POST MARKET STUDY TO EVALUATE SAFETY AND EFFECTIVENESS OF THE INNFOCUS MICROSHUNT™ (MIDI ARROW) IN PATIENTS WITH PRIMARY OPEN ANGLE GLAUCOMA

Protocol INN-007

STATISTICAL ANALYSIS PLAN

NCT02177123

Sponsor: SANTEN

V1.1

05MAR2018

Post market study
To evaluate safety and effectiveness of the Innfocus Microshunt™ (MIDI Arrow) in patients with primary open angle glaucoma

Statistical Analysis Plan

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MEDPASS INTERNATIONAL	**STATISTICAL ANALYSIS PLAN**	INN-007_SAP_V1.1 redacted.doc1 **Sponsor :** SANTEN **Device :** MICROSHUNT **Protocol Nr:** INN-007 **MedPass Project Nr:** 376-01-13

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SIGNATURE PAGE

POST MARKET STUDY
TO EVALUATE SAFETY AND EFFECTIVENESS OF THE INNFOCUS MICROSHUNT™ (MIDI ARROW) IN PATIENTS WITH PRIMARY OPEN ANGLE GLAUCOMA

Version 1.1

[redacted]

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LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

AE	Adverse Event
BSS	Balanced Salt Solution
CE	Conformité Européenne (European Conformity)
CI	Confidence Interval
CSR	Clinical Study Report
FUP	Follow-up
IMS	Innfocus MicroShunt Implant
IOP	Intraocular Pressure
ITT	Intention-to-Treat
NAE	Number of Adverse Events
NDEV	Number of Deviations
OD	Oculus Dexter
OS	Oculus Sinister
PP	Per protocol
Q1-Q3	First and third quartiles
SAE	Serious Adverse Event
SAF	Safety Population
SAP	Statistical Analysis Plan
S.D.	Standard Deviation
SOC/PT	System Organ Class/Preferred Term
VA	Visual Acuity

1. OVERVIEW

This statistical analysis plan (SAP) describes the planned statistical analyses of the data collected in the course of INN-007, a post-market study evaluating safety and effectiveness of the Innfocus Microshunt™ (MIDI Arrow) in patients with primary open angle glaucoma.

This SAP provides additional details concerning the statistical analyses outlined in the Protocol INN-007 (version 1.3 dated 17MAR2014).

1.1. Study Objective

The objective of this study is to collect additional safety and effectiveness data on the InnFocus MicroShunt (MIDI Arrow) in patients suffering from primary open angle glaucoma who are inadequately controlled on maximum tolerated medical therapy with intraocular pressure ≥ 18 mmHg and ≤ 35 mmHg and/or where glaucoma progression warrants surgery.

1.2. Study Design

This is a prospective, multicentric, single arm post-market study with a CE marked device conducted at up to 4 European locations in which each patient meeting the inclusion criteria and not excluded per the exclusion criteria are implanted with a InnFocus MicroShunt in the anterior chamber of the eye. Patients are followed for 24 months with an expected enrolment period of up to 12 months. Safety of the InnFocus MicroShunt is confirmed with indirect and direct microscopic evaluation of the implanted and non-implanted eyes pre and post operatively, and at defined follow-up intervals for hypotony, inflammation, infection, migration of the shunt, visual acuity (VA), as well as a number of other defined potential complications. The effectiveness of the shunt is evaluated by measurement of intraocular pressure at defined intervals.

1.3. Study Plan

1.3.1. Patient's Follow-up

10 visits are scheduled:

- Visit 1 : Qualifying assessment and Preop - Baseline
- Visit 2 : Procedure - Day 0 (Operative day)
- Visit 3 : Day 1 ± 0 day Follow-up
- Visit 4 : Day 7 ± 1 day Follow-up
- Visit 5 : Week 4 ± 2 day Follow-up
- Visit 6 : Month 3 ± 1 week Follow-up
- Visit 7 : Month 6 ± 1 week Follow-up
- Visit 8 : Month 9 ± 2 weeks Follow-up
- Visit 9 : Month 12 ± 2 weeks Follow-up
- Visit 10 : Month 24 ± 2 weeks Follow-up

1.3.2. Study Device use

The study device is the InnFocus MicroShunt™ (IMS) Drainage Implant. The InnFocus MicroShunt was CE marked in January 25, 2012. In its review for CE marking the notified body has approved the instructions for use.

1.3.3. Study Assessments

The following flowchart applies to the study:

Assessment Forms	Qualifying Assessment & Preop Forms	Day			Week	Months				
		0	1	7	4	3	6	9	12	24
Patient Eligibility/ Informed Consent	X	Operative Day								
Medical History/Pregnancy test*	X									
Pachymetry	X									
Visual Acuity	X		X	X	X	X	X	X	X	X
Slit Lamp	X		X	X	X	X	X	X	X	X
Seidel Test			X	X	X	X	X	X	X	X
Tonometry	X		X	X	X	X	X	X	X	X
Motility Evaluation	X						X		X	X
Gonioscopy	X									
Ophthalmoscopy	X		X	X	X	X	X	X	X	X
Perimetry	X								X	X
Concomitant Medication	X		X	X	X	X	X	X	X	X
Adverse Events			X	X	X	X	X	X	X	X

* for non-menopausal women

Acceptable Visit Windows:

- Day 0 : Operative day
- Day 1 : ± 0 day
- Day 7 : ± 1 day
- Week 4 : ± 2 days
- Month 3 : ± 1 week
- Month 6 : ± 1 week
- Month 9 : ± 2 weeks
- Month 12 : ± 2 weeks
- Month 24 : ± 2 weeks

2. STATISTICAL METHODS

2.1. General Statistical Considerations

All statistical analyses will be made on the locked database, after a careful review of the data in order to identify the protocol deviations and their potential impact on endpoints analysis (bias in result).

2.1.1. Time Points Definition

Baseline data is defined as the last available observation recorded before the first study device exposition for the patient.

Visit (n) data is defined as the last available observation on or before the Visit (n) time point following the first study device exposition for the patient.

2.1.2. Handling Missing Data

- The following imputation methods will be used to handle the missing medication start date:

Date	Type of Missing Date	Handling of Missing Date
Medication Start date (e.g., YYYY-MM-DD	Completely missing	No imputation will be applied.
	Only YYYY is available	Use the first day of YYYY to impute the missing month and date parts of the medication start date
	YYYY and MM are available but DD is missing	Use the first day of MM to impute the missing date part of the medication start date
Medication Stop date (e.g., YYYY-MM-DD	Completely missing	No imputation will be applied. Medication will be considered ongoing at Study Exit.
	Only YYYY is available	Use the last day of YYYY to impute the missing month and date parts of the medication stop date
	YYYY and MM are available but DD is missing	Use the last day of MM to impute the missing date part of the medication stop date

The same methods will be used to handle the missing AE start date.

- For each success endpoint defined in section 2.4.4.2., the missing IOP score at the Month 12 visit will be imputed by the last observed IOP score before considering other criteria. No imputation of missing values is planned for any other parameters. In all applicable cases, reported analysis will mention the number of missing observations for each outcome relatively to the considered analysis set (SAF, ITT or PP).

2.1.1. Handling of Data Collected after Re-operation

As data collected after glaucoma re-operation may be confounded by the re-operation, IOP data collected after re-operation will be excluded from the summary of IOP and IOP reduction. For patients who experienced any re-operation, the number of glaucoma medications will be set to missing at visits after the re-operation; Procedure- or device-related AEs that occurred after the re-operation will also be excluded from AE summaries.

2.1.2. Descriptive Statistics in Summary Tables

- *Continuous variables* will be summarized using standard quantitative statistics: number of non-missing observations, mean, standard deviation, median, quartiles and range (minimum and maximum observed values). The number of missing observations will also be specified.
- *Categorical variables* will be summarized using classical frequency statistics: number of non-missing observations and percentages by categories. Except for the binary endpoints defined in

section 2.4.4.2. for which missing IOP data will be imputed, percentages will be calculated on the number of non-missing observations, and will be displayed using one decimal. The number of missing observations will also be specified.

2.1.3. Inferential Analysis

- Confidence intervals:

The 95% bilateral confidence interval of the mean will be calculated for continuous variable if pertinent.

For categorical variables, if pertinent, the 95% asymptotic confidence interval will be calculated if theoretical assumptions are verified. If this is not the case, and the corresponding proportion is 0% or 100%, then the Agresti-Coull confidence interval will be calculated instead. In all other cases, the exact confidence interval will be calculated.

