Impact of idebenone on pulmonary morbidity, including bronchopulmonary adverse events, in Duchenne muscular dystrophy (DMD)

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Background

Respiratory function decline in DMD

- In DMD, respiratory function declines due to progressive muscle weakness, typically beginning while patients are still able to walk, and crossing the “lower limit of normal” (forced vital capacity (FVC) <60%).
- The patient may then fall into a vicious cycle of respiratory decline, with poor airway clearance, and increased bronchopulmonary adverse events (BAEs), requiring hospitalization.
- The risk of respiratory complications is linked to patients crossing clinical thresholds of respiratory function, with the risk of BAEs such as respiratory illness and related hospitalization increasing.
- Glucocorticoids (GCs) delay the onset of respiratory function decline by 2-3 years, but not the rate of decline. However, a significant proportion of DMD patients are not taking GCs, resulting in an unmet need for disease modifying medical therapies.
- Idebenone is an oral drug in development for DMD patients with concomitant GCs, and may be used as an alternative to conventional treatment.

Methods

- We further assessed data from the DELOS trial (Figure 1) to demonstrate the potential of idebenone to reduce early respiratory morbidity in adolescent patients with DMD by delaying the time to reach clinically relevant respiratory function thresholds, and the frequency of BAEs.
- Clinically relevant thresholds for FVC% at, were compiled following a review of standard of care guidelines.
- We compared the number of patients (idebenone vs placebo) crossing these thresholds (FVC% < 80% vs placebo) with patients treated with placebo (Figure 3).
- Patients treated with idebenone, 19.4% (n = 6) had a total of 7 events, lasting a total of 82 days. In patients treated with placebo, 51.5% (n = 17) had a total of 28 events, lasting a total of 222 days.
- Hospitalizations for respiratory reasons were also reduced in patients treated with idebenone. One patient in the idebenone group was hospitalized for 3 days, whereas in the placebo-treated group, 4 patients were hospitalized for a total of 30 days.

Results

- Crossing clinically relevant thresholds of 50%, 40% and 30% FVC% at, correlated to an increased risk of respiratory complications in patients with DMD (Table 1).
- Fewer patients taking idebenone fell below any of the clinically relevant FVC% at, thresholds (idebenone: 34%; placebo 57%) or experienced a BAE, resulting in a hazard ratio of 0.50 (95% CI: 0.26, 0.97; p = 0.039) in favor of idebenone (Figure 4).

Conclusion

- Crossing clinically relevant thresholds of 50%, 40% and 30% FVC% at, correlate to an increased risk of respiratory complications in patients with DMD.
- Time above all clinically relevant FVC% at, thresholds was extended in patients treated with idebenone compared to patients receiving placebo.
- Fewer idebenone-treated patients experienced a ≥10% decline in FVC% at.
- Treatment with idebenone reduced the risk of BAEs and hospital admissions due to respiratory reasons compared to patients receiving placebo.
- These exploratory data support the efficacy and utility of idebenone in DMD patients not taking GCs, a population for which no other treatment is available.

References


For more information please visit www.santhera.com

Acknowledgments

DELOS Study Group

Conflict of interest

- O. Mayer and G. Buyse are paid consultants for Santhera and are investigators in prior/current studies with idebenone in DMD.
- G. Buyse is co-inventor of relevant patent applications.
- S. Hasham, C. Rummey and Catherine Lawrence are employees of Santhera Pharmaceuticals.