Cipaglucosidase alfa/miglustat versus alglucosidase alfa/placebo in late-onset Pompe disease: PROPEL study subgroup analyses

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INTRODUCTION

Pompe disease is a rare, autosomal recessive lysosomal storage disorder caused by pathological accumulation of glycogen in tissues of the skeletal and cardiac muscle, heart, and brain owing to a deficiency in the lysosomal enzyme α-glucosidase (also known as acid maltase). This deficiency impairs the breakdown of glycogen to glucose in lysosomes, leading to accumulation of glycogen. The most severe form, infantile Pompe disease (IPD), presents in early infancy with clinical manifestations such as hypotonia, feeding difficulties, and heart failure and is generally lethal before age 2. Late-onset Pompe disease (LOPD) occurs later in life (age ≥18 years), and may present with a less severe disease course.

METHODS

• The PROPEL study (NCT03752192) was a Phase 3, randomized, double-blind, active-controlled trial to assess the efficacy and safety of cipaglucosidase alfa/miglustat in adults with late onset Pompe disease (LOPD) compared with alglucosidase alfa/placebo.
• The report presents prespecified and post hoc subgroup analyses based on enzyme replacement therapy (ERT) status, baseline 6-minute walk distance (6MWD), and baseline percent predicted sitting forced vital capacity (FVC).

RESULTS

In the overall PROPEL study, patients (n=122) were randomized to receive cipaglucosidase alfa/miglustat (n=65) or alglucosidase alfa/placebo (n=57). The primary endpoint was the change in mean 6MWD from baseline to week 52 in the overall population (n=122). An exploratory endpoint was the change in mean FVC from baseline to week 52 in the overall population (n=122).

Post hoc subgroup analyses

1. ERT status

• In the overall PROPEL study population, FVC showed a nominally statistically significant and clinically meaningful improvement at week 52 in patients with late-onset Pompe disease (IPD) compared with alglucosidase alfa/placebo (nominal P=0.02 for both 6MWD and FVC). In the alglucosidase alfa/placebo group, mean 6MWD declined over time (mean [SE] 6MWD to week 52=−15.6 [8.3] m and −10.1 [2.1] m, respectively, nominal two-tailed P=0.005). (Figure 6).

2. Baseline 6MWD categories

• Cipaglucosidase alfa/miglustat was favoured over alglucosidase alfa/placebo in the overall population and in patients in both the ≥300 m and <300 m categories at week 52. In the ≥300 m category, mean 6MWD increased over time (mean [SE] 6MWD to week 52=+13.6 [8.3] m and +16.9 [8.8] m, respectively, nominal two-tailed P=0.047). In the <300 m category, mean 6MWD declined over time (mean [SE] 6MWD to week 52=−20.0 [4.6] m and −15.6 [8.3] m, respectively, nominal two-tailed P=0.071).

3. Baseline FVC categories

• Cipaglucosidase alfa/miglustat was favoured over alglucosidase alfa/placebo in the overall population and in patients in both the ≥55% and <55% categories at week 52. In the ≥55% category, mean FVC increased over time (mean [SE] FVC to week 52=+13.6 [8.3] m and +16.9 [8.8] m, respectively, nominal two-tailed P=0.047). In the <55% category, mean FVC declined over time (mean [SE] FVC to week 52=−15.6 [8.3] m and −10.1 [2.1] m, respectively, nominal two-tailed P=0.005).

CONCLUSIONS

• In the overall study population including ERT naive and ERT experienced patients, cipaglucosidase alfa/miglustat showed positive effects on clinically meaningful improvements on motor and respiratory functions compared with approved ERT, regardless of baseline 6MWD and FVC assessments, and across both prespecified and post hoc subgroup analyses.
• Cipaglucosidase alfa/miglustat demonstrated a similar safety profile to that of alglucosidase alfa/placebo.

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References