Clinical trial results:
A Randomized, Double-Blind, Multi-Dose, Placebo-Controlled Study to Evaluate the Efficacy and Safety of REGN5069 in Patients with Pain due to Osteoarthritis of the Knee

Summary

EudraCT number	2018-004730-15
Trial protocol	GB PL BG ES
Global end of trial date	29 October 2020

Results information

Result version number	v1 (current)
This version publication date	16 September 2021
First version publication date	16 September 2021

Trial information

Trial identification

Sponsor protocol code	R5069-OA-1849

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03956550
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 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	29 October 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 October 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the efficacy of REGN5069 compared to placebo in subjects with pain due to radiographically-confirmed osteoarthritis (OA) of the knee who had a history of inadequate joint pain relief or intolerance to current analgesic therapy.

Protection of trial subjects:

This clinical 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 GCP and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 May 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 51
Country: Number of subjects enrolled	Moldova, Republic of: 64
Country: Number of subjects enrolled	Poland: 56
Country: Number of subjects enrolled	Ukraine: 41
Country: Number of subjects enrolled	Georgia: 47
Worldwide total number of subjects	259
EEA total number of subjects	56

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)	137
From 65 to 84 years	121
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

The study was conducted in 5 countries and 12 sites participated in enrollment. It consisted of screening period up to 30 days, followed by a 12-week randomized, double-blind, placebo-controlled treatment period, a 24-week follow-up period, and end-of-study phone call approximately 52 weeks after first dose. Study was terminated at 36 weeks..

Pre-assignment

Screening details:

A total of 259 subjects randomized in 1:1:1 ratio to receive REGN5069 at 100 mg IV Q4W or at 1000 mg IV Q4W, or matching placebo Q4W. Subjects received 3 fixed-dose IV infusions at baseline, week 4 & week 8.

171 subjects randomized to receive REGN5069 (86 subjects in 100 mg Q4W group & 85 in 1000 mg Q4W group) & 88 randomized to receive placebo.

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	Placebo

Arm description:

Subjects received matching placebo intravenously every 4 weeks (Q4W)

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Matching dose administered intravenously every 4 weeks (Q4W)

Arm title	REGN5069 100 mg Q4W

Arm description:

Subjects received 100 milligrams (mg) of REGN5069 intravenously every 4 weeks (Q4W)

Arm type	Active comparator
Investigational medicinal product name	REGN5069
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

IV dose Q4W

Arm title	REGN5069 1000 mg Q4W

Arm description:

Subjects received 1000 milligrams (mg) of REGN5069 intravenously every 4 weeks (Q4W)

Arm type	Active comparator

Investigational medicinal product name	REGN5069
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

IV Q4W

Number of subjects in period 1	Placebo	REGN5069 100 mg Q4W	REGN5069 1000 mg Q4W
Started	88	86	85
Completed	18	14	15
Not completed	70	72	70
Consent withdrawn by subject	5	5	6
Adverse event, non-fatal	-	1	-
Sponsor decision	65	66	64

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received matching placebo intravenously every 4 weeks (Q4W)	
Reporting group title	REGN5069 100 mg Q4W
Reporting group description:	
Subjects received 100 milligrams (mg) of REGN5069 intravenously every 4 weeks (Q4W)	
Reporting group title	REGN5069 1000 mg Q4W
Reporting group description:	
Subjects received 1000 milligrams (mg) of REGN5069 intravenously every 4 weeks (Q4W)	

Reporting group values	Placebo	REGN5069 100 mg Q4W	REGN5069 1000 mg Q4W
Number of subjects	88	86	85
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)	51	45	41
From 65-84 years	36	41	44
85 years and over	1	0	0
Age Continuous			
Full analysis set population (FAS): includes all randomized subjects			
Units: years			
arithmetic mean	63.5	63.9	64.7
standard deviation	± 8.27	± 7.39	± 8.30
Sex: Female, Male			
Full analysis set population (FAS): includes all randomized subjects			
Units: Subjects			
Female	64	74	68
Male	24	12	17
Race/Ethnicity, Customized			
Full analysis set population (FAS): includes all randomized subjects			
Units: Subjects			
White	83	85	81
Black or African American	5	1	4
Asian	0	0	0
American Indian or Alaska Native	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Not reported	0	0	0
Other	0	0	0

Ethnicity (NIH/OMB)			
Full analysis set population (FAS): includes all randomized subjects			
Units: Subjects			
Hispanic or Latino	4	1	2
Not Hispanic or Latino	84	85	83
Unknown or Not Reported	0	0	0
Western Ontario and McMaster Osteoarthritis Index (WOMAC) Pain Subscale Score			
The WOMAC index has 24 parameters grouped in 3 subscales (pain-5 questions, physical function-17 questions & stiffness-2 questions), with 0-10 grading of each question. Each subscale score is summed up, divided by number of questions, & each is reported using Numerical Rating Scale (NRS) score 0-10. Total score equaled the sum of normalized subscale scores divided by 3 & reported using NRS score of 0-10. Higher scores equal worse pain, stiffness & functional limitations. Here 'n' = number of evaluable subjects at the specific time point.			
Units: Scores on a scale			
arithmetic mean	6.68	6.24	6.47
standard deviation	± 1.257	± 1.203	± 1.150

Reporting group values	Total		
Number of subjects	259		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	137		
From 65-84 years	121		
85 years and over	1		
Age Continuous			
Full analysis set population (FAS): includes all randomized subjects			
Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Full analysis set population (FAS): includes all randomized subjects			
Units: Subjects			
Female	206		
Male	53		
Race/Ethnicity, Customized			
Full analysis set population (FAS): includes all randomized subjects			
Units: Subjects			
White	249		
Black or African American	10		
Asian	0		
American Indian or Alaska Native	0		
Native Hawaiian or Other Pacific Islander	0		
Not reported	0		

Other	0		
Ethnicity (NIH/OMB)			
Full analysis set population (FAS): includes all randomized subjects			
Units: Subjects			
Hispanic or Latino	7		
Not Hispanic or Latino	252		
Unknown or Not Reported	0		
Western Ontario and McMaster Osteoarthritis Index (WOMAC) Pain Subscale Score			
The WOMAC index has 24 parameters grouped in 3 subscales (pain-5 questions, physical function-17 questions & stiffness-2 questions), with 0-10 grading of each question. Each subscale score is summed up, divided by number of questions, & each is reported using Numerical Rating Scale (NRS) score 0-10. Total score equaled the sum of normalized subscale scores divided by 3 & reported using NRS score of 0-10. Higher scores equal worse pain, stiffness & functional limitations. Here 'n' = number of evaluable subjects at the specific time point.			
Units: Scores on a scale			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Subjects received matching placebo intravenously every 4 weeks (Q4W)	
Reporting group title	REGN5069 100 mg Q4W
Reporting group description: Subjects received 100 milligrams (mg) of REGN5069 intravenously every 4 weeks (Q4W)	
Reporting group title	REGN5069 1000 mg Q4W
Reporting group description: Subjects received 1000 milligrams (mg) of REGN5069 intravenously every 4 weeks (Q4W)	

Primary: Change from Baseline to Week 12 in the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain Subscale Score

End point title	Change from Baseline to Week 12 in the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain Subscale Score
End point description: The WOMAC index has 24 parameters grouped in 3 subscales (pain-5 questions, physical function-17 questions & stiffness-2 questions), with 0-10 grading of each question. Each subscale score is summed up, divided by number of questions, & each is reported using Numerical Rating Scale (NRS) score 0-10. Total score = sum of normalized subscale scores divided by 3 & reported using NRS score of 0-10. Higher scores equal worse pain, stiffness & functional limitations. Full Analysis Set (FAS) population included all randomized subjects; Here 'n' = number of evaluable subjects at a specific time point.	
End point type	Primary
End point timeframe: Baseline to Week 12	

End point values	Placebo	REGN5069 100 mg Q4W	REGN5069 1000 mg Q4W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	84	80	82	
Units: Scores on a scale				
least squares mean (standard error)	-2.09 (± 0.188)	-2.37 (± 0.191)	-1.98 (± 0.190)	

Statistical analyses

Statistical analysis title	Placebo, REGN5069 1000 mg Q4W
Comparison groups	Placebo v REGN5069 1000 mg Q4W

Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.689
Method	Mixed models analysis

Statistical analysis title	Placebo, REGN5069 100 mg Q4W
Comparison groups	REGN5069 100 mg Q4W v Placebo
Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2978
Method	Mixed models analysis

Secondary: Change from Baseline to Week 12 in WOMAC Total Score

End point title	Change from Baseline to Week 12 in WOMAC Total Score

End point description:

The WOMAC index has 24 parameters grouped in 3 subscales (pain-5 questions, physical function-17 questions & stiffness-2 questions), with 0-10 grading of each question. Each subscale score is summed up, divided by number of questions, & each is reported using Numerical Rating Scale (NRS) score 0-10. Total score equaled the sum of normalized subscale scores divided by 3 & reported using NRS score of 0-10. Higher scores equal worse pain, stiffness & functional limitations. FAS population included all randomized subjects; Here 'n' = number of evaluable subjects at the specific time point.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	REGN5069 100 mg Q4W	REGN5069 1000 mg Q4W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	84	80	82	
Units: Scores on a scale				
least squares mean (standard error)	-1.83 (± 0.177)	-2.15 (± 0.179)	-1.81 (± 0.181)	

Statistical analyses

Statistical analysis title	Placebo, REGN5069 100 mg Q4W
Comparison groups	Placebo v REGN5069 100 mg Q4W

Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1973
Method	Mixed models analysis

Statistical analysis title	Placebo, REGN5069 1000 mg Q4W
Comparison groups	Placebo v REGN5069 1000 mg Q4W
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.942
Method	Mixed models analysis

Secondary: Change from Baseline to Week 12 in WOMAC Physical Function Subscale Score

End point title	Change from Baseline to Week 12 in WOMAC Physical Function Subscale Score

End point description:

The WOMAC index has 24 parameters grouped in 3 subscales (pain-5 questions, physical function-17 questions & stiffness-2 questions), with 0-10 grading of each question. Each subscale score is summed up, divided by number of questions, & each is reported using Numerical Rating Scale (NRS) score 0-10. Total score equaled the sum of normalized subscale scores divided by 3 & reported using NRS score of 0-10. Higher scores equal worse pain, stiffness & functional limitations. FAS population included all randomized subjects; Here 'n' = number of evaluable subjects at the specific time point.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	REGN5069 100 mg Q4W	REGN5069 1000 mg Q4W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	84	80	82	
Units: Scores on a scale				
least squares mean (standard error)	-1.74 (± 0.180)	-2.09 (± 0.183)	-1.75 (± 0.182)	

Statistical analyses

Statistical analysis title	Placebo, REGN5069 1000 mg Q4W
Comparison groups	Placebo v REGN5069 1000 mg Q4W

Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9719
Method	Mixed models analysis

Statistical analysis title	Placebo, REGN5069 100 mg Q4W
Comparison groups	Placebo v REGN5069 100 mg Q4W
Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1597
Method	Mixed models analysis

Secondary: Change from Baseline to Week 12 in Patient Global Assessment (PGA) Score

End point title	Change from Baseline to Week 12 in Patient Global Assessment (PGA) Score

End point description:

The Patient Global Assessment of OA (PGA) is a subject-rated assessment of current disease state on a 5-point Likert scale (1 = very good; 2 = good; 3 = fair; 4 = poor; and 5 = very poor). Full analysis set population (FAS): included all randomized subjects; Here 'n' = number of evaluable subjects at this time interval

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	REGN5069 100 mg Q4W	REGN5069 1000 mg Q4W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	84	80	82	
Units: Scores on a scale				
least squares mean (standard error)	-0.59 (± 0.076)	-0.75 (± 0.078)	-0.80 (± 0.078)	

Statistical analyses

Statistical analysis title	Placebo, REGN5069 100 mg Q4W
Comparison groups	Placebo v REGN5069 100 mg Q4W

Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1365
Method	Mixed models analysis

Statistical analysis title	Placebo, REGN5069 1000 mg Q4W
Comparison groups	Placebo v REGN5069 1000 mg Q4W
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0604
Method	Mixed models analysis

Secondary: Change from Baseline to Week 12 in WOMAC Stiffness Subscale Score

End point title	Change from Baseline to Week 12 in WOMAC Stiffness Subscale Score

End point description:

The WOMAC index has 24 parameters grouped in 3 subscales (pain-5 questions, physical function-17 questions & stiffness-2 questions), with 0-10 grading of each question. Each subscale score is summed up, divided by number of questions, & each is reported using Numerical Rating Scale (NRS) score 0-10. Total score equaled the sum of normalized subscale scores divided by 3 & reported using NRS score of 0-10. Higher scores equal worse pain, stiffness & functional limitations. FAS population included all randomized subjects; Here 'n' = number of evaluable subjects at the specific time point.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	REGN5069 100 mg Q4W	REGN5069 1000 mg Q4W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	84	80	82	
Units: Scores on a scale				
least squares mean (standard error)	-1.70 (± 0.214)	-2.20 (± 0.217)	-1.88 (± 0.217)	

Statistical analyses

Statistical analysis title	Placebo, REGN5069 1000 mg Q4W
Comparison groups	Placebo v REGN5069 1000 mg Q4W

Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5487
Method	Mixed models analysis

Statistical analysis title	Placebo, REGN5069 100 mg Q4W
Comparison groups	Placebo v REGN5069 100 mg Q4W
Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0989
Method	Mixed models analysis

Secondary: Percentage of Subjects with ≥30% Improvement in WOMAC Pain Subscale Score

End point title	Percentage of Subjects with ≥30% Improvement in WOMAC Pain Subscale Score

End point description:

The WOMAC index has 24 parameters grouped in 3 subscales (pain-5 questions, physical function-17 questions & stiffness-2 questions), with 0-10 grading of each question. Each subscale score is summed up, divided by number of questions, & each is reported using Numerical Rating Scale (NRS) score 0-10. Total score equaled the sum of normalized subscale scores divided by 3 & reported using NRS score of 0-10. Higher scores equal worse pain, stiffness & functional limitations. FAS population included all randomized subjects; Here 'n' = number of evaluable subjects at the specific time point.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	REGN5069 100 mg Q4W	REGN5069 1000 mg Q4W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	86	85	
Units: Percentage of subjects				
number (not applicable)	51.1	58.1	47.1	

Statistical analyses

Statistical analysis title	Placebo, REGN5069 1000 mg Q4W
Comparison groups	Placebo v REGN5069 1000 mg Q4W

Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5747
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Placebo, REGN5069 100 mg Q4W
Comparison groups	Placebo v REGN5069 100 mg Q4W
Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3572
Method	Cochran-Mantel-Haenszel

Secondary: Number of Non-Serious and Serious Treatment-Emergent Adverse Events (TEAEs) through End of Study

End point title	Number of Non-Serious and Serious Treatment-Emergent Adverse Events (TEAEs) through End of Study

End point description:

An adverse event (AE) is any untoward medical occurrence in a subject administered a study drug which may or may not have a causal relationship with the study drug. Treatment-emergent AEs (TEAEs) are AEs that developed or worsened during the treatment period. Safety Analysis Set (SAF): included all randomized subjects who received any study drug.

End point type	Secondary

End point timeframe:

Baseline to Week 36

End point values	Placebo	REGN5069 100 mg Q4W	REGN5069 1000 mg Q4W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	85	84	
Units: Number of events				
Non-Serious TEAEs	78	42	55	
Serious TEAEs	0	2	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Imaging Abnormalities Consistent with Adjudicated Arthropathies through End of Study

End point title	Number of Imaging Abnormalities Consistent with Adjudicated Arthropathies through End of Study

End point description:

Adjudicated arthropathy is an umbrella term referring to Rapidly Progressive Osteoarthritis Type 1 (RPOA-1), Rapidly Progressive Osteoarthritis Type 2 (RPOA-2), subchondral insufficiency fractures (SIF) and osteonecrosis (ON) confirmed by an arthropathy adjudication committee. Safety Analysis Set (SAF): included all randomized subjects who received any study drug

End point type	Secondary

End point timeframe:

