Australasian Neuromuscular Network

Clinical Trials:UPDATE

Exon Skipping

"A Phase II, Double Blind, Exploratory, Parallel-group, Placebo-controlled Clinical Study to Assess Two Dosing Regimens of GSK2402968 for Efficacy, Safety, Tolerability and Pharmacokinetics in Ambulant Subjects With Duchenne Muscular Dystrophy" - GlaxoSmithKline (GSK)

Duchenne muscular dystrophy (DMD) is caused by a mutation in the dystrophin gene, a gene that codes for the protein dystrophin, an important structural component of muscle fibres. Boys with DMD do not make dystrophin in their muscles. Prosensa and GSK have shown in a smaller trial that a compound called PRO051/GSK2402968 can 'skip' the mutation and can restore dystrophin production. With an increase in dystrophin production, the ultimate aim is to improve and maintain muscle function and strength.

Exon skipping is the most promising therapeutic strategy at present for DMD. This particular study is aimed at those patients with a mutation in a section of the dystrophin gene called exon 51- affecting approx. 13% of the DMD population.

This international study, including two Australian sites, is currently underway to assess the safety and efficacy of two dosing regimes (continuous and intermittent dose) administered over 48 weeks in 54 ambulant boys aged 5 years and over. Recruitment has been finalised and the study is expected to be completed in September 2012.

This is an intensive study for patients, their families and the study coordinators, as the frequency of testing and types of testing involved require regular visits to hospital; however this is necessary to generate the detailed information required to determine dosing regimes for optimal benefits to patients.

For further details, contact:
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Ataluren (Also known as PTC124)

Ataluren also works to form a functioning protein, however its mechanism is different to that used in exon skipping. In this approach, the machinery that produces the protein is corrected to allow a longer and functioning form of the protein, dystrophin, to be produced.

Early studies resulted in the slowing of muscle weakness, however two doses were assessed in the trial and only the lower dose had an effect. A new multi-centre trial is planned to start in December this year to collect additional information to draw more conclusive results and to allow patients enrolled in previous trials to have access to the ataluren.

Sydney and Melbourne sites will be involved in this trial - please keep an eye out for further information.

INSIDE

If you know anyone who would be interested in joining the ANN, please forward this newsletter to them. Membership is free. Email: info@ann.org.au

IN THE SPOTLIGHT:
Fazio-Londe Disease

Fazio-Londe disease is a very rare neuromuscular disease, resembling spinal muscular atrophy, which particularly affects the lower cranial nerves, causing slowly-progressive bulbar weakness and swallowing difficulties. Affected children often present in infancy with hypotonia and failure to thrive. Respiratory insufficiency is common. Similarities between this condition and Brown-Violetto-Van Laere syndrome, a rare neurological disorder which can present in infancy with neurological deterioration with hypotonia, respiratory insufficiency and early death, or later in life with deafness and progressive ponto-bulbar palsy, have long been recognised. Muscle biopsy may show fibre type grouping, mild type 1 fibre predominance, or mild myopathic abnormalities.

The genetic basis of Fazio-Londe disease has now been shown to be recessive mutations in the C20orf54 gene, which encodes the human homolog of a rat riboflavin transporter, which also cause Brown-Violetto-Van Laere syndrome. Both of these conditions show clinical and pathologic overlap with multiple acyl-CoA dehydrogenation defect (MADD), an inherited defect of mitochondrial fatty acid beta-oxidation, and may be responsive to treatment with riboflavin.

Possible patients should be investigated with a carnitine/acylcarnitine profile and urine organic acid testing, and should receive a trial of high-dose riboflavin.

References:

Bosch AM, Nico GG, Abeling M et al. Brown-Vialetto-Van Laere and Fazio Londe syndrome is associated with a riboflavin transporter defect mimicking mild MADD: a new inborn error of metabolism with potential treatment. J Inherit Metab Dis 2011;34:159-164.

Green P, Wiseman M, Crow YJ, et al. Brown-Vialetto-Van Laere syndrome, a pontobulbar palsy with deafness, is caused by mutations in c20orf54. Am J Hum Genet 2020; 12;86(3):485-489.

Guidelines & Standards of Care

Best Practice Guidelines on Molecular Diagnostics for Duchenne/Becker muscular dystrophies

Specimen Collection

Emergency Guidelines

Diagnosis and management of limb girdle muscular dystrophy

A Dutch guideline for the treatment of scoliosis in neuromuscular disorders

Diagnosis and management of Duchenne muscular dystrophy

Diagnosis and management of Spinal Muscular Atrophy (SMA)

Diagnosis and management of facioscapulohumeral muscular dystrophy (FSHD)

Available on the ANN website

NEW!

CONGENITAL MUSCULAR DYSTROPHY OUTCOME MEASURES

Available for download HERE and in the news section of the ANN website

ICNA&AOCN

Brisbane, Queensland

27th May - 1st June, 2012

12th International Child Neurology Congress and 11th Asian and Oceanian Congress of Child Neurology

The ICNC will be held jointly with the 11th Asian and Oceanian Congress of Child Neurology, and promises to attract a large international audience. As in the past congresses, the Scientific Program will be of the highest caliber, emphasizing not only the latest developments and advances in child neurology, but also a review of current standard of care in the practice of child neurology. Participants from all over the world will be able to engage in collegial exchange of ideas in a friendly and warm atmosphere.

An attractive socio-cultural program is also being planned, and participants and their families will be able to enjoy both the diversity and uniqueness that Australia has to offer. Therefore, it is with great enthusiasm that we urge you to join us in Brisbane, May 2012 in what we anticipate to be a memorable scientific, academic and social experience.

Harry T. Chugani, M.D.

President, The International Child Neurology Association (ICNA)

There are a number of exciting themes in the program including:

- New developments in epilepsy
- Genetic developments and technologies in child neurology in the 21st Century
- Neurodevelopmental outcomes: global perspectives
- Cutting edge management in cerebral palsy
- CNS infection: African and Asian perspectives
- New developments in neurometabolic diseases

Confirmed speakers include:

Prof James Barkovich	University of California
Prof Samuel F Berkovic	University of Melbourne
Prof Josep Dalmau	University of Barcelona
Prof Gabrielle A. deVeber	The Hospital for Sick Children (SickKids), Canada
Prof Donna Ferriero	University of California
Prof Ikuya Nonaka	National Center of Neurology and Psychiatry, Japan

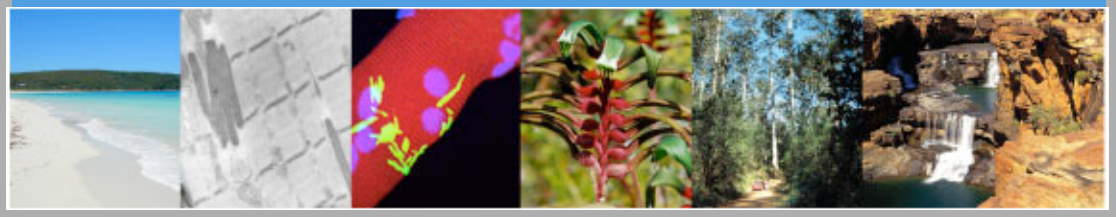
For more information, visit www.icnc2012.com

We are planning an ANN meeting as a satellite to the World Muscle Society meeting in Perth (October 9-13) - please mark this in your diaries!

WMS 2012

Perth, Western Australia
9th-13th October, 2012

17th International Congress of the World Muscle Society



This is an outstanding opportunity for everyone in Australia in the neuromuscular diseases community to listen to and meet many of the world's leading researchers in this field.

The Local Organising Committee would particularly like to draw the attention of the ANN members to the associated Training Course (8th and 9th October) that includes both clinical and pathological teaching by some of the best in the world.

The Training Course, held in conjunction with each Annual Congress, is limited to 40 places and is highly recommended for junior clinicians, pathologists and molecular geneticists.

For more information about the conference, and to register your interest, visit www.wms2012.com