



Clinical trial results:

A 6-MONTH, MULTICENTER, PHASE 3, OPEN-LABEL EXTENSION SAFETY STUDY OF OTO-104 GIVEN AT 3-MONTH INTERVALS BY INTRATYMPANIC INJECTION IN SUBJECTS WITH UNILATERAL MENIERE'S DISEASE

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2016-000766-29 |
| Trial protocol | GB BE DE IT |
| Global end of trial date | 05 September 2017 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 13 December 2021 |
| First version publication date | 13 December 2021 |

Trial information

Trial identification

| | |
|-----------------------|------------|
| Sponsor protocol code | 104-201610 |
|-----------------------|------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02768662 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Otonomy, Inc. |
| Sponsor organisation address | 4796 Executive Drive, San Diego, United States, 92121 |
| Public contact | Medical Information, Otonomy Inc., medinfo@otonomy.com |
| Scientific contact | Medical Information, Otonomy Inc., medinfo@otonomy.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 | 08 June 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 05 September 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 05 September 2017 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The objective is to assess the safety of repeat intratympanic injections of 12 mg OTO-104 at 3-month intervals in an open-label study in subjects with unilateral Meniere's disease.

Protection of trial subjects:

Not Applicable

Background therapy:

Subjects were permitted to continue medications for relief of symptoms related to Meniere's disease during the course of the study. Intermittent use of vestibular suppressants and anti-emetics was allowed as symptomatic relief medications. Subjects were allowed to take betahistine as well.

Evidence for comparator:

Not Applicable - no comparator

| | |
|---|--------------|
| Actual start date of recruitment | 20 July 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 | United Kingdom: 83 |
| Country: Number of subjects enrolled | Poland: 23 |
| Country: Number of subjects enrolled | Belgium: 6 |
| Country: Number of subjects enrolled | France: 4 |
| Country: Number of subjects enrolled | Germany: 17 |
| Country: Number of subjects enrolled | Italy: 9 |
| Worldwide total number of subjects | 142 |
| EEA total number of subjects | 59 |

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) | 123 |
| From 65 to 84 years | 19 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

This was a 6-month, multicenter, Phase 3, open-label extension safety study in subjects with unilateral Meniere's disease that had previously completed the Phase 2 (104-201403) or Phase 3 (104-201508) studies.

Pre-assignment

Screening details:

Subjects that completed one of the prior studies were asked if they wanted to participate in this study and if so, they signed an informed consent.

Period 1

| | |
|------------------------------|----------------------------|
| Period 1 title | Treatment (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Blinding implementation details:

This was an open-label study and therefore, no blinding was required.

Arms

| | |
|-----------|---------|
| Arm title | OTO-104 |
|-----------|---------|

Arm description:

dexamethasone suspension in a solution of poloxamer 407

| | |
|--|--------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | OTO-104 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intratympanic use |

Dosage and administration details:

The tympanic membrane was anesthetized by covering the external surface of the inferior-posterior quadrant with topical lidocaine or lidocaine/prilocaine cream. 200 microliters of a 6% w/v suspension of dexamethasone (12 mg) was administered via intratympanic injection by inserting the needle into the inferior-posterior quadrant of the tympanic membrane at the level of the round window.

| Number of subjects in period 1 | OTO-104 |
|------------------------------------|---------|
| Started | 142 |
| Completed | 90 |
| Not completed | 52 |
| Consent withdrawn by subject | 4 |
| Subject received saccotomy | 1 |
| Adverse event, non-fatal | 1 |
| Missing reason for discontinuation | 1 |
| Study terminated by sponsor | 43 |
| Lost to follow-up | 2 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | Treatment |
|-----------------------|-----------|

Reporting group description:

All subjects that received at least one intratympanic injection of OTO-104.

| Reporting group values | Treatment | Total | |
|------------------------|-----------|-------|--|
| Number of subjects | 142 | 142 | |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 123 | 123 | |
| From 65-84 years | 19 | 19 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 77 | 77 | |
| Male | 65 | 65 | |

Subject analysis sets

| | |
|----------------------------|--------|
| Subject analysis set title | Safety |
|----------------------------|--------|

| | |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

The safety analysis set included all subjects who received at least one dose of study drug.

| Reporting group values | Safety | | |
|------------------------|--------|--|--|
| Number of subjects | 142 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 123 | | |
| From 65-84 years | 19 | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 77 | | |
| Male | 65 | | |

End points

End points reporting groups

| | |
|--|-----------------|
| Reporting group title | OTO-104 |
| Reporting group description: dexamethasone suspension in a solution of poloxamer 407 | |
| Subject analysis set title | Safety |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: The safety analysis set included all subjects who received at least one dose of study drug. | |

Primary: Tympanic Membrane Perforation

| | |
|---|--|
| End point title | Tympanic Membrane Perforation ^[1] |
| End point description: Perforations were rated as "Present" or "Not Present"; if a subject did not receive an otoscopy, then the perforation is listed as "Missing". | |
| End point type | Primary |
| End point timeframe: Up to 6 months; otoscopy examinations were performed at 3 and 6 months in the ear that received the injection(s). | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The primary endpoint for this study was safety in nature and as such, no additional statistics were performed other than summary statistics.

| End point values | OTO-104 | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 142 | | | |
| Units: ears | | | | |
| Present | 0 | | | |
| Not Present | 92 | | | |
| Missing | 50 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Day 1 to end of study, which could have been up to Month 6.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

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|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 18.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | OTO-104 |
|-----------------------|---------|

Reporting group description:

dexamethasone suspension in a solution of poloxamer 407

| Serious adverse events | OTO-104 | | |
|---|---|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 142 (2.82%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Invasive ductal breast carcinoma | Additional description: Subject was diagnosed with invasive ductal breast carcinoma on Day 85. The event was considered not related to study drug was ongoing at the date of last contact. | | |
| subjects affected / exposed | 1 / 142 (0.70%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pancreatic carcinoma | Additional description: Subject as diagnosed with pancreatic carcinoma on Day 54. Treatment included surgery, which was planned, not yet performed at the date of last contact. The event was considered not related to study drug. | | |
| subjects affected / exposed | 1 / 142 (0.70%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | Additional description: Subject had anemia on Day 1. The subject was hospitalized and received blood transfusions from Day 22 to Day 27, when the event was considered resolved and the subject was discharged. | | |
| subjects affected / exposed | 1 / 142 (0.70%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain upper | Additional description: Subject had 3 Serious adverse events: abdominal pain upper, constipation, and helicobacter infection on Day 34. Treatment included lansoprazole, clarithromycin, metronidazole, and Laxido sachets. The event | | |

| | | | |
|---|--|--|--|
| resolved 4 days later. | | | |
| subjects affected / exposed | 1 / 142 (0.70%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Constipation | Additional description: Subject had 3 Serious adverse events: abdominal pain upper, constipation, and helicobacter infection on Day 34. Treatment included lansoprazole, clarithromycin, metronidazole, and Laxido sachets. The event resolved 4 days later. | | |
| subjects affected / exposed | 1 / 142 (0.70%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Helicobacter infection | Additional description: Subject had 3 Serious adverse events: abdominal pain upper, constipation, and helicobacter infection on Day 34. Treatment included lansoprazole, clarithromycin, metronidazole, and Laxido sachets. The event resolved 4 days later. | | |
| subjects affected / exposed | 1 / 142 (0.70%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 2 %

| | | | |
|---|-------------------|--|--|
| Non-serious adverse events | OTO-104 | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 37 / 142 (26.06%) | | |
| Injury, poisoning and procedural complications | | | |
| Procedural dizziness | | | |
| subjects affected / exposed | 3 / 142 (2.11%) | | |
| occurrences (all) | 3 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 4 / 142 (2.82%) | | |
| occurrences (all) | 4 | | |
| Dizziness | | | |
| subjects affected / exposed | 3 / 142 (2.11%) | | |
| occurrences (all) | 3 | | |
| General disorders and administration site conditions | | | |
| Injection site discomfort | | | |
| subjects affected / exposed | 3 / 142 (2.11%) | | |
| occurrences (all) | 3 | | |

| | | | |
|--|---------------------------------|--|--|
| <p>Ear and labyrinth disorders</p> <p>Tinnitus</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>5 / 142 (3.52%)</p> <p>5</p> | | |
| <p>Vertigo</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>4 / 142 (2.82%)</p> <p>4</p> | | |
| <p>Meniere's disease</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>3 / 142 (2.11%)</p> <p>3</p> | | |
| <p>Gastrointestinal disorders</p> <p>Nausea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>3 / 142 (2.11%)</p> <p>3</p> | | |
| <p>Musculoskeletal and connective tissue disorders</p> <p>Arthralgia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>3 / 142 (2.11%)</p> <p>3</p> | | |
| <p>Infections and infestations</p> <p>Nasopharyngitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>3 / 142 (2.11%)</p> <p>3</p> | | |
| <p>Urinary tract infection</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>3 / 142 (2.11%)</p> <p>3</p> | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|--|
| 26 April 2016 | <ul style="list-style-type: none">- Added EudraCT number to title page- Removed telephone as a method to report SAEs.- Added safety fax number as a back-up contact method for reporting SAEs. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported