



## Clinical trial results:

### **A PHASE IV, PROSPECTIVE, OPEN-LABEL, MULTICENTRE, SINGLE ARM, 3-MONTH PROOF OF CONCEPT STUDY TO ASSESS THE EFFECT OF IKERVIS® 1MG/ML (CICLOSPORIN) EYE DROPS ADMINISTERED ONCE DAILY ON THE QUALITY OF VISION IN DRY EYE DISEASE (DED) PATIENTS WITH SEVERE KERATITIS**

#### **Summary**

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2016-003497-40 |
| Trial protocol           | FR             |
| Global end of trial date | 11 July 2018   |

#### **Results information**

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 15 December 2021 |
| First version publication date | 15 December 2021 |

#### **Trial information**

##### **Trial identification**

|                       |           |
|-----------------------|-----------|
| Sponsor protocol code | NVG16E128 |
|-----------------------|-----------|

##### **Additional study identifiers**

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03237936 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### **Sponsors**

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | SANTEN SAS   |
| Sponsor organisation address | Genavenir IV, 1 rue Pierre Fontaine, EVRY, France,                       |
| Public contact               | Elsa LLOBET-MERKLING, EURAXI PHARMA,<br>e.llobetmerkling@euraxipharma.fr |
| Scientific contact           | Elsa LLOBET-MERKLING, EURAXI PHARMA,<br>e.llobetmerkling@euraxipharma.fr |

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                       | 10 November 2020 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 11 July 2018     |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 11 July 2018     |
| Was the trial ended prematurely?                     | No               |

Notes:

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**General information about the trial**

Main objective of the trial:

To assess the effect on the quality of vision of IKERVIS® (1mg/ml ciclosporin) eye drops administered once daily in adult dry eye disease (DED) patients with severe keratitis following 3 months of treatment.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements.

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 28 March 2017 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | No            |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |            |
|--------------------------------------|------------|
| Country: Number of subjects enrolled | France: 17 |
| Worldwide total number of subjects   | 17         |
| EEA total number of subjects         | 17         |

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)                      | 12 |
| From 65 to 84 years                       | 5  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Study was conducted in 3 sites in France.

### Pre-assignment

Screening details:

Overall, 20 patients were screened for the study and 19 patients were enrolled (1 screen failure patient). 2 patients withdrew before receiving any study medication and 17 patients were included in the FAS and safety populations.

### Period 1

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

### Arms

|                  |                      |
|------------------|----------------------|
| <b>Arm title</b> | IKERVIS® 1 mg/mL CsA |
|------------------|----------------------|

Arm description:

Participants received IKERVIS® (1mg/mL CsA) eye drops administered once daily during the 3-month study period.

|  |                     |
|--|---------------------|
| Arm type                               | Experimental        |
| Investigational medicinal product name | IKERVIS®            |
| Investigational medicinal product code |                     |
| Other name                             |                     |
| Pharmaceutical forms                   | Eye drops, emulsion |
| Routes of administration               | Ocular use          |

Dosage and administration details:

During the 3-month study treatment period, each patient was instructed to instil one drop of study medication (IKERVIS®, 1mg/mL CsA) into the lower conjunctival sac of each eye once daily at bedtime.

|                                       |                      |
|---------------------------------------|----------------------|
| <b>Number of subjects in period 1</b> | IKERVIS® 1 mg/mL CsA |
| Started                               | 17                   |
| Full Analysis Set (FAS)               | 17                   |
| Completed                             | 16                   |
| Not completed                         | 1                    |
| Decision of Santen Promotor           | 1                    |

## Baseline characteristics

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | overall trial |
|-----------------------|---------------|

Reporting group description: -

| Reporting group values                                | overall trial | Total |  |
|---|---------------|-------|--|
| Number of subjects                                    | 17            | 17    |  |
| Age categorical                                       |               |       |  |
| Units: Subjects                                       |               |       |  |
| In utero  |               | 0     |  |
| Preterm newborn infants<br>(gestational age < 37 wks) |               | 0     |  |
| Newborns (0-27 days)                                  |               | 0     |  |
| Infants and toddlers (28 days-23<br>months)           |               | 0     |  |
| Children (2-11 years)                                 |               | 0     |  |
| Adolescents (12-17 years)                             |               | 0     |  |
| Adults (18-64 years)                                  |               | 0     |  |
| From 65-84 years                                      |               | 0     |  |
| 85 years and over                                     |               | 0     |  |
| Age continuous  |               |       |  |
| Units: years  |               |       |  |
| arithmetic mean                                       | 61.9          |       |  |
| standard deviation                                    | ± 12.7        | -     |  |
| Gender categorical                                    |               |       |  |
| Units: Subjects                                       |               |       |  |
| Female  | 13            | 13    |  |
| Male  | 4             | 4     |  |

## End points

### End points reporting groups

|  |                      |
|--|----------------------|
| Reporting group title  | IKERVIS® 1 mg/mL CsA |
| Reporting group description:<br>Participants received IKERVIS® (1mg/mL CsA) eye drops administered once daily during the 3-month study period. |                      |
| Subject analysis set title   | Primary Endpoint     |
| Subject analysis set type  | Full analysis        |
| Subject analysis set description:<br>A total of 17 patients were included in the study.  |                      |

### Primary: Spearman's coefficient of correlation between the change from baseline in VMR measured with FVA system at Month 3 and the change from baseline in the CFS at Month 3.

|                                    |  |
|------------------------------------|--|
| End point title                    | Spearman's coefficient of correlation between the change from baseline in VMR measured with FVA system at Month 3 and the change from baseline in the CFS at Month 3. <sup>[1]</sup> |
| End point description:             |  |
| End point type                     | Primary  |
| End point timeframe:<br>At Month 3 |  |

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: This study is estimating the correlation of two measures VMR change and CFS change within the same group. No further statistical analyses were planned for this endpoint.

|  |                              |  |  |  |
|--|------------------------------|--|--|--|
| <b>End point values</b>                      | IKERVIS® 1 mg/mL CsA         |  |  |  |
| Subject group type                           | Reporting group              |  |  |  |
| Number of subjects analysed                  | 17                           |  |  |  |
| Units: Spearman's coefficient of correlation |                              |  |  |  |
| number (confidence interval 95%)             | -0.7028 (-0.8797 to -0.3158) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Correlation between the change from baseline in variance of OSI measured with double pass aberrometer at Month 3 and the change from baseline in the CFS at Month 3.

|                        |   |
|------------------------|---|
| End point title        | Correlation between the change from baseline in variance of OSI measured with double pass aberrometer at Month 3 and the change from baseline in the CFS at Month 3. <sup>[2]</sup> |
| End point description: |   |
| End point type         | Primary   |

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End point timeframe:

At Month 3

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Notes:

[2] - 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: This study is estimating the correlation of two measures OSI variance change and CFS change within the same group. No further statistical analyses were planned for this endpoint.

|  |                             |  |  |  |
|--|-----------------------------|--|--|--|
| <b>End point values</b>                      | IKERVIS® 1 mg/mL CsA        |  |  |  |
| Subject group type                           | Reporting group             |  |  |  |
| Number of subjects analysed                  | 17                          |  |  |  |
| Units: Spearman's coefficient of correlation |                             |  |  |  |
| number (confidence interval 95%)             | -0.0384 (-0.5087 to 0.4515) |  |  |  |

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From the time the patient gave informed consent until the final trial visit.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 19.1 |
|--------------------|------|

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | Overall study |
|-----------------------|---------------|

Reporting group description: -

| Serious adverse events                            | Overall study  |  |  |
|---|----------------|--|--|
| Total subjects affected by serious adverse events |                |  |  |
| subjects affected / exposed                       | 0 / 17 (0.00%) |  |  |
| number of deaths (all causes)                     | 0              |  |  |
| number of deaths resulting from adverse events    | 0              |  |  |

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

| Non-serious adverse events                            | Overall study   |  |  |
|---|-----------------|--|--|
| Total subjects affected by non-serious adverse events |                 |  |  |
| subjects affected / exposed                           | 9 / 17 (52.94%) |  |  |
| Eye disorders   |                 |  |  |
| Eye Irritation  |                 |  |  |
| subjects affected / exposed                           | 3 / 17 (17.65%) |  |  |
| occurrences (all)                                     | 3               |  |  |
| Dry eye   |                 |  |  |
| subjects affected / exposed                           | 2 / 17 (11.76%) |  |  |
| occurrences (all)                                     | 2               |  |  |
| Eye Burns   |                 |  |  |
| subjects affected / exposed                           | 1 / 17 (5.88%)  |  |  |
| occurrences (all)                                     | 1               |  |  |
| Eyelid oedema   |                 |  |  |
| subjects affected / exposed                           | 1 / 17 (5.88%)  |  |  |
| occurrences (all)                                     | 1               |  |  |

|                             |                |  |  |
|-----------------------------|----------------|--|--|
| PHOTOPHOBIA                 |                |  |  |
| subjects affected / exposed | 1 / 17 (5.88%) |  |  |
| occurrences (all)           | 1              |  |  |
| VISUAL ACUITY REDUCED       |                |  |  |
| subjects affected / exposed | 1 / 17 (5.88%) |  |  |
| occurrences (all)           | 1              |  |  |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date        | Amendment   |
|-------------|---|
| 03 May 2017 | Modification of an inclusion criteria, allowing to include patients rated 3 for the corneal fluorescein staining (CFS) test; specifying that certain exclusion criteria only applies to the eligible eye to be used for the statistical analysis, adding an assessment (non-corrected visual acuity). |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported