Clinical trial results:
A PHASE 3 RANDOMIZED, DOUBLE-BLIND, PLACEBOCONTROLLED STUDY ASSESSING THE EFFICACY OF ANTI-BET V 1 MONOCLONAL ANTIBODIES TO REDUCE SYMPTOMS OF SEASONAL ALLERGIC RHINITIS

Summary

EudraCT number	2020-004094-52
Trial protocol	DE DK BE
Global end of trial date	24 August 2021

Results information

Result version number	v1 (current)
This version publication date	08 September 2022
First version publication date	08 September 2022

Trial information

Trial identification

Sponsor protocol code	R5713-5714-5715-ALG-2001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04709575
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Regeneron Pharmaceuticals, Inc
Sponsor organisation address	777 Old Saw Mill River Road, Tarrytown, NY, United States, 10591
Public contact	Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 844-734-6643, clinicaltrials@regeneron.com
Scientific contact	Clinical Trial Management, Regeneron Pharmaceuticals, Inc, 001 1-844-734-6643, 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	24 August 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 August 2021
Global end of trial reached?	Yes
Global end of trial date	24 August 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to assess the reduction of allergic symptoms as measured by combined symptom and medication score (CSMS) during birch pollen season after a single dose of REGN5713-5714-5715 versus placebo

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 January 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 31
Country: Number of subjects enrolled	Canada: 118
Country: Number of subjects enrolled	Denmark: 37
Country: Number of subjects enrolled	Germany: 130
Country: Number of subjects enrolled	United States: 37
Worldwide total number of subjects	353
EEA total number of subjects	198

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	336
From 65 to 84 years	17
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

589 participants screened, 353 randomized and from these 349 treated. 4 participants were randomized but not treated. Reasons not randomized: 235 did not meet I/E criteria, 1 withdrew consent.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	REGN5713-5714-5715

Arm description:

REGN5713-5714-5715 administered subcutaneously

Arm type	Experimental
Investigational medicinal product name	REGN5713-5714-5715
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous powder
Routes of administration	Subcutaneous use

Dosage and administration details:

Single SC dose, 900 mg

Investigational medicinal product name	REGN5713-5714-5715 placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous powder
Routes of administration	Subcutaneous use

Dosage and administration details:

Single SC dose, 600 mg

Arm title	Placebo Only

Arm description:

Placebo matching REGN5713-5714-5715 administered subcutaneously

Arm type	Placebo

No investigational medicinal product assigned in this arm

Number of subjects in period 1	REGN5713-5714-5715	Placebo Only
Started	176	177
Completed	166	172
Not completed	10	5
Consent withdrawn by subject	6	2
Adverse event, non-fatal	1	-
Lost to follow-up	2	2
Protocol deviation	1	1

Baseline characteristics

Reporting groups	
Reporting group title	REGN5713-5714-5715
Reporting group description:	
REGN5713-5714-5715 administered subcutaneously	
Reporting group title	Placebo Only
Reporting group description:	
Placebo matching REGN5713-5714-5715 administered subcutaneously	

Reporting group values	REGN5713-5714-5715	Placebo Only	Total
Number of subjects	176	177	353
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	167	169	336
From 65-84 years	9	8	17
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	39.6	42.1	
standard deviation	± 14.15	± 14.36	-
Sex: Female, Male Units: Participants			
Female	102	102	204
Male	74	75	149
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	2	4
Not Hispanic or Latino	172	174	346
Unknown or Not Reported	2	1	3
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	3	10	13
Native Hawaiian or Other Pacific Islander	1	0	1
Black or African American	1	2	3
White	165	161	326
More than one race	0	0	0
Unknown or Not Reported	6	3	9

End points

End points reporting groups

Reporting group title	REGN5713-5714-5715
Reporting group description: REGN5713-5714-5715 administered subcutaneously	
Reporting group title	Placebo Only
Reporting group description: Placebo matching REGN5713-5714-5715 administered subcutaneously	

Primary: Combined symptom and medication score (CSMS) in participants who receive a single dose of REGN5713-5714-5715 versus placebo

End point title	Combined symptom and medication score (CSMS) in participants who receive a single dose of REGN5713-5714-5715 versus placebo
End point description: CSMS is calculated by adding the Daily Medication Score (DMS) and Total Symptom Score (TSS) together, with scores ranging between 0 (none) and 38 (severe).	
End point type	Primary
End point timeframe: Until the end of Birch Pollen Season, up to Week 16	

End point values	REGN5713-5714-5715	Placebo Only		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	171	172		
Units: Scores on a Scale				
least squares mean (standard error)	7.503 (± 0.6545)	8.498 (± 0.6534)		

Statistical analyses

Statistical analysis title	Linear-Mixed Effect Model
Comparison groups	REGN5713-5714-5715 v Placebo Only
Number of subjects included in analysis	343
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0497
Method	LS Mean Difference
Parameter estimate	linear mixed-effect model
Point estimate	-0.995

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9886
upper limit	-0.0011

Secondary: Total symptom score (TSS), averaged over the duration of the birch pollen season, in participants who receive a single dose of REGN5713-5714-5715 versus placebo

End point title	Total symptom score (TSS), averaged over the duration of the birch pollen season, in participants who receive a single dose of REGN5713-5714-5715 versus placebo

End point description:

TSS is a combined score of TOSS and TNSS. TNSS and TOSS are scored as in part 1 each for a combined TSS of 0 (none) to 18 (severe)

End point type	Secondary

End point timeframe:

Until the end of Birch Pollen Season, up to Week 16

End point values	REGN5713-5714-5715	Placebo Only		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	171	172		
Units: Percentage of Participants				
least squares mean (standard error)	5.19 (± 0.397)	5.62 (± 0.396)		

Statistical analyses

No statistical analyses for this end point

Secondary: Total nasal symptom score (TNSS), averaged over the duration of the birch pollen season, in participants who receive a single dose of REGN5713-5714-5715 versus placebo

End point title	Total nasal symptom score (TNSS), averaged over the duration of the birch pollen season, in participants who receive a single dose of REGN5713-5714-5715 versus placebo

End point description:

Total nasal symptom score (TNSS) is from 0 to 12 and is based on assessment of 4 nasal symptoms graded on a Likert scale ranging from 0 (none) to 3 (severe) for congestion, itching, and rhinorrhea, and from 0 (none) to 3 (5 or more sneezes) for sneezing.

End point type	Secondary

End point timeframe:

Until the end of Birch Pollen Season, up to Week 16

End point values	REGN5713-5714-5715	Placebo Only		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	171	172		
Units: Percentage of Participants				
least squares mean (standard error)	3.76 (± 0.278)	4.00 (± 0.277)		

Statistical analyses

No statistical analyses for this end point

Secondary: Total ocular symptom score (TOSS), averaged over the duration of the birch pollen season, in participants who receive a single dose of REGN5713-5714-5715 versus placebo

End point title	Total ocular symptom score (TOSS), averaged over the duration of the birch pollen season, in participants who receive a single dose of REGN5713-5714-5715 versus placebo

End point description:

Total ocular symptom score is 0 to 6 and is based on itching/redness/gritty feeling and tearing/watering; each of the 2 symptoms is graded 0 (absent), 1 (mild), 2 (moderate), and 3 (severe)

End point type	Secondary

End point timeframe:

Until the end of Birch Pollen Season, up to Week 16

End point values	REGN5713-5714-5715	Placebo Only		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	171	172		
Units: Percentage of Participants				
least squares mean (standard error)	1.43 (± 0.150)	1.62 (± 0.150)		

Statistical analyses

No statistical analyses for this end point

Secondary: Daily medication score (DMS), averaged over the duration of the birch pollen season, in participants who receive a single dose of REGN5713-5714-5715 versus placebo

End point title	Daily medication score (DMS), averaged over the duration of the birch pollen season, in participants who receive a single dose of REGN5713-5714-5715 versus placebo

End point description:

The Daily Medication Score (DMS) is calculated by adding points for each pre-specified medication taken as follows: desloratadine 5 mg 6 points/dose; maximum daily score 6 points, olopatadine 1 mg/mL each drop 1.5 points/drop; maximum daily score 6 points, mometasone furoate 50 ug/dose 2.0 points/spray; maximum daily score 8 points). The scale is 0 (minimum) to 20 (maximum)

End point type	Secondary

End point timeframe:

Until the end of Birch Pollen Season, up to Week 16

End point values	REGN5713-5714-5715	Placebo Only		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	171	172		
Units: Percentage of Participants				
least squares mean (standard error)	2.316 (± 0.3993)	2.882 (± 0.3986)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of Participants with Treatment-Emergent Adverse Events (TEAEs) throughout the study

End point description:

Number of participants with any Treatment Emergent Adverse Events (TEAEs)

End point type	Secondary

End point timeframe:

Up to Day 127

End point values	REGN5713-5714-5715	Placebo Only		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	176		
Units: Count of Participants	92	85		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Serious TEAEs throughout the study

End point title	Number of Participants with Serious TEAEs throughout the study

End point description:

End point type	Secondary

End point timeframe:

Up to Day 127

End point values	REGN5713-5714-5715	Placebo Only		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	176		
Units: Count of Participants	3	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to the end of study in birch SPT mean wheal diameter in participants who receive a single dose of REGN5713-5714-5715 versus placebo

End point title	Change from baseline to the end of study in birch SPT mean wheal diameter in participants who receive a single dose of REGN5713-5714-5715 versus placebo

End point description:

End point type	Secondary

End point timeframe:

Baseline through Day 127

End point values	REGN5713-5714-5715	Placebo Only		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	171	172		
Units: millimeters				
least squares mean (standard error)	-3.139 (± 0.5086)	0.553 (± 0.5067)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from baseline to the end of study in birch SPT mean wheal diameter in participants who receive a single dose of REGN5713-5714-5715 versus placebo

End point title	Percent change from baseline to the end of study in birch SPT mean wheal diameter in participants who receive a single dose of REGN5713-5714-5715 versus placebo

End point description:

End point type	Secondary

End point timeframe:
Baseline through Day 127

End point values	REGN5713-5714-5715	Placebo Only		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	171	172		
Units: Percentage				
least squares mean (standard error)	-26.38 (± 5.179)	8.17 (± 5.160)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum concentration of REGN5713 over the study duration

End point title	Serum concentration of REGN5713 over the study duration[1]

End point description:

End point type	Secondary

End point timeframe:
Up to Day 127

Notes:
[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was presented for this endpoint

End point values	REGN5713-5714-5715			
Subject group type	Reporting group			
Number of subjects analysed	172			
Units: mg/L				
arithmetic mean (standard deviation)				
Day 0	0 (± 0)			
Day 56	10.0 (± 3.97)			
Day 112	2.53 (± 1.57)			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum concentration of REGN5714 over the study duration

End point title	Serum concentration of REGN5714 over the study duration[2]

End point description:

End point type	Secondary

End point timeframe:

Up to Day 127

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was presented for this endpoint

End point values	REGN5713-5714-5715			
Subject group type	Reporting group			
Number of subjects analysed	172			
Units: mg/L				
arithmetic mean (standard deviation)				
Day 0	0 (± 0)			
Day 56	14.7 (± 4.68)			
Day 112	4.82 (± 2.16)			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum concentration of REGN5715 over the study duration

End point title	Serum concentration of REGN5715 over the study duration[3]

End point description:

End point type	Secondary

End point timeframe:

Up to Day 127

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis was presented for this endpoint

End point values	REGN5713-5714-5715			
Subject group type	Reporting group			
Number of subjects analysed	172			
Units: mg/L				
arithmetic mean (standard deviation)				
Day 0	0 (± 0)			
Day 56	16.6 (± 5.34)			
Day 112	5.34 (± 2.35)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with treatment emergent anti-drug antibodies to REGN5713 throughout the study

End point title	Percentage of Participants with treatment emergent anti-drug antibodies to REGN5713 throughout the study

End point description:

End point type	Secondary

End point timeframe:

Up to Day 127

End point values	REGN5713-5714-5715	Placebo Only		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	168	171		
Units: Percentage of Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with treatment emergent anti-drug antibodies to REGN5715 throughout the study

End point title	Percentage of Participants with treatment emergent anti-drug antibodies to REGN5715 throughout the study

End point description:

End point type	Secondary

End point timeframe:

Up to Day 127

End point values	REGN5713-5714-5715	Placebo Only		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	168	171		
Units: Percentage of Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with treatment emergent anti-drug antibodies to REGN5714 throughout the study

End point title	Percentage of Participants with treatment emergent anti-drug antibodies to REGN5714 throughout the study

End point description:

End point type	Secondary

End point timeframe:

Up to Day 127

End point values	REGN5713-5714-5715	Placebo Only		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	168	171		
Units: Percentage of Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of "Well Days"

End point title	Number of "Well Days"

End point description:

"Well Days" are defined as days when rescue medication is not utilized and the Total symptom score (TSS) is ≤2/18

End point type	Secondary

End point timeframe:

Until the end of Birch Pollen Season, up to Week 16

End point values	REGN5713-5714-5715	Placebo Only		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	171	172		
Units: Days				
least squares mean (standard error)	8.3 (± 1.42)	8.6 (± 1.42)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 28 weeks	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	R5713-5714-5715 900 mg
Reporting group description: REGN5713-5714-5715 administered subcutaneously	
Reporting group title	Placebo
Reporting group description: Placebo matching REGN5713-5714-5715 administered subcutaneously	

Serious adverse events	R5713-5714-5715 900 mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 173 (1.73%)	0 / 176 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 173 (0.58%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Thermal burn			
subjects affected / exposed	1 / 173 (0.58%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 173 (0.58%)	0 / 176 (0.00%)	
occurrences causally related to treatment / all	0 / 1	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	R5713-5714-5715 900 mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 173 (18.50%)	43 / 176 (24.43%)	
Injury, poisoning and procedural complications			
Vaccination complication			
subjects affected / exposed	17 / 173 (9.83%)	22 / 176 (12.50%)	
occurrences (all)	26	29	
Nervous system disorders			
Headache			
subjects affected / exposed	15 / 173 (8.67%)	19 / 176 (10.80%)	
occurrences (all)	19	22	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 173 (2.89%)	9 / 176 (5.11%)	
occurrences (all)	5	9	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported