RWD131

Investigating resource costs and the experiences of patients and healthcare professionals in the treatment of Fabry disease with enzyme replacement therapy: a multi-country study

Ian Keyzor,[1] Ana Maria Martins,[2] Sema Kalkan Uçar,[3] Hiroyuki Yamakawa,[4] Yin-Hsiu Chien,[5] Nur Arslan,[6] Dau-Ming Niu,[7] Leyla Tümer,[8] Joseph D. Giuliano,[9] Simon Shohet,[1] Laura Baldock,[10] Mano Andiappan[10]

[1]Amicus Therapeutics Ltd, Marlow, UK; [2]Universidade Federal de São Paulo, São Paulo, Brazil; [3]Ege University Medical Faculty, Izmir, Turkey; [4]Keio University, Keio, Japan; [5]National Taiwan University Hospital, Taipei City, Taiwan; [6]Dokuz Eylul University Faculty of Medicine, İzmir, Turkey; [7]Taipei Veterans General Hospital, Taipei City, Taiwan; [8]Gazi University Hospital, Ankara, Turkey; [9]Amicus Therapeutics, Inc, Philadelphia, PA, USA; [10]OPEN Health, Marlow, UK

OBJECTIVES

- Enzyme replacement therapies (ERTs) offer valuable treatment options for patients with Fabry disease (FD).
- However, ERTs must be prepared and administered as intravenous (IV) infusions every 2 weeks in a hospital setting.
- We wanted to better understand the resource requirements associated with ERT infusions, as well as explore the possibility of burden and impacts on health-related quality of life (HRQoL) and work productivity for patients with FD and their caregivers.

METHODS

- The source population for this time and motion study was adult patients with FD and their caregivers, recruited from four countries (Brazil, Taiwan, Japan and Turkey).
- Patients had to have attended the participating hospitals, treatment centres or community healthcare facilities for administration of ERT (agalsidase alfa or agalsidase beta) as part of their routine treatment and received ≥4 doses of ERT for the treatment of FD.
- A study protocol was implemented (NCT04281537) and local ethics approval was obtained for each participating site.
- Assessments included total healthcare professional (HCP) and patient time associated with ERT infusion, out-of-pocket expenses, patient HRQoL (as measured by the 12-Item Short Form Health Survey [SF-12]), well-being (World Health Organization – Five Well-Being Index [WHO-5]), levels of fatigue (bespoke Fatigue Likert Scale), work productivity (Work Productivity and Activity Impairment [WPAI] questionnaire), and burden of care provision for the caregivers. For the time and motion component, up to three ERT infusion episodes were observed per patient.

RESULTS

- Between 2020 and 2022, 76 patients undergoing ERT infusions within the hospital setting and 6 caregivers met the eligibility criteria (**Table 1**).
- Baseline demographic and clinical characteristics are presented in **Table 1**.

Table 1. Baseline demographic, clinical and employment characteristics

	Overall	Brazil	Taiwan	Japan	Turkey
Patient characteristics					
Participants	76	23	30	4	19
Women (%)	41	57	33	25	37
Mean (±SD) age at time of infusion, years	43.0 (16.4)	32.5 (12.5)	50.5 (14.5)	53.1 (8.7)	41.9 (17.6)
Mean (±SD) age at FD diagnosis, years	41.1 (17.1)	30.1 (13.3)	49.8 (14.4)	48.6 (10.3)	39.0 (18.8)
Mild FD, n (%)	12 (15.8)	7 (30.4)	2 (6.7)	0	3 (37.5)*
Moderate FD, n (%)	53 (69.7)	14 (60.9)	24 (80)	4 (100)	0
Severe FD, n (%)	11 (14.5)	2 (8.7)	4 (13.3)	0	5 (62.5)*
Patients employed (%)	49	44	63	50	31
Caregivers' characteristics					
Participants	6	N/A	5	N/A	1
Women (%)	83	N/A	80	N/A	100
Caregivers employed (%)	67	N/A	80	N/A	0

*Based on non-missing data.
SD, standard deviation. FD severity was determined using the following baseline information (type of FD [classical/non classical]). If type is unavailable, it was inferred at enrolment from number of organs involved (per medical history), estimated glomerular filtration rate, urine protein, left ventricular mass index and white blood cell alpha-galactosidase levels.

- The total time HCPs spent in the preparation and administration of ERT is presented in **Table 2A** and **Figure 1**.
- The total time spent on all activities was 157.1 min (2.6 hours) in Taiwan, 139.5 min (2.3 hours) in Japan and 174.6 min (2.9 hours) in Turkey (**Table 2B** and **Figure 1**).
- The results highlight the considerable time burden associated with the preparation and administration of a single dose of ERT, as well as highlighting variations between countries, including during the post-infusion administration period, which included completing clinical documentation.

Table 2. Total time spent by HCPs in the preparation and administration of ERT (A) by ERT treatment and (B) by country*

A)

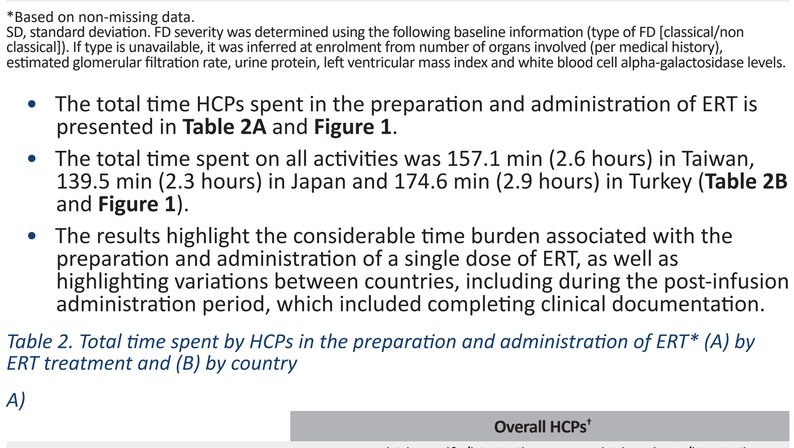
	Overall HCPs†	
Mean time (SD)‡	Agalsidase alfa/biosimilar (n=28)	Agalsidase beta/biosimilar (n=48)
Pre-infusion time in minutes	25.1 (6.5)	27.4 (22.8)
Infusion time in minutes	82.2 (23.1)	139.3 (59.4)

B)

Mean time (SD)‡	Taiwan (n=30)	Japan (n=4)	Turkey (n=19)
ERT pre-infusion time in minutes	38.8 (21.9)	31.0 (15.2)	22.9 (7.5)
ERT infusion time in minutes	103.6 (31.3)	84.0 (49.3)	142.6 (70.3)
ERT post-administration in minutes	14.7 (12.6)	24.5 (8.9)	9.2 (7.5)
Total time, all activities in minutes	157.1 (60.5)	139.5 (58.8)	174.6 (74.7)

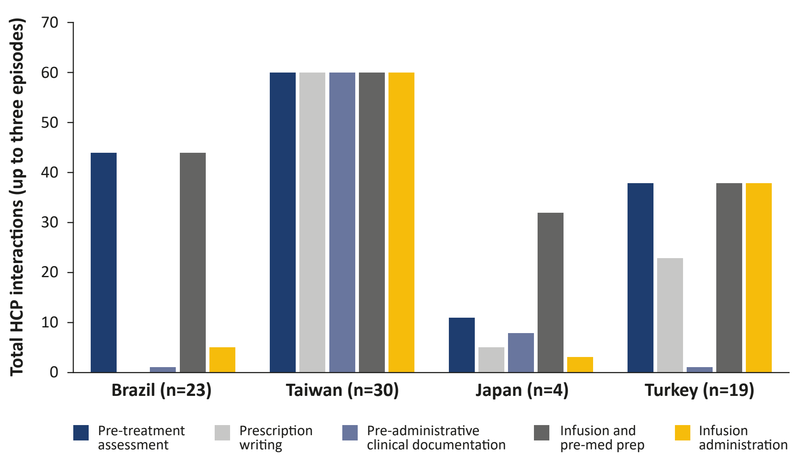
*Activities included consultation for pre-treatment assessment; prescription writing; pre-administration clinical documentation; infusion (and pre-medication) preparation activities; and administration of IV agalsidase alfa or agalsidase beta (including administration of pre-medications).
†Includes HCPs from Brazil, Taiwan, Japan and Turkey.
‡n value refers to number of patients, and the time measurements are the average per ERT infusion episode based on a maximum of three episodes per patient.

Figure 1. Total time spent by HCPs on ERT infusion and related activities



- The results indicate that ERT administration comprised the largest amount of time spent by HCPs in all countries (**Table 2** and **Figure 1**).
- With regard to total HCP interactions as shown in **Figure 2**, the results also highlight the substantial number of HCP interactions, across a variety of activities, relating to ERT infusion episodes.

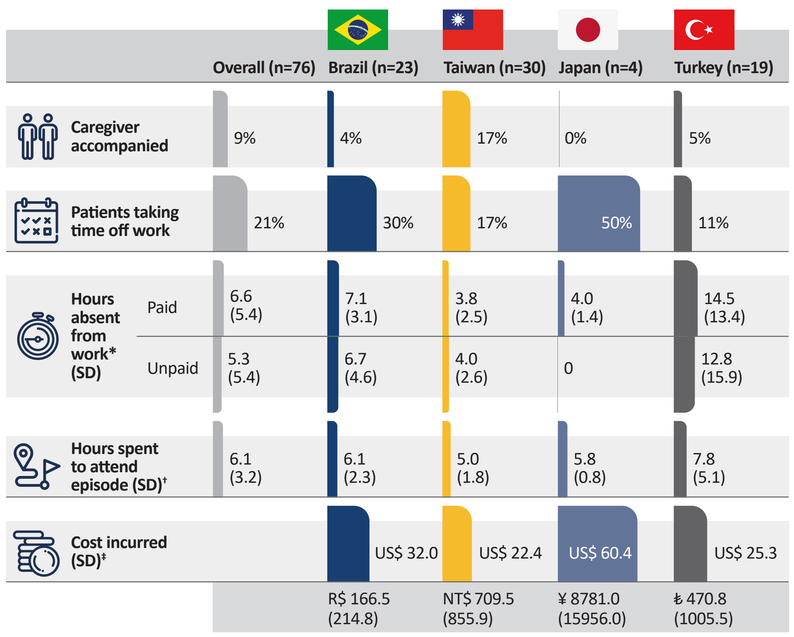
*Figure 2. Total individual HCP (physician, nurse, pharmacist, other) interactions needed (across all infusion episodes [up to three per patient])**



*The number of HCP interactions is calculated across all ERT infusion episodes observed in the study (ie up to three per patient). The number of HCP interactions for each country may be more than the n value as several activities are recorded per episode for each patient and each patient could have multiple episodes.

- The HCP activities involved in an ERT infusion episode varied considerably between the participating countries (**Figure 2**). Taiwanese sites reported the highest levels of HCP resources at each stage of infusion.
- All activities relating to the administration of treatment, assessment, monitoring and completion of documentation were led by nurses.

Figure 3. Total patient time (hours/min) to attend episode, their costs (ie out-of-pocket expenses) and work-related absence associated with attendances



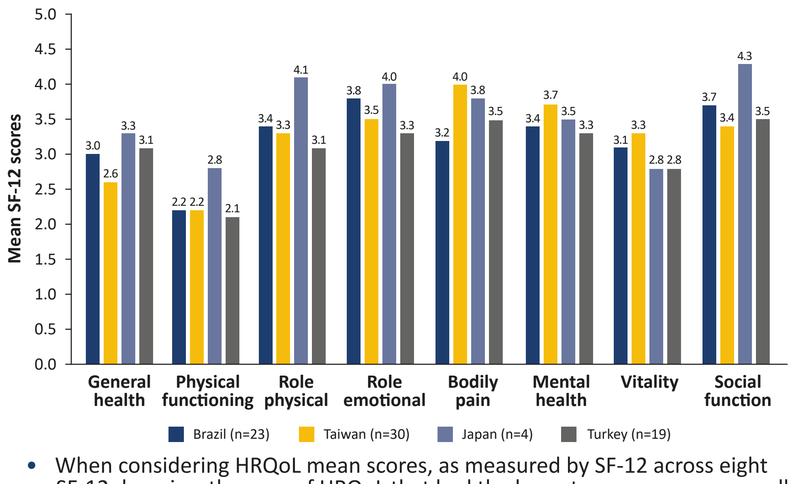
SD, standard deviation.
*Mean.
†Mean time spent outside of the house (including at hospital) to attend episode (door to door).
‡Mean cost incurred by patients to attend, in US$ and local currency.

- In addition to physical time spent in hospital, there were also substantial time and opportunity costs incurred by patients throughout the day (**Figure 3**).
- In the overall cohort, patients required a mean of 364.1 min (6.1 hours) from leaving home to travel, attend their infusion appointment and return home. This ranged from a mean of 298.9 min (5.0 hours) in the Taiwanese cohort to a mean of 467.4 min (7.8 hours) in the Turkish cohort (**Figure 3**).
- In the overall cohort, 21% (n=16/76) of patients had to take time off work to attend their ERT appointment. There was some variation observed across countries: 30% (n=7/23) in Brazil, 17% (n=5/30) in Taiwan, 50% (n=2/4) in Japan and 11% (n=2/19) in Turkey. In the overall cohort, patients attending the infusion appointment required a mean (SD) of 6.6 (5.4) paid hours and a mean (SD) of 5.3 (5.4) unpaid hours absence from work (**Figure 3**).
- The results also demonstrate the additional time and out-of-pocket costs incurred by caregivers (n=6) accompanying a patient with FD for the administration of a single dose of ERT (with agalsidase alfa or agalsidase beta).
- In the overall cohort, caregivers spent a mean of 160 min (2.7 hours) travelling to the appointment. Fifty percent (n=3) of caregivers took time off work to attend ERT. Caregiver costs were reported in the Taiwanese setting and showed that a mean (SD) total of 2085.0 (1728.6) NT$ (USD 65.7) out-of-pocket costs were incurred by caregivers in relation to supporting the patient with ERT attendance.

HRQoL

- At an individual country level (**Figure 4**), there was some consistency between countries on HRQoL (SF-12) score domains impacted.
- For the SF-12, all domains have a maximum value of 5 except physical functioning, where the maximum score is 3. Higher scores indicate better HRQoL.

Figure 4. Mean HRQoL scores for each SF-12 domain stratified by country



- When considering HRQoL mean scores, as measured by SF-12 across eight SF-12 domains, the area of HRQoL that had the lowest mean score across all countries was physical functioning. Of the remaining domains, general health and vitality appeared to be most impacted (**Figure 4**).
- The study found variability in the mean (SD) WHO-5 raw scores (that capture well-being) across countries (scored out of a possible 25, with higher scores indicating better well-being).
- For the overall cohort, the mean (SD) total WHO-5 score was 15.1 (5.6). When stratified by country, the mean (SD) total scores were 14.3 (6.0) for Brazil, 16.9 (4.4) for Taiwan, 16.8 (7.9) for Japan and 13.1 (5.6) for Turkey.
- Using the bespoke Fatigue Likert Scale (1 = not at all tired; 5 = extremely tired), in the overall cohort, the mean (SD) score during the infusion was 2.4 (1.4).
- When considering change in fatigue between the ERT infusion and the evening of the infusion, the mean (SD) change was –0.2 (1.4) (indicating a trend towards patients being more fatigued the evening of the infusion).
- When considering change in fatigue levels between the ERT infusion and the period occurring 1–7 days after the infusion, the mean (SD) change was 0.1 (1.3) (indicating a trend towards patients being less fatigued). However, due to small numbers, statistical significance could not be tested.

Work productivity (measured by the WPAI questionnaire)

- The mean (SD) percent of work time missed due to health (absenteeism score) was 5.0 (9.5)% 1–7 days after first observed ERT infusion, and 3.7 (7.3)% for the day immediately after the infusion (**Table 3**). This equates to more than a standard missed working day associated with each infusion.
- The mean (SD) percent impairment while working due to health (presenteeism) was 28.6 (29.5)% 1–7 days after first observed ERT infusion, and 22.6 (24.9)% for the day immediately after the infusion (**Table 3**).
- The study also provided insight into wider areas of impact for caregivers. For example, of the 6 caregivers who participated in the study, two-thirds reported having to change their personal plans, and half reported experiencing confinement and inconvenience.

Table 3. Summary of WPAI scores (as impairment percentages)

	Absenteeism score (percent work time missed due to health)	Presenteeism score (percent impairment while working due to health)	Work productivity loss score (percent overall work impairment due to health)	Activity impairment score (percent activity impairment due to health)
1–7 days after initial ERT infusion				
Mean (SD)	5.0 (9.5)	28.6 (29.5)	28.9 (27.7)	30.8 (29.3)
Median	0.0	20.0	20.0	20.0
IQR	0.0–6.5	0.0–50.0	0.0–49.1	10.0–50.0
Range	0.0–42.9	0.0–100.0	0.0–88.6	0.0–100.0
Day of next ERT infusion (ie, approx. 15 days after initial infusion)				
Mean (SD)	3.7 (7.3)	22.6 (24.9)	25.7 (26.4)	32.3 (30.4)
Median	0.0	15.0	20.0	20.0
IQR	0.0–5.4	0.0–30.0	0.0–36.7	10.0–57.5
Range	0.0–32.4	0.0–90.0	0.0–90.0	0.0–100.0

SD, standard deviation; IQR, interquartile range.

Strengths

- For the first time, this study quantified the time and costs associated with ERT beyond the number of visits, providing a more complete picture of the impact from multiple perspectives (HCP, patient and caregiver).
- The data were observed directly thus recall bias was minimised.
- Despite being a rare disease, the total number of patients was reasonable and the coverage spanned a range of different countries.

Limitations

- This study was purely descriptive; no *a priori* hypotheses were tested and no control for confounding was carried out, nor was any statistical testing for differences between groups or time points performed.
- Time and motion studies can raise the risk of observers interfering with care patterns by their presence (ie Hawthorne effect) and the precision of study data given the possibility of human timing errors.
- Data and results relied upon centres being willing to participate during the COVID-19 pandemic, completeness of patient and caregiver answers, and experience of staff members, which all may have introduced bias.
- The younger patients who were less well represented in the cohorts may have had higher carer requirements, thus underestimating carer burden.
- Data need to be interpreted carefully when aggregated across countries with different healthcare systems.

CONCLUSIONS

- The study highlighted the considerable time burden associated with the preparation and administration of a single dose of ERT, with the overall time spent by HCPs (in different countries) on all activities, including pre-infusion, infusion and post-infusion activities ranging between approximately 2 to 3 hours per infusion episode.
- The study found that a large overall time was required by patients to attend their infusion episode (5–8 hours) in addition to the high-cost burden it entails.
- Additionally, the subsequent burden on their working life was demonstrated by more than a standard working day being missed for each infusion for some patients, as well as an impact on work productivity. Additionally, two-thirds of caregivers reported having to change their personal plans, and half reported experiencing confinement and inconvenience.
- The resulting data for before, during and after ERT infusion episodes provide insights for patients receiving ERT infusion, the caregivers supporting them, and the healthcare system administering treatment. This could be used to further optimise ERT workflow, as well as enable more accurate comparisons to alternative treatments such as oral chaperone therapies for FD.

Acknowledgements

We would like to thank the local CRAs, HCPs, and the staff at the participating sites who identified and approached study participants and collected data, as well as the patients with Fabry disease and their caregivers who participated in this study. We would also like to thank the wider study team at OPEN Health, a healthcare consultancy company specialising in real world evaluation who supported Amicus Therapeutics, Inc and the authors in the design and conduct of this research, and analysis of the results.

Medical writing assistance was provided by Lucy Wust, MSc, of Cogent (an AMICULUM agency), funded by Amicus Therapeutics, Inc.

This study was funded by Amicus Therapeutics, Inc.

The presenter, Ian Keyzor, and co-authors, Simon Shohet and Joesph D. Giuliano, are employees of, and hold stock in, Amicus Therapeutics, Inc.

Presenting author email address: ikeyzor@amicusrx.com

Please scan this QR code with your smartphone camera or app to obtain a copy of this poster.

This study was supported by Amicus Therapeutics, Inc.

Presented at the annual meeting of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Europe, Vienna, Austria; 6–9 November 2022.