Clinical trial results:
Therapeutic Equivalence (non-inferiority), Randomized, Observer-blind, two Parallel Group, Clinical Trial for Comparing the Efficacy and Tolerability of a new Generic Formulation of Travoprost 40g/ml Eye Drops Free of Preservatives vs. TRAVATAN® 40g/ml Eye Drops in Patients with Open Angle Glaucoma, or Ocular Hypertension, already on Treatment with IOP-lowering Drugs and Low Intraocular Pressure (IOP21 mmHg)

Summary

EudraCT number	2014-002576-91
Trial protocol	GR
Global end of trial date	18 December 2015

Results information

Result version number	v1 (current)
This version publication date	29 December 2021
First version publication date	29 December 2021

Trial information

Trial identification

Sponsor protocol code	Becro/OV/Travoprost

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	OmniVision
Sponsor organisation address	Lindberghstraße 9, Puchheim, Germany, 82178
Public contact	CLINICAL TRIAL INFORMATION, BECRO, +30 210 6729037, trials@becro.gr
Scientific contact	CLINICAL TRIAL INFORMATION, BECRO, +30 210 6729037, trials@becro.gr

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	20 December 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this clinical trial is to demonstrate the non-inferiority of the generic investigational medicinal product containing preservative-free Travoprost 40µg/ml in comparison with the commercially available preservative-containing comparator TRAVATAN® 40µg/ml (Alcon Laboratories Ltd UK) in the treatment of open angle glaucoma or ocular hypertension by examining the average change of diurnal IOP measured between last visit and baseline.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 October 2014
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	Greece: 200
Worldwide total number of subjects	200
EEA total number of subjects	200

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)	66
From 65 to 84 years	124

85 years and over	10

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Potential patients are evaluated for eligibility at a pre-study screening visit (SV) seven to one days before starting the clinical trial.

Period 1

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

Blinding implementation details:

The clinical trial was performed as observer-blind because of the differences in the primary packaging of both drugs. The investigational medicinal product (test) is a preservative-free preparation (Polyquad is excluded), in single dose containers while the reference product Travatan® is in multiple dose containers. Consequently, the clinical trial site had to have blind and not-blind clinical trial personnel.

Arms

Are arms mutually exclusive?	Yes
Arm title	Travoprost

Arm description:

A new preservative-free formulation of Travoprost 40µg/ml Eye Drops solution (Test product-T)

Arm type	Experimental
Investigational medicinal product name	Preservative-free Travoprost
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops, solution
Routes of administration	Topical use

Dosage and administration details:

Products will be self-administered by the patient, as indicated: One drop in the affected eye(s) once daily in the evening, approximately at 21:00.

Arm title	Travatan

Arm description:

Marketed Travatan® including preservative (Reference).

Arm type	Active comparator
Investigational medicinal product name	Travatan® 40µg/ml eye drops solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops, solution
Routes of administration	Topical use

Dosage and administration details:

Products will be self-administered by the patient, as indicated: One drop in the affected eye(s) once daily in the evening, approximately at 21:00.

Notes:

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

Justification: The clinical trial was performed as observer-blind because of the differences in the primary packaging of both drugs. The investigational medicinal product (test) is a preservative-free preparation (Polyquad is excluded), in single dose containers while the reference product Travatan® is in multiple dose containers. Consequently, the clinical trial site had to have blind and not-blind clinical trial

personnel.

Number of subjects in period 1	Travoprost	Travatan
Started	101	99
Completed	77	80
Not completed	24	19
Patients had incomplete IOP data	9	7
Protocol deviation	15	12

Baseline characteristics

Reporting groups	
Reporting group title	Travoprost
Reporting group description:	
A new preservative-free formulation of Travoprost 40µg/ml Eye Drops solution (Test product-T)	
Reporting group title	Travatan
Reporting group description:	
Marketed Travatan® including preservative (Reference).	

Reporting group values	Travoprost	Travatan	Total
Number of subjects	101	99	200
Age categorical Units: Subjects			
Adults (18-64 years)	29	37	66
From 65-84 years	70	54	124
85 years and over	2	8	10
Gender categorical Units: Subjects			
Female	51	47	98
Male	50	52	102

End points

End points reporting groups	
Reporting group title	Travoprost
Reporting group description:	
A new preservative-free formulation of Travoprost 40µg/ml Eye Drops solution (Test product-T)	
Reporting group title	Travatan
Reporting group description:	
Marketed Travatan® including preservative (Reference).	
Subject analysis set title	Per Protocol Population
Subject analysis set type	Per protocol
Subject analysis set description:	
The non-inferiority of the Test was proven based on the per protocol population: 157 patients, 77 in Test and 80 in Reference.	
Subject analysis set title	Intent-to-treat (ITT) Population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All randomized patients (N=200) were evaluated for safety as these subjects received at least one dose of the study medication.	

Primary: mean diurnal IOP change from baseline to last visit	
End point title	mean diurnal IOP change from baseline to last visit
End point description:	
End point type	Primary
End point timeframe:	
From baseline to last visit (week 4)	

End point values	Travoprost	Travatan		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	80		
Units: mmHg				
arithmetic mean (standard deviation)				
mean IOP at baseline	15.619 (± 2.531)	15.404 (± 2.410)		
mean IOP at week 1	15.322 (± 2.531)	15.638 (± 2.198)		
mean IOP at week 2	15.240 (± 2.513)	15.640 (± 2.150)		
mean IOP at week 4	15.194 (± 2.453)	15.785 (± 2.070)		

Statistical analyses

Statistical analysis title	Mean change in diurnal IOP
Statistical analysis description:	
The primary endpoint was the mean diurnal IOP change from baseline to last visit and the primary	

efficacy analysis was planned and carried out as a test of non-inferiority. Then, the analysis of covariance (ANCOVA) model was used to analyse the mean change in diurnal IOP with baseline IOP as the covariate, and treatment as factor. The treatment difference and a two-sided 95% confidence interval (CI) for the difference are calculated.

Comparison groups	Travoprost v Travatan
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.731
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.237
upper limit	0.225
Variability estimate	Standard deviation

Secondary: mean change in IOP between baseline and week 1

End point title	mean change in IOP between baseline and week 1
End point description:	
End point type	Secondary
End point timeframe:	
From baseline to week 1	

End point values	Travoprost	Travatan		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	80		
Units: mmHg				
arithmetic mean (standard deviation)				
mean IOP at baseline	15.619 (± 2.531)	15.404 (± 2.410)		
mean IOP at week 1	15.322 (± 2.531)	15.638 (± 2.198)		

Statistical analyses

Statistical analysis title	Analysis of secondary end point, baseline to wk 1
Comparison groups	Travoprost v Travatan

Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.483
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.921
upper limit	-0.045
Variability estimate	Standard deviation

Secondary: mean change in IOP between baseline and week 2

End point title	mean change in IOP between baseline and week 2
End point description:	
End point type	Secondary
End point timeframe:	
From baseline to week 2	

End point values	Travoprost	Travatan		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	80		
Units: mmHg				
arithmetic mean (standard deviation)				
mean IOP at baseline	15.619 (± 2.531)	15.404 (± 2.410)		
mean IOP at week 1	15.322 (± 2.531)	15.638 (± 2.198)		
mean IOP at week 2	15.240 (± 2.513)	15.640 (± 2.150)		

Statistical analyses

Statistical analysis title	Analysis of secondary end point, baseline to wk 2
Comparison groups	Travoprost v Travatan

Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.555
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.032
upper limit	-0.078
Variability estimate	Standard deviation

Secondary: proportion of patients with measured IOP <21 mmHg at the end of study (week 4)

End point title	proportion of patients with measured IOP <21 mmHg at the end of study (week 4)

End point description:

End point type	Secondary

End point timeframe:

At week 4

End point values	Travoprost	Travatan		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	80		
Units: percent				
number (not applicable)				
Percent	98.7	100		

Statistical analyses

No statistical analyses for this end point

Secondary: proportion of patients with measured IOP <21 mmHg during the study

End point title	proportion of patients with measured IOP <21 mmHg during the study

End point description:

End point type	Secondary

End point timeframe:

From baseline to week 4

End point values	Travoprost	Travatan		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	80		
Units: percent				
number (not applicable)				
Percent	97.4	100		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
All adverse events (AEs) that occurred during the study were documented.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	12.1

Reporting groups	
Reporting group title	Travoprost
Reporting group description:	
Travoprost 40µg/ml Eye Drops Free of Preservatives	
Reporting group title	Travatan
Reporting group description:	
Travatan® 40µg/ml Eye Drops	

Serious adverse events	Travoprost	Travatan	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 101 (0.00%)	0 / 99 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Travoprost	Travatan	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 101 (14.85%)	12 / 99 (12.12%)	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 101 (0.99%)	0 / 99 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Allergic reaction			
subjects affected / exposed	0 / 101 (0.00%)	1 / 99 (1.01%)	
occurrences (all)	0	1	
Eye disorders			

Conjunctival hyperaemia			
subjects affected / exposed	6 / 101 (5.94%)	3 / 99 (3.03%)	
occurrences (all)	6	3	
Stinging			
subjects affected / exposed	0 / 101 (0.00%)	3 / 99 (3.03%)	
occurrences (all)	0	3	
Foreign body sensation			
subjects affected / exposed	3 / 101 (2.97%)	4 / 99 (4.04%)	
occurrences (all)	3	4	
Eye dryness			
subjects affected / exposed	1 / 101 (0.99%)	3 / 99 (3.03%)	
occurrences (all)	1	3	
Eye redness			
subjects affected / exposed	0 / 101 (0.00%)	1 / 99 (1.01%)	
occurrences (all)	0	1	
Conjunctivitis			
subjects affected / exposed	1 / 101 (0.99%)	0 / 99 (0.00%)	
occurrences (all)	1	0	
Itching			
subjects affected / exposed	0 / 101 (0.00%)	2 / 99 (2.02%)	
occurrences (all)	0	2	
Blepharitis			
subjects affected / exposed	1 / 101 (0.99%)	1 / 99 (1.01%)	
occurrences (all)	1	1	
Blurred vision			
subjects affected / exposed	2 / 101 (1.98%)	0 / 99 (0.00%)	
occurrences (all)	2	0	
Visual acuity reduction			
subjects affected / exposed	0 / 101 (0.00%)	1 / 99 (1.01%)	
occurrences (all)	0	1	
Eye burning			
subjects affected / exposed	3 / 101 (2.97%)	0 / 99 (0.00%)	
occurrences (all)	3	0	
Eye irritation			
subjects affected / exposed	1 / 101 (0.99%)	0 / 99 (0.00%)	
occurrences (all)	1	0	

Photopsia subjects affected / exposed occurrences (all)	1 / 101 (0.99%) 1	0 / 99 (0.00%) 0	
Skin and subcutaneous tissue disorders Dermatitis subjects affected / exposed occurrences (all)	1 / 101 (0.99%) 1	0 / 99 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported