Clinical trial results:
A phase IV study on the changes in ocular signs and symptoms in patients with ocular hypertension or open-angle glaucoma switched from Ganfort® eye drops (bimatoprost 0.03%/timolol 0.5%) to Taptiqom® eye drops (tafluprost 0.0015%/timolol 0.5%)

Summary

EudraCT number	2014-005273-37
Trial protocol	FI DE IT
Global end of trial date	25 May 2016

Results information

Result version number	v1 (current)
This version publication date	21 March 2019
First version publication date	21 March 2019
Summary attachment (see zip file)	Ganfort_CSR synopsis (Ganfort_CSR synopsis.pdf)

Trial information

Trial identification

Sponsor protocol code	201450

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Santen Oy
Sponsor organisation address	Niittyhaankatu 20, PO BOX 33, Tampere, Finland, FIN-33721
Public contact	Global Medical Affairs, Santen Oy, 358 32848863,
Scientific contact	Global Medical Affairs, Santen Oy, 358 32848863,

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	31 January 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 May 2016
Global end of trial reached?	Yes
Global end of trial date	25 May 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study is to investigate whether changes in ocular signs or symptoms occur when patients with OHT or OAG (POAG or PEX) are switched from Ganfort® eye drops (FDC of bimatoprost 0.03% and timolol 0.5%) to Taptiqom® eye drops (FDC of tafluprost 0.0015% and timolol 0.5%).

Protection of trial subjects:

The investigator (or designated doctor) gave each patient, prior to inclusion in the study, verbal and written information regarding the objectives and procedures of the study and the possible risks involved. The patientswere informed about their right to withdraw from the study at any time without the need to give a reason. The investigator (or designated doctor) obtained the written informed consent from all patients before any study related procedures were undertaken. The patient and the investigator (or designated doctor who gave the information) signed the informed consent form (ICF). The patients were timely informed of any new information that could have affected their willingness to continue in the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 June 2015
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	United Kingdom: 13
Country: Number of subjects enrolled	Finland: 10
Country: Number of subjects enrolled	Germany: 73
Country: Number of subjects enrolled	Italy: 27
Worldwide total number of subjects	123
EEA total number of subjects	123

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)	47
From 65 to 84 years	75
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

This was an open-label, multinational, multicenter, phase IV study planned to enroll 120 patients diagnosed with ocular hypertension or open-angle glaucoma (OAG). OAG included patients with primary open-angle glaucoma (POAG) or pseudoexfoliative glaucoma (PEX).

Pre-assignment

Screening details:

Patients who had been regular users of Ganfort® for at least 4 weeks prior to screening were eligible to enter the study. Ganfort® had to be taken once-daily in the evening. At the Screening/Baseline visit PF or BAK-preserved Ganfort® was switched to PF Taptiqom®.

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Taptiqom
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Tafluprost and timolol
Investigational medicinal product code	
Other name	Taptiqom
Pharmaceutical forms	Eye drops
Routes of administration	Ocular use

Dosage and administration details:

One drop of the study medication was administered once daily at 21:00 in the affected eye(s). The drops were administered in the temporal lower conjunctival cul de sac of the eye(s). Every effort was made to administer the study drops at the given time, but if extremely necessary, a deviation of one hour was allowed in the timing of administration.

Number of subjects in period 1	Taptiqom
Started	123
Completed	114
Not completed	9
Consent withdrawn by subject	4
Adverse event, non-fatal	5

Baseline characteristics

Reporting groups	
Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	123	123	
Age categorical Units: Subjects			
Adults (18-64 years)	47	47	
From 65-84 years	75	75	
85 years and over	1	1	
Age continuous Units: years			
arithmetic mean	66.49		
standard deviation	± 10.26	-	
Gender categorical Units: Subjects			
Female	68	68	
Male	55	55	

Subject analysis sets	
Subject analysis set title	Safety dataset
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety dataset included all enrolled patients who had received at least one dose of study treatment and had a subsequent safety measurement.

Subject analysis set title	ITT dataset
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The ITT dataset included all enrolled patients who had received at least one dose of study treatment and had at least one post-baseline outcome measurement available (ocular symptom or ocular sign).

Subject analysis set title	12-week ITT dataset
Subject analysis set type	Intention-to-treat

Subject analysis set description:

the patients continued the study up to 12 weeks

Reporting group values	Safety dataset	ITT dataset	12-week ITT dataset
Number of subjects	123	121	114
Age categorical Units: Subjects			
Adults (18-64 years)	47	47	46
From 65-84 years	75	73	68
85 years and over	1	1	0
Age continuous Units: years			
arithmetic mean	66.49	66.47	66.14

standard deviation	± 10.26	± 10.34	± 10.27

Gender categorical Units: Subjects			
Female	68	66	65
Male	55	55	49

End points

End points reporting groups

Reporting group title	Taptiqom
Reporting group description: -	
Subject analysis set title	Safety dataset
Subject analysis set type	Safety analysis
Subject analysis set description:	
The safety dataset included all enrolled patients who had received at least one dose of study treatment and had a subsequent safety measurement.	
Subject analysis set title	ITT dataset
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The ITT dataset included all enrolled patients who had received at least one dose of study treatment and had at least one post-baseline outcome measurement available (ocular symptom or ocular sign).	
Subject analysis set title	12-week ITT dataset
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
the patients continued the study up to 12 weeks	

Primary: Worst ocular symptom

End point title	Worst ocular symptom
End point description:	
End point type	Primary
End point timeframe:	
12-week changes from Screening/Baseline	

End point values	ITT dataset	ITT dataset	12-week ITT dataset	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	121	121	114	
Units: patients				
None	0	0	45	
Trace	0	0	22	
Mild	47	47	35	
Moderate	62	62	11	
Severe	12	12	1	

Statistical analyses

Statistical analysis title	Change from screening
Comparison groups	ITT dataset v 12-week ITT dataset

Number of subjects included in analysis	235
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Primary: Conjunctival redness/hyperemia

End point title	Conjunctival redness/hyperemia

End point description:

End point type	Primary

End point timeframe:

12-week changes from Screening/Baseline

End point values	ITT dataset	12-week ITT dataset		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	121	114		
Units: patients				
"0"	0	26		
"0.5"	0	10		
"1"	1	43		
"1.5"	0	22		
"2"	80	13		
"2.5"	17	0		
"3"	21	0		
"3.5"	1	0		
"4"	1	0		

Statistical analyses

Statistical analysis title	Change from screening
Comparison groups	12-week ITT dataset v ITT dataset
Number of subjects included in analysis	235
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
During the study	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups	
Reporting group title	overall trial

Reporting group description: -

Serious adverse events	overall trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 123 (1.63%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrioventricular block second degree			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Arterial occlusive disease			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 123 (35.77%)		
Vascular disorders			
Arterial occlusive disease			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Hypotension			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
General disorders and administration site conditions			
Condition aggravated			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	3 / 123 (2.44%)		
occurrences (all)	3		
Reproductive system and breast disorders			
Breast swelling			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 123 (2.44%)		
occurrences (all)	3		
Oropharyngeal pain			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Investigations			
Intraocular pressure increased			
subjects affected / exposed	3 / 123 (2.44%)		
occurrences (all)	3		
Body temperature increased			

subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Ultrasound kidney			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Fall	Additional description: Ocular adverse event : 1, Non-ocular adverse event : 1		
subjects affected / exposed	2 / 123 (1.63%)		
occurrences (all)	2		
Superficial injury of eye			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Ligament sprain			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Skin injury			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Dysgeusia			
subjects affected / exposed	2 / 123 (1.63%)		
occurrences (all)	2		
Headache			
subjects affected / exposed	11 / 123 (8.94%)		
occurrences (all)	11		
Somnolence			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Eye disorders			
Lacrimation increased			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Eye pruritus			

subjects affected / exposed occurrences (all)	1 / 123 (0.81%) 1		
Eyelid haematoma subjects affected / exposed occurrences (all)	1 / 123 (0.81%) 1		
Ocular hyperaemia subjects affected / exposed occurrences (all)	2 / 123 (1.63%) 2		
Optic disc haemorrhage subjects affected / exposed occurrences (all)	1 / 123 (0.81%) 1		
Visual acuity reduced subjects affected / exposed occurrences (all)	1 / 123 (0.81%) 1		
Eyelid irritation subjects affected / exposed occurrences (all)	1 / 123 (0.81%) 1		
Gastrointestinal disorders			
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 123 (0.81%) 1		
Diarrhoea subjects affected / exposed occurrences (all)	1 / 123 (0.81%) 1		
Nausea subjects affected / exposed occurrences (all)	1 / 123 (0.81%) 1		
Skin and subcutaneous tissue disorders			
Pruritus subjects affected / exposed occurrences (all)	1 / 123 (0.81%) 1		
Urticaria subjects affected / exposed occurrences (all)	1 / 123 (0.81%) 1		
Renal and urinary disorders			

Dysuria			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Renal cyst			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 123 (1.63%)		
occurrences (all)	2		
Back pain			
subjects affected / exposed	2 / 123 (1.63%)		
occurrences (all)	2		
Myalgia			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Infections and infestations			
Eye infection			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Gastroenteritis			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	1 / 123 (0.81%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	4 / 123 (3.25%)		
occurrences (all)	4		

Periodontitis subjects affected / exposed occurrences (all)	1 / 123 (0.81%) 1		
Rhinitis subjects affected / exposed occurrences (all)	3 / 123 (2.44%) 3		

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