CHALLENGES OF GAUCHER DISEASE TYPE 2 AND 3 PATIENTS TO ACCESS TREATMENT DUE TO FDA LABEL

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INTRODUCTION

- Gaucher disease (GD) is a rare (prevalence: 0.7-1.75:100,000) autosomal recessive lysosomal storage disorder (LSD) caused by mutations in the *GBA1* gene.[1]
- GD is classified into 3 phenotypes according to age of onset and extent of neurologic involvement.[1-3]

  Type 1 GD
  Chronic, non-neuronopathic; accounts for ≥90% of cases; may remain asymptomatic or become symptomatic; mean age of symptom onset: 20.4 years

  Type 2 GD
  Acute, neuronopathic; accounts for ≤5% of cases; severe, early neurological impairment beginning at 3-6 months of age; mean survival age: 11.7 months

  Type 3 GD
  Chronic, neuronopathic; accounts for ~5% of cases; symptom severity varies; neurological symptoms often appear <2 years of age
- Enzyme replacement therapy (ERT) with imiglucerase, taliglucerase alfa, or velaglucerase alfa is standard of care treatment for adult and pediatric patients with type 1 GD with progressing or significant signs of disease.[2,4-6]
- No therapies are currently approved by the United States Food and Drug Administration for the treatment of type 2 or 3 GD.
  - However, ERT effectively treats visceral symptoms in patients with type 2 or 3 GD, to improve overall quality of life and extend longevity.[1-3,7]
- Patients with type 2 and 3 GD were surveyed to understand challenges related to treatment access, with the aim of working with regulators to revise the indications of available treatments to cover patients with type 3 GD.

METHODS

- A 13-question survey was developed by Gaucher Community Alliance (GCA), with input from industry partners.
- The survey was hosted by Google Forms and promoted via the GCA email list (distribution, ~1200), Facebook, and Instagram and was sent to GCA board members with family members diagnosed with type 2 or 3 GD.
- Respondents were notified in the survey instructions that the GCA intended to publish the findings.
- The survey was open to respondents between April 1, 2024, and May 28, 2024.
- Survey results were analyzed using RStudio Desktop and Microsoft Excel.

Survey Questions

- Do you or your family member have a diagnosis of type 2 or 3 Gaucher disease?
- At what age was the diagnosis made?
- Are you or your family member receiving treatment for type 2 or 3 Gaucher disease?
- If the patient is receiving treatment, at what age did treatment begin?
- If the patient is receiving treatment, how often are they receiving it?
- If you or your loved one are receiving treatment, which treatment are you currently taking?
- Which treatment(s) has the patient used in the past?
- Where is the patient getting treatment?
- Was it difficult to access treatment? Please explain any struggle with getting access to treatment.
- Did the patient and/or family have input into the type of treatment?
- Does the patient currently attend school?
- Does the patient work?
- Comments

RESULTS

Respondents

- 31 individuals responded to the survey.
- All respondents reported a diagnosis with type 3 GD or having a family member with type 2 or 3 GD.

RESULTS

Current Age (n=29)[a]

Median	Mean
72 months	113 months

[a]Two patients were excluded from analysis (deceased, n=2).

Age at Diagnosis (n=31)

Median	Mean
13 months	18.2 months

Age Treatment Began (n=29)[b]

Median	Mean
12.5 months	29 months

[b]Two patients were excluded from analysis (awaiting treatment, n=1; died before receiving treatment, n=1).

Time from Diagnosis to Treatment Initiation (n=28)[c]

Median	Mean
1 month	11 months

[c]Three patients were excluded from analysis (awaiting treatment, n=1; died before receiving treatment, n=1; age of treatment initiation preceded age of diagnosis, n=1).

Treatment Frequency (n=30)[d]

Biweekly	Weekly
52%	48%

[d]One patient was excluded from analysis (died before receiving treatment, n=1).

Current Treatment (n=28)[e,f]

Imiglucerase	Velaglucerase alfa
62%	34%
Taliglucerase alfa	**Venglustat**
3%	3%

[e]One respondent reported that the patient was receiving both imiglucerase and the investigational product venglustat. [f]Three patients were excluded from analysis (deceased, n=1; awaiting treatment, n=1; died before receiving treatment, n=1).

Treatment Switching (n=29)[g]

24%	7%
switched treatment	>1 prior treatment

[g]Two patients were excluded from analysis (died before receiving treatment, n=1; awaiting treatment, n=1).

Treatment Access (n=29)[h]

69% reported difficulty accessing treatment

[h]Two respondents did not answer the survey question.

School & Work Status (n=29)

52%	13%	42%
attend school	work	neither attend school nor work

[a]Two patients were excluded from analysis (deceased, n=2).

Respondent Comments on Treatment Access

"XXX is a verbal, ambulatory, smart, loving kindergartner. The insurance fights for enzyme replacement therapy have lasted for over 12 months (combined). This places our family under huge amounts of undue stress for her health and ability to thrive with treatment."

"Our insurance denied treatment due to FDA label requirements being type 1 and 4 years old and older. Our son was only 13 months. It took going out of state and seeing a specialty in LSDs and over at least 6 months of denials, appeals, peer to peer, submitting scientific articles, before finally being able to establish stable treatment."

"Access to this treatment is everyone's human right and treatment is very important to increase the quality of life of patients and to prevent the accumulation in their bodies. The patient should have access to treatment no matter what type he has, because living is a human right and should not take it away from the profit of any person or country authority."

"Getting approval for and access to treatment was a significant challenge following diagnosis. Despite the data reflecting the significant health and treatment benefits of early diagnosis and treatment for GD patients, my medical insurance carrier initially denied coverage on the basis that enzyme replacement therapy would be off label and therefore not covered under 2 grounds: 1) ERT not being FDA approved for treatment of Type 3 GD and 2) ERT not being FDA approved for treatment of children with GD under 2 years of age. Multiple rounds of appeals and peer to peer meetings resulted in the same denial of coverage, putting my son's health and prognosis at significant risk of complications and deteriorating conditions."

"I wish the FDA would approve ERT for children under 4 as research and studies show that it gives the child a better prognosis. Every day I am sending more documents to the insurance and getting denials, it is another day my daughters are without treatment getting sicker."

"These children/adults are fighting the fight for their lives and any medication that helps that fight should be completely accessible."

"The absolute headache it is to actually get my medication approved left me without [treatment] from the month of January - March this year."

CONCLUSION

Nearly all patients were receiving treatment for type 2 or 3 GD.

Respondents reported a patient burden related to difficulty accessing treatment.

Treatment access is often delayed as providers and families work with payors to coordinate coverage.

Regulatory approval of treatments indicated for type 3 GD would likely reduce the patient burden related to treatment access.

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