



Clinical trial results:

A Randomized Double-Blind Placebo-Controlled Study of the LEPR Agonist Antibody REGN4461 for the Treatment of Metabolic Abnormalities in Patients with Familial Partial Lipodystrophy

Summary

EudraCT number	2021-000138-33
Trial protocol	ES FR
Global end of trial date	18 April 2024

Results information

Result version number	v1 (current)
This version publication date	03 May 2025
First version publication date	03 May 2025

Trial information

Trial identification

Sponsor protocol code	R4461-PLD-20100
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05088460
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)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 April 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	18 April 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Two cohorts were studied based on leptin levels. Cohort A was composed of participants with baseline leptin <8.0 ng/mL & Cohort B was composed of participants with baseline leptin 8.0 to ≤20.0 ng/mL.

The primary objectives evaluated participants in Cohort A only:

- effect of REGN4461 on fasting triglycerides (TG) in participants with elevated baseline fasting TG
- effect of REGN4461 on hyperglycemia in participants with elevated baseline Hemoglobin A1c (HbA1c)

Secondary objectives evaluated:

Cohort B & the combined set of Cohorts A plus B:

- effect of REGN4461 on fasting TG levels in participants with hypertriglyceridemia
- effect of REGN4461 on glycemic control in participants with hyperglycemia

Cohorts A & B separately, & the combined set of Cohorts A plus B:

- effect of REGN4461 on liver fat in participants with hepatic steatosis
- effect of REGN4461 on hunger
- safety & tolerability of REGN4461
- concentration profile of REGN4461 over time
- immunogenicity

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 February 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Türkiye: 4
Country: Number of subjects enrolled	United States: 16
Worldwide total number of subjects	20
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
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Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	20
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 66 participants were screened, of whom 20 were randomized and received study treatment.

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, Data analyst, Assessor

Blinding implementation details:

Double-blind treatment for 12 weeks followed by 12 weeks of single-blind treatment

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm 1 Cohort A: Placebo to REGN4461

Arm description:

Participants randomized to Arm 1 received placebo for 12 weeks during the DBTP followed by crossover to REGN4461 treatment for 12 weeks during the SBTP.

Arm type	Placebo
Investigational medicinal product name	mibavademab
Investigational medicinal product code	REGN4461
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

REGN4461 for 12 weeks during SBTP

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

Dosage and administration details:

Matching Placebo for 12 weeks during DBTP

Arm title	Arm 2 Cohort A: REGN4461 to REGN4461
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Arm description:

Participants randomized to Arm 2 received REGN4461 treatment for 12 weeks during the DBTP followed by an additional 12 weeks of REGN4461 treatment during the SBTP.

Arm type	Experimental
Investigational medicinal product name	mibavademab
Investigational medicinal product code	REGN4461
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

REGN4461 for 24 weeks

Arm title	Arm 1 Cohort B: Placebo to REGN4461
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Arm description:

Participants randomized to Arm 1 received placebo for 12 weeks during the DBTP followed by crossover to REGN4461 treatment for 12 weeks during the SBTP.

Arm type	Experimental
Investigational medicinal product name	mibavademab
Investigational medicinal product code	REGN4461
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

REGN4461 for 12 weeks during SBTP

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

Dosage and administration details:

Matching Placebo for 12 weeks during DBTP

Arm title	Arm 2 Cohort B: REGN4461 to REGN4461
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Arm description:

Participants randomized to Arm 2 received REGN4461 treatment for 12 weeks during the DBTP followed by an additional 12 weeks of REGN4461 treatment during the SBTP.

Arm type	Experimental
Investigational medicinal product name	mibavademab
Investigational medicinal product code	REGN4461
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

REGN4461 for 24 weeks

Number of subjects in period 1	Arm 1 Cohort A: Placebo to REGN4461	Arm 2 Cohort A: REGN4461 to REGN4461	Arm 1 Cohort B: Placebo to REGN4461
Started	6	6	4
Completed treatment during DBTP	5 ^[1]	6	4
Completed treatment during SBTP	5 ^[2]	5 ^[3]	3 ^[4]
Completed	6	6	4

Number of subjects in period 1	Arm 2 Cohort B: REGN4461 to REGN4461
Started	4
Completed treatment during DBTP	4
Completed treatment during SBTP	4
Completed	4

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: 1 participant completed the DBTP but was prematurely discontinued before entering the SBTP at the request of the sponsor due to the early study termination.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: 1 participant prematurely discontinued study treatment before completing SBTP at the request of the sponsor due to the early study termination.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: 1 participant prematurely discontinued before completing the DBTP at the request of the sponsor due to the early study termination.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: 1 participant prematurely discontinued before completing the DBTP at the request of the sponsor due to the early study termination.

Baseline characteristics

Reporting groups

Reporting group title	Arm 1 Cohort A: Placebo to REGN4461
Reporting group description:	
Participants randomized to Arm 1 received placebo for 12 weeks during the DBTP followed by crossover to REGN4461 treatment for 12 weeks during the SBTP.	
Reporting group title	Arm 2 Cohort A: REGN4461 to REGN4461
Reporting group description:	
Participants randomized to Arm 2 received REGN4461 treatment for 12 weeks during the DBTP followed by an additional 12 weeks of REGN4461 treatment during the SBTP.	
Reporting group title	Arm 1 Cohort B: Placebo to REGN4461
Reporting group description:	
Participants randomized to Arm 1 received placebo for 12 weeks during the DBTP followed by crossover to REGN4461 treatment for 12 weeks during the SBTP.	
Reporting group title	Arm 2 Cohort B: REGN4461 to REGN4461
Reporting group description:	
Participants randomized to Arm 2 received REGN4461 treatment for 12 weeks during the DBTP followed by an additional 12 weeks of REGN4461 treatment during the SBTP.	

Reporting group values	Arm 1 Cohort A: Placebo to REGN4461	Arm 2 Cohort A: REGN4461 to REGN4461	Arm 1 Cohort B: Placebo to REGN4461
Number of subjects	6	6	4
Age categorical			
Units: Subjects			
Adults (18-64 years)	6	6	4
Age Continuous			
Units: years			
arithmetic mean	40.5	43.8	48.0
standard deviation	± 16.79	± 13.47	± 11.97
Sex: Female, Male			
Units: participants			
Female	5	6	3
Male	1	0	1
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	6	6	3
More than one race	0	0	0
Unknown or Not Reported	0	0	1
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	6	6	4
Unknown or Not Reported	0	0	0

Fasting Triglycerides Serum Concentration Units: milligrams per deciliter (mg/dL) geometric mean full range (min-max)	1100.9 405 to 5681	737.8 308 to 2487	675.0 426 to 1534
Hemoglobin A1c (HbA1c) Units: Percentage (%) arithmetic mean standard deviation	8.8 ± 1.62	8.2 ± 1.76	6.9 ± 0.91

Reporting group values	Arm 2 Cohort B: REGN4461 to REGN4461	Total	
Number of subjects	4	20	
Age categorical Units: Subjects			
Adults (18-64 years)	4	20	
Age Continuous Units: years arithmetic mean standard deviation	40.3 ± 12.82	-	
Sex: Female, Male Units: participants			
Female	4	18	
Male	0	2	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	1	1	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	3	18	
More than one race	0	0	
Unknown or Not Reported	0	1	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	4	20	
Unknown or Not Reported	0	0	
Fasting Triglycerides Serum Concentration Units: milligrams per deciliter (mg/dL) geometric mean full range (min-max)	336.2 150 to 1376	-	
Hemoglobin A1c (HbA1c) Units: Percentage (%) arithmetic mean standard deviation	8.6 ± 2.06	-	

End points

End points reporting groups

Reporting group title	Arm 1 Cohort A: Placebo to REGN4461
Reporting group description: Participants randomized to Arm 1 received placebo for 12 weeks during the DBTP followed by crossover to REGN4461 treatment for 12 weeks during the SBTP.	
Reporting group title	Arm 2 Cohort A: REGN4461 to REGN4461
Reporting group description: Participants randomized to Arm 2 received REGN4461 treatment for 12 weeks during the DBTP followed by an additional 12 weeks of REGN4461 treatment during the SBTP.	
Reporting group title	Arm 1 Cohort B: Placebo to REGN4461
Reporting group description: Participants randomized to Arm 1 received placebo for 12 weeks during the DBTP followed by crossover to REGN4461 treatment for 12 weeks during the SBTP.	
Reporting group title	Arm 2 Cohort B: REGN4461 to REGN4461
Reporting group description: Participants randomized to Arm 2 received REGN4461 treatment for 12 weeks during the DBTP followed by an additional 12 weeks of REGN4461 treatment during the SBTP.	
Subject analysis set title	Arm 1 Combined Cohort A + B: Placebo to REGN4461
Subject analysis set type	Full analysis
Subject analysis set description: "Arm 1 Cohort A" and "Arm 1 Cohort B" combined	
Subject analysis set title	Arm 2 Combined Cohort A + B: REGN4461 to REGN4461
Subject analysis set type	Full analysis
Subject analysis set description: "Arm 2 Cohort A" and "Arm 2 Cohort B" combined	
Subject analysis set title	DBTP Arm 1 Cohort A: Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Participants randomized to Arm 1 received placebo for 12 weeks during the DBTP.	
Subject analysis set title	DBTP Arm 2 Cohort A: REGN4461
Subject analysis set type	Full analysis
Subject analysis set description: Participants randomized to Arm 2 received REGN4461 treatment for 12 weeks during the DBTP.	
Subject analysis set title	DBTP Arm 1 Cohort B: Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Participants randomized to Arm 1 received placebo for 12 weeks during the DBTP.	
Subject analysis set title	DBTP Arm 2 Cohort B: REGN4461
Subject analysis set type	Full analysis
Subject analysis set description: Participants randomized to Arm 2 received REGN4461 treatment for 12 weeks during the DBTP.	
Subject analysis set title	DBTP Arm 1 Combined Cohort A + B: Placebo
Subject analysis set type	Full analysis
Subject analysis set description: DBTP "Arm 1 Cohort A" and "Arm 1 Cohort B" combined	
Subject analysis set title	DBTP Arm 2 Combined Cohort A + B: REGN4461
Subject analysis set type	Full analysis
Subject analysis set description: DBTP "Arm 2 Cohort A" and "Arm 2 Cohort B" combined	
Subject analysis set title	SBTP Arm 1 Cohort A: Placebo to REGN4461

Subject analysis set type	Full analysis
Subject analysis set description: Participants randomized to Arm 1 received placebo for 12 weeks during the DBTP followed by crossover to REGN4461 treatment for 12 weeks during the SBTP.	
Subject analysis set title	SBTP Arm 2 Cohort A: REGN4461 to REGN4461
Subject analysis set type	Full analysis
Subject analysis set description: Participants randomized to Arm 2 received REGN4461 treatment for 12 weeks during the DBTP followed by an additional 12 weeks of REGN4461 treatment during the SBTP.	
Subject analysis set title	SBTP Arm 1 Cohort B: Placebo to REGN4461
Subject analysis set type	Full analysis
Subject analysis set description: Participants randomized to Arm 1 received placebo for 12 weeks during the DBTP followed by crossover to REGN4461 treatment for 12 weeks during the SBTP.	
Subject analysis set title	SBTP Arm 2 Cohort B: REGN4461 to REGN4461
Subject analysis set type	Full analysis
Subject analysis set description: Participants randomized to Arm 2 received REGN4461 treatment for 12 weeks during the DBTP followed by an additional 12 weeks of REGN4461 treatment during the SBTP.	
Subject analysis set title	SBTP Arm 1 Combined Cohort A + B: Placebo to REGN4461
Subject analysis set type	Full analysis
Subject analysis set description: SBTP "Arm 1 Cohort A" and "Arm 1 Cohort B" combined	
Subject analysis set title	SBTP Arm 2 Combined Cohort A + B: REGN4461 to REGN4461
Subject analysis set type	Full analysis
Subject analysis set description: SBTP "Arm 2 Cohort A" and "Arm 2 Cohort B" combined	
Subject analysis set title	Arm 1 Cohort A: Placebo to REGN4461
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subgroup of Participants with Screening HbA1C>7%	
Subject analysis set title	Arm 2 Cohort A: REGN4461 to REGN4461
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subgroup of Participants with Screening HbA1C>7%	
Subject analysis set title	Arm 1 Cohort B: Placebo to REGN4461
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subgroup of Participants with Screening HbA1C>7%	
Subject analysis set title	Arm 2 Cohort B: REGN4461 to REGN4461
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subgroup of Participants with Screening HbA1C>7%	
Subject analysis set title	Arm 1 Combined Cohort A + B: Placebo to REGN4461
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subgroup of Participants with Screening HbA1C>7%	
Subject analysis set title	Arm 2 Combined Cohort A + B: REGN4461 to REGN4461
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subgroup of Participants with Screening HbA1C>7%	

Primary: Percent change from baseline to week 12 in fasting serum triglyceride (TG) (Cohort A)

End point title	Percent change from baseline to week 12 in fasting serum triglyceride (TG) (Cohort A) ^{[1][2]}
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End point description:

Percentage change in fasting serum TG was reported for participants with elevated baseline fasting TG (> 200 mg/dL) and with baseline leptin < 8.0 ng/mL (Cohort A). Full Analysis Set (FAS): All randomized participants who received any study drug in the double-blind treatment period (DBTP) and had at least 1 post-baseline assessment.

End point type	Primary
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End point timeframe:

Baseline to week 12

Notes:

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

Justification: Only summary statistics were planned for this endpoint.

[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: Arms reported per protocol.

End point values	Arm 1 Cohort A: Placebo to REGN4461	Arm 2 Cohort A: REGN4461 to REGN4461		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	6		
Units: percentage				
arithmetic mean (standard deviation)	-11.30 (± 46.306)	-38.97 (± 16.998)		

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline to week 12 in hemoglobin A1c (HbA1c) (Cohort A)

End point title	Change from baseline to week 12 in hemoglobin A1c (HbA1c) (Cohort A) ^[3]
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End point description:

Change in HbA1c was reported for participants with elevated baseline HbA1c (> 7.0%) and with baseline leptin < 8.0 ng/mL (Cohort A). FAS: All randomized participants who received any study drug in the DBTP and had at least 1 post-baseline assessment.

End point type	Primary
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End point timeframe:

Baseline to week 12

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: Only summary statistics were planned for this endpoint.

End point values	Arm 1 Cohort A: Placebo to REGN4461	Arm 2 Cohort A: REGN4461 to REGN4461		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	4	5		
Units: percentage of glycated hemoglobin				
arithmetic mean (standard deviation)	-0.05 (± 0.451)	-1.08 (± 1.108)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from baseline to week 12 in fasting serum TG (Cohorts B and A + B)

End point title	Percent change from baseline to week 12 in fasting serum TG (Cohorts B and A + B) ^[4]
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End point description:

Percent change in fasting serum TG was reported for participants with elevated baseline fasting TG (>200 mg/dL) in Cohort B and Cohorts A + B. FAS: All randomized participants who received any study drug in the DBTP and had at least 1 post-baseline assessment.

End point type	Secondary
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End point timeframe:

Baseline to week 12

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Arms reported per protocol.

End point values	Arm 1 Cohort B: Placebo to REGN4461	Arm 2 Cohort B: REGN4461 to REGN4461	Arm 1 Combined Cohort A + B: Placebo to REGN4461	Arm 2 Combined Cohort A + B: REGN4461 to REGN4461
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	4	4	9	10
Units: percentage				
arithmetic mean (standard deviation)	36.78 (± 44.863)	-35.59 (± 8.754)	10.07 (± 49.689)	-37.62 (± 13.752)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from baseline to weeks 12 and 24 in fasting serum TG (Study Arm 1)

End point title	Percent change from baseline to weeks 12 and 24 in fasting serum TG (Study Arm 1) ^[5]
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End point description:

Percent change in fasting serum TG was reported for participants in Study Arm 1. FAS: All randomized participants who received any study drug in the DBTP and had at least 1 post-baseline assessment.

Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure, and "Number analyzed" is the number of participants evaluated at each time point.

End point type	Secondary
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End point timeframe:

Baseline, Week 12, Week 24

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: Arms reported per protocol.

End point values	Arm 1 Cohort A: Placebo to REGN4461	Arm 1 Cohort B: Placebo to REGN4461	Arm 1 Combined Cohort A + B: Placebo to REGN4461	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	5	4	9	
Units: percentage				
arithmetic mean (standard deviation)				
Week 12 (n=5, 4, 9)	-11.30 (\pm 46.306)	36.78 (\pm 44.863)	10.07 (\pm 49.689)	
Week 24 (n=5, 2, 7)	-29.79 (\pm 35.109)	-8.96 (\pm 13.673)	-23.84 (\pm 30.923)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to week 12 in HbA1c (Cohorts B and A + B)

End point title	Change from baseline to week 12 in HbA1c (Cohorts B and A + B)
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End point description:

Change in HbA1c was reported for participants with elevated baseline HbA1c (>7.0%) in Cohort B and Cohorts A + B. FAS: All randomized participants who received any study drug in the DBTP and had at least 1 post-baseline assessment.

End point type	Secondary
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End point timeframe:

Baseline to week 12

End point values	Arm 1 Cohort B: Placebo to REGN4461	Arm 2 Cohort B: REGN4461 to REGN4461	Arm 1 Combined Cohort A + B: Placebo to REGN4461	Arm 2 Combined Cohort A + B: REGN4461 to REGN4461
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	3	6	8
Units: percentage of glycated hemoglobin				
arithmetic mean (standard deviation)	-0.20 (\pm 0.283)	-0.90 (\pm 0.964)	-0.10 (\pm 0.379)	-1.01 (\pm 0.988)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from baseline to weeks 12 and 24 in fasting serum TG (Study Arm 2)

End point title	Percent change from baseline to weeks 12 and 24 in fasting serum TG (Study Arm 2) ^[6]
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End point description:

Percent change in fasting serum TG was reported for participants in Study Arm 2. FAS: All randomized participants who received any study drug in the DBTP and had at least 1 post-baseline assessment. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure, and "Number analyzed" is the number of participants evaluated at each time point.

End point type	Secondary
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End point timeframe:

Baseline, Week 12, Week 24

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: Arms reported per protocol.

End point values	Arm 2 Cohort A: REGN4461 to REGN4461	Arm 2 Cohort B: REGN4461 to REGN4461	Arm 2 Combined Cohort A + B: REGN4461 to REGN4461	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	6	4	10	
Units: percentage				
arithmetic mean (standard deviation)				
Week 12 (n=6, 4, 10)	-38.97 (± 16.998)	-35.59 (± 8.754)	-37.62 (± 13.752)	
Week 24 (n=4, 4, 8)	-30.77 (± 48.883)	-5.30 (± 51.158)	-18.04 (± 48.282)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to weeks 12 and 24 in HbA1c (Study Arm 1)

End point title	Change from baseline to weeks 12 and 24 in HbA1c (Study Arm 1) ^[7]
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End point description:

Change from baseline in HbA1c was reported for participants in Study Arm 1. FAS: All randomized participants who received any study drug in the DBTP and had at least 1 post-baseline assessment. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure, and "Number analyzed" is the number of participants evaluated at each time point.

End point type	Secondary
End point timeframe:	
Baseline, Week 12, Week 24	
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: Arms reported per protocol.	

End point values	Arm 1 Cohort A: Placebo to REGN4461	Arm 1 Cohort B: Placebo to REGN4461	Arm 1 Combined Cohort A + B: Placebo to REGN4461	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	5	4	9	
Units: percentage of glycated hemoglobin				
arithmetic mean (standard deviation)				
Week 12 (n=5, 4, 9)	-0.10 (± 0.406)	0.13 (± 0.427)	0.00 (± 0.406)	
Week 24 (n=5, 3, 8)	-0.78 (± 0.694)	0.13 (± 0.802)	-0.44 (± 0.826)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to weeks 12 and 24 in HbA1c (Study Arm 2)

End point title	Change from baseline to weeks 12 and 24 in HbA1c (Study Arm 2) ^[8]
End point description:	
Change from baseline in HbA1c was reported for participants in Study Arm 2. FAS: All randomized participants who received any study drug in the DBTP and had at least 1 post-baseline assessment. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure, and "Number analyzed" is the number of participants evaluated at each time point.	
End point type	Secondary
End point timeframe:	
Baseline, Week 12, Week 24	
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: Arms reported per protocol.	

End point values	Arm 2 Cohort A: REGN4461 to REGN4461	Arm 2 Cohort B: REGN4461 to REGN4461	Arm 2 Combined Cohort A + B: REGN4461 to REGN4461	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	6	4	10	
Units: percentage of glycated hemoglobin				
arithmetic mean (standard deviation)				
Week 12 (n=6, 4, 10)	-0.92 (± 1.068)	-0.78 (± 0.826)	-0.86 (± 0.931)	

Week 24 (n=5, 4, 9)	-0.98 (\pm 1.357)	-0.50 (\pm 1.068)	-0.77 (\pm 1.188)	
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Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to weeks 12 and 24 in fasting glucose (Study Arm 1)

End point title	Change from baseline to weeks 12 and 24 in fasting glucose (Study Arm 1) ^[9]
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End point description:

Change from baseline in fasting glucose was reported for participants in Study Arm 1. FAS: All randomized participants who received any study drug in the DBTP and had at least 1 post-baseline assessment. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure, and "Number analyzed" is the number of participants evaluated at each time point.

End point type	Secondary
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End point timeframe:

Baseline, Week 12, Week 24

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: Arms reported per protocol.

End point values	Arm 1 Cohort A: Placebo to REGN4461	Arm 1 Cohort B: Placebo to REGN4461	Arm 1 Combined Cohort A + B: Placebo to REGN4461	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	5	4	9	
Units: milligrams per deciliter (mg/dL)				
arithmetic mean (standard deviation)				
Week 12 (n=5, 4, 9)	4.8 (\pm 29.55)	0.0 (\pm 60.37)	2.7 (\pm 42.54)	
Week 24 (n=5, 2, 7)	7.2 (\pm 29.65)	-15.5 (\pm 6.36)	0.7 (\pm 26.75)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to weeks 12 and 24 in fasting glucose (Study Arm 2)

End point title	Change from baseline to weeks 12 and 24 in fasting glucose (Study Arm 2) ^[10]
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End point description:

Change from baseline in fasting glucose was reported for participants in Study Arm 2. FAS: All randomized participants who received any study drug in the DBTP and had at least 1 post-baseline assessment. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure, and "Number analyzed" is the number of participants evaluated at each time

point.

End point type	Secondary
End point timeframe:	
Baseline, Week 12, Week 24	

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: Arms reported per protocol.

End point values	Arm 2 Cohort A: REGN4461 to REGN4461	Arm 2 Cohort B: REGN4461 to REGN4461	Arm 2 Combined Cohort A + B: REGN4461 to REGN4461	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	6	4	10	
Units: mg/dL				
arithmetic mean (standard deviation)				
Week 12 (n=6, 4, 10)	-5.2 (± 36.55)	-19.5 (± 22.87)	-10.9 (± 31.17)	
Week 24 (n=4, 4, 8)	1.8 (± 26.35)	-12.3 (± 58.59)	-5.3 (± 42.71)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from baseline to weeks 12 and 24 in liver fat magnetic resonance imaging-derived proton density fat fraction (MRI-PDFF) (Study Arm 1)

End point title	Percent change from baseline to weeks 12 and 24 in liver fat magnetic resonance imaging-derived proton density fat fraction (MRI-PDFF) (Study Arm 1) ^[11]
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End point description:

Percent change from baseline in MRI-PDFF was reported for participants with baseline MRI-PDFF ≥8.5% in Study Arm 1. FAS: All randomized participants who received any study drug in the DBTP and had at least 1 post-baseline assessment. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure, and "Number analyzed" is the number of participants evaluated at each time point. "99999" = SD not calculable with n=1

End point type	Secondary
End point timeframe:	
Baseline, Week 12, Week 24	

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: Arms reported per protocol.

End point values	Arm 1 Cohort A: Placebo to REGN4461	Arm 1 Cohort B: Placebo to REGN4461	Arm 1 Combined Cohort A + B: Placebo to REGN4461	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	3	2	5	
Units: percentage				
arithmetic mean (standard deviation)				
Week 12 (n=3, 2, 5)	-11.44 (± 18.576)	-0.74 (± 9.919)	-7.16 (± 15.214)	
Week 24 (n=2, 1, 3)	-47.21 (± 22.176)	44.81 (± 99999)	-16.54 (± 55.394)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from baseline to weeks 12 and 24 in liver fat MRI-PDFF (Study Arm 2)

End point title	Percent change from baseline to weeks 12 and 24 in liver fat MRI-PDFF (Study Arm 2) ^[12]
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End point description:

Percent change from baseline in MRI-PDFF was reported for participants with baseline liver fat MRI-PDFF ≥8.5% in Study Arm 2. FAS: All randomized participants who received any study drug in the DBTP and had at least 1 post-baseline assessment. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure, and "Number analyzed" is the number of participants evaluated at each time point.

End point type	Secondary
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End point timeframe:

Baseline, Week 12, Week 24

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: Arms reported per protocol.

End point values	Arm 2 Cohort A: REGN4461 to REGN4461	Arm 2 Cohort B: REGN4461 to REGN4461	Arm 2 Combined Cohort A + B: REGN4461 to REGN4461	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	4	4	8	
Units: percentage				
arithmetic mean (standard deviation)				
Week 12 (n=4, 4, 8)	-17.05 (± 25.788)	-18.80 (± 17.300)	-17.92 (± 20.351)	
Week 24 (n=4, 3, 7)	-24.33 (± 27.151)	-19.53 (± 19.324)	-22.27 (± 22.353)	

Statistical analyses

Secondary: Change from baseline to weeks 12 and 24 on the daily lipodystrophy hunger questionnaire - highest hunger score

End point title	Change from baseline to weeks 12 and 24 on the daily lipodystrophy hunger questionnaire - highest hunger score
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End point description:

The daily lipodystrophy hunger questionnaire was developed to assess hunger related behaviors among patients with lipodystrophy. The highest hunger score asked participants to rate their highest hunger that day on a scale from 0 to 4, with higher scores representing the higher perceived hunger. A negative change from baseline indicated a reduction in perceived hunger. FAS: All randomized participants who received any study drug in the DBTP and had at least 1 post-baseline assessment. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure, and "Number analyzed" is the number of participants evaluated at each time point.

End point type	Secondary
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End point timeframe:

Baseline, Week 12, Week 24

End point values	Arm 1 Cohort A: Placebo to REGN4461	Arm 2 Cohort A: REGN4461 to REGN4461	Arm 1 Cohort B: Placebo to REGN4461	Arm 2 Cohort B: REGN4461 to REGN4461
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	4	4
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=6, 6, 4, 4, 10, 10)	-0.060 (± 0.9009)	-0.538 (± 0.4679)	-0.240 (± 0.2483)	-0.415 (± 0.7539)
Week 24 (n=5, 5, 3, 4, 8, 9)	-0.330 (± 0.3684)	-0.018 (± 0.6228)	-0.383 (± 0.1550)	-0.285 (± 0.6180)

End point values	Arm 1 Combined Cohort A + B: Placebo to REGN4461	Arm 2 Combined Cohort A + B: REGN4461 to REGN4461		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	10		
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=6, 6, 4, 4, 10, 10)	-0.132 (± 0.6929)	-0.489 (± 0.5614)		
Week 24 (n=5, 5, 3, 4, 8, 9)	-0.350 (± 0.2919)	-0.137 (± 0.5975)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to weeks 12 and 24 on the daily lipodystrophy hunger questionnaire - lowest hunger score

End point title	Change from baseline to weeks 12 and 24 on the daily lipodystrophy hunger questionnaire - lowest hunger score
End point description: The daily lipodystrophy hunger questionnaire was developed to assess hunger related behaviors among patients with lipodystrophy. The lowest hunger score asked participants to rate their lowest hunger that day on a scale from 0 to 4, with higher scores indicating higher perceived hunger. A negative change from baseline score indicated a reduction in perceived lowest hunger. FAS: All randomized participants who received any study drug in the DBTP and had at least 1 post-baseline assessment. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure, and "Number analyzed" is the number of participants evaluated at each time point.	
End point type	Secondary
End point timeframe: Baseline, Week 12, Week 24	

End point values	Arm 1 Cohort A: Placebo to REGN4461	Arm 2 Cohort A: REGN4461 to REGN4461	Arm 1 Cohort B: Placebo to REGN4461	Arm 2 Cohort B: REGN4461 to REGN4461
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	4	4
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=6, 6, 4, 4, 10, 10)	0.185 (± 0.8013)	-0.475 (± 0.4630)	-0.338 (± 0.4287)	-0.173 (± 0.3625)
Week 24 (n=5, 5, 3, 4, 8, 9)	-0.128 (± 0.0622)	0.046 (± 0.6776)	-0.103 (± 0.2230)	0.308 (± 0.9603)

End point values	Arm 1 Combined Cohort A + B: Placebo to REGN4461	Arm 2 Combined Cohort A + B: REGN4461 to REGN4461		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	10		
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=6, 6, 4, 4, 10, 10)	-0.024 (± 0.7006)	-0.354 (± 0.4328)		
Week 24 (n=5, 5, 3, 4, 8, 9)	-0.119 (± 0.1288)	0.162 (± 0.7710)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to weeks 12 and 24 on the daily lipodystrophy hunger questionnaire - felt hungry score

End point title	Change from baseline to weeks 12 and 24 on the daily
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End point description:

The daily lipodystrophy hunger questionnaire was developed to assess hunger related behaviors among patients with lipodystrophy with higher scores indicating higher perceived hunger. A negative change from baseline score indicated a reduction in perceived hunger. FAS: All randomized participants who received any study drug in the DBTP and had at least 1 post-baseline assessment. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure, and "Number analyzed" is the number of participants evaluated at each time point.

End point type	Secondary
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End point timeframe:

Baseline, Week 12, Week 24

End point values	Arm 1 Cohort A: Placebo to REGN4461	Arm 2 Cohort A: REGN4461 to REGN4461	Arm 1 Cohort B: Placebo to REGN4461	Arm 2 Cohort B: REGN4461 to REGN4461
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	4	4
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=6, 6, 4, 4, 10, 10)	0.248 (± 0.8642)	-0.550 (± 0.5334)	-0.168 (± 0.2900)	0.008 (± 0.9139)
Week 24 (n=5, 5, 3, 4, 8, 9)	0.016 (± 0.3932)	0.120 (± 0.4374)	-0.183 (± 0.0603)	-0.138 (± 0.6595)

End point values	Arm 1 Combined Cohort A + B: Placebo to REGN4461	Arm 2 Combined Cohort A + B: REGN4461 to REGN4461		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	10		
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=6, 6, 4, 4, 10, 10)	0.082 (± 0.6993)	-0.327 (± 0.7206)		
Week 24 (n=5, 5, 3, 4, 8, 9)	-0.059 (± 0.3163)	0.006 (± 0.5265)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to weeks 12 and 24 on the daily lipodystrophy hunger questionnaire - fullness score

End point title	Change from baseline to weeks 12 and 24 on the daily lipodystrophy hunger questionnaire - fullness score
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End point description:

The daily lipodystrophy hunger questionnaire was developed to assess hunger related behaviors among patients with lipodystrophy. The fullness score asked participants to rate how often they felt full after

eating that day on a scale from 0 to 4, with higher scores indicating higher feeling of fullness. A negative change from baseline indicated a reduced feeling of fullness. FAS: All randomized participants who received any study drug in the DBTP and had at least 1 post-baseline assessment. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure, and "Number analyzed" is the number of participants evaluated at each time point.

End point type	Secondary
End point timeframe:	
Baseline, Week 12, Week 24	

End point values	Arm 1 Cohort A: Placebo to REGN4461	Arm 2 Cohort A: REGN4461 to REGN4461	Arm 1 Cohort B: Placebo to REGN4461	Arm 2 Cohort B: REGN4461 to REGN4461
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	4	4
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=6, 6, 4, 4, 10, 10)	0.063 (± 1.1988)	-0.267 (± 0.5381)	-1.180 (± 0.3764)	-0.535 (± 0.5736)
Week 24 (n=5, 5, 3, 4, 8, 9)	-0.182 (± 0.6474)	0.012 (± 0.6474)	-1.193 (± 0.6630)	-0.178 (± 0.8032)

End point values	Arm 1 Combined Cohort A + B: Placebo to REGN4461	Arm 2 Combined Cohort A + B: REGN4461 to REGN4461		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	10		
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12 (n=6, 6, 4, 4, 10, 10)	-0.434 (± 1.1216)	-0.374 (± 0.5383)		
Week 24 (n=5, 5, 3, 4, 8, 9)	-0.561 (± 0.7994)	-0.072 (± 0.6793)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with treatment-emergent adverse events (TEAEs)

End point title	Number of participants with treatment-emergent adverse events (TEAEs)
End point description:	
The DB SAF included all participants who received any double-blind study drug in DBTP. The single-blind safety analysis set (SB SAF) included all randomized participants who received any single-blind study drug in the single-blind treatment period (SBTP).	
End point type	Secondary

End point timeframe:

Up to Day 169

End point values	DBTP Arm 1 Cohort A: Placebo	DBTP Arm 2 Cohort A: REGN4461	DBTP Arm 1 Cohort B: Placebo	DBTP Arm 2 Cohort B: REGN4461
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	6	4	4
Units: participants	4	5	4	4

End point values	DBTP Arm 1 Combined Cohort A + B: Placebo	DBTP Arm 2 Combined Cohort A + B: REGN4461	SBTP Arm 1 Cohort A: Placebo to REGN4461	SBTP Arm 2 Cohort A: REGN4461 to REGN4461
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	10	5	6
Units: participants	8	9	3	5

End point values	SBTP Arm 1 Cohort B: Placebo to REGN4461	SBTP Arm 2 Cohort B: REGN4461 to REGN4461	SBTP Arm 1 Combined Cohort A + B: Placebo to REGN4461	SBTP Arm 2 Combined Cohort A + B: REGN4461 to REGN4461
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	4	8	10
Units: participants	3	4	6	9

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of REGN4461 in Serum

End point title	Concentrations of REGN4461 in Serum
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End point description:

PK analysis set: All randomized participants who received any study drug and had at least 1 non-missing measurement of REGN4461 concentration following the first dose of study drug. Here, "Overall Number of Participants Analyzed" is the number of participants evaluable for this outcome measure, and "Number analyzed" is the number of participants evaluated at each time point.

End point type	Secondary
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End point timeframe:

Weeks 0, 1, 2, 3, 4, 5, 6, 9, 12, 13, 14, 15, 16, 17, 18, 21, 28, 32 and 36. Weeks 0 and 12 collected pre- and post-dose. All other time points were only pre-dose.

End point values	Arm 1 Combined Cohort A + B: Placebo to REGN4461	Arm 2 Combined Cohort A + B: REGN4461 to REGN4461		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	10		
Units: milligrams per liter (mg/L)				
arithmetic mean (standard deviation)				
Week 0 (pre-dose) (n=10, 10)	0 (± 0)	0 (± 0)		
Week 0 (post-dose) (n=10, 10)	0 (± 0)	232 (± 83.8)		
Week 1 (pre-dose) (n=9, 8)	0 (± 0)	64.3 (± 24.9)		
Week 2 (pre-dose) (n=9, 10)	0 (± 0)	52.5 (± 13.3)		
Week 3 (pre-dose) (n=10, 8)	0 (± 0)	60.2 (± 19.0)		
Week 4 (pre-dose) (n=8, 10)	0 (± 0)	58.8 (± 23.8)		
Week 5 (pre-dose) (n=10, 10)	0 (± 0)	62.0 (± 36.1)		
Week 6 (pre-dose) (n=10, 10)	0 (± 0)	68.8 (± 38.8)		
Week 9 (pre-dose) (n=10, 9)	0 (± 0)	79.6 (± 49.2)		
Week 12 (pre-dose) (n=8, 10)	0 (± 0)	87.1 (± 57.8)		
Week 12 (post-dose) (n=8, 10)	252 (± 50.7)	87.6 (± 49.7)		
Week 13 (pre-dose) (n=8, 10)	62.4 (± 17.5)	97.6 (± 68.6)		
Week 14 (pre-dose) (n=8, 10)	56.6 (± 17.6)	92.8 (± 68.0)		
Week 15 (pre-dose) (n=8, 10)	64.2 (± 29.6)	90.5 (± 59.1)		
Week 16 (pre-dose) (n=8, 10)	68.8 (± 24.3)	103 (± 76.4)		
Week 17 (pre-dose) (n=8, 10)	73.4 (± 30.8)	92.1 (± 73.3)		
Week 18 (pre-dose) (n=8, 10)	75.1 (± 27.1)	95.0 (± 79.3)		
Week 21 (pre-dose) (n=8, 9)	89.3 (± 40.0)	72.9 (± 51.4)		
Week 28 (pre-dose) (n=10, 10)	10.9 (± 12.0)	16.0 (± 23.4)		
Week 32 (pre-dose) (n=9, 10)	0.0663 (± 0.0705)	0.189 (± 0.281)		
Week 36 (pre-dose) (n=9, 10)	0.0110 (± 0.0330)	0.0373 (± 0.0788)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with treatment-emergent anti-drug antibody (ADA) response

End point title	Number of participants with treatment-emergent anti-drug antibody (ADA) response
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End point description:

ADA analysis set: All treated participants who received any amount of study drug and had at least one non-missing anti-drug antibody result following the first dose of study drug.

End point type	Secondary
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End point timeframe:

Up to Day 281

End point values	Arm 1 Combined Cohort A + B: Placebo to REGN4461	Arm 2 Combined Cohort A + B: REGN4461 to REGN4461		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	10		
Units: participants	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From signing of informed consent up to day 281 (end of study)

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	27.0
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Reporting groups

Reporting group title	DBTP Arm 1 Cohort A: Placebo
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Reporting group description:

Participants randomized to Arm 1 received placebo for 12 weeks during the DBTP.

Reporting group title	DBTP Arm 2 Cohort A: REGN4461
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Reporting group description:

Participants randomized to Arm 2 received REGN4461 treatment for 12 weeks during the DBTP.

Reporting group title	SBTP Arm 1 Cohort A: Placebo to REGN4461
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Reporting group description:

Participants randomized to Arm 1 received placebo for 12 weeks during the DBTP followed by crossover to REGN4461 treatment for 12 weeks during the SBTP.

Reporting group title	SBTP Arm 2 Cohort A: REGN4461 to REGN4461
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Reporting group description:

Participants randomized to Arm 2 received REGN4461 treatment for 12 weeks during the DBTP followed by an additional 12 weeks of REGN4461 treatment during the SBTP.

Reporting group title	SBTP Arm 1 Cohort B: Placebo to REGN4461
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Reporting group description:

Participants randomized to Arm 1 received placebo for 12 weeks during the DBTP followed by crossover to REGN4461 treatment for 12 weeks during the SBTP.

Reporting group title	SBTP Arm 2 Cohort B: REGN4461 to REGN4461
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Reporting group description:

Participants randomized to Arm 2 received REGN4461 treatment for 12 weeks during the DBTP followed by an additional 12 weeks of REGN4461 treatment during the SBTP.

Reporting group title	DBTP Arm 1 Cohort B: Placebo
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Reporting group description:

Participants randomized to Arm 1 received placebo for 12 weeks during the DBTP.

Reporting group title	DBTP Arm 2 Cohort B: REGN4461
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Reporting group description:

Participants randomized to Arm 2 received REGN4461 treatment for 12 weeks during the DBTP.

Serious adverse events	DBTP Arm 1 Cohort A: Placebo	DBTP Arm 2 Cohort A: REGN4461	SBTP Arm 1 Cohort A: Placebo to REGN4461
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	1 / 5 (20.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Vascular disorders			

Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 5 (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 disorders			
Angina pectoris			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (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			
Pancreatitis acute			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 5 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 5 (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
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	SBTP Arm 2 Cohort A: REGN4461 to REGN4461	SBTP Arm 1 Cohort B: Placebo to REGN4461	SBTP Arm 2 Cohort B: REGN4461 to REGN4461
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 4 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (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			
Angina pectoris			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 4 (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
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 4 (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
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (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	DBTP Arm 1 Cohort B: Placebo	DBTP Arm 2 Cohort B: REGN4461	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	DBTP Arm 1 Cohort A: Placebo	DBTP Arm 2 Cohort A: REGN4461	SBTP Arm 1 Cohort A: Placebo to REGN4461
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	6 / 6 (100.00%)	3 / 5 (60.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	1	5	0
Peripheral swelling			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Decreased appetite			
subjects affected / exposed	0 / 6 (0.00%)	2 / 6 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Chills			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Infusion site extravasation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Injection site reaction			
subjects affected / exposed	0 / 6 (0.00%)	2 / 6 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	10	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			

Vaginal cyst subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	1 / 5 (20.00%) 1
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0
Cough subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	0 / 5 (0.00%) 0
Snoring subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0
Psychiatric disorders			
Affect lability subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0
Insomnia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	1 / 5 (20.00%) 1
Bipolar I disorder subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0
Poor quality sleep subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0
Suicidal ideation subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	0 / 5 (0.00%) 0
Investigations			
Carbohydrate antigen 19-9 increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	1 / 5 (20.00%) 1
Blood pressure increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	0 / 5 (0.00%) 0

Aspartate aminotransferase increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram abnormal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Haematocrit increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Arterial injury			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Infusion related reaction			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Congenital, familial and genetic disorders			
Muscular dystrophy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			

Left ventricular hypertrophy subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0
Bundle branch block left subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0
Cardiac failure subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0
Defect conduction intraventricular subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0
Nervous system disorders			
Dizziness subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	3 / 6 (50.00%) 3	0 / 5 (0.00%) 0
Cognitive disorder subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0
Carpal tunnel syndrome subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0
Brain fog subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0
Migraine subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0
Mononeuropathy subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0
Neuralgia			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0
Presyncope subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0
Lethargy subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	0 / 5 (0.00%) 0
Restless legs syndrome subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	1 / 5 (20.00%) 2
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0
Iron deficiency anaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	1 / 5 (20.00%) 1
Splenomegaly subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0
Eye disorders Photophobia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	2 / 6 (33.33%) 2	1 / 5 (20.00%) 1
Diarrhoea subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 2	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0
Dyspepsia			

subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Abdominal distension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Ascites			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Duodenal ulcer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 6 (0.00%)	2 / 6 (33.33%)	1 / 5 (20.00%)
occurrences (all)	0	2	1
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	2 / 6 (33.33%)	1 / 5 (20.00%)
occurrences (all)	0	2	1
Gastrointestinal wall thickening			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Plicated tongue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Retching			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Varices oesophageal			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Seborrhoeic dermatitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Acne			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Dermatitis contact			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Skin exfoliation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1

Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	2 / 6 (33.33%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	4	1	0
Back pain			
subjects affected / exposed	1 / 6 (16.67%)	2 / 6 (33.33%)	0 / 5 (0.00%)
occurrences (all)	1	2	0
Groin pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Flank pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Influenza			
subjects affected / exposed	2 / 6 (33.33%)	2 / 6 (33.33%)	0 / 5 (0.00%)
occurrences (all)	2	2	0
Gastroenteritis viral			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0

COVID-19			
subjects affected / exposed	1 / 6 (16.67%)	2 / 6 (33.33%)	0 / 5 (0.00%)
occurrences (all)	1	2	0
Bacterial infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Oral candidiasis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Pharyngitis streptococcal			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	3	0	0
Bronchitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Onychomycosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Fungal infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Diverticulitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Otitis externa			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Otitis media			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	2 / 5 (40.00%)
occurrences (all)	0	0	2
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	3 / 6 (50.00%)	1 / 5 (20.00%)
occurrences (all)	0	3	1
Tooth infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 6 (33.33%)	1 / 5 (20.00%)
occurrences (all)	0	4	5
Hyperphagia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			

subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	2 / 5 (40.00%)
occurrences (all)	0	2	3
Hyponatraemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Increased appetite			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	SBTP Arm 2 Cohort A: REGN4461 to REGN4461	SBTP Arm 1 Cohort B: Placebo to REGN4461	SBTP Arm 2 Cohort B: REGN4461 to REGN4461
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)	3 / 3 (100.00%)	4 / 4 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infusion site extravasation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Injection site reaction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	2 / 4 (50.00%)
occurrences (all)	0	0	2
Reproductive system and breast disorders			
Vaginal cyst			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Snoring			

subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0
Psychiatric disorders			
Affect lability			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Bipolar I disorder			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Poor quality sleep			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Suicidal ideation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Investigations			
Carbohydrate antigen 19-9 increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram abnormal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			

subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0
Haematocrit increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 3 (0.00%) 0	1 / 4 (25.00%) 1
Injury, poisoning and procedural complications			
Foot fracture subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 3 (0.00%) 0	1 / 4 (25.00%) 1
Fall subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 3 (33.33%) 1	0 / 4 (0.00%) 0
Arterial injury subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0
Infusion related reaction subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 2	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0
Congenital, familial and genetic disorders			
Muscular dystrophy subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0
Cardiac disorders			
Left ventricular hypertrophy subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0
Bundle branch block left subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 3 (0.00%) 0	1 / 4 (25.00%) 1
Cardiac failure subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0
Defect conduction intraventricular subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0
Nervous system disorders			

Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Cognitive disorder			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Carpal tunnel syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Brain fog			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Migraine			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Mononeuropathy			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Neuralgia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Presyncope			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Restless legs syndrome			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0
Iron deficiency anaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0
Splenomegaly subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0
Eye disorders Photophobia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 3 (0.00%) 0	1 / 4 (25.00%) 1
Diarrhoea subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	2 / 3 (66.67%) 2	1 / 4 (25.00%) 1
Dyspepsia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0
Abdominal distension subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 3 (33.33%) 1	0 / 4 (0.00%) 0
Ascites subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0
Gastritis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Duodenal ulcer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Dry mouth			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal wall thickening			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Plicated tongue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Retching			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Varices oesophageal			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Stomatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Acne			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0

Rash			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin exfoliation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			

subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Groin pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Influenza			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Bacterial infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pharyngitis streptococcal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Bronchitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Cellulitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Onychomycosis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Fungal infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Diverticulitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Oral herpes			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Otitis externa			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	3 / 4 (75.00%)
occurrences (all)	0	0	4
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	1	0

Paronychia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0
Vulvovaginal candidiasis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 2	1 / 3 (33.33%) 1	0 / 4 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 3 (0.00%) 0	1 / 4 (25.00%) 1
Tooth infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 3 (0.00%) 0	1 / 4 (25.00%) 1
Metabolism and nutrition disorders			
Hypoglycaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0
Hyperphagia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 3 (0.00%) 0	1 / 4 (25.00%) 1
Hyperglycaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0
Hyponatraemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 3 (0.00%) 0	0 / 4 (0.00%) 0
Increased appetite subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 3 (0.00%) 0	1 / 4 (25.00%) 1
Non-serious adverse events	DBTP Arm 1 Cohort B: Placebo	DBTP Arm 2 Cohort B: REGN4461	
Total subjects affected by non-serious adverse events subjects affected / exposed	4 / 4 (100.00%)	4 / 4 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Melanocytic naevus subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Vascular disorders			
Hypertension subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Hypotension subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
General disorders and administration site conditions			
Fatigue subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 4 (25.00%) 2	
Peripheral swelling subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Asthenia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Decreased appetite subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Chills subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 4 (25.00%) 1	
Chest discomfort subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Infusion site extravasation subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Injection site reaction subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	1 / 4 (25.00%) 2	
Non-cardiac chest pain			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Oedema peripheral</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 4 (0.00%)</p> <p>0</p> <p>0 / 4 (0.00%)</p> <p>0</p> <p>0 / 4 (0.00%)</p> <p>0</p>	<p>1 / 4 (25.00%)</p> <p>1</p> <p>1 / 4 (25.00%)</p> <p>1</p> <p>0 / 4 (0.00%)</p> <p>0</p>	
<p>Reproductive system and breast disorders</p> <p>Vaginal cyst</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 4 (0.00%)</p> <p>0</p>	<p>0 / 4 (0.00%)</p> <p>0</p>	
<p>Respiratory, thoracic and mediastinal disorders</p> <p>Oropharyngeal pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Cough</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Snoring</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 4 (0.00%)</p> <p>0</p> <p>0 / 4 (0.00%)</p> <p>0</p> <p>0 / 4 (0.00%)</p> <p>0</p>	<p>0 / 4 (0.00%)</p> <p>0</p> <p>0 / 4 (0.00%)</p> <p>0</p> <p>0 / 4 (0.00%)</p> <p>0</p>	
<p>Psychiatric disorders</p> <p>Affect lability</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Insomnia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Bipolar I disorder</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Poor quality sleep</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Suicidal ideation</p>	<p>0 / 4 (0.00%)</p> <p>0</p> <p>0 / 4 (0.00%)</p> <p>0</p> <p>0 / 4 (0.00%)</p> <p>0</p> <p>0 / 4 (0.00%)</p> <p>0</p> <p>0 / 4 (0.00%)</p> <p>0</p>	<p>0 / 4 (0.00%)</p> <p>0</p> <p>0 / 4 (0.00%)</p> <p>0</p> <p>0 / 4 (0.00%)</p> <p>0</p>	

subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Investigations			
Carbohydrate antigen 19-9 increased subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Blood pressure increased subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Electrocardiogram abnormal subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 4 (0.00%) 0	
Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Haematocrit increased subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Injury, poisoning and procedural complications			
Foot fracture subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Fall subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Arterial injury subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Infusion related reaction			

subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	2 / 4 (50.00%) 2	
Congenital, familial and genetic disorders Muscular dystrophy subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 4 (0.00%) 0	
Cardiac disorders Left ventricular hypertrophy subjects affected / exposed occurrences (all) Bundle branch block left subjects affected / exposed occurrences (all) Cardiac failure subjects affected / exposed occurrences (all) Defect conduction intraventricular subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0	0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0	
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Cognitive disorder subjects affected / exposed occurrences (all) Carpal tunnel syndrome subjects affected / exposed occurrences (all) Brain fog subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Migraine	0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 1 / 4 (25.00%) 3	0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 1 / 4 (25.00%) 1	

subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Mononeuropathy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Neuralgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Presyncope			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	
Lethargy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Restless legs syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	2	0	
Iron deficiency anaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Splenomegaly			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Photophobia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			

Abdominal pain		
subjects affected / exposed	2 / 4 (50.00%)	1 / 4 (25.00%)
occurrences (all)	2	1
Diarrhoea		
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	2	0
Dyspepsia		
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	1
Abdominal distension		
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	1	0
Vomiting		
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	1	0
Ascites		
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	1	0
Gastritis		
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0
Duodenal ulcer		
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0
Dry mouth		
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	1	0
Constipation		
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0
Nausea		
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	1
Gastrointestinal wall thickening		
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0

Plicated tongue subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Retching subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 4 (0.00%) 0	
Varices oesophageal subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Stomatitis subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 4 (0.00%) 0	
Skin and subcutaneous tissue disorders			
Seborrhoeic dermatitis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Acne subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Rash subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Pruritus subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 4 (0.00%) 0	
Hyperhidrosis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Erythema subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Dermatitis contact subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 4 (0.00%) 0	
Alopecia			

subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Skin exfoliation subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 4 (0.00%) 0	
Skin lesion subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Renal and urinary disorders Nephrolithiasis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 4 (25.00%) 2	
Haematuria subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 4 (25.00%) 1	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 4 (0.00%) 0	
Pain in extremity subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 4 (25.00%) 1	
Back pain subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Groin pain subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Flank pain subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 4 (0.00%) 0	
Myalgia subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	1 / 4 (25.00%) 1	
Neck pain			

subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis viral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
COVID-19			
subjects affected / exposed	1 / 4 (25.00%)	2 / 4 (50.00%)	
occurrences (all)	1	2	
Bacterial infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Oral candidiasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Pharyngitis streptococcal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Bronchitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Cellulitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Onychomycosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Nasopharyngitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Fungal infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	

Diverticulitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Oral herpes			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Otitis externa			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Otitis media			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Sinusitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Paronychia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Vulvovaginal candidiasis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 4 (25.00%)	2 / 4 (50.00%)	
occurrences (all)	1	2	
Tooth infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	
occurrences (all)	0	1	

Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	
occurrences (all)	1	0	
Hyperphagia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Hyperglycaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Hyponatraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
Increased appetite			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 May 2022	The main purpose of the amendment was to change the SC weekly maintenance dose of REGN4461.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported