September 15th, 2021

Dear SMA Community,

In response to your request, we are pleased to share with you information on the ASCEND study, a new global, clinical trial planned to be initiated by Biogen.

While great progress has been made in recent years to treat SMA, there are opportunities to further improve outcomes and quality of life for patients. The ASCEND study aims to evaluate whether treatment with an investigational higher dose of nusinersen has the potential to improve clinical outcomes and address unmet medical needs in patients with later-onset SMA previously treated with risdiplam.[1-3]

ASCEND study overview

The ASCEND study will assess if nusinersen at an investigational higher dose may address outstanding clinical needs among later-onset SMA patients treated with risdiplam who want to make a change in their treatment regimen. This includes both adults who have been treated with nusinersen prior to risdiplam, as well as children, teens and adults who have only been treated with risdiplam and have not previously received nusinersen.

Study design

The ASCEND protocol has been submitted to regulatory authorities. ASCEND is planned to be an approximately 2.5-year study and aims to enrol up to 135 later-onset, non-ambulatory (unable to walk independently) SMA patients aged 5-39. All participants must have been treated with the maximum dose of 5 mg of risdiplam before joining the study and be willing and able to change their treatment regimen to a higher dose of nusinersen. Further eligibility criteria also apply. All participants will receive 2 initial doses of 50 mg two weeks apart, followed by a maintenance dose of 28 mg every 4 months over the remaining study period. The 50 mg and 28 mg doses of nusinersen are not
approved doses and are higher than the currently approved 12 mg nusinersen dose. These higher doses are also being evaluated in the DEVOTE study.[4]

Patient outcomes

In this study, efficacy is planned to be assessed using Revised Upper Limb Module (RULM). Additional clinical outcomes include safety, Hammersmith Functional Motor Scale Expanded (HFMSE) and caregiver burden. A neuron protein called neurofilament, will be explored as a biological marker of disease activity. In participants aged 13 years and older, upper limb fine motor function will also be assessed using a mobile application.

Timing

We expect the first eligiblepatients will be enrolled in the ASCEND study later in 2021. Further information on the study will soon be available on https://clinicaltrials.gov/.

Working in partnership

A consultation process with the SMA community has been conducted in order to shape the design of this study and ensure that the clinical outcome measures being used are those that matter most to patients.

We are grateful to all the families, caregivers and investigators who continue to help us improve care for families affected by SMA.

As a team we remain a dedicated, committed partner to this community and will continue to be available to provide updates in the future, when requested.

Best Regards,
Michaela Hrdlickova
Director Patient Advocacy SMA, Europe/Canada/Partner Markets, Biogen

References:

1. Mercuri E. et al. SUNFISH Part 2: Efficacy and safety of risdiplam (RG7916) in patients with Type 2 or non-ambulant Type 3 spinal muscular atrophy (SMA). SMA Europe Feb 5-7, 2020 presentation.
2. Evrysdi US FDA Summary Basis of Approval (SBA) documents. Clinical Review(s): Page 67, table 15. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2020/213535Orig1s000MedR.pdf Accessed: July 2021. Accessed September 2021.
3. European Medicines Agency. EMA/216061/2021 – Evrysdi EPAR. Available at: https://www.ema.europa.eu/en/documents/assessment-report/evrysdi-epar-public-assessment-report_en.pdf. Accessed September 2021.
4. Clinicaltrials.gov. Study of Nusinersen (BIIB058) in Participants With Spinal Muscular Atrophy (DEVOTE). Available at: https://clinicaltrials.gov/ct2/show/NCT04089566. Accessed September 2021.