Clinical trial results:
A Phase II/III, Randomized, Double-Masked, Vehicle-Controlled, Efficacy, Safety and Tolerability Study of Chloroprocaine 3% Gel Eye Drops in healthy volunteers

Summary

EudraCT number	2020-000465-17
Trial protocol	AT
Global end of trial date	03 December 2020

Results information

Result version number	v1 (current)
This version publication date	12 May 2022
First version publication date	12 May 2022

Trial information

Trial identification

Sponsor protocol code	CHL.3-02-2019

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04753710
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sintetica SA
Sponsor organisation address	Via Penate 5, Mendrisio, Switzerland, 6850
Public contact	Department of Clinical Pharmacology, Medical University of Vienna, +43 14040029810, klin-pharmakologie@meduniwien.ac.at
Scientific contact	Department of Clinical Pharmacology, Medical University of Vienna, +43 14040029810, klin-pharmakologie@meduniwien.ac.at

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	25 June 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 December 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess efficacy of Chloroprocaine 3% ophthalmic gel in healthy subjects

Protection of trial subjects:

Following inclusion/exclusion criteria were assessed:
Inclusion criteria
Signed and dated ICF
Healthy male or female aged from 18 to 90 years
No clinically significant ocular or systemic disease
Ability to orally respond to pain
Ability to follow the visit schedule.
Exclusion criteria
Ophthalmic exclusion criteria:
Eye movement disorder
Dacryocystitis and all other pathologies of tears drainage system
History of Inflammatory ocular disease
Corneal, epithelial, stromal or endothelial, residual or evolutionary disease
History of ocular traumatism, infection or inflammation within the last 3 months
Best corrected visual acuity < 1/10
History of ophthalmic surgical complication
Systemic/non ophthalmic exclusion criteria:
General history:
Deafness
Excessive anxiety
Any other medical or surgical history, disorder or disease such as acute or chronic severe organic disease: hepatic, endocrine neoplastic, hematological diseases, severe psychiatric illness, etc and/or any complicating factor or structural abnormality judged by the investigator to be incompatible with the study
Allergic history: Known hypersensitivity to one of the components of the study medications or to test products
Specific non-inclusion criteria for women:
Pregnancy, lactation
Women without an effective method of contraception
OR
Women not hysterectomized, not menopaused nor surgically sterilized
Exclusion criteria related to general conditions:
Inability of subject to understand the study procedures and thus inability to give informed consent
Non-compliant subject
Participation in another clinical study
Already included once in this study
Ward of court
Subject not covered by the Social Security
Exclusion criteria related to previous and concomitant medications (within 15 days prior screening)
Use of systemic opioids and opioid drugs
Topical ocular treatment with anesthetic action
Use of systemic analgesic drugs,except paracetamol, which will be allowed after V2

Background therapy:

not applicable

Evidence for comparator:

not applicable

Actual start date of recruitment	01 June 2020
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	Austria: 107
Worldwide total number of subjects	107
EEA total number of subjects	107

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)	107
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was performed in 2 parts. In part 1: 36 subjects received treatment and completed the study. in part 2: 60 were randomized, 40 in the CHL 3% gel and 20 in the vehicle group.
Part 1:
Group 1: 1 drop
Group 2: 3 drops
Group 3: 3+3 times
Part 2: 3 drops

Pre-assignment

Screening details:

The screening examination was to be performed before the start of the experiments and was identical for Part 1 and Part 2 and occurred at Visit 1 (Day -30 to Day -7).
Informed consent,Pregnancy test if applicable,Demography,Ocular and systemic medical and surgical history,previous and conc meds,Slit lamp examination, etc as per incl/excl criteria

Period 1

Period 1 title	Part 1
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

The study was carried out in a double-masked fashion. Therefore, the investigators and study site staff as well as the study participants were not informed about the treatment dispensed.
Drug accountability was also to be performed by designated personnel only

Arms

Are arms mutually exclusive?	Yes
Arm title	Chloroprocaine

Arm description:

Chloroprocaine hydrochloride 3% eye gel for instillation

Arm type	Experimental
Investigational medicinal product name	Chloroprocaine gel 3%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye gel
Routes of administration	Conjunctival use

Dosage and administration details:

In Part 1, 3 groups for single and multiple instillations (1 drop, 3 drops and 3+3 drops). In each group, 9 subjects were to be randomized to receive CHL 3% gel and 3 subjects were to receive the vehicle as control in the right eye.
After Part 1 was completed, an internal independent board was to review safety endpoints of data collected from these first subjects and to advise to go on with further enrolment.

Arm title	Vehicle

Arm description:

Vehicle for Chloroprocaine hydrochloride 3% eye gel for instillation

Arm type	Placebo

Investigational medicinal product name	Vehicle
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye gel
Routes of administration	Conjunctival use

Dosage and administration details:

In Part 1, 3 groups for single and multiple instillations (1 drop, 3 drops and 3+3 drops). In each group, 9 subjects were to be randomized to receive CHL 3% gel and 3 subjects were to receive the vehicle as control in the right eye.
After Part 1 was completed, an internal independent board was to review safety endpoints of data collected from these first subjects and to advise to go on with further enrolment.

Number of subjects in period 1	Chloroprocaine	Vehicle
Started	27	9
Completed	27	9

Period 2

Period 2 title	Part 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

The study was carried out in a double-masked fashion. Therefore, the investigators and study site staff as well as the study participants were not informed about the treatment dispensed.
Drug accountability was also to be performed by designated personnel only.

Arms

Are arms mutually exclusive?	Yes
Arm title	Chloroprocaine

Arm description:

Chloroprocaine hydrochloride 3% eye gel for instillation

Arm type	Experimental
Investigational medicinal product name	Chloroprocaine hydrochloride 3% eye gel
Investigational medicinal product code	CAS number: 3858-89-7
Other name	
Pharmaceutical forms	Eye gel
Routes of administration	Conjunctival use

Dosage and administration details:

After Part 1 was completed, an internal independent board was to review safety endpoints of data collected from these first subjects and to advise to go on with further enrolment.
If no safety concerns had arisen, in Part 2 efficacy, safety and tolerability were to be assessed in 60 healthy subjects for the 3 drops dose regimen. Forty (40) subjects were to receive CHL 3% gel and 20

the vehicle (2:1 randomization) in the right eye.

Arm title	Vehicle

Arm description:

Vehicle for Chloroprocaine hydrochloride 3% eye gel for instillation

Arm type	Placebo
Investigational medicinal product name	Vehicle
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye gel
Routes of administration	Conjunctival use

Dosage and administration details:

After Part 1 was completed, an internal independent board was to review safety endpoints of data collected from these first subjects and to advise to go on with further enrolment.
If no safety concerns had arisen, in Part 2 efficacy, safety and tolerability were to be assessed in 60 healthy subjects for the 3 drops dose regimen. Forty (40) subjects were to receive CHL 3% gel and 20 the vehicle (2:1 randomization) in the right eye.

Number of subjects in period 2	Chloroprocaine	Vehicle
Started	27	9
Completed	40	20

Joined	13	11
Late recruitment	13	11
Late recruitment reason	part 2 of the trial	part 2 of the trial

Period 3

Period 3 title	Overall
Is this the baseline period?	Yes[1]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

The study was carried out in a double-masked fashion. Therefore, the investigators and study site staff as well as the study participants were not informed about the treatment dispensed.
Drug accountability was also to be performed by designated personnel only.

Arms

Are arms mutually exclusive?	Yes

Arm title	Chloroprocaine

Arm description:

Chloroprocaine hydrochloride 3% eye gel for instillation

Arm type	Experimental
Investigational medicinal product name	Chloroprocaine hydrochloride 3% eye gel
Investigational medicinal product code	CAS number: 3858-89-7
Other name	
Pharmaceutical forms	Eye gel
Routes of administration	Conjunctival use

Dosage and administration details:

In Part 1, 3 groups (12 subjects per group) for single and multiple instillations (1 drop, 3 drops and 3+3 drops). In each group, 9 subjects were to be randomized to receive CHL 3% gel and 3 subjects were to receive the vehicle as control in the right eye.
After Part 1 was completed, an internal independent board was to review safety endpoints of data collected from these first subjects and to advise to go on with further enrolment.
If no safety concerns had arisen, in Part 2 efficacy, safety and tolerability were to be assessed in 60 healthy subjects for the 3 drops dose regimen. Forty (40) subjects were to receive CHL 3% gel and 20 the vehicle (2:1 randomization) in the right eye.

Arm title	Vehicle

Arm description:

Vehicle for Chloroprocaine hydrochloride 3% eye gel for instillation

Arm type	Placebo
Investigational medicinal product name	Vehicle
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye gel
Routes of administration	Conjunctival use

Dosage and administration details:

In Part 1, 3 groups (12 subjects per group) for single and multiple instillations (1 drop, 3 drops and 3+3 drops). In each group, 9 subjects were to be randomized to receive CHL 3% gel and 3 subjects were to receive the vehicle as control in the right eye.
After Part 1 was completed, an internal independent board was to review safety endpoints of data collected from these first subjects and to advise to go on with further enrolment.
If no safety concerns had arisen, in Part 2 efficacy, safety and tolerability were to be assessed in 60 healthy subjects for the 3 drops dose regimen. Forty (40) subjects were to receive CHL 3% gel and 20 the vehicle (2:1 randomization) in the right eye.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: The overall was entered as baseline period since it is the period matching both part, 1 and 2

Number of subjects in period 3[2]	Chloroprocaine	Vehicle
Started	40	20
Completed	67	29

Joined	27	9
part 1 + part 2 of the trial	27	-
part 1 + part 2 of tthe trial	-	9

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 107 subjects have been screened. 96 were enrolled and 11 were screening failure

Baseline characteristics

Reporting groups

Reporting group title	Overall

Reporting group description: -

Reporting group values	Overall	Total	
Number of subjects	96	96	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	96	96	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	28.1		
standard deviation	± 9.3	-	
Gender categorical Units: Subjects			
Female	52	52	
Male	44	44	

Subject analysis sets

Subject analysis set title	Pooled Safety set
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety population considered in the pooled analysis included the total number of subjects participating in the safety populations of Part 1 (36) and Part 2 (60) respectively

Subject analysis set title	Enrolled set_Part 1
Subject analysis set type	Safety analysis

Subject analysis set description:

number of subject who received either IMP or placebo during Part 1

Subject analysis set title	Enrolled set_Part 2_safety
Subject analysis set type	Safety analysis

Subject analysis set description:

All patients enrolled in the Part 2, for which there is evidence that they used study medication and for whom any follow-up information is available.

Subject analysis set title	Enrolled set_Part 2_FAS
Subject analysis set type	Full analysis

Subject analysis set description:

All patients enrolled in the Part 2 for which any follow-up efficacy information is available.

Subject analysis set title	Enrolled set_Part 2_PP
Subject analysis set type	Per protocol

Subject analysis set description:

All patients of the Part 2 FAS who did not show any major protocol violation

Reporting group values	Pooled Safety set	Enrolled set_Part 1	Enrolled set_Part 2_safety
Number of subjects	96	36	60
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)	96		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean	28.1		
standard deviation	± 9.3	±	±
Gender categorical			
Units: Subjects			
Female	52		
Male	44		

Reporting group values	Enrolled set_Part 2_FAS	Enrolled set_Part 2_PP	
Number of subjects	60	59	
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	±	±	
Gender categorical			
Units: Subjects			
Female			
Male			

End points

End points reporting groups

Reporting group title	Chloroprocaine

Reporting group description:

Chloroprocaine hydrochloride 3% eye gel for instillation

Reporting group title	Vehicle

Reporting group description:

Vehicle for Chloroprocaine hydrochloride 3% eye gel for instillation

Reporting group title	Chloroprocaine

Reporting group description:

Chloroprocaine hydrochloride 3% eye gel for instillation

Reporting group title	Vehicle

Reporting group description:

Vehicle for Chloroprocaine hydrochloride 3% eye gel for instillation

Reporting group title	Chloroprocaine

Reporting group description:

Chloroprocaine hydrochloride 3% eye gel for instillation

Reporting group title	Vehicle

Reporting group description:

Vehicle for Chloroprocaine hydrochloride 3% eye gel for instillation

Subject analysis set title	Pooled Safety set
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety population considered in the pooled analysis included the total number of subjects participating in the safety populations of Part 1 (36) and Part 2 (60) respectively

Subject analysis set title	Enrolled set_Part 1
Subject analysis set type	Safety analysis

Subject analysis set description:

number of subject who received either IMP or placebo during Part 1

Subject analysis set title	Enrolled set_Part 2_safety
Subject analysis set type	Safety analysis

Subject analysis set description:

All patients enrolled in the Part 2, for which there is evidence that they used study medication and for whom any follow-up information is available.

Subject analysis set title	Enrolled set_Part 2_FAS
Subject analysis set type	Full analysis

Subject analysis set description:

All patients enrolled in the Part 2 for which any follow-up efficacy information is available.

Subject analysis set title	Enrolled set_Part 2_PP
Subject analysis set type	Per protocol

Subject analysis set description:

All patients of the Part 2 FAS who did not show any major protocol violation

Primary: anesthesia: proportion of success_Part 2_FAS

End point title	anesthesia: proportion of success_Part 2_FAS

End point description:

To assess efficacy of Chloroprocaine 3% ophthalmic gel in healthy subjects. For this, we assessed the proportion of subjects gaining full anesthesia of the ocular surface 5 minutes after administration of Chloroprocaine 3% ophthalmic gel. (the intent was to collect and only report data for Participants who were in Part 2)

End point type	Primary

End point timeframe:

at visit 2, day 1.
Anesthesia success is defined as full anesthesia of the ocular surface 5 minutes after administration of the IP.

End point values	Chloroprocaine	Vehicle	Enrolled set_Part 2_FAS	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	40	20	60	
Units: yes/no				
Anesthesia success_YES	38	4	42	
Anesthesia success_NO	2	16	18	

Statistical analyses

Statistical analysis title	Anesthesia proportion of success in V2_FAS
Comparison groups	Chloroprocaine v Vehicle
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.0001
Method	Z-test

Notes:

[1] - The proportion of subjects with successful anesthesia at Visit 2 was 95.0% (38 subjects) for CHL 3% gel and 20.0% (4 subjects) with the vehicle. The difference was statistically significant (p<0.0001) with a CI 95%

Primary: anesthesia: proportion of success_Part 2 _PP

End point title	anesthesia: proportion of success_Part 2 _PP

End point description:

To assess efficacy of Chloroprocaine 3% ophthalmic gel in healthy subjects. For this, we assessed the proportion of subjects gaining full anesthesia of the ocular surface 5 minutes after administration of Chloroprocaine 3% ophthalmic gel. (the intent was to collect and only report data for Participants who were in Part 2)

End point type	Primary

End point timeframe:

at visit 2, day 1
Anesthesia success is defined as full anesthesia of the ocular surface 5 minutes after administration of the IP.

End point values	Chloroprocaine	Vehicle	Enrolled set_Part 2_PP	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	39	20	59	
Units: yes/no				
Anesthesia success/YES	37	4	41	
Anesthesia success/NO	2	16	18	

Statistical analyses

Statistical analysis title	Anesthesia proportion of success in V2_PP
Comparison groups	Chloroprocaine v Vehicle
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Z-test

Primary: Duration of anesthesia (min) for all subjects – FAS, Part 2

End point title	Duration of anesthesia (min) for all subjects – FAS, Part 2

End point description:

When considering all subjects, anesthesia duration lasted longer after administration of CHL3% gel than after the vehicle, with median (min, max) values of 19.3 (0-44.3) min and 0 (0-39.3) min, respectively. No anesthesia was achieved in the majority of subjects in the vehicle group. Mean values were 22.92±10.15 min for CHL 3% gel and 3.86±9.85 min for the vehicle. Differences in anesthesia duration between treatments were statistically significant (p<0.0001).

End point type	Primary

End point timeframe:

visit 2, day 1

End point values	Chloroprocaine	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	20		
Units: minute				
median (full range (min-max))	19.3 (0 to 44.3)	0 (0 to 39.3)		

Statistical analyses

Statistical analysis title	Duration of anesthesia for all subjects_FAS_Part2
Comparison groups	Chloroprocaine v Vehicle

Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Wilcoxon (Mann-Whitney)

Secondary: Time to anesthesia (min) for all subjects – FAS, Part 2

End point title	Time to anesthesia (min) for all subjects – FAS, Part 2

End point description:

Data for all subjects in each treatment group (40 subjects in the CHL 3 % gel and 20 in the vehicle group) were analyzed. Subjects not achieving anesthesia were assigned a value of 5 min for time to obtain anesthesia.
When considering all subjects, the median time to anesthesia was the same in the CHL 3% gel group, whereas it occurred after 5 min in the vehicle group. Mean values were 1.03±1.15 min and 4.13±1.78 min in the CHL 3% gel and vehicle group, respectively. The difference for time to anesthesia between the two treatments was statistically significant (p<0.0001).

End point type	Secondary

End point timeframe:

visit 2, day 1

End point values	Chloroprocaine	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	20		
Units: minute				
median (full range (min-max))	0.67 (0.67 to 5)	5 (0.67 to 5)		

Statistical analyses

Statistical analysis title	Time to anesthesia for all subjects – FAS, Part 2
Comparison groups	Chloroprocaine v Vehicle
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	< 0.0001
Method	Wilcoxon (Mann-Whitney)

Notes:

[2] - Results on the PPS confirmed FAS results

Secondary: Cochet Bonnet assessment at Visit 2 – FAS, Part 2

End point title	Cochet Bonnet assessment at Visit 2 – FAS, Part 2

End point description:

End point type	Secondary

End point timeframe:

at visit 2, day 1

End point values	Chloroprocaine	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	20		
Units: mm				
arithmetic mean (standard deviation)	1.54 (± 9.61)	56.84 (± 7.11)		

Statistical analyses

Statistical analysis title	Cochet Bonnet assessment at Visit 2_FAS_Part 2

Statistical analysis description:

Concerns touching pressure (mm) measured in the right eye at Visit 2 mm. Median values were to be derived for both arms and were compared using a non-parametric hypothesis test (i.e. Mann-Whitney test).

Comparison groups	Chloroprocaine v Vehicle
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Wilcoxon (Mann-Whitney)

Secondary: arterial pressure_all groups

End point title	arterial pressure_all groups

End point description:

Mean arterial pressure (mmHg) is defined as the average pressure in a patient's arteries during one cardiac cycle. It is considered a better indicator of perfusion to vital organs than systolic blood pressure (SBP).

End point type	Secondary

End point timeframe:

up to 8 days

End point values	Chloroprocaine	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	29		
Units: mmHg				
geometric mean (standard deviation)				
Visit 1_screening	95.4 (± 8.6)	94.4 (± 9.1)		
Visit 2_pre dose	96.4 (± 8.4)	94.1 (± 9.2)		
Visit 2_post dose	94.9 (± 8.1)	94.2 (± 8.8)		
Visit 4_fup	94.9 (± 8.0)	93.7 (± 9.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: heart rate_all groups

End point title	heart rate_all groups

End point description:

End point type	Secondary

End point timeframe:

up to 8 days

End point values	Chloroprocaine	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	29		
Units: beats/min				
arithmetic mean (standard deviation)				
Visit 1_screening	74.6 (± 11.3)	75.1 (± 10.9)		
Visit 2_pre dose	75.9 (± 11.6)	75.9 (± 11.3)		
Visit 2_post dose	68.7 (± 12.5)	71.4 (± 11.6)		
Visit 4_fup	75.4 (± 11.5)	74.6 (± 11.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Visual analogue scale analysis_all groups

End point title	Visual analogue scale analysis_all groups

End point description:

100 mm visual analogue scale ws used for assessing ocular symptoms as burning, stinging, itching, foreign body sensation.

End point type	Secondary

End point timeframe:

up to day 8

End point values	Chloroprocaine	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	29		
Units: millimetre(s)				
arithmetic mean (standard deviation)				
Burning_screening_right eye	0.6 (± 2.2)	1.7 (± 4.8)		
Burning_visit 2 pre dose_right eye	0.8 (± 3.5)	0.0 (± 0.2)		
Burning_visit 2 post dose_right eye	4.1 (± 8.2)	1.2 (± 3.4)		
Burning_visit 4 fup_right eye	0.4 (± 1.7)	0.0 (± 0.2)		
Foreign body sensation_screening_right eye	0.4 (± 2.2)	1.8 (± 6.5)		
Foreign body sensation_visit 2 pre dose_right eye	0.3 (± 1.6)	0.8 (± 3.2)		
Foreign body sensation_visit 2 post dose_right eye	5.7 (± 9.7)	8.5 (± 13.7)		
Foreign body sensation_visit 4 fup_right eye	0.4 (± 2.0)	0.4 (± 1.9)		
Itching_screening_right eye	1.6 (± 5.3)	3.1 (± 10.4)		
Itching_visit 2 pre dose_right eye	1.5 (± 5.4)	1.8 (± 5.4)		
Itching_visit 2 post dose_right eye	2.1 (± 6.3)	0.3 (± 1.1)		
Itching_visit 4 up_right eye	1.1 (± 4.4)	0.7 (± 2.2)		
Stinging_screening_right eye	0.2 (± 1.0)	0.3 (± 1.7)		
Stinging_visit 2 pre dose_right eye	0.2 (± 0.9)	0.3 (± 1.3)		
Stinging_visit 2 post dose_right eye	1.5 (± 3.3)	1.7 (± 4.0)		
Stinging_visit 4 fup_right eye	0.4 (± 1.9)	0.1 (± 0.4)		
Burning_screening_left eye	0.8 (± 2.6)	1.4 (± 3.9)		
Burning_visit 4 fup_left eye	0.2 (± 1.0)	0.4 (± 1.9)		
Foreign body sensation_screening_left eye	0.5 (± 2.8)	1.1 (± 5.2)		
Foreign body sensation_visit 4 fup_left eye	0.3 (± 1.4)	0.6 (± 2.8)		
Itching_screening_left eye	1.3 (± 4.6)	2.7 (± 10.0)		
Itching_visit 4 fup_left eye	0.7 (± 3.4)	1.0 (± 3.5)		
Stinging_screening_left eye	0.4 (± 1.7)	0.7 (± 2.8)		
Stinging_visit 4 fup_left eye	0.2 (± 1.0)	0.1 (± 0.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Best corrected visual acuity_all groups

End point title	Best corrected visual acuity_all groups

End point description:

Far best-corrected visual acuity was to be measured using the standard ETDRS acuity charts.

End point type	Secondary

End point timeframe:

at visit 1 (screening) and at visit 4 (follow up).

End point values	Chloroprocaine	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	29		
Units: score				
arithmetic mean (standard deviation)				
Visual acuity_screening_right eye	87.9 (± 4.4)	89.2 (± 4.6)		
Visual acuity_visit 4 fup_right eye	88.7 (± 4.6)	89.2 (± 3.7)		
Visual acuity_screening_left eye	87.3 (± 4.8)	87.8 (± 3.1)		
Visual acuity_visit 4 fup_left eye	88.1 (± 5.1)	88.0 (± 3.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Intraocular pressure

End point title	Intraocular pressure

End point description:

Intraocular pressure was to be measured with a slit-lamp mounted Goldmann applanation tonometer. Before each measurement one drop of oxybuprocainhydrochloride combined with sodium fluorescein was to be used for local anesthesia of the cornea.

End point type	Secondary

End point timeframe:

at visit 1 (screening) and at visit 4 (follow up)

End point values	Chloroprocaine	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	29		
Units: mmHg				
arithmetic mean (standard deviation)				
IOP_screening_right eye	14.0 (± 2.6)	14.0 (± 2.3)		
IOP_visit 4 fup_right eye	13.6 (± 2.6)	13.3 (± 2.0)		
IOP_screening_left eye	14.3 (± 2.5)	13.7 (± 2.1)		
IOP_visit 4 fup_left eye	13.9 (± 2.7)	13.3 (± 1.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Fundus evaluation analysis_all groups

End point title	Fundus evaluation analysis_all groups

End point description:

Fundoscopy at the slit lamp.
Indirect ophthalmoscopy was to be performed at the slit lamp using a +90 diopters Volk lens.

End point type	Secondary

End point timeframe:

at visit 1 (screening) and at visit 4 (follow up)

End point values	Chloroprocaine	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	29		
Units: number of subjects				
Fundoscopy_screening_right eye_normal	67	29		
Fundoscopy_screening_right eye_not normal	0	0		
Fundoscopy_visit 4 fup_right eye_normal	67	29		
Fundoscopy_visit 4 fup_right eye_not normal	0	0		
Fundoscopy_screening_left eye_normal	67	29		
Fundoscopy_screening_left eye_not normal	0	0		
Fundoscopy_visit 4 fup_left eye_normal	67	29		
Fundoscopy_visit 4 fup_left eye_not normal	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Corneal fluorescein staining analysis_all groups

End point title	Corneal fluorescein staining analysis_all groups

End point description:

Minims-Fluorescein Sodium 2.0% eye drops were to be used to detect corneal epithelial defects using slit lamp biomicroscopy. As grading scale for corneal damage, the NEI/Industry Workshop guidelines were to be used4. The cornea was to be divided into 5 sectors (central, superior, inferior, nasal and temporal), each of which is scored on a scale of 0–3, whereas 0 means no staining and 3 means maximum staining, with a maximal score of 15.
Total score is reported in the results.

End point type	Secondary

End point timeframe:

at visit 1 (screening) and at visit 4 (follow up)

End point values	Chloroprocaine	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	29		
Units: score				
arithmetic mean (standard deviation)				
Corneal staining_screening_right eye	0.0 (± 0.0)	0.0 (± 0.2)		

Corneal staining_visit 4 follow up_right eye	0.0 (± 0.0)	0.0 (± 0.0)		
Corneal staining_screening_left eye	0.0 (± 0.0)	0.0 (± 0.2)		
Corneal staining_visit 4 follow up_left eye	0.0 (± 0.0)	0.0 (± 0.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Slit lamp examination analysis_all groups

End point title	Slit lamp examination analysis_all groups

End point description:

Slit lamp biomicroscopy was to be performed for the following parameters: Conjunctival redness, anterior chamber flare, conjunctival chemosis, eyelid swelling, eyelid redness and cornea were to be graded on a 4 point scale: (0) none, (1) mild, (2) moderate, (3) severe.
The full data results are in the attached document.
No statistically significant differences of clinical signs between treatment groups were observed at any time point of the study.

End point type	Secondary

End point timeframe:

up to day 8 (visit 4)

End point values	Chloroprocaine	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	29		
Units: number of subjects	0	0		

Attachments (see zip file)	CSR_slit lamp examination_all groups.pdf

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Start of monitoring: from immediately after the signature of the informed consent
End of monitoring: last follow-up visit/Early Termination Visit (ETV)

Adverse event reporting additional description:

An AE occurring after the last follow-up visit/ETV and coming to knowledge of the investigator (e.g. by spontaneous reporting by study subjects) was to be recorded only if it was an ADR, according to the investigator's judgment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Global incidence of subjects with TEAE and serious TEAE

Reporting group description:

Global incidence of subjects with treatment-emergent adverse events and serious treatment-emergent adverse events – Safety set

Serious adverse events	Global incidence of subjects with TEAE and serious TEAE		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 96 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Global incidence of subjects with TEAE and serious TEAE		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	58 / 96 (60.42%)		
Investigations			
Intraocular pressure increased			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences (all)	1		
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences (all)	1		

Injury, poisoning and procedural complications Ligament sprain subjects affected / exposed occurrences (all)	 1 / 96 (1.04%) 1		
Cardiac disorders Bradycardia subjects affected / exposed occurrences (all)	 5 / 96 (5.21%) 5		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Presyncope subjects affected / exposed occurrences (all) Syncope subjects affected / exposed occurrences (all)	 7 / 96 (7.29%) 7 1 / 96 (1.04%) 1 1 / 96 (1.04%) 1		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Instillation site pain subjects affected / exposed occurrences (all) Pain subjects affected / exposed occurrences (all) Sensation of foreign body subjects affected / exposed occurrences (all)	 1 / 96 (1.04%) 1 1 / 96 (1.04%) 1 1 / 96 (1.04%) 1 4 / 96 (4.17%) 4		
Eye disorders Conjunctival haemorrhage subjects affected / exposed occurrences (all) Conjunctival hyperaemia	 2 / 96 (2.08%) 2		

subjects affected / exposed	10 / 96 (10.42%)		
occurrences (all)	11		
Conjunctival oedema			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences (all)	1		
Dry eye			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences (all)	2		
Eye irritation			
subjects affected / exposed	9 / 96 (9.38%)		
occurrences (all)	9		
Mydriasis			
subjects affected / exposed	24 / 96 (25.00%)		
occurrences (all)	24		
Ocular hyperaemia			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences (all)	1		
Vision blurred			
subjects affected / exposed	3 / 96 (3.13%)		
occurrences (all)	3		
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	2 / 96 (2.08%)		
occurrences (all)	2		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			

Pruritus subjects affected / exposed occurrences (all)	1 / 96 (1.04%) 1		
Infections and infestations COVID-19 subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Rhinitis subjects affected / exposed occurrences (all) Tonsillitis subjects affected / exposed occurrences (all)	 1 / 96 (1.04%) 1 3 / 96 (3.13%) 3 1 / 96 (1.04%) 1 1 / 96 (1.04%) 1		

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