Long-term follow-up of cipaglucosidase alfa/miglustat in ambulatory patients with Pompe disease: an open-label Phase I/II study (ATB200-02)

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Disclosure information (Barry J. Byrne)

- **I have the following financial relationships to disclose:**
  - Co-founder of Aavanti Bio, Inc.

- **I will discuss the following off-label use and/or investigational use in my presentation:**
  - 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

- The study was funded by Amicus Therapeutics, Inc.

Background

- Pompe disease is a rare lysosomal disorder characterized by progressive loss of muscle and respiratory function due to GAA deficiency[1,2]
- ERT with rhGAA, alglucosidase alfa, is the first approved treatment for the disease[3]
  - While alglucosidase alfa has been shown to improve prognosis,[4] some patients do not respond, and many do not show a sustained benefit;[5] thus, substantial unmet clinical needs remain[5]
- Cipaglucosidase alfa plus miglustat is an investigational, two-component therapy for Pompe disease comprised of cipaglucosidase alfa, a novel bis-M6P-enhanced rhGAA, administered in conjunction with miglustat, an enzyme stabilizer[6,7]
- Results from the PROPEL study, a 52-week, Phase III study of cipaglucosidase alfa plus miglustat versus alglucosidase alfa plus placebo in patients with Pompe disease were recently published; the open-label extension of this study is ongoing[7]
- Data from a Phase I/II study (ATB200-02) may provide a further understanding of the long-term effect of this investigational therapy

GAA, acid α-glucosidase; ERT, enzyme replacement therapy; M6P, mannose-6-phosphate; rhGAA, recombinant human GAA. 1. Hers HG. *Biochem J* 1963;86:11–6; 2. Kishnani PS *et al. Genet Med* 2006;8:267–88; 3. Genzyme. Lumizyme prescribing information. Available at: www.accessdata.fda.gov/drugsatfda_docs/label/2020/125291s151lbl.pdf (accessed Feb 2022); 4. van der Ploeg AT *et al. N Engl J Med* 2010;362:1396–406; 5. Harlaar L *et al. Neurology* 2019;93:e1756–67; 6. Xu S *et al. JCI Insight* 2019;4:e125358; 7. Schoser B *et al. Lancet Neurol* 2021;20:1027–37.

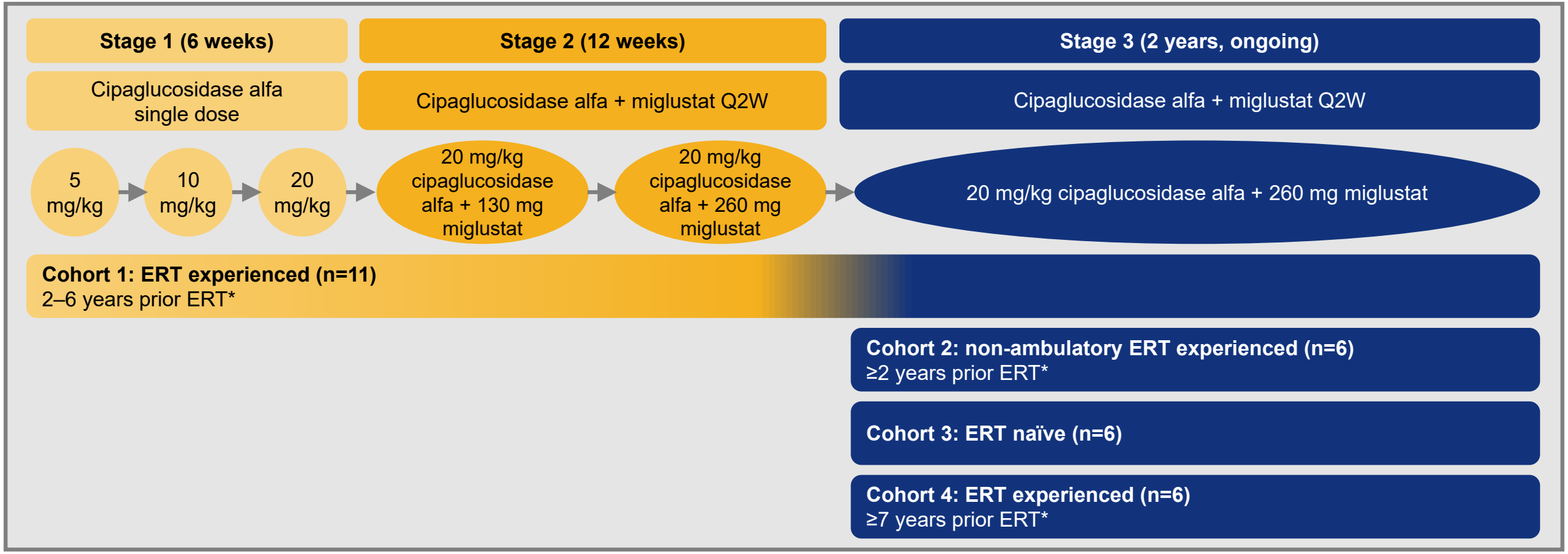
ATB200-02 overview

ATB200-02 (NCT02675465) is an **ongoing, open-label, Phase I/II clinical trial** that aimed to evaluate the **safety, tolerability, pharmacokinetics, pharmacodynamics,** and **efficacy** of **cipaglucosidase alfa plus miglustat** in adults with **Pompe disease**

Here, we report **up to 36 months of efficacy and safety data** for ambulatory patients with Pompe disease in the ATB200-02 study

Phase I/II ATB200-02 study design

- The ATB200-02 study is conducted in 17 centers across 6 countries, with 4 cohorts of patients enrolled at staggered timepoints



*With 20 mg/kg alglucosidase alfa Q2W. Q2W, every 2 weeks.

Summary of endpoints and cohorts reported

Assessments	ERT experienced*		ERT naïve Cohort 3
	Cohort 1 (2–6 years)	Cohort 4 (≥7 years)	
Motor function • 6MWD	Pooled data		✓
Respiratory function • FVC	Pooled data		✓
Muscle strength • MMT lower extremity score	Pooled data		✓
Biomarkers • Hex4 and CK	Pooled data		✓
Safety	Pooled data		✓
	Pooled data		

- Available data for cohort 2, non-ambulatory ERT-experienced patients, are presented in the Supplement, which is available via QR code

*With 20 mg/kg alglucosidase alfa Q2W. 6MWD, 6-minute walk distance; CK, creatine kinase; FVC, forced vital capacity; Hex4, glucose tertasaccharide; MMT, manual muscle test; QR, quick response.

Baseline characteristics and patient disposition

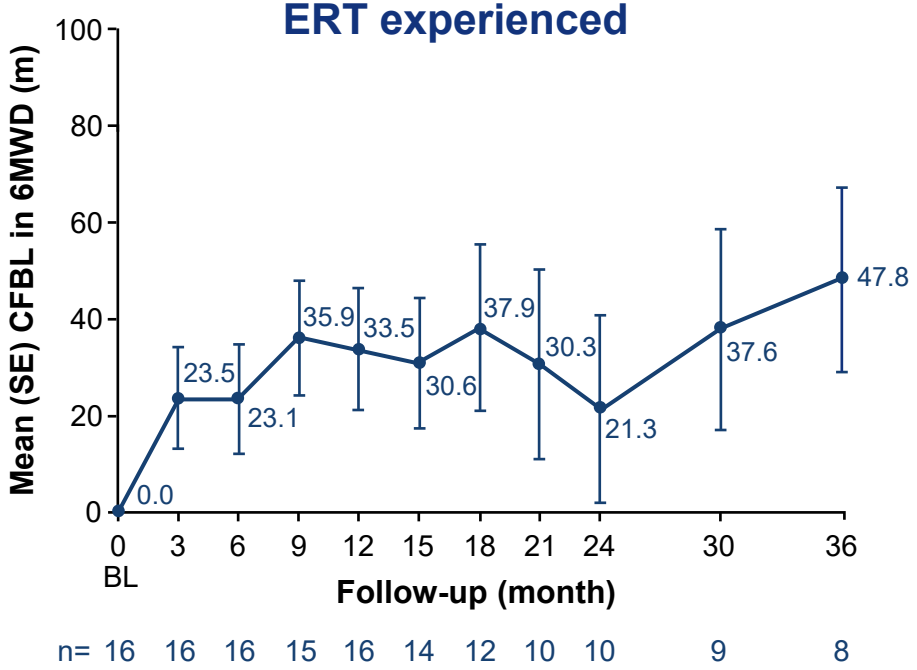
	ERT experienced		ERT naïve
	Cohort 1 2–6 years prior ERT n=11	**Cohort 4** ≥7 years prior ERT n=6	**Cohort 3** n=6
Baseline characteristics			
Median (range) age, years	49.4 (28–66)	40.8 (20–65)	49.3 (24–65)
Sex, M:F	9:2	2:4	1:5
Mean (SD) time on alglucosidase alfa, years	4.7 (1.4)	9.4 (1.2)	N/A*
Mean (SD) 6MWD, m	397.2 (96.8)	387.3 (161.3)	396.0 (75.2)
Mean (SD) sitting FVC, % predicted	52.6 (13.9)	65.3 (21.1)	55.8 (19.1)
Mean (SD) MMT lower extremity score	31.8 (1.9)	27.3 (3.7)	29.0 (1.7)
Patient disposition			
Ongoing in study, n (%)	9 (82)	6 (100)	6 (100)

- Due to the staggered timing of patient enrollment, the number of patients with data currently available decreases at later timepoints in this ongoing study

*1 ERT-naïve patient had received 1 dose of alglucosidase alfa >6 months prior to study entry. m, meters; M:F, male:female; N/A, not applicable; SD, standard deviation.

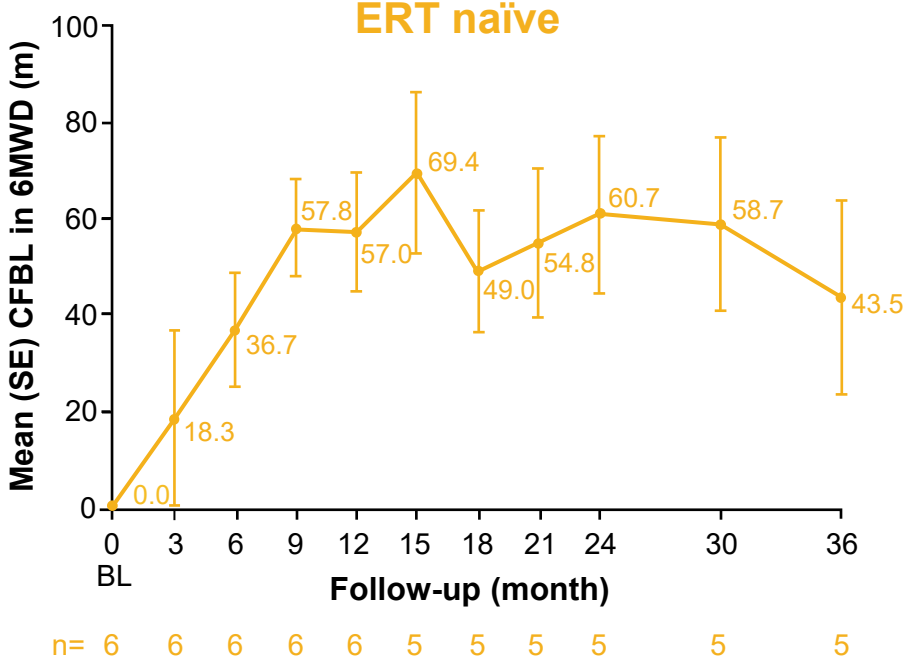
Motor function: CFBL in 6MWD

ERT experienced



- Patients showed durable mean improvements from baseline in 6MWD up to 36 months
- After 12, 24 and 36 months of follow-up, 6MWD improved numerically from baseline in **13/16**, **8/10**, and **6/8** patients, respectively

ERT naïve

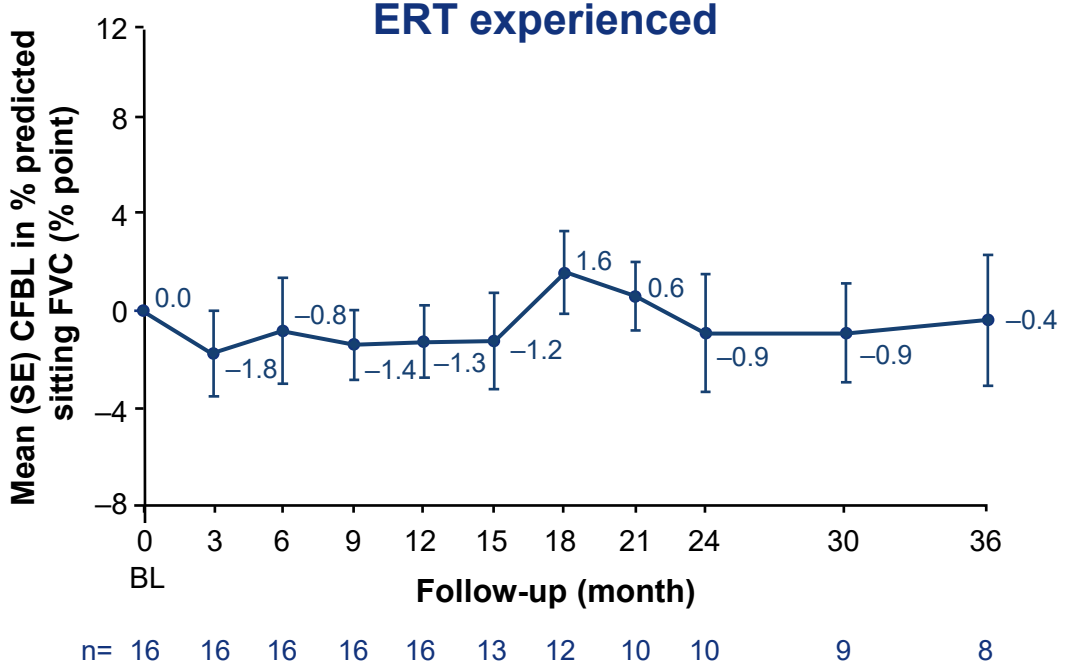


- Patients showed durable mean improvements from baseline in 6MWD up to 36 months
- After 12, 24 and 36 months of follow-up, 6MWD improved numerically from baseline in **6/6**, **5/5**, and **4/5** patients, respectively

BL, baseline; CFBL, change from baseline; SE, standard error.

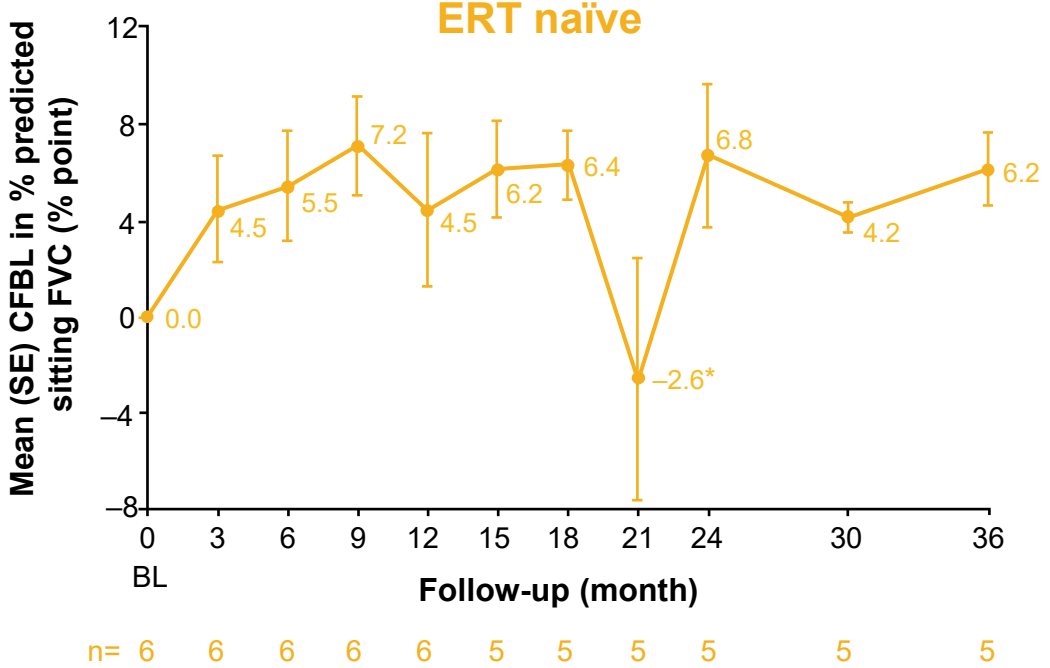
Respiratory function: CFBL in FVC

ERT experienced



- Mean CFBL in FVC was generally stable for up to 36 months of follow-up
- After 12, 24 and 36 months of follow-up, FVC improved (>3% points) or remained stable (±3% points) from baseline in **9/16**, **6/10**, and **6/8** patients, respectively

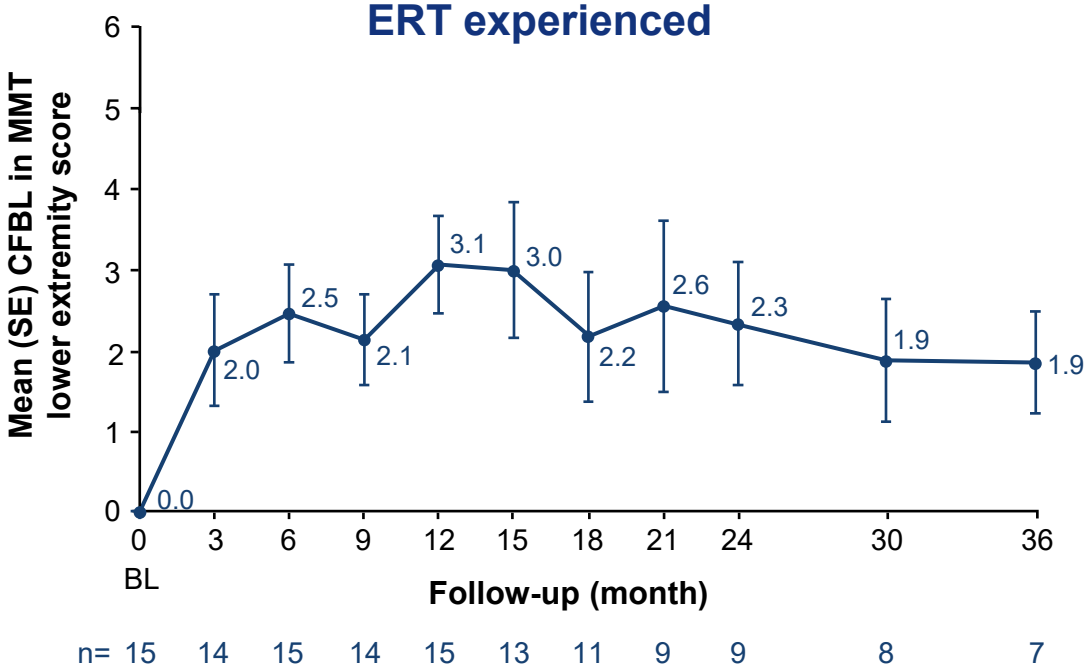
ERT naïve



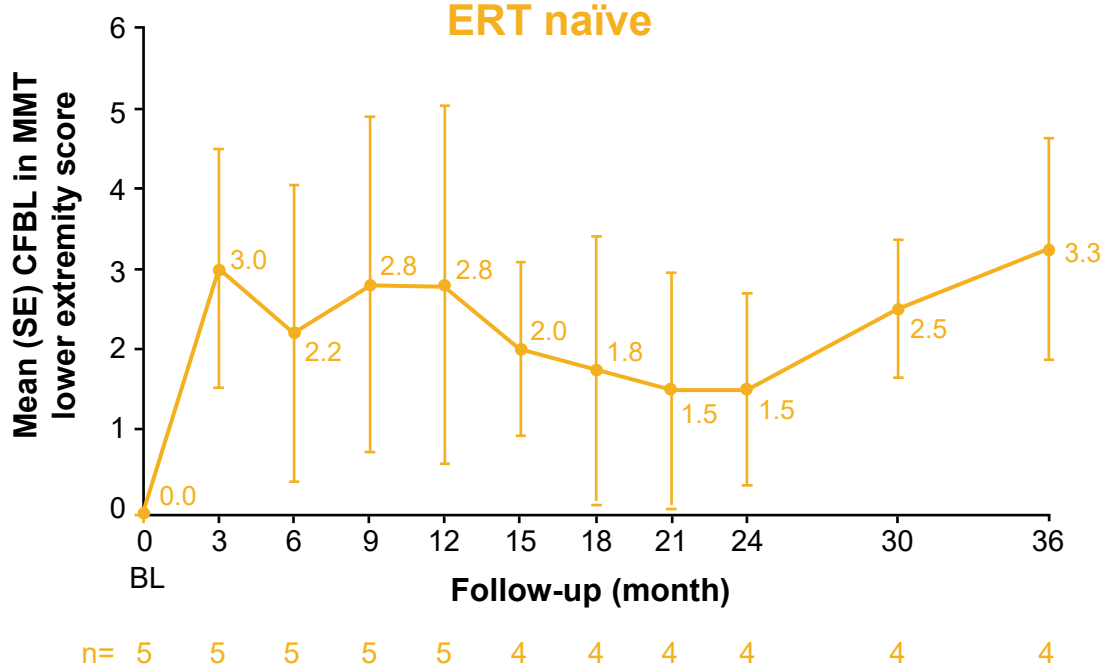
- Mean CFBL in FVC improved numerically from baseline for up to 36 months of follow-up
- After 12, 24 and 36 months of follow-up, FVC improved (>3% points) or remained stable (±3% points) from baseline in **5/6**, **5/5**, and **5/5** patients, respectively

*One patient in the ERT-naïve cohort experienced a large drop in % predicted FVC at month 21, which returned to previous levels at the following visit (month 24).

Muscle strength: CFBL in MMT lower extremity score

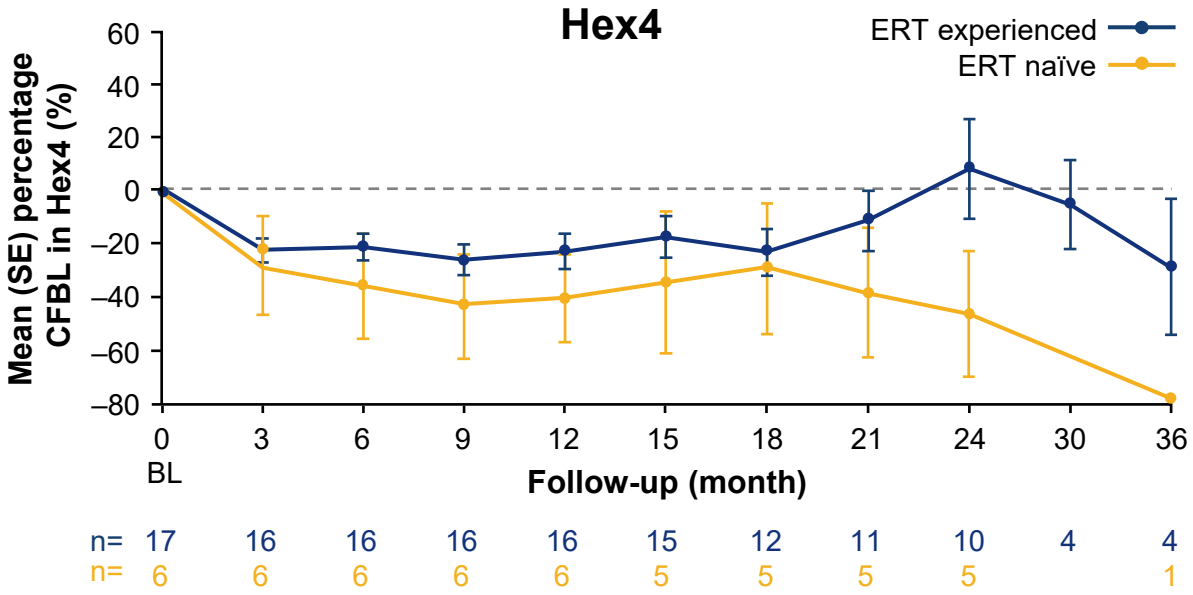


- Mean change in MMT lower extremity score improved numerically from baseline and improvements were maintained for up to 36 months of follow-up

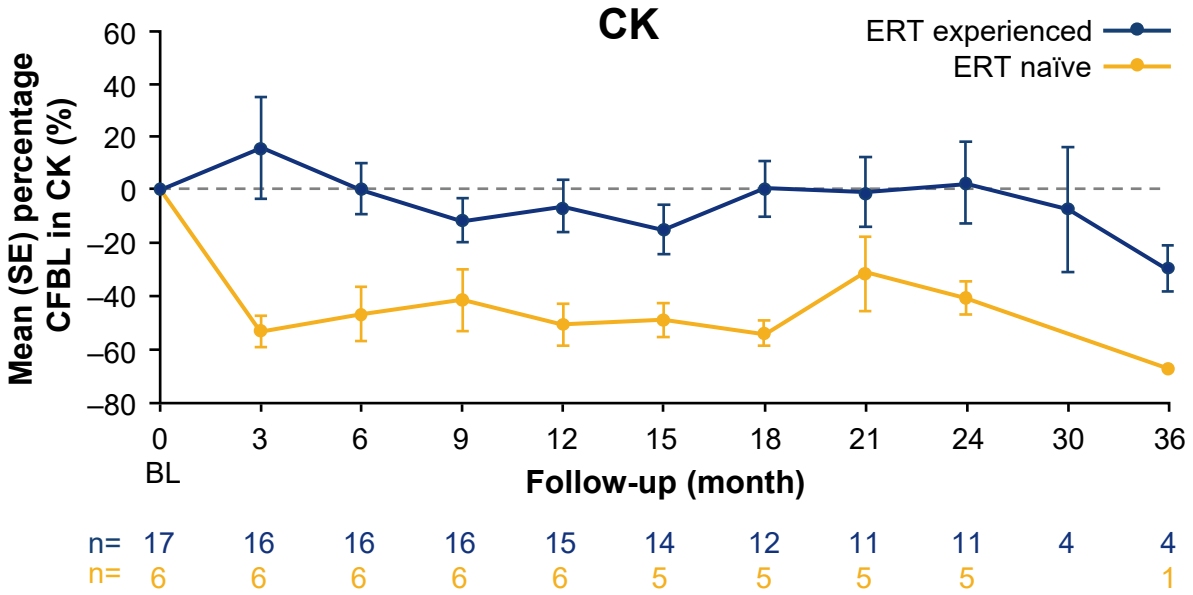


- Mean change in MMT lower extremity score improved numerically from baseline and improvements were maintained for up to 36 months of follow-up

Biomarkers: % CFBL in Hex4 and CK levels



- During 36 months of follow-up, cipaglucosidase alfa/miglustat was generally associated with mean reductions from baseline in urine Hex4, with greater reductions in ERT-naïve patients
- After 12, 24 and 36 months of follow-up, Hex4 levels decreased numerically from baseline in **13/16**, **6/10**, and **3/4 ERT-experienced patients**, and in **5/6**, **4/5**, and **1/1 ERT-naïve patients**, respectively



- During 36 months of follow-up, cipaglucosidase alfa/miglustat was associated with either stable levels of, or mean reductions from baseline, in plasma CK, with greater reductions in ERT-naïve patients
- After 12, 24 and 36 months of follow-up, CK levels decreased numerically from baseline in **10/15**, **6/11**, and **4/4 ERT-experienced patients**, and in **6/6**, **5/5**, and **1/1 ERT-naïve patients**, respectively

Safety summary

	ERT experienced n=17	ERT naïve n=6	Overall N=23
TEAEs, n (%)	17 (100)	6 (100)	23 (100)
TEAEs potentially related to treatment	11 (65)	3 (50)	14 (61)
Serious TEAEs	3 (18)	2 (33)	5 (22)
Serious TEAEs potentially related to treatment	1 (6)	1 (17)	2 (9)
TEAEs leading to study withdrawal	1 (6)*	0 (0)	1 (4)
TEAEs leading to death	0 (0)	0 (0)	0 (0)
IARs	7 (41)	2 (33)	9 (39)

- Mean (SD) duration of treatment was 37.2 (14.48),19.9 (4.13) and 36.9 (12.14) months in cohorts 1 (prior ERT 2–6 years), 4 (prior ERT ≥7 years) and 3 (ERT naive), respectively
- The most common TEAEs included fall, nasopharyngitis and arthralgia; most TEAEs were mild or moderate in severity and did not lead to study withdrawal

*Diffuse large B-cell lymphoma. IAR, infusion-associated reaction; TEAE, treatment-emergent adverse event with onset date on or after first dose of study drug.

Conclusions

- **Results from up to 36 months of follow-up in ambulatory patients from the ATB200-02 study of cipaglucosidase alfa plus miglustat show:**
  - **ERT-experienced patients** had **durable mean improvements from baseline in motor function** that were **sustained for up to 36 months** of follow-up, while **respiratory function was stable and maintained** over the same period: an improvement relative to the expected decline in many patients receiving long-term ERT[1]
  - **ERT-naïve patients** showed **durable mean improvements from baseline in motor and respiratory function** that were **sustained for up to 36 months** of follow-up
  - Mean levels of two biomarkers, **Hex4 and CK**, **were either stable or decreased from baseline up to 36 months** of follow-up, with decreases **most notable in the ERT-naïve cohort**
  - The **safety profile of cipaglucosidase alfa plus miglustat** was **similar to** that reported for **alglucosidase alfa**[2]

1. Harlaar L *et al. Neurology* 2019;93:e1756–67; 2. van der Ploeg AT *et al. N Engl J Med* 2010; 362:1396–406.

Acknowledgments and QR codes

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Presentation PDF

Supplement

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