An Open-Label, Multicenter, Extension Trial to Evaluate the Long-Term Safety and Efficacy of Apitegromab in Patients with Type 2 and Type 3 Spinal Muscular Atrophy Who Completed Previous Investigational Trials of Apitegromab

Published: 20-12-2022
Last updated: 30-11-2024

This study has been transitioned to CTIS with ID 2024-511654-42-00 check the CTIS register for the current data. -Evaluate the long-term safety and tolerability of apitegromab in patients with Type 2 and Type 3 SMA-Evaluate the long-term efficacy of...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Neuromuscular disorders
Study type	Interventional

Summary

ID

NL-OMON53608

Source
ToetsingOnline

Brief title
SRK-015-004

Condition

- Neuromuscular disorders

Synonym
neuromuscular disease, SMA

Research involving

Human

Sponsors and support

Primary sponsor: Scholar Rock Inc.
Source(s) of monetary or material Support: Industry

Intervention

Keyword: Phase 3, Spinal Muscular Atrophy

Outcome measures

Primary outcome

-Incidence of TEAEs and SAEs by severity

Secondary outcome

- Hammersmith Functional Motor Scale Expanded (HFMSE) total score at prespecified time points (excludes TOPAZ Cohort 1 patients)

- Revised Upper Limb Module (RULM) total score at prespecified time points (excludes TOPAZ Cohort 1 patients)

- Number of World Health Organization (WHO) motor development milestones attained at prespecified time points (excludes TOPAZ Cohort 1 patients)

- Revised Hammersmith Scale (RHS) total score and results for 6-Minute Walk Test, 30-Second Sit-to-Stand, 10-Meter Walk/Run (from the RHS), and timed rise from floor (from the RHS) at prespecified time points (TOPAZ Cohort 1 patients only)

-Presence or absence of antidrug antibody (ADA) against apitegromab in serum from blood samples

Study description

Background summary

SMA is a whole-body disease (Wirth 2020). Although the SMN upregulator (also referred to as SMN corrector) therapies approved
for the treatment of SMA have been shown to significantly improve clinical outcomes by preventing or reducing the decline in motor
function, patients may continue to suffer from substantial motor functional impairment because targeted SMN upregulator therapies
focus on SMN-dependent pathways and do not directly impact skeletal muscle to reverse the atrophy that has already taken place
(Mercuri 2018, Mercuri 2020).
Consequently, there remains an unmet medical need for a complementary therapeutic strategy, namely muscle-directed therapy,
that may address muscle atrophy and thereby improve motor function in patients with SMA. Through its novel mechanism of action
as a selective inhibitor of
myostatin activation, apitegromab (SRK-015) has the potential to produce a clinically meaningful effect on motor function in a broad
population of patients with SMA who are being treated with background SMN upregulator therapies (e.g., nusinersen [SPINRAZA®]
or risdiplam [EVRYSDI®]) (SPINRAZA Food and Drug Administration [FDA] Prescribing Information [PI] 2020, SPINRAZA Summary
of Product Characteristics [SmPC] 2021,
EVRYSDI FDA PI 2021, EVRYSDI SmPC 2021).

Study objective

This study has been transitioned to CTIS with ID 2024-511654-42-00 check the CTIS register for the current data.

-Evaluate the long-term safety and tolerability of apitegromab in patients with Type 2 and Type 3 SMA
-Evaluate the long-term efficacy of apitegromab by assessing changes in motor function outcome measures at prespecified time points
-Further evaluate the immunogenicity of apitegromab

Study design

This Phase 3 trial will continue to evaluate the safety and efficacy of apitegromab in ambulatory and nonambulatory patients with Type 2 and Type 3 SMA who have completed a previous apitegromab trial (i.e., TOPAZ or SAPPHIRE). This global trial will be conducted at approximately 55 trial sites.
The trial will include Baseline, Treatment, and Safety Follow-up Periods.

Approximately 260 male and female patients who are >=2 years of age with Type 2 and Type 3 SMA will receive apitegromab 20 mg/kg every 4 weeks by intravenous (IV) infusion during the 104-week Treatment Period. Dosing every 4 weeks should be targeted. However, a ±7*day window around each
dosing visit (with a minimum of 21 days and a maximum of 35 days between doses) is allowed without consultation with the Sponsor.

Intervention

N/A

Study burden and risks

- The study lasts a total of approximately 76 weeks for patients.
- Additional hospital visits, additional physical tests, including a pregnancy test.
- A total of approximately 110ml of blood is taken. This amount is not a problem (for comparison: a blood donation means that 500 ml of blood is taken each time). Possible side effects of blood tests include fainting, soreness and tenderness at the injection site and, in rare cases, infection.
- If the study drug does not work for the patient, he/she may see an increase in his/her disease symptoms.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)

Inclusion criteria

1. Informed consent document signed by the patient if the patient is legally an adult. If the patient is legally a minor, informed consent document signed by the patient's parent or legal guardian and patient's oral or written assent obtained, if applicable and in accordance with the regulatory and legal requirements of the participating location.
2. Patients who have completed the Phase 2 TOPAZ (Study SRK-015-002) trial or the Phase 3 SAPPHIRE (Study SRK-015-003) trial.
3. Estimated life expectancy >2 years from Baseline (Day 1).
4. Able to receive study drug infusions and provide blood samples through the use of a peripheral IV or a long-term IV access device that the patient has placed for reasons independent from the trial (i.e., for background medical care and not for the purpose of receiving apitegromab in the trial), throughout the trial.
5. Able to adhere to the requirements of the protocol.
6. Females of childbearing potential must have a negative pregnancy test at Baseline and agree to use at least 1 acceptable method of contraception throughout the trial and for 20 weeks after the last dose of apitegromab. Female patients who are expected to have reached reproductive maturity by the end of the trial must agree to adhere to trial-specific contraception requirements.

Exclusion criteria

1. Patient permanently discontinued study treatment during the feeder trial (i.e., TOPAZ or SAPPHIRE).
2. Nutritional status that was not stable over the past 6 months and is not anticipated to be stable throughout the trial or medical necessity for a gastric/nasogastric feeding tube, where the majority of feeds are given by this route, as assessed by the investigator.

3. Patient is currently enrolled in any investigational drug trial other than TOPAZ or SAPPHIRE.
4. Prior history of severe hypersensitivity reaction or intolerance to SMNtargeted therapies.
5. Prior history of severe hypersensitivity reaction or intolerance to apitegromab.
6. Use of chronic daytime noninvasive ventilatory support for >16 hours daily in the 2 weeks before dosing, or anticipated to regularly receive such daytime ventilator support chronically throughout the trial.
7. Any acute or comorbid condition interfering with the well-being of the patient at the patient's last visit in TOPAZ or SAPPHIRE, including active systemic infection, the need for acute treatment, or inpatient observation due to any reason.
8. Pregnant or breastfeeding.
9. Any other condition or clinically significant laboratory result or ECG value that, in the opinion of the Investigator, may compromise safety or compliance, would preclude the patient from successful completion of the trial, or interfere with the interpretation of the results.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	21-11-2023
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	Apitegromab
Generic name:	Apitegromab

Ethics review

Approved WMO Date:	20-12-2022
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	07-03-2023
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	21-11-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	07-12-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
Other	2022□001771□14
EU-CTR	CTIS2024-511654-42-00
EudraCT	EUCTR2022-001771-14-NL
CCMO	NL82994.028.22