Clinical trial results:
A Phase 2 interventional, multicenter, randomized open label study to determine the effective and tolerable dose of KAF156 and Lumefantrine Solid Dispersion Formulation in combination, given once daily for 1, 2 and 3-days to adults and children with uncomplicated Plasmodium falciparum malaria

Summary

EudraCT number	2020-003284-25
Trial protocol	Outside EU/EEA
Global end of trial date	28 June 2021

Results information

Result version number	v1 (current)
This version publication date	11 January 2022
First version publication date	11 January 2022

Trial information

Trial identification

Sponsor protocol code	CKAF156A2202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03167242
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 June 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 June 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to determine the effective doses of KAF156 combined with LUM-SDF given daily over 1, 2, or 3 days for treatment of uncomplicated malaria caused by P. falciparum.

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	02 August 2017
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: 29
Country: Number of subjects enrolled	Côte d'Ivoire: 40
Country: Number of subjects enrolled	Gabon: 42
Country: Number of subjects enrolled	Vietnam: 41
Country: Number of subjects enrolled	Thailand: 7
Country: Number of subjects enrolled	Kenya: 137
Country: Number of subjects enrolled	India: 2
Country: Number of subjects enrolled	Mozambique: 30
Country: Number of subjects enrolled	Uganda: 134
Country: Number of subjects enrolled	Mali: 62
Worldwide total number of subjects	524
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)	0
Children (2-11 years)	179
Adolescents (12-17 years)	197
Adults (18-64 years)	148
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from 13 sites in 10 countries.

Pre-assignment

Screening details:

Before being enrolled in the study, participants underwent a prescreening evaluation to ascertain the Plasmodium falciparum parasitemia count.

Period 1

Period 1 title	Overall Study (overall period)
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	PK Run-in Cohort: KAF 200 mg and LUM 960 mg QD for 1 day

Arm description:

Participants received a single oral dose of KAF156 200 mg and LUM-SDF 960 mg

Arm type	Experimental
Investigational medicinal product name	KAF156
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered in combination with LUM-SDF once daily (QD) for 1 day at 200 mg.

Investigational medicinal product name	Lumefantrine Solid Dispersion Formulation
Investigational medicinal product code	
Other name	LUM-SDF / LUM
Pharmaceutical forms	Oral solution in sachet
Routes of administration	Oral use

Dosage and administration details:

Administered in combination with KAF156 once daily (QD) for 1 day at 960 mg.

Arm title	Part A - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day

Arm description:

Participants received a single oral dose of KAF156 400 mg and LUM-SDF 960 mg

Arm type	Experimental
Investigational medicinal product name	Lumefantrine Solid Dispersion Formulation
Investigational medicinal product code	
Other name	LUM-SDF / LUM
Pharmaceutical forms	Oral solution in sachet
Routes of administration	Oral use

Dosage and administration details:

Administered in combination with KAF156 oncedaily (QD) for 1 day at 960 mg.

Investigational medicinal product name	KAF156
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered in combination with LUM-SDF once daily (QD) for 1 day at 400 mg.

Arm title	Part A - Cohort 2: KAF 800 mg and LUM 960 mg QD for 1 day

Arm description:

Participants received a single oral dose of KAF156 800 mg and LUM-SDF 960 mg

Arm type	Experimental
Investigational medicinal product name	Lumefantrine Solid Dispersion Formulation
Investigational medicinal product code	
Other name	LUM-SDF / LUM
Pharmaceutical forms	Oral solution in sachet
Routes of administration	Oral use

Dosage and administration details:

Administered in combination with KAF156 oncedaily (QD) for 1 day at 960 mg.

Investigational medicinal product name	KAF156
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered in combination with LUM-SDF once daily (QD) for 1 day at 800 mg.

Arm title	Part A - Cohort 3: KAF 400 mg and LUM 960 mg QD for 2 days

Arm description:

Participants received KAF156 400 mg and LUM-SDF 960 mg once daily via oral administration for 2 days

Arm type	Experimental
Investigational medicinal product name	Lumefantrine Solid Dispersion Formulation
Investigational medicinal product code	
Other name	LUM-SDF / LUM
Pharmaceutical forms	Oral solution in sachet
Routes of administration	Oral use

Dosage and administration details:

Administered in combination with KAF156 oncedaily (QD) for 2 days at 960 mg.

Investigational medicinal product name	KAF156
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered in combination with LUM-SDF once daily (QD) for 2 days at 400 mg.

Arm title	Part A - Cohort 4: KAF 200 mg and LUM 480 mg QD for 3 days

Arm description:

Participants received KAF156 200 mg and LUM-SDF 480 mg once daily via oral administration for 3 days

Arm type	Experimental
Investigational medicinal product name	KAF156
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details: Administered in combination with LUM-SDF once daily (QD) for 3 days at 200 mg.	
Investigational medicinal product name	Lumefantrine Solid Dispersion Formulation
Investigational medicinal product code	
Other name	LUM-SDF / LUM
Pharmaceutical forms	Oral solution in sachet
Routes of administration	Oral use
Dosage and administration details: Administered in combination with KAF156 oncedaily (QD) for 3 days at 480 mg.	
Arm title	Part A - Cohort 5: KAF 400 mg and LUM 480 mg QD for 3 days
Arm description: Participants received KAF156 400 mg and LUM-SDF 480 mg once daily via oral administration for 3 days	
Arm type	Experimental
Investigational medicinal product name	Lumefantrine Solid Dispersion Formulation
Investigational medicinal product code	
Other name	LUM-SDF / LUM
Pharmaceutical forms	Oral solution in sachet
Routes of administration	Oral use
Dosage and administration details: Administered in combination with KAF156 oncedaily (QD) for 3 days at 480 mg.	
Investigational medicinal product name	KAF156
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Administered in combination with LUM-SDF once daily (QD) for 3 days at 400 mg.	
Arm title	Part A - Cohort 6: KAF 400 mg and LUM 960 mg QD for 3 days
Arm description: Participants received KAF156 400 mg and LUM-SDF 960 mg once daily via oral administration for 3 days	
Arm type	Experimental
Investigational medicinal product name	KAF156
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Administered in combination with LUM-SDF once daily (QD) for 3 days at 400 mg.	
Investigational medicinal product name	Lumefantrine Solid Dispersion Formulation
Investigational medicinal product code	
Other name	LUM-SDF / LUM
Pharmaceutical forms	Oral solution in sachet
Routes of administration	Oral use
Dosage and administration details: Administered in combination with KAF156 oncedaily (QD) for 3 days at 960 mg.	
Arm title	Part A - Cohort 7: Coartem
Arm description: Participants received Coartem twice daily via oral administration for 3 days	
Arm type	Active comparator

Investigational medicinal product name	Coartem
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Administered twice daily for 3 days as active comparator

Arm title	Part B - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day

Arm description:

Participants received a single oral dose of KAF156 400 mg and LUM-SDF 960 mg

Arm type	Experimental
Investigational medicinal product name	Lumefantrine Solid Dispersion Formulation
Investigational medicinal product code	
Other name	LUM-SDF / LUM
Pharmaceutical forms	Oral solution in sachet
Routes of administration	Oral use

Dosage and administration details:

Administered in combination with KAF156 oncedaily (QD) for 1 day at 960 mg.

Investigational medicinal product name	KAF156
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered in combination with LUM-SDF once daily (QD) for 1 day at 400 mg.

Arm title	Part B - Cohort 2: KAF 400 mg and LUM 960 mg QD for 2 days

Arm description:

Participants received KAF156 400 mg and LUM-SDF 960 mg once daily via oral administration for 2 days

Arm type	Experimental
Investigational medicinal product name	Lumefantrine Solid Dispersion Formulation
Investigational medicinal product code	
Other name	LUM-SDF / LUM
Pharmaceutical forms	Oral solution in sachet
Routes of administration	Oral use

Dosage and administration details:

Administered in combination with KAF156 oncedaily (QD) for 2 days at 960 mg.

Investigational medicinal product name	KAF156
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered in combination with LUM-SDF once daily (QD) for 2 days at 400 mg.

Arm title	Part B - Cohort 3: KAF 400 mg and LUM 960 mg QD for 3 days

Arm description:

Participants received KAF156 400 mg and LUM-SDF 960 mg once daily via oral administration for 3 days

Arm type	Experimental

Investigational medicinal product name	Lumefantrine Solid Dispersion Formulation
Investigational medicinal product code	
Other name	LUM-SDF / LUM
Pharmaceutical forms	Oral solution in sachet
Routes of administration	Oral use

Dosage and administration details:

Administered in combination with KAF156 oncedaily (QD) for 3 days at 960 mg.

Investigational medicinal product name	KAF156
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered in combination with LUM-SDF once daily (QD) for 3 days at 400 mg.

Arm title	Part B - Cohort 4: Coartem

Arm description:

Participants received Coartem twice daily via oral administration for 3 days

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

Dosage and administration details:

Administered twice daily for 3 days as active comparator

Notes:

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

Justification: It is consistent

Number of subjects in period 1	PK Run-in Cohort: KAF 200 mg and LUM 960 mg QD for 1 day	Part A - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day	Part A - Cohort 2: KAF 800 mg and LUM 960 mg QD for 1 day
Started	12	51	51
Full Analysis Set (FAS)	12	51	51
Pharmacokinetics (PK) Analysis Set	12	47 [2]	51
Per-Protocol Set (PPS)	12	50	48
Completed	12	50	48
Not completed	0	1	3
Patient/Guardian Decision	-	1	2
Lost to follow-up	-	-	1
Missing	-	-	-

Number of subjects in period 1	Part A - Cohort 3: KAF 400 mg and LUM 960 mg QD for 2 days	Part A - Cohort 4: KAF 200 mg and LUM 480 mg QD for 3 days	Part A - Cohort 5: KAF 400 mg and LUM 480 mg QD for 3 days
Started	51	54	51
Full Analysis Set (FAS)	51	54	51
Pharmacokinetics (PK) Analysis Set	46 [3]	48 [4]	46 [5]

Per-Protocol Set (PPS)	48 [6]	47 [7]	44 [8]
Completed	50	53	49
Not completed	1	1	2
Patient/Guardian Decision	1	1	1
Lost to follow-up	-	-	1
Missing	-	-	-

Number of subjects in period 1	Part A - Cohort 6: KAF 400 mg and LUM 960 mg QD for 3 days	Part A - Cohort 7: Coartem	Part B - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day
Started	52	27	53
Full Analysis Set (FAS)	52	27	52
Pharmacokinetics (PK) Analysis Set	45 [9]	24 [10]	48 [11]
Per-Protocol Set (PPS)	43 [12]	25 [13]	48 [14]
Completed	50	26	52
Not completed	2	1	1
Patient/Guardian Decision	-	-	-
Lost to follow-up	2	1	-
Missing	-	-	1

Number of subjects in period 1	Part B - Cohort 2: KAF 400 mg and LUM 960 mg QD for 2 days	Part B - Cohort 3: KAF 400 mg and LUM 960 mg QD for 3 days	Part B - Cohort 4: Coartem
Started	53	45	24
Full Analysis Set (FAS)	53	45	24
Pharmacokinetics (PK) Analysis Set	46 [15]	41 [16]	24
Per-Protocol Set (PPS)	46 [17]	40 [18]	22 [19]
Completed	53	43	23
Not completed	0	2	1
Patient/Guardian Decision	-	1	-
Lost to follow-up	-	1	1
Missing	-	-	-

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: Numbers are consistent

[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: Numbers are consistent

[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: Numbers are consistent

[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: Numbers are consistent

[6] - 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: Numbers are consistent

[7] - 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: Numbers are consistent

[8] - 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: Numbers are consistent

[9] - 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: Numbers are consistent

[10] - 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: Numbers are consistent

[11] - 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: Numbers are consistent

[12] - 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: Numbers are consistent

[13] - 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: Numbers are consistent

[14] - 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: Numbers are consistent

[15] - 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: Numbers are consistent

[16] - 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: Numbers are consistent

[17] - 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: Numbers are consistent

[18] - 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: Numbers are consistent

[19] - 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: Numbers are consistent

Baseline characteristics

Reporting groups	
Reporting group title	PK Run-in Cohort: KAF 200 mg and LUM 960 mg QD for 1 day
Reporting group description:	
Participants received a single oral dose of KAF156 200 mg and LUM-SDF 960 mg	
Reporting group title	Part A - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day
Reporting group description:	
Participants received a single oral dose of KAF156 400 mg and LUM-SDF 960 mg	
Reporting group title	Part A - Cohort 2: KAF 800 mg and LUM 960 mg QD for 1 day
Reporting group description:	
Participants received a single oral dose of KAF156 800 mg and LUM-SDF 960 mg	
Reporting group title	Part A - Cohort 3: KAF 400 mg and LUM 960 mg QD for 2 days
Reporting group description:	
Participants received KAF156 400 mg and LUM-SDF 960 mg once daily via oral administration for 2 days	
Reporting group title	Part A - Cohort 4: KAF 200 mg and LUM 480 mg QD for 3 days
Reporting group description:	
Participants received KAF156 200 mg and LUM-SDF 480 mg once daily via oral administration for 3 days	
Reporting group title	Part A - Cohort 5: KAF 400 mg and LUM 480 mg QD for 3 days
Reporting group description:	
Participants received KAF156 400 mg and LUM-SDF 480 mg once daily via oral administration for 3 days	
Reporting group title	Part A - Cohort 6: KAF 400 mg and LUM 960 mg QD for 3 days
Reporting group description:	
Participants received KAF156 400 mg and LUM-SDF 960 mg once daily via oral administration for 3 days	
Reporting group title	Part A - Cohort 7: Coartem
Reporting group description:	
Participants received Coartem twice daily via oral administration for 3 days	
Reporting group title	Part B - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day
Reporting group description:	
Participants received a single oral dose of KAF156 400 mg and LUM-SDF 960 mg	
Reporting group title	Part B - Cohort 2: KAF 400 mg and LUM 960 mg QD for 2 days
Reporting group description:	
Participants received KAF156 400 mg and LUM-SDF 960 mg once daily via oral administration for 2 days	
Reporting group title	Part B - Cohort 3: KAF 400 mg and LUM 960 mg QD for 3 days
Reporting group description:	
Participants received KAF156 400 mg and LUM-SDF 960 mg once daily via oral administration for 3 days	
Reporting group title	Part B - Cohort 4: Coartem
Reporting group description:	
Participants received Coartem twice daily via oral administration for 3 days	

Reporting group values	PK Run-in Cohort: KAF 200 mg and LUM 960 mg QD for 1 day	Part A - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day	Part A - Cohort 2: KAF 800 mg and LUM 960 mg QD for 1 day
Number of subjects	12	51	51
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0

Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	2	1
Adolescents (12-17 years)	10	25	25
Adults (18-64 years)	2	24	25
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	17.8	22.3	21.3
standard deviation	± 10.25	± 13.53	± 10.69
Sex: Female, Male			
Units: Participants			
Female	6	26	24
Male	6	25	27
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	7	7
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	12	44	44
White	0	0	0
More than one race	0	0	0
Unknown or Not Reported	0	0	0

Reporting group values	Part A - Cohort 3: KAF 400 mg and LUM 960 mg QD for 2 days	Part A - Cohort 4: KAF 200 mg and LUM 480 mg QD for 3 days	Part A - Cohort 5: KAF 400 mg and LUM 480 mg QD for 3 days
Number of subjects	51	54	51
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	29	31	33
Adults (18-64 years)	22	23	18
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	21.1	23.3	20.3
standard deviation	± 11.09	± 14.68	± 11.90
Sex: Female, Male			
Units: Participants			
Female	21	26	25
Male	30	28	26

Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	7	9	7
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	43	45	44
White	1	0	0
More than one race	0	0	0
Unknown or Not Reported	0	0	0

Reporting group values	Part A - Cohort 6: KAF 400 mg and LUM 960 mg QD for 3 days	Part A - Cohort 7: Coartem	Part B - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day
Number of subjects	52	27	53
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	1	53
Adolescents (12-17 years)	31	13	0
Adults (18-64 years)	21	13	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	20.0	20.9	6.6
standard deviation	± 9.49	± 12.28	± 2.86
Sex: Female, Male Units: Participants			
Female	20	13	31
Male	32	14	22
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	7	4	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	45	23	52
White	0	0	0
More than one race	0	0	0
Unknown or Not Reported	0	0	0

Reporting group values	Part B - Cohort 2: KAF 400 mg and LUM 960 mg QD for 2 days	Part B - Cohort 3: KAF 400 mg and LUM 960 mg QD for 3 days	Part B - Cohort 4: Coartem
Number of subjects	53	45	24

Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	53	45	24
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	6.2	6.9	5.9
standard deviation	± 2.90	± 2.60	± 2.21
Sex: Female, Male Units: Participants			
Female	29	20	15
Male	24	25	9
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	52	45	24
White	0	0	0
More than one race	0	0	0
Unknown or Not Reported	0	0	0

Reporting group values	Total		
Number of subjects	524		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	179		
Adolescents (12-17 years)	197		
Adults (18-64 years)	148		
From 65-84 years	0		
85 years and over	0		
Age Continuous Units: Years			
arithmetic mean			
standard deviation	-		

Sex: Female, Male Units: Participants			
Female	256		
Male	268		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	50		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	473		
White	1		
More than one race	0		
Unknown or Not Reported	0		

End points

End points reporting groups

Reporting group title	PK Run-in Cohort: KAF 200 mg and LUM 960 mg QD for 1 day
Reporting group description:	
Participants received a single oral dose of KAF156 200 mg and LUM-SDF 960 mg	
Reporting group title	Part A - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day
Reporting group description:	
Participants received a single oral dose of KAF156 400 mg and LUM-SDF 960 mg	
Reporting group title	Part A - Cohort 2: KAF 800 mg and LUM 960 mg QD for 1 day
Reporting group description:	
Participants received a single oral dose of KAF156 800 mg and LUM-SDF 960 mg	
Reporting group title	Part A - Cohort 3: KAF 400 mg and LUM 960 mg QD for 2 days
Reporting group description:	
Participants received KAF156 400 mg and LUM-SDF 960 mg once daily via oral administration for 2 days	
Reporting group title	Part A - Cohort 4: KAF 200 mg and LUM 480 mg QD for 3 days
Reporting group description:	
Participants received KAF156 200 mg and LUM-SDF 480 mg once daily via oral administration for 3 days	
Reporting group title	Part A - Cohort 5: KAF 400 mg and LUM 480 mg QD for 3 days
Reporting group description:	
Participants received KAF156 400 mg and LUM-SDF 480 mg once daily via oral administration for 3 days	
Reporting group title	Part A - Cohort 6: KAF 400 mg and LUM 960 mg QD for 3 days
Reporting group description:	
Participants received KAF156 400 mg and LUM-SDF 960 mg once daily via oral administration for 3 days	
Reporting group title	Part A - Cohort 7: Coartem
Reporting group description:	
Participants received Coartem twice daily via oral administration for 3 days	
Reporting group title	Part B - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day
Reporting group description:	
Participants received a single oral dose of KAF156 400 mg and LUM-SDF 960 mg	
Reporting group title	Part B - Cohort 2: KAF 400 mg and LUM 960 mg QD for 2 days
Reporting group description:	
Participants received KAF156 400 mg and LUM-SDF 960 mg once daily via oral administration for 2 days	
Reporting group title	Part B - Cohort 3: KAF 400 mg and LUM 960 mg QD for 3 days
Reporting group description:	
Participants received KAF156 400 mg and LUM-SDF 960 mg once daily via oral administration for 3 days	
Reporting group title	Part B - Cohort 4: Coartem
Reporting group description:	
Participants received Coartem twice daily via oral administration for 3 days	

Primary: Part A and Part B: Number of participants with Polymerase Chain Reaction (PCR)-corrected adequate clinical and parasitological response (ACPR) at Day 29

End point title	Part A and Part B: Number of participants with Polymerase Chain Reaction (PCR)-corrected adequate clinical and parasitological response (ACPR) at Day 29[1][2]

End point description:

PCR-corrected ACPR defined as the absence of parasitaemia was evaluated at Day 29 (i.e., 28 days post first dose) based on the short half-life of the study drugs. Microscopic species identification was confirmed and determined by PCR genotyping methods to establish malaria recrudescence/reinfection.

A participant was considered as PCR-corrected ACPR at Day 29 if the participant did not meet any of the criteria of early treatment failure, late clinical failure or late parasitological failure and was absence of parasitaemia on Day 29 irrespective of axillary temperature unless the presence of parasitaemia after 7 days was due to reinfection based on PCR. A presence of parasitaemia after 7 days of treatment initiation was considered as a reinfection only if the parasitaemia was clear before Day 8 and none of the parasite strain(s) detected on Day 8 or later matched with the parasite strain at baseline based on PCR.

No statistical analysis was planned for this primary outcome.

End point type	Primary

End point timeframe:

28 days post first dose

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this endpoint

[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: No statistical analysis was planned for this endpoint

End point values	Part A - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day	Part A - Cohort 2: KAF 800 mg and LUM 960 mg QD for 1 day	Part A - Cohort 3: KAF 400 mg and LUM 960 mg QD for 2 days	Part A - Cohort 4: KAF 200 mg and LUM 480 mg QD for 3 days
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	48	48	47
Units: Participants	46	45	47	47

End point values	Part A - Cohort 5: KAF 400 mg and LUM 480 mg QD for 3 days	Part A - Cohort 6: KAF 400 mg and LUM 960 mg QD for 3 days	Part A - Cohort 7: Coartem	Part B - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	43	25	48
Units: Participants	44	42	25	37

End point values	Part B - Cohort 2: KAF 400 mg and LUM 960 mg QD for 2 days	Part B - Cohort 3: KAF 400 mg and LUM 960 mg QD for 3 days	Part B - Cohort 4: Coartem	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	46	40	22	
Units: Participants	42	38	21	

Statistical analyses

No statistical analyses for this end point

Primary: PK Run-in: Area under the blood concentration-time curve over the last 24 hours after treatment dose (AUC0-24h) of KAF156

End point title	PK Run-in: Area under the blood concentration-time curve over the last 24 hours after treatment dose (AUC0-24h) of KAF156[3][4]

End point description:

Pharmacokinetic (PK) parameters were calculated based on KAF156 blood concentrations determined by a validated liquid chromatography and tandem mass spectrometry (LC-MS/MS) method. AUC0-24h was determined using non-compartmental methods.

No statistical analysis was planned for this primary outcome.

End point type	Primary

End point timeframe:

0, 1, 3, 6, 12, 18 and 24 hours post-dose

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this endpoint

[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: No statistical analysis was planned for this endpoint

End point values	PK Run-in Cohort: KAF 200 mg and LUM 960 mg QD for 1 day			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: hours*µg/mL				
geometric mean (geometric coefficient of variation)	5.35 (± 34.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part A and Part B: Number of participants with Polymerase Chain Reaction (PCR)-uncorrected adequate clinical and parasitological response (ACPR)

End point title	Part A and Part B: Number of participants with Polymerase Chain Reaction (PCR)-uncorrected adequate clinical and parasitological response (ACPR)[5]

End point description:

PCR-uncorrected ACPR defined as the absence of parasitaemia was evaluated at days 15, 29 and 43 (i.e., 14, 28 and 42 days post first dose).

A participant was considered as PCR-uncorrected ACPR at Days 15, 29 or 43 if the participant did not meet any of the criteria of early treatment failure, late clinical failure or late parasitological failure and was absence of parasitaemia on Days 15, 29 or 43 irrespective of axillary temperature.

End point type	Secondary

End point timeframe:

14, 28 and 42 days post first dose

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: No statistical analysis was planned for this endpoint

End point values	Part A - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day	Part A - Cohort 2: KAF 800 mg and LUM 960 mg QD for 1 day	Part A - Cohort 3: KAF 400 mg and LUM 960 mg QD for 2 days	Part A - Cohort 4: KAF 200 mg and LUM 480 mg QD for 3 days
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	51	51	54
Units: Participants				
Day 14 post-dose	49	47	51	53
Day 28 post-dose	46	40	48	51
Day 42 post-dose	42	36	45	45

End point values	Part A - Cohort 5: KAF 400 mg and LUM 480 mg QD for 3 days	Part A - Cohort 6: KAF 400 mg and LUM 960 mg QD for 3 days	Part A - Cohort 7: Coartem	Part B - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	52	27	52
Units: Participants				
Day 14 post-dose	50	51	27	51
Day 28 post-dose	45	47	26	34
Day 42 post-dose	41	45	19	29

End point values	Part B - Cohort 2: KAF 400 mg and LUM 960 mg QD for 2 days	Part B - Cohort 3: KAF 400 mg and LUM 960 mg QD for 3 days	Part B - Cohort 4: Coartem	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	45	24	
Units: Participants				
Day 14 post-dose	52	43	24	
Day 28 post-dose	41	36	15	
Day 42 post-dose	33	31	11	

Statistical analyses

No statistical analyses for this end point

Secondary: Part A and Part B: Number of participants with Polymerase Chain Reaction (PCR)-corrected adequate clinical and parasitological response (ACPR)

End point title	Part A and Part B: Number of participants with Polymerase Chain Reaction (PCR)-corrected adequate clinical and parasitological response (ACPR)[6]

End point description:

PCR-corrected ACPR defined as the absence of parasitaemia was evaluated at days 15 and 43 (i.e., 14 and 42 days post first dose). Microscopic species identification was confirmed and determined by PCR genotyping methods to establish malaria recrudescence/reinfection.

A participant was considered as PCR-corrected ACPR at Day 15 or Day 43 if the participant did not meet any of the criteria of early treatment failure, late clinical failure or late parasitological failure and was absence of parasitaemia on Day 15 or Day 43 irrespective of axillary temperature unless the presence of parasitaemia after 7 days was due to reinfection based on PCR. A presence of parasitaemia after 7 days of treatment initiation was considered as a reinfection only if the parasitaemia was clear before Day 8 and none of the parasite strain(s) detected on Day 8 or later matched with the parasite strain at baseline based on PCR.

End point type	Secondary

End point timeframe:

14 and 42 days post first dose

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: No statistical analysis was planned for this endpoint

End point values	Part A - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day	Part A - Cohort 2: KAF 800 mg and LUM 960 mg QD for 1 day	Part A - Cohort 3: KAF 400 mg and LUM 960 mg QD for 2 days	Part A - Cohort 4: KAF 200 mg and LUM 480 mg QD for 3 days
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	48	48	47
Units: Participants				
Day 14 post-dose	48	46	48	47
Day 42 post-dose	45	44	46	46

End point values	Part A - Cohort 5: KAF 400 mg and LUM 480 mg QD for 3 days	Part A - Cohort 6: KAF 400 mg and LUM 960 mg QD for 3 days	Part A - Cohort 7: Coartem	Part B - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	43	25	48
Units: Participants				
Day 14 post-dose	44	43	25	47
Day 42 post-dose	43	41	24	36

End point values	Part B - Cohort 2: KAF 400 mg and LUM 960 mg QD for 2 days	Part B - Cohort 3: KAF 400 mg and LUM 960 mg QD for 3 days	Part B - Cohort 4: Coartem	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	46	40	22	
Units: Participants				
Day 14 post-dose	45	40	22	
Day 42 post-dose	37	37	20	

Statistical analyses

No statistical analyses for this end point

Secondary: Part A and Part B: Number of participants with recrudescence events

End point title	Part A and Part B: Number of participants with recrudescence events[7]

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 must be confirmed by PCR analysis.

End point type	Secondary

End point timeframe:

42 days post first dose

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: No statistical analysis was planned for this endpoint

End point values	Part A - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day	Part A - Cohort 2: KAF 800 mg and LUM 960 mg QD for 1 day	Part A - Cohort 3: KAF 400 mg and LUM 960 mg QD for 2 days	Part A - Cohort 4: KAF 200 mg and LUM 480 mg QD for 3 days
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	51	51	54
Units: Participants	4	3	1	1

End point values	Part A - Cohort 5: KAF 400 mg and LUM 480 mg QD for 3 days	Part A - Cohort 6: KAF 400 mg and LUM 960 mg QD for 3 days	Part A - Cohort 7: Coartem	Part B - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	52	27	52
Units: Participants	0	2	0	12

End point values	Part B - Cohort 2: KAF 400 mg and LUM 960 mg QD for 2 days	Part B - Cohort 3: KAF 400 mg and LUM 960 mg QD for 3 days	Part B - Cohort 4: Coartem	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	45	24	
Units: Participants	7	3	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Part A and Part B: Number of participants with reinfection events

End point title	Part A and Part B: Number of participants with reinfection events[8]

End point description:

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

End point type	Secondary

End point timeframe:

42 days post first dose

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: No statistical analysis was planned for this endpoint

End point values	Part A - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day	Part A - Cohort 2: KAF 800 mg and LUM 960 mg QD for 1 day	Part A - Cohort 3: KAF 400 mg and LUM 960 mg QD for 2 days	Part A - Cohort 4: KAF 200 mg and LUM 480 mg QD for 3 days
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	51	51	54
Units: Participants	3	7	4	7

End point values	Part A - Cohort 5: KAF 400 mg and LUM 480 mg QD for 3 days	Part A - Cohort 6: KAF 400 mg and LUM 960 mg QD for 3 days	Part A - Cohort 7: Coartem	Part B - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	52	27	52
Units: Participants	8	2	8	11

End point values	Part B - Cohort 2: KAF 400 mg and LUM 960 mg QD for 2 days	Part B - Cohort 3: KAF 400 mg and LUM 960 mg QD for 3 days	Part B - Cohort 4: Coartem	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	45	24	
Units: Participants	10	9	10	

Statistical analyses

No statistical analyses for this end point

Secondary: Part A and Part B: Fever clearance time (FCT)

End point title	Part A and Part B: Fever clearance time (FCT)[9]

End point description:

Fever Clearance Time (FCT) is defined as the 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. In case a participant received rescue medication before (fever) clearance, the time to event was censored at the first use of rescue medication.

End point type	Secondary

End point timeframe:

42 days post first dose

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: No statistical analysis was planned for this endpoint

End point values	Part A - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day	Part A - Cohort 2: KAF 800 mg and LUM 960 mg QD for 1 day	Part A - Cohort 3: KAF 400 mg and LUM 960 mg QD for 2 days	Part A - Cohort 4: KAF 200 mg and LUM 480 mg QD for 3 days
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	7	8	15
Units: Hours				
arithmetic mean (standard error)	18.7 (± 3.09)	22.5 (± 6.09)	20.3 (± 4.92)	16.6 (± 3.48)

End point values	Part A - Cohort 5: KAF 400 mg and LUM 480 mg QD for 3 days	Part A - Cohort 6: KAF 400 mg and LUM 960 mg QD for 3 days	Part A - Cohort 7: Coartem	Part B - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	9	5	9
Units: Hours				
arithmetic mean (standard error)	17.5 (± 2.65)	19.2 (± 2.92)	26.3 (± 7.67)	23.5 (± 10.26)

End point values	Part B - Cohort 2: KAF 400 mg and LUM 960 mg QD for 2 days	Part B - Cohort 3: KAF 400 mg and LUM 960 mg QD for 3 days	Part B - Cohort 4: Coartem	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	10	5	
Units: Hours				
arithmetic mean (standard error)	17.3 (± 7.4)	13.8 (± 3.68)	22.9 (± 12.78)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK Run-in, Part A and Part B: Parasite Clearance time (PCT)

End point title	PK Run-in, Part A and Part B: Parasite Clearance time (PCT)

End point description:

Parasite Clearance Time (PCT) is defined as the time from the first dose until the first total and continued disappearance of asexual parasite forms which remained at least a further 48 hours. In case a participant received rescue medication before (parasite) clearance, the time to event was censored at the first use of rescue medication.

End point type	Secondary

End point timeframe:

42 days post first

End point values	PK Run-in Cohort: KAF 200 mg and LUM 960 mg QD for 1 day	Part A - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day	Part A - Cohort 2: KAF 800 mg and LUM 960 mg QD for 1 day	Part A - Cohort 3: KAF 400 mg and LUM 960 mg QD for 2 days
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	51	51	51
Units: Hours				
arithmetic mean (standard error)	49.9 (± 4.35)	48.4 (± 3.5)	46.6 (± 3.93)	39.9 (± 2.46)

End point values	Part A - Cohort 4: KAF 200 mg and LUM 480 mg QD for 3 days	Part A - Cohort 5: KAF 400 mg and LUM 480 mg QD for 3 days	Part A - Cohort 6: KAF 400 mg and LUM 960 mg QD for 3 days	Part A - Cohort 7: Coartem
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	51	52	27
Units: Hours				
arithmetic mean (standard error)	51.4 (± 3.97)	49.7 (± 3.72)	48.1 (± 4.24)	50.0 (± 12.82)

End point values	Part B - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day	Part B - Cohort 2: KAF 400 mg and LUM 960 mg QD for 2 days	Part B - Cohort 3: KAF 400 mg and LUM 960 mg QD for 3 days	Part B - Cohort 4: Coartem
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	53	45	24
Units: Hours				
arithmetic mean (standard error)	42.6 (± 2.62)	47.0 (± 2.79)	41.9 (± 2.58)	35.6 (± 2.82)

Statistical analyses

No statistical analyses for this end point

Secondary: PK Run-in, Part A and Part B: Number of participants with parasitaemia

End point title	PK Run-in, Part A and Part B: Number of participants with parasitaemia

End point description:

Parasitaemia is the quantitative content of parasites in the blood determined by microscopy examination validated methods. Only Plasmodium Falciparum asexual form is used for parasitaemia assessments.

12 h post last dose n= (12, 50, 50, 49, 52, 50, 51, 27, 51, 53, 45, 24)
24 h post last dose n= (12, 49, 51, 51, 54, 50, 50, 27, 51, 52, 44, 24)
48 h post last dose n= (12, 50, 51, 51, 53, 49, 52, 26, 51, 52, 44, 24)

End point type	Secondary

End point timeframe:

14, 28 and 42 days post last dose

End point values	PK Run-in Cohort: KAF 200 mg and LUM 960 mg QD for 1 day	Part A - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day	Part A - Cohort 2: KAF 800 mg and LUM 960 mg QD for 1 day	Part A - Cohort 3: KAF 400 mg and LUM 960 mg QD for 2 days
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	51	51	51
Units: Participants				
12 h post last dose	12	46	46	44
24 h post last dose	11	39	41	38
48 h post last dose	3	13	9	8

End point values	Part A - Cohort 4: KAF 200 mg and LUM 480 mg QD for 3 days	Part A - Cohort 5: KAF 400 mg and LUM 480 mg QD for 3 days	Part A - Cohort 6: KAF 400 mg and LUM 960 mg QD for 3 days	Part A - Cohort 7: Coartem
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	51	52	27
Units: Participants				
12 h post last dose	52	49	49	22
24 h post last dose	46	42	34	14
48 h post last dose	12	10	11	4

End point values	Part B - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day	Part B - Cohort 2: KAF 400 mg and LUM 960 mg QD for 2 days	Part B - Cohort 3: KAF 400 mg and LUM 960 mg QD for 3 days	Part B - Cohort 4: Coartem
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	53	45	24
Units: Participants				
12 h post last dose	48	48	42	22
24 h post last dose	41	42	36	17

48 h post last dose	4	10	5	1

Statistical analyses

No statistical analyses for this end point

Secondary: Part A and Part B: Area under the blood concentration-time curve over the last 24 hours after last treatment dose (AUC0-24h) of KAF156

End point title	Part A and Part B: Area under the blood concentration-time curve over the last 24 hours after last treatment dose (AUC0-24h) of KAF156[10]

End point description:

Pharmacokinetic (PK) parameters were calculated based on KAF156 blood concentrations determined by a validated liquid chromatography and tandem mass spectrometry (LC-MS/MS) method. AUC0-24h was determined using non-compartmental methods.

End point type	Secondary

End point timeframe:

3, 6, 18 and 24 hours post last dose

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: No statistical analysis was planned for this endpoint

End point values	Part A - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day	Part A - Cohort 2: KAF 800 mg and LUM 960 mg QD for 1 day	Part A - Cohort 3: KAF 400 mg and LUM 960 mg QD for 2 days	Part A - Cohort 4: KAF 200 mg and LUM 480 mg QD for 3 days
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	44	41	43
Units: hours*µg/mL				
geometric mean (geometric coefficient of variation)	9.84 (± 41.5)	21.7 (± 41.7)	9.95 (± 131.9)	5.91 (± 29.2)

End point values	Part A - Cohort 5: KAF 400 mg and LUM 480 mg QD for 3 days	Part A - Cohort 6: KAF 400 mg and LUM 960 mg QD for 3 days	Part B - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day	Part B - Cohort 2: KAF 400 mg and LUM 960 mg QD for 2 days
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	41	48	0[11]
Units: hours*µg/mL				
geometric mean (geometric coefficient of variation)	11 (± 79.3)	10.9 (± 57.4)	11 (± 47.7)	()

Notes:

[11] - Not performed as per the study design for Part B dosing regimens of 2 and 3 days.

End point values	Part B - Cohort 3: KAF 400 mg and LUM 960 mg QD for 3 days			
Subject group type	Reporting group			
Number of subjects analysed	0[12]			
Units: hours*µg/mL				
geometric mean (geometric coefficient of variation)	()			

Notes:

[12] - Not performed as per the study design for Part B dosing regimens of 2 and 3 days.

Statistical analyses

No statistical analyses for this end point

Secondary: Part A and Part B: Maximum Peak Observed Concentration (Cmax) of KAF156

End point title	Part A and Part B: Maximum Peak Observed Concentration (Cmax) of KAF156[13]

End point description:

Pharmacokinetic (PK) parameters were calculated based on KAF156 blood concentrations determined by a validated liquid chromatography and tandem mass spectrometry (LC-MS/MS) method. Cmax was determined using non-compartmental methods.

End point type	Secondary

End point timeframe:

3, 6, 18, 24, 27, 30, 48, 51, 54, 68, 72 and 168 hours post last dose

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: No statistical analysis was planned for this endpoint

End point values	Part A - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day	Part A - Cohort 2: KAF 800 mg and LUM 960 mg QD for 1 day	Part A - Cohort 3: KAF 400 mg and LUM 960 mg QD for 2 days	Part A - Cohort 4: KAF 200 mg and LUM 480 mg QD for 3 days
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	44	40	43
Units: ng/mL				
geometric mean (geometric coefficient of variation)	653 (± 43.9)	1470 (± 46.5)	1060 (± 83.9)	665 (± 30.3)

End point values	Part A - Cohort 5: KAF 400 mg and LUM 480 mg QD for 3 days	Part A - Cohort 6: KAF 400 mg and LUM 960 mg QD for 3 days	Part B - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day	Part B - Cohort 2: KAF 400 mg and LUM 960 mg QD for 2 days
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	41	48	46
Units: ng/mL				
geometric mean (geometric coefficient of variation)	1470 (± 30.9)	1320 (± 32.7)	714 (± 49.4)	1060 (± 48.4)

End point values	Part B - Cohort 3: KAF 400 mg and LUM 960 mg QD for 3 days			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	1380 (± 29.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Run-in and Part A: Elimination half-life (T½) of KAF156

End point title	PK Run-in and Part A: Elimination half-life (T½) of KAF156[14]

End point description:

Pharmacokinetic (PK) parameters were calculated based on KAF156 blood concentrations determined by a validated liquid chromatography and tandem mass spectrometry (LC-MS/MS) method. T½ was determined using non-compartmental methods.

End point type	Secondary

End point timeframe:

0, 1, 3, 6, 12, 18, 24, 27, 30, 36, 48, 72, 96 and 168 hours post last dose

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: No statistical analysis was planned for this endpoint

End point values	PK Run-in Cohort: KAF 200 mg and LUM 960 mg QD for 1 day	Part A - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day	Part A - Cohort 2: KAF 800 mg and LUM 960 mg QD for 1 day	Part A - Cohort 3: KAF 400 mg and LUM 960 mg QD for 2 days
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	4	6	4
Units: Hours				
arithmetic mean (standard deviation)	25.0 (± 8.81)	25.4 (± 5.32)	29.9 (± 9.95)	31.0 (± 3.86)

End point values	Part A - Cohort 4: KAF 200 mg and LUM 480 mg QD for 3 days	Part A - Cohort 5: KAF 400 mg and LUM 480 mg QD for 3 days	Part A - Cohort 6: KAF 400 mg and LUM 960 mg QD for 3 days	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	9	2	
Units: Hours				

arithmetic mean (standard deviation)	35.8 (± 19.4)	28.4 (± 3.49)	26.6 (± 4.15)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK Run-in and Part A: Time to Reach Maximum Blood Concentrations (Tmax) of KAF156

End point title	PK Run-in and Part A: Time to Reach Maximum Blood Concentrations (Tmax) of KAF156[15]

End point description:

Pharmacokinetic (PK) parameters were calculated based on KAF156 blood concentrations determined by a validated liquid chromatography and tandem mass spectrometry (LC-MS/MS) method. Tmax was determined using non-compartmental methods.

End point type	Secondary

End point timeframe:

0, 1, 3, 6, 12, 18, 24, 30, 48, 96 and 168 hours post last dose

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: No statistical analysis was planned for this endpoint

End point values	PK Run-in Cohort: KAF 200 mg and LUM 960 mg QD for 1 day	Part A - Cohort 1: KAF 400 mg and LUM 960 mg QD for 1 day	Part A - Cohort 2: KAF 800 mg and LUM 960 mg QD for 1 day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	5	6	
Units: Hours				
arithmetic mean (standard deviation)	4.23 (± 1.55)	39.8 (± 77.3)	5.99 (± 3.11)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from first dose of study treatment until end of study treatment plus 40, 41 or 42 days post treatment depending on whether the participant received treatment during 1, 2 or 3 consecutive days respectively.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	KAF200mg/@LUM960mg-1D@(PK Run-in)
Reporting group description: KAF200mg/@LUM960mg-1D@(PK Run-in)	
Reporting group title	KAF400mg/@LUM960mg-1D
Reporting group description: KAF400mg/@LUM960mg-1D	
Reporting group title	KAF800mg/@LUM960mg-1D
Reporting group description: KAF800mg/@LUM960mg-1D	
Reporting group title	KAF400mg/@LUM960mg-2D
Reporting group description: KAF400mg/@LUM960mg-2D	
Reporting group title	KAF200mg/@LUM480mg-3D
Reporting group description: KAF200mg/@LUM480mg-3D	
Reporting group title	KAF400mg/@LUM480mg-3D
Reporting group description: KAF400mg/@LUM480mg-3D	
Reporting group title	KAF400mg/@LUM960mg-3D
Reporting group description: KAF400mg/@LUM960mg-3D	
Reporting group title	Coartem
Reporting group description: Coartem	

Serious adverse events	KAF200mg/@LUM960mg-1D@(PK Run-in)	KAF400mg/@LUM960mg-1D	KAF800mg/@LUM960mg-1D
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	7 / 103 (6.80%)	1 / 51 (1.96%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	0 / 12 (0.00%)	0 / 103 (0.00%)	0 / 51 (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
Aspartate aminotransferase			
subjects affected / exposed	0 / 12 (0.00%)	0 / 103 (0.00%)	0 / 51 (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
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 12 (0.00%)	3 / 103 (2.91%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	0 / 12 (0.00%)	2 / 103 (1.94%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	0 / 12 (0.00%)	1 / 103 (0.97%)	0 / 51 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 103 (0.00%)	0 / 51 (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
Hepatobiliary disorders			
Hepatitis acute			
subjects affected / exposed	0 / 12 (0.00%)	1 / 103 (0.97%)	0 / 51 (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
Jaundice			
subjects affected / exposed	0 / 12 (0.00%)	1 / 103 (0.97%)	0 / 51 (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

