dfnet better data. better insights. better care.

Statistical Analysis Plan

Protocol Title	A Phase 2b randomized, open-label, controlled, single center study in Plasmodium falciparum-infected and uninfected adults age 18-55 years old in Kenya to evaluate the efficacy of the delayed, fractional dose RTS,S/AS01 $_E$ malaria vaccine in subjects treated with artemisinin combination therapy plus primaquine
Protocol Number	CVIA 078, version 5.1, 24 May 2021
Sponsor	PATH
Principal Investigator	[redacted]
Co-Principal Investigator	
Version	4.0
Date	Apr 15th, 2023
ClinicalTrials.gov NCT Number	NCT04661579

Statistical Analysis Plan (SAP) Approval Form

PATH Reviewer Signature
This signature indicates approval for this SAP.

Typed Name/Title	Signature	Date
[redacted] Statistician, PATH	[redacted]	14-Apr-2023

Author Signature
This signature indicates that appropriate and accurate information has been included in this SAP.

Typed Name/Title	Signature	Date
[redacted] Data Sciences Lead, DF/Net Research, Inc.	[redacted]	14-Apr-2023

Revision History

Version	Date	Summary of Revision
0.1	March 22, 2021	Initial version
0.2	April 02, 2021	Added Shells
0.3	April 16, 2021	Clean version for ERC
0.4	May 3, 2021	Updated shells
1.0	May 17, 2021	Final version
1.1	May 18th 2021	Small update to clarify the Total cohort for efficacy and ATP cohort for efficacy population definition
2.0	May 20th 2022	Updated the protocol version, Co-PI, and the values that define a positive result for Anti-CS results
2.1	Sep 27th 2022	Added a new section on the Timing of Analysis
3.0	Nov 2nd 2022	Finalized for signature
3.1	Jan 31st 2023	Updated the start of at risk to 7 days after dose 3 instead of 14 days after dose 3. Updated the shells
3.2	Feb 28th 2023	Added survival curves for exploratory analysis and updated the list of TLF shells
4.0	Mar 5th 2023	Finalized for signature
	Apr 14th 2023	Updated the model for immunogenicity group comparisons and associated TLF shells

Table of Contents

1. LIST OF ABBREVIATIONS 11
2. INTRODUCTION 13
2.1 Background and rationale 13
2.2 Study Objectives 13
2.2.1 Primary Objective 13
2.2.2 Secondary Objective 13
2.2.3 Exploratory Objective 14
2.3 Study Design and Study Endpoints 14
2.3.1 Study Design 14
2.3.2 Study Endpoints 15
2.4 Randomization and Treatment Assignment 17
2.5 Sample Size and Power Considerations 18
3. GENERAL CONSIDERATIONS FOR DATA ANALYSES 20
3.1 Statistical Hypotheses 20
3.2 Definition of Populations to be Analyzed (Analysis Datasets) 20
3.2.1 Enrolled population 20
3.2.2 Total vaccinated cohort (TVC) 20
3.2.3 Safety analysis population 20
3.2.4 According to protocol (ATP) cohort for efficacy 21
3.2.5 Total cohort for efficacy 21
3.2.6 ATP cohort for immunogenicity 21
3.3 Time Window for Analysis 21
3.4 Missing Data and Outliers 23
3.4.1 Missing Data 23
3.4.2 Outliers 23
3.5 Data Handling Conventions and Transformations 23
3.6 Statistical Summaries, Confidence Intervals and P values 23
3.7 Multiple Comparisons/Multiplicity 24

3.8 Interim Analysis and Final Analysis 24
3.9 Statistical Software 24
4. SUBJECT DISPOSITION 25
4.1 Subject Enrollment 25
4.2 Disposition of Subjects 25
4.3 Eligibility Criteria 25
5. SUBJECT CHARACTERISTICS AND ADHERENCE 26
5.1 Baseline Demographics and Characteristics 26
5.2 Subject Characteristics at Each Visit 26
5.3 Visit and Vaccination Adherence, Sample Availability 26
5.4 Anti-Malarial Compliance 26
5.5 Protocol Deviations 26
6. ANALYSIS OF THE PRIMARY EFFICACY ENDPOINT 27
7. ANALYSIS OF THE SECONDARY ENDPOINT(S) 28
7.1 Secondary Efficacy 28
7.2 Immunogenicity 28
7.3 Safety Analyses 29
7.3.1 Definition 29
7.3.2 Analysis of Safety Endpoints 30
8. EXPLORATORY ANALYSES 32
9. LIST OF TABLES, LISTINGS AND FIGURES 33
10. TLF SHELLS 34
11. TIMING OF ANALYSIS 34
DEMOGRAPHICS TABLES 37
Table 10.1.1: Enrollment Status by Group 37
Table 10.1.2: Summary of eligibility criteria 38
Table 10.1.3: Summary of Demographics by Treatment (TVC, total efficacy cohort and Per Protocol Populations) 39
Table 10.1.4: Summary of HLA Typing by Treatment (TVC Population) 41
Table 10.1.5: Protocol Deviations 42

Table 10.1.6: Medical History 43
Table 10.1.7: Vital Signs 44
Table 10.1.8: Physical Examination 45
Table 10.1.9: Prior Medications 46
Table 10.1.10: Concomitant Medications 47
Table 10.1.11: Vaccine Administration 48
Table 10.1.12: Anti-Malarial Compliance 49
TABLE 10.1.13.1: VISIT ATTENDANCE (EPOCH 1) 50
TABLE 10.1.13.2: VISIT ATTENDANCE (EPOCH 2) 51
TABLE 10.1.13.3: VISIT ATTENDANCE (EPOCH 3) 52
VACCINE EFFICACY TABLES 53
Table 10.2.1.1 and 2. Vaccine efficacy (Group 1 vs Group 4): First Infection Events (FIEs) of *P. falciparum* during the Active Detection of Infection period by HIV status and overall (ATP cohort for efficacy and Total cohort for efficacy) 53
Table 10.2.2.1 and 2 Vaccine efficacy (Group 2 vs Group 5): First Infection Events (FIEs) of P. falciparum during the Active Detection of Infection period by HIV status and overall (ATP cohort for efficacy and Total cohort for efficacy) 54
Table 10.2.3.1 and 2 Vaccine efficacy (Group 1 vs Group 2): First Infection Events (FIEs) of *P. falciparum* during the Active Detection of Infection period by HIV status and overall (ATP cohort for efficacy and Total cohort for efficacy) 55
Table 10.2.4.1 and 2 Vaccine efficacy (Group 4 vs Group 5): First Infection Events (FIEs) of *P. falciparum* during the Active Detection of Infection period by HIV status and overall (ATP cohort for efficacy and Total cohort for efficacy) 56
Table 10.2.5.1 and 2 Summary of subjects at risk, person-time, number of FIEs and incidence rate (ATP cohort for efficacy and Total cohort for efficacy) for Group 1 and 4 57
Table 10.2.6.1 and 2 Summary of subjects at risk, person-time, number of FIEs and incidence rate (ATP cohort for efficacy and Total cohort for efficacy) for Group 2 and 5 58
Table 10.2.7.1 and 2 Summary of median time to FIEs and hazards (ATP cohort for efficacy and Total cohort for efficacy) 59
IMMUNOGENICITY TABLES 60
Table 10.3.1.1 and 2: Number and Percentage of Subjects with anti-CS NANP Antibody Titer/Avidity Equal to or above Cut-off (seropositive) and GMTs (ATP cohort for immunogenicity and Total vaccinated cohort) 60

Table 10.3.2.1 and 2: Number and Percentage of Subjects with Anti-CS C-term Antibody Titer/Avidity Equal to or above Cut-off and GMTs (ATP cohort for immunogenicity and Total cohort for efficacy) 61

Table 10.3.3.1 and 2: Number and Percentage of Subjects with Anti-HBsAb Titer Equal to or above Cut-off and GMTs (ATP cohort for immunogenicity and Total vaccinated cohort) 61

Table 10.3.4.1 and 2 : Geometric Fold Rise in Anti-CS NANP Antibody Titer at Each Post-Vaccination Timepoint Compared to Screening (ATP cohort for immunogenicity and Total vaccinated cohort) 62

Table 10.3.5.1 and 2: Geometric Fold Rise in Anti-CS C-term Antibody Titer at Each Post-Vaccination Timepoint Compared to Screening (ATP cohort for immunogenicity and Total vaccinated cohort) 62

Table 10.3.6.1 and 2: Geometric Fold Rise in Anti-HBsAb Titer at Each Post-Vaccination Timepoint Compared to Screening (ATP cohort for immunogenicity and Total vaccinated cohort) 62

SAFETY TABLES 63

Table 10.4.1.1: Overall Safety Profile by Treatment (Safety Population) 63

Table 10.4.1.2: Frequency of Local Solicited Adverse Events by Treatment and Severity (Safety Population) 64

Table 10.4.1.3: Frequency of Systemic Solicited Adverse Events by Treatment and Severity (Safety Population) 65

Table 10.4.1.4: Summary of Unsolicited Adverse Events by Treatment (Safety Population) . 67

Table 10.4.1.5: Summary of Unsolicited Adverse Events by Treatment, Severity and Relationship to Study Treatment (Safety Population) 68

Table 10.4.1.6: Summary of Serious Adverse Events by Treatment (Safety Population) 70

Table 10.4.1.7: Frequency of Local Solicited Adverse Events by Treatment, Injection Period, and Severity (Safety Population) 71

Table 10.4.1.8: Frequency of Systemic Solicited Adverse Events by Treatment, Injection Period, and Severity (Safety Population) 72

Table 10.4.1.9: Summary of Adverse Events of Special Interest by Treatment (Safety Population) 74

Table 10.4.1.10: Summary of Adverse Events (Safety Population) 75

Table 10.4.1.11: Summary of Recurrent Adverse Events (Safety Population) 77

Table 10.4.1.12: Summary of Adverse Events that Persisted beyond 6 Days Post-IP Administration (Safety Population) 79

Table 10.4.1.13: Exploration of Group Comparisons for Common Adverse Events (Safety Population) 80
Table 10.4.1.14: Safety Lab Data out of Range (Safety Population) 81
Table 10.4.1.15: Summary of Safety Lab Results (Safety Population) 82
Table 10.4.1.16: Summary of Hemoglobinopathy Results (Safety Population) 83
Table 10.4.1.17: Summary of Urine Pregnancy Test Results (Safety Population) 84
Table 10.4.1.18: Summary of All Non-Serious Adverse Events by Treatment (Safety Population) 85
12. DEMOGRAPHICS LISTINGS 86
Listing 10.1.1: Protocol Deviations 86
Listing 10.1.2: Enrollment Status, Demographics and Subject Disposition 87
Listing 10.1.3: Eligibility Criteria Not Met 88
Listing 10.1.4: Listing of All Eligibility Criteria 89
Listing 10.1.5: Baseline Demographics 90
Listing 10.1.6: HIV Status and HLA Typing 91
Listing 10.1.7: Prior Medications 92
Listing 10.1.8: Concomitant Medication 93
Listing 10.1.9: Medical History 94
Listing 10.1.10.1: Visit Attendance (Epoch 1) 95
Listing 10.1.10.2: Visit Attendance (Epoch 2) 96
Listing 10.1.10.3: Visit Attendance (Epoch 3) 97
Listing 10.1.11: Vaccine administration 98
Listing 10.1.12: Anti-Malarials 99
Listing 10.1.13: Vital Signs 100
Listing 10.1.14: Physical Examinations 101
13. SAFETY LISTINGS 102
Listing 10.2.1: Solicited Adverse Events (Safety Population) 102
Listing 10.2.2: Unsolicited Adverse Events (Safety Population) 103
Listing 10.2.3: Serious Adverse Events (Safety Population) 104
Listing 10.2.4: Adverse Events of Special Interest (Safety Population) 105

Listing 10.2.5: Safety Laboratory Results (Safety Population) 106
Listing 10.2.6: Hemoglobinopathy Tests Results (Safety Population) 107
Listing 10.2.7: Urine Pregnancy Tests for Female Subjects (Safety Population) 108
14. IMMUNOGENICITY LISTING 109
Listing 10.3.1: Listing of Antibody Titers/Avidity 109
15. VACCINE EFFICACY LISTING 110
Listing 10.4.1 Listing of First Infection Events (FIEs) 110
Listing 10.4.2 Listing of Parasitemia Test Results (ADI) 111
16. DEMOGRAPHICS FIGURES 112
Figure 10.1.1: CONSORT Diagram 112
17. VACCINE EFFICACY FIGURES 114
Figure 10.2.1: Kaplan-Meier survival curve for FIEs in Groups 1 and 4. 114
Figure 10.2.2: Kaplan-Meier survival curve for FIEs in Groups 1 and 4 stratified by HIV status. 115
Figure 10.2.3: Kaplan-Meier survival curve for FIEs in Groups 2 and 5. 116
Figure 10.2.4: Kaplan-Meier survival curve for FIEs in Groups 2 and 5 stratified by HIV status. 117
Figure 10.2.5: Kaplan-Meier survival curve for FIEs in Groups 1 and 2 117
Figure 10.2.6: Kaplan-Meier survival curve for FIEs in Groups 4 and 5 117
Figure 10.2.7: Scaled Schoenfeld residuals with 95% confidence interval versus time for Groups 1 and 4 FIEs during the entire study period (ATP cohort for efficacy) 118
Figure 10.2.8: Scaled Schoenfeld residuals with 95% confidence interval versus time for Groups 2 and 5 FIEs during the entire study period (ATP cohort for efficacy) 119
Figure 10.2.9: Scaled Schoenfeld residuals with 95% confidence interval versus time for Groups 1 and 2 FIEs during the entire study period (ATP cohort for efficacy) 119
Figure 10.2.10: Scaled Schoenfeld residuals with 95% confidence interval versus time for Groups 4 and 5 FIEs during the entire study period (ATP cohort for efficacy). 119
18. IMMUNOGENICITY FIGURES 120
Figure 10.3.1: Reverse Cumulative Distribution Curves for Anti-CS NANP Antibody Titers in Each Group (ATP cohort for immunogenicity) 120
Figure 10.3.2: Reverse Cumulative Distribution Curves for Anti-CS C-term Antibody Titers in Each Group (ATP cohort for immunogenicity) 120

Figure 10.3.3: Reverse Cumulative Distribution Curves for Anti-HBsAb Titers in Each Group (ATP cohort for immunogenicity)..... 120

1. LIST OF ABBREVIATIONS

ADI	Active Detection of infection
AE	Adverse Event
AESI	Adverse event of special interest
A/L	Artemether/lumefantrine
ALT	Alanine aminotransferase
ATP	According to protocol
anti-HBs	Antibody to hepatitis B surface antigen
AS01	GSK's proprietary adjuvant system containing QS21, MPL, and liposomes
CBC	Complete Blood Count
CDC	Centers for Disease Control and Prevention
CI	Confidence interval
CMI	Cell-mediated immunity
CRF	Case report form
ELISA	Enzyme-linked immunosorbent assay
GCP	Good Clinical Practice
GMFRs	Geometric Mean Fold Rises
GMT	Geometric Mean Titer
CS	Circumsporozoite protein
DHA/Pip	Dihydroartemisinin-piperaquine
ELISA	Enzyme-linked immunosorbent assay
GMT	Geometric Mean Titer
H_0	Null hypothesis
H_1	Alternative hypothesis
Hb	Haemoglobin
HBsAb	Hepatitis B surface antibody
HBsAg	Hepatitis B surface antigen
HIV	Human immunodeficiency virus
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
IDMC	Independent Data Monitoring Committee
IgG	Immunoglobulin G
IP	Investigational Product
LD PQ	Low dose primaquine
AESI	Adverse Events of Special Interest
MMRM	Mixed Model for Repeated Measures
MedDRA	Medical Dictionary for Regulatory Activities
NIH	National Institutes of Health
P. falciparum	*Plasmodium falciparum*
PBMCs	Peripheral Blood Mononuclear Cells
PCR	Polymerase chain reaction

PLT	Platelet
PT	Preferred Term
RTS,S	Protein comprising CS and hepatitis B surface antigen
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SOC	System Organ Class
TVC	Total vaccine cohort
VE	Vaccine efficacy
WBC	White blood count
WHO	World Health Organization

2. INTRODUCTION

The main goal of this study is to assess the efficacy of RTS,S/AS01$_E$, a candidate vaccine against malaria caused by *Plasmodium falciparum*, in adults positive for *P. falciparum* by PCR at baseline, but have been treated with anti-malarial medications to clear the parasite before receiving multiple doses of the vaccine. The goal is to overcome the reduced vaccine efficacy (hypo-responsiveness to the vaccine) reported in actively or chronically infected adults.

2.1 Background and rationale

In previous clinical trials for the RTS,S/AS01$_E$ vaccine, it has been reported that the vaccine has been less effective in adults in endemic regions. Adults living in areas of moderate to high malaria transmission often have co-existing asymptomatic circulating blood stage *P. falciparum* parasites that results from multiple exposures to infective mosquito bites. This has been recognized as inducing a level of immunologic hypo-responsiveness that may impede the development of a protective immune response following immunization. We hypothesize that treatment of malaria infection in individuals prior to immunization with the RTS,S/AS01 vaccine will reset the immune response to the vaccine and result in an increased vaccine efficacy.

The rationale of the trial is to compare the vaccine efficacy of RTS,S/AS01$_E$ in two groups of adults who differ with the presence/absence of baseline PCR-positive parasitemia. Both groups receive the same anti-malarial treatment to clear parasites or to prevent infection (prophylaxis) prior to immunization. A rabies comparator vaccine (Abhayrab) is administered to two parallel groups to assess the absolute vaccine efficacy (VE) against *P. falciparum* parasitemia and to investigate whether sub-optimal immune responses in previously infected or concurrently infected adults is a general phenomenon independent of the vaccine antigen.

2.2 Study Objectives

2.2.1 Primary Objective

To evaluate the vaccine efficacy assessed by time to first *P. falciparum* infection in RTS,S/AS01$_E$ vaccinated adults who are positive for *P. falciparum* by PCR at baseline and treated to clear parasites compared to adults administered a comparator Rabies vaccine (Abhayrab) who are also positive for *P. falciparum* by PCR at baseline and treated to clear parasites.

2.2.2 Secondary Objective

Efficacy

The secondary efficacy objective is to assess vaccine efficacy by time to first *P. falciparum* infection by PCR in RTS,S/AS01$_E$ vaccinated adults who are negative for *P. falciparum* at baseline and are provided anti-malarial chemo-prophylaxis versus the vaccine efficacy against *P.*

falciparum of a comparator rabies vaccine that are administered to adults who are also negative for *P. falciparum* at baseline and receive the same anti-malarial chemo-prophylaxis.

Safety

There are several secondary safety objectives for the trial:

- To assess the safety of RTS,S/AS01$_E$ in terms of serious adverse events (SAEs) during the whole study period (from Dose 1 to study conclusion)
- To assess the safety and reactogenicity of RTS,S/AS01$_E$ in terms of solicited local and systemic adverse events within 7 days after each vaccination in the first 50 subjects in groups 1 and 2, and in all 35 subjects from Group 3.
- To assess the safety of RTS,S/AS01$_E$ in terms of unsolicited adverse events within 28 days after each vaccination

Immunogenicity

The secondary immunogenicity objective is to assess the level & avidity of anti-circumsporozoite (CS) antibody, and that of hepatitis B surface antibodies (HBsAb), for groups 1, 2 and 3.

[redacted]

2.3 Study Design and Study Endpoints

2.3.1 Study Design

The five groups for this study are summarized in Table 1. The schedules for immunization and anti-malarial treatment are listed in Table 2.

Table 1. The five study groups and their descriptors (from protocol)

Group	Vaccine	Sample size	Baseline Parasitemia	Anti-malarial Rx	Anti-malarial Rx rationale
Group 1	RTS,S/AS01$_E$	164	+	+	Clear parasites
Group 2	RTS,S/AS01$_E$	128	-	+	Prophylaxis
Group 3	RTS,S/AS01$_E$	35	+	-	-
Group 4	Rabies	164	+	+	Clear parasites
Group 5	Rabies	128	-	+	Prophylaxis
	total	**619**			

Table 2. The schedule of immunization and anti-malarial treatment (from protocol).

Group	Month -1	Month 0 (Vaccine 1)	1-2 wks before Vx dose 2	Month 1 (Vaccine 2)	1 wk before Vx dose 3	Month 7 (Vaccine 3)	Month 8 to 14
Group 1	DHA/Pip + LD PQ	RTS,S/AS01$_E$	DHA/Pip + LD PQ	RTS,S/AS01$_E$	A/L + LD PQ	1/5th dose RTS,S/AS01$_E$	ADI
Group 2	DHA/Pip + LD PQ	RTS,S/AS01$_E$	DHA/Pip + LD PQ	RTS,S/AS01$_E$	A/L + LD PQ	1/5th dose RTS,S/AS01$_E$	ADI
Group 3	-	RTS,S/AS01$_E$	-	RTS,S/AS01$_E$	-	1/5th dose RTS,S/AS01$_E$	-
Group 4	DHA/Pip + LD PQ	Rabies	DHA/Pip + LD PQ	Rabies	A/L + LD PQ	Rabies	ADI
Group 5	DHA/Pip + LD PQ	Rabies	DHA/Pip + LD PQ	Rabies	A/L + LD PQ	Rabies	ADI

Group 1. Subjects have detectable *P. falciparum* parasitemia at baseline measured by PCR. Anti-malarial treatment with DHA/Pip to clear asexual stage and young gametocyte parasites plus LD PQ to clear mature gametocytes will be given 4 weeks prior to immunization with RTS,S/AS01$_E$. A 2nd course of DHA/Pip plus Primaquine will be given 2 weeks before second RTS,S/AS01$_E$ immunization. One week before 3rd RTS,S/AS01$_E$ immunization, a three-day course of A/L plus Primaquine will be administered to clear infection.

Group 2. Subjects have no detectable *P. falciparum* parasitemia as measured by PCR at enrolment. The same anti-malarial treatment regimen as for Group 1 will be administered before each dose of RTS,S/AS01$_E$ immunization as chemo-prophylaxis against *P. falciparum*.

Group 3. Subjects have detectable *P. falciparum* parasitemia at baseline measured by PCR but will not receive any anti-malarial medications to clear PCR-positive parasites. This group includes 35 subjects and is included only for immunological assessment and not for vaccine efficacy.

Group 4. Subjects have detectable *P. falciparum* parasitemia at baseline measured by PCR and will receive the same anti-malarial treatment on the same schedule as subjects in group 1. However, subjects in Group 4 will be administered the Abhayrab rabies vaccine instead of RTS,S/AS01 $_E$.

Group 5. Subjects have no detectable *P. falciparum* parasitemia as measured by PCR at enrolment and will receive the same anti-malarial treatment on the same schedule as subjects in group 2. Similarly, subjects in Group 5 will be administered the Abhayrab rabies vaccine instead of RTS,S/AS01 $_E$.

2.3.2 Study Endpoints

The primary endpoint

The primary endpoint is defined as the time to first PCR-detectable malaria infection in Groups 1 and 4 during the ADI phase of the study. Vaccine efficacy for subject in (Group 1) who are immunized with RTS,S/AS01 E vaccine will be compared to volunteers in Group 4 who are immunization with a comparator rabies vaccine.

Secondary Endpoints

Secondary endpoint for vaccine efficacy:

The secondary endpoint is defined as the time to first PCR-detectable malaria infection in Groups 2 and 5 during the ADI phase of the study. Vaccine efficacy in group 2 subjects who are administered RTS,S/AS01 E will be compared to volunteers in Group 5 who are immunized with a comparator rabies vaccine.

Secondary endpoint for safety:

- Frequency count and proportion of subjects reporting serious adverse events (SAEs) during the whole study period
- Frequency count and proportion of subjects reporting solicited local and systemic adverse events within 7 days after each vaccination
- Frequency count and proportion of subjects reporting unsolicited adverse events within 28 days after each vaccination

Secondary endpoint for immunogenicity:

- Anti-circumsporozoite (CS) antibody levels & avidity for subject in Groups 1,2 and 3.
- Hepatitis B surface antibody (HBsAb) levels for subjects in Groups 1,2 and 3.

[redacted]

[redacted]

2.4 Randomization and Treatment Assignment

This study is an open label study and eligible subjects will be stratified by baseline parasitemia status and block randomized. Among those positive for parasitemia at baseline a total of 363 will be randomized. The first 105 will be randomized in a 1:1:1 ratio with 35 subjects assigned to each of Groups 1, 3 and 4. The next 258 subjects with baseline parasitemia will be randomized in a 1:1 ratio to Groups 1 and 4 with a total of 129 additional subjects per group. Two hundred fifty-six subjects that are negative for parasitemia at baseline will be randomized with an 1:1 ratio to Groups 2 and 5. This randomization schedule will result in a total of 164, 128, 35, 164, and 128 for Groups 1 through 5, respectively (Table 1). In addition, HIV infection status will be noted prior to randomization, and individuals will be stratified across the groups to the extent possible. The proportion of subjects per group that are HIV positive rate for the groups will be capped near 20% for each group. The randomization scheme and the randomization lists with their block sizes used for the study is shown in Figure 1.

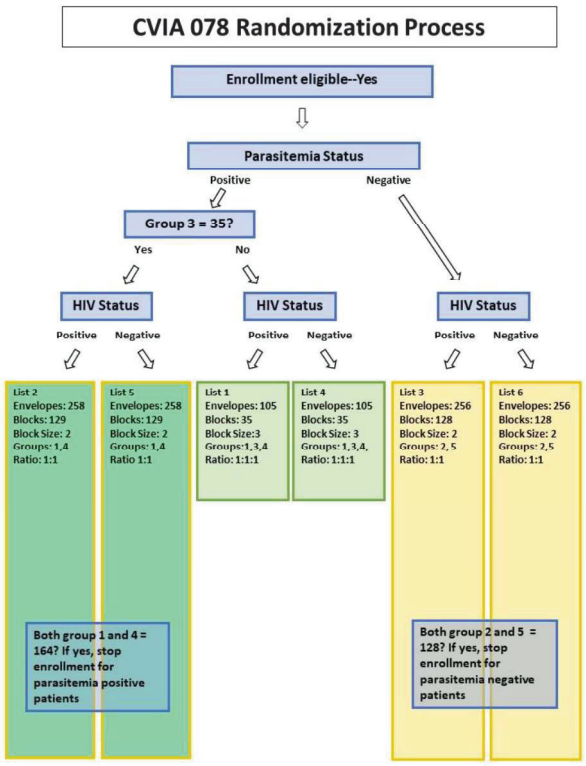


Figure 1. The schematic diagram of the randomization process for the study (from randomization plan). The HIV positive rate for each group are capped near 20%.

2.5 Sample Size and Power Considerations

This is a Phase 2b study to assess the vaccine efficacy of RTS,S/AS01 E in adults in a malaria endemic region. The statistical analysis will measure vaccine efficacy using Cox proportional hazards regression model (time to first PCR-positive infection). An attack rate of 40% over 6 months has been assumed as a conservative estimate in an epidemiologic setting of perennial transmission in Western Kenya. A fixed vaccine efficacy of 50% is a conservative assumption according to the estimated vaccine efficacy.

Using an event-based design and assuming 10% drop out of the enrolled population and a one-sided α=0.025, the following table lists the power and required number of events to conduct the analysis.

Table 3. Sample Size Calculations (from protocol)

Power	N to enroll per group	Total events required to conduct analysis	Endpoint
90%	164	92	Primary (Group 1 vs 4)
80%	128	72	Secondary (Group 2 vs 5)

The impact of the event-driven design is that the study will continue to follow up until 92 first PCR-positive infection events, subsequently referred to as events, have been observed in aggregate between Groups 1 and 4, and 72 events have been observed in the aggregate of Groups 2 and 5. If the aggregate numbers of events have been reached prior to 24 weeks of ADI, study actives will continue to occur through the end of the ADI. If the aggregate number of events during ADI does not reach the cutoff indicated in Table 3, then the ADI will be extended up to 48 weeks or until the total number of events is reached, whichever occurs first. This will require the PCR lab to provide timely aggregated reports of event counts (across Group 1 plus 4; and Group 2 plus 5) and may result in more than the required events for either the primary or secondary endpoint.

An additional cross-sectional PCR will be performed at the Study Termination Visit, but these PCR results will not count toward the study endpoints.

Based on these assumptions we estimate a greater than 90% probability of observing the required number of events for the primary and secondary analyses by 6.9 months. However, larger dropout rates and/or a lower attack rate might extend the amount of follow-up time necessary to accumulate the required number of events.

The sample size for the immunologic sub-cohort (CMI assays in all subjects in RTS,S/AS01 E groups 1, 2, and 3) is based on logistical considerations and the feasibility of the collection and processing of PBMCs. Analysis of these exploratory endpoints and inter-group differences will be descriptive in nature.

3. GENERAL CONSIDERATIONS FOR DATA ANALYSES

3.1 Statistical Hypotheses

The primary and secondary hypotheses will be assessed using Cox proportional hazards regression (time to first PCR-positive infection). These hypotheses tests will be supplemented with two-sided confidence intervals for the hazard ratios as described below.

The null (H_0) and alternative (H_1) hypotheses for the primary analysis of time to first malaria infection in Groups 1 and 4 is as follows:

> H_0: Among adults positive for *P. falciparum* at baseline the hazard rate for first malaria infection for RTS,S/AS01$_E$ vaccinated adults (Group 1) is not different than that of adults administered the comparator rabies vaccine (Group 4) as measured by the hazard ratio.
>
> H_1: Among adults positive for *P. falciparum* at baseline the hazard rate for malaria infection for RTS,S/AS01$_E$ vaccinated adults (Group 1) is different than that of adults administered the comparator rabies vaccine (Group 4) as measured by the hazard ratio.

The null and alternative hypotheses for the secondary efficacy analysis of time to first malaria infection in Groups 2 and 5 is as follows:

> H_0: Among adults negative for *P. falciparum* at baseline the hazard rate for malaria infection for RTS,S/AS01$_E$ vaccinated adults (Group 2) is not different than that of adults administered the comparator rabies vaccine (Group 5) as measured by the hazard ratio.
>
> H_1: Among adults negative for *P. falciparum* at baseline the hazard rate for first malaria infection for RTS,S/AS01$_E$ vaccinated adults (Group 2) is different than that of adults administered the comparator rabies vaccine (Group 5) as measured by the hazard ratio.

3.2 Definition of Populations to be Analyzed (Analysis Datasets)

3.2.1 Enrolled population

All subjects who have provided written informed consent, regardless of the subject's screening, randomization, and vaccination status in the study.

3.2.2 Total vaccinated cohort (TVC)

All subjects in the enrolled population who are randomized and received at least one vaccination.

3.2.3 Safety analysis population

All subjects in the TVC for which any safety data is available. All safety analyses will be performed using this population. The denominators for different safety endpoints may vary according to the number of subjects with available data for the specific endpoint.

3.2.4 According to protocol (ATP) cohort for efficacy

The ATP cohort for efficacy will include all subjects included in the TVC with no major protocol deviations that are determined to potentially interfere with the efficacy assessment of the study vaccine and contributed to the time at risk starting 7 days after the third dose. The membership in this study population will be determined in a blinded fashion at a data review meeting attended by the sponsor Medical Officer, the site PI/Co-PI, and the sponsor Statistician. The list of criteria used to exclude subjects from ATP, including anti-malarial administration and other relevant analysis protocol deviations, will be finalized before database freeze. The details can be found in the Note to File (NTF) from the meeting.

3.2.5 Total cohort for efficacy

Given the potential for some participants to receive COVID-19 vaccine during the study, an additional total efficacy cohort is defined to include all TVC subjects who receive all three doses of RTS,S/AS01$_E$ vaccine or comparator and contribute to time at risk starting 7 days after the third dose.

3.2.6 ATP cohort for immunogenicity

The ATP cohort for immunogenicity will include all subjects included in the TVC with no major protocol deviations that are determined to potentially interfere with the immunogenicity assessment of the study vaccine. This population will serve as the primary analysis population for the immunogenicity endpoints. The population will be adapted by time point to include all eligible subjects' data up to the time of disqualifying protocol deviation. The criteria used to exclude subjects from this cohort will include but not limited to: performed blood samplings for immunogenicity according to protocol intervals; did not use any medication or blood products forbidden by the protocol; did not have any reported underlying medical condition influencing immune responses. Similarly, the membership in this study population will be determined in a blinded fashion at a data review meeting attended by the sponsor, investigator, and DFnet and finalized before database freeze. The details can be found in the Note to File (NTF) from the meeting.

3.3 Time Window for Analysis

Study day will be calculated as the actual date minus date of the first dose of vaccine (Day 1) + 1 and will be used to show start/ stop day of assessments and events. If the event date is partial or missing, the corresponding study day and study duration will appear partial or missing in the listings.

Study day is defined to account for potential deviation from the visit schedule and unscheduled visits, all by-visit summary tables, unless otherwise specified, will be based on analysis visits, which will be assigned based on time window around the scheduled visit days below. However, listings will include all scheduled, unscheduled, retest and early withdrawal data. In general:

- unscheduled measurements will not be included if they do not fall within the analysis window listed below, but will contribute to the baseline value, or best/worst case value where required (e.g. shift table).
- for retest measurements (with same visit number assigned or fall within the same time window as another measurement), the last available measurement for that visit will be used with the exception for ADI visits where the first result will be used.
- early withdrawal data will be mapped to the next available visit number.

The following general time windows will be used:

Table 4. Time windows for Analysis

Scheduled time point	Study Day Window
Visit 2	Day -29 to -25
Visit 5	Day -3 to 4
Visit 7	Day 8 to 10
Visit 11	Day 26 to 32
Visit 12	Day 36 to 38
Visit 13	Day 54 to 60
Visit 14	Day 188 to 192
Visit 17	Day 194 to 200
Visit 18	Day 204 to 206
Visit 19	Day 208 to 214
Visit 20	Day 221 to 229
Visit 21	Day 242 to 250
Visit 22	Day 263 to 271
Visit 23	Day 284 to 292
Visit 24	Day 305 to 313
Visit 25	Day 326 to 334
Visit 26	Day 347 to 355
Visit 27	Day 368 to 376
Visit 28	Day 389 to 397
Visit 29	Day 410 to 418
Visit 30	Day 431 to 439
Visit 31	Day 452 to 460
Visit 32	Day 473 to 481
Visit 33	Day494 to 502
Visit 34	Day 514 to 523
Visit 35	Day 536 to 544

3.4 Missing Data and Outliers

3.4.1 Missing Data

Non-missing ELISA data are considered validated. Missing ELISA data are considered non-retrievable. They will not be imputed and will be analyzed as if they were randomly missing. For subjects who discontinue from the study, their immunogenicity data collected before discontinuation will be analyzed under the analysis populations as applicable.

If severity or relationship to the IP administration for a reported AE or serious adverse event (SAE) is missing, an independent category "Missing" will be reported. If a start or stop date associated with a reported concomitant medication, AE, or SAE is incomplete or missing, the following rules will be applied:

- If the day of the start date is missing and the month and year of the start date are known, compare the start month and year to the month and year of visits 1 – 3. If the start month and year match exactly one of visits 1 – 3, then use the day of the date of that matched visit; otherwise use the 15th day of the month.
- If either month or year is missing, no imputations will be done.

If stop date for a concomitant medication/medical history (AE or SAE) is missing, the medication/medical history will be considered ongoing.

If the study termination date is missing, it will not be imputed.

3.4.2 Outliers

Graphic inspection for outliers will be performed. No data will be excluded from the primary and secondary analyses, including any outliers. All transformations of the study data will be pre-specified.

3.5 Data Handling Conventions and Transformations

The antibody titers will be transformed using log10 transformation for geometric mean analyses. Data will be back transformed to the original scale for presentation.

3.6 Statistical Summaries, Confidence Intervals and P values

Continuous data will be summarized by vaccination group with number of observations (n), mean, standard deviation (SD), median, Interquartile range, minimum, and maximum; Categorical results will be summarized by number of participants (n) and percentage (%) of subjects per vaccination group and visit. Unless otherwise specified, all statistical tests will be two-sided with a significance level of 0.05 and a 95% CI will be provided for estimates, as appropriate.

3.7 Multiple Comparisons/Multiplicity

No multiplicity adjustments will be performed.

3.8 Interim Analysis and Final Analysis

There is no planned interim analysis for the study.

A final analysis on all efficacy, safety and immunogenicity data will be performed after the study ends, when all additional safety data has been collected following the last subject's last study visit and the database is cleaned and locked.

3.9 Statistical Software

All statistical analyses will be performed using SAS® software version 9.4 or later.

4. SUBJECT DISPOSITION

4.1 Subject Enrollment

Expected and actual subject enrollment will be tabulated by study group. The number and proportion of screened subjects meeting and not meeting entry criteria will also be tabulated.

4.2 Disposition of Subjects

Subject disposition will be summarized by study group. The following information will be tabulated. Summaries of subject disposition will be prepared for all subjects, including the number and percent enrolled, screened, randomized, and administered antimalarials and vaccines [T.10.1.1, L.10.1.2], as well as a CONSORT diagram [F.10.1.1] describing study participation and discontinuation. The reasons for screen failures, discontinuations, and population exclusions will be summarized and listed [T.10.1.5, L.10.1.1].

4.3 Eligibility Criteria

The inclusion and exclusion criteria used for screening in this study are listed in the protocol. The subjects excluded from the study for failing each inclusion/exclusion criteria and exclusion criteria will be listed and summarized [T.10. 1.2, L.10.1.3]

5. SUBJECT CHARACTERISTICS AND ADHERENCE

5.1 Baseline Demographics and Characteristics

Baseline demographics and characteristics, including age, height, weight, BMI, sex, race, and HIV status will be summarized for the TVC, total efficacy cohort and per protocol populations by vaccination group using descriptive statistics (mean, standard deviation, median, interquartile range, minimum and maximum for continuous features and rates for categorical features). [T.10.1.3, L.10.1.4]

Medical history will be tabulated by Medical Dictionary for Regulatory Activities (MedDRA v23) System Organ Class (SOC), Preferred Term (PT) and vaccination group. For the TVC population, medical history will be listed and summarized by category [T.10.1.6, L.10.1.9]. Using the World Health Organization (WHO, version: Mar2020) Drug Dictionary, prior and concomitant medications will be tabulated by anatomical therapeutic chemical (ATC) classification, preferred drug name and vaccination group [T.10.1.9, T.10.1.10, L.10.1.7, L.10.1.8].

5.2 Subject Characteristics at Each Visit

Vital signs [T.10.1.7] and physical exam results [T.10.1.8] collected at other visits will be summarized for the TVC, total cohort for efficacy and per protocol populations by vaccination group.

Listings of vital signs [L.10.1.13] and physical exam results [L.10.1.14] at each applicable time point will be provided at participant-level.

5.3 Visit and Vaccination Adherence, Sample Availability

A summary and listing of visit attendance [T.10.1.13.1-3, L.10.1.10.1-3] will be prepared, in addition to a summary and listing of vaccine administration and sample collection/availability for each sample [T.10.1.11, L.10.1.11].

5.4 Anti-Malarial Compliance

The detailed information on the administration of three anti-malarials used in this study will be listed for the SAF population, including number of tablets dispensed, number of tablets returned, date, time, and compliance of dosing. Furthermore, since anti-malarial treatment does not allow for missed doses, their compliances will be listed by visits and summarized as the number and percentage of participants who have missed at least one dose of anti-malarials [T.10.1.12, L.10.1.12].

5.5 Protocol Deviations

A summary and listing of protocol deviations will be prepared [T.10.1.5, L.10.1.1].

6. ANALYSIS OF THE PRIMARY EFFICACY ENDPOINT

Vaccine efficacy against the first PCR-positive *P. falciparum* infection among adults who were *P. falciparum* positive at baseline will be assessed using Cox proportional hazards regression model with a covariate for group assignment to compare Groups 1 and 4. Specifically, the elapsed time starting 7 days after the third vaccination to the first PCR-positive *P. falciparum* detection or censoring will be analyzed. Time at risk will be presented as person years at risk (PYAR) dividing the days at risk by 365.25. As HIV status is a stratification factor in the randomization, it will be also included as covariate. An exploratory analysis, including Age, Gender and other baseline features might also be included as stratifications for the model if there is a randomization imbalance. Listing of FIEs and parasitemia testing results during ADI will be provided [L10.4.1 and L10.4.2].

The vaccine efficacy estimates (1-hazard ratio), 95% CI, and p-values will be calculated from this model using the Wald test. Ties will be handled using the Efron method [T.10.2.1]. In addition, tests and graphs based on the scaled Schoenfeld residuals will be used to assess the proportional hazard assumption [F10.2.5]. The interaction between HIV status and group assignment will be evaluated using a Wald test.

Descriptive statistics for each vaccination group and visit, the number of subjects at risk, person-time, number of PCR-confirmed first *P. falciparum* events and incidence rate will be tabulated [T.10.2.5]. The censoring rules are summarized in table 5. Similar tables will describe the median time-to-event and accumulative hazard from the cox regression model [T.10.2.7]. Survival curves for each vaccine group will be calculated non-parametrically, tabulated and presented graphically overall and by HIV status using the Kaplan-Meier method [F10.1.1-2].

This analysis will be conducted using both the ATP cohort for efficacy and the total cohort for efficacy.

7. ANALYSIS OF THE SECONDARY ENDPOINT(S)

7.1 Secondary Efficacy

Vaccine efficacy against the first PCR-positive *P. falciparum* infection among adults who were *P. falciparum* negative at baseline will be assessed using Cox proportional hazards regression with a covariate for group assignment to compare Groups 2 and 5. Similarly, HIV status, age, gender and other features might also be included as stratifications for the model. The vaccine efficacy estimates (1-hazard ratio), 95% CI, and p-values will be calculated from this model using the Wald test. Ties will be handled using the Efron method [T.10.2.2].

Table 5. Censoring rules

Situation	Censoring Rules
The FIEs for Groups 1&4 and 2&5 reached in Epoch 2	The entire period of epoch 2 (1st ADI period)
The FIEs for Groups 1&4 and 2&5 reached in Epoch 3	The visit when the number of FIEs for both groups reached their targets during 2nd ADI period
The FIEs for Groups 1&4 and 2&5 did not reach at the end of Epoch 3	The entire period of epoch 2 and 3 (1st and 2nd ADI period)
Early withdrawal	The last visit available
Subjects treated with non-protocol anti-malarial during either ADI period	The last visit before anti-malarials were administration

Similar descriptive statistics table as in the primary efficacy endpoint will be provided, as well as a table for median time to event and accumulative hazard and the Kaplan-Meier survival curves for each vaccination group overall and stratified by HIV status [T.10.2.6, T.10.2.7, F.10.2.3-4]. And this analysis will be conducted using both the ATP cohort for efficacy and the total cohort for efficacy.

7.2 Immunogenicity

There are two antibodies, anti-CS, an antibody against both central repeat region (NANP) and C-terminal region of circumsporozoite protein, and anti-HBs (against hepatitis B surface protein), will be included in antibody response analysis of secondary immunogenicity endpoints for Groups 1-3 (Table 6). The antibody titer and avidity against the NANP or C-terminal of CS protein will be analyzed for visits 2, 5, 11, 13, 17, 20, 27 and 35. Anti-HBs antibody titer will be analyzed for visits 2, 5, 11 and 20. The analysis will be based on the ATP for immunogenicity cohort unless a significant number of subjects have missing data (>10%), then a secondary analysis based on the TVC will be performed to complement the ATP analysis. For estimation of the geometric mean titer (GMT), geometric mean ratio (fold increases), and corresponding confidence limits, analyses will incorporate censoring where appropriate and log-scale coefficients will be back-transformed in order to compute the estimate and corresponding confidence limits for the relevant quantity.

To calculate the fold increases in the antibody titer, an ELISA titer for a given sample being tested for anti-CS antibody levels will be considered seropositive if its value is greater than the following Lower Limit of Quantifications (LLOQs): anti-CS NANP (1XPBS) 54.1 1/DIL, anti-CS NANP (4M UREA) 37.9 1/DIL, anti-CS C-Term (1XPBS) 89.4 1/DIL, anti-CS C-term (4M UREA) 37.5 1/DIL. ELISA titers for the anti-HBs antibody will be considered positive if its value is greater than 10 mIU/mL. Samples that do not generate above or equal to the cut-offs will be reported as LLOQ for analysis purposes. Geometric Mean Fold Rises (GMFRs) will be computed using standard two-sample methods for the log difference of the within-subject increase from baseline, with corresponding CIs computed via *t*-distribution, utilizing the antilog transformation to present the ratio. Analyses of binary variables will include 95% CIs computed via the Clopper-Pearson method, and antibody response rates between each other among Groups 1-3 will be compared using either Fisher's exact test or Chi-square test. Furthermore, at each visit, GMT will be compared among groups 1, 2 and 3 by a mixed model for repeated measures with the log-transformed antibody titer as dependent variable, groups, HIV status and their interaction term as covariates and subject as a random effect. Compound symmetry will be

assumed for the covariance structure. The comparison of the ratios of GMT (estimated treatment differences between groups at all post baseline visits) will be estimated from a similar mixed model for repeated measures.

Table 6. Sampling Visits for Immunogenicity Assessment (from Appendix F of protocol)

SAMPLES COLLECTED FOR IMMUNOGENICITY	Visit #	2	5	6	7	11	13	17	20	27	Termination Visit
	Study day	-27	1	2	8	29	57	197	225	372	TBD*
Secondary endpoint - Groups 1, 2, 3											
Serum	anti-CS NANP levels	●	●			●	●	●	●	●	●
	anti-CS NANP avidity	●	●			●	●	●	●	●	●
	anti-CS C-term levels	●	●			●	●	●	●	●	●
	anti-CS C-term avidity	●	●			●	●	●	●	●	●
	anti-HbsAb antibodies	●	●			●			●		

The number and proportion of subjects exhibiting positive responses and their GMTs will be assessed for each antigen (anti-CS NANP or anti-CS C-term) and conditions (1XPBS or 4M Urea), including the number and proportion exhibiting a seroresponse (defined as a positive response among subjects negative at baseline) [T.10.3.1-3]. Individual fold increases will be listed and summarized as GMFRs by vaccination groups and visits. Subjects showing ≥ 2, 3 and 4-fold rises in their antibody titers will also be listed individually by visits and summarized by vaccination groups and visits [T.10.3.4-6]. Additionally, the distribution of antibody titers against three antigens will be summarized using reverse cumulative distribution curves [F.10.3.1-3]. A listing of titer values will also be included [L.10.3.1].

7.3 Safety Analyses

7.3.1 Definition

Solicited Adverse Event

Solicited AEs are pre-specified local and systemic AEs that occur relatively more frequently or are known to be associated with immunization, which are monitored actively as potential indicators of vaccine reactogenicity. The following specific solicited local and systemic AEs and their intensity scales will be monitored for this study and listed in Table 7:

Table 7. Intensity Scales for Solicited Symptoms in Adults

Pain at injection site	0	Absent
	1	Painful on touch
	2	Painful when limb is moved
	3	Pain that prevents normal activity
Swelling at injection site	0	Absent
	1	Present and is easily tolerated
	2	Present and interferes with normal activity
	3	Present and prevents normal activity
Fever	0	<37.5ºC (99.5ºF)
	1	37.5ºC (99.5ºF) to 38.0ºC (100.4ºF)
	2	>38.0ºC (>100.4ºF) to 39.0ºC (102.1ºF)
	3	>39.0ºC (102.1ºF)
Headache	0	Normal
	1	Headache feeling is easily tolerated
	2	Headache feeling interferes with normal activity
	3	Headache feeling prevents normal activity
	0	Gastrointestinal symptoms normal
	1	Gastrointestinal symptoms that are easily tolerated
	2	Gastrointestinal symptoms that interfere with normal activity

Gastrointestinal symptoms	3	Gastrointestinal symptoms that prevent normal activity
Fatigue	0	Normal
	1	Fatigue that is easily tolerated
	2	Fatigue that interferes with normal activity
	3	Fatigue that prevents normal activity
Muscle ache	0	Absent
	1	Muscle ache that is easily tolerated
	2	Muscle ache that interferes with normal activity
	3	Muscle ache that prevents normal activity

Unsolicited Adverse Events

Unsolicited AEs are any AEs reported spontaneously by the subject, observed by the study staff during study visits or those identified during review of medical records or source documents. Solicited AEs with an onset after the seven-day solicitation period will be considered unsolicited AEs. In the absence of a diagnosis, abnormal physical examination findings or abnormal clinical safety laboratory test results that are assessed by the investigator to be clinically significant will be recorded as an AE.

Adverse Events of Special Interest

AESIs are unsolicited AEs of specific interest for safety monitoring include all seizures occurring within 30 days post-vaccination, meningitis and potential immune-mediated diseases (pIMDs). The full list of pIMDs can be found in the protocol.

Serious Adverse Event

An SAE is any AE that results in any of the following outcomes:

- Death
- Is life-threatening (i.e., the subject was, in the opinion of the investigator, at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe)
- Requires inpatient hospitalization or prolongation of existing hospitalization
- Results in persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
- Congenital anomaly or birth defect
- Important medical event that may not result in one of the above outcomes but may jeopardize the health of the study subject or may require medical or surgical intervention to prevent one of the outcomes listed above

7.3.2 Analysis of Safety Endpoints

All safety assessments will take place using the safety analysis population, according to the vaccination groups. All subject-based percentages (solicited/unsolicited AEs, clinical safety laboratory abnormalities, etc.) will be supplemented with two-sided 95% CIs computed via the Clopper-Pearson method. Individual summaries (denominators for percentages) will be limited to the number of subjects within the appropriate analysis population with data available for analysis for the given endpoint. When an AE occurs more than once for a subject, the subject will be only counted once for the corresponding PT according to the maximum severity of the events.

The overall safety profile for overall and each group will be summarized by the number of all solicited adverse events, the frequencies of local and systemic adverse events among them, the number of unsolicited events, the number and the percentages of subjects with any unsolicited adverse events, the number of adverse events of special interest, the number and the percentages of subjects with any adverse events of special interest, the number of adverse events, the number and the percentages of subjects with any adverse events [T.10.4.1.1].

All solicited AEs will be summarized according to defined severity grading scales. Frequencies and percentages of subjects experiencing each solicited AE will be presented for each symptom severity [T.10.4.1.2-3, T.10.4.1.7-8]. Summary tables showing the occurrence of any local or systemic solicited AE overall and solicited AEs that persist up to 7 days post-administration of IP overall will also be presented [T.10.4.1.12]. Data listings of all solicited AEs will be provided

by subject [L.10.2.1]. For common AEs group comparisons, including each preferred terms, frequency of signs and symptoms and the occurrences of Grade 4 solicited and unsolicited general reactions, will be explored and tested using Fisher's exact test [T.10.4.1.13]. In addition to safety population, these analyses will be also performed using the TVC analysis population.

All unsolicited AEs with onset occurring up to 28 days after each vaccine dose will be assessed as either related or not related to IP by the investigator and will be recorded. Additionally, all AESIs/SAEs throughout the study will be summarized [T.10.4.1.6, T10.4.1.9]. The original verbatim terms used by investigators to identify AEs in the eCRFs will be mapped to PTs using MedDRA. The AEs will then be grouped by MedDRA PTs into frequency tables according to SOC. All reported AEs, as well as AEs assessed by the investigator as related to IP, will be summarized according to SOC, PT within SOC, and severity [T.10.4.1.4-5]. Data listings sorted by subject will be provided [L.10.2.2].

A summary table [T.10.4.1.10] will be prepared for unsolicited AEs comprised of the following categories:

- Unsolicited AEs
- Related unsolicited AEs
- AESIs
- Related AESIs
- SAEs
- Related SAEs
- SAEs leading to death
- Unsolicited AEs leading to subject discontinuation

An additional summary table will be provided including all AEs excluding SAEs, i.e., all solicited, unsolicited, and AESIs [T.10.3.1.18]. A descriptive summary of recurrent AEs [T.14.3.1.11] will also be generated. Listings of AESIs and SAEs sorted by subject will also be provided [L.10.2.3-4]

For clinical safety laboratory data collected on the same day of the first dose of vaccination, individual hemoglobin, WBC count, platelet count, ALT, and creatinine values will be presented as number of subjects out of range (above and below normal range as appropriate) and tabulated by study group [T.10.4.1.14]. In addition, summary statistics of the lab result values will be presented, including mean, standard deviation (SD), 95% CIs, median, and interquartile range [T.10.4.1.15]. A listing of lab results will also be included [L.10.2.5].

Hemoglobinopathy test result at screening and urine pregnancy test results at screening, Visit 2, 5, 8 and 17, will also be listed [L.10.2.6-7] and summarized by overall and each group [T.10.4.1.16-17].

