CLINICAL TRIAL CONSULTANTS AB

CONFIDENTIAL

Statistical Analysis Plan (SAP)

(Combined SAD, MAD and Part IV)

Sponsor:	*Gesynta Pharma AB*
Study code:	*GS-1001*
CTC project no:	*225-45-2018*
Study title:	*A Phase I, placebo-controlled, double-blind, first-in-human study to investigate safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of GS-248 solution in healthy subjects and patients with systemic sclerosis (SSc)*
SAP version and date:	*Draft version 0.1 05MAR2020* *Draft version 0.2 11MAR2020* *Final version 1.0 17MAR2020*

1 VERSION HISTORY

This Statistical Analysis Plan (SAP) for study GS-1001 is based on the protocol dated 29MAY2019.

Table 1 SAP Version History Summary

SAP version	Approval Date	Changes	Rationale
0.1	04MAR2020		Internal review
0.2	11MAR2020		Sponsor review
1.0			Original version

2 INTRODUCTION

This Statistical Analysis Plan (SAP) gives details regarding the statistical analyses for the comparison between treatment groups in the Part I (SAD), Part II (MAD) and Part IV of the study. Data presentation outlined in the final Clinical study protocol (CSP) for the study *GS-1001.* Any changes from the final CSP are given in Section 0.
A separate SAP have been constructed for each part of the study: GS-1001_SAP_v.1.0_11DEC2019 - SAD, GS-1001SAP_v.1.0_13FEB2020 - MAD and GS-1001_SAP_v.1.0_27FEB2020 - Part IV. Some of the analyses described in this SAP will supersede the analyses presented in each separate SAP, but for all TLF will the descriptive statistics tables be including both the Part II (MAD) and Part IV data using the FAS population. Data from the Part I (SAD) of the study will only be used in specific analyses of the exploratory endpoints (cohort number 3 to 6).

3 CLINICAL STUDY DETAILS

3.1 Clinical Study Objectives and Endpoints

Table 2 – Study objectives and endpoints

Objects	Estimands/Endpoints
Primary	
Been included in previous SAP's: ***1. To determine the safety and tolerability following oral single and multiple ascending doses of GS-248 (solution) in healthy subjects and patients with SSc.***	*Included in previous SAPs:* *1.1 Frequency, severity and seriousness of adverse events (AEs)* *1.2 Clinically significant changes in:* • *12-lead electrocardiogram (ECG)* • *Vital signs* • *Safety laboratory parameters* • *Physical examinations*
Secondary	
Included in previous SAP's: ***1. To evaluate the PK of GS-248 in healthy subjects.***	*Included in previous SAP's:* *1.1 Part I: area under the curve from time 0 to time t (AUC_{0-t}), AUC from time 0 to infinity ($AUC_{0-\infty}$), terminal half-life ($T_{½}$), maximum plasma concentration (C_{max}), time to C_{max} (T_{max}), dose proportionality (based on AUC and C_{max}), apparent total body clearance following extravascular administration (CL/F) and apparent volume of distribution following extravascular administration (V_z/F).* *1.2 Part II and III after first dose interval: AUC_{0-t}, $T_{½}$, T_{max}, C_{max}, dose proportionality (based on AUC and C_{max}).* *1.3 Part II and III after last dose interval: AUC_{0-t}, AUC at steady state (AUC_{ss}), $T_{½}$, T_{max}, C_{max}, observed concentration at the end of a dosing interval, immediately before next administration (C_{trough} from the 2 doses preceding the last dose), dose proportionality (based on AUC_{ss} and C_{max}), CL/F, V_z/F and accumulation ratio.*
Tertiary/Exploratory	
1. To evaluate the PD effects of GS-248 and celecoxib by determination of microsomal Prostaglandin E synthase-1 (mPGES-1) activity (Prostaglandin E_2 [PGE_2] levels) in a whole blood assay (WBA).	*1.1 Ex vivo* determination of mPGES-1 activity (PGE_2 levels) in a WBA.

2. To explore the PD effects of GS-248 in plasma (asymmetric dimethylarginine [ADMA] and L-arginine) and urine (arachidonic acid [AA] metabolites) and additional exploratory inflammatory biomarkers in healthy subjects and patients with SSc.	*2.1* AA metabolites in urine captured pre-dose administration and during 24 h post-dose o -alfa-hydroxy-9,15-dioxo-13,14-dihydro-2,3,4,5, tetranor-prostan-1,20-dioic acid (PGEM). o 2,3-dinor-6-ketoprostaglandin F1α (PGIM). o 11-dehydro-thromboxane B_2 (TXM). *2.2* ADMA in plasma. *2.3* L-arginine in Plasma.
3. To explore the PD effects of celecoxib in plasma (ADMA and L-arginine) and urine (AA metabolites) and additional exploratory inflammatory biomarkers in healthy subjects after 10 days twice daily dosing to enable exploratory comparisons with GS-248 treated subjects.	*3.1* AA metabolites in urine captured pre-dose administration and during 24 h post-dose. o -alfa-hydroxy-9,15-dioxo-13,14-dihydro-2,3,4,5, tetranor-prostan-1,20-dioic acid (PGEM). o 2,3-dinor-6-ketoprostaglandin F1α (PGIM). o 11-dehydro-thromboxane B_2 (TXM). *3.2* ADMA in plasma. *3.3* L-arginine in Plasma.
4. To explore potential metabolites of GS-248 in plasma and urine (including metabolites in safety testing [MIST])	*4.1* Collection of plasma and urine for future analysis of potential metabolites after single and multiple dosing with GS-248. *4.2* Plasma and urine samples will be saved for future biomarker analyses e.g. further AA metabolite profiling in plasma and urine and inflammatory biomarkers in plasma and urine

3.2 Clinical Study Design

This is a FIH, double-blind, parallel-group, randomised, placebo-controlled study designed to evaluate the safety, tolerability, PK and PD of single and multiple ascending oral doses of GS-248 in healthy subjects. In addition, an exploratory comparison of the PD effects between celecoxib and GS-248 will be performed.
Study GS-1001 include three parts: Part I (SAD), Part II (MAD) and Part IV (celecoxib). Part III (SSc patient) in this study was cancelled.
Part I (single ascending dose [SAD]): safety, tolerability, PK and PD of single ascending oral doses of GS-248 in healthy male and female subjects.
Part II (multiple ascending dose [MAD]): safety, tolerability, PK and PD of multiple ascending oral doses of GS-248 in healthy male and female subjects during 10 days administration.
Part III (SSc patients): cancelled.
Part IV (celecoxib): PD of multiple oral doses of celecoxib (200 mg BID) in healthy males and females during 10 days administration.

3.3 Statistical Hypotheses

No statistical hypotheses have been made in any of the study parts.

3.4 Number of Subjects

The total number of subjects included in the study (Part I, Part II and Part IV) were 80.

- Part I (SAD): 48 subjects were randomised and dosed (6 cohorts, each of 8 subjects with 6 subjects receiving GS-248 (1mg, 5mg, 8mg, 40mg, 100mg and 300mg) and 2 receiving placebo).
- Part II (MAD): 24 subjects were randomised and dosed (3 cohorts, each of 8 subjects with 6 subjects receiving GS-248 (20mg, 60mg and 180mg) and 2 receiving placebo).
- Part III in the study was cancelled.
- Part IV (celecoxib): 8 subjects were randomised and dosed (1 cohort with 8 subjects receiving 200mg celecoxib BID).

3.5 Methods of Assigning Subject to IMP

See section 3.4

3.6 Blinding

Part I (SAD) and Part II (MAD) were conducted in double-blinded fashion and the allocation of treatments were not disclosed until clean file was declared, and the database were locked for each part. GS-248 and the placebo are identical in appearance.
Part IV (celecoxib) was a non-placebo controlled, non-randomised and open study.

4 STATISTICAL AND ANALYTICAL PLANS

4.1 Sample Size Determination

No formal sample size calculations have been performed for any part in this study. The proposed sample size is considered sufficient to provide adequate information for the study objective.

4.2 Definition of Analysis Sets

Safety Analysis Set

Not applicable.

Full Analysis Set

The Full Analysis Set (FAS) of each part will consist of all subjects/patients who have been randomised and received at least one dose of IMP and who have at least one post-baseline assessment of efficacy data.

Per Protocol Analysis Set

Not applicable.

PK Analysis Set

Not applicable.

Use of analysis set

The FAS population will be used for all analyses presented in this SAP.
Safety analysis set and Per protocol analysis set (PPS) will not be used in any part or in any analysis.

4.3 Definition of Baseline

Baseline measurement is defined as the latest measurement prior to first dose of each IMP (for WBA will this be defined as 24h pre-dose).

4.4 Summary Statistics

In general, all data collected will be presented with summary statistics and given in subject data listings. Summary statistics will include at least number of subjects, 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 and visit where applicable. Subject data listings will be sorted by treatment, dose, subject and timing of assessments.

4.5 Significance Level

All hypothesis testing will use a significance level of 5%.

4.6 Multiple Comparisons/Multiplicity

No adjustment for multiple comparison/multiplicity will be performed, all significant statistical findings, must be reviewed for medical relevance.

4.7 Handling of Dropouts, Missing Data and Outliers

Outliers will be included in summary tables and listings and will not be handled separately in any analyses. No imputation of data will be performed, however a sensitivity analysis will be applied when specific data are missing (applicable for the exploratory endpoints).
Values which are below detection limit will be set to 50% of detection limit.

4.8 Sensitivity analysis

For the exploratory endpoints will a sensitivity approach be performed, i.e. for data which is missing will two set of tables be produced. The first one with all data included and other with data for subjects with complete data.

4.9 Adjustment for Covariates

No adjustments for covariates have or will be performed.

4.10 Examination of Subgroups

No examination of the subgroups has or will be performed.

4.11 Blind Review

Not applicable.

5 SUBJECTS

5.1 Subject Disposition

The number of subjects that entered the study, withdrawn subjects, completed subjects and the number of subjects at each visit will be summarised by treatment group.

5.2 Baseline Characteristics and Demographics

The baseline characteristics and demographics have been described in the previous SAP's, GS-1001SAP_v.10_11DEC2019- SAD, GS-1001SAP_v.10_13FEB2020- MAD and GS-1001SAP_v.10_27FEB2020- Part IV. The tables for Part II (MAD) and Part IV (celecoxib) will be combined.

6 TREATMENT INFORMATION AND EXTENT OF EXPOSURE

6.1 Active Treatment

The number of subjects on each IMP will be tabulated using listings and summary statistics.

6.2 Prior and Concomitant Medications

Prior and concomitant medication data have been listed and tabulated by ATC code for each part in the study. It has been specified in previous SAP´s. Prior and concomitant medications were coded according to the World Health Organization (WHO) Anatomic Therapeutic Chemical (ATC) classification system.

7 STATISTICAL METHODOLOGY

All parameters will be presented by treatment group and visit using summary statistics. Additional statistical analyses are specified below.

7.1 Primary Endpoint(s) Analysis

Definition of endpoint(s)

The primary endpoints have been described in the previous SAP's, GS-1001SAP_v.10_11DEC2019- SAD, GS-1001SAP_v.1.0_13FEB2020- MAD and GS-1001SAP_v.10_27FEB2020- Part IV. The tables for Part II (MAD) and Part IV (celecoxib) will be combined.

7.2 Secondary Endpoint(s) Analysis

Definition of endpoint(s)

Secondary endpoints have been estimated for Part I (SAD) and Part II (MAD), described in GS-1001_SAP_v.1.0_11DEC2019 - SAD, GS-1001_SAP_v.1.0_13FEB2020 - MAD.

7.3 Tertiary/Exploratory Endpoint(s) Analysis

7.3.1.1 Analysis of mPGES-1 activity (PGE_2 levels) levels using whole blood assay

PGE_2 levels will be estimated for the absolute and percent change from pre-dose to both day 1 and day 10 subsequent timepoints. The change will be presented using summary statistics (one table per variable and comparison) and bar graphs (one graph per variable and comparison). The difference between all treatment groups, see table 3, will be analysed using Wilcoxon Rank Sum test and the p-values will be presented in a separate table (the Wilcoxon Rank sum test will only be applied for the changes between pre-dose and 24h value).

Table 3 – Comparison between treatment groups

Pairwise comparison groups	
Placebo	MAD 20mg
Placebo	MAD 60mg
Placebo	MAD 180mg
Placebo	Celecoxib
Celecoxib	MAD 20mg
Celecoxib	MAD 60mg
Celecoxib	MAD 180mg
MAD 20mg	MAD 60mg
MAD 20mg	MAD 180mg
MAD 60mg	MAD 180mg

A bar graph for the absolute and relative changes between pre-dose and Day 1 (24h) including treatment groups from SAD (cohorts 3 to 6 - 5mg, 40mg, 100, mg and 300mg), MAD (20mg, 60mg and 180mg), celexocib 200 mg BID and Placebo, see table 4, including p-values in comparison to Placebo (using all placebo subjects in one group).

Table 4 – Comparison between treatment groups

Pairwise comparison groups	
Placebo	MAD 20mg
Placebo	MAD 60mg
Placebo	MAD 180mg
Placebo	Celecoxib
Placebo	SAD 5mg
Placebo	SAD 40mg
Placebo	SAD 100mg
Placebo	SAD 300mg
Celecoxib	MAD 20mg
Celecoxib	MAD 60mg
Celecoxib	MAD 180mg
Celecoxib	SAD 5mg
Celecoxib	SAD 40mg
Celecoxib	SAD 100mg
Celecoxib	SAD 300mg
MAD 20mg	MAD 60mg
MAD 20mg	MAD 180mg
MAD 20mg	SAD 5mg
MAD 20mg	SAD 40mg
MAD 20mg	SAD 100mg
MAD 20mg	SAD 300mg
MAD 60mg	MAD 180mg
MAD 60mg	SAD 5mg
MAD 60mg	SAD 40mg
MAD 60mg	SAD 100mg
MAD 60mg	SAD 300mg
SAD 5mg	SAD 40mg
SAD 5mg	SAD 100mg
SAD 5mg	SAD 300mg
SAD 40mg	SAD 100mg
SAD 40mg	SAD 300mg
SAD 100mg	SAD 300mg

A bar graph for Part I (SAD), cohorts 3 to 6 (5mg, 40mg, 100mg and 300mg), the within subject changes between pre-dose and Day 1 (24h) (both absolute and percent) with Wilcoxon test in comparison to placebo will be applied and presented in graphs.

