

# MONTHLY Feature

## Highlights from MDA's Virtual Clinical Trial Session

The MDA Virtual Clinical Trial Session, held on March 24, 2020, via webinar, provided a forum for more than a dozen speakers to present exciting results from recent clinical trials. The talks encompassed a wide range of neuromuscular diseases, including Duchenne muscular dystrophy (DMD), amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), facioscapulohumeral muscular dystrophy (FSHD), myasthenia gravis (MG), giant axonal neuropathy (GAN), and X-linked myotubular myopathy (XLMTM). Many of the results discussed in these trials provide hope for the future of neuromuscular disease treatment.

### SMA studies

Two trials further investigating the efficacy of Zolgensma in SMA patients, the STRONG Phase 1 study and the STRIVE Phase 3 study, revealed encouraging results. In the STRONG study, 6- to 60-month-old patients who could sit but not stand or walk were treated with Zolgensma to determine the safety/tolerability and optimal dose of the viral gene therapy. Younger patients tended to see greater improvement in HFMSE score and achievement of motor milestones than 2- to 5-year-old patients. In the STRIVE study, patients under 6 months old with the most severe type of SMA were treated with a one-time dose of Zolgensma. The gene therapy provided significant benefit compared to untreated natural history in survival, CHOP INTEND scores, and independent sitting. These two trials further demonstrate the efficacy of SMN gene replacement therapy in SMA and continue to instill confidence that Zolgensma can benefit patients.

### DMD studies

In the MoveDMD Phase 2 trial, the non-steroidal compound edasalonexent, an oral NF- $\kappa$ B inhibitor, was studied for up to 150 weeks of treatment in 4- to 7-year-old boys with DMD. Edasalonexent facilitated normal growth patterns in patients without the adverse effects typically seen with high-dose steroids, indicating it may have the potential to be disease modifying. A Phase 3 trial with edasalonexent is currently underway. Another study in DMD patients sought to determine the safety, efficacy, and PK/PD of the antisense oligonucleotide



suvodirsen in a Phase 1 open-label extension trial. Following 12 or 22 weeks of treatment, it was determined that there was no change from baseline in dystrophin expression, and therefore the development of suvodirsen has been discontinued. The results of the study are still being fully analyzed and could provide important information to help advance the development of other novel DMD treatments.

### XLMTM study

A Phase 1/2 open-label trial in XLMTM patients, ASPIRO, investigated the safety/efficacy of a gene therapy targeting the MTM1 gene, which is mutated in XLMTM. Patients were randomized into ascending dose cohorts and treated with a single infusion of the viral vector therapy. Almost all patients demonstrated clinically meaningful improvements in motor and respiratory function following treatment, suggesting this could be a viable approach for all XLMTM patients.

### ALS study

In an effort to develop a disease-modifying treatment for ALS, patients received autologous infusion of expanded Tregs, a subpopulation of T-lymphocytes that suppress inflammation. The Treg infusions were safe and well tolerated in all patients and Treg suppressive function correlated with slowing of disease progression; however, the benefits of the infusions were not sustained following cessation of treatment. These promising results revealed clear but transient clinical benefit following Treg therapy and provide hope that optimization of this approach could yield a novel disease-modifying therapy in ALS.