中華民國人類遺傳學會 2024 春季會

2024 THGS Spring Symposium

Genome sequencing: challenges and opportunities

3/10 日

臺大醫院國際會議中心

301 廳

指導單位：

衛生福利部 Ministry of Health and Welfare

主辦單位：

國家衛生研究院 National Health Research Institutes

中華民國人類遺傳學會 TAIWAN HUMAN GENETICS SOCIETY

合辦單位：

台大醫院兒童醫院 NTUCH

國立臺灣大學醫學院附設醫院兒童醫院 National Taiwan University Children's Hospital

中華民國人類遺傳學會
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方菊雄　林清淵
張建國　蔡世峯
魏耀揮

秘書長

簡穎秀

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PROGRAM AGENDA

March 10th 2024 (Sunday)

NTUH International Convention Center, R301
(No. 2, Xuzhou Road, Zhongzheng District 100, Taipei City.)

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08:20-08:50	Registration			*Poster Set up*
08:50-09:00	Opening Remark		Fuu-Jen Tsai	
09:00-12:10	***<Session I> The Challenges and Solutions of Undiagnosed Diseases***			
09:00-09:50	**Undiagnosed Diseases Network in the USA, Program Overview**	Danica Novacic	Hung-Yi Chiou	*Poster Viewing 3F / Lobby*
09:50-10:40	**Let Us Treasure and Share Our Exceptions: Story on Discovery of New Diseases**	Kenjiro Kosaki		
10:40-11:00	Coffee Break			*Poster Session 3F / Lobby*
11:00-11:50	**Korean Genetic Diagnosis Program for Rare Diseases**	Jong-Hee Chae	Wuh-Liang Hwu	*Poster Viewing 3F / Lobby*
11:50-12:10	**The Undiagnosed Disease Platform in Taiwan**	Ni-Chung Lee		
12:10-13:00	Lunch Time			
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13:30-14:00	**[Special Lecture] From Variants to Therapies: Progress in Treating Patients with Inherited Skin Diseases**	John McGrath	Chao-Kai Hsu	
14:00-17:00	***<Session II> Genome screening: Current status and Ethics Consideration***			
14:00-14:40	**Ethics in Genomic Screening: How to Consider in gNBS?**	Daniel Fu-Chang Tsai	Yin-Hsiu Chien	
14:40-15:10	**Genetic Studies of Genodermatoses: Personal Experience in Epidermolysis Bullosa**	Chao-Kai Hsu	Hsiang-Yu Lin	
15:10-15:40	**Organ Transplant Donor and Recipient Perspectives**	Feng-Jung Yang		
15:40-16:00	Coffee Break			*Poster Removal*
16:00-16:30	**Carrier Screening**	Ming Chen	Pei-Lung Chen	
16:30-17:00	**How Polygenetic Risk Score Contributes to Human Leukocyte Antigen Disease Association?**	Fuu-Jen Tsai		
17:00-17:10	Award & Closing Ceremony		Fuu-Jen Tsai	

08:50-09:00 Opening Remark

PRESIDENT

蔡輔仁 Fuu-Jen Tsai

Taiwan Human Genetic Society

PRESENT POSITION

Vice President and Distinguished Professor of Pediatrics, China Medical University
Chief, Department of Medical Research and Medical Genetics, China Medical University Hospital
President, Taiwan Human Genetics Society
President, Taiwan Foundation for Rare Disorders

EDUCATION

MD, China Medical University
Ph.D., Institute of Chinese Medicine, China Medical University

BRIEF CHRONOLOGY OF EMPLOYMENT

Dean, College of Chinese Medicine, China Medical University
Dean, Office of Research and Development, China Medical University

SELECTED PUBLICATIONS

1. The genome-wide association study of serum IgE levels demonstrated a shared genetic background in allergic diseases. Lu HF, Chou CH, Lin YJ, Uchiyama S, Terao C, Wang YW, Yang JS, Liu TY, Wong HS, Chen SC, Tsai FJ*. Clin Immunol. 2024 Mar;260:109897.
2. Identification of the efficacy of parentage testing based on bi-allelic autosomal single nucleotide polymorphism markers in Taiwanese population. Chen YC, Lin WD, Liu TY, Tsai FJ*. Forensic Sci Med Pathol. 2024 Feb 12. d
3. Risk of depression in patients with pneumoconiosis: A population-based retrospective cohort study. Lee HM, Liu DY, Hsu HL, Yu TL, Yu TS, Shen TC, Tsai FJ*. J Affect Disord. 2024 Feb 16:S0165-0327(24)00366-5.
4. Acupuncture's long-term impact on depression prevention in primary dysmenorrhea: A 19-year follow-up of a Taiwan cohort with neuroimmune insights. Liao CC, Lin CL, Tsai FJ, Chien CH, Li JM. J Affect Disord. 2024 Jan 1;344:48-60.
5. The largest genome-wide association study for breast cancer in Taiwanese Han population. Hsu YC, Chen HL, Cheng CF, Chattopadhyay A, Chen PS, Lin CC, Chiang HY, Liu TY, Huang CH, Kuo CC, Chuang EY, Lu TP, Tsai FJ. Breast Cancer Res Treat. 2024 Jan;203(2):291-306.

09:00-10:40 <Session I> The Challenges and Solutions of Undiagnosed Diseases

MODERATOR

邱弘毅 Hung-Yi Chiou

PRESENT POSITION

Distinguished Investigator and Director
Institute of Population Health Sciences, National Health Research Institutes, Taiwan

EDUCATION

1996	Ph.D. - Epidemiology of National Taiwan University
1989	M.S. - Public Health of National Taiwan University
1985	B.S. - Public Health of National Taiwan University

BRIEF CHRONOLOGY OF EMPLOYMENT

2013/10-Present	President-Elected, APACPH, Asia-Pacific Academic Consortium for Public Health
2020/09-Present	Distinguished Investigator and Director, Institute of Population Health Sciences, National Health Research Institutes, Taiwan
2020/07-Present	Board Director, International Cooperation and Development Fund ICDF
2019/10-Present	Supervisor, Taiwan Public Health Association
2017/10-Present	Finance Vice President, APACPH, Asia-Pacific Academic Consortium for Public Health
2017/04-Present	Distinguished Professor, Master program in Applied Molecular Epidemiology, Taipei Medical University
2017/02-Present	President, Taiwan Society for Development of Long-Term Care and Senior Health Management

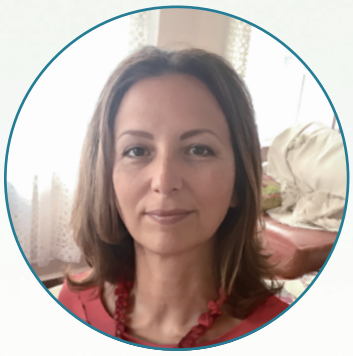
SELECTED PUBLICATIONS

1. Lam F, Liao CC, Chen TL, Huang YM, Lee YJ, Chiou HY (2023, Jun). Share Outcomes after surgery in patients with and without recent influenza: a nationwide population-based study. Front Med (Lausanne).
2. Bui C, Lin LY, Lin CJ, Chiu YW, Chiou HY. (2023, Mar). Association betweenclustering of unhealthy behaviors and depressive symptom among adolescents in Taiwan: A nationwide cross-sectional survey. Front Public Health.

09:00-09:50 Undiagnosed Diseases Network in the USA, Program Overview

SPEAKER

Danica (Donna) Novacic



PRESENT POSITION

Undiagnosed Diseases Program (UDP), NHGRI, NIH, Staff Physician, Internal Medicine

EDUCATION

2005/08	Residency - Internal Medicine, University of Maryland Medical School
2001/04	Medical School, University of Maryland
1996/08	Post-Bac Pre-Medical - University of Maryland, Baltimore County
1988-1991	B.A. - Accounting, Loyola College, Baltimore, Maryland

BRIEF CHRONOLOGY OF EMPLOYMENT

2009/01-2015/03	University of Maryland Baltimore Washington Medical Center Hospitalist and Medical Director of Inpatient Team, Internal Medicine Hospitalist Group
2005/06-2008/12	Internal Medicine Medical Resident and Researcher, University of Maryland Medical System, Baltimore MD
1991-1995	Accountant, C.W. Amos & Co. Regional Public Accounting Firm Departments of Management Information Systems Audit and Taxation
1989-1990	Property management, EG Rock Property Management

SELECTED PUBLICATIONS

1. Erdinc D et al, Pathological variants in TOP3A cause distinct disorders of mitochondrial and nuclear genome stability. EMBO Mol Med. 2023 May 8;15(5):e16775. doi: 10.15252/emmm.202216775. Epub 2023 Apr 4. PMID: 37013609; PMCID: PMC10165364.
2. Schoch K, et al, Clinical sites of the Undiagnosed Diseases Network: unique contributions to genomic medicine and science. Genet Med. 2021 Feb;23(2):259-271. doi: 10.1038/s41436-020-00984-z. Epub 2020 Oct 23. PMID: 33093671; PMCID: PMC7867619.
3. Beck DB et al, Somatic Mutations in UBA1 and Severe Adult-Onset Autoinflammatory Disease, N Engl J Med. 2020 Dec 31;383(27):2628-2638. doi: 10.1056/ NEJMoa2026834. Epub 2020 Oct 27.PMID: 33108101
4. Ray EC, Boyd-Shiwarski CR, Liu P, Novacic D, Cassiman D, SGLT2 Inhibitors for Treatment of Refractory Hypomagnesemia: A Case Report of 3 Patients, Kidney Medicine (2020), doi: 10.1016/j.xkme.2020.01.010.

Undiagnosed Diseases Network in the USA, Program Overview
- Abstract -

Danica Novacic, MD

Millions of people in the United States are living with some form of a rare or previously undocumented, poorly understood disease. The vast majority of these have a genetic etiology or predisposition driven by genetic polymorphisms that are not well understood. The United States National Center for Advancing Translational Sciences (NCATS) identifies about 10,000 diseases considered rare which taken together, amount to millions of patients. Despite this, most physicians in the community infrequently identify a patient with a specific rare or undiagnosed condition. Often there is a lack of insight or time to recognize a rare syndrome, lack of tools to establish an accurate diagnosis, and lack of resources to manage and treat these conditions. In many instances this results in years of misdiagnosis and failed treatments for these patients. Those unable to secure any diagnosis are unable to draw on resources such as needed services or treatment where one may exist. Although a physician may infrequently encounter a specific rare disease, in totality there is a large unmet need to care for this large population of people with rare, poorly understood conditions. Amongst them are not only rare, but also many patients that have no discernible diagnosis even after genetic testing. They are truly “undiagnosed” and have no central guidelines to manage their care. Yet there is so much to learn from these patients. To address this need, the Undiagnosed Diseases Program was established at the United States National Institutes of Health (NIH) under the Human Genome Research Institute in 2008. The program was funded by the NIH Common Fund as a pilot program to thoroughly investigate undiagnosed medical cases that eluded diagnosis and may have a yet unclear genetic basis. The goals are to assist in obtaining an accurate diagnosis, to discover new diseases and provide insight into human genetics. We select patients that have no diagnosis despite objective findings on testing. We preform extensive phenotyping and genetic testing. If clinical genetic testing does not yield a diagnosis, then an agnostic analysis pipeline is employed. Pathologic genetic findings are confirmed wherever possible with functional testing in our translational lab or in animal models thru collaboration with our animal model core. Cases are published wherever possible to contribute to general knowledge of pathophysiology and genomics. Since 2008 our program has expanded to the Undiagnosed Diseases Network with additional clinical sites across the US and internationally as the UDN-I, Undiagnosed Disease Network International. I will present the organizational structure and logistical workings of our program as well as show example cases moving thru the protocol process.

09:50-10:40 Let Us Treasure and Share Our Exceptions: Story on Discovery of New Diseases

SPEAKER

Kenjiro Kosaki

PRESENT POSITION

Director and Professor, Center for Medical Genetics, Keio University School of Medicine

EDUCATION

1998	Ph.D. - Keio University, Doctor of Medical Science, Tokyo, Japan
1989	M.D. - Keio University, Tokyo, Japan
1985	B.S. - Keio University, Tokyo, Japan

BRIEF CHRONOLOGY OF EMPLOYMENT

2012/06-Present	Director, Center for Medical Genetics Professor of Medical Genetics, Keio University School of Medicine, Tokyo, Japan
2003/05-2011/05	Chief, Division of Medical Genetics and Dysmorphology Associate Professor of Pediatrics, Keio University School of Medicine, Tokyo, Japan
1999/04-2003/04	Chief, Division of Medical Genetics and Dysmorphology, Assistant Professor of Pediatrics, Keio University School of Medicine, Tokyo, Japan
1998/09-1999/03	Instructor of Medical Genetics, Department of Pediatrics, Keio University School of Medicine, Tokyo, Japan

SELECTED PUBLICATIONS

1. Kuroda A, Namkoong H, Iwami E, Tsutsumi A, Nakajima T, Shinoda H, Katada Y, Iimura J, Suzuki H, Kosaki K, Terashima T. X-linked inheritance of primary ciliary dyskinesia and retinitis pigmentosa due to RPGR variant: A case report and literature review. Respirol Case Rep. 2023 Oct 31;11(12):e01240. doi: 10.1002/rcr2.1240. eCollection 2023 Dec.
2. Kurosawa R, Iida K, Ajiro M, Awaya T, Yamada M, Kosaki K, Hagiwara M. PDIVAS: Pathogenicity predictor for Deep-Intronic Variants causing Aberrant Splicing. BMC Genomics. 2023 Oct 10;24(1):601. doi: 10.1186/s12864-023-09645-2.
3. Arai H, Noguchi A, Shina K, Otaka S, Takahashi I, Kosaki K, Takahashi T. A child with branchio-oto-renal spectrum disorder carrying an SIX1 variant. Pediatr Int. 2023 Jan-Dec;65(1):e15638. doi: 10.1111/ped.15638.

Let us treasure and share our exceptions: Story on discovery of new diseases
- Abstract -

Kenjiro Kosaki, MD, PhD

Professor William Bateson, who coined the term “genetics”, left the message “Treasure your exception” to young geneticists. We all value this phrase because even a limited number of patients can teach us a scientific truth. Classic syndromes as cataloged in the textbook "Smith's Recognizable Patterns of Human Malformation" were established mostly through intuitional analysis of exceptional cases by gifted syndromologists and causative genes were identified afterwards by basic scientists. The invention of next-generation sequencing has revolutionized the approach to new disease discovery in that hypothesis pondered one or two exceptional patients can be confirmed through genomic studies and follow-up model organism studies in a strait forward manner. Our laboratory has shown that variants in PDGFRB, CDC42, DHX9, DPYSL2 (CRMP2), CTR9, CDK19, and CNOT2 are associated with previously unknown human genetic diseases. Among those genes, activating pathogenic variants in PDGFRB cause the so-called Kosaki overgrowth syndrome [KOGS], which is characterized by overgrowth, skeletal abnormalities including craniosynostosis, and aneurysm formation of the systemic vessels. More than ten patients with this entity have been identified globally and the entity has been cataloged in the most recent edition of Smith's textbook mentioned above.

Tyrosine kinase inhibitors [TKIs] have shown promising suppressive effect on KOGS-associated activating mutations and an international consortium for developing therapy has been organized. Using gene editing, we have developed the mouse model of KOGS and demonstrated that mice with activating Pdgfrb variants recapitulate the human phenotype, including craniosynostosis. The use of the mouse model will help us to screen the best TKI for treatment of KOGS. Our collaborators have also shown that somatic (i.e., mosaic) activating variants in PDGFRB in humans are associated with cerebral arterial aneurysm. The use of TKIs was effective in suppressing the dilatation of cerebral arteries in mice. Therefore, a therapeutic effect of TKIs is expected in not only exceptional patients with KOGS but also a large number of non-syndromic patients with cerebral arterial aneurysm. It is encouraging to look back that scientific evidence learnt from only two patients in my clinic has evolved to have therapeutic relevance to countless patients with brain aneurysm through global collaboration.

11:00-12:10 <Session I> The Challenges and Solutions of Undiagnosed Diseases

MODERATOR

胡務亮 Wuh-Liang Hwu

PRESENT POSITION

Distinguished Research Fellow, Center for Precision Medicine, China Medical University Hospital
Professor Emeritus, Department of Pediatrics, College of Medicine, National Taiwan University
Adjunct Attending Physician, Department of Medical Genetics, National Taiwan University Hospital

EDUCATION

1992-1997	Ph.D. - Institute of Molecular Medicine, National Taiwan University, Taipei, Taiwan
1978-1984	M.D. - College of Medicine, National Taiwan University, Taipei, Taiwan

BRIEF CHRONOLOGY OF EMPLOYMENT

1990-2023	Attending Physician, Department of Medical Genetics and Pediatrics, National Taiwan University Hospital, Taipei, Taiwan
2010-2023	Professor, Department of Pediatrics, National Taiwan University Hospital, Taipei, Taiwan
2018-2021	Deputy Director, Department of Pediatrics, National Taiwan University Hospital, Taipei, Taiwan
2006-2012	Director, Department of Medical Genetics, National Taiwan University Hospital, Taipei, Taiwan

SELECTED PUBLICATIONS

1. Hwu WL. Disorders of bioamine metabolism. 4th Asia pacific course: Early diagnosis and early treatment of inherited metabolic disease. Recordati Rare Disease Foundation. Tokyo, Nov 23-25, 2023
2. Hwu WL. Long term clinical trials for eladocagene exuparvovec, a gene therapy for AADC deficiency. PLENARY, 30th Annual Congress European Society of Gene and Cell Therapy (ESGCT), Brussels, Belgium, Oct 24, 2023

11:00-11:50 Korean Genetic Diagnosis Program for Rare Diseases

SPEAKER

Jong-Hee Chae

PRESENT POSITION

Professor, Department of Genomic Medicine, Seoul National University Hospital, Department of Pediatrics, Seoul National University College of Medicine, Division of Pediatric Neurology, Seoul National University Children's Hospital, Seoul Korea
Director, Rare Disease Center, SNUH

EDUCATION

2002	Ph.D. - Seoul National University, College of Medicine, Seoul Korea
1992	M.D. - Seoul National University, College of Medicine, Seoul Korea

ACADEMIC TRAINING

2015	Korean Board of Medical Genetics
2007	Korean Board of Pediatric Neurology
1997	Korean Board of Pediatrics
1992	Licensed to Practice of Medicine in Korea

PROFESSIONAL ORGANIZATION AND SOCIETIES

2022-Present	Vice-President, Korean Child Neurology Society
2015-Present	Executive Board, Asian Oceanian Muscle Center
2019-Present	Director, Coordinating Center, Korea Rare Disease Network
2021-Present	Chair, Scientific Committee Korean Society of Medical Genetics& Genomics

PUBLICATIONS

230 Peer Review SCI Publications
Major Research Interests:

- Medical genetics and genomics in Rare diseases
- Neuromuscular disorders
- Neurodevelopmental Disorders
- Mitochondrial disorders
- Neurodegenerative diseases

Korean Genetic Diagnosis Program for Rare Diseases
- Abstract -

Jong-Hee Chae, MD, PhD

Over the past decade, the field of genetic diagnosis for rare diseases has undergone a significant paradigm shift, thanks to advancements in molecular genetics. In response to these changes, we have developed a stepwise approach to the genetic diagnosis of rare diseases. For known genetic rare diseases, we offer a range of genetic analyses, including microarray, single gene tests, and NGS-based panel tests, which are partially or fully covered by government insurance. For undiagnosed rare diseases, our team has been actively involved in the Korean Undiagnosed Disease Program (K-UDP) since its pilot launch in 2017. Our initial goal was to validate a concept and develop a system that is compatible with Korea's medical environment. Buoyed by our early results and the observed potential, we received a three-year grant from the government, followed by an additional two-year extension, leading to the formal establishment of the K-UDP. Throughout its operation, the K-UDP has successfully diagnosed approximately 40% of patients who were previously undiagnosed. Our involvement has also led to the discovery of new genes and fostered international collaborations. Beyond its clinical impact, we have put together a team of basic scientists with expertise in animal modeling, protein structure, iPSCs, cell signaling, and proteomics. This interdisciplinary collaboration has deepened our understanding of gene functions and has facilitated the sharing of research insights.

This presentation will outline the strategy for genetic diagnosis of rare diseases in Korea and detail our six-year journey with the K-UDP. We aim to share our experiences, challenges, and achievements, highlighting our collaborative efforts and the importance of further communication with Taiwan, the Asian network, and globally.

11:50-12:10 The Undiagnosed Disease Platform in Taiwan

SPEAKER

李妮鍾 Ni-Chung Lee

PRESENT POSITION

Attending Physician, Department of Medical Genetics, NTUH
Clinical Professor, Department of Pediatrics, College of Medicine, NTU
Adjunct Professor, Genome and Systems Biology Degree Program, NTU

EDUCATION

2014	Ph.D., Graduate Institute of Clinical Medicine, College of Medicine, National Taiwan University
1999	M.D., Medical College, National Yang-Ming University

BRIEF CHRONOLOGY OF EMPLOYMENT

2021-Present	Clinical Professor, Department of Pediatrics, National Taiwan University Hospital, Taipei, Taiwan
2005-Present	Adjunct Professor, Genome and Systems Biology Degree Program, NTU
2016-2021	Clinical Associate Professor, Department of Pediatrics, National Taiwan University Hospital, Taipei, Taiwan
2013-2016	Clinical Associate Professor, Department of Pediatrics, National Taiwan University Hospital, Taipei, Taiwan

SELECTED PUBLICATIONS

1. Hsu RH, Lee CH, Chien YH, Lin SP, Hung MZ, Chen NC, Lin YL, Hwu WL, Lee NC. Utility of whole-exome sequencing for patients with multiple congenital anomalies with or without intellectual disability/developmental delay in East Asia population. Mol Genet Genomic Med. 2023 Feb 27:e2160.
2. Chu CM, Yu HH, Kao TL, Chen YH, Lu HH, Wu ET, Yang YL, Lin CH, Lin SY, Tsai MM, Chien YH, Hwu WL, Chen WP, Lee NC, Tseng CK. A missense variant in the nuclear localization signal of DKC1 causes Hoyeraal-Hreidarsson syndrome. NPJ Genom Med. 2022 Oct 30;7(1):64. (Co-corresponding author)
3. Lee NC, Chien YH, Wang CH, Wong SL, Peng SS, Tsai FJ, Hwu WL. Safety and efficacy of eliglustat combined to enzyme replacement therapy for lymphadenopathy in patients with Gaucher disease type 3. Mol Genet Metab Rep. 2022 Apr 19;31:100867.

The Undiagnosed Disease Platform in Taiwan
- Abstract -

Ni-Chung Lee, MD, PhD

The Undiagnosed Disease Network (UDN) in Taiwan operates under the umbrella of the Optimizing Pediatric Healthcare Network, an initiative sanctioned by the government in 2020. Its primary aim is to establish a specialized core hospital dedicated to diagnosing and caring for pediatric patients afflicted with complex or rare diseases. In tandem, the network has instituted a Pediatric Undiagnosed Disease Platform (Pediatric UDP), supported by an Expert Consultation Committee, to augment the diagnostic process. Since 2022, the Pediatric UDP has streamlined its services by centralizing contact through a single point of access for patients who meet enrollment criteria. The program's focus lies on intricate cases requiring multidisciplinary care and individuals who have undergone numerous examinations without receiving a definitive diagnosis. It also extends support to critically ill patients in the intensive care unit. This holistic approach encompasses genetic testing and analysis, employing methodologies such as Whole Exome Sequencing (WES), Whole Genome Sequencing (WGS), and RNA sequencing. Furthermore, the program offers the option to reanalyze existing data to provide a more thorough evaluation. Following meticulous analysis, the program facilitates discussions on clinical data and test results, culminating in the provision of personalized treatment and care plans tailored to each patient's unique circumstances. Presently, ten remote hospitals, including those in eastern and outlying islands, participate in this network, convening regular case discussion meetings. To date, 33 consultations have been received, with 31 cases enrolled in the program. The diagnostic yield currently stands at 30.3%, with the remaining cases awaiting diagnosis. For those without a diagnosis, regular reanalysis and the utilization of new sequencing technologies may be implemented.

13:30-14:00 [Special Lecture]
From Variants to Therapies: Progress in Treating Patients with Inherited Skin Diseases

MODERATOR

許釗凱 Chao-Kai Hsu

PRESENT POSITION

Professor, Department of Dermatology, College of Medicine, National Cheng Kung University, Taiwan

EDUCATION

2010-2017	Ph.D., Institute of Clinical Medicine, College of Medicine, National Cheng Kung University, Taiwan
1996-2003	M.D., Department of Medicine, Medical College of Medicine, National Cheng Kung University, Taiwan

BRIEF CHRONOLOGY OF EMPLOYMENT

2023/08-Present	Professor, Department of Dermatology, College of Medicine, National Cheng Kung University, Taiwan
2022/08-Present	Director, Genetic Center, National Cheng Kung University Hospital, Taiwan
2018/08-2023/07	Associate Professor, Department of Dermatology, College of Medicine, National Cheng Kung University, Taiwan
2014/08-2018/08	Assistant Professor, Department of Dermatology, National Cheng Kung University Hospital, Taiwan

SELECTED PUBLICATIONS

1. Tu WT, Chen PC, Chen WR, Wang JY, Huang YT, Wu YH, Su CL, Tang YA, Iwata H, Natsuga K, Chao SC, Sun HS, Tang MJ, Lee JYY, McGrath JA, Hsu CK. Mutational analysis of epidermolysis bullosa in Taiwan by whole-exome sequencing complemented by RNA sequencing: a series of 77 patients. Orphanet J Rare Dis. 2022 Dec;17(1):451.
2. Chen YF, Lu HC, Hou PC, Lin YC, Aala WJ, Onoufriadis A, McGrath JA, Chen YL, Hsu CK. Plasma metabolomic profiling reflects the malnourished and chronic inflammatory state in recessive dystrophic epidermolysis bullosa. J Dermatol Sci. 2022 Aug;107(2):82-88.
3. Hou PC, Wang HT, Abhee S, Tu WT, McGrath JA, Hsu CK. Investigational Treatments for Epidermolysis Bullosa. Am J Clin Dermatol. 2021 Nov;22(6):801-817.

