Clinical trial results:
A randomized, open-label, multicenter study to compare efficacy, safety and tolerability of KLU156 with Coartem® in the treatment of uncomplicated Plasmodium falciparum malaria in adults and children 5 kg body weight followed by an Extension phase with repeated KLU156 treatment

Summary

EudraCT number	2022-002675-10
Trial protocol	Outside EU/EEA
Global end of trial date	25 November 2025

Results information

Result version number	v1 (current)
This version publication date	09 June 2026
First version publication date	09 June 2026

Trial information

Trial identification

Sponsor protocol code	CKLU156A12301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05842954
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 November 2025
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 November 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to confirm the efficacy of KLU156 in adults and children ≥ 10 kg body weight suffering from uncomplicated malaria caused by P. falciparum (with or without other Plasmodium spp. co-infection) by demonstrating that KLU156 is non-inferior to Coartem (noninferiority margin = 5%) based on the PCR-corrected ACPR at Day 29.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 March 2024
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Burkina Faso: 379
Country: Number of subjects enrolled	Congo, The Democratic Republic of the: 198
Country: Number of subjects enrolled	Côte d'Ivoire: 242
Country: Number of subjects enrolled	Gabon: 80
Country: Number of subjects enrolled	Ghana: 163
Country: Number of subjects enrolled	Kenya: 175
Country: Number of subjects enrolled	Mali: 110
Country: Number of subjects enrolled	Niger: 8
Country: Number of subjects enrolled	Rwanda: 163
Country: Number of subjects enrolled	Tanzania, United Republic of: 56
Country: Number of subjects enrolled	Uganda: 89
Country: Number of subjects enrolled	Zambia: 57
Worldwide total number of subjects	1720
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)	53
Children (2-11 years)	1042
Adolescents (12-17 years)	314
Adults (18-64 years)	307
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients were screened at 35 centers in 13 countries across Sub-Saharan Africa and India.

Period 1

Period 1 title	Core Phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor[1]

Arms

Are arms mutually exclusive?	Yes
Arm title	KLU156 (Participants with ≥10 kg Body Weight)

Arm description:

KLU156 once daily (QD) for 3 days under fed conditions (light meal).

Arm type	Experimental
Investigational medicinal product name	KLU156
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Oral use. KLU156 (400/480 mg) was the dose for patients with a bodyweight ≥ 35kg. Patients < 35kg took a fraction of the dose according to weight group as defined in the protocol.

Arm title	Coartem (Participants with ≥10 kg Body Weight)

Arm description:

Coartem twice a day (BID) for 3 days under fed conditions.

Arm type	Active comparator
Investigational medicinal product name	Coartem
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Oral use. Dosing was selected based on patient’s body weight as per product's label.

Arm title	KLU156 (Participants with <10 kg Body Weight)

Arm description:

KLU156 once daily (QD) for 3 days under fed conditions (light meal).

Arm type	Experimental
Investigational medicinal product name	KLU156
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Oral use. KLU156 (400/480 mg) was the dose for patients with a bodyweight ≥ 35kg. Patients < 35kg took a fraction of the dose according to weight group as defined in the protocol.

Arm title	Coartem (Participants with <10 kg Body Weight

Arm description:

Coartem twice a day (BID) for 3 days under fed conditions.

Arm type	Active comparator
Investigational medicinal product name	Coartem
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Oral use. Dosing was selected based on patient's body weight as per product's label.

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: assessor blinded

Number of subjects in period 1	KLU156 (Participants with ≥10 kg Body Weight)	Coartem (Participants with ≥10 kg Body Weight)	KLU156 (Participants with <10 kg Body Weight)
Started	836	832	24
Safety set	830	831	24
Modified randomized set (mRAS)	836	832	0 [2]
Modified safety set	830	831	0 [3]
Completed	767	824	14
Not completed	69	8	10
Adverse event, non-fatal	62	5	9
Protocol Deviation	-	1	-
Technical Problems	-	-	1
Guardian Decision	1	1	-
Not Treated in Core	6	1	-

Number of subjects in period 1	Coartem (Participants with <10 kg Body Weight
Started	28
Safety set	27
Modified randomized set (mRAS)	0 [4]
Modified safety set	0 [5]
Completed	27
Not completed	1
Adverse event, non-fatal	-
Protocol Deviation	-
Technical Problems	-

Guardian Decision	-
Not Treated in Core	1

Notes:

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Milestone provided to define analysis population

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Milestone provided to define analysis population

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Milestone provided to define analysis population

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Milestone provided to define analysis population

Period 2

Period 2 title	Extension Phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor[6]

Blinding implementation details:

assessor blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	KLU156 (≥10 kg Body Weight Entering from Core KLU156 Arm)

Arm description:

KLU156 once daily (QD) for 3 days under fed conditions (light meal).

Arm type	Experimental
Investigational medicinal product name	KLU156
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Oral use. KLU156 (400/480 mg) was the dose for patients with a bodyweight ≥ 35kg. Patients < 35kg took a fraction of the dose according to weight group as defined in the protocol.

Arm title	KLU156 (≥10 kg Body Weight Entering from Core Coartem Arm)

Arm description:

KLU156 once daily (QD) for 3 days under fed conditions (light meal).

Arm type	Experimental

Investigational medicinal product name	KLU156
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Oral use. KLU156 (400/480 mg) was the dose for patients with a bodyweight ≥ 35kg. Patients < 35kg took a fraction of the dose according to weight group as defined in the protocol.

Arm title	KLU156 (<10 kg Body Weight Entering from Core KLU156 Arm)

Arm description:

KLU156 once daily (QD) for 3 days under fed conditions (light meal).

Arm type	Experimental
Investigational medicinal product name	KLU156
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Oral use. KLU156 (400/480 mg) was the dose for patients with a bodyweight ≥ 35kg. Patients < 35kg took a fraction of the dose according to weight group as defined in the protocol.

Notes:

[6] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: assessor blinded

Number of subjects in period 2[7]	KLU156 (≥10 kg Body Weight Entering from Core KLU156 Arm)	KLU156 (≥10 kg Body Weight Entering from Core Coartem Arm)	KLU156 (<10 kg Body Weight Entering from Core KLU156 Arm)
Started	190	203	2
Completed	190	203	2

Notes:

[7] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Milestone provided to define analysis population

Baseline characteristics

Reporting groups	
Reporting group title	KLU156 (Participants with ≥10 kg Body Weight)
Reporting group description: KLU156 once daily (QD) for 3 days under fed conditions (light meal).	
Reporting group title	Coartem (Participants with ≥10 kg Body Weight)
Reporting group description: Coartem twice a day (BID) for 3 days under fed conditions.	
Reporting group title	KLU156 (Participants with <10 kg Body Weight)
Reporting group description: KLU156 once daily (QD) for 3 days under fed conditions (light meal).	
Reporting group title	Coartem (Participants with <10 kg Body Weight
Reporting group description: Coartem twice a day (BID) for 3 days under fed conditions.	

Reporting group values	KLU156 (Participants with ≥10 kg Body Weight)	Coartem (Participants with ≥10 kg Body Weight)	KLU156 (Participants with <10 kg Body Weight)
Number of subjects	836	832	24
Age Categorical Units: participants			
Infants and toddlers (28 days-23 months)	13	9	18
Children (2-11 years)	506	515	6
Adolescents (12-17 years)	162	152	0
Adults (18-64 years)	152	155	0
From 65-84 years	3	1	0
Age Continuous Units: years			
arithmetic mean	12.13	11.94	1.60
standard deviation	± 10.46	± 9.91	± 0.47
Sex: Female, Male Units: participants			
Female	419	395	15
Male	417	437	9
Race/Ethnicity, Customized Units: Subjects			
Black or African American	816	813	24
Race Not Reported	19	19	0
Race Unknown	1	0	0

Reporting group values	Coartem (Participants with <10 kg Body Weight	Total	
Number of subjects	28	1720	
Age Categorical Units: participants			
Infants and toddlers (28 days-23 months)	14	54	

Children (2-11 years)	14	1041	
Adolescents (12-17 years)	0	314	
Adults (18-64 years)	0	307	
From 65-84 years	0	4	
Age Continuous			
Units: years			
arithmetic mean	1.80		
standard deviation	± 0.60	-	
Sex: Female, Male			
Units: participants			
Female	14	843	
Male	14	877	
Race/Ethnicity, Customized			
Units: Subjects			
Black or African American	28	1681	
Race Not Reported	0	38	
Race Unknown	0	1	

Subject analysis sets

Subject analysis set title	Coartem (Participants with <10 kg Body Weight)
Subject analysis set type	Full analysis

Subject analysis set description:

Coartem twice a day (BID) for 3 days under fed conditions.

Reporting group values	Coartem (Participants with <10 kg Body Weight)		
Number of subjects	27		
Age Categorical			
Units: participants			
Infants and toddlers (28 days-23 months)	13		
Children (2-11 years)	14		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
Age Continuous			
Units: years			
arithmetic mean	1.80		
standard deviation	± 0.60		
Sex: Female, Male			
Units: participants			
Female	14		
Male	13		
Race/Ethnicity, Customized			
Units: Subjects			
Black or African American	27		
Race Not Reported	0		
Race Unknown	0		

End points

End points reporting groups

Reporting group title	KLU156 (Participants with ≥10 kg Body Weight)
Reporting group description: KLU156 once daily (QD) for 3 days under fed conditions (light meal).	
Reporting group title	Coartem (Participants with ≥10 kg Body Weight)
Reporting group description: Coartem twice a day (BID) for 3 days under fed conditions.	
Reporting group title	KLU156 (Participants with <10 kg Body Weight)
Reporting group description: KLU156 once daily (QD) for 3 days under fed conditions (light meal).	
Reporting group title	Coartem (Participants with <10 kg Body Weight
Reporting group description: Coartem twice a day (BID) for 3 days under fed conditions.	
Reporting group title	KLU156 (≥10 kg Body Weight Entering from Core KLU156 Arm)
Reporting group description: KLU156 once daily (QD) for 3 days under fed conditions (light meal).	
Reporting group title	KLU156 (≥10 kg Body Weight Entering from Core Coartem Arm)
Reporting group description: KLU156 once daily (QD) for 3 days under fed conditions (light meal).	
Reporting group title	KLU156 (<10 kg Body Weight Entering from Core KLU156 Arm)
Reporting group description: KLU156 once daily (QD) for 3 days under fed conditions (light meal).	
Subject analysis set title	Coartem (Participants with <10 kg Body Weight)
Subject analysis set type	Full analysis
Subject analysis set description: Coartem twice a day (BID) for 3 days under fed conditions.	

Primary: Core phase: PCR-corrected Adequate Clinical and Parasitological Response (ACPR) at Day 29

End point title	Core phase: PCR-corrected Adequate Clinical and Parasitological Response (ACPR) at Day 29[1]
End point description: PCR-corrected Adequate Clinical and Parasitological Response (ACPR) at Day 29 is defined as the percentage of participants who are clinically well and have no recrudescence (reappearance of the original malaria infection) by 29 days after treatment, with PCR genotyping used to distinguish new infections from recrudescence. This primary outcome was applicable to the non-US submission.	
End point type	Primary
End point timeframe: Day 29 (i.e., 28 days post-first dose administration)	

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: Protocol amendment increased the minimum body weight requirement for study participation from ≥ 5 kg to ≥ 10 kg and revised the statistical analysis plan to exclude patients < 10 kg from the main analyses.

End point values	KLU156 (Participants with ≥10 kg Body Weight)	Coartem (Participants with ≥10 kg Body Weight)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	657	686		
Units: percentage of participants				
number (confidence interval 95%)	97.4 (95.9 to 98.5)	94.0 (92.0 to 95.7)		

Statistical analyses

Statistical analysis title	Analysis
Comparison groups	KLU156 (Participants with ≥10 kg Body Weight) v Coartem (Participants with ≥10 kg Body Weight)
Number of subjects included in analysis	1343
Analysis specification	Pre-specified
Analysis type	
Method	Wilson uncorrected method
Parameter estimate	Risk difference (RD)
Point estimate	3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	5.6

Primary: Core phase: Uncorrected ACPR (US NDA Submission) at Day 29

End point title	Core phase: Uncorrected ACPR (US NDA Submission) at Day

End point description:

Uncorrected ACPR at Day 29 is defined as the percentage of participants who are clinically well and have no malaria parasite reappearance detected by Day 29 after treatment, without using parasite genotyping to distinguish new infections from recrudescence of the original infection. This primary outcome was applicable to US New Drug Application (NDA) submission.

End point type	Primary

End point timeframe:

Day 29

Notes:

[2] - 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: Protocol amendment increased the minimum body weight requirement for study participation from ≥ 5 kg to ≥ 10 kg and revised the statistical analysis plan to exclude patients < 10 kg from the main analyses.

End point values	KLU156 (Participants with ≥10 kg Body Weight)	Coartem (Participants with ≥10 kg Body Weight)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	726	722		
Units: percentage of participants				
number (confidence interval 95%)	85.3 (82.5 to 87.8)	82.1 (79.1 to 84.9)		

Statistical analyses

Statistical analysis title	Analysis
Comparison groups	KLU156 (Participants with ≥10 kg Body Weight) v Coartem (Participants with ≥10 kg Body Weight)
Number of subjects included in analysis	1448
Analysis specification	Pre-specified
Analysis type	
Method	Wilson uncorrected method
Parameter estimate	Risk difference (RD)
Point estimate	3.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	6.9

Secondary: Core phase: PCR-corrected ACPR at Days 22 and 43

End point title	Core phase: PCR-corrected ACPR at Days 22 and 43[3]

End point description:

To confirm the efficacy of KLU156 by assessing PCR-corrected ACPR at additional time points.

End point type	Secondary

End point timeframe:

Days 22 and 43 (i.e., 21 and 42 days post-first dose administration)

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: Protocol amendment increased the minimum body weight requirement for study participation from ≥ 5 kg to ≥ 10 kg and revised the statistical analysis plan to exclude patients < 10 kg from the main analyses.

End point values	KLU156 (Participants with ≥10 kg Body Weight)	Coartem (Participants with ≥10 kg Body Weight)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	664	713		
Units: percentage of participants				
number (confidence interval 95%)				

Day 22 n=664,713	98.9 (97.8 to 99.6)	96.5 (94.9 to 97.7)		
Day 43/End of Core Phase n=626,627	94.6 (92.5 to 96.2)	91.7 (89.3 to 93.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Core phase: Uncorrected ACPR at Days 22 and 43

End point title	Core phase: Uncorrected ACPR at Days 22 and 43[4]

End point description:

To confirm the efficacy of KLU156 by assessing uncorrected ACPR at additional time points.

