

Action Duchenne Conference, London, 23 – 24 October 2009

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One of the highlights of the conference was the range of drug treatments that may show promise for increasing dystrophin expression in Duchenne Muscular Dystrophy, however they are still in the “clinical trials” stage in their development.

The Dutch pharmaceutical company Prosensa has recently formed an alliance with GlaxoSmithKline. The new collaboration will mean that GSK has a worldwide license to develop and market Prosensa’s lead drug PRO-051, which is now entering a Phase III clinical trial in order to determine how effective the drug is clinically in a large group of boys. This drug would be suitable for 13% of patients because it can treat a cluster of mutations, which could be by-passed by skipping exon 51. We all understand that families, support groups and healthcare professionals want a cure immediately but these safety trials are necessary before drugs can be launched on the market.

PRO-051 is an example of an “antisense oligonucleotide”, a drug which has the capacity to skip an exon and thereby correct the reading frame of DMD transcripts aiming at the synthesis of a largely functional dystrophin protein, rather like a genetic “band-aid” or plaster. Different mutations in the gene require different oligonucleotide drugs. Prosensa’s PRO-051 is designed to skip exon 51, and since the conference results from the Phase I/II clinical trial have been presented, which showed stable dystrophin expression and that the delivery of the drug was well tolerated by all the boys treated. The drug was also demonstrated to be safe; boys have been treated for 14 weeks and will continue to be treated for 2 years as an extension of the study.



Prosensa are also developing another drug, PRO-044, which designed to skip exon 44 and is in the very early stages of testing, and is undergoing Phase I/II trials to determine its safety.

AVI Biopharma (a US pharmaceutical company) is testing a drug called AVI-4568, another antisense oligonucleotide designed to skip exon 51, and create a “patch” in the mutated dystrophin gene. New data was shown at the conference to show that this drug is safe, but it has not yet shown to be effective. The same company is also at the early stages of development of a drug called AVI-5038 in the US which aims to skip exon 50.

Researchers in Cambridge are also investigating the possibility of creating one exon-skipping drug that can potentially skip multiple exons, but this is at the early stages of investigation.

Ataluren (previously called PTC-124) is a drug designed to overcome “nonsense mutations”. The results of a clinical trial to determine whether this drug can affect walking, activity, muscle function and strength, and whether the drug can be given for a long period of time, are due soon. It is important to note that this drug is only experimental at this stage.

The conference not only focussed on drug trials, but also emphasised the fact that appropriate management improves survival. As respiratory and cardiac complications are the major threats to health in Duchenne’s, a strong emphasis at the conference was placed on respiratory support, cardiac surveillance and the established benefit of steroid therapy and regular stretching in prolonging strength and function in boys with the condition. Indeed, worldwide standards of care in the management of Duchenne’s for health professionals have recently been published in Lancet Neurology and a ‘family-friendly’ version is in preparation, and will be available soon.

Dr. Nick Hart, Clinical Research Consultant, Guy's & St. Thomas' NHS Foundation gave an impressive talk on respiratory care, showing how quality of life and life expectancy has substantially increased since the dawn of non-invasive ventilation at home (sometimes known as BiPAP) for older boys. Work at the Lane Fox respiratory unit in London has also shown that with long-term respiratory support at home, boys with Duchenne spend less time in hospital if admitted with an acute respiratory problem, and are far less likely to need invasive ventilation or to spend time in Intensive Care.

This was further emphasised by Dr. Anita Simonds from the Royal Brompton Hospital in London who showed that young men with Duchenne Muscular Dystrophy are living longer due to good cardiology care, early treatment of infection and respiratory support in the home. These aspects in the management of the health of our boys is extremely important, regardless of future drug therapies. Dr. Simonds also quoted a recent study which suggested that patients with neuromuscular disease with nocturnal hypoventilation (night-time breathing problems) are likely to deteriorate and develop daytime problems +/- progressive night-time symptoms within 2 years and may benefit from the early introduction of night time ventilator support.

Prof. Terry Partridge (Washington, USA) gave a review on stem cell research, and detailed the research being conducted worldwide to introduce donor cells into the body to repair damaged muscle cells in patients with Duchenne's. This is an enormous scientific and clinical challenge, which is at a very early stage of investigation and unfortunately at this stage nothing is on the horizon from a therapeutic viewpoint.

Among the parallel sessions was a physiotherapy workshop, where Pamela Foley and Eóin Ó Rathallaigh, Senior Physiotherapists at the CRC Muscle Clinic, were invited to assist with Dr. Michelle Eagle from Newcastle in teaching a group of parents from as far afield as South Africa and Australia. It was an interesting opportunity to help mothers and fathers brush up on their home stretching programmes, and gave parents the experience of how the stretches feel on each other.

Overall the conference provided an excellent summary of best practice medical, cardiac and respiratory and physiotherapy management for young people with Duchenne Muscular Dystrophy, which is consistent with healthcare provided in Ireland. It also gave a valuable insight into the research and development of potential new drug therapies, some of which are at an advanced stage of clinical testing; these new drugs may be able to stimulate the synthesis of better quality dystrophin in skeletal and cardiac muscle and hopefully improve function and prognosis.