2.1.4. Data Listings

Patient data listings will be selected data supportive of summary statistical tables, including derived/calculated data from statistical process. These key data listings will be performed on selected analysis sets according to the focus of the listings.

2.2. Sample size calculation

Despite relatively large variability, a credible level of performance at the 1-year follow-up for the primary endpoint is at least above 50%. As a result, to demonstrate that the incidence of success using IMS was >50%, sample size calculations were conducted with NQuery software and a one group Chi-Square test, in a bilateral situation, with 5% alpha level and 80% power.

The table below summarises the sample size calculation.

Test significance level, alpha	0.05
1 or 2 sided test?	2
Null hypothesis proportion	50%
Alternative proportion	65%
Power (%)	80
N	85

To allow for patients dropping out before the 1-year follow-up visit, the final sample size was increased to 100 patients. A total of 100 patients with a goal of 25 patients at each selected centre were planned to be enrolled.

2.3. Analysis Sets

2.3.1. Definition of patient populations

Three (3) populations are defined:

- The Safety population (SAF) will include all patients who have signed the informed consent / enrolled in the study.
- The Intent-to-Treat (ITT) population will include all patients from the SAF who received the assigned therapy under evaluation (InnFocus MicroShunt).

- The Per Protocol (PP) population will include all ITT patients without any major protocol deviations.

2.3.2. Protocol Deviations

On a case-by-case basis, all protocol deviations will be reviewed and will be classified as “minor” or “major” according to the possible impact expected on primary results.

Patients meeting at least one of the following major deviations will be excluded from the PP population.

- Did not meet at least one inclusion criterion, or
- Did not meet at least one exclusion criterion

Follow-up visits out of the pre-specified visit windows described in section 1.3.3 will be listed and summarized.

2.4. Statistical Analyses

2.4.1. Patient Disposition and Follow-up

2.4.1.1. Patient Populations, follow-ups and withdrawals

The number of patients present at each visit, as well as the reasons for study exit will be presented by population.

2.4.1.2. Protocol Deviations

The focus of protocol deviations description will be on major deviations as defined in section 2.3.2.

Frequency of patients with at least one major protocol deviation will be summarized on the ITT population, by deviation category.

Major as well as minor protocol deviations will be detailed in a patients’ data listing.

2.4.2. Demographics and other baseline characteristics

Descriptive statistical data will be used to draw up a recapitulation of the ITT patients’ characteristics at baseline.

2.4.2.1. Demographics

- Gender,
- Age (years),
- Study eye.

2.4.2.2. Disease history

- Glaucoma diagnosis,
- Lens status,
- Cataract grade of phakic eyes,
- Systemic disease,
- Previous ocular laser surgeries,
- Previous incisional surgeries.

2.4.2.3. *Efficacy data at baseline*

- Baseline VA,
- Reasons for VA < 7 at baseline,
- Baseline IOP,
- Baseline Gonioscopy results,
- Baseline diplopia,
- Baseline motility.

2.4.3. Procedure characteristics

Descriptive statistical data will be used to draw up a recapitulation of ITT patients' characteristics at procedure.

- Antiproliferative treatment used,
- Antiproliferative treatment dose (mg/mL),
- Antiproliferative treatment duration (min),
- Number of laser shields used,
- Volume of Balanced Salt Solution (BSS) rinse used (cc),
- Number of devices opened,
- Length of conjunctival flap (mm),
- Length of MIDI Arrow,
- Implant position,
- Intraoperative medications,
- Intraoperative medications classes,
- Implanted and not implanted devices.

2.4.3.1. *Not implanted devices*

- Sterile package damaged,
- Product damaged.

2.4.3.2. *Implanted devices*

- Grade of ease to position MIDI Arrow,
- Grade of ease to position MIDI Arrow into the anterior chamber,
- Flow through MIDI Arrow into the anterior chamber.

2.4.3.3. *Complications and surgical time*

- Intraoperative complications,
- Surgical time (min).

2.4.4. Performance primary endpoints

The primary endpoint analysis will be performed on the ITT and the PP population.

2.4.4.1. *IOP reduction*

Primary analysis consists of the analysis of the IOP reduction at each post-operative visit.

2.4.4.2. Success Definitions

In this study, *success* is defined as:

- For eyes under study with baseline IOP ≥18 to ≤21 mmHg, success will be measured as an eye under study which achieves an IOP reduction of 20% or greater with no reoperation for glaucoma or loss of light perception vision. A reoperation to better the aqueous drainage like a trabeculectomy or an implantation of another drainage implant is considered a failure as it does not fulfill the criteria for success mentioned above.
- For eyes under study with baseline IOP >21 mmHg, success will be measured as an eye under study with IOP<21 mmHg and IOP reduction from baseline of 20% or greater with no reoperation for glaucoma or loss of light perception vision

Qualified success is defined as an eye under study which requires supplemental medical therapy to maintain controlled levels of intraocular pressure

Complete success is an eye under study which is not on supplemental medical therapy to obtain controlled levels of intraocular pressure.

All success endpoints are primarily assessed at Month 12 and Month 24. Success rates will be calculated at Month 6, Month 9, Month 12, and Month 24, with the missing data imputed using the last-observation-carried-forward approach before considering other success criteria.

Success was not defined in the protocol for eyes under study with baseline IOP <18 mmHg as it was not expected to enroll eyes with baseline IOP <18 mmHg per the inclusion criterion on baseline IOP. However, if patients in this case are enrolled, to follow the intention-to-treat principle, these ineligible studied eyes will be included in the ITT analysis of all success endpoints, with the same definition of success for studied eyes with baseline IOP>=18 and <=21 mmHg.

2.4.5. Performance secondary endpoints

The secondary endpoint analysis will be performed on the ITT population and by visit.

- Visual acuity per visit in the Study eye,
- Visual acuity per visit in the Fellow eye,
- Visual acuity (quantitative) per visit,
- Visual acuity compared to baseline value per visit,
- Visual acuity loss per visit,
- IOP per visit in the Study eye,
- IOP per visit in the Fellow eye,
- Bleb per visit,
- Diplopia per visit,
- Motility per visit,
- Motility problems appeared after the procedure,
- Re-operations.

2.4.6. Safety analysis

Safety analysis will be analysed on the SAF or ITT population as appropriate.

The 55 AE types pre-defined by Innfocus in the AE eCRF will be analysed separately to meet the FDA's expectation.

Adverse events have been coded using the MedDRA dictionary version 19.

2.4.6.1. Seidel test

- Seidel test results per visit

2.4.6.2. Sites reported adverse events

- Total number of Adverse events types and the corresponding number and percentage of patients by eye (Study eye/Fellow eye),
- Adverse events severity by eye (Study eye/Fellow eye),
- Summary of adverse events.

2.4.6.3. Device or procedure related AE

- Summary of device/procedure related AEs,
- Occurrence of device/procedure related AEs.

2.4.7. Concomitant Medications

Concomitant medications will be summarized on the ITT population. Medications have been classified by Anatomical-Therapeutic-Chemical (ATC) levels and the preferred drug name coded using the World Health Organization Drug Dictionary Enhanced (WHO-DEE; March 2017 version).

- Status of glaucoma medication use regarding the time of procedure,
- Concomitant medications by class,
- Need of glaucoma supplemental treatment per visit,
- Number of glaucoma supplemental treatments per visit,
- Percentage of glaucoma medications per visit.

The number of glaucoma supplemental treatments at a visit is derived as the number of glaucoma medication classes the patient was receiving at that visit. For example, if a patient was receiving a glaucoma medication of class A (monotherapy), a glaucoma medication of class B (monotherapy), together with a glaucoma medication of class A+B (combination therapy) at baseline, then the number of glaucoma supplemental treatments at baseline was 2 (A and B) for this patient. The WHO-DEE ATC Level 4 will be used to determine the primary glaucoma medication class (e.g., Beta blocking agents, Carbonic anhydrase inhibitors, Parasympathomimetics, Prostaglandin analogues, or Sympathomimetics in glaucoma therapy). For glaucoma supplemental treatment that combines multiple glaucoma medications of different classes, the secondary glaucoma medication class(es) will be determined by Santen Clinical Scientist and added to the INN-007 coded medication spreadsheet.

2.4.8. Additional Analysis

The following parameters will be presented for the ITT population.

- Protocol deviations,
- Baseline visual field classes,
- Success by baseline visual field classes per visit,

- IOP by baseline IOP range per visit,
- Visual acuity recovery per visit,
- Visual field per visit,
- Change in visual field per visit (quantitative),
- Change in visual field per visit (qualitative),
- Total number of Adverse events (SOC/PT) and the corresponding number and percentage of patients by eye (Study eye/Fellow eye),
- Total number of Device related AEs (SOC/PT) and the corresponding number and percentage of patients by eye (Study eye/Fellow eye),
- Total number of Procedure related AEs (SOC/PT) and the corresponding number and percentage of patients by eye (Study eye/Fellow eye),
- Total number of Serious adverse events (SOC/PT) and the corresponding number and percentage of patients by eye (Study eye/Fellow eye),
- Total number of Device related SAEs (SOC/PT) and the corresponding number and percentage of patients by eye (Study eye/Fellow eye),
- Total number of Procedure related SAEs (SOC/PT) and the corresponding number and percentage of patients by eye (Study eye/Fellow eye),
- Total number of Non-ocular adverse events and the corresponding number and percentage of patients by eye (Study eye/Fellow eye).

2.5. Derived Criteria Calculation

- A patient will be considered as fulfilling the eligibility criteria if:
  - Inclusion Criteria 1 to 5 are ticked “Yes”, AND
  - Exclusion Criteria 1 to 46 are ticked “No”, AND
  - Baseline IOP ≥ 18 and ≤ 35 mmHg.
- Duration between two dates t_1 and t_2 will be calculated as: $Duration(t_1,t_2)= t_2-(t_1+1)$
- Concomitant treatment:
  - If the visit date is between or equal to the start and the end of the concomitant treatment,
  - If the visit date is after or equal to the start of the concomitant treatment and the treatment is ongoing or the end is missing,
  - If the visit date is before or equal to the end of the concomitant treatment and the start is missing.

If for a concomitant treatment there are two different end of treatment, the highest is kept. When the concomitant treatment has an end of but is also indicated as ongoing, the date with the end is privileged.

- The eye receiving a glaucoma medication classes will be the following:
  - “Treatment ongoing after the procedure”: if t_1 is prior or equal to *tp* and, *tp* is posterior to t_2 or t_2 is missing.
  - “Treatment stopped before the procedure”: if t_2 is prior to *tp.*
  - “Treatment begun after the procedure”: if *tp* is prior to t_1.

  Where t_1 is the treatment start date, t_2 the treatment stop date and *tp* the date of procedure.
- The number of glaucoma supplemental treatments is calculated as the number of glaucoma medication classes (see Section 2.4.7 for more details).
- Derived criterion “IOP (mmHg)” will be calculated as follows:
  - If the study eye is the right eye (OD) then $IOP\_mean=mean(right\ IOP_1,\ right\ IOP_2)$

- If the study eye is the left eye (OS) then *IOP_mean=mean(left IOP_1, left IOP_2)*

Where IOP_1 is the IOP result n°1 and IOP_2 the IOP result n°2.

- Derived criterion "Baseline Gonioscopy results" will be derived as follows:
  - If the Study eye is the right eye (OD) then the gonioscopy of the right eye is reported.
  - If the Study eye is the left eye (OS) then the gonioscopy of the left eye is reported.
- Derived criterion "Motility" classes will calculated as follows:
  - "Motility < 100": $mean(m_1, m_2, m_3, m_4)<100$
  - "Motility = 100": $mean(m_1, m_2, m_3, m_4)=100$

Where m_1 is the motility upward, m_2 the motility to the right; m_3 the motility downward and m_4 the motility to the left.

- Derived criterion "Length of MIDI Arrow" will be defined as follows:
  - If "Implanted length of MIDI Arrow" is ticked then the length will be "8.5 mm".
  - If "Implanted length of MIDI Arrow" is "Other" then the other length will be reported.
- Derived criterion "Volume of BSS Rinse Used" classes will be the following:
  - "10 cc": if the specification is equal to 10.
  - "20 cc": if the volume category is recorded to "20 cc".
  - "More": if the volume category is recorded to "More".
- Derived criterion "Intraoperative medications" will be defined as "Yes" if medications will be informed since the date of procedure is recorded.
- Derived criterion "Implanted and not implanted devices" classes will be defined as followed:
  - "Implanted": if the "current section number" is equal to the "total section number" and the specification of the device evaluation is not recorded "Not implanted".
  - "Not implanted": the opposite definition of "Implanted".
- Derived criterion "Surgical time (min) will be calculated as: $time=(t_2-t_1)/60$

  Where *t1* is the surgical start time and *t2* the surgical stop time.
- Derived criteria "IOP reduction" and "Percentage IOP reduction" will be calculated at each visit as
  - $Reduc(i)=IOP\_mean_i - IOP\_mean_{pre}$
  - $Percentage\ Reduc(i)=((IOP\_mean_i - IOP\_mean_{pre})/IOP\_mean_{pre})*100$

  Where IOP_mean_{pre} is the IOP mean recorded during the pre-operative visit. IOP_mean_i *is the* IOP mean for the visit *i* where $i = (4,\ldots,11)$ which are the Follow-up Day 1 visit to Follow-up 24 month.
- Derived criterion "study success" will be defined as follows:
  - IOP reduction ≥20% in patients with baseline IOP ≥18 and ≤21 mmHg with no reoperation or loss of light perception vision, or;
  - IOP <21 mmHg and IOP reduction from baseline of ≥20% in patients with baseline IOP >21 mmHg with no reoperation or loss of light perception vision.
- Derived criterion "Motility problems appeared after the procedure" classes will be defined at each visit as follows:
  - "No worsening motility": if $mot_i>mot_{pre}$
  - "Motility problem appeared": if $mot_i<mot_{pre}$

Where mot_{pre} is the mean of motility for the pre-operative visit and mot_i is the mean of motility for the visit *i* and $i = (4,\ldots,11)$ which are the Follow-up Day 1 visit to Follow-up 24 month.

3. STATISTICAL SOFTWARE

All statistical outputs (summary tables and data listings) will be generated using SAS® version 9.4.

4. STATISTICAL TABLES, LISTINGS AND FIGURES (TABLE OF CONTENTS)

4.1. Statistical Tables

4.1.1. Patient Disposition and Follow-up

4.1.1.1. Patient Populations, follow-ups and withdrawals

Table 1: Patients follow-ups and study exits by population (Type 5)

4.1.2. Demographics and other baseline characteristics

4.1.2.1. Demographics

Table 2: Gender (Type 4)

Table 3: Age (years) (Type 1)

Table 4: Study eye (Type 4)

4.1.2.2. Disease history

Table 5: Glaucoma diagnosis (Type 4)

Table 6: Lens Status (Type 5)

Table 7: Cataract grade of phakic eyes (Type 5)

Table 8: Systemic disease (Type 5)

Table 9: Previous ocular laser surgeries (Type 5)

Table 10: Previous incisional surgeries (Type 5)

4.1.2.3. Efficacy data at baseline

Table 11: Baseline VA (Type 4)

Table 12: Reasons for VA < 7 at baseline (Type 4)

Table 13: Baseline IOP (Type 3a)

Table 14: Baseline Gonioscopy results (Type 4)

Table 15: Baseline Diplopia (Type 4)

Table 16: Baseline Motility (Type 4)

4.1.3. Procedure characteristics

Table 17: Antiproliferative treatment used (Type 4)

Table 18: Antiproliferative treatment dose (mg/mL) (Type 1)

Table 19: Antiproliferative treatment duration (min) (Type 1)

4.1.3.1. Not implanted devices

4.1.3.2. Implanted devices

4.1.3.3. Complications and surgical time

4.1.4. Performance primary endpoints

4.1.4.1. Percentage of IOP reduction

4.1.4.2. Study Success

4.1.5. Performance secondary endpoints

4.1.6. Safety analysis

4.1.6.1. Seidel test

4.1.6.2. Sites reported Adverse Events

4.1.6.3. Device or procedure related AE

4.1.7. Concomitant Medications

4.1.8. Additional Analysis

4.2. Listings

4.2.1. Study patients

4.2.1.1. Protocol deviations

4.2.2. Demographics and other baseline characteristics

4.2.2.1. Disease history

4.2.2.2. Efficacy data at baseline

4.2.2.3. Procedure description

4.2.2.4. Not implanted devices

4.2.2.5. Implanted devices

Listing 12: Implanted devices lot number

Listing 13: Other implanted devices evaluation

4.2.2.6. Complications and surgical time

Listing 14: Surgical time (ascending order)

4.2.3. Performance primary endpoints

Listing 15: FUP VA loss of at least 2 Monoyer lines

Listing 16: FUP IOP extreme values

Listing 17: FUP diplopia

Listing 18: FUP motility less than 100%

Listing 19: Motility problems after the procedure

Listing 20: Re-operation reasons and delay from procedure

4.2.4. Safety analysis

4.2.4.1. Adverse events

Listing 21: Adverse events

4.2.5. Concomitant treatments

Listing 22: Other medications classes (given to only one eye)

Listing 23: Glaucoma treatments taken after the procedure

Listing 24: All medications (except intra-operative)

4.2.6. Additional Anlaysis

Listing 25: Non-ocular adverse events

4.3. Figures

4.3.1. Additional Analysis tables

Figure 1: Glaucoma medications pre-procedure vs W4

Figure 2: Glaucoma medications pre-procedure vs M3

Figure 3: Glaucoma medications pre-procedure vs M6

Figure 4: Glaucoma medications pre-procedure vs M9

Figure 5: Glaucoma medications pre-procedure vs M12

5. LAYOUT OF THE STATISTICAL TABLES

5.1. Quantitative variables

5.1.1. Type 1: Without group

Variable	N	Missing	Mean	S.D.	Median	Min,Max	Q1-Q3
Var 1	XX	XX	XX.X	XX.X	XX.X	XX.X, XX.X	[XX.X ; XX.X]

5.1.1. Type 2 : Without group and by population or visit

		N	Missing	Mean	S.D.	Median	Min,Max	Q1-Q3	95% CI
Var 1	Population 1 (or Visit 1)	XX	XX	XX.X	XX.X	XX.X	XX.X, XX.X	[XX.X ; XX.X]	[XX.X - XX.X]
	Population 2 (or Visit 2)	XX	XX	XX.X	XX.X	XX.X	XX.X, XX.X	[XX.X ; XX.X]	[XX.X - XX.X]

5.1.2. Type 3a : With group and by population or visit

		Group	N	Missing	Mean	S.D.	Median	Min,Max	Q1-Q3
Var 1	Population 1 (or Visit 1)	Group1	XX	XX	XX.X	XX.X	XX.X	XX.X, XX.X	[XX.X ; XX.X]
		Group2	XX	XX	XX.X	XX.X	XX.X	XX.X, XX.X	[XX.X ; XX.X]
	Population 2 (or Visit 2)	Group1	XX	XX	XX.X	XX.X	XX.X	XX.X, XX.X	[XX.X ; XX.X]
		Group2	XX	XX	XX.X	XX.X	XX.X	XX.X, XX.X	[XX.X ; XX.X]

5.1.1. Type 3b : With group and by population or visit

			Group1	Group 2
Var 1	Population 1 (or Visit 1)	N	XX	XX
		Mean	XX.X	XX.X
		S.D.	XX.X	XX.X
		Median	XX.X	XX.X
		Min,Max	XX.X, XX.X	XX.X, XX.X
		Q1-Q3	XX.X - XX.X	XX.X - XX.X
		Missing	XX	XX
	Population 2 (or Visit 2)	N	XX	XX
		Mean	XX.X	XX.X
		S.D.	XX.X	XX.X

			Group1	Group 2
		Median	XX.X	XX.X
		Min,Max	XX.X, XX.X	XX.X, XX.X
		Q1-Q3	XX.X - XX.X	XX.X - XX.X
		Missing	XX	XX

5.2. Qualitative variables

5.2.1. Type 4 : Without group and by population or visit

		Population 1 (or Visit 1) (N=XX)	Population 2 (or Visit 2) (N=XX)
Var 1	N	XX	XX
	Var 1 – Mod 1	XX (XX.X %)	XX (XX.X %)
	Var 1 – Mod 2	XX (XX.X %)	XX (XX.X %)
	95% CI (Yes)*	[XX.X % - XX.X %]	[XX.X % - XX.X %]
	Missing*	XX	XX

*If needed

5.2.2. Type 5 : Without group, with conditional variable and by population or visit (with 95% CI)

		Population 1 (or Visit 1) (N=XX)	Population 2 (or Visit 2) (N=XX)
Var 1	N	XX	XX
	Var 1 – Mod 1	XX (XX.X %)	XX (XX.X %)
	Var 1 – Mod 2	XX (XX.X %)	XX (XX.X %)
	95% CI (Yes)*	[XX.X % - XX.X %]	[XX.X % - XX.X %]
	Var 2 – Mod 1	XX (XX.X %)	XX (XX.X %)
	95% CI (Yes)*	[XX.X % - XX.X %]	[XX.X % - XX.X %]
	Var 2 – Mod 2	XX (XX.X %)	XX (XX.X %)
	95% CI (Yes)*	[XX.X % - XX.X %]	[XX.X % - XX.X %]
	Missing*	XX	XX

*if needed

5.2.3. Type 6 : By group

		Population (N=XX)		
		Group 1 (N=XX)	Group 2 (N=XX)	Total (N=XX)*
Var 1	N	XX	XX	XX
	Var 1 – Mod 1	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
	Var 1 – Mod 2	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
	95% CI (Yes)*	[XX.X % - XX.X %]	[XX.X % - XX.X %]	[XX.X % - XX.X %]
	Missing*	XX	XX	XX

*If needed

5.2.4. Type 7 : By group and by population or visit

			Population (N=XX)		
			Group 1 (N=XX)	Group 2 (N=XX)	Total (N=XX)*
Var 1	Population 1 (or Visit 1)	N	XX	XX	XX
		Var 1 – Mod 1	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
		Var 1 – Mod 2	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
		95% CI (Yes)*	[XX.X % - XX.X %]	[XX.X % - XX.X %]	[XX.X % - XX.X %]
		Missing	XX	XX	XX
	Population 2 (or Visit 2)	N	XX	XX	XX
		Var 1 – Mod 1	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
		Var 1 – Mod 2	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
		95% CI (Yes)*	[XX.X % - XX.X %]	[XX.X % - XX.X %]	[XX.X % - XX.X %]
		Missing	XX	XX	XX

*If needed

5.3. Others

5.3.1. Type 8 : Medications/ complications

Medication	Population 1 (N=XX)
At least one	XX (XX.X %)
Med 1	XX (XX.X %)
Med 2	XX (XX.X %)
Med 3	XX (XX.X %)
Med 4	XX (XX.X %)
Med 5	XX (XX.X %)

5.3.2. Type 9 : Adverse Event with or without conditional variable

	Population 1 (N=XX)			Population 2 (N=XX)			Population 3 (N=XX)		
Sites reported Adverse Event Type	NAE (1)	n (2)	% (3)	NAE (1)	n (2)	% (3)	NAE (1)	n (2)	% (3)
ALL	XX	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X
AE 1	XX	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X
AE 1 – Mod 1	XX	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X
AE 1 – Mod 2	XX	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X
AE 2	XX	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X
AE 2 – Mod 1	XX	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X
AE 2 – Mod 2	XX	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X

(1) NAE: Number of Adverse Events
(2) n: number of eyes
(3) %: percentage of eyes (%=n/N)

5.3.3. Type 10 : Summary of Adverse Event

	Population 1 (N=XX)		
Number and percentage of	N	%	95 % CI
Var 1	XX	XX.X	[XX.X% - XX.X %]
Var 2	XX	XX.X	[XX.X% - XX.X %]
Var 3	XX	XX.X	[XX.X% - XX.X %]

5.3.4. Type 11 : Concomitant medications

	Population 1 (N=XX)	
Number and percentage of	N	%
ALL		
Med 1	XX	XX.X
Med 2	XX	XX.X
Med 3	XX	XX.X

5.3.5. Type 12 : Protocol deviation

	ITT (N=101)		
Deviation / Specify	NDEV (1)	n (2)	% (3)
ALL	XX	XX	XX.X
Visit out of window	XX	XX	XX.X
Visit 1	XX	XX	XX.X
Visit 2	XX	XX	XX.X
Inclusion/Exclusion criteria not respected	XX	XX	XX.X

	ITT (N=101)		
Deviation / Specify	NDEV (1)	n (2)	% (3)
Inclusion Criterion N°1 = NO	XX	XX	XX.X
Exclusion Criterion N°1 = YES	XX	XX	XX.X
Glaucoma treatment not stoppped before the procedure	XX	XX	XX.X

(1) NDEV: Number of deviations
(2) n: Number of eyes with at least one deviation
(3) %: the corresponding percentage of eyes (n*100/N, with N=total number of eyes)