



## 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
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#### 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:

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**Results analysis stage**

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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:

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**General information about the trial**

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Main objective of the trial:

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

Protection of trial subjects:

Patients were monitored for any possible adverse events occurred 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:

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**Population of trial subjects**

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**Subjects enrolled per country**

Country: Number of subjects enrolled	Italy: 99
Worldwide total number of subjects	99
EEA total number of subjects	99

Notes:

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**Subjects enrolled per age group**

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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
<b>Arm title</b>	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).

<b>Arm title</b>	Arm B PP
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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).

<b>Number of subjects in period 1</b>	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 efficacy 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	

<b>Reporting group values</b>	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

<b>Reporting group values</b>	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 efficacy 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

<b>Statistical analysis title</b>	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 <sup>[1]</sup>
P-value	= 0.506 <sup>[2]</sup>
Method	Fisher exact

Notes:

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

[2] - p=0.506 at 3 months.

Both tests are not statistically significant

<b>Statistical analysis title</b>	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 <sup>[3]</sup>
P-value	= 0.671 <sup>[4]</sup>
Method	Fisher exact

Notes:

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

[4] - p=0.657 at 3 months.

Both tests are not statistically significant

### 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.
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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	39	40	43	44

### Statistical analyses

<b>Statistical analysis title</b>	evaluation of compliance between groups pp
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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 <sup>[5]</sup>
P-value	= 1 <sup>[6]</sup>
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

<b>Statistical analysis title</b>	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 <sup>[7]</sup>
P-value	= 1 <sup>[8]</sup>
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.
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End point description:

End point type	Secondary
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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

<b>Statistical analysis title</b>	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 <sup>[9]</sup>
P-value	= 0.372 <sup>[10]</sup>
Method	Fisher exact

Notes:

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

[10] - P=0.187 at 3 months.

Both tests are not statistically significant

<b>Statistical analysis title</b>	Reduction in Khalfa questionnaire (ITT)
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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 <sup>[11]</sup>
P-value	= 0.831 <sup>[12]</sup>
Method	Fisher exact

Notes:

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

[12] - p=0.191 at 3 months.

Both tests are not statistically 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
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	24
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### Reporting groups

Reporting group title	Olevia
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Reporting group description:

Subjects treated by Olevia.

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

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

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported