Clinical trial results:
A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study Assessing the Efficacy and Safety of Anti-Spike SARS-CoV-2 Monoclonal Antibodies in Preventing SARS-CoV-2 Infection in Household Contacts of Individuals Infected with SARS-CoV-2

Summary

EudraCT number	2020-003654-71
Trial protocol	RO GR
Global end of trial date	04 October 2021

Results information

Result version number	v1 (current)
This version publication date	18 April 2022
First version publication date	18 April 2022

Trial information

Trial identification

Sponsor protocol code	R10933-10987-COV-2069

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Regeneron Pharmaceuticals, Inc.
Sponsor organisation address	777 Old Saw Mill River Rd., Tarrytown, United States, 10591
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)	EMEA-002964-PIP01-21, EMEA-002964-PIP01-21
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes
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	04 October 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 October 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This randomized, double-blind, placebo-controlled master protocol assessed the safety, tolerability, and efficacy of casirivimab+imdevimab in adult subjects and pediatric subjects who are household contacts of the first known household member infected with SARS-CoV-2 (index case).

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with the International Conference on Harmonisation (ICH) guidelines for Good Clinical Practice (GCP) and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 July 2020
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: 3075
Country: Number of subjects enrolled	Romania: 97
Country: Number of subjects enrolled	Moldova, Republic of: 126
Worldwide total number of subjects	3298
EEA total number of subjects	97

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)	1
Adolescents (12-17 years)	145
Adults (18-64 years)	2867
From 65 to 84 years	274

85 years and over	11

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Of 3375 participants screened, 3298 participants were randomized and 3270 participants were treated. 77 participants were screen failures and 28 participants were randomized but not treated.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort A: Placebo of R10933 + R10987

Arm description:

Cohort A: Placebo of R10933 + R10987 Adult and Adolescent Subjects (≥12years) Who Are SARS-CoV-2 RT-qPCR negative at baseline

Arm type	Placebo
Investigational medicinal product name	Placebo for casirivimab and placebo for imdevimab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

1 to 4 injections in the abdomen or thigh
• SC: For adults and pediatric participants ≥10 kg. Investigators had the option to use an infusion pump for SC administration of study drug containing the combined
volume with both mAbs.

Arm title	Cohort A: R10933 + R10987

Arm description:

Cohort A: R10933 + R10987 Adult and Adolescent Subjects (≥12years) Who Are SARS-CoV-2 RT-qPCR negative at baseline

Arm type	Experimental
Investigational medicinal product name	casirivimab (REGN10933) and imdevimab (REGN10987)
Investigational medicinal product code	R10933 + R10987
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

1 to 4 injections in the abdomen or thigh
• SC: For adults and pediatric participants ≥10 kg. Investigators had the option to use an infusion pump for SC administration of study drug containing the combined volume with both mAbs.

Arm title	Cohort A1: Placebo of R10933 + R10987

Arm description:

Cohort A1: Placebo of R10933 + R10987 Pediatric Subjects (<12 years) with SARS-CoV-2 RT-qPCR Negative

Arm type	Placebo

Investigational medicinal product name	Placebo for casirivimab and placebo for imdevimab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

1 to 4 injections in the abdomen or thigh
• SC: pediatric participants ≥10 kg. Investigators had the option to use an infusion pump for SC administration of study drug containing the combined volume with both mAbs.

Arm title	Cohort B: Placebo of R10933 + R10987

Arm description:

Cohort B: Placebo of R10933 + R10987 Adult and Adolescent Subjects (≥12years) Who Are SARS-CoV-2 RT-qPCR Positive

Arm type	Placebo
Investigational medicinal product name	Placebo for casirivimab and placebo for imdevimab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

1 to 4 injections in the abdomen or thigh
• SC: For adults and pediatric participants ≥10 kg. Investigators had the option to use an infusion pump for SC administration of study drug containing the combined
volume with both mAbs.

Arm title	Cohort B: R10933 + R10987

Arm description:

Cohort B: R10933 + R10987 Adult and Adolescent Subjects (≥12years) who Are SARS-CoV-2 RT-qPCR Positive

Arm type	Experimental
Investigational medicinal product name	casirivimab (REGN10933) and imdevimab (REGN10987)
Investigational medicinal product code	R10933 + R10987
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

1 to 4 injections in the abdomen or thigh
• SC: For adults and pediatric participants ≥10 kg. Investigators had the option to use an infusion pump for SC administration of study drug containing the combined volume with both mAbs.

Arm title	Undetermined: Placebo of R10933 + R10987

Arm description:

Undetermined: Placebo of R10933 + R10987 Adult and Adolescent subjects (≥12 years) whose baseline RT-qPCR status was inconclusive or missing

Arm type	Placebo
Investigational medicinal product name	Placebo for casirivimab and placebo for imdevimab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

1 to 4 injections in the abdomen or thigh
• SC: For adults and pediatric participants ≥10 kg. Investigators had the option to use an infusion pump for SC administration of study drug containing the combined
volume with both mAbs.

Arm title	Undetermined: R10933 + R10987

Arm description:

Undetermined: R10933 + R10987 Adult and Adolescent subjects (≥12 years) whose baseline RT-qPCR status was inconclusive or missing

Arm type	Experimental
Investigational medicinal product name	casirivimab (REGN10933) and imdevimab (REGN10987)
Investigational medicinal product code	R10933 + R10987
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

1 to 4 injections in the abdomen or thigh
• SC: For adults and pediatric participants ≥10 kg. Investigators had the option to use an infusion pump for SC administration of study drug containing the combined volume with both mAbs.

Number of subjects in period 1	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987	Cohort A1: Placebo of R10933 + R10987
Started	1430	1441	1
Randomized and treated	1428	1439	1
Completed	1343	1368	1
Not completed	87	73	0
Adverse event, serious fatal	2	3	-
Physician decision	1	2	-
Consent withdrawn by subject	46	40	-
Lost to follow-up	38	28	-

Number of subjects in period 1	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987	Undetermined: Placebo of R10933 + R10987
Started	173	166	53
Randomized and treated	170	165	44
Completed	150	157	41
Not completed	23	9	12
Adverse event, serious fatal	-	-	-
Physician decision	2	-	2
Consent withdrawn by subject	18	6	8
Lost to follow-up	3	3	2

Number of subjects in period 1	Undetermined: R10933 + R10987
Started	34
Randomized and treated	23
Completed	22
Not completed	12
Adverse event, serious fatal	-
Physician decision	5
Consent withdrawn by subject	6

Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	Cohort A: Placebo of R10933 + R10987
Reporting group description:	
Cohort A: Placebo of R10933 + R10987 Adult and Adolescent Subjects (≥12years) Who Are SARS-CoV-2 RT-qPCR negative at baseline	
Reporting group title	Cohort A: R10933 + R10987
Reporting group description:	
Cohort A: R10933 + R10987 Adult and Adolescent Subjects (≥12years) Who Are SARS-CoV-2 RT-qPCR negative at baseline	
Reporting group title	Cohort A1: Placebo of R10933 + R10987
Reporting group description:	
Cohort A1: Placebo of R10933 + R10987 Pediatric Subjects (<12 years) with SARS-CoV-2 RT-qPCR Negative	
Reporting group title	Cohort B: Placebo of R10933 + R10987
Reporting group description:	
Cohort B: Placebo of R10933 + R10987 Adult and Adolescent Subjects (≥12years) Who Are SARS-CoV-2 RT-qPCR Positive	
Reporting group title	Cohort B: R10933 + R10987
Reporting group description:	
Cohort B: R10933 + R10987 Adult and Adolescent Subjects (≥12years) who Are SARS-CoV-2 RT-qPCR Positive	
Reporting group title	Undetermined: Placebo of R10933 + R10987
Reporting group description:	
Undetermined: Placebo of R10933 + R10987 Adult and Adolescent subjects (≥12 years) whose baseline RT-qPCR status was inconclusive or missing	
Reporting group title	Undetermined: R10933 + R10987
Reporting group description:	
Undetermined: R10933 + R10987 Adult and Adolescent subjects (≥12 years) whose baseline RT-qPCR status was inconclusive or missing	

Reporting group values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987	Cohort A1: Placebo of R10933 + R10987
Number of subjects	1430	1441	1
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	0	0
Children (2-11 years)	0	0	1
Adolescents (12-17 years)	47	52	0
Adults (18-64 years)	1272	1263	0
From 65-84 years	105	125	0
85 years and over	6	1	0
Age Continuous Units: years			
arithmetic mean	42.4	42.1	10.0
standard deviation	± 15.71	± 15.99	± 0.0

Sex: Female, Male Units: participants			
Female	738	780	0
Male	692	661	1
Race/Ethnicity, Customized Units: Subjects			
White	1193	1196	1
Black or African American	161	164	0
Asian	37	42	0
American Indian or Alaska Native	5	4	0
Native Hawaiian or Other Pacific Islander	2	3	0
Other	32	32	0

Reporting group values	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987	Undetermined: Placebo of R10933 + R10987
Number of subjects	173	166	53
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	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	20	23	2
Adults (18-64 years)	130	127	45
From 65-84 years	21	15	5
85 years and over	2	1	1
Age Continuous Units: years			
arithmetic mean	41.8	39.5	41.8
standard deviation	± 18.1	± 17.81	± 16.73
Sex: Female, Male Units: participants			
Female	97	80	21
Male	76	86	32
Race/Ethnicity, Customized Units: Subjects			
White	149	140	46
Black or African American	11	9	4
Asian	8	11	3
American Indian or Alaska Native	1	1	0
Native Hawaiian or Other Pacific Islander	0	0	0
Other	4	5	0

Reporting group values	Undetermined: R10933 + R10987	Total	
Number of subjects	34	3298	

Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	1	
Adolescents (12-17 years)	1	145	
Adults (18-64 years)	30	2867	
From 65-84 years	3	274	
85 years and over	0	11	
Age Continuous Units: years			
arithmetic mean	39.0		
standard deviation	± 15.3	-	
Sex: Female, Male Units: participants			
Female	20	1736	
Male	14	1562	
Race/Ethnicity, Customized Units: Subjects			
White	29	2754	
Black or African American	1	350	
Asian	2	103	
American Indian or Alaska Native	0	11	
Native Hawaiian or Other Pacific Islander	0	5	
Other	2	75	

End points

End points reporting groups

Reporting group title	Cohort A: Placebo of R10933 + R10987
Reporting group description:	
Cohort A: Placebo of R10933 + R10987 Adult and Adolescent Subjects (≥12years) Who Are SARS-CoV-2 RT-qPCR negative at baseline	
Reporting group title	Cohort A: R10933 + R10987
Reporting group description:	
Cohort A: R10933 + R10987 Adult and Adolescent Subjects (≥12years) Who Are SARS-CoV-2 RT-qPCR negative at baseline	
Reporting group title	Cohort A1: Placebo of R10933 + R10987
Reporting group description:	
Cohort A1: Placebo of R10933 + R10987 Pediatric Subjects (<12 years) with SARS-CoV-2 RT-qPCR Negative	
Reporting group title	Cohort B: Placebo of R10933 + R10987
Reporting group description:	
Cohort B: Placebo of R10933 + R10987 Adult and Adolescent Subjects (≥12years) Who Are SARS-CoV-2 RT-qPCR Positive	
Reporting group title	Cohort B: R10933 + R10987
Reporting group description:	
Cohort B: R10933 + R10987 Adult and Adolescent Subjects (≥12years) who Are SARS-CoV-2 RT-qPCR Positive	
Reporting group title	Undetermined: Placebo of R10933 + R10987
Reporting group description:	
Undetermined: Placebo of R10933 + R10987 Adult and Adolescent subjects (≥12 years) whose baseline RT-qPCR status was inconclusive or missing	
Reporting group title	Undetermined: R10933 + R10987
Reporting group description:	
Undetermined: R10933 + R10987 Adult and Adolescent subjects (≥12 years) whose baseline RT-qPCR status was inconclusive or missing	
Subject analysis set title	Anti-drug Antibodies Analysis Set (AAS)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
The Anti-drug Antibodies Analysis set (AAS) includes all treated subjects who received study drug and had at least 1 non-missing ADA result after study drug administration. The AAS is based on the actual treatment received.	
Subject analysis set title	NAb Analysis Set
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
NAb analysis set includes all treated subjects who received any study drug (active or placebo), have at least one non-missing anti-casirivimab or anti-imdevimab antibody result following the first dose of study drug (active or placebo), and either tested negative at all ADA sampling times or tested positive for ADA with at least one non-missing NAb result after first dose of the study drug (active or placebo).	
Subject analysis set title	PKAS Analysis Set
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
PK analysis set (PKAS) includes all treated subjects who received any study drug and had at least 1 non-missing casirivimab or imdevimab concentration measurement following study drug administration, respectively. The PK analysis set is based on the actual treatment received (as treated) rather than as randomized.	

Primary: Cohort A: Percentage of participants who have a symptomatic RT-qPCR confirmed SARS-CoV-2 infection (broad-term) during the EAP

End point title	Cohort A: Percentage of participants who have a symptomatic RT-qPCR confirmed SARS-CoV-2 infection (broad-term) during the EAP[1]

End point description:

Symptomatic SARS-CoV-2 infection (broad-term) is defined as a positive central lab SARS-CoV-2 RT-qPCR result (either NP, nasal or saliva) associated with signs and symptoms with the onset date occurring within 14 days of a positive RT-qPCR during the EAP. Percentage estimated by Logistic Regression.

End point type	Primary

End point timeframe:

Up to 1 month

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: This endpoint is only applicable to participants in Cohort A.

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	752	753		
Units: Percentage of Participants				
number (not applicable)	7.8	1.4		

Statistical analyses

Statistical analysis title	Cohort A: R10933 + R10987 and Placebo
Comparison groups	Cohort A: R10933 + R10987 v Cohort A: Placebo of R10933 + R10987
Number of subjects included in analysis	1505
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.09
upper limit	0.332

Primary: Cohort B: Percentage of Participants who Subsequently Develop Signs and Symptoms (Broad-Term) within 14 Days of a Positive RT-qPCR at Baseline or during the EAP

End point title	Cohort B: Percentage of Participants who Subsequently Develop Signs and Symptoms (Broad-Term) within 14 Days of

	a Positive RT-qPCR at Baseline or during the EAP[2]

End point description:

End point type	Primary

End point timeframe:

Up to 8 months

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: This endpoint is only applicable to participants in Cohort B

End point values	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	100		
Units: Percentage of Participants				
number (not applicable)	42.5	28.4		

Statistical analyses

Statistical analysis title	Cohort B: R10933 + R10987 and Placebo
Comparison groups	Cohort B: R10933 + R10987 v Cohort B: Placebo of R10933 + R10987
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.038
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.298
upper limit	0.966

Primary: Cohort A and Cohort B: Number of participants with at least one treatment-emergent adverse event (TEAEs) and severity of TEAEs

End point title	Cohort A and Cohort B: Number of participants with at least one treatment-emergent adverse event (TEAEs) and severity of TEAEs[3][4]

End point description:

End point type	Primary

End point timeframe:

Up to 8 months

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: This endpoint is only applicable to participants in Cohort A

[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: This endpoint is only applicable to participants in Cohort A and Cohort B.

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1428	1439	170	165
Units: Participants				
# of participants with at least one TEAE	512	405	88	60
# of participants with at least one Grade 1 TEAE	384	284	61	51
# of participants with at least one Grade 2 TEAE	98	95	21	7
# of participants with at least one Grade 3 TEAE	26	21	6	2
# of participants with at least one Grade 4 TEAE	2	2	0	0
# of participants with at least one Grade 5 TEAE	2	3	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort A and Cohort B: Percentage of Participants with high viral load in Nasopharyngeal (NP) swab samples during the EAP

End point title	Cohort A and Cohort B: Percentage of Participants with high viral load in Nasopharyngeal (NP) swab samples during the EAP[5]
End point description:	
High viral load (> 4 log 10 copies/ml)	
End point type	Secondary
End point timeframe:	
Up to 1 month	

Notes:

[5] - 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: This endpoint is only applicable to participants in Cohort A and Cohort B.

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	749	745	101	98
Units: Percentage of Participants				
number (not applicable)	11.3	1.6	62.6	40.5

Statistical analyses

Statistical analysis title	Cohort A: R10933 + R10987 and Placebo
Comparison groups	Cohort A: R10933 + R10987 v Cohort A: Placebo of R10933 + R10987
Number of subjects included in analysis	1494
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.069
upper limit	0.236

Statistical analysis title	Cohort B: R10933 + R10987 and Placebo
Comparison groups	Cohort B: R10933 + R10987 v Cohort B: Placebo of R10933 + R10987
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0024
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.228
upper limit	0.728

Secondary: Cohort A: Number of weeks of symptomatic RT-qPCR confirmed SARS-CoV-2 infection (broad term) during the EAP

End point title	Cohort A: Number of weeks of symptomatic RT-qPCR confirmed SARS-CoV-2 infection (broad term) during the EAP[6]

End point description:

End point type	Secondary

End point timeframe:

Up to 1 month

Notes:

[6] - 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: This endpoint is only applicable to participants in Cohort A

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	752	753		
Units: weeks				
arithmetic mean (standard deviation)	0.25 (± 1.135)	0.02 (± 0.181)		

Statistical analyses

Statistical analysis title	Cohort A: R10933 + R10987 and Placebo
Comparison groups	Cohort A: R10933 + R10987 v Cohort A: Placebo of R10933 + R10987
Number of subjects included in analysis	1505
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Wilcoxon (Mann-Whitney)

Secondary: Cohort A and Cohort B: Number of weeks of high viral load in NP swab samples during the EAP

End point title	Cohort A and Cohort B: Number of weeks of high viral load in NP swab samples during the EAP[7]

End point description:

High viral load (> 4 log 10 copies/ml)

End point type	Secondary

End point timeframe:

Up to 1 month

Notes:

[7] - 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: This endpoint is only applicable to participants in Cohort A and Cohort B.

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	749	745	101	98
Units: weeks				
arithmetic mean (standard deviation)	0.18 (± 0.554)	0.02 (± 0.154)	0.81 (± 0.758)	0.49 (± 0.677)

Statistical analyses

Statistical analysis title	Cohort B: R10933 + R10987 and Placebo
Comparison groups	Cohort B: Placebo of R10933 + R10987 v Cohort B: R10933 + R10987
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Cohort A: R10933 + R10987 and Placebo
Comparison groups	Cohort A: Placebo of R10933 + R10987 v Cohort A: R10933 + R10987
Number of subjects included in analysis	1494
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Wilcoxon (Mann-Whitney)

Secondary: Cohort A: Number of weeks of RT-qPCR confirmed SARS-CoV-2 infection (regardless of symptoms) during the EAP

End point title	Cohort A: Number of weeks of RT-qPCR confirmed SARS-CoV-2 infection (regardless of symptoms) during the EAP[8]

End point description:

End point type	Secondary

End point timeframe:

Up to 1 month

Notes:

[8] - 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: This endpoint is only applicable to participants in Cohort A

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	752	753		
Units: weeks				
arithmetic mean (standard deviation)	0.31 (± 0.854)	0.05 (± 0.260)		

Statistical analyses

Statistical analysis title	Cohort A: R10933 + R10987 and Placebo
Comparison groups	Cohort A: R10933 + R10987 v Cohort A: Placebo of R10933 + R10987
Number of subjects included in analysis	1505
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Wilcoxon (Mann-Whitney)

Secondary: Cohort A: Percentage of participants who have a RT-qPCR confirmed SARS-CoV-2 infection (regardless of symptoms) during the EAP

End point title	Cohort A: Percentage of participants who have a RT-qPCR confirmed SARS-CoV-2 infection (regardless of symptoms) during the EAP[9]

End point description:

End point type	Secondary

End point timeframe:

Up to 1 month

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: This endpoint is only applicable to participants in Cohort A

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	752	753		
Units: Percentage of Participants				
number (not applicable)	14.56	5.00		

Statistical analyses

Statistical analysis title	Cohort A: R10933 + R10987 and Placebo
Comparison groups	Cohort A: R10933 + R10987 v Cohort A: Placebo of R10933 + R10987

Number of subjects included in analysis	1505
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.208
upper limit	0.456

Secondary: Cohort A: Percentage of participants in placebo group with a RT-qPCR confirmed SARS-CoV-2 infection during the EAP with an index case participating in study R10933-10987-COV-2067 (NCT04425629)

End point title	Cohort A: Percentage of participants in placebo group with a RT-qPCR confirmed SARS-CoV-2 infection during the EAP with an index case participating in study R10933-10987-COV-2067 (NCT04425629)[10]

End point description:

End point type	Secondary

End point timeframe:

Up to 1 month

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: This endpoint is only applicable to participants in Cohort A

End point values	Cohort A: Placebo of R10933 + R10987			
Subject group type	Reporting group			
Number of subjects analysed	186			
Units: Percentage of Participants				
number (not applicable)				
% with index case receiving R10933+R10987 in 2067	19.8			
% with index case receiving placebo in 2067	19.6			
% with index case treatment in 2067 not available	10.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort A: Percentage of participants with a symptomatic RT-qPCR confirmed SARS-CoV-2 infection (CDC definition) during the EAP

End point title	Cohort A: Percentage of participants with a symptomatic RT-qPCR confirmed SARS-CoV-2 infection (CDC definition) during the EAP[11]

End point description:

Symptomatic SARS-CoV-2 infection (CDC definition) is defined as a positive central lab SARS-CoV-2 RT-qPCR result (either NP, nasal or saliva) associated with signs and symptoms with the onset date occurring within 14 days of a positive RT-qPCR during the EAP. Percentage estimated by Logistic Regression.

End point type	Secondary

End point timeframe:

Up to 1 month

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: This endpoint is only applicable to participants in Cohort A

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	752	753		
Units: Percentage of participants				
number (not applicable)	5.9	0.8		

Statistical analyses

Statistical analysis title	Cohort A: R10933 + R10987 and Placebo
Comparison groups	Cohort A: Placebo of R10933 + R10987 v Cohort A: R10933 + R10987
Number of subjects included in analysis	1505
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.051
upper limit	0.286

Secondary: Cohort A: Number of weeks of symptomatic RT-qPCR-confirmed SARS-CoV-2 infection (CDC definition) during the EAP

End point title	Cohort A: Number of weeks of symptomatic RT-qPCR-confirmed SARS-CoV-2 infection (CDC definition) during the EAP[12]

End point description:

End point type	Secondary

End point timeframe:

Up to 1 month

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: This endpoint is only applicable to participants in Cohort A

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	752	753		
Units: weeks				
arithmetic mean (standard deviation)	0.21 (± 1.042)	0.01 (± 0.128)		

Statistical analyses

Statistical analysis title	Cohort A: R10933 + R10987 and Placebo
Comparison groups	Cohort A: R10933 + R10987 v Cohort A: Placebo of R10933 + R10987
Number of subjects included in analysis	1505
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Wilcoxon (Van Elteren Test)

Secondary: Cohort A: Percentage of participants who have a symptomatic RT-qPCR confirmed SARS-CoV-2 infection (strict-term) during the EAP

End point title	Cohort A: Percentage of participants who have a symptomatic RT-qPCR confirmed SARS-CoV-2 infection (strict-term) during the EAP[13]

End point description:

End point type	Secondary

End point timeframe:

Up to 1 month

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: This endpoint is only applicable to participants in Cohort A

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	752	753		
Units: Percentage of participants				
number (not applicable)	2.8	0.2		

Statistical analyses

Statistical analysis title	Cohort A: R10933 + R10987 and Placebo
Comparison groups	Cohort A: R10933 + R10987 v Cohort A: Placebo of R10933 + R10987
Number of subjects included in analysis	1505
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.02
upper limit	0.37

Secondary: Cohort A: Number of weeks of symptomatic RT-qPCR confirmed SARS-CoV-2 infection (strict-term) during the EAP

End point title	Cohort A: Number of weeks of symptomatic RT-qPCR confirmed SARS-CoV-2 infection (strict-term) during the EAP[14]

End point description:

End point type	Secondary

End point timeframe:

Up to 1 month

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: This endpoint is only applicable to participants in Cohort A

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	752	753		
Units: weeks				
arithmetic mean (standard deviation)	0.12 (± 0.843)	0.00 (± 0.084)		

Statistical analyses

Statistical analysis title	Cohort A: R10933 + R10987 and Placebo
Comparison groups	Cohort A: R10933 + R10987 v Cohort A: Placebo of R10933 + R10987
Number of subjects included in analysis	1505
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Wilcoxon (Van Elteren Test)

Secondary: Cohort A: Percentage of participants who have a RT-qPCR confirmed SARS-CoV-2 infections at each week in the EAP

End point title	Cohort A: Percentage of participants who have a RT-qPCR confirmed SARS-CoV-2 infections at each week in the EAP[15]

End point description:

End point type	Secondary

End point timeframe:

Week 1, Week 2, Week 3, Week 4

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: This endpoint is only applicable to participants in Cohort A

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	752	753		
Units: Percentage of participants				
number (not applicable)				
Week 1	8.9	3.1		
Week 2	8.5	1.1		
Week 3	7.7	0.7		
Week 4	5.6	0.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort A: Percentage of participants who have a symptomatic RT-qPCR confirmed SARS-CoV-2 infection (broad-term) at each week in the EAP

End point title	Cohort A: Percentage of participants who have a symptomatic RT-qPCR confirmed SARS-CoV-2 infection (broad-term) at each week in the EAP[16]

End point description:

End point type	Secondary

End point timeframe:

Week 1, Week 2, Week 3, Week 4

Notes:

[16] - 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: This endpoint is only applicable to participants in Cohort A

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	752	753		
Units: Percentage of participants				
number (not applicable)				
Week 1	5.2	1.2		
Week 2	4.8	0.4		
Week 3	3.3	0.0		
Week 4	2.1	0.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort A: Time-weighted average of viral load from the first positive SARS CoV-2 RT-qPCR in NP swab samples (that has an onset during the EAP) until the third weekly visit after the first positive test during the EAP

End point title	Cohort A: Time-weighted average of viral load from the first positive SARS CoV-2 RT-qPCR in NP swab samples (that has an onset during the EAP) until the third weekly visit after the first positive test during the EAP[17]

End point description:

End point type	Secondary

End point timeframe:

Up to 1 month

Notes:

[17] - 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: This endpoint is only applicable to participants in Cohort A

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107	36		
Units: log10 copies/mL				
least squares mean (standard error)	3.065 (± 0.243)	0.942 (± 0.317)		

Statistical analyses

Statistical analysis title	Cohort A: R10933 + R10987 and Placebo
Comparison groups	Cohort A: R10933 + R10987 v Cohort A: Placebo of R10933 + R10987
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Difference of LS Means
Point estimate	-2.123
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.707
upper limit	-1.539
Variability estimate	Standard error of the mean
Dispersion value	0.295

Secondary: Cohort A: Time-weighted average of viral load from the first positive SARS-CoV-2 RT-qPCR in NP swab samples (that has an onset during the EAP) until the second weekly visit after the first positive test during the EAP

End point title	Cohort A: Time-weighted average of viral load from the first positive SARS-CoV-2 RT-qPCR in NP swab samples (that has an onset during the EAP) until the second weekly visit after the first positive test during the EAP[18]

End point description:

End point type	Secondary

End point timeframe:

Up to 1 month

Notes:

[18] - 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: This endpoint is only applicable to participants in Cohort A

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107	36		
Units: log10 copies/mL				
least squares mean (standard error)	3.689 (± 0.281)	1.205 (± 0.368)		

Statistical analyses

Statistical analysis title	Cohort A: R10933 + R10987 and Placebo
Comparison groups	Cohort A: Placebo of R10933 + R10987 v Cohort A: R10933 + R10987
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Difference of LS Means
Point estimate	-2.483
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.161
upper limit	-1.806
Variability estimate	Standard error of the mean
Dispersion value	0.342

Secondary: Cohort A: Maximum SARS-CoV-2 RT-qPCR viral load in NP swab samples among individuals with ≥1 RT-qPCR positive that has an onset during the EAP

End point title	Cohort A: Maximum SARS-CoV-2 RT-qPCR viral load in NP swab samples among individuals with ≥1 RT-qPCR positive that has an onset during the EAP[19]

End point description:

End point type	Secondary

End point timeframe:

Up to 1 month

Notes:

[19] - 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: This endpoint is only applicable to participants in Cohort A

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107	36		
Units: log10 copies/mL				
least squares mean (standard error)	6.133 (± 0.301)	3.705 (± 0.402)		

Statistical analyses

Statistical analysis title	Cohort A: R10933 + R10987 and Placebo
Comparison groups	Cohort A: Placebo of R10933 + R10987 v Cohort A: R10933 + R10987
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Difference of LS Mean
Point estimate	-2.428
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.196
upper limit	-1.659
Variability estimate	Standard error of the mean
Dispersion value	0.389

Secondary: Cohort A: SARS-CoV-2 RT-qPCR viral load in NP swab samples corresponding to the onset of first positive RT-qPCR during the EAP

End point title	Cohort A: SARS-CoV-2 RT-qPCR viral load in NP swab samples corresponding to the onset of first positive RT-qPCR during the EAP[20]

End point description:

End point type	Secondary

End point timeframe:

Up to 1 month

Notes:

[20] - 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: This endpoint is only applicable to participants in Cohort A

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107	36		
Units: log10 copies/mL				
least squares mean (standard error)	6.141 (± 0.305)	3.700 (± 0.396)		

Statistical analyses

Statistical analysis title	Cohort A: R10933 + R10987 and Placebo
Comparison groups	Cohort A: Placebo of R10933 + R10987 v Cohort A: R10933 + R10987
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Difference of LS Mean
Point estimate	-2.441
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.194
upper limit	-1.688
Variability estimate	Standard error of the mean
Dispersion value	0.381

Secondary: Cohort A: Area under the curve (AUC) in viral load from the first positive SARS-CoV-2 RT-qPCR NP swab samples detected during the EAP until the first confirmed negative test

End point title	Cohort A: Area under the curve (AUC) in viral load from the first positive SARS-CoV-2 RT-qPCR NP swab samples detected during the EAP until the first confirmed negative test[21]

End point description:

End point type	Secondary

End point timeframe:

Up to 8 months

Notes:

[21] - 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: This endpoint is only applicable to participants in Cohort A

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	33		
Units: log10 copies/mL				
arithmetic mean (standard deviation)	65.982 (± 47.6933)	19.700 (± 14.8257)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort A: Total Number of medically attended visits in emergency rooms or urgent care centers related to a RT-qPCR confirmed SARS-CoV-2 infection that has an onset during the EAP

End point title	Cohort A: Total Number of medically attended visits in emergency rooms or urgent care centers related to a RT-qPCR confirmed SARS-CoV-2 infection that has an onset during the EAP[22]

End point description:

Medically attended visits referred to hospitalizations, Emergency Room visits, or visits at an Urgent Care center.

End point type	Secondary

End point timeframe:

Up to 1 month

Notes:

[22] - 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: This endpoint is only applicable to participants in Cohort A

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	752	753		
Units: medically attended visits	9	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort A: Percentage of participants with at least 1 COVID-19-related hospitalization or emergency room visit associated with a positive RT-qPCR during the EAP or all-cause death

End point title	Cohort A: Percentage of participants with at least 1 COVID-19-related hospitalization or emergency room visit associated with a positive RT-qPCR during the EAP or all-cause death[23]

End point description:

End point type	Secondary

End point timeframe:

Up to 1 month

Notes:

[23] - 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: This endpoint is only applicable to participants in Cohort A

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	752	753		
Units: Percentage of Participants				
number (not applicable)	0.5	0.0		

Statistical analyses

Statistical analysis title	Cohort A: R10933 + R10987 and Placebo

Statistical analysis description:

Testing if there is an association between the observed results and treatment received

Comparison groups	Cohort A: Placebo of R10933 + R10987 v Cohort A: R10933 + R10987
Number of subjects included in analysis	1505
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0621
Method	Fisher exact

Secondary: Cohort A: Percentage of participants requiring medically attended visits in emergency rooms or urgent care centers related to a RT-qPCR confirmed SARS CoV-2 infection that has an onset during the EAP

End point title	Cohort A: Percentage of participants requiring medically attended visits in emergency rooms or urgent care centers related to a RT-qPCR confirmed SARS CoV-2 infection that has an onset during the EAP[24]

End point description:

End point type	Secondary

End point timeframe:

Up to 1 month

Notes:

[24] - 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: This endpoint is only applicable to participants in Cohort A

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	752	753		
Units: Percentage of participants				
number (not applicable)	1.1	0.0		

Statistical analyses

Statistical analysis title	Cohort A: R10933 + R10987 and Placebo
Statistical analysis description: Testing if there is an association between the observed results and treatment received’	
Comparison groups	Cohort A: Placebo of R10933 + R10987 v Cohort A: R10933 + R10987
Number of subjects included in analysis	1505
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0038
Method	Fisher exact

Secondary: Cohort A: Percentage of participants hospitalized related to a RT-qPCR confirmed SARS-CoV-2 infection that has an onset during the EAP

End point title	Cohort A: Percentage of participants hospitalized related to a RT-qPCR confirmed SARS-CoV-2 infection that has an onset during the EAP[25]
End point description:	
End point type	Secondary
End point timeframe: Up to 8 months	

Notes:

[25] - 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: This endpoint is only applicable to participants in Cohort A

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	752	753		
Units: Percentage of participants				
number (not applicable)	0.1	0.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort A: Number of days of hospital and intensive care unit (ICU) stay in participants hospitalized for a RT-qPCR confirmed SARS-CoV-2 infection that has an onset during the EAP

End point title	Cohort A: Number of days of hospital and intensive care unit (ICU) stay in participants hospitalized for a RT-qPCR confirmed SARS-CoV-2 infection that has an onset during the EAP[26]

End point description:

End point type	Secondary

End point timeframe:

Up to 8 months

Notes:

[26] - 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: This endpoint is only applicable to participants in Cohort A

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	752	753		
Units: Days				
arithmetic mean (standard deviation)	0.01 (± 0.401)	0.00 (± 0.000)		

Statistical analyses

Statistical analysis title	Cohort A: R10933 + R10987 and Placebo
Comparison groups	Cohort A: Placebo of R10933 + R10987 v Cohort A: R10933 + R10987
Number of subjects included in analysis	1505
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.363
Method	Wilcoxon (Rank Sum)

Secondary: Cohort A: Number of days missed for daily responsibilities due to a RT-qPCR confirmed SARS-CoV-2 infection that has an onset during the EAP

End point title	Cohort A: Number of days missed for daily responsibilities due to a RT-qPCR confirmed SARS-CoV-2 infection that has an onset during the EAP[27]

End point description:

Daily responsibilities including work (employed adults) or school (students), daycare or family obligations/responsibilities (childcare or eldercare)

End point type	Secondary

End point timeframe:

Up to 1 month

Notes:

[27] - 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: This endpoint is only applicable to participants in Cohort A

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	752	753		
Units: days				
arithmetic mean (standard deviation)	0.98 (± 4.659)	0.15 (± 1.276)		

Statistical analyses

Statistical analysis title	Cohort A: R10933 + R10987 and Placebo
Comparison groups	Cohort A: Placebo of R10933 + R10987 v Cohort A: R10933 + R10987
Number of subjects included in analysis	1505
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Wilcoxon (Van Elteren Test)

Secondary: Cohort A: Proportion of baseline seropositive participants (based on central lab test) with TEAEs and severity of TEAEs

End point title	Cohort A: Proportion of baseline seropositive participants (based on central lab test) with TEAEs and severity of TEAEs[28]

End point description:

End point type	Secondary

End point timeframe:

Up to 8 months

Notes:

[28] - 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: This endpoint is only applicable to participants in Cohort A

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	296	337		
Units: participants				
with at least one TEAE	79	83		

with at least one serious TEAE	5	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort A and Cohort B: Incidence and Severity of symptomatic SARS-CoV-2 infections during the EAP

End point title	Cohort A and Cohort B: Incidence and Severity of symptomatic SARS-CoV-2 infections during the EAP[29]

End point description:

End point type	Secondary

End point timeframe:

Up to Day 29

Notes:

[29] - 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: This endpoint is only applicable to participants in Cohort A and Cohort B.

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1428	1439	170	165
Units: subjects				
Total Symptomatic COVID-19	81	15	57	35
Grade 1 Symptomatic COVID-19	68	11	43	33
Grade 2 Symptomatic COVID-19	11	4	12	2
Grade 3 Symptomatic COVID-19	2	0	2	0
Grade 4 Symptomatic COVID-19	0	0	0	0
Grade 5 Symptomatic COVID-19	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort A and Cohort B: Incidence and Severity of symptomatic SARS-CoV-2 infections during the Follow-Up Period

End point title	Cohort A and Cohort B: Incidence and Severity of symptomatic SARS-CoV-2 infections during the Follow-Up Period[30]

End point description:

End point type	Secondary

End point timeframe:

Up to Day 225

Notes:

[30] - 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: This endpoint is only applicable to participants in Cohort A and Cohort B.

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1428	1439	170	165
Units: Subjects				
Total Symptomatic COVID-19	68	14	1	1
Grade 1 Symptomatic COVID-19	50	12	1	1
Grade 2 Symptomatic COVID-19	14	2	0	0
Grade 3 Symptomatic COVID-19	4	0	0	0
Grade 4 Symptomatic COVID-19	0	0	0	0
Grade 5 Symptomatic COVID-19	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort A and Cohort B: Incidence and Severity of symptomatic SARS-CoV-2 infections in Seronegative subjects during the EAP

End point title	Cohort A and Cohort B: Incidence and Severity of symptomatic SARS-CoV-2 infections in Seronegative subjects during the EAP[31]

End point description:

End point type	Secondary

End point timeframe:

Up to Day 29

Notes:

[31] - 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: This endpoint is only applicable to participants in Cohort A and Cohort B.

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1067	1028	114	109
Units: Subjects				
Total Symptomatic COVID-19	74	12	47	32
Grade 1 Symptomatic COVID-19	64	9	35	30
Grade 2 Symptomatic COVID-19	9	3	10	2
Grade 3 Symptomatic COVID-19	1	0	2	0

Grade 4 Symptomatic COVID-19	0	0	0	0
Grade 5 Symptomatic COVID-19	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort A and Cohort B: Incidence and Severity of symptomatic SARS-CoV-2 infections in Seronegative subjects during the Follow-Up Period

End point title	Cohort A and Cohort B: Incidence and Severity of symptomatic SARS-CoV-2 infections in Seronegative subjects during the Follow-Up Period[32]

End point description:

End point type	Secondary

End point timeframe:

Up to Day 226

Notes:

[32] - 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: This endpoint is only applicable to participants in Cohort A and Cohort B.

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1067	1028	114	109
Units: subjects				
Total Symptomatic COVID-19	64	10	1	1
Grade 1 Symptomatic COVID-19	47	8	1	1
Grade 2 Symptomatic COVID-19	14	2	0	0
Grade 3 Symptomatic COVID-19	3	0	0	0
Grade 4 Symptomatic COVID-19	0	0	0	0
Grade 5 Symptomatic COVID-19	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort A and Cohort B: Incidence and Severity of symptomatic SARS-CoV-2 infections in Seropositive subjects during the EAP

End point title	Cohort A and Cohort B: Incidence and Severity of symptomatic SARS-CoV-2 infections in Seropositive subjects during the EAP[33]

End point description:

End point type	Secondary

End point timeframe:

Up to Day 29

Notes:

[33] - 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: This endpoint is only applicable to participants in Cohort A and Cohort B.

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	296	337	43	48
Units: subjects				
Total Symptomatic COVID-19	6	3	6	3
Grade 1 Symptomatic COVID-19	3	2	5	3
Grade 2 Symptomatic COVID-19	2	1	1	0
Grade 3 Symptomatic COVID-19	1	0	0	0
Grade 4 Symptomatic COVID-19	0	0	0	0
Grade 5 Symptomatic COVID-19	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort A and Cohort B: Incidence and Severity of symptomatic SARS-CoV-2 infections in Seropositive subjects during the Follow-Up Period

End point title	Cohort A and Cohort B: Incidence and Severity of symptomatic SARS-CoV-2 infections in Seropositive subjects during the Follow-Up Period[34]

End point description:

End point type	Secondary

End point timeframe:

Up to Day 225

Notes:

[34] - 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: This endpoint is only applicable to participants in Cohort A and Cohort B.

End point values	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933 + R10987	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	296	337	43	48
Units: Subjects				
Total Symptomatic COVID-19	3	3	0	0
Grade 1 Symptomatic COVID-19	3	3	0	0
Grade 2 Symptomatic COVID-19	0	0	0	0
Grade 3Symptomatic COVID-19	0	0	0	0

Grade 4 Symptomatic COVID-19	0	0	0	0
Grade 5 Symptomatic COVID-19	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort B: Number of weeks of symptomatic SARS-CoV-2 infection (broad-term) within 14 days of a positive RT-qPCR at baseline or during the EAP

End point title	Cohort B: Number of weeks of symptomatic SARS-CoV-2 infection (broad-term) within 14 days of a positive RT-qPCR at baseline or during the EAP[35]

End point description:

End point type	Secondary

End point timeframe:

Up to 8 months

Notes:

[35] - 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: This endpoint is only applicable to participants in Cohort B

End point values	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	100		
Units: weeks				
arithmetic mean (standard deviation)	1.64 (± 3.493)	0.90 (± 2.586)		

Statistical analyses

Statistical analysis title	Cohort B: Placebo of R10933 + R10987 and Placebo
Comparison groups	Cohort B: Placebo of R10933 + R10987 v Cohort B: R10933 + R10987
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0273
Method	Wilcoxon (Van Elteren Test)

Secondary: Cohort B: Percentage of participants with Asymptomatic Infection who develop signs and symptoms (CDC definition) within 14 days of a positive RT-qPCR at baseline or during the EAP

End point title	Cohort B: Percentage of participants with Asymptomatic Infection who develop signs and symptoms (CDC definition) within 14 days of a positive RT-qPCR at baseline or during the EAP[36]

End point description:

End point type	Secondary

End point timeframe:

Up to 1 month

Notes:

[36] - 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: This endpoint is only applicable to participants in Cohort B

End point values	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	100		
Units: percentage of participants				
number (not applicable)	39.7	26.3		

Statistical analyses

Statistical analysis title	Cohort B: Placebo of R10933 + R10987 and Placebo
Comparison groups	Cohort B: Placebo of R10933 + R10987 v Cohort B: R10933 + R10987
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.046
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.299
upper limit	0.989

Secondary: Cohort B: Percentage of participants who subsequently develop signs and symptoms (strict-term) within 14 days of a positive RT-qPCR at baseline or during the EAP

End point title	Cohort B: Percentage of participants who subsequently develop signs and symptoms (strict-term) within 14 days of a positive RT-qPCR at baseline or during the EAP[37]

End point description:

End point type	Secondary

End point timeframe:

Up to 1 month

Notes:

[37] - 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: This endpoint is only applicable to participants in Cohort B

End point values	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	100		
Units: Percentage of Participants				
number (not applicable)	18.5	9.7		

Statistical analyses

Statistical analysis title	Cohort B: R10933 + R10987 and Placebo
Comparison groups	Cohort B: Placebo of R10933 + R10987 v Cohort B: R10933 + R10987
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0721
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.207
upper limit	1.07

Secondary: Cohort B: Number of weeks of symptomatic SARS-CoV-2 infection (CDC definition) within 14 days of a positive RT-qPCR at baseline or during the EAP

End point title	Cohort B: Number of weeks of symptomatic SARS-CoV-2 infection (CDC definition) within 14 days of a positive RT-qPCR at baseline or during the EAP[38]

End point description:

End point type	Secondary

End point timeframe:

Up to 8 months

Notes:

[38] - 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: This endpoint is only applicable to participants in Cohort B

End point values	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	100		
Units: weeks				
arithmetic mean (standard deviation)	1.71 (± 3.569)	0.88 (± 2.584)		

Statistical analyses

Statistical analysis title	Cohort B: Placebo of R10933 + R10987 and Placebo
Comparison groups	Cohort B: Placebo of R10933 + R10987 v Cohort B: R10933 + R10987
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.026
Method	Wilcoxon (Mann-Whitney)

Secondary: Cohort B: Number of weeks of symptomatic SARS-CoV-2 infection (Strict-term definition) within 14 days of a positive RT-qPCR at baseline or during the EAP

End point title	Cohort B: Number of weeks of symptomatic SARS-CoV-2 infection (Strict-term definition) within 14 days of a positive RT-qPCR at baseline or during the EAP[39]

End point description:

End point type	Secondary

End point timeframe:

Up to 8 months

Notes:

[39] - 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: This endpoint is only applicable to participants in Cohort B

End point values	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	100		
Units: weeks				
arithmetic mean (standard deviation)	0.68 (± 1.889)	0.40 (± 1.876)		

Statistical analyses

Statistical analysis title	Cohort B: Placebo of R10933 + R10987 and Placebo
Comparison groups	Cohort B: Placebo of R10933 + R10987 v Cohort B: R10933 + R10987
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0614
Method	Wilcoxon (Mann-Whitney)

Secondary: Cohort B: Change in viral load from baseline to day 8 visit in NP swab samples

End point title	Cohort B: Change in viral load from baseline to day 8 visit in NP swab samples[40]

End point description:

End point type	Secondary

End point timeframe:

Up to day 8 visit

Notes:

[40] - 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: This endpoint is only applicable to participants in Cohort B.

End point values	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	95		
Units: log10 copies/mL				
least squares mean (standard error)	-1.543 (± 0.238)	-3.004 (± 0.239)		

Statistical analyses

Statistical analysis title	Cohort B: Placebo of R10933 + R10987 and Placebo
Comparison groups	Cohort B: Placebo of R10933 + R10987 v Cohort B: R10933 + R10987

Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-1.461
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.127
upper limit	-0.795
Variability estimate	Standard error of the mean
Dispersion value	0.337

Secondary: Cohort B: Change in viral load from baseline to day 15 visit in NP swab samples

End point title	Cohort B: Change in viral load from baseline to day 15 visit in NP swab samples[41]

End point description:

End point type	Secondary

End point timeframe:

Up to day 15 visit

Notes:

[41] - 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: This endpoint is only applicable to participants in Cohort B.

End point values	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	95		
Units: log10 copies/mL				
least squares mean (standard error)	-4.014 (± 0.195)	-4.864 (± 0.199)		

Statistical analyses

Statistical analysis title	Cohort B: Placebo of R10933 + R10987 and Placebo
Comparison groups	Cohort B: Placebo of R10933 + R10987 v Cohort B: R10933 + R10987

Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0026
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	-0.3
Variability estimate	Standard error of the mean
Dispersion value	0.279

Secondary: Cohort B: Time-weighted average change from baseline in viral load (log10 copies/mL) in NP swab samples until the day 22 visit

End point title	Cohort B: Time-weighted average change from baseline in viral load (log10 copies/mL) in NP swab samples until the day 22 visit[42]

End point description:

End point type	Secondary

End point timeframe:

Day 22

Notes:

[42] - 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: This endpoint is only applicable to participants in Cohort B

End point values	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	95		
Units: log10 copies/mL				
least squares mean (standard error)	-2.639 (± 0.136)	-3.580 (± 0.137)		

Statistical analyses

Statistical analysis title	Cohort B: Placebo of R10933 + R10987 and Placebo
Comparison groups	Cohort B: Placebo of R10933 + R10987 v Cohort B: R10933 + R10987

Number of subjects included in analysis	191
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.321
upper limit	-0.559
Variability estimate	Standard error of the mean
Dispersion value	0.193

Secondary: Cohort B: AUC in viral load from the first positive SARS-CoV-2 RT-qPCR NP swab samples detected during the EAP to the first confirmed negative test

End point title	Cohort B: AUC in viral load from the first positive SARS-CoV-2 RT-qPCR NP swab samples detected during the EAP to the first confirmed negative test[43]

End point description:

End point type	Secondary

End point timeframe:

Up to 8 months

Notes:

[43] - 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: This endpoint is only applicable to participants in Cohort B

End point values	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	98		
Units: log10 copies/mL				
least squares mean (standard error)	82.008 (± 4.328)	55.964 (± 4.201)		

Statistical analyses

Statistical analysis title	Cohort B: R10933 + R10987 and Placebo
Comparison groups	Cohort B: Placebo of R10933 + R10987 v Cohort B: R10933 + R10987

Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Difference of LS Mean
Point estimate	-26.045
Confidence interval	
level	95 %
sides	2-sided
lower limit	-37.973
upper limit	-14.117
Variability estimate	Standard error of the mean
Dispersion value	6.041

Secondary: Cohort B: Maximum SARS-CoV-2 RT-qPCR viral load in NP swab samples in participants with 1 or more positive test that has an onset during the EAP

End point title	Cohort B: Maximum SARS-CoV-2 RT-qPCR viral load in NP swab samples in participants with 1 or more positive test that has an onset during the EAP[44]

End point description:

End point type	Secondary

End point timeframe:

Up to 8 months

Notes:

[44] - 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: This endpoint is only applicable to participants in Cohort B

End point values	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	98		
Units: log10 copies/mL				
least squares mean (standard error)	4.731 (± 0.238)	3.336 (± 0.240)		

Statistical analyses

Statistical analysis title	Cohort B: R10933 + R10987 and Placebo
Comparison groups	Cohort B: Placebo of R10933 + R10987 v Cohort B: R10933 + R10987

Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Difference of LS Mean
Point estimate	-1.395
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.063
upper limit	-0.727
Variability estimate	Standard error of the mean
Dispersion value	0.338

Secondary: Cohort B: Number of medically attended visits in emergency rooms or urgent care centers related to RT-qPCR confirmed SARS-CoV-2 infection that has an onset at baseline or during the EAP

End point title	Cohort B: Number of medically attended visits in emergency rooms or urgent care centers related to RT-qPCR confirmed SARS-CoV-2 infection that has an onset at baseline or during the EAP[45]

End point description:

End point type	Secondary

End point timeframe:

Up to 1 month

Notes:

[45] - 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: This endpoint is only applicable to participants in Cohort B

End point values	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	100		
Units: Medically attended visits				
arithmetic mean (standard deviation)	0.06 (± 0.234)	0.00 (± 0.000)		

Statistical analyses

Statistical analysis title	Cohort B: Placebo of R10933 + R10987 and Placebo
Comparison groups	Cohort B: Placebo of R10933 + R10987 v Cohort B: R10933 + R10987

Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0138
Method	Wilcoxon (Mann-Whitney)

Secondary: Cohort B: Percentage of participants requiring medically attended visits in emergency rooms or urgent care centers related to a RT-qPCR confirmed SARS CoV-2 infection that has an onset at baseline or during the EAP

End point title	Cohort B: Percentage of participants requiring medically attended visits in emergency rooms or urgent care centers related to a RT-qPCR confirmed SARS CoV-2 infection that has an onset at baseline or during the EAP[46]

End point description:

End point type	Secondary

End point timeframe:

Up to 1 month

Notes:

[46] - 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: This endpoint is only applicable to participants in Cohort B

End point values	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	100		
Units: Percentage of participants				
number (not applicable)	5.8	0.0		

Statistical analyses

Statistical analysis title	Cohort B: Placebo of R10933 + R10987 and Placebo

Statistical analysis description:

Testing if there is an association between the observed results and treatment received

Comparison groups	Cohort B: Placebo of R10933 + R10987 v Cohort B: R10933 + R10987
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0292
Method	Fisher exact

Secondary: Cohort B: Percentage of participants hospitalized related to a RT-qPCR

confirmed SARS-CoV-2 infection that has an onset at baseline or during the EAP	
End point title	Cohort B: Percentage of participants hospitalized related to a RT-qPCR confirmed SARS-CoV-2 infection that has an onset at baseline or during the EAP[47]

End point description:

End point type	Secondary

End point timeframe:

Up to 8 months

Notes:

[47] - 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: This endpoint is only applicable to participants in Cohort B

End point values	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	100		
Units: Percentage of participants				
number (not applicable)	2.9	0.0		

Statistical analyses

Statistical analysis title	Cohort B: Placebo of R10933 + R10987 and Placebo

Statistical analysis description:

Testing if there is an association between the observed results and treatment received

Comparison groups	Cohort B: R10933 + R10987 v Cohort B: Placebo of R10933 + R10987
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2466
Method	Fisher exact

Secondary: Cohort B: Number of days missed for daily responsibilities (where applicable) due to a RT-qPCR confirmed SARS-CoV-2 infection that has an onset at baseline or during the EAP	
End point title	Cohort B: Number of days missed for daily responsibilities (where applicable) due to a RT-qPCR confirmed SARS-CoV-2 infection that has an onset at baseline or during the EAP[48]

End point description:

End point type	Secondary

End point timeframe:

Up to 1 month

Notes:

[48] - 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: This endpoint is only applicable to participants in Cohort B

End point values	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	100		
Units: Days				
arithmetic mean (standard deviation)	5.69 (± 8.802)	5.18 (± 8.940)		

Statistical analyses

Statistical analysis title	Cohort B: Placebo of R10933 + R10987 and Placebo
Comparison groups	Cohort B: Placebo of R10933 + R10987 v Cohort B: R10933 + R10987
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7861
Method	Wilcoxon (Van Elteren Test)

Secondary: Cohort B: Number of days of hospital and intensive care unit (ICU) stay in participants hospitalized for a RT-qPCR confirmed SARS-CoV-2 infection that has an onset at baseline or during the EAP

End point title	Cohort B: Number of days of hospital and intensive care unit (ICU) stay in participants hospitalized for a RT-qPCR confirmed SARS-CoV-2 infection that has an onset at baseline or during the EAP[49]

End point description:

End point type	Secondary

End point timeframe:

Up to 8 months

Notes:

[49] - 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: This endpoint is only applicable to participants in Cohort B

End point values	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	100		
Units: days				

arithmetic mean (standard deviation)	0.38 (± 2.671)	0.00 (± 0.000)		

Statistical analyses

Statistical analysis title	Cohort B: R10933 + R10987 and Placebo
Comparison groups	Cohort B: Placebo of R10933 + R10987 v Cohort B: R10933 + R10987
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0842
Method	Wilcoxon (Mann-Whitney)

Secondary: Concentrations of REGN10933 in serum over time

End point title	Concentrations of REGN10933 in serum over time

End point description:

End point type	Secondary

End point timeframe:

0 Days Post-Dose, 28 Days Post-Dose, 56 Days Post-Dose, 112 Days Post-Dose, 168 Days Post-Dose, 224 Days Post-Dose

End point values	PKAS Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	170			
Units: milligrams per liter (mg/L)				
arithmetic mean (standard deviation)				
0 Days Post-Dose (n=133)	0.613 (± 3.97)			
28 Days Post-Dose (n=122)	28.7 (± 14.5)			
56 Days Post-Dose (n=140)	14.3 (± 8.22)			
112 Days Post-Dose (n=113)	4.29 (± 7.74)			
168 Days Post-Dose (n=132)	1.45 (± 3.34)			
224 Days Post-Dose (n=139)	0.498 (± 1.01)			

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of REGN10987 in serum over time

End point title	Concentrations of REGN10987 in serum over time

End point description:

End point type	Secondary

End point timeframe:

0 Days Post-Dose, 28 Days Post-Dose, 56 Days Post-Dose, 112 Days Post-Dose, 168 Days Post-Dose, 224 Days Post-Dose

End point values	Anti-drug Antibodies Analysis Set (AAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	170			
Units: mg/L				
arithmetic mean (standard deviation)				
0 Days Post-Dose (n=133)	0.601 (± 4.18)			
28 Days Post-Dose (n=122)	23.4 (± 11.8)			
56 Days Post-Dose (n=140)	10.2 (± 6.53)			
112 Days Post-Dose (n=113)	2.65 (± 6.17)			
168 Days Post-Dose (n=132)	0.768 (± 2.40)			
224 Days Post-Dose (n=139)	0.198 (± 0.617)			

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity as measured by anti-drug antibodies (ADAs) to REGN10933

End point title	Immunogenicity as measured by anti-drug antibodies (ADAs) to REGN10933

End point description:

End point type	Secondary

End point timeframe:

Up to 8 months

End point values	Anti-drug Antibodies Analysis Set (AAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	3201			
Units: participants				
Negative	2863			

Pre-Existing Immunoreactivity	84			
Treatment Boosted Response	1			
Treatment Emergent Response	253			

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity as measured by anti-drug antibodies (ADAs) to REGN10987

End point title	Immunogenicity as measured by anti-drug antibodies (ADAs) to REGN10987

End point description:

End point type	Secondary

End point timeframe:

Up to 8 months

End point values	Anti-drug Antibodies Analysis Set (AAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	3201			
Units: participants				
Negative	2751			
Pre-Existing Immunoreactivity	105			
Treatment Boosted Response	9			
Treatment Emergent Response	336			

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity as Measured by Neutralizing Anti-drug Antibody (NAb) to REGN10933

End point title	Immunogenicity as Measured by Neutralizing Anti-drug Antibody (NAb) to REGN10933

End point description:

End point type	Secondary

End point timeframe:

Up to 8 months

End point values	NAb Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	3199			
Units: participants				
ADA Negative	2863			
Pre-existing immunoreactivity; Negative NAb-	79			
Pre-existing immunoreactivity; NAb+	5			
Treatment-emergent & Treatment-boosted; NAb-	215			
Treatment-emergent & Treatment-boosted; NAb+	37			

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity as Measured by Neutralizing Anti-drug Antibody (NAb) to REGN10987

End point title	Immunogenicity as Measured by Neutralizing Anti-drug Antibody (NAb) to REGN10987

End point description:

End point type	Secondary

End point timeframe:

Up to 8 months

End point values	NAb Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	3199			
Units: participants				
ADA Negative	2751			
Pre-Existing Immunoreactivity; NAb-	39			
Pre-Existing Immunoreactivity; NAb+	66			
Treatment-emergent & Treatment-boosted; NAb-	156			
Treatment-emergent & Treatment-boosted; NAb+	187			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to Day 226	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	Cohort A: Placebo of R10933 + R10987
Reporting group description: Placebo of R10933 + R10987 Adult and Adolescent Subjects (≥12years) Who Are SARS-CoV-2 RT-qPCR negative at baseline	
Reporting group title	Cohort A: R10933+R10987
Reporting group description: Cohort A: R10933+R10987 Adult and Adolescent Subjects (≥12years) who are SARS-CoV-2 RT-qPCR negative at baseline	
Reporting group title	Cohort A1: Placebo of R10933 + R10987
Reporting group description: Placebo of R10933 + R10987 Pediatric Subjects (<12 years) with SARS-CoV-2 RT-qPCR Negative at baseline	
Reporting group title	Cohort B: Placebo of R10933 + R10987
Reporting group description: Cohort B: Placebo of R10933 + R10987 Adult and Adolescent Subjects (≥12years) Who Are SARS-CoV-2 RT-qPCR Positive at baseline	
Reporting group title	Cohort B: R10933 + R10987
Reporting group description: Cohort B: R10933 + R10987 Adult and Adolescent Subjects (≥12years) Who Are SARS-CoV-2 RT-qPCR Positive at baseline	
Reporting group title	Undetermined: Placebo of R10933 + R10987
Reporting group description: Undetermined: Placebo of R10933 + R10987 Adult and Adolescent subjects (≥12 years) whose baseline RT-qPCR status was inconclusive or missing	
Reporting group title	Undetermined: R10933 + R10987
Reporting group description: Undetermined: R10933 + R10987 Adult and Adolescent subjects (≥12 years) whose baseline RT-qPCR status was inconclusive or missing	

Serious adverse events	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933+R10987	Cohort A1: Placebo of R10933 + R10987
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 1428 (1.61%)	24 / 1439 (1.67%)	0 / 1 (0.00%)
number of deaths (all causes)	2	3	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive ductal breast carcinoma			

subjects affected / exposed	1 / 1428 (0.07%)	0 / 1439 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervix carcinoma recurrent			
subjects affected / exposed	0 / 1428 (0.00%)	1 / 1439 (0.07%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Essential hypertension			
subjects affected / exposed	1 / 1428 (0.07%)	0 / 1439 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive urgency			
subjects affected / exposed	1 / 1428 (0.07%)	0 / 1439 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	2 / 1428 (0.14%)	1 / 1439 (0.07%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pre-eclampsia			
subjects affected / exposed	0 / 1428 (0.00%)	1 / 1439 (0.07%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Breast haematoma			
subjects affected / exposed	1 / 1428 (0.07%)	0 / 1439 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicidal ideation			

subjects affected / exposed	2 / 1428 (0.14%)	0 / 1439 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mania			
subjects affected / exposed	1 / 1428 (0.07%)	0 / 1439 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Schizophrenia			
subjects affected / exposed	0 / 1428 (0.00%)	1 / 1439 (0.07%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Gun shot wound			
subjects affected / exposed	1 / 1428 (0.07%)	0 / 1439 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	1 / 1428 (0.07%)	0 / 1439 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue injury			
subjects affected / exposed	1 / 1428 (0.07%)	0 / 1439 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	0 / 1428 (0.00%)	1 / 1439 (0.07%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Burns second degree			
subjects affected / exposed	0 / 1428 (0.00%)	1 / 1439 (0.07%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			

subjects affected / exposed	0 / 1428 (0.00%)	1 / 1439 (0.07%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural complication			
subjects affected / exposed	0 / 1428 (0.00%)	1 / 1439 (0.07%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	0 / 1428 (0.00%)	1 / 1439 (0.07%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural inflammation			
subjects affected / exposed	0 / 1428 (0.00%)	1 / 1439 (0.07%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 1428 (0.00%)	2 / 1439 (0.14%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 1428 (0.00%)	1 / 1439 (0.07%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic lung injury			
subjects affected / exposed	0 / 1428 (0.00%)	1 / 1439 (0.07%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 1428 (0.07%)	0 / 1439 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Acute myocardial infarction			

subjects affected / exposed	0 / 1428 (0.00%)	2 / 1439 (0.14%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 1428 (0.00%)	1 / 1439 (0.07%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	0 / 1428 (0.00%)	1 / 1439 (0.07%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	1 / 1428 (0.07%)	0 / 1439 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 1428 (0.00%)	1 / 1439 (0.07%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 1428 (0.00%)	1 / 1439 (0.07%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 1428 (0.00%)	1 / 1439 (0.07%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 1428 (0.00%)	0 / 1439 (0.00%)	0 / 1 (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
Hepatobiliary disorders			

Cholelithiasis			
subjects affected / exposed	1 / 1428 (0.07%)	0 / 1439 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 1428 (0.00%)	1 / 1439 (0.07%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	0 / 1428 (0.00%)	1 / 1439 (0.07%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 1428 (0.00%)	1 / 1439 (0.07%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			
subjects affected / exposed	5 / 1428 (0.35%)	0 / 1439 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	3 / 1428 (0.21%)	0 / 1439 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	2 / 1428 (0.14%)	1 / 1439 (0.07%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	1 / 1428 (0.07%)	2 / 1439 (0.14%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 1428 (0.07%)	0 / 1439 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Scrotal abscess			
subjects affected / exposed	1 / 1428 (0.07%)	0 / 1439 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 1428 (0.07%)	1 / 1439 (0.07%)	0 / 1 (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
Abscess limb			
subjects affected / exposed	0 / 1428 (0.00%)	1 / 1439 (0.07%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gangrene			
subjects affected / exposed	0 / 1428 (0.00%)	1 / 1439 (0.07%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 1428 (0.00%)	1 / 1439 (0.07%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 1428 (0.00%)	1 / 1439 (0.07%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue infection			

subjects affected / exposed	0 / 1428 (0.00%)	1 / 1439 (0.07%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987	Undetermined: Placebo of R10933 + R10987
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 170 (2.94%)	1 / 165 (0.61%)	0 / 44 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Cervix carcinoma recurrent			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Vascular disorders			
Essential hypertension			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Hypertensive urgency			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Pre-eclampsia			

subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Reproductive system and breast disorders			
Breast haematoma			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Mania			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Schizophrenia			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Injury, poisoning and procedural complications			
Gun shot wound			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Humerus fracture			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Soft tissue injury			

subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Ankle fracture			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Burns second degree			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Foot fracture			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Post procedural complication			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Post procedural haemorrhage			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Post procedural inflammation			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Road traffic accident			
subjects affected / exposed	0 / 170 (0.00%)	1 / 165 (0.61%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			

subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Traumatic lung injury			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Acute myocardial infarction			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Cardiac failure congestive			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Cardio-respiratory arrest			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Syncope			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Transient ischaemic attack			

subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Pancreatitis acute			
subjects affected / exposed	1 / 170 (0.59%)	0 / 165 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Cholecystitis acute			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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			
COVID-19			

subjects affected / exposed	2 / 170 (1.18%)	0 / 165 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	2 / 170 (1.18%)	0 / 165 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Pneumonia			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Pyelonephritis			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Scrotal abscess			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Sepsis			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Abscess limb			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Gangrene			

subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Gastroenteritis			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Osteomyelitis			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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
Soft tissue infection			
subjects affected / exposed	0 / 170 (0.00%)	0 / 165 (0.00%)	0 / 44 (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

Serious adverse events	Undetermined: R10933 + R10987		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 23 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cervix carcinoma recurrent			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Essential hypertension			

subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypertensive urgency			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pre-eclampsia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Breast haematoma			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mania			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Schizophrenia			

subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Gun shot wound			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Humerus fracture			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Soft tissue injury			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ankle fracture			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Burns second degree			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Foot fracture			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Post procedural complication			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Post procedural haemorrhage			

subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Post procedural inflammation				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Road traffic accident				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tibia fracture				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Traumatic lung injury				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Cardiac arrest				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardio-respiratory arrest				

subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis acute			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholecystitis acute			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COVID-19 pneumonia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Scrotal abscess			

subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abscess limb			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gangrene			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteomyelitis			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Soft tissue infection			
subjects affected / exposed	0 / 23 (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	Cohort A: Placebo of R10933 + R10987	Cohort A: R10933+R10987	Cohort A1: Placebo of R10933 + R10987
Total subjects affected by non-serious adverse events			
subjects affected / exposed	247 / 1428 (17.30%)	96 / 1439 (6.67%)	0 / 1 (0.00%)
Infections and infestations			
COVID-19			
subjects affected / exposed	148 / 1428 (10.36%)	29 / 1439 (2.02%)	0 / 1 (0.00%)
occurrences (all)	149	32	0
Asymptomatic COVID-19			
subjects affected / exposed	119 / 1428 (8.33%)	71 / 1439 (4.93%)	0 / 1 (0.00%)
occurrences (all)	119	73	0

Non-serious adverse events	Cohort B: Placebo of R10933 + R10987	Cohort B: R10933 + R10987	Undetermined: Placebo of R10933 + R10987
Total subjects affected by non-serious adverse events			
subjects affected / exposed	63 / 170 (37.06%)	41 / 165 (24.85%)	10 / 44 (22.73%)
Infections and infestations			
COVID-19			
subjects affected / exposed	58 / 170 (34.12%)	35 / 165 (21.21%)	4 / 44 (9.09%)
occurrences (all)	59	35	4
Asymptomatic COVID-19			
subjects affected / exposed	6 / 170 (3.53%)	7 / 165 (4.24%)	7 / 44 (15.91%)
occurrences (all)	6	7	7

Non-serious adverse events	Undetermined: R10933 + R10987		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 23 (8.70%)		
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Asymptomatic COVID-19			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 July 2020	Amendment 1: The purpose of this amendment is to change the collection of respiratory samples for SARS-CoV-2 reverse-transcriptase quantitative polymerase chain reaction (RT-qPCR) from nasal swabs and saliva samples to nasopharyngeal (NP) swab samples due to analysis of data from baseline samples from the REGN10933+REGN10987 treatment studies, where study patients were sampled by NP swabs, nasal swabs, and saliva for side-by-side comparison.
27 August 2020	Amendment 2: The primary purpose of this amendment is to remove the requirement for subjects to have at least 48 hours of sustained exposure to the index case.
07 October 2020	Amendment 3: The primary purpose of this amendment is to include adolescent subjects aged 12 years to less than 18 years in the study. The inclusion of adolescent subjects is considered relevant to the populations at risk for infection with SARS-CoV-2.
24 November 2020	Amendment 4: The primary purposes of this amendment are 1) to change from 2 primary endpoints to 1 primary endpoint, 2) to increase the sample size, 3) to allow for the inclusion of pediatric subjects aged <12 years, 4) to allow for the inclusion of women who are pregnant or breastfeeding
19 January 2021	Amendment 5: The primary purpose of this amendment is to describe the verification of the sample size assumptions used to design the study
25 March 2021	Amendment 6: The primary purpose of this amendment is to revise and add objectives and endpoints, as well as to define the statistical testing hierarchy for the primary and key secondary endpoints.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported