



Clinical trial results:

An open label extension study to evaluate the safety, tolerability and efficacy of

AIN457 in patients with relapsing-remitting multiple sclerosis.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2011-001629-25 |
| Trial protocol | CZ |
| Global end of trial date | 02 June 2014 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 13 July 2016 |
| First version publication date | 24 July 2015 |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | CAIN457B2201E1 |
|-----------------------|----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01433250 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Novartis Pharma AG |
| Sponsor organisation address | CH-4002, Basel, Switzerland, |
| Public contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, |
| Scientific contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, |

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 | 02 June 2014 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 02 June 2014 |
| Global end of trial reached? | Yes |
| Global end of trial date | 02 June 2014 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

To assess the long term safety and tolerability of secukinumab in patients with RRMS who participated in the core CAIN457B2201 phase II PoC study.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 28 February 2012 |
| 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 | Czech Republic: 8 |
| Country: Number of subjects enrolled | Russian Federation: 20 |
| Country: Number of subjects enrolled | Ukraine: 11 |
| Worldwide total number of subjects | 39 |
| EEA total number of subjects | 8 |

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) | 39 |

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

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This was a multicenter, open-label, non-randomized, non-controlled trial that aimed at providing access to active treatment for at least 1 year to patients who had completed the core CAIN457B2201 study (24 weeks), in order to collect long-term safety data

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | AIN/AIN |

Arm description:

AIN core 24 weeks/AIN extension 1 year

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Secukinumab |
| Investigational medicinal product code | AIN457 |
| Other name | |
| Pharmaceutical forms | Powder for solution for injection/infusion |
| Routes of administration | Intramuscular and intravenous use |

Dosage and administration details:

10 mg/kg i.v. at the start of Week 1 and then

| | |
|------------------|---------|
| Arm title | PBO/AIN |
|------------------|---------|

Arm description:

placebo first 24 weeks/ AIN extension for 52 weeks

| | |
|--|--|
| Arm type | Placebo |
| Investigational medicinal product name | Secukinumab |
| Investigational medicinal product code | AIN457 |
| Other name | |
| Pharmaceutical forms | Powder for solution for injection/infusion |
| Routes of administration | Intramuscular and intravenous use |

Dosage and administration details:

10 mg/kg i.v. at the start of Week 1 and then

| Number of subjects in period 1 | AIN/AIN | PBO/AIN |
|---------------------------------------|---------|---------|
| Started | 22 | 17 |
| Completed | 19 | 14 |
| Not completed | 3 | 3 |
| Consent withdrawn by subject | 3 | 2 |
| Protocol deviation | - | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | AIN/AIN |
|-----------------------|---------|

Reporting group description:

AIN core 24 weeks/AIN extension 1 year

| | |
|-----------------------|---------|
| Reporting group title | PBO/AIN |
|-----------------------|---------|

Reporting group description:

placebo first 24 weeks/ AIN extension for 52 weeks

| Reporting group values | AIN/AIN | PBO/AIN | Total |
|---|---------|---------|-------|
| Number of subjects | 22 | 17 | 39 |
| 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) | 22 | 17 | 39 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous Units: Years | | | |
| arithmetic mean | 36.1 | 34.2 | |
| standard deviation | ± 10 | ± 8.71 | - |
| Gender, Male/Female Units: Participants | | | |
| Female | 12 | 12 | 24 |
| Male | 10 | 5 | 15 |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 1 | 0 | 1 |
| Not Hispanic or Latino | 20 | 16 | 36 |
| Unknown or Not Reported | 1 | 1 | 2 |

End points

End points reporting groups

| | |
|--|---------|
| Reporting group title | AIN/AIN |
| Reporting group description: AIN core 24 weeks/AIN extension 1 year | |
| Reporting group title | PBO/AIN |
| Reporting group description: placebo first 24 weeks/ AIN extension for 52 weeks | |

Primary: Measure: number of subjects with adverse events, number of abnormalities in safety assessments

| | |
|--|---|
| End point title | Measure: number of subjects with adverse events, number of abnormalities in safety assessments ^[1] |
| End point description: Safety outcomes will be described in Adverse events section as there was not an efficacy primary outcome | |
| End point type | Primary |
| End point timeframe: up to 97 weeks | |

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: No prespecified analysis were planned for this outcome measure

| End point values | AIN/AIN | PBO/AIN | | |
|-----------------------------|-------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 ^[2] | 17 | | |
| Units: participants | 0 | 0 | | |

Notes:

[2] - No prespecified statistical analysis was planned for this outcome measure

Statistical analyses

No statistical analyses for this end point

Secondary: Distribution of patients with relapses to end of study (EOS) (all subjects)

| | |
|--|---|
| End point title | Distribution of patients with relapses to end of study (EOS) (all subjects) |
| End point description: Description: number of relapses based on neurological assessments and EDSS | |
| End point type | Secondary |
| End point timeframe: up to 97 weeks | |

| End point values | AIN/AIN | PBO/AIN | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 | 17 | | |
| Units: Participants | 9 | 5 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number lesions measured in the brain by magnetic resonance imaging. T1 Weighted MRI

| | |
|------------------------|---|
| End point title | Number lesions measured in the brain by magnetic resonance imaging. T1 Weighted MRI |
| End point description: | Measures of absolute number of gadolinium [Gd]-enhancing lesions on T1-weighted scans |
| End point type | Secondary |
| End point timeframe: | up to 97 weeks |

| End point values | AIN/AIN | PBO/AIN | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 | 17 | | |
| Units: lesions | | | | |
| arithmetic mean (full range (min-max)) | | | | |
| week 13 T1 (n=22, 16) | 0.8 (0 to 4) | 2 (0 to 15) | | |
| week 25 T1 (n=22, 16) | 0.6 (0 to 5) | 1.9 (0 to 20) | | |
| week 37 T1 (n=22, 15) | 1 (0 to 5) | 0.8 (0 to 4) | | |
| week 53 T1 (n=14, 6) | 0.3 (0 to 3) | 0.3 (0 to 1) | | |
| wk 73 T1 (n=11,9) | 0.6 (0 to 3) | 0.2 (0 to 1) | | |
| EOT (n=15,13) | 0.7 (0 to 5) | 0.5 (0 to 3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number lesions measured in the brain by magnetic resonance imaging. T2 Weighted MRI

| | |
|------------------------|---|
| End point title | Number lesions measured in the brain by magnetic resonance imaging. T2 Weighted MRI |
| End point description: | Measures of absolute number of gadolinium [Gd]-enhancing lesions on T2-weighted lesions |
| End point type | Secondary |
| End point timeframe: | upto 97 weeks |

| End point values | AIN/AIN | PBO/AIN | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 | 17 | | |
| Units: lesions | | | | |
| arithmetic mean (full range (min-max)) | | | | |
| week 13 T2 (n=22, 16) | 1.3 (0 to 7) | 2.2 (0 to 12) | | |
| week 25 T2 (n=22, 16) | 0.8 (0 to 6) | 2.4 (0 to 21) | | |
| week 37 T2 (n=22, 15) | 1.3 (0 to 5) | 1.3 (0 to 6) | | |
| week 53 T2 (n=14, 6) | 0.4 (0 to 4) | 0.7 (0 to 3) | | |
| wk 73 T2 (n=11,9) | 1.3 (0 to 5) | 0.9 (0 to 5) | | |
| EOT T2 (n=15,13) | 1.1 (0 to 4) | 0.07 (0 to 3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Brain Volume at end of study.

| | |
|---|---|
| End point title | Change in Brain Volume at end of study. |
| End point description: | |
| Change in volume from start to end of study | |
| End point type | Secondary |
| End point timeframe: | |
| up to 97 weeks | |

| End point values | AIN/AIN | PBO/AIN | | |
|--------------------------------------|----------------------------|--------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 | 17 | | |
| Units: ml | | | | |
| arithmetic mean (standard deviation) | -14.8968 (\pm 63.73027) | -30.4346 (\pm 31.218) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Measure of disability: Expanded Disability Status Scale (EDSS).

| | |
|--|---|
| End point title | Measure of disability: Expanded Disability Status Scale (EDSS). |
| End point description: | |
| The EDSS is a scale for assessing neurological impairment in MS (Kurtzke 1983) including (1) a series of scores in each of eight functional systems, and (2) the EDSS steps (ranging from 0 (normal) to 10 | |

(death due to MS). The functional systems are Visual, Brain Stem, Pyramidal, Cerebellar, Sensory, Bowel and Bladder, Cerebral and Other functions.

| | |
|--------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline to End of Study | |

| End point values | AIN/AIN | PBO/AIN | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 | 17 | | |
| Units: participants | | | | |
| Baseline score 0 | 1 | 0 | | |
| Baseline score 1.0 | 0 | 2 | | |
| Baseline score 1.5 | 5 | 5 | | |
| Baseline score 2.0 | 5 | 2 | | |
| Baseline score 2.5 | 1 | 1 | | |
| Baseline score 3.0 | 2 | 4 | | |
| Baseline score 3.5 | 2 | 0 | | |
| Baseline score 4.0 | 1 | 1 | | |
| Baseline score 4.5 | 2 | 2 | | |
| Baseline score 5.0 | 1 | 0 | | |
| Baseline score 6.0 | 1 | 0 | | |
| WK25 score 0 | 2 | 0 | | |
| WK25 score 1 | 1 | 2 | | |
| WK25 score 1.5 | 4 | 5 | | |
| WK25 score 2.0 | 4 | 1 | | |
| WK25 score 2.5 | 2 | 1 | | |
| WK25 score 3.0 | 2 | 4 | | |
| WK25 score 4.0 | 1 | 1 | | |
| WK25 score 4.5 | 3 | 1 | | |
| WK25 score 5.0 | 1 | 0 | | |
| WK25 score 5.5 | 0 | 1 | | |
| WK25 score 6.0 | 1 | 0 | | |
| WK25 score 6.5 | 1 | 0 | | |
| Safety Week 53 score 0 | 1 | 0 | | |
| Safety Week 53 score 1.0 | 1 | 1 | | |
| Safety Week 53 score 1.5 | 3 | 3 | | |
| Safety Week 53 score 2.0 | 4 | 0 | | |
| Safety Week 53 score 3.0 | 1 | 1 | | |
| Safety Week 53 score 3.5 | 1 | 0 | | |
| Safety Week 53 score 4.0 | 0 | 1 | | |
| Safety Week 53 score 5.0 | 1 | 0 | | |
| Safety Week 53 score 5.5 | 2 | 0 | | |
| Safety Week 53 score 6.0 | 1 | 0 | | |
| WK73 score 0 | 1 | 1 | | |
| WK73 score 1.0 | 2 | 1 | | |
| WK73 score 1.5 | 1 | 5 | | |
| WK73 score 2.0 | 2 | 0 | | |
| WK73 score 3.0 | 0 | 1 | | |
| WK73 score 4.0 | 1 | 0 | | |

| | | | | |
|----------------------------|---|---|--|--|
| WK73 score 5.5 | 1 | 0 | | |
| WK73 score 6.0 | 1 | 0 | | |
| End of treatment score 0 | 1 | 1 | | |
| End of treatment score 1.0 | 2 | 1 | | |
| End of treatment score 1.5 | 2 | 5 | | |
| End of treatment score 2.0 | 2 | 1 | | |
| End of treatment score 2.5 | 2 | 1 | | |
| End of treatment score 3.0 | 0 | 3 | | |
| End of treatment score 3.5 | 1 | 0 | | |
| End of treatment score 4.0 | 2 | 0 | | |
| End of treatment score 4.5 | 0 | 1 | | |
| End of treatment score 5.5 | 0 | 1 | | |
| End of treatment score 6.0 | 1 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All Adverse events are reported in this record from First Patient First Treatment until Last Patient Last Visit.

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 16.0 |

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | PBO/AIN |
|-----------------------|---------|

Reporting group description:

PBO/AIN

| | |
|-----------------------|---------|
| Reporting group title | AIN/AIN |
|-----------------------|---------|

Reporting group description:

AIN/AIN

| Serious adverse events | PBO/AIN | AIN/AIN | |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 2 / 22 (9.09%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Radius fracture | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 22 (4.55%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Osteochondrosis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 22 (4.55%) | |
| 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: 5 %

| Non-serious adverse events | PBO/AIN | AIN/AIN | |
|---|-----------------|-----------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 8 / 17 (47.06%) | 7 / 22 (31.82%) | |
| Investigations | | | |
| C-reactive protein increased | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 22 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 22 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Varicose vein | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 2 / 22 (9.09%) | |
| occurrences (all) | 0 | 2 | |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 22 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Cardiomyopathy | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 22 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 22 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Migraine | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 22 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Gastrointestinal disorders | | | |
| Gastritis | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 22 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Reproductive system and breast disorders | | | |
| Uterine cervical erosion | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 22 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|--|---------------------|---------------------|--|
| Cough subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 2 / 22 (9.09%) 2 | |
| Psychiatric disorders Anxiety disorder subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 2 / 22 (9.09%) 2 | |
| Infections and infestations Cystitis subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 22 (0.00%) 0 | |
| Laryngitis subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 22 (0.00%) 0 | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 2 | 1 / 22 (4.55%) 1 | |
| Pharyngitis subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 2 / 22 (9.09%) 3 | |
| Respiratory tract infection viral subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 2 | 2 / 22 (9.09%) 3 | |
| Rhinitis subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 22 (0.00%) 0 | |
| Metabolism and nutrition disorders Overweight subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 22 (0.00%) 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 21 February 2013 | This amendment was issued in order to prolong access to active treatment to all patients enrolled in the current CAIN457B2201E1 study until they could participate in another extension study. For this purpose additional treatment visits were scheduled and described. All patients continued to receive only active treatment throughout the study course. In addition this amendment included an adjustment of the frequency at which some assessments were scheduled in order to align with the ongoing secukinumab program. These changes were not expected to have an impact on the safety of the intended study population, analysis of results and the scientific value of the trial. |

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.

Further development of secukinumab in MS is not being pursued and the extension study in MS, CAIN457B2201E1, was terminated. Termination of this study was not related to the safety or tolerability concerns observed in the study.

Notes: