

FINAL PROGRAM & BOOK OF ABSTRACTS

XII NEUROMEDITERRANÉE 2012

2-4 NOVEMBER, 2012 NICOSIA - CYPRUS

The Cyprus

Institute of Neurology & Genetics



*Διαφορετικοί ασθενείς. Διαφορετικές ανάγκες.

Για πλήρεις συνταγογραφικές πληροφορίες αυμβουλευτείτε την Περίληψη Χαρακτηριστικών του Προϊόντος που δημοσιεύεται σε επόμενη σελίδα



Η Merck Serono είνοι ένος κλάδος της Merck



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> Βοηθήστε να γίνουν τα φάρμακα πιο ασφαλή: Συμπληρώστε την "ΚΙΤΡΙΝΗ ΚΑΡΤΑ" Αναφέρατε:

- · ΟΛΕΣ τις ανεπιθύμητες ενέργειες
- για τα ΝΕΑ Φάρμακα Ν
- τις ΣΟΒΑΡΕΣ ανεπιθύμητες ενέργειες
- για τα ΓΝΩΣΤΑ Φάρμακα

Κατηγορία Οργάνου Συσπίματος	Πολύ συχνές	Συχνές	Όχι συχνές	Μη γνωστές*
Λοιμώξεις και παρασπώσεις			Απόστημα στο σημείο της ένεστης	Λαμώξεις στο αημείο της ένεσης, συμπεριλαμβανομένης κυπαρπίδα
Διαταριακές του αιμοποιπτικού και του λεμφικού συστήματος	Ουδετεροπενία, λεμφοτιενία, λευκοτιενία, θρομβοτιενία, αναιμία			Θραμβωτική θραμβατιενική παριφύρα/Αιμαλυτικό συραιμικό αύνδραμο
Διαταριακές του ανοσοποιπτικού συστήματος				Αναφυλακτικές αντιδράσεις
Διαταρακές του ενδοκρινικού συστήματος			Δυσλεπουργία του Θυρεσειδούς συτινότερο εμφαινζόμενη ως υποθυ- ρεσειδιαμός ή υπερθυρεσειδιαμός	
Ψυχιατρικές διαταραχές		Κατάθλιψη, αῦτινία		Απόπειρα αυτοκτονίας
Διαταρακές του νευρικού συστήματος	Κεφαλαλγία			Στασμοί, παροδικά νευρολογικά συμπτώματα (τ.κ. υπαισθησία, μιλικός οποσμός, παρασθησία, δυσκολία στο βάδιομο, μιασικε- λετική σκαμμική που μπορεί για προσομοιάζουν με εξάροση πολατιλής συλέρυνσης
Οφθαλμικές διατοραχές				Αγγειακή διαταριοκή του αμφιβίκπτροειδούς (n.x. αμφιβίκπτροειδο πάθεια, βαμβιακόμορφα εξιδριώματα και απόφραξη της αμφιβίκιστρο ειδικής φλέβος ή αριτηρίας
Αγγειακές διατοραχές				Θρομβοεμβολικά επεισόδια
Διαταρακές του αναπνευστικού συστήματος, του θώρακα και του μετοθωρακίου				Δύστνοιο
Διαταριακές του γοστρεντερικού		Διάρραια, έμετος, ναυπία		
Διαταριακές του ήπατος και των χοληφόρων				Ηπατική ανεπάρκεια, ππατήτδα με ή χωρίς ίκτερο
Διαταριαχές του δέρματος και του υποδόριου κατού		Κνταμός, εξάνθημα, ερυθημο- τώδες εξάνθημα, κηλιδαβλατι- δώδες εξάνθημα		Αγγειοαίδημα, κιλίδωση, πολύμαρφο ερύθημα, δερματικές αντιδρά- σεις τύπου πολύμορφου ερυθήματος, σύνδρομο Stevens Johnson, αλωπεκία
Δισταρακές του μυσσκελετικού αυστήματος και του συνδετικού ιστού		Μυαλγία, αρθραλγία		Επαγόμενος από φάρμακα ερυθηματώδης λάκος
Γενικές διαταρακές και καταστάσεις της οδού χορήγησης	Ολεγμονή στο αημείο της ένεαης, αντίδραση στο αημείο της ένεαης, γρηπιώδη συμπτώματο	Άλγος στο σημείο της ένεσης, κόπωση, ρίγη, πυριετός	Νέκρωση στο σημείο της ένεσης, μάζα στο σημείο της ένεσης	
Παρακλινικές εξετάσεις	Ασυμπωματική αύξηση των τρανσαμινασών	Μεγάλη αύξηση των τρανσαμινιασών		

δυολαγμόρις τη συρισκύρι απη θαρατιός μη ΠέτΗ. Η έγτο Τουρίου ποτοκάντολει μης του που-μήμα στο σχροτάλης και ο Τουρχουσιά στραι τη ζητάχης του κοιτομάτια περιοξία ποι του όποι αυρίου ματά τη στοριάτη ματρία τη ματρία τη ματρία τη ματρία τη ματρία τη ματρία τη ματρία απο το ματρία τη ματρία απο το ματρία τη ματρία απο το ματρία τη μ δύνου/αφέλους της συνεχιζόμενης Θερατιείας με Rebit. Η χρήση διαφάρων τενιγκών ο Rebit αναμένεται να παρουσιάσουν το τυπικόγριπτώδες σύνδραμό των ιντερτερονών εινός του πρώτου εξο-μήνου μετά πιν έναρξη πης θεραπείας. Περίπου 30% των ασθενών θα παρουσιάσουν αντιδράσεις στο σημείο Ref or galaxies more productions more of provides collegations were proposed and consultation of provides in weight program. Enjoyout 30: were indexed and productions were approximately to provide in weight provides and provides and provides and provides and provides to provide in collegations and provides and p ра на продократи рака на разпрото на констранција и на на террионитри са террионитри са террионитри са террионитри са террионитри са террионитри на протоката и проток Протоката и протокатата и протоката и прот οια «Κοτοποίη τρήματοι όλοιτης Πολέξα (πραφρά τη βητ. - Τρίρι απο Νοιου στο Κοραμαζία) μης πλογολογιά δράτη ματοιοχράτη βητ. Τλαγραφρά τη βητ. - Τρίρι απο Νοιου στο Κοραμαζία. Τρίρι ποι διαγρά το δράτη ματοιοχράτη τη βητ. Τρίατη βητο δράτη το με πιν ενδογενή ανθρώτινη ιντερφερόνη βήτα. Παράγεται σε κύπαρα θηλαστικών (ωσθήκη κινεζικου κρικη

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Αριθμός συμβάντων Εκτίμηση ΚΜ	144 85.8%	106 62.5%			
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Αρθμός συμβάνιων Εκτίμηση ΚΜ	60 37,5%	33 20.6%			
			52%	0,48 [0,31 - 0,73]	<0,001
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MÉDOC ENDRORUN					
τετρογώνων (SE)	2,58(0,30)	0,50 (0,06)	81%	0,19 [0,14 - 0,26]	⊲0,001

* fw - τρες φορές την εβδομάδο

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**m - peoplemic micRopath

Λεπεμερή πληραφοριακά στοτείο για το προϊόν είναι διαθέσιμαι στην ιστο οθίδα του Ευρωπαϊκού. Οργανισμού Παια μέσων http://www.ema.eurora.eur



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Welcome

Dear Colleagues, Dear Friends,

On behalf of the organizing committee we cordially invite you to the XIIth Neuromediterranée Conference that will take place in Nicosia, Cyprus, November 2-4, 2012.

Neuromediterranée has a long tradition of excellent science and networking covering all aspects of neurology, bringing together clinicians and scientists from all countries around the Mediterranean to present the latest advances and discuss key challenges in neurology. For this year a rich scientific program features presentations by world experts on topics such as neurodegenerative disorders, neurological complications of systemic disease, neuropediatrics, neurooncology, brain injury, neurorehabilitation and pain, all areas of great importance for the Mediterranean region and beyond.

Organized by the **Cyprus Institute of Neurology and Genetics**, the **Cyprus Neurological Society**, and the **Neuromediterranée Society**, this year's conference will coincide with the Cyprus Presidency of the European Union. This special occasion emphasizes the bridging role of Cyprus in promoting peace and collaboration between Europe and the Mediterranean region. Cyprus epitomizes the Mediterranean past, present and future, finding itself between three continents and in the crossroads of different religions and civilizations throughout the long and stormy history of the island.

In these times of difficult political and economical challenges in the region and beyond, we strongly believe that cooperation, exchange of information and ideas, and promotion of excellence in medicine and science through international meetings like this will strengthen our collaboration and provide hope for a better future in the region and the world.

Nicosia, the capital of Cyprus offers many historical and cultural attractions. Located in the center of the island it also offers easy access to the costal cities and the forested mountains. The conference will be hosted by the Cyprus Institute of Neurology and Genetics, the largest neurological center as well as a leading academic and research institution in Cyprus, offering a stimulating environment for a productive meeting.

We look forward to welcoming you in Cyprus

On behalf of the organising committee





Committees

ORGANIZING COMMITTEE

Kleopas A. Kleopa Eleni Zamba-Papanicolaou Savvas Papacostas George Kaponides Costas Michaelides Lefkos T Middleton Andreas Hadjisavvas

INTERNATIONAL SCIENTIFIC COMMITTEE/ BOARD OF THE NEUROMEDITERRANEE SOCIETY

Georges Serratrice, France Jean Pouget, France Antonio Federico, Italy Jean-Marc Leger, France Lefkos T Middleton, UK Claude Desnuelle, France Piraye Serdaroglu, Turkey Kleopas A Kleopa, Cyprus Jera Kruja, Albania Riadh Gouider, Tunisia Mohamed El Tamawy, Egypt Nazha Birouk, Morocco Yehuda Schapira, Israel Fadi Abou-Mrad, Lebanon



Organised by:

- ✓ The Cyprus Institute of Neurology & Genetics and the Cyprus School of Molecular Medicine
- ✓ Cyprus Neurological Society
- ✓ Neuromediterranée Society







CYPRUS NEUROLOGICAL SOCIETY







FRIDAY, NOV. 2

Session A: Time: Chairperson: NOVEL THERAPEUTICS 17.00-18.30 K. Kleopa

Fr. A.1

17.00-17.30

Leonidas Stefanis, University of Athens and Biomedical Research Foundation of the Academy of Athens, Greece Enhancement of Chaperone-Mediated Autophagy as a therapeutic strategy in Parkinson's Disease

Fr. A.2

17.30-18.00

Michael Krams, Johnson&Johnson, New Brunswick, USA CNS drug trials – innovative clinical development strategies

Fr. A.3

18.00-18.30

Arie Stangou, King's College Hospital, London, UK Advances in the management of the familial and hereditary amyloidoses

FRIDAY, NOV. 2

18.30-18.45 OPENING CEREMONY OF THE NEUROMEDITERRANÉE 2012

George Serratrice Neuromediterranée Society

Kleopas A. Kleopa The Cyprus Institute of Neurology and Genetics

George Kaponides Cyprus Neurological Society

18-45-19-30 KEYNOTE LECTURE

Demetris Michaelides Professor of Archaeology, University of Cyprus Archaeological findings of medical nature in Cyprus

19.30-21.30 Cocktail reception

SATURDAY, NOV. 3

Session B:	NEURODEGENERATIVE DISORDERS			
Time:	9.00-12.30			
Chairperson:	L. Middleton			
Sat. B.1 Lofkes Middleten	Imperial College London, UK	9.00-9.30		
	Parkinson's associated dementias. Is th	nere a link?		
Sat. B.2		9.30-10.00		
Michel Goedert, N	Nedical Research Council Laboratory of N			
Biology, Cambridg Pathogenesis of tl				
i amogenesis oi n	le labopullies			
Sat. B.3		10.00-10.30		
	el Aviv University, Israel htia a separate entity?			
Coffee break, pos	ter presentations	10.30-11.00		
Sat. B.4 11.00-11.				
Maria Grazia Spillantini, University of Cambridge, UK				
The role of Alpha	-synuclein in Parkinson's disease			
Sat. B.5		11.30-12.00		
-	Imperial College London, UK			
Gene merapy in P	arkinson's disease			
Sat. B.6		12.00-12.30		
Richard Reynolds, Imperial College London, UK Mechanisms of neurodegeneration in multiple sclerosis				
Lunch		12.30-14.00		

SATURDAY, NOV. 3

Session C:	NEUROLOGICAL COMPLICATIONS SYSTEMIC DISEASE	OF		
Time:	14.00-18.00			
Chairperson:	J.M. Leger			
Sat. C.1 Jean Pouget, Paris Inflammatory myo		14.00-14.30		
Sat. C.2 Zohar Argov, Hadassah-Hebrew University Medical Center, Jerusalem, Israel Neuromuscular complications of systemic medications				
Sat. C.3 Jean-Marc Leger, Hôpital Pitié-Salpêtrière, Paris, France Neuropathy in the context of infection				
Coffee break, pos	ter presentations	15.30-16.00		
Sat. C.4 16:00-16.30 Guido Cavaletti, University of Milan-Bicocca, Monza, Italy Chemotherapy-induced peripheral neuropathy				
	Lebanese University, Beirut, Lebanon I tions of neurological disease	16.30-17:00		

SELECTED ORAL PRESENTATIONS - Session 1 Chairperson: S. Papacostas

Sat. C.6 Antonio Federico, University of Siena, Italy Adult-onset parkinsonism and hypermanganesaemia - a novel recessive syndrome caused by SLC30A10 mutation and Kufor-Rakeb (ATP13A2/PARK9) syndrome

Sat. C.7

Antonios Kerasnoudis, University, Bochum, Germany The role of neuromuscular ultrasound in the diagnostic of immune mediated neuropathies

Sat. C.8

Marios C. Pantzaris, George N. Loukaides, Evangelia E. Ntzani, Ioannis S. Patrikios

¹PALUPA Medical Ltd, ²The Cyprus Institute of Neurology and Genetics, ³University of Ioannina School of Medicine, ⁴European University Cyprus A Novel Oral Formula (PLP10) for the Treatment of Relapsing Remitting Multiple Sclerosis: A Proof-of-Concept, Randomized, Placebo-controlled, Double-blind Clinical Trial

Sat. C.9

K. Kyriacou, R. Papacharalambous, A. Hadiisavvas and T. Kyriakides Departments of Electron Microscopy and Neuropathology The Cyprus Institute of Neurology and Genetics, Nicosia, Cyprus The contribution of electron microscopy in the diagnosis of a case of childhood vacuolar myopathy

17.15-17.30

17.30-17.45

17.45-18.00

17.00-17.15

SUNDAY, NOV. 4

Session D:	NEUROPEDIATRICS, NEUROMUSCULAR &
	NEUROONCOLOGY
Time:	9.00-11.00
Chairperson:	K. Kleopa

Sun. D.1 9.00-9.30 Athanasios Covanis, Aghia Sophia Children's Hospital, Athens, Greece Myoclonic syndromes from early infancy to adolescence

Sun. D.29.30-10.00Francois Kamar, Beirut, Lebanon9.30-10.00Current & Future Treatment trends in High Grade Gliomas

Sun. D.3 Kleopas A. Kleopa, Cyprus Institute of Neurology & Genetics, Nicosia, Cyprus Paraneoplastic and non-paraneoplastic disorders of the voltage-gated potassium channel complex

Coffee break, poster presentations

10.30-11.00

SUNDAY, NOV. 4

Session E:	BRAIN INJURY, STROKE, PAIN &
	REHABILITATION
Time:	11.00-13.30
Chairperson:	G. Kaponides

Sun. E.111.00-11.20George Kaponides, Limassol, CyprusPharmacological options in rehabilitation of traumatic brain injury

Sun. E.2 11.20-11.40 Savvas Papacostas, Cyprus Institute of Neurology & Genetics, Nicosia, Cyprus Psychiatric Co-morbidity in Epilepsy

Sun. E.3 11.40-12.10 Constantin Potagas, University of Athens, Greece Evolution of aphasia in the rehabilitation from stroke

Sun. E.4 Ekaterini Kosma, Psychiatric Hospital of Athens, Dromokaition, Greece Phychopharmacology of chronic Neuropathic Pain

SUNDAY. NOV. 4

SELECTED ORAL PRESENTATIONS – Session II Chairperson: E. Zamba-Papanicolaou

Sun. E.5

Marilena Theodorou, Nektarios Poullos, Christine Kopp, Sabrina Astner, Anca Ligia Grosu, Michael Molls

Clinic and Policlinic for Radiotherapy and Radiation Oncology, Klinikum rechts der Isar, Technical University of Munich, Germany

Brain tumors: Radiosurgery and Stereotactic High Precision Radiotherapy

Sun. E.6

Carlo Bertoncelli University Hospital Chu-Lenval, Nice, France **Rehabilitation strategies in Neuropediatrics**

Sun. E.7

¹Payman Salamati, ²Mohammad Barkhordari, ³Kambiz Sotoudeh, ⁴Zohrehsadat Naii

¹Sina Trauma and Surgery Research Center, Tehran University of Medical Sciences; ²Department of Pediatrics, Tehran University of Medical Sciences; ³Department of Pathology, Tehran University of Medical Sciences: ⁴Research and Sciences Center of Azad University, Iran **Stereotyping Movement in Children**

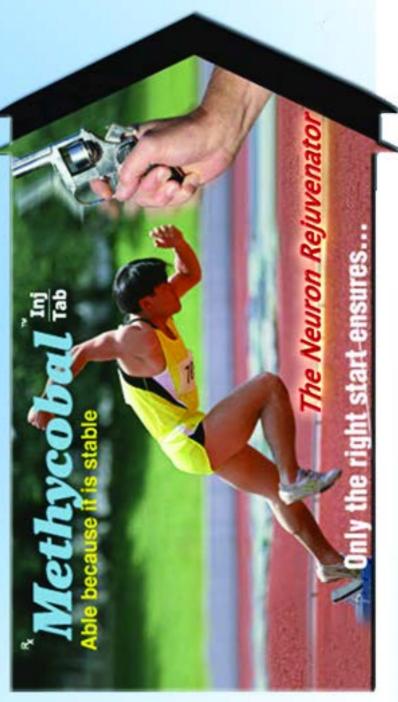
End of the congress, concluding remarks

12.45-13.00

13.00-13.15

12 30-12 45



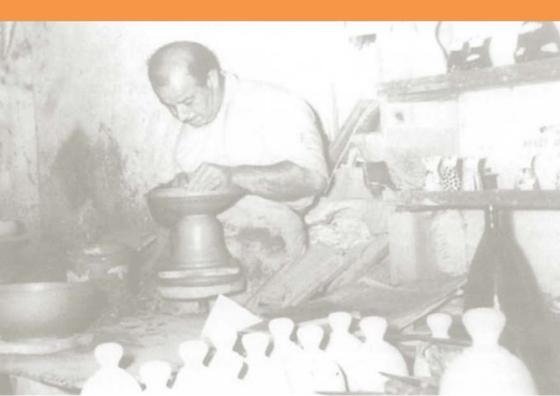




Medilink Pharmaceuticals Ltd P.O. Box 28576, 1640 Nicosia Tel: 22319282

Invited

Abstracts



Sat. B.3

Vascular cognitive impairment Amos D. Korczyn Tel Aviv University, Israel

Abstract - The epidemic proportions of dementia in old age are a cause of great concern for the medical profession and the society at large. It is customary to consider Alzheimer's disease (AD) as the most common cause of dementia, and vascular dementia (VaD) as being the second. This dichotomous view of a primary neurodegenerative disease as opposed to a disorder where extrinsic factors cause brain damage led to separate lines of research in these two entities.

New biomarkers, particularly the introduction of modern neuroimaging and cerebrospinal fluid changes, have, in recent years, helped to identify anatomical and chemical changes of VaD and of AD. However, recently accumulated data suggest that the two disorders have additive effects and probably interact with each other, since older people most commonly harbour both neurodegenerative and vascular still what degree primary chanaes. lt is unknown to the neurodegenerative processes and vascular chanaes occur independently or interact with each other. Furthermore, epidemiological studies have shown "vascular" risk factors to be associated with AD.

Therefore, a clear distinction between AD and cognitive impairment due to vascular changes cannot be made in most demented people and is furthermore unhelpful. Moreover, in the absence of efficacious treatment for the primary degenerative process, special attention must be given to vascular component even in patients with presumed mixed pathology.

Symptomatic treatment of VaD is similar to that given to AD, although it is less effective than in AD. For prevention of dementia it is important to treat aggressively all relevant factors, in particular risk factors for stroke, even in stroke survivors who do not show evidence of cognitive decline or only mild changes.

Sat. B.6

Mechanisms of neurodegeneration in multiple sclerosis Richard Reynolds, Roberta Magliozzi, Owain Howell

Centre for Neuroscience, Division of Brain Sciences, Imperial College London

Abstract - Accumulating neuronal loss and axon damage are thought to be responsible for many aspects of clinical progression in multiple sclerosis (MS), but little is known concerning the mechanisms involved. Recent studies of cortical pathology in secondary progressive MS have shown that the presence of extensive grey matter lesions (GMLs) organised associates with increased and diffuse meninaeal inflammation and correlates with a more rapidly progressive disease course. We have investigated the hypothesis that diffusion of proinflammatory cytokines from the meninges into the brain parenchyma could be responsible for this pathology. A quantitative analysis of subpial GMLs and normal appearing GM of the motor cortex from MS cases, with and without substantial meningeal infiltrates, revealed a significant gradient of neuronal loss from the pial surface only in cases with organised meningeal infiltrates. Immunohistochemical analysis revealed the presence of tumour necrosis factor (TNF) and interferongamma (IFNg) expressing cells in the meningeal infiltrates and TNFexpressing microglia in active GMLs. Gene expression profiling of the same lesions demonstrated the upregulation of multiple genes and pathways directly regulated by TNF and IFNg, and in particular genes involved in TNF mediated cell apoptosis/survival signalling. Increased meningeal inflammation gave rise to a shift in the balance of TNF signalling from the TNFR2 and NFkB anti-apoptotic pathway towards TNFR1 pro-apoptotic signalling, in keeping with the stimulation of TNFR1 gene expression by IFNY. These results support the hypothesis that an inflammatory milieu in the cerebral meninges could give rise to subpial cortical grey matter pathology, including neuronal loss, in MS.

Neuromuscular complications of systemic medications Zohar Argov

Kanrich Prof of Neuromuscular Disorders at the Department of Neurology, Hadassah Hebrew-University Medical Center, Jerusalem, Israel

Abstract - Drug induced neuromuscular disorders are not rare in clinical practice. If identified early, these are usually reversible conditions but sometimes are potentially serious and rarely even lethal. The lecture will present the various disorders through clinical cases and dilemmas of their management to enhance the relevance between the theory and the clinical practice. Drug induced myopathies may appear as myalgia only or as chronic weakness (with or without pain). Acute rhabdomyolysis can also be induced by medications. Emphasis will be made on the more commonly used drugs that may cause myopathy, especially the statins. New findings related to the immune pathogenesis of statin myopathy will be discussed. Drug induced impairment of neuromuscular transmission may present itself as unmasking of a known myasthenic condition or aggravating it, but also as an acute episode in the operative and post operative period as well as in the intensive care unit. The more drugs that may aggravate myasthenia and their recognition will be reviewed.

Neuropathy in the context of infection

Jean-Marc Leger

National Referral Center for Neuromuscular Diseases / Hôpital de la Salpêtrière and University Paris VI, Paris, France

Abstract - A number of disorders of the peripheral nervous system may be related to an infectious disease. Infection with Borrelia burgdoferi (Lyme's disease) is followed by early and rather distinctive neurologic syndrome in about 15% of untreated patients. This consists of a cranial neuropathy, radiculoneuropathy, or a lymphocytic meningitis, often in combination. These syndromes often improve spontaneously over several months, but improve faster with antibiotic therapy. In contrast, the chronic manifestations, mainly a predominantly sensory neuropathy, do not generally resolve spontaneously, and may partially improve with antibiotic therapy. Peripheral neuropathy is a common complication of HIV infection. Four types have been reported : distal symmetric polyneuropathy which mainly occurs in patients with advanced immunosuppression; inflammatory demyelinating polyradiculoneuropathy which is mainly observed in patients who are otherwise asymptomatic of HIV infection; mononeuropathy and multifocal mononeuropathy, which may occur early in the course as a self-limited inflammatory neuropathy, or as a manifestation of lifethreatening systemic CMV infection; and acute lumbosacral polyradiculopathy which has been reported in late stage of the disease. Other infectious processes associated with peripheral neuropathy include leprosy, hepatitis C virus (HCV) infection and West Nile virus infection. Combination of HCV infection and mixed cryoglobulinemia is frequently associated with either acute multifocal mononeuropathy, or distal polyneuropathy, which may improve with anti-retroviral therapies. West Nile virus infection is responsible for encephalopathy and axonal predominantly motor polyneuropathy.

Chemotherapy-induced peripheral neuropathy Guido Cavaletti

University of Milan-Bicocca, Monza, Italy

Abstract - Chemotherapy-induced Peripheral Neuropathy (CIPN) is a side-effect that could occur during and after chemotherapy treatment.

It is not an infrequent condition. It is second only to haematological toxicities and it is related to widely-used drugs (platinum compounds, taxanes, vinka-alkaloids, proteasome inhibitors).

CIPN generally consists of an axonal long-dependent peripheral neuropathy; its features are mainly sensory, even though some patients could develop a mild distal weakness. Main complaints referred by patients are related to both positive (paresthesia/disesthesia) both negative (hypoesthesia on different modalities) sensory symptoms, distributed in a stocking/glove fashion. Sensory alterations are usually slightly different, in dependence of the specific kind of drug administered (for example sensory ataxia is more common with platinum compounds).

CIPN, apart from being quite frequent, is highly relevant from a clinical point of view since it affects negatively Quality of Life (QoL) in a population of long-survival patients.

Thus, in recent years many efforts have been employed to better understand its mechanisms and to find a preventive and/or curative treatment.

At the present moment an efficacious treatment has not yet been discovered. A reason for this could be the following: clinical trials performed so far were made even more difficult by the lack of a solid end-point to be selected in clinical trials, since there is not yet a gold standard in CIPN assessment. In particular, it is not yet clear which clinimetric tool(s) could be more useful and the precise role of NCS and QOL questionnaire in this specific setting. Recently, a study has been published aimed to answer this still unmet clinical and scientific need: CI-Perinoms Study. It has demonstrated good validity and reliability findings for a set of selected outcome measures. Subsequent responsiveness study is to be held by the same group, thus possibly solving those pending questions.

Efforts in end-points selection should also be performed in combination with a genomic approach, to discover specific individual risk factors for CIPN. A careful selection of "genomic targets" could be recommended to design these studies: pathways that could be possibly involved in nerve damage should be aimed first. In the next few years initial answers could be expected to be given, in the hope of discovering a treatment for this potentially curable iatrogenic neuropathy.

Cardiac manifestations of neurological disease Fadi Abou-Mrad

Assistant Professor of Neurology & Medical Ethics, Lebanese University Medical Director, Saint Charles Hospital President, Lebanese Society of Neurology

Abstract - The cardiac complications of certain neurologic diseases have been well recognized for over 50 years. They are benign in most circumstances. Serious arrhythmias and myocardial infarctions, may occur. The link to most of these cardiac derangements is a transient or chronic autonomic dysfunction, depending on the specific neurologic disease. Myocardial infarcts, left ventricular dysfunction. and arrhythmias are well-recognized complications of subarachnoid hemorrhage, intracranial bleed, and ischemic strokes. Seizures may present with atonia or sudden death from asystole. Degenerative brain disorders, namely the synucleinopathies, may affect the central control areas or peripheral ganglia of the autonomic nervous system, causing autonomic dysfunction. In addition, cardiac conduction defects and cardiomyopathy are also common in certain neuromuscular disorders such as dystrophies and mitochondrial myopathies.

Sun. D.1

Myoclonic syndromes from early infancy to adolescence Athanasios Covanis MD, DCH, PhD

Emeritus Director, Neurology Department, The children's hospital "Agia Sophia", Athens, Greece

Abstract - The past few decades several distinct syndromes have been recognized in families and individuals. Advances in electroclinical correlation during video-EEG, brain imaging, magneto-EEG, family studies, linkage analyses and molecular genetics have contributed very much. The 2010 ILAE Commission on Classification and Terminology classifies electro clinical syndromes according to the age at onset.

Myoclonic seizures in childhood and adolescence whether massive, bilateral, symmetrical or fragmented constitute a heterogeneous group of syndromes with variable clinical and EEG characteristics and prognosis. Several myoclonic syndromes have been identified in childhood and adolescent and some of them are expressed incompletely in infancy and early childhood. The ILAE Task Force on Classification has recognized some of them, while other syndromes are in development and others having myoclonic seizures in their phenotype e.g., Eyelid myoclonia and absences, are accepted as seizure type. For many years the epileptologists have been characterized as "lumpers" and "splitters". It is not surprising that almost all splitters are epileptologists dealing with children.

Myoclonic epilepsy syndromes in infancy, childhood and adolescent, belong either to the group of encephalopathies (Early myoclonic encephalopathy, Dravet syndrome, Myoclonic encephalopathy in nonprogressive disorders, Lennox-Gastaut syndrome) or to the idiopathic group. In the idiopathic group there are syndromes where myoclonic seizures are the only seizure-type or the predominant type syndromes where both myoclonic and absence seizures and predominate in the phenotype. For example in myoclonic epilepsy of infancy/childhood and juvenile myoclonic epilepsy, myoclonic seizures predominate in the phenotype, while in eyelid myoclonia and absences (Jeavons syndrome), facial myoclonia with absences and epilepsy with myoclonic absences (Tassinari syndrome) myoclonic and absence seizures predominate. All these syndromes may not have, or may have to a variable degree, positive response to intermittent photic stimulation.

Early and correct diagnosis based on clinical and EEG characteristics, using correct methodology, will guide us to early and correct treatment which subsequently contributes to a better prognosis. For myoclonic syndromes sodium channel blocker drugs are contra-indicated. The correct diagnosis will also help us to choose material for genetic studies in identifying specific single gene defects or multiple interrelated defects.

Sun. D.3

Paraneoplastic and non-paraneoplastic disorders of the voltage-gated potassium channel complex

Kleopas A. Kleopa

Cyprus Institute of Neurology & Genetics, Nicosia, Cyprus

Abstract - A spectrum of increasingly recognized neurological disorders has been associated with autoimmunity to protein components of the voltage-gated potassium channel (VGKC) complex. VGKC antibodies have been reported in association with three main clinical syndromes: neuromyotonia, Morvan's syndrome (MoS) and limbic encephalitis (LE). Neuromyotonia is a syndrome of peripheral nerve hyperexcitability characterized by muscle cramps and stiffness. In MoS, symptoms of neuromyotonia are associated with autonomic and central nervous system dysfunction, with frequent insomnia. Patients with LE typically present with amnesia, confusion, seizures and personality change or psychosis, with discrete hippocampal abnormalities on brain MRI. In addition to these syndromes, VGKC-antibodies have also been identified in some patients with idiopathic epilepsy and late-onset dystonic epilepsy. These disorders share in common a relatively favorable response to immunotherapies if recognized early, although paraneoplastic cases tend to have a worse prognosis.

Recent studies have provided new insights into the antigenic targets of disease causing antibodies and their clinical correlates. Although initially antibodies were thought to bind directly to VGKC, subsequent studies revealed that in most cases they bound to another protein component of the VGKC complex, either Lgi1 or Caspr2, and rarely Tag-1. Most LE patients have antibodies against Lgi1 which is prominently expressed in CNS neurons and axon terminals that play critical roles in excitability, but is not significantly expressed in peripheral nerves. In contrast, NMT patients usually have antibodies against Caspr2, which is an essential component of the VGKC complex in peripheral axons, as well as in central neurons that promote arousal. The majority of MoS patients have both Lgi1 and Caspr2 antibodies, which may explain the combination of PNS and CNS phenotypes.

Searching for an underlying neoplasm is indicated in Caspr2-Ab+ cases with MoS and neuromyotonia, although the majority are nonparaneoplastic. Underlying tumors are mostly thymomas and some MoS cases have a history of myasthenia. In contrast, Lgi1 antibodies in LE patients are usually not associated with any underlying malignancy.

Sun. E.3

The evolution of aphasia after stroke

Constantin Potagas

Dept of Neurology, University of Athens, Aeginiteion Hospital, Athens, Greece

Abstract - Aphasia occurs in about one third of strokes: in the majority of people in developed countries vascular lesions of left hemisphere in the acute stage lead to important deficits in expression, processing and comprehension of language. In the post-stroke phase, aphasia usually has a spontaneous tendency for more or less complete recovery, and is an example of the ways the brain may adapt to a lesion.

There is much clinical experience in the natural course of aphasia after stroke, though the really documented clinical studies are few. On the other hand. clinical attitudes can also rely on research neurophysiological data confirming that amelioration is the consequence of some kind of reorganization of cerebral activity in the two brain hemispheres; however, the precise mechanisms sustaining this phenomenon still remain unknown and unpredictable. Functional neuroimaging techniques allow us to follow the functional state of the brain during the period of recovery. Some of these results point out to the role of the non-affected right hemisphere in the recovery from aphasia, while, others point out to the role of the perilesional regions of the left hemisphere.

Functional recovery may be observed essentially during the first few months post stroke. However, independent of the evolution of linguistic capacities per se (i.e. scores in the aphasia batteries), it is very important to focus on communicational abilities, which depend mainly on personality traits and are independent of the quality of language processing itself. A number of aspects of aphasia and of the communication deficit may improve even many years after the stroke, if sufficient care and speech therapy is provided. There are some studies and results on the effects of specific and intensive treatment, the effects of some pharmaceutical agents and of the transcranial magnetic stimulation.

It is also known that aphasic deficits and hemiplegia are associated very frequently with depression, leading to major handicap with many secondary consequences. Hence, a major medical issue is avoidance, prevention, and remediation of secondary effects due to wrong strategies (such as care givers attitudes, fear for using compensatory communication strategies, inhibition of utilization of remaining skills) and isolation of the aphasic person.

Sun. E.4 Phychopharmacology of chronic Neuropathic Pain

Ekaterini Kosma

Psychiatric Hospital of Athens, Dromokaition, Greece

Abstract - Pain is subjective sensory experience that serves a vital function. However pain can be transformed from an adaptive process into a disease state that implicates pathophysiological mechanisms such as peripheral and central sensitization.

This type of pain is called neuropathic, since it develops as a result of a lesion affecting the somatosensory nervous system. Clinically is characterized by throbbing shooting or stabbing pain and exaggerated and prolonged painful response to noxious or even non-noxious stimuli.

Neuropathic pain conditions are often chronic in their course and they range from very well established states such as trigeminal neuralgia and diabetic peripheral neuropathy to less well understood entities such as fibromyalgia or the so called functional somatic syndromes. Independently of the aetiology, neuropathic pain is in most cases intractable and refractory to treatment with common analgesics. On the other hand patients may benefit from a wide variety of psychotropic agents. In addition, chronic neuropathic pain shares many clinical and pathophysiological features with common psychiatric diseases, mainly anxiety and depression and this has been recently one of the main goals of basic research.

All the above have changed entirely our perspective for the management of neuropathic pain in the aspect that medications now target on modulating specific malfunctioning CNS circuits rather on treating causes or symptoms.

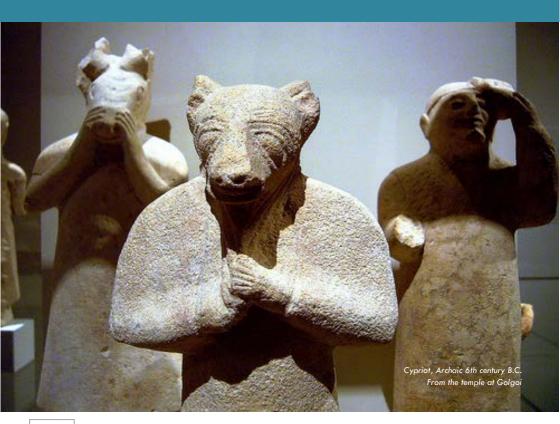
Second generation anticonvulsants such as gabapentin and pregabalin bind to the alpha 2 delta subunit of voltage sensitive calcium channels and produce analgesic effect by reducing calcium influx and excessive stimulation of post-synaptic neurons. Other classes of anticonvulsants such as oxcarbamazepine, lamotrigine and topiramate reduce pain by acting on voltage gated sodium channels.

Serotonin and norepinephrine re-uptakeee inhibitors such as venlafaxine and duloxetine are potent antidepressants and at the same time exert aanalgesicic effect by facilitating neurotransmission in descending inhibitory pathways at the level of the dorsal horns. Evenmore, drugs that are typically used to treat psychosis, such as olanzapine clozapine and amisulpiride have shown to be effective in selected cases although their analgesic mechanism has not been identified up to now. Many psychotropic drugs are recommended nowadays as first-line treatment options. However. several limitations regarding pharmacological treatment should considered. auidelines be For example, most of the medications licensed have only be examined in certain neuropathic entities such as diabetic peripheral neuropathy or postherpetic neuralgia. Another limitation is that medications' efficacy as well as adverse effects in randomized clinical trials have only been examined for 12 weeks or less and also there are only very few headto-head studies that allow comparisons in regard to long term efficacy and adverse events.

Finally it is very common to administer a combination of various drugs in order to achieve a satisfactory pain relief however this practice remains largely empirical, since it has not been confirmed in large randomized studies.

Selected Oral

Presentations



Adult-onset parkinsonism and hypermanganesaemia - a novel recessive syndrome caused by SLC30A10 mutation and Kufor-Rakeb (ATP13A2/PARK9) syndrome

Antonio Federico

Department of Neurological, Neurosurgical and Behavioural Sciences, University of Siena, Italy

Abstract - **Background:** In 2012 a new syndrome related to manganese transport impairement has been contemporary described by our group (Quadri, Federico et al. 2012) and by Tuschl et al (2012). Individuals with homozygous frameshift SLC30A10 mutation developed a recessive neurologic syndrome characterized by adult-onset parkinsonism, severe hypermanganesaemia, polycythemia, and chronic hepatic disease. This gene encoded protein belongs to a large family of membrane transporters. It's highly expressed in the brain, including the basal ganglia, and in the human liver, where explaned an important role in the manganese homeostasis. In individuals with homozygous loss of function SLC30A10 mutations, the manganese excretion is severely defective, leading to metal accumulation in the liver, the bloodstream, the brain, and other peripheral tissues. This syndrome delineates a primary disease of manganese metabolism and identifies SLC30A10 as a critical regulator of the manganese transport.

Methods: We describe the follow-up after 16 months of chelation therapy, in a 60-years patient born to consanguineous parents with adult-onset parkinsonism, severe hypermanganesaemia, polycythaemia, and chronic hepatic disease, from the original family. Patient received cycles of chelation therapy with disodium calcium edetate five days a month, every two months.

Discussion: After the first infusion cycle at dose of 10 mg/kg twice daily, urinary levels of manganese were considerably increased, but blood manganese levels were still very hight (133 mcg/L, n.r. 3.0-8.0). After tenth cycle of therapy the dose was increased to 20 mg/kg: blood manganese levels were within normal range (4.2 mcg/L, n.r. 3.0-8.0) with significant improvement of the extrapyramidal motor symtoms. Chelation therapy were well tolerated and the laboratory investigation showed a normal renal function during all cycles. We applied the Unified Parkinson's Disease Rating Scale (Part III) to follow the longitudinal course of disease: the score was decreased by 22 points than the first evaluation (27 points). T1-weighted brain MRI, that showed at the first observation bilateral, symmetrical hyperintensies at the level of the caudate and lentiform nuclei, thalamus, corticospinal

tract, medial cerebral peduncle, substantia nigra, posterior pons, and bulbar olives, was unchanged.

These data suggest that early diagnosis and treatment cause a remarkable clinical improvement and arrest the disease's progression. We will also report manganese abnormalities in two siblings affected by Kufor Rakeb disease, a disorder related to ATP13A2 dysfunction with parkinsonism discussing the role of manganese in the regulation of basal ganglia functions and its relationship to oxidative stress.

The role of neuromuscular ultrasound in the diagnostic of immune mediated neuropathies

Antonios Kerasnoudis

Neurological Department, St. Josef Hospital, Ruhr University, Bochum, Germany

Abstract - "The immune-mediated neuropathies are a diverse group of syndromes. Their diagnosis is based in classical cases, on the distribution pattern of peripheral nerve impairment and the results of nerve conduction studies (NCS). In some cases though, the clinical presentation may be subtle, so that extended differential diagnostic workup (cerebrospinal-fluid examination, laboratory tests, nerve biopsy) may be needed.

NCS remain nowadays fundamental not only for the diagnosis, but also for the follow-up and measurement of response to immune-treatment in these type of neuropathies. New challenges arise though, on how best to acquire a static and dynamic imaging of the nerves, aiming to provide a complementary and holistic approach to the nerve impairment. As ultrasound technology continoues to improve, nerve imaging has become more detailed and allows visualisation of nerve fascicles and small structural changes, which will move nerve imaging closer to the type of detail that can be seen in biopsy material. Neuromuscular ultrasound has been able to detect thickened or swollen roots, peripheral nerves or plexus, findings that are consistent with ongoing inflammation, especially in cases of chronic inflammatory demyelinating polyneuropathy (CIDP). Similar findings have been described also in Guillain-Barré syndrome (GBS), multifocal-motor neuropathy (MMN) and multifocal-acquired demyelinating sensory and motor neuropathy (MADSAM). Although these figures are rewarding to both physicians and patients, it remains unknown, whether ultrasound could be a reliable method for follow-up and measurement of response to immune-treatment.

This review provides a timely-update on the ultrasound findings of different immune-mediated neuropathies, while possible future possibilities of neuromuscular ultrasound are also discussed."

A Novel Oral Formula (PLP10) for the Treatment of Relapsing Remitting Multiple Sclerosis: A Proof-of-Concept, Randomized, Placebo-controlled, Double-blind Clinical Trial

Marios C. Pantzaris^{1,2}, George N. Loukaides^{1,2}, Evangelia E. Ntzani³ & Ioannis S. Patrikios^{1,4}

¹PALUPA Medical Ltd, ²The Cyprus Institute of Neurology and Genetics, ³University of Ioannina School of Medicine, ⁴European University Cyprus

Abstract - Rationale: Available multiple sclerosis (MS) treatments are products of reductionism. partially effective with no (re)myelinating/neuroprotective abilities associated with significant side-effects. We aimed to assess whether our novel interventions, formulated based on systems medicine (SM), comprising specific polyunsaturated fatty acids (PUFA) and vitamins reduce disease activity in patients with relapsing remitting (RR)MS. Methods: We contacted a 30-month randomized, double-blind, placebo-controlled, proof-ofconcept clinical study at the CING. Of a total of 80 patients, 20 were randomly assigned to receive intervention A (DHA/ EPA (3:1 w/w) omega-3, LA/ GLA (2:1 w/w) omega-6 FA, omega-3/omega-6 (1:1 w/w), other specific PUFA, monounsaturated FA, minor quantity of specific saturated FA, vitamin A and vitamin E), 20 to receive Vtocopherol, intervention C, 20 to receive the combination of A and C, intervention B (PLP10) and 20 to receive placebo, as an oral solution, once daily. The primary end point was the annual relapse rate (ARR) and the secondary end point was the time to disability progression. ISRCTN87818535.

Results: PLP10 reduced the ARR (primary end-point) by 58% (95% Cl 0.10 to 0.79, p=0.016) and significantly reduced the risk of sustained progression of disability (secondary end-point) by 86% over the 2-year period (Hr, 0.11; 95% Cl 0.01-0.97, p=0.047) vs. placebo. More patients in the PLP10 (72%) vs. placebo group (20%) were free from new or enlarging T2-weighted lesions on brain MRI over the 2-year study. No adverse events were reported. Interventions A and C showed no significant efficacy.

Conclusion: PLP10 treatment significantly reduced the ARR, and the risk of sustained disability progression without any adverse or significant side effects. This is the first clinical study of SM approach formula holding strong promise as an effective treatment for RRMS.

Sat. C.9

The contribution of electron microscopy in the diagnosis of a case of childhood vacuolar myopathy

K. Kyriacou, R. Papacharalambous, A. Hadjisavvas and T. Kyriakides Departments of Electron Microscopy and Neuropathology The Cyprus Institute of Neurology and Genetics, Nicosia, Cyprus

Abstract - Vacuolar myopathies comprise a heterogeneous group of disorders which share as their main histopathological feature the presence of vacuoles. Electron microscopy provides important information on the characteristics and contents of the vacuoles, and is crucial for the diagnosis of lysosomal myopathies. Several entities are included and in this presentation we report on a case, which may present a new type of autophagic vacuolar myopathy with unique sarcolemmal features. The case is a six and a half year old girl, referred because of difficulty walking and a tendency to fall easily. Fetal movements had been normal and family history was negative for a neuromuscular disease. The patient managed to walk at the age of two but was always a slow walker with a tendency to fall and having in particular difficulties with climbing stairs. On examination she had a myopathic face, diffuse hypotrophic musculature and she was hypotonic. Nerve conduction study was normal but with a myopathic EMG. A muscle biopsy showed the presence of vacuoles which stained positive staining for spectrin, dystrophin, laminin and dystrolgycans. In addition positive staining was seen for acetylcholinesterase, C5b9 and LAMP-2 antibodies. The vacuoles were evident with H+E staining and contained basophilic material: they were also positive for acid phosphatase and non-specific esterase. By electron microscopy the vacuolar membranes had basal laming on the luminal side of the membrane which confirmed that vacuolar membranes had sarcolemmal features. Electron microscopy also showed the presence of electron dense myeloid type material within the subsarcolemmal vacuoles and there was reduplication of the basal lamina.

Sun. E.5

Brain tumors: Radiosurgery and Stereotactic High Precision Radiotherapy

Marilena Theodorou, Nektarios Poullos, Christine Kopp, Sabrina Astner, Anca Ligia Grosu, Michael Molls

Clinic and Policlinic for Radiotherapy and Radiation Oncology, Klinikum rechts der Isar, Technical University of Munich, Germany

Abstract - "Stereotactic Radiation and Radiosurgery are special techniques to deliver precisely directed, high dose radiation that tightly conforms to an intracranial target to create a desired radiobiologic response while minimizing radiation dose to surrounding normal tissue. For an exact tumor definition we use the Fusion of CT, MRI and PET-scan in special treatment planning system. By this way the safe margin is minimized so that the side effects are low and at the same time the dose for the tumor is high. According to the national and international studies the local tumor control is more than 90 %.

With these techniques we can radiate tumors in complicated anatomically location that they are inoperable. The Radiosurgery delivers the high dose in a single fraction while the Stereotactic radiation delivers the high dose in fractionated schedule. The indications for these special techniques are the brain metastasis, brain tumor such as glioma recurrent, acusticneurinoma, meningioma, chordom, glomus tumor, hypophysis tumor, craniopharyngioma, medulloblastoma, ependymoma.

We present our experience from Munich for Radiosurgery and Stereotactic high Precision Radiation for Brain Tumors so that our publicated Researches."

Sun. E.6

Rehabilitation strategies in Neuropediatrics Carlo Bertoncelli

University Hospital Chu-Lenval, Nice (France)

Abstract - "Focused physiotherapy may cover important role on the whole of rehabilitation strategies dedicated to children with neurological diseases. In France, Neuropediatric Hospital Unit is usually called EEAPs (Etablissemet pour Enfants et Adolescent Polyhandicapés: Institute for children and adolescent with multiple disabilities).

EEAP of the University Hospital Lenval of Nice takes care of children with several neurological and psychological associated pathologies. Their clinical picture contains an enormous variety of deficiencies: neuro-developmental disorders, cerebral palsy, epilepsy, nutrition, visual, hearing, communication and intellectual disabilities.

From 2005 to 2012 our EEAP accommodated 72 patients, residents and day hospital.

Our objective was to develop a personal plan of management, including physical, occupational, and speech therapy, recreational and social milieu, as well as family and community resources. We aimed to optimize functional physical therapy intervention.

During these years we structured our rehabilitation strategy based on epidemiology, severity, and comorbidity of neurological deficits and psychopathological factors.

We endeavored to adapt the outcomes of our researches into clinical interventions by:

- 1. Collecting etiological data of patients
- 2. Analysing epidemiological information that could help us to preview individual semiology. We have found both neurological and psychopathological factors to be statistically associated to epilepsy

Additionally by:

- 3. Choosing neurological and psychopathological adapted assessment tools
- 4. Projecting and programming global and focused rehabilitation tasks
- 5. Practicing physical therapy based on these data We reviewed the effectiveness of the following physical therapy interventions as:

a. Comprehensive physical therapy approaches; b. Upper extremity treatments; c. Postural and Balance training; d. Strength training; e. Cardiovascular fitness/aerobic programmes; f. Constraint-induced therapy

g. Sensorimotor therapy (Bobath).

Sun. E.7

Stereotyping Movement in Children

¹Payman Salamati, ²Mohammad Barkhordari, ³Kambiz Sotoudeh, ⁴Zohrehsadat Naji

¹Sina Trauma and Surgery Research Center, Tehran University of Medical Sciences; ²Department of Pediatrics, Tehran University of Medical Sciences; ³Department of Pathology, Tehran University of Medical Sciences; ⁴Research and Sciences Center of Azad University

Abstract - **Objective:** To study the frequency of stereotyping movements (SM) in children. Methods: Using a multistage sampling method, we selected 300 children from 13 day care centers and primary schools in Urmia (Western Azarbaijan Province) in Iran. Data collection involved parent interviews in the presence of the children.

Results: Three hundred children (167 boys and 133 girls) were included in the study. Nearly 50% (149 out of 300) had one type of SM. The frequency of different types of stereotyping movements was as follows: bruxism 16%, head banging 13%, hair pulling 8%, nails biting 7% and thumb sucking 6%. There were not any significant relationships between sex and various SM varieties- except for head banging, which was more common in boys (p < 0.001). There were no significant associations between parents' education or occupation and presence of any type of SM (p > 0.05).

Conclusion: The frequency of stereotyping movements is high in children. More comprehensive studies are recommended.





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BIBΛΙΟΓΡΑΦΙΑ: 1. Jacobs LD. et al. Ann Neurol 1996;39:285-94 2. AVONEX Π.Χ.Π. Συνταγογραφικές πληροφορίες σε επόμενη σελίδα Αναστάσιο Μέγαρο, Γωνία Λεωφ. Αθαλάσσας & Ι. Χατζηιωσήφ Γρ. 402, 4ος όροφος, 2024 Στρόβολος, Κύπρος Τηλ: +357 22769946, Φαξ: +357 22769978 e-mail: info_cyprus@genesispharma.com www.genesispharma.com



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Το ασσευρία στοιχοια υποριγωον στι πορίστης το αγτιτροίες στοιχού αυτορισμικόν ετριποροιες στριπαίες μέτη τράτης το ΑΥΟΝΕΧ κατό την κητη. Το ασσευρία στοιχοια υποριγωον στι πορίστης το αγτιτροίες στοιχού αυτορισμού το αγτιτροίες στοιχού αυτορισμού το αντιτροίες στοιχού αυτορισμού το αγτιτροίες στοιχού αυτορισμού το αγτιτροίες στοιχού αυτορισμού το αντιτροίες στοιχού αυτορισμού το αγτιτροίες στοιχού αυτορισμού αυτορισμού αυτορισμού αυτορισμού το αγτιτροίες στοιχού αυτορισμού αυτορισμού αυτορισμού αυτορισμού το αντιτροίες στοιχού αυτορισμού αυτορισμου αυτορισμου αυτορισμού αυτορισμου αυτορισμου αυτορ the expension of the standard and δα tradition mapplicing layer on provinging table global in the juin geologican traditions in yoon layer in an any power before the uncertain and a global Adverse juin EDSS and 10 Juin 25 4 million in uncertain and a global Adverse juin EDSS and 10 Juin 25 4 million in a constraint analysis of the θηκαν σε αγωγή με AVONEX. 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Posters

Dysregulation of axonal cytoskeleton in a mouse model of X-linked Charcot-Marie-Tooth Disease

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Abstract - Mutations affecting the gap junction (GJ) protein connexin32 (Cx32) cause the X-linked Charcot-Marie-Tooth disease (CMT1X). Although Cx32 is expressed by myelinating Schwann cells, patients with CMT1X develop relatively early axonal degeneration, which correlates best with chronic disability. Our recent studies in *Gjb1*-null mice at the age of 2-4 months showed that compared to wild type (WT) littermates, the diameter of myelinated axons was progressively reduced in *Gjb1*-null mice. Furthermore, neurofilaments were progressively dephosphorylated and more densely packed. As a result of these cytoskeletal changes, fast axonal transport was slower in distal axons of mutant compared to WT animals, with reduced accumulation of synaptic vesicle-associated proteins after ligation and increased expression of beta-amyloid precursor protein and tau.

Here we investigated the signaling mechanisms regulating axonal neurofilament phosphorylation focusing on major kinases and phosphatases involved in neurofilament phosphorylation. Interestingly, ERK1/2 kinase, as well as PP2A phosphatase, was localized in noncompact myelin areas, in close proximity to GJs formed by Cx32. Another kinase, Cdk5, was more diffusely localized along the axon. Biochemical analysis showed altered amounts of ERK1/2, PP2A and Cdk5 as well as their upstream activators in Gjb1-null nerves. Moreover, the expression of two type alpha ATPase channels was reduced. Finally, assessment of mitochondria in mutant axons showed significantly increased density in Gib1-null axons, which may have implications for energy supply to the axon. These findings clarify for the first time the mechanisms of early axonal pathology that are independent of demyelination in this mouse model of CMT1X. Our results may lead to future therapeutic targets for this and other types of inherited neuropathy.

Funded by Cyprus Telethon

Umbilical cord blood stem cell ability relieve neurologic deficits in rat intracerebral hemorrhage model

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Abstract - Human umbilical cord blood (HUCB) is now considered as a valuable source for stem cell-based therapies. Previous studies showed that intravascular injection of the HUCB significantly improves neurological functional recovery in a model of intracerebral hemorrhage (ICH). To extend these findings, we examined the behavioral recovery and injured volume in the presence of increasing doses of human umbilical cord blood derived mononuclear cells (HUC-MCs) after intracerebral hemorrhage in rats.

The experimental ICH was induced by intrastriatal administration of bacterial collagenase IV in adult rats. One day after the surgery, the rats were randomly divided into 4 groups to receive intravenously either BrdU positive human UC-MCs (4 ? 106, 8 ? 106 and 16 ? 106 cells in 1 ml saline, n = 10, respectively) as treated groups or the same amount of saline as lesion group (n = 10). There was also one group (control n = 10) that received only the vehicle solution of collagenase. The animals were evaluated for 14 days with modified limb placing and corner turn tests. The transplanted human UC-MCs were also detected by immunohistochemistry with labeling of BrdU.

Two weeks after infusion, there was a significant recovery in the behavioral performance when 4 ? 106 or more UC-MCs were delivered (P < 0.05-0.001). Injured volume measurements disclosed an inverse relationship between UC-MCs dose and damage reaching significance at the higher UC-MCs doses. Moreover, human UC-MCs were localized by immunohistochemistry only in the injured area.

Intravenously transplanted UC-MCs can accelerate the neurological function recovery of ICH rat and diminish the striatum lesion size by demonstrating a dose relationship between them.

Complement C1Q ablation accelerates amyloid formation in a mouse model of TTRMet30 Amyloidotic Neuropathy

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Abstract - Penetrance and age of onset of TTRMet30 amyloidotic neuropathy varies significantly among different populations. Penetrance in Sweden, Cyprus and Portugal are 2%, 28% and 80% while age of onset is 52, 46 and 32 years respectively1. Genetic and epigenetic factors are speculated to play a role. There is good pathological data to implicate the participation of complement in the pathogenic cascades in peripheral nerve tissue 2. We have recently demonstrated a correlation within between age of onset and C1Q polymorphisms in the Cypriot cohoet of patients with TTRMet30 amyloidotic neuropathy suggesting that this is a genetic modifier 3. The object of the current study was to evaluate the role of complement C1Q in the available mouse model of the disease, the TTRKO/Met30+/+.

Gene therapy for inherited neuropathy

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Abstract - X-linked Charcot Marie-Tooth disease (CMT1X) leads to progressive distal muscle weakness and sensory loss and is one of the commonest forms of inherited neuropathies. The disease is caused by a large number of mutations in the GJB1 gene encoding the gap junction protein connexin32 (Cx32). Cx32 forms important channels of communication between the layers of the myelin sheath in peripheral nerves and is necessary for the homeostasis and survival of the myelinating cells and the axon. Transgenic disease models generated in our lab as well as clinical-genetic analysis of large number of patients have demonstrated that most CMT1X mutations result in loss of Cx32 function and failure to form gap junctions. Therefore, replacement of the normal gene may be an effective strategy to treat the disease. For this purpose, we have generated a novel 3rd generation lentiviral vector to allow gene delivery to peripheral nerves. In this vector, Cx32 is under the control of the mouse 2', 3'-cyclic nucleotide phosphodiesterase (CNP) promoter, which specifically drives expression in myelinating cells of the Central and Peripheral Nerve System. The expression cassette also includes a green fluorescent protein (EGFP) as a marker. We have successfully produced lentiviral vector particles and delivered them to the CNS and peripheral nerves. Our initial studies show widespread expression of EGFP in Schwann following intraneural injection, as well as in oligodendrocytes following stereotactic brain injection. These results indicate that gene replacement therapy is feasible and may lead to correction of the gap junction loss in myelinating cells of the CNS and PNS.

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Oxaliplatin-induced hyperexcitation of rat sciatic nerve fibers: an intra-axonal study

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Abstract - Oxaliplatin is an agent that is used extensively in gastrointestinal cancer chemotherapy. The agent's major dose-limiting toxicity is peripheral neuropathy that can manifest as a chronic or an acute syndrome. Oxaliplatin-induced acute neuropathy is caused by an alteration of the biophysical properties of voltage-gated sodium channels. However, sodium channel blockers have not been successful at preventing acute neuropathy in the clinical setting. We report intraaxonal recordings from the isolated rat sciatic nerve preparation under the effect of oxaliplatin. The depolarization phase of single action potentials remains intact with a duration of 0.52 ± 0.02 ms (n=68) before and 0.55 \pm 0.01 ms (n=68) after 1-5 h of exposure to 150 μ m oxaliplatin (unpaired t-test, P>0.05) whereas there is a significant broadening of the repolarization phase (2.16 \pm 0.10 ms, n=68, before and 5.90 \pm 0.32 ms after, n=68, unpaired t-test, P<0.05). Apart from changes in spike shape, oxaliplatin also had drastic concentration- and time-dependent effects on the firing responses of fibers to short stimuli. In the intra-axonal recordings, three groups of firing patterns were indentified. The first group shows bursting (internal frequency 90 - 130 Hz, n=88), the second shows a characteristic plateau (at -19.27 ± 2.84 mV, n=31, with durations ranging from 45 - 140 ms depending on the exposure time), and the third combines a plateau and a bursting period. Our results implicate the voltage-gated potassium channels as additional oxaliplatin targets, opening up new perspectives for the pharmacological prevention of peripheral neuropathy.

Frequency of anxiety and depression symptoms in patients suffering from chronic pain

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Abstract - **Background and aims**: Identifying and alleviating any psychiatric comorbidity is considered crucial in the therapeutic approach for chronic pain regardless of patients' pain status. The aim of the present study was to identify the frequency of anxiety and depression symptoms in a patient population suffering from chronic pain.

Methods: A total of 483 patients, 193 men and 290 women with chronic pain symptoms were referred to our Clinic from General Practitioners or other specialities in a period of 4 years. Patients underwent a thorough clinical interview and examination and underwent laboratory and neuroimaging examination when needed. All patients were prompted to complete the Hospital Anxiety and Depression (HADS) questionnaire, and scores over 10 were considered positive for either anxiety or depression symptoms. Patients with a psychiatric history were not included in the sample.

Results: The mean age of patients was 49.3 years for men and 47.6 for women. HADS scores showed that out of 193 men with chronic pain, 38 presented anxiety and/or depression symptoms and out of 290 women, 101 displayed anxiety and/or depression symptoms. The results were also verified by the clinical evaluation of the patients.

Conclusions: A large proportion of patients with chronic pain also suffer from symptoms of anxiety and/or depression and the percentage is even higher for women. Even if these symptoms do not constitute a distinct psychiatric disorder and regardless of patients' pain status, therapeutic approach for chronic pain requires to take these symptoms into account, in order to achieve optimal care.

Major psychiatric disorders identified during interview in patients referred for chronic pain

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Abstract - **Background and aims:** Psychological suffering takes the form of pain complaints leading to chronic functional impairment if major psychiatric symptoms are undiagnosed. The purpose of this report is to demonstrate the importance of a thorough patient interview prior to any intervention for chronic pain.

Methods: 483 chronic pain cases were referred to our Clinic from General Practitioners or other specialities during 4 years. Patients underwent a thorough patient interview by both a neurologist and a psychologist prior to any investigation and treatment approach. Two patients, as described below, were identified with an undiagnosed psychiatric disorder, and this was considered a treatment priority. Results: The first was a 58 years-old male who reported severe headache that had emerged after a brain surgery. He believed that a metallic clip was left into his brain and that among others could command him and could direct his movements in space. The patient was referred to a psychiatrist who diagnosed "paranoid schizophrenia" and prescribed neuroleptics. 4 weeks later the patient was free of symptoms. The second patient was a 64 years-old female with a constant severe chronic thoracic pain. She claimed she could "listen to" her pain and she could only be relieved when lying down, so the pain would eventually dissolve. She was diagnosed with "psychotic depression" and after appropriate treatment symptoms were partially remitted.

Conclusions: Medically unexplained chronic pain may sometimes involve major psychiatric disorders. A thorough patient interview before any intervention for chronic pain is considered a priority.

Predicting the progression of cognitive impairment in memory clinics Andry Giannakou, Chris Metcalfe, Yoav Ben-Shlomo, Margaret Newson, Sarah Cullum

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Abstract - Neuropsychological tests are routinely undertaken at memory clinics to help diagnose Mild Cognitive Impairment (MCI) and Dementia. For those patients found to have MCI it would be clinically valuable to be able to distinguish patients at high risk of progressing to Dementia. The aim is to develop a prognostic algorithm using neuropsychological test performance, in order to estimate the probability of progressing to dementia in patients with MCI. The cohort providing data of patients who attended the BRACE memory clinic in Bristol, UK comprises 643 MCI patients, 268 of whom were observed to progress to Dementia. To inform our analysis, a systematic search of the published literature and conducted for which meta-analysis were and indication of neuropsychological tests can distinguish those MCI patients at risk of progressing to dementia. This resulted in 38 articles fulfilling the inclusion criteria.

Subsequently the meta-analysis revealed that the most predominant domains associated with progression to dementia were Memory, Learning, and Language. Using the BRACE data, the best subset of neuropsychological tests to predict dementia was found to be compromising the tests of Mini Mental State Examination (MMSE), the Immediate Recall of the Story Test and the total score of Hopkins Verbal Learning Test (HVLT).

First reported cases of oculo-dento-digital dysplasia (ODDD) in Cyprus, caused by a novel GJA1 mutation

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Abstract - Oculo-dento-digital dysplasia (ODDD) is an autosomal dominant condition which manifests with a characteristic facial gestalt (typically a "pinched" nose with hypoplastic alae nasi and thin nares), microphthalmia, cutaneous syndactyly of the 3rd, 4th and 5th digits (syndactyly, type III), and other skeletal abnormalities. Radiographs usually reveal hyperplasia of the body of the mandible and broadening of the tubular bones. Several authors have noted spasticity and hyperreflexia as well as white matter changes and calcification of the basal ganglia. Loddenkemper et al. (2002) noted that spastic bladder or gait disturbances were the most frequent neurologic presentations starting in the second decade of life. Paznekas et al., (2003) demonstrated mutations in the gap junction alpha 1 (GJA1) gene (encoding Cx43) as the cause of the condition.

We report a mother and a daughter clinically affected with ODDD. Both were heterozygous for a novel three nucleotide deletion in the open reading frame of exon 2 of the GJA1 gene (c.397_399delAAG) resulting in the deletion of the amino acid lysine at codon 133 (p.Lys133Del). This in-frame deletion lies within the intracellular loop of the Cx43 protein. Within the same region, five missense mutations (p.lle130Thr, p.Lys134Glu, p.Lys134Asn, p.Gly138Ser and p.Gly138Arg) have previously been shown to be pathogenic (Paznekas et al. 2003 and Richardson et al. 2004). In addition, screening of 110 healthy Cypriot controls has proved negative for this deletion. We are therefore proposing that the p.Lys133Del is pathogenic due to possible conformational changes on Cx43. Further functional studies to ascertain pathogenicity are currently underway.

*Equal contribution

An unusual cause of seizures and eye malformations. First report of two Cypriot patients with Mowat-Wilson syndrome

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Abstract - Mowat-Wilson syndrome (MWS) is a mental retardation / multiple congenital anomaly syndrome caused by heterozygous mutations or deletions in the ZEB2 gene. It manifests with a characteristic facial gestalt, the presence of moderate to severe mental retardation, epilepsy and multiple congenital anomalies such as Hirschsprung disease, genitourinary anomalies, heart defects, agenesis of the corpus callosum and eye anomalies. Eye structural anomalies are not a common feature of MWS as they are described in only 4 % of the published cases. We report two new MWS patients, both of whom present with structural eye anomalies namely iris/optic nerve colobomata.

Patient 1 was initially examined in infancy and had distinct facial features, bilateral iris colobomata, hypotonia, global developmental delay, and constipation. Brain imaging did not reveal any CNS malformations. Seizures were first reported at the age of 12 years. Mutation analysis revealed a de novo c.652delC ZEB2 mutation thus confirming the clinical diagnosis. Patient 2 was examined at birth because of multiple congenital anomalies (heart anomalies, unilateral iris coloboma and partial aniridia, hypospadias) and distinct facial features. Mild hypotonia and developmental delay without seizures are recorded to date. Mutation analysis showed a de novo c.2769C>G (p.Tyr923X) mutation in exon 8 of the ZEB2 gene.

MWS is a relatively recently delineated condition usually caused by de novo ZEB2 mutations, although rare cases of sibling recurrence have been observed. We report two new cases presenting with ocular malformations (colobomata), suggesting that these anomalies should be included in the spectrum of the MWS.

Neurogenic Vestibular Evoked Potentials: Unique Scalp Waveforms Specific to Bilateral High Intensity Sound Stimulation are Probably Vestibular in Origin

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Abstract - **Objective:** Sound-evoked vestibular responses are a recently discovered phenomenon. It is believed to be due to the fact that the saccule is located close to the stapes footplate. Using the right type of sound, one can elicit eddy currents in the endolymph and stimulate the saccular macular. Our group has previously published the existence of unique neurogenic vestibular waveforms specific to this form of stimulation given unilaterally, but of low amplitude (0.1-0.2 uV). The purpose of this study is to use bilateral sound stimulation to obtain vestibular specific waveforms of higher amplitude that may be more clinically useful. The rationale for this is that the brain would be expected to respond more meaningfully to stimulation of both saccules, which would normally happen under conditions of vertical acceleration. Materials and

Methods: Ten physiological normal volunteers were examined, and several derivations from the scalp surface were used for recording. Responses were compared between two sound stimulation conditions: (1) 70 dB nHL clicks, known to stimulate the cochlea, and (2) 125 dB pSPL 500Hz tone, known to stimulate both the saccule and the cochlea. Results: Waveforms of high amplitude (0.2-0.4 uV), specific to the second sound condition were obtained at the following derivations: P3-F7, P4-F8, P3-P4 and P4-F3.

Conclusions: Waveforms that are probably vestibular in origin have been found so far to be preferentially located over the parietal areas. The higher amplitude responses compared to unilateral stimulation reported earlier may make these responses more clinically useful to locate lesions along the vestibular pathway.

Effect of Perindopril on oxidative status in rat hippocampus Tahereh Mashhoody^a, Fatemeh Zal^b, Masoumeh Emamghoreishi^c, Karim Rastegar^a

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Abstract - Oxidative stress and renin- angiotensin system are both involved in the pathophysiology of most of the systemic and central disorders as well as in aging. Angiotensin converting enzyme (ACE) inhibitors, well known for their cardiovascular effects, have also shown antioxidant properties in pathologic conditions. This study aimed to evaluate the effect of ACE inhibition on physiologic oxidative status of the brain. Normal male rats were divided into four groups of 7-9 rats each. Groups were treated orally by perindopril at the doses of 1, 2, 4 mg/kg/day or normal saline as the control for four weeks. At the end of the treatment period the reduced and oxidized alutathione (GSH and GSSG respectively) and malondialdehyd (MDA), the product of lipid peroxidation, were measured in the rats' hippocampus. The GSH and the ratio of GSH to GSSG increased dose dependently and were significantly higher in the group treated with 2 mg perindopril than the control group (p < 0.05). There was not any significant change in MDA and GSSG. This study demonstrated for the first time that ACE inhibition may promote anti- oxidant defense in the brain of normal healthy subjects.

ΠΟΛΛΑΠΛΗ ΣΚΛΗΡΥΝΣΗ



ΥΨΗΛΈΣ ΠΡΟΣΔΟΚΙΈΣ και Η ΔΥΝΑΜΗ ΝΑ ΠΡΑΓΜΑΤΟΠΟΙΗΘΟΥΝ



biogen idec

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* Polman CH, et al, N Engl J Med. 2006;354:899-910.

Συνταγογραφικές πληροφορίες σε επόμενη σελίδα



1. OKOMALIA TOY APPRAKEYTIKOV (PROIONTOL 1754691 300 mg. nurób daluaz tem prozonań fi balujance; moc ź typor, 7. DIODTINK AK DIODTINK I KA DIODTINKI I KA DIOD

MCPMM Take Obduszy via mapoceni folkularzne ruce tyck tych mapoceni folkularzne ruce dyrafter. A funkce Earlier Mapoceni folkularzne i mapoceni folkularzne ruce dyrafter a funkci folkularzne i mapoceni folk απροτητή στα αστοκείς με αφρατη η ητοπιο (κολοπουργία). Τα Ιδιατρικος πτιστούρις το ΤΥΧΑΡΕ στοποδιακικο τα παιδι σε αρτοριος γινιακς κατώ τη χρόγηση, βιντι παρόγροφ 6.3 [πρότις οχρήτης Ελθογίδα] αρτίζης τη Ο διήτης στημαι με τη αφαίοι τη οι οραμασικου πρώτης την τοπο τη χρόγηση. βιντι παρόγροφ 6.4 [πρότις οχρήτης Ελθογίδα] αρτίζης τη Ο διήτης στημαι με τη αφαίοι τη οι οραμασικο πρώτης την ποι μα πρακοίολου/στοι κατή Τι δρόκεια της σχομαιή (Ελ. παρόγροφ 6.8], η έχορη πρότι το γίνεται γιο διάστημα τα απάρισται υπαρακοίολου/στοι κατή Τι δρόκεια της σχοματή βιαθη τη συργασία τη τη αφαίο τη τη αρτοριατική τη αρτοριατή τη αρτόρια τη απόματη απόματη απόματη τη ματαρακοίολου/στοι κατή Τι δρόκεια της σχοριστη το αρτοριστη στη οιλολομοίη της της τορίας παι απόματης τη αρτοριστη απόματη απόματη απόματη απόματη απόματη απόματη απόματη απόματη απόματη απόμα τη αρτοριστη τη διαδική της τη αρτοριστη στη τη αρτοριστη στη αρτόρια τη τη αρτοριστη στη αρτοριστη απόμα τη αρτοριστη απόμα τη αρτοριστη απόμα τη αρτοριστη απόμα τη αρτοριστη απόματη απόμα τη αρτοριστη απόματη α entime care in hologia na o sequences any mangingers as 1. Episiona molumizante luxacoyerapionatales (PML). Advince ju ca Ergluso Advince exampación localizati, puncti la vero anice as a conconstructivativa conductiva, tray una facilitaria vero la conconstructivativa éspansia: na overseguén majolo fo reculur mos elas as aconsourcementales (punctiva) constructiva e seguences advinces ano espansia B. Intimp: nanoproductiva e seguences advinces (punctiva) constructiva e seguences advinces ano espansia de punction advinces advinces advinces advinces (punctiva) constructiva e seguences advinces με απόθειας που έκαι αριτικεί για αποιώματα καιτά του κά. 2. Οι ασθεική που έχοιν και τους τρας παράγιστε κυδιών για PML (β), κίωτί αποτις του αποιώματα του και μ.Ο. και αίχου και αρία διαθαιστικαι με TMRM για παραστάσει που 2 τηται οι είχου λίαι προητούμετη διαρματική αναστοαποτικτική διατράχους αυχαιτικό μαγλατιρο κάλους για PML. 20 οθείταις που έχοιν και τους τρας παράγοτης κυδιώνους η Εβρατίαι με αναστοαποτικτική διατράχους αυχαιτικό μαγλατιρο κάλους για PML. 20 οθείταις που έχοιν και τους τρας παράγοτης κυδιώνους η Εβρατίαι με αναστοαποτικτική διατράχους αυχαιτικό μαγλατιρο κάλους για PML. 20 οθείταις που έχοιν και τους τρας παράγοτης κυδιώνους για PML ανασμάζιας απόθεικαι της αυτοξής τους Παρασχράφους του ποριώνης τα Εποιλινήταρο Οθείτας Αρμάριστης. Τα τη συσματοποίηση τοι κοίλου τραι η κατό τη άρδακεια έχοιται τους ΤΟΥΚΑΡΕ, εξατάσεις για αποιόματα αυτά το του J.C. παράχουν πάτοροαρίας στήριξης. Η διασμασία αυτομικού η κατό τη άρδακεια έχοιται τους του ΤΟΚΑΡΕ, εξατάσεις για αποιόματα αυτά του σύ J.C. παράχουν πάτοροαρίας στήριξης. Η διασμασία αυτομούταται η επαλοτη τη διαδικαι έχοι του ΤΟΚΑΡΕ, εξατάσεις για αποιόματα αυτά του α.J.C. παράχουν πάτοροαρίας στήριξης. Η διασμασία αυτοματότικαι τη αριτο του δυζη διαδικό τη διαδιάσμαι μαι ποριάστη του τη του μάριστης τη στη αυτομάζης του διαδικά της του ποριαματικά του του του αυτά του αλομοι απόρις του διαδικόμαι μαι παράγεια του μαριτικής της αρομοριας επισμάζης. Η διαδικά του αποιματικαι τα του του μαρισκή ότη παράγραταται διαδιάσμαι ματοποιρίατη μαριστη του του του του διαδιάσι της προτικής αυτό του του Το του του μορισκή στη στατότη του τη αποτά του του του διάδια της παραστάσεις τη του του αποιματικαι τη του του μορισκή αντιστη του του του του του του διάδια τη ματοποίο διασια τη αποιματικά τη τη του του του του τη του του αρισκή διατη τη αποτήσει τη τη τη του του του του διάδια τη ματοποιά τη στα του του του του του του του διάδιου αυτοματικό τη του του τη του του αρισκή απότη τη του τη του του του του του πολιστα του του του του του του τ ατ τοτά χρονία δαστήματα αλάλη τη δροτεία. Νετά από 2 πη δια αι ασθακάς έρτίται τα απραχύριστη τα νάται για τον κάλονα γιο PMA, μετ TSSRRI Aν υπάρχου υπότοις το PML, περιστέρο χρήτης PML Aν υπάρχαι αποτάτηται και ότα συσκράτιστη PML. Ο υλουκός απολές θα πράτια να οδρίοληται τον απότης το PML, περιστέρο χρήτης PML Aν υπάρχαι αποτάτητα και ότα συσκράτιστη PML. Ο υλουκός απολές θα πράτια να οδρίοληται τον απότης PML The παρισίναι μαρήτης PML Aν υπάρχαι αποτάτητα και ότα συσκράτιστα τη PML. Ο υλουκός απολές παριστέρια αδρίολητης τη απότα αυτικρικάς PML Παιάναι παριστικής απότης PML Αν υπάρχαι αποτάτητα και ότα ματικριτάτητα το διατολογιατικής το αριστάριστα το αναιτάτητα τη PML Το διατολογιστικής διατολογιστικής διατολογιστικής διαλογιστικής διαδογιστικής της διαστολογιστικής τη απότα αυτικρικάς PML Το διαχό απότα το διατολογιστικής διαδογιστικης διαδογιστικής της διαστολογιστικής τη απότα αυτικρικής PML Το διαδο το αποτάδομαζη το αντίδιατη διαγογιστικής διαδογιστικής της διαστολογιστικής τη απότα αυτικρικός αυτικρίας διαστολογιστικής διαδογιστικής διαφορίας της διαδογιστικής αιδιαδογιστικής της παριστηρίους της διαστολογιστικής διαστολογιστικής της συστατολογιστικής διαδογιστικής της διαστολογιστικής απότα διαδογιστηρίας της απότα αυτικρής διαδογιστικής διαστολογιστικούς της της αυτολογιστης διαδογιστης διαδογιστης απότα διαδογιστηρίας της της παριστηρίος διαδογιστικής διαστολογιστικούς της της αυτικρίας της αντηροχής αυτολογιστης απότα διαστολογιστης της παριστηρίος συστηρίας της αυτολογιστης της αυτολογιστης διαδογιστης διαδογιστης διαδογιστης απότα διαστολογιστης διαδογιστης της αυτολογιστης της αυτολογιστης της αυτολογιστης διαδογιστης διαδογιστης διαδογιστης απότα διαστολογιστης της παριστηρίος συστηρίας της αυτολογιστη της της αυτολογιστης της αυτολογιστης διαδογιστης διαδογιστης διαδογιστης διαδογιστης της αυτολογιστης αυτολογιστης της αυτολογιστης της διαδογιστης διαδογιστης διαδογιστης διαδογιστης διαδογιστης διαδογιστης της αυτολογιστης διαδογιστης της αυτολογιστης αυτολογιστης διαδογιστης α στορογια τομουγίας στοιούς μαι μησια το ποια στοστρορο Αποτος με πω του συρασιο τοματία με η 11 συστή τρατια προσουσουστα την από της του συράφως Η 55 το ποι ποιαποροστησιο ποτις μαρικαι ή αρλαγματι την ποιαρφηρία ματη την ποιαρφηρία « απόληξη θεσιστική συμματίση της ευχητίζεισης φέριμας»; κατή την αλαφάμη από την PRL για προστατιας πληροφορίες, βλης Προφορίας τα Ιστροφορία καταιλούτητας Ο τομης δαρίστης Αλλαγματία ματο ευσοφορία τοματία την κατά την αλαφόρι το αράψης πληροφορίας τη αποροιατία της τομησίας το ποια την αποροιατική την αλαφόρι τη ποιαρφηρία το τομος του ποια την αποροιατική την ποιαρφορία της του τομούτης αράφης του Το 1549 κ. καιμας στα αδικότεις με όστο το Circin, οι στοία τηται αποροιατισμέση όπου πήρας σημαγική συνοστρόπης. Σπότος

Οι ιπροί τράτια να άξιολογούν κάθε μεμονωμένη τερίπτυση ώστε να προσδορίζουν κατά πόσο υπάρχουν στοχία ανοσοκαταστολής των από την διαφής θεραποίας με TS46H (8), παρόγραφο 43), Σε λινικός δοιωμέ όθοης 3 για του χρέτης το προτοποιρικός που τραγό αργήστη απριστοποιάτιζα να συχατηριτική με αυξιαμότι αυτοριτική μαρία μαριατική του τράτης το τραγό τη του τράτης μηριματοτράτης τη αποτράτη του του τράτης μηριματοτράτης τη αποτράτης του τράτης μηριματοτράτης του τράτης από τράτης του τράτης από τράτης τράτης του τράτης από τράτης του τράτης από τράτης του τράτης από τράτης του τράτης από τράτης του τράτης από τράτης του τράτης από του τράτης από του τράτης του τράτης του τράτης του τράτης τράτης του τραι του τράτης του τράτης του τράτης του τράτης του τ εφομοειναική προίτησα κατικά για ματά τη διαστή του παίδιαπό ενόξατα τα σύχητα τα επιτράθητη αποσοσιασταίτοι ή διαγή. Από θα δηστία να λαβάθεται απορατικά ματό για πάτα ματό της το απορατικά της απορατικής της το απορατικής της το παίδιατου Βραχοχρίας χροητήσες σταροδιαό του χρηρισποιεύται για της σηματίπιση των υπορατικώ θα καχαίτηταν μα ειδάρτη των λαμάζεται Καινικός διαμές Γλαμόχια του Τλθθαί της υπορατικός το απόρα της της σηματίπιση των υπορατικώ θα καχαίτηταν μα ειδάρτη των λαμάζεται Όποι διαλικάται σε 10 m χωριοζου απο) 50 θαι της το αραμοειατικής πορίου παράς της 70 που 16 406 της ιστάριστας Το ποι διαλικάτα σε 10 m χωριοζου απορο 50 ητημί (1954) από τα φαιρισευτικά της σύστας διαχώς το της της διαγό Το 17540 θαι απορατικής το απορατικής της διαγή της αποραίες της διαγότητας της συσταροτικής της συσταροτικής Το 17540 θαι αποράσει της το απορατικής της διαγή της αποραίες της διαγή της συσταροτικής της συσταροτικής της της απορατικής της της απορατικής της συσταρου της της συσταροτικής της της συσταροι της της συσταροτικής της συσταροι της της συσταροτικής της συσταροτικής της συσταροι της της συσταροτικής της συσταροι της της συσταροτικής της συσταροι της συσταροτικής της συσταροι της συσταροτικής της συσταροι της της συσταροι της συσταροι της συσταροι της συσταροτικής της συσταροτικής της συσταροτικής της συσταροτικής της συσταροι της συσταροτικής της συσταροι της συσταροτις συσταροτικής της συσταροτις της συσταροτικής της συσταροτικής της συσταροι της συσταροτικής της συσταροι της συσταροι της συσταροτικής της συσταροι της συσταροτικής της συσταροι της συσταροτικής της συσταροι της συσταροτις συσταροτης συσταροι της συσταροτης συσταροτης συσταροτης συσταροτης της συσταροτης συσταροι της συσταροτης συσταροτης συσταροτης συσταροτης συσταροτης συσταροτη апрет селенорале ту сурсковно та отсложе медатила отклица, от селеното и покуление от екропните сучут, и от 1-земен та е прет се очучута у та орбок клуза по обще клучута, бе курски у клучанте (клуза срайка 54 Горийрта, катера на рекула 54 Горийрта, катера 54 Горийрта, 154 Горийрта, катера 54 Горийрта, 154 Горийрта, 54 Горийрт πρέτει να αξατοτεί η ειχρίπτως ποιοτής της θειροπείος, με το TK48H. Ογλουχία F.Ο TK48H στοικομέται το σλομίτωτο γολα. Η ποξιαστιτο το τολομίτωτο γολα. Η ποξιαστιτο το πολομίτωτο γολα. Η ποξιαστι το πολομίτωτο το πολομίτωτο το πολομίτωτο το πολομίτωτο το πολομίτατο πολομίτατο το πολομίτατο πολομίτατο το πολομίτατο πολομιστη πολομίτατο πολομίτατο πολομίτατο πολ της δετολος περιόδου του μάτεται το 5.5% του ασθεινό που υπάβλήθηκαι το θεραπία μα παίτεμπολο ανίσκρα αναπλάμητα ευίργος το αφοράκοι μοικού αγιωσι 28.6% Η Η μαγίατης πορίτηται αστατήματια κατραγία που πορύσμαν από δωμές καρίας μου αρόγμας με εισοικού φάρμαια αι ασθεικά με ανάρμονη από πλαίος ήτατ το παίτεμπολο μαράτη από προιοποίρματη διαση, ανοράβηκον μας ΟΔη, καιτά, και κλιώνη και αρίας από αθεικά με ανάρμονη από πλαίος ήτατ το παίτεμπολο παρουπάζισται τη ανοιτόμμη διαση, ανοράβηκον μας ΟΔη, καιτά, και κλιώνη και αρίας προτημώρικας έρως πορης Κπάλλογος ανατιθμάτηνα ισφορικά κατάτερίας από παρουπάζισται διαση, ανοράβηκον μας ΟΔη, καιτά, και κλιώνη και αρίας προτημώρικας έρως ανοιτής που αποράβησης με το εικοικοί φάρμαση παρουπάζισται παρουπάζια. Οι αντιθμάτηται τη ανοιτόμετη από αφούρα από εκείτη που αποράβησης με το εικοικοί φάρμαση παρουπάζισται παρουπάζια. Οι αντιθμάτηται τη ανοιτήστα τη αρία τη αρία τη αρία τη αριατική τη αρίας τη αρίας τη αρίας τη αρίας τη αρίας τη αριατόματη τη αριατικής τη αρίας τα αριατόμεται τη αριατόμεται τη αριατόμεται. Οι αντιθμάτηται τη αρίας τη αριατόμεται τη αρίας τη αριατήρης τη αριατήρης τη αρίας τη αριατήρης τη αριατήρης τη αριατήρης τη αριατήρης τη αριατήρης τη αριατήρης τη αρίας τη αριατήρης τη αριατήρης τη αριατήρης τη αριατήρης τη αριατήρης αριατήρης απόριας τη αριατήρης τη τη αριατήρης τη τη αριατήρης αριατήρης απόρισης αριατήρης τη αριατή ότις με το κοινού όφραιο ταριλαβάτοντο (Δθα), τουτία, καίται διάδουτας μέγη, Απλήρδιας ιπτρισυρθητός Τρ. Επτις Δετηχύεικες Ανικές δουμές συρθούς αυ αστοθετίες με 20. Το πόδρο ιστη χραιοθητός μεριοδύτηση το λήβραιο της άγραις το μοιρίας το ποριστικός της ποριστικός της ποριστικός το ποριστικός το ποριστικός το ποριστικός το ποριστικός το ποριστικός της ποριστικός της ποριστικός το ποριστικός το ποριστικός το ποριστικός το ποριστικός το ποριστικός της ποριστικός το ποριστικός ποριστικός το ποριστικός το ποριστικός πο «απία, ματος και Εδαιη (β), παφήρορο 44, Α, μπά από περίου 4 μήκας έχοπτίας υπόραι υποίρι για απμάνους παριουία οποιομάτινα, είτα μαι μαιανόμης αποτιλαμοποιήτητας τη διλουρίας μαφότης αυβάλητοι να στουτώ ματη τέγχους που μπορού ναι οποιρισμούται μαι μαι απόμας αποτιζατικής τη ματηρικής τη τη πρωτή πετιτή εξίτουπ, μάδομόνο ότι μπορού ναι οποιρισμούται για αυβάρι τη μαιανόμης αποτιλαμούται τη ματηρικής τη τη πρωτή πετιτή εξίτουπ, μάδομόνο ότι μπορού ναι αρισμοριάτης της μπομασήρης αποτιλαμότης το ματήρου δια ματήρου τη ματορικό τη αυτό απόμη ματηρικούται τη αποίοματι τη αρισμούται τη αποιρισμική τη τη πρωτή της μπομασήρης τη αυτό τη ματορικού αποριασία απόματατα. Κομμάζεις ο αμπαρίας διαριτικής της TML και αναμαριούς λομμάζεις 25 δεπετις διαρίζεις το διατήρι διαβόρι το αιοικού αραμότου. Τη έχοση το μαθματήρης της τη πρωτή τη διαριτικής τη τη διαριτικής τη αρισμής τη τη αρισμής τη τη απόμη τη παιδιατική αίδου τοι αποις αθοιότης το μαιοικό αρισμότεις. Τη εποιρισμότη διαριότης της TML και αναμαρίας διαμμάζεις διαμπαρίας τη τη προτήρια τη αρισμούτης της TML και αναμαριατός λομμάζεις 15 οποις τη παιδιατική αδιαρία το αιοικοι αρισμούς αρισμότεις. Τη έχοι τη μαίο ματηρικής τη αρισμής τη τη διαριάζη τη αρισμής τη τη αλισμότη τη αρισμής τη τη διαριάτης της τη στη αρισμής της τη διαριάτης της τη διαριάτης της στη στηρικής τη αρισμής της τη διαριάτης της στηρικής της τη αρισμής της τη διαριάτης της στηρικής της της διαριάτης της διαριας της στηρικής της της διαριότης της διαριας της στηρικής της στηρης της στηρικής της της στηρικής της της στηρικής της της στηρικής της απ' ότι σε ασθενείς του ελάμθαναν το εικουικό φάρμακο. Κατά την εμπειρία μετά την κικλοφορία του πορίφιτρε στην αγορά, μπήρξαν αγορορές απ οτι σε σσέσκις που καιμορικό το ακοίνο φορμίακ. Απαι την μπορία μετα την κυλοισφαία του προίστις στην στρος, υπηρέα στοιρομος από το σσέσκις που καιμορικό το ακοίνο φορμίακ. Απαι την μπορία μετα την κυλοισφαία του προίστις στην στρος ματηρέα πλασφάρεια μπατιτικά την απορία την απορία την από τη δάρκοα των λουμέων και υπήρξα στοιρόμουτης την υστάλλη θεραπαία. Αναφάρειαν επιματιτικά την απορία. Η ματιτικά την απόρεται την μουμέανο του υπήρξα στοιρόμουτη με την υστάλλη θε από την αυτολοφορία στην απορά. Η PML συτήθως σδητεί σε οφορή αναπρία η θέκατο (βλ. παράτραφο 4.4). Ηταπικά παρατατικά λιθόροματι дио на токороди си то трак. О так котора котран ко красн котрана такато де на радироват. На таката нарактако на правития соврем патами Крайна содрем уталики година предлакулянация, сторандей каката правита. Пота раконородст правития с ток на токата и на токата и совеката на предлака на 2 таката на токата предлака на каката на предлак патами с токата предлака на совеката на предлака на 2 таката на предлака на совеката на предлака на совеката Патами с предлака на предлака на совеката на предлака предлака на совеката на предлака на совеката на предлака Патаката предлаката предлака на совеката на предлака предлака на совеката на предотока на совеката на предлака на совеката Пата на предлака на предлака на совеката на предлака на совеката на предлака на совеката на предлака на совеката λεφούπτρα, μονούπορ, προιτόφια, βοστάφια, ο ματάγοι το μάρουπορα, Αλάζοτας των οδιτατρόψων δεν παρατηρήθηκαι. Ο ουζότας τω αργικότι τημέν τη ελεφούπταρ, προιτόφια, βοστάφης προπόβου Αμαίρισταν στα διότες των οδιτατρόψων δεν παρατηρήθηκαι μαζι αλύ da μάρας τιμές παράμπουν αντός των φοιολογιών επιλικών. Κατά τη δάρισκαι της θεραπίας με "TS46BI παρατηρήθηκαι μαζι αμασοραίτη μίζαμα μαγία. Τό αξι ότης το προπόβου δια μάρας το το προτό της διαστικότης της το προτηρήθηκαι μαζι ματοραίζει μίζα της αματολογικάς μπάρης της προτηρίας το προτης θεραπίας τιμές, αυτήθες αυτός 16 φβολρουπό της το μάρας πους ματοβολίς τους αυτολογικές μπάβητές επίστρεφια της ποριτής θεραπίας τιμές, αυτήθες αυτός 16 φβολρουπό της τολοματίας της ΤΑ ΚΑΤΟΚΟΓΤΗ ΑΔΕΙΑΚΤΙΚΟΛΟΓΑΙΑΣ Ειν ήθεται τη θεπισιάτη τους Δύδι ή μαρχηριά το μάταταξια αυτάρχες 27 πους 28 ΤΗ ΕΝΕΡΟΙΑΤΗΝΑ ΑΜΟΕΕΡΟΙΑΤΗΣΤΟ ΤΗ ΚΑΙΝΕΙΟΓΕ ΤΟ ΚΟΙΝΟΓΙΑ ΤΟ ΚΟΙΝΟΓΙΑ ΤΟ ΚΑΙΝΟΓΙΑ ΤΟ ΤΟ ΚΕΙΝΟΓΙΑ ΤΟ ΚΟΙΝΟΓΙΑ ΤΟ ΚΑΙΝΟΓΙΑ ΤΟ ΚΑΙΝΟΓΙΑ ΤΟ ΤΟ ΚΑΙΝΟΓΙΑ ΤΟ ΚΑΙΝΟΓΙΑ ΤΟ ΤΟ ΚΑΙΝΟΓΙΑ ΤΟ ΤΟ ΚΑΙΝΟΓΙΑ ΤΟ ΚΑΙΝΟΓΙΑ ΤΟ ΤΟ ΚΑΙΝΟΓΙΑ ΤΟ ΚΑΙΝΟΓΙΑ ΤΟ ΤΟ ΚΑΙΝΟΓΙΑ ΤΟ ΤΟ ΚΑΙΝΟΓΙΑ ΤΟ ΤΟ ΚΑΙΝΟΓΙΑ ΤΟ ΚΑΙΝΟΓΙΑ ΤΟ ΤΟ ΤΕ ΓΕΓΟΥΓΙΑ ΤΟ ΤΟ ΚΑΙΝΟΓΙΑ ΤΟ ΤΟ ΚΑΙΝ λεμφοκύτταρα, μονοκύτταρα, πωσινόφιλα, Βασεόφιλα και εμπύρηνα ερυθροκύτταρα, Αμξήσεις των ουδετερόφιλων δεν παραπτρήθηκαν. Οι αυξήσεις



Αναστάσιο Μέγαρο, Γωνία Λεωφ. Αθαλάσσας & Ι. Χατζηιωσήφ Γρ. 402, 4ος όροφος, 2024 Στρόβολος, Κύπρος Τηλ: +357 22769946, Φαξ: +357 22769978 e-mail: info_cyprus@genesispharma.com www.genesispharma.com



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The favourable efficacy and safety profiles of Zebinix® (eslicarbazepine acetate) 800 and 1200 mg, including the sustained efficacy for at least 1 year and the lack of major concerns related to rash, hyponatraemia or body weight increase, indicate that Zebinix® (eslicarbazepine acetate) is a valuable addition to the current armamentarium of AEDs as an adjunctive therapy for refractory partial-onset seizures.

Almeida L, Bialer M and Soares-da-Silva P, Eslicarbazepine Acetate. In: Shorvon SD, Perucca E, Engel J Jr., editors. The Treatment of Epilepsy. 3rd ed. Oxford: Wiley-Blackweil; @2009. p. 485-98.

ZEBINIX® 800 mg, each tablet contains 800 mg of eslicarbazepine acetate and can be divided into equal doses Therapeutic indications: ZEBINIX® 800 mg is indicated as adjunctive therapy in adults with partial-onset seizures with or without secondary generalisation. Posology and method of administration: ZEBINIX® 800 mg must be added to existing anticonvulsant therapy. The recommended starting dose is 400 mg once daily which should be increased to 800 mg once daily after one or two weeks. Based on individual response, the dose may be increased to 1,200 mg once daily. Contraindications: Hypersensitivity to the active substance, to other carboxamide derivatives (e.g. carbamazepine, oxcarbazepine) or to any of the excipients. Known second or third degree atrioventricular (AV) block. Special warnings and precautions for use: Caution should be exercised in the treatment of patients with renal impairment and the cose should be adjusted according to creatinine clearance. In patients with CLCR <30 mL/min use is not recommended due to insufficient data, Eslicarbazepine acetate should be used with caution in patients with mild to moderate hepatic impairment and is not recommended in patients with severe hepatic impairment. Interaction with be used with caution in patients with mild to moderate hepatic impairment and is not recommended in patients with severe hepatic impairment. **Interaction with other medicinal products:** Eslicarbazepine showed an inducing effect on the metabolism of medicinal products that are mainly eliminated by metabolism through CYP3A4. A study in healthy subjects showed an average decrease of 50% in systemic exposure to simvastatin when co-administered with eslicarbazepine acetate 800 mg once daily, most likely caused by an induction of CYP3A4. An increase of the simvastatin when co-administered with eslicarbaze-epine acetate. In a study in healthy subjects there was an average decrease of 36 39% in systemic exposure to Rosuvastatin in healthy subjects when co-administered with eslicarbazepine acetate 1,200 mg once daily. The mechanism for this reduction is unknown, but could be due to interference of transporter activity for rosuvastatin alone or in combination with induction of its metabolism. Since the relationship between exposure and drug activity is unclear, the monitoring of response to therapy (e.g., cholesterol levels) is recommended. Administration of eslicarbazepine acetate 1,200 mg once daily to female subjects using a combined oral contraceptive showed an average decrease of 37% and 42% in systemic exposure to lexonorgestrel and ethnylestradio, respectively, most likely caused by an induction of CYF3A4. Therefore, women of childbearing potential must use adequate contraception during treatment with Zebinks^m, and up to the of the current menstruation cycle after the treatment has been discontinued. In a study in healthy subjects, concomitant administration of eslicarbazepine, acetate 800 mg once daily and carbamazepine 400 mg twice daily resulted in an average decrease of 32% in exposure to lewosure to the active metabolite eslicarbazepine, acetate 800 mg once daily and carbamazepine 400 mg twice daily resulted in an average decrease of 32% in exposure to the active metabolite esilicarhazepine, most likely caused by an induction of glucuronidation. No change in exposure to carbamazepine or its metabolite carbamazepine. individual response, the dose of eslicarbazepine acetate may need to be increased if used concomitantly with carbamazepine. Undesirable effects: In placebo-controlled studies involving 1,192 adult patients with partial-onset seizures (856 patients treated with eslicarbazepine acetate and 336 treated with placebo), 45.3% of patients treated with eslicarbazepine acetate and 24.4% of patients treated with placebo experienced adverse reactions. Adverse reactions were usually mild to moderate in intensity and occurred predominantly during the first weeks of treatment with esticarbazepine acetate. Adverse reactions, which occurred at an incidence greater than placebo and numerically present in more than 1 patient are listed by System Organ Class and frequency (very common $\geq 1/10$, common $\geq 1/100$ to <1/100, uncommon $\geq 1/100$ to <1/100, or <1/100, or <1/100, the <1/100 to <1/100 to <1/100 to <1/100 to <1/100. The <1/100 to <1/100abnormal coordination, disturbance in attention, tremor, diplopia, vision blurred, vertigo, nausea, vomiting, diarrhea, rash, fatigue, gait disturbance. Uncommon: Anaemia, hypersensitivity, hypothyroidism, increased appetite, docreased appetite, hypothyroidism, activitie, de Insomnia, apathy, depression, nervousness, agitation, irritability, attention deficit/hyperactivity disorder, confusional state, mood swings, crying, psychomotor retardation, stress, psychotic disorder, memory impairment, balance disorder, amnesia, hypersomnia, sedation, aphasia, dysaesthesia, dystonia, lethargy, parosmia, autonomic nervous system imbalance, cerebellar ataxia, cerebellar syndrome, grand mal convulsion, neuropathy peripheral, sleep phase rhythm disturbance, nystagmus, speech disorder, dysarthria, hypoaesthesia, ageusia, burning sensation, vision disturbance, oscillopsia, binocular eye movement disorder, ocular hyperaemia, saccadic eye movement, eye pain, ear pain, hypoacusis, tinnitus, palpitations, bradycardia, sinus bradycardia, hypertension, hypotension, orthostatic hypotension, dysphonia, epistaxis, chest pain, dyspepsia, gastritis, abdominal pain, dry mouth, abdominal discomfort, abdominal distension, duodenitis, epigastric discomfort, gingival hyperplasia, gingivitis, irritable bowel syndrome, melaena, odynophagia, stomach discomfort, stomatitis, toothache, liver disorder, alopecia, dry skin, hyperhidrosis, erythema, nall disorder, skin disorder, myalgia, back pain, neck pain, nocturia, urinary tract infection, menstruation irregular, asthenia, malaise, chills, oedema peripheral, adverse drug reaction, peripheral coldness, blood pressure decreased, weight decreased, blood pressure diastolic decreased, blood pressure systolic decreased, blood sodium decreased, haematocrit decreased, haemoglobin decreased, heart rate increased, the pressure increased, biolog pressure system outputs about note treased, internation outputs and increased, internation outputs and increased, triangloan outputs and internation of the accessed and the system outputs and internation of the accessed and the system outputs and the syste

Pregnancy Registry: To provide information regarding the effects of in utero exposure to ZEBINIX® physicians are advised to enroll pregnant patients taking ZEBINIX® in the International Registry of Antiepilepitic Drugs and Pregnancy (EURAP). More information can be found at the website http://www.eurapinternational.org/ BIAL-Portela & C® S.A. Sponsors the EURAP Pregnancy Registry to advance scientific knowledge abcut safety and outcomes in pregnant women being treated with antiepileptic drugs including esticarbazepine acetate (ZEBINIX®) and to respond to a requirement of the Committee for Medicinal Products for Human Use (CHMP) to address missing information on safety in pregnancy.

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