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Patient Descriptions of the Benefits of a Reduced Cornstarch Dose Regimen in a Phase 3 Trial of DTX401 for Glycogen Storage Disease Type Ia

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OBJECTIVE

Glycogen Storage Disease type Ia (GSDIa) is a rare, inherited, autosomal recessive disease of glucose-6-phosphatase deficiency (G6Pase)[1] requiring frequent consumption of exogenous glucose (e.g., uncooked cornstarch, Glycosade®), scheduled meals high in complex carbohydrates, and vigilant monitoring of blood glucose levels. Despite best efforts for management, individuals living with GSDIa are at risk for severe hypoglycemia that may result in seizure, coma, or death; and increased risk for lactic acidosis, hyperlipidemia, hyperuricemia and long-term complications (e.g., liver, renal, metabolic, obesity, growth, among others).[2] Qualitative interviews explored treatment experiences in a Phase 3, double-blind, randomized, placebo-controlled crossover study of DTX401, an investigational gene therapy for individuals ≥8 years with GSDIa (NCT05139316). This research describes participant perspectives on changes in cornstarch dose frequency (the number of total daily doses and total nighttime doses of cornstarch taken daily) at study Week.

METHODS

Phase 3 trial participants were randomized in a 1:1 ratio at Baseline to receive a single, blinded infusion of either DTX401 or Placebo. At Week 48, eligible participants received a second blinded infusion, marking the crossover point of the trial. DTX401 group participants received DTX401 at Baseline and Crossover DTX401 participants received DTX401 at Week 48. Following ethics approval, 60-minute web-based telephone interviews were conducted by Lumanity, an independent company with expertise in patient-centered outcomes research, using semi-structured interview guides at Week 96. Interviews were audio-recorded, transcribed, and coded by Lumanity. Data for participants reporting changes in cornstarch dose frequency were content analyzed and thematic results summarized.

RESULTS

A total of N=38 interviews (Crossover [Placebo → DTX401] group, n=20; DTX401 group, n=18) were conducted at Week 96 and included in the qualitative analysis. This sample included 66% (n=25/38) adult participants ≥ 18 years and 34% (n=13/38) pediatric participants ages 8 to <18 years. Among DTX401-treated participants with available data at Week 96 (n=33), 88% (n=29) reduced and 12% (n=4) had no change or increased total daily cornstarch dose at Week 96. For participants who reduced total daily cornstarch dose at Week 96, 86% (n=25/29) described improved, 7% (n=2/29) described no change, 3% (n=1/29) described mixed, and 3% (n=1/29) described worsened overall quality of life (QoL) at the same timepoint (Table 1A). Results were similar for those who reduced nighttime cornstarch dose at Week 96 (Table 2A). Those describing improved QoL commonly cited benefits of a reduced regimen, improved appearance, more freedom/ independence, more flexible diet, and ability to live a more normal life (Table 1, Figure 1). One participant reporting mixed QoL described both lifestyle benefits of the reduced regimen and improved physical health, yet difficulties attending work/school due to study burden. One participant reporting worsened QoL cited difficulties attending work/school due to continued low blood sugars. Improved QoL was also described by most participants who had no change/increased total daily and nighttime cornstarch dose at Week 96 (Table 1B, 2B), though fewer participants with no change/increase in nighttime dose reported ability to live a more normal life.

CONCLUSIONS

Trial participants who reduced cornstarch dose frequency following DTX401 treatment commonly reported reduced regimen burden and associated improvements in quality of life.

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Overall Quality of Life (QoL)

Table 1. Perceived Change in Overall QoL by Change in TOTAL DAILY Cornstarch Dose Frequency at Week 96

Table 1A. Among Participants with Reduced TOTAL DAILY Cornstarch Dose[1] Frequency at Week 96 (N=29)				
Change in Overall QoL	Crossover DTX401 (n=16)	DTX401 (n=13)	Total (N=29)	Key Reason(s)
	% (n)[3]			
Improved	88 (14)	84 (11)	86 (25)	Less Cornstarch/Glycosade®; Improved Appearance; More Freedom/Independence; Overall Improvement
No Change	6 (1)	8 (1)	7 (2)	N/A
Mixed Change[2]	6 (1)	0 (0)	3 (1)	Less Cornstarch/Glycosade®; Improved Physical Health; Negative Impact on Ability to Work/Attend School (due to study burden)
Worsened	0 (0)	8 (1)	3 (1)	Negative Impact on Ability to Work/Attend School (due to continued low blood sugars)

Table 1B. Among Participants with No Change or Increase in TOTAL DAILY Cornstarch Dose Frequency at Week 96 (N=4)				
Change in Overall QoL	Crossover DTX401 (n=2)	DTX401 (n=2)	Total (N=4)	Key Reason(s)
	% (n)			
Improved	100 (2)	100 (2)	100 (4)	Improved Appearance; More Freedom/Independence; More Flexible Diet
No Change	0 (0)	0 (0)	0 (0)	N/A
Mixed Change	0 (0)	0 (0)	0 (0)	N/A
Worsened	0 (0)	0 (0)	0 (0)	N/A

[1] *Total Daily Cornstarch Dose Frequency* reflects the total number of doses of cornstarch and/or Glycosade® consumed in a 24-hour period (daytime + nighttime).
[2] Participants coded as *Mixed Change* reported aspects of both improved and worsened quality of life.
[3] Percentages may not total 100% due to rounding.
[4] The two participants with reduced nighttime cornstarch dose frequency reporting mixed and worsened QoL are the same two participants with reduced nighttime cornstarch dose frequency reporting mixed and worsened QOL.

Table 2. Perceived Change in Overall QoL by Change in NIGHTTIME[4] Cornstarch Dose Frequency at Week 96

Table 2A. Among Participants with Reduced NIGHTTIME Cornstarch Dose Frequency at Week 96 (N=16)				
Change in Overall QoL	Crossover DTX401 (n=8)	DTX401 (n=8)	Total (N=16)	Key Reason(s)
	% (n)			
Improved	88 (7)	88 (7)	88 (14)	Less Cornstarch/Glycosade®; Improved Appearance; More Freedom/Independence; More Flexible Diet
No Change	0 (0)	0 (0)	0 (0)	N/A
Mixed Change	12 (1)[4]	0 (0)	6 (1)	Less Cornstarch/Glycosade®; Improved Physical Health, Study Burden, Negative Impact on Ability to Work/Attend School (due to study burden)
Worsened	0	12 (1)	6 (1)[4]	Negative Impact on Ability to Work/Attend School (due to continued low blood sugars)

Table 2B. Among Participants with No Change or Increase in NIGHTTIME Cornstarch Dose Frequency at Week 96 (N=8)				
Change in Overall QoL	Crossover DTX401 (n=4)	DTX401 (n=4)	Total (N=8)	Key Reason(s)
	% (n)			
Improved	75 (3)	100 (4)	88 (7)	Improved Blood Sugar Levels
No Change	25 (1)	0 (0)	12 (1)	N/A
Mixed Change	0 (0)	0 (0)	0 (0)	N/A
Worsened	0 (0)	0 (0)	0 (0)	N/A

Participant Descriptors of QoL Improvements

Figure 1. Reasons for improved quality of life among those who reduced total daily and nighttime cornstarch dose frequency



Ability to Live a More 'Normal' Life

Table 3. Perceived Change in Ability to Live a More Normal Life by Change in TOTAL DAILY Cornstarch Dose Frequency at Week 96

Among Participants Who Reduced TOTAL DAILY Cornstarch Dose Frequency at Week 96 (N=29)			
Ability to Live a More Normal Life	Crossover DTX401 (n=16)	DTX401 (n=13)	Total (N=29)
	% (n)		
Yes	69 (11)	77 (10)	72 (21)
No	19 (3)	23 (3)	21 (6)
Unsure	6 (1)	0 (0)	3 (1)
Data Missing	6 (1)	0 (0)	3 (1)

Among Participants Who Had No Change or Increase in TOTAL DAILY Cornstarch Dose Frequency at Week 96 (N=4)			
Ability to Live a More Normal Life	Crossover DTX401 (n=2)	DTX401 (n=2)	Total (N=4)
	% (n)		
Yes	100 (2)	50 (1)	75 (3)
No	0 (0)	50 (1)	25 (1)
Unsure	0 (0)	0 (0)	0 (0)
Data Missing	0 (0)	0 (0)	0 (0)

Table 4. Perceived Change in Ability to Live a More Normal Life by Change in NIGHTTIME Cornstarch Dose Frequency at Week 96

Among Participants Who Reduced Nighttime Cornstarch Dose Frequency at Week 96 (N=16)			
Ability to Live a More Normal Life	Crossover DTX401 (n=8)	DTX401 (n=8)	Total % (N=16)
	% (n)		
Yes	88 (7)	88 (7)	88 (14)
No	12 (1)	12 (1)	12 (2)
Unsure	0 (0)	0 (0)	0 (0)
Data Missing	0 (0)	0 (0)	0 (0)

Among Participants Who Had No Change or Increase in Nighttime Cornstarch Dose Frequency at Week 96 (N=8)			
Ability to Live a More Normal Life	Crossover DTX401 (n=4)	DTX401 (n=4)	Total (N=8)
	% (n)		
Yes	50 (2)	25 (1)	38 (3)
No	25 (1)	75 (3)	50 (4)
Unsure	0 (0)	0 (0)	0 (0)
Data Missing	25 (1)	0 (0)	12 (1)

- ***"So, I'm no longer waking up every four hours to get out of bed and take corn starch and – so I can just sleep through that time. And I also sleep better and deeper, because I'm not waking up in the middle of the night."*** *(DTX401 group participant that reduced nighttime cornstarch dose frequency, described improved QoL and ability to live a more normal life)*
- ***"I feel so much more – I hate to say it like this, but like normal now. Like just kind of – I feel a lot more secure in like everyday life knowing I don't have to really worry about it as much, and it's kind of nice. [Q: And do you feel like you're able to live a more normal life now?] Absolutely…Just freedom of it all. I can do sleepovers now. I can go on trips with my friends. I can kind of live without being tethered to somebody else, which has been incredible for me. I have a lot more self-reliance now and kind of self-sufficiency of it all, and I know what I can and can't do."*** *(DTX401 group pediatric participant that reduced total daily dose frequency, described improved QoL and ability to live a more normal life)*
- ***"I feel like I can make more plans, arrange more trips, worry less about it getting in the way of my work, about having to pause activities to take cornstarch. Worries have significantly decreased."*** *(Crossover DTX401 group participant that reduced total daily cornstarch dose frequency, described improved QoL and ability to live a more normal life)*
- ***"I'd say [my life has] changed a lot, and mostly in – for the better once I stopped taking cornstarch completely. [I am] feeling better. I've been able to wake up better…And just overall feel a lot better."*** *(Crossover DTX401 group participant that reduced total daily cornstarch dose frequency and described improved QoL and ability to live a more normal life)*
- ***"Lots of airplane trips. Lots of hospital stays. Lots of the home health nurse coming in and poking you…I don't like that…Oh, we got behind on school last year a little bit. [Good change was needing] a little less cornstarch."*** *(Crossover DTX401 pediatric participant/caregiver, mixed change in overall quality of life)*

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