Clinical trial results:
Efficacy and Safety Assessment of T4030 Eye Drops versus Ganfort® UD
in Ocular Hypertensive or Glaucomatous Patients.

Summary

EudraCT number	2020-003979-18
Trial protocol	FR PL HU BG BE ES IT
Global end of trial date	13 April 2023

Results information

Result version number	v1 (current)
This version publication date	10 November 2023
First version publication date	10 November 2023

Trial information

Trial identification

Sponsor protocol code	LT4030-301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04898387
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Laboratoires Thea
Sponsor organisation address	12 rue Louis Blériot, Clermont-Ferrand, France, 63017
Public contact	Research and Development Department, Laboratoires THEA, Sandrine.Guyon@theapharma.com
Scientific contact	Research and Development Department, Laboratoires THEA, Sandrine.Guyon@theapharma.com

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	11 July 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 April 2023
Global end of trial reached?	Yes
Global end of trial date	13 April 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the non-inferiority of T4030 (unpreserved fixed combination of bimatoprost 0.01% and timolol 0.1%) with Ganfort UD (unpreserved fixed combination of bimatoprost 0.03% and timolol 0.5% eye drops) in terms of efficacy.

Protection of trial subjects:

Protection of trial subjects:
Different assessments were done during subject visits in order to ensure subject safety:
• Assessment of the conjunctival hyperaemia on McMonnies photographic scale in each eye.
• Corneal fluorescein staining according to Oxford grading scheme in each eye.
• Far Best Corrected Visual Acuity in each eye.
• Ocular tolerance assessed by the investigator and by the patient.
• Ocular and systemic AE reporting.

All AEs experienced by a patient, irrespective of the suspected causality, was monitored until the event has resolved or stabilised at a level acceptable to the investigator and Medical expert, until there is a satisfactory explanation for the changes observed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 March 2021
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	Poland: 86
Country: Number of subjects enrolled	Spain: 18
Country: Number of subjects enrolled	United Kingdom: 11
Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	Bulgaria: 149
Country: Number of subjects enrolled	Czechia: 7
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Hungary: 9
Country: Number of subjects enrolled	Italy: 51
Country: Number of subjects enrolled	India: 85
Country: Number of subjects enrolled	Ukraine: 15
Country: Number of subjects enrolled	Russian Federation: 58
Country: Number of subjects enrolled	Tunisia: 58

Worldwide total number of subjects	554
EEA total number of subjects	327

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)	282
From 65 to 84 years	264
85 years and over	8

Subject disposition

Recruitment

Recruitment details:

554 patients (from 645 screened patients) were randomised in the study: 554 patients in the intent-to-treat (ITT) set, 553 in the Safety set, 550 in the modified-ITT (mITT) set and 508 in the per-protocol (PP) set. The recuitment started on 26-MAR-2021 and was completed on 9-Nov -2022 and the last pateint completed tcompleted on 13-Apr-2023

Pre-assignment

Screening details:

Patient with both eyes with diagnosed OHT or open-angle glaucoma currently treated with a first-line monotherapy and insufficiently controlled in the opinion of the investigator, and requiring a dual therapy (bitherapy). Incl/Excl criteria checked at screening visit, then patients discontinued their current treatment to start wash-out period.

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	Investigator[1]

Blinding implementation details:

The 2 different treatment kits (T4030 and Ganfort) were identical in external packaging. The identity of the IMP given to each patient was not known by the masked investigator or masked authorised collaborator in charge of the ophthalmic examination and questionnaires, or individuals from the Sponsor in charge of medical evaluation of the data. The masked investigator delegated the recording of used and unused IMPs, to the hospital pharmacy or to a trained collaborator

Arms

Are arms mutually exclusive?	Yes
Arm title	T4030

Arm description:

T4030 : PF fixed combination bimatoprost 0.01% and timolol 0.1% eye drops presented in UD
The patient administered the assigned treatment T4030 once daily at 20:00 (±1 h) in the conjunctival cul-de-sac of each eye for the 3-month treatment period from the randomisation visit (Day 1; Visit #2) to the final visit (Week 12; Day 85±7 days; Visit #4).

Arm type	Experimental
Investigational medicinal product name	T4030
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye gel in single-dose container
Routes of administration	Ocular use

Dosage and administration details:

The patient administered the assigned treatment (T4030) once daily at 20:00 (±1 h) in the conjunctival cul-de-sac of each eye for 12 weeks.

Arm title	Ganfort

Arm description:

Ganfort : PF fixed combination bimatoprost 0.03% and timolol 0.5% eye drops presented in UD
The patient administered the assigned treatment Ganfort once daily at 20:00 (±1 h) in the conjunctival cul-de-sac of each eye for the 3-month treatment period from the randomisation visit (Day 1; Visit #2) to the final visit (Week 12; Day 85±7 days; Visit #4).

Arm type	Active comparator

Investigational medicinal product name	Ganfort
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye gel in single-dose container
Routes of administration	Ocular use

Dosage and administration details:

The patient administered the assigned treatment (Ganfort) once daily at 20:00 (±1 h) in the conjunctival cul-de-sac of each eye for 12 weeks.

Notes:

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

Justification: The identity of the IMP given to each patient was not known by the masked investigator or masked authorised collaborator in charge of the ophthalmic examination and questionnaires, or individuals from the Sponsor in charge of medical evaluation of the data. The masked investigator delegated the recording of used and unused IMPs, to the hospital pharmacy or to a trained collaborator

Number of subjects in period 1	T4030	Ganfort
Started	280	274
Completed	273	262
Not completed	7	12
Consent withdrawn by subject	3	2
Adverse event, non-fatal	1	8
Unknown	2	1
Lost to follow-up	1	-
Covid 19	-	1

Baseline characteristics

Reporting groups	
Reporting group title	T4030

Reporting group description:

T4030 : PF fixed combination bimatoprost 0.01% and timolol 0.1% eye drops presented in UD
The patient administered the assigned treatment T4030 once daily at 20:00 (±1 h) in the conjunctival cul-de-sac of each eye for the 3-month treatment period from the randomisation visit (Day 1; Visit #2) to the final visit (Week 12; Day 85±7 days; Visit #4).

Reporting group title	Ganfort

Reporting group description:

Ganfort : PF fixed combination bimatoprost 0.03% and timolol 0.5% eye drops presented in UD
The patient administered the assigned treatment Ganfort once daily at 20:00 (±1 h) in the conjunctival cul-de-sac of each eye for the 3-month treatment period from the randomisation visit (Day 1; Visit #2) to the final visit (Week 12; Day 85±7 days; Visit #4).

Reporting group values	T4030	Ganfort	Total
Number of subjects	280	274	554
Age categorical Units: Subjects			
Adults (18-64 years)	140	142	282
From 65-84 years	136	128	264
85 years and over	4	4	8
Gender categorical Units: Subjects			
Female	148	168	316
Male	132	106	238

Subject analysis sets	
Subject analysis set title	mITT T4030
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

T4030 arm : All randomised patients having received at least one dose of IMP T4030 with at least one baseline and one post-randomisation efficacy assessment on treatment and considered as-randomised. m-ITT set will be the primary population for efficacy analysis

Subject analysis set title	mITT Ganfort
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Ganfort arm : All randomised patients having received at least one dose of IMP Ganfort with at least one baseline and one post-randomisation efficacy assessment on treatment and considered as-randomised. m-ITT set will be the primary population for efficacy analysis

Reporting group values	mITT T4030	mITT Ganfort	
Number of subjects	276	274	
Age categorical Units: Subjects			
Adults (18-64 years)	138	142	
From 65-84 years	134	128	
85 years and over	4	4	

Gender categorical Units: Subjects			
Female	147	168	
Male	129	106	

End points

End points reporting groups

Reporting group title	T4030

Reporting group description:

T4030 : PF fixed combination bimatoprost 0.01% and timolol 0.1% eye drops presented in UD
The patient administered the assigned treatment T4030 once daily at 20:00 (±1 h) in the conjunctival cul-de-sac of each eye for the 3-month treatment period from the randomisation visit (Day 1; Visit #2) to the final visit (Week 12; Day 85±7 days; Visit #4).

