Clinical trial results:
Phase 2/3, Open-Label, Comparative Trial Of Azithromycin Plus Chloroquine Versus Artemether-Lumefantrine For The Treatment Of Uncomplicated Plasmodium Falciparum Malaria In Children In Africa

Summary

EudraCT number	2014-004163-21
Trial protocol	Outside EU/EEA
Global end of trial date	07 September 2010

Results information

Result version number	v1 (current)
This version publication date	27 April 2016
First version publication date	08 July 2015

Trial information

Trial identification

Sponsor protocol code	A0661157

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00677833
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer Clinical Trials.gov Call Center, Pfizer Inc , 001 8007181021, ClinicalTrials.govCallCenter@pfizer.com
Scientific contact	Pfizer Clinical Trials.gov Call Center, Pfizer Inc , 001 8007181021, ClinicalTrials.govCallCenter@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	04 August 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 September 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To confirm the hypothesis that azithromycin used in combination with chloroquine was non-inferior to artemether- Lumefantrine for the treatment of symptomatic, uncomplicated malaria due to Plasmodium Falciparum (P. Falciparum) in children in Africa.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 June 2008
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	2 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Ghana: 99
Country: Number of subjects enrolled	Côte d'Ivoire: 30
Country: Number of subjects enrolled	Mali: 80
Country: Number of subjects enrolled	Burkina Faso: 90
Country: Number of subjects enrolled	Kenya: 62
Worldwide total number of subjects	361
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	43

Children (2-11 years)	309
Adolescents (12-17 years)	9
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited in 2 age-based Cohorts. Cohort 1= Subjects between 5-12 years of age, assumed to have some degree of immunity and at less risk for untoward outcome. After demonstration of successful treatment, safety and tolerability in Cohort 1, subjects between >=6 months of age to <=59 months of age were enrolled in Cohort 2.

Pre-assignment

Screening details:

Subjects were enrolled in 2 cohorts based on different age criteria. All Subjects in Cohort 1 met the age criteria whereas 3 Subjects enrolled in Cohort 2 were slightly older than 5 years (by less than 2 months).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: Azithromycin + Chloroquine

Arm description:

Azithromycin/Chloroquine administered orally once daily for 3 days as a combination tablet on Days 0, 1, 2. The combination tablets were administered on the basis of body weight approximately 30 milligram per kilogram (mg/kg) Azithromycin + approximately 10 mg base/kg Chloroquine base. Cohort 1 included subjects between greater than or equal to (>=) 5 years of age and less than or equal to (<=) 12 years of age.

Arm type	Experimental
Investigational medicinal product name	Azithromycin/Chloroquine combination tablet
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Azithromycin/Chloroquine administered orally once daily for 3 days as a combination tablet (300 mg Azithromycin and 100 mg Chloroquine or 150 mg Azithromycin and 50 mg Chloroquine) on Days 0, 1, 2.

Arm title	Cohort 1: Artemether + Lumefantrine

Arm description:

Artemether/Lumefantrine administered orally once daily for 3 days as a combination tablet on Days 0, 1, 2. Cohort 1 included subjects between >=5 years of age and <=12 years of age.

Arm type	Active comparator
Investigational medicinal product name	Artemether/Lumefantrine combination tablet
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Artemether/Lumefantrine administered orally once daily for 3 days as a combination tablet (20 mg Artemether and 120 mg Lumefantrine) on Days 0, 1, 2.

Arm title	Cohort 2: Azithromycin + Chloroquine

Arm description:

Azithromycin/Chloroquine administered orally once daily for 3 days as a combination tablet on Days 0,

1, 2. The combination tablets were administered on the basis of body weight approximately 30 milligram/kilogram (mg/kg) Azithromycin + approximately 10 mg base/kg Chloroquine base. Cohort 2 included subjects between >=6 months of age to <=59 months of age.

Arm type	Experimental
Investigational medicinal product name	Azithromycin/Chloroquine combination tablet
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Azithromycin/Chloroquine administered orally once daily for 3 days as a combination tablet (300 mg Azithromycin and 100 mg Chloroquine or 150 mg Azithromycin and 50 mg Chloroquine) on Days 0, 1, 2.

Arm title	Cohort 2: Artemether + Lumefantrine

Arm description:

Artemether/Lumefantrine administered orally once daily for 3 days as a combination tablet on Days 0, 1, 2. Cohort 2 included subjects between >=6 months of age to <=59 months of age.

Arm type	Active comparator
Investigational medicinal product name	Artemether/Lumefantrine combination tablet
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Artemether/Lumefantrine administered orally once daily for 3 days as a combination tablet (20 mg Artemether and 120 mg Lumefantrine) on Days 0, 1, 2.

Number of subjects in period 1	Cohort 1: Azithromycin + Chloroquine	Cohort 1: Artemether + Lumefantrine	Cohort 2: Azithromycin + Chloroquine
Started	55	51	124
Completed	51	51	122
Not completed	4	0	2
Consent withdrawn by subject	4	-	1
Lost to follow-up	-	-	1

Number of subjects in period 1	Cohort 2: Artemether + Lumefantrine
Started	131
Completed	128
Not completed	3
Consent withdrawn by subject	3
Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1: Azithromycin + Chloroquine
Reporting group description:	
Azithromycin/Chloroquine administered orally once daily for 3 days as a combination tablet on Days 0, 1, 2. The combination tablets were administered on the basis of body weight approximately 30 milligram per kilogram (mg/kg) Azithromycin + approximately 10 mg base/kg Chloroquine base. Cohort 1 included subjects between greater than or equal to (>=) 5 years of age and less than or equal to (<=) 12 years of age.	
Reporting group title	Cohort 1: Artemether + Lumefantrine
Reporting group description:	
Artemether/Lumefantrine administered orally once daily for 3 days as a combination tablet on Days 0, 1, 2. Cohort 1 included subjects between >=5 years of age and <=12 years of age.	
Reporting group title	Cohort 2: Azithromycin + Chloroquine
Reporting group description:	
Azithromycin/Chloroquine administered orally once daily for 3 days as a combination tablet on Days 0, 1, 2. The combination tablets were administered on the basis of body weight approximately 30 milligram/kilogram (mg/kg) Azithromycin + approximately 10 mg base/kg Chloroquine base. Cohort 2 included subjects between >=6 months of age to <=59 months of age.	
Reporting group title	Cohort 2: Artemether + Lumefantrine
Reporting group description:	
Artemether/Lumefantrine administered orally once daily for 3 days as a combination tablet on Days 0, 1, 2. Cohort 2 included subjects between >=6 months of age to <=59 months of age.	

Reporting group values	Cohort 1: Azithromycin + Chloroquine	Cohort 1: Artemether + Lumefantrine	Cohort 2: Azithromycin + Chloroquine
Number of subjects	55	51	124
Age categorical Units: Subjects			
6 months – less than 5 years	0	0	123
5 years – 12 years	55	51	1
Gender categorical Units: Subjects			
Female	28	21	50
Male	27	30	74

Reporting group values	Cohort 2: Artemether + Lumefantrine	Total	
Number of subjects	131	361	
Age categorical Units: Subjects			
6 months – less than 5 years	129	252	
5 years – 12 years	2	109	
Gender categorical Units: Subjects			
Female	65	164	
Male	66	197	

End points

End points reporting groups

Reporting group title	Cohort 1: Azithromycin + Chloroquine

Reporting group description:

Azithromycin/Chloroquine administered orally once daily for 3 days as a combination tablet on Days 0, 1, 2. The combination tablets were administered on the basis of body weight approximately 30 milligram per kilogram (mg/kg) Azithromycin + approximately 10 mg base/kg Chloroquine base. Cohort 1 included subjects between greater than or equal to (>=) 5 years of age and less than or equal to (<=) 12 years of age.

Reporting group title	Cohort 1: Artemether + Lumefantrine

Reporting group description:

Artemether/Lumefantrine administered orally once daily for 3 days as a combination tablet on Days 0, 1, 2. Cohort 1 included subjects between >=5 years of age and <=12 years of age.

Reporting group title	Cohort 2: Azithromycin + Chloroquine

Reporting group description:

Azithromycin/Chloroquine administered orally once daily for 3 days as a combination tablet on Days 0, 1, 2. The combination tablets were administered on the basis of body weight approximately 30 milligram/kilogram (mg/kg) Azithromycin + approximately 10 mg base/kg Chloroquine base. Cohort 2 included subjects between >=6 months of age to <=59 months of age.

Reporting group title	Cohort 2: Artemether + Lumefantrine

Reporting group description:

Artemether/Lumefantrine administered orally once daily for 3 days as a combination tablet on Days 0, 1, 2. Cohort 2 included subjects between >=6 months of age to <=59 months of age.

Primary: Percentage of Subjects With Polymerase Chain Reaction (PCR)-Corrected Adequate Clinical and Parasitologic Response (ACPR) at Day 28 in the Modified Intent-to-treat (mITT) Population

End point title	Percentage of Subjects With Polymerase Chain Reaction (PCR)-Corrected Adequate Clinical and Parasitologic Response (ACPR) at Day 28 in the Modified Intent-to-treat (mITT) Population[1]

End point description:

ACPR(PCR-corrected) was defined as asexual P. falciparum parasitologic clearance at Day 28 irrespective of axillary, oral, rectal, or tympanic temperature, without previously meeting the criteria of Early Treatment Failure(ETF) or PCR-corrected Late Treatment Failure(LTF)(which includes PCR-corrected Late Clinical Failures[LCF]-see measure description in secondary outcome measure 9 and 10, and PCR-corrected Late Parasitologic Failures(LPF)– see measure description in secondary outcome measure 11 and 12).PCR-corrected refers to the use of molecular testing to differentiate recrudescence from reinfection in the context of an efficacy evaluation. mITT:treated subjects who met disease criteria(blood smears positive for P.falciparum monoinfection;asexual parasitemia=1000-100,000 parasites/microliter[mcL];fever/history of fever >=38 degree Celsius[C][rectal],37.2 degree C[axillary] or >=37.5 degree C[oral] within last 24 hours).Subjects in Ivory Coast center excluded from analysis.

End point type	Primary

End point timeframe:

Day 28

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 was a screening cohort, meant for safety evaluation, but not included in the efficacy assessments.

End point values	Cohort 2: Azithromycin + Chloroquine	Cohort 2: Artemether + Lumefantrine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	120	126		
Units: Percentage of Subjects				
number (confidence interval 95%)	89.27 (82.77 to 95.77)	98.37 (95.59 to 100)		

Statistical analyses

Statistical analysis title	ACPR (PCR-corrected) at Day 28 For mITT population

Statistical analysis description:

A two-sided 95 percent (%) confidence interval (CI) for the difference in ACPR (PCR corrected) proportions [(AZ-CQ)–(AL)] using the normal approximation to the binomial with continuity correction was constructed based on the estimated ACPR (PCR-corrected) proportions from the Kaplan-Meier curves and their standard errors estimated by the greenwood formula. The drug (AZ-CQ) was considered non-inferior with respect to this primary endpoint if the lower bound of this 95% CI was >= -10% points.

Comparison groups	Cohort 2: Artemether + Lumefantrine v Cohort 2: Azithromycin + Chloroquine
Number of subjects included in analysis	246
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Method	Kaplan-Meier curves
Parameter estimate	ACPR percent difference
Point estimate	-9.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.02
upper limit	-2.18

Notes:

[2] - Null hypothesis: proportion of subjects with ACPR (PCR-corrected) of Azithromycin/Chloroquine (AZ-CQ) at Day 28 is less than that of Artemether/Lumefantrine (AL); Alternative hypothesis: proportion of subjects with ACPR (PCR-corrected) of AZ-CQ at Day 28 is greater than or equal (non-inferior) to that of AL by a non-inferiority margin of -0.1.

Primary: Percentage of Subjects With PCR-corrected ACPR at Day 28 in Per-Protocol (PP) Population

End point title	Percentage of Subjects With PCR-corrected ACPR at Day 28 in Per-Protocol (PP) Population[3]

End point description:

ACPR (PCR-corrected) was defined as asexual P.falciparum parasitologic clearance at Day 28 irrespective of axillary, oral, rectal, or tympanic temperature, without previously meeting the criteria of ETF (see measure description in secondary outcome measures 7 and 8) or PCR-corrected LTF (which includes PCR-corrected LCF - see measure description in secondary outcome measure 9 and 10, and PCR-corrected LPF – see measure description in secondary outcome measure 11 and 12). PCR-corrected refers to the use of molecular testing to differentiate recrudescence from reinfection in the context of an efficacy evaluation. Per-Protocol (PP) population was a subset of the mITT population, who received all 3 days of study medication to which they were assigned. For ACPR efficacy endpoints, subjects in Ivory Coast center excluded from PP population.

End point type	Primary

End point timeframe:

Day 28

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Cohort 1 was a screening cohort, meant for safety evaluation, but not included in the efficacy assessments.

End point values	Cohort 2: Azithromycin + Chloroquine	Cohort 2: Artemether + Lumefantrine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	114	124		
Units: Percentage of Subjects				
number (confidence interval 95%)	93.08 (87.32 to 98.84)	99.16 (96.97 to 100)		

Statistical analyses

Statistical analysis title	ACPR (PCR-corrected) at Day 28 For PP population

Statistical analysis description:

A two-sided 95 percent (%) confidence interval (CI) for the difference in ACPR (PCR corrected) proportions [(AZ-CQ)−(AL)] using the normal approximation to the binomial with continuity correction was constructed based on the estimated ACPR (PCR-corrected) proportions from the Kaplan-Meier curves and their standard errors estimated by the greenwood formula. The drug (AZ-CQ) was considered non-inferior with respect to this primary endpoint if the lower bound of this 95% CI was >= -10% points.

Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine
Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Method	Kaplan-Meier curves
Parameter estimate	ACPR percent difference
Point estimate	-6.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.1
upper limit	-0.05

Notes:

[4] - Null hypothesis: proportion of subjects with ACPR (PCR-corrected) of AZ-CQ at Day 28 is less than that of AL; Alternative hypothesis: proportion of Subjects with ACPR (PCR-corrected) of AZ-CQ at Day 28 is greater than or equal (non-inferior) to that of AL by a non-inferiority margin of -0.1.

Secondary: Percentage of Subjects With PCR-corrected ACPR in the mITT Population

End point title	Percentage of Subjects With PCR-corrected ACPR in the mITT Population[5]

End point description:

ACPR (PCR-corrected) was defined as asexual P.falciparum parasitologic clearance on Days 7, 14, 21, 35, 42 irrespective of axillary, oral, rectal, or tympanic temperature, without previously meeting the criteria of ETF (see measure description in secondary outcome measures 7 and 8) or PCR-corrected LTF (which includes PCR-Corrected LCF- see measure description in secondary outcome measure 9 and 10, and PCR-corrected LPF – see measure description in secondary outcome measure 11 and 12). PCR-corrected refers to the use of molecular testing to differentiate recrudescence from reinfection in the context of an efficacy evaluation. mITT population. For ACPR efficacy endpoints, subjects in Ivory Coast center excluded from mITT population.

End point type	Secondary

End point timeframe:

Days 7, 14, 21, 35, 42

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 was a screening cohort, meant for safety evaluation, but not included in the efficacy assessments.

End point values	Cohort 2: Azithromycin + Chloroquine	Cohort 2: Artemether + Lumefantrine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	120	126		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Day 7	94.17 (89.55 to 98.78)	99.21 (97.25 to 100)		
Day 14	92.47 (87.3 to 97.64)	99.21 (97.24 to 100)		
Day 21	91.59 (86.04 to 97.14)	98.37 (95.65 to 100)		
Day 35	89.27 (82.68 to 95.86)	96.19 (91.85 to 100)		
Day 42	87.55 (80.08 to 95.03)	96.19 (91.79 to 100)		

Statistical analyses

Statistical analysis title	Estimates for Day 7

Statistical analysis description:

A two-sided 95% CI for the difference in ACPR (PCR-corrected) proportions [(AZ-CQ)–(AL)] using the normal approximation to the binomial with continuity correction was constructed based on the estimated ACPR proportions from the Kaplan-Meier curves and their standard errors estimated by the greenwood formula.

Comparison groups	Cohort 2: Artemether + Lumefantrine v Cohort 2: Azithromycin + Chloroquine
Number of subjects included in analysis	246
Analysis specification	Pre-specified
Analysis type	superiority
Method	Kaplan-Meier curves
Parameter estimate	ACPR percent difference
Point estimate	-5.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.93
upper limit	-0.15

Statistical analysis title	Estimates for Day 14

Statistical analysis description:

A two-sided 95% CI for the difference in ACPR (PCR-corrected) proportions [(AZ-CQ)–(AL)] using the

normal approximation to the binomial with continuity correction was constructed based on the estimated ACPR proportions from the Kaplan-Meier curves and their standard errors estimated by the greenwood formula.

Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine
Number of subjects included in analysis	246
Analysis specification	Pre-specified
Analysis type	superiority
Method	Kaplan-Meier curves
Parameter estimate	ACPR percent difference
Point estimate	-6.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.15
upper limit	-1.32

Statistical analysis title	Estimates for Day 21

Statistical analysis description:

A two-sided 95% CI for the difference in ACPR (PCR-corrected) proportions [(AZ-CQ)–(AL)] using the normal approximation to the binomial with continuity correction was constructed based on the estimated ACPR proportions from the Kaplan-Meier curves and their standard errors estimated by the greenwood formula.

Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine
Number of subjects included in analysis	246
Analysis specification	Pre-specified
Analysis type	superiority
Method	Kaplan-Meier curves
Parameter estimate	ACPR percent difference
Point estimate	-6.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.82
upper limit	-0.75

Statistical analysis title	Estimates for Day 35

Statistical analysis description:

A two-sided 95% CI for the difference in ACPR (PCR-corrected) proportions [(AZ-CQ)–(AL)] using the normal approximation to the binomial with continuity correction was constructed based on the estimated ACPR proportions from the Kaplan-Meier curves and their standard errors estimated by the greenwood formula.

Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine

Number of subjects included in analysis	246
Analysis specification	Pre-specified
Analysis type	superiority
Method	Kaplan-Meier curves
Parameter estimate	ACPR percent difference
Point estimate	-6.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.59
upper limit	0.76

Statistical analysis title	Estimates for Day 42

Statistical analysis description:

A two-sided 95% CI for the difference in ACPR (PCR-corrected) proportions [(AZ-CQ)–(AL)] using the normal approximation to the binomial with continuity correction was constructed based on the estimated ACPR proportions from the Kaplan-Meier curves and their standard errors estimated by the greenwood formula.

Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine
Number of subjects included in analysis	246
Analysis specification	Pre-specified
Analysis type	superiority
Method	Kaplan-Meier curves
Parameter estimate	ACPR percent difference
Point estimate	-8.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.08
upper limit	-0.18

Secondary: Percentage of Subjects With PCR-corrected ACPR in PP Population

End point title	Percentage of Subjects With PCR-corrected ACPR in PP Population[6]

End point description:

ACPR (PCR-corrected) was defined as asexual P.falciparum parasitologic clearance on Days 7, 14, 21, 35, 42 irrespective of axillary, oral, rectal, or tympanic temperature, without previously meeting the criteria of ETF (see measure description in secondary outcome measures 7 and 8) or PCR-corrected LTF (which includes PCR-corrected LCF - see measure description in secondary outcome measure 9 and 10, and PCR-corrected LPF – see measure description in secondary outcome measure 11 and 12). PCR-corrected refers to the use of molecular testing to differentiate recrudescence from reinfection in the context of an efficacy evaluation. PP population. For ACPR efficacy endpoints, subjects in Ivory Coast center were excluded from the PP population. Here "99999" in the CI signifies not available (NA). CI was not calculable as standard error for 100% rate could not be estimated from Kaplan-Meier method.

End point type	Secondary

End point timeframe:

Days 7, 14, 21, 35, 42

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 was a screening cohort, meant for safety evaluation, but not included in the efficacy assessments.

End point values	Cohort 2: Azithromycin + Chloroquine	Cohort 2: Artemether + Lumefantrine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	114	124		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Day 7	98.25 (95.39 to 100)	100 (-99999 to 99999)		
Day 14	96.46 (92.59 to 100)	100 (-99999 to 99999)		
Day 21	95.53 (91.1 to 99.96)	99.16 (97.03 to 100)		
Day 35	93.08 (87.22 to 98.95)	96.96 (92.9 to 100)		
Day 42	91.29 (84.31 to 98.28)	96.96 (92.84 to 100)		

Statistical analyses

Statistical analysis title	Estimates for Day 21

Statistical analysis description:

A two-sided 95% CI for the difference in ACPR (PCR-corrected) proportions [(AZ-CQ)–(AL)] using the normal approximation to the binomial with continuity correction was constructed based on the estimated ACPR proportions from the Kaplan-Meier curves and their standard errors estimated by the greenwood formula.

Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine
Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	superiority
Method	Kaplan-Meier curves
Parameter estimate	ACPR percent difference
Point estimate	-3.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.4
upper limit	1.14

Statistical analysis title	Estimates for Day 35

Statistical analysis description:

A two-sided 95% CI for the difference in ACPR (PCR-corrected) proportions [(AZ-CQ)–(AL)] using the normal approximation to the binomial with continuity correction was constructed based on the estimated ACPR proportions from the Kaplan-Meier curves and their standard errors estimated by the greenwood formula.

Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine
Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	superiority
Method	Kaplan-Meier curves
Parameter estimate	ACPR percent difference
Point estimate	-3.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.79
upper limit	3.04

Statistical analysis title	Estimates for Day 42

Statistical analysis description:

A two-sided 95% CI for the difference in ACPR (PCR-corrected) proportions [(AZ-CQ)–(AL)] using the normal approximation to the binomial with continuity correction was constructed based on the estimated ACPR proportions from the Kaplan-Meier curves and their standard errors estimated by the greenwood formula.

Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine
Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	superiority
Method	Kaplan-Meier curves
Parameter estimate	ACPR percent difference
Point estimate	-5.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.55
upper limit	2.22

Secondary: Percentage of Subjects With PCR-uncorrected ACPR in the mITT Population

End point title	Percentage of Subjects With PCR-uncorrected ACPR in the mITT Population[7]

End point description:

ACPR (PCR-uncorrected) was defined as asexual P.falciparum parasitologic clearance on Days 7, 14, 21, 28, 35, 42 irrespective of axillary, oral, rectal, or tympanic temperature, without previously meeting the criteria of ETF (see measure description in secondary outcome measures 7 and 8) or PCR-uncorrected LTF (which includes PCR-uncorrected LCF - see measure description in secondary outcome measure 9 and 10, and PCR-uncorrected LPF – see measure description in secondary outcome measure 11 and 12). PCR-uncorrected: not adjusted for molecular testing which determined recrudescence or true failures from reinfection. mITT population. For ACPR efficacy endpoints, subjects in Ivory Coast center were excluded from mITT population.

End point type	Secondary

End point timeframe:

Days 7, 14, 21, 28, 35, 42

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 was a screening cohort, meant for safety evaluation, but not included in the efficacy assessments.

End point values	Cohort 2: Azithromycin + Chloroquine	Cohort 2: Artemether + Lumefantrine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	120	126		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Day 7	94.17 (89.55 to 98.78)	99.21 (97.25 to 100)		
Day 14	89.08 (83.05 to 95.11)	96.79 (93.28 to 100)		
Day 21	67.87 (59.02 to 76.72)	82.96 (75.91 to 90.01)		
Day 28	51.55 (42.07 to 61.02)	73.31 (65.1 to 81.52)		
Day 35	44.67 (35.24 to 54.11)	62.91 (54 to 71.82)		
Day 42	37.8 (28.58 to 47.02)	56.29 (47.12 to 65.46)		

Statistical analyses

Statistical analysis title	Estimates for Day 7

Statistical analysis description:

A two-sided 95% CI for the difference in ACPR (PCR-uncorrected) proportions [(AZ-CQ)–(AL)] using the normal approximation to the binomial with continuity correction was constructed based on the estimated ACPR proportions from the Kaplan-Meier curves and their standard errors estimated by the greenwood formula.

Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine
Number of subjects included in analysis	246
Analysis specification	Pre-specified
Analysis type	superiority
Method	Kaplan-Meier curves
Parameter estimate	ACPR percent difference
Point estimate	-5.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.93
upper limit	-0.15

Statistical analysis title	Estimates for Day 14

Statistical analysis description:

A two-sided 95% CI for the difference in ACPR (PCR-uncorrected) proportions [(AZ-CQ)–(AL)] using the normal approximation to the binomial with continuity correction was constructed based on the estimated

ACPR proportions from the Kaplan-Meier curves and their standard errors estimated by the greenwood formula.

Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine
Number of subjects included in analysis	246
Analysis specification	Pre-specified
Analysis type	superiority
Method	Kaplan-Meier curves
Parameter estimate	ACPR percent difference
Point estimate	-7.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.54
upper limit	-0.88

Statistical analysis title	Estimates for Day 21

Statistical analysis description:

A two-sided 95% CI for the difference in ACPR (PCR-uncorrected) proportions [(AZ-CQ)–(AL)] using the normal approximation to the binomial with continuity correction was constructed based on the estimated ACPR proportions from the Kaplan-Meier curves and their standard errors estimated by the greenwood formula.

Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine
Number of subjects included in analysis	246
Analysis specification	Pre-specified
Analysis type	superiority
Method	Kaplan-Meier curves
Parameter estimate	ACPR percent difference
Point estimate	-15.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.24
upper limit	-3.94

Statistical analysis title	Estimates for Day 28

Statistical analysis description:

A two-sided 95% CI for the difference in ACPR (PCR-uncorrected) proportions [(AZ-CQ)–(AL)] using the normal approximation to the binomial with continuity correction was constructed based on the estimated ACPR proportions from the Kaplan-Meier curves and their standard errors estimated by the greenwood formula.

Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine

Number of subjects included in analysis	246
Analysis specification	Pre-specified
Analysis type	superiority
Method	Kaplan-Meier curves
Parameter estimate	ACPR percent difference
Point estimate	-21.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-34.14
upper limit	-9.39

Statistical analysis title	Estimates for Day 35

Statistical analysis description:

A two-sided 95% CI for the difference in ACPR (PCR-uncorrected) proportions [(AZ-CQ)–(AL)] using the normal approximation to the binomial with continuity correction was constructed based on the estimated ACPR proportions from the Kaplan-Meier curves and their standard errors estimated by the greenwood formula.

Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine
Number of subjects included in analysis	246
Analysis specification	Pre-specified
Analysis type	superiority
Method	Kaplan-Meier curves
Parameter estimate	ACPR percent difference
Point estimate	-18.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.05
upper limit	-5.43

Statistical analysis title	Estimates for Day 42

Statistical analysis description:

A two-sided 95% CI for the difference in ACPR (PCR-uncorrected) proportions [(AZ-CQ)–(AL)] using the normal approximation to the binomial with continuity correction was constructed based on the estimated ACPR proportions from the Kaplan-Meier curves and their standard errors estimated by the greenwood formula.

Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine
Number of subjects included in analysis	246
Analysis specification	Pre-specified
Analysis type	superiority
Method	Kaplan-Meier curves
Parameter estimate	ACPR percent difference
Point estimate	-18.49

Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.33
upper limit	-5.65

Secondary: Percentage of Subjects With PCR-uncorrected ACPR in PP Population

End point title	Percentage of Subjects With PCR-uncorrected ACPR in PP Population[8]

End point description:

ACPR (PCR-uncorrected) was defined as asexual P.falciparum parasitologic clearance on Days 7, 14, 21, 28, 35, 42 irrespective of axillary, oral, rectal, or tympanic temperature, without previously meeting the criteria of ETF (see measure description in secondary outcome measures 7 and 8) or PCR-uncorrected LTF (which includes PCR-uncorrected LCF - see measure description in secondary outcome measure 9 and 10, and PCR-uncorrected LPF – see measure description in secondary outcome measure 11 and 12). PCR-uncorrected: not adjusted for molecular testing which determined recrudescence or true failures from reinfection. PP population. For ACPR efficacy endpoints, subjects in Ivory Coast center were excluded from the PP population. Here "99999" in the CI signifies not available (NA). CI is not calculable when rate is 100%.

End point type	Secondary

End point timeframe:

Days 7, 14, 21, 28, 35, 42

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Cohort 1 was a screening cohort, meant for safety evaluation, but not included in the efficacy assessments.

End point values	Cohort 2: Azithromycin + Chloroquine	Cohort 2: Artemether + Lumefantrine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	114	124		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Day 7	98.25 (95.39 to 100)	100 (-99999 to 99999)		
Day 14	92.89 (87.69 to 98.08)	97.56 (94.42 to 100)		
Day 21	70.56 (61.67 to 79.45)	83.62 (76.65 to 90.6)		
Day 28	54.28 (44.57 to 63.98)	73.9 (65.71 to 82.08)		
Day 35	47.04 (37.31 to 56.77)	63.41 (54.49 to 72.34)		
Day 42	39.8 (30.24 to 49.36)	56.74 (47.54 to 65.94)		

Statistical analyses

Statistical analysis title	Estimates for Day 14

Statistical analysis description:

A two-sided 95% CI for the difference in ACPR (PCR-uncorrected) proportions [(AZ-CQ)–(AL)] using the

normal approximation to the binomial with continuity correction was constructed based on the estimated ACPR proportions from the Kaplan-Meier curves and their standard errors estimated by the greenwood formula.

Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine
Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	superiority
Method	Kaplan-Meier curves
Parameter estimate	ACPR percent difference
Point estimate	-4.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.6
upper limit	1.25

Statistical analysis title	Estimates for Day 21

Statistical analysis description:

A two-sided 95% CI for the difference in ACPR (PCR-uncorrected) proportions [(AZ-CQ)–(AL)] using the normal approximation to the binomial with continuity correction was constructed based on the estimated ACPR proportions from the Kaplan-Meier curves and their standard errors estimated by the greenwood formula.

Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine
Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	superiority
Method	Kaplan-Meier curves
Parameter estimate	ACPR percent difference
Point estimate	-13.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.21
upper limit	-1.92

Statistical analysis title	Estimates for Day 28

Statistical analysis description:

A two-sided 95% CI for the difference in ACPR (PCR-uncorrected) proportions [(AZ-CQ)–(AL)] using the normal approximation to the binomial with continuity correction was constructed based on the estimated ACPR proportions from the Kaplan-Meier curves and their standard errors estimated by the greenwood formula.

Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine

Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	superiority
Method	Kaplan-Meier curves
Parameter estimate	ACPR percent difference
Point estimate	-19.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-32.16
upper limit	-7.08

Statistical analysis title	Estimates for Day 35

Statistical analysis description:

A two-sided 95% CI for the difference in ACPR (PCR-uncorrected) proportions [(AZ-CQ)–(AL)] using the normal approximation to the binomial with continuity correction was constructed based on the estimated ACPR proportions from the Kaplan-Meier curves and their standard errors estimated by the greenwood formula.

Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine
Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	superiority
Method	Kaplan-Meier curves
Parameter estimate	ACPR percent difference
Point estimate	-16.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.42
upper limit	-3.33

Statistical analysis title	Estimates for Day 42

Statistical analysis description:

A two-sided 95% CI for the difference in ACPR (PCR-uncorrected) proportions [(AZ-CQ)–(AL)] using the normal approximation to the binomial with continuity correction was constructed based on the estimated ACPR proportions from the Kaplan-Meier curves and their standard errors estimated by the greenwood formula.

Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine
Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	superiority
Method	Kaplan-Meier curves
Parameter estimate	ACPR percent difference
Point estimate	-16.94

Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.04
upper limit	-3.83

Secondary: Percentage of Subjects With Early Treatment Failure (ETF) in the mITT Population (PCR-corrected)

End point title	Percentage of Subjects With Early Treatment Failure (ETF) in the mITT Population (PCR-corrected)[9]

End point description:

ETF defined as subjects who met the following criteria:
1. Developed signs of severe malaria or clinical deterioration that required rescue medication on Days 0, 1, 2 or 3, in the presence of P. falciparum parasitemia
2. Last available asexual P. falciparum parasite count on Day 2 greater than the first available parasite count on Day 0 (Baseline), irrespective of axillary, oral or rectal temperature.
3. Parasitemia (P. falciparum) on Day 3 with fever or
4. Last available P. falciparum parasite count on Day 3 >=25% of the first available parasite count on Day 0 (Baseline).
PCR-corrected refers to the use of molecular testing to differentiate recrudescence from reinfection in the context of an efficacy evaluation. mITT population, subjects in Ivory Coast center were excluded from mITT population.

End point type	Secondary

End point timeframe:

Day 0 up to Day 3

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Cohort 1 was a screening cohort, meant for safety evaluation, but not included in the efficacy assessments.

End point values	Cohort 2: Azithromycin + Chloroquine	Cohort 2: Artemether + Lumefantrine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	120	126		
Units: Percentage of Subjects				
number (not applicable)	5.83	0.79		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With ETF in PP Population (PCR-corrected)

End point title	Percentage of Subjects With ETF in PP Population (PCR-corrected)[10]

End point description:

ETF defined as subjects who met the following criteria:
1. Developed signs of severe malaria or clinical deterioration that required rescue medication on Days 0, 1, 2 or 3, in the presence of P. falciparum parasitemia
2. Last available asexual P. falciparum parasite count on Day 2 greater than the first available parasite count on Day 0 (Baseline), irrespective of axillary, oral or rectal temperature.

3. Parasitemia (P. falciparum) on Day 3 with fever or
4. Last available P. falciparum parasite count on Day 3 >=25% of the first available parasite count on Day 0 (Baseline).
PCR-corrected refers to the use of molecular testing to differentiate recrudescence from reinfection in the context of an efficacy evaluation. PP population, subjects in Ivory Coast center were excluded from the PP population.

End point type	Secondary

End point timeframe:

Day 0 up to Day 3

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 was a screening cohort, meant for safety evaluation, but not included in the efficacy assessments.

End point values	Cohort 2: Azithromycin + Chloroquine	Cohort 2: Artemether + Lumefantrine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	114	124		
Units: Percentage of Subjects				
number (not applicable)	1.75	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Late Clinical Failure (LCF) in the mITT Population (PCR-corrected)

End point title	Percentage of Subjects With Late Clinical Failure (LCF) in the mITT Population (PCR-corrected)[11]

End point description:

LCF included subjects who met any of the following criteria:
1. Development of signs of severe malaria or clinical deterioration requiring rescue medication after Day 3 in the presence of P.falciparum parasitemia, without previously meeting any of the criteria of ETF (see measure description in secondary outcome measures 5 and 6)
2. Presence of P.falciparum parasitemia and fever on any day from Day 4 onward, without previously meeting any of the criteria of ETF (see measure description in secondary outcome measures 5 and 6).
PCR-corrected refers to the use of molecular testing to differentiate recrudescence from reinfection in the context of an efficacy evaluation.
mITT population, subjects in Ivory Coast center were excluded from mITT population.

End point type	Secondary

End point timeframe:

Days 7, 14, 21, 28, 35, 42

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 was a screening cohort, meant for safety evaluation, but not included in the efficacy assessments.

End point values	Cohort 2: Azithromycin + Chloroquine	Cohort 2: Artemether + Lumefantrine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	120	126		
Units: Percentage of Subjects				
number (not applicable)				
Day 7	0	0		
Day 14	0	0		
Day 21	0	0		
Day 28	0	0		
Day 35	0	0		
Day 42	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With LCF in PP Population (PCR-corrected)

End point title	Percentage of Subjects With LCF in PP Population (PCR-corrected)[12]

End point description:

LCF included subjects who met any of the following criteria:
1. Development of signs of severe malaria or clinical deterioration requiring rescue medication after Day 3 in the presence of P.falciparum parasitemia, without previously meeting any of the criteria of ETF (see measure description in secondary outcome measures 5 and 6)
2. Presence of P.falciparum parasitemia and fever on any day from Day 4 onward, without previously meeting any of the criteria of ETF (see measure description in secondary outcome measures 5 and 6).
PCR-corrected refers to the use of molecular testing to differentiate recrudescence from reinfection in the context of an efficacy evaluation.
PP population, subjects in Ivory Coast center were excluded from the PP population.

End point type	Secondary

End point timeframe:

Days 7, 14, 21, 28, 35, 42

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 was a screening cohort, meant for safety evaluation, but not included in the efficacy assessments.

End point values	Cohort 2: Azithromycin + Chloroquine	Cohort 2: Artemether + Lumefantrine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	114	124		
Units: Percentage of Subjects				
number (not applicable)				
Day 7	0	0		
Day 14	0	0		
Day 21	0	0		
Day 28	0	0		
Day 35	0	0		

Day 42	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Late Parasitologic Failure (LPF) in the mITT Population (PCR-corrected)

End point title	Percentage of Subjects With Late Parasitologic Failure (LPF) in the mITT Population (PCR-corrected)[13]

End point description:

LPF: Presence of P. falciparum parasitemia in the mITT population on any day from Day 7 onward and the absence of fever without previously meeting any of the criteria of ETF (see measure description in secondary outcome measures 5 and 6) or LCF (see measure description in secondary outcome measure 7 and 8). PCR-corrected refers to the use of molecular testing to differentiate recrudescence from reinfection in the context of an efficacy evaluation. mITT population, subjects in Ivory Coast center were excluded from mITT population.

End point type	Secondary

End point timeframe:

Days 7, 14, 21, 28, 35, 42

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 was a screening cohort, meant for safety evaluation, but not included in the efficacy assessments.

End point values	Cohort 2: Azithromycin + Chloroquine	Cohort 2: Artemether + Lumefantrine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	120	126		
Units: Percentage of subjects				
number (not applicable)				
Day 7	0	0		
Day 14	1.67	0		
Day 21	2.5	0.79		
Day 28	4.17	0.79		
Day 35	4.17	2.38		
Day 42	5	2.38		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With LPF in PP Population (PCR-corrected)

End point title	Percentage of Subjects With LPF in PP Population (PCR-corrected)[14]

End point description:

LPF: Presence of P. falciparum parasitemia in the PP population on any day from Day 7 onward and the absence of fever without previously meeting any of the criteria of ETF (see measure description in secondary outcome measures 5 and 6) or LCF (see measure description in secondary outcome measure 7 and 8). PCR-corrected refers to the use of molecular testing to differentiate recrudescence from reinfection in the context of an efficacy evaluation. PP population, subjects in Ivory Coast center were excluded from the PP population.

End point type	Secondary

End point timeframe:

Days 7, 14, 21, 28, 35, 42

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 was a screening cohort, meant for safety evaluation, but not included in the efficacy assessments.

End point values	Cohort 2: Azithromycin + Chloroquine	Cohort 2: Artemether + Lumefantrine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	114	124		
Units: Percentage of subjects				
number (not applicable)				
Day 7	0	0		
Day 14	1.75	0		
Day 21	2.63	0.81		
Day 28	4.39	0.81		
Day 35	4.39	2.42		
Day 42	5.26	2.42		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Asexual Parasitologic Response (PCR-corrected)

End point title	Percentage of Subjects With Asexual Parasitologic Response (PCR-corrected)[15]

End point description:

Percentage of Subjects who were cleared of asexual parasites. Asexual parasite clearance - clearance of asexual P.falciparum parasitemia within 7 days of initiation of treatment without subsequent recurrence (PCR-corrected) through the day of consideration. PCR-corrected refers to the use of molecular testing to differentiate recrudescence from reinfection in the context of an efficacy evaluation. mITT population. "n"=Subjects who were evaluable at specified time points for each arm, respectively.

End point type	Secondary

End point timeframe:

Days 7, 14, 21, 28, 35, 42

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 was a screening cohort, meant for safety evaluation, but not included in the efficacy assessments.

End point values	Cohort 2: Azithromycin + Chloroquine	Cohort 2: Artemether + Lumefantrine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	120[16]	128[17]		
Units: Percentage of Subjects				
number (not applicable)				
Day 7 (n=120, 128)	93.33	99.22		
Day 14 (n=120, 127)	91.67	99.21		
Day 21 (n=120, 128)	90.83	98.44		
Day 28 (n=120, 127)	89.17	98.43		
Day 35 (n=120, 128)	89.17	96.88		
Day 42 (n=120, 127)	88.33	96.85		

Notes:

[16] - Subjects with evaluable data, including subjects in Ivory Coast center.

[17] - Subjects with evaluable data, including subjects in Ivory Coast center.

Statistical analyses

Statistical analysis title	Asexual Parasitologic Response for Day 7
Statistical analysis description: Day 7.	
Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
Method	large sample approximation to binomial
Parameter estimate	Percent difference
Point estimate	-5.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.02
upper limit	-0.75

Statistical analysis title	Asexual Parasitologic Response for Day 14
Statistical analysis description: Day 14.	
Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
Method	large sample approximation to binomial
Parameter estimate	Percent difference
Point estimate	-7.55

Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.14
upper limit	-1.95

Statistical analysis title	Asexual Parasitologic Response for Day 21
Statistical analysis description: Day 21.	
Comparison groups	Cohort 2: Artemether + Lumefantrine v Cohort 2: Azithromycin + Chloroquine
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
Method	large sample approximation to binomial
Parameter estimate	Percent difference
Point estimate	-7.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.61
upper limit	-1.6

Statistical analysis title	Asexual Parasitologic Response for Day 28
Statistical analysis description: Day 28.	
Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
Method	large sample approximation to binomial
Parameter estimate	Percent difference
Point estimate	-9.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.64
upper limit	-2.87

Statistical analysis title	Asexual Parasitologic Response for Day 35
Statistical analysis description: Day 35.	
Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine

Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
Method	large sample approximation to binomial
Parameter estimate	Percent difference
Point estimate	-7.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.45
upper limit	-0.97

Statistical analysis title	Asexual Parasitologic Response for Day 42
Statistical analysis description:	
Day 42.	
Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
Method	large sample approximation to binomial
Parameter estimate	Percent difference
Point estimate	-8.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.43
upper limit	-1.6

Secondary: Percentage of Subjects With Gametocytologic Response

End point title	Percentage of Subjects With Gametocytologic Response[18]

End point description:

Gametocyte response/absence/clearance: Clearance of P.falciparum gametocytemia (PCR-uncorrected) (attainment of 2 consecutive zero gametocyte counts) without subsequent recurrence through the day of consideration. PCR-uncorrected: not adjusted for molecular testing which determined recrudescence or true failures from reinfection. mITT population. "n"=subjects who were evaluable at specified time points for each arm, respectively.

End point type	Secondary

End point timeframe:

Days 7, 14, 21, 28, 35, 42

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 was a screening cohort, meant for safety evaluation, but not included in the efficacy assessments.

End point values	Cohort 2: Azithromycin + Chloroquine	Cohort 2: Artemether + Lumefantrine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	122[19]	130[20]		
Units: Percentage of Subjects				
number (not applicable)				
Day 7 (n=122, 129)	81.97	91.47		
Day 14 (n=122, 130)	81.15	91.54		
Day 21 (n=122, 130)	80.33	93.08		
Day 28 (n=122, 130)	81.97	93.08		
Day 35 (n=122, 130)	81.97	92.31		
Day 42 (n=122, 130)	80.33	91.54		

Notes:

[19] - Subjects with evaluable data, including subjects in the Ivory Coast center.

[20] - Subjects with evaluable data, including subjects in the Ivory Coast center.

Statistical analyses

Statistical analysis title	Gametocytologic Response for Day 7
Statistical analysis description: Day 7.	
Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine
Number of subjects included in analysis	252
Analysis specification	Pre-specified
Analysis type	superiority
Method	large sample approximation to binomial
Parameter estimate	Percent difference
Point estimate	-9.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.27
upper limit	-0.74

Statistical analysis title	Gametocytologic Response for Day 14
Statistical analysis description: Day 14.	
Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine
Number of subjects included in analysis	252
Analysis specification	Pre-specified
Analysis type	superiority
Method	large sample approximation to binomial
Parameter estimate	Percent difference
Point estimate	-10.39

Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.23
upper limit	-1.55

Statistical analysis title	Gametocytologic Response for Day 21
Statistical analysis description: Day 21.	
Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine
Number of subjects included in analysis	252
Analysis specification	Pre-specified
Analysis type	superiority
Method	large sample approximation to binomial
Parameter estimate	Percent difference
Point estimate	-12.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.45
upper limit	-4.04

Statistical analysis title	Gametocytologic Response for Day 28
Statistical analysis description: Day 28.	
Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine
Number of subjects included in analysis	252
Analysis specification	Pre-specified
Analysis type	superiority
Method	large sample approximation to binomial
Parameter estimate	Percent difference
Point estimate	-11.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.62
upper limit	-2.6

Statistical analysis title	Gametocytologic Response for Day 35
Statistical analysis description: Day 35.	
Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine

Number of subjects included in analysis	252
Analysis specification	Pre-specified
Analysis type	superiority
Method	large sample approximation to binomial
Parameter estimate	Percent difference
Point estimate	-10.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.97
upper limit	-1.71

Statistical analysis title	Gametocytologic Response for Day 42
Statistical analysis description:	
Day 42.	
Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine
Number of subjects included in analysis	252
Analysis specification	Pre-specified
Analysis type	superiority
Method	large sample approximation to binomial
Parameter estimate	Percent difference
Point estimate	-11.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.14
upper limit	-2.28

Secondary: Fever Clearance Time

End point title	Fever Clearance Time[21]
End point description:	
Calculated as time of first occurrence of two consecutive time points with temperature less than (<) 38.0 degrees C/100.4 degrees Fahrenheit (F) (rectal), 37.2 degrees C/99.0 degrees F (axillary), or <37.5 degrees C/99.5 degrees F (oral). mITT population, including subjects in the Ivory Coast center.	
End point type	Secondary
End point timeframe:	
Baseline to Day 42	

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 was a screening cohort, meant for safety evaluation, but not included in the efficacy assessments.

End point values	Cohort 2: Azithromycin + Chloroquine	Cohort 2: Artemether + Lumefantrine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	131		
Units: Hours				
median (full range (min-max))	24 (1 to 504)	24 (1 to 336)		

Statistical analyses

Statistical analysis title	Fever Clearance Time

Statistical analysis description:

Time to event data was analyzed using the Kaplan-Meier curve.

Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine
Number of subjects included in analysis	255
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2564
Method	Kaplan-Meier, log rank

Secondary: Asexual Plasmodium Falciparum Parasite Clearance Time

End point title	Asexual Plasmodium Falciparum Parasite Clearance Time[22]

End point description:

Defined as time to first of two consecutive zero asexual P. falciparum parasite (PCR-corrected) counts, regardless of recurrence of parasitemia later. PCR-corrected refers to the use of molecular testing to differentiate recrudescence from reinfection in the context of an efficacy evaluation. mITT population, including subjects in the Ivory Coast center.

End point type	Secondary

End point timeframe:

Baseline to Day 42

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 was a screening cohort, meant for safety evaluation, but not included in the efficacy assessments.

End point values	Cohort 2: Azithromycin + Chloroquine	Cohort 2: Artemether + Lumefantrine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	131		
Units: Hours				
median (full range (min-max))	48 (24 to 504)	24 (1 to 48)		

Statistical analyses

Statistical analysis title	Asexual P Falciparum Parasite Clearance Time

Statistical analysis description:

Time to event data was analyzed using the Kaplan-Meier curve.

Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine
Number of subjects included in analysis	255
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Kaplan-Meier, log rank

Secondary: Nadir Hemoglobin Level

End point title	Nadir Hemoglobin Level[23]

End point description:

Nadir hemoglobin for each Subject was defined as the minimum hemoglobin values obtained from Day 0 through Day 3. mITT population, including Subjects in the Ivory Coast center.

End point type	Secondary

End point timeframe:

Day 0 through Day 3

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 was a screening cohort, meant for safety evaluation, but not included in the efficacy assessments.

End point values	Cohort 2: Azithromycin + Chloroquine	Cohort 2: Artemether + Lumefantrine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	131		
Units: grams per deciliter (g/dL)				
arithmetic mean (standard deviation)	9.63 (± 1.53)	9.82 (± 1.61)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Nadir Hemoglobin Level at Days 14, 28, and 42

End point title	Change From Nadir Hemoglobin Level at Days 14, 28, and

End point description:

Change from nadir= observation minus nadir. Nadir defined as the minimum value for each subject on Days 0-3. mITT population. "n"=subjects who were evaluable at specified time points for each arm, respectively.

End point type	Secondary

End point timeframe:

Day 14, 28, 42

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 was a screening cohort, meant for safety evaluation, but not included in the efficacy assessments.

End point values	Cohort 2: Azithromycin + Chloroquine	Cohort 2: Artemether + Lumefantrine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	122[25]	128[26]		
Units: g/dL				
arithmetic mean (standard error)				
Change at Day 14 (n=122, 127)	0.52 (± 0.11)	0.44 (± 0.13)		
Change at Day 28 (n=122, 127)	1.15 (± 0.11)	0.96 (± 0.13)		
Change at Day 42 (n=122, 128)	1.29 (± 0.12)	1.14 (± 0.14)		

Notes:

[25] - Subjects with evaluable data, including subjects in the Ivory Coast center.

[26] - Subjects with evaluable data, including subjects in the Ivory Coast center.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Recurrence of Parasitemia

End point title	Time to Recurrence of Parasitemia[27]

End point description:

Time from the day of clearance to the time of recurrence of asexual P.falciparum parasitemia (PCR-uncorrected). mITT population, including subjects in the Ivory Coast center. Here "9.9999" indicates median as median time to recurrence could not be calculated for subjects in the Artemether-Lumefantrine treatment groups since fewer than 50% of the subjects experienced recurrent parasitemia during the study.

End point type	Secondary

End point timeframe:

Baseline (Day 0) to Day 42

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 was a screening cohort, meant for safety evaluation, but not included in the efficacy assessments.

End point values	Cohort 2: Azithromycin + Chloroquine	Cohort 2: Artemether + Lumefantrine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	131		
Units: Days				
median (full range (min-max))	34 (2 to 42)	9.9999 (7 to 43)		

Statistical analyses

Statistical analysis title	Time to Recurrence of Parasitemia

Statistical analysis description:

Time to event data was analyzed using the Kaplan-Meier curve.

Comparison groups	Cohort 2: Azithromycin + Chloroquine v Cohort 2: Artemether + Lumefantrine
Number of subjects included in analysis	255
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0006
Method	Kaplan-Meier, log rank

Secondary: Number of Subjects With Recurrent Parasitemia Versus Baseline Plasmodium Falciparum Chloroquine Resistance Transporter (PfCRT) Status

End point title	Number of Subjects With Recurrent Parasitemia Versus Baseline Plasmodium Falciparum Chloroquine Resistance Transporter (PfCRT) Status[28]

End point description:

End point type	Secondary

End point timeframe:

Baseline to Day 42

Notes:

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 was a screening cohort, meant for safety evaluation, but not included in the efficacy assessments.

End point values	Cohort 2: Azithromycin + Chloroquine	Cohort 2: Artemether + Lumefantrine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[29]	0[30]		
Units: Subjects				

Notes:

[29] - Data for this outcome measure was not analyzed as per change in planned analysis.

[30] - Data for this outcome measure was not analyzed as per change in planned analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With PfCRT in True Failures

End point title	Percentage of Subjects With PfCRT in True Failures[31]

End point description:

A genetic marker, P.falciparum chloroquine resistance transporter (PfCRT), indicative of P.falciparum chloroquine resistance was to be determined from blood blots obtained on Day 0 and at the time of treatment failure. Treatment failure was defined as any of the following events that a subject experienced from Day 0 through the Day 42 visit: ETF (see measure description in secondary outcome measures 5 and 6), LCF (PCR corrected) (see measure description in secondary outcome measure 7 and 8), or LPF (PCR corrected) (see measure description in secondary outcome measure 9 and 10). Recrudescence of asexual P.falciparum parasites was considered treatment failure. Data for this outcome measure was not analyzed as per change in planned analysis.

End point type	Secondary

End point timeframe:

Baseline to Day 42

Notes:

[31] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 was a screening cohort, meant for safety evaluation, but not included in the efficacy assessments.

End point values	Cohort 2: Azithromycin + Chloroquine	Cohort 2: Artemether + Lumefantrine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[32]	0[33]		
Units: Percentage of subjects				
number (not applicable)				

Notes:

[32] - Data for this outcome measure was not analyzed as per change in planned analysis.

[33] - Data for this outcome measure was not analyzed as per change in planned analysis.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 35 days after last dose of study drug

Adverse event reporting additional description:

The same event may appear as both an AE and a SAE.However, what is presented are distinct events.An event may be categorized as serious in one subject and as nonserious in another subject, or one subject may have experienced both a serious and nonserious event during the study. EU BR specific AE tables were generated separately using latest coding.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	COHORT1- AZITHROMYCIN/CHLOROQUINE

Reporting group description:

Azithromycin/Chloroquine administered orally once daily for 3 days as a combination tablet on Days 0, 1, 2. The combination tablets were administered on the basis of body weight approximately 30 milligram per kilogram (mg/kg) Azithromycin + approximately 10 mg base/kg Chloroquine base. Cohort 1 included subjects between >= 5 years of age and <= 12 years of age.

Reporting group title	COHORT1- ARTEMETHER/LUMEFANTRINE

Reporting group description:

Artemether/Lumefantrine administered orally once daily for 3 days as a combination tablet on Days 0, 1, 2. Cohort 1 included subjects between >=5 years of age and <=12 years of age.

Reporting group title	COHORT2- AZITHROMYCIN/CHLOROQUINE

Reporting group description:

Azithromycin/Chloroquine administered orally once daily for 3 days as a combination tablet on Days 0, 1, 2. The combination tablets were administered on the basis of body weight approximately 30 milligram/kilogram (mg/kg) Azithromycin + approximately 10 mg base/kg Chloroquine base. Cohort 2 included subjects between >=6 months of age to <=59 months of age.

Reporting group title	COHORT2- ARTEMETHER/LUMEFANTRINE

Reporting group description:

Artemether/Lumefantrine administered orally once daily for 3 days as a combination tablet on Days 0, 1, 2. Cohort 2 included subjects between >=6 months of age to <=59 months of age.

Serious adverse events	COHORT1-AZITHROMYCIN/CHLOROQUINE	COHORT1-ARTEMETHER/LUMEFANTRINE	COHORT2-AZITHROMYCIN/CHLOROQUINE
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 55 (1.82%)	2 / 51 (3.92%)	0 / 124 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations			
Hepatitis B			
subjects affected / exposed	0 / 55 (0.00%)	1 / 51 (1.96%)	0 / 124 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaria			
subjects affected / exposed	1 / 55 (1.82%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 51 (1.96%)	0 / 124 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	COHORT2-ARTEMETHER/LUMEFANTRINE		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 131 (0.76%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Nervous system disorders			
Convulsion			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Hepatitis B			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malaria			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			

subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	COHORT1-AZITHROMYCIN/CHLOROQUINE	COHORT1-ARTEMETHER/LUMEFANTRINE	COHORT2-AZITHROMYCIN/CHLOROQUINE
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 55 (72.73%)	36 / 51 (70.59%)	103 / 124 (83.06%)
Vascular disorders			
Pallor			
subjects affected / exposed	1 / 55 (1.82%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	1 / 124 (0.81%)
occurrences (all)	0	0	1
Chills			
subjects affected / exposed	2 / 55 (3.64%)	2 / 51 (3.92%)	3 / 124 (2.42%)
occurrences (all)	2	2	3
Fatigue			
subjects affected / exposed	1 / 55 (1.82%)	2 / 51 (3.92%)	0 / 124 (0.00%)
occurrences (all)	1	2	0
Feeling hot			
subjects affected / exposed	1 / 55 (1.82%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	1	0	0
Inflammation			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 55 (0.00%)	1 / 51 (1.96%)	3 / 124 (2.42%)
occurrences (all)	0	1	3
Product taste abnormal			

subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	1 / 124 (0.81%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	4 / 55 (7.27%)	3 / 51 (5.88%)	17 / 124 (13.71%)
occurrences (all)	4	3	20
Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	1	0	0
Vaginal inflammation			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	1 / 124 (0.81%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 55 (5.45%)	6 / 51 (11.76%)	15 / 124 (12.10%)
occurrences (all)	4	7	16
Dyspnoea			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	1 / 124 (0.81%)
occurrences (all)	0	0	1
Epistaxis			
subjects affected / exposed	3 / 55 (5.45%)	0 / 51 (0.00%)	1 / 124 (0.81%)
occurrences (all)	4	0	1
Nasal congestion			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 55 (1.82%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 55 (0.00%)	1 / 51 (1.96%)	4 / 124 (3.23%)
occurrences (all)	0	1	4
Tachypnoea			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	1 / 124 (0.81%)
occurrences (all)	0	0	1
Psychiatric disorders			

Irritability			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	0	0	0
Restlessness			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	0	0	0
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 55 (0.00%)	1 / 51 (1.96%)	0 / 124 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Scratch			
subjects affected / exposed	0 / 55 (0.00%)	1 / 51 (1.96%)	0 / 124 (0.00%)
occurrences (all)	0	1	0
Thermal burn			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	0	0	0
Wound			
subjects affected / exposed	0 / 55 (0.00%)	2 / 51 (3.92%)	2 / 124 (1.61%)
occurrences (all)	0	3	2
Congenital, familial and genetic disorders			
Phimosis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Atrioventricular block first degree			
subjects affected / exposed	1 / 55 (1.82%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 51 (1.96%)	1 / 124 (0.81%)
occurrences (all)	0	1	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 55 (1.82%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	1	0	0
Headache			

subjects affected / exposed	8 / 55 (14.55%)	5 / 51 (9.80%)	4 / 124 (3.23%)
occurrences (all)	9	7	4
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 51 (1.96%)	2 / 124 (1.61%)
occurrences (all)	0	1	2
Lymphadenopathy			
subjects affected / exposed	0 / 55 (0.00%)	1 / 51 (1.96%)	1 / 124 (0.81%)
occurrences (all)	0	1	1
Splenomegaly			
subjects affected / exposed	0 / 55 (0.00%)	3 / 51 (5.88%)	1 / 124 (0.81%)
occurrences (all)	0	3	1
Thrombocytopenia			
subjects affected / exposed	1 / 55 (1.82%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 55 (1.82%)	2 / 51 (3.92%)	0 / 124 (0.00%)
occurrences (all)	1	2	0
Eye disorders			
Conjunctival pallor			
subjects affected / exposed	0 / 55 (0.00%)	1 / 51 (1.96%)	0 / 124 (0.00%)
occurrences (all)	0	1	0
Eye swelling			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 55 (0.00%)	1 / 51 (1.96%)	0 / 124 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	10 / 55 (18.18%)	5 / 51 (9.80%)	4 / 124 (3.23%)
occurrences (all)	11	5	6
Abdominal pain upper			

subjects affected / exposed	0 / 55 (0.00%)	1 / 51 (1.96%)	0 / 124 (0.00%)
occurrences (all)	0	1	0
Anal pruritus			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	1 / 124 (0.81%)
occurrences (all)	0	0	1
Colitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	2 / 55 (3.64%)	1 / 51 (1.96%)	4 / 124 (3.23%)
occurrences (all)	2	2	4
Enteritis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	1 / 124 (0.81%)
occurrences (all)	0	0	1
Gastrointestinal sounds abnormal			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	1 / 124 (0.81%)
occurrences (all)	0	0	1
Mucous stools			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	1 / 124 (0.81%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	3 / 55 (5.45%)	2 / 51 (3.92%)	0 / 124 (0.00%)
occurrences (all)	3	2	0
Stomatitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	11 / 55 (20.00%)	5 / 51 (9.80%)	38 / 124 (30.65%)
occurrences (all)	12	6	44
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	0 / 55 (0.00%)	1 / 51 (1.96%)	0 / 124 (0.00%)
occurrences (all)	0	1	0
Dermatitis atopic			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	0	0	0

Pruritus			
subjects affected / exposed	9 / 55 (16.36%)	1 / 51 (1.96%)	8 / 124 (6.45%)
occurrences (all)	9	1	8
Pruritus generalised			
subjects affected / exposed	2 / 55 (3.64%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	2	0	0
Rash			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	2 / 124 (1.61%)
occurrences (all)	0	0	2
Rash generalised			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	2 / 124 (1.61%)
occurrences (all)	0	0	2
Rash papular			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	0	0	0
Skin ulcer			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	0	0	0
Swelling face			
subjects affected / exposed	1 / 55 (1.82%)	1 / 51 (1.96%)	1 / 124 (0.81%)
occurrences (all)	1	1	1
Urticaria			
subjects affected / exposed	1 / 55 (1.82%)	0 / 51 (0.00%)	1 / 124 (0.81%)
occurrences (all)	1	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 55 (0.00%)	1 / 51 (1.96%)	0 / 124 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal pain			
subjects affected / exposed	0 / 55 (0.00%)	1 / 51 (1.96%)	0 / 124 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	1 / 55 (1.82%)	1 / 51 (1.96%)	0 / 124 (0.00%)
occurrences (all)	1	2	0
Pain in extremity			

subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 55 (0.00%)	1 / 51 (1.96%)	0 / 124 (0.00%)
occurrences (all)	0	1	0
Amoebiasis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	0	0	0
Bacterial infection			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	1 / 124 (0.81%)
occurrences (all)	0	0	1
Blister infected			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	0	0	0
Body tinea			
subjects affected / exposed	0 / 55 (0.00%)	1 / 51 (1.96%)	0 / 124 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 51 (0.00%)	4 / 124 (3.23%)
occurrences (all)	1	0	4
Bronchopneumonia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 55 (0.00%)	3 / 51 (5.88%)	3 / 124 (2.42%)
occurrences (all)	0	3	3
Dysentery			
subjects affected / exposed	0 / 55 (0.00%)	1 / 51 (1.96%)	1 / 124 (0.81%)
occurrences (all)	0	1	1
Ear infection			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	1 / 124 (0.81%)
occurrences (all)	0	0	1
Fungal skin infection			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	0	0	0

Furuncle			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	1 / 124 (0.81%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	2 / 124 (1.61%)
occurrences (all)	0	0	2
Giardiasis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 51 (1.96%)	0 / 124 (0.00%)
occurrences (all)	0	1	0
Helminthic infection			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	0	0	0
Hepatitis A			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	0	0	0
Infection parasitic			
subjects affected / exposed	14 / 55 (25.45%)	11 / 51 (21.57%)	37 / 124 (29.84%)
occurrences (all)	14	11	39
Malaria			
subjects affected / exposed	5 / 55 (9.09%)	4 / 51 (7.84%)	26 / 124 (20.97%)
occurrences (all)	5	4	26
Mumps			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	1 / 124 (0.81%)
occurrences (all)	0	0	1
Oral herpes			
subjects affected / exposed	1 / 55 (1.82%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	1	0	0
Otitis media			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	1 / 124 (0.81%)
occurrences (all)	0	0	1
Otitis media acute			
subjects affected / exposed	0 / 55 (0.00%)	1 / 51 (1.96%)	0 / 124 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	2 / 124 (1.61%)
occurrences (all)	0	0	2

Respiratory tract infection			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	2 / 124 (1.61%)
occurrences (all)	0	0	3
Rhinitis			
subjects affected / exposed	2 / 55 (3.64%)	1 / 51 (1.96%)	2 / 124 (1.61%)
occurrences (all)	2	1	2
Septic rash			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 55 (0.00%)	1 / 51 (1.96%)	0 / 124 (0.00%)
occurrences (all)	0	1	0
Staphylococcal skin infection			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	0	0	0
Subcutaneous abscess			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	0	0	0
Tinea capitis			
subjects affected / exposed	5 / 55 (9.09%)	2 / 51 (3.92%)	2 / 124 (1.61%)
occurrences (all)	5	2	2
Tonsillitis			
subjects affected / exposed	0 / 55 (0.00%)	1 / 51 (1.96%)	0 / 124 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	6 / 55 (10.91%)	4 / 51 (7.84%)	9 / 124 (7.26%)
occurrences (all)	6	4	13
Urinary tract infection			
subjects affected / exposed	1 / 55 (1.82%)	0 / 51 (0.00%)	0 / 124 (0.00%)
occurrences (all)	1	0	0
Viral rash			
subjects affected / exposed	0 / 55 (0.00%)	0 / 51 (0.00%)	1 / 124 (0.81%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	3 / 55 (5.45%)	3 / 51 (5.88%)	9 / 124 (7.26%)
occurrences (all)	3	3	10

Non-serious adverse events	COHORT2-ARTEMETHER/LUMEFANTRINE		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	99 / 131 (75.57%)		
Vascular disorders			
Pallor			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	3 / 131 (2.29%)		
occurrences (all)	3		
Chills			
subjects affected / exposed	5 / 131 (3.82%)		
occurrences (all)	5		
Fatigue			
subjects affected / exposed	3 / 131 (2.29%)		
occurrences (all)	3		
Feeling hot			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences (all)	0		
Inflammation			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	2 / 131 (1.53%)		
occurrences (all)	2		
Product taste abnormal			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	27 / 131 (20.61%)		
occurrences (all)	31		
Reproductive system and breast			

disorders			
Balanoposthitis			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences (all)	0		
Vaginal inflammation			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	13 / 131 (9.92%)		
occurrences (all)	14		
Dyspnoea			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	2 / 131 (1.53%)		
occurrences (all)	2		
Tachypnoea			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences (all)	1		
Psychiatric disorders			
Irritability			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences (all)	1		
Restlessness			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences (all)	1		

Investigations Electrocardiogram QT prolonged subjects affected / exposed occurrences (all)	 0 / 131 (0.00%) 0		
Injury, poisoning and procedural complications Scratch subjects affected / exposed occurrences (all) Thermal burn subjects affected / exposed occurrences (all) Wound subjects affected / exposed occurrences (all)	 0 / 131 (0.00%) 0 1 / 131 (0.76%) 1 1 / 131 (0.76%) 1		
Congenital, familial and genetic disorders Phimosis subjects affected / exposed occurrences (all)	 0 / 131 (0.00%) 0		
Cardiac disorders Atrioventricular block first degree subjects affected / exposed occurrences (all) Tachycardia subjects affected / exposed occurrences (all)	 0 / 131 (0.00%) 0 1 / 131 (0.76%) 2		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	 0 / 131 (0.00%) 0 4 / 131 (3.05%) 4		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Lymphadenopathy	 4 / 131 (3.05%) 4		

subjects affected / exposed	0 / 131 (0.00%)		
occurrences (all)	0		
Splenomegaly			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences (all)	0		
Thrombocytopenia			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences (all)	0		
Eye disorders			
Conjunctival pallor			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences (all)	0		
Eye swelling			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences (all)	1		
Periorbital oedema			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	14 / 131 (10.69%)		
occurrences (all)	16		
Abdominal pain upper			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences (all)	0		
Anal pruritus			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences (all)	1		
Colitis			

subjects affected / exposed	1 / 131 (0.76%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	8 / 131 (6.11%)		
occurrences (all)	8		
Enteritis			
subjects affected / exposed	2 / 131 (1.53%)		
occurrences (all)	2		
Gastrointestinal sounds abnormal			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences (all)	0		
Mucous stools			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences (all)	1		
Stomatitis			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	13 / 131 (9.92%)		
occurrences (all)	14		
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences (all)	0		
Dermatitis atopic			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	2 / 131 (1.53%)		
occurrences (all)	2		
Pruritus generalised			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences (all)	0		

Rash			
subjects affected / exposed	2 / 131 (1.53%)		
occurrences (all)	2		
Rash generalised			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences (all)	0		
Rash papular			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences (all)	1		
Skin ulcer			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences (all)	1		
Swelling face			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences (all)	0		
Urticaria			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences (all)	1		
Infections and infestations			
Abscess limb			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences (all)	1		
Amoebiasis			

subjects affected / exposed	1 / 131 (0.76%)			
occurrences (all)	1			
Bacterial infection				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences (all)	1			
Blister infected				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences (all)	1			
Body tinea				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences (all)	1			
Bronchitis				
subjects affected / exposed	9 / 131 (6.87%)			
occurrences (all)	9			
Bronchopneumonia				
subjects affected / exposed	2 / 131 (1.53%)			
occurrences (all)	2			
Conjunctivitis				
subjects affected / exposed	2 / 131 (1.53%)			
occurrences (all)	2			
Dysentery				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences (all)	1			
Ear infection				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences (all)	1			
Fungal skin infection				
subjects affected / exposed	2 / 131 (1.53%)			
occurrences (all)	2			
Furuncle				
subjects affected / exposed	5 / 131 (3.82%)			
occurrences (all)	6			
Gastroenteritis				
subjects affected / exposed	5 / 131 (3.82%)			
occurrences (all)	6			
Giardiasis				

subjects affected / exposed	0 / 131 (0.00%)			
occurrences (all)	0			
Helminthic infection				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences (all)	1			
Hepatitis A				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences (all)	1			
Infection parasitic				
subjects affected / exposed	31 / 131 (23.66%)			
occurrences (all)	33			
Malaria				
subjects affected / exposed	19 / 131 (14.50%)			
occurrences (all)	19			
Mumps				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences (all)	1			
Oral herpes				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences (all)	1			
Otitis media				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences (all)	1			
Otitis media acute				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences (all)	1			
Pneumonia				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences (all)	0			
Respiratory tract infection				
subjects affected / exposed	8 / 131 (6.11%)			
occurrences (all)	8			
Rhinitis				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences (all)	1			
Septic rash				

subjects affected / exposed	1 / 131 (0.76%)		
occurrences (all)	1		
Skin infection			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences (all)	0		
Staphylococcal skin infection			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences (all)	1		
Subcutaneous abscess			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences (all)	1		
Tinea capitis			
subjects affected / exposed	2 / 131 (1.53%)		
occurrences (all)	2		
Tonsillitis			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	12 / 131 (9.16%)		
occurrences (all)	14		
Urinary tract infection			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences (all)	1		
Viral rash			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	5 / 131 (3.82%)		
occurrences (all)	5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 December 2007	1. The primary endpoint was changed from asexual P. falciparum parasite clearance rate at Day 28 to adequate clinical and parasitological response (ACPR) at Day 28 2. The primary endpoint (ACPR) was also changed to be based on PCR-corrected data rather than using uncorrected data. 3. Secondary endpoint changed from % Late treatment failure (LTF) to % Late Clinical Failures (LCF)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Cohort 1 was a screening cohort, meant for safety evaluation, but not included in the efficacy assessments.

Notes: