Clinical trial results:
High-Resolution Assessment of Coronary Plaques in a Global Evolocumab Randomized Study (HUYGENS)

Summary

EudraCT number	2017-003236-37
Trial protocol	CZ HU IT
Global end of trial date	21 January 2021

Results information

Result version number	v1 (current)
This version publication date	12 November 2021
First version publication date	12 November 2021

Trial information

Trial identification

Sponsor protocol code	20160184

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03570697
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States, 91320
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	21 January 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 January 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of evolocumab on fibrous cap thickness (FCT) in subjects with non-ST-elevation acute coronary syndrome (NSTE-ACS) who are taking maximally tolerated statin therapy.

Protection of trial subjects:

This study was conducted in accordance with the protocol and with:
- Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines
- Applicable International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines
- Applicable ICH laws and regulations

The investigator or his/her delegated representative explained to the subject, or his/her legally authorized representative, the aims, methods, anticipated benefits, and potential hazards of the study before any protocol-specific screening procedures or any investigational product(s) were administered, and answered all questions regarding the study.

Background therapy:

High-intensity statin treatment with atorvastatin ≥ 40 mg daily or equivalent as background therapy

Investigators up-titrated statin therapy to the maximally tolerated dose, in accordance with local guidelines, prior to randomization.

Evidence for comparator: -

Actual start date of recruitment	19 November 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	Australia: 2
Country: Number of subjects enrolled	Czechia: 10
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Hungary: 45
Country: Number of subjects enrolled	Italy: 23
Country: Number of subjects enrolled	Netherlands: 78
Worldwide total number of subjects	164
EEA total number of subjects	162

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)	104
From 65 to 84 years	60
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 23 research centers in Australia (2), Czech Republic (2), Germany (2), Hungary (4), Italy (6), and the Netherlands (7), from November 2018 to December 2019.

Pre-assignment

Screening details:

Participants were randomized 1:1 into 2 treatment groups: evolocumab 420 mg subcutaneously (SC) monthly (QM) or placebo SC QM.

Randomization was stratified by current statin use (> 4 weeks or ≤ 4 weeks) at screening.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo SC injection QM for 48 weeks. Background maximally tolerated statin therapy for the duration of the study participation.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in cartridge
Routes of administration	Subcutaneous use

Dosage and administration details:

Matching placebo was administered in accordance with instructions in the Investigational Product Instruction Manual (IPIM) and the Information for Use (IFU). The subject (or designee) must have had demonstrated competency, as per site judgment, at administration of SC injections before self-administration was permitted.

Arm title	Evolocumab

Arm description:

Evolocumab 420 mg SC injection QM for 48 weeks. Background maximally tolerated statin therapy for the duration of the study participation.

Arm type	Experimental
Investigational medicinal product name	Evolocumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in cartridge
Routes of administration	Subcutaneous use

Dosage and administration details:

Evolocumab was administered in accordance with instructions in the IPIM and the IFU. The subject (or designee) must have had demonstrated competency, as per site judgment, at administration of SC injections before self-administration was permitted.

Number of subjects in period 1	Placebo	Evolocumab
Started	82	82
Received at least 1 dose of study drug	81	80
Completed	76	79
Not completed	6	3
Adverse event, serious fatal	2	-
Consent withdrawn by subject	4	2
Lost to follow-up	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo SC injection QM for 48 weeks. Background maximally tolerated statin therapy for the duration of the study participation.	
Reporting group title	Evolocumab
Reporting group description:	
Evolocumab 420 mg SC injection QM for 48 weeks. Background maximally tolerated statin therapy for the duration of the study participation.	

Reporting group values	Placebo	Evolocumab	Total
Number of subjects	82	82	164
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	60.4	61.1	
standard deviation	± 9.4	± 10.0	-
Sex: Female, Male Units:			
Female	26	20	46
Male	56	62	118
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	4	5
Not Hispanic or Latino	81	78	159
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
Asian	1	1	2
White	80	79	159
Other, Not Specified	1	2	3
Stratification Factor: Statin Use at Screening Units: Subjects			
> 4 weeks of statin use	20	19	39
≤ 4 weeks of statin use	62	63	125
Minimum Fibrous Cap Thickness (FCT)			
Minimum FCT as determined by optical coherence tomography (OCT). Minimum FCT for a participant is defined as the minimum of all minimum FCT measurements within each individual frame across all frames of that participant. Higher value of FCT indicates a better situation. Full Analysis Set; n=81, 80			
Units: µm			
arithmetic mean	54.6	56.6	
standard deviation	± 15.1	± 17.8	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo SC injection QM for 48 weeks. Background maximally tolerated statin therapy for the duration of the study participation.	
Reporting group title	Evolocumab
Reporting group description:	
Evolocumab 420 mg SC injection QM for 48 weeks. Background maximally tolerated statin therapy for the duration of the study participation.	

Primary: Absolute Change From Baseline in Minimum FCT

End point title	Absolute Change From Baseline in Minimum FCT
End point description:	
Absolute change from baseline in minimum FCT in a matched segment of artery as determined by OCT. Minimum FCT for a participant is defined as the minimum of all minimum FCT measurements within each individual frame across all frames of that participant. Higher value of FCT indicates a better situation. Full Analysis Set: all participants who received at least 1 dose of study drug.	
End point type	Primary
End point timeframe:	
Baseline, week 50	

End point values	Placebo	Evolocumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	80		
Units: µm				
least squares mean (standard error)	21.5 (± 5.2)	42.7 (± 5.1)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Evolocumab
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.015
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	21.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	4.7
upper limit	37.7
Variability estimate	Standard error of the mean
Dispersion value	7.9

Secondary: Percent Change From Baseline in Minimum FCT

End point title	Percent Change From Baseline in Minimum FCT

End point description:

Percent change from baseline in minimum FCT in a matched segment of artery as determined by OCT. Minimum FCT for a participant is defined as the minimum of all minimum FCT measurements within each individual frame across all frames of that participant. Higher value of FCT indicates a better situation.

Full Analysis Set: all participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, week 50

End point values	Placebo	Evolocumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	80		
Units: percent change				
least squares mean (standard error)	44.30 (± 11.76)	81.76 (± 10.94)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Evolocumab
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.041
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	37.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.63
upper limit	73.31

Variability estimate	Standard error of the mean
Dispersion value	17.04

Secondary: Absolute Change From Baseline in Mean Minimum FCT

End point title	Absolute Change From Baseline in Mean Minimum FCT

End point description:

Absolute change from baseline in mean minimum FCT for all images assessed in an individual participant as determined by OCT. Minimum FCT for a participant is defined as the minimum of all minimum FCT measurements within each individual frame across all frames of that participant. Higher value of FCT indicates a better situation.

Full Analysis Set: all participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, week 50

End point values	Placebo	Evolocumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	80		
Units: µm				
least squares mean (standard error)	29.78 (± 6.88)	62.29 (± 5.95)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Evolocumab
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.003
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	32.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.67
upper limit	52.35
Variability estimate	Standard error of the mean
Dispersion value	9.52

Secondary: Absolute Change From Baseline in the Maximum Lipid Arc

End point title	Absolute Change From Baseline in the Maximum Lipid Arc

End point description:

Absolute change from baseline in the maximum lipid arc in a matched segment of artery as determined by OCT. Lower value of lipid arc indicates a better situation.

Full Analysis Set: all participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, week 50

End point values	Placebo	Evolocumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	81		
Units: degrees				
least squares mean (standard error)	-31.4 (± 9.0)	-57.5 (± 7.4)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Evolocumab
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.032
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-49.6
upper limit	-2.4
Variability estimate	Standard error of the mean
Dispersion value	11.4

Secondary: Absolute Change from Baseline in Minimum FCT in Lipid Rich Plaques

End point title	Absolute Change from Baseline in Minimum FCT in Lipid Rich Plaques

End point description:

Absolute change from baseline in minimum FCT in lipid rich plaques as determined by OCT. Lipid rich plaques are defined as minimum FCT less than 120 µm and lipid arc greater than 90° in at least 3 consecutive images as determined by OCT. Higher value of FCT indicates a better situation.

Full Analysis Set: all participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe: Baseline, week 50

End point values	Placebo	Evolocumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	80		
Units: µm				
least squares mean (standard error)	24.6 (± 5.5)	40.6 (± 5.5)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Evolocumab
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.036
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	16
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.1
upper limit	31
Variability estimate	Standard error of the mean
Dispersion value	7.5

Secondary: Absolute Change from Baseline in Maximum Lipid Arc in Lipid Rich Plaques

End point title	Absolute Change from Baseline in Maximum Lipid Arc in Lipid Rich Plaques

End point description:

Absolute change from baseline in maximum lipid arc in lipid rich plaques. Lipid rich plaques are defined as minimum FCT less than 120 µm and lipid arc greater than 90° in at least 3 consecutive images as determined by OCT. Lower value of lipid arc indicates a better situation.

Full Analysis Set: all participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, week 50

End point values	Placebo	Evolocumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	80		
Units: degrees				
least squares mean (standard error)	-31.9 (± 8.1)	-61.9 (± 7.9)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Evolocumab
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.005
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-30
Confidence interval	
level	95 %
sides	2-sided
lower limit	-50.5
upper limit	-9.5
Variability estimate	Standard error of the mean
Dispersion value	10.4

Secondary: Absolute Change From Baseline in Lipid Core Length in Lipid Rich Plaques

End point title	Absolute Change From Baseline in Lipid Core Length in Lipid Rich Plaques

End point description:

Absolute change from baseline in lipid core length in lipid rich plaques. Lipid rich plaques are defined as minimum FCT less than 120 µm and lipid arc greater than 90° in at least 3 consecutive images as determined by OCT. Lower value of lipid core length indicates a better situation.

Full Analysis Set: all participants who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, week 50

End point values	Placebo	Evolocumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	80		
Units: mm				
least squares mean (standard error)	-3.33 (± 0.64)	-5.76 (± 0.61)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Evolocumab
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.003
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-2.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.04
upper limit	-0.82
Variability estimate	Standard error of the mean
Dispersion value	0.81

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event (AE) reporting period is from the 1st dose of IP up to and including 30 days after the last dose of IP date or the EOS date (Week 52) whichever is earlier.

Adverse event reporting additional description:

Serious adverse events and other adverse events are reported for all participants who received at least one dose of study drug. All-cause mortality is reported for all participants randomized.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	EvoMab 420 MG QM

Reporting group description:

Evolocumab 420 mg SC injection QM for 48 weeks. Background maximally tolerated statin therapy for the duration of the study participation.

Reporting group title	Placebo QM

Reporting group description:

Placebo SC injection QM for 48 weeks. Background maximally tolerated statin therapy for the duration of the study participation.

Serious adverse events	EvoMab 420 MG QM	Placebo QM	
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 80 (16.25%)	16 / 81 (19.75%)	
number of deaths (all causes)	0	2	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 80 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	1 / 80 (1.25%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Arteriosclerosis			

subjects affected / exposed	1 / 80 (1.25%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 80 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary hypertensive crisis			
subjects affected / exposed	0 / 80 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	1 / 80 (1.25%)	0 / 81 (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			
Carotid artery restenosis			
subjects affected / exposed	0 / 80 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pain			
subjects affected / exposed	0 / 80 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 80 (1.25%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			

subjects affected / exposed	0 / 80 (0.00%)	3 / 81 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	1 / 80 (1.25%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	0 / 80 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 80 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Coronary artery disease			
subjects affected / exposed	1 / 80 (1.25%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	1 / 80 (1.25%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation			
subjects affected / exposed	1 / 80 (1.25%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 80 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebrobasilar insufficiency			

subjects affected / exposed	1 / 80 (1.25%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Normocytic anaemia			
subjects affected / exposed	1 / 80 (1.25%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal wall haematoma			
subjects affected / exposed	0 / 80 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ulcerative			
subjects affected / exposed	1 / 80 (1.25%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal angiodysplasia			
subjects affected / exposed	1 / 80 (1.25%)	0 / 81 (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			
Intervertebral disc disorder			
subjects affected / exposed	1 / 80 (1.25%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 80 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Enterococcal infection			

subjects affected / exposed	1 / 80 (1.25%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis staphylococcal			
subjects affected / exposed	0 / 80 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 80 (1.25%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetic metabolic decompensation			
subjects affected / exposed	0 / 80 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lactic acidosis			
subjects affected / exposed	0 / 80 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	EvoMab 420 MG QM	Placebo QM	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 80 (38.75%)	30 / 81 (37.04%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 80 (7.50%)	5 / 81 (6.17%)	
occurrences (all)	7	5	
Hypotension			
subjects affected / exposed	3 / 80 (3.75%)	1 / 81 (1.23%)	
occurrences (all)	3	1	
Cardiac disorders			

Angina pectoris			
subjects affected / exposed	4 / 80 (5.00%)	7 / 81 (8.64%)	
occurrences (all)	4	7	
Bradycardia			
subjects affected / exposed	2 / 80 (2.50%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 80 (0.00%)	2 / 81 (2.47%)	
occurrences (all)	0	2	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 80 (3.75%)	2 / 81 (2.47%)	
occurrences (all)	3	2	
Non-cardiac chest pain			
subjects affected / exposed	2 / 80 (2.50%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	2 / 80 (2.50%)	1 / 81 (1.23%)	
occurrences (all)	2	1	
Diarrhoea			
subjects affected / exposed	3 / 80 (3.75%)	4 / 81 (4.94%)	
occurrences (all)	3	4	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 80 (2.50%)	3 / 81 (3.70%)	
occurrences (all)	2	3	
Epistaxis			
subjects affected / exposed	3 / 80 (3.75%)	0 / 81 (0.00%)	
occurrences (all)	3	0	
Oropharyngeal pain			
subjects affected / exposed	2 / 80 (2.50%)	2 / 81 (2.47%)	
occurrences (all)	3	2	
Rhinorrhoea			

subjects affected / exposed	2 / 80 (2.50%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	0 / 80 (0.00%)	2 / 81 (2.47%)	
occurrences (all)	0	2	
Rash			
subjects affected / exposed	1 / 80 (1.25%)	2 / 81 (2.47%)	
occurrences (all)	1	3	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 80 (2.50%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Muscle spasms			
subjects affected / exposed	0 / 80 (0.00%)	3 / 81 (3.70%)	
occurrences (all)	0	3	
Myalgia			
subjects affected / exposed	5 / 80 (6.25%)	6 / 81 (7.41%)	
occurrences (all)	6	6	
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 80 (1.25%)	2 / 81 (2.47%)	
occurrences (all)	1	2	
Pneumonia			
subjects affected / exposed	2 / 80 (2.50%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	2 / 80 (2.50%)	0 / 81 (0.00%)	
occurrences (all)	2	0	
Glucose tolerance impaired			
subjects affected / exposed	0 / 80 (0.00%)	2 / 81 (2.47%)	
occurrences (all)	0	2	

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