



Clinical trial results:

A Randomized, Double-blind, Placebo-controlled, Study to Investigate the Safety, Pharmacokinetics, and Pharmacodynamics of Garadacimab in Participants with Idiopathic Pulmonary Fibrosis

Summary

EudraCT number	2021-003162-12
Trial protocol	DE DK AT PL IT BE ES
Global end of trial date	02 January 2024

Results information

Result version number	v1 (current)
This version publication date	07 December 2024
First version publication date	07 December 2024

Trial information

Trial identification

Sponsor protocol code	CSL312_2002
-----------------------	-------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05130970
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CSL Behring LLC
Sponsor organisation address	1020 First Avenue, King of Prussia, Pennsylvania, United States, 19406
Public contact	Trial Registration Coordinator, CSL Behring LLC, +1 610-878-4000, clinicaltrials@cs Behring.com
Scientific contact	Trial Registration Coordinator, CSL Behring LLC, +1 610-878-4000, clinicaltrials@cs Behring.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
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	22 March 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	02 January 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to investigate the safety of Garadacimab in participants with Idiopathic pulmonary fibrosis (IPF).

Protection of trial subjects:

This study was carried out in accordance with the International Council for Harmonisation (ICH) Good Clinical Practice (GCP) guidelines, the ethical principles that have their origin in the Declaration of Helsinki, all applicable national and local regulations, and Standard Operating Procedures for clinical research and development at CSL Behring. The study protocol and all amendments were approved by the Independent Ethics Committees (IEC)/ institutional review boards (IRBs) of the participating centers. Participant informed consent was obtained and documented according to the provisions of ICH GCP and applicable regulatory requirements. Written informed consent was provided by each participant before any protocol-specific procedures were carried out.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 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	Poland: 9
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Denmark: 5
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	United Kingdom: 8
Country: Number of subjects enrolled	United States: 40
Country: Number of subjects enrolled	Australia: 1
Worldwide total number of subjects	81
EEA total number of subjects	31

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)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	5
From 65 to 84 years	73
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 47 study sites in 11 countries (Australia, Austria, Belgium, Canada, Denmark, Germany, Italy, Poland, Spain, the United Kingdom [UK], and the United States of America [USA]). No participants from Italy were enrolled in the study.

Pre-assignment

Screening details:

A total of 131 potential participants were screened for eligibility. Out of these, 81 participants met all selection criteria and were enrolled in the study, and 50 individuals failed to meet the selection criteria and were not enrolled in the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Garadacimab

Arm description:

Participants received garadacimab intravenous (IV) loading dose followed by 3 subcutaneous (SC) doses.

Arm type	Experimental
Investigational medicinal product name	Garadacimab
Investigational medicinal product code	CSL312
Other name	Factor XIIa antagonist monoclonal antibody
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

Participants received garadacimab IV loading dose followed by 3 SC doses.

Arm title	Placebo
------------------	---------

Arm description:

Participants received a matching placebo IV loading dose, followed by 3 SC doses.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

Participants received a matching placebo IV loading dose, followed by 3 SC doses.

Number of subjects in period 1	Garadacimab	Placebo
Started	40	41
Completed	38	36
Not completed	2	5
Adverse event, serious fatal	1	1
Consent withdrawn by subject	1	1
Physician decision	-	1
Death	-	1
Lost to follow-up	-	1

Baseline characteristics

Reporting groups

Reporting group title	Garadacimab
Reporting group description: Participants received garadacimab intravenous (IV) loading dose followed by 3 subcutaneous (SC) doses.	
Reporting group title	Placebo
Reporting group description: Participants received a matching placebo IV loading dose, followed by 3 SC doses.	

Reporting group values	Garadacimab	Placebo	Total
Number of subjects	40	41	81
Age categorical Units: Subjects			
Less than or equal to (\leq 18) years	0	0	0
Between 18 and 65 years	2	3	5
Greater than or equal to (\geq) 65 years	38	38	76
Age continuous Units: years			
arithmetic mean	72.6	72.9	
standard deviation	\pm 6.19	\pm 6.17	-
Gender categorical Units: Subjects			
Female	14	21	35
Male	26	20	46

End points

End points reporting groups

Reporting group title	Garadacimab
Reporting group description: Participants received garadacimab intravenous (IV) loading dose followed by 3 subcutaneous (SC) doses.	
Reporting group title	Placebo
Reporting group description: Participants received a matching placebo IV loading dose, followed by 3 SC doses.	

