



Clinical trial results:

Open-labeled, randomized, comparative clinical study of efficacy and safety of Levofloxan 0,5% eye drops in patients with Acute Bacterial Conjunctivitis.

Summary

EudraCT number	2012-003664-41
Trial protocol	BG
Global end of trial date	27 June 2014

Results information

Result version number	v1 (current)
This version publication date	11 February 2020
First version publication date	11 February 2020

Trial information

Trial identification

Sponsor protocol code	PMS/LEVO-001-06-2012
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Balkanpharma-Razgrad AD
Sponsor organisation address	68 "Aprilsko vastanie" Blvd. , Razgrad, Bulgaria,
Public contact	Research and Development, Balkanpharma-Razgrad AD, +359 84613303, office@razgrad.bg
Scientific contact	Research and Development, Balkanpharma-Razgrad AD, +359 84613303, office@razgrad.bg

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	27 June 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 June 2014
Global end of trial reached?	Yes
Global end of trial date	27 June 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- Evaluation of therapeutically effect of Levofloxan 0,5% eye drops in patients with Acute Bacterial Conjunctivitis.
- Comparative evaluation of efficacy of Levofloxan 0,5% eye drops with respect to the comparator

Protection of trial subjects:

Prior to the start of the study, the study protocol, the informed consent and assent documents, patient instruction sheets, as well as any advertising materials used to recruit patients were submitted to Bulgarian Drug Agency (BDA) and ethics committees for multicenter trials (ECMT). The BDA/ECMTs reviewed all documents and approved required documents. Consistent with both the BDA/ECMT's requirements and all applicable regulations, the Investigators periodically provided study updates to the BDA/ECMT's. A patient provided informed consent, and children signed an approved assent form when appropriate. This study was conducted in accordance with Good Clinical Practices (GCP) and the ethical principles that have their origins in the Declaration of Helsinki.

Background therapy:

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Evidence for comparator:

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Actual start date of recruitment	26 July 2012
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	Bulgaria: 70
Worldwide total number of subjects	70
EEA total number of subjects	70

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)	61
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from 2 study centers located in Bulgaria.

Pre-assignment

Screening details:

70 subjects with bacterial conjunctivitis were randomized and treated with Levofloxan eye drops or Oftaquix eye drops.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

The study was conducted as open with regard to the IMPs. In the Information for the patient, detailed information was provided in accessible language on the investigational medicinal products, the usual dosage and method of administration. The manufacturer of the medicine was specified.

Arms

Are arms mutually exclusive?	Yes
Arm title	Levofloxan

Arm description:

Levofloxan 0.5% eye drops, solution

Arm type	Experimental
Investigational medicinal product name	Levofloxan 0.5% eye drops
Investigational medicinal product code	A
Other name	
Pharmaceutical forms	Eye drops, solution
Routes of administration	Ophthalmic use

Dosage and administration details:

Days 1-2: 1-2 drops every 2 (two) hours in the affected eye/eyes

Days 3-7: 1-2 drops 4 times daily in the affected eye/eyes

Average duration of treatment: 5 days.

Arm title	Oftaquix
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Arm description:

Oftaquix 0.5% eye drops, solution

Arm type	Experimental
Investigational medicinal product name	Oftaquix 0.5% eye drops
Investigational medicinal product code	B
Other name	
Pharmaceutical forms	Eye drops, solution
Routes of administration	Ophthalmic use

Dosage and administration details:

Days 1-2: 1-2 drops every 2 (two) hours in the affected eye/eyes

Days 3-7: 1-2 drops 4 times daily in the affected eye/eyes

Average duration of treatment: 5 days.

Number of subjects in period 1	Levofloxan	Oftaquix
Started	35	35
Completed	33	29
Not completed	2	6
Consent withdrawn by subject	2	6

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial
Reporting group description: -	

Reporting group values	Overall Trial	Total	
Number of subjects	70	70	
Age categorical			
Units: Subjects			
Adults (18-64 years)	61	61	
From 65-84 years	9	9	
Age continuous			
Units: years			
arithmetic mean	44.5		
standard deviation	± 14.45	-	
Gender categorical			
Units: Subjects			
Female	35	35	
Male	35	35	

Subject analysis sets

Subject analysis set title	Levofloxan
Subject analysis set type	Sub-group analysis
Subject analysis set description: Levofloxan 0.5% eye drops	
Subject analysis set title	Oftaquix
Subject analysis set type	Sub-group analysis
Subject analysis set description: Oftaquix 0.5% eye drops	

Reporting group values	Levofloxan	Oftaquix	
Number of subjects	33	29	
Age categorical			
Units: Subjects			
Adults (18-64 years)	30	24	
From 65-84 years	3	5	
Age continuous			
Units: years			
arithmetic mean	43.0	46.0	
standard deviation	± 13.96	± 14.86	
Gender categorical			
Units: Subjects			
Female	15	16	
Male	18	13	

End points

End points reporting groups

Reporting group title	Levofloxan
Reporting group description: Levofloxan 0.5% eye drops, solution	
Reporting group title	Oftaquix
Reporting group description: Oftaquix 0.5% eye drops, solution	
Subject analysis set title	Levofloxan
Subject analysis set type	Sub-group analysis
Subject analysis set description: Levofloxan 0.5% eye drops	
Subject analysis set title	Oftaquix
Subject analysis set type	Sub-group analysis
Subject analysis set description: Oftaquix 0.5% eye drops	

Primary: Evaluation of therapeutical effect of Levofloxan 0,5% eye drops in patients with Acute Bacterial Conjunctivitis

End point title	Evaluation of therapeutical effect of Levofloxan 0,5% eye drops in patients with Acute Bacterial Conjunctivitis
End point description: Evaluation of therapeutic effect of Levofloxan 0,5% eye drops in patients with Acute Bacterial Conjunctivitis.	
End point type	Primary
End point timeframe: Visit 1, Visit 2 and Visit 3	

End point values	Levofloxan	Oftaquix		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	33	29		
Units: subjects	33	29		

Statistical analyses

Statistical analysis title	Therapeutic effect - Ocular signs and symptoms
Statistical analysis description: Therapeutic results after both treatments on the Ocular signs and symptoms - Ocular signs and symptoms (anamnestic data).	
Comparison groups	Oftaquix v Levofloxan

Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	= 0.05
Method	Fisher exact
Parameter estimate	Chi-square = 0.344; p-value =0.755

Notes:

[1] - Main clinical parameters were measured, compared and assessed. Evaluation of clinical signs and symptoms, such as photosensitivity, pain, burning, itching, irritation and eyelid sticking were carried out according to a preliminary prepared scale.

Statistical analysis title	Therapeutic effect - Microbiological examination
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Statistical analysis description:

Evaluation of main clinical parameter - microbiological findings.

Comparison groups	Levofloxan v Oftaquix
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority ^[2]
P-value	= 0.05
Method	Fisher exact
Parameter estimate	Chi-square = 2.542; p-value=0.155

Notes:

[2] - Main clinical parameter microbiological findings was measured, compared and assessed.

Statistical analysis title	Therapeutic effect - Clinical examination
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Statistical analysis description:

Clinical examination.

Comparison groups	Levofloxan v Oftaquix
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05
Method	Fisher exact
Parameter estimate	Chi-square = 0.000; p-value=1.00

Primary: Comparative evaluation of efficacy of Levofloxan 0,5% eye drops with respect to the comparator

End point title	Comparative evaluation of efficacy of Levofloxan 0,5% eye drops with respect to the comparator
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End point description:

In order to assess the therapeutic equivalence, the following primary end-points were evaluated and compared:
microbiological findings, rate of eradication of the causative agent and data of biomicroscopy.

End point type	Primary
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End point timeframe:

Visit 1, Visit 2, Visit 3

End point values	Levofloxan	Oftaquix		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	33	29		
Units: subject	33	29		

Statistical analyses

Statistical analysis title	Microbiological findings and rate of eradication
Statistical analysis description: A microbiological examinations were provided aimed at isolating the bacterial cause, determining its susceptibility to levofloxacin and assessing the degree of eradication.	
Comparison groups	Levofloxan v Oftaquix
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05
Method	Fisher exact
Parameter estimate	Chi-square = 2.542; p-value =0.155

Statistical analysis title	Biomicroscopical exam. - Conjunctival discharge A
Statistical analysis description: Biomicroscopical examination results for Conjunctival discharge after application of Levofloxan 0.5% eye drops. Mean and 95% confidence intervals refer to the percent of remaining without significant improvement volunteers at the last (3-rd) visit.	
Comparison groups	Levofloxan v Oftaquix
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.09

Statistical analysis title	Biomicroscopical exam. - Conjunctival discharge B
Statistical analysis description: Biomicroscopical examination results for Conjunctival discharge after application of Oftaquix 0.5% eye drops. Mean and 95% confidence intervals refer to the percent of remaining without significant improvement volunteers at the last (3-rd) visit.	
Comparison groups	Levofloxan v Oftaquix

Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.32

Statistical analysis title	Biomicrosc exam. - Bulbar conjunctival injection A
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Statistical analysis description:

Biomicroscopical examination results for Bulbar conjunctival injection after application of Levofloxan 0.5% eye drops.

Mean and 95% confidence intervals refer to the percent of remaining without significant improvement volunteers at the last (3-rd) visit.

Comparison groups	Oftaquix v Levofloxan
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.15

Statistical analysis title	Biomicrosc exam. - Bulbar conjunctival injection B
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Statistical analysis description:

Biomicroscopical examination results for Bulbar conjunctival injection after application of Oftaquix 0.5% eye drops.

Mean and 95% confidence intervals refer to the percent of remaining without significant improvement volunteers at the last (3-rd) visit.

Comparison groups	Levofloxan v Oftaquix
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.18

Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.39

Statistical analysis title	Biomicr. exam. Palpebral conjunctival injection A
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Statistical analysis description:

Biomicroscopical examination results for Palpebral conjunctival injection after application of Levofloxan 0.5% eye drops.

Mean and 95% confidence intervals refer to the percent of remaining without significant improvement volunteers at the last (3-rd) visit.

Comparison groups	Levofloxan v Oftaquix
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.09

Statistical analysis title	Biomicr. exam. Palpebral conjunctival injection B
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Statistical analysis description:

Biomicroscopical examination results for Palpebral conjunctival injection after application of Oftaquix 0.5% eye drops.

Mean and 95% confidence intervals refer to the percent of remaining without significant improvement volunteers at the last (3-rd) visit.

Comparison groups	Levofloxan v Oftaquix
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.39

Statistical analysis title	Comparative evaluation of efficacy - Clinical exam
Statistical analysis description:	
Comparative evaluation of efficacy of Levofloxan 0.5% eye drops with respect to the comparator - clinical examination	
Comparison groups	Levofloxan v Oftaquix
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05
Method	Fisher exact
Parameter estimate	Chi-square = 0.000; p-value =1.00

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit until Last Patient Last Visit.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.0
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Reporting groups

Reporting group title	Levofloxan eye drops, solution
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Reporting group description: -

Reporting group title	Oftaquix eye drops, solution
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Reporting group description: -

Serious adverse events	Levofloxan eye drops, solution	Oftaquix eye drops, solution	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 33 (0.00%)	0 / 29 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Levofloxan eye drops, solution	Oftaquix eye drops, solution	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 33 (0.00%)	0 / 29 (0.00%)	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: Throughout the study, none of the participants reported an adverse event.

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