Baseline to Week 36

End point values	Placebo	REGN5069 100 mg Q4W	REGN5069 1000 mg Q4W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	85	84	
Units: Number of events				
Baseline Up to and Including Week 12 Visit	1	0	0	
After Week 12 Visit, Up to and Including Week 36	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Presence of Anti-REGN5049 Antibody Development through End of Study

End point title	Number of Subjects with Presence of Anti-REGN5049 Antibody Development through End of Study

End point description:

Anti-Drug Antibody (ADA) Analysis Set: included all treated subjects who received any amount of study drug (active or placebo [safety analysis set (SAF)]) & had at least one non-missing anti-REGN5069 antibody result after first dose of study drug or placebo. ADA analysis set based on actual treatment received. Immunogenicity will be characterized by ADA responses & titers.

End point type	Secondary

End point timeframe:

Baseline to Week 36

End point values	Placebo	REGN5069 100 mg Q4W	REGN5069 1000 mg Q4W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	84	83	82	
Units: Subjects				
Negative	82	83	78	
Pre-Existing Immunoreactivity	1	0	4	
Treatment-Boosted Response	0	0	0	
Treatment-Emergent Response	1	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AE) and Serious Adverse Events (SAE) were collected from time of informed consent signature and then at each visit until the end of follow-up (week 36) for AEs and end of study (week 52) for SAEs. The study terminated early at 36 weeks.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects received matching placebo intravenously every 4 weeks (Q4W)

Reporting group title	REGN5069 1000 mg IV Q4W

Reporting group description:

Subjects received 1000 milligrams (mg) of REGN5069 intravenously every 4 weeks (Q4W)

Reporting group title	REGN5069 100 mg IV Q4W

Reporting group description:

Subjects received 100 milligrams (mg) of REGN5069 intravenously every 4 weeks (Q4W)

Serious adverse events	Placebo	REGN5069 1000 mg IV Q4W	REGN5069 100 mg IV Q4W
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 88 (3.41%)	0 / 84 (0.00%)	3 / 85 (3.53%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Meniscus injury			
subjects affected / exposed	1 / 88 (1.14%)	0 / 84 (0.00%)	0 / 85 (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
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 88 (0.00%)	0 / 84 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Transient ischaemic attack			

subjects affected / exposed	0 / 88 (0.00%)	0 / 84 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	1 / 88 (1.14%)	0 / 84 (0.00%)	0 / 85 (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
Dizziness			
subjects affected / exposed	0 / 88 (0.00%)	0 / 84 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 88 (1.14%)	0 / 84 (0.00%)	0 / 85 (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
COVID-19			
subjects affected / exposed	0 / 88 (0.00%)	0 / 84 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 88 (0.00%)	0 / 84 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo	REGN5069 1000 mg IV Q4W	REGN5069 100 mg IV Q4W
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 88 (54.55%)	36 / 84 (42.86%)	33 / 85 (38.82%)
Nervous system disorders			
Headache			
subjects affected / exposed	30 / 88 (34.09%)	20 / 84 (23.81%)	19 / 85 (22.35%)
occurrences (all)	64	47	36

Gastrointestinal disorders			
Toothache			
subjects affected / exposed	10 / 88 (11.36%)	0 / 84 (0.00%)	5 / 85 (5.88%)
occurrences (all)	15	0	7
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	9 / 88 (10.23%)	8 / 84 (9.52%)	3 / 85 (3.53%)
occurrences (all)	14	8	4
Arthralgia			
subjects affected / exposed	6 / 88 (6.82%)	7 / 84 (8.33%)	9 / 85 (10.59%)
occurrences (all)	7	9	17
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	11 / 88 (12.50%)	7 / 84 (8.33%)	4 / 85 (4.71%)
occurrences (all)	14	10	4
Urinary tract infection			
subjects affected / exposed	9 / 88 (10.23%)	5 / 84 (5.95%)	4 / 85 (4.71%)
occurrences (all)	14	6	5

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 September 2019	Added end of study phone call to collect long-term information on subject status; Study duration, end of study definition were updated for accuracy; study analysis plan updated

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
29 October 2020	Study terminated early due to lack of efficacy for indication of pain for osteoarthritis.	-

Notes:

Limitations and caveats

None reported