Medical Media Release

Suspicion Index for Niemann-Pick type C disease published in Neurology journal

Important step to support physicians in identifying patients who should undergo further testing for this rare disease in order to achieve earlier diagnosis

ALLSCHWIL, SWITZERLAND – Thursday 19 April 2012 - Actelion Ltd (SIX: ATLN). A Suspicion Index for Niemann-Pick type C disease (NP-C) has been developed to help physicians unfamiliar with the disease understand the key signs and symptoms and consider NP-C as a possible diagnosis. The Suspicion Index, published on the Neurology website this week, attributes a numeric value to each of the individual symptoms common for the disease.¹ By adding up the values for the symptoms presenting in a specific patient, physicians generate a total score which indicates whether or not the patient should be referred on to a specialist center for further investigation.

NP-C disease is a rare genetic condition primarily affecting children and teenagers, although the clinical manifestations of the disease can become apparent at any age. It is estimated that the incidence of NP-C is approximately one in 120,000 live births,² but as diagnosis of NP-C can be delayed for many years due to its complex and often non-specific clinical presentation, this may be an underestimation. Early diagnosis is vital to ensure patients and carers can access appropriate support and early treatment, which may help delay the progression of the neurological manifestations of the disease.³

Professor Frits Wijburg of the Academic Medical Center in Amsterdam and involved in the development of the Suspicion Index says: “From a physician’s point of view the Suspicion Index works both as a reminder of the complex and varied symptoms characteristic of NP-C, as well as support in making the right referral decision. It is our hope that the Suspicion Index will contribute to reducing the time to diagnosis for more patients to ensure that they can receive the support and treatment they require.”

The Suspicion Index was developed by a group of international experts in the field of NP-C. The group categorized the signs and symptoms of the condition into visceral, neurological and psychiatric domains. Through a retrospective chart review in seven centers in Europe and
Australia, the importance of each sign and symptom was evaluated and attributed an individual value, according to their relative association with positive NP-C diagnosis. It was established that once more common diseases were ruled out, the symptoms, their combination and the patient's family history provided a risk prediction score for NP-C that could help inform referral decisions. Ultimately, the Suspicion Index was developed as a paper-based referral aid, designed to be simple to use in clinical practice.

Professor Wijburg comments: “We were very focused on developing a tool that would be of genuine use to physicians. It needed to be easy to understand and quick and simple to use during or following a consultation. The Suspicion Index has been proven to be both specific and sensitive in the evaluation of risk of NP-C and we hope that it will help physicians recognize the signs of this rare condition and ensure that their patients are appropriately referred to specialists.”

The NP-C Suspicion Index is also available online at www.npc-si.com, providing physicians unfamiliar with NP-C with a simple-to-use and interactive screening tool. Alongside the online NP-C Suspicion Index tool, www.npc-si.com contains information about how the tool was developed and also provides an overview of the visceral, neurological and psychiatric symptoms of NP-C. The website is intended for physicians outside of the United States only.

The Suspicion Index was developed through a retrospective review of 216 patients across three different groups; NP-C positive cases confirmed by classical or variant filipin staining (n=71), NP-C negative cases confirmed by negative filipin staining (n=64) and controls with at least one characteristic symptom of NP-C (n=81). NP-C signs and symptoms categorized into visceral, neurological or psychiatric domains were evaluated both within and across domains. Symptoms identified as being particularly strong predictors of the disease included neonatal jaundice, enlarged spleen, vertical supranuclear gaze palsy (impairment of vertical eye movement), gelastic cataplexy (sudden weakness or collapse associated with strong emotion) and cognitive decline, along with parents or siblings diagnosed with NP-C. Vertical supranuclear gaze palsy and gelastic cataplexy were identified as the strongest predictors of NP-C. Once other common diseases have been ruled out, a Suspicion Index total score of less than 40 indicates a low probability of NP-C, a score between 40 and 69 suggests that follow-up examination is required and a score over 70 indicates that a patient should be referred directly to a specialist center.

The Suspicion Index has been developed in collaboration with a scientific committee comprising NP-C experts and its development has been sponsored by Actelion Pharmaceuticals Ltd.

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Notes to the Editor

About Niemann-Pick type C disease (NP-C)
NP-C disease is a rare, fatal, neurodegenerative, genetic condition, primarily affecting children and teenagers although the clinical manifestations can become apparent at any age. The symptoms are caused by the storage of some lipids - such as glycosphingolipids and cholesterol - within certain tissues in the body, including the brain. It is invariably progressive and most patients die within five to ten years of diagnosis; for the majority the disease is fatal during childhood.

Neurological deterioration is the key feature of the disease and can manifest itself as clumsy body movements, balance problems, slow and slurred speech, difficulty in swallowing, problems with eye movements and seizures. Intellectual decline is also common. In the final stages of the disease the child or young adult is frequently bedridden, has little muscle control and is intellectually impaired. Diagnosis of the disease can be difficult and may take years due to the rarity and heterogeneity of the condition. A treatment has been available throughout Europe since 2009 to treat NP-C disease; however there is no specific drug therapy approved in the United States.

About Actelion Pharmaceuticals Ltd
Actelion Ltd is a biopharmaceutical company with its corporate headquarters in Allschwil/Basel, Switzerland. Actelion developed the first treatment for Niemann-Pick type C (NP-C) disease, Zavesca® (miglustat), which was approved in 2009 for the treatment of progressive neurological manifestations in adult patients and pediatric patients with NP-C. Miglustat is approved for the treatment of NP-C in 43 markets worldwide, including the European Union, Japan, Canada, Australia and Switzerland.

Actelion, founded in late 1997, is a leading player in innovative science. Actelion’s over 2,500 employees focus on the discovery, development and marketing of innovative drugs for significant unmet medical needs. Actelion shares are traded on the SIX Swiss Exchange (ticker symbol: ATLN) as part of the Swiss blue-chip index SMI (Swiss Market Index SMI®).

References
1. Wijburg FA, Sedel F, Pineda M, et al. Development of a Suspicion Index to Aid Diagnosis of Niemann-Pick Disease Type C. Neurology. Published online ahead of print April 18, 2012; DOI 10.1212/WNL.0b013e3182563b82

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