STATISTICAL ANALYSIS PLAN

"MULTICENTRIC CLINICAL INVESTIGATION ON THE USE OF SINGLE-DOSE OPHTHALMIC SOLUTION BASED ON SODIUM HYALURONATE IN THE TREATMENT OF EYE DISCOMFORT IN PARTICULAR IN CASE OF OCULAR DRYNESS"

Version 1 –October 10th, 2023

STUDY CODE: 052/SI Hyalistil Bio PF Mono

Post Market Clinical Follow up (PMCF)

(Observational Study-Profit)

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Statistical Analysis Plan Status: DRAFT

Clinical Investigation Plan No.: 052/SI Hyalistil Bio PF Mono

Study Type: Post Market Clinical Follow up (PMCF) (Prospective, observational, non-interventional clinical investigation)

Products Name: Hyalistil Bio PF Mono

Date of Issue: *October 10th, 2023*

Study Title

Multicentric clinical investigation on the use of single-dose ophthalmic solution based on sodium hyaluronate in the treatment of eye *discomfort* in particular in case of ocular dryness

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LIST OF ABBREVIATION

AE	Adverse Events
CI	Confidence intervals
DED	Dry eye disease
DEQS	Questionnaire about Eye Symptoms and Daily Life
FAS	Full Analysis Set
IGAS	Investigator Global Assessment of Safety
IOP	Intraocular Pressure
ITT	Intent-to-Treat
LLT	Lowest level term
LOCF	Last observation carried forward method
MedDRA	Medical Dictionary for Regulatory Activities
NEI	National Eye Institute Scale
PP	Per Protocol
PPS	Per Protocol Set
PT	Preferred Term
QOL	Quality of Life
SANDE	Questionnaire Symptom Assessment in Dry Eye
SAP	Statistical Analysis Plan
SEAE	Study-emergent adverse event
SD	Standard Deviation
SOC	System/Organ class
TFBUT	Tear Film Break-up Time

1. CHANGE HISTORY RECORD

1.1. Statistical Analysis Plan

Statisitcal Analysis Plan version	Statisitcal Analysis Plan date	Description of changes	Amendment version	Amendment date
1	October 10th 2023	First version	-	-

1.2. Clinical Investigation Plan

Clinical Investigation Plan version	Clinical Investigation Plan date	Description of changes	Amendment version	Amendment date
1	October 10th 2022	First release	-	-
2	March 14th,2023	Second release	052/SI Hyalistil Bio PF Mono/EM version 1 of March 14th,2023	March 14th,2023

1.3. CRF

CRF version	CRF date	Description of changes	Amendment version	Amendment date
1.0	March 9rd 2023	First release	-	-
2.0	May 29th, 2023	Second release		
3.0	July 24th, 2023	Third release		

2. RATIONAL AND BACKGROUND

Dry eye disease (DED) is a common clinical problem as over 7 million people in the United States experience dry eye symptoms. Symptoms of DED include a sensation of dry eyes, foreign body sensation, irritation, burning, tearing, ocular pain, and itching, among others. DED affects quality of life and work productivity, and patients with moderate to severe DED may experience reduced visual function in addition to ocular dysfunction.

DED is a multi-factorial disease, defined by a loss of homeostasis of the tear film and accompanied by ocular symptoms, in which tear film instability and hyper-osmolarity, ocular surface inflammation and damage, and neuro-sensory abnormalities play etiological roles.

Hyalistil BIO PF (listed in the Medical Device Technical File as HA MONO 0.2% Phosp. Free-) is sterile medical devices (eye drops) for ophthalmic use containing 0.2% sodium hyaluronate. The device is presented in unidose containers phosphate-free. Therefore, HA MONO 0.2% Phosp. Free- is indicated to lubricate and hydrate the ocular surface able to provide a stable coating on the surface of the eye performing a moisturizing and lubricating action on the ocular surface, thus allowing a temporary relief to burning, irritation and all dry-eye related discomfort.

In addition, the device assures the protection of the ocular surface during the healing processes.

Moreover, since the presence of phosphates in ophthalmic formulations may rarely cause, in patients with compromised cornea, corneal deposits or corneal opacities [1,2], HA MONO 0.2% Phosp. Free- is a specific formulation without phosphates (and alternative buffer systems) mainly indicated in all cases of ocular discomfort and ocular dryness due to (as example) dry eye syndrome, ocular surgery, allergy, environmental factors (sun exposure, wind, smoke, pollution, conditioned air), excessive use of computer monitors, contact lenses use, aging, Moreover, they protect the ocular surface during the process of wound healing after corneal abrasions.

One-two drops of HA MONO 0.2% Phosp. Free- should be instilled in the conjunctival fornix three to four times daily, unless otherwise indicated.

No safety concerns have been identified and reported on the leaflet with the exception of occasional burning and local irritation upon instillation.

Under these premises, considering that HA-MONO-0.2%-Phosp.free was marketed in Italy with the name “Hyalistil Bio PF”, the purpose of this prospective observational investigational plan is to assess the clinical performance, tolerance, and safety of Hyalistil Bio PF device after 35 ± 4 days of treatment in patients affected by eye *discomfor*t in particular in case of ocular dryness.

3. CLINICAL INVESTIGATION OBJECTIVES

3.1. Primary objective

- Evaluation of Tear film break-up time with fluorescein (TFBUT) at Study Termination Visit (*Day 35 ± 4 of treatment*) compared to Visit 1 (*Day 0 of treatment - baseline*).

3.2.Secondary objective

The secondary objectives were:

Clinical Performance

- Evaluation of the change in total score (score from 6 to 33, considering a normal score 0-33) resulting from the sum of the corneal staining score (score from 0 to 15) and conjunctival staining score (score from 0 to 18) with fluorescein using the National Eye Institute Scale (NEI) at Visit 2 *(Day 14 ± 2 of treatment)* and at the Study Termination Visit *(Day 35 ± 4 of treatment)* compared to Visit 1 *(Day 0 of treatment - baseline);*
- Evaluation of the tear film stability per group as objectified by the tear break up time with fluorescein (TFBUT) at Study Termination Visit *(Day 35 ± 4 of treatment)* compared to Visit 2 (*Day 14 ± 2 of treatment*).
- Changes about Best Corrected Visual Acuity (BCVA) measured by the "*Early Treatment Diabetic Retinopathy Study*" (ETDRS) at Visit 2 (*Day 14 ± 2 of treatment*) and Study Termination Visit *(Day 35 ± 4 of treatment)* compared to Visit 1*(Day 0 of treatment – baseline)*.

Patient reported outcomes

- To compare patients reported outcomes (PRO) measures per group, including:
  - Patient's reported symptoms (SANDE) at Visit 2 (*Day 14 ± 2 of treatment*) and Study Termination Visit *(Day 35 ± 4 of treatment)* compared to Visit 1*(Day 0 of treatment – baseline)*.
  - Evaluation of the degree of satisfaction to the treatment reported by patients through the use of the visual analogue scale (VAS)[##], at the Study Termination Visit (*Day 35 ± 4 of treatment*).
  - Assessment of the quality of life (QOL)[###] by "Questionnaire about Eye Symptoms and Daily Life" (DEQS) at Study Termination Visit (Day 35 ± 4 of treatment) compared to Visit 1 (Day 0 of treatment - baseline).

3.3. Safety Evaluations

- Evaluation of safety of daily instillation of ophthalmic solution during all the study period through:
  - ✓ Investigator Global Assessment of Safety (IGAS): using the 4-point scale:1= very good safety, 2 =good safety, 3 = moderate safety and 4 = poor safety. IGAS was evaluated at the Study Termination Visit. [Time Frame: Study Termination Visit];
  - ✓ Evaluation of reported adverse events/incidents. [Time Frame: During the treatment period];
  - ✓ Evaluation of intraocular pressure (IOP) [Time frame: Visit 1, Visit 2 and Study

Termination Visit];

According to clinical practice, the Investigator will perform all clinical evaluations on both eyes of the individual patient.
In the case that both eyes are affected by ocular dry eye, the statistical analysis will be performed considering the eye with the lowest level of TFBUT score "worse eye". If the level of TFBUT score at baseline is the same in both eyes, then the eye with the highest level of NEI score will be designated as the "worse eye". If the level of NEI score at baseline is the same in both eyes, then the right eye will be designated as the "worse eye."

4. CLINICAL INVESTIGATION DESIGN

This clinical investigation is a multicentric prospective observational open-label, non-interventional clinical investigation evaluation, during the conventional clinical practice, the performance and safety of the daily instillation of Hyalistil Bio PF device in the treatment of patients affected by eye *discomfor*t in particular in case of ocular dryness.
The clinical evaluation period was run approximately for 4 months from first patient first visit (FPFV) March 14th, 2023, to last patient last visit (LPLV) August 3tr, 2023. All patients were followed from enrolment until study end date, which was occur when, in compliance with the normal clinical practice, the last patient was undergo the Study Termination Visit (35± 4 days from the first instillation of study product).

4.1. Study visits and procedures

In this observational clinical investigation, each enrolled patient will be evaluated during 3 scheduled visits. A written informed consent will be obtained before any study assessment or procedure. The first patient first visit (FPFV) is defined as the 1st visit to the clinical site by the 1st screened patient. The "Last Patient Last Visit" (LPLV) is defined as the last visit to the clinical site by the last patient (i.e., the last visit foreseen by the study clinical investigation plan), independently of whether the patient completed or withdrew from the study.

Visit 1 (screening-enrolment)

The following procedures were performed:

- Explanation to the patient of study aims, procedures and possible risks of the observational study;
- Informed consent signature;
- Allocation screening number;
- Demographic data collection;
- In case of female patients (collection of information on pregnancy or breastfeeding self-reported by the patient);
- Medical and surgical history/current medical conditions;
- Prior/concomitant ocular and systemic medications;
- Ocular examination of both eyes:
  - External Ocular Examination;
  - BCVA test through the ETDRS at 4 m distance;
  - Symptom Assessment in Dry Eye by SANDE questionnaire;

- Evaluation of Intraocular pressure (IOP);
- Tear film break-up time with fluorescein (TFBUT)ϕ;
- Ocular surface staining (NEI score) with fluorescein;

- DEQS questionnaire administration;
  - Patient eligibility: inclusion/exclusion criteria evaluation;
  - Assignment of the study and allocation patient clinical investigational number;
  - Generation of unique subject identifiers code;
  - Medical device dispensation;
  - Beginning of the treatment*.

The Investigator will be dispensed to the patients 5 boxes of medical device each containing 30 single-dose containers of medical device for the following 35±4 days. After completing the baseline evaluation, patients will start the study treatment as instructed through self-instillation of medical device under investigation at home*.
Patients were return to the clinical site on day 14±2 from the first instillation of medical device under investigation (Visit 2).

Visit 2 (on the 14th day from the first instillation of medical device under investigation (MD)) (window ± 2 days)***

The following procedures will be performed:
- Assessment of treatment compliance;
- Current medical conditions;
- Concomitant medications;
- Evaluation of any reported adverse events/incidents**;
- Ocular examination of both eyes:
  - External Ocular Examination;
  - BCVA test through the ETDRS at 4 m distance;
  - Symptom Assessment in Dry Eye by SANDE questionnaire;
  - Evaluation of Intraocular pressure (IOP);
  - Tear film break-up time with fluorescein (TFBUT)ϕ;
  - Ocular surface staining (NEI score) with fluorescein;

Patients were return to the clinical site on day 35±4 days from the first instillation of medical device under investigation (Study Termination Visit).

Study Termination Visit (on the 35th day from the first instillation of medical device under investigation) (window ± 4 days)

The final visit is defined as the visit performed on 35 ± 4 days after the first instillation of medical device under investigation°.

In case of premature study discontinuation, patients will undergo an Early Termination Visit (ETV)'.

The following procedures will be performed:
- Assessment of treatment compliance (reconciliation of the amount of used single dose containers and empty/unused medical device boxes returned by patients to the centre)§;
- Current medical conditions;

- Concomitant medications;
- Evaluation of any reported adverse events/incidents**;
- Ocular examination of both eyes:
  - External Ocular Examination;
  - BCVA test through the ETDRS at 4 m distance;
  - Symptom Assessment in Dry Eye by SANDE questionnaire;
  - Evaluation of Intraocular pressure (IOP);
  - Tear film break-up time with fluorescein (TFBUT)ϕ;
  - Ocular surface staining (NEI score) with fluorescein;
- Administration of the VAS scale on the degree of satisfaction to the treatment;
- DEQS questionnaire administration;
- Evaluation of the safety of the experimental product through the compilation of the IGAS scale;
- Restitution of remaining medical devices§.

* Start of the treatment (window + 1 day).
** In case of adverse events/incidents all assessments considered necessary by the Investigator was performed, including the possible suspension of treatment.
*** Variable because it is based on the planned visit schedule according to clinical practice for the individual patient Visit 2 (windows of ± 2 days).
° All patients enrolled were treated for 35 days. The Study Termination Visit is variable because it is based on the planned visit schedule according to clinical practice for the individual patient (window ± 4 days).
§ Restitution of the amount of used single dose containers and empty/unused medical device boxes returned by patients to the centre.
'In case of premature study discontinuation, patients were undergoing an Early Termination Visit (ETV). During the ETV the patients will return the amount of used single dose containers and empty/unused medical device boxes returned by patients to the centre·
 The "unique subject identifiers code" consists of the 5-digit screening number (e.g. S1001, S1002,….S1028 etc.), and, if applicable, the 4-digit subject clinical investigational number (e.g. 1001, 1002,…1028 etc.). Specifically, the first subject clinical investigational number was referred to the study site.
Allocation screening number and subject clinical investigational number are separated by slashes (e.g. "S1001/1001"). (e.g. "S1001/1001" for site number 1, "S2001/2001" for site number 2).
ϕ The TFBUT value will be recorded as the average of 3 measurements.

4.2. Treatment Administration

All patients meeting the inclusion and exclusion criteria

4.3. Randomization and Blinding

Not applicable: open-label clinical investigation

4.4. Clinical Investigation Scheme

Study Procedure	Visit 1 (screening- enrolment- start of treatment)*	Visit 2*** (on the 14th day from the first instillation of medical device) (window ± 2 days)	Study termination Visit° (on the 35th day from the first instillation of medical device) (window ± 4 days)
Informed Consent	√		
Allocation screening number	√		
Demographic data collection	√		
Medical and surgical history	√		
Current medical conditions	√	√	√
Prior ocular local and systemic medication	√		
Concomitant ocular local and systemic medication		√	√
External Ocular Examination	√	√	√
BCVA evaluation through ETDRS grade	√	√	√
SANDE questionnaire	√	√	√
Evaluation of Intraocular pressure (IOP)	√	√	√
Ocular surface staining (Fluorescein- NEI score)	√	√	√
Tear Film Break-up Time$^{\phi}$ (TFBUT- Fluorescein)	√	√	√
Administration of DEQS$^{\#\#\#}$ questionnaire	√		√
Inclusion/Exclusion Criteria	√		

Enrolment and allocation subject clinical investigational number	√		
Generation of unique subject identifiers code□	√		
Medical device dispensing*	√		
Check Compliance (check proper treatment with medical device, use of other medication and medical devices)		√	√
Medical device restitution§ '			√
Evaluation of satisfaction to the treatment by VAS scale			√
Evaluation of IGAS			√
Adverse events /Incidents**		√	√

* Start of the treatment (window + 1 day).

** In case of adverse events/incidents all assessments considered necessary by the Investigator will be performed, including the possible suspension of treatment.

*** Variable because it is based on the planned visit schedule according to clinical practice for the individual patient Visit 2 (windows of ± 2 days).

° All patients enrolled will be treated for 35± 4 days. The Study Termination Visit is variable because it is based on the planned visit schedule according to clinical practice for the individual patient (window ± 4 days).

§ Restitution of the amount of used single dose containers and empty/unused medical device boxes returned by patients to the centre.

'In case of premature study discontinuation, patients will undergo an Early Termination Visit (ETV). During the ETV the patients will return the amount of used single dose containers and empty/unused medical device boxes returned by patients to the centre.

□ The "unique subject identifiers code" consists of the 5-digit screening number (e.g. S1001, S1002,….S1028 etc.), and, if applicable, the 4-digit subject clinical investigational number (e.g. 1001, 1002,…1028 etc.). Specifically, the first subject clinical investigational number was referred to the study site.
Allocation screening number and subject clinical investigational number are separated by slashes (e.g. "S1001/1001"). (e.g. "S1001/1001" for site number 1, "S2001/2001" for site number 2).

ϕ The TFBUT value will be recorded as the average of 3 measurements.

###In the event that, for both trial centers, the DEQS questionnaire is not available, the assessment of the quality of the life will be performed by the DEQ-5 questionnaire.

5. PRIMARY AND SECONDARY OUTCOMES^

5.1. Primary Endpoints#

- *Clinical performance:*

-25 % increase from Visit 1 (*Day 0 of treatment - baseline*) to Study Termination Visit (*Day 35 ± 4 of treatment*) of tear film break-up time with fluorescein (TFBUT)ϕ [Time frame: Visit 1 and Study Termination Visit].

For more details see paragraph 13 and the list and samples of tables, figures and graphs, reported in paragraph 15.

5.2. Secondary Endpoints

- Reduction from baseline (*Visit 1- Day 0 of treatment*) in the corneal and conjunctival fluorescein staining score using the NEI scale.

Fluorescein staining of the ocular surface is assessed as the total sum of the corneal and conjunctival subregions.

- Corneal Fluorescein Staining (NEI score, sum of 5 subregions, maximum score 15. Each subregion will have a maximum score of 3.
(0=no staining, 3 = maximum staining).
- Conjunctival Fluorescein Staining (NEI score, sum of 6 subregions, maximum score 18. Each subregion will have a maximum score of 3.
(0=no staining, 3 = maximum staining).
[Time frame: Visit 1, Visit 2 and Study Termination Visit].

- Tear film break-up time with fluorescein (TFBUT)ϕ. [Time frame: Visit 2 and Study Termination Visit].
- BCVA is measured using the standard Early Treatment Diabetic Retinopathy Study (ETDRS) acuity chart and reported in ETDRS letters. [Time frame: Visit 1, Visit 2 and Study Termination Visit];
- *Patient reported outcomes:*

Change in intensity## and frequency of dry eye symptoms assessed by completing the questionnaire SANDE. [Time frame: Visit 1, Visit 2 and Study Termination Visit].

In the questionnaire SANDE, the term "intensity" has the same meaning than "severity".

- ###Evaluation of the degree of satisfaction to the treatment reported by patients through the use of the visual analogue scale (VAS)###, ranging from 0 to 100 mm, at Study Termination Visit (*Day 35 ± 4 of treatment*). [Time frame: Study Termination Visit].

Patients will be asked to rate their degree of satisfaction to the treatment and answer the following questions:

- "I feel satisfied using this treatment? ",
- "With this treatment, I have a feeling of freshness?",
- "With this treatment, I have a feeling of relief?",

- "This treatment contributed to reduce my pain due to eye dryness?",
- "This treatment is comfortable? ",

Patients will be asked to place a vertical mark on a horizontal line, from 0 to100 mm, to indicate the degree of satisfaction to the treatment, where:

✓ 0-10 mm=none
✓ 11-30 mm=very mild
✓ 31-50 mm=mild
✓ 51-70 mm=moderate
✓ 71-90 mm=strong
✓ 91-100 mm=very strong.

- Assessment of the quality of life (QOL) by "Questionnaire about Eye Symptoms and Daily Life" (DEQS) at Study Termination Visit (Day 35 ± 4 of treatment) compared to Visit 1 (Day 0 of treatment - baseline). [Time frame: Visit 1 and Study Termination Visit].

For more details see paragraph 13 and the list and samples of tables, figures and graphs, reported in paragraph 15.

~~###In the event that, for both trial centers, the DEQS questionnaire is not available, the assessment of the quality of the life will be performed by the DEQ-5 questionnaire.~~

According to clinical practice, the Investigator will perform all clinical evaluations on both eyes of the individual patient.
In the case that both eyes are affected by ocular dry eye, the statistical analysis will be performed considering the eye with the lowest level of TFBUT score "worse eye". If the level of TFBUT score at baseline is the same in both eyes, then the eye with the highest level of NEI score will be designated as the "worse eye". If the level of NEI score at baseline is the same in both eyes, then the right eye will be designated as the "worse eye."

5.3. Safety Endpoints

Evaluation of safety parameters

Evaluation of safety of daily instillation of ophthalmic solution during all the study period through:

- Evaluation of safety of daily instillation of ophthalmic solution during all the study period through:
- Investigator Global Assessment of Safety (IGAS): using the 4-point scale:1= very good safety, 2 =good safety, 3 = moderate safety and 4 = poor safety. IGAS will be evaluated at the Study Termination Visit. [Time Frame: Study Termination Visit];
- Evaluation of reported adverse events/incidents. [Time Frame: During the treatment period].
- Evaluation of intraocular pressure (IOP) [Time frame: Visit 1, Visit 2 and Study Termination Visit];
- Evaluation of *compliance* through verification of correct instillation of the medical device,

counting of single dose containers and boxes. [Time Frame: Visit 2 and Study Termination Visit].

^According to clinical practice, the Investigator will perform all clinical evaluations on both eyes of the individual patient.
The statistical analysis will be performed considering right eye as the "study eye."
#The primary end point will be evaluated on the ITT population and in PP population.
ϕThe TFBUT value will be recorded as the average of 3 measurements.

6. PLANNED ANALYSIS

6.1. Interim Analysis
No interim analysis is planned.

6.2. Final Analysis
Final analysis will be performed according to the current version of the protocol (version 2 of March 14th, 2023) and to this Statistical Analysis Plan (version 1 of October 10th, 2023), after data cleaning operations and Data Base (DB) Lock will be performed.
The statistical analysis will be performed using SAS 9.4 for Windows (SAS Institute Inc., Cary, NC, USA).

7. SAMPLE SIZE AND STATISTICAL POWER CONSIDERATION
A previous study reported by De-Hita-Cantalejo C, et al 2022 [3], baseline level of TFBUT of 6.23±1.75 in patients with moderate dry eye disease. After 30 days of treatment with tear eyedrops containing hyaluronic acid 0.3%, TFBUT was 8.10 ± 2.06 s. To detect a 25% of increase of TFBUT at Study Termination Visit compared to the baseline (Visit 1) (mean difference 1.56, s.d. 1,91), considering an alpha = 0.01 (two-tailed) and a power of 1 – ß = 0.80, 23 patients are required (Wilcoxon signed-rank test). Taking into account an expected dropout of 20%, it is expected to enroll a total of 28 patients.

8. ANALYSIS POPULATIONS
8.1. Screening Failures
Screening failures will be defined as patients who provided informed consent but who were not enrolled ~~randomised~~. Screening Failures will be summarised and presented by a total count.
More details regarding the patient distribution well be described in the consort figure as reported in paragraph 15.1.

8.2 Total Set
The total set will be defined as all patients who provided informed consent as documented on the 'Informed Consent' eCRF page. The total set will be summarized and presented by a total count (without study treatment categorization).

8.3. Intent-to-Treat Population (ITT)

The performance analysis will be performed on the full intent to treat population (ITT) population. The ITT population consisted of all enrolled patients who receive at least one dose of the study experimental product. The patients with no treatment applied at all and the patients who do not have any available data after the first dose of treatment should be excluded from the analysis.

8.4. Per-Protocol (PP) Population

The per protocol set (PPS) will be used for supportive performance analysis. The PPS consisted of patients in the ITT who did not have any major protocol violation.

8.5. Safety Population

The safety population, used for all safety analyses, consisted of all patients who received at least one dose of the medical device.

9.GENERAL ISSUES FOR STATISTICAL ANALYSIS

9.1Definitions, Derived Variables and Datasets

Variable (CRF)	Variable	Type	Description
md_dispensing_q7; checkcomp_and_mdret_q3.	Treat_time	Continuous	Treatment duration
age	Age	Continuous	Age
sex_at_birth	Sex	Discrete	Sex
race	Race	Discrete	Race
eoe_q3; eoe_q4;	Ext_oc_ex	Discrete	External ocular examination
mh_part1_q1; mh_part1_q1_ongoing; mh_part1_q2; mh_part1_q2_ongoing; mh_part1_q3; mh_part1_q3_ongoing; mh_part1_q4; mh_part1_q4_ongoing; mh_part1_q5; mh_part1_q5_ongoing; mh_part1_q6; mh_part1_q6_ongoing; otherprevious_cdiseases; table_otherprevious_cd1.	Med_hist	Discrete	Medical history
concomitant_q1; concomitant_q2; concomitant_q3;	Conc_med	Discrete	Concomitant medications

concomitant_q4.			
tfbut_q2_od; tfbut_q3_od; tfbut_q4_od; tfbut_q2_os; tfbut_q3_os; tfbut_q4_os; tfbut_q5_od_a; tfbut_q5_os_a.	TFBUT	Continuous	Tear film break-up time with fluorescein
cornea_od_totalscore_a; cornea_os_totalscore_a; conjunctiva_od_totalscore_c; conjunctiva_od_totalscore_d; cornea_conjunctiva_os_b_d; cornea_conjunctiva_od_a_c;	NEI_total NEI_cornea NEI_conjunt	Continuous	National Eye Institute Scale
eoe_q5;	BCVA	Continuous	Best Corrected Visual Acuity
sande_q3_severity; sande_q4_frequency; sande_qc_score2;	SANDE_total SANDE_sev SANDE_freq	Continuous	Symptom Assessment in Dry Eye
vasscale_q2; vasscale_cornea_q1; vasscale_cornea_q2; vasscale_cornea_q3; vasscale_cornea_q4; vasscale_cornea_q5;	VAS1 VAS2 VAS3 VAS4 VAS5	Continuous	Degree of satisfaction to the treatment
sensazione_deqs; secchezzaoculare; doloreagliocchi; stanchezzaoculare; pesantezzadellepalpedre; rossoreagliocchi; sensazione_deqs_1; secchezzaoculare_1; doloreagliocchi_1; stanchezzaoculare_1; rossoreagliocchi_1; deqs_q13; deqs_q14; deqs_q15; deqs_3. GES	DEQS_sum_score DEQS_subscale1 DEQS_subscale2	Continuous	Questionnaire about Eye Symptoms and Daily Life
igas_q1	IGAS	Discrete	(Investigator Global Assessment of Safety)

Incident_adverseevent_q1; incident_adverseevents_q2; incident_adverseevent_q3; endofstudy2_q4;	Adv_event_Inc	Discrete	Adverse events/incidents
iop_q2_od; Iop_q2_os;	IOP	Continuous	Evaluation of intraocular pressure
checkcompliance_q1; checkcompliance_q2; checkcompl_and_mdret_q3;	Compliance	Continuous/Discrete	Evaluation of compliance through verification of correct instillation of the medical device

10. STATISTICAL METHODS

Descriptive analysis will be performed by using absolute rate, percentage and frequency tables for qualitative variables.
Normally distributed continuous data will be reported as minimum, maximum, mean and standard deviation, whereas non- normally distributed data as medians and IQR.
Categorical variables will be analyzed by using Yates-corrected chi-square test or Fisher's exact test when appropriate. The McNemar's test will be used to analyze paired nominal data. Differences in endpoints between baseline and different timepoints will be assessed using paired t-test for normally distributed data, whereas the Wilcoxon signed-rank test will be used for non-normally distributed data.
Data distribution will be evaluated through the Kolmogorov-Smirnov test.
A p-value <0.05 will be considered statistically significant.
Analysis will be performed using SAS version 9.4 for Windows (SAS Institute Inc., Cary, NC, USA).

10.1. General Issues for Statistical Analysis

All data will be summarized and listed as appropriate. ~~Performance data will be summarized and listed for the overall population.~~
Performance data will be summarized, listed and described in table for the overall population.
There are no subgroups.
For more details see paragraph 13 and the list and samples of tables, figures and graphs, reported in paragraph 15.

10.2 Definitions, Derived Variables and Datasets

10.2.1 Baseline Values

Data collected at the screening/baseline visit (Visit 1), before the beginning of the treatment, are considered as baseline values.
The last observation carried forward method (LOCF) was used to replace missing data in each performance endpoints.
Baseline and demographic characteristics of the patients will be summarized by using appropriate descriptive statistics.
For more details see paragraph 11.1.

10.2.2 Demographic Data

Demographic data (age, sex, race) were summarized using mean, SD, minimum, maximum, median, lower quartile and upper quartile for continuous variables and number of patients (frequency) and percentage per category for categorical variables.

10.2.3 Duration of Exposure

All patients will be followed from enrolment until study end date, which will occur when, in compliance with the normal clinical practice, the last patient will be patient to the study termination visit (30 days from the first application of study product) (window ±4 day).
For each patient enrolled, the duration of exposure per patient will be estimated as the number of days between the first and last treatment administration. Mean and SD, minimum and maximum number of days of treatment will be reported.

10.2.4 Treatment Compliance

Treatment duration per patient will be estimated as the number of days between the first and last treatment administration. Absolute rate and percentage of days of treatment will be reported.
Compliance will be estimated as the percentage of administrations given with respect to the administrations planned. Compliance will be also reported categorical as <50%, 50-80% and >80%. In particular:
1. <50% = Poor Compliance
2. 50-80% = Moderate Compliance
3. >80% = Good Compliance

Details by patients about compliance well be reported

10.2.5. Methods for Withdrawals and Missing Data

Reasons for withdrawal will be considered and patients will be entered in the analysis on the basis the reason for withdrawal.
If the primary performance measurement at Visit 2 is missing, it will be imputed with the score at baseline. If the primary performance measurement at Study Termination Visit is missing, it will be imputed with the score at Visit 2, if it is not missing, or otherwise with the score at baseline.

10.2.6. Adverse Events

Adverse events will be mapped to a Medical Dictionary for Regulatory Activities (MedDRA)

version 19.1 preferred term and system organ classification.
If a patient has multiple adverse events within the same system organ class in the treatment period, the subject will only be counted once at the system organ class level in adverse event frequency tables. Should an event have a missing severity or relationship, it will be classified as having the highest severity and/or strongest relationship to study medication.
Summaries of incidence rates (frequencies and percentages) of individual AEs by MedDRA system organ class and preferred term will be prepared. Such summaries will be displayed for all TEAEs, TEAEs by maximum severity, and TEAEs by strongest relationship to clinical investigation medical device.
Serious AEs and AEs leading to discontinuation of investigational product will also be summarized.
All adverse events reported will be listed for individual patients showing both verbatim and preferred terms.
Any adverse event with a missing onset date will be considered to be a TEAE occurring during the treatment period.

10.2.7. Premature Discontinuation

Dropout patients will be defined as patients who prematurely discontinued the study. Patients who had stopped the study treatment but were still being followed in the study were not considered as dropouts.
All data available until the premature discontinuation will be taken into account.

10.3 Multicenter Studies Considerations

Not applicable.

10.4 Multiple Comparisons and Multiplicity

When necessary, the multiplicity-adjusted *p*-value will be calculated by multiplying the unadjusted *p*-value by the number of times compared.

10.5 Data Safety Monitoring Board (DSMB)

Not applicable.

11 STUDY PATIENTS

11.1 Disposition of Patients

Patient disposition will be presented in terms of the numbers and percentages of patients who completed the study and discontinued from the study patients who are not discontinued from the study will be considered study completers. The disposition of the patients will be described in the

CONSORT figure.
The number and percentage of patients prematurely discontinued from the study and the reasons for study discontinuation will be for all enrolled patients. The reasons for study discontinuation that will be summarized include: AE, protocol violation, administrative reasons (e.g., inability to continue, lost to follow up), Sponsor termination of study, patient choice, and other. A patient listing will be provided that includes the date of and reason for premature study discontinuation.

11.2 Protocol Deviations

Protocol deviations will be registered in the monitoring visits reports, performed during the study. Protocol deviations will be described in Table and in Listing.
The number and percentage of patients with any, major, and minor protocol deviations will be summarized for all enrolled patients. Major protocol deviations are defined as protocol deviations that may impact primary performance endpoint; other protocol deviations are classified as minor. Protocol deviations will be assessed prior to database lock and unmasking. The number and percentage of patients with any protocol deviation will also be summarized for the following categories: Informed Consent, Inclusion / Exclusion, Instillation of investigational product. Improper Protocol Procedures at Site, Site's Failure to Report Serious Adverse Event (SAE) / AE, Visit Out of Window, patient's Use of Prohibited Concomitant Medication, and Other. A patient listing will be provided that includes the date, description of each deviation and the classification of whether the deviation was judged to be major or minor.
The Sponsor will consider the following criteria for exclusion of a patient from the PPS:

- Impossibility to assess the compliance with investigational medical product application (patients who have not returned the amount of used single dose containers and/or empty/unused medical device boxes);
- Missing primary performance data;
- Failure to satisfy any inclusion/exclusion criteria;
- Intake of prohibited medications.

12PERFORMANCE ANALYSIS

12.1 Analysis datasets

See Section 10.

12.2 Demographics and Baseline Characteristics

Demographic (age, gender, ethnic origin) and baseline characteristics (vital signs, weight, height, medical history, and physical examination) will be summarized by using minimum, maximum, mean, standard deviation or median and IQR for continuous variables and number of patients and percentage per category for categorical variables.

12.3 Measurements of Treatment Compliance

Details by patients will be reported and compliance will be estimated as the percentage of administrations given with respect to the administrations planned.

$$Compliance\ (\%) = \frac{Numbers\ of\ vial\ dispensed - Number\ of\ unused\ vials\ returned}{Number\ of\ doses\ planned}$$

Compliance will be presented categorical as <50% 50-80% and >80%, were:
1) <50% = Poor Compliance
2) 50-80% = Moderate Compliance
3) >80% = Good Compliance

No further analyses will be planned on compliance. All other collected data including diary information on treatment compliance will be evaluated during the BDRM for relevant protocol deviations and will be listed.

13 ANALYSIS OF PERFORMANCE

13.1 Primary performance endpoint

The primary endpoint consists in the assessment of 25 % increase from Visit 1 (*Day 0 of treatment - baseline*) to Study Termination Visit (*Day 35 ± 4 of treatment*) of tear film break-up time with fluorescein (TFBUT)$^{\phi}$. The data will be reported (change vs baseline) as minimum, maximum, mean, standard deviation or median and IQR. According to the data distribution, paired t-test or Wilcoxon signed-rank test will be used to test the statistical significance of the change from baseline to each time points. [Time frame: Visit 1, and Study Termination Visit].

Patients with a Tear Film Break-up Time TFBUT test ≤ 10 in the study eye (study eye) at the screening visits are eligible for enrollment.

TFBUT will be measured by determining the time to tear break-up. The TFBUT will be performed after instillation of 5 µl of 2% preservative-free sodium fluorescein solution into the inferior conjunctival cul-de-sac of each eye. The patient will be instructed to blink several times to thoroughly mix the fluorescein with the tear film. To achieve maximum fluorescence, the examiner should wait approximately 30 seconds after instillation before evaluating TFBUT. With the aid of a slit lamp at 10X magnification using cobalt blue illumination, the examiner will monitor the integrity of the tear film, noting the time it takes to form lacunae (clear spaces in the tear film) from the time that the eye is opened after the last blink. This measurement will be performed within 10 seconds maximum. The TFBUT will be measured twice during the first minute after the instillation of the fluorescein. The TFBUT value will be the average of 3 measurements.

13.2 Secondary objective

The secondary objectives were:

Clinical Performance

- Changes in NEI score from baseline will be summarized as minimum, maximum, mean,

standard deviation or median and IQR. Paired t-test or Wilcoxon signed-rank test will be used to test the statistical significance of the change from baseline to each timepoints. [Time frame: Visit 1, Visit 2 and Study Termination Visit].
The cornea is divided into five sectors (central, superior, inferior, nasal and temporal), each of which is scored on a scale of 0–3, with a maximal score of 15. Both nasally and temporally, the conjunctiva is divided into a superior paralimbal area, an inferior paralimbal area and a peripheral area with a grading scale of 0–3 and with a maximal total score of 18 for the nasal and temporal conjunctiva.
For a better reading it is also essential not to use an intense illumination beam, which may reduce the contrast and lead to an underestimation of grading.

- Changes in TFBUT from baseline will be reported as minimum, maximum, mean standard deviation or median and IQR. Paired t-test or Wilcoxon signed-rank will be used to test the statistical significance of the change from baseline to each timepoints. [Time frame: Visit 2, and Study Termination Visit].

- Change in the BVCA scores will be summarized as minimum, maximum, mean, standard deviation or median and IQR. Paired t-test or Wilcoxon signed-rank test will be used to test the statistical significance. Details of changes (i.e., difference in BVCA scores between baseline and end of treatment) will be summarized as well. [Time frame: Visit 1, Visit 2 and Study Termination Visit].

- Best Corrected Visual Acuity BCVA was measured using the standard Early Treatment Diabetic Retinopathy Study (ETDRS) acuity chart lighting, and procedures and reported in Best-corrected visual acuity is measured at all trial visits using standard charts, (chart 1 is used for testing the visual acuity of the RIGHT eye; Chart 2 for testing the LEFT eye). Patients should not be allowed to see any of the charts before the examination.
A distance of 4 meters is required between the patient's eyes and the visual acuity chart. With the box light off, not more than 15 foot-candles of light (161.4 Lux) should fall on the center of the chart. To measure the amount of light, the room is set up for visual acuity testing, but with the box light off. The light meter is placed at the fourth line from the top of the chart, with its back against the chart and the reading is taken. If more than one line available for testing visual acuity, the visual acuity of an individual patient should be measured in the same line at each visit, if possible. If different lines are used to test visual acuity, they must each meet the same standards.

Patient reported outcomes:

- Change in the SANDE scores will be summarized as minimum, maximum, mean, standard deviation or median and IQR. Paired t-test or Wilcoxon signed-rank test will be used to test the statistical significance. Details of changes (i.e., difference in SANDE scores between

baseline and end of treatment) will be summarized as well. [Time frame: Visit 1, Visit 2 and Study Termination Visit].

The SANDE questionnaire is a short questionnaire to evaluate both the intensity and frequency of dry eye using a 100 mm VAS. The patient's symptoms of ocular dryness and/or irritation will be quantified on the scale based on two questions assessing both severity and frequency of symptoms. For the assessment, patients mark the point that they feel represents their perception of their current state on the 100 mm VAS line. The VAS score is determined by measuring in millimeters from the left-hand end of the line to the point that the patient marks. The SANDE scores will be then evaluated for the 2 questions severity (0-100) and frequency (0-100). To simplify the procedure the patient will be informed that to provided anchors for the question measuring the frequency of symptoms, the extreme left of the 100 mm line indicated "rarely" and the extreme right indicated "all of the time". Similarly, for the question that measured the severity of symptoms, the words "very mild" and "very severe" were placed at the left and right ends of the 100 mm line, respectively.

At each visit, only one assessment is performed aggregating the situation for both eyes (i.e. no separate assessment per study eye).

Data collected from the SANDE questionnaire were calculated by multiplying the frequency score by the severity score and obtaining the square root.

- VAS will be summarized reporting the number of patients and related percentage in each category. [Time frame: Study Termination Visit].

Patients will be asked to rate their degree of satisfaction to the treatment and answer the following questions:

- "I feel satisfied using this treatment? ",
- "With this treatment, I have a feeling of freshness?",
- "With this treatment, I have a feeling of relief?",
- "This treatment contributed to reduce my pain due to eye dryness?",
- "This treatment is comfortable? ",

Patients will be asked to place a vertical mark on a horizontal line, from 0 to100 mm, to indicate the degree of satisfaction to the treatment, where:

✓ 0-10 mm=none
✓ 11-30 mm=very mild
✓ 31-50 mm=mild
✓ 51-70 mm=moderate
✓ 71-90 mm=strong
✓ 91-100 mm=very strong.

- Changes from baseline in DEQS for each subscale and total score will be summarized as minimum, maximum, mean, standard deviation or median and IQR. Paired t-test or Wilcoxon signed-rank test will be used to test the statistical significance of the change from baseline to the study termination. [Time frame: Visit 1 and Study Termination Visit].

The DEQS questionnaire consists of 15 questions divided in two subscales: the Bothersome Ocular Symptoms (six questions) and the Impact on Daily Life (nine questions). Each question is assessed using two-step scales. The first step is to assess the frequency of symptoms and disability, and the second is to assess the degree of severity. The frequency is scored on a 5-point Likert scale ranging from 0 to 4 (0 = never, 4=always). When the answer was "never," then the respondent could skip to the next question; but when any frequency was reported (1–4), the respondent had to rate the degree of severity, which was scored on a 4-point Likert scale ranging from 1 to 4, with a larger number indicating a greater burden.
The total score of the answer will be calculated using the summation of the degree scores of all questions answered multiplied by 25 and divided by the total number of questions answered. The total score ranging from 0 to 100, with a higher score, represented greater disability.

$$Total\ summary\ score = \frac{(Sum\ of\ the\ degree\ scores\ for\ all\ questions\ answered X\ 25)}{Total\ number\ of\ questions\ answered}$$

Subscale scores will be calculated similarly, using only the item from each subscale.

- GENERAL EYES STATUS (GES) will be summarized as minimum, maximum, mean, standard deviation or median and IQR. Paired t-test or Wilcoxon signed-rank test will be used to test the statistical significance of the change from baseline to the study termination. [Time frame: Visit 1 and Study Termination Visit].
  GENERAL EYES STATUS will be assessed using the degree scores of a question answered using the 6-point scale:1= Estremamente bene, 2 = Molto bene, 3 = Bene, 4 = Male, 5= Molto male and 6= Estremamente male.

Safety Evaluation:

- IGAS will be summarized reporting the number of patients and related percentage in each category. [Time frame: Study Termination Visit].
  The Safety of medical device will be assessed using the Investigator Global Assessment of Safety (IGAS): using the 4-point scale:1= very good safety, 2 =good safety, 3 = moderate safety and 4 = poor safety. IGAS will be evaluated during the Study Termination Visit. [Time Frame: Study Termination Visit].

- Incidents will be coded using the last updated version of the MedDRA dictionary to give a preferred term (PT) and a system/organ class term (SOC) for each event. The number of patients who experienced at least one incident, study product-related incidents, serious incidents, and the number of patients withdrawn due to an incident will be summarized. The frequency of incidents will be presented overall, by SOC and PT, and additional grouping by severity and relationship to the observed treatment will be performed. [Time Frame: During the treatment period].

- Changes from baseline in IOP will be summarized as minimum, maximum, mean, standard deviation or median and IQR. Paired t-test or Wilcoxon signed-rank will be used to test the statistical significance of the change from baseline to each timepoints. [Time frame: Visit 1, Visit 2 and Study Termination Visit].

  Intraocular pressure (IOP) measurement was performed using a Goldmann applanation tonometer after topical anesthesia with unpreserved 0.4% oxybuprocaine hydrochloride.

Moreover, for each endpoint, a delta % calculation will be performed.

14. CHANGES IN THE PLANNED ANALYSES

No deviations in the conduct of the study or the planned analysis are anticipated. Should any deviations from the analyses specified in the authorized statistical analysis plan arise, such deviations will be documented in the final clinical study report.

15. LIST AND SAMPLES OF TABLES, FIGURES AND GRAPHS

The following lists of tables might not be exhaustive. Additional tables can be produced if necessary.

For each comparison of the various quantitative endpoints (visit 2 versus visit 1 and visit 3 versus visit 1) the descriptive statistics of the endpoint at the two visits will first be calculated and then the P-value will be calculated to assess the statistical significance of the difference. This difference will also be reported as a percentage from baseline.

15.1 LIST AND SAMPLES OF FIGURES

1 DISPOSITION OF PATIENTS

Figure 1 Patient's disposition by CONSORT.

15.2 LIST AND SAMPLES OF TABLES

1 TREATMENT DURATION

Table 1 Treatment duration ITT population

2 DEMOGRAPHICS AND OTHER BASELINE DATA

Table 2.1.1 Demographic characteristics (screened patients) Age
Table 2.1.2 Demographic characteristics of Age

Table 2.1.2 Demographic characteristics (screened patients) Sex
Table 2.1.3 Demographic characteristics (screened patients) Race

Table 2.2.1 Demographic characteristics (ITT population) Age
Table 2.2.2 Demographic characteristics (ITT population) Sex

Table 2.2.3 Demographic characteristics (ITT population) Race

Table 2.3.1 Demographic characteristics (PP population) Age
Table 2.3.2 Demographic characteristics (PP population) Sex
Table 2.3.3 Demographic characteristics (PP population) Race

Table 2.4.2.1 Medical history (Visit 1: ITT population)
Table 2.4.2.2 Medical history (Visit 2: ITT population)
Table 2.4.2.3 Medical history (Visit 3: ITT population)
Table 2.4.2.4 Concomitant medications (ITT population)
Table 2.4.3.1 Medical history (Visit 1: PP population)
Table 2.4.3.2 Medical history (Visit 2: PP population)
Table 2.4.3.3 Medical history (Visit 3: PP population)
Table 2.4.3.4 Concomitant medications (PP population)

3 COMPLIANCE DATA
Table 3.1 % Administered doses over the planned doses (ITT population)
Table 3.2 % Administered doses over the planned doses (PP population)

4 PERFORMANCE DATA (PRIMARY ENDPOINTS)

Table 4.1.1 TFBUT ITT population (v1) vs (v3)
Table 4.1.2 Delta % TFBUT ITT population (v1) vs (v3)
Table 4.2.1 TFBUT PP population (v1) vs (v3)
Table 4.2.2 Delta % TFBUT PP population (v1) vs (v3)

5 PERFORMANCE DATA (SECONDARY ENDPOINTS)
-NEI Scale ITT population
Table 5.1.1 TOTAL SCORE NEI ITT population (v1) vs (v3)
Table 5.2.1 TOTAL SCORE NEI ITT population (v1) vs (v2)
Table 5.3.1 TOTAL SCORE CORNEA ITT population (v1) vs (v3)
Table 5.3.2 TOTAL SCORE CORNEA ITT population (v1) vs (v2)
Table 5.4.1 TOTAL SCORE CONJUNCTIVA ITT population (v1) vs (v3)
Table 5.4.2 TOTAL SCORE CONJUNCTIVA ITT population (v1) vs (v2)

-TFBUT ITT POPULATION
Table 5.5.1 TFBUT ITT population (v1) vs (v2)

-Questionnaire SANDE ITT population
Table 5.6.1 TOTAL SCORE SANDE ITT population (v1) vs (v3)
Table 5.7.1 TOTAL SCORE SANDE ITT population (v1) vs (v2)

Table 5.8.1 SEVERITY DRYNESS/IRRITATION ITT population (v1) vs (v3)
Table 5.8.2 SEVERITY DRYNESS/IRRITATION ITT population (v1) vs (v2)

Table 5.9.1 FREQUENCY DRYNESS/IRRITATION ITT population (v1) vs (v3)
Table 5.9.2 FREQUENCY DRYNESS/IRRITATION ITT population (v1) vs (v2)

-Questionnaire VAS ITT population

Table 5.10.1 Question "I feel satisfied using this treatment? ", ITT population
Table 5.10.2 Question "With this treatment, I have a feeling of freshness?", ITT population.
Table 5.10.3 Question "With this treatment, I have a feeling of relief?", ITT
Table 5.10.4 Question "This treatment contributed to reduce my pain due to eye dryness?", ITT population
Table 5.10.5 Question "This treatment is comfortable? ", ITT population
Table 5.10.6 Total score VAS, ITT population

-DEQS ITT POPULATION
Table 5.11.1.1 DEQS Summary score ITT population (v1) vs (v3)
Table 5.11.2.1 DEQS Bothersome Ocular Symptoms subscale ITT population (v1) vs (v3)
Table 5.11.3.1 DEQS Impact on Daily Life subscale ITT population (v1) vs (v3)
Table 5.11.4.1 DEQS-GES ITT population (v1) vs (v3)

-IGAS
Table 5.12.1 IGAS ITT populations

-IOP ITT POPULATION
Table 5.13.1 IOP ITT population (v1) vs (v3)
Table 5.14.1 IOP ITT population (v1) vs (v2)

16. LIST OF LISTING

FIGURE 1: Patient deposition

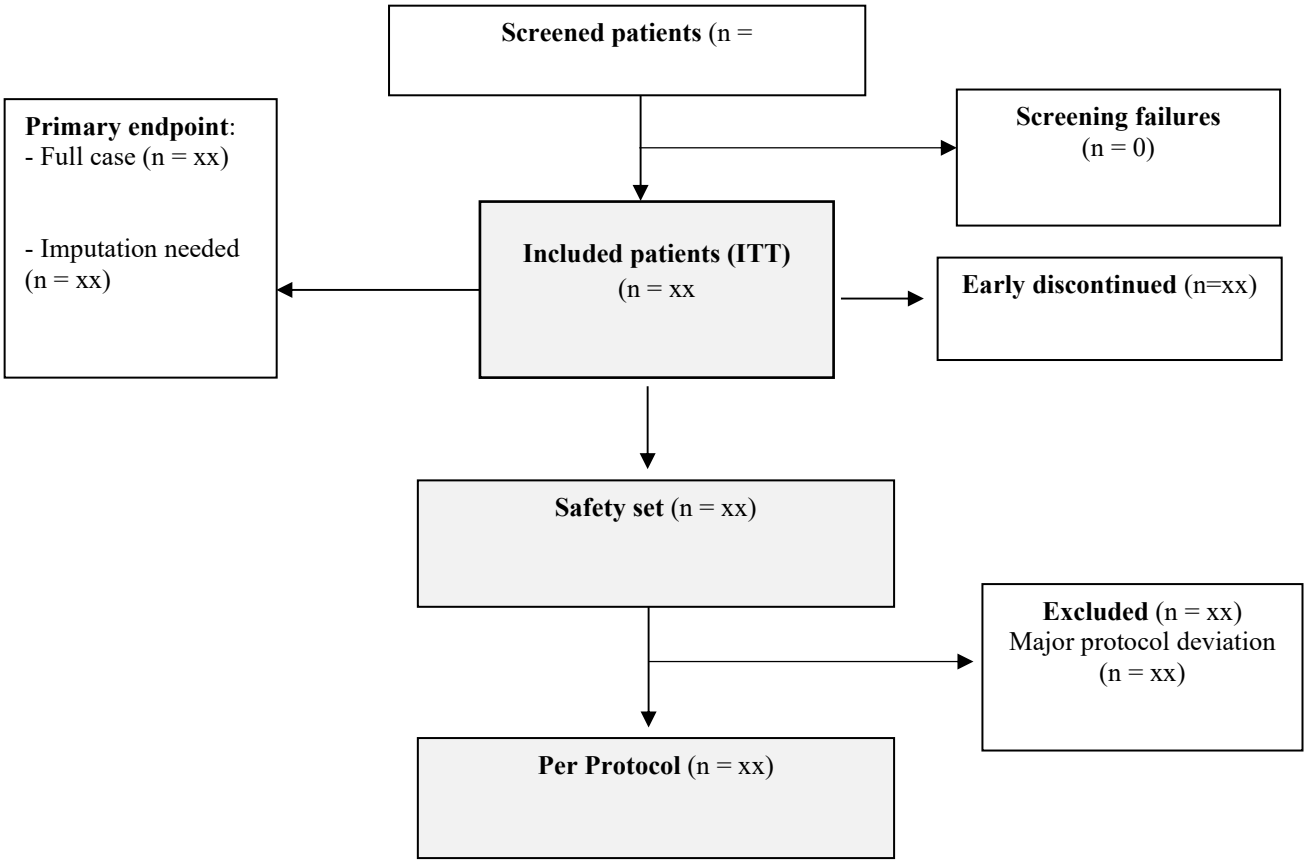

Table 1

ITT population

Analysis variable: ***Treatment duration***

Mean	*Std Dev*	*Min*	*Max*	*N*	*lower quartile*	*Median*	*upper quartile*
x.xx	x.xx	x.xx	x.xx	xx	x.xx	x.xx	x.xx

Test for Normality

Test	*Statistic*		*P-value*	
Shapiro-Wilk	W	x.xxx	Pr < W	x.xxx
Kolmogorov-Smirnov	D	x.xxx	Pr > D	x.xxx
Cramer-von Mises	W-Qu	x.xxx	Pr > W-Qu	x.xxx
Anderson-Darling	A-Qu	x.xxx	Pr > A-Qu	x.xxx

Program SAS 9.4 ('Local', X64_10HOME) date xx XXX xxxx

Table 2.1.1 Demographics and other baseline data

Screened patients

Analysis variable: ***Age***

Mean	*Std Dev*	*Min*	*Max*	*N*	*lower quartile*	*Median*	*upper quartile*
x.xx	x.xx	x.xx	x.xx	xx	x.xx	x.xx	x.xx

Test for Normality

Test		*Statistic*	*P-value*	
Shapiro-Wilk	W	x.xxx	Pr < W	x.xxx
Kolmogorov-Smirnov	D	x.xxx	Pr > D	x.xxx
Cramer-von Mises	W-Qu	x.xxx	Pr > W-Qu	x.xxx
Anderson-Darling	A-Qu	x.xxx	Pr > A-Qu	x.xxx

Program SAS 9.4 ('Local', X64_10HOME) date xx XXX xxxx

Table 2.1.2 Demographics and other baseline data

Screened patients

Sex

	N	*%*
Male	X	xx.xx
Female	X	xx.xx

Program SAS 9.4 ('Local', X64_10HOME) date xx XXX xxxx

Table 2.1.3 Demographics and other baseline data

Screened patients

Race

	N	*%*
Caucasian	x	xx.xx
Xxxxx	x	xx.xx
Xxxxx	x	xx.xx

Program SAS 9.4 ('Local', X64_10HOME) date xx XXX xxxx

Table 2.2.1 Demographics and other baseline data

ITT population

Analysis variable: ***Age***

Mean	*Std Dev*	*Min*	*Max*	*N*	*lower quartile*	*Median*	*upper quartile*
x.xx	x.xx	x.xx	x.xx	xx	x.xx	x.xx	x.xx

Test for Normality

Test		*Statistic*		*P-value*
Shapiro-Wilk	W	x.xxx	Pr < W	x.xxx
Kolmogorov-Smirnov	D	x.xxx	Pr > D	x.xxx
Cramer-von Mises	W-Qu	x.xxx	Pr > W-Qu	x.xxx
Anderson-Darling	A-Qu	x.xxx	Pr > A-Qu	x.xxx

Age (classes, years)

	N	*%*
[18-64]	x	xx.xx
>65	x	xx.xx

Age by sex

Analysis variable: ***Age males***

Mean	*Std Dev*	*Min*	*Max*	*N*	*lower quartile*	*Median*	*upper quartile*
x.xx	x.xx	x.xx	x.xx	xx	x.xx	x.xx	x.xx

Test for Normality

Test		*Statistic*	*P-value*	
Shapiro-Wilk	W	x.xxx	Pr < W	x.xxx
Kolmogorov-Smirnov	D	x.xxx	Pr > D	x.xxx
Cramer-von Mises	W-Qu	x.xxx	Pr > W-Qu	x.xxx
Anderson-Darling	A-Qu	x.xxx	Pr > A-Qu	x.xxx

Analysis variable: ***Age females***

Mean	*Std Dev*	*Min*	*Max*	*N*	*lower quartile*	*Median*	*upper quartile*
x.xx	x.xx	x.xx	x.xx	xx	x.xx	x.xx	x.xx

Test for Normality

Test		*Statistic*	*P-value*	
Shapiro-Wilk	W	x.xxx	Pr < W	x.xxx
Kolmogorov-Smirnov	D	x.xxx	Pr > D	x.xxx
Cramer-von Mises	W-Qu	x.xxx	Pr > W-Qu	x.xxx
Anderson-Darling	A-Qu	x.xxx	Pr > A-Qu	x.xxx

Program SAS 9.4 ('Local', X64_10HOME) date xx XXX xxxx

Table 2.2.2 Demographics and other baseline data

ITT population

Sex

	N	*%*
Male	x	xx.xx
Female	x	xx.xx

Program SAS 9.4 ('Local', X64_10HOME) date xx XXX xxxx

Table 2.2.3 Demographics and other baseline data

ITT population

Race

	N	*%*
Caucasian	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx

Program SAS 9.4 ('Local', X64_10HOME) date xx XXX xxxx

Table 2.3.1 Demographics and other baseline data

PP population

Analysis variable: ***Age***

Mean	*Std Dev*	*Min*	*Max*	*N*	*lower quartile*	*Median*	*upper quartile*
x.xx	x.xx	x.xx	x.xx	xx	x.xx	x.xx	x.xx

Test for Normality

Test		*Statistic*		*P-value*
Shapiro-Wilk	W	x.xxx	Pr < W	x.xxx
Kolmogorov-Smirnov	D	x.xxx	Pr > D	x.xxx
Cramer-von Mises	W-Qu	x.xxx	Pr > W-Qu	x.xxx
Anderson-Darling	A-Qu	x.xxx	Pr > A-Qu	x.xxx

Age (classes, years)

	N	*%*
[18-64]	x	xx.xx
>65	x	xx.xx

Program SAS 9.4 ('Local', X64_10HOME) date xx XXX xxxx

Table 2.3.2 Demographics and other baseline data

PP population

Sex

	N	*%*
Male	x	xx.xx
Female	x	xx.xx

Program SAS 9.4 ('Local', X64_10HOME) date xx XXX xxxx

Table 2.3.3 Demographics and other baseline data

PP population

Race

	N	*%*
Caucasian	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx

Program SAS 9.4 ('Local', X64_10HOME) date xx XXX xxxx

Table 2.4.2.1 Demographics and other baseline data

ITT population

Medical history (Visit 1)

	N	*%*
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx

Program SAS 9.4 ('Local', X64_10HOME) date xx XXX xxxx

Table 2.4.2.2 Demographics and other baseline data

ITT population

Medical history (Visit 2)

	N	*%*
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx

Program SAS 9.4 ('Local', X64_10HOME) date xx XXX xxxx

Table 2.4.2.3 Demographics and other baseline data

ITT population

Medical history (Visit 3)

	N	*%*
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx

Program SAS 9.4 ('Local', X64_10HOME) date xx XXX xxxx

Table 2.4.2.4 Demographics and other baseline data

ITT population

Concomitant medications

	N	*%*
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx

Program SAS 9.4 ('Local', X64_10HOME) date xx XXX xxxx

Table 2.4.3.1 Demographics and other baseline data

PP population

Medical history (Visit 1)

	N	*%*
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx

Program SAS 9.4 ('Local', X64_10HOME) date xx XXX xxxx

Table 2.4.3.2 Demographics and other baseline data

PP population

Medical history (Visit 2)

	N	*%*
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx

Program SAS 9.4 ('Local', X64_10HOME) date xx XXX xxxx

Table 2.4.3.3 Demographics and other baseline data

PP population

Medical history (Visit 3)

	N	*%*
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx

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Table 2.4.3.4 Demographics and other baseline data

PP population

Concomitant medications

	N	*%*
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx
xxxxx	x	xx.xx

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Table 3.1 % Administered doses over the planned doses

ITT population

% Administered doses over the planned doses

		N	*%*
xxxxx		x	xx.xx
xxxxx		x	xx.xx
xxxxx		x	xx.xx
xxxxx		x	xx.xx
xxxxx		x	xx.xx
xxxxx		x	xx.xx
xxxxx		x	xx.xx
<50 %	*Poor Compliance*	x	xx.xx
50-80 %	*Moderate Compliance*	x	xx.xx
> 80 %	*Good Compliance*	x	xx.xx

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Table 3.2 % Administered doses over the planned doses

PP population

% Administered doses over the planned doses

xxxxx		x	xx.xx
xxxxx		x	xx.xx
xxxxx		x	xx.xx
xxxxx		x	xx.xx
xxxxx		x	xx.xx
xxxxx		x	xx.xx
xxxxx		x	xx.xx
		N	*%*
<50 %	*Poor Compliance*	x	xx.xx
50-80 %	*Moderate Compliance*	x	xx.xx
> 80 %	*Good Compliance*	x	xx.xx

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Table 4.1.1 TFBUT ITT population (v1) vs (v3)

ITT population

TFBUT v1 vs v3

Variable: TFBUT Visit 1

Test for Normality				
Test	*Statistic*		*P-value*	
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: TFBUT Visit 3

Test for Normality				
Test	*Statistic*		*P-value*	
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: Difference TFBUT Visit 3 – Visit 1

Basic Statistical Measures

Location		*Variability*	
Mean	x.xx	Std dev	x.xx
Median	x.xx	Variance	x.xx
Mode	x.xx	Range	x.xx
		Interquartile range	x.xx

Location test: Mu0=0

Test	*Statistic*		*P-value*	
Student's T	t	x.xxx	Pr > |t|	x.xxxx
sign	M	xx	Pr >= |M|	x.xxxx
Signed rank	S	x.xxx	Pr >= |S|	x.xxxx

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Table 4.1.2 Delta % TFBUT ITT population v1-v3

Analysis variable: Delta % TFBUT v1-v3

Mean	*Std Dev*	*Min*	*Max*	*N*	*Lower quartile*	*Median*	*Upper quartile*
x.xx	x.xx	x.xx	x.xx	xx	x.xx	x.xx	x.xx

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Table 4.2.1 TFBUT PP population (v1) vs (v3)

PP population
TFBUT v1 vs v3

Variable: TFBUT Visit 1

Test for Normality				
Test	*Statistic*		*P-value*	
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: TFBUT Visit 3

Test for Normality				
Test	*Statistic*		*P-value*	
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*

Variable: DifferenceTFBUT Visit 3 – Visit 1

Basic Statistical Measures

Location		*Variability*	
Mean	x.xx	Std dev	x.xx
Median	x.xx	Variance	x.xx
Mode	x.xx	Range	x.xx
		Interquartile range	x.xx

Location test: Mu0=0

Test	*Statistic*			
Student's T	t	x.xxx	Pr > |t|	x.xxxx
sign	M	xx	Pr >= |M|	x.xxxx
Signed rank	S	x.xxx	Pr >= |S|	x.xxxx

Program SAS 9.4 ('Local', X64_10HOME) date xxXXxxxx

Table 4.2.2 Delta % TFBUT PP population v1-v3

Analysis variable: Delta % TFBUT v1-v3

Mean	*Std Dev*	*Min*	*Max*	*N*	*Lower quartile*	*Median*	*Upper quartile*
x.xx	x.xx	x.xx	x.xx	xx	x.xx	x.xx	x.xx

Table 5.1.1 TOTAL SCORE NEI ITT population (v1) vs (v3)

ITT population

TOTAL SCORE NEI v1 vs v3

Variable TOTAL SCORE NEI Visit 1

Test for Normality

Test		*Statistic*		*P-value*	
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx	
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx	
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx	
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx	

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: TOTAL SCORE NEI Visit 3

Test for Normality

Test		*Statistic*		*P-value*	
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx	
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx	
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx	
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx	

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*

Variable: Difference TOTAL SCORE NEI Visit 3 – Visit 1

Basic Statistical Measures

Location		*Variability*	
Mean	x.xx	Std dev	x.xx
Median	x.xx	Variance	x.xx
Mode	x.xx	Range	x.xx
		Interquartile range	x.xx

Location test: Mu0=0

Test	*Statistic*		*P-value*	
Student's T	t	x.xxx	Pr > |t|	x.xxxx
sign	M	xx	Pr >= |M|	x.xxxx
Signed rank	S	x.xxx	Pr >= |S|	x.xxxx

Program SAS 9.4 ('Local', X64_10HOME) date xxXXXxxxx

Table 5.2.1 TOTAL SCORE NEI ITT population (v1) vs (v2)

ITT population

TOTAL SCORE NEI v1 vs v2

Variable TOTAL SCORE NEI Visit 1

Test for Normality

Test		*Statistic*		*P-value*
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: TOTAL SCORE NEI Visit 2

Test for Normality

Test		*Statistic*		*P-value*
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*

Variable: Difference TOTAL SCORE NEI Visit 2 – Visit 1

Basic Statistical Measures

Location		*Variability*	
Mean	x.xx	Std dev	x.xx
Median	x.xx	Variance	x.xx
Mode	x.xx	Range	x.xx
		Interquartile range	x.xx

Location test: Mu0=0

Test	*Statistic*		*P-value*	
Student's T	t	x.xxx	Pr > |t|	x.xxxx
sign	M	xx	Pr >= |M|	x.xxxx
Signed rank	S	x.xxx	Pr >= |S|	x.xxxx

Program SAS 9.4 ('Local', X64_10HOME) date xxXXXxxxx

Table 5.3.1 TOTAL SCORE CORNEA ITT population (v1) vs (v3)

ITT population

TOTAL SCORE CORNEA v1 vs v3

Variable TOTAL SCORE CORNEA Visit 1

Test for Normality

Test		*Statistic*		*P-value*
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: TOTAL SCORE CORNEA Visit 3

Test for Normality

Test		*Statistic*		*P-value*
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*

Variable: Difference TOTAL SCORE CORNEA Visit 3 – Visit 1

Basic Statistical Measures

Location		*Variability*	
Mean	x.xx	Std dev	x.xx
Median	x.xx	Variance	x.xx
Mode	x.xx	Range	x.xx
		Interquartile range	x.xx

Location test: Mu0=0

Test	*Statistic*		*P-value*	
Student's T	t	x.xxx	Pr > |t|	x.xxxx
sign	M	xx	Pr >= |M|	x.xxxx
Signed rank	S	x.xxx	Pr >= |S|	x.xxxx

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Table 5.3.2 TOTAL SCORE CORNEA ITT population (v1) vs (v2)

ITT population

TOTAL SCORE CORNEA v1 vs v2

Variable TOTAL SCORE NEI Visit 1

Test for Normality

Test		*Statistic*		*P-value*
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: TOTAL SCORE CORNEA Visit 2

Test for Normality

Test		*Statistic*		*P-value*
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*

Variable: Difference TOTAL SCORE CORNEA Visit 2 – Visit 1

Basic Statistical Measures

Location		*Variability*	
Mean	x.xx	Std dev	x.xx
Median	x.xx	Variance	x.xx
Mode	x.xx	Range	x.xx
		Interquartile range	x.xx

Location test: Mu0=0

Test	*Statistic*		*P-value*	
Student's T	t	x.xxx	Pr > |t|	x.xxxx
sign	M	xx	Pr >= |M|	x.xxxx
Signed rank	S	x.xxx	Pr >= |S|	x.xxxx

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Table 5.4.1 TOTAL SCORE CONJUNCTIVA ITT population (v1) vs (v3)

ITT population

TOTAL SCORE CONJUNCTIVA v1 vs v3

Variable TOTAL SCORE CONJUNCTIVA Visit 1

Test for Normality

Test		*Statistic*		*P-value*
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: TOTAL SCORE CONJUNCTIVA Visit 3

Test for Normality

Test		*Statistic*		*P-value*
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: Difference TOTAL SCORE CONJUNCTIVA Visit 3 – Visit 1

Basic Statistical Measures

Location		*Variability*	
Mean	x.xx	Std dev	x.xx
Median	x.xx	Variance	x.xx
Mode	x.xx	Range	x.xx
		Interquartile range	x.xx

Location test: Mu0=0

Test	*Statistic*		*P-value*	
Student's T	t	x.xxx	Pr > |t|	x.xxxx
Sign	M	xx	Pr >= |M|	x.xxxx
Signed rank	S	x.xxx	Pr >= |S|	x.xxxx

Program SAS 9.4 ('Local', X64_10HOME) date xxXXXxxxx

Table 5.4.2 TOTAL SCORE CONJUNCTIVA ITT population (v1) vs (v2)

ITT population

TOTAL SCORE CONJUNCTIVA v1 vs v2

Variable TOTAL SCORE CONJUNCTIVA Visit 1

Test for Normality

Test		*Statistic*		*P-value*
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: TOTAL SCORE CONJUNCTIVA Visit 2

Test for Normality

Test		*Statistic*		*P-value*
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*

Variable: Difference TOTAL SCORE CONJUNCTIVA Visit 2 – Visit 1

Basic Statistical Measures

Location		*Variability*	
Mean	x.xx	Std dev	x.xx
Median	x.xx	Variance	x.xx
Mode	x.xx	Range	x.xx
		Interquartile range	x.xx

Location test: Mu0=0

Test	*Statistic*		*P-value*	
Student's T	t	x.xxx	Pr > |t|	x.xxxx
sign	M	xx	Pr >= |M|	x.xxxx
Signed rank	S	x.xxx	Pr >= |S|	x.xxxx

Program SAS 9.4 ('Local', X64_10HOME) date xxXXXxxxx

Table 5.5.1 TFBUT ITT population (v1) vs (v2)

ITT population

TFBUT v1 vs v2

Variable TFBUT Visit 1

Test for Normality				
Test	*Statistic*		*P-value*	
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable:* TFBUT *Visit 2

Test for Normality				
Test	*Statistic*		*P-value*	
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*

Variable: Difference TFBUT Visit 2 – Visit 1

Basic Statistical Measures

Location		*Variability*	
Mean	x.xx	Std dev	x.xx
Median	x.xx	Variance	x.xx
Mode	x.xx	Range	x.xx
		Interquartile range	x.xx

Location test: Mu0=0

Test	*Statistic*		*P-value*	
Student's T	t	x.xxx	Pr > |t|	x.xxxx
sign	M	xx	Pr >= |M|	x.xxxx
Signed rank	S	x.xxx	Pr >= |S|	x.xxxx

Program SAS 9.4 ('Local', X64_10HOME) date xxXXXxxxx

Table 5.6.1 TOTAL SCORE SANDE ITT population (v1) vs (v3)

ITT population

TOTAL SCORE SANDE v1 vs v3

Variable TOTAL SCORE SANDE Visit 1

Test for Normality

Test		*Statistic*		*P-value*
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: TOTAL SCORE SANDE Visit 3

Test for Normality

Test		*Statistic*		*P-value*
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*

Variable: Difference TOTAL SCORE SANDE Visit 3 – Visit 1

Basic Statistical Measures

Location		*Variability*	
Mean	x.xx	Std dev	x.xx
Median	x.xx	Variance	x.xx
Mode	x.xx	Range	x.xx
		Interquartile range	x.xx

Location test: Mu0=0

Test	*Statistic*		*P-value*	
Student's T	t	x.xxx	Pr > |t|	x.xxxx
sign	M	xx	Pr >= |M|	x.xxxx
Signed rank	S	x.xxx	Pr >= |S|	x.xxxx

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Table 5.7.1 TOTAL SCORE SANDE ITT population (v1) vs (v2)

ITT population

TOTAL SCORE SANDE v1 vs v2

Variable TOTAL SCORE SANDE Visit 1

Test for Normality

Test		*Statistic*		*P-value*
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: TOTAL SCORE SANDE Visit 2

Test for Normality

Test		*Statistic*		*P-value*
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: Difference TOTAL SCORE SANDE Visit 2 – Visit 1

Basic Statistical Measures

Location		*Variability*	
Mean	x.xx	Std dev	x.xx
Median	x.xx	Variance	x.xx
Mode	x.xx	Range	x.xx
		Interquartile range	x.xx

Location test: Mu0=0

Test	*Statistic*		*P-value*	
Student's T	t	x.xxx	Pr > |t|	x.xxxx
sign	M	xx	Pr >= |M|	x.xxxx
Signed rank	S	x.xxx	Pr >= |S|	x.xxxx

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Table 5.8.1 SEVERITY DRYNESS/IRRITATION ITT population (v1) vs (v3)

ITT population

SEVERITY DRYNESS/IRRITATION v1 vs v3

Variable SEVERITY DRYNESS/IRRITATION Visit 1

Test for Normality

Test		*Statistic*		*P-value*
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: SEVERITY DRYNESS/IRRITATION Visit 3

Test for Normality

Test		*Statistic*		*P-value*
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: Difference SEVERITY DRYNESS/IRRITATION Visit 3 – Visit 1

Basic Statistical Measures

Location		*Variability*	
Mean	x.xx	Std dev	x.xx
Median	x.xx	Variance	x.xx
Mode	x.xx	Range	x.xx
		Interquartile range	x.xx

Location test: Mu0=0

Test	*Statistic*		*P-value*	
Student's T	t	x.xxx	Pr > |t|	x.xxxx
Sign	M	xx	Pr >= |M|	x.xxxx
Signed rank	S	x.xxx	Pr >= |S|	x.xxxx

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Table 5.8.2 SEVERITY DRYNESS/IRRITATION ITT population (v1) vs (v2)

ITT population

SEVERITY DRYNESS/IRRITATION v1 vs v2

Variable SEVERITY DRYNESS/IRRITATION Visit 1

Test for Normality

Test		*Statistic*		*P-value*
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: SEVERITY DRYNESS/IRRITATION Visit 2

Test for Normality

Test		*Statistic*		*P-value*
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*

Variable: Difference SEVERITY DRYNESS/IRRITATION Visit 2 – Visit 1

Basic Statistical Measures

Location		*Variability*	
Mean	x.xx	Std dev	x.xx
Median	x.xx	Variance	x.xx
Mode	x.xx	Range	x.xx
		Interquartile range	x.xx

Location test: Mu0=0

Test	*Statistic*		*P-value*	
Student's T	t	x.xxx	Pr > |t|	x.xxxx
sign	M	xx	Pr >= |M|	x.xxxx
Signed rank	S	x.xxx	Pr >= |S|	x.xxxx

Program SAS 9.4 ('Local', X64_10HOME) date xxXXXxxxx

Table 5.9.1 FREQUENCY DRYNESS/IRRITATION ITT population (v1) vs (v3)

ITT population

FREQUENCY DRYNESS/IRRITATION v1 vs v3

Variable FREQUENCY DRYNESS/IRRITATION Visit 1

Test for Normality

Test		*Statistic*		*P-value*
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: FREQUENCY DRYNESS/IRRITATION Visit 3

Test for Normality

Test		*Statistic*		*P-value*
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: Difference FREQUENCY DRYNESS/IRRITATION Visit 3 – Visit 1

Basic Statistical Measures

Location		*Variability*	
Mean	x.xx	Std dev	x.xx
Median	x.xx	Variance	x.xx
Mode	x.xx	Range	x.xx
		Interquartile range	x.xx

Location test: Mu0=0

Test	*Statistic*		*P-value*	
Student's T	t	x.xxx	Pr > |t|	x.xxxx
Sign	M	xx	Pr >= |M|	x.xxxx
Signed rank	S	x.xxx	Pr >= |S|	x.xxxx

Program SAS 9.4 ('Local', X64_10HOME) date xxXXXxxxx

Table 5.9.2 FREQUENCY DRYNESS/IRRITATION ITT population (v1) vs (v2)

ITT population

FREQUENCY DRYNESS/IRRITATION v1 vs v2

Variable FREQUENCY DRYNESS/IRRITATION Visit 1

Test for Normality

Test		*Statistic*		*P-value*
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: FREQUENCY DRYNESS/IRRITATION Visit 2

Test for Normality

Test		*Statistic*		*P-value*
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*

Variable: Difference FREQUENCY DRYNESS/IRRITATION Visit 2 – Visit 1

Basic Statistical Measures

Location		*Variability*	
Mean	x.xx	Std dev	x.xx
Median	x.xx	Variance	x.xx
Mode	x.xx	Range	x.xx
		Interquartile range	x.xx

Location test: Mu0=0

Test	*Statistic*		*P-value*	
Student's T	t	x.xxx	Pr > |t|	x.xxxx
sign	M	xx	Pr >= |M|	x.xxxx
Signed rank	S	x.xxx	Pr >= |S|	x.xxxx

Program SAS 9.4 ('Local', X64_10HOME) date xxXXXxxxx

Table 5.10.1 VAS Question "I feel satisfied using this treatment? ", ITT population

VAS1		
	N	*%*
0-10 mm=none	x	x.xx
11-30 mm=very mild	x	x.xx
31-50 mm=mild	x	x.xx
51-70 mm=moderate	x	x.xx
71-90 mm=strong	x	x.xx
91-100 mm=very strong	x	x.xx

Program SAS 9.4 ('Local', X64_10HOME) date xxXXXxxxx

Table 5.10.2 VAS Question "With this treatment, I have a feeling of freshness? ", ITT population

VAS2		
	N	*%*
0-10 mm=none	x	x.xx
11-30 mm=very mild	x	x.xx
31-50 mm=mild	x	x.xx
51-70 mm=moderate	x	x.xx
71-90 mm=strong	x	x.xx
91-100 mm=very strong	x	x.xx

Program SAS 9.4 ('Local', X64_10HOME) date xxXXXxxxx

Table 5.10.3 VAS Question "With this treatment, I have a feeling of relief?", ITT population

	VAS3	
	N	*%*
0-10 mm=none	x	x.xx
11-30 mm=very mild	x	x.xx
31-50 mm=mild	x	x.xx
51-70 mm=moderate	x	x.xx
71-90 mm=strong	x	x.xx
91-100 mm=very strong	x	x.xx

Program SAS 9.4 ('Local', X64_10HOME) date xxXXXxxxx

Table 5.10.4 VAS Question "This treatment contributed to reduce my pain due to eye dryness?"", ITT population

	VAS4	
	N	*%*
0-10 mm=none	x	x.xx
11-30 mm=very mild	x	x.xx
31-50 mm=mild	x	x.xx
51-70 mm=moderate	x	x.xx
71-90 mm=strong	x	x.xx
91-100 mm=very strong	x	x.xx

Program SAS 9.4 ('Local', X64_10HOME) date xxXXXxxxx

Table 5.10.5 VAS Question "This treatment is comfortable?, ITT population

	VAS5	
	N	*%*
0-10 mm=none	x	x.xx
11-30 mm=very mild	x	x.xx
31-50 mm=mild	x	x.xx
51-70 mm=moderate	x	x.xx
71-90 mm=strong	x	x.xx
91-100 mm=very strong	x	x.xx

Program SAS 9.4 ('Local', X64_10HOME) date xxXXXxxxx

Table 5.10.6 Total score VAS , ITT population

Analysis variable: ***Total score VAS***

Mean	*Std Dev*	*Min*	*Max*	*N*	*lower quartile*	*Median*	*upper quartile*
x.xx	x.xx	x.xx	x.xx	xx	x.xx	x.xx	x.xx

Test for Normality

Test		*Statistic*	*P-value*	
Shapiro-Wilk	W	x.xxx	Pr < W	x.xxx
Kolmogorov-Smirnov	D	x.xxx	Pr > D	x.xxx
Cramer-von Mises	W-Qu	x.xxx	Pr > W-Qu	x.xxx
Anderson-Darling	A-Qu	x.xxx	Pr > A-Qu	x.xxx

Program SAS 9.4 ('Local', X64_10HOME) date xx XXX xxxx

Table 5.11.1.1 DEQS Summary score ITT population (v1) vs (v3)

ITT population

DEQS Summary score v1 vs v3

Variable* DEQS Summary score *Visit 1

Test for Normality

Test		*Statistic*		*P-value*
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: DEQS Summary score Visit 3

Test for Normality

Test		*Statistic*		*P-value*
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: Difference DEQS Summary score Visit 3 – Visit 1

Basic Statistical Measures

Location		*Variability*	
Mean	x.xx	Std dev	x.xx
Median	x.xx	Variance	x.xx
Mode	x.xx	Range	x.xx
		Interquartile range	x.xx

Location test: Mu0=0

Test	*Statistic*		*P-value*	
Student's T	t	x.xxx	Pr > |t|	x.xxxx
sign	M	xx	Pr >= |M|	x.xxxx
Signed rank	S	x.xxx	Pr >= |S|	x.xxxx

Program SAS 9.4 ('Local', X64_10HOME) date xxXXXxxxx

Table 5.11.2.1 DEQS Bothersome Ocular Symptoms subscale ITT population (v1) vs (v3)

ITT population

DEQS subscale1 v1 vs v3

Variable** DEQS subscale1 **Visit 1

Test for Normality

Test		*Statistic*		*P-value*
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: DEQS subscale1 Visit 3

Test for Normality

Test		*Statistic*		*P-value*
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: Difference DEQS subscale1 Visit 3 – Visit 1

Basic Statistical Measures

Location		*Variability*	
Mean	x.xx	Std dev	x.xx
Median	x.xx	Variance	x.xx
Mode	x.xx	Range	x.xx
		Interquartile range	x.xx

Location test: Mu0=0

Test	*Statistic*		*P-value*	
Student's T	t	x.xxx	Pr > |t|	x.xxxx
sign	M	xx	Pr >= |M|	x.xxxx
Signed rank	S	x.xxx	Pr >= |S|	x.xxxx

Program SAS 9.4 ('Local', X64_10HOME) date xxXXXxxxx

Table 5.11.3.1 DEQS Impact on Daily Life subscale ITT population (v1) vs (v3)

ITT population

DEQS subscale2 v1 vs v3

Variable DEQS subscale2 Visit 1

Test for Normality				
Test	*Statistic*		*P-value*	
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: DEQS subscale2 Visit 3

Test for Normality				
Test	*Statistic*		*P-value*	
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: Difference DEQS subscale2 Visit 3 – Visit 1

Basic Statistical Measures

Location		*Variability*	
Mean	x.xx	Std dev	x.xx
Median	x.xx	Variance	x.xx
Mode	x.xx	Range	x.xx
		Interquartile range	x.xx

Location test: Mu0=0

Test	*Statistic*		*P-value*	
Student's T	t	x.xxx	Pr > |t|	x.xxxx
sign	M	xx	Pr >= |M|	x.xxxx
Signed rank	S	x.xxx	Pr >= |S|	x.xxxx

Program SAS 9.4 ('Local', X64_10HOME) date xxXXXxxxx

Table 5.11.4.1 DEQS GES ITT population (v1) vs (v3)

ITT population

DEQS GES v1 vs v3

Variable DEQS GES Visit 1

Test for Normality				
Test	*Statistic*		*P-value*	
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: DEQS GES Visit 3

Test for Normality				
Test	*Statistic*		*P-value*	
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: Difference DEQS GES Visit 3 – Visit 1

Basic Statistical Measures

Location		*Variability*	
Mean	x.xx	Std dev	x.xx
Median	x.xx	Variance	x.xx
Mode	x.xx	Range	x.xx
		Interquartile range	x.xx

Location test: Mu0=0

Test	*Statistic*		*P-value*	
Student's T	t	x.xxx	Pr > |t|	x.xxxx
sign	M	xx	Pr >= |M|	x.xxxx
Signed rank	S	x.xxx	Pr >= |S|	x.xxxx

Program SAS 9.4 ('Local', X64_10HOME) date xxXXXxxxx

Table 5.12.1 IGAS Investigator Global Assessment of Safety, ITT population

IGAS		
	N	*%*
1 very good safety	x	x.xx
2 good safety	x	x.xx
3 moderate safety	x	x.xx
4 poor safety	x	x.xx

Program SAS 9.4 ('Local', X64_10HOME) date xxXXXxxxx

Table 5.13.1 IOP Intraocular Pressure, ITT population (v1) vs (v3)

ITT population

IOP *v1 vs v3*

Variable IOP Visit 1

Test for Normality				
Test		*Statistic*	*P-value*	
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: IOP Visit 3

Test for Normality				
Test		*Statistic*	*P-value*	
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: Difference IOP Visit 3 – Visit 1

Basic Statistical Measures

Location		*Variability*	
Mean	x.xx	Std dev	x.xx
Median	x.xx	Variance	x.xx
Mode	x.xx	Range	x.xx
		Interquartile range	x.xx

Location test: Mu0=0

Test	*Statistic*		*P-value*	
Student's T	t	x.xxx	Pr > |t|	x.xxxx
sign	M	xx	Pr >= |M|	x.xxxx
Signed rank	S	x.xxx	Pr >= |S|	x.xxxx

Program SAS 9.4 ('Local', X64_10HOME) date xxXXXxxxx

Table 5.14.1 IOP Intraocular Pressure, ITT population (v1) vs (v2)

ITT population

IOP *v1 vs v2*

Variable IOP Visit 1

Test for Normality				
Test		*Statistic*	*P-value*	
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: IOP Visit 2

Test for Normality				
Test		*Statistic*	*P-value*	
Shapiro-Wilk	W	x.xxxx	Pr < W	x.xxxx
Kolmogorov-Smirnov	D	x.xxxx	Pr > D	x.xxxx
Cramer-von Mises	W-Qu	x.xxxx	Pr > W-Qu	x.xxxx
Anderson-Darling	A-Qu	x.xxxx	Pr > A-Qu	x.xxxx

N	*Mean*	*Std dev*	*Min*	*Max*	*Lower quartile*	*Median*	*Upper quartile*
x	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Variable: Difference IOP Visit 2 – Visit 1

Basic Statistical Measures

Location		*Variability*	
Mean	x.xx	Std dev	x.xx
Median	x.xx	Variance	x.xx
Mode	x.xx	Range	x.xx
		Interquartile range	x.xx

Location test: Mu0=0

Test	*Statistic*		*P-value*	
Student's T	t	x.xxx	Pr > |t|	x.xxxx
sign	M	xx	Pr >= |M|	x.xxxx
Signed rank	S	x.xxx	Pr >= |S|	x.xxxx

Program SAS 9.4 ('Local', X64_10HOME) date xxXXXxxxx

Sample listing

Listings will be issued as PDF files. Mock listings are reported in the following section.

Listing 1 ITT Population datasets

PATIENT	VISIT	VAR 1	VAR 2	VAR 3	VAR 4	VAR 5	VAR 6	VAR 7	VAR 8	VAR 9	VAR 10	VAR 11	VAR 12	VAR 13
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-xx.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-xx.x	x	x	x	x.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	x.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	xx.x	xx	xx	xx	xx.x	-x.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	x.x	xx	xx	xx	xx.x	x.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-x.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	x.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	x.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xxx	xx.x	xx	xx	xx	xx.x	-x.x	xx	xx	xx	xx.x	x.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	xx.x	xx	xx	xx	xx.x	x.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-xx.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-xx.x	xx	x	x	x.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-x.x	xx	x	x	x.x	-xx.x

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Listing 2 PP Population datasets

PATIENT	VISIT	VAR 1	VAR 2	VAR 3	VAR 4	VAR 5	VAR 6	VAR 7	VAR 8	VAR 9	VAR 10	VAR 11	VAR 12	VAR 13
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-xx.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-xx.x	x	x	x	x.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	x.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	xx.x	xx	xx	xx	xx.x	-x.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	x.x	xx	xx	xx	xx.x	x.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-x.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	x.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	x.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xxx	xx.x	xx	xx	xx	xx.x	-x.x	xx	xx	xx	xx.x	x.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	xx.x	xx	xx	xx	xx.x	x.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-xx.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-xx.x	xx	x	x	x.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-x.x	xx	x	x	x.x	-xx.x

Listing 3 ITT Population datasets DEQS

PATIENT	VISIT	VAR 1	VAR 2	VAR 3	VAR 4	VAR 5	VAR 6	VAR 7	VAR 8	VAR 9	VAR 10	VAR 11	VAR 12	VAR 13
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-xx.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-xx.x	x	x	x	x.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	x.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	xx.x	xx	xx	xx	xx.x	-x.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	x.x	xx	xx	xx	xx.x	x.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-x.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	x.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	x.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xxx	xx.x	xx	xx	xx	xx.x	-x.x	xx	xx	xx	xx.x	x.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	xx.x	xx	xx	xx	xx.x	x.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-xx.x	xx	xx	xx	xx.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-xx.x	xx	x	x	x.x	-xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x	-x.x	xx	x	x	x.x	-xx.x

Listing 4 ITT Population datasets VAS

PATIENT	VISIT	VAR 1	VAR 2	VAR 3	VAR 4	VAR 5	VAR 6	VAR 7
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x
XXxxx-xxx	x	xx	xxx	xx.x	xx	xx	xx	xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x
XXxxx-xxx	x	xx	xx	xx.x	xx	xx	xx	xx.x

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