



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

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