INTERNATIONAL ALLIANCE OF ALS/MND ASSOCIATIONS

Cytokinetics – Reldasemtiv Summer 2019

Background

Cytokinetics is a company that was founded in 1997 to develop treatments targeting impairments in muscle function. The initial drug used in ALS trials, called tirasemtiv, showed promising results in a Phase 2 clinical trial (BENEFIT-ALS) in 2014, followed by a Phase 3 clinical trial (VITALITY-ALS) that failed to show any significant positive effects on the disease. One of the key problems with tirasemtiv was tolerability. Despite targeting muscle, it also entered the brain and caused nausea, dizziness and other symptoms that were considered safe, but not particularly tolerable, as it caused participants to drop out of trials, thereby reducing the statistical power needed to determine any benefit.

Prior to the completion of the Phase 3 trial, Cytokinetics also began a Phase 2 trial of reldasemtiv, which had all the muscle benefits of tirasemtiv, without the ability to cross into the central nervous system and cause the dizziness, nausea, etc. This was a large Phase 2 clinical trial (over 400 participants) that had vastly improved tolerance, but did not meet it's goals of showing statistically significant slowing of breathing capacity, disease progression rate or muscle strength. However, as the dosing was only for 12 weeks and the trends were in the direction of a positive result, the interpretation is is not necessarily that of a failed trial, but rather one that would need further testing to determine if reldasemtiv has value for treating ALS.

Recommendation

Currently there is no knowledge as to whether reldasemtiv works to improve muscle function or slow disease progression in ALS. Results from the Phase 2 clinical trial show increased tolerance and safety compared to tirasemtiv and potentially promising results on disease progression, breathing function and muscle strength that would need a Phase 3 clinical trial to examine with any significance. As of May 2019 it is unknown if there will be a Phase 3 trial.

Further information

The SAC will continue to monitor Cytokinetics and reldasemtiv, and provide updates to the Alliance as they are needed or requested.