Expanding horizons for patients with Pompe disease: Using data to guide clinical practice

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Recorded following 29th Annual Congress of the World Muscle Society, Prague, Czechia, 8–12 October 2024, and 21st Annual WORLD*Symposium,* San Diego, CA, USA, 3–7 February 2025

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Treating Pompe disease for the long-term and in the real world

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119: Retrospective cohort study evaluating the disease burden of patients with Pompe disease treated with ERT in the United States

Pillai NR, et al.

Patient cohort N=105 **IOPD:** n=50 **LOPD:** n=55

Comorbidities of interest

	Respiratory	Ambulatory	GI	CV
IOPD	84.5%	57.4%	67.8%	16.9%
LOPD	79.4%	54.3%	33.4%	28.7%

Cumulative incidence of most comorbidities, particularly respiratory infections, increased over time

Patterns of ERT use

	IOPD	LOPD
Discontinued 1st ERT after 12 months	35.3%	33.0%
Discontinued 1st ERT after 24 months	48.7%	54.5%
Had a change in ERT dose	42.4%	20.6%
ERT dose decrease	36.4%	14.7%
ERT dose increase	14.7%	17.6%

Utilization of support/therapy services

	ITI/IVIg	Ambulatory	Respiratory	Occupational	Speech	Nutritional	Physical
IOPD	48.6%	8.3%	15.1%	27.8%	59.5%	47.3%	66.9%
LOPD	1.8%	11.1%	17.0%	3.7%	3.9%	11.2%	31.8%

The use of occupational, speech and physical therapy increased over time for both groups

Pompe disease causes a substantial disease burden for patients despite standard-of-care ERT, suggesting alternative treatments are needed

CV, cardiovascular; ERT, enzyme replacement therapy; GI, gastrointestinal; IOPD, infantile-onset Pompe disease; ITI, immune tolerance induction; IVIg, intravenous immunoglobulin; LOPD, late-onset Pompe disease. Pillai NR, et al. Presented at 21st Annual WORLD*Symposium* 2025. San Diego, CA, USA. 3–7 February 2025. Abstr. 119.

331: Retrospective cohort study evaluating the economic burden of patients with Pompe disease treated with ERT in the United States

Steiner RD, et al.

Patient cohort N=105 **IOPD:** n=50 **LOPD:** n=55

Healthcare resource utilization, %

	IOPD	LOPD
Used ≥1 outpatient services	94.0	89.1
Require ≥1 all-cause hospitalization	46	29
Require ≥1 Pompe-related hospitalization	44	24
Mean, n		
All-cause outpatient visits PMPM	8.7	3.9
Pompe-related outpatient visits PMPM	5.2	1.7

Healthcare costs:

	IOPD	LOPD
All-cause (total)	$950,380	$1,857,823
All-cause (PMPM)	$31,658	$56,615
ERT pharmacy (total)	$211,536	$566,938
ERT pharmacy (PMPM)	$7,046	$17,277
Pompe-related* (total)	$804,918	$1,329,693
Pompe-related* (PMPM)	$25,999	$39,344

The majority of costs were outpatient- or ERT-related

Pompe disease causes a substantial economic burden for patients treated with ERT, primarily due to outpatient visits and ERT prescription costs, highlighting the need for new, less expensive treatments

*Pompe-related healthcare costs included outpatient, hospitalization and prescription costs.
ERT, enzyme replacement therapy; IOPD, infantile-onset Pompe disease; LOPD, late-onset Pompe disease; PMPM, per member per month.
Steiner RD, et al. Presented at 21st Annual WORLD*Symposium* 2025. San Diego, CA, USA. 3–7 February 2025. Abstr. 331.

248: Pompe disease in Sweden: A real-world evidence study investigating disease burden, treatment patterns for ERT and concomitant medications

Nordin S, et al.

Insights on treatment patterns in a Swedish cohort

	LOPD (n=14)	IOPD (n=5)
Disease prevalence at CSTP, per 1 million	**1.3**	**0.5**
Mean age at diagnosis, years (SD)	**43.2** (22.3)	**0.5** (0.5)
Mean time from symptom onset to diagnosis, years (SD)	**9.5** (13.5)	*
Median time from symptom onset to diagnosis, years (IQR)	**5.4** (2.3–8.2)	*
Median time from diagnosis to ERT initiation, years (95% CI)	**1.5** (0.5–16.6)	*

Biweekly ERT dose

LOPD (n=9): **20 mg/kg** (standard dose)
IOPD (n=5): **24.0 mg/kg** (SD ±8.9)
(maximum 40.0 mg/kg)

In patients with LOPD (n=14):

receiving concomitant respiratory-management medication

6 patients required ventilation/other respiratory management

age at first requirement

62.8 years

Diagnoses prior to LOPD

- **71%** Symptoms, signs and abnormal clinical/ laboratory findings not elsewhere classified
- **53%** Endocrine, nutritional and metabolic diseases
- **53%** Nervous system diseases
- **41%** Respiratory system diseases

*Not reported in published abstract. CI, confidence interval; CSTP, cross-sectional timepoint; ERT, enzyme replacement therapy; IOPD, infantile-onset Pompe disease; IQR, interquartile range; LOPD, late-onset Pompe disease; SD, standard deviation. Nordin S, et al. Presented at 21st Annual WORLD*Symposium* 2025. San Diego, CA, USA. 3–7 February 2025. Abstr. 248.

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225: POM-005: A global, prospective, observational registry of people living with Pompe disease

McIntosh P, et al.

POM-005 (NCT06121011): A global, prospective, observational registry to assess clinical outcomes in people living with Pompe disease, regardless of current/previous therapy status

Inclusion criteria

People with IOPD or LOPD based on documented GAA enzyme deficiency and/or GAA genotyping, regardless of time since diagnosis

Data from a long-term cohort of patients from CIPA + MIG in clinical trials/early access programmes continuing therapy post-approval

Ineligible: Patients currently receiving investigational therapy for Pompe in a clinical trial, compassionate use or expanded-use programme

- **~100 study sites** globally
- **500 participants anticipated**
  - 1st participant enrolled: February 2024
- Study completion: ~December 2034
- ≥5 years prospective follow-up
- Data at enrolment will include historical data (≤5 years prior)

Objectives

- Long-term real-world effectiveness (e.g. biomarkers, motor and pulmonary function)
- Long-term safety (e.g. IARs, pregnancy exposure)
- HR-QoL and PROs
- Characterize disease natural history

CIPA, cipaglucosidase alfa; GAA, acid alpha-glucosidase; HR-QoL, health-related quality of life; IAR, infusion-associated reactions; IOPD, infantile-onset Pompe disease; LOPD, late-onset Pompe disease; MIG, miglustat; PRO, patient reported outcome. McIntosh P, et al. Presented at 21st Annual WORLD*Symposium* 2025. San Diego, CA, USA. 3–7 February 2025. Abstr. 225.

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Treatment switching for patients with Pompe disease

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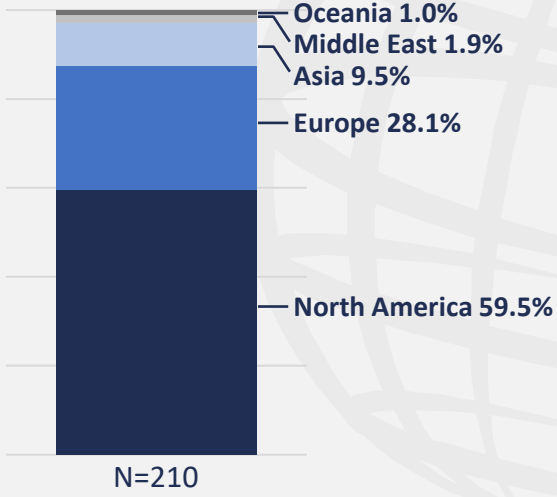
P668: Pompe Registry: Real-world experience of patients with LOPD who switched therapy from alglucosidase alfa (ALG) to avalglucosidase alfa (AVA)

Schoser B, et al.

Baseline characteristics (Data download: 5 April 2024)	Patients
Pompe Registry patients with LOPD who had switched treatments, N	210
Time on ALG pre-switch	
<5 years, n (%)	85 (40.5%)
≥5 years, n (%)	125 (59.5%)
Females, n (%)	110 (52.4%)
Age at Pompe disease diagnosis, n	209
Mean, years (SD)	35.2 (21.41)
Mean patients on ALG <5 years pre-switch, years (SD)	33.7 (22.39)
Mean patients on ALG ≥5 years pre-switch, years (SD)	34.5 (20.74)
Median, years (min, max)	35.6 (0, 77.5)
Median patients on ALG <5 years pre-switch, years (min, max)	34.7 (0, 70.6)
Median patients on ALG ≥5 years pre-switch, years (min, max)	36.4 (0, 77.5)

Distribution of patients with LOPD by region of residence



Most (59.5%; 125/210) patients with LOPD in the Pompe Registry, who had switched treatment from ALG to AVA, **had received ALG for ≥5 years pre-switch**

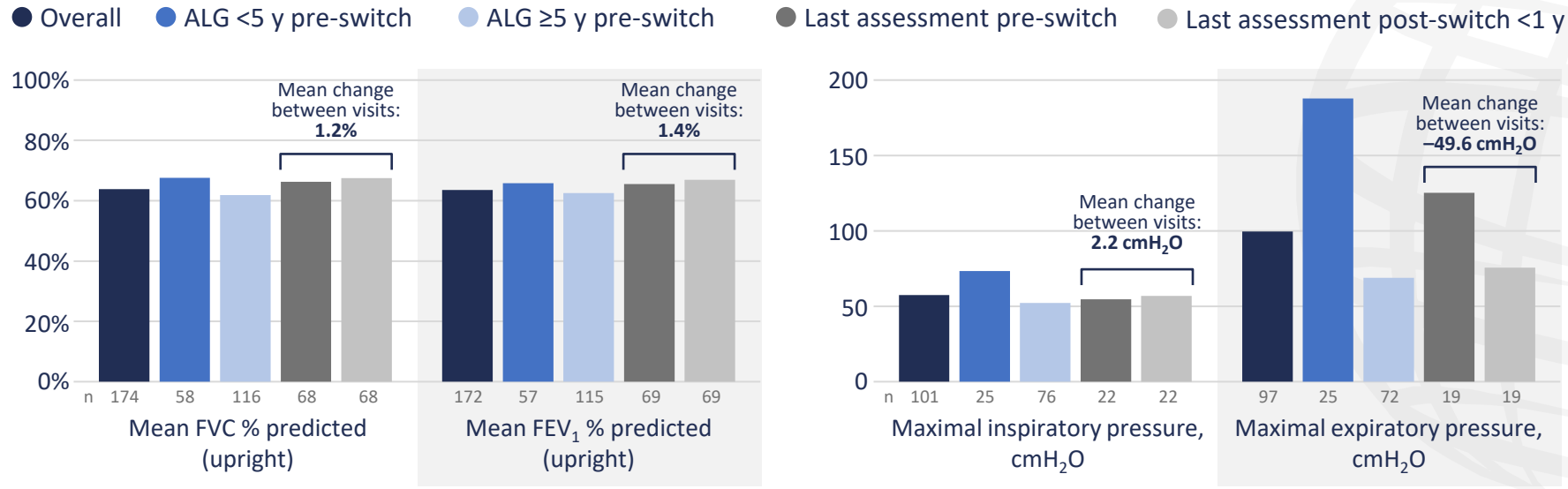
ALG, alglucosidase alfa; AVA, avalglucosidase alfa; LOPD, late-onset Pompe disease; SD, standard deviation.

Schoser B, et al. Presented at: 29th Annual Congress of the World Muscle Society 2024, Prague, Czechia. 8–12 October 2024. P668.

P668: Pompe Registry: Real-world experience of patients with LOPD who switched therapy from alglucosidase alfa (ALG) to avalglucosidase alfa (AVA)

Schoser B, et al.

Pulmonary function



Preliminary results showed that effectiveness measures of **respiratory outcomes** were **relatively stable**

ALG, alglucosidase alfa; AVA, avalglucosidase alfa; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity.

Schoser B, et al. Presented at: 29th Annual Congress of the World Muscle Society 2024, Prague, Czechia. 8–12 October 2024. P668.

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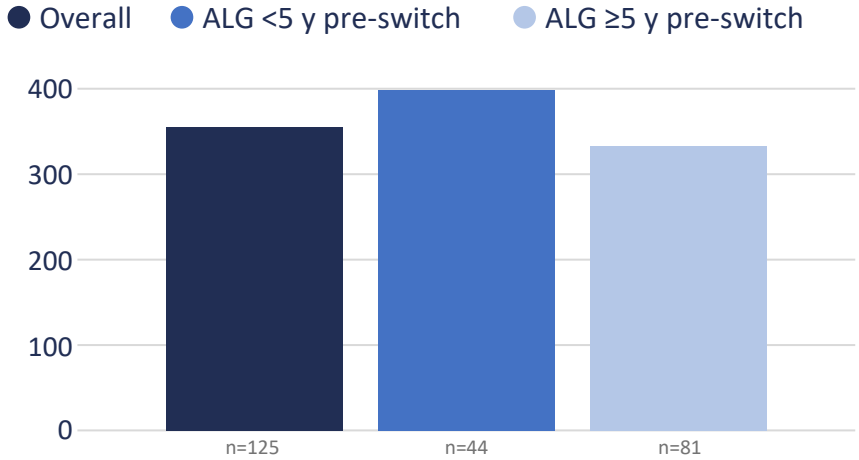
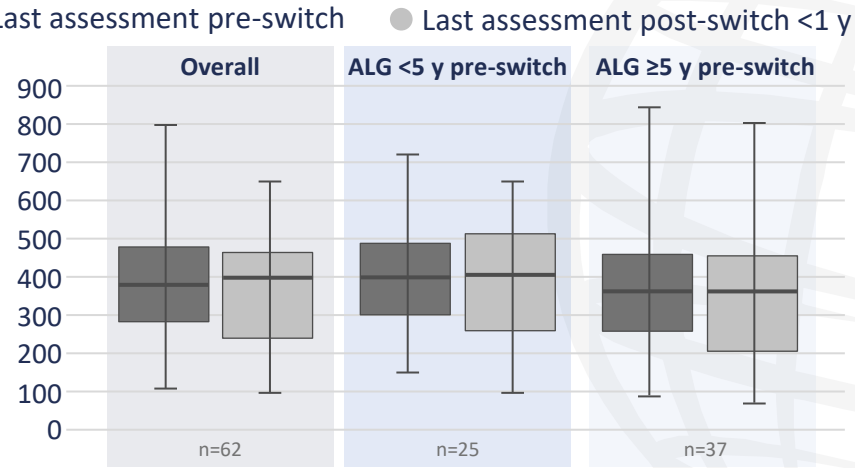
Schoser B, et al.

Motor function



Mean 6MWT distance at last assessment pre-switch from ALG to AVA for patients with LOPD, m



6MWT distance at last assessment pre-switch and last assessment within 1 y post-switch,* m

Preliminary results showed that effectiveness measures of **motor outcomes** were **relatively stable**

*Bottom and top of box indicate 25th and 75th percentiles; line within the box indicates median; whiskers indicate 5th and 95th percentiles.
6MWT, 6-minute walk test; ALG, alglucosidase alfa; AVA, avalglucosidase alfa; LOPD, late-onset Pompe disease.
Schoser B, et al. Presented at: 29th Annual Congress of the World Muscle Society 2024, Prague, Czechia. 8–12 October 2024. P668.

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P668: Pompe Registry: Real-world experience of patients with LOPD who switched therapy from alglucosidase alfa (ALG) to avalglucosidase alfa (AVA)

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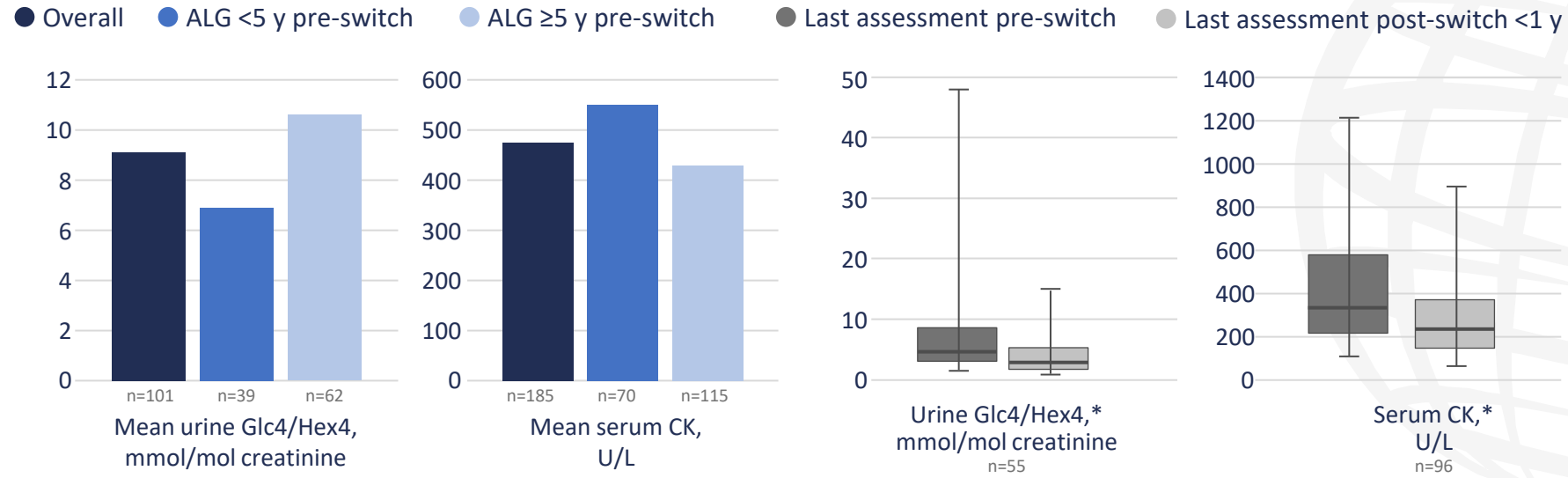
Biomarkers



Preliminary results showed that **biomarkers associated with disease burden decreased (improved) after treatment switch**

*Bottom and top of box indicate 25th and 75th percentiles; line within the box indicates median; whiskers indicate 5th and 95th percentiles.

ALG, alglucosidase alfa; AVA, avalglucosidase alfa; CK, creatine kinase; Glc4/Hex4, glucose tetrasaccharide/hexose tetrasaccharide; LOPD, late-onset Pompe disease.

Schoser B, et al. Presented at: 29th Annual Congress of the World Muscle Society 2024, Prague, Czechia. 8–12 October 2024. P668.

303: Clinically important improvements in 6MWD and FVC in adults with LOPD switching from alglucosidase alfa (ALG) to cipaglucosidase alfa plus miglustat (CIPA + MIG) in the PROPEL study

Schoser B, et al.

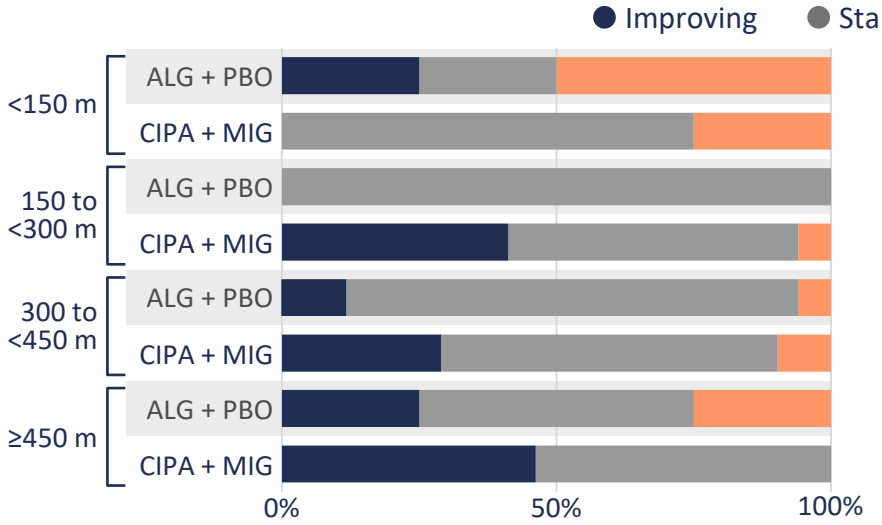
Baseline characteristics	CIPA + MIG (n=65)	ALG + PBO (n=30)
Median age, years (range)*	48.0 (21–74)	46.5 (24–66)
Median age at diagnosis, years (range)*	39.0 (1–63)	39.0 (7–62)
Males, n (%)	28 (43.1)	14 (46.7)
Median ERT duration, years (IQR)*	7.6 (4.3–10.2)	7.1 (3.8–10.4)
ERT duration, n (%)		
≥2 to <3 years	4 (6.2)	5 (16.7)
≥3 to <5 years	16 (24.6)	6 (20.0)
≥5 years	45 (69.2)	64 (67.4)
Mean 6MWD, meters (SD)†	346.9 (110.2)	334.6 (114.0)
Mean predicted sitting FVC, % (SD)†	67.9 (19.1)	67.5 (21.0)

*Data from Kishnani PS, et al. *J Patient Rep Outcomes.* 2024;8:132. †Data from Schoser B, et al. *Lancet Neurol.* 2021;20:1027–37.
6MWD, 6-minute walk distance; ALG, alglucosidase alfa; CIPA, cipaglucosidase alfa; ERT, enzyme replacement therapy; FVC, forced vital capacity; IQR, interquartile range; LOPD, late-onset Pompe disease; MIG, miglustat; PBO, placebo; SD, standard deviation.
Schoser B, et al. Presented at: WORLD*Symposium* 2025, San Diego, CA, USA. 3–7 February 2025. Abstr. 303.

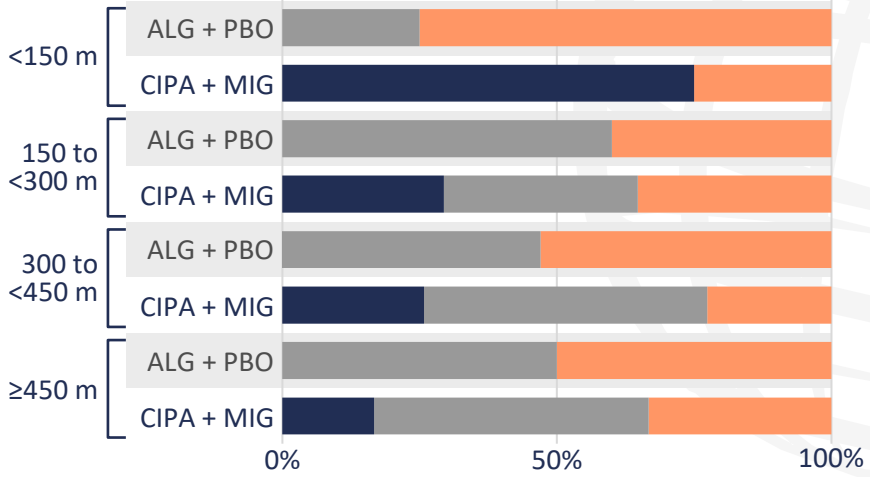
303: Clinically important improvements in 6MWD and FVC in adults with LOPD switching from alglucosidase alfa (ALG) to cipaglucosidase alfa plus miglustat (CIPA + MIG) in the PROPEL study

Schoser B, et al.

Response level by baseline 6MWD: Based on 6MWD CFBL to week 52 and MCID* (%)



Response level by baseline 6MWD: Based on predicted FVC CFBL to week 52 and MCID† (%)



*Response levels (number of responders) determined: improving, 6MWD CFBL to week 52 ≥MCID; stable, −MCID <6MWD CFBL to week 52 <MCID; worsening, 6MWD CFBL to week 52 ≤−MCID.
†Response levels (number of responders) determined: improving, FVC CFBL to week 52 ≥3%; stable, −3% <FVC CFBL to week 52 <3%; worsening, FVC CFBL to week 52 ≤−3%.
6MWD, 6-minute walk distance; ALG, alglucosidase alfa; CFBL, change from baseline; CIPA, cipaglucosidase alfa; FVC, forced vital capacity; LOPD, late-onset Pompe disease; MCID, minimal clinically important difference; MIG, miglustat; PBO, placebo.

Schoser B, et al. Presented at: WORLD*Symposium* 2025, San Diego, CA, USA. 3–7 February 2025. Abstr. 303.

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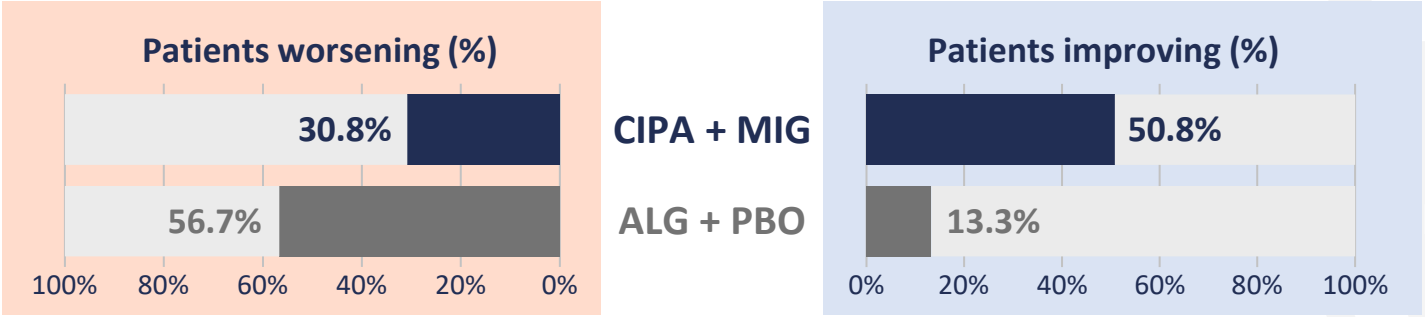
Schoser B, et al.

Overall proportion of patients with clinically relevant improvement or worsening in 6MWD and/or FVC after switching ERT in PROPEL



Around **half** as many patients treated with CIPA + MIG **worsened** compared with ALG

Nearly **4**× as many patients who switched to CIPA + MIG **improved** in 6MWD and/or FVC vs those remaining on ALG

More patients achieved clinically relevant improvement in 6MWD and/or FVC and fewer worsened with CIPA + MIG vs ALG

6MWD, 6-minute walk distance; ALG, alglucosidase alfa; CIPA, cipaglucosidase alfa; ERT, enzyme replacement therapy; FVC, forced vital capacity; LOPD, late-onset Pompe disease; MCID, minimal clinically important difference; MIG, miglustat; PBO, placebo.

Schoser B, et al. Presented at: WORLD*Symposium* 2025, San Diego, CA, USA. 3–7 February 2025. Abstr. 303.

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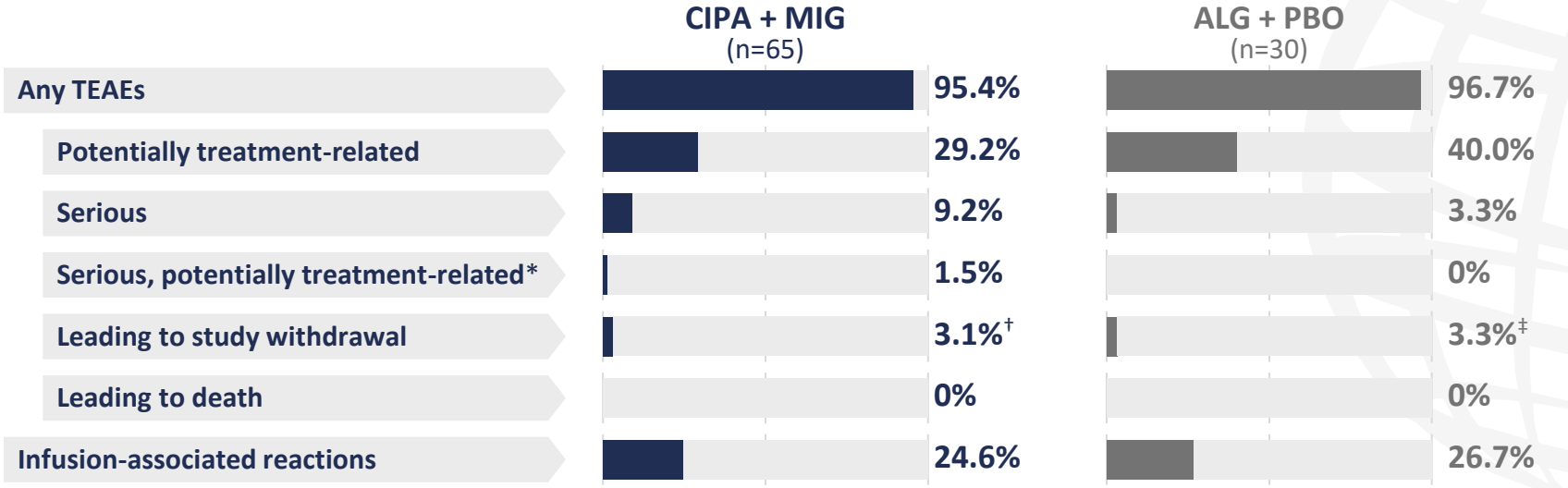
Schoser B, et al.

Safety



Safety profiles of CIPA + MIG and ALG + PBO in the ERT-experienced PROPEL study population were similar

*Relatedness to treatment determined by the investigator. †Anaphylactic reaction and chills. ‡Cerebrovascular accident (stroke) unrelated to study drug.
6MWD, 6-minute walk distance; ALG, alglucosidase alfa; CIPA, cipaglucosidase alfa; ERT, enzyme replacement therapy; FVC, forced vital capacity; LOPD, late-onset Pompe disease; MIG, miglustat; PBO, placebo; TEAE, treatment-emergent adverse event. Schoser B, et al. Presented at: WORLD*Symposium* 2025, San Diego, CA, USA. 3–7 February 2025. Abstr. 303.

46: CIPA plus MIG in LOPD: Two non-ambulatory patients switching from high-dose, high-frequency ALG

Byrne BJ, et al.

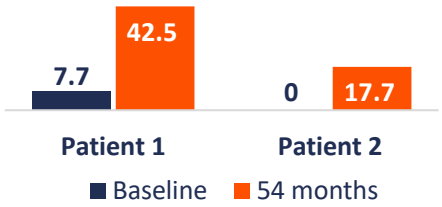
CIPA + MIG showed long-term benefits with few AEs

N=2

- Aged 18–25 years during study
- Diagnosed before age 2 years
- Patient 1: female; Patient 2: male
- Same genotype (C.1210G>A;C.1924G>T)

- Receiving ALG since age 4–6 years
- Weekly high-dose (40 mg/kg)

Upper body QMT Score, kg



Following switch to CIPA + MIG:

- Patients reported improvement in overall physical well-being
- Physicians mainly rated health status as improved
- uHex4 and sCK ↓ vs baseline at every assessment

CIPA + MIG: well-tolerated with 11 TEAEs in total by data cut-off*

- No serious TEAEs reported
- No infusion-related reactions
- None were deemed treatment-related, apart from fatigue in Patient 2

70: Outcomes of a pediatric patient with LOPD switching from high-dose, high-frequency ALG to standard-dose CIPA + MIG

DeArmey S, et al.

Improvement or stability seen over 160 weeks' treatment

N=1

- Male, aged 1 year at diagnosis (in 2006)
- On ALG for 14 years before switching to standard-dose CIPA + MIG on entering study ATB200-04

- Aged 15 at baseline
- Transitioned to approved CIPA + MIG at age 18 years

Improvements in motor function (baseline to week 156):

- +48.7 m — 6MWD
- –1.3 s — 4-stair climb test
- –0.6 s — Chair test
- –2.2% — Δ sitting FVC (% pred.)

SGIC and PGIC
Showed stability or improvement vs baseline at every visit to week 156

CIPA + MIG: Similar safety outcomes to those seen in adults

- All AEs were non-serious, and mild or moderate in severity

*Data cut off: 13 December 2021. 6MWD, 6-minute walk distance; AE, adverse event; ALG, alglucosidase alfa; CIPA, cipaglucosidase alfa; FVC, forced vital capacity; LOPD, late-onset Pompe disease; MIG, miglustat; PGIC, Physician Global Impression of Change; pred., predicted; QMT, quantitative muscle test; sCK, serum creatine kinase; SGIC, Subject Global Impression of Change; TEAE, treatment-emergent AE; uHex4, urine hexose tetrasaccharide.

1. Byrne BJ, et al. Presented at: World Muscle Society Congress 2024, Prague, Czech Republic. 8–12 October 2024. Abstr. 657P, and WORLD*Symposium* 2025, San Diego, CA. USA. 3–7 February 2025. Abstr. 46; 2. DeArmey S, et al. Presented at: WORLD*Symposium* 2025, San Diego, CA, USA. 3–7 February 2025. Abstr. 70.

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Applying data to clinical practice for patients with Pompe disease

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139: Miglustat: a first-in-class enzyme stabilizer for LOPD

Hopkin RJ, et al.

Impact of MIG on functional outcomes of CIPA

- MIG stabilizes CIPA at pH 7.4 (blood)
- MIG increased exposure to CIPA in Gaa –/– mice and resulted in an improvement in glycogen clearance and grip strength
- MIG increases CIPA exposure in humans by a greater extent than mice

Change in AUC of total GAA-protein concentration with CIPA + MIG in mice and humans

 ↑ 6.8%

 ↑ 28.5%

Safety profile of CIPA + MIG from pooled analysis of 3 trials (N=151)

Any TEAE	98.7%
TEAE related to MIG only	13.9%
Serious TEAE related to MIG only	0

In a head-to-head study (PROPEL); CIPA + MIG has a similar safety profile to ALG

CIPA + MIG is associated with a **reduction in Hex4 and CK levels** vs CIPA alone

The combination of CIPA + MIG improves delivery of rhGAA, reduces biomarker levels, and is well tolerated in adults with LOPD

AUC, area under curve; ALG, alglucosidase alfa; CIPA, cipaglucosidase alfa; CK, creatine kinase; GAA, acid alpha-glucosidase gene; Hex4, hexose tetrasaccharide; LOPD, late-onset Pompe disease; MIG, miglustat; rhGAA, recombinant human acid α-glucosidase; TEAE, treatment-emergent adverse event.

Hopkin RJ, et al. Presented at 21st Annual WORLD*Symposium* 2025. San Diego, CA, USA. 3–7 February 2025. Abstr. 139.

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236: AT845 gene replacement therapy for LOPD: An update on safety and preliminary efficacy data from FORTIS, a phase I/II open-label clinical study

Mozaffar T, et al.

Patient cohort N=6

Safety

All liver events
(ALT/AST increases observed in 5 of the 6 participants and deemed possibly related to AT845)
have been **asymptomatic**
and have
responded to immunosuppressive treatment with glucocorticoid therapy

Efficacy

- A clear transduction of AT845 was seen
- Patients demonstrated marked improvement in muscle GAA levels and activity

Discontinued ERT* — n=5

Remain off ERT — n=5

- FVC
- 6MWT
- PROMIS-fatigue
- R-PAct

Assessments stable for first 4 participants for ≤2-years post-dosing, including following ERT withdrawal

Patients receiving AT845 remained clinically stable while off ERT for at least 1 year and up to 3.5 years

*At 10, 15, 15, 17 and 24 weeks, respectively.
6MWT, 6-minute walk test; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ERT, enzyme replacement therapy; FVC, forced vital capacity; GAA, acid alpha-glucosidase; LOPD, late-onset Pompe diseases; PROMIS, Patient Reported Outcomes Measurement Information System; R-PAct, Rasch-built Pompe-specific activity.

Mozaffar T, et al. Presented at 21st Annual WORLD*Symposium* 2025. San Diego, CA, USA. 3–7 February 2025. Abstr. 236.