# Effect of apitegromab on PEDI-CAT and PROMIS Fatigue questionnaire at 36 months in patients with spinal muscular atrophy

P234

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## Introduction

- Spinal muscular atrophy (SMA) is characterized by neuronal degeneration and muscle atrophy[1]
- Apitegromab is an investigational, fully human monoclonal antibody that is being investigated in SMA and has been shown to inhibit the pro- and latent forms of myostatin, therefore directly targeting muscle atrophy[2]
- The 52-week treatment period of the TOPAZ study of apitegromab showed improvements in muscle function and in the Pediatric Evaluation of Disability Inventory Computer Adaptive Test (PEDI-CAT) and the Patient-Reported Outcomes Measurement Information System (PROMIS) Fatigue questionnaire in patients with SMA Type 2 and nonambulatory Type 3, suggesting the potential of restoring muscle strength to improve patient/caregiver reported outcomes

## Objective

- To evaluate daily activities and mobility domains of the PEDI-CAT alongside the PROMIS Fatigue questionnaire for patients with Type 2 and nonambulatory Type 3 SMA who continue to receive apitegromab (20 mg/kg) for 36 months

## Methods

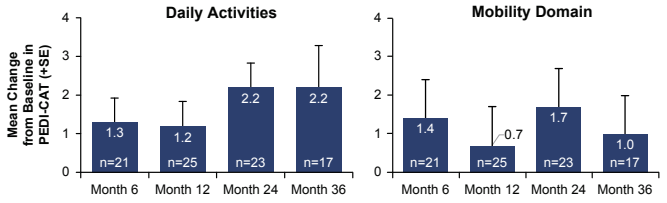
### Study design and treatment interventions

- TOPAZ (NCT03921528) is an ongoing multicenter, phase 2, active treatment study to evaluate the safety and efficacy of apitegromab in patients (2–21 years old) with Types 2 and 3 SMA at 16 sites across the US and Europe
- The study consisted of a 28-day screening period and a 52-week treatment period. Patients who completed the 52-week treatment period had the option to enroll in up to three 52-week extension periods for a total of 36 months (enrollment was dependent upon completion of the prior extension period)
- In the 52-week treatment period, patients were divided into 3 cohorts: 2 open-label cohorts of patients with ambulatory Type 3 SMA (Cohort 1) and Type 2 SMA or nonambulatory Type 3 SMA (Cohort 2), and 1 Type 2 SMA randomized double-blind cohort, randomized to either low- (2 mg/kg) or high-dose (20 mg/kg) apitegromab (Cohort 3)
- In the extension periods, patients originally receiving 2 mg/kg in the primary treatment period switched to 20 mg/kg, while all patients on 20 mg/kg continued their dose
- This report focuses on patients with Type 2 and nonambulatory Type 3 SMA who received apitegromab for 36 months as part of the TOPAZ extension study
- The PEDI-CAT assessed (via caregiver proxy) 2 domains of function: daily activities and mobility
- The PROMIS Fatigue questionnaire (via caregiver proxy) was used to assess a range of self-reported symptoms, from mild tiredness to debilitating exhaustion that may interfere with functioning. Parents served as proxy reporters for their children

## Results

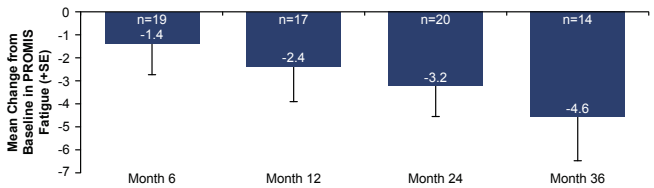
- Of 58 patients enrolled in the TOPAZ study, 57 completed the primary treatment period and enrolled in the extension study (1 patient withdrew from the study)
- Of 57 patients enrolled in the extension period, 6 discontinued: 2 withdrew consent due to concerns with COVID-19, and 4 patients receiving apitegromab monotherapy (not being treated with nusinersen) discontinued due to lack of benefit or scheduling difficulty
- PEDI-CAT domain scores were improved versus baseline over 36 months (**Figure 1**)
- Improvements in the PROMIS Fatigue questionnaire were sustained over 36 months (**Figure 2**)

**Figure 1. Improvements in PEDI-CAT Daily Activities and Mobility Domain Are Sustained Over 36 Months**




This analysis population included nonambulatory patients 2–21 years old receiving either low-dose (2 mg/kg) or high-dose (20 mg/kg) apitegromab (inclusive of patients in Cohort 3 who transitioned from 2 mg/kg to 20 mg/kg in Year 2). Error bars represent standard error of the means.
PEDI-CAT, Pediatric Evaluation of Disability Inventory Computer Adaptive Test; SE, standard error.

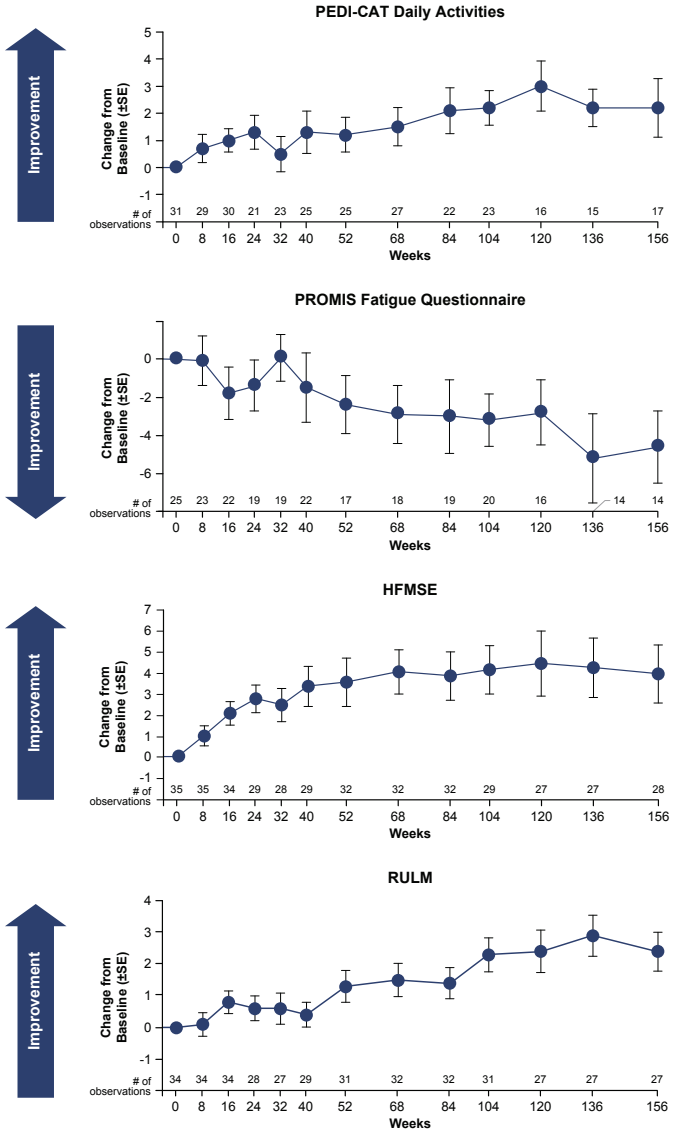
**Figure 2. PROMIS Fatigue Questionnaire Improvement Over 36 Months**




This analysis population included nonambulatory patients from Cohorts 2 & 3, 2–21 years old, receiving either low-dose (2 mg/kg) or high-dose (20 mg/kg) apitegromab (inclusive of patients in Cohort 3 who transitioned from 2 mg/kg to 20 mg/kg in Year 2). Error bars represent the standard error of the means.
PROMIS, Patient-Reported Outcomes Measurement Information System; SE, standard error.

- Results on patient/caregiver-reported outcomes are consistent with improvements in motor function as assessed by the Hammersmith Functional Motor Scale–Expanded (HFSME) and Revised Upper Limb Module (RULM) (**Figure 3**)

**Figure 3. Patient-Reported Outcomes and Motor Function Measures Over 36 Months**




HFMSE, Hammersmith Functional Motor Scale–Expanded; PEDI-CAT, Pediatric Evaluation of Disability Inventory-Computer Adaptive Test; PROMIS, Patient-Reported Outcomes Measurement Information System; RULM, Revised Upper Limb Module; SE, standard error.

## Conclusions

- Patient-reported outcomes are consistent with improvements in motor function as assessed by the HFSME and RULM
- Treatment with apitegromab was associated with sustained improvements in patient/caregiver-reported outcomes of function and perceived fatigue over 36 months in patients with SMA

### References

1. Kolb SJ, Kissel JT. *Neurol Clin*. 2015;33(4):831-846.
2. Pirruccello-Straub M, et al. *Sci Rep*. 2018;8(1):2292.

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### Disclosures

**TOC** is the lead principal investigator of the TOPAZ trial; and a consultant and/or advisory board member for AveXis/Novartis, Biogen, Pfizer, and Roche/Genentech. **BTD** has served as an ad hoc scientific advisory board member for AveXis/Novartis Gene Therapies, Biogen, Pfizer, Sarepta Therapeutics, Vertex, and Roche/Genentech; steering committee chair for Roche FIREFISH and MANATEE studies, and DSMB member for Amicus Inc. and Lexeo Therapeutics; he has no financial interests in these companies. He has received research support from the National Institutes of Health/National Institute of Neurological Disorders and Stroke, the Slaney Family Fund for SMA, the Spinal Muscular Atrophy Foundation, CureSMA, and Working on Walking Fund; received grants from Ionis Pharmaceuticals, Inc. for the ENDEAR, CHERISH, CS2/CS12 studies; from Biogen for CS11; and from AveXis, Sarepta Pharmaceuticals, Novartis (AveXis), PTC Therapeutics, Roche, Scholar Rock, and Fibrogen; and has received royalties for books and online publications from Elsevier and UpToDate, Inc. **JWD** has received consulting fees from Biogen, Cytokinetics, Ionis Pharmaceuticals, NGT, Pfizer, Roche, and Sarepta Therapeutics; license fees or royalty payments from Athena Diagnostics; and research funding from Biogen, Cytokinetics, NGT, Roche, Sanofi-Genzyme, and Sarepta Therapeutics. **JMK** was site principal investigator for clinical trials sponsored by Novartis Gene Therapies, Inc., Biogen, and Scholar Rock. **EM, AN,** and **AP** have nothing to disclose. **TD** has received honoraria for scientific advisory boards or consultancy from Biogen, Novartis, F. Hoffmann-La Roche, Genentech, Pfizer, Sarepta Therapeutics, Audentes, Astellas, and Dyne. **LL, MS,** and **SB** are employees of Scholar Rock.

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