13:30-14:00 [Special Lecture]
From Variants to Therapies: Progress in Treating Patients with Inherited Skin Diseases

SPEAKER

John McGrath

BIOGRAPHY

John McGrath is the Academic Head of St John's Institute of Dermatology in London where he also runs the Genetic Skin Disease Group. He holds the Mary Dunhill Chair in Cutaneous Medicine at King's College London and is Honorary Consultant Dermatologist to the Guy's and St Thomas' National Health Service Foundation Trust. He is also currently a Yu-Shan Fellow at the National Cheng Kung University in Tainan. His expertise is in genodermatoses, discovering genes and testing experimental therapies to improve patient care. He has held several leadership positions within European dermatology including serving as President for the European Society for Dermatological Research and the European Dermatology Forum. He has published >550 articles and will become editor-in-chief of the British Journal of Dermatology from July 2024.

From variants to therapies: progress in treating patients with inherited skin diseases.
- Abstract -

John McGrath, MD, PhD

The advent of next generation sequencing has led to a plethora of new genetic discoveries in the field of inherited skin diseases. Since 2009, there have been over 200 “genodermatoses” matched to specific gene pathology, including the identification of more than 50 brand new diseases. As in other fields, the new data have boosted mainstream molecular diagnostics for patients with widespread adoption of targeted gene panel screening for various categories of genodermatoses, such a skin fragility disorders, ichthyoses, and ectodermal dysplasias. Major improvements for patients with inherited skin diseases, thus far however, have been somewhat limited. Strategies to correct the primary gene defects through gene and cell-based approaches have created exciting science but to the benefit of just a few individuals and at great expense. More affordable and generalizable are complementary approaches to address disease mechanisms and patient symptoms. Two strategies have emerged: one is to start with an available drug (e.g. a biologic or small molecule) and to test widely in various disorders to see who might benefit; the other is to undertake multi-omic characterization of patient skin and blood to define disease signatures and thus deliver stratified or personalized prescribing. Both approaches are generating clinical gains. This presentation will reflect on recent progress in trying to address the unmet therapeutic needs of patients with inherited skin diseases, highlighting some recent successes but also the scale of trying to deliver effective treatments for most patients and to improve their quality of life.

14:00-14:40 <Session II> Genome screening: Current status and Ethics Consideration

MODERATOR

簡穎秀 Yin-Hsiu Chien

PRESENT POSITION

Visiting Staff, Department of Medical Genetics and Pediatrics, National Taiwan University Hospital, Taipei.
Clinical Professor, National Taiwan University College of Medicine, National Taiwan University, Taipei, Taiwan.
Head, Department of Medical Genetics, National Taiwan University Hospital, Taipei.

EDUCATION

Ph.D., Graduate Institute of Clinical Medicine, National Taiwan University, College of Medicine, Taipei, Taiwan.
M.D., Chang Gung Medical Collage, Taoyuan, Taiwan.

BRIEF CHRONOLOGY OF EMPLOYMENT

Resident in Pediatrics, Department of Pediatrics, National Taiwan University Hospital.
Clinical Fellow in Pediatric Allergy, Asthma and Immunology, Department of Pediatrics, National Taiwan University Hospital.
Clinical Fellow in Pediatrics Genetics and metabolisms, Department of Pediatrics, National Taiwan University Hospital.
Lecturer / Clinical Assistant Professor / Clinical Associate Professor, Department of Pediatrics, National Taiwan University College of Medicine.

SPECIALTIES

1. Pediatrics
2. Allergy and Immunology
3. Medical Genetics
4. Inborn errors of Metabolisms

14:00-14:40 Ethics in Genomic Screening: How to Consider in gNBS?

SPEAKER

蔡甫昌 Daniel Fu-Chang Tsai

PRESENT POSITION

Professor, Department & Graduate Institute of Medical Education and Bioethics, National Taiwan University College of Medicine
Attending Physician, Department of Medical Research, National Taiwan University Hospital
Director, Ethics Center of NTUH.
Director, Center for Biomedical Ethics, National Taiwan University
Head of Taiwan Unit, International Chair in Bioethics

EDUCATION

1999	Ph.D. in Health care ethics, Center for Social Ethics and Policy, The University of Manchester, United Kingdom
1989	M.D., National Taiwan University College of Medicine, Taiwan

BRIEF CHRONOLOGY OF EMPLOYMENT

2014-Present	Professor, Department & Research Institute of Medical Education & Bioethics, National Taiwan University College
2010-2014	Director, Department of Social Medicine, National Taiwan University College of Medicine
2013-2014	Professor, Department of Social Medicine, National Taiwan University College of Medicine

SELECTED PUBLICATIONS

1. Tsai, D.F.C. (2023) Genetic Testing Ethics, Taipei, Taiwan: National Taiwan University College of Medicine Press.
2. Tsai, D.F.C. (2021). Biomedical Research Ethics. Taipei, Taiwan: National Taiwan University College of Medicine Press.
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Ethics in Genomic Screening: How to Consider in gNBS?
- Abstract -

Daniel Fu-Chang Tsai, MD, PhD

This speech will investigate the ethical issues and policy in genomic screening. Common types and principles of population based genetic screening are first introduced. The ethical issues of population-based genetic screening which include practical and theoretical perspectives are analyzed. The national policies of the US, UK and France will be summarized and presented. Then the speaker will focus on the ethical considerations in genomic new born screen gNBS. At the rapid changing landscape of genomic testing, developing professional clinical practice guidelines for genomic screening is an important and timely task for the THGS.

MODERATOR

林翔宇 Hsiang-Yu Lin

PRESENT POSITION

Director, Division of Genetics and Metabolism, Department of Pediatrics, MacKay Memorial Hospital, Taipei, Taiwan
Director, Rare Disease Center, MacKay Memorial Hospital, Taipei, Taiwan
Director, Department of Medical Research, MacKay Children's Hospital, Taipei, Taiwan
Professor, Department of Medicine, MacKay Medical College, New Taipei City, Taiwan and MacKay Junior College of Medicine, Nursing and Management, Taipei, Taiwan

EDUCATION

Ph.D., Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan
M.D., School of Medicine, Taipei Medical University, Taipei, Taiwan

BRIEF CHRONOLOGY OF EMPLOYMENT

2006-Present	Attending Physician, Department of Pediatrics, MacKay Memorial Hospital, Taipei, Taiwan
2010-2011	Postdoctoral researcher, Ohio State University, USA
2015-Present	Director, Division of Genetics and Metabolism, Department of Pediatrics, MacKay Memorial Hospital, Taipei, Taiwan
2020-Present	Director, Rare Disease Center, MacKay Memorial Hospital, Taipei, Taiwan
2023-Present	Director, Department of Medical Research, MacKay Children's Hospital, Taipei, Taiwan
2020-Present	Professor, Department of Medicine, MacKay Medical College, New Taipei City, Taiwan and MacKay Junior College of Medicine, Nursing and Management, Taipei, Taiwan

SELECTED PUBLICATIONS

1. Hsiang-Yu Lin, Lee CL, Tu YR, Chang YH, Niu DM, Chang CY, Chiu PC, Chou YY, Hsiao HP, Tsai MC, Chao MC, Tsai LP, Yang CF, Su PH, Pan YW, Lee CH, Chu TH, Chuang CK, Lin SP. uantitative DNA Methylation Analysis and Epigenotype-Phenotype Correlations in Taiwanese Patients with Silver-Russell Syndrome. Int J Med Sci. 2024;21(1):8-18. (SCI)

14:40-15:10 Genetic Studies of Genodermatoses: Personal Experience in Epidermolysis Bullosa

SPEAKER

許釗凱 Chao-Kai Hsu

PRESENT POSITION

Professor, Department of Dermatology, College of Medicine, National Cheng Kung University, Taiwan

EDUCATION

2010-2017	Ph.D., Institute of Clinical Medicine, College of Medicine, National Cheng Kung University, Taiwan
1996-2003	M.D., Department of Medicine, Medical College of Medicine, National Cheng Kung University, Taiwan

BRIEF CHRONOLOGY OF EMPLOYMENT

2023/08-Present	Professor, Department of Dermatology, College of Medicine, National Cheng Kung University, Taiwan
2022/08-Present	Director, Genetic Center, National Cheng Kung University Hospital, Taiwan
2018/08-2023/07	Associate Professor, Department of Dermatology, College of Medicine, National Cheng Kung University, Taiwan
2014/08-2018/08	Assistant Professor, Department of Dermatology, National Cheng Kung University Hospital, Taiwan

SELECTED PUBLICATIONS

1. Tu WT, Chen PC, Chen WR, Wang JY, Huang YT, Wu YH, Su CL, Tang YA, Iwata H, Natsuga K, Chao SC, Sun HS, Tang MJ, Lee JYY, McGrath JA, Hsu CK. Mutational analysis of epidermolysis bullosa in Taiwan by whole-exome sequencing complemented by RNA sequencing: a series of 77 patients. Orphanet J Rare Dis. 2022 Dec;17(1):451.
2. Chen YF, Lu HC, Hou PC, Lin YC, Aala WJ, Onoufriadis A, McGrath JA, Chen YL, Hsu CK. Plasma metabolomic profiling reflects the malnourished and chronic inflammatory state in recessive dystrophic epidermolysis bullosa. J Dermatol Sci. 2022 Aug;107(2):82-88.
3. Hou PC, Wang HT, Abhee S, Tu WT, McGrath JA, Hsu CK. Investigational Treatments for Epidermolysis Bullosa. Am J Clin Dermatol. 2021 Nov;22(6):801-817.

Genetic Studies of Genodermatoses: Personal Experience in Epidermolysis Bullosa
- Abstract -

Chao-Kai Hsu, MD, PhD

Epidermolysis bullosa (EB) is a heterogeneous group of hereditary skin diseases characterized by skin fragility. Primary data on Taiwanese population remain scarce. We gathered clinical information from EB patients at National Cheng Kung University Hospital from January, 2012, to December, 2023. Diagnostic tests including transmission electron microscopy, immunofluorescence studies, and whole-exome sequencing (WES) were performed. The pathogenicity of novel splice-site variants was determined through reverse transcriptase-PCR of skin mRNA followed by Sanger and/or RNA sequencing. We have compiled a dataset of 120 patients, encompassing subtypes including EB simplex, junctional EB, and dystrophic EB. In our approach to molecular diagnosis, WES served as the first-line tool, successfully identifying pathogenic variants in more than 95% of our patient families. The pathogenic variants involved KRT5, KRT14, PLEC, COL17A1, LAMB3, LAMA3, ITGB4, and COL7A1 genes. The distinct clinical presentation and molecular pathology of EB in Taiwan expand our understanding of this disorder. In addition, we found that WES is an effective first-line diagnostic tool for identifying EB-associated variants, and RNA sequencing provides a valuable complement to WES when multiple potentially pathogenic splice-site variants are found. In the presentation, I will outline the protocol we currently employ and provide illustrations of some exemplary cases.

15:10-15:40 Organ Transplant Donor and Recipient Perspectives

SPEAKER

楊豐榮 Feng-Jung Yang

PRESENT POSITION

2006/07-Present	Attending Physician, Department of Internal Medicine, National Taiwan University Hospital Yun-Lin Branch
2019/04-Present	Director of Rare Disease Center, National Taiwan University Hospital Yun-Lin Branch
2016/08-Present	Medical Secretariat, National Taiwan University Hospital Yun-Lin Branch

EDUCATION

PhD, Graduate Institute of Clinical Medicine, College of Medicine, National Taiwan University, Taipei City, Taiwan
Master in Medical Science, Graduate Institute of Clinical Medicine, College of Medicine, National Taiwan University, Taipei City, Taiwan
Executive Master of Business Administration, College of Management, National Taiwan University, Taipei City, Taiwan

2015/11-2016/02	Research Scholar, Jonathan Schneck's Lab, Department of Pathology, Johns Hopkins University School of Medicine, USA
2017/06-2019/06	Executive Master of Health Administration (EMHA), The Institute of Health Policy and Management, National Taiwan University, Taipei City, Taiwan

BRIEF CHRONOLOGY OF EMPLOYMENT

2020/02-Present	Clinical Assistant Professor, Internal Medicine, College of Medicine, National Taiwan University
2019/08-Present	Adjunct Attending Physicians, Department of Medical Genetics, National Taiwan University Hospital
2006/07-Present	Adjunct Attending Physicians, Department of Internal Medicine, National Taiwan University Hospital
2006/07-Present	Attending Physician, Department of Internal Medicine, National Taiwan University Hospital Yun-Lin Branch

SELECTED PUBLICATIONS

1. Hsueh HW, Weng WC, Fan PC, Chien YH, Yang FJ, Lee WT, et al. The diversity of hereditary neuromuscular diseases: Experiences from molecular diagnosis. J Formos Med Assoc. 2022;121(12):2574-83.
2. Weng HL, Yang FJ, Chien YH, Chen PR, Lin ZX, Lee NC, Hwu WL. Lessons for the clinical nephrologist: dietary management of adult-onset type II citrullinemia in chronic kidney disease: a nutritional dilemma. J Nephrol. 2020;33(5):1111-3.
3. Lin YS, Yang FJ. Lymphovenous Anastomosis for Treating Lymphedema in IgG4-Related Disease. Plast Reconstr Surg Glob Open. 2020;8(9):e3111.

Organ Transplant Donor and Recipient Perspectives
- Abstract -

Feng-Jung Yang, MD, PhD

The growing accessibility and falling costs of genetic sequencing techniques have expanded the utilization of genetic testing in clinical practice. Genetic evaluation has been increasingly used for living donation to identify genetic diseases in potential candidates, especially younger ones and other organ involvement. However, genetic testing on asymptomatic living donors has many challenges and uncertainties. Not all transplant practitioners are aware of the limitations of genetic testing, are comfortable with selecting testing methods, comprehending test results, or providing counsel, and many do not have access to a genetic counselor or a clinical geneticist. Although genetic testing can be a valuable tool in living kidney donor evaluation, its overall benefit in donor evaluation has not been demonstrated, and it can also lead to confusion, inappropriate donor exclusion, or misleading reassurance. Until more published data becomes available, this lecture provides genetic counselors with information on the responsible use of genetic testing in evaluating living donor candidates.

16:00-17:00 <Session II> Genome screening: Current status and Ethics Consideration

MODERATOR

陳沛隆 Pei-Lung Chen

PRESENT POSITION

Professor, Graduate Institute of Medical Genomics and Proteomics, National Taiwan University
Attending Physician, Department of Medical Genetics, National Taiwan University Hospital

EDUCATION

2003-2009	Ph.D., Human Genetics and Molecular Biology Program, Institute of Genetic Medicine, Johns Hopkins School of Medicine
2000-2002	Master of Medical Science, Graduate Institute of Clinical Medicine, NTU
1988-1995	M.D., College of Medicine, NTU

BRIEF CHRONOLOGY OF EMPLOYMENT

2023-Present	Professor, Graduate Institute of Medical Genomics and Proteomics, NTU
2019-Present	Director, Graduate Institute of Medical Genomics and Proteomics, NTU
2016-2023	Associate Professor, Graduate Institute of Medical Genomics and Proteomics, NTU
2011-2016	Assistant Professor, Graduate Institute of Medical Genomics and Proteomics, NTU
2013	Laboratory Director, Laboratory of Molecular Genetic Diagnostics, NTUH

SELECTED PUBLICATIONS

1. Hsu et al. (2023, Dec). Complete genomic profiles of 1496 Taiwanese reveal curated medical insights. Journal of Advanced Research, https://doi.org/10.1016/j.jare.2023.12.018
2. Lin et al. (2022, Sep). Profiling genes encoding the adaptive immune receptor repertoire with gAIRR Suite. Frontiers in Immunology, 13:922513
3. Chan et al. (2022, Apr). Predicted protein structure variations indicate the clinical presentation of CYP4V2-related Bietti crystalline dystrophy. Retina, 42(4):797-806
4. Lin et al. (2021, Oct). Hearing impairment with mono-allelic GJB2 variants: a GJB2 cause or non-GJB2 cause? Journal of Molecular Diagnostics, 23(10):1279-1291
5. Chen et al. (2021, Feb). Genetic characteristics and epidemiology of inherited retinal degeneration in Taiwan. npj Genomic Medicine, 6(1):1-8.

16:00-16:30 Carrier Screening

SPEAKER

陳明　Ming Chen

PRESENT POSITION

Chief Medical Director, Changhua Christian Hospital, Taiwan
Professor, Dept. Post-Baccalaureate Medicine, NCHU, Taiwan

EDUCATION

2008	Ph.D., NTU
2002	MSc with distinction in Medical Genetics
1995	M.D., NTU

BRIEF CHRONOLOGY OF EMPLOYMENT

2018	Professor, certified by DOE of Taiwanese government
2015	Associate Professor
2008	Associate Professor
2006	Lecturer
2004-Present	Department of Obstetrics and Gynecology, CCH, Taiwan
2003-2004	Dept. Medical Genetics, NTUH, Taiwan

SELECTED PUBLICATIONS

1. Wu WJ et al., Wu WJ#, Ma GC#, Chang TY, Lee MH, Lin WH, Chen M*. (2023, Sep) Outcome and etiology of fetal pleural effusion, fetal ascites, and hydrops fetalis after fetal intervention: retrospective observational cohort from a single institution. Ultrasound Obstet Gynecol, 2023 Sep 28. doi: 10.1002/uog.27501. Online ahead of print.
2. Chen M, Shen MC*, Chang SP, Ma GC, Huang YC, Lin CY. (2022, Nov). Origin and timing of de novo variants implicated in type 2 von Willebrand disease. Journal of Cellular and Molecular Medicine, 2022 Nov;26(21):5403-5413. doi: 10.1111/jcmm.17563. Epub 2022 Oct 13.
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Carrier Screening
- Abstract -

Ming Chen, MD, PhD

In 2021 ACMG published its practice resource regarding screening of autosomal recessive and X-linked conditions during pregnancy and preconception (Gregg A et al., GIM 2021), a paper being proposed mostly due to the increase adoption of NGS into clinical practice in reproductive medicine, with fertility treatments and maternal-fetal-medicine included. This speaker will first illustrate the key points presented in this practice resource, and discusses the experience from his group, regarding the false positive/false negative examples, to present the evolving nature of this kind of genetic tests. Like those previously emerging tests in the past two decades, such evolution was also seen, for example, in the adoption of chromosome microarray into daily clinical practice, of which the speaker's group is also one of the first few teams to utilize it into reproductive genetics. Limitations instead of the power of these NGS-based tests will be highlighted in this brief talk.

16:30-17:00 How Polygenetic Risk Score Contributes to Human Leukocyte Antigen Disease Association?

SPEAKER

蔡輔仁 Fuu-Jen Tsai

PRESENT POSITION

Vice President and Distinguished Professor of Pediatrics, China Medical University
Chief, Department of Medical Research and Medical Genetics, China Medical University Hospital
President, Taiwan Human Genetics Society
President, Taiwan Foundation for Rare Disorders

EDUCATION

MD, China Medical University
Ph.D., Institute of Chinese Medicine, China Medical University

BRIEF CHRONOLOGY OF EMPLOYMENT

Dean, College of Chinese Medicine, China Medical University
Dean, Office of Research and Development, China Medical University

SELECTED PUBLICATIONS

1. The genome-wide association study of serum IgE levels demonstrated a shared genetic background in allergic diseases. Lu HF, Chou CH, Lin YJ, Uchiyama S, Terao C, Wang YW, Yang JS, Liu TY, Wong HS, Chen SC, Tsai FJ*. Clin Immunol. 2024 Mar;260:109897.
2. Identification of the efficacy of parentage testing based on bi-allelic autosomal single nucleotide polymorphism markers in Taiwanese population. Chen YC, Lin WD, Liu TY, Tsai FJ*. Forensic Sci Med Pathol. 2024 Feb 12. d
3. Risk of depression in patients with pneumoconiosis: A population-based retrospective cohort study. Lee HM, Liu DY, Hsu HL, Yu TL, Yu TS, Shen TC, Tsai FJ*. J Affect Disord. 2024 Feb 16:S0165-0327(24)00366-5.
4. Acupuncture's long-term impact on depression prevention in primary dysmenorrhea: A 19-year follow-up of a Taiwan cohort with neuroimmune insights. Liao CC, Lin CL, Tsai FJ, Chien CH, Li JM. J Affect Disord. 2024 Jan 1;344:48-60.
5. The largest genome-wide association study for breast cancer in Taiwanese Han population. Hsu YC, Chen HL, Cheng CF, Chattopadhyay A, Chen PS, Lin CC, Chiang HY, Liu TY, Huang CH, Kuo CC, Chuang EY, Lu TP, Tsai FJ. Breast Cancer Res Treat. 2024 Jan;203(2):291-306.

How Polygenetic Risk Score Contributes to Human Leukocyte Antigen Disease Association?
- Abstract -

Fuu-Jen Tsai, MD, PhD

The human leukocyte antigen (HLA) genes are known to play a crucial role in various human diseases. Notably, the associations between HLA alleles and phenotypes exhibit significant population specificity. Therefore, it is imperative to discern the impact of HLA genes on diverse traits across different populations. Recently, the application of polygenic risk scores (PRS), derived from the cumulative effect sizes of genotypes associated with specific diseases, has emerged as a powerful tool for predicting the risk of future disease development. Interestingly, the integration HLA information to PRS has proven valuable in predicting Type I diabetes. Furthermore, the PRS for immunoglobulin E (IgE) not only correlates with serum IgE levels but also exhibits associations with asthma in both Taiwanese and Japanese populations. These observations suggest the potential utility of PRS, enabling proactive measures for high-risk individuals before the onset of symptoms. Leveraging PRS in HLA-related diseases holds promise for advancing our understanding and application of precision medicine.

APPRECIATION & ACKNOWLEDGMENT

感謝有您與我們一起，為遺傳與罕見疾病的診斷與治療共同努力！

Thank you for being with us and working together for the diagnosis and treatment of genetic and rare diseases!

*按英文字母排序 **Arrange in alphabetical order**

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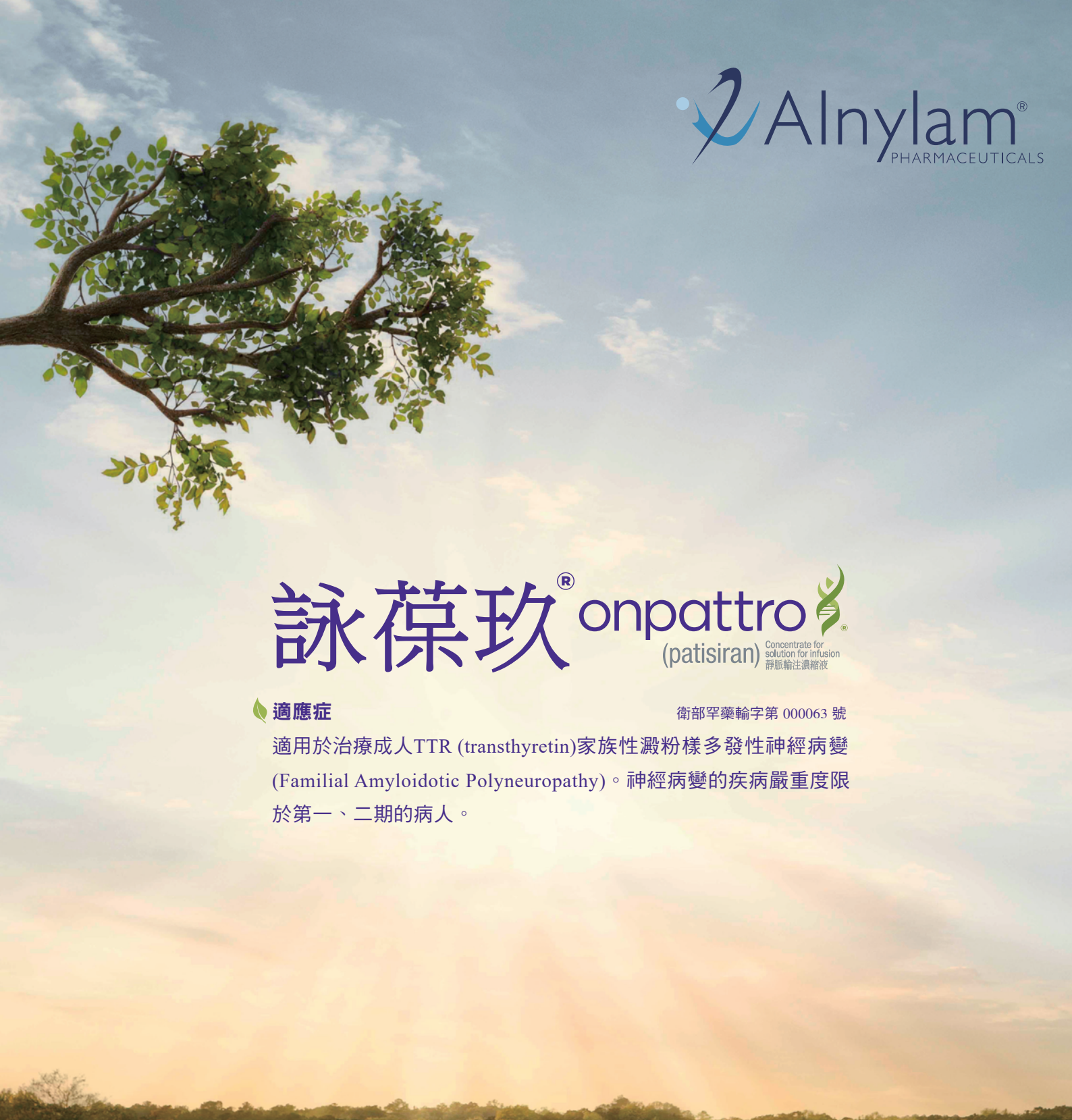

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紫福拉利注射劑 Givlaari Solution for Injection

北市衛藥廣字第112090075號

1.藥品名稱 紫福拉利注射劑 **2.組成與劑型** 每毫升溶液中含有 200mg givosiran sodium，相當於 189mg 的 givosiran。 每個小瓶中含有 200mg givosiran sodium，相當於 189mg 的 givosiran。 劑型：注射液。**3.臨床特性 3.1 適應症** 適用於治療成人急性肝臟型紫質症(AHP, acute hepatic porphyria)。 **3.2 劑量及給藥方法** 應在有紫質症治療經驗的醫療專業人員的監督下開始治療。 **用法用量** Givlaari 的建議劑量為每月一次 2.5 mg/kg，以皮下注射給藥。劑量依實際體重計算。給病人的劑量(mg)和體積(mL)應按以下方式計算： 病人體重(kg)× 劑量(2.5 mg/kg)=要給予的藥物總量(mg)。總量(mg)除以小瓶濃度(189mg/mL)=要注射的藥品總體積(mL)。**漏打** 如果漏打，應盡快給藥，並在給予漏打的劑量後恢復每月間隔給藥。 **對不良反應的劑量調整** 對於有臨床相關轉氨酶升高的病人，若給藥中斷後有改善，則可以考慮以每月一次 1.25 mg/kg 的劑量恢復使用。特殊族群 *老年* 65 歲以上的病人無需調整劑量。 *肝功能不全* 65 歲以上的病人無需調整劑量。 輕度肝功能不全(膽紅素 ≤ 1xULN (Upper Limit of Normal)、天門冬氨酸轉氨酶(AST)> 1×ULN 或膽紅素> 1×ULN – 1.5×ULN)的病人無需調整劑量。尚未對中度或重度肝功能不全病人進行 Givlaari 的試驗。 *腎功能不全* 對於輕度，中度或重度腎功能不全（預估腎小球濾過率[eGFR]≥15 至 <90 mL/min/1.73m²)的病人，無需調整劑量。尚未對患有終末期腎病的病人或接受透析的病人進行 Givlaari 的試驗。 *小兒* 尚未確立 Givlaari 在小兒的安全性和有效性。 給藥方法 僅可用於皮下。 本品為可立即使用的單次使用小瓶裝。 · Givlaari 的注射量應根據建議以體重計算。 · 可接受的最大單次注射量為 1.5 mL。如果劑量大於 1 mL，則需要一個以上的小瓶。 · 高於 1.5 mL 的劑量應以多次注射的方式給藥(每月總劑量均分至每個注射器，每次注射的體積大致相同)，以最大程度地減少因注射量而可能引起的注射部位不適感。 · 本品應於腹部皮下注射。其他可用注射部位包括大腿或上臂。 · 對於後續注射或劑量，建議輪替注射不同位置。 · 本品不應注射於疤痕組織或發紅、發炎或腫脹的位置。 **3.3 禁忌症** 對主成分或所列的任何賦形劑嚴重過敏(例如過敏反應[anaphylaxis])。 **3.4 特殊警告和使用注意事項** 患有急性間歇性紫質症(AIP, acute intermittent porphyria)以外的 AHP 亞型的病人 除 AIP 以外的 AHP 亞型(遺傳性糞紫質症(HCP)、異位型紫質症(VP)和 ALAD 缺乏紫質症(ADP))病人的療效和安全性數據有限。在評估這些罕見的 AHP 亞型的風險利益時，應列入考量。 過敏反應(anaphylactic reaction) 在臨床試驗中，過敏反應發生於一名有過敏性哮喘史和異位性體質的病人。應 監測過敏反應的徵象和症狀。如果發生過敏反應，應立即停藥，並應採取適當的醫療措施。 轉氨酶升高 曾在 givosiran 治療的病人中觀察到轉氨酶升高。轉氨酶升高主要發生在開始治療後 3 到 5 個月之間。 在開始治療之前應進行肝功能檢查。在治療的前 6 個月應每月重複進行這些檢查，此後依臨床需要進行。對於臨床相關的轉氨酶升高，應考慮中斷或終止治療。如果轉氨酶數值在中斷治療後有所改善，可以考慮以 1.25mg/kg的劑量恢復治療。較低劑量的療效和安全性方面的數據有限，尤其是對於轉氨酶已升高之病人。在轉氨酶升高中斷給藥後，尚無關於將 1.25mg/kg 劑量增加至 2.5mg/kg 的數據。 對腎功能的影響 曾有接受 givosiran 治療期間血清肌酸酐升高和 eGFR 降低的報告。在安慰劑對照試驗中，第 3 個月肌酸酐升高的中位數為 6.5 μ mol/L(0.07mg/dL)，繼續接受每月 2.5mg/kg givosiran 治療後，在第 6 個月得到解決或穩定。 在接受 givosiran 治療期間建議依臨床需要進行腎功能監測。曾在部份已有腎臟疾病的病人中，觀察到腎功能進一步的惡化；對這類病人，需要在治療期間仔細監測腎功能。 血中同半胱胺酸(homocysteine)升高 AHP 病人、維生素缺乏或慢性腎病病人可能會有血中同半胱胺酸濃度升高。在givosiran治療期間，曾觀察到血中同半胱胺酸濃度較治療前升高(請參閱第8 節)。治療期間的血中同半胱胺酸濃度升高與 givosiran 的臨床關聯仍未知。然而，同半胱胺酸濃度升高於先前被認為與增加血栓栓塞(thromoboembolic)事件風險有關。 建議在治療開始前檢測血中同半胱胺酸濃度以及在 givosiran 治療期間監測其變化。對於血中同半胱胺酸濃度升高的病人，可考慮補充維生素 B6。**3.5 交互作用** 在一個臨床藥物交互作用試驗中，givosiran 導致肝臟中某些 CYP450 酶的活性微弱至中度降低，從而增加了血漿暴露：· CYP1A2：caffeine 的 Cmax 增加 1.3 倍，AUC0-∞增加 3.1 倍 · CYP2D6：dextromethorphan 的 Cmax 增加 2.0 倍，AUC0-∞增加 2.4 倍 · CYP2C19：omeprazole 的 Cmax 增加 1.1 倍，AUC0-∞增加 1.6 倍 · CYP3A4：midazolam 的 Cmax 增加 1.2 倍，AUC0-∞增加 1.5 倍 · CYP2C9：對 losartan 的暴露無影響 · 在進行 Givlaari 治療期間時使用為 CYP1A2 或 CYP2D6 受質的藥物時，建議謹慎使用，因為本品可能會增加或延長其治療效果，或改變其不良反應。應考慮依據核准的藥品仿單減少 CYP1A2 或 CYP2D6 受質的劑量。 **3.6 特殊族群注意事項** 懷孕 目前缺乏或僅有有限的孕婦使用 givosiran 的數據。動物研究顯示在有母體毒性時會產生生殖毒性。在已考量到對婦女的預期健康益處和對胎兒的潛在風險的情況下，可考慮在懷孕期間使用本品。 **動物數據** 在懷孕兔子進行的胚胎-胎兒發育試驗中，於器官生成期間(妊娠期 7–19 天)以 0.5、 1.5 和 5mg/kg/day 的劑量，或在妊娠第 7 天以 20 mg/kg 的劑量以皮下注射方式給予 givosiran。 Givosiran 是具有母體毒性的，因在所有試驗劑量下都造成母體體重增加之減少，且 1.5mg/kg/day 以上會導致胚胎植入後之損失增加。在 20 mg/kg 時觀察到胸骨節骨變異的發生率增加。依體表面積估算，兔子接受 1.5 mg/kg/day 劑量為最大建議人體劑量(MRHD)2.5mg/kg/month(標準化後為 0.089 mg/kg/day)的 5 倍。在雌性大鼠的生育力和胚胎-胎兒發育聯合試驗中，在器官生成期間(妊娠期 6–17 天)以 0.5 至 5 mg/kg/day 的劑量用皮下注射方式給予 givosiran。5 mg/kg/day 的劑量(依體表面積估算，為標準化後 MRHD 的 9 倍)與骨骼變異(恥骨不完全骨化)相關並產生母體毒性。 在一項產前和產後發育試驗中，在妊娠第 7、13 和 19 天以及產後第 6、12 和 18天以皮下注射方式給予懷孕大鼠高達 30 mg/kg 的劑量，並未觀察到母體毒性或子代發育受影響。 哺乳 尚不清楚 givosiran 是否會分泌到乳汁。不能排除對新生兒/嬰兒的風險。已知的動物藥效學/毒理學顯示 givosiran 會分泌到乳汁(請參閱第 10 節)。必須考慮哺育母乳對孩子的益處和治療對婦女的益處，來決定是否停止哺乳或中斷/放棄Givlaari 治療。有生育能力的女性與男性 在大鼠試驗中，未觀察到 givosiran 對生育力具顯著影響。**3.7 不良反應** 安全性摘要 使用 givosiran 治療的病人中最常被回報的不良反應是注射部位反應(ISR)(36%)、噁心(32.4%)和疲倦(22.5%)。導致治療中斷的不良反應是轉氨酶升高(0.9%)和過敏反應(0.9%)。所選不良反應的描述 **肝功能檢查** 在安慰劑對照試驗中，有 7 名(14.6%)接受 givosiran 治療的病人及 1 例(2.2%)接受安慰劑治療的病人的 ALT 升高達 ULN 的 3 倍以上。有 5 名接受 givosiran 治療轉氨酶升高的病人，在以 2.5mg/kg 持續治療後得到解決。遵照計劃書，一名ALT 超過 ULN8 倍的病人(異位型紫質症)終止治療，一名 ALT 大於 ULN 5 倍的病人中斷治療並以 1.25 mg/kg 的劑量恢復用藥。兩名病人的 ALT 升高均得到緩解。**注射部位反應** 在安慰劑對照和開放標籤的臨床試驗中，有 36%的病人報告了注射部位反應且嚴重程度一般為輕度或中度，多數為短暫性且未經治療即可緩解。最常報告的症狀包括紅斑，疼痛和瘙癢。7.8%的注射發生注射部位反應且未導致治療中斷。三名病人(2.7%)在給予下一劑量後在先前的注射部位經歷了單一、短暫、記憶性的紅斑反應(recall reaction)。**免疫原性** 在安慰劑對照和開放標籤的臨床試驗中，111 名 AHP 病人中有 1 名(0.9%)在使用givosiran 的治療過程中發生了治療中出現的抗藥物抗體(ADA)。ADA 效價低且短暫，沒有證據顯示對本品的臨床功效、安全性、藥動學或藥效學特性有影響。藥商：艾拉倫股份有限公司

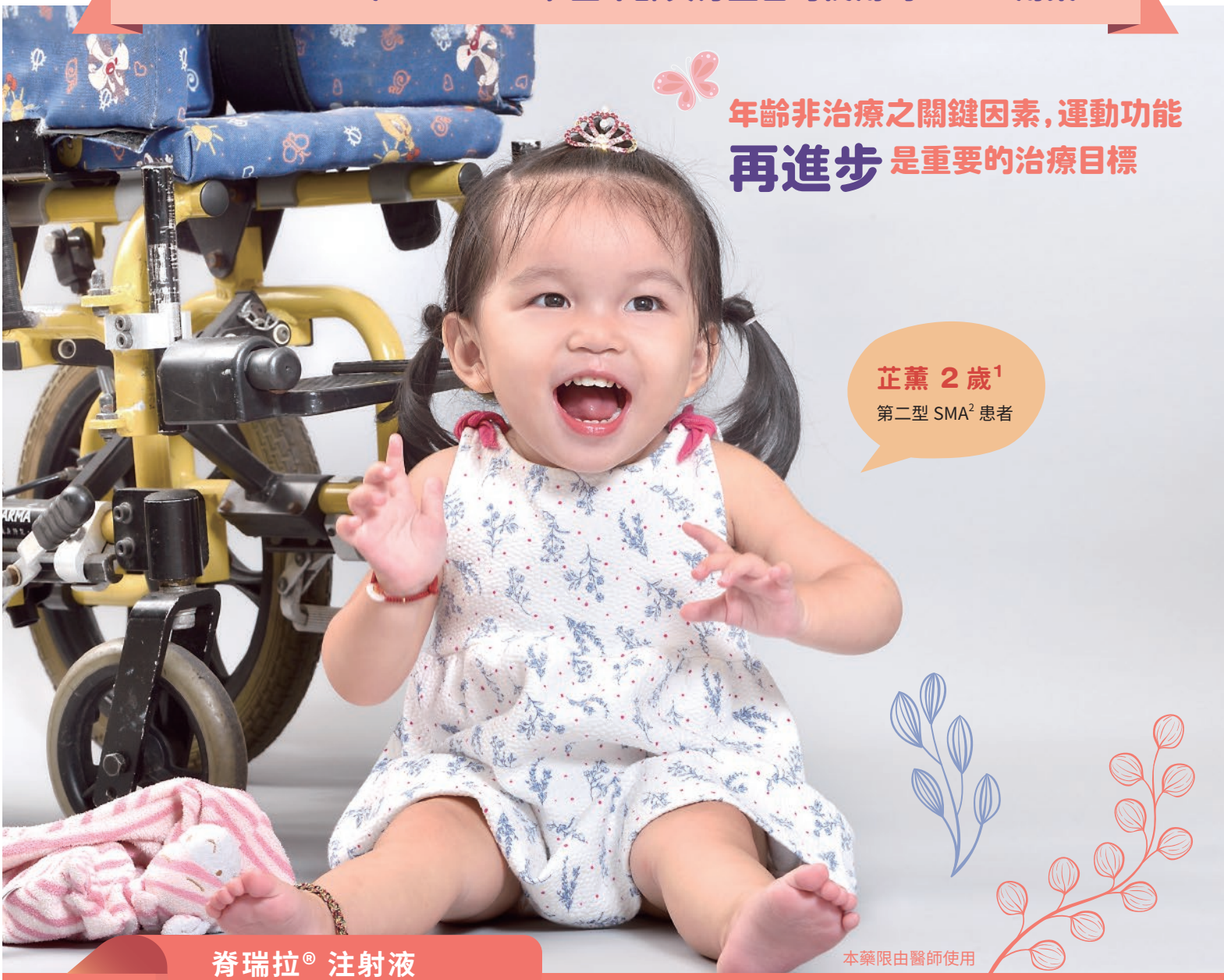
地址：台北市信義區松智路 1 號 11 樓(1146/1147 室)　TFDA PI: 2023-08-04 此為簡易仿單，完整產品資訊，請參照完整仿單。

AS1-TWN-00012

SPINRAZA®
(nusinersen) 12 mg solution for injection

Biogen

SPINRAZA® (nusinersen) 全年齡與分型皆可使用的 SMA 用藥



年齡非治療之關鍵因素，運動功能再進步是重要的治療目標

芷薰 2 歲[1]
第二型 SMA[2] 患者

本藥限由醫師使用

脊瑞拉® 注射液
SPINRAZA® solution for injection

成分組成：每個 5 毫升的小瓶含有相當於 12 毫克的 nusinersen。每毫升含有 2.4 毫克的nusinersen。
適應症：經基因確診之 SMA 脊髓性肌肉萎縮症病人，其 *SMN2* 為 2 或 3 套或已出現症狀之 SMA 第一、二、三型病人，但不適用於已使用呼吸器每天 12 小時以上且連續超過 30 天者。
劑量及投藥方式：Spinraza 治療應只能由具脊髓性肌肉萎縮症 (SMA) 照護經驗的醫師開始。建議劑量為每次給藥 12 毫克 (5 毫升) 確診後應儘早開始治療。起始治療包含四次療程，於第 0, 14, 28, 以及第 63 天給予；之後的維持治療應為每 4 個月給藥一次。
錯過或延遲劑量
起始劑量：儘早給予延遲或錯過的劑量，且兩個劑量須至少間隔 14 天；後續的劑量從前一次劑量給藥日起算，依處方給藥間隔給予。例如，第三次起始劑量延遲 30 天至第 58 天給藥 (未依原訂時程在第 28 天給藥)，則第四次起始劑量應依處方間隔在 35 天後的第 93 天給藥 (非依原訂時程在第 63 天給藥)，之後的維持劑量將從第 93 天起算，間隔每 4 個月給予維持劑量一次。
維持劑量：自前次劑量延遲 >4 至 <8 個月：儘早給予延遲的維持劑量；然後下個維持劑量依原訂時程給藥，且兩個劑量給藥時間須至少間隔 14 天，接著自前一次劑量 4 個月後給予維持劑量，並每 4 個月重覆給藥一次。自前次劑量延遲 ≥ 8 至 <16 個月：儘早給予錯過的劑量，14 天後再給予下個劑量，接著自前一次劑量 4 個月後給予維持劑量，並每 4 個月重覆給藥一次。自前次劑量延遲 ≥16 至 <40 個月：儘早給予錯過的劑量，14 天後再給予下個劑量，接著 14 天後再第三次給藥，接著自前一次劑量 4 個月後給予維持劑量，並每 4 個月重覆給藥一次。自前次劑量延遲 ≥40 個月：依處方的給藥時程 (第 0, 14, 28 和 63 天) 再次給予完整的起始治療劑量，接著自前一次劑量 4 個月後給予維持劑量，並每 4 個月重覆給藥一次。Spinraza 是以腰椎穿刺於脊髓腔內使用。治療應由執行腰椎穿刺經驗豐富的專業醫護人員給藥。
禁忌：對本品中所含之主成分或任何賦形劑過敏。
特別的警語和使用注意事項：
腰椎穿刺步驟：腰椎穿刺步驟的部分存在發生不良反應的風險 (例如頭痛，背痛，嘔吐)。這種給藥途徑在年紀非常小的病人和脊柱側彎的病人中可能有潛在的困難性。
血小板減少和凝血異常：在投與其他皮下或靜脈內給藥之反義寡核苷酸後，曾經觀察到凝血異常和血小板減少，包括急性嚴重血小板減少。如果有臨床上的須要，在 Spinraza 給藥之前，建議進行血小板和凝血實驗室檢測。
腎毒性：在投與其他皮下或靜脈內給藥之反義寡核苷酸後，曾經觀察到腎毒性。如果有臨床上的須要，建議進行尿蛋白檢測 (最好是使用早晨第一次尿液檢體)。
水腦症：在上市後，曾有接受 nusinersen 治療的病人被報導發生與腦膜炎或出血無關的交通性水腦症 (communicating hydrocephalus)。
交互作用：沒有進行交互作用研究。
懷孕和哺乳：作為一個預防措施，最好避免在懷孕期間使用 Spinraza。Nusinersen 或其代謝是否會分泌到乳汁仍未知。
操作機械能力：Nusinersen 對開車和使用機器能力沒有影響或其影響是可忽略的。
副作用/不良反應：很常見與腰椎穿刺相關的不良反應 (發生頻率 ≥1/10)：背疼、頭痛、嘔吐。
上市後的經驗：上市後與 Spinraza 給藥相關的不良反應：腦膜炎，過敏 (例如血管性水腫，蕁麻疹和丘疹)，頭痛，無菌性腦膜炎，嘔吐，背痛。發生頻率未知。上市後曾觀察到交通性水腦症(communicating hydrocephalus)。
藥理特性：
藥物治療分組：其他用於肌肉骨骼系統疾病的藥物 ATC code: M09AX07
作用機轉：Nusinersen 是一種反義寡核苷酸 (antisense oligonucleotide, ASO)，可增加外顯子 7 (exon 7)被包含在 *SMN2* 信使核糖核酸 (mRNA) 轉錄物中的比率，當 *SMN2* mRNA 被產生時，將可被轉譯為具功能的全長度 SMN 蛋白質。
儲存特別注意事項：儲存在冰箱 (2°C - 8°C)。不要冷凍

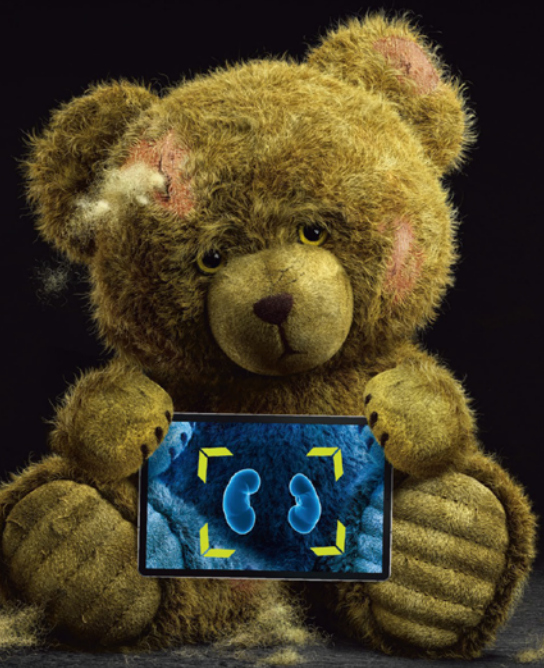
1. 拍照時年齡 2. Spinal muscular atrophy, 脊髓性肌肉萎縮症
*此為真實病人照片，台灣百健已取得照片肖像權。

台灣百健有限公司
110台北市信義區忠孝東路五段68號20樓A2
(國泰置地廣場大樓)
TEL：(02)8729-7970

衛部罕藥輸字第 000057 號
北市衛藥廣字第 113010032 號
Biogen-231726-TWN-12/2023

美商百傲萬里生技股份有限公司台灣分公司
台北市敦化南路二段97號2樓
電話：02-7711-1090 • 02-7711-1091
APAC-PKU-00044 March 2022

孩童所不能承受之"癢"



LIVMARLI 可以顯著降低血清膽酸量 (sBA) 與膽汁鬱積搔癢症，為阿拉吉歐症候群患者 (Alagille Syndrome, ALGS) 提供一種全新的治療選擇[1,2]

邁芮倍® LIVMARLI® (maralixibat) 是首個批准用於治療年齡 1 歲以上的 ALGS 病人的膽汁鬱積搔癢症

迴腸膽酸轉運體抑制劑 (IBATi) 的作用機轉

- LIVMARLI 對於 ALGS 具有新的作用機轉，減少從迴腸末端膽酸的再吸收 (主要為鹽類形式)，進而減少膽汁鬱積相關的搔癢症狀

LIVMARLI 的療效

- 顯著改善膽汁鬱積搔癢症[1,2]
- 改善黃色瘤與膽固醇量[**,1,2]
- 血清中膽酸量 (sBA) 顯著降低[1,2]
- 改善生長、睡眠、健康相關生活品質[2,4]
- 6 年無事件存活期 (Event Free Survival) 顯著改善[*,3]

LIVMARLI 安全性

- 完整的安全性與耐受性資料[1]
- 5 年以上的安全性資料作為佐證[1]

邁芮倍® 口服溶液　LIVMARLI® (maralixibat chloride)　衛部罕藥輸字第 000093 號

適應症：用於治療 1 歲以上的阿拉吉歐症候群 (Alagille Syndrome, ALGS)病人的膽汁鬱積搔癢症。**用法用量**：建議劑量為每日一次 380 mcg/kg，在當天第一餐的 30 分鐘前服用，起始劑量為 190 mcg/kg，每日口服一次；一週後，視耐受情況調升至 380 mcg/kg 每日一次。對於體重超過 70 kg 的病人，每日最大劑量體積為 3 mL 或 28.5 mg。**禁忌**：無。**警語與注意事項**：取得基準期肝臟檢測結果並於治療期間持續監測。如在沒有其他成因的情況下發生異常，可考慮調降劑量或中斷治療。如有持續性或復發性肝臟檢測結果異常，則考慮停用治療。未曾在患有肝硬化的 ALGS 病人中進行評估，須監測病人肝臟檢測結果與肝臟相關不良反應。腹瀉、腹痛和嘔吐為接受 LIVMARLI 治療的病人中最常見的胃腸道不良反應。如出現腹瀉、腹痛和/或嘔吐且未發現其他病因，請考慮調降 LIVMARLI 的劑量或中斷 LIVMARLI 的給藥。針對腹瀉或嘔吐，請監測有無脫水並及時治療。如果病人發生持續性腹瀉，或有腹瀉合併血便、嘔吐、需要治療之脫水或發燒等徵象和症狀，應考慮中斷 LIVMARLI 給藥。取得基準期血清脂溶性維生素 (FSV) 的濃度並在治療期間持續進行監測，同時監測任何相關臨床表徵。**特殊族群注意事項**：由於口服給藥後全身吸收量低，因此在建議的臨床劑量下，母體使用 LIVMARLI 後預期不會導致可測的胎兒藥物暴露。LIVMARLI 在阿拉吉歐症候群兒童病人中治療膽汁鬱積搔癢的安全性和療效，已在一項針對 1 至 15 歲病人 (N = 31) 的試驗中確立。LIVMARLI 的安全性和療效尚未在未滿 1 歲或 65 歲以上成年病人中的病人中確立。**副作用**：最常見的任何分級不良反應 (≥ 5%) 是腹瀉 (55.8%)、腹痛 (53.5%)、嘔吐 (40.7%)、脂溶性維生素缺乏 (25.6%)、肝臟檢測結果異常 (18.6%)、胃腸道出血 (10.4%) 和骨折 (9.3%)。**須由醫師處方使用。請將本品儲存於 25°C 以下。使用前請詳閱衛服部核准之 LIVMARLI 中文仿單**

References:
1. 衛生福利部食品藥物管理署西藥、醫療器材、特定用途化粧品許可證查詢 https://info.fda.gov.tw/MLMS/H0001.aspx
2. Gonzales E, Hardikar W, Stormon M, et al. Efficacy and safety of maralixibat treatment in patients with Alagille syndrome and cholestatic pruritus (ICONIC): a randomised phase 2 study. Lancet. 2021;398:1581-92.
3. Hansen BE, Vandriel SM, Vig P, et al. Event-free survival of maralixibat-treated patients with Alagille syndrome compared to a real-world cohort from GALA. Hepatology. Published online December 25, 2023.
4. Kamath BM, Goldstein A, Howard R, et al. Maralixibat Treatment Response in Alagille Syndrome is Associated with Improved Health-Related Quality of Life. J Pediatr. 2023;252:68-75.e5.

* 臨床事件定義：膽道分流術、肝代償不全、肝移植或死亡。

** 改善程度不一。[1]

ALGS：阿拉吉歐症候群；sBA：血清膽酸；IBATi：迴腸膽酸轉運體抑制劑；MoA：作用機制。

產品詳細資訊
請參考完整仿單

MTR-CAN108-2024-00001　北市衛藥廣字第 113010284 號

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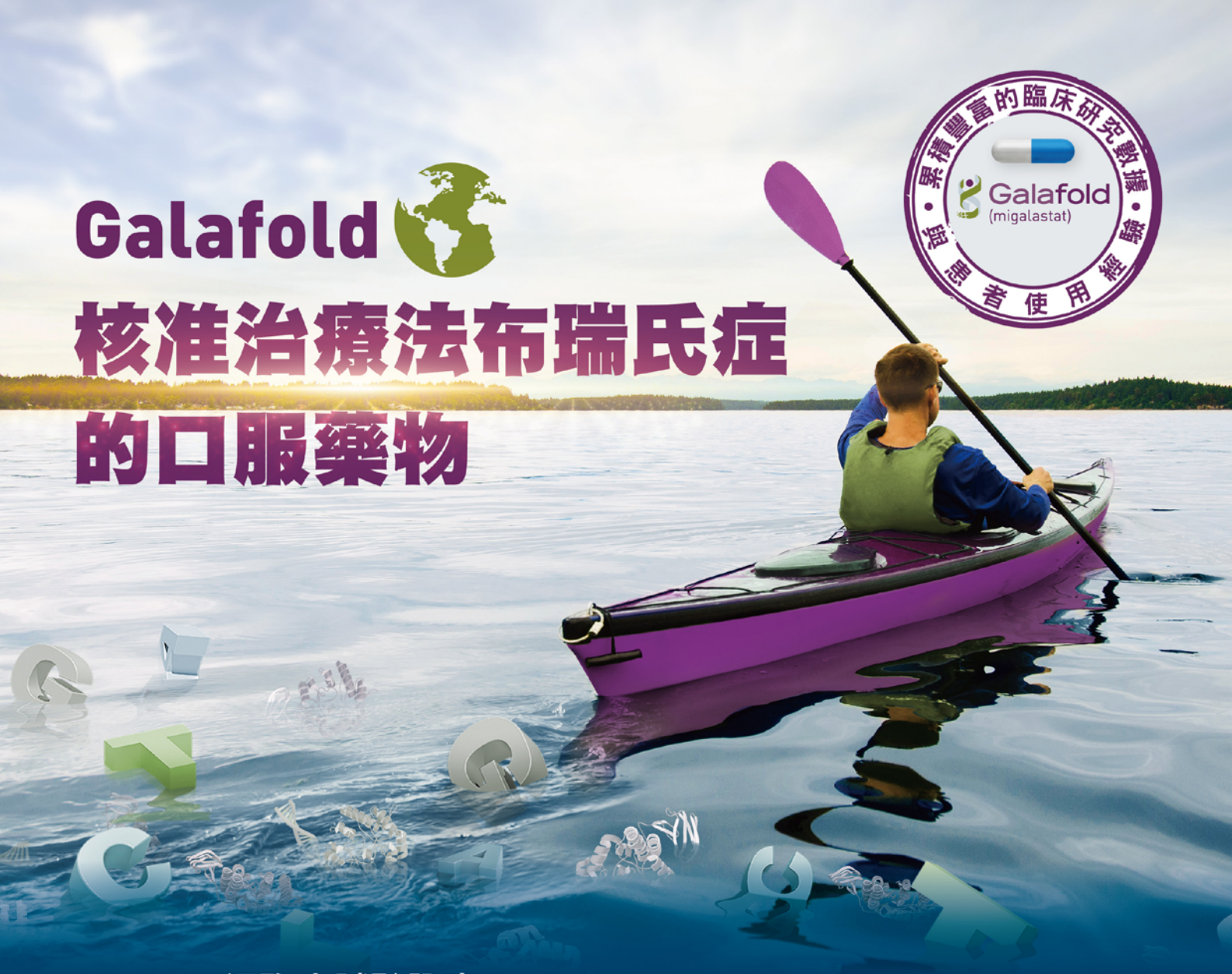

Galafold

核准治療法布瑞氏症的口服藥物

Galafold 經臨床試驗證實
在法布瑞氏症 amenable mutation 患者使用後
達到心臟 LVMi 顯著降低、腎臟功能維持穩定等多重器官臨床指標*

衛部罕藥輸字第 000060 號　北市衛藥廣字第 112040085 號

加厲伏藥品處方資訊摘要： 1. **藥品名稱：**加厲伏膠囊 123 毫克 (**衛部罕藥輸字第 000060 號**) 2. **主要成分：**每粒膠囊內含 migalastat hydrochloride，相當於 migalastat 123 毫克 3. **治療適應症：**加厲伏 適用於已確診為法布瑞氏症且於體外試驗確定為可符合性基因突變 (amenable mutation) 的 16 歲 (含) 以上病人。4. **劑量與給藥方式：**加厲伏 應由具有診治法布瑞氏症經驗的專科醫師監督給藥。加厲伏 不適合與酵素替代療法同時給藥。，**劑量：**成年病人與 16 歲以上 (含 16 歲) 青春期病人的 加厲伏 建議劑量為每間隔 1 日1 次，每次在固定的時間服用 加厲伏 123 毫克 (1 粒)，**給藥方式：**口服給藥。加厲伏與食物併用時，在體內的暴露量大約減少 40%，因此飯前與飯後 2 小時內不可服用加厲伏，這樣病人至少有 4 小時空腹狀態，這段時間內病人可以飲用包含碳酸飲料在內的澄清的流質飲料。對病人最好的方式是每間隔 1 日 1 次，每次在固定的時間服用加厲伏。加厲伏膠囊應整粒吞服，不可切開、碾碎或咀嚼。**加厲伏仿單中禁忌、警告與注意事項 4.3 禁忌** 對主成分或對仿單中第 6.1 節內所列出的賦形劑過敏者禁用。**4.4 警告與注意事項** 已開始使用或改用 migalastat 的病人應定期 (每 6 個月) 監測腎功能、心電圖與生化檢驗。當臨床狀況明顯惡化時，應再度作臨床評估或考慮停用加厲伏。加厲伏不適用於具有非可符合性突變的病人 (參見仿單中第 5.1 節)。未曾看到以加厲伏治療的病人有蛋白尿減少的情形。嚴重腎功能不全 (腎絲球過濾率小於 30 mL/min/1.73 m²) 的病人，不建議使用加厲伏 (參見仿單中第 5.2 節)。有少數的資料顯示加厲伏單次劑量與一次輸注標準酵素取代療法併用會造成 agalsidase 在體內動態濃度最多增加達到 5 倍。該試驗也指出 agalsidase 不影響 migalastat 的藥品動力學。加厲伏不適合與酵素替代療法同時給藥。**4.5 與其他藥物的交互作用以及各種形式的交互作用** 依據體外實驗資料，migalastat 不是 CYP1A2、2B6 或 3A4 的誘導劑。而且，migalastat 也不是 CYP1A2、2A6、2B6、 2C8、 2C9、 2C19、 2D6、 2E1 或 3A4/5 的受質或抑制劑。Migalastat 不是 MDR1 或 BCRP 的受質，也不是 BCRP、MDR1 或 BSEP 等人類外排轉運蛋白的抑制劑。此外，migalastat 不是 MATE1、MATE2-K、OAT1、OAT3 或 OCT2 的受質，也不是 OATP1B1、OATP1B3、OAT1、 OAT3、OCT1、OCT2、MATE1 或 MATE2-K 等人類攝入轉運蛋白的抑制劑。**4.6 生育、懷孕與授乳** 可能懷孕的女性病人/男性與女性病人的避孕 有可能懷孕且未避孕的女性病人不可使用加厲伏。懷孕 孕婦服用 加厲伏 的資料很少。在兔子試驗中觀察到，只有達到對雌兔有毒性劑量時才出現生長發育毒性(參見仿單中第5.3節)。懷孕期間不可服用 加厲伏。餵奶 未知加厲伏是否會排放於人類乳汁中，不過，曾發現 migalastat 出現於正在餵奶的大鼠乳汁中，因此，喝母奶的嬰兒也可能有暴露於 migalastat 的風險。應衡量母親接受加厲伏治療的效益與餵奶帶給嬰兒的風險何者重要，來決定應停止餵奶或停用加厲伏。生育 未曾研究 加厲伏 對人類生育力的影響。實驗顯示雄性大鼠接受所評估的各劑量之 migalastat 後，出現短暫不孕。藥物停用 4 週後可以完全恢復生育能力。其他 iminosugars 治療的前臨床實驗也有類似的結果 (參見仿單中第 5.3 節)。加厲伏不影響雌性大鼠的生育能力。**4.7 對駕駛與操作機具的影響** 加厲伏對駕駛或操作機具的能力無影響或影響極小。**4.8 不良反應** 安全性摘要 加厲伏最常見的副作用是頭痛，大約有 10% 病人出現頭痛。副作用列表 發生頻次類別的定義為：極常見 (≥1/10)、常見 (≥1/100 到 <1/10)、少見 (≥1/1,000 到 <1/100)、罕見 (≥1/10,000 到 <1/1,000)、極罕見 (<1/10,000) 以及不明 (現有資料無法估算)。在每種頻次類別中，依據系統器官分類將副作用發生率由高至低順序排列。表一、完整的不良反應列表，請參見仿單。疑似副作用的通報 藥品批准上市後的疑似副作用通報相當重要，如此可持續監測該藥品的效益/風險平衡。專業醫護人員必須將所有疑似副作用透過全國副作用通報系統進行通報。**4.9 過量中毒** 若發生過量中毒，應給予一般性醫療處置。當加厲伏用量達到 1250mg 或 2000mg 時，最常出現的副作用報告分別是頭痛與頭暈。

詳細處方資料備索、僅供專業醫療人員參考

*** References:** Galafold 藥品仿單。

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AMI_GAL_FAB_202303002 (Mar 2023)

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* 參考資料：DIACOMIT® 戴克癲產品仿單，採法國研究數據計算，處方資訊摘要如下：

【品名】戴克癲膠囊 250 毫克、500 毫克 DIACOMIT Hard Capsules 250 mg、500 mg

【適應症】用於嬰兒期嚴重肌痙攣性癲癇（SMEI, Dravet's syndrome）病人，僅服用 clobazam 及 valproate 無法充分控制癲癇發作時，併 DIACOMIT 作為輔助治療難治的全身性強直陣攣性發作（generalized tonic-clonic seizure）。

【用量】

Stiripentol 劑量以每公斤體重用量（mg/kg）計算。每日總劑量應分成 2 或 3 次服用。最高建議總劑量為 3000mg/day。

一開始 Stiripentol 併用 clobazam 與 valproate 的輔助療法應逐步增加劑量至建議劑量 50 mg/kg/day。Stiripentol 的劑量應逐漸增加，從 20 mg/kg/day 開始一個星期，接著 30 mg/kg/day 一個星期，之後的劑量調升應依據年齡。

【其他抗癲癇藥物劑量調整】

其他抗癲癇藥物與 stiripentol 併用時之劑量調整關於潛在的藥物交互作用，雖然目前沒有充分的藥理學資料，但基於臨床經驗，其他抗癲癇藥物與 stiripentol 併用時，建議以下調整劑量及服藥時間。

Clobazam：在樞紐性試驗中，開始併用 stripentol 時，clobazam 每日劑量為 0.5 mg/kg/day，通常分成 2 次使用。當產生不良反應或 clobazam 過量之臨床徵兆時（如：嗜睡、肌張力減退或幼兒煩躁），每日總劑量應每週減少 25%。

Valproate：一般認為 stiripentol 與 valproate 潛在代謝性交互作用不大，因此，當併用 stiripentol 時，不需調整 valproate 劑量，除非有臨床安全性的考量。在樞紐性試驗中，開始併用 stiripentol 時，valproate 每日總劑量不超過 30 mg/kg/day，當腸胃方面發生不良反應時（如：食慾不振、體重減輕）valproate 每日總劑量應每週減少 10 mg/kg/day。

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有效成分及含量：主成分：Risdiplam，每個黃褐色瓶內裝有 2.0 g 乾粉，內含 60 mg 的 Risdiplam。

適應症：適用於治療經基因確診且已出現症狀之脊髓性肌肉萎縮症 (SMA) 第一、二、三型病人，但不適用於已使用呼吸器每天十二小時以上且連續超過三十天者。

用法用量：使用途徑：口服或腸道給藥每天口服 EVRYSDI 一次，每天大約在同一時間投予，使用所附之口服餵藥器投予藥物。每日建議劑量取決於 SMA 病人的年齡和體重：・16天到 <2個月：0.15 mg/kg・2個月到 <2歲： 0.20 mg/kg・≥ 2歲（體重 < 20 kg)：0.25 mg/kg・≥ 2歲（體重 ≥ 20 kg)：5 mg。

作用機轉：Risdiplam 是一種存活運動神經元2 (Survival of Motor Neuron 2, SMN2) 前信使核糖核酸的剪接調節劑 (pre-mRNA splicing modifier)，被設計用於治療因5q 染色體突變導致 SMN 蛋白缺陷所引起的 SMA。缺乏功能性 SMN 蛋白質是所有 SMA 類型的病理生理學致病機轉。Risdiplam 修正 *SMN2* 的剪接，將排除外顯子7 (exon 7) 平衡調整為外顯子7納入至 mRNA 轉錄物中，從而增加 *SMN2* 基因轉譯為具功能性且穩定的 SMN 蛋白質。因此，Risdiplam 藉由增加和維持功能性 SMN 蛋白質的濃度來治療 SMA。Risdiplam 會均勻地分佈到身體的所有部位，包括藉由穿過血腦障壁到中樞神經系統 (CNS)，從而導致 CNS 和全身的 SMN 蛋白質增加。血漿中的Risdiplam 濃度和血液中的 SMN 蛋白質濃度反映了其在組織中的分佈和藥效學作用，如大腦和肌肉。臨床試驗中，Risdiplam 會使 SMN 蛋白質增加，在治療開始的四週內，血中 SMN 蛋白質的中位數變化為基期的2倍以上。對嬰兒發病型和晚發型 SMA 的受試者，達兩年的治療期間內，增加的 SMN 蛋白質一直維持。

禁忌、警語及注意事項：・EVRYSDI 禁用於已知對 Risdiplam 或其任何賦形劑過敏的病人。・在動物研究中觀察到胚胎-胎兒毒性。女性病人應告知具有生育力的病人此風險，且女性病人必須在治療期間使用高效避孕方式，直到投予最後一劑 EVRYSDI 後至少1個月為止，而男性病人則直到投予最後一劑後4個月為止。・EVRYSDI 不應在懷孕期間使用，除非對母親的益處超過對胎兒的潛在風險。如果懷孕婦女需要接受 EVRYSDI 的治療，應明確告知她對胎兒的潛在風險。・男性病人在治療期間和直到投予最後一劑 EVRYSDI 後4個月內都不應捐獻精子。目前尚不清楚EVRYSDI 是否會分泌於人類母乳中。建議在 EVRYSDI 治療期間不要餵母乳。具有生育力的男性和女性病人應遵守以下避孕要求：・具有生育力的女性病人應在 EVRYSDI 治療期間採用高效的避孕方式，直到最後一劑給藥後至少1個月。・男性病人及其具有生育力的女性伴侶應在 EVRYSDI 治療期間同時採用高效的避孕藥方式，直到最後一劑給藥後至少4個月。

副作用/不良反應：在 EVRYSDI 臨床試驗中，嬰兒發病型 SMA 受試者觀察到的最常見不良反應是發熱(48.4%)、皮疹(27.4%)和腹瀉（16.1%)。晚發型 SMA 受試者觀察到的最常見不良反應是發熱(21.7%)、頭痛(20.0%)和腹瀉(16.7%)和皮疹(16.7%)。上述不良反應的發生並沒有確切的時間或特定的臨床表現，且在持續接受 EVRYSDI 治療的情況之下，這些不良反應的症狀通常仍逐漸緩解。Risdiplam 主要是由黃素單氧化酶 (flavin monooxygenase) 1 和 3 （FMO1 和 3）代謝，也能由 CYP1A1、2J2、3A4 和 3A7 代謝。Risdiplam 並非人類多重抗藥性蛋白1 (human multidrug resistance protein 1; MDR1) 的受質。當 EVRYSDI 與 CYP3A抑制劑併用時不需調整劑量。

產品詳細資訊，請參考完整仿單。

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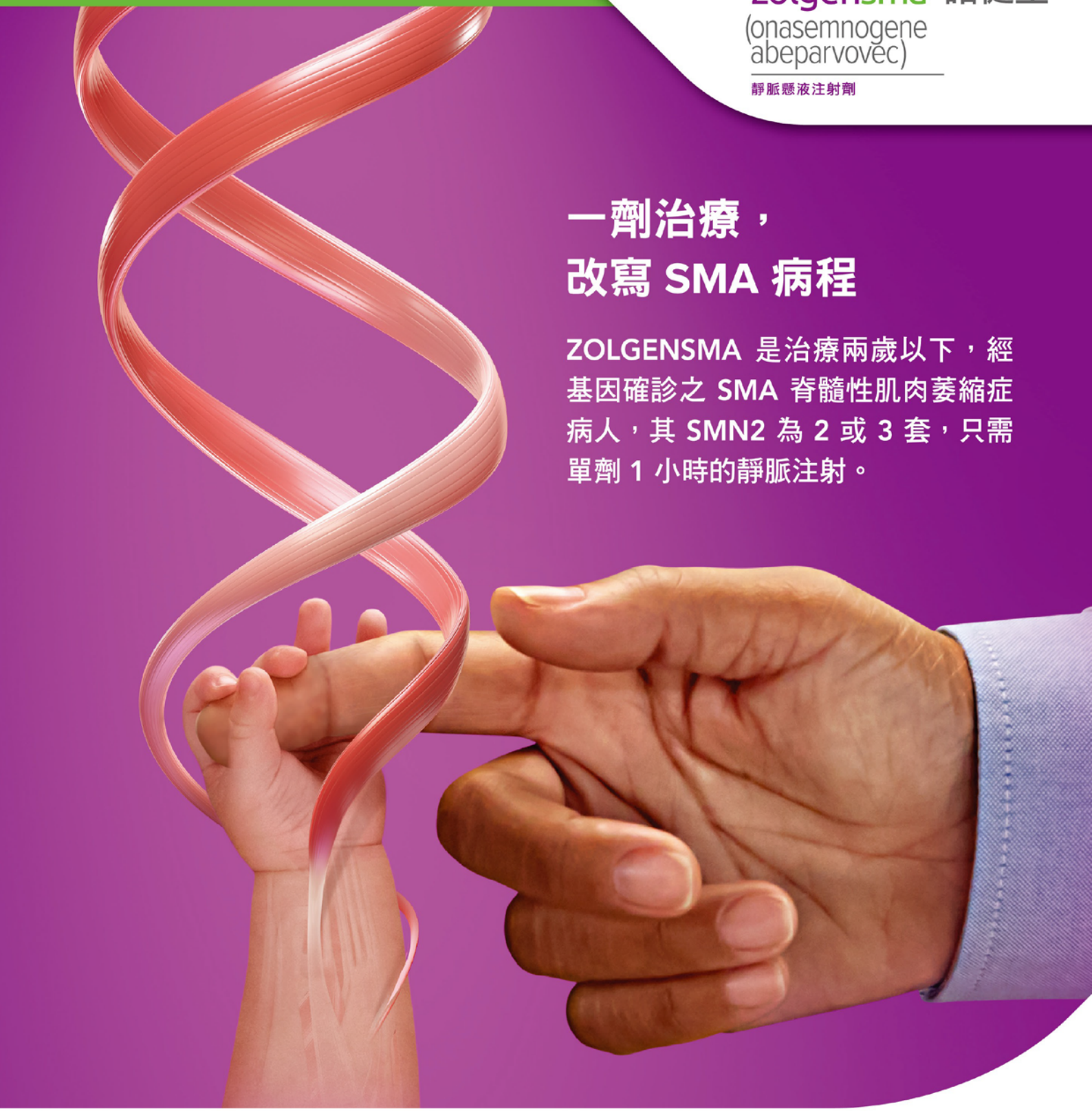

一劑治療，改寫 SMA 病程

ZOLGENSMA 是治療兩歲以下，經基因確診之 SMA 脊髓性肌肉萎縮症病人，其 SMN2 為 2 或 3 套，只需單劑 1 小時的靜脈注射。

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適應症治療 兩歲以下，經基因確診之 SMA 脊髓性肌肉萎縮症病人，其 SMN2 為 2 或 3 套，但不適用於已使用呼吸器每天 12 小時以上且連續超過30天者。**用量與用法** 應在臨床中心啟動並執行治療，並由具 SMA 病人治療經驗的醫師負責監督。在給予 Zolgensma 前，需要進行基期實驗室檢測，包含：使用經適當驗證的檢測法對 AAV9 抗體進行測試、丙胺酸轉胺酶 (ALT)、天門冬胺酸轉胺酶 (AST)、總膽紅素、白蛋白、凝血酶原時間、部分凝血活酶時間 (PTT) 和國際標準化比值 (INR)、肌酸酐、全血細胞計數 (包括血紅素和血小板計數) 及肌鈣蛋白I。在確定 Zolgensma 治療的時機時，必須考量在給藥後是否需要密切監測肝臟功能、血小板計數和肌鈣蛋白I，以及是否需要皮質類固醇治療。在發生急性或慢性未獲控制的活動性感染時，應延遲治療直到感染緩解或得到控制。**用量：**僅適用於單劑靜脈輸注。病人將接受一劑名義劑量為 1.1 x 10^{14}vg/kg 的 onasemnogene abeparvovec。**免疫調節療程：**第 9 血清型腺相關病毒載體 (AAV9) 殼體的免疫反應會在給予 Zolgensma 後產生。這可能導致肝臟轉胺酶上升、肌鈣蛋白I 上升、或是血小板計數降低。為了抑制免疫反應，建議使用皮質類固醇進行免疫調節。在可行的情況下，在給予 Zolgensma 輸注前後，應適當調整病人疫苗接種的時程，以因應同時給予的皮質類固醇治療。**禁忌症** 對下列活性物質或任一賦形劑過敏者：氨基丁三醇、氯化鎂、氯化鈉、泊洛沙姆 188、鹽酸 (調整 pH)、注射用水。**警語及注意事項/不良反應** 追蹤性：為改善生物醫療產品追蹤性，應明確記錄給藥產品的名稱及批號。對抗 AAV9 的既有免疫力：在 Zolgensma 輸注前，應檢測病人體內是否存在 AAV9 抗體。若 AAV9 抗體效價通報高於 1:50，則可能需要重新檢測。晚期 SMA：Zolgensma 對病人症狀的效益，取決於在接受治療時的疾病負擔程度，早期治療可能會帶來較高的效益。儘管晚期症狀性 SMA 病人將無法達到與未受影響的健康同齡人相同的粗大動作發展，但他們可能會依照治療時疾病的進展，在臨床上受益於基因替代療法。免疫原性：輸注 Zolgensma 後，將發生對於第 9 血清型腺相關病毒載體 (AAV9) 殼體的免疫反應，包含生成對抗 AAV9 殼體的抗體，和以T細胞為媒介的免疫反應。肝毒性：施用 AAV 載體可能導致轉胺酶上升，其可能是嚴重反應。在接受輸注後，應監測肝臟功能 (AST、ALT、總膽紅素) 至少 3 個月，在其他時間則視臨床指示而定。如果懷疑肝臟損傷，則建議進一步檢查 (例如：白蛋白，凝血酶原時間、PTT 以及 INR)。免疫媒介型肝毒性可能需要調整皮質類固醇的治療療程，包括更長的治療時間、劑量增加，或將皮質類固醇逐漸減少的時間延長。其他可能會發生以下不良反應：血小板減少症、血栓性微血管病變、肌鈣蛋白I 上升。載體嵌入 (vector integration) 可能導致致癌性的理論風險：重組 AAV 有可能發生載體隨機嵌入人類 DNA 中的罕見情況。有關嵌入事件之整體臨床相關性尚不清楚，但理論上可能有導致致癌性之風險。免疫調節療程：不應在具活動性感染的同時展開免疫調節治療，無論是急性 (例如急性呼吸道感染或急性肝炎) 或未獲控制慢性感染。脫離：發生暫時 Zolgensma 脫離，主要經由身體排泄物排出。應告知照護者及病人家屬下列對於適當處理病人糞便的說明。鈉含量：此藥品每 mL 含有 4.6 mg 的鈉。每瓶 5.5 mL 的小瓶含有 25.3 mg 的鈉，且每瓶 8.3 mL 小瓶含有 38.2 mg 的鈉。不良反應 (僅列出發生頻率≥1/10)：肝臟酵素升高。

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