Clinical Trial Results: Study to Evaluate Arthroplasty Specimens in the Phase 3 Fasinumab Program for Osteoarthritis of the Knee and Hip

Summary	
EudraCT number	2018-001618-13
Trial protocol	GB PL
Global end of trial date	25 Aug 2020
Results information	
Results version number	v1(current)

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Trial information	
Trial identification	
Sponsor protocol code	R475-OA-1816
Additional study identifiers	
ISRCTN number	-
US NCT number	NCT03949673
WHO universal trial number (UTN)	-
Sponsors	
Sponsor organisation name	Regeneron Pharmaceuticals, Inc.
Sponsor organisation address	777 Old Saw Mill River Rd., Tarrytown, United States, 10591
Public contact	Clinical Trial Management, Regeneron Pharmaceuticals, Inc., clinicaltrials@regeneron.com
Scientific contact	Clinical Trial Management, Regeneron Pharmaceuticals, Inc., clinicaltrials@regeneron.com
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
Results analysis stage	
Analysis stage	Final
Date of interim/final analysis	25 Aug 2020

Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	25 Aug 2020
Was the trial ended prematurely?	Yes
General information about the trial	
Main objective of the trial	The objective of this exploratory study was to evaluate the cellular and connective tissue composition of joints from subjects with osteoarthritis (OA) who have been treated with fasinumab, compared with those treated with placebo or non-steroidal anti-inflammatory drugs (NSAID), in one of the following fasinumab phase 3 parent studies: R475-PN- 1523 (2015-003783-36), R475-OA-1611 (2016-005020-29) or R475-OA-1688 (2017-001702-15).
Protection of trial subjects	This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with the International Conference on Harmonisation (ICH) guidelines for Good Clinical Practice (GCP) and applicable regulatory requirements.
Actual start date of recruitment	08 Apr 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No
Population of trial subjects	
Number of subjects enrolled per country	
Country: Number of subjects enrolled	Poland: 1
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	United States: 10
Worldwide total number of subjects	20
EEA total number of subjects	10
Number of subjects enrolled per age group	
In utero	0
Preterm newborn - 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)	9
From 65 to 84 years	11
85 years and over	0

Subject disposition	
Recruitment	
Recruitment details	This study was initiated 08 Apr 2019 and included only subjects that received at least 1 dose of study drug in one of the 3 parent studies: R475-PN-1523 (2015-003783-36), R475-OA-1611 (2016-005020-29), or R475-OA-1688 (2017-001702-15).
Period 1	
Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised; No investigational medicinal product (IMP) was administered in this study.
Arms	
Are arms mutually exclusive	Yes
Arm title	Placebo
Arm description	Placebo was administered in the parent studies; joint tissue samples for this study were collected for subjects who voluntarily elected to have knee or hip joint arthroplasty during the parent studies
Arm title	NSAID
Arm description	Non-steroidal anti-inflammatory drugs (NSAID) were administered in the parent studies; joint tissue samples for this study were collected for subjects who voluntarily elected to have knee or hip joint arthroplasty during the parent studies
Arm title	Fasinumab
Arm description	Fasinumab was administered in the parent studies; joint tissue samples for this study were collected for subjects who voluntarily elected to have knee or hip joint arthroplasty during the parent studies.

Baseline characteristics	
Baseline characteristics subject population	Arthroplasty analysis set: All subjects who are enrolled in this study, have histological

	evaluation data and is based on the treatment received in their parent study (as treated).
Baseline characteristics reporting groups	
Reporting group title	Placebo
Reporting group description	Placebo was administered in the parent studies; joint tissue samples for this study were collected for subjects who voluntarily elected to have knee or hip joint arthroplasty during the parent studies
Reporting group title	NSAID
Reporting group description	Non-steroidal anti-inflammatory drugs (NSAID) were administered in the parent studies; joint tissue samples for this study were collected for subjects who voluntarily elected to have knee or hip joint arthroplasty during the parent studies
Reporting group title	Fasinumab
Reporting group description	Fasinumab was administered in the parent studies; joint tissue samples for this study were collected for subjects who voluntarily elected to have knee or hip joint arthroplasty during the parent studies.

Reporting group values	Placebo	NSAID	Fasinumab	Total
Number of subjects	2	5	13	20
Units: Subjects				
Age continuous				
Units: years				
arithmetic mean (standard deviation)	60.5 (7.8)	60.2 (7.7)	67.3 (8.2)	
Gender categorical				
Units: Subjects				
Female	2	3	7	12
Male	0	2	6	8

End points	
End points reporting groups	
Reporting group title	Placebo

Reporting group description	Placebo was administered in the parent studies; joint tissue samples for this study were collected for subjects who voluntarily elected to have knee or hip joint arthroplasty during the parent studies
Reporting group title	NSAID
Reporting group description	Non-steroidal anti-inflammatory drugs (NSAID) were administered in the parent studies; joint tissue samples for this study were collected for subjects who voluntarily elected to have knee or hip joint arthroplasty during the parent studies
Reporting group title	Fasinumab
Reporting group description	Fasinumab was administered in the parent studies; joint tissue samples for this study were collected for subjects who voluntarily elected to have knee or hip joint arthroplasty during the parent studies.

Primary: Descriptive histological evaluation of the synovium, cartilage, and bone.

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End point title	Descriptive histological evaluation of the synovium, cartilage, and bone.
End point description	The endpoint for this exploratory study is descriptive histological evaluation of the synovium, cartilage, and bone.
End point type	Primary
End point timeframe	From time of randomization into parent study until 24 weeks following last dose of study drug
Subject population	Arthroplasty analysis set: All subjects who are enrolled in this study, have histological evaluation data and is based on the treatment received in their parent study (as treated).

End point values	Placebo	NSAIDs	Fasinumab
Number of subjects analysed	2	5	13
Subjects with subarticular fracture or bony collapse	0	2	6

Statistical analysis title	N/A
Statistical analysis description	No formal hypothesis testing was performed in this exploratory study

Adverse events

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Adverse events information	
Timeframe for reporting adverse events	Safety was not analyzed or collected specifically for this sub-study
Adverse event reporting additional description	Subjects followed screening and pre-randomization requirements of their parent study and if they decided to undergo a joint replacement during the parent study, they could consent to this sub-study. Safety data was collected during the parent studies.

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? Yes The study was anticipated to close in February 2021 but ended prematurely on 25 Aug 2020 (date of global last arthroplasty surgery for last subject enrolled) due to lack of enrollment.
Limitations and caveats
Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.
This exploratory sub-study terminated early due to low enrollment. As of the date of this results report, R475-PN- 1523 (2015-003783-36), R475-OA-1611 (2016-005020-29) and R475-OA-1688 (2017-001702-15) are still ongoing and not all analyses of data from this study have been conducted. Additional results may be available in the future.