End point type	Secondary

End point timeframe:

Days 22 and 43 (i.e., 21 and 42 days post-first dose administration)

Notes:

[4] - 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: Protocol amendment increased the minimum body weight requirement for study participation from ≥ 5 kg to ≥ 10 kg and revised the statistical analysis plan to exclude patients < 10 kg from the main analyses.

End point values	KLU156 (Participants with ≥10 kg Body Weight)	Coartem (Participants with ≥10 kg Body Weight)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	726	722		
Units: percentage of participants				
number (confidence interval 95%)				
Day 22 n=726,722	90.1 (87.7 to 92.2)	92.1 (89.9 to 94.0)		
Day 43/End of Core Phase n=726,722	74.4 (71.0 to 77.5)	72.6 (69.2 to 75.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Core phase: Percentage of Participants With Recrudescence

End point title	Core phase: Percentage of Participants With Recrudescence[5]

End point description:

Recrudescence is defined as appearance of asexual parasites after clearance of initial infection with a genotype identical to that of parasites present at baseline. Recrudescence had to be confirmed by PCR analysis.

End point type	Secondary

End point timeframe:

Days 22, 29 and 43

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: Protocol amendment increased the minimum body weight requirement for study participation from ≥ 5 kg to ≥ 10 kg and revised the statistical analysis plan to exclude patients < 10 kg from the main analyses.

End point values	KLU156 (Participants with ≥10 kg Body Weight)	Coartem (Participants with ≥10 kg Body Weight)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	667	711		
Units: percentage of participants				
Day 8 to Day 22 n=667,711	0	6		
Day 23 to Day 29 n=658,680	3	15		
Day 30 to Day 43 n=626,615	12	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Core phase: Percentage of Participants With New Infection

End point title	Core phase: Percentage of Participants With New Infection[6]

End point description:

New infection is defined as appearance of asexual parasites after clearance of initial infection with a genotype different from those parasites present at baseline. New infection had to be confirmed by PCR analysis.

End point type	Secondary

End point timeframe:

Days 22, 29 and 43

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: Protocol amendment increased the minimum body weight requirement for study participation from ≥ 5 kg to ≥ 10 kg and revised the statistical analysis plan to exclude patients < 10 kg from the main analyses.

End point values	KLU156 (Participants with ≥10 kg Body Weight)	Coartem (Participants with ≥10 kg Body Weight)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	667	711		
Units: percentage of participants				
Day 8 to Day 22 n=667,711	4	19		
Day 23 to Day 29 n=657,674	15	46		
Day 30 to Day 43 n=625,608	66	64		

Statistical analyses

No statistical analyses for this end point

Secondary: Core phase: Fever Clearance Time

End point title	Core phase: Fever Clearance Time[7]

End point description:

Fever clearance time is defined as time from the first dose until the first time the axillary body temperature decreased below and remained below 37.5°C axillary or 38.0°C oral/tympanic/rectal for at least a further 24 hours.

End point type	Secondary

End point timeframe:

Up to Day 3

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: Protocol amendment increased the minimum body weight requirement for study participation from ≥ 5 kg to ≥ 10 kg and revised the statistical analysis plan to exclude patients < 10 kg from the main analyses.

End point values	KLU156 (Participants with ≥10 kg Body Weight)	Coartem (Participants with ≥10 kg Body Weight)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	726	722		
Units: hours				
median (confidence interval 95%)	6.3 (6.0 to 11.6)	11.9 (11.4 to 12.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Core phase: Parasite Clearance Time

End point title	Core phase: Parasite Clearance Time[8]

End point description:

Parasite clearance time is defined as time from the first dose until the first total and continued disappearance of asexual parasite forms which remained at least a further 48 hours.

End point type	Secondary

End point timeframe:

Up to Day 3

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: Protocol amendment increased the minimum body weight requirement for study participation from ≥ 5 kg to ≥ 10 kg and revised the statistical analysis plan to exclude patients < 10 kg from the main analyses.

End point values	KLU156 (Participants with ≥10 kg Body Weight)	Coartem (Participants with ≥10 kg Body Weight)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	726	722		
Units: hours				
median (confidence interval 95%)	37.6 (36.2 to 46.9)	36.0 (35.9 to 36.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Core phase: Gametocyte Clearance Time

End point title	Core phase: Gametocyte Clearance Time[9]

End point description:

To confirm the efficacy of KLU156 by assessing gametocyte clearance between the two treatment arms

End point type	Secondary

End point timeframe:

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: Protocol amendment increased the minimum body weight requirement for study participation from ≥ 5 kg to ≥ 10 kg and revised the statistical analysis plan to exclude patients < 10 kg from the main analyses.

End point values	KLU156 (Participants with ≥10 kg Body Weight)	Coartem (Participants with ≥10 kg Body Weight)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	726	722		
Units: hours				
median (confidence interval 95%)	35.9 (24.0 to 48.0)	48.0 (36.0 to 159.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Core phase: Percentage of Participants With Parasitemia

End point title	Core phase: Percentage of Participants With Parasitemia[10]

End point description:

For the parasitemia assessment, blood sampling can be done by means of a finger prick except when the timing for parasitology assessments coincides with time for clinical laboratory tests, in which case, blood sample can be taken from the venous blood collected for clinical laboratory analyses.

End point type	Secondary

End point timeframe:

12, 24, 48 and 72 hours after treatment

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: Protocol amendment increased the minimum body weight requirement for study participation from ≥ 5 kg to ≥ 10 kg and revised the statistical analysis plan to exclude patients < 10 kg from the main analyses.

End point values	KLU156 (Participants with ≥10 kg Body Weight)	Coartem (Participants with ≥10 kg Body Weight)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	724	721		
Units: percentage of participants				
number (confidence interval 95%)				
12 Hours n=719,721	96.9 (95.40 to 98.07)	92.0 (89.72 to 93.84)		
24 Hours n=723,720	86.3 (83.58 to 88.73)	62.5 (58.85 to 66.05)		
48 Hours n=721,721	15.0 (12.45 to 17.80)	9.0 (7.03 to 11.35)		
72 Hours n=724,719	0.8 (0.30 to 1.80)	1.7 (0.87 to 2.90)		

Statistical analyses

No statistical analyses for this end point

Secondary: Core phase: Clearance of Gametocytes in Participants With Gametocytemia at Baseline

End point title	Core phase: Clearance of Gametocytes in Participants With Gametocytemia at Baseline[11]

End point description:

Assessed by microscopy. Baseline was pre-first dose administration.

End point type	Secondary

End point timeframe:

From baseline up to Day 43

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: Protocol amendment increased the minimum body weight requirement for study participation from ≥ 5 kg to ≥ 10 kg and revised the statistical analysis plan to exclude patients < 10 kg from the main analyses.

End point values	KLU156 (Participants with ≥10 kg Body Weight)	Coartem (Participants with ≥10 kg Body Weight)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	726	722		
Units: percentage of participants				
number (not applicable)				
Day 1: Present at 6 Hours	4.4	4.7		

Day 1: Absent at 6 Hours	94.1	95.3		
Day 1: Present at 12 Hours	4.5	4.7		
Day 1: Absent at 12 Hours	94.5	95.2		
Day 2: Present at 24 Hours	3.9	6.2		
Day 2: Absent at 24 Hours	95.7	93.5		
Day 2: Present at 36 Hours	2.3	3.6		
Day 2: Absent at 36 Hours	97.2	96.1		
Day 3: Present	1.1	98.8		
Day 3: Absent	3.2	96.7		
Day 4: Present	1.0	1.9		
Day 4: Absent	98.8	97.6		
Day 8: Present	0.1	1.8		
Day 8: Absent	99.2	97.0		
Day 22: Present	0	0.3		
Day 22: Absent	93.5	97.5		
Day 29: Present	0	0.1		
Day 29: Absent	97.1	97.1		
Day 43/End of Core Phase: Present	0.1	0.3		
Day 43/End of Core Phase: Absent	97.2	96.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Core phase: Percentage of Participants With Treatment-emergent Adverse Events (TEAEs) and AEs of Grade 3 Severity or Higher

End point title	Core phase: Percentage of Participants With Treatment-emergent Adverse Events (TEAEs) and AEs of Grade 3 Severity or Higher[12]

End point description:

Incidence and severity of TEAEs by treatment group, including changes in vital signs, electrocardiograms (ECGs), and laboratory results qualifying and reported as AEs. Severity was graded according to the Common Terminology Criteria for Adverse Events (CTCAE): Grade 1 (Mild), Grade 2 (Moderate), Grade 3 (Severe), Grade 4 (Life-threatening), and Grade 5 (Death).

End point type	Secondary

End point timeframe:

Day 43

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: Protocol amendment increased the minimum body weight requirement for study participation from ≥ 5 kg to ≥ 10 kg and revised the statistical analysis plan to exclude patients < 10 kg from the main analyses.

End point values	KLU156 (Participants with ≥10 kg Body Weight)	Coartem (Participants with ≥10 kg Body Weight)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	830	831		
Units: percentage of participants				
number (not applicable)				

All TEAEs	444	422		
TEAEs of Grade 3 Severity or Higher	2.5	2.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Core phase: Percentage of Participants With Treatment-emergent Serious Adverse Events (SAEs), Graded by Severity

End point title	Core phase: Percentage of Participants With Treatment-emergent Serious Adverse Events (SAEs), Graded by Severity[13]

End point description:

Incidence and severity of treatment-emergent SAEs by treatment group, including changes in vital signs, electrocardiograms (ECGs), and laboratory results qualifying and reported as AEs. Severity was graded according to the Common Terminology Criteria for Adverse Events (CTCAE): Grade 1 (Mild), Grade 2 (Moderate), Grade 3 (Severe), Grade 4 (Life-threatening), and Grade 5 (Death).

End point type	Secondary

End point timeframe:

Day 43

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: Protocol amendment increased the minimum body weight requirement for study participation from ≥ 5 kg to ≥ 10 kg and revised the statistical analysis plan to exclude patients < 10 kg from the main analyses.

End point values	KLU156 (Participants with ≥10 kg Body Weight)	Coartem (Participants with ≥10 kg Body Weight)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	830	831		
Units: percentage of participants				
Grade 2	2	5		
Grade 3	5	1		
Grade 4	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Extension phase: PCR-corrected ACPR

End point title	Extension phase: PCR-corrected ACPR[14]

End point description:

To evaluate PCR-corrected ACPR over repeated treatment with KLU156 in adults and children ≥ 10 kg of body weight suffering from uncomplicated malaria caused by P. falciparum (with or without other Plasmodium spp. co-infection). Patients were instructed to return to the study site whenever symptoms suggestive of malaria occurred. At each suspected malaria episode, eligibility for KLU156 treatment was reassessed, including confirmation of malaria diagnosis.

End point type	Secondary

End point timeframe:

Up to Day 29 for each KLU156 treatment episode

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: Protocol amendment increased the minimum body weight requirement for study participation from ≥ 5 kg to ≥ 10 kg and revised the statistical analysis plan to exclude patients < 10 kg from the main analyses.

End point values	KLU156 (Participants with ≥10 kg Body Weight)			
Subject group type	Reporting group			
Number of subjects analysed	342			
Units: percentage of participants				
number (confidence interval 95%)				
1st KLU156 Treatment n=342	98.0 (95.8 to 99.2)			
2nd KLU156 Treatment n=214	97.2 (94.0 to 99.0)			
3rd+KLU156 includes 3rd, 4th, 5th, 6th groups n=59	100.0 (93.9 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Extension Phase: Uncorrected ACPR

End point title	Extension Phase: Uncorrected ACPR[15]

End point description:

To evaluate uncorrected ACPR over repeated treatment with KLU156 in adults and children ≥ 10 kg of body weight suffering from uncomplicated malaria caused by P. falciparum (with or without other Plasmodium spp. co-infection).

End point type	Secondary

End point timeframe:

Up to Day 29 for each KLU156 treatment episode

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: Protocol amendment increased the minimum body weight requirement for study participation from ≥ 5 kg to ≥ 10 kg and revised the statistical analysis plan to exclude patients < 10 kg from the main analyses.

End point values	KLU156 (Participants with ≥10 kg Body Weight)			
Subject group type	Reporting group			
Number of subjects analysed	362			
Units: percentage of participants				
number (confidence interval 95%)				

1st KLU156 Treatment n=362	86.5 (82.5 to 89.8)			
2nd KLU156 Treatment n=222	87.4 (82.3 to 91.5)			
3rd+KLU156 includes 3rd, 4th, 5th, 6th groups n=59	88.1 (77.1 to 95.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Extension phase: Percentage of Participants With KLU156-related AEs by Malaria Episode

End point title	Extension phase: Percentage of Participants With KLU156-related AEs by Malaria Episode[16]

End point description:

To assess the safety and tolerability over repeated treatment with KLU156 in adults and children ≥ 10 kg of body weight suffering from uncomplicated malaria caused by P. falciparum (with or without other Plasmodium spp. co-infection).

End point type	Secondary

End point timeframe:

Up to approximately 18 months

Notes:

[16] - 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: Protocol amendment increased the minimum body weight requirement for study participation from ≥ 5 kg to ≥ 10 kg and revised the statistical analysis plan to exclude patients < 10 kg from the main analyses.

End point values	KLU156 (Participants with ≥10 kg Body Weight)			
Subject group type	Reporting group			
Number of subjects analysed	393			
Units: percentage of participants				
number (not applicable)				
1st KLU156 Treatment n=393	12.2			
2nd KLU156 Treatment n=230	9.1			
3rd+KLU156 includes 3rd, 4th, 5th, 6th groups n=62	11.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Extension phase: Percentage of Participants With SAEs by Severity and Malaria Episode

End point title	Extension phase: Percentage of Participants With SAEs by Severity and Malaria Episode[17]

End point description:

To assess the safety and tolerability over repeated treatment with KLU156 in adults and children ≥ 10 kg of body weight suffering from uncomplicated malaria caused by P. falciparum (with or without other Plasmodium spp. co-infection).

End point type	Secondary

End point timeframe:

Up to approximately 18 months

Notes:

[17] - 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: Protocol amendment increased the minimum body weight requirement for study participation from ≥ 5 kg to ≥ 10 kg and revised the statistical analysis plan to exclude patients < 10 kg from the main analyses.

End point values	KLU156 (Participants with ≥10 kg Body Weight)			
Subject group type	Reporting group			
Number of subjects analysed	393			
Units: percentage of participants				
1st KLU156 Treatment n=393	0			
2nd KLU156 Treatment n=230	0			
3rd+KLU156 includes 3rd, 4th, 5th, 6th groups n=62	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Extension phase: Gametocyte Carriage Over Time

End point title	Extension phase: Gametocyte Carriage Over Time[18]

End point description:

To assess gametocyte carriage over time by malaria episode in the extension phase

End point type	Secondary

End point timeframe:

Up to Day 29 for each KLU156 treatment episode

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: Protocol amendment increased the minimum body weight requirement for study participation from ≥ 5 kg to ≥ 10 kg and revised the statistical analysis plan to exclude patients < 10 kg from the main analyses.

