STATISTICAL ANALYSIS PLAN
FOR DSMB / INTERIM ANALYSES

AN OPEN LABEL STUDY TO ASSESS THE EFFICACY, SAFETY, TOLERABILITY AND PHARMACOKINETICS OF A SINGLE DOSE OF MMV390048 IN ADULT PATIENTS WITH ACUTE, UNCOMPLICATED ***PLASMODIUM VIVAX*** OR ***FALCIPARUM*** MALARIA MONOINFECTION OVER A 35 DAY PERIOD

MMV_MMV390048_16_02

Author	Martina Wibberg, CRO Trial Statistician
Version	Version 1, Final
Date of version	10-Mar-2017
Approved by customer	Cristina Donini, Project Director MMV, Hilary Johnstone, Clinical Research Physician

Signatures

Author: **Martina Wibberg, Senior Biostatistician** **DATAMAP GmbH**	10 Mar 2017 (Date)	(Signature)
Approved by: **Cristina Donini, PharmD, PhD** **Project Director, MMV**	27 MAR 2017 (Date)	(Signature)
Hilary Johnstone, MBChB **Clinical Research Physician**	(Date)	Digitally signed by Hilary Johnstone DN: cn=Hilary Johnstone, o=HJ Clinical Trial Consultancy cc., ou, email=hjohnstone@hjclinical.com, c=ZA Reason: I am approving this document Date: 2017.03.16 14:03:28 +02'00' (Signature)

Document - History

Version	Date	Responsible	Change information
Draft 1	30-Jan-2017	M. Wibberg	
Draft 2	15-Feb-2017	M. Wibberg	Implementation of comments from first review cycle
Draft 3	1-Mar-2017	M. Wibberg	Implementation of comments from review cycle by DSMB members
Final	10-Mar-2017	M. Wibberg	No further changes from draft 3; track changes accepted and document finalized

List of a bbreviations

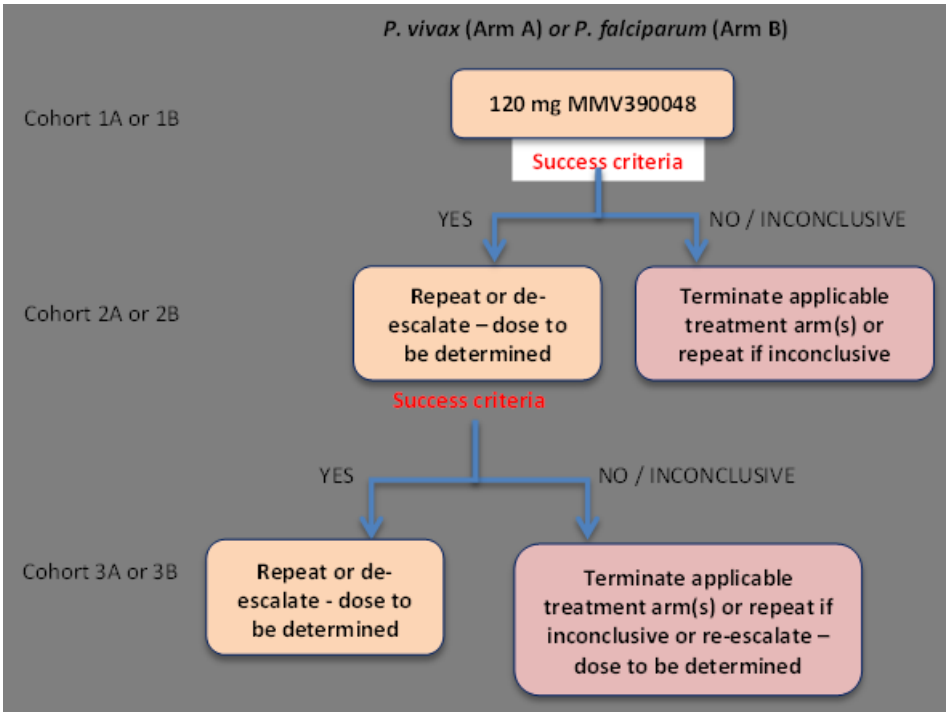
ACPR	Adequate Clinical and Parasitological Response
AE	Adverse Event
ALT	Alanine Amino Transferase
AST	Aspartate Amino Transferase
AUC	Area Under the Plasma Concentration Time Curve
BMI	Body Mass Index
BP	Blood Pressure
Cmax	Maximum plasma concentration
DSMB	Data Safety Monitoring Board
ECG	Electrocardiogram
ETF	Early Treatment Failure
LCF	Late Clinical Failure
LPF	Late Parasitological Failure
MedDRA	Medical Dictionary for Regulatory Activities
mITT	Microbiological Intent-to-Treat
P. falciparum	Plasmodium falciparum
P. vivax	Plasmodium vivax
PCR	Polymerase Chain Reaction
PK	Pharmacokinetic
PT	Preferred Term
QTcF	Corrected QT interval, Fridericia
QTcB	Corrected QT interval, Bazett
RBC	Red Blood Cells (erythrocytes)
SAE	Serious Adverse Event
SAS	Statistical Analysis System
SRT	Safety Review Team
t1/2	Estimated terminal phase half life
tmax	Time to reach maximum plasma concentration
ULN	Upper Limit of Normal
WBC	White Blood Cells (leukocytes)
WHO	World Health Organization

Table of Contents

1. Introduction

This analysis plan is based on the study protocol MMV_MMV390048_16_02, v1.2 dated 26 Jan 2017 and the DSMB Charter dated 26 Jan 2017

The study is designed to enroll 17 patients into each of the planned cohorts as per the following flow chart:



The DSMB will review safety and efficacy data to decide on the further study proceed, as per DSMB Charter.

Up to two interim analyses per malaria arm, i.e., 4 in total, are planned, after each of the first 2 cohorts in each arm completes its Day 14 assessment.

The purpose of the first interim analyses after Cohorts 1A and 1B, respectively, is to determine if the respective malaria arm must be stopped for futility or if enrolment of a second cohort is indicated. The arm will be stopped for futility if no more than 10 out of the 17 patients are responders for the primary ACPR endpoint. If there are 11 to 17 responders out of 17 patients, a second cohort of 17 patients may be enrolled. The dose for Cohort 2 will be determined based on the responder rate in Cohort 1 and corresponding safety and pharmacokinetic data. Second interim analyses will occur after each of Cohorts 2A and 2B. The purpose of these analyses is to determine:

- if a dose should be stopped for futility
- whether or not enrolment of a third cohort is required and to select the appropriate dose for that cohort. If two distinct dose levels have been tested in Cohorts 1 and 2, a dose-response logistic regression model may be fitted to support the termination and dose selection decisions.

The interim analyses will be conducted on data to at least Day 14 of each cohort. If PCR correction data are not available at the time of the interim analyses, decisions regarding dose and cohort progression may be based on the crude adequate clinical and parasitological response (ACPR, for definition see Section 3 below) for both P. vivax and P. falciparum.

2. Decision rules for interim analyses

As stated in the study protocol, the following rules will be applied to decide upon study progression at the time point of the interim analyses:

After Cohorts 1A/1B

- After the first cohort, the arm will be terminated for futility if less than 11 out of 17 patients (or less than a minimum of 60% of patients) are ACPR responsive on Day 14.
- If the arm is not terminated for futility after Cohort 1, Cohort 2 may be enrolled to investigate
    - a lower dose if at least 14 out of 17 patients from Cohort 1 were responders (the response rate was greater than 80%, i.e., success criteria were met), or
    - a repeat dose if 11 to 13 out of 17 patients from Cohort 1 were responders (the response rate was greater than 60% but less than 80%, i.e., the data were regarded as inconclusive).

After Cohorts 2A/2B

- If Cohort 2 investigated a lower dose than Cohort 1:
    - the same progression criteria described for Cohort 1 will be applied to Cohort 2 to determine whether a further dose de-escalation or dose repeat is permitted.
    - the safety review team (SRT) may elect to re-escalate to an intermediate dose depending on the success criteria at the doses from Cohorts 1 and 2.
- If Cohort 2 investigated the same dose as Cohort 1:
    - the arm will be terminated for futility if less than 25 out of 34 patients from both cohorts (or 72% or less of cumulative patients from both cohorts) were ACPR on Day 14.
    - if the arm is not terminated for futility after Cohorts 1 and 2, Cohort 3 may be enrolled to investigate:
        - a lower dose if at least 28 out of 34 patients from both cohorts were responders (the cumulative response rate was greater than 80%i.e. success criteria were met), or
        - a repeat dose if 25 to 27 out of 34 patients from both cohorts were responders (the cumulative response rate was greater than 72% but less than 80% i.e. the data were regarded as inconclusive).

Throughout:

- At any stage, the SRT may elect to repeat a dose rather than de-escalate even though success criteria may have been met.

The minimum Day 14 ACPR responder count to meet the cohort success criteria will be 14 out of 17 patients. Assuming a binomial distribution, the point estimate of the response rate with 14 out of 17 responders will be 82.4% with the lower margin of the 90% confidence interval (Clopper-Pearson method) greater than 60% (60.4% to 95.0%). A responder count of 11 to 13 out of 17 patients will be regarded as inconclusive and the dose may be repeated in a subsequent cohort. The maximum Day 14 ACPR responder count to declare futility of a dose level after one cohort will be 10 out of 17 patients (response rate of 58.8% or less) and will be associated with a risk of false conclusion of futility of less than 0.1% (alpha <0.001) assuming that the true population response is at least 90%.

If a particular dose is repeated, the minimum combined Day 14 ACPR responder count across the two cohorts to meet the success criteria will be 28 out of 34 patients (82.4% response rate; 90% confidence interval of 68.1% to 92.0%). A responder count of 25 to 27 out of 34 patients will be regarded as inconclusive and the dose may be repeated in a third cohort. The maximum combined Day 14 ACPR responder count to declare futility of a dose level after two cohorts will be 24 out of 34 (response rate of 70.6% or less) and will be associated with a risk of false conclusion of futility of less than 0.2% (alpha <0.002) assuming that the true population response is at least 90%.

If a particular dose is repeated across three cohorts, a combined Day 14 ACPR responder count across the three cohorts of at least 41 out of 51 patients (80.4% response rate; 90% confidence interval of 69.0% to 89.0%) will be required to meet the dose success criteria. An observed response rate across the three cohorts of 78.4% or less (at most 40 out of 51 patients) will be associated with a risk of false conclusion of futility of less than 2% (alpha <0.011) assuming that the true population response is at least 90%.

DSMB safety reports and interim analyses will be provided by DATAMAP GmbH, Freiburg, Germany using SAS®, Version 9.3 or higher in a Unix environment.

3. Definitions and data conventions

Baseline

Baseline for analysis purposes will be defined as the last measurement prior to the study drug administration, i.e. in general the Day 0, pre-dose assessment. Only if the Day 0, pre-dose is missing the screening assessment will be used instead.

Study days and hours since dosing

Study days will be calculated as actual date minus date of study drug intake, i.e., the day of the study drug intake will be defined as Day 0.

Hours since dosing will be calculated based on the date and time of the actual measurement in relation to the date and time of study drug intake.

In all calculations time of dose will be the time of the initial dose, i.e., irrespective of vomiting.

Calculation of Body Mass Index (BMI)

BMI will be calculated as weight (kg) / [height (m)]^2.

BMI will be rounded to one decimal place.

Calculation of Age

Age will be calculated from the date of the screening visit and the date of birth and will be presented as integer value. If the date of birth is not available the age entered on the CRF will be used.

The following SAS code will be used to calculate age where '&dob' is the date of birth and '&dat' is the date of visit 1

floor((intck('MONTH',&dob,&dat)-(day(&dat)<day(&dob)))/12).

Fever

Fever will be defined as axillary body temperature ≥37.5°C, or oral, rectal or tympanic body temperature ≥38°C.

Parasitemia

Parasitemia will be defined as a P. vivax or P. falciparum asexual forms count >0.

Crude adequate clinical and parasitological response (ACPR)

Crude ACPR at Day 14 will be defined as the absence of parasitemia (thick smear) on Day 14, irrespective of temperature, in patients who did not previously meet any of the criteria of early treatment failure, late clinical failure or late parasitological failure.

PCR corrected ACPR

The PCR corrected ACPR (P. falciparum only) at Day 14 will be defined as the absence of parasitemia (thick smear) on Day 14, irrespective of temperature, in patients who did not previously meet any of the criteria of early treatment failure, late clinical failure or late parasitological failure, after adjustment for parasitemia due to new infections by genotyping using PCR techniques.

Early treatment failure (ETF)

ETF is defined as one of the following:

- Development of any clinical complications (WHO definition of complicated/severe malaria, WHO [2012]) on Days 1, 2 or 3 with parasitemia
- Parasitemia >100,000/µL on Days 0, 1, 2 or 3 with or without fever
- A ≥25% increase in parasitemia compared to baseline during the period up to 24 hours after dosing for P. vivax malaria or up to 12 hours after dosing for P. falciparum malaria, with or without fever, and together with any of the following:
  - clinical decline;
  - lack of clinical improvement; or
  - significant decrease in platelet count defined as:
    - a >20% reduction from baseline for patients with a baseline platelet count between 50,000/mm^3 and 74,999/mm^3 (thrombocytopenia grade 2), or
    - a drop in platelet count to <50,000/mm^3 for patients with a baseline platelet count ≥75,000/mm3
- Parasitemia >baseline with or without fever, between >24 and 48 hours after dosing for P. vivax and between >12 and 36 hours after dosing for P. falciparum;
- Any parasitemia with fever, or parasitemia >25% of baseline with or without fever, between >48 and 72 hours after dosing for P. vivax and between >36 and 60 hours after dosing for P. falciparum;
- Failure to clear all parasites by microscopy associated with axillary temperature ≥37.5°C or oral/rectal/tympanic temperature ≥38°C, between >72 and 96 hours for P. vivax and >60 and 96 hours for P. falciparum.

Late Clinical Failure (LCF)

LCF is defined as the presence of any of the following between Day 4 and 14 in a patient who did not previously meet any of the criteria of ETF:

- Danger signs,
- Severe malaria, or
- Parasitemia with fever.

Late Parasitological Failure (LPF)

LPF is defined as the recurrence of parasitemia between Day 4 and 14 without fever in a patient who did not previously meet any of the criteria of ETF or LCF.

4. Analysis s ets

All DSMB summaries will be based on all enrolled patients of the corresponding cohort who received any amount of study medication (safety set).

The interim efficacy analyses will be based on the microbiological ITT (mITT) analysis set which will consist of all patients from the safety set with parasitologically confirmed malaria at baseline and at least one post-baseline efficacy assessment (clinical and parasitological data), and for whom no major protocol deviations are reported with the potential to affect the evaluation of efficacy. Protocol deviations leading to exclusion from the mITT analysis will be defined in a separate document.

The pharmacokinetic analysis (if data available at the time point of the DSMB/interim analyses) will be based on the pharmacokinetic set defined as all patients in the safety set who have at least one quantifiable post dose plasma concentration.

5. Patient disposition

A summary table of patient disposition will be provided, presenting per cohort

- The number of patients screened, treated, completed study, prematurely discontinued study.
- The reasons for premature discontinuation.

The number of patients who actually reached the Day 14 visit but have not yet completed / discontinued will also be displayed (since DSMB / interim analysis is supposed to occur when all patients of a cohort have reached Day 14), labelled "Ongoing at Day 14".

A listing of patient disposition data will be provided.

6. Demographic data and baseline characteristics

Standard summary statistics (number of available observations, mean, standard deviation, quartiles, minimum, median, maximum), or the number (%) of patients will be used, as appropriate. The following demographics and baseline characteristics will be provided to the DSMB:

- Patient demographics: sex, race, age, body weight, height, body mass index (BMI), BMI category (<25 kg/m², >=25 kg/m²).
- Baseline disease characteristics:
  - Pre-dose P. vivax / P. falciparum asexual forms count (/µL), screening P. vivax / P. falciparum gametocytes count (/µL), screening P. vivax / P. falciparum total count (sum of asexual forms and gametocytes) determined by both microscopy and qPCR with descriptive measures.
  - Pre-dose body temperature with descriptive measures and with number (%) of patients with or without fever at baseline, as defined in Section 3, number (%) of patients with history of fever within 24 hours.
  - Pre-dose malaria signs and symptoms with number (%) of patients

Listings of demographic data and baseline characteristics will be provided.

7. Concomitant medication

Concomitant medication will be listed by patient. These will include ATC classification and WHO preferred terms.

8. Safety analyses

8.1 Adverse events

All adverse events (AEs) will be coded according to the most recent version of the MedDRA dictionary. Only treatment emergent AEs will be considered, i.e. AEs which newly started or increased in intensity after the study drug administration. For all summaries the worst case approach will be taken, i.e. the maximum severity by patient will be summarised, as will the closest relationship to study drug. Although every effort will be taken on the data management side to avoid missing data, a missing category will be added to the tables, if needed.

The following AE summaries will be generated:

- An overview table of the number (%) of patients with any AE, any SAE, any study drug related AE/SAE, any AE leading to withdrawal.
- Number (%) of patients with AEs by MedDRA primary system organ class and preferred term, including the number of events. The number of events will be defined as all occurrences of an AE, i.e., if a patient reported headache twice, it will be counted as two events.
- Number (%) of patients with study drug related AEs by MedDRA primary system organ class and preferred term, including the number of events.
- Number (%) of patients with serious AEs by MedDRA primary system organ class and preferred term, including the number of events.
- Number (%)of patients with serious drug-related AEs by MedDRA primary system organ class and preferred term, including the number of events.
- Listings of all AEs and of all serious AEs.

8.2 Dermatotoxicity

Potential dermatotoxicity will be evaluated based on the occurrence of the following AEs:

- Dermatitis
- Rash (rash, erythematous rash, macular rash, papular rash, maculo-papular rash, pruritic rash, pustular rash, vesicular rash)

MedDRA dictionary preferred terms related to "rash" and dermatitis as per the attached excel spreadsheet will be used to identify potential dermatitis events. These will then be flagged in the AE listings and will be subject to a medical review.

MEDDRA_terms_to identify_potential der

8.3 Clinical laboratory data

8.3.1 Haematotoxicity

For haemoglobin, incidence rates of patients having a haemoglobin fall of more than 2 g/dl (i.e., a decrease from baseline < -2 g/dL) will be summarized.

For absolute neutrophils the number (%)of patients with a value below 1,000 /µL post baseline will be provided.

Spaghetti plots of haemoglobin values, absolute neutrophil counts and platelets until Day 14 (absolute values and changes from baseline) for all patients will be provided.

A summary table with descriptive statistics of platelets over time and changes from baseline will be provided.

8.3.2 Hepatotoxicity

The number (%)of patients with treatment emergent liver enzyme elevations as defined below will be summarized. Treatment emergent is defined as not meeting the criterion at any pre-treatment measurement.

- ALT or AST > 3*ULN with appearance / worsening of fatigue, nausea, vomiting, fever, rash, or eosinophilia
- ALT or AST > 5*ULN (raise rapidly in less than 4 weeks or persists for >2 weeks
- ALT or AST > 8*ULN
- ALT or AST > 3*ULN and Bilirubin > 2*ULN, at the same time point, if conjugated bilirubin >35% (Potential Hy's law cases).

The following figures will be provided for liver enzyme data of all patients:

- Scatter plot of peak bilirubin versus peak ALT (e-dish graph).
- Spaghetti plots of liver function tests and of their changes from baseline over time (AST, ALT, total bilirubin, alkaline phosphatase).

Listings of all clinical laboratory data per patient will be provided. Potentially notably abnormal values, as defined above will be flagged.

8.4 ECG data

8.4.1 Cardiotoxicity

The number (%) of patients with treatment emergent QTc values based on Fridericia's formula as defined in the DMC DSMB Charter and below will be summarized. Treatment emergent is defined as not meeting the criterion at any pre-treatment measurement.

- QTcF prolongation >60 ms
- QTcF at any time >450 ms

The same will be repeated for QTc values calculated based on Bazett's formula, even though not mentioned in the DSMB Charter and study protocol.

Potential QTc prolongations will be evaluated by tabulating the changes from pre dose (Day 0) ECG to each time point and worst post baseline (highest post dosing value) according to the categories:

- <= 0 msec (no change, decrease)
- > 0 - < 30 msec
- 30 - 60 msec
- > 60 msec

Further, absolute post dose QTc values will be summarized with the following categories:

- <= 450 msec
- >450 - < 480 msec
- >480 - < 500 msec
- >500 msec

will be summarised per time point and for the highest post dose value. These tabulations will be presented for QTcF and QTcB.

Box-whisker plots of QTcF and QTcB values over time will be provided.

A listing of all ECG data per patient will be provided with the above values flagged accordingly.

8.5 Vital signs

Spaghetti plots of vital signs over time and of corresponding changes from baseline will be provided.

9. Efficacy analyses

9.1 Primary efficacy endpoints

The primary efficacy endpoints are crude ACPR for P. vivax and PCR-corrected ACPR for P. falciparum.

The number (%) of ACPR responders (PCR-corrected ACPR responders for P. falciparum, if available) and the associated 95% confidence interval calculated according to the Clopper Pearson method will be displayed. Further, the number (%) of treatment failures and the reason for treatment failure (ETF, LPF, LCF) will be tabulated.

The interim efficacy analyses will be performed using the mITT set.

Listings of all parasite count data determined by microscopy by patient, of PCR correction results, if available and of parasite count data determined by qPCR, if available will be provided.

10. Pharmacokinetic (PK) data

If available, PK data will be listed and graphically displayed by patient over time (reported values and log-transformed values). Further listings of PK concentration data and individual summary values (C_{max}, t_{max}, area under the plasma concentration curve [AUC]) will be provided. The latter will also be summarized by cohort with geometric mean and CV% for C_{max} and AUC and with median and range for t_{max}.

11. List of outputs

12. Table shells

DSMB Table 1 Patient disposition (Safety set)
(Page 1 of 1)

	Cohort XX	Cohort YY
Patients enrolled	xxx (100.0)	
Patients treated	xx (xx.x)	
Patients completed	xx (xx.x)	
Patient continuing at Day 14	xx (xx.x)	
Withdrawn from study prematurely	xx (xx.x)	
Reason 1	xx (xx.x)	
Reason 2	xx (xx.x)	
Reason 3	xx (xx.x)	

etc.

Note: Percentages are based on the number of enrolled patients.

Programming note: Display all potential reasons for withdrawal from the CRF, even if no patient fulfilled the reason.

RELATED TO ALL TABLES
Data for all cohorts recruited up to the time point of the DSMB analysis will be displayed (one column per cohort).

DSMB Table 2 Demographic characteristics at screening (Safety set)
(Page 1 of 3)

Variable/ Statistic/Category	Cohort XX (N=xx)	Cohort YY (N=xx)
Gender, n (%)		
Male	xx (xx.x)	
Female	xx (xx.x)	
Age (years)		
Available observations	xx	
Mean	xx.x	
Standard deviation	x.xx	
Minimum	xx	
Q1	xx.x	
Median	xx	
Q3	xx.x	
Maximum	xx	
Race, n (%)		
Caucasian	xx (xx.x)	
Black	xx (xx.x)	
Asian/Oriental	xx (xx.x)	
Other	xx (xx.x)	

Missing values were not included in the calculation of percentages.
Body mass index = weight in kg / (height in m)**2

DSMB Table 2 Demographic characteristics at screening (Safety set)
(Page 2 of 3)

Variable/ Statistic/Category	Cohort XX (N=xx)	Cohort YY (N=xx)
Height (cm)		
Available observations	xx	
Mean	xxx.x	
Standard deviation	xx.xx	
Minimum	xxx	
Q1	xxx	
Median	xxx.x	
Q3	xxx	
Maximum	xxx	
Body weight (kg)		
Available observations	xx	
Mean	xx.x	
Standard deviation	x.xx	
Minimum	xx.x	
Q1	xx.x	
Median	xx.x	
Q3	xx.x	
Maximum	xx.x	

Missing values were not included in the calculation of percentages.
Body mass index = weight in kg / (height in m)**2

DSMB Table 2 Demographic characteristics at screening (Safety set)
(Page 3 of 3)

Variable/ Statistic/Category	Cohort XX (N=xx)	Cohort YY (N=xx)
Body mass index (kg/m**2)		
Available observations	xx	
Mean	xx.xx	
Standard deviation	x.xxx	
Minimum	xx.x	
Q1	xx.xx	
Median	xx.xx	
Q3	xx.xx	
Maximum	xx.x	
Body mass index category , n (%)		
<= 25 kg/m**2	xx (xx.x)	
>25 kg/m**2	xx (xx.x)	
Missing	x (-)	

Missing values were not included in the calculation of percentages.
Body mass index = weight in kg / (height in m)**2

DSMB Table 3 Baseline disease characteristics (Safety set)
(Page 1 of 3)

Variable/ Statistic/Category	Cohort XX (N=xx)	Cohort YY (N=xx)
Pre - dose asexual parasites (/uL) determined by microscopy		
Available observations	xx	
Geometric mean *	xxxx.x	
Mean	xxxx.x	
Standard deviation	xxxx.x	
Minimum	xxxx.x	
Q1	xxxx.x	
Median	xxxx.x	
Q3	xxxx.x	
Maximum	xxxx.x	
Pre - dose g ametocytes determined by microscopy, n (%)		
Yes	xx (xx.x)	
No	xx (xx.x)	
Pre - dose total p arasites (/uL) determined by microscopy		
Available observations	xx	
Geometric mean *	xxxx.x	
Mean	xxxx.x	
Standard deviation	xxxx.x	
Minimum	xxxx.x	
Q1	xxxx.x	
Median	xxxx.x	
Q3	xxxx.x	
Maximum	xxxx.x	

* Geometric mean was only calculated if all counts were > 0.

DSMB Table 3 Baseline disease characteristics (Safety set)
(Page 2 of 3)

Variable/ Statistic/Category	Cohort XX (N=xx)	Cohort YY (N=xx)
Pre - dose asexual parasites (/uL) determined by qPCR		
Available observations	xx	
Geometric mean *	xxxx.x	
Mean	xxxx.x	
Standard deviation	xxxx.x	
Minimum	xxxx.x	
Q1	xxxx.x	
Median	xxxx.x	
Q3	xxxx.x	
Maximum	xxxx.x	
Pre - dose g ametocytes determined by qPCR, n (%)		
Yes	xx (xx.x)	
No	xx (xx.x)	

* Geometric mean was only calculated if all counts were >0.

DSMB Table 3 Baseline disease characteristics (Safety set)
(Page 3 of 3)

Variable/ Statistic/Category	Cohort XX (N=xx)	Cohort YY (N=xx)
Pre - dose b ody temperature, n (%)		
No fever	xx (xx.x)	
Fever	xx (xx.x)	
Descriptive statistics (°C)		
Available observations	xx	
Mean	xx.x	
Standard deviation	x.xx	
Minimum	xx.x	
Q1	xx.x	
Median	xx.x	
Q3	xx.x	
Maximum	xx.x	

DSMB Table 4 Pre-dose signs and symptoms of malaria (Safety set)

(Page 1 of n)

Malaria symptoms	Cohort XX (N=xx) n (%)	Cohort YY (N=xx)
Any	xx (xx.x)	
Symptom 1	xx (xx.x)	
Symptom 2	xx (xx.x)	
etc.		

DSMB Table 5.1 Overview of adverse events (Safety set)

(Page 1 of 1)

	Cohort XX (N=xx)	Cohort YY (N=xx)
Number (%) of patients with	n (%)	
Any adverse event	xx (xx.x)	
Any drug - related adverse event	xx (xx.x)	
Any serious adverse event	xx (xx.x)	
Any serious drug - related adverse event	xx (xx.x)	
Any adverse event leading to death	xx (xx.x)	
Any adverse event leading to withdrawal from study	xx (xx.x)	

DSMB Table 5.2 Incidence of all adverse events by MedDRA primary system organ class and preferred term (Safety set)
(Page 1 of n)

Primary system organ class Preferred term	Cohort XX (N=xx) n (%) /# events	Cohort YY (N=xx)
At least one adverse event	xx (xx.x) / xx	
Primary system organ class 1	xx (xx.x) / xx	
Preferred term 1	xx (xx.x) / xx	
Preferred term 2	xx (xx.x) / xx	
Primary system organ class 2	xx (xx.x) / xx	
Preferred term 1	xx (xx.x) / xx	
Preferred term 2	xx (xx.x) / xx	
etc.		

A patient with more than one adverse events within a primary system organ class is counted only once for that class.

DSMB Table 5.3 Incidence of adverse events considered to be study drug related by MedDRA primary system organ class and preferred term (Safety set)

Programming note: Same shell as Table 5.2;

DSMB Table 5.4 Incidence of all adverse events by MedDRA primary system organ class, preferred term and maximal severity (Safety set)

(Page 1 of n)

Maximal severity	Primary SOC	Preferred term	Cohort XX (N=xx) n (%)	Cohort YY (N=xx) n (%)
Total	At least one AE	Total	xxx (xx.x)	
Mild			xxx (xx.x)	
Moderate			xxx (xx.x)	
Severe			xxx (xx.x)	
Total	Primary SOC	Total	xxx (xx.x)	
Mild			xxx (xx.x)	
Moderate		Preferred term 1	xxx (xx.x)	
			xxx (xx.x)	
etc.				

If a patient reported more than one adverse event within the same category, the worst severity was summarised.
A patient with more than one adverse event within a primary system organ class is counted only once for that class.

DSMB Table 5.5 Incidence of all adverse events considered to be study drug related by MedDRA primary system organ class, preferred term and maximal severity (Safety set)

Programming note: Same shell as Table 5.4

DSMB Table 5.6 Incidence of serious adverse events by MedDRA primary system organ class and preferred term (Safety set)

Programming note: Same shell as Table 5.2

DSMB Table 5.7 Incidence of serious adverse events considered to be study drug related by MedDRA primary system organ class and preferred term (Safety set)

Programming note: Same shell as Table 5.2 ; Additional footnote: Study drug related = possibly, probably or definitely related to study drug.

DSMB Table 5.8 Incidence of adverse events related to dermatotoxicity by MedDRA primary system organ class and preferred term

Programming note: Same shell as Table 5.2; Present dermatotoxicity related AEs.

DSMB Table 6 Number (%) of patients with treatment emergent potential haematotoxicity (Safety set)
(Page 1 of 1)

Time point	Criterion	Cohort XX (N=xx) n /m (%)	Cohort YY (N=xx)
At any time post dose	Haemoglobin change > - 2 g/dL	xx / xx (xx.x)	
	Abs. neutrophil count <1,000 /uL	xx / xx (xx.x)	
At any time post dose until Day 14 inclusive	Haemoglobin change > - 2 g/dL	xx / xx (xx.x)	
	Abs. neutrophil count <1,000 /uL	xx / xx (xx.x)	
24 h post dose	Haemoglobin change > - 2 g/dL	xx / xx (xx.x)	
	Abs. neutrophil count <1,000 /uL	xx / xx (xx.x)	
48 h post dose	Haemoglobin change > - 2 g/dL	xx / xx (xx.x)	
	Abs. neutrophil count < 1,000 /uL	xx / xx (xx.x)	
Day 7	Haemoglobin change > - 2 g/dL	xx / xx (xx.x)	
	Abs. neutrophil count <1,000 /uL	xx / xx (xx.x)	
Day 10/11	Haemoglobin change > - 2 g/dL	xx / xx (xx.x)	
	Abs. neutrophil count <1,000 /uL	xx / xx (xx.x)	
etc.			

n is the number of patients fulfilling the criterion at the time point of interest.
m is the number of patients with a corresponding measurement at the time point of interest.
Treatment emergent = present after dosing but not present before dosing.

DSMB Table 7 Number (%) of patients with treatment emergent liver enzyme elevation (Safety set)

(Page 1 of 1)

Time point				Cohort XX (N=xx) n /m (%)	Cohort YY (N=xx)
At any time post dose	ALT or AST > 3*ULN			xx / xx (xx.x)	
	ALT or AST > 5 *ULN			xx / xx (xx.x)	
	ALT or AST > 8 *ULN			xx / xx (xx.x)	
	ALT or AST > 3*ULN	and Bilirubin >	2*ULN	xx / xx (xx.x)	
At any time post dose until Day 14 inclusive	ALT or AST > 3*ULN			xx / xx (xx.x)	
	ALT or AST > 5 *ULN			xx / xx (xx.x)	
	ALT or AST > 8 *ULN			xx / xx (xx.x)	
	ALT or AST > 3*ULN	and Bilirubin >	2*ULN	xx / xx (xx.x)	
24 h post dose	ALT or AST > 3*ULN			xx / xx (xx.x)	
	ALT or AST > 5 *ULN			xx / xx (xx.x)	
	ALT or AST > 8 *ULN			xx / xx (xx.x)	
	ALT or AST > 3*ULN	and Bilirubin >	2*ULN	xx / xx (xx.x)	
etc.					

n is the number of patients fulfilling the criterion at the time point of interest.
m is the number of patients with a corresponding measurement at the time point of interest.
For combined criteria, the criteria have to be fulfilled at the same visit.
Treatment emergent = present after dosing but not present before dosing.

DSMB Table 8 Summary of platelets and changes form baseline in platelets over time (Safety set)
(Page 1 of 1)

	Time point	n	Mean	SD	Minimum	Q1	Median	Q3	Maximum
Cohort XX (N=xx)									
Absolute values	Baseline	xx	xxx.x	xx.xx	xxx	xxx.x	xxx.x	xxx.x	xxx
	12 hours	xx	xxx.x	xx.xx	xxx	xxx.x	xxx.x	xxx.x	xxx
	24 hours	xx	xxx.x	xx.xx	xxx	xxx.x	xxx.x	xxx.x	xxx
	48 hours	xx	xxx.x	xx.xx	xxx	xxx.x	xxx.x	xxx.x	xxx
	Day 7	xx	xxx.x	xx.xx	xxx	xxx.x	xxx.x	xxx.x	xxx
	Day 10	xx	xxx.x	xx.xx	xxx	xxx.x	xxx.x	xxx.x	xxx
	etc.	xx	xxx.x	xx.xx	xxx	xxx.x	xxx.x	xxx.x	xxx
Changes from baseline	12 hours	xx	xx.x	xx.xx	xx	xx.x	xx.x	xx.x	xx
	24 hours	xx	xx.x	xx.xx	xx	xx.x	xx.x	xx.x	xx
	etc.								

DSMB Table 9 Number (%) of patients with treatment emergent potential notably abnormal QTcF or QTcB values (Safety set)
(Page 1 of 1)

Time point		Cohort XX (N=xx) n /m (%)	Cohort YY (N=xx)
At any time post dose	QTcF > 450 ms	xx / xx (xx.x)	
	QTcF increase from baseline >60 ms	xx / xx (xx.x)	
	QTcB > 450 ms	xx / xx (xx.x)	
	QTcB increase from baseline >60 ms	xx / xx (xx.x)	
At any time post dose until Day 14 inclusive	QTcF > 450 ms	xx / xx (xx.x)	
	QTcF increase from baseline >60 ms	xx / xx (xx.x)	
	QTcF > 450 ms	xx / xx (xx.x)	
	QTcF increase from baseline >60 ms	xx / xx (xx.x)	
24 h post dose	QTcF > 450 ms	xx / xx (xx.x)	
	QTcF increase from baseline >60 ms	xx / xx (xx.x)	

etc.

n is the number of patients fulfilling the criterion at the time point of interest.
m is the number of patients with a corresponding measurement at the time point of interest.
Treatment emergent = present after dosing but not present before dosing.

DSMB Table 10 Number (%) of patients by QTcF / QTcB category and change from pre dose in QTcF / QTcB category (Safety set)
(Page 1 of 1)

Time point	Criterion	Cohort XX n / m (%)	Cohort YY (N=xx)
At any time post dose	Absolute values		
	<=450 msec	xx / xx (xx.x)	
	>450 - 480 msec	xx / xx (xx.x)	
	>480 - 500 msec	xx / xx (xx.x)	
	>=500 msec	xx / xx (xx.x)	
	Increase between actual value and pre dose		
	<= 0 msec (decrease)	xx / xx (xx.x)	
	>0 - 30 msec	xx / xx (xx.x)	
	>30 – 60 msec	xx / xx (xx.x)	
	>60 msec	xx / xx (xx.x)	
At any time post dose until Day 14 inclusive	….		
24 h post dose			
etc.			

n is the number of patients fulfilling the criterion at the time point of interest.
m is the number of patients with a corresponding measurement at the time point of interest.
Programming note: Continue with further time points and QTcB

DSMB Table 11 Number (%) of patients with Day 14 ACPR response (mITT set)

(Page 1 of 1)

		Cohort XX (N=xx)	Cohort YY (N=xx)
Crude ACPR	Available observations	xx	
	Number (%) of patients with ACPR	xx (xx.x)	
	95% Clopper Pearson confidence interval	(xx.x, xx.x)	
	Number (%) of treatment failures	xx (xx.x)	
	Early treatment failure	xx (xx.x)	
	Late clinical failure	xx (xx.x)	
	Late parasitological failure	xx (xx.x)	
PCR corrected ACPR	Available observations	xx	
	Number (%) of patients with ACPR	xx (xx.x)	
	95% Clopper Pearson confidence interval	(xx.x, xx.x)	
	Number (%) of treatment failures	xx (xx.x)	
	Early treatment failure	xx (xx.x)	
	Late clinical failure	xx (xx.x)	
	Late parasitological failure	xx (xx.x)	

The minimum Day 14 ACPR responder count to meet the cohort success criteria is 14 out of 17 patients.
A responder count of 11 to 13 out of 17 patients is regarded as inconclusive and the dose may be repeated in a subsequent cohort.
The maximum Day 14 ACPR responder count to declare futility of a dose level after one cohort is 10 out of 17 patien ts.

Programming note: PCR-corrected ACPR only for P. falciparum and only if available. Footnotes will be adjusted if the same dose is repeated during the study.

DSMB Table 12 Plasma pharmacokinetic variable of MMV390048

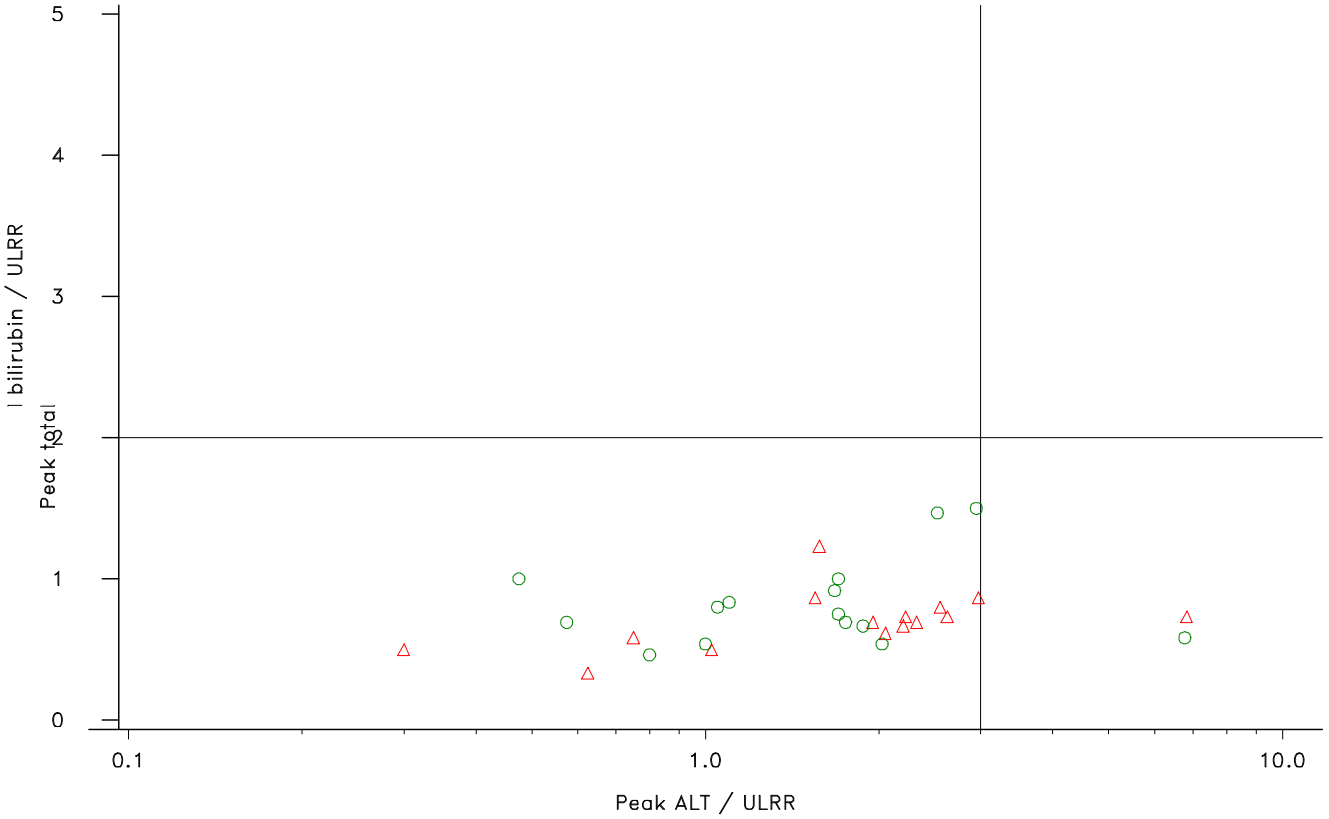
(Page 1 of 1)

Variable	Statistic	Cohort XX (N=xx)	Cohort YY (N=xx)
Cmax	n	xx	
	geometric mean	xxx.x	
	CV%	xxx.x	
tmax	n	xx	
	Median	xx.x	
	Minimum	xx.x	
	Maximum	xx.x	
AUC(last)	n	xx	
	geometric mean	xxx.x	
	CV%	xxx.x	
AUC(inf)	n	xx	
	geometric mean	xxx.x	
	CV%	xxx.x	

Programming note: will only be delivered if PK data is available.

DSMB Figure 1 Scatter plot of peak post dose total bilirubin versus peak ALT until and including Day 14 (Safety set)
(Page 1 of 1)

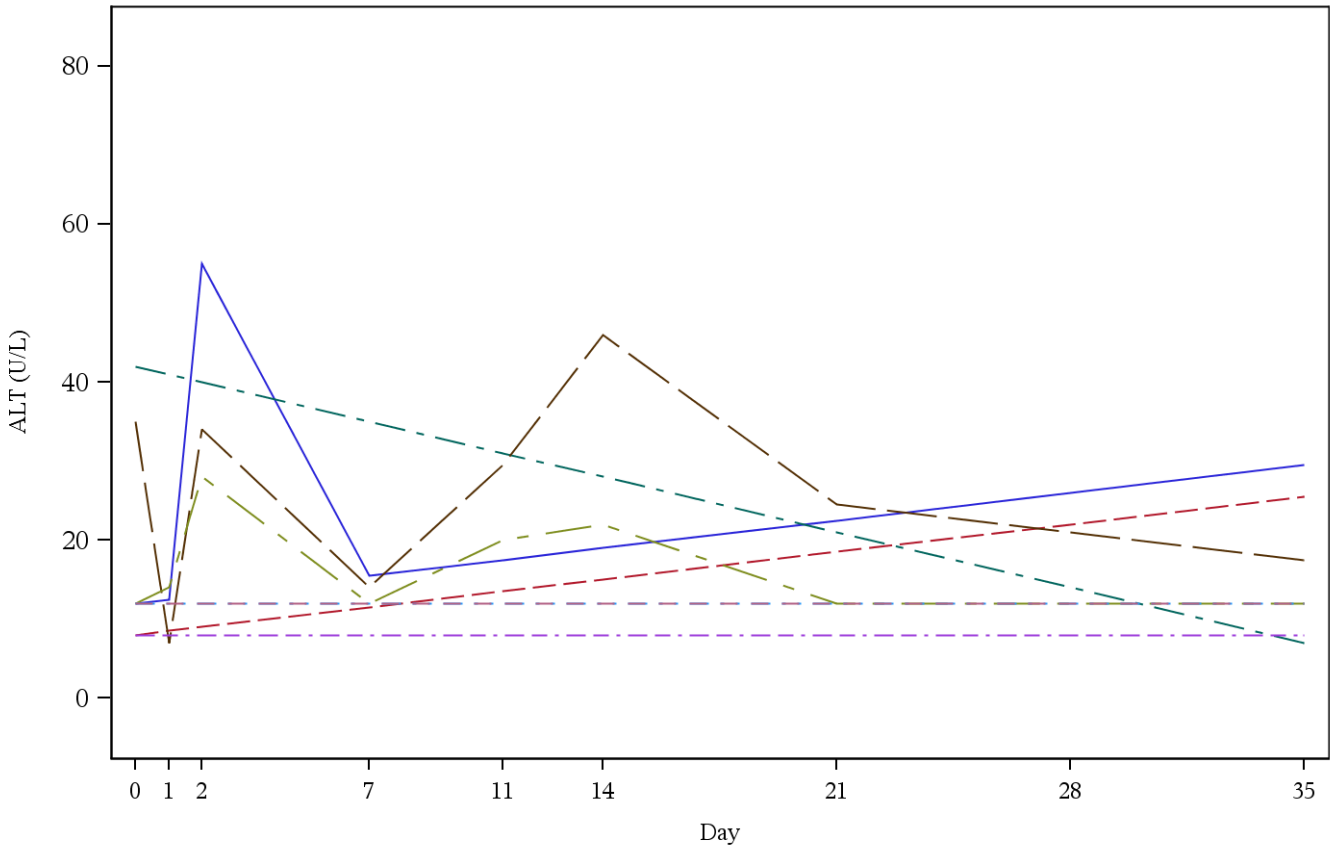
Cohort XX: P. xxxxxxxx, xxx mg



Programming note: The figure will be similar to the above. The same symbol will be used for all patients.

DSMB Figure 2 Spaghetti plot of haemoglobin and changes from baseline in haemoglobin over time (Safety set)
(Page 1 of 2)

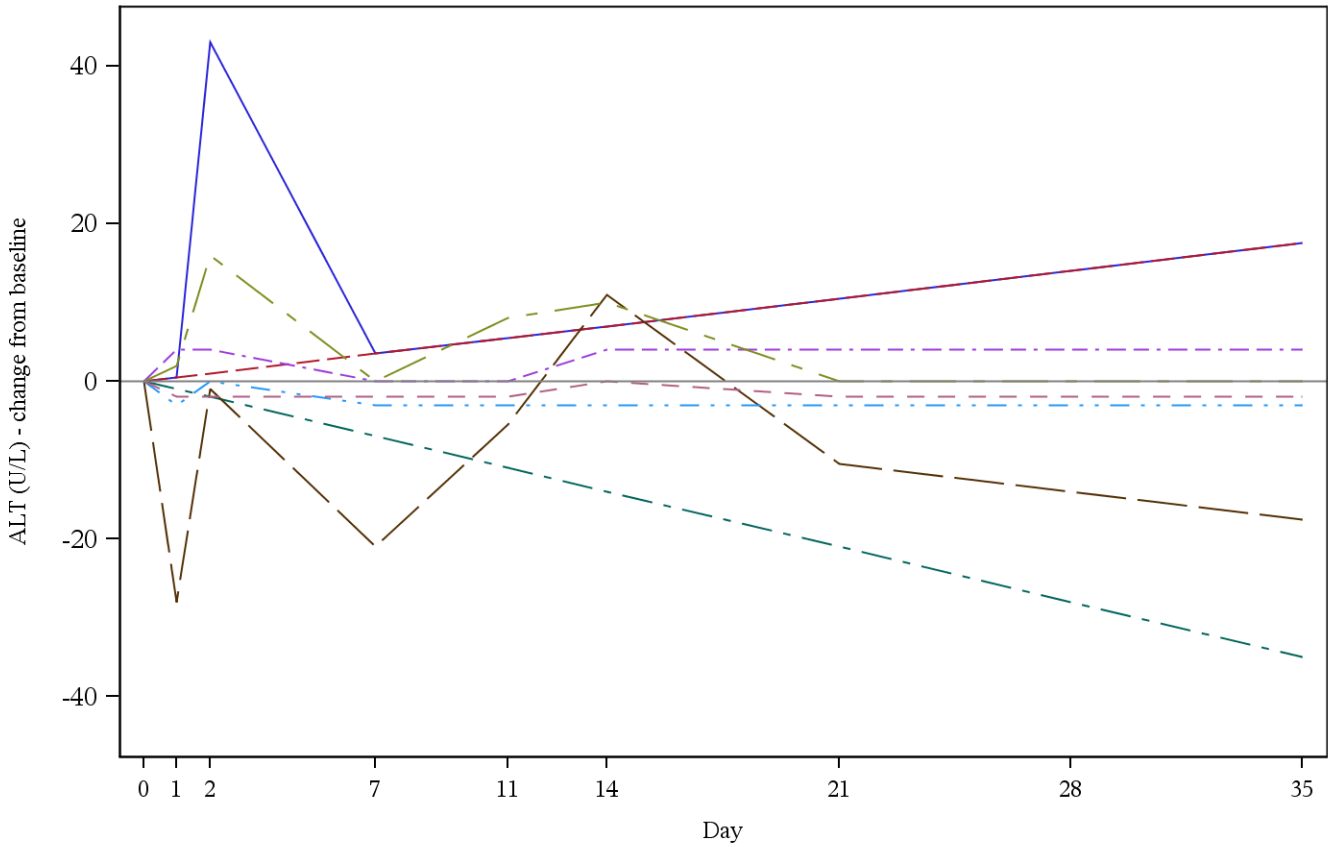
Cohort XX: P. xxxxxxxx, xxx mg



Programming note: Figure will be similar to the above. Unit and y axis will be changed appropriately. Present changes from baseline scatterplot on second page. Days 21, 28 and 35 will only be displayed if data available.

DSMB Figure 2 Spaghetti plot of haemoglobin and changes from baseline in haemoglobin over time (Safety set)
(Page 2 of 2)

Cohort XX: P. xxxxxxxx, xxx mg



Programming note: Figure will be similar to the above. Unit and y axis will be changed appropriately. Present changes from baseline scatterplot on second page. Days 21, 28 and 35 will only be displayed if data available.

DSMB Figure 3 Spaghetti plot of absolute neutrophils and changes from baseline in absolute neutrophils over time (Safety set)
Programming note: Same layout as Figure 2 for absolute neutrophils

DSMB Figure 4 Spaghetti plot of platelets and changes from baseline in platelets over time (Safety set)
Programming note: Same layout as Figure 2 for platelets

DSMB Figure 5 Spaghetti plot of ALT and changes from baseline in ALT over time (Safety set)
Programming note: Same layout as Figure 2 for ALT

DSMB Figure 6 Spaghetti plot of AST and changes from baseline in AST over time (Safety set)
Programming note: Same layout as Figure 2 for AST

DSMB Figure 7 Spaghetti plot of total bilirubin and changes from baseline in total bilirubin over time (Safety set)
Programming note: Same layout as Figure 2 for total bilirubin

DSMB Figure 8 Spaghetti plot of alkaline phosphatase and changes from baseline in alkaline phosphatase over time (Safety set)
Programming note: Same layout as Figure 2 for alkaline phosphatase

DSMB Figure 9 Spaghetti plot of systolic blood pressure and changes from baseline in systolic blood pressure over time (Safety set)

Programming note: Same layout as Figure 2 for systolic blood pressure. If necessary due to the amount of assessment time points, results obtained during the first 3 days will be shown separately.

DSMB Figure 10 Spaghetti plot of diastolic blood pressure and changes from baseline in diastolic blood pressure over time (Safety set)

Programming note: Same layout as Figure 2 for diastolic blood pressure. If necessary due to the amount of assessment time points, results obtained during the first 3 days will be shown separately.

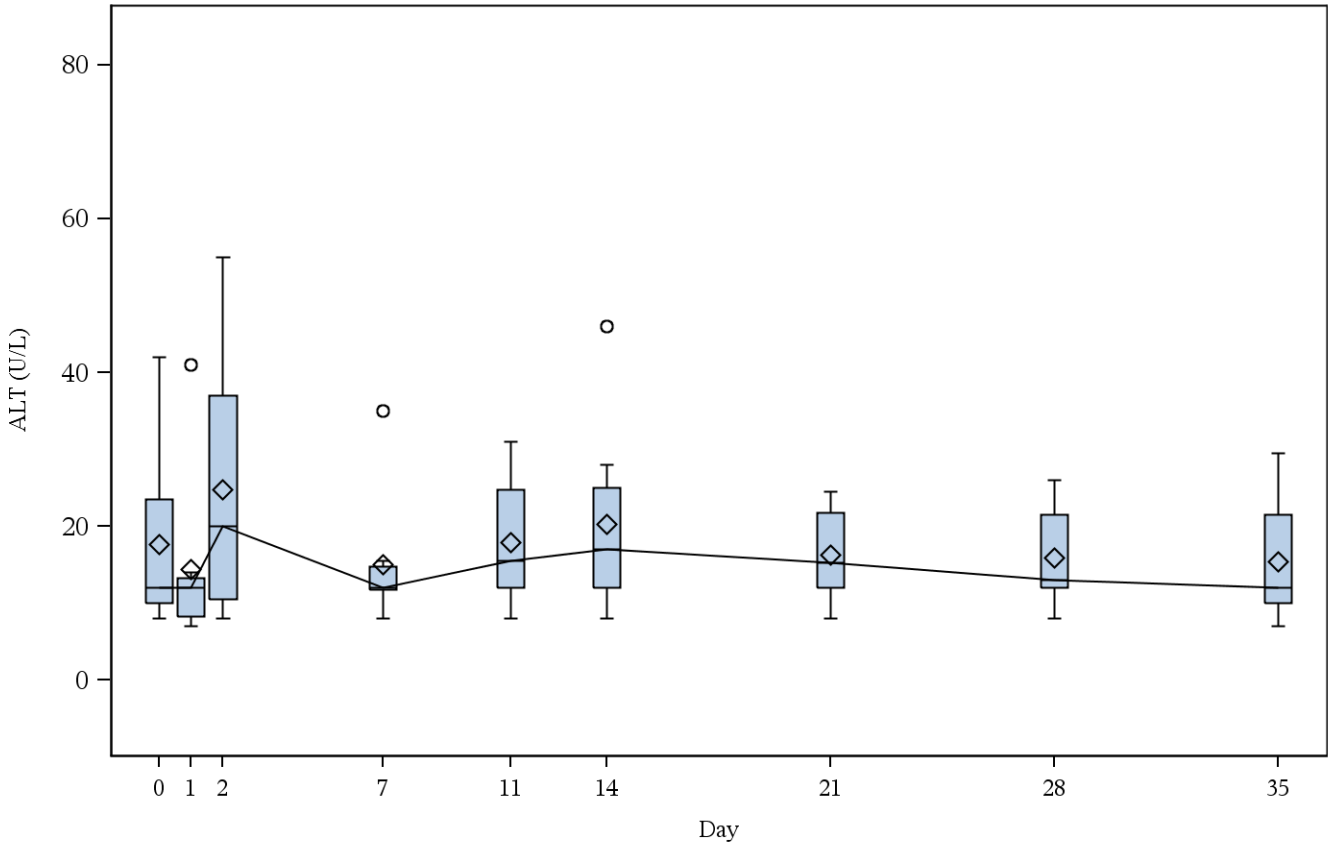
DSMB Figure 11 Spaghetti plot of pulse rate and changes from baseline in pulse rate over time (Safety set)

Programming note: Same layout as Figure 2 for pulse. If necessary due to the amount of assessment time points, results obtained during the first 3 days will be shown separately.

DSMB Figure 12 Spaghetti plot of body temperature and changes from baseline in body temperature over time (Safety set)

Programming note: Same layout as Figure 2 for pulse. If necessary due to the amount of assessment time points, results obtained during the first 3 days will be shown separately.

DSMB Figure 13 Box-Whisker plot of QTcF values over time (Safety set)



Programming note: This figure will be similar to the above showing QTcF values from the ECGs. The axes will be adjusted and labelled accordingly.

DSMB Figure 14 Box-Whisker plot of QTcB values over time (Safety set)

Programming note: Same layout as Figure 10

DSMB Figure 15 PK concentrations over time by patient (Safety set)

Programming note: This figure will display the individual PK concentration measurements by patient over time. The data for each patient will be displayed in a separate curve and several plots (4 or 6) will displayed on one page. Both log transformed and raw values.

DSMB Listing 1 Study completion (Safety set)
(Page 1 of n)

Cohort XX: P. xxxxxxxx, xxx mg

Pat. No.	Age/ Sex/ Race	Completed	Date/day of withdrawal/ completion	Primary reason for withdrawal
xxx xx	xx /F/Bl	No	ddMMMyyyy/x	xxxxxxxxxxxxxxxxxxxx
etc.				

DSMB Listing 2 Protocol deviations (Safety set)

(Page 1 of n)

Cohort XX: P. xxxxxxxx, xxx mg

Pat. No.	Age/ Sex/ Race	Protocol deviation	Details	Deviation day/day
xxxx	xx/F/Black	xxxxxxxxxxxx	xxxxxxxxxxxxxxxxxxxx	
etc.				

DSMB Listing 3 Demographic data (Safety set)
(Page 1 of n)

Cohort XX: P. xxxxxxxx, xxx mg

Pat. No.	Age/ Sex/ Race	Year of birth	Date of enrolment	Height (cm)	Body weight (kg)	BMI (kg/m**2)	Ethnicity
xxxx	xx /F/ Black	yyyy	ddMMMyyyy	xxx	xx.x	xx.x	xxxxxxxxxxxxx
etc.							

BMI = Weight (kg)/[Height (m)]**2

DSMB Listing 4 Blood film microscopy data (Safety set)

(Page 1 of n)

Cohort XX: P. xxxxxxxx, xxx mg

Pat. No.	Age/ Sex/ Race	Visit	Collection date/ day/time hours since dosing	P. <xxxxxx> x /µL asexual	gametocytes	Other species xxxxxx	ovale	malariae
xxxx	xx/F/ Black	D0	ddMMMyyyy/xx/hh:mm/xx.x	xx,xxx	0	No	No	No
			ddMMMyyyy/xx/hh:mm/xx.x	xx,xxx	xx	No	No	No
			ddMMMyyyy/xx/hh:mm/xx.x	xx,xxx	0			
etc.								

Programming note: For P. vivax cohorts present P. vivax counts; for P. falciparum cohort present P. falciparum counts in <xxxxxx> column and the other specimen under "Other". If available, add PCR result in case of re-appearance of parasites.

DSMB Listing 5 qPCR data (Safety set)

(Page 1 of n)

Cohort XX: P. xxxxxxxx, xxx mg

Pat. No.	Age/ Sex/ Race	Visit	Collection date/ day/time hours since dosing	P. <xxxxxx>x /µL asexual	gametocytes	Other species xxxxxx	ovale	malariae
xxxx	xx /F/ Black	D0	ddMMMyyyy/xx/hh:mm/xx.x	xx,xxx	0	No	No	No
			ddMMMyyyy/xx/hh:mm/xx.x	xx,xxx	xx	No	No	No
			ddMMMyyyy/xx/hh:mm/xx.x	xx,xxx	0			
etc.								

Programming note: For P. vivax cohorts present P. vivax counts; for P. falciparum cohort present P. falciparum counts in <xxxxxx> column and the other specimen under "Other".

DSMB Listing 6 Study drug administration (Safety set)
(Page 1 of n)

Cohort XX: P. xxxxxxxx, xxx mg

Pat. No.	Age/ Sex/ Race	Date/time of dosing	Number of tablets	Patient vomited	Date/time of vomiting	Dose repeated	Number of tablets	Date/time of repeat dose	Repeat dose vomited
xxxx	xx /F/ Black	ddMMMyyyy/hh:mm	xx	Yes	ddMMMyyyy/hh:mm	Yes		ddMMMyyyy/ hh:mm	Yes

etc.

DSMB Listing 7 Adverse events (Safety set)
(Page 1 of n)

Cohort XX: P. xxxxxxxx, xxx mg

Pat. No.	Age/ Sex/ Race	SAE	Adverse event INVESTIGATOR TERM/ Preferred term/SOC	Start date/ day	Stop day/ day	Severity	Relationship with Study drug	(1)	(2)	Action taken	Outcome
xxxx	xx /F/Bl	No	XXXXXXXXXXXX/ * xxxxxxxxxxxxx/xxxx	ddMMMyyyy/ xx	ddMMMyyyy/ xx	mild	possible	none	none	none	resolved
etc.											

Day 0 is defined as the date of study drug administration.
Action taken: 1 = Patient withdrawn from study , 2 = Concomitant medication, 3 = Hospitalization required or prolonged
4 = Administration of non - drug therapy , 5 = Other actions taken, please specify
(1) Definitive anti malaria therapy, (2) malaria
* Potential dermatotoxicity event

DSMB Listing 8 Haematology values, by parameter (Safety set)
(Page 1 of n)

Cohort XX: P. xxxxxxxx, xxx mg

Pat. No.	Age/ Sex/ Race	Parameter	Unit	Normal range	Visit	Sampling date/ time/hours since	day/ dose	Value/ (L/H)		Clinically significant
xxxx	xx /F/Black	Haemoglobin	g/dL	xx.x - xx.x	Day 0	ddMMMyyyy/ 0	/hh:mm /xxx.x	xx.x /	L	No
					24 hours	ddMMMyyyy/ 3	/hh:mm /xxx.x	xx.x /	H	Yes
					48 hours	ddMMMyyyy/ 7	/hh:mm /xxx.x	xx.x /	L	No

etc.

Note: Day 0 is defined as the date of study drug administration.
L denotes a value below the normal range, H a value above the normal range.

Programming note: Haematology variables haemoglobin, haematocrit, erythrocytes (RBC), platelets, reticulocytes, white blood cells (WBC), neutrophils, lymphocytes, monocytes, eosinophils, basophils will be presented. Decimal places will be adapted as appropriate.

DSMB Listing 9 Biochemistry values, by parameter (Safety set)
(Page 1 of n)

Cohort XX: P. xxxxxxxx, xxx mg

Pat. No.	Age/ Sex/ Race	Parameter	Unit	Normal range	Visit	Sampling date/ day/ time/hours since dose	Value/ (L/H)	Clinically significant
xxxx	xx /F/Black	AST	U/L	xx.x - xx.x	Day 0	ddMMMyyyy/ 0 /hh:mm/xxx.x	xx.x / L	No
					24 hours	ddMMMyyyy/ 3 /hh:mm/xxx.x	xx.x / H	Yes
					48 hours	ddMMMyyyy/ 7 /hh:mm/xxx.x	xx.x / L	No

etc.

Note: Day 0 is defined as the date of study drug administration.
L denotes a value below the normal range, H a value above the normal range.

Programming note: Biochemistry variables sodium, potassium, creatinine, glucose, total and conjugated bilirubin (conjugated only if total bilirubin is elevated), AST, ALT, alkaline phosphatase, creatinine kinase, and haptoglobin (only if patient had haemogl obin related adverse event of special interest) will be presented. Decimal places will be adapted as appropriate.

DSMB Listing 10 ECG data (Safety set)
(Page 1 of n)

Cohort XX: P. xxxxxxxx, xxx mg

Pat. No.	Age/ Sex/ Race	Visit	ECG date/day/time/ hours since dose	PR (ms)	QRS (ms)	RR (ms)	QT (ms)	QTc Fridericia (ms)	QTc Fridericia Change from baseline	QTc Bazett (ms)	QTc Bazett Change from baseline
xxxx	xx /F/ xxxx	Day 0	ddMMMyyyy/xx/hh:mm/xx	xx	xx	xx	xx	xxx	xxx	xxx	xx
				xx	xx	xx	xx	xxx	xxx	xxx #	xx *

etc.

Note: Day 0 is defined as the date of study drug administration.
QTc (Fridericia / Bazett): # >450 ms, * change from baseline >60 ms.

DSMB Listing 11 ECG abnormalities (Safety set)
(Page 1 of n)

Cohort XX: P. xxxxxxxx, xxx mg

Pat. No.	Age/ Sex/ Race	Visit	ECG date/day/time/ hours since dose	Clinically significant abnormalities	Abnormality details
xxxx	xx/F/Black	Day x	ddMMMyyyy/xx/hh:mm/xx	yes	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
etc.					

DSMB Listing 12 Vital signs (Safety set)
(Page 1 of n)

Cohort XX: P. xxxxxxxx, xxx mg

Pat. No.	Age/ Sex/ Race	Visit	Vital signs date/day/time/ hours since dose		Pulse (bpm)	Systolic BP (mmHg)	Diastolic BP (mmHg)	Body temperature (degree C)	Location of temp. measurement
xxxx	xx /F/ xxxx	Day 0 , Hour 0	ddMMMyyyy/xx/hh:mm/xx	x.x	xx	xxx	xx	xx.x	axillary
		Day 0, Hour 2	ddMMMyyyy/xx/hh:mm/xx	x.x	xx	xxx	xx	xx.x	axillary
		Day 0, Hour 4	ddMMMyyyy/xx/hh:mm/xx	x.x	xx	xxx	xx	xx.x	axillary

etc.

Note: Day 0 is defined as the date of study drug administration.
BP = blood pressure.

DSMB Listing 13 Individual pharmacokinetic concentration data (Pharmacokinetic set)
(Page 1 of n)

Cohort XX: P. xxxxxxxx, xxx mg

Pat. No.	Age/ Sex/ Race	Scheduled time point	Sampling date/day/time/ hours since dose	Concentration (unit)	Concentration (log transformed)
xxxx	xx /F/ xxxx	Day 0 , Hour 0	ddMMMyyyy/xx/hh:mm/xx x.x	xx.x	xx.x
		Day 0, Hour 2	ddMMMyyyy/xx/hh:mm/xx x.x	xx.x	xx.x
		Day 0, Hour 4	ddMMMyyyy/xx/hh:mm/ xx x.x	xx.x	xx.x

etc.

Note: Day 0 is defined as the date of study drug administration.

Programming note: Only provided when data are available.

DSMB Listing 14 Pharmacokinetic summary data (Pharmacokinetic set)
(Page 1 of n)

Cohort XX: P. xxxxxxxx, xxx mg

Pat. No.	Age/ Sex/ Race	Cmax (unit)	tmax (hours)	AUC(last) (unit)	AUC(inf) (unit)
xxxx	xx /F/ Black				
etc.					

Programming note: Only provided when data are available.

DSMB Listing 15 Concomitant medication (Safety set)
(Page 1 of n)

Cohort XX: P. xxxxxxxx, xxx mg

Pat. No.	Age/ Sex/ Race	Treatment INVESTIGATOR TERM Preferred term	/ATC class	Dose / unit / frequency / route	Date/day started	Date/day stopped/	Reason for use
xxxx	xx/F/Bl	xxxxxxxxxxxxxxxx xxxxxxxxxxxxxx	/xxxxxxxx	xxxxxxxx	ddMMMyyyy/xx	ddMMMyyyy/xx	xxxxxxxxxxxxxxxx
etc.							

Note: Day 0 is defined as the date of study drug administration.

DSMB Listing 16 Patient profiles (Safety set)
(Page 1 of n)

This will be a by patient listing of all data collected relevant to the safety and efficacy.