Clinical trial results:
A Multicenter, Open-label, Single-arm, Study to Evaluate Safety and Tolerability of Repatha in Patients With Homozygous Familial Hypercholesterolemia (HoFH) in India (RAMAN)

Summary

EudraCT number	2020-005111-51
Trial protocol	Outside EU/EEA
Global end of trial date	27 November 2019

Results information

Result version number	v1 (current)
This version publication date	04 December 2020
First version publication date	04 December 2020

Trial information

Trial identification

Sponsor protocol code	20170199

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03403374
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States,
Public contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com
Scientific contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.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	27 November 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 November 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to characterize the safety and tolerability in homozygous familial hypercholesterolemia (HoFH) patients in India exposed to 12 weeks of evolocumab (Repatha).

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonisation (ICH) Good Clinical Practice (GCP), Declaration of Helsinki, and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines. The investigator or his/her designee informed the subject of all aspects pertaining to the subject's participation in the study before any screening procedures were performed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 August 2018
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	India: 30
Worldwide total number of subjects	30
EEA total number of subjects	0

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)	13
Adults (18-64 years)	16
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 10 study centers in India. The first participant was enrolled on 04 August 2018 and the last participant was enrolled on 29 August 2019.

Pre-assignment

Screening details:

This study included a screening period of up to 4 weeks.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Evolocumab

Arm description:

Evolocumab 420 mg subcutaneous (SC) once monthly (QM) or every 2 weeks (Q2W; for participants on apheresis).

Arm type	Experimental
Investigational medicinal product name	evolocumab
Investigational medicinal product code	AMG 145
Other name	Repatha® EvoMab
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered by SC injection via autoinjector (AI)/pen

Number of subjects in period 1	Evolocumab
Started	30
Completed	29
Not completed	1
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	Evolocumab
Reporting group description:	
Evolocumab 420 mg subcutaneous (SC) once monthly (QM) or every 2 weeks (Q2W; for participants on apheresis).	

Reporting group values	Evolocumab	Total	
Number of subjects	30	30	
Age Categorical Units: participants			
Adolescents (12 - 17 years old)	13	13	
Adults (18 - 64 years old)	16	16	
Adults (65 - 84 years old)	1	1	
Age Continuous Units: years			
arithmetic mean	23.2		
standard deviation	± 13.1	-	
Sex: Female, Male Units:			
Female	13	13	
Male	17	17	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	30	30	
Unknown or Not Reported	0	0	
Race/Ethnicity, Customized Units: Subjects			
Asian	30	30	
Low-Density Lipoprotein Cholesterol (LDL-C) Units: mg/dL			
arithmetic mean	473.5		
standard deviation	± 135.2	-	
Apolipoprotein B (ApoB) Units: mg/dL			
arithmetic mean	275.3		
standard deviation	± 69.1	-	
Lipoprotein(a) (Lp[a]) Units: nmol/L			
arithmetic mean	201.3		
standard deviation	± 177.6	-	

End points

End points reporting groups

Reporting group title	Evolocumab

Reporting group description:

Evolocumab 420 mg subcutaneous (SC) once monthly (QM) or every 2 weeks (Q2W; for participants on apheresis).

Primary: Number of Participants With Treatment-Emergent Adverse Events (TEAEs)

End point title	Number of Participants With Treatment-Emergent Adverse Events (TEAEs)[1]

End point description:

Includes both serious and non-serious TEAEs. Adverse event (AE): any untoward medical occurrence in a participant. Serious AE (SAE): an AE that meets 1 on the following serious criteria: fatal; life-threatening; requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity; congenital anomaly/birth defect; other medically important serious event. TEAE: any AE starting on or after the first dose of study drug and up to and including 30 days after the last dose of study drug or the end of study date, whichever is earlier.

End point type	Primary

End point timeframe:

12 weeks

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: Descriptive statistics are presented, per protocol.

End point values	Evolocumab			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: participants	10			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline to Week 12 in Low-Density Lipoprotein Cholesterol (LDL-C)

End point title	Percent Change From Baseline to Week 12 in Low-Density Lipoprotein Cholesterol (LDL-C)

End point description:

End point type	Secondary

End point timeframe:

baseline, week 12

End point values	Evolocumab			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: percentage				
arithmetic mean (standard deviation)	-6.4 (± 22.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline to Week 12 in Apolipoprotein B (ApoB)

End point title	Percent Change From Baseline to Week 12 in Apolipoprotein B (ApoB)

End point description:

End point type	Secondary

End point timeframe:
baseline, week 12

End point values	Evolocumab			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: percentage				
arithmetic mean (standard deviation)	-6.0 (± 19.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline to Week 12 in Lipoprotein(a) (Lp[a])

End point title	Percent Change From Baseline to Week 12 in Lipoprotein(a) (Lp[a])

End point description:

End point type	Secondary

End point timeframe:
baseline, week 12

End point values	Evolocumab			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: percentage				
arithmetic mean (standard deviation)	-0.2 (± 26.2)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Fatal adverse events: from first dose date to the end of study date (week 12). Non-fatal adverse events: from the first dose of study drug up to 30 days after the last dose (at week 8) or until the end of study date (week 12), whichever was earlier.

Adverse event reporting additional description:

Treatment-emergent adverse events (TEAEs) are presented. TEAE: any AE starting on or after the first dose of study drug and up to and including 30 days after the last dose of study drug or the end of study date, whichever is earlier.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Evolocumab

Reporting group description:

Evolocumab 420 mg subcutaneous (SC) once monthly (QM) or every 2 weeks (Q2W; for participants on apheresis).

Serious adverse events	Evolocumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 30 (6.67%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Evolocumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 30 (26.67%)		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Injection site swelling			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Peripheral swelling			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Diabetic wound			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Skin fissures			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Arthritis			

subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Infections and infestations			
Pyoderma			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Varicella			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		

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