Clinical trial results:
Phase 3, Double-Blind, Placebo-Controlled Trial to Evaluate the Efficacy and Safety of Apitegromab (SRK-015) in Patients with Later-Onset Spinal Muscular Atrophy Receiving Background Nusinersen or Risdiplam Therapy

Summary

EudraCT number	2021-005314-34
Trial protocol	BE DE FR ES NL IT PL
Global end of trial date	18 December 2024

Results information

Result version number	v1 (current)
This version publication date	03 January 2026
First version publication date	03 January 2026

Trial information

Trial identification

Sponsor protocol code	SRK-015-003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05156320
WHO universal trial number (UTN)	-
Other trial identifiers	IND: 136872

Notes:

Sponsors

Sponsor organisation name	Scholar Rock, Inc.
Sponsor organisation address	301 Binney Street, 3rd Floor, Cambridge, MA, United States, 02142
Public contact	Clinical Information Desk, Scholar Rock, Inc., +1 857259 3860 , clinicaltrials@scholarrock.com
Scientific contact	Clinical Information Desk, Scholar Rock, Inc., +1 857259 3860 , clinicaltrials@scholarrock.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002951-PIP02-21
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 December 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 December 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to assess the efficacy of apitegromab (SRK-015) compared with placebo using the Hammersmith Functional Motor Scale Expanded (HFMSE) in subjects 2 through 12 years old.

Protection of trial subjects:

This study was designed and monitored in accordance with Sponsor procedures, which comply with the ethical principles of the International Council for Harmonisation (ICH) on GCP guidance and in accordance with the Declaration of Helsinki (Version 2013). The study was also conducted in accordance with national and local legal requirements and in accordance with United States (US) Investigational New Drug regulations (21 Code of Federal Regulations [CFR] 56) and the European Union (EU)'s Commission Directive 2005/28/EC of 8 April 2005.

Background therapy:

Nusinersen or Risdiplam.

Evidence for comparator: -

Actual start date of recruitment	12 February 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 8
Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	Poland: 16
Country: Number of subjects enrolled	Spain: 15
Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	France: 16
Country: Number of subjects enrolled	Germany: 16
Country: Number of subjects enrolled	Italy: 31
Country: Number of subjects enrolled	United States: 71
Worldwide total number of subjects	188
EEA total number of subjects	109

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	148
Adolescents (12-17 years)	33
Adults (18-64 years)	7
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects took part in this multicenter study in Belgium, France, Germany, Italy, Netherland, Spain, Poland, United Kingdom and the United States from 28 March 2022 to 18 December 2024. Subjects with Type 2 and Type 3 spinal muscular atrophy (SMA) were enrolled into either the Main Efficacy Population (MEP) or the Exploratory Subpopulation (EXP).

Pre-assignment

Screening details:

Study included a Screening Period, a Treatment Period, and a Follow-Up Period. A total of 216 subjects were screened of which 188 subjects (156 subjects in the MEP, and 32 subjects in the EXP) were randomized.

Period 1

Period 1 title	Overall Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

The sponsor, subjects, parents or caregivers, Investigators, and site personnel, with the exception of the designated unblinded personnel (eg, site Pharmacist), were blinded to treatment assignments.

Arms

Are arms mutually exclusive?	Yes
Arm title	Main Efficacy Population: Placebo

Arm description:

Subjects aged 2-12 years received apitegromab matching placebo, IV infusion, Q4W, over a period of 1-2 hours during the 52-week Treatment Period.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

Apitegromab matching placebo, IV infusion, Q4W, over a period of 1-2 hours.

Arm title	Main Efficacy Population: Apitegromab 10 mg/kg

Arm description:

Subjects aged 2-12 years received apitegromab 10 mg/kg, IV infusion, Q4W over a period of 1-2 hours during the 52-week Treatment Period.

Arm type	Experimental
Investigational medicinal product name	Apitegromab
Investigational medicinal product code	
Other name	SRK-015
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

Apitegromab 10 mg/kg, IV infusion, Q4W, over a period of 1-2 hours.

Arm title	Main Efficacy Population: Apitegromab 20 mg/kg

Arm description:

Subjects aged 2-12 years received apitegromab 20 mg/kg, IV infusion, Q4W over a period of 1-2 hours

during the 52-week Treatment Period.

Arm type	Experimental
Investigational medicinal product name	Apitegromab
Investigational medicinal product code	
Other name	SRK-015
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

Apitegromab 20 mg/kg, IV infusion, Q4W, over a period of 1-2 hours.

Arm title	Exploratory Subpopulation: Placebo

Arm description:

Subjects aged 13-21 years received apitegromab matching placebo, IV infusion, Q4W over a period of 1-2 hours during the 52-week Treatment Period.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

Apitegromab matching placebo, IV infusion, Q4W, over a period of 1-2 hours.

Arm title	Exploratory Subpopulation: Apitegromab 20 mg/kg

Arm description:

Subjects aged 13-21 years received apitegromab 20 mg/kg, IV infusion, Q4W over a period of 1-2 hours during the 52-week Treatment Period.

Arm type	Experimental
Investigational medicinal product name	Apitegromab
Investigational medicinal product code	
Other name	SRK-015
Pharmaceutical forms	Injection/infusion
Routes of administration	Infusion

Dosage and administration details:

Apitegromab 20 mg/kg, IV infusion, Q4W, over a period of 1-2 hours.

Number of subjects in period 1	Main Efficacy Population: Placebo	Main Efficacy Population: Apitegromab 10 mg/kg	Main Efficacy Population: Apitegromab 20 mg/kg
Started	50	53	53
Completed	50	53	52
Not completed	0	0	1
Consent withdrawn by subject	-	-	-
Other	-	-	1

Number of subjects in period 1	Exploratory Subpopulation: Placebo	Exploratory Subpopulation: Apitegromab 20 mg/kg
Started	10	22

Completed	10	21
Not completed	0	1
Consent withdrawn by subject	-	1
Other	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Main Efficacy Population: Placebo
Reporting group description:	
Subjects aged 2-12 years received apitegromab matching placebo, IV infusion, Q4W, over a period of 1-2 hours during the 52-week Treatment Period.	
Reporting group title	Main Efficacy Population: Apitegromab 10 mg/kg
Reporting group description:	
Subjects aged 2-12 years received apitegromab 10 mg/kg, IV infusion, Q4W over a period of 1-2 hours during the 52-week Treatment Period.	
Reporting group title	Main Efficacy Population: Apitegromab 20 mg/kg
Reporting group description:	
Subjects aged 2-12 years received apitegromab 20 mg/kg, IV infusion, Q4W over a period of 1-2 hours during the 52-week Treatment Period.	
Reporting group title	Exploratory Subpopulation: Placebo
Reporting group description:	
Subjects aged 13-21 years received apitegromab matching placebo, IV infusion, Q4W over a period of 1-2 hours during the 52-week Treatment Period.	
Reporting group title	Exploratory Subpopulation: Apitegromab 20 mg/kg
Reporting group description:	
Subjects aged 13-21 years received apitegromab 20 mg/kg, IV infusion, Q4W over a period of 1-2 hours during the 52-week Treatment Period.	

Reporting group values	Main Efficacy Population: Placebo	Main Efficacy Population: Apitegromab 10 mg/kg	Main Efficacy Population: Apitegromab 20 mg/kg
Number of subjects	50	53	53
Age categorical Units: Subjects			
2 years to 18 years			
Age continuous Units: years			
arithmetic mean	8.1	7.4	7.9
standard deviation	± 2.46	± 2.57	± 2.46
Gender categorical Units: Subjects			
Female	25	23	26
Male	25	30	27
Race Units: Subjects			
Asian	2	2	4
Black or African American	1	1	0
White	41	35	40
Other	1	3	0
Not Reported or Unknown	5	12	9

Reporting group values	Exploratory Subpopulation: Placebo	Exploratory Subpopulation: Apitegromab 20 mg/kg	Total
Number of subjects	10	22	188

Age categorical Units: Subjects			
2 years to 18 years			0
Age continuous Units: years			
arithmetic mean	15.2	16.1	
standard deviation	± 1.75	± 2.59	-
Gender categorical Units: Subjects			
Female	5	15	94
Male	5	7	94
Race Units: Subjects			
Asian	0	0	8
Black or African American	0	2	4
White	6	14	136
Other	0	0	4
Not Reported or Unknown	4	6	36

End points

End points reporting groups

Reporting group title	Main Efficacy Population: Placebo
Reporting group description:	
Subjects aged 2-12 years received apitegromab matching placebo, IV infusion, Q4W, over a period of 1-2 hours during the 52-week Treatment Period.	
Reporting group title	Main Efficacy Population: Apitegromab 10 mg/kg
Reporting group description:	
Subjects aged 2-12 years received apitegromab 10 mg/kg, IV infusion, Q4W over a period of 1-2 hours during the 52-week Treatment Period.	
Reporting group title	Main Efficacy Population: Apitegromab 20 mg/kg
Reporting group description:	
Subjects aged 2-12 years received apitegromab 20 mg/kg, IV infusion, Q4W over a period of 1-2 hours during the 52-week Treatment Period.	
Reporting group title	Exploratory Subpopulation: Placebo
Reporting group description:	
Subjects aged 13-21 years received apitegromab matching placebo, IV infusion, Q4W over a period of 1-2 hours during the 52-week Treatment Period.	
Reporting group title	Exploratory Subpopulation: Apitegromab 20 mg/kg
Reporting group description:	
Subjects aged 13-21 years received apitegromab 20 mg/kg, IV infusion, Q4W over a period of 1-2 hours during the 52-week Treatment Period.	
Subject analysis set title	Main Efficacy Population: Apitegromab 10 mg/kg + 20 mg/kg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All subjects aged 2-12 years who received apitegromab 10 mg/kg or 20 mg/kg, IV infusion, Q4W, over a period of 1-2 hours during the 52-week Treatment Period.	

Primary: Change From Baseline in Hammersmith Functional Motor Scale Expanded (HFMSE) Total Score at Week 52

End point title	Change From Baseline in Hammersmith Functional Motor Scale Expanded (HFMSE) Total Score at Week 52[1]
End point description:	
The HFMSE assesses the physical abilities of patients with Type 2 and Type 3 SMA. It comprises of 33 items graded on a scale of 0, 1, or 2, where 0 denotes unable, 1 denotes performed with modification or adaptation, and 2 denotes performed without modification or adaptation. The overall score is the sum of the scores for all activities with a maximum achievable score of 66. Higher scores indicate increased motor function. Modified Intention-to-Treat (MITT) Set, defined as all subjects who received at least 1 dose of study drug and had at least 1 postbaseline evaluable HFMSE assessment.	
End point type	Primary
End point timeframe:	
Baseline, Week 52	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Applicable treatment arms were assessed for analysis.

End point values	Main Efficacy Population: Placebo	Main Efficacy Population: Apitegromab 10 mg/kg	Main Efficacy Population: Apitegromab 20 mg/kg	Main Efficacy Population: Apitegromab 10 mg/kg + 20 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	50	53	53	106
Units: score on a scale				

least squares mean (standard error)	-1.2 (± 0.66)	1.0 (± 0.64)	0.2 (± 0.64)	0.6 (± 0.48)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
MMRM includes the fixed effects of treatment group, visit, treatment group-by-visit interaction, baseline HFMSE total score, baseline HFMSE total score-by-visit interaction, type of SMN Therapy (i.e., nusinersen or risdiplam), and age at initiation of SMN Therapy (>=5 and <5 years). Comparison was presented by the difference between apitegromab group versus placebo.	
Comparison groups	Main Efficacy Population: Placebo v Main Efficacy Population: Apitegromab 10 mg/kg + 20 mg/kg
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0192
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	3.32
Variability estimate	Standard error of the mean
Dispersion value	0.76

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
MMRM includes the fixed effects of treatment group, visit, treatment group-by-visit interaction, baseline HFMSE total score, baseline HFMSE total score-by-visit interaction, type of SMN Therapy (i.e., nusinersen or risdiplam), and age at initiation of SMN Therapy (>=5 and <5 years).	
Comparison groups	Main Efficacy Population: Placebo v Main Efficacy Population: Apitegromab 20 mg/kg
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1149
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.34
upper limit	3.13

Variability estimate	Standard error of the mean
Dispersion value	0.88

Secondary: Change From Baseline in Revised Upper Limb Module (RULM) Total Score at Week 52

End point title	Change From Baseline in Revised Upper Limb Module (RULM) Total Score at Week 52[2]

End point description:

The RULM is an assessment of upper limb function in nonambulatory patients with SMA that was performed for patients who were 30 months of age or older at baseline. The 19 scored items assess functions that relate to everyday life, such as placing hands from lap, pressing a button, and picking up a token. With the exception of 1 activity with a binary score, these items are scored 0, 1, or 2, where 0 denotes unable, 1 denotes able with modification, and 2 denotes able with no modification. The maximum score achievable is 37. MITT Set, defined as all subjects who received at least 1 dose of study drug and had at least 1 postbaseline evaluable HFMSE assessment.

End point type	Secondary

End point timeframe:

Baseline, Week 52

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Applicable treatment arms were assessed for analysis.

End point values	Main Efficacy Population: Placebo	Main Efficacy Population: Apitegromab 10 mg/kg	Main Efficacy Population: Apitegromab 20 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	53	53	
Units: score on a scale				
least squares mean (standard error)	0.1 (± 0.40)	0.7 (± 0.39)	0.8 (± 0.38)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With >=3-Point Change From Baseline in the HFMSE Total Score at Week 52

End point title	Percentage of Subjects With >=3-Point Change From Baseline in the HFMSE Total Score at Week 52[3]

End point description:

Percentage of subjects treated with apitegromab who achieved a specific number of points of HFMSE improvement from baseline were reported. The HFMSE assesses the physical abilities of patients with Type 2 and Type 3 SMA. It comprises of 33 items graded on a scale of 0, 1, or 2, where 0 denotes unable, 1 denotes performed with modification or adaptation, and 2 denotes performed without modification or adaptation. The overall score is the sum of the scores for all activities with a maximum achievable score of 66. Higher scores indicate increased motor function. MITT Set, defined as all subjects who received at least 1 dose of study drug and had at least 1 postbaseline evaluable HFMSE assessment.

End point type	Secondary

End point timeframe:

Week 52

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Applicable treatment arms were assessed for analysis.

End point values	Main Efficacy Population: Placebo	Main Efficacy Population: Apitegromab 10 mg/kg	Main Efficacy Population: Apitegromab 20 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	53	53	
Units: percentage of subjects				
number (not applicable)	13.5	34.2	25.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Number of World Health Organization (WHO) Motor Development Milestones Attained at Week 52

End point title	Change From Baseline in Number of World Health Organization (WHO) Motor Development Milestones Attained at Week 52[4]

End point description:

The WHO Multicenter Growth Reference Study performance criteria was utilized to assess the WHO motor development milestones of subjects with Type 2 and nonambulatory Type 3 SMA enrolled in Cohort 2 and Cohort 3 relative to baseline. The WHO motor development milestones are a set of 6 distinct gross motor milestones that are considered to be universal and fundamental to acquiring the ability to walk independently. They include 1) sitting without support, 2) hands and knees crawling, 3) standing with assistance, 4) walking with assistance, 5) standing alone, and 6) walking without assistance. Each item is recorded as 1 (unable), 2 (refusal), 3 (Yes) or 9 (did not test). The number of 3s was counted as the final score. The minimum was 0, which means no motor milestones were achieved; the maximum was 6, which means all 6 milestones were achieved. MITT Set, defined as all subjects who received at least 1 dose of study drug and had at least 1 postbaseline evaluable HFMSE assessment.

End point type	Secondary

End point timeframe:

Baseline, Week 52

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Applicable treatment arms were assessed for analysis.

End point values	Main Efficacy Population: Placebo	Main Efficacy Population: Apitegromab 10 mg/kg	Main Efficacy Population: Apitegromab 20 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	53	53	
Units: motor milestone				
least squares mean (standard error)	0.0 (± 0.10)	0.1 (± 0.09)	0.1 (± 0.09)	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Treatment Emergent Adverse Events (TEAEs) and Severe Adverse Events (SAEs)

End point title	Incidence of Treatment Emergent Adverse Events (TEAEs) and Severe Adverse Events (SAEs)

End point description:

A Treatment Emergent Adverse Events (TEAE) is defined as an adverse event that started or worsened in severity after the start of the first dose of study drug. The Safety Set is defined as all randomized subjects who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

From start of study up to end of study (Day 505)

End point values	Main Efficacy Population: Placebo	Main Efficacy Population: Apitegromab 10 mg/kg	Main Efficacy Population: Apitegromab 20 mg/kg	Exploratory Subpopulation: Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	53	53	10
Units: subjects				
TEAEs	43	51	46	9
SAEs	5	9	12	1

End point values	Exploratory Subpopulation: Apitegromab 20 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: subjects				
TEAEs	19			
SAEs	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From start of study up to end of study (Day 505)	
Adverse event reporting additional description:	
The Safety Set included all randomized subjects who received at least 1 dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups	
Reporting group title	Pooled Population (Apitegromab 10 mg/kg + 20 mg/kg Combined)
Reporting group description:	
Type 2 SMA and Nonambulatory Type 3 SMA, ages 2 through 21 years old at Screening. Participants were randomized to receive apitegromab 10 mg/kg or 20 mg/kg for up to 52 weeks.	
Reporting group title	Pooled Population (Apitegromab 10 mg/kg)
Reporting group description:	
Type 2 SMA and Nonambulatory Type 3 SMA, ages 2 through 21 years old at Screening. Participants were randomized to receive apitegromab 10 mg/kg for up to 52 weeks.	
Reporting group title	Pooled Population (Apitegromab 20 mg/kg)
Reporting group description:	
Type 2 SMA and Nonambulatory Type 3 SMA, ages 2 through 21 years old at Screening. Participants were randomized to receive apitegromab 20 mg/kg for up to 52 weeks.	
Reporting group title	Comparator: Comparator: Pooled Population (Placebo)
Reporting group description:	
Type 2 SMA and Nonambulatory Type 3 SMA, ages 2 through 21 years old at Screening. Participants were randomized to receive Placebo for up to 52 weeks.	

Serious adverse events	Pooled Population (Apitegromab 10 mg/kg + 20 mg/kg Combined)	Pooled Population (Apitegromab 10 mg/kg)	Pooled Population (Apitegromab 20 mg/kg)
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 128 (16.41%)	9 / 53 (16.98%)	12 / 75 (16.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 128 (0.78%)	0 / 53 (0.00%)	1 / 75 (1.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Immune thrombocytopenia			

subjects affected / exposed	1 / 128 (0.78%)	1 / 53 (1.89%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	2 / 128 (1.56%)	1 / 53 (1.89%)	1 / 75 (1.33%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 128 (0.78%)	0 / 53 (0.00%)	1 / 75 (1.33%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	2 / 128 (1.56%)	2 / 53 (3.77%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atelectasis			
subjects affected / exposed	1 / 128 (0.78%)	1 / 53 (1.89%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 128 (0.78%)	0 / 53 (0.00%)	1 / 75 (1.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	1 / 128 (0.78%)	0 / 53 (0.00%)	1 / 75 (1.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 128 (0.00%)	0 / 53 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal and connective tissue disorders			
Scoliosis			
subjects affected / exposed	2 / 128 (1.56%)	1 / 53 (1.89%)	1 / 75 (1.33%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle contracture			
subjects affected / exposed	1 / 128 (0.78%)	0 / 53 (0.00%)	1 / 75 (1.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic misalignment			
subjects affected / exposed	0 / 128 (0.00%)	0 / 53 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	7 / 128 (5.47%)	3 / 53 (5.66%)	4 / 75 (5.33%)
occurrences causally related to treatment / all	0 / 8	0 / 3	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenovirus infection			
subjects affected / exposed	2 / 128 (1.56%)	0 / 53 (0.00%)	2 / 75 (2.67%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	2 / 128 (1.56%)	1 / 53 (1.89%)	1 / 75 (1.33%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	1 / 128 (0.78%)	1 / 53 (1.89%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterovirus infection			
subjects affected / exposed	1 / 128 (0.78%)	0 / 53 (0.00%)	1 / 75 (1.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal infection			
subjects affected / exposed	1 / 128 (0.78%)	1 / 53 (1.89%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metapneumovirus infection			
subjects affected / exposed	1 / 128 (0.78%)	1 / 53 (1.89%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	1 / 128 (0.78%)	1 / 53 (1.89%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 128 (0.78%)	1 / 53 (1.89%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhinovirus infection			
subjects affected / exposed	1 / 128 (0.78%)	0 / 53 (0.00%)	1 / 75 (1.33%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	1 / 128 (0.78%)	1 / 53 (1.89%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	0 / 128 (0.00%)	0 / 53 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection viral			
subjects affected / exposed	0 / 128 (0.00%)	0 / 53 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			

Dehydration			
subjects affected / exposed	3 / 128 (2.34%)	2 / 53 (3.77%)	1 / 75 (1.33%)
occurrences causally related to treatment / all	0 / 4	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic acidosis			
subjects affected / exposed	1 / 128 (0.78%)	1 / 53 (1.89%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Comparator: Comparator: Pooled Population (Placebo)		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 60 (10.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Immune thrombocytopenia			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			

Acute respiratory failure				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atelectasis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epistaxis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Urticaria				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Scoliosis				
subjects affected / exposed	2 / 60 (3.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Muscle contracture				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pelvic misalignment				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Adenovirus infection			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enterovirus infection			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal infection			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metapneumovirus infection			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia viral			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory syncytial virus infection			

subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rhinovirus infection				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Viral infection				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory syncytial virus bronchiolitis				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection viral				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolic acidosis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Pooled Population (Apitegromab 10 mg/kg + 20 mg/kg Combined)	Pooled Population (Apitegromab 10 mg/kg)	Pooled Population (Apitegromab 20 mg/kg)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	115 / 128 (89.84%)	51 / 53 (96.23%)	64 / 75 (85.33%)
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	8 / 128 (6.25%)	6 / 53 (11.32%)	2 / 75 (2.67%)
occurrences (all)	10	8	2
Fall			
subjects affected / exposed	8 / 128 (6.25%)	6 / 53 (11.32%)	2 / 75 (2.67%)
occurrences (all)	10	8	2
Vascular disorders			
Haematoma			
subjects affected / exposed	4 / 128 (3.13%)	3 / 53 (5.66%)	1 / 75 (1.33%)
occurrences (all)	5	4	1
Nervous system disorders			
Headache			
subjects affected / exposed	27 / 128 (21.09%)	12 / 53 (22.64%)	15 / 75 (20.00%)
occurrences (all)	45	16	29
Dizziness			
subjects affected / exposed	4 / 128 (3.13%)	3 / 53 (5.66%)	1 / 75 (1.33%)
occurrences (all)	6	3	3
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	33 / 128 (25.78%)	18 / 53 (33.96%)	15 / 75 (20.00%)
occurrences (all)	60	37	23
Fatigue			
subjects affected / exposed	8 / 128 (6.25%)	3 / 53 (5.66%)	5 / 75 (6.67%)
occurrences (all)	16	7	9
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	4 / 128 (3.13%)	4 / 53 (7.55%)	0 / 75 (0.00%)
occurrences (all)	4	4	0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	29 / 128 (22.66%)	16 / 53 (30.19%)	13 / 75 (17.33%)
occurrences (all)	42	23	19

Diarrhoea			
subjects affected / exposed	13 / 128 (10.16%)	9 / 53 (16.98%)	4 / 75 (5.33%)
occurrences (all)	19	15	4
Abdominal pain			
subjects affected / exposed	10 / 128 (7.81%)	5 / 53 (9.43%)	5 / 75 (6.67%)
occurrences (all)	14	5	9
Nausea			
subjects affected / exposed	7 / 128 (5.47%)	4 / 53 (7.55%)	3 / 75 (4.00%)
occurrences (all)	11	7	4
Abdominal pain upper			
subjects affected / exposed	6 / 128 (4.69%)	3 / 53 (5.66%)	3 / 75 (4.00%)
occurrences (all)	7	4	3
Constipation			
subjects affected / exposed	5 / 128 (3.91%)	1 / 53 (1.89%)	4 / 75 (5.33%)
occurrences (all)	5	1	4
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	31 / 128 (24.22%)	16 / 53 (30.19%)	15 / 75 (20.00%)
occurrences (all)	42	25	17
Rhinorrhoea			
subjects affected / exposed	12 / 128 (9.38%)	6 / 53 (11.32%)	6 / 75 (8.00%)
occurrences (all)	14	8	6
Oropharyngeal pain			
subjects affected / exposed	10 / 128 (7.81%)	6 / 53 (11.32%)	4 / 75 (5.33%)
occurrences (all)	11	6	5
Nasal congestion			
subjects affected / exposed	7 / 128 (5.47%)	2 / 53 (3.77%)	5 / 75 (6.67%)
occurrences (all)	9	3	6
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	15 / 128 (11.72%)	10 / 53 (18.87%)	5 / 75 (6.67%)
occurrences (all)	26	14	12
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	11 / 128 (8.59%)	7 / 53 (13.21%)	4 / 75 (5.33%)
occurrences (all)	13	9	4

Myalgia			
subjects affected / exposed	8 / 128 (6.25%)	3 / 53 (5.66%)	5 / 75 (6.67%)
occurrences (all)	11	3	8
Pain in extremity			
subjects affected / exposed	7 / 128 (5.47%)	5 / 53 (9.43%)	2 / 75 (2.67%)
occurrences (all)	8	6	2
Scoliosis			
subjects affected / exposed	6 / 128 (4.69%)	4 / 53 (7.55%)	2 / 75 (2.67%)
occurrences (all)	6	4	2
Muscle contracture			
subjects affected / exposed	5 / 128 (3.91%)	1 / 53 (1.89%)	4 / 75 (5.33%)
occurrences (all)	6	1	5
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	32 / 128 (25.00%)	15 / 53 (28.30%)	17 / 75 (22.67%)
occurrences (all)	50	21	29
Upper respiratory tract infection			
subjects affected / exposed	28 / 128 (21.88%)	12 / 53 (22.64%)	16 / 75 (21.33%)
occurrences (all)	40	16	24
Rhinitis			
subjects affected / exposed	16 / 128 (12.50%)	8 / 53 (15.09%)	8 / 75 (10.67%)
occurrences (all)	17	8	9
Ear infection			
subjects affected / exposed	13 / 128 (10.16%)	5 / 53 (9.43%)	8 / 75 (10.67%)
occurrences (all)	18	8	10
Gastroenteritis			
subjects affected / exposed	12 / 128 (9.38%)	7 / 53 (13.21%)	5 / 75 (6.67%)
occurrences (all)	16	8	8
COVID-19			
subjects affected / exposed	9 / 128 (7.03%)	5 / 53 (9.43%)	4 / 75 (5.33%)
occurrences (all)	9	5	4
Pharyngitis streptococcal			
subjects affected / exposed	6 / 128 (4.69%)	4 / 53 (7.55%)	2 / 75 (2.67%)
occurrences (all)	8	6	2
Influenza			

subjects affected / exposed	5 / 128 (3.91%)	3 / 53 (5.66%)	2 / 75 (2.67%)
occurrences (all)	6	4	2
Urinary tract infection			
subjects affected / exposed	4 / 128 (3.13%)	0 / 53 (0.00%)	4 / 75 (5.33%)
occurrences (all)	5	0	5
Respiratory syncytial virus infection			
subjects affected / exposed	3 / 128 (2.34%)	3 / 53 (5.66%)	0 / 75 (0.00%)
occurrences (all)	3	3	0
Bronchitis			
subjects affected / exposed	2 / 128 (1.56%)	2 / 53 (3.77%)	0 / 75 (0.00%)
occurrences (all)	2	2	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 128 (3.13%)	3 / 53 (5.66%)	1 / 75 (1.33%)
occurrences (all)	4	3	1

Non-serious adverse events	Comparator: Comparator: Pooled Population (Placebo)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	51 / 60 (85.00%)		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	4 / 60 (6.67%)		
occurrences (all)	4		
Fall			
subjects affected / exposed	4 / 60 (6.67%)		
occurrences (all)	5		
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	12 / 60 (20.00%)		
occurrences (all)	35		
Dizziness			

subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 4		
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all)	 17 / 60 (28.33%) 18 2 / 60 (3.33%) 2		
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	 5 / 60 (8.33%) 6		
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all)	 10 / 60 (16.67%) 14 1 / 60 (1.67%) 1 2 / 60 (3.33%) 3 7 / 60 (11.67%) 8 3 / 60 (5.00%) 4 1 / 60 (1.67%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	 12 / 60 (20.00%) 14		

Rhinorrhoea subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 3		
Oropharyngeal pain subjects affected / exposed occurrences (all)	7 / 60 (11.67%) 8		
Nasal congestion subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 2		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	5 / 60 (8.33%) 8		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3		
Myalgia subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1		
Pain in extremity subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 2		
Scoliosis subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 4		
Muscle contracture subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	14 / 60 (23.33%) 19		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	18 / 60 (30.00%) 33		

Rhinitis subjects affected / exposed occurrences (all)	6 / 60 (10.00%) 13		
Ear infection subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 4		
Gastroenteritis subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 4		
COVID-19 subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 5		
Pharyngitis streptococcal subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3		
Influenza subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 4		
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1		
Respiratory syncytial virus infection subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0		
Bronchitis subjects affected / exposed occurrences (all)	6 / 60 (10.00%) 6		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 August 2022	The primary reasons for amending the SRK-015-003 protocol were to add collection of antidrug antibodies at various visits, align the timing of vital sign and hypersensitivity monitoring, Change the version of the Columbia-Suicide Severity Rating Scale (C SSRS) to the Children's "baseline/screening" and the Children's "since last visit," which are more appropriate for clinical trials, continue blinding of treatment assignment for patients, Investigators, and site personnel until the completion of the extension trial to reduce the chances of introducing bias in measures assessed in the extension trial, clarify that the interim analysis and stopping the trial for early efficacy are optional and to clarify the time allowed between apitegromab doses, the required timing for pharmacokinetic (PK)-matched electrocardiograms (ECGs), eligibility for the extension trial, the end of study visit for patients who enroll in the extension trial, and overdose language/reporting procedures.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported