



## Clinical trial results:

**An exploratory, open-label, single centre, phase II, proof of concept study of gevokizumab treatment in patients with Schnitzler syndrome.**

### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2013-002562-39  |
| Trial protocol           | NL              |
| Global end of trial date | 04 January 2016 |

### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1 (current)  |
| This version publication date  | 27 April 2017 |
| First version publication date | 27 April 2017 |

### Trial information

#### Trial identification

|                       |               |
|-----------------------|---------------|
| Sponsor protocol code | CL2-78989-018 |
|-----------------------|---------------|

#### Additional study identifiers

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

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Institut de Recherches Internationales Servier  |
| Sponsor organisation address | 50 rue Carnot, Suresnes, France,  |
| Public contact               | ITP (Innovative Therapeutic Pole), Institut de Recherches Internationales Servier, +33 15572 4366, clinicaltrials@servier.com |
| Scientific contact           | ITP (Innovative Therapeutic Pole), Institut de Recherches Internationales Servier, +33 15572 4366, clinicaltrials@servier.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:

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**Results analysis stage**

|  |                 |
|--|-----------------|
| Analysis stage                                       | Final           |
| Date of interim/final analysis                       | 04 January 2016 |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 04 January 2016 |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 04 January 2016 |
| Was the trial ended prematurely?                     | No              |

Notes:

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**General information about the trial**

Main objective of the trial:

The objective of this study is to explore the efficacy and safety of gevokizumab in patients with Schnitzler syndrome.

Protection of trial subjects:

This study was conducted in accordance with Good Clinical Practice standards, ethical principles stated in the Declaration of Helsinki and applicable regulatory requirements. After the subject has ended his/her participation in the trial, the investigator provided appropriate medication and/or arranged access to appropriate care for the patient.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 05 December 2013 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

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**Population of trial subjects****Subjects enrolled per country**

|                                      |                |
|--------------------------------------|----------------|
| Country: Number of subjects enrolled | Netherlands: 3 |
| Worldwide total number of subjects   | 3              |
| EEA total number of subjects         | 3              |

Notes:

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**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)                      | 0 |
| From 65 to 84 years                       | 3 |
| 85 years and over                         | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Males or females aged  $\geq 18$  years with diagnosis of Schnitzler syndrome at least one year prior, and with active Schnitzler syndrome disease as defined by the presence of at least 2 of 3 clinical criteria (from rash, fever (defined as  $\geq 38^{\circ}\text{C}$ ) and bone or arthritis pain) and elevated CRP levels  $\geq 30$  mg/L, and without clinical signs of tuberculosis.

### Period 1

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

### Arms

|  |                        |
|--|------------------------|
| Arm title                              | Gevokizumab            |
| Arm description: -                     |                        |
| Arm type                               | Experimental           |
| Investigational medicinal product name | Gevokizumab            |
| Investigational medicinal product code | S78989                 |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Subcutaneous use       |

Dosage and administration details:

Gevokizumab was administered to 3 patients with starting dose of 60 mg and were to receive maximum dose of 180 mg per 2-week period over a 2-year treatment duration.

| Number of subjects in period 1 | Gevokizumab |
|--------------------------------|-------------|
| Started                        | 3           |
| Completed                      | 3           |

## Baseline characteristics

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### Reporting groups

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Treatment period |
|-----------------------|------------------|

Reporting group description: -

| Reporting group values | Treatment period | Total |  |
|------------------------|------------------|-------|--|
| Number of subjects     | 3                | 3     |  |
| Age categorical        |                  |       |  |
| Units: Subjects        |                  |       |  |
| From 65-84 years       | 3                | 3     |  |
| Gender categorical     |                  |       |  |
| Units: Subjects        |                  |       |  |
| Female                 | 2                | 2     |  |
| Male                   | 1                | 1     |  |

## End points

### End points reporting groups

|                                |             |
|--------------------------------|-------------|
| Reporting group title          | Gevokizumab |
| Reporting group description: - |             |

### Primary: no primary criterion

|                        |                                     |
|------------------------|-------------------------------------|
| End point title        | no primary criterion <sup>[1]</sup> |
| End point description: |                                     |

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

As the study was exploratory, no primary endpoint was defined.

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: As no primary endpoint was defined for this exploratory study, no statistical analysis was performed.

|                             |                  |  |  |  |
|-----------------------------|------------------|--|--|--|
| <b>End point values</b>     | Gevokizumab      |  |  |  |
| Subject group type          | Reporting group  |  |  |  |
| Number of subjects analysed | 0 <sup>[2]</sup> |  |  |  |
| Units: no unit              |                  |  |  |  |

Notes:

[2] - As the study was exploratory, no primary endpoint was defined.

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All adverse events which occurred during the treatment period are presented here.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 18.0 |
|--------------------|------|

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Gevokizumab |
|-----------------------|-------------|

Reporting group description: -

| Serious adverse events                            | Gevokizumab    |  |  |
|---|----------------|--|--|
| Total subjects affected by serious adverse events |                |  |  |
| subjects affected / exposed                       | 1 / 3 (33.33%) |  |  |
| number of deaths (all causes)                     | 0              |  |  |
| number of deaths resulting from adverse events    | 0              |  |  |
| Reproductive system and breast disorders          |                |  |  |
| Cervical dysplasia                                |                |  |  |
| subjects affected / exposed                       | 1 / 3 (33.33%) |  |  |
| occurrences causally related to treatment / all   | 0 / 1          |  |  |
| deaths causally related to treatment / all        | 0 / 0          |  |  |

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

| Non-serious adverse events                            | Gevokizumab     |  |  |
|---|-----------------|--|--|
| Total subjects affected by non-serious adverse events |                 |  |  |
| subjects affected / exposed                           | 3 / 3 (100.00%) |  |  |
| Injury, poisoning and procedural complications        |                 |  |  |
| Animal bite   |                 |  |  |
| subjects affected / exposed                           | 1 / 3 (33.33%)  |  |  |
| occurrences (all)                                     | 1               |  |  |
| Fall  |                 |  |  |
| subjects affected / exposed                           | 1 / 3 (33.33%)  |  |  |
| occurrences (all)                                     | 1               |  |  |
| Head injury   |                 |  |  |

|  |   |  |  |
|--|---|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Vaccination complication</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>1 / 3 (33.33%)</p> <p>1</p> <p>1 / 3 (33.33%)</p> <p>1</p>   |  |  |
| <p>Nervous system disorders</p> <p>Somnolence</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>1 / 3 (33.33%)</p> <p>1</p>  |  |  |
| <p>General disorders and administration site conditions</p> <p>Fatigue</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Feeling cold</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>General physical health deterioration</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Malaise</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 3 (33.33%)</p> <p>2</p> <p>1 / 3 (33.33%)</p> <p>1</p> <p>1 / 3 (33.33%)</p> <p>1</p> <p>1 / 3 (33.33%)</p> <p>1</p> |  |  |
| <p>Gastrointestinal disorders</p> <p>Abdominal pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Abdominal pain upper</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Diarrhoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dry mouth</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dyspepsia</p>                     | <p>1 / 3 (33.33%)</p> <p>1</p> <p>1 / 3 (33.33%)</p> <p>1</p> <p>2 / 3 (66.67%)</p> <p>3</p> <p>1 / 3 (33.33%)</p> <p>1</p> |  |  |

|  |   |  |  |
|--|---|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Eructation</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Nausea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>1 / 3 (33.33%)</p> <p>1</p> <p>1 / 3 (33.33%)</p> <p>1</p> <p>1 / 3 (33.33%)</p> <p>1</p>                                |  |  |
| <p>Reproductive system and breast disorders</p> <p>Atrophic vulvovaginitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>1 / 3 (33.33%)</p> <p>1</p>  |  |  |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>Cough</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Epistaxis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Nasal congestion</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Oropharyngeal pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 3 (33.33%)</p> <p>2</p> <p>1 / 3 (33.33%)</p> <p>1</p> <p>1 / 3 (33.33%)</p> <p>3</p> <p>1 / 3 (33.33%)</p> <p>1</p> |  |  |
| <p>Psychiatric disorders</p> <p>Insomnia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Stress</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>1 / 3 (33.33%)</p> <p>1</p> <p>1 / 3 (33.33%)</p> <p>1</p>   |  |  |
| <p>Musculoskeletal and connective tissue disorders</p> <p>Arthralgia</p>   |   |  |  |



|                                       |                |  |  |
|---------------------------------------|----------------|--|--|
| subjects affected / exposed           | 1 / 3 (33.33%) |  |  |
| occurrences (all)                     | 2              |  |  |
| Back pain                             |                |  |  |
| subjects affected / exposed           | 1 / 3 (33.33%) |  |  |
| occurrences (all)                     | 1              |  |  |
| Metatarsalgia                         |                |  |  |
| subjects affected / exposed           | 1 / 3 (33.33%) |  |  |
| occurrences (all)                     | 1              |  |  |
| Musculoskeletal stiffness             |                |  |  |
| subjects affected / exposed           | 1 / 3 (33.33%) |  |  |
| occurrences (all)                     | 1              |  |  |
| Myalgia                               |                |  |  |
| subjects affected / exposed           | 1 / 3 (33.33%) |  |  |
| occurrences (all)                     | 1              |  |  |
| Neck pain                             |                |  |  |
| subjects affected / exposed           | 1 / 3 (33.33%) |  |  |
| occurrences (all)                     | 1              |  |  |
| Osteoarthritis                        |                |  |  |
| subjects affected / exposed           | 1 / 3 (33.33%) |  |  |
| occurrences (all)                     | 1              |  |  |
| Infections and infestations           |                |  |  |
| Bronchitis viral                      |                |  |  |
| subjects affected / exposed           | 1 / 3 (33.33%) |  |  |
| occurrences (all)                     | 1              |  |  |
| Cystitis                              |                |  |  |
| subjects affected / exposed           | 1 / 3 (33.33%) |  |  |
| occurrences (all)                     | 1              |  |  |
| Gastrointestinal viral infection      |                |  |  |
| subjects affected / exposed           | 2 / 3 (66.67%) |  |  |
| occurrences (all)                     | 2              |  |  |
| Oral herpes                           |                |  |  |
| subjects affected / exposed           | 1 / 3 (33.33%) |  |  |
| occurrences (all)                     | 4              |  |  |
| Respiratory tract infection bacterial |                |  |  |
| subjects affected / exposed           | 1 / 3 (33.33%) |  |  |
| occurrences (all)                     | 1              |  |  |

|   |                |  |  |
|---|----------------|--|--|
| Sinusitis                               |                |  |  |
| subjects affected / exposed             | 1 / 3 (33.33%) |  |  |
| occurrences (all)                       | 1              |  |  |
| Upper respiratory tract infection       |                |  |  |
| subjects affected / exposed             | 1 / 3 (33.33%) |  |  |
| occurrences (all)                       | 1              |  |  |
| Viral upper respiratory tract infection |                |  |  |
| subjects affected / exposed             | 2 / 3 (66.67%) |  |  |
| occurrences (all)                       | 3              |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment  |
|-----------------|--|
| 16 July 2014    | At inclusion, the starting dose of gevokizumab was increased to 180 mg; as no patient was recruited after the amendment, all included patients received a starting dose of 60 mg as per initial protocol. For on-going patients, the maximum authorised dose was increased up to 180 mg gevokizumab per 2-week period if deemed appropriate by the investigator according to the patient's clinical response over the 2-year treatment period. |
| 21 October 2014 | The overall follow-up of patient was extended from 1 to 2 years.   |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported