Effect of Idebenone on Bronchopulmonary Adverse Events and Hospitalizations in Patients with Duchenne Muscular Dystrophy (DMD)

O. H. Mayer1, C. McDonald1, T. Meier3, M. Leimonen4, G. M. Buyse4

1Children’s Hospital of Philadelphia - Philadelphia, PA/US, 2UC Davis - Sacramento, CA/US, 3Santhera Pharmaceuticals - Liestal/CH, 4University Hospitals Leuven - Leuven/BF on behalf of the DELOS Study Group

Duchenne Muscular Dystrophy (DMD) is the most common form of muscular dystrophy, resulting in progressive loss of respiratory muscle strength. 1,2 As a result, patients with DMD are typically at a higher risk for bronchopulmonary adverse events (BAEs).2,3 These BAEs include upper and lower respiratory tract infections and related complications, where patients often require antibiotics or hospitalization.4–6

Pathologic findings in patients with DMD, including muscle strength.1–3 As a result, patients with DMD are typically at a higher risk for bronchopulmonary adverse events (BAEs).2,3 These BAEs include upper and lower respiratory tract infections and related complications, where patients often require antibiotics or hospitalization.4–6. 

Idebenone (Raxone®) is in development as an oral tablet and in clinical trials in DMD, is administered as 300 mg three times daily (with meals). Idebenone is a short-chain benzoquinone, capable of stimulating mitochondrial electron flux, and cellular energy production, resulting in increased ATP production and decreased reactive oxygen species (ROS).8

Background

Objectives

• Evaluate the impact of idebenone on the incidence and duration of BAEs, systemic use of antibiotics and the number and duration of hospitalizations due to respiratory complications in patients with DMD.

• We can achieve this by further, post-hoc analyses of the dataset from the Phase 3, placebo-controlled trial (DELOS).8

Methods

• In the Phase 3, placebo-controlled trial (DELOS), idebenone decreased loss of respiratory function, measured by percent predicted changes in: Peak Expiratory Flow (PEF%p), Forced Vital Capacity (FVC%p) and Forced Expiratory Volume in 1 second (FEV1%p) over 52 weeks in DMD patients aged 10–18 years not using concomitant glucocorticoids (GCs).8

• In a post-hoc analysis, we assessed the incidence and duration of BAEs, systemic use of antibiotics and the number and duration of hospitalizations due to respiratory complications.8

• Clinically relevant BAEs (evaluated by an independent pulmonologist, in a blinded manner) included: pneumonia, upper respiratory tract infection, respiratory failure, and acute respiratory failure.8

Results

• Six patients (19.4%) on idebenone reported 7 BAEs compared with 17 patients (51.5%; p=0.0130) in favor of idebenone (Table 1).

• The cumulative frequency of use of antibiotics (allowing for multiple use per patient) resulted in a HR of 0.52 (95% CI: 0.226, 1.217; p = 0.1330), in favor of idebenone (Figure 2).

Conclusion

• The results of this post-hoc analysis indicate that the protective effect of idebenone on pulmonary function was associated with reduced incidence of BAEs, reduced need for systemic antibiotic treatment and less hospitalizations in 10–18 year old patients with DMD not using GC.9

Table 1. Number (%) of patients experiencing bronchopulmonary events (BAEs), including those requiring hospitalization7

<table>
<thead>
<tr>
<th>Analyses</th>
<th>Subjects</th>
<th>Total number of BAEs</th>
<th>Cumulative days with BAEs</th>
<th>Subjects hospitalized</th>
<th>Days in hospital</th>
</tr>
</thead>
<tbody>
<tr>
<td>Idebenone</td>
<td>6 (19.4%)</td>
<td>17 (51.5%)</td>
<td>7</td>
<td>82</td>
<td>3</td>
</tr>
<tr>
<td>Placebo</td>
<td>13 (39.4%)</td>
<td>28</td>
<td>222</td>
<td>4</td>
<td>30</td>
</tr>
</tbody>
</table>

References


Figure 1. Mean cumulative frequency of BAEs

Figure 2. Mean cumulative frequency of antibiotic use

Acknowledgments

O. Mayer, C. McDonald and G. Buyn are paid consultants for Santhera Pharmaceuticals and also participated in prior/current studies with idebenone in DMD. G.Buyn is co-inventor of relevant patent applications.

T. Meier and M. Leimonen are employees of Santhera Pharmaceuticals who are involved in idebenone development for DMD. O. Mayer, C. McDonald and G. Buyn are paid consultants for Santhera Pharmaceuticals who are involved in idebenone development for DMD.