



Clinical trial results:

A Phase 2a, Open-Label Study Assessing the Pharmacokinetics, Safety, Tolerability, and Immunogenicity of a Single Dose of Subcutaneous Anti-Spike SARS-CoV-2 Monoclonal Antibodies Casirivimab and Imdevimab in High-Risk Pediatric Subjects Under 12 Years of Age

Summary

EudraCT number	2021-004590-30
Trial protocol	Outside EU/EEA
Global end of trial date	01 June 2022

Results information

Result version number	v1 (current)
This version publication date	15 December 2022
First version publication date	15 December 2022

Trial information

Trial identification

Sponsor protocol code	R10933-10987-COV-2121
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04992273
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Regeneron Pharmaceuticals, Inc.
Sponsor organisation address	777 Old Saw Mill River Road, Tarrytown, United States, NY
Public contact	Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 8447346643, clinicaltrials@regeneron.com
Scientific contact	Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 8447346643, clinicaltrials@regeneron.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-002964-PIP01-21
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 June 2022
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	01 June 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This was an open-label, phase 2a study to assess the pharmacokinetics, safety, tolerability, and immunogenicity of casirivimab+imdevimab in participants <12 years old who were not infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) but are at high risk to develop severe coronavirus disease 2019 (COVID-19) if they became infected.

Protection of trial subjects:

It is the responsibility of both the sponsor and the investigator(s) to ensure that this clinical study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with the ICH guidelines for GCP and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 September 2021
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 States: 7
Worldwide total number of subjects	7
EEA total number of subjects	0

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)	1
Children (2-11 years)	6
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 7 participants were screened & enrolled into Group A (≥ 10 kg to < 40 kg). One discontinued at week 9 (lost to follow-up). Participants were subsequently divided into 2 groups: 2 participants in Group A1 (≥ 20 kg to < 40 kg) & 5 in Group A2 (≥ 10 kg to < 20 kg) & received different doses. All participants were enrolled & treated.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
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Arm title	≥ 20 kg to < 40 kg
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Arm description:

Single dose of casirivimab+imdevimab, that was the body weight dose equivalent to the 1200 mg adult dose (600 mg of casirivimab and 600 mg of imdevimab) administered as 1 to 4 subcutaneous (SC) injections based on body weight.

Arm type	Experimental
Investigational medicinal product name	casirivimab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

600 milligram (mg) administered as 1 to 4 subcutaneous (SC) injections based on body weight

Investigational medicinal product name	imdevimab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

600 milligram (mg) administered as 1 to 4 subcutaneous (SC) injections based on body weight

Arm title	≥ 10 kg to < 20 kg
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Arm description:

Single dose of casirivimab+imdevimab, that was the body weight dose equivalent to the 1200 mg adult dose (600 mg of casirivimab and 600 mg of imdevimab) administered as 1 to 4 subcutaneous (SC) injections based on body weight.

Arm type	Experimental
Investigational medicinal product name	casirivimab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

600 milligram (mg) administered as 1 to 4 subcutaneous (SC) injections based on body weight

Investigational medicinal product name	imdevimab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

600 milligram (mg) administered as 1 to 4 subcutaneous (SC) injections based on body weight

Number of subjects in period 1	≥20 kg to <40 kg	≥10 kg to <20 kg
Started	2	5
Completed	2	4
Not completed	0	1
Lost to follow-up	-	1

Baseline characteristics

Reporting groups

Reporting group title	≥20 kg to <40 kg
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Reporting group description:

Single dose of casirivimab+imdevimab, that was the body weight dose equivalent to the 1200 mg adult dose (600 mg of casirivimab and 600 mg of imdevimab) administered as 1 to 4 subcutaneous (SC) injections based on body weight.

Reporting group title	≥10 kg to <20 kg
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Reporting group description:

Single dose of casirivimab+imdevimab, that was the body weight dose equivalent to the 1200 mg adult dose (600 mg of casirivimab and 600 mg of imdevimab) administered as 1 to 4 subcutaneous (SC) injections based on body weight.