Primary: Number of Participants With Treatment-emergent (TE) Serious Adverse Events (SAEs)

End point title	Number of Participants With Treatment-emergent (TE) Serious Adverse Events (SAEs) ^[1]
End point description: A TE SAE is defined as an SAE reported at or after the start of the first administration of study treatment. A SAE is defined as any untoward medical occurrence that at any dose results in: death, life-threatening event, initial or prolongation of existing hospitalization, disability or incapacity, congenital anomaly or birth defect, or any other medically significant event. This analysis was performed on the safety analysis set (SAS). The SAS was defined as all participants who received any portion of an IV infusion or SC injection of garadacimab or placebo.	
End point type	Primary
End point timeframe: Up to 22 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: Justification: Primary end point data were summarized by frequency counts and percentages as per protocol; no primary hypothesis was planned.	

End point values	Garadacimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	41		
Units: Participants	5	2		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With TE SAEs

End point title	Percentage of Participants With TE SAEs ^[2]
End point description: A TE SAE is defined as an SAE reported at or after the start of the first administration of study treatment. A SAE is defined as any untoward medical occurrence that at any dose results in: death, life-threatening event, initial or prolongation of existing hospitalization, disability or incapacity, congenital anomaly or birth defect, or any other medically significant event. This analysis was performed on the SAS. The SAS was defined as all participants who received any portion of an IV infusion or SC injection of garadacimab or placebo.	
End point type	Primary

End point timeframe:

Up to 22 weeks

Notes:

[2] - 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: Justification: Primary end point data were summarized by frequency counts and percentages as per protocol; no primary hypothesis was planned.

End point values	Garadacimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	41		
Units: Percentage of participants				
number (not applicable)	12.5	4.9		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With TE Adverse Events of Special Interests (AESIs)

End point title	Number of Participants With TE Adverse Events of Special Interests (AESIs) ^[3]
-----------------	---

End point description:

The following TEAEs were considered as AESIs: Bleeding events that were abnormal in the opinion of the investigator, thromboembolic events (non-systemic thrombosis [e.g., localized thrombosis associated with vascular access] was not considered an AESI), and severe hypersensitivity including anaphylaxis. This analysis was performed on the SAS. The SAS was defined as all participants who received any portion of an IV infusion or SC injection of garadacimab or placebo.

End point type	Primary
----------------	---------

End point timeframe:

Up to 22 weeks

Notes:

[3] - 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: Justification: Primary end point data were summarized by frequency counts and percentages as per protocol; no primary hypothesis was planned.

End point values	Garadacimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	41		
Units: Participants	2	0		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With TE-AESIs

End point title	Percentage of Participants With TE-AESIs ^[4]
-----------------	---

End point description:

The following TEAEs were considered as AESIs: Bleeding events that were abnormal in the opinion of the Investigator, Thromboembolic events (non-systemic thrombosis [e.g., localized thrombosis associated with vascular access] was not considered an AESI), and Severe hypersensitivity including anaphylaxis. This analysis was performed on the SAS. The SAS was defined as all participants who received any portion of an IV infusion or SC injection of garadacimab or placebo.

End point type	Primary
----------------	---------

End point timeframe:

Up to 22 weeks

Notes:

[4] - 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: Justification: Primary end point data were summarized by frequency counts and percentages as per protocol; no primary hypothesis was planned.

End point values	Garadacimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	41		
Units: Percentage of participants				
number (not applicable)	5.0	0.0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Garadacimab Induced Anti-drug Antibodies (ADAs) in Plasma

End point title	Number of Participants With Garadacimab Induced Anti-drug Antibodies (ADAs) in Plasma ^[5]
-----------------	--

End point description:

This analysis was performed on the SAS. The SAS was defined as all participants who received any portion of an IV infusion or SC injection of garadacimab or placebo. Here, number of subjects analyzed (N) included all subjects who were evaluated for this endpoint. Number analyzed (n), included all subjects who were evaluated for this endpoint for the specified timepoint.

End point type	Primary
----------------	---------

End point timeframe:

At Day 36 and Day 92 after the first treatment

Notes:

[5] - 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: Justification: Primary end point data were summarized by frequency counts and percentages as per protocol; no primary hypothesis was planned.

End point values	Garadacimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	37		
Units: Participants				
At Day 36 (n=39,37)	1	2		
At Day 92 (n=38, 36)	1	1		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Garadacimab Induced ADAs in Plasma

End point title	Percentage of Participants With Garadacimab Induced ADAs in Plasma ^[6]
-----------------	---

End point description:

This analysis was performed on the SAS. The SAS was defined as all participants who received any portion of an IV infusion or SC injection of garadacimab or placebo. Here, number of subjects analyzed (N) included all subjects who were evaluated for this endpoint. Number analyzed (n), included all subjects who were evaluated for this endpoint for the specified timepoint.

End point type	Primary
----------------	---------

End point timeframe:

At Day 36 and Day 92 after the first treatment

Notes:

[6] - 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: Justification: Primary end point data were summarized by frequency counts and percentages as per protocol; no primary hypothesis was planned.

End point values	Garadacimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	37		
Units: Percentage of participants				
number (not applicable)				
At Day 36 (n= 39, 37)	2.6	5.4		
At Day 92 (n= 38, 36)	2.6	2.8		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With TE Clinically Significant Abnormalities in Laboratory Assessments Reported as Adverse Events (AEs)

End point title	Number of Participants With TE Clinically Significant Abnormalities in Laboratory Assessments Reported as Adverse Events (AEs) ^[7]
-----------------	---

End point description:

This analysis was performed on the SAS. The SAS was defined as all participants who received any portion of an IV infusion or SC injection of garadacimab or placebo.

End point type	Primary
----------------	---------

End point timeframe:

Up to 14 weeks after treatment

Notes:

[7] - 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: Justification: Primary end point data were summarized by frequency counts and percentages as per protocol; no primary hypothesis was planned.

End point values	Garadacimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	41		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With TE Clinically Significant Abnormalities in Laboratory Assessments Reported as AEs

End point title	Percentage of Participants With TE Clinically Significant Abnormalities in Laboratory Assessments Reported as AEs ^[8]
-----------------	--

End point description:

This analysis was performed on the SAS. The SAS was defined as all participants who received any portion of an IV infusion or SC injection of garadacimab or placebo.

End point type	Primary
----------------	---------

End point timeframe:

Up to 14 weeks after treatment

Notes:

[8] - 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: Justification: Primary end point data were summarized by frequency counts and percentages as per protocol; no primary hypothesis was planned.

End point values	Garadacimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	41		
Units: Percentage of participants				
number (not applicable)	0.0	0.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Trough Plasma Concentration (C_{trough}) After Subcutaneous (SC) Administration of Garadacimab

End point title	Trough Plasma Concentration (C _{trough}) After Subcutaneous (SC) Administration of Garadacimab ^[9]
-----------------	---

End point description:

This analysis was performed on pharmacokinetic analysis set (PKS). The PKS was defined as all participants in the SAS who received ≥ 1 dose of garadacimab with ≥ 1 measurable concentration of garadacimab after administration. Here, number of subjects analyzed (N) included all subjects who were evaluated for this endpoint. Number analyzed (n), included all subjects who were evaluated for this endpoint for the specified timepoint.

End point type	Secondary
----------------	-----------

End point timeframe:

At Day 36 and Day 64

Notes:

[9] - 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: As planned, statistics are reported for all PK parameters for the garadacimab arms only.

End point values	Garadacimab			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: Microgram/millilitre (mg/mL)				
arithmetic mean (standard deviation)				
At Day 36 (n=37)	16.445 (± 6.0362)			
At Day 64 (n=35)	17.123 (± 7.9383)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Plasma Concentration (C_{max}) (Last SC Dosing Interval Only) of Garadacimab

End point title	Maximum Plasma Concentration (C _{max}) (Last SC Dosing Interval Only) of Garadacimab ^[10]
-----------------	--

End point description:

This analysis was performed on PKS. The PKS was defined as all participants in the SAS who received ≥ 1 dose of garadacimab with ≥ 1 measurable concentration of garadacimab after administration. Here, the Overall Number of Participants Analyzed (N) included all participants who were evaluated for this outcome measure.

End point type	Secondary
----------------	-----------

End point timeframe:

After dosing on Day 64

Notes:

[10] - 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: As planned, statistics are reported for all PK parameters for the garadacimab arms only.

End point values	Garadacimab			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: ug/mL				
arithmetic mean (standard deviation)	37.41 (± 15.507)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Maximum Plasma Concentration (T_{max}) (Last SC Dosing

Interval Only) of Garadacimab

End point title	Time to Maximum Plasma Concentration (Tmax) (Last SC Dosing Interval Only) of Garadacimab ^[11]
-----------------	---

End point description:

This analysis was performed on PKS. The PKS was defined as all participants in the SAS who received ≥ 1 dose of garadacimab with ≥ 1 measurable concentration of garadacimab after administration. Here, the Overall Number of Participants Analyzed (N) included all participants who were evaluated for this outcome measure.

End point type	Secondary
----------------	-----------

End point timeframe:

After dosing on Day 64

Notes:

[11] - 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: As planned, statistics are reported for all PK parameters for the garadacimab arms only.

End point values	Garadacimab			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: Hours (h)				
median (full range (min-max))	165.4585 (45.250 to 478.633)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-time Curve Over the Dose Interval (AUC0-tau) (Last SC Dosing Interval Only) of Garadacimab

End point title	Area Under the Plasma Concentration-time Curve Over the Dose Interval (AUC0-tau) (Last SC Dosing Interval Only) of Garadacimab ^[12]
-----------------	--

End point description:

This analysis was performed on PKS. The PKS was defined as all participants in the SAS who received ≥ 1 dose of garadacimab with ≥ 1 measurable concentration of garadacimab after administration. Here, the Overall Number of Participants Analyzed (N) included all participants who were evaluated for this outcome measure.

End point type	Secondary
----------------	-----------

End point timeframe:

After dosing on Day 64

Notes:

[12] - 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: As planned, statistics are reported for all PK parameters for the garadacimab arms only.

End point values	Garadacimab			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: h*ug/mL				
arithmetic mean (standard deviation)	18094.6128 (\pm 6977.9036)			

Statistical analyses

No statistical analyses for this end point

Secondary: Ctrough After IV Administration of Garadacimab

End point title	Ctrough After IV Administration of Garadacimab ^[13]
-----------------	--

End point description:

This analysis was performed on PKS. The PKS was defined as all participants in the SAS who received ≥ 1 dose of garadacimab with ≥ 1 measurable concentration of garadacimab after administration. Here, the Overall Number of Participants Analyzed (N) included all participants who were evaluated for this outcome measure.

End point type	Secondary
----------------	-----------

End point timeframe:

At Day 8

Notes:

[13] - 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: As planned, statistics are reported for all PK parameters for the garadacimab arms only.

End point values	Garadacimab			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: ug/mL				
arithmetic mean (standard deviation)	18.6054 (\pm 7.9685)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax After IV Administration of Garadacimab

End point title	Cmax After IV Administration of Garadacimab ^[14]
-----------------	---

End point description:

This analysis was performed on PKS. The PKS was defined as all participants in the SAS who received ≥ 1 dose of garadacimab with ≥ 1 measurable concentration of garadacimab after administration. Here, the Overall Number of Participants Analyzed (N) included all participants who were evaluated for this outcome measure.

End point type	Secondary
----------------	-----------

End point timeframe:

After dosing on Day 1

Notes:

[14] - 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: As planned, statistics are reported for all PK parameters for the garadacimab arms only.

End point values	Garadacimab			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: ug/mL				
arithmetic mean (standard deviation)	79.636 (± 31.4406)			

Statistical analyses

No statistical analyses for this end point

Secondary: Tmax After IV Administration of Garadacimab

End point title	Tmax After IV Administration of Garadacimab ^[15]
End point description: This analysis was performed on PKS. The PKS was defined as all participants in the SAS who received ≥ 1 dose of garadacimab with ≥ 1 measurable concentration of garadacimab after administration.	
End point type	Secondary
End point timeframe: After dosing on Day 1	

Notes:

[15] - 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: As planned, statistics are reported for all PK parameters for the garadacimab arms only.

End point values	Garadacimab			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: h				
median (full range (min-max))	0.1000 (0.017 to 0.967)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in FXIIa-mediated Kallikrein Activity

End point title	Mean Change From Baseline in FXIIa-mediated Kallikrein Activity
End point description: This analysis was performed on pharmacodynamic analysis set (PDS). The PDS was defined as all participants in the SAS for whom analysis results were obtained for ≥ 1 of the exploratory biomarkers of interest. Here, the Overall Number of Participants Analyzed (N) included all participants who were	

evaluated for this outcome measure.

End point type	Secondary
End point timeframe:	
Baseline, and at Day 92	

End point values	Garadacimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	32		
Units: nmol/L/mins				
arithmetic mean (standard deviation)	-0.0258 (\pm 0.0657)	0.0072 (\pm 0.0706)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Percentage of Baseline in FXIIa-mediated Kallikrein Activity

End point title	Mean Percentage of Baseline in FXIIa-mediated Kallikrein Activity
-----------------	---

End point description:

Percent baseline is calculated by using the formula visit value / baseline value multiplied by 100, percent baseline is reported as percentage in the outcome measure. This analysis was performed on PDS. The PDS was defined as all participants in the SAS for whom analysis results were obtained for ≥ 1 of the exploratory biomarkers of interest. Here, number of subjects analyzed (N) included all subjects who were evaluated for this endpoint.

End point type	Secondary
End point timeframe:	
Baseline, and at Day 92	

End point values	Garadacimab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	32		
Units: percent baseline				
arithmetic mean (standard deviation)	129.56 (\pm 215.689)	124.83 (\pm 68.872)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 22 weeks

Adverse event reporting additional description:

This analysis was performed on the SAS. The SAS was defined as all participants who received any portion of an IV infusion or SC injection of garadacimab or placebo.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	26.1
--------------------	------

Reporting groups

Reporting group title	Garadacimab
-----------------------	-------------

Reporting group description:

Participants received garadacimab IV loading dose followed by 3 SC doses.

Reporting group title	Placebo
-----------------------	---------

Reporting group description:

Participants received a matching placebo IV loading dose, followed by 3 SC doses.

Serious adverse events	Garadacimab	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 40 (12.50%)	2 / 41 (4.88%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	1	1	
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Idiopathic pulmonary fibrosis			
subjects affected / exposed	3 / 40 (7.50%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute respiratory failure			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pneumothorax spontaneous subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

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

Non-serious adverse events	Garadacimab	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 40 (45.00%)	19 / 41 (46.34%)	
Investigations			
C-reactive protein increased			
subjects affected / exposed	1 / 40 (2.50%)	3 / 41 (7.32%)	
occurrences (all)	3	3	
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 40 (5.00%)	4 / 41 (9.76%)	
occurrences (all)	3	6	
Headache			
subjects affected / exposed	2 / 40 (5.00%)	1 / 41 (2.44%)	
occurrences (all)	2	1	
Presyncope			
subjects affected / exposed	2 / 40 (5.00%)	0 / 41 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			

Fatigue subjects affected / exposed occurrences (all)	3 / 40 (7.50%) 4	3 / 41 (7.32%) 4	
Non-cardiac chest pain subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 3	1 / 41 (2.44%) 1	
Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 3	0 / 41 (0.00%) 0	
Diarrhoea subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2	5 / 41 (12.20%) 8	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2	5 / 41 (12.20%) 5	
Dyspnoea subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1	4 / 41 (9.76%) 6	
Idiopathic pulmonary fibrosis subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2	1 / 41 (2.44%) 1	
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2	0 / 41 (0.00%) 0	
Infections and infestations Bronchitis subjects affected / exposed occurrences (all)	3 / 40 (7.50%) 4	2 / 41 (4.88%) 2	
COVID-19 subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2	2 / 41 (4.88%) 2	
Urinary tract infection			

subjects affected / exposed	3 / 40 (7.50%)	1 / 41 (2.44%)	
occurrences (all)	4	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 November 2021	<ul style="list-style-type: none">• Clarified the process for breaking the blind in an emergency situation.
18 January 2022	<ul style="list-style-type: none">• Modified study halting criteria.
18 October 2022	<ul style="list-style-type: none">• Removed exclusion criterion 8 to allow administration of non-live influenza virus vaccines or SARS-CoV-2 vaccines before and during study participation.• Updated the Schedule of Assessments to clarify the INR and prothrombin measurement procedures• Revised wording in exclusion criterion 12 to clarify that standard of care medication was also prohibited during the Treatment and Observation Period.• Revised wording for SC administration regarding anatomical site of injection and the number of injections per dose.• Added an additional citation and reference for DLCO.• Low-dose aspirin was specifically mentioned in the table of permitted therapies.• For clarification, the wording for halting criteria due to ECG prolongation was revised.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported