



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 (Oftaquin®). 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 + Dexamethason e | Levofloxacin | Dexamethason e | |
|----------------------------------|-------------------------------------|-----------------|---------------------------|--|
| 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 occurrences (all) | 0 / 42 (0.00%) 0 | 0 / 42 (0.00%) 0 | 1 / 41 (2.44%) 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