Reporting group values	≥20 kg to <40 kg	≥10 kg to <20 kg	Total
Number of subjects	2	5	7
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	1	1
Children (2-11 years)	2	4	6
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	9.5	3.0	
standard deviation	± 2.12	± 1.58	-
Sex: Female, Male			
Units: Participants			
Female	1	4	5
Male	1	1	2
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	1	1
White	2	4	6
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	1	0	1
Not Hispanic or Latino	1	5	6

Unknown or Not Reported	0	0	0
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Subject analysis sets

Subject analysis set title	≥10 kg to <40 kg
Subject analysis set type	Full analysis

Subject analysis set description:

Single dose of casirivimab+imdevimab, that was the body weight dose equivalent to the 1200 mg adult dose administered as 1 to 4 subcutaneous (SC) injections based on body weight.

Reporting group values	≥10 kg to <40 kg		
Number of subjects	7		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	1		
Children (2-11 years)	6		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age Continuous			
Units: Years			
arithmetic mean			
standard deviation	±		
Sex: Female, Male			
Units: Participants			
Female			
Male			
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native			
Asian			
Native Hawaiian or Other Pacific Islander			
Black or African American			
White			
More than one race			
Unknown or Not Reported			
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino			
Not Hispanic or Latino			
Unknown or Not Reported			

End points

End points reporting groups

Reporting group title	≥20 kg to <40 kg
Reporting group description: Single dose of casirivimab+imdevimab, that was the body weight dose equivalent to the 1200 mg adult dose (600 mg of casirivimab and 600 mg of imdevimab) administered as 1 to 4 subcutaneous (SC) injections based on body weight.	
Reporting group title	≥10 kg to <20 kg
Reporting group description: Single dose of casirivimab+imdevimab, that was the body weight dose equivalent to the 1200 mg adult dose (600 mg of casirivimab and 600 mg of imdevimab) administered as 1 to 4 subcutaneous (SC) injections based on body weight.	
Subject analysis set title	≥10 kg to <40 kg
Subject analysis set type	Full analysis
Subject analysis set description: Single dose of casirivimab+imdevimab, that was the body weight dose equivalent to the 1200 mg adult dose administered as 1 to 4 subcutaneous (SC) injections based on body weight.	

Primary: Concentrations of casirivimab+imdevimab in serum over time

End point title	Concentrations of casirivimab+imdevimab in serum over time ^[1]
End point description: Concentrations reported in milligrams per Liter (mg/L)	
End point type	Primary
End point timeframe: Up to 24 weeks	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics were performed on this outcome measure.

End point values	≥10 kg to <40 kg			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: mg/L				
arithmetic mean (standard deviation)				
Day 0	0 (± 0)			
Day 14	239.0 (± 36.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment-Emergent Adverse Events (TEAEs)

End point title	Number of Participants with Treatment-Emergent Adverse Events (TEAEs)
End point description:	

End point type	Secondary
End point timeframe:	
Through end of study, approximately 24 weeks	

End point values	≥20 kg to <40 kg	≥10 kg to <20 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	5		
Units: Participants	2	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Severity of TEAEs

End point title	Severity of TEAEs
End point description:	
End point type	Secondary
End point timeframe:	
Through end of study, approximately 24 weeks	

End point values	≥20 kg to <40 kg	≥10 kg to <20 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	5		
Units: Participants				
Infections and Infestations - Grade 1	1	1		
Infections and Infestations - Grade 2	1	1		
Infections and Infestations - Grade 3	0	0		
Infections and Infestations - Grade 4	0	0		
Infections and Infestations - Grade 5	0	0		
Respiratory disorders - Grade 1	0	1		
Respiratory disorders - Grade 2	1	1		
Respiratory disorders - Grade 3	0	0		
Respiratory disorders - Grade 4	0	0		
Respiratory disorders - Grade 5	0	0		
Nervous system disorders - Grade 1	0	1		
Nervous system disorders - Grade 2	0	0		
Nervous system disorders - Grade 3	0	0		
Nervous system disorders - Grade 4	0	0		
Nervous system disorders - Grade 5	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Grade ≥ 3 Injection Site Reactions

End point title | Number of Participants with Grade ≥ 3 Injection Site Reactions

End point description:

End point type | Secondary

End point timeframe:

Through Day 4

End point values	≥ 20 kg to <40 kg	≥ 10 kg to <20 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	5		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with grade ≥ 3 hypersensitivity reactions

End point title | Number of participants with grade ≥ 3 hypersensitivity reactions

End point description:

End point type | Secondary

End point timeframe:

Through Day 4

End point values	≥ 20 kg to <40 kg	≥ 10 kg to <20 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	5		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity as measured by ADA to imdevimab over time

End point title Immunogenicity as measured by ADA to imdevimab over time

End point description:

Negative response

End point type Secondary

End point timeframe:

Up to 24 weeks

End point values	≥20 kg to <40 kg	≥10 kg to <20 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	4		
Units: Participants	2	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity as measured by anti-drug antibodies (ADA) to casirivimab over time

End point title Immunogenicity as measured by anti-drug antibodies (ADA) to casirivimab over time

End point description:

Negative response

End point type Secondary

End point timeframe:

Up to 24 weeks

End point values	≥20 kg to <40 kg	≥10 kg to <20 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	4		
Units: Participants	2	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity as measured by neutralizing antibodies (NAb) to casirivimab over time

End point title	Immunogenicity as measured by neutralizing antibodies (NAb) to casirivimab over time			
End point description:				
End point type	Secondary			
End point timeframe:				
Up to 24 weeks				

End point values	≥20 kg to <40 kg	≥10 kg to <20 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[2]	0 ^[3]		
Units: Antibodies				
number (not applicable)				

Notes:

[2] - Neutralizing antibody (NAb) analysis data was not collected.

[3] - Neutralizing antibody (NAb) analysis data was not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity as measured by NAb to imdevimab over time

End point title	Immunogenicity as measured by NAb to imdevimab over time			
End point description:				
End point type	Secondary			
End point timeframe:				
Up to 24 weeks				

End point values	≥20 kg to <40 kg	≥10 kg to <20 kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[4]	0 ^[5]		
Units: Antibodies				
number (not applicable)				

Notes:

[4] - Neutralizing antibody (NAb) analysis data was not collected.

[5] - Neutralizing antibody (NAb) analysis data was not collected.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose to week 24

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.0
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Reporting groups

Reporting group title	Group A2 \geq 10 kg to <20 kg
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Reporting group description:

Single dose of casirivimab+imdevimab, that was the body weight dose equivalent to the 1200 mg adult dose administered as 1 to 4 subcutaneous (SC) injections based on body weight.

Reporting group title	Group A1 \geq 20 kg to <40 kg
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Reporting group description:

Single dose of casirivimab+imdevimab, that was the body weight dose equivalent to the 1200 mg adult dose administered as 1 to 4 subcutaneous (SC) injections based on body weight.

Serious adverse events	Group A2 \geq 10 kg to <20 kg	Group A1 \geq 20 kg to <40 kg	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Group A2 \geq 10 kg to <20 kg	Group A1 \geq 20 kg to <40 kg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 5 (60.00%)	2 / 2 (100.00%)	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 5 (20.00%)	1 / 2 (50.00%)	
occurrences (all)	1	1	
Cough variant asthma			

subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 2 (0.00%) 0	
Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 2 (50.00%) 1	
Infections and infestations			
COVID-19 subjects affected / exposed occurrences (all)	2 / 5 (40.00%) 2	1 / 2 (50.00%) 1	
Pneumonia viral subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 2 (50.00%) 1	
Gastroenteritis subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 2 (0.00%) 0	
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 2 (50.00%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 September 2021	Updated route of administration in participants with lower body weight (subcutaneous rather than intramuscular), included additional sample collections for drug concentration assessment at later time points, and addition of an adverse event of special interest (AESI).
08 March 2022	Updates included shortening length of follow-up period from 225 days to 169 days (32 weeks to 24 weeks), and to add that the end of study visit (EOS) visit is required to be performed in person.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
23 December 2021	The study was paused for new enrollment on 23 Dec 2021 due to the increasing prevalence of the Omicron-lineage variants and the lack of sufficient neutralization by casirivimab+imdevimab of Omicron-lineage variants in vitro. Study was not restarted and was terminated on 28 Jun 2022. The participants who had been enrolled prior to the pause date continued to participate in study visits and study activities according to the protocol.	-

Notes:

Limitations and caveats

None reported