STATISTICAL ANALYSIS PLAN

A single centre, open label, pilot phase Ib study to investigate blood stage malaria infection after Direct Venous Inoculation of cryopreserved Plasmodium falciparum (NF54 strain) Sporozoites (PfSPZ-DVI) in malaria naïve healthy adult volunteers

Protocol:	MMV_PfSPZ-DVI Blood Stage_19_01
SGS LS number:	BE-80-1914715
Development phase:	Ib
Sponsor:	Medicines for Malaria Venture (MMV)
SAP version number:	Final 1.0
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PROTOCOL HISTORY

Protocol:		
Version or ID	**Date (ddMMMyyyy)**	**Impact of the changes on the statistical analysis**
Final 1.0	17DEC2019	NAP
Final 2.0	27JAN2020	Including substantial amendment 1: no impact on the statistical analysis.
Final 3.0	24JUN2020	Including substantial amendment 2: no impact on the statistical analysis.

This statistical analysis plan (SAP) only considers the last version of the protocol, and of the protocol amendments, as listed above.

LIST OF ABBREVIATIONS

ADaM	analysis data model
AE	adverse event
ALP	alkaline phosphatase
ALT	alanine transaminase
aPTT	activated partial thromboplastin time
AST	aspartate transaminase
β-HCG	β-human chorionic gonadotropin
BMI	body mass index
bpm	beats per minute
CI	confidence interval
CMV	cytomegalovirus
CRF	case report form
CRP	C-reactive protein
DBP	diastolic blood pressure
DVI	direct venous inoculation
DY	relative day
EBV	Epstein Barr Virus
ECG	electrocardiogram
eGFR	estimated glomerular filtration rate
EOS	end of study
FSH	follicle stimulating hormone
GGT	gamma-glutamyl transferase
HbsAg	hepatitis B surface antigen
HCV	hepatitis C virus
HIV	human immunodeficiency virus
HR	heart rate
ICF	informed consent form
ICH	International Council for Harmonisation
IgM	immunoglobulin M
INR	international normalised ratio
LDH	lactate dehydrogenase
log10PRR48	log10 parasite reduction ratio per 48 h

log10PRR48,max	maximum log10 parasite reduction ratio per 48 h
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
MedDRA	Medical Dictionary for Regulatory Activities
NAP	not applicable
NCE	new chemical entities
PC50	parasite clearance half-life
PC99	predicted time to reach parasite clearance of 99%
PCR	polymerase chain reaction
PD	pharmacodynamic
PfSPZ	P. falciparum sporozoites
PfSPZ-DVI Challenge	inoculation of P. falciparum sporozoites through direct venous inoculation
PMR	parasite multiplication rate
PMR48	parasite multiplication rate standardised to 48 h
PMRLC	parasite multiplication rate per life cycle (if not 48 h)
PRR	parasite reduction ratio
PT	prothrombin time
QTc	corrected QT interval
QTcB	Bazett's corrected QT interval
QTcF	Fridericia's corrected QT interval
RBC	red blood cell
rRT-PCR	real-time reverse transcription polymerase chain reaction
SAP	statistical analysis plan
SAF	safety analysis set
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SBP	systolic blood pressure
SCR	all screened subject's analysis set
SD	standard deviation
SE	standard error
SGS LS	SGS Life Sciences
SOP	standard operating procedure
STAT	statistics

TLF	tables, listings and figures
ULN	upper limit of normal
varATS	the acidic terminal segment in Plasmodium falciparum var genes
VIS	volunteer infection study
VS	vital signs
WBC	white blood cell
WHO	World Health Organisation
WI	work instruction

DEFINITION OF TERMS

baseline	An initial measurement of a condition that is taken at an early time point and used for comparison over time to look for changes. The study specific definition is in section 5.2.2.
case report form (CRF)	A printed, optical, or electronic document designed to record protocol required information to be reported to the sponsor for each trial subject.
display	Analysis table, figure or listing
phase	Interval of time in the planned conduct of a study associated with a specific purpose: for example, screening, treatment, follow-up.
round half up tie-breaking rule	Convention to round values ending with 5 to positive infinity. The round half up rule is implemented in the SAS® ROUND function.

Examples:

Database value	Rounded value
-1.35	-1.3
-1.25	-1.2
1.25	1.3
1.35	1.4

significant digit	All digits of a number used to express it to the required degree of accuracy, starting from the first non-zero digit.
post-baseline-emergent abnormality	Any post-baseline abnormality that was not present at baseline (e.g. haemoglobin normal at baseline and grade 1 post-baseline; glucose low at baseline and high post-baseline.

TABLE OF CONTENTS

1. INTRODUCTION

This SAP describes the final statistical analysis to be performed for the MMV_PfSPZ-DVI Blood Stage_19_01 (BE-80-1914715) study.

This SAP covers the pharmacodynamic (PD), safety, and general characteristics parts of the statistical analysis. It specifies the analysis displays to be presented and describes the methods and procedures in a more elaborated way than in the statistical methods section of the protocol. The parasite transcriptomics analysis is not in the scope of this SAP but will be described by the Institute of Tropical Medicine and reported separately.

The statistical analysis will process and present the results following the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) standards, in particular the ICH-E3, ICH-E6, and ICH-E9 guidelines.

1.1 STUDY OBJECTIVES

According to the protocol, the primary objectives of this study are:

- To evaluate the safety and tolerability associated with blood-stage malaria infection in naïve healthy participants after PfSPZ-DVI Challenge.
- To characterise key stages in the blood-stage parasite growth profile in malaria infection in naïve healthy participants after PfSPZ-DVI Challenge.

According to the protocol, the secondary objectives of this study are:

- To determine the safety and tolerability of Riamet® in blood-stage malaria infection in naïve healthy participants after PfSPZ-DVI Challenge.
- To characterise the blood-stage parasite profile in malaria infection in naïve healthy participants after PfSPZ-DVI Challenge before Riamet® administration.
- To characterise the blood-stage parasite clearance profile of Riamet® in malaria infection in naïve healthy participants after PfSPZ-DVI Challenge.

According to the protocol, the exploratory objective of this study is to characterise the individual variability of blood-stage parasite profile.

1.2 STUDY DESIGN

This is a single-centre, open-label, Phase Ib study designed to assess if intravenous bolus injection of approximately 3200 P. falciparum (NF54 strain) sporozoites can be safely administered to achieve blood-stage parasitaemia with a kinetics/PCR profile that will allow for the future characterisation of antimalarial blood-stage activity of NCEs in a relatively small number of participants during early drug development.

Up to 16 healthy, malaria-naïve males and females, aged 18-55 years, will be enrolled in a maximum of 2 cohorts (up to 8 participants per cohort; a participant may be enrolled in one cohort only). Enrolment into the cohorts will proceed sequentially, with two target levels of parasitaemia previously achieved in healthy participants enrolled in malaria VIS at other study sites, i.e., 5000 parasites/mL blood in Cohort 1 and 10000 parasites/mL blood in Cohort 2.

Each participant will be admitted to the clinical unit in the morning of Day -1 and inoculated with approximately 3200 P. falciparum sporozoites (NF54 strain) by DVI on Day 1. Participants will be discharged 2 h post inoculation on Day 1 and will be monitored daily via phone call from Day 2 until Day 6 to solicit any AEs. Participants will come to the clinical unit daily from Day 7 until Day 9 and together with the malaria clinical score, the presence of parasites will be assessed once daily by a specific qPCR targeting the varATS (the acidic terminal segment in Plasmodium falciparum var genes) multigenic family; this to accurately describe parasite growth even in case PCR positivity, i.e., a qPCR outcome ≥250 parasites per mL blood, is confirmed this early (very low probability and with low densities). Participants will be confined to the clinical unit from Day 10 in the morning. qPCR will be performed and malaria clinical score assessed twice daily and participants will be administered registered antimalarial therapy, i.e., Riamet®, when the following criteria are met:

1. Cohort 1: ≥5000 parasites/mL blood or earlier if a participant has a malaria clinical score >6 or at Investigator's discretion.

2. Cohort 2: ≥10000 parasites/mL blood or earlier if a participant has a malaria clinical score >6 or at Investigator's discretion.

The registered 3-day antimalarial therapy regimen will be further administered and monitored. qPCR assessments of parasitaemia will be carried out at multiple time points (2, 6, 8, 12, 16, 24, 36, 48 and 72 h) following initiation of Riamet® and malaria clinical score will be assessed twice daily during confinement in the clinical unit. Safety and tolerability will be monitored during the whole study duration, specific assessments will be done at periodic pre-specified time points from Day 10 and for at least 72 h after initiating antimalarial therapy, i.e., during confinement in the clinical unit. If an intolerance or contraindication to Riamet® develops, Malarone® will be administered.

Upon parasite clearance (defined as a qPCR value below the limit of quantification of 50 parasites per mL blood after initiating antimalarial therapy) and at least 72 h after initiating antimalarial therapy (estimated to occur on or before Day 19 and on or before Day 22 for Cohort 1 and Cohort 2, respectively), and if clinically well, participants will be discharged from the clinical unit and will be followed up for safety assessments, clinical evaluation and malaria qPCR in the clinical unit at the EOS visit on Day 28.

All participants inoculated with PfSPZ-DVI Challenge will commence antimalarial therapy no later than Day 24 for both cohorts, regardless if they reach pre-defined cohort-specific PCR parasitaemia/malaria clinical score thresholds. Participants who start antimalarial therapy on Day 24 will only be discharged from confinement at the end of the EOS visit on Day 28.

The schedule of assessments is in appendix 9.2.

After evaluation of data from Cohort 1, the Safety Review Team decided to continue with Cohort 2 (8 participants) using a threshold of 5000 parasites/mL.

1.3 EXPECTED SAMPLE SIZE

Up to 16 participants will be enrolled in 2 cohorts of 8 participants per cohort. In agreement with the Sponsor, additional participants may be recruited in each cohort, to replace discontinuations for non-safety reasons and achieve the required cohort size.

This is an exploratory study focusing on the methodology of malaria inoculation in healthy participants, thus no formal sample size calculation is performed.

1.4 RANDOMISATION AND BLINDING

Participants are not randomised. As participants are confirmed to be eligible for the study, they will be assigned a single unique identifier across the study and will be enrolled sequentially in one of the two cohorts.

All participants will be inoculated with PfSPZ-DVI Challenge and receive registered antimalarial therapy, i.e. Riamet® (Malarone® if an intolerance or contraindication to Riamet® develops).

As this is an open-label study, blinding is not applicable.

1.5 INTERIM ANALYSIS

No interim analyses are foreseen.

1.6 SOFTWARE

SAS version 9.4 or later will be used for programming.

Monolix for modelling parasite growth.

1.7 VALIDATION MODEL

SGS Life Sciences (SGS LS) – Clinical Research statistics (STAT) standard operating procedures (SOPs) and work instructions (WIs) as effective at the project start will be followed throughout the project, provided the applicable regulatory requirements are still met.

ADaMs and TLFs related to the time to first PCR positivity and time to parasitaemia of ≥5000 parasites per mL blood will be validated according to model C. All other tables/figures/listings follow validation model B (see SOP.STAT.020):

- Model B: review by an independent person
- Model C: review by an independent person and independent programming of the parameters indicated in this SAP

2. PHARMACODYNAMIC ANALYSES

2.1 PHARMACODYNAMICS

2.1.1 Available data

Parasitaemia is assessed by qPCR at the time points indicated in appendix 9.2.

2.1.2 Endpoints and derivation rules

The following primary endpoint parameters will be derived:

- Time to first PCR positivity in days: (datetime in seconds of first positive parasitaemia - datetime in seconds of inoculation) / (24*60*60)
  - Positive parasitaemia is defined as qPCR outcome (MBTESTCD = PARADENS) ≥ 250 asexual parasites per mL.
  - Subjects with absence of positive parasitaemia will be excluded.
- Parasitaemia at first PCR positivity defined as qPCR outcome ≥ 250 asexual parasites per mL
- Time to parasitaemia of ≥5000 parasites per mL blood in days: (datetime in seconds of first parasitaemia of ≥5000 parasites per mL blood - datetime in seconds of inoculation) / (24*60*60)
  - In the absence of parasitaemia of ≥5000 parasites per mL blood, the duration will be censored. The censoring datetime will be set to the datetime of first administration of antimalarial treatment. If the date of antimalarial treatment is (partially) missing the censored duration will be set to 28 days.
- Parasitaemia at the first time of ≥5000 parasites per mL blood
- Time to first dose of treatment with Riamet®: (datetime of first dose of Riamet® - datetime of inoculation) / (24*60*60)
- Parasitaemia at first dose of treatment with Riamet®

The following secondary endpoint parameter will be derived:

- Time to parasite clearance: (datetime of first PCR below the limit of quantification - datetime of first dose of Riamet®) / (24*60*60)
  - PCR below the limit of quantification is defined as (MBTESTCD = PARADENS) < 50 asexual parasites per mL.

(Partially) missing times will be imputed as specified in section 5.3.2.

For the creation of the graphs of parasitaemia by time point, the individual subject assessments will be mapped as follows:

- Time from first PCR positivity (days) = (datetime of assessment - datetime of first PCR positivity) / (24*60*60)
  - (Partially) missing times will be imputed as specified in section 5.3.2.

2.1.3 Inferential statistics

2.1.3.1 SECONDARY ENDPOINTS:

***Blood-stage parasite profile before* treatment with Riamet®**

To characterise the blood-stage parasite profile before treatment with Riamet® is initiated, first, a log-linear mixed effect model will be fitted to the measured parasitaemia (in count/mL, transformed on natural log scale) data prior to Riamet® administration. In this model, for each individual i:

$$\begin{cases} \dfrac{d\ log\ Parasitaemia_i}{dt} = GR_i \\ logParasitaemia_{0,i} = logF_{inoc,i} + logP_{inoc} - logV_{blood} \end{cases}$$

where t is the time in hours since inoculation, GR_i is the individual parasitaemia growth rate (measured in 1/hour) , Parasitaemia$_{o,i}$ is the individual parasitaemia at time of inoculation ($t = 0$), $F_{inoc,i}$ is the individual inoculum viability, P_{inoc} is the inoculum size, which is fixed to 3200 parasites, and V_{blood} is the blood volume (in mL units) which is fixed to 5000 mL for all individuals:

If the measured parasitaemia profile shows a cyclic behaviour due to synchronicity of the parasites and their sequestration during the late stages of their lifecycle, an attempt will be made to model this behaviour using the following extended version of the log-linear model:

$$\begin{cases} \dfrac{d\ log\ Parasitaemia_i}{dt} = GR_i \\ log\ Parasitaemia_{0,i} = logF_{inoc,i} + logP_{inoc} - logV_{blood} \\ logParasitaemia_{visible,i} = log\ Parasitaemia_i + log\left\{1 - 0.5F_{max,i}\left[1 - \cos\left(\dfrac{2\pi(t/24 - \mathrm{D}_{t,i})}{P_{len,i}}\right)\right]\right\} \end{cases}$$

where $Parasitaemia_{visible,i}$ denotes the measured parasitaemia, $\mathrm{D}_{t,i} = \phi_i P_{len,i}$, $F_{max,i}$ denotes the individual maximum fraction of hidden parasites, $P_{len,i}$ denotes the individual period length of the oscillation (in hours), and ϕ_i denotes the individual oscillation phase.

Parameter estimation will be performed using Monolix (Antony, France: Lixoft SAS). By default, all of the model parameters described above will be estimated, including their inter-individual variability (IIV) distributions. If, due to limited data size, the relative standard error (RSE) of the estimates exceeds 40%, the modeler may decide to fix the IIV for some of the parameters to previous estimates based on pooled data from induced blood-stage malaria VIS studies. By default, the models should assume independence of the parameters in their uncertainty and IIV distributions. If, during the model exploration, indications appear of a strong correlation between specific pairs of parameters, both, in their uncertainty and/or IIV distributions, the modeler may attempt to explicitly estimate such parameter correlations. Data below the limit of quantification will be included in the dataset and flagged as censored observations.

The following parameters will be determined from the population fits of the data:

- Parasite growth rate expressed as the parasite multiplication rate (PMR) standardised to 48 h (PMR_{48}), i.e., ratio of the parasite density at a specific time point to the parasite density 48 h earlier. Based on the population estimates for the GR parameter in the log-linear mixed effect model, PMR_{48} will be reported in log10 units: , i.e. $PMR_{48} = \frac{48GR}{\log(10)}$
- If cycles are observed and if their estimated period is not 48 h, parasite growth rate expressed as the PMR per life cycle (PMR_{LC}). Based on the population estimates for the GR and P_{len} parameters in the extended log-linear mixed effect model, PMR_{LC} will be reported in log10 units: $PMR_{LC} = \frac{P_{len}GR}{\log(10)}$.
- Predicted time to reach parasitaemia thresholds of first positive PCR, ≥5000 parasites per mL blood for Cohorts 1 and 2. All these quantities should be calculated at the population level by solving for t the linear equations

  $$logX = logParasitaemia_0 + GR \times t$$

  where $X \in \{250, 5000\}$ and $\log_{10} Parasitaemia_0$ and GR are the population estimates for parasitaemia at time of inoculation and parasitaemia growth rates respectively.

To determine confidence intervals for the population mean, parameters will be sampled from uncertainty.

Blood-stage parasite clearance profile after treatment with Riamet®

To characterise the blood-stage parasite clearance profile of Riamet® in malaria infection in naïve healthy participants after PfSPZ-DVI challenge; a log-linear model will be fitted to the parasitaemia data observed from the administration of the treatment onwards.

For each participant i:

$$\log_{10} Parasitaemia_{ij} = \beta_{0,i} + \beta_{1,i} t_{ij} + \varepsilon_{ij}$$

Where t_{ij} is the time in hours since administration of antimalarial treatment, $\beta_{0,i}$ and $\beta_{1,i}$ are the participant's intercept and slope, respectively, and ε_{ij} the error terms. For each participant i, $\beta_{0,i}$ is the $\log_{10}$(Parasitaemia at initiation of antimalarial treatment) and $-\beta_{1,i}$ is the clearance rate constant.

The following algorithm will be used to remove potential lag and/or tail phases of the parasitaemia clearance profile, in order to determine the optimal log-linear decay regression (Marquart et al, 2015 see section 7). The algorithm considers removing parasitaemia data points in an iterative process from both ends of the parasitaemia curve, i.e. a combination of removing values from the tail phase and removing values from the lag phase.

The optimal log-linear regression model for a participant is deemed an appropriate fit if the overall model p-value < 0.001.

Iteration process to determine the optimal log-linear decay curve:

For each participant:

- Step 1: Fit the full model - fit a linear regression (as defined by the previous equation) to all m parasitaemia values of participant i
- Step 2: Fit two models:
  - Fit linear regression model to $m-1$ parasitaemia values, removing the first observation
  - Fit linear regression model to $m-1$ parasitaemia values, removing the last observation
- Step 3: Determine the best model of Step 2a and Step 2b, defined as the model corresponding to the minimum overall model p-value
- Step 4: Of the best model defined in Step 3, repeat Step 2 and Step 3 in an iterative process until a minimum of four observations remain.
- Step 5: Of the $m-3$ best models selected per iteration (including the full model [Step 1]), the optimal model is defined by the minimum overall model p-value.

The following parameters will be calculated from the estimates of the optimal linear regression model for participant i:

- $\log_{10}$ parasite reduction ratio per 48 h ($\log_{10}\text{PRR}_{48}$), i.e., ratio of the parasite density at a specific time point to the parasite density 48 h later and expressed in $\log_{10}$
  - $\log_{10}\text{PRR}_{48_i} = -48\beta_{1,i}$
- Parasite clearance half-life (PC50), i.e., time taken for the parasite density to be reduced by 50% after the first dose administration of Riamet®
  - $PC50_i = \log_{10}(2)\left(\frac{48\ hours}{\log_{10}\text{PRR}_{48_i}}\right) = \frac{\log_{10}(2)}{-\beta_{1,i}}$
- Predicted time to reach parasite clearance of 99% (PC99) is calculated solving for t the linear equation

$$\log_{10} X = \hat{\beta}_{0,i} + \hat{\beta}_{1,i} \times t$$

where $\hat{\beta}_{0,i}$ is the participant's estimated $\log_{10}$(Parasitaemia at initiation of Riamet®), $\hat{\beta}_{1,i}$ the opposite of clearance rate constant, and X the Parasitaemia at initiation of Riamet® / 100. Thus:

$$PC99_i = \frac{\log_{10}(100)}{-\beta_{1,i}}$$

Note: when computing descriptive statistics per cohort and overall of the above estimated parameters, the summary statistics will be estimated by using the inverse-variance method to calculate the weighted average linear regression slope ($\bar{\beta}_1$) and corresponding standard error [SE($\bar{\beta}_1$)] (Hartung et al, 2008 see section 7). Descriptive statistics are based only on the participants whose optimal regression model overall p-value < 0.001.

2.1.3.2 EXPLORATORY ENDPOINTS:

To characterise the individual variability the results of modelling the blood-stage parasite profile with a log-linear or cyclic growth model whichever best describes the data (Section 2.1.3.1) will be used. Based on the individual parameter estimates from

the NLME model the inter-individual variability of the parasite growth rate and the predicted time to reach parasitaemia threshold of first positive PCR, ≥5000 parasites per mL blood for Cohorts 1 and 2 will be calculated according to corresponding equations from Section 2.1.3.1. In case that the IIV can be estimated for all parameters, prediction intervals for these variables will be determined based on 1000 samples of individual parameters from the estimated IIV.

2.1.4 Presentation of results

All parasitaemia tables, listings and figures will be presented for the PD set. As a sensitivity analysis the tables and figures will also be presented for the modified PD set. In this set subjects with a PCR assessment below the limit of quantification (<50 parasites per mL) after first PCR positivity (>250 parasites per mL) but before first antimalarial treatment administration will be excluded.

All parasitaemia data will be listed, including all derived parameters. The onset date of antimalarial treatment administration will be added to the listing.

Primary endpoints:

Descriptive statistics (N, geometric mean, geometric SD, 95% CI, minimum, maximum) will be provided for the following primary endpoints per cohort and overall:

- Time to first PCR positivity
- Parasitaemia at first PCR positivity
- Parasitaemia at the time of ≥5000 parasites per mL blood
- Time to first dose of treatment with Riamet®
- Parasitaemia at first dose of treatment with Riamet®

Time to parasitaemia of ≥5000 parasites per mL blood will be analysed using Kaplan-Meier time to event analysis per cohort and overall. The number of events, number of censored observations, 25th percentile, median and 75th percentile with 95% CI will be presented.

The number and proportion of participants with presence of positive PCR and parasitaemia of ≥5000 parasites per mL blood between inoculation with PfSPZ-DVI Challenge and Day 28 will be summarised per cohort. Corresponding two-sided 90% Exact Clopper-Pearson confidence limits will be presented as well.

Parasitaemia actual values in the base-10 logarithmic scale will be summarised by means of descriptive statistics at each analysis visit. The visits will be grouped by analysis phase.

Graphs of the median actual values over time and spaghetti plots of the individual participants will be prepared for parasitaemia in the base-10 logarithmic scale. The median plot will be shown from the Day 7 assessment to the assessment 72 h following initiation of Riamet®. The spaghetti plots will be shown from the subject's first PCR positivity to parasite clearance. For the spaghetti plots, different plotting symbols will be used on the first assessment when antimalarial treatment was given.

For all time to event parameters, Kaplan-Meier plots per cohort and overall will be presented.

Secondary endpoints:

Blood-stage parasite profile before treatment with Riamet®

Parameter estimates for fixed (mean parameter value) and random (inter-individual and residual variability) effects values will be tabulated including their standard error and shrinkage for the inter-individual variability.

To characterise the blood-stage parasite profile the mean, 90%-CI will be provided for:

- PMR_{48}
- PMR_{LC} (if cycles are observed and their estimated period is not 48 h)
- Predicted time to reach parasitaemia threshold of first positive PCR, ≥5000 parasites per mL blood for Cohorts 1 and 2

Blood-stage parasite clearance profile after treatment with Riamet®

The model estimates and derived parameters resulting from the optimal log-linear decay regression model of each subject will be tabulated.

To characterise the blood-stage parasite clearance profile of Riamet® descriptive statistics (N, geometric mean, geometric SD, 95% CI, minimum, maximum) will be provided for time to parasite clearance per cohort and overall.

The following cohort parameters will be estimated based on the weighted average slope and standard error of the subjects with the optimal regression model having a p-value <0.001. N, mean, 95% CI, minimum and maximum will be shown.

- $\log_{10}$ parasite reduction ratio per 48 h ($\log_{10}PRR_{48}$)
- Parasite clearance half-life (PC50)
- Predicted time to reach parasite clearance of 99% (PC99)

For each subject, the regression slope with 95% CI, $\log_{10}PRR_{48}$ with 95% CI and overall model p-value of all the fitted models leading to the selection of the optimal log-linear model will be listed. The optimal model of each subject will be flagged.

A Kaplan-Meier plot per cohort and overall will be presented for the time to parasite clearance.

Exploratory endpoints:

Summary statistics of all individual parameters (cohort 1 and cohort 2) of the log-linear growth model will be tabulated to show the inter-individual variability of the parasite growth rate of predicted time to reach parasitaemia threshold of first positive PCR, ≥5000 parasites per mL blood by geometric mean, standard deviation (including their 95% CI), and the range. In case that the IIV could be estimated for all parameters, the 90% prediction interval and the median will be reported.

3. SAFETY ANALYSES

3.1 ADVERSE EVENTS

3.1.1 Available data

Adverse events (AEs) are coded into system organ classes and preferred terms using the medical dictionary for regulatory activities (MedDRA). For each AE, start and stop date(time)s are collected as well as grade, severity, a seriousness flag, relatedness to PfSPZ inoculum, relatedness to Riamet®, relatedness to Malarone®, action taken towards PfSPZ inoculum, action taken towards Riamet®, action taken towards Malarone®, outcome and a flag for AEs of special interest.

To determine severity of Adverse Events, including the 14 signs/symptoms as part of the Malaria Clinical Score, we use the CTCAE grading scale grade 1 - 5.

3.1.2 Derivation rules

Based on their start date(time), AEs will be allocated to the phase during which they started. Each AE will therefore be reported in only one phase. Phases are defined in section 5.2.1. In case the AE start date(time) is incomplete or missing and the AE could consequently be allocated to more than one phase, a worst-case allocation will be done as detailed below:

- Screening phase vs. challenge phase: AE will be allocated to the challenge phase unless the available parts of the AE start or stop date(time) provide evidence for allocating to the screening phase.
- Challenge phase vs. rescue phase: AE will be allocated to the rescue phase unless the available parts of the AE start or stop date(time) provide evidence for allocating to the challenge phase.

A fatal AE is defined as an AE with outcome ‘fatal’.

An AE for which the antimalarial treatment was discontinued is defined as an AE with action taken ‘Permanently discontinued’ towards Riamet® or Malarone®.

Treatment-relatedness will be assessed for PfSPZ inoculum, Riamet® and Malarone®. It will be dichotomised as follows in tables:

- Treatment-related: Related/Suspected or missing.
- Not treatment-related: Not related/Not suspected or Not Applicable.

AE onset and duration will be calculated as follows when start and stop dates are fully known:

- AE onset day / hour (vs. first PfSPZ Challenge administration) =
  - AE start date > date of first inoculation: AE start date – date of first inoculation + 1 day
  - AE start date < date of first inoculation: AE start date – date of first inoculation
  - AE start date = date of first inoculation (AE start datetime – datetime of first inoculation)/(60*60)

- AE onset day / hour (vs. start of phase) =
  - AE start date > analysis phase start date: AE start date – analysis phase start date + 1 day
  - AE start date = analysis phase start date (AE start datetime – analysis phase start datetime)/(60*60)
- AE duration (days) =
  - AE end date – AE start date + 1 day
  - study discontinuation date – AE start date + 1 day (when the AE start date is fully known but the AE is not resolved at the end of the study)
    In this case the duration will be presented as ">x days".

(Partially) missing times will be imputed as specified in section 5.3.2.

3.1.3 Presentation of results

Tables will present only AEs that start after the PfSPZ Challenge inoculation. Pre-inoculation AEs will only be listed. Unless stated otherwise, tables will not be shown by phase.

An overview table will show the number and percentage of subjects with at least one event and the number of events for the following:

- AEs
- Serious AEs
- Grade ≥ 3 AEs
- Fatal AEs
- AEs related to PfSPZ inoculum
- AEs related to antimalarial treatment
- AEs related to Riamet®
- AEs related to Malarone®
- Serious AEs related to PfSPZ inoculum
- AEs for which the study was discontinued
- AEs for which the antimalarial treatment was discontinued
- AEs for which Riamet® was discontinued
- AEs for which Malarone® was discontinued
- AEs of special interest
- AEs of special interest related to PfSPZ inoculum
- AEs of special interest related to antimalarial treatment

Summary tables by MedDRA system organ class and preferred term will show the number and percentage of subjects with at least one event. The table of AEs will additionally show the number of events.

Separate tables will be prepared for the following:

- AEs
- Serious AEs
- Grade ≥ 3 AEs
- AEs related to PfSPZ inoculum
- AEs related to antimalarial treatment (overall, related to Riamet® and related to Malarone®)
- Serious AEs related to PfSPZ inoculum
- AEs for which the antimalarial treatment was discontinued (overall, Riamet® discontinued and Malarone® discontinued)
- AEs of special interest related to PfSPZ inoculum
- AEs of special interest related to antimalarial treatment (overall, related to Riamet® and related to Malarone®)

Additionally, a summary table by MedDRA preferred term will show the number and percentage of subjects with at least one event, by descending order of frequency (number of subjects with events in the total group).

All AEs, including pre-inoculation events will be listed. Separate listings will be prepared for serious AEs, AEs after antimalarial treatment administration, AEs for which the study was discontinued, AEs for which the antimalarial treatment was discontinued (Riamet® or Malarone®), fatal AEs and AEs for which another action is taken. A listing showing all coding information will be prepared as well.

3.2 CLINICAL LABORATORY EVALUATION

3.2.1 Available data

Per protocol, the following laboratory parameters are expected:

- Biochemistry: Liver biochemistry: albumin, AST, ALT, alkaline phosphatase (ALP), gamma glutamyl aminotransferase (GGT), total and direct bilirubin and total serum proteins; Biochemistry other than liver: sodium, potassium, chloride, bicarbonate, urate, inorganic phosphate, creatinine, estimated glomerular filtration rate (eGFR), glucose, lactate dehydrogenase (LDH), blood urea nitrogen (BUN) and creatine phosphokinase (CPK); C-reactive protein (CRP); High sensitive troponin T;
- Haematology: haemoglobin, haematocrit, RBC count, mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), mean corpuscular volume (MCV), white blood cell (WBC) count, platelet count, reticulocytes, neutrophils, eosinophils, basophils, lymphocytes and monocytes;
- Coagulation: prothrombin time (PT), international normalised ratio (INR), activated partial thromboplastin time (aPTT);
- Urinalysis: dipstick for glucose, protein, nitrite, pH and occult blood; microscopic examination for WBC, RBC and casts.

Normal ranges are available as provided by the laboratory. Based on the Regulatory Agency's recommendation, the Clinically Acceptable Ranges for Clinically Important Study Inclusion Laboratory Tests (including total and conjugated bilirubin) have been added in Attachment 4 of the protocol to guide inclusion/exclusion of study participants.

3.2.2 Derivation rules

The following abnormality categories will be defined:

- Low: value < lower limit of normal range
- Normal: lower limit of normal range ≤ value ≤ upper limit of normal range
- High: value > upper limit of normal range

Note:

- Classification will be done in standardised units, using non-imputed values and limits.
- For the worst-case analysis visit, as defined in section 5.2.5, an additional category low + high is defined in case there are both low and high values.
- If not straightforward how to categorise urinalysis results, a worst-case approach will be used. A value of '4 to 6' with normal range '0 to 5' will thus be classified as normal for predose assessments but as high for post-dose assessments.

Additionally, for liver enzymes, the following elevation categories will be defined:

- ALT or AST >3 x Upper Limit of Normal (ULN);
- ALT or AST >5 x ULN;
- ALT or AST >8 x ULN;
- ALT or AST >3 x ULN and total bilirubin >2 x ULN at the same time point, together with a conjugated bilirubin fraction (direct bilirubin / total bilirubin) > 35% (Potential Hy's law cases).

3.2.3 Presentation of results

The statistical analysis will present results in standardised units.

Continuous laboratory parameters will be summarised by means of descriptive statistics at each analysis visit. Actual values and changes from baseline will be tabulated. Categorical parameters will be listed only.

Laboratory abnormalities will be presented as cross-tabulations of the abnormality at each post-baseline analysis visit and at the worst-case analysis visit versus the baseline abnormality. Numbers of subjects with post-baseline-emergent abnormalities will also be shown.

Additionally, a frequency table showing the liver enzyme elevation categories for the highest post-inoculation values will be prepared.

All laboratory data will be listed, but only for subjects with any post-baseline abnormality or clinically significant value.

Spaghetti plots of the individual subjects' actual values over time will be prepared for liver biochemistry parameters, CRP and haemoglobin. For the spaghetti plots, the median will also be plotted.

3.3 VITAL SIGNS

3.3.1 Available data

The following vital signs parameters are collected: supine heart rate, supine systolic (SBP) and diastolic blood pressure (DBP), oral body temperature and body weight.

3.3.2 Derivation rules

Abnormalities are defined in below table.

	Heart rate (bpm)	**SBP (mmHg)**	**DBP (mmHg)**	**Temperature (°C)**	**Weight (kg)**
Low	<40	<90	<45	<35.0	<50
Normal	40-100	90-150	45-90	35.0-37.5	50-120
High	>100	>150	>90	>37.5	>120

Note: For the worst-case analysis visit, as defined in section 5.2.5, an additional category low + high is defined in case there are both low and high values.

For the figures, the median assessment of first antimalarial treatment administration will be calculated starting from the individual vital signs first assessments which follow the first administration. In case the median is found to be between two assessments the first of the two will be selected.

3.3.3 Presentation of results

Vital signs parameters will be summarised by means of descriptive statistics at each analysis visit. Actual values and changes from baseline will be tabulated.

Abnormalities will be presented as cross-tabulations of the abnormality at each post-baseline analysis visit versus the baseline abnormality and as cross-tabulations of the worst-case abnormality versus the baseline abnormality. Numbers of subjects with post-baseline-emergent abnormalities will also be shown.

All vital signs data will be listed, but only for subjects with any post-baseline abnormality or clinically significant value.

Spaghetti plots of the individual subjects' actual values over time will be prepared for heart rate and body temperature. For the spaghetti plots, the median will also be plotted. The median time to first antimalarial treatment administration will be shown.

3.4 ELECTROCARDIOGRAMS

3.4.1 Available data

The following electrocardiogram (ECG) parameters will be collected: heart rate (HR), QRS interval, PR interval, QT interval and corrected QT interval (Bazett and Fridericia). Recordings will be performed in triplicate.

3.4.2 Derivation rules

Mean values of the triplicates will be calculated per time point and rounded as detailed in section 5.3.4. Throughout the analysis, including the derivation of baseline and abnormalities, the mean values will be used. Individual triplicate values will only be listed.

Abnormalities for HR, QRS, PR and QTc interval are defined in below table.

	HR (bpm)	PR (ms)	QRS (ms)	QTc (ms)
Low	<40	<120	-	-
Normal	40-100	120-220	≤120	≤450 for males, ≤470 for females
High	>100	>220	>120	>450 for males, >470 for females

Note: For the worst-case analysis visit, as defined in section 5.2.5, an additional category low + high is defined in case there are both low and high values.

For QTc interval changes (ms), the following categories are defined:

- ≤ 30 (normal)
- >30; ≤ 60
- > 60

Note: The worst-case, as defined in section 5.2.5, is the highest value and associated change.

3.4.3 Presentation of results

Uncorrected QT interval will only be listed.

Continuous ECG parameters will be summarised by means of descriptive statistics at each analysis visit. Actual values and changes from baseline will be tabulated.

Abnormalities of the actual values will be presented as cross-tabulations of the abnormality at each post-baseline analysis visit, and at the worst-case analysis visit versus the baseline abnormality. Numbers of subjects with post-baseline-emergent abnormalities will also be shown.

Abnormalities of the QTc changes will be presented as tabulations of the change abnormality at each post-baseline analysis visit and at the worst-case analysis visit. Cumulative numbers of subjects with change abnormalities will also be shown.

All ECG data will be listed, but only for subjects with any post-baseline abnormality or clinically significant value or change.

Spaghetti plots of the individual subjects' actual values over time will be prepared for QTcF and QTcB. For the spaghetti plots, the median will also be plotted.

3.5 MALARIA CLINICAL SCORE

3.5.1 Available data

The following 14 signs/symptoms frequently associated with malaria will be graded using a 4-point scale (absent: 0; mild: 1; moderate: 2; severe: 3): headache, myalgia (muscle ache), arthralgia (joint ache), fatigue/lethargy, malaise (general discomfort/ uneasiness), chills/shivering/rigors, sweating/hot spells, anorexia, nausea, vomiting, abdominal discomfort, fever, tachycardia and hypotension.

3.5.2 Derivation rules

Malaria clinical score is calculated as the sum of all (14) malaria sign and symptoms scores (maximum score is 42). Missing individual scores will be imputed as detailed in section 5.3.1. The score will be rounded as detailed in section 5.3.4.

For malaria clinical score and individual signs and symptoms, a worst-case analysis visit, as defined in section 5.2.5 will be derived.

For the creation of the graphs of malaria clinical score and parasitaemia/C-reactive protein together, the individual subject assessments will be mapped as follows:

- Time from PfSPZ inoculation (days) = (datetime of assessment - datetime of inoculation) / (24*60*60)
    - (Partially) missing times will be imputed as specified in section 5.3.2.

For the figures, the median assessment of first antimalarial treatment administration will be calculated starting from the individual MCS first assessments which follow the first administration. In case the median is found to be between two assessments the first of the two will be selected.

3.5.3 Presentation of results

For the malaria clinical score, actual values and changes from baseline will be evaluated by means of descriptive statistics at each time point and at the worst-case analysis visit (by phase and overall).

Individual malaria signs and symptoms scores will be presented as frequency tabulations at the worst-case analysis visit (by phase and overall). Numbers and percentage of subjects with any post-baseline non-zero score will also be shown.

Malaria signs and symptoms and clinical score will be listed. The onset date of antimalarial treatment administration will be added to the listing.

Malaria clinical scores of more than 6 will be listed. The baseline score value, the corresponding parasitaemia values at those analysis visits and the onset date of antimalarial treatment administration will be added to the listing.

Spaghetti plots of the individual subjects' actual values over time will be prepared for malaria clinical score. For the spaghetti plots, the median will also be plotted and different plotting symbols will be used at the time point of first antimalarial treatment administration and at the time point of peak parasitaemia. The median time to first antimalarial treatment administration will be shown.

Spaghetti plots of the individual subjects' actual values over time will be prepared for malaria clinical score and parasitaemia together. These plots will be shown per cohort

and per individual subject. The same type of plot will be prepared for malaria clinical score and C-reactive protein together.

3.6 PHYSICAL EXAMINATIONS

Abnormal physical examination findings will be listed.

4. GENERAL CHARACTERISTICS ANALYSES

4.1 SUBJECT DISPOSITION

The following subject data will be tabulated:

- The number of subjects in each analysis set
- Dates of first signed informed consent, last visit and last contact (overall only)
- The number and percentage of subjects who completed or discontinued the study as documented on the study termination page and the number and percentage of subjects for each study discontinuation reason

All information collected in the CRF concerning allocation, study discontinuation, antimalarial treatment discontinuation and information on phases will be listed. The phases listing will also include the start and stop dates of antimalarial treatment administration.

4.2 PROTOCOL DEVIATIONS AND ELIGIBILITY

The number and percentage of subjects with major protocol deviations will be tabulated, overall and per class of deviation.

All available information concerning major protocol deviations, violations on eligibility criteria and subjects not inoculated with PfSPZ-DVI Challenge will be listed.

4.3 DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

4.3.1 Available data

The following parameters will be available:

- Demographics: sex, age, race, ethnicity, height, body weight at screening, date of signing informed consent form (ICF), smoking habits
- Screening laboratory tests: Viral serology: hepatitis A IgM antibody, HbsAg, anti-HCV antibody, hepatitis D antibody (only in subjects positive for HbsAg), hepatitis E IgM antibody, CMV IgM antibody, EBV IgM antibody and HIV; Urine drug screen (amphetamines, barbiturates, benzodiazepines, cannabinoids, cocaine and opiates) and alcohol breath test. In all female participants, serum β-HCG at screening and at the EOS visit, urine β-HCG on Day-1 and FSH at screening. rRT-PCR test on nasopharyngeal swab to screen for infection with SARS-CoV-2 at screening and prior to confinement to the study site on Day 10
- Standing and supine heart rate, standing and supine systolic (SBP) and diastolic blood pressure (DBP)
- Beck depression inventory (question 9 - suicidal thoughts - and total score)

4.3.2 Derivation rules

The following parameters will be derived:

- Body mass index (BMI) at screening (kg/m²) = (body weight at screening (kg)) / (height (m))²

  Note: The BMI will only be recalculated and rounded as detailed in section 5.3.4 when not available in the database.
- Smoking status:
  - Non-smoker: SUOCCUR = N
  - Ex-smoker: SUOCCUR = Y and non-missing smoking end date
  - Smoker: SUOCCUR = Y and missing smoking end date
- Orthostatic change = value in supine position – value in standing position
- Beck depression inventory interpretation:
  - 0-10: Normal
  - 11-16: Mild mood disturbance
  - 17-20: Borderline clinical depression
  - 21-30: Clinical depression
  - 31-40: Severe depression
  - >40: Extreme depression

4.3.3 Presentation of results

Demographics will be presented using descriptive statistics for age, height, body weight and BMI and frequency tabulations for sex, race, ethnicity and smoking status.

Orthostatic change and Beck depression inventory will be presented using descriptive statistics for the total score and frequency tabulations for interpretation.

All demographic data will be listed. Separate listings will also be created for smoking history, orthostatic changes, Beck depression inventory, screening laboratory tests, pregnancy tests (including EOS result) and rRT-PCR tests.

4.4 MEDICAL HISTORY AND CONCOMITANT DISEASES

4.4.1 Available data

Medical history and concomitant diseases findings are coded using the medical dictionary for regulatory activities (MedDRA) into system organ classes and preferred terms. For each finding, a start and stop date or ongoing flag is collected.

4.4.2 Derivation rules

The following parameters will be derived:

- Medical history finding: not ongoing at screening (MHENRTPT =BEFORE)
- Concomitant disease finding: still ongoing at screening (MHENRTPT = ONGOING)

4.4.3 Presentation of results

Medical history and concomitant diseases will be tabulated separately. Each table will show:

- The number and percentage of subjects with and without findings
- The number and percentage of subjects with findings by system organ class and preferred term

All medical history and concomitant diseases data will be listed separately.

4.5 PRIOR AND CONCOMITANT THERAPIES

4.5.1 Available data

All therapies (excluding antimalarial treatment) are coded using WHO-DRUG. ATC selection is performed. ATC coding up to level 4 is available in the clinical database. For each therapy, a start date or prior flag and stop date or ongoing flag are collected.

For antimalarial treatment the start and end date(times) and the dose will be recorded.

4.5.2 Derivation rules

Based on their start and stop date(time), prior and concomitant therapies will be allocated to each phase during which they were administered. A therapy can therefore be reported in more than one phase.

Phases are defined in section 5.2.1. Therapies with (partially) missing dates will be allocated to each phase unless the available parts of the therapy start or stop date(time) provide evidence the therapy was not taken during that phase.

4.5.3 Presentation of results

The number and percentage of subjects with and without therapies and the number and percentage of subjects with therapies by ATC class (level 4) and generic term will be tabulated by phase and overall. Blank ATC levels, if any, will be shown as ‘not available’ in the tables.

A frequency table will be prepared showing the timing of antimalarial treatment administration (prior to day 24 / on day 24) and the generic name (Riamet® / Malarone®).

The number and percentage of subjects who completed or discontinued the antimalarial treatment as documented on the treatment termination page and the number and percentage of subjects for each discontinuation reason will be tabulated.

All prior and concomitant therapies data will be listed. A separate listing will be prepared for antimalarial treatment administration.

4.6 EXPOSURE TO CHALLENGE AGENT

4.6.1 Available data

For the challenge agent (PfSPZ-DVI) the administration date(time) and the dose will be recorded.

4.6.2 Derivation rules

Not applicable.

4.6.3 Presentation of results

All exposure to challenge agent data will be listed.

5. GENERAL METHODOLOGY

5.1 ANALYSIS SETS

5.1.1 Analysis sets

The following analysis sets will be considered in the statistical analysis:

All screened subjects set (SCR):	subjects who *signed an informed consent* to participate in this study
Safety analysis set (SAF):	subjects who were *inoculated* with PfSPZ-DVI Challenge
PD analysis set:	subjects from the safety analysis set with at least one available PD data who received all Riamet® doses and who experienced no major protocol deviations with relevant impact on PD data
Modified PD analysis set (m-PD):	subjects from the PD analysis set excluding subjects with a PCR assessment below the limit of quantification (<50 parasites per mL) after first PCR positivity (>250 parasites per mL) but before first antimalarial treatment administration

Notes:

- Having signed an informed consent is defined as having a complete informed consent signature date in the database.
- Being inoculated with PfSPZ-DVI Challenge is defined as having an exposure date of PfSPZ-DVI Challenge or any information confirming this exposure present in the database.
- Major protocol deviations with impact on PD data will be identified with DVSCAT. DVSCAT = 'MISSING DATA EXPECTED PER PROTOCOL' indicates no impact on PD.

Unless specified otherwise, the safety analysis set will be used for the analysis of demographics and other general characteristics and for the safety/tolerability analysis. The PD analysis set will be used for pharmacodynamic statistical analysis. The modified PD analysis set will be used as a sensitivity analysis for the pharmacodynamic statistical analysis.

Protocol deviations will be reviewed and exclusion of subjects from the analysis sets will be decided during final data review prior to database lock.

5.1.2 As planned versus as actual analysis

Not applicable.

5.2 PHASES AND TIME POINTS

5.2.1 Phases

All events and assessments will be allocated to phases. Seconds in the time part will be ignored.

Phase	Start	End
Screening	Date of signing the ICF, with 00:00 added as time part	First inoculation date(time) – 1 minute
Challenge	First inoculation date(time)	First antimalarial treatment administration date(time) – 1 minute
Rescue	First antimalarial treatment administration date(time)	Date of last contact, with 23:59 added as time part

Per definition, and for each subject, the first phase starts on the date of the earliest available ICF signature, and the last available phase ends on the date of last contact, with 23:59 added as time part.

AEs and concomitant therapies will be allocated to phases as described in sections 3.1.2 and 4.5.2 respectively. All other assessments will be allocated to phases based on the assessment date(time).

In case of (partially) missing date(time) fields, the visit label will be used to allocate to the correct phase. If this is not possible (unscheduled visits or visits on a turning point between phases), assessments will be handled as follows:

- Screening phase vs. challenge phase: assessments will be allocated to the challenge phase unless the available parts of the assessments start or stop date(time) provide evidence for allocating to the screening phase.
- Challenge phase vs. rescue phase: assessments will be allocated to the rescue phase unless the available parts of the assessments start or stop date(time) provide evidence for allocating to the challenge phase.

5.2.2 Baseline and change from baseline

The baseline value is the last available and non-missing value before the inoculation of PfSPZ-DVI Challenge. If all values are missing, the baseline will be reported as missing.

Change from baseline is defined as:

Change from baseline at time point t = value at time point t – baseline value.

5.2.3 Relative day

Relative days (DY) will be calculated according to the following rule:

- Concerned date < reference date: DY = concerned date – reference date
- Concerned date ≥ reference date: DY = concerned date – reference date + 1

The reference date is the date of inoculation of PfSPZ-DVI Challenge.

5.2.4 Analysis visits

For assessments after the reference date, the analysis will use the visits and time points indicated on the subject's case report form (CRF). Unscheduled assessments after the reference date will only be listed.

The screening value is the last available and non-missing value before day -1. This value corresponds to the screening visit, except in case of retesting. Reason for this approach is the use of retest results for subject eligibility assessment.

The day -1 value is the last available and non-missing value performed on the date of day -1.

Baseline is defined in section 5.2.2.

5.2.5 Worst-case

A worst-case analysis visit will be created for parameters for which abnormalities are defined to summarise values considered as the worst-case. For abnormalities it is derived per parameter and in case both the lowest and the highest values are considered abnormal, a subject can have two worst-case analysis visits for a same parameter, which will be shown in tables as a combined high+low category. For malaria signs and symptoms, the worst-case corresponds to the highest score and is also derived per sign/symptom.

All non-missing post-baseline values, including unscheduled assessments and follow-up will be considered when deriving the worst-case analysis visit.

Worst-case will be derived both by phase (challenge/rescue) as relevant and overall.

5.3 IMPUTATION AND ROUNDING RULES

5.3.1 Missing values

For the calculation of the malaria clinical score, missing individual signs and symptom scores will be imputed with the mean of all non-missing scores.

No other imputation will be done of missing values.

5.3.2 Handling partially or completely missing dates in calculations

For the time to event parasitaemia parameters, assessment datetimes used in the figures and AE onset hours, partially missing time parts will be imputed with zero (e.g. if minutes and seconds are missing time will be set to hh:00:00).

Note: If imputation of the start datetime results in a start datetime posterior to the stop datetime, the start datetime will be imputed with the stop datetime. If imputation of the stop datetime results in a stop datetime anterior to the start datetime, the stop datetime will be imputed with the start datetime.

No other date(time) imputation will be performed.

5.3.3 Values below or above a threshold

Safety values expressed as below (or above) the limit of quantification will be imputed by the value of the quantification limit itself.

Parasitaemia values below the limit of quantification (50 parasites/mL) will be imputed by 1 parasite per mL blood, which is equivalent to zero in the logarithmic scale.

Listings will always show the non-imputed values.

5.3.4 Rounding of derived variables

Derived variables will be rounded to the appropriate number of significant digits (see Definition of terms) at display level:

- Malaria clinical score will be rounded to 1 decimal.
- Mean of triplicates, mean scores and BMI will be rounded to 1 decimal.
- AE onset hour will be rounded to 1 decimal.
- Time to event parameters and log10(parasitaemia) will be rounded to 1 decimal.
- Other derived PD parameters will be rounded to 2 decimals.

Rounding will be done using the round half to up rule (see Definition of terms).

5.3.5 Outliers

There will be no outlier detection. All measured values will be included in the analyses.

5.4 PRESENTATION OF RESULTS

5.4.1 Calculation of descriptive statistics and percentages

For continuous parameters, full descriptive statistics will only be presented if there are at least 2 non-missing observations. Alternatively, only the number of non-missing data points and mean are shown.

Descriptive statistics of the general and safety parameters will include the number of non-missing data points, the arithmetic mean, the standard deviation (SD), the median, minimum and maximum.

Descriptive statistics of the pharmacodynamic endpoints will include the number of non-missing data points, the arithmetic or geometric mean and SD, the corresponding 95% confidence interval (CI), minimum and maximum. Geometric mean, geometric SD and CI are calculated as the exponentials of the arithmetic mean, SD and corresponding CI (based on t-distribution, without continuity correction) of the log-transformed data.

Mean, geometric mean, median, SD, geometric SD and CI will be presented with one more decimal place than the individual values. Minimum and maximum will be presented with the same number of decimal places than the individual values.

P-values will be presented with four decimal places, ratios with three decimal places and test statistics with two decimal places.

For event-type data, the denominator will be all subjects in the analysis set and phase. All cohorts will be shown, even if no events are present.

For frequency tabulations and cross-tabulations, missing values will not be included in the denominator count when computing percentages. For cross-tabulations of post-baseline results versus baseline results, a ‘missing’ category will be shown for baseline results if applicable.

Percentages will be shown with one decimal place.

5.4.2 Presentation of treatments

The following labels will be used in the tables, listings and figures:

- Cohort 1
- Cohort 2

In the analysis, a grand total will be added to summarise all subjects over cohorts except for parameters defined only for cohort 2. Grand totals will be shown last.

5.4.3 Ordering in tables, figures and listings

All tables and figures will be presented per cohort, unless specified otherwise.

All listings will be ordered by cohort, subject, analysis visit and time point, unless specified otherwise.

Tables will be sorted first by cohort, then by time point.

In tables and figures showing several parameters, each parameter will begin on a new page and parameters will be sorted alphabetically, within the parameter category if applicable.

6. CHANGES TO THE PLANNED ANALYSIS

6.1 CHANGES NOT COVERED BY PROTOCOL AMENDMENTS BEFORE DATABASE LOCK

- The inoculation set is renamed as safety analysis set and will be used for the general and safety analyses instead of the safety analysis set defined in the protocol as "all inoculated participants who received any treatment" (see protocol section 9.1).
- Time to first PCR positivity (defined as qPCR outcome ≥ 250 asexual parasites per mL blood): in the absence of positive PCR, the endpoint will not be derived instead of imputing the duration by 28 days.
- Time to parasitaemia of >= 5000 parasites per mL blood: summarised using Kaplan Meier estimates instead of geometric mean (95% CI), SD and range.
- Endpoints related to the 10000 parasites per mL blood are removed from the analysis since the threshold for Cohort 2 was modified to 5000 parasites per mL blood.
- log10PRR48, PC50 and PC99 are estimated using the weighted average slope and standard error of the subjects with the optimal regression model having a p-value <0.001.

6.2 CHANGES NOT COVERED BY PROTOCOL AMENDMENTS AFTER DATABASE LOCK

Not applicable.

6.3 CHANGES TO THE FINAL STATISTICAL ANALYSIS PLAN

Not applicable.

7. REFERENCES

ICH Topic E6(R2) Guideline for Good Clinical Practice – Step 4, 9 November 2016.

ICH guideline E14: the clinical evaluation of QT/QTc interval prolongation and proarrhythmic potential for non-antiarrhythmic drugs (R3) – questions and answers, January 2016.

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8. LIST OF TABLES, LISTINGS AND FIGURES

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9. APPENDICES

9.1 SAS CODE

Blood-stage parasite clearance profile:

```
data ds;
   set ...;
   laval = log10(aval);
run;

proc glm data = ds alpha = 0.05;
   by usubjid;
   model laval = areltm / clparm;
run;
```

9.2 SCHEDULE OF ASSESSMENTS

Assessments			**Challenge, treatment and follow-up**								
Study Day/Event	**Screening Visit Day -28 to Day -2**	**Day -1**[Error! Reference source not found.]	**Day 1**		**Day 2-6**	**Day 7-9**	**Day 10: Start of Confinement in Clinical Unit**	**Day of First PCR ≥250 Parasites/mL Until Day of First PCR ≥5000 Parasites/mL**	**Day of First PCR ≥5000 Parasites/mL Until ≥72 h After Initiating Antimalarial Therapy**	**Day of Discharge From Confinement: Day of Parasite Clearance (0 Parasites/mL) AND ≥72 h After Initiating Antimalarial Therapy**	**EOS Visit Day 28**[Error! Reference source not found.]
Time point (h) in relation to *Pf*SPZ-DVI Challenge			**0**[Error! Reference source not found.]	**2**						**Estimated On or Before Day 19**	
Ambulatory visit	X					X					X
Ambulatory visit (SARS-CoV-2 test)	X					X					
Confinement in clinical unit[Error! Reference source not found.]		X	X				X	X	X	(X)	
Discharge from clinical unit				X						X	(X)
Telephonic Monitoring for AEs					X						
Eligibility criteria	X	X									
Informed consent[Error! Reference source not found.]	X										
Demographics	X										
Medical and social history	X										
Beck Depression Inventory	X										

Assessments	**Screening Visit**		**Challenge, treatment and follow-up**								**EOS Visit**
Study Day/Event	**Day -28 to Day -2**	**Day -1**[Error! Reference source not found.]	**Day 1**		**Day 2-6**	**Day 7-9**	**Day 10: Start of Confinement in Clinical Unit**	**Day of First PCR ≥250 Parasites/mL Until Day of First PCR ≥5000 Parasites/mL**	**Day of First PCR ≥5000 Parasites/mL Until ≥72 h After Initiating Antimalarial Therapy**	**Day of Discharge From Confinement: Day of Parasite Clearance (0 Parasites/mL) AND ≥72 h After Initiating Antimalarial Therapy**	**Day 28**[Error! Reference source not found.]
Time point (h) in relation to *Pf*SPZ-DVI Challenge			**0**[Error! Reference source not found.]	**2**						**Estimated On or Before Day 19**	
Alcohol & drug screen[Error! Reference source not found.]	X	X									
Height & weight[Error! Reference source not found.]	X	X									X
Physical examination[Error! Reference source not found.]	X	X					X	X	X	X	X
Vital signs[Error! Reference source not found.]	X	X	X	X			X	X	X	X	X
12-lead ECG[Error! Reference source not found.]	X								X		
Viral serology[Error! Reference source not found.]	X										
Pregnancy test[Error! Reference source not found.]	X	X									X
DVI of *Pf*SPZ Challenge			X								
Riamet®[Error! Reference source not found.]									X[Error! Reference source not found.]		
Malaria Clinical Score[Error! Reference source not found.]			X			X	X	X	X	X	X
Haematology & liver biochemistry[Error! Reference source not found.]	X	X				X	X	X	X	X	X

Assessments	Screening Visit Day -28 to Day -2		Challenge, treatment and follow-up								EOS Visit Day 28[Error! Reference source not found.]
Study Day/Event		**Day -1**[Error! Reference source not found.]	**Day 1**		**Day 2-6**	**Day 7-9**	**Day 10: Start of Confinement in Clinical Unit**	**Day of First PCR ≥250 Parasites/mL Until Day of First PCR ≥5000 Parasites/mL**	**Day of First PCR ≥5000 Parasites/mL Until ≥72 h After Initiating Antimalarial Therapy**	**Day of Discharge From Confinement: Day of Parasite Clearance (0 Parasites/mL) AND ≥72 h After Initiating Antimalarial Therapy**	
Time point (h) in relation to *Pf*SPZ-DVI Challenge			**0**[Error! Reference source not found.]	**2**						**Estimated On or Before Day 19**	
Biochemistry other than liver[Error! Reference source not found.]	X	X					X		X		X
CRP analysis[Error! Reference source not found.]		X				X	X	X	X	X	X
Coagulation parameters[Error! Reference source not found.]	X	X				X	X	X	X	X	X
rRT-PCR for SARS-CoV-2	X[r]					X[s]					
qPCR for parasites[Error! Reference source not found.]			X			X	X	X	X	X	X
Parasite Transcriptomics[Error! Reference source not found.]						X	X	X	X	X	X
Previous medications	X										
Concomitant medications	X---X										
AEs	X---X										
SAE reporting	X---X										

β-HCG: β-human chorionic gonadotropin, AE: adverse event, aPTT: activated partial thromboplastin time, CMV: cytomegalovirus, CRP: C-reactive protein, DVI: direct venous inoculation, EBV: Epstein Barr Virus, ECG: electrocardiogram, EOS: end of study, FSH: follicle stimulating hormone, HbsAg: hepatitis B surface antigen , HCV: hepatitis C virus, HIV: human immunodeficiency virus, IgM: immunoglobulin M, INR: international normalized ratio, *Pf*SPZ: *Plasmodium falciparum* sporozoites, PT: prothrombin time, qPCR: quantitative polymerase chain reaction, rRT-PCR: real-time reverse transcription polymerase chain reaction, SAE: serious adverse event, SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

a. Assessments begin as of participant confinement in the clinical unit and must be completed and safety assessment outcomes must be available before *Pf*SPZ-DVI Challenge on Day 1.

b. On Day 1, assessments begin as of 3 h before challenge (except for urinalysis assessments, morning void allowed). The assessments indicated must be completed and safety assessment outcomes must be available before *Pf*SPZ-DVI Challenge inoculation.

c. Confinement to the clinical unit will occur as follows:

- Participants will be admitted to the clinical unit in the morning of Day -1 and discharged from confinement 2 h post *Pf*SPZ-DVI Challenge on Day 1.
- Participants will be admitted to the clinical unit in the morning of Day 10 and discharged on Day of discharge from confinement (Day of parasite clearance AND ≥72 h after initiating antimalarial therapy), estimated to occur on or before Day 19. Of note, participants who commence antimalarial therapy on Day 24 (see **Error! Reference source not found.**) will only be discharged from confinement at the end of the EOS visit on Day 28.

d. No study-related procedure is to be performed before voluntarily signing of the informed consent form.

e. Alcohol breath test and urine dipstick screening for drug abuse.

f. Height to be measured at screening only; body weight to be measured at screening, at admission on Day -1 and at the EOS visit.

g. Physical examination will be conducted:

- once at screening and once on Day -1;
- once on Day 10 (upon admission to clinical unit for confinement);
- once within 24 h after first PCR ≥250 parasites/mL;
- once within 24 h after first PCR ≥5000 parasites/mL;
- once at pre-discharge from clinical unit on Day of discharge from confinement (Day of parasite clearance AND ≥72 h after initiating antimalarial therapy); and
- once at the EOS.

Full physical examination will be conducted at screening, on Day -1, within ±24 h after first PCR ≥250 parasites/mL and at the EOS visit on Day 28. Targeted (symptom-driven) physical examination will be performed on the other time points in case malaria clinical score >6.

h. Vital signs (blood pressure and pulse) will be measured after remaining in a supine position for at least 10 min. All measurements will be performed as follows:

- once at screening and once on Day -1;
- on Day 1 (pre and post *Pf*SPZ-DVI Challenge);
- twice daily from Day 10 (admission to clinical unit for confinement) onwards until Day of discharge from confinement (Day of parasite clearance AND ≥72 h after initiating antimalarial therapy); and
- once at the EOS.

Body temperature (sublingual) will also be assessed, and this whenever the malaria clinical score will be evaluated (see **Error! Reference source not found.**).
At screening, orthostatic changes to blood pressure and pulse rate will also be assessed: participants will be requested to stand after completion of the supine measurements and blood pressure and pulse rate will be recorded after at least 2 min in the standing position.

i. 12-lead ECGs recordings will be performed in triplicate after participants have remained in a supine position for at least 10 min. All recordings will be performed as follows:

- once at screening; and
- once on Days 2 and 3 of antimalarial therapy.

j. Serological testing for HIV, hepatitis A IgM antibody, HbsAg, anti-HCV antibody, hepatitis D antibody (only in subjects positive for HbsAg), hepatitis E IgM antibody, CMV IgM antibody and EBV IgM antibody, to determine eligibility for the study.

k. Pregnancy testing consists of serum β-HCG assessments at screening and at the EOS visit and a urine β-HCG assessment on Day-1.

l. Every participant will be prescribed a 3-day oral course of Riamet® (20 mg artemether and 120 mg lumefantrine tablets) (see Protocol Section 5.1). The first dose should be taken as soon as possible when a PCR threshold of 5000 parasites/mL is achieved or earlier if a participant has a malaria clinical score >6 or at Investigator's discretion. Of note, all participants inoculated with *Pf*SPZ-DVI Challenge will commence antimalarial therapy no later than Day 24, regardless if they reach the pre-defined cohort-specific PCR parasitaemia/malaria clinical score thresholds (i.e., 5000 parasites/mL blood and/or a malaria clinical score ≥6) (see Protocol Section 4.3).

If an intolerance or contraindication to Riamet® develops since inclusion, Malarone® will be administered (see Protocol Section 5.1).

m. Malaria clinical score for malaria signs and symptoms and the vital sign parameter body temperature (sublingual) (see **Error! Reference source not found.**) are assessed:

- on Day 1 (pre-*Pf*SPZ-DVI Challenge);
- once daily during ambulatory visits on Day 7, 8 and 9;
- twice daily from Day 10 (admission to clinical unit for confinement) onwards until Day of discharge from confinement (Day of parasite clearance AND ≥72 h after initiating antimalarial therapy); and
- once at the EOS.

n. Haematology and liver biochemistry laboratory tests will be performed after overnight fast for at least 8 h (see Protocol Section 4.3):

- once at screening and once on Day -1;
- once during ambulatory visit on Day 7;
- once on Day 10 (upon admission to clinical unit for confinement);
- once within 24 h after first PCR ≥250 parasites/mL;
- once on Day of first PCR ≥5000 parasites/mL AND prior to initiating antimalarial therapy (non-fasted state allowed);
- once at pre-discharge from clinical unit on Day of discharge from confinement (Day of parasite clearance AND ≥72 h after initiating antimalarial therapy); and
- once at the EOS.

  Troponin T will be measured at screening (fasted state), at baseline prior to inoculation on Day -1 (fasted state), and on Days 1, 2 and 3 of antimalarial therapy (non-fasted state).
  FSH will be measured at screening in all women.

o. Biochemistry laboratory tests other than liver (including urinalysis; morning void allowed) will be performed after overnight fast for at least 8 h (see Protocol Section 4.3):

- once at screening and once on Day -1;
- once on Day 10 (upon admission to clinical unit for confinement);
- once on Day of first PCR ≥5000 parasites/mL AND prior to initiating antimalarial therapy (non-fasted state allowed); and
- once at the EOS.

p. CRP laboratory tests will be performed at the following time points:

- on Day -1;
- once during ambulatory visit on Day 7;
- once on Day 10 (upon admission to clinical unit for confinement);
- once within 24 h after first PCR ≥250 parasites/mL;
- once on Day of first PCR ≥5000 parasites/mL AND prior to initiating antimalarial therapy;
- on Days 2 and 3 of antimalarial therapy;
- once at pre-discharge from clinical unit on Day of discharge from confinement (Day of parasite clearance AND ≥72 h after initiating antimalarial therapy); and
- once at the EOS.

q. INR, PT and aPTT laboratory tests will be performed once at screening and once on Day -1. On the other time points thereafter, only the INR test will be performed.

r. A nasopharyngeal swab will be taken at an ambulatory visit during screening up to Day -2 (preferably as close as possible to the day of admission, based on test capacity and according to national laws) from participants who are still eligible to be enrolled in the study after completing all other screening tests. An rRT-PCR test will be performed on these swabs to screen for infection with SARS-CoV-2.

s. A nasopharyngeal swab will be taken prior to confinement to the study site on Day 10, based on test capacity and according to national laws.

t. Blood samples for the assessment of parasitaemia by qPCR will be drawn at the following time points:

- on Day 1 (pre-*Pf*SPZ-DVI Challenge);
- once daily during ambulatory visits on Day 7, 8 and 9;
- twice daily from Day 10 (admission to clinical unit for confinement) onwards until Day of first PCR ≥5000 parasites/mL AND prior to initiating antimalarial therapy;
- at multiple time points (2, 6, 8, 12, 16, 24, 36, 48 and 72 h) following initiation of Riamet®;
- once on Day of discharge from confinement (Day of parasite clearance AND ≥72 h after initiating antimalarial therapy); and
- once at the EOS.

All qPCR blood samples will be drawn for immediate analysis, except for the ones drawn at the multiple time points during Riamet® therapy.

u. Blood samples for parasite transcriptomics will be drawn at the following time points:

- once daily during ambulatory visits on Day 7, 8 and 9;
- once daily from Day 10 (admission to clinical unit for confinement) onwards until Day of discharge from confinement (Day of parasite clearance AND ≥72 h after initiating antimalarial therapy); and
- once at the EOS.

v. All participants will be asked non-leading questions to determine the occurrence of any AEs at the EOS visit.

Of note, for participants who commence antimalarial therapy on Day 24 (**Error! Reference source not found.**), the Day of discharge from confinement will coincide with the EOS. In this case, applicable assessments will not be performed in duplicate.

MOCK TABLES, LISTINGS AND FIGURES

A single centre, open label, pilot phase Ib study to investigate blood stage malaria infection after Direct Venous Inoculation of cryopreserved Plasmodium falciparum (NF54 strain) Sporozoites (PfSPZ-DVI) in malaria naïve healthy adult volunteers

Protocol:	MMV_PfSPZ-DVI Blood Stage_19_01
SGS LS number:	BE-80-1914715
Development phase:	Ib
Sponsor:	Medicines for Malaria Venture (MMV)
Mock TLF version number:	Final 1.0
SAP version date:	11FEB2021

SIGNATURE PAGE

Name and function	Date (ddMMMyyyy)	Signature
SGS-LS author(s):		
Daniel Izquierdo Juncàs, Biostatistician	11FEB2021	DocuSigned by: Daniel Izquierdo Juncas Signer Name: Daniel Izquierdo Juncas Signing Reason: I am the author of this document Signing Time: 11-Feb-2021 | 16:10 CET 690E658303D54613A9EC59ED7BAE2148
Bastiaan Jansen, Biostatistical Coordinator	11FEB2021	DocuSigned by: bastiaan Jansen Signer Name: bastiaan Jansen Signing Reason: I approve this document Signing Time: 11-Feb-2021 | 16:23 CET 15ADFC6D3E734686B167F978EA41202B
Sponsor's approval: The approver agrees the tables, listings and figures of the statistical analysis will be created according to this document.		
Farouk Chughlay, Project and Medical Director		DocuSigned by: Signer Name: Farouk Chughlay Signing Reason: I approve this document Signing Time: 11-Feb-2021 | 07:55 PST 6A2C1E232AEB48DFA6A544CF570BF27F
Myriam El Gaaloul Director, Clinical Sciences		DocuSigned by: Myriam El Gaaloul Signer Name: Myriam El Gaaloul Signing Reason: I approve this document Signing Time: 13-Feb-2021 | 01:24 PST C2CA71F33AA843DAB327CC3B36DFB37C

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1.3.3 Vital signs

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2. GENERAL LAYOUT OF A TLF

2.1 SOFTWARE USED

SAS version 9.4 or later will be used for programming. TLFs will be transferred to MS WORD.

2.2 LAYOUT SPECIFICATIONS IN SAS

SAS TITLE1, left will identify the project by Sponsor protocol number. In case of a blinded testrun, the analysis version will be added, or a note that fake treatments were used.

SAS TITLE1, right will show the SAS datetime stamp of the table creation (batch submit datetime).

SAS TITLE2 will present the page numbering, right aligned, in the format “PAGE X OF Y”.

SAS TITLE3 will contain the TLF’s identification in the form TABLE 14.x.x.x, LISTING 16.2.x.x and FIGURE 14.x.x.x followed by the title. The title itself and the TLF number are copied from the SAP.

SAS TITLE4 will draw a horizontal dotted line (“-------“) over the entire width of the page.

SAS TITLE5 will show the analysis population.

SAS TITLE6 through 10 may be used to provide further information, when deemed useful.

Example:

```
1 STUDY IDENTIFIER - ANALYSIS VERSION                                                                        SAS DATE AND TIME
2                                                                                                                  PAGE X OF Y
3 TABLE 14.x.x.x: <TABLE TITLE>
4 ------------------------------------------------------------------------------------------------------------------------------
5 POPULATION: ALL SUBJECTS
6
7
8
9
10
```

Footnotes will be added in SAS, as deemed appropriate by the programmer. Footnotes will be used to improve the readability of the output.

Output will be left-aligned and all text will be in CAPITALS, except for specific test units.

The following SAS page setup will be used:

- LSIZE = 139
- PSIZE = 43

Dates are formatted using the SAS date9. format: ddMMMyyyy . E.g., 16SEP1970.

The format of times follows a 24h clock as hh:mm, from 00:00 till 23:59. 24:00 equals 00:00 on the next day.

Datetime fields are formatted using the SAS datetime13. or datetime15. format: ddMMMyyyy:hh:mm

2.3 LAYOUT SPECIFICATIONS IN MS WORD

All tables and listings will be generated in ASCII text files by SAS, and then converted into MS Word documents, using font COURIER NEW 8pt. (like in these Mock TLFs).

Page layout:

- landscape
- paper size: A4
- margins in MS Word, in cm:

Top	3.2
Bottom	3.2
Left	2.2
Right	2.2
Gutter	0
Header, from edge	0.97
Footer, from edge	0.94

2.4 GENERAL TABLE LAYOUT

2.4.1 Standard layout for descriptive statistics on continuous parameters

Use of decimal places in descriptive statistics:

- Mean, geometric mean, median, SD, geometric SD and CI will be presented with one more decimal place than the individual values.
- Minimum, maximum and range will be presented with the same number of decimal places than the individual values.
- P-values will be presented with four decimal places, ratios with three decimal places and estimates and test statistics with two decimal places.

PARAMETER 1 (unit)

	n	Mean	S.E.	S.D.	95% C.I. *	Min	Median	Max
COHORT 1 (N=XX)								
SCREENING	XX	XX.XXX	XX.XXX	XX.XXX	(XX.XXX ; XX.XXX)	XX.XX	XX.XXX	XX.XX
BASELINE	XX	XX.XXX	XX.XXX	XX.XXX	(XX.XXX ; XX.XXX)	XX.XX	XX.XXX	XX.XX
TIME POINT 3	XX	XX.XXX	XX.XXX	XX.XXX	(XX.XXX ; XX.XXX)	XX.XX	XX.XXX	XX.XX
TIME POINT 4	XX	XX.XXX	XX.XXX	XX.XXX	(XX.XXX ; XX.XXX)	XX.XX	XX.XXX	XX.XX
FOLLOW-UP	XX	XX.XXX	XX.XXX	XX.XXX	(XX.XXX ; XX.XXX)	XX.XX	XX.XXX	XX.XX
COHORT 2 (N=XX)								
SCREENING	XX	XX.XXX	XX.XXX	XX.XXX	(XX.XXX ; XX.XXX)	XX.XX	XX.XXX	XX.XX
BASELINE	XX	XX.XXX	XX.XXX	XX.XXX	(XX.XXX ; XX.XXX)	XX.XX	XX.XXX	XX.XX
TIME POINT 3	XX	XX.XXX	XX.XXX	XX.XXX	(XX.XXX ; XX.XXX)	XX.XX	XX.XXX	XX.XX
TIME POINT 4	XX	XX.XXX	XX.XXX	XX.XXX	(XX.XXX ; XX.XXX)	XX.XX	XX.XXX	XX.XX
FOLLOW-UP	XX	XX.XXX	XX.XXX	XX.XXX	(XX.XXX ; XX.XXX)	XX.XX	XX.XXX	XX.XX

Etc.

* CONFIDENCE INTERVAL FOR MEAN

2.4.2 Standard layout for frequency tabulations

It is possible that the width of tables is too much to fit on one page (due to the number of treatments / columns). In that case, the page break will attempt to keep information of one treatment together. I.e., the break will not be made between "n" and "%".

Zero frequencies are shown, but classes that were not observed in any treatment or missing values, are not presented.

Percentages will be shown with 1 decimal place (xx.x%). It is allowed that "100.0%" is presented as "100%" to save space.

An example for a categorical variable:

	COHORT 1 (N=XX)		COHORT 2 (N=XX)		ALL SUBJECTS (N=XX)	
PARAMETER AND CLASS	n	%	n	%	n	%
PARAMETER 1						
CLASS 1	XX	XX.X	XX	XX.X	XX	XX.X
CLASS 2	XX	XX.X	XX	XX.X	XX	XX.X
TOTAL	XX	100	XX	100	XX	100
PARAMETER 2						
CLASS 1	XX	XX.X	XX	XX.X	XX	XX.X
CLASS 2	XX	XX.X	XX	XX.X	XX	XX.X
CLASS 3	XX	XX.X	XX	XX.X	XX	XX.X
TOTAL	XX	100	XX	100	XX	100
PARAMETER 3						
CLASS 1	XX	XX.X	XX	XX.X	XX	XX.X
TOTAL	XX	100	XX	100	XX	100

2.4.3 Standard layout for table containing descriptive statistics and frequency tabulations

In case a table contains descriptive statistics as well as tabulations (for example for demographic parameters), the following presentation will be used:

	COHORT 1 (N=XX)	COHORT 2 (N=XX)	ALL SUBJECTS (N=XX)
PARAMETER 1 (unit)			
n	XX	XX	XX
Mean (S.D)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
S.E.	X.X	X.X	X.X
95% C.I. *	(XX.X; XX.X)	(XX.X; XX.X)	(XX.X; XX.X)
Median	XX.X	XX.X	XX.X
Min; Max	(XX; XX)	(XX; XX)	(XX; XX)
PARAMETER 2 (unit)			
n	XX	XX	XX
Mean (S.D)	XX.X (XX.X)	XX.X (XX.X)	XX.X (XX.X)
S.E.	X.X	X.X	X.X
95% C.I. *	(XX.X; XX.X)	(XX.X; XX.X)	(XX.X; XX.X)
Median	XX.X	XX.X	XX.X
Min; Max	(XX; XX)	(XX; XX)	(XX; XX)
PARAMETER 3			
CLASS 1	XX XX.X	XX XX.X	XX XX.X
CLASS 2	XX XX.X	XX XX.X	XX XX.X
TOTAL	XX 100	XX 100	XX 100
PARAMETER 4			
CLASS 1	XX XX.X	XX XX.X	XX XX.X
CLASS 2	XX XX.X	XX XX.X	XX XX.X
TOTAL	XX 100	XX 100	XX 100

* CONFIDENCE INTERVAL FOR MEAN
THE DENOMINATOR FOR THE PERCENTAGE CALCULATIONS IS THE TOTAL NUMBER OF SUBJECTS PER COHORT IN THE SAFETY SET, EXCLUDING MISSING VALUES.

2.4.4 Standard layout of an analysis table of contents

Per section of the analysis a table of contents is created automatically. Below an example:

```
STUDY IDENTIFIER - ANALYSIS VERSION                                                                                    SAS DATE AND TIME

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-------------------------------------------------------------------------------------------------------------------------------------------

 DISPLAY / LISTING
 ---------------------------------------------------------------------------------------------------------------------------------------

 LISTING 16.2.1.1: SUBJECT DISPOSITION: ALLOCATION
 TABLE 14.1.1.1: SUBJECT DISPOSITION: TABULATION OF THE STUDY TERMINATION
 TABLE 14.1.1.2: SUBJECT DISPOSITION: TABULATION OF THE NUMBER OF SUBJECTS IN EACH ANALYSIS POPULATION
 LISTING 16.2.1.2: SUBJECT DISPOSITION: STUDY TERMINATION
 LISTING 16.2.1.3: SUBJECT DISPOSITION: STUDY ANALYSIS PERIODS
 LISTING 16.2.1.4: SUBJECT DISPOSITION: OVERALL LISTING OF VISITS AND ASSESSMENTS
 LISTING 16.2.1.5: SUBJECT DISPOSITION: ELIGIBILITY CRITERIA - VIOLATIONS
 LISTING 16.2.1.6: SUBJECT DISPOSITION: ELIGIBILITY CRITERIA - EXEMPTIONS
 LISTING 16.2.1.7: SUBJECT DISPOSITION: PROTOCOL DEVIATIONS
 LISTING 16.2.1.8: SUBJECT DISPOSITION: NO-TREATMENT SUBJECTS
 LISTING 16.2.1.9: SUBJECT DISPOSITION: COMMENTS
 LISTING 16.2.1.10: USE OF STUDY MEDICATION: ACTUAL DATA
 TABLE 14.1.2.1: DEMOGRAPHIC DATA: DESCRIPTIVE STATISTICS
 LISTING 16.2.2.1: DEMOGRAPHIC DATA: DEMOGRAPHIC PARAMETERS
 LISTING 16.2.2.2: DEMOGRAPHIC DATA: SCREENING TESTS
 LISTING 16.2.2.3: DEMOGRAPHIC DATA: MEDICAL HISTORY ABNORMALITIES
 LISTING 16.2.2.4: DEMOGRAPHIC DATA: CONCOMITANT DISEASES
 LISTING 16.2.2.5: PHYSICAL EXAMINATIONS
```

2.5 GENERAL FIGURE LAYOUT

Please be aware that all graphs shown in this document are mock-graphs. Points, lines, axes and legends are not always study specific and are therefore described explicitly below each graph.

General programmer notes:

- Figures should be made at a high resolution and with an easily readable font size for legend and axis labels and values.
- Markers and lines should be of sufficient size and width.
- Labels of X- and Y-axis will be centred.
- Colours, line types and symbols should be used in a consistent way throughout the analysis.
- Colours, line types and symbols should be used keeping in mind figures are often printed in grey scale.

3. MOCK TABLES

3.1 GENERAL CHARACTERISTICS

3.1.1 Subject disposition

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TABLE 14.1.1.1: ANALYSIS SETS

ANALYSIS SET: ALL SCREENED SUBJECTS

ANALYSIS SET	COHORT 1 n	COHORT 1 %	COHORT 2 n	COHORT 2 %	ALL SUBJECTS n	ALL SUBJECTS %
ALL SCREENED SUBJECTS SET	XX		XX		XX	
SAFETY ANALYSIS SET	XX	100	XX	100	XX	100
PHARMACODYNAMICS ANALYSIS SET	XX	XX.X	XX	XX.X	XX	XX.X
MODIFIED PHARMACODYNAMICS ANALYSIS SET	XX	XX.X	XX	XX.X	XX	XX.X

THE DENOMINATOR FOR THE PERCENTAGE CALCULATIONS IS THE TOTAL NUMBER OF SUBJECTS PER COHORT IN THE SAFETY SET.

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TABLE 14.1.1.2: FIRST AND LAST CONTACT IN THE STUDY

ANALYSIS SET: ALL SCREENED SUBJECTS

DATE OF FIRST ICF (1):	ddMMMyyyy
DATE OF LAST VISIT (2):	ddMMMyyyy
DATE OF LAST CONTACT (3):	ddMMMyyyy

NOTES: (1): SIGNATURE DATE ON THE INFORMED CONSENT FORM OF THE FIRST SUBJECT.
(2): DATE OF THE LAST VISIT IN THE STUDY (INCLUDING UNSCHEDULED VISITS).
(3): LAST DATE OF CONTACT WITH ANY SUBJECT IN THE STUDY.

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TABLE 14.1.1.3: STUDY DISCONTINUATION

ANALYSIS SET: SAFETY

SUBJECT STATUS	COHORT 1 (N=XX) n	%	COHORT 2 (N=XX) n	%	ALL SUBJECTS (N=XX) n	%
COMPLETED	XX	XX.X	XX	XX.X	XX	XX.X
DISCONTINUED	XX	XX.X	XX	XX.X	XX	XX.X
ADVERSE EVENT	XX	XX.X	XX	XX.X	XX	XX.X
SUBJECT LOST TO FOLLOW-UP	XX	XX.X	XX	XX.X	XX	XX.X

THE DENOMINATOR FOR THE PERCENTAGE CALCULATIONS IS THE TOTAL NUMBER OF SUBJECTS PER COHORT IN THE SAFETY SET.

3.1.2 Protocol deviations and eligibility

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TABLE 14.1.1.4: MAJOR PROTOCOL DEVIATIONS

ANALYSIS SET: SAFETY

PRESENCE AND CLASS	COHORT 1 (N=XX) n	%	COHORT 2 (N=XX) n	%	ALL SUBJECTS (N=XX) n	%
NO MAJOR DEVIATIONS	XX	XX.X	XX	XX.X	XX	XX.X
ANY MAJOR DEVIATION	XX	XX.X	XX	XX.X	XX	XX.X
FORBIDDEN THERAPY	XX	XX.X	XX	XX.X	XX	XX.X
PROCEDURE DEVIATION	XX	XX.X	XX	XX.X	XX	XX.X

THE DENOMINATOR FOR THE PERCENTAGE CALCULATIONS IS THE TOTAL NUMBER OF SUBJECTS PER COHORT IN THE SAFETY SET.

3.1.3 Demographic and other baseline characteristics

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TABLE 14.1.2.1: DEMOGRAPHIC DATA

ANALYSIS SET: SAFETY

	COHORT 1 (N=XX)	COHORT 2 (N=XX)	ALL SUBJECTS (N=XX)
AGE (years)			
n	XX	XX	XX
Mean (S.D.)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)
Median	XX.X	XX.X	XX.X
Min; Max	(XX; XX)	(XX; XX)	(XX; XX)
HEIGHT (cm)			
n	XX	XX	XX
Mean (S.D.)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)
Median	XX.X	XX.X	XX.X
Min; Max	(XX; XX)	(XX; XX)	(XX; XX)
WEIGHT AT SCREENING (kg)			
n	XX	XX	XX
Mean (S.D.)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)
Median	XX.X	XX.X	XX.X
Min; Max	(XX; XX)	(XX; XX)	(XX; XX)
BMI AT SCREENING (kg/m²)			
n	XX	XX	XX
Mean (S.D.)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)
Median	XX.X	XX.X	XX.X
Min; Max	(XX; XX)	(XX; XX)	(XX; XX)
SEX (n %)			
FEMALE	XX XX.X	XX XX.X	XX XX.X
MALE	XX XX.X	XX XX.X	XX XX.X
TOTAL	XX 100	XX 100	XX 100
RACE (n %)			
BLACK	XX XX.X	XX XX.X	XX XX.X
CAUCASIAN/WHITE	XX XX.X	XX XX.X	XX XX.X
TOTAL	XX 100	XX 100	XX 100

ETHNICITY (n %)						
HISPANIC/LATINO	XX	XX.X	XX	XX.X	XX	XX.X
NOT HISPANIC/LATINO	XX	XX.X	XX	XX.X	XX	XX.X
TOTAL	XX	100	XX	100	XX	100
SMOKING STATUS (n %)						
EX-SMOKER	XX	XX.X	XX	XX.X	XX	XX.X
NON-SMOKER	XX	XX.X	XX	XX.X	XX	XX.X
SMOKER	XX	XX.X	XX	XX.X	XX	XX.X
TOTAL	XX	100	XX	100	XX	100

THE DENOMINATOR FOR THE PERCENTAGE CALCULATIONS IS THE TOTAL NUMBER OF SUBJECTS PER COHORT IN THE SAFETY SET, EXCLUDING MISSING VALUES.

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TABLE 14.1.2.2: ORTHOSTATIC CHANGE IN VITAL SIGNS AT SCREENING

ANALYSIS SET: SAFETY

SYSTOLIC BLOOD PRESSURE (mmHg)

	COHORT 1 (N=XX)	COHORT 2 (N=XX)	ALL SUBJECTS (N=XX)
SUPINE RESULT			
n	XX	XX	XX
Mean (S.D.)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)
Median	XX.X	XX.X	XX.X
Min; Max	(XX; XX)	(XX; XX)	(XX; XX)
STANDING RESULT			
n	XX	XX	XX
Mean (S.D.)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)
Median	XX.X	XX.X	XX.X
Min; Max	(XX; XX)	(XX; XX)	(XX; XX)
ORTHOSTATIC CHANGE			
n	XX	XX	XX
Mean (S.D.)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)
Median	XX.X	XX.X	XX.X
Min; Max	(XX; XX)	(XX; XX)	(XX; XX)

ORTHOSTATIC CHANGE = VALUE IN SUPINE POSITION - VALUE IN STANDING POSITION.

Programmer notes: repeat the table by parameter: systolic blood pressure, diastolic blood pressure and heart rate.

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TABLE 14.1.2.3: BECK DEPRESSION INVENTORY AT SCREENING

ANALYSIS SET: SAFETY

	COHORT 1 (N=XX)	COHORT 2 (N=XX)	ALL SUBJECTS (N=XX)
BECK DEPRESSION INVENTORY TOTAL SCORE			
n	XX	XX	XX
Mean (S.D.)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)
Median	XX.X	XX.X	XX.X
Min; Max	(XX; XX)	(XX; XX)	(XX; XX)
BECK DEPRESSION INVENTORY INTERPRETATION			
NORMAL	XX XX.X	XX XX.X	XX XX.X
MILD MOOD DISTURBANCE	XX XX.X	XX XX.X	XX XX.X
BORDERLINE CLINICAL DEPRESSION	XX XX.X	XX XX.X	XX XX.X
TOTAL	XX 100	XX 100	XX 100

THE DENOMINATOR FOR THE PERCENTAGE CALCULATIONS IS THE TOTAL NUMBER OF SUBJECTS PER COHORT IN THE SAFETY SET, EXCLUDING MISSING VALUES.

3.1.4 Medical history and concomitant diseases

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TABLE 14.1.2.4: MEDICAL HISTORY

ANALYSIS SET: SAFETY

SYSTEM ORGAN CLASS AND PREFERRED TERM	COHORT 1 (N=XX) n	%	COHORT 2 (N=XX) n	%	ALL SUBJECTS (N=XX) n	%
NO MEDICAL HISTORY FINDINGS	XX	XX.X	XX	XX.X	XX	XX.X
WITH ANY MEDICAL HISTORY FINDING	XX	XX.X	XX	XX.X	XX	XX.X
EYE DISORDERS	XX	XX.X	XX	XX.X	XX	XX.X
CATARACT	XX	XX.X	XX	XX.X	XX	XX.X
GASTROINTESTINAL DISORDERS	XX	XX.X	XX	XX.X	XX	XX.X
DUODENAL ULCER	XX	XX.X	XX	XX.X	XX	XX.X
UMBILICAL HERNIA	XX	XX.X	XX	XX.X	XX	XX.X
INFECTIONS AND INFESTATIONS	XX	XX.X	XX	XX.X	XX	XX.X
APPENDICITIS	XX	XX.X	XX	XX.X	XX	XX.X
TUBERCULOSIS	XX	XX.X	XX	XX.X	XX	XX.X

THE DENOMINATOR FOR THE PERCENTAGE CALCULATIONS IS THE TOTAL NUMBER OF SUBJECTS PER COHORT IN THE SAFETY SET.

Programmer notes: repeat similar table for concomitant diseases:

TABLE 14.1.2.5: CONCOMITANT DISEASES

3.1.5 Prior and concomitant therapies

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TABLE 14.1.2.6: PRIOR AND CONCOMITANT THERAPIES BY ATC CLASS (LEVEL 4) AND GENERIC TERM

ANALYSIS SET: SAFETY

ANALYSIS PHASE = OVERALL

ATC CLASS (LEVEL 4) AND GENERIC TERM	COHORT 1 (N=XX) n	%	COHORT 2 (N=XX) n	%	ALL SUBJECTS (N=XX) n	%
NO THERAPIES TAKEN	XX	XX.X	XX	XX.X	XX	XX.X
WITH THERAPIES TAKEN	XX	XX.X	XX	XX.X	XX	XX.X
ANALGESICS	XX	XX.X	XX	XX.X	XX	XX.X
PARACETAMOL	XX	XX.X	XX	XX.X	XX	XX.X
ULTRACET	XX	XX.X	XX	XX.X	XX	XX.X
ZOLMITRIPTAN	XX	XX.X	XX	XX.X	XX	XX.X
CARDIAC THERAPY	XX	XX.X	XX	XX.X	XX	XX.X
CAFFEINE	XX	XX.X	XX	XX.X	XX	XX.X
IBUFROFEN	XX	XX.X	XX	XX.X	XX	XX.X

Etc.

ANALYSIS PHASE = SCREENING

Etc.

THE DENOMINATOR FOR THE PERCENTAGE CALCULATIONS IS THE TOTAL NUMBER OF SUBJECTS PER COHORT AND PER ANALYSIS PHASE IN THE SAFETY SET.

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TABLE 14.1.2.7: ANTIMALARIAL TREATMENT

ANALYSIS SET: SAFETY

	COHORT 1 (N=XX) n	%	COHORT 2 (N=XX) n	%	ALL SUBJECTS (N=XX) n	%
START OF ANTIMALARIAL TREATMENT						
PRIOR TO DAY 24	XX	XX.X	XX	XX.X	XX	XX.X
ON DAY 24	XX	XX.X	XX	XX.X	XX	XX.X
TOTAL	XX	100	XX	100	XX	100
ANTIMALARIAL TREATMENT ADMINISTERED						
MALARONE 250/100 mg	XX	XX.X	XX	XX.X	XX	XX.X
RIAMET 20/120 mg	XX	XX.X	XX	XX.X	XX	XX.X
TOTAL	XX	100	XX	100	XX	100

THE DENOMINATOR FOR THE PERCENTAGE CALCULATIONS IS THE TOTAL NUMBER OF SUBJECTS PER COHORT IN THE SAFETY SET.

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TABLE 14.1.2.8: ANTIMALARIAL TREATMENT DISCONTINUATION

ANALYSIS SET: SAFETY

SUBJECT STATUS	COHORT 1 (N=XX) n	%	COHORT 2 (N=XX) n	%	ALL SUBJECTS (N=XX) n	%
COMPLETED	XX	XX.X	XX	XX.X	XX	XX.X
DISCONTINUED	XX	XX.X	XX	XX.X	XX	XX.X
ADVERSE EVENT	XX	XX.X	XX	XX.X	XX	XX.X
SUBJECT LOST TO FOLLOW-UP	XX	XX.X	XX	XX.X	XX	XX.X

THE DENOMINATOR FOR THE PERCENTAGE CALCULATIONS IS THE TOTAL NUMBER OF SUBJECTS PER COHORT IN THE SAFETY SET.

3.2 PHARMACODYNAMICS

Programmer note: all PD tables shown in this section will be repeated for the m-PD analysis set with adjusted numbering (e.g. 14.2.3.1.2).

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TABLE 14.2.3.1.1: TIME TO FIRST PCR POSITIVITY (DAYS): DESCRIPTIVE STATISTICS

ANALYSIS SET: PD

	n	Geom. Mean	95% C.I. <a>	Geom S.D.	Min; Max
COHORT 1 (N=XX)	XX	XX.XXX	XX.XXX; XX.XXX	XX.XXX	XX.XX
COHORT 2 (N=XX)	XX	XX.XXX	XX.XXX; XX.XXX	XX.XXX	XX.XX
ALL SUBJECTS (N=XX)	XX	XX.XXX	XX.XXX; XX.XXX	XX.XXX	XX.XX

<a> TWO-SIDED 95% CONFIDENCE INTERVAL ON THE GEOMETRIC MEAN.
POSITIVE PARASITAEMIA IS DEFINED AS qPCR OUTCOME ≥ 250 PARASITES PER mL BLOOD.
ONLY SUBJECTS THAT REACHED POSITIVE PARASITAEMIA ARE INCLUDED.

Programmer note: repeat Table 14.2.3.1.1 excluding the last footnote for:

TABLE 14.2.3.2.1: PARASITAEMIA AT FIRST PCR POSITIVITY (PARASITES/mL): DESCRIPTIVE STATISTICS

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TABLE 14.2.3.3.1: TIME TO PARASITAEMIA OF ≥5000 PARASITES PER mL BLOOD (DAYS): KAPLAN MEIER ESTIMATES

ANALYSIS SET: PD

	COHORT 1 (N=XX)	COHORT 2 (N=XX)	ALL SUBJECTS (N=XX)
25th QUANTILE (95% CI)	XX.X (XX.X; XX.X)	XX.X (XX.X; XX.X)	XX.X (XX.X; XX.X)
MEDIAN (95% CI)	XX.X (XX.X; XX.X)	XX.X (XX.X; XX.X)	XX.X (XX.X; XX.X)
75th QUANTILE (95% CI)	XX.X (XX.X; XX.X)	XX.X (XX.X; XX.X)	XX.X (XX.X; XX.X)
NUMBER ASSESSED	XX	XX	XX
NUMBER CENSORED	XX	XX	XX
NUMBER OF EVENTS <a>	XX	XX	XX

<a> SUBJECTS WITH PARASITAEMIA OF ≥5000 PARASITES PER mL BLOOD.

Programmer note: repeat Table 14.2.3.1.1 for:

TABLE 14.2.3.4.1: PARASITAEMIA AT THE TIME OF ≥5000 PARASITES PER mL BLOOD (PARASITES/mL): DESCRIPTIVE STATISTICS

TABLE 14.2.3.5.1: TIME TO FIRST DOSE OF TREATMENT WITH RIAMET (DAYS): DESCRIPTIVE STATISTICS

TABLE 14.2.3.6.1: PARASITAEMIA AT FIRST DOSE OF TREATMENT WITH RIAMET (PARASITES/mL): DESCRIPTIVE STATISTICS

In the previous tables the footnotes will be adapted accordingly.

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TABLE 14.2.3.7.1: INCIDENCE OF PARASITAEMIA

ANALYSIS SET: PD

	POSITIVE PARASITAEMIA <a>			PARASITAEMIA OF ≥5000 PARASITES PER mL BLOOD <b>		
	n	%	90% C.I. <c>	n	%	90% C.I. <c>
COHORT 1 (N=XX)	XX	XX.X	XX.X; XX.X	XX	XX.X	XX.X; XX.X
COHORT 2 (N=XX)	XX	XX.X	XX.X; XX.X	XX	XX.X	XX.X; XX.X
ALL SUBJECTS (N=XX)	XX	XX.X	XX.X; XX.X	XX	XX.X	XX.X; XX.X

<a> INCIDENCE OF POSITIVE PARASITAEMIA BETWEEN INOCULATION WITH PfSPZ AND DAY 28.
<b> INCIDENCE OF PARASITAEMIA OF ≥5000 PARASITES PER mL BLOOD BETWEEN INOCULATION WITH PfSPZ AND DAY 28.
<c> TWO-SIDED 90% EXACT CLOPPER-PEARSON CONFIDENCE INTERVAL.

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TABLE 14.2.3.8.1: BLOOD-STAGE PARASITE PROFILE: LOG-LINEAR MIXED MODEL ESTIMATES

ANALYSIS SET: PD

PARAMETER	VALUE	RSE	SHRINKAGE	COMMENT
Typical parameters				
GR			-	Parasite growth rate (1/hour)
Finoc			-	Inoculum viability (-)
Pinoc			-	Inoculum size (-)
Inter-individual variability				
omega(GR)				LogNormal
omega(Finoc)				LogNormal
omega(Pinoc)				LogNormal
Correlation of random effects				
corr(GR,Finoc)			-	Correlation coefficient
corr(GR,Pinoc)			-	Correlation coefficient
corr(Finoc,Pinoc)			-	Correlation coefficient
...			-	...
Parameter-Covariate relationships				
beta_GR(AGE)			-	AGE in Years on GR
beta_GR(WT0)			-	Weight in kg on GR
beta_GR(SEX_0)			-	Gender female on GR
...			-	...
Residual variability				
error_PROP1				Proportional Error (fraction) - Parasitemia
error_ADD1				Absolute Error - Parasitemia
Objective function		-		-
AIC		-		-
BIC		-		-

Model: ../PATH/TO/MODEL/DIRECTORY, Significant digits: 3 (Objective function rounded to closest integer value), omega values reported in standard deviation.

Programmer note 1: In the previous table, rows for correlation of random effects and rows for Parameter-Covariate relationships can be added or removed, depending on the final selected model.

Programmer note 2: In the previous table, the path to the model directory in the footnote should be adapted accordingly.

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TABLE 14.2.3.9.1: BLOOD-STAGE PARASITE PROFILE: EXTENDED LOG-LINEAR MIXED MODEL ESTIMATES

ANALYSIS SET: PD

PARAMETER	VALUE	RSE	SHRINKAGE	COMMENT
Typical parameters				
GR			-	Parasite growth rate (1/hour)
Finoc			-	Inoculum viability (-)
Pinoc			-	Inoculum size (-)
Fmax			-	Maximum fraction of hidden parasites (-)
Phi			-	Oscillation phase (-)
Plen			-	Period length of the oscillation (h)
Inter-individual variability				
omega(GR)				LogNormal
omega(Finoc)				LogNormal
omega(Pinoc)				LogNormal
omega(Fmax)				LogNormal
omega(Phi)				LogNormal
omega(Plen)				LogNormal
Correlation of random effects				
corr(GR,Finoc)			-	Correlation coefficient
corr(GR,Pinoc)			-	Correlation coefficient
corr(Finoc,Pinoc)			-	Correlation coefficient
...			-	...
Parameter-Covariate relationships				
beta_GR(AGE)			-	AGE in Years on GR
beta_GR(WT0)			-	Weight in kg on GR
beta_GR(SEX_0)			-	Gender female on GR
...			-	...
Residual variability				
error_PROP1				Proportional Error (fraction) - Parasitemia
error_ADD1				Absolute Error - Parasitemia
Objective function		-		-
AIC		-		-
BIC		-		-

Model: ../PATH/TO/MODEL/DIRECTORY, Significant digits: 3 (Objective function rounded to closest integer value), omega values reported in standard deviation.

Programmer note 1: The table should be included only if such an extended log-linear model had been estimated (refer to SAP section 2.1.3.1).

Programmer note 2: In the previous table, rows for correlation of random effects and rows for Parameter-Covariate relationships can be added or removed, depending on the final selected model.

Programmer note 3: In the previous table, the path to the model directory in the footnote should be adapted accordingly.

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TABLE 14.2.3.10.1: BLOOD-STAGE PARASITE PROFILE: MODEL DERIVED POPULATION PARAMETERS

ANALYSIS SET: PD

PARAMETER	MEAN	95%-CI
Parasitaemia multiplication rate (log10)		
PMR_48h <a>	X.XX	X.XX; X.XX<c>
PMR_Plen <b>	X.XX	X.XX; X.XX<c>
Predicted time to reach parasitaemia thresholds (h)		
TIME_PCRPOS <a>	XXX.X	XXX.X; XXX.X<d>
TIME_PCR5000 <a>	XXX.X	XXX.X; XXX.X<d>
TIME_PCRPOS <b>	XXX.X	XXX.X; XXX.X<d>
TIME_PCR5000 <b>	XXX.X	XXX.X; XXX.X<d>

POPULATION PARAMETER ESTIMATES OBTAINED UPON SAMPLING OF 1'000 SETS OF MODEL POPULATION PARAMETERS FROM THE UNCERTAINTY DISTRIBUTION:
MEAN: SAMPLE ARITHMETIC MEAN FOR PARASITAEMIA MULTIPLICATION RATE; SAMPLE GEOMETRIC MEAN FOR PREDICTED TIME TO REACH PARASITAEMIA THRESHOLDS, I.E. EXP(MEAN(LOG-TRANSFORMED TIMES));
95%-CI: 95% CONFIDENCE INTERVAL FOR THE MEAN (SEE FOOTNOTES <c> and <d>).

<a> derivation based on the log-linear mixed model;
<b> derivation based on the extended log-linear mixed model.
<c> calculated as -1.96*S.E.+MEAN; 1.96*S.E.+MEAN, where S.E. denotes the standard error of MEAN, i.e. S.E.=S.D./SQRT(1'000) with S.D. denoting the sample standard deviation.
<d> calculated as EXP(-1.96*S.E. + LOG(MEAN)); EXP(1.96*S.E. + LOG(MEAN)), where S.E=S.D./SQRT(1'000) with S.D. denoting the sample standard deviation of the log-transformed times.

Programmer note 1: Rows corresponding to the extended log-linear model <b> to be omitted if such model had not been inferred (refer to SAP section 2.1.3.1).

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TABLE 14.2.3.11.1: BLOOD-STAGE PARASITE PROFILE: MODEL DERIVED PARAMETERS BASED ON INDIVIDUAL PARAMETER ESTIMATES

ANALYSIS SET: PD

PARAMETER	N	MEAN (RSE)	S.D.	95%-PI	RANGE
Parasitaemia multiplication rate (log10)					
PMR_48h <a>	XX	X.XX (XX%<c>)	X.XX	X.XX; X.XX	X.XX; X.XX
PMR_Plen <b>	XX	X.XX (XX%<c>)	X.XX	X.XX; X.XX	X.XX; X.XX
Predicted time to reach parasitaemia thresholds (h)					
TIME_PCRPOS <a>	XX	XXX.X (XX%<d>)	XXX.X	XXX.X; XXX.X	XXX.X; XXX.X
TIME_PCR5000 <a>	XX	XXX.X (XX%<d>)	XXX.X	XXX.X; XXX.X	XXX.X; XXX.X
TIME_PCRPOS <b>	XX	XXX.X (XX%<d>)	XXX.X	XXX.X; XXX.X	XXX.X; XXX.X
TIME_PCR5000 <b>	XX	XXX.X (XX%<d>)	XXX.X	XXX.X; XXX.X	XXX.X; XXX.X

SUMMARY STATISTICS OF INDIVIDUAL PARAMETER ESTIMATES:
N: NUMBER OF INDIVIDUALS;
MEAN: ARITHMETIC MEAN FOR PARASITAEMIA MULTIPLICATION RATE; GEOMETRIC MEAN FOR PREDICTED TIME TO REACH PARASITAEMIA THRESHOLDS;
S.D.: STANDARD DEVIATION;
RSE: RELATIVE STANDARD ERROR FOR MEAN (IN PERCENTILES; see footnotes <c> and <d>);
95%-PI: 95% PREDICTION INTERVAL (see footnote <e>);
RANGE: OBSERVED MINIMUM AND MAXIMUM.

<a> derivation based on log-linear mixed model;
<b> derivation based on extended log-linear mixed model.
<c> relative standard error of ARITHMETIC MEAN in percentile calculated as S.D./SQRT(N)/MEAN*100;
<d> relative standard error of GEOMETRIC MEAN in percentile calculated as S.D.(LOG-TRANSFORMED TIMES)/SQRT(N - 1)*100;
<e> 95% prediction interval calculated as -t(N-1,0.025,0.975)*S.D.+ ARITHMETIC MEAN; t(N-1,0.025,0.975)*S.D.+ ARITHMETIC MEAN, where t(N-1,0.025,0.975) denotes the Student t-value for N-1 degrees of freedom. Note that these procedure assumes normal distribution of the variable.

Programmer note 1: Derived parameters for the extended log-linear model <b> should be omitted if such model had not been inferred (refer to SAP section 2.1.3.1).

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TABLE 14.2.3.12.1: BLOOD-STAGE PARASITE PROFILE: MODEL DERIVED PARAMETERS BASED ON SIMULATED INDIVIDUAL PARAMETER VALUES

ANALYSIS SET: PD

PARAMETER	MEAN	95%-PI
Parasitaemia multiplication rate (log10)		
PMR_48h <a>	X.XX	X.XX; X.XX
PMR_Plen <b>	X.XX	X.XX; X.XX
Predicted time to reach parasitaemia thresholds (h)		
TIME_PCRPOS <a>	XXX.X	XXX.X; XXX.X
TIME_PCR5000 <a>	XXX.X	XXX.X; XXX.X
TIME_PCRPOS <b>	XXX.X	XXX.X; XXX.X
TIME_PCR5000 <b>	XXX.X	XXX.X; XXX.X

SUMMARY STATISTICS UPON SIMULATING 1'000 SETS OF POPULATION PARAMETERS (SAMPLING FROM UNCERTAINTY DISTRIBUTION) AND 1'000 SETS OF INDIVIDUAL PARAMETER VALUES (SAMPLING FROM IIV DISTRIBUTION) FOR EACH POPULATION (IN TOTAL 1'000'000 SETS OF INDIVIDUAL PARAMETER VALUES):
MEAN: SAMPLE ARITHMETIC MEAN FOR PARASITAEMIA MULTIPLICATION RATE; SAMPLE GEOMETRIC MEAN FOR PREDICTED TIME TO REACH PARASITAEMIA THRESHOLDS;
95%-PI: 95% PREDICTION INTERVAL CALCULATED FROM THE 0.025TH AND 0.975TH SAMPLE QUANTILES.

<a> derivation based on log-linear mixed model;
<b> derivation based on extended log-linear mixed model.

Programmer note 1: The table should be included only if the model parameter IIV distribution could be estimated for all model parameters (refer to SAP section 2.1.3.1).

Programmer note 2: Derived parameters for the extended log-linear model <b> should be omitted if such model had not been inferred (refer to SAP section 2.1.4).

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TABLE 14.2.3.13.1: BLOOD-STAGE PARASITE CLEARANCE PROFILE: INDIVIDUAL LOG-LINEAR MODEL ESTIMATES

ANALYSIS SET: PD

COHORT = COHORT 1
SUBJECT = XXX

	ESTIMATE	S.E.	95% C.I.	P-VALUE
MODEL ESTIMATES:				
INTERCEPT	XX.X	XX.X	XX.X; XX.X	
TIME	XX.X	XX.X	XX.X; XX.X	X.XX <a>
DERIVED PARAMETERS:				
LOG10PRR48	XX.X		XX.X; XX.X	
PC50	XX.X		XX.X; XX.X	
PC99	XX.X		XX.X; XX.X	
TYPE 3 TESTS OF FIXED EFFECTS:				
TIME				X.XX <b>

<a> P-VALUE BASED ON T-TEST.
<b> P-VALUE BASED ON F-TEST.
LOG10PRR48 = LOG10 PARASITE REDUCTION RATIO PER 48h; PC50 = PARASITE CLEARANCE HALF-LIFE (HOURS); PC99 = TIME TO REACH PARASITE CLEARANCE OF 99% (HOURS).
ESTIMATES RESULTING FROM THE OPTIMAL LOG-LINEAR REGRESSION MODEL WITH TIME AS INDEPENDENT VARIABLE.

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TABLE 14.2.3.14.1: BLOOD-STAGE PARASITE CLEARANCE PROFILE: DESCRIPTIVE STATISTICS

ANALYSIS SET: PD

TIME TO PARASITE CLEARANCE (DAYS)

	n	Geom. Mean	95% C.I. <a>	Geom. S.D.	Min; Max
COHORT 1 (N=XX)	XX	XX.XXX	XX.XXX; XX.XXX	XX.XXX	XX;XX
COHORT 2 (N=XX)	XX	XX.XXX	XX.XXX; XX.XXX	XX.XXX	XX;XX
ALL SUBJECTS (N=XX)	XX	XX.XXX	XX.XXX; XX.XXX	XX.XXX	XX;XX

<a> TWO-SIDED 95% CONFIDENCE INTERVAL ON THE GEOMETRIC MEAN.

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TABLE 14.2.3.14.1: BLOOD-STAGE PARASITE CLEARANCE PROFILE: DESCRIPTIVE STATISTICS

ANALYSIS SET: PD

LOG10 PARASITE REDUCTION RATIO PER 48h (LOG10PRR48)

	n	Mean	95% C.I.	Min; Max
COHORT 1 (N=XX)	XX	XX.XXX	XX.XXX; XX.XXX	XX;XX
COHORT 2 (N=XX)	XX	XX.XXX	XX.XXX; XX.XXX	XX;XX
ALL SUBJECTS (N=XX)	XX	XX.XXX	XX.XXX; XX.XXX	XX;XX

SUMMARY STATISTICS ESTIMATED BY USING THE INVERSE-VARIANCE METHOD TO CALCULATE THE WEIGHTED AVERAGE LINEAR REGRESSION SLOPE AND CORRESPONDING STANDARD ERROR.
ONLY SUBJECTS WHOSE OPTIMAL LOG-LINEAR REGRESSION MODEL OVERALL P-VALUE < 0.001 ARE INCLUDED.

Programmer notes:

- *Show the table for all parameters starting in a new page in the following order: time to parasite clearance, $log_{10}PRR_{48}$, PC50, PC99.*

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TABLE 14.2.3.15.1: DESCRIPTIVE STATISTICS OF LOG10(PARASITAEMIA) ACTUAL VALUES

ANALYSIS SET: PD

ANALYSIS PHASE ANALYSIS VISIT	COHORT 1 (N=XX)	COHORT 2 (N=XX)	ALL SUBJECTS (N=XX)
SCREENING			
DAY 1, PREDOSE			
n	XX	XX	XX
Mean (S.D)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)
Median	XX.X	XX.X	XX.X
Min; Max	(XX; XX)	(XX; XX)	(XX; XX)
95% C.I. <a>	(XX; XX)	(XX; XX)	(XX; XX)
CHALLENGE			
DAY 7			
n	XX	XX	XX
Mean (S.D)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)
Median	XX.X	XX.X	XX.X
Min; Max	(XX; XX)	(XX; XX)	(XX; XX)
95% C.I. <a>	(XX; XX)	(XX; XX)	(XX; XX)
DAY 8			
n	XX	XX	XX
Mean (S.D)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)
Median	XX.X	XX.X	XX.X
Min; Max	(XX; XX)	(XX; XX)	(XX; XX)
95% C.I. <a>	(XX; XX)	(XX; XX)	(XX; XX)
ETC.			
RESCUE			
RIAMET DAY 1, 2H			
n	XX	XX	XX
Mean (S.D)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)
Median	XX.X	XX.X	XX.X
Min; Max	(XX; XX)	(XX; XX)	(XX; XX)
95% C.I. <a>	(XX; XX)	(XX; XX)	(XX; XX)

<a> TWO-SIDED 95% CONFIDENCE INTERVAL ON THE ARITHMETIC MEAN.

3.3 SAFETY

3.3.1 Adverse events

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TABLE 14.3.1.1: ADVERSE EVENTS OVERVIEW

ANALYSIS SET: SAFETY

	COHORT 1 (N=XX)			COHORT 2 (N=XX)			ALL SUBJECTS (N=XX)		
TOTAL NUMBER OF SUBJECTS WITH:	n	%	m	n	%	m	n	%	m
AT LEAST ONE AE	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X	XX
AT LEAST ONE SERIOUS AE	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X	XX
AT LEAST ONE GRADE ≥ 3 AE	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X	XX
AT LEAST ONE FATAL AE	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X	XX
AT LEAST ONE AE RELATED TO PfSPZ INOCULUM	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X	XX
AT LEAST ONE AE RELATED TO ANTIMALARIAL TREATMENT	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X	XX
AT LEAST ONE AE RELATED TO RIAMET	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X	XX
AT LEAST ONE AE RELATED TO MALARONE	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X	XX
AT LEAST ONE SERIOUS AE RELATED TO PfSPZ INOCULUM	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X	XX
AT LEAST ONE AE FOR WHICH THE STUDY WAS DISCONTINUED	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X	XX
AT LEAST ONE AE FOR WHICH THE ANTIMALARIAL TREATMENT WAS DISCONTINUED	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X	XX
AT LEAST ONE AE FOR WHICH RIAMET WAS DISCONTINUED	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X	XX
AT LEAST ONE AE FOR WHICH MALARONE WAS DISCONTINUED	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X	XX
AT LEAST ONE AE OF SPECIAL INTEREST	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X	XX
AT LEAST ONE AE OF SPECIAL INTEREST RELATED TO PfSPZ INOCULUM	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X	XX
AT LEAST ONE AE OF SPECIAL INTEREST RELATED TO ANTIMALARIAL TREATMENT	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X	XX

n= NUMBER OF SUBJECTS WITH EVENT, m = NUMBER OF EVENTS, AE = ADVERSE EVENT.
THE DENOMINATOR FOR THE PERCENTAGE CALCULATIONS IS THE TOTAL NUMBER OF SUBJECTS PER COHORT IN THE SAFETY SET.
ONLY ADVERSE EVENTS THAT STARTED AFTER PfSPZ INOCULATION ARE SHOWN.
RELATED IS DEFINED AS RELATED/SUSPECTED TO CHALLENGE AGENT/ANTIMALARIAL TREATMENT ACCORDING TO THE INVESTIGATOR, OR A MISSING RELATEDNESS.

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TABLE 14.3.1.2: ADVERSE EVENTS BY MEDDRA SYSTEM ORGAN CLASS AND PREFERRED TERM

ANALYSIS SET: SAFETY

	COHORT 1 (N=XX)			COHORT 2 (N=XX)			ALL SUBJECTS (N=XX)		
SYSTEM ORGAN CLASS AND PREFERRED TERM	n	%	m	n	%	m	n	%	m
ANY AE	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X	XX
GASTROINTESTINAL DISORDERS	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X	XX
DIARRHOEA	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X	XX
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X	XX
FATIGUE	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X	XX
FEELING HOT	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X	XX
INJECTION SITE ERYTHEMA	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X	XX
INFECTIONS AND INFESTATIONS	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X	XX
RHINITIS	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X	XX
PNEUMONIA	XX	XX.X	XX	XX	XX.X	XX	XX	XX.X	XX

Etc.

n= NUMBER OF SUBJECTS WITH EVENT, m = NUMBER OF EVENTS, AE = ADVERSE EVENT.
THE DENOMINATOR FOR THE PERCENTAGE CALCULATIONS IS THE TOTAL NUMBER OF SUBJECTS PER COHORT IN THE SAFETY SET.
ONLY ADVERSE EVENTS THAT STARTED AFTER PfSPZ INOCULATION ARE SHOWN.

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TABLE 14.3.1.3: ADVERSE EVENTS BY MEDDRA PREFERRED TERM BY DESCENDING ORDER OF FREQUENCY

ANALYSIS SET: SAFETY

	COHORT 1 (N=XX)		COHORT 2 (N=XX)		ALL SUBJECTS (N=XX)	
PREFERRED TERM	n	%	n	%	n	%
DIARRHOEA	XX	XX.X	XX	XX.X	XX	XX.X
FATIGUE	XX	XX.X	XX	XX.X	XX	XX.X
FEELING HOT	XX	XX.X	XX	XX.X	XX	XX.X
INJECTION SITE ERYTHEMA	XX	XX.X	XX	XX.X	XX	XX.X
RHINITIS	XX	XX.X	XX	XX.X	XX	XX.X
PNEUMONIA	XX	XX.X	XX	XX.X	XX	XX.X

Etc.

n= NUMBER OF SUBJECTS WITH EVENT, AE = ADVERSE EVENT.
THE DENOMINATOR FOR THE PERCENTAGE CALCULATIONS IS THE TOTAL NUMBER OF SUBJECTS PER COHORT IN THE SAFETY SET.
ONLY ADVERSE EVENTS THAT STARTED AFTER PfSPZ INOCULATION ARE SHOWN.

Programmer note: the adverse events will be sorted by descending order of frequency in the all subjects group.

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TABLE 14.3.1.4: SERIOUS ADVERSE EVENTS BY MEDDRA SYSTEM ORGAN CLASS AND PREFERRED TERM

ANALYSIS SET: SAFETY

SYSTEM ORGAN CLASS AND PREFERRED TERM	COHORT 1 (N=XX) n	%	COHORT 2 (N=XX) n	%	ALL SUBJECTS (N=XX) n	%
ANY AE	XX	XX.X	XX	XX.X	XX	XX.X
GASTROINTESTINAL DISORDERS	XX	XX.X	XX	XX.X	XX	XX.X
DIARRHOEA	XX	XX.X	XX	XX.X	XX	XX.X
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	XX	XX.X	XX	XX.X	XX	XX.X
FATIGUE	XX	XX.X	XX	XX.X	XX	XX.X
FEELING HOT	XX	XX.X	XX	XX.X	XX	XX.X
INJECTION SITE ERYTHEMA	XX	XX.X	XX	XX.X	XX	XX.X
INFECTIONS AND INFESTATIONS	XX	XX.X	XX	XX.X	XX	XX.X
RHINITIS	XX	XX.X	XX	XX.X	XX	XX.X
PNEUMONIA	XX	XX.X	XX	XX.X	XX	XX.X

Etc.

n= NUMBER OF SUBJECTS WITH EVENT, AE = ADVERSE EVENT.
THE DENOMINATOR FOR THE PERCENTAGE CALCULATIONS IS THE TOTAL NUMBER OF SUBJECTS PER COHORT IN THE SAFETY SET.
ONLY ADVERSE EVENTS THAT STARTED AFTER PfSPZ INOCULATION ARE SHOWN.

Programmer note: repeat Table 14.2.1.4 for:

TABLE 14.3.1.5: GRADE 3 OR MORE ADVERSE EVENTS BY MEDDRA SYSTEM ORGAN CLASS AND PREFERRED TERM

TABLE 14.3.1.6: PfSPZ INOCULUM RELATED ADVERSE EVENTS BY MEDDRA SYSTEM ORGAN CLASS AND PREFERRED TERM

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TABLE 14.3.1.7: ANTIMALARIAL TREATMENT RELATED ADVERSE EVENTS BY MEDDRA SYSTEM ORGAN CLASS AND PREFERRED TERM

ANALYSIS SET: SAFETY

ANTIMALARIAL TREATMENT = RIAMET OR MALARONE

SYSTEM ORGAN CLASS AND PREFERRED TERM	COHORT 1 (N=XX) n	%	COHORT 2 (N=XX) n	%	ALL SUBJECTS (N=XX) n	%
ANY AE	XX	XX.X	XX	XX.X	XX	XX.X
GASTROINTESTINAL DISORDERS	XX	XX.X	XX	XX.X	XX	XX.X
DIARRHOEA	XX	XX.X	XX	XX.X	XX	XX.X
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	XX	XX.X	XX	XX.X	XX	XX.X
FATIGUE	XX	XX.X	XX	XX.X	XX	XX.X
FEELING HOT	XX	XX.X	XX	XX.X	XX	XX.X
INJECTION SITE ERYTHEMA	XX	XX.X	XX	XX.X	XX	XX.X
INFECTIONS AND INFESTATIONS	XX	XX.X	XX	XX.X	XX	XX.X
RHINITIS	XX	XX.X	XX	XX.X	XX	XX.X
PNEUMONIA	XX	XX.X	XX	XX.X	XX	XX.X

ANTIMALARIAL TREATMENT = RIAMET
Etc.

n= NUMBER OF SUBJECTS WITH EVENT, AE = ADVERSE EVENT.
THE DENOMINATOR FOR THE PERCENTAGE CALCULATIONS IS THE TOTAL NUMBER OF SUBJECTS PER COHORT IN THE SAFETY SET.
ONLY ADVERSE EVENTS THAT STARTED AFTER PfSPZ INOCULATION ARE SHOWN.

Programmer note: repeat Table 14.2.1.4 for:

TABLE 14.3.1.8: SERIOUS PfSPZ INOCULUM RELATED ADVERSE EVENTS BY MEDDRA SYSTEM ORGAN CLASS AND PREFERRED TERM

Programmer note: repeat Table 14.2.1.8 for:

TABLE 14.3.1.9: ADVERSE EVENTS FOR WHICH THE ANTIMALARIAL TREATMENT WAS DISCONTINUED BY MEDDRA SYSTEM ORGAN CLASS AND PREFERRED TERM

Programmer note: repeat Table 14.2.1.4 for:

TABLE 14.3.1.10: ADVERSE EVENTS OF SPECIAL INTEREST RELATED TO PfSPZ INOCULUM BY MEDDRA SYSTEM ORGAN CLASS AND PREFERRED TERM

Programmer note: repeat Table 14.2.1.8 for:

TABLE 14.3.1.11: ADVERSE EVENTS OF SPECIAL INTEREST RELATED TO ANTIMALARIAL TREATMENT BY MEDDRA SYSTEM ORGAN CLASS AND PREFERRED TERM

3.3.2 *Clinical laboratory evaluation*

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TABLE 14.3.2.1: DESCRIPTIVE STATISTICS OF LABORATORY TEST RESULTS

ANALYSIS SET: SAFETY

LABORATORY CATEGORY: LABORATORY PARAMETER 1 (unit)

	ACTUAL VALUES			CHANGES FROM BASELINE		
	COHORT 1 (N=XX)	COHORT 2 (N=XX)	ALL SUBJECTS (N=XX)	COHORT 1 (N=XX)	COHORT 2 (N=XX)	ALL SUBJECTS (N=XX)
BASELINE						
n	XX	XX	XX			
Mean (S.D)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)			
Median	XX.X	XX.X	XX.X			
Min; Max	(XX; XX)	(XX; XX)	(XX; XX)			
DAY X						
n	XX	XX	XX	XX	XX	XX
Mean (S.D)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min; Max	(XX; XX)	(XX; XX)	(XX; XX)	(XX; XX)	(XX; XX)	(XX; XX)
DAY X						
n	XX	XX	XX	XX	XX	XX
Mean (S.D)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min; Max	(XX; XX)	(XX; XX)	(XX; XX)	(XX; XX)	(XX; XX)	(XX; XX)
DAY X						
n	XX	XX	XX	XX	XX	XX
Mean (S.D)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min; Max	(XX; XX)	(XX; XX)	(XX; XX)	(XX; XX)	(XX; XX)	(XX; XX)

Etc.

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TABLE 14.3.2.2: CROSS-TABULATION OF LABORATORY ABNORMALITIES VERSUS BASELINE

ANALYSIS SET: SAFETY

LABORATORY CATEGORY: LABORATORY PARAMETER 1 (unit)

COHORT/ ANALYSIS VISIT	ABNORMALITY	N	%	N'	%	ABNORMALITY AT BASELINE: LOW n	%	NORMAL n	%	HIGH n	%	MISSING n	%
COHORT 1 (N=XX)													
DAY 7	LOW	XX	XX.X	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	XX	XX.X
	TOTAL	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
WORST-CASE POST-BASELINE	LOW	XX	XX.X	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	XX	XX.X
	LOW + HIGH	XX	XX.X	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	XX.X	XX	XX.X
WORST-CASE CHALLENGE	LOW	XX	XX.X	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
	LOW + HIGH	XX	XX.X	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	XX.X	XX	XX.X
WORST-CASE RESCUE	LOW	XX	XX.X	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
	TOTAL	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
COHORT 2 (N=XX)													
DAY 7	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	XX	XX.X
	TOTAL	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X

Etc.

N = TOTAL NUMBER OF SUBJECTS PER ABNORMALITY WITHIN EACH COHORT AND ANALYSIS VISIT
N' = TOTAL NUMBER OF SUBJECTS WITH A POST-BASELINE EMERGENT ABNORMALITY WITHIN EACH COHORT AND ANALYSIS VISIT
THE WORST-CASE ANALYSIS VISIT CONSIDERS ALL POST-BASELINE ASSESSMENTS, INCLUDING UNSCHEDULED ASSESSMENTS, AND IS SHOWN OVERALL AND BY ANALYSIS PHASE.
THE DENOMINATOR FOR THE PERCENTAGE CALCULATIONS IS THE TOTAL NUMBER OF SUBJECTS PER COHORT AND PER ANALYSIS VISIT IN THE SAFETY SET, EXCLUDING SUBJECTS WITH MISSING VALUES PER COHORT AND PER ANALYSIS VISIT.

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TABLE 14.3.2.3: LIVER ENZYME ELEVATION CATEGORIES

ANALYSIS SET: SAFETY

CRITERION	COHORT 1 (N=XX) n	%	COHORT 2 (N=XX) n	%	ALL SUBJECTS (N=XX) n	%
ALT						
> 8XULN	XX	XX.X	XX	XX.X	XX	XX.X
> 5XULN	XX	XX.X	XX	XX.X	XX	XX.X
> 3XULN	XX	XX.X	XX	XX.X	XX	XX.X
AST						
> 8XULN	XX	XX.X	XX	XX.X	XX	XX.X
> 5XULN	XX	XX.X	XX	XX.X	XX	XX.X
> 3XULN	XX	XX.X	XX	XX.X	XX	XX.X
ALT OR AST						
> 8XULN	XX	XX.X	XX	XX.X	XX	XX.X
> 5XULN	XX	XX.X	XX	XX.X	XX	XX.X
> 3XULN	XX	XX.X	XX	XX.X	XX	XX.X
TOTAL BILIRUBIN > 2XULN	XX	XX.X	XX	XX.X	XX	XX.X
CONJUGATED BILIRUBIN FRACTION >35%	XX	XX.X	XX	XX.X	XX	XX.X
POTENTIAL HY'S LAW CASE	XX	XX.X	XX	XX.X	XX	XX.X

THE DENOMINATOR FOR THE PERCENTAGE CALCULATIONS IS THE TOTAL NUMBER OF SUBJECTS PER COHORT IN THE SAFETY SET, EXCLUDING SUBJECTS WITH MISSING VALUES.
FOR EACH OF THE CRITERIA, THE HIGHEST POST-BASELINE VALUE IS CONSIDERED.
POTENTIAL HY'S LAW CASE: ALT OR AST > 3XULN AND TOTAL BILIRUBIN > 2XULN AT THE SAME SAMPLE, TOGETHER WITH A CONJUGATED BILIRUBIN FRACTION >35%.

3.3.3 Vital signs

The analysis tables for vital signs parameters are largely identical to the laboratory tables.

TABLE 14.3.3.1: DESCRIPTIVE STATISTICS OF VITAL SIGNS

TABLE 14.3.3.2: CROSS-TABULATION OF VITAL SIGNS ABNORMALITIES VERSUS BASELINE

3.3.4 Electrocardiograms (ECG)

The analysis tables for ECG parameters are largely identical to the laboratory tables.

TABLE 14.3.4.1: DESCRIPTIVE STATISTICS OF ECG

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TABLE 14.3.4.2: CROSS-TABULATION OF ECG ABNORMALITIES VERSUS BASELINE

ANALYSIS SET: SAFETY

ECG PARAMETER 1 (unit)

						ABNORMALITY AT BASELINE							
						LOW		NORMAL		HIGH		MISSING	
COHORT / ANALYSIS VISIT	ABNORMALITY	N	%	N'	%	n	%	n	%	n	%	n	%
COHORT 1 (N=XX)													
RIAMET DAY 2	LOW	XX	XX.X	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	XX	XX.X
	TOTAL	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
RIAMET DAY 3	LOW	XX	XX.X	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	XX	XX.X
	TOTAL	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
WORST-CASE POST-BASELINE	LOW	XX	XX.X	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	XX	XX.X
	LOW + HIGH	XX	XX.X	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	XX.X	XX	XX.X
COHORT 2 (N=XX)													
RIAMET DAY 2	LOW	XX	XX.X	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	XX	XX.X
	TOTAL	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X

Etc.

N = TOTAL NUMBER OF SUBJECTS PER ABNORMALITY WITHIN EACH COHORT AND ANALYSIS VISIT
N' = TOTAL NUMBER OF SUBJECTS WITH A POST-BASELINE EMERGENT ABNORMALITY WITHIN EACH COHORT AND ANALYSIS VISIT
THE WORST-CASE ANALYSIS VISIT CONSIDERS ALL POST-BASELINE ASSESSMENTS, INCLUDING UNSCHEDULED ASSESSMENTS.
THE DENOMINATOR FOR THE PERCENTAGE CALCULATIONS IS THE TOTAL NUMBER OF SUBJECTS PER COHORT AND PER ANALYSIS VISIT IN THE SAFETY SET, EXCLUDING SUBJECTS WITH MISSING VALUES PER COHORT AND PER ANALYSIS VISIT.

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TABLE 14.3.4.3: TABULATION OF QTC CHANGE ABNORMALITIES

ANALYSIS SET: SAFETY

QTcB INTERVAL (ms)

	COHORT 1 (N=XX)				COHORT 2 (N=XX)				ALL SUBJECTS (N=XX)			
	n	%	cN'	%	n	%	cN'	%	n	%	cN'	%
RIAMET DAY 2												
> 60	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
]30,60]	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
<= 30 (NORMAL)	XX	XX.X			XX	XX.X			XX	XX.X		
TOTAL	XX	100			XX	100			XX	100		
RIAMET DAY 3												
> 60	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
]30,60]	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
<= 30 (NORMAL)	XX	XX.X			XX	XX.X			XX	XX.X		
TOTAL	XX	100			XX	100			XX	100		
WORST-CASE POST-BASELINE												
> 60	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
]30,60]	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X	XX	XX.X
<= 30 (NORMAL)	XX	XX.X			XX	XX.X			XX	XX.X		
TOTAL	XX	100			XX	100			XX	100		

cN' = CUMULATIVE NUMBER OF SUBJECTS WITH A QTC CHANGE ABNORMALITY WITHIN EACH COHORT AND ANALYSIS VISIT
THE WORST-CASE ANALYSIS VISIT CONSIDERS ALL POST-BASELINE ASSESSMENTS, INCLUDING UNSCHEDULED ASSESSMENTS.
THE DENOMINATOR FOR THE PERCENTAGE CALCULATIONS IS THE TOTAL NUMBER OF SUBJECTS PER COHORT AND PER ANALYSIS VISIT IN THE SAFETY SET, EXCLUDING SUBJECTS WITH MISSING VALUES PER COHORT AND PER ANALYSIS VISIT.

3.3.5 Malaria clinical score

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TABLE 14.3.5.1: DESCRIPTIVE STATISTICS OF MALARIA CLINICAL SCORE

ANALYSIS SET: SAFETY

	ACTUAL VALUES			CHANGES FROM BASELINE		
	COHORT 1 (N=XX)	COHORT 2 (N=XX)	ALL SUBJECTS (N=XX)	COHORT 1 (N=XX)	COHORT 2 (N=XX)	ALL SUBJECTS (N=XX)
BASELINE						
n	XX	XX	XX			
Mean (S.D)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)			
Median	XX.X	XX.X	XX.X			
Min; Max	(XX; XX)	(XX; XX)	(XX; XX)			
DAY 7						
n	XX	XX	XX	XX	XX	XX
Mean (S.D)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min; Max	(XX; XX)	(XX; XX)	(XX; XX)	(XX; XX)	(XX; XX)	(XX; XX)
DAY 8						
n	XX	XX	XX	XX	XX	XX
Mean (S.D)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min; Max	(XX; XX)	(XX; XX)	(XX; XX)	(XX; XX)	(XX; XX)	(XX; XX)
WORST-CASE POST-BASELINE						
n	XX	XX	XX	XX	XX	XX
Mean (S.D)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)	XX.X (X.X)
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Min; Max	(XX; XX)	(XX; XX)	(XX; XX)	(XX; XX)	(XX; XX)	(XX; XX)

Etc.

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TABLE 14.3.5.2: FREQUENCY TABLE OF THE WORST-CASE INDIVIDUAL MALARIA SIGNS AND SYMPTOMS

ANALYSIS SET: SAFETY

ANALYSIS PHASE = CHALLENGE + RESCUE

	COHORT 1 (N=XX)		COHORT 2 (N=XX)		ALL SUBJECTS (N=XX)	
MALARIA SIGN/SYMPTOM	n	%	n	%	n	%
ANY SYMPTOM						
0	XX	XX.X	XX	XX.X	XX	XX.X
1	XX	XX.X	XX	XX.X	XX	XX.X
2	XX	XX.X	XX	XX.X	XX	XX.X
3	XX	XX.X	XX	XX.X	XX	XX.X
TOTAL	XX	100	XX	100	XX	100
HEADACHE						
0	XX	XX.X	XX	XX.X	XX	XX.X
1	XX	XX.X	XX	XX.X	XX	XX.X
2	XX	XX.X	XX	XX.X	XX	XX.X
3	XX	XX.X	XX	XX.X	XX	XX.X
TOTAL	XX	100	XX	100	XX	100
MYALGIA						
0	XX	XX.X	XX	XX.X	XX	XX.X
1	XX	XX.X	XX	XX.X	XX	XX.X
2	XX	XX.X	XX	XX.X	XX	XX.X
3	XX	XX.X	XX	XX.X	XX	XX.X
TOTAL	XX	100	XX	100	XX	100
ARTHRALGIA						
0	XX	XX.X	XX	XX.X	XX	XX.X
1	XX	XX.X	XX	XX.X	XX	XX.X
2	XX	XX.X	XX	XX.X	XX	XX.X
3	XX	XX.X	XX	XX.X	XX	XX.X
TOTAL	XX	100	XX	100	XX	100

Etc.

ANALYSIS PHASE = CHALLENGE

Etc.

0=ABSENT; 1=MILD; 2=MODERATE; 3=SEVERE
THE DENOMINATOR FOR THE PERCENTAGE CALCULATIONS IS THE TOTAL NUMBER OF SUBJECTS PER COHORT IN THE SAFETY SET, EXCLUDING SUBJECTS WITH MISSING VALUES.
THE WORST-CASE IS THE HIGHEST POST-BASELINE SCORE WITHIN THE ANALYSIS PHASE AND IS DERIVED PER SIGN/SYMPTOM.
ANY SYMPTOM SHOWS THE WORST-CASE SEVERITY OF THE SIGN/SYMPTOM WITH THE HIGHEST SEVERITY.

Programmer notes:

- *All malaria signs and symptoms will be shown (headache, myalgia, arthralgia, fatigue/lethargy, malaise, chills/shivering/rigors, sweating/hot spells, anorexia, nausea, vomiting, abdominal discomfort, fever, tachycardia and hypotension)*

4. MOCK LISTINGS

4.1 GENERAL CHARACTERISTICS

4.1.1 Subject disposition

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LISTING 16.2.1.1: ALLOCATION

ANALYSIS SET: ALL SCREENED SUBJECTS

SUBJECT NUMBER	DATETIME OF SIGNING INFORMED CONSENT [1]	COHORT	SAF	PD	m-PD
XXXX	ddMMMyyyy:hh:mm	COHORT 1	YES	NO	NO
XXXX	ddMMMyyyy:hh:mm	COHORT 1	YES	YES	YES
XXXX	ddMMMyyyy:hh:mm	COHORT 2	YES	YES	YES
XXXX	ddMMMyyyy:hh:mm	COHORT 1	YES	YES	YES
XXXX	ddMMMyyyy:hh:mm	COHORT 2	YES	NO	NO
XXXX	ddMMMyyyy:hh:mm	COHORT 1	YES	YES	YES
XXXX	ddMMMyyyy:hh:mm	COHORT 1	YES	NO	NO
XXXX	ddMMMyyyy:hh:mm	COHORT 2	YES	YES	YES
XXXX	ddMMMyyyy:hh:mm	COHORT 2	YES	YES	NO
XXXX	ddMMMyyyy:hh:mm	COHORT 1	YES	YES	YES
XXXX	ddMMMyyyy:hh:mm	COHORT 2	NO	NO	NO
XXXX	ddMMMyyyy:hh:mm	COHORT 1	YES	YES	NO

ETC…

[1] DATETIME OF THE EARLIEST AVAILABLE INFORMED CONSENT FORM SIGNATURE.

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LISTING 16.2.1.2: ANALYSIS PHASES

ANALYSIS SET: SAFETY

COHORT	SUBJECT NUMBER	DATETIME OF INOCULATION	FIRST USE OF ANTIMALARIAL TREATMENT	LAST USE OF ANTIMALARIAL TREATMENT	DISCONTINUATION DATE	ANALYSIS PHASE	START	STOP	DURATION (DAYS)
COHORT 1	XXXXXX	ddMMMyyyy:hh:mm	ddMMMyyyy:hh:mm	ddMMMyyyy:hh:mm	ddMMMyyyy	SCREENING	ddMMMyyyy:hh:mm	ddMMMyyyy:hh:mm	XX
						CHALLENGE	ddMMMyyyy:hh:mm	ddMMMyyyy:hh:mm	XX
						RESCUE	ddMMMyyyy:hh:mm	ddMMMyyyy:hh:mm	XX
	XXXXXX	ddMMMyyyy:hh:mm	ddMMMyyyy:hh:mm	ddMMMyyyy:hh:mm	ddMMMyyyy	SCREENING	ddMMMyyyy:hh:mm	ddMMMyyyy:hh:mm	XX
						CHALLENGE	ddMMMyyyy:hh:mm	ddMMMyyyy:hh:mm	XX
						RESCUE	ddMMMyyyy:hh:mm	ddMMMyyyy:hh:mm	XX
	XXXXXX	ddMMMyyyy:hh:mm	ddMMMyyyy:hh:mm	ddMMMyyyy:hh:mm	ddMMMyyyy	SCREENING	ddMMMyyyy:hh:mm	ddMMMyyyy:hh:mm	XX
						CHALLENGE	ddMMMyyyy:hh:mm	ddMMMyyyy:hh:mm	XX
						RESCUE	ddMMMyyyy:hh:mm	ddMMMyyyy:hh:mm	XX
COHORT 2	XXXXXX	ddMMMyyyy:hh:mm	ddMMMyyyy:hh:mm	ddMMMyyyy:hh:mm	ddMMMyyyy	SCREENING	ddMMMyyyy:hh:mm	ddMMMyyyy:hh:mm	XX
						CHALLENGE	ddMMMyyyy:hh:mm	ddMMMyyyy:hh:mm	XX
						RESCUE	ddMMMyyyy:hh:mm	ddMMMyyyy:hh:mm	XX

ETC…

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LISTING 16.2.1.3: STUDY AND ANTIMALARIAL TREATMENT DISCONTINUATION

ANALYSIS SET: SAFETY

		DATE OF DISCONTINUATION			STUDY DISCONTINUATION		ANTIMALARIAL TREATMENT DISCONTINUATION	
COHORT	SUBJECT NUMBER	STUDY	ANTIMALARIAL TREATMENT	DAYS [1]	TYPE	REASON	TYPE	REASON
COHORT 1	XXXXXX	ddMMMyyyy	ddMMMyyyy	XX	COMPLETED		COMPLETED	
	XXXXXX	ddMMMyyyy	ddMMMyyyy	XX	COMPLETED		COMPLETED	
	XXXXXX	ddMMMyyyy	ddMMMyyyy	XX	DISCONTINUED	ADVERSE EVENT (SEQ XX): PREFERRED TERM	DISCONTINUED	ADVERSE EVENT (SEQ XX): PREFERRED TERM
COHORT 2	XXXXXX	ddMMMyyyy	ddMMMyyyy	XX	ONGOING		ONGOING	

ETC…

[1] NUMBER OF DAYS IN STUDY AT DATE OF DISCONTINUATION, CALCULATED WITH REFERENCE TO THE DATE OF INOCULATION.

4.1.2 Protocol deviations and eligibility

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LISTING 16.2.2.1: MAJOR PROTOCOL DEVIATIONS

ANALYSIS SET: SAFETY

COHORT	SUBJECT NUMBER	TYPE	DEVIATION CLASS	DEVIATION	DEVIATION (SPECIFICATION)
COHORT 1	XXXX	MAJOR	PROCEDURE DEVIATION	NO COMPLIANCE WITH ASSESSMENT WINDOW	PK URINE COLLECTION X-XH POSTDOSE, STARTED XH XXMIN. EARLIER
				NO COMPLIANCE WITH VISIT SCHEDULES	VISIT X DONE X DAY LATER
	XXXX	MAJOR	PROCEDURE DEVIATION	NO COMPLIANCE WITH ASSESSMENT WINDOW	ECG PXDX XX MIN.POSTDOSE, DONE XX MIN. EARLIER
					ECG PXDX XH. POSTDOSE, DONE X MIN. EARLIER
					PK URINE COLLECTION X-XH POSTDOSE, STARTED XXMIN. EARLIER
				NO COMPLIANCE WITH VISIT SCHEDULES	VISIT X DONE X DAY LATER
	XXXX	MAJOR	TREATMENT DEVIATION	NO COMPLIANCE WITH STUDY MED. INTAKE	MEDICATION XX MIN. INFUSION, DOSE NOT GIVEN COMPLETELY
		MAJOR	PROCEDURE DEVIATION	NO COMPLIANCE WITH ASSESSMENT WINDOW	PK BLOOD SAMPLING XH POSTDOSE, DONE X MIN. EARLIER
					ECG XXMIN. POSTDOSE, DONE XX MIN. EARLIER
					ECG XH. POSTDOSE, DONE XX MIN. EARLIER
				NO COMPLIANCE WITH VISIT SCHEDULES	VISIT X DONE X DAY LATER
	XXXX	MAJOR	SELECTION CRITERIA	SELECTION CRITERIA NOT MET	SELECTION CRITERIA ARE NOT MET (EX03, EX10)

ETC…

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LISTING 16.2.2.2: VIOLATIONS ON ELIGIBILITY CRITERIA

ANALYSIS SET: SAFETY

COHORT	SUBJECT NUMBER	TYPE	CRITERION	ANSWER
COHORT 1	XXXX	INCLUSION	9.BODY WEIGHT OF AT LEAST 50 KG AND A BODY MASS INDEX (BMI) OF 19.0 TO 30.0 KG/M2	NO
COHORT 2	XXXX	INCLUSION	9.BODY WEIGHT OF AT LEAST 50 KG AND A BODY MASS INDEX (BMI) OF 19.0 TO 30.0 KG/M2	NO
		EXCLUSION	17.PERSONAL HISTORY OF MALARIA	YES

NOTE: ONLY VIOLATIONS ARE SHOWN.

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LISTING 16.2.2.3: NO-INOCULATED SUBJECTS

ANALYSIS SET: ALL SCREENED SUBJECTS MINUS SAFETY

SUBJECT NUMBER	STUDY TERMINATION REASON
XXXX	OTHER: PERSONAL REASON
XXXX	SUBJECT DID NOT FULFILL ALL INCLUSION/EXCLUSION CRITERIA
XXXX	OTHER: PERSONAL REASON
XXXX	SUBJECT DID NOT FULFILL ALL INCLUSION/EXCLUSION CRITERIA
XXXX	SUBJECT DID NOT FULFILL ALL INCLUSION/EXCLUSION CRITERIA
XXXX	OTHER: BLOOD SAFETY RESULTS
XXXX	OTHER: BLOOD SAFETY RESULTS
XXXX	SUBJECT WITHDREW CONSENT

ETC…

4.1.3 Demographic and other baseline characteristics

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LISTING 16.2.4.1: DEMOGRAPHIC DATA

ANALYSIS SET: SAFETY

COHORT	SUBJECT NUMBER	PD	DATE OF SIGNING INFORMED CONSENT	AGE (years)	HEIGHT (cm)	WEIGHT (kg)	BMI (kg/m²)	SEX	COUNTRY	RACE	ETHNICITY
COHORT 1	XXX	YES	ddMMMyyyy	XX	XXX	XX.X	XX.X	MALE	BELGIUM	WHITE	HISPANIC OR LATINO
	XXX	YES	ddMMMyyyy	XX	XXX	XX.X	XX.X	MALE	BELGIUM	WHITE	NOT HISPANIC OR LATINO
	XXX	YES	ddMMMyyyy	XX	XXX	XX.X	XX.X	MALE	FRANCE	WHITE	HISPANIC OR LATINO
	XXX	YES	ddMMMyyyy	XX	XXX	XX.X	XX.X	MALE	BELGIUM	WHITE	HISPANIC OR LATINO
	XXX	NO	ddMMMyyyy	XX	XXX	XX.X	XX.X	MALE	BELGIUM	WHITE	HISPANIC OR LATINO
COHORT 2	XXX	YES	ddMMMyyyy	XX	XXX	XX.X	XX.X	MALE	FRANCE	WHITE	NOT HISPANIC OR LATINO
	XXX	YES	ddMMMyyyy	XX	XXX	XX.X	XX.X	FEMALE	FRANCE	WHITE	HISPANIC OR LATINO
	XXX	YES	ddMMMyyyy	XX	XXX	XX.X	XX.X	MALE	FRANCE	WHITE	NOT HISPANIC OR LATINO

ETC…

SCREENING HEIGHT, WEIGHT AND BMI ARE LISTED.

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LISTING 16.2.4.2: SMOKING HISTORY

ANALYSIS SET: SAFETY

			SMOKING HABITS			
COHORT	SUBJECT NUMBER	STATUS	QUANTITY	FREQUENCY	START DATE	STOP DATE
COHORT 1	XXX	SMOKER	4 CIGARETTE	QD	ddMMMyyyy	
	XXX	EX-SMOKER	1 CIGARETTE	QD	ddMMMyyyy	ddMMMyyyy
	XXX	NON-SMOKER				
COHORT 2	XXX	SMOKER	3 CIGARETTE	QD	ddMMMyyyy	
	XXX	SMOKER	2 CIGARETTE	QD	ddMMMyyyy	
	XXX	EX-SMOKER	7 CIGARETTE	QD	ddMMMyyyy	ddMMMyyyy
ETC…						

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LISTING 16.2.4.3: ORTHOSTATIC CHANGE IN VITAL SIGNS AT SCREENING

ANALYSIS SET: SAFETY

				HEART RATE (beats/min)			SYSTOLIC BLOOD PRESSURE (mmHg)			DIASTOLIC BLOOD PRESSURE (mmHg)		
COHORT	SUBJECT NUMBER	ASSESSMENT DATE	USE [1]	SUPINE	STANDING	CHANGE	SUPINE	STANDING	CHANGE	SUPINE	STANDING	CHANGE
COHORT 1	XXX	ddMMMyyyy		XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX
	XXX	ddMMMyyyy		XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX
COHORT 2	XXX	ddMMMyyyy		XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX
	XXX	ddMMMyyyy		XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX
	XXX	ddMMMyyyy		XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX
	XXX	ddMMMyyyy		XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX
		ddMMMyyyy	NO	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX

ETC…

[1] NO = SAMPLE NOT USED IN ANALYSIS TABLES AND FIGURES.
ORTHOSTATIC CHANGE = VALUE IN SUPINE POSITION - VALUE IN STANDING POSITION.

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LISTING 16.2.4.4: BECK DEPRESSION INVENTORY AT SCREENING

ANALYSIS SET: SAFETY

COHORT	SUBJECT NUMBER	ASSESSMENT DATETIME	SUICIDAL THOUGHTS? (Q9)	TOTAL SCORE	INTERPRETATION
COHORT 1	XXX	ddMMMyyyy:hh:mm	XXX	XXX	NORMAL
	XXX	ddMMMyyyy:hh:mm	XXX	XXX	MILD MOOD DISTURBANCE
COHORT 2	XXX	ddMMMyyyy:hh:mm	XXX	XXX	NORMAL
	XXX	ddMMMyyyy:hh:mm	XXX	XXX	BORDERLINE CLINICAL DEPRESSION
	XXX	ddMMMyyyy:hh:mm	XXX	XXX	NORMAL
	XXX	ddMMMyyyy:hh:mm	XXX	XXX	NORMAL

ETC…

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LISTING 16.2.4.5: SCREENING LABORATORY TESTS

ANALYSIS SET: SAFETY

A) URINE DRUG SCREEN AND ETHANOL

			DRUG SCREENING		ETHANOL	
COHORT	SUBJECT NUMBER	ANALYSIS VISIT	ASSESSMENT DATETIME	RESULT	ASSESSMENT DATETIME	RESULT
COHORT 1	XXX	SCREENING	ddMMMyyyy:hh:mm	NEGATIVE	ddMMMyyyy:hh:mm	NEGATIVE
		DAY -1	ddMMMyyyy:hh:mm	NEGATIVE	ddMMMyyyy:hh:mm	NEGATIVE
	XXX	SCREENING	ddMMMyyyy:hh:mm	NEGATIVE	ddMMMyyyy:hh:mm	NEGATIVE
		DAY -1	ddMMMyyyy:hh:mm	NEGATIVE	ddMMMyyyy:hh:mm	NEGATIVE
	XXX	SCREENING	ddMMMyyyy:hh:mm	NEGATIVE	ddMMMyyyy:hh:mm	NEGATIVE
	XXX	SCREENING	ddMMMyyyy:hh:mm	NEGATIVE	ddMMMyyyy:hh:mm	NEGATIVE
COHORT 2	XXX	SCREENING	ddMMMyyyy:hh:mm	NEGATIVE	ddMMMyyyy:hh:mm	NEGATIVE
		DAY -1	ddMMMyyyy:hh:mm	NEGATIVE	ddMMMyyyy:hh:mm	NEGATIVE

ETC…

B) VIRAL SEROLOGY AT SCREENING

COHORT	SUBJECT NUMBER	ASSESSMENT DATETIME	HEPATITIS A VIRUS ANTIBODY	HEPATITIS B SURFACE ANTIGEN	HEPATITIS C VIRUS ANTIBODY	HEPATITIS E VIRUS ANTIBODY	CYTOMEGALOVIRUS ANTIBODY	EPSTEIN BARR VIRUS ANTIBODY	HIV SEROLOGY
COHORT 1	XXX	ddMMMyyyy:hh:mm	POSITIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE
	XXX	ddMMMyyyy:hh:mm	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE
	XXX	ddMMMyyyy:hh:mm	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE
	XXX	ddMMMyyyy:hh:mm	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE
	XXX	ddMMMyyyy:hh:mm	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE
	XXX	ddMMMyyyy:hh:mm	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE
COHORT 2	XXX	ddMMMyyyy:hh:mm	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE
	XXX	ddMMMyyyy:hh:mm	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE

ETC…

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LISTING 16.2.4.6: PREGNANCY TESTS

ANALYSIS SET: SAFETY

COHORT	SUBJECT NUMBER	ANALYSIS VISIT	ASSESSMENT DATETIME	SPECIMEN TYPE	HCG RESULT
COHORT 1	XXX	SCREENING	ddMMMyyyy:hh:mm	SERUM	XX
		DAY -1	ddMMMyyyy:hh:mm	URINE	NEGATIVE
		END OF STUDY	ddMMMyyyy:hh:mm	SERUM	XX
	XXX	SCREENING	ddMMMyyyy:hh:mm	SERUM	XX
		DAY -1	ddMMMyyyy:hh:mm	URINE	NEGATIVE

ETC…

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LISTING 16.2.4.7: rRT-PCR TESTS FOR SARS-CoV-2 INFECTION

ANALYSIS SET: SAFETY

COHORT	SUBJECT NUMBER	ANALYSIS VISIT	ASSESSMENT DATETIME	RESULT
COHORT 1	XXX	SCREENING	ddMMMyyyy:hh:mm	NEGATIVE
		DAY 9	ddMMMyyyy:hh:mm	NEGATIVE
	XXX	SCREENING	ddMMMyyyy:hh:mm	NEGATIVE
		DAY 9	ddMMMyyyy:hh:mm	NEGATIVE

ETC…

4.1.4 Medical history and concomitant diseases

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LISTING 16.2.4.8: MEDICAL HISTORY

ANALYSIS SET: SAFETY

COHORT	SUBJECT NUMBER	SYSTEM ORGAN CLASS	PREFERRED TERM	VERBATIM	START DATE	END DATE	COMMENTS
COHORT 1	XXX	GASTROONTESTINAL DISORDERS	DIARRHOEA	DIARRHOEA	ddMMMyyyy	ddMMMyyyy	
			ABDOMINAL HERNIA	ABDOMINAL HERNIA	ddMMMyyyy	ddMMMyyyy	XXXXXXXXXXXXXXXXX
		INFECTIONS AND INFESTATIONS	ABSCESS	ABSCESES	ddMMMyyyy	ddMMMyyyy	
	XXX	PSYCHIATRIC DISORDERS	DEPRESSION	DEPRESSION	ddMMMyyyy	ddMMMyyyy	
	XXX	PSYCHIATRIC DISORDERS	INSOMNIA	INSOMNIA	ddMMMyyyy	ddMMMyyyy	

ETC…

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LISTING 16.2.4.9: CONCOMITANT DISEASES

ANALYSIS SET: SAFETY

COHORT	SUBJECT NUMBER	SYSTEM ORGAN CLASS	PREFERRED TERM	VERBATIM	START DATE	COMMENTS
COHORT 1	XXX	GASTROINTESTINAL DISORDERS	DIARRHOEA	DIARRHOEA	ddMMMyyyy	
			ABDOMINAL HERNIA	ABDOMINAL HERNIA	ddMMMyyyy	
		INFECTIONS AND INFESTATIONS	ABSCESS	ABSCESES	ddMMMyyyy	
	XXX	PSYCHIATRIC DISORDERS	DEPRESSION	DEPRESSION	ddMMMyyyy	XXXXXXXXXXXXXXXXXXXXXX
	XXX	PSYCHIATRIC DISORDERS	INSOMNIA	INSOMNIA	ddMMMyyyy	

ETC…

4.1.5 Prior and concomitant therapies

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LISTING 16.2.4.10: PRIOR AND CONCOMITANT THERAPIES

ANALYSIS SET: SAFETY

COHORT 1

SUBJECT NUMBER	ANALYSIS PHASE	ATC CLASS (LEVEL 4) GENERIC TERM	--------THERAPY----- START DATE	END DATE	DOSE, FREQ, ROUTE	INDICATION	COMMENTS
XXXX	SCREENING	DIHYDROPYRIDINE DERIVATIVES AMLODIPINE	ddMMMyyyy	ddMMMyyyy	10 mg QD PO	HIGH BLOOD PRESSURE (MEDICAL HISTORY)	
	CHALLENGE	PROGESTOGENS MEDROXYPROGESTERONE ACETATE	ddMMMyyyy	ddMMMyyyy	150 mg 1X IM	CONTRACEPTIVE	
	RESCUE	PROGESTOGENS MEDROXYPROGESTERONE ACETATE	ddMMMyyyy	ONGOING	150 mg 1X IM	CONTRACEPTIVE	
XXXX	SCREENING	PROGESTOGENS MEDROXYPROGESTERONE ACETATE	ddMMMyyyy	ddMMMyyyy	150 mg 1X IM	CONTRACEPTIVE	
	CHALLENGE	ANILIDES PARACETAMOL	ddMMMyyyy	ddMMMyyyy	1000 mg T.I.D. PO	AE (SEQ X): PREFERRED TERM	
	RESCUE	PENICILLINS WITH EXTENDED SPECTRUM AMOXICILLIN	ddMMMyyyy	ddMMMyyyy	250 mg T.I.D. PO	AE (SEQ X): PREFERRED TERM	
		AMASE INHIBITORS AUGMENTIN /00756801/	ddMMMyyyy	ddMMMyyyy	375 mg T.I.D. PO	AE (SEQ X): PREFERRED TERM	
ETC…							

COHORT 2

ETC…

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LISTING 16.2.4.11: ANTIMALARIAL TREATMENT

ANALYSIS SET: SAFETY

COHORT	SUBJECT NUMBER	DAY IN STUDY[1]	GENERIC TERM	DOSING DATETIME	NUMBER OF TABLETS	DOSE/TABLET
COHORT 1	XXXX	12	RIAMET	ddMMMyyyy:hh:mm	XX	20/120 MG/TABLET
		13	RIAMET	ddMMMyyyy:hh:mm	XX	20/120 MG/TABLET
		14	RIAMET	ddMMMyyyy:hh:mm	XX	20/120 MG/TABLET
	XXXX	13	RIAMET	ddMMMyyyy:hh:mm	XX	20/120 MG/TABLET
		14	RIAMET	ddMMMyyyy:hh:mm	XX	20/120 MG/TABLET
		15	RIAMET	ddMMMyyyy:hh:mm	XX	20/120 MG/TABLET
	XXXX	18	RIAMET	ddMMMyyyy:hh:mm	XX	20/120 MG/TABLET
		18	MALARONE	ddMMMyyyy:hh:mm	XX	250/100 MG/TABLET

ETC…

[1] NUMBER OF DAYS IN STUDY AT DATE OF ANTIMALARIAL TREATMENT, CALCULATED WITH REFERENCE TO THE DATE OF INOCULATION.

4.1.6 Comments

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LISTING 16.2.4.12: COMMENTS

ANALYSIS SET: SAFETY

COHORT	SUBJECT NUMBER	REFERENCE	COMMENT
COHORT 1	XXXX	LBSEQ: XX	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
		VSSEQ: XX	XXXXXXXXXXXXXXXXXXXXXXXXXXXX
	XXXX	EGSEQ: XX	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
		LBSEQ: XX	XXXXXXXXXXXXXXXXXXXXXXXXXXXX
COHORT 2	XXXX	EGSEQ: XX	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
		PESEQ: XX	XXXXXXXXXXXXXXXXXXXXXXXXXXXX

ETC…

4.1.7 Exposure to challenge agent

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LISTING 16.2.5.1: EXPOSURE TO CHALLENGE AGENT

ANALYSIS SET: SAFETY

COHORT	SUBJECT NUMBER	PfSPZ CHALLENGE DATETIME	DOSE	ADMINISTRATION ROUTE	FORMULATION
COHORT 1	XXXX	ddMMMyyyy:hh:mm	X.XXX	XXXXXXXX	XXXXXXXXX
	XXXX	ddMMMyyyy:hh:mm	X.XXX	XXXXXXXX	XXXXXXXXX
	XXXX	ddMMMyyyy:hh:mm	X.XXX	XXXXXXXX	XXXXXXXXX
	XXXX	ddMMMyyyy:hh:mm	X.XXX	XXXXXXXX	XXXXXXXXX
	XXXX	ddMMMyyyy:hh:mm	X.XXX	XXXXXXXX	XXXXXXXXX

ETC…

4.2 PHARMACODYNAMICS

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LISTING 16.2.6.1: PARASITAEMIA

ANALYSIS SET: PD

COHORT 1

SUBJECT NUMBER	m-PD	FIRST ANTIMALARIAL TREATMENT DATETIME	ANALYSIS VISIT	DAY [1]	SAMPLE DATETIME	USE [2]	qPCR RESULT (p/mL) [3]
XXXX	YES	ddMMMyyyy:hh:mm	BASELINE	1	ddMMMyyyy:hh:mm		XX
			DAY 7	7	ddMMMyyyy:hh:mm		XX
			DAY 8	8	ddMMMyyyy:hh:mm		XX
			DAY 9	9	ddMMMyyyy:hh:mm		XX
			DAY 10	10	ddMMMyyyy:hh:mm		XX
			DAY 11	11	ddMMMyyyy:hh:mm		XX
			DAY 12	12	ddMMMyyyy:hh:mm		XX $
			DAY 13	13	ddMMMyyyy:hh:mm		XX $
			DAY 14 *	14	ddMMMyyyy:hh:mm		XX $
			UNSCHEDULED *	15	ddMMMyyyy:hh:mm	NO	XX
			UNSCHEDULED *	16	ddMMMyyyy:hh:mm	NO	XX
			DAY 21	21	ddMMMyyyy:hh:mm		XX

ETC…

[1] DAY VS. INOCULATION, DAYS ON WHICH ANTIMALARIAL TREATMENT IS TAKEN ARE FLAGGED (*).
[2] NO = NOT USED IN ANALYSIS TABLES AND FIGURES.
[3] POSITIVE qPCR RESULTS (≥250 PARASITES PER ML BLOOD) ARE FLAGGED ($).

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LISTING 16.2.6.2: PARASITAEMIA ENDPOINTS

ANALYSIS SET: PD

COHORT 1

SUBJECT NUMBER	m-PD	TIME TO POSITIVE PARASITAEMIA (DAYS)	PARASITAEMIA AT FIRST POSITIVE PCR (PARASITES/mL)	TIME TO ≥5000 PARASITES (DAYS)[1]	PARASITAEMIA AT ≥5000 PARASITES (PARASITES/mL)	TIME TO FIRST DOSE OF RIAMET (DAYS)	PARASITAEMIA AT FIRST DOSE OF RIAMET (PARASITES/mL)	TIME TO PARASITE CLEARENCE (DAYS)
XXXX	YES	XX	XXXX	XX°	-	XX	XXXX	XX
XXXX	YES	XX	XXXX	XX	XXXX	XX	XXXX	XX
XXXX	NO	XX	XXXX	XX	XXXX	XX	XXXX	XX
XXXX	YES	XX	XXXX	XX	XXXX	XX	XXXX	XX

ETC…

[1] ABSENCE OF EVENT IS FLAGGED (°).
POSITIVE PARASITAEMIA IS DEFINED AS qPCR OUTCOME ≥250 PARASITES PER mL BLOOD.
PARASITE CLEARANCE IS DEFINED AS qPCR OUTCOME BELOW THE LIMIT OF QUANTIFICATION (<50 PARASITES PER mL BLOOD).

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LISTING 16.2.6.3: BLOOD-STAGE PARASITE CLEARANCE PROFILE: ITERATION PROCESS TO DETERMINE THE OPTIMAL LOG-LINEAR MODEL

ANALYSIS SET: PD

COHORT 1

SUBJECT NUMBER	USE m-PD	[1]	ITERATION	TIME ESTIMATE (95% CI)	LOG10PRR48 (95% CI)	P-VALUE [2]	OPTIMAL FLAG [3]
XXXX	YES	YES	1	XX (XX;XX)	XX (XX;XX)	XXX	
			2	XX (XX;XX)	XX (XX;XX)	XXX	
			3	XX (XX;XX)	XX (XX;XX)	XXX	YES
			4	XX (XX;XX)	XX (XX;XX)	XXX	
XXXX	YES	YES	1	XX (XX;XX)	XX (XX;XX)	XXX	
			2	XX (XX;XX)	XX (XX;XX)	XXX	
			3	XX (XX;XX)	XX (XX;XX)	XXX	
			4	XX (XX;XX)	XX (XX;XX)	XXX	
			5	XX (XX;XX)	XX (XX;XX)	XXX	YES
			6	XX (XX;XX)	XX (XX;XX)	XXX	

ETC…

[1] YES = SUBJECT INCLUDED IN THE DESCRIPTIVE STATISTICS OF DERIVED PARAMETERS OF THE LOG-LINEAR MODEL FOR PARASITE CLEARANCE. A SUBJECT IS INCLUDED WHEN THE OPTIMAL LOG-LINEAR REGRESSION MODEL P-VALUE < 0.001.
[2] OVERALL MODEL P-VALUE BASED ON F-TEST.
[3] OPTIMAL MODEL IS DEFINED BY THE MINIMUM OVERALL MODEL P-VALUE.

4.3 SAFETY

4.3.1 Adverse events

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LISTING 16.2.7.1: ADVERSE EVENTS

ANALYSIS SET: SAFETY

COHORT 1

SUBJECT NUMBER	ANALYSIS PHASE	PREFERRED TERM (VERBATIM) [1]	ADVERSE EVENT START DATETIME	ADVERSE EVENT STOP DATETIME	OUT [2]	TOX [3]	SI [4]	REL [5]	REL [6]	REL [7]	ACT [8]	ACT [9]	ACT [10]	RX [11]	ONSET [12]	ONSET [13]	DUR [14]
XXXX	SCREENING	NONE															
	CHALLENGE	PAIN NOS (XXXXXXXXX)	ddMMMyyyy:hh:mm	ddMMMyyyy:hh:mm	REC	GR1	NO	NO	NO	NO	NO	NO	NO	NO	XXX	XXX	XXX
		PULMONARY EMBOLISM (XXXXXXXXX) *	ddMMMyyyy:hh:mm	ONGOING	REC	GR1	NO	NO	NO	NO	NO	NO	NO	YES	XXX	XXX	>XXX
		TINEA PEDIS (XXXXXXXXX)	ddMMMyyyy:hh:mm	ddMMMyyyy:hh:mm	REC	GR2	YES	NO	NO	NO	NO	NO	NO	NO	XXX	XXX	XXX
		VEIN WALL HYPERTROPHY (XXXXXXXXX)	ddMMMyyyy:hh:mm	ddMMMyyyy:hh:mm	REC	GR1	NO	NO	NO	NO	NO	NO	NO	NO	XXX	XXX	XXX
XXXX	SCREENING	NONE															
	CHALLENGE	NONE															
	RESCUE	DIARRHOEA NOS (XXXXXXXXX)	ddMMMyyyy:hh:mm	MMMyyyy	REC	GR3	YES	YES	YES	YES	NO	NO	NO	NO	XXX	XXX	XXX
		DIZZINESS (XXXXXXXXX)	ddMMMyyyy:hh:mm	ddMMMyyyy:hh:mm	REC	GR1	NO	YES	YES	YES	NO	NO	NO	NO	XXX	XXX	XXX
		PAIN IN FOOT (XXXXXXXXX) !	UNKNOWN	ddMMMyyyy:hh:mm	REC	GR1	NO	NO	NO	NO	NO	NO	NO	YES			
		VOMITING NOS (XXXXXXXXX)	ddMMMyyyy:hh:mm	ddMMMyyyy:hh:mm	REC	GR1	NO	NO	NO	NO	PER	PER	PER	YES	XXX	XXX	XXX

ETC…

[1] SAES ARE FLAGGED WITH *. AES FOR WHICH ANOTHER ACTION IS TAKEN ARE FLAGGED WITH (!).
[2] OUTCOME: REC = RECOVERED/RESOLVED; RECI = RECOVERING/RESOLVING; NREC = NOT RECOVERED/NOT RESOLVED; RECS = RECOVERED WITH SEQUELAE; FAT = FATAL; UNK = UNKNOWN.
[3] AE TOXICITY: GR1 = GRADE 1-MILD; GR2 = GRADE 2-MODERATE; GR3 = GRADE 3-SEVERE; GR4 = GRADE 4-LIFE-THREATENING; GR5 = GRADE 5-DEATH.
[4] SI: ADVERSE EVENT OF SPECIAL INTEREST.
[5,6,7] RELATIONSHIP TO PfSPZ INOCULUM, RIAMET, MALARONE: NO=NOT RELATED/NOT SUSPECTED; YES=RELATED/SUSPECTED; NAP=NOT APPLICABLE.
[8,9,10] ACTION TAKEN TOWARDS PfSPZ INOCULUM, RIAMET, MALARONE: PER=PERMANENTLY DISCONTINUED; NO=NO ACTION TAKEN; UNK=UNKNOWN; NAP=NOT APPLICABLE.
[11] RX: CONCOMITANT THERAPY STARTED BECAUSE OF THE AE.
[12] ONSET: DAY OF ONSET VERSUS FIRST PfSPZ INOCULATION, OR TIME OF ONSET IF ON DAY 1.
[13] ONSET: DAY OF ONSET VERSUS START OF THE ANALYSIS PHASE, OR TIME OF ONSET IF ON DAY OF START OF THE ANALYSIS PHASE.
[14] DURATION: DURATION (DAYS) OF THE INDIVIDUAL EVENT.

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LISTING 16.2.7.2: SERIOUS ADVERSE EVENTS

ANALYSIS SET: SAFETY

COHORT 1

SUBJECT NUMBER	ANALYSIS PHASE	PREFERRED TERM (VERBATIM)	ADVERSE EVENT START DATETIME	ADVERSE EVENT STOP DATETIME	SAE REASON [1]	OUT [2]	TOX [3]	SI [4]	REL [5]	REL [6]	REL [7]	ACT [8]	ACT [9]	ACT [10]	RX [11]	ONSET [12]	ONSET [13]	DUR [14]
XXXX	CHALLENGE	PAIN NOS (XXXXXXXXX)	ddMMMyyyy:hh:mm	ddMMMyyyy:hh:mm	OMI	REC	GR1	NO	NO	NO	NO	NO	NO	NO	NO	XXX	XXX	XXX
		PULMONARY EMBOLISM (XXXXX)	ddMMMyyyy:hh:mm	ONGOING	HOS	REC	GR1	NO	NO	NO	NO	NO	NO	NO	YES	XXX	XXX	>XXX
		VEIN WALL HYPERTROPHY (XX)	ddMMMyyyy:hh:mm	ddMMMyyyy:hh:mm	OMI	REC	GR2	YES	NO	NO	NO	NO	NO	NO	NO	XXX	XXX	XXX
XXXX	RESCUE	VOMITING NOS (XXXXXXXXX)	ddMMMyyyy:hh:mm	ddMMMyyyy:hh:mm	OMI	REC	GR1	NO	YES	YES	YES	NO	NO	NO	NO	XXX	XXX	XXX

ETC…

[1] DTH = RESULTS IN DEATH; LIF = LIFE-THREATENING; HOS = REQUIRES OR PROLONGS HOSPITALISATION; DIS = RESULTS IN DISABILITY; CON = CONGENITAL ANOMALY; OMI = OTHER MEDICAL IMPORTANT AE.
[2] OUTCOME: REC = RECOVERED/RESOLVED; RECI = RECOVERING/RESOLVING; NREC = NOT RECOVERED/NOT RESOLVED; RECS = RECOVERED WITH SEQUELAE; FAT = FATAL; UNK = UNKNOWN.
[3] AE TOXICITY: GR1 = GRADE 1-MILD; GR2 = GRADE 2-MODERATE; GR3 = GRADE 3-SEVERE; GR4 = GRADE 4-LIFE-THREATENING; GR5 = GRADE 5-DEATH.
[4] SI: ADVERSE EVENT OF SPECIAL INTEREST.
[5,6,7] RELATIONSHIP TO PfSPZ INOCULUM, RIAMET, MALARONE: NO=NOT RELATED/NOT SUSPECTED; YES=RELATED/SUSPECTED; NAP=NOT APPLICABLE.
[8,9,10] ACTION TAKEN TOWARDS PfSPZ INOCULUM, RIAMET, MALARONE: PER=PERMANENTLY DISCONTINUED; NO=NO ACTION TAKEN; UNK=UNKNOWN; NAP=NOT APPLICABLE.
[11] RX: CONCOMITANT THERAPY STARTED BECAUSE OF THE AE.
[12] ONSET: DAY OF ONSET VERSUS FIRST PfSPZ INOCULATION, OR TIME OF ONSET IF ON DAY 1.
[13] ONSET: DAY OF ONSET VERSUS START OF THE ANALYSIS PHASE, OR TIME OF ONSET IF ON DAY OF START OF THE ANALYSIS PHASE.
[14] DURATION: DURATION (DAYS) OF THE INDIVIDUAL EVENT.

Programmer note: repeat listing 16.2.7.1 for:

LISTING 16.2.7.3: FATAL ADVERSE EVENTS

LISTING 16.2.7.4: ADVERSE EVENTS FOR WHICH THE STUDY WAS DISCONTINUED

LISTING 16.2.7.5: ADVERSE EVENTS FOR WHICH THE ANTIMALARIAL TREATMENT WAS DISCONTINUED

LISTING 16.2.7.6: ADVERSE EVENTS AFTER ADMINISTRATION OF ANTIMALARIAL TREATMENT

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LISTING 16.2.7.7: ADVERSE EVENTS FOR WHICH ANOTHER ACTION IS TAKEN

ANALYSIS SET: SAFETY

COHORT 1

SUBJECT NUMBER	ANALYSIS PHASE	PREFERRED TERM (VERBATIM)	OTHER ACTION TAKEN
XXXX	CHALLENGE	PAIN NOS (XXXXXXXXX)	XXXXXXXXXXXXXXXXXXXXXXXXXX
		PULMONARY EMBOLISM (XXXXXXXXX)	XXXXXXXXXXXXXXXXXXXXXXXXXX
XXXX	RESCUE	DIARRHOEA NOS (XXXXXXXXX)	XXXXXXXXXXXXXXXXXXXXXXXXXX
		DIZZINESS (XXXXXXXXX)	XXXXXXXXXXXXXXXXXXXXXXXXXX
		VOMITING NOS (XXXXXXXXX)	XXXXXXXXXXXXXXXXXXXXXXXXXX

ETC…

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LISTING 16.2.7.8: ADVERSE EVENTS: CODING INFORMATION

ANALYSIS SET: SAFETY

COHORT 1

SYSTEM ORGAN CLASS	HIGH LEVEL GROUP TERM	HIGH LEVEL TERM	PREFERRED TERM	LOWER LEVEL TERM	VERBATIM	SUBJECT NUMBER
GASTROINTESTINAL DISORDERS	DENTAL AND GINGIVAL CONDITIONS	DENTAL AND PERIODONTAL INFECTIONS AND INFLAMMATIONS	DENTAL CARIES	CARIES DENTAL	CARIES DENTAL	XXX
		DENTAL DISORDERS NEC	TOOTH DISORDER	TOOTH DISORDER	TOOTH DISORDER	XXX
	GASTROINTESTINAL MOTILITY AND DEFAECATION CONDITIONS	DIARRHOEA (EXCL INFECTIVE)	DIARRHOEA	DIARRHOEA	DIARRHEA	XXX
				LOOSE STOOLS	LOOSE STOOLS	XXX
						XXX
						XXX
						XXX
INFECTIONS AND INFESTATIONS	INFESTATIONS - PATHOGEN UNSPECIFIED	UPPER RESPIRATORY TRACT INFECTIONS	NASOPHARYNGITIS	COMMON COLD	COMMON COLD	XXX
						XXX
						XXX
						XXX
	VIRAL INFECTIOUS DISORDERS	VIRAL INFECTIONS NEC	GASTROENTERITIS VIRAL	GASTROENTERITIS VIRAL	GASTROENTERITIS VIRAL	XXX
			VIRAL UPPER RESPIRATORY TRACT INFECTION	UPPER RESPIRATORY TRACT INFECTION VIRAL NOS	UPPER RESPIRATORY TRACT INFECTION VIRAL	XXX

ETC…

4.3.2 Physical examinations

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LISTING 16.2.7.9: PHYSICAL EXAMINATIONS ABNORMALITIES

ANALYSIS SET: SAFETY

COHORT	SUBJECT NUMBER	ANALYSIS VISIT	ASSESSMENT DATETIME	CRF BODY SYSTEM	DESCRIPTION (VERBATIM)	CLINICAL SIGNIFICANT
COHORT 1	XXXXXX	DAY -1	ddMMMyyyy:hh:mm	EARS, NOSE & THROAT	ANGINA (NOT TREATED)	NO
	XXXXXX	DAY -1	ddMMMyyyy:hh:mm	MUSCULOSKELETAL	BACK PAIN	NO
	XXXXXX	DAY 10	ddMMMyyyy:hh:mm	SKIN	SCARS (UPPER THORAX) CNS	NO
	XXXXXX	END OF STUDY	ddMMMyyyy:hh:mm	MUSCULOSKELETAL	MOVEMENT-PAIN + CREPITATIO IN BOTH KNEES CNS	YES
	XXXXXX	DAY 10	ddMMMyyyy:hh:mm	MUSCULOSKELETAL	HIGH MUSCULAR TENSION (NECK)	NO
	XXXXXX	DAY 10	ddMMMyyyy:hh:mm	MUSCULOSKELETAL	MUSC. TENSION SHOULDER-NECK-MUSC. (NCS)	NO

ETC…

ONLY ABNORMALITIES ARE SHOWN.

4.3.3 Clinical laboratory evaluation

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LISTING 16.2.8.1: LABORATORY TEST RESULTS FOR SUBJECTS WITH ABNORMAL VALUES

ANALYSIS SET: SAFETY

COHORT 1
SUBJECT NUMBER (SEX) = XXXXXXXXX (MALE)

LABORATORY TEST (UNIT)	ANALYSIS PHASE	ANALYSIS VISIT	SAMPLE DATETIME	USE [1]	RESULT	CHG [2]	NORMAL RANGE	ABN [3]	FAS TED	CSA [4]	COMMENT
TEST 1 (UNIT)	SCREENING	SCREENING	ddMMMyyyy:hh:mm		XX		XX-XX		YES	NO	XXXXXXXXXXXXX
		DAY -1	ddMMMyyyy:hh:mm		XX		XX-XX		YES	NO	XXXXXXXXXX
	CHALLENGE	DAY X	ddMMMyyyy:hh:mm		XX	XX	XX-XX	H	YES	NO	
		DAY X	ddMMMyyyy:hh:mm		XX	XX	XX-XX	H	YES	NO	
		DAY X	ddMMMyyyy:hh:mm		XX	XX	XX-XX	H	YES	NO	
	RESCUE	DAY X	ddMMMyyyy:hh:mm		XX	XX	XX-XX		YES	NO	
		DAY X	ddMMMyyyy:hh:mm		XX	XX	XX-XX		YES	NO	
		DAY X	ddMMMyyyy:hh:mm		XX	XX	XX-XX		YES	NO	
		DAY X	ddMMMyyyy:hh:mm		XX	XX	XX-XX		NO	NO	
TEST 2 (UNIT)	SCREENING	SCREENING	ddMMMyyyy:hh:mm		XX		XX-XX		YES	NO	
		DAY -1	ddMMMyyyy:hh:mm		XX		XX-XX		YES	NO	
	CHALLENGE	DAY X	ddMMMyyyy:hh:mm		XX	XX	XX-XX		YES	NO	
		DAY X	ddMMMyyyy:hh:mm	NO	XX	XX	XX-XX		YES	NO	
		DAY X	ddMMMyyyy:hh:mm		XX	XX	XX-XX		YES	NO	

ETC…

[1] NO = SAMPLE NOT USED IN ANALYSIS TABLES AND FIGURES.
[2] CHANGE FROM BASELINE VALUE.
[3] ABNORMALITY: H = ABNORMALLY HIGH VALUE / L = ABNORMALLY LOW VALUE COMPARED TO THE NORMAL RANGE.
[4] SAMPLE WITH CLINICALLY SIGNIFICANT ABNORMALITIES (CRF DATA).

4.3.4 Vital signs

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LISTING 16.2.9.1: VITAL SIGNS RESULTS FOR SUBJECTS WITH ABNORMAL VALUES

ANALYSIS SET: SAFETY

COHORT 1

SUBJECT NUMBER	ANALYSIS PHASE	ANALYSIS VISIT	VITAL SIGN DATETIME	USE [1]	CSA [2]	SUPINE SBP (mmHg) TEST RESULT	CHG [3]	ABN [4]	SUPINE DBP (mmHg) TEST RESULT	CHG [3]	ABN [4]	HEART RATE (bpm) TEST RESULT	CHG [3]	ABN [4]	TEMPERATURE (°C) TEST RESULT	CHG [3]	ABN [4]	WEIGHT (kg) TEST RESULT	CHG [3]	ABN [4]
XXXX	SCREENING	SCREENING	ddMMMyyyy:hh:mm			XX			XX			XX			XX.X			XX		
		DAY -1	ddMMMyyyy:hh:mm			XX			XX			XX			XX.X			XX		
	CHALLENGE	BASELINE	ddMMMyyyy:hh:mm		NO	XX	XX		XX	XX		XX	XX	L	XX.X	X.X		XX	XX	
		TIME POINT 4	ddMMMyyyy:hh:mm			XX	XX		XX	XX		XX	XX		XX.X	X.X		XX	XX	
		TIME POINT 5	ddMMMyyyy:hh:mm	NO		XX	XX		XX	XX		XX	XX		XX.X	X.X	H	XX	XX	
XXXX	SCREENING	SCREENING	ddMMMyyyy:hh:mm			XX	XX		XX	XX		XX	XX		XX.X	X.X	H	XX	XX	
		DAY -1	ddMMMyyyy:hh:mm			XX	XX		XX	XX		XX	XX		XX.X	X.X	H	XX	XX	
	CHALLENGE	BASELINE	ddMMMyyyy:hh:mm			XX	XX		XX	XX		XX	XX		XX.X	X.X		XX	XX	
		TIME POINT 4	ddMMMyyyy:hh:mm			XX	XX		XX	XX		XX	XX		XX.X	X.X		XX	XX	
		TIME POINT 5	ddMMMyyyy:hh:mm			XX	XX		XX	XX		XX	XX		XX.X	X.X		XX	XX	

ETC…

[1] NO = NOT USED IN ANALYSIS TABLES AND FIGURES.
[2] CLINICALLY SIGNIFICANT ABNORMALITY (CRF DATA).
[3] CHANGE FROM BASELINE VALUE.
[4] ABNORMALITY: H = ABNORMALLY HIGH VALUE / L = ABNORMALLY LOW VALUE COMPARED TO THE NORMAL RANGE.

4.3.5 ECG

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LISTING 16.2.10.1: ECG RESULTS FOR SUBJECTS WITH ABNORMAL VALUES

ANALYSIS SET: SAFETY

COHORT 1
SUBJECT NUMBER (SEX) =XXXXXXXX (MALE)

						HEART RATE (bpm)			PR (ms)			QRS (ms)			
ANALYSIS PHASE	ANALYSIS VISIT	ECG TRIPLET	ECG DATETIME	USE [1]	CSA [2]	TEST RESULT	CHG [3]	ABN [4]	TEST RESULT	CHG [3]	ABN [4]	TEST RESULT	CHG [3]	ABN [4]	COMMENT/MORPHOLOGY
SCREENING	SCREENING	ECG 1	ddMMMyyyy:hh:mm	NO	NO	XXX		L	XXX			XXX			
		ECG 2	ddMMMyyyy:hh:mm	NO	NO	XXX		L	XXX			XXX			
		ECG 3	ddMMMyyyy:hh:mm	NO	NO	XXX		L	XXX			XXX			XXXXXXXXX
		MEAN	ddMMMyyyy:hh:mm		NO	XXX		L	XXX			XXX			
CHALLENGE	BASELINE	ECG 1	ddMMMyyyy:hh:mm	NO		XXX			XXX			XXX			
		ECG 2	ddMMMyyyy:hh:mm	NO		XXX			XXX			XXX			
		ECG 3	ddMMMyyyy:hh:mm	NO		XXX			XXX			XXX			
		MEAN	ddMMMyyyy:hh:mm			XXX			XXX			XXX			
	TIME POINT 3	ECG 1	ddMMMyyyy:hh:mm	NO	NO	XXX	XXX	L	XXX	XX	H	XXX	XX	H	
		ECG 2	ddMMMyyyy:hh:mm	NO	NO	XXX	XXX	L	XXX	XX	H	XXX	XX	H	XXXXXXXXXXXXX
		ECG 3	ddMMMyyyy:hh:mm	NO	NO	XXX	XXX	L	XXX	XX	H	XXX	XX	H	
		MEAN	ddMMMyyyy:hh:mm		NO	XXX	XXX	L	XXX	XX	H	XXX	XX	H	

ETC…

[1] NO = NOT USED IN ANALYSIS TABLES AND FIGURES.
[2] CLINICALLY SIGNIFICANT ABNORMALITY (CRF DATA).
[3] CHANGE FROM BASELINE VALUE.
[4] ABNORMALITY: H = ABNORMALLY HIGH VALUE / L = ABNORMALLY LOW VALUE COMPARED TO THE NORMAL RANGE.

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LISTING 16.2.10.1: ECG RESULTS FOR SUBJECTS WITH ABNORMAL VALUES

ANALYSIS SET: SAFETY

COHORT 1
SUBJECT NUMBER (SEX) = XXXXXXXX (MALE)

						QT (ms)				QTcB (ms)				QTcF (ms)			
ANALYSIS PHASE	ANALYSIS VISIT	ECG TRIPLET	ECG DATETIME	USE [1]	CSA [2]	TEST RESULT	ABN	CHG [3]	ABN	TEST RESULT	ABN	CHG [3]	ABN	TEST RESULT	ABN	CHG [3]	ABN
SCREENING	SCREENING	ECG 1	ddMMMyyyy:hh:mm	NO	NO	XXX	H			XXX	H			XXX	H		
		ECG 2	ddMMMyyyy:hh:mm	NO	NO	XXX	H			XXX	H			XXX	H		
		ECG 3	ddMMMyyyy:hh:mm	NO	NO	XXX	H			XXX	H			XXX	H		
		MEAN	ddMMMyyyy:hh:mm		NO	XXX	H			XXX	H			XXX	H		
CHALLENGE	BASELINE	ECG 1	ddMMMyyyy:hh:mm	NO		XXX				XXX				XXX			
		ECG 2	ddMMMyyyy:hh:mm	NO		XXX				XXX				XXX			
		ECG 3	ddMMMyyyy:hh:mm	NO		XXX				XXX				XXX			
		MEAN	ddMMMyyyy:hh:mm			XXX				XXX				XXX			
	TIME POINT 3	ECG 1	ddMMMyyyy:hh:mm	NO	NO	XXX		XXX	[30,60]	XXX		XXX	[30,60]	XXX		XXX	
		ECG 2	ddMMMyyyy:hh:mm	NO	NO	XXX		XXX	[30,60]	XXX		XXX	[30,60]	XXX		XXX	
		ECG 3	ddMMMyyyy:hh:mm	NO	NO	XXX		XXX	[30,60]	XXX		XXX	[30,60]	XXX		XXX	
		MEAN	ddMMMyyyy:hh:mm		NO	XXX		XXX	[30,60]	XXX		XXX	[30,60]	XXX		XXX	

ETC…

[1] NO = NOT USED IN ANALYSIS TABLES AND FIGURES.
[2] CLINICALLY SIGNIFICANT ABNORMALITY (CRF DATA).
[3] CHANGE FROM BASELINE VALUE.
[4] ABNORMALITY: H = ABNORMALLY HIGH VALUE / L = ABNORMALLY LOW VALUE COMPARED TO THE NORMAL RANGE.

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LISTING 16.2.10.2: ECG INTERPRETATION AND MORPHOLOGY FOR SUBJECTS WITH ANY ABNORMAL INTERPRETATION

ANALYSIS SET: SAFETY

COHORT 1
SUBJECT NUMBER (SEX) = XXXXXXXX (MALE)

ANALYSIS VISIT	ECG DATETIME	USE [1]	INTERPRETATION	CSA [2]	FINDING	COMMENT
SCREENING	ddMMMyyyy:hh:mm	NO	ABNORMAL	YES		XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
BASELINE	ddMMMyyyy:hh:mm	NO	ABNORMAL	NO	XXXXXXXXXX	
TIMEPOINT 3	ddMMMyyyy:hh:mm	NO	ABNORMAL	NO		XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX

ETC…

[1] NO = NOT USED IN ANALYSIS TABLES AND FIGURES.
[2] CLINICALLY SIGNIFICANT ABNORMALITY (CRF DATA).

4.3.6 Malaria clinical score

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LISTING 16.2.11.1: MALARIA SIGNS AND SYMPTOMS

ANALYSIS SET: SAFETY

COHORT 1

SUBJECT NUMBER	FIRST ANTIMALARIAL TREATMENT DATETIME	ANALYSIS VISIT	DAY [1]	ASSESSMENT DATETIME	USE [2]	MCS ACT	MCS CHG	HEA	MYA	ART	FAT	MAL	CHI	SWE	ANO	NAU	VOM	ABD	FEV	TAC	HYP
XXXX	ddMMMyyyy:hh:mm	BASELINE	1	ddMMMyyyy:hh:mm		XX.X	XX.X	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
		DAY 7	7	ddMMMyyyy:hh:mm		XX.X	XX.X	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
		DAY 8	8	ddMMMyyyy:hh:mm		XX.X	XX.X	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
		DAY 9	9	ddMMMyyyy:hh:mm		XX.X	XX.X	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
		DAY 10	10	ddMMMyyyy:hh:mm		XX.X	XX.X	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
		DAY 11	11	ddMMMyyyy:hh:mm		XX.X	XX.X	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
		DAY 12	12	ddMMMyyyy:hh:mm		XX.X	XX.X	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
		DAY 13	13	ddMMMyyyy:hh:mm		XX.X	XX.X	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
		DAY 14	14 *	ddMMMyyyy:hh:mm		XX.X	XX.X	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
		UNSCHED	15 *	ddMMMyyyy:hh:mm	NO	XX.X	XX.X	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
		UNSCHED	16 *	ddMMMyyyy:hh:mm	NO	XX.X	XX.X	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
		DAY 21	21	ddMMMyyyy:hh:mm		XX.X	XX.X	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX

ETC…

[1] DAY VS. INOCULATION, DAYS ON WHICH ANTIMALARIAL TREATMENT IS TAKEN ARE FLAGGED (*).
[2] NO = NOT USED IN ANALYSIS TABLES AND FIGURES.
MCS=MALARIA CLINICAL SCORE (/42); ACT=ACTUAL VALUE; CHG=CHANGE FROM BASELINE.
MALARIA SIGNS AND SYMPTOMS: HEADACHE, MYALGIA, ARTHRALGIA, FATIGUE/LETHARGY, MALAISE, CHILLS/SHIVERING/RIGORS, SWEATING/HOT SPELLS, ANOREXIA, NAUSEA, VOMITING, ABDOMINAL DISCOMFORT, FEVER, TACHYCARDIA, HYPOTENSION.

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LISTING 16.2.11.2: MALARIA CLINICAL SCORES > 6 AND PARASITAEMIA

ANALYSIS SET: SAFETY

COHORT 1

								PARASITAEMIA		
	FIRST ANTIMALARIAL					MCS				RESULT
SUBJECT NUMBER	TREATMENT DATETIME	ANALYSIS VISIT	DAY [1]	ASSESSMENT DATETIME	USE [2]	ACT	CHG	ANALYSIS VISIT	ASSESSMENT DATETIME	(p/mL) [3]
XXXX	ddMMMyyyy:hh:mm	BASELINE	1	ddMMMyyyy:hh:mm		XX.X	XX.X	BASELINE	ddMMMyyyy:hh:mm	XX.X
		DAY 11	11	ddMMMyyyy:hh:mm		XX.X	XX.X	DAY 11	ddMMMyyyy:hh:mm	XX.X $
		DAY 12	12	ddMMMyyyy:hh:mm		XX.X	XX.X	DAY 12	ddMMMyyyy:hh:mm	XX.X $
		DAY 13	13	ddMMMyyyy:hh:mm		XX.X	XX.X	DAY 13	ddMMMyyyy:hh:mm	XX.X $
		DAY 14	14 *	ddMMMyyyy:hh:mm		XX.X	XX.X	DAY 14	ddMMMyyyy:hh:mm	XX.X $
		UNSCHED	15 *	ddMMMyyyy:hh:mm	NO	XX.X	XX.X	DAY 14	ddMMMyyyy:hh:mm	XX.X $

ETC…

[1] DAY VS. INOCULATION, DAYS ON WHICH ANTIMALARIAL TREATMENT IS TAKEN ARE FLAGGED (*).
[2] NO = NOT USED IN ANALYSIS TABLES AND FIGURES.
[3] POSITIVE qPCR RESULTS (≥ 250 PARASITES PER ML BLOOD) ARE FLAGGED ($).
MCS=MALARIA CLINICAL SCORE (/42); ACT=ACTUAL VALUE; CHG=CHANGE FROM BASELINE.

5. TEMPLATE FIGURES

5.1 PHARMACODYNAMICS

Programmer note: all PD figures shown in this section will be repeated for the m-PD set with adjusted numbering (e.g. 14.2.3.1.2).

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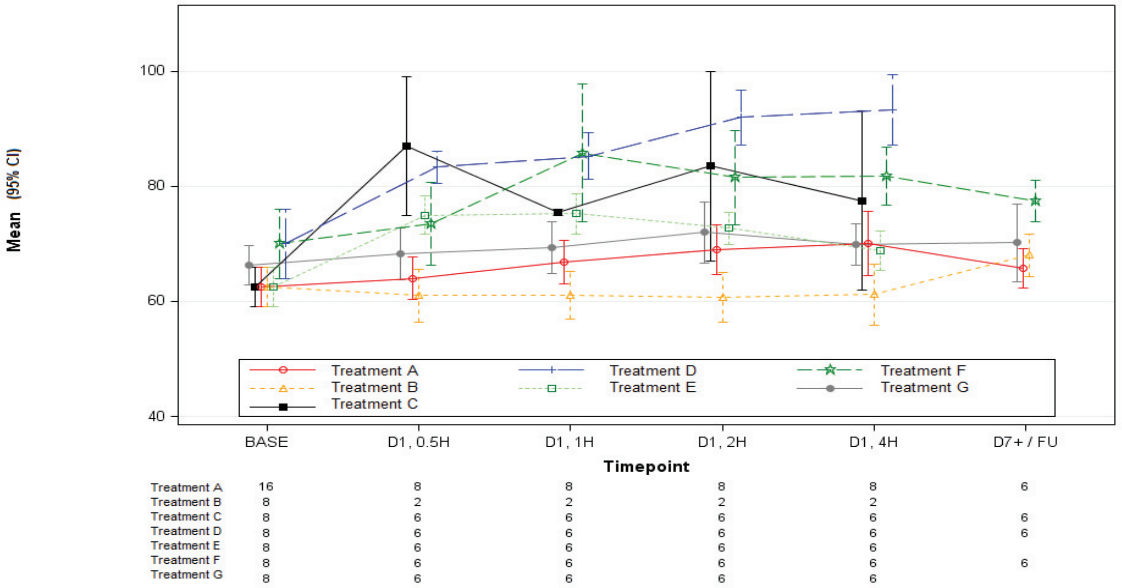
FIGURE 14.2.3.1.1: BLOOD-STAGE PARASITE PROFILE: MEDIAN PARASITAEMIA ACTUAL VALUES OVER TIME

ANALYSIS SET: PD



Treatment A	16	8	8	8	8	6
Treatment B	8	2	2	2	2	
Treatment C	8	6	6	6	6	6
Treatment D	8	6	6	6	6	6
Treatment E	8	6	6	6	6	
Treatment F	8	6	6	6	6	6
Treatment G	8	6	6	6	6	

Programmer notes:

- *One line per cohort and for all subjects.*
- *Legend: Cohort 1, Cohort 2, All subjects.*
- *X-axis 'Analysis Time Point' will show scheduled time points from Day 7 to Riamet Day 4, 72h.*
- *Y-axis label: 'log10(Parasitaemia)'.*
- *No CI interval will be shown.*
- *Jittering should be allowed to distinguish overlapping symbols.*

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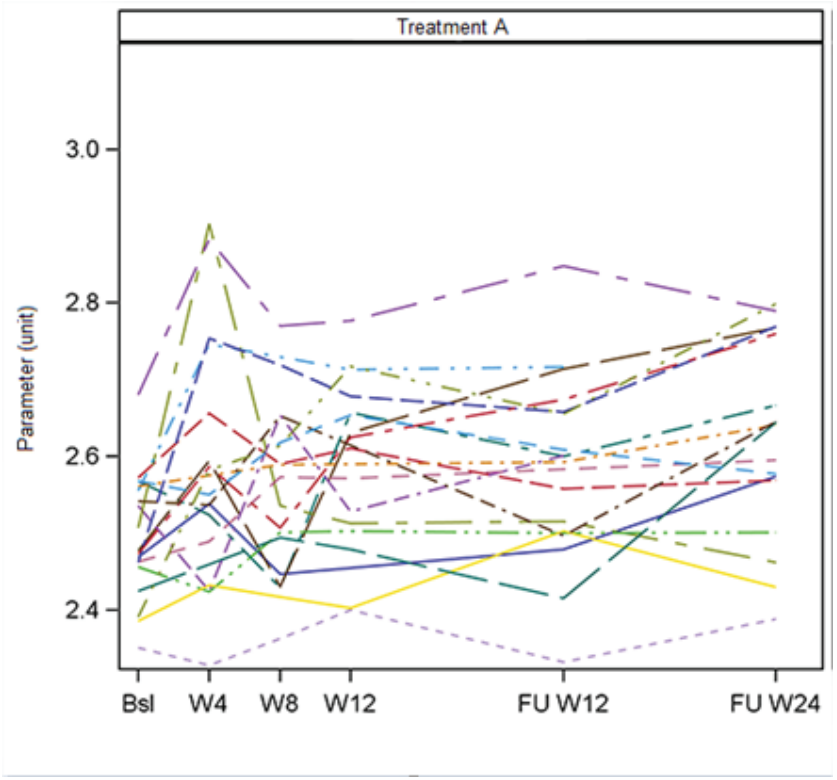
FIGURE 14.2.3.2.1: BLOOD-STAGE PARASITE PROFILE: INDIVIDUAL PARASITAEMIA ACTUAL VALUES OVER TIME

ANALYSIS SET: PD



Programmer notes:

- *A separate plot per cohort and all subjects starting in a new page.*
- *One line per subject.*
- *Legend: Subject numbers.*
- *X-axis label: 'Time from first PCR positivity (days)'.*
- *Y-axis label: 'log10(Parasitaemia)'.*
- *For each subject, show the assessments from the subject's first PCR positivity to parasite clearance.*
- *Different plotting symbols will be used on the first assessment when antimalarial treatment was given and will be denoted by a footnote.*

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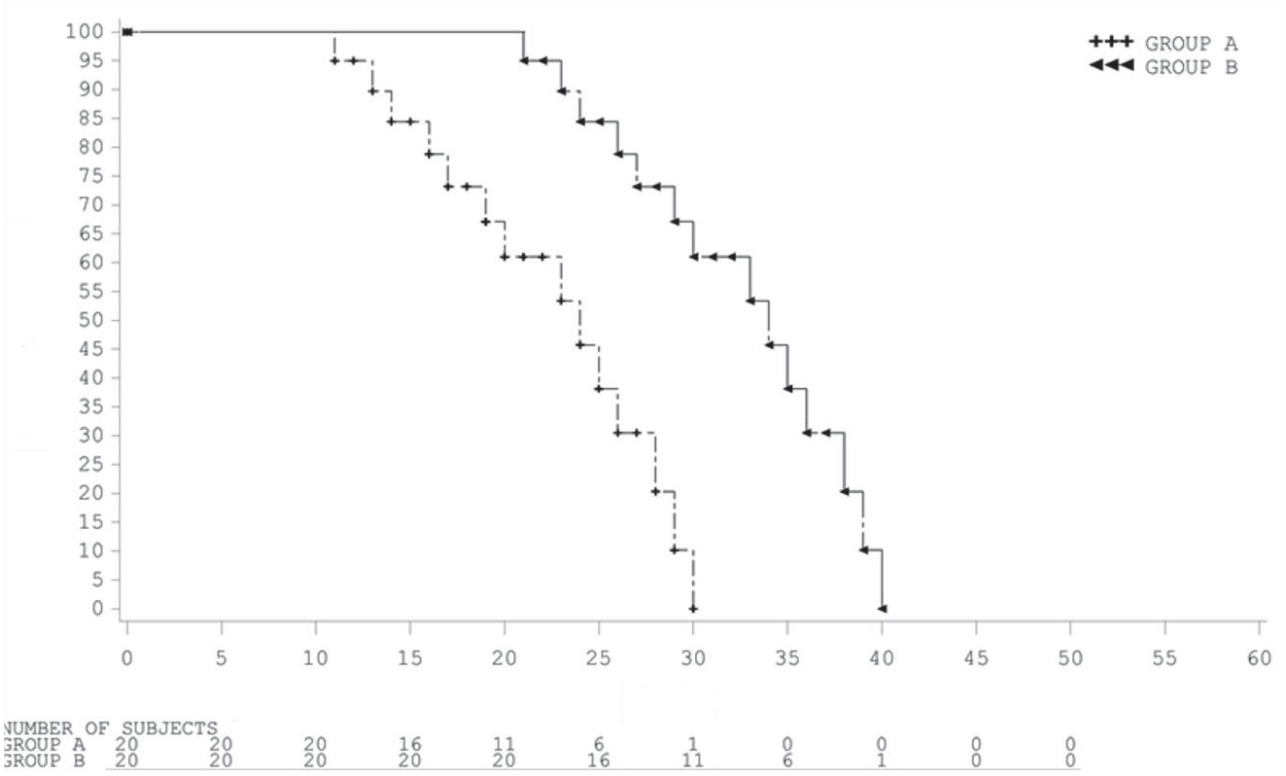
FIGURE 14.2.3.3.1: TIME TO FIRST PCR POSITIVITY: KAPLAN MEIER PLOT

ANALYSIS SET: PD



NUMBER OF SUBJECTS										
GROUP A	20	20	20	16	11	6	1	0	0	0	0
GROUP B	20	20	20	20	20	16	11	6	1	0	0

POSITIVE PARASITAEMIA IS DEFINED AS qPCR OUTCOME ≥ 250 PARASITES PER mL BLOOD.

Programmer notes:

- *One line per cohort and all subjects.*
- *X-axis label: 'Time from PfSPZ inoculation (days)'.*
- *Y-axis label: 'Probability (%)'.*

Programmer note: repeat Figure 14.2.3.3.1 for:

FIGURE 14.2.3.4.1: TIME TO PARASITAEMIA OF ≥5000 PARASITES PER mL BLOOD: KAPLAN MEIER PLOT

FIGURE 14.2.3.5.1: TIME TO FIRST DOSE OF TREATMENT WITH RIAMET: KAPLAN MEIER PLOT

FIGURE 14.2.3.6.1: TIME TO PARASITE CLEARANCE: KAPLAN MEIER PLOT

The footnotes and axes will be adapted accordingly.

5.2 SAFETY

5.2.1 Clinical laboratory evaluation

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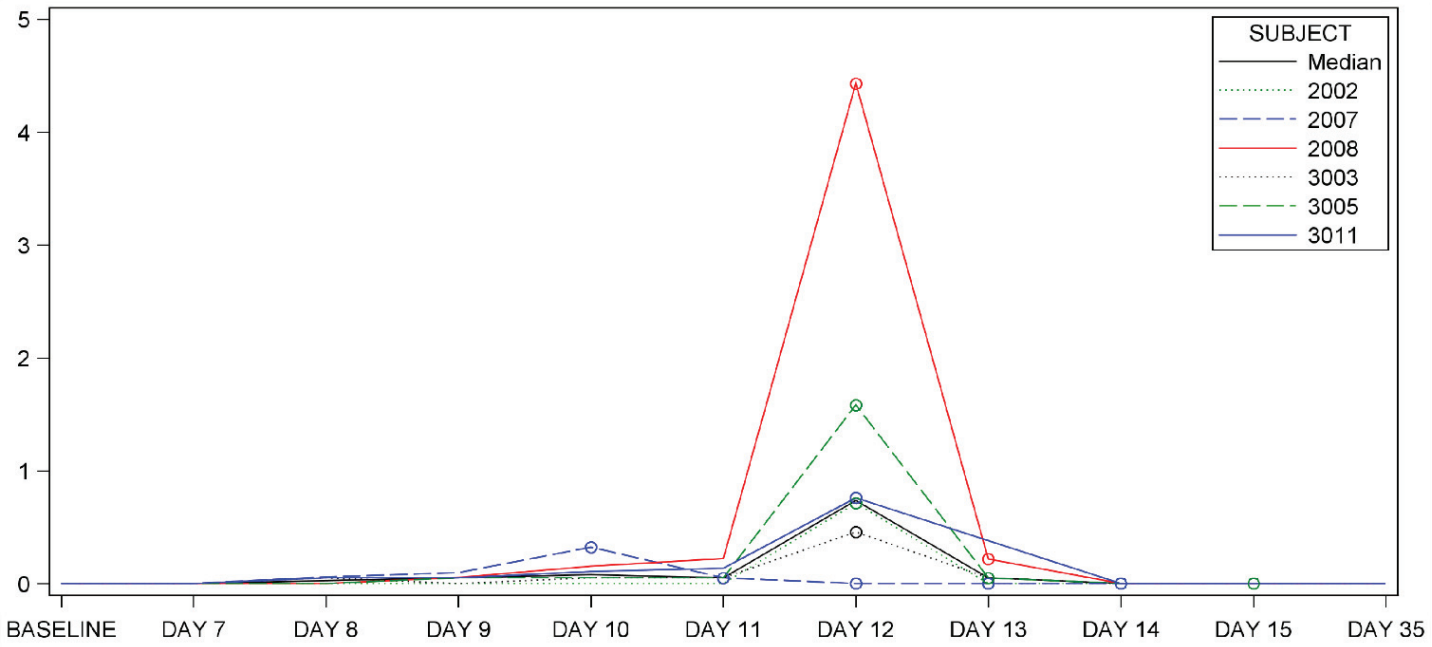
FIGURE 14.3.2.1: INDIVIDUAL LABORATORY TEST ACTUAL VALUES OVER TIME

ANALYSIS SET: SAFETY



Programmer notes:

- *A separate plot per cohort and all subjects starting in a new page.*
- *One line per subject and one line for the median.*
- *X-axis 'Analysis Time Point' will show scheduled time points.*
- *Label Y-axis will be the laboratory test result.*
- *The following laboratory parameters will be shown in separate plots: liver biochemistry parameters (albumin, AST, ALT, ALP, GGT, total and direct bilirubin and total serum proteins), CRP and haemoglobin.*

5.2.2 Vital signs

The analysis figures for vital signs parameters are largely identical to the laboratory figures.

FIGURE 14.3.3.1: INDIVIDUAL VITAL SIGNS ACTUAL VALUES OVER TIME

Programmer notes:

- *The following vital signs parameters will be shown in separate plots: heart rate and body temperature.*
- *The median time to first antimalarial treatment administration will be shown with a reference line.*

5.2.3 ECG

The analysis figures for ECG parameters are largely identical to the laboratory figures.

FIGURE 14.3.4.1: INDIVIDUAL ECG ACTUAL VALUES OVER TIME

Programmer note: the following ECG parameters will be shown in separate plots: QTcF and QTcB.

5.2.4 Malaria clinical score

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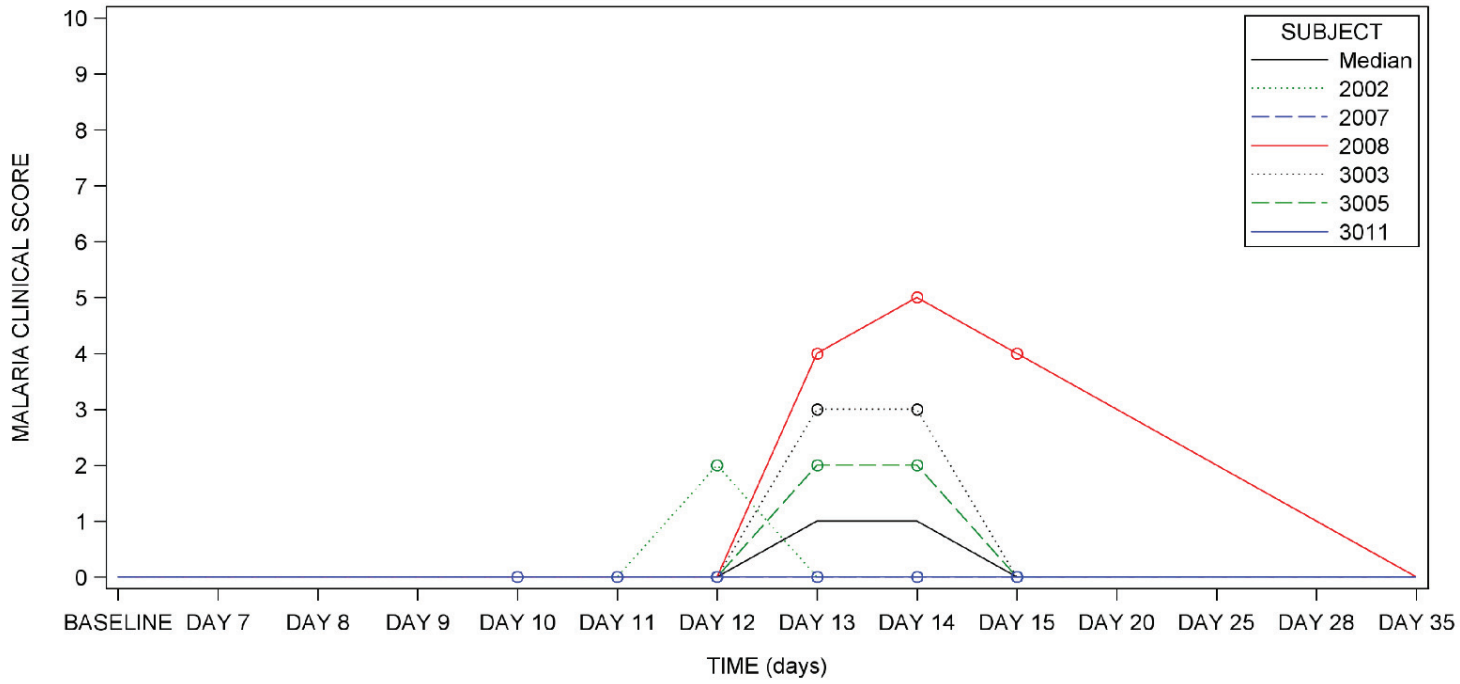
FIGURE 14.3.5.1: INDIVIDUAL MALARIA CLINICAL SCORE ACTUAL VALUES OVER TIME

ANALYSIS SET: SAFETY



Programmer notes:

- *A separate plot per cohort and all subjects starting in a new page.*
- *One line per subject and one line for the median.*
- *X-axis 'Analysis Time Point' will show scheduled time points.*
- *Label Y-axis will be 'Malaria clinical score'.*
- *Different symbols will be used for the time points where antimalarial treatment was taken for the first time and for the time point of peak parasitaemia. They will be specified in a footnote.*
- *The median time to first antimalarial treatment administration will be shown with a reference line.*

Programmer note: repeat Figure 14.3.5.1 for:

FIGURE 14.3.5.2: INDIVIDUAL MALARIA CLINICAL SCORE AND PARASITAEMIA ACTUAL VALUES OVER TIME

FIGURE 14.3.5.3: INDIVIDUAL MALARIA CLINICAL SCORE AND CRP ACTUAL VALUES OVER TIME

- *Each figure will show a separate plot per cohort starting in a new page followed by a separate plot per individual subject starting in a new page.*
- *One line per subject and parameter. I.e. individual subjects plots will have 2 lines; cohort plots will have 2*8 = 16 lines (if no missing data).*
- *X-axis 'Time from PfSPZ inoculation (days)' will show the relative time in days of the individual subject assessments.*
- *Label Y-axis will be 'Malaria clinical score' on the left Y-axis and 'log10(Parasitaemia)' / 'CRP (unit)' on the right Y-axis.*
- *The first antimalarial treatment administration will be shown with a reference line.*

Certificate Of Completion

Envelope Id: 7A8080D29B54469F91469E9C4688E6A0 Status: Completed

Subject: Please DocuSign: MMV_PfSPZ-DVI Blood Stage_19_01_SAP_v1.0.docx, MMV_PfSPZ-DVI Blood Stage_19_01...

Source Envelope:

Document Pages: 167 Signatures: 8 Envelope Originator:

Certificate Pages: 6 Initials: 0 Daniel Izquierdo Juncas

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2/11/2021 4:03:36 PM daniel.izquierdojuncas@sgs.com

Signer Events	Signature	Timestamp
bastiaan Jansen bastiaan.jansen@sgs.com Biostatistical Coordinator - Senior Statistician SGS BE Security Level: Email, Account Authentication (Required)	bastiaan Jansen Signature Adoption: Pre-selected Style Signature ID: 15ADFC6D-3E73-4686-B167-F978EA41202B Using IP Address: 81.243.99.25 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document I approve this document	Sent: 2/11/2021 4:09:51 PM Viewed: 2/11/2021 4:21:30 PM Signed: 2/11/2021 4:23:23 PM
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Daniel Izquierdo Juncas daniel.izquierdojuncas@sgs.com Biostatistician SGS LS Security Level: Email, Account Authentication (Required)	Daniel Izquierdo Juncas Signature Adoption: Pre-selected Style Signature ID: 690E6583-03D5-4613-A9EC-59ED7BAE2148 Using IP Address: 165.225.93.35 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I am the author of this document I am the author of this document	Sent: 2/11/2021 4:09:51 PM Viewed: 2/11/2021 4:10:01 PM Signed: 2/11/2021 4:11:35 PM
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Signer Events	Signature	Timestamp
Farouk Chughlay chughlayf@mmv.org Project and Medical Director Farouk Chughlay Security Level: Email, Account Authentication (Required)	 Signature Adoption: Drawn on Device Signature ID: 6A2C1E23-2AEB-48DF-A6A5-44CF570BF27F Using IP Address: 83.228.139.243 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document I approve this document	Sent: 2/11/2021 4:23:28 PM Viewed: 2/11/2021 4:54:18 PM Signed: 2/11/2021 4:55:13 PM
Electronic Record and Signature Disclosure: Accepted: 2/5/2021 11:52:45 AM ID: cbc1c9da-6caf-461d-9c71-c22138d857b0		
Myriam El Gaaloul elgaaloulm@mmv.org Security Level: Email, Account Authentication (Required)	Myriam El Gaaloul Signature Adoption: Pre-selected Style Signature ID: C2CA71F3-3AA8-43DA-B327-CC3B36DFB37C Using IP Address: 213.55.244.6 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document I approve this document	Sent: 2/11/2021 4:23:28 PM Viewed: 2/13/2021 10:14:26 AM Signed: 2/13/2021 10:25:38 AM
Electronic Record and Signature Disclosure: Accepted: 2/13/2021 10:14:26 AM ID: 672a0588-36b7-450e-bb09-e42c22631e93		

In Person Signer Events	Signature	Timestamp

Editor Delivery Events	Status	Timestamp

Agent Delivery Events	Status	Timestamp

Intermediary Delivery Events	Status	Timestamp

Certified Delivery Events	Status	Timestamp

Carbon Copy Events	Status	Timestamp
Ann Mallinus ann.mallinus@sgs.com Management Assistant Biostatistics SGS Belgium NV Security Level: Email, Account Authentication (Required) **Electronic Record and Signature Disclosure:** Not Offered via DocuSign	COPIED	Sent: 2/13/2021 10:25:43 AM

Witness Events	Signature	Timestamp

Notary Events	Signature	Timestamp

Envelope Summary Events	Status	Timestamps
Envelope Sent	Hashed/Encrypted	2/11/2021 4:09:52 PM
Certified Delivered	Security Checked	2/13/2021 10:14:26 AM
Signing Complete	Security Checked	2/13/2021 10:25:38 AM
Completed	Security Checked	2/13/2021 10:25:43 AM

Payment Events	Status	Timestamps

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