Statistical Analysis Plan (SAP)

AAA 1002 / NCT number: NCT02328027

Phase I-IIa study of safety, tolerance, pharmacokinetics, dosimetry and benefice of early nuclear medicine imaging of 99mTc-rhAnnexin V-128 in patients with rheumatoid arthritis or ankylosing spondylitis

Prepared for:

Advanced Accelerator Applications

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Sommario

REVISION HISTORY

Date	Author	Initial/ Release Version #
26/01/2018	[redacted]	Initial
Date	New Version #	Summary of Changes

1 List of abbreviations

AAA	Advanced Accelerator Applications
ACR	American College of Rheumatology
AE	Adverse Event
ALT	Alanine Transaminase
AS	Ankylosing Spondylitis
ASAS	Assessment of Spondylo-Arthritis Society
AST	Aspartate Transaminase
ATC	Anatomical Therapeutic Chemical
AUC	Area Under the Curve
BASDAI	Bath Ankylosing Spondylitis Disease Activity Index
BASFI	Bath Ankylosing Spondylitis Functional Index
BASMI	Bath Ankylosing Spondylitis Metrology Index
Bi-DMARD	Biological Disease Modifying Anti-Rheumatic Drug
BMI	Body Mass Index
BP	Blood Pressure
CFR	Code of Federal Regulations
Cl	Clearance
CRF	Case Report Form
DMARD	Disease Modifying Anti-Rheumatic Drug
DPD	Deoxypyridinoline
ECG	Electrocardiogram
EDC	Electronic Data Capture
ELISA	Enzyme-Linked Immunosorbent Assay
EULAR	European League Against Rheumatism
HR	Heart Rate
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IL-6	anti-interleukine 6
ITT	intention-to-treat
MedDRA	Medical Dictionary for Regulatory Activities

MIRD	Medical Internal Radiation Dose
NSAID	Non-Steroidal Anti-Inflammatory Drug
NYHA	New York Heart Association
OLINDA/EXM	Organ Level INternal Dose Assessment/EXponential Modeling
[redacted]	[redacted]
[redacted] CRO	[redacted] Contract Research Organization
PK	Pharmacokinetic
PT	Preferred Term
RA	Rheumatoid Arthritis
ROI	Region Of Interest
RR	Respiratory Rate
RTF	Rich Text Format
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SEC-HPLC	Size-Exclusion HPLC- High-Performance Liquid Chromatography
SOC	System Organ Class
SOP	Standard Operating Procedure
SPECT	Single-Photon Emission Computed Tomography
SS	Safety Set
t1/2	Half-life
TEAE	Treatment Emergent Adverse Event
TNF	tumour necrosis factor
ULN	Upper Limit of Normal
Vz	Volume of distribution
WHO DDE	World Health Organization Drug Dictionary

2 INTRODUCTION

The purpose of this statistical analysis plan (SAP) is to provide a detailed description of the planned analyses of safety and tolerability data that have been outlined in the clinical study protocol AAA 1002.

This SAP is based on the AAA 1002 Protocol Amendment n°4 dated 16 December 2014, entitled "Phase I-IIa study of safety, tolerance, pharmacokinetics, dosimetry and benefice of early nuclear medicine imaging of 99mTc-rhAnnexin V-128 in patients with rheumatoid arthritis or ankylosing spondylitis".

This plan provides the basis for the statistical sections of the AAA 1002 clinical study report as described in the E3 Guideline on the Structure and Content of Clinical Study Reports issued by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).

This SAP was finalized before final lock of the database as per the E9 ICH Guideline on Statistical Principles for Clinical Trials.

3 STUDY OBJECTIVES

This Phase I-IIa study will be undertaken to determine the safety, tolerability, bio-distribution and ability of early imaging with 99mTc-rhAnnexin V-128 to predict response to treatment in 20 patients with diagnosed rheumatoid arthritis (RA) or ankylosing spondylitis (AS).

The objectives of this study are:

- To determine the safety and tolerability of imaging with 99mTc-rhAnnexin V-128.
- To determine the biodistribution, pharmacokinetics and radiation dosimetry of 99mTc-rhAnnexin V-128
- To demonstrate the time-dependent distribution and localization of 99mTc-rhAnnexin V-128 both in RA and AS patients
- To determine ability of early imaging with 99mTc-rhAnnexin V-128 to evaluate the presence of lesions before and after short term treatment of either RA or AS patients

4 STUDY DESIGN

4.1 Overall Study Design

This is a monocentric, open label, Phase I-IIa study. Patients who have signed the informed consent and are eligible for study participation according to the inclusion and exclusion criteria will receive a single intravenous bolus of 99mTc-rhAnnexin V-128 on Day 1 and a single intravenous bolus of 99mTc-rhAnnexin V-128 6 weeks later (+/- 2 weeks). All patients will start a new RA or AS treatment on Day 2 (Figure 1). In order to minimize the risks for the study population, patients will be enrolled with a minimum of 2-week interval.
Study duration is of 4 months +/- 2 weeks (including the screening period). Eligible patients will receive two injections: one on Day 1 and a second administration 6 weeks +/- 2 weeks later. The end of the study is defined as the moment that the last enrolled patient has completed 18 days follow-up after completing the second 99mTc-rhAnnexin V-128 administration. An

additional blood sample for immunological assay is required 3 months after the first administration of the 99mTc-rhAnnexin V-128 (Day 90 ± 14 days) in case of positive anti-Annexin antibodies outcome in previous examination.

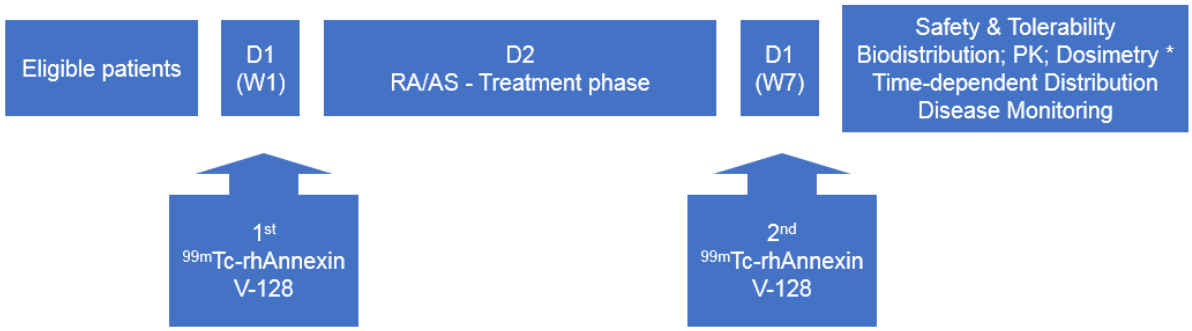

Figure 1: Study flowchart (*: up to 10 patients)

4.2 Expected Sample Size

The number of patients in this study is not based on statistical power considerations. The planned sample includes 20 patients with Day 56 assessments which are believed to provide sufficient data to assess the general safety and tolerability of 99mTc-rhAnnexin V-128. Patients will be recruited with a ratio of 1:1 RA:AS. Any patient who has not completed Day 56 assessment will be replaced by a patient from the same group (RA or AS). It is expected that about 10% of patients will not complete their Day 56 assessments; therefore, approximately 23 patients will be recruited. In addition, 10 patients enrolled in the study will be asked to participate in a dosimetry and PK study, irrespective of the group they are part of (RA or AS). Out of the first 6 patients, at least 3 patients must take part in the dosimetry and PK sub-study.

Considering the very slow recruitment rate of this study, AAA, the sponsor decided to stop study recruitment by end of September 2017. With an 80% or more of the planned sample size evaluable for analysis, the sample size is still considered to be sufficient for assessing the primary objective. Regarding secondary objectives, a thorough data review will be organised before finalizing the SAP in order to assess the relevance of conducting all or part of the corresponding statistical analyses.

4.3 Enrolment

For the purpose of this study, an “enrolled patient” is a patient who has signed the informed consent and meets all inclusion and exclusion criteria to participate in the study.
Patients with RA will be diagnosed based on ACR/EULAR10 (Classification Criteria for Rheumatoid Arthritis) and will thereafter be evaluated with DAS 28 (Disease Activity Score Calculator for Rheumatoid Arthritis). Patients with AS will be diagnosed based on the ASAS (Classification Criteria for Axial and Peripheral Spondyloarthritis). Each patient will be anonymized and identified with a patient ID number. A unique subject identification number (Patient ID) will be assigned at the start of the Screening Period to each subject who signs the informed consent form until the study termination of the patient. This number will identify the subject throughout the study. Patient IDs will include the 2-digit country code number (SW) and a 3-digit subject number (ex: SW001 for first subject in). In both groups of patients – i.e. RA and AS patients – the introduction of a Bi-DMARD (biological disease-modifying antirheumatic drug) treatment should be indicated at the moment of inclusion in the study. The Bi-DMARD therapy should start on Day 2 of the study. RA patients must have been treated at

least with one DMARD (methotrexate, leflunomide and sulfasalazine) or a combination of them in the last 3 months – before inclusion - and this/these DMARD(s) will be continued in this study. Otherwise, RA patients must have been previously treated with Bi-DMARD before administration of the new Bi-DMARD treatment. The non-response of the previous Bi-DMARD treatment must be documented. AS patients must at least have been treated with NSAID in the last 3 months before inclusion and they should be under the same NSAID treatment during the last 4 weeks before inclusion. For RA patients, anti-tumour necrosis factor (TNF) antibodies, anti-interleukine 6 (IL-6) antibodies and abatacept therapies are to be considered and are authorized in Switzerland as first line Bi-DMARD agents in RA. On the contrary, anti-CD 20 positive lymphocytes antibodies can only be used, if one anti-TNF therapy failed. In the AS patients group, only anti-TNF antibodies can be considered, if NSAID are not sufficient. Ten patients enrolled in the study will be asked to participate in a dosimetry and PK sub-study, irrespective of the group they are part of (RA or AS).

The patient is free to withdraw from the study for any reason and at any time without giving reason for doing so and without penalty or prejudice. It is also possible that the Sponsor or Swissmedic request termination of the study if there are concerns about conduct or safety.

A patient may be withdrawn from the study if:

- A serious adverse event (SAE) occurs.
- The patient fails to comply with the evaluations or other requirements of the study.
- The patient starts treatment with one of the medications disallowed. The final decision to withdraw a patient who starts treatment with disallowed medication will be made by the Sponsor following consulting of the Investigator.

A patient must be withdrawn from the study if:

- The Investigator considers it, for safety reasons, to be in the best interest of the patient.
- The patient withdraws his/her consent.
- The patient is pregnant.

If withdrawal occurs for any reason, the Investigator must determine the primary reason for a patient's withdrawal from the study. The date and reason for discontinuation must be documented in the CRF. For patients who are lost to follow-up (i.e., those patients whose status is unclear because they fail to appear for study visits without stating an intention to withdraw), the Investigator should show 'due diligence' by documenting in the source documents steps taken to contact the patient, e.g., dates of telephone calls, registered letters, etc.

4.4 Treatment

The single dose vial (rhAnnexin V-128: 0.40 mg) will be reconstituted with 740 MBq (20 mCi) of 99mTc. The labelling reaction requires 90 minutes and the reconstituted radiolabelled product is stable for 6 h. For the purpose of this study, it is recommended to administer the reconstituted solution within 4 hours after completion of the labelling reaction. The drug is administered at a dose of 250 MBq as a single intravenous bolus over 10-20 seconds at Day 1 and at 6 weeks (42 days) +/- 2 weeks after the first administration.

4.5 Inclusion/Exclusion Criteria

4.5.1 Inclusion Criteria

1. Patients diagnosed with RA based on ACR/EULAR 2010 criteria (score ≥ 6), OR Patients diagnosed with AS based on the ASAS criteria. Patients with RA must have serology assessment performed and documented.at the time of enrolment.
2. Patient with RA active disease (DAS > 2,6) and the introduction of a Bi-DMARD treatment should be indicated. RA patients must at least have been treated with DMARD (methotrexate, leflunomide and sulfasalazine) or combination of these treatments for at least 3 months. Treatment will be pursued while on study. OR RA patients must have been previously treated with Bi-DMARD before initiation of the new Bi-DMARD treatment. The non-response of the previous Bi-DMARD treatment must be documented. OR Patients with ankylosing spondylitis with insufficiently controlled disease while under NSAID and indication for Bi-DMARD. These patients must be under NSAID for at least 3 months and 99mTc-rhAnnexin V-128 in patients with rheumatoid arthritis or ankylosing spondylitis Protocol Amendment n°4, 16 December 2014 Page 26 of 67 under the same NSAID for at least 1 month prior to enrolment.
3. ≥ 18 years old
4. Karnofsky performance status ≥ 80%
5. Negative Pregnancy test for women with childbearing potential
6. For women with childbearing potential, use of two reliable means of contraception (e.g., hormonal contraceptive, patch, vaginal ring, intrauterine device, associated with other barrier method of contraception such as the use of condoms), throughout their participation in the study
7. Absence of ECG anomaly
8. Written ICF signed

4.5.2 Exclusion Criteria

1. Pregnancy or lactation
2. Liver impairment (ALT, AST or Bilirubin > 2 ULN) at screening visit or baseline
3. Kidney impairment (serum creatinine > 1.5 mg/dL)
4. History of congestive heart failure (NYHA III & IV)
5. History of malignant disease within 5 years
6. History of any disease or relevant physical or psychiatric condition or abnormal physical finding which may interfere with the study objectives at the investigator judgment
7. Known hypersensitivity to the investigational drug or any of its components
8. Participation to another clinical trial within 4 weeks before study inclusion except for patients who have participated or who are currently participating in an interventional study without any study drug administration.

4.6 Demographic and Baseline Characteristics Assessments

Demographic data is collected at Visit V0 (Screening/Baseline) and include month and year of birth, age in years, gender (Male or Female) and ethnicity. This data also includes:

- Medical history
- Results of pregnancy test
- Physical examination (including height, weight and BMI)
- Vital signs (blood pressure, heart rate)
- Previous and current medications (taken at least two weeks before the screening visit and those ongoing at screening), including the RA and AS treatment
- Electrocardiogram (ECG) 12-lead
- Laboratory assessment (haematology, biochemistry, urinalysis)
- Immunogenicity (by ELISA)

4.7 Previous, Current and Concomitant medication assessments

Any previous and concomitant medications (including the specific RA/AS treatments as per the protocol) are recorded at visit V0 (taken at least two weeks before the screening visit and those ongoing at screening) and at each subsequent visit. At subsequent visits, only new therapy or changes in therapy since the previous visit are recorded.

4.8 99mTc-DPD-bone scintigraphy and whole body planar imaging

All patients will have a baseline DPD-99m-Tc bone scan if not already performed within 8 weeks before rhAnnexin V-128 administration.
Then a whole body planar imaging will be performed prior to any treatment.

4.9 Safety

4.9.1 Adverse Events

AEs will be reported from signing the informed consent onwards until the last study-related procedure. If the information of an untoward medical occurrence is collected before starting the intake of study medication, this information will be listed as a pre-treatment AE during statistical analysis. AEs that occurred after the first intake of study medication will be considered as treatment emergent for the analysis.
All AEs occurring during the study are to be followed up until resolved or judged to be no longer clinically significant, or until they become chronic to the extent that they can be fully characterized. An assessment should be made at the last study-related visit for each patient (See Study Protocol for more details).

4.9.2 Laboratory Parameters

Laboratory tests (haematology, coagulation, blood chemistry and urinalysis) will be monitored before and after the Day 1 visit, with additional samples at 24 hours (only for patients participating to the PK substudy), 30, 42 and 90 study day.

4.9.3 Vital Signs, Physical Examination and ECG

Vital signs will be recorded at each study visit.
Physical Examination will be performed at screening, 42 and 90 study day.
Twelve-lead ECG will be performed at screening, dosing (Day 1), 24 hours (only for patients participating in the substudy), 30, 42 and 90 study day.

4.10 Pharmacokinetics and Dosimetry

For first 3 patients included into the subgroup of PK and dosimetry study, blood sample will be collected at Day 2 For the first 3 patients participating to the PK substudy, a further 10 ml of venous blood samples will be drawn at nominal times of 0, 5, 10, 15, 30, 60 minutes as well as 2 hrs, 4hrs and 24 hrs post administration. Depending upon the results in those 3 patients, the timeframe for dosimetry measurements and PK will be confirmed or modified with a time-point at 3 hrs (instead of 2 hrs) and 6 hrs (instead of 4 hrs) for the following 7 enrolled patients in the sub-study.
Urine sample will be collected within 24 hrs prior to 99mTc-rhAnnexin V-128 administration, preferable just prior to its administration (0 h sample) to achieve bladder emptying. Urine collections will be obtained and volume recorded, possibly in the time intervals 0-1 h, 1 h – 4 hrs, 4 hrs -16 hrs, 16 hrs – 24 hrs post administration. Dual 2 mL aliquots of urine from each period will be counted in a gamma counter at local laboratory

4.11 Immunogenicity

Assays for anti-rhAnnexin V-128 IgG and IgM antibodies will be performed in serum samples by ELISA. For this purpose 10mL blood samples will be collected at baseline, at Day 30 ± 3 days and at Day 56 ± 14 days. An additional sample is required 3 months after the first administration of the 99mTc-rhAnnexin V-128 (Day 90 ± 14 days) in case of positive anti-Annexin antibodies outcome in previous examinations.

5 STUDY SCHEMA

Study Procedures	Screening (±4 weeks)	Day 1	24 hours[1]	Day 30 ±3 days	Day 42 ±2weeks	Day 56 ±2weeks	Day 90 ±2weeks
Written informed consent	x						
Inclusion/exclusion criteria	x						
Medical history	x						
Concomitant medications including RA and AS treatment	x	x	x	x	x	x	x
Disease assessment (BASDAI, BASFI, BASMI for AS for AS patients, DAS28 scales including Ultrasound assessments for RA patients)	x				x		x
Physical examination	x				x		x
Vital signs (BP and HR)	x	x	x	x	x	x	x
Lab analysis (haematology, biochemistry; urine)	x		x	x	x		x
Venous/urine sampling (PK and dosimetry)[2]		x[1]	x				
Immunogenicity by ELISA[3]	x			x		x	x
Urine SEC-HPLC analysis[1,4]		x	x				
Pregnancy test	x	x			x		
Standard 12-lead ECG	x	x	x	x	x		x
rh-Annexin V-128 administration[6]		x			x		
Bone scintigraphy[7]	x						
Whole Body scintigraphic imaging[5]		x	x		x		
Adverse Events	x	x	x	x	x	x	x

6 STUDY ENDPOINTS

The following study endpoints are derived from the clinical study protocol objectives.

6.1 Safety endpoints (Primary)

Safety endpoints will be evaluated by:
1. Serious and non-serious adverse event assessments
2. Abnormal haematology, coagulation, blood chemistry, urinalysis laboratory tests
3. Change from baseline of ECG parameters (including HR heart rate, RR interval, PR interval, QRS width and QT interval)
4. Change from baseline of vital signs

6.2 Pharmacokinetics and Dosimetry (Secondary - only for patients participating to the dosimetry and pk substudy)

Pharmacokinetics and dosimetry will be assessed by:

1. Serial measurements of rhAnnexin V-128 concentrations (by ELISA) from serum samples
    a. Annexin concentrations in serum
    b. Annexin PK parameters: AUC, Vz, Cl and elimination t1/2
2. Serial measurements of radioactivity in whole blood and serum samples
    a. Whole blood and serum concentrations of total radioactivity
    b. Whole blood and serum PK parameters for total radioactivity: AUC, t1/2
3. Serial measurements of radioactivity in urine samples
    a. % excretion of total radioactivity in urine
    b. SEC-HPLC analysis – as a function of time to assess chemical status and presence of Annexin related species
4. Radiation dose to the organ of interests (particularly the kidneys), effective dose equivalent and effective dose

6.3 Immunogenicity

Immunogenicity will be evaluated by Anti-rhAnnexin V-128 IgG and IgM antibodies assessment (by ELISA) at baseline and at 30 and 56 days post-administration. An additional sample at 90 days will be taken only in case of positive anti-Annexin antibodies outcome in previous examinations.

6.4 Disease Assessment

BASDAI (Bath Ankylosing Spondylitis Disease Activity Index), BASFI (Bath Ankylosing Spondylitis Functional Index) and BASMI (Bath Ankylosing Spondylitis Metrology Index) scores for AS patients will be presented as a descriptive table at each visit.
DAS28 and ACR/EULAR scores for RA patients will be presented as a descriptive table at each visit.

6.5 Imaging assessments

To assess the suitability of 99mTc-rhAnnexin V-128 imaging for detecting RA or AS lesions before and after short term treatment by observing qualitatively the number and location of lesions at each imaging point and calculating the intensity of lesion uptake (specific) as well as quantitatively through assessment of radiotracer uptake by geometric mean of counts/ROI on anterior and posterior planar images. Only patients with available anterior and posterior planar imaging data at 1h and at 2h post-injection at both Day 1 and Day 42 assessments will be considered for this analysis.

7 STATISTICAL METHODS OF ANALYSIS

7.1 General Principles

All tables, figures, listings and inference analyses will be produced using Stata-files (Stata12.1 [redacted] USA).

7.1.1 Standards:

- All tables and figures other than dosimetry and PK will be grouped by subjects' disease (RA/AS), and will also include a total column for all patients receiving Annexin. Dosimetry and PK tables and figures will only include the total of patients in the PK/dosimetry population (not separated by disease group).
- Summary tables and listings will use Courier New font of size 9 with a default page orientation of landscape.
- The code is made of 5 digits, resulting from the combination of the site identification letter "SW" and the subject number.
- Any CRF data, third party electronic data (such as clinical laboratory data) as well as any corresponding derived variable listed will be presented sorted by subject unless otherwise specified.
- Flags for abnormal laboratory parameters will be displayed in the individual subject data listings. For the classification of abnormal laboratory values, the individual normal and safety ranges of the central laboratory will be used and will be displayed in the listings.
- Categorical variables will be presented using number of subjects in the analysis population (N), number of subjects with non-missing observations (n), and frequency and percentages by category. Denominators for calculation of percentages will be taken as the number of subjects with non-missing observations (n) in the specified population unless otherwise stated.
- Continuous variables will be presented using number of subjects in the analysis population (N), number of subjects with non-missing observations (n), mean, standard deviation (abbreviated as "SD" in statistical tables), median, quartiles, minimum and maximum.
- All hypothesis testing will be considered exploratory. Unless stated otherwise, statistical tests conducted will be two-sided at a level of p=0.05, although care will be taken to avoid over-emphasis on nominal significance levels. No adjustments for multiplicity issues will be made in this study.

- Dates will be presented as DDMMMYYYY.
- Times will be presented in hours and minutes using a 24 hour clock (i.e. hh:mm).
- Numeric values will be decimal point aligned.
- Character values will be left aligned.
- The tables, listings and figures will be delivered in a RTF format.

7.1.2 Handling of Missing Data and Data from Unscheduled or Repeat Visits

No imputations of missing data will be used in the analysis of safety data and PK/Dosimetry. In particular for PK, a minimum number of 3 valid time points is required for including the subject in the PK analysis.

For summary statistics, only data from scheduled visits will be used. Data from unscheduled visits or repeat tests will not be used when descriptive statistics are presented by visit. However, all observed data including repeat tests and unscheduled visits will be presented in assessments of max and min changes on treatment, shift tables and in listings. Missing data will appear as blank.

7.1.3 Handling of Outliers

If outliers are identified, sensitivity analyses eliminating the outlier effects will be performed when relevant and their results compared to those of analyses which include all the data.

7.1.4 Rounding

Data will be presented to the observed number of decimal places. In general, minimums and maximums will be presented to the same level of accuracy as the raw data; means, medians and standard deviation (SD) will be presented to 1 further decimal place. Percentages will be presented to 1 decimal place. P-value (significance level) will be presented with 4 decimal places. P-values below 0.0001 will be presented as <0.0001.

7.1.5 Computation of Derived Data

7.1.5.1 Derivation of Body Mass Index (BMI)

BMI is the ratio between weight (Kilograms) and height² (meters²). The results are rounded to the first decimal.

7.1.5.2 Derivation of Activity Measurement of Effective administered dose (MBq)

Activity measurement of the effective administered dose is derived as the difference between the measured radioactivity of the pre-injection total dose in the syringe (in MBq) and the measured radioactivity of the post-injection residual dose remaining in the syringe (in MBq).

7.1.5.3 Derivation of difference between two dates

For any other event, the duration between 2 dates will be derived using the following formula:

- Duration in Days = (End Date – Start Date) + 1

7.1.5.4 Coding of Variables Using Standard Dictionaries

Medical history, Concomitant medications and adverse events (AE) description will be coded using version 208.10 of the Medical Dictionary for Regulatory Activities (MedDRA). Prior and concomitant medications will be coded using the World Health Organization Drug Dictionary Enhanced (WHO DDE version Q3 2017), and grouped by ATC code level 3.

7.1.5.5 Baseline definition

Baseline is defined as the latest available observation before the study drug administration.

7.2 Protocol Deviations

Protocol deviations are defined as deviations from the procedures outlined in the protocol. Protocol deviations will be provided by the sponsor prior to database lock and summarized in table grouped by major or minor classification.

7.3 Analysis Set Definitions

Taking in account the study design, the particular investigated imaging product administered (two single administrations at V1 and V4) all analyses will be performed on the safety population (Safety Set), which will be comprised of all eligible subjects who have been administered at least one study treatment. The Safety Set (SS) population is equivalent to the intention-to-treat (ITT) population.
Individuals having any major deviations will not be excluded from the SS population.

Subjects participating to the PK/Dosimetry substudy will be included into the PK population which will be used for PK and Dosimetry analysis.

Listings and screening assessments will be generated using the Screened set of subjects that does not exclude the screening failures.

7.4 Subject Disposition

Frequency distributions will be given for the number of subjects enrolled, treated, withdrawn, and who completed the study assessment periods.

Frequency distributions for the reason of withdrawal will be presented: percentages will be calculated on the basis of the whole safety set. Primary reason for which subjects have been withdrawn from the study at any time will be presented, including the following:

- at their own request or at the request of their legally authorized representative; or
- If, in the Investigator's opinion, continuation in the study would be detrimental to the subject's well-being.

In all cases, the reason for withdrawal must be recorded in the subject's medical records and on the eCRF. If the reason is not known, the reason must be investigated to establish whether the reason was due to an adverse event, and, if so, this must be reported in accordance with the procedures as indicated in the study protocol.

7.5 Description of Demographic and Baseline Characteristics

All variables related to demographics and medical history will be summarized on the safety set.
For medical history, the number and percentage of subjects will be summarized by MedDRA classification preferred term.
Frequency distributions will be given for the number of subjects in the Safety set.

All characteristics will be grouped also by RA/AS subjects' disease.

7.6 Extent of Exposure

Summary statistics of the volume of drug injected in mL as well as the actual dose in MBq and MBq/kg will be summarized in the safety dataset by RA/AS patient disease groups and total and by 1st and 2nd injection.

7.7 Evaluation of Safety

The safety analyses will be performed on the Safety set. All safety analyses will be performed considering the treatment received by the subjects.
Safety will be evaluated by abnormal renal function, hepatic function and coagulation laboratory tests and treatment emergent serious and non-serious adverse event assessments over the study period.
No formal hypothesis testing will be carried out.
No imputations will be used in the analysis of safety data.

7.8 Adverse Events

All AEs reported after the first dose (treatment emergent adverse events, TEAEs) will be summarized and their occurrence rate, will be presented by MedDRA system organ class (SOC) and preferred term (PT), overall and by worst severity level. Within a SOC, PT will be presented in descending order of overall occurrence.
Relationship to the investigational product will be assessed by presenting separately all AEs and AEs at least possibly related to study drug (i.e. cause = study treatment and relationship = probable or possible).
Pre-treatment AE will just be presented in the listings.

7.8.1 Adverse Event occurrence rate

The occurrence rate of a given AE (i.e. proportion of subjects who experienced an AE) will be calculated by dividing the number of subjects who experienced this AE by the total number of subjects in the Safety set.
When calculating occurrence rates, if a subject has the same AE preferred term reported more than once, then the subject will be reported only once using the worst AE attribute.
Occurrence rate will be presented overall and by worst severity level (i.e. in case a patient experienced several times the same AE, only the worst severity level will be presented in the summary table by severity category).

7.8.2 Adverse Events Tabulation

Calculated AE duration will be indicated in the listing.

Onset day of an AE will be calculated if both the AE start date and date of dosing are complete and is calculated as:

- Onset day for AE = (AE start date – Date of first dose) + 1 (only if AE start date >= First dose date)

Duration of an AE will be calculated if both the AE stop and start dates are complete and is calculated as:

- Duration of an AE = (AE stop date – AE start date) + 1

In cases where the start date of an AE is completely known but the AE has not yet resolved at the end of the study, duration of an AE will be calculated as:

- Duration of an unresolved AE = (Study termination date – AE start date) + 1

These observations will be flagged in listings with a greater than sign (i.e. >) prior to presentation of the duration.

In case of AE partial dates: if only the day is missing then the first day of the month will be used for start dates and the last day of the month will be used for end dates. In case the AE started on the same month than the first dose and the AE start day is missing, the partial date will be replaced by the first dose date.

If the month is missing no imputation will be done.

If duration of an AE cannot be calculated, the information will be missing from the listing.

Incidence rates, frequencies and summary tabulations will be provided for:
- All TEAEs
- All Treatment Emergent Serious AEs (TESAEs)
- All Treatment Emergent Serious AEs (TESAEs) by severity
- All TEAEs leading to permanent treatment discontinuation
- All TEAEs by severity
- All TESAEs by drug-event relationship
- All TEAEs by drug-event relationship
- All TEAEs leading to death

7.9 Safety Laboratory Evaluation

Summary statistics (n, mean, SD, median, quartiles, minimum, maximum) will be presented at each assessment time point for each continuous laboratory assessment, including routine haematology, chemistry and urinary panels. Summary statistics changes from baseline will also be presented. For categorical variables the outputs will be generated according to the section 7.1.1.

For the classification of abnormal laboratory values, the individual normal range of the laboratory will be used.

7.10 Electrocardiogram

Electrocardiogram (Standard 12-lead ECGs) at each visit will be classified as:

- Normal
- Abnormal, i.e. changes Not Clinically Significant
- Abnormal, i.e. changes Clinically Significant

Summary statistics (n, mean, SD, median, quartiles, minimum, maximum) of ECG parameters will be presented at each assessment time point.
Summary statistics of change from baseline of ECG parameters (including heart rate (HR), RR interval, PR interval, QRS width and QT/QTc interval) will also be presented.

7.11 Vital Signs

Summary statistics (n, mean, SD, median, quartiles, minimum, maximum) of vital signs will be presented at each assessment time point. Summary statistics of changes from baseline will also be presented.

Number and percentage of subjects with shift changes from baseline will be tabulated in Shift Tables for each vital sign assessment.

The following normal ranges for vital signs will be used:

Systolic blood pressure	BETWEEN 90 AND 150 (mm Hg)
Diastolic blood pressure	BETWEEN 45 AND 90 (mm Hg)
Heart Rate	BETWEEN 40 AND 100 (beats/min)

Listings of all vital signs will be presented.

7.12 Physical Examinations

Summary statistics (n, mean, SD, median, quartiles, minimum, maximum) of weight and BMI will be presented at each assessment time point.

Physical examination data from complete physical examinations will be listed by subject.

7.13 Prior and Concomitant Medications

Prior and Concomitant medications will be presented grouped by RA/AS patient disease groups and total using summary tables and will be classified according to whether they were taken before baseline or either started or taken during the study period.
Number and percentage of subjects will be summarized by World Health Organization Drug Dictionary Enhanced (WHO DDE version Q3 2017), and grouped by ATC code level 3.
Use of concomitant medications will also be presented in listings by subject.
Medications will be defined as prior if stop date is not missing, and less than the date of the first administration of the investigated imaging product, concomitant otherwise.
Medications will be considered as both prior and concomitant when the start date is before the administration of the investigated imaging product and stop date is after the administration of the investigated imaging product, or unknown or marked as ongoing and when the start date is unknown and the stop date is after the administration of the investigated imaging product, or marked as ongoing.
Medications with incomplete start or stop dates will be considered concomitant medications if it is possible that they could have been concomitant medications.

7.14 Pharmacokinetics and Dosimetry

Standard non-compartmental analysis will be conducted for the calculation of usual pharmacokinetic parameters such as AUC, Vz, Cl and elimination half-life, using serum concentration-time data. Mean serum area under the concentration-time curve will be determined using the linear trapezoidal rule and extrapolated to infinity using the plasma elimination rate constant.
All pharmacokinetic parameters will be calculated for each subject, and summary statistics (n, mean, SD) will be tabulated.

The quantitative in vivo biodistribution of the 99mTc-rhAnnexin V-128 will be determined through whole-body planar imaging. In addition, a SPECT/CT will be performed by regions in order to generate relevant dosimetry data after extrapolation for the reconstruction with OLINDA software.
Radiation dose to the organ of interests (particularly the kidneys), effective dose equivalent and effective dose will be calculated following the MIRD committee guidelines using the OLINDA/EXM software.

Summary statistics (n, mean, SD, median, quartiles, minimum, maximum) of PK and dosimetry parameters will be tabulated.

7.15 Immunogenicity

Immunogenicity will be presented as a descriptive table of Anti-rhAnnexin V-128 IgG and IgM antibodies assessment (by ELISA) at screening and at 30 and 56 days post-administration plus an addition sample taken at day 90 in case of previous positive result.

7.16 Disease Assessment

BASDAI, BASFI and BASMI scores for AS patients will be presented as a descriptive table at each visit.

DAS28 and ACR/EULAR scores for RA patients will be presented as a descriptive table at each visit.

7.17 99mTc-rhAnnexin V-128 Scintigraphy

Descriptive statistics of the imaging findings with report of location and intensity of lesions at each imaging time point will be reported to determine the most suitable imaging time point post injection.
An association between annexin scintigraphy results and disease assessments (see Section 7.16) will be presented to assess diagnostic concordance.
These analyses will be taken care of by AAA's study physician and results will appended to the clinical study report.

7.18 Other Data

Other data, including informed consents, study administration and analysis sets will be listed by subject.

7.19 Changes to the Planned Analysis

There were no changes to the planned statistical analysis.

8 DELIVERABLES

8.1 Statistical Outputs Validation

[redacted] CRO seeks to ensure the quality of the results provided for the study in the form of tables and listings, and the derived datasets used in their creation according to [redacted] CRO Standard Operating Procedures (SOP).
The entire set of tables, listings, and figures will be checked for accuracy, completeness, and consistency prior to inclusion in the final clinical study report.

8.2 Data Capture and Verification

Data generated in this study will be handled according to [redacted] CRO's Standard Operating Procedures. The data will be recorded in the CRF by the Investigator and then entered in a fully validated 21 CFR Part 11 compliant electronic data management system. A full detailed description of data management procedures used in this study is described in the Data Management Operating Plan for this study.

8.3 Data Sets Creation and Transfer

Analysis data sets including labels and formats will be generated from the data management system according to [redacted] CRO Standard Operating Procedures (SOP).
Analysis data sets will be created as follows: raw data sets will be extracted from the EDC system in SAS XPT format; raw data sets will then be transformed using Stat transfer to generate analysis data sets in Stata format.

9 REFERENCES

- Clinical Study Protocol AAA 1002: "Phase I-IIa study of safety, tolerance, pharmacokinetics, dosimetry and benefice of early nuclear medicine imaging of 99mTc-rhAnnexin V-128 in patients with rheumatoid arthritis or ankylosing spondylitis".
- International Conference on Harmonization. Structure and content of clinical study reports. E3. Finalized November 1995.
- International Conference on Harmonization. Statistical principles for clinical trials. E9. Adopted February 1998.

10 APPENDICES

10.1 List of tables

Number	Table Title	Analysis set
14.1.1	Subject Disposition	Screened
14.1.2	Summary of Protocol Deviations	Safety
14.1.3	Demographics and Baseline Characteristics	Safety
14.1.4	Medical History	Safety
14.1.5	Prior Medications	Safety
14.1.6	Concomitant Medications	Safety
14.1.7	Extent of Exposure: Summary of injected Dose of the investigated imaging product.	Safety
14.2.1	Blood and serum concentrations of total radioactivity	PK
14.2.2	Blood and serum area under the concentration-time curve (AUC) and terminal half-life (t1/2) of total radioactivity after intravenous 99mTc-rhAnnexin V-128	PK
14.2.3	Summary of Percent excretion of total radioactivity in urine	PK
14.2.4	Summary of Serum concentrations of rhAnnexin V-128 based on ELISA analysis	PK
14.2.5	Summary of Volume of distribution (Vz) and systemic clearance (Cl) of rhAnnexin V-128 based on ELISA analysis	PK
14.2.6	Summary of SEC-HPLC analysis results	PK
14.3.1.1	Overall Summary of TEAEs	Safety
14.3.1.2	Occurrence of TEAEs – Number and percentage of subjects by System Organ Class and Preferred Term	Safety
14.3.1.3	Occurrence of Serious TEAEs – Number and percentage of subject by System Organ Class and Preferred Term	Safety
14.3.1.4	Occurrence of TEAEs Leading to permanent treatment discontinuation – Number and percentage of subject by System Organ Class and Preferred Term	Safety
14.3.1.5	Occurrence of Serious TEAEs Severity – Number and percentage of subject by System Organ Class and Preferred Term	Safety
14.3.1.6	Occurrence of Serious TEAEs Relationship to study drugs – Number and Percentage of Subjects by System Organ Class, and Preferred Term	Safety

Number	Table Title	Analysis set
14.3.1.7	Occurrence of TEAEs Relationship to study drugs – Number and Percentage of Subjects by System Organ Class, and Preferred Term	Safety
14.3.1.8	Occurrence of TEAEs Severity – Number and Percentage of Subject by System Organ Class and Preferred Term	Safety
14.3.2	Listing of Deaths and Other Serious Adverse Events	Safety
14.3.4.1	Listing of Laboratory Safety Values for Subjects with Clinically Significant Abnormal Laboratory Values	Safety
14.3.4.2	Haematology parameters at each visit and change from baseline	Safety
14.3.4.3	Biochemistry parameters at each visit and change from baseline	Safety
14.3.4.4	Urinalysis parameters at each visit and change from baseline	Safety
14.3.5	Disease Assessment (BASDAI, BASFI, BASMI, DAS28, ACR/EULAR scores) at each visit and change from baseline	Safety
14.3.6	Listing of Anti-Annexin V-128 IgG and IgM antibodies Reactive results	Safety
14.3.7	Physical examination at each visit	Safety
14.3.8.1	Vital signs at each visit and change from baseline	Safety
14.3.8.2	Vital signs – Shifts from baseline	Safety
14.3.9.1	Overall Electrocardiogram interpretation	Safety
14.3.9.2	Electrocardiogram parameters at each visit and change from baseline	Safety

10.2 List of Figures

Number	Figure Title	Analysis Set	Shell type
14.2.1	Annexin V-128 serum time-concentration linear graphs	PK	1
14.2.2	Annexin V-128 serum time-concentration semilog graphs	PK	1
14.2.3	Annexin V-128 serum Area Under the Curves	PK	2
14.2.4	Radioactivity levels in whole blood samples graph	PK	1
14.2.5	Radioactivity levels in serum samples graph	PK	1
14.2.6	Radioactivity levels in urine samples graph	PK	1
14.3.1	ECG parameters change from baseline box plot	Safety	3

10.3 List of Listings

Number	Listing Title	Analysis set
16.2.1.1	Study Populations	Screened
16.2.1.2	Screen Failures	Screened
16.2.1.3	Early Termination/Study completion	Screened
16.2.2	Protocol deviations	Screened
16.2.3	Subjects excluded from the Efficacy Analysis Set	Screened
16.2.4.1	Demographics and Baseline Characteristics	Screened
16.2.4.2	Informed Consents	Screened
16.2.4.3.1	Inclusion Criteria Definitions	Screened
16.2.4.3.2	Inclusion Criteria	Screened
16.2.4.4.1	Exclusion Criteria Definitions	Screened
16.2.4.4.2	Exclusion Criteria	Screened
16.2.4.5	Medical History	Screened
16.2.4.6	Physical examination	Screened
16.2.4.7	Vital Signs	Screened
16.2.4.8	Electrocardiograms	Screened
16.2.4.9	Prior and Concomitant Medications	Screened
16.2.4.10	Disease Assessment	Screened
16.2.4.11	Blood and Urine Samples Assessment	Screened
16.2.4.12	Haematology tests results	Screened
16.2.4.13	Biochemistry tests results	Screened
16.2.4.14	Urinalysis tests results	Screened
16.2.4.15	Immunogenicity Samples Assessment	Screened
16.2.4.16	Immunogenicity Tests Result	Screened
16.2.4.17	Bone Scintigraphy	Screened
16.2.4.18	Whole Body Planar Imaging	Screened
16.2.4.19	Pregnancy tests results	Screened
16.2.5.1	Study Treatment Administration	Screened
16.2.5.2	Visit Dates	Screened
16.2.6.1	PK serum Results	PK
16.2.6.2	Dosimetry Whole Blood Results	PK
16.2.6.3	Dosimetry Serum Results	PK
16.2.6.4	Dosimetry Urine Results	PK
16.2.7.1	Adverse Events	Screened
16.2.7.2	Serious Adverse Events	Screened
16.2.7.3	Fatal Adverse Events	Screened
16.2.7.4	Drug Related Adverse Events	Screened

Number	Listing Title	Analysis set
16.2.7.5	Adverse Events Leading to study drug discontinuation	Screened

10.4 Table Shells

The footnotes are displayed on the last page of each table.

Table 14.1.1: Subject Disposition
Population: Screened

Disposition Reason	RA n (%)	AS n (%)	V-128 Total n (%)
Screened	xxx	xxx	xxx
Screen Failures [1]	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Reason 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Reason 2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
...	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Treated with Study Drug	xxx	xxx	xxx
Completed Treatment [2]	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Completed PK/PD sub-study [2]	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Withdrew from Treatment [2]	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Adverse event	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Discretion of the Investigator or sponsor	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Protocol violation	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Subject withdrew consent	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Lost to follow-up	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Death	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Other	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

[1] Percentages are based on the number of screened subjects.
[2] Percentages are based on the number of treated subjects.

Data source: listings 16.x.x.x, 16.x.x.x. and 16.x.x.x
Source code: xxxx.ssc. Date/time of run: DDMMMYYYY:HH:MM.

Table 14.1.2: Summary of Protocol Deviations
Population: Safety

Deviation Type	RA (N=xxx) n (%)	AS (N=xxx) n (%)	V-128 Total (N=xxx) n (%)
Major	xxx	xxx	xxx
Type 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Type 2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
...	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Minor	xxx	xxx	xxx
Type 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Type 2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
....	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

Data source: listings 16.1.4
Source code: xxxx.ssc. Date/time of run: DDMMMYYYY:HH:MM.

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Table 14.1.3: Demographics and Baseline Characteristics
Population: Safety

Summary Statistics	RA (N=xxx) n (%)	AS (N=xxx) n (%)	V-128 Total (N=xxx) n (%)
Age (year)			
n	Xx	Xx	Xx
Mean (SD)	xx.x (x.xx)	xx.x (x.xx)	xx.x (x.xx)
Median	xx.x	xx.x	xx.x
Min, Max	(xx,xx)	(xx,xx)	(xx,xx)
Gender, n(%)			
Male	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Female	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Race, n(%)			
White	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Black	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Asian	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Other	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

Data source: listings 16.x.x.x.x and 16.x.x.x.x
Source code: xxxx.ssc. Date/time of run: DDMMMYYYY:HH:MM.

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Table 14.1.4: Medical History
Population: Safety

System Organ Class [1]	Preferred Term [1]	RA (N=xxx) n (%)	AS (N=xxx) n (%)	V-128 Total (N=xxx) n (%)
Any Medical History	With History/Condition	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
System Organ Class	Any History of Class	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
	Term 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
	Term 2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
	. . .	. . .	. . .	. . .
System Organ Class	Any History of Class	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
	Term 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
	Term 2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
	. . .	. . .	. . .	. . .
System Organ Class	Any History of Class	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
	Term 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
	. . .	. . .	. . .	. . .

Data source: listing 16.x.x.x.x
Source code: xxxx.ssc. Date/time of run: DDMMMYYYY:HH:MM.
[1] Medical Dictionary for Regulatory Activities, Version xx.x

Table 14.1.5: Prior Medication
Population: Safety

ATC level 3 [1]	Drug name	RA (N=xxx) n (%)	AS (N=xxx) n (%)	V-128 Total (N=xxx) n (%)
Any Medication		**xxx (xx.x)**	**xxx (xx.x)**	**xxx (xx.x)**
ATC 1	Any Medication of ATC	**xxx (xx.x)**	**xxx (xx.x)**	**xxx (xx.x)**
	Drug name1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
	Drug name2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
ATC 2	Any Medication of ATC	**xxx (xx.x)**	**xxx (xx.x)**	**xxx (xx.x)**
	Drug name1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
	Drug name2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
ATC 3	Any Medication of ATC	**xxx (xx.x)**	**xxx (xx.x)**	**xxx (xx.x)**
	Drug name1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
	Drug name2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

Data source: listings 16.x.x.x.x and 16.x.x.x.x
Source code: xxxx.ssc. Date/time of run: DDMMMYYYY:HH:MM.
[1] WHODrug dictionary Version xx.xx

Table 14.1.6: Concomitant Medication
Population: Safety

ATC level 3[1]	Drug name	RA (N=xxx) n (%)	AS (N=xxx) n (%)	V-128 Total (N=xxx) n (%)
Any Medication		**xxx (xx.x)**	**xxx (xx.x)**	**xxx (xx.x)**
ATC 1	Any Medication of ATC	**xxx (xx.x)**	**xxx (xx.x)**	**xxx (xx.x)**
	Drug name1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
	Drug name2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
ATC 2	Any Medication of ATC	**xxx (xx.x)**	**xxx (xx.x)**	**xxx (xx.x)**
	Drug name1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
	Drug name2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
ATC 3	Any Medication of ATC	**xxx (xx.x)**	**xxx (xx.x)**	**xxx (xx.x)**
	Drug name1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
	Drug name2	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

Data source: listings 16.x.x.x.x and 16.x.x.x.x
Source code: xxxx.ssc. Date/time of run: DDMMMYYYY:HH:MM.
[1] WHODrug dictionary Version xx.xx

Table 14.1.7 Extent of Exposure: Summary of Injected Dose of the investigated imaging product
Population: Safety (N=xx)

	Statistics	RA (N=xxx)	AS (N=xxx)	V-128 Total (N=xxx)
1st Injection				
Volume Injected (ml)	n	XXX	XXX	XXX
	Total	XXXXX	XXXXX	XXXXX
	Mean	XXX.X	XXX.X	XXX.X
	SD	XXX.XX	XXX.XX	XXX.XX
	Median	XXX.X	XXX.X	XXX.X
	Min, Max	XXX, XXX	XXX, XXX	XXX, XXX
Actual Dose (MBq)	n	XXX	XXX	XXX
	Total	XXXXX	XXXXX	XXXXX
	Mean	XXX.X	XXX.X	XXX.X
	SD	XXX.XX	XXX.XX	XXX.XX
	…	XXX.X	XXX.X	XXX.X
Actual Dose (MBq/kg)[1]	n	XXX	XXX	XXX
	Total	XXXXX	XXXXX	XXXXX
	Mean	XXX.X	XXX.X	XXX.X
	…	XXX.XX	XXX.XX	XXX.XX
2nd Injection				
... Repeat above summaries				

[1] The weight for 1st injection is the one measured at screening
Data source: listing 16.x.x.x
Source code: xxxx.ssc. Date/time of run: DDMMMYYYY:HH:MM.

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Table 14.2.1: Blood and serum concentrations of total radioactivity

Population: PK (N=xx)

Parameter	Nominal timepoint relative to dose time	Statistic	V-128 (N=xxx)
Blood concentration of total radioactivity	0 min	n	xxx
		Mean (SD)	xx.xx(xx.x)
		Geometric mean (CV)	xx.xx(xx.x)
		Median	xx.x
		Min, Max	xx.x, xx.x
	5 min	n	xxx
		Mean (SD)	xx.xx(xx.x)
		Geometric mean (CV)	xx.xx(xx.x)
		Median	xx.x
		Min, Max	xx.x, xx.x
	…. etc	....	….
Serum concentration of total radioactivity	0 min	n	xxx
		Mean (SD)	xx.xx(xx.x)
		Geometric mean (CV)	xx.xx(xx.x)
		Median	xx.x
		Min, Max	xx.x, xx.x

Data source: listing 16.x.x.x
Source code: xxxx.ssc. Date/time of run: DDMMMYYYY:HH:MM.

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Table 14.2.2: Blood and serum area under the concentration-time curve (AUC)
and terminal half-life (t1/2) of total radioactivity after intravenous 99mTc-rhAnnexin V-128
Population: PK (N=XX)

Parameter	Sample Type	Statistic	V-128 (N=xxx)
AUC (ngEq/min.mL)	Blood	n	xxx
		Mean (SD)	xx.xx(xx.x)
		Geometric mean (CV)	xx.xx(xx.x)
		Median	xx.x
		Min, Max	xx.x, xx.x
	Serum	n	xxx
		Mean (SD)	xx.xx(xx.x)
		Geometric mean (CV)	xx.xx(xx.x)
		Median	xx.x
		Min, Max	xx.x, xx.x
	Blood/serum	....	….
Terminal t1/2 (min)	Blood	n	xxx
		Mean (SD)	xx.xx(xx.x)
		Geometric mean (CV)	xx.xx(xx.x)
		Median	xx.x
		Min, Max	xx.x, xx.x

Data source: listing 16.x.x.x
Source code: xxxx.ssc. Date/time of run: DDMMMYYYY:HH:MM.

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Table 14.2.3: Summary of Percent excretion of total radioactivity in urine

Population: PK (N=xx)

Timepoint	Statistic	V-128 (N=xxx)
Before treatment	n	xxx
	Mean (SD)	xx.xx(xx.x)
	Geometric mean (CV)	xx.xx(xx.x)
	Median	xx.x
	Min, Max	xx.x, xx.x
Up to 1h	n	xxx
	Mean (SD)	xx.xx(xx.x)
	Geometric mean (CV)	xx.xx(xx.x)
	Median	xx.x
	Min, Max	xx.x, xx.x
1h->4hrs	n	xxx
	Mean (SD)	xx.xx(xx.x)
	Geometric mean (CV)	xx.xx(xx.x)
	Median	xx.x
	Min, Max	xx.x, xx.x

Data source: listing 16.x.x.x
Source code: xxxx.ssc. Date/time of run: DDMMMYYYY:HH:MM.

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Table 14.2.4: Summary of Serum concentrations (ng/mL) of rhAnnexin V-128 based on ELISA analysis

Population: PK (N=xx)

Timepoint	Statistic	V-128 (N=xxx)
Before treatment	n	xxx
	Mean (SD)	xx.xx(xx.x)
	Geometric mean (CV)	xx.xx(xx.x)
	Median	xx.x
	Min, Max	xx.x, xx.x
5 minutes	n	xxx
	Mean (SD)	xx.xx(xx.x)
	Geometric mean (CV)	xx.xx(xx.x)
	Median	xx.x
	Min, Max	xx.x, xx.x
10 minutes	n	xxx
	Mean (SD)	xx.xx(xx.x)
	Geometric mean (CV)	xx.xx(xx.x)
	Median	xx.x
	Min, Max	xx.x, xx.x

Data source: listings 16.X.X
Source code: xxxx.ssc. Date/time of run: DDMMMYYYY:HH:MM.

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Table 14.2.5: Summary of Volume of distribution (Vz) and systemic clearance (Cl) of rhAnnexin V-128 based on ELISA analysis.

Population: PK (N=xx)

Parameter	Statistic	V-128 (N=xxx)
Volume of distribution (Vz)	n	xxx
	Mean (SD)	xx.xx(xx.x)
	Geometric mean (CV)	xx.xx(xx.x)
	Median	xx.x
	Min, Max	xx.x, xx.x
systemic clearance (Cl)	n	xxx
	Mean (SD)	xx.xx(xx.x)
	Geometric mean (CV)	xx.xx(xx.x)
	Median	xx.x
	Min, Max	xx.x, xx.x

Data source: listings 16.x.x
Source code: xxxx.ssc. Date/time of run: DDMMMYYYY:HH:MM.

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Table 14.2.6 Summary of SEC-HPLC analysis results
Population: PK (N=xx)

Species found	Visit	Statistics	Score
XXXXX	Day 1	n	XXX
		Total	XXXXX
		Mean	XXX.X
		SD	XXX.XX
		Median	XXX.X
		Min, Max	XXX, XXX
	24 Hours	n	XXX
		Total	XXXXX
		Mean	XXX.X
		SD	XXX.XX
		Median	XXX.X
		Min, Max	XXX, XXX

Data source: listing 16.x.x.x
Source code: xxxx.ssc. Date/time of run: DDMMMYYYY:HH:MM

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Table 14.3.1.1 Overall Summary of TEAEs
Population: Safety (N=xx)

AE Category	RA (N=xx) n(%)[Events]	AS (N=xx) n(%)[Events	V-128 Total (N=xx) n(%)[Events
Treatment emergent AEs	xx (xx.x)[xx]	xx (xx.x)[xx]	xx (xx.x)[xx]
Treatment emergent adverse drug reactions	xx (xx.x)[xx]	xx (xx.x)[xx]	xx (xx.x)[xx]
Treatment emergent SAEs	xx (xx.x)[xx]	xx (xx.x)[xx]	xx (xx.x)[xx]
Treatment emergent serious adverse drug reactions	xx (xx.x)[xx]	xx (xx.x)[xx]	xx (xx.x)[xx]
Treatment emergent AEs leading to withdrawal	xx (xx.x)[xx]	xx (xx.x)[xx]	xx (xx.x)[xx]
Treatment emergent AEs leading to death	xx (xx.x)[xx]	xx (xx.x)[xx]	xx (xx.x)[xx]
...			

Data source: Listing 16.2.x.x.x
Source code: xxxx.ssc. Date/time of run: DDMMMYYYY:HH:MM.

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Table 14.3.1.2 Occurrence of TEAEs – Number and Percentage of Subjects by System Organ Class and Preferred Term
Population: Safety

System Organ Class(1)	Preferred Term(1)	RA (N=xx) n (%)	AS (N=xx) n (%)	V-128 Total (N=xx) n (%)
Any adverse event		xx (xx.x)	xx (xx.x)	xx (xx.x)
SOC 1	Any SOC 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Term 3	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Term 4	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Term 5	xx (xx.x)	xx (xx.x)	xx (xx.x)
SOC 2	Any SOC 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Term 11	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Term 21	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Term 31	xx (xx-x)	xx (xx-x)	xx (xx-x)
	Term 41	xx (xx-x)	xx (xx-x)	xx (xx-x)
	Term 51	xx (xx-x)	xx (xx-x)	xx (xx-x)

[1] Coding Dictionary MedDRA, Version XX.X
Note: Occurrences are based on the number of subjects who had one or more event with the same PT within the same SOC
Data source: Listing 16.2.x.x.x
Source code: xxxx.ssc. Date/time of run: DDMMMYYYY:HH:MM.

Versions:

- 14.3.1.3 Occurrence of Serious TEAEs – Number and percentage of subject by System Organ Class and Preferred Term
- 14.3.1.4 Occurrence of TEAEs leading to permanent treatment discontinuation – Number and percentage of subject by System Organ Class and Preferred Term

Table 14.3.1.5 Occurrence of Serious TEAEs by Severity – Number and Percentage of Subjects by System Organ Class and Preferred Term
Population: Safety (N=xx)

System Organ Class / Preferred Term [1]	Severity [2]	RA (N=xx) n (%)	AS (N=xx) n (%)	V-128 Total (N=xx) n (%)
All	Mild	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Moderate	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Severe	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Life threatening	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Fatal	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class 1	Mild	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Moderate	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Severe	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Life threatening	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Fatal	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	Mild	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Moderate	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Severe	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Life threatening	xx (xx.x)	xx (xx.x)	xx (xx.x)
...	Fatal	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class 2		xx (xx-x)	xx (xx-x)	xx (xx-x)
...		...	...	...

Note: Occurrences are based on the number of subjects who had one or more event with the same PT within the same SOC
Data source: Listing 16.2.x.x.x
Source code: xxxx.ssc. Date/time of run: DDMMMYYYY:HH:MM.
[1] Coding Dictionary MedDRA, Version xx.x
[2] Worst Severity for each AE is considered

Versions:

- 14.3.1.6 Occurrence of TEAEs by Severity – Number and Percentage of Subjects by System Organ Class and Preferred Term

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Table 14.3.1.7 Occurrence of Serious TEAEs by Relationship to study drugs – Number and Percentage of Subjects by System Organ Class, and Preferred Term
Population: Safety (N=xx)

System Organ Class [1]	Preferred Term[1]	RA (N=xx) n (%)	AS (N=xx) n (%)	V-128 (N=xx) n (%)
Any adverse event		xx (xx.x)	xx (xx.x)	xx (xx.x)
DRUG RELATED		xx (xx.x)	xx (xx.x)	xx (xx.x)
SOC 1		xx (xx.x)	xx (xx.x)	xx (xx.x)
	PT 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
	PT 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
NOT DRUG RELATED		xx (xx.x)	xx (xx.x)	xx (xx.x)
SOC 2		xx (xx.x)	xx (xx.x)	xx (xx.x)
	PT 3	xx (xx.x)	xx (xx.x)	xx (xx.x)
	PT 4	xx (xx.x)	xx (xx.x)	xx (xx.x)
SOC 3		xx (xx.x)	xx (xx.x)	xx (xx.x)
	PT 5	xx (xx.x)	xx (xx.x)	xx (xx.x)
SOC 4		xx (xx.x)	xx (xx.x)	xx (xx.x)
	PT 6	xx (xx.x)	xx (xx.x)	xx (xx.x)
	PT 7	xx (xx.x)	xx (xx.x)	xx (xx.x)
	PT 8	xx (xx.x)	xx (xx.x)	xx (xx.x)
SOC 5		xx (xx-x)	xx (xx-x)	xx (xx-x)
	PT 9	...	...	...
	PT 10	...	...	...
..				

Note: Occurrences are based on the number of subjects who had one or more event with the same PT within the same SOC
Data source: Listing 16.2.x.x.x
Source code: xxxx.ssc. Date/time of run: DDMMMYYYY:HH:MM.
[1] Coding Dictionary MedDRA, Version xx.x

Versions:

Table 14.3.1.8 Occurrence of TEAEs by Relationship to study drugs – Number and Percentage of Subjects by System Organ Class, and Preferred Term

Table 14.3.2 Listing of Deaths and Other Serious Adverse Events
Population: Safety (N=xx)

Cohort: XXX

Subject	SAE No.	System Organ Class/ Preferred Term [1]/ Verbatim [1]/	Event date	Event Duration (Days)	Time to Event (Days)	Outcome	Severity	Action(s) taken with study treatment	Relationship with study treatment	Serious criteria
xxxxx	X	Xxxxxxxxxxxxxxxxxxxxxx/ Xxxxxxxxxxxxxxxxxxxxxx/ Xxxxxxxxxxxxxxxxxxxxx	DDMMMYYYY	XX	XX	Fatal	Fatal	Permanently discontinued	Unrelated	Results in death
xxxxx	X	Xxxxxxxxxxxxxxxxxxxxxx/ Xxxxxxxxxxxxxxxxxxxxxx/ Xxxxxxxxxxxxxxxxxxxxx	DDMMMYYYY	XX	XX	Recovered/ resolved	Severe	None/continued	Related	
XX	X	Xxxxxxxxxxxxxxxxxxxxxx/ Xxxxxxxxxxxxxxxxxxxxxx/ Xxxxxxxxxxxxxxxxxxxxx	DDMMMYYYY	XX	XX	Recovered/ resolved	Severe	None/continued	Related	Life-threatening/ Requires/prolongs hospitalization

Data source: listings 16.x.x.x.x. and 16.x.x.x.x
Source code: xxxx.ssc. Date/time of run: DDMMMYYYY:HH:MM.
[1] Coding Dictionary MedDRA, Version xx.x

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Table 14.3.4.1: Listing of Laboratory Safety Values for Subjects with Clinically Significant Abnormal Laboratory Values
Population: Safety (N=xx)

Cohort: XXX

Subject	Visit	Date	Time	Laboratory test	Result	Unit	Lower range	Upper range	Alert flag
XX-XXX-XX	Screening	DDMMMYYYY	XX:XX	XXXXXX	XXX.X	XXX	XXX	XXX	H
	Day 1	DDMMMYYYY	XX:XX	XXXXXX	XXX.X	XXX	XXX	XXX	L
XX-XXX-XX		DDMMMYYYY	XX:XX	XXXXXX	XXX.X	XXX	XXX	XXX	L
...	....	...	...	...	...	...	...	...	...

Data source: listings 16.x.x.x.x, 16.x.x.x.x
Source code: xxxx.ssc. Date/time of run: DDMMMYYYY:HH:MM.

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Table 14.3.4.2: Haematology parameters at each visit and change from baseline
Population: Safety

Test(unit)	Visit	Statistics	RA (N=xx)		AS (N=xx)		V-128 Total (N=xx)	
			Raw	Change from Baseline	Raw	Change from Baseline	Raw	Change from Baseline
WBC (xx/yy)	Baseline [1]	n	x		x		x	
		Mean	xx		xx		xx	
		SD	x.x		x.x		x.x	
		Median	xx.x		xx.x		xx.x	
		Min; Max	xx ; xxx		xx ; xxx		xx ; xxx	
	Day 30	n	x	x	x	x	x	x
		Mean	xx	xx	xx	xx	xx	xx
		SD	x.x	x.x	x.x	x.x	x.x	x.x
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min; Max	xx ; xxx	xx ; xxx	xx ; xxx	xx ; xxx	xx ; xxx	xx ; xxx
	.....							
	Day 90	n	x	x	x	x	x	x
		Mean	xx	xx	xx	xx	xx	xx
		SD	x.x	x.x	x.x	x.x	x.x	x.x
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min; Max	xx ; xxx	xx ; xxx	xx ; xxx	xx ; xxx	xx ; xxx	xx ; xxx

Data source: listings 16.x.x.x.x and 16.x.x.x.x.
Source code: xxxx.ssc. Date/time of run: DDMMMYYYY:HH:MM.
[1] Baseline is defined as the latest available observation before drug administration.

Versions:

- 14.3.4.3 Biochemistry parameters at each visit and change from baseline
- 14.3.4.4 Urinalysis parameters at each visit and change from baseline

Note: Categorical variables will be presented in the last page using number of subjects in the analysis population (N), number of subjects with non-missing observations (n), and frequency and percentages by category. See here below:

Test	Visit	Result	RA (N=xx) n (%)	AS (N=xx) n (%)	V-128 Total (N=xx) n (%)
Urine Proteins (dipstick)	Screening				
		Positive	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Negative	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Day 30				
		Positive	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Negative	xx (xx.x)	xx (xx.x)	xx (xx.x)

Percentages are based on the number of subjects in the safety population.

Table 14.3.5 Disease Assessment (BASDAI, BASFI, BASMI, DAS28, ACR/EULAR scores)
at each visit and change from baseline
Population: Safety (N=xxx)

Assessment scale	Visit	Statistics	RA (N=xx)		AS (N=xx)	
			Raw Score	Change from baseline	Raw Score	Change from baseline
BASDAI	Baseline	N	XXX		XXX	
		Total	XXXXX		XXXXX	
		Mean	XXX.X		XXX.X	
		SD	XXX.XX		XXX.XX	
		Median	XXX.X		XXX.X	
		Min, Max	XXX, XXX		XXX, XXX	
	Day 42	N	XXX	XXX	XXX	XXX
		Total	XXXXX	XXXXX	XXXXX	XXXXX
		Mean	XXX.X	XXX.X	XXX.X	XXX.X
		SD	XXX.XX	XXX.XX	XXX.XX	XXX.XX
		Median	XXX.X	XXX.X	XXX.X	XXX.X
		Min, Max	XXX, XXX	XXX, XXX	XXX, XXX	XXX, XXX

Data source: listing 16.x.x.x8
Source code: xxxx.ssc. Date/time of run: DDMMMYYYY:HH:MM

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Table 14.3.6 Listing of Anti-Annexin V-128 IgG and IgM antibodies Reactive results
Population: Safety (N=xx)

Cohort: XXX

Subject	Visit	Result	Absorbance (OD)
XX-XXX	Screening	Reactive	X.XXX
XX-XXX	Day 56	Reactive	X.XXX
XX-XXX	Day 90	Reactive	X.XXX

Data source: listings 16.x.x.x.x. and 16.x.x.x.x
Source code: xxxx.ssc. Date/time of run: DDMMMYYYY:HH:MM.

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Table 14.3.7: Physical examination at each visit
Population: Safety

Test (unit)	Visit	Statistic	RA (N=XXX)	AS (N=XXX)	V-128 Total (N=XXX)
Weight	Screening	n	XXX	XXX	XXX
(kg)		Mean	XXX.XX	XXX.XX	XXX.XX
		SD	XXX.XXX	XXX.XXX	XXX.XXX
		Median	XXX.XX	XXX.XX	XXX.XX
		Min, Max	XXX.X, XXX.X	XXX.X, XXX.X	XXX.X, XXX.X
	Day 42	n	XXX	XXX	XXX
		Mean	XXX.XX	XXX.XX	XXX.XX
		SD	XXX.XXX	XXX.XXX	XXX.XXX
		Median	XXX.XX	XXX.XX	XXX.XX

Data source: listings 16.x.x.x.x and 16.x.x.x.x.
Source code: xxxx.ssc. Date/time of run: DDMMMYYYY:HH:MM.
Physical examination includes: height, weight, BMI

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Table 14.3.8.1 Vital Signs at each visit and change from baseline
Population: Safety

Test (unit)	Visit	Statistic	RA (N=xx)		AS (N=xx)		V-128 Total (N=xx)	
			Raw	Change from Baseline	Raw	Change from Baseline	Raw	Change from Baseline
Systolic Blood Pressure Supine (xx/yy)	Baseline[1]	n	XXX		XXX		XXX	
		Mean	XXX.XX		XXX.XX		XXX.XX	
		SD	XXX.XXX		XXX.XXX		XXX.XXX	
		Median	XXX.XX		XXX.XX		XXX.XX	
		Min, Max	XXX.X, XXX.X		XXX.X, XXX.X		XXX.X, XXX.X	
	Day 2	n	XXX	XXX	XXX	XXX	XXX	XXX
		Mean	XXX.XX	XXX.XX	XXX.XX	XXX.XX	XXX.XX	XXX.XX
		SD	XXX.XXX	XXX.XXX	XXX.XXX	XXX.XXX	XXX.XXX	XXX.XXX
		Median	XXX.XX	XXX.XX	XXX.XX	XXX.XX	XXX.XX	XXX.XX
		Min, Max	XXX.X,XXX.X	XXX.X,XXX.X	XXX.X,XXX.X	XXX.X,XXX.X	XXX.X,XXX.X	XXX.X,XXX.X
	Etc...							

[1] Baseline is defined as the latest available observation before drug administration.
Data source: listings 16.x.x.x.x and 16.x.x.x.x.
Source code: xxxx.ssc. Date/time of run: DDMMMYYYY:HH:MM.
Vital sign includes: blood pressure, heart rate

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Table 14.3.8.2 Vital Signs – Shifts from baseline
Population: Safety

Cohort: RA (N=xx)

Test (unit)	Visit	Result	Baseline Result				
			Low	Normal	High	Missing	Total
			n (%)	n (%)	n (%)	n (%)	n (%)
Systolic Blood Pressure Supine (xx/yy)	Day 2	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		High	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Missing	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (100)
	Day 30	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		High	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Missing	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (100)
	Etc...						

[1] Baseline is defined as the latest available observation before drug administration.
Percentages are based on the number of patients with at least one available baseline or post-baseline result.
Data source: listings 16.x.x.x.x and 16.x.x.x.x.
Source code: xxxx.ssc. Date/time of run: DDMMMYYYY:HH:MM.
Vital sign includes: blood pressure, heart rate

Programming note: Continue table for all treatment groups and total.

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Table 14.3.9.1: Overall Electrocardiogram interpretation
Population: Safety

Visit	ECG interpretation	RA (N=XXX) n (%)	AS (N=XXX) n (%)	V-128 Total (N=XXX) n (%)
Baseline [1]				
	Not Done	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
	Normal	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
	Abnormal, Not Clinically Significant	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
	Abnormal, Clinically Significant	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
24 hours				
	Not Done	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
	Normal	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
	Abnormal, Not Clinically Significant	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
	Abnormal, Clinically Significant	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
.....	.....			
.....	.....			
.....	.....			

[1] Baseline is defined as the latest available observation before drug administration.

Data source: listings 16.x.x.x.x and 16.x.x.x.x
Source code: xxxx.ssc. Date/time of run: DDMMMYYYY:HH:MM.

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Table 14.3.9.2: Electrocardiogram parameters at each visit and change from baseline
Population: Safety

Test(unit)	Visit	Statistics	RA (N=xx)		AS (N=xx)		V-128 Total (N=xx)	
			Raw	Change from Baseline	Raw	Change from Baseline	Raw	Change from Baseline
HR (xx/yy)	Baseline [1]	n	x		x		x	
		Mean	xx		xx		xx	
		SD	x.x		x.x		x.x	
		Median	xx.x		xx.x		xx.x	
		Min; Max	xx ; xxx		xx ; xxx		xx ; xxx	
	Day 30	n	x	x	x	x	x	x
		Mean	xx	xx	xx	xx	xx	xx
		SD	x.x	x.x	x.x	x.x	x.x	x.x
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min; Max	xx ; xxx	xx ; xxx	xx ; xxx	xx ; xxx	xx ; xxx	xx ; xxx
	.....							
	Day 90	n	x	x	x	x	x	x
		Mean	xx	xx	xx	xx	xx	xx
		SD	x.x	x.x	x.x	x.x	x.x	x.x
		Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
		Min; Max	xx ; xxx	xx ; xxx	xx ; xxx	xx ; xxx	xx ; xxx	xx ; xxx

Data source: listings 16.x.x.x.x and 16.x.x.x.x.
Source code: xxxx.ssc. Date/time of run: DDMMMYYYY:HH:MM.
ECG includes: HR, RR interval, PR interval, QRS interval, QT interval
[1] Baseline is defined as the latest available observation before drug administration.

10.5 Figure Shells

The figure will be presented according to the following shells.

10.5.1 Shell 1 – Concentration of

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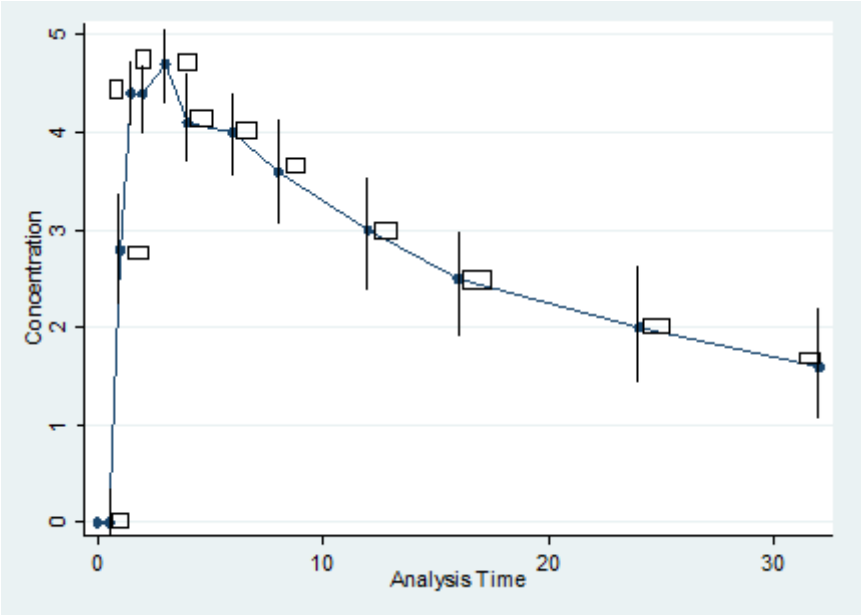
Figure 14.x.x.x Mean of
Population: xxxxxxxx (N=xx)



Note:xxxx
Data source: <14.x.x.x.x:datalisting name>
Source code:<name of program>.sas
Date/time of run: DDMMMYYYY:hh:mm

10.5.2 Shell 2 – AUC

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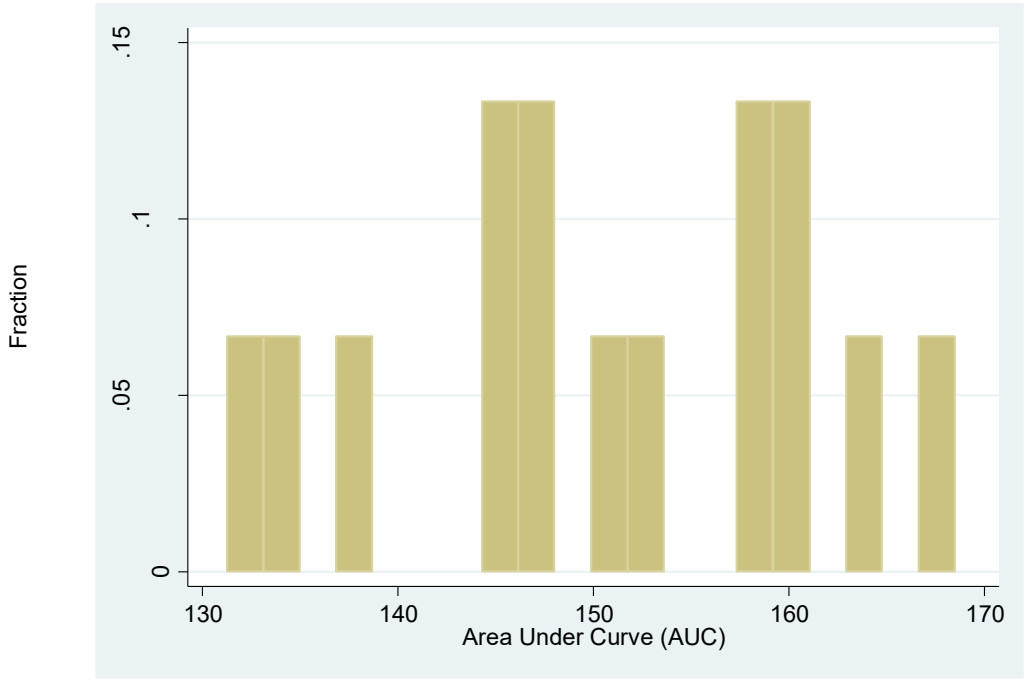
Figure 14.x.x.x Area Under the Curves
Population: xxxxxxxx (N=xx)



[redacted]

10.5.3 Shell 3 – Box-Plot

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Figure 14.x.x.x Box-Plot of
Population: xxxxxxxx (N=xx)