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Multiple Myeloma: genesis, diagnosis, and treatment

Overview on the disease with an English-Chinese terminographic repertoire

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“Happiness can be found, even in the darkest of times, if one only remembers to turn on the light.”

- J. K. Rowling -

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前言

该研究对比分析了与多发性骨髓瘤有关的专业术语的中英文之间的差异。由于在中国没有一本用中文解释的医学词典，无法提供一个明确性的多发性骨髓瘤定义，我们只参照《牛津英语词典》提供的定义。《牛津英语词典》将多发性骨髓瘤（MM）定义为“浆细胞的恶性克隆性增殖，通常在骨骼中引起多发性细胞瘤，通常与血液和尿液中出现的异常蛋白质有关，也叫骨髓瘤病”。多发性骨髓瘤，又叫MM，是一种比较常见的恶性肿瘤，在2020年全球发病率为16万，而死亡率显示为10.6万。多发性骨髓瘤经常被定义为发达国家特有的疾病，但这种说法不够全面。事实上，虽然在发达国家多发性骨髓瘤的发病率确实较高，但这并不是因为人口的易感性较高，而是因为诊断率较高，中国的这种情况特别明显。中国的发病率比发达国家更低，但是这种数据后面有两种重要的原因：第一就是中国人本身的身体特点，第二就是中国的诊断率低。关于身体特点，中国人的生活方式和营养习惯对他们的身体有保护作用。关于诊断率，在中国诊断率比发达国家低，这就是因为中国医生没能识别多发性骨髓瘤的症状，而把它诊断为其他疾病。

由于在过去几年里在全世界范围内多发性骨髓瘤的发病率都有所增长，因此有必要建立一种明确的共同术语，以确保高效和持续的知识、现场经验和关键信息的跨国界交流，从而提高患者预期寿命和生活质量。

本论文旨在建立多发性骨髓瘤有关的英汉术语库。该术语库不仅适用于从事医学翻译工作的专业人士，还可作为处理该疾病或从事医学研究的医生和学者在日常工作中的参考。选择英汉互译，主要是因为中国和美国是多发性骨髓瘤治疗和药物发展主要研究中心，不断产生新发现并推动该领域的发展。

本术语库被设想纳入数据库，作为MultiTerm，在计算机辅助翻译（CAT）软件中使用，作为Trados®（由SDL MultiTerm开发）。术语卡片使用文字处理器Microsoft Word编写，并符合标准通用标记语言（SGML）的要求。SGML是一种被ISO（ISO 8879:1986 SGML）定义为标准的原语言，它的定义用于编写文本的代码，以便于使用计算机工具进行传输和存储。

这个术语库包括158张卡片，旨在澄清与多发性骨髓瘤相关的主要关键术语，涵盖疾病描述、诊断工具、治疗和疼痛管理等方面。这个术语库为多发性骨髓瘤术语的描述提供了一个起点，随着研究的进展，它可以进一步补充和扩展。

本论文分为三部分：第一部分是对多发性骨髓瘤的总体概述；第二部分为英汉术语库；第三部分是英汉和汉英词汇表。

如第一段所述，多发性骨髓瘤是一种比较常见的血液病，以各种症状为特征，可表现为不同的形式。本论文的第一部分又分为四个章节，涉及疾病的描述、分期、诊断和治疗方案。

第一章介绍多发性骨髓瘤的发病机制、危险因素和分期，其中，对多发性骨髓瘤的分期系统进行了详细的介绍。这不仅在确定预期寿命和症状分类方面起着关键作用，而且对选择最适合的治疗方案也至关重要。在疾病的发展过程中，可以指认三个阶段：首先是单克隆免疫球蛋白增生症（MGUS），在这种情况下，疾病完全无症状；第二阶段是冒烟的多发性骨髓瘤（SMM），其特点是恶性细胞的增加，但尚未出现明显的症状；最后一段是有症状的多发性骨髓瘤，这不仅是疾病的最后阶段，而且也是最复杂的阶段，因为需要进行更细致的治疗。

第二章的重点是症状和诊断。首先，我们将澄清CRAB症状（高钙血症、肾功能损伤、贫血和骨病变）与非CRAB症状之间的区别，并强调CRAB症状对预期寿命和生活质量的影响。实际上，CRAB症状通常在疾病已经广泛扩散到肌体时才会出现，因此在疾病的这一阶段治疗效果很不理想。在诊断工具和标准这两个方面，我们主要参照国际骨髓瘤工作组（IMWG）的标准及其发展。随着时间的推移，IMWG标准改近了多发性骨髓瘤的诊断流程，发展了更准确的预测和诊断手法。此外，考虑到多发性骨髓瘤是一种多方面的疾病，我们将对有关实验室检查、造影学和细胞遗传学调查等不同诊断检查提供概述。

第三章专门介绍多发性骨髓瘤治疗中使用的不同治疗药物，如烷化剂、免疫调节剂、蛋白酶体抑制剂和单克隆抗体，描述了这些药物的作用机制、给药途径和副作用，并将对不同治疗阶段的病人接受自体干细胞移植（ASCT）的可能性、药物组合和治疗方案进行讨论。

第四章提供关了目前药物实验和开发的概述，主要讨论三种治疗药物： 1. 组蛋白去乙酰化酶抑制剂（HDACi）；2.BCL-2抑制剂；3. 选择性核输出抑制剂。本章还介绍美国的临床试验，描述经由FDA或EMA批准的药物的主要相关试验。

本论文的第二部分专注于术语库，其中包括术语卡和书目卡。第二部分的主要目是提供对多发性骨髓瘤（MM）描述中主要相关术语的全面理解。在编制术语卡的过程中，我特别关注两个相关领域，即<context>并<synonym>。由于许多医学术语非常特殊且难以理解，我们努力为每个术语提供背景，以进一步说明已提供的<definition>的内容。

关于<synonyms>领域，医学语言的一个特点是用于描述同一疾病、模式或化学制剂的同义词数量很大，正因为如此，所有的同义词以缩写和首字母方式被列在每张卡片的最后部分。值得注意的是，在许多情况下，来自英文全称的缩写（缩略语或首字母）在中文中也以同样的方式使用，尽管缺乏严格的对应关系。书目卡包括在起草术语卡时使用的系统收集来源，用于填写<Source>。

本论文的最后一部分是英中和中英词汇表，它提供每个术语的英文、中文和拼音之间的对应关系，并总结本论文第二部分的信息。这一部分的目的是为那些已经读过术语卡的人提供快速参考。

鉴于本论文是对多发性骨髓瘤描述中使用的技术语言研究的初步阶段，而且术语库还可以进一步补充，该研究还对多发性骨髓瘤的研究进展做一个简单的介绍。事实上，虽然多发性骨髓瘤是一种不治之症，但医生对它的进展并造成因素的了解不多。在“Tao of Myeloma”文章中，Lawrence提出一种描述多发性骨髓瘤的创新方法，他利用传统中医术语来介绍多发性骨髓瘤的特点，并提出一个新的研究框架，这可能会改变医学研究的视角，从而影响相关语言。在文章中，多发性骨髓瘤被定义为“道”，由阴（代表浆细胞生物学）和阳（代表癌症生物学）组成，与疾病进展过程中发生的变化有关。阴和阳在肌体中共存，并且相互依赖，因此，在开发药物和治疗过程中，应将它们作为一个整体考虑，否则只选择针对其中一个元素对待可能会进一步损害肌体。整体观对临床试验和药物开发的结果有很大影响。事实上，过去药物开发的主要关注点是找到一个“灵丹妙药”，这个“灵丹妙药”成了肌体疾病中的干扰因素，因此应该成为治疗重点。为此，现在的主要关注点已经转移到整体观点，即同时考虑多种因素。这一转变是由于人们日益认识到人体是个“复杂”的系统，所以应该从整体角度来看，而不是从线性角度来分析。在这种情况下，有证据表明，蛋白酶体抑制剂和免疫调节剂是同时治疗阴（浆细胞生物学）和阳（癌症生物学）最有希望的选择，可以提高治愈成功率和患者的预期寿命。为了进一步提高患者的生活质量，并最终了解哪些是采取行动的杠杆点，以便有效减少疾病对患者的影响，未来需要从更全面的角度来分析多发性骨髓瘤的复杂动态，并在多发性骨髓瘤阴阳之间取得更精确的平衡。

综上所述，本论文并不是一个全面的多发性骨髓瘤的术语库，但它更好地奠定术语改进和整合的长期工作的基础，这不仅考虑到科学的进步，也考虑到分析视角和研究框架的转变。

Preface

The Oxford English Dictionary defines Multiple Myeloma (MM) as "a malignant clonal proliferation of plasma cells, typically causing multiple lytic tumours in bones and usually associated with the presence of abnormal proteins in the blood and urine".[1] MM is a relatively common malignancy and in 2020 its worldwide incidence was 160,000, while mortality showed a value of 106,000.[2] MM is often defined as a disease proper of developed countries, but this statement is often misinterpreted. Indeed, while it is true that the incidence of MM is higher in developed countries than in developing ones, this does not depend on the higher susceptibility of the population but rather on higher rates of diagnosis. This dynamic is perfectly reflected by the Chinese situation: while, on one hand, the Chinese population is physically less prone to develop the disease, on the other hand, the great gap between the incidence of MM in China and in developed countries is mainly determined by the lack of proper and timed diagnosis.

As in the last years an increase in the incidence of MM has been registered worldwide, a clear and shared common language is necessary to ensure efficient and continuous exchange of knowledge, field experience and key information across borders to improve life expectancies and quality of life.

The present works aims at identifying an English – Chinese terminographic repertoire employed in the description of MM. The terminographic repertoire is not only addressed to interpreters and translators who work in the medical field, but it may also work as a reference point for physicians and scholars who are dealing with the disease in the daily practice or who are working in the medical research. The choice to opt for an English – Chinese correspondence is mainly determined by the geographical location of the greatest research hubs in this field; indeed, China and USA represent the avant-garde in treatment and in drug development for MM, constantly producing new knowledge and developments.

The present terminographic repertoire has been conceived to be included into databases as MultiTerm, employed within Computer Assisted Translation (CAT) software, as Trados® (developed by SDL MultiTerm). The terminographic cards have been written with the word processor Microsoft Word, respecting the Standard Generalized Markup Language (SGML), a metalanguage defined as standard ISO (ISO 8879:1986 SGML), which defines the code used to draft texts mean to be transmitted and stored with computer tools.[3]

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[1] Lesley BROWN, et al., *Oxford Dictionary of English*, Oxford, Oxford University Press, 2013.
[2] Heinz LUDWIG, et al., "Multiple Myeloma Incidence and Mortality Around the Globe; Interrelations Between Health Access and Quality, Economic Resources, and Patient Empowerment", *Oncologist*, 25, 9, 2020, 1406-1413.
[3] International Standard Organization. ISO, ISO 8879:1986. Information processing — Text and office systems — Standard Generalized Markup Language (SGML), in "ISO official website", 2020, https://www.iso.org/standard/16387.html, (last access May 22, 2023).

The terminographic compilation includes 158 cards, meant to clarify the main key terms in disease description, diagnostic tolls, treatment, and management of pain at the state of art. This compilation, therefore, represents a starting point in the terminographic description of MM and it is open to further additions and expansions as the research in this fields progresses and new words to describe drugs and approaches are developed.

The present dissertation is three folded: in section 1, a general overview over MM is provided; section 2 includes English – Chinese terminographic repertoire; section 3 is dedicated to the English – Chinese and Chinese – English glossary, whose main scope it to sum up the information provided by the terminographic cards in section 2.

As mentioned in the first paragraph, MM is a relatively common hematologic disease characterized by a variety of symptoms, and that may manifest in different forms. The first section of this dissertation, which is in turn divided into four paragraphs, deals with the description of disease, staging, diagnosis, and treatment options.

Chapter 1 deals with pathogenesis, risk factors and staging of the disease. In this chapter, great attention is devoted to the staging system of MM which plays a crucial role not only in determining life expectancies and in symptoms classification, but also in deciding which is the most appropriate treatment option. Three stages are identified in the disease progress, respectively Monoclonal Gammopathy of Undermined Significance (MGUS), in which the disease is totally silent, Smouldering Multiple Myeloma (SMM), characterized by an increase in the malignant cells and symptomatic Multiple Myeloma, which is the last stage of the illness and the most complex to deal with.

Chapter 2 is focused on symptoms and diagnosis. In first place, the distinction between CRAB (hypercalcemia, Renal insufficiency, Anemia and Bone lesions) and non-CRAB symptoms will be clarified, highlighting the effects of the presence of CRAB on life expectancies and quality of life. Indeed, these symptoms usually manifest themselves when the disease is already well diffused into the organism and thus when any attempt to reduce the burden of the illness is limited. Regarding diagnostic tools and criteria, a great focus will be casted on the International Myeloma Working Group (IMWG) criteria and on its development which, throughout time, revolutionized MM diagnostic procedures allowing anticipated and more precise diagnosis. Furthermore, considering that MM is a multifaced diseases, an overview over the diverse diagnostic exam as laboratory test, imaging and cytogenetic investigation will be provided.

Chapter 3 is dedicated to the description of the different treatment agents used in MM therapy, as alkylating agents, immunomodulatory drugs, proteasome inhibitors and monoclonal antibodies. Once their mechanism of actions, administration routes and toxicity have been

described, drugs combinations and treatment options will be discussed in relation to different treatment phases and to the possibility for the patient to undergo Autologous Stem Cell Transplantation (ASCT).

Chapter 4 provides the reader with an overview over the current drug experimentation and development, focusing on the three most promising treatment agents: 1. Histone Deacetylase Inhibitors (HDAC); 2. BCL-2 Inhibitors; 3. Exportin Inhibitors. This chapter will also give a glimpse on the American clinical trial sector, describing the main and most relevant trials which ended up the approval of a drug by FDA or EMA.

The second section of the present dissertation is dedicated to the terminographic repertoire which consists of terminographic and bibliographic cards whose main objective is to provide readers with a complete comprehension of the most relevant terms in the description of the disease. In realizing the terminographic cards great attention will be casted on two relevant fields, respectively <context> and <synonyms>. Indeed, since many medical terms are very specific and of difficult comprehension, a great effort has been made to provide each term with a context that can further clarify the information already provided by the field <definition>.

Concerning the field <synonyms>, a peculiarity of the medical language can be found in the consistent number of synonyms used to describe the same disease, pattern, or chemical agent; because of this, all the synonyms as well as acronyms and initials are listed in the last part of each card to facilitate the understanding of medical texts that may use to different terms to refer to same element or concept. Noteworthy is that in many cases the abbreviations (acronyms or initials) which come from the English full form are used in the same way also in Chinese, regardless of the lack of strict correspondence.

Bibliographic cards include the systematic collection of sources used in the drafting of terminology card, used to fill in the <Source> field.

The last section of the present work is reserved to the English – Chinese and Chinese – English glossary, which summarizes the information of section 2 by simply providing the correspondence between the English, Chinese and pinyin version of each term. This section is meant to work as a quick reference for those who already read the terminographic cards but did not memorize the whole compilation of terms.

Given that this dissertation represents the preliminary stage of the research on the technical language used in the description of MM and that the terminographic compilation is open to further addition, a brief consideration should be made on the progress in the research of MM. Indeed, while it is clear that MM is an incurable disease, little is known about its progression and the triggering factors that determine the shift from the inactive stage of the

disease to the active one. In the article "Tao of Myeloma",[4] Lawrence presents an innovative way to describe MM, making use of Traditional Chinese Medicine (TMC) terminology, and proposing a new framework of study which may change the medical research perspective and consequently affecting the related language. In the article, MM is defined as "Tao", made of Yin, represented by the plasma cell biology and of Yang, represented by the cancer biology and associated with the changes that occur during the progress of the disease. Yin and Yang coexist in the organism and are dependent one on another, so, when developing drugs and treatments, they should be targets as a single element, otherwise the choice to target only one of them could further damage the organism. The decision to opt for a holistic view or not, strongly affects the results of clinical trials and drug development. Indeed, while in the past the main concern in drug development was to find a "magic bullet" which constitutes the disrupting element in the organism and that should thus be the target of treatment and therapies, nowadays the main concern shifted to a holist perspective which takes into consideration multiple elements at the same time. This shift is the result of the rising awareness that diseases are "complex" and that they should be analysed from a global perspective and not on a linear basis. In this context, evidence shows that Proteasome Inhibitors and Immunomodulatory agents are promising options in treating both Yin (plasma cell biology) and Yang (cancer biology) at the same time, maximizing the rate of success and the life expectancy of patients. In the future, in order to further improve patients' quality of life and eventually understanding which are the leverage points on which to act to effectively reduce the impact of the disease on patients, a greater holistic perspective in the analysis of MM complex dynamics and a more precise balance between MM Yin and Yang will be needed.

All this considered, the present dissertation does not claim to be a comprehensive terminographic repertoire on MM to be univocally applied but it better lays the foundations of a continuous work of terminographic improvement and integration, which takes into account not only the scientific progress but also the shifts in analysis perspectives and research frameworks.

[4] Lawrence H. BOISE, et al., "The Tao of Myeloma", Blood, 124, 12, 2014, 1873-1879.

SECTION I

CHAPTER 1

Multiple Myeloma: the disease and the staging

1.1 Basic characteristics of Multiple Myeloma

1.1.1 Biological characteristics

Multiple Myeloma (MM) is a hematologic malignancy characterized by the proliferation and the accumulation of plasma cells in the bone marrow, which synthetizes monoclonal immunoglobulin (Ig) protein (also called M-protein), leading to end-organ damage.

The progress of MM can be divided into three phases: the first one called Monoclonal Gammopathy of Undetermined Significance (MGUS); the second one called Smouldering Multiple Myeloma (SMM) and the third one, which is the final stage of the disease, which is intra or extra-medullary, symptomatic Multiple Myeloma.

The first stage of the disease is characterized by the asymptomatic presence of the malignancy and by a M-protein below 1.5 g/dl.[5] The rate of progression from MGUS to MM is roughly 1% every year.

The second stage of the disease is characterized by an increase of neoplastic plasma cells and of M-protein (superior to 3 g/dL), but by the absence of organ damage and CRAB symptoms (hypercalcemia, renal failure, anaemia, and bone lesion).[6] In SMM, the risk of progression to MM is higher than in MGUS with a rate of 10% every year, within 5 years from the diagnosis.[7]

The final stage of the disease is characterized by a high level of M-protein, hypercalcemia, osteolytic lesions, kidney damage, immunodeficiency, and renal function impairment.[8]

Different studies show that MM is an heterogenous disease;[9] indeed, once the neoplastic clone has been created, the tumour cells can differentiate themselves due to stochastic, external events which are independent one to another. One of the causes that may lead to these modifications is the competition between the tumour cells to get nutrients and other vital resources. These stochastic modifications play a great role in determining the characteristics of

[5] Neha KORDE, et al., "Monoclonal gammopathy of undetermined significance (MGUS) and smoldering multiple myeloma (SMM): novel biological insights and development of early treatment strategies", *Blood*, 117, 21, 2011, 5573-5581.
[6] Vincent RAJKUMAR, et al., "Smoldering Multiple Myeloma", *Blood*, 125, 20, 2015, 3069-3075.
[7] Robert A. KYLE, et al., "Clinical course and prognosis of smoldering (asymptomatic) multiple myeloma", *The New England journal of medicine*, 356, 25, 2007, 2582-2590.
[8] Anuj MAHINDRA, et al., "Multiple myeloma: biology of the disease", *Blood reviews*, 24, 1, 2010, 5-11.
[9] Niccolò BOLLI, et al., "Heterogeneity of genomic evolution and mutational profiles in multiple myeloma", *Nature communications*, 5, 2014, 2997.

the disease itself, as different patients may have different traits but also the therapy itself may alter the development of the disease.[10]

1.1.1.1 Genesis of Multiple Myeloma

To have a complete picture of MM it is primarily necessary to understand how this disease originates. As we stated in the introduction, MM is monoclonal B-cell malignancy which can develop through different stages: an inactive stage in which tumour cells are non-proliferating mature plasma cells; an active stage with a limited percentage (<1%) of proliferating plasma blasts and a fulminant stage characterized by an increase in the plasma blasts and a diffusion of the disease out of the bone marrow.

Normally, cells deputed to carry out B lymphocytopoiesis, undergo a rearrangement of V (variable region), D (diversity region) and J (joining region) sequences of the genes coding heavy chains (IgH) and of the V and J sequences of the genes coding for the light chains (IgL) of the immunoglobulins. The outcome of this process is the creation of *naïve* B-cells, which will move from the bone marrow to lymphoid organs where will find the antigen.

B-cells may, at this point, face two different situations: in the first one, they will become short-lived plasma cells which will stay in secondary lymphoid tissue; in the second case, the encounter of B-cells with protein-based antigens will determine the germinal centre reaction and the production of Memory B-Cells (MBC) and plasma blasts. Plasma blasts and MBC will then migrate back to the bone marrow (homing process) and will differentiate into long-lived plasma cells thanks to the interactions with the medullary microenvironment.[11][12] This process of transformation is not determined by a single event, but it is the results of multiple stochastic genomic alterations undergone by the tumour cells.[13] The changes that happens on a cellular level correspond to the changes in the different stages of the disease, from those that have a limited impact on the individual, to those that are more aggressive and implies stronger clinical manifestations.

The rearrangement of the cells of B lymphocytopoiesis is thought to be promoted by the break of the DNA double-strand, caused by the Activation-Induced Cytidine Deaminase (AID

[10] Jonathan J. KEATS, et al., "Clonal competition with alternating dominance in multiple myeloma", *Blood*, 120, 5, 2012, 1067-1076.
[11] Abul ABBAS, et al., *Cellular and Molecular Immunology,* Amsterdam, Elsevier, 2021.
[12] Niccolò BOLLI, Francesco DI RAIMONDO, "Mieloma Multiplo: biologia, criteri diagnostici e prognostici", *Seminari di ematologia clinica,* 2016, 5-18.
[13] Jens G LOHR, et al., "Widespread genetic heterogeneity in multiple myeloma: implications for targeted therapy", *Cancer cell*, 25, 1, 2014, 91-101.

enzyme).[14] Considering this, the risk of developing any sort of plasma cell cancer is connected to the physiological mechanisms of production of antibody response.

Myeloma cells (observable in Figure 1) can be identified as tumoral cells originated from the maturation process that takes place into the secondary lymphoid organs. They are characterized by a strong dependence on BM and represent the "malignant counterparts of post-Germinal Center (GC) long-lived PCs".[15] MM cells, once reached the bone marrow, will interact with the microenvironment, and will stimulate the production of neoplastic clones.

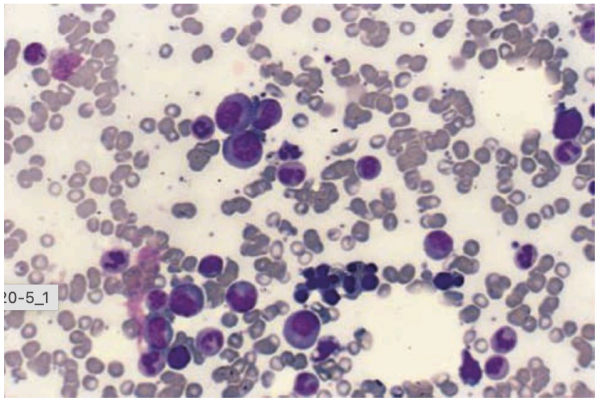

Figure 1: Myeloma Cells. The larger cells with concentric nuclei are the myeloma cells

1.1.1.2 Medullary microenvironment

In the above paragraph, the medullary microenvironment has been mentioned so it is needed to clarify what the medullary microenvironment is. The medullary microenvironment consists of two different sections: the cellular compartment and the non-cellular compartment. The former consists of hematopoietic elements as stem cells, lipocytes and platelets, and non-hematopoietic elements as grow factors and cytokines. The latter consists of Extracellular Matrix Protein (ECM).

MM is characterized by a modification of the regulation process carried out by cell-signalling molecules. The effects of such modification can be observed in the survival and proliferation of the malignant clone B-cell, but also in the appearance of osteolytic lesions and in the resistance to diverse treatments. Osteolytic lesions and drug resistance are mainly determined by mechanisms of cells adhesions in which the main contribution is provided by Bone Marrow Stromal Cells (BMSC).[16] This process of cells adhesion starts when circulating

[14] David GONZÁLEZ, et al., "Immunoglobulin gene rearrangements and the pathogenesis of multiple myeloma", *Blood*, 110, 9, 2007, 3112-3121.
[15] Marta CHESI, P. Leif BERSAGEL, "Molecular pathogenesis of multiple myeloma: basic and clinical updates", *International journal of hematology*, 97, 3, 2013, 313-323.
[16] Constantine S. MITSIADES, et al., "The role of the bone microenvironment in the pathophysiology and therapeutic management of multiple myeloma: interplay of growth factors, their receptors and stromal interactions", *European journal of cancer,* 42, 11, 2006, 1564-1573.

tumoral cells adhere to the tissue of bone marrow thanks to their adhesion molecules; this will lead to the activation of paths of intracellular signal transduction. The activation of these pathways will determine inhibition of apoptosis, bone damage and drug resistance.

Medullary microenvironment will also play a great role in the development of relapsed MM; indeed, research shows that tumoral B-cells are able to modify themselves according to the external environment and therefore are able to perpetuate the disease autonomously.[17]

1.1.1.3 Angiogenesis

The angiogenesis plays a crucial role in the development of MM. Tumour angiogenesis is a multistep process which originates from the increase in the need of oxygen and nutrients in tissues, and it is characterized by the appearance of vascular structures made of disorganized and premature blood vessels. This process is mainly determined by the imbalance between anti-angiogenic and pro-angiogenic factors in favour of the last one which leads to the proliferation of new blood vessels.[18] One of the main factors which stimulates the angiogenesis is the growth of the tumour mass.

It has been showed that, in patients with MM, the medullary microenvironment is characterized by a high density of blood vessels, compared to healthy patients. In MM, the angiogenic process is strongly connected to the degree of diffusion of tumour cells into the bone marrow and to the stage of the disease; indeed, in MGUS and SMM, the angiogenic process has not started yet. The "angiogenic switch" takes place when the tumour mass is of considerable size, and it is started by the secretion of the Vascular Endothelial Grow Factor (VEGF) which stimulates the proliferation of blood vessels.

Overall, angiogenesis contributes to the nourishment, growth and spread of tumour cells and to the development of osteolytic lesions; these two main contributions of angiogenesis make it clear that it is a trait proper of the disease in its active stage.[19]

1.1.1.4 Osteolytic lesions

The last paragraph of this section will be devoted to osteolytic lesions (Figure 2) which are one of the main traits of MM and predispose the individual to calcinosis, hypercalcemia, mobility issues, fracture, and strong pain. Osteolytic lesions may be caused by a modification of the bone remodelling process (process in which the mature bone tissue is removed from the skeleton and

[17] Bruno PAIVA, et al., "Differentiation stage of myeloma plasma cells: biological and clinical significance." *Leukemia*, 31, 2, 2017, 382-392.
[18] Nektaria MAKRILIA, et al., "The role of angiogenesis in solid tumors: an overview", *European journal of internal medicine*, 20, 7, 2009, 663-671.
[19] Nikhil MUNSHI, "Increased bone marrow microvessel density in newly diagnosed multiple myeloma carries a poor prognosis", *Seminars in oncology,* 28, 6, 2001, 565-569.

replaced with new one). This modification may be produced by two different situations: the first one refers to the stimulation of the process of osteoclast genesis, which causes the osteoclast hyper-activation.[20] The expression "osteoclast hyper-activation" refers to an increase in the activity of the osteoclasts which are responsible for the disintegration of the bone matrix. The second situation refers to the reduction of the osteoblastic activity, which consists in a reduction the activity of creation of the bone matrix.[21]

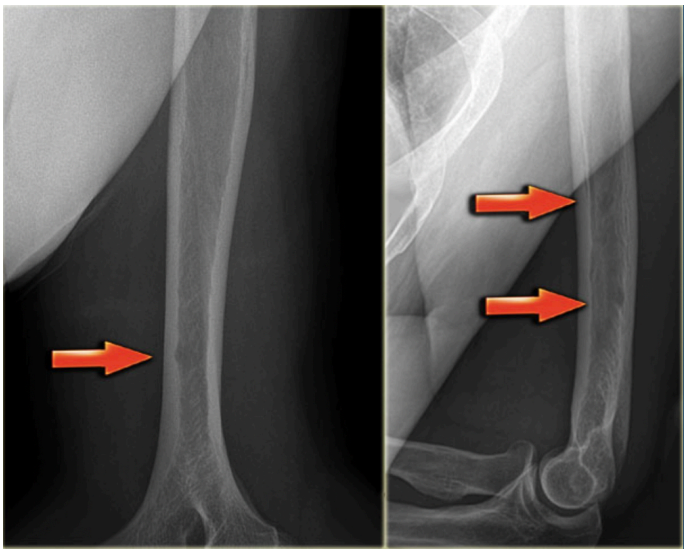

Figure 2:Multiple osteolytic lesions in the humerus

1.1.2 Epidemiology

In this section an overview about the epidemiology of MM will be provided. Firstly, data related to the incidence and the prevalence of the disease on a worldwide level will be described, subsequently some detailed information about the epidemiology of MM in the USA, Italy and China will be presented.

1.1.2.1 Worldwide level epidemiology

MM is a moderately common disease associated with older age and mainly diffused in developed countries.

According to the Global Cancer Observatory (GLOBOCAL), in 2018, MM accounted for 0,9% of all the cancer diagnoses, with approximately 160,000 cases globally,[22] representing the second most common hematologic malignancy after lymphoma.

[20] G. David ROODMAN, "Pathogenesis of myeloma bone disease", *Leukemia*, 23, 3, 2009, 435-441.
[21] G. David ROODMAN, "Pathogenesis of myeloma bone disease", *Journal of cellular biochemistry,* 109, 2, 2010, 283-291.
[22] Global Cancer Observatory: Cancer Today, International Agency for Research on Cancer, Lyon, France. Available online: https://gco.iarc.fr/today/home (last access March 2, 2023).

Since 1990, the global incidence of MM registered an increase of 126%,[23] with a peak in is developed countries as Australia, New Zealand, USA, and Europe, which shows the highest incidence.

The ethnic analysis carried out within the population of the USA has showed that MM is more common in black people rather than in white ones; the incidence of MM in black people is almost two times the incidence of MM in white people, and furthermore, the age of development of the disease tends to be lower, with a higher number of patients diagnosed before the age of 60. On the other hand, Asian people, especially Chinese and Japanese, tend to be less exposed to the development of the disease.

Epidemiological studies showed that MM is more diffused in men rather than in women, with a ratio of 1.5.[24] Of the total 160,000 cases in 2018, 90,000 cases were male, while 70,000 were female.[25] The disease is also more diffused in older people rather than in younger ones; the median age for the diagnosis is 66 to 70 years; only 10% of the patients were diagnosed before they turned 50, and the percentage decrease to 2% for the patients that were diagnosed before they turned 40.[26]

With regards to the mortality rate, in 2018, MM mortality rate accounted for 1,1% of all the cancer deaths, with 106,000 registered deaths. The risk of death by MM is slightly higher in men rather than in women.[27] In the last decades, the rate of survival has increased significantly due to the development of effective therapy and improvement of the general living conditions. This improvement is shown by the extended survival of patients with relapsed MM, indeed, before 2000 the survival expectancy was less than 12 moths, while after 2000 it reached 24 months.[28]

The risk of death and the rate of survival are also strongly related to the stage at which the disease is diagnosed; indeed, if the disease is diagnosed when it is still localized (only 5% of all the diagnosed cases), the survival rate over 5 years is 74,8%, while if it diagnosed when it is already systemic (95% of all the diagnosed cases) the rate of survival over 5 years decreases to 52,9%.[29] In Figure 3, it is possible to see the incidence and mortality rate; the diagram makes

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[23], Andrew J. COWAN, et al., "Global Burden of Multiple Myeloma: A Systematic Analysis for the Global Burden of Disease Study 2016", *JAMA oncology*, 4, 9, 2018, 1221-1227.

[24] The ratio was calculated dividing the incidence of the disease in man (2.1/100,000) by the incidence of the disease in women (1.4/100,000).

[25] Freddy BRAY, et al., "Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries", *CA: a cancer journal for clinicians,* 68, 6, 2018, 394-424.

[26] Anuj MAHINDRA, et al., "Multiple myeloma: biology of the disease", *Blood reviews*, 24, 1, 2010, 5-11.

[27] Global Cancer Observatory: Cancer Today, International Agency for Research on Cancer, Lyon, France. Available online: https://gco.iarc.fr/today/home (last access March 2, 2023).

[28] Shaji K. KUMAR, et al., "Improved survival in multiple myeloma and the impact of novel therapies", *Blood*, 111, 5, 2008, 2516-2520.

[29] Nadia HOWLANDER, et al., *SEER Cancer Statistics Review 1975-2016*, National Cancer Institute: Bethesda, 2019.

it clear that the disease is more diffused in developed countries rather than in developing or underdeveloped ones.

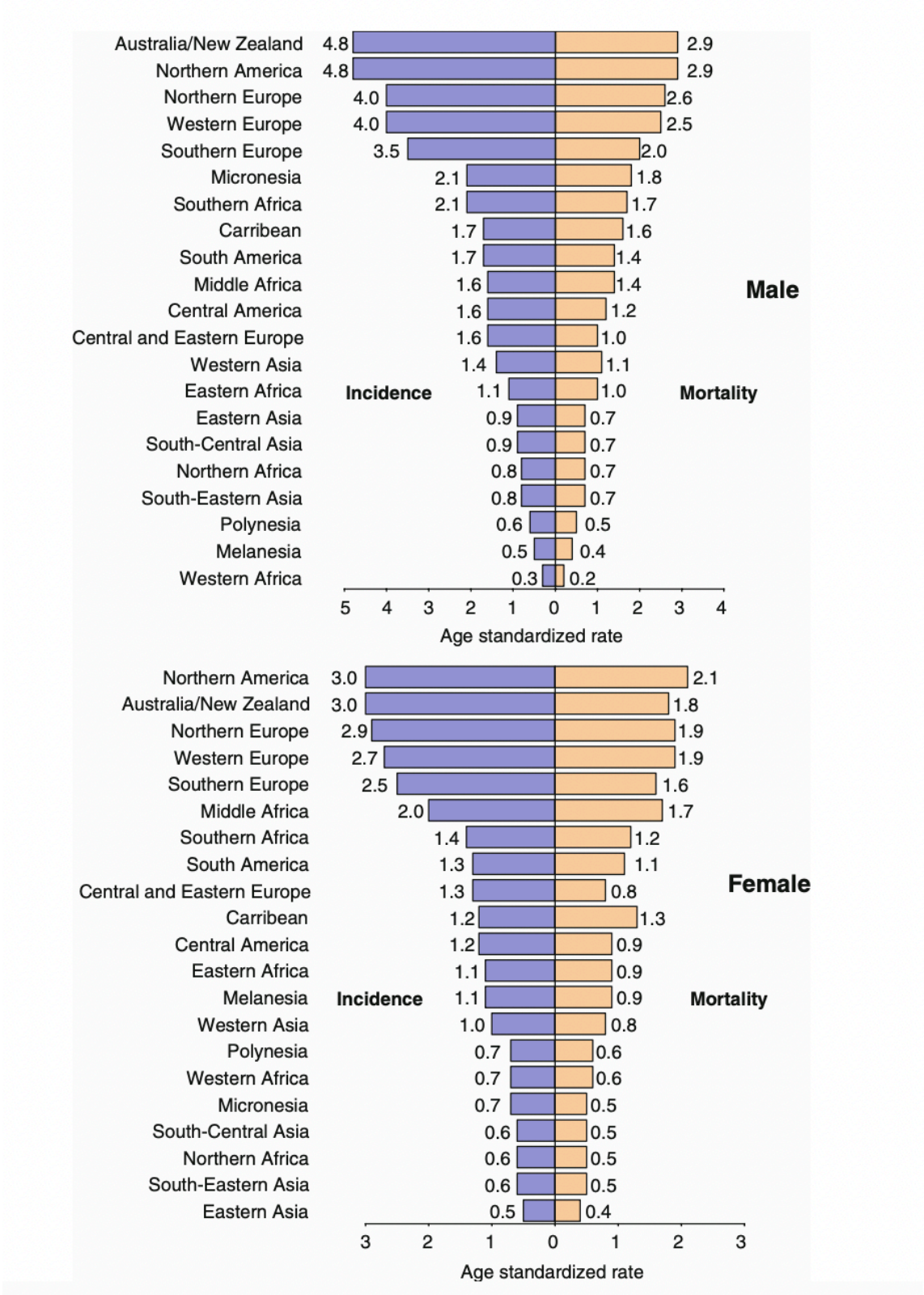

Figure 3: Incidence and mortality rates for MM

1.1.2.2 US epidemiology

The most recent data related to the diffusion of MM in the US report a total of 32,000 cases in 2020, making MM the 14th most common neoplasm and consisting of 1,8% of all cancer diagnosis. Currently, the median incidence rate for MM in US is 7.0/100,000,[30] with an incidence rate of 8.0/100,000 for men and an incidence rate of 5.2/100,000 for women.

Epidemiological data provided by the United States Department of Health and Human Services (HHS) provided some evidence about the fact that MM could be associated to the agricultural work, since the extended exposure to the chemical alachlor is demonstrated to be one of the main causes of lymphohemopoietic cancers.[31] Other occupations that have been associated with a high risk of developing MM include miners, sheer-metal workers and workers exposed to wood-dust.[32]

Mortality rate due to MM has decreased sharply in the last decades; indeed, in 2020, the mortality rate in the US was 3.3/100,000, while in 1994, it was 4.0/100,000. In 2020, 12,800 people died due to MM, accounting for 2,1% of all the cancer deaths.[33]

1.1.2.3 Italy epidemiology

In Italy, MM represents 10% of all the haematological neoplasms diagnosed every year. MM accounts for 1,3% of all the cancers diagnosed among women and 1,2% of all the cancers diagnosed among men. As in the USA and on a global level, also in Italy, MM is more common among men rather than in women; indeed, data shows an incidence of 8.1/100,000 for women and 9.5/100,000 for men.[34] According to the data provided by AIRTUM (Associazione Italiana Registro Tumori) referring to 2015, the general incidence is 8.8/100,000 with an Overall Survival (OS) of 76% over 1 year and 42% over 5 years.[35]

Research carried out on the Italian population shows that a greater risk of developing the disease is associated with the extended exposure to toxic agents as pesticides, petroleum derivatives and ionizing radiations. Some investigation has been conducted also on genetic factors which may be a cause of a higher risk of developing the disease; however, even though

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[30] Nadia HOWLANDER, et al., *SEER Cancer Statistics Review 1975-2016*, National Cancer Institute: Bethesda, 2019.

[31] Won Jin LEE, et al., "Cancer incidence among pesticide applicators exposed to alachlor in the Agricultural Health Study", *American journal of epidemiology*, 159, 4, 2004, 373-80.

[32] Lin FRITSCHI, Jack SIEMIATYCKI, "Lymphoma, myeloma and occupation: results of a case-control study", *International journal of cancer*, 67, 4, 1996, 498-503.

[33] Nadia HOWLANDER, et al., *SEER Cancer Statistics Review 1975-2016*, National Cancer Institute: Bethesda, 2019.

[34] Lorenza SCOTTI, et al., "Epidemiologia del mieloma multiplo e caratteristiche cliniche dei pazienti", *Giornale Italiano di Farmacoeconomia e Farmacoutilizzazione*, 10, 2, 2018, 23-30.

[35] Katia MANCUSO, *Mieloma multiplo: identificazione di fattori prognostici, biomarcatori di risposta alla terapia, evoluzione clonale e di terapie innovative e personalizzate*, [Dissertation thesis], Alma Mater Studiorum Università di Bologna. Dottorato di ricerca in Oncologia, ematologia e patologia, 33 Ciclo, 2021.

some family clusters have been described, there is no evidence that the transmission of the disease is hereditary.

As reported by a study conducted by the INT (Istituto Nazionale Tumori) in Milan, 16% of the patients with MM exhibited renal or cardiovascular comorbidities and 17% of the patients do not receive treatment as MM is diagnosed in a too advanced stage.[36]

1.1.2.4 China epidemiology

As mentioned in the first paragraph, the incidence of MM in the Asian population is relatively low compared to the one in Caucasians or in the black population.

According to data provided by the National Medical Insurance Database, gathered from January 1, 2012, to December 31, 2016, in China, MM incidence is 1.15/100,000, which is significantly lower compared to USA or Europe. However, it is noteworthy than in China, the incidence of MM is strongly dependent upon the geographical area; indeed, northern, and eastern China show high rates of MM compared to the rest of China. This difference may be determined by differences in climate, lifestyle patterns but also in genetic background (taller individual are proved to be more exposed to the development of the disease).[37]

Differently of USA and Europe, in China the median age of MM patients is 58 years, roughly 10 years younger than Caucasians. The reason behind this gap could be found in ethnic disparity, considering the great differences existing between bone geometry, strength and quality of Asians and Caucasians.[38]

Another difference in the Chinese epidemiology refers to the diffusion of the disease in men and women; while in USA and Europe men tend to be more exposed to MM, in China not only women are more prone to develop the disease but also the age at which it is diagnosed is lower than in men. Indeed, as in figure 4, while the peak for women is registered between 55 and 59 years old, the peak for men is registered between 64 and 74 years old.[39] It should be considered that the diffusion of MM has shown an intense increase in the last 3 years, which casts the light on the necessity to establish an effective disease prevention and to pursue the path of the research to develop new treatments and therapies.

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[36] Giovanni CORRAO, et al., "Rwd Study for Epidemiology and Characateristics of Patients with Multiple Myeloma in Italy", *Blood,* 128, 22, 2016.
[37] Lauren TERAS, et al., "Body size and multiple myeloma mortality: a pooled analysis of 20 prospective studies", *British journal of haematology*, 166, 5, 2014, 667-676.
[38] Anna L. KEPLEY, et al., "Differences in bone quality and strength between Asian and Caucasian young men", *Osteoporosis international: a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA,* 28, 2, 2017, 549-558.
[39] Shengfeng WANG, et al., "Prevalence and Incidence of Multiple Myeloma in Urban Area in China: A National Population-Based Analysis", *Frontiers in Oncology,* 9, 1513, 2020.

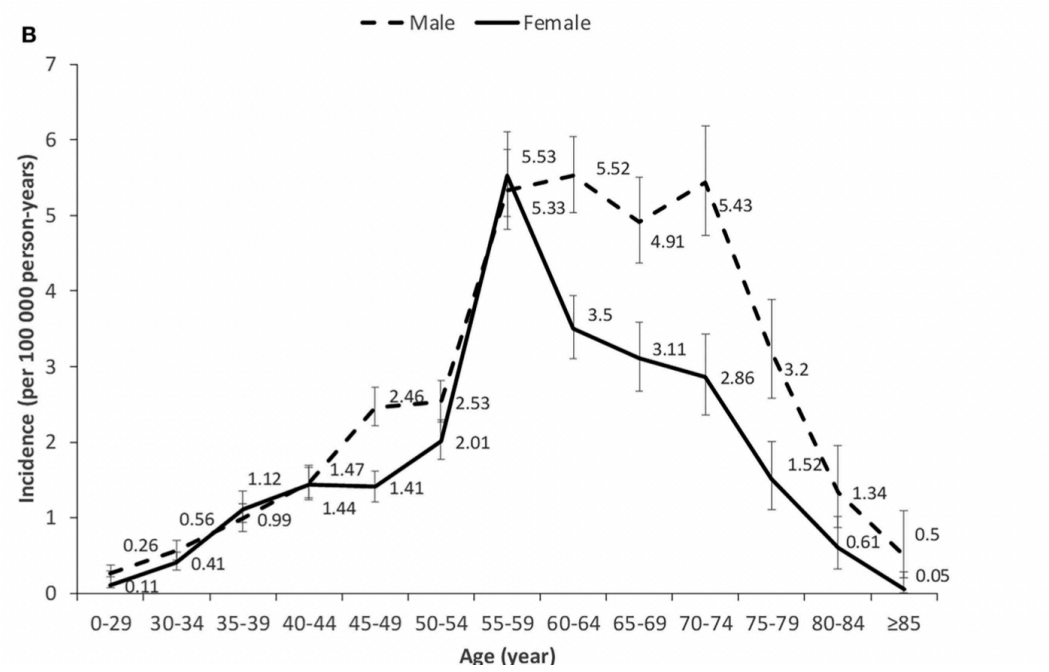

Figure 4: Incidence of Multiple Myeloma in 2016 based on gender and age.

1.2 Multiple Myeloma risk factors

As we explained above, MM is a multifaced disease with many factors concurring in its development and in its peculiar traits. MM is also characterized by a variety of risk factors, both biological, as genetic peculiarities, age, ethnic group, and precursor diseases but also environmental, usually related to occupation and exposition to chemicals. Some of these variables as for instance ethnic group and age, do not only play the role of risk factors but also of prognostic factors; some others, as obesity, can also appear as a comorbidity, being therefore one of the factors that can increase the risk of developing the disease, but at the same time one of the consequences of the disease itself. In the last years, there has been a growing effort in the identification of risk factors, which may lead to new prevention measures as well as to a reduction of mortality rate.

1.2.1 Biological risk factors

Age

Generally, the incidence of haematological malignancies increases with age, and MM does not represent an exception to this paradigm. As explained in the epidemiology section, the median age for the diagnosis of MM is 70 years, and limited is the number of patients that are diagnosed before the age of 65.[40] The rate of survival and the efficiency of treatments decreases with age;

[40] Rafael RÍOS-TAMAYO, et al., "Trends in survival of multiple myeloma: a thirty-year population-based study in a single institution", *Cancer epidemiology*, 39, 5, 2015, 693-699.

indeed, patients diagnosed before 65 years old exhibit a rate of survival of at least 7.7 years, while those diagnosed after 65 years old, exhibit a rate of survival of 3.4 years.[41] The increasing rate of mortality that follows the older age is mainly determined by a lower tolerance to the treatments, a higher discontinuity rate in the drug assumption, and by a limited physical response to the treatment due to the weakness of the organism itself. An element of considerable relevance can also be found in the higher number of comorbidities that are developed by the older organism, which determines poor outcomes in the patients with MM.

All considered, it is possible to say that MM mainly affects elders and that the older is the patient, the more limited are the possibilities of recovery and survival.

Ethnic group and social status

Studies about ethnic group as a risk factor for MM provide controversial results: for instance, the study conducted by Surveillance, Epidemiology and End Results (SEER) did not highlight any difference, concluding that the discrepancy in the incidences in black and white people was not consistent.[42] A similar result was obtained by a study which used Fluorescent in Situ Hybridization (FISH) testing to look for genetic foundations of the greater risk of developing MM in black people.[43] On the other hand, the Mayo Clinic study showed disparities in the treatment response with consequents differences in the disease itself.[44]

Considering different studies concerning the role of ethnic group belonging in the development of the illness, the most likely conclusion is that there is no substantial genetic and biological variation in the response to the disease, but the differences emerging in the rate of survival and in the drug efficiency may be determined by the socio-economical context.[45] Indeed, patients who belong to a lower social status are characterized by a delay in seeking for medical attention and this leads to a farther advancement of the disease. Determinants of this delay can be found in the absence of health insurance, low income, and marital status.

Type 2 Diabetes

An increased risk of MM has been pinpointed in patients with type 2 diabetes mellitus (DM2). This increase is mainly associated with the appearance of lymphoproliferative disorders which

[41] Cecilie H. BLIMARK., et al., "Outcome and survival of myeloma patients diagnosed 2008-2015. Real-world data on 4904 patients from the Swedish Myeloma Registry", *Haematologica*, 103, 3, 2018, 506-513.
[42] Hakan KAYA, et al., "Impact of age, race and decade of treatment on overall survival in a critical population analysis of 40,000 multiple myeloma patients", *International journal of hematology*, 95, 1, 2012, 64-70.
[43] Angela BAKER, et al., "Uncovering the biology of multiple myeloma among African Americans: a comprehensive genomics approach", *Blood*, 121, 16, 2013, 3147-3152.
[44] Sikander AILAWADHI, et al., "Racial disparity in utilization of therapeutic modalities among multiple myeloma patients: a SEER-medicare analysis", *Cancer medicine*, 6, 12, 2017, 2876-2885.
[45] David SAVAGE, et al., "Race, poverty, and survival in multiple myeloma", *Cancer*, 54, 12, 1984, 3085-3094.

lead to uncontrolled proliferation of neoplastic plasma cells, determined by chronic immune stimulation and lymphocyte activation.[46] The OS of MM patients who also have been diagnosed with DM2 is 1.22 which is significantly lower than the one of patients who does not have this pathology.

Other risk factors

An increased risk in developing MM can be determined by the presence of other illnesses that affects the organism as autoimmune disease, thyroid disease, or inflammatory disorders. The term "autoimmune disease" comprises a great variety of illnesses, such as ankylosing spondylitis and systemic sclerosis which are shown to produce a significant increase in the possibility to develop the active form of MM.[47] A significant increase in the rate of development of MM was also demonstrated in women who were previously diagnosed with pernicious anaemia.[48]

1.2.2 Environmental risk factors

Obesity

Obesity is one of the biggest problems in health as it leads to an increase in the risk for DM2, cardiovascular diseases and cancers. Obesity constitutes both a risk factor and a comorbidity in MM; overweight (BMI - Body-Mass Index 25.0-29.9) and obesity (BMI ≥30) are thought to determine, respectively, a 12% and 27% increase in risk of developing MM. Generally speaking, an increase in BMI of 5 kg/m^2 determines an increase of 12% in the incidence of MM and of 21% in the mortality rate.[49] On the other hand, there is no evidence that underweight may increase or decrease the risk of developing MM.[50]

According to the World Health Organization (WHO), 20% of all the cancers that are diagnosed every year are obesity-related and the percentage increases to 40% if overweight is considered.[51] 32% of all the Newly-Diagnosed Multiple Myeloma (NDMM) patients are obese, and this usually determines a higher drug-resistance due to a higher BMI, but also to a lower OS

[46] Jorge J. CASTILLO, et al., "Increased incidence of non-Hodgkin lymphoma, leukemia, and myeloma in patients with diabetes mellitus type 2: a meta-analysis of observational studies", *Blood*, 119, 21, 2012, 4845-4850.
[47] Kari HEMMINKI, et al., "Effect of autoimmune diseases on incidence and survival in subsequent multiple myeloma", *Journal of Hematology & Oncology,* 5, 59, 2012.
[48] Ann W. HSING, et al., "Pernicious anemia and subsequent cancer. A population-based cohort study", *Cancer,* 71, 3, 1993, 745-750.
[49] Andrew G. RENEHAN, et al., "Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies", *Lancet,* 371, 9612, 2008, 569-578.
[50] Julie BRITTON, et al., "Anthropometric characteristics and non-Hodgkin's lymphoma and multiple myeloma risk in the European Prospective Investigation into Cancer and Nutrition (EPIC)", *Haematologica*, 93, 11, 2008, 1666-1677.
[51] Brooke STEELE, et al., "Vital Signs: Trends in Incidence of Cancers Associated with Overweight and Obesity - United States, 2005-2014", *MMWR. Morbidity and mortality weekly report*, 66, 39, 2017, 1052-1058.

since the organism itself is already compromised and therefore exhibits a lower resistance to the disease. Furthermore, it should be considered that obese individuals have high levels of pro-inflammatory cytokine interleukin-6 (IL-6), which is produced partially by the adipocytes and constitutes a "potent myeloma cell grow factor".[52] It has been shown that high levels of IL-6 strongly affect patients, determining a rapid progress of MM.[53]

Occupation

Several occupations have been associated with a higher risk of developing MM, such as for farmers, firefighters, and hairdressers. All of these occupations are characterized by a high and extended exposure to chemicals and metals, so it is possible to affirm that all of the occupations where the individual is exposed to higher levels of chemical agents and metal dust show a higher possibility to develop the active form of MM.

Since 1970, farming has been associated with a 46% increase in risk of developing MM for men and 33% for women; [54] the higher risk is determined by the exposure to dichlorodiphenyltrichloroethane (DDT), pesticides, phenoxyacetics, and chlorophenols. DDT is a strong insecticide which was used until 1972 in the USA and until 1978 in Italy; it was prohibited due to its dangerous ecological effects, especially on birds and marine life. DDT is a stable substance which accumulates in the human tissue, determining high probabilities of developing lung and liver cancers as well as malignant lymphoma.[55] Another relevant element which increases the risk for farmers to develop MM is determined by prolonged antigenic stimulation; this condition implies an over-production of cells which increases the probability that mutations in cells occur, leading to the formation of a neoplasm.

In firefighters, the risk of being diagnosed with MM increases of about 50%,[56] mainly determined by the exposure to metals such as cadmium and antimony as well as to chemical substances such as benzene, toluene, and formaldehyde. The risk of developing MM in firefighters increases significantly with the duration of the employment, so this should encourage the development of innovative protective equipment as well as the improvement of

[52] Alice WALLIN, Susanna C. LARSSON, "Body mass index and risk of multiple myeloma: a meta-analysis of prospective studies", *European journal of cancer,* 47, 11, 2011, 1606-1615.
[53] Ninglin GE, Stuart RUDIKOFF, "Insulin-like growth factor I is a dual effector of multiple myeloma cell growth", *Blood*, 96, 8, 2000, 2856-2861.
[54] Carla PERROTTA, et al., "Multiple myeloma and farming. A systematic review of 30 years of research. Where next?", *Journal of occupational medicine and toxicology,* 3, 27, 2008.
[55] Shirikant KASHYAP, et al., "Carcinogenicity of DDT (dichlorodiphenyl trichloroethane) in pure inbred Swiss mice", *International journal of cancer*, 19, 5, 1977, 725-729.
[56] Grace K. LEMASTERS, et al., "Cancer risk among firefighters: a review and meta-analysis of 32 studies", *Journal of occupational and environmental medicine*, 48, 11, 2006, 1189-1202.

ventilations systems in the firehouses, in order to allow firefighters to perform their job without excessively compromising their health.

With regards to hairdressers, the increase in risk is approximately 40%[57] and it is caused by the exposure to chemicals present in shampoo, conditioners, colorants, and bleaches, as well as to volatiles propellants and solvents from hairspray. Several studies show the carcinogenic potential of these products[58] and the International Agency for Research on Cancer (IARC) corroborated the tests by affirming that the occupational exposure of hairdressers is "probably carcinogenic". The increased risk of cancer in hairdressers represents a serious concern for the society since the potential illness of all the individuals employed in this sector may lead to high health expenditure. To avoid the potentially critical situation derived by a consistent increase in the MM cases, improvements in hygienic measures and in ventilation systems should be implemented in the salons.

Exposure to chemicals

The exposure to chemicals which may not be related to a specific occupation but may be found in specific environments or situations is also proved to be a significant risk factor. Exposure to methylene chloride (dichloromethane) is considered one of the higher risk factors in the development of the disease. Methylene chloride is used as a propellant in aerosols and as a solvent in paint remover and drugs.[59] Benzene is another proven risk factor for acute MM;[60] benzene is mainly used as a solvent in the chemical industry, but it is also used in the synthetization of drugs and in the production of plastic materials.

Exposure to Ionizing Radiation

Research related to the effect of ionizing radiation as a risk factor for MM are controversial; indeed, studies based on the data of the atomic-bomb survivors associated the exposure to ionizing radiation to a higher risk of developing MM.[61] However, later evaluations of the same data found some discrepancies to the first analysis and did not confirm the connection between the exposure to ionizing ration and MM. Considering the general limited exposure of patients

[57] Carla PERROTTA, et al., "Multiple myeloma and farming. A systematic review of 30 years of research. Where next?", *Journal of occupational medicine and toxicology,* 3, 27, 2008.
[58] John G. BABISH, et al., "Urinary mutagens in cosmetologists and dental personnel", *Journal of toxicology and environmental health*, 34, 2, 1991, 197-206.
[59] Michael HOLBROOK, "Methylene chloride", *Kirk-Othmer Encyclopedia of Chemical Technology,* 16, 2003, 371-380.
[60] Paul D. MORRIS, et al., "Toxic substance exposure and multiple myeloma: a case-control study", *Journal of the National Cancer Institute*, 76, 6, 1986, 987-994.
[61] Dominik ALEXANDER, et al., "Multiple Myeloma: a review of the epidemiologic literature", *International Journal of Cancer,* 120, 12, 2007, 40-61.

to radiations, nowadays there are no sufficient data to prove whether ionizing radiations are a concrete risk factor in the development of MM.

1.3 The Staging of the disease

The great heterogeneity of MM clinical manifestations and progress conveys the need to identify precise parameters which can assist oncologists and physicians in the distinction of the disease in a high-risk and aggressive stage from the one in the low-risk stage. Thanks to this distinction it will be possible to predict and estimate drug and therapies responses.

Regarding MM staging system, three staging systems must be presented: Durie-Salmon System, International Staging System (ISS) and Revised International Staging System (R-ISS). The Durie-Salmon System represents the first attempt to provide a reference system for the progress of MM, but since its criteria are currently considered obsolete, the R-ISS constitutes the most updated system, and it is thus the one that is mostly used, even if it still presents some criticalities.

1.3.1 Durie–Salmon System

The Durie-Salmon (DS) System was introduced in 1975 by Brian Durie and Sydney Salmon and constitutes the first classification system for MM. Durie and Salmon study was meant to show how myeloma mass was related to clinical manifestations, response to treatment and patients' survival rate. According to their study, the most significant clinical manifestations associated with tumour mass are osteolytic lesions, level of M-component, level of haemoglobin and level of calcium.

This system identifies three clinical stages (I, II, III), each of which distinguishes a precise tumour size which becomes progressively bigger moving from stage I to stage III. Each stage is also differentiated in two varieties (A and B) which provide information about the renal functioning based on the presence of serum creatinine; indeed, creatinine is a major indicator of response to treatments and higher rate of survival. "A" refers to a normal renal functioning while "B" corresponds to an abnormal renal functioning (A – Creatinine < 2mg/dL; B – Creatinine ≥ 2mg/dL).[62]

Stage I of DS shows a low myeloma cell mass and a good response to treatment; stage II has an intermediate tumour mass and neither good or poor response to treatment; stage III is

[62] Brian G. DURIE, Sydney E. SALMON, "A clinical staging system for multiple myeloma. Correlation of measured myeloma cell mass with presenting clinical features, response to treatment, and survival", *Cancer*, 36, 3, 1975, 842-854.

characterized by a high cell mass, poor response to treatment and low survival perspectives (Table 1).

Stage I	All the following: Hb > 10g/dL Normal calcium No or Single bone lesion Low M-component production	Low tumour mass <$0.5x10^{12}/m^2$
Stage II	Between stage I and stage III	Intermediate tumour mass $0.5\text{-}1.2x10^{12}/m^2$
Stage III	Any of the following: Hb < 8.5g/dL Calcium <12 mg/dL Multiple Osteolytic lesions and fractures High M-component production	High tumour mass >$1.2x10^{12}/m^2$

Table 1:Durie-Salmon Staging System

1.3.2 International Staging System (ISS)

The International Staging System was introduced in 2005; it distinguishes 3 stages of MM, based on two main parameters: the level of serum *β_2-microglobulin* and the level of serum albumin (Table 2).

Stage I	Serum *β_2-microglobulin < 3.5 mg/L* *Serum albumin ≥ 3.5 g/dL*
Stage II	Not stage I or III[63]
Stage III	Serum *β_2-microglobulin > 5.5 mg/L*

Table 2: ISS Staging System

The three stages of ISS are strongly related to the prognosis of MM: stage I implies an OS of 62 months, stage II implies an OS of 44 months and stage II implies an OS of 29 months.[64]

The capability to estimate the median survival of the patient, depends upon the two main variables that are used to assess the stage: the level of serum β_2-microglobulin is strongly related to the size of the neoplasm and to the degree of renal impairment, while the low level of serum albumin reflects the high level of IL-6.*[65]*

Even if the ISS classification provides a more equal distribution of the patients among the three stages of MM compared to the DS, there are still some similarities that can be found

[63] Stage II identifies two possible situations: serum β_2-microglobulin < 3.5 mg/L but serum albumin < 3.5 g/dL; or serum β_2-microglobulin between 3.5 and 5.5 mg/L, regardless of the serum albumin level.

[64] Antonio PALUMBO, et al., "Revised International Staging System for Multiple Myeloma: A Report From International Myeloma Working Group", *Journal of clinical oncology: official journal of the American Society of Clinical Oncology*, 33, 26, 2015, 2863-2869.

[65] Joth L. JACOBSON, et al., "A new staging system for multiple myeloma patients based on the Southwest Oncology Group (SWOG) experience", *British journal of haematology*, 122, 3, 2003, 441-450.

between the two systems. The OS identified by stage I of ISS is exactly the same of the stage IA of the DS system and the characteristics of patients of ISS stage III correspond to those of patients in DS stage IIIA. Particularly interesting is that the stage III of ISS, corresponds to stage I, II and III of DS system in the B variable, regardless of the size of the tumour.

The replacement of the DS system with the ISS is mainly determined by the greater prognostic accuracy of the ISS and because the tests conducted to assess the level of serum β_2-microglobulin and serum albumin are inexpensive and therefore widely available.

1.3.3 Revised International Staging System (R-ISS)

In 2015, the International Myeloma Working Group (IMWG), revised the ISS, providing an improved system named Revised ISS. The R-ISS adds to the traditional ISS two new variables: the level of serum Lactate DeHydrogenase (LDH) and the presence of Chromosomal Abnormalities (CAs) (Table 3).

Stage I	Serum *β_2-microglobulin < 3.5 mg/L* *Serum albumin ≥ 3.5 g/dL* No high-risk chromosomal abnormalities (presence of standard-risk chromosomal abnormalities) Normal LDH
Stage II	Not R-ISS stage I or III
Stage III	Serum *β_2-microglobulin > 5.5 mg/L* High-risk chromosomal abnormalities High LDH

Table 3: R-ISS staging system

CAs tracked with to interphase Fluorescent In Situ Hybridization (iFISH) constitute a crucial element in defining the biological features of MM; indeed, the presence of standard-risk CAs correspond to an OS of 50.5 months, while the presence of high-risk CAs halve the OS to 24.5 months. The enormous gap in the OS existing between the two conditions indicates the high relevance of this data in defining the prognosis.

LDH is another significant element as it is an indicator of the aggressiveness of the disease; indeed, high levels of LDH denote high proliferation of the tumour mass, and the presence of extraosseous or extramedullary disease, which sensibly shortens the OS.[66]

The R-ISS represents the most complete staging system available now and it plays a crucial role in the outlining the prognosis of MM as it allows to define both Progression-free survival (PFS) and OS. According to R-ISS, 5 years PFS, is 55% in R-ISS stage I, 36% in R-

[66] Bart BARLOGIE, et al., "High serum levels of lactic dehydrogenase identify a high-grade lymphoma-like myeloma", *Annals of internal medicine*, 110, 7, 1989, 521-525.

ISS stage II and 24% in R-ISS stage III; while 5 years OS, is 82% in R-ISS stage I, 62% in R-ISS stage II and 40% in R-ISS stage III.

However, even if R-ISS is now the most accurate and the most complete staging system available, there are still some criticalities and limits to its efficiency; indeed, since MM is an heterogenous disease which may appear in different forms, especially in R-ISS II patients, in some cases it is necessary to provide some more detailed subclassifications.[67] Furthermore, it should also be taken into account that R-ISS does not consider the presence of circulating neoplastic plasma cells and the presence of extra-medullary disease, which have been proven, in the last years, to be extremely relevant in the prognosis of MM.

As can been seen from the description of DS, ISS and R-ISS systems, the process of defining a complete staging system for MM is an ongoing and complex process which requires constant improvement and modifications based on the advent of new therapies and on the increase of the OS. Since continuous research on MM is carried out every day, it is highly probable that the R-ISS will be revised in few years in order to implement new discoveries coming from trials and experimentation.

[67] Since it is not the aim of this thesis to provide detailed information about the staging system of MM, for further clarification about the subclassification of MM, see: Sung-Hoon JUNG, et al., "A prognostic scoring system for patients with multiple myeloma classified as stage II with the Revised International Staging System", *British journal of haematology* vol. 181,5 (2018): 707-710.

CHAPTER 2

Diagnosis: clinical manifestations, criteria, and tolls

2.1 Clinical manifestations

MM is an heterogenous disease which can manifest through a variety of symptoms, but it may also be totally asymptomatic and thus being diagnosed by chance when patients undergo blood examinations.

When considering MM symptoms, a main distinction should be made between CRAB and non-CRAB manifestations. The former refers to the main four clinical manifestations of MM, while the latter comprehends all the other symptoms that may appear in MM patients but that do not follow any specific pattern, such as infections, spinal cord compression and psychological illnesses. Estimates show that at presentation, 6% of patients with symptomatic MM, present both CRAB and non-CRAB, 20% only present non-CRAB manifestations and 71% show at least one CRAB manifestation.[68]

Even if CRAB symptoms tend to be present in most of the patients, while non-CRAB manifestations depend on stochastic events, CRAB symptoms should not be used as the only criteria to diagnose MM because, as we mentioned above, there is 1/5 of patients who only presents non-CRAB manifestations. Furthermore, there is no data supporting the hypothesis according to which the presence of CRAB symptoms in the initial stage may be more relevant that the presence of non-CRAB symptoms.

2.1.1 CRAB manifestations

The acronym CRAB refers to the main clinical manifestations of MM which include hyperCalcemia, Renal insufficiency, Anaemia and Bone lesions. CRAB are caused by uncontrolled proliferation of neoplastic plasma cells in the bone marrow, increased production of monoclonal immunoglobulin and autocrine and paracrine production of cytokines. CRAB symptoms help oncologist and physicians to distinguish the active form of MM from the asymptomatic one, thus playing a crucial role in determining prognosis, therapy, and timing of antineoplastic therapy.[69]

[68] Cecile BLIMARK, et al., "Multiple myeloma and infections: a population-based study on 9253 multiple myeloma patients", *Haematologica*, 100, 1, 2015, 107-113.
[69] Angela DISPENZIERI, Robert KYLE, "Multiple myeloma: clinical features and indications for therapy", *Best practice & research. Clinical haematology*, 18, 4, 2005, 553-568.

Hypercalcemia

Being present in more than 20% of MM patients,[70] osteolytic hypercalcemia is the most common metabolic complication of MM, and it may result from direct bone resorption or from local processing of cytokines and prostaglandins activation of osteoclasts, which stimulate bone resorption.[71] Hypercalcemia is frequently identified through level of serum calcium >11 mg/dL, but as the only analysis of serum calcium is often unreliable, the concentration of ionized calcium should also be tested.[72] Hypercalcemia clinical manifestations depends mainly upon the stage of the illness: the disease is often asymptomatic when the calcium levels are <3 mmol/L, while it becomes symptomatic when calcium levels are 3-4 mmol/L. Symptomatic hypercalcemia manifests itself through nausea, renal colic, anorexia and abdominal pain, while in the acute phase polyuria and polydipsia may arise. If the levels of calcium are >4 mmol/L, the patients may suffer from hypercalcaemic crisis, which may be fatal. Hypercalcemia is normally treated in first place with intravenous hydration of normal saline to restore the calciuresis and if necessary, the patients can also be treated with intravenous bisphosphonate therapy.[73]

Renal insufficiency

Renal insufficiency is one of the most common features of MM which may work as a wake-up call for the diagnosis. Renal impairment can be found in 20% of the patients at diagnosis and in 30% of patients during progression and may result in significant morbidity.[74] Patients who are affected by severe renal failure are characterized by a higher risk of mortality, with a 30% increase compared to those that do not suffer from renal impairment.[75] Renal insufficiency is mainly caused by hyperproduction and nephrotoxicity of IgL. IgLs obstruct the renal tubule of the nephron creating the so called "casts", resulting in the classic myeloma Cast Nephropathy (CN); CN often progress to tubular necrosis, which is particularly common around the tubules filled with fractured casts.

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[70] David GOLTZMAN, *Approach to Hypercalcemia*, in "Endotext", 2019, https://www.endotext.org/chapter/approach-to-hypercalcemia/, (last access March 15, 2023).

[71] Lewis JAMES, *Ipercacelmia*, in "Manuale MSD. Versione per professionisti", 2021, https://www.msdmanuals.com/it-it/professionale/malattie-endocrine-e-metaboliche/squilibri-elettrolitici/ipercalcemia?query=ipercalcemia, (last access March 14, 2023).

[72] Robert B. PAYNE, et al., "Interpretation of serum total calcium: effects of adjustment for albumin concentration on frequency of abnormal values and on detection of change in the individual", *Journal of clinical pathology*, 32, 1, 1979, 56-60.

[73] Jennifer WALSH, et al., "SOCIETY FOR ENDOCRINOLOGY ENDOCRINE EMERGENCY GUIDANCE: Emergency management of acute hypercalcaemia in adult patients", *Endocrine connections*, 5, 5, 2016, G9-G11.

[74] Katia MANCUSO, *Mieloma multiplo: identificazione di fattori prognostici, biomarcatori di risposta alla terapia, evoluzione clonale e di terapie innovative e personalizzate*, [Dissertation thesis], Alma Mater Studiorum Università di Bologna. Dottorato di ricerca in Oncologia, ematologia e patologia, 33 Ciclo, 2021.

[75] Joan BLADÉ, et al., "Renal failure in multiple myeloma: presenting features and predictors of outcome in 94 patients from a single institution", *Archives of internal medicine*, 158, 17, 1998, 1889-1893.

According to IMWG criteria published in 2014,[76] renal function should be evaluated according to the creatinine clearance which provides more accurate information about the glomerular filtrate. If creatinine clearance is ≤ 40ml/min, renal functioning is compromised due to the light chain deposition nephropathy. The diagnosis of CN can also be made through renal biopsy, which could reduce the risks for the patient and the costs for the hospital, but which is less common than the analysis of creatine clearance and it is not part of the routine analysis.[77] CN is often treated in first place with glucocorticoids, which provide doctors with the necessary amount of time to choose the best pharmacological treatment. Subsequently, patients are often treated with monoclonal antibodies, proteasome inhibitors and immunomodulatory drugs, which correspond to the main treatments of MM.[78]

Anaemia

Anaemia is a typical trait of MM as it is present in almost 60% of patients.[79] Myeloma-associated anaemia is usually normocytic, normochromic anaemia, in which "the circulating red blood cells (RBC) are the same size (normocytic) and have a normal red colour (normochromic)"[80] and the level of haemoglobin is ≤ 10 g/dL.[81] Normocytic, normochromic anaemia is primarily caused by: 1. erythropoietin deficiency, which leads to impaired production of RBCs and it is mainly determined by the release of IL-6; [82] 2. release of pro-inflammatory cytokines which causes the upregulation of the hepcidin (main modulator of iron metabolism), resulting in iron trapping and low levels of iron circulation;[83] 3. decrease in RBC survival.
The main symptoms of normocytic, normochromic anaemia can be found in fatigue, dizziness, migraine.

[76] S. Vincent RAJKUMAR, et al., "International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma", *The Lancet. Oncology*, 15, 12, 2014. e538-48.
[77] Guillermo A., HERRERA, "Renal manifestations of plasma cell dyscrasias: an appraisal from the patients' bedside to the research laboratory", *Annals of diagnostic pathology*, 4, 3, 2000, 174-200.
[78] Simone A. MINNIE, Geoffrey R. HILL, "Immunotherapy of multiple myeloma", *The Journal of clinical investigation*, 130, 4, 2020, 1565-1575.
[79] Gunnar BIRGEGÅRD, et al., "Evaluation of anaemia in patients with multiple myeloma and lymphoma: findings of the European CANCER ANAEMIA SURVEY", *European journal of haematology*, 77, 5, 2006, 378-386.
[80] Gizem YILMAZ, Hira SHAIKH, "Normochromic Normocytic Anemia", in *StatPearls*, Treasure Island, StatPearls Publishing, 2022.
[81] Giampaolo TALAMO, et al., "Beyond the CRAB symptoms: a study of presenting clinical manifestations of multiple myeloma", *Clinical lymphoma, myeloma & leukemia*, 10, 6, 2010, 464-468.
[82] Pellegrino MUSTO, et al., "Clinical results of recombinant erythropoietin in transfusion-dependent patients with refractory multiple myeloma: role of cytokines and monitoring of erythropoiesis", *European journal of haematology*, 58, 5, 1997, 314-319.
[83] Chia-Yu WANG, Jodie L. BABITT, "Hepcidin regulation in the anemia of inflammation", *Current opinion in hematology*, 23, 3, 2016, 189-197.

Bone lesions

Bone lesions[84] are one of the most common MM symptoms; indeed, at diagnosis, 30% of the patients have multiple fractures, caused mainly by bone rarefaction, while 70% show osteolytic lesions on radiography.[85]

Bone lesions are determined by a variety of different causes as reduced effectives of humoral immunity and cell-mediated immunity and suppression of normal IgM production. These conditions lead to immunoparesis (which implies a global decrease of normal Ig) whose main cause can be found in the increased production of cytokines by neoplastic plasma cells (PC) and BMSC. Osteolytic lesions are frequent in vertebral bodies and vertebroplasty can be used to control the immediate pain and to stabilizes the interested area.

The presence of osteolytic lesions may be identified through whole body Computed Tomography (CT), Positron Emission Tomography/Computed Tomography (PET-CT), or whole body Nuclear Magnetic Resonance (NMR).[86]

2.1.2 Non-CRAB manifestations

It should be noted that besides CRAB symptoms, other relevant clinical manifestations can be present in MM patients, as infections, hyper viscosity syndrome, neurological impairment, spinal cord compression and mental health issues. It is noteworthy that MM patients with non-CRAB manifestations are generally male and of a younger age, compared to those with CRAB symptoms.

Infections

Patients with MM are affected by abnormalities of humoral immunity, which present themselves through impaired antibody formation. These abnormalities are caused by the release of infective subunits of Ribonucleic Acid (RNA) by the myeloma tumour cells; the subunits produce some alterations in the expression of the immunoglobulin receptors on the surface of B lymphocytes, which lead to impaired antibody formation.[87] Due to the presence of this peculiar condition, MM patients are especially vulnerable to infections; indeed, recurring infections represent an initial manifestation in 25% of the MM patients. Furthermore, 75% of the patients will probably

[84] The terms "bone lesions" and "osteolytic lesions" will be used as synonymies in this paragraph. The term "osteolytic lesion" is more used in the medical field, while "bone lesions" is a term of common use.
[85] Robert A. KYLE, "Multiple myeloma: review of 869 cases", *Mayo Clinic proceedings*, 50,1,1975, 29-40.
[86] Niccolò BOLLI, Francesco DI RAIMONDO, "Mieloma Multiplo: biologia, criteri diagnostici e prognostici", *Seminari di ematologia clinica,* 2016, 5-18.
[87] Franco PARADISI, et al., "Infections in multiple myeloma", *Infectious disease clinics of North America*, 15, 2, 2001, 373-384.

develop a strong infection during the progress of the illness and 50% of MM patients will die because of an infection.[88]

It should be considered that the susceptibility to infections varies according to the stage of the illness as well as to the treatments to which the patient is subjected (patients in the first two month of chemotherapy are high-risk patients while after the first two months, the risk of infections declines).

Infections can be divided into different categories: 1. Infections caused by the disease (i.e. pneumococcal infection); 2. Infections induced by the disease and worsened by therapeutic agents (i.e. respiratory tract infections); 3. Infection caused only by therapeutic agents (i.e. urinary infections).[89] The most common infections that affect MM patients are urinary and respiratory tracts infections, which may lead to sepsis, and pneumococcal infections, which often work as wake-up call for further investigation for underlying MM.[90] Among MM recurrent infections, the most severe is Invasive Aspergillosis which occurs mainly in advanced stage II and in stage III and it last proximately 19 days, leading to a less than 500/mm^3 neutrophil count. Invasive Aspergillosis is a leading cause of death in MM patients that are highly treated.[91]

It should be noted that, even though these infections belong to different categories, there is no significant prevalence of any of the three categories as patients are equally infected by disease itself, hospital environment and drugs and medicaments they have been administered.

Hyper viscosity syndrome

"Hyper viscosity syndrome is the result of impaired blood flow especially in the microvasculature"[92] and it is determined by high haematocrit levels and by high concentration of blood-proteins. In hyper viscosity large aggregates of RBC can cause significant occlusions leading to multiple organs failure and to fatal outcome. In MM, RBC aggregates are found in peripheral blood, and they are known as "rouleaux".[93] These "rouleaux" made of three to twelve RBC are dispersed in the whole body by the movement of blood, significantly increasing the risk of thromboembolic events involving venous and arterial circulation, which may lead to

[88] Cecile BLIMARK, et al., "Multiple myeloma and infections: a population-based study on 9253 multiple myeloma patients", *Haematologica*, 100, 1, 2015, 107-113.
[89] Donald LOURIA, "Introduction and epidemiology", The American Journal of Medecine, 76, 3, 414-420, 1984.
[90] Eddy BARASCH, et al., "Pneumococcaemia as a presenting sign in 3 cases of multiple myeloma", *Scandinavian journal of haematology*, 36, 2, 1986, 229-231.
[91] Oliver LORTHOLARY, et al., "Invasive aspergillosis as an opportunistic infection in nonallografted patients with multiple myeloma: a European Organization for Research and Treatment of Cancer/ Invasive Fungal Infections Cooperative Group and the Intergroupe Français du Myélome", *Clinical infectious diseases: an official publication of the Infectious Diseases Society of America*, 30, 1, 2000, 41-46.
[92] Hau C. KWAAN, "Hyperviscosity in plasma cell dyscrasias", *Clinical hemorheology and microcirculation*, 55, 1, 2013, 75-83.
[93] Oguz K. BASKURT, Herbert J. MEISELMAN, "Erythrocyte aggregation: basic aspects and clinical importance", *Clinical hemorheology and microcirculation*, 53, 1-2, 2013, 23-37.

ischemic attacks and strokes. In blood-proteins, the variable that may give rise to hyper viscosity is the molecular size; indeed, the abnormal proteins produced in MM are characterized by a larger molecular size. It is when Ig concentration reaches 3 g/dL that viscosity will increase to 4-5 centipoise causing hyper viscosity.[94]

Since hyper viscosity limits the flow of blood to the central nervous system, vertigo, migraine, deafness, and dizziness could manifest in patients. If untreated or underestimated, hyper viscosity can cause have serious consequences as multiple organs ischemia.

Spinal Cord compression and Radiculopathy

Spinal cord compression is a relatively common clinical manifestation of MM which occurs in 5% of MM patients. Spinal cord compression may be caused by vertebral collapse or by the extradural extension of plasmacytoma,[95] and it is often associated with weakness of legs, loss of sensation in the saddle area and buttocks pain. Since spinal cord compression cause severe pain which may strongly affect patients' quality of life, it should be immediately treated with high-dose corticosteroids, which provides both pain relief and improvement of neurological functions.[96] Spinal cord compression may also result in radiculopathy, which refers to the damage of the nerve roots in the area where they leave the spinal cord. Even though, the pain caused by radiculopathy is more intense that the one due to spinal cord compression, the actual threat to the patient is less serious and the condition can be treated with immediate corticosteroids and systemic chemotherapy.

Psychological symptoms

Anxiety, distress, and depression are the most common psychological issues that emerge in MM patients; indeed, considering only those cases of clinical relevance,[97] 26.7% of MM patients suffer from anxiety, while 23.6% suffer from depression.[98] In particular, depression is proven to increase after stem cell transplantation as full recovery is often not possible and together with the toxicity of the maintenance treatment, the general quality of life of MM patients decreases.[99]

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[94] Hau C. KWANN, "Role of plasma proteins in whole blood viscosity: a brief clinical review", *Clinical hemorheology and microcirculation*, 44, 3, 2010, 167-176.
[95] Warwick BENSON, et al., "Spinal-cord compression in myeloma", *British medical journal*, 1 ,6177, 1979, 1541-1544.
[96] Angela DISPENZIERI, Robert A. KYLE, "Neurological aspects of multiple myeloma and related disorders", *Best practice & research. Clinical haematology*, 18, 4, 2005, 673-688.
[97] The clinical relevance was measured according to the Hospital Anxiety and Depression Scale (HADS).
[98] Christina RAMSENTHALER, et al., "Prevalence of symptoms in patients with multiple myeloma: a systematic review and meta-analysis", *European journal of haematology*, 97, 5, 2016.
[99] Sarah ACASTER, et al., "Impact of the treatment-free interval on health-related quality of life in patients with multiple myeloma: a UK cross-sectional survey", *Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer,* 21, 2, 2013.

The concern about quality of life is still underrated in MM research, both in the evaluation of the patient's treatment and in the supportive care guidelines.[100] However, the persistence of mental health issues in MM patients should cast a light on the criteria used to appoint patients for palliative care; indeed, the decision to provide patients with palliative care should not be only dependent upon clinical response to the treatment but should also take into consideration the emotional response, otherwise a substantial number of patients will be excluded even if they could benefit from supportive and palliative services.[101]

2.2 MM diagnostic criteria and tools

Multiple Myeloma diagnosis is primarily based on IMWG criteria, which were firstly published in 2003 and then revised in 2014. Since MM is a multifaced disease, it requires multiple and diverse diagnostic exams and test including laboratory exams, imaging, and cytogenetic investigation.

2.2.1 IMWG diagnostic criteria

In 2003, IMWG firstly published criteria for the diagnosis of MM. In 2014, the IMWG revised the existing criteria improving the definition of CRAB manifestations and adding three new malignancy biomarkers, indicators of imminent organ damage (see Table 4).

According to IMGW 2003 criteria, only patients with CRAB manifestations could be diagnosed with MM; this way, patients were starting the treatment only when severe end-organ damage had already occurred without the possibility to prevent the degeneration of the disease leading to a significant reduction in the OS.

The criteria established in 2003 were acceptable when treatment options were limited and had substantially toxic effect on patients; however, nowadays, treatment and diagnostic techniques have greatly improved, making 2003 criteria obsolete and limiting for patients OS.[102]

Concerning the CRAB symptoms, according to the new IMWG criteria, to diagnose renal impairment the analysis of the creatinine level (> 2 mg/dL) is not sufficient anymore, but the analysis of the level of the creatinine clearance is needed (≤ 40ml/min). Furthermore, in the evaluation of the extension of osteolytic lesions, CT and PET-CT have been added to the traditional skeletal radiograph to have more precise information.[103]

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[100] Pieter SONNEVELD, et al., "Review of health-related quality of life data in multiple myeloma patients treated with novel agents", *Leukemia*, 27, 10, 2013, 1959-1969.
[101] Melanie KRIPP, et al., "Patients with malignant hematological disorders treated on a palliative care unit: prognostic impact of clinical factors", *Annals of hematology*, 93, 2, 2014.
[102] Robert A. KYLE, S. Vincent RAJKUMAR, "Monoclonal gammopathies of undetermined significance", *Best practice & research. Clinical haematology*, 18, 4, 2005, 689-707.
[103] S. Vincent RAJKUMAR, et al., "International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma", *The Lancet. Oncology*, 15, 12, 2014. e538-48.