7.3.1.2 AA metabolites in urine

The AA metabolites that will be analysed in urine are PGEM, PGIM and TXM. The AA metabolite concentration will be normalised by urine creatinine concentration and total excretion over 24 hours will be calculated:

- Actual concentration data
- Values normalised by urine creatinine concentration
  - Formula : $^{ng}/_{mg} = \frac{AA\ metabolite\ (^{ng}/_{mL}) * 1000}{U-creatinine\ (mmol/L) * 113\ (g/mol)}$
- Calculated total excretion over 24 h (described in previous SAP as Normalised values for urine volume)
  - Formula: $ng = AA\ metabolite\ (^{ng}/_{mL}) * urine\ volume\ (ml)$

Each metabolite will be estimated for the absolute and percent change from pre-dose to post-dose. The changes will be presented using summary statistics (one table per variable and comparison) and bar graphs (one graph per variable and comparison). The difference between all treatment groups, see table 3, will be analysed using Wilcoxon Rank Sum test and tabulated.

7.3.1.3 ADMA, L-Arginine

ADMA/L-arginine and L-arginine will be estimated for the absolute and percent change from pre-dose to 2h, 8h and 24h. The change will be presented using summary statistics (one table per variable and comparison) and bar graphs (one graph per variable and comparison). The different between all treatment groups, see table 3, will be analysed using Wilcoxon Rank Sum test and will be presented in a table.

7.3.1.4 Renal creatinine clearance 24 h (ClCr):

Formula:

- AeCreatinine (mmol/24h) = Total sum over 24 hours of U-Creatinine (mmol/L) * U-Volume (L), as calculated for each urine fraction and summarized.
  - ClCr (L/h) = AeCreatinine (mmol)*1000 / [24 (h)*P-Creatinine (umol/L)]
    - ClCr (mL/min) = ClCr (L/h) * 1000/60

P-creatinine at day -1 and day 9 will be used for the MAD cohorts in the calculations, for the celecoxib cohort will screening and follow-up values be used.
Renal creatinine clearance will be presented in a table including Wilcoxon rank sum test p-value for the comparison between all the treatment groups.

7.4 Discontinuation

Subjects who discontinue from IMP treatment will be tabulated. The reason for discontinuation will be given. For discontinuation due to AE, the AEs will be given.

7.5 Other Analyses

Further analyses may be performed on an ad-hoc basis.

7.6 Interim Analysis

No interim analysis will be performed.

8 CHANGES FROM THE CSP

- There will be no Part III (patients with systematic sclerosis).
- The analyses for metabolites in safety testing (MIST) will not be included in the SAP or the CSR. MIST may be analysed in the future.
- One non-substantial amendment to the CSP. L-arginine should be analysed as well and have been added in the SAP.
- The future exploratory analyses of biomarkers and GS-248 metabolites will not be included in the SAP, may be analysed in the future.
- PGE_2 levels for Day 1 will be compared between the treatment groups: Part I (SAD) cohorts 3 to 6, Part II (MAD) and Part IV (celecoxib).
- PGE_2 levels will be compared and analysed using Wilcoxon Rank Sum test between the treatment groups: Part II (MAD) and Part IV (celecoxib).
- AA metabolites (PGEM, PGIM and TXM) will be compared and analysed using Wilcoxon Rank Sum test between the treatment groups: Part II (MAD) and Part IV (celecoxib).
- ADMA and L-arginine will be compared and analysed using Wilcoxon Rank Sum test between the treatment groups: Part II (MAD) and Part IV (celecoxib).

9 STATISTICAL DELIVERABLES

The following documents have been delivered:

- SAP Part I (SAD)
- TLF Part I (SAD)
- SAP Part II (MAD) (superseded with this version)
- TLF Part II (MAD) (superseded with this version)
- SAP Part IV (celecoxib) (superseded with this version)

The following documents will be delivered:

- Combined SAP
- Statistical analyses and summary tables

10 SOFTWARE

All statistical analyses will be performed using SAS Version 9.4 (SAS institute, Cary, NC) and all PK parameters will be calculated by non-compartmental analysis (NCA) using the software Phoenix WinNonlin® version 8.1 or later (Certara, U.S.A.).

11 APPROVAL

Issued by:

Fredrik Hansson
Responsible Biostatistician
CTC Representative

18MAR2020
Date (dd-Mmm-yyyy)

Approved by:

Sponsor Representative

18MAR2020
Date (dd-Mmm-yyyy)

12 SUPPORTIVE DOCUMENTATION

12.1 Appendix 1 – List of Abbreviations

Abbreviation of term	Explanation
AE	Adverse Event
ATC	Anatomical-Therapeutic-Chemical
CF	Clean File
CRF	Case Report Form
CSP	Clinical study protocol
CTC	Clinical Trial Consultants AB
FAS	Full Analysis Set
FIH	First in Human
IMP	Investigational medicinal product
MAD	Multiple Ascending Dose
MedDRA	Medical Dictionary for Regulatory Affairs
PGEM	11-alfa-hydroxy-9,15-dioxo-13,14-dihydro-2,3,4,5, tetranor-prostan-1,20-dioic acid
PGIM	2,3-dinor-6-ketoprostaglandin F1α
PK	Pharmacokinetic
PT	Preferred term
PPS	Per Protocol Set
SAD	Single Ascending Dose
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System
SD	Standard Deviation
TXT	11-dehydro-thromboxane B_2
WHO	World Health Organization

12.2Appendix 2 – Changes to Protocol-Planned Analyses

13 STATISTICAL OUTPUT LAUOUT

13.1Tables

Table 14.1.1 Baseline characteristics and demographics ([analysis set])

		GS-248 20 mg (N=X)	GS-248 60 mg (N=X)	GS-248 180 mg (N=X)	All GS-248 (N=X)	PLACEBO (N=X)	[All GS-248 and PLACEBO]	Celecoxib (N=X)X)
Age (years)	n/nmiss	x/x	x/x	x/x	x/x	x/x	x/x	x/x
	Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
	Median (Min, Max)	x.x (x, x)	x.x (x, x)	x.x (x, x)	x.x (x, x)	x.x (x, x)	x.x (x,x)	x.x (x,x)
Body Mass Index (kg/m2)	n/nmiss	x/x	x/x	x/x	x/x	x/x	x/x	x/x
	Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
	Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
Height (cm)	n/nmiss	x/x	x/x	x/x	x/x	x/x	x/x	x/x
	Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
	Median (Min, Max)	x.x (x, x)	x.x (x, x)	x.x (x, x)	x.x (x, x)	x.x (x, x)	x.x (x,x)	x.x (x,x)
Weight (kg)	n/nmiss	x/x	x/x	x/x	x/x	x/x	x/x	x/x
	Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
	Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x,x.x)	x.xx (x.x,x.x)
Sex	Female	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)

		GS-248 20 mg (N=X)	GS-248 60 mg (N=X)	GS-248 180 mg (N=X)	All GS-248 (N=X)	PLACEBO (N=X)	[All GS-248 and PLACEBO]	Celecoxib (N=X)X)
	Male	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)
Ethnicity	Hispanic Or Latino	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)
	Not Hispanic Or Latino	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)
Race	American Indian Or Alaska Native	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)
	Asian	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)
	Black or African American	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)
	Native Hawaiian or other Pacific Islander	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)
	White	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)	x (x.x%)

```
[STUDYID] Summarised demographics data.
Data based on the [analysis set].
SAS program: summary_demographics.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]
```

Table 14.1.2.1. Subject disposition MAD ([analysis set])

	Total
Subjects screened	x
- Screen failures	x
- Withdrawal of consent prior to randomisation	x
- Reserves	x
- Other	x
Randomised	x
- GS-248 20 mg	x
- GS-248 60 mg	x
- GS-248 180 mg	x
- PLACEBO	x
Withdrawn subjects	x
- Withdrawal of consent	x
- Lost to follow-up	x
- Non-compliance	x
- Significant AE	x
- Other	x
Completed subjects	x
- GS-248 20 mg	x
- GS-248 60 mg	x
- GS-248 180 mg	x
- PLACEBO	x
Included in safety analysis set	x
Included in full analysis set	x

	Total
Included in per protocol analysis set	x
Included in PK analysis set	x
Subjects at VISIT 1 SCREENING	x
Subjects at VISIT 2	x
Subjects at VISIT 3	x
Subjects at VISIT 4	x
Subjects at VISIT 5	x
Subjects at VISIT 6	x
Subjects at VISIT 7	x
Subjects at VISIT 8	x
Subjects at VISIT 9 FOLLOW-UP	x

Table 14.1.2.2. Subject disposition Celecoxib ([analysis set])

	Total
Subjects screened	x
- Screen failures	x
- Withdrawal of consent prior to treatment	x
- Reserves	x
- Other	x
Included	x
- Celecoxib	x
Withdrawn subjects	x
- Withdrawal of consent	x
- Lost to follow-up	x
- Non-compliance	x
- Significant AE	x
- Other	x
Completed subjects	x
- Celecoxib	x
Included in safety analysis set	x
Included in full analysis set	x
Included in per protocol analysis set	x
Subjects at VISIT 1 SCREENING	x
Subjects at VISIT 2	x
Subjects at PHONE CALL/DOSING AT HOME	x
Subjects at VISIT 4	x
Subjects at VISIT 5 FOLLOW-UP	x

Table 14.1.3. Medical history events by system organ class and preferred term ([analysis set])

	GS-248 20 mg (N=X)		GS-248 60 mg (N=X)		GS-248 180 mg (N=X)		[All GS-248] (N=X)		PLACEBO (N=X)		[All GS-248 and PLACEBO] (N=X)		celecoxib (N=X)	
System organ class Preferred term	n(%)	m	n(%)	m	n(%)	m	n(%)	m	n(%)	m	n(%)	m	n(%)	m
Total	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**
SOC 1	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**
SOC 1 PT 1	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
SOC 1 PT 2	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
SOC 1 PT 3	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
SOC 2	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**
SOC 2 PT 1	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
SOC 2 PT 2	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x

n, number of subjects; m, number of events
Percentages are based on the number of subjects in the treatment period included in the [analysis set]
[STUDYID] Medical history events by system organ class and preferred term, [analysis set], SAS program: mh_summary_by_soc_and_pt.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]

Table 14.1.4 Concomitant medications ([analysis set])

	GS-248 20 mg (N=X)		GS-248 60 mg (N=X)		GS-248 180 mg (N=X)		[All GS-248] (N=X)		PLACEBO (N=X)		[All GS-248 and PLACEBO] (N=X)		celecoxib (N=X)	
ATC level 4 ATC level 5	n(%)	m	n(%)	m	n(%)	m	n(%)	m	n(%)	m	n(%)	m	n(%)	m
Total	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	x	**x(x.x%)**	**x**
ATC 4	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	x	**x(x.x%)**	**x**
ATC 5	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x

n, number of subjects; m, number of events;
Percentages are based on the number of subjects in the full analysis set

Table 14.1.5 Study drug administration ([analysis set])

Treatment	Treatment duration (days)	N
GS-248 20 mg	x	x
GS-248 60 mg	x	x
GS-248 180 mg	x	x
Celecoxib 200 mg BID	x	x

Table 14.2.1.1. Overview of adverse events ([analysis set])

	GS-248 20 mg (N=X)		GS-248 60 mg (N=X)		GS-248 180 mg (N=X)		[All GS-248] (N=X)		PLACEBO (N=X)		[All GS-248 and PLACEBO] (N=X)		celecoxib (N=X)	
	n(%)	m	n(%)	m	n(%)	m	n(%)	m	n(%)	m	n(%)	m	n(%)	m
Any AE	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
Any SAE	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
Any AE leading to withdrawal	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
Any AE leading to death	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
Causality														
Possibly Related	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
Probably Related	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
Unlikely Related	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
Severity														
Mild	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
Moderate	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
Severe	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
Life-threatening	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
Death	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x

n, number of subjects; m, number of events
Percentages are based on the number of subjects in the treatment period included in the [analysis set].
Adverse events that occurred during screening are omitted from summary.
[STUDYID] Overview of adverse events, [analysis set], SAS program: ae_summary_tables.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]

14.2.1.1: FAS

Table 14.2.1.2. Adverse events by system organ class and preferred term ([analysis set])

	GS-248 20 mg (N=X)		GS-248 60 mg (N=X)		GS-248 180 mg (N=X)		[All GS-248] (N=X)		PLACEBO (N=X)		[All GS-248 and PLACEBO] (N=X)		celecoxib (N=X)	
System organ class Preferred term	n(%)	m	n(%)	m	n(%)	m	n(%)	m	n(%)	m	n(%)	m	n(%)	m
Total	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**
SOC 1s	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**
SOC 1 PT 1	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
SOC 1 PT 2	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
SOC 1 PT 3	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)		x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
SOC 2	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**
SOC 2 PT 1	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
SOC 2 PT 2	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x

n, number of subjects; m, number of events
Percentages are based on the number of subjects in the treatment period included in the [analysis set]
[STUDYID] Adverse events by system organ class and preferred term, [analysis set], SAS program: ae_summary_by_soc_and_pt.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]

Table 14.2.3.1. ECG ([analysis set])

Assessment (unit)	Result Category	Assessment timepoint		GS-248 20 mg	GS-248 60 mg	GS-248 180 mg	PLACEBO	Celecoxib
[Parameter 1] (unit)	Measured value	[Assessment timepoint 1]	n	x	x	x	x	x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
		[Assessment timepoint 2]	n	x	x	x	x	x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
	Absolute change from baseline	[Assessment timepoint 2]	n	x	x	x	x	x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
	Relative change from baseline (%)	[Assessment timepoint 2]	n	x	x	x	x	x
			Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
			Median (Min, Max)	x.x (x, x)	x.x (x, x)	x.x (x, x)	x.x (x, x)	x.x (x, x)

Data based on [ANALYSIS SET].
[STUDYID] [DOMAIN]: [PARAMETER CATEGORY], SAS program: descriptive_stat_tables.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]

Parameters: Heart rate, PQ/PR, QRS, QT and QTcF intervals.

Table 14.2.3.2. ECG interpretation ([analysis set])

			GS-248 20 mg	GS-248 60 mg	GS-248 180 mg	PLACEBO	Celecoxib
Assessment	Assessment timepoint	Result					
[Parameter 1]	[Assessment timepoint 1]	[RESULT 1]	x(x.x%)/X	x(x.x%)/X	x(x.x%)/X	x(x.x%)/X	x(x.x%)/X
		[RESULT 2]	x(x.x%)/X	x(x.x%)/X	x(x.x%)/X	x(x.x%)/X	x(x.x%)/X
	[Assessment timepoint 2]	[RESULT 1]	x(x.x%)/X	x(x.x%)/X	x(x.x%)/X	x(x.x%)/X	x(x.x%)/X
		[RESULT 2]	x(x.x%)/X	x(x.x%)/X	x(x.x%)/X	x(x.x%)/X	x(x.x%)/X

Data based on [ANALYSIS SET].
[STUDYID] [DOMAIN]: [PARAMETER CATEGORY], SAS program: descriptive_stat_tables.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]

Table 14.2.3.3. ECG – Shift table ([analysis set])

Subcategory for ECG	Parameter	Treatment	Assessment timepoint	Result	NORMAL n (%)	ABNORMAL CS n (%)	ABNORMAL NCS n (%)	MISSING n (%)	TOTAL n (%)
12-LEAD	Interpretation	GS-248 20 mg (N=X)	[Assessment timepoint 1]	NORMAL	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)
				ABNORMAL CS	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)
				ABNORMAL NCS	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)
				MISSING	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)
				TOTAL	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)

Data based on [ANALYSIS SET].
[STUDYID] [DOMAIN]: [PARAMETER CATEGORY], SAS program: descriptive_stat_tables.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]

Table 14.3.4.1. Vital signs ([analysis set])

[Layout same as ECG table]

```
Data based on [ANALYSIS SET].
[STUDYID] [DOMAIN]: [PARAMETER CATEGORY], SAS program: descriptive_stat_tables.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]
```

Parameters: Systolic and diastolic blood pressure, pulse and body temperature.

Table 14.3.5.1. Safety laboratory results – clinical chemistry ([analysis set])

[Layout same as ECG table]

```
Data based on [ANALYSIS SET].
[STUDYID] [DOMAIN]: [PARAMETER CATEGORY], SAS program: descriptive_stat_tables.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]
```

Clinical chemistry: alanine aminotransferase, albumin, alkaline phosphatase, aspartate aminotransferase, direct bilirubin, bilirubin, calcium, creatinine, estimated glomerular filtration, cholesterol, C reactive protein, cystatin C, gamma glutamyl transferase, glucose, Lactate dehydrogenase, osmolality, phosphate, potassium, sodium and urea nitrogen.

Table 14.3.5.2. Safety laboratory results – haematology ([analysis set])

[Layout same as ECG table]

```
Data based on [ANALYSIS SET].
[STUDYID] [DOMAIN]: [PARAMETER CATEGORY], SAS program: descriptive_stat_tables.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]
```

Hematology: erythrocyte, hematocrit, hemoglobin, leukocytes, lymphocytes, monocytes, neutrophils, eosinophils, basophils, mean corpuscular and platelet count.

Table 14.3.5.3. Safety laboratory results – coagulation ([analysis set])

[Layout same as ECG table]

```
Data based on [ANALYSIS SET].
[STUDYID] [DOMAIN]: [PARAMETER CATEGORY], SAS program: descriptive_stat_tables.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]
```

Coagulation: activated partial thromboplastin time and prothrombin complex international normalized ratio.

Table 14.3.5.4. Safety laboratory results - urinalysis ([analysis set])

[Layout same as ECG interpretation table]

```
Data based on [ANALYSIS SET].
[STUDYID] [DOMAIN]: [PARAMETER CATEGORY], SAS program: descriptive_stat_tables.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]
```

Urinalysis: bilirubin, erythrocytes, glucose, ketones, leucocytes, nitrite, pH, protein, specific gravity and urobilinogen.

Table 14.3.5.5. Safety laboratory results - shift table ([analysis set])

[Layout same as ECG shift table]

```
Data based on [ANALYSIS SET].
[STUDYID] [DOMAIN]: [PARAMETER CATEGORY], SAS program: descriptive_stat_tables.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]
```

Table 14.3.6.1. Physical examinations ([analysis set])

[Layout same as ECG interpretation table]

```
Data based on [ANALYSIS SET].
[STUDYID] [DOMAIN]: [PARAMETER CATEGORY], SAS program: descriptive_stat_tables.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]
```

Table 14.3.6.2 Physical examinations - shift table ([analysis set])

[Layout same as ECG shift table]

```
Data based on [ANALYSIS SET].
[STUDYID] [DOMAIN]: [PARAMETER CATEGORY], SAS program: descriptive_stat_tables.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]
```

Parameters: head, eyes, ears, nose, throat, skin, thyroid, neurological, lungs, cardiovascular, abdomen (liver and spleen), lymph nodes and extremities.

Table 14.3.1.x. PK parameters ([analysis set])

Assessment (unit)	Result Category		GS-248 20 mg	GS-248 60 mg	GS-248 180 mg
[Parameter 1] (unit)	Measured value	n	x	x	x
		Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
		Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
		Geometric Mean (CV%)	xx.xx (xx.x)	xx.xx (xx.x)	xx.xx (xx.x)
		n	x	x	x
		Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
		Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
		Geometric Mean (CV%)	xx.xx (xx.x)	xx.xx (xx.x)	xx.xx (xx.x)

Data based on [ANALYSIS SET].
[STUDYID] [DOMAIN]: [PARAMETER CATEGORY], SAS program: descriptive_stat_tables.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]

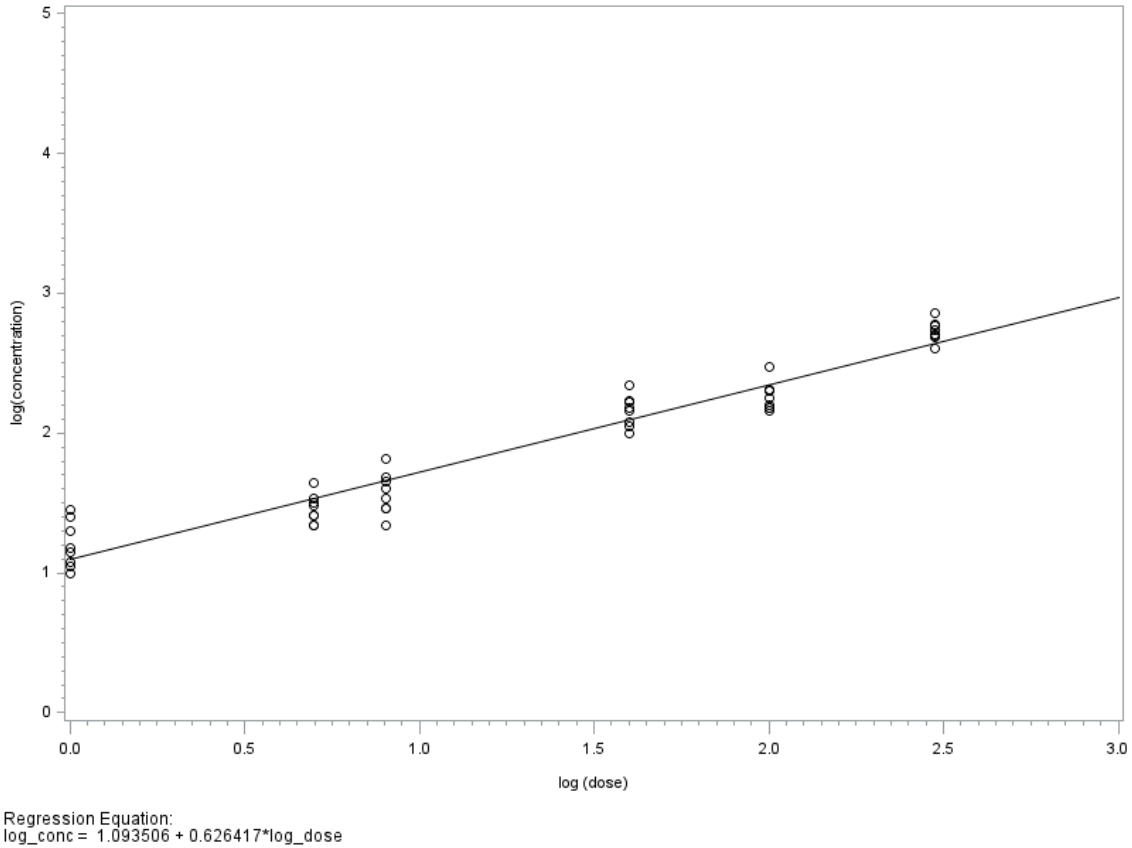
PK parameters: $AUC_{0\text{-}t}$, AUC_{ss}, $T_{½}$, T_{max}, C_{max}, V_z/F, CL/F, AUC_D and C_{max_D}

Table 14.3.2.x. PK concentrations ([analysis set])

				GS-248 20 mg	GS-248 60 mg	GS-248 180 mg
Assessment (unit)	Result Category	Assessment timepoint				
[Parameter 1] (unit)	Measured value	[Assessment timepoint 1]	n/BLQ/ULQ	x/x/x	x/x/x	x/x/x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
			Geometric Mean (CV%)	xx.xx (xx.x)	xx.xx (xx.x)	xx.xx (xx.x)
		[Assessment timepoint 2]	n/BLQ/ULQ	x/x/x	x/x/x	x/x/x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
			Geometric Mean (CV%)	xx.xx (xx.x)	xx.xx (xx.x)	xx.xx (xx.x)

Data based on [ANALYSIS SET].
[STUDYID] [DOMAIN]: [PARAMETER CATEGORY], SAS program: descriptive_stat_tables.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]

Figure 14.3.3.1.x. Dose proportionality after a first dose based on AUC0-t and Cmax ([analysis set])



[STUDYID] Dose proportionality of [parameter], [analysis set], SAS program: dose_prop.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]

Figure 14.3.3.2.x. Dose proportionality after a last dose interval based on AUCss and Cmax ([analysis set])

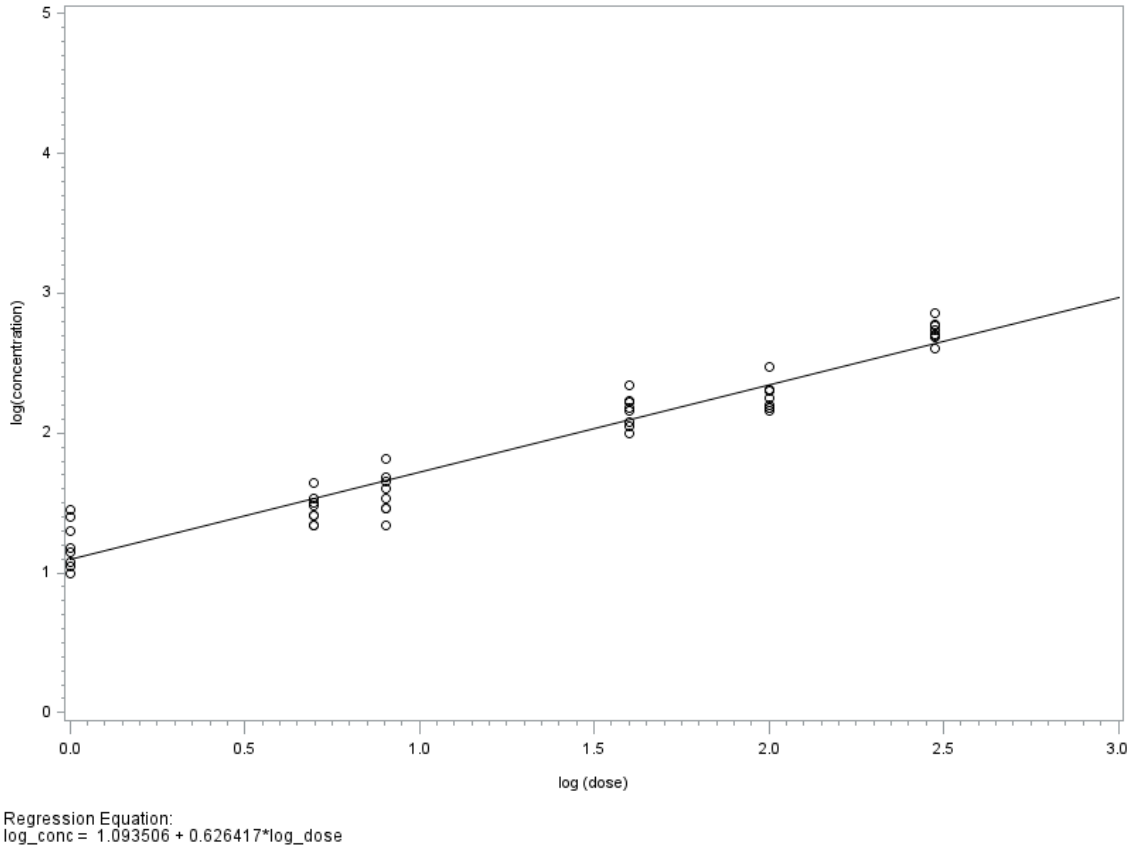


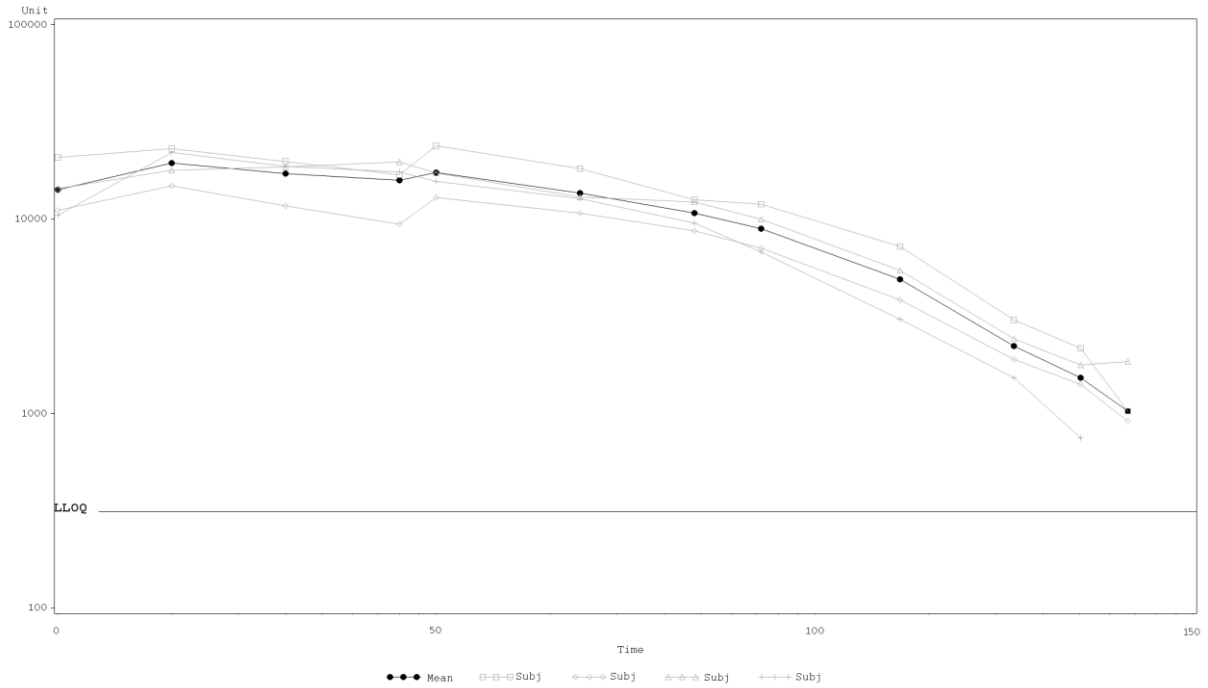
Table 14.3.3.3.1. PK parameter data used to present dose proportionality ([analysis set])

Assessment (unit)	Dose interval	Dose group		Subject 1	Subject 2	Subject 3	Subject 4	Subject 5	Subject 6
[Parameter 1] (unit)	First/last dose interval	Dose group 1 (x mg)	Subject ID	21xx	21xx	21xx	21xx	21xx	21xx
			value	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
			log(value)	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
			log(dose)	0	0	0	0	0	0
		Dose group 2 (x mg)	…	…	…	…	…	…	…

[STUDYID] Dose proportionality, [analysis set], SAS program: dose_prop.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]

PK parameters: Cmax, AUC_{0-t} and AUC_{ss}

Figure 14.3.4.x. PK concentrations ([analysis set])



*The figure will be based on geometric mean

Table 14.4.1.1. PGE2 levels in WBA SAD cohorts ([analysis set])

Assessment (unit)	Result Category	Assessment timepoint		GS-248 5 mg	GS-248 40 mg	GS-248 100 mg	GS-248 300	PLACEBO
[Parameter 1] (unit)	Measured value	[Assessment timepoint 1]	n	x	x	x	x	x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
		[Assessment timepoint 2]	n	x	x	x	x	x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
	Absolute change from baseline	[Assessment timepoint 2]	n	x	x	x	x	x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
			Wilcoxon between groups p-value	x.xxxx	x.xxxx	x.xxxx		x.xxxx
	Relative change from baseline (%)	[Assessment timepoint 2]	n	x	x	x	x	x
			Mean (SD)	x.x (x.x)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.x (x, x)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
			Wilcoxon between groups p-value	x.xxxx	x.xxxx	x.xxxx		x.xxxx

Data based on [ANALYSIS SET]. All p-values in comparison to PLACEBO.
[STUDYID] [DOMAIN]: [PARAMETER CATEGORY], SAS program: descriptive_stat_tables.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]

Parameters: WBA-DMSO, WBA-MF63, mPGES-1 activity

Table 14.4.1.2. P-values for pairwise comparisons between all dose groups for PGE2 levels Day 1([analysis set])

Figure 14.4.2.x. PGE2 levels Day 1 for all dose groups([analysis set])

Bar graph with SEM presenting Day 1 24 h post dose relative change from baseline values for all cohorts (SAD, MAD and Celecoxib)

Figure 14.4.3.x. PGE2 levels Day 1 for all dose groups ([analysis set])

Bar graph with p values presenting absolute and relative change from baseline for all dose groups. Graphs presented by dose group and all timepoints (one graph per dose group).

Table 14.4.4.1. PGE2 levels in WBA MAD cohorts and Celecoxib group ([analysis set])

Assessment (unit)	Result Category	Assessment timepoint		GS-248 20 mg	GS-248 60 mg	GS-248 180 mg	PLACEBO	Celecoxib
[Parameter 1] (unit)	Measured value	[Assessment timepoint 1]	n	x	x	x	x	x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
		[Assessment timepoint 2]	n	x	x	x	x	x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
	Absolute change from baseline	[Assessment timepoint 2]	n	x	x	x	x	x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
			Wilcoxon between groups p-value	x.xxxx	x.xxxx	x.xxxx		x.xxxx
	Relative change from baseline (%)	[Assessment timepoint 2]	n	x	x	x	x	x
			Mean (SD)	x.x (x.x)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.x (x, x)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
			Wilcoxon between groups p-value	x.xxxx	x.xxxx	x.xxxx		x.xxxx

Data based on [ANALYSIS SET]. All p-values in comparison to PLACEBO.
[STUDYID] [DOMAIN]: [PARAMETER CATEGORY], SAS program: descriptive_stat_tables.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]

Parameters: WBA-DMSO, WBA-MF63, mPGES-1 activity

Table 14.4.4.2. P-values for pairwise comparisons between all dose groups for PGE2 levels MAD cohorts and Celecoxib ([analysis set])

Figure 14.4.5.x. PGE2 levels Day 1 and Day 10 MAD cohorts and Celecoxib ([analysis set])

Bar graph with SEM presenting Day 1 and Day 10 24 h post dose relative change from baseline values for MAD cohorts and Celecoxib. Graphs presented by timepoint.

Figure 14.4.6.x. PGE2 levels Day 1 and Day 10 MAD cohorts and Celecoxib ([analysis set])

Bar graph with p values presenting absolute and relative change from baseline for MAD cohorts and Celecoxib. Graphs presented by dose group and all timepoints (one graph per dose group).

Table 14.5.1.x. AA metabolites ([analysis set])

Assessment (unit)	Result Category	Assessment timepoint		GS-248 20 mg	GS-248 60 mg	GS-248 180 mg	PLACEBO	Celecoxib
[Parameter 1] (unit)	Measured value	[Assessment timepoint 1]	n	x	x	x	x	x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
		[Assessment timepoint 2]	n	x	x	x	x	x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
	Absolute change from baseline	[Assessment timepoint 2]	n	x	x	x	x	x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
			Wilcoxon between groups p-value	x.xxxx	x.xxxx	x.xxxx		x.xxxx
	Relative change from baseline (%)	[Assessment timepoint 2]	n	x	x	x	x	x
			Mean (SD)	x.x (x.x)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.x (x, x)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
			Wilcoxon between groups p-value	x.xxxx	x.xxxx	x.xxxx		x.xxxx

Data based on [ANALYSIS SET]. All p-values in comparison to PLACEBO.
[STUDYID] [DOMAIN]: [PARAMETER CATEGORY], SAS program: descriptive_stat_tables.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]

Parameters: 11-alfa-hydroxy-9,15-dioxo-13,14-dihydro-2,3,4,5, tetranor-prostan-1,20-dioic acid (PGEM), 2, 3-dinor-6-ketoprostaglandin F1α (PGIM), 11-dehydro-thromboxane B_2 (TXM).

Table 14.5.1.y. P-values for pairwise comparisons between all dose groups for AA metabolites

Figure 14.5.2.x. AA metabolite levels Day 1 and Day 10 MAD cohorts and Celecoxib ([analysis set])

Bar graph with SEM presenting Day 1 and Day 10 24 h post dose relative change from baseline values for MAD cohorts and Celecoxib. Graphs presented by timepoint.

Figure 14.5.3.x. AA metabolites levels Day 1 and Day 10 MAD cohorts and Celecoxib ([analysis set])

Bar graph with p values presenting absolute and relative change from baseline for MAD cohorts and Celecoxib. Graphs presented by dose group and all timepoints (one graph per dose group).

Table 14.6.1.x. ADMA/L-Arg and L-Arg in plasma ([analysis set])

Assessment (unit)	Result Category	Assessment timepoint		GS-248 20 mg	GS-248 60 mg	GS-248 180 mg	PLACEBO	Celecoxib
[Parameter 1] (unit)	Measured value	[Assessment timepoint 1]	n	x	x	x	x	x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
		[Assessment timepoint 2]	n	x	x	x	x	x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
	Absolute change from baseline	[Assessment timepoint 2]	n	x	x	x	x	x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
			Wilcoxon between groups p-value	x.xxxx	x.xxxx	x.xxxx		x.xxxx
	Relative change from baseline (%)	[Assessment timepoint 2]	n	x	x	x	x	x
			Mean (SD)	x.x (x.x)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.x (x, x)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
			Wilcoxon between groups p-value	x.xxxx	x.xxxx	x.xxxx		x.xxxx

Data based on [ANALYSIS SET]. All p-values in comparison to PLACEBO.
[STUDYID] [DOMAIN]: [PARAMETER CATEGORY], SAS program: descriptive_stat_tables.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]

Parameters: ADMA/L-Arg, L-Arg

Table 14.6.1.y. P-values for pairwise comparisons between all dose groups for ADMA/L-Arg and L-Arg levels

Figure 14.6.2.x. ADMA/L-Arg and L-Arg levels Day 1 and Day 10 MAD cohorts and Celecoxib ([analysis set])

Bar graph with SEM presenting Day 1 and Day 10 24 h post dose relative change from baseline values for MAD cohorts and Celecoxib. Graphs presented by timepoint.

Figure 14.6.3.x. ADMA/L-Arg and L-Arg levels Day 1 and Day 10 MAD cohorts and Celecoxib ([analysis set])

Bar graph with p values presenting absolute and relative change from baseline for MAD cohorts and Celecoxib. Graphs presented by dose group and all timepoints (one graph per dose group).

Table 14.7.1.1. Renal creatinine clearance ClCr ([analysis set])

Assessment (unit)	Result Category	Assessment timepoint		GS-248 20 mg	GS-248 60 mg	GS-248 180 mg	PLACEBO	Celecoxib
[Parameter 1] (unit)	Measured value	[Assessment timepoint 1]	n	x	x	x	x	x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
		[Assessment timepoint 2]	n	x	x	x	x	x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
	Absolute change from baseline	[Assessment timepoint 2]	n	x	x	x	x	x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
			Wilcoxon between groups p-value	x.xxxx	x.xxxx	x.xxxx		x.xxxx
	Relative change from baseline (%)	[Assessment timepoint 2]	n	x	x	x	x	x
			Mean (SD)	x.x (x.x)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.x (x, x)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
			Wilcoxon between groups p-value	x.xxxx	x.xxxx	x.xxxx		x.xxxx

Data based on [ANALYSIS SET]. All p-values in comparison to PLACEBO.
[STUDYID] [DOMAIN]: [PARAMETER CATEGORY], SAS program: descriptive_stat_tables.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]

Table 14.7.1.2. P-values for pairwise comparisons between all dose groups for Renal creatinine clearance ClCr

Listings

Listing 16.2.1. Discontinued subjects (All subjects)

Listing 16.2.2. Protocol deviations (All subjects)

Listing 16.2.3.1 Subject excluded from Per protocol set (All subjects)

Listing 16.2.3.2 Population definitions (All subjects)

Listing 16.2.3.3 Non-eligible subjects (All subjects)

Listing 16.2.4.1. Demography (Full analysis set)

Listing 16.2.4.2. Medical history (Full analysis set)

Listing 16.2.4.3 Adverse events as screening, part 1 (Full analysis set)

Listing 16.2.4.4 Adverse events as screening, part 2 (Full analysis set)

Listing 16.2.5.1 Prior and concomitant medications (Full analysis set)

Listing 16.2.5.2. Exposure (Full analysis set)

Listing 16.2.6.1. Adverse events, part 1 (Full analysis set)

Listing 16.2.6.2. Adverse events, part 2 (Full analysis set)

Listing 16.2.6.3. Serious adverse events, part 1 (Full analysis set)

Listing 16.2.6.4. Serious adverse events, part 2 (Full analysis set)

Listing 16.2.6.5. Serious adverse events, seriousness criteria (Full analysis set)

Listing 16.2.7. ECG measurements (Full analysis set)

Listing 16.2.8. Vital signs (Full analysis set)

Listing 16.2.9.1 Laboratory values (Full analysis set)

Listing 16.2.9.2 Abnormal laboratory values (Full analysis set)

Listing 16.2.9. Physical examinations (Full analysis set)

Listing 16.2.10.1. GS-248 concentration (Full analysis set)

Listing 16.2.10.3. Pharmacokinetic parameters of GS-248 (Full analysis set)

Listing 16.2.10.5. PGE2 levels in WBA (Full analysis set)

Listing 16.2.11.1. AA metabolites in urine ([analysis set])

Listing 16.2.11.2. ADMA in plasma ([analysis set])

Listing 16.2.11.3. L-Arg in plasma ([analysis set])

Listing 16.2.11.4. Biomarkers and GS-248 metabolites ([analysis set])

Listing 16.2.12. Disposition (All subjects)

Listing 16.2.13. Subject visits (All subjects)

Listing 16.2.14. Subject elements (All subjects)