Clinical trial results:
Phase III study, double blind, placebo controlled, to evaluate the efficacy and the safety of an omega-3 based drug, in patients with primary tinnitus.

Summary

EudraCT number	2015-003514-24
Trial protocol	IT
Global end of trial date	17 October 2018

Results information

Result version number	v1 (current)
This version publication date	27 April 2022
First version publication date	27 April 2022

Trial information

Trial identification

Sponsor protocol code	OLEV01/2015

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	IBSA Farmaceutici Italia srl
Sponsor organisation address	Via Martiri di Cefalonia, 2, Lodi, Italy, 26900
Public contact	CRO, Informa PRO S.r.l., +39 065758926, segreteria@informa.pro
Scientific contact	CRO, Informa PRO S.r.l., +39 065758926, segreteria@informa.pro

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	15 November 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 October 2018
Global end of trial reached?	Yes
Global end of trial date	17 October 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluation of the efficacy and safety of Olevia (omega-3 polyunsatured acid based drug) in both genders patients affected by primary tinnitus.

Protection of trial subjects:

Patients were monitored for any possible adverse events ocurred between each visits.

Background therapy: -

Evidence for comparator:

NA

Actual start date of recruitment	05 September 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	Italy: 99
Worldwide total number of subjects	99
EEA total number of subjects	99

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)	80
From 65 to 84 years	19
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First Patient First Visit: 05-09-2016; Last Patient First Visit: 27-03-2018; Last Patient Last Visit: 17-10-2018
The trial was conducted on 5 Sites: Site 01 - Salerno; Site 02 - Bologna; Site 03- Catanzaro; Site 04- Pisa; Site 05- Torino.

Pre-assignment

Screening details:

14 subjects did not meet the Inclusion/Exclusion Criteria.

Pre-assignment period milestones

Number of subjects started	99
Number of subjects completed	99

Period 1

Period 1 title	Baseline (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A PP

Arm description:

Subjects treated with Olevia

Arm type	Experimental
Investigational medicinal product name	Olevia 1000 mg
Investigational medicinal product code	042639029
Other name	OMEGAIBSA2
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

2000 mg/die for the first 2 months (2 capsule); 1000 mg/die for the third month (1 capsule).

Arm title	Arm B PP

Arm description:

Subjects treated with placebo

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

2000 mg/die for the first 2 months (2 capsule); 1000 mg/die for the third month (1 capsule).

Number of subjects in period 1	Arm A PP	Arm B PP
Started	49	50
Completed	39	41
Not completed	10	9
Lost to Follow up	3	3
Physician decision	1	3
Consent withdrawn by subject	1	1
Adverse event, non-fatal	5	-
Lack of compliance	-	1
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Arm A PP
Reporting group description:	
Subjects treated with Olevia	
Reporting group title	Arm B PP
Reporting group description:	
Subjects treated with placebo	

Reporting group values	Arm A PP	Arm B PP	Total
Number of subjects	49	50	99
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)	41	42	83
From 65-84 years	8	8	16
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	20	17	37
Male	29	33	62

Subject analysis sets	
Subject analysis set title	Arm A ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects with at least one efficay parameter assessment.	
Subject analysis set title	Arm B ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects with at least one efficacy parameter assessment.	
Subject analysis set title	Arm A PP
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects completed the study according to Protocol	
Subject analysis set title	Arm B PP
Subject analysis set type	Per protocol
Subject analysis set description:	
Subjects completed the study according to Protocol	

Reporting group values	Arm A ITT	Arm B ITT	Arm A PP
Number of subjects	45	45	39
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)	37	37	31
From 65-84 years	8	8	8
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	18	14	16
Male	27	31	23

Reporting group values	Arm B PP		
Number of subjects	41		
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)	34		
From 65-84 years	7		
85 years and over	0		
Gender categorical Units: Subjects			
Female	12		
Male	29		

End points

End points reporting groups

Reporting group title	Arm A PP
Reporting group description: Subjects treated with Olevia	
Reporting group title	Arm B PP
Reporting group description: Subjects treated with placebo	
Subject analysis set title	Arm A ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects with at least one efficay parameter assessment.	
Subject analysis set title	Arm B ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description: Subjects with at least one efficacy parameter assessment.	
Subject analysis set title	Arm A PP
Subject analysis set type	Per protocol
Subject analysis set description: Subjects completed the study according to Protocol	
Subject analysis set title	Arm B PP
Subject analysis set type	Per protocol
Subject analysis set description: Subjects completed the study according to Protocol	

Primary: Evaluation of the level of reduction of the primary tinnitus, through THI scale, in both groups.

End point title	Evaluation of the level of reduction of the primary tinnitus, through THI scale, in both groups.
End point description:	
End point type	Primary
End point timeframe: 2 months and 3 months after baseline visit.	

End point values	Arm A PP	Arm B PP	Arm A ITT	Arm B ITT
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	39	41	45	45
Units: THI	24	22	27	24

Statistical analyses

Statistical analysis title	Evaluation of reduction in scale THI (PP)

Statistical analysis description:

Subjects reduction in scale THI (PP)

Comparison groups	Arm B PP v Arm A PP
Number of subjects included in analysis	80
Analysis specification	Post-hoc
Analysis type	non-inferiority[1]
P-value	= 0.506 [2]
Method	Fisher exact

Notes:

[1] - Two tailed test, alpha error = 0.05

[2] - p=0.506 at 3 months.
Both tests are not statisticaly significant

Statistical analysis title	Evaluation of reduction in scale THI (ITT)

Statistical analysis description:

Subjects reduction in scale THI (ITT)

Comparison groups	Arm A ITT v Arm B ITT
Number of subjects included in analysis	90
Analysis specification	Post-hoc
Analysis type	non-inferiority[3]
P-value	= 0.671 [4]
Method	Fisher exact

Notes:

[3] - Two tailed test, alpha error = 0.05

[4] - p=0.657 at 3 months.
Both tests are not statisticaly signinficant

Secondary: Evaluation of level of compliance to treatment through, in both groups.

End point title	Evaluation of level of compliance to treatment through, in both groups.

End point description:

End point type	Secondary

End point timeframe:

2 months and 3 months after baseline visit

End point values	Arm A PP	Arm B PP	Arm A ITT	Arm B ITT
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	39	41	45	45
Units: questionnary	39	40	43	44

Statistical analyses

Statistical analysis title	evaluation of compliance between groups pp

Statistical analysis description:

evaluation of subject completing compliance

Comparison groups	Arm B PP v Arm A PP
Number of subjects included in analysis	80
Analysis specification	Post-hoc
Analysis type	non-inferiority[5]
P-value	= 1 [6]
Method	Fisher exact

Notes:

[5] - Two tailed test, alpha error = 0.05

[6] - p value =1 at three months
both test are not staistical significant

Statistical analysis title	evaluation of compliance between groups ITT
Comparison groups	Arm A ITT v Arm B ITT
Number of subjects included in analysis	90
Analysis specification	Post-hoc
Analysis type	non-inferiority[7]
P-value	= 1 [8]
Method	Fisher exact

Notes:

[7] - Two tailed test, alpha error = 0.05

[8] - p value =1 at three months
both test are not statistical significant

Secondary: Evaluation of the grade of reduction of hyperacusis.

End point title	Evaluation of the grade of reduction of hyperacusis.

End point description:

End point type	Secondary

End point timeframe:

2 months and 3 months after baseline visit

End point values	Arm A PP	Arm B PP	Arm A ITT	Arm B ITT
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	39	41	45	45
Units: questionnaire	14	19	18	20

Statistical analyses

Statistical analysis title	Reduction in Khalfa questionnaire (PP)

Statistical analysis description:

Number of subjects reduction in Khalfa questionnaire (PP)

Comparison groups	Arm A PP v Arm B PP

Number of subjects included in analysis	80
Analysis specification	Post-hoc
Analysis type	non-inferiority[9]
P-value	= 0.372 [10]
Method	Fisher exact

Notes:

[9] - Two tailed test, alpha error=0.05

[10] - P=0.187 at 3 months.
Both tests are not statisticaly significant

Statistical analysis title	Reduction in Khalfa questionnaire (ITT)

Statistical analysis description:

Number of subjects reduction in Khalfa questionnaire (ITT)

Comparison groups	Arm A ITT v Arm B ITT
Number of subjects included in analysis	90
Analysis specification	Post-hoc
Analysis type	non-inferiority[11]
P-value	= 0.831 [12]
Method	Fisher exact

Notes:

[11] - Two tailed test, alpha error=0.05

[12] - p=0.191 at 3 months.
Both tests are not statisticaly significant

Adverse events

Adverse events information	
Timeframe for reporting adverse events: During all the study, from signature ICF to end of study.	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	24
Reporting groups	
Reporting group title	Olevia
Reporting group description: Subjects treated by Olevia.	
Reporting group title	Placebo
Reporting group description: Subjects treated by Placebo	

Serious adverse events	Olevia	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 49 (0.00%)	0 / 51 (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	Olevia	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 49 (20.41%)	3 / 51 (5.88%)	
Investigations			
Hypertransaminasaemia	Additional description: MedDRA Cod. 10054889		
subjects affected / exposed	1 / 49 (2.04%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Hypercholesterolaemia	Additional description: MedDRA Cod. 10020603		
subjects affected / exposed	1 / 49 (2.04%)	1 / 51 (1.96%)	
occurrences (all)	1	1	
Injury, poisoning and procedural complications			

Subcutaneous haematoma	Additional description: MedDRA Cod. 10022117.		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 49 (2.04%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Hypotension	Additional description: MedDRA Cod. 10021106		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 49 (2.04%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Paraesthesia	Additional description: MedDRA Cod. 10033987		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 49 (2.04%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Tinnitus	Additional description: MedDRA Cod. 10048029		
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 49 (4.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal pain upper	Additional description: MedDRA Cod. 10064906		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 49 (2.04%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Constipation	Additional description: MedDRA Cod. 10010774		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 49 (2.04%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Erythema	Additional description: MedDRA Cod. 10015150		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 49 (2.04%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			

Headache	Additional description: MedDRA Cod. 10028411		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 49 (2.04%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Hypertriglyceridaemia	Additional description: MedDRA Cod. 10020870		
subjects affected / exposed	0 / 49 (0.00%)	2 / 51 (3.92%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 February 2016	1) Background rational extension. 2) Added Follow Up Visit (Visit V4) 6 months after Baseline Visit. 3) At Drop Out section was added "Not compliance to treatment".

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported