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SKIP-NMD reports progress on skipping exon 53

Encouraging results on the successful completion of the first part of a clinical trial to skip exon 53 in boys with Duchenne muscular dystrophy have been reported at the SKIP-NMD Consortium meeting that took place in Sardinia from the 24-25 June 2015.

The SKIP-NMD project

The SKIP-NMD project, led by Professor Francesco Muntoni, London, is funded by the European Union and involves 10 partners from Europe and the USA. The aim is to carry out a clinical trial to test the benefit of a new drug to skip exon 53 (SRP-4053) to understand how well it restores production of the dystrophin protein and improves motor ability in boys with Duchenne muscular dystrophy. The trial is taking place at the Muscle Centres in London, Newcastle, Rome and Paris and is carried out in collaboration with the US biopharmaceutical company Sarepta Therapeutics.

The study follows promising results of clinical trials to skip exon 51 and the companies involved are currently working with the regulatory agencies in the US and Europe to speedily bring this drug to the market. It is now crucial to make exon skipping technology available to as many boys as possible and the SKIP-NMD project is an important initiative to achieve this. About 8% of all boys with Duchenne muscular dystrophy have a mutation that could be treated by skipping exon 53.

Results of the clinical trial

The first part of the clinical trial carried out by the SKIP-NMD Consortium was a placebo controlled study aimed at finding the most efficient dose of SRP-4053, a so-called dose escalating study. During the trial three different doses were tested. Twelve boys took part in the trial and were divided into four groups. Three groups received one of the doses of SRP-4053 while one group received an inactive substance, a placebo.

It was great to hear at the meeting that an optimal dose was found and that no significant problems were reported in any of the boys. The researchers have also now received the green light to start the second part of the study.

This second phase consists of two parts aimed at studying the long term benefits of the most efficient dose of SRP-4053. Firstly, all boys that participated in the first part of the study will now receive the optimal dose of SRP-4053 even those that had previously received placebo. Secondly, the researchers are now recruiting an additional 12 boys to a new study who will receive the most efficient dose over a period of 48 weeks. This is aimed to study the benefit of the SRP-4053 in a larger population of boys.

If you are interested in the study and want to find out more please read the eligibility criteria below.

Results of other SKIP-NMD studies

At the meeting, results of other studies included in the SKIP-NMD project were also discussed. These are aimed at finding new biomarkers and non–invasive tests to assess the benefit of potential drugs and treatments in clinical trials, for example, investigating for the first time whether MRI could do this. This has already resulted in the start of a large natural history study recruiting

boys with Duchenne muscular dystrophy that are not eligible for the exon 53 study. MRI and other non-invasive but highly technological tests will be studied in great detail to better understand how they can be used in clinical trials to measure differences in muscle strength and endurance.

The next step

The next vital step to fully understand the benefit of SRP-4053 will be the recruitment of 36 boys required for the second part of the clinical trial. The trial will consist of two groups and participants must have the following criteria:

Group 1 (12 boys): This group will receive SRP-4053. Participants must have a confirmed diagnosis of Duchenne muscular dystrophy and have a deletion amenable to exon 53 skipping (e.g., deletions of exons such as 42-52, 45-52, 47-52, 48-52, 49-52, 50-52, 52, or 54-58).

Group 2 (24 boys): This group will be the untreated control group. Participants must have an established clinical diagnosis of Duchenne muscular dystrophy with confirmed genomic deletion of exon(s) not amenable to exon 53 skipping. Boys in the untreated control group will not receive SRP-4053 and will be on a reduced assessment schedule. This means that they will be seen only every 3-6 months and there will be no biopsies required. Taking part in the untreated control group will not preclude participation in future Sarepta trials involving active treatment.

Generally, although other requirements may apply, boys who meet the following criteria may participate in Part 2 of this clinical trial either in the SRPT-4053 treated group or the untreated control group if they:

- are between six to 15 years old
- can walk at least 250m in six minutes
- a Northstar score above 17 is required
- have stable respiratory and heart function
- have been on a stable dose of corticosteroids for at least 6 months
- enrolment into another clinical study would exclude participation in this study

Please visit the project website at http://www.skip-nmd.eu/for additional information. You can also read more about this clinical trial at www.clinicaltrials.gov. There is also a video aimed at young boys to explain what is happening during this trial which can be found at https://www.youtube.com/watch?v=wG6GPnAcEQY&feature=youtu.be

If you have any further question or wish to discuss the study please give us a ring on