Clinical trial results:
A Double-Masked, Randomised, Placebo-Controlled, Parallel-Group, 12-Week, Phase 2 Study to Investigate the Safety and Efficacy of Ripasudil (K-321) Eye Drops After Descemetorhexis in Patients with Fuchs Endothelial Corneal Dystrophy

Summary

EudraCT number	2019-003280-22
Trial protocol	DE DK
Global end of trial date	27 June 2022

Results information

Result version number	v1 (current)
This version publication date	12 July 2025
First version publication date	12 July 2025

Trial information

Trial identification

Sponsor protocol code	K-321-201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04250207
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Kowa Research Institute, Inc.
Sponsor organisation address	430 Davis Drive, Suite 200, Morrisville, United States, 27560
Public contact	Shona Pendse, MD, MMSc, Kowa Research Institute, Inc., studyrecruitment@kowaus.com
Scientific contact	Shona Pendse, MD, MMSc, Kowa Research Institute, Inc., studyrecruitment@kowaus.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:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 September 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 June 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to investigate the effect of K-321 dosed for 12 weeks on central ECD in patients with FECD after descemetorhexis.

Protection of trial subjects:

The study was conducted in accordance with the World Medical Association Declaration of Helsinki; ICH GCP; General Data Protection Regulation or Directive 2001/20/EC (in the EU); the FDA GCP, as described in 21 CFR Parts 11, 50, 54, 56, and 312 and Health Insurance Portability and Accountability Act (in the US); and the laws and regulations of the country where the study was conducted. Prior to the initiation of any study procedures, each patient signed and dated an approved informed consent form. Each patient was assured of his/her right to withdraw from the study at any time.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 June 2020
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	Australia: 8
Country: Number of subjects enrolled	United States: 34
Country: Number of subjects enrolled	Denmark: 2
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Spain: 15
Worldwide total number of subjects	65
EEA total number of subjects	23

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)	30
From 65 to 84 years	35
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

After obtaining informed consent at Visit 1, the patient returned for the descemetorhexis operation and randomly assigned to treatment after 1 to 4 weeks (Visit 2). At Visit 2, each patient's eligibility for study participation was confirmed, which included the requirement of a successful descemetorhexis operation.

Period 1

Period 1 title	Treatment Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	K-321 QID

Arm description: -

Arm type	Experimental
Investigational medicinal product name	K-321
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops, solution in single-dose container
Routes of administration	Ophthalmic use

Dosage and administration details:

K-321 ophthalmic solution 0.4% dosed QID (K-321 QID)

Arm title	K-321 BID

Arm description: -

Arm type	Experimental
Investigational medicinal product name	K-321
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops, solution in single-dose container
Routes of administration	Ophthalmic use

Dosage and administration details:

K-321 ophthalmic solution 0.4% dosed BID (K-321 BID)

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo matching K-321
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops, solution in single-dose container
Routes of administration	Ophthalmic use

Dosage and administration details:

K-321 Placebo

Number of subjects in period 1	K-321 QID	K-321 BID	Placebo
Started	21	22	22
Completed	21	22	22

Period 2	
Period 2 title	40 Week Follow-up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor
Arms	
Are arms mutually exclusive?	Yes
Arm title	K-321 QID
Arm description: Follow-up	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	K-321 BID
Arm description: Follow-up	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Placebo
Arm description: Follow-up	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 2	K-321 QID	K-321 BID	Placebo
Started	21	22	22
Completed	21	21	20
Not completed	0	1	2
Rescue keratoplasty	-	-	1
Withdrawal by patient	-	1	1

Baseline characteristics

Reporting groups	
Reporting group title	K-321 QID
Reporting group description: -	
Reporting group title	K-321 BID
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	K-321 QID	K-321 BID	Placebo
Number of subjects	21	22	22
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
arithmetic mean	64.7	65.1	65.3
standard deviation	± 12.28	± 9.68	± 9.00
Gender categorical Units: Subjects			
Female	16	13	20
Male	5	9	2

Reporting group values	Total		
Number of subjects	65		
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 standard deviation	- 		
Gender categorical Units: Subjects			
Female Male	49 16		

Subject analysis sets

Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

The FAS consisted of all patients who had a successful descemetorhexis procedure, were randomly assigned to receive double-masked study drug, received at least 1 dose of study drug in the study eye, and had at least 1 assessment of central corneal ECD performed after the descemetorhexis procedure on the study eye. (An assessment of "cannot perform due to corneal oedema" was considered a valid assessment for inclusion in the FAS.)

Subject analysis set title	Safety Set (SFS)
Subject analysis set type	Safety analysis

Subject analysis set description:

The SFS consisted of all patients who received any study drug.

Reporting group values	Full Analysis Set (FAS)	Safety Set (SFS)	
Number of subjects	65	65	
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years arithmetic mean standard deviation	 65.0 ± 10.23	 65.0 ± 10.23	
Gender categorical Units: Subjects			
Female Male	49 16	49 16	

End points

End points reporting groups

Reporting group title	K-321 QID
Reporting group description: -	
Reporting group title	K-321 BID
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	K-321 QID
Reporting group description: Follow-up	
Reporting group title	K-321 BID
Reporting group description: Follow-up	
Reporting group title	Placebo
Reporting group description: Follow-up	
Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis
Subject analysis set description: The FAS consisted of all patients who had a successful descemetorhexis procedure, were randomly assigned to receive double-masked study drug, received at least 1 dose of study drug in the study eye, and had at least 1 assessment of central corneal ECD performed after the descemetorhexis procedure on the study eye. (An assessment of "cannot perform due to corneal oedema" was considered a valid assessment for inclusion in the FAS.)	
Subject analysis set title	Safety Set (SFS)
Subject analysis set type	Safety analysis
Subject analysis set description: The SFS consisted of all patients who received any study drug.	

Primary: Central Corneal ECD at Week 12

End point title	Central Corneal ECD at Week 12
End point description: Assessed by Cornea Image Analysis Reading Center (CIARC) and was based on assessments performed by specular microscopy.	
End point type	Primary
End point timeframe: Baseline to Week 12	

End point values	K-321 QID	K-321 BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	22	22	
Units: cells/square millimeter				
arithmetic mean (standard deviation)	530.86 (± 312.453)	468.02 (± 322.361)	228.05 (± 297.860)	

Statistical analyses

Statistical analysis title	Central Corneal ECD at Week 12
Comparison groups	K-321 BID v Placebo
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0344
Method	Wilcoxon rank sum test

Statistical analysis title	Central Corneal ECD at Week 12
Comparison groups	K-321 QID v Placebo
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0065
Method	Wilcoxon rank sum test

Secondary: Time to Return of Corneal Thickness to Less than or Equal to Baseline Corneal Thickness

End point title	Time to Return of Corneal Thickness to Less than or Equal to Baseline Corneal Thickness

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 52

End point values	K-321 QID	K-321 BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	22	22	
Units: Days				
median (confidence interval 95%)	50.0 (35.0 to 110.0)	50.0 (34.0 to 66.0)	165.0 (112.0 to 366.0)	

Statistical analyses

Statistical analysis title	Time to Achieve No Corneal Oedema of Study Eye
Comparison groups	Placebo v K-321 QID
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0259
Method	Logrank

Statistical analysis title	Time to Achieve No Corneal Oedema of Study Eye
Comparison groups	K-321 BID v Placebo
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0068
Method	Logrank

Secondary: Time to No Corneal Oedema

End point title	Time to No Corneal Oedema
End point description:	

End point type	Secondary
End point timeframe:	
Baseline to Week 52	

End point values	K-321 QID	K-321 BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	22	22	
Units: Days				
median (confidence interval 95%)	35.0 (22.0 to 64.0)	51.5 (50.0 to 269.0)	267.0 (141.0 to 365.0)	

Statistical analyses

Statistical analysis title	Time to Achieve No Corneal Oedema of Study Eye
Comparison groups	K-321 QID v Placebo

Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0021
Method	Logrank

Statistical analysis title	Time to Achieve No Corneal Oedema of Study Eye
Comparison groups	K-321 BID v Placebo
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1696
Method	Logrank

Secondary: Time to Achieve Central Corneal ECD 700 cells/mm2 or more

End point title	Time to Achieve Central Corneal ECD 700 cells/mm2 or more
End point description:	

End point type	Secondary
End point timeframe:	
Baseline to Week 52	

End point values	K-321 QID	K-321 BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	22[1]	22[2]	
Units: Days				
median (confidence interval 95%)	141.0 (83.0 to 363.0)	181.0 (113.0 to 9999)	273.0 (135.0 to 9999)	

Notes:

[1] - 9999 = NA: Median upper limit unestimable as curve < 0.50.

[2] - 9999 = NA: Median upper limit unestimable as curve < 0.50.

Statistical analyses

Statistical analysis title	Time to Achieve Central Corneal ECD 700 cells/mm2
Comparison groups	K-321 QID v Placebo
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1209
Method	Logrank

Statistical analysis title	Time to Achieve Central Corneal ECD 700 cells/mm2
Comparison groups	K-321 BID v Placebo
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7116
Method	Logrank

Secondary: Central Corneal ECD at Week 52

End point title	Central Corneal ECD at Week 52

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 52

End point values	K-321 QID	K-321 BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	22	22	
Units: cells/square millimeters				
arithmetic mean (standard deviation)	751.45 (± 407.259)	633.05 (± 313.372)	431.79 (± 327.488)	

Statistical analyses

Statistical analysis title	Central Corneal ECD at Week 52
Comparison groups	K-321 QID v Placebo
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0047
Method	Wilcoxon Rank Sum Test

Statistical analysis title	Central Corneal ECD at Week 52
Comparison groups	K-321 BID v Placebo

Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0625
Method	Wilcoxon Rank Sum Test

Secondary: Proportion of patients who achieve central corneal ECD of 700 cells/mm2 or more at Week 12

End point title	Proportion of patients who achieve central corneal ECD of 700 cells/mm2 or more at Week 12

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 12

End point values	K-321 QID	K-321 BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	21	16	
Units: Patients				
number (not applicable)				
Number	6	4	2	
Percent	28.6	19.0	12.5	

Statistical analyses

Statistical analysis title	Proportion of patients who achieve central corneal
Comparison groups	K-321 QID v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4227
Method	Fisher exact

Statistical analysis title	Proportion of patients who achieve central corneal
Comparison groups	K-321 BID v Placebo

Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6796
Method	Fisher exact

Secondary: Proportion of patients who achieve central corneal ECD of 700 cells/mm2 or more at Week 52

End point title	Proportion of patients who achieve central corneal ECD of 700 cells/mm2 or more at Week 52

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 52

End point values	K-321 QID	K-321 BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	18	15	
Units: percent				
number (not applicable)				
Number	15	8	5	
Percent	78.9	44.4	33.3	

Statistical analyses

Statistical analysis title	Central corneal ECD of 700 cells/mm2 or more
Comparison groups	K-321 QID v Placebo
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0135
Method	Fisher exact

Statistical analysis title	Central corneal ECD of 700 cells/mm2 or more
Comparison groups	K-321 BID v Placebo

Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5154
Method	Pearson Chi-square test

Secondary: Change in Central Corneal Thickness from Baseline at Week 12

End point title	Change in Central Corneal Thickness from Baseline at Week 12
End point description:	

End point type	Secondary
End point timeframe:	
Baseline to Week 12	

End point values	K-321 QID	K-321 BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	21	21	
Units: micrometer				
arithmetic mean (standard deviation)	0.59 (± 86.332)	-22.69 (± 61.127)	100.19 (± 137.191)	

Statistical analyses

Statistical analysis title	Change from Baseline in Central Corneal Thickness
Comparison groups	K-321 QID v Placebo
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0127
Method	Wilcoxon rank sum test

Statistical analysis title	Change from Baseline in Central Corneal Thickness
Comparison groups	K-321 BID v Placebo
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0014
Method	Wilcoxon rank sum test

Secondary: Change in Central Corneal Thickness from Baseline at Week 52

End point title	Change in Central Corneal Thickness from Baseline at Week 52
End point description:	

End point type	Secondary
End point timeframe:	
Baseline to Week 52	

End point values	K-321 QID	K-321 BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	21	21	
Units: micrometer				
arithmetic mean (standard deviation)	-6.74 (± 65.888)	-25.88 (± 44.360)	55.29 (± 155.649)	

Statistical analyses

Statistical analysis title	Change in Central Corneal Thickness at Week 52
Comparison groups	K-321 QID v Placebo
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5181
Method	Wilcoxon rank sum test

Statistical analysis title	Change in Central Corneal Thickness at Week 52
Comparison groups	K-321 BID v Placebo
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1898
Method	Wilcoxon rank sum test

Secondary: Percentage Change from Baseline in Central Corneal Thickness at Week 12

End point title	Percentage Change from Baseline in Central Corneal Thickness at Week 12
End point description:	

End point type	Secondary

End point timeframe: Baseline to Week 12

End point values	K-321 QID	K-321 BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	21	17	
Units: percent				
arithmetic mean (standard deviation)	0.73 (± 15.895)	-3.65 (± 9.467)	10.70 (± 17.611)	

Statistical analyses

Statistical analysis title	Difference to Placebo
Comparison groups	K-321 QID v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0608
Method	Wilcoxon rank sum test

Statistical analysis title	Difference to Placebo
Comparison groups	K-321 BID v Placebo
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0071
Method	Wilcoxon rank sum test

Secondary: Percentage Change from Baseline in Central Corneal Thickness at Week 52

End point title	Percentage Change from Baseline in Central Corneal Thickness at Week 52

End point description:

End point type	Secondary

End point timeframe:
Baseline to Week 52

End point values	K-321 QID	K-321 BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	18	15	
Units: percent				
arithmetic mean (standard deviation)	-2.90 (± 8.634)	-5.63 (± 5.614)	-3.68 (± 11.182)	

Statistical analyses

Statistical analysis title	Difference to Placebo
Comparison groups	K-321 QID v Placebo
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.555
Method	Wilcoxon rank sum test

Statistical analysis title	Compared to Placebo
Comparison groups	K-321 BID v Placebo
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8718
Method	Wilcoxon rank sum test

Secondary: Proportion of patients who achieve corneal thickness less than or equal to baseline corneal thickness at Week 12

End point title	Proportion of patients who achieve corneal thickness less than or equal to baseline corneal thickness at Week 12
End point description:	
End point type	Secondary
End point timeframe: Baseline to Week 12	

End point values	K-321 QID	K-321 BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	21	18	
Units: participants				
number (not applicable)				
Number	13	17	5	

Percent	65.0	81.0	27.8	

Statistical analyses

Statistical analysis title	Difference to Placebo
Comparison groups	K-321 QID v Placebo
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.0218
Method	Pearson Chi-square test

Statistical analysis title	Difference to Placebo
Comparison groups	K-321 BID v Placebo
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0013
Method	Fisher exact

Secondary: Proportion of patients who achieve corneal thickness less than or equal to baseline corneal thickness at Week 52

End point title	Proportion of patients who achieve corneal thickness less than or equal to baseline corneal thickness at Week 52

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 52

End point values	K-321 QID	K-321 BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	18	16	
Units: percent				
number (not applicable)				
Number	14	15	13	
Percent	77.8	83.3	81.3	

Statistical analyses

Statistical analysis title	Difference to Placebo
Comparison groups	K-321 QID v Placebo
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.9999
Method	Fisher exact

Statistical analysis title	Difference to Placebo
Comparison groups	K-321 BID v Placebo
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.9999
Method	Fisher exact

Secondary: Proportion of patients who achieve no corneal oedema at Week 12

End point title	Proportion of patients who achieve no corneal oedema at Week 12

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 12

End point values	K-321 QID	K-321 BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	22	22	
Units: participants				
number (not applicable)				
Number	17	12	2	
Percent	81.0	54.5	9.1	

Statistical analyses

Statistical analysis title	Difference to Placebo
Comparison groups	K-321 QID v Placebo
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Fisher exact

Statistical analysis title	Difference to Placebo
Comparison groups	K-321 BID v Placebo
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0028
Method	Fisher exact

Secondary: Proportion of patients who achieve no corneal oedema at Week 52

End point title	Proportion of patients who achieve no corneal oedema at Week 52

End point description:

End point type	Secondary

End point timeframe:

Baseline to Week 52

End point values	K-321 QID	K-321 BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	22	22	
Units: Participants				
number (not applicable)				
Number	17	13	13	
Percent	81.0	59.1	59.1	

Statistical analyses

Statistical analysis title	No corneal oedema at Week 52
Comparison groups	K-321 QID v Placebo
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1854
Method	Fisher exact

Statistical analysis title	No corneal oedema at Week 52
Comparison groups	K-321 BID v Placebo
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.9999
Method	Pearson Chi-square test

Adverse events

Adverse events information

Timeframe for reporting adverse events:

52 Weeks

Adverse event reporting additional description:

All AEs were collected starting from the time that the patient gave consent until the date of completion or withdrawal from the study. Adverse events were deemed to be treatment-emergent if the onset date was on or after the date of first treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	K-321 QID
Reporting group description: -	
Reporting group title	K-321 BID
Reporting group description: -	
Reporting group title	Placebo

Reporting group description: -

Serious adverse events	K-321 QID	K-321 BID	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	3 / 22 (13.64%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Alcohol rehabilitation			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Terminal ileitis			

subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	K-321 QID	K-321 BID	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 21 (57.14%)	11 / 22 (50.00%)	14 / 22 (63.64%)
Investigations			
Intraocular pressure increased			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	2 / 22 (9.09%)
occurrences (all)	0	1	4
Injury, poisoning and procedural complications			
Wrist fracture			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Eye disorders			
Conjunctival hyperaemia			
subjects affected / exposed	3 / 21 (14.29%)	3 / 22 (13.64%)	0 / 22 (0.00%)
occurrences (all)	3	3	0

Corneal degeneration			
subjects affected / exposed	2 / 21 (9.52%)	1 / 22 (4.55%)	1 / 22 (4.55%)
occurrences (all)	2	1	1
Eye pruritus			
subjects affected / exposed	1 / 21 (4.76%)	3 / 22 (13.64%)	0 / 22 (0.00%)
occurrences (all)	1	3	0
Photophobia			
subjects affected / exposed	1 / 21 (4.76%)	2 / 22 (9.09%)	2 / 22 (9.09%)
occurrences (all)	1	3	2
Punctate keratitis			
subjects affected / exposed	1 / 21 (4.76%)	2 / 22 (9.09%)	1 / 22 (4.55%)
occurrences (all)	1	2	1
Vision blurred			
subjects affected / exposed	1 / 21 (4.76%)	2 / 22 (9.09%)	3 / 22 (13.64%)
occurrences (all)	1	2	4
Visual acuity reduced			
subjects affected / exposed	1 / 21 (4.76%)	3 / 22 (13.64%)	0 / 22 (0.00%)
occurrences (all)	1	4	0
Corneal oedema			
subjects affected / exposed	4 / 21 (19.05%)	2 / 22 (9.09%)	7 / 22 (31.82%)
occurrences (all)	4	3	10
Eye pain			
subjects affected / exposed	0 / 21 (0.00%)	2 / 22 (9.09%)	5 / 22 (22.73%)
occurrences (all)	0	3	5
Corneal disorder			
subjects affected / exposed	0 / 21 (0.00%)	2 / 22 (9.09%)	1 / 22 (4.55%)
occurrences (all)	0	2	1
Foreign body sensation in eyes			
subjects affected / exposed	0 / 21 (0.00%)	2 / 22 (9.09%)	1 / 22 (4.55%)
occurrences (all)	0	2	1
Diplopia			
subjects affected / exposed	0 / 21 (0.00%)	2 / 22 (9.09%)	0 / 22 (0.00%)
occurrences (all)	0	2	0
Eye Allergy (study eye)			
subjects affected / exposed	2 / 21 (9.52%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0

Eye allergy (non-study eye) subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 2	0 / 22 (0.00%) 0	0 / 22 (0.00%) 0
Eye irritation subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0	2 / 22 (9.09%) 2	1 / 22 (4.55%) 1
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1	2 / 22 (9.09%) 2	0 / 22 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported