INTERNATIONAL ALLIANCE OF ALS/MND ASSOCIATIONS

Biogen – SOD1 Antisense Oligonucleotide (BIIB067 – Tofersen) – Spring 2020

Background

Biogen partnered with Ionis Pharmaceuticals to advance a type of therapy called antisense oligonucleotides (ASOs), which are biological substances that can block the production of a specific gene/protein target. The first ASO target for ALS is superoxide dismutase 1 (SOD1); the first gene discovered to cause ALS back in 1993. A small change in the composition of the SOD1 gene leads to an abnormal SOD1 protein. Over the years, it was determined that this abnormal protein causes ALS, not by losing its normal, protective function, but by becoming toxic to motor neurons. An ASO that blocks SOD1 production was suggested as a logical treatment target.

A phase 1 clinical trial of tofersen (the SOD1 ASO) with 50 participants was run at 17 sites in the United States, Europe and Canada with the goal of assessing safety, tolerability and understanding how it acts inside the human body. The study showed that these goals were met and a secondary measure of whether there was reduced SOD1 in the cerebrospinal fluid (a biomarker of effect) was also significantly achieved. Furthermore, there was a trend towards slowing of ALS progression in three measures including functional decline, respiratory function and muscle strength. This means that the treatment seemed to be very effective at slowing the loss of these three measures, but the number of participants was too low to form conclusions with statistical certainty.

As a result of these findings, Biogen has extended the current phase 1 trial into an immediate phase 3 trial that will add participants and aim to determine if the effect on disease course is significant enough to warrant an application for approval and availability to people living with ALS as quickly as possible. As of Spring 2020, this trial is still recruiting.

Biogen and Ionis are currently collaborating on two other antisense oligonucleotide clinical trials. One is targeting the most common genetic mutation in ALS, called C9ORF72, and is already recruiting in phase 1 at several multinational sites. C9ORF72 mutations are the most commonly found genetic alteration in hereditary/familial ALS, but they are also found in about 5-10% of sporadic cases. The other will target a gene encoding a protein called ataxin-2 and will aim to treat certain people with sporadic ALS. It is anticipated that this strategy will be used to target other genes in the years to come.

Recommendation

At present, we only know that tofersen is safe and tolerable, and do not know if it actually works to slow progression. As a result, it should be explained that the results of the phase 1 were promising and the current phase 3 trial is aiming to have an answer by the late 2020 or early 2021.