Disease Burden and Unmet Needs: Results from a New Survey in Adult Patients Receiving Enzyme Replacement Therapy for Pompe Disease in the United Kingdom

Adam J,[1] Muir A,[2] Patel N,[3] Wilson J[4]

[1]MPS Commercial, Amersham, Buckinghamshire, UK; [2]Association for Glycogen Storage Disease-UK, Droxford, Southampton, UK; [3]Amicus Therapeutics, Cranbury, NJ, USA; [4]Amicus Therapeutics, Marlow, UK

INTRODUCTION

- Pompe disease is a rare, autosomal recessive, multisystemic lysosomal disorder caused by functional deficiency of acid α-glucosidase (GAA), which leads to accumulation of glycogen in the lysosome in all tissues[1,2]
- Progressive glycogen accumulation results in a spectrum of disease severity and can lead to organ failure and/or death. Skeletal muscle weakness and respiratory difficulties are common manifestations of Pompe disease[1]; however, clinical manifestations and disease progression are variable[3]
- Currently the only specific drug treatment for Pompe disease is enzyme replacement therapy (ERT) with recombinant human GAA alglucosidase alfa[4,5]
  - Although ERT has been shown to slow the rate of progression for patients with Pompe disease,[6] clinical outcomes vary greatly among patients[7]
  - Therapy does not reverse disease manifestations due to several limitations, including poor targeting to skeletal muscles, minimal impact on autophagic defects, and antibody response to ERT[7,8]
- Despite the availability of ERT, many patients with Pompe disease continue to experience difficulties in daily life[9]

OBJECTIVE

- To assess current unmet needs in the management and treatment of Pompe disease

METHODS

Study Design

- The Association for Glycogen Storage Disease (AGSD)-UK conducted a patient survey to understand the following:
  - Heterogeneity of Pompe disease
  - Patient journey, including duration of disease, time on treatment, and response to treatment
  - Effects of disease burden on daily living for patients with Pompe disease
- Patients were identified and invited to participate in the survey via their membership in the ASGD-UK
- All patients provided informed consent before accessing the survey
- Patients completed the 88-question survey online and could skip questions that were not applicable to them

Inclusion Criteria

- ≥18 years of age
- Confirmed diagnosis of Pompe disease
- Currently receiving ERT
- Able to read, understand, and complete the online survey

RESULTS

Patients

- A total of 25 patients participated in the study, and the survey completion rate was 92%
- Demographics and treatment information are shown in **Table 1**
- 80% of participants (20/25) reported regularly taking medications in addition to ERT, including nutritional supplements (6/25), psychiatric medications (6/25), and medications that treat high blood pressure (6/25), pain (4/25), pulmonary disorders (3/25), gastrointestinal symptoms (2/25), osteoporosis (2/25), and stroke (2/25)

Table 1. Patient Demographics and Treatment Information

	Patients n=25
Age, years, mean (min, max)	51.6 (25, 81)
Sex, M:F	16:9
Ethnic background, n (%)	
Caucasian	18 (72)
Mixed ethnicity	1 (4)
Did not specify	6 (24)
Duration of ERT, years, mean (SD)	8.7 (4.2)
Age at initiation of ERT, years, mean (SD)	42.4 (15.5)
Other regular, concomitant medications, n (%)	20 (80)

ERT=enzyme replacement therapy; max=maximum; min=minimum; SD=standard deviation.

Motor Function Impairment and Fatigue Symptoms

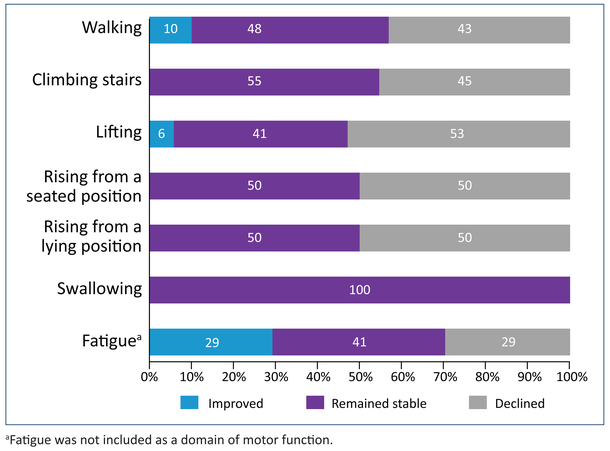
- The overwhelming majority of respondents reported difficulty with walking, climbing stairs, lifting, rising from a seated or lying position, and fatigue (**Table 2**), and most (86%) required walking assistance
- About half of the respondents reported a decline for each of the motor functions surveyed during ERT with the exception of swallowing, for which all 3 respondents who reported difficulties were stable. Fatigue worsened during ERT in 29% of respondents (**Figure 1**)

Table 2. Current Symptoms of Motor Function Impairment and Fatigue

	Patients reporting difficulty m/n (%)	Age difficulty started Mean±SD, years	Difficulty started before ERT m/n (%)
Walking[a]	21/23 (91)	29.6±10.2	18/21 (86)
Climbing stairs	21/22 (95)	34.5±15.6	14/20 (70)
Lifting[b]	17/21 (81)	38.1±18.8	9/17 (53)
Rising from a seated position	19/21 (90)	36.2±16.0	12/18 (67)
Rising from a lying position	18/20 (90)	38.3±15.2	11/18 (61)
Swallowing	3/21 (14)	46.0±41.0	2/3 (67)
Fatigue	17/20 (85)	32.5±16.2	14/17 (82)

[a]Patients reported difficulty in the following aspects of walking: walking uphill, walking downhill, running, walking long distance, and other. Different ages of onset were reported for each of the above aspects. The table shows the age of onset for difficulty walking long distance.
[b]Lifting objects weighing approximately 2.5 kg.
m=number of respondents reporting the specified outcome; n=number of respondents to the specific question.

Figure 1. Impact of ERT on Motor Function and Fatigue



[a]Fatigue was not included as a domain of motor function.

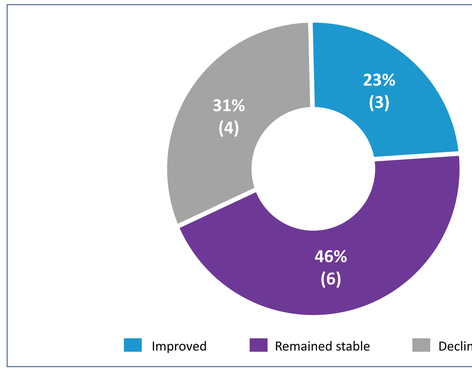
Respiratory Function Impairment

- Breathing difficulty was reported in 13 (62%) patients (**Table 3**)
- All 13 respondents reported using a ventilator that required them to use a face mask, nasal mask, mouthpiece, full face visor, or helmet (a non-invasive ventilator assistive device); usage ranged from 8-24 hours a day
  - Mean±SD age at first ventilator use was 38.1±17.2 years
- In these patients, breathing difficulty had remained stable, declined, or improved in 46%, 31%, and 23% of patients, respectively, during ERT (**Figure 2**)

Table 3. Aspects of Breathing Difficulty

	Patients reporting difficulty n/m (%)	Age at onset Median, years
Shortness of breath	8/21 (38)	28
Excessive daytime sleepiness	6/21 (29)	23
Morning headache	8/21 (38)	25
Unable to lie flat	10/21 (48)	40
Other	2/21 (10)	NA

Figure 2. Impact of ERT on Breathing Difficulty



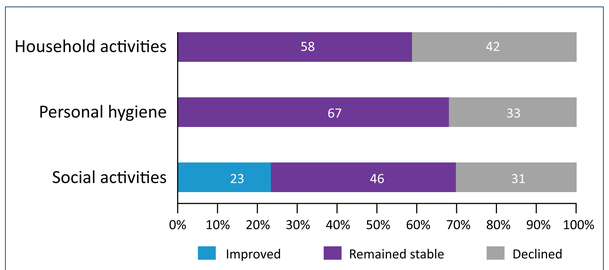
Difficulty with Activities of Daily Living

- 84% (21/25) of patients reported an impaired ability to work, and two-thirds or more reported difficulty with household activities, social activities, and personal hygiene (**Table 4**)
- 68% (13/19) of patients reported difficulty with household activities, 67% (10/15) reported difficulty with personal hygiene, and 69% (9/13) reported difficulty with social activities prior to ERT
- Although about half of patients reported that their ability to perform activities of daily living remained stable during ERT, more than a third of respondents reported a decline (**Figure 3**)

Table 4. Current Difficulty with Activities of Daily Living

	Patients reporting difficulty m/n (%)	Age difficulty started Mean±SD, years
Household activities	19/20 (90)	40.3±15.5
Personal hygiene	15/20 (75)	37.3±14.8
Social activities	13/20 (65)	45.1±15.0

Figure 3. Impact of ERT on Difficulty With Activities of Daily Living



CONCLUSIONS

- Patients with Pompe disease experience significant physical and social burdens
- Among ERT-treated patients surveyed, approximately half reported a decline while receiving ERT in motor function, such as ambulation, climbing stairs, and rising from a seated or lying position
- 42% of ERT-treated patients surveyed experienced a decline in their ability to perform household activities, 33% experienced a decline in their ability to maintain personal hygiene, and 31% experienced a decline in their ability to participate in social activities while receiving ERT
- Despite the availability of ERT, significant unmet medical needs remain

REFERENCES

1. Kishnani PS et al. *Genet Med.* 2006;8(5):267-288.
2. Bijvoet AGA et al. *Hum Mol Gen.* 1998;7(1):53-62.
3. van der Meijden JC et al. *J Inherit Metab Dis.* 2015;38(3):495-503.
4. Lumizyme [package insert]. Cambridge, MA: Genzyme Corporation; 2014.
5. Myozyme [summary of product characteristics]. Amsterdam, The Netherlands: Genzyme Corporation; 2011.
6. Toscano A, Schoser B. *J Neurol.* 2013;260(4):951-959.
7. Xu S et al. *JCI Insight.* 2019;4(5):e125358.https://doi.org/10.1172/jci.insight.125358.
8. Schoser B et al. *J Neurol.* 2017;264(4):621-630.
9. Schoser B et al. *BMC Neurol.* 2017;17(1):202.

ACKNOWLEDGMENTS

Third-party medical writing assistance was provided by ApotheCom (Yardley, PA) and was supported by Amicus Therapeutics, Inc.

DISCLOSURE

Conflict of interest

JA and AM have no conflicts to disclose. NP and JW are employees of Amicus Therapeutics and own stock/stock options in Amicus.

This study was supported by Amicus Therapeutics, Inc.

Adam J et al. Disease burden and unmet needs: results from a new survey in adult patients receiving enzyme replacement therapy for Pompe disease in the United Kingdom. Presented at the 2019 Muscle Study Group Annual Scientific Meeting; September 20-22, 2019; Snowbird, UT, USA.