9. LIST OF TABLES, LISTINGS AND FIGURES

Table 10.1.1	Enrollment Status by Group
Table 10.1.2	Summary of eligibility criteria
Table 10.1.3	Summary of Demographics by Treatment (TVC, total cohort for efficacy and Per Protocol Population)
Table 10.1.4	Summary of HIV Status and HLA Typing by Treatment (TVC, total cohort for efficacy and Per Protocol Population)
Table 10.1.5	Protocol Deviations
Table 10.1.6	Medical History
Table 10.1.7	Vital Signs
Table 10.1.8	Physical Examination
Table 10.1.9	Prior Medications
Table 10.1.10	Concomitant Medications
Table 10.1.11	Vaccine Administration
Table 10.1.12	Anti-Malarial Compliance
Table 10.1.13.1	Visit Attendance (Epoch 1)
Table 10.1.13.2	Visit Attendance (Epoch 2)
Table 10.1.13.3	Visit Attendance (Epoch 3)
Table 10.2.1.1 and 2	Vaccine efficacy (Group 1 vs Group 4): First Infection Events (FIEs) of P. falciparum during the Active Detection of Infection period by HIV status and overall (ATP cohort for efficacy and total cohort for efficacy)
Table 10.2.2.1 and 2	Vaccine efficacy (Group 2 vs Group 5): First Infection Events (FIEs) of P. falciparum during the Active Detection of Infection period by HIV status and overall (ATP cohort for efficacy and total cohort for efficacy)
Table 10.2.3.1 and 2	Vaccine efficacy (Group 1 vs Group 2): First Infection Events (FIEs) of P. falciparum during the Active Detection of Infection period by HIV status and overall (ATP cohort for efficacy and total cohort for efficacy)
Table 10.2.4.1 and 2	Vaccine efficacy (Group 4 vs Group 5): First Infection Events (FIEs) of P. falciparum during the Active Detection of Infection period by HIV status and overall (ATP cohort for efficacy and total cohort for efficacy)
Table 10.2.5.1 and 2	Summary of subjects at risk, person-time, number of FIEs and incidence rate (ATP cohort for efficacy and total cohort for efficacy) for Group 1 and 4
Table 10.2.6.1 and 2	Summary of subjects at risk, person-time, number of FIEs and incidence rate (ATP cohort for efficacy and total cohort for efficacy) for Group 2 and 5
Table 10.2.7.1 and 2	Summary of median time to FIEs and hazard rates (ATP cohort for efficacy and total cohort for efficacy)
Table 10.3.1.1 and 2	Number and Percentage of Subjects with anti-CS NANP Antibody Titer/Avidity Equal to or above Cut-off (seropositive) and GMTs (ATP cohort for immunogenicity and Total vaccinated cohort)
Table 10.3.2.1 and 2	Number and Percentage of Subjects with Anti-CS C-term Antibody Titer/Avidity Equal to or above Cut-off and GMTs (ATP cohort for immunogenicity and Total vaccinated cohort)
Table 10.3.3.1 and 2	Number and Percentage of Subjects with Anti-HBsAb Titer Equal to or above Cut-off and GMTs (ATP cohort for immunogenicity and Total vaccinated cohort)
Table 10.3.4.1 and 2	Geometric Fold Rise in Anti-CS NANP Antibody Titer at Each Post-Vaccination Timepoint Compared to Screening (ATP cohort for immunogenicity and Total vaccinated cohort)
Table 10.3.5.1 and 2	Geometric Fold Rise in Anti-CS C-term Antibody Titer at Each Post-Vaccination Timepoint Compared to Screening (ATP cohort for immunogenicity and Total vaccinated cohort)
Table 10.3.6.1 and 2	Geometric Fold Rise in Anti-HBsAb Titer at Each Post-Vaccination Timepoint Compared to Screening (ATP cohort for immunogenicity and Total vaccinated cohort)
Table 10.4.1.1	Overall Safety Profile by Treatment (Safety Population)
Table 10.4.1.2	Frequency of Local Solicited Adverse Events by Treatment and Severity (Safety Population)
Table 10.4.1.3	Frequency of Systemic Solicited Adverse Events by Treatment and Severity (Safety Population)
Table 10.4.1.4	Summary of Unsolicited Adverse Events by Treatment (Safety Population)
Table 10.4.1.5	Summary of Unsolicited Adverse Events by Treatment, Severity and Relationship to Study Treatment (Safety Population)
Table 10.4.1.6	Summary of Serious Adverse Events by Treatment (Safety Population)
Table 10.4.1.7	Frequency of Local Solicited Adverse Events by Treatment, Injection Period, and Severity (Safety Population)
Table 10.4.1.8	Frequency of Systemic Solicited Adverse Events by Treatment, Injection Period, and Severity (Safety Population)
Table 10.4.1.9	Summary of Adverse Events of Special Interest by Treatment (Safety Population)
Table 10.4.1.10	Summary of Adverse Events (Safety Population)
Table 10.4.1.11	Summary of Recurrent Adverse Events (Safety Population)
Table 10.4.1.12	Summary of Adverse Events that Persisted beyond 6 Days Post-IP Administration (Safety Population) 47

Table 10.4.1.13	Exploration of Group Comparisons for Common Adverse Events (Safety Population)
Table 10.4.1.14	Safety Lab Data out of Range (Safety Population)
Table 10.4.1.15	Summary of Safety Lab Results (Safety Population)
Table 10.4.1.16	Summary of Hemoglobinopathy Results (Safety Population)
Table 10.4.1.17	Summary of Urine Pregnancy Test Results (Safety Population)
Table 10.4.1.18	Summary of All Non-Serious Adverse Events by Treatment (Safety Population)
Listing 10.1.1	Protocol Deviations
Listing 10.1.2	Enrollment Status, Demographics and Subject Disposition
Listing 10.1.3	Eligibility Criteria Not Met
Listing 10.1.4	Listing of All Eligibility Criteria
Listing 10.1.5	Baseline Demographics
Listing 10.1.6	HIV Status and HLA Typing
Listing 10.1.7	Prior Medications
Listing 10.1.8	Concomitant Medication
Listing 10.1.9	Medical History
Listing 10.1.10.1	Visit Attendance (Epoch 1)
Listing 10.1.10.2	Visit Attendance (Epoch 2)
Listing 10.1.10.3	Visit Attendance (Epoch 3)
Listing 10.1.11	Vaccine administration
Listing 10.1.12	Anti-Malarials
Listing 10.1.13	Vital Signs
Listing 10.1.14	Physical Examinations
Listing 10.2.1	Solicited Adverse Events (Safety Population)
Listing 10.2.2	Unsolicited Adverse Events (Safety Population)
Listing 10.2.3	Serious Adverse Events (Safety Population)
Listing 10.2.4	Adverse Events of Special Interest (Safety Population)
Listing 10.2.5	Safety Laboratory Results (Safety Population)
Listing 10.2.6	Hemoglobinopathy Tests Results (Safety Population)
Listing 10.2.7	Urine Pregnancy Tests for Female Subjects (Safety Population)
Listing 10.3.1	Listing of Antibody Titers/Avidity
Listing 10.4.1	Listing of FIEs
Listing 10.4.2	Listing of Parasitemia Test Results
Figure 10.1.1	CONSORT Diagram
Figure 10.2.1	Kaplan-Meier survival curve for FIEs in Groups 1 and 4.
Figure 10.2.2	Kaplan-Meier survival curve for FIEs in Groups 1 and 4 stratified by HIV status.
Figure 10.2.3	Kaplan-Meier survival curve for FIEs in Groups 2 and 5.
Figure 10.2.4	Kaplan-Meier survival curve for FIEs in Groups 2 and 5 stratified by HIV status.
Figure 10.2.5	Kaplan-Meier survival curve for FIEs in Groups 1 and 2.
Figure 10.2.6	Kaplan-Meier survival curve for FIEs in Groups 4 and 5.
Figure 10.2.7	Scaled Schoenfeld residuals with 95% confidence interval versus time for Groups 1 and 4 FIEs during the entire study period (ATP cohort for efficacy)
Figure 10.2.8	Scaled Schoenfeld residuals with 95% confidence interval versus time for Groups 2 and 5 FIEs during the entire study period (ATP cohort for efficacy)
Figure 10.2.10	Scaled Schoenfeld residuals with 95% confidence interval versus time for Groups 1 and 2 FIEs during the entire study period (ATP cohort for efficacy)
Figure 10.2.11	Scaled Schoenfeld residuals with 95% confidence interval versus time for Groups 4 and 5 FIEs during the entire study period (ATP cohort for efficacy)
Figure 10.3.1	Reverse Cumulative Distribution Curves for Anti-CS NANP Antibody Titers in Each Group (ATP cohort for immunogenicity)
Figure 10.3.2	Reverse Cumulative Distribution Curves for Anti-CS C-term Antibody Titers in Each Group (ATP cohort for immunogenicity)
Figure 10.3.3	Reverse Cumulative Distribution Curves for Anti-HBsAb Titers in Each Group (ATP cohort for immunogenicity)

10. TLF SHELLS

The TLF shells are included in a separate document/attached in the end.

11. TIMING OF ANALYSIS

Upon completion of last visit for the final participant and availability of immunogenicity results, a partial lock of the database will be realized, and a topline analysis will be initiated to include the results for safety, efficacy and immunogenicity. Immunogenicity results will include the data available before the partial lock. Upon collection of the remainder of the data for immunogenicity and final database lock, the final analysis on immunogenicity will be performed.

TFL Shells for Protocol CVIA 078; RTS,S/AS10E corresponding to SAP v3.1

Protocol title: A Phase 2b randomized, open-label, controlled, single center study in Plasmodium falciparum-infected and uninfected adults age 18-55 years old in Kenya to evaluate the efficacy of the delayed, fractional dose RTS,S/AS01 E malaria vaccine in subjects treated with artemisinin combination therapy plus primaquine
Date created: v0.1 April 06th, 2021
Updated: v0.3 April 16th, **2021,**
Updated: v0.4, May 3rd, 2021,
Updated: v1.0/v1.1 May 17-18th, 2021 added Total cohort for efficacy population for efficacy summary tables and Total vaccinated cohort for immunogenicity summary tables
Updated: Jan 31st,2023, removed change from baseline and toxicity grades from safety lab summaries and listings; updated TLF headers and footers
Updated: Feb 28th, 2023, added two efficacy tables (Groups 1 vs 2 and 4 vs 5), four survival curves (groups 1 vs 2 and groups 4 vs 5), two residual plots and two efficacy listings (FIEs and parasitemia test results)
Updated: Mar 5th, 2023, finalized to v4.0 for signature and updated again on April 14th, updated the model for the pairwise comparisons of immunogenicity and the TLF shells associated with.

DEMOGRAPHICS TABLES

Table 10.1.1: Enrollment Status by Group

	Group 1 (N=)	Group 2 (N=)	Group 3 (N=)	Group 4 (N=)	Group 5 (N=)	Total (N=)
Informed Consent signed						xxxx
Eligible						xxxx
Randomized	xxxx	xxxx	xxxx	xxxx	xxxx	xxxx
Randomized but received no study product at D1	xx	xx	xx	xx	xx	xx
Received study product at D1	xx	xx	xx	xx	xx	xx
Subjects who completed study	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Received study product at D1 who discontinued early	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Adverse Event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Death	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Lost to follow-up	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Physician decision	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Eligibility criteria not met	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Withdrawal by subject	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Study terminated by sponsor	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Protocol deviation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Total vaccinated cohort,	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Safety analysis population,	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ATP for efficacy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ATP for immunogenicity	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Total cohort for efficacy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Total cohort for immunogenicty	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

N: Number of subjects in each group.
Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).
Denominator of percentage is number of subjects randomized and received at least one dose of IP.

Table 10.1.2: Summary of eligibility criteria

	Total n (%)
Informed Consent Signed	xxxx
Subjects who met all eligibility criteria	xx (xx.x%)
Subjects who did not satisfy at least one eligibility criterion	xx (xx.x%)
Subjects who did not meet at least one Inclusion Criterion	xx (xx.x%)
Subject has provided signed or thumb printed and dated informed consent form	xx (xx.x%)
Subject has stated willingness to comply with all study procedures and availability for the duration of the study.	xx (xx.x%)
xxxxxxxxxxxxxxx	xx (xx.x%)
Subjects who met at least one Exclusion Criterion	xx (xx.x%)
Subject has planned administration/administration of a vaccine not foreseen by the study protocol from within 30 days before the first dose of study vaccine until 30 days after the last dose of study vaccine.	xx (xx.x%)
Subject has prior receipt of any rabies vaccine or experimental malaria vaccine.	xx (xx.x%)
xxxxxxxxxxxxxxxxxxxxxxxxx	xx (xx.x%)
	xx (xx.x%)
	xx (xx.x%)
	xx (xx.x%)
	xx (xx.x%)
	xx (xx.x%)

Denominator of percentage is number of subjects screened.

Table 10.1.3: Summary of Demographics by Treatment (TVC, total efficacy cohort and Per Protocol Populations)

	Statistics	Group 1 (N=)	Group 2 (N=)	Group 3 (N=)	Group 4 (N=)	Group 5 (N=)	Overall (N=)
Age	n						
	Mean (SD)						
	Median						
	Q1, Q3						
	Min, Max						
Sex	**n (%)**						
Female	xx(xx.x%)						
Male	xx(xx.x%)						
Ethnicity	**n (%)**						
Luo	xx(xx.x%)						
Luhya	xx(xx.x%)						
Not reported	xx(xx.x%)						
Unknown	xx(xx.x%)						
Other	xx(xx.x%)						
Race	**n (%)**						
White	xx(xx.x%)						
Black	xx(xx.x%)						
Not reported	xx(xx.x%)						
Unknown	xx(xx.x%)						
Other	xx(xx.x%)						
HIV Status	n(%)						
Positive	xx(xx.x%)						
Negative	xx(xx.x%)						
Own Bednet?	**n (%)**						
Yes	xx(xx.x%)						
No	xx(xx.x%)						
Sleep Under Net?	**n (%)**						
Yes	xx(xx.x%)						
Once a week	xx(xx.x%)						
2-3 times a week	xx(xx.x%)						
4-6 times a week	xx(xx.x%)						
Daily	xx(xx.x%)						
No	xx(xx.x%)						

Indoor residual spray within the past year	**n (%)**
Yes	xx(xx.x%)
No	xx(xx.x%)
Height	n
	Mean (SD)
	Median
	Q1, Q3
	Min, Max
Weight	n
	Mean (SD)
	Median
	Q1, Q3
	Min, Max
BMI	n
	Mean (SD)
	Median
	Q1, Q3
	Min, Max

N: total number of subjects in each group
n: total number of subjects in each category
Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).

Table 10.1.4: Summary of HLA Typing by Treatment (TVC Population)

	Group 1 (N=)	Group 2 (N=)	Group 3 (N=)	Group 4 (N=)	Group 5 (N=)	Overall (N=)
HLA subtype 1: xxxx	xx(xx.x%)	xx(xx.x%)	xx(xx.x%)	xx(xx.x%)	xx(xx.x%)	xx(xx.x%)
HLA subtype 2: xxxx	xx(xx.x%)	xx(xx.x%)	xx(xx.x%)	xx(xx.x%)	xx(xx.x%)	xx(xx.x%)
HLA subtype 3: xxxx	xx(xx.x%)	xx(xx.x%)	xx(xx.x%)	xx(xx.x%)	xx(xx.x%)	xx(xx.x%)
…						
Repeat for other HLA Class 1 and 2 subtypes						

N: total number of subjects in each group

Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).

Table 10.1.5: Protocol Deviations

Protocol Deviation Type/classification	Group 1 (N=)	Group 2 (N=)	Group 3 (N=)	Group 4 (N=)	Group 5 (N=)	Total (N=)
Deviation Types						
Eligibility	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Informed consent	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Randomization error	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Antimalarial drugs administered incorrectly	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
IP administered incorrectly	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
IP administration missed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missed visit	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Out-of-window visit	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Specimen not collected	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Procedure done incorrectly	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Procedure not done	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Deviation Classifications						
Major	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Minor	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

N: total number of subjects in each group

Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).

Table 10.1.6: Medical History

System Organ Class/ Preferred Term	Group 1 (N=)	Group 2 (N=)	Group 3 (N=)	Group 4 (N=)	Group 5 (N=)	Total (N=)
System Organ Class #1						
Preferred term #1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term #2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term #3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
….	…	…..	…	…..	…..	….
System Organ Class #2						
Preferred term #1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term #2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term #3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
..	…	…..	…	…..	…..	….
System Organ Class #3						
Preferred term #1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term #2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term #3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
..	…	…..	…	…..	…..	….

N: total number of subjects in each group

Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).

Table 10.1.7: Vital Signs

Parameter/ Visit	Group 1	Group 2	Group 3	Group 4	Group 5	Overall
Pulse Rate (beats/ min) at Screening						
N	xx	xx	xx	xx	xx	xx
Mean (SD)	xx .xx (xx.xx)	xx .xx (xx.xx)	xx .xx (xx.xx)	xx .xx (xx.xx)	xx .xx (xx.xx)	xx .xx (xx.xx)
Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Q1, Q3	xx .xx, xx.xx	xx .xx, xx.xx	xx .xx, xx.xx	xx .xx, xx.xx	xx .xx, xx.xx	xx .xx, xx.xx
Min, Max	xx .xx, xx.xx	xx .xx, xx.xx	xx .xx, xx.xx	xx .xx, xx.xx	xx .xx, xx.xx	xx .xx, xx.xx
Pulse Rate (beats/ min) Visit 5						
N	xx	xx	xx	xx	xx	xx
Mean (SD)	xx .xx (xx.xx)	xx .xx (xx.xx)	xx .xx (xx.xx)	xx .xx (xx.xx)	xx .xx (xx.xx)	xx .xx (xx.xx)
Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Q1, Q3	xx .xx, xx.xx	xx .xx, xx.xx	xx .xx, xx.xx	xx .xx, xx.xx	xx .xx, xx.xx	xx .xx, xx.xx
Min, Max	xx .xx, xx.xx	xx .xx, xx.xx	xx .xx, xx.xx	xx .xx, xx.xx	xx .xx, xx.xx	xx .xx, xx.xx
Pulse Rate (beats/ min) Visit 8						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx .xx (xx.xx)	xx .xx (xx.xx)	xx .xx (xx.xx)	xx .xx (xx.xx)	xx .xx (xx.xx)	xx .xx (xx.xx)
Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Q1, Q3	xx .xx, xx.xx	xx .xx, xx.xx	xx .xx, xx.xx	xx .xx, xx.xx	xx .xx, xx.xx	xx .xx, xx.xx
Min, Max	xx .xx, xx.xx	xx .xx, xx.xx	xx .xx, xx.xx	xx .xx, xx.xx	xx .xx, xx.xx	xx .xx, xx.xx
…..						
(Display rows for additional visits and the other categories of vital signs, including oral temperature, and blood pressures)						

N: total number of subjects in each group

Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).

Table 10.1.8: Physical Examination

Body System	Group 1 (N=)	Group 2 (N=)	Group 3 (N=)	Group 4 (N=)	Group 5 (N=)	Total (N=)
General appearance at Visit 5						
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abnormal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not done	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
General appearance Visit 11						
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abnormal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not done	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
General appearance at Visit 17						
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abnormal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not done	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
						….
(Display additional rows for the other categories of physical exam)						

N: total number of subjects in each group

Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).

