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Scientific Programme

Venue: Grand Ballroom, Level 3, JW Marriott Hotel, Admiralty, Hong Kong SAR

	14 November 2020, Saturday
08:00 - 08:10	Registration
08:10 - 08:45	Movement Disorders Symposium 1 Chairperson/Judge: Dr Germaine Chan
	Clinical trials targeting alpha-synuclein in Parkinson disease Anthony E Lang
08:45 – 09:30	Dissertation Highlights Chairpersons: <i>Dr Yannie Soo, Dr WK Cheng</i> Judge: <i>Dr Patrick Li</i>
	A retrospective study of stroke in Chinese young adults in a local tertiary centre <i>Chris Chau</i>
	Factors predicting favourable outcome for mechanical thrombectomy in patients with acute ischaemic stroke Kelvin PK Cheung
	Clinical, morphological, and genetic studies of a cohort of Hong Kong Chinese patients with a novel pathogenic <i>FLNC</i> nonsense mutation Gene Gao
	Clinical presentation and course of patients with motor neuron disease: a tertiary centre experience in Hong Kong Christina YT Ho
09:35 – 10:00	Intermission / Poster Viewing Session Chairperson: Dr Herrick Lau Judges: Dr Gardian Fong, Dr Colin Lui
	Clinical, cerebrospinal fluid, and radiological profiles of cryptococcal meningitis in patients with or without HIV CH Cheung
	Development and results of intraarterial intervention for acute ischaemic stroke in New Territories West Cluster MS Chi
	Bilateral globus pallidus internus deep brain stimulation for a 4-year-old girl with GNAO1 mutation—related status dystonia: case report and literature review Hilary HC Kwok
	Intravenous tenecteplase for suspected acute large vessel occlusion anterior circulation strokes $WTLo$
10:00 - 11:30	Education Session Chairperson/Judge: Dr KL Shiu
	Clinical approach of weakness SH Ng
11:30 – 11:45	Opening Ceremony (Guest of Honour: Dr Tony Ko, Chief Executive, The Hospital Authority)
11:45 – 12:45	BI Stroke Symposium Chairperson/Judge: Dr KY Cheung
	Stroke prevention in neurological perspective: what should we consider? Ken Butcher

14 NOVEMBER 2020, Saturday

12:45 - 13:45

Free Paper Presentations

Chairpersons/Judges: Dr Nelson Cheung, Dr Betty Ng, Dr WC Fong

Ischaemic strokes during direct oral anticoagulant usage: how compliance matters

Bonaventure YM Ip

Association between basilar artery diameter and stroke risk in Chinese patients with Fabry disease

YLT Lam

Clinical course of transthyretin familial amyloid polyneuropathy with p.Ala117Ser mutation

LPNg

Quantitative muscle strength assessment in late-onset Pompe disease and its correlation with 6-minute-walk test: a 4-year longitudinal study

Winnie WM Yau

13:45 - 14:45

Movement Disorders Symposium 2

Chairperson/Judge: Dr Mandy Au Yeung

Deep brain stimulation surgery for movement disorders other than Parkinson disease

Michael Lee

Nonmotor symptoms and personalised medicine of Parkinson disease in 2020 $\it K\,Ray\,Chaudhuri$

14:45 - 15:00

Intermission / Sponsor Acknowledgement Time

15:00 - 16:30

UCB Epilepsy Symposium

Chairperson/Judge: Dr Howan Leung

Real world evidence of anti-epileptic drugs benefit to patients with epilepsy Manuel Toledo

Tetratogenicity of anti-epileptic drugs

Torbjörn Tomson

	15 November 2020, Sunday
08:00 - 08:15	Registration
08:15 - 09:15	Neuro-degenerative Disease Symposium Chairperson/Judge: Dr Carlin Chang
	Amyotrophic lateral sclerosis update and a review of novel therapeutic strategies Lorne Zinman
09:15 - 11:00	Neuromuscular Disease Symposium
	(Co-organised with Hong Kong Society of Neuromuscular Diseases) Chairperson/Judge: Dr CN Lee
	The role of serology in the modern era of myositis Andrew Mammen
	Diagnosis, treatment, and pathogenesis of immune-mediated necrotising myopathy Andrew Mammen
	Spinal muscular atrophy: new treatment and challenge Sophelia Chan
11:15 – 12:15	Stroke Symposium
	(Co-organised with Hong Kong Stroke Society) Chairperson/Judge: <i>Prof Thomas Leung</i>
	Clinical application of the RAPID software Greg Albers
12:15 - 12:30	Intermission / Sponsor Acknowledgement Time
12:30 – 13:15	Novartis Migraine Symposium Chairperson/Judge: Dr Shirley Cheung
	CGRP-based monoclonal antibodies in migraine management: a review and the Singapore experience KH Ho
13:15 – 14:00	Astra Zeneca Stroke Symposium Chairperson/Judge: Dr Gary Lau
	Secondary prevention with potent P2Y12 inhibitor in minor acute ischaemic stroke or high-risk transient ischaemic attack *Lawrence Wong**
14:00 – 15:00	Daiichi Sankyo Stroke Symposium Chairperson/Judge: <i>Dr Richard Li</i>
	Cerebrovascular risk management and anticoagulation: scientific evidence and clinical decision on non-vitamin K antagonist oral anticoagulants Hans-Christoph Diener
	Stroke prevention in atrial fibrillation. Our local perspective and roadmap to future care Yannie Soo
15:00 – 15:15	Intermission / Sponsor Acknowledgement Time
15:15 – 16:45	Biogen Hereditary Neurological Diseases Symposium Chairperson/Judge: Dr Sheng Bun
	Management of adult patients with spinal muscular atrophy Tim Hagenacker
	FLNC-related myofibrillar myopathy in Hong Kong: histopathology and genetics Hencher Lee, Shun Wong
16:45 – 16:50	Closing Ceremony and Award Presentations

Movement Disorders Symposium 1 Clinical trials targeting alpha-synuclein in Parkinson disease

Anthony E Lang University of Toronto

 α -synuclein aggregation in the form of Lewy pathology (Lewy bodies and Lewy neurites) is the hallmark of Parkinson disease. The toxic effects of pathological α -synuclein are believed to trigger a number of pathogenic mechanisms that contribute to the progressive neurodegenerative process. Cell-to-cell transmission of pathological α -synuclein (eg, oligomers) is believed to underlie the disease progression, possibly in a caudal-rostral fashion up the brainstem and eventually involving the cerebral cortex (the Braak hypothesis). There have been increasing efforts to develop disease-modifying therapies that target α -synuclein in various ways, including synthesis, aggregation, degradation, and propagation. This lecture reviews the role of α -synuclein in the pathogenesis of Parkinson disease, the various approaches to address the contribution of this pathogenic protein, and the current status of treatments targeting α -synuclein in human trials.

A retrospective study of stroke in Chinese young adults in a local tertiary centre

DH 1

Chris Chau Queen Elizabeth Hospital, Hong Kong

Background: Young ischaemic stroke comprises 5% to 10% of all strokes. Aetiologies are more diverse than for adult strokes. Data on the impact on patients and society are few, especially in Asia localities. We aim to review the demographics, risk factors, aetiologies and outcome of young ischaemic stroke patients in a regional centre in Hong Kong.

Methods: Patients aged 18 to 45 years admitted between 2016 and 2018 for ischaemic stroke were included. Clinical, laboratory and radiological findings were reviewed. Stroke aetiologies were classified by the Baltimore-Washington and TOAST classification. Outcomes studied included modified Rankin score (mRS), modified Barthel Index (mBI) and ischaemic stroke recurrence. Categorical comparison of outcomes was performed stratified by age and aetiologies.

Results: A total of 94 patients with median age 40 years were included. Mean follow-up duration was 2.29 years. The majority (92%) had mild strokes (NIHSS score 0-8). Vascular risks factors were prevalent: 46.8% had hypertension, 60.6% had hyperlipidaemia and 34.0% had diabetes or pre-diabetes. Small vessel occlusion was the most common aetiology by both the Baltimore-Washington and TOAST classification. Upon hospital discharge, 87.2% patients remained independent (mRS 0-2). Case fatality was 3.2%. Calculated recurrent ischaemic stroke incidence proportion was 1.85% per person-year. A trend of association with ischaemic stroke recurrence was observed for cardioembolic stroke.

Conclusion: Young ischaemic stroke patients in our centre had a high prevalence of vascular risk factors. The most common aetiology was small vessel occlusion. The majority remained independent. Short-term ischaemic stroke recurrence was low. Literature review however suggested significant long-term mortality and health burden.

Factors predicting favourable outcome for mechanical thrombectomy in patients with acute ischaemic stroke

Kelvin PK Cheung

Department of Medicine and Geriatrics, Tuen Mun Hospital, Hong Kong

Background: Multiple randomised controlled trials have demonstrated that mechanical thrombectomy is superior to medical therapy for acute ischaemic stroke with anterior circulation large vessel occlusion.

Objective: The aim of the study was to describe the outcome of acute ischaemic stroke patients undergoing mechanical thrombectomy and investigate the predictors of favourable prognosis in this group of patients after thrombectomy.

Methods: A retrospective cohort study was conducted on 91 patients with acute ischaemic stroke secondary to anterior circulation large vessel occlusion who received mechanical thrombectomy from January 2015 to August 2019 in Tuen Mun Hospital, Hong Kong. Modified Rankin scale (mRS) was used to evaluate the outcome of the patients 3 months after mechanical thrombectomy. Related factors of favourable outcome were analysed using univariate and multivariate logistic regression.

Results: 42.9% (39/91) of patients were functionally independent (modified Rankin scale of ≤2) at 3 months after receiving endovascular treatment. 28.6% (26/91) of patients achieved modified Barthel index of ≥90 at 3 months. Mortality was 20.9% (19/91). 11.0% (10/91) of patients had symptomatic intracranial haemorrhage. Outpatient status upon referral for mechanical thrombectomy was associated with a better functional outcome significantly (P=0.007). History of ischaemic heart disease (P=0.029) and high post 24 hours National Institute of Health Stroke Scale (P<0.001) were associated with worse functional outcome significantly.

Conclusion: Functional outcome and mortality after mechanical thrombectomy in a locoregional hospital of Hong Kong are in line with international trials. Outpatient stroke, history of ischaemic heart disease, and post 24 hours National Institute of Health Stroke Scale are significant prognostic predictors of functional outcome.

Clinical, morphological, and genetic studies of a cohort of Hong Kong Chinese patients with a novel pathogenic *FLNC* nonsense mutation

DH 3

Gene Gao University of Hong Kong, Hong Kong

Myofibrillar myopathy type 5 (MFM5) is a rare autosomal dominant genetic myopathy caused by mutation of the FLNC gene encoding filamin-C, one of the Z-disk associated proteins, that helps in maintaining myofibril assembly, remodelling, and maintenance. The clinical manifestation of MFM5 varies corresponding to the difference of FLNC mutation types and locations. Although myofibrillar myopathy can be characteristically recognised by muscle histopathological analyses, the precise molecular aetiology cannot be readily discerned without genetic testing. Although series of myofibrillar myopathy cohorts have been reported in American, German, Italian, and French populations, no Chinese population cohort data are currently available. In this study, we identified a cohort of Hong Kong Chinese MFM5 patients with genetic confirmation of a novel FLNC heterozygous c.8129G>A (p.Trp2710Ter) nonsense pathogenic mutation. Clinical, radiological, histopathological, and genetic studies of these symptomatic MFM5 patients were conducted across different generations within these families. A comparison was made with other reported Caucasian myofibrillar myopathy cohorts. In our study, the majority of MFM5 patients had symptom onset at age >40 years. The weakness of lower limb distal muscles was firstly presented, and it progressed slowly to affect both proximal and upper limb muscles. Large fibre axonal peripheral neuropathy, restrictive lung disease, and cardiac dysfunction were observed as concomitant manifestations in patients with MFM5. Although MFM5 exhibited heterogeneous clinical manifestations even among affected members in the same family, its muscle magnetic resonance imaging pattern was consistent and muscle biopsy histopathological findings were characteristic. The use of muscle ultrasonography-magnetic resonance imaging and muscle biopsy yielded high accuracy and reduced surgical complications. Genetic testing by next-generation sequencing targeting myopathy-related genes detected a novel FLNC heterozygous c.8129G>A nonsense mutation in the exon 48 at the dimerisation domain of filamin-C, which formed a premature termination codon and resulted in mRNA translation termination and protein truncation. The recurrent presence of this FLNC nonsense mutation among different unrelated families implied its founder effect among Hong Kong Chinese populations. Understanding the clinical, morphological, and genetic characteristics of MFM5 in Chinese populations enables early recognition and diagnosis of the disease, understanding disease mechanisms, and promoting exploration of potential therapeutics.

Clinical presentation and course of patients with motor neuron disease: a tertiary centre experience in Hong Kong

Christina YT Ho Queen Elizabeth Hospital, Hong Kong

Motor neuron disease is a devastating neurodegenerative condition that most patients ultimately develop severe complications leading to respiratory failure and death. In this study, the clinical course of 41 patients who attended a multidisciplinary clinic of a tertiary neurology referral centre in Hong Kong over a 9.5-year follow-up period was analysed. This is one of the first local studies that explores the clinical features and progression of Chinese patients with motor neuron disease. The mean patient age at symptom onset was 57.3 years, with half of the patients presented with pure limb weakness at onset. The 5-year survival rate was 34.1%, with a mean survival time from the symptom onset of 70.3 months and a mean age of death at 64 years. In this cohort, clinical progression as represented by Δ FS1 was the only factor that was found to be associated with patients' overall survival time and the time to respiratory failure from symptom onset. Riluzole use of more than 6 months and body mass index at first presentation to HMV clinic were both positively correlated with the time to respiratory failure, despite no significant effect on survival was demonstrated. The use of NIV was not associated with significant survival benefit in our population. Further studies and statistical analysis might be needed to translate Δ FS1 into a potential surrogate marker for prediction of patients' overall prognosis and survival.

Clinical, cerebrospinal fluid, and radiological profiles of cryptococcal meningitis in patients with or without HIV

P 1

CH Cheung, B Sheng, WT Wong, HH Kwan, LP Ng, YLT Lam, HSB Lam Department of Medicine and Geriatrics, Princess Margaret Hospital, Hong Kong

² Department of Pathology, Princess Margaret Hospital, Hong Kong

Background: We aim to review characteristics of cryptococcal meningitis in patients with or without HIV at our hospital.

Methods: Patients admitted to Princess Margaret Hospital during January 2009 to December 2019 with *Cryptococcus* species grown on cerebrospinal fluid (CSF) culture were included for analysis. We reviewed their demographics, predisposing conditions, clinical, CSF, and radiological features, treatment, and outcomes.

Results: A total of 24 patients aged 21 to 80 (mean, 51) years were identified. 75% of patients were HIV positive; others had predisposing conditions that require immunosuppressive treatment. Non-HIV infected patients were older (60.8 vs 47.5 years). Common clinical presentations included fever (67%), headache (50%), reduced consciousness or confusion (38%), and seizure (13%). For CSF findings, 67% had an opening pressure of ≥20 cm H2O, up to 55 cm H2O; 63% had CSF pleocytosis; and 63% had elevated CSF protein. CSF in one patient grew Cryptococcus gattii, whereas all others grew Cryptococcus neoformans. The majority of computed tomographic scans showed only ischaemic changes. Nine of them were assessed with magnetic resonance imaging, and five of them revealed abnormal findings, namely leptomeningeal enhancement and multifocal enhancing mass lesions. Apart from standard antifungal treatment, three patients required courses of intensive lumbar punctures (eg, daily) for symptom relief. The mortality rate was 33%. At 1-year follow-up, all survivors were ambulatory and functionally independent.

Conclusion: Cryptococcal meningitis can affect patients with HIV and patients with underlying immunocompromised states. While its clinical presentation is diverse, markedly elevated opening pressure is a common feature and may indicate the need for serial lumbar punctures for symptomatic relief. Radiological findings were more likely to be appreciated on magnetic resonance imaging than on computed tomography. With early diagnosis and appropriate treatment, the outcome is satisfactory at our hospital.

Development and results of intraarterial intervention for acute ischaemic stroke in New Territories West Cluster

MS Chi, YP Fu, YC Wong, CB Tan, J Siu, HY Lau, SM Wong, CX Chan, LY Chan, BL Man, KL Shiu, KY Cheung, KK Ma, CF Cheung, ML Li, LK Tsoi, PK Cheung, HY Se, CK Yuen
Department of Medicine and Geriatrics, Tuen Mun Hospital, Hong Kong

Background: Tuen Mun Hospital provides acute stroke services for New Territories West region. We have provided intraarterial thrombolysis since 2004 and mechanical thrombectomy since 2009. Before mid-2015, patients were mainly with contraindications to intravenous thrombolysis (iv-rtPA) such as taking anticoagulant and presented in 4.5 to 6 hours. Since mid-2015, we have performed intraarterial thrombectomy for patients with large vessels occlusion on top of usual iv-rtPA if eligible. We present our results and compare the patient outcomes before and after mid-2015.

Methods: All patients who received intraarterial intervention for acute ischaemic stroke in Tuen Mun Hospital from 2004 to September 2020 were included. Patient age, initial National Institute of Health Stroke Scale (NIHSS) score, thrombolysis in cerebral infarction score, 24-hour NIHSS score, and 3-month modified Rankin Scale score were recorded. Recanalisation was defined as thrombolysis in cerebral infarction score of 2B or above. Early neurological recovery was defined as NIHSS score improved by ≥8 or reaching 0-1 at 24 hours. Results: Before mid-2015, 60 patients (mean age, 62.4 years) with a mean NIHSS score of 14.4 underwent intraarterial intervention. Of them, 8% received iv-rtPA and 93% received intraarterial thrombolysis. 61% achieved recanalisation and only 25% had early neurological recovery. The symptomatic haemorrhage rate was 5%. At 3 months, 48% of them achieved functional independence and the mortality was 12%. After mid-2015, 121 patients (mean age, 69 years) with a mean NIHSS score of 19.9 underwent intraarterial intervention. Of them, 62% received iv-rtPA and the recanalisation rate was 83%. 44% had early neurological recovery. The symptomatic haemorrhage rate remained 5%. At 3 months, 34% had functional independence and the mortality was 20%.

Conclusions: After the new workflow for intraarterial thrombectomy for acute ischaemic stroke, we achieved a higher recanalisation rate (83% vs 61%) and a higher rate of patients with early neurological improvement (44% vs 25%), with a similar rate of symptomatic haemorrhage (5%). Older age and more severe stroke in the recent cases could explain the less favourable 3-month outcome.

