



Clinical trial results:

Assessing the therapeutic efficacy and safety of an 11-hydroxysteroid dehydrogenase type 1 inhibitor (AZD4017) in idiopathic intracranial hypertension (IIH).

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2013-003643-31 |
| Trial protocol | GB |
| Global end of trial date | 10 February 2017 |

Results information

| | |
|-----------------------------------|--|
| Result version number | v1 (current) |
| This version publication date | 29 August 2019 |
| First version publication date | 29 August 2019 |
| Summary attachment (see zip file) | 11 β -Hydroxysteroid Dehydrogenase Type 1 inhibition in Idiopathic Intracranial (IIHDT results preprint.pdf) |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | RG_13-022 |
|-----------------------|-----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02017444 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | University of Birmingham |
| Sponsor organisation address | Edgbaston, Birmingham, United Kingdom, B15 2TT |
| Public contact | Dr Birgit Whitman, University of Birmingham, +44 1214158011, B.Whitman@bham.ac.uk |
| Scientific contact | Dr Birgit Whitman, University of Birmingham, +44 1214158011, B.Whitman@bham.ac.uk |

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 | 25 January 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 19 December 2016 |
| Global end of trial reached? | Yes |
| Global end of trial date | 10 February 2017 |
| 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 evaluate whether 12 weeks of a 11 β -hydroxysteroid dehydrogenase inhibitor (AZD4017) is effective and safe for reducing the raised intracranial pressure (pressure of fluid around the brain) observed in patients with idiopathic intracranial hypertension, compared to a placebo ('dummy' drug with no active properties).

In the original grant application and early versions of the protocol, the primary outcome measure was stated as the change in ICP between baseline and 12 weeks. Following adoption of the study by the University of Birmingham Clinical Trials Unit, the primary outcome was changed to ICP at 12 weeks, with adjustment for baseline ICP in the analysis. This change was made blind to any data analysis.

Protection of trial subjects:

The trial was discussed with potential participants and written information presented detailing the exact nature of the trial and the potential risks involved. It was clearly stated that participants were free to withdraw from the trial at any time and for any reason, with no obligation to give the reason for withdrawal and without affecting their future care.

Since the effects of AZD4017 on unborn children are unknown, participants had pregnancy tests before randomisation and at intervals throughout the trial. Participants were also required to use one form of highly effective contraception.

Informed by earlier trials investigating AZD4017, a panel of safety bloods were monitored throughout the trial, including renal function, liver function, thyroid function and creatine kinase.

An independent Data Monitoring and Ethics Committee reviewed data including Adverse Events and safety blood results.

Background therapy:

Although weight loss is generally advised for patients with IIH, the management of IIH varies considerably owing to a lack of supporting evidence.

During trial design and registration, there was no evidence supporting the use of any particular medical treatment for IIH.

For progressive or acute deterioration of vision in IIH, surgical techniques such as cerebrospinal fluid (CSF) shunting, optic nerve sheath fenestration, or venous sinus stenting have been used to prevent blindness. However, there is limited evidence to support these surgical interventions.

Evidence for comparator:

AZD4017 was compared to placebo rather than a current medical treatment of IIH due to the lack of evidence for any other active treatment noted above.

| | |
|---|---------------|
| Actual start date of recruitment | 25 April 2014 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United Kingdom: 31 |
| Worldwide total number of subjects | 31 |
| EEA total number of subjects | 31 |

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) | 31 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

A total of 31 participants were recruited from 3 UK NHS Trusts between April 2014 and August 2016.

Pre-assignment

Screening details:

Patients were eligible for pre-screening (slit lamp examination for papilloedema Frisen grading ≥ 1 and a blood test) if they were female, ≥ 18 years old, with a confirmed diagnosis of active IIH (Modified Dandy criteria). Screening before randomisation then involved a lumbar puncture to confirm raised ICP and a urine pregnancy test.

Period 1

| | |
|------------------------------|-----------------------------------|
| Period 1 title | Treatment period (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Assessor |

Blinding implementation details:

The trial drug and placebo was blinded, randomised, and packaged by Almac, contract manufacturing organisation on behalf of AstraZeneca. If unblinding was required, unblinding codes were held in the Pharmacy Departments of each Trust, as well as by the Trial Statistician with reasons for unblinding to be recorded.

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | AZD4017 |

Arm description:

An oral selective 11 β -HSD1 inhibitor, AZD4017, at 400mg twice daily for 12 weeks.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | AZD4017 |
| Investigational medicinal product code | n/a |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

400mg twice daily (am and pm) for 12 weeks

| | |
|------------------|-------------|
| Arm title | Placebo arm |
|------------------|-------------|

Arm description:

A matched placebo 400mg twice daily for 12 weeks.

| | |
|--|----------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | n/a |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

400mg twice daily (am and pm) for 12 weeks

| Number of subjects in period 1 | AZD4017 | Placebo arm |
|---------------------------------------|---------|-------------|
| Started | 17 | 14 |
| Completed | 17 | 12 |
| Not completed | 0 | 2 |
| Physician decision | - | 1 |
| Protocol deviation | - | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | AZD4017 |
|-----------------------|---------|

Reporting group description:

An oral selective 11 β -HSD1 inhibitor, AZD4017, at 400mg twice daily for 12 weeks.

| | |
|-----------------------|-------------|
| Reporting group title | Placebo arm |
|-----------------------|-------------|

Reporting group description:

A matched placebo 400mg twice daily for 12 weeks.

| Reporting group values | AZD4017 | Placebo arm | Total |
|--|-----------|-------------|-------|
| Number of subjects | 17 | 14 | 31 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 17 | 14 | 31 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous | | | |
| Age in years | | | |
| Units: years | | | |
| arithmetic mean | 30.1 | 32.4 | |
| standard deviation | ± 5.9 | ± 8 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 17 | 14 | 31 |
| Male | 0 | 0 | 0 |
| Ethnicity | | | |
| Units: Subjects | | | |
| White British | 16 | 13 | 29 |
| Asian/Asian British - Pakistani | 1 | 0 | 1 |
| Asian/Asian British - Other Asian | 0 | 1 | 1 |
| Number on acetazolamide | | | |
| Units: Subjects | | | |
| Number on acetazolamide | 6 | 4 | 10 |
| Not on acetazolamide | 11 | 10 | 21 |
| IIH Symptoms | | | |
| Headache | | | |
| Units: Subjects | | | |
| Headache | 16 | 14 | 30 |
| No headache | 1 | 0 | 1 |
| Frisén Grading, number | | | |

| | | | |
|----------------------------------|--------|--------|----|
| Worst eye only | | | |
| Units: Subjects | | | |
| Frisén Grade 1 | 4 | 2 | 6 |
| Frisén Grade 2 | 9 | 5 | 14 |
| Frisén Grade 3 | 0 | 3 | 3 |
| Frisén Grade 4 | 2 | 1 | 3 |
| Frisén Grade 5 | 1 | 0 | 1 |
| Not recorded | 1 | 3 | 4 |
| IIH Symptoms | | | |
| Visual loss | | | |
| Units: Subjects | | | |
| Visual loss | 4 | 8 | 12 |
| No visual loss | 13 | 6 | 19 |
| IIH Symptoms | | | |
| Pulsatile tinnitus | | | |
| Units: Subjects | | | |
| Pulsatile tinnitus | 12 | 13 | 25 |
| No Pulsatile tinnitus | 5 | 1 | 6 |
| IIH Symptoms | | | |
| Diplopia | | | |
| Units: Subjects | | | |
| Diplopia | 7 | 5 | 12 |
| No Diplopia | 10 | 9 | 19 |
| IIH Symptoms | | | |
| Transient visual obscurations | | | |
| Units: Subjects | | | |
| Transient visual obscurations | 6 | 6 | 12 |
| No Transient visual obscurations | 11 | 8 | 19 |
| Opening LP pressure, cmCSF | | | |
| Units: cmCSF | | | |
| arithmetic mean | 33.7 | 32.7 | - |
| standard deviation | ± 6.3 | ± 4.8 | - |
| Weight, kg | | | |
| Units: kilograms | | | |
| arithmetic mean | 97.9 | 108.4 | - |
| standard deviation | ± 21.3 | ± 42.3 | - |
| BMI (weight (kg)/ height (m2) | | | |
| Units: kg/m2 | | | |
| arithmetic mean | 37.3 | 41.2 | - |
| standard deviation | ± 7.2 | ± 16.6 | - |
| HIT-6 score | | | |
| Units: HIT-6 | | | |
| arithmetic mean | 63.8 | 63.4 | - |
| standard deviation | ± 8.2 | ± 8.1 | - |
| Perimetric mean deviation | | | |
| Worst eye only | | | |
| Units: dB | | | |
| arithmetic mean | -6.1 | -3.4 | - |
| standard deviation | ± 5.4 | ± 6.8 | - |
| Log visual acuity | | | |
| Worst eye only | | | |

| | | | |
|---|---------|---------|---|
| Units: LVA | | | |
| arithmetic mean | 0.08 | 0.13 | |
| standard deviation | ± 0.23 | ± 0.22 | - |
| Log contrast sensitivity | | | |
| Worst eye only | | | |
| Units: LCS | | | |
| arithmetic mean | 1.63 | 1.63 | |
| standard deviation | ± 0.22 | ± 0.16 | - |
| OCT, thickness in µm | | | |
| Average retinal nerve fibre layer, worst eye only | | | |
| Units: µm | | | |
| arithmetic mean | 152 | 158.4 | |
| standard deviation | ± 68.7 | ± 83 | - |
| OCT, thickness in µm | | | |
| Maximum retinal nerve fibre, worst eye only | | | |
| Units: µm | | | |
| arithmetic mean | 320.2 | 290 | |
| standard deviation | ± 117.2 | ± 102.4 | - |
| Average Frisén grading | | | |
| Worst eye only | | | |
| Units: Frisén grading | | | |
| arithmetic mean | 2.19 | 2.27 | |
| standard deviation | ± 1.17 | ± 0.9 | - |

End points

End points reporting groups

| | |
|---|-------------|
| Reporting group title | AZD4017 |
| Reporting group description: An oral selective 11 β -HSD1 inhibitor, AZD4017, at 400mg twice daily for 12 weeks. | |
| Reporting group title | Placebo arm |
| Reporting group description: A matched placebo 400mg twice daily for 12 weeks. | |

Primary: Primary clinical outcome, mean ICP at 12 weeks

| | |
|--|--|
| End point title | Primary clinical outcome, mean ICP at 12 weeks |
| End point description: | |
| End point type | Primary |
| End point timeframe: Baseline to 12 weeks | |

| End point values | AZD4017 | Placebo arm | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 ^[1] | 12 ^[2] | | |
| Units: cmCSF | | | | |
| arithmetic mean (standard deviation) | 29.7 (\pm 5.2) | 31.3 (\pm 6.7) | | |

Notes:

[1] - 1 participant unable to complete LP for ICP at week 12

[2] - 2 participants withdrawn before timepoint

Statistical analyses

| | |
|---|--------------------------------|
| Statistical analysis title | Primary outcome |
| Statistical analysis description: The primary outcome is to examine the effect of AZD4017 on ICP, as measured by lumbar puncture in cmCSF, from baseline to 12 weeks. The primary outcome measure is the difference in ICP at 12 weeks. Analysis is by intention-to-treat. A linear regression model will be used to compare the ICP at 12 weeks between the two arms, adjusting for baseline ICP. | |
| Comparison groups | Placebo arm v AZD4017 |
| Number of subjects included in analysis | 28 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[3] |
| P-value | = 0.2 |
| Method | Regression, Linear |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -2.8 |

| | |
|----------------------|--------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.1 |
| upper limit | 1.5 |
| Variability estimate | Standard deviation |

Notes:

[3] - Negative values in the adjusted mean difference between treatment arms favour AZD4017.

Secondary: Secondary clinical outcome: Log Visual Acuity

| | |
|------------------------|---|
| End point title | Secondary clinical outcome: Log Visual Acuity |
| End point description: | |
| Worst eye only | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to 12 weeks | |

| End point values | AZD4017 | Placebo arm | | |
|--------------------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 12 | | |
| Units: LogMAR | | | | |
| arithmetic mean (standard deviation) | 0.06 (\pm 0.15) | 0.09 (\pm 0.18) | | |

Statistical analyses

| | |
|---|--------------------------------|
| Statistical analysis title | Visual acuity |
| Comparison groups | AZD4017 v Placebo arm |
| Number of subjects included in analysis | 28 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[4] |
| P-value | = 0.5 |
| Method | Regression, Linear |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.03 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.12 |
| upper limit | 0.07 |
| Variability estimate | Standard deviation |

Notes:

[4] - Negative values in the adjusted mean difference between treatment arms favour AZD4017.

Secondary: Secondary clinical outcome: Log contrast sensitivity

| | |
|-----------------|--|
| End point title | Secondary clinical outcome: Log contrast sensitivity |
|-----------------|--|

| | |
|--|-----------|
| End point description: worst eye only | |
| End point type | Secondary |
| End point timeframe: Baseline to 12 weeks | |

| End point values | AZD4017 | Placebo arm | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 13 | 10 | | |
| Units: LCS | | | | |
| arithmetic mean (standard deviation) | 1.65 (± 0.15) | 1.66 (± 0.12) | | |

Statistical analyses

| | |
|---|--------------------------------|
| Statistical analysis title | Log Contrast Sensitivity |
| Comparison groups | AZD4017 v Placebo arm |
| Number of subjects included in analysis | 23 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[5] |
| P-value | = 0.7 |
| Method | Regression, Linear |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.02 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.15 |
| upper limit | 0.11 |
| Variability estimate | Standard deviation |

Notes:

[5] - Negative values in the adjusted mean difference between treatment arms favour AZD4017.

Secondary: Secondary clinical outcome: Perimetric mean deviation

| | |
|--|---|
| End point title | Secondary clinical outcome: Perimetric mean deviation |
| End point description: worst eye only | |
| End point type | Secondary |
| End point timeframe: Baseline to 12 weeks | |

| End point values | AZD4017 | Placebo arm | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 17 | 12 | | |
| Units: dB | | | | |
| arithmetic mean (standard deviation) | -3.4 (± 3.2) | -2.2 (± 3.1) | | |

Statistical analyses

| Statistical analysis title | Perimetric mean deviation |
|---|--------------------------------|
| Comparison groups | AZD4017 v Placebo arm |
| Number of subjects included in analysis | 29 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[6] |
| P-value | = 0.8 |
| Method | Regression, Linear |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2 |
| upper limit | 2.7 |
| Variability estimate | Standard deviation |

Notes:

[6] - Negative values in the adjusted mean difference between treatment arms favour AZD4017.

Secondary: Secondary clinical outcome: OCT retinal nerve fibre layer average

| | |
|------------------------|---|
| End point title | Secondary clinical outcome: OCT retinal nerve fibre layer average |
| End point description: | |
| Worst eye only | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to 12 weeks | |

| End point values | AZD4017 | Placebo arm | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 15 | 11 | | |
| Units: µm | | | | |
| arithmetic mean (standard deviation) | 139.7 (± 56.3) | 143.2 (± 78.7) | | |

Statistical analyses

| | |
|---|--------------------------------|
| Statistical analysis title | OCT RNFL average |
| Comparison groups | AZD4017 v Placebo arm |
| Number of subjects included in analysis | 26 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[7] |
| P-value | = 1 |
| Method | Regression, Linear |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -34 |
| upper limit | 34.1 |
| Variability estimate | Standard deviation |

Notes:

[7] - Negative values in the adjusted mean difference between treatment arms favour AZD4017.

Secondary: Secondary clinical outcome: OCT retinal nerve fibre layer maximum

| | |
|------------------------|---|
| End point title | Secondary clinical outcome: OCT retinal nerve fibre layer maximum |
| End point description: | |
| Worst eye only | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to 12 weeks | |

| End point values | AZD4017 | Placebo arm | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 15 | 11 | | |
| Units: µm | | | | |
| arithmetic mean (standard deviation) | 305.5 (± 122.3) | 277 (± 133.1) | | |

Statistical analyses

| | |
|---|--------------------------------|
| Statistical analysis title | OCT RNFL maximum |
| Comparison groups | AZD4017 v Placebo arm |
| Number of subjects included in analysis | 26 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[8] |
| P-value | = 0.9 |
| Method | Regression, Linear |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -4.5 |

| | |
|----------------------|--------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -68.1 |
| upper limit | 59.1 |
| Variability estimate | Standard deviation |

Notes:

[8] - Negative values in the adjusted mean difference between treatment arms favour AZD4017.

Secondary: Secondary clinical outcome: Average Frisén grading

| | |
|------------------------|--|
| End point title | Secondary clinical outcome: Average Frisén grading |
| End point description: | |
| Worst eye only | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to 12 weeks | |

| End point values | AZD4017 | Placebo arm | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 12 | | |
| Units: Frisén grading | | | | |
| arithmetic mean (standard deviation) | 1.56 (± 0.96) | 2.25 (± 0.87) | | |

Statistical analyses

| | |
|--|--------------------------------|
| Statistical analysis title | Average Frisén grading |
| Statistical analysis description: | |
| Negative values in the adjusted mean difference between treatment arms favour AZD4017. | |
| Comparison groups | AZD4017 v Placebo arm |
| Number of subjects included in analysis | 28 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[9] |
| P-value | = 0.06 |
| Method | Regression, Linear |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.4 |
| upper limit | 0.03 |
| Variability estimate | Standard deviation |

Notes:

[9] - Negative values in the adjusted mean difference between treatment arms favour AZD4017.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs and SAEs were reported from the signing of the consent form to the end of the follow-up period at week 16. SAEs were to be reported within 24 hours of the site becoming aware of it.

Adverse event reporting additional description:

AEs were collected whether or not related to the IMP.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|----|
| Dictionary version | 14 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | AZD4017 |
|-----------------------|---------|

Reporting group description: -

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description: -

| Serious adverse events | AZD4017 | Placebo | |
|---|---|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 14 (7.14%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Nervous system disorders | | | |
| Deterioration of IIH symptoms | Additional description: Expected progression of condition | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 14 (7.14%) | |
| 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: 0 %

| Non-serious adverse events | AZD4017 | Placebo | |
|---|------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 16 / 17 (94.12%) | 11 / 14 (78.57%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Neoplasia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Cardiac disorders | | | |

| | | | |
|---|--|-----------------------|--|
| Cardiovascular subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 1 / 14 (7.14%) 1 | |
| Nervous system disorders Neurological subjects affected / exposed occurrences (all) | 7 / 17 (41.18%) 18 | 3 / 14 (21.43%) 6 | |
| General disorders and administration site conditions Genito-urinary subjects affected / exposed occurrences (all) | 2 / 17 (11.76%) 2 | 1 / 14 (7.14%) 1 | |
| Allergies subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 14 (0.00%) 0 | |
| Other | Additional description: Reasons for other included: tiredness, hot sweats, flu like symptoms, disrupted sleep, toothache/infection, breast pain, menstrual problems for more than 3 weeks, mouth ulcers, a cold, transient nausea, and height headaches. | | |
| subjects affected / exposed occurrences (all) | 7 / 17 (41.18%) 9 | 5 / 14 (35.71%) 6 | |
| Ear and labyrinth disorders Eyes, ear, nose, Throat subjects affected / exposed occurrences (all) | 12 / 17 (70.59%) 22 | 6 / 14 (42.86%) 14 | |
| Immune system disorders Immunological subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 14 (7.14%) 1 | |
| Gastrointestinal disorders Gastrointestinal subjects affected / exposed occurrences (all) | 8 / 17 (47.06%) 22 | 3 / 14 (21.43%) 3 | |
| Respiratory, thoracic and mediastinal disorders Respiratory subjects affected / exposed occurrences (all) | 4 / 17 (23.53%) 4 | 3 / 14 (21.43%) 3 | |
| Skin and subcutaneous tissue disorders Dermatological | | | |

| | | | |
|--|-----------------------|-----------------------|--|
| subjects affected / exposed occurrences (all) | 2 / 17 (11.76%) 4 | 5 / 14 (35.71%) 8 | |
| Psychiatric disorders Psychological subjects affected / exposed occurrences (all) | 4 / 17 (23.53%) 8 | 4 / 14 (28.57%) 8 | |
| Endocrine disorders Endocrine subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 1 / 14 (7.14%) 1 | |
| Musculoskeletal and connective tissue disorders Musculoskeletal subjects affected / exposed occurrences (all) | 6 / 17 (35.29%) 13 | 7 / 14 (50.00%) 10 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 19 November 2014 | Substantial Amendment 1: To improve recruitment: Introducing patient compensation; switching subset of follow up visits to telephone visits to ease patient burden. |
| 13 August 2015 | Substantial Amendment 2: Change from single- to multi-centre trial; Removal of eligibility criteria requiring patients to be within 6 months of confirmed IIH diagnosis. |
| 26 October 2015 | Substantial Amendment 3: Correction of stratification text in randomisation section of protocol to reflect changing from single- to multi-centre trial. |
| 17 November 2015 | Substantial Amendment 4: Clarification of safety bloods required and their reporting/review timelines |
| 07 July 2016 | Substantial Amendment 5: Clarification to IIH symptom recording |
| 04 January 2017 | Substantial Amendment 6: Change to statistical analysis proposed in protocol (from change over 12 weeks to mean difference between arms) |

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.

The pre-print of the results has not been peer-reviewed as of July 2019.

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/28923789>