Clinical trial results:
Aqueous humour concentrations after topical apPlication of combinEd levofloxacin dexamethasone eye dRops and of its single components: a randoMized, assEssor-blinded, parallel-group study in patients undergoing cataract surgery - iPERME

Summary

EudraCT number	2018-001149-15
Trial protocol	IT
Global end of trial date	06 December 2018

Results information

Result version number	v1 (current)
This version publication date	16 August 2020
First version publication date	16 August 2020

Trial information

Trial identification

Sponsor protocol code	LevoDesa_05-2017

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	NTC SRL
Sponsor organisation address	Via dei Gracchi, 35, Milano, Italy, 20146
Public contact	Dr. Federico Bertocchi , NTC SRL, 0039 0243850436, federico.bertocchi@ntcpharma.com
Scientific contact	Dr. Federico Bertocchi , NTC SRL, 0039 0243850436, federico.bertocchi@ntcpharma.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	25 March 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 December 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the penetration of levofloxacin/dexamethasone 21-phosphate into the aqueous humour after ocular administration in combination or as single active ingredients.

Protection of trial subjects:

The trial will be conducted in accordance with International Conference on Harmonisation Good Clinical Practice (ICH GCP) and all applicable laws and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 September 2018
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	Italy: 125
Worldwide total number of subjects	125
EEA total number of subjects	125

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)	17
From 65 to 84 years	96
85 years and over	12

Subject disposition

Recruitment

Recruitment details:

Study Period:
• Date of first enrolment: 4 September 2018
• Date study finalized (last patient last visit): 6 December 2018
Study centres:
• U.O. Oculistica Universitaria, Azienda Ospedaliera Universitaria Pisana, Presidio Ospedaliero di Cisanello, Pisa;
• Clinica Oculistica, Presidio Ospedale San Paolo, Milan.

Pre-assignment

Screening details:

Planned sample size n.120; randomized patients n.125; screened patients n.133 (1 patient screened for both eyes).

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor[1]

Arms

Are arms mutually exclusive?	Yes
Arm title	Levofloxacin + Dexamethasone

Arm description:

Levofloxacin 0.5% + DSP 0.132% (w/v) eye drops (TEST product). One ml contains levofloxacin hemihydrate 5.12 mg, corresponding to 5 mg of levofloxacin, and DSP 1.32 mg, corresponding to 1 mg of dexamethasone;
Administration route: ocular instillation;
Dose and regimen: two 30 µl doses 30 minutes apart, one 90 ± 15 minutes prior to surgery and the other 60 ± 15 minutes prior to surgery (each dose contains 150 µg anhydrous levofloxacin and 39.6 µg DSP).

Arm type	Experimental
Investigational medicinal product name	Levofloxacin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops, solution
Routes of administration	Ocular use

Dosage and administration details:

Administration route: ocular instillation;

Dose and regimen: two 30 µl doses 30 minutes apart, one 90 ± 15 minutes prior to surgery and the other 60 ± 15 minutes prior to surgery (each dose contains 150 µg anhydrous levofloxacin and 39.6 µg DSP).

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops, solution
Routes of administration	Ocular use

Dosage and administration details:

Administration route: ocular instillation
Dose and regimen: two 30 µl doses 30 minutes apart, one 90 ± 15 minutes prior to surgery and the other 60 ± 15 minutes prior to surgery (each dose contains 150 µg anhydrous levofloxacin and 39.6 µg DSP).

Arm title	Levofloxacin

Arm description:

Levofloxacin 0.5% eye drops (Oftaquix®). One ml contains 5,12 mg of levofloxacin hemihydrate equal to 5 mg of levofloxacin;
Administration route: ocular instillation;
Dose and regimen: two 30 µl doses 30 minutes apart, one 90 ± 15 minutes prior to surgery and the other 60 ± 15 minutes prior to surgery (each dose contains 150 µg anhydrous levofloxacin).

Arm type	Experimental
Investigational medicinal product name	Levofloxacin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops, solution
Routes of administration	Ocular use

Dosage and administration details:

Administration route: ocular instillation;

Dose and regimen: two 30 µl doses 30 minutes apart, one 90 ± 15 minutes prior to surgery and the other 60 ± 15 minutes prior to surgery (each dose contains 150 µg anhydrous levofloxacin).

Arm title	Dexamethasone

Arm description:

Dexamethasone sodium phosphate 0.15% eye drops (Tamesad®). One ml contains 1.5 mg of DSP corresponding to 1.14 mg/ml of dexamethasone;
Administration route: ocular instillation;
Dose and regimen: two 26 µl doses 30 minutes apart, one 90 ± 15 minutes prior to surgery and the other 60 ± 15 minutes prior to surgery (each dose containing 39 µg DSP).

Arm type	Experimental
Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops, solution
Routes of administration	Ocular use

Dosage and administration details:

Administration route: ocular instillation;

Dose and regimen: two 26 µl doses 30 minutes apart, one 90 ± 15 minutes prior to surgery and the other 60 ± 15 minutes prior to surgery (each dose containing 39 µg DSP).

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: This is a randomized, assessor-blinded, parallel-group study.

Number of subjects in period 1	Levofloxacin + Dexamethasone	Levofloxacin	Dexamethasone
Started	42	42	41
Completed	42	42	41

Baseline characteristics

Reporting groups	
Reporting group title	Levofloxacin + Dexamethasone
Reporting group description:	
Levofloxacin 0.5% + DSP 0.132% (w/v) eye drops (TEST product). One ml contains levofloxacin hemihydrate 5.12 mg, corresponding to 5 mg of levofloxacin, and DSP 1.32 mg, corresponding to 1 mg of dexamethasone; Administration route: ocular instillation; Dose and regimen: two 30 µl doses 30 minutes apart, one 90 ± 15 minutes prior to surgery and the other 60 ± 15 minutes prior to surgery (each dose contains 150 µg anhydrous levofloxacin and 39.6 µg DSP).	
Reporting group title	Levofloxacin
Reporting group description:	
Levofloxacin 0.5% eye drops (Oftaquix®). One ml contains 5,12 mg of levofloxacin hemihydrate equal to 5 mg of levofloxacin; Administration route: ocular instillation; Dose and regimen: two 30 µl doses 30 minutes apart, one 90 ± 15 minutes prior to surgery and the other 60 ± 15 minutes prior to surgery (each dose contains 150 µg anhydrous levofloxacin).	
Reporting group title	Dexamethasone
Reporting group description:	
Dexamethasone sodium phosphate 0.15% eye drops (Tamesad®). One ml contains 1.5 mg of DSP corresponding to 1.14 mg/ml of dexamethasone; Administration route: ocular instillation; Dose and regimen: two 26 µl doses 30 minutes apart, one 90 ± 15 minutes prior to surgery and the other 60 ± 15 minutes prior to surgery (each dose containing 39 µg DSP).	

Reporting group values	Levofloxacin + Dexamethasone	Levofloxacin	Dexamethasone
Number of subjects	42	42	41
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	7	4	6
From 65-84 years	33	31	32
85 years and over	2	7	3
Age continuous Units: years			
median	72.45	75.38	74.59
standard deviation	± 7.60	± 8.38	± 8.00
Gender categorical Units: Subjects			
Female	27	21	21
Male	15	21	20
Race Units: Subjects			
American Indian or Alaska Native	0	0	0

Asian	0	1	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	1	0
White	42	40	40
More than one race	0	0	0
Unknown or Not Reported	0	0	0

Reporting group values	Total		
Number of subjects	125		
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)	17		
From 65-84 years	96		
85 years and over	12		
Age continuous			
Units: years			
median			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	69		
Male	56		
Race			
Units: Subjects			
American Indian or Alaska Native	0		
Asian	2		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	1		
White	122		
More than one race	0		
Unknown or Not Reported	0		

End points

End points reporting groups

Reporting group title	Levofloxacin + Dexamethasone

Reporting group description:

Levofloxacin 0.5% + DSP 0.132% (w/v) eye drops (TEST product). One ml contains levofloxacin hemihydrate 5.12 mg, corresponding to 5 mg of levofloxacin, and DSP 1.32 mg, corresponding to 1 mg of dexamethasone;
Administration route: ocular instillation;
Dose and regimen: two 30 µl doses 30 minutes apart, one 90 ± 15 minutes prior to surgery and the other 60 ± 15 minutes prior to surgery (each dose contains 150 µg anhydrous levofloxacin and 39.6 µg DSP).

Reporting group title	Levofloxacin

Reporting group description:

Levofloxacin 0.5% eye drops (Oftaquix®). One ml contains 5,12 mg of levofloxacin hemihydrate equal to 5 mg of levofloxacin;
Administration route: ocular instillation;
Dose and regimen: two 30 µl doses 30 minutes apart, one 90 ± 15 minutes prior to surgery and the other 60 ± 15 minutes prior to surgery (each dose contains 150 µg anhydrous levofloxacin).

Reporting group title	Dexamethasone

Reporting group description:

Dexamethasone sodium phosphate 0.15% eye drops (Tamesad®). One ml contains 1.5 mg of DSP corresponding to 1.14 mg/ml of dexamethasone;
Administration route: ocular instillation;
Dose and regimen: two 26 µl doses 30 minutes apart, one 90 ± 15 minutes prior to surgery and the other 60 ± 15 minutes prior to surgery (each dose containing 39 µg DSP).

Primary: Aqueous Humour Concentration of Levofloxacin

End point title	Aqueous Humour Concentration of Levofloxacin[1]

End point description:

Defined as the concentration of levofloxacin into the aqueous humour in all the three arms: Levofloxacin + Dexamethasone, Dexamethasone and Levofloxacin. The concentration of levofloxacin has been measured by LC tandem mass spectrometry.

End point type	Primary

End point timeframe:

90±15 min after the first administration of the study treatments

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: No formal statistical hypothesis had been formulated. All analyses were descriptive in nature and no inferential statistical analyses were planned.

End point values	Levofloxacin + Dexamethasone	Levofloxacin	Dexamethasone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	42	41	
Units: nmol/mL				
median (confidence interval 95%)	1.970 (1.648 to 2.292)	2.151 (1.708 to 2.594)	0 (0 to 0)	

Statistical analyses

No statistical analyses for this end point

Primary: Aqueous Humour Concentration of Dexamethasone 21-phosphate

End point title	Aqueous Humour Concentration of Dexamethasone 21-phosphate[2]

End point description:

Defined as the concentration of dexamethasone 21-phosphate into the aqueous humour in all the three arms: Levofloxacin + Dexamethasone, Dexamethasone and Levofloxacin. The concentration of dexamethasone 21- phosphate has been measured by LC tandem mass spectrometry.

End point type	Primary

End point timeframe:

90±15 min after the first administration of the study treatments

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: No formal statistical hypothesis had been formulated. All analyses were descriptive in nature and no inferential statistical analyses were planned.

End point values	Levofloxacin + Dexamethasone	Levofloxacin	Dexamethasone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	42	41	
Units: nmol/mL				
median (confidence interval 95%)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	

Statistical analyses

No statistical analyses for this end point

Primary: Aqueous Humour Concentration of Dexamethasone

End point title	Aqueous Humour Concentration of Dexamethasone[3]

End point description:

Defined as the concentration of dexamethasone into the aqueous humour in all the three arms: Levofloxacin + Dexamethasone, Dexamethasone and Levofloxacin.The concentration of dexamethasone has been measured by LC tandem mass spectrometry.

End point type	Primary

End point timeframe:

90±15 min after the first administration of the study treatments

Notes:

[3] - 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: No formal statistical hypothesis had been formulated. All analyses were descriptive in nature and no inferential statistical analyses were planned.

End point values	Levofloxacin + Dexamethasone	Levofloxacin	Dexamethasone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	42	41	
Units: nmol/mL				
median (confidence interval 95%)	0.030 (0.025 to 0.035)	0 (0 to 0)	0.042 (0.035 to 0.048)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline to the study completion, approximately 2 hours

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Levofloxacin + Dexamethasone

Reporting group description:

Levofloxacin 0.5% + DSP 0.132% (w/v) eye drops (TEST product). One ml contains levofloxacin hemihydrate 5.12 mg, corresponding to 5 mg of levofloxacin, and DSP 1.32 mg, corresponding to 1 mg of dexamethasone;
Administration route: ocular instillation;
Dose and regimen: two 30 µl doses 30 minutes apart, one 90 ± 15 minutes prior to surgery and the other 60 ± 15 minutes prior to surgery (each dose contains 150 µg anhydrous levofloxacin and 39.6 µg DSP).

Reporting group title	Levofloxacin

Reporting group description:

Levofloxacin 0.5% eye drops (Oftaquix®). One ml contains 5,12 mg of levofloxacin hemihydrate equal to 5 mg
of levofloxacin;
Administration route: ocular instillation;
Dose and regimen: two 30 µl doses 30 minutes apart, one 90 ± 15 minutes prior to surgery and the other 60 ±
15 minutes prior to surgery (each dose contains 150 µg anhydrous levofloxacin).

Reporting group title	Dexamethasone

Reporting group description:

Dexamethasone sodium phosphate 0.15% eye drops (Tamesad®). One ml contains 1.5 mg of DSP corresponding to 1.14 mg/ml of dexamethasone;
Administration route: ocular instillation;
Dose and regimen: two 26 µl doses 30 minutes apart, one 90 ± 15 minutes prior to surgery and the other 60 ± 15 minutes prior to surgery (each dose containing 39 µg DSP).

Serious adverse events	Levofloxacin + Dexamethasone	Levofloxacin	Dexamethasone
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	0 / 41 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	Levofloxacin + Dexamethasone	Levofloxacin	Dexamethasone
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	1 / 41 (2.44%)
Eye disorders			
Mild Mydriasis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 42 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	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