Bilateral globus pallidus internus deep brain stimulation for a 4-year-old girl with GNAO1 mutation-related status dystonia: case report and literature review

P 3

Hilary HC Kwok, XL Zhu, KY Lau, David YC Chan, Emily KY Chan, Danny TM Chan, Eva LW Fung, Anne YY Chan Prince of Wales Hospital, Hong Kong

GNAO1 mutation is a rare condition. It can manifest with hyperkinetic movement disorder during childhood with life-threatening exacerbations (status dyskinesia) refractory to medical treatment. Deep brain stimulation (DBS) is emerging as an effective treatment to abolish dyskinetic crisis in patients with GNAO1 mutation. As of 2019, 15 cases of GNAO1 mutation-associated hyperkinetic movement disorder treated with DBS have been reported. We report on a 4-year-old girl with a de novo GNAO1 mutation who had status dystonia triggered by a viral infection. She had a severe exacerbation of dystonia refractory to medical treatment and complicated by rhabdomyolysis requiring paediatric intensive care unit (PICU) stay. In January 2020, she underwent bilateral globus pallidus internus (GPi) DBS. DBS was switched on soon after the operation. Significant improvement of hyperkinetic movement was noted in the early post-operative period. Medications were stepped down and nasogastric tube was removed at 1 month after surgery. There were no further exacerbations of dystonia. The Global Judgement of Severity by Abnormal Involuntary Movement Scale score improved from 4/4 during PICU stay in August 2019 to 3/4 before DBS in January 2020 to 2/4 at 10-month follow-up. The Fahn-Marsden score improved from 108/120 during PICU stay to 106.5/120 before DBS to 64.5/120 at 10-month follow-up. Our result is encouraging and consistent with that in the literature. Long-term follow-up is needed. DBS in young children is challenging. High wound and hardware-related complication rates have been reported. Lead migration is likely as the child grows.

Intravenous tenecteplase for suspected acute large vessel occlusion anterior circulation strokes

WT Lo, WC Fong, YF Cheung, KW Fong, LT Chan, HF Chan, M Ismail, TC Li, CC Chan, CH Chan, CO Luk, SK Chau, YT Ho, CM Lui, WY Kwok, MK Yuen, ST Chan, CS Fong, HF Or.
Department of Medicine, Queen Elizabeth Hospital, Hong Kong

Background: Tenecteplase (TNK) is a thrombolytic administered as a single intravenous bolus. It has higher fibrin affinity and is potentially better in clot lysis. The American Heart Association stroke guideline includes the option of intravenous TNK for patients eligible to undergo mechanical thrombectomy. Since May 2020, pilot use of TNK (0.25 mg/kg) for patients with suspected large vessel occlusion has been implemented at Queen Elizabeth Hospital. Patients with suspected large vessel occlusion are those with National Institute of Health Stroke Scale (NIHSS) score of ≥ 6 plus cortical signs or evident middle cerebral artery sign. Computed tomography angiography was not performed.

Methods: We compared patients with suspected large vessel occlusion of anterior circulation treated with either TNK or alteplase using the same criteria. Baseline demographics, vascular risk factors, treatment parameters were compared. Safety outcomes included the symptomatic intracerebral haemorrhage rate and 30-day all-cause mortality. Efficacy outcomes were improvement of ≥ 8 and ≥ 4 scores in NIHSS at 24 hours after thrombolysis.

Results: From May to September 2020, 21 patients with suspected large vessel occlusion in the anterior circulation were treated with TNK. They were compared with 30 patients treated with alteplase from January to September 2020. For the TNK patients, the mean age was 71.8 years, the median baseline NIHSS score was 19, and the median Alberta Stroke Program Early Computed Tomography Score was 9. At 24 hours, more patients in the TNK group than the alteplase group had improvement in NIHSS of \geq 8 points (42.9% vs 23.3%) and of \geq 4 points (57.1% vs 43.3%), but the difference was not significant. No patients in the TNK group had symptomatic intracerebral haemorrhage. There were no significant differences in symptomatic intracerebral haemorrhage and 30-day all-cause mortality between the groups.

Conclusion: For patients with suspected large vessel occlusion, TNK is safe and of potentially better efficacy than alteplase.

Clinical approach of weakness

ES 1

SH Ng

Tuen Mun Hospital and Pok Oi Hospital, Hong Kong

This talk focuses on the bedside component of the clinical approach of weakness, which led to my landmark diagnosis of the first Hong Kong case of Hirayama disease in 2006 and the first Chinese case of McLeod syndrome in 2012. Some causes for weakness are discussed such as benign monomelic amyotrophy, cervical spondylotic amyotrophy, idiopathic inflammatory myositis, Guillain-Barre syndrome atypical subtypes, and familial distal myopathy. In addition, two landmark projects introduced by me are discussed: the combined neuro-oncology clinic on nasopharyngeal carcinoma post-therapy neurological complications since 1980, and the functional neurological disorders rehabilitation programme. The talk is in two parts with a 5-minute break. Finally, four neurology puzzles are given to the audience to discuss.

BI Stroke Symposium

Stroke prevention in neurological perspective: what should we consider?

Ken Butcher

Prince of Wales Clinical School, University of New South Wales, Australia

Patients with atrial fibrillation are at increased risk of stroke, particularly if they have had a prior episode of an ischaemic stroke or a transient ischaemic attack (TIA). Twice-daily treatment with 110 mg or 150 mg dabigatran have demonstrated more favourable safety and efficacy profiles, compared with warfarin, and the effects were consistent in patients with previous stroke or TIA. In emergency conditions (such as urgent surgery or uncontrolled bleeding), patients treated with non-vitamin K antagonist oral anticoagulants may need to use reversal agents. In Hong Kong, only dabigatran has the specific reversal agent idarucizumab to reverse the anticoagulation effects. Three-factor prothrombin complex concentrate (3F-PCC) remains the choice of reversal agent for emergency conditions associated with fXa inhibitors. In a retrospective analysis on risk of thrombosis, bleeding, and mortality in patients receiving direct oral anticoagulants with 3F-PCC reversal for major bleeding or emergency operations in local hospital, the overall 30-day mortality was 32.7%, and death due to thrombosis or bleeding in major bleeding group accounted for 62.5% of cases. Prof Butcher will give an overview of the current advances of secondary stroke prevention and how these advances may affect current clinical practice. He will describe how the availability of specific reversal agents adds to the management strategies and optimises therapeutic outcomes in neurological conditions such as ischaemic stroke and intracranial haemorrhage.

Ischaemic strokes during direct oral anticoagulant usage: how compliance matters

FP 1

Bonaventure YM Ip, Yannie OY Soo, Thomas W Leung Division of Neurology, Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong

Background: Understanding the clinical characteristics, aetiologies, and treatment options of ischaemic stroke during direct oral anticoagulant (DOAC) usage may inform treatment and prevention strategies. **Methods:** We retrospectively analysed the stroke severity, rates of large vessel occlusion, reperfusion therapy,

and mortality of consecutive patients who developed ischaemic stroke during DOAC usage from 2010 to 2018 in a university hospital in Hong Kong at 2-year intervals. We analysed these clinical outcomes with respect to the compliance to DOAC.

Results: Among ischaemic stroke patients with known atrial fibrillation, DOAC usage before stroke onset increased significantly from 2010 to 2018 (P=0.01). 102 patients developed ischaemic stroke during DOAC usage. Compared with patients who were non-compliant or had interruption of DOAC, compliant patients had a lower median National Institute of Health Stroke Scale score (7 vs 16, P=0.015) and lower odds for large vessel occlusion (odds ratio=0.369, 95% confidence interval=0.156-0.872, P=0.023). Nonetheless, 1-year all-cause mortality was not statistically different (P=0.29). Lower proportion of compliant patients received reperfusion therapy even if presented with therapeutic window (30% vs 83.3%, P<0.001). Compliant patients had higher percentage of alternative causative stroke aetiologies besides atrial fibrillation (46.9% vs 9.7%, P<0.001).

Conclusion: Compliance to DOAC was associated with lower risk of large vessel occlusion and stroke disability. However, the low rate of reperfusion therapy in ischaemic stroke during DOAC usage warrants further researches in DOAC level testing and antidote use in thrombolysis triage to enhance the safety of its delivery.

Association between basilar artery diameter and stroke risk in Chinese patients with Fabry disease

YLT Lam, B Sheng, YP Chu, WT Wong, HH Kwan, LP Ng, CH Cheung Department of Medicine and Geriatrics, Princess Margaret Hospital, Hong Kong

Introduction: Fabry disease is an X-linked lysosomal storage disorder caused by mutation of a-galactosidase A gene. As the disease progresses, it is typically associated with end-organ damage, in which cerebrovascular events remain one of the most debilitating complications to occur with little warning. Vertebrobasilar dolichoectasia, a characteristic cerebral finding in Fabry disease, has been reported to be associated with higher stroke risk. This study aims to evaluate the correlation between basilar artery diameter with stroke occurrence in Chinese patients with Fabry disease.

Methods: We retrospectively reviewed 19 patients who were diagnosed with Fabry disease and had magnetic resonance imaging of the brain performed during their disease course. The association between stroke occurrence with different neuroimaging markers including deep white matter hyperintensities, periventricular hyperintensities, and basilar artery diameter were assessed. FAZEKAS rating scale was used to quantify the burden of hyperintense signal abnormalities on neuroimaging, in which deep white matter and periventricular hyperintensities were individually graded by a score of 0 to 3 on its amount of high signal intensity.

Results: A total of 13 men and 6 women aged 57.5 ± 11.5 years were included. Three (15.7%) patients developed ischaemic stroke; two of them demonstrated cortical infarcts. The mean basilar artery diameter was 3.67 ± 0.67 mm; larger diameters were observed in patients with stroke than those without (4.60 ± 0.58 mm vs 3.50 ± 0.47 mm, P=0.002). Basilar artery diameter moderately correlated with more extensive white matter changes (correlation coefficient=0.46, P=0.046) and stroke occurrence (correlation coefficient=0.58, P=0.009). **Conclusion:** Larger basilar artery diameter is associated with more extensive white matter changes and higher occurrence of cerebrovascular events. Baseline neuroimaging is recommended for patients diagnosed with Fabry disease, as basilar artery diameter serves as a screening tool in predicting stroke risk.

Clinical course of transthyretin familial amyloid polyneuropathy with p.Ala117Ser mutation

FP 3

LP Ng, B Sheng, WT Wong, HH Kwan, YLT Lam, CH Cheung Princess Margaret Hospital, Hong Kong

Background: Transthyretin familial amyloid polyneuropathy (FAP) is an autosomal dominant inheritable disease. Typically, patients develop progressive peripheral polyneuropathy, autonomic neuropathy, and restrictive cardiomyopathy secondary to the amyloid deposition. The missense mutation p.Ala117Ser is particularly prevalent among those with FAP in Southern China. We aim to study the phenotype of FAP in Hong Kong Chinese carrying this mutation.

Method: A descriptive case series of 11 carriers with p.Ala117Ser mutation from six unrelated families.

Results: Six symptomatic and five pre-symptomatic mutation carriers were included. The median age of pre-symptomatic carriers was 42. For symptomatic patients, the median age of symptom onset was 56 (range, 33-62) years. Two remained in FAP stage I at 13 and 15 years after symptom onset, one in FAP stage II at 3 years after symptom onset, and three in stage III after disease progression for 4, 17, and 19 years. The first presenting symptom was limb numbness in four and gastrointestinal discomfort in two patients. Three patients had carpal tunnel syndrome as initial presentation of neuropathy. All six symptomatic patients developed full-blown peripheral neuropathy and different degrees of gastrointestinal upset. Five had heart failure in the later years with two in New York Heart Association class II, two in class III, and one in class IV. The mean lapse time from neuropathy to heart failure was 8.4 (range, 1-14) years. A 70-year-old woman in FAP stage I and New York Heart Association class II had sudden cardiac death, which raised concern on whether cardiac amyloidosis could be more susceptible to malignant arrhythmia at a relatively preserved cardiac function.

Conclusion: FAP patients with p.Ala117Ser tend to present with neuropathy, commonly as carpal tunnel syndrome. Most patients have different gastrointestinal upsets and cardiomyopathy. The disease course is variable. Pre-symptomatic mutation carriers should be screened regularly as early as mid-20s to capture the disease emergence.

FP 4

Quantitative muscle strength assessment in late-onset Pompe disease and its correlation with 6-minute-walk test: a 4-year longitudinal study

Winnie WM Yau, Candy YY Leung, Ellen LM Yu, B Sheng Physiotherapy Department, Princess Margaret Hospital, Hong Kong

Background: Late-onset Pompe disease is a rare hereditary disease characterised by progressive limb girdle myopathy and weakness of respiratory muscles. Enzyme replacement therapy is its long-term treatment. This study aimed to evaluate any longitudinal change in quantitative muscle (assessed with a handheld dynamometer) and forced vital capacity in supine position (FVC-Sup), and to investigate the correlations between functional measures with the 6-minute-walk test (6MWT).

Methods: We retrospectively reviewed annual assessment documents of six men and two women with late-onset Pompe disease who were on enzyme replacement therapy from April 2016 to October 2019 in our centre. The studied outcomes were 6MWT, hip flexion, knee extension, handgrip strength, and FVC-sup. Data were analysed by linear mixed effects models and Spearman rank correlation coefficients.

Results: The mean age at diagnosis was 23.9 ± 8.2 years, and the mean age at start of enzyme replacement therapy was 31.9 ± 10.9 years. Over 4 years, there was significant decline in 6MWT (slope: -8.16 m [95% CI= -16.2 m to -0.13 m], P=0.047) and FVC-sup (slope: -2.70% [95% CI= -2.70% to -2.70%], p<0.001). The 6MWT was positively correlated with hip flexion (ρ =0.531, P=0.006), knee extension (ρ =0.612, P=0.001), handgrip strength (ρ =0.575, P=0.003), and FVC-sup (ρ =0.527, P=0.014).

Conclusion: Our cohort had significant decline in functional activity and respiratory function despite enzyme replacement therapy. Functional performance correlated positively with limb weakness and respiratory dysfunction. Physical interventions targeting at improving strength may be an option to slow down the decline.

Movement Disorders Symposium 2

S 3

Deep brain stimulation surgery for movement disorders other than Parkinson disease

Michael Lee

Pamela Youde Nethersole Eastern Hospital, Hong Kong

Since its introduction in 1987, deep brain stimulation has emerged as a standard therapeutic option for various movement disorders refractory to pharmacological treatment. Parkinson disease and essential tremor are the FDA-approved indications. In Hong Kong, more than 300 patients have undergone deep brain stimulation surgery since 1997. Patients with other movement disorders also benefit from deep brain stimulation surgery. In this session, cases of refractory cervical dystonia and Tourette syndrome will be shared.

Movement Disorders Symposium 2 Nonmotor symptoms and personalised medicine of Parkinson disease in 2020

K Ray Chaudhuri King's College Hospital, United Kingdom

The treatment of Parkinson disease (PD) remains underpinned by levodopa and other dopamine replacement therapies. Although dopamine replacement therapies, in particular levodopa, have the ability to improve the motor symptoms of PD, motor complications still affect the treatment strategies in PD. PD is considered a multisystem, multi-neurotransmitter dysfunction—related heterogeneous disorder. Biomarker-driven evidence suggests that PD is a complex disease that can manifest with non-dopaminergic syndromes. Characteristics of these patients with nonmotor subtypes have been described. Therefore, generic prescribing of dopamine replacement therapies may not be sufficient for some patients. We need to be aware of the 'one size does not fit all' concept regarding treatment. Consideration of specific personal needs and the clinical phenotype of patients before prescribing is the basis of personalised medicine.

UCB Epilepsy Symposium Real world evidence of anti-epileptic drugs benefit to patients with epilepsy

S 5

Manuel Toledo Neurology Department, Valle de Hebron Hospital, Spain

Clinical trials are often developed under conditions, which not reflect the daily practice. However, many of the endpoints and secondary results obtained from them can extrapolated in our daily practice. Data from real-life series are presented in parallel to clinical trials results.

S 7

UCB Epilepsy Symposium Tetratogenicity of anti-epileptic drugs

Torbjörn Tomson

Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden

Maternal use of antiepileptic drugs (AEDs) is associated with an increased risk of birth defects in the offspring. The teratogenic risks on foetuses associated with AED use depends partly on the time of exposure. The risk of structural teratogenicity--major congenital malformations (MCM)—has been associated with exposure in early pregnancy, whereas exposure throughout pregnancy may cause adverse effects on growth and neurobehavioural development. Prospective registries and meta-analyses have better defined the risk of MCMs in offspring exposed to individual AEDs at different dose levels. Valproate is the drug with the highest risk, whereas the prevalence of MCMs is lowest with lamotrigine, levetiracetam, and oxcarbazepine. For valproate, phenobarbital, phenytoin, carbamazepine, and lamotrigine, the risk of MCMs is dose-dependent. Prenatal exposure to valproate has also been confirmed to cause an increased risk of cognitive impairments and autistic traits. Studies have shown topiramate to be associated with growth restrictions in the offspring. This information enables a more rational AED selection in women of childbearing potential and evidence-based counselling on optimisation of AED treatment before conception. Recent studies have shown that changes in AED selection are associated with reduced rates of MCM.

Neuro-degenerative Disease Symposium Amyotrophic lateral sclerosis update and a review of novel therapeutic strategies

Lorne Zinman

Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada

Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease characterised by the progressive degeneration of the upper and lower motor neurons. There remains an incomplete understanding of disease pathophysiology and current interventions only mildly slow disease progression. This presentation will provide an update on ALS epidemiology, progression, prognosis and management. Novel therapeutic targets and innovative treatment strategies will also be reviewed. These recent advances will assist in transforming ALS from a terminal to a treatable disease.

Neuromuscular Disease Symposium The role of serology in the modern era of myositis

Andrew Mammen

Johns Hopkins Myositis Center, Baltimore, MD, USA

Inflammatory myopathies are a heterogeneous family of systemic autoimmune diseases that include dermatomyositis, antisynthetase syndrome, immune-mediated necrotising myopathy, and inclusion body myositis. Many patients with inflammatory myopathies have myositis-specific autoantibodies that define distinct phenotypic subtypes. In addition, some patients have one or more myositis-associated autoantibodies (MAA) that are associated with certain clinical features. In this presentation, Dr Mammen will discuss how myositis-specific and -associated autoantibodies can be used to diagnose and manage patients with inflammatory myopathies.

Neuromuscular Disease Symposium Diagnosis, treatment, and pathogenesis of immune-mediated necrotising myopathy

Andrew Mammen

Johns Hopkins Myositis Center, Baltimore, MD, USA

Immune-mediated necrotising myopathy (IMNM) is a distinct type of inflammatory myopathy characterised by muscle biopsies with myofibre necrosis and regeneration but without prominent endomysial inflammation or perifascicular atrophy. Patients with IMNM can be further subdivided into those with anti-HMG-CoA reductase autoantibodies, those with anti-SRP autoantibodies, and those without a known myositis-specific autoantibody. Each of these subtypes is characterised by unique immunogenetic risk factors, prognosis, and optimal treatment strategies. In this presentation, Dr Mammen will discuss the diagnosis, prognosis, treatment, and pathogenesis of each IMNM subtype.

Neuromuscular Disease Symposium Spinal muscular atrophy: new treatment and challenge

Sophelia Chan

Department of Paediatrics and Adolescent Medicine, LSK Faculty of Medicine, The University of Hong Kong, Hong Kong

Spinal muscular atrophy (SMA) is a hereditary neuromuscular disorder with an autosomal recessive inheritance and a spectrum of clinical presentations from the severe lethal infantile-onset SMA type I to the adult-onset SMA type IV. The disease is caused by mutations of the SMN1 gene leading to deficiencies of SMN protein. Additionally, the number of copies of SMN2 gene, a disease-modifier gene, which produces a small quantity of SMN protein, plays a major role in determining the clinical severity of the disease. Without diseasemodifying drugs, all patients have progressive weakness and deterioration of health over time. The effect on patients and their families is profound. This presentation will explain how the improved understandings of the molecular basis and natural history of SMA support the development of novel therapeutic strategies; as well as recognise the impact of the standardised care on outcomes. Therapeutic strategies in the pipeline, ranging from the modulation of SMN2 encoded transcripts to SMN1 gene replacement therapy, will be evaluated. This presentation will also share the local experience of the Hong Kong SMA treatment programme with nusinersen, which was started in 2018. The changes in motor outcome, health-related quality of life, and cerebrospinal fluid neurofilament level, pre-and-post-treatment, will be appraised. The way forward, which includes advancing the pre-symptomatic diagnosis and screening programme, establishing a transition of care programme, and setting up monitoring programme to determine the long-term impacts of the diseasemodifying treatments and further improvements in the supportive care, will be discussed.

Stroke Symposium Clinical application of the RAPID software

S 11

Greg Albers Stanford University Medical Center, Palo Alto, CA, USA

RAPID MR Perfusion software was first tested in the DEFUSE 2 study where it was shown to identify patients who could benefit from reperfusion up to 12 hours after symptom onset. Subsequently, RAPID computed tomography perfusion was validated in the SWIFT PRIME and EXTEND IA trials that showed the highest good outcome rates and largest treatment benefits among the early window thrombectomy studies. Both of the late window thrombectomy trials, DEFUSE 3 and DAWN, used RAPID for selection of all enrolled patients. Currently, the software is been used to select patients for the CHARM and TIMELESS studies. RAPID is the only software approved by US Food and Drug Administration to select patients for thrombectomy. Recently RAPID has expanded to include modules that detect brain haemorrhage, large vessel occlusion, and ASPECT scores. Recent data regarding the validation of these modules will be presented.

Novartis Migraine Symposium

CGRP-based monoclonal antibodies in migraine management: a review and the Singapore experience

KH Ho Gleneagles Hospital, Singapore

Traditional oral migraine prophylactic drugs are associated with a low rate of compliance and retention over time. This problem is related to a high incidence of adverse effects. Identification of the CGRP pathway as a major mediator of migraine symptoms has led to the development of oral anti-CGRP drugs and monoclonal antibodies against the CGRP receptor or molecule. The four US Food and Drug Administration—approved monoclonals show an excellent efficacy and tolerability profile in episodic and chronic migraine treatment. Real-life experience with Erenumab in Singapore confirms its efficacy in episodic and chronic migraine, even with co-morbidities and after previous inadequate response to multiple prophylactic agents. Erenumab was very well-tolerated in the Singapore population.

S 13

Astra Zeneca Stroke Symposium

Secondary prevention with potent P2Y12 inhibitor in minor acute ischaemic stroke or high-risk transient ischaemic attack

Lawrence Wong

Department of Medicine and Therapeutics, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong

Patients who had an acute ischaemic stroke or transient ischaemic attack may experience a subsequent potentially avoidable stroke. Trials have suggested that dual antiplatelet therapy is effective in preventing stroke after an ischaemic stroke or transient ischaemic attack. A large-scale trial THALES showed that ticagrelor, which is a direct-acting antiplatelet agent not dependent on metabolic activation, reversibly binds and inhibits the P2Y12 receptor on platelets, combined with aspirin for 30 days are superior to aspirin alone in preventing stroke or death by 17% in patients with non-severe, non-cardioembolic ischaemic stroke or high-risk transient ischaemic attack. The risk for severe bleeding events was 0.5% in the aspirin plus ticagrelor group and 0.1% in the aspirin group. The THALES trial further elucidated the benefits and risks of dual antiplatelet therapy in patients with acute cerebral ischaemia in a global setting.

S14&S15

Daiichi Sankyo Stroke Symposium

Cerebrovascular risk management and anticoagulation: scientific evidence and clinical decision on non-vitamin K antagonist oral anticoagulants

Hans-Christoph Diener Medical Faculty, University Duisburg-Essen, Germany

Stroke prevention in atrial fibrillation. Our local perspective and roadmap to future care

Yannie Soo

Division of Neurology, Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong

Anticoagulation in atrial fibrillation is the most effective therapy for secondary stroke prevention. Non-vitamin K antagonist oral anticoagulant is the preferred anticoagulant option for stroke prevention in atrial fibrillation. The benefit is recognised in patients at higher risk for ischaemic events and/or bleeding. In this session, the management of atrial fibrillation with non-vitamin K antagonist oral anticoagulants for secondary stroke prevention is discussed. Through case studies, we will learn from clinical practice the anticoagulation strategy to minimise cerebrovascular outcomes.

Biogen Hereditary Neurological Diseases Symposium Management of adult patients with spinal muscular atrophy

S 16

Tim Hagenacker
Department of Neurology; University Hospital Essen, Germany

Spinal muscular atrophy (SMA) is a progressive disease and has profound lifetime implications for patients and their families. Those affected need long-term multidisciplinary medical and supportive care to maintain functional mobility, independence, and quality of life. Nusinersen is approved for the treatment of all types and stages of SMA in patients of all age. Clinical trials have shown improvements in motor function in infants and children treated with the drug. The effectiveness of nusinersen on older children and adults rely on real-world studies. To date, small real-world studies in the US and Germany have reported motor function stabilisation or improvements in adult patients treated with nusinersen. In an observational adult cohort study, the mean Hammersmith Functional Motor Scale-Expanded scores were significantly increased compared with baseline, and 40% of patients were able to achieve clinically meaningful improvement (≥3 points increase) in scores. Although nusinersen seems to be beneficial to adult patients, there are practical challenges before initiating treatment. Patient-reported outcomes are increasingly important in determining treatment efficacy, especially in severely affected adult patients, in whom common motor function tests might not be applicable. Future studies should focus on the long-term effects of nusinersen. It is important to initiate treatment as early as possible in patients with SMA to prevent further loss of motor function.

Biogen Hereditary Neurological Diseases Symposium FLNC-related myofibrillar myopathy in Hong Kong: histopathology and genetics

Hencher Lee, ¹ Shun Wong²

¹ Department of Pathology, Princess Margaret Hospital, Hong Kong

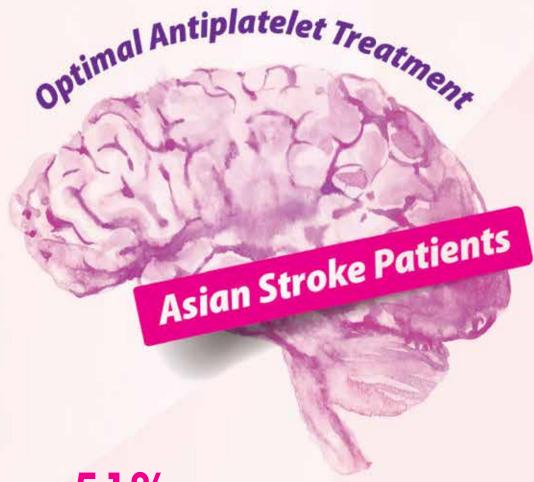
² St Paul's Hospital, Hong Kong

The clinicopathological features and genetics of FLNC-related myofibrillar myopathy in Hong Kong Chinese are discussed. We also demonstrate the evidence of founder effect associated with this Hong Kong variant LRG_879t1:c.8129G>A.

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51% risk reduction of recurrent ischaemic stroke*1

CSPS.com

Cilostazol Stroke Prevention Study for Antiplatelet Combination

Abbreviated Prescribing Information²

PLETAAL (cilostazol) 50 mg tablets. INDICATION: 1) Improvement of the maximal and pain-free walking distances in patients with intermittent claudication, who do not have rest pain and who do not have evidence of peripheral tissue necrosis (peripheral arterial disease Fontaine stage II); 2) Prevention of recurrence of cerebral infarction (excluding cardiogenic cerebral embolism). DOSAGE: 100 mg twice a day before breakfast and evening meal. CONTRAINDICATION: Known hypersensitivity to cilostazol or to any of the excipients; severe renal impairment; moderate or severe hepatic impairment; congestive heart failure; pregnancy; patients with known predisposition to bleeding, with hemorrhage, with any history of ventricular tachycardia, ventricular fibrillation or multifocal ventricular ectopics, with prolongation of the QTc interval, with a history of severe tachyarrhythmia; patients taking concomitantly 2 or more antiplatelet or anticoagulant agents; unstable angina pectoris, myocardial infarction within the last 6 months, or a coronary intervention in the last 6 months. WARNINGS AND PRECAUTIONS: may induce tachycardia, palpitation, tachyarrhythmia and/or hypotension. Monitor use in patients with stable coronary disease. Caution exercised for patients with atrial or ventricular ectopy, and patients with atrial fibrillation or flutter. Patients should be warned to report bleeding episode. Stop treatment in case of retinal bleeding. Stop 5 days before surgery. Rare report of haematological abnormalities. ADVERSE REACTIONS: ecchymosis, oedema (peripheral, face), anorexia, headache, dizziness, palpitation, tachycardia, angina pectoris, arrhythmia, ventricular extrasystoles, rhinitis, pharyngitis, rash, pruritus, chest pain, asthenia diarrhoea and abnormal stools, DRUG INTERACTIONS: Extensively metabolised by CYP enzymes; reduce dose to 50 mg twice daily for patients on strong CYP3A4 or CYP2C19 inhibitors. Caution when co-administering with any other agent having the potential to reduce blood pressure. Please see full Pre

Further information available upon request:

Otsuka Pharmaceutical (H.K.) Ltd.

21/F, East Exchange Tower, 38 Leighton Road, Causeway Bay, Hong Kong. Tel: 2881 6299 Fax: 2577 5206

*non-cardioembolic ischaemic stroke

References:

1. Toyoda K., et al. *Lancet Neurol*. 2019 Jun; 18(6): 539-548. 2. Pletaal Package Insert





Aimovig Important note: Before prescribing, consult full prescribing information. Presentation: Solution for injection, subcutaneous use: 1 mL prefiled pen contains 70 mg of erenumab. Indications: Aimovig is indicated for prophylaxis of migraine in adults who have at least 4 migraine days per month. Dosage and administration: Adults: The recommended dose of Aimovig is 70 mg administered subcutaneously every 4 weeks. Some patients may benefit from a obage of 140 mg every 4 weeks. Aimovig is intended for patient self-administration in the abdomen, thigh, or, if someone else is giving the injection, also into the outer area of the upper arm. Administration should be performed by an individual who have shown no response after 3 months of treatment. Evaluation of the need to continue treatment in patients who have shown no response after 3 months of treatment. Evaluation of the need to continue treatment is recommended regularly thereafter. The entire contents of the Aimovig pre-filled pen should be given to discontinuing treatment in patients who have shown no response after 3 months of treatment. Evaluation of the need to continue treatment is recommended regularly thereafter. The entire contents of the Aimovig pre-filled pen should be injected. Special populations patients with careful and effectiveness of Aimovig has not been studied in pediatric patients. No dose adjustment is necessary in patients with contained the patients are recommended regularly thereafter. The entire contents of the Aimovig pre-filled pen should be given to distinct the patients with careful patients. However, the patients is necessary as the pharmacokinetics of erenumab are not affected by age. Renal impairment. Volument is necessary in patients with real patients. Pregnand, Indiana the patients are reactions and patients. Warnings and precautions: Pregnandy, Indiana and Pregnandy Indiana. Pregnandy Indiana are administration. The patients with respect to the active substance or to any of the excipients. Warnings and precautions: Pregna

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