The major innovation of the IMWG criteria of 2014 can be found in the three new malignancy biomarkers which includes: level of plasma cells in the bone marrow, serum Free Light Chain (sFLC) ratio, and identification of focal lesions through Magnetic Resonance Imaging (MRI). The presence of one of these three biomarkers is considered sufficient to start the treatment, regardless of whether CRAB symptoms appear or not; this way, time for diagnosis can be shortened, improving patients OS.

Regarding the level of plasma cells in the bone marrow, patients are considered eligible for therapy when Bone Marrow Plasma Cells (BMPC) are higher than 60%. The level of BMPC can be assessed through bone marrow aspirate or biopsy examination and if discrepancies arise between the two exams, the higher value should be considered as the most relevant.[104]

Concerning sFLC, the normal ratio ranges between 0.26 and 1.65, but in patients with plasma cells disorders, an excessive production of one of the two light chains type (κ and λ) occurs resulting in an abnormal FLC ratio.[105] The IMWG established that patients with a sFLC over 100 are eligible for immediate treatment, as the risk of progression to symptomatic MM in two years is 82% and the possibility to incur in severe renal failure or other CRAB symptoms is up to 27%.[106]

The last of the three new criteria is the presence of at least one focal lesion identified through MRI. If the lesions identified are smaller than 5mm (< 5mm), the MRI should be complemented by CT or PET-CT to assess their presence and start the MM therapy.

The new criteria introduced in 2014 represent a great step forward in the treatment and diagnosis of MM as they can sensibly reduce the time needed in the identification of MM, also reducing the cases of delay in diagnosis, which account for a great percentage of the avoidable premature deaths. Furthermore, since end-organ damage is not anymore, a compulsory manifestation to start the treatment, the general OS of patients is substantially increasing.

Monoclonal Gammopathy of Undermined Significance (MGUS)
1. Serum monoclonal component < 30 g/L 2. Clonal bone marrow plasma cells < 10% 3. Absence of end-organ damage such as hypercalcemia, anaemia, renal insufficiency, bone lesion (CRAB)
Smouldering Multiple Myeloma (SMM)
1. Serum monoclonal component ≥ 30 g/L 2. Bone marrow plasma cells ≥ 10% and < 60%

[104] S. Vincent RAJKUMAR, et al., "Methods for estimation of bone marrow plasma cell involvement in myeloma: predictive value for response and survival in patients undergoing autologous stem cell transplantation", *American journal of hematology*, 68, 4, 2001, 269-275.
[105] Angela DISPENZIERI, et al., "International Myeloma Working Group guidelines for serum-free light chain analysis in multiple myeloma and related disorders", *Leukemia*, 23, 2, 2009, 215-224.
[106] Jeremy T. LARSEN, et al., "Serum free light chain ratio as a biomarker for high-risk smoldering multiple myeloma", *Leukemia*, 27, 4, 2013, 941-946.

3. Absence of Myeloma Defining Events (MDE)
Multiple Myeloma (MM)
1. Bone marrow plasma cells ≥ 10% and presence of plasmacytoma 2. Presence of one or more of the Myeloma Defining Events (MDE): Organ damage related to MM (CRAB) a. C (hyper calcemia): calcemia > 11mg/dL b. R (renal insufficiency): creatinine clearance < 40 mL/min or serum creatinine > 2 mg/dL c. A (Anaemia): Hb < 10g/dL d. B (bone lesions): 1 or more osteolytic lesions identified through CT or PET/CT One or more malignancy biomarker: e. Medullary plasma cells ≥ 60% f. sFLC ratio (involved/uninvolved) > 100 g. > 1 focal lesion identified through MRI

Table 4: IMWG criteria for plasmacellular discrasia diagnosis

2.2.2 Diagnostic Tools

Given the multifaced nature of MM, a variety of exams and laboratory analysis are carried out to assess the presence of the illness in the symptomatic or asymptomatic form. In this section, considering the parameters provided by the IMWG in 2014, the most relevant laboratory and instrumental analysis will be examined.

2.2.2.1 Laboratory investigation

Serum and urine exam

In order to assess the presence of the malignant PC clone, it is necessary define, both in the serum and in the urine, the quantity and the quality of the Monoclonal Component (MC) which can consist of a whole Immunoglobulin (Ig) made of two heavy chains and two light chains (see figure 5) or by a fragment of the Ig made only of light chains. To do so, Serum Protein Electrophoresis (SPEP),[107] serum Immunofixation (IFE),[108] Urine Protein Electrophoresis (UPEP) and urine IFE should be carried out.[109] Usually, SPEP and UPEP are carried out on a urine or serum sample collected no more than 24 hours before the test and in 80% of the patients M-protein is found, leading to the diagnosis of MM.[110]

To complete the diagnosis, patients are advised to carry out complete blood count, analysis of serum and urine creatinine, analysis of LDH level and analysis of serum albumin

[107] Serum Protein Electrophoresis (SPEP) is a laboratory exam which, according to physical properties, separates proteins within the given sample. It is used to identify MM and other protein disorders.
[108] Serum Immunofixation (IFE) is a laboratory exam which measures the presence of protein in the blood, to assess the presence of specific illnesses.
[109] Robert A. KYLE, S. Vincent RAJKUMAR, "Criteria for diagnosis, staging, risk stratification and response assessment of multiple myeloma", *Leukemia*, 23, 1, 2009, 3-9.
[110] James BERENSON, *Mieloma Multiplo*, in "Manuale MSD. Versione per professionisti", 2021, https://www.msdmanuals.com/it-it/professionale/ematologia-e-oncologia/disturbi-plasmacellulari/mieloma-multiplo?query=mieloma%20multiplo, (last access March 20, 2023).

and *β₂-microglobulin* level. While blood count and analysis of creatinine are necessary to highlight the potential or imminent end-organ damage, analysis of LDH, serum albumin and *β₂-microglobulin* are crucial to identify the stage of the disease according to the ISS.

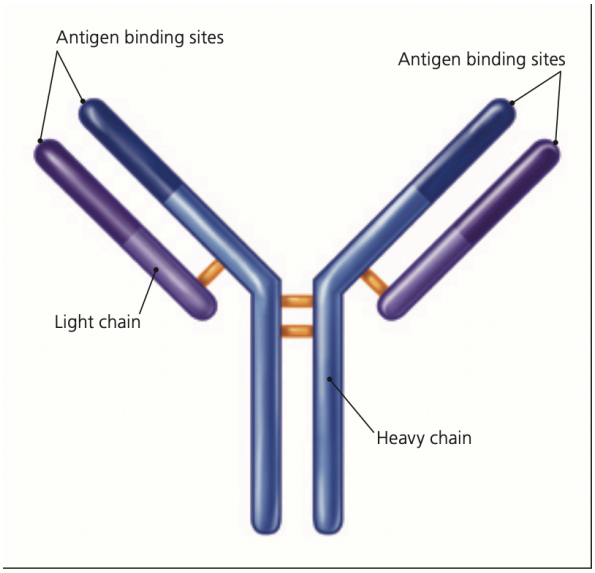

Figure 5: Ig molecule containing heavy chains and light chains

Bone marrow exam

Medullary biopsy and medullary aspiration are used to assess the presence of plasma cells in the bone marrow and should be performed on those patients whose level of proteins in serum or urine are abnormal. Once these examinations have been completed, FISH will be carried out on the sample drawn from the bone marrow to evaluate the chromosomal set and verify whether plasma cells are malignant or not.[111] The bone marrow exams play a relevant role in the definition of the prognosis as the results can strongly impact the OS of the patient.

2.2.2.2 Instrumental investigation

The use of instrumental techniques for examining skeletal pathology and identifying potential extramedullary spread of the disease is crucial for diagnostic, prognostic and therapeutic assessment purposes throughout and after the treatment.[112] In the last few years, several new imaging practices as Whole-Body Low-Dose Computed Tomography (WBLD-CT), NMR and PET-TC have been introduced, and they have been added to the IMWG criteria for the diagnosis of MM, as the preferred methods to assess the presence of osteolytic lesions.

[111] Evangelos TERPOS, et al., "Management of bone disease in multiple myeloma", *Expert review of hematology*, 7, 1, 2014.
[112] Elena ZAMAGNI, et al., "Imaging in multiple myeloma: How? When?", *Blood*, 133, 7, 2019, 644-651.

Radiologic exam (X-Ray)

Whole-body X-Ray was, in the past, the main exam to assess the presence of osteolytic lesions, but now have been progressively substituted by the new techniques, as WBLD-CT. The main reason behind the decline in the use of X-Ray consists in the fact the X-Ray highlights lesions only when there is the involvement of at least 50% of the local bone mass, which often results in underestimation of the skeletal disease.[113]

Whole-Body Low-Dose Computed Tomography (WBLD-CT)

The WBLD-CT represents now the "gold standard" in the identification of osteolytic lesions and in the estimation of the risk of fracture and it also works as a guide for biopsy and radiotherapy planification. As we said in the above paragraph, the WBLD-CT substituted the traditional X-Ray in the identification of osteolytic lesions because of its greater precision and its greater capability of noticing even small lesions.[114] It should be noted that, WBLD-CT not only provides with more sensitivity in noticing the osteolytic lesions, but also allows the diagnosis of pathologic fractures.

Nuclear Magnetic Resonance (NMR)

NMR is mainly used in the analysis of the spinal column; indeed, the traditional NMR with contrast agent is able to identify the medullary spread of the tumour in T1 and T2 sequences, where the lesions are, respectively, hypointense and hyperintense.[115] NMR is characterized by a high level sensitivity which permits to identify the lesions even in the axial skeleton, thus playing a crucial role in the differentiation of SMM or MM. NMR is also relevant in differentiating vertebral fractures caused by MM or vertebral fractures caused by osteoporosis, in describing the entity of medullary compression, and in the evaluation of the need for surgical intervention.[116]

Whole-body MRI constitutes an advanced version of NMR, which does not require the use of contrast agent and it is ever faster in its execution (only 20 minutes).

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[113] Evangelos TERPOS, et al., "Advances in imaging and the management of myeloma bone disease", *Journal of clinical oncology: official journal of the American Society of Clinical Oncology*, 29, 14, 2011, 1907-1915.

[114] Kelechi PRINCEWILL, et al., "Multiple myeloma lesion detection with whole body CT versus radiographic skeletal survey", *Cancer investigation*, 31, 3, 2013, 206-11.

[115] T1 and T2 constitute two sequences of the NMR: in T1, the release of energy leads to the baseline alignment of protons, while in T2, due to the transfer of energy, the protons are oscillating. In T1, where the lesions are hypointense, they look darker than the other part of the body in the NMR, while in T2, where the lesions are hyperintense, they look brighter than the rest. The two images in T1 and T2 should be regarded as complementary as considered together.

[116] Angela RAGO, "Inquadramento diagnostico del Mieloma Multiplo", *Atti della Accademia Lancisiana,* 65, 2, 2021, 78-84.

Positron Emission Tomography – Computed Tomography (PET-TC)

The PET-TC combines metabolic data with anatomical one, allowing the analysis of the metabolism of osteolytic lesions based on the extent of the glucose uptake (thus differentiating active lesions and inactive ones). PET-TC, thus, allows the identification of metabolically active lesions with a resolution power of 5mm and it is mainly used in the identification of the presence of extramedullary malignant cells as well as in the analysis of the patient's response to the therapy.[117] According to the new IMWG criteria, the presence of lesions in the PET-TC is considered a sufficient evidence to start the chemotherapeutical treatment.

Considering the different methodologies described above, IMWG recommends WBLD-CT and PET-TC to evaluate the presence and the extension of the osteolytic lesions (PET-TC is especially required when there is suspect of extramedullary presence of malignant cells); if the exam results are negative, whole-body NMR is used to identify possible focal lesions which would lead to a final diagnosis of MM.

In the evaluation of the response to the therapy, the preferred instrumental investigation depends mainly on the exams carried out to diagnose MM in first place: if PET-TC was negative at the beginning, WBLD-CT is recommended in second instance, while if PET-TC was positive, the test will be retaken to evaluate the progress of the illness and the response to the therapy, allowing an adequate comparison.[118]

2.2.3 The relevance of time in diagnosis

As we saw, MM is a disease whose primary phase is often silent and when symptoms start to arise the disease is already in its advanced stage. Given that, the time in which the disease is diagnosed is crucial to determine the prognosis and the OS of the patients.

In many cases, MM is diagnosed by chance when patients undergo their annual complete blood count, but in other cases, patients who show symptoms as fatigue and bone pain consult their General Practitioner (GP) several times before the final diagnosis.[119] Delay in the diagnosis is proven to be one of the main causes of mortality rate in MM patients, as 11% to 23% of MM

[117] Sree Harsha TIRUMANI, et al., "Role of FDG-PET/CT in Extramedullary Multiple Myeloma: Correlation of FDG-PET/CT Findings With Clinical Outcome", *Clinical nuclear medicine*, 41, 1, 2016, 7-13.
[118] Elena ZAMAGNI, Michele CAVO, "The role of imaging techniques in the management of multiple myeloma", *British journal of haematology*, 159, 5, 2012, 499-513.
[119] Georgios LYRATZOPOULOS, et al., "Variation in number of general practitioner consultations before hospital referral for cancer: findings from the 2010 National Cancer Patient Experience Survey in England", *The Lancet, Oncology*, 13, 4, 2012, 353-65.

cases are diagnosed with delay.[120] This delay may be determined by a variety of different causes, as late presentation of patients, wrong diagnosis by GP themselves or inefficiency of healthcare system.[121]

Late presentation is mainly caused by the fact that patients may underestimate the first symptoms of MM, ascribing them to an excess of stress, to incorrect seating positions or to low blood pressure. However, even if patients have some consideration of their symptoms, they may present themselves to the wrong practitioner as physiotherapists, physiatrists, or orthopaedics, who will try to solve the single symptom instead of considering the whole system.

With regards to cases of wrong diagnosis, nowadays, new diagnostic techniques render possible the diagnosis of MM in its early stage, but the main obstacle that needs to be overcome is the recognition of the possibility of MM by GP, who usually attributes early MM symptoms, as back pain, to other less serious and more common conditions. Indeed, since MM is a relatively rare disease and its early symptoms are common and attributable to several other disease, single symptoms have low Positive Predictive Value (PPV)[122] which renders difficult the initial diagnosis. However, it should be noted that, while PPV in single symptoms is low, the occurrence of more symptoms together as sever back pain, nosebleeds and hypercalcemia should be regarded as a clear indicator of MM and initial tests should be carried out. Several guidelines have been released to facilitate the diagnosis of MM by GP, listing some "red flag" features that should lead to more in-depth exams.[123]

Significant delay may also be determined by the structural problems in the healthcare system; indeed, due to the unavailability of resources and personnel, great time is needed for patients to take the necessary exams that would lead to the diagnosis of MM and long time is also required to start the therapy once the diagnosis has been made.

All things considered, delay in the diagnosis of MM constitute a highly relevant clinical problem which may be mitigated by a more interdisciplinary approach in diagnosis, by a deepen knowledge of the symptoms of MM and of their occurrence and by an improvement in coordination between GP and specialists. However, the main problem in the delay of both diagnosis and treatment stays in the inefficiency of the healthcare system, which is not

[120] Giulia GRAZIANI, et al., "Time from first symptom onset to the final diagnosis of multiple myeloma (MM) - possible risks and future solutions: retrospective and prospective 'Deutsche Studiengruppe MM' (DSMM) and 'European Myeloma Network' (EMN) analysis", *Leukemia & lymphoma*, 61, 4, 2020.
[121] C. KARIYAWASAN, et al., "Multiple myeloma: causes and consequences of delay in diagnosis", *QJM: monthly journal of the Association of Physicians*, 100, 10, 2007, 635-640.
[122] Elizabeth SHEPHARD, et al., "Quantifying the risk of multiple myeloma from symptoms reported in primary care patients: a large case-control study using electronic records,", *The British journal of general practice: the journal of the Royal College of General Practitioners*, 65, 631, 2015, 106-113.
[123] For further information see: Nicholas HENSCHKE, et al., "Red flags to screen for malignancy in patients with low-back pain", *The Cochrane database of systematic reviews*, 2, 2013.

adequately providing services to patients, and whose efficiency depends mainly on political decisions.

CHAPTER 3

Incurable disease: treatment and pain therapy

3.1 Treatment agents

Therapy for MM started in 1950s with alkylating agents and corticosteroids, which exhibited high effectiveness in first place. Until 1980s, MM standard of care consisted in the two-drugs combination melphalan-prednisone (MP), with which Objective Response Rate (ORR) reached 50% and Complete Remission (CR) could be seen in 5-10% of the patients. To improve the effectiveness of the therapy, different chemotherapeutical drugs were combined, giving birth to VAD (vincristine, doxorubicin, dexamethasone) treatment. VAD treatment showed a higher response rate, but didn't increase the OS, which, as in MP treatment, was almost 3 years.[124]

In 1980s, melphalan-based chemotherapy, followed by Autologous Stem Cell Transplantation (ASCT), opened the way to a new treatment era; in 1990s, it was demonstrated that ASCT was superior to traditional chemotherapeutical treatments in terms of PFS and OS, especially for patients below the age of 60.[125]

In the early 2000, a pivotal change in the therapeutical approach for MM was elicited by the introduction of the "new drugs": non-antiblastic[126] agents that effectively act on neoplastic plasma cells and on medullary microenvironment and whose role is crucial in promoting the growth of neoplastic clones and in inducing resistance to therapy. Thanks to them, the clinical outcome of MM patients improved greatly, regardless of the stage of the disease and the age of the patient. These "new drugs" can be divided into three categories:

1. Immunomodulatory drugs (IMiD) as thalidomide, lenalidomide and pomalidomide.
2. Proteasome inhibitors (PI) as bortezomib, carfilzomib and ixazomib.
3. Monoclonal antibodies (mAb) as daratumumab and isatuximab.

In the next paragraphs, action mechanisms and toxicity of the drugs that MM patients have been administered to since 1950 will be analysed. It should be noted that this section will provide information also about those treatments that are not in use anymore but which hold a role in the past therapy of MM.

[124] Diana SAMSON, et al., "Infusion of vincristine and doxorubicin with oral dexamethasone as first-line therapy for multiple myeloma", *Lancet,* 2, 8668, 1989, 882-885.
[125] Michel ATTAL, Jean-Luc HAROUSSEAU, "Standard therapy versus autologous transplantation in multiple myeloma", *Hematology/oncology clinics of North America*, 11, 1, 1997, 133-146.
[126] The term "antiblastic" can be used as a synonym of "chemotherapeutical", therefore, the "non-antiblastic agents" are all of those drugs, who do not belong to the family of alkylating agents or corticosteroids.

3.1.1 Alkylating agents

Alkylating agents constitute the first category of drugs used for the treatment of MM. The main property of alkylating agents consists in damaging the DNA by inserting alkylating groups in DNA strands, causing the inhibition of the replication process. Once the alkylating group has been inserted, the DNA strand breaks, leading to abnormal RNA transcription which results in apoptosis as the cell is not able to complete the synthesis of proteins.[127]

Melphalan

Melphalan (Phelinun®) is the first alkylating agent that has been found effective in treating MM. In 1969, the combination between melphalan and prednisone became the standard of care in the treatment for MM, as it showed significant positive effects. However, melphalan is not used anymore, since the "new drugs", described in the following paragraphs, have been showing greater outcomes and lower toxicity. Melphalan main action mechanism consists in the inhibition of DNA and RNA synthesis. Since melphalan is metabolized by the liver and then it is eliminated by the kidneys, dose reduction may be needed if the patient suffers from renal impartment; indeed, if kidney function is reduced, melphalan accumulates in the organism resulting in bone marrow suppression.[128] The most common toxicities of melphalan are bone marrow suppression, nausea, and vomiting.

Cyclophosphamide

Cyclophosphamide (Endoxan Baxter®) is another alkylating agent which is used in the treatment of MM at a higher rate compared to melphalan. Cyclophosphamide main action mechanism consists in inhibiting and interfering with DNA replication and with RNA production. Phoramide mustard, the active metabolite of cyclophosphamide, establishes cross-links with the DNA, leading to cell apoptosis. Cyclophosphamide is administered orally, and this facilitate and hasten the absorption by the organism. Common side effects of cyclophosphamide administration include nausea, hair loss and immunosuppression, while severe side effects are infertility, allergic reactions, and cardiotoxicity. Severe side effects mainly arise when the patient is administered cumulative doses of cyclophosphamide.[129]

[127] Anastazja POCZTA, et al., "Treatment of Multiple Myeloma and the Role of Melphalan in the Era of Modern Therapies-Current Research and Clinical Approaches", *Journal of clinical medicine*, 10, 9, 2021.
[128] Gibbons CORNWELL, et al., "Influence of renal failure on myelosuppressive effects of melphalan: Cancer and Leukemia Group B experience", *Cancer treatment reports*, 66, 3, 1982, 475-481.
[129] Jemianne JIA, et al., "Chemotherapy-related complications in the kidneys and collecting system: an imaging perspective", *Insights into imaging*, 6, 4, 2015, 479-487.

3.1.2 VAD and VND

As described in the previous paragraph, melphalan-based treatment constituted the standard for MM treatment for long time. The most common combination was melphalan-prednisone, which produced a 50% response rate with a median survival of 3 years.[130] However, since CR rates were low, new studies were carried out, resulting in VAD treatment (vincristine,[131] doxorubicin,[132] dexamethasone[133]), which was particularly recommended for patients for which alkylating agents were not effective.[134] Due to the high level of toxicity in VAD treatment, which led to serious infections and cardiovascular complications in most patients, VAD-hybrids treatments were explored. VND (vincristine, mitoxantrone,[135] dexamethasone) is the first developed VAD-hybrid in which doxorubicin is substituted with mitoxantrone. Since it is believed that the main results of VAD treatment are related to the presence of dexamethasone, the substitution of doxorubicin with mitoxantrone did not reduce in any way the effectiveness of the treatment, but it only contributed to the reduction of its toxicity.

VAD and VND side effects are mainly haematological, and they include granulocytopenia and myelosuppression. The former is a condition in which the number of granulocytes is lower than normal, while the latter, particularly strong in VND treatment, is a condition in which bone marrow reduces its activity; both Adverse Events (AEs) lead to recurrent infection and severe infective morbidity. Considering non-haematological side effects, the main concern is referred to cardiac issues such as heart failure, myocardial infarction, and angina,[136] which do not show any significant occurrence difference in VAD or VND treatment.

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[130] Walter GREGORY, et al., "Combination chemotherapy versus melphalan and prednisolone in the treatment of multiple myeloma: an overview of published trials", *Journal of clinical oncology: official journal of the American Society of Clinical Oncology*, 10, 2, 1992, 334-342.

[131] Vincristine is a chemotherapeutical drug which belongs to the family of alkaloids. The main action mechanism of vincristine consists in stopping the process of proliferation of the neoplastic cells by inhibiting the capability of the cell to separate into new cells. The main side effects of vincristine are recurrent infections, hair loss, numbness, and abdominal and muscular pain.

[132] Doxorubicin is a chemotherapeutical drug which belongs to the family of anthracycline. The main action mechanism of doxorubicin consists in reducing the growth of cancer cells by blocking a specific enzyme which is responsible for the division and growth of the cells. The main side effects of doxorubicin are recurrent infections, numbness, diarrhea, and weight gain.

[133] Dexamethasone is a drug belonging to the family of corticosteroids. Dexamethasone is used to treat inflammation, which may have different origins, and it often used in combination with chemotherapeutical drug, to reduce the side effects of the main treatment.

[134] Garry FORGESON, et al., "Infused vincristine and adriamycin with high dose methylprednisolone (VAMP) in advanced previously treated multiple myeloma patients", *British journal of cancer*, 58, 4, 1988, 469-473.

[135] Mitoxantrone is a chemotherapeutical drug. The main action mechanism of mitoxantrone consists in inhibiting the reproduction of neoplastic cells and reducing the presence of grow factors. The main side effects of mitoxantrone are recurrent infections, hair loss and tiredness. Compared to doxorubicin, it is characterized by limited side effects, and this is one of the main reasons behind the substitution.

[136] Michele CAVO, et al., "Melphalan-prednisone versus alternating combination VAD/MP or VND/MP as primary therapy for multiple myeloma: final analysis of a randomized clinical study", *Haematologica*, 87, 9, 2002, 934-942.

3.1.3 Autologous Stem Cell transplantation (ASCT)

ASCT is the main non-drug treatment in MM therapy and the great improvement in MM patients' OS can be attributable to it. ASCT led to an improvement is average OS equal to 12 months,[137] and generally the OS in five years is 52%.[138] Different factors as comorbidities, age and performance status influence the feasibility of the procedure and even if ASCT is the treatment that provides the most benefit to patients and Treatment-Related Mortality (TRM) is only 1-2%,[139] it may not represent the best choice in all situations.

ASCT can be distinguished in early ASCT (carried out immediately after the induction therapy) or delayed ASCT (resorted as a salvage therapy at the moment of first relapse). Different studies, the main carried out by Mayo Clinic, tried to assess whether early ASCT is more effective than delayed ASCT, but there are no sufficient data to come to a final conclusion. However, considering the impact on quality of life determined by high-dose chemotherapy and its economic burden, if there is no specific preference on the side of the patient, early ASCT is recommended. It may be preferrable to opt for delayed ASCT only if the patient is well tolerating and responding to the initial therapy and the risk of progression is low.

ASCT can be performed once or twice (tandem ASCT) according to the specific condition of the patient. In tandem ASCT, the patient will receive a second transplant once he recovered from the first one.[140] Different studies[141][142] showed an improvement in PFS, when ASCT is performed twice, but they all failed to show any improvement in OS, mainly because of treatment significant toxicity, which in the long run affects the possibility to increase the survival rate. Since no significant benefits can be obtained from tandem ASCT, patients are considered for this procedure only when they show a high-risk disease with no complete response after the first transplant.

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[137] David H. VESOLE, "Transplantation for multiple myeloma: who, when how often? Patient selection and goals", *Blood*, 102, 10, 2003, 3471-3472.

[138] Michel ATTAL, et al., "A prospective, randomized trial of autologous bone marrow transplantation and chemotherapy in multiple myeloma. Intergroupe Français du Myélome", *The New England journal of medicine*, 335, 2, 1996, 91-97.

[139] Morie A. GERTZ, et al. "Autologous stem cell transplant in 716 patients with multiple myeloma: low treatment-related mortality, feasibility of outpatient transplant, and effect of a multidisciplinary quality initiative", *Mayo Clinic proceedings*, 83, 10, 2008, 1131-1138.

[140] Bart BARLOGIE, et al., "Superiority of tandem autologous transplantation over standard therapy for previously untreated multiple myeloma", *Blood*, 89, 3, 1997, 789-793.

[141] Umit Yavuz MALKAN, et al., "Comparison of single and double autologous stem cell transplantation in multiple myeloma patients", *Open medicine,* 16, 1, 2021, 192-197.

[142] Michele CAVO, et al., "Double Autologous Stem Cell Transplantation Significaly Prolongs Progression-Free Survival and Overall Survival in Comparison with Single Autotransplantation in Newly Diagnosed Multiple Myeloma: An Analysis of Phase 3 EMN02/HO95 Study", *Blood*, 130, 401, 2017.

3.1.4 Immunomodulatory drugs (IMiD)

IMiDs represent the first category of the "new drugs" which deeply changed MM treatment, moving away from the massive use of alkylating agents and constituting a key element in the backbone of MM therapy. IMiDs are characterized by a pleotropic mechanism[143] of action, which allows inhibition of proliferation of adhesion cells and stimulation of apoptosis. It should be noted that IMiDs act on the medullary microenvironment inhibiting angiogenesis, altering cytokines secretion, and hampering the osteoclastogenic proliferation.[144] The main IMiDs are thalidomide, lenalidomide, and pomalidomide, whose specific characteristics will be analysed in the following paragraphs.

Thalidomide

Thalidomide is a derivative of glutamic acid, which was used in 1950s as a sedative. Once its effects and effectiveness as immunomodulatory and anti-angiogenic agent were demonstrated, it was approved for the treatment of MM in 2006 and in 2008, respectively by FDA (US Food and Drug Administration) and EMA (European Medicine Agency).

Thalidomide works mainly as an inhibitor of angiogenesis[145] and of secretion of IL-6 which is crucial for the survival and the expansion of the neoplastic clone.[146] Furthermore, thalidomide contributes to the reduction of interaction between neoplastic cells and medullary microenvironment since it inhibits the secretion of the adhesion molecules.[147]

The main drawback in the use of thalidomide is its high level of toxicity: moderate side effects are asthenia, drowsiness, bradycardia, skin rush and gastrointestinal disorders. In the long run (>1 year), Peripheral Neuropathy (PN) is the most common side effect of thalidomide and the one that mostly affects patients' Quality of Life (QOL). PN is a condition that affects sensory nerves, altering patients' perception of temperature, touch, and pain, but it can also affect motor nerves, leading to numbness, muscles cramps, lack of coordination and weakness. The most severe complication related to the administration of thalidomide is Deep Vein Thrombosis (DVT), which is found in 25% of the patients and usually requires additional

[143] "Pleiotropic mechanisms" refers to the phenomenon according to which a single gene leads to multiple phenotypic traits.
[144] Hang QUACH, et al., Hang, "Mechanism of action of immunomodulatory drugs (IMiDS) in multiple myeloma", *Leukemia*, 24, 1, 2010, 22-32.
[144] Ana Pilar GONZÁLEZ RODRIGUEZ, "Management of the adverse effects of lenalidomide in multiple myeloma", *Advances in therapy*, 28, 1, 2011, 1-10.
[145] Robert J. D'AMATO, et al., "Thalidomide is an inhibitor of angiogenesis", *Proceedings of the National Academy of Sciences of the United States of America*, 91, 9, 1994, 4082-4085.
[146] Andre MOREIRA, et al., "Thalidomide exerts its inhibitory action on tumor necrosis factor alpha by enhancing mRNA degradation", *The Journal of experimental medicine*, 177, 6, 1993, 1675-1680.
[147] Annalisa MERCURIO, et al., "A Mini-Review on Thalidomide: Chemistry, Mechanisms of Action, Therapeutic Potential and Anti-Angiogenic Properties in Multiple Myeloma", *Current medicinal chemistry*, 24, 25, 2017, 2736-2744.

therapies to reduce the risk of death.[148] After thalidomide, other two IMiDs were developed: lenalidomide (second generation IMiD) and pomalidomide (third generation IMiD).

Lenalidomide

Lenalidomide (Revlimid®) was approved in 2006 by FDA and in 2008 by EMA for the treatment of Relapsed/Refractory Multiple Myeloma (RRMM); in 2017 it was also approved as first-line therapy for patients that would have undergone ASCT and in 2018 it was approved as maintenance therapy after ASCT.

Lenalidomide works mainly as an inhibitor of angiogenesis and of proliferation of neoplastic cells, since it reduces secretion of adhesion molecules.[149] Thalidomide and lenalidomide effects are similar, but lenalidomide is preferred to thalidomide for is greater effectiveness and for its limited toxicity. Indeed, even if lenalidomide implies side effects as asthenia, skin rush, myelotoxicity, and higher exposition to infection, PN is not a complication of its administration, determining better outcomes for patients.[150]

It should be noted that, since lenalidomide is excreted via urinary tract in its unmodified form, adjustment in dosage should be made according to renal function, in order not to increase renal impairment.[151]

Pomalidomide

Pomalidomide is a third generation IMiD approved in 2013 by FDA and subsequently by EMA for the treatment of RRMM. Pomalidomide effects are the same as lenalidomide, but the main difference between second and third generation IMiD is that the latter is excreted in form of inactive metabolite, thus not constituting a threat for kidneys. The main side effects of pomalidomide administration are asthenia, myelotoxicity and DVT.[152]

3.1.5 Proteasome Inhibitors (PI)

Proteasome Inhibitors constitute the second category of the so-called "new drugs" and the most common are bortezomib, carfilzomib, ixazomib. Proteasome is a multi-enzymatic cytoplasmic

[148] Antonio PALUMBO, et al., "Consensus guidelines for the optimal management of adverse events in newly diagnosed, transplant-ineligible patients receiving melphalan and prednisone in combination with thalidomide (MPT) for the treatment of multiple myeloma", *Annals of hematology*, 89, 8, 2010, 803-811.
[149] Hang QUACH, et al., Hang, "Mechanism of action of immunomodulatory drugs (IMiDS) in multiple myeloma", *Leukemia*, 24, 1, 2010, 22-32.
[150] Ana Pilar GONZÁLEZ RODRIGUEZ, "Management of the adverse effects of lenalidomide in multiple myeloma", *Advances in therapy*, 28, 1, 2011, 1-10.
[151] Nianhang CHEN, et al., "Clinical Pharmacokinetics and Pharmacodynamics of Lenalidomide", *Clinical pharmacokinetics*, 56, 2, 2017, 139-152.
[152] Meletios DIMOPOULOS, et al., "Safety and efficacy of pomalidomide plus low-dose dexamethasone in STRATUS (MM-010): a phase 3b study in refractory multiple myeloma", *Blood*, 128, 4, 2016, 497-503.

complex, responsible for degradation of most of damaged or non-functioning intracellular proteins; PIs inhibit proteasome itself, leading to a process of direct apoptosis.[153] Because of the abnormal protein synthesis determined by the presence of neoplastic cells, MM takes great advantage from this drug category, as proteasome is a key element in the regulation of different cellular processes including proliferation, apoptosis, and angiogenesis.[154]

Bortezomib

Bortezomib (Velcade®) is the first-generation proteasome inhibitor, and it was firstly approved in 2003 by EMA for the treatment of RRMM, and only after it was approved also for first-line treatment. In first place, bortezomib was administered intravenously but different studies showed that subcutaneous administration could reduce its toxicity, and now this second procedure represents the standard for administration.[155]

The main action mechanism of bortezomib depends upon its capability to reversibly binds itself to and inhibit the proteasome 20S proteolytic site, leading to protein accumulation and activation of apoptotic mechanisms.[156]

Other secondary action mechanisms of bortezomib include apoptosis stimulation, drug-resistance inhibition and reduction of pro-inflammatory cytokines which play a great role in leading to cast nephropathy.[157] Bortezomib main side effects are PN (present in 40% of the patients), thrombocytopenia (present in 30% of the patients) and myelotoxicity.[158]

Carfilzomib and Ixazomib

Carfilzomib (Kyprolis®) and ixazomib (Ninlaro®) constitute second generation PIs and they have both been approved by FDA and EMA for the treatment of RRMM. Carfilzomib, administered intravenously, is characterized by a more selective and irreversible bond with

[153] David J MCCONKEY, Keyi ZHU, "Mechanisms of proteasome inhibitor action and resistance in cancer", *Drug resistance updates: reviews and commentaries in antimicrobial and anticancer chemotherapy*, 11, 4-5, 2008, 164-179.
[154] Keiji TANAKA, "The proteasome: overview of structure and functions", *Proceedings of the Japan Academy. Series B, Physical and biological sciences*, 85, 1, 2009, 12-36.
[155] Philippe MOREAU, et al., "Subcutaneous versus intravenous administration of bortezomib in patients with relapsed multiple myeloma: a randomised, phase 3, non-inferiority study", *The Lancet. Oncology*, 12, 5, 2011, 431-440.
[156] Kristin BREITSCHOPF, et al., "Ubiquitin-mediated degradation of the proapoptotic active form of bid. A functional consequence on apoptosis induction", *The Journal of biological chemistry*, 275, 28, 2000, 21648-21652.
[157] Wanqiu ZHU, Wenming CHEN, "Bortezomib-based treatment for multiple myeloma patients with renal impairment: A systematic review and meta-analysis of observational studies", *Medicine*, 95, 46, 2016.
[158] Antonia FIELD-SMITH, et al., "Bortezomib (Velcadetrade mark) in the Treatment of Multiple Myeloma", *Therapeutics and clinical risk management*, 2, 3, 2006, 271-279.

proteasome (compared with bortezomib), [159] while ixazomib, administered orally, is characterized by a selective bond which is, contrary to carfilzomib, reversible.

Concerning the side effects of carfilzomib, it leads to arterial hypertension, heart failure and ischemic heart disease. Since its main effects are related to heart diseases, before administration, heart screening and blood pressure monitoring are advised. On the other hand, ixazomib side effects include gastrointestinal diseases (nausea, vomit, and diarrhoea), myelotoxicity and rashes.[160]

3.1.6 Monoclonal Antibody (mAb)

Monoclonal antibodies directed towards neoplastic, medullary microenvironment and immune system cells targets constitute a great shift in the treatment of MM; indeed, because of their limited toxicity, they are becoming more and more popular compared to IMiDs and PIs. Monoclonal antibodies act on the apoptotic process, creating interference in the signalling mechanisms leading to cell death, and inhibiting the production of new cells and adhesion molecules.

Regarding mAb toxicity, AEs are mainly related to the Infusion Related Reactions (IRR) which can be found in 10% of the patients, especially after the first infusion.[161] The main drugs belonging to this category are daratumumab and isatuximab, both targeting the CD38 antibody[162].

Daratumumab

Daratumumab (Darzalex®) is the first mAb discovered to be effective against MM, both in monotherapy and in combination with other drugs. Daratumumab bond with CD38 antibody leads to cell death due to immune mechanisms as Antibody-Dependent Cellular Cytotoxicity (ADCC).[163] Daratumumab was approved for the treatment of RRMM in 2015 by FDA, and in 2016 by EMA. It is administered only after three prior therapy lines or when MM is refractory to other treatments, and it is often used in the treatment of first relapse due to its high level of

[159] Eli MUCHTAR, et al., "A practical review on carfilzomib in multiple myeloma", *European journal of haematology*, 96, 6, 2016, 564-577.
[160] Sara BRINGHEN, et al., "Prevention, monitoring and treatment of cardiovascular adverse events in myeloma patients receiving carfilzomib A consensus paper by the European Myeloma Network and the Italian Society of Arterial Hypertension", *Journal of internal medicine*, 286, 1, 2019, 63-74.
[161] Niels VAN DE DONK, et al., "Clinical efficacy and management of monoclonal antibodies targeting CD38 and SLAMF7 in multiple myeloma", *Blood*, 127, 6, 2016, 681-695.
[162] CD38 is an antibody universally present in MM cells, which is mainly relevant for the adhesion, migration and signaling events and it belongs to the family of glycoproteins.
[163] ADCC is an immune system's process which is used to eliminate neoplastic cells. In this process when a neoplastic cell is recognized, natural killer cells will capture the target cell and inject them with cytotoxic factors which will kill the neoplastic cell.

effectiveness in reducing the risk of progression. In first place, daratumumab was administered intravenously with a 7-hours long infusion which strongly affected patients' quality of life and healthcare resources;[164] however, in the last years a subcutaneous formulation of daratumumab has been developed, reducing the burden for patients and for the health system, shortening the administration process and reducing AEs related to IRR.

Daratumumab toxicity can be considered favourable as the AEs are limited. The most common AEs are related, as mentioned before, to IRR (recorder in 43 to 71% of patients), and they may manifest as nausea, throat irritation and vomiting.[165] In case of IRR, the infusion should be temporarily suspended and restarted once symptoms have been resolved. It is advised to restart the infusion at a lower rate and gradually increase it, until reaching the previous level. More severe side effects are recurrent infections, found in 38% of the patients, which may lead to other pathologies as neutropenia (19% of the patients), anaemia, and thrombocytopenia.[166]

Isatuximab

Isatuximab (Sarclisa®) is a mAb which, as daratumumab, targets the CD38 antibody. Differently from daratumumab, isatuximab leads to direct apoptosis and it has a stronger inhibiting effect on the antibody, [167] mitigating the medullary immunosuppressive microenvironment. Isatuximab action mechanisms include induction of indirect anti-neoplastic activity and restoration of immune function in the bone marrow.[168] Isatuximab can work as a single agent, but it is almost always employed in combination with pomalidomide and dexamethasone for the treatment of RRMM.[169]

Remarkable in isatuximab is its limited toxicity especially when employed as a single agent, which makes it available for patients with other comorbidities or of an older age. As in daratumumab, also in isatuximab, the main side effects are IRR, which may manifest in form of fatigue, nausea and cough and they are present in 20% to 40% of the patients. Concerning most

[164] European Medicines Agency, DARZALEX. Summary of Product Characteristics, in "European Medicine Agency. Science, Medicine, Health", 2023, https://www.ema.europa.eu/en/medicines/human/EPAR/darzalex, (last access March 24, 2023).
[165] Michel DELFORGE, Heinz LUDWIG, "How I manage the toxicities of myeloma drugs", *Blood*, 129, 17, 2017, 2359-2367.
[166] Catarina GERALDES, et al., "Practical Considerations for the Daratumumab Management in Portuguese Routine Clinical Practice: Recommendations From an Expert Panel of Hematologists", *Frontiers in oncology*, 11, 2022.
[167] Thomas G. MARTIN, et al., "Therapeutic Opportunities with Pharmacological Inhibition of CD38 with Isatuximab", *Cells*, 8, 12, 2019.
[168] Xiaoyan FENG, et al., "Targeting CD38 Suppresses Induction and Function of T Regulatory Cells to Mitigate Immunosuppression in Multiple Myeloma", *Clinical cancer research: an official journal of the American Association for Cancer Research*, 23, 15, 2017, 4290-4300.
[169] Michel ATTAL, et al., "Isatuximab plus pomalidomide and low-dose dexamethasone versus pomalidomide and low-dose dexamethasone in patients with relapsed and refractory multiple myeloma (ICARIA-MM): a randomised, multicentre, open-label, phase 3 study", *Lancet,* 394, 10214, 2019, 2096-2107.

severe toxicities, lymphopenia, neutropenia, and thrombocytopenia are the most common, affecting respectively 34%, 12% and 17% of the patients.[170]

3.2 Treatment basic phases

The decision on whether start a treatment in NDMM patients depends on IMWG criteria; indeed, patients will be submitted to therapy as soon as active MM is diagnosed (active MM depends on presence of CRAB or Myeloma Defining Events).

NDMM patients can be submitted to different treatments according to several factors as clinical manifestation, age, performance status, risk status, comorbidities, and drug availability. QOL is another relevant element that should be considered when deciding the right treatment; indeed, since MM patients are mainly subjected to long-term treatments, physicians should try to opt for those whose impact on daily life is limited and that can be better tolerated by patients. Generally, three different kinds of patients can be identified:

1. Young patients (≤ 65 years) without severe comorbidities.
2. Patients whose age is between 65 and 70 years who are considered "fit" (the term "fit" implies that patients have good organ function and that do not show cardiorespiratory pathologies).
3. Patients ≥ 70 years or patients with severe comorbidities.

In the first two cases, patients may be considered for the ASCT, while in the last case, the patient will be treated with conventional chemotherapy together with the "new drugs". Furthermore, in patients that are considered "fit", three-drug combinations, instead of two-drug combinations are advised as they produce better outcomes in a shorter time.

It should be considered that the greatest struggle in the treatment of MM is the insurgence of RRMM, which requires ad hoc therapy based on previous treatments, drug-resistance, and patient's physical condition.

3.2.1 Initial therapy for patients eligible for ASCT

ASCT represents the greatest improvement in the treatment for young MM patients as it substantially increased PFS, extends OS of 12 months and in some patients even achieves Minimal Residual Disease (MRD) negative state.[171]

Currently, high dose melphalan (HDM) chemotherapy followed by ASCT is considered the "gold standard" in the treatment of NDMM patients whose age is between 65 and 70 years

[170] Thomas MARTIN, et al., "Phase I trial of isatuximab monotherapy in the treatment of refractory multiple myeloma", *Blood Cancer Journal,* 9, 41, 2019.
[171] Vincent RAJKUMAR, Shaji KUMAR, "Multiple myeloma current treatment algorithms", *Blood cancer journal*, 10, 94, 2020.

and who do not show relevant comorbidities. Concerning Tandem ASCT, it has been introduced in the 1990s to increase CR and duration of PFS in NDMM patients, but nowadays it is practiced only in limited cases due to its high toxicity; for example, patients who failed to show CR or Partial Response (PR) after first transplant are good candidates for tandem ASCT.[172]

ASCT is forerun by induction regimens which can be constituted by different drugs according to needs and physical conditions of patients. The first induction regimen used in the treatment of MM was VAD, but it has been substituted by the "new drugs" due their better outcomes and reduced toxicity.

Three combinations of drugs have been proved to be particularly effective in the induction therapy: VD (bortezomib-dexamethasone), VCD (bortezomib-cyclophosphamide-dexamethasone) and VTD (bortezomib-thalidomide-dexamethasone). VD combination opened the wat to bortezomib-based combinations in the treatment of MM. VD compared to VAD has been shown to be particularly efficient in terms of response rate and PFS post-ASCT.[173] The addition of cyclophosphamide (alkylating agent) to VD combination has given birth to a three-drug regimen (VCD) which has furtherly increased response rate and CR rates.[174]

The latest development in the induction therapy consists in VTD regimen, characterized by the substitution of cyclophosphamide with the first-generation IMiD, thalidomide. The three-drug combination has shown great results both in terms of PFS and OS, superior to other therapeutical regimens.[175]

Comparing the effectiveness of VCD and VTD induction therapies, VTD has been associated to a greater rate of Very Good Partial Rate (VGPR) and to a higher Objective Response Rate (ORR), with lower hematologic toxicity.[176] VCD and VTD are also recommended for the treatment of patients with cast nephropathy, as major adjustments in dosage are not required and therapy is well tolerated without worsening renal impairment.[177]

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[172] Michel ATTAL, et al., "Single versus double autologous stem-cell transplantation for multiple myeloma", *The New England journal of medicine*, 349, 26, 2003, 2495-2502.
[173] Jean-Luc HAROUSSEAU, et al., "Bortezomib plus dexamethasone as induction treatment prior to autologous stem cell transplantation in patients with newly diagnosed multiple myeloma: results of an IFM phase II study", *Haematologica*, 91, 11, 2006, 1498-1505.
[174] Craig REEDER, et al., "Cyclophosphamide, bortezomib and dexamethasone induction for newly diagnosed multiple myeloma: high response rates in a phase II clinical trial", *Leukemia*, 23, 7, 2009, 1337-1341.
[175] Laura ROSINOL, et al., "Superiority of bortezomib, thalidomide, and dexamethasone (VTD) as induction pretransplantation therapy in multiple myeloma: a randomized phase 3 PETHEMA/GEM study", *Blood*, 120, 8, 2012, 1589-1596.
[176] Michele CAVO, et al., "Bortezomib-thalidomide-dexamethasone (VTD) is superior to bortezomib-cyclophosphamide-dexamethasone (VCD) as induction therapy prior to autologous stem cell transplantation in multiple myeloma", *Leukemia*, 29, 12, 2015, 2429-2431.
[177] Meletios DIMOPOULOS, et al., "Renal impairment in patients with multiple myeloma: a consensus statement on behalf of the International Myeloma Working Group", *Journal of clinical oncology: official journal of the American Society of Clinical Oncology*, 28, 33, 2010, 4976-4984.

Overall, induction therapies based on a three-drug combination in which two elements are bortezomib and IMiD as thalidomide have been shown to be particularly effective, reaching a CR of 33% and a MRD of 29%. The substitution of thalidomide with the second generation IMiD, lenalidomide (VTD), further reduces neurological toxicity, leading to decreased percentages of patients that develop neuropathy during the therapy. The reduced toxicity of lenalidomide also allows the longer administration of VTD, maximizing the outcomes before moving to ASCT. [178]

In the last years, many trials have been evaluating the possibility to add daratumumab to VTD in induction therapy before ASCT, and in consolidation therapy right after ASCT. The phase III trial "Cassiopeia" showed that the combination D-VTD led to an increase in CR and in MRD with minor toxicity,[179] suggesting that D-VTD could become the new standard of care in NDMM patients eligible for ASCT.

3.2.2 Initial therapy for patients not eligible for ASCT

As underlined in the ASCT section, not all the patients are eligible for ASCT, mainly because of age, performance status and comorbidities. However, nowadays, many different options are available for those patients and to decide which is the best approach, it is necessary to divide patients in different groups. To do so, the frailty score, based on the integration of the Activities of Daily Living scale (ADL), the Instrumental Activities of Daily Living scale (IADL) and the Charlson Comorbidity Index (CCI), is used to assess number and severity of comorbidities with particular attention to cardiocirculatory, respiratory, hepatic, and renal function.

Thanks to frailty scores, patients can be divided into fit patients, intermediate-fit patients, and unfit-frail patients. For the first class of patients, full-dose IMiDs or PIs, associated with corticosteroids or alkylating agents can be used; while for the last two classes of patients, reduced dosage therapies are preferred, and the recourse the palliative therapies is advised when the patient is no longer responsive to the treatment.[180]

In first place, the basic treatment for patients who were not eligible for the ASCT was the two-drug combination melphalan-prednisone (MP), which determined a 50% response rate but no improvement in OS and CR lower than 5%. Significant improvements in the treatment of non-eligible ASCT patients have been determined by the introduction of the "new drugs"

[178] Laura ROSIGNOL, et al., "Bortezomib, lenalidomide, and dexamethasone as induction therapy prior to autologous transplant in multiple myeloma", *Blood*, 134, 16, 2019, 1337-1345.
[179] Murielle ROUSSEL, et al., "Bortezomib, thalidomide, and dexamethasone with or without daratumumab for transplantation-eligible patients with newly diagnosed multiple myeloma (CASSIOPEIA): health-related quality of life outcomes of a randomised, open-label, phase 3 trial", *The Lancet. Haematology*, 7, 12, 2020, e874-e883.
[180] Antonio PALUMBO, et al., "Geriatric assessment predicts survival and toxicities in elderly myeloma patients: an International Myeloma Working Group report", *Blood*, 125, 13, 2015, 2068-2074.

which led to a significant increase in response rate, PFS and OS. The first regimens that have been experimented included three-drug combinations as melphalan-prednisone-thalidomide (MPT) and melphalan-prednisone-bortezomib (MPV), which showed significant improvements concerning ORR, PFS and OS compared to MP.[181] MPT is not used anymore because it has been replaced with lenalidomide-dexamethasone (RD) regimen, which is proven to lead to higher ORR (22%), PFS (25,5 months) and OS (60 months) and which is now the standard of care for patients not eligible for ASCT. If possible, considering financial means and drug availability, RD should be administered until disease progression without any interruption.[182]

Concerning MPV regimen, the employment of bortezomib instead of thalidomide is shown to drive to ORR of 71% and CR of 30%; furthermore, a follow-up of 60 months highlighted an improvement of 23% in OS (also in patients of more than 75 years).[183] Nowadays, the MPV treatment is, together with the RD regimen, the standard of care in first line treatment for non-eligible ASCT patients.

Great hopes rely in the bortezomib-lenalidomide-dexamethasone (VRD) combination which could eventually become the new standard of care. VRD showed great results in trials for the treatment of NDMM patients not eligible for the ASCT; indeed, even if the treatment has not yet been approved by EMA, several stage II trials showed its effectiveness and high tolerability. Precisely because of its high tolerability and limited toxicity, VRD can potentially be used without any time limits.[184] The main drawback in the VRD treatment lies in its high cost; indeed, as the treatment should be administered as long as the disease proceeds, it will result in a very expensive and burdening therapy.

Lastly, noteworthy is the relevance of mAbs in first-line therapy; for instance, daratumumab associated to RD treatment showed a greater rate of response together with a higher PFS.[185]

Overall, many different options are available for patients who are not eligible for ASCT and continuous research is carried out to improve the pharmacological treatments. Indeed, more

[181] Peter FAYERS, et al., "Thalidomide for previously untreated elderly patients with multiple myeloma: meta-analysis of 1685 individual patient data from 6 randomized clinical trials", *Blood*, 118, 5, 2011, 1239-1247.
[182] Lofti BENBOUBKER, et al., "Lenalidomide and dexamethasone in transplant-ineligible patients with myeloma", *The New England journal of medicine*, 371, 10, 2014, 906-917.
[183] Jesús SAN MIGUEL, et al., "Persistent overall survival benefit and no increased risk of second malignancies with bortezomib-melphalan-prednisone versus melphalan-prednisone in patients with previously untreated multiple myeloma", *Journal of clinical oncology: official journal of the American Society of Clinical Oncology*, 31, 4, 2013, 448-455.
[184] Elizabeth K. O'DONNEL, et al., "A phase 2 study of modified lenalidomide, bortezomib and dexamethasone in transplant-ineligible multiple myeloma", *British journal of haematology*, 182, 2, 2018, 222-230.
[185] Thierry FACON, et al., "Daratumumab plus Lenalidomide and Dexamethasone for Untreated Myeloma", *The New England journal of medicine*, 380, 22, 2019, 2104-2115.

and more physicians are trying to substitute ASCT with pharmacological treatments to reduce the burden and the negative implications over patients' quality of life.

3.2.3 Maintenance Therapy

Maintenance therapy consists in a long-term treatment (1-2 years) whose main goal is to preserve results obtained with previous treatments, prolonging PFS and OS.

In first place, chemotherapeutic drugs as interferon (IFN) and glucocorticoids were used in the maintenance therapy but their low effectiveness, together with high toxicity in the long run, opened the road to the "new drugs". Thalidomide has been widely used in the maintenance therapy after ASCT, both as a single agent or in combination with prednisone, showing great results in PFS, but with no increase in OS.[186] The lack of response in terms of OS can be attributed to the high toxicity of thalidomide in the long run, which can results in polyneuropathy and thromboembolic events; indeed, the severity of these comorbidities could lead to discontinuous administration or even to treatment interruption.[187]

As for induction therapy, also in maintenance therapy, thalidomide has been substituted by the second generation IMiD, lenalidomide, which constitutes the standard of care for the maintenance therapy, as established by FDA and EMA. The employment of lenalidomide instead of thalidomide, increases PFS, Event Free Survival (EFS) and OS; however, the treatment also increases the risk of developing Secondary Primary Malignancies (SPM).[188]

Concerning the use of PIs in maintenance therapy, the recourse to Bortezomib-based treatments have shown greater results in terms of PFS, CR and OS, compared to thalidomide- and lenalidomide-based treatments.[189] The more relevant drawbacks in the use of bortezomib-based treatments lie in its compulsory parenteral administration and in the frequent onset of polyneuropathy, which significantly affects patients' quality of life, and which may lead to the interruption of the treatment. Nevertheless, several studies showed that bortezomib

[186] Andrew SPENCE, et al., "Consolidation therapy with low-dose thalidomide and prednisolone prolongs the survival of multiple myeloma patients undergoing a single autologous stem-cell transplantation procedure", *Journal of clinical oncology: official journal of the American Society of Clinical Oncology*, 27, 11, 2009, 1788-1793.

[187] Yuki KAGOYA, et al., "Thalidomide maintenance therapy for patients with multiple myeloma: meta-analysis", *Leukemia research*, 36, 8, 2012, 1016-1021.

[188] Philip MCCARTHY, et al., "Lenalidomide Maintenance After Autologous Stem-Cell Transplantation in Newly Diagnosed Multiple Myeloma: A Meta-Analysis", *Journal of clinical oncology: official journal of the American Society of Clinical Oncology*, 35, 29, 2017, 3279-3289.

[189] Pieter SONNEVELD, et al., "Bortezomib induction and maintenance treatment in patients with newly diagnosed multiple myeloma: results of the randomized phase III HOVON-65/ GMMG-HD4 trial", *Journal of clinical oncology: official journal of the American Society of Clinical Oncology*, 30, 24, 2012, 2946-2955.

neurotoxicity can be partially diminished by reducing its administration from twice a week to once a week.[190]

Overall, considering the different possibilities available for maintenance therapy, the best option considering PFS, OS and toxicity is lenalidomide-based treatment, the only maintenance therapy now approved by FDA and EMA.

3.2.4 Treatment of relapsed/refractory MM

Despite the introduction of the "new drugs", the natural progress of MM is characterized by the inevitable upswing of the disease till reaching the "relapsed/refractory" phase in which the disease develops drug resistance. Furthermore, after each treatment cycle, the remission duration decreases, leading closer and closer relapses.

The choice of treatment for RRMM depends upon a variety of aspects as general characteristics of the patient (age, performance status, comorbidities), previous treatments and disease stage at the moment of the relapse. Generally speaking, physicians recommend the employment of IMiD- or PI-based therapeutical regimens, resorting to those drugs that have not been previously used in first-line treatment. The two main drugs used in the treatment of RRMM are bortezomib and lenalidomide, but several other therapies as daratumumab-, carfilzomib- and ixazomib-based treatments are available.

Bortezomib was the first of the "new drugs" approved by FDA and EMA for the treatment of RRMM. Bortezomib can be used as a single agent, but it is preferred in combination with dexamethasone (VD) for its greater response rate and OS, associated with a low toxicity.[191] In the last years, new trials tested the effectives of VD associated with other drugs as doxorubicin, which showed a greater effectiveness but also a higher toxicity.[192]

Lenalidomide, second generation IMiD, is also often deployed in the treatment of RRMM in combination with dexamethasone (RD). The two-drug combination has been approved by FDA and EMA in 2006 and it showed great response rate (60%) and OS (38 months).[193] RD represents the backbone of RRMM treatment, and on this base, it is possible to compose more elaborate treatments by adding second-generation PIs or mAbs. Furthermore, in

[190] María-Victoria MATEOS, et al., "Bortezomib, melphalan, and prednisone versus bortezomib, thalidomide, and prednisone as induction therapy followed by maintenance treatment with bortezomib and thalidomide versus bortezomib and prednisone in elderly patients with untreated multiple myeloma: a randomised trial", *The Lancet. Oncology*, 11, 10, 2010, 934-941.
[191] Paul RICHARDSON, et al., "Bortezomib or high-dose dexamethasone for relapsed multiple myeloma", *The New England journal of medicine*, 352, 24, 2005, 2487-2498.
[192] Antonio PALUMBO, et al., "Bortezomib, doxorubicin and dexamethasone in advanced multiple myeloma", *Annals of oncology: official journal of the European Society for Medical Oncology*, 19, 6, 2008, 1160-1165.
[193] Meletios DIMOPOULOS, et al., "Lenalidomide plus dexamethasone for relapsed or refractory multiple myeloma", *The New England journal of medicine*, 357, 21, 2007, 2123-2132.

case in which patients' age is below 65 and performance status is "fit", it is also possible to opt for salvage ASCT. This option is not frequently used, and it is available only for those patients who did not resort to ASCT before, or for those who successfully responded to ASCT as a first-line treatment (remission duration >18 months) and were not subjected to tandem ASCT.

It should be considered that physicians are now trying to build up a "systemic approach" which consists in global therapeutical approaches that take into consideration all the different treatment options during the entire progress of the disease, moving away from the step-by-step approach.[194]

3.3 Pain management

Since MM is still incurable what is more relevant in the last stages of the disease is to relieve patients' pain, improving quality of life. MM patients are often affected by chronic pain, derived mainly from bone lesions, present in up to 70% of MM population.[195] Furthermore, even if the percentage of patients who survive to MM is increasing thanks to new treatments, it should be considered that many of them suffer from "cancer survivor" syndrome, which is characterized by fatigue, depression, insomnia, chronic pain, and overall worsened quality of life.[196]

In the following paragraphs, the three main pain management options are described; noteworthy is that pain management and supportive care are mainly directed to relieve patients from bone pain, which is proven to be the most crippling clinical manifestation in MM.
This paragraph will not take into consideration treatments that are meant to solve severe clinical manifestations derived by MM treating agents, as peripheral neuropathy, hypertension, or other cardiac issues.

3.3.1 Antiresorptive Therapy

European Society for Medical Oncology (ESMO) recommends the use of antiresorptive treatments in MM patients who show severe bone pain. Bone disease, as seen in chapter 1 and 2, is a common feature in MM and can manifest itself through bone pain (80%), fractures (60%) and spinal cord compression (3%).[197] Bisphosphonates and the recently approved denosumab constitute the two main antiresorptive treatments; according to IMGW recommendations, they should be administered for a maximum of two years, eventually restarting the therapy if necessary. Bisphosphonates and denosumab lead to the same positive effects, but they differ in

[194] Chor CHIM, et al., "Management of relapsed and refractory multiple myeloma: novel agents, antibodies, immunotherapies and beyond", *Leukemia*, 32, 2, 2018, 252-262.
[195] Russell K. PORTENOY, "Treatment of cancer pain", *Lancet,* 377, 2011, 2236-2247.
[196] Charles SHAPIRO, "Cancer Survivorship", *The New England journal of medicine*, 379, 25, 2018, 2438-2450.
[197] Abdul HAMEED, et al., "Bone disease in multiple myeloma: pathophysiology and management", *Cancer growth and metastasis*, 7, 2014, 33-42.

toxicity levels; indeed, denosumab shows a lower toxicity, provoking limited AEs. The main difference existing between the two therapies consists in the fact that while denosumab inhibits osteoclast precursors, bisphosphonates inhibit mature osteoclasts.[198]

Bisphosphonates

Bisphosphonates (BPs) represent the backbone of MM pain management, and their action mechanisms include inhibition of bone resorption, elimination of bone-derived grow factors and apoptotic effect on osteoclasts. Secondary pharmacological effects of BPs include anti-angiogenic influence and inhibition of the osteoclastic activity.[199]

BPs proved to be effective in the reduction of pathological vertebral fractures, bone pain and Skeletal Related Events (SRE),[200] and they are characterized by a limited toxicity. Acute reaction to treatment has been reported only in first intravenous infusions (20-30%) and there is no significant evidence that it occurred also in subsequent infusions. Musculoskeletal syndrome is a common side effect of BPs, and it is characterized by intense muscular pain.[201] The most severe AEs of BPs are renal impairment and osteonecrosis of the jaw (ONJ) which are related to treatment dosage and duration. Concerning the risk of renal impairment, if patients incur in kidney issues during the treatment, it will be sufficient to stop BPs administration and restart it at a lower dose when the renal function returns. For patients whose renal function is already compromised BPs treatment should not be considered, and they should be advised for denosumab treatment, which showed limited effects on renal function.

With regard to ONJ, patients with MM exhibit the highest incidence of ONJ and this is related to the administration of zoledronic acid, the most common BPs. In 60% of the cases, jaw lesions heal in a year after stopping the administration of zoledronic acid, while they can be worsened by tooth extraction and jaw surgery.[202] It is advisable that, before starting BPs, patients carry out a complete dental evaluation to solve all the potential issue before the beginning of the therapy.

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[198] Daniel A. GOLDSTEIN, "Denosumab for bone lesions in multiple myeloma - what is its value?", *Haematologica*, 103, 5, 2018, 753-754.
[199] Rahul MHASKAR, et al., "Bisphosphonates in multiple myeloma: an updated network meta-analysis", *The Cochrane database of systematic reviews*, 12, 12, 2017, 108-112.
[200] *Ibidem*
[201] Seth M. ARUM, "New developments surrounding the safety of bisphosphonates", *Current opinion in endocrinology, diabetes, and obesity*, 15, 6, 2008, 508-513.
[202] Ashraf BADROS, et al., "Osteonecrosis of the jaw in multiple myeloma patients: clinical features and risk factors", *Journal of clinical oncology: official journal of the American Society of Clinical Oncology*, 24, 6, 2006, 945-952.

Denosumab

Denosumab is a fully human mAb, approved by FDA in 2018 for the treatment of MM, especially in the prevention of SREs. Denosumab is administered monthly subcutaneously, and no dosage adjustment is required for specific pathologies. Its main action mechanism consists in targeting RANKL, a stimulator produced by MM cells,[203] which is crucial in survival and proliferation of osteoclast. By doing so, denosumab leads to inhibition of neoplastic cell activation and of resorptive activities while increasing neoplastic cells apoptosis. The administration of denosumab reduces reduce bone pain, leading to a significant improvement in patient's quality of life.[204]

Denosumab represents the main alternative to BPs in the antiresorptive therapy, especially for those patients who show renal impairment, since it is better tolerated by the organism. However, concerning OS and frequency of SRE, no significant differences has been found between the two treatments, as both lead to a decrease in the number of SRE, with no relevant improvement in OS.

Concerning the side effects of denosumab, neutropenia is the most common adverse clinical manifestation (15% of the patients), while pneumonia is the most severe one, but its appearance is limited (8% of the patients).[205]

3.3.2 Vertebroplasty

Vertebroplasty is a surgical procedure in which polymethylmethacrylate (PMMA) (bone cement) is injected into the broken vertebral bone to relieve pain, increase mobility, and improve performance status.[206] It is advised to patients that show vertebral compression fractures (VCFs) but that are not affected by spinal cord compression. Indeed, early vertebroplasty in patients with VCFs can help avoiding the risk of a "domino effect" in which the VCFs cause extreme stress in posterior muscles, leading to a stronger pain.[207] Vertebroplasty can be distinguished in "early" and "delayed"; the former is advised when acute VCFs and severe pain are experienced, while the latter should be performed after bisphosphonates therapy, if pain burden is not

[203] Orhan SEZER et al., "RANK ligand and osteoprotegerin in myeloma bone disease",*Blood*, 101, 6, 2003, 2094-2098.
[204] Saroj VADHAN-RAJ, et al., "Clinical benefit in patients with metastatic bone disease: results of a phase 3 study of denosumab versus zoledronic acid", *Annals of oncology: official journal of the European Society for Medical Oncology*, 23, 12, 2012, 3045-3051.
[205] Noopur RAJE, et al., "Denosumab versus zoledronic acid in bone disease treatment of newly diagnosed multiple myeloma: an international, double-blind, double-dummy, randomised, controlled, phase 3 study", *The Lancet. Oncology*, 19, 3, 2018, 370-381.
[206] Paula GARLAND, et al., "Percutaneous vertebroplasty to treat painful myelomatous vertebral deposits-long-term efficacy outcomes", *Annals of hematology*, 90, 1, 2011, 95-100.
[207] Mohamed A. HUSSEIN, et al., "The role of vertebral augmentation in multiple myeloma: International Myeloma Working Group Consensus Statement", *Leukemia*, 22, 8, 2008, 1479-1484.

unbearable and if VFCs are not in the acute stage. It may be necessary to perform multiple procedures if bone damage is extensive and in doing so the optimum solution is to act on three or four vertebrae each time, to reduce the post-surgical pain.[208] After the surgery, a physical rehabilitation program is recommended to maximize the effects of the procedure as well as shortening the recovery process.

The most common complications of vertebroplasty are radiculopathy[209] and root compression, but their incidence is limited to 1-2% of treated patients.[210] Extravasation of cement in the vertebral foramina, occurs in a high rate of patients (38 to 72,5%), but it does cause nerve root compression or paraplegia only in 2% of the reported cases, thus constituting a non-significant risk.[211] The positive outcomes of this surgical treatment are related to two principal factors: in first place, PMMA has a cytotoxic effect which leads to apoptosis in the neoplastic cells; secondly, the heat derived from the polymerization of PMMA partially destroys nerve roots, limiting the pain coming from radiculopathy.[212]

3.3.3 Analgesics

Analgesics constitute the most obvious way to control pain in patients affected by chronical conditions as they can significantly improve quality of life by reducing pain perception. However, even if it is advisable to start analgesics administration as soon as active MM is diagnosed, careful pain assessment should be carried out before starting any treatment. Pain assessment includes two main examinations: physical examinations meant to localize pain source, to verify presence of comorbidities and to detect possible allergies, and psychological evaluation meant to estimate pain impact on sleep, daily activities, mood, and quality of life and to assess the presence of possible psychological issues that may require pharmacological treatment.[213] Pain assessment should also clarify whether pain is nociceptive or neuropathic; the former is caused by continuous tissue damage and it includes bone pain, while the latter is caused by damages in the nervous system and it comprehends spinal cord compression.[214] Usually,

[208] Mohamed A. HUSSEIN, et al., "The role of vertebral augmentation in multiple myeloma: International Myeloma Working Group Consensus Statement", *Leukemia*, 22, 8, 2008, 1479-1484.
[209] Radiculopathy is the injury or the irritation of the spinal cord nerve root, which is often caused by the compression of the nerve and can lead to sever pain, muscle weakness and occasional numbness.
[210] Flaminia COLUZZI, et al., "Pain Management in Patients with Multiple Myeloma: An Update", *Cancers*, 11, 2019.
[211] Jean-Denis LAREDO, Bassam HAMZE, "Complications of percutaneous vertebroplasty and their prevention", *Seminars in ultrasound, CT, and MR*, 26, 2, 2005, 65-80.
[212] Lin-Huei CHEN, et al., "Percutaneous vertebroplasty for pathological vertebral compression fractures secondary to multiple myeloma", *Archives of orthopaedic and trauma surgery*, 132, 6, 2012, 759-764.
[213] Michael BENNETT, et al., "Standards for the management of cancer-related pain across Europe-A position paper from the EFIC Task Force on Cancer Pain", *European journal of pain,* 23, 4, 2019, 660-668.
[214] Virginia SUN, et al., "Barriers to pain assessment and management in cancer survivorship", *Journal of cancer survivorship: research and practice*, 2,1, 2008. 65-71.

nociceptive pain, compared to neuropathic pain, requires a shorter and less complicated treatment to reach steady pain control.

Since one of the most common clinical manifestations in MM is renal impairment, administration of non-steroid anti-inflammatory drugs (NSAIDs) is not recommended due to its potential nephrotoxicity.[215] Mild pain, however, may not require the recourse to opioids and in this case the best option for the patients is paracetamol (Tachipirina®), which provides adequate analgesic effect.

In case of moderate or severe pain, the administration of opioids constitutes the backbone of MM management of pain. Opioids, when possible, are administered orally but subcutaneous administration may be required when patients are affected by severe and acute pain. Since opioids are the strongest analgesics available and because of related risk of developing addictions, the choice of opioids treatment should be carefully evaluated by physicians, oncologists, and phycologists.

The most common opioids in the treatment of MM are buprenorphine (Suboxone®) and fentanyl (Effentora®) as they do not require dosage adaptation and they are available also for patients with severe kidney-failure.

Alternatively, codeine (Paracodina®) and morphine (Oramorph®) are also available, but they are not advisable in those patients with limited renal function, as they could accumulate into the organism worsening renal impairment. It should be noted that morphine is the strongest opioid available, especially in its oral form, thus it may be considered the as best choice to relieve patients from acute pain, but it could determine adverse consequences on kidney functioning. Oxycodone (Targin®) and hydromorphone (Jurnista®) are available for all the MM patients, regardless of renal functioning, but they require dosage adaptation due to their significant toxicity.

Generally speaking, opioids are characterized by limited toxicity and the most common side effects are nausea, bowel dysfunction, drowsiness and hallucinations; however, since they are often administered for long periods of time, correct and prompt management of AEs is necessary to grant patients with the highest possible living standards.[216]

It should be noted that in many in MM patients, opioids therapies are supported by additional medications, since the opioid analgesic effect is not sufficient to relieve the neuropathic pain.[217] Indeed, opioids' clinical efficiency will diminish with time, leading the

[215] Marie FALLON, et al., "Management of cancer pain in adult patients: ESMO Clinical Practice Guidelines", *Annals of oncology: official journal of the European Society for Medical Oncology*, 29, 4, 2018, 166-191.
[216] Ramsin BENYAMIN et al., "Opioid complications and side effects", *Pain physician*, 11, 2, 2008, 105-120.
[217] Efklidis RAPTIS, et al., "Pregabalin vs. opioids for the treatment of neuropathic cancer pain: a prospective, head-to-head, randomized, open-label study", *Pain practice: the official journal of World Institute of Pain*, 14, 1, 2014, 32-42.

patients to increase the dosage, implement other complementary drugs or switch to another class of opioids, to increase response rate.[218]

[218] Sebastiano MERCADANTE, "Opioid rotation for cancer pain: rationale and clinical aspects", *Cancer*, 86, 9, 1999, 1856-1866.

CHAPTER 4

Multiple Myeloma: new drugs and future directions

As we saw in the previous chapter, several improvements have been made in the treatment of MM, leading to a significant increase in the OS. However, MM is still an incurable disease in which there is no proof of "completely recovered" patients; current drugs are meant to reduce pain and proliferation of the neoplastic cells but there is no drug that is proven to lead to complete disappearance of the disease. For this reason, several new trials have been started and new therapeutic agents are continuously under consideration; furthermore, new combination of existing drugs, who showed not to be effective as single agents, are the object of many ongoing trials. In this chapter, the three most promising agents will be analysed, and notions related to their mechanisms of action, clinical development and tolerability will be presented.

4.1 Histone Deacetylase Inhibitors

Histone Deacetylase (HDAC) Inhibitors constitute a class of chemotherapeutical agents whose main action is reducing the neoplastic cell proliferation by inhibiting the HDAC and promoting neoplastic cells apoptosis.[219] HDAC are proteins which constitute the main component of the chromatin, and they are responsible for the regulation of protein degradation and DNA transcription, which takes place through the process of histone acetylation.[220]

Histone acetylation is one of the main epigenetic mechanisms of gene expression regulation: the acetylation of the histone leads to the opening of chromatin which allows the access of the enzymes necessary to DNA duplication and transcription. On the other hand, the deacetylation of the histone prevents the access of enzymes to chromatin, preventing the duplication of DNA and leading to gene silencing.[221]

In MM, an aberrant expression of HDAC linked to great proliferation of neoplastic cells is present, determining shorter PFS and limited OS. Precisely because of the great proliferation of HDAC, many therapies are focusing on the employment of HDAC inhibitors as they showed to be a promising option, especially in combination with other chemotherapeutical agents and "new drugs". The most promising HDAC inhibitor is panobinostat (Farydak®), a non-selective inhibitor of different deacetylases, which has recently been approved by FDA and EMA in three-

[219] Dharshan SIVARAJ, et al., "Panobinostat for the management of multiple myeloma", *Future oncology,* 13, 6, 2017, 477-488.
[220] Paul G. RICHARDSON, et al., "Panobinostat: a novel pan-deacetylase inhibitor for the treatment of relapsed or relapsed and refractory multiple myeloma", *Expert review of anticancer therapy*, 15, 7, 2015, 737-748.
[221] Philip D. GREGORY, et al, "Histone acetylation and chromatin remodeling", *Experimental cell research*, 265, 2, 2001, 195-202.

drugs combination for the treatment of RRMM.[222] Panobinostat as a maintenance therapy is still under evaluation and it has not yet achieved the approval of FDA.

4.1.1. Mechanisms of action

As above mentioned, panobinostat is a non-selective inhibitor of different deacetylases, and it constitutes a unique and innovative approach in the inhibition of proliferation and survival of neoplastic cells. Panobinostat is administered orally, and it is characterized by quick absorption and metabolization. Panobinostat acts on the HDAC leading to inhibition of DNA replication, gene transcription and protein degradation, showing an overall reduction of cells proliferation and an increased cytotoxicity. It is interesting that the cytotoxic effect of panobinostat is affecting only neoplastic cells while normal cells seem to be immune, thus reducing the insurgence of adverse events.[223]

When used in combination with bortezomib, panobinostat shows a peculiar action mechanism: the action of bortezomib leads to the accumulation of protein within the cell, which ends up in an aggresome formation. The presence of this aggresome stimulates cells' degradation induced by deacetylation process.[224] However, the presence of panobinostat inhibits the deacetylation process, blocking the breakdown of proteins. The result of this complex mechanism is cell apoptosis; indeed, the excessive presence of proteins produces signals that induce the cells to start apoptosis.[225]

4.1.2 Clinical development

Panobinostat development is mainly based on five major trials from phase I to phase III. The first trials investigated the role of panobinostat as a single agent, but they did not produce any significant result since the outcomes were poor and the level of toxicity high.[226] PANORAMA is the main trial in the research of panobinostat for RRMM treatment and it includes a phase II and phase III clinical trial which tested the effects of panobinostat in combination with bortezomib and dexamethasone. The main difference existing between the two trials is that PANORAMA 2 is a single-arm phase II study, while PANORAMA 1 is a double-blinded phase

[222] Jacob P. LAUBACH, et al., "Panobinostat for the Treatment of Multiple Myeloma", *Clinical cancer research: an official journal of the American Association for Cancer Research*, 21, 21, 2015, 4767-4773.
[223] Wenlin SHAO, et al., "Potential anticancer activity of the pan-deacetylase inhibitor panobinostat (LBH589) as a single agent in multiple myeloma", *Blood*, 126, 23, 2015, 3026.
[224] Peter, ATADJA, "Development of the pan-DAC inhibitor panobinostat (LBH589): successes and challenges", *Cancer letters*, 280, 2, 2009, 233-241.
[225] Teru HIDESHIMA, et al., "Mechanism of action of proteasome inhibitors and deacetylase inhibitors and the biological basis of synergy in multiple myeloma", *Molecular cancer therapeutics*, 10, 11, 2011, 2034-2042.
[226] Daniel DEANGELO, et al., "Phase Ia/II, two-arm, open-label, dose-escalation study of oral panobinostat administered via two dosing schedules in patients with advanced hematologic malignancies", *Leukemia*, 27, 8, 2013, 1628-1636.

III trial. These two studies have been crucial in the approval of the three-drug combination; indeed, if panobinostat as a single agent has not been approved yet for the treatment of MM, the three-drug combination has shown to be effective.

The research on panobinostat as a single agent or in combination with other agents is still ongoing and future results are expected to further improve the treatment of RRMM. In the following paragraphs the two phases of the PANORAMA trial will be presented, taking as a base the two official reports approved by Novartis International AG (sponsor of the trial) and published by "Blood" and "The Lancet. Oncology" respectively in 2013 and 2014.

4.1.2.1 Phase II trial: PANORAMA 2

PANORAMA 2 is a "phase 2, two-stage, single-arm, open-label, multicenter study of oral panobinostat in combination with bortezomib and dexamethasone".[227] The main objectives of the study were to assess the ORR, the Minimal Response (MR), the Duration of the Response (DoR), the PFS and the OS; great attention was also paid to tolerability and safety of the three-drug combination. The trial started in 2010 and concluded in 2017, with last update published on December 21, 2017. The patients' sample consisted of ≥ 18 years old patients with RRMM, refractory to bortezomib, who received at least two prior treatments that included an IMiD.

The trial consisted of two phases: the former consisted of 8 three-weeks cycles of oral panobinostat, intravenous bortezomib and oral dexamethasone, while the latter included six-week cycles of panobinostat and reduced doses of bortezomib and dexamethasone. Patients were allowed to take part in the second phase of the trial only if they showed positive outcomes at the end of the first phase; the second phase treatment was administered until death, withdrawal of consent, toxicity, or disease progression.

At the end of the trial, results showed that DoR was 6 months, PFS was 5.4 months and median OS was 8.3 months; the overall response rate (34.5%) showed that the three-drug combination is effective in the treatment of RRMM with minor and manageable toxicities, which did not lead to the discontinuation or the suspension of the treatment. The most common Adverse Events (AEs) included diarrhoea (70.9%), fatigue (69.1%), thrombocytopenia (65.5%), nausea (60.0%) and anaemia (47.3%).[228] Most of these AEs were managed with dose reduction or temporary interruption of the treatment but none of them led to the complete suspension. The most severe AE is peripheral neuropathy which manifested in 67.3% of the patients, mainly as a result of the administration of bortezomib.

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[227] Paul RICHARDSON, et al., "PANORAMA 2: panobinostat in combination with bortezomib and dexamethasone in patients with relapsed and bortezomib-refractory myeloma", *Blood*, 122, 14, 2013, 2331-2337.
[228] *Ibidem*

Overall, PANORAMA 2 trial obtained response in 34.5% of the patients, showing the potentially effective role of panobinostat-bortezomib-dexamethasone combination in the treatment of RRMM.[229]

4.1.2.2 Phase III trial: PANORAMA 1

PANORAMA 1 is a "multicentre, randomized, placebo-controlled, double-blind phase 3 trial",[230] whose main endpoints were the assessment of PFS, OR and safety of administration of panobinostat, bortezomib and dexamethasone. The trial started in 2009 and concluded in 2020, with the last update published on March 17, 2020.

Patients' sample included ≥ 18 years old patients with RRMM who have been subjected to 1-3 previous treatments and who were not refractory to bortezomib. 768 patients were enrolled in the trial, and they were randomly divided into two arms: 387 people were assigned to the panobinostat arm, while 381 patients were assigned to the placebo arm. All the patients were administered with dexamethasone and bortezomib but only half of them received the panobinostat.

The study consisted of two phases: the former included 8 three-week cycles in which patients were administered with oral panobinostat, oral dexamethasone and intravenous bortezomib, the latter included 4 six-week cycles in which the dosage of dexamethasone and bortezomib was reduced. The trial mechanism is similar to the one of PANORAMA 2, but the main difference is that half of the sample was administered with placebo instead of panobinostat. Patients were admitted to the second phase of the trial only if they obtained positive outcomes at the end of the first phase; patients that during the trial showed intolerance to panobinostat, placebo or bortezomib were forced to leave the trial, while those who showed intolerance to dexamethasone could continue the trial with a two-drug combination.

Trial results showed that PFS, OS and median response were longer in the panobinostat arm than in the placebo one; however, the rate of AEs insurgence was also higher in the panobinostat arm, indeed 96% of panobinostat patients showed some kind of AEs compared to the 82% in the placebo group. Noteworthy is that the median duration of the treatment was shorter in the panobinostat arm due to the insurgence of AEs and disease progression. The most common moderate AEs were diarrhoea, fatigue, and asthenia while severe AEs included peripheral neuropathy, thrombocytopenia and pneumonia and manifested in 60% of the patients

[229] Paul RICHARDSON, et al., "New drugs for myeloma", *The oncologist*, 12, 6, 2007, 664-689.
[230] Jesús F. SAN-MIGUEL, et al., "Panobinostat plus bortezomib and dexamethasone versus placebo plus bortezomib and dexamethasone in patients with relapsed or relapsed and refractory multiple myeloma: a multicentre, randomised, double-blind phase 3 trial", *The Lancet. Oncology*, 15, 11, 2014, 1995-1206.

in the panobinostat arm. Overall, 8% of the patients in the panobinostat arm died during the treatment and 36% were forced to leave the trial because of extremely severe AEs.

Considering the above-mentioned results, panobinostat led to a significant extension in the PFS but no difference was observed in the OS. Concerning the safety of the therapy, higher toxicity was observed in the panobinostat treatment mainly determined by the overlapping of the side effects of panobinostat and bortezomib; it should be noted that the toxicity of the therapy could be improved by reducing the dose of bortezomib and limiting the administration to once per week.[231]

4.1.3 Tolerability

Panobinostat as a single agent and in combination with dexamethasone and bortezomib is generally considered as safe and highly tolerable by patients; indeed, even if patients aged >75 years and patients with hepatic impairment are advised to start the treatment with reduced dosage, panobinostat administration is not limited by age, gender, or race.[232] It should be noted that even though the toxicity profile of panobinostat is generally positive, mechanisms for coping with AEs and alleviating their effects should be developed and considered carefully.

Panobinostat AEs include mainly gastrointestinal, haematological, and cardiac toxicities, but peripheral neuropathy (18%) and pneumonia (13%) can also occur, especially when panobinostat is not administered as a single agent.[233] The most common gastrointestinal AEs are diarrhoea (25%), vomiting and fatigue (24%).[234] Even with the reduction of the dosage, fatigue and diarrhoea represent the AEs which mostly result in therapy discontinuation (25%) and they should be managed with antiemetics, proper hydration, and antidiarrheal medications.

Concerning haematological side effects, the most frequent are thrombocytopenia (67%), lymphopenia (54%) and neutropenia (35%); in most of the cases these AEs can be alleviated by discontinuous administration of panobinostat.[235]

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[231] Sara BRINGHEN, et al., "Efficacy and safety of once-weekly bortezomib in multiple myeloma patients", *Blood*, 116, 23, 2010, 4745-4753.

[232] Novartis Europharm Limited, *Farydak hard capsules: EU summary of product characteristics*, 2015, https://www.ema.europa.eu/en/medicines/human/EPAR/farydak, (accessed on 3 April 2023).

[233] Sarah L. GREIG, "Panobinostat: A Review in Relapsed or Refractory Multiple Myeloma", *Targeted oncology*, 11, 1, 2016, 107-114.

[234] Jesús F. SAN-MIGUEL, et al., "Phase Ib study of panobinostat and bortezomib in relapsed or relapsed and refractory multiple myeloma", *Journal of clinical oncology: official journal of the American Society of Clinical Oncology*, 31, 29, 2013, 3696-3703.

[235] Jesús F. SAN-MIGUEL, et al., "Panobinostat plus bortezomib and dexamethasone versus placebo plus bortezomib and dexamethasone in patients with relapsed or relapsed and refractory multiple myeloma: a multicentre, randomised, double-blind phase 3 trial", *The Lancet. Oncology*, 15, 11, 2014, 1995-1206.

Cardiac toxicities are rare, and they can be reduced by periodical ECG and monitoring of electrolytic levels.[236] Patients with prior angina, myocardial infections and congestive heart failure should not be initiated to panobinostat-based treatments.[237]

4.2 BCL-2 Inhibitors

BCL-2 is one of the most important anti-apoptotic proteins and it plays a crucial role in the survival of MM cells, since it facilitates the evasion from apoptosis. The process of apoptosis is strongly dependent upon the balance existing between pro-apoptotic proteins as BAX and BAK and anti-apoptotic proteins as BCL-2; indeed, the activation of pro-apoptotic proteins induces apoptosis, which in turn is inhibited by the BCL-2 proteins. BCL-2 proteins, usually overexpressed in patients affected by malignancies, inhibit apoptosis by isolating pro-apoptotic proteins, thus promoting the resistance to therapy and the survival of cells, regardless of whether they are neoplastic or normal cells.[238]

Venetoclax (Venclexta®) is a powerful and selective, orally available, BCL-2 inhibitor and it is crucial in the regulation of cells death by intrinsic apoptosis.[239] Venetoclax constitutes the only BCL-2 inhibitor approved by FDA; however, it should be noted that it has not yet been approved for the treatment of MM, but it has been approved for the treatment of other haematological diseases as Chronic Lymphocytic Leukaemia (CLL). Venetoclax main action mechanisms consist in easy binding with BCL-2, causing interference in the signal of apoptosis inhibition, thus leading to the apoptotic pathway.[240] Properly because of its affinity with BCL-2, Venetoclax constitutes a promising agent in the treatment of MM, and it is currently the object of many ongoing trials.

4.2.1 Mechanisms of action

As mentioned in the above paragraph, BCL-2 and other anti-apoptotic proteins are overexpressed in MM cells since the bone marrow promotes the expression of BCL-2 family

[236] Jacob P. LAUBACH, et al., "Panobinostat for the Treatment of Multiple Myeloma", *Clinical cancer research: an official journal of the American Association for Cancer Research*, 21, 21, 2015, 4767-4773.
[237] Novartis Europharm Limited, *Farydak hard capsules: EU summary of product characteristics*, 2015, https://www.ema.europa.eu/en/medicines/human/EPAR/farydak, (accessed on 3 April 2023).
[238] Guillaume LESSENE, et al., "BCL-2 family antagonists for cancer therapy", *Nature reviews. Drug discovery*, 7, 12, 2008, 989-1000.
[239] Avi ASHKENAZI, et al., "From basic apoptosis discoveries to advanced selective BCL-2 family inhibitors", *Nature reviews. Drug discovery*, 16, 4, 2017, 273-284.
[240] Masa LASICA, Mary Ann ANDERSON, "Review of Venetoclax in CLL, AML and Multiple Myeloma", *Journal of personalized medicine*, 11, 463, 2021.

proteins, thus leading to massive proliferation of neoplastic cells and promotion of disease survival.[241]

This proliferation mechanism, backbone of MM progress, is interrupted by the presence of venetoclax, the strongest BCL-2 inhibitor, which by inhibiting BCL-2 induces the onset of apoptotic process.[242] It should be noted that the effectiveness of venetoclax is influenced by the relationship existing between MM cells and BCL-2; indeed, since MM is an heterogeneous disease, some neoplastic cells may be more dependents on BCL-2 than others, being therefore more sensitive to apoptosis and leading to more positive outcomes.[243]

Venetoclax showed anti-neoplastic activities when deployed as a single agent, but it is proven to be more effective when combined with dexamethasone and bortezomib, since a strong increase in the cell death has been registered.[244] Indeed, not only venetoclax intensifies bortezomib activity but simultaneously dexamethasone increases neoplastic cells dependence on BCL-2, thus determining a greater sensitivity to the treatment.[245] Due to this proved efficacy in a three-drug combination, different other combinations are under investigations.

Even if venetoclax has not been yet approved by FDA or EMA for the treatment of MM, several trials showed it effectiveness especially in NDMM patients which show high BCL-2 expression, while its role in the treatment of RRMM is still under consideration and it is the object of many phase III trials. In patients with RRMM, venetoclax-based therapies are potentially threatening because patients would be excessively exposed to life-threatening infections due to immunosuppression derived from multiple previous treatments.[246]

4.2.2 Clinical development

Since venetoclax has not been approved yet by FDA or EMA for the treatment of MM, several trials are taking place to demonstrate its effectives and its potential benefits. Many trials are testing the effectiveness of venetoclax in combination with other agents as IMiDs and PIs; indeed, two- or three-drug regimens phase I trials showed that combined regimens are more effective than the employment of the drug as a single agent. In particular, two combinations showed to be promising: the former is venetoclax-dexamethasone-bortezomib which already

[241] Mats PETTERSSON, et al., "Expression of the bcl-2 gene in human multiple myeloma cell lines and normal plasma cells", *Blood*, 79, 2, 1992, 495-502.
[242] Hamid EHSAN, et al., "Role of Venetoclax in the Treatment of Relapsed and Refractory Multiple Myeloma", *Journal of hematology*, 10, 3, 2021, 89-97.
[243] Cyrille TOUZEAU, et al., "The Bcl-2 specific BH3 mimetic ABT-199: a promising targeted therapy for t(11;14) multiple myeloma", *Leukemia*, 28, , 2014, 210-212.
[244] Shannon M. MATULIS, et al., "Dexamethasone treatment promotes Bcl-2 dependence in multiple myeloma resulting in sensitivity to venetoclax", *Leukemia*, 30, 5, 2016, 1086-1093.
[245] *Ibidem*
[246] Hamid EHSAN, et al., "Role of Venetoclax in the Treatment of Relapsed and Refractory Multiple Myeloma", *Journal of hematology*, 10, 3, 2021, 89-97.

reached phase III trials, while the latter is venetoclax-daratumumab-dexamethasone, whose investigation is still at the beginning. The NCT03314181 trial is a phase I/II trial, in which the second combination is under investigation; the trial started is 2018 and it estimates to conclude in 2025.

While for the ventoclax-daratumumab-dexamethasone combination there is no sufficient data to confirm its effectiveness, in the case of venetoclax-dexamethasone-bortezomib combination the BELLINI trial, started in 2016 and concluded in 2022, proved the effectiveness of the therapy. In the following paragraph detailed information about the BELLINI trial will be provided, based on the report published in 2022 and approved by the sponsor of the trial, AbbVie Inc., and on the information provided by the official governmental clinical trial page.[247]

4.2.2.1 Phase III trial: BELLINI

BELLINI[248] is a "randomized, double-blind, placebo-controlled, multicentre, phase 3 trial",[249] whose main endpoints are the assessment of PFS, ORR, OS, and quality of life in administration of venetoclax, bortezomib and dexamethasone. The trial started in 2016 and concluded in 2022, with last update published on August 24, 2022.[250]

Patient's sample consisted in ≥ 18 years old patients with RRMM, who received 1-3 previous treatments and whose level of BCL-2 was high; patients who were refractory to PIs or that had been already treated with BCL-2 inhibitors were excluded.[251] 291 patients were enrolled in the trial and they were randomly divided into two arms: 194 patients were administered with venetoclax-bortezomib-dexamethasone, while 97 patients were administered placebo-bortezomib-dexamethasone.

The study consisted in 9 twenty-one-day cycles and undetermined number of thirty-five-day cycles; indeed, after the last twenty-one-day cycle, the treatment would have been administered with thirty-five-day cycles until disease progression, death, or withdrawal of consent. In the first eight cycles, patients were administered with oral venetoclax, subcutaneous bortezomib and oral dexamethasone, from the ninth cycle on the dosage of dexamethasone and bortezomib was reduced. Venetoclax dose reduction was admitted only in case of severe and

[247] For further information on US government approved clinical trial see: https://clinicaltrials.gov/
[248] The clinical trial official name is: A Phase 3, Multicenter, Randomized, Double Blind Study of Bortezomib and Dexamethasone in Combination With Either Venetoclax or Placebo in Subjects With Relapsed or Refractory Multiple Myeloma Who Are Sensitive or Naïve to Proteasome Inhibitors.
[249] Shaji K. KUMAR, et al., "Venetoclax or placebo in combination with bortezomib and dexamethasone in patients with relapsed or refractory multiple myeloma (BELLINI): a randomised, double-blind, multicentre, phase 3 trial", *The Lancet. Oncology*, 21, 12, 2020, 1630-1642.
[250] U.S. National Library of Medicine. ClinicalTrials.gov, *A study evaluating Venetoclax (ABT-199) in Multiple Myeloma Subjects who are receiving bortezomib and dexamethasone as a standard therapy (BELLINI*), https://clinicaltrials.gov/ct2/show/NCT02755597?term=BELLINI&draw=2&rank=3, (last access 4 April 2023).
[251] *Ibidem*

continuous toxicity and manifestation of AEs. Together with the main therapy, patients were also administered with antibacterial prophylaxis to reduce the rate of infections.

Concerning results, the trial showed a PFS of 22.4 months, which was significantly higher compared to the one in the placebo arm; the same can be said for the ORR, which increased in the venetoclax arm (82%), with great portion of patients who showed very good partial response (26%). 63% of the patients in the venetoclax arm were forced to discontinue the treatment because of the occurrence of AEs.

AEs were present in 99% of the patients regardless of whether they were part of the placebo or of the venetoclax arm; however, severe AEs were more common in the venetoclax arm. The most common side effects of the three-drug regimen were neutropenia (18%), diarrhoea (15%) and thrombocytopenia (15%); while the most severe was pneumonia, which manifested in 14% of the patients in the venetoclax arm.

Noteworthy is that with the administration of venetoclax the rate of infection and the rate of fatal infection increased dramatically; indeed, more than half of the deaths in the venetoclax arm were associated with infections. Generally speaking, an imbalance in the mortality rate was registered within the two arms with a consistent number of deaths occurring in the venetoclax arm. Several hypotheses were formulated to explain this increased death's rate, but conclusive results have not been obtained yet.

In conclusion, BELLINI phase III trial showed an improvement in the ORR and PFS, but it also ended with an increased death's rete, leading an adverse risk-benefit outline.[252]

4.2.3 Tolerability

Venetoclax, both as a single agent and in combination with dexamethasone and bortezomib, is considered to have a toxicity profile which is acceptably safe and it is particularly suitable for long-term therapies, common in RRMM patients who have been strongly pre-treated.[253]

When used as a single agent, the most common AEs are haematological and gastrointestinal: the former includes mainly thrombocytopenia (26%), neutropenia (21%) and anaemia (14%), while the latter includes nausea (47%), diarrhoea (36%) and vomiting (21%).[254] Most severe AEs comprehend pneumonia (8%) and sepsis (5%), which, however, are far less common than the haematological or gastrointestinal ones.

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[252] Shaji K. KUMAR, et al., "Venetoclax or placebo in combination with bortezomib and dexamethasone in patients with relapsed or refractory multiple myeloma (BELLINI): a randomised, double-blind, multicentre, phase 3 trial", *The Lancet. Oncology*, 21, 12, 2020, 1630-1642.
[253] Iuliana VAXMAN, et al., "Venetoclax for the treatment of multiple myeloma", *Expert review of hematology*, 11, 12, 2018, 915-920.
[254] Shaji K. KUMAR, et al., "Efficacy of venetoclax as targeted therapy for relapsed/refractory t(11;14) multiple myeloma", *Blood*, 130, 22, 2017, 2401-2409.

When used in combination with dexamethasone and bortezomib, the most common AEs are diarrhoea, neutropenia, and thrombocytopenia, while the most severe one is pneumonia, which is however less common.[255] It should be noted that, since optimal doses for venetoclax administration have not been established, professionals should be careful in administering it at high dose, since it can cause strong myelosuppression thus leading the patient to be particularly susceptible to infections.[256]

4.3 Exportin inhibitors

Proteins belonging to the mammalian family of karyopherin constitute the biggest group of transport receptors. Based on their transport signs, mammalian proteins can be divided in importins, responsible for the relocation of cells into the nucleus, and exportins, responsible for the relocation of cells outside the nucleus.[257] Exportin 1 (XPO1) is a mammalian protein responsible for the export and inactivation of tumour suppressor proteins, immune response regulators, cell-cycle regulators and chemotherapeutic targets.[258] XPO1 is usually overexpressed in neoplastic cells, both in solid and hematologic tumours, and this leads to the strengthening of oncoproteins translation, which causes aggressive disease, poor therapeutical outcomes, and reinforced drug resistance especially to PIs and IMiDs.[259] Because of its pleiotropic nature, XPO1 represents a new and promising target for MM therapy.

Selinexor (Xpovio®) is a strong, selective, fully synthetic, and orally bioavailable inhibitor of nuclear exportin, which, by specifically binding with XPO1, leads to the activation of tumour suppressor proteins and inhibition of the oncoproteins translation.[260] Selinexor has not been approved yet by FDA for the treatment of MM as a single agent, but, in 2019 it was approved in combination with dexamethasone for the treatment of RRMM in patients who received at least three prior treatments and that are refractory to two IMiDs and mAb.[261]

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[255] Shaji K. KUMAR, et al., "Venetoclax or placebo in combination with bortezomib and dexamethasone in patients with relapsed or refractory multiple myeloma (BELLINI): a randomised, double-blind, multicentre, phase 3 trial", *The Lancet. Oncology*, 21, 12, 2020, 1630-1642.
[256] Courtney D. DINARDO, et al., "Azacitidine and Venetoclax in Previously Untreated Acute Myeloid Leukemia", *The New England journal of medicine*, 383, 7, 2020, 617-629.
[257] Klaus PODAR, et al., "Selinexor for the treatment of multiple myeloma", *Expert opinion on pharmacotherapy*, 21, 4, 2020, 399-408.
[258] Giovanni Luca GRAVINA, et al., "Nucleo-cytoplasmic transport as a therapeutic target of cancer", *Journal of hematology & oncology*, 7, 85, 2014.
[259] Manisha BHUTANI, et al., "Investigation of a gene signature to predict response to immunomodulatory derivatives for patients with multiple myeloma: an exploratory, retrospective study using microarray datasets from prospective clinical trials", *The Lancet. Haematology*, 4, 9, 2017, e443-e451.
[260] Lior GOLOMB, et al., "Importin 7 and exportin 1 link c-Myc and p53 to regulation of ribosomal biogenesis", *Molecular cell*, 45, 2, 2012, 222-232.
[261] US-FDA, FDA grants accelerated approval to Selinexor for multiple myeloma, 2019, https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-selinexor-multiple-myeloma, (last access April 5, 2023).

4.3.1 Mechanisms of action

Selinexor is a Selective Inhibitor of Nuclear Exportin (SINE), which inhibits exportin's basic functions by establishing a covalent bond with it. The inhibition of XPO1 leads to oncoproteins retention and Tumour Suppressor Proteins (TSP) activation which cause apoptosis in the neoplastic cells, without affecting normal cells.[262]

Selinexor is proved to be more effective when combined with dexamethasone with which it shows a synergic activity; indeed, selinexor enhances the activity of dexamethasone, increasing the effectiveness both in transcriptional and repression functions.[263] The increased effectiveness of the two-drug combination has been proved by significant increases in the ORR. It should be noted that the two-drug combination has been tested only on RRMM patients that have been strongly pre-treated, while there is no evidence of its effectiveness in NDMM patients.

4.3.2 Clinical development

As mentioned in the introductive paragraph, selinexor in combination with dexamethasone has been approved by FDA in 2019 for the treatment of RRMM; however, its use as a single agent or in combination with other agents has not received approval yet. Furthermore, it should be noted that the approval of the two-drug combination was firstly rejected by the FDA because of its potential high toxicity[264] but then it was granted with accelerated approval after the conclusion of the STORM trial and the publication of its positive results. With regards to the EU, EMA has not granted approval for selinexor-based treatments considering that toxicity is more relevant than the positive outcomes.

At the moment, since a variety of phase I trials and *in vitro* studies showed selinexor's synergic action with various targeted therapies and chemotherapeutical agents,[265] 60 trials are evaluating its effectiveness and toxicity as a monotherapy or in combination with other agents.[266] Except for selinexor-dexamethasone therapy, also the three-drug combination, selinexor-dexamethasone-bortezomib, which is currently undergoing a phase III trial, showed to be particularly promising.

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[262] Yu-Tzu TAI, et al., "CRM1 inhibition induces tumor cell cytotoxicity and impairs osteoclastogenesis in multiple myeloma: molecular mechanisms and therapeutic implications", *Leukemia*, 28, 1, 2014, 155-165.
[263] Trinayan KASHYAP, et al., "Selinexor, a Selective Inhibitor of Nuclear Export (SINE) compound, acts through NF-κB deactivation and combines with proteasome inhibitors to synergistically induce tumor cell death", *Oncotarget*, 7, 48, 2016, 78883-78895.
[264] Klaus PODAR, et al., "Selinexor for the treatment of multiple myeloma", *Expert opinion on pharmacotherapy*, 21, 4, 2020, 399-408.
[265] Alessandro ALLEGRA, et al., "Selective Inhibitors of Nuclear Export in the Treatment of Hematologic Malignancies", *Clinical lymphoma, myeloma & leukemia*, 19, 11, 2019, 689-698.
[266] Klaus PODAR, et al., "Selinexor for the treatment of multiple myeloma", *Expert opinion on pharmacotherapy*, 21, 4, 2020, 399-408.

Concerning the selinexor-dexamethasone combination, the STORM trial (part I and part II) played a pivotal role in the acceptance of this two-drug treatment which showed to be effective in heavily pre-treated patients with RRMM; with regards to the three-drug combination, the ongoing BOSTON trial is showing encouraging results with high rates of response. In the following paragraphs, detailed information about STORM and BOSTON trials will be provided, based on the results published in January 2023 by the main sponsor of the trials, Karyopharm Therapeutics Inc, on the official governmental clinical trial website.[267][268]

4.3.2.1 STORM

STORM[269] is a "phase IIb, single-arm, multicenter, open-label study",[270] whose main endpoints are ORR, DoR, PFS and OS. The trial started in January 2015 and concluded in January 2023, with last update on January 26, 2023.[271] The trial consisted in two parts which enrolled two different samples but followed the same drug administration path and obtained similar results, which were then elaborated to produce a uniform outcome that could prove the validity of the therapy.

Patient's sample consisted in ≥ 18 years old patients with RRMM. Inclusion criteria included disease refractory to IMiDs, PIs, daratumumab and glucocorticoids; while exclusion criteria included presence of active smouldering MM, plasma cell leukaemia, amyloidosis, and painful peripheral neuropathy. In part 1, 79 patients, quad- or penta-refractory to MM and with a median age of 63 years, were enrolled;[272] while in part 2, 122 patients, with a median age of 65 years, were enrolled.

Patients, in both part 1 and 2, were subjected to four-week cycles with twice a week administration of high-dose oral selinexor and low-dose dexamethasone until disease

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[267] U.S. National Library of Medicine. ClinicalTrials.gov, *Selinexor treatment of Refractory Myeloma (STORM),* https://clinicaltrials.gov/ct2/show/NCT02336815?term=STORM%2C+selinexor&draw=2&rank=1, (last access April 6, 2023).

[268] U.S. National Library of Medicine. ClinicalTrials.gov, *Bortezomib, Selinexor, and Dexamethasone in Patients With Multiple Myeloma (BOSTON),* https://clinicaltrials.gov/ct2/show/NCT03110562?term=selinexor+BOSTON&draw=2&rank=1, (last access April 6, 2023).

[269] Official name of the study as published on the official page of the trial in U.S. National Trial Library of Medicine. ClinicalTrial.gov: A Phase 2b, Open-Label, Single-Arm Study of Selinexor (KPT-330) Plus Low-Dose Dexamethasone (Sd) in Patients With Multiple Myeloma Previously treated With Lenalidomide, Pomalidomide, Bortezomib, Carfilzomib, and an Anti-CD38 Monoclonal Antibody (mAb) Daratumumab, and Refractory to Prior Treatment With Glucocorticoids, an Immunomodulatory Agent, a Proteasome Inhibitor, and an the Anti-CD38 mAb Daratumumab.

[270] Ajai CHARI, et al., "Oral Selinexor-Dexamethasone for Triple-Class Refractory Multiple Myeloma", *The New England journal of medicine*, 381, 8, 2019, 727-738.

[271] U.S. National Library of Medicine. ClinicalTrials.gov, *Selinexor treatment of Refractory Myeloma (STORM),* https://clinicaltrials.gov/ct2/show/NCT02336815?term=STORM%2C+selinexor&draw=2&rank=1, (last access April 6, 2023).

[272] Klaus PODAR, et al., "Selinexor for the treatment of multiple myeloma", *Expert opinion on pharmacotherapy*, 21, 4, 2020, 399-408.

progression, withdrawal of consent or unbearable adverse events. Furthermore, to control nausea, one of the most common AEs, patients were also administered with antiemetics. The average treatment duration was 9.0 weeks. Concerning the results of the trial, in part 1, ORR was 21%, median DoR was 5 months, PFS was 2 months[273] and OS was 9.00 months.[274] In part 2, 26% of the patients showed partial or better response and the median DoR was 4.4 months. PFS was 3.7 months and OS was 8.6 months, showing positive outcomes and great effectiveness of the two-drug combination.

With regards to AEs, they are one of the most complex aspects of the STORM trial; indeed, even if the results obtained were positive, the rate of occurrence of AEs was very high, leading to the questioning of whether the positive outcomes could compensate the high level of toxicity. The most common AEs were thrombocytopenia and fatigue which occurred in 73% of the patients, nausea present in 72% of the patients, and anaemia arisen in 67% of the patients. Regarding most severe AEs, these included pneumonia and sepsis, which occurred in 63% of the patients. AEs caused the discontinuation of the treatment in 18% of the patients, while 80% were forced to opt for dose reduction and to add supportive care to reduce the physical burden and to improve quality of life. Since dose reduction was frequent, the therapy could benefit from a shift to weekly dosing instead of twice a week administration, which would allow an easier platelet control, reducing the haematological AEs.[275]

It should be considered that given patients' initial disease condition, little space was available to act and prevent disease progression and this is the main reason behind the administration of high dose selinexor, meant to maximize the results in the shortest time. However, high dose selinexor enhanced its toxicity, which can be significantly improved with dose modification and supportive care.[276]

[273] Adeel MASOOD, et al., "Efficacy and safety of selinexor-based regimens for relapsed/refractory multiple myeloma: a systematic review of literature", *Annals of hematology*, 101, 12, 2022, 2601-2610.
[274] Klaus PODAR, et al., "Selinexor for the treatment of multiple myeloma", *Expert opinion on pharmacotherapy*, 21, 4, 2020, 399-408.
[275] Joshua RICHTER, et al., "Selinexor in relapsed/refractory multiple myeloma", *Therapeutic advances in hematology*, 11, 2020.
[276] Ajar CHARI, et al., "Results of the Pivotal STORM Study (part 2) in Penta-Refractory Multiple Myeloma (MM): Deep and Durable Responses with Oral Selinexor Plus Low Dose Dexamethasone in Patients with Penta-Refractory MM", *Blood*, 132, 2, 2018, 598.

4.3.2.2 BOSTON

BOSTON[277] is an ongoing "phase 3, open-label, global, randomized, controlled trial",[278] whose main endpoints are PFS, ORR, OS, and evaluation of the clinical benefits of the three-drug combination, selinexor-dexamethasone-bortezomib, compared to the two-drug combination, dexamethasone-bortezomib in RRMM patients. The study started in 2016 and it has not concluded yet, even if the recruiting period is closed; the last update was published in January 2023.[279]

Patients' sample consists in ≥ 18 years old patients with RRMM, which received 1-3 previous different treatments; exclusion criteria included presence of light-chain amyloidosis and painful peripheral neuropathy. 402 patients were enrolled in the study: 195 were allocated in the selinexor-dexamethasone-bortezomib arm, while 207 were allocated in the dexamethasone-bortezomib arm. Patients in the former arm are administered weekly with oral selinexor, subcutaneous bortezomib and oral dexamethasone in five-week cycles, while patients in the latter arm are administered with subcutaneous bortezomib and oral dexamethasone in three-week cycles. If needed, patients are also administered with supportive therapies to minimize burden of the AEs; in particular, all the patients are administered with hydroxy tryptamine to control nausea and vomit. Since the trial is still ongoing is not possible to define the average duration of the treatment, but if no complication arises it can be administered until disease progression. Decision to stop the therapy ahead of schedule may be determined by withdrawal of consent, physician decision or uncontrollable side effects. Overall, until January 2023, the main reason for treatment anticipated conclusion or discontinuation can be found in disease progression, with limited part of the sample giving up because of the toxicity of the agents.

Concerning the results collected until January 2023, PFS in the selinexor arm was 13.9 months which was significantly longer than the one obtained in the other arm (11.0 months); ORR was also higher in the selinexor arm reaching a value of 76.4%. It is not possible to provide data in relation to the OS, since a longer follow-up is necessary to determine a scientific valuable

[277] Official name of the study as published on the official page of the trial in U.S. National Trial Library of Medicine. ClinicalTrial.gov: A Phase 3 Randomized, Controlled, Open-label Study of Selinexor, Bortezomib, and Dexamethasone (SVd) Versus Bortezomib and Dexamethasone (Vd) in Patients with Relapsed or Refractory Multiple Myeloma (RRMM).

[278] Sebastian GROSICKI, et al., "Once-per-week selinexor, bortezomib, and dexamethasone versus twice-per-week bortezomib and dexamethasone in patients with multiple myeloma (BOSTON): a randomised, open-label, phase 3 trial", *Lancet,* 396, 10262, 2020, 1563-1573.

[279] U.S. National Library of Medicine. ClinicalTrials.gov, *Bortezomib, Selinexor, and Dexamethasone in Patients With Multiple Myeloma (BOSTON),* https://clinicaltrials.gov/ct2/show/NCT03110562?term=selinexor+BOSTON&draw=2&rank=1, (last access April 6, 2023).

data; however, at January 2023, 24% of the selinexor arm patients died, while in the other arm 30% of the patients deceased.

If in the STORM trial the toxicity was a problematic issue, in the BOSTON trial the AEs configuration considerably improved; indeed only 21% of the patients were forced to discontinue treatment because of AEs and the majority of them were located in the dexamethasone-bortezomib arm. The most common side effects are fatigue, nausea, vomit, and thrombocytopenia but they manifested in limited percentage. Severe AEs included pneumonia, sepsis and infections, and their occurrence rate was the same among the two arms; furthermore, deaths due to their insurgence was limited to 2% of the patients in both arms.

Overall, it can be stated that the toxicity profile of the selinexor-dexamethasone-bortezomib combination is acceptable, and the AEs can be easily managed through dose reduction and supportive care; furthermore, the therapy shows a significantly lower rate of insurgence of peripheral neuropathy compared to the bortezomib-dexamethasone treatment, improving patients' quality of life.

All things considered, even if the trial is not concluded yet, promising data have been published, showing the high potential of this new therapy which could eventually become the new standard of care in the treatment of RRMM.

4.3.3 Tolerability

Tolerability represents a major issue for selinexor administration; indeed, even if it showed promising activity especially in highly refractory MM, its clinical use may be compromised by its high toxicity. Toxicity constituted the main reason for which the combination of dexamethasone and selinexor was firstly rejected by FDA and it is still the main concern in its approval by EMA. The main reason behind the insurgence of innumerable side effects lies in the fact that selinexor is used in patients that have been heavily pre-treated and whose organism is already extremely susceptible; because of this, patients need to be carefully monitored and dose adjustment as well as supportive therapies should be provided when necessary. It should be noted that since many trials are still ongoing and various selinexor-based combinations are still to be explored, there is no indication of the optimal dosage of selinexor, but it is to be defined on the expected results and on the physical condition of the patient.

As showed in the BOSTON trial, selinexor toxicity can be reduced when the agent is combined with other agents as bortezomib, which not only increases the efficiency of the two-drug regimen, but also reduces the insurgence of AEs.[280]

[280] Nizar J. BAHLIS, et al., "Selinexor plus low-dose bortezomib and dexamethasone for patients with relapsed or refractory multiple myeloma", *Blood*, 132, 24, 2018, 2546-2554.

The main side effects of selinexor-based treatments are gastrointestinal and haematological. Gastrointestinal AEs include mainly nausea, vomit, anorexia, and diarrhoea; while the most common haematological AEs are thrombocytopenia, anaemia, and neutropenia.[281]

To relieve AEs' burden and to improve patient's quality of life, antiemetics and erythropoietin stimulating agents (ESAs) are usually administered as supportive care;[282] indeed, anaemia and nausea are the most QoL affecting side effects and they need to be properly managed to provide patients with the needed relief.[283]

[281] Dan T. VOGL, et al., "Selective Inhibition of Nuclear Export With Oral Selinexor for Treatment of Relapsed or Refractory Multiple Myeloma", *Journal of clinical oncology: official journal of the American Society of Clinical Oncology*, 36, 9, 2018 859-866.

[282] Maria GAVRIATOPOULOU, et al., "Integrated safety profile of selinexor in multiple myeloma: experience from 437 patients enrolled in clinical trials", *Leukemia*, 34, 9, 2020, 2430-2440.

[283] Joshua RICHTER, et al., "Selinexor in relapsed/refractory multiple myeloma", *Therapeutic advances in hematology*, 11, 2020.

SECTION II

TERMINOGRAPHIC CARDS

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>multiple myeloma

<Morphosyntax>noun group

<Usage label>main term

<Source>^Mahindra, et al. 2010^:1

<Lexica>Found in ^Merriam/Webster 2016^

<Definition>Multiple Myeloma (MM) is a clonal B-cell malignancy characterized by the aberrant expansion of plasma cells within the bone marrow, as well as at extramedullary sites.

<Source>^Mahindra, et al. 2010^:1

<Context>Multiple Myeloma arises in most cases from monoclonal gammopathy of undetermined significance or smouldering MM, which are characterized by the presence of M-protein, bone marrow plasmacytosis, and renal impairment attributable to the plasma cell proliferation disorder. The risk of progression to MM is substantially different between MGUS and SMM, about 1% per year versus 10–20% per year, respectively.

<Source>^Mahindra, et al. 2010^:1

<Concept field>haematology

<Related words>^neoplasm^

<Type of relation>super.

<Related words>^plasma cells^

<Type of relation>general

<Related words>^monoclonal gammopathy of undermined significance^

<Type of relation>sub.

<Related words>^smouldering Multiple Myeloma^

<Type of relation>sub.

<Synonyms>The terms “plasma cell myeloma”, “myelomatosis” and “kahler disease” are synonyms to “multiple myeloma” but they are hardly used to identify the disease.

<en>plasma cell myeloma

<Morphosyntax>noun group

<Usage label>uncommon

<Source>^National Cancer institute dictionary 2022^, https://www.cancer.gov/publications/dictionaries/cancer-terms/def/plasma-cell-myeloma

<en>myelomatosis
<Morphosyntax>noun
<Usage label>uncommon
<Source>^Bommer, et al. 2018^

<en>kahler disease
<Morphosyntax>noun group
<Usage label>uncommon
<Source>^National Cancer institute dictionary 2022^, https://www.cancer.gov/publications/dictionaries/cancer-terms/def/plasma-cell-myeloma

<en>MM
<Morphosyntax>noun
<Category>initials
<Usage label>common
<Source>^Mahindra, et al. 2010^:1
<Variant of>multiple myeloma

<zh>多发性骨髓瘤
<Morphosyntax>noun group
<Source>^路瑾，等2020^:2
<Definition>多发性骨髓瘤是一种浆细胞恶性增殖性疾病，其特征为异常浆细胞没润骨路和/或软组织，并产生大量单克隆免疫球蛋白或轻链。
<Source>^路瑾，等2020^:2
<Context>由于浆细胞属于分化成熟的细胞，所以大多数多发性骨髓瘤是一种疾病进展相对缓慢、恶性程度相对较低的恶性肿瘤。但也有少数病情进展快,恶性程度较高。最常见的临床表现为骨质破坏、肾功能不全、贫血、高钙血症、反复感染以及高黏滞血症等。
<Source>^路瑾，等2020^:2-3
<Concept field>血液学
<Related words>^恶性肿瘤^

<Type of relation>super.

<Related words>^浆细胞^

<Type of relation>general

<Related words>^意义不明的单克隆丙种球蛋白^

<Type of relation>sub.

<Related words>^冒烟性多发性骨髓瘤^

<Type of relation>sub.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>plasma cell

<Morphosyntax>noun group

<Usage label>main term

<Source>^Allen/Sharma 2022^

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Plasma cells are differentiated B-lymphocyte white blood cells capable of secreting immunoglobulin or antibody.

<Source>^Allen/Sharma 2022^

<Context>Plasma cells play a significant role in the adaptive immune response, namely, being the main cells responsible for human immunity.

<Source>^Allen/Sharma 2022^

<Concept field>histology

<Related words>^multiple Myeloma^

<Type of relation>general

<Related words>B cell

<Type of relation>sub.

<Related words>lymphocyte

<Type of relation>coord.

<Synonyms>The term “plasmacyte” is synonym to “plasma cell” and it is commonly used to identify the lymphocyte secreting immunoglobulins.

<en>plasmacyte

<Morphosyntax>noun

<Usage label>common

<Source>^Merriam/Webster 2016^

<en>PL
<Morphosyntax>noun
<Category>initials
<Source>^Allen/Sharma 2022^
<Variant of>plasma cell

<zh>浆细胞
<Morphosyntax>noun group
<Source>^路瑾，等2020^:2
<Definition>浆细胞是B淋巴细胞在抗原刺激下分化增殖的一种终末细胞，可合成和分泌免疫球蛋白。
<Source>^路瑾，等2020^:2
<Context>正常人体内有许多不同的浆细胞克隆，而浆细胞疾病则是由单克隆浆细胞异常增殖浸润及分泌M蛋白，同时正常浆细胞功能受到抑制导致的一组疾病，包括意义未明单克隆免疫球蛋白血症、多发性骨髓瘤、系统性轻链型淀粉样变性、髓外浆细胞瘤和孤立性骨髓瘤、POEMS综合征、浆细胞白血病、有肾脏损害意义的单克隆免疫球蛋白病等。
<Source>^路瑾，等2020^:2
<Concept field>组织学
<Related words>^多发性骨髓瘤^
<Type of relation>general
<Related words>淋巴细胞
<Type of relation>coord.
**
<Subject>医学与卫生 / Medicine & health (610)
<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)
<en>M Protein
<Morphosyntax>noun group
<Usage label>main term
<Source>^Batuman 2020^:54
<Lexica>Found in ^Merriam/Webster 2016^

<Definition>M proteins are monoclonal immune globulin fragments or intact immune globulins produced by usually a malignant cone of plasma cells or B cells.
<Source>^Batuman 2020^:54
<Context>Since M proteins are produced by plasma cells or B cells, and their presence in blood or urine indicates clonal proliferation of either of these cell lines, that is, multiple myeloma (plasma cells), or lymphomas (B cells). M proteins fragments have relatively unrestricted access to kidneys and kidney tubules, causing an expanding spectrum of kidney disorders caused by deposition of intact immune globulins or their fragments in the glomeruli or along the kidney tubules.
<Source>^Batuman 2020^:54
<Concept field>histology
<Related words>^plasma cell^
<Type of relation>super.
<Related words>antibody
<Type of relation>super.
<Synonyms>The terms “monoclonal immunoglobulin” and “paraprotein” are synonym to “M-protein” and they are commonly used.

<en>monoclonal immunoglobulin
<Morphosyntax>noun group
<Usage label>common
<Source>^Batuman 2020^:55

<en>paraprotein
<Morphosyntax>noun group
<Usage label>common
<Source>^Batuman 2020^:54

<zh>单克隆免疫球蛋白
<Morphosyntax>noun group
<Usage label>main term
<Source>^Kumar 2022^, https://bestpractice.bmj.com/topics/zh-cn/891
<Definition>单克隆蛋白是单个浆细胞克隆产生的异常免疫同质性免疫球蛋白或其片段。
<Source>^Kumar 2022^, https://bestpractice.bmj.com/topics/zh-cn/891

<Context>单克隆蛋白可能是基础淋巴组织恶性肿瘤的结果，可能是无症状性浆细胞克隆扩增的一部分，并且可以是单克隆丙种球蛋白病的潜在异常表现。这些浆细胞可见于骨髓、外周循环或软组织内。它们通常可在骨髓检查中发现，其中克隆性浆细胞的存在可能伴随或不伴随浆细胞比例的绝对增加。

<Source>^Kumar 2022^, https://bestpractice.bmj.com/topics/zh-cn/891

<Concept field>组织学

<Related words>^浆细胞^

<Type of relation>super.

<Related words>抗体

<Type of relation>super.

<Synonym>“M 蛋白”和“单克隆免疫球蛋白”是近义词。

<zh>M 蛋白

<Morphosyntax>noun group

<Usage label>common

<Source>^路瑾，等 2020^:2

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>monoclonal gammopathy of undermined significance

<Morphosyntax>noun group

<Usage label>main term

<Source>^Korde, et al 2011^:5573

<Lexica>Found in ^Merriam/Webster 2016^

<Definition>Monoclonal Gammopathy of Undermined Significance (MGUS) is an asymptomatic plasma cell dyscrasia that is present in more than 3% of the general white population older than age 50 and has an average multiple myeloma progression risk of 1% per year.

<Source>^Korde, et al 2011^:5573

<Context>Monoclonal Gammopathy of Undermined Significance (MGUS) is present in more than 3% of the general white population older than age 50 and has an average multiple myeloma progression risk of 1% per year. The aetiology of MGUS remains unclear and it is a current

topic of investigation, but different studies have demonstrated that most cases of multiple myeloma are preceded by MGUS.
<Source>^Korde, et al 2011^:5573
<Concept field>haematology
<Related words>^multiple myeloma^
<Type of relation>super.
<Related words>^smouldering multiple myeloma^
<Type of relation>coord.
<Synonyms>The term “monoclonal gammopathy of undermined significance” is often substituted by its initials “MGUS”.

<en>MGUS
<Morphosyntax>noun
<Category>initials
<Usage label>common
<Source>^Korde, et al 2011^:5573
<Variant of>monoclonal gammopathy of undermined significance

<zh>意义未明的单克隆免疫球蛋白病
<Morphosyntax>noun group
<Source>^Berenson 2021^, https://www.msdmanuals.cn/home/blood-disorders/plasma-cell-disorders/multiple-myeloma
<Definition>意义未明的单克隆丙种球蛋白病是指异常但非恶性浆细胞生成的单克隆抗体积聚。
<Source>^Berenson 2021^, https://www.msdmanuals.cn/home/blood-disorders/plasma-cell-disorders/multiple-myeloma
<Context>意义未明的单克隆免疫球蛋白病在老年男性中最为常见；通常不会引起任何问题。但这种疾病有时会发展成更严重的疾病。如果您的血液中含有大量的这种蛋白，务必定期接受检查，这样一旦病情有所恶化，您便能尽早接受治疗。如果病情未恶化，则无需对意义未明的单克隆丙种球蛋白病进行治疗。
<Source>^Mayo Clinic 2021^
<Concept field>血液学
<Related words>^多发性骨髓瘤^
<Type of relation>super.

<Related words>^冒烟性多发性骨髓瘤^

<Type of relation>coord.

<Synonym>“MGUS”和“意义未明的单克隆免疫球蛋白病”是近义词。

<zh>MGUS

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^Berenson 2021^

<Variant of>意义未明的单克隆免疫球蛋白病

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>smouldering multiple myeloma

<Morphosyntax>noun group

<Usage label>main term

<Source>^Korde 2011^:5573

<Definition>Smouldering Multiple Myeloma (SMM) is asymptomatic plasma cell disorder which carries a high risk of progression to active multiple myeloma (10% per year the first 5 years).

<Source>^Korde 2011^:5573

<Context>SMM is characterized by serum M-protein level >3 g/dL and/or clonal plasma cell population in bone marrow <10%, while maintaining lack of end-organ damage. Risk of progression from SMM to multiple myeloma is 10% per year for the first 5 years, 3% per year for the next 5 years, and 1% for the subsequent 10 years.

<Source>^Korde 2011^:5574

<Concept field>haematology

<Related words>^multiple myeloma^

<Type of relation>super.

<Related words>^monoclonal gammopathy of undermined significance^

<Type of relation>coord.

<Synonyms>The expression “Smouldering Multiple Myeloma” is often substituted by its initials “SMM”.

<en>SMM

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^Korde 2011^:5573

<Variant of>smouldering multiple myeloma

<zh>冒烟性多发性骨髓瘤

<Morphosyntax>noun group

<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/diseases-conditions/mgus/symptoms-causes/syc-20352362

<Definition>冒烟性多发性骨髓瘤（SMM）是一种异质性极高的无症状浆细胞病，病程介于意义未明的单克隆丙种球蛋白血症（MGUS）与多发性骨髓瘤（MM）之间。

<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/diseases-conditions/mgus/symptoms-causes/syc-20352362

<Context>冒烟性多发性骨髓瘤表示：血清 M 蛋白≥3g / dL 或 24 h 尿单克隆蛋白≥0.5g，和（或）骨髓单克隆浆细胞的比例介于 10%～60%，无骨髓瘤相关事件。SMM 在诊断后 5 年内进展为 MM 的风险约为每年 10%，6～10 年内则为每年 3%，而后降为每年 1%。

<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/diseases-conditions/mgus/symptoms-causes/syc-20352362

<Concept field>血液学

<Related words>^多发性骨髓瘤^

<Type of relation>super.

<Related words>^意义未明的单克隆免疫球蛋白病^

<Type of relation>coord.

<Synonym>“SMM”和“冒烟性多发性骨髓瘤”是近义词。

<zh>SMM

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^Korde 2011^:5573

<Variant of>冒烟性多发性骨髓瘤

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>hypercalcemia

<Morphosyntax>noun

<Source>^Turner 2017^:270

<Lexica>Found in ^Merriam/Webster 2016^

<Definition>Hypercalcemia is a common disorder normally caused by primary hyperparathyroidism (PHPT) or malignancy. It is characterized by high serum calcium concentration in the biochemical screen.

<Source>^Turner 2017^:270

<Context>Hypercalcemia accounts for approximately 0.6% of all acute medical admissions. Its prevalence in the general population is up to 1/1,000. The classical symptomatic presentation of hypercalcemia is seen relatively rarely in the developed world, it is more common the asymptomatic presentation of the disease. Severe hypercalcemia (>3.5 mmol/L) requires emergency management, based on intravenous rehydration with normal saline, while asymptomatic mild hypercalcemia is amenable to conservative management.

<Source>^Turner 2017^:270

<Concept field>symptoms

<Related words>CRAB symptoms

<Type of relation>super.

<Related words>^osteolytic lesion^

<Type of relation>coord.

<Related words>^immunodeficiency^

<Type of relation>coord.

<Related words>^anaemia^

<Type of relation>coord.

<Related words>renal impairment

<Type of relation>coord.

<zh>高钙血症

<Morphosyntax>noun group

<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/diseases-conditions/hypercalcemia/symptoms-causes/syc-20355523

<Definition>高钙血症是血液中钙水平高于正常值的疾病。血液中钙含量过高会削弱骨骼，产生肾结石，并干扰心脏和大脑的运作。

<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/diseases-conditions/hypercalcemia/symptoms-causes/syc-20355523

<Context>高钙血症通常由甲状旁腺功能亢进所致。高钙血症的其他病因包括癌症、某些其他疾病、某些药物，以及服用过多钙和维生素 D 补充剂。高钙血症体征和症状的程度从无症状到重度不等。如果您的高钙血症较轻微，您可能不会出现任何体征或症状。更严重病例产生的体征和症状与血液中的高钙含量所影响的身体部位相关。

<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/diseases-conditions/hypercalcemia/symptoms-causes/syc-20355523

<Concept field>症状

<Related words>CRAB 症状

<Type of relation>super.

<Related words>^溶骨性病变^

<Type of relation>coord.

<Related words>^免疫缺陷^

<Type of relation>coord.

<Related words>^贫血^

<Type of relation>coord.

<Related words>肾功能损伤

<Type of relation>coord.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>osteolytic lesion

<Morphosyntax>noun group

<Usage label>main term

<Source>^Merz, et al. 2022^:2

<Definition>Osteolytic lesions (OL) are areas of circumscribed bone loss caused by malignant PC infiltration.

<Source>^Merz, et al. 2022^:2

<Context>Osteolytic lesions (OL) characterize symptomatic multiple myeloma. OL can be visualized by positron emission computed tomography (PET/CT) in up to 80% of patients, but

their underlying biology remains to be clarified. Some patients show subtotal plasma cells infiltration of the bone marrow in the iliac crest without signs of bone destruction while in the same patients, plasma cells cause bone disease in distant locations such as the vertebral bodies. Therefore, OL might represent regions of increased infiltration as well as areas containing biologically different PC.

<Source>^Merz, et al. 2022^:2

<Concept field>symptoms

<Related words>CRAB symptoms

<Type of relation>super.

<Related words>^hypercalcemia^

<Type of relation>coord.

<Related words>^immunodeficiency^

<Type of relation>coord.

<Related words>^anaemia^

<Type of relation>coord.

<Related words>renal impairment

<Type of relation>coord.

<Synonyms>The term “osteolytic lesion” is often substituted by its initials “OL”.

<en>OL

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^Merz, et al. 2022^:2

<Variant of>osteolytic lesion

<zh>溶骨性病变

<Morphosyntax>noun group

<Source>^路瑾，等2020^:176

<Definition>溶骨性病变是多发性骨髓瘤的基本病变之一。溶骨性病变是是骨质流失区，所以出现此病变，病人易发生骨折。

<Source>^路瑾，等2020^:176

<Concept field>症状

<Related words>CRAB症状

<Type of relation>super.

<Related words>^高钙血症^

<Type of relation>coord.

<Related words>^免疫缺陷^

<Type of relation>coord.

<Related words>^贫血^

<Type of relation>coord.

<Related words>肾功能损伤

<Type of relation>coord.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>immunodeficiency

<Morphosyntax>noun

<Source>^Raje/Dinakar 2015^:599

<Lexica>Found in ^Merriam/Webster 2016^

<Definition>Immunodeficiency is a group of heterogeneous disorders with immune system abnormalities that lead to an abnormal production of antibodies. It is characterized by recurrent infections, autoimmunity, lymphoproliferation and malignancy.

Source>^Raje/Dinakar 2015^:599

<Context>The overall clinical picture is dictated by the specific type of underlying immune defect. Based on the type of immunodeficiency disorders, the types of infections can vary. Some immunodeficiency disorders are characterized by cutaneous, respiratory, or gastrointestinal tract granulomas caused by immune dysregulation. Atopic features such as asthma, atopic dermatitis, and food allergies can be observed in some patients.

Source>^Raje/Dinakar 2015^:599-600

<Concept field>symptoms

<Related words>^hypercalcemia^

<Type of relation>coord.

<Related words>^osteolytic lesion^

<Type of relation>coord.

<Related words>renal impairment

<Type of relation>coord.

<zh>免疫缺陷

<Morphosyntax>noun group

<Source>^张文静，等 2021^:796

<Definition>免疫缺陷是一类由免疫细胞和（或）分子缺陷所致的异质性疾病。

<Source>^张文静，等 2021^:796

<Context>免疫缺陷通常以反复和（或）严重感染、自身免疫、自身炎症、肿瘤和过敏性疾病的风险增加为特征。前几者已见于较多的报道,而过敏相对少,尤其是过敏中的食物过敏在国内文献中提及甚少. 截止 2019 年国际免疫学联合会（IUIS）统计,免疫缺陷病已达 430 种。

<Source>^张文静，等 2021^:796

<Concept field>症状

<Related words>^高钙血症^

<Type of relation>coord.

<Related words>^溶骨性病变^

<Type of relation>coord.

<Related words>肾功能损伤

<Type of relation>coord.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield> 解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>plasmablast

<Morphosyntax>noun group

<Source>^Nutt, et al. 2015^:160

<Lexica>Found in ^Merriam/Webster 2016^

<Definition>Plasmablasts are the rapidly produced and short-lived effector cells of the early antibody response.

<Source>^Nutt, et al. 2015^:160

<Context>Plasmablast are dividing cells which have migratory potential and can further mature into plasma cells, which do not divide. Plasmablasts also develop B cells which are characterized by their capacity to secrete large amounts of antibodies.

<Source>^Nutt, et al. 2015^:160

<Concept field>histology

<Related words>^plasma cell^

<Type of relation>super.

<Related words>neoplastic clone

<Type of relation>general

<zh>浆母细胞

<Morphosyntax>noun group

<Usage label>main term

<Source>^生物通 2023^，https://www.ebiotrade.com/newsf/2022-9/202297153051262.htm

<Definition>浆母细胞是短寿命的活化B细胞，可在分裂时分泌抗体。

<Source>^生物通 2023^，https://www.ebiotrade.com/newsf/2022-9/202297153051262.htm

<Context>为了有效地产生抗体，B细胞最终从初始状态分化为分泌抗体的浆母细胞和浆细胞。浆母细胞的早期抗体应答可能来自T细胞依赖性和非依赖性活化。浆母细胞群可以来自B1细胞、MZ B细胞、FO B细胞和记忆B细胞，并有可能进一步成熟为浆细胞。

<Source>^生物通 2023^，https://www.ebiotrade.com/newsf/2022-9/202297153051262.htm

<Concept field>组织学

<Related words>^浆细胞^

<Type of relation>super.

<Related words>肿瘤性克隆

<Type of relation>general.

<Synonym>“原浆细胞”和“浆母细胞”是近义词；但是“浆母细胞”是不常使用的。

<zh>原浆细胞

<Morphosyntax>noun group

<Usage label>uncommon

<Source>^A+ 医 学 百 科 2001^ ， http://www.a-hospital.com/w/%E6%B5%86%E6%AF%8D%E7%BB%86%E8%83%9E

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>lymphopoiesis

<Morphosyntax>noun

<Source>^Sue, et al. 2018^:89

<Lexica>Found in ^Merriam/Webster 2016^

<Definition>Lymphopoiesis is a tightly regulated sequence of events that leads to the expression of a functional antigen receptor on the surface of the lymphocyte.
<Source>^Sue, et al. 2018^:89
<Context>In lymphopoiesis, for B lymphocytes, it is the B-cell receptor (BCR) that represents surface immunoglobulin molecule, and for T lymphocytes, it is the T-cell receptor (TCR) complex. Cellular micro-environment, transcription factors, and posttranscriptional regulators such as microRNAs, cytokines, and chemokines, along with silencing or activation of certain genes at different stages of lineage commitment, are some of the multiple factors contributing to a successful and mature lymphocyte.
<Source>^Sue, et al. 2018^:89
<Concept field>histology
<Related words>lymphocytes
<Type of relation>sub.
<Related words>^VJD rearrangement^
<Type of relation>general

<zh>淋巴细胞增殖
<Morphosyntax>noun group
<Source>^邵安良，等 2019^:1355
<Definition>淋巴细胞增殖是机体免疫应答过程的一个重要阶段，抗原刺激淋巴细胞产生各种细胞因子或白介素，这些细胞因子或白介素将激活并刺激淋巴细胞分化，从而使增殖反应放大。
<Source>^邵安良，等 2019^:1355
<Context>T 细胞或 B 细胞受特异性抗原或非特异性有丝分裂原刺激后，细胞代谢和形态发生变化，主要发生一系列增殖反应，进而影响机体内的免疫应答（包括刺激效应与抑制效应）。检测淋巴细胞增殖水平是细胞免疫研究和临床免疫功能检测的一种常用方法。
<Source>^邵安良，等 2019^:1355
<Concept field>组织学
<Related words>淋巴细胞
<Type of relation>sub.
<Related words>^VJD 重组^
<Type of relation>general
**
<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>VDJ rearrangement

<Morphosyntax>noun group

<Source>^Das, et al. 2011^:163

<Definition>VDJ recombination is the process by which immunoglobulins are assembled for expression during B-lymphocyte development.

<Source>^Das, et al. 2011^:163

<Context>VDJ process has two major outcomes, the generation of a functional diversified V gene and the expression of a single type of receptor per B-lymphocyte. This combinatorial diversification uses the diversity of the different V, D, and J gene segments present in the germline to generate one set of diverse combinations. The same process occurs between the V and J gene segment pools to create a chimeric segment that encodes the variable region of the L-chain.

<Source>^Das, et al. 2011^:163

<Concept field>cytology

<Related words>immunoglobulin

<Type of relation>sub.

<Related words>B-lymphocyte

<Type of relation>sub.

<Related words>variable segment

<Type of relation>sub.

<Related words>diversity segment

<Type of relation>sub.

<Related words>joining segment

<Type of relation>sub.

<zh>VJD 重组

<Morphosyntax>noun group

<Source>^Slabodkin, et al. 2021^:2209

<Definition>可变 (V)、多样性 (D) 和连接 (J) 免疫球蛋白 (Ig) 基因片段之间的重组过程决定了个体的初始 Ig 库，因此决定了（自动）抗原识别。

<Source>^Slabodkin, et al. 2021^:2209

<Context>VDJ 重组遵循可以统计建模的概率规则，但是 VDJ 重组规则是否在个体之间存在差异仍然未知。如果这些规则不同，则会以个体特异性概率生成相同的（自动）抗原特异性 Ig 序列，这表明可用的 Ig 序列空间能是个体特异性的。

<Source>^Slabodkin, et al. 2021^:2209

<Concept field>细胞学

<Related words>免疫球蛋白

<Type of relation>sub.

<Related words>B-淋巴细胞

<Type of relation>sub.

<Related words>可变基因片段

<Type of relation>sub.

<Related words>多样性基因片段

<Type of relation>sub.

<Related words>连接基因片段

<Type of relation>sub.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>immunoglobulin light chain

<Morphosyntax>noun group

<Usage label>main term

<Source>^Nakano, et al. 2011^:843

<Lexica>Found in ^Merriam/Webster 2016^

<Definition>Immunoglobulin light chain (IgLC) is a component of antibodies, while its free form is observed in the circulation, which originates from 10 to 40% excess synthesis over heavy chain, in B cells.

<Source>^Nakano, et al. 2011^:843

<Context>Light chains are asynchronously synthesized on the different ribosomes; because of the excess production of light chains over heavy chains and their secretion competency, excess light chain is secreted as a free form. The excess production of light chain over heavy chain maintains a constant intracellular pool of light chains. This pool of light chains mediates the release of the relatively insoluble heavy chains from their ribosomes and hampers the formation of toxic heavy chain aggregates.

<Source>^Nakano, et al. 2011^:843

<Concept field>histology
<Related words>^heavy chains^
<Type of relation>coord.
<Related words>antibody
<Type of relation>sub.
<Related words>B cell
<Type of relation>super.
<Synonyms>The term “immunoglobulin light chain” is often substituted by its initials “IgLC”.

<en>IgLC
<Morphosyntax>noun
<Category>initials
<Usage label>common
<Source>^Nakano, et al. 2011^:843
<Variant of>immunoglobulin light chain

<zh>免疫球蛋白轻链
<Morphosyntax>noun group
<Usage label>main term
<Source>^安必奇生物^, https://www.abace-biology.com/tech-antibody-structure.htm
<Definition>免疫球蛋白轻链是免疫球蛋白的多肽链。轻链含有一系列重复的、同源性的单元，每一单元大约有 110 个氨基酸残基，它们独立折叠成球状，称为球蛋白功能区（domain）。
<Source>^安必奇生物^, https://www.abace-biology.com/tech-antibody-structure.htm
<Context>轻链大大约由 214 个氨基酸残基组成，通常不含碳水化合物。每条轻链含有两个由链内二硫键所组成的环肽。轻链共有两型：kappa(κ)与 lambda(λ)。
<Source>cf.^安必奇生物^, https://www.abace-biology.com/tech-antibody-structure.htm
<Concept field>组织学
<Related words>^免疫球蛋白重链^
<Type of relation>coord.
<Related words>抗体
<Type of relation>sub.
<Related words>B 细胞

<Type of relation>super.

<Synonyms>“免疫球蛋白轻链”、“L 链”、“轻链” 是近义词。“轻链”是最常用的词。

<zh>L 链

<Morphosyntax>noun

<Category>initials

<Usage label>uncommon

<Source>^安必奇生物^, https://www.abace-biology.com/tech-antibody-structure.htm

<zh>轻链

<Morphosyntax>noun

<Usage label>common

<Source>^安必奇生物^, https://www.abace-biology.com/tech-antibody-structure.htm

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>immunoglobulin heavy chain

<Morphosyntax>noun group

<Source>^Janeway, et al. 2005^

<Lexica>Found in ^Merriam/Webster 2016^

<Definition>Immunoglobulin heavy chains are a component of immunoglobulin. An Ig molecule is made up of 2 identical heavy chains and disulphide bonds link the heavy chain to a light chain and link the two heavy chains together.

<Source>cf.^Janeway, et al. 2005^

<Context>Each Ig heavy chain has a variable (V) region containing the antigen-binding site and a constant (C) region that determines the isotype of the antibody and provides signalling functions. The heavy chain V region is encoded by 1 each of 3 types of genes: Variable genes, joining genes and diversity genes.

<Source>cf.^Janeway, et al. 2005^

<Concept field>histology

<Related words>^light chain^

<Type of relation>coord.

<Related words>antibody

<Type of relation>sub.

<Related words>B cell

<Type of relation>super.

<zh>免疫球蛋白重链

<Morphosyntax>noun group

<Usage label>main term

<Source>^安必奇生物^, https://www.abace-biology.com/tech-antibody-structure.htm

<Definition>免疫球蛋白重链是分子质量较大的肽链。重链都含有一系列重复的、同源性的单元，每一单元大约有 110 个氨基酸残基，它们独立折叠成球状，称为球蛋白功能区。

<Source>cf.^安必奇生物^, https://www.abace-biology.com/tech-antibody-structure.htm

<Context>重链大约含 450~550 个氨基酸残基。每条重链含有 4~5 个链内二硫键所组成的肽环。由于氨基酸组成的排列顺序以及二硫键的位置、数目等的不同，因此不同重链的抗原性也不同，根据重链抗原性的不同可将其分为五类，分别以希腊字母 γ、α、μ、δ、和 ε 表示，并以此将免疫球蛋白相应地分为 IgG、 IgA、 IgM、IgD 和 IgE。

<Source>^安必奇生物^, https://www.abace-biology.com/tech-antibody-structure.htm

<Concept field>组织学

<Related words>^免疫球蛋白轻链^

<Type of relation>coord.

<Related words>抗体

<Type of relation>sub.

<Related words>B 细胞

<Type of relation>super.

<Synonyms>“免疫球蛋白重链”、“H 链”、“重链”是近义词。“重链”是最常用的词。

<zh>H 链

<Morphosyntax>noun

<Category>initials

<Usage label>uncommon

<Source>^安必奇生物^, https://www.abace-biology.com/tech-antibody-structure.htm

<zh>重链

<Morphosyntax>noun

<Usage label>common

<Source>^安必奇生物^, https://www.abace-biology.com/tech-antibody-structure.htm

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>memory B-cells

<Morphosyntax>noun group

<Source>^Palm/Henry 2019^

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Memory B-cells are defined as long-lived and quiescent cells that are poised to quickly respond to antigen upon recall.

<Source>^Palm/Henry 2019^

<Context>Memory B cells and antibody-secreting cells (ASCs) are the product of antigen activation and, most often, interaction with cognate T helper cells. Although generation of memory B cells does require ligation of CD40 (protein required for the activation of antigen), an early burst of both memory B cells and ASCs can form independently of Germinal Centers, as well as in T-cell independent responses. In contrast, activation and differentiation of B cells within Germinal Centers allow the generation of plasma cells of high affinity that will then migrate to the bone marrow, where they can survive for decades and provide long-term humoral protection. They persist in the absence of antigen for decades after the original exposure. Although they exist in multiple lymphoid organs, the bone marrow is the home of the majority of plasma cells.

<Source>^Palm/Henry 2019^

<Concept field>histology

<Related words>antigen

<Type of relation>general

<Related words>B-cell

<Type of relation>super.

<Related words>germinal center

<Type of relation>general.

<zh>记忆B细胞

<Morphosyntax>noun group

<Source>^贾卫红，等 2009^:362

<Definition>记忆性B细胞（BM）是初次免疫应答后克隆消除保留下来的高亲和力细胞，它们有其独特的表型以及特殊的生物活性，如同Bm相似的异质性及其活化特点。
<Source>^贾卫红，等 2009^:362
<Context>记忆性B细胞对浆细胞的产生、抗体的生成以及持久的免疫保护起关键的作用。对其记忆机制还不完全明了，但最近有报道指出，Bm的长期免疫记忆机制在免疫应答及免疫保护方面起着重要的作用，在临床治疗及疫苗研制方面也起着一定的指导作用。
<Source>^贾卫红，等 2009^:362
<Concept field>组织学
<Related words>抗原
<Type of relation>general
<Related words>B 细胞
<Type of relation>super.
<Related words>生发中心
<Type of relation>general.
<Synonym>“BM”和“记忆B细胞”是近义词。

<zh>BM
<Morphosyntax>noun
<Category>initials
<Usage label>common
<Source>^贾卫红，等 2009^
<Variant of>记忆 B 细胞
**
<Subject>医学与卫生 / Medicine & health (610)
<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)
<en>activation-induced cytidine deaminase
<Morphosyntax>noun group
<Source>^Gómez-González/Aguilera 2007^:8408
<Definition>Activation-induced cytidine deaminase (AID) is a specific B cell enzyme believed to be responsible for the initiation of somatic hypermutation (SHM) and class switch recombination (CSR) during B cell differentiation.
<Source>^Gómez-González/Aguilera 2007^:8408

<Context>Activation-induced cytidine deaminase acts directly on DNA, the natural target for AID action in the variable and switch (S) regions for SHM and CSR, respectively. The specific mechanisms of AID function are still unclear, but evidence suggests that the preferential target of AID may be ssDNA (single strand DNA). Transient formation of ssDNA during transcription facilitates AID action.
<Source>^ Gómez-González/Aguilera 2007^:8408
<Concept field>histology
<Related words>^lymphopoiesis^
<Type of relation>super.
<Related words>B-cell
<Type of relation>general
<Related words>DNA
<Type of relation>general
<Synonyms>The term “activation-induced cytidine deaminase” is often substituted by its initials “AID”.

<en>AID
<Morphosyntax>noun
<Category>initials
<Usage label>common
<Source>^Gómez-González/Aguilera 2007^:8408
<Variant of>activation-induced cytidine deaminase

<zh>活化诱导性胞苷脱氨酶
<Morphosyntax>noun group
<Source>^周光全/顾伟英 2016^:350
<Definition>活化诱导胞嘧啶核苷脱氨酶是一种酵素作为基因的诱导突变体，将胞嘧啶脱氧核糖核苷酸脱氨转变为尿嘧啶脱氧核糖核苷酸，从而引起基因突变山。
<Source>^周光全/顾伟英 2016^:350
<Context>激活诱导的胞苷脱氨酶(AID)对于通过同种型类别转换和体细胞突变产生 Ig 多样性至关重要，然后直接影响克隆选择。活化的 B 细胞在稳定状态下形成生发中心并促进 B 细胞库的持续多样化。
<Source>^Bao, et al. 2022^:2632
<Concept field>组织学

<Related words>^淋巴细胞增殖^

<Type of relation>super.

<Related words>B细胞

<Type of relation>general

<Related words>DNA

<Type of relation>general

<Synonym>“活化诱导性胞苷脱氨酶”和“AID”是近义词。

<zh>AID

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^Bao, et al. 2022^:2632

<Variant of>活化诱导性胞苷脱氨酶

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>hemopoietic microenvironment

<Morphosyntax>noun group

<Source>^Mayani, et al. 1992^:225

<Definition>Hemopoietic microenvironment is a highly organized structure that regulates the location and physiology of Hemopoietic/progenitor cell (HPC).

<Source>^Mayani, et al. 1992^:225

<Context>The hemopoietic microenvironment is composed of stromal cells (fibroblasts, macrophages, endothelial cells, adipocytes), accessory cells (T lymphocytes, monocytes), and their products (extracellular matrix and cytokines). Microenvironmental cells can regulate hemopoiesis by interacting directly (cell-to-cell contact) with HPC and/or by secreting regulatory molecules that influence, in a positive or negative manner, HPC growth. Functional abnormalities of the hemopoietic microenvironment may be implicated in the manifestation of certain haematological disorders.

<Source>^Mayani, et al. 1992^:225

<Concept field>histology

<Related words>hemopoietic stem cell

<Type of relation>sub.

<Related words>^extracellular matrix^

<Type of relation>sub.

<Related words>^bone marrow stromal cell^

<Type of relation>sub.

<Related words>hemopoiesis

<Type of relation>general

<Synonym>The terms “hemopoietic microenvironment”, “hematopoietic microenvironment” and “medullary microenvironment” are synonyms and are all equally used.

<en>hematopoietic microenvironment

<Morphosyntax>noun

<Usage>common

<Source>^Greenberger 1991^:65

<en>medullary microenvironment

<Morphosyntax>noun

<Usage>common

<Source>^Mancuso 2021^:9

<zh>造血微环境

<Morphosyntax>noun group

<Source>^宫跃敏/程涛 2015^:74

<Definition>造血微环境是由一群组织细胞和细胞外基质构成的，通过细胞间接触和信号分子的作用维持和调控造血干细胞（HSC）的局部组织微环境。

<Source>^宫跃敏/程涛 2015^:74

<Context>造血微环境功能单元称为 niche。按解剖位置，骨髓造血微环境可分为骨内膜微环境和血管微环境，前者主要由成骨细胞、破骨细胞等组成，后者主要由血管内皮细胞。其他 niche 细胞包括 Nestin+间充质干细胞（MSC）、巨噬细胞、无髓鞘 Schwann 细胞等。

<Source>^宫跃敏/程涛 2015^:74

<Concept field>组织学

<Related words>造血干细胞

<Type of relation>sub.

<Related words>^细胞外基质^

<Type of relation>sub.

<Related words>^骨髓基质细胞^

<Type of relation>sub.

<Related words>造血作用

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>extracellular matrix

<Morphosyntax>noun group

<Usage label>main term

<Source>^Frantz, et al. 2010^:4195

<Definition>The extracellular matrix (ECM) is the noncellular component present within all tissues and organs and provides not only essential physical scaffolding for the cellular constituents but also initiates crucial biochemical and biomechanical cues that are required for tissue morphogenesis, differentiation and homeostasis.

<Source>^Frantz, et al. 2010^:4195

<Context>Although, the ECM is composed of water, proteins and polysaccharides, each tissue has an ECM with a unique composition and topology that is generated during tissue development through a dynamic and reciprocal, biochemical and biophysical dialogue between the various cellular components (e.g. epithelial, fibroblast, adipocyte, endothelial elements) and the evolving cellular and protein microenvironment. The ECM is a highly dynamic structure that is constantly being remodelled, either enzymatically or non-enzymatically, and its molecular components are subjected to a myriad of post-translational modifications. Through these physical and biochemical characteristics, the ECM generates the biochemical and mechanical properties of each organ, such as its tensile and compressive strength and elasticity, and also mediates protection by a buffering action that maintains extracellular homeostasis and water retention.

<Source>^Frantz, et al. 2010^:4195

<Concept field>histology

<Related words>^hemopoietic microenvironment^

<Type of relation>super.

<Related words>extracellular matrix protein

<Type of relation>sub.
<Synonyms>The term “extracellular matrix” is often substituted by its initials “ECM”.

<en>ECM
<Morphosyntax>noun
<Category>initials
<Usage label>common
<Source>^Frantz, et al. 2010^:4195
<Variant of>extracellular matrix

<zh>细胞外基质
<Morphosyntax>noun group
<Usage label>main term
<Source>^CORNING Biocoat™^, https://www.unimed.com.tw/upload/200522_053950.pdf
<Definition>细胞外基质是由动物细胞合成并分泌至胞外的大分子糖蛋白，和其所组成的复杂网状结构；细胞外基质的成份决定结缔组织的特性，常见的成份有collagen、fibronectin、及laminin等等。
<Source>^CORNING Biocoat™^, https://www.unimed.com.tw/upload/200522_053950.pdf
<Context>细胞与局部ECM之间的相互作用显示出细胞内的影响。这可能促进细胞迁移、分裂和其它细胞反应。其中一些反应包括基因表达和细胞信号级联的改变。此外，已知ECM与信号分子结合，信号分子在ECM降解时释放。由于动物细胞需要有降解和重塑细胞外基质的能力，因此，细胞通常具有分解细胞外基质所必需的酶。ECM的降解和重塑对包括血管分支在内的健康组织生长具有重要意义。另一方面，当癌细胞在体内扩散时，细胞外基质重塑也有助于癌细胞的转移。
<Source>^MyJove Corporation^, https://www.jove.com/science-education/10695/the-extracellular-matrix?language=Chinese
<Concept field>组织学
<Related words>^造血微环境^
<Type of relation>super.
<Related words>细胞外基质蛋白
<Type of relation>sub.
<Synonym>“ECM”和“细胞外基质”是近义词。

<zh>ECM
<Morphosyntax>noun
<Category>initials
<Usage label>common
<Source>^MyJove Corporation^, https://www.jove.com/science-education/10695/the-extracellular-matrix?language=Chinese
<Variant of>细胞外基质
**
<Subject>医学与卫生 / Medicine & health (610)
<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)
<en>bone marrow stromal cell
<Morphosyntax>noun group
<Usage label>main term
<Source>^Bianco, et al. 2001^:180
<Definition>Bone marrow stromal cells are progenitors of skeletal tissue components such as bone, cartilage, the haematopoiesis-supporting stroma, and adipocytes.
<Source>^Bianco, et al. 2001^:180
<Context>Marrow stromal cells showed an unexpected differentiation potential into neural tissue or muscle grant them membership in the diverse family of putative somatic stem cells. These cells exist in a number of post-natal tissues that display transgermal plasticity; that is, the ability to differentiate into cell types phenotypically unrelated to the cells in their tissue of origin. BMST have a variety of property with enormous potential therapeutic application.
<Source>cf.^Bianco, et al. 2001^:180-181
<Concept field>histology
<Related words>^osteolytic lesion^
<Type of relation>general
<Synonyms>The term “bone marrow stromal cell” is often substituted by its initials “BMSC”.

<en>BMSC
<Morphosyntax>noun
<Category>initials
<Usage label>common
<Source>^Bianco, et al. 2001^:180
<Variant of>bone marrow stromal cell

<zh>骨髓基质细胞

<Morphosyntax>noun group

<Usage label>main term

<Source>^姚红英/李小兵 2005^:123

<Definition>骨髓基质细胞是指从骨髓中分离出来后，在体外长期的细胞培养中能够附着生长的、非造血系统源的细胞。

<Source>^姚红英/李小兵 2005^:123

<Context>BMSC 在骨髓腔内相互连接成连续网状结构，通过散布于造血细胞中的基质扩展，使骨与骨髓在物理和生理上成为功能统一的结构。非造血系统中早期的BMST外表与前成骨细胞相似且分裂活跃，但在造血功能活跃的骨髓中，其有丝分裂为静止状态。骨髓基质形成动脉外膜并顺其延至窦腔。

<Source>^姚红英/李小兵 2005^:123

<Concept field>组织学

<Related words>^溶骨性病变^

<Type of relation>general

<Synonym>“BMSC”和“骨髓基质细胞”是近义词。

<zh>BMSC

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^姚红英/李小兵 2005^:123

<Variant of>骨髓基质细胞

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>signal transduction

<Morphosyntax>noun group

<Usage label>main term

<Source>^Torres/Forman 2006^:10

<Definition>Signal transduction refers to all biochemical processes by which cells translate extracellular signals originating from their environment into specific responses.

<Source>^Torres/Forman 2006^:10

<Context>Signal transduction is thought to occur through tightly organized networks in which protein–protein interactions and reversible assembly of signalling complexes are controlled by a small number of modular domains. Signal transduction is critical in regulating the lung nonrespiratory functions. Secretion of mucins by bronchial epithelial cells and surfactant by type II alveolar epithelial cells, phagocytosis and the respiratory burst by alveolar macrophages, production of cytokines by various cells, replacement of various cell types by cell division, and differentiation are among processes that are highly regulated through signalling pathways in the lung. Aberrant signal transduction underlies pathological changes such as fibroblast proliferation and cancer.
<Source>^Torres/Forman 2006^:10
<Concept field>histology

<zh>细胞信号转导
<Morphosyntax>noun group
<Source>^Sino Biological Inc.^, https://cn.sinobiological.com/research/signal-transduction
<Definition>细胞信号转导指细胞外信使分子携带的信息转化为影响细胞生物学功能的过程。
<Source>^Sino Biological Inc.^, https://cn.sinobiological.com/research/signal-transduction
<Context>细胞信号转导涉及检测、放大和整合各种外部信号，产生诸如酶活性、基因表达或离子通道活性变化等反应。细胞信号转导是许多重要物理过程的基本机制。细胞信号转导起始于细胞外信使分子及其受体之间的相互作用，如生长因子、细胞外基质和细胞粘附分子，例如细胞粘附信号中的整联蛋白、神经递质和神经递质受体。然后，信号是通过第二信使或蛋白激酶（蛋白磷酸化）在细胞内进行传递。细胞内信号转导之后，可调节细胞应答，例如转录因子发生的变化。
<Source>^Sino Biological Inc.^, https://cn.sinobiological.com/research/signal-transduction
<Concept field>组织学
**
<Subject>医学与卫生 / Medicine & health (610)
<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)
<en>apoptosis
<Morphosyntax>noun group
<Usage label>main term
<Lexica>Found in ^Merriam/Webster 2016^

<Source>^Elmore 2007^:495
<Definition>Apoptosis is a distinctive and important mode of “programmed” cell death, which involves the genetically determined elimination of cells.
<Source>^Elmore 2007^:495
<Context>The process of programmed cell death, or apoptosis, is generally characterized by distinct morphological characteristics and energy-dependent biochemical mechanisms. Apoptosis is considered a vital component of various processes including normal cell turnover, proper development and functioning of the immune system, hormone-dependent atrophy, embryonic development and chemical-induced cell death. Inappropriate apoptosis (either too little or too much) is a factor in many human conditions including neurodegenerative diseases, ischemic damage, autoimmune disorders, and many types of cancer. The ability to modulate the life or death of a cell is recognized for its immense therapeutic potential.
<Source>^Elmore 2007^:495
<Concept field>histology
<Related words>osteoporosis
<Type of relation>general
<Related words>drug resistance
<Type of relation>general
<Synonyms>The terms “cell suicide” and “programmed cell death” are synonyms to “apoptosis”; while the use of the expression “cells suicide” is not very common, the expression “programmed cell death” is frequently used to substitute the term “apoptosis” or in combination with it.

<en>cell suicide
<Morphosyntax>noun group
<Usage label>uncommon
<Source>^Merriam/Webster 2016^

<en>programmed cell death
<Morphosyntax>noun group
<Usage label>common
<Source>^Merriam/Webster 2016^

<zh>细胞凋亡
<Morphosyntax>noun group

<Usage label>main term

<Source>^楊繼江 2005^:9

<Definition>细胞凋亡是在生物进化中保存下来的一种导致细胞程序性死亡的基本调节机制。

<Source>^楊繼江 2005^:9

<Context>根据细胞的种类不同可产生各种不同的细胞凋亡传导途径。细胞凋亡与自身免疫性疾病、病毒感染性疾病、神经变异性疾病等多种疾病的发生、发展相关。

<Source>^楊繼江 2005^:9

<Concept field>组织学

<Related words>骨质疏松症

<Type of relation>general

<Related words>耐药性

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>relapsed refractory multiple myeloma

<Morphosyntax>noun group

<Usage label>main term

<Source>^Sonneveld/Broijl 2016^:396

<Definition>Relapsed/refractory MM (RRMM) is defined as a disease which becomes non-responsive or progressive on therapy or within 60 days of the last treatment in patients who had achieved a minimal response (MR) or better on prior therapy.

<Source>^Sonneveld/Broijl 2016^:396

<Context>RRMM is still inevitable in the majority of patients, including those who achieved deep remissions becoming progressively shorter. Criteria for RRMM include the IMWG criteria for progressive disease (PD), progressive disease on treatment or after at least minimal response (MR), or progressive disease ≤60 days following the most recent treatment, the absence of at least minimal response on a given therapy (primary refractory disease), the presence of PD criteria in the absence of features for RRMM, or primary refractory MM. Treatment goals vary among patients with RRMM and should consider disease control, extension of survival, and maintenance of quality of life (QoL). Specifically, in frail MM patients, treatment should focus

on symptom relief rather than on attaining a deep and durable response. In contrast, in patients with aggressive disease, treatment should be initiated immediately.
<Source>^Podar/Leleu 2021^
<Concept field>haematology
<Related words>^multiple myeloma^
<Type of relation>super.
<Related words>drug resistance
<Type of relation>general
<Synonyms>The term “relapsed refractory multiple myeloma” is often substituted by its initials “RRMM”.

<en>RRMM
<Morphosyntax>noun
<Category>initials
<Usage label>common
<Source>^Podar/Leleu 2021^
<Variant of>relapsed refractory multiple myeloma

<zh>复发难治性多发性骨髓瘤
<Morphosyntax>noun group
<Usage label>main term
<Source>^施菊妹 2014^，https://www.haodf.com/neirong/wenzhang/1367968924.html
<Definition>复发且难治性 MM 是指对挽救性治疗无反应，或在接受末次治疗达微小缓解(MR)后，60 天内出现疾病进展的患者。
<Source>^施菊妹 2014^，https://www.haodf.com/neirong/wenzhang/1367968924.html
<Context>残留的骨髓瘤干细胞是 MM 复发的根源，而其生物学改变以及耐药克隆的增加是MM耐药的主要原因。同时药物转运障碍、骨髓微环境和克隆性浆细胞相互作用、细胞黏附等因素也在 MM 耐药中发挥重要作用。因此，复发、难治 MM 的治疗关键在于尽可能清除骨髓瘤王细胞，千扰骨髓瘤细胞和骨髓微环不境之间的相互作用，从而延缓疾病复发，克服 MM 的耐药性。
<Source>^施菊妹 2014^，https://www.haodf.com/neirong/wenzhang/1367968924.html
<Concept field>血液学
<Related words>^多发性骨髓瘤^

<Type of relation>super.

<Related words>耐药性

<Type of relation>general

<Synonym>“复发难治性MM”和“复发难治性多发性骨髓瘤”是近义词。

<zh>复发难治性 MM

<Morphosyntax>noun

<Category>abbreviation

<Usage label>common

<Source>^施菊妹 2014^，https://www.haodf.com/neirong/wenzhang/1367968924.html

<Variant of>复发难治性多发性骨髓瘤

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>angiogenesis

<Morphosyntax>noun

<Usage label>main term

<Source>^Makrilia, et al. 2009^:663

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Angiogenesis is the physiological process of the formation of new blood vessels from pre-existing ones.

<Source>^Makrilia, et al. 2009^:663

<Context>Multiple molecules regulate angiogenesis, such as the vascular endothelial growth factor, angiopoietins, the fibroblast growth factor, the platelet-derived growth factor, and the transforming growth factor-β. Angiogenesis plays an important role in the growth, progression and metastasis of a tumour. Inhibiting the angiogenic process or targeting existing tumour vessels can be used for treatment of tumours as an alternative or in parallel with conventional chemotherapy.

<Source>^Makrilia, et al. 2009^:663

<Concept field>haematology

<Related words>^multiple myeloma^

<Type of relation>super.

<Related words>blood vessel

<Type of relation>sub.

<Related words>^vascular endothelial growth factor^

<Type of relation>sub.

<zh>血管新生

<Morphosyntax>noun group

<Source>^陳俊宏 2014^, https://highscope.ch.ntu.edu.tw/wordpress/?p=26705

<Definition>血管新生是人体一种正常的生理现象。当组织中需要血管时，有一些促使因子的分泌量会增加，以造就新血管的生长机会。

<Source>^陳俊宏 2014^, https://highscope.ch.ntu.edu.tw/wordpress/?p=26705

<Context>血管新生和癌细胞的生长亦有重大关系。癌细胞本身或周围的结缔组织，会分泌许多促使血管新生的物质，例如血管内皮细胞生长因子（VEGF），这些物质会活化血管内皮细胞，形成新的微血管。肿瘤内新生的血管系统和正常组织大不相同，这些血管弯弯曲曲异常混乱，没有任何规则可循。血管内的血液流速也很怪异，有些流动快速，有些则血流迟滞。这些种种异常的情形，造成肿瘤内微环境状况特殊，同时也使得肿瘤的治疗窒碍难行。由于血管新生是肿瘤生长坐大的必经过程，理论上若能适时抑制血管新生，应能抑制肿瘤的生长。根据这项理论，目前医学上发展出一种抗癌的新策略，称为“抗血管新生疗法”。

<Source>^陳俊宏 2014^, https://highscope.ch.ntu.edu.tw/wordpress/?p=26705

<Concept field>血液学

<Related words>^多发性骨髓瘤^

<Type of relation>super.

<Related words>血管

<Type of relation>sub.

<Related words>^血管内皮生长因子^

<Type of relation>sub.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>angiogenic switch

<Morphosyntax>noun group

<Source>^Baeriswyl/Christofori 2009^:329

<Definition>Angiogenic switch refers to a time-restricted event during tumour progression where the balance between pro- and anti-angiogenic factors tilts towards a pro-angiogenic outcome, resulting in the transition from dormant avascularised hyperplasia to outgrowing vascularized tumour and eventually to malignant tumour progression.
<Source>^Baeriswyl/Christofori 2009^:329
<Context>As the angiogenic switch is controlled by changes in the fine-tuned balance between pro- and anti-angiogenic factors secreted either by tumour cells or by cells of the tumour microenvironment, various angiogenic factors and different cells of the tumour microenvironment contribute to the occurrence of the angiogenic switch. To inhibit the angiogenic switch various pro- and anti-angiogenic therapies that are currently tested in clinical trials or are already in clinical use.
<Source>^Baeriswyl/Christofori 2009^:329
<Concept field>cytology
<Related words>^angiogenesis^
<Type of relation>super.
<Related words>blood vessel
<Type of relation>sub.
<Related words>^vascular endothelial growth factor^
<Type of relation>sub.
<Related words>tumour mass
<Type of relation>sub.

<zh>血管新生开关
<Morphosyntax>noun group
<Source>^吴銘斌，等 2004^:125
<Definition>这种血管新生开关是基于平衡假说，由血管新生促进因子与抑制因子两者互相撷抗所控制。在不同种类肿瘤，血管新生开关启动的时间点，可发生在转变为恶性肿瘤之前、转变为恶性肿瘤的同时、或转变为恶性肿瘤之后发生。
<Source>^吴銘斌，等 2004^:125
<Context>肿瘤的生长与血管新生是密不可分的，当肿瘤长到 1-2 mm 大小以上时，即必须有血管新生开关启动的现象才能维持肿瘤继续生长。抗血管新生疗法是一种新型对抗癌症的策略。借着降低血管新生促进因子或增加血管新生抑制因子等方法，特异性地抑制肿瘤血管的内皮细胞，而造成肿瘤的萎缩，称之为蛰伏疗法。使用抗血管新生疗法于

治疗肿瘤，是以肿瘤血管的内皮细胞为攻击标的，而非肿瘤细胞本身为攻击标的，所以抗血管新生疗法比起传统化学疗法是更具疗效的潜力。

<Source>^吳銘斌，等 2004^:125

<Concept field>细胞学

<Related words>^血管新生^

<Type of relation>super.

<Related words>血管

<Type of relation>sub.

<Related words>^血管内皮生长因子^

<Type of relation>sub.

<Related words>肿瘤肿块

<Type of relation>sub.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>vascular endothelial growth factor

<Morphosyntax>noun group

<Usage label>main term

<Lexica>Found in ^Merriam/Webster 2016^

<Source>^Melincovici, et al. 2018^:455

<Definition>Vascular endothelial growth factor (VEGF) represents a growth factor with important pro-angiogenic activity, having a mitogenic and an anti-apoptotic effect on endothelial cells, increasing the vascular permeability, promoting cell migration, etc.. Due to these effects, it actively contributes in regulating the normal and pathological angiogenic processes.

<Source>^Melincovici, et al. 2018^:455

<Context>VEGF plays an important role in pathological angiogenesis, inducing the development and progression of certain pathological conditions in the postnatal period, such as: tumour growth and metastasis, macular degeneration, diabetic retinopathy, inflammatory processes (e.g., rheumatoid arthritis), ischemic processes (myocardial ischemia), preeclampsia, etc. In humans, the VEGF family includes several members that perform various functions.

<Source>^Melincovici, et al. 2018^:455

<Concept field>histology

<Related words>^angiogenesis^

<Type of relation>super.
<Related words>^angiogenic switch^
<Type of relation>general
<Related words>blood vessel
<Type of relation>general
<Related words>tumour mass
<Type of relation> general
<Synonyms>The term “vascular endothelial growth factor” is often substituted by its initials “VEGF”.

<en>VEGF
<Morphosyntax>noun
<Category>initials
<Source>^Melincovici, et al. 2018^:455
<Variant of>vascular endothelial growth factor

<zh>血管内皮生长因子
<Morphosyntax>noun group
<Usage label>main term
<Source>^Abcam plc^, https://www.abcam.cn/cancer/the-role-of-vegf-in-angiogenesis-3
<Definition>血管内皮生长因子（VEGF）是新血管形成的关键因素。VEGF 能诱导已有血管的再生（血管再生）或新血管的生长（血管发生），因此是胚胎发育、血管修复的关键。VEGF 还能被实体瘤所用，促进实体瘤的生长。
<Source>^Abcam plc^, https://www.abcam.cn/cancer/the-role-of-vegf-in-angiogenesis-3
<Context>VEGF 在不同类型的细胞（比如肌肉细胞、神经元细胞）中均有活性，但是它主要作用于内皮细胞。胚胎发育过程中，可观察到 VEGF 高表达；在此过程中，VEGF 与多种胚胎发育因子协同控制新血管的形成。出生后，VEGF 的表达显著减少。但是，在进行伤口愈合或骨折修复的组织中，VEGF 的局部表达水平会上调。VEGF 及其家族成员的免疫组化分析与多种癌症的预后相关。
<Source>^Abcam plc^, https://www.abcam.cn/cancer/the-role-of-vegf-in-angiogenesis-3
<Concept field>组织学
<Related words>^血管新生^
<Type of relation>super.
<Related words>^血管新生开关^

<Type of relation>general

<Related words>血管

<Type of relation>general

<Related words>肿瘤肿块

<Type of relation>general

<Synonym>“VEFG”和“血管内皮生长因子”是近义词。

<zh>VEGF

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^Abcam plc^, https://www.abcam.cn/cancer/the-role-of-vegf-in-angiogenesis-3

<Variant of>血管内皮生长因子

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>calcinosis

<Morphosyntax>noun

<Usage label>main term

<Source>^Elahmar, et al. 2022^:980

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Calcinosis refers to deposition of calcium salts (hydroxyapatite and calcium phosphate crystal) in the skin.

<Source>cf.^Elahmar, et al. 2022^:980

<Context>Calcinosis within the extracellular matrix of the dermis and subcutaneous tissue is a frequent manifestation of adult and paediatric systemic autoimmune rheumatic diseases, specifically systemic sclerosis, dermatomyositis, mixed connective tissue disease, and systemic lupus erythematosus. Calcinosis can be classified into 5 subtypes: dystrophic, metastatic, idiopathic, tumoral, and calciphylaxis. Dystrophic presents as nodules, plaques, extensive small dermal, or large subcutaneous deposits; metastatic is seen occasionally in the skin subcutaneous tissue as hard nodules located mainly in the vicinity of large joints; idiopathic is characterized by multiple, asymptomatic nodules, which begin to appear in childhood or in early adult life; tumoral presents as large subcutaneous calcium deposits near joints and pressure areas; calciphylaxis shows subcutaneous nodules of infarction vessel and necrotizing skin ulcers.

<Source>cf.^Elahmar, et al. 2022^:980-981

<Concept field>symptoms

<Related words>^hypercalcemia^

<Type of relation>coord.

<Related words>^osteolytic lesion^

<Type of relation>super.

<Synonyms>The term “calcinosis cutis” is a synonym to “calcinosis” but it is hardly used.

<en>calcinosis cutis

<Morphosyntax>noun

<Usage label>uncommon

<Source>^Elahmar, et al. 2022^:980

<zh>皮肤钙化

<Morphosyntax>noun group

<Source>^Fernandez/Ward 2021^, https://www.uptodate.com/contents/zh-Hans/calcinosis-cutis-etiology-and-patient-evaluation

<Definition>皮肤钙化是指不可溶的钙盐在皮肤和皮下组织中沉积。

<Source>^Fernandez/Ward 2021^, https://www.uptodate.com/contents/zh-Hans/calcinosis-cutis-etiology-and-patient-evaluation

<Context>根据钙沉积的病因，皮肤钙化有 5 种类型：营养不良性、转移性、特发性、医源性和钙化防御。1.营养不良性皮肤钙化–由局部组织损伤导致，全身钙代谢正常。2.转移性皮肤钙化–病因是钙或磷代谢异常，导致钙沉积在皮肤和皮下组织中。3.特发性皮肤钙化–没有任何基础组织损伤和代谢障碍时发生的皮肤钙化。4.医源性皮肤钙化–钙盐沉积于皮肤是对其他疾病进行医疗干预的副作用。5.钙化-钙化表现为中小血管的钙化，特别是真皮或皮下组织的钙化。这被认为是由于钙和磷酸盐的代谢紊乱而发生的；常常存在甲状旁腺功能亢进。

<Source>^Fernandez/Ward 2021^, https://www.uptodate.com/contents/zh-Hans/calcinosis-cutis-etiology-and-patient-evaluation

<Concept field>症状

<Related words>^高钙血症^

<Type of relation>coord.

<Related words>^溶骨性病变^

<Type of relation>super.
**
<Subject>医学与卫生 / Medicine & health (610)
<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)
<en>bone remodelling
<Morphosyntax>noun group
<Source>^Hadjidakis/Androulakis 2006^:385
<Definition>Bone remodelling is a process which involves the removal of mineralized bone by osteoclasts followed by the formation of bone matrix through the osteoblasts that subsequently be-come mineralized.
<Source>^Hadjidakis/Androulakis 2006^:385
<Context>The remodelling cycle consists of three consecutive phases: resorption, during which osteoclasts digest old bone; reversal, when mononuclear cells appear on the bone surface; and formation, when osteoblasts lay down new bone until the resorbed bone is completely replaced. Bone remodelling serves to adjust bone architecture to meet changing mechanical needs and it helps to repair microdamage in bone matrix preventing the accumulation of old bone.
<Source>^Hadjidakis/Androulakis 2006^:385
<Concept field>histology
<Related words>^osteolytic lesion^
<Type of relation>general
<Related words>^osteoclast^
<Type of relation>general
<Related words>^osteoblast^
<Type of relation>general

<zh>骨重塑
<Morphosyntax>noun group
<Source>^王雪娥/陳明宏 2004^:68
<Definition>骨重塑是指老旧的骨组织由饮骨细胞吸收后，再由成骨细胞形成新骨，这是—个反覆循环的反应。
<Source>^王雪娥/陳明宏 2004^:68
<Context>骨重塑生化标记随着每天的日韵律、每月的月经周期、每年的季节变化，及饮食、运动和任何改变骨重塑的因素等，呈波动性变化。生体骨重塑的活性与本衡，可以藉由测量血液或尿液中的生化标记，包括触骨标记如胶原蛋白片断、造骨标记如碱性

磷酸酶，来作为判断依据。骨质流失是因旧骨的吸收速率大于新骨的形成速率，开始于中年以后或更早，许多疾病或是生理状态上雌激素的缺乏会加重此种不衡。

<Source>^王雪娥/陳明宏 2004^:68

<Concept field>组织学

<Related words>^溶骨性病变^

<Type of relation>general

<Related words>^破骨细胞^

<Type of relation>general

<Related words>^成骨细胞^

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>osteoclast

<Morphosyntax>noun

<Source>^Boyce, et al. 2009^:171

<Lexica>Found in ^Merriam-Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Osteoclasts are the cells that degrade bone to initiate normal bone remodelling and mediate bone loss in pathologic conditions by increasing their resorptive activity.

<Source>^Boyce, et al. 2009^:171

<Context>Osteoclasts are derived from precursors in the monocyte lineage that circulate in the blood after their formation in the bone marrow. These osteoclast precursors (OCPs) are attracted to sites on bone surfaces destined for resorption and fuse with one another to form the multinucleated cells that resorb calcified matrixes under the influence of osteoblastic cells in bone marrow. OCPs and osteoclasts regulate the differentiation of osteoblast precursors and the movement of hematopoietic stem cells from the bone marrow to the bloodstream; they participate in immune responses and secrete cytokines that can affect their own functions and those of other cells in inflammatory and neoplastic processes affecting bone.

<Source>^Boyce, et al. 2009^:171

<Concept field>histology

<Related words>^osteoblast^

<Type of relation>coord.

<Related words>^bone remodelling^

<Type of relation>super.

<Related words>^osteolytic lesion^

<Type of relation>general

<zh>破骨细胞

<Morphosyntax>noun group

<Source>^石玉 2021^:504

<Definition>破骨细胞是一种个体大、多细胞核、在体内负责吸收骨基质的细胞，同时也是维持骨稳态的主要细胞种类。

<Source>^石玉 2021^:504

<Context>破骨细胞是骨骼系统中重要的细胞类型，直接参与并影响成 年个体的骨骼重建。由破骨细胞介导的骨吸收共同调控着骨稳态；如果骨形成与骨吸收的平衡被打破，极易造成骨量丢失，进而导致骨质疏松的发生。因此，研究对破骨细胞的分化、活性和功能的调控机制对于更好地了解骨质疏松的发病原理以及 发现新的治疗方案至关重要。

<Source>cf.^石玉 2021^:502

<Concept field>组织学

<Related words>^成骨细胞^

<Type of relation>coord.

<Related words>^骨重塑^

<Type of relation>super.

<Related words>^溶骨性病变^

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>osteoblast

<Morphosyntax>noun

<Source>^Bassi, et al. 2011^:95

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Osteoblasts are mononucleate cuboid cells that are responsible for bone formation.

<Source>^Bassi, et al. 2011^:95

<Context>Osteoblasts originate from immature mesenchymal stem cells, which can also differentiate and give rise to chondrocytes, muscle, fat, ligament, and tendon cells. Mesenchymal stem cells undergo several transcription steps to form mature osteoblast cells.

Osteoblasts produce alkaline phosphatase, an enzyme that is involved in the mineralization of bone. Alkaline phosphatase is an early marker of osteoblast differentiation, and its increased expression is associated with the progressive differentiation of osteoblasts.
<Source>cf.^Bassi, et al. 2011^:95-96
<Concept field>histology
<Related words>^osteoclast^
<Type of relation>coord.
<Related words>^bone remodelling^
<Type of relation>super.
<Related words>^osteolytic lesion^
<Type of relation>general

<zh>成骨细胞
<Morphosyntax>noun group
<Usage label>main term
<Source>^陈珺，等 2017^:1491
<Definition>成骨细胞是维持骨代谢平衡的主要功能细胞，负责骨基质的合成、分泌和矿化。
<Source>^陈珺，等 2017^:1491
<Context>成骨细胞数量和功能情况直接影响着代谢性骨病的发生发展，因此，研究不同因素对成骨细胞的调节作用，也是目前代谢性骨病药物研发的主要内容。
<Source>^陈珺，等 2017^:1491
<Concept field>组织学
<Related words>^破骨细胞^
<Type of relation>coord.
<Related words>^骨重塑^
<Type of relation>super.
<Related words>^溶骨性病变^
<Type of relation>general
**
<Subject>化学和相关科学 / Chemistry and allied sciences (540)
<Subfield>有机化学/ Organic chemistry (547)
<en>alachlor

<Morphosyntax>noun

<Usage label>main term

<Source>^National Center for Biotechnology Information 2023^, https://pubchem.ncbi.nlm.nih.gov/compound/Alachlor

<Definition>Alachlor is an aromatic amide that is N-(2,6 diethypheniyl)acetamide substituted by a methoxymethyl group at the nitrogen atom while one of the hydrogens of the methyl group has been replaced by a chlorine atom. It has a role as an herbicide, an environmental contaminant, and a xenobiotic.

<Source>^National Center for Biotechnology Information 2023^, https://pubchem.ncbi.nlm.nih.gov/compound/Alachlor

<Context>Alachlor is an organochlorine compound, a monocarboxylic acid amide and an aromatic amide. Alachlor belongs to the family of Anilides. Alachlor is a selective preemergent herbicide used on food crops.

<Source>^National Center for Biotechnology Information 2023^, https://pubchem.ncbi.nlm.nih.gov/compound/Alachlor

<Concept field>chemical compounds

<Synonyms>“metachlor” and “alachlor” are synonyms and they are both commonly used to identify this herbicide.

<en>metachlor

<Morphosyntax>noun

<Usage label>common

<Source>^National Center for Biotechnology Information 2023^, https://pubchem.ncbi.nlm.nih.gov/compound/Alachlor

<zh>甲草胺

<Morphosyntax>noun

<Source>^徐磊 2019^, http://www.agroinfo.com.cn/other_detail_7367.html

<Definition>甲草胺是防除多种一年生单子叶和某些双子叶杂草的选择性旱地芽前除草剂。

<Source>^徐磊 2019^, http://www.agroinfo.com.cn/other_detail_7367.html

<Context>甲草胺常用于大豆、玉米、花生、棉花、马铃薯、甘蔗、油菜等作物田，防除稗草、马唐、蟋蟀草、狗尾草、秋稗、臂形草、马齿苋、苋、轮生粟米草、藜、蓼等一年生禾本科杂草和阔叶杂草。甲草胺主要作用于芽前，通过杂草的芽鞘吸收，阻碍其

蛋白质合成，进而导致杂草死亡。对已出土杂草无效，一般防除效果甲草胺低于异丙甲草胺和乙草胺。由于甲草胺对水生生物有极高毒性，可能对水体环境产生不良影响，故只能使用于旱地。

<Source>^徐磊 2019^, http://www.agroinfo.com.cn/other_detail_7367.html

<Concept field>化合物

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病的发病率和预防/ Incidence and prevention of disease (614)

<en>fluorescent in situ hybridization

<Morphosyntax>noun group

<Usage label>main term

<Source>^Cui, et al. 2016^:1

<Lexica>Found in ^Oxford Concise Medical Dictionary 2020^

<Definition>Fluorescence in situ hybridization (FISH) is a hybridization-based macromolecule recognition tool which uses DNA fragments incorporated with fluorophore-coupled nucleotides as probes to examine the presence or absence of complementary sequences in fixed cells or tissues under a fluorescent microscope.

<Source>^Cui, et al. 2016^:1

<Context>Fluorescence in situ hybridization was initially developed as a physical mapping tool to delineate genes within chromosomes. Its high analytical resolution to a single gene level and high sensitivity and specificity enabled an immediate application for genetic diagnosis of constitutional common aneuploidies, microdeletion/microduplication syndromes, and subtelomeric rearrangements. FISH has also been used to detect infectious microbias and parasites like malaria in human blood cells. Clinical application of FISH technology had upgraded classical cytogenetics to molecular cytogenetics.

<Source>^Cui, et al. 2016^:1-2

<Concept field>laboratory test

<Related words>bone marrow

<Type of relation>general

<Related words>chromosomal set

<Type of relation>general

<Related words>^plasma cell^

<Type of relation>general

<Synonyms>The term “fluorescent in situ hybridization” is often substituted by its initials “FISH”.

<en>FISH
<Morphosyntax>noun
<Category>acronym
<Usage label>
<Source>^Cui, et al. 2016^:1
<Variant of>fluorescent in situ hybridization

<zh>萤光原位杂交
<Morphosyntax>noun group
<Usage label>main term
<Source>^義大醫療財團法人。醫學檢驗部 2023^，https://exdep.edah.org.tw/cp/index.php/2017-06-26-08-19-55/2017-06-28-09-06-14/539-fish-analysis
<Definition>萤光原位杂交（FISH）是一种细胞遗传学技术，可以用来对核酸进行检测和定位。萤光标记的核酸探针只和具有高度相似性的核酸杂交，可用于染色体上基因的定位。
<Source>^義大醫療財團法人。醫學檢驗部 2023^，https://exdep.edah.org.tw/cp/index.php/2017-06-26-08-19-55/2017-06-28-09-06-14/539-fish-analysis
<Context>萤光原位杂交(FISH)，检测染色体某区域是否有缺失。须注意：FISH 无法侦测某些致病遗传缺失，如染色体缺失不在侦测区域内、点突变或臂内倒位，遗传诊断需配合细胞遗传学分析结果与临床资讯。
<Source>^義大醫療財團法人。醫學檢驗部 2023^，https://exdep.edah.org.tw/cp/index.php/2017-06-26-08-19-55/2017-06-28-09-06-14/539-fish-analysis
<Concept field>实验室检查
<Related words>骨髓
<Type of relation>general
<Related words>染色体组
<Type of relation>general

<Related words>^浆细胞^

<Type of relation>general

<Synonym>“FISH”和“萤光原位杂交”是近义词。

<zh>FISH

<Morphosyntax>noun

<Category>acronym

<Usage label>common

<Source>^義大醫療財團法人。醫學檢驗部 2023^，https://exdep.edah.org.tw/cp/index.php/2017-06-26-08-19-55/2017-06-28-09-06-14/539-fish-analysis

<Variant of>萤光原位杂交

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>diabetes mellitus

<Morphosyntax>noun group

<Usage label>main term

<Source>^America Diabetes Association 2011^:62

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Diabetes mellitus is a group of metabolic diseases characterized by hyperglycaemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycaemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels.

<Source>^America Diabetes Association 2011^:62

<Context>The basis of the abnormalities in carbohydrate, fat, and protein metabolism in diabetes is deficient action of insulin on target tissues. Deficient insulin action results from inadequate insulin secretion and/or diminished tissue responses to insulin at one or more points in the complex pathways of hormone action. Symptoms of marked hyperglycaemia include polyuria, polydipsia, weight loss, sometimes with polyphagia, and blurred vision. The vast majority of cases of diabetes fall into two broad etiopathogenetic categories. In one category, type 1 diabetes, the cause is an absolute deficiency of insulin secretion. In the other, much more prevalent category, type 2 diabetes, the cause is a combination of resistance to insulin action and an inadequate compensatory insulin secretory response.

<Source>^America Diabetes Association 2011^:62-63

<Concept field>risk factor

<Related words>type 1 Diabetes

<Type of relation>sub.

<Related words>type 2 Diabetes

<Type of relation>sub.

<Synonyms>The term “diabetes” is a synonym to “diabetes mellitus” and it is commonly used.

<en>diabetes

<Morphosyntax>noun

<Usage label>common

<Source>^America Diabetes Association 2011^:62

<zh>糖尿病

<Morphosyntax>noun

<Usage label>main term

<Source>^World Trade Organization 2023^, https://www.who.int/zh/news-room/fact-sheets/detail/diabetes

<Definition>糖尿病是一种慢性病。当胰腺产生不了足够胰岛素或者人体无法有效地利用所产生的胰岛素时，就会出现糖尿病。胰岛素是一种调节血糖的荷尔蒙。高血糖或血糖升高是糖尿病失控的常见后果，随着时间的推移会对人体的许多系统（特别是神经和血管）带来严重损害。

<Source>^World Trade Organization 2023^, https://www.who.int/zh/news-room/fact-sheets/detail/diabetes

<Context>糖尿病患者出现健康问题的风险更高，包括心脏病发作、卒中和肾衰竭。糖尿病会损害眼睛中的血管，从而导致永久性视力损失。许多糖尿病患者因神经损伤和血流不畅而出现脚部问题。这可能导致足部溃疡，并可能导致截肢。1 型糖尿病的特征是胰岛素分泌不足，需要每日输入胰岛素。2 型糖尿病影响身体使用糖（葡萄糖）作为能量的方式。它阻止身体正确使用胰岛素，如果不治疗，会导致血糖升高。

<Source>^World Trade Organization 2023^, https://www.who.int/zh/news-room/fact-sheets/detail/diabetes

<Concept field>风险因素

<Related words>1型糖尿病

<Type of relation>sub.

<Related words>2型糖尿病

<Type of relation>sub.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>ankylosing spondylitis

<Morphosyntax>noun group

<Usage label>main term

<Source>^Yaseen 2022^, https://www.msdmanuals.com/professional/musculoskeletal-and-connective-tissue-disorders/joint-disorders/ankylosing-spondylitis

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Ankylosing spondylitis is the prototypical spondyloarthropathy and a systemic disorder characterized by inflammation of the axial skeleton, large peripheral joints, and digits; nocturnal back pain; back stiffness; accentuated kyphosis; constitutional symptoms; aortitis; cardiac conduction abnormalities; and anterior uveitis.

<Source>^Yaseen 2022^, https://www.msdmanuals.com/professional/musculoskeletal-and-connective-tissue-disorders/joint-disorders/ankylosing-spondylitis

<Context>Ankylosing spondylitis is 3 times more frequent in men than in women and begins most often between ages 20 and 40. The most frequent manifestation of ankylosing spondylitis is inflammatory back pain, but disease can begin in peripheral joints, especially in children and women, and rarely with acute iridocyclitis (iritis, anterior uveitis). Other early symptoms and signs are diminished chest expansion from diffuse costovertebral involvement, and occasionally fatigue, anorexia, weight loss, and anaemia.

<Source>^Yaseen 2022^, https://www.msdmanuals.com/professional/musculoskeletal-and-connective-tissue-disorders/joint-disorders/ankylosing-spondylitis

<Concept field>risk factor

<Related words>autoimmune disease

<Type of relation>super.

<Related words>^system sclerosis^

<Type of relation>general

<Related words>^pernicious anaemia^

<Type of relation>general

<Synonyms>The terms “spondylitis”, “Marie-Strümpell disease” and “rheumatoid spondylitis” are all synonyms of the term “Ankylosing spondylitis”; however, while the terms

“spondylitis” is of common use, the terms “Marie-Strümpell disease” and “rheumatoid spondylitis” are not commonly used and are reserved to very technical context.

<en>spondylitis
<Morphosyntax>noun
<Usage label>common
<Source>^Oxford Concise Medical Dictionary 2020^

<en>Marie-Strümpell disease
<Morphosyntax>noun group
<Usage label>uncommon
<Source>^Merriam/Webster 2016^

<en>rheumatoid spondylitis
<Morphosyntax>noun group
<Usage label>uncommon
<Source>^Merriam/Webster 2016^

<zh>强直性脊柱炎
<Morphosyntax>noun group
<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/diseases-conditions/ankylosing-spondylitis/symptoms-causes/syc-20354808
<Definition>强直性脊柱炎是一种炎症性疾病，随着时间的推移可能导致脊柱中部分骨骼（椎骨）融合。
<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/diseases-conditions/ankylosing-spondylitis/symptoms-causes/syc-20354808
<Context>强直性脊柱炎降低脊柱灵活性，可能导致弓形姿势。如果肋骨受累，可能难以进行深呼吸。体征和症状通常始于青年时期。强直性脊柱炎无法治愈，但是治疗可以减轻症状并可能延缓病情进展。强直性脊柱炎在早期可能会出现下背部和髋部的疼痛和僵硬等症状。颈部疼痛和疲劳也很常见。随着时间的推移，症状可能会加重、改善或不定期停止。
<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/diseases-conditions/ankylosing-spondylitis/symptoms-causes/syc-20354808
<Concept field>风险因素

<Related words>自身免疫性疾病

<Type of relation>super.

<Related words>^全身性硬化症^

<Type of relation>general

<Related words>^巨幼细胞性贫血^

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>systemic sclerosis

<Morphosyntax>noun group

<Usage label>main term

<Source>^Nevares 2022^, https://www.msdmanuals.com/professional/musculoskeletal-and-connective-tissue-disorders/autoimmune-rheumatic-disorders/systemic-sclerosis

<Lexica>Found in ^Oxford Concise Medical Dictionary 2020^

<Definition>Systemic sclerosis is a rare chronic disease of unknown cause characterized by diffuse fibrosis and vascular abnormalities in the skin, joints, and internal organs (especially the oesophagus, lower gastrointestinal tract, lungs, heart, and kidneys).

<Source>^Nevares 2022^, https://www.msdmanuals.com/professional/musculoskeletal-and-connective-tissue-disorders/autoimmune-rheumatic-disorders/systemic-sclerosis

<Context>Systemic sclerosis common symptoms include Raynaud syndrome, polyarthralgia, dysphagia, heartburn, and swelling and eventually skin tightening and contractures of the fingers. Lung, heart, and kidney involvement accounts for most deaths. Diagnosis is clinical, but laboratory tests support the diagnosis and aid in prognostication. Specific treatment is difficult, and emphasis is often on treatment of complications. Systemic sclerosis is classified as: limited systemic sclerosis in which patients develop skin tightening over the face and distal to the elbows and knees and may also have gastroesophageal reflux disease; generalized systemic sclerosis with diffuse skin involvement, in which patients have Raynaud syndrome and gastrointestinal (GI) complications; systemic sclerosis sine scleroderma, in which patients have systemic sclerosis–related antibodies and visceral manifestations of the disease but no skin tightening.

<Source>^Nevares 2022^, https://www.msdmanuals.com/professional/musculoskeletal-and-connective-tissue-disorders/autoimmune-rheumatic-disorders/systemic-sclerosis

<Concept field>risk factors

<Related words>autoimmune disease
<Type of relation>super.
<Related words>^ankylosing spondylitis^
<Type of relation>general
<Related words>^pernicious anaemia^
<Type of relation>general
<Synonyms>The term “scleroderma” is a synonym to “system sclerosis” and it is commonly used.

<en>scleroderma
<Morphosyntax>noun
<Usage label>common
<Source>^Oxford Concise Medical Dictionary 2020^

<zh>全身性硬化症
<Morphosyntax>noun
<Usage label>main term
<Source>^陳依伶，等 2016^
<Definition>全身性硬化症(SSc)是以微血管病变为主的自体免疫疾病。免疫的失调、纤维母细胞的功能异常导致自体免疫抗体形成、血管壁异常增生、组织缺血以及细胞外基质增生沉积，持续的免疫系统活化发炎导致皮肤与内脏器官的纤维化与失能。
<Source>^陳依伶，等 2016^
<Context>典型的临床表现有 CREST(calcinosis, Raynaud’s phenomenon, oesophageal motility dysfunction, sclerodactyly, and telangiectasia)，严重导致间质性肺疾病、肺高压、急性肾衰竭危机。在 2013 年由美国风湿病学会与欧洲抗风湿病联盟一同制定了新的归类标准，新标准纳入了特定甲褶血管镜检查特异血管表现，除了能提早确诊外更提高了硬皮症诊断的专一度与敏感度。
<Source>^陳依伶，等 2016^
<Concept field>风险因素
<Related words>自身免疫性疾病
<Type of relation>super.
<Related words>^强直性脊柱炎^
<Type of relation>general

<Related words>^巨幼细胞性贫血^

<Type of relation>general

<Synonym>“硬皮症”,“SSc”和“全身性硬化症”是近义词。

<zh>硬皮症

<Morphosyntax>noun

<Usage label>common

<Source>^陳依伶，等 2016^

<zh>SSc

<Morphosyntax>noun

<Category>initials

<Source>^陳依伶，等 2016^

<Variant of>全身性硬化症

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>pernicious anaemia

<Morphosyntax>noun group

<Usage label>main term

<Source>^Muhajir, et al. 2020^:1

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Pernicious anaemia is an autoimmune disorder affecting the gastric mucosa with impaired absorption of dietary cobalamin (vitamin B12) resulting in B12 deficiency.

<Source>^Muhajir, et al. 2020^:1

<Context>Pernicious anaemia symptoms manifest insidiously and rarely raise clinical suspicion, since they are often present in other conditions as well, leading to a missed or delayed diagnosis. Tiredness, memory loss, and poor concentration are the most common symptoms. Some patients present with gastrointestinal symptoms such as dyspepsia before development of anaemia. Peripheral neuropathy is an early neurological manifestation of pernicious anaemia, which causes reversible paraesthesia and numbness.

<Source>^Muhajir, et al. 2020^:1-2

<Concept field>risk factor

<Related words>immune disease

<Type of relation>super.
<Related words>^ankylosing spondylitis^
<Type of relation>general
<Related words>^systemic sclerosis^
<Type of relation>general
<Synonyms>The term “Addisonian anaemia” is a synonym to “pernicious anaemia” but it is hardly used to identify the disease.

<en>addisonian anaemia
<Morphosyntax>noun group
<Usage label>uncommon
<Source>^Merriam/Webster 2016^

<zh>巨幼细胞性贫血
<Morphosyntax>noun
<Usage label>main term
<Source>^Braunstein 2021,^ https://www.msdmanuals.cn/professional/hematology-and-oncology/anemias-caused-by-deficient-erythropoiesis/megaloblastic-macrocytic-anemias
<Definition>巨幼细胞性贫血通常是缺乏维生素 B12 或叶酸所致的免疫疾病。
<Source>^Braunstein 2021,^ https://www.msdmanuals.cn/professional/hematology-and-oncology/anemias-caused-by-deficient-erythropoiesis/megaloblastic-macrocytic-anemias
<Context>导致巨幼细胞性贫血的最常见的原因是维生素 B12 缺乏，维生素 B12 急用障碍，叶酸缺乏。诊断通常基于全血细胞计数和外周涂片，通常显示大红细胞性贫血伴细胞不等和异形红细胞增多症、大的椭圆形红细胞（大卵圆细胞）、Howell-Jolly 小体（细胞核的残留碎片）、高分节的中性粒细胞、和网织红细胞减少症。巨幼细胞性贫血隐匿性发展，直到贫血严重时才会出现症状。胃肠道表现很常见，包括腹泻、舌炎和食欲不振。神经系统表现，包括周围神经病变、步态不稳，如病程延长，可发展为永久性的。
<Source>^Braunstein 2021,^ https://www.msdmanuals.cn/professional/hematology-and-oncology/anemias-caused-by-deficient-erythropoiesis/megaloblastic-macrocytic-anemias
<Concept field>风险因素
<Related words>自身免疫性疾病
<Type of relation>super.
<Related words>^强直性脊柱炎^

<Type of relation>general

<Related words>^全身性硬化症^

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>interleukin-6

<Morphosyntax>noun group

<Usage label>main term

<Source>^Scheller, et al. 2011^:878

<Lexica>Found in ^Merriam/Webster 2016^

<Definition>Interleukin-6 is a cytokine involved in inflammation, infection responses and in the regulation of metabolic, regenerative, and neural processes.

<Source>cf.^Scheller, et al. 2011^:878

<Context>In classic signalling, interleukin-6 stimulates target cells via a membrane bound interleukin-6 receptor, which upon ligand binding associates with the signalling receptor protein gp130. Interestingly, only few cells express membrane bound interleukin-6 receptor whereas all cells display gp130 on the cell surface. While cells, which only express gp130, are not responsive to interleukin-6 alone, they can respond to a complex of interleukin-6 bound to a naturally occurring soluble form of the interleukin-6 receptor. Regenerative or anti-inflammatory activities of interleukin-6 are mediated by classic signalling whereas pro-inflammatory responses of interleukin-6 are rather mediated by trans-signalling. This is important since therapeutic blockade of interleukin-6 by the neutralizing anti-interleukin-6 receptor monoclonal antibody tocilizumab has recently been approved for the treatment of inflammatory diseases.

<Source>^Scheller, et al. 2011^:878

<Concept field>histology

<Related words>adipocytes

<Type of relation>super

<Synonyms>“Pro-inflammatory cytokine interleukin 6”, “IL-6” and “interleukin-6” are synonyms, but while the first one represents the full form, and it is not frequently used, “IL-6” and “Interleukin-6” are both abbreviation of the full form. “Interleukin-6” is considered as the main term and it is the one that is most frequently used, while “IL-6” is properly used as an abbreviation.

<en>pro-inflammatory cytokine interleukin 6
<Morphosyntax>noun group
<Category>full form
<Usage label>uncommon
<Source>^Wallin/Larsson 2011^
<Variant of>interleukin-6

<en>IL-6
<Morphosyntax>noun
<Category>initials
<Source>^Merriam/Webster 2016^
<Variant of>interleukin-6

<zh>白细胞介素-6
<Morphosyntax>noun
<Usage label>main term
<Source>^林丽艳，等 2008^:681
<Definition>白细胞介素-6(IL-6)是多功能炎性细胞因子，是炎性介质网络的关键成份，在炎症反应中起重要作用。作为抗炎症细胞因子或远期细胞因子可平衡前炎症细胞因子或早期细胞因子的损伤效应，起到一定的保护作用。
<Source>^林丽艳，等 2008^:681
<Context>体内 IL-6 的水平上升，可以导致多种疾病如:类风湿性关节炎、肾小球肾炎的肾小球增殖，克罗恩病(CD)和 Castleman 氏病等。有研究表明，在炎症、感染和患有某些肿瘤等情况下，血清中 IL-6 的含量会有不同程度上升因此 IL-6 水平可作为判别病情严重程度的灵敏指标并可藉此判断患者的预后。
<Source>^林丽艳，等 2008^:681
<Concept field>组织学
<Related words>脂肪细胞
<Type of relation>super.
<Synonym>“IL-6”和“白细胞介素-6”是近义词。

<zh>IL-6
<Morphosyntax>noun

<Category>initials

<Source>^林丽艳，等 2008^:681

<Variant of>白细胞介素-6

**

<Subject>化学和相关科学 / Chemistry and allied sciences (540)

<Subfield>有机化学/ Organic chemistry (547)

<en>DDT

<Morphosyntax>initials

<Usage label>main term

<Source>^Kuswandi et al. 2017^:316

<Lexica>Found in ^Oxford Dictionary of English 2013^

<Definition>DDT, chemically known as 1,1,1-trichloro-2,2-bis(4-chlorophenyl)ethane is one of the most widely used organochlorine pesticides in the world.

<Source>^Kuswandi et al. 2017^:316

<Context>Commercial grade DDT also contains the compounds dichlorodiphenyldichloroethylene (DDE) and dichloro-diphenyldichloroethane (DDD), both of which are also metabolites of DDT and have similar chemical properties. DDT is an organochlorine compound that was introduced for commercial use in 1945 and was used heavily in populated areas for vector control and in agriculture for pest control. DDT is an extremely persistent compound due to its near insolubility in water and tendency to bioaccumulate in fatty tissue and biomagnify throughout trophic levels. By 1972, DDT use was banned in the United States and worldwide production and use began to decrease as well. Despite the injurious impacts on the environment and potential adverse health effects in humans, DDT is still produced; in fact, global production actually appears to be increasing.

<Source>^Cheremisinoff/Rosenfeld 2011^:247

<Concept field> Chemical compounds

<Related words>pesticide

<Type of relation>super.

<Related words>^phenoxyacetic acid^

<Type of relation>general

<Related words>^chlorophenol^

<Type of relation>general

<Related words>^dichloromethane^

<Type of relation>general

<Synonyms>The term “DDT” can be substituted by its full form “Dichlorodiphenyltrichloroethane”.

<en>dichlorodiphenyltrichloroethane
<Morphosyntax>noun
<Category>full form
<Source>^Kuswandi, et al. 2017^:316
<Variant of>DDT

<zh>滴滴涕
<Morphosyntax>noun
<Usage label>main term
<Source>^香港特別行政區政府。食物安全中心 2017^，https://www.cfs.gov.hk/tc_chi/programme/programme_rafs/programme_rafs_fc_02_02.html
<Definition>滴滴涕是一种活性范围很广泛的有机氯杀虫剂，用来防控森林及农作物的昆虫、家居害虫、病媒传播的疾病，例如疟疾、伤寒等。
<Source>^香港特別行政區政府。食物安全中心 2017^，https://www.cfs.gov.hk/tc_chi/programme/programme_rafs/programme_rafs_fc_02_02.html
<Context>滴滴涕无处不在，可经其生产、运输、应用和处置的过程进入环境。由于滴滴涕可能对环境和人类健康带来不良影响，不少国家已禁止使用滴滴涕。滴滴涕会对神经系统造 成急性影响，并且可损害多种动物的生殖系统及。
<Source>^香港特別行政區政府。食物安全中心 2017^，https://www.cfs.gov.hk/tc_chi/programme/programme_rafs/programme_rafs_fc_02_02.html
<Concept field>化合物
<Related words>害剂
<Type of relation>super.
<Related words>^苯氧乙酸^
<Type of relation>general
<Related words>^氯酚^
<Type of relation>general
<Related words>^二氯甲烷^
<Type of relation>general
**

<Subject>化学和相关科学 / Chemistry and allied sciences (540)

<Subfield>有机化学/ Organic chemistry (547)

<en>phenoxyacetic acid

<Morphosyntax>noun group

<Usage label>main term

<Source>^National Center for Biotechnology Information^, https://pubchem.ncbi.nlm.nih.gov/compound/Phenoxyacetic-acid

<Lexica>Found in ^Oxford Dictionary of English 2013^

<Definition>Phenoxyacetic acid is a monocarboxylic acid that is the O-phenyl derivative of glycolic acid.

<Source>^National Center for Biotechnology Information^, https://pubchem.ncbi.nlm.nih.gov/compound/Phenoxyacetic-acid

<Context>It is used in the manufacture of pharmaceuticals, pesticides, fungicides and dyes. It has a role as a human xenobiotic metabolite, an Aspergillus metabolite, a plant growth retardant and an allergen.

<Source>^National Center for Biotechnology Information^, https://pubchem.ncbi.nlm.nih.gov/compound/Phenoxyacetic-acid

<Concept field>chemical compound

<Related words>pesticides

<Type of relation>general

<Related words>^DDT^

<Type of relation>general

<Related words>^chlorophenol^

<Type of relation>general

<Related words>^dichloromethane^

<Type of relation>general

<Synonyms>“2-phenoxyacetic acid”, “phenoxyethanoic acid” and “phenoxyacetic acid” are synonyms. The term “2-phenoxyacetic acid” is not frequently used while the term “phenoxyethanoic acid” is commonly used in substitution to the main term.

<en>2-phenoxyacetic acid

<Morphosyntax>noun group

<Usage label>uncommon

<Source>^National Center for Biotechnology Information^, https://pubchem.ncbi.nlm.nih.gov/compound/Phenoxyacetic-acid

<en>phenoxyethanoic acid

<Morphosyntax>noun group

<Usage label>common

<Source>^National Center for Biotechnology Information^, https://pubchem.ncbi.nlm.nih.gov/compound/Phenoxyacetic-acid

<zh>苯氧乙酸

<Morphosyntax>noun

<Usage label>main term

<Source>^物竞化学品数据库^, http://www.basechem.org/chemical/1649

<Definition>苯氧乙酸，分子式 $C_8H_8O_3$, 是除草剂、植物激素和中枢神经兴奋药的中间体，也是测定钍的试剂。由苯酚与氯乙酸在碱性溶液中进行缩合，然后酸化制得苯氧基乙酸。

<Source>^物竞化学品数据库^, http://www.basechem.org/chemical/1649

<Context>苯氧乙酸是在抗生素发酵，制药工业中用于头孢、氯酯醒，特别是青霉素 V 中的先驱。工业中苯氧乙酸用于杀菌剂、角蛋白脱落、作为染料、杀虫剂和其它有机物的中间体、调味品、实验室试剂。

<Source>^物竞化学品数据库^, http://www.basechem.org/chemical/1649

<Concept field>化合物

<Related words>害剂

<Type of relation>general

<Related words>^滴滴涕^

<Type of relation>general

<Related words>^氯酚^

<Type of relation>general

<Related words>^二氯甲烷^

<Type of relation>general

**

<Subject>化学和相关科学 / Chemistry and allied sciences (540)

<Subfield>有机化学/ Organic chemistry (547)

<en>chlorophenols

<Morphosyntax>noun

<Usage label>main term

<Source>^Badanthadka/Mehendale 2014^:896
<Definition>Chlorophenols are a group of chemicals produced by electrophilic halogenation of phenol with chlorine.
<Source>^Badanthadka/Mehendale 2014^:896
<Context>There are 5 basic types and 19 different chlorophenols. Some chlorophenols are used as pesticides and herbicides. Others are used as antiseptics and disinfectants. Pentachlorophenol is the most important compound in this group.
<Source>^Badanthadka/Mehendale 2014^:896
<Concept field>chemical compounds
<Related words>pesticides
<Type of relation>general
<Related words>^DDT^
<Type of relation>general
<Related words>^phenoxyacetic acid^
<Type of relation>general
<Related words>^dichloromethane^
<Type of relation>general
<Synonyms>The term “chlorophenol” can be substituted by its full form “chlorinated phenols”, but the full form is not frequently used.

<en>chlorinated phenols
<Morphosyntax>noun group
<Category>full form
<Usage label>uncommon
<Source>^Exon 1984^:508
<Variant of>chlorophenols

<zh>氯酚
<Morphosyntax>noun
<Usage label>main term
<Source>^AG. AFIRM Group 2021^:1
<Definition>氯酚是一组人造化学品，历来被用作杀虫剂或被转化为杀虫剂。
<Source>^AG. AFIRM Group 2021^:1
<Context>氯酚通常被用作杀虫剂，或被转化成杀虫剂，历来被用作储存和运输过程中纺织品和皮革材料的防腐剂。氯酚也可作为杂质存在于染料生产中所用的原料中。有些

氯酚可用作印花色浆的防腐剂。在用元素氯漂白纺织品或纸张之后，以及在废水或饮用水的消毒过程中，可以在废水中产生和发现氯酚。

<Source>^AG. AFIRM Group 2021^:1

<Concept field>化合物

<Related words>害剂

<Type of relation>general

<Concept field>化合物

<Related words>^滴滴涕^

<Type of relation>general

<Related words>^苯氧乙酸^

<Type of relation>general

<Related words>^二氯甲烷^

<Type of relation>general

<Synonym>“氯酚”和“含氯苯酚”是近义词。

<zh>含氯苯酚

<Morphosyntax>noun

<Usage label>uncommon

<Source>^AG. AFIRM Group 2021^:1

**

<Subject>化学和相关科学 / Chemistry and allied sciences (540)

<Subfield>有机化学/ Organic chemistry (547)

<en>dichloromethane

<Morphosyntax>noun

<Usage label>main term

<Lexica>Found in ^Oxford Dictionary of English 2013^

<Source>^National Center for Biotechnology Information^, https://pubchem.ncbi.nlm.nih.gov/compound/Methylene-Chloride

<Definition>Methylene Chloride is a clear, colourless, non-flammable, volatile liquid chlorinated hydrocarbon with a sweet, pleasant smell and emits highly toxic fumes of phosgene when heated to decomposition.

<Source>^National Center for Biotechnology Information^, https://pubchem.ncbi.nlm.nih.gov/compound/Methylene-Chloride

<Context>Methylene chloride is primarily used as a solvent in paint removers, but is also used in aerosol formulations, as a solvent in the manufacture of pharmaceuticals, as a degreasing agent, in electronics manufacturing and as an ethane foam blowing agent. Methylene chloride is a possible mutagen and is reasonably anticipated to be a human carcinogen. Methylene chloride does not occur naturally in the environment. The acute (short-term) effects of methylene chloride inhalation in humans consist mainly of nervous system effects including decreased visual, auditory, and motor functions, but these effects are reversible once exposure ceases. The effects of chronic (long-term) exposure to methylene chloride suggest that the central nervous system (CNS) is a potential target in humans and animals.
<Source>^National Center for Biotechnology Information^, https://pubchem.ncbi.nlm.nih.gov/compound/Methylene-Chloride
<Concept field>chemical compound
<Related words>pesticides
<Type of relation>general
<Related words>^DDT^
<Type of relation>general
<Related words>^phenoxyacetic acid^
<Type of relation>general
<Related words>^chlorophenols^
<Type of relation>general
<Synonyms>The term “dichloromethanes”” can be substituted by its full form “methylene chloride”, but it is not frequently used.

<en>methylene chloride
<Morphosyntax>noun group
<Category>full name
<Usage label>uncommon
<Source>^National Center for Biotechnology Information^, https://pubchem.ncbi.nlm.nih.gov/compound/Methylene-Chloride
<Variant of> dichloromethane

<zh>二氯甲烷
<Morphosyntax>noun group
<Usage label>main term
<Source>^江宏哲，等^，http://nehrc.nhri.org.tw/toxic/toxfaq_detail_en.php?id=68

<Definition>二氯甲烷是一种带有淡淡甜味的无色液体，且它在环境中并不会自然产生。
<Source>^江宏哲，等^，http://nehrc.nhri.org.tw/toxic/toxfaq_detail_en.php?id=68
<Context>二氯甲烷被用來當作工業用溶劑或者是油漆清除劑，也使用在一些噴霧器、殺蟲劑產品及感光底片的製造過程中。若吸入大量的二氯甲烷會感到搖晃不穩、暈眩、噁心、且手指或腳趾會感到麻木或刺痛；而當在執行需要手眼協調的工作時吸入較少量的二氯甲烷則會造成注意力及細心程度降低。皮膚若接觸到二氯甲烷則會造成皮膚發紅及灼傷。世界衛生組織(WHO)已確定二氯甲烷可能會造成人類的癌症。
<Source>^江宏哲，等^，http://nehrc.nhri.org.tw/toxic/toxfaq_detail_en.php?id=68
<Concept field>化合物
<Related words>害剂
<Type of relation>general
<Concept field>化合物
<Related words>^滴滴涕^
<Type of relation>general
<Related words>^苯氧乙酸^
<Type of relation>general
<Related words>^氯酚^
**
<Subject>医学与卫生 / Medicine & health (610)
<Subfield>疾病的发病率和预防 / Incidence & prevention of disease (614)
<en>international staging system
<Morphosyntax>noun group
<Usage label>main term
<Source>^Greipp, et al 2005^:1
<Definition>The International Staging System (ISS) is a simple, reliable staging system for multiple myeloma that can be applied internationally for patient classification and stratification. ISS is based on two variables, Serum β_2-microglobulin and serum albumin.
<Source>cf.^Greipp, et al 2005^:1
<Context>Serum β_2-microglobulin and serum albumin were selected from the various potential prognostic factors both because of the statistical power in various models as well as the known wide availability of these two simple inexpensive laboratory tests. Serum β_2-microglobulin is widely recognized as the single most important variable predicting survival as it reflects not only tumour mass and renal function but also other parameters, including immune function,

while a low albumin may reflect effects on the liver by interleukin-6 produced by the microenvironment of myeloma cells.

<Source>cf.^Greipp, et al 2005^:5-6-7

<Concept field>staging system

<Related words>Durie-Salmon Staging system

<Type of relation>general

<Related words>^revised international staging system^

<Type of relation>general

<Synonyms>The term “International Staging System” is often substituted by its initials “ISS”.

<en>ISS

<Morphosyntax>noun

<Category>acronym

<Source>^Greipp, et al 2005^:1

<Variant of>international Staging System

<zh>国际分期系统

<Morphosyntax>noun

<Usage label>main term

<Source>cf.^杜辰星，等 2017^:113

<Definition>国际分期系统（ISS）是一个简单有效的 MM 预后分期系统。国际分期系统主要虑 β2-MG 及血清白蛋白水平。

<Source>cf.^杜辰星，等 2017^:113

<Context>国际骨髓瘤基金会于 2005 年建立了国际分期系统。国际分期系统(ISS)包括三期：I期为 β2-MG 水平<3.5 mg/L，白蛋白水平≥3.5 g/dL；II期为不符合I期与III期者；III期为 β2-MG 水平≥5.5 mg/L，ISS I、II、III期 MM 患者的中位 OS 期分别为 62、44、29 个月。

<Source>cf.^杜辰星，等 2017^:113

<Concept field>分期系统

<Related words>Durie-Salmon 分期系统

<Type of relation>general

<Related words>^修订的国际分期系统^

<Type of relation>general

<Synonyms>“ISS”和“国际分期系统”是近义词。

<zh>ISS
<Morphosyntax>noun
<Category>initials
<Source>cf.^杜辰星，等 2017^:113
<Variant of>国际分期系统
**
<Subject>医学与卫生 / Medicine & health (610)
<Subfield>疾病的发病率和预防 / Incidence & prevention of disease (614)
<en>revised international staging system
<Morphosyntax>noun group
<Usage label>main term
<Source>^Palumbo et al. 2015^:2863
<Definition>The R-ISS staging system is a new risk stratification algorithm with an improved prognostic power which includes CA and LDH parameters.
<Source>cf.^Palumbo, et al. 2015^:2863
<Context>The International Staging System (ISS) is a simple risk stratification algorithm based on two parameters: serum β_2-microglobulin and serum albumin. The R-ISS introduce chromosomal abnormalities (CA) and serum lactate dehydrogenase (LDH). CA detected by interphase fluorescent in situ hybridization (iFISH), are a key element to define the biologic features of MM, while LDH is a relevant bio-marker in MM. LDH level above the upper limit of normal denotes an increased disease aggressiveness and suggests high proliferation rate and/or the presence of tumour mass, in particular extramedullary and extraosseous disease.
<Source>cf.^Palumbo, et al. 2015^:2863-2864
<Concept field>staging system
<Related words>durie-salmon staging system
<Type of relation>general
<Related words>^international staging system^
<Type of relation>general
<Synonyms>The term “revised international staging system” is often substituted by its initials “R-ISS”.

<en>R-ISS

<Morphosyntax>noun

<Category>initials

<Source>^Palumbo, et al. 2015^:2863

<Variant of>revised international staging system

<zh>修订的国际分期系统

<Morphosyntax>noun

<Usage label>main term

<Source>^卢静，等 2017^:476

<Definition>修订的国际分期系统（R-ISS）是最新的 MM 分期系统，R-ISS 纳入了细胞遗传学因素和血清 LDH 作为判断预后的指标。

<Source>cf.^卢静，等 2017^:476

<Context>由于国际分期系统（ISS）在新药时期已不能完全满足目前临床需求，因此在 2015 年，国际骨髓瘤工作组依据 11 个临床试验中心的数据，总结了 4445 例新诊断的 MM 患者的临床资料，更新修订的国际分期系统。R-ISS 能更好地区分初诊 MM 患者的 OS 时间，尤其对年轻、未行移植患者的预后评估价值较为突出。

<Source>cf.^卢静，等 2017^:475-476

<Concept field>分期系统

<Related words>durie-salmon 分期系统

<Type of relation>general

<Related words>^国际分期系统^

<Type of relation>general

<Synonyms>“R-ISS”和“修订的国际分期系统”是近义词

<zh>R-ISS

<Morphosyntax>noun

<Category>initials

<Source>^卢静，等 2017^:475

<Variant of>修订的国际分期系统

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>creatinine

<Morphosyntax>noun group

<Usage label>main term

<Source>^Mayer/Donnelly 2013^:615

<Lexica>Found in ^Merriam/Webster 2016^

<Definition>Creatinine is a nitrogenous waste product produced by the breakdown of creatine, which is an important part of muscle.

<Source>^Mayer/Donnelly 2013^:615

<Context>Creatinine is filtered mainly by the kidney. Any changes in levels of creatinine in the blood are related to excretion and therefore reflect kidney function. Higher creatinine level can be indicative of dehydration. A serum creatinine test measures the amount of creatinine in the blood; it is an indirect indicator of renal glomerular filtration rate.

<Source>^Mayer/Donnelly 2013^:615

<Concept field>histology

<Related words>durie-salmon staging system

<Type of relation>general

<Related words>renal impairment

<Type of relation>general

<Synonyms>The term “creat” is a synonym to “creatinine” but it is not frequently used.

<en>creat

<Morphosyntax>noun

<Usage label>uncommon

<Source>^Mayer/Donnelly 2013^:615

<zh>肌酸酐

<Morphosyntax>noun

<Usage label>main term

<Source>^新隆醫事檢驗所^，https://www.sl-lab.com.tw/creatinine/

<Definition>肌酐酸是人体肌肉中肌酸的分解产物，属于代谢废物的一种，由肾脏将其排出至尿中。

<Source>^新隆醫事檢驗所^，https://www.sl-lab.com.tw/creatinine/

<Context>肌酐酸是非常稳定的肾功能指标，常用于评估肾功能障碍的严重程度及肾脏病的病情监控。当肾功能出现障碍时，代谢功能降低，肌酐酸会累积在血中而无法排出

体外，导致血中浓度上升，因此可借血液肌酐酸浓度来判定肾功能的好坏。一般血液肌酐酸经多次测定均在 2.0mg/dl 以上时，为广义的肾功能衰竭。

<Source>^新隆醫事檢驗所^，https://www.sl-lab.com.tw/creatinine/

<Concept field>组织学

<Related words>durie-salmon 分期系统

<Type of relation>general

<Related words>肾功能损伤

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>albumin

<Morphosyntax>noun

<Source>^Moman 2022^, https://www.ncbi.nlm.nih.gov/books/NBK459198/

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Albumin is a small globular protein with a molecular weight of 66.5 kilodaltons (kDa). It consists of 585 amino acids which are organized into three repeated homologous domains and are made up of two separate sub-domains, A and B.

<Source>^Moman 2022^, https://www.ncbi.nlm.nih.gov/books/NBK459198/

<Context>Albumin represents half of the total protein content of plasma in healthy human patients. Albumin is synthesized by liver hepatocytes and rapidly excreted into the bloodstream. Serum albumin functions as a significant modulator of plasma oncotic pressure and transporter of endogenous and exogenous ligands. In clinical medicine, serum albumin can be measured via standard serum laboratory testing, and this measure has been advocated as a marker for an individual patient's nutritional status. As a laboratory value, serum albumin can also aid clinicians regarding insight into patients' liver function or the ability to biosynthesize proteins and factors vital to total body homeostasis.

<Source>^Moman 2022^, https://www.ncbi.nlm.nih.gov/books/NBK459198/

<Concept field>histology

<Related words>^international staging system^

<Type of relation>general

<Related words>^β_2-microglobulin^

<Type of relation>coord.

<zh>白蛋白

<Morphosyntax>noun

<Usage label>main term

<Source>^ 南 京 建 成 生 物 工 程 研 究 所 2014^ ，http://www.njjcbio.com/contents.asp?cid=5&wid=2&id=827

<Definition>白蛋白是属于球蛋白的一种蛋白质；白蛋白是由肝实质细胞合成.

<Source>^ 南 京 建 成 生 物 工 程 研 究 所 2014^ ，http://www.njjcbio.com/contents.asp?cid=5&wid=2&id=827

<Context>白蛋白是血浆中含量最多的蛋白质，占血浆总蛋白的 40%-60%。白蛋白广泛分布在各种动植物中，在人体血液，组织液中含有白蛋白，它最重要的作用是维持胶体渗透压。在肝功能检查中，检查白蛋白的作用是根据白蛋白的检查结果来判断某些疾病。一般情况下，白蛋白增高主要见于血液浓缩而致相对性增高，如严重脱水和休克、严重烧伤、急性出血、慢性肾上腺皮质功能减低症。白蛋白降低常见于肝硬化合并腹水及其他肝功能严重损害(如急性肝坏死、中毒性肝炎等)营养不良、慢性消耗性疾病、糖尿病、严重出血肾病综合征等。

<Source>^ 南 京 建 成 生 物 工 程 研 究 所 2014^ ，http://www.njjcbio.com/contents.asp?cid=5&wid=2&id=827

<Concept field>组织学

<Related words>^国际分期系统^

<Type of relation>general

<Related words>^β_2微球蛋白^

<Type of relation>coord.

<Synonyms>“白蛋白”和“清蛋白”是近义词。

<zh>清蛋白

<Morphosyntax>noun

<Usage label>uncommon

<Source>^ 南 京 建 成 生 物 工 程 研 究 所 2014^ ，http://www.njjcbio.com/contents.asp?cid=5&wid=2&id=827

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>β_2-microglobulin

<Morphosyntax>noun group

<Usage label>main term

<Source>^Bernier 1980^:323

<Lexica>Found in ^Merriam/Webster 2016^

<Definition>β_2-microglobulin is a low molecular weight protein with sequence homology to immunoglobulins.

<Source>^Bernier 1980^:323

<Context>Under normal conditions β_2-microglobulin is synthesized and shed by many cells, particularly lymphocytes, and is detectable in the circulation of normal individuals. Because of its small size it is normally filtered readily at the glomerulus and is catabolized by proximal tubular cells of the kidney. Impaired renal function and hyperproduction of β_2-microglobulin are both associated with increased serum levels.

<Source>^Bernier 1980^:323

<Concept field>histology

<Related words>^international staging system^

<Type of relation>general

<Related words>^albumin^

<Type of relation>coord.

<zh>β_2 微球蛋白

<Morphosyntax>noun

<Usage label>main term

<Source>^天津市肿瘤医院（天津医科大学肿瘤医院）2021^，http://www.tjmuch.com/system/2021/05/11/030005810.shtml

<Definition>β_2 微球蛋白（β_2-MG）是一种内源性低分子量血清蛋白质，由淋巴细胞和其他大多数的有核细胞分泌，在免疫应答中起重要作用。

<Source>^天津市肿瘤医院（天津医科大学肿瘤医院）2021^，http://www.tjmuch.com/system/2021/05/11/030005810.shtml

<Context>血清 β2-MG 极易通过肾小球滤过膜，滤过的 β2-MG 99.9%被近曲小管细胞重吸收和降解。临床上检测血或尿中的 β2-MG 浓度为临床肾功能测定、肾移植成活、糖尿病肾病、重金属镉、汞中毒以及某些恶性肿瘤的临床诊断提供较早、可靠和灵敏的指标。血 β2-MG 是以淋巴细胞增殖性疾病的主要标志物，如多发性骨髓瘤，血 β2-MG 浓度明显增加。

<Source>^ 天 津 市 肿 瘤 医 院 (天 津 医 科 大 学 肿 瘤 医 院) 2021^ ，http://www.tjmuch.com/system/2021/05/11/030005810.shtml

<Concept field>组织学

<Related words>^国际分期系统^

<Type of relation>general

<Related words>^白蛋白^

<Type of relation>coord.

<Synonyms>“β_2-MG”和“β_2 微球蛋白”是近义词。

<zh>β_2-MG

<Morphosyntax>noun

<Category>initials

<Source>^ 天 津 市 肿 瘤 医 院 (天 津 医 科 大 学 肿 瘤 医 院) 2021^ ，http://www.tjmuch.com/system/2021/05/11/030005810.shtml

<Variant of>β_2 微球蛋白

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>lactate dehydrogenase

<Morphosyntax>noun group

<Usage label>main term

<Source>^Farhana/Lappin 2022^, https://www.ncbi.nlm.nih.gov/books/NBK557536/

<Lexica>Found in ^Merriam/Webster 2016^

<Definition>Lactate dehydrogenase (LDH) is an important enzyme of the anaerobic metabolic pathway. It belongs to the class of oxidoreductases and its function is to catalyse the reversible conversion of lactate to pyruvate.

<Source>^Farhana/Lappin 2022^, https://www.ncbi.nlm.nih.gov/books/NBK557536/

<Context>Lactate dehydrogenase is ubiquitously present in all tissues and serves as an important checkpoint of gluconeogenesis and DNA metabolism. Conditions that can cause increased LDH in the blood may include liver disease, anaemia, heart attack, bone fractures, muscle trauma, cancers, and infections such as encephalitis, meningitis, encephalitis, and HIV. Many cancers cause a general increase in LDH levels; thus it can be a non-specific tumour marker.

<Source>^Farhana/Lappin 2022^, https://www.ncbi.nlm.nih.gov/books/NBK557536/

<Concept field>histology
<Related words>^revised international staging system^
<Type of relation>general
<Related words>chromosomal abnormalities
<Type of relation>coord.
<Synonyms>“Lactic dehydrogenase” and “LDH” are synonyms to “Lactate Dehydrogenase”. The first term is not frequently used while the initials are frequently used in substitution to the full term

<en>lactic dehydrogenase
<Morphosyntax>noun group
<Usage label>uncommon
<Source>^Merriam/Webster 2016^

<en>LDH
<Morphosyntax>noun
<Usage label>common
<Category>initials
<Source>^Farhana/Lappin 2022^, https://www.ncbi.nlm.nih.gov/books/NBK557536/
<Variant of>lactate dehydrogenase

<zh>乳酸脱氢酶
<Morphosyntax>noun
<Usage label>main term
<Source>^郑雪香，等 2020^
<Definition>乳酸脱氢酶（LDH）是糖酵解途径中一种重要的酶，广泛存在于组织细胞中，其中以肝脏中活性最高，其次为心脏、骨骼肌、肾脏。
<Source>^郑雪香，等 2020^
<Context>乳酸脱氢酶用于体外定量测定血清或血浆中的乳酸脱氢酶。在临床医学上乳酸脱氢酶用于心肌梗塞，肝硬化，肾病以及流行性肝炎疾病的体外辅助诊断。
<Source>^富士胶片和光纯药株式会社^，https://diagnostic-wako.fujifilm.com/cn/products/clinical-diagnostics-reagents/ldh.html
<Concept field>组织学
<Related words>^修订的国际分期系统^

<Type of relation>general

<Related words>^染色体异常^

<Type of relation>coord.

<Synonyms>“LDH”和“乳酸脱氢酶”是近义词。

<zh>LDH

<Morphosyntax>noun

<Category>initials

<Source>^郑雪香，等 2020^

<Variant of>乳酸脱氢酶

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>CRAB symptoms

<Morphosyntax>noun group

<Source>^Nakaya, et al. 2017^:16

<Definition>The acronym CRAB summarizes the most typical clinical manifestations of multiple myeloma, these being hypercalcemia, renal failure, anaemia, and bone disease.

<Source>^Nakaya, et al. 2017^:16

<Context>CRAB factors can be used to distinguish between active, symptomatic multiple myeloma and its precursor states, monoclonal gammopathy of undermined significance and smouldering myeloma. The distinction is relevant not only for classification and diagnosis, but also for therapy. CRAB factors are criteria for deciding when to initiate chemotherapy and are known to suggest the prognosis of multiple myeloma. With advances in technology and science, it is unclear whether the presence of CRAB factors is associated with the prognosis of myeloma treated with novel agents.

<Source>^Nakaya, et al. 2017^:16

<Concept field>symptoms

<Related words>^hypercalcemia^

<Type of relation>sub.

<Related words>renal insufficiency

<Type of relation>sub.

<Related words>^anaemia^

<Type of relation>sub.

<Related words>^osteolytic lesion^

<Type of relation>sub.

<zh>CRAB 症状

<Morphosyntax>noun group

<Source>^ 刘 琼 芝 、 秦 璐 2022^, https://wjw.hunan.gov.cn/wjw/xxgk/gzdt/dfxx/202204/t20220419_22739948.html

<Definition>CRAB 症状是多发性骨髓瘤的典型症状，“C”为高钙血症，“R”为肾功能损伤，“A”为贫血，“B”为骨痛。

<Source>^ 刘 琼 芝 、 秦 璐 2022^, https://wjw.hunan.gov.cn/wjw/xxgk/gzdt/dfxx/202204/t20220419_22739948.html

<Context>高钙血症，骨髓瘤细胞造成溶骨性损伤，使大量钙释放到血液中，表现为恶心、呕吐、嗜睡、意识模糊等；肾功能损伤，有高达 50%左右的活动性骨髓瘤患者在其疾病过程中发生，临床上以肌酐高和蛋白尿最为多见；贫血，骨髓中大量骨髓瘤细胞的存在会影响红细胞的生成，同时促红细胞生成素生成不足，患者会出现贫血，常表现为疲劳、虚弱、头晕、心悸等；骨痛，70%初诊多发性骨髓瘤患者是以骨痛为主要症状就诊，常累及脊柱、肋骨等，可至病理性骨折。

<Source>^ 刘 琼 芝 、 秦 璐 2022^, https://wjw.hunan.gov.cn/wjw/xxgk/gzdt/dfxx/202204/t20220419_22739948.html

<Concept field>症状

<Related words>^高钙血症^

<Type of relation>sub.

<Related words>肾功能损伤<Type of relation>sub.

<Related words>^贫血^

<Type of relation>sub.

<Related words>^溶骨性病变^

<Type of relation>sub.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>anaemia

<Morphosyntax>noun

<Usage label>main term

<Source>^National Heart, Lung and Blood institute 2022^, https://www.nhlbi.nih.gov/health/anemia

<Lexica>Found in ^Merriam/Webster 2016^

<Definition>Anaemia is a condition that develops when blood produces a lower-than-normal amount of healthy red blood cells.

<Source>^National Heart, Lung and Blood institute 2022^, https://www.nhlbi.nih.gov/health/anemia

<Context>There are many types of anaemia, including: Iron-deficiency anaemia, Vitamin B12-deficiency anaemia, Haemolytic anaemia. Mild anaemia is a common and treatable condition. Anaemia can also be chronic. The most common type of anaemia is iron-deficiency anaemia. Some people are at a higher risk for anaemia, including women during their menstrual periods and pregnancy. Anaemia may also be a sign of a more serious condition, such as bleeding in stomach, inflammation from an infection, kidney disease, cancer, or autoimmune diseases.

<Source>^National Heart, Lung and Blood institute 2022^, https://www.nhlbi.nih.gov/health/anemia

<Concept field>symptoms

<Related words>^CRAB symptoms^

<Type of relation>super.

<Related words>^hypercalcemia^

<Type of relation>sub.

<Related words>renal insufficiency

<Type of relation>sub.

<Related words>^osteolytic lesion^

<Type of relation>sub.

<zh>贫血

<Morphosyntax>noun

<Source>^世界卫生组织^，https://www.who.int/zh/health-topics/anaemia#tab=tab_3

<Lexica>Found in ^现代汉语词典 2013^

<Definition>贫血指血液中红细胞数量过少或血红蛋白浓度低于正常水平。

<Source>^世界卫生组织^，https://www.who.int/zh/health-topics/anaemia#tab=tab_3

<Context>贫血最常见的原因有：营养不良，特别是缺铁，但缺乏叶酸、维生素 B12 和 A 也是重要原因；血红蛋白病；以及疟疾、结核病、艾滋病毒和寄生虫感染等传染病。贫血是一个严重的全球公共卫生问题，尤其影响到幼儿和孕妇。缺铁性贫血最常见，治

疗可通过改变饮食，相对容易。而其他性质的贫血需采取健康干预措施，可能较难获得。准确描述贫血的特征对于了解贫血的负担和流行病学、规划公共卫生干预措施以及在整个生命过程中对患者进行临床医疗至关重要。

<Source>^世界卫生组织^，https://www.who.int/zh/health-topics/anaemia#tab=tab_3

<Concept field>症状

<Related words>^CRAB 症状^

<Type of relation>super.

<Related words>^高钙血症^

<Type of relation>sub.

<Related words>肾功能损伤

<Type of relation>sub.

<Related words>^溶骨性病变^

<Type of relation>sub.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>人体生理学 / Human physiology (612)

<en>autocrine signalling

<Morphosyntax>noun group

<Source>^King 2007^:63

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Autocrine signalling means the production and secretion of an extracellular mediator by a cell followed by the binding of that mediator to receptors on the same cell to initiate signal transduction.

<Source>^King 2007^:63

<Context>Pure autocrine signalling in which one cell type stimulates itself is relatively uncommon in normal physiology but can be an important feature of some pathologic conditions such as cancer in which tumour cell proliferation may be driven by autocrine signalling.

<Source>^King 2007^:63

<Concept field>physiology

<Related words>^CRAB symptoms^

<Type of relation>super.

<Related words>^M Protein^

<Type of relation>general

<Related words>^paracrine signalling^

<Type of relation>coord.

<zh>自分泌信号传送

<Morphosyntax>noun group

<Source>^ 深 梦 健 康 管 理 2017^ ，https://mp.weixin.qq.com/s?__biz=MzA3NTcxMzkyNg==&mid=2451226690&idx=3&sn=393b0e7889789b00633eacf5d8813ab9&chksm=888823cabbff5b5bdb78c19eb8026583926b4133a4c937605c0de1183081ff667240c3807bf29&scene=27

<Definition>在自分泌传讯中，细胞传送信号给自己，细胞释放一个化学信号跟它自己表面的受体结合。

<Source>^ 深 梦 健 康 管 理 2017^ ，https://mp.weixin.qq.com/s?__biz=MzA3NTcxMzkyNg==&mid=2451226690&idx=3&sn=393b0e7889789b00633eacf5d8813ab9&chksm=888823cabbff5b5bdb78c19eb8026583926b4133a4c937605c0de1183081ff667240c3807bf29&scene=27

<Context>自分泌传讯有其重要性：它帮助细胞保持完整性并正确地分裂。这在发育过程中相当重要，有助于细胞强化它们的特性。

<Source>^ 深 梦 健 康 管 理 2017^ ，https://mp.weixin.qq.com/s?__biz=MzA3NTcxMzkyNg==&mid=2451226690&idx=3&sn=393b0e7889789b00633eacf5d8813ab9&chksm=888823cabbff5b5bdb78c19eb8026583926b4133a4c937605c0de1183081ff667240c3807bf29&scene=27

<Concept field>生理学

<Related words>^CRAB 症状^

<Type of relation>super.

<Related words>^单克隆免疫球蛋白^

<Type of relation>general

<Related words>^旁分泌传讯^

<Type of relation>coord.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>人体生理学 / Human physiology (612)

<en>paracrine signalling

<Morphosyntax>noun group

<Source>^King 2007^:63

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Paracrine signalling means secretion of mediators by one cell that acts on other cells in its immediate vicinity.

<Source>^King 2007^:63

<Context>Paracrine signalling is common since many mediators have a relatively short half-life and so must act quickly after they are secreted if they are to have an effect. Paracrine signalling facilitates the organization of localized tissue responses such as inflammation or angiogenesis by focusing the action of mediators within a small geographic area.

<Source>^King 2007^:63

<Concept field>physiology

<Related words>^CRAB symptoms^

<Type of relation>super.

<Related words>^M Protein^

<Type of relation>general

<Related words>^autocrine signalling^

<Type of relation>coord.

<zh>旁分泌传讯

<Morphosyntax>noun group

<Source>^深梦健康管理2017^，https://mp.weixin.qq.com/s?__biz=MzA3NTcxMzkyNg==&mid=2451226690&idx=3&sn=393b0e7889789b00633eacf5d8813ab9&chksm=888823cabbff5b5bdb78c19eb8026583926b4133a4c937605c0de1183081ff667240c3807bf29&scene=27

<Definition>旁分泌传讯发生在跨越短距离的两个细胞之间，在旁分泌传讯细胞传送信号给另一个细胞。

<Source>cf.^深梦健康管理2017^，https://mp.weixin.qq.com/s?__biz=MzA3NTcxMzkyNg==&mid=2451226690&idx=3&sn=393b0e7889789b00633eacf5d8813ab9&chksm=888823cabbff5b5bdb78c19eb8026583926b4133a4c937605c0de1183081ff667240c3807bf29&scene=27

<Context>旁分泌传讯让细胞与其近邻彼此协调运转和作用。突触传讯是旁分泌传讯的一个例子，是在两个神经元之间的微小间隙间发生信号传输。

<Source>cf.^深梦健康管理2017^，https://mp.weixin.qq.com/s?__biz=MzA3NTcxMzkyNg==&mid=2451226690&idx=3&

sn=393b0e7889789b00633eacf5d8813ab9&chksm=88823cabbff5b5bdb78c19eb8026583926b4133a4c937605c0de1183081ff667240c3807bf29&scene=27

<Concept field>生理学

<Related words>^CRAB 症状^

<Type of relation>super.

<Related words>^单克隆免疫球蛋白^

<Type of relation>general

<Related words>^自分泌信号传送^

<Type of relation>coord.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>cytokine

<Morphosyntax>noun

<Source>^Zhang/An 2007^:27

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Cytokines are small, secreted proteins released by cells that have a specific effect on the interactions and communications between cells.

<Source>^Zhang/An 2007^:27

<Context>Cytokine is a general name; other names include lymphokine (cytokines made by lymphocytes), monokine (cytokines made by monocytes), chemokine (cytokines with chemotactic activities), and interleukin (cytokines made by one leukocyte and acting on other leukocytes). Cytokines may act on the cells that secrete them (autocrine action), on nearby cells (paracrine action), or in some instances on distant cells (endocrine action). Cytokines are redundant in their activity, meaning similar functions can be stimulated by different cytokines. They are often produced in a cascade, as one cytokine stimulates its target cells to make additional cytokines.

<Source>^Zhang/An 2007^:27-28

<Concept field>histology

<Related words>^autocrine signalling^

<Type of relation>super.

<Related words>^paracrine signalling^

<Type of relation>super.

<zh>细胞因子

<Morphosyntax>noun group

<Source>^ThermoFisher Scientific^, https://www.thermofisher.cn/cn/zh/home/life-science/cell-analysis/cell-analysis-learning-center/immunology-at-work/proinflammatory-cytokines-overview.html

<Definition>细胞因子是一个通用术语，指的是当体内有病原体时机体会分泌各种调节炎症的蛋白细胞因子，能够刺激、募集和扩增免疫细胞。

<Source>^ThermoFisher Scientific^, https://www.thermofisher.cn/cn/zh/home/life-science/cell-analysis/cell-analysis-learning-center/immunology-at-work/proinflammatory-cytokines-overview.html

<Context>细胞因子包括白细胞介素（IL）、趋化因子、干扰素和肿瘤坏死因子（TNF）。细胞因子根据免疫反应的性质及其产生来源进行细分。细胞因子分为促炎性和抗炎性两种。关键的促炎细胞因子是 IL-1、IL-6 和 TNF-α。促炎细胞因子通常调节免疫细胞的生长、活化、分化以及归巢至感染部位，最终控制并根除细胞内病原体。

<Source>^ThermoFisher Scientific^, https://www.thermofisher.cn/cn/zh/home/life-science/cell-analysis/cell-analysis-learning-center/immunology-at-work/proinflammatory-cytokines-overview.html

<Concept field>组织学

<Related words>^自分泌信号传送^

<Type of relation>super.

<Related words>^旁分泌传讯^

<Type of relation>super.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>prostaglandin

<Morphosyntax>noun

<Source>^Pettipher 1998^:2024

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Prostaglandins are acidic lipids which can be enzymatically produced by most mammalian cell types in response to mechanical, chemical or immunological stimuli.

<Source>^Pettipher 1998^:2024

<Context>The unsaturated fatty acid arachidonic acid is the precursor for the synthesis of the major classes of prostaglandins and leukotrienes, collectively 6-keto-PGFta known as eicosanoids. The primary prostaglandins have all been detected in elevated levels at sites of acute and chronic inflammation. Prostaglandins produced at a site of injury contribute to the signs and symptoms of inflammation.
<Source>^Pettipher 1998^:2024
<Concept field>cytology
<Related words>^hypercalcemia^
<Type of relation>super.
<Related words>bone resorption
<Type of relation>general
<Related words>^cytokines^
<Type of relation>coord.

<zh>前列腺素
<Morphosyntax>noun group
<Source>^ 科 技 部 高 瞻 自 然 科 學 教 學 平 台 2010^, https://highscope.ch.ntu.edu.tw/wordpress/?p=9265
<Definition>前列腺素（PG） 是一类激素，最早是由前列腺分泌物所分离出来的，含有五元脂肪环，并接上两条侧链及官能基，其中官能机包括有羧酸基、羟基、酮类及碳-碳双键。
<Source>^ 科 技 部 高 瞻 自 然 科 學 教 學 平 台 2010^, https://highscope.ch.ntu.edu.tw/wordpress/?p=9265
<Context>前列腺素有很多种不同的结构和作用，不同的结构则根据分子中五元脂肪环上取代基主要是羟基和氢的不同将 PG 分为 A、B、C、D、E、F 等类型，分别用 PGA、PGB、PGC、PGD、PGE、PGF 等表示。前列腺素可以表现出很多种不同的生理以及病理活性。举例来说，前列腺素可引起的发炎、发烧、疼痛等反应。
<Source>^ 科 技 部 高 瞻 自 然 科 學 教 學 平 台 2010^, https://highscope.ch.ntu.edu.tw/wordpress/?p=9265
<Concept field>组织学
<Related words>^高钙血症^
<Type of relation>super.
<Related words>骨吸收

<Type of relation>general

<Related words>^细胞因子^

<Type of relation>coord.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>polyuria

<Morphosyntax>noun

<Source>^Sanders 2009^:216

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Polyuria is a urine output greater than 3.0 L/day.

<Source>^Sanders 2009^:216

<Context>Four main disorders cause polyuria: psychogenic polydipsia (psychosis), dipsogenic Diabetes Insipidus (DI) (defect in thirst center), central neurogenic DI (defect in ADH secretion), and nephrogenic DI (defect in ADH action on the kidney). Polyuria also may occur from osmotic diuresis in such conditions as diabetes mellitus (glucose), recovery from renal failure (urea), and intravenous infusions (saline, mannitol).

<Source>^Sanders 2009^:216

<Concept field>symptoms

<Related words>^hypercalcemia^

<Type of relation>super.

<Related words>^polydipsia^

<Type of relation>coord.

<zh>多尿

<Morphosyntax>noun

<Source>^Maddukuri 2021^ ， https://www.msdmanuals.cn/professional/genitourinary-disorders/symptoms-of-genitourinary-disorders/polyuria?query=%E5%A4%9A%E5%B0%BF

<Definition>多尿指每天尿量>3L。

<Source>^Maddukuri 2021^ ， https://www.msdmanuals.cn/professional/genitourinary-disorders/symptoms-of-genitourinary-disorders/polyuria?query=%E5%A4%9A%E5%B0%BF

<Context>由于 ADH（称为精氨酸血管升压素）可促进集合管水的重吸收，ADH 减少，则尿量增加，使得血渗透压回到正常水平。包含任何以下过程的疾病可产生多尿：持续

的水分摄入增多（烦渴），ADH 分泌减少（中枢性尿崩症），外周 ADH 敏感性下降（肾性尿崩症），溶质性利尿。

<Source>^Maddukuri 2021^ ， https://www.msdmanuals.cn/professional/genitourinary-disorders/symptoms-of-genitourinary-disorders/polyuria?query=%E5%A4%9A%E5%B0%BF

<Concept field>症状

<Related words>^高钙血症^

<Type of relation>super.

<Related words>^多渴^

<Type of relation>coord.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>polydipsia

<Morphosyntax>noun

<Source>^Kotagiri/Sridhara 2023^, https://www.ncbi.nlm.nih.gov/books/NBK562251/

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Polydipsia is a condition where there is excess consumption of fluids leading to polyuria with diluted urine and, ultimately, hyponatremia.

<Source>^Kotagiri/Sridhara 2023^, https://www.ncbi.nlm.nih.gov/books/NBK562251/

<Context>Polydipsia can be categorized into two types. 1) Psychogenic polydipsia and 2) Dipsogenic polydipsia. As the name suggests, psychogenic polydipsia is seen in patients with psychiatric disorders. Dipsogenic polydipsia, also called compulsory water drinking, is seen mostly in people who consciously drink large quantities of water to maintain a healthy lifestyle or in those whose hypothalamus is affected. Compulsory water drinking is perceived to improve, maintain good health, and is on the rise of late given the popularity of lifestyle programs. Psychogenic polydipsia is seen in many psychiatric conditions but is more commonly seen in schizophrenic patients.

<Source>^Kotagiri/Sridhara 2023^, https://www.ncbi.nlm.nih.gov/books/NBK562251/

<Concept field>symptoms

<Related words>^hypercalcemia^

<Type of relation>super.

<Related words>^polyuria^

<Type of relation>coord.

<zh>多渴

<Morphosyntax>noun

<Source>^Srinivasan 2023^，https://bestpractice.bmj.com/topics/zh-cn/865

<Definition>烦渴是过度或异常的口渴，伴随摄入过量的水或液体。

<Source>^Srinivasan 2023^，https://bestpractice.bmj.com/topics/zh-cn/865

<Context>心因性烦渴（PPD），又称原发性烦渴，是一种烦渴，其特征是自主摄入过多的水，经常见于患有精神障碍和/或神经发育障碍的患者。患者表现出找水和过度饮水行为，有时候伴低钠血症和水中毒。精神性烦渴的并发症包括失禁和遗尿症、膀胱扩张和肾积水、肾脏和充血性心力衰竭、骨质疏松症和相关病理性骨折。

<Source>^Srinivasan 2023^，https://bestpractice.bmj.com/topics/zh-cn/865

<Concept field>症状

<Related words>^高钙血症^

<Type of relation>super.

<Related words>^多尿^

<Type of relation>coord.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>cast nephropathy

<Morphosyntax>noun group

<Usage label>main term

<Source>^Shahrier/Bonsib 2020^:71

<Definition>Cast nephropathy (“myeloma kidney”) is a disease resulting from acute tubular injury due to the intratubular formation of large, eosinophilic, PAS-negative, and often cracked or fractured casts composed of a restricted light chain.

<Source>^Shahrier/Bonsib 2020^:71

<Context>The updated International Myeloma Working Group consensus criteria recognize cast nephropathy as a myeloma-defining condition. The casts form in the distal tubules and collecting ducts and may extend into the adjacent interstitium. They may elicit an inflammatory response that includes neutrophils, histiocytes, and sometimes multinucleated giant cells. Immunohistochemical demonstration of light chain restriction is required for diagnosis.

<Source>^Shahrier/Bonsib 2020^:71

<Concept field>symptoms

<Related words>renal impairment
<Type of relation>super.
<Related words>^immunoglobulin light chains^
<Type of relation>general
<Related words>^acute tubular necrosis^
<Type of relation>sub.
<Related words>^creatinine clearance^
<Type of relation>sub.
<Related words>^glucocorticoids^
<Type of relation>general
<Synonyms>The term “myeloma kidney” is a synonym to “cast nephropathy” but it is hardly used to identify the disease.

<en>myeloma kidney
<Morphosyntax>noun group
<Usage label>uncommon
<Source>^Shahrier/Bonsib 2020^:71

<zh>管型肾病
<Morphosyntax>noun group
<Source>^The Binding Site^, https://www.bindingsite.com.cn/%E5%AD%A6%E6%9C%AF/%E8%82%BE%E8%84%8F%E5%92%8C%E6%B5%86%E7%BB%86%E8%83%9E%E7%96%BE%E7%97%85/%E7%AE%A1%E5%9E%8B%E8%82%BE%E7%97%85/
<Definition>管型肾病是多发性骨髓瘤中引起严重急性肾损伤的主要原因。管型肾病中，远端肾小管被塔姆霍斯福尔蛋白（尿调节素）相关的单克隆游离轻链形成的蜡样沉积物堵塞。
<Source>^The Binding Site^, https://www.bindingsite.com.cn/%E5%AD%A6%E6%9C%AF/%E8%82%BE%E8%84%8F%E5%92%8C%E6%B5%86%E7%BB%86%E8%83%9E%E7%96%BE%E7%97%85/%E7%AE%A1%E5%9E%8B%E8%82%BE%E7%97%85/
<Context>血清游离轻链值≥500 毫克/升表示不明原因急性肾损伤患者患有管型肾病。在透析依赖型急性肾损伤患者中，治疗后血清游离轻链持续降低与肾脏恢复和患者生存率改善有关。

<Source>^The Binding Site^, https://www.bindingsite.com.cn/%E5%AD%A6%E6%9C%AF/%E8%82%BE%E8%84%8F%E5%92%8C%E6%B5%86%E7%BB%86%E8%83%9E%E7%96%BE%E7%97%85/%E7%AE%A1%E5%9E%8B%E8%82%BE%E7%97%85/

<Concept field>症状

<Related words>肾功能损伤

<Type of relation>super.

<Related words>^免疫球蛋白轻链^

<Type of relation>general

<Related words>^急性肾小管坏死^

<Type of relation>sub.

<Related words>^肌酐清除率^

<Type of relation>sub.

<Related words>^糖皮质激素^

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>acute tubular necrosis

<Morphosyntax>noun group

<Usage label>main term

<Source>^Latif 2021^, https://medlineplus.gov/ency/article/000512.htm#:~:text=Acute%20tubular%20necrosis%20(ATN)%20is,it%20passes%20through%20the%20kidneys

<Definition>Acute tubular necrosis (ATN) is a kidney disorder involving damage to the tubule cells of the kidneys, which can lead to acute kidney failure. The tubules are tiny ducts in the kidneys that help filter the blood when it passes through the kidneys.

<Source>^Latif 2021^, https://medlineplus.gov/ency/article/000512.htm#:~:text=Acute%20tubular%20necrosis%20(ATN)%20is,it%20passes%20through%20the%20kidneys

<Context>ATN is often caused by a lack of blood flow and oxygen to the kidney tissues (ischemia of the kidneys). It may also occur if the kidney cells are damaged by a poison or harmful substance. ATN is one of the most common structural changes that can lead to acute kidney failure. ATN is a common cause of kidney failure in people who are in the hospital. ATN

can be caused by medicines that are toxic to the kidneys. In most people, ATN is reversible. The goal of treatment is to prevent life-threatening complications of acute kidney failure.
<Source>^Latif 2021^, https://medlineplus.gov/ency/article/000512.htm#:~:text=Acute%20tubular%20necrosis%20(ATN)%20is,it%20passes%20through%20the%20kidneys
<Concept field>symptoms
<Related words>renal impairment
<Type of relation>super.
<Related words>^immunoglobulin light chains^
<Type of relation>general
<Related words>^cast nephropathy^
<Type of relation>super.
<Related words>^creatinine clearance^
<Type of relation>sub.
<Related words>^glucocorticoids^
<Type of relation>general
<Synonyms>The term “acute tubular necrosis” is often substituted by its initials “ATN”.

<en>ATN
<Morphosyntax>noun
<Category>initials
<Usage label>common
<Source>^Latif 2021^, https://medlineplus.gov/ency/article/000512.htm#:~:text=Acute%20tubular%20necrosis%20(ATN)%20is,it%20passes%20through%20the%20kidneys
<Variant of>acute tubular necrosis

<zh>急性肾小管坏死
<Morphosyntax>noun group
<Usage label>main term
<Source>^高點醫護網^，https://doctor.get.com.tw/m/Journal/detail.aspx?no=402989
<Definition>急性肾小管坏死(ATN)，当各种原因引起肾功能在短期内急剧下降，血清肌酸酐（SCr）每天上升 0.5mg/dl，出现氮质代谢废物滞留体内及尿量减少的一种临床症候群。

<Source>^高點醫護網^，https://doctor.get.com.tw/m/Journal/detail.aspx?no=402989

<Context>急性肾小管坏死(ATN)，是急性腎功能衰竭最常见的类型。主要表现为肾丝球滤过率明显降低、进行性氮质血症，以及肾小管重吸收障碍和排泄功能低下所致的水、电解质与酸碱失衡。肾小管坏死的主要病因可概括为肾缺血和肾毒性损害两大类。

<Source>^高點醫護網^，https://doctor.get.com.tw/m/Journal/detail.aspx?no=402989

<Concept field>症状

<Related words>肾功能损伤

<Type of relation>super.

<Related words>^免疫球蛋白轻链^

<Type of relation>general

<Related words>^管型肾病^

<Type of relation>super.

<Related words>^肌酐清除率^

<Type of relation>sub.

<Related words>^糖皮质激素^

<Type of relation>general

<Synonym>“急性肾小管坏死”和“ATP”是近义词。

<zh>ATP

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^高點醫護網^，https://doctor.get.com.tw/m/Journal/detail.aspx?no=402989

<Variant of>急性肾小管坏死

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>creatinine clearance

<Morphosyntax>noun group

<Usage label>main term

<Source>Shahbaz/Gupta 2022, https://www.ncbi.nlm.nih.gov/books/NBK544228/

<Definition>Creatinine clearance (CrCl) is the volume of blood plasma cleared of creatinine per unit time.

<Source>Shahbaz/Gupta 2022, https://www.ncbi.nlm.nih.gov/books/NBK544228/
<Context>The measurement of accurate renal function is vital for the routine care of patients. The glomerular filtration rate (GFR) describes the flow rate of filtered fluid through the kidneys. The biochemical marker creatinine found in serum and urine is commonly used in the estimation of GFR. Both CrCl and GFR can be measured using the comparative values of creatinine in blood and urine. Creatinine clearance can also be estimated using serum creatinine levels.
<Source>Shahbaz/Gupta 2022, https://www.ncbi.nlm.nih.gov/books/NBK544228/
<Concept field>cytology
<Related words>renal impairment
<Type of relation>super.
<Related words>^immunoglobulin light chains^
<Type of relation>general
<Related words>^cast nephropathy^
<Type of relation>super.
<Related words>^acute tubular nephrosis^
<Type of relation>super.
<Related words>^glucocorticoids^
<Type of relation>general
<Synonyms>The term “creatinine clearance” is often substituted by its initials “CrCl”.

<en>CrCl
<Morphosyntax>noun
<Category>initials
<Usage label>common
<Source>Shahbaz/Gupta 2022, https://www.ncbi.nlm.nih.gov/books/NBK544228/
<Variant of>creatinine clearance

<zh>肌酐清除率
<Morphosyntax>noun group
<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/tests-procedures/creatinine-test/about/pac-20384646
<Definition>肌酐清除率是衡量肾脏将肌酐从血流中滤出以通过尿液排出的能力的指标。
<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/tests-procedures/creatinine-test/about/pac-20384646

<Context>肌酐清除率通常根据 24 小时尿液样本中的肌酐测量值和相同时间段内采集的血清样本确定。肌酐清除率报告为毫升肌酐/分钟/体表面积（mL/min/BSA）。低于您所在年龄组的正常范围的结果可能提示肾功能不良或影响肾脏血流的状况。

<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/tests-procedures/creatinine-test/about/pac-20384646

<Concept field>细胞学

<Related words>肾功能损伤

<Type of relation>super.

<Related words>^免疫球蛋白轻链^

<Type of relation>general

<Related words>^管型肾病^

<Type of relation>super.

<Related words>^急性肾小管坏死^

<Type of relation>super.

<Related words>^糖皮质激素^

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>人体生理学 / Human physiology (612)

<en>glucocorticoids

<Morphosyntax>noun

<Usage label>main term

<Source>^Chourpiliadis/Chourpiliadis 2022^, https://www.ncbi.nlm.nih.gov/books/NBK560897/

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Glucocorticoids are steroid hormones produced from the cortex of adrenal glands

<Source>^Chourpiliadis/Chourpiliadis 2022^, https://www.ncbi.nlm.nih.gov/books/NBK560897/

<Context>Glucocorticoids have a pivotal role in the glucose, protein, and fat metabolism of the body. They originate from steroid precursors and are synthesized primarily in the zona fasciculata of the adrenal cortex. Their medical significance arises from their anti-inflammatory, anti-allergic, and immune-suppressive role in the body, and this particular role used for medical treatment purposes. The essential glucocorticoid in the body is cortisol.

<Source>^Chourpiliadis/Chourpiliadis 2022^, https://www.ncbi.nlm.nih.gov/books/NBK560897/

<Concept field>physiology

<Related words>renal impairment

<Type of relation>super.

<Related words>^immunoglobulin light chains^

<Type of relation>general

<Related words>^cast nephropathy^

<Type of relation>super.

<Related words>^acute tubular nephrosis^

<Type of relation>super.

<Related words>^creatinine clearance^

<Type of relation>general

<zh>糖皮质激素

<Morphosyntax>noun group

<Source>^国家化妆品质量检验检测中心 2016^，http://www.gjhzp.org.cn/zjyjy_hzp/infodetail/?infoid=0a3189ff-b77b-4a74-9d9b-a4fc4108ac5a&categoryNum=004001

<Definition>糖皮质激素是由肾上腺皮质中束状带分泌的一类甾体激素，具有调节糖、脂肪、和蛋白质的生物合成和代谢的作用，还具有抗炎作用。

<Source>^国家化妆品质量检验检测中心 2016^，http://www.gjhzp.org.cn/zjyjy_hzp/infodetail/?infoid=0a3189ff-b77b-4a74-9d9b-a4fc4108ac5a&categoryNum=004001

<Context>糖皮质激素是一类临床药物，在抗炎、抗敏等方面具有显著的效果。医学上广泛用于治疗皮炎、湿疹等疾病，但必须严格在医生的指导下使用。滥用糖皮质激素对皮肤的伤害很大，因此它属于化妆品的禁用物质。

<Source>^国家化妆品质量检验检测中心 2016^，http://www.gjhzp.org.cn/zjyjy_hzp/infodetail/?infoid=0a3189ff-b77b-4a74-9d9b-a4fc4108ac5a&categoryNum=004001

<Concept field>生理学

<Related words>肾功能损伤

<Type of relation>super.

<Related words>^免疫球蛋白轻链^

<Type of relation>general

<Related words>^管型肾病^

<Type of relation>super.

<Related words>^急性肾小管坏死^

<Type of relation>super.

<Related words>^肌酐清除率^

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>normocytic normochromic anaemia

<Morphosyntax>noun group

<Source>^Yilmaz/Shaikh 2023^, https://www.ncbi.nlm.nih.gov/books/NBK565880/

<Lexica>Found in ^Merriam/Webster 2016^

<Definition>Normocytic normochromic anaemia is the type of anaemia in which the circulating red blood cells (RBCs) are the same size (normocytic) and have a normal red colour (normochromic).

<Source>Yilmaz/Shaikh 2023, https://www.ncbi.nlm.nih.gov/books/NBK565880/

<Context>Normocytic normochromic anaemia differs from other forms of anaemia because the average size and haemoglobin content of the RBCs are typically within normal limits. RBCs typically appear similar to normal cells under microscopic examination, though in some cases, there may be variations in size and shape that equalize one another, resulting in average values within the normal range. Normocytic normochromic anaemia most commonly occurs as a result of miscellaneous chronic infections and systemic diseases. Most normocytic anaemias appear to be the outcome of the impaired production of RBCs. Management depends primarily on treating the underlying cause of anaemia.

<Source>Yilmaz/Shaikh 2023, https://www.ncbi.nlm.nih.gov/books/NBK565880/

<Concept field>symptoms

<Related words>^CRAB symptoms^

<Type of relation>super.

<Related words>blood cell

<Type of relation>sub.

<Related words>^erythropoietin^

<Type of relation>sub.

<Related words>^hepcidin^

<Type of relation>sub.

<zh>正细胞性正色素性贫血

<Morphosyntax>noun group

<Source>^我附近的健康食品 2022^，https://zh-cn.healthy-food-near-me.com/normocytic-normochromic-anemia/

<Definition>正细胞正色素性贫血是一大类贫血，其特征在于血象的某些变化。

<Source>^我附近的健康食品 2022^，https://zh-cn.healthy-food-near-me.com/normocytic-normochromic-anemia/

<Context>正常色素性贫血的定义包括血液的颜色指示剂。 它表征了红细胞与血红蛋白的饱和程度，血红蛋白赋予红细胞一种特征颜色。正细胞性贫血可能与各种病理有关，包括：肾功能衰竭和内分泌腺疾病，血液癌症，或转移扩散到全身，缺铁性贫血。

<Source>^我附近的健康食品 2022^，https://zh-cn.healthy-food-near-me.com/normocytic-normochromic-anemia/

<Concept field>症状

<Related words>^CRAB 症状^

<Type of relation>super.

<Related words>血球

<Type of relation>sub.

<Related words>^促红细胞生成素^

<Type of relation>sub.

<Related words>^铁调素^

<Type of relation>sub.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>erythropoietin

<Morphosyntax>noun

<Usage label>main term

<Source>^Schoener/Borger 2023^, https://www.ncbi.nlm.nih.gov/books/NBK536997/

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Erythropoietin (EPO) is a glycoprotein hormone, naturally produced by the peritubular cells of the kidney, that stimulates red blood cell production.
<Source>^Schoener/Borger 2023^, https://www.ncbi.nlm.nih.gov/books/NBK536997/
<Context>Renal cortex peritubular cells produce most EPO in the human body. Partial pressure of oxygen (PO2) directly regulates EPO production. The lower the pO2, the greater the production of EPO. Erythropoietin stimulating agents (ESAs) are recombinant versions of EPO produced pharmacologically. ESAs are generally indicated in conditions where there is impaired red blood cell production. This activity will highlight the mechanism of action, adverse event profile, pharmacology, monitoring, and relevant interactions of ESAs in light of the natural physiology of erythropoietin, pertinent for members of the interprofessional team in the treatment of patients with conditions where these agents are indicated.
<Source>^Schoener/Borger 2023^, https://www.ncbi.nlm.nih.gov/books/NBK536997/
<Concept field>cytology
<Related words>^CRAB symptoms^
<Type of relation>super.
<Related words>blood cell
<Type of relation>sub.
<Related words>^normocytic normochromic anaemia^
<Type of relation>super.
<Related words>^hepcidin^
<Type of relation>coord.
<Synonyms>The term “erythropoietin” is often substituted by its acronym “EPO”; while its full form “endogenous erythropoietin” is not frequently used.

<en>EPO
<Morphosyntax>noun
<Category>acronym
<Usage label>common
<Source>^Oxford Concise Medical Dictionary 2020^:270
<Variant of>erythropoietin

<en>endogenous erythropoietin
<Morphosyntax>noun group
<Category>full form
<Usage label>uncommon

<Source>^Schoener/Borger 2023^, https://www.ncbi.nlm.nih.gov/books/NBK536997/
<Variant of>erythropoietin

<zh>促红细胞生成素
<Morphosyntax>noun group
<Usage label>main term
<Source>^也龙，等，2019^:662
<Definition>促红细胞生成素（EPO）是一种疏水性糖蛋白，主要由哺乳动物肾脏分泌。
<Source>^也龙，等，2019^:662
<Context>研究表明 EPO 是红细胞成熟关键因素，可以促进红系祖细胞生长、增殖、分化和成熟，诱导红细胞特定蛋白表达，从而增加红细胞数量。EPO 最早用于治疗肾性贫血，之后逐渐用于纠正创伤和外科手术引起的贫血。
<Source>^也龙，等，2019^:662
<Concept field>细胞学
<Related words>^CRAB 症状^
<Type of relation>super.
<Related words>血球
<Type of relation>sub.
<Related words>^正细胞性正色素性贫血^
<Type of relation>super.
<Related words>^铁调素^
<Type of relation>coord.
<Synonyms>“EPO”和“促红细胞生成素”是近义词。

<zh>EPO
<Morphosyntax>noun
<Category>acronym
<Usage label>common
<Source>^也龙，等，2019^:662
<Variant of>促红细胞生成素
**
<Subject>医学与卫生 / Medicine & health (610)
<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>hepcidin

<Morphosyntax>noun

<Source>^Ganz 2016^:1916

<Lexica>Found in ^Oxford Concise Medical Dictionary 2020^

<Definition>Hepcidin is an iron-regulating peptide hormone made in the liver.

<Source>^Ganz 2016^:1916

<Context>Hepcidin controls the delivery of iron to blood plasma from intestinal cells absorbing iron, from erythrocyte-recycling macrophages, and from iron-storing hepatocytes. Hepcidin acts by binding to and inactivating the sole cellular iron exporter, ferroportin, which delivers iron to plasma from all iron-transporting cells. In a classical endocrine feedback system, hepcidin production is stimulated by plasma iron and iron stores. Increased erythropoietic activity suppresses hepcidin, which leads to increased iron absorption and release of iron from stores, matching iron supply to increased demand. Pathologically increased concentrations of hepcidin are seen in iron-refractory iron deficiency anaemia, in anaemia of inflammation, and anaemia of chronic kidney disease where increased hepcidin limits the availability of iron for erythropoiesis. Its central involvement in a variety of iron disorders makes hepcidin an important target for diagnostic and therapeutic applications.

<Source>^Ganz 2016^:1916

<Concept field>cytology

<Related words>^CRAB symptoms^

<Type of relation>super.

<Related words>blood cell

<Type of relation>sub.

<Related words>^normocytic normochromic anaemia^

<Type of relation>super.

<Related words>^erythropoietin^

<Type of relation>coord.

<zh>铁调素

<Morphosyntax>noun

<Usage label>main term

<Source>^范斯斌，等 2015^:977

<Definition>铁调素（Hepcidin）是肝细胞合成的小分子肽类激素，在机体铁稳态调控中发挥着枢纽作用。

<Source>^范斯斌，等 2015^:977

<Context>Hepcidin 作用于肠道刷状缘上皮细胞、肝脾单核-网状内皮细胞的铁通道蛋白（Ferroportin），促进其细胞内吞而被降解，从而减少肠道对外源食物铁的吸收，抑制单核-网状内皮系统储存池铁的释放，使机体处于限制性铁利用状态。Hepcidin 表达调控异常是多种铁代谢失衡的关键环节。针对 Hepcidin 的分子靶向治疗可有效纠正失衡的铁稳态，对于铁过载或限制性铁利用障碍性疾病有潜在的临床应用价值。

<Source>^范斯斌，等 2015^:977

<Concept field>细胞学

<Related words>^CRAB 症状^

<Type of relation>super.

<Related words>血球

<Type of relation>sub.

<Related words>^正细胞性正色素性贫血^

<Type of relation>super.

<Related words>^促红细胞生成素^

<Type of relation>coord.

<Synonyms>“Hepcidin”和“铁调素”是近义词，文章上常用引文的名字。

<zh>hepcidin

<Morphosyntax>noun

<Usage label>common

<Category>translation

<Source>^范斯斌，等 2015^:977

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>immunoparesis

<Morphosyntax>noun

<Usage label>main term

<Source>^Chahin, et al. 2022^

<Definition>Immunoparesis is defined as the suppression of one or more of the uninvolved immunoglobulins, AKA, polyclonal immunoglobulin.

<Source>^Chahin, et al. 2022^

<Context>Immunoparesis is a distinguishing feature of multiple myeloma, smouldering multiple myeloma, and monoclonal gammopathy of unknown significance (MGUS). The extent of immunoparesis is an independent prognostic factor in patients with newly diagnosed multiple myeloma. Myeloma patients with suppressed uninvolved immunoglobulins at diagnosis have shorter median overall survival (OS) and progression-free survival (PFS). There is a clear association between the high incidence of immunoglobulin suppression and a higher risk of infection. Intuitively, this contributes to the poorer survival in patients with immunoparesis.
<Source>^Chahin, et al. 2022^
<Concept field>symptoms
<Related words>^osteolytic lesion^
<Type of relation>general
<Related words>^osteoporosis^
<Type of relation>general

<zh>免疫不全麻痹
<Morphosyntax>noun group
<Usage label>main term
<Source>^周小钢，等 2014^:1115
<Definition>免疫不全麻痹（也称为多克隆低丙种球蛋白血症）是多克隆免疫球蛋白产生受抑的现象。
<Source>^周小钢，等 2014^:1115
<Context>免疫不全麻痹在意义未明的单克隆免疫球蛋白血症(MGUS)进展为 MM 具有预测作用。在冒烟型骨髓瘤(SMM)中，免疫不全麻痹也与疾病进展至症状性 MM 相关。新药时代，免疫不全麻痹的改善率不断增加。
<Source>^周小钢，等 2014^:1115
<Concept field>症状
<Related words>^溶骨性病变^
<Type of relation>general
<Related words>^骨质疏松症^
<Type of relation>general
<Synonyms>“多克隆低丙种球蛋白血症”和“免疫不全麻痹”是近义词，但是“多克隆低丙种球蛋白血症”是不常用的。

<zh>多克隆低丙种球蛋白血症

<Morphosyntax>noun group

<Usage label>uncommon

<Source>^周小钢，等 2014^:1115

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>osteoporosis

<Morphosyntax>noun

<Usage label>main term

<Source>^NHS. National Health System UK 2022^, https://www.nhs.uk/conditions/osteoporosis/

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Osteoporosis is a health condition that weakens bones, making them fragile and more likely to break.

<Source>^NHS. National Health System UK 2022^, https://www.nhs.uk/conditions/osteoporosis/

<Context>Osteoporosis is not usually painful until a bone is broken, but broken bones in the spine are a common cause of long-term pain. A broken bone is often the first sign of osteoporosis. Treatment for osteoporosis is based on treating and preventing broken bones and taking medicine to strengthen your bones.

<Source>^NHS. National Health System UK 2022^, https://www.nhs.uk/conditions/osteoporosis/

<Concept field>symptoms

<Related words>^osteolytic lesion^

<Type of relation>general

<Related words>^immunoparesis^

<Type of relation>general

<zh>骨质疏松症

<Morphosyntax>noun group

<Source>^ 中华人民共和国国家卫生健康委员会 2012^, http://www.nhc.gov.cn/wjw/jbyfykz/201304/2fb324d3cc0947bc9b7cf9b84fc5c851.shtml

<Definition>骨质疏松症是一种全身性疾病，它的主要特征是骨矿物质含量低下、骨结构破坏、骨强度降低、易发生骨折。

<Source>^ 中华人民共和国国家卫生健康委员会 2012^, http://www.nhc.gov.cn/wjw/jbyfykz/201304/2fb324d3cc0947bc9b7cf9b84fc5c851.shtml

<Context>骨质疏松症是第四位常见的慢性疾病，也是中老年最常见的骨骼疾病。骨折是骨质疏松症的严重后果，常是部分骨质疏松症患者的首发症状和就诊原因。骨质疏松性骨折是脆性骨折，通常在日常负重、活动、弯腰和跌倒后发生。髋部骨折后第一年内由于各种并发症死亡率达到20－25%。存活者中50%以上会有不同程度的残疾。疼痛、驼背、身高降低和骨折是骨质疏松症的特征性表现。富含钙、低盐和适量蛋白质的均衡饮食对预防骨质疏松有益。

<Source>^ 中华人民共和国国家卫生健康委员会 2012^, http://www.nhc.gov.cn/wjw/jbyfykz/201304/2fb324d3cc0947bc9b7cf9b84fc5c851.shtml

<Concept field>症状

<Related words>^溶骨性病变^

<Type of relation>general

<Related words>^免疫不全麻痹^

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>invasive aspergillosis

<Morphosyntax>noun group

<Usage label>main term

<Source>^Thornton 2010^:187

<Definition>Invasive aspergillosis (IA) caused by the fungus Aspergillus fumigatus is a frequent and life-threatening complication of chemotherapy and bone marrow transplantation with high rates of mortality and morbidity.

<Source>^Thornton 2010^:187

<Context>Diagnosis of IA is complex and can only be confirmed by identification of the fungus in biopsy samples. Capturing tissue for diagnosis is in itself hazardous, and because of this many patients receive empirical antifungal treatment rather than undergo biopsy. However, the treatment carries with it significant side effects and is prohibitively expensive. Because of this, attempts have been made to develop specific and sensitive diagnostic tests that can be used to

track the early onset of infection and permit rational administration of antifungal drugs. The commercial Platelia enzyme immunoassay (EIA) is an assay that has found widespread use in IA diagnosis.
<Source>^Thornton 2010^:187
<Concept field>infections
<Related words>aspergillus fumigatus
<Type of relation>sub.
<Related words>chemotherapy
<Type of relation>general
<Related words>bone marrow transplantation
<Type of relation>general
<Synonyms>The term “invasive aspergillosis” is often substituted by its initials “IA”.

<en>IA
<Morphosyntax>noun
<Category>initials
<Usage label>common
<Source>^Thornton 2010^:187
<Variant of>invasive aspergillosis

<zh>侵袭性肺麴菌病
<Morphosyntax>noun group
<Source>^邱宗佑 2021^
<Definition>侵袭性肺麴菌病（IPA）为进展快速且死亡率高的感染性疾病，以往常见于免众功能严重不全的病人，近年来发生在非免疫功能不全病人身上的案例也有不断上升的趋势。
<Source>^邱宗佑 2021^
<Context>及早诊断并开始治疗是降低死亡率的关键之一，然而侵袭性肺麴菌病的临床症状不具特异性，在疾病早期常臾细菌性肺炎产生混淆，如何尽早诊断仍是临床上的一大挑战。治疗侵袭性肺麴菌病的抗征菌药物分别有 polyenes、triazolesy 以及 echinocandins；在选择抗征菌药物时，除了参考现行治疗指引建议，病人的疾病严重程度、肝肾功能、现状用药等因素都是需要考量的重点。
<Source>^邱宗佑 2021^

<Concept field>感染

<Related words>薰烟麴菌

<Type of relation>sub.

<Related words>化学疗法

<Type of relation>general

<Related words>骨髓移植

<Type of relation>general

<Synonyms>“IPA”和“侵袭性肺麴菌病”是近义词。

<zh>IPA

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^邱宗佑 2021^

<Variant of>侵袭性肺麴菌病

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>hyper viscosity

<Morphosyntax>noun group

<Usage label>main term

<Source>^Perez Rogers/Estes 2023^, https://www.ncbi.nlm.nih.gov/books/NBK518963/

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Hyperviscosity (HVS) is an oncologic emergency that is characterized by red blood cell shape deformity or a pathological increase in serum proteins, red blood cells (RBC), white blood cells (WBC), or platelets.

<Source>cf.^Perez Rogers/Estes 2023^, https://www.ncbi.nlm.nih.gov/books/NBK518963/

<Context>The most common cause of HVS is Waldenstrom macroglobulinemia (WM), and therefore, the term HVS is typically used to describe an increase in serum proteins. Management consists of supportive care with intravenous fluids, plasmapheresis, and treatment of the underlying haematological condition. An increase in blood viscosity can be caused either by a deformity of the shape of red blood cells (RBCs) which causes RBC aggregation and decreased blood flow or by any pathological elevation of the components of blood. This includes RBC, WBC, platelets, or serum proteins. This increase in viscosity causes sluggish blood flow, relative

decreased microvascular circulation, and hypoperfusion of tissues. The severity of clinical symptoms is directly related to the increased levels of serum viscosity, with progressively more severe symptoms occurring as the individual patient's serum viscosity increases.
<Source>^Perez Rogers/Estes 2023^, https://www.ncbi.nlm.nih.gov/books/NBK518963/
<Concept field>haematology
<Related words>blood cell
<Type of relation>sub.
<Related words>^rouleaux^
<Type of relation>sub.
<Synonyms>The term "hyper viscosity" is often substituted by its initials "HVS", while its full form "hyper viscosity syndrome" is not frequently used.

<en>hyper viscosity syndrome
<Morphosyntax>noun group
<Category>full form
<Usage label>uncommon
<Source>^Perez Rogers/Estes 2023^, https://www.ncbi.nlm.nih.gov/books/NBK518963/
<Variant of>hyper viscosity

<en>HVS
<Morphosyntax>noun
<Category>initials
<Usage label>common
<Source>^Perez Rogers/Estes 2023^, https://www.ncbi.nlm.nih.gov/books/NBK518963/
<Variant of>hyper viscosity

<zh>血液高度黏稠症候群
<Morphosyntax>noun group
<Usage label>main term
<Source>^涂松昀 2020^
<Definition>血液高度黏稠症候群 (HVS)是一种血液肿瘤急症，肇因于血液黏稠度上升而产生症状。
<Source>^涂松昀 2020^

<Context>血液黏稠度上升时，血流流速会下降，造成全身小血管循环不佳而使组织灌流不足。此外血液中的蛋白质(抗体)浓度上升也会影响血小板作用，而使凝血功能出现异常。临床症状的严重程度会随着血液黏稠度上升而增加。出血是最常见的表现，因血小板功能异常而 产生牙龈、鼻黏膜、或消化道出血。血液高度黏稠症候群典型症状为黏膜出血、神经功能缺损、视觉变化，配合 血液检验、黏稠度诊断。急性期以生理食盐水输注、血浆置换、及依临床症状给予支持性治疗为主，后续转 介血液肿瘤专科治疗。

<Source>^涂松昀 2020^

<Concept field>血液学

<Related words>血球

<Type of relation>sub.

<Related words>^缗錢狀紅血球凝集^

<Type of relation>sub.

<Synonyms>“HVS”和“血液高度黏稠症候群”是近义词。

<zh>HVS

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^涂松昀 2020^

<Variant of>血液高度黏稠症候群

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>rouleaux

<Morphosyntax>noun

<Usage label>main term

<Source>^Baskurt/Meiselman 2013^:23

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Rouleaux are two-dimensional structures that are formed by face-to-face contact of red blood cells (RBC) into linear arrays whose shape is similar to a stack of coins.

<Source>cf.^Baskurt/Meiselman 2013^:23

<Context>Human red blood cells (RBC) are able to aggregate to form two- and three-dimensional structures when suspended in aqueous solutions containing large plasma proteins or polymers. These structures form at stasis or when fluid shear forces are sufficiently low and can be dispersed by higher shear forces; the aggregation process is reversible when shear forces are decreased or eliminated. The formation of these structures is affected by factors such as available space and the level of cell-to-cell attractive forces. RBC aggregation is a relatively fast process with time constants of about seconds for initial rouleau formation and somewhat longer for forming three-dimensional aggregates. Therefore, RBC aggregates may form in various parts of the circulatory system.
<Source>^Baskurt/Meiselman 2013^:23-24
<Concept field>cytology
<Related words>blood cell
<Type of relation>sub.
<Related words>^hyper viscosity^
<Type of relation>sub.

<zh>缗錢狀紅血球凝集
<Morphosyntax>noun group
<Source>^吳泰民 2016^
<Definition>缗钱状红血球凝集是指血液抹片上的红血球呈条状凝集，看起来像以前的调钱串，条状可呈分枝或不分枝。
<Source>^吳泰民 2016^
<Context>在临床上，病人若有血液循环问题，心血管疾病，输用这种“缗钱状红血球凝集“之血品，容易在微小血管造成阻塞。红血球凝集的机转仍不甚清楚，理论之一为 Bridging，造桥理论，另一为 Depletion，排除理论。前者为血清内大分子聚集在红血球之间，后者为大分子在血清内压迫红血球之间的聚合物，然而，去凝集的机转与血管内机械性的血流型态(Shear force)，Shear 指类似剪羊毛的动作，它增加时凝集会降低；排斥力则与红血球表面的弹性能量有关。
<Source>^吳泰民 2016^
<Concept field>细胞学
<Related words>血球
<Type of relation>sub.
<Related words>^血液高度黏稠症候群^

<Type of relation>sub.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>epidural spinal cord compression

<Morphosyntax>noun group

<Usage label>main term

<Source>^Prasad/Schiff 2005^:15

<Definition>Epidural spinal-cord compression (ESSC) can be defined as the compressive indentation, displacement, or encasement of the thecal sac that surrounds the spinal cord or cauda equina by spinal epidural metastases (SEM) or by locally advanced cancer.

<Source>^Prasad/Schiff 2005^:15

<Context>ESSC can occur by posterior extension of a vertebral body mass, which results in compression of the anterior aspect of the spinal cord, by anterior extension of a mass arising from the dorsal elements, or by growth of a mass invading the vertebral foramen.

<Source>^Prasad/Schiff 2005^:15

<Concept field>symptoms

<Related words>^corticosteroids^

<Type of relation>general

<Related words>^radiculopathy^

<Type of relation>sub.

<Synonyms>The terms “spinal cord compression” and “malignant spinal cord compression” are synonym to “M-protein” and they are commonly used. The term “epidural spinal cord compression” is often substituted by its initials “ESSC”.

<en>spinal cord compression

<Morphosyntax> noun group

<Usage label>common

<Source>^Prasad/Schiff 2005^:15

<en>malignant spinal cord compression

<Morphosyntax> noun group

<Usage label>common

<Source>^Prasad/Schiff 2005^:15

<en>ESSC

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^Prasad/Schiff 2005^:15

<Variant of>epidural spinal cord compression

<zh>恶性脊髓压迫症

<Morphosyntax>noun group

<Usage label>main term

<Source>^田卫伟，等 2017^:639

<Definition>恶性脊髓压迫症（SCC）是指脊椎或椎管内占位性病变（肿瘤转移或原发）引起脊髓、脊神经根及其供应血管受压，造成脊髓及脊神经根功能缺陷的临床综合征。

<Source>^田卫伟，等 2017^:639

<Context>若恶性脊髓压迫症得不到及时诊治，常常发生截瘫、大小便困难等不可逆的神经损害，严重影响患者生活质量。由于发病率低，该病早期诊断、治疗方式仍在探索中。

<Source>^田卫伟，等 2017^:639

<Concept field>症状

<Related words>^皮质类固醇^

<Type of relation>general

<Related words>^神经根疾病^

<Type of relation>sub.

<Synonyms>“SCC”和“恶性脊髓压迫症”是近义词。

<zh>SCC

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^田卫伟，等 2017^:639

<Variant of>恶性脊髓压迫症

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>corticosteroids

<Morphosyntax>noun

<Source>^Hodgens/Sharman 2022^, https://www.ncbi.nlm.nih.gov/books/NBK554612/

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Corticosteroids are synthetic analogues of the natural steroid hormones produced by the adrenal cortex and include glucocorticoids and mineralocorticoids.

<Source>^Hodgens/Sharman 2022^, https://www.ncbi.nlm.nih.gov/books/NBK554612/

<Context>The term corticosteroids in practice, however, is generally used to refer to the glucocorticoid effect. Glucocorticoids are primary stress hormones that regulate a variety of physiologic processes and are essential for life. Corticosteroids are among the most widely prescribed drug classes worldwide. Corticosteroids are used at physiologic doses as replacement therapy in cases of adrenal insufficiency and supraphysiologic doses in treatments for anti-inflammatory and immunosuppressive effects. Corticosteroids produce anti-inflammatory and immunosuppressive effects, protein and carbohydrate metabolic effects, water and electrolyte effects, central nervous system effects, and blood cell effects.

<Source>^Hodgens/Sharman 2022^, https://www.ncbi.nlm.nih.gov/books/NBK554612/

<Concept field>pharmacology

<Related words>^epidural spinal cord compression^

<Type of relation>general

<Related words>^radiculopathy^

<Type of relation>general

<zh>皮质类固醇

<Morphosyntax>noun group

<Source>^默沙东诊疗手册^，https://www.msdmanuals.cn/home/multimedia/table/corticosteroids-uses-and-side-effects

<Definition>皮质类固醇是与皮质醇（或称可的松）具有相同作用的合成物，皮质醇是由肾上腺外层（皮质）产生的一种类固醇激素，因此称作“皮质类固醇”。

<Source>^默沙东诊疗手册^，https://www.msdmanuals.cn/home/multimedia/table/corticosteroids-uses-and-side-effects

<Context>皮质类固醇和皮质醇化学性质相关，但是作用不同，皮质醇（如睾酮）由身体产生，有时会被运动员滥用。很多合成的皮质类固醇比皮质醇的作用更强，作用的持续时间也更长。皮质类固醇是现有的最强效抗炎药物。长期使用皮质类固醇药物，特别

是大剂量时，尤其是通过口或静脉给药时，总会产生很多不良反应，几乎涉及人体的每个器官。

<Source>^默沙东诊疗手册^，https://www.msdmanuals.cn/home/multimedia/table/corticosteroids-uses-and-side-effects

<Concept field>药理学

<Related words>^恶性脊髓压迫症^

<Type of relation>general

<Related words>^神经根疾病^

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>radiculopathy

<Morphosyntax>noun

<Usage label>main term

<Source>^OrthoInfo^, https://orthoinfo.aaos.org/en/diseases--conditions/cervical-radiculopathy-pinched-nerve/

<Lexica>Found in ^Merriam/Webster 2016^

<Definition>Cervical radiculopathy, commonly called a "pinched nerve," is the compression or irritation of a nerve in the neck, where it branches away from the spinal cord.

<Source>^OrthoInfo^, https://orthoinfo.aaos.org/en/diseases--conditions/cervical-radiculopathy-pinched-nerve/

<Context>Cervical radiculopathy may cause pain that radiates into the shoulder and/or arm, as well as muscle weakness and numbness. Cervical radiculopathy most often arises from degenerative changes that occur in the spine as we age or from an injury that causes a herniated, or bulging, intervertebral disk. In most cases, cervical radiculopathy responds well to conservative treatment that includes medication and physical therapy.

<Source>^OrthoInfo^, https://orthoinfo.aaos.org/en/diseases--conditions/cervical-radiculopathy-pinched-nerve/

<Concept field>symptoms

<Related words>^epidural spinal cord compression^

<Type of relation>super.

<Related words>^corticosteroids^

<Type of relation>general
<Synonyms>The term “pinched nerve” is a synonym to “radiculopathy”, and it is commonly used.

<en>pinched nerve
<Morphosyntax>noun group
<Usage label>common
<Source>^OrthoInfo^, https://orthoinfo.aaos.org/en/diseases--conditions/cervical-radiculopathy-pinched-nerve/

<zh>神经根疾病
<Morphosyntax>noun group
<Usage label>main term
<Source>^Rubin 2022^, https://www.msdmanuals.cn/home/brain-spinal-cord-and-nerve-disorders/peripheral-nerve-and-related-disorders/nerve-root-disorders
<Definition>神经根疾病是一种病情由突发或长期压迫脊神经根引起。
<Source>^Rubin 2022^, https://www.msdmanuals.cn/home/brain-spinal-cord-and-nerve-disorders/peripheral-nerve-and-related-disorders/nerve-root-disorders
<Context>神经根疾病通常由椎间盘突出或脊柱骨关节炎引起。这些疾病可导致疼痛、感觉异常和/或身体供应区域肌肉无力。医生根据影像学检查、电诊断检查以及确定病因的检查的结果来诊断神经根疾病。如果可能，医生会治疗病因，并给予药物缓解疼痛，包括非处方止痛药（如非甾体类抗炎药或对乙酰氨基酚）和皮质类固醇。
<Source>^Rubin 2022^, https://www.msdmanuals.cn/home/brain-spinal-cord-and-nerve-disorders/peripheral-nerve-and-related-disorders/nerve-root-disorders
<Concept field>症状
<Related words>^恶性脊髓压迫症^
<Type of relation>super.
<Related words>^皮质类固醇^
<Type of relation>general
<Synonyms>“神经根病”和“神经根疾病”是近义词。

<zh>神经根病
<Morphosyntax>noun group
<Usage label>common

<Source>^Rubin 2022^, https://www.msdmanuals.cn/home/brain-spinal-cord-and-nerve-disorders/peripheral-nerve-and-related-disorders/nerve-root-disorders

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病的发病率和预防/ Incidence and prevention of disease (614)

<en>serum protein electrophoresis

<Morphosyntax>noun group

<Usage label>main term

<Source>^O'Connell, et al. 2005^:105

<Definition>Serum protein electrophoresis is a laboratory examination in which proteins are separated based on their physical properties, the subsets of these proteins are used in interpreting the results.

<Source>^O'Connell, et al. 2005^:105

<Context>Serum protein electrophoresis is used to identify patients with multiple myeloma and other serum protein disorders. Many subspecialists include serum protein electrophoresis screening in the initial evaluation for numerous clinical conditions. In electrophoresis, serum is placed on a specific medium, and a charge is applied. The net charge (positive or negative) and the size and shape of the protein commonly are used in differentiating various serum proteins. Several subsets of serum protein electrophoresis are available. The names of these subsets are based on the method that is used to separate and differentiate the various serum components.

<Source>^O'Connell, et al. 2005^:105

<Concept field>laboratory test

<Related words>^serum immunofixation^

<Type of relation>coord.

<Related words>^urine protein electrophoresis^

<Type of relation>coord.

<Related words>^urine immunofixation^

<Type of relation>coord.

<Synonyms>The term "serum protein electrophoresis" is often substituted by its acronym "SPEP".

<en>SPEP

<Morphosyntax>noun

<Category>acronym

<Usage label>common

<Source>^O'Connell, et al. 2005^:105
<Variant of>serum protein electrophoresis

<zh>血清蛋白电泳
<Morphosyntax>noun group
<Usage label>main term
<Source>^Alvaran Tuazon 2019^, https://www.sscesa.com/article/2087113-overview
<Definition>血清蛋白电泳(SPEP)是一种简单、廉价的基于净电荷、大小和形状分离蛋白质的方法。
<Source>^Alvaran Tuazon 2019^, https://www.sscesa.com/article/2087113-overview
<Context>血清中主要有两种蛋白质白蛋白以及球蛋白。白蛋白是血清中主要的蛋白质成分，在离阳性电极最近的地方有最大的峰。球蛋白在血清总蛋白中所占比例要小得多，但它是血清蛋白电泳解释的主要焦点。各种疾病状态或条件会改变电泳中蛋白质的模式，例如单克隆丙种球蛋白病，多克隆丙种球蛋白病。
<Source>^Alvaran Tuazon 2019^, https://www.sscesa.com/article/2087113-overview
<Concept field>实验室检查
<Related words>^血清免疫固定电泳^
<Type of relation>coord.
<Related words>^尿免蛋白电泳^
<Type of relation>coord.
<Related words>^尿免疫固定电泳^
<Type of relation>coord.
<Synonyms>"SPEP"和"血清蛋白电泳"是近义词。

<zh>SPEP
<Morphosyntax>noun
<Category>acronym
<Usage label>common
<Source>^Alvaran Tuazon 2019^, https://www.sscesa.com/article/2087113-overview
<Variant of>血清蛋白电泳
**
<Subject>医学与卫生 / Medicine & health (610)
<Subfield>疾病的发病率和预防/ Incidence and prevention of disease (614)

<en>serum immunofixation
<Morphosyntax>noun group
<Usage label>main term
<Source>^Pestronk/Lopate 2005^:2181
<Definition>Serum immunofixation is the most sensitive method for identifying and characterizing M proteins in the serum.
<Source>^Pestronk/Lopate 2005^:2181
<Context>Immunofixation involves two steps. First, six aliquots of the test specimen are applied to an agarose gel. Electrophoresis separates the proteins in the specimen according to net charge. In the second fixation steps, five of the electrophoresis lanes are individually stained with antibodies to immunoglobulin (Ig) G, IgA, IgM, and κ and λ light chains, while the sixth lane has a protein fixative applied. Finally, an amido black solution stains the antigen-antibody complexes and the fixed proteins in the sixth lane. Immunofixation, since it is the most sensitive method for detecting M proteins, is the preferred method in the laboratory evaluation of neuropathies. Other methods, such as serum protein electrophoresis, may not detect some M proteins.
<Source>^Pestronk/Lopate 2005^:2181
<Concept field>laboratory test
<Related words>^serum protein electrophoresis^
<Type of relation>coord.
<Related words>^urine protein electrophoresis^
<Type of relation>coord.
<Related words>^urine immunofixation^
<Type of relation>coord.
<Synonyms>The term “serum immunofixation” is often substituted by its acronym “sIFE”.

<en>sIFE
<Morphosyntax>noun
<Category>acronym
<Usage label>common
<Source>^Pestronk/Lopate 2005^:2181
<Variant of>serum immunofixation

<zh>血清免疫固定电泳
<Morphosyntax>noun group

<Usage label>main term

<Source>^Sohu Inc. 2020^, https://www.sohu.com/a/385808258_120051826

<Definition>血清免疫固定电泳是指对血清中的各种蛋白成分进行分离，用于区分蛋白的类型。

<Source>cf.^Sohu Inc. 2020^, https://www.sohu.com/a/385808258_120051826

<Context>检测过程包括琼脂凝胶蛋白电泳和免疫沉淀两个步骤的操作。血清免疫固定电泳可检测 IgG、IgM、IgA 等及 κ 轻链、λ 轻链。血清免疫固定电泳常用于单克隆免疫球蛋白增殖病、本周氏蛋白和游离轻链病、重链病、多组分单克隆免疫球蛋白病、定位蛋白图谱中的寡克隆、多克隆免疫球蛋白病等多种免疫疾病的辅助诊断。

<Source>^Sohu Inc. 2020^, https://www.sohu.com/a/385808258_120051826

<Concept field>实验室检查

<Related words>^血清蛋白电泳^

<Type of relation>coord.

<Related words>^尿免蛋白电泳^

<Type of relation>coord.

<Related words>^尿免疫固定电泳^

<Type of relation>coord.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病的发病率和预防/ Incidence and prevention of disease (614)

<en>urine protein electrophoresis

<Morphosyntax>noun group

<Usage label>main term

<Source>^Jenkins 2009^:119

<Definition>Urine protein electrophoresis is a test meant to find a light chain myeloma producing an excess of free light chains (Bence Jones protein); it is an important part of a myeloma screen.

<Source>cf.^Jenkins 2009^:119

<Context>A band in the urine protein electropherogram may also result from an intact monoclonal immunoglobulin, especially if the patient has poor renal function. Immunofixation is important in defining the nature of the band and in distinguishing between Bence Jones protein and an intact monoclonal protein originating from the serum. From the urine electropherogram

we can also tell if the proteinuria is of glomerular origin with a predominance of albumin, or if it has tubular components with excretion of smaller molecular weight proteins.

<Source>^Jenkins 2009^:119-120

<Concept field>laboratory test

<Related words>^serum protein electrophoresis^

<Type of relation>coord.

<Related words>^serum immunofixation^

<Type of relation>coord.

<Related words>^urine immunofixation^

<Type of relation>coord.

<Synonyms>The term “urine protein electrophoresis” is often substituted by its acronym “UPEP”.

<en>UPEP

<Morphosyntax>noun

<Category>acronym

<Usage label>common

<Source>^Jenkins 2009^:119

<Variant of>urine protein electrophoresis

<zh>尿免蛋白电泳

<Morphosyntax>noun group

<Source>^李贵芳，等 2011^:2353

<Definition>尿蛋白电泳，对尿蛋白组成成分进行测定，判断尿蛋白来源,有利于早期肾脏损伤的诊断和肾脏病变的部位及程度的评。

<Source>^李贵芳，等 2011^:2353

<Context>用于肾脏疾病诊断的传统肾功能测定，只能大体了解肾脏功能的情况，不能判断肾脏损伤的部位和程度。尿液成分的分析，尤其是尿蛋白电泳成分分析，根据各组分的出现与否及含量判断肾脏损伤的部位和程度，已成为肾脏疾病诊断的手段，尤其是早期肾脏损伤的判断标准。该方法操作简便省时，灵敏度高，重复性好。

<Source>^李贵芳，等 2011^:2353

<Concept field>实验室检查

<Related words>^血清蛋白电泳^

<Type of relation>coord.

<Related words>^血清免疫固定电泳^

<Type of relation>coord.

<Related words>^尿免疫固定电泳^

<Type of relation>coord.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病的发病率和预防/ Incidence and prevention of disease (614)

<en>urine immunofixation

<Morphosyntax>noun group

<Usage label>main term

<Source>^Abraham, et al. 2013^:1147

<Definition>Urine Immunofixation electrophoresis (IFE) is a test which establish the presence and isotype of a monoclonal immunoglobulin M-protein in urine.

<Source>cf.^Abraham, et al. 2013^:1147

<Context>Although serum is the most common sample source, urine may also be examined to detect and/or characterize M-proteins or their fragments. UIFE has several advantages, including rapid turn-around time, increased sensitivity, better resolution, and ease of interpretation.

<Source>^Abraham, et al. 2013^:1147

<Concept field>laboratory test

<Related words>^serum protein electrophoresis^

<Type of relation>coord.

<Related words>^serum immunofixation^

<Type of relation>coord.

<Related words>^urine protein electrophoresis^

<Type of relation>coord.

<Synonyms>The term “urine immunofixation electrophoresis” is a synonym to “urine immunofixation” but it is not frequently used, while the term “urine immunofixation” is often substituted by its acronym “UIFE”.

<en>urine immunofixation electrophoresis

<Morphosyntax> noun group

<Usage label>uncommon

<Source>^Abraham, et al. 2013^:1147

<en>UIFE

<Morphosyntax>noun

<Category>acronym

<Usage label>common

<Source>^Abraham, et al. 2013^:1147

<Variant of>urine immunofixation

<zh>尿免疫固定电泳

<Morphosyntax>noun group

<Source>^孙国华，等 2004^:207

<Definition>尿免疫固定电泳用于区分尿蛋白的类型，评价肾脏的损害部位及损伤程度。

<Source>^孙国华，等 2004^:207

<Context>免疫固定电泳方法具有检测敏感性好，特异度高，方法简便省时，结果直观，易于分析，胶片易于保存等优点。

<Source>^孙国华，等 2004^:207

<Concept field>实验室检查

<Related words>^血清蛋白电泳^

<Type of relation>coord.

<Related words>^血清免疫固定电泳^

<Type of relation>coord.

<Related words>^尿免蛋白电泳^

<Type of relation>coord.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>外科及相关医学专业 / Surgery & related medical specialties (617)

<en>bone marrow aspiration and biopsy

<Morphosyntax>noun group

<Usage label>main term

<Source>^Tomasian/Jennings 2022^:81

<Definition>Bone marrow aspiration and biopsy (BMAB) is an essential and minimally invasive diagnostic intervention for evaluation of hematologic abnormalities, nonhematologic malignancies, metabolic abnormalities, tumour treatment response and bone marrow

transplantation, hematologic tumour staging, and suspected infection in patients with fever of unknown origin.

<Source>^Tomasian/Jennings 2022^:81

<Context>In most clinical scenarios, aspiration of bone marrow and core bone marrow biopsy provide complementary diagnostic information, and both specimens are routinely obtained during the same intervention in clinical practice. Bone marrow aspiration specimens are valuable for assessment of differential cell counts, characterization of cell morphology, cytogenetic (chromosome) analysis, molecular diagnostics, and for cytometry evaluation. Bone marrow core biopsy specimen provide information on marrow cellularity, accurate characterization of hematopoietic elements such as number of megakaryocytes, detection of marrow infiltration by tumour including hematopoietic malignancies and metastases, granulomatous or metabolic marrow infiltration, and infection. The posterior iliac crest serves as the preferred and most common target site for BMAB due to technical ease considering superficial location and lack of critical structures along needle trajectory.

<Source>^Tomasian/Jennings 2022^:81

<Concept field>surgical procedure

<Related words>^fluorescent in situ hybridization^

<Type of relation>general

<Related words>chromosomal set

<Type of relation>general

<Synonyms>The term “bone marrow aspiration and biopsy” is often substituted by its initials “BMAB”.

<en>BMAB

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^Tomasian/Jennings 2022^:81

<Variant of>bone marrow aspiration and biopsy

<zh>骨髓活检和穿刺

<Morphosyntax>noun group

<Source>Mayo Clinic 2021, https://www.mayoclinic.org/zh-hans/tests-procedures/bone-marrow-biopsy/about/pac-20393117

<Definition>骨髓穿刺和骨髓活检是采集和检查骨髓（一些较大骨骼中的海绵状组织）的程序。在做骨髓穿刺时，医生会用针抽取液态部分的样本。在做骨髓活检时，医生会用针抽取固态部分的样本。

<Source>Mayo Clinic 2021, https://www.mayoclinic.org/zh-hans/tests-procedures/bone-marrow-biopsy/about/pac-20393117

<Context>骨髓穿刺和骨髓活检可以显示骨髓是否健康，是否在制造正常数量的血细胞。医生通过这些医疗程序诊断并监测血液和骨髓疾病（包括一些癌症），以及原因不明的发热。尽管骨髓穿刺可以单独进行，但它通常与骨髓活检相结合。这两项程序可以统称为骨髓检查。

<Source>Mayo Clinic 2021, https://www.mayoclinic.org/zh-hans/tests-procedures/bone-marrow-biopsy/about/pac-20393117

<Concept field>外科手术

<Related words>^萤光原位杂交^

<Type of relation>general

<Related words>染色体组

<Type of relation>general

<Synonyms>“骨髓检查”和“骨髓活检和穿刺”是近义词。

<zh>骨髓检查

<Morphosyntax>noun group

<Usage label>common

<Source>Mayo Clinic 2021, https://www.mayoclinic.org/zh-hans/tests-procedures/bone-marrow-biopsy/about/pac-20393117

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病的发病率和预防/ Incidence and prevention of disease (614)

<en>radiography

<Morphosyntax>noun

<Source>^Berger, et al. 2018^:138

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Radiography is the process of creating two-dimensional projection images by exposing an anatomy of interest to X-rays and measuring the attenuation they undergo when passing through the object.

<Source>^Berger, et al. 2018^:138

<Context>Radiography is a very common form of X-ray imaging and is used in clinics around the globe. The main application area is the examination of fractures and changes of the skeletal system. Here, the high attenuation coefficient of bones compared to the surrounding tissue delivers a good contrast and allows for distinct detection and classification of fractures. Moreover, radiography can be used to detect changes of a bone's consistency or density, e. g., in case of osteoporosis or bone cancer.

<Source>^Berger, et al. 2018^:138

<Concept field>instrumental examination

<Related words>^X-rays^

<Type of relation>sub.

<Related words>^low-dose computed tomography^

<Type of relation>general

<Related words>^nuclear magnetic resonance^

<Type of relation>general

<Related words>^magnetic resonance imaging^

<Type of relation>general

<Related words>^positron emission tomography^

<Type of relation>general

<Related words>^positron emission tomography/computed tomography^

<Type of relation>general

<Related words>^computed tomography^

<Type of relation>general

<zh>造影

<Morphosyntax>noun

<Source>^现代汉语词典 2013^:1626

<Lexica>Found in ^现代汉语词典 2013^

<Definition>造影是一种快速、无痛的检测，可产生体内结构的图像，特别是骨骼。

<Source>cf.^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/tests-procedures/x-ray/about/pac-20395303

<Context>X 射线束穿过您的身体，根据 X 射线穿过的材料的密度，它们将以不同的量被吸收。诸如骨骼和金属之类的致密材料在 X 射线检查中显示为白色。肺中的空气显示

为黑色。脂肪和肌肉显示为灰色阴影。对于某些类型的 造影检查，医生将向您的体内注入造影剂（例如碘或钡），以提供更多图像细节。

<Source>cf.^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/tests-procedures/x-ray/about/pac-20395303

<Concept field>仪器检查

<Related words>^X 射线^

<Type of relation>sub.

<Related words>^低剂量电脑断层术^

<Type of relation>general

<Related words>^核磁共振^

<Type of relation>general

<Related words>^磁共振成像^

<Type of relation>general

<Related words>^正电子发射断层成像^

<Type of relation>general

<Related words>^正电子电脑断层扫描^

<Type of relation>general

<Related words>^计算机断层^

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病的发病率和预防/ Incidence and prevention of disease (614)

<en>X-rays

<Morphosyntax>noun, plural

<Source>^Berger, et al. 2018^:119

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>X-rays are electromagnetic rays which follow the rules of electromagnetic radiation.

<Source>cf.^Berger, et al. 2018^:119.

<Context>X-rays have the ability to penetrate matter, yet the amount of penetrating X- ray photons is material-dependent. Their ability to penetrate human tissue is in fact the reason why they can be used to get information on internal organs.

<Source>^Berger, et al. 2018^:125

<Concept field>instrumental examination

<Related words>^radiography^

<Type of relation>super.

<Related words>^low-dose computed tomography^

<Type of relation>general

<Related words>^nuclear magnetic resonance^

<Type of relation>general

<Related words>^magnetic resonance imaging^

<Type of relation>general

<Related words>^positron emission tomography^

<Type of relation>general

<Related words>^positron emission tomography/computed tomography^

<Type of relation>general<Related words>^computed tomography^

<Type of relation>general

<zh>X 射线

<Morphosyntax>noun

<Usage label>main term

<Source>^新华社 2017^, https://ihep.cas.cn/kxcb/kjqy/201708/t20170817_4849433.html

<Lexica>Found in ^现代汉语词典 2013^

<Definition>X 射线，又称伦琴射线、爱克斯射线或 X 光，是波长很短的一种电磁波，其特征是波长非常短，频率非常高。

<Source>^新华社 2017^, https://ihep.cas.cn/kxcb/kjqy/201708/t20170817_4849433.html

<Context>X 射线是由于原子在能量相差悬殊的两个能级之间的跃迁而产生的粒子流，波长介于 0.01 纳米到 10 纳米之间，是一种介于紫外线和 γ 射线之间的电磁辐射。光学光谱是原子中外层的电子跃迁时发射出来的，而 X 射线光谱是原子中最靠内层的电子跃迁时发出来的，X 射线在电场磁场中不发生偏转。因此，X 射线是不带电的粒子流。这种肉眼看不见的射线穿透本领非常高，能穿透许多对可见光不透明的物质，如墨纸、书本、木料等，还可以使许多固体材料产生可见的荧光，使空气电离以及照相底片感光等效应。

<Source>^新华社 2017^, https://ihep.cas.cn/kxcb/kjqy/201708/t20170817_4849433.html

<Concept field>仪器检查

<Related words>^造影^

<Type of relation>super.

<Related words>^低剂量电脑断层术^

<Type of relation>general

<Related words>^核磁共振^

<Type of relation>general

<Related words>^磁共振成像^

<Type of relation>general

<Related words>^正电子发射断层成像^

<Type of relation>general

<Related words>^正电子电脑断层扫描^

<Type of relation>general

<Related words>^计算机断层^

<Type of relation>general

<Synonyms>“伦琴射线”，“爱克斯射”，“X 光”和“X 射线”是近义词。

<zh>伦琴射线

<Morphosyntax>noun group

<Usage label>uncommon

<Source>^新华社 2017^, https://ihep.cas.cn/kxcb/kjqy/201708/t20170817_4849433.html

<zh>爱克斯射

<Morphosyntax>noun group

<Usage label>uncommon

<Source>^新华社 2017^, https://ihep.cas.cn/kxcb/kjqy/201708/t20170817_4849433.html

<zh>X 光

<Morphosyntax>noun

<Usage label>common

<Source>^新华社 2017^, https://ihep.cas.cn/kxcb/kjqy/201708/t20170817_4849433.html

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病的发病率和预防/ Incidence and prevention of disease (614)

<en>low-dose computed tomography

<Morphosyntax>noun group

<Usage label>main term

<Source>^National Cancer Institute^, https://www.cancer.gov/publications/dictionaries/cancer-terms/def/low-dose-computed-tomography

<Definition>Low-dose computer tomography is a procedure that uses a computer linked to an x-ray machine that gives off a very low dose of radiation to make a series of detailed pictures of areas inside the body.

<Source>^National Cancer Institute^, https://www.cancer.gov/publications/dictionaries/cancer-terms/def/low-dose-computed-tomography

<Context>In low-dose computer tomography, the pictures are taken from different angles and are used to create 3-D views of tissues and organs. Low-dose computed tomography is recommended as a screening test for adults who have a high risk of developing lung cancer based on their age and smoking history. Also called LDCT and low-dose CT scan.

<Source>^National Cancer Institute^, https://www.cancer.gov/publications/dictionaries/cancer-terms/def/low-dose-computed-tomography

<Concept field>instrumental examination

<Related words>^radiography^

<Type of relation>super.

<Related words>^X-rays^

<Type of relation>general

<Related words>^nuclear magnetic resonance^

<Type of relation>general

<Related words>^magnetic resonance imaging^

<Type of relation>general

<Related words>^positron emission tomography^

<Type of relation>general

<Related words>^positron emission tomography/computed tomography^

<Type of relation>general

<Related words>^computed tomography^

<Type of relation>general

<Synonyms>The term “low-dose CT scan” is a synonym to “low-dose computed tomography” but it is not commonly used, while the term “low-dose computed tomography” is often substituted by its initials “LDCT”.

<en>low-dose CT scan
<Morphosyntax>noun group
<Usage label>uncommon
<Source>^National Cancer Institute^, https://www.cancer.gov/publications/dictionaries/cancer-terms/def/low-dose-computed-tomography

<en>LDCT
<Morphosyntax>noun
<Category>initials
<Usage label>common
<Source>^National Cancer Institute^, https://www.cancer.gov/publications/dictionaries/cancer-terms/def/low-dose-computed-tomography
<Variant of>low-dose computed tomography

<zh>低剂量电脑断层术
<Morphosyntax>noun
<Usage label>main term
<Source> 永越健康管理中心 2016, https://www.eonway.com/%E4%BD%8E%E5%8A%91%E9%87%8F%E9%9B%BB%E8%85%A6%E6%96%B7%E5%B1%A4%E8%82%BA%E7%99%8C%E7%AF%A9%E6%AA%A2%E7%AD%94%E5%95%8F%E7%AF%87/#:~:text=%E3%80%8C%E4%BD%8E%E5%8A%91%E9%87%8F%E9%9B%BB%E8%85%A6%E6%96%B7%E5%B1%A4%E8%A1%93,%E7%9A%84%E9%9B%BB%E8%85%A6%E6%96%B7%E5%B1%A4%E8%A1%93%E6%AA%A2%E6%9F%A5%E3%80%82
<Definition>低剂量电脑断层术(LDCT)是电脑断层术检查的一种，检查时，我们将 X 光球管输出的剂量降低，自然人体所接受的辐射量就会降低。
<Source> 永越健康管理中心 2016, https://www.eonway.com/%E4%BD%8E%E5%8A%91%E9%87%8F%E9%9B%BB%E8%8

5%A6%E6%96%B7%E5%B1%A4%E8%82%BA%E7%99%8C%E7%AF%A9%E6%AA%A2%E7%AD%94%E5%95%8F%E7%AF%87/#:~:text=%E3%80%8C%E4%BD%8E%E5%8A%91%E9%87%8F%E9%9B%BB%E8%85%A6%E6%96%B7%E5%B1%A4%E8%A1%93,%E7%9A%84%E9%9B%BB%E8%85%A6%E6%96%B7%E5%B1%A4%E8%A1%93%E6%AA%A2%E6%9F%A5%E3%80%82

<Context>一般而言，它的辐射剂量约为传统的胸部电脑断层检查剂量(约 5~7mSv)的1/6~1/10，然而它在节功能上不逊于传统的电脑断层术检查。不需注射显影剂。过去估量上扫描一次低剂量电脑断层术约等于照了标准正面及侧面胸部 X 光 1~2.2 倍。

<Source> 永越健康管理中心 2016, https://www.eonway.com/%E4%BD%8E%E5%8A%91%E9%87%8F%E9%9B%BB%E8%85%A6%E6%96%B7%E5%B1%A4%E8%82%BA%E7%99%8C%E7%AF%A9%E6%AA%A2%E7%AD%94%E5%95%8F%E7%AF%87/#:~:text=%E3%80%8C%E4%BD%8E%E5%8A%91%E9%87%8F%E9%9B%BB%E8%85%A6%E6%96%B7%E5%B1%A4%E8%A1%93,%E7%9A%84%E9%9B%BB%E8%85%A6%E6%96%B7%E5%B1%A4%E8%A1%93%E6%AA%A2%E6%9F%A5%E3%80%82

<Concept field>仪器检查

<Related words>^造影^

<Type of relation>super.

<Related words>^X 射线^

<Type of relation>general

<Related words>^核磁共振^

<Type of relation>general

<Related words>^磁共振成像^

<Type of relation>general

<Related words>^正电子发射断层成像^

<Type of relation>general

<Related words>^正电子电脑断层扫描^

<Type of relation>general

<Related words>^计算机断层^

<Type of relation>general

<Synonyms>“LDCT”和“低剂量电脑断层术”是近义词。

<zh>LDCT

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source> 永 越 健 康 管 理 中 心 2016, https://www.eonway.com/%E4%BD%8E%E5%8A%91%E9%87%8F%E9%9B%BB%E8%85%A6%E6%96%B7%E5%B1%A4%E8%82%BA%E7%99%8C%E7%AF%A9%E6%AA%A2%E7%AD%94%E5%95%8F%E7%AF%87/#:~:text=%E3%80%8C%E4%BD%8E%E5%8A%91%E9%87%8F%E9%9B%BB%E8%85%A6%E6%96%B7%E5%B1%A4%E8%A1%93,%E7%9A%84%E9%9B%BB%E8%85%A6%E6%96%B7%E5%B1%A4%E8%A1%93%E6%AA%A2%E6%9F%A5%E3%80%82

<Variant of>低剂量电脑断层术

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病的发病率和预防/ Incidence and prevention of disease (614)

<en>nuclear magnetic resonance

<Morphosyntax>noun group

<Usage label>main term

<Source>^Xiao, et al. 2022^:517

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Nuclear magnetic resonance (NMR) is a test which analyses the composition of substances qualitatively and even quantitatively by studying the absorption of electro-magnetic radiation (4900 MHz) by atomic nuclei and can provide information about the chemical structure and molecular dynamics of molecules.

<Source>^Xiao, et al. 2022^:517

<Context>Nuclear magnetic resonance does not damage the sample and is a non-destructive testing technique. NMR spectrometers are mainly divided into high-resolution NMR spectrometers and broad-line NMR spectrometers, which are used to measure liquid and solid samples, respectively. High-resolution NMR spectroscopy is most commonly used, and it is an important means to identify the structure of organic compounds. Another commonly used NMR technology is NMR imaging technology, which can be used to visually and vividly display the distribution of membrane foulant along the flow routes in the membrane module.

<Source>^Xiao, et al. 2022^:517-518

<Concept field>instrumental examination

<Related words>^radiography^

<Type of relation>super.

<Related words>^X-rays^

<Type of relation>general

<Related words>^low-dose computed tomography^

<Type of relation>general

<Related words>^magnetic resonance imaging^

<Type of relation>general

<Related words>^positron emission tomography^

<Type of relation>general

<Related words>^positron emission tomography/computed tomography^

<Type of relation>general

<Related words>^computed tomography^

<Type of relation>general

<Synonyms>The term “nuclear magnetic resonance” is often substituted by its initials “NMR”.

<en>NMR

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^Xiao, et al. 2022^:517

<Variant of>nuclear magnetic resonance

<zh>核磁共振

<Morphosyntax>noun

<Source>^史全水 2006^:82

<Lexica>Found in ^现代汉语词典 2013^

<Definition>核磁共振分析技术是利用物理原理,通过对核磁共振谱线特征参数的测定来分析物质的分子结构与性质。

<Source>^史全水 2006^:82

<Context>核磁共振不破坏被测样品的内部结构，是一种无损检测方法。

<Source>^史全水 2006^:82

<Concept field>仪器检查

<Related words>^造影^

<Type of relation>super.

<Related words>^X 射线^

<Type of relation>general

<Related words>^低剂量电脑断层术^

<Type of relation>general

<Related words>^磁共振成像^

<Type of relation>general

<Related words>^正电子发射断层成像^

<Type of relation>general

<Related words>^正电子电脑断层扫描^

<Type of relation>general

<Related words>^计算机断层^

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病的发病率和预防/ Incidence and prevention of disease (614)

<en>magnetic resonance imaging

<Morphosyntax>noun group

<Usage label>main term

<Source>^Katti, et al. 2011^:65

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Magnetic resonance imaging (MRI) is a non-invasive method of mapping the internal structure and certain aspects of function within the body.

<Source>^Katti, et al. 2011^:65

<Context>MRI uses nonionizing electromagnetic radiation and appears to be without exposure-related hazard. It employs radio frequency (RF) radiation in the presence of carefully controlled magnetic fields in order to produce high quality cross-sectional images of the body in any plane. The MR Image is constructed by placing the patient inside a large magnet, which induces a relatively strong External magnetic field. This causes the nuclei of many atoms in the body, including Hydrogen, to align them with the magnetic field and later application of RF signal, Energy is released from the body, detected and used to construct the MR image by Computer.

<Source>^Katti, et al. 2011^:65

<Concept field>instrumental examination

<Related words>^radiography^

<Type of relation>super.

<Related words>^X-rays^

<Type of relation>general
<Related words>^low-dose computed tomography^
<Type of relation>general
<Related words>^nuclear magnetic resonance^
<Type of relation>general
<Related words>^positron emission tomography^
<Type of relation>general
<Related words>^positron emission tomography/computed tomography^
<Type of relation>general
<Related words>^computed tomography^
<Type of relation>general
<Synonyms>The term “magnetic resonance imaging” is often substituted by its initials “MRI”.

<en>MRI
<Morphosyntax>noun
<Category>initials
<Usage label>common
<Source>^Katti, et al. 2011^:65
<Variant of>magnetic resonance imaging

<zh>磁共振成像
<Morphosyntax>noun group
<Usage label>main term
<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/tests-procedures/mri/about/pac-20384768
<Definition>磁共振成像（MRI）是一种医学成像技术，利用磁场和计算机生成的无线电波来创建人体器官和组织的详细图像。
<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/tests-procedures/mri/about/pac-20384768
<Context>MRI 是一种检查器官、组织和骨骼系统的无创方法。大多数的磁共振成像机都是大型的管状磁体。躺在磁共振成像机内时，磁场会暂时重组体内的水分子。无线电波会使这些排列好的原子产生微弱的信号，并将其用于创建各个横截面 MRI 图像——就像一条面包中的多个切片。MRI 机器还能生成可从不同角度查看的三维图像。

<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/tests-procedures/mri/about/pac-20384768

<Concept field>仪器检查

<Related words>^造影^

<Type of relation>super.

<Related words>^X 射线^

<Type of relation>general

<Related words>^低剂量电脑断层术^

<Type of relation>general

<Related words>^核磁共振^

<Type of relation>general

<Related words>^正电子发射断层成像^

<Type of relation>general

<Related words>^正电子电脑断层扫描^

<Type of relation>general

<Related words>^计算机断层^

<Type of relation>general

<Synonyms>“MRI”和“磁共振成像”是近义词。

<zh>MRI

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/tests-procedures/mri/about/pac-20384768

<Variant of>磁共振成像

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病的发病率和预防/ Incidence and prevention of disease (614)

<en>positron emission tomography

<Morphosyntax>noun group

<Usage label>main term

<Source>^Mikla/Mikla 2014^:53

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^
<Definition>Positron emission tomography, also referred to as PET imaging or a PET scan, is a nuclear medicine technique that produces 3D images (pictures) of metabolic processes in the body and allows visualizing the body at the cellular and functional levels.
<Source>^Mikla/Mikla 2014^:53
<Context>PET system detects pairs of gamma rays emitted indirectly by a positron-emitting radionuclide (tracer), which is introduced into the body on a biologically active molecule. PET scanning provides information about the body's chemistry not available through other procedures. Unlike CT (computerized tomography) or MRI (magnetic resonance imaging), techniques that look at anatomy or body form, PET studies metabolic activity or body function and disease processes. In the last decade, the clinical value of PET as an imaging modality has become increasingly apparent. Medical professionals in the fields of oncology, cardiology, and neurology have been using PET techniques to assess metabolism in their respective evaluations of cancer, damaged heart tissue, and brain disorders.
<Source>^Mikla/Mikla 2014^:53
<Concept field>instrumental examination
<Related words>^radiography^
<Type of relation>super.
<Related words>^X-rays^
<Type of relation>general
<Related words>^low-dose computed tomography^
<Type of relation>general
<Related words>^nuclear magnetic resonance^
<Type of relation>general
<Related words>^magnetic resonance imaging^
<Type of relation>general
<Related words>^positron emission tomography/computed tomography^
<Type of relation>general
<Related words>^computed tomography^
<Type of relation>general
<Synonyms>The term "PET scan" is a synonym to "positron emission tomography" but it is not commonly used, while the term "positron emission tomography" is often substituted by its initials "PET".

<en>PET scan

<Morphosyntax>noun group
<Usage label>uncommon
<Source>^Mikla/Mikla 2014^:53

<en>PET
<Morphosyntax>noun
<Category>initials
<Usage label>common
<Source>^Mikla/Mikla 2014^:53
<Variant of>positron emission tomography

<zh>正电子发射断层成像
<Morphosyntax>noun group
<Usage label>main term
<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/tests-procedures/pet-scan/about/pac-20385078
<Definition>正电子发射断层成像（PET）扫描是一种影像学检查，可以显示组织和器官的代谢或生化功能。
<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/tests-procedures/pet-scan/about/pac-20385078
<Context>PET 扫描会使用放射性药物（示踪剂）来显示正常和异常的代谢活动。PET 扫描通常可以在疾病出现在其他成像检查（如计算机断层成像（CT）和磁共振成像（MRI）之前检测到疾病中示踪剂的异常代谢。医生通常会将示踪剂注射到手或手臂的静脉中。然后，示踪剂会聚集在体内代谢或生化活动水平较高的区域，这些区域往往可以准确定位疾病的位置。PET 成像一般与 CT 或 MRI 相结合，称为 PET-CT 或 PET-MRI 扫描。
<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/tests-procedures/pet-scan/about/pac-20385078
<Concept field>仪器检查
<Related words>^造影^
<Type of relation>super.
<Related words>^X 射线^
<Type of relation>general

<Related words>^低剂量电脑断层术^

<Type of relation>general

<Related words>^核磁共振^

<Type of relation>general

<Related words>^磁共振成像^

<Type of relation>general

<Related words>^正电子电脑断层扫描^

<Type of relation>general

<Related words>^计算机断层^

<Type of relation>general

<Synonyms>“PET”，“PET 扫描”和“正电子发射断层成像”是近义词。

<zh>PET 扫描

<Morphosyntax>noun group

<Usage label>common

<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/tests-procedures/pet-scan/about/pac-20385078

<zh>PET

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/tests-procedures/pet-scan/about/pac-20385078

<Variant of>正电子发射断层成像

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病的发病率和预防/ Incidence and prevention of disease (614)

<en>positron emission tomography/computed tomography

<Morphosyntax>noun group

<Usage label>main term

<Source>^Kapoor, et al. 2004^:523

<Definition>PET–computed tomography (CT) is a unique combination of the cross-sectional anatomic information provided by CT and the metabolic information provided by PET, which are acquired during a single examination and fused.
<Source>^Kapoor, et al. 2004^:523
<Context>Positron emission tomography (PET) performed with 2-[fluorine-18]fluoro-2-deoxy-d-glucose (FDG) has proved valuable in providing important tumour-related qualitative and quantitative metabolic information that is critical to diagnosis and follow-up. FDG PET–CT offers several advantages over PET alone; the most important is the ability to accurately localize increased FDG activity to specific normal or abnormal anatomic locations, which may be difficult or even impossible with PET alone.
<Source>^Kapoor, et al. 2004^:523
<Concept field>**i**nstrumental examination
<Related words>^radiography^<Type of relation>super.
<Related words>^X-rays^
<Type of relation>general
<Related words>^low-dose computed tomography^
<Type of relation>general
<Related words>^nuclear magnetic resonance^
<Type of relation>general
<Related words>^magnetic resonance imaging^
<Type of relation>general
<Related words>^positron emission tomography^
<Type of relation>general
<Related words>^computed tomography^
<Type of relation>general
<Synonyms>The term “PET–computed tomography” is a synonym to “positron emission tomography” and is commonly used; the term “positron emission tomography/computed tomography” is also often substituted by its initials “PET-TC”.

<en>PET–computed tomography
<Morphosyntax>noun group
<Usage label>common
<Source>^Kapoor, et al. 2004^:523

<en>PET-TC

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^Kapoor, et al. 2004^:523

<Variant of>positron emission tomography/computed tomography

<zh>正电子电脑断层扫描

<Morphosyntax>noun group

<Usage label>main term

<Source>^香港綜合腫瘤中心^，https://www.hkioc.com.hk/zh-hant/screening-and-diagnosis/positron-emission-tomography-pet-ct/

<Definition>正电子电脑断层扫描，简称正电子扫描或 PET-CT Scan，是结合了正电子扫描和电脑扫描的技术。

<Source>^香港綜合腫瘤中心^，https://www.hkioc.com.hk/zh-hant/screening-and-diagnosis/positron-emission-tomography-pet-ct/

<Context>正电子扫描的原理是利用放射同位素，将身体细胞新陈代谢的情况影像化。另一方面，电脑扫描利用 X 光从不同角度收集身体结构的数据，除了可制造高清影像，亦可收集体内的辐射衰减数据，用作构成精确的 PET-CT 影像。透过结合两者结果，医生便可将正电子扫描显示的放射同位素讯号，对应电脑扫描所显示的器官或组织位置，得出准确的病变位置和病况。

<Source>^香港綜合腫瘤中心^，https://www.hkioc.com.hk/zh-hant/screening-and-diagnosis/positron-emission-tomography-pet-ct/

<Concept field>仪器检查

<Related words>^造影^

<Type of relation>super.

<Related words>^X 射线^

<Type of relation>general

<Related words>^低剂量电脑断层术^

<Type of relation>general

<Related words>^核磁共振^

<Type of relation>general

<Related words>^磁共振成像^

<Type of relation>general

<Related words>^正电子发射断层成像^

<Type of relation>general

<Related words>^计算机断层^

<Type of relation>general

<Synonyms>“PET-TC Scan”，“正电子扫描”和“正电子电脑断层扫描”是近义词。

<zh>PET-TC Scan

<Morphosyntax>noun group

<Usage label>common

<Source>^ 香 港 綜 合 腫 瘤 中 心 ^ ， https://www.hkioc.com.hk/zh-hant/screening-and-diagnosis/positron-emission-tomography-pet-ct/

<zh>正电子扫描

<Morphosyntax>noun

<Usage label>common

<Source>^ 香 港 綜 合 腫 瘤 中 心 ^ ， https://www.hkioc.com.hk/zh-hant/screening-and-diagnosis/positron-emission-tomography-pet-ct/

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<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病的发病率和预防/ Incidence and prevention of disease (614)

<en>computed tomography

<Morphosyntax>noun group

<Usage label>main term

<Source>^Mikla/Mikla 2014^:23

<Lexica>Found in ^Merriam/Webster 2016^

<Definition>Computed tomography (CT) is a diagnostic procedure that uses special X-ray equipment to create cross-sectional pictures of human body.

<Source>^Mikla/Mikla 2014^:23

<Context>Computerized tomography is nearly an ideal form of tomography yielding sequence images of thin consecutive slices of the patient. Moreover, CT provides the opportunity to localize resultant image in three dimensions. Unlike conventional, classical tomography, computerized tomography does not suffer from interference from structures in the patient outside the slice being imaged. This is achieved by irradiating only thin slices of the patient with a fan-shaped beam. Transaxial images (tomograms) of the patient’s anatomy can give more

selective information than conventional planar projection radiographs. Compared to planar radiography, CT images have superior contrast resolution. CT images are produced using X-ray technology and powerful computers.
<Source>^Mikla/Mikla 2014^:25
<Concept field>instrumental examination
<Related words>^radiography^
<Type of relation>super.
<Related words>^X-rays^
<Type of relation>general
<Related words>^low-dose computed tomography^
<Type of relation>general
<Related words>^nuclear magnetic resonance^
<Type of relation>general
<Related words>^magnetic resonance imaging^
<Type of relation>general
<Related words>^positron emission tomography^
<Type of relation>general
<Related words>^positron emission tomography/computed tomography^
<Type of relation>general
<Synonyms>The terms “computerized tomography” and “CAT scan” are synonyms to “computed tomography” and they are commonly used; the term “computed tomography” is also often substituted by its initials “CT”.

<en>CAT scan
<Morphosyntax>noun group
<Usage label>uncommon
<Source>^Mikla/Mikla 2014^:24

<en>computerized tomography
<Morphosyntax>noun group
<Usage label>uncommon
<Source>^Mikla/Mikla 2014^:24

<en>CT
<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^Mikla/Mikla 2014^:23

<Variant of>computed tomography

<zh>计算机断层

<Morphosyntax>noun group

<Usage label>main term

<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/tests-procedures/ct-scan/about/pac-20393675

<Definition>计算机断层（CT）扫描组合了一系列从身体周围不同角度拍摄的 X 光图像，并运用计算机进行处理，以创建体内骨骼、血管和软组织的横截面图像（切片）。

<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/tests-procedures/ct-scan/about/pac-20393675

<Context>CT 扫描影像可获得比普通 X 光片更详细的信息。CT 扫描有很多用途，但是特别适合快速检查可能因车祸或其他类型的创伤而导致内部损伤的患者。CT 扫描可用于以可视化的方式检查人体的几乎所有部位，诊断疾病或损伤以及计划医学、外科或放射治疗。

<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/tests-procedures/ct-scan/about/pac-20393675

<Concept field>仪器检查

<Related words>^造影^

<Type of relation>super.

<Related words>^X 射线^

<Type of relation>general

<Related words>^低剂量电脑断层术^

<Type of relation>general

<Related words>^核磁共振^

<Type of relation>general

<Related words>^磁共振成像^

<Type of relation>general

<Related words>^正电子发射断层成像^

<Type of relation>general

<Related words>^正电子电脑断层扫描^

<Type of relation>general

<Synonyms>“CT”，“CT 扫描”和“计算机断层”是近义词。

<zh>CT 扫描

<Morphosyntax>noun group

<Usage label>common

<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/tests-procedures/ct-scan/about/pac-20393675

<zh>CT

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/tests-procedures/ct-scan/about/pac-20393675

<Variant of>计算机断层

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>alkylating agents

<Morphosyntax>noun group

<Source>National Institute of Diabetes and Digestive and Kidney Diseases 2015, https://www.ncbi.nlm.nih.gov/books/NBK547849/

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Alkylating agents are a class of antineoplastic or anticancer drugs which act by inhibiting the transcription of DNA into RNA and thereby stopping the protein synthesis.