The physical examination includes the following body system or part: 1. General appearance; 2. Skin; 3. Lymph nodes; 4. HEENT; 5. Neck; 6. Respiratory/pulmonary; 7. Cardiovascular; 8. Abdomen; 9. Musculoskeletal; 10. Neurological; 11. Extremities; 12. Other

Table 10.1.9: Prior Medications

ATC Level/ Preferred Term	Group 1 (N=)	Group 2 (N=)	Group 3 (N=)	Group 4 (N=)	Group 5 (N=)	Total (N=)
ATC Classification #1						
Preferred term #1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term #2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term #3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ATC Classification #2						
Preferred term #1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term #2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term #3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ATC Classification #3						
Preferred term #1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term #2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term #3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
…						….

N: total number of subjects in each group

Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).

Table 10.1.10: Concomitant Medications

ATC Level/ Preferred Term	Group 1 (N=)	Group 2 (N=)	Group 3 (N=)	Group 4 (N=)	Group 5 (N=)	Total (N=)
ATC Classification #1						
Preferred term #1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term #2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term #3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ATC Classification #2						
Preferred term #1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term #2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term #3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ATC Classification #3						
Preferred term #1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term #2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred term #3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

N: total number of subjects in each group
Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).

Table 10.1.11: Vaccine Administration

Group	Visit 5-Dose1	Visit 11-Dose2	Visit 17-Dose3	# of subjects who received all three vaccine doses
Group 1 (N=)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Group 2 (N=)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Group 3 (N=)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Group 4 (N=)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Group 5 (N=)	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 %)

N: total number of subjects in each group

Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).

Table 10.1.12: Anti-Malarial Compliance

Group	Visit 2		Visit 3	Visit 4	Visit 8		Visit 9	Visit 10	Visit 14		Visit 15	Visit 16	Full Compliance
	DHA/Pip	LD PQ	DHA/Pip	DHA/Pip	DHA/Pip	LD PQ	DHA/Pip	DHA/Pip	A/L	LD PQ	A/L	A/L	
Group 1 (N=)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Group 2 (N=)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Group 4 (N=)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Group 5 (N=)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	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 %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)

xx: represents the number of subjects who took the full dose of anti-malarials.

N: total number of subjects in each group

Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 4: Rabies with anti-malarials to clear parasites. Group 5: Rabies with anti-malarials to prevent infection (prophylaxis)

DHA/Pip: Dihydroartemisinin-piperaquine; LD PQ: Low dose primaquine; A/L: Artemether/lumefantrine (Coartem)

TABLE 10.1.13.1: VISIT ATTENDANCE (EPOCH 1)

Group	Treatment and immunoization (Epoch 1)									
	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8	Visit 9	…	Repeat until Visit 18
Group 1 (N=)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)		
Group 2 (N=)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)		
Group 3 (N=)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)		
Group 4 (N=)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)		
Group 5 (N=)	xx (xx.x %)	xx (xx.x %)	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 %)	xx (xx.x %)	xx (xx.x %)		

N: total number of subjects in each group

Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).

TABLE 10.1.13.2: VISIT ATTENDANCE (EPOCH 2)

Group	Active Detection of Infection (Epoch 2)								
	Visit 19	Visit 20	Visit 21	Visit 22	Visit 23	Visit 24	Visit 25	Visit 26	Visit 27
Group 1 (N=)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Group 2 (N=)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Group 3 (N=)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Group 4 (N=)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Group 5 (N=)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	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 %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)

N: total number of subjects in each group

Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).

TABLE 10.1.13.3: VISIT ATTENDANCE (EPOCH 3)

Group	Active Detection of Infection-Extension (Epoch 3)							
	Visit 28	Visit 29	Visit 30	Visit 31	Visit 32	Visit 33	Visit 34	Visit 35
Group 1 (N=)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Group 2 (N=)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Group 3 (N=)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Group 4 (N=)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Group 5 (N=)	xx (xx.x %)	xx (xx.x %)	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 %)	xx (xx.x %)	xx (xx.x %)

N: total number of subjects in each group
Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).

VACCINE EFFICACY TABLES

Table 10.2.1.1 and 2. Vaccine efficacy (Group 1 vs Group 4): First Infection Events (FIEs) of *P. falciparum* during the Active Detection of Infection period by HIV status and overall (ATP cohort for efficacy and Total cohort for efficacy)

First or only infection	Group 1 (RTS,S)				Group 4 (Rabies)				Vaccine Efficacy				Adjusting variable	Interaction VE
	N	Events	PYAR	Rate	N	Event	PYAR	Rate	Efficacy	LL	UL	P value	P value	P value
Overall unadjusted	xxx	xxx	xxxx.x	x.xx	xxx	xxx	xxx	xxxx.x	xx.xx	xx.xx	xx.xx	x.xxx		
Adjusted by HIV									xx.xx	xx.xx	xx.xx	x.xxx	x.xxx	x.xxx
HIV positive	xxx	xxx	xxxx.x	x.x	xxx	xxx	xxx	xxxx.x						
HIV negative	Xxx	xxx	xxxx.x	x.x	xxx	xxx	xxx	xxxx.x						

N = total number of subjects at risk in each group (without missing values)
Events = number of subjects having at least one confirmed *P. falciparum* infection detected by PCR in each group
PYAR = sum of follow-up period (censored at the first occurrence of a confirmed *P. falciparum* infection) expressed in years
Events/PYAR = Incidence rate of subjects reporting one event
LL, UL = 95% Lower and Upper confidence limits
Efficacy (%) = Vaccine Efficacy adjusted by gender (Cox regression model, 1-adjusted HR (Hazard ratio))
p-values for vaccine efficacy and statistically significant covariates are from Cox regression model and interaction vaccine efficacy p-value is from HIV status and treatment Group term.
For the multivariable analysis, HIV (positive vs negative) will be included, and the next variables will be considered: Age (tertile 1-3), Gender (male vs female), the more significant between Ethnicity and Race, the most significant between Own bednet, Sleep under bednet and Indoor residual spray (IRS) and the most significant between Height, Weight and BMI (tertile 1-3). Any potential confounding factor will be identified with p-value lower than 0.1.

Table 10.2.2.1 and 2 Vaccine efficacy (Group 2 vs Group 5): First Infection Events (FIEs) of P. falciparum during the Active Detection of Infection period by HIV status and overall (ATP cohort for efficacy and Total cohort for efficacy)

First or only infection	Group 2 (RTS,S)				Group 5 (Rabies)				Vaccine Efficacy				Adjusting variable	Interaction VE
	N	Events	PYAR	Rate	N	Event	PYAR	Rate	Efficacy	LL	UL	P value	P value	P value
Overall unadjusted	Xxx	xxx	xxxx.x	x.xx	xxx	xxx	xxx	xxxx.x	xx.xx	xx.xx	xx.xx	x.xxx		
Adjusted by HIV									xx.xx	xx.xx	xx.xx	x.xxx	x.xxx	x.xxx
HIV positive	Xxx	xxx	xxxx.x	x.x	xxx	xxx	xxx	xxxx.x						
HIV negative	Xxx	xxx	xxxx.x	x.x	xxx	xxx	xxx	xxxx.x						

N = total number of subjects at risk in each group (without missing values)
Events = number of subjects having at least one confirmed *P. falciparum* infection detected by PCR in each group
PYAR = sum of follow-up period (censored at the first occurrence of a confirmed *P. falciparum* infection) expressed in years
Events/PYAR = Incidence rate of subjects reporting one event
LL, UL = 95% Lower and Upper confidence limits
Efficacy (%) = Vaccine Efficacy adjusted by gender (Cox regression model, 1-adjusted HR (Hazard ratio))
p-values for vaccine efficacy and statistically significant covariates are from Cox regression model and interaction vaccine efficacy p-value is from HIV status and treatment Group term.
For the multivariable analysis, HIV (positive vs negative) will be included, and the next variables will be considered: Age (tertile 1-3), Gender (male vs female), the more significant between Ethnicity and Race, the most significant between Own bednet, Sleep under bednet and Indoor residual spray (IRS) and the most significant between Height, Weight and BMI (tertile 1-3). Any potential confounding factor will be identified with p-value lower than 0.1.

Table 10.2.3.1 and 2 Vaccine efficacy (Group 1 vs Group 2): First Infection Events (FIEs) of *P. falciparum* during the Active Detection of Infection period by HIV status and overall (ATP cohort for efficacy and Total cohort for efficacy)

First or only infection	Group 1 (RTS,S)				Group 2 (RTS,S)				Vaccine Efficacy				Adjusting variable	Interaction VE
	N	Events	PYAR	Rate	N	Event	PYAR	Rate	Efficacy	LL	UL	P value	P value	P value
Overall unadjusted	Xxx	xxx	xxxx.x	x.xx	xxx	xxx	xxx	xxxx.x	xx.xx	xx.xx	xx.xx	x.xxx		
Adjusted by HIV									xx.xx	xx.xx	xx.xx	x.xxx	x.xxx	x.xxx
HIV positive	Xxx	xxx	xxxx.x	x.x	xxx	xxx	xxx	xxxx.x						
HIV negative	Xxx	xxx	xxxx.x	x.x	xxx	xxx	xxx	xxxx.x						

N = total number of subjects at risk in each group (without missing values)
Events = number of subjects having at least one confirmed *P. falciparum* infection detected by PCR in each group
PYAR = sum of follow-up period (censored at the first occurrence of a confirmed *P. falciparum* infection) expressed in years
Events/PYAR = Incidence rate of subjects reporting one event
LL, UL = 95% Lower and Upper confidence limits
Efficacy (%) = Vaccine Efficacy adjusted by gender (Cox regression model, 1-adjusted HR (Hazard ratio))
p-value from Cox regression model
For the multivariable analysis, HIV (positive vs negative) will be included, and the next variables will be considered: Age (tertile 1-3), Gender (male vs female), the more significant between Ethnicity and Race, the most significant between Own bednet, Sleep under bednet and Indoor residual spray (IRS) and the most significant between Height, Weight and BMI (tertile 1-3). Any potential confounding factor will be identified with p-value lower than 0.1.

Table 10.2.4.1 and 2 Vaccine efficacy (Group 4 vs Group 5): First Infection Events (FIEs) of *P. falciparum* during the Active Detection of Infection period by HIV status and overall (ATP cohort for efficacy and Total cohort for efficacy)

First or only infection	Group 4 (Rabies)				Group 5 (Rabies)				Vaccine Efficacy				Adjusting variable	Interaction VE
	N	Events	PYAR	Rate	N	Event	PYAR	Rate	Efficacy	LL	UL	P value	P value	P value
Overall unadjusted	Xxx	xxx	xxxx.x	x.xx	xxx	xxx	xxx	xxxx.x	xx.xx	xx.xx	xx.xx	x.xxx		
Adjusted by HIV									xx.xx	xx.xx	xx.xx	x.xxx	x.xxx	x.xxx
HIV positive	Xxx	xxx	xxxx.x	x.x	xxx	xxx	xxx	xxxx.x						
HIV negative	Xxx	xxx	xxxx.x	x.x	xxx	xxx	xxx	xxxx.x						

N = total number of subjects at risk in each group (without missing values)
Events = number of subjects having at least one confirmed *P. falciparum* infection detected by PCR in each group
PYAR = sum of follow-up period (censored at the first occurrence of a confirmed *P. falciparum* infection) expressed in years
Events/PYAR = Incidence rate of subjects reporting one event
LL, UL = 95% Lower and Upper confidence limits
Efficacy (%) = Vaccine Efficacy adjusted by gender (Cox regression model, 1-adjusted HR (Hazard ratio))
p-value from Cox regression model
For the multivariable analysis, HIV (positive vs negative) will be included, and the next variables will be considered: Age (tertile 1-3), Gender (male vs female), the more significant between Ethnicity and Race, the most significant between Own bednet, Sleep under bednet and Indoor residual spray (IRS) and the most significant between Height, Weight and BMI (tertile 1-3). Any potential confounding factor will be identified with p-value lower than 0.1.

Table 10.2.5.1 and 2 Summary of subjects at risk, person-time, number of FIEs and incidence rate (ATP cohort for efficacy and Total cohort for efficacy) for Group 1 and 4

	Group 1 (RTS/S)				Group 4 (Rabies)				Overall			
	N	Events	PYAR	Rate	N	Events	PYAR	Rate	N	Events	PYAR	Rate
Visit 19	Xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x
Visit 20	Xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x
Visit 21	Xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x
Visit 22	Xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x
Visit 23	Xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x
Visit 24	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x
Visit 25	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x
Visit 26	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x
Visit 27	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x
…												
If the targets are not reach by the end of Epoch 2, then ADI period will extended to when the target is reached or the end of the extension ADI period												

N = number of subjects at risk in each group at each visit (without missing values)
Events = number of subjects having at least one confirmed *P. falciparum* infection detected by PCR
PYAR = sum of follow-up period (censored at the first occurrence of a confirmed *P. falciparum* infection) expressed in years
Events/PYAR = Incidence rate of subjects reporting one event
No parasitemia testing has been recorded for unscheduled visits.

Commented [JA1]: Why is this footnote removed?
Commented [JJ2R1]: There were no parasitemia data for unscheduled visits during ADI
Commented [JA3R1]: Could you please include in the footnote that no parasitemia data for unscheduled visits was registered.

Please note that there are several AEs that are malaria, but I have not check if they were during the ADI epochs.
Commented [JJ4R1]: Updated

Table 10.2.6.1 and 2 Summary of subjects at risk, person-time, number of FIEs and incidence rate (ATP cohort for efficacy and Total cohort for efficacy) for Group 2 and 5

	Group 2 (RTS/S)				Group 5 (Rabies)				Overall			
	N	Events	PYAR	Rate	N	Events	PYAR	Rate	N	Events	PYAR	Rate
Visit 19	xxx				xxx				xxx			
Visit 20	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x
Visit 21	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x
Visit 22	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x
Visit 23	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x
Visit 24	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x
Visit 25	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x
Visit 26	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x
Visit 27	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x	xxx	xx	xx.x	x.x
…												
If the targets are not reach by the end of Epoch 2, then ADI period will extended to when the target is reached or the end of the extension ADI period												

N = number of subjects at risk in each group at each visit (without missing values)
Events = number of subjects having at least one confirmed *P. falciparum* infection detected by PCR
PYAR = sum of follow-up period (censored at the first occurrence of a confirmed *P. falciparum* infection) expressed in years
Events/PYAR = Incidence rate of subjects reporting one event
No parasitemia testing has been recorded for unscheduled visits.

Table 10.2.7.1 and 2 Summary of median time to FIEs and hazards (ATP cohort for efficacy and Total cohort for efficacy)

	Group1 (N=)	Group2 (N=)	Group4 (N=)	Group5 (N=)	Overall (N=)
Median time to FIEs (IQR)	xxx(xxx.x-xxx.x)	xxx(xxx.x-xxx.x)	xxx(xxx.x-xxx.x)	xxx(xxx.x-xxx.x)	xxx(xxx.x-xxx.x)
Hazard (95% CI)	x.xx(x.xx-x.xx)	x.xx(x.xx-x.xx)	x.xx(x.xx-x.xx)	x.xx(x.xx-x.xx)	x.xx(x.xx-x.xx)

N = number of subjects at risk in each group (without missing values)
Median time to FIEs (expressed in years) and hazard are derived from KM and cox regression model respectively.

IMMUNOGENICITY TABLES

Table 10.3.1.1 and 2: Number and Percentage of Subjects with anti-CS NANP Antibody Titer/Avidity Equal to or above Cut-off (seropositive) and GMTs (ATP cohort for immunogenicity and Total vaccinated cohort)

			Group 1	Group 2	Group 3
Anti-CS NANP (1XPBS) seroresponse	**Visit**	**Statistics**			
	Visit 2	N	xx	xx	Xx
		N	xx	xx	Xx
		%	xx.x	xx.x	xx.x
		LL, UL	xx.x	xx.x	xx.x
	Repeat for visits 11, 13, 17, 10 and 27 and the termination visit				
Repeat for Anti-CS NANP (4M Urea)					
Anti-CS NANP (1XPBS) GMT					
	Visit 2	Titer	xxx.x	xxx.x	xxx.x
		LL, UL	xxx.xx-xx.x	xxx.xx-xx.x	xxx.xx-xx.x
		Min, Max	xxx.x-xxx.x	xxx.x-xxx.x	xxx.x-xxx.x
		p-value	1 vs 2 (x.xxx)	2 vs 3 (x,xxx)	1 vs 3 (x.xxx)
	Repeat for visits 11, 13, 17, 10 and 27 and the termination visit				
Repeat for Anti-CS NANP (4M Urea) GMT and					

Anti-CS NANP
Avidity Index

Abbreviations: GMT = Geometric Mean Titer; N = Total number of subjects; n = Number of seropositive subjects; % = Percentage; LL = Lower limit of 95% CI; UL = Upper limit of 95% CI; Min = Minimum; Max = Maximum;
p-values for pairwise comparisons are computed from mixed model for repeated measures using avidity index or log transformed antibody titers (Anti-CS NANP (1XPBS) and Anti-CS NANP (4M Urea)) and their interaction term as dependent variables and groups and HIV status as covariates and subject as random effect;
Seropositivity criteria: antibody titer > LLOQ, lower limit of quantification

Table 10.3.2.1 and 2: Number and Percentage of Subjects with Anti-CS C-term Antibody Titer/Avidity Equal to or above Cut-off and GMTs (ATP cohort for immunogenicity and Total cohort for efficacy)

Same shell as T.10.3.1

Table 10.3.3.1 and 2: Number and Percentage of Subjects with Anti-HBsAb Titer Equal to or above Cut-off and GMTs (ATP cohort for immunogenicity and Total vaccinated cohort)

Same shell as T.10.3.1 except only antibody titer is assayed and the visits are 2, 5, 11 and 20.

Table 10.3.4.1 and 2 : Geometric Fold Rise in Anti-CS NANP Antibody Titer at Each Post-Vaccination Timepoint Compared to Screening (ATP cohort for immunogenicity and Total vaccinated cohort)

								95% CI		>= 2			>= 3			>= 4		
Antibody	**Group**	**N**	**Visit**	**GMT**	**Baseline GMT**	**Ratio Order**	**Ratio Value**	**LL**	**UL**	**n**	**% (95% CI)**	**p-value**	**n**	**% (95% CI)**	**p-value**	**n**	**% (95% CI)**	**p-value**
Anti-CS NANP	1		V11	xx.x	xx.x	V11/V5	xx.x	xx.x	xx.x	xx	xx.x (xx.x, xx.x)	1 vs 2 (x.xxx)	xx	xx.x (xx.x, xx.x)	1 vs 2 (x.xxx)	xx	xx.x(xx.x, xx.x)	1 vs 2 (x.xxx)
	2		V11	xx.x	xx.x	V11/V5	xx.x	xx.x	xx.x	xx	xx.x (xx.x, xx.x)	2 vs 3 (x.xxx)	xx	xx.x (xx.x, xx.x)	2 vs 3 (x.xxx)	xx	xx.x(xx.x, xx.x)	2 vs 3 (x.xxx)
	3		V11	xx.x	xx.x	V11/V5	xx.x	xx.x	xx.x	xx	xx.x (xx.x, xx.x)	1 vs 3 (x.xxx)	xx	xx.x (xx.x, xx.x)	1 vs 3 (x.xxx)	xx	xx.x(xx.x, xx.x)	1 vs 3 (x.xxx)
	Repeat for visits 13, 17, 10 and 27 and the termination visit																	

Abbreviations: GMT = Geometric Mean Titer; N = Total number of subjects; n = Number of seropositive subjects; % = Percentage; LL = Lower limit of 95% CI; UL = Upper limit of 95% CI; Min = Minimum; Max = Maximum;

p-values for pairwise comparisons are computed from mixed model for repeated measures using log transformed fold increase (Anti-CS NANP (1XPBS) and Anti-CS NANP (4M Urea)) and their interaction term as dependent variables and groups and HIV status as covariates and subject as random effect;

>=2, >=3 and >=4 responder rates and their 95% CIs are calculated through Clopper-Pearson method and p-values are calculated through Fisher's test or Chi-Square test.

Table 10.3.5.1 and 2: Geometric Fold Rise in Anti-CS C-term Antibody Titer at Each Post-Vaccination Timepoint Compared to Screening (ATP cohort for immunogenicity and Total vaccinated cohort)

Same shell as T.10.3.4.1 and 2

Table 10.3.6.1 and 2: Geometric Fold Rise in Anti-HBsAb Titer at Each Post-Vaccination Timepoint Compared to Screening (ATP cohort for immunogenicity and Total vaccinated cohort)

Same shell as T.10.3.4.1 and 2

SAFETY TABLES

Table 10.4.1.1: Overall Safety Profile by Treatment (Safety Population)

	Group 1 (N=) n (%) [CI]	Group 2 (N=) n (%) [CI]	Group 3 (N=) n (%) [CI]	Group 4 (N=) n (%) [CI]	Group 5 (N=) n (%) [CI]	Total (N=) n (%) [CI]
Number of Local Solicited Adverse Events	xxx	xxx	xxx	xxx	xxx	xxx
Number of Subjects with any Local Solicited Adverse Events	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
Number of Systemic Solicited Adverse Events	xxx	xxx	xxx	xxx	xxx	xxx
Number of Subjects with any Systemic Solicited Adverse Events	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
Number of Unsolicited Adverse Events	xxx	xxx	xxx	xxx	xxx	xxx
Number of Subjects with any Unsolicited Adverse Events	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
Number of Adverse Events of Special Interest (AESIs)	xxx	xxx	xxx	xxx	xxx	xxx
Number of Subjects with any Adverse Events of Special Interest (AESIs)	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
Number of Serious Adverse Events (SAEs)	xxx	xxx	xxx	xxx	xxx	xxx
Number of Subjects with any Serious Adverse Events (SAEs)	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]

N: total number of subjects in each group; n = Number of subjects; % = Percentage; CI = Confidence interval.
Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).
All confidence intervals are two-sided 95% via Clopper-Pearson method.
Denominator for percentage is subjects in safety population.

Table 10.4.1.2: Frequency of Local Solicited Adverse Events by Treatment and Severity (Safety Population)

	Group 1 (N=) n (%) [CI]	Group 2 (N=) n (%) [CI]	Group 3 (N=) n (%) [CI]	Group 4 (N=) n (%) [CI]	Group 5 (N=) n (%) [CI]	Total (N=) n (%) [CI]
Any Events	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Total	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Grade 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Grade 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Grade 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Pain at SOI	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Total	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Grade 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Grade 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Grade 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
(Repeat for Swelling at SOI)						

N: total number of subjects in each group; n = Number of subjects; % = Percentage; CI = Confidence interval.
Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).
Denominator for percentage is subjects in safety population.
Subject counted once at highest severity grade.
All confidence intervals are two-sided 95% via Clopper-Pearson method
Local solicited Adverse Events include: Pain at site of injection (Pain at SOI); Swelling at injection site; Each event has intensity scores 0-3 with 0 for no adverse event and 3 for the adverse event that prevents normal activity (for details see protocol for detail)

Table 10.4.1.3: Frequency of Systemic Solicited Adverse Events by Treatment and Severity (Safety Population)

	Group 1 (N=) n (%) [CI]	Group 2 (N=) n (%) [CI]	Group 3 (N=) n (%) [CI]	Group 4 (N=) n (%) [CI]	Group 5 (N=) n (%) [CI]	Total (N=) n (%) [CI]
Any Events						
Total	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Grade 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Grade 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Grade 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Fever						
Total	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Grade 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Grade 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Grade 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
(Repeat for Fatigue, Headache, Muscle ache, and Gastrointestinal Symptoms)						

N: total number of subjects in each group; n = Number of subjects; % = Percentage; CI = Confidence interval.
Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).
Denominator for percentage is subjects in safety population for whom memory aid data was available.
Subject counted once at highest severity grade.
All confidence intervals are two-sided 95% via Clopper-Pearson method
Systemic Solicited Adverse Events include: Fever; Headache; Gastrointestinal symptoms (nausea, vomiting, diarrhea and/or abdominal pain); Fatigue; Muscle ache. Each event has intensity scores 0-3 with 0 for no adverse event and 3 for the adverse event that prevents normal activity. For fever, 0: <37.5°C (99.5°F); 1: 37.5°C (99.5°F) to 38.0°C (100.4°F); 2: >38.0°C (>100.4°F) to 39.0°C (102.1°F); 3: >39.0°C (102.1°F) (for additional details see protocol)

Table 10.4.1.4: Summary of Unsolicited Adverse Events by Treatment (Safety Population)

	Group 1 (N=) n (%) [CI]	Group 2 (N=) n (%) [CI]	Group 3 (N=) n (%) [CI]	Group 4 (N=) n (%) [CI]	Group 5 (N=) n (%) [CI]	Total (N=) n (%) [CI]
All Systems						
	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
System Organ Class 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Preferred Term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Preferred Term 3						
System Organ Class 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Preferred Term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Preferred Term 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]

N: total number of subjects in each group; n = Number of subjects; % = Percentage; CI = Confidence interval.
Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).
xx= Number of Events
Subject counted once per adverse event term.
All confidence intervals are two-sided 95% via Clopper-Pearson method.

Table 10.4.1.5: Summary of Unsolicited Adverse Events by Treatment, Severity and Relationship to Study Treatment (Safety Population)

	Group 1 (N=) n (%) [CI]	Group 2 (N=) n (%) [CI]	Group 3 (N=) n (%) [CI]	Group 4 (N=) n (%) [CI]	Group 5 (N=) n (%) [CI]	Total (N=) n (%) [CI]
All Systems						
Total	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
Grade 1	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
Grade 2	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
Grade 3	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
Related	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
Grade 1	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
Grade 2	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
Grade 3	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
Not Related	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
Grade 1	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
Grade 2	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
Grade 3	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
System Organ Class 1	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
Total	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
Grade 1	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
Grade 2	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]

Grade 3	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
(Repeat similarly for other SOCs and PTs)						

N: total number of subjects in each group; n = Number of subjects; % = Percentage; CI = Confidence interval.
Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).
xx= Number of Events
All confidence intervals are two-sided 95% via Clopper-Pearson method.
Subjects who experience one or more episodes of the same adverse event are counted once at highest severity grade and relatedness

Table 10.4.1.6: Summary of Serious Adverse Events by Treatment (Safety Population)

	Group 1 (N=) n (%) [CI]	Group 2 (N=) n (%) [CI]	Group 3 (N=) n (%) [CI]	Group 4 (N=) n (%) [CI]	Group 5 (N=) n (%) [CI]	Total (N=) n (%) [CI]
All Systems						
	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
System Organ Class 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Preferred Term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Preferred Term 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
System Organ Class 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Preferred Term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Preferred Term 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
(Repeat similarly for other SOCs and PTs)						

N: total number of subjects in each group; n = Number of subjects; % = Percentage; CI = Confidence interval.
Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).
xx= Number of Events
Subjects who experience one or more episodes of the same adverse event are counted once
All confidence intervals are two-sided 95% via Clopper-Pearson method.

Table 10.4.1.7: Frequency of Local Solicited Adverse Events by Treatment, Injection Period, and Severity (Safety Population)

	Group 1 (N=)			Repeat for Groups 2-5 and Total
	Injection 1 Day 1-7 n (%) [CI]	**Injection 2 Day 29-35 n (%) [CI]**	**Injection 3 Day 197-203 n (%) [CI]**	
Any Events	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	
Total	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	
Grade 1	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	
Grade 2	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	
Grade 3	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	
Pain at SOI	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	
Total	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	
Grade 1	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	
Grade 2	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	
Grade 3	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	
(Repeat for Swelling at SOI)				

N: total number of subjects in each group; n = Number of subjects; % = Percentage; CI = Confidence interval.
Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).
Solicited AEs are collected on the day of vaccine administration and for six days following each injection (Day 1-7).
Denominator for percentage is subjects in safety population.
All confidence intervals are two-sided 95% via Clopper-Pearson method.
Local solicited Adverse Events include: Pain at site of injection (Pain at SOI); Swelling at injection site.

Table 10.4.1.8: Frequency of Systemic Solicited Adverse Events by Treatment, Injection Period, and Severity (Safety Population)

	Group 1 (N=)			Repeat for Groups 2-5 and Total
	Injection 1 Day 1-7 n (%) [CI]	Injection 2 Day 29-35 n (%) [CI]	Injection 3 Day 197-203 n (%) [CI]	
Any Events	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	
Total	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	
Grade 1	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	
Grade 2	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	
Grade 3	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	
Fatigue	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	
Total	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	
Grade 1	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	
Grade 2	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	
Grade 3	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	
(Repeat for Fever, Headache, ect.)				

N: total number of subjects in each group; n = Number of subjects; % = Percentage; CI = Confidence interval.
Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).
Solicited AEs are collected on the day of vaccine administration and for six days following each injection (Day 1-7).
Denominator for percentage is subjects in safety population
All confidence intervals are two-sided 95% via Clopper-Pearson method.

Systemic Solicited Adverse Events include: Fever; Headache; Gastrointestinal symptoms (nausea, vomiting, diarrhea and/or abdominal pain); Fatigue; Muscle ache. Each event has intensity scores 0-3 with 0 for no adverse event and 3 for the adverse event that prevents normal activity. For fever, Grade 0: <37.5ºC (99.5ºF); Grade 1: 37.5ºC (99.5ºF) to 38.0ºC (100.4ºF); Grade 2: >38.0ºC (>100.4ºF) to 39.0ºC (102.1ºF); Grade 3: >39.0ºC (102.1ºF) (for additional details see protocol)

Table 10.4.1.9: Summary of Adverse Events of Special Interest by Treatment (Safety Population)

	Group 1 (N=) n (%) [CI]	Group 2 (N=) n (%) [CI]	Group 3 (N=) n (%) [CI]	Group 4 (N=) n (%) [CI]	Group 5 (N=) n (%) [CI]	Total (N=) n (%) [CI]
All Systems	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
System Organ Class 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Preferred Term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Preferred Term 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
System Organ Class 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Preferred Term 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Preferred Term 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
(Repeat similarly for other SOCs and PTs)						

N: total number of subjects in each group; n = Number of subjects; % = Percentage; CI = Confidence interval.
Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).
Subjects who experience one or more episodes of the same adverse event are counted once
All confidence intervals are two-sided 95% via Clopper-Pearson method.

Table 10.4.1.10: Summary of Adverse Events (Safety Population)

	Group 1 (N=) n (%) [CI]	Group 2 (N=) n (%) [CI]	Group 3 (N=) n (%) [CI]	Group 4 (N=) n (%) [CI]	Group 5 (N=) n (%) [CI]	Total (N=) n (%) [CI]
Number of Unsolicited Adverse Events	xxx	xxx	xxx	xxx	xxx	xxx
Number of Subjects with any Unsolicited Adverse Events	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
Number of Related Unsolicited Adverse Events	xxx	xxx	xxx	xxx	xxx	xxx
Number of Subjects with any Related Unsolicited Adverse Events	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
Number of Adverse Events of Special Interest (AESIs)	xxx	xxx	xxx	xxx	xxx	xxx
Number of Subjects with any Adverse Events of Special Interest (AESIs)	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
Number of Related Adverse Events of Special Interest	xxx	xxx	xxx	xxx	xxx	xxx
Number of Subjects with any Related Adverse Events of Special Interest	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
Number of Serious Adverse Events (SAEs)	xxx	xxx	xxx	xxx	xxx	xxx
Number of Subjects with any Serious Adverse Events (SAEs)	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
Number of Related Serious Adverse Events	xxx	xxx	xxx	xxx	xxx	xxx
Number of Subjects with any Related Serious Adverse Events	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
Number of Serious Adverse Events leading to death.	xxx	xxx	xxx	xxx	xxx	xxx
Number of Subjects with any Serious Adverse Events leading to death.	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
Number of Unsolicited Adverse Events leading to subject discontinuation	xxx	xxx	xxx	xxx	xxx	xxx
Number of Subjects with any Unsolicited Adverse Events leading to subject discontinuation.	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]

N: total number of subjects in each group; n = Number of subjects; % = Percentage; CI = Confidence interval.

Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).
All confidence intervals are two-sided 95% via Clopper-Pearson method.
Denominator for percentage is subjects in safety population for whom memory aid data was available.

Table 10.4.1.11: Summary of Recurrent Adverse Events (Safety Population)

	Episodes of AEs of this Type per Subject	Group 1 (N=) n (%) [CI]	Group 2 (N=) n (%) [CI]	Group 3 (N=) n (%) [CI]	Group 4 (N=) n (%) [CI]	Group 5 (N=) n (%) [CI]	Total (N=) n (%) [CI]
Local Solicited							
Pain at SOI							
	2	xx	xx	xx	xx	xx	xx
	3	xx	xx	xx	xx	xx	xx
(Repeat for Swelling at SOI)							
Systemic Solicited							
Fever	2	xx	xx	xx	xx	xx	xx
	3	xx	xx	xx	xx	xx	xx
(Repeat for Fatigue, Headache, Muscle ache, Gatrointestinal Symptoms)							
Unsolicited Adverse Events							
System Organ Class 1							
Preferred Term 1	2	xx	xx	xx	xx	xx	xx
	3	xx	xx	xx	xx	xx	xx
	4+	xx	xx	xx	xx	xx	xx
Preferred Term 2	2	xx	xx	xx	xx	xx	xx
	3	xx	xx	xx	xx	xx	xx
	4+	xx	xx	xx	xx	xx	xx
System Organ Class 2							
Preferred Term 1	2	xx	xx	xx	xx	xx	xx
	3	xx	xx	xx	xx	xx	xx
	4+	xx	xx	xx	xx	xx	xx
Preferred Term 2	2	xx	xx	xx	xx	xx	xx
	3	xx	xx	xx	xx	xx	xx
	4+	xx	xx	xx	xx	xx	xx
Repeat for other SOCs and PTs							

N: total number of subjects in each group; n = Number of subjects; % = Percentage; CI = Confidence interval
Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).
Subjects who experience one or more episodes of the same adverse event are counted once
All confidence intervals are two-sided 95% via Clopper-Pearson method.
Only Adverse Events that have count of occurrences greater than or equal to 2 will be included.

Table 10.4.1.12: Summary of Adverse Events that Persisted beyond 6 Days Post-IP Administration (Safety Population)

	Group 1 (N=) n (%) [CI]	Group 2 (N=) n (%) [CI]	Group 3 (N=) n (%) [CI]	Group 4 (N=) n (%) [CI]	Group 5 (N=) n (%) [CI]	Total (N=) n (%) [CI]
Any Events	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
Total						
Grade 1						
Grade 2						
Grade 3						
Local						
Pain at SOI						
Total						
Grade 1						
Grade 2						
Grade 3						
(Repeat for Swelling at SOI)						
Systemic						
Fever						
Total						
Grade 1						
Grade 2						
Grade 3						
(Repeat for Fatigue, Headache, Muscle ache and gastrointestinal symptoms)						

N: total number of subjects in each group; n = Number of subjects; % = Percentage; CI = Confidence interval
Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).
Subjects who experience one or more episodes of the same adverse event are counted once
All confidence intervals are two-sided 95% via Clopper-Pearson method.
All solicited Adverse Events that persisted beyond 6 days post-IP administration.

Table 10.4.1.13: Exploration of Group Comparisons for Common Adverse Events (Safety Population)

	Group 1 (N=) n (%) [CI]	Group 2 (N=) n (%) [CI]	Group 3 (N=) n (%) [CI]	Group 4 (N=) n (%) [CI]	Group 5 (N=) n (%) [CI]	Total (N=) n (%) [CI]	P-value
Pain at SOI							
Yes	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	0.xxx
No	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	
Swell at SOI							
Yes	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	0.xxx
No	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	
(Repeat for Fever, Headache, Gastrointestinal symptoms (nausea, vomiting, diarrhea and/or abdominal pain), Fatigue and Muscle ache)							

Subjects who experience one or more episodes of the same adverse event are counted once
All confidence intervals are two-sided 95% via Clopper-Pearson method.
p-values are calculated using Fisher's Exact Test.
This table can be expanded to cover other group comparisons, including each preferred terms, grade 4 solicited and unsolicited reactions ect.

Table 10.4.1.14: Safety Lab Data out of Range (Safety Population)

	Group 1 (N=) n (%) [CI]	Group 2 (N=) n (%) [CI]	Group 3 (N=) n (%) [CI]	Group 4 (N=) n (%) [CI]	Group 5 (N=) n (%) [CI]	Total (N=) n (%) [CI]
Hemoglobin						
Screening						
Low	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
High	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Visit 5						
Low	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
High	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
(Repeat for WBC, Platelets, ALT, Creatinine)						

N = total number of subjects in each group; n = Number of subjects; %=Percentage; CI = Confidence interval.
Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).
All confidence intervals are two-sided 95% via Clopper-Pearson method.

Table 10.4.1.15: Summary of Safety Lab Results (Safety Population)

	Group 1 (N=)	Group 2 (N=)	Group 3 (N=)	Group 4 (N=)	Group 5 (N=)	Total (N=)
Hemoglobin at Screening						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
95% CI	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Hemoglobin at Visit 5						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
95% CI	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
(Repeat for WBC, Platelet, ALT, Creatinine)						

N = total number of subjects in each group.

Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).

All confidence intervals are two-sided 95% via t-distribution.

Table 10.4.1.16: Summary of Hemoglobinopathy Results (Safety Population)

	Group 1 (N=) n (%) [CI]	Group 2 (N=) n (%) [CI]	Group 3 (N=) n (%) [CI]	Group 4 (N=) n (%) [CI]	Group 5 (N=) n (%) [CI]	Total (N=) n (%) [CI]
Sickle cell screen						
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Heterozygous	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Homozygous	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
G6PD						
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Deficient	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Alpha-thalassemia						
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Heterozygous	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]
Homozygous	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]	[xx.x-xx.x]

N = total number of subjects in each group; n = Number of subjects; %=Percentage; CI = Confidence interval.
Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).
All confidence intervals are two-sided 95% via Clopper-Pearson method.

Table 10.4.1.17: Summary of Urine Pregnancy Test Results (Safety Population)

	Group 1 (N=) n (%) [CI]	Group 2 (N=) n (%) [CI]	Group 3 (N=) n (%) [CI]	Group 4 (N=) n (%) [CI]	Group 5 (N=) n (%) [CI]	Total (N=) n (%) [CI]
Screening						
Positve	x	x	x	x	x	x
Negative	xx	xx	xx	xx	xx	xx
N/A	xx	xx	xx	xx	xx	xx
Visit 2						
Positve	x	x	x	x	x	x
Negative	xx	xx	xx	xx	xx	xx
N/A	xx	xx	xx	xx	xx	xx
Visit 5						
Positve	x	x	x	x	x	x
Negative	xx	xx	xx	xx	xx	xx
N/A	xx	xx	xx	xx	xx	xx
Repeat for Visit 8 and 17						

N = total number of subjects in each group; n = Number of subjects; %=Percentage; CI = Confidence interval.
Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).

Table 10.4.1.18: Summary of All Non-Serious Adverse Events by Treatment (Safety Population)

	Group 1 (N=) n (%) [CI]	Group 2 (N=) n (%) [CI]	Group 3 (N=) n (%) [CI]	Group 4 (N=) n (%) [CI]	Group 5 (N=) n (%) [CI]	Total (N=) n (%) [CI]
All Non-Serious Adverse Events	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]	xx (xx.x%) [xx.x-xx.x]
System Organ Class 1						
Preferred Term 1						
Preferred Term 2						
Preferred Term 3						
System Organ Class 2						
Preferred Term 1						
Preferred Term 2						
Preferred Term 3						

N = total number of subjects in each group; n = Number of subjects; %=Percentage; CI = Confidence interval.
Denominator for percentage is subjects in the safety population.
Subjects who experience one or more episodes of the same adverse event are counted once.
Solicited AEs are included in the table within categories of system organ class and preferred term.
All confidence intervals are two-sided 95% via Clopper-Pearson method.
Group 1: RTS,S/AS01E with anti-malarials to clear parasites; Group 2: RTS,S/AS01E with anti-malarials to prevent infection (prophylaxis); Group 3: RTS,S/AS01E without anti-malarials treatment to clear parasites; Group 4: Rabies with anti-malarials to clear parasites; Group 5: Rabies with anti-malarials to prevent infection (prophylaxis).

12. DEMOGRAPHICS LISTINGS

Listing 10.1.1: Protocol Deviations

Subject ID	Group	Date Occurred	Date Reported	Category	Brief Description
xxxxx	Groups 1-5	ddMMMyyyy	ddMMMyyyy	xxxx	xxxxxxxxxx

The following deviation categories are included for the study:

- Eligibility
- Informed consent
- Randomization error
- Antimalarial drugs administered incorrectly
- IP administered incorrectly
- IP administration missed
- Missed visit
- Out-of-window visit
- Specimen not collected
- Procedure done incorrectly
- Procedure not done
- Other

Listing 10.1.2: Enrollment Status, Demographics and Subject Disposition

Subject ID	Informed Consent Signed/ Date of Informed Consent	Eligible	Randomized	Group	Reactogenicity Cohorts?	Sex/Age (Years)	Race/Ethnicity	Completed Study?	Date of Completion/ Early Termination	Reason for Early Termination
xxx	Yes/xxxxxx	No	No	xxx	(Yes/No)	Female/39	xxx/xxxx	No	xxxx	xxxxxxxxxxxxxx
xxx	Yes/xxxxxx	Yes	Yes	xxx		xxx	xxx/xxxx	Yes	xxxx	

Listing 10.1.3: Eligibility Criteria Not Met

Subject ID	Eligibility Criteria	Criteria Description
xxxxx	Inclusion Criteria	Subject has provided signed or thumb printed and dated informed consent form. xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
	Exclusion Criteria	Subject has planned administration/administration of a vaccine not foreseen by the study protocol from within 30 days before the first dose of study vaccine until 30 days after the last dose of study vaccine. xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx

Listing 10.1.4: Listing of All Eligibility Criteria

Eligibility Criteria	Criteria Description
Inclusion Criteria	Subject has provided signed or thumb printed and dated informed consent form. xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
Exclusion Criteria	Subject has planned administration/administration of a vaccine not foreseen by the study protocol from within 30 days before the first dose of study vaccine until 30 days after the last dose of study vaccine. xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx

Listing 10.1.5: Baseline Demographics

Subject ID	Group	Age (years)	Race	Sex	Ethnicity	Weight (unit)	Height (unit)	BMI (unit)
xxxxx	xxx	xx	xxxxxx	x	xxxxxx	xx.x	xxx.x	xx.x

Listing 10.1.6: HIV Status and HLA Typing

Subject ID	Group	HIV Test Date/Time	HIV Status	Buccal Swab Date/Time	HLA Typing Date/Time
xxxxx	xxx	ddMMMyyyy/hh:mm	Negative/Positive	ddMMMyyyy/hh:mm	HLA-A

Listing 10.1.7: Prior Medications

Subject ID	Group	Start Date/ End Date	ATC Level 4/ Preferred Term/ Medication Name	Dose/ Unit	Route/ Freq
Xxx	xxxx	ddMMMyyyy/ (ddMMMyyyy)	xxxx/xxx/xxx	xxxx/xxx	xxxx/xxxx

Listing 10.1.8: Concomitant Medication

Subject ID	Group	Start Date/ End Date	ATC Level 4/ Preferred Term/ Medication Name	Dose/ Unit	Route/ Freq
Xxx	xxxx	ddmmmyyyy/ (ddmmmyyyy or ONGOING)	xxxx/xxx/xxx	xxxx/xxx	xxxx/xxxx

Listing 10.1.9: Medical History

Subject ID	Group	Start Date / End Date	System Organ Class	Preferred Term
Xxxx	xxxx	ddMMMyyyy / ddMMMyyyy or ongoing ddMMMyyyy / ddMMMyyyy or ongoing	xxxxxx	xxxxxxx

Listing 10.1.10.1: Visit Attendance (Epoch 1)

Subject ID	Group	Treatment and immunization (Epoch 1)								
		Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8	Visit 9	Repeat until Visit 18
xxxx	xxxx	(Yes/ No)	(Yes/ No)	(Yes/ No)	(Yes/ No)	(Yes/ No)	(Yes/ No)	(Yes/ No)	(Yes/ No)	

Listing 10.1.10.2: Visit Attendance (Epoch 2)

Subject ID	Group	Active Detection of Infection (Epoch 2)								
		Visit 19	Visit 20	Visit 21	Visit 22	Visit 23	Visit 24	Visit 25	Visit 26	Visit 27
xxxx	xxxx	(Yes/ No)	(Yes/ No)	(Yes/ No)	(Yes/ No)	(Yes/ No)	(Yes/ No)	(Yes/ No)	(Yes/ No)	(Yes/ No)

Listing 10.1.10.3: Visit Attendance (Epoch 3)

Subject ID	Group	Active Detection of Infection-Extension (Epoch 3)							
		Visit 28	Visit 29	Visit 30	Visit 31	Visit 32	Visit 33	Visit34	Visit 35
xxxx	xxxx	(Yes/ No)	(Yes/ No)	(Yes/ No)	(Yes/ No)	(Yes/ No)	(Yes/ No)	(Yes/ No)	(Yes/ No)

Listing 10.1.11: Vaccine administration

Subject ID	Group	Visit Number	Vaccine Dose	Vaccination Date
xxxx	xxxx	Xxx	xxx	ddMMMyyyy

Listing 10.1.12: Anti-Malarials

Subject ID	Group	Visit Number	Anti-Malarials Taken	Date/Time	Number of tablets dispensed	Number of tablets returned	Full dose?
xxxx	xxxx	Xxx	xxx	ddMMMyyyy:hh:mm	x	x	(Yes/No)

Listing 10.1.13: Vital Signs

Subject ID	Group	Parameter	Visit	Date: Time	Results (Units)
			Screening		
xxx	xxxx	Pulse Rate	(Visit 1 or 2)	ddmmmyyyy: hh:mm	xx (beats/min))
			Visit 5	ddmmmyyyy: hh:mm	xx (beats/min))
			Visit 8	ddmmmyyyy: hh:mm	xx (beats/min))
			Visit 11	ddmmmyyyy: hh:mm	xx (beats/min))
			Visit 17	ddmmmyyyy: hh:mm	xx (beats/min))
			…		
		Systolic Blood Pressure		ddmmmyyyy: hh:mm	
			Screening (Visit 1 or 2)		xxx (mmHg))
			Visit 5	ddmmmyyyy: hh:mm	xxx (mmHg))
			Visit 8	ddmmmyyyy: hh:mm	xxx (mmHg))
			Visit 11	ddmmmyyyy: hh:mm	xxx (mmHg))
			Visit 17	ddmmmyyyy: hh:mm	xxx (mmHg))
			…		
			Repeat for Oral Temperature and diastolic Blood Pressure		
Repeat for other subjects					

Listing 10.1.14: Physical Examinations

Subject ID	Group	Body System	Visit	Date/Time of Exam	Results/ Description	Clinically Significant?
xxxxx	x	Abdomen	Screening	ddmmmyyyy:hh:mm	Normal	(Yes/No)
			Visit 5	ddmmmyyyy:hh:mm	Normal	(Yes/No)
			Visit 11	ddmmmyyyy:hh:mm	Normal	(Yes/No)
			Visit 17	ddmmmyyyy:hh:mm	Normal	(Yes/No)
		Repeat other body systems				

Repeat other subjects

13. SAFETY LISTINGS

Listing 10.2.1: Solicited Adverse Events (Safety Population)

Subject ID	Group	Reported at Visit	Type	AE Term	Maximum Severity	Start Date	Stop Date	Duration (in days) *	Days from Most Recent Vaccination**
xxxxx		xxx	Local	Pain at SOI	Grade 2	xxx	xxxx	xxxx	2
				Swelling at SOI	Grade 1	xxx	xxxx	xxxx	3
			Systemic	Headache	Grade 1	xxx	xxxx	xxxx	1

* Duration= AE stop date – AE start date + 1
** Difference between AE start date and most recent vaccination date + 1.

Listing 10.2.2: Unsolicited Adverse Events (Safety Population)

Subject ID	Group	AE Term	MedDRA Preferred Term/ System Organ Class	Start Date	Outcome/ Outcome Date	Duration (in days) *	Days from Most Recent Vaccination**	Severity/ Relation to Study Treatment	Action Taken with Study Treatment/Action Taken with Antimalarials	AESI?	SAE?
xxxxx	xxx	xxx									

* Duration= AE stop date – AE start date + 1
** Difference between AE start date and most recent vaccination date + 1.

Listing 10.2.3: Serious Adverse Events (Safety Population)

Subject ID	Group	AE Term	MedDRA Preferred Term/ System Organ Class	Start Date	Outcome/ Outcome Date	Duration (in days) *	Days from Most Recent Vaccination**	Severity/ Relation to Study Treatment	Action Taken with Study Treatment?	Serious Adverse Event Category
xxxxx	xxx	xxx								

* Duration= AE stop date – AE start date + 1
** Difference between AE start date and most recent vaccination date + 1.

Listing 10.2.4: Adverse Events of Special Interest (Safety Population)

Subject ID	Group	AE Term	MedDRA Preferred Term/ System Organ Class	Start Date	Outcome/ Outcome Date	Duration (in days) *	Days from Most Recent Vaccination**	Severity/ Relation to Study Treatment	Action Taken with Study Treatment?	Serious Adverse Event?
xxxxx	xxx	xxx								

* Duration= AE stop date – AE start date + 1
** Difference between AE start date and most recent vaccination date + 1.

Listing 10.2.5: Safety Laboratory Results (Safety Population)

Subject ID	Group	Sex	Test Name	Visit	Date	Results	Normal / Abnormal
xxxxx	xxx	xxx	Hemoglobin	1	ddMMMyyyy	xx	Normal
xxxxx	xxx	xxx	Hemoglobin	5	ddMMMyyyy	xx	Normal

Listing 10.2.6: Hemoglobinopathy Tests Results (Safety Population)

Subject ID	Group	Sex	Test Name	Date	Results
xxxxx	xxx	xxx	Sickle Cell Screen	ddMMMyyyy	xx
	xxx	xxx	G6P	ddMMMyyyy	xx
	xxx	xxx	Alpha-thalassemia	ddMMMyyyy	xx
Repeat for other subjects					

Listing 10.2.7: Urine Pregnancy Tests for Female Subjects (Safety Population)

Subject ID	Group	Sex	Visit	Date	Results
xxxxx	xxx	F	1	ddMMMyyyy	Negative
xxxxx	xxx	F	5	ddMMMyyyy	Negative
xxxxx	xxx	F	8	ddMMMyyyy	Negative
xxxxx	xxx	F	11	ddMMMyyyy	Negative
xxxxx	xxx	F	17	ddMMMyyyy	Negative
Repeat for other subjects					

14. IMMUNOGENICITY LISTING

Listing 10.3.1: Listing of Antibody Titers/Avidity

Subject ID	Timepoint	Date-time of Sample Draw	Anti- CS NANP Titer (unit)	Anti- CS NANP Avidity (unit)	Anti-CS C-term Titer (unit)	Anti-CS C-term Avidity (unit)	Anti-HBsAb Titer (unit)
xxxxx	V2	ddMMMyyyy/hh:mm					
	V5						
	V11						
	V13						
	V17						
	V20						
	V27						
Repeat as other subjects							

15. VACCINE EFFICACY LISTING

Listing 10.4.1 Listing of First Infection Events (FIEs)

Subject ID	Group	Per Protocol Population for Efficacy	Start Date at Risk	End Date at Risk	At Risk Time (yrs)	Event
xxxxx	Group 1	Y	ddMMMyyyy	ddMMyyyy	x.xx	Yes/No

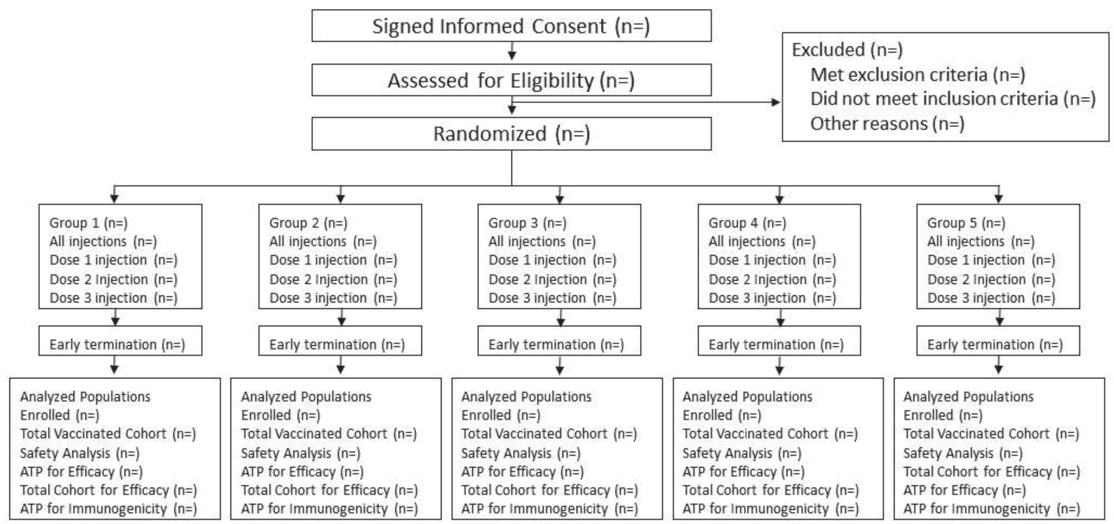
Listing 10.4.2 Listing of Parasitemia Test Results (ADI)

Subject ID	Group	Visit	Date of Sample Collection	Parasitemia Test Results
xxxxx	Group 1	Visit 19	ddMMMyyyy	Positive/Negative

16. DEMOGRAPHICS FIGURES

Figure 10.1.1: CONSORT Diagram

CONSORT Diagram for CVIA 078 RTS,S/AS01$_E$



17. VACCINE EFFICACY FIGURES

Figure 10.2.1: Kaplan-Meier survival curve for FIEs in Groups 1 and 4.

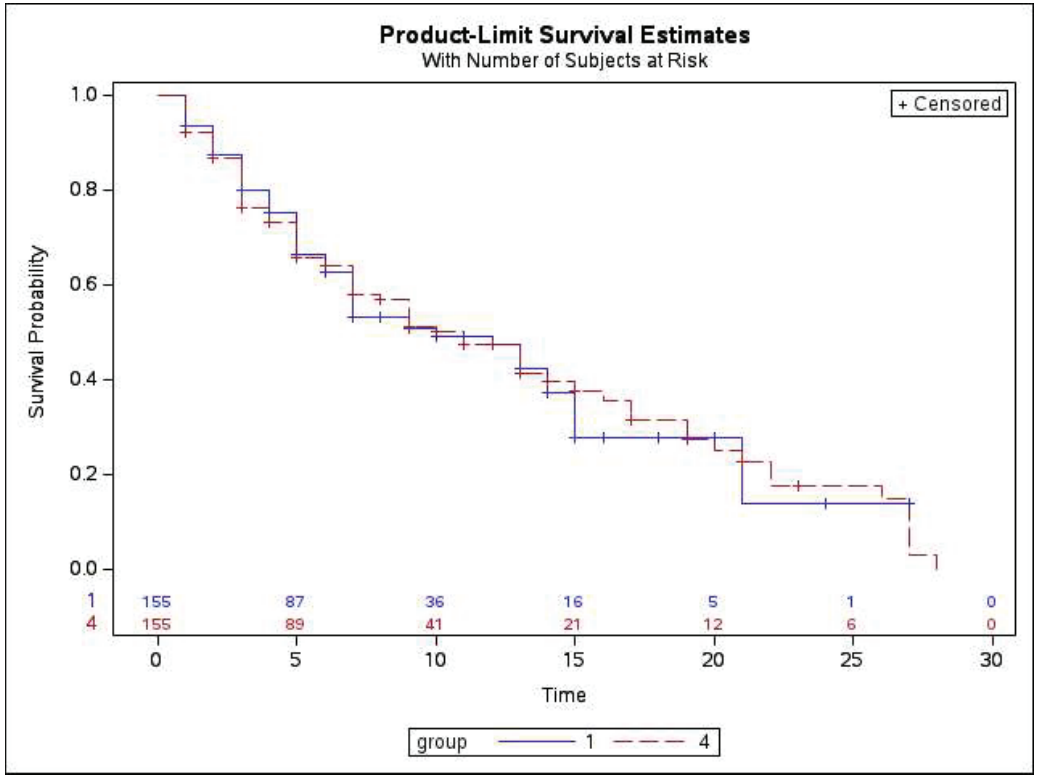


Figure 10.2.2: Kaplan-Meier survival curve for FIEs in Groups 1 and 4 stratified by HIV status.

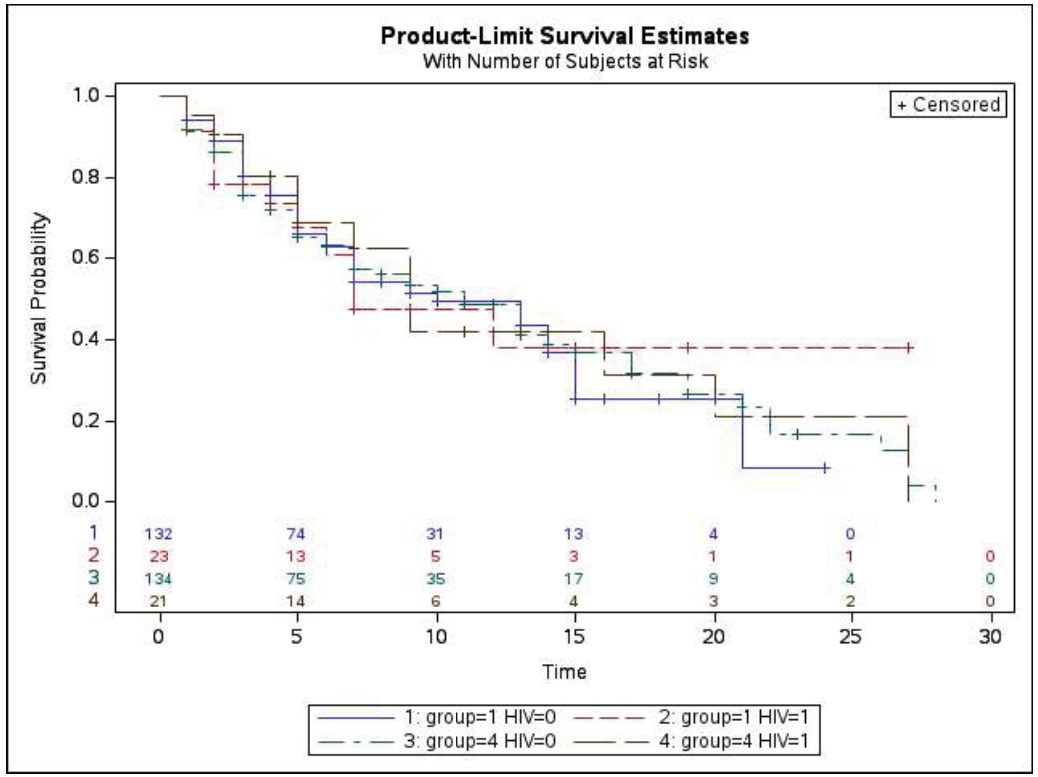


Figure 10.2.3: Kaplan-Meier survival curve for FIEs in Groups 2 and 5.

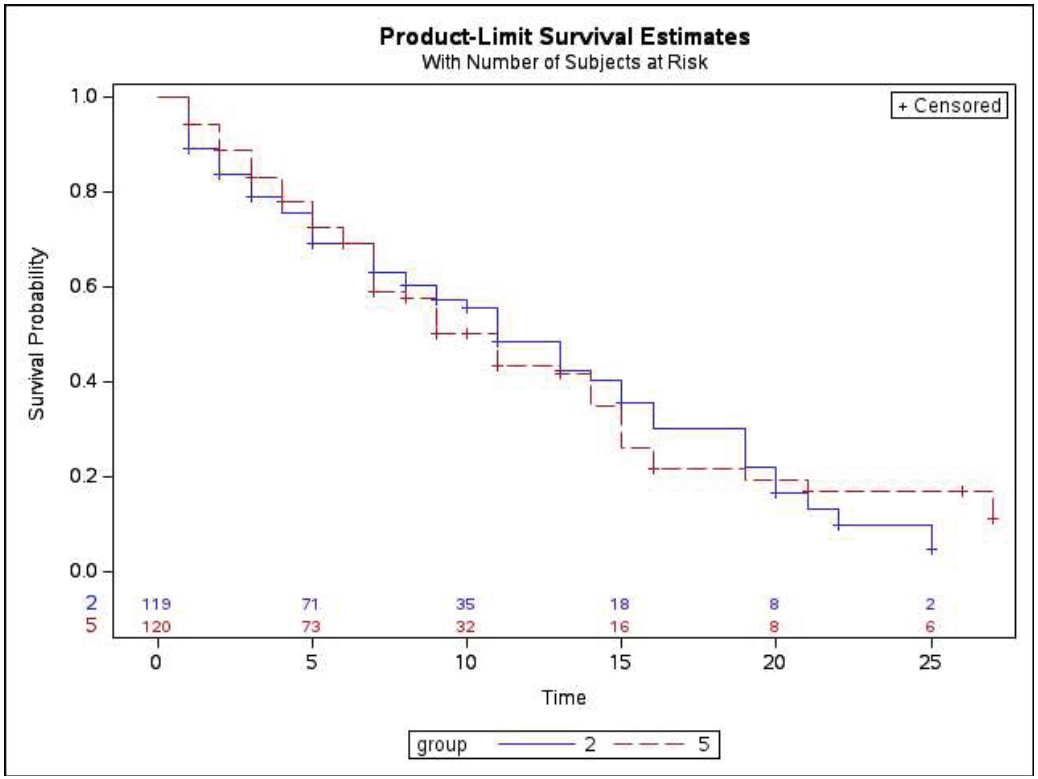
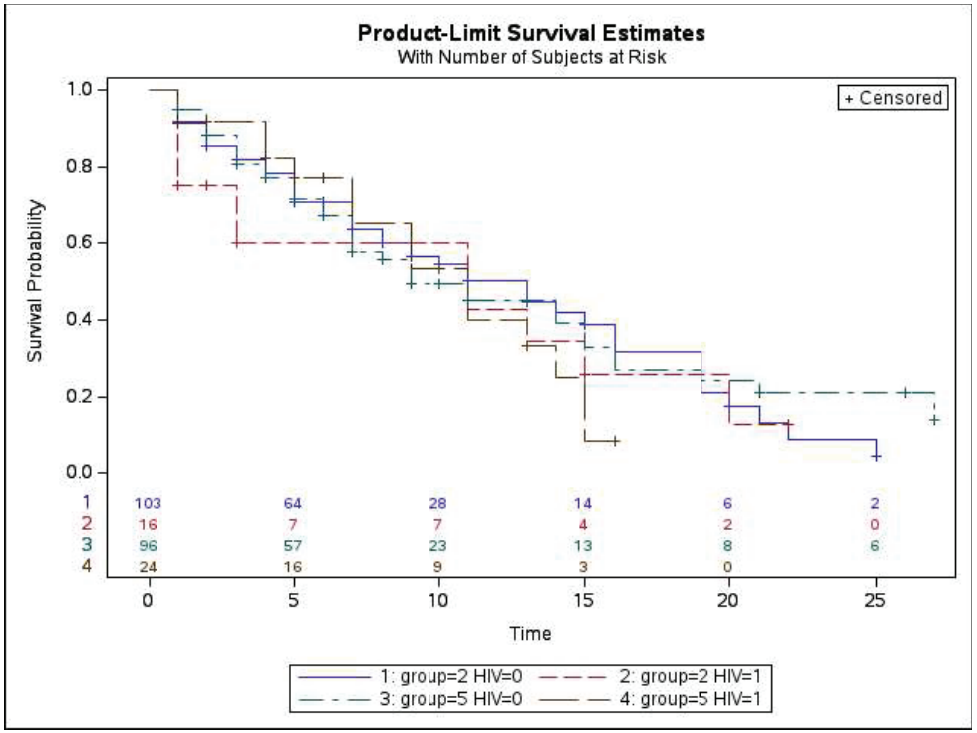


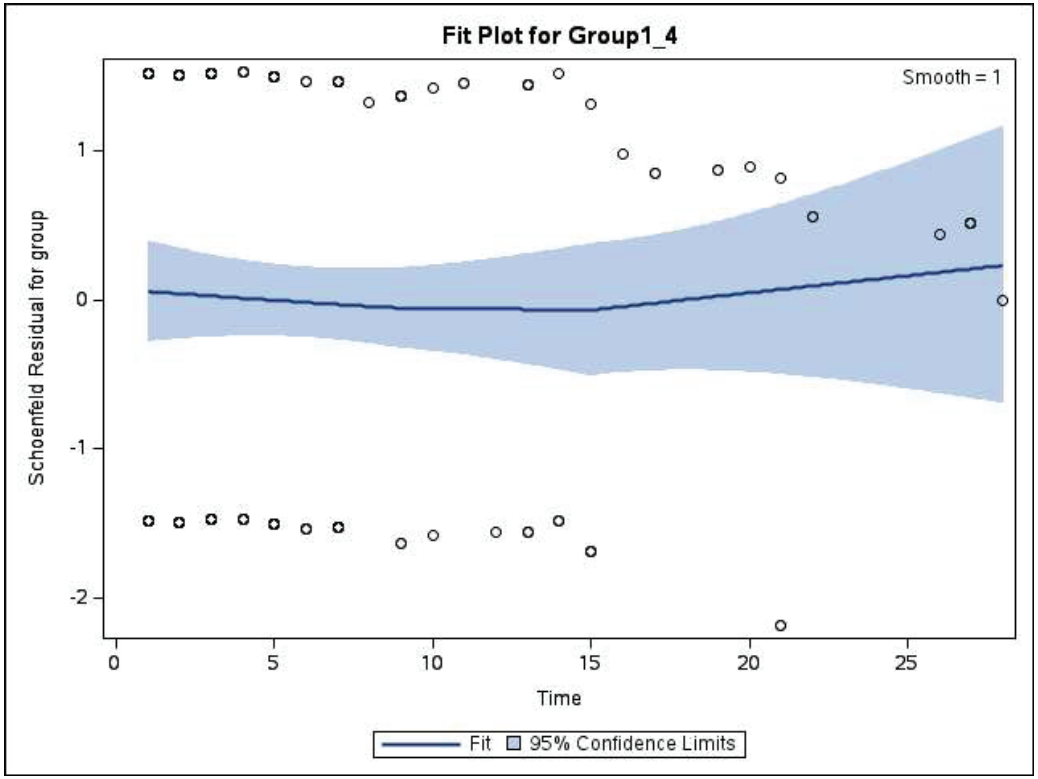
Figure 10.2.4: Kaplan-Meier survival curve for FIEs in Groups 2 and 5 stratified by HIV status.



Repeat the same survival curves for groups 1 and 2, groups 4 and 5

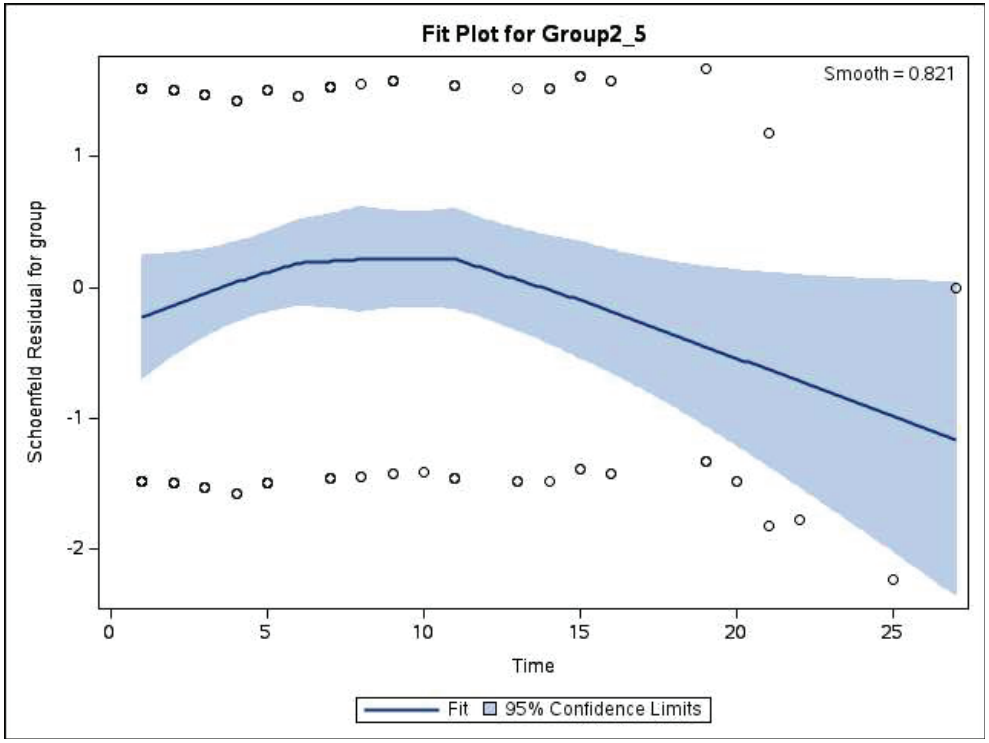
Figure 10.2.5: Kaplan-Meier survival curve for FIEs in Groups 1 and 2
Figure 10.2.6: Kaplan-Meier survival curve for FIEs in Groups 4 and 5

Figure 10.2.7: Scaled Schoenfeld residuals with 95% confidence interval versus time for Groups 1 and 4 FIEs during the entire study period (ATP cohort for efficacy)



p-value=x.xxx

Figure 10.2.8: Scaled Schoenfeld residuals with 95% confidence interval versus time for Groups 2 and 5 FIEs during the entire study period (ATP cohort for efficacy)



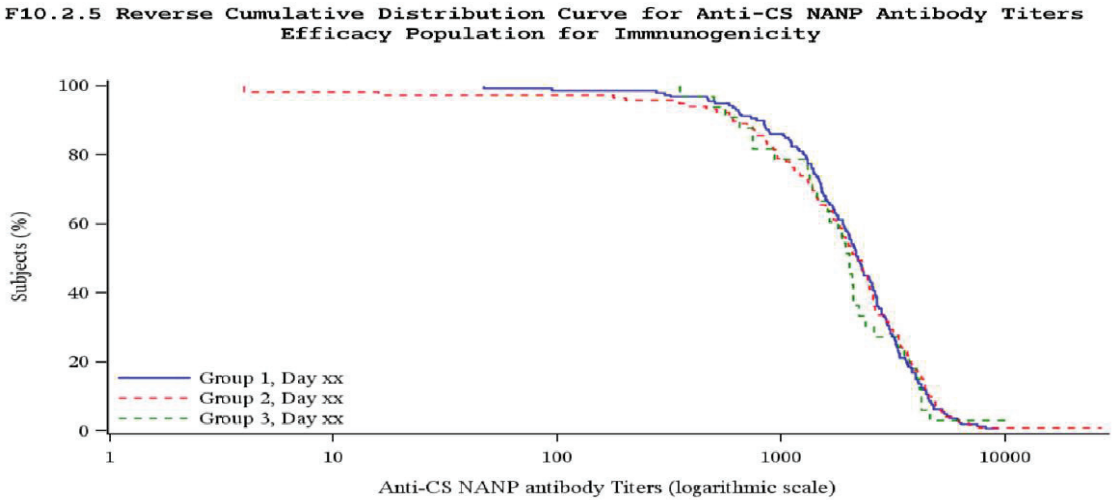
p-value=x.xxx

Repeat the same residual plots for groups 1 and 2, groups 4 and 5:

Figure 10.2.9: Scaled Schoenfeld residuals with 95% confidence interval versus time for Groups 1 and 2 FIEs during the entire study period (ATP cohort for efficacy)
Figure 10.2.10: Scaled Schoenfeld residuals with 95% confidence interval versus time for Groups 4 and 5 FIEs during the entire study period (ATP cohort for efficacy).

18. **IMMUNOGENICITY FIGURES**

Figure 10.3.1: Reverse Cumulative Distribution Curves for Anti-CS NANP Antibody Titers in Each Group (ATP cohort for immunogenicity)



Repeat the same plots for Anti-CS C-terminal and Anti-HBsAb titers in Figures 10.2.6 and 10.2.7

Figure 10.3.2: Reverse Cumulative Distribution Curves for Anti-CS C-term Antibody Titers in Each Group (ATP cohort for immunogenicity)

Figure 10.3.3: Reverse Cumulative Distribution Curves for Anti-HBsAb Titers in Each Group (ATP cohort for immunogenicity)