Reporting group title	Ganfort

Reporting group description:

Ganfort : PF fixed combination bimatoprost 0.03% and timolol 0.5% eye drops presented in UD
The patient administered the assigned treatment Ganfort once daily at 20:00 (±1 h) in the conjunctival cul-de-sac of each eye for the 3-month treatment period from the randomisation visit (Day 1; Visit #2) to the final visit (Week 12; Day 85±7 days; Visit #4).

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Subject analysis set title	mITT Ganfort
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Ganfort arm : All randomised patients having received at least one dose of IMP Ganfort with at least one baseline and one post-randomisation efficacy assessment on treatment and considered as-randomised. m-ITT set will be the primary population for efficacy analysis

Primary: Change from baseline in IOP

End point title	Change from baseline in IOP

End point description:

The primary efficacy endpoint is the change from Baseline (Day 1) to Week 12 in IOP at 08:00 in the study eye.
The study eye is defined as the eligible eye with the highest IOP at baseline at 08:00. In case of no IOP difference between both eyes, the right eye will be considered as the study eye.

End point type	Primary

End point timeframe:

The primary efficacy endpoint is the change from Baseline (Day 1) to Week 12 in IOP at 08:00 in the study eye.

End point values	mITT T4030	mITT Ganfort		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	276	274		
Units: mmHg				
least squares mean (standard error)	-11.01 (± 0.17)	-10.97 (± 0.17)		

Statistical analyses

Statistical analysis title	Change from Baseline in IOP at 08:00 at week 12

Statistical analysis description:

To assess the efficacy of T4030, on the change from Baseline in IOP at 08:00, a Mixed Model for Repeated Measures (MMRM) approach was used.
The model will include as fixed factors, treatment, scheduled visit time point (Week 6 and Week 12), baseline IOP as covariates, treatment by visit interaction, baseline IOP by visit interaction, and patient as random factor. The Restricted Maximum Likelihood (REML) estimation approach will be used, and the default covariance structure will be unstructured.

Comparison groups	mITT T4030 v mITT Ganfort
Number of subjects included in analysis	550
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Adjusted Mean Difference
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.51
upper limit	0.43
Variability estimate	Standard error of the mean
Dispersion value	0.24

Notes:

[1] - The non-inferiority testing will be performed based on a two-sided 95% CI on the mean difference in change from baseline in IOP after 12 weeks of treatment.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event reporting from start of the treatement (Day 1) until follow-up Phone call (4 weeks±7 days after the last Investigational Medicinal Product (IMP) instillation)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Safety Set T4030
Reporting group description: -	
Reporting group title	Safety Set Ganfort

Reporting group description: -

Serious adverse events	Safety Set T4030	Safety Set Ganfort	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 278 (0.36%)	2 / 275 (0.73%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Rectal Cancer			
subjects affected / exposed	1 / 278 (0.36%)	0 / 275 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19 Pneumonia			
subjects affected / exposed	0 / 278 (0.00%)	1 / 275 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complicated appendicitis			
subjects affected / exposed	0 / 278 (0.00%)	1 / 275 (0.36%)	
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	Safety Set T4030	Safety Set Ganfort	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 278 (12.95%)	56 / 275 (20.36%)	
General disorders and administration site conditions			
Instillation site irritation			
subjects affected / exposed	9 / 278 (3.24%)	19 / 275 (6.91%)	
occurrences (all)	9	26	
Eye disorders			
Conjunctival hyperaemia			
subjects affected / exposed	27 / 278 (9.71%)	37 / 275 (13.45%)	
occurrences (all)	30	37	

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