



Clinical trial results:

A Phase 2a, multi-center, single-blind, within-subject, placebo-controlled study to assess the pharmacodynamics of ACT-709478 in subjects with photosensitive epilepsy

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2017-000494-36 |
| Trial protocol | DE FR |
| Global end of trial date | 25 April 2018 |

Results information

| | |
|--------------------------------|--|
| Result version number | v2 (current) |
| This version publication date | 07 November 2019 |
| First version publication date | 25 May 2019 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data setChange of Sponsor. |

Trial information

Trial identification

| | |
|-----------------------|------------|
| Sponsor protocol code | AC-083-103 |
|-----------------------|------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03239691 |
| 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 | 22 November 2018 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 25 April 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To assess the pharmacodynamics by means of the change in intermittent photic stimulation induced photoparoxysmal response in male and female subjects with photosensitive epilepsy following single dose administration of ACT-709478.

Protection of trial subjects:

Prior to the start of the study and implementation of the amendments, Independent Ethics Committees were consulted, i.e., review panels that were responsible for ensuring the protection of the rights, safety, and well being of human subjects involved in a clinical investigation.

Background therapy:

Subjects were allowed to be on stable background treatment (i.e., no dose changes within 4 weeks prior to screening and no changes foreseen during the study) with a maximum of 2 concomitant antiepileptic drugs. During the whole study duration, they received the antiepileptic drugs according to their regular administration schedule.

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 06 October 2017 |
| 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 | Germany: 5 |
| Worldwide total number of subjects | 5 |
| EEA total number of subjects | 5 |

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) | 5 |

| | |
|---------------------|---|
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study was conducted in 2 countries and 5 sites

Pre-assignment

Screening details:

A screening evaluation was performed within 3–28 days before first study treatment administration for male subjects and female subjects of non-childbearing potential and within 10–28 days before first study treatment administration for female subjects of childbearing potential.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Non-randomised - controlled |
| Blinding used | Single blind |
| Roles blinded | Subject |

Blinding implementation details:

For safety reasons, this study was conducted in a single-blind fashion. The investigator and study site personnel, the monitors, and the sponsor knew on which study days placebo or ACT-709478 was administered. In contrast, the subjects remained blinded to the study treatment until study closure. The investigational treatment and its matching placebo were indistinguishable.

Arms

| | |
|-----------|---|
| Arm title | ACT-709478 single-dose / placebo administration |
|-----------|---|

Arm description:

Each subject was to receive both placebo and a single dose of active treatment on consecutive days. Placebo was to be administered in the morning of Day 1 and Day 3, and ACT-709478 in the morning of Day 2.

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | ACT-709478 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Hard gelatin capsules for oral administration formulated at a strength of 100 mg.

| | |
|--|---------------|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Matching placebo available as matching capsules for oral administration.

| Number of subjects in period 1 | ACT-709478 single-dose / placebo administration |
|---------------------------------------|---|
| Started | 5 |
| Completed | 4 |
| Not completed | 1 |
| Treatment discontinuation | 1 |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|---------------|
| Reporting group title | Overall trial |
| Reporting group description: - | |

| Reporting group values | Overall trial | Total | |
|------------------------------------|---------------|-------|--|
| Number of subjects | 5 | 5 | |
| Age categorical Units: Subjects | | | |

| | | | |
|---|------------------|---|--|
| Age continuous Units: years arithmetic mean full range (min-max) | 35.6 19 to 57 | - | |
| Gender categorical Units: Subjects | | | |
| Female | 5 | 5 | |

| | | | |
|--|----------------------|---|--|
| BMI Units: kg/m2 arithmetic mean full range (min-max) | 25.8 23.3 to 29.2 | - | |
|--|----------------------|---|--|

End points

End points reporting groups

| | |
|---|---|
| Reporting group title | ACT-709478 single-dose / placebo administration |
| Reporting group description: Each subject was to receive both placebo and a single dose of active treatment on consecutive days. Placebo was to be administered in the morning of Day 1 and Day 3, and ACT-709478 in the morning of Day 2. | |

Primary: Positive response described as complete suppression of photoparoxysmal response or a clinically relevant reduction in the standardized photosensitive range

| | |
|------------------------|--|
| End point title | Positive response described as complete suppression of photoparoxysmal response or a clinically relevant reduction in the standardized photosensitive range ^[1] |
| End point description: | |

| | |
|--|---------|
| End point type | Primary |
| End point timeframe: From Day 2 to Day 10 | |

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: See version 1.

| End point values | ACT-709478 single-dose / placebo administration | | | |
|-----------------------------|---|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 3 | | | |
| Units: Positive response | | | | |
| Subject 1 | 0 | | | |
| Subject 2 | 1 | | | |
| Subject 3 | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time (hours) to onset of positive response

| | |
|---|--|
| End point title | Time (hours) to onset of positive response |
| End point description: Defined by the first time point after ACT-709478 administration at which complete suppression of PPR or reduction in SPR ≥ 3 units compared to baseline is achieved at least at 2 consecutive time points. | |
| End point type | Secondary |
| End point timeframe: From Day 2 to Day 10 | |

| | | | | |
|-----------------------------|--|--|--|--|
| End point values | ACT-709478 single-dose / placebo administration | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 3 | | | |
| Units: Hours | | | | |
| Subject 2 - Eye closure | 55 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Duration (hours) of positive response

| | |
|---|---------------------------------------|
| End point title | Duration (hours) of positive response |
| End point description: Defined as the time elapsed between the time point of onset of the positive response and the last time point of the positive response after ACT-709478 administration | |
| End point type | Secondary |
| End point timeframe: From Day 2 to Day 10 | |

| | | | | |
|-----------------------------|--|--|--|--|
| End point values | ACT-709478 single-dose / placebo administration | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 3 | | | |
| Units: Hours | | | | |
| Subject 2 - Eye closure | 143 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum SPR reduction

| | |
|--|-----------------------|
| End point title | Maximum SPR reduction |
| End point description: Defined as the largest reduction in SPR achieved at any time point compared to baseline during the positive response after ACT-709478 administration | |
| End point type | Secondary |

End point timeframe:
From Day 2 to Day 10

| | | | | |
|-----------------------------|--|--|--|--|
| End point values | ACT-709478 single-dose / placebo administration | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 3 | | | |
| Units: SPR reduction | | | | |
| Subject 2 - Eye closure | 5 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time (hours) to maximum SPR reduction

| | |
|-----------------|---------------------------------------|
| End point title | Time (hours) to maximum SPR reduction |
|-----------------|---------------------------------------|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Day 2 to Day 10

| | | | | |
|-----------------------------|--|--|--|--|
| End point values | ACT-709478 single-dose / placebo administration | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 3 | | | |
| Units: Hours | | | | |
| Subject 2 - Eye closure | 127 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events treatment-emergent for placebo (from placebo administration on Day 1 up to ACT-709478 administration on Day 2) and ACT-709478 (from ACT-709478 administration on Day 2 up to EOS).

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 21.0 |

Reporting groups

| | |
|--------------------------------|------------|
| Reporting group title | ACT-709478 |
| Reporting group description: - | |
| Reporting group title | Placebo |
| Reporting group description: - | |

| Serious adverse events | ACT-709478 | Placebo | |
|---|----------------|---------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 5 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Nervous system disorders | | | |
| generalized tonic-clonic seizure | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 5 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | ACT-709478 | Placebo | |
|---|-----------------|----------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 5 / 5 (100.00%) | 3 / 5 (60.00%) | |
| Injury, poisoning and procedural complications | | | |
| Post procedural discomfort | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Nervous system disorders | | | |

| | | | |
|--|----------------|----------------|--|
| Dizziness | | | |
| subjects affected / exposed | 2 / 5 (40.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Disturbance in attention | | | |
| subjects affected / exposed | 2 / 5 (40.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Headache | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| Hyperaesthesia | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Myoclonus | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 2 / 5 (40.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Application site hypersensitivity | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Chills | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Feeling of body temperature change | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Catheter site haematoma | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| Pre-existing condition improved | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Ear and labyrinth disorders | | | |

| | | | |
|---|---------------------|---------------------|--|
| Hyperacusis subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | 0 / 5 (0.00%) 0 | |
| Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | 0 / 5 (0.00%) 0 | |
| Psychiatric disorders Sleep disorder subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | 1 / 5 (20.00%) 1 | |
| Tension subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 1 / 5 (20.00%) 2 | |
| Euphoric mood subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | 0 / 5 (0.00%) 0 | |
| Initial insomnia subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 1 / 5 (20.00%) 1 | |
| Nightmare subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | 0 / 5 (0.00%) 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 12 July 2017 | Amendment 1 was a substantial amendment finalized before the start of the clinical conduct of the study. This amendment was issued in response to two requests expressed by BfArM: 1) The inclusion of the submission of a protocol amendment in the procedure to continue the study, e.g., with an intermediate dose, if a stopping criterion is met for dose escalation. 2) The C-SSRS was added in order to exclude subjects with a history of suicidal thoughts or attempted suicide and to monitor the subjects for signs of suicidal thoughts or suicidal behavior during the course of the study. |
| 28 November 2017 | Amendment 2 specified the change of sponsorship of the study from Actelion Pharmaceuticals Ltd to Idorsia Pharmaceuticals Ltd, effective from 1 March 2018 |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to the late occurrence, the positive response in one subject was not considered relevant.

Notes: