Clinical trial results:
A multi-center, open-label, randomized, study to assess the onset of platelet aggregation inhibition after a single subcutaneous injection of ACT-246475 in adults with acute myocardial infarction

Summary

EudraCT number	2018-000765-36
Trial protocol	BE
Global end of trial date	10 November 2018

Results information

Result version number	v1 (current)
This version publication date	03 November 2019
First version publication date	03 November 2019

Trial information

Trial identification

Sponsor protocol code	ID-076A202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03487445
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Idorsia Pharmaceuticals Ltd
Sponsor organisation address	Hegenheimermattweg 91, Allschwil, Switzerland, 4123
Public contact	Clinical Trial Disclosure Desk, Idorsia Pharmaceuticals Ltd, clinical-trials-disclosure@idorsia.com
Scientific contact	Clinical Trial Disclosure Desk, Idorsia Pharmaceuticals Ltd, clinical-trials-disclosure@idorsia.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	04 March 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 November 2018
Global end of trial reached?	Yes
Global end of trial date	10 November 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to assess the inhibition of adenosine diposphate (ADP)-mediated platelet aggregation 30 min after a single subcutaneous (s.c.) injection of selatogrel (ACT-246475) in subjects with acute myocardial infarction (AMI) receiving conventional antithrombotic treatment (e.g., aspirin, chronic oral P2Y12 receptor antagonists, anticoagulants).

Protection of trial subjects:

Prior to the start of the study, each study site consulted an independent ethics committee, i.e., a review panel that was responsible for ensuring the protection of the rights, safety, and well-being of human subjects involved in a clinical investigation. The protocol and any material provided to the subject (such as a subject information sheet or description of the study used to obtain informed consent) were reviewed and approved by the appropriate Independent ethics committee before study was started.

Eligible subjects presented with acute myocardial infarction (AMI; ST-segment elevation myocardial infarction [STEMI] or non-STEMI [NSTEMI]), a life-threatening condition, and therefore fulfilled the ICH-GCP definition of vulnerable subjects ("persons in emergency situations"). Accordingly, a specific process for obtaining consent was implemented in compliance with local regulations and approved by the independent ethics committee.

An Independent Safety Event Committee had overall responsibility for safeguarding the interests of subjects.

Background therapy:

Standard treatment of AMI was allowed including anticoagulants. Ticagrelor was the only oral P2Y12 receptor antagonist allowed to be initiated during the study and its administration was possible only after selatogrel administration. Use of fibrinolytics or GPIIb/IIIa inhibitors was prohibited unless required for bail-out. All other standard-of-care treatments for AMI were allowed without restriction.

Evidence for comparator:

Not applicable.

Actual start date of recruitment	10 July 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	Belgium: 14
Country: Number of subjects enrolled	Israel: 1
Country: Number of subjects enrolled	Switzerland: 33
Worldwide total number of subjects	48
EEA total number of subjects	14

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)	18
From 65 to 84 years	29
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

The study was conducted between 10 July 2018 and 10 November 2018.

Pre-assignment

Screening details:

Of the 48 subjects screened and randomized, 47 subjects were treated. One subject randomized to the 8 mg selatogrel arm did not receive the study treatment for administrative reasons (study treatment in quarantine).

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Selatogrel - 8mg

Arm description:

A single 8 mg dose of selatogrel (ACT-246475) was administered via a single subcutaneous (s.c.) injection in the thigh.

Arm type	Experimental
Investigational medicinal product name	Selatogrel
Investigational medicinal product code	ACT-246475
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

ACT-246475 for s.c. administration was supplied in sealed glass vials at a strength of 20 mg. The vials contained 22 mg of lyophilized ACT-246475A (hydrochloride salt of ACT-246475) for reconstitution with 1 mL of water for injection. The stock solution was diluted with 1 mL of NaCl 0.9% to obtain the required final concentration for injection ensuring the same volume of injection for both doses. The injected volume was 0.8 mL for all subjects. Administration was performed at the investigational site by qualified personnel.

Arm title	Selatogrel - 16 mg

Arm description:

A single 16 mg dose of selatogrel (ACT-246475) was administered via a single subcutaneous (s.c.) injection in the thigh.

Arm type	Experimental
Investigational medicinal product name	Selatogrel
Investigational medicinal product code	ACT-246475
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

ACT-246475 for s.c. administration was supplied in sealed glass vials at a strength of 20 mg. The vials contained 22 mg of lyophilized ACT-246475A (hydrochloride salt of ACT-246475) for reconstitution with 1 mL of water for injection. The injected volume was 0.8 mL for all subjects. Administration was performed at the investigational site by qualified personnel.

Number of subjects in period 1	Selatogrel - 8mg	Selatogrel - 16 mg
Started	25	23
Completed	24	23
Not completed	1	0
Administrative reasons	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Selatogrel - 8mg
Reporting group description:	
A single 8 mg dose of selatogrel (ACT-246475) was administered via a single subcutaneous (s.c.) injection in the thigh.	
Reporting group title	Selatogrel - 16 mg
Reporting group description:	
A single 16 mg dose of selatogrel (ACT-246475) was administered via a single subcutaneous (s.c.) injection in the thigh.	

Reporting group values	Selatogrel - 8mg	Selatogrel - 16 mg	Total
Number of subjects	25	23	48
Age categorical Units: Subjects			
Adults (18-64 years)	10	8	18
From 65-84 years	14	15	29
85 years and over	1	0	1
Age continuous Units: years			
arithmetic mean	64.3	68.0	
standard deviation	± 12.5	± 10.3	-
Gender categorical Units: Subjects			
Female	8	5	13
Male	17	18	35
Race Units: Subjects			
Asian	1	2	3
White	23	21	44
Other	1	0	1
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	25	23	48
Body mass index Units: kg/m^2			
arithmetic mean	27.92	26.78	
standard deviation	± 4.75	± 3.74	-

End points

End points reporting groups

Reporting group title	Selatogrel - 8mg
Reporting group description:	
A single 8 mg dose of selatogrel (ACT-246475) was administered via a single subcutaneous (s.c.) injection in the thigh.	
Reporting group title	Selatogrel - 16 mg
Reporting group description:	
A single 16 mg dose of selatogrel (ACT-246475) was administered via a single subcutaneous (s.c.) injection in the thigh.	

Primary: Number of subjects achieving a PD response

End point title	Number of subjects achieving a PD response[1]
End point description:	
The primary PD endpoint was the response to treatment, defined for each subject as a P2Y12 reaction units (PRU) value < 100 at 30 min post-dose, as measured via the VerifyNow® assay. The PRU indicates the extent of (residual) ADP-mediated platelet aggregation, specific to the P2Y12 receptor.	
End point type	Primary
End point timeframe:	
30 minutes post treatment administration	

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: A statistical analysis comparing the two doses was not planned. The main analysis (mFAS, treatment dose as received) of treatment effect on the primary endpoint was conducted independently for each dose, i.e., 8 and 16 mg, at 0.025 type I error level, with null hypothesis defined as a proportion of responding patients less or equal to 50%. If this null hypothesis was rejected, a subsequent null hypothesis of treatment effect less or equal to 85% was tested at a 0.025 level.

End point values	Selatogrel - 8mg	Selatogrel - 16 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23[2]	22[3]		
Units: number of subjects				
Number of responders at 30 minutes	21	21		

Notes:

[2] - Modified full analysis set (all subjects with a 30-min post dose VerifyNow(R) blood sample analysis)

[3] - Modified full analysis set (all subjects with a 30-min post dose VerifyNow(R) blood sample analysis)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment emergent adverse events (TEAEs) were those adverse events with onset date/time after the date/time of study drug administration and up to 48 hours after the date/time of study treatment administration.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Selatogrel - 8 mg
Reporting group description: -	
Reporting group title	Selatogrel - 16 mg

Reporting group description: -

Serious adverse events	Selatogrel - 8 mg	Selatogrel - 16 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 24 (4.17%)	1 / 23 (4.35%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Ventricular tachycardia			
subjects affected / exposed	1 / 24 (4.17%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Selatogrel - 8 mg	Selatogrel - 16 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 24 (50.00%)	7 / 23 (30.43%)	
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Vascular pseudoaneurysm			

subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Aortic stenosis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	1	
Arteriovenous fistula			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Hypertension			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Hypotension			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Cardiac failure			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	1	
Extrasystoles			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Mitral valve stenosis			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	1	
Nodal rhythm			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Ventricular tachycardia			
subjects affected / exposed	3 / 24 (12.50%)	2 / 23 (8.70%)	
occurrences (all)	3	2	
Nervous system disorders			

Dizziness			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	1	
Pleural effusion			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	1	
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Confusional state			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	1	
Delirium			
subjects affected / exposed	1 / 24 (4.17%)	0 / 23 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Herpes zoster			
subjects affected / exposed	0 / 24 (0.00%)	1 / 23 (4.35%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	3 / 24 (12.50%)	2 / 23 (8.70%)	
occurrences (all)	3	2	
Hypokalaemia			

subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 1	0 / 23 (0.00%) 0	

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