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Long-term efficacy and safety of cipaglucosidase alfa/miglustat in ambulatory patients with Pompe disease: a Phase III open-label extension study (ATB200-07)

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Introduction and objectives

- Pompe disease is a rare, multisystemic, heterogeneous disorder characterized by progressive loss of muscle and respiratory function due to acid α-glucosidase (GAA) deficiency, an enzyme responsible for degrading lysosomal glycogen.[1–3]
- Enzyme replacement therapy (ERT) with alglucosidase alfa, a recombinant human GAA (rhGAA), was the first approved Pompe-disease-specific treatment,[4–7] while avalglucosidase alfa has received marketing authorization in several countries for infantile-onset Pompe disease (IOPD) and/or late-onset Pompe disease (LOPD).[8]
- Cipaglucosidase alfa plus miglustat (cipa/mig) is a novel, two-component therapy for Pompe disease comprising cipaglucosidase alfa, a novel bis-mannose-6-phosphate-enriched rhGAA, administered in conjunction with miglustat, an enzyme stabilizer.[9,10]
- The Phase III double-blind ATB200-03 PROPEL study (NCT03729362) compared cipa/mig with alglucosidase alfa/placebo (alg/pla) in adults with LOPD over 52 weeks.[10]
- The ongoing open-label extension (OLE) of PROPEL, ATB200-07 (NCT04138277), evaluates the long-term efficacy and safety of cipa/mig. Here we report data from the first year of the OLE.

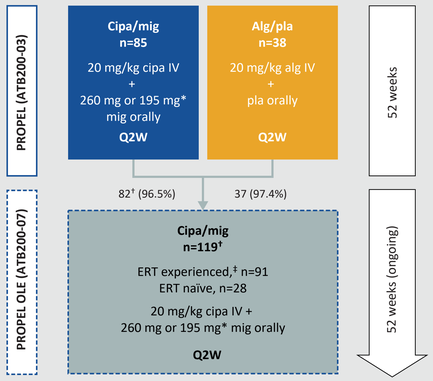
Conclusions

- ERT-experienced patients who were treated with cipa/mig through PROPEL and the OLE showed improvements from baseline in 6-minute walk distance (6MWD) and biomarker levels and remained stable in forced vital capacity (FVC) through PROPEL. All outcomes remained stable through the OLE to week 104.
- For ERT-naïve patients who were treated with cipa/mig through PROPEL and the OLE, 6MWD and biomarker levels improved through PROPEL and remained stable through the OLE. FVC declined through PROPEL and stabilized over the OLE.
- ERT-experienced patients who were treated with alg/pla during PROPEL remained stable in 6MWD and worsened in FVC and biomarker levels, and stabilized or improved after switching to cipa/mig in the OLE.
- ERT-naïve patients who were treated with alg/pla during PROPEL and switched to cipa/mig in the OLE showed a similar pattern in 6MWD and FVC to ERT-naïve patients who were treated with cipa/mig throughout.
- No new safety signals were identified in the OLE.
- Overall, data demonstrate that treatment with cipa/mig up to 104 weeks was associated with a durable effect and was well tolerated, supporting the long-term benefits of cipa/mig treatment for patients with LOPD.

Methods

- For patients who completed PROPEL, the first infusion of the OLE was scheduled approximately 2 weeks after the last dose to ensure continuity
  - ERT-experienced patients are defined as those treated with ERT prior to their participation in PROPEL
  - ERT-naïve patients had not been treated with ERT prior to PROPEL.
- Enrollment criteria for ATB200-07 can be found in the Supplement.
- 90.8% of patients remained in the OLE through week 52.

Study design: patients who completed the PROPEL study continued cipa/mig treatment or switched from alg/pla to cipa/mig



Reported outcomes

Motor function
- 6MWD (% predicted)

Respiratory function
- FVC (% predicted)

Biomarkers
- Hex4 (mmol/mol)
- CK (U/L)

Safety
- TEAEs
- IARs

Efficacy and biomarker data are reported as change from the PROPEL baseline to OLE week 52 (104 weeks after the PROPEL baseline)

*260 mg miglustat for patients weighing ≥50 kg and 195 mg for patients weighing ≥40 kg to <50 kg; †Includes one patient who enrolled in ATB200-07 but was never dosed; ‡ERT-experienced patients are defined as those treated with ERT (alg) prior to their participation in the PROPEL study. CK, creatine kinase; Hex4, hexose tetrasaccharide; IAR, infusion-associated reaction; IV, intravenous; Q2W, every 2 weeks; TEAE, treatment-emergent adverse event.

Patient disposition and baseline characteristics

- Of the 123 patients who enrolled in PROPEL, 119 enrolled in the OLE, and 118 of these received study treatment. Further information on patient disposition can be found in the Supplement.
- Of these, 90 (76.3%) patients were ERT experienced and 28 (23.7%) were ERT naïve at the PROPEL baseline.
- Baseline characteristics of the patients in PROPEL have been described. The mean (standard deviation [SD]) duration of ERT for ERT-experienced patients in PROPEL was 7.3 (3.5) years and was similar between treatment groups.[10]

Baseline characteristics of OLE participants

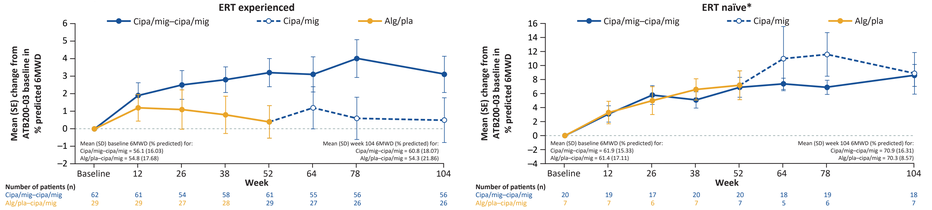
	Cipa/mig–cipa/mig n=81*	Alg/pla–cipa/mig n=37
Median (range) age, years	49 (20–75)	47 (23–67)
Male patients, n (%)	33 (40.7)	19 (51.4)
Race, n (%)		
Asian	3 (3.7)	1 (2.7)
Japanese	2 (2.5)	4 (10.8)
Black or African American	0	1 (2.7)
White	71 (87.7)	30 (81.1)
Other	5 (6.2)	1 (2.7)
ERT experienced, n (%)	61 (75.3)	29 (78.4)
Median (Q1–Q3) ERT duration, years†	7.6 (4.3–10.2)	7.1 (3.8–10.4)

*Excludes one patient who enrolled in ATB200-07 but was never dosed; †For ERT-experienced patients only.

Results

Motor function (% predicted 6MWD)

Improvement from the PROPEL baseline in % predicted 6MWD for the cipa/mig group was maintained throughout the OLE for ERT-experienced and ERT-naïve patients

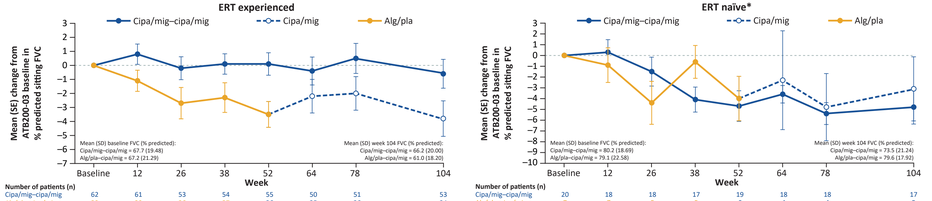


*Excludes one outlier. SD, standard deviation; SE, standard error.

- ERT-experienced and -naïve patients treated with cipa/mig throughout showed durable improvements in % predicted 6MWD in PROPEL that were maintained throughout the OLE to week 104.
- ERT-experienced and -naïve patients who received alg/pla in PROPEL and switched to cipa/mig in the OLE showed stability in % predicted 6MWD throughout the OLE.

Respiratory function (sitting % predicted FVC)

Sitting % predicted FVC remained stable in ERT-experienced and ERT-naïve patients throughout the OLE for both PROPEL treatment groups

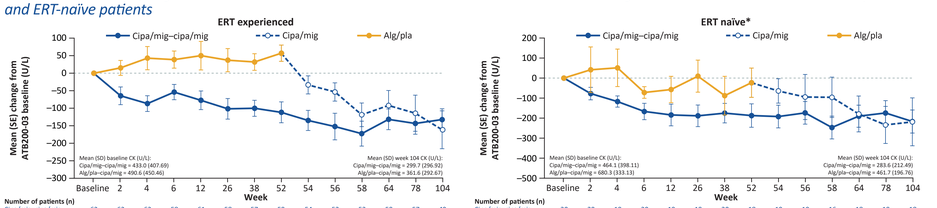


*Excludes one outlier. SD, standard deviation; SE, standard error.

- ERT-experienced patients treated with cipa/mig throughout remained stable, while patients who received alg/pla in PROPEL experienced a decline in sitting % predicted FVC that stabilized after switching to cipa/mig in the OLE.
- ERT-naïve patients in both treatment groups experienced some decline in PROPEL that stabilized in the OLE with no further decline in FVC to week 104.

Biomarkers

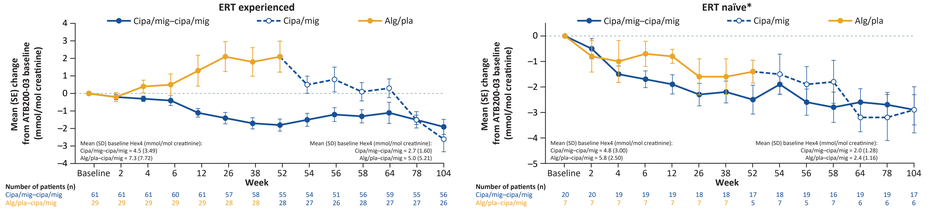
Serum CK levels: cipa/mig treatment was associated with a durable reduction in serum CK during PROPEL and the OLE in both ERT-experienced and ERT-naïve patients



*Excludes one outlier. SD, standard deviation; SE, standard error.

- ERT-experienced and -naïve patients treated with cipa/mig throughout showed a decline in serum CK levels during PROPEL that was maintained throughout the OLE.
- ERT-experienced and -naïve patients who received alg/pla in PROPEL showed a slight increase or stability in serum CK levels to week 52, and a marked decline after switching to cipa/mig in the OLE.

Urine Hex4 levels: cipa/mig treatment was associated with a durable reduction in urine Hex4 during PROPEL and the OLE in both ERT-experienced and ERT-naïve patients



*Excludes one outlier. SD, standard deviation; SE, standard error.

- ERT-experienced patients treated with cipa/mig throughout experienced a decline in urine Hex4 levels in PROPEL that stabilized during the OLE. ERT-experienced patients who received alg/pla in PROPEL experienced an increase in Hex4 and a marked decline after switching to cipa/mig in the OLE.
- ERT-naïve patients experienced a decline in Hex4 levels during PROPEL in both treatment groups that stabilized or declined further during the OLE to week 104.

Safety

The safety profile was similar for patients who continued cipa/mig treatment from the start of PROPEL and those who switched from alg/pla

	Cipa/mig–cipa/mig n=85*	Alg/pla–cipa/mig n=37†
TEAEs, n (%)	84 (98.8)	36 (97.3)
TEAEs potentially related to treatment	37 (43.5)	15 (40.5)
Serious TEAEs	14 (16.5)	6 (16.2)
Serious TEAEs potentially related to treatment‡	1 (1.2)	2 (5.4)
TEAEs leading to study withdrawal during OLE	1 (1.2)§	2 (5.4)‖
TEAEs leading to death	0 (0)	0 (0)
IARs	27 (31.8)	10 (27.0)

*Includes data from patients treated with cipa/mig in PROPEL who may or may not have continued cipa/mig in the OLE, including data from both PROPEL and the OLE; †Includes data from the OLE only; ‡Relatedness to treatment was determined by the investigator; §Urticaria; ‖Urticaria and hypotension, and anaphylaxis.

- Most TEAEs were mild to moderate in severity.
- The most common TEAEs included fall, headache, arthralgia, nasopharyngitis, myalgia and back pain.
- Three patients withdrew from the study due to TEAEs experienced during the OLE.
- No new safety signals were identified during the OLE.

Acknowledgments and disclosures

The authors thank the patients, their families, and Pompe disease patient organizations, as well as the ATB200-07 study investigators.

Amicus Therapeutics' investigational therapy, cipaglucosidase alfa/miglustat, is in development for the treatment of Pompe disease and is not approved by any regulatory agency at this time.

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References

1. Cabello JF *et al. Orphan Drugs Res Rev* 2017;7:1–10.
2. Hers HG. *Biochem J* 1963;86:11–16.
3. Kishnani PS *et al. Genet Med* 2006;8:267–88.
4. Tarnopolsky M *et al. Can J Neurol Sci* 2016;43:472–85.
5. van der Ploeg AT *et al. Eur J Neurol* 2017;24:768–e31.
6. Cupler EJ *et al. Muscle & Nerve* 2012;45:319–33.
7. European Medicines Agency. EPAR for Myozyme®. Available at: https://www.ema.europa.eu/en/medicines/human/EPAR/myozyme (accessed December 2022).
8. Genzyme Corporation. Nexviazyme™ prescribing information. Available at: https://products.sanofi.us/nexviazyme/nexviazyme.pdf (accessed December 2022).
9. Xu S *et al. JCI Insight* 2019;4:e125358.
10. Schoser B *et al. Lancet Neurol* 2021;20:1027–37.

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