<Source>National Institute of Diabetes and Digestive and Kidney Diseases 2015, https://www.ncbi.nlm.nih.gov/books/NBK547849/

<Context>Alkylating agents substitute alkyl groups for hydrogen atoms on DNA, resulting in the formation of cross links within the DNA chain and thereby resulting in cytotoxic, mutagenic, and carcinogenic effects. This action occurs in all cells, but alkylating agents have their primary effect on rapidly dividing cells which do not have time for DNA repair. Cancer cells are among the most affected because they are among the most rapidly dividing cells. The end result of the

alkylation process results in the misreading of the DNA code and the inhibition of DNA, RNA, and protein synthesis and the triggering of programmed cell death (apoptosis) in rapidly proliferating tumor cells. The alkylating agents all have major toxicities, but the predominant toxicities are to the bone marrow and gastrointestinal tract.

<Source>National Institute of Diabetes and Digestive and Kidney Diseases 2015, https://www.ncbi.nlm.nih.gov/books/NBK547849/

<Concept field>alkylating agents

<Related words>^melphalan^

<Type of relation>sub.

<Related words>^cyclophosphamide^

<Type of relation>sub.

<Related words>VAD treatment

<Type of relation>sub.

<Related words>VND treatment

<Type of relation>sub.

<zh>烷化剂

<Morphosyntax>noun group

<Source> 中国疾病预防控制中心，https://www.phsciencedata.cn/Share/wiki/wikiView?id=83a840c9-87a7-4f3d-aa78-840689735819

<Definition>烷化剂是一种药物具有一个或多个高度活跃的烷化基团，并能与机体的核酸，特别是 DNA 结合，被结合的 DNA 功能受到抑制并产生染色体的碎裂或堆聚。

<Source> 中国疾病预防控制中心，https://www.phsciencedata.cn/Share/wiki/wikiView?id=83a840c9-87a7-4f3d-aa78-840689735819

<Context>双功能或多功能烷化剂抗癌效果最强，由于它能使核酸的链产生交叉联结，有些烷化剂进入体内，在未经代谢激活之前并无烷化作用，环磷酰胺就是个突出的例子。

<Source> 中国疾病预防控制中心，https://www.phsciencedata.cn/Share/wiki/wikiView?id=83a840c9-87a7-4f3d-aa78-840689735819

<Concept field>烷化剂

<Related words>^美法仑^

<Type of relation>sub.

<Related words>^环磷酰胺^

<Type of relation>sub.

<Related words>VAD 治疗

<Type of relation>sub.

<Related words>VND 治疗

<Type of relation>sub.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>melphalan

<Morphosyntax>noun

<Usage label>main term

<Source>^Betcher/Burnham 1990^:35

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Melphalan is an alkylating agent whose structure incorporates the alkylating agents nitrogen mustard and phenylalanine. The chemical name for melphalan is L-alanine. Melphalan is also known as Alkeran, L-PAM, L-sarcolysin, and L-phenyfafanine mustard.

<Source>^Betcher/Burnham 1990^:35

<Context>Melphalan is a bifunctional alkylating agent that is cytotoxic either by forming cross-links with deoxyribonucleic acid (ANA) or DNA protein complexes. It appears to act as a non-cell cycle specific agent. Melphalan has been administered orally for a wide variety of malignancies including cancer of the breast and ovary as well as multiple myeloma.

<Source>^Betcher/Burnham 1990^:35

<Concept field>alkylating agents

<Related words>^alkylating agents^

<Type of relation>super

<Related words>^prednisone^

<Type of relation>coord.

<Related words>^cyclophosphamide^

<Type of relation>coord.

<Related words>VAD treatment

<Type of relation>coord.

<Related words>VND treatment

<Type of relation>coord.

<Synonyms>The terms “alkeran”, “L-PAM”, “L-sarcolysin”and “L-phenyfafanine mustard” are synonyms to “melphalan” but they are hardly used to identify the alkylating agent, while the chemical name “L-alanine” is frequently used.

<en>L-alanine
<Morphosyntax>noun group
<Usage label>common
<Source>^Betcher/Burnham 1990^:35

<en>alkeran
<Morphosyntax>noun
<Usage label>uncommon
<Source>^Betcher/Burnham 1990^:35

<en>L-PAM
<Morphosyntax>noun group
<Usage label>uncommon
<Source>^Betcher/Burnham 1990^:35

<en>L-sarcolysin
<Morphosyntax>noun group
<Usage label>uncommon
<Source>^Betcher/Burnham 1990^:35

<en>L-phenyfafanine mustard
<Morphosyntax>noun group
<Usage label>uncommon
<Source>^Betcher/Burnham 1990^:35

<zh>美法仑
<Morphosyntax>noun
<Usage label>main term
<Source>^药物性肝损伤专业网^，http://www.hepatox.org/drug/show/160
<Definition>美法仑是一种苯丙氨酸氮芥，也是一种与环磷酰胺和苯丁酸氮相似的烷化剂。

<Source>^药物性肝损伤专业网^，http://www.hepatox.org/drug/show/160

<Context>美法仑可引起 DNA 修饰和交联，从而抑制 DNA、RNA 和蛋白质合成，最终导致快速分裂中的细胞程序性死亡（细胞凋亡）。美法仑当前的适应症包括多发性骨髓瘤和一些形式的卵巢癌，通常与其他抗肿瘤药剂联合使用。骨髓抑制治疗方案中也应用美法仑为造血干细胞移植做好准备。常见副作用与氮芥以及其他烷化剂相同，包括恶心、呕吐腹泻、脱发、瘙痒、骨髓抑制、皮疹和超敏反应。

<Source>^药物性肝损伤专业网^，http://www.hepatox.org/drug/show/160

<Concept field>烷化剂

<Related words>^烷化剂^

<Type of relation>super.

<Related words>^泼尼松^

<Type of relation>coord.

<Related words>^环磷酰胺^

<Type of relation>coord.

<Related words>VAD 治疗

<Type of relation>coord.

<Related words>VND 治疗

<Type of relation>coord.

<Synonyms>“威克瘤”和“美法仑”是近义词。

<zh>威克瘤

<Morphosyntax>noun group

<Usage label>common

<Source>^ 藥 劑 部 2021^, https://www.chimei.org.tw/main/cmh_department/59012/info/5500/A5500042.html

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>prednisone

<Morphosyntax>noun

<Source>^Puckett, et al., 2022^, https://www.ncbi.nlm.nih.gov/books/NBK534809/

<Lexica>Found in ^Merriam/Webster 2016^

<Definition>Prednisone is a synthetic, anti-inflammatory glucocorticoid that derives from cortisone. It is biologically inert and converted to prednisolone in the liver.
<Source>^Puckett, et al., 2022^, https://www.ncbi.nlm.nih.gov/books/NBK534809/
<Context>Prednisone is an FDA-approved, delayed-release corticosteroid indicated as an anti-inflammatory or immunosuppressive agent to treat a broad range of diseases, including immunosuppressive/endocrine, rheumatic, collagen, dermatologic, allergic states, ophthalmic, respiratory, hematologic, neoplastic, oedematous, gastrointestinal, acute exacerbations of multiple sclerosis, and as an anti-inflammatory and an antineoplastic agent. Prednisone is a prodrug to prednisolone, which mediates its glucocorticoid effects. Prednisone is a synthetic glucocorticoid that has both anti-inflammatory and immunomodulating properties.
<Source>^Puckett, et al., 2022^, https://www.ncbi.nlm.nih.gov/books/NBK534809/
<Concept field>alkylating agents
<Related words>^alkylating agents^
<Type of relation>super.
<Related words>^melphalan^
<Type of relation>coord.
<Related words>^cyclophosphamide^
<Type of relation>coord.
<Related words>VAD treatment
<Type of relation>coord.
<Related words>VND treatment
<Type of relation>coord.

<zh>泼尼松
<Morphosyntax>noun
<Source>^圣裘德儿童研究医院 2023^，https://together.stjude.org/zh-cn/diagnosis-treatment/%E8%8D%AF%E7%89%A9%E6%B8%85%E5%8D%95/prednisone.html
<Definition>泼尼松是一种类固醇皮质激素，也可用作化疗药物。泼尼松也可用于治疗炎症、过敏和哮喘以及皮疹和肾上腺问题。
<Source>^圣裘德儿童研究医院 2023^，https://together.stjude.org/zh-cn/diagnosis-treatment/%E8%8D%AF%E7%89%A9%E6%B8%85%E5%8D%95/prednisone.html
<Context>随着患者的成长，泼尼松的适用剂量会发生变化。需通过抽取外周血检测血钾水平。治疗可能会给某些患者造成长期影响或迟发效应，这些影响可能在治疗结束后数月或数年内持续或发生。

<Source>^ 圣 裘 德 儿 童 研 究 医 院 2023^， https://together.stjude.org/zh-cn/diagnosis-treatment/%E8%8D%AF%E7%89%A9%E6%B8%85%E5%8D%95/prednisone.html

<Concept field>烷化剂

<Related words>^烷化剂^

<Type of relation>super.

<Related words>^美法仑^

<Type of relation>coord.

<Related words>^环磷酰胺^

<Type of relation>coord.

<Related words>VAD 治疗

<Type of relation>coord.

<Related words>VND 治疗

<Type of relation>coord.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>cyclophosphamide

<Morphosyntax>noun

<Source>^Ogino/Tadi 2022^, https://www.ncbi.nlm.nih.gov/books/NBK553087/

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Cyclophosphamide is a nitrogen mustard that exerts its anti-neoplastic effects through alkylation.

<Source>^Ogino/Tadi 2022^, https://www.ncbi.nlm.nih.gov/books/NBK553087/

<Context>Cyclophosphamide is a medication primarily used in the management and treatment of neoplasms, including multiple myeloma, sarcoma, and breast cancer. The majority of the antineoplastic effects of cyclophosphamide are due to the phosphoramide mustard formed from the metabolism of the drug by liver enzymes. In addition to antimitotic and antineoplastic effects, cyclophosphamide has immunosuppressive effects and selectivity for T cells. High-dose cyclophosphamide is used in eradication therapy of malignant hematopoietic cells, while lower dosages have shown merit for use in selective immunomodulation of regulatory T cells.

<Source>^Ogino/Tadi 2022^, https://www.ncbi.nlm.nih.gov/books/NBK553087/

<Concept field>alkylating agents

<Related words>^alkylating agents^

<Type of relation>super.

<Related words>^melphalan^

<Type of relation>coord.

<Related words>^prednisone^

<Type of relation>coord.

<Related words>^phosphoramide mustard^

<Type of relation>sub.

<Related words>VAD treatment

<Type of relation>coord.

<Related words>VND treatment

<Type of relation>coord.

<zh>环磷酰胺

<Morphosyntax>noun group

<Source>^Barnes, et al. 2018^, https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD010908.pub2/full/zh_HANS

<Definition>环磷酰胺是一种高度有效的免疫抑制剂，在诱导和维持自身免疫性和炎症性疾病的缓解方面已表现出有效性。

<Source>^Barnes, et al. 2018^, https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD010908.pub2/full/zh_HANS

<Context>环磷酰胺随着潜在的毒性，包括恶心，出血性膀胱炎，膀胱癌，骨髓抑制，机会性感染的风险增加，以及血液和实体器官恶性肿瘤。

<Source>^Barnes, et al. 2018^, https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD010908.pub2/full/zh_HANS

<Concept field>烷化剂

<Related words>^烷化剂^

<Type of relation>super.

<Related words>^美法仑^

<Type of relation>coord.

<Related words>^泼尼松^

<Type of relation>coord.

<Related words>^磷酰胺氮芥^

<Type of relation>sub.

<Related words>VAD 治疗

<Type of relation>coord.

<Related words>VND 治疗

<Type of relation>coord.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>phosphoramide mustard

<Morphosyntax>noun group

<Usage label>main term

<Source>^National Center for Biotechnology Information 2023^, https://pubchem.ncbi.nlm.nih.gov/compound/Phosphoramide-mustard

<Definition 1>Phosphoramide mustard is a nitrogen mustard and a phosphorodiamide.

<Definition 2>Phosphoramide Mustard is one of a number of chemically related alkylating agents with antineoplastic properties.

<Source>^National Center for Biotechnology Information 2023^, https://pubchem.ncbi.nlm.nih.gov/compound/Phosphoramide-mustard

<Context>Most phosphoramide mustards are administered as prodrugs that undergo reductive activation in hypoxic environments to yield cytotoxic metabolites. Phosphoramide mustards are also immunosuppressants, mutagens and teratogens.

<Source>^National Center for Biotechnology Information 2023^, https://pubchem.ncbi.nlm.nih.gov/compound/Phosphoramide-mustard

<Concept field>alkylating agents

<Related words>^alkylating agents^

<Type of relation>super.

<Related words>^melphalan^

<Type of relation>coord.

<Related words>^prednisone^

<Type of relation>coord.

<Related words>^cyclophospamide^

<Type of relation>sub.

<Related words>VAD treatment

<Type of relation>coord.

<Related words>VND treatment

<Type of relation>coord.

<Synonyms>The term “phosphamide mustard” is a synonym to “phosphoramide mustard” and it is commonly used.

<en>phosphamide mustard

<Morphosyntax>noun group

<Usage label>common

<Source>^National Center for Biotechnology Information 2023^, https://pubchem.ncbi.nlm.nih.gov/compound/Phosphoramide-mustard

<zh>磷酰胺氮芥

<Morphosyntax>noun group

<Usage label>main term

<Source>^MedChemExpress^, https://www.medchemexpress.cn/phosphoramide-mustard.html

<Definition>磷酰胺氮芥是环磷酰胺(HY-17420)的活性代谢物，具有抗肿瘤活性。

<Source>^MedChemExpress^, https://www.medchemexpress.cn/phosphoramide-mustard.html

<Context>磷酰胺氮芥能诱导 DNA 损伤。

<Source>^MedChemExpress^, https://www.medchemexpress.cn/phosphoramide-mustard.html

<Concept field>烷化剂

<Related words>^烷化剂^

<Type of relation>super.

<Related words>^美法仑^

<Type of relation>coord.

<Related words>^泼尼松^

<Type of relation>coord.

<Related words>^环磷酰胺^

<Type of relation>sub.

<Related words>VAD 治疗

<Type of relation>coord.

<Related words>VND 治疗

<Type of relation>coord.

<Synonyms>“Phosphoramide mustard”和“磷酰胺氮芥”是近义词。

<zh>phosphoramide mustard

<Morphosyntax>noun group

<Category>translation

<Usage label>common

<Source>^MedChemExpress^, https://www.medchemexpress.cn/phosphoramide-mustard.html

<Variant of>磷酰胺氮芥

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>vincristine

<Morphosyntax>noun

<Source>^Yoneda/Cross 2010^:493

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Vincristine is a vinca alkaloid used primarily in the treatment of leukaemia, lymphomas, neuroblastoma, and sarcomas.

<Source>^Yoneda/Cross 2010^:493

<Context>Pulmonary toxicity has been well described when vincristine is used in combination with other chemotherapeutic agents. However, it is not generally believed to be the major contributing factor. When vincristine is used in combination with bleomycin, doxorubicin, cyclophosphamide, procarbazine, prednisone, and gemcitabine, patients experience serious pulmonary toxicity believed to be due to an interaction between bleomycin and gemcitabine.

<Source>^Yoneda/Cross 2010^:493-494

<Concept field>alkylating agents

<Related words>VAD treatment

<Type of relation>super.

<Related words>VND treatment

<Type of relation>super.

<Related words>^doxorubicin^

<Type of relation>coord.

<Related words>^dexamethasone^

<Type of relation>coord.

<Related words>^mitoxantrone^

<Type of relation>coord.

<Related words>^neutropenia^

<Type of relation>general

<Related words>^myelosuppression^

<Type of relation>general

<zh>长春新碱

<Morphosyntax>noun

<Source>^張 卓 然 2022^， https://www.healthymatters.com.hk/zh/medicines/docetaxel-in-hong-kong/

<Definition>长春新碱是一种抗肿瘤药，可抑制微管蛋白连接在一起形成微管，因此抑制癌细胞分裂。因此，它可用于治疗肺癌、脑癌、血液癌和其他癌症。

<Source>^張 卓 然 2022^， https://www.healthymatters.com.hk/zh/medicines/docetaxel-in-hong-kong/

<Context>长春新碱是只可以静脉注射。每周往静脉注射 1.4-1.5 mg/m2 一次，最高可用每周 2 mg，可能与其他药物一同使用。其后剂量将根据身体反应和耐受性进行调整。长春新碱的常见副作用包括但不限于高血压、脱发、头痛、腹泻、脱水、感染风险增加和脑神经紊乱。

<Source>^張 卓 然 2022^， https://www.healthymatters.com.hk/zh/medicines/docetaxel-in-hong-kong/

<Concept field>烷化剂

<Related words>VAD 治疗

<Type of relation>super.

<Related words>VND 治疗

<Type of relation>super.

<Related words>^阿霉素^

<Type of relation>coord.

<Related words>^地塞米松^

<Type of relation>coord.

<Related words>^米托蒽醌^

<Type of relation>coord.

<Related words>^嗜中性白血球缺乏症^

<Type of relation>general

<Related words>^骨髓抑制^

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>doxorubicin

<Morphosyntax>noun

<Source>^Yoneda/Cross 2010^:491

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Doxorubicin is a cytotoxic anthracycline antibiotic typically used in combination with other chemotherapeutic agents in the treatment of a variety of carcinomas including breast cancer, Hodgkin's and non-Hodgkin's lymphoma, leukaemia, bronchogenic carcinoma, gastric carcinoma, sarcomas, and thyroid carcinoma.

<Source>^Yoneda/Cross 2010^:491

<Context>Doxorubicin cytotoxic effect on malignant and normal cells is believed to be related to inhibition of nucleotide replication and the function of DNA and RNA polymerases by nucleotide base intercalation, binding to the lipid component of the cell membrane, and inhibition of topoisomerase II. Pulmonary toxicity has been reported with variable frequency when doxorubicin has been used in combination with G-CSF or other chemotherapeutic agents in the treatment of a variety of malignancies. Doxorubicin alone or in combination with other chemotherapeutic agents appears to potentiate radiation pneumonitis.

<Source>^Yoneda/Cross 2010^:491

<Concept field>alkylating agents

<Related words>VAD treatment

<Type of relation>super.

<Related words>VND treatment

<Type of relation>super.

<Related words>^vincristine^

<Type of relation>coord.

<Related words>^dexamethasone^

<Type of relation>coord.

<Related words>^mitoxantrone^

<Type of relation>coord.

<Related words>^neutropenia^

<Type of relation>general

<Related words>^myelosuppression^

<Type of relation>general

<zh>阿霉素

<Morphosyntax>noun

<Usage label>main term

<Source>^吕雪丽，等 2021^:613

<Definition>阿霉素是临床上常见的抗肿瘤药物之一，在体内有广泛的非选择性分布特点。

<Source>^吕雪丽，等 2021^:613

<Context>阿霉素又称多柔比星，临床上注射用盐酸多柔比星（辉瑞）适应症为急性白血病、淋巴瘤、软组织和骨肉瘤、儿童恶性肿瘤及成人实体瘤的治疗，尤其用于乳腺癌和肺癌。

<Source>^吕雪丽，等 2021^:618

<Concept field>烷化剂

<Related words>VAD 治疗

<Type of relation>super.

<Related words>VND 治疗

<Type of relation>super.

<Related words>^长春新碱^

<Type of relation>coord.

<Related words>^地塞米松^

<Type of relation>coord.

<Related words>^米托蒽醌^

<Type of relation>coord.

<Related words>^嗜中性白血球缺乏症^

<Type of relation>general

<Related words>^骨髓抑制^

<Type of relation>general

<Synonyms>“多柔比星”和“阿霉素”是近义词。

<zh>多柔比星

<Morphosyntax>noun

<Usage label>common

<Source>^吕雪丽，等 2021^:618

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>dexamethasone

<Morphosyntax>noun

<Source>^Moore 2018^:488

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition 1>Dexamethasone is a synthetic corticosteroid, a fluorinated derivative of prednisolone, and an isomer of bethamasone.

<Definition 2>Dexamethasone is a corticosteroid that has been widely used in the perioperative setting to pre- vent postoperative nausea and vomiting.

<Source>^Moore 2018^:488

<Context>Historically, dexamethasone has been used to treat a number of conditions, and its effectiveness has been well established in treating cerebral oedema and the resultant increases in intracranial pressure due to tumours and metastatic lesions. Also well-established is dexamethasone's role as an antiemetic during the perioperative period. Dexamethasone is believed to exhibit its postoperative antinausea and antivomiting effects by reducing surgery-induced inflammation because of its inhibition of prostaglandin synthesis. The analgesic effects of dexamethasone come from inhibition of phospholipase that is necessary for the inflammatory chain reaction along both the cyclooxygenase and lipoxygenase pathways.

<Source>^Moore 2018^:488

<Concept field>alkylating agents

<Related words>VAD treatment

<Type of relation>super.

<Related words>VND treatment

<Type of relation>super.

<Related words>^vincristine^

<Type of relation>coord.

<Related words>^doxorubicin^

<Type of relation>coord.

<Related words>^mitoxantrone^

<Type of relation>coord.

<Related words>^neutropenia^

<Type of relation>general

<Related words>^myelosuppression^

<Type of relation>general

<zh>地塞米松

<Morphosyntax>noun

<Source>^莫一凡，等 2023^:915

<Definition>地塞米松是一种常见的糖皮质激素药物，可以预防术后恶心和呕吐，提高患者术后恢复的质量。

<Source>^莫一凡，等 2023^:915

<Context>具有强大的抗炎、抗过敏、抗休克等作用，能有效减少炎症早期渗出、水肿和局部毛细血管扩张。地塞米松经常被用作辅助剂，以增强局部麻醉的效果并延长持续时间。常见的应用途径包括静脉注射和神经周给药，研究证实这两种途径都能阻断延长周围神经阻滞的作用时间。

<Source>^莫一凡，等 2023^:915

<Concept field>烷化剂

<Related words>VAD 治疗

<Type of relation>super.

<Related words>VND 治疗

<Type of relation>super.

<Related words>^长春新碱^

<Type of relation>coord.

<Related words>^阿霉素^

<Type of relation>coord.

<Related words>^米托蒽醌^

<Type of relation>coord.

<Related words>^嗜中性白血球缺乏症^

<Type of relation>general

<Related words>^骨髓抑制^

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>mitoxantrone

<Morphosyntax>noun

<Source>^Evison, et al. 2016^:248

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Mitoxantrone is a synthetic anthracenedione originally developed to improve the therapeutic profile of the anthracyclines and is commonly applied in the treatment of breast and prostate cancers, lymphomas, and leukaemia.
<Source>^Evison, et al. 2016^:248
<Context>Across the world, mitoxantrone has been approved for the treatment of numerous cancers. More specifically, mitoxantrone is effective in the treatment of acute nonlymphocytic leukaemia (ANLL), acute lymphoblastic leukaemia (ALL), and AML when applied alone or in combi- nation with cytarabine, an antimetabolite. More recently, mitoxantrone has also been applied in the treatment of prostate cancer. Given its minimal toxicities relative to doxorubicin, mitoxantrone has been incorporated into therapeutic regimens in lieu of doxorubicin for the treatment of breast cancer and lymphoma. Generally, regimens implementing mitoxantrone are better tolerated, yet are slightly less effective in achieving anticancer activity as compared to doxorubicin.
<Source>^Evison, et al. 2016^:251-252
<Concept field>alkylating agents
<Related words>VAD treatment
<Type of relation>super.
<Related words>VND treatment
<Type of relation>super.
<Related words>^vincristine^
<Type of relation>coord.
<Related words>^doxorubicin^
<Type of relation>coord.
<Related words>^dexamethasone^
<Type of relation>coord.
<Related words>^neutropenia^
<Type of relation>general
<Related words>^myelosuppression^
<Type of relation>general

<zh>米托蒽醌
<Morphosyntax>noun
<Usage label>main term
<Source>^中国临床肿瘤学会（CSCO）淋巴瘤专家委员会 2022^:258

<Definition>米托蒽醌是一种蒽醌类抗肿瘤药，其化学名称为 1，4-二羟基-5，8-双[[2-[（2-羟乙基）氨基]乙基]氨基]-9，10-蒽醌二盐酸盐，分子式为 C22H28N4O6·2（HCl）。
<Source>^中国临床肿瘤学会（CSCO）淋巴瘤专家委员会 2022^:258
<Context>米托蒽醌的主要作用机制为通过氢键结合插入 DNA，引起 DNA 结构的交联和断裂；能够干扰 RNA，同时也是具有解旋和修复受损 DNA 作用的拓扑异构酶II的有效抑制剂，其对体外培养的增殖性和非增殖性人类细胞均有杀伤作用，为细胞周期非特异性药物。盐酸米托蒽醌脂质体注射液是普通米托蒽醌注射液剂型的改良和升级，其活性成分为米托蒽醌，脂质体包裹并没有改变米托蒽醌固有的作用机制。
<Source>^中国临床肿瘤学会（CSCO）淋巴瘤专家委员会 2022^:258
<Concept field>烷化剂
<Related words>VAD 治疗
<Type of relation>super.
<Related words>VND 治疗
<Type of relation>super.
<Related words>^长春新碱^
<Type of relation>coord.
<Related words>^阿霉素^
<Type of relation>coord.
<Related words>^地塞米松^
<Type of relation>coord.
<Related words>^嗜中性白血球缺乏症^
<Type of relation>general
<Related words>^骨髓抑制^
<Type of relation>general
**
<Subject>医学与卫生 / Medicine & health (610)
<Subfield>疾病 / Diseases (616)
<en>neutropenia
<Morphosyntax>noun
<Source>^Spoor, et al. 2019^:149
<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Neutropenia is a primary immunodeficiency disease that is associated with recurrent bacterial infections, auto-inflammatory and auto-immune phenomena, haematological malignancy, and neuro-psychiatric manifestations.
<Source>^Spoor, et al. 2019^:149
<Context>Neutropenia is a dangerous and potentially fatal condition that renders patients vulnerable to recurrent infections. Its severity is commensurate with the absolute count of neutrophil granulocytes in the circulation. In the past decades, a number of genes has been discovered that are responsible for congenital neutropenia. By perturbation of mitochondrial energy metabolism, vesicle trafficking or synthesis of functional proteins, these mutations cause a maturation arrest in myeloid precursor cells in the bone marrow. Apart from these isolated forms, congenital neutropenia is associated with a multiplicity of syndromic diseases that includes among others: oculocutaneous albinism, metabolic diseases, and bone marrow failure syndromes.
<Source>^Spoor, et al. 2019^:149
<Concept field>adverse events
<Related words>VAD treatment
<Type of relation>super.
<Related words>VND treatment
<Type of relation>super.
<Related words>^vincristine^
<Type of relation>coord.
<Related words>^doxorubicin^
<Type of relation>coord.
<Related words>^dexamethasone^
<Type of relation>coord.
<Related words>^mitoxantrone^
<Type of relation>coord.
<Related words>^myelosuppression^
<Type of relation>general

<zh>嗜中性白血球缺乏症
<Morphosyntax>noun group
<Source>^林育聖，等 2008^:393

<Definition>嗜中性白血球缺乏症定义为血中绝对嗜中性白血球数目(ANC)低于1,500/mm3，此定义相当明确，除了以相当严格标准审视新生儿以及某些特定黑人、犹太人族群外，公认可应用于所有年龄层与人种。

<Source>^林育聖，等 2008^:393

<Context>嗜中性白血球缺乏症于临床医疗实务中，不论是已出现症状的门诊、住院病患，或是无症状的体检民众，都有不少案例经由血液检验结果发现此一现象。当血中中性球数目减少至 1,000/mm3 以下时会造成感染机会增加，此为每位临床医疗工作者皆必须提高警觉的。

<Source>^林育聖，等 2008^:393

<Concept field>不良事件

<Related words>VAD 治疗

<Type of relation>super.

<Related words>VND 治疗

<Type of relation>super.

<Related words>^长春新碱^

<Type of relation>coord.

<Related words>^阿霉素^

<Type of relation>coord.

<Related words>^地塞米松^

<Type of relation>coord.

<Related words>^米托蒽醌^

<Type of relation>general

<Related words>^骨髓抑制^

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>myelosuppression

<Morphosyntax>noun

<Source>^National Cancer Institute^, https://www.cancer.gov/publications/dictionaries/cancer-terms/def/myelosuppression

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Myelosuppression is a condition in which bone marrow activity is decreased, resulting in fewer red blood cells, white blood cells, and platelets. Myelosuppression is a side effect of some cancer treatments.
<Source>cf.^National Cancer Institute^, https://www.cancer.gov/publications/dictionaries/cancer-terms/def/myelosuppression
<Context>Myelosuppression is a common and anticipated adverse effect of cytotoxic chemotherapy. Myelosuppression is potentially life threatening because of the infection and bleeding complications of neutropenia and thrombocytopenia.
<Source>^Carey 2003^:691-692
<Concept field>adverse events
<Related words>VAD treatment
<Type of relation>super.
<Related words>VND treatment
<Type of relation>super.
<Related words>^vincristine^
<Type of relation>coord.
<Related words>^doxorubicin^
<Type of relation>coord.
<Related words>^dexamethasone^
<Type of relation>coord.
<Related words>^mitoxantrone^
<Type of relation>coord.
<Related words>^neutropenia^
<Type of relation>general

<zh>骨髓抑制
<Morphosyntax>noun group
<Usage label>main term
<Source>^出境医^，https://zhiliao.chujingyi.cn/gsyz
<Definition>骨髓抑制，也称为“骨髓功能抑制”，是放化疗或使用某些免疫抑制剂，如硫唑嘌呤、氟尿嘧啶、阿糖胞苷等所产生的副作用，导致骨髓中造血干细胞的活性下降，主要表现为血液中白细胞、血小板、红细胞的减少。
<Source>^出境医^，https://zhiliao.chujingyi.cn/gsyz

<Context>大多数化疗药物都可以引起不同程度的骨髓抑制。主要表现为血小板减低，可出现身体各个部位的出血、便血、尿血、皮肤出现不明原因瘀血，关节肌肉疼痛、虚弱感强等；贫血，可表现为稍有活动就出现呼吸困难，眼睑、皮肤、甲床、口腔、牙龈苍白；白细胞低，易出现伤口化脓、肿胀、发红，易感冒等。在肿瘤治疗过程中出现不同程度的骨髓抑制，如外周血多系或单系的下降，这会使临床医师被迫推迟化疗疗程，影响疾病疗效，严重者还会出现严重感染，甚至死亡。

<Source>^出境医^，https://zhiliao.chujingyi.cn/gsyz

<Concept field>不良事件

<Related words>VAD 治疗

<Type of relation>super.

<Related words>VND 治疗

<Type of relation>super.

<Related words>^长春新碱^

<Type of relation>coord.

<Related words>^阿霉素^

<Type of relation>coord.

<Related words>^地塞米松^

<Type of relation>coord.

<Related words>^米托蒽醌^

<Type of relation>general

<Related words>^嗜中性白血球缺乏症^

<Type of relation>general

<Synonyms>“骨髓功能抑制”和“骨髓抑制”是近义词。

<zh>骨髓功能抑制

<Morphosyntax>noun group

<Usage label>common

<Source>^出境医^，https://zhiliao.chujingyi.cn/gsyz

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>外科及相关医学专业 / Surgery & related medical specialties (617)

<en>autologous stem cell transplantation

<Morphosyntax>noun group

<Usage label>main term

<Source>^Muraro, et al. 2017^:391

<Definition>Autologous stem cell transplantation (ASCT) is a multistep procedure that enables destruction of the immune system and its reconstitution from autologous stem cells.

<Source>^Muraro, et al. 2017^:391

<Context>Stem cell (SC) transplantation is a well-established multistep procedure designed to replace the blood and lymphoid systems of a patient with a new one derived from autologous stem cells. The procedure has been used extensively in the past 50 years for the treatment of aggressive haematological malignancies, such as leukaemia and lymphoma. The ASCT procedure comprises four main steps: SC mobilization, SC harvesting, ablative conditioning and SC re-infusion.

<Source>^Muraro, et al. 2017^:391

<Concept field>non-drug treatment

<Related words>tandem ASCT

<Type of relation>general

<Related words>stem cell

<Type of relation>sub.

<Synonyms>The term “autologous stem cell transplantation” is often substituted by its initials “ASTC”.

<en>ASTC

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^Muraro, et al. 2017^:391

<Variant of>autologous stem cell transplantation

<zh>自体幹細胞移植

<Morphosyntax>noun group

<Usage label>main term

<Source>^IWMF 2015^ , https://iwmf.com/wp-content/uploads/2020/10/%E4%B8%AD%E6%96%87%E7%89%88Stem_Cell_Transplantation_Fact_Sheet.pdf

<Definition>自体幹細胞移植(又称 ASCT)，是病患本身既是捐赠者亦是干细胞接受者—干细胞的来源是该病患本人的血液；藉由生长因子或细胞因子此类生物化学试剂，来诱导存在于骨髓中的干细胞使之移至血液中。

<Source>^IWMF 2015^ , https://iwmf.com/wp-content/uploads/2020/10/%E4%B8%AD%E6%96%87%E7%89%88Stem_Cell_Transplantation_Fact_Sheet.pdf

<Context>自体幹細胞移植的目标是藉由调理疗方（预备疗方），如高剂量化疗和/或放射疗法，来消灭接受者体内的癌细胞，紧接着以早先从病患本身血液收集到的干细胞进行移植，来取代或抢救骨髓。注入干细胞之后，干细胞移生植入骨髓内的速度相当快速，通常是 12-14 天。

<Source>^IWMF 2015^ , https://iwmf.com/wp-content/uploads/2020/10/%E4%B8%AD%E6%96%87%E7%89%88Stem_Cell_Transplantation_Fact_Sheet.pdf

<Concept field>非药物干预

<Related words>串联 ASCT

<Type of relation>general

<Related words>干细胞

<Type of relation>sub.

<Synonyms>“ASCT”和“自体幹細胞移植”是近义词。

<zh>ASCT

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^IWMF 2015^ , https://iwmf.com/wp-content/uploads/2020/10/%E4%B8%AD%E6%96%87%E7%89%88Stem_Cell_Transplantation_Fact_Sheet.pdf

<Variant of>自体幹細胞移植

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>immunomodulatory drug

<Morphosyntax>noun group

<Usage label>main term

<Source>^Bascones-Martinez, et al. 2014^:25

<Definition>Immunomodulatory drugs are agents which modify the response of the immune system by increasing (immunostimulators) or decreasing (immunosuppressives) the production of serum antibodies.

<Source>^Bascones-Martinez, et al. 2014^:25

<Context>Immunomodulators act at different levels of the immune system. Therefore, different kinds of drugs have been developed that selectively either inhibit or intensify the specific populations and subpopulations of immune responsive cells. Immunostimulators are prescribed to enhance the immune response against infectious diseases, tumours, primary or secondary immunodeficiency, and alterations in antibody transfer, among others. Immunosuppressive drugs are used to reduce the immune response against transplanted organs and to treat autoimmune diseases such as pemphigus, lupus, or allergies.

<Source>^Bascones-Martinez, et al. 2014^:25

<Concept field>new drugs

<Related words>^thalidomide^

<Type of relation>sub.

<Related words>^asthenia^

<Type of relation>general

<Related words>^bradycardia^

<Type of relation>general

<Related words>^peripheral neuropathy^

<Type of relation>general

<Related words>^deep vein thrombosis^

<Type of relation>general

<Related words>^lenalidomide^

<Type of relation>sub.

<Related words>^pomalidomide^

<Type of relation>sub.

<Synonyms>The term “immunomodulatory drug” is often substituted by its acronym “IMiD”.

<en>IMiD

<Morphosyntax>noun

<Category>acronym

<Usage label>common

<Source>^Bascones-Martinez, et al. 2014^:25
<Variant of>immunomodulatory drug

<zh>免疫调节剂
<Morphosyntax>noun group
<Source>^上海医学会儿科学分会免疫学组 2018^:651
<Definition>免疫调节剂是具有调节机体免疫功能的药物，可以用于治疗免疫功能低下和/或紊乱所引起的疾病。
<Source>^上海医学会儿科学分会免疫学组 2018^:651
<Context>免疫调节剂具有药物的特性，并对机体免疫功能具有增强或抑制以及双向调节作用。免疫调节剂也包含生物反应修饰剂(BRMs)的概念。BRMs 是指某种可调节宿主免疫系统并与之互相作用的物质。根据免疫调节剂对机体免疫作用的不同，可以分为免疫增强剂、免疫抑制剂、双向免疫调节剂。免疫增强剂可刺激机体免疫系统中的某一环节，增强免疫功能；免疫抑制剂具有抑制免疫系统中某一环节的作用，从而抑制机体的免疫功能；双向免疫调节剂的作用大部分是多靶点、多部位对免疫平衡的调节，维持机体的自稳。
<Source>^上海医学会儿科学分会免疫学组 2018^:651
<Concept field>新药
<Related words>^沙利度股^
<Type of relation>sub.
<Related words>^无力^
<Type of relation>general
<Related words>^心动过缓^
<Type of relation>general
<Related words>^周围神经病变^
<Type of relation>general
<Related words>^深静脉血栓形成^
<Type of relation>general
<Related words>^来那度胺^
<Type of relation>sub.
<Related words>^泊马度胺^
<Type of relation>sub.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>thalidomide

<Morphosyntax>noun

<Source>^Franks, et al. 2004^:1802

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>The thalidomide molecule is a racemic glutamic acid analogue, consisting of S(–) and R(+) enantiomers that interconvert under physiological conditions. The S(–) form potently inhibits release of tumour necrosis factor (TNF) α from peripheral mononuclear blood cells, whereas the R(+) form seems to act as a sedative, probably mediated by sleep receptors in the forebrain.

<Source>^Franks, et al. 2004^:1802-1803

<Context>Results of molecular studies have resulted in the identification of several mechanisms whereby thalidomide is active in multiple myeloma. These include reduction of cell adhesion in multiple myelomas and related drug resistance; induction of apoptosis; inhibition of angiogenesis in the bone marrow; and augmentation of immunity of multiple myelomas through stimulation of natural killer cells (with subsequent increase of interleukin-2-mediated T-cell proliferation) and increase in cytotoxicity of natural killer cells.

<Source>^Franks, et al. 2004^:1804

<Concept field>new drugs

<Related words>^immunomodulatory drug^

<Type of relation>super.

<Related words>^asthenia^

<Type of relation>sub.

<Related words>^bradycardia^

<Type of relation>sub.

<Related words>^peripheral neuropathy^

<Type of relation>sub.

<Related words>^deep vein thrombosis^

<Type of relation>sub.

<Related words>^lenalidomide^

<Type of relation>coord.

<Related words>^pomalidomide^

<Type of relation>coord.

<zh>沙利度股

<Morphosyntax>noun

<Source>^路瑾，等 2020^:61

<Definition>沙利度股是一种免疫调节剂，其作用机制有免疫调节、抑制血管新生的作用。

<Source>^路瑾，等 2020^:61

<Context>多发性骨髓瘤在化疗方案的基础上联合沙利度胺可以提高缓解率，此外沙利度胺也用于多发性骨髓瘤维持和复发难治性骨髓瘤。沙利度胺在化疗过程中抑制肿瘤细胞的同时会对机体正常组织细胞产生不同程度的不良反应，根据沙利度胺的说明书,它的副作用主要表现为倦息、嗜睡、眩晕、皮疹、恶心、腹胀、便秘、面部水肿、周围神经炎、变态反应、血细胞减少、心动过缓，还可能会引起深静脉血栓形成、继发第二肿瘤及严重的致畸性。

<Source>^路瑾，等 2020^:62

<Concept field>新药

<Related words>^免疫调节剂^

<Type of relation>super.

<Related words>^无力^

<Type of relation>sub.

<Related words>^心动过缓^

<Type of relation>sub.

<Related words>^周围神经病变^

<Type of relation>sub.

<Related words>^深静脉血栓形成^

<Type of relation>sub.

<Related words>^来那度胺^

<Type of relation>coord.

<Related words>^泊马度胺^

<Type of relation>coord.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>asthenia

<Morphosyntax>noun

<Usage label>main term

<Source>^Kauffman/Kemmin 2014^:117

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Asthenia, is an ill-defined condition characterized by generalized weakness and usually involving mental and physical fatigue.

<Source>^Kauffman/Kemmin 2014^:117

<Context>The patient undergoing radiation therapy or chemotherapy may suffer from asthenia and thus may not tolerate the rigors of rehabilitation as defined by the Medicare system (twice-a-day treatments as inpatients in rehabilitation units or a minimum of three times a week in the home or outpatient setting). Other factors that may contribute to asthenia include anaemia, malnutrition, infection, metabolic disorders and the use of medications such as methyldopa (Aldomet), Bactrim, Cardizem (Diltiazem), dexamethasone (Decadron), Donnatal, amitriptyline (Elavil), propranolol (Inderal), digoxin (Lanoxin), metoprolol (Lopressor), Novahistine, promethazine (Phenergan), Relafen (Nabumetone), co-careldopa (Sinemet) and alprazolam (Xanax). Asthenia is a factor in the rehabilitation of many frail patients.

<Source>^Kauffman/Kemmin 2014^:117

<Concept field>adverse events

<Related words>^immunomodulatory drug^

<Type of relation>super.

<Related words>^thalidomide^

<Type of relation>super.

<Related words>^bradycardia^

<Type of relation>coord.

<Related words>^peripheral neuropathy^

<Type of relation>coord.

<Related words>^deep vein thrombosis^

<Type of relation>coord.

<Related words>^lenalidomide^

<Type of relation>general

<Related words>^pomalidomide^

<Type of relation>general

<Synonyms>The terms “weakness” and “debility” are synonyms to “asthenia”, and they are commonly used.

<en>weakness

<Morphosyntax>noun

<Usage label>common

<Source>^Merriam/Webster 2016^:61

<en>debility

<Morphosyntax>noun

<Usage label>common

<Source>^Merriam/Webster 2016^:61

<zh>无力

<Morphosyntax>noun

<Usage label>main term

<Source>^Levin 2021^ ， https://www.msdmanuals.cn/professional/neurologic-disorders/symptoms-of-neurologic-disorders/weakness

<Lexica>Found in ^现代汉语词典 2013^

<Definition>无力是肌肉力量的缺失。

<Source>^Levin 2021^ ， https://www.msdmanuals.cn/professional/neurologic-disorders/symptoms-of-neurologic-disorders/weakness

<Context>尽管很多病人在感到疲劳或者功能限制的时候，即使肌肉力量是正常的，也使用无力来表达。无力可能影响部分或多个肌群，可能突发或逐渐进展。根据病因可能出现其他症状。特定肌肉群的虚弱可导致眼球运动障碍，构音障碍，吞咽困难或呼吸衰弱。

<Source>^Levin 2021^ ， https://www.msdmanuals.cn/professional/neurologic-disorders/symptoms-of-neurologic-disorders/weakness

<Concept field>不良事件

<Related words>^免疫调节剂^

<Type of relation>super.

<Related words>^沙利度股^

<Type of relation>super.

<Related words>^心动过缓^

<Type of relation>coord.

<Related words>^周围神经病变^

<Type of relation>coord.

<Related words>^深静脉血栓形成^

<Type of relation>coord.

<Related words>^来那度胺^

<Type of relation>general

<Related words>^泊马度胺^

<Type of relation>general

<Synonyms>“乏力”和“无力”是近义词。

<zh>乏力

<Morphosyntax>noun

<Usage label>common

<Source>^Levin 2021^ , https://www.msdmanuals.cn/professional/neurologic-disorders/symptoms-of-neurologic-disorders/weakness

<zh>虚弱

<Morphosyntax>noun

<Usage label>common

<Source>^Zhao 2013^

<zh>衰弱

<Morphosyntax>noun

<Usage label>common

<Source>^Zhao 2013^

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>bradycardia

<Morphosyntax>noun

<Source>^Sidhu/Marine 2020^:265

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Bradycardia is a commonly observed arrhythmia, defined as a heart rate of less than 50–60 bpm.

<Source>^Sidhu/Marine 2020^:265

<Context>Bradycardia can be observed as a normal phenomenon in young athletic individuals, and in patients as part of normal aging or disease. Pathology that produces bradycardia may occur within the sinus node, atrioventricular (AV) nodal tissue. Given the overlap of heart rate ranges with non-pathologic changes, assessment of symptoms is a critical component in the evaluation and management of bradycardia. Common symptoms of bradycardia include syncope, presyncope, transient dizziness or light-headedness, fatigue, dyspnoea on exertion, heart failure symptoms, or confusion resulting from cerebral hypoperfusion. Treatment should rarely be prescribed solely on the basis of a heart rate lower than an arbitrary cut-off or a pause above certain duration.

<Source>^Sidhu/Marine 2020^:265

<Concept field>adverse events

<Related words>^immunomodulatory drug^

<Type of relation>super.

<Related words>^thalidomide^

<Type of relation>super.

<Related words>^asthenia^

<Type of relation>coord.

<Related words>^peripheral neuropathy^

<Type of relation>coord.

<Related words>^deep vein thrombosis^

<Type of relation>coord.

<Related words>^lenalidomide^

<Type of relation>general

<Related words>^pomalidomide^

<Type of relation>general

<zh>心动过缓

<Morphosyntax>noun group

<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/diseases-conditions/bradycardia/symptoms-causes/syc-20355474

<Definition>心动过缓是指心跳较慢。成人休息时的心跳是每分钟 60 至 100 次。如果有心动过缓，心跳会少于每分钟 60 次。

<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/diseases-conditions/bradycardia/symptoms-causes/syc-20355474

<Context>如果心率极慢且心脏无法向身体供应足够的富氧血液，心动过缓可能是个严重问题。如果发生这种情况，您可能会感觉头晕目眩、非常疲劳或虚弱，并伴有气短。有时，心动过缓不会引起任何症状或并发症。如果心动过缓严重，可能需要植入起搏器来帮助心脏保持适当的心率。

<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/diseases-conditions/bradycardia/symptoms-causes/syc-20355474

<Concept field>不良事件

<Related words>^免疫调节剂^

<Type of relation>super.

<Related words>^沙利度股^

<Type of relation>super.

<Related words>^无力^

<Type of relation>coord.

<Related words>^周围神经病变^

<Type of relation>coord.

<Related words>^深静脉血栓形成^

<Type of relation>coord.

<Related words>^来那度胺^

<Type of relation>general

<Related words>^泊马度胺^

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>peripheral neuropathy

<Morphosyntax>noun group

<Usage label>main term

<Source>^Rubin 2022^, https://www.msdmanuals.com/professional/neurologic-disorders/peripheral-nervous-system-and-motor-unit-disorders/peripheral-neuropathy

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Peripheral neuropathy is dysfunction of one or more peripheral nerves (the part of a nerve distal to the root and plexus).

<Source>^Rubin 2022^, https://www.msdmanuals.com/professional/neurologic-disorders/peripheral-nervous-system-and-motor-unit-disorders/peripheral-neuropathy
<Context>Peripheral Neuropathy includes numerous syndromes characterized by varying degrees of sensory disturbances, pain, muscle weakness and atrophy, diminished deep tendon reflexes, and vasomotor symptoms, alone or in any combination. Initial classification is based on history and physical examination. Electromyography and nerve conduction studies (electrodiagnostic testing) help localize the lesion and determine whether the pathophysiology is primarily axonal (often metabolic) or demyelinating (often autoimmune). Treatment is aimed mainly at the cause.
<Source>^Rubin 2022^, https://www.msdmanuals.com/professional/neurologic-disorders/peripheral-nervous-system-and-motor-unit-disorders/peripheral-neuropathy
<Concept field>adverse events
<Related words>^immunomodulatory drug^
<Type of relation>super.
<Related words>^thalidomide^
<Type of relation>super.
<Related words>^asthenia^
<Type of relation>coord.
<Related words>^bradycardia^
<Type of relation>coord.
<Related words>^deep vein thrombosis^
<Type of relation>coord.
<Related words>^lenalidomide^
<Type of relation>general
<Related words>^pomalidomide^
<Type of relation>general
<Synonyms>The term “peripheral neuropathy” is often substituted by its initials “PN”.

<en>PN
<Morphosyntax>noun
<Category>initials
<Usage label>common
<Source>^Rubin 2022^, https://www.msdmanuals.com/professional/neurologic-disorders/peripheral-nervous-system-and-motor-unit-disorders/peripheral-neuropathy
<Variant of>peripheral neuropathy

<zh>周围神经病变

<Morphosyntax>noun group

<Source>Mayo Clinic 2021, https://www.mayoclinic.org/zh-hans/diseases-conditions/peripheral-neuropathy/symptoms-causes/syc-20352061

<Definition>周围神经病变是由大脑和脊髓外的神经（周围神经）受损所致，通常会导致无力、麻木和疼痛，往往发生于手部和脚部。

<Source>Mayo Clinic 2021, https://www.mayoclinic.org/zh-hans/diseases-conditions/peripheral-neuropathy/symptoms-causes/syc-20352061

<Context>周围神经病变可能由外伤、感染、代谢问题、遗传原因和接触毒素所引起。最常见的原因之一是糖尿病。周围神经病变患者通常将疼痛描述为刀刺痛、灼痛或刺痛。许多情况下，症状（尤其是由可治疗的病症引起的症状）可改善。药物可以减轻周围神经病变的疼痛。

<Source>Mayo Clinic 2021, https://www.mayoclinic.org/zh-hans/diseases-conditions/peripheral-neuropathy/symptoms-causes/syc-20352061

<Concept field>不良事件

<Related words>^免疫调节剂^

<Type of relation>super.

<Related words>^沙利度股^

<Type of relation>super.

<Related words>^无力^

<Type of relation>coord.

<Related words>^心动过缓^

<Type of relation>coord.

<Related words>^深静脉血栓形成^

<Type of relation>coord.

<Related words>^来那度胺^

<Type of relation>general

<Related words>^泊马度胺^

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>deep vein thrombosis
<Morphosyntax>noun group
<Usage label>main term
<Source>^Tachil 2014^:309
<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^
<Definition>Deep vein thrombosis (DVT) is a condition where a blood clot develops in the veins, which are blood vessels that take blood back to the heart (as opposed to arteries).
<Source>^Tachil 2014^:309
<Context>DVT develops in the legs, although it rarely can affect the arms and also the veins inside the abdomen and the brain. DVT can be asymptomatic, but often present with nonspecific symptoms like leg discomfort or ache or sensation of warmth. The classical symptoms are pain, tenderness, swelling, or blue or reddish discoloration of the limb. If the DVT occurs in the abdomen or cerebral veins, these can present as abdominal pain or persistent headache, respectively. The symptoms of DVT are shortness of breath, chest pain, palpitations (feeling of heart-racing), or sudden collapse.
<Source>^Tachil 2014^:309
<Concept field>adverse events
<Related words>^immunomodulatory drug^
<Type of relation>super.
<Related words>^thalidomide^
<Type of relation>super.
<Related words>^asthenia^
<Type of relation>coord.
<Related words>^bradycardia^
<Type of relation>coord.
<Related words>^peripheral neuropathy^
<Type of relation>coord.
<Related words>^lenalidomide^
<Type of relation>general
<Related words>^pomalidomide^
<Type of relation>general
<Synonyms>The term “deep vein thrombosis” is often substituted by its initials “DVT”.

<en>DVT
<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^Tachil 2014^:309

<Variant of>deep vein thrombosis

<zh>深静脉血栓形成

<Morphosyntax>noun group

<Usage label>main term

<Source>^Douketis 2022^ ， https://www.msdmanuals.cn/home/heart-and-blood-vessel-disorders/venous-disorders/deep-vein-thrombosis-dvt

<Definition>深静脉血栓形成（DVT）是在肢体（通常是小腿或大腿）或骨盆深静脉的血液凝结。

<Source>^Douketis 2022^ ， https://www.msdmanuals.cn/home/heart-and-blood-vessel-disorders/venous-disorders/deep-vein-thrombosis-dvt

<Context>DVT 是肺栓塞的主要原因。DVT 由静脉回流受损，导致内皮损伤或功能紊乱，或引起高凝状态的状况所引起。DVT 可能无症状或引起肢端疼痛和肿胀。诊断依赖病史和体格检查，确诊依赖客观检查，通常为超声多普勒检查。当怀疑 DVT 时进行 D-二聚体检查，阴性结果有助于除外 DVT，而阳性结果不具有特异性，需要进行其他检查以证实 DVT。治疗通常是抗凝。

<Source>^Douketis 2022^ ， https://www.msdmanuals.cn/home/heart-and-blood-vessel-disorders/venous-disorders/deep-vein-thrombosis-dvt

<Concept field>不良事件

<Related words>^免疫调节剂^

<Type of relation>super.

<Related words>^沙利度股^

<Type of relation>super.

<Related words>^无力^

<Type of relation>coord.

<Related words>^心动过缓^

<Type of relation>coord.

<Related words>^周围神经病变^

<Type of relation>coord.

<Related words>^来那度胺^

<Type of relation>general

<Related words>^泊马度胺^

<Type of relation>general

<Synonyms>“DVT”和“深静脉血栓形成”是近义词。

<zh>DVT

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^Douketis 2022^ ， https://www.msdmanuals.cn/home/heart-and-blood-vessel-disorders/venous-disorders/deep-vein-thrombosis-dvt

<Variant of>深静脉血栓形成

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>lenalidomide

<Morphosyntax>noun

<Usage label>main term

<Source>^Hegde/Schmidt 2007^:524

<Lexica>Found in ^Oxford Concise Medical Dictionary 2020^

<Definition>Lenalidomide is a derivative of thalidomide differing in the presence of an amino moiety in the 4-position and removal of one of the carbonyls of the phthaloyl ring.

<Source>^Hegde/Schmidt 2007^:524

<Context>Lenalidomide evolved from a structural-based effort to eliminate the adverse effects (somnolence, neuropathy, and teratogenicity) of thalidomide while maintaining or enhancing the appealing attributes. Complimentary to inhibition of pro-inflammatory cytokines, lenalidomide also increases the secretion of anti- inflammatory cytokines, such as IL-10. Furthermore, lenalidomide inhibits secretion of angiogenic cytokines. Due to its immunomodulatory and antiangiogenic properties, lenalidomide has the potential for a wide spectrum of therapeutic applications.

<Source>^Hegde/Schmidt 2007^:524

<Concept field>new drugs

<Related words>^immunomodulatory drug^

<Type of relation>super.

<Related words>^thalidomide^

<Type of relation>coord.

<Related words>^asthenia^

<Type of relation>general

<Related words>^bradycardia^

<Type of relation>general.

<Related words>^peripheral neuropathy^

<Type of relation>general.

<Related words>^deep vein thrombosis^

<Type of relation>general

<Related words>^pomalidomide^

<Type of relation>coord.

<zh>来那度胺

<Morphosyntax>noun

<Source>^路瑾，等 2020^:62

<Definition>来那度胺是一种沙利度胺类似制剂，与沙利度胺相似，它被认为可多靶位攻击浆细胞微环境，使其调亡、抑制其血管生成和细胞因子环路,并产生其他诸如免疫调节、抗肿瘤等作用。

<Source>^路瑾，等 2020^:62

<Context>来那度胺已通过美国食品药品管理局(FDA)批准,用于初治、复发难治多发性骨髓瘤病人的诱导治疗和维持治疗中。来那度胺、硼替佐米联合地塞米松的诱导治疗方案可显著加深初治病人缓解深度,带来无进展生存时间获益。来那度胺联合地塞米松用于复发难治多发性骨髓瘤病人，总缓解率为 60%，中位总生存期约 38 个月。采用来那度胶维持治疗若达到 2 年以上，也可以在总生存期上获益。

<Source>^路瑾，等 2020^:63

<Concept field>新药

<Related words>^免疫调节剂^

<Type of relation>super.

<Related words>^沙利度股^

<Type of relation>coord.

<Related words>^无力^

<Type of relation>general

<Related words>^心动过缓^

<Type of relation>general

<Related words>^周围神经病变^

<Type of relation>general

<Related words>^深静脉血栓形成^

<Type of relation>general

<Related words>^泊马度胺^

<Type of relation>coord.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>pomalidomide

<Morphosyntax>noun

<Usage label>main term

<Source>^Gerson, et al. 2018^:866

<Lexica>Found in ^Oxford Concise Medical Dictionary 2020^

<Definition>Pomalidomide is a third-generation member of the immunomodulatory drugs (IMiDs) class.

<Source>^Gerson, et al. 2018^:866

<Context>In addition to its immunomodulatory and antiangiogenic activity, pomalidomide has direct activity against myeloma cells, affecting gene expression, and promoting apoptosis and cell cycle arrest. In vitro studies showed that pomalidomide was active in cell lines resistant to thalidomide and lenalidomide. The most common severe adverse events are myelosuppression (anaemia, neutropenia, and thrombocytopenia), infections, and fatigue. Venous thromboembolic events were observed in early-phase studies and subsequent trials have required thromboprophylaxis, under which the rate of VTE with pomalidomide is less than 5%.

<Source>^Gerson, et al. 2018^:866

<Concept field>new drugs

<Related words>^immunomodulatory drug^

<Type of relation>super.

<Related words>^thalidomide^

<Type of relation>coord.

<Related words>^asthenia^

<Type of relation>general

<Related words>^bradycardia^

<Type of relation>general

<Related words>^peripheral neuropathy^

<Type of relation>general

<Related words>^deep vein thrombosis^

<Type of relation>general

<Related words>^lenalidomide^

<Type of relation>coord.

<zh>泊马度胺

<Morphosyntax>noun

<Source>^路瑾，等 2020^:163

<Definition>泊马度胺是继沙利度胺和来那度胺后的第三代免疫调节剂，通过多重作用机制来抑制主发性骨髓瘤。

<Source>^路瑾，等 2020^:163

<Context>2013 年经美国 FDA 批准用于治疗至少经过两种治疗无效(包括来那度胺和硼替佐米)和最后—次治疗后 60d 内病情恶化的多发性骨髓瘤病人。在体外细胞学试验，泊马度胺能够抑制来那度胺耐药多发性骨髓瘤细胞株的增殖，与地塞米松协同作用诱导来那度胺-敏感、来那度胺-耐药细胞株肿瘤细胞凋亡。泊马度胺治疗伴有不良细胞遗传学的多发性骨髓瘤病人。

<Source>^路瑾，等 2020^:163

<Concept field>新药

<Related words>^免疫调节剂^

<Type of relation>super.

<Related words>^沙利度股^

<Type of relation>coord.

<Related words>^无力^

<Type of relation>general

<Related words>^心动过缓^

<Type of relation>general

<Related words>^周围神经病变^

<Type of relation>general

<Related words>^深静脉血栓形成^

<Type of relation>general

<Related words>^来那度胺^

<Type of relation>coord.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>proteasome inhibitor

<Morphosyntax>noun group

<Usage label>main term

<Source>^Alexa-Stratulat, et al. 2017^:13

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Proteasome inhibitors are a class of cytotoxic drugs that exert their anticancer effect through reversibly inhibiting the chymotrypsin-like catalytic activity of the proteasome which is involved in intracellular protein degradation.

<Source>^Alexa-Stratulat, et al. 2017^:13

<Context>Proteasome inhibitors are an important new class of drugs for the treatment of multiple myeloma and mantle cell lymphoma, and they are currently in clinical trials for additional types of cancer. Proteasome inhibitors also function as immunosuppressants, inhibit bone resorption, and may have other applications. Bortezomib was the first proteasome inhibitor to be US Food and Drug Administration (FDA)-approved in 2003, followed by carfilzomib in 2012 and ixazomib in 2015—other compounds are currently in clinical trials.

<Source>^Fricker 2020^:458

<Concept field>new drugs

<Related words>^proteasome^

<Type of relation>sub.

<Related words>^bortezomib^

<Type of relation>sub.

<Related words>^thrombocytopenia^

<Type of relation>general

<Related words>^carfilzomib^

<Type of relation>sub.

<Related words>^ixazomib^

<Type of relation>sub.

<Synonyms>The term “proteasome inhibitor” is often substituted by its initials “PI”.

<en>PI

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^McConkey/Zhu 2008^:164

<Variant of>proteasome inhibitor

<zh>蛋白酶体抑制剂

<Morphosyntax>noun group

<Source>^林渝樺 2021^，https://www.healthnews.com.tw/article/49504

<Definition>蛋白酶体抑制剂是一种标靶药物，可以选择性抑制细胞内蛋白酶体的功能，细胞无法回收老化及受损的蛋白质，当细胞内累积的老废蛋白质无法被分解时，将诱发细胞自我凋亡，达到毒杀骨髓瘤细胞的效果。

<Source>^林渝樺 2021^，https://www.healthnews.com.tw/article/49504

<Context>蛋白酶体抑制剂是治疗多发性骨髓瘤相当重要的药物，主要透过阻断癌细胞清除分解代谢产物的能力，借以达到毒杀骨髓瘤细胞的效果。目前蛋白酶体抑制剂有三种，分为针剂与口服两剂型；两者皆为针剂剂型，第一代药物以皮下注射为主（静脉注射的神经病变副作用大），第二代药物则是静脉注射，施打原则是以三至四周为一次疗程，一周施打一至两次，连续二至三周，休息一周。

<Source>^林渝樺 2021^，https://www.healthnews.com.tw/article/49504

<Concept field>新药

<Related words>^蛋白酶体^

<Type of relation>sub.

<Related words>^硼替佐米^

<Type of relation>sub.

<Related words>^血小板减少症^

<Type of relation>general

<Related words>^卡非佐米^

<Type of relation>sub.

<Related words>^伊沙佐米^

<Type of relation>sub.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>proteasome

<Morphosyntax>noun

<Source>^Fricker 2020^:458

<Lexica>Found in ^Oxford Concise Medical Dictionary 2020^

<Definition>The proteasome is a large, multicatalytic protein complex that degrades many cellular proteins.

<Source>^Fricker 2020^:458

<Context>The proteasome complex is not a single entity but exists in many different forms due to variations in the composition of catalytic subunits, structural subunits, regulatory subunits, and posttranslational modifications. Multiple proteasome forms are typically present in a single cell type, and this can change in a dynamically regulated process. There is variation between cell types and tissues, suggesting that the proteasome is optimized for each cell's function. Various proteasome forms have dramatic differences in their substrate preferences and generate distinct sets of peptides. In some studies, different proteasome forms have been found to show altered sensitivity to proteasome inhibitors. All proteasomes contain a common core, referred to as the 20S proteasome (based on its Svedberg sedimentation coefficient). This 20S core particle is about 700 kDa and contains 14 α and 14 β subunits arranged into four rings with a hollow center.

<Source>^Fricker 2020^:460

<Concept field>cytology

<Related words>^proteasome inhibitor^

<Type of relation>super

<Related words>^bortezomib^

<Type of relation>general

<Related words>^thrombocytopenia^

<Type of relation>general

<Related words>^carfilzomib^

<Type of relation>general

<Related words>^ixazomib^

<Type of relation>general

<zh>蛋白酶体

<Morphosyntax>noun

<Source>^陈佳文，等 2017^:518

<Definition>蛋白酶体是非溶酶体蛋白水解复合物，呈高度保守的圆桶状结构，主要存在于细胞核与细胞质中，可特异性降解泛素化蛋白质，维持细胞内蛋白质平衡及稳定，调控细胞的代谢和增殖。

<Source>^陈佳文，等 2017^:518

<Context>蛋白酶体通过泛素-蛋白酶体系统(UPS)实现降解蛋白功能。细胞内蛋白酶体大部分为 26S 蛋白酶体，由 1 个 20S 核心结构及 2 个 19S 调节结构组成。泛素化蛋白和(或)错误折叠蛋白的积累，可导致细胞凋亡。由于 MM 细胞具有遗传不稳定和快速增殖的特点，其更依赖于蛋白酶体，以去除错误折叠或损伤的蛋白质。

<Source>^陈佳文，等 2017^:518

<Concept field>细胞学

<Related words>^蛋白酶体抑制剂^

<Type of relation>super.

<Related words>^硼替佐米^

<Type of relation>general

<Related words>^血小板减少症^

<Type of relation>general

<Related words>^卡非佐米^

<Type of relation>general

<Related words>^伊沙佐米^

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>bortezomib

<Morphosyntax>noun

<Source>^Gerson, et al. 2018^:867

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Bortezomib (pyrazylcarbonyl-Phe-Leu-boronate) is a dipeptidyl boronic acid that is a specific and selective inhibitor of the 26S proteasome.

<Source>^Gerson, et al. 2018^:867

<Context>The Boron atom interacts reversibly with the catalytic threonine residue of the proteasome, primarily inhibiting its chymotrypsin-like activity. The inhibition of the ubiquitin–proteasome pathway with bortezomib was demonstrated to arrest the growth of malignant cells

(breast, colon, prostate tumour cell lines, Burkitt lymphoma, adult T-cell leukaemia, Lewis lung carcinoma, CLL, and myeloma cell lines) and sensitize them to chemotherapeutic agents (5-FU, cisplatin, taxol, doxorubicin, CPT-11, and gemcitabine). Bortezomib mediates these effects through multiple mechanisms by regulating the expression of proteins involved in cell cycle progression, oncogenesis, apoptosis, and, more recently, DNA repair.
<Source>^Gerson, et al. 2018^:868
<Concept field>new drugs
<Related words>^proteasome inhibitor^
<Type of relation>super.
<Related words>^proteasome^
<Type of relation>general
<Related words>^thrombocytopenia^
<Type of relation>sub.
<Related words>^carfilzomib^
<Type of relation>coord.
<Related words>^ixazomib^
<Type of relation>coord.

<zh>硼替佐米
<Morphosyntax>noun
<Source>^中华人民共和国国家知识产权局 2016^:1
<Definition>硼替佐米是一种合成的高选择性 26S 蛋白酶体糜蛋白酶样活性的可逆抑制剂，主要通过阻断细胞内多种调控细胞调亡及信号传导的蛋白质的降解，导致肿瘤细胞的死亡。
<Source>^中华人民共和国国家知识产权局 2016^:1
<Context>硼替佐米是首个用于临床研究的蛋白酶体抑制剂，在单独或联合其它药物时，显现出优越的抗肿瘤作用和用药的安全性，与许多药物合用呈协同或增敏作用。同时，硼替佐米在其它类型的浆细胞疾病、急性髓系白血病及某些实体瘤的治疗上，也被报道具有良好的疗效。
<Source>^中华人民共和国国家知识产权局 2016^:1
<Concept field>新药
<Related words>^蛋白酶体抑制剂^
<Type of relation>super.

<Related words>^蛋白酶体^

<Type of relation>general

<Related words>^血小板减少症^

<Type of relation>sub.

<Related words>^卡非佐米^

<Type of relation>coord.

<Related words>^伊沙佐米^

<Type of relation>coord.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>thrombocytopenia

<Morphosyntax>noun

<Source>^Greenberg/Kaled 2013^:428

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Thrombocytopenia is defined as a platelet count less than 150,000/mL. It is considered to be mild when the platelet count is between 70,000 and 150,000/mL, and severe if less than 20,000/mL.

<Source>^Greenberg/Kaled 2013^:428

<Context>Thrombocytopenia can occur from a decreased bone marrow production, increased destruction of platelets, and sequestration. Most individuals are asymptomatic if the platelet count is 50,000/mL or greater. Surgical procedures may be performed when the platelet count is 50,000/mL or greater. Bleeding from minimal trauma may occur with a platelet count of 30,000/mL or less, and spontaneous bleeding may occur when the platelet count is less than 10,000/mL. Spontaneous bleeding may occur in the mucosa, skin, lungs, gastrointestinal tract, central nervous system, and genitourinary tract.

<Source>^Greenberg/Kaled 2013^:428

<Concept field>adverse events

<Related words>^proteasome inhibitor^

<Type of relation>super.

<Related words>^proteasome^

<Type of relation>general

<Related words>^bortezomib^

<Type of relation>super.

<Related words>^carfilzomib^

<Type of relation>general

<Related words>^ixazomib^

<Type of relation>general

<zh>血小板减少症

<Morphosyntax>noun group

<Usage label>main term

<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/diseases-conditions/thrombocytopenia/symptoms-causes/syc-20378293

<Definition>血小板减少症是指循环血液中的血小板数量低于 150,000/微升。

<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/diseases-conditions/thrombocytopenia/symptoms-causes/syc-20378293

<Context>血小板减少症可能是由于骨髓疾病如白血病或免疫系统问题引起的。也可能是服用某些药物的副作用。血小板减少症可以是轻微的，引起很少的体征或症状。极少数情况下，血小板的数量会低到出现危险的内出血。

<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/diseases-conditions/thrombocytopenia/symptoms-causes/syc-20378293

<Concept field>不良事件

<Related words>^蛋白酶体抑制剂^

<Type of relation>super.

<Related words>^蛋白酶体^

<Type of relation>general

<Related words>^硼替佐米^

<Type of relation>super.

<Related words>^卡非佐米^

<Type of relation>general

<Related words>^伊沙佐米^

<Type of relation>general

<Synonyms>“血小板计数低”和“血小板减少症”是近义词。

<zh>血小板计数低

<Morphosyntax>noun group

<Usage label>uncommon

<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/diseases-conditions/thrombocytopenia/symptoms-causes/syc-20378293

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>carfilzomib

<Morphosyntax>noun

<Source>^Gerson, et al. 2018^:868

<Definition>Carfilzomib is a second-generation proteasome inhibitor that selectively inhibits the chymotrypsin-like activity of the proteasome and is active in bortezomib-resistant patients.

<Source>^Gerson, et al. 2018^:868

<Context>Carfilzomib induces irreversible inhibition (once carfilzomib binds to its active site within the barrel of the proteasome, the proteasome is permanently inactivated, and new proteasomes must be synthesized to restore proteasome activity) compared with the reversible effects of bortezomib (duration of proteasome inhibition lasts about 72 h). Carfilzomib appears to be less likely to cause peripheral neuropathy and is safe in patients with renal impairment. Higher response rates are observed when carfilzomib is used in combination with other agents such as lenalidomide and low-dose dexamethasone.

<Source>^Gerson, et al. 2018^:868-869

<Concept field>new drugs

<Related words>^proteasome inhibitor^

<Type of relation>super.

<Related words>^proteasome^

<Type of relation>general

<Related words>^bortezomib^

<Type of relation>coord.

<Related words>^thrombocytopenia^

<Type of relation>general

<Related words>^ixazomib^

<Type of relation>coord.

<zh>卡非佐米

<Morphosyntax>noun

<Source>^陈佳文，等 2017^:519

<Definition>卡非佐米是经静脉给药的环氧甲酮四肽 PI，通这特异性抑制蛋白酶体的糜蛋白醇样蛋白水解活性，从而诱导 MM 细胞调亡。

<Source>^陈佳文，等 2017^:519

<Context>卡非佐米以其高度选择性及不可逆抑制性，在对 MM 患者的疗效和安全性上较硼替佐米更具有优势。此外,卡非佐米所致的神经毒性和神经退行性变较硼替佐米显著减少 1。主要适用于接受过 2 种及以上治疗方案(包括免疫调节剂和硼替佐米在内）无效或复发的 MM 患者。

<Source>^陈佳文，等 2017^:519

<Concept field>新药

<Related words>^蛋白酶体抑制剂^

<Type of relation>super.

<Related words>^蛋白酶体^

<Type of relation>general

<Related words>^硼替佐米^

<Type of relation>coord.

<Related words>^血小板减少症^

<Type of relation>general

<Related words>^伊沙佐米^

<Type of relation>coord.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>ixazomib

<Morphosyntax>noun

<Source>^Gerson, et al. 2018^:869

<Definition>Ixazomib is a boronic acid-containing peptide with chymotrypsin- and caspase-like proteasome inhibitory activity, formulated for oral administration.

<Source>^Gerson, et al. 2018^:869

<Context>Haematologic adverse events appear to be a class effect associated with proteasome inhibitors; ixazomib cause transient, cyclical thrombocytopenia, with platelet counts dropping and then returning to baseline prior to the next cycle of treatment. Ixazomib may cause transient rash.

<Source>^Gerson, et al. 2018^:869

<Concept field>new drugs

<Related words>^proteasome inhibitor^

<Type of relation>super.

<Related words>^proteasome^

<Type of relation>general

<Related words>^bortezomib^

<Type of relation>coord.

<Related words>^thrombocytopenia^

<Type of relation>general

<Related words>^carlfizomib^

<Type of relation>coord.

<zh>伊沙佐米

<Morphosyntax>noun

<Source>^路瑾，等 2020^:66

<Definition>伊沙佐米是全球首个口服蛋白酶体抑制剂，通过选择性抑制 20S 蛋白酶体发挥治疗 MM 的作用。

<Source>^路瑾，等 2020^:66

<Context>伊莎佐米在体外可诱导多发性骨髓瘤细胞系调亡，对经硼替佐米、来那度胺和地塞米松等多种药物治疗后复发病人的骨髓瘤细胞仍具有细胞毒作用。其突出优点是周围神经炎明显低于硼替佐米。伊沙佐米对初治 MM 治疗效果良好，起效迅速,安全性高，其与来那度胺和地塞米松组成的全口服方案(IRd)为病人提供了便利，也为初发 MM 病人提供了“无化疗”的治疗选择。

<Source>^路瑾，等 2020^:66

<Concept field>新药

<Related words>^蛋白酶体抑制剂^

<Type of relation>super.

<Related words>^蛋白酶体^

<Type of relation>general

<Related words>^硼替佐米^

<Type of relation>coord.

<Related words>^血小板减少症^

<Type of relation>general

<Related words>^卡非佐米^

<Type of relation>coord.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>monoclonal antibody

<Morphosyntax>noun group

<Usage label>main term

<Source>^Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases 2012^, https://www.ncbi.nlm.nih.gov/books/NBK548844/

<Lexica>Found in ^Oxford Concise Medical Dictionary 2020^

<Definition>Monoclonal antibodies are immunoglobulins that have a high degree of specificity (mono-specificity) for an antigen or epitope.

<Source>^Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases 2012^, https://www.ncbi.nlm.nih.gov/books/NBK548844/

<Context>Monoclonal antibodies are typically derived from a clonal expansion of antibody producing malignant human plasma cells. Monoclonal antibodies have broad clinical and experimental medical uses. Use of monoclonal antibodies is currently broadening to therapy of severe, nonmalignant conditions including asthma, atopic dermatitis, migraine headaches, hypercholesterolemia, osteoporosis, bacterial diseases (such as anthrax) and viral infections (such as COVID-19).

<Source>^Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases 2012^, https://www.ncbi.nlm.nih.gov/books/NBK548844/

<Concept field>new drugs

<Related words>^hemopoietic microenvironment^

<Type of relation>general

<Related words>^daratumumab^

<Type of relation>sub.

<Related words>^antibody-dependent cellular cytotoxicity^

<Type of relation>general

<Related words>^isatuximab^

<Type of relation>sub.

<Related words>^lymphopenia^

<Type of relation>general

<Synonyms>The term “monoclonal antibody” is often substituted by its acronym “mAb”.

<en>mAb

<Morphosyntax>noun

<Category>acronym

<Usage label>common

<Source>^Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases 2012^, https://www.ncbi.nlm.nih.gov/books/NBK548844/

<Variant of>monoclonal antibody

<zh>单克隆抗体

<Morphosyntax>noun group

<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/diseases-conditions/cancer/in-depth/monoclonal-antibody/art-20047808

<Definition>单克隆抗体是实验室生产的分子，旨在作为替代抗体，恢复、增强、修改或模仿免疫系统对不需要的细胞（如癌细胞）进行的攻击。

<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/diseases-conditions/cancer/in-depth/monoclonal-antibody/art-20047808

<Context>单克隆抗体旨在以不同的方式起作用，例如：标记癌细胞，阻碍细胞生长，防止血管生长，阻断免疫系统抑制剂，直接攻击癌细胞，提供放射治疗，提供化疗。许多单克隆抗体已经批准用于治疗多种不同类型的癌症。临床试验正在研究新药物和现有单克隆抗体的新用途。单克隆抗体通过静脉（静脉内）。一些单克隆抗体药物可以与其他治疗结合使用，例如化疗或激素疗法。

<Source>^Mayo Clinic 2021^, https://www.mayoclinic.org/zh-hans/diseases-conditions/cancer/in-depth/monoclonal-antibody/art-20047808

<Concept field>新药

<Related words>^造血微环境^

<Type of relation>general

<Related words>^达雷妥尤单抗^

<Type of relation>sub.

<Related words>^抗体依赖的细胞介导的细胞毒性^

<Type of relation>general

<Related words>^伊莎妥昔单抗^

<Type of relation>sub.

<Related words>^淋巴细胞减少^

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>daratumumab

<Morphosyntax>noun

<Usage label>main term

<Source>^Kalis 2017^:83

<Definition>Daratumumab is a human immunoglobulin (IgG1) monoclonal antibody directed against CD38, which is highly expressed on myeloma cells.

<Source>^Kalis 2017^:83

<Context>Daratumumab (Darzalex) is a first-in-class inhibitor of CD38 and the first monoclonal antibody approved for treatment of myeloma. In November 2015, the US Food and Drug Administration (FDA) granted accelerated approval to daratumumab for the treatment of patients with myeloma who have received at least three prior lines of therapy, including a PI and an IMiD, or who are double refractory to a PI and an IMiD. Furthermore, daratumumab has been shown to induce immunomodulatory effects. CD38 is expressed on subsets of regulatory T cells, B cells, and monocytes, indicating these cells are sensitive to treatment with daratumumab. By targeting and eliminating these cells, daratumumab removes a mechanism of immuno- suppression and enables an antimyeloma response.

<Source>^Kalis 2017^:83

<Concept field>new drugs

<Related words>^monoclonal antibody^

<Type of relation>super

<Related words>^antibody-dependent cellular cytotoxicity^

<Type of relation>sub.

<Related words>^isatuximab^

<Type of relation>coord.

<Related words>^lymphopenia^

<Type of relation>general

<zh>达雷妥尤单抗

<Morphosyntax>noun

<Source>^赵艾琳，等 2022^:3304

<Definition>达雷妥尤单抗是人源化、IgG1κ 型抗 CD38 单克隆抗体，通过补体依赖的细胞毒作用、抗体依赖细胞介导的细胞毒作用、抗体依赖的细胞吞噬作用、Fcγ 介导的单抗交联、CD38 酶活性的调节等诱导 MM 细胞凋亡。

<Source>^赵艾琳，等 2022^:3304

<Context>研究报道泊马度胺与达雷妥尤单抗治疗有协同作用。达雷妥尤单抗总体安全性较好，常见的不良事件为感染、输液相关不良反应、血小板减少。

<Source>^赵艾琳，等 2022^:3310

<Concept field>新药

<Related words>^单克隆抗体^

<Type of relation>super.

<Related words>^抗体依赖的细胞介导的细胞毒性^

<Type of relation>sub.

<Related words>^伊莎妥昔单抗^

<Type of relation>coord.

<Related words>^淋巴细胞减少^

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>人体生理学 / Human physiology (612)

<en>antibody-dependent cellular cytotoxicity

<Morphosyntax>noun group

<Usage label>main term

<Source>^Gómez Román, et al. 2014^:1

<Definition>Antibody-dependent cellular cytotoxicity (ADCC), also called antibody-dependent cell-mediated cytotoxicity, is an immune mechanism through which Fc receptor-bearing effector cells can recognize and kill antibody-coated target cells expressing tumour- or pathogen-derived antigens on their surface.

<Source>^Gómez Román, et al. 2014^:1

<Context>Four main stages and mechanisms leading to the antibody-dependent effector-mediated killing of the target cell can be identified: (1) Recognition of the target cell and Fc receptor cross-linking on the surface of the effector cell; (2) phosphorylation of immunoreceptor tyrosine-based activation motifs (ITAMs) by cellular kinases within the effector cell; (3)

triggering of three main downstream signalling pathways in the effector cell, resulting in cytotoxic granule polarization and release; and (4) killing of the target cell via the predominant perforin/granzyme cell death pathway.
<Source>^Gómez Román, et al. 2014^:1
<Concept field>immune mechanism
<Related words>^monoclonal antibody^
<Type of relation>super.
<Related words>^daratumumab^
<Type of relation>super.
<Related words>^isatuximab^
<Type of relation>general
<Related words>^lymphopenia^
<Type of relation>coord.
<Synonyms>The term “antibody-dependent cellular cytotoxicity” is often substituted by its initials “ADCC”.

<en>ADCC
<Morphosyntax>noun
<Category>initials
<Usage label>common
<Source>^Gómez Román, et al. 2014^:1
<Variant of>antibody-dependent cellular cytotoxicity

<zh>抗体依赖的细胞介导的细胞毒性
<Morphosyntax>noun group
<Usage label>main term
<Source>^LabEx^, https://www.u-labex.com/article-adcc.html
<Definition>抗体依赖的细胞介导的细胞毒性（ADCC）是指抗体的 Fab 段结合病毒感染的细胞或肿瘤细胞的抗原表位，其 Fc 段与杀伤细胞（NK 细胞、巨噬细胞等）表面的 FcR 结合，介导杀伤细胞直接杀伤靶细胞。
<Source>^LabEx^, https://www.u-labex.com/article-adcc.html
<Context>抗体依赖细胞介导的细胞毒作用（ADCC）是抗体发挥作用的方式之一。ADCC 是一种抗体依赖的细胞杀伤作用，一般为自然杀伤细胞（NK）介导。抗体 Fab

端结合靶细胞表面抗原，Fc 端结合 NK 细胞表面的 Fc 受体 CD16,将靶细胞与 NK 细胞拉近距离，并激活 NK 细胞释放颗粒酶和穿孔素等，最终导致靶细胞被裂解。

<Source>^LabEx^, https://www.u-labex.com/article-adcc.html

<Concept field>免疫机制

<Related words>^单克隆抗体^

<Type of relation>super.

<Related words>^达雷妥尤单抗^

<Type of relation>super.

<Related words>^伊莎妥昔单抗^

<Type of relation>general

<Related words>^淋巴细胞减少^

<Type of relation>coord.

<Synonyms>“ADCC”和“抗体依赖的细胞介导的细胞毒性”是近义词。

<zh>ADCC

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^LabEx^, https://www.u-labex.com/article-adcc.html

<Variant of>抗体依赖的细胞介导的细胞毒性

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>isatuximab

<Morphosyntax>noun

<Source>^European Medicines Agency^, https://www.ema.europa.eu/en/documents/product-information/sarclisa-epar-product-information_en.pdf

<Definition 1>Isatuximab is an immunoglobulin G1 (IgG1) monoclonal antibody (mAb) produced from a mammalian cell line.

<Definition 2>Isatuximab is an IgG1-derived monoclonal antibody that binds to a specific extracellular epitope of CD38 receptor.

<Source>^European Medicines Agency^, https://www.ema.europa.eu/en/documents/product-information/sarclisa-epar-product-information_en.pdf

<Context>In vitro, isatuximab acts through IgG Fc-dependent mechanisms including antibody dependent cell mediated cytotoxicity (ADCC), antibody dependent cellular phagocytosis (ADCP), and complement dependent cytotoxicity (CDC). Furthermore, isatuximab can also trigger tumour cell death by induction of apoptosis via an Fc-independent mechanism. In vitro, isatuximab blocks the enzymatic activity of CD38 which catalyses the synthesis and hydrolysis of cyclic ADP-ribose (cADPR), a calcium mobilizing agent. The combination of isatuximab and pomalidomide in vitro enhances cell lysis of CD38 expressing multiple myeloma cells by effector cells (ADCC), and by direct tumour cell killing compared to that of isatuximab alone.
<Source>^European Medicines Agency^, https://www.ema.europa.eu/en/documents/product-information/sarclisa-epar-product-information_en.pdf
<Concept field>new drugs
<Related words>^monoclonal antibody^
<Type of relation>super.
<Related words>^daratumumab^
<Type of relation>coord.
<Related words>^antibody-dependent cellular cytotoxicity^
<Type of relation>general
<Related words>^lymphopenia^
<Type of relation>sub.

<zh>伊莎妥昔单抗
<Morphosyntax>noun
<Source>^刘燕/陶洁 2020^:538
<Definition>伊莎妥昔单抗是一种人源化、CD38IgG1 单克隆抗体，能选择性地结合于 CD38 的特异性表位。
<Source>^刘燕/陶洁 2020^:538
<Context>由于 CD38 在恶性浆细胞上呈高表达且分布均匀，而在正常淋巴细胞和髓细胞，以及非造血细胞上表达相对较低，使其成为有潜力的 MM 治疗靶点。伊莎妥昔单抗通过清除 CD38＋的免疫抑制细胞发挥作用，其作用机制包括 Fc 依赖性免疫效应机制、直接凋亡活性和免疫调节效应。此外，伊莎妥昔单抗还可以抑制 CD38 的细胞外酶活性，改变 Ca2＋稳态，从而发挥抗 MM 作用。
<Source>^刘燕/陶洁 2020^:538
<Concept field>新药

<Related words>^单克隆抗体^

<Type of relation>super.

<Related words>^达雷妥尤单抗^

<Type of relation>coord.

<Related words>^抗体依赖的细胞介导的细胞毒性^

<Type of relation>general

<Related words>^淋巴细胞减少^

<Type of relation>sub.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>lymphopenia

<Morphosyntax>noun

<Usage label>main term

<Source>^Dale 2023^, https://www.msdmanuals.com/professional/hematology-and-oncology/leukopenias/lymphocytopenia

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Lymphopenia is a total lymphocyte count of < 1000/mcL (1 × 109/L) in adults or < 3000/mcL (< 3 × 109/L) in children < 2 years.

<Source>^Dale 2023^, https://www.msdmanuals.com/professional/hematology-and-oncology/leukopenias/lymphocytopenia

<Context>Lymphopenia is often transient when caused by many viral and bacterial infections, sepsis, corticosteroid treatment, and stress responses. Lymphopenia may also reflect impaired lymphocyte production arising from destruction of thymic or lymphoid architecture. Lymphopenia per se generally causes no symptoms. Patients with lymphopenia experience recurrent infections or develop infections with unusual organisms. Lymphopenia is also a risk factor for the development of cancers and for autoimmune disorders.

<Source>^Dale 2023^, https://www.msdmanuals.com/professional/hematology-and-oncology/leukopenias/lymphocytopenia

<Concept field>adverse events

<Related words>^monoclonal antibody^

<Type of relation>general

<Related words>^daratumumab^

<Type of relation>general

<Related words>^antibody-dependent cellular cytotoxicity^

<Type of relation>general

<Related words>^isatuximab^

<Type of relation>super.

<Synonyms>The term “lymphocytopenia” is synonym to “lymphopenia” and it is commonly used.

<en>lymphocytopenia

<Morphosyntax>noun

<Usage label>common

<Source>^Oxford Concise Medical Dictionary 2020^:453

<zh>淋巴细胞减少

<Morphosyntax>noun group

<Source>^Territo 2021^, https://www.msdmanuals.cn/professional/hematology-and-oncology/leukopenias/lymphocytopenia

<Definition>淋巴细胞减少指成人淋巴细胞总数<1000/mcL（<1×109/L)，<2 岁儿童<3000/mcL（<3×109/L)。

<Source>^Territo 2021^, https://www.msdmanuals.cn/professional/hematology-and-oncology/leukopenias/lymphocytopenia

<Context>淋巴细胞减少可能是获得性或遗传性。医源性淋巴细胞减少常由细胞毒性化疗、放疗或给予抗淋巴细胞球蛋白（或其他淋巴细胞抗体）所引起。淋巴细胞减少可能发生于淋巴瘤，自身免疫性疾病，如系统性红斑狼疮、类风湿性关节炎、重症肌无力及胃肠道疾病或缩窄性心包炎所致的蛋白质丢失性肠病。遗传性淋巴细胞减少主要由以下原因引起严重的联合免疫缺陷病，Wiskott-Aldrich 综合征。其结局包括机会感染、恶性肿瘤和自身免疫性疾病的发病风险增加。根据潜在疾病进行治疗。

<Source>^Territo 2021^, https://www.msdmanuals.cn/professional/hematology-and-oncology/leukopenias/lymphocytopenia

<Concept field>不良事件

<Related words>^单克隆抗体^

<Type of relation>super.

<Related words>^达雷妥尤单抗^

<Type of relation>general

<Related words>^抗体依赖的细胞介导的细胞毒性^

<Type of relation>coord.

<Related words>^伊莎妥昔单抗^

<Type of relation>super.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>interferon

<Morphosyntax>noun

<Usage label>main term

<Source>^Chow/Gale 2015^:1808

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Interferons (IFNs) are crucial cytokines of antimicrobial, antitumor, and immunomodulatory activity.

<Source>^Chow/Gale 2015^:1808

<Context>The three types of IFN (I, II, and III) are classified by their receptor specificity and sequence homology. IFNs are produced and secreted by cells in response to specific stimuli. Beyond the canonical pathways, IFNs operate on intricate levels of complexity that impart their pleiotropic effects. IFN responses are cell type and context specific, with overlapping, but often distinct, transcriptional output. Type I IFNs can enhance IFN-γ signalling by activating STAT1 homodimers. Type III IFN stimulation can enhance responsiveness to IFN-γ. These pathways regulate mRNA translation, autophagy, and other cellular functions, and together they form a complex network that confers the many facets of IFN response.

<Source>^Chow/Gale 2015^:1808

<Concept field>chemotherapeutic agents

<Related words>maintenance therapy

<Type of relation>super.

<Related words>glucocorticoids

<Type of relation>coord.

<Related words>new drugs

<Type of relation>coord.

<Related words>^polyneuropathy^

<Type of relation>sub.

<Synonyms>The term “interferon” is often substituted by its initials “IFN”.

<en>IFN

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^Chow/Gale 2015^:1808

<Variant of>interferon

<zh>干扰素

<Morphosyntax>noun

<Usage label>main term

<Source>^ThermoFisher Scientific^, https://www.thermofisher.cn/cn/zh/home/life-science/cell-analysis/cell-analysis-learning-center/immunology-at-work/interferons-overview.html

<Lexica>Found in ^现代汉语词典 2013^

<Definition>干扰素（IFN）受体蛋白是宿主细胞分泌的一类细胞因子，可调节免疫应答。

<Source>^ThermoFisher Scientific^, https://www.thermofisher.cn/cn/zh/home/life-science/cell-analysis/cell-analysis-learning-center/immunology-at-work/interferons-overview.html

<Context>当存在病原体时，通常由宿主细胞释放干扰素，周围未感染的细胞感知后激活适当的细胞防御机制，以便消除病原体。IFN 细胞因子根据其结合的不同干扰素受体分为三种类型（I 型、II 型和 III 型）（表 1）；每种 IFN 细胞因子诱导一种特定的免疫反应。此外，IFN 细胞因子介导信号会促进主要组织相容性 I 类和 II 类分子（MHC I，MHC II）的上调，并活化许多下游信号级联，从而生成抗病毒防御机制。

<Source>^ThermoFisher Scientific^, https://www.thermofisher.cn/cn/zh/home/life-science/cell-analysis/cell-analysis-learning-center/immunology-at-work/interferons-overview.html

<Concept field>化疗剂

<Related words>维持治疗

<Type of relation>super.

<Related words>糖皮质激素

<Type of relation>coord.

<Related words>新药

<Type of relation>coord.

<Related words>^多发性神经病^

<Type of relation>sub.

<Synonyms>“IFN”和“干扰素”是近义词。

<zh>IFN

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^ThermoFisher Scientific^, https://www.thermofisher.cn/cn/zh/home/life-science/cell-analysis/cell-analysis-learning-center/immunology-at-work/interferons-overview.html

<Variant of>干扰素

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>polyneuropathy

<Morphosyntax>noun

<Source>^Rubin 2022^, https://www.msdmanuals.com/professional/neurologic-disorders/peripheral-nervous-system-and-motor-unit-disorders/polyneuropathy?query=polyneuropathy

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>A polyneuropathy is a diffuse peripheral nerve disorder that is not confined to the distribution of a single nerve or a single limb and typically is relatively symmetrical bilaterally.

<Source>^Rubin 2022^, https://www.msdmanuals.com/professional/neurologic-disorders/peripheral-nervous-system-and-motor-unit-disorders/polyneuropathy?query=polyneuropathy

<Context>Symptoms of polyneuropathy may appear suddenly or develop slowly and become chronic depending on the cause. Because pathophysiology and symptoms are related, polyneuropathies are often classified by area of dysfunction: Myelin, Vasa nervorum, Axon. Polyneuropathies may be acquired or inherited. Polyneuropathy is suspected in patients with diffuse or multifocal sensory deficits, weakness without hyperreflexia, or both. Treatment of polyneuropathy focuses on correcting the causes when possible; a causative drug or toxin can be eliminated, or a dietary deficiency can be corrected. If the cause cannot be corrected, treatment focuses on minimizing disability and pain.

<Source>^Rubin 2022^, https://www.msdmanuals.com/professional/neurologic-disorders/peripheral-nervous-system-and-motor-unit-disorders/polyneuropathy?query=polyneuropathy

<Concept field>adverse events

<Related words>maintenance therapy

<Type of relation>super.

<Related words>^interferon^

<Type of relation>super.

<zh>多发性神经病

<Morphosyntax>noun group

<Usage label>main term

<Source>^中国公众健康网2014^，http://www.chealth.org.cn/mon/diseases/article/MA144005317.html

<Definition>多发性神经病，又称末梢神经病，是不同病因引起的，表现为四肢远端对称性的或非对称性的运动、感觉以及自主神经功能障碍性疾病。

<Source>^中国公众健康网2014^，http://www.chealth.org.cn/mon/diseases/article/MA144005317.html

<Context>周围神经的损伤，常是完全性的，一般均有周围神经的感觉、运动和自主神经纤维受累的共同症状。症状通常同时出现，呈四肢远端对称性分布，由远端向近端扩展。各种原因引起的多发性神经炎，均应早期足量地应用维生素 B1、维生素 B2、维生素 B6、维生素 B12 及维生素 C 等。疼痛剧烈患者可选用止痛剂、卡马西平、苯妥英钠或阿米替林。

<Source>^中国公众健康网2014^，http://www.chealth.org.cn/mon/diseases/article/MA144005317.html

<Concept field>不良事件

<Related words>维持治疗

<Type of relation>super.

<Related words>^干扰素^

<Type of relation>super.

<Synonyms>“末梢神经病”和“多发性神经病”是近义词。

<zh>末梢神经病

<Morphosyntax>noun group

<Usage label>uncommon

<Source>^ 中 国 公 众 健 康 网 2014^ ，

http://www.chealth.org.cn/mon/diseases/article/MA144005317.html

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>bisphosphonates

<Morphosyntax>noun

<Usage label>main term

<Source>^Levy/Roodman 2009^:109

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Bisphosphonates are carbon-containing derivatives of pyrophosphoric acid that allow chemical substitution on the carbon to optimize bisphosphonates' affinity for bone and their activity against osteoclasts.

<Source>^Levy/Roodman 2009^:109

<Context>The pharmacologic effects of bisphosphonates result from both their high affinity for bone through their similarity to pyrophosphonates and their ability to inhibit osteoclasts. Other effects of bisphosphonates shown by in vitro studies include antiangiogenic effects and effects on the marrow microenvironmental cells, immune cells, and cancer cells. In patients with MM, their primary effect is to inhibit osteoclast activity. Overall, bisphosphonates are very safe drugs for treating patients with MM. The most common toxicity associated with bisphosphonate therapy is renal toxicity since these drugs are cleared by the kidney. Usually, the renal toxicity can be managed by simply stopping the bisphosphonate and waiting until renal function returns to within 10% of baseline. The bisphosphonate is then restarted at a lower dose (in the case of zoledronic acid) or using a prolonged infusion time (for pamidronate). An emerging complication for patients receiving bisphosphonate therapy is osteonecrosis of the jaw (ONJ).

<Source>^Levy/Roodman 2009^:109-110

<Concept field>antiresorptive drug

<Related words>^denosumab^

<Type of relation>sub.

<Related words>^osteonecrosis of the jaw^

<Type of relation>sub.

<Related words>^zoledronic acid^

<Type of relation>sub.

<Synonyms>The term “bisphosphonates” is often substituted by its initials “BPs”.

<en>BPs
<Morphosyntax>noun
<Category>initials
<Usage label>common
<Source>^Levy/Roodman 2009^:109
<Variant of>bisphosphonates

<zh>双膦酸盐类
<Morphosyntax>noun
<Usage label>main term
<Source>^潘剑，等 2017^:29
<Definition>双膦酸盐类（BPs）药物是一种强有力的破骨细胞抑制剂，临床上被广泛应用于预防或治疗由破骨细胞活性增强所致的各种骨质降解类疾病，如骨质疏松症、Paget's 病、多发性骨髓瘤、恶性肿瘤骨转移及肿瘤源性高钙血症等。
<Source>^潘剑，等 2017^:29
<Context>近年来，BPs 也开始用于治疗一些口腔疾病，如应用于牙周炎，可改善牙周病状况并促进骨的再生和矿化，也有记载将其应用于种植牙治疗。目前临床上 BPs 常用的是第二、三代，如唑来膦酸、阿仑膦酸、帕米膦酸等。双膦酸盐相关性颌骨坏死（BRONJ）作为使用 BPs 药物引起的严重不良反应。
<Source>^潘剑，等 2017^:29
<Concept field>抗骨化药物
<Related words>^地舒单抗^
<Type of relation>sub.
<Related words>^颌骨坏死^
<Type of relation>sub.
<Related words>^唑来膦酸^
<Type of relation>sub.
<Synonyms>“BPs”和“双膦酸盐类”是近义词。

<zh>BPs
<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^潘剑，等 2017^:29

<Variant of>双膦酸盐类

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>denosumab

<Morphosyntax>noun

<Usage label>main term

<Source>^Zhou/Dempster 2013^:1788

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Denosumab is a human monoclonal antibody with high affinity and specificity for receptor activator of nuclear factor kappaB ligand (RANKL), an essential mediator of the formation, activity, and survival of osteoclasts.

<Source>^Zhou/Dempster 2013^:1788

<Context>By neutralizing the activity of RANKL, denosumab inhibits osteoclastic bone resorption and reduces bone turnover, consequently increasing BMD and reducing the risk of new vertebral fractures, nonvertebral, and hip fractures.

<Source>^Zhou/Dempster 2013^:1788

<Concept field>antiresorptive drug

<Related words>^bisphosphonates^

<Type of relation>super.

<Related words>^osteonecrosis of the jaw^

<Type of relation>sub.

<Related words>^zoledronic acid^

<Type of relation>coord.

<zh>地舒单抗

<Morphosyntax>noun

<Usage label>main term

<Source>^施雅分，等 2013^:118

<Definition>地舒单抗（Denosumab）是一种人类 IgG2 单株抗体制剂，会与 RANKL 结合，为 RANKL 抑制剂。

<Source>^施雅分，等 2013^:118

<Context>RANKL 是一种蛋白质，由造骨细胞生成，促使破骨细胞先驱物 (osteoclast precursor)成熟，形成破骨细胞，然后破骨细胞作用在骨骼，溶出骨骼内的钙质，造成骨质的流失。Denosumab 可针对 RANKL 产生作用，抑制 RANKL 和破骨细胞的结合，抑制破骨细胞活化，避免骨质的流失，因而增加骨质密度，使骨折风险降低。

<Source>^施雅分，等 2013^:118-119

<Concept field>抗骨化药物

<Related words>^双膦酸盐类^

<Type of relation>super.

<Related words>^颌骨坏死^

<Type of relation>sub.

<Related words>^唑来膦酸^

<Type of relation>coord.

<Synonyms>“Denosumab”和“地舒单抗”是近义词。

<zh>denosumab

<Morphosyntax>noun

<Category>translation

<Usage label>common

<Source>^施雅分，等 2013^:118

<Variant of>地舒单抗

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>osteonecrosis of the jaw

<Morphosyntax>noun group

<Usage label>main term

<Source>^Anastasilakis, et al. 2022^:1442

<Definition>Osteonecrosis of the jaw (ONJ) is a rare but serious condition manifested as one or more necrotic bone lesions that are exposed or can be probed through an intraoral or extraoral fistula in the maxillofacial region and persist for at least 8 weeks without response to appropriate therapy.

<Source>^Anastasilakis, et al. 2022^:1442

<Context>ONJ is more commonly located in the mandible but can be detected at both jaws. It may be accompanied by pain, inflammation, erythema, suppuration, and loose teeth. Although ONJ may occur spontaneously, in most cases it is the result of a dental procedure, for example, a tooth extraction or oral surgery. The occurrence of ONJ was initially associated with BP administration and named bisphosphonate related ONJ (BRONJ).
<Source>^Anastasilakis, et al. 2022^:1442
<Concept field>adverse events
<Related words>^bisphosphonates^
<Type of relation>super.
<Related words>^denosumab^
<Type of relation>super.
<Related words>^zoledronic acid^
<Type of relation>super.
<Synonyms>The term “osteonecrosis of the jaw” is often substituted by its initials “ONJ”.

<en>ONJ
<Morphosyntax>noun
<Category>initials
<Usage label>common
<Source>^Anastasilakis, et al. 2022^:1442
<Variant of>osteonecrosis of the jaw

<zh>颌骨坏死
<Morphosyntax>noun group
<Usage label>main term
<Source>^Goodman 2021^, https://www.msdmanuals.cn/professional/musculoskeletal-and-connective-tissue-disorders/osteonecrosis/medication-related-osteonecrosis-of-the-jaw-mronj
<Definition>颌骨坏死是口腔病变累及裸露的下颌骨或上颌骨。它可能会引起疼痛或可以是无症状的。
<Source>^Goodman 2021^, https://www.msdmanuals.cn/professional/musculoskeletal-and-connective-tissue-disorders/osteonecrosis/medication-related-osteonecrosis-of-the-jaw-mronj
<Context>ONJ 可自行发生，或在拔牙、外伤、大剂量静滴双膦酸盐治疗或大剂量地诺单抗 120mg（如癌症治疗）后引起。ONJ 可能是骨髓炎而不是真正的骨坏死，特别是显

影后使用双膦酸盐。骨外露存在至少 8 周可以做出诊断。治疗措施包括局部清创术，抗生素和口腔冲洗。

<Source>^Goodman 2021^, https://www.msdmanuals.cn/professional/musculoskeletal-and-connective-tissue-disorders/osteonecrosis/medication-related-osteonecrosis-of-the-jaw-mronj

<Concept field>不良事件

<Related words>^双膦酸盐类^

<Type of relation>super.

<Related words>^地舒单抗^

<Type of relation>super.

<Related words>^唑来膦酸^

<Type of relation>super.

<Synonyms>“ONJ”和“颌骨坏死”是近义词。

<zh>ONJ

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^Goodman 2021^, https://www.msdmanuals.cn/professional/musculoskeletal-and-connective-tissue-disorders/osteonecrosis/medication-related-osteonecrosis-of-the-jaw-mronj

<Variant of>颌骨坏死

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>zoledronic acid

<Morphosyntax>noun group

<Usage label>main term

<Source>^European Medicines Agency 2019^, https://www.ema.europa.eu/en/medicines/human/EPAR/zoledronic-acid-accord

<Lexica>Found in ^Oxford Concise Medical Dictionary 2020^

<Definition>Zoledronic Acid Accord is a medicine used to prevent bone complications in adults with advanced cancer that is affecting the bone.

<Source>^European Medicines Agency 2019^, https://www.ema.europa.eu/en/medicines/human/EPAR/zoledronic-acid-accord

<Context>The active substance in Zoledronic Acid Accord, zoledronic acid, is a bisphosphonate. It stops the action of the osteoclasts, the cells in the body that are involved in breaking down the bone tissue. This reduces bone loss. The reduction of bone loss helps to make bones less likely to break, which is useful in preventing fractures in cancer patients with bone metastases. Patients with tumours can have high levels of calcium in their blood, released from the bones. By preventing the breakdown of bones, Zoledronic Acid Accord also helps to reduce the amount of calcium released into the blood.

<Source>^European Medicines Agency 2019^, https://www.ema.europa.eu/en/medicines/human/EPAR/zoledronic-acid-accord

<Concept field>antiresorptive drugs

<Related words>^bisphosphonates^

<Type of relation>super.

<Related words>^denosumab^

<Type of relation>coord.

<Related words>^osteonecrosis of the jaw^

<Type of relation>sub.

<Synonyms>The term “zolendrate” is synonym to “zoledronic acid” but it not commonly used.

<en>zolendronate

<Morphosyntax>noun

<Usage label>uncommon

<Source>^Oxford Concise Medical Dictionary 2020^:837

<zh>唑来膦酸

<Morphosyntax>noun

<Source>^彭六保 2007^:237

<Definition>唑来膦酸是第 3 代二膦酸盐药物，能够抑制骨吸收，降低血钙水平。

<Source>^彭六保 2007^:237

<Context>唑来膦酸可用于治疗恶性高钙血症(15 min 静脉滴注 4 mg)，绝经后骨质疏松症(每年给药 1 次,15 min 静脉滴注 4 mg)，控制恶性肿瘤骨转移(每 3～4 wk 给药 1 次,15 min 静脉滴注 4 mg)，可显著降低骨相关事件(SREs)的发生率，推迟 SREs 的发生，缓解骨痛等症状。唑来膦酸高效且使用方便，不良反应少，耐受性好，有助于提高病人的生存质量。

<Source>^彭六保 2007^:237

<Concept field>抗骨化药物

<Related words>^双膦酸盐类^

<Type of relation>super.

<Related words>^地舒单抗^

<Type of relation>coord.

<Related words>^颌骨坏死^

<Type of relation>sub.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>vertebroplasty

<Morphosyntax>noun

<Usage label>main term

<Source>^Jay/Ahn 2013^:297

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Vertebroplasty (VP) is a minimally invasive image-guided procedure involving the injection of bone cement into a vertebral body fracture in an effort to improve pain and stability of the fracture.

<Source>^Jay/Ahn 2013^:297

<Context>The most common indication for VP is treatment of painful acute and subacute vertebral body compression fractures (VF) in patients who have failed to respond to a 4- to 6-week course of appropriate medical therapy. By far, the most common underlying aetiology of painful VF is osteoporosis. Other frequently encountered causes are metastatic disease, multiple myeloma, and painful aggressive haemangiomas. Allergy to PMMA or other bone cement products preclude VP. Relative contraindications include disruption of the posterior vertebral body wall or tumour extension into the spinal canal.

<Source>^Jay/Ahn 2013^:297-298

<Concept field>non-drug treatment

<Related words>^polymethylmethacrylate^

<Type of relation>sub.

<Related words>vertebral compression fractures

<Type of relation>general

<Related words>^epidural spinal cord compression^

<Type of relation>general

<Related words>^radiculopathy^

<Type of relation>sub.

<Related words>paraplegia

<Type of relation>sub.

<Synonyms>The term “vertebroplasty” is often substituted by its initials “VP”.

<en>VP

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^Jay/Ahn 2013^:297

<Variant of>vertebroplasty

<zh>椎体成形术

<Morphosyntax>noun group

<Usage label>main term

<Source>^赵必增，等 2001^

<Definition>椎体成形术(VP)，即通过椎弓根或直接向椎体内注人人工骨方法，以达到增疆椎体强度和稳定性、防止塌陷、缓解腰背疼痛，甚至部分饮复椎体高度的目的。

<Source>^赵必增，等 2001^

<Context>使用前配制骨水泥，要有足够的粘稠度，往骨水泥内掺人碗酸饮或钛粉或钨粉以利于术中透视。对多发椎体压缩骨折的，可先对较严重椎体施行椎体成形术，因为具体哪此或哪个椎休引起疼痛不清楚，故视疼痛缓解情况，必要时再行剩余椎体的手术。

<Source>^赵必增，等 2001^

<Concept field>非药物干预

<Related words>^聚甲基丙烯酸甲酯^

<Type of relation>sub.

<Related words>脊柱压缩性骨折

<Type of relation>general

<Related words>^恶性脊髓压迫症^

<Type of relation>general

<Related words>^神经根疾病^

<Type of relation>sub.

<Related words>截瘫

<Type of relation>sub.

<Synonyms>“VP”和“椎体成形术”是近义词。

<zh>VP

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^赵必增，等 2001^

<Variant of>椎体成形术

**

<Subject>化学和相关科学 / Chemistry and allied sciences (540)

<Subfield>无机化学/ Inorganic chemistry (546)

<en>polymethylmethacrylate

<Morphosyntax>noun

<Usage label>main term

<Source>^Ottenbrite/Javan 2005^:106

<Definition>Poly(methylmethacrylate) (PMMA) is an amorphous, transparent, and hydrophobic thermoplastic polymer that is very hard and stiff but brittle and notch sensitive.

<Source>^Ottenbrite/Javan 2005^:106

<Context>Methylmethacrylate (PMMA) is used extensively as a medical adhesive. It is used as bone cement to secure prostheses, such as hip replacements and dental crowns. In orthopaedic surgery, PMMA cement is injected into the collapsed vertebra to reconstruct back injuries. Although this procedure does not re-expend the collapsed vertebra, it seems to alleviate pain by reinforcing and stabilizing the fracture. PMMA is used extensively in maxillofacial augmentation to improve the skin contours and reduce depressions in the skin due to scars, injury, or lines.

<Source>^Ottenbrite/Javan 2005^:106

<Concept field>chemical compounds

<Related words>^vertebroplasty^

<Type of relation>super.

<Related words>vertebral compression fractures

<Type of relation>general

<Related words>^epidural spinal cord compression^

<Type of relation>general
<Related words>^radiculopathy^
<Type of relation>general
<Related words>paraplegia
<Type of relation>general
<Synonyms>The term “methyl methacrylate” is a synonym to “polymethylmethacrylate” and it is commonly used; furthermore, the term “polymethylmethacrylate” is often substituted by its initials “PMMA”.

<en>methylmethacrylate
<Morphosyntax>noun
<Usage label>common
<Source>^Ottenbrite/Javan 2005^:106

<en>PMMA
<Morphosyntax>noun
<Category>initials
<Usage label>common
<Source>^Ottenbrite/Javan 2005^:106
<Variant of>polymethylmethacrylate

<zh>聚甲基丙烯酸甲酯
<Morphosyntax>noun group
<Usage label>main term
<Source>^Sigma-Aldrich LLC^，https://www.sigmaaldrich.cn/CN/zh/product/aldrich/182230
<Definition>聚甲基丙烯酸甲酯（PMMA）是无定形、透明的热塑性聚合物。
<Source>^Sigma-Aldrich LLC^，https://www.sigmaaldrich.cn/CN/zh/product/aldrich/182230
<Context>PMMA 的折射率为 1.49，因而被认为是光学聚合物。因此，它被用于光纤。由于其较低的吸水能力和生物相容性，它在生物应用中得到应用。PMMA/HA（羟基磷灰石）复合材料已经用于生物医学应用，例如牙科、矫形保持器和骨替代物。
<Source>^Sigma-Aldrich LLC^，https://www.sigmaaldrich.cn/CN/zh/product/aldrich/182230
<Concept field>化合物
<Related words>^椎体成形术^
<Type of relation>super.

<Related words>脊柱压缩性骨折

<Type of relation>general

<Related words>^恶性脊髓压迫症^

<Type of relation>general

<Related words>^神经根疾病^

<Type of relation>general

<Related words>截瘫

<Type of relation>general

<Synonyms>“PMMA”和“聚甲基丙烯酸甲酯”是近义词。

<zh>PMMA

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^Sigma-Aldrich LLC^，https://www.sigmaaldrich.cn/CN/zh/product/aldrich/182230

<Variant of>聚甲基丙烯酸甲酯

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>NDSAID

<Morphosyntax>noun group

<Usage label>main term

<Source>^Ghlichloo/Gerriets 2022^, https://www.ncbi.nlm.nih.gov/books/NBK547742/

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>NSAIDs (Nonsteroidal anti-inflammatory drugs) are a drug class FDA-approved for use as antipyretic, anti-inflammatory, and analgesic agents.

<Source>^Ghlichloo/Gerriets 2022^, https://www.ncbi.nlm.nih.gov/books/NBK547742/

<Context>NSAIDs are typically divided into groups based on their chemical structure and selectivity. The main mechanism of action of NSAIDs is the inhibition of the enzyme cyclooxygenase (COX). There are two cyclooxygenase isoenzymes, COX-1 and COX-2. Most of the NSAIDs are nonselective and inhibit both COX-1 and COX-2. NSAIDs have well-known adverse effects affecting the gastric mucosa, renal system, cardiovascular system, hepatic system, and hematologic system.

<Source>^Ghlichloo/Gerriets 2022^, https://www.ncbi.nlm.nih.gov/books/NBK547742/

<Concept field>analgesics

<Related words>^paracetamol^

<Type of relation>sub.

<Related words>^opioids^

<Type of relation>coord.

<Related words>renal impairment

<Type of relation>general

<Synonyms>The acronym “NSAID” can be substituted by its full form “non-steroidal anti-inflammatory drugs”.

<en>non-steroidal anti-inflammatory drugs

<Morphosyntax>noun group

<Category>full form

<Usage label>common

<Source>^Ghlichloo/Gerriets 2022^, https://www.ncbi.nlm.nih.gov/books/NBK547742/

<Variant of>NSAID

<zh>解热镇痛抗炎药

<Morphosyntax>noun group

<Usage label>main term

<Source>^赵冰 2014^:8

<Definition>解热镇痛抗炎药是一类具有解热、止痛、多数还有抗炎、抗风湿作用的药物。由于化学结构及抗炎机制与糖皮质激素(甾体类抗炎药)不同，故又称为非甾体抗炎药(NSAIDs)。

<Source>^赵冰 2014^:8

<Context>NSAIDs 的作用机理主要是通过抑制环加氧酶(COX)而抑制前列腺素(PGs)的合成，缓解或消除 PGs(特别是 PGE2)的致痛、致热和致炎作用。阿司匹林是本类药物的代表，故此类药物也称为“阿司匹林类药物”。

<Source>^赵冰 2014^:9

<Concept field>镇痛药

<Related words>^对乙酰氨基酚^

<Type of relation>sub.

<Related words>^阿片类药物^

<Type of relation>coord.

<Related words>肾功能损伤

<Type of relation>general

<Synonyms>“NSAID”和“解热镇痛抗炎药”是近义词。

<zh>NSAID

<Morphosyntax>noun

<Category>acronym

<Usage label>common

<Source>^赵冰 2014^:8

<Variant of>解热镇痛抗炎药

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>paracetamol

<Morphosyntax>noun

<Usage label>main term

<Source>^Jóźwiak-Bebenista/Nowak 2014^:11

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Paracetamol/acetaminophen is one of the most popular and most commonly used analgesic and antipyretic drugs around the world, available without a prescription, both in mono- and multi-component preparations.

<Source>^Jóźwiak-Bebenista/Nowak 2014^:11

<Context>Paracetamol is the drug of choice in patients that cannot be treated with non-steroidal anti-inflammatory drugs (NSAID), such as people with bronchial asthma, peptic ulcer disease, haemophilia, salicylate-sensitized people, children under 12 years of age, pregnant or breastfeeding women. It is recommended as a first-line treatment of pain associated with osteoarthritis. The mechanism of action is complex and includes the effects of both the peripheral (COX inhibition), and central (COX, serotonergic descending neuronal pathway, L-arginine/NO pathway, cannabinoid system) antinociception processes. Paracetamol is well tolerated drug and produces few side effects from the gastrointestinal tract, however, despite that, every year, has seen a steadily increasing number of registered cases of paracetamol-induced liver intoxication all over the world.

<Source>^Jóźwiak-Bebenista/Nowak 2014^:11

<Concept field>analgesics

<Related words>^NSAIDs^

<Type of relation>super

<Related words>^opioids^

<Type of relation>general.

<Related words>renal impairment

<Type of relation>general

<Synonyms>The term “acetaminophen” is synonym to “paracetamol”, but it is not frequently used.

<en>acetaminophen

<Morphosyntax>noun

<Usage label>uncommon

<Source>^Merriam/Webster 2016^:567

<zh>对乙酰氨基酚

<Morphosyntax>noun group

<Source>^中国人民共和国中央人民政府 2008^，http://www.gov.cn/govweb/fwxx/jk/2008-12/03/content_1166929.htm

<Definition>对乙酰氨基酚是一种解热镇痛常用药，经常配伍用于普通感冒、关节痛、神经痛等疾病的对症治疗。

<Source>^中国人民共和国中央人民政府 2008^，http://www.gov.cn/govweb/fwxx/jk/2008-12/03/content_1166929.htm

<Context>对乙酰氨基酚用于疼痛、发热的对症治疗，并不能控制病情发展，且每日用药量不宜过大，用药时间不宜过长，症状控制后应及时停药。长期大剂量使用对乙酰氨基酚可致肾疾病，包括肾乳头坏死性肾衰竭，尤其是肾功能低下者，可出现肾绞痛或急性肾衰（少尿，尿毒症）。因此，肾功能不全患者长期应用，有增加肾脏毒性的危险。

<Source>^中国人民共和国中央人民政府 2008^，http://www.gov.cn/govweb/fwxx/jk/2008-12/03/content_1166929.htm

<Concept field>镇痛药

<Related words>^解热镇痛抗炎药^

<Type of relation>super.

<Related words>^阿片类药物^

<Type of relation>general

<Related words>肾功能损伤

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>opioids

<Morphosyntax>noun

<Usage label>main term

<Source>^National Institute of Diabetes and Digestive and Kidney Diseases 2020^, https://www.ncbi.nlm.nih.gov/books/NBK547864/

<Lexica>Found in ^Merriam/Webster 2016^

<Definition>The opioids are a large class of medications related in structure to the natural plant alkaloids found in opium that are derived from the resin of the opium poppy, Papaver somniferous.

<Source>^National Institute of Diabetes and Digestive and Kidney Diseases 2020^, https://www.ncbi.nlm.nih.gov/books/NBK547864/

<Context>The natural alkaloids are also referred to as opiates and include morphine and codeine. Synthetic derivatives include heroin, fentanyl, hydromorphone, methadone, buprenorphine and others. The opioids have a variety of clinical effects but are predominantly known and used for their profound pain-relieving effects. However, the distinctive feature of the analgesia induced by the opioids is the lack of loss of consciousness. The pain is often described as less intense, but still present although better tolerated. Thus, the opioids do not decrease or treat the cause of the painful stimulus, but rather decrease its perception. Most opioids have similar effects and side effects, although pharmacokinetic differences, tissue distribution, and receptor type specificity probably account for the variation in effects of the various synthetic and semisynthetic derivatives of morphine. Morphine is considered the prototype opiate, against which other agents are measured for their analgesic effects as well as adverse side effects.

<Source>^National Institute of Diabetes and Digestive and Kidney Diseases 2020^, https://www.ncbi.nlm.nih.gov/books/NBK547864/

<Concept field>analgesics

<Related words>^NSAIDs^

<Type of relation>coord.

<Related words>^buprenorphine^

<Type of relation>sub.

<Related words>^fentanyl^

<Type of relation>sub.

<Related words>^morphine^

<Type of relation>sub.

<Related words>^oxycodone^

<Type of relation>sub.

<Related words>^hydromorphone^

<Type of relation>sub

<zh>阿片类药物

<Morphosyntax>noun group

<Source>^Krieger 2021^, https://www.mayoclinic.org/zh-hans/diseases-conditions/prescription-drug-abuse/expert-answers/what-are-opioids/faq-20381270

<Definition>阿片类药物是一类止痛药的总称，通过与细胞内的阿片受体相互作用来缓解疼痛。

<Source>^Krieger 2021^, https://www.mayoclinic.org/zh-hans/diseases-conditions/prescription-drug-abuse/expert-answers/what-are-opioids/faq-20381270

<Context>阿片类药物可以由罂粟植物制成，例如吗啡（Kadian、Ms Contin 等），也可以在实验室合成，例如芬太尼（Actiq、Duragesic 等）。当阿片类药物通过血液传播并附着于脑细胞中的阿片受体时，脑细胞会释放信号，抑制对疼痛的感知，增强愉悦感。

<Source>^Krieger 2021^, https://www.mayoclinic.org/zh-hans/diseases-conditions/prescription-drug-abuse/expert-answers/what-are-opioids/faq-20381270

<Concept field>镇痛药

<Related words>^解热镇痛抗炎药^

<Type of relation>coord.

<Related words>^丁丙诺啡^

<Type of relation>sub.

<Related words>^芬太尼^

<Type of relation>sub.

<Related words>^吗啡^

<Type of relation>sub.

<Related words>^羟考酮^

<Type of relation>sub.

<Related words>^氢吗啡酮^

<Type of relation>sub

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>buprenorphine

<Morphosyntax>noun

<Source>^Evans/Easthope 2003^:2001

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Buprenorphine is a synthetic opioid which is lipophilic, water soluble and has a low molecular weight; these properties allow for tissue penetration and make it suitable for transdermal delivery.

<Source>^Evans/Easthope 2003^:2001

<Context>Buprenorphine is a partial agonist at μ opioid receptors and an antagonist at κ receptors and binds to both receptors with high affinity. Effects on analgesia appear to occur as a result of μ-agonist activity. Binding to and dissociation from the μ-receptor is slow; therefore, the effects of buprenorphine are slow in onset and long in duration. Buprenorphine produces dose-related analgesia and is about 25–50 times more potent than an equivalent dose (by weight) of morphine.

<Source>^Evans/Easthope 2003^:2001

<Concept field>analgesics

<Related words>^NSAIDs^

<Type of relation>general

<Related words>^opioids^

<Type of relation>super.

<Related words>^fentanyl^

<Type of relation>coord.

<Related words>^morphine^

<Type of relation>coord.

<Related words>^oxycodone^

<Type of relation>coord.

<Related words>^hydromorphone^

<Type of relation>coord.

<zh>丁丙诺啡

<Morphosyntax>noun

<Usage label>main term

<Source>^储靖，陈宁 2009^:271

<Definition>丁丙诺啡，又称盐酸丁丙诺啡，属于阿片受体激动一拮抗药，主要激动μ受体，对δ受体也有一定的激动作用，而对κ受体则有不同程度的拮抗作用。

<Source>^储靖，陈宁 2009^:271

<Context>丁丙诺啡对 μ 受体有很大亲和力，并缓慢释放。镇痛作用强且持久。它能有效减轻术中及术后疼痛与各种急慢性疼痛，成瘾性很低，同时对阿片成瘾治疗有效。用药后，血浆药物峰值浓度在静脉注射后 30 min 出现，半衰期约 3 h，血浆蛋白结合率约为96%。经静脉注射常用剂量为0.15一O.3 mg。不良反应少，主要表现有嗜睡、头晕、恶心和(或)呕吐。

<Source>^储靖，陈宁 2009^:271

<Concept field>镇痛药

<Related words>^解热镇痛抗炎药^

<Type of relation>general

<Related words>^阿片类药物^

<Type of relation>super.

<Related words>^芬太尼^

<Type of relation>coord.

<Related words>^吗啡^

<Type of relation>coord.

<Related words>^羟考酮^

<Type of relation>coord.

<Related words>^氢吗啡酮^

<Type of relation>coord.

<Synonyms>“盐酸丁丙诺啡”和“丁丙诺啡”是近义词。

<zh>盐酸丁丙诺啡

<Morphosyntax>noun group

<Usage label>common

<Source>^储靖，陈宁 2009^:271

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>fentanyl

<Morphosyntax>noun

<Source>^Poklis 1995^:439

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Fentanyl [N-(1-phenethyl-4-piperidyl) propionanilide] is a synthetic narcotic analgesic of high potency and a short duration of action.

<Source>^Poklis 1995^:439

<Context>Fentanyl is available for intravenous injection, as a transdermal patch and a lozenge dosage form. The drug is 80 times more potent than morphine. The incidence of incomplete amnesia, hypotension or hypertension are less than that associated with morphine and the duration of respiratory depression is shorter. For these reasons, it is the primary analgesic in surgical procedures performed in the US. It is indicated as a preanesthetic medication, a primary anaesthetic and a postsurgical anaesthetic. It is a popular drug of abuse among health care professionals. Diversion of pharmaceutical fentanyl preparations, as well as the availability of illicitly synthesized potent and highly toxic fentanyl analogues have resulted in numerous overdose deaths.

<Source>^Poklis 1995^:439

<Concept field>analgesics

<Related words>^NSAIDs^

<Type of relation>general

<Related words>^opioids^

<Type of relation>super.

<Related words>^buprenorphine^

<Type of relation>coord.

<Related words>^morphine^

<Type of relation>coord.

<Related words>^oxycodone^

<Type of relation>coord.

<Related words>^hydromorphone^

<Type of relation>coord.

<zh>芬太尼

<Morphosyntax>noun

<Source>^ 圣 裘 德 儿 童 研 究 医 院 2023^， https://together.stjude.org/zh-cn/diagnosis-treatment/%E8%8D%AF%E7%89%A9%E6%B8%85%E5%8D%95/%E8%8A%AC%E5%A4%AA%E5%B0%BC.html

<Definition>芬太尼是一种用于控制疼痛的阿片类药物。

<Source>^ 圣 裘 德 儿 童 研 究 医 院 2023^， https://together.stjude.org/zh-cn/diagnosis-treatment/%E8%8D%AF%E7%89%A9%E6%B8%85%E5%8D%95/%E8%8A%AC%E5%A4%AA%E5%B0%BC.html

<Context>芬太尼具有不同的剂型和规格。对于在服用其他止痛药时仍有疼痛感的患者，可使用这种药物来缓解严重或持续疼痛。芬太尼还可以在手术期间用于控制疼痛。速效剂型包括舌下含服片剂和喷雾剂、口服锭剂、口腔片剂、可溶膜剂和鼻喷雾剂。芬太尼也可以通过皮肤贴片给药。皮肤贴片会以更慢的速度持续释放药物，可用于更慢性或持续性的疼痛。

<Source>^ 圣 裘 德 儿 童 研 究 医 院 2023^， https://together.stjude.org/zh-cn/diagnosis-treatment/%E8%8D%AF%E7%89%A9%E6%B8%85%E5%8D%95/%E8%8A%AC%E5%A4%AA%E5%B0%BC.html

<Concept field>镇痛药

<Related words>^解热镇痛抗炎药^

<Type of relation>general

<Related words>^阿片类药物^

<Type of relation>super.

<Related words>^丁丙诺啡^

<Type of relation>coord.

<Related words>^吗啡^

<Type of relation>coord.

<Related words>^羟考酮^

<Type of relation>coord.

<Related words>^氢吗啡酮^

<Type of relation>coord.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>morphine

<Morphosyntax>noun

<Source>^Christrup 1997^:116

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition 1>Morphine is the most important and widely used strong opioid analgesic compound presently available for the treatment of chronic severe pain.

<Definition 2>Morphine is a naturally occurring alkaloid present in the poppy plant Pupuver somniferurn.

<Source>^Christrup 1997^:116

<Context>Morphine is a member of the morphinan-framed alkaloids, which are present in the poppy plant. The drug is soluble in water, but its solubility in lipids is poor. In man, morphine-3-glucuronide (M3G) and morphine-6-glumronide (M6G) are the major metabolites of morphine. The metabolism of morphine occurs not only in the liver but may also take place in the brain and the kidneys.

<Source>^Christrup 1997^:116

<Concept field>analgesics

<Related words>^NSAIDs^

<Type of relation>general

<Related words>^opioids^

<Type of relation>super.

<Related words>^buprenorphine^

<Type of relation>coord.

<Related words>^fentanyl^

<Type of relation>coord.

<Related words>^oxycodone^

<Type of relation>coord.

<Related words>^hydromorphone^

<Type of relation>coord.

<zh>吗啡

<Morphosyntax>noun

<Source>^葉名倉 2010^，https://highscope.ch.ntu.edu.tw/wordpress/?p=9253

<Definition>吗啡是天然的鸦片剂或麻醉剂，可当心理和精神上具高效能的镇静、止痛、麻醉的药物，在临床医学上，吗啡被视为解除难以忍受之痛苦、疼痛的基本药物。

<Source>^葉名倉 2010^，https://highscope.ch.ntu.edu.tw/wordpress/?p=9253

<Context>吗啡的止痛功能是直接作用在中枢神经系统上，对于药物成瘾有极高的潜在力且耐药性会在身理心理迅速产生依赖性。

<Source>^葉名倉 2010^，https://highscope.ch.ntu.edu.tw/wordpress/?p=9253

<Concept field>镇痛药

<Related words>^解热镇痛抗炎药^

<Type of relation>general

<Related words>^阿片类药物^

<Type of relation>super.

<Related words>^丁丙诺啡^

<Type of relation>coord.

<Related words>^芬太尼^

<Type of relation>coord.

<Related words>^羟考酮^

<Type of relation>coord.

<Related words>^氢吗啡酮^

<Type of relation>coord.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>oxycodone

<Morphosyntax>noun

<Source>^Sadiq, et al. 2022^, https://www.ncbi.nlm.nih.gov/books/NBK482226/

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Oxycodone is a semisynthetic opioid with agonistic properties on mu, kappa, and delta-type opioid receptors, with the strongest affinity being for mu-type receptors.

<Source>^Sadiq, et al. 2022^, https://www.ncbi.nlm.nih.gov/books/NBK482226/

<Context>Oxycodone is an opioid agonist prescription medication. The oxycodone immediate-release formulation is FDA-approved for the management of acute or chronic moderate to severe pain, for which other treatments do not suffice, and for which the use of opioid medication is appropriate. The extended-release formulation is FDA-approved for the management of pain severe enough to require continuous (24 hours per day) long-term opioid treatment and for which there are no alternative options to treat the pain. The oxycodone to morphine dose equivalent ratio is approximately 1 to 1.5 for immediate-release and 1 to 2 for extended-release

formulations. As with other opioids, oxycodone causes hyperpolarization and reduced excitability of neurons in the central nervous system (CNS).

<Source>^Sadiq, et al. 2022^, https://www.ncbi.nlm.nih.gov/books/NBK482226/

<Concept field>analgesics

<Related words>^NSAIDs^

<Type of relation>general

<Related words>^opioids^

<Type of relation>super.

<Related words>^buprenorphine^

<Type of relation>coord.

<Related words>^fentanyl^

<Type of relation>coord.

<Related words>^morphine^

<Type of relation>coord.

<Related words>^hydromorphone^

<Type of relation>coord.

<zh>羟考酮

<Morphosyntax>noun

<Source>^张杜枭，等 2014^:527

<Definition>羟考酮是由蒂巴因改造合成的阿片类中枢神经镇痛药。

<Source>^张杜枭，等 2014^:527

<Context>羟考酮能产生强烈的快感、镇痛和镇静作用，并具有类似吗啡的依赖性。临床上用于缓解中度至重度疼痛，但也被非法使用，特别是作为奥施康定销售的长效药物。羟考酮的半衰期在 3.5 至 5.5 小时之间，但其主要代谢物去甲羟考酮和羟吗啉酮可在尿液中检测到 2-4 天。

<Source>^Meridian Bioscience^, https://www.meridianbioscience.com/cn/lifescience/products/antibodies-antigens/doa/oxycodone/

<Concept field>镇痛药

<Related words>^解热镇痛抗炎药^

<Type of relation>general

<Related words>^阿片类药物^

<Type of relation>super.

<Related words>^丁丙诺啡^

<Type of relation>coord.

<Related words>^芬太尼^

<Type of relation>coord.

<Related words>^吗啡^

<Type of relation>coord.

<Related words>^氢吗啡酮^

<Type of relation>coord.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>hydromorphone

<Morphosyntax>noun

<Usage label>main term

<Source>^Murray/Hagen 2005^:57

<Lexica>Found in ^Merriam/Webster 2016^

<Definition>Hydromorphone is a semi-synthetic opioid that has been used widely for acute pain, chronic cancer pain and to a lesser extent, in chronic non-malignant pain.

<Source>^Murray/Hagen 2005^:57

<Context>Hydromorphone is structurally very similar to morphine; it differs from morphine by the presence of a 6-keto group and the hydrogenation of the double bond at the 7-8 position of the molecule. Hydromorphone is available in the following oral preparations: powder, solution, immediate- release tablet, and modified-release tablet. Hydromorphone can be administered parenterally by intravenous, intramuscular, and sub-cutaneous routes. Hydromorphone can be given via the epidural route. Hydromorphone appears to have similar analgesic properties to morphine and a similar side effect profile.

<Source>^Murray/Hagen 2005^:58

<Concept field>analgesics

<Related words>^NSAIDs^

<Type of relation>general

<Related words>^opioids^

<Type of relation>super.

<Related words>^buprenorphine^

<Type of relation>coord.

<Related words>^fentanyl^

<Type of relation>coord.

<Related words>^morphine^

<Type of relation>coord.

<Related words>^oxycodone^

<Type of relation>coord.

<Synonyms>The term “dihydromorphinone” is synonym to “hydromorphone”, but it is not frequently used.

<en>dihydromorphinone

<Morphosyntax>noun

<Usage label>uncommon

<Source>^Merriam/Webster 2016^:349

<zh>氢吗啡酮

<Morphosyntax>noun

<Source>^简文亭，等 2014^:1204

<Definition>氢吗啡酮是一种半合成的阿片类镇痛药，主要作用于阿片μ受体，并在较小程度上作用于δ受体。

<Source>^简文亭，等 2014^:1204

<Context>氢吗啡酮镇痛作用是吗啡的 5~8 倍，起效快，主要代谢产物无活性，不良反应少于吗啡，适合用于急慢性疼痛以及癌症疼痛的治疗，临床应用安全有效。氢吗啡酮剂型较多，可通过肌内注射、静脉注射、口服、皮下注射、硬膜外注射等方式给药。氢吗啡酮适用于缓解各种原因引起的中强度疼痛，如围手术期中、重度疼痛的镇痛，急性疼痛，慢性疼痛，肿瘤疼痛,临终宽慰治疗等，有时用于镇咳和镇静。

<Source>^简文亭，等 2014^:1204

<Concept field>镇痛药

<Related words>^解热镇痛抗炎药^

<Type of relation>general

<Related words>^阿片类药物^

<Type of relation>super.

<Related words>^丁丙诺啡^

<Type of relation>coord.

<Related words>^芬太尼^

<Type of relation>coord.

<Related words>^吗啡^

<Type of relation>coord.

<Related words>^羟考酮^

<Type of relation>coord.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>histone deacetylase

<Morphosyntax>noun group

<Usage label>main term

<Source>^Seto/Yoshida 2014^:1

<Definition>Histone deacetylases (HDACs) are enzymes that catalyse the removal of acetyl functional groups from the lysine residues of both histone and nonhistone proteins.

<Source>^Seto/Yoshida 2014^:1

<Context>In humans, there are 18 HDAC enzymes that use either zinc- or NAD+-dependent mechanisms to deacetylate acetyl lysine substrates. Although removal of histone acetyl epigenetic modification by HDACs regulates chromatin structure and transcription, deacetylation of nonhistone controls diverse cellular processes. HDAC inhibitors are already known potential anticancer agents and show promise for the treatment of many diseases.

<Source>^Seto/Yoshida 2014^:1

<Concept field>cytology

<Related words>^histone deacetylase inhibitor^

<Type of relation>coord.

<Related words>^histone acetylation^

<Type of relation>super.

<Related words>^chromatin^

<Type of relation>sub.

<Related words>^panobinostat^

<Type of relation>coord.

<Related words>^aggresome^

<Type of relation>general

<Synonyms>The term “histone deacetylase” is often substituted by its initials “HDAC”.

<en>HDAC

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^Seto/Yoshida 2014^:1

<Variant of>histone deacetylase

<zh>组蛋白去乙酰化酶

<Morphosyntax>noun group

<Usage label>main term

<Source>^李丹丹，等 2019^:37

<Definition>组蛋白去乙酰化酶是一类调节组蛋白和非组蛋白赖氨酸残基去乙酰化的酶，与转录调控、细胞周期、蛋白转运和血管发生等密切相关。

<Source>^李丹丹，等 2019^:37

<Context>HDACs 作为一种重要的翻译后修饰酶，能将核小体核心组蛋白氨基末端的赖氨酸残基中的乙酰基去除，使得染色体发生凝聚，从而阻止转录激活子进入其靶位点，导致转录抑制。HDACs 还可通过作用于一些非组蛋白，如转录因子、结构蛋白、蛋白激酶等，从而影响基因的表达。

<Source>^李丹丹，等 2019^:37

<Concept field>细胞学

<Related words>^组蛋白去乙酰化酶抑制剂^

<Type of relation>coord.

<Related words>^组蛋白赖氨酸乙酰化^

<Type of relation>super.

<Related words>^染色质^

<Type of relation>sub.

<Related words>^帕比司他^

<Type of relation>coord.

<Related words>^蛋白质沉淀聚集体^

<Type of relation>general

<Synonyms>“HDAC”和“组蛋白去乙酰化酶”是近义词。

<zh>HDAC

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^李丹丹，等 2019^:37

<Variant of>组蛋白去乙酰化酶

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>histone deacetylase inhibitor

<Morphosyntax>noun group

<Usage label>main term

<Source>^Kim/Bae 2011^:166

<Definition>Histone deacetylase (HDAC) inhibitors are a relatively new class of anti-cancer agents that play important roles in epigenetic or non-epigenetic regulation, inducing death, apoptosis, and cell cycle arrest in cancer cells.

<Source>^Kim/Bae 2011^:166

<Context>A large number of HDAC inhibitors have been purified from natural sources or have been synthesized. HDAC inhibitors can be structurally grouped into at least four classes: hydroxamates, cyclic peptides, aliphatic acids and benzamides. HDAC inhibitors are well tolerated and clinically effective against hematologic cancers, even though they have poor anti-cancer activity against solid tumours when used as a monotherapy.

<Source>^Kim/Bae 2011^:167-168

<Concept field>new drugs

<Related words>^histone deacetylase^

<Type of relation>coord.

<Related words>^histone acetylation^

<Type of relation>super.

<Related words>^chromatin^

<Type of relation>sub.

<Related words>^panobinostat^

<Type of relation>sub.

<Related words>^aggresome^

<Type of relation>general

<Synonyms>The term “HDAC inhibitor” is synonym to “histone deacetylase inhibitor” and it is commonly used.

<en>HDAC inhibitor
<Morphosyntax>noun group
<Usage label>common
<Source>^Kim/Bae 2011^:167

<zh>组蛋白去乙酰化酶抑制剂
<Morphosyntax>noun group
<Usage label>main term
<Source>^方晨，等 2021^:204
<Definition>组蛋白去乙酰化酶抑制剂（HDACi）作为一类表观遗传调控药物，在调控细胞周期、增殖分化及活性中发挥重要作用。
<Source>^方晨，等 2021^:204
<Context>近年来，研究发现 HDACi 不仅能够调节细胞生物学特征，还与肿瘤 ICIs 耐药的改善密切相关。因此，HDACi 提高 ICIs 疗效的相关机制研究对肿瘤免疫治疗具有重要意义。
<Source>^方晨，等 2021^:204
<Concept field>新药
<Related words>^组蛋白去乙酰化酶^
<Type of relation>coord.
<Related words>^组蛋白赖氨酸乙酰化^
<Type of relation>super.
<Related words>^染色质^
<Type of relation>sub.
<Related words>^帕比司他^
<Type of relation>sub.
<Related words>^蛋白质沉淀聚集体^
<Type of relation>general
<Synonyms>“HDACi”和“组蛋白去乙酰化酶抑制剂”是近义词。

<zh>HDACi

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^方晨，等 2021^:204

<Variant of>组蛋白去乙酰化酶抑制剂

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>人体生理学 / Human physiology (612)

<en>histone acetylation

<Morphosyntax>noun group

<Usage label>main term

<Source>^Schwarzer 2008^:592

<Definition>Histone acetylation is a reversible and covalent modification of histone proteins introduced at the ε-amino groups of lysine residues.

<Source>^Schwarzer 2008^:592

<Context>The precise balance of the acetylated and deacetylated state of histones is an important feature of gene regulation. Imbalances can be found in many human cancers and often result from alterations in HDAC and HAT activities. In this context overexpression or aberrant recruitment of HDACs by oncoproteins are common in human cancers, as well as mutations in HAT encoding genes.

<Source>^Schwarzer 2008^:594

<Concept field>epigenetic mechanism

<Related words>^histone deacetylase^

<Type of relation>sub.

<Related words>^histone deacetylase inhibitor^

<Type of relation>sub.

<Related words>^chromatin^

<Type of relation>sub.

<Related words>^panobinostat^

<Type of relation>general

<Related words>^aggresome^

<Type of relation>general

<Synonyms>The term “lysine acetylation of histones” is synonym to “histone acetylation” but it is not commonly used to identify the epigenetic process.

<en>lysine acetylation of histones

<Morphosyntax>noun group

<Usage label>uncommon

<Source>^Schwarzer 2008^:592

<zh>组蛋白赖氨酸乙酰化

<Morphosyntax>noun group

<Source>^曹端方，杨娜 2015^:978

<Definition>组蛋白赖氨酸乙酰化是一种组蛋白翻译后修饰，在染色质重塑和基因表达调控等方面发挥重要作用，这种修饰在体内受到组蛋白乙酰化酶和去乙酰化酶的高度动态调控。

<Source>^曹端方，杨娜 2015^:978

<Context>组蛋白翻译后修饰(PTMs)主要包括乙酰化、甲基化、磷酸化、泛素化、SUMO 化和 ADP 核糖基化修饰等。其中发生在赖氨酸侧链着氨基上的组蛋白乙酰化修饰是最早被发现的组蛋白翻译后修饰之一，四膜虫 GCN5 和人源 Rpd3 是最早被鉴定的组蛋白乙酰化酶和去乙酰化酶。很早以来，人们就认识到组蛋白乙酰化修饰与染色质结构和基因转录调控密切相关。组蛋白乙酰化修饰呈特异性的高度动态变化，它的调控是由组蛋白乙酰化转移酶(HAT)和组蛋白去乙酰化酶(HDAC)共同实现的。

<Source>^曹端方，杨娜 2015^:978

<Concept field>表观遗传机制

<Related words>^组蛋白去乙酰化酶^

<Type of relation>sub.

<Related words>^组蛋白去乙酰化酶抑制剂^

<Type of relation>sub.

<Related words>^染色质^

<Type of relation>sub.

<Related words>^帕比司他^

<Type of relation>general

<Related words>^蛋白质沉淀聚集体^

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>chromatin

<Morphosyntax>noun

<Usage label>main term

<Source>^Gross, et al. 2015^:1158

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Chromatin is a complex of proteins, RNA and DNA that constitutes the physiological state of the genome.

<Source>^Gross, et al. 2015^:1158

<Context>Its basic structure is essentially the same in nearly all eukaryotes, from single-celled yeasts to the most complex multicellular organisms (exceptions include the chromatin of dinoflagellates and vertebrate sperm). Its fundamental role is to package the genome in a sufficiently compact form that allows comparatively very large molecules of DNA to fit inside the cell's nucleus.

<Source>^Gross, et al. 2015^:1158

<Concept field>cytology

<Related words>^histone deacetylase^

<Type of relation>super.

<Related words>^histone deacetylase inhibitor^

<Type of relation>super.

<Related words>^histone acetylation^

<Type of relation>super.

<Related words>^panobinostat^

<Type of relation>general

<Related words>^aggresome^

<Type of relation>general

<zh>染色质

<Morphosyntax>noun

<Source>^朱婷婷 2016^

<Definition 1>染色质本质是 DNA 分子缠绕在组蛋白八聚体，并压缩到一个特定的程度。

<Definition 2>染色质是一个动态结构，负责组织基因组信息并且综合外部和内部信号，并最终确定在不同细胞类型，不同的发育时间节点，响应于不同的刺激时，哪些基因被表达，哪些不表达。

<Source>^朱婷婷 2016^

<Context>关于染色质，其广义的定义还包括其他染色质相关蛋白。染色质结构的高度压缩形式、异染色质、松散压缩形式都被称作常染色质。该结构是动态的；染色质结构的改变可以影响细胞核中 DNA 参与的进程：如转录、复制、修复和重组。染色质表观遗传变化可由以下情况引起：非正常组蛋白（组蛋白变体）的添加，ATP 依赖的染色质重塑导致的染色质结构改变，组蛋白尾部化学标记的添加（组蛋白修饰）和 DNA 碱基上甲基基团的添加（DNA 甲基化)。

<Source>^朱婷婷 2016^

<Concept field>细胞学

<Related words>^组蛋白去乙酰化酶^

<Type of relation>super.

<Related words>^组蛋白去乙酰化酶抑制剂^

<Type of relation>super.

<Related words>^组蛋白赖氨酸乙酰化^

<Type of relation>super.

<Related words>^帕比司他^

<Type of relation>general

<Related words>^蛋白质沉淀聚集体^

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>panobinostat

<Morphosyntax>noun

<Source>^Sivaraj, et al. 2017^:477

<Definition>Panobinostat is a pan-deacetylase inhibitor that impedes protein destruction by disturbing the enzymatic activity of deacetylases

<Source>^Sivaraj, et al. 2017^:477

<Context>Panobinostat is rapidly absorbed after oral administration and is extensively metabolized. Panobinostat was shown to influence multiple pathways that are essential to the biology of MM in several nonclinical studies. Panobinostat acts synergistically with bortezomib, and this has been shown via in vitro as well as in vivo models. Alterations in protein degradation pathways.

<Source>cf.^Sivaraj, et al. 2017^:479

<Concept field>new drugs

<Related words>^histone deacetylase^

<Type of relation>general

<Related words>^histone deacetylase inhibitor^

<Type of relation>super.

<Related words>^histone acetylation^

<Type of relation>general

<Related words>^chromatin^

<Type of relation>general

<Related words>^aggresome^

<Type of relation>sub.

<Related words>^antiemetics^

<Type of relation>general

<Related words>^angina pectoris^

<Type of relation>general

<zh>帕比司他

<Morphosyntax>noun

<Usage label>main term

<Source>^孙琦/高大 2021^:5147

<Definition>帕比司他(Panobinostat)是一种组蛋白脱乙酰酶(HDAC)抑制剂，HDAC 活性的抑制导致组蛋白的乙酰化增加，导致染色体松弛的表观遗传学改变，导致转录激活，诱导一些转化细胞的细胞周期停滞或细胞凋亡，而不影响健康细胞。

<Source>^孙琦/高大 2021^:5147

<Context>帕比司他 20 mg 联合硼替佐米、沙利度胺和地塞米松治疗复发性多发性骨髓瘤是一种有效且耐受性良好的方案。Panobinostat 加硼替佐米和地塞米松(PAN-BTZ-Dex)导致在 3 期 PANORAMA 1 试验中复发或复发且难治性多发性骨髓瘤患者的无进展生存期(PFS)显著高于安慰剂加硼替佐米和地塞米松。

<Source>^孙琦/高大 2021^:5147

<Concept field>新药

<Related words>^组蛋白去乙酰化酶^

<Type of relation>general

<Related words>^组蛋白去乙酰化酶抑制剂^

<Type of relation>super.

<Related words>^组蛋白赖氨酸乙酰化^

<Type of relation>general

<Related words>^染色质^

<Type of relation>general

<Related words>^蛋白质沉淀聚集体^

<Type of relation>sub.

<Related words>^止吐药^

<Type of relation>general

<Related words>^心绞痛^

<Type of relation>general

<Synonyms>“panobinostat”和“帕比司他”是近义词。

<zh>panobinostat

<Morphosyntax>noun

<Category>translation

<Usage label>common

<Source>^孙琦/高大 2021^:5147

<Variant of>帕比司他

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>aggresome

<Morphosyntax>noun

<Usage label>main term

<Source>^Corboy, et al. 2005^:305

<Definition>Aggresomes are dynamic structures, formed as a general response to an overload of improperly folded proteins.

<Source>^Corboy, et al. 2005^:305

<Context>Aggresome formation is not an arbitrary, indiscriminate event, but is instead part of a highly organized and regulated process designed to deliver both the inclusions and the degradation machinery to a single locale. Aggresomes have since been shown to form from misfolding and aggregation of an ever-widening spectrum of cytoplasmic, transmembrane, and

secretory proteins, suggesting a general feature of the cell's attempts to deal with these potentially toxic species. Aggresomes likely represent the end point of a normal cellular function gone awry when the burden of misfolded protein cannot be adequately handled. Aggresomes are located at the microtubule organizing center (MTOC) surrounding the centrioles.
<Source>^Corboy, et al. 2005^:305-306-312
<Concept field>cytology
<Related words>^histone deacetylase^
<Type of relation>general
<Related words>^histone deacetylase inhibitor^
<Type of relation>general
<Related words>^histone acetylation^
<Type of relation>general
<Related words>^chromatin^
<Type of relation>general
<Related words>^panobinostat^
<Type of relation>super.
<Related words>^antiemetics^
<Type of relation>general
<Related words>^angina pectoris^
<Type of relation>general

<zh>蛋白质沉淀聚集体
<Morphosyntax>noun group
<Usage label>main term
<Source>^北京大学生物医学前沿创新中心 2021^，https://www.research.pku.edu.cn/bdkyjz/1350480.htm
<Definition>蛋白质沉淀聚集体(aggresomes)是通过液-液相分离机制形成的无膜细胞器，在细菌对抗逆境和抗生素耐药中发挥了关键作用。
<Source>^北京大学生物医学前沿创新中心 2021^，https://www.research.pku.edu.cn/bdkyjz/1350480.htm
<Context>蛋白质沉淀聚集体在显微镜明场下呈现为分布在细菌胞内的小黑点，在细胞遭遇外界压力（营养缺乏、抗生素攻击）时形成，促进细胞进入休眠状态；在外界环境改善后，aggresomes 被清除，细菌重新恢复生长。

<Source>^ 北 京 大 学 生 物 医 学 前 沿 创 新 中 心 2021^ ，
https://www.research.pku.edu.cn/bdkyjz/1350480.htm
<Concept field>细胞学
<Related words>^组蛋白去乙酰化酶^
<Type of relation>general
<Related words>^组蛋白去乙酰化酶抑制剂^
<Type of relation>general
<Related words>^组蛋白赖氨酸乙酰化^
<Type of relation>general
<Related words>^染色质^
<Type of relation>general
<Related words>^帕比司他^
<Type of relation>super.
<Related words>^止吐药^
<Type of relation>general
<Related words>^心绞痛^
<Type of relation>general
<Synonyms>“aggresome”和“蛋白质沉淀聚集体”是近义词。

<zh>aggresome
<Morphosyntax>noun
<Category>translation
<Usage label>common
<Source>^ 北 京 大 学 生 物 医 学 前 沿 创 新 中 心 2021^ ，
https://www.research.pku.edu.cn/bdkyjz/1350480.htm
<Variant of>蛋白质沉淀聚集体
**
<Subject>医学与卫生 / Medicine & health (610)
<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)
<en>antiemetic
<Morphosyntax>noun
<Usage label>main term
<Source>^Chadha/Silakari 2018^:301

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^
<Definition>Antiemetics are a class of drugs effective in the treatment of nausea and vomiting.
<Source>^Chadha/Silakari 2018^:301
<Context>These drugs are particularly used for the treatment of motion sickness, cancer chemotherapy, and drug-induced nausea and vomiting. The structure–activity relationship developed for this class of drugs highlighted the importance of an aromatic center (to form hydrophobic interactions), a basic amine moiety (form hydrogen bonds with the receptor), and a carbonyl linker (provide proper distance between the two moieties).
<Source>^Chadha/Silakari 2018^:301
<Concept field>supportive drugs
<Related words>^histone deacetylase^
<Type of relation>general
<Related words>^histone deacetylase inhibitor^
<Type of relation>general
<Related words>^histone acetylation^
<Type of relation>general
<Related words>^chromatin^
<Type of relation>general
<Related words>^panobinostat^
<Type of relation>general
<Related words>^aggresome^
<Type of relation>general
<Related words>^angina pectoris^
<Type of relation>general

<zh>止吐药
<Morphosyntax>noun group
<Source>^前瞻产业研究院2015^，http://baike.qianzhan.com/detail/bk_66c6883d.html#comment
<Definition>止吐药是指防止或减轻恶心和呕吐的药物，通过不同环节抑制呕吐反应。
<Source>^前瞻产业研究院2015^，http://baike.qianzhan.com/detail/bk_66c6883d.html#comment
<Context>虽然止吐药在分类上属于消化系统药物的范畴，但在临床上却主要用在抗肿瘤药物所致的呕吐治疗中，在肿瘤辅助治疗领域占有很重要的位置。止吐药目前主要有

以下几类，分别通过不同的环节来抑制催吐化学感受区而止吐：1)噻嗪类药物，2)抗组织胺药物，3)多巴胺(DA)，4)抗胆碱能药，5)5-羟色胺受体拮抗剂(5-HT3)，6)其他止吐药。

<Source>^ 前瞻产业研究院 2015^ ，http://baike.qianzhan.com/detail/bk_66c6883d.html#comment

<Concept field>支持性药物

<Related words>^组蛋白去乙酰化酶^

<Type of relation>general

<Related words>^组蛋白去乙酰化酶抑制剂^

<Type of relation>general

<Related words>^组蛋白赖氨酸乙酰化^

<Type of relation>general

<Related words>^染色质^

<Type of relation>general

<Related words>^帕比司他^

<Type of relation>general

<Related words>^蛋白质沉淀聚集体^

<Type of relation>general

<Related words>^心绞痛^

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>angina pectoris

<Morphosyntax>noun group

<Usage label>main term

<Source>^Alaeddini 2018^, https://emedicine.medscape.com/article/150215-overview

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Angina pectoris is the result of myocardial ischemia caused by an imbalance between myocardial blood supply and oxygen demand.

<Source>^Alaeddini 2018^, https://emedicine.medscape.com/article/150215-overview

<Context>Angina is a common presenting symptom (typically, chest pain) among patients with coronary artery disease (CAD). In patients with CAD, efforts should be made to lower the low-

density lipoprotein (LDL) level (eg, with a statin). Patients with established CAD and low HDL levels are at high risk for recurrent events and should be targeted for aggressive nonpharmacologic and pharmacologic treatment.
<Source>^Alaeddini 2018^, https://emedicine.medscape.com/article/150215-overview
<Concept field>cardiac disease
<Related words>^histone deacetylase^
<Type of relation>general
<Related words>^histone deacetylase inhibitor^
<Type of relation>general
<Related words>^histone acetylation^
<Type of relation>general
<Related words>^chromatin^
<Type of relation>general
<Related words>^panobinostat^
<Type of relation>general
<Related words>^aggresome^
<Type of relation>general
<Related words>^antiemetic^
<Type of relation>general
<Synonyms>The term “angina” is synonym to “angina pectoris” and it is commonly used to identify the disease.

<en>angina
<Morphosyntax>noun
<Usage label>common
<Source>^Alaeddini 2018^, https://emedicine.medscape.com/article/150215-overview

<zh>心绞痛
<Morphosyntax>noun group
<Source>^Sweis/Jivan 2022^, https://www.msdmanuals.cn/professional/cardiovascular-disorders/coronary-artery-disease/angina-pectoris?query=%E5%BF%83%E7%BB%9E%E7%97%9B
<Definition>心绞痛是由于一过性心肌缺血（非梗死）导致心前区不适或压迫感的一类临床综合征。

<Source>^Sweis/Jivan 2022^, https://www.msdmanuals.cn/professional/cardiovascular-disorders/coronary-artery-disease/angina-pectoris?query=%E5%BF%83%E7%BB%9E%E7%97%9B

<Context>典型的心绞痛由劳累或情绪应激所诱发，通过休息或舌下含服硝酸甘油可缓解。通过症状、心电图和心肌成像进行诊断。治疗手段包括抗血小板药物、硝酸酯类、beta 受体阻滞剂、钙通道阻滞剂、ACEI、他汀类，以及冠状动脉成形术或冠状动脉旁路移植术。

<Source>^Sweis/Jivan 2022^, https://www.msdmanuals.cn/professional/cardiovascular-disorders/coronary-artery-disease/angina-pectoris?query=%E5%BF%83%E7%BB%9E%E7%97%9B

<Concept field>心脏病

<Related words>^组蛋白去乙酰化酶^

<Type of relation>general

<Related words>^组蛋白去乙酰化酶抑制剂^

<Type of relation>general

<Related words>^组蛋白赖氨酸乙酰化^

<Type of relation>general

<Related words>^染色质^

<Type of relation>general

<Related words>^帕比司他^

<Type of relation>general

<Related words>^蛋白质沉淀聚集体^

<Type of relation>general

<Related words>^止吐药^

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病的发病率和预防/ Incidence and prevention of disease (614)

<en>objective response rate

<Morphosyntax>noun group

<Usage label>main term

<Source>^Sachdev, et al. 2022^:1

<Definition>Objective response rate (ORR) is defined as the percentage of patients who achieve a response, which can either be complete response (complete disappearance of lesions) or partial response (reduction in the sum of maximal tumour diameters by at least 30% or more).
<Source>^Sachdev, et al. 2022^:1
<Context>ORR is a poor marker of drug efficacy as it doesn't correlate with improvement in survival. Despite this poor correlation with survival, one reason for the frequent use of ORR as an endpoint in cancer drug trials is the hypothesis that a malignant tumour would not shrink spontaneously, if not for the drug.
<Source>^Sachdev, et al. 2022^:1
<Concept field>clinical endpoint
<Related words>^duration of response^
<Type of relation>coord.
<Related words>^complete response^
<Type of relation>coord.
<Related words>^time to progression^
<Type of relation>coord.
<Related words>^time to treatment failure^
<Type of relation>coord.
<Related words>^disease free survival^
<Type of relation>coord.
<Related words>^progression free survival^
<Type of relation>coord.
<Related words>^overall survival^
<Type of relation>coord.
<Related words>^health-related quality of life^
<Type of relation>coord.
<Synonyms>The term "objective response rate" is often substituted by its initials "ORR".

<en>ORR
<Morphosyntax>noun
<Category>initials
<Usage label>common
<Source>^Sachdev, et al. 2022^:1
<Variant of>objective response rate

<zh>客观缓解率

<Morphosyntax>noun group

<Usage label>main term

<Source>^国家药监局 2019^，http://www.gov.cn/xinwen/2019-09/18/content_5430886.htm

<Definition>ORR 定义为肿瘤体积缩小达到预先规定值并能维持最低时限要求的患者比例。

<Source>^国家药监局 2019^，http://www.gov.cn/xinwen/2019-09/18/content_5430886.htm

<Context>ORR 为完全缓解（CR）与部分缓解（PR）的比例之和，ORR 不包括疾病稳定（SD），排除了疾病自然病程的影响，相比疾病控制率（DCR），ORR 可更可靠反映药物的抗肿瘤活性，是单臂临床试验常用替代终点。

<Source>^国家药监局 2019^，http://www.gov.cn/xinwen/2019-09/18/content_5430886.htm

<Concept field>临床终点

<Related words>^缓解持续时间^

<Type of relation>coord.

<Related words>^完全缓解^

<Type of relation>coord.

<Related words>^访视的至进展时间^

<Type of relation>coord.

<Related words>^至治疗失败时间^

<Type of relation>coord.

<Related words>^无疾病存活期^

<Type of relation>coord.

<Related words>^无进展生存期^

<Type of relation>coord.

<Related words>^总生存期^

<Type of relation>coord.

<Related words>^健康生活品质^

<Type of relation>coord.

<Synonyms>“ORR”和“客观缓解率”是近义词。

<zh>ORR

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^国家药监局 2019^，http://www.gov.cn/xinwen/2019-09/18/content_5430886.htm

<Variant of>客观缓解率

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病的发病率和预防/ Incidence and prevention of disease (614)

<en>duration of response

<Morphosyntax>noun group

<Usage label>main term

<Source>^AstraZeneca Pcl 2018^, https://www.astrazeneca-us.com/media/astrazeneca-us-blog/2018/clinical-trial-endpoints-in-cancer-research-four-terms-you-should-know-09242018.html#

<Definition>Duration of response, or DoR, is the length of time that a tumour continues to respond to treatment without the cancer growing or spreading.

<Source>^AstraZeneca Pcl 2018^, https://www.astrazeneca-us.com/media/astrazeneca-us-blog/2018/clinical-trial-endpoints-in-cancer-research-four-terms-you-should-know-09242018.html#

<Context>Cancer drugs that demonstrate improved DoR can produce a durable, meaningful delay in disease progression, as opposed to a temporary response without any lasting benefit.

<Source>^AstraZeneca Pcl 2018^, https://www.astrazeneca-us.com/media/astrazeneca-us-blog/2018/clinical-trial-endpoints-in-cancer-research-four-terms-you-should-know-09242018.html#

<Concept field>clinical endpoint

<Related words>^objective response rate^

<Type of relation>coord.

<Related words>^complete response^

<Type of relation>coord.

<Related words>^time to progression^

<Type of relation>coord.

<Related words>^time to treatment failure^

<Type of relation>coord.

<Related words>^disease free survival^

<Type of relation>coord.

<Related words>^progression free survival^

<Type of relation>coord.

<Related words>^overall survival^

<Type of relation>coord.

<Related words>^health-related quality of life^

<Type of relation>coord.

<Synonyms>The term “duration of response” is often substituted by its initials “DoR”.

<en>DoR

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^AstraZeneca Pcl 2018^, https://www.astrazeneca-us.com/media/astrazeneca-us-blog/2018/clinical-trial-endpoints-in-cancer-research-four-terms-you-should-know-09242018.html#

<Variant of>duration of response

<zh>缓解持续时间

<Morphosyntax>noun group

<Usage label>main term

<Source>^国家药监局 2019^，http://www.gov.cn/xinwen/2019-09/18/content_5430886.htm

<Definition>缓解持续时间(DOR)定义为肿瘤第一次评估为客观缓解至第一次评估为 PD 或 PD 前任何原因死亡的时间，反映了 ORR 的持续时间。

<Source>^国家药监局 2019^，http://www.gov.cn/xinwen/2019-09/18/content_5430886.htm

<Concept field>临床终点

<Related words>^客观缓解率^

<Type of relation>coord.

<Related words>^完全缓解^

<Type of relation>coord.

<Related words>^访视的至进展时间^

<Type of relation>coord.

<Related words>^至治疗失败时间^

<Type of relation>coord.

<Related words>^无疾病存活期^

<Type of relation>coord.

<Related words>^无进展生存期^

<Type of relation>coord.

<Related words>^总生存期^

<Type of relation>coord.

<Related words>^健康生活品质^

<Type of relation>coord.

<Synonyms>“DOR”和“缓解持续时间”是近义词。

<zh>DOR

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^国家药监局 2019^，http://www.gov.cn/xinwen/2019-09/18/content_5430886.htm

<Variant of>缓解持续时间

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病的发病率和预防/ Incidence and prevention of disease (614)

<en>complete response

<Morphosyntax>noun group

<Usage label>main term

<Source>^Delgado/Guddati 2021^:1125

<Definition>Complete response (CR) is defined as the lack of detectable evidence of tumour.

<Source>^Delgado/Guddati 2021^:1125

<Context>Imaging studies and histopathology are used to measure CR which can be used as a surrogate or primary endpoint depending on the specific disease or context of use. For example: CR in the setting of multiple myeloma therapy has proven to be clinically relevant as it conveys a survival advantage associated with improved OS and prolonged EFS in specific treatment studies.

<Source>^Delgado/Guddati 2021^:1125

<Concept field>clinical endpoint

<Related words>^objective response rate^

<Type of relation>coord.

<Related words>^duration of response^

<Type of relation>coord.

<Related words>^time to progression^

<Type of relation>coord.

<Related words>^time to treatment failure^

<Type of relation>coord.

<Related words>^disease free survival^

<Type of relation>coord.

<Related words>^progression free survival^

<Type of relation>coord.

<Related words>^overall survival^

<Type of relation>coord.

<Related words>^health-related quality of life^

<Type of relation>coord.

<Synonyms>The term “complete response” is often substituted by its initials “CP”.

<en>CP

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^Delgado/Guddati 2021^:1125

<Variant of>complete response

<zh>完全缓解

<Morphosyntax>noun group

<Usage label>main term

<Source>^健康全记录 2019^，https://www.qitaijk.cn/index.php/cms/show-1614.html

<Definition>完全缓解是指各种症状、体征以及肿瘤有关的生化改变完全消失，至少持续 4 周，在此期间没有新病灶的出现。

<Source>^健康全记录 2019^，https://www.qitaijk.cn/index.php/cms/show-1614.html

<Context>病情稳定指治疗前后病变范围无变化或增、减均未超过原病灶大小的 1/4 并无新病灶出现至少持续 4 周。一般来说，医生会在病人接受 2 到 3 周期化疗后，进行全面检查评价疗效，以决定进一步的治疗方案。

<Source>^健康全记录 2019^，https://www.qitaijk.cn/index.php/cms/show-1614.html

<Concept field>临床终点

<Related words>^客观缓解率^

<Type of relation>coord.

<Related words>^缓解持续时间^

<Type of relation>coord.

<Related words>^访视的至进展时间^

<Type of relation>coord.

<Related words>^至治疗失败时间^

<Type of relation>coord.

<Related words>^无疾病存活期^

<Type of relation>coord.

<Related words>^无进展生存期^

<Type of relation>coord.

<Related words>^总生存期^

<Type of relation>coord.

<Related words>^健康生活品质^

<Type of relation>coord.

<Synonyms>“CR”和“完全缓解”是近义词。

<zh>CR

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^国家药监局 2019^，http://www.gov.cn/xinwen/2019-09/18/content_5430886.htm

<Variant of>完全缓解

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病的发病率和预防/ Incidence and prevention of disease (614)

<en>time to progression

<Morphosyntax>noun group

<Usage label>main term

<Source>^Delgado/Guddati 2021^:1123

<Definition>Time to progression (TTP) is defined as the time from randomization until first evidence of disease progression.

<Source>^Delgado/Guddati 2021^:1123

<Context>The value of TTP's assessment has the potential to be adversely affected by disease characteristics unique to each patient including inter-tumour variation and the tumour's natural growth rate. In response, researchers have proposed a patient personalized "TTP ratio" as an additional parameter to measure the effectiveness of targeted therapy. This variant of TTP compares tumour growth both on and off treatment, serving as an intra-patient control for natural tumour growth rate.
<Source>^Delgado/Guddati 2021^:1123
<Concept field>clinical endpoint
<Related words>^objective response rate^
<Type of relation>coord.
<Related words>^duration of response^
<Type of relation>coord.
<Related words>^complete response^
<Type of relation>coord.
<Related words>^time to treatment failure^
<Type of relation>coord.
<Related words>^disease free survival^
<Type of relation>coord.
<Related words>^progression free survival^
<Type of relation>coord.
<Related words>^overall survival^
<Type of relation>coord.
<Related words>^health-related quality of life^
<Type of relation>coord.
<Synonyms>The term "time to progression" is often substituted by its initials "TTP".

<en>TTP
<Morphosyntax>noun
<Category>initials
<Usage label>common
<Source>^Delgado/Guddati 2021^:1123
<Variant of>time to progression

<zh>访视的至进展时间
<Morphosyntax>noun group

<Usage label>main term

<Source>^国家药监局 2019^，http://www.gov.cn/xinwen/2019-09/18/content_5430886.htm

<Definition>访视的至进展时间(TTP)定义为从随机化至出现肿瘤客观进展的时间，不包括死亡。

<Source>^国家药监局 2019^，http://www.gov.cn/xinwen/2019-09/18/content_5430886.htm

<Context>TTP 能精确反映治疗带来的近期生存获益，由于排除了死亡，TTP 对治疗临床获益的相关性差于 PFS 和 TTF。

<Source>^国家药监局 2019^，http://www.gov.cn/xinwen/2019-09/18/content_5430886.htm

<Concept field>临床终点

<Related words>^客观缓解率^

<Type of relation>coord.

<Related words>^缓解持续时间^

<Type of relation>coord.

<Related words>^完全缓解^

<Type of relation>coord.

<Related words>^至治疗失败时间^

<Type of relation>coord.

<Related words>^无疾病存活期^

<Type of relation>coord.

<Related words>^无进展生存期^

<Type of relation>coord.

<Related words>^总生存期^

<Type of relation>coord.

<Related words>^健康生活品质^

<Type of relation>coord.

<Synonyms>“TTP”和“访视的至进展时间”是近义词。

<zh>TTP

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^国家药监局 2019^，http://www.gov.cn/xinwen/2019-09/18/content_5430886.htm

<Variant of>访视的至进展时间

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病的发病率和预防/ Incidence and prevention of disease (614)

<en>time to treatment failure

<Morphosyntax>noun group

<Usage label>main term

<Source>^Williams/Padzur 2006^:277

<Definition>Time to treatment failure (TTF) is often defined as the time from randomization to discontinuation of treatment for any reason, including progression of disease, treatment toxicity, and death.

<Source>^Williams/Padzur 2006^:277

<Context>TTF is an end point that combines efficacy and measures of safety and tolerability; it is seldom useful for regulatory purposes. Separate analyses of the components of TTF (TTP, survival, and toxicity) are preferred end points.

<Source>^Williams/Padzur 2006^:277

<Concept field>clinical endpoint

<Related words>^objective response rate^

<Type of relation>coord.

<Related words>^duration of response^

<Type of relation>coord.

<Related words>^complete response^

<Type of relation>coord.

<Related words>^time to progression^

<Type of relation>coord.

<Related words>^disease free survival^

<Type of relation>coord.

<Related words>^progression free survival^

<Type of relation>coord.

<Related words>^overall survival^

<Type of relation>coord.

<Related words>^health-related quality of life^

<Type of relation>coord.

<Synonyms>The term “time to treatment failure” is often substituted by its initials “TTF”.

<en>TTF

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^Williams/Padzur 2006^:277

<Variant of>time to treatment failure

<zh>至治疗失败时间

<Morphosyntax>noun group

<Usage label>main term

<Source>^国家药监局 2019^，http://www.gov.cn/xinwen/2019-09/18/content_5430886.htm

<Definition>TTF 定义为从随机化至治疗失败或退出试验的时间，退出试验的原因可为患者要求、疾病进展、死亡或不良事件等。

<Source>^国家药监局 2019^，http://www.gov.cn/xinwen/2019-09/18/content_5430886.htm

<Context>与 PFS 相比，TTF 覆盖了非疾病进展导致的退出，并可包括疾病进展后的继续治疗，是综合的临床终点。因 TTF 不能充分将药物的疗效和耐受性等因素区分，当前，不常用于抗肿瘤药物确证性研究的主要研究终点。

<Source>^国家药监局 2019^，http://www.gov.cn/xinwen/2019-09/18/content_5430886.htm

<Concept field>临床终点

<Related words>^客观缓解率^

<Type of relation>coord.

<Related words>^缓解持续时间^

<Type of relation>coord.

<Related words>^完全缓解^

<Type of relation>coord.

<Related words>^访视的至进展时间^

<Type of relation>coord.

<Related words>^无疾病存活期^

<Type of relation>coord.

<Related words>^无进展生存期^

<Type of relation>coord.

<Related words>^总生存期^

<Type of relation>coord.

<Related words>^健康生活品质^

<Type of relation>coord.

<Synonyms>“TTF”和“至治疗失败时间”是近义词。

<zh>TTF

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^国家药监局 2019^，http://www.gov.cn/xinwen/2019-09/18/content_5430886.htm

<Variant of>至治疗失败时间

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病的发病率和预防/ Incidence and prevention of disease (614)

<en>disease free survival

<Morphosyntax>noun group

<Usage label>main term

<Source>^Kilickap, et al. 2018^:2

<Definition>DFS is defined as the time to the development of new disease following complete radiological resolution of tumour after curative treatment with surgery, radiotherapy or chemoradiotherapy.

<Source>^Kilickap, et al. 2018^:2

<Context>DFS is used in clinical trials in which the benefit of adjuvant therapy is evaluated in patients with no sign of disease following curative treatment. DFS better reflects OS in patient groups with long-term survival expectancy.

<Source>^Kilickap, et al. 2018^:5

<Concept field>clinical endpoint

<Related words>^objective response rate^

<Type of relation>coord.

<Related words>^duration of response^

<Type of relation>coord.

<Related words>^complete response^

<Type of relation>coord.

<Related words>^time to progression^

<Type of relation>coord.

<Related words>^time to treatment failure^

<Type of relation>coord.
<Related words>^progression free survival^
<Type of relation>coord.
<Related words>^overall survival^
<Type of relation>coord.
<Related words>^health-related quality of life^
<Type of relation>coord.
<Synonyms>The term “disease free survival” is often substituted by its initials “DFS”.

<en>DFS
<Morphosyntax>noun
<Category>initials
<Usage label>common
<Source>^Kilickap, et al. 2018^:2
<Variant of>disease free survival

<zh>无疾病存活期
<Morphosyntax>noun group
<Usage label>main term
<Source>^財團法人醫藥品查驗中心 2019^:18
<Definition>无疾病存活期(DFS)定义为从随机分配至疾病复发或任何原因死亡之期间，常作为辅助性治疗之疗效指标。
<Source>^財團法人醫藥品查驗中心 2019^:18
<Context>DFS 可作为加速核准的合理替代性指标、支持一般核准的替代性指标，甚至可直接视为具临床益处的疗效指标，但需考量疾病特性、药品使用时机、药效强度现行标准治疗、及风险益处评估而决定。
<Source>^財團法人醫藥品查驗中心 2019^:18
<Concept field>临床终点
<Related words>^客观缓解率^
<Type of relation>coord.
<Related words>^缓解持续时间^
<Type of relation>coord.
<Related words>^完全缓解^

<Type of relation>coord.

<Related words>^访视的至进展时间^

<Type of relation>coord.

<Related words>^至治疗失败时间^

<Type of relation>coord.

<Related words>^无进展生存期^

<Type of relation>coord.

<Related words>^总生存期^

<Type of relation>coord.

<Related words>^健康生活品质^

<Type of relation>coord.

<Synonyms>“DFS”和“无疾病存活期”是近义词。

<zh>DFS

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^財團法人醫藥品查驗中心 2019^:18

<Variant of>无疾病存活期

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病的发病率和预防/ Incidence and prevention of disease (614)

<en>progression free survival

<Morphosyntax>noun group

<Usage label>main term

<Source>^Delgado/Guddati 2021^:1122

<Definition>Progression free survival (PFS) is defined as the time from randomization until first evidence of disease progression or death.

<Source>^Delgado/Guddati 2021^:1122

<Context>PFS is a popular surrogate endpoint since fewer patients are needed to obtain the data that becomes available early in the trial. PFS also provides the benefit of objective evaluation without being influenced by subsequent therapies or crossovers. PFS has drawn more attention as a clinical endpoint for its ability to assess treatment paradigms that include multi-stage

therapies. However, PFS's use as a clinical endpoint is debatable because prolonged PFS does not always result in an extended survival.

<Source>^Delgado/Guddati 2021^:1122-1123

<Concept field>clinical endpoint

<Related words>^objective response rate^

<Type of relation>coord.

<Related words>^duration of response^

<Type of relation>coord.

<Related words>^complete response^

<Type of relation>coord.

<Related words>^time to progression^

<Type of relation>coord.

<Related words>^time to treatment failure^

<Type of relation>coord.

<Related words>^disease free survival^

<Type of relation>coord.

<Related words>^overall survival^

<Type of relation>coord.

<Related words>^health-related quality of life^

<Type of relation>coord.

<Synonyms>The term "progression free survival" is often substituted by its initials "PFS".

<en>PFS

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^Delgado/Guddati 2021^:1122

<Variant of>progression free survival

<zh>无进展生存期

<Morphosyntax>noun group

<Usage label>main term

<Source>^国家药监局 2019^，http://www.gov.cn/xinwen/2019-09/18/content_5430886.htm

<Definition>无进展生存期（PFS）定义为从随机化至出现肿瘤客观进展或全因死亡的时间，是 OS 的替代终点。

<Source>^国家药监局 2019^，http://www.gov.cn/xinwen/2019-09/18/content_5430886.htm

<Context>PFS 包括了任何原因导致的死亡，与 OS 相关性更高，且不受后续治疗影响，是随机对照设计临床试验最常用的替代终点。PFS 为 OS 的替代终点，PFS 获益能否转化为 OS 具有不确定性，多种非治疗因素可使 PFS 的差异达到统计学意义——预后因素分层不均衡、选择了较弱的对照治疗、甚至疗效评价时间点的设计等。

<Source>^国家药监局 2019^，http://www.gov.cn/xinwen/2019-09/18/content_5430886.htm

<Concept field>临床终点

<Related words>^客观缓解率^

<Type of relation>coord.

<Related words>^缓解持续时间^

<Type of relation>coord.

<Related words>^完全缓解^

<Type of relation>coord.

<Related words>^访视的至进展时间^

<Type of relation>coord.

<Related words>^至治疗失败时间^

<Type of relation>coord.

<Related words>^无疾病存活期^

<Type of relation>coord.

<Related words>^总生存期^

<Type of relation>coord.

<Related words>^健康生活品质^

<Type of relation>coord.

<Synonyms>“PFS”和“无进展生存期”是近义词。

<zh>PFS

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^国家药监局 2019^，http://www.gov.cn/xinwen/2019-09/18/content_5430886.htm

<Variant of>无进展生存期

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病的发病率和预防/ Incidence and prevention of disease (614)

<en>overall survival

<Morphosyntax>noun group

<Usage label>main term

<Source>^Delgado/Guddati 2021^:1122

<Definition>Overall survival (OS) is defined as the time from randomization to death.

<Source>^Delgado/Guddati 2021^:1122

<Context>Since the goal of cancer treatment is generally to extend survival, OS is often referred to as the gold standard endpoint in oncology clinical trials. OS is a patient-centered endpoint that is easy to measure, and it is definite since the final time point is death. OS has limited use in diseases that are slowly progressing and have an expected long-term survival. As a primary clinical endpoint, OS can also be influenced by non-cancer deaths since the end- point is defined as time from randomization to death of any cause.

<Source>^Delgado/Guddati 2021^:1122

<Concept field>clinical endpoint

<Related words>^objective response rate^

<Type of relation>coord.

<Related words>^duration of response^

<Type of relation>coord.

<Related words>^complete response^

<Type of relation>coord.

<Related words>^time to progression^

<Type of relation>coord.

<Related words>^time to treatment failure^

<Type of relation>coord.

<Related words>^disease free survival^

<Type of relation>coord.

<Related words>^progression free survival^

<Type of relation>coord.

<Related words>^health-related quality of life^

<Type of relation>coord.

<Synonyms>The term “overall survival” is often substituted by its initials “OS”.

<en>OS

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^Delgado/Guddati 2021^:1122

<Variant of>overall survival

<zh>总生存期

<Morphosyntax>noun group

<Usage label>main term

<Source>^国家药监局 2019^，http://www.gov.cn/xinwen/2019-09/18/content_5430886.htm

<Definition>总生存期（OS）定义为从随机化到任何因素导致患者死亡的时间。OS 的判定精确可靠，不易偏倚，常作为首选终点。

<Source>^国家药监局 2019^，http://www.gov.cn/xinwen/2019-09/18/content_5430886.htm

<Context>OS 的定义明确、客观稳健，是反映患者生存获益的金标准，但试验耗时长且需较大样本量。以 OS 为主要终点的临床试验需采用随机对照设计，常需较大样本量和更长的随访时间，易受到交叉和后续治疗影响。OS 率定义为自随机化至指定时间节点同一试验组内生存的受试者所占的比例，为 OS 的中间临床终点，在既往研究中可作为次要终点，随机临床试验中，可通过 OS 率的比较观察到治疗组的获益，如 1 年 OS 率。

<Source>^国家药监局 2019^，http://www.gov.cn/xinwen/2019-09/18/content_5430886.htm

<Concept field>临床终点

<Related words>^客观缓解率^

<Type of relation>coord.

<Related words>^缓解持续时间^

<Type of relation>coord.

<Related words>^完全缓解^

<Type of relation>coord.

<Related words>^访视的至进展时间^

<Type of relation>coord.

<Related words>^至治疗失败时间^

<Type of relation>coord.

<Related words>^无疾病存活期^

<Type of relation>coord.

<Related words>^无进展生存期^

<Type of relation>coord.

<Related words>^健康生活品质^

<Type of relation>coord.

<Synonyms>“OS”和“总生存期”是近义词。

<zh>OS

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^国家药监局 2019^，http://www.gov.cn/xinwen/2019-09/18/content_5430886.htm

<Variant of>总生存期

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病的发病率和预防/ Incidence and prevention of disease (614)

<en>health-related quality of life

<Morphosyntax>noun group

<Usage label>main term

<Source>^Delgado/Guddati 2021^:1125

<Definition>Health-related quality of life (HRQoL) is an evaluation of a patient’s quality of life with respect to health status over time.

<Source>cf.^Delgado/Guddati 2021^:1125

<Context>HRQoL is an important measure that is patient reported and demonstrates clinical benefit. Quality of life is often used as a secondary clinical endpoint to compare treatments that have similar effects with differences in toxicity, but it can also be used as a co-primary endpoint with OS. HRQoL is usually assessed using a set of four core questions developed by the Centers for Disease Control and Prevention (CDC).

<Source>^Delgado/Guddati 2021^:1125

<Concept field>clinical endpoint

<Related words>^objective response rate^

<Type of relation>coord.

<Related words>^duration of response^

<Type of relation>coord.

<Related words>^complete response^

<Type of relation>coord.

<Related words>^time to progression^

<Type of relation>coord.
<Related words>^time to treatment failure^
<Type of relation>coord.
<Related words>^disease free survival^
<Type of relation>coord.
<Related words>^progression free survival^
<Type of relation>coord.
<Related words>^overall survival^
<Type of relation>coord.
<Synonyms>The term “health-related quality of life” is often substituted by its initials “HRQoL”.

<en>HRQoL
<Morphosyntax>noun
<Category>initials
<Usage label>common
<Source>^Delgado/Guddati 2021^:1125
<Variant of>health-related quality of life

<zh>健康生活品质
<Morphosyntax>noun group
<Usage label>main term
<Source>^于勝宗，等 2009^:1
<Definition>健康生活品质(HRQOL)纳入了疾病以及健康状态的概念，探讨健康 对个人生理、心理以及社会功能的影响，涵盖了生理与精神层面的生活品质。
<Source>^于勝宗，等 2009^:1
<Context>近年来已成为临床与公共卫生上用来评估个人健康的重要工具，并借此获得比生理及临床诊断上更完整的身体功能与疾病存活资讯。有学者指出，大多数的常见的慢性疾病对华人的健康生活品质会造成 影响。
<Source>^于勝宗，等 2009^:1-4
<Concept field>临床终点
<Related words>^客观缓解率^
<Type of relation>coord.
<Related words>^缓解持续时间^

<Type of relation>coord.

<Related words>^完全缓解^

<Type of relation>coord.

<Related words>^访视的至进展时间^

<Type of relation>coord.

<Related words>^至治疗失败时间^

<Type of relation>coord.

<Related words>^无疾病存活期^

<Type of relation>coord.

<Related words>^无进展生存期^

<Type of relation>coord.

<Related words>^总生存期^

<Type of relation>coord.

<Synonyms>“HRQOL”和“健康生活品质”是近义词。

<zh>HRQOL

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^于勝宗，等 2009^:1

<Variant of>健康生活品质

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>BCL-2

<Morphosyntax>noun

<Usage label>main term

<Source>^Ofengeim, et al. 2011^:82

<Definition>The Bcl-2 proteins are a family of structurally related proteins that serve as central regulators of intrinsic programmed cell death.

<Source>^Ofengeim, et al. 2011^:82

<Context>Bcl-2 family proteins are classified as either antiapoptotic or proapoptotic proteins. Antiapoptotic members localize to the cytosol and to the mitochondrial and endoplasmic reticulum membrane. Proapoptotic members are thought to induce cell death by inhibiting the

antiapoptotic family members. The balance between antiapoptotic and proapoptotic Bcl-2 family members has long been thought to determine the functional integrity of the mitochondrial outer membrane and commitment to cell death.

<Source>^Ofengeim, et al. 2011^:82-83

<Concept field>cytology

<Related words>^BAX^

<Type of relation>super.

<Related words>^BAK^

<Type of relation>super.

<Related words>^BCL-2 inhibitor^

<Type of relation>coord.

<Related words>^venetoclax^

<Type of relation>general

<Synonyms>The terms “Bcl-2 protein” is a synonym to “BCL-2” and it is commonly used.

<en>Bcl-2 protein

<Morphosyntax>noun group

<Usage label>common

<Source>^Ofengeim, et al. 2011^:82

<zh>B 细胞淋巴瘤−2

<Morphosyntax>noun group

<Usage label>main term

<Source>^健愉冯，等 2019^:1477

<Definition>B 细胞淋巴瘤−2(Bcl-2)家族蛋白是凋亡途径的重要组分，其功能异常与多种疾病相关，包括癌症、神经退行性疾病和自身免疫疾病等。

<Source>^健愉冯，等 2019^:1477

<Context>Bcl-2 家族蛋白在调控线粒体功能和细胞色素 C 等的释放中起重要作用。Bcl-2 家族蛋白主要有三大类：抑凋亡蛋白亚家族，促凋亡蛋白亚家族，包括 Bax、Bak 和 Bok 等；另一类促凋亡蛋白只含有 BH3 结构域，即 BH3-only 亚家族。在过去几年中，许多针对不同 Bcl-2 成员的药物已经被开发并进入临床阶段。

<Source>^健愉冯，等 2019^:1477-1479

<Concept field>细胞学

<Related words>^BAX^

<Type of relation>super.

<Related words>^BAK^

<Type of relation>super.

<Related words>^Bcl-2 抑制剂^

<Type of relation>coord.

<Related words>^维奈克拉^

<Type of relation>general

<Synonyms>“Bcl-2”和“B 细胞淋巴瘤−2”是近义词。

<zh>Bcl-2

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^健愉冯，等 2019^:1477

<Variant of>B 细胞淋巴瘤−2

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>BAX

<Morphosyntax>noun

<Source>^Liu, et al. 2016^:313

<Definition>Bax, a central cell death regulator, is an indispensable gateway to mitochondrial dysfunction and a major pro-apoptotic member of the Bcl-2 family proteins that control apoptosis in normal and cancer cells.

<Source>^Liu, et al. 2016^:313

<Context>Bax activation induces mitochondrial membrane permeabilization, thereby leading to the release of apoptotic factor cytochrome c and consequently cancer cell death. Multi-domain pro-apoptotic proteins Bax and Bak are essential executive proteins responsible for MOMP and a requisite gateway to mitochondrial dysfunction as well as cell death. Bax is expressed in essentially all organs, indicating that it may be a regulator of apoptosis in various cell types. Bax is also involved in the endoplasmic reticulum (ER) signalling pathway which plays a decisive role in many cellular events especially in cell death via crosstalk with mitochondrial pathways.

<Source>^Liu, et al. 2016^:313-314-316

<Concept field>cytology

<Related words>^BCL-2^

<Type of relation>sub.

<Related words>^BAK^

<Type of relation>coord.

<Related words>^BCL-2 inhibitor^

<Type of relation>general

<Related words>^venetoclax^

<Type of relation>general

<zh>Bax

<Morphosyntax>noun

<Source>^冯健愉，等 2019^:1480

<Definition>Bax 是一种可溶性的蛋白分子，主要位于细胞质中，但当凋亡发生时，它会从胞质转移到线粒体并与线粒体膜相结合。

<Source>^冯健愉，等 2019^:1480

<Context>当细胞受到凋亡刺激时，Bax 发生构象变化，其 C-端的 α9 被释放，暴露了疏水袋状结构，有利于其与其他 Bcl-2 分子之间通过 BH3 结构域而相互作用。内源性细胞凋亡是由 Bax 蛋白将线粒体外膜通透化(MOMP)引发的。Bax 在健康的细胞中是无活性的并且存在于胞质中。在应激细胞中，Bcl-2 家族中的促凋亡蛋白被激活后，反过来激活 Bax。被激活的 Bax 蛋白发生构象变化并且嵌入到线粒体外膜(MOM)中。

<Source>^冯健愉，等 2019^:1480-1482

<Concept field>细胞学

<Related words>^B 细胞淋巴瘤−2^

<Type of relation>sub.

<Related words>^BAK^

<Type of relation>coord.

<Related words>^Bcl-2 抑制剂^

<Type of relation>generak

<Related words>^维奈克拉^

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>BAK

<Morphosyntax>noun

<Source>^Graber, et al. 1999^:74

<Definition>Bak is a pro-apoptotic member of the Bcl-2 family whose genes are involved in regulation of programmed cell death.

<Source>^Graber, et al. 1999^:74

<Context>As Bak is a pro-apoptotic member of the Bcl-2 family, Bak overexpression in peritumorous areas of chronic inflammation suggest that there is extensive activation of programmed cell death in these areas. Bak was hardly expressed in circulating lymphocytes and macrophages, suggesting that programmed cell death in areas of chronic inflammation surrounding pancreatic cancer cells is induced after having entered the perifocal tissue.

<Source>^Graber, et al. 1999^:79-80

<Concept field>cytology

<Related words>^BCL-2^

<Type of relation>sub.

<Related words>^BAX^

<Type of relation>coord.

<Related words>^BCL-2 inhibitor^

<Type of relation>general

<Related words>^venetoclax^

<Type of relation>general

<zh>Bak

<Morphosyntax>noun

<Source>^Park, et al. 2021^:8500

<Definition>Bak 是主要的促凋亡 Bcl2 家族成员，也是凋亡细胞死亡所需的分子。

<Source>^Park, et al. 2021^:8500

<Context>Bak 表达增加与患者的不良预后相关，表明 Bak 蛋白是治疗的一个有吸引力的靶标。Bak 结合促进 Bak 寡聚化和激活其促凋亡功能的线粒体启动。

<Source>^Park, et al. 2021^:8500

<Concept field>细胞学

<Related words>^B 细胞淋巴瘤−2^

<Type of relation>sub.

<Related words>^BAX^

<Type of relation>coord.

<Related words>^Bcl-2 抑制剂^

<Type of relation>general

<Related words>^维奈克拉^

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>BCL-2 inhibitor

<Morphosyntax>noun group

<Usage label>main term

<Source>^National Cancer Institute^, https://www.cancer.gov/publications/dictionaries/cancer-drug/def/bcl-2-inhibitor-bcl201

<Definition>BCL-2 inhibitor is a selective inhibitor of the anti-apoptotic protein B-cell lymphoma 2 (Bcl-2), with potential pro-apoptotic and antineoplastic activities.

<Source>cf.^National Cancer Institute^, https://www.cancer.gov/publications/dictionaries/cancer-drug/def/bcl-2-inhibitor-bcl201

<Context>Upon administration, Bcl-2 inhibitor (BCL201) binds to and inhibits the activity of Bcl-2. This restores apoptotic processes in tumour cells. Bcl-2 protein is overexpressed in many cancers and plays an important role in the negative regulation of apoptosis; its expression is associated with increased drug resistance and tumour cell survival.

<Source>^National Cancer Institute^, https://www.cancer.gov/publications/dictionaries/cancer-drug/def/bcl-2-inhibitor-bcl201

<Concept field>new drugs

<Related words>^BCL-2^

<Type of relation>coord.

<Related words>^BAX^

<Type of relation>super.

<Related words>^BAK^

<Type of relation>super.

<Related words>^venetoclax^

<Type of relation>sub.

<Synonyms>The terms “servier-1” and “BCL201” are synonym to “BCL-2 inhibitor” but they are not commonly used.

<en>servier-1

<Morphosyntax>noun

<Usage label>uncommon

<Source>^National Cancer Institute^, https://www.cancer.gov/publications/dictionaries/cancer-drug/def/bcl-2-inhibitor-bcl201

<en>BCL201

<Morphosyntax>noun

<Category>code name

<Usage label>uncommon

<Source>^National Cancer Institute^, https://www.cancer.gov/publications/dictionaries/cancer-drug/def/bcl-2-inhibitor-bcl201

<Variant of>BCL-2 inhibitor

<zh>Bcl-2 抑制剂

<Morphosyntax>noun group

<Source>^上海申银万国证券研究所有限公司 2019^:1

<Definition>Bcl-2 抑制剂通过抑制阻止细胞凋亡的 Bcl-2 蛋白来修复细胞凋亡过程。

<Source>^上海申银万国证券研究所有限公司 2019^:1

<Context>Bcl-2 抑制剂展现优异的首次人体临床数据。目前，全球仅有一款 Bcl-2 抑制剂维奈托克获批上市，FDA 已批准其用于治疗一线和二线慢性淋巴细胞白血病(CLL/SLL)和一线急性髓系白血病(AML)。

<Source>^上海申银万国证券研究所有限公司 2019^:1

<Concept field>新药

<Related words>^B 细胞淋巴瘤−2^

<Type of relation>coord.

<Related words>^BAX^

<Type of relation>super.

<Related words>^BAK^

<Type of relation>super.

<Related words>^维奈克拉^

<Type of relation>sub.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>venetoclax

<Morphosyntax>noun

<Usage label>main term

<Source>^Kumar, et al. 2020^:1631

<Definition>Venetoclax is a highly selective, potent, oral BCL2 inhibitor that induces apoptosis in multiple myeloma cell lines and primary multiple myeloma cells in vitro.

<Source>^Kumar, et al. 2020^:1631

<Context>Multiple myeloma cells with a high dependency on BCL-2 protein for survival are particularly sensitive to venetoclax-induced apoptosis. However, multiple myeloma is heterogeneous in its dependence on BCL-2 for survival, meaning that BCL-2 inhibition is less effective in some patients than others. Combination of venetoclax with drugs that can increase BCL-2 dependency could be an effective therapeutic strategy for targeting survival pathways in multiple myeloma. Preclinical studies have shown that both the glucocorticoid dexamethasone and the proteasome inhibitor bortezomib can increase BCL-2 dependency in multiple myeloma cells.

<Source>^Kumar, et al. 2020^:1631

<Concept field>new drugs

<Related words>^BCL-2^

<Type of relation>coord.

<Related words>^BAX^

<Type of relation>super.

<Related words>^BAK^

<Type of relation>super.

<Related words>^BCL-2 inhibitors^

<Type of relation>super.

<Related words>^sepsis^

<Type of relation>sub.

<zh>维奈克拉

<Morphosyntax>noun

<Usage label>main term

<Source>^宗李红，等 2021^:862

<Definition>维奈克拉(VEN)是一种选择性小分子 BCL-2 抑制剂，已在临床前研究中显示出可诱导依赖 BCL-2 生存的恶性细胞凋亡。

<Source>^宗李红，等 2021^:862

<Context>VEN 联合去甲基化药物(HMA)或低剂量阿糖胞苷成为 75 岁及以上、不适合强化疗的初治 AML 患者的治疗新选择，能够使患 者获得更长的总生存期和更高缓解率。

<Source>^宗李红，等 2021^:862

<Concept field>新药

<Related words>^B 细胞淋巴瘤−2^

<Type of relation>coord.

<Related words>^BAX^

<Type of relation>super.

<Related words>^BAK^

<Type of relation>super.

<Related words>^Bcl-2 抑制剂^

<Type of relation>super.

<Related words>^败血症^

<Type of relation>sub.

<Synonyms>“VEN”和“维奈克拉”是近义词。

<zh>VEN

<Morphosyntax>noun

<Category>acronym

<Usage label>common

<Source>^宗李红，等 2021^:862

<Variant of>维奈克拉

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>sepsis

<Morphosyntax>noun

<Usage label>main term

<Source>^Purcarea/Sovaila 2020^:130

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^

<Definition>Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.

<Source>^Purcarea/Sovaila 2020^:130

<Context>Sepsis is a heterogenous syndrome that characterizes the body's overwhelming and life-threatening response to an infection, and it represents the main driver of mortality from infection. Risk factors for sepsis development are an age of 65 or more, or younger than 1 year, or the presence of concomitant chronic conditions. Sepsis therapy principles comprise fluid resuscitation and hemodynamic support, antibiotics and source control, and a series of adjunctive measures.

<Source>^Purcarea/Sovaila 2020^:129-130

<Concept field>adverse events

<Related words>^BCL-2 inhibitors^

<Type of relation>super.

<Related words>^venetoclax^

<Type of relation>super.

<zh>败血症

<Morphosyntax>noun group

<Source>^世界卫生组织 2017^, https://apps.who.int/gb/ebwha/pdf_files/EB140/B140_12-ch.pdf

<Lexica>Found in ^现代汉语词典 2013^

<Definition>败血症是宿主对感染的反应失调引起的危及生命的器官功能障碍。

<Source>^世界卫生组织 2017^, https://apps.who.int/gb/ebwha/pdf_files/EB140/B140_12-ch.pdf

<Context>败血症发生于身体对损伤其自身组织和器官的感染作出反应时。如果不能及时识别 和管理，它可能导致感染性休克，多器官功能衰竭乃至死亡。败血症的发生和频率取决于许多宿主、病原体和卫生系统反应因素的复杂相互作用。人口和社会因素，如饮食和生活方式(例如，使用烟草和酒精)、贫困、性别和种族，也会影响到败血症的发生。卫生保健系统的享有，特别是重 症监护，以及护理的及时性和质量，也与败血症的发生及其死亡率有关。

<Source>^世界卫生组织 2017^, https://apps.who.int/gb/ebwha/pdf_files/EB140/B140_12-ch.pdf

<Concept field>不良事件

<Related words>^Bcl-2 抑制剂^

<Type of relation>super.

<Related words>^维奈克拉^

<Type of relation>super.

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>karyopherin

<Morphosyntax>noun

<Usage label>main term

<Source>^Hall 2019^:107

<Definition>Karyopherins, also known as importins or exportins, are a superfamily of nuclear transport receptors that facilitate the translocation of proteins, RNAs, and ribonuclear particles across the NPC in a Ran GTP hydrolase-dependent process.

<Source>^Hall 2019^:107

<Context>The conserved Karyopherin (Kap) family of nuclear transport receptors mediate the majority of transport of macromolecules, especially of proteins, across the NPC into the nucleus (importins), out of the nucleus (exportins) or in both directions (biportins). Of the 20 Kaps identified in human cells, 10 are importins, 5 are exportins, 3 are biportins and the functions of 2 Kaps remain unknown. Kaps are critically involved in many eukaryotic cellular processes that include response to the environment, signal transduction, regulation and maintenance of the cell cycle.

<Source>^Wing, et al. 2022^:307-308

<Concept field>cytology

<Related words>^Exportin 1^

<Type of relation>sub.

<Related words>^selective inhibitor of nuclear export^

<Type of relation>sub.

<Related words>^tumour suppressor gene^

<Type of relation>general.

<Related words>^selinexor^

<Type of relation>sub.

<Related words>^amyloidosis^

<Type of relation>general

<Related words>^erythropoietin stimulating agent^

<Type of relation>general
<Synonyms>The terms “importin” and “exportin” are synonym to “karyopherin” and they are commonly used.

<en>importin
<Morphosyntax>noun
<Usage label>common
<Source>^Hall 2019^:107

<en>exportin
<Morphosyntax>noun
<Usage label>common
<Source>^Hall 2019^:107

<zh>核转运蛋白
<Morphosyntax>noun group
<Source>^樊静/朱运松 2003^:85
<Definition>核转运蛋白是在真核细胞中广泛存在的一类重要的蛋白质，其成员数目众多，并且有新成员正在不断地被发现。
<Source>^樊静/朱运松 2003^:85
<Context>核转运蛋白与不同底物结合时，呈现出不同的构象，它也是由 2 或 3 个螺旋所组成的延伸的超螺旋结构。核转运蛋白完成对大分子蛋白质的穿越核膜的转运，并且以这一作用为基础，参与了细胞的信号转导，细胞分裂及生长发育，细胞调亡等重要生命活动。
<Source>^樊静/朱运松 2003^:85
<Concept field>细胞学
<Related words>^核输出蛋白 1^
<Type of relation>sub.
<Related words>^选择性核输出抑制剂^
<Type of relation>sub.
<Related words>^肿瘤抑制基因^
<Type of relation>general.
<Related words>^塞利尼索^

<Type of relation>sub.

<Related words>^淀粉样变性^

<Type of relation>general

<Related words>^红细胞生成刺激剂^

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>XPO1

<Morphosyntax>noun group

<Usage label>main term

<Source>^Azizian/Li 2020^:1

<Definition>XPO1 is a nuclear export receptor with a pleiotropic role in transporting a plethora of proteins and RNA species, including rRNAs, snRNAs, mRNA, microRNAs, and tRNAs.

<Source>^Azizian/Li 2020^:1

<Context>Originally named as CRM1 (chromosomal region maintenance 1), XPO1 was identified in Schizosaccharomyces pombe as a gene required for maintaining higher-order chromosome structure. Subsequently, it was shown to function as a shuttling protein, mediating the nuclear export of proteins and mRNAs in Saccharomyces cerevisiae and renamed as XPO1. XPO1 is frequently overexpressed and/or mutated in human cancers and functions as an oncogenic driver. Suppression of XPO1-mediated nuclear export, therefore, presents a unique therapeutic strategy.

<Source>^Azizian/Li 2020^:1

<Concept field>cytology

<Related words>^karyopherin^

<Type of relation>super.

<Related words>^selective inhibitor of nuclear export^

<Type of relation>coord.

<Related words>^tumour suppressor gene^

<Type of relation>sub.

<Related words>^selinexor^

<Type of relation>coord.

<Related words>^amyloidosis^

<Type of relation>general

<Related words>^erythropoietin stimulating agent^

<Type of relation>general
<Synonyms>The term “XPO1” can be substituted by its full form “exportin 1”.

<en>exportin 1
<Morphosyntax>noun
<Category>full form
<Usage label>common
<Source>^Azizian/Li 2020^:1
<Variant of>XPO1

<zh>核输出蛋白 1
<Morphosyntax>noun group
<Usage label>main term
<Source>^中国临床肿瘤学会（CSCO）白血病专家委员会，中国临床肿瘤学会（CSCO）淋巴瘤专家委员会 2023^:65
<Definition>核输出蛋白 1（XPO1）也被称为染色体区域稳定蛋白 1（CRM1），是主要肿瘤抑制蛋白（TSP）、生长调节蛋白（GRP）的唯一核输出受体，也是当前研究最广泛、最关键的核输出蛋白。
<Source>^中国临床肿瘤学会（CSCO）白血病专家委员会，中国临床肿瘤学会（CSCO）淋巴瘤专家委员会 2023^:65
<Context>核输出蛋白 1（XPO1）是人体关键的核输出蛋白，也是血液肿瘤治疗的有效靶点。塞利尼索作为首个 XPO1 抑制剂，已被美国食品药品管理局（FDA）批准用于复发难治多发性骨髓瘤（MM）。
<Source>^中国临床肿瘤学会（CSCO）白血病专家委员会，中国临床肿瘤学会（CSCO）淋巴瘤专家委员会 2023^:65
<Concept field>细胞学
<Related words>^核转运蛋白^
<Type of relation>super.
<Related words>^选择性核输出抑制剂^
<Type of relation>coord.
<Related words>^肿瘤抑制基因^
<Type of relation>sub.
<Related words>^塞利尼索^

<Type of relation>coord.

<Related words>^淀粉样变性^

<Type of relation>general

<Related words>^红细胞生成刺激剂^

<Type of relation>general

<Synonyms>“染色体区域稳定蛋白 1”，“XPO1”，“CRM1”和“核输出蛋白 1”是近义词。

<zh>染色体区域稳定蛋白 1

<Morphosyntax>noun group

<Usage label>uncommon

<Source>^中国临床肿瘤学会（CSCO）白血病专家委员会，中国临床肿瘤学会（CSCO）淋巴瘤专家委员会 2023^:65

<zh>XPO1

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^中国临床肿瘤学会（CSCO）白血病专家委员会，中国临床肿瘤学会（CSCO）淋巴瘤专家委员会 2023^:65

<Variant of>核输出蛋白 1

<zh>CRM1

<Morphosyntax>noun

<Category>initials

<Usage label>uncommon

<Source>^中国临床肿瘤学会（CSCO）白血病专家委员会，中国临床肿瘤学会（CSCO）淋巴瘤专家委员会 2023^:65

<Variant of>染色体区域稳定蛋白 1

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>selective inhibitor of nuclear export

<Morphosyntax>noun group

<Usage label>main term
<Source>^Jardin, et al. 2016^:924
<Definition>Selective inhibitors of nuclear export (SINE) compounds, a new class of small molecule inhibitors, have been shown to effectively target XPO1 and retain TSPs in the nucleus.
<Source>^Jardin, et al. 2016^:924
<Context>Selective inhibitors of nuclear export (SINEs) directed against nuclear exportin-1 (XPO1) have demonstrated anti-tumour efficacy in several haematological malignancies. Given that protein transport regulation through XPO1 across the nuclear membrane is essential to normal cells, SINEs disturb normal immune homeostasis resulting in side effects such as cytopenia.
<Source>^Wang, et al. 2021^:1-2
<Concept field>new drugs
<Related words>^karyopherin^
<Type of relation>super.
<Related words>^exportin 1^
<Type of relation>coord.
<Related words>^tumour suppressor gene^
<Type of relation>sub.
<Related words>^selinexor^
<Type of relation>sub.
<Related words>^amyloidosis^
<Type of relation>general
<Related words>^erythropoietin stimulating agent^
<Type of relation>general
<Synonyms>The term “selective inhibitor of nuclear export” is often substituted by its initials “SINE”.

<en>SINE
<Morphosyntax>noun
<Category>acronym
<Usage label>common
<Source>^Jardin, et al. 2016^:924
<Variant of>selective inhibitors of nuclear export

<zh>选择性核输出抑制剂

<Morphosyntax>noun group

<Usage label>main term

<Source>^Benkova, et al. 2020^:1

<Definition>选择性核输出抑制剂(SINE)是新一代 XPO1 抑制剂，正在研究作为一种有前途的靶向抗癌疗法。

<Source>^Benkova, et al. 2020^:1

<Context>选择性核输出抑制剂（SINE）化合物可阻断多种肿瘤抑制蛋白（例如 p53、IkB、p21）的核输出，导致其于核内积累并活化从而发挥抗肿瘤作用；另外 SINE 化合物还可减少多种与 elF4E 结合的致癌基因 mRNA（c-Myc、Bcl-2、Bcl-6、cyclin D）的出核及转化，使肿瘤细胞选择性凋亡。

<Source>^德琪醫藥有限公司 2020^:1

<Concept field>新药

<Related words>^核转运蛋白^

<Type of relation>super.

<Related words>^核输出蛋白 1^

<Type of relation>coord.

<Related words>^肿瘤抑制基因^

<Type of relation>sub.

<Related words>^塞利尼索^

<Type of relation>sub.

<Related words>^淀粉样变性^

<Type of relation>general

<Related words>^红细胞生成刺激剂^

<Type of relation>general

<Synonyms>“SINE”和“选择性核输出抑制剂”是近义词。

<zh>SINE

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^Benkova, et al. 2020^:1

<Variant of>选择性核输出抑制剂

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>解剖学、细胞学和组织学 / Human anatomy, cytology & histology (611)

<en>tumour suppressor gene

<Morphosyntax>noun group

<Usage label>main term

<Source>^Joyce, et al. 2022^ https://www.ncbi.nlm.nih.gov/books/NBK532243/

<Lexica>Found in ^Merriam/Webster 2016^

<Definition>Tumour suppressor genes are important genes that act within the genome to regulate several cellular functions.

<Source>^Joyce, et al. 2022^ https://www.ncbi.nlm.nih.gov/books/NBK532243/

<Context>These genes can be broadly classified based on their role in cell growth/cell cycle progression, cell proliferation, DNA repair mechanisms, and other crucial cellular signalling functions such as the apoptosis induction. Without functional tumour suppressor genes, there is a high risk of dysregulated cell growth that is a well-known mechanism for the development of cancers. There are even familial cancer syndromes associated with the loss of function germline mutations of specific tumour suppressor genes like Li-Fraumeni syndrome with the loss of TP53.

<Source>^Joyce, et al. 2022^ https://www.ncbi.nlm.nih.gov/books/NBK532243/

<Concept field>cytology

<Related words>^karyopherin^

<Type of relation>super.

<Related words>^exportin 1^

<Type of relation>super.

<Related words>^selective inhibitor of nuclear export^

<Type of relation>super.

<Related words>^selinexor^

<Type of relation>general

<Related words>^amyloidosis^

<Type of relation>general

<Related words>^erythropoietin stimulating agent^

<Type of relation>general

<zh>肿瘤抑制基因

<Morphosyntax>noun group

<Usage label>main term

<Source>^孙开来 1998^:50

<Definition>抑癌基因又称肿瘤抑制基因或抗癌基因，是能够抑制细胞的恶性转化，对正常细胞的增殖起负性调节作用的基因。

<Source>^孙开来 1998^:50

<Context>抑癌基因是当前肿瘤遗传学和分子生物学研究的前沿和热点。抑癌基因失活后，正常细胞增殖失控，转化成肿瘤细胞。

<Source>^孙开来 1998^:50

<Concept field>细胞学

<Related words>^核转运蛋白^

<Type of relation>super.

<Related words>^核输出蛋白 1^

<Type of relation>super.

<Related words>^选择性核输出抑制剂^

<Type of relation>super.

<Related words>^塞利尼索^

<Type of relation>general

<Related words>^淀粉样变性^

<Type of relation>general

<Related words>^红细胞生成刺激剂^

<Type of relation>general

<Synonyms>“抗癌基因”和“肿瘤抑制基因”是近义词。

<zh>抗癌基因

<Morphosyntax>noun group

<Usage label>common

<Source>^孙开来 1998^:50

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>selinexor

<Morphosyntax>noun

<Source>^Podar, et al., 2020^:340

<Definition>Selinexor (XPOVIOTM, formerly KPT-330, Karyopharm Therapeutics) is a first-in-class, slowly reversible, fully synthetic, oral SINE compound developed by structure-based drug design.
<Source>^Podar, et al., 2020^:340
<Context>Selinexor induces cell cycle arrest and apoptosis of various solid and hematologic tumour cells, with single-agent activity in DLBCL, AML, and MM. The capacity of selinexor to cross the blood-brain barrier makes it a promising candidate for the treatment of central nervous and meningeal manifestation of MM. Despite the promising anti-MM activity of selinexor, its broad clinical use may be challenged by its toxicity. Side effects in patients receiving selinexor include GI and neurological side effects (emesis, nausea, decreased appetite and weight, constipation, delirium, and confusional state), neutropenia, thrombocytopenia, anaemia, fatigue, upper respiratory infections, hyponatremia, and blurred vision.
<Source>^Podar, et al., 2020^:340-341-344
<Concept field>new drugs
<Related words>^karyopherin^
<Type of relation>super.
<Related words>^exportin 1^
<Type of relation>super.
<Related words>^selective inhibitor of nuclear export^
<Type of relation>super.
<Related words>^tumour suppressor gene^
<Type of relation>general
<Related words>^amyloidosis^
<Type of relation>sub.
<Related words>^erythropoietin stimulating agent^
<Type of relation>general

<zh>塞利尼索
<Morphosyntax>noun
<Usage label>main term
<Source>^快赴康海外医疗 2022^，https://www.kuaifukang.com/3810.html
<Definition>塞利尼索(selinexor)是一种一流的口服选择性核出口抑制剂(SINE)化合物。
<Source>^快赴康海外医疗 2022^，https://www.kuaifukang.com/3810.html

<Context>Selinexor 通过与核输出蛋白 XPO1 结合并抑制其起作用，导致肿瘤抑制蛋白在细胞核中的积累。这重新启动并扩增了它们的肿瘤抑制功能，并且被认为导致癌细胞中细胞凋亡的选择性诱导，同时在很大程度上保留了正常细胞。Selinexor 已被 FDA 授予多发性骨髓瘤和 DLBCL 的孤儿指定。

<Source>^快赴康海外医疗 2022^，https://www.kuaifukang.com/3810.html

<Concept field>新药

<Related words>^核转运蛋白^

<Type of relation>super.

<Related words>^核输出蛋白 1^

<Type of relation>super.

<Related words>^选择性核输出抑制剂^

<Type of relation>super.

<Related words>^肿瘤抑制基因^

<Type of relation>general

<Related words>^淀粉样变性^

<Type of relation>sub.

<Related words>^红细胞生成刺激剂^

<Type of relation>general

<Synonyms>“selinexor”和“塞利尼索”是近义词。

<zh>selinexor

<Morphosyntax>noun

<Category>translation

<Usage label>common

<Source>^快赴康海外医疗 2022^，https://www.kuaifukang.com/3810.html

<Variant of>塞利尼索

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>疾病 / Diseases (616)

<en>amyloidosis

<Morphosyntax>noun

<Usage label>main term

<Source>^Baker/Rice 2012^:3

<Lexica>Found in ^Merriam/Webster 2016; Oxford Concise Medical Dictionary 2020^
<Definition>Amyloidosis is a rare disorder in which insoluble amyloid proteins are deposited in body organs, causing abnormal protein build-up in tissues, and eventually leading to organ dysfunction and death.
<Source>^Baker/Rice 2012^:3
<Context>Approximately 60 heterogeneous amyloidogenic proteins have been identified, 27 of these associated with known human disease. The unifying feature of these proteins is their tendency to form β-pleated sheets aligned in an antiparallel fashion. These sheets then form rigid, nonbranching fibrils that resist proteolysis and cause mechanical disruption and local oxidative stress in affected organs such as the heart, liver, kidneys, and gastrointestinal tract.
<Source>^Baker/Rice 2012^:3
<Concept field>adverse events
<Related words>^selective inhibitor of nuclear export^
<Type of relation>general
<Related words>^tumour suppressor gene^
<Type of relation>general
<Related words>^selinexor^
<Type of relation>super.
<Related words>^erythropoietin stimulating agent^
<Type of relation>general

<zh>淀粉样变性
<Morphosyntax>noun group
<Source>^杜鹃/侯健 2017^:469
<Definition>淀粉样变性(Amyloidosis)是由于淀粉样蛋白沉积在细胞外基质，造成沉积部位组织和器官损伤的一组疾病，可累及肾脏、心脏、肝脏、皮肤软组织、外周神经、肺、腺体、血管等多种器官和组织。
<Source>^杜鹃/侯健 2017^:469
<Context>至今发现，大约有 31 种不同蛋白质沉积导致不同类型淀粉样变性疾病的发生，而系统性轻链型(AL 型)淀粉样变性是临床最常见的一种类型。AL 型淀粉样变性可累及多个脏器，因此临床表现形式多样，2/3 的患者以乏力起病，这主要归因于纳差、厌食导致营养不良，约 50%的患者在就诊时体重下降明显。肾脏、心脏是受累频率最高的器官，其次为肝脏、周围神经、胃肠道等。
<Source>^杜鹃/侯健 2017^:469-470

<Concept field>不良事件

<Related words>^选择性核输出抑制剂^

<Type of relation>general

<Related words>^肿瘤抑制基因^

<Type of relation>general

<Related words>^塞利尼索^

<Type of relation>super.

<Related words>^红细胞生成刺激剂^

<Type of relation>general

**

<Subject>医学与卫生 / Medicine & health (610)

<Subfield>药理学和治疗学 / Pharmacology & therapeutics (615)

<en>erythropoietin stimulating agent

<Morphosyntax>noun group

<Usage label>main term

<Source>^Schoener/Borger 2023^, https://www.ncbi.nlm.nih.gov/books/NBK536997/

<Definition>Erythropoietin stimulating agents (ESAs) are recombinant versions of EPO produced pharmacologically via recombinant DNA technology in cell cultures.

<Source>^Schoener/Borger 2023^, https://www.ncbi.nlm.nih.gov/books/NBK536997/

<Context>ESAs are generally indicated in conditions where there is impaired red blood cell production. The two primary FDA-approved indications for ESAs are anaemia secondary to chronic kidney disease and chemotherapy-induced anaemia in patients with cancer. Erythropoietin stimulating agents are contraindicated in patients with hypersensitivity to non-human mammal-derived products because of ESA production methods. ESAs containing benzyl alcohol are contraindicated in neonates, peripartum mothers, and breastfeeding mothers due to the risk for gasping syndrome. This syndrome causes gasping respirations, renal failure, and neurological deterioration in neonates, resulting from severe metabolic acidosis.

<Source>^Schoener/Borger 2023^, https://www.ncbi.nlm.nih.gov/books/NBK536997/

<Concept field>supportive drugs

<Related words>^selective inhibitor of nuclear export^

<Type of relation>general

<Related words>^tumour suppressor gene^

<Type of relation>general

<Related words>^selinexor^

<Type of relation>general

<Related words>^amyloidosis^

<Type of relation>general

<Synonyms>The term “erythropoietin stimulating agent” is often substituted by its initials “ESA”.

<en>ESA

<Morphosyntax>noun

<Category>initials

<Usage label>common

<Source>^Schoener/Borger 2023^, https://www.ncbi.nlm.nih.gov/books/NBK536997/

<Variant of>erythropoietin stimulating agent

<zh>红细胞生成刺激剂

<Morphosyntax>noun group

<Usage label>main term

<Source>^赵玉超，等 2022^

<Definition>红细胞生成刺激剂(ESA)是肾性贫血最重要的治疗药物。

<Source>^赵玉超，等 2022^

<Context>ESA 通过激活 EPO 受体促进骨髓红系造血，是肾性贫血的重要治疗措施，作为 ESA 的主要药物，EPO 被广泛应用于临床。随着 ESA 的广泛应用，其安全性持续受到学者们关注，其中 ESA 继发的血压升高一直是 ESA 应用的焦点，由于第一代 ESA 即 EPO 的广泛应用，目前对 ESA 与高血压关系的研究主要聚焦在 EPO 上。

<Source>^赵玉超，等 2022^

<Concept field>支持性药物

<Related words>^选择性核输出抑制剂^

<Type of relation>general

<Related words>^肿瘤抑制基因^

<Type of relation>general

<Related words>^塞利尼索^

<Type of relation>general

<Related words>^淀粉样变性^

<Type of relation>general

<Synonyms>“ESA”和“红细胞生成刺激剂”是近义词。

<zh>ESA
<Morphosyntax>noun
<Category>initials
<Usage label>common
<Source>^赵玉超，等 2022^
<Variant of>红细胞生成刺激剂

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SECTION III

English – Chinese glossary
英/汉词典

<en> 英语	<zh> 中文	Pinyin 拼音
Activation-induced cytidine deaminase	活化诱导性甘肝脱氨酶	Huóhuà yòudǎo xìng gān gān tuō ān méi
Acute tubular necrosis	急性肾小管坏死	Jíxìng shèn xiǎoguǎn huàisǐ
Aggresome	蛋白质沉淀聚集体	Dànbáizhí chéndiàn jùjí tǐ
Alachlor	甲草胺	Jiǎ cǎo àn
Albumin	白蛋白	Bái dànbái
Alkylating agents	烷化剂	Wán huà jì
Amyloidosis	淀粉样变性	Diànfěn yàng biànxìng
Anaemia	贫血	Pínxuě
Angina pectoris	心绞痛	Xīnjiǎotòng
Angiogenesis	血管新生	Xuèguǎn xīnshēng
Angiogenic switch	血管新生开关	Xuèguǎn xīnshēng kāiguān
Ankylosing spondylitis	强直性脊柱炎	Qiángzhí xìng jǐzhù yán
Antibody-dependent cellular cytotoxicity	抗体依赖的细胞介导的细胞毒性	Kàngtǐ yīlài de xìbāo jiè dǎo de xìbāo dúxìng
Antiemetic	止吐药	Zhǐ tǔ yào
Aplastic anaemia	再生障碍性贫血	Zàishēng zhàng'ài xìng pínxiě
Apoptosis	细胞凋亡	Xìbāo diāo wáng
Asthenia	无力	Wúlì
Autocrine signalling	自分泌信号传送	Zì fèn mì xìnhào chuánsòng
Autologous stem cell transplantation	自体幹細胞移植	Zìtǐ gànxìbāo yízhí
BAK	Bak	Bak
BAX	Bax	Bax
BCL-2	B 细胞淋巴瘤−2	B xìbāo línbā liú −2
BCL-2 inhibitor	Bcl-2 抑制剂	Bcl-2 yìzhì jì
Bisphosphonates	双膦酸盐类	Shuāng lìn suān yán lèi
Bone marrow aspiration and biopsy	骨髓活检和穿刺	Gǔsuǐ huójiǎn hé chuāncì
Bone marrow stromal cell	骨髓基质细胞	Gǔsuǐ jīzhì xìbāo
Bone remodelling	骨重塑	Gǔ chóng sù
Bortezomib	硼替佐米	Péng tìzuǒ mǐ
Bradycardia	心动过缓	Xīndòngguò huǎn
Buprenorphine	丁丙诺啡	Dīng bǐng nuò fēi
Calcinosis	皮肤钙化	Pífū gàihuà
Carfilzomib	卡非佐米	Kǎ fēi zuǒ mǐ
Cast nephropathy	管型肾病	Guǎn xíng shènbìng
Chlorophenol	氯酚	Lǜ fēn
Chromatin	染色质	Rǎnsè zhí
Complete response	完全缓解	Wánquán huǎnjiě

Computed tomography	计算机断层	Jìsuànjī duàncéng
Corticosteroids	皮质类固醇	Pízhí lèigùchún
CRAB symptoms	CRAB 症状	CRAB zhèngzhuàng
Creatinine	肌酸酐	Jī suāngān
Creatinine clearance	肌酐清除率	Jīgān qīngchú lǜ
Cyclophospamide	环磷酰胺	Huán lín xiān'àn
Cytokine	细胞因子	Xìbāo yīnzǐ
Daratumumab	达雷妥尤单抗	Dá léi tuǒ yóu dān kàng
DDT	滴滴涕	Dīdītì
Deep vein thrombosis	深静脉血栓形成	Shēn jìngmài xiě shuān xíngchéng
Denosumab	地舒单抗	De shū dān kàng
Dexamethasone	地塞米松	De sāi mǐsōng
Diabetes Mellitus	糖尿病	Tángniàobìng
Dichloromethane	二氯甲烷	Èr lǜ jiǎwán
Disease free survival	无疾病存活期	Wú jíbìng cúnhuó qí
Doxorubicin	阿霉素	Ā méi sù
Duration of response	缓解持续时间	Huǎnjiě chíxù shíjiān
Epidural spinal cord compression	恶性脊髓压迫症	Èxìng jǐsuǐ yāpò zhèng
Erythropoietin	促红细胞生成素	Cù hóngxìbāo shēngchéng sù
Erythropoietin stimulating agent	红细胞生成刺激剂	Hóngxìbāo shēngchéng cìjī jì
Extracellular matrix	细胞外基质	Xìbāo wài jīzhì
Fentanyl	芬太尼	Fēn tài ní
Fluorescent in situ hybridization	荧光原位杂交	Yíngguāng yuán wèi zájiāo
Functional module	功能模块	Gōngnéng mókuài
Genome	基因组	Jīyīnzǔ
Glucocorticoids	糖皮质激素	Táng pízhí jīsù
Health-related quality of life	健康生活品质	Jiànkāng shēnghuó pǐnzhí
Hematopoietic microenvironment	造血微环境	Zàoxiě wēi huánjìng
Hepcidin	铁调素	Tiě diào sù
Histone acetylation	组蛋白赖氨酸乙酰化	Zǔ dànbái lài ān suān yǐxiān huà
Histone deacetylase	组蛋白去乙酰化酶	Zǔ dànbái qù yǐxiān huà méi
Histone deacetylase inhibitor	组蛋白去乙酰化酶抑制剂	Zǔ dànbái qù yǐxiān huà méi yìzhì jì
Hydromorphone	氢吗啡酮	Qīng mǎfēi tóng
Hyper viscosity	血液高度黏稠症候群	Xiěyè gāodù niánchóu zhènghòuqún
Hypercalcemia	高钙血症	Gāo gài xiě zhèng
Immunodeficiency	免疫缺陷	Miǎnyì quēxiàn
Immunoglobulin heavy chains	免疫球蛋白重链	Miǎnyì qiú dànbái zhòng liàn

Immunoglobulin light chains	免疫球蛋白轻链	Miǎnyì qiú dànbái qīng liàn
Immunomodulatory drug	免疫调节剂	Miǎnyì tiáojié jì
Immunoparesis	免疫不全麻痹	Miǎnyì bùquán mábì
Interferon	干扰素	Gānrǎo sù
Interleukin-6	白细胞介素-6	Báixìbāo jiè sù - 6
International Staging System	国际分期系统	Guójì fēnqí xìtǒng
Invasive aspergillosis	侵袭性肺麴菌病	Qīnxí xìng fèi qū jùn bìng
Isatuximab	伊莎妥昔单抗	Yī shā tuǒ xī dān kàng
Ixazomib	伊沙佐米	Yī shā zuǒ mǐ
Karyopherin	核转运蛋白	Hé zhuǎnyùn dànbái
Lactate dehydrogenase	乳酸脱氢酶	Rǔsuān tuō qīng méi
Lenalidomide	来那度胺	Lái nà dù àn
Leukaemia	白血病	Báixiěbìng
Leverage point	杠杆点	Gànggǎn diǎn
Low-dose computed tomography	低剂量电脑断层术	Dī jìliàng diànnǎo duàncéng shù
Lymphopenia	淋巴细胞减少	Línbā xìbāo jiǎnshǎo
Lymphopoiesis	淋巴细胞增殖	Línbā xì xìbāo zēng jī
Magnetic resonance imaging	磁共振成像	Cí gòngzhèn chéngxiàng
Melphalan	美法仑	Měi fǎ lún
Memory B-cell	记忆 B 细胞	Jìyì B xìbāo
Mitoxantrone	米托蒽醌	Mǐ tuō ēn kūn
Monoclonal antibody	单克隆抗体	Dān kèlóng kàngtǐ
Monoclonal gammopathy of undermined significance	意义未明的单克隆免疫球蛋白	Yìyì wèimíng de dān kèlóng miǎnyì qiú dànbái
Monoclonal immunoglobulin	单克隆免疫球蛋白	Dān kèlóng miǎnyì qiú dànbái
Morphine	吗啡	Mǎfēi
Multiple Myeloma	多发性骨髓瘤	Duōfā xìng gǔsuǐ liú
Myelosuppression	骨髓抑制	Gǔsuǐ yìzhì
NDSAID	解热镇痛抗炎药	Jiě rè zhèn tòng kàng yán yào
Necrosis	坏死	Huàisǐ
Neutropenia	嗜中性白血球缺乏症	Shì zhōng xìng báixiěqiú quēfá zhèng
Normocytic normochromic anaemia	正细胞性正色素性贫血	Zhèng xìbāo xìng zhèng sèsù xìng pínxiě
Nuclear magnetic resonance	核磁共振	Hécí gòngzhèn
Objective response rate	客观缓解率	Kèguān huǎnjiě lǜ
Opioids	阿片类药物	Āpiàn lèi yàowù
Osteoblast	成骨细胞	Chéng gǔ xìbāo
Osteoclast	破骨细胞	Pò gǔ xìbāo
Osteolytic lesion	溶骨性病变	Róng gǔ xìng bìngbiàn
Osteonecrosis of the jaw	颌骨坏死	Gé gǔ huàisǐ
Osteoporosis	骨质疏松症	Gǔ zhí shūsōng zhèng
Overall survival	总生存期	Zǒng shēngcún qī

Oxycodone	羟考酮	Qiǎng kǎo tóng
Panobinostat	帕比司他	Pà bǐ sī tā
Paracetamol	对乙酰氨基酚	Duì yǐxiān ānjī fēn
Paracrine signalling	旁分泌传讯	Páng fēnmì chuánxùn
Peripheral neuropathy	周围神经病变	Zhōuwéi shénjīng bìngbiàn
Pernicious anaemia	巨幼细胞性贫血	Jù yòu xìbāo xìng pínxuě
Phenoxyacetic acid	苯氧乙酸	Běn yǎng yǐsuān
Phosphoramide mustard	磷酰胺氮芥	Lín xiān'àn dàn jiè
Plasma cell	浆细胞	Jiāng xìbāo
Plasmablast	原浆细胞	Yuán jiāng xìbāo
Polydipsia	多渴	Duō kě
Polygenic disease	多基因疾病	Duō jīyīn jíbìng
Polymethylmethacrylate	聚甲基丙烯酸甲酯	Jù jiǎ jī bǐngxīsuān jiǎ zhǐ
Polyneuropathy	多发性神经病	Duōfā xìng shénjīngbìng
Polyuria	多尿	Duō niào
Pomalidomide	泊马度胺	Pō mǎ dù àn
Positron emission tomography	正电子发射断层成像	Zhèng diànzǐ fāshè duàncéng chéngxiàng
Positron emission tomography/computed tomography	正电子电脑断层扫描	Zhèng diànzǐ diànnǎo duàncéng sǎomiáo
Prednisone	泼尼松	Pō ní sōng
Progression free survival	无进展生存期	Wú jìnzhǎn shēngcún qī
Prostaglandin	前列腺素	Qiánlièxiàn sù
Proteasome	蛋白酶体	Dànbáiméi tǐ
Proteasome inhibitor	蛋白酶体抑制剂	Dànbáiméi tǐ yìzhì jì
Radiculopathy	神经根疾病	Shénjīng gēn jíbìng
Radiography	造影	Zàoyǐng
Relapsed Refractory Multiple Myeloma	复发难治性多发性骨髓瘤	Fù fà nánzhì xìng duōfā xìng gǔsuǐ liú
Revised International Staging System	修订的国际分期系统	Xiūdìng de guójì fēnqí xìtǒng
Rouleaux	缗錢狀紅血球凝集	Mín qián zhuàng hóngxiěqiú níngjí
Selective inhibitor of nuclear export	选择性核输出抑制剂	Xuǎnzé xìng hé shūchū yìzhì jì
Selinexor	塞利尼索	Sāi lì ní suǒ
Sepsis	败血症	Bàixiězhèng
Serum immunofixation	血清免疫固定电泳	Xuěqīng miǎnyì gùdìng diànyǒng
Serum protein electrophoresis	血清蛋白电泳	Xuěqīng dànbái diànyǒng
Signal transduction	细胞信号转导	Xìbāo xìnhào zhuǎn dǎo
Smouldering multiple myeloma	冒烟性多发性骨髓瘤	Mào yān xìng duōfā xìng gǔsuǐ liú
Systemic sclerosis	全身性硬化症	Quánshēn xìng yìnghuà zhèng

Thalidomide	沙利度股	Shā lì dù gǔ
Thrombocytopenia	血小板减少症	Xuèxiǎobǎn jiǎnshǎo zhèng
Time to progression	访视的至进展时间	Fǎng shì de zhì jìnzhǎn shíjiān
Time to treatment failure	至治疗失败时间	Zhì zhìliáo shībài shíjiān
Tumour suppressor gene	肿瘤抑制基因	Zhǒngliú yìzhì jīyīn
Urine immunofixation	尿免疫固定电泳	Niào miǎnyì gùdìng diànyǒng
Urine protein electrophoresis	尿免蛋白电泳	Niào miǎn dànbái diànyǒng
Vascular endothelial grow factor	血管内皮生长因子	Xiěguǎn nèipí shēngzhǎng yīnzǐ
VDJ Arrangement	VDJ 重组	Chóngzǔ
Venetoclax	维奈克拉	Wéi nài kèlā
Vertebroplasty	椎体成形术	Chuí tǐ chéngxíng shù
Vincristine	长春新碱	Zhǎngchūn xīn jiǎn
X-rays	X 射线	X shèxiàn
XPO1	核输出蛋白 1	Hé shūchū dànbái 1
Zoledronic acid	唑来膦酸	Zuò lái lìn suān
β_2-microglobulin	β_2 微球蛋白	β_2 wēi qiú dànbái

Chinese – English glossary
汉/英词典

Pinyin 拼音	<zh> 中文	<en> 英语
Ā méi sù	阿霉素	Doxorubicin
Āpiàn lèi yàowù	阿片类药物	Opioids
B xìbāo línbā liú −2	B 细胞淋巴瘤−2	BCL-2
Bái dànbái	白蛋白	Albumin
Báixìbāo jiè sù - 6	白细胞介素-6	Interleukin-6
Báixiěbìng	白血病	Leukaemia
Bàixiězhèng	败血症	Sepsis
Bak	Bak	BAK
Bax	Bax	BAX
Bcl-2 yìzhì jì	Bcl-2 抑制剂	BCL-2 inhibitor
Běn yǎng yǐsuān	苯氧乙酸	Phenoxyacetic acid
Chéng gǔ xìbāo	成骨细胞	Osteoblast
Chóngzǔ	VDJ 重组	VDJ Arrangement
Chuí tǐ chéngxíng shù	椎体成形术	Vertebroplasty
Cí gòngzhèn chéngxiàng	磁共振成像	Magnetic resonance imaging
CRAB zhèngzhuàng	CRAB 症状	CRAB symptoms
Cù hóngxìbāo shēngchéng sù	促红细胞生成素	Erythropoietin
Dá léi tuǒ yóu dān kàng	达雷妥尤单抗	Daratumumab
Dān kèlóng kàngtǐ	单克隆抗体	Monoclonal antibody
Dān kèlóng miǎnyì qiú dànbái	单克隆免疫球蛋白	Monoclonal immunoglobulin
Dànbáiméi tǐ	蛋白酶体	Proteasome
Dànbáiméi tǐ yìzhì jì	蛋白酶体抑制剂	Proteasome inhibitor
Dànbáizhí chéndiàn jùjí tǐ	蛋白质沉淀聚集体	Aggresome
De sāi mǐsōng	地塞米松	Dexamethasone
De shū dān kàng	地舒单抗	Denosumab
Dī jìliàng diànnǎo duàncéng shù	低剂量电脑断层术	Low-dose computed tomography
Diànfěn yàng biànxìng	淀粉样变性	Amyloidosis
Dīdītì	滴滴涕	DDT
Dīng bǐng nuò fēi	丁丙诺啡	Buprenorphine
Duì yǐxiān ānjī fēn	对乙酰氨基酚	Paracetamol
Duō jīyīn jíbìng	多基因疾病	Polygenic disease
Duō kě	多渴	Polydipsia
Duō niào	多尿	Polyuria
Duōfā xìng gǔsuǐ liú	多发性骨髓瘤	Multiple Myeloma

Duōfā xìng shénjīngbìng	多发性神经病	Polyneuropathy
Èr lǜ jiǎwán	二氯甲烷	Dichloromethane
Èxìng jǐsuǐ yāpò zhèng	恶性脊髓压迫症	Epidural spinal cord compression
Fǎng shì de zhì jìnzhǎn shíjiān	访视的至进展时间	Time to progression
Fēn tài ní	芬太尼	Fentanyl
Fù fà nánzhì xìng duōfā xìng gǔsuǐ liú	复发难治性多发性骨髓瘤	Relapsed Refractory Multiple Myeloma
Gànggǎn diǎn	杠杆点	Leverage point
Gānrǎo sù	干扰素	Interferon
Gāo gài xiě zhèng	高钙血症	Hypercalcemia
Gé gǔ huàisǐ	颌骨坏死	Osteonecrosis of the jaw
Gōngnéng mókuài	功能模块	Functional module
Gǔ chóng sù	骨重塑	Bone remodelling
Gǔ zhí shūsōng zhèng	骨质疏松症	Osteoporosis
Guǎn xíng shènbìng	管型肾病	Cast nephropathy
Guójì fēnqí xìtǒng	国际分期系统	International Staging System
Gǔsuǐ huójiǎn hé chuāncì	骨髓活检和穿刺	Bone marrow aspiration and biopsy
Gǔsuǐ jīzhì xìbāo	骨髓基质细胞	Bone marrow stromal cell
Gǔsuǐ yìzhì	骨髓抑制	Myelosuppression
Hé shūchū dànbái 1	核输出蛋白 1	XPO1
Hé zhuǎnyùn dànbái	核转运蛋白	Karyopherin
Hécí gòngzhèn	核磁共振	Nuclear magnetic resonance
Hóngxìbāo shēngchéng cìjī jì	红细胞生成刺激剂	Erythropoietin stimulating agent
Huàisǐ	坏死	Necrosis
Huán lín xiān'àn	环磷酰胺	Cyclophospamide
Huǎnjiě chíxù shíjiān	缓解持续时间	Duration of response
Huóhuà yòudǎo xìng gān gān tuō ān méi	活化诱导性甘肝脱氨酶	Activation-induced cytidine deaminase
Jī suāngān	肌酸酐	Creatinine
Jiǎ cǎo àn	甲草胺	Alachlor
Jiāng xìbāo	浆细胞	Plasma cell
Jiànkāng shēnghuó pǐnzhí	健康生活品质	Health-related quality of life
Jiě rè zhèn tòng kàng yán yào	解热镇痛抗炎药	NDSAID
Jīgān qīngchú lǜ	肌酐清除率	Creatinine clearance
Jìsuànjī duàncéng	计算机断层	Computed tomography
Jíxìng shèn xiǎoguǎn huàisǐ	急性肾小管坏死	Acute tubular necrosis
Jìyì B xìbāo	记忆 B 细胞	Memory B-cell
Jīyīnzǔ	基因组	Genome
Jù jiǎ jī bǐngxīsuān jiǎ zhǐ	聚甲基丙烯酸甲酯	Polymethylmethacrylate
Jù yòu xìbāo xìng pínxuě	巨幼细胞性贫血	Pernicious anaemia
Kǎ fēi zuǒ mǐ	卡非佐米	Carfilzomib

Kàngtǐ yīlài de xìbāo jiè dǎo de xìbāo dúxìng	抗体依赖的细胞介导的细胞毒性	Antibody-dependent cellular cytotoxicity
Kèguān huǎnjiě lǜ	客观缓解率	Objective response rate
Lái nà dù àn	来那度胺	Lenalidomide
Lín xiān'àn dàn jiè	磷酰胺氮芥	Phosphoramide mustard
Línbā xì xìbāo zēng jī	淋巴细胞增殖	Lymphopoiesis
Línbā xìbāo jiǎnshǎo	淋巴细胞减少	Lymphopenia
Lǜ fēn	氯酚	Chlorophenol
Mǎfēi	吗啡	Morphine
Mào yān xìng duōfā xìng gǔsuǐ liú	冒烟性多发性骨髓瘤	Smouldering multiple myeloma
Měi fǎ lún	美法仑	Melphalan
Mǐ tuō ēn kūn	米托蒽醌	Mitoxantrone
Miǎnyì bùquán mábì	免疫不全麻痹	Immunoparesis
Miǎnyì qiú dànbái qīng liàn	免疫球蛋白轻链	Immunoglobulin light chains
Miǎnyì qiú dànbái zhòng liàn	免疫球蛋白重链	Immunoglobulin heavy chains
Miǎnyì quēxiàn	免疫缺陷	Immunodeficiency
Miǎnyì tiáojié jì	免疫调节剂	Immunomodulatory drug
Mín qián zhuàng hóngxiěqiú níngjí	缗錢狀紅血球凝集	Rouleaux
Niào miǎn dànbái diànyǒng	尿免蛋白电泳	Urine protein electrophoresis
Niào miǎnyì gùdìng diànyǒng	尿免疫固定电泳	Urine immunofixation
Pà bǐ sī tā	帕比司他	Panobinostat
Páng fēnmì chuánxùn	旁分泌传讯	Paracrine signalling
Péng tìzuǒ mǐ	硼替佐米	Bortezomib
Pífū gàihuà	皮肤钙化	Calcinosis
Pínxuě	贫血	Anaemia
Pízhí lèigùchún	皮质类固醇	Corticosteroids
Pò gǔ xìbāo	破骨细胞	Osteoclast
Pō mǎ dù àn	泊马度胺	Pomalidomide
Pō ní sōng	泼尼松	Prednisone
Qiǎng kǎo tóng	羟考酮	Oxycodone
Qiángzhí xìng jǐzhù yán	强直性脊柱炎	Ankylosing spondylitis
Qiánlièxiàn sù	前列腺素	Prostaglandin
Qīng mǎfēi tóng	氢吗啡酮	Hydromorphone
Qīnxí xìng fèi qū jùn bìng	侵袭性肺麴菌病	Invasive aspergillosis
Quánshēn xìng yìnghuà zhèng	全身性硬化症	Systemic sclerosis
Rǎnsè zhí	染色质	Chromatin
Róng gǔ xìng bìngbiàn	溶骨性病变	Osteolytic lesion
Rǔsuān tuō qīng méi	乳酸脱氢酶	Lactate dehydrogenase
Sāi lì ní suǒ	塞利尼索	Selinexor
Shā lì dù gǔ	沙利度股	Thalidomide

Shēn jìngmài xiě shuān xíngchéng	深静脉血栓形成	Deep vein thrombosis
Shénjīng gēn jíbìng	神经根疾病	Radiculopathy
Shì zhōng xìng báixiěqiú quēfá zhèng	嗜中性白血球缺乏症	Neutropenia
Shuāng lìn suān yán lèi	双膦酸盐类	Bisphosphonates
Táng pízhí jīsù	糖皮质激素	Glucocorticoids
Tángniàobìng	糖尿病	Diabetes Mellitus
Tiě diào sù	铁调素	Hepcidin
Wán huà jì	烷化剂	Alkylating agents
Wánquán huǎnjiě	完全缓解	Complete response
Wéi nài kèlā	维奈克拉	Venetoclax
Wú jíbìng cúnhuó qí	无疾病存活期	Disease free survival
Wú jìnzhǎn shēngcún qī	无进展生存期	Progression free survival
Wúlì	无力	Asthenia
X shèxiàn	X 射线	X-rays
Xìbāo diāo wáng	细胞凋亡	Apoptosis
Xìbāo wài jīzhì	细胞外基质	Extracellular matrix
Xìbāo xìnhào zhuǎn dǎo	细胞信号转导	Signal transduction
Xìbāo yīnzǐ	细胞因子	Cytokine
Xiěguǎn nèipí shēngzhǎng yīnzǐ	血管内皮生长因子	Vascular endothelial grow factor
Xiěyè gāodù niánchóu zhènghòuqún	血液高度黏稠症候群	Hyper viscosity
Xīndòngguò huǎn	心动过缓	Bradycardia
Xīnjiǎotòng	心绞痛	Angina pectoris
Xiūdìng de guójì fēnqí xìtǒng	修订的国际分期系统	Revised International Staging System
Xuǎnzé xìng hé shūchū yìzhì jì	选择性核输出抑制剂	Selective inhibitor of nuclear export
Xuèguǎn xīnshēng	血管新生	Angiogenesis
Xuèguǎn xīnshēng kāiguān	血管新生开关	Angiogenic switch
Xuěqīng dànbái diànyǒng	血清蛋白电泳	Serum protein electrophoresis
Xuěqīng miǎnyì gùdìng diànyǒng	血清免疫固定电泳	Serum immunofixation
Xuèxiǎobǎn jiǎnshǎo zhèng	血小板减少症	Thrombocytopenia
Yī shā tuǒ xī dān kàng	伊莎妥昔单抗	Isatuximab
Yī shā zuǒ mǐ	伊沙佐米	Ixazomib
Yíngguāng yuán wèi zájiāo	荧光原位杂交	Fluorescent in situ hybridization
Yìyì wèimíng de dān kèlóng miǎnyì qiú dànbái	意义未明的单克隆免疫球蛋白	Monoclonal gammopathy of undermined significance
Yuán jiāng xìbāo	原浆细胞	Plasmablast
Zàishēng zhàng'ài xìng pínxiě	再生障碍性贫血	Aplastic anaemia

Zàoxiě wēi huánjìng	造血微环境	Hematopoietic microenvironment
Zàoyǐng	造影	Radiography
Zhǎngchūn xīn jiǎn	长春新碱	Vincristine
Zhèng diànzǐ diànnǎo duàncéng sǎomiáo	正电子电脑断层扫描	Positron emission tomography/computed tomography
Zhèng diànzǐ fāshè duàncéng chéngxiàng	正电子发射断层成像	Positron emission tomography
Zhèng xìbāo xìng zhèng sèsù xìng pínxiě	正细胞性正色素性贫血	Normocytic normochromic anaemia
Zhǐ tǔ yào	止吐药	Antiemetic
Zhì zhìliáo shībài shíjiān	至治疗失败时间	Time to treatment failure
Zhǒngliú yìzhì jīyīn	肿瘤抑制基因	Tumour suppressor gene
Zhōuwéi shénjīng bìngbiàn	周围神经病变	Peripheral neuropathy
Zì fèn mì xìnhào chuánsòng	自分泌信号传送	Autocrine signalling
Zìtǐ gànxìbāo yízhí	自体幹細胞移植	Autologous stem cell transplantation
Zǒng shēngcún qī	总生存期	Overall survival
Zǔ dànbái lài ān suān yǐxiān huà	组蛋白赖氨酸乙酰化	Histone acetylation
Zǔ dànbái qù yǐxiān huà méi	组蛋白去乙酰化酶	Histone deacetylase
Zǔ dànbái qù yǐxiān huà méi yìzhì jì	组蛋白去乙酰化酶抑制剂	Histone deacetylase inhibitor
Zuò lái lìn suān	唑来膦酸	Zoledronic acid
β_2 wēi qiú dànbái	β_2微球蛋白	β_2-microglobulin

Abbreviations

Abbreviation	Full form
MM	Multiple Myeloma
MGUS	Monoclonal Gammopathy of Undermined Significance
SMM	Smouldering Multiple Myeloma
MBC	Memory B-cell
IgH	Immunoglobulin Heavy Chain
IgL	Immunoglobulin Light Chain
AID	Activation-Induced Cytidine Deaminase
GC	Germinal Center
ECM	Extracellular Matrix Protein
BMSC	Bone Marrow Stromal Cell
VEGF	Vascular Endothelial Grow Factor
GLOBOCAN	Global Center Observatory
HHS	US Department of Health and Human Services
AIRTRUM	Associazione Italiana Registro Tumori
OS	Overall Survival
INT	Istituto Nazionale Tumori
SEER	Surveillance, Epidemiology and End Results
FISH	Fluorescent in Situ Hybridization
DM2	Type 2 Diabetes Mellitus
BMI	Body Mass Index
WHO	World Health Organization
NDMM	Newly Diagnosed Multiple Myeloma
IL-6	Interleukin 6
DDT	Dichlorodiphenyltrichloroethane
IARC	International Agency for Research on Cancer
ISS	International Staging System
R-ISS	Revised International Staging System
DS	Durie-Salmon Staging System
IMWG	International Myeloma Working Group
LDH	Lactate Dehydrogenase
CA	Chromosomal Abnormalities
iFISH	Interphase Fluorescent in Situ Hybridization
PFS	Progression-Free Survival
CN	Cast Nephropathy
RBC	Red Blood Cell
PC	Plasma Cell
CT	Computed Tomography
PET-TC	Positron-Emission Tomography / Computed Tomography
NMR	Nuclear Magnetic Resonance
RNA	Ribonucleic Acid
sFLC	Serum Free Light Chain
MRI	Magnetic Resonance Imaging
BMPC	Bone Marrow Plasma Cell
MC	Monoclonal Component
Ig	Immunoglobulin
SPEP	Serum Protein Electrophoresis
IFE	Immunofixation

UPEP	Urine Protein Electrophoresis
WBLD-CT	Whole-body Low-dose Computed Tomography
GP	General Practitioner
PPV	Positive Predictive Value
MP	Melphalan-Prednisone
ORR	Objective Response Rate
CR	Complete Remission
VAD	Vincristine-Doxorubicin-Dexamethasone
ASCT	Autologous Stem Cell Transplantation
IMiD	Immunomodulatory drugs
PI	Proteasome Inhibitor
mAb	Monoclonal Antibody
VND	Vincristine-Mitoxantrone-Dexamethasone
AEs	Adverse Events
TRM	Treatment Related Mortality
FDA	Food and Drug Administration
EMA	European Medicine Agency
PN	Peripheral Neuropathy
QOL	Quality of Life
DVT	Deep Vein Thrombosis
RRMM	Relapsed/Refractory Multiple Myeloma
IRR	Infusion Related Reaction
ADCC	Antibody-Dependent Cellular Cytotoxicity
MRD	Minimal Residual Disease
HDM	High-dose Melphalan
PR	Partial Response
VD	Bortezomib-Dexamethasone
VCD	Bortezomib-Cyclophosphamide-Dexamethasone
VTD	Bortezomib-Thalidomide-Dexamethasone
VGPR	Very Good Partial Response
ORR	Objective Response Rate
ADL	Activities of Daily Living
IADL	Instrumental Activities of Daily Living
CCI	Charlson Comorbidity Index
MPT	Melphalan-Prednisone-Thalidomide
MPV	Melphalan-Prednisone-Bortezomib
RD	Lenalidomide-Dexamethasone
VRD	Bortezomib-Lenalidomide-Dexamethasone
IFN	Interferon
EFS	Event-Free Survival
SPM	Secondary Primary Malignancies
ESMO	European Society for Medical Oncology
BP	Bisphosphonate
SRE	Skeletal Related Event
ONJ	Osteonecrosis of the Jaw
PMMA	Polymethylmethacrylate
VCF	Vertebral Compression Fracture
NSAID	Non-Steroid Anti-inflammatory Drugs
HDAC	Histone Deacetylase
MR	Minimal Response

DoR	Duration of Response
SINE	Selective Inhibitor of Nuclear Exportin
TSP	Tumour Suppression Protein

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Images and Tables

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Figure 2

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