



## 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
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##### 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, e.llobetmerkling@euraxipharma.fr
Scientific contact	Elsa LLOBET-MERKLING, EURAXI PHARMA, 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**

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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**

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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**

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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

Arm title	IKERVIS® 1 mg/mL CsA
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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.

Number of subjects in period 1	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
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Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	17	17	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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 65-84 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: 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: 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: 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
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.1
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### Reporting groups

Reporting group title	Overall study
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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