Clinical trial results:
Intraocular pressure and tolerability Study of Preservative Free Bimatoprost 0.03% Unit Dose (BUDPF) or preservative free Latanoprost 0.005% Unit Dose (LUDPF) (Monoprost®) in patients with Ocular hypertension or glaucoma: A Randomized, single masked, 3 month cross-over, Investigator led, European multicentre Trial (SPORT)

Summary

EudraCT number	2013-003490-10
Trial protocol	BE AT PT GB IT
Global end of trial date	17 February 2015

Results information

Result version number	v1 (current)
This version publication date	14 November 2021
First version publication date	14 November 2021
Summary attachment (see zip file)	SPORT Report Synopsis (Imp 16-5-4 01 Study_Report_Data_SPORT_synopsis.pdf)

Trial information

Trial identification

Sponsor protocol code	ECR-GLC-2013-06

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01975714
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AIBILI
Sponsor organisation address	Azinhaga de Santa Comba, Celas, Coimbra, Portugal, 3000-548
Public contact	EVICR.net Coordinating Centre, AIBILI (EVICR.net), +351 239480142, 4c@aibili.pt
Scientific contact	EVICR.net Coordinating Centre, AIBILI (EVICR.net), +351 239480142, 4c@aibili.pt

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	07 April 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 February 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to compare the difference in mean Intraocular pressure values between the 2 groups at 6 months.

Protection of trial subjects:

The trial was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki and its amendment in October 2000, Edinburgh, Scotland, the European Guidelines on Good Clinical Practice (GCP) and the International Conference on Harmonisation (ICH) Guidelines.
The Investigator ensured that each patient was fully informed about the nature and objective of the study and possible risks associated with participation. Patients indicated assent to participate in the study by personally signing and dating the written informed consent form. The process of obtaining informed consent was documented in the patient's source documents. The informed consent form used in this study, and any changes made during the course of the study, were prospectively approved by the Ethics Committees (EC). The Investigator retained the original of each patient's signed informed consent form and gave a copy to the patient.
Eligible patients were only included in the study after providing written (witnessed, where required by law or regulation), EC-approved informed consent. In cases where the patient's representative gave consent, the patient was informed about the study to the extent possible given his/her understanding. If the patient was capable of doing so, he/she indicated assent by personally signing and dating the written informed consent document or a separate assent form. Informed consent was obtained before conducting any study-specific procedures (i.e. all of the procedures described in the protocol).
Women of child bearing potential were informed that taking the study medication may involve unknown risks to the fetus if pregnancy were to occur during the study and agree that in order to participate in the study they must adhere to the contraception requirement for the duration of the study.

Background therapy: -
Evidence for comparator: -

Actual start date of recruitment	22 October 2013
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	Portugal: 12
Country: Number of subjects enrolled	Italy: 17
Country: Number of subjects enrolled	Belgium: 20
Country: Number of subjects enrolled	Austria: 6
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	Switzerland: 10

Worldwide total number of subjects	67
EEA total number of subjects	57

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)	32
From 65 to 84 years	32
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

Studied period (years): 1 year, 4 months
First enrolment: 22-Oct-2013
Last completed: 17-Feb-2015

Pre-assignment

Screening details:

72 patients were screened, 5 of which did not meet the eligibility criteria

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Monitor, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	BUDPF/ LUDPF
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	BUDPF
Investigational medicinal product code	S01EE03
Other name	
Pharmaceutical forms	Eye drops, solution in single-dose container
Routes of administration	Ophthalmic use
Dosage and administration details: 0.03% preservative free	
Investigational medicinal product name	LUDPF
Investigational medicinal product code	S01EE01
Other name	
Pharmaceutical forms	Eye drops, solution in single-dose container
Routes of administration	Ophthalmic use
Dosage and administration details: 0.005% preservative free	
Arm title	LUDPF/ BUDPF
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	BUDPF
Investigational medicinal product code	S01EE03
Other name	
Pharmaceutical forms	Eye drops, solution in single-dose container
Routes of administration	Ophthalmic use
Dosage and administration details: 0.03% preservative free	
Investigational medicinal product name	LUDPF
Investigational medicinal product code	S01EE01
Other name	
Pharmaceutical forms	Eye drops, solution in single-dose container

Routes of administration	Ophthalmic use
Dosage and administration details: 0.005% preservative free	

Number of subjects in period 1	BUDPF/ LUDPF	LUDPF/ BUDPF
Started	33	34
Completed	33	34

Period 2	
Period 2 title	overall trial
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind[1]
Roles blinded	Investigator, Data analyst, Assessor, Subject, Monitor, Carer
Arms	
Are arms mutually exclusive?	Yes
Arm title	BUDPF/ LUDPF
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	BUDPF
Investigational medicinal product code	S01EE03
Other name	
Pharmaceutical forms	Eye drops, solution in single-dose container
Routes of administration	Ophthalmic use
Dosage and administration details: 0.03% preservative free	
Investigational medicinal product name	LUDPF
Investigational medicinal product code	S01EE01
Other name	
Pharmaceutical forms	Eye drops, solution in single-dose container
Routes of administration	Ophthalmic use
Dosage and administration details: 0.005% preservative free	
Arm title	LUDPF/ BUDPF
Arm description: -	
Arm type	Experimental

Investigational medicinal product name	BUDPF
Investigational medicinal product code	S01EE03
Other name	
Pharmaceutical forms	Eye drops, solution in single-dose container
Routes of administration	Ophthalmic use
Dosage and administration details:	
0.03% preservative free	
Investigational medicinal product name	LUDPF
Investigational medicinal product code	S01EE01
Other name	
Pharmaceutical forms	Eye drops, solution in single-dose container
Routes of administration	Ophthalmic use
Dosage and administration details:	
0.005% preservative free	

Notes:

[1] - The roles blinded appear to be inconsistent with a double blind trial.

Justification: A classic double blinded trial has both investigator and patient blinded. In this study the investigator was blinded, as was the technician that measured the primary outcome and the statistician, but the patients knew the medication they were taking. As both were active drugs, there was no placebo effect applicable. The system complained when selecting single blind so we selected double.

Number of subjects in period 2	BUDPF/ LUDPF	LUDPF/ BUDPF
Started	33	34
Completed	33	34

Baseline characteristics

Reporting groups	
Reporting group title	BUDPF/ LUDPF
Reporting group description: -	
Reporting group title	LUDPF/ BUDPF

Reporting group description: -

Reporting group values	BUDPF/ LUDPF	LUDPF/ BUDPF	Total
Number of subjects	33	34	67
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)	14	18	32
From 65-84 years	17	15	32
85 years and over	2	1	3
Adults	0	0	0
Gender categorical Units: Subjects			
Female	21	16	37
Male	12	18	30
Intraocular pressure Units: mmHg			
arithmetic mean	19.2	19.2	
standard deviation	± 3.32	± 4.61	-

End points

End points reporting groups

Reporting group title	BUDPF/ LUDPF
Reporting group description: -	
Reporting group title	LUDPF/ BUDPF
Reporting group description: -	
Reporting group title	BUDPF/ LUDPF
Reporting group description: -	
Reporting group title	LUDPF/ BUDPF
Reporting group description: -	

Primary: Intraocular pressure

End point title	Intraocular pressure
End point description:	
End point type	Primary
End point timeframe:	
6 months - baseline	

End point values	BUDPF/ LUDPF	LUDPF/ BUDPF		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	34		
Units: mmHg				
arithmetic mean (standard deviation)	15.9 (± 2.8)	13.9 (± 2.61)		

Statistical analyses

Statistical analysis title	Linear mixed effects model

Statistical analysis description:

For this analysis a linear mixed model approach was used to compare the two groups (Model 1). Specifically, the Treatment (LUDPF vs BUDPF) at 6 months was used as a fixed effect factor with the two levels representing the two groups. The model included the baseline IOP (i.e. the IOP with no treatments) as a covariate and the Center as random effect to correct for the correlation among patient measurements from the same center

Comparison groups	BUDPF/ LUDPF v LUDPF/ BUDPF
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.01
Method	Mixed models analysis
Parameter estimate	Effect size
Point estimate	1.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	2.5

Notes:

[1] - Linear mixed effects model

Adverse events

Adverse events information	
Timeframe for reporting adverse events: month 6	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	15

Reporting groups	
Reporting group title	Bimatoprost
Reporting group description: this was the active drug when AE was reported	
Reporting group title	Latanoprost
Reporting group description: this drug was the active when AE was reported	

Serious adverse events	Bimatoprost	Latanoprost	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 67 (2.99%)	2 / 67 (2.99%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 67 (1.49%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Rectal fistula repair			
subjects affected / exposed	1 / 67 (1.49%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Rectal haemorrhage			
subjects affected / exposed	0 / 67 (0.00%)	1 / 67 (1.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			

Intervertebral disc protrusion			
subjects affected / exposed	0 / 67 (0.00%)	1 / 67 (1.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Bimatoprost	Latanoprost	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 67 (28.36%)	12 / 67 (17.91%)	
Injury, poisoning and procedural complications			
Laceration			
subjects affected / exposed	0 / 67 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Skeletal injury			
subjects affected / exposed	0 / 67 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Knee operation			
subjects affected / exposed	1 / 67 (1.49%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Retinal migraine			
subjects affected / exposed	1 / 67 (1.49%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 67 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	1 / 67 (1.49%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Tinnitus			

subjects affected / exposed	2 / 67 (2.99%)	0 / 67 (0.00%)	
occurrences (all)	2	0	
Eye disorders			
Asthenopia			
subjects affected / exposed	1 / 67 (1.49%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Blepharal pigmentation			
subjects affected / exposed	1 / 67 (1.49%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Conjunctival hyperaemia			
subjects affected / exposed	1 / 67 (1.49%)	1 / 67 (1.49%)	
occurrences (all)	1	1	
Dark circles under eyes			
subjects affected / exposed	1 / 67 (1.49%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Diabetic retinal oedema			
subjects affected / exposed	0 / 67 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Dry eye			
subjects affected / exposed	2 / 67 (2.99%)	0 / 67 (0.00%)	
occurrences (all)	2	0	
Erythema of eyelid			
subjects affected / exposed	1 / 67 (1.49%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Eye irritation			
subjects affected / exposed	0 / 67 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Eye pain			
subjects affected / exposed	1 / 67 (1.49%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Eye pruritus			
subjects affected / exposed	1 / 67 (1.49%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Foreign body sensation in eyes			
subjects affected / exposed	1 / 67 (1.49%)	0 / 67 (0.00%)	
occurrences (all)	1	0	

Vision blurred			
subjects affected / exposed	2 / 67 (2.99%)	0 / 67 (0.00%)	
occurrences (all)	2	0	
Visual acuity reduced			
subjects affected / exposed	1 / 67 (1.49%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 67 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Large intestine polyp			
subjects affected / exposed	1 / 67 (1.49%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 67 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Influenza			
subjects affected / exposed	0 / 67 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	2	
Nasopharyngitis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Oral herpes			
subjects affected / exposed	0 / 67 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Only primary analysis results were posted.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/26907933