

## **Advances in experimental therapies for neuromuscular diseases**

The improved understanding of the genetic basis and molecular events leading to muscle degeneration in muscular dystrophies, coupled with advances in small molecules aimed at interfering with gene transcription, has very rapidly moved in the last decade from proof of concept studies in relevant cellular and animal models to phase I; II; and III clinical trials in Duchenne muscular dystrophy, the most common of the severe and childhood onset muscular dystrophies. These approaches take advantages of the properties of antisense induced forced splicing, and restoration of the open reading frame in patients with out of frame deletions.

Preclinical studies in myotonic dystrophy are also rapidly advancing, aimed at using small molecules that induce or ameliorate alternative splicing dysregulation which characterize this condition. Interfering with RNA processing is also very rapidly moving forward for spinal muscular atrophy, a form of motorneuron disease that mostly affects children

The pace of the development of these novel genetic approaches to treat neuromuscular diseases is exciting and one of the fastest in recent drug development program.

Nevertheless the outcome of clinical trials, in all these rare conditions, is influenced by a significant level of clinical variability. The implication of this is acute in tailored therapeutic approaches, as these therapies only target a subset of patients affected by the condition and randomised placebo controlled studies, already difficult for the most common conditions, are impossible for the rarer genetic variants.

While these exciting developments go forward, the importance of patient selection and what to measure is proving fundamental. Functional outcome measures, and biochemical outcome measures have been refined, and are continuously refined in order to capture effect of these novel therapies.

In my presentation I will summarise the status of the art of the clinical and preclinical work being performed in this field.

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