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EXPANDING THE THERAPEUTIC LANDSCAPE OF SMA: SAFETY AND EFFICIENCY OF APITEGROMAB

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ABSTRACT

Spinal muscular atrophy (SMA) is a genetic disease caused by mutations in the Survival Motor Neuron 1 (SMN1) gene, leading to a deficiency of the SMN protein and progressive degradation of motor neurons and muscle atrophy.
Currently, three therapies are available that increase SMN protein levels: nusinersen, risdiplam, and onasemnogene abeparvovec; however, many patients still struggle with persistent motor function deficits. For this reason, an additional form of treatment is needed.
The myostatin inhibitor apitegromab is a fully human monoclonal antibody that selectively inhibits the activation of promyostatin and the latent form of myostatin, thereby preventing the release of active myostatin, a negative regulator of muscle growth.
The Phase 2 TOPAZ trial demonstrated that apitegromab led to considerable improvements in motor function over 12 months, particularly in younger, nonambulatory patients, where the 20 mg/kg dose resulted in a mean increase in the Hammersmith Functional Motor Scale Expanded (HFMSE) of 7.1 points.
Long-term analysis after 36 months from the TOPAZ OLE Study confirmed the durability of these benefits, with nonambulatory patients showing a mean increase of 4.0 points in HFMSE and 2.4 points in RULM. The pivotal phase 3 SAPPHIRE study provided evidence of apitegromab's efficacy. In children aged 2-12 years, a statistically significant improvement of 1.8 points on the HFMSE scale was achieved (p=0.019). In all studies, apitegromab was well tolerated and demonstrated a favorable safety profile. These results show that apitegromab is an effective adjunctive therapy in SMA.

KEYWORDS

Apitegromab, Spinal Muscular Atrophy, Myostatin Inhibitor, Myostatin

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Introduction

Spinal muscular atrophy (SMA) is a severe neuromuscular disorder that progressively worsens and is caused by a mutation or deletion in the Survival Motor Neuron 1 (SMN 1) gene. When functional SMN1 is absent, the body relies on SMN2, which produces a dysfunctional protein due to a splicing defect that skips exon 7. As a result, SMN protein levels are low, leading to degeneration of alpha motor neurons in the spinal cord and muscle atrophy. (Ahmad et al., 2016; D'Amico et al., 2011)

Recently, treatments targeting SMN, such as nusinersen, risdiplam, and onasemnogene abeparvovec, have significantly improved patient care by helping motor neurons survive longer. However, there is still a lot of room for improvement. Patients who begin treatment after symptoms have already started often suffer from ongoing muscle denervation, atrophy, and functional limitations because these therapies cannot reverse the preexisting muscle loss. (Day et al., 2022)

Myostatin inhibitors are drugs developed to block myostatin (GDF-8), a protein that limits muscle growth. These inhibitors promote muscle tissue growth and boost strength, which is important for conditions such as muscle atrophy. (Nielsen et al., 2021)

A prominent option in this category is apitegromab (SRK-015), a fully human monoclonal antibody that targets only inactive myostatin precursors. By binding to these forms, it prevents their conversion into the active protein that hinders muscle growth. This specific approach allows apitegromab to improve muscle condition while maintaining a low risk of adverse events. (Day et al., 2022).

The aim of this study is to evaluate the safety and efficacy of apitegromab as an adjunct to standard SMN-targeting therapy to improve motor function in patients with SMA types 2 and 3.

Methods

This review is based on an analysis of scientific publications from 2011 to 2026 on the safety and efficacy of apitegromab (SRK-015) in spinal muscular atrophy (SMA). PubMed searches were conducted using the following keywords: apitegromab, SRK-015, myostatin inhibitor, and spinal muscular atrophy. Priority was given to phase II and III randomized controlled trials, including the TOPAZ trial, its open-label extension (OLE), and the SAPPHIRE trial. Data extraction focused on endpoints such as motor function assessed using the Hammersmith Functional Motor Scale Expanded (HFMSE) and Revised Upper Limb Module (RULM) scales, as well as adverse events.

Background

Pathophysiology of SMA

Spinal muscular atrophy (SMA) is a genetic neuromuscular disorder inherited in an autosomal recessive manner. It is caused by a deletion or mutation of the Survival Motor Neuron 1 (SMN1) gene and, consequently, SMN protein deficiency. This causes degeneration of spinal cord motor neurons and muscle atrophy. On chromosome 5 at locus 5q13, there are two nearly identical genes responsible for producing the SMN protein: the SMN1 gene, directly responsible for SMA, and the SMN2 gene. The SMN2 gene differs from SMN1 by a single nucleotide (transition 840C > T in exon 7). This change leads to alternative splicing and deletion of exon 7. As a result, the SMN2 gene produces a reduced amount of full-length SMN protein. (D'Amico et al., 2011) Disease severity depends on the amount of functional SMN protein produced by the SMN2 gene, so the number of SMN2 copies is the primary modifier of SMA progression—the more copies of SMN2, the milder the course. (Ahmad et al., 2016)

Standard Therapies in SMA

Currently, three drugs are approved by the FDA and EMA that aim to boost the production of functional SMN protein: nusinersen, risdiplam, and onasemnogene abeparvovec. (Chaytow et al., 2021)

Nusinersen is the first drug approved by the FDA in 2016 for the treatment of children and adults with SMA. (Kakazu et al., n.d.-a) Nusinersen is an antisense oligonucleotide that binds to a specific sequence in the pre-mRNA of the SMN2 gene. Through this binding, the drug modulates splicing by promoting the inclusion of exon 7 in the mature RNA chain. Thanks to the inclusion of exon 7, the SMN2 gene produces a greater amount of functional SMN protein, which is essential for the survival of motor neurons. (Chaytow et al., 2021) In the CHERISH study, the safety and efficacy of nusinersen were evaluated in patients with later-onset SMA (symptoms after age 6 months). (Mercuri et al., 2018) The study showed that patients receiving nusinersen achieved a clinically significant improvement in motor neuron function. After 15 months of treatment, the treated group showed a mean increase of 3.9 points on the HFMSE scale, while the control group showed a decline of 1.0 points. An improvement of at least 3 points on this scale was achieved by 57% of children treated with nusinersen, compared with 26% in the placebo group. The trials confirmed nusinersen's favorable safety profile. The frequency of adverse events was similar in the nusinersen and control groups. The most common adverse events related to the administration route (lumbar puncture) are post-procedure headache, back pain, and vomiting. (Mercuri et al., 2018) Although nusinersen's introduction to SMA treatment has brought many benefits, this therapy also comes with certain limitations. Primarily, the drug's administration route requires repeated lumbar punctures, which carry potential complications and can be challenging for some patients, such as those with scoliosis. Additionally, the drug has limited penetration through the blood-brain barrier, and its distribution is restricted outside the central nervous system. (Day et al., 2022)

Onasemnogene abeparvovec is a groundbreaking gene replacement therapy specifically developed for the treatment of SMA. The therapy has achieved recognition as a major breakthrough in SMA management, particularly for infants diagnosed with the most severe form of the disease, SMA type 1. Clinical trials, including the pivotal START and STR1VE studies, have demonstrated that onasemnogene abeparvovec substantially improves motor function as well as overall quality of life, with a high percentage of treated children achieving important developmental milestones such as independent sitting and survival without the need for permanent ventilation. (Mendell et al., 2021; Mercuri et al., 2021) Despite its revolutionary nature, onasemnogene abeparvovec has its limitations. Its extraordinarily high cost—approximately $2.1 million per dose—has raised major ethical and accessibility concerns, especially in low-resource settings. (Pearson et al., 2019) Furthermore, potential side effects, particularly related to liver function, call for careful patient monitoring, adding an additional degree of complexity to its clinical use. (Chand et al., 2021) Despite a few shortcomings, Onasemnogene abeparvovec constitutes a major breakthrough in the treatment of SMA, showcasing the key role of innovative gene therapies in managing rare and severe genetic disorders.

Risdiplam is another medication used to treat spinal muscular atrophy. By enhancing the production of the SMN protein through modulation of SMN2 pre-mRNA splicing, risdiplam increases levels of functional SMN protein, thereby promoting motor neuron health and function. (Kakazu et al., n.d.-b) Approved by the U.S. Food and Drug Administration (FDA) in 2020, risdiplam has appeared as a significant therapeutic option, especially due to its oral route of administration. (Sitas et al., n.d.) Risdiplam promotes the inclusion of exon 7, thereby increasing the expression of full-length *SMN2* mRNA and functional SMN protein. (Baranello et al., 2021a) First, it was studied in animal models of spinal muscular atrophy, in which risdiplam increased functional SMN protein levels in the central nervous system and nonneuronal tissues. (Poirier et al., 2018; Ratni et al., 2018) Later, risdiplam was studied through rigorous clinical trials, including the SUNFISH and FIREFISH trials, which demonstrated considerable improvements in motor function across various age groups, particularly in infants and children with different SMA types. (Baranello et al., 2021; Mah et al., 2023; Mercuri et al., 2022)

Despite SMN-dependent therapies being a major breakthrough in SMA treatment, they still have limitations. First, their effectiveness depends on the timing of treatment initiation. Damage to motor axons begins prenatally and is followed by rapid neuronal degeneration after birth. Therefore, earlier initiation of treatment often leads to better outcomes. (Kong et al., 2021) Some older SMA patients did not receive treatment early enough due to the lack of available therapies at the time, failure to meet treatment inclusion criteria, and delays in diagnosis. This delay in initiating treatment reduces the effectiveness of SMN-dependent therapy in these patients. Furthermore, even with early treatment initiation, many patients do not achieve maximum scores on motor scales (e.g., HFMSE) and fail to reach all developmental milestones. (Day et al., 2022) Additionally, a challenge is the limited systemic distribution of certain drugs like nusinersen, whose action is confined to the central nervous system. Studies show that SMA affects not only motor neurons but also peripheral tissues, including muscles. (Yeo & Darras, 2021) Therefore, it is emphasized that ideal treatment should be two-pronged: optimizing neuron function (via SMN) and directly strengthening the muscle component (via SMN-independent mechanisms, e.g., myostatin inhibition). (Day et al., 2022)

Myostatin inhibitors

Myostatin (GDF-8) is a protein from the TGF-β superfamily and acts as a strong negative regulator of muscle mass growth. It is mainly produced by skeletal muscle cells as an inactive precursor (pro-myostatin). (Gnazzo et al., 2025) The conversion of pro-myostatin to its active form occurs in two steps. The first step involves cleavage by the furin protease, producing a latent form that remains inactive. Then, a second cleavage by proteases such as BMP-1/TLD, TLL-1, and TLL-2 generates the active form. Active myostatin binds to the ActRIIA and ActRIIB receptors, triggering intracellular pathways (e.g., SMAD2/3 or MAPK). This signaling inhibits myogenesis and upregulates genes responsible for muscle atrophy. Therefore, myostatin inhibition is a promising SMA treatment strategy. This therapy is SMN-independent and targets muscle tissue directly. Myostatin inhibitors aim to reduce atrophy, improve muscle strength, and offer additional support for patients who do not fully respond to standard SMN-dependent therapy. (Abati et al., 2022) Unfortunately, most myostatin inhibitors showed low specificity and blocked other molecules from the TGF-beta superfamily. This led to a high incidence of adverse effects. (Nielsen et al., 2021) Current research focuses on more selective molecules, such as apitegromab, which show significantly fewer adverse effects.

Apitegromab - SRK-015

Apitegromab is a fully human monoclonal antibody being investigated as a therapy to improve motor function in patients with spinal muscular atrophy (SMA) and other conditions associated with muscle atrophy. Unlike other myostatin inhibitors, apitegromab binds specifically to the inactive form of myostatin — pro-myostatin and the latent form of myostatin, blocking its conversion into the active form by blocking tolloid proteases' access to the cleavage site in the prodomain. (Barrett et al., 2021; Pirruccello-Straub et al., 2018) A major advantage of apitegromab over other myostatin inhibitors is its lack of binding to other TGFβ family factors, including GDF11, Activin A, BMP9 and 10, and TGFβ1. Thanks to this, apitegromab offers a better safety profile and greater precision of action than previous generations of inhibitors. (Barrett et al., 2021)

Results

Phase 2 TOPAZ Study

The TOPAZ Study (Crawford, Darras, et al., 2024) was a multicenter, phase 2 clinical trial evaluating the safety, tolerability, and efficacy of apitegromab (SRK-015) in patients with spinal muscular atrophy (SMA) types 2 and 3. The goal of the study was to determine whether a selective myostatin inhibitor could improve motor function in patients undergoing standard SMN-dependent therapies.

In the clinical trial, a total of 58 individuals aged 2 to 21 years with SMA types 2 and 3 participated. Patients were recruited at 16 centers in the United States and Europe. The study groups were divided into 3 cohorts depending on age, disease severity, and treatment history. Cohort 1 included 23 patients aged 5 to 21 years with ambulatory type 3 SMA. It was divided into two subgroups: the first group received apitegromab at 20 mg/kg as monotherapy, and the second received apitegromab in combination with nusinersen. Cohort 2 included 15 non-ambulatory patients aged 5–21 years with SMA types 2 or 3. All in this cohort received apitegromab 20 mg/kg in combination with nusinersen. Nusinersen treatment in these patients had to be initiated after the age of 5 years. Cohort 3 included 20 non-ambulatory patients with type 2 SMA aged 2 years and older. Patients were randomized into two groups: the first received apitegromab at 2 mg/kg, and the second at 20 mg/kg. All patients in this cohort were treated with nusinersen, initiated before age 5 years. Additionally, all participants had to have an estimated life expectancy >2 years from screening. In cohort 1, participants needed a Revised Hammersmith Scale (RHS) score no greater than 63; in cohorts 2 and 3, an HFMSE score no less than 10. The study design is summarized in Table 1.

Participants were excluded from the study, among other reasons, if they had a tracheostomy, required chronic daytime noninvasive ventilatory support for >16 hours per day during the 2 weeks before dosing, had severe scoliosis or contractures, or had used glucocorticosteroids within 60 days before screening.

Apitegromab was administered every 28 days until day 364. Participants receiving nusinersen had to receive their maintenance dose ≥ 24 hours after apitegromab or ≥ 14 days before the scheduled apitegromab dose.

To assess the primary efficacy endpoints of treatment, two motor function scales designed for SMA patients were used: the HFMSE for individuals in the non-ambulatory cohort (cohorts 2 and 3) and the RHS for the ambulatory cohort (cohort 1). The HFMSE is an expanded scale that represents the gold standard in assessing motor function in patients with SMA types 2 and 3. It consists of 33 items scored from 0 to 2 points. The maximum possible score in this scale is 66. The higher the HFMSE score, the better the patient's motor function. An increase of ≥3 points on this scale is considered a clinically significant improvement in motor function.

Changes from baseline in the total scores on these scales were evaluated.

In cohort 1, the mean change in the RHS score was −0.3 points from baseline. For the group receiving apitegromab alone, the mean change was −0.4 points (95% CI −3.9 to 3.1). The group receiving apitegromab combined with nusinersen had a mean change of −0.3 points (95% CI −2.0 to 1.4).

In Cohort 2, the mean increase on the HFMSE scale was 0.6 points. The majority of patients (64.3%) achieved stabilization or improvement in the primary outcome measure.

In cohort 3, the mean change in HFMSE from baseline at 12 months was 6.2 points. Patients receiving the higher dose of apitegromab (20 mg/kg) (n=8) demonstrated a mean improvement of 7.1 points on the HFMSE scale; 5 participants (62.5%) achieved an increase of ≥5 points, and 3 participants (37.5%) achieved an increase of ≥10 points. In the lower-dose group (2 mg/kg)(n=9), the mean change from baseline in HFMSE was 5.3 points; 5 participants (55.6%) achieved an increase of ≥3 points, and 5 (55.6%) achieved an increase of ≥ 5 points.

The TOPAZ trial results present a favorable safety profile for apitegromab in patients with SMA types 2 and 3. The most frequently reported adverse events associated with apitegromab were headache, pyrexia, upper respiratory tract infections, cough, and nasopharyngitis. No deaths or serious adverse events directly attributable to apitegromab were reported. Only one participant (1.7%) discontinued the trial because of muscle fatigue, which occurred before initiation of apitegromab therapy. No hypersensitivity reactions to the drug were observed.

Table 1. TOPAZ Trial Design. Adapted from "Safety and Efficacy of Apitegromab in Patients With Spinal Muscular Atrophy Types 2 and 3: The Phase 2 TOPAZ Study", by Crawford, Darras, Day, et al., 2024

	Cohort 1	**Cohort 2**	**Cohort 3**
Participants	Ambulatory type 3 SMA Age 5-21 years n=23 RHS scores ≤ 63	Type 2 or nonambulatory type 3 SMA Age 5-21 years n=15 Concomitant nusinersen started ≥ 5 years HFMSE scores ≥ 10	Nonambulatory type 2 SMA Age ≥ 2 years n=20 Concomitant nusinersen started ≥ 5 years HFMSE scores ≥ 10
Design	Open-label, single-arm Two subgroups, apitegromab alone or with nusinersen 20 mg/kg apitegromab IV every 4 weeks 12-month treatment period	Open-label, single-arm 20 mg/kg apitegromab IV every 4 weeks 12-month treatment period	Open-label, blinded randomization (1:1) to 2 mg/kg or 20 mg/kg apitegromab IV every 4 weeks 12-month treatment period
Primary Objectives	Safety Mean change from baseline in RHS	Safety Mean change from baseline in HFMSE	Safety Mean change from baseline in HFMSE

HFMSE - Hammersmith Functional Motor Scale Expanded, RHS - Revised Hammersmith Scale

TOPAZ OLE

The TOPAZ OLE Study (Crawford, Day, et al., 2024) is an open-label extension of the phase 2 TOPAZ study designed to evaluate the long-term (36-month) efficacy and safety of apitegromab. Eligible participants were those who completed the primary 12-month treatment period in the TOPAZ study. Of the 58 participants enrolled in TOPAZ, 57 completed the study and enrolled in the extension study. Data analysis concentrated on the nonambulatory patient group (35 participants). All participants in the extension phase received apitegromab at a dose of 20 mg/kg every 4 weeks via intravenous infusion. All patients were concurrently treated with nusinersen.

Efficacy assessments included evaluation of motor function using the HFMSE (Hammersmith Functional Motor Scale–Expanded) and RULM (Revised Upper Limb Module**)** scales, as well as monitoring achievement of WHO developmental motor milestones. Quality of life and fatigue levels were assessed using caregiver-reported outcomes from the PEDI-CAT (Pediatric Evaluation of Disability Inventory Computer Adaptive Test**)** and PROMIS Fatigue (Patient-Reported Outcomes Measurement Information System Fatigue**)** questionnaires. Treatment safety was monitored through reporting of treatment-related adverse events, physical examinations, laboratory tests, 12-lead ECGs, and testing for antidrug antibodies.

Results from the 36-month TOPAZ OLE study demonstrated sustained and continued improvement in motor function among nonambulatory patients with SMA types 2 and 3. In the HFMSE scale, the total nonambulatory population (ages 2–21 years) had a mean change from baseline of +4.0 points. In the subgroup of children aged 2–12 years, the mean change was +4.8 points. Assessment of upper limb function using the RULM scale in all nonambulatory patients (ages 2–21 years) showed a mean increase of 2.4 points, and in the subgroup aged 2–12 years, the mean increase was 2.8 points. Analyses of the HFMSE and RULM scales excluded data from 7 patients who underwent scoliosis surgery.

Improvements in these scales were consistent with caregiver-reported outcomes regarding daily activities (PEDI-CAT) and reduced fatigue (PROMIS Fatigue).

The safety profile of apitegromab after 36 months of treatment remains favorable and consistent with the 12-month results from the TOPAZ study. Treatment-related adverse events were mild to moderate in severity. The most frequently reported events were pyrexia (48.6%), nasopharyngitis (45.7%), COVID-19 infection (40.0%), vomiting (40.0%), and upper respiratory tract infections (31.4%). Although 40% of patients experienced at least one serious adverse event, none were deemed related to apitegromab administration. No deaths were reported, and no hypersensitivity reactions to the drug were observed. No patients developed antidrug antibodies, confirming the molecule's low immunogenicity.

Phase 3 SAPPHIRE Study

The SAPPHIRE Study (Crawford et al., 2025) is a phase 3 trial evaluating the efficacy and safety of apitegromab. The study was a double-blind, placebo-controlled trial lasting 52 weeks. Inclusion criteria were strictly defined. Participants had to have confirmed nonambulatory SMA type 2 or 3 and be aged 2–21 years, with an estimated life expectancy >2 years at screening. Patients were required to have an HFMSE score between 10 and 45 at screening and to be undergoing standard SMA therapy with nusinersen for at least 10 months or risdiplam for at least 6 months. Patients previously treated with gene therapy (onasemnogene abeparvovec) or apitegromab, or those with severe scoliosis or contractures (defined as grade 3 per Common Terminology Criteria for Adverse Events or likely affecting motor function assessments), were excluded.

A total of 188 participants were enrolled in the study. Participants were split into two groups based on age. The first group consisted of patients aged 2–12 years (n=156), who were randomly assigned to 3 subgroups: 53 received apitegromab at 20 mg/kg, 53 at 10 mg/kg, and 50 received a placebo. The second group consisted of older patients aged 13–21 years (n=32), who were allocated in a 2:1 ratio to apitegromab 20 mg/kg (n=22) and placebo (n=10).

The primary tool for assessing apitegromab treatment efficacy was the HFMSE scale. Additionally, upper limb function was evaluated using the RULM scale, and the achievement of new WHO developmental motor milestones was monitored.

Of the 156 participants in the 2-12 years age group, 155 (99%) completed the study, and of the 32 participants in the 13-21 years age group, 31 (97%) completed the study. Two participants receiving apitegromab 20 mg/kg (one from the 2-12 years group and one from the 13-21 years group) discontinued participation, and neither discontinuation was due to adverse events.

In the 2-12 years age group, the combined HFMSE results for the 10 mg/kg and 20 mg/kg apitegromab groups, compared with placebo, showed a mean improvement of 1.8 points (p=0.019). Comparison of the 20 mg/kg dose alone versus placebo yielded a mean improvement of 1.4 points (p=0.11). In the 13-21 years age group, the HFMSE scale showed a mean increase of 1.8 points (20 mg/kg apitegromab vs placebo).

The SAPPHIRE study demonstrated that apitegromab has a favorable safety profile comparable to placebo. The nature of adverse events corresponded to the natural course of SMA and to the background treatment with nusinersen and risdiplam. The most frequently reported adverse events were pyrexia, nasopharyngitis, cough, vomiting, upper respiratory tract infections, and headache. Adverse events occurring at least 5% more frequently in patients receiving apitegromab compared to placebo included vomiting, diarrhea, gastroenteritis, rhinorrhea, and pneumonia. No deaths or serious adverse reactions related to apitegromab administration occurred during the study.

A summary of the mentioned studies, comparing phase, population, primary efficiency endpoint, and results, is presented in **Table 2**.

Table 2. Summary of TOPAZ, TOPAZ OLE, and SAPPHIRE Trials

Study	Phase/design	Population	Primary efficiency endpoint	Results
TOPAZ	Phase 2, open-label	Patients with SMA type 2 and 3, aged 2 to 21 years	Change in HFMSE (or RHS - cohort 1) from baseline at 12 months	Cohort 3 - Mean HFMSE increase of **+7.1 points** (20 mg/kg) and **+5.3 points** (2 mg/kg) Cohort 2 - Mean HFMSE increase of **+0.6 points** Cohort 1 - Mean RHS change of **-0.3 points**
TOPAZ OLE	Long-term extension	Participants from TOPAZ who continued treatment	Maintenance of HFMSE and RULM over 36 months	Mean HFMSE change was **+4.0**, and mean RULM change was **+2.4**
SAPPHIRE	Phase 3, randomized, placebo-controlled, double-blind	Patients with SMA type 2 and 3 receiving SMN-targeted therapy aged 2 to 21 years	Change in HFMSE from baseline at 12 months	**Ages 2–12:** Statistically significant difference of **1.8 points** in HFMSE vs. placebo (p=0.019) **Ages 13–21:** A **1.8-point** difference in HFMSE vs. placebo

SMA - Spinal Muscular Atrophy, HFMSE - Hammersmith Functional Motor Scale Expanded, RHS - Revised Hammersmith Scale, RULM - Revised Upper Limb Module

Conclusions

Clinical trials of apitegromab (TOPAZ, TOPAZ OLE, SAPPHIRE) indicate the breakthrough significance of this therapy as the first method directly supporting muscle function in patients with SMA types 2 and 3. The trials confirmed the clinical efficacy of apitegromab, with considerable improvements in motor function in participants. The SAPPHIRE study demonstrated improvement in motor function on the HFMSE scale by an average of +1.8 points compared to placebo. Results from the TOPAZ OLE study after 36 months confirmed that the effects of apitegromab treatment are durable and deepen over longer periods. Additionally, all trials confirmed apitegromab's favorable safety profile and showed that it is well tolerated by patients. The SAPPHIRE study showed that the frequency of adverse events was similar to that of the placebo group. Moreover, no serious adverse events or deaths directly related to the drug were reported. It was also demonstrated that patients do not develop antibodies against the drug, attesting to its low immunogenicity. Results obtained using questionnaires in the TOPAZ OLE study indicate a real improvement in patients' quality of life. Data reported by caregivers via the PROMIS Fatigue questionnaire indicated reduced fatigue among patients, and PEDI-CAT scale results indicated improved independence in daily activities.

The studies demonstrated that selective myostatin inhibition significantly improves motor function in patients with SMA types 2 and 3 and, due to its high selectivity, has a favorable safety profile. These results position apitegromab as a key adjunctive therapy to standard SMA treatments, enabling patients not only to halt disease progression but also to regain lost motor functions and improve quality of life.

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