End point values	KLU156 (Participants with ≥10 kg Body Weight)			
Subject group type	Reporting group			
Number of subjects analysed	362			
Units: percentage of participants				
number (not applicable)				

1st KLU156 Treatment, Present at Day 3 n=362	1.1			
1st KLU156 Treatment, Absent at Day 3 n=362	98.9			
2nd KLU156 Treatment Present at Day 3 n=222	0.5			
2nd KLU156 Treatment Absent at Day 3 n=222	99.1			
3rd+KLU156 Groups 3, 4, 5, 6 Pres. at Day 3 n=59	0			
3rd+KLU156 Groups 3, 4, 5, 6 Abs. at Day 3 n=59	100			
1st KLU156 Treatment, Present at Day 4 n=362	0.8			
1st KLU156 Treatment, Absent at Day 4 n=362	98.9			
2nd KLU156 Treatment Present at Day 4 n=222	0			
2nd KLU156 Treatment Absent at Day 4 n=222	100			
3rd+KLU156 Groups 3, 4, 5, 6 Pres. at Day 4 n=59	0			
3rd+KLU156 Groups 3, 4, 5, 6 Abs. at Day 4 n=59	100			
1st KLU156 Treatment, Present at Day 8 n=362	0			
1st KLU156 Treatment, Absent at Day 8 n=362	99.4			
2nd KLU156 Treatment Present at Day 8 n=222	0			
2nd KLU156 Treatment Absent at Day 8 n=222	100			
3rd+KLU156 Groups 3, 4, 5, 6 Pres. at Day 8 n=59	0			
3rd+KLU156 Groups 3, 4, 5, 6 Abs. at Day 8 n=59	100			
1st KLU156 Treatment, Present at Day 29 n=362	0			
1st KLU156 Treatment, Absent at Day 29 n=362	98.9			
2nd KLU156 Treatment Present at Day 29 n=222	0			
2nd KLU156 Treatment Absent at Day 29 n=222	99.1			
3rd+KLU156 Groups 3, 4, 5, 6 Pres. at Day 29 n=59	0			
3rd+KLU156 Groups 3, 4, 5, 6 Abs. at Day 29 n=59	100			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from the first dose of study treatment until the end of study treatment plus a follow-up period, up to a maximum of approximately 20 months.

Adverse event reporting additional description:

The safety set included all participants who took at least one dose of study drug during the treatment period of the study. Safety data are reported for all treated patients, regardless of body weight.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	28.1

Reporting groups

Reporting group title	Core Phase:@KLU156
Reporting group description:	
Core Phase:@KLU156	
Reporting group title	Core Phase:@Coartem
Reporting group description:	
Core Phase:@Coartem	
Reporting group title	Extension KLU156 (Entering from Core Phase Coartem Arm)
Reporting group description:	
KLU156 once daily (QD) for 3 days under fed conditions (light meal) in extension.	
Reporting group title	Extension KLU156 (Entering from Core Phase KLU156 Arm)
Reporting group description:	
KLU156 once daily (QD) for 3 days under fed conditions (light meal) in extension.	
Reporting group title	Extension@Phase:@Total
Reporting group description:	
Extension@Phase:@Total	
Reporting group title	Core Phase:@Total
Reporting group description:	
Core Phase:@Total	

Serious adverse events	Core Phase:@KLU156	Core Phase:@Coartem	Extension KLU156 (Entering from Core Phase Coartem Arm)
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 854 (1.05%)	10 / 858 (1.17%)	0 / 203 (0.00%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 854 (0.00%)	1 / 858 (0.12%)	0 / 203 (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

Hepatic enzyme increased			
subjects affected / exposed	1 / 854 (0.12%)	0 / 858 (0.00%)	0 / 203 (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
Liver function test increased			
subjects affected / exposed	0 / 854 (0.00%)	1 / 858 (0.12%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Lower limb fracture			
subjects affected / exposed	0 / 854 (0.00%)	1 / 858 (0.12%)	0 / 203 (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
Snake bite			
subjects affected / exposed	0 / 854 (0.00%)	1 / 858 (0.12%)	0 / 203 (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
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	1 / 854 (0.12%)	0 / 858 (0.00%)	0 / 203 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 854 (0.35%)	1 / 858 (0.12%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Intussusception			
subjects affected / exposed	1 / 854 (0.12%)	0 / 858 (0.00%)	0 / 203 (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
Vomiting			

subjects affected / exposed	1 / 854 (0.12%)	0 / 858 (0.00%)	0 / 203 (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
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 854 (0.12%)	0 / 858 (0.00%)	0 / 203 (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
Furuncle			
subjects affected / exposed	1 / 854 (0.12%)	0 / 858 (0.00%)	0 / 203 (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
Hepatitis viral			
subjects affected / exposed	0 / 854 (0.00%)	1 / 858 (0.12%)	0 / 203 (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	0 / 854 (0.00%)	2 / 858 (0.23%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media acute			
subjects affected / exposed	0 / 854 (0.00%)	1 / 858 (0.12%)	0 / 203 (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
Pneumonia			
subjects affected / exposed	1 / 854 (0.12%)	1 / 858 (0.12%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 854 (0.12%)	0 / 858 (0.00%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Extension KLU156 (Entering from Core Phase KLU156 Arm)	Extension@Phase:@ Total	Core Phase:@Total
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 192 (0.00%)	0 / 395 (0.00%)	19 / 1712 (1.11%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 192 (0.00%)	0 / 395 (0.00%)	1 / 1712 (0.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic enzyme increased			
subjects affected / exposed	0 / 192 (0.00%)	0 / 395 (0.00%)	1 / 1712 (0.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test increased			
subjects affected / exposed	0 / 192 (0.00%)	0 / 395 (0.00%)	1 / 1712 (0.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Lower limb fracture			
subjects affected / exposed	0 / 192 (0.00%)	0 / 395 (0.00%)	1 / 1712 (0.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Snake bite			
subjects affected / exposed	0 / 192 (0.00%)	0 / 395 (0.00%)	1 / 1712 (0.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	0 / 192 (0.00%)	0 / 395 (0.00%)	1 / 1712 (0.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	0 / 192 (0.00%)	0 / 395 (0.00%)	4 / 1712 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Intussusception			
subjects affected / exposed	0 / 192 (0.00%)	0 / 395 (0.00%)	1 / 1712 (0.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 192 (0.00%)	0 / 395 (0.00%)	1 / 1712 (0.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 192 (0.00%)	0 / 395 (0.00%)	1 / 1712 (0.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Furuncle			
subjects affected / exposed	0 / 192 (0.00%)	0 / 395 (0.00%)	1 / 1712 (0.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis viral			
subjects affected / exposed	0 / 192 (0.00%)	0 / 395 (0.00%)	1 / 1712 (0.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaria			
subjects affected / exposed	0 / 192 (0.00%)	0 / 395 (0.00%)	2 / 1712 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media acute			
subjects affected / exposed	0 / 192 (0.00%)	0 / 395 (0.00%)	1 / 1712 (0.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	0 / 192 (0.00%)	0 / 395 (0.00%)	2 / 1712 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 192 (0.00%)	0 / 395 (0.00%)	1 / 1712 (0.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Core Phase:@KLU156	Core Phase:@Coartem	Extension KLU156 (Entering from Core Phase Coartem Arm)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	358 / 854 (41.92%)	319 / 858 (37.18%)	52 / 203 (25.62%)
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	22 / 854 (2.58%)	8 / 858 (0.93%)	6 / 203 (2.96%)
occurrences (all)	24	9	6
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	72 / 854 (8.43%)	72 / 858 (8.39%)	10 / 203 (4.93%)
occurrences (all)	74	74	10
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	80 / 854 (9.37%)	108 / 858 (12.59%)	10 / 203 (4.93%)
occurrences (all)	81	117	10
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	170 / 854 (19.91%)	39 / 858 (4.55%)	16 / 203 (7.88%)
occurrences (all)	171	39	17
Infections and infestations			
Malaria			
subjects affected / exposed	136 / 854 (15.93%)	197 / 858 (22.96%)	21 / 203 (10.34%)
occurrences (all)	138	203	21

Non-serious adverse events	Extension KLU156 (Entering from Core	Extension@Phase:@ Total	Core Phase:@Total

	Phase KLU156 Arm)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	55 / 192 (28.65%)	107 / 395 (27.09%)	677 / 1712 (39.54%)
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	10 / 192 (5.21%)	16 / 395 (4.05%)	30 / 1712 (1.75%)
occurrences (all)	11	17	33
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	9 / 192 (4.69%)	19 / 395 (4.81%)	144 / 1712 (8.41%)
occurrences (all)	11	21	148
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	10 / 192 (5.21%)	20 / 395 (5.06%)	188 / 1712 (10.98%)
occurrences (all)	11	21	198
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	21 / 192 (10.94%)	37 / 395 (9.37%)	209 / 1712 (12.21%)
occurrences (all)	22	39	210
Infections and infestations			
Malaria			
subjects affected / exposed	23 / 192 (11.98%)	44 / 395 (11.14%)	333 / 1712 (19.45%)
occurrences (all)	24	45	341

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 May 2025	This amendment increased the minimum body weight requirement for study participation from ≥ 5 kg to ≥ 10 kg and revised the statistical analysis plan to exclude patients < 10 kg from the main analyses due to palatability issues of the formulation (vomiting/spitting out the study medication) observed in children < 10 kg. Additional protocol updates included the addition of gametocyte clearance time by microscopy as a secondary endpoint, clarification of the limit of total allowable blood volume collected during the study, definition of Hy's Law, guidance for potential cases to be reported as serious adverse events, and addition of analyses for patients < 10 kg.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported