



## Clinical trial results:

### A multi-center, double-blind, placebo-controlled phase II study of the efficacy and safety of canakinumab in subjects with Schnitzler syndrome

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2010-024156-28   |
| Trial protocol           | DE               |
| Global end of trial date | 21 December 2017 |

#### Results information

|                                   |   |
|-----------------------------------|---|
| Result version number             | v1 (current)  |
| This version publication date     | 16 September 2021   |
| First version publication date    | 16 September 2021   |
| Summary attachment (see zip file) | Publication (Krause et al. CAN in SchS JACI 2017.pdf)<br>Publication (Krause et. al. CAN in SchS extension JACI 2020.pdf) |

#### Trial information

##### Trial identification

|                       |               |
|-----------------------|---------------|
| Sponsor protocol code | CACZ885DDE03T |
|-----------------------|---------------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Charité - University Hospital of Berlin  |
| Sponsor organisation address | Charitéplatz 1, Berlin, Germany, 10117   |
| Public contact               | Clinical Trials Information, Charité - University Hospital of Berlin, +49 030450-518-342, karoline.krause@charite.de |
| Scientific contact           | Clinical Trials Information, Charité - University Hospital of Berlin, +49 030450-518-342, karoline.krause@charite.de |

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                       | 21 December 2017 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 21 December 2017 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

To assess the effect of canakinumab on the clinical signs and symptoms of Schnitzler Syndrome (SchS)

Protection of trial subjects:

Canakinumab (Ilaris®, L04AC04, Novartis International AG, CH-4002 Basel, Switzerland) is a recombinant high-affinity monoclonal antibody that neutralizes IL-1 $\beta$ , a key mediator of local and systemic inflammatory reactions. Canakinumab is indicated for adults and children over 4 years for treatment of cryopyrin-associated periodic syndromes (CAPS) including familial cold autoinflammatory syndrome (FCAS), MuckleWells syndrome (MWS) and neonatal onset multi-system inflammatory disease (NOMID/CINCA). In addition, it has been successfully tested for gout, systemic juvenile idiopathic arthritis (SJIA) and other autoinflammatory diseases. On the basis of the good response to treatment with anakinra it is supposed that canakinumab may be highly effective in SchS too. Safety assessment included adverse event reporting and routine clinical and laboratory assessments. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 01 June 2011 |
| 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 | Germany: 20 |
| Worldwide total number of subjects   | 20          |
| EEA total number of subjects         | 20          |

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) | 20 |
| From 65 to 84 years  | 0  |
| 85 years and over    | 0  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

The study started 05.07.2011 and ended on 21.12.2017. There were 15 patients who completed the whole study period of 4 years.

### Period 1

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

### Arms

|                              |         |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes     |
| <b>Arm title</b>             | Placebo |

Arm description: -

|  |                          |
|--|--------------------------|
| Arm type                               | Placebo                  |
| Investigational medicinal product name | Placebo                  |
| Investigational medicinal product code |                          |
| Other name                             |                          |
| Pharmaceutical forms                   | Suspension for injection |
| Routes of administration               | Subcutaneous use         |

Dosage and administration details:

Subjects received placebo (identical with study drug apart from active ingredient)

|                  |             |
|------------------|-------------|
| <b>Arm title</b> | Canakinumab |
|------------------|-------------|

Arm description: -

|  |                          |
|--|--------------------------|
| Arm type                               | Active comparator        |
| Investigational medicinal product name | Canakinumab              |
| Investigational medicinal product code |                          |
| Other name                             |                          |
| Pharmaceutical forms                   | Suspension for injection |
| Routes of administration               | Subcutaneous use         |

Dosage and administration details:

The first part was an initial 7-day double-blind, placebo-controlled study of a single subcutaneous dose of canakinumab 150 mg. The second part was a 16-week open-label follow-up to establish the optimal dose of canakinumab, 150 or 300 mg, and to assess adverse responses.

| <b>Number of subjects in period 1</b> | Placebo | Canakinumab |
|---------------------------------------|---------|-------------|
| Started                               | 13      | 7           |
| Completed                             | 13      | 7           |

## Baseline characteristics

### Reporting groups

|                                |             |
|--------------------------------|-------------|
| Reporting group title          | Placebo     |
| Reporting group description: - |             |
| Reporting group title          | Canakinumab |
| Reporting group description: - |             |

| Reporting group values                                | Placebo | Canakinumab | Total |
|---|---------|-------------|-------|
| Number of subjects                                    | 13      | 7           | 20    |
| Age categorical<br>Units: Subjects                    |         |             |       |
| In utero  | 0       | 0           | 0     |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0       | 0           | 0     |
| Newborns (0-27 days)                                  | 0       | 0           | 0     |
| Infants and toddlers (28 days-23<br>months)           | 0       | 0           | 0     |
| Children (2-11 years)                                 | 0       | 0           | 0     |
| Adolescents (12-17 years)                             | 0       | 0           | 0     |
| Adults (18-64 years)                                  | 13      | 7           | 20    |
| From 65-84 years                                      | 0       | 0           | 0     |
| 85 years and over                                     | 0       | 0           | 0     |
| Gender categorical<br>Units: Subjects                 |         |             |       |
| Female  | 5       | 4           | 9     |
| Male  | 8       | 3           | 11    |

## End points

### End points reporting groups

|                                |             |
|--------------------------------|-------------|
| Reporting group title          | Placebo     |
| Reporting group description: - |             |
| Reporting group title          | Canakinumab |
| Reporting group description: - |             |

### Primary: The effect of canakinumab of canakinumab on the clinical signs and symptoms of SchS measured by physicians global assessment

|                                      |  |
|--------------------------------------|--|
| End point title                      | The effect of canakinumab of canakinumab on the clinical signs and symptoms of SchS measured by physicians global assessment <sup>[1][2]</sup> |
| End point description:<br>see report |  |
| End point type                       | Primary  |
| End point timeframe:<br>57 months    |  |

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 report

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: See report

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| <b>End point values</b>                   | Canakinumab     |  |  |  |
| Subject group type                        | Reporting group |  |  |  |
| Number of subjects analysed               | 7               |  |  |  |
| Units: Physician global assessment (0-20) |                 |  |  |  |
| median (inter-quartile range (Q1-Q3))     | 4 (0 to 5)      |  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information<sup>[1]</sup>

Timeframe for reporting adverse events:

During the whole trial

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 21.0 |
|--------------------|------|

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | 17 Patients |
|-----------------------|-------------|

Reporting group description:

See manuskript

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: See manuskript

| Serious adverse events  | 17 Patients   |  |  |
|---|---|--|--|
| Total subjects affected by serious adverse events                   |   |  |  |
| subjects affected / exposed   | 7 / 17 (41.18%)   |  |  |
| number of deaths (all causes)                                       | 1   |  |  |
| number of deaths resulting from adverse events                      | 0   |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |  |  |
| Leiomyoma   |   |  |  |
| subjects affected / exposed   | 1 / 17 (5.88%)  |  |  |
| occurrences causally related to treatment / all                     | 0 / 1   |  |  |
| deaths causally related to treatment / all                          | 0 / 0   |  |  |
| Injury, poisoning and procedural complications                      |   |  |  |
| Craniocerebral injury   | Additional description: Due to assault; recovered               |  |  |
| subjects affected / exposed   | 1 / 17 (5.88%)  |  |  |
| occurrences causally related to treatment / all                     | 0 / 1   |  |  |
| deaths causally related to treatment / all                          | 0 / 0   |  |  |
| Blood and lymphatic system disorders                                |   |  |  |
| Multiple Myeloma  |   |  |  |
| subjects affected / exposed   | 1 / 17 (5.88%)  |  |  |
| occurrences causally related to treatment / all                     | 0 / 1   |  |  |
| deaths causally related to treatment / all                          | 0 / 0   |  |  |
| Gastrointestinal disorders  |   |  |  |
| Hernia inguinal   | Additional description: Worsening of inguinal hernia; recovered |  |  |



|   |   |  |  |
|---|---|--|--|
| subjects affected / exposed                     | 1 / 17 (5.88%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1   |  |  |
| deaths causally related to treatment / all      | 0 / 0   |  |  |
| Respiratory, thoracic and mediastinal disorders |   |  |  |
| Pneumonia with consecutive paraplegia           |   |  |  |
| subjects affected / exposed                     | 1 / 17 (5.88%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1   |  |  |
| deaths causally related to treatment / all      | 0 / 0   |  |  |
| Hepatobiliary disorders                         |   |  |  |
| Cholelithiasis                                  |   |  |  |
| subjects affected / exposed                     | 1 / 17 (5.88%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1   |  |  |
| deaths causally related to treatment / all      | 0 / 0   |  |  |
| Infections and infestations                     |   |  |  |
| Sepsis  | Additional description: Sepsis due to atypical mycobacteriosis; fatal outcome |  |  |
| subjects affected / exposed                     | 1 / 17 (5.88%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1   |  |  |
| deaths causally related to treatment / all      | 0 / 1   |  |  |

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

|   |                |  |  |
|---|----------------|--|--|
| <b>Non-serious adverse events</b>                     | 17 Patients    |  |  |
| Total subjects affected by non-serious adverse events |                |  |  |
| subjects affected / exposed                           | 0 / 17 (0.00%) |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported