Treatment effects and perceptions among apitegromab-treated patients with Type 2/3 spinal muscular atrophy: patient and caregiver interviews from the TOPAZ clinical trial

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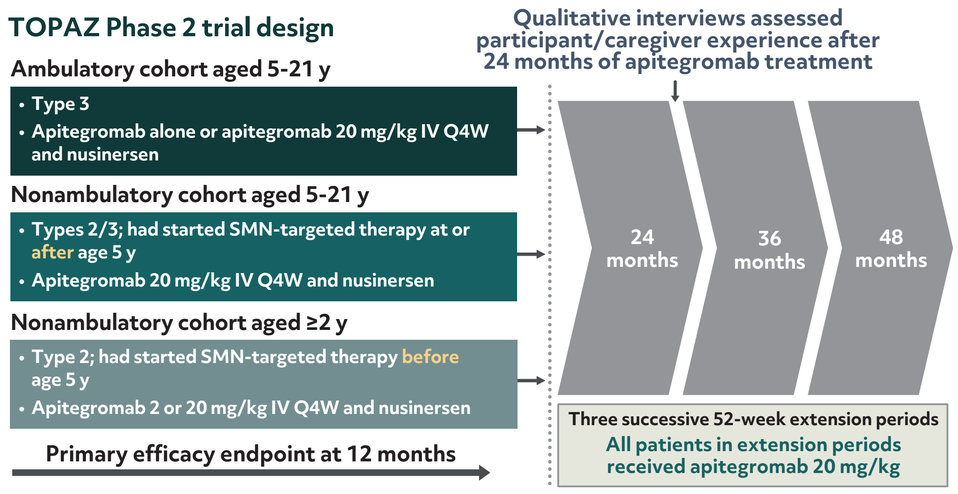
INTRODUCTION

- Despite advances in the diagnosis and treatment of spinal muscular atrophy (SMA), people with SMA and their caregivers report significant unmet needs, including gaining muscle strength, stabilizing or achieving new motor function, and reducing fatigue[1,2]
- Comprehensive evaluation of new treatments for SMA requires the use of outcome measures that adequately capture symptomatic themes that go undetected with current motor function scales
- Apitegromab is an investigational, fully human monoclonal antibody that inhibits the activation of myostatin, a negative regulator of muscle mass[3,4]
- In the Phase 2 TOPAZ trial (NCT03921528; **Figure 1**), apitegromab improved motor function and had sustained clinical benefit in participants with SMA who were concurrently receiving nusinersen[3,4]

Figure 1. TOPAZ trial design[4]



IV, intravenous; Q4W, once every 4 weeks; SMN, survival motor neuron.

OBJECTIVES

- Gain a deeper understanding of the patient experience of SMA before and during TOPAZ through participant and caregiver assessments of the impact of receiving apitegromab and whether benefits were considered meaningful
- Inform future research on apitegromab (eg, endpoints of interest to individuals with SMA and their caregivers)

METHODS

- Researchers conducted qualitative phone interviews (≈2 hours) 24 months after the start of treatment in TOPAZ
  - Participants reported their/their child's experience with 16 symptoms of SMA and 6 related impacts on their daily lives
  - Interview transcripts were analyzed qualitatively; results are presented descriptively

RESULTS

Participants

- 11 caregivers of pediatric participants and 1 participant > age 10 years were interviewed (**Table 1**)
- All participants were nonambulatory at time of enrollment in TOPAZ, with baseline HFMSE and RULM scores consistent with that of the overall TOPAZ nonambulatory population (23.9 and 25.1, respectively)[4]

Table 1. Baseline demographics and motor function scores

Participant characteristic[a]	All (N=12)	Participant > age 10 y (n=1)	Pediatric participants (n=11)
Age, mean±SD (min, max), y	6.5±4.0 (2, 16)	16	5.6±2.8 (2, 10)
Nusinersen exposure, mean±SD (min, max), mo	25.9±5.6 (13, 31)	29.3	25.6±5.8 (13, 31)
Baseline HFMSE score, mean (SD)	23.2 (10.1)	–	–
Baseline RULM score, mean (SD)	25.5 (6.7)[b]	–	–

[a]Participant characteristics are reported for TOPAZ baseline. [b]For RULM score, n=11.
HFMSE, Hammersmith Functional Motor Scale–Expanded; RULM, Revised Upper Limb Module; SD, standard deviation.

SMA symptoms and impacts

- All participants/caregivers reported muscle-related SMA symptoms and impacts on their/their child's daily lives at TOPAZ enrollment (**Table 2**)

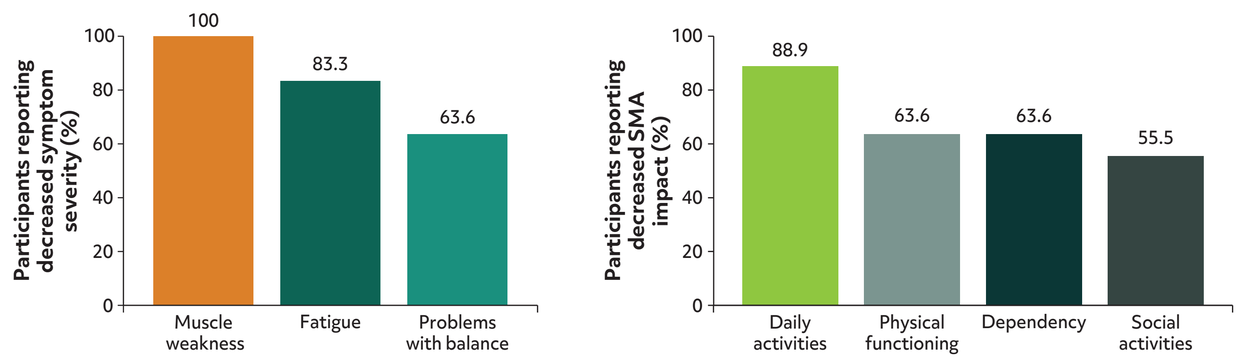
Table 2. Frequently reported symptoms and impacts of SMA in participants treated with nusinersen prior to TOPAZ[a]

Symptom, n/N	All (N=12)
Muscle weakness	12/12
Fatigue	12/12
Balance	11/12
Physical functioning	11/12
Dependency	11/12
Daily activities	9/12
Social activities	9/12

[a]Symptoms and impacts were reported for the time of enrollment in TOPAZ.
HFMSE, Hammersmith Functional Motor Scale–Expanded; RULM, Revised Upper Limb Module; SMA, spinal muscular atrophy.

These symptoms coincided with low baseline HFMSE and RULM scores and negative impacts on their/their child's wellbeing

Figure 2. Participants reporting SMA improvements 24 months post initiation of apitegromab



SMA, spinal muscular atrophy.

- After 24 months of apitegromab treatment, participants/caregivers reported:
  - Improvement in muscle strength, balance, fatigue, and impact of SMA (**Figure 2**)
  - Decreased overall symptoms compared with ratings prior to participation in TOPAZ; no increases in severity were reported (**Figure S1**, accessible by QR code)
  - Achievement of new skills that bolstered independence and confidence (**Figure 3**)

Figure 3. Participant testimonials[a]

[a]Participant testimonials have been edited for readability. Participant ages are reported for TOPAZ baseline.
SMA, spinal muscular atrophy.

Motor function scores

- Participant HFMSE and RULM scores were stable or increased across 24 months of treatment with apitegromab (**Figure S2**, accessible by QR code)
  - Mean (standard error) changes from baseline to 24 months in HFMSE and RULM scores were +5.2 (2.16) and +2.9 (1.00) points, respectively

CONCLUSIONS

- All participants/caregivers reported improved motor function symptoms, new motor skills, and decreased SMA impacts—despite variability in motor function scale changes—after 24 months of apitegromab treatment
- Improvements in muscle and fatigue that may not be fully captured by motor function scales may be perceived by patients as meaningful, enhancing independence and the ability to perform activities of daily living
- These results underscore the utility of qualitative assessments in capturing SMA disease burden and perceived treatment benefits and their impact on daily life, which may go undetected with motor function scales alone

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