Clinical trial results:
Open, Observer-blind, two Parallel Group, Randomized, Multicentric Clinical Phase III Trial on the Comparison of Efficacy and Tolerability of a New Preservative-free Formulation of the Fixed Combination Latanoprost 50 µg/ml and Timolol 5 mg/ml Eye Drops vs. Xalacom? Eye Drops in Patients with Primary Open Angle Glaucoma or Ocular Hypertension

Summary

EudraCT number	2011-005339-15
Trial protocol	ES
Global end of trial date	05 March 2014

Results information

Result version number	v1 (current)
This version publication date	12 April 2021
First version publication date	12 April 2021

Trial information

Trial identification

Sponsor protocol code	QTM/OMN0211

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	OmniVision GmbH
Sponsor organisation address	Lindberghstraße 9, Puchheim, Germany, 82178
Public contact	Sponsor, OmniVision GmbH, clinicalconsultant@omnivision.de
Scientific contact	Sponsor, OmniVision GmbH, clinicalconsultant@omnivision.de

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	02 April 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 March 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To confirm the clinical non-inferiority of the preservative-free fixed combination Latanoprost/ Timolol eye drops compared with the marketed preservative-containing Xalacom? eye drops by the average decrease of diurnal IOP measured between the first and last visit

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	02 January 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	Spain: 165
Worldwide total number of subjects	165
EEA total number of subjects	165

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)	165
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All patients provided written informed consent to participate in the study prior to being screened. At screening, IOP evaluation was performed by two separate measurements one hour apart to confirm the eligibility of the patient concerning the inclusion criterion IOP ≤21 mmHg.
170 patients were assessed for eligibility, 165 were randomized.

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	Subject

Blinding implementation details:

The clinical trial was performed as observer-blind because of the differences in the packaging of both drugs. The investigational medicinal product is a preservative-free preparation, which has a special container closure system. Patients and non-blind personnel were cautioned not to reveal the clinical trial assignment to the blind evaluator.

Arms

Are arms mutually exclusive?	Yes
Arm title	Latanoprost 50 µg/ml and Timolol 5 mg/ml

Arm description:

New Preservative-free Formulation of the Fixed Combination Latanoprost 50 µg/ml and Timolol 5 mg/ml Eye Drops

Arm type	Experimental
Investigational medicinal product name	preservative-free combination of Latanoprost (50 µg/ml), Timolol (5 µg/ml)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops
Routes of administration	Topical use

Dosage and administration details:

Dose: One drop in each eye once daily in the evening at 21:00 (± 15 minutes)

Arm title	Xalacom

Arm description:

The current preparations of Xalacom™ contain latanoprost 50 micrograms, 6.8 mg timolol maleate equivalent to 5 mg timolol and 200 microgram of the excipient benzalkonium chloride (BAC) in 1ml solution.

Arm type	Active comparator
Investigational medicinal product name	Xalacom™ (Pfizer)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops
Routes of administration	Topical use

Dosage and administration details:

Dose: One drop in each eye once daily in the evening at 21:00 (± 15 minutes)

Number of subjects in period 1	Latanoprost 50 µg/ml and Timolol 5 mg/ml	Xalacom
Started	82	83
Completed	73	75
Not completed	9	8
Did not receive allocated intervention	1	-
Lost to follow-up	8	8

Baseline characteristics

Reporting groups	
Reporting group title	Latanoprost 50 µg/ml and Timolol 5 mg/ml
Reporting group description:	
New Preservative-free Formulation of the Fixed Combination Latanoprost 50 µg/ml and Timolol 5 mg/ml Eye Drops	
Reporting group title	Xalacom
Reporting group description:	
The current preparations of Xalacom™ contain latanoprost 50 micrograms, 6.8 mg timolol maleate equivalent to 5 mg timolol and 200 microgram of the excipient benzalkonium chloride (BAC) in 1ml solution.	

Reporting group values	Latanoprost 50 µg/ml and Timolol 5 mg/ml	Xalacom	Total
Number of subjects	82	83	165
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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
arithmetic mean	66.961	65.824	
standard deviation	± 9.5297	± 12.3016	-
Gender categorical			
Units: Subjects			
Female	53	51	104
Male	20	24	44
Not recorded	9	8	17

End points

End points reporting groups

Reporting group title	Latanoprost 50 µg/ml and Timolol 5 mg/ml

Reporting group description:

New Preservative-free Formulation of the Fixed Combination Latanoprost 50 µg/ml and Timolol 5 mg/ml Eye Drops

Reporting group title	Xalacom

Reporting group description:

The current preparations of Xalacom™ contain latanoprost 50 micrograms, 6.8 mg timolol maleate equivalent to 5 mg timolol and 200 microgram of the excipient benzalkonium chloride (BAC) in 1ml solution.

Subject analysis set title	Difference_evaluation
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Non inferiority of diurnal intraocular pressure difference between baseline and end of treatment (day 28) for the investigational drug compared with the comparator have been calculated.
To calculate non inferiority, treatment difference and a two-sided 95% confidence interval (CI) for the difference have been calculated.

Primary: Diurnal IOP difference between baseline and end of treatment (day 28)

End point title	Diurnal IOP difference between baseline and end of treatment (day 28)[1]

End point description:

Non inferiority of diurnal intraocular pressure difference between baseline and end of treatment (day 28) for the investigational drug compared with the comparator have been calculated.
To calculate non inferiority, treatment difference and a two-sided 95% confidence interval (CI) for the difference have been calculated .
The preservative-free fixed composition of Latanoprost/Timolol eye drops is considered to be non-inferior to the marketed Xalacom™ including preservative because the upper limit of the 95% CI of the difference is <1.5 mmHg.

To be reported: the difference between both eyes intraocular pressure measured after 28 days of treatment with Latanoprost/Timolol versus Xalacom (covariate: initial intraocular pressure).

End point type	Primary

End point timeframe:

difference between baseline and end of treatment (day 28)

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: Due to missing data concerning the statistical analysis this section cannot be completed.

End point values	Difference_evaluation			
Subject group type	Subject analysis set			
Number of subjects analysed	148			
Units: mmHg				
arithmetic mean (confidence interval 95%)	0.317 (-0.198 to 0.832)			

Statistical analyses

No statistical analyses for this end point

Secondary: Average decrease of diurnal IOP measured between baseline and day 7

End point title	Average decrease of diurnal IOP measured between baseline and day 7

End point description:

End point type	Secondary

End point timeframe:

From baseline to day 7.

End point values	Latanoprost 50 µg/ml and Timolol 5 mg/ml	Xalacom		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	75		
Units: mmHg				
arithmetic mean (standard error)				
Mean IOP day 1	17.562 (± 0.226)	17.988 (± 0.223)		
Mean IOP day 7	17.217 (± 0.237)	17.342 (± 0.234)		

Statistical analyses

No statistical analyses for this end point

Secondary: Average decrease of diurnal IOP measured between baseline and day 14

End point title	Average decrease of diurnal IOP measured between baseline and day 14

End point description:

End point type	Secondary

End point timeframe:

From baseline to day 14.

End point values	Latanoprost 50 µg/ml and Timolol 5 mg/ml	Xalacom		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	75		
Units: mmHg				
arithmetic mean (standard error)				

Mean IOP day 1	17.562 (± 0.226)	17.988 (± 0.223)		
Mean IOP day 7	17.217 (± 0.237)	17.342 (± 0.234)		
Mean IOP day 14	17.210 (± 0.221)	17.444 (± 0.218)		

Statistical analyses

No statistical analyses for this end point

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 the end of the study.

End point values	Latanoprost 50 µg/ml and Timolol 5 mg/ml	Xalacom		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	83		
Units: percent				
number (not applicable)				
percent	100	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	not specified
Dictionary version	N/A

Reporting groups	
Reporting group title	Latanoprost/Timolol
Reporting group description: -	
Reporting group title	Xalacom
Reporting group description: -	

Serious adverse events	Latanoprost/Timolol	Xalacom	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 81 (0.00%)	0 / 83 (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	Latanoprost/Timolol	Xalacom	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 81 (3.70%)	1 / 83 (1.20%)	
Injury, poisoning and procedural complications			
Trauma			
subjects affected / exposed	0 / 81 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Eye disorders			
Gritty sensation in the left eye			
subjects affected / exposed	1 / 81 (1.23%)	0 / 83 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Constipation			

subjects affected / exposed	1 / 81 (1.23%)	0 / 83 (0.00%)	
occurrences (all)	1	0	
Stomach discomfort			
subjects affected / exposed	1 / 81 (1.23%)	0 / 83 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Upper respiratory tract infection			
subjects affected / exposed	1 / 81 (1.23%)	0 / 83 (0.00%)	
occurrences (all)	1	0	
irritative cough			
subjects affected / exposed	0 / 81 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Headache			
subjects affected / exposed	1 / 81 (1.23%)	0 / 83 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Pruritus on face			
subjects affected / exposed	1 / 81 (1.23%)	0 / 83 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 81 (1.23%)	0 / 83 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 April 2012	V1. 1-03-2012 New Sites included: H. San Carlos, H. Reina Sofía
10 May 2012	V2. 2-04-2012 New Sites included: Puerta del Mar, V. Macarena, Carlos Haya, Torrecárdenas, Virgen de las Nieves
10 October 2012	V3. 8-08-2012 Change in a Inclusion Criterion
13 December 2012	V4. 22-10-2012 New Sites included: H. La Paz, H. La Fe, ICR
07 March 2013	V5. 17-01-2013 New Principal Investigator of Torrecárdenas hospital
09 May 2013	V6. 4-04-2013 New sites included: H. Morales Meseguer, H. de La Vega

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported