Clinical trial results:
A Phase 2a, Double-Blind, Randomized, Placebo-Controlled, Repeated Administration, Crossover Study to Establish Safety, Tolerability, and Efficacy of PresbiDrops in Presbyopic Subjects

Summary

EudraCT number	2016-001091-30
Trial protocol	SI
Global end of trial date	26 June 2017

Results information

Result version number	v1 (current)
This version publication date	24 August 2019
First version publication date	24 August 2019

Trial information

Trial identification

Sponsor protocol code	FG-PRE-101

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Orasis
Sponsor organisation address	Maskit, Herzliya, Israel, 4673312
Public contact	Elad Kedar, CEO, ORASIS Pharmaceuticals Ltd, 972 98877745, elad.kedar@orasis-pharma.com
Scientific contact	Elad Kedar, CEO, ORASIS Pharmaceuticals Ltd, 972 98877745, elad.kedar@orasis-pharma.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	25 July 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 July 2016
Global end of trial reached?	Yes
Global end of trial date	26 June 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary
To establish safety and tolerability of repeated administration of PresbiDrops in presbyopic subjects

Protection of trial subjects:

1. 24/7 availability of principal investigators
2. Medical experts available on behalf of the company and from insurance coverage

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2016
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	Slovenia: 13
Country: Number of subjects enrolled	Israel: 24
Worldwide total number of subjects	37
EEA total number of subjects	13

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)	37
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening assessments was conducted within a 21-day period prior to the start of therapy, including demographics, medical history, concomitant medication recording, urine pregnancy test (for females of childbearing potential), and ophthalmic examinations.

Pre-assignment period milestones

Number of subjects started	37
Number of subjects completed	37

Period 1

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

Blinding implementation details:

Treatment order (investigational product or placebo) was dependent on randomization sequence assignment.
Eligible subjects were randomly assigned in a 1:1 ratio to one of two treatment sequences of multiple administrations of drug and placebo. A master randomization list was generated by MediStat, Ltd., indexed by randomization number.

Arms

Are arms mutually exclusive?	Yes
Arm title	treatment 1

Arm description:

PresbiDrops followed by placebo

Arm type	Experimental
Investigational medicinal product name	Presbidrops
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops, solution
Routes of administration	Ophthalmic use

Dosage and administration details:

self-administered by the subject over two weeks (one drop in each eye every morning)

Investigational medicinal product name	Placebo for presbidrops
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ear/eye drops, solution
Routes of administration	Ophthalmic use

Dosage and administration details:

one drop per eye

Arm title	treatment 2

Arm description:

placebo followed by PresbiDrops

Arm type	Experimental
Investigational medicinal product name	Placebo for presbidrops
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ear/eye drops, solution
Routes of administration	Ophthalmic use

Dosage and administration details:
one drop per eye

Investigational medicinal product name	Presbidrops
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops, solution
Routes of administration	Ophthalmic use

Dosage and administration details:
self-administered by the subject over two weeks (one drop in each eye every morning)

Number of subjects in period 1	treatment 1	treatment 2
Started	18	19
Completed	15	19
Not completed	3	0
Lost to follow-up	3	-

Period 2

Period 2 title	Follow up period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	treatment 1

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Presbidrops
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops, solution
Routes of administration	Ophthalmic use

Dosage and administration details:
self-administered by the subject over two weeks (one drop in each eye every morning)

Arm title	placebo

Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Presbidrops
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Eye drops, solution
Routes of administration	Ophthalmic use

Dosage and administration details:

self-administered by the subject over two weeks (one drop in each eye every morning)

Number of subjects in period 2	treatment 1	placebo
Started	15	19
Completed	15	19

Baseline characteristics

Reporting groups	
Reporting group title	Treatment Phase

Reporting group description: -

Reporting group values	Treatment Phase	Total	
Number of subjects	37	37	
Age categorical			
Men and women between 40 and 65 years of age (inclusive)			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	37	37	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Mean - 51.3, SD - 4.6			
Units: years			
arithmetic mean	51.3		
standard deviation	± 4.6	-	
Gender categorical			
Units: Subjects			
Female	22	22	
Male	15	15	

End points

End points reporting groups

Reporting group title	treatment 1
Reporting group description: PresbiDrops followed by placebo	
Reporting group title	treatment 2
Reporting group description: placebo followed by PresbiDrops	
Reporting group title	treatment 1
Reporting group description: -	
Reporting group title	placebo
Reporting group description: -	

Primary: 2 line improvement - treatment vs. placebo

End point title	2 line improvement - treatment vs. placebo
End point description:	
End point type	Primary
End point timeframe: Study duration	

End point values	treatment 1	treatment 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	19		
Units: percent				
number (not applicable)	15	19		

Statistical analyses

Statistical analysis title	Rate of responders by treatment
Comparison groups	treatment 1 v treatment 2
Number of subjects included in analysis	34
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: AEs were collected throughout the study starting from Baseline through the Follow-up visit- 45 days	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0
Reporting groups	
Reporting group title	Presbidrops
Reporting group description: Each participant received presbidrops during the study	
Reporting group title	Placebo for presbidrops
Reporting group description: Every subject received placebo for presbidrops	

Serious adverse events	Presbidrops	Placebo for presbidrops	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 37 (0.00%)	0 / 37 (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	Presbidrops	Placebo for presbidrops	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 37 (75.68%)	23 / 37 (62.16%)	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 37 (8.11%)	0 / 37 (0.00%)	
occurrences (all)	3	0	
General disorders and administration site conditions			
Administration site discomfort			
subjects affected / exposed	5 / 37 (13.51%)	5 / 37 (13.51%)	
occurrences (all)	5	5	
Eye disorders			

Conjunctival hyperaemia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Administration site dryness			
subjects affected / exposed	3 / 37 (8.11%)	0 / 37 (0.00%)	
occurrences (all)	4	0	
Burning sensation			
subjects affected / exposed	16 / 37 (43.24%)	4 / 37 (10.81%)	
occurrences (all)	37	4	
Administration site pain			
subjects affected / exposed	7 / 37 (18.92%)	2 / 37 (5.41%)	
occurrences (all)	13	2	
Vision blurred			
subjects affected / exposed	22 / 37 (59.46%)	20 / 37 (54.05%)	
occurrences (all)	51	40	

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