Update 08.09.2021/

7th Duchenne CAB Meeting
April - July 2021

The Duchenne CAB held its 7th meeting between April and July 2021. Due to the COVID-19 pandemic, the meetings were again held virtually via video conference. Twelve Duchenne CAB members from twelve countries met with five companies in six separate meetings during this period, in addition to executing a number of internal preparation and recap meetings.

Some of the main topics discussed:

- Addressing pre-existing antibodies and the potential to re-dose gene therapy: Duchenne CAB members were provided an overview of four potential approaches to circumvent the issue of pre-existing anti-bodies to AAV vectors used in gene therapy studies. Although none of these approaches are currently in use, they are being explored to find a potential solution in the coming years. These approaches are:
    - Biologic: anti-FcRn antibodies that may reduce pre-existing antibodies by up to 80% for around 60 days
    - Enzymatic: an enzyme called IdeS can digest other antibodies and seems to remove 90-95% of antibodies for a few days, which could provide a window for gene therapy administration
    - Immunoadsorption: remove antibodies using plasmapheresis (removing and replacing some of the blood plasma), though the question remains as to whether this method could remove enough antibodies to enable safe administration of gene therapy
    - Cloaking: encasing AAV in exosomes (PEGylation) to minimize their interaction with pre-existing antibodies

  Challenges:
    - It may prove necessary to utilize a combination of these approaches in order to abolish enough of the antibodies to enable administration of the gene therapy
    - There is a risk that the pre-existing antibodies could come back at an even higher level following treatment, which might lead to safety risks in the subsequent weeks
    - More research is needed to determine efficacy and potential safety risks of these approaches

- Studies to better understand seroprevalence (prevalence of pre-existing antibodies) in various regions of the world are underway

- Discussions around the relevance and applicability of various currently validated surveys proposed for use in clinical trials (Health Resource Utility, Work Productivity and Impairment, Caregiver Global Impression of Severity and others), and specific aspects related to DMD to keep in mind during analysis of the data collected

- Reducing the burden of clinical trials and subsequent follow-up by initiating remote consent, home assessments, telemedicine, use of wearable devices etc. whilst providing flexibility for participants who prefer to visit the clinic

- Introduction of a "Care Package" for trial participants at hospital visits, containing a schedule of events for the day, hospital plan, introduction to the relevant surveys/PROs to provide better context, including goals, guidance and glossary of terms, as well as water and snacks

- Policies to be put in place before starting clinical trials, i.e. sibling protocols, compassionate use policies, recruitment policy including a statement on international and cross-border participation

- The Duchenne CAB was happy to be informed that its advice on one of the wearables previously used in clinical trials in DMD has been integrated into a new design, e.g. the device is now waterproof, smaller and lighter, less obtrusive, more comfortable etc.

Announcement:
Next official Duchenne CAB dates are 13 – 16 October 2021. As these meetings will again be virtual and there are requests for eight individual meetings, they will begin in September and continue through October.

Inquiries:
If you have any questions concerning the Duchenne CAB or any issues you would like to bring to our attention, please contact the Duchenne CAB Coordinator: sally@duchennedatafoundation.org