CONFIDENTIAL

Statistical Analysis Plan (SAP)

Sponsor:	Kontigo Care AB Påvel Snickares Gränd 12 753 20 Uppsala Sweden
Study code:	KCClin01
Study title:	A first-in-human explorative pilot study in healthy volunteers measuring eye parameters with a new mobile phone application for future monitoring of patients in treatment of substance use disorder.
Date:	7-Aug-2023

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1 LIST OF ABBREVIATIONS

ADE – Adverse Device Effect

AE – Adverse Event

ASADE – Anticipated Serious Adverse Device Effect

BMI – Body Mass Index

CIP – Clinical Investigational Plan

D1 – Phenethylamines

D2 – Benzodiazepines

D3 – Cannabinoids

D4 – Opioids

ECG – Electrocardiography

eCRF – Electronic Case Report Form

FAS – Full Analysis Set

IMD – Investigational Medical Device

LC-MS/MS – Liquid Chromatography Tandem Mass-Spectroscopy

NC – Non-convergence

NY – Horizontal nystagmus

PLR – Pupillary light reflex

QC – Quality Control

SADE – Serious Adverse Device Effect

SAE – Serious Adverse Event

SAP – Statistical Analysis Plan

SAS – Statistical Analysis System

SD – Standard Deviation

2 INTRODUCTION

This Statistical Analysis Plan (SAP) is specific for the clinical investigation KCClin01 and gives details regarding the statistical analyses and data presentation outlined in the final Clinical Investigation Plan (CIP) dated 31-Mar-2023 (Approved in Amendment 1). Changes from the final CIP are given in Section 8.

Statistical methods are given in the CIP. However, since the statistical methods in the CIP was written the statistical knowledge has increased and several deviations from the CIP are presented in this plan.

3 CLINICAL INVESTIGATION DETAILS

3.1 Clinical Investigation Objectives

3.1.1 Primary objective

- Evaluate if self-administered pupillometry using a mobile phone application can be used to collect pupillograms before and under the influence of phenethylamines, benzodiazepines, cannabinoids, and opioids (D1-D4).

3.1.2 Secondary objectives

- Evaluate if self-administered pupillometry using a mobile phone application, after refining the method for establishing pupillograms, can be used to collect pupillograms before and under the influence of each medicinal product (D1-D4).
- Evaluate if self-administered pupillometry using a mobile phone application can be used for indicating use of each medicinal product (D1-D4).
- Evaluate the correlation between pupillometric variables and concentration in plasma over time for each medicinal product (D1-D4).
- Evaluate the maximum time after medicine intake (D1-D4) when pupillometric variables differ from baseline.
- Evaluate if a combination of different pupillometric variables can be used for indicating use of each medicinal product (D1-D4).
- Collect usability data to evaluate if the user-interface of Previct Drugs is suitable to be used by users.

3.1.3 Safety objective

Evaluate the safety of using the mobile phone application Previct Drugs for collecting self-administered pupillometry data.

3.2 Clinical Investigation Design

KCCLin01 is a pre-market, explorative, early feasibility, pilot, controlled clinical investigation designed to collect initial clinical data on Previct Drugs. The clinical data collected in this early feasibility study is an important step in the product development of Previct Drugs as the data is required for continuing the development of the mathematical models and algorithms for drug detection.

This first clinical investigation will give valuable information on the feasibility of Previct Drugs function to measure pupils and eye movements and to evaluate if there are any changes in the pupillometric parameters before and after intake of a medicinal product. It will also provide information on the usability of the device. Drug intake is simulated by a controlled single application of commonly therapeutically used medicinal products from the following classes of drugs: phenethylamines (D1), benzodiazepines (D2), cannabinoids (D3), and opioids (D4).

The investigation will enroll and follow adult male and female healthy volunteers, i.e., subjects, for collection of baseline data during one week in the subject's home environment and thereafter performance of a single administration of one of the four medicinal products of interest (D1-D4) at

the site in a controlled setting. The investigation population will consist of 44 subjects (11 subjects per arm) fulfilling the eligibility criteria for the clinical investigation. The dropout rate is estimated to 10% and hence a total of 48 subjects (12 in each treatment arm) will be recruited. The subjects will be recruited in the Netherlands.

Each subject will be randomized to exactly one of the treatment arms. The drug will be applied to the subjects one time.

The duration of the investigation is estimated to approximately 5.5 months with a recruitment period of 5 months.

3.3 Number of Subjects

The investigation aims to enroll 11 subjects, i.e., healthy volunteers, per medicinal product group that have completed the clinical investigation until the telephone follow-up call. For four medicinal products, the total will be 44 subjects. In order to take account for a drop-out rate of 10%, 12 subjects will be included per medicinal product group and in total 48 subjects in the clinical investigation.

The sample size of this clinical investigation is not based on any mathematical grounds as this in an explorative trial and no formal hypotheses will be tested.

3.4 Methods of Assigning Subject to Device Groups

Once a subject has consented for study participation, the subject will be given a unique subject identification (subject ID) number. If the subject fulfills all inclusion criteria and none of the exclusion criteria, the subject will be seen as eligible.

Randomization to one of the four medicinal products will take place at visit 1. Randomization will be based on which criteria the subject fulfils as for each medicinal product there should be at least 3 subjects with bright eyes (defined as blue, green, or grey) and at least 3 subjects with dark eyes (defined as brown), at least 2 subjects between 18-25 years old and at least 2 subjects between 50-65 years old. A subject can fulfill several of these criteria.

The subject will be allocated to the next available randomization number according to the randomization list and the associated medicinal product will thereafter be administered at visit 2 according to this CIP.

For further details related to the randomization procedure, see KC09-115 Randomization procedure KCClin01_ RevB_8-May-2023.

3.5 Blinding

Neither the subject nor the site personnel are blinded. The drug type randomization will be known for the site personnel from opening the randomization envelope at Visit 1. However, the subject will not be informed about drug type until initiation of Visit 2.

4 STATISTICAL AND ANALYTICAL PLANS

4.1 Sample Size Justification

As this is an early feasibility and explorative investigation, the sample size is not derived from a formal sample size calculation as no hypothesis is pre-defined.

4.2 Definition of Analysis Sets

4.2.1 Full Analysis Set (FAS)

FAS is defined as all subjects included in the clinical investigation with at least one pupillometric test under influence of one of the medicinal products.

It is assumed all enrolled subjects fulfill the eligibility (entry) criteria. If this is not the case it will be considered to exclude incorrectly enrolled subjects from the FAS.

Data from subjects that are excluded – if any – from the FAS will not be used for efficacy analyses but all collected data will be used in the safety evaluation.

4.2.2 Use of Analysis Sets

All analyses will be performed on the Full Analyses Set (FAS).

4.3 Definition of Baseline

Baseline will be defined as all Previct Drugs tests performed at visit 2 before administration of the medicinal product at the same light condition.

4.4 Summary Statistics

All data collected from patients included in the FAS will be presented with summary statistics, i.e. number of observations, number of missing observations, minimum value, median value, maximum value and standard deviation for continuous data and frequency and percentage for categorical data.

Summary statistics will include number of subjects with data, number of subjects with missing data, mean, standard deviation, median, minimum and maximum for continuous data and frequency and percentage for categorical data.

Table with summary statistics will be divided by treatment group, visit and relevant stratification factors such as the light conditions.

Examples of tables for presentation of data are given in Table 1 and Table 2.

Table 1. Example of a table presenting data for a continuous variable

Statistica	Group 1	Group 2	Group 3	Group 4
N	X	X	X	X
Missing	X	X	X	X
Min	X.XX	X.XX	X.XX	X.XX
Median	X.XX	X.XX	X.XX	X.XX
Mean	X.XX	X.XX	X.XX	X.XX
Standard deviation	X.XX	X.XX	X.XX	X.XX

Table 2. Example of a table presenting data for a categorical variable

Statistica	Group 1	Group 2	Group 3	Group 4
Missing	X (%)	X (%)	X (%)	X (%)
Category 1	X (%)	X (%)	X (%)	X (%)
Category 2	X (%)	X (%)	X (%)	X (%)
:	:	:	:	:
:	:	:	:	:
Category n	X (%)	X (%)	X (%)	X (%)

4.5 Significance Level

This early feasibility and exploratory investigation do not incorporate any historical controls or comparators. Only descriptive statistics will be used.

All presented p-values (if any) will be two-sided.

4.6 Multiple Comparisons/Multiplicity

This is an early feasibility and exploratory investigation, meaning no confirmatory hypotheses will be tested and no adjustment for multiplicity will be done.

4.7 Handling of Drop-outs, Missing Data and Outliers

Available data from prematurely withdrawn subjects will be included in the analysis. Missing data will not be imputed.

4.8 Adjustment for Covariates

The analysis of covariance model will not be used. However, the strength of the light between the different mobile phone models may affect the outcome, and the influence on the results in the clinical investigation will be investigated based on mobile phone model by in addition to pooling results over both mobile phone models. Each model will be analysed seperately as well.

4.9 Multicenter Studies

This is a single center clinical investigation and hence no adjustment for multicenter clinical investigations are applicable.

4.10 Examination of Subgroups

All analyses will be performed separately for each drug-group (treatment group). However, these groups are not considered to be "sub-groups".

Sub-group analyses will be applied considering each stratification factor at the randomization to be sub-groups.

4.11 Blind Review

No blind review analyses will be conducted.

5 SUBJECTS

5.1 Subject Disposition

The number of subjects that entered the clinical investigation, withdrawn subjects, completed subjects and the number of subjects at each visit will be summarized in total and by medicinal drug allocation.

5.2 Baseline Characteristics and Demographics

Demographics (e.g., age, gender, weight, length, BMI, eye color), and baseline characteristics (e.g., health examination variables, relevant medical and surgical history, relevant concomitant medication, history of alcohol and drug usage) will be presented by means of summary statistics, for each treatment group.

6 TREATMENT INFORMATION AND EXTENT OF EXPOSURE

6.1 Active Treatment

This is an early feasibility with no actual treatment involved. All subjects will be allocated to the same medical device (Previct Drugs).

6.2 Placebo Treatment

Not applicable.

6.3 Extent of Exposure

One Previct Drugs measurement consists of three different tests:

- Cross Eye Test (NC)
- Nystagmus Test (NY)
- Contraction Test (PLR)

Measurements described below are all related to one test set including the three different eye tests.

At visit 1, the first measurements of Previct Drugs take place once the subject has been assessed as eligible. The subject performs three (3) duplicate measurements with Previct Drugs in two different ambient light conditions, i.e., in total 6 measurements.

Between visit 1 and visit 2 the subject is instructed to perform measurements with Previct Drugs in the home environment. Three (3) measurements are to be performed per day, once in the morning, once in the mid of the day, and once in the evening.

Visit 2 is performed 1 week after visit 1 (+/- 2 days). The subject performs three (3) replicate measurements with Previct Drugs in two different ambient light conditions.

The subject is then administered with the randomized medicinal product. Measurements with Previct Drugs, blood sampling for LC-MS/MS analysis and collection of vital signs are thereafter performed according to Table 3.

Table 3. At visit 2: Measurements with Previct Drugs, blood sampling for LC-MS/MS analysis and collection of vital signs were thereafter performed according to the following schedule

Hour (approx.)	Activity
0	• Administration of medicine • Collection of vital signs • 1 measurement with Previct Drugs in light condition 1 • Wait ~10 minutes • 1 measurement with Previct Drugs in light condition 2
0.5	**For subject administered with cannabinoids only:** • Blood sampling for LC-MS/MS • 1 measurement with Previct Drugs in light condition 1 • Wait ~10 minutes • 1 measurement with Previct Drugs in light condition 2
1	• Blood sampling for LC-MS/MS • Collection of vital signs • **2** measurements with Previct Drugs in light condition 1 • Wait ~10 minutes • **2** measurements with Previct Drugs in light condition 2
2	• Blood sampling for LC-MS/MS • Collection of vital signs • **2** measurements with Previct Drugs in light condition 1 • Wait ~10 minutes • 2 measurements with Previct Drugs in light condition 2

Hour (approx.)	Activity
3	• Blood sampling for LC-MS/MS • Collection of vital signs • 2 measurements with Previct Drugs in light condition 1 • Wait ~10 minutes • 2 measurements with Previct Drugs in light condition 2
4	• Blood sampling for LC-MS/MS • Collection of vital signs • 1 measurement with Previct Drugs in light condition 1 • Wait ~10 minutes • 1 measurement with Previct Drugs in light condition 2
5	• Blood sampling for LC-MS/MS • Collection of vital signs • 1 measurement with Previct Drugs in light condition 1 • Wait ~10 minutes • 1 measurement with Previct Drugs in light condition 2

6.4 Compliance of Investigational Medical Device (IMD)

During each measurement the Previct Drugs app will inform if the conducted test was approved. If not approved, the subject will be asked to re-do the measurement. If the test cannot be conducted, the subject continues to the next test, or completes the test set, as applicable.

Performed and successful tests are documented in the eCRF for Visit 1 and Visit 2. The number of attempts per test is not documented in the eCRF. During the on-site visits, compliance is overseen by site personnel. Sponsor is the only part receiving the Previct Drugs data output and can overview the compliance of the home testing period, as well as approved tests during Visit 1 or Visit 2 with data output discrepancies. Non-compliance related to Previct drugs measurements will be documented by the Sponsor, and where applicable be reported as Protocol Deviations.

6.5 Concomitant Medications

Subjects are allowed to continue their regular medication during the clinical investigation. However, individuals with ongoing treatment with medications which may interfere with eye measurements, or which may interfere with any of the medicinal products to be used, will not be included in this investigation.

Relevant concomitant medication will be presented descriptively, for each treatment group.

7 STATISTICAL METHODOLOGY

All statistical analyses will be performed separately for each medicinal product. No comparisons will be performed between the medicinal product groups. The two ambient light conditions will also be analyzed separately.

Baseline and safety variables will be given descriptively, for each medicinal product group.

For comparison of change within subject the Wilcoxon signed rank test will be used for continuous data and the McNemar test for binary data.

7.1 Primary efficacy endpoint

7.1.1 Definition

For each medicinal product (D1-D4), the fraction of collected pupillometry data from the mobile phone application at baseline and under the influence of D1-D4, which can be transformed into pre-defined key features using native pupillograms.

7.1.2 Analysis

Fraction of collected pupillometry data using native pupillogram. For each of the measurements PLR, NC, and NY, each measurements quality control (QC) will approve the measurements or not using the native pupillogram. For each subject, the proportion of approved measurements over all measurements during day 2 will be calculated for each of PLR, NC, and NY. The distribution over subjects for each medicinal product will be given by summary statistics.

7.1.3 Presentation

The presentation of summary statistics will mainly be in tables. Graphics may be used as well.

7.2 Secondary Efficacy Endpoints

7.2.1 Definitions

Secondary 1

For each medicinal product (D1-D4), the fraction of collected pupillometry data from the mobile phone application at baseline and under the influence of D1-D4, which can be transformed into pre-defined key features using refined pupillograms.

Secondary 2

For each medicinal product (D1-D4), change in key features from baseline to the LC-MS/MS verified peak concentration in plasma after administration of medicinal product at visit 2 using native or refined pupillograms.

Secondary 3

For each medicinal product (D1-D4), analysis and plot the correlation between key features and plasma concentration over time using native or refined pupillograms.

Secondary 4

For each medicinal product (D1-D4), change in key features from baseline to 5 hours after administration of medicinal product at visit 2 using native or refined pupillograms.

Secondary 5

For each medicinal product (D1-D4), test known combinations of key features that changes from baseline to the LC-MS/MS verified peak concentration in plasma after administration of medicinal product at visit 2 using native or refined pupillograms.

Secondary 6

User-friendliness of Previct Drugs evaluated by the subject at Visit 2.

7.2.2 Analyses

Secondary 1

For each of the measurements PLR, NC, and NY, each measurements QC control will approve the measurements or not using the native pupillogram. For each subject, the proportion of approved measurements over all measurements during day 2 will be calculated for each of PLR, NC, and NY. The distribution over subjects for each medicinal product will be presented by means of summary statistics.

Secondary 2 and 4

Analyses for the second and fourth secondary endpoint will be changes in key features within subjects from baseline to time points under influence of medicinal product with verified peak concentration in plasma and up to 5 hours. For continuous variables the mean values will be used and for ordered categorical variables the last observation will be used. If the QC has not approved a measurement that

measurement will not be used in the analyses. These analyses will be performed both for the native and the refined pupillograms.

For comparison of change within subject the Wilcoxon signed rank test will be used for continuous data and the McNemar test for binary data.

Secondary 3

The two following correlation analyses will be performed between pupillometry key features and plasma concentrations:

- Correlations between change from baseline to verified peak plasma concentration between pupillometry data and plasma concentrations using Spearman correlation and scatter plots.
- For each subject, calculate Spearman correlation coefficient between plasma concentration and pupillometry key features for all measurements during visit 2. These Spearman correlation coefficients will be analyzed over subjects with Fisher's one sample non-parametric permutation test.

Selected important analyses will be illustrated graphically with individual plots over time, boxplots over time, and scatterplots for correlations.

Secondary 5

The change of known combinations of key features from baseline to verified peak concentration will be analyzed in the same way as described for the second secondary endpoint above.

Secondary 6

User-friendliness of Predict Drugs evaluated by a Subject usability Questionnaire at visit 2 will only be analyzed descriptively with numbers and percentages.

7.2.3 Presentation

The presentation of summary statistics will mainly be in tables. Graphics may be used as well.

7.3 Safety Endpoints

7.3.1 Definitions

For full details on Adverse Events (AEs), Adverse Device Effects (ADEs), Serious Adverse Events (SAEs), Serious Adverse Device Effects (SADEs) and Unanticipated Serious Adverse Device Effect (USADE) please see KC09-104 Clinical Investigation Plan_KCClin01_RevC_31Mar2023.

Adverse Event (AE)

Untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users, or other persons, whether or not related to the investigational medical device and whether anticipated or unanticipated.

Note 1: This definition includes events related to the investigational medical device or the comparator.

Note 2: This definition includes events related to the procedures involved.

Note 3: For users or other persons, this definition is restricted to events related to the use of investigational medical devices or comparators.

Adverse Device Effect (ADE)

Adverse event related to the use of an investigational medical device.

Note 1: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.

Note 2: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.

Note 3: This includes 'comparator' if the comparator is a medical device.

Serious Adverse Event (SAE)

Adverse event that led to any of the following:

a) death,
b) serious deterioration in the health of the subject, users, or other persons as defined by one or more of the following:
    i. A life-threatening illness or injury, or
    ii. A permanent impairment of a body structure or a body function including chronic diseases, or
    iii. In-subject or prolonged hospitalization, or
    iv. medical or surgical intervention to prevent life-threatening illness or injury, or permanent impairment to a body structure or a body function,
c) foetal distress, foetal death, a congenital abnormality, or birth defect including physical or mental impairment.

Note: Planned hospitalization for pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event.

Serious Adverse Device Effect (SADE)

Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

Serious safe threat

Signal from any adverse event or device deficiency that indicates an imminent risk of death or a serious deterioration in the health in subjects, users, or other persons, and that requires prompt remedial action for other subjects, users, or other persons.

Note: This would include events that are of significant and unexpected nature such that they become alarming as a potential serious health hazard or possibility of multiple deaths occurring at short intervals.

Unanticipated Serious Adverse Device Effect (USADE)

Serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current risk assessment.

Note: Anticipated Serious Adverse Device Effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk assessment.

AEs will be documented as reported in the eCRF, without use of specific coding dictionaries.

7.3.2 Analyses

No statistical analyses are planned for safety parameters.

7.3.3 Presentation

AE/ADE:

The following summaries of AEs and SAEs will be given by for each medicinal product group and in total:

- Total number of AEs
- Total number of unique AEs
- Total number of unique, related AEs

- Total number (%) of subjects with at least one AE
- Total number (%) of subjects with at least one related AE
- Total number (%) which had AE as reason for premature discontinuation of IMD

Severity, action taken, concomitant therapy started, and subject outcome of the AEs will be given in data listings only. AEs, which were reason for premature discontinuation of IMD, will be listed separately.

Depending on the number of AEs reported, the most frequently reported (e.g., in more than 5% of the subjects) AEs might be summarized separately.

The total number of SAEs and subjects with a least one SAE will always be given. Further summaries of SAEs depending on the number of SAEs observed.

SAE/SADE:

SAEs/SADEs, if any, will be listed only.

7.4 Interim Analysis

No interim analyses are planned.

8 CHANGES FROM THE CIP

Statistical methods are given in the CIP. However, the biostatistician involved in writing the CIP has been replaced and will not be involved in the remaining part of the clinical investigation. The previous biostatistician has been replaced by biostatistician Mikael Åström, who has, to the best of his knowledge and experience, modified the planned analyses, methods, and strategies according to his preferences. In addition, since the statistical methods in the CIP was written the statistical knowledge of the purpose of the clinical investigation has increased. Consequently, several deviations from the CIP are presented in this SAP.

The main changes are presented in Table *4*.

Table 4. Main changes in the SAP compared to the CIP regarding statistical methods and strategies

Text in the CIP	Changes and reasons in the SAP
It is stated in the CIP that "Changes within subjects from baseline, without medicinal product, to time points under influence of medicinal product in key features will be analyzed with Fisher's non-parametric permutation test for paired observation for continuous variables and with Sign test for ordinal and dichotomous variables."	• "Fisher's non-parametric permutation test": This test is not well known from the literature. The more used non-parametric method is the Wilcoxon signed rank test, which will be used to test the null-hypothesis of no change over time for continuous and ordered categorical data • "Sign test for ordinal and dichotomous variables": This method is not judged to be the most efficient test for changes over time for ordinal values. The Wilcoxon signed rank test will be used instead. For dichotomous data (=having two possible values) the Binary test will be used instead.
It is written in the CIP: "These spearman correlation coefficients will be analyzed over subjects with Fisher's one sample non-parametric permutation test."	The Spearman correlation coefficient is a parameter that can take any value between -1 and +1 where the absolute value indicates level of relations between two variables. However, analyzing over subjects is considered the best option. In addition, the test is not well-known (see above).

Text in the CIP	Changes and reasons in the SAP
In the CIP it is stated "For each subject, the proportion of approved measurements over all measurements during day 2 will be calculated for each of PLR, NC, and NY"	The "proportion of approved measurements" may not be possible to calculate based on the data in the database. Therefore, this analysis may be conducted but is not mandatory.
It is stated in the CIP: "The distribution over subjects for each medicinal product will be given with mean, SD, median, minimum, and maximum."	It is always important to present number of missing for each variable and that will be added.
It is stated in the CIP: "Continuous variables and changes in continuous variables will be described by mean, SD, median, minimum, and maximum"	It is always important to present number of missing for each variable and that will be added.
It is stated in the CIP "Change in categorical variables will be given as increase, no change and decrease"	This is a classification that is not considered necessary and will decrease the statistical sensitivity (power) and therefore replaced by given then changes numerically.
In the CIP it is stated: "Selected important analyses will be illustrated graphically with individual plots over time, boxplots over time, and scatterplots for correlations."	It is not specified which variables that will be presented by showing graphics. As this is a part of showing the data descriptively tables will be the first choice for each variable and graphics only shown when contributing to the understanding of the data.
It is stated in the CIP: "User-friendliness of Predict Drugs evaluated by a Subject usability Questionnaire at visit 2 will only be analyzed descriptively with numbers and percentages."	This sentence indicate that it would be possible to use other methods than just descriptive statistics. However, as these data are collected only once and there is no comparison between the drug groups it is not possible to do anything else than presenting the data descriptively and then this is presented already in the general statistical methodology section.
It is stated in the CIP: "This early feasibility and exploratory investigation does not incorporate any historical controls or comparators. Only descriptive statistics will be used. P-values will only be reported descriptively"	This information is no longer considered propriate and are thus not repeated in the SAP.
The CIP states that baseline will be defined as the last three measurements prior to Previct Drugs tests performed at visit 2 before administration of the medicinal product.	This is changed so that baseline is considered all available measurements prior to Previct Drugs tests performed visit 2 before administration of the medicinal product.

9 STATISTICAL DELIVERABLES

The following statistical deliverables will be prepared and provided:

- SAP
  - This document and hereby delivered.
- Statistical analyses and summary tables
  - This will delivered as the result of the statistical analyses and as well used as background material for the Clinical Investigational Report (CIR).
- Appendices with patient data listings:
  - Randomization scheme and codes
    - Not applicable in this study as this is an open labeled clinical investigation.
  - Discontinued subjects

- This is a part of the clean file documentation but will as well be delivered as a part of the Statistical Report.

- CIP deviations
  - This is a part of the clean file documentation but will as well be delivered as a part of the Statistical Report.
- Patients excluded from the efficacy analyses
  - Subjects excluded from FAS will be reported as described above.
- Demographic
  - This will be included in the Statistical Report and in the CIR.
- Exposure to IMD
  - This will be included in the Statistical Report and in the CIR.
- Individual efficacy response (both primary and secondary variables)
  - This is not applicable in this clinical investigation considering the design. However, all relevant efficacy data will be presented by subject and as summary statistics.
- Adverse event
  - This will be included in the Statistical Report and in the CIR.
- Listing of individual laboratory measurements
  - This will be included in the Statistical Report and in the CIR.
- Vital signs
  - This will be included in the Statistical Report and in the CIR.
- ECG
  - This will be included in the Statistical Report and in the CIR.
- Physical examination
  - This will be included in the Statistical Report and in the CIR.

10 SOFTWARE

The statistical software used will be described in the statistical analysis report and is assumed to be Excel (latest available version in Office 365), STATA (version 16.0) and StatXact (version 11.1.0).

11 REFERENCES

- KC09-104 Clinical Investigation Plan_KCClin01_RevC_31Mar2023.

12 APPROVAL

Issued by:

Mikael Åström, Biostatistician
Devicia Representative

Date (dd-Mmm-yyyy)

Approved by:

Markku Hämäläinen, CSO
Sponsor Representative

Date (dd-Mmm-yyyy)