Statistical Analysis Plan

FINAL

Subject´s preference regarding hearing performance and functionality using a new sound processor

Single-center, prospective, open within-subject comparison with randomised device test order

CBAS5731

2019-05-06

Table of Contents

1 STUDY DETAILS

1.1 Study Objectives

The objectives of this clinical investigation is to investigate the subject´s overall preference, hearing performance and self-reported assessments with the Osia 2 Sound Processor (Investigational device) and the Osia Sound Processor (Comparator).

The safety objectives are to assess the frequency of Adverse Events, the usage of concomitant medication/treatment and the amount of Device deficiencies.

1.2 Study Design

This clinical investigation is an open, single-centre, prospective, within-subject comparison, with 2-3 visits over a period of 6 weeks. The data for the overall objectives will be collected at Visit 1 and at Visit 3. Subjects enrolled will all be previous participants in the CBAS5539 study conducted at the same clinic. No new implantations will be performed. A randomisation will be performed regarding the device test order at Visit 3 and each subject will be compared to his/her own questionnaire answers from Visit 1 and test results at Visit 3.

1.2.1 Flow chart

Procedures and timing	Visit 1	Visit 2/ Contact*	Visit 3
Day/Week/Month	Day 0	14 days	6 weeks
Time window		± 5 days	± 5 days
Demographics	X		
Medical history	X		
Eligibility criteria	X		
Audiogram	X		
Baseline characteristics	X		
Informed consent	X		
Sound Processor Fitting			
Magnet choice	X[1]	X[3]	
Digital link calibration (DLC)	X[1]	X[3]	
Feedback measurement	X[1]	X[3]	
BC Direct	X[1]	X[3]	
Fine tuning[1]	X[1]	X[3]	
Randomised device test order			X
Thresholds audiometry, free-field			X
Speech recognition in noise			X
Speech recognition in quiet			X
APHAB	X[2]		X[1]
SSQ	X[2]		X[1]
QUEST	X[2]		X[1]
Comfort and Specific usage: Comfort, magnet choice, battery life, SoftWear pad, Safety line	X[2]		X[1]
Wireless accessories			X[1]
Subject´s overall preference			X[4]
Adverse events	X	X	X
Device deficiency	X	X	X
Concomitant treatment	X	X	X
Extra visit			

*Visit 2 is optional as a Visit. Can be done by contact via phone call
[1] Investigational device
[2] With Comparator
[3] As required, Investigational device
[4] Investigational Device vs Comparator

1.3 Investigational device and comparator

The investigational device is the Osia 2 Sound Processor (Osia 2 SP) and will be compared to the Osia Sound Processor (Osia SP).

1.4 Sample Size

Only subjects who completed the CBAS5539 clinical investigation at the Melbourne site will be included in this clinical investigation. No sample size calculation is made. Up to 12 subjects will be included.

2 STUDY POPULATIONS

2.1 Definition of Study Populations

2.1.1 Full Analysis Set

Full analysis set consist of all subjects attending the 6 weeks visit. Safety population consists of all subjects attending Visit 1.

3 STUDY VARIABLES

3.1 Baseline Variables

3.1.1 Demographics and Baseline Characteristics

The following demographic data will be recorded at Visit 1:

- Age collected as date of birth (month and year)
- Gender
- Ethnicity

During Visit 1, a number of baseline characteristics will be recorded:

- Treatment ear (indicate left or right)
- Type of hearing loss: (Conductive, Mixed or SSD)
- Aetiology: (chronic) infection, tumour, trauma, malfunction, otosclerosis, other reason

3.1.2 Medical History

The following information will be recorded at Visit 1:

- Current concomitant medication and treatments and 6 months back.

3.1.3 Prior and Concomitant Medications

All medications and treatments given, will be reported by ATC coding.

3.1.4 Audiogram

Unaided audiometric threshold measures (including both air- and bone conduction thresholds) should demonstrate that the subject has a conductive hearing loss, mixed hearing loss or SSD and is a suitable subject for the Osia 2 SP as per the third inclusion criteria.

3.2 Measurements

Measurements to compare the subjects' overall preference regarding the Osia 2 SP and Osia SP

- Preferred choice made by selection between Osia 2 SP and Osia SP (OSIA SP/OSIA 2 SP/No preference)
    - What influenced his/her decision (following choices shall be ticked)
        - Hearing performance (Yes/No)
        - Sound quality (Yes/No)
        - Aesthetic (Yes/No)
        - Comfort and sound processor ease of use (Yes/No)
        - Possibility to use Wireless accessories (Yes/No)
        - Possibility of iPhone pairing (Yes/No)
        - Other (Yes/No)
- Self-reported assessments
    - Abbreviated Profile of Hearing Aid Benefit (APHAB) at visit 1 and visit 3 and comparison between visit 1 and 3
    - Speech, Spatial, and Qualities of Hearing Scale (SSQ) at visit 1 and visit 3 and comparison between visit 1 and 3. Each item, scale and the total should be reported.
    - Self-reported assessment regarding satisfaction and usability (QUEST version 2) at visit 1 and visit 3 and comparison between visit 1 and 3
        - Dimensions (1-5)
        - Weight (1-5)
        - Adjustments (1-5)
        - Safety (1-5)
        - Durability (1-5)
        - Easy to use (1-5)
        - Comfort (1-5)
        - Effectiveness (1-5)
        - Sum of Dimensions (1-5), Weight (1-5), Adjustments (1-5), Safety (1-5), Durability (1-5), Easy to use (1-5), Comfort (1-5) and Effectiveness (1-5)
        - Which three items are the most important?
- Audiometric thresholds in free field at visit 3 for Osia SP and Osia 2 SP and the difference between Osia SP and Osia 2 SP
    - Thresholds audiometry, free-field [PTA4, Mean of 0.5, 1, 2 and 4 kHz].
    - Thresholds audiometry, free-field [0.25, 0.5, 0.75, 1.0, 1.5, 2.0, 3.0, 4.0, 6.0 and 8.0 kHz].
- Speech recognition tests in quiet and noise at visit 3 for Osia SP and Osia 2 SP and the difference between Osia SP and Osia 2 SP

- Adaptive speech in noise [speech-to-noise ratio, 50% speech understanding]. Osia 2 SP vs Osia SP at 6 weeks
- Speech in quiet [% correctly perceived words at 50dB, 65dB and 80dB SPL]. Osia 2 SP vs Osia SP at 6 weeks.

Measurements to assess the subjects' experience regarding Comfort and specific usage

- Subjective experience regarding comfort and specific usage during the last 6 weeks at visit 1 and visit 3 and comparison between visit 1 and 3 where applicable
  - Comfort (VAS)
  - Magnet choice
    - Strength selected at visit 1 (1/2/3/4)
    - Did the subject change strength at visit 3 and if so from what to what strength? If the subject changed the magnet strength at visit 2 this will be presented as a change at visit 3.
  - On average, how many hours per day did you use the sound processor? (hours)
  - Battery life (free text, only listed)
  - SoftWear pad use (Yes/No)
    - Change of soft pad how often (free text, only listed)
  - Safety line use (Yes/No)
  - Wireless accessories (Yes/No) (only at visit 3)
    - Accessory: (Cochlear Wireless Phone-clip/iPhone/Cochlear Baha Remote Control 2/Cochlear Wireless Mini-microphone 2+)
    - Did the subject use this accessory during the 6 week period? (Yes/No)
    - In which situations was this accessory used? (free text, only listed)
    - On average, how many hours per day was this accessory
    - used? (free text, only listed)
    - Benefits in using this accessory? (free text, only listed)
    - Difficulties in using this accessory? (free text, only listed)

3.3 Safety Variables

3.3.1 Adverse Events

All adverse events from visit 1 to visit 3 will be collected by the following categories:

- Adverse Event (AE), Adverse Event of Special Interest (AESI)
- Adverse Device Effect (ADE) (Definitely, Probably and Possibly related)
- Serious Adverse Event (SAE)
- Serious Adverse Device Effect (SADE) (Definitely, Probably and Possibly related)

- Unanticipated Serious Adverse Device Effect (USADE)

All Adverse events will be coded using CTCAE v5.0.

3.3.2 Device deficiency

The device deficiency will be classified into a category which will be reported by device type.

Category:

- Identity
- Quality
- Durability
- Reliability
- Safety
- Performance
- Connectivity
- Other

Device type:

- Implant
- Sound Processor
- Accessory
- Software

4 STATISTICAL METHODOLOGY

4.1 General Methodology

No formal statistical testing will be made between Osia 2 SP and Osia SP. The study is not dimensioned to present or test significances by groups/subgroups.

All variables will be presented descriptively by Osia 2 SP and Osia SP where applicable. The change/difference between Osia 2 SP and Osia SP (with 95% confidence interval for the mean difference) will be calculated and presented.

Continuous variables will be presented with mean, standard deviation, standard error of the mean, median, minimum, maximum and number and categorical variables with number and percentage.

All measurements will be made on the Full analysis set except for the safety variables which will be presented for the Safety population. All tests will be two-tailed and conducted at 0.05 significance level. All analyses will be performed by using SAS® v9.4 (Cary, NC).

4.2 Patient Disposition and Data Sets Analyzed

The number of subjects included in each of the Full analysis set and safety populations will be summarized. The number and percentage of subjects randomized and treated will be presented. Subjects who completed the study and subjects who withdrew from study prematurely will also be presented with a breakdown of the reasons for withdrawal from the Full analysis set and safety populations.

4.3 Protocol Violations/Deviations

A list of protocol deviations will be produced.

4.4 Demographics and Baseline Characteristics

Demographics and baseline characteristics will be summarized in the Full analysis set and analysed according to the methods described in section “General Methodology” above.

4.5 Audiogram

Unaided audiometric threshold measures will be presented by both air- and bone conduction thresholds and by conductive/mixed hearing loss or SSD both unmasked and masked.

4.6 Prior and Concomitant Medications

Prior and concomitant medication will be summarized by higher level anatomical therapeutic chemical classification (ATC) group and generic term for the Safety population.

4.7 Efficacy Analyses

4.7.1 Overall preference and Experience regarding Comfort and specific usage measurements

Results will be presented at visit 1 (Osia SP) and at visit 3 (Osia 2 SP) and where applicable the change from visit 1 to visit 3 will also be presented according to the methods described in section “General Methodology” above. For audiometric thresholds in free field and Speech recognition tests in quiet and noise at visit 3 for Osia SP and Osia 2 SP and the difference between Osia SP and Osia 2 SP will be presented.

Summaries will be presented by tabulations and figures (where applicable). Figures showing Osia SP and Osia 2 SP and the difference Osia SP and Osia 2 SP will be produced. An alternative to the difference figure would be to present Osia SP values on the x-axis and Osia 2 SP on the y-axis.

4.8 Safety Analyses

4.8.1 Adverse Events and device deficiency

Number of adverse events and number of subjects with adverse events will be presented by CTCAE SOC and CTCAE PT. The presentation will be made by Adverse Event (AE), Adverse Event of Special Interest (AESI), Adverse Device Effect (ADE), Adverse event related to the use of an investigational medical device, Serious Adverse Event (SAE), Serious Adverse Device Effect (SADE) and Unanticipated Serious Adverse Device Effect (USADE).

The coding of the adverse event will be performed according to the Common Terminology Criteria for Adverse Events, CTCAE classification.

Number of device deficiencies (category) and number of subjects with device deficiencies will be presented. The presentation will be made by Device type; Implant, Sound Processor, Accessory and Software.

5 INTERIM ANALYSES

No interim analysis will be performed.

6 CHANGES OF ANALYSIS FROM PROTOCOL

No changes from the protocol is made.

7 LISTING OF TABLE, FIGURES AND LISTINGS

7.1 Listing of Tables

Table Number	Table Title
14.1.1	Patient Disposition and Data Sets Analyzed (FAS)
14.1.2	Demographics and Baseline Characteristics (FAS)
14.1.3.1	Prior Medications (Safety population)
14.1.3.2	Concomitant Medications (Safety population)
14.1.4	Audiogram (Safety population)
14.2.1.1	Overall preference - Preferred choice (FAS)
14.2.1.2	Overall preference - APHAB (FAS)
14.2.1.3	Overall preference - SSQ (FAS)
14.2.1.4	Overall preference - QUEST (FAS)
14.2.1.5	Overall preference - Thresholds audiometry, free-field (FAS)
14.2.1.6	Overall preference - Adaptive speech in noise and Speech in quite (FAS)
14.2.2	Subjective experience regarding Comfort and specific usage (FAS)
14.3.1.1	Adverse Events (Safety population)
14.3.1.2	Adverse Device Effects (Safety population)
14.3.1.3	Serious Adverse Events (Safety population)
14.3.1.4	Serious Adverse Device Effects (Safety population)
14.3.1.5	Serious Adverse Device Effect (Safety population)
14.3.1.6	Unanticipated Serious Adverse Device Effect (Safety population)
14.3.2.1	Device deficiency - Implant (Safety population)
14.3.2.2	Device deficiency - Sound Processor (Safety population)
14.3.2.3	Device deficiency - Accessory (Safety population)
14.3.2.4	Device deficiency - Software (Safety population)

7.2 Listing of Figures

Figures will be produced as defined in statistical methodology.

7.3 Listing of Listings

List will be produced later.

8 REFERENCES

9 APPENDIX