秋季會

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

THGS

21-22 OCT ,2023

中華民國人類遺傳學會
Taiwan Human Genetic Society

Address / 104台北市中山區長春路20號6樓
TEL / (02)-2521-8355　　E-mail / thgs1999@thgs.org.tw
Website / www.thgs.org.tw

理事長

蔡輔仁

理事

牛道明　　李妮鍾　　林炫沛
林翔宇　　邱寶琴　　胡務亮
陳沛隆　　陳　明　　陳燕彰
楊佳鳳　　趙美琴　　蔡立平
鐘育志　財團法人罕見疾病基金會

監事

方菊雄　　林清淵
張建國　　蔡世峯
魏耀揮

秘書長

簡穎秀

秋季會 THGS

Table of CONTENT

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

Program AGENDA

October 21st 2023 (Saturday)

Shangri-La Far Eastern Tainan
(89 Section West, University Road, Tainan 70146 Taiwan)

TIME	TOPIC	SPEAKER	MODERATOR
13:00-13:50	Registration / Poster/ Exhibition		
13:50-14:00	Opening Remark	President Fuu-Jen Tsai	
14:00-15:20	**<Keynote Lecture> New Trends in Precision Medicine**		
14:00-14:30	New Trends in Precision Medicine of Cancer Genomics	Prof. Jan-Gowth Chang	Prof. Shuan-Pei Lin
14:30-14:40	Q&A		
14:40-15:10	New Trends in Precision Medicine of Pharmacogenomics	Dr. Wen-Hui Ku	
15:10-15:20	Q&A		
15:20-15:40	Coffee Break		
15:40-18:20	**<Plenary Lecture> New Mechanisms in Diagnosis and Treatment of Rare Disease**		
15:40-16:10	Inherited Cholestatic Liver Disease and Novel Therapies	Prof. Huey-Ling Chen	Prof. Wuh-Liang Hwu
16:10-16:20	Q&A		
16:20-16:50	Metabolic Bone Diseases: Diagnosis and Management	Prof. Keiichi Ozono (JP/Online)	
16:50-17:00	Q&A		
17:00-17:30	Familial Amyloidosis	Prof. Kon-Ping Lin	
17:30-17:40	Q&A		
17:40-18:10	mRNA: A New Hope for Rare Diseases	Dr. Paolo Martini, CSO	
18:10-18:15	Q&A		
18:15-18:20	Closing Remark	President Fuu-Jen Tsai	
18:20-19:00	Dinner Time		
19:00-20:30	**<Special Program> Case Discussion**		
19:00-20:30	Case Discussion		Director Pao-Chin Chiu Director Li-Ping Tsai Prof. Ni-Chung Lee

13:50-14:00 Opening Remark

PRESIDENT

蔡輔仁 Fuu-Jen Tsai

Taiwan Human Genetic Society

PRESENT PROFESSIONAL ASSIGNMENT

中國醫藥大學副校長暨特聘教授

EDUCATION

Ph.D., Institute of Chinese Medicine, China Medical University, Taiwan.
M.D., China Medical University, Taichung, Taiwan.

BRIEF CHRONOLOGY OF EMPLOYMENT

2020/07 - Present	**President**, Taiwan Human Genetics Society
2015/08 - Present	**Distinguished Professor of Pediatrics**, China Medical University
2013/08 - Present	**Vice President**, China Medical University
2009/08 - Present	**Chief**, Department of Medical Research, China Medical University Hospital
2009/08 - 2015/08	**Dean**, Office of Research and Development, China Medical University
2006/08 - Present	**Chief**, Genetic Center, China Medical University Hospital
2003/10 - 2009/10	**Dean**, College of Chinese Medicine, China Medical University
2002/03 - 2005/03	**President**, Taiwan Human Genetics Society
2001/10 - Present	**Professor of Pediatrics**, China Medical University
2001/03 - 2003/10	**Chief**, Department of Pediatrics, China Medical University Hospital
1998 - Present	**Chief**, Department of Medical Genetics, China Medical University Hospital

SELECTED PUBLICATIONS

1. Chiou JS, Cheng CF, Liang WM, Chou CH, Wang CH, Lin WD, Chiu ML, Cheng WC, Lin CW, Lin TH, Liao CC, Huang SM, Tsai CH, Lin YJ, Tsai FJ*. Your height affects your health: genetic determinants and health-related outcomes in Taiwan. BMC Med. 2022 Jul 13;20(1):250.
2. Chang CY, Chiang AJ, Lai MT, Yan MJ, Tseng CC, Lo LC, Wan L, Li CJ, Tsui KH, Chen CM, Hwang T, Tsai FJ*, Sheu JJ. A More Diverse Cervical Microbiome Associates with Better Clinical Outcomes in Patients with Endometriosis: A Pilot Study. Biomedicines. 2022 Jan 14;10(1):174.
3. Cheng CF, Liao KY, Lee KJ, Tsai FJ*. A Study to Evaluate Accuracy and Validity of the EFAI Computer-Aided Bone Age Diagnosis System Compared With Qualified Physicians. Front Pediatr. 2022 Apr 8;10:829372.

14:00-15:20 <Keynote Lecture> New Trends in Precision Medicine

MODERATOR

林炫沛 Shuan-Pei Lin

Founding Director,
Rare Disease Center, Director of Division of Biochemical Genetics,
Department of Medical Research, MacKay Memorial Hospital,
Taipei, Taiwan.

PRESENT PROFESSIONAL ASSIGNMENT

Professor, Department of Medicine, MacKay Medical College,
Department of Infant and Early Childhood Care, National Taipei University of Nursing and Health Sciences, Taipei, Taiwan.

EDUCATION

Researcher, Yale University, School of Medicine, Division of Human Genetics.
M.D., Kaohsiung Medical University, Kaohsiung, Taiwan.

BRIEF CHRONOLOGY OF EMPLOYMENT

2014/01 - Present	**Professor**, Department of Medicine, Mackay Medical College and Department of Infant and Child Care, National Taipei University of Nursing and Health Sciences
2013/01 - Present	**Co-founder and Board Director**, Asia Pacifc MPS Network (APMN)
2010/03 - Present	**Board Member**, Asian Congress of Inherited Metabolic Diseases (ACIMD)
2008/10 - Present	**Honorary President**, Taiwan MPS Society, Taipei, Taiwan
2005/11 - Present	**Committee Member**, Committee of Academic Affairs, Taipei Medical Association, Taipei, Taiwan
2000/07 - Present	**Committee Member**, Committee of Early Intervention Program, MacKay Memorial Hospital, Taipei, Taiwan
1999/06 - Present	**Board Director**, Taiwan Human Genetics Society
1998/02 - Present	**Board Director**, Down Syndrome Foundation of R.O.C., Taipei, Taiwan

SELECTED PUBLICATIONS

1. Okur I, Ezgu F, Giugliani R, Muschol N, Koehn A, Amartino H, Harmatz P, de Castro Lopez MJ, Couce ML, Lin SP, Batzios S, Cleary M, Solano M, Peters H, Lee J, Nestrasil I, Shaywitz AJ, Maricich SM, Kuca B, Kovalchin J, Zanelli E. Longitudinal natural history of pediatric subjects affected with mucopolysaccharidosis IIIB. J Pediatr 2022 Oct;249:50-58.e2.doi: 10.1016/j.jpeds.2022.06.005
2. Muschol N, Koehn A, von Cossel K, Okur I, Ezgu F, Harmatz P, de Castro Lopez MJ, Couce ML, Lin SP, Batzios S, Cleary M, Solano M, Nestrasil I, Kaufman B, Shaywitz AJ, Maricich SM, Kuca B, Kovalchin J, Zanelli E. A phase I/II study on intracerebroventricular tralesinidase alfa in patients with Sanfilippo syndrome type B. J Clin Invest. 2023 Jan 17;133(2):e165076.
3. Lin HY, Chang SY, Teng HH, Wu HJ, Li HY, Cheng CC, Chuang CK, Lin HY, Lin SP, Cheng WC. Discovery of small-molecule protein stabilizers toward exogenous alpha-l-iduronidase to reduce the accumulated heparan sulfate in mucopolysaccharidosis type I cells. Eur J Med Chem. 2023 Feb 5;247

Dr. Shuan-Pei Lin has published more than 330 papers since 1984.

秋季會 THGS

14:00-14:30 New Trends in Precision Medicine of Cancer Genomics

SPEAKER

張建國 Jan-Gowth Chang

Chair Professor,
Department of Bioinformatics and Medical Engineering,
Asia University, Taichung, Taiwan.

EDUCATION

M.D., Kaohsiung Medical University, Kaohsiung, Taiwan.

BRIEF CHRONOLOGY OF EMPLOYMENT

主任, 中國醫藥大學附設醫院 - 精準醫學中心

研究副院長, 中國醫藥大學附設醫院

副院長, 高雄醫學大學附設中和紀念醫院

主任, 高雄醫學大學附設中和紀念醫院 - 檢驗部/臨床醫學研

SELECTED PUBLICATIONS

1. Shie MY, Fang HY, Kan KW, Ho CC, Tu CY, Lee PC, Hsueh PR, Chen CH, Lee AK, Tien N, Chen JX, Shen YC, Chang JG, Shen YF, Lin TJ, Wang B, Hung MC, Cho DY, Chen YW. Highly Mimetic Ex Vivo Lung-Cancer Spheroid-Based Physiological Model for Clinical Precision Therapeutics. Adv Sci (Weinh). 2023 Apr 21:e2206603.
2. Jhuang KF, Hsu ML, Chen YC, Chang JG, Zouali M. DNA methylation trajectories during innate and adaptive immune responses of human B lymphocytes. Immunology. 2023 Feb 10.
Lin MR, Chou PH, Huang KJ, Ting J, Liu CY, Chou WH, Lin GH, Chang JG, Ikegawa S, Wang ST,
3. Chang WC. Whole-Exome Sequencing Identifies Genetic Variants for Severe Adolescent Idiopathic Scoliosis in a Taiwanese Population. J Pers Med. 2022 Dec 23;13(1):32.
4. Chang JG, Tu SJ, Huang CM, Chen YC, Chiang HS, Lee YT, Yen JC, Lin CL, Chung CC, Liu TC, Chang YS. Single-cell RNA sequencing of immune cells in patients with acute gout. Sci Rep. 2022 Dec 22;12(1):22130.
5. Chang YS, Tu SJ, Chen HD, Hsu MH, Chen YC, Chao DS, Chung CC, Chou YP, Chang CM, Lee YT, Yen JC, Jeng LB, Chang JG. Integrated genomic analyses of hepatocellular carcinoma. Hepatol Int. 2023 Feb;17(1):97-111.
6. Chang YS, Chao DS, Chung CC, Chou YP, Chang CM, Lin CL, Chu HW, Chen HD, Liu TY, Juan YH, Chang SJ, Chang JG. Cancer carrier screening in the general population using whole-genome sequencing. Cancer Med. 2023 Jan;12(2):1972-1983.

New Trends in Precision Medicine of Cancer Genomics
- Abstract -

Author / 張建國 Jan-Gowth Chang

在癌症的研究及臨床應用方面，由The Cancer Genome Atlas (TCGA)及The Pan-Cancer Analysis of Whole Genomes (PCAWG)的研究成果，使我們全面性的了解癌症的基因體、表觀基因體及表現體的變化及臨床治療的方向，再加上The Circulating Cell-free Genome Atlas study (CCGA)的研究，讓我們可以從血液中看到癌症基因體及表觀基因體的變化，因而可以更早期的檢測出癌症的產生，及未來治療的方向。同時，也由於人類微生物體的研究(Human Microbiome Project)，讓我們了解各種疾病與人類微生物體的關係，特別是與癌症病人免疫力及治療效果的關係，再加上同時利用第二代及第三代基因體定序技術，讓我們可以了解整個人類基因體變化，包括大段的結構性變化、甲基化及表現體的修飾等等。基因體定序的價格也急速下降至200美元左右，而生物資訊分析也更方便和快速，現在已進入真正的精準醫學的臨床應用時代。

14:40-15:10 New Trends in Precision Medicine of Pharmacogenomics

SPEAKER

顧文輝 Wen-Hui Ku

Chief Executive Officer and Chief,
Department of Molecular Pathology,
Taipei Institute of Pathology, Taipei, Taiwan.

PRESENT PROFESSIONAL ASSIGNMENT

Pathologist, Department of Molecular Pathology, Taipei Institute of Pathology, Taipei.

EDUCATION

M.D., Department of Medicine, National Taiwan University, Taipei, Taiwan.

BRIEF CHRONOLOGY OF EMPLOYMENT

2018 - Present	**Chief Executive Officer and Chief,** Department of Molecular Pathology, Taipei Institute of Pathology, Taipei
2015 - 2017	**Chief**, Department of Molecular Pathology and **Chief**, Department of Clinical Pathology, Taipei Institute of Pathology, Taipei
2014 - 2015	**Attending Pathologist**, Laboratory of Molecular Medicine, Department of Research and Education, Taipei Institute of Pathology, Taipei
2010 - Present	**Committee member**, Molecular Pathology, Taiwan Society of Pathology, Taipei
2007 - 2014	**Attending Pathologist**, Department of Pathology and Laboratory Medicine, Sun Yat-Sen Cancer Center, Taipei
2002 - 2007	**Resident**, Anatomical Pathology and Laboratory Medicine, Sun Yat-Sen Cancer Center, Taipei
2001 - 2002	**Resident**, Internal Medicine, National Taiwan University Hospital, Taipei

SELECTED PUBLICATIONS

1. The Ring Study: an international comparison of PD-L1 diagnostic assays and their interpretation in non-small cell lung cancer, head and neck squamous cell cancer and urothelial cancer, Yu SL, Hsiao YJ, Cooper WA, Choi YL, Avilés-Salas A, Chou TY, Coudry R, Raskin GA, Fox SB, Huang CC, Jeon YK, Ko YH, Ku WH, Kwon GY, Leslie C, Lin MC, Lou PJ, Neto CS, Ramírez SM, Savelov N, Shim HS, Torres CL, Werneck I, Zavalishina L, Chen YM, Pathology (2023) 55(1): 19-30.
2. Treatment outcomes and FGFR alterations in unresectable locally advanced or metastatic urothelial cancer in Taiwan, J. Li, Y. Feng, C. Chen, W. Ku, H. Huang, W.J. Huang, ESMO 2022. Annals of Oncology (2022) 33 (suppl_7): S785-S807.

New Trends in Precision Medicine of Pharmacogenomics
- Abstract -

Author / 顧文輝 Wen-Hui Ku

Though the human genomics data is increasing available, implementing these into clinical practice has been still slow. However, implementation of pharmacogenomics into clinical practice has already shown to improve success rates on the drug discovery and development process. Pharmacogenomics is just one of components in precision medicine. Multimodal algorithms that incorporating both clinical and genetic factors, as well as other -omic biomarkers, are essential. Artificial Intelligence and other robust instruments such as mass spectrophotometry, may help us to overcome the challenges of implementation of pharmacogenomics into clinical practice in the future.

秋季會 THGS

Symposium

NOTEPAD

15:40-18:05 <Plenary Lecture> New Mechanisms in Diagnosis and Treatment of Rare Disease

MODERATOR

胡務亮 Wuh-Liang Hwu

Senior Attending Physician,
Division of Genetics and Metabolism,
Department of Pediatrics

PRESENT PROFESSIONAL ASSIGNMENT

Professor, Department of Pediatrics at National Taiwan University Hospital

EDUCATION

Ph.D., National Taiwan University
Fellowship, Johns Hopkins University

BRIEF CHRONOLOGY OF EMPLOYMENT

2006 - 2012	**Department Head**, Department of Medical Genetics, National Taiwan University Hospital
1999 - 2002	**Inaugural President**, Taiwan Human Genetics Society
1999 - Present	**Board Member**, Taiwan Foundation for Rare Disorders

SELECTED PUBLICATIONS

1. Tai CH, Lee NC, Chien YH, Byrne BJ, Muramatsu SI, Tseng SH, Hwu WL. Long-Term Efficacy and Safety of Eladocagene Exuparvovec in Patients with AADC Deficiency. Mol Ther. 2022 Feb 2;30(2):509-518.
2. Hwu PW, Kiening K, Anselm I, Compton DR, Nakajima T, Opladen T, Pearl PL, Roubertie A, Roujeau T, Muramatsu SI. Gene therapy in the putamen for curing AADC deficiency and Parkinson's disease. EMBO Mol Med. 2021 Sep 7;13(9):e14712.
3. Chien YH, Lee NC, Tseng SH, Tai CH, Muramatsu S, Byrne BJ, Hwu WL. Efficacy and safety of AAV2 gene therapy in children with aromatic L-amino acid decarboxylase deficiency: an open-label, phase 1/2 trial. Lancet Child Adolesc Health 2017 Dec; 1: 265–73
4. Hwu WL, Muramatsu S, Tseng SH, Tzen KY, Lee NC, Chien YH, Snyder RO, Byrne BJ, Tai CH, Wu RM. Gene therapy for aromatic L-amino acid decarboxylase deficiency. Sci Transl Med. 2012 May 16;4(134):134ra61.

秋季會 THGS

15:40-16:10 Inherited Cholestatic Liver Disease and Novel Therapies

SPEAKER

陳慧玲 Huey-Ling Chen

Professor and Director,
Department of Medical Education & Bioethics /
Graduate Institute of Medical Education & Bioethics,
National Taiwan University College of Medicine, Taiwan.

PRESENT PROFESSIONAL ASSIGNMENT

主任/所長, 臺灣大學醫學教育暨生醫倫理學科暨研究所

教授, 臺大醫學院小兒科

醫務秘書, 臺大醫院

主治醫師, 臺大醫院兒童醫院小兒消化科

主治醫師, 臺大醫院肝炎中心

館長, 臺大醫學院醫學人文博物館

EDUCATION

Ph.D., Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine
M.D., School of Medicine, National Taiwan University College of Medicine

BRIEF CHRONOLOGY OF EMPLOYMENT

教授, 台大醫學院醫學系一般醫學科

專科訓練, 台大醫院小兒部住院醫師、小兒消化次

理事長, 臺灣小兒消化醫學會

秘書長, 台灣小兒消化醫學會

肝臟委員會主席, 亞太小消化學會

訪問學者, 加拿大卑詩大學癌症中心

SELECTED PUBLICATIONS

1. Chen CB, Hsu JS, Chen PL, Wu JF, Li HY, Liou BY, Chang MH, Ni YH, Hwu WL, Chien YH, Chou YY, Yang YJ, Lee NC, Chen HL*. Combining Panel-Based Next-Generation Sequencing and Exome Sequencing for Genetic Liver Diseases. J Pediatr. 2023, Epub
2. Chen HL, Li HY, Wu JF, Wu SH, Chen HL, Yang YH, Hsu YH, Liou BY, Chang MH, Ni YH. Panel-Based Next-Generation Sequencing for the Diagnosis of Cholestatic Genetic Liver Diseases: Clinical Utility and Challenges. J Pediatr. 2019 Feb;205:153-9.

Inherited Cholestatic Liver Disease and Novel Therapies
- Abstract -

Author / 陳慧玲 Huey-Ling Chen

Tremendous progress has been made in the field of genetic liver diseases in the recent decade. Monogenetic diseases causing liver diseases have been identified increasingly. This talk will highlight the progress in diagnosis and management of inherited cholestatic liver diseases, including the inborn errors of bile acid metabolism (IEBAM), Alagille syndrome, progressive familial intrahepatic cholestasis (PFIC), etc. These disorders result in common consequences of decreased bile flow, decreased intestinal absorption of fats and fat-soluble vitamins, and chronic liver injuries leading to cirrhosis or live failure. Alagille syndrome, caused by Jag 1 mutation, causes cholestasis, and also intractable skin itching, multiple organ involvement, and growth impairment. In IEBAM, one of multiple steps in BA synthesis is impaired, resulting in failure to produce normal BA and accumulation of abnormal BA and intermediate metabolites, which is treatable by supplementation of primary bile acids. PFIC is a group of ever-increasing numbers of genetic diseases that may progress to cirrhosis at various age. Genetic analysis has helped unravel the disease mechanisms, and helps to better understand the spectra of phenotypes associated with mutations in each gene. Current mainstay of treatment includes disease specific treatment, partial biliary diversion surgery, and liver transplantation. The recently developed new drug: the ileal bile acid transporter (IBAT), also known as the apical sodium-dependent bile acid transporter (ASBT) inhibitors, have been approved to be used in treating Alagille syndrome and PFIC. Different responses to medical and surgical management, based on genetic etiology and molecular mechanisms, are being actively investigated. Progress toward precision medicine in liver disease is anticipated.

秋季會 THGS

16:20 - 16:50 Metabolic Bone Diseases: Diagnosis and Management

SPEAKER

Keiichi Ozono

Professor Emeritus,
Osaka University, Japan.

EDUCATION

M.D., Osaka University Medical School
Ph.D., Osaka University Medical School

BRIEF CHRONOLOGY OF EMPLOYMENT

Present	Center for Promoting Treatment of Intractable Diseases, ISEIKAI International General Hospital
2002 - 2023	**Professor**, Head Department of Pediatrics, Osaka University, Graduate School of Medicine
1999 - 2002	**Visiting Professor**, Osaka University Graduate School of Medicine
1994 - 2002	**Department Head**, Department of Environmental Medicine, Osaka Medical Center and Research Institute for Maternal and Child Health
1992 - 1994	**Staff**, Department of Clinical Investigation, Osaka Medical Center and Research Institute for Maternal and Child Health
1991 - 1992	**Visiting staff**, Department of pediatrics, Osaka University Medical School
1989 - 1991	**Research Associate**, Department of Pediatrics and Cell Biology (Dr. J. Wesley Pike's laboratory), Baylor College of Medicine, Houston Tx
1986 - 1989	**Senior Resident**, Department of pediatrics, Osaka University Hospital
1983 - 1985	**Staff**, Department of pediatrics, Osaka Tondabayashi Hospital
1982 - 1983	**Resident**, Department of pediatrics, Osaka University Hospital

SELECTED PUBLICATIONS

1. Ishihara Y, Ohata Y, Takeyari S, Kitaoka T, Fujiwara M, Nakano Y, Yamamoto K, Yamada C, Yamamoto K, Michigami T, Mabe H, Yamaguchi T, Matsui K, Tamada I, Namba N, Yamamoto A, Etoh J, Kawaguchi A, Kosugi R, Ozono K, Kubota T. Genotype-phenotype analysis, and assessment of the importance of the zinc-binding site in PHEX in Japanese patients with X-linked hypophosphatemic rickets using 3D structure modeling. Bone. 2021 Jul 30;153:116135.
2. Kubota T, Fukumoto S, Cheong HI, Michigami T, Namba N, Ito N, Tokunaga S, Gibbs Y, Ozono K. Long-term outcomes for Asian patients with X-linked hypophosphataemia: rationale and design of the SUNFLOWER longitudinal, observational cohort study. BMJ Open. 2020 Jun 29;10(6):e036367.

Metabolic Bone Diseases: Diagnosis and Management
- Abstract -

Author / Keiichi Ozono

X-linked hypophosphatemic rickets (XLH, OMIM 307800) is an inheritable disorder characterized by growth retardation, rachitic and osteomalatic bone disease, and dental abscesses. It is the most common form of heritable rickets, occurring in 3.9/100,000 live birth and a prevalence ranging from 1.7-4.8/100,000 persons. In XLH patients, laboratory findings show hypophosphatemia, phosphaturia, and low or inappropriately normal levels of serum 1,25(OH)2D. The overproduction of fibroblast growth factor 23 (FGF23) is the pathogenesis of the hypophosphatemia in XLH. FGF23, a member of the FGF family, decreases the expression of type 2a and 2c sodium-phosphate transporters (NPT2a and NPT2c) in renal tubules which results in the reduction of phosphate (Pi) reabsorption. It also decreases the activation of vitamin D through the up- and down-regulation of 1-alpha hydroxylase and 24-hydroxylase, respectively. Collectively, disorders associated with the increased levels of FGF23 including XLH, autosomal dominant, autosomal recessive and tumor induced type are called FGF23-related hypophosphatemic rickets and osteomalacia. In Japan, the intact form of FGF is measured in the ordinary clinical practice.

In the 1990s, the genetic basis of XLH was discovered that the loss of function variants in phosphate regulating endopeptidase homolog X-linked (PHEX) gene. More than 650 recurrent PHEX variants have been reported in Human Gene Mutation Database (HGMD: http://www.hgmd.cf.ac.uk/ac/index.php, accessed January 2023) as a cause of XLH. The PHEX gene encodes for a protein which is a member of the M13 family of membrane-bound metalloproteases expressing in osteoblasts, osteocytes, and odontoblasts but not in kidney tubules. To date, however, the function of the PHEX protein has not been revealed, so that it remains to be elucidated how the deficiency of PHEX leads to the overproduction of FGF23. Although some studies have analyzed the genotype-phenotype correlation for PHEX variants, no conclusion has been reached to reveal the important functional domain of PHEX for the elevated FGF23. However, the genetic test for PHEX helps diagnose XLH. In our experience, the genetic analysis of 39 Japanese XLH patients from 28 unrelated pedigrees were performed and found missence or nonsence variants, splicing variants and small in/del variants.

Conventional therapy for XLH consists of oral phosphate salts supplementation and active vitamin D medication. In 2018, burosumab, a neutralizing antibody to FGF23 was approved for the treatment of patients with XLH in the European Union and the USA, and in Japan in 2019 since some clinical trials showed efficacy of it. Regarding this advance in XLH treatment, it becomes more important to clear the genotype-phenotype correlation to choose the best therapy for each patient.

17:00 - 17:30 Familial Amyloidosis

SPEAKER

林恭平 Kon-Ping Lin

Doctor with Contract,
Neurological Institute,
Taipei Veterans General Hospital, Taipei, Taiwan.

PRESENT PROFESSIONAL ASSIGNMENT

Doctor with Contract, Neurological Institute, Taipei Veterans General Hospital
Assistant Professor, National Yang Ming Chiao Tung University

EDUCATION

Research Fellow, Department of Hematology Oncology, Medical School,
Texas Medical Center, Houston, Texas, USA
Visiting Fellow, Department of Clinical, Neuroscience,
Medical School, Royal Free Hospital, London, UK
Fellow, EMG Laboratory, Department of Neurology, Taipei Veterans General Hospital
Resident, Department of Neurology, Taipei Veterans General Hospital

BRIEF CHRONOLOGY OF EMPLOYMENT

Attending Physician, Department of Neurology, Taipei Veterans General Hospital
Director, Taiwan Neurological Society
Secretary-general, Taiwan Society of Clinical Neurophysiology

SELECTED PUBLICATIONS

1. Adams D, Gonzalez-Duarte A, O'Riordan WD, Yang CC, Ueda M1, Kristen AV, Tournev I, Schmidt HH, Coelho T, Berk JL, Lin KP, Vita G, Attarian S, Planté-Bordeneuve V, Mezei MM, Campistol JM, Buades J, Brannagan TH 3rd, Kim BJ, Oh J, Parman Y, Sekijima Y, Hawkins PN, Solomon SD, Polydefkis M, Dyck PJ, Gandhi PJ, Goyal S, Chen J, Strahs AL, Nochur SV, Sweetser MT, Garg PP, Vaishnaw AK, Gollob JA, Suhr OB. Patisiran, an RNAi Therapeutic, for Hereditary Transthyretin Amyloidosis. N Engl J Med. 2018 Jul 5;379(1):11-21.
2. Tsai PC, Liao YC, Jih KY, Soong BW, Lin KP, Lee YC. Genetic analysis of ANXA11 variants in a Han Chinese cohort with amyotrophic lateral sclerosis in Taiwan. Neurobiol Aging. 2018 Jul 10. pii: S0197-4580(18)30253-7.
3. Chao HC, Liao YC, Liu YT, Guo YC, Chang FP, Lee YC, Lin KP.* Clinical and genetic profiles of hereditary transthyretin amyloidosis in Taiwan. Ann Clin Transl Neurol. 2019 Apr 9;6(5):913-922

Familial Amyloidosis
- Abstract -

Author / 林恭平 Kon-Ping Lin

Most of the amyloid transthyretin (ATTR) patients had a peripheral neuropathy with variable autonomic symptoms. The average age at disease onset (AO) was 58.2 ± 7.2 years, and the male patients had an earlier AO (56.6 ± 5.7 years versus 61.8 ± 8.9 years, p = 0.013). Electrophysiological studies revealed a generalized axonal neuropathy and isolated median neuropathy in 84.5% and 15.5% of the patients, respectively. Up to 80% of the patients with ATTR had symptomatic or subclinical cardiac involvement. Six TTR mutations were identified in the participants. Among them, p.Glu89Asp was a novel mutation and p.Ala97Ser was the most common one, accounting for 91.2% of the ATTR pedigrees. Detailed haplotype analyses demonstrated a shared haplotype in the 47 patients (14 families) with the p.Ala97Ser mutation, suggesting a founder effect.

The recent approval of three drugs for the treatment of TTR amyloidosis, both hereditary and wild-type, has opened a new era in the care of these diseases. ATTR amyloidosis is embedded in its pathophysiology, and the drugs target critical steps of the amyloid cascade. In addition to liver transplant, which removes the pathogenic variants, the introduction of gene silencers has allowed the suppression of both wild type and mutant transthyretin (TTR), thus extending the potential therapeutic range to wild-type cardiac amyloidosis. The kinetic stabilisation of TTR using small molecules has proved to be clinically effective both for amyloid neuropathy and cardiomyopathy. Gene silencers and kinetic stabilizers were recently approved on the basis of the outcome of phase III trials

17:40 - 18:10 mRNA: A New Hope for Rare Diseases

SPEAKER

Paolo Martini

Chief Scientific Officer
International Therapeutics Research Centers and
Founder of Moderna Rare Diseases, Moderna, Inc

PRESENT PROFESSIONAL ASSIGNMENT

Chief Scientific Officer, International Therapeutics Research Centers
Founder of Moderna Rare Diseases, Moderna, Inc.

EDUCATION

Ph.D., Molecular Endocrinology, University of Milano, Italy

BRIEF CHRONOLOGY OF EMPLOYMENT

2015/10 - Present	**Chief Scientific Officer**, Moderna
2007/01 - 2015/09	**Shire Pharmaceutical Senior Director**, Discovery Biology and Translational Research
2001/06 - 2006/11	Serono Pharmaceutical Group Leader

SELECTED PUBLICATIONS

1. mRNA therapy restores euglycemia and prevents liver tumors in murine model of glycogen storage disease.
   Cao J, Choi M, Guadagnin E, Soty M, Silva M, Verzieux V, Weisser E, Markel A, Zhuo J, Liang S, Yin L, Frassetto A, Graham AR, Burke K, Ketova T, Mihai C, Zalinger Z, Levy B, Besin G, Wolfrom M, Tran B, Tunkey C, Owen E, Sarkis J, Dousis A, Presnyak V, Pepin C, Zheng W, Ci L, Hard M, Miracco E, Rice L, Nguyen V, Zimmer M, Rajarajacholan U, Finn PF, Mithieux G, Rajas F, Martini PGV, Giangrande PH. Nat Commun. 2021 May 25;12(1):3090. doi: 10.1038/s41467-021-23318-2. PMID: 34035281
2. Systemic Messenger RNA Therapy as a Treatment for Methylmalonic Acidemia.
   An D, Schneller JL, Frassetto A, Liang S, Zhu X, Park JS, Theisen M, Hong SJ, Zhou J, Rajendran R, Levy B, Howell R, Besin G, Presnyak V, Sabnis S, Murphy-Benenato KE, Kumarasinghe ES, Salerno T, Mihai C, Lukacs CM, Chandler RJ, Guey LT, Venditti CP, Martini PGV.
   Cell Rep. 2017 Dec 19;21(12):3548-3558. doi: 10.1016/j.celrep.2017.11.081.
   PMID: 29262333

mRNA: A New Hope for Rare Diseases
- Abstract -

Author / Paolo Martini

Following decades of research in molecular biology and biochemistry, therapeutic messenger RNAs (mRNA) are emerging as a new class of medicines with broad applicability including the potential to treat rare genetic metabolic disorders.

Recent advances in mRNA technology, including modifications to the mRNA itself, along with improvements to the delivery vehicle, have transformed the utility of mRNA as a potential therapy to restore or replace different types of therapeutic proteins. This includes systemic intracellular therapeutics which aim to deliver mRNA inside cells as a therapeutic approach for diseases caused by a missing or defective intracellular protein.

Preliminary data from studies in propionic acidemia (PA) and methylmalonic acidemia (MMA) have demonstrated mRNA-based therapy restored functional protein to therapeutically - relevant levels in target organs, with sustained and reproducible pharmacology following each dose administration and no dose-limiting toxicities observed.

19:00-20:30 <Special Program> Case Discussion

MODERATOR

邱寶琴 Pao-Chin Chiu

Director,
Genetic Counseling Center,
Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan.

PRESENT PROFESSIONAL ASSIGNMENT

主任, 高雄榮民總醫院 遺傳諮詢中心

主治醫師, 高雄榮民總醫院 兒童新陳代謝科

主治醫師, 高雄榮民總醫院 兒童醫學遺傳科

主治醫師, 高雄榮民總醫院 兒童內分泌科

EDUCATION

M.D., National Yang Ming Chaio Tung University

BRIEF CHRONOLOGY OF EMPLOYMENT

主治醫師, 高雄榮民總醫院 兒童醫學部

主任, 高雄榮民總醫院 遺傳諮詢中心

美國馬里蘭州約翰霍普金斯醫學中心/德州貝勒醫學中心/科羅拉多州丹佛醫學中心進修

SELECTED PUBLICATIONS

1. A novel deep intronic variant strongly associates with Alkaptonuria Chien-Yi Lai 1,2,3, I-Jung Tsai2, Pao-Chin Chiu4, David B. Ascher 5,6,7,8, Yin-Hsiu Chien 1,2, Yu-Hsuan Huang1, Yi-Lin Lin1, Wuh-Liang Hwu1,2 and Ni-Chung Lee Genomic Medicine (2021) 6:89.
2. Epigenotype, Genotype, and Phenotype Analysis of Taiwanese Patients with Silver–Russell Syndrome Hsiang-Yu Lin 1,2,3,4,5,6 , Chung-Lin Lee 1,2,4,6,7,8, Sisca Fran 3, Ru-Yi Tu 3, Ya-Hui Chang 2,6, Dau-Ming Niu 7,8,9,Chia-Ying Chang 10, Pao-Chin Chiu 11, Yen-Yin Chou 12, Hui-Pin Hsiao 13, Meng-Che Tsai 12 , Mei-Chyn Chao 14,Li-Ping Tsai 15,16, Chia-Feng Yang 9, Pen-Hua Su 17, Yu-Wen Pan 12 , Chen-Hao Lee 18, Tzu-Hung Chu 19,Chih-Kuang Chuang 3,20,* and Shuan-Pei Lin 1,2,3,6,21, J. Pers. Med. 2021, 11, 1197.
3. Quantitative DNA Methylation Analysis and Epigenotype-Phenotype Correlations in Taiwanese Patientswith Beckwith-Wiedemann Syndrome Hsiang-Yu Lin 1,2,3,4,5,6 , Chung-Lin Lee 1,2,4,6,7,8, Sisca Fran 3, Ru-Yi Tu 3, Ya-Hui Chang 2,6, Dau-Ming Niu 7,8,9,Chia-Ying Chang 10, Pao Chin Chiu 11, Yen-Yin Chou 12, Hui-Pin Hsiao 13, Chia-Feng Yang 9 , Meng-Che Tsai 12 ,Tzu-Hung Chu 14, Chih-Kuang Chuang 3,15,* and Shuan-Pei Lin 1,2,3,6,16 J. Pers. Med. 2021, 11, 1066.

19:00-20:30 <Special Program> Case Discussion

MODERATOR

蔡立平 Li-Ping Tsai

Director,
Medical Genetic Center,
Taipei Tzu Chi Hospital, Taipei, Taiwan.

PRESENT PROFESSIONAL ASSIGNMENT

副主任, 台北慈濟醫院醫療部

主任, 台北慈濟醫院遺傳醫學中心

主治醫師, 台北慈濟醫院兒科部

EDUCATION

M.D., School of Medicine, Taipei Medical University

BRIEF CHRONOLOGY OF EMPLOYMENT

2022 - Present	Associate Professor, Department of Pediatrics, School of Medicine, Tzu Chi University
2020 - Present	Director, Medical Genetic Center, Taipei Tzu Chi Hospital
2013 - 2021	Assistant Professor, Department of Pediatrics, School of Medicine, Tzu Chi University
2010 - 2020	Director, Department of Pediatrics, Taipei Tzu Chi Hospital
2009 - 2020	Deputy Director, Department of Medical Education, Taipei Tzu Chi Hospital
2005 - 2010	Visiting Staff in Pediatrics, Taipei Tzu Chi Hospital
1999 - 2000	Visiting Scientist, Department of Human Genetics, UCLA, USA
1996 - 2005	Visiting Staff in Pediatrics, Taipei Municipal Women/Children Hospital
1993 - 1995	Medical Genetic Fellow, National Taiwan University Hospital
1989 - 1993	Pediatric Resident, Taipei Municipal Women/Children Hospital

SELECTED PUBLICATIONS

1. Hwu WL, Chuang SC, Tsai LP, Chang MH, Chuang SM, Wang TR. Glucose-6-phosphatase gene G327A mutation is common in Chinese patients with glycogen storage disease type Ia. Human Molecular Genetics. 1995;4:1095-6. (SCI)
2. Hwu WL, Tsai LP, Wang WC, Chuang SC, Wang PJ, Wang TR. Arylsulfatase A pseudodeficiency in Chinese. Human Genetics. 1996;97:148-9. (SCI)

19:00-20:30 <Special Program> Case Discussion

MODERATOR

李妮鍾 Ni-Chung Lee

Clinical Professor,
Department of Pediatrics, College of Medicine,
National Taiwan University.

PRESENT PROFESSIONAL ASSIGNMENT

Attending Physician, Department of Medical Genetics, National Taiwan University Hospital
Clinical Professor, Department of Pediatrics, College of Medicine,
National Taiwan University

EDUCATION

Ph.D., Graduate Institute of Clinical Medicine, College of Medicine, National Taiwan University
M.D., Medical College, National Yang Ming Chiao Tung University

BRIEF CHRONOLOGY OF EMPLOYMENT

Dr. Lee is a clinical associate professor at the National Taiwan University Hospital (NTUH). She had her PhD degree from NTU. Her research interests include the diagnosis and treatment of pediatric patients with rare diseases. In the diagnosis, she involves in the clinical application of next generation sequencing for pediatric rare diseases. About the treatment, she conducted gene therapy researches for AADC deficiency, Pompe disease and several rare diseases.

SELECTED PUBLICATIONS

1. 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.
2. Lin YL, Chang PC, Hsu C, Hung MZ, Chien YH, Hwu WL, Lai F, Lee NC. Comparison of GATK and DeepVariant by trio sequencing. Sci Rep. 2022 Feb 2;12(1):1809.
3. Lee NC, Chang KL, In 't Groen SLM, de Faria DOS, Huang HJ, Pijnappel WWMP, Hwu WL, Chien YH. Outcome of Later-Onset Pompe Disease Identified Through Newborn Screening. J Pediatr. 2022 Jan 4:S0022-3476(21)01279-8.
4. Lai CY, Tsai IJ, Chiu PC, Ascher DB, Chien YH, Huang YH, Lin YL, Hwu WL, Lee NC. A novel deep intronic variant strongly associates with Alkaptonuria. NPJ Genom Med. 2021 Oct 22;6(1):89.
5. Huang YH, Su TC, Wang CH, Wong SL, Chien YH, Wang YT, Hwu WL, Lee NC. RNA-seq of peripheral blood mononuclear cells of congenital generalized lipodystrophy type 2 patients. Sci Data. 2021 Oct 13;8(1):265.

秋季會 THGS

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

Alnylam PHARMACEUTICALS
CHALLENGE ACCEPTED

CANbridge 北海康成

DKSH

EXCELSIOR 科懋生物科技股份有限公司

Giddi 吉帝藥品股份有限公司 Giddi Pharma Company Limited

KYOWA KIRIN 台灣協和麒麟股份有限公司

moderna 莫德納台灣

Roche

sanofi

詠葆玖® onpattro®

(patisiran) Concentrate for solution for infusion 靜脈輸注濃縮液

適應症

衛部罕藥輸字第 000063 號

適用於治療成人TTR (transthyretin)家族性澱粉樣多發性神經病變(Familial Amyloidotic Polyneuropathy)。神經病變的疾病嚴重度限於第一、二期的病人。

詠葆玖靜脈輸注濃縮液 2 毫克/毫升
Onpattro 2 mg/mL concentrate for solution for infusion
衛部罕藥輸字第 000063 號 本藥限由醫師使用

1.藥品名稱 詠葆玖靜脈輸注濃縮液 2 毫克/毫升 **2.組成與劑型** 每 mL 含有 2.1 mg 的 patisiran sodium，相當於 2.0 mg 的 patisiran。白色至灰白色、乳白色的靜脈輸注用濃縮液（無菌濃縮液）均質溶液（pH：6.4-7.5）。**3.臨床特性** **3.1 適應症** 適用於治療成人 TTR (transthyretin) 家族性澱粉樣多發性神經病變 (Familial Amyloidotic polyneuropathy)，神經病變的疾病嚴重度限於第一、二期的病人。**3.2 劑量及給藥方法** 用法用量 Onpattro 的建議劑量是每公斤體重 300 微公克 (300 μg/kg)，每 3 週靜脈輸注一次。對於體重≥100kg 的病人，最大建議劑量為 30 mg。所有病人應在 Onpattro 治療前接受前置用藥，以降低輸注相關反應 (infusion-related reactions, IRR) 的風險。在 Onpattro 給藥當天靜脈輸注前至少 60 分鐘以上，給予下列各藥品：靜脈注射皮質類固醇 (dexamethasone 10 mg 或等效藥品)、口服 paracetamol (500 mg)，靜脈注射 H1 受體阻斷劑 (diphehydramine 50 mg 或等效藥品)、靜脈注射 H2 受體阻斷劑 (ranitidine 50 mg 或等效藥品)。若前置用藥無法取得或無法耐受靜脈注射，可以口服給予等效藥品。如果需要，可以給予額外或更高劑量的一種或多種前置用藥以降低 IRR 的風險。**漏服劑量** 如果在漏服劑量的 3 天內給予 Onpattro，則應根據病人的原時程繼續給藥。如果在漏服劑量超過 3 天後給予 Onpattro，則應在此後每 3 週繼續給藥。特殊族群 老年病人 ≥65 歲的病人無需調整劑量。肝功能不全 輕度肝功能不全的病人不需調整劑量 (膽紅素≤ 1×ULN 及 AST> 1×ULN，或膽紅素> 1.0-1.5×ULN 及任何 AST)。Onpattro 尚未在中度或重度肝功能不全病人中進行研究，除非預期的臨床益處超過潛在風險，否則不應使用於這些病人。腎功能不全 輕度或中度腎功能不全病人不需調整劑量 (預估腎小球濾過率[eGFR]≥30 至<90 mL/min/1.73 m²)。Onpattro 尚未在嚴重腎功能不全或末期腎病病人中進行研究，除非預期的臨床益處超過潛在風險，否則不應使用於這些病人。兒童 Onpattro 在 18 歲以下兒童或青少年的安全性及有效性尚未確立。給藥方法 Onpattro 用於靜脈注射。Onpattro 在靜脈輸注前必須稀釋。**3.3 禁忌症** 對主成分或任何賦形劑的嚴重過敏反應（例如嚴重急性過敏反應）。**3.4 特殊警告和使用注意事項** 輸注相關反應 (IRR) IRR 最常見的症狀 (≥2%的病人) 是潮紅、背痛、噁心、腹痛、呼吸困難和頭痛。IRR 也可能包含低血壓及暈厥。如果發生 IRR，應依臨床狀況，考慮減緩或中斷輸注並給予醫療處置 (例如皮質類固醇或其他症狀治療)。如果中斷輸注，則可以在症狀消退後考慮以較慢的輸注速率恢復輸注。若發生嚴重或危及生命的 IRR，應停止輸注 Onpattro。維生素 A 缺乏症 接受 Onpattro 治療的病人應每天口服補充約 2500IU 的維生素 A，以減少因維生素 A 缺乏所引起的眼部毒性的潛在風險。**3.5 與其他藥物的交互作用及其他形式的交互作用** 除了在體外試驗有對 CYP2B6 的誘導性和時間依賴性的抑制性外，Onpattro 預期不會受細胞色素 P450 酶抑制劑或誘導劑的影響或引起藥物-藥物交互作用。**3.6 生育、懷孕和哺乳** 有生育可能的女性 在開始治療前應排除懷孕可能，並且有生育可能的婦女應採取有效的避孕措施。如果女性打算懷孕，應停用 Onpattro 和維生素 A，並應監測血清維生素 A 濃度並使其在嘗試受孕前回復正常。懷孕 沒有關於孕婦使用 Onpattro 的資訊。如果發生意外懷孕，特別是在第一孕期，應對胎兒進行嚴密監測。有生育可能的婦女在 Onpattro 治療期間必須採取有效的避孕措施。哺乳 尚不清楚 Onpattro 是否會分泌至母乳中。應考量哺乳對兒童的益處以及治療對女性的益處，決定是否停止哺乳或停用 Onpattro。生育力 沒有關於 Onpattro 對人類生育能力影響的資訊。**3.7 不良反應** 安全性摘要 在 Onpattro 治療的病人中最常被通報的不良反應是周邊水腫 (29.7%) 和輸注相關反應 (18.9%)。唯一導致停用 Onpattro 的不良反應是輸注相關反應 (0.7%)。**輸注相關反應** IRR 的症狀包括但不限於：關節痛或疼痛 (包括背部、頸部或肌肉骨骼疼痛)、潮紅 (包括面部紅斑或皮膚發熱)、噁心、腹痛、呼吸困難或咳嗽、胸部不適或胸痛、頭痛、皮疹、搔癢、發冷、頭暈、疲倦、心率增加或心悸、低血壓 (可能包含昏厥)、高血壓、面部水腫。周邊水腫 在 Onpattro 治療病人中，事件頻率隨著時間的推移而降低。其他特殊族群 肝臟移植接受者 在一個包含 23 例 hATTR 澱粉樣病變病人且在肝臟移植後有多發性神經病變的開放標記臨床試驗中，patisiran 的安全性特性與之前的臨床試驗一致。

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
TFDA PI: 2022/10/29
此為簡易仿單，完整產品資訊，請參照完整仿單。

衛藥廣字第112030021號

For X-linked hypophosphatemia (XLH)

CRYSVITA®
burosumab

北市衛藥廣字第 110030092 號

作用機轉

XLH 的成因是由於纖維母細胞生長因子 23 (FGF23) 的過度表現，過多的 FGF23 進而抑制腎小管磷酸鹽再吸收與腎臟 1,25 - dihydroxy 維生素 D 之製造。
Burosumab 與 FGF23 結合並抑制它的生物活性，藉此恢復腎小管對磷酸鹽的再吸收並提升血中 1,25 - dihydroxy 維生素 D 的濃度。

適應症

性聯遺傳型低磷酸鹽症 (X - Linked Hypophosphatemia, XLH):
適用於 1 歲以上兒童與青少年，及合併有 XLH 相關骨骼疾病之成人。

10mg 衛部罕菌疫輸字第 000030 號
20mg 衛部罕菌疫輸字第 000031 號
30mg 衛部罕菌疫輸字第 000032 號

藥物詳細資訊請參見衛福部最新核准之仿單
僅供醫療人員參考
處方藥品請參考衛福部核准仿單，
使用前請詳閱仿單警語及注意事項。

KYOWA KIRIN
台灣協和麒麟股份有限公司
台北市中山區中山北路二段68號 9樓

戴克癲膠囊
DIACOMIT®
(stiripentol)
Committed to controlling seizures

為您守護怕熱的卓飛天使

創新 Dravet syndrome 適應症藥物

- 71.4% 病患癲癇發作頻率降低超過50%
- 42.9% 病患無癲癇發生
- 戴克癲組21位病患產生輕微的副作用(嗜睡、食慾不振)，安慰劑組則有 13 位，病患耐受性佳。

* 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。

BIOCODEX EXCELSIOR

本藥限由醫師處方使用，使用前請詳閱說明書警語及注意事項。
戴克癲膠囊250毫克：衛部罕藥輸字第000067號 戴克癲膠囊500毫克：衛部罕藥輸字第000070號
北市衛藥廣字第111040151號

藥商：科懋生物科技股份有限公司
地址：臺北市南港區園區街3 號14 樓之6 電話：(02) 2655-7568
04-2023-DCMC-2022-TW-1017-AD

Cerezyme®
imiglucerase

THE CEREZYME® EXPERIENCE

一個照亮未來道路的傳奇藥物

Cerezyme® 已證實具有長期療效、完整確立的安全性資料，以及 20 年在真實世界中治療高雪氏症的經驗。[1-3]

- 在內臟和血液學參數中顯示出療效[4,5*]
- 在兒童中顯示出療效[7,13-15*]
- 降低了疾病嚴重程度的關鍵生物標記[9]
- 在特定骨骼參數中顯示出療效[6,10-12]
- 已確立的安全性資料[1-3]

Cerezyme 降低了高雪氏症的影響· 並在高雪氏症病人中持續改善其內臟、血液學和特定骨骼的參數。[4-6,10-12]

* Gaucher Registry 試驗中的 Cerezyme 治療組為一開始接受 alglucerase 或 imiglucerase 治療並繼接受長期 imiglucerse 治療的病人 [4,7-8,10-13]

雪瑞素® 400 U Cerezyme® 400 U | 衛部罕菌疫輸字第 000015 號 | 本藥限由醫師處方使用

簡易處方資訊 **1 適應症** (1) 第一型高雪氏症 Cerezyme (imiglucerase 凍晶注射劑) 用於需要長期酵素替代療法，並經診斷確認為第一型高雪氏症且併發下列症狀之兒童或成人病患：a. 貧血 b. 血小板減少症 c. 骨病變 d. 肝臟腫大或脾臟腫大 (2) 第三型高雪氏症改善高雪氏症症狀，包括貧血、血小板減少症、肝臟或脾臟腫大、骨病變，但對於神經學症狀無效。**2 劑量及給藥方式** Cerezyme (imiglucerase 凍晶注射劑) 經由靜脈輸注投予 1-2 小時，劑量應依每個病患個別調整，起始劑量範圍可依體重自 2.5 U/kg 每星期三次至 60 U/kg 每二星期一次。60 U/kg 每二星期一次是目前資料中最常用的劑量。疾病的嚴重性是以較高劑量開始治療或增加給藥次數的指標，劑量之調整應以個人為準，依據病患之臨床表現的定期多項評估是否達到治療的目的而酌予增加或減少。兒科病人 兒科病人不需調整劑量。尚未確定 Cerezyme 對高雪氏症病人因慢性神經病變造成的神經性症狀有效，因此無治療此類症狀的建議用藥劑量療程。作用機轉 本藥品配製稀釋後，應以靜脈輸注給藥，Cerezyme 最初幾次的輸注速率不可超過每分鐘 0.5U/kg，之後可提高輸注速率但最高不可超過每分鐘 1U/kg，提高輸注速率應在專業醫護人員監督下進行。當病人經過幾個月的 Cerezyme 輸注，已經習慣輸注且耐受性良好的情況下，可考慮讓病人在家裡輸注，病人是否可以家中輸注應由主治醫師評估決定，決定由病人或照顧者自行在家輸注 Cerezyme 後，應先由專業醫護人員在診間給予訓練，指導病人或照顧者輸注技術與如何作治療紀錄，當病人在輸注當中出現不良反應時應立即停止輸注尋求專業醫護人員幫助，後續輸注可能得在診間進行，在家輸注時必須維持一定的劑量與輸注速率，只有在專業醫護人員的監督下才能改變劑量與輸注速率。給予本藥品前應如何配製與稀釋，請參見第 6.6 節。**3 劑型及劑量** Cerezyme® 為白色至灰白色濃縮粉末，配製後成為輸注溶液。**4 禁忌** 對本藥品主成分或任何賦形劑過敏者禁用 (參見第 4.1 節)。**4.1 警告與注意事項** 過敏反應 現有資料經過 ELISA 篩選處理再作放射免疫沉澱確定分析顯示，在第一年治療時，接受治療的病人中約有 15% 出現 imiglucerase 的 IgG 抗體，會出現 IgG 抗體者大多在治療 6 個月內就會出現，治療 12 個月後就很少出現抗雪瑞素的抗體了，因此對治療反應下降之病人應定期檢驗是否有出現抗 imiglucerase 的 IgG 抗體。有 imiglucerase 抗體的病人比較容易出現過敏反應 (參見第 4.8 節)，若病人疑似出現過敏反應，建議檢測是否有 imiglucerase 抗體，本藥品如同其他輸注蛋白質類製劑可能發生極嚴重過敏型態之過敏反應，一旦出現這類反應應立即停止輸注 Cerezyme，並參考現行急救治療標準作法給予適當的支持性治療。以 Cerezyme (imiglucerase) 治療過去曾出現抗體或出現各種 Ceredase (alglucerase) 過敏反應症狀之病人應特別小心。賦形劑 本藥品含鈉，且給藥時會加入 0.9% 氯化鈉靜脈輸液，病人可視狀況決定是否採用限鈉飲食。**4.2 與其他藥物之交互作用以及各種形式的交互作用** 未曾作過交互作用試驗。**4.3 生育力、懷孕與授乳** 從 150 位懷孕病人 (主要從主動通報與文獻回顧獲得) 使用經驗分析得知 Cerezyme 有助於控制住孕期潛在的高雪氏症，此外這些資料顯示 Cerezyme 不會造成胎兒畸形，不過這些統計證據偏低，胎兒死亡報告相當罕見，且不清楚是跟 Cerezyme 治療有關還是跟高雪氏症疾病本身有關。未曾以動物實驗研究 Cerezyme 對懷孕、胚胎/胎兒發育、分娩以及產後新生兒發育之影響，不知 Cerezyme 是否會通過胎盤而影響發育中的胎兒。已經懷孕或計畫懷孕的高雪氏症病人應謹慎評估治療對懷孕的利弊得失，高雪氏症的疾病活性在懷孕時與產後都會提高，包括骨骼症狀危險性提高、血球細胞更加缺乏、出血以及增加輸血需求；已知懷孕與授乳都會影響母體內鈣平衡並加速骨轉換率，使高雪氏症的骨骼問題加劇。為了獲得最佳健康狀況，未曾接受過治療的女性病人在進行治療前先採取避孕措施；已經在接受 Cerezyme 治療中的懷孕病人可考慮繼續治療，依據病人需求與治療反應調整劑量並密切監測高雪氏症臨床症狀與懷孕狀況。未知主成分是否會分泌於人類乳汁中，一般而言酵素很可能會在兒童胃腸道中被消化。**4.4 對駕駛與操作機械之影響** Cerezyme 不影響 (或幾乎不影響) 駕駛與操作機械。**4.5 不良反應** 下表依據器官分類與發生頻率列出各種不良反應 (常見 (1/100 到 <1/10)、不常見 (1/1,000 到 <1/100) 以及罕見 (1/10,000 到 <1/1,000))，各列中的不良反應依據嚴重程度遞減順序排列。

神經系統問題	不常見	頭暈、頭痛、感覺異常*
心臟問題	不常見	心悸*, 發紺*
血管問題	不常見	潮紅*, 低血壓*
呼吸道、胸腔與縱膈腔問題	常見	呼吸困難*, 咳嗽*
腸胃道問題	不常見	嘔吐、噁心、腹絞痛、腹瀉
免疫系統問題	常見	過敏反應
	罕見	無防禦性過敏反應
皮膚與皮下組織問題	常見	蕁麻疹/血管水腫*、搔癢*、皮疹*
骨骼肌與結締組織問題	不常見	關節痛、背痛*
一般性與給藥部位問題	不常見	輸注部位不適、輸注部位燒灼感、輸注部位腫脹、注射部位無菌性膿瘍、胸部不適*、發燒、寒顫、疲累

全部病人中約有 3% 出現可能是過敏反應的症狀 (上表中標示*者)，這類症狀在輸注期間或輸注後很快出現，且通常對抗組織胺加上/或類固醇有反應，一旦出現這類症狀應 建議病人停止輸注並聯繫主治醫師。**4.9 過量** 未曾有過量報告，曾有病人用過每 2 週一次，每次每公斤體重 240 單位的劑量。**5 藥理特性 5.1 藥效學特性** 藥理分類：酵素類-Imiglucerase (具巨噬細胞專一性之重組β-葡萄糖腦苷脂酶) ATC碼：A16AB02。高雪氏症是一種罕見退化性遺傳代謝疾病，由於體內缺乏一種酸性β-葡萄糖腦苷脂酶的溶小體酵素所造成，此酵素會將葡萄糖神經醯胺 (glucosylceramide 一種細胞膜上重要的脂質結構主成分) 裂解為葡萄糖與腦苷脂，罹患高雪氏症病人因葡萄糖神經醯胺降解作用不足導致葡萄糖神經醯胺大量蓄積在巨噬細胞溶小體 (稱為"高雪氏細胞") 中，以致於產生廣泛的續發性病變。高雪氏細胞一般出現在肝臟、脾臟與骨髓中，偶爾也會在肺臟、腎臟與小腸中，臨床上，高雪氏症是一種異質性基因表現型，最常見的病徵為肝脾腫大、血小板缺乏、貧血與骨骼病變，骨骼病變是高雪氏症病人最常出現的退化與失能的特徵，骨骼病變包括骨髓浸潤、骨壞死、骨痛與骨危象、缺骨與骨質疏鬆、病理性骨折與生長受損，高雪氏症病人的葡萄糖製造增加、休息時能量消耗率也增加，因此容易精神不振與惡質症，高雪氏症病人也會有輕微發炎問題，此外，高雪氏症與免疫球蛋白異常之危險性增加有關，這些異常包括高免疫球蛋白血症、多株γ球蛋白病變、意義不明的單株免疫球蛋白病變 (MGUS) 以及多發性骨髓瘤，高雪氏症的自然病程會一直惡化，一段時間後各種器官都會可能出現不可逆併發症，其臨床症狀會使生活品質變差，高雪氏症病人罹病率高且較多早年死亡。兒童階段就出現各種主客觀症狀的病人是屬於比較嚴重的高雪氏症，高雪氏症會導致生長遲緩與青春期延遲。已知高雪氏症會併發肺動脈高血壓，已作過脾臟切除手術者出現肺動脈高血壓的風險增加，大部分病人接受 Cerezyme 治療後可降低脾臟切除手術需求，越早開始接受 Cerezyme 治療，併發肺動脈高血壓的風險越低，建議在高雪氏症確定診斷後定期評估是否有肺動脈高血壓問題，一旦病人被診斷出有肺動脈高血壓應接受足夠劑量的 Cerezyme 治療以確保原來的高雪氏症有被控制住，且應考慮加用針對肺動脈高血壓的治療。Imiglucerase (具巨噬細胞專一性之重組 β 葡萄糖腦苷脂酶) 能取代受損的酵素活性將葡 萄糖神經醯胺水解，從而矯正各種病理生理問題預防後續之病變，Cerezyme 能縮小脾臟與肝臟體積，改善血小板減少症與貧血問題或使之恢復正常，減輕或完全消除骨頭疼痛與骨危象，Cerezyme 能降低休息時能量消耗率，Cerezyme 能改善高雪氏症病人心智或體能等各方面之生活品質，Cerezyme 能降低幾丁三糖酶 (chitotriosidase)，幾丁三糖酶為葡萄糖神經醯胺蓄積在巨噬細胞之生物標記且對治療有反應，Cerezyme 可使高雪氏症兒童病人的青春期發育恢復正常，趕上生長，使病人成年後有正常的身高與骨礦物質密度。以 Cerezyme 治療獲得的改善程度依給藥劑量而定，通常週轉率高的器官組織如血液系 統改善率會比週轉率低的器官如骨組織來得快，一項包含一大群第一型高雪氏症病人(528 人) 的世代試驗之 ICGG 高雪氏症登錄分析顯示，Cerezyme 對血液與內臟 (血小板數、血色素濃度、脾臟與肝臟體積等各指標的效果在 15、30 及 60U/kg，每2週一次的範圍下有時間與劑量依賴性，每兩週給予 60 U/kg 的病人比接受較低劑量的病人較快獲得改善，治療效果也比較好。同樣地，一項包含 342 位病人的 ICGG 高雪氏症登錄分析顯示，以 Cerezyme 每 2 週一次，每次 60U/kg 給藥治療 8 年後，病人骨礦物質密度恢復正常 (以雙能量 X 光吸收儀 DXA 來檢驗)，但給予每 2 週一次，每次 15 或 30 單位等較低劑量之病人則未恢復正常 (Wenstrup et al, 2007)。一項包含 2 個世代病人之研究，一組給予劑量為每 4 週一次，每次劑量中位數為 80U/kg，另一組每 4 週一次，每次劑量中位數為 30 U/kg，結果對於骨髓負荷評分 ≥ 6 之病人而言，給予較高劑量的病人 (33%；22人) 在 Cerezyme 治療 24 個月後比給予較低劑量世代 (10%；13人) 病人多降低 2 個評分 (de Fost, 2006)。以 Cerezyme 每 2 週一次每次給予 60U/kg 治療後 3 個月後就可看到骨頭疼痛獲得改善，治療 12 個月後能降低骨危象，治療 24 個月後可改善骨礦物質密度 (Sims et al, 2008)。一般輸注頻率為每 2 週一次 (參見第 4.2 節)，曾對已經穩定下來仍殘存第一型高雪氏症之成年病人進行維持劑量試驗，在相同累積劑量下，給藥間隔由每 2 週 (以下稱 Q2) 一次改為每 4 週 (以下稱 Q4) 一次，將血色素、血小板、肝脾體積、骨危象與骨病變從基線起產生的變化組成一個已定義之複合療效終點，將血液與內臟各指標達到或維持已建立之高雪氏症治療目標則為額外的療效終點，結果 Q4 組病人有 63% 在 24 個月時達到複合療效終點，Q2 組則有 81% 達到，95% 信賴區間顯示此差異無統計意義 (-0.357, 0.058)，Q4 組病人有 89% 達到療效目標為主之療效終點，Q2 組則有 100% 達到，95% 信賴區間顯示此差異無統計意義 (-0.231, 0.060)，對某些已經穩定的第一型高雪氏症之成年病人可考慮使用 Q4 輸注療法，不過此種用法臨床資料不多。**5.2 藥物動力學特性** 在 1 小時的靜脈輸注中，四種劑量 (7.5, 15, 30, 60 U/kg) 的 imiglucerase 皆可在 30 分鐘內達到酵素活性的穩定狀態，停止輸注之後，血漿酵素活性以 3.6 到 10.4 分鐘的半衰期快速下降，血漿的廓清率為 9.8 至 20.3mL/min/kg (平均值 ± 標準差：14.5 ± 4.0 mL/min/kg)，依體重校正過之分布體積為 0.09 到 0.15 L/kg (0.12 ± 0.02 L/kg)，這些數值不因劑量或輸注時間不同而受影響。以上數據是歸納自每一劑量與每一輸注速率對一或二位病人所得到的研究結果。**5.3 臨床前安全性** 依據安全性藥理學、單次或多次劑量毒性以及基因毒性等各種傳統實驗所得之非臨床資料顯示，此藥品對人體無害。**6. 製劑特性 6.1 賦形劑** Mannitol, USP、Trisodium Citrate, USP、Disodium Hydrogen Citrate, USP、Polysorbate 80, NF。**6.2 不相容性** 缺乏不相容性試驗資料，本藥品絕對不可與其他藥品混合使用。**6.3 已稀釋藥品之儲存** 已稀釋溶液 ：以微生物安全性觀點而言，藥品稀釋後應立即使用，若無法立即使用，使用前藥品存放的條件是使用者的責任，同時在 2°C-8°C 且避光情況下最多不可放置 24 小時。**6.4 儲存注意事項** 需儲存於 2°C - 8°C。已稀釋藥品之儲存請參考第 6.3 節。**6.5 容器材質與包裝規格** Cerezyme 填充於 20 毫升第一型硼矽玻璃 (透明) 注射瓶中，瓶蓋含一個矽丁基瓶塞與一個防拆封易掀蓋。為了確保每一注射瓶中含有足夠藥量提供精準調劑，每瓶皆多填充 0.6 毫升。包裝規格：每盒含 1、5 或 25 支注射劑，並非所有包裝規格都有販售。**6.6 廢棄藥品丟棄須知** Cerezyme 每瓶限用一次。本藥品中的濃縮粉末以靜脈輸注給藥前，應先用注射用水配製後，再以 0.9% 氯化鈉輸注溶液稀釋之。依據個別病人所需劑量計算應配製之注射劑瓶數，自冰箱中取出所需瓶數。偶爾可對劑量作小幅度調整以避免需丟棄部分未用到的藥品，只要每個月的投予劑量維持不變，可將給藥劑量四捨五入至接近整瓶注射劑的劑量。無菌操作技術 **配製** 每一注射劑需用 10.2 毫升注射用水加以配製，不可以注射用水強力衝擊藥品粉末，應輕輕混合避免溶液起泡。配製後溶液體積應為 10.6 毫升，配製後酸鹼值約為 6.1。配製溶液應為透明無色無異物之液體，接著再加以稀釋，稀釋前應以目視檢查注射瓶配製後溶液是否有異物或褪色情形，若有雜質或褪色應丟棄勿使用，配製後要立即稀釋，不可放著等待下次使用。**稀釋** 配製後每毫升溶液中含 imiglucerase 40 單位，每瓶配製後溶液體積應足以精準抽出 10 毫升 (相當於 400 單位)，將每瓶所抽出的 10 毫升溶液集合起來，再以 0.9% 氯化鈉注射用水稀釋成總體積 100 到 200 毫升，輕輕地混合此輸注溶液。建議給予此稀釋溶液時，使用附在輸注管線上的低蛋白結合之 0.2μm 濾膜過濾，以除去所有蛋白質顆粒，此舉不會使 imiglucerase 活性降低，稀釋後溶液應在 3 小時內給予，本藥品以 0.9% 氯化鈉輸注溶液稀釋後，其化學穩定性在 2°C- 8°C 且避光環境下最多可維持 24 小時，不過，微生物安全性則視配製與稀釋時是否確實使用無菌操作技術而定。Cerezyme 不含防腐劑，任何未用完或須丟棄之藥品應依據當地法規處理。原料藥製造廠：Genzyme Corporation (Allston Facility) 500 Soldiers Field Rd., Allston, MA 02134, USA Lonza Biologics, Inc. | 101 International Drive, Pease International Trade Port, Portsmouth, New Hampshire, 03801, U.S.A. | 充填廠：Genzyme Ireland Limited | IDA Industrial Park, Old Kilmeaden Road, Waterford, Ireland. | 包裝貼標廠：Genzyme Corporation (Northborough Facility) 11 Forbes Road, Northborough, MA 01532, USA | 藥商：賽諾菲股份有限公司 地址：臺北市信義區松仁路 3 號 7 樓 **詳細仿單內容請詳閱衛服部食藥署核准仿單** Cerezyme 400U API_C_TW201912 (TW201705-SmPC2013)

Reference:
1. Cerezyme Summary of Product Characteristics (SmPC) Genzyme Europe B.V. [December 2018].
2. Mistry PK, Batista JL, Andersson HC, et al. Transformation in pretreatment manifestations of Gaucher disease type 1 during two decades of alglucerase/imiglucerase enzyme replacement therapy in the Internation Collaborative Gaucher Group (ICGG) Gaucher Registry. *Am J Hematol.* 2017;92(9):929-939. doi:10.1002/ajh.24801.
3. Serratrice C, Carballo S, Serratrice J, Stirnemann J. Imiglucerase in the management of Gaucher disease type 1: an evidence-based review of its place in therapy. *Core Evid.* 2016;11:37-47.
4. Weinreb NJ, Goldblatt J, Villalobos J, et al. Long-term clinical outcomes in type 1 Gaucher disease following 10 years of imiglucerase treatment. *J Inherit Metab Dis.* 2013;36(3):543-553. doi:10.1007/s10545-012-9528-4.
5. Grabowski GA, Barton NW, Pastores G, et al. Enzyme therapy in type 1 Gaucher disease: comparative efficacy of mannose-terminated glucocerebrosidase from natural and recombinant sources. *Ann Intern Med.* 1995;122(1):33-39.
6. Sims KB, Pastores GM, Weinreb NJ, et al. Improvement of bone disease by imiglucerase (Cerezyme) therapy in patients with skeletal manifestations of type 1 Gaucher disease: results of a 48-month longitudinal cohort study. *Clin Genet.* 2008;73(5):430-440. doi:10.1111/j. 1399-0004.2008.00978.x.
7. Andersson H, Kaplan P, Kacena K, Yee J. Eight-year clinical outcomes of long-term enzyme replacement therapy for 884 children with Gaucher disease type 1. *Pediatrics.* 2008;122(6):1182-1190. doi:10.1542/ peds.2007-2144.
8. El-Beshlawy A, Tylki-Szymanska A, Vellodi A, et al. Long-term hematological, visceral, and growth outcomes in children with Gaucher disease type 3 treated with Gaucher disease type 3 treated with imiglucerase in the International Collaborative Gaucher Grooup Gaucher Registry. Mol Genet Metab. 2017;120(1-2):47-56. doi:10.1016/j.ymgme.2016. 12.001.
9. Murugesan V, Chuang WL, Liu J, et al. Glucosylsphingosine is a key biomarker of Gaucher disease. *Ann J Hematol.* 2016;91(11):1082-1089. doi:10. 1002/ajh.24491.
10. Wenstrup RJ, Kacena KA, Kaplan P, et al. Effect of enzyme replacement therapy with imiglucerase on BMD in type 1 Gaucher disease. *J Bone Miner Res.* 2007;22(1):119-126.
11. Charrow J, Dulisse B, Grabowski GA, Weinreb NJ. The effect of enzyme replacement therapy on bone crisis and bone pain in patients with type 1 Gaucher disease. *Clin Genet.* 2007;71(3):205-211.
12. Mistry PK, Deegan P, Vellodi A, Cole JA, Yeh M, Weinreb NJ. Timing of initiation of enzyme replacement therapy ather diagnosis of type 1 Gaucher disease: effect on incidence of avascular necrosis. *Br J Haematol.* 2009;147(4):561-570. doi:10.1111/j. 1365-2141. 200907872.x.
13. Mistry PK, Weinreb NJ, Kaplan P, Cole JA, Gwosdow AR, Hangartner T. Osteopenia in Gaucher disease develops early in life: response to imiglucerase enzyme therapy in children, adolescents and adults. Blood Cells Mol Dis. 2011;46(1):66-72. doi:10.1016/j.bcmd.2010.10.011.
14. El-Beshlawy A, Ragab L, Youssry I, et al. Enzyme replacement therapy and bony in Egyptian paediatric Gaucher disease patients. *J Inherit Metab Dis.* 2006;29(1):92-98.
15. Kauli R, Zaizov R, Lazar L, et al. Delayed growth and puberty in patients with Gaucher disease type 1: natural history and effect of splenectomy and/or enzyme replacement therapy. *Isr Med Assoc J.* 2000;2(2):158-163.

sanofi
賽諾菲股份有限公司
台北市信義區11010松仁路3號7樓
電話：(02)2176-5588 傳真：(02)2176-5590

北市衛藥廣字第 112080235 號
MAT-TW-2301032-0.1-08/2023
製作日期：Aug-2023

吉帝藥品股份有限公司
Giddi Pharma Company Limited

Professional
Passion
Integrity
Caring
Responsibility

Your Partner on Rare Disease Care

Giddi Pharma Company Limited
Taichung office: 6F, No.216-5, Sec. 2, Suiyuan Rd, Taichung 406, Taiwan
Taipei office: 7F, No.43, Lane 115, Sec. 2, Chung Shan N. Rd, Taipei 104, Taiwan
Tel: 886-4-22473356 Fax: 886-4-22473365
Tel: 886-2-25110757 Fax: 886-2-25113757

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。

Market Expansion Services by www.dksh.com　DKSH

藥商名稱：台灣大昌華嘉股份有限公司 DKSH Taiwan Ltd.
藥商地址：臺北市內湖區堤頂大道 2 段 407 巷 20 弄 1、3、5、7 號 10 樓，及 22、24、26 號 10 樓及 22 號 10 樓之 1
訂購專線：0800-865-688

Galafold® (migalastat)

口服給藥，為多重器官帶來療效

AMI_GAL_FAB_202303002 (Mar 2023)

moderna®

this changes everything

造訪莫德納官網
獲得更多資訊

成為莫德納好夥伴
定時收到最新資訊
（僅限醫師填寫）

TW-MRNA-2300017