Skin and subcutaneous tissue disorders			
Petechiae			
subjects affected / exposed	0 / 12 (0.00%)	0 / 103 (0.00%)	0 / 51 (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			
COVID-19			
subjects affected / exposed	0 / 12 (0.00%)	0 / 103 (0.00%)	0 / 51 (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
Plasmodium falciparum infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 103 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 103 (0.00%)	0 / 51 (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
Sepsis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 103 (0.00%)	0 / 51 (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

Serious adverse events	KAF400mg/@LUM960mg-2D	KAF200mg/@LUM480mg-3D	KAF400mg/@LUM480mg-3D
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 104 (4.81%)	2 / 54 (3.70%)	1 / 51 (1.96%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 104 (0.00%)	0 / 54 (0.00%)	0 / 51 (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
Aspartate aminotransferase			

subjects affected / exposed	0 / 104 (0.00%)	1 / 54 (1.85%)	0 / 51 (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
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 104 (1.92%)	1 / 54 (1.85%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	2 / 104 (1.92%)	0 / 54 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	0 / 104 (0.00%)	0 / 54 (0.00%)	0 / 51 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 104 (0.96%)	0 / 54 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatitis acute			
subjects affected / exposed	0 / 104 (0.00%)	0 / 54 (0.00%)	0 / 51 (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
Jaundice			
subjects affected / exposed	0 / 104 (0.00%)	0 / 54 (0.00%)	0 / 51 (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
Skin and subcutaneous tissue disorders			
Petechiae			

subjects affected / exposed	0 / 104 (0.00%)	0 / 54 (0.00%)	0 / 51 (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			
COVID-19			
subjects affected / exposed	1 / 104 (0.96%)	0 / 54 (0.00%)	0 / 51 (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
Plasmodium falciparum infection			
subjects affected / exposed	0 / 104 (0.00%)	0 / 54 (0.00%)	0 / 51 (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
Pneumonia			
subjects affected / exposed	0 / 104 (0.00%)	0 / 54 (0.00%)	0 / 51 (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
Sepsis			
subjects affected / exposed	1 / 104 (0.96%)	0 / 54 (0.00%)	0 / 51 (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

Serious adverse events	KAF400mg/@LUM960mg-3D	Coartem	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 97 (2.06%)	3 / 51 (5.88%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 97 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase			
subjects affected / exposed	0 / 97 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 97 (0.00%)	3 / 51 (5.88%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood bilirubin increased			
subjects affected / exposed	1 / 97 (1.03%)	2 / 51 (3.92%)	
occurrences causally related to treatment / all	0 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	0 / 97 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 97 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatitis acute			
subjects affected / exposed	0 / 97 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	0 / 97 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Petechiae			
subjects affected / exposed	1 / 97 (1.03%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			

subjects affected / exposed	0 / 97 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasmodium falciparum infection			
subjects affected / exposed	0 / 97 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 97 (1.03%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 97 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	KAF200mg/@LUM960mg-1D@(PK Run-in)	KAF400mg/@LUM960mg-1D	KAF800mg/@LUM960mg-1D
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 12 (58.33%)	69 / 103 (66.99%)	37 / 51 (72.55%)
Investigations			
Blood phosphorus increased			
subjects affected / exposed	4 / 12 (33.33%)	0 / 103 (0.00%)	0 / 51 (0.00%)
occurrences (all)	4	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 12 (8.33%)	5 / 103 (4.85%)	5 / 51 (9.80%)
occurrences (all)	1	6	5
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	0 / 12 (0.00%)	4 / 103 (3.88%)	4 / 51 (7.84%)
occurrences (all)	0	4	4
Nervous system disorders			

Headache			
subjects affected / exposed	0 / 12 (0.00%)	16 / 103 (15.53%)	10 / 51 (19.61%)
occurrences (all)	0	17	13
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 12 (0.00%)	5 / 103 (4.85%)	0 / 51 (0.00%)
occurrences (all)	0	6	0
Eosinophilia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 103 (0.00%)	2 / 51 (3.92%)
occurrences (all)	0	0	2
Thrombocytopenia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 103 (0.97%)	3 / 51 (5.88%)
occurrences (all)	0	1	3
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 12 (0.00%)	20 / 103 (19.42%)	5 / 51 (9.80%)
occurrences (all)	0	22	5
Treatment failure			
subjects affected / exposed	0 / 12 (0.00%)	3 / 103 (2.91%)	3 / 51 (5.88%)
occurrences (all)	0	3	3
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 12 (0.00%)	3 / 103 (2.91%)	3 / 51 (5.88%)
occurrences (all)	0	3	3
Diarrhoea			
subjects affected / exposed	0 / 12 (0.00%)	1 / 103 (0.97%)	4 / 51 (7.84%)
occurrences (all)	0	1	4
Vomiting			
subjects affected / exposed	0 / 12 (0.00%)	8 / 103 (7.77%)	8 / 51 (15.69%)
occurrences (all)	0	8	8
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 12 (0.00%)	7 / 103 (6.80%)	3 / 51 (5.88%)
occurrences (all)	0	7	4
Infections and infestations			

Bronchitis			
subjects affected / exposed	1 / 12 (8.33%)	2 / 103 (1.94%)	0 / 51 (0.00%)
occurrences (all)	1	2	0
Infection parasitic			
subjects affected / exposed	1 / 12 (8.33%)	0 / 103 (0.00%)	0 / 51 (0.00%)
occurrences (all)	1	0	0
Malaria			
subjects affected / exposed	0 / 12 (0.00%)	28 / 103 (27.18%)	8 / 51 (15.69%)
occurrences (all)	0	29	8
Upper respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	15 / 103 (14.56%)	6 / 51 (11.76%)
occurrences (all)	0	15	6

Non-serious adverse events	KAF400mg/@LUM960mg-2D	KAF200mg/@LUM480mg-3D	KAF400mg/@LUM480mg-3D
Total subjects affected by non-serious adverse events			
subjects affected / exposed	68 / 104 (65.38%)	30 / 54 (55.56%)	32 / 51 (62.75%)
Investigations			
Blood phosphorus increased			
subjects affected / exposed	0 / 104 (0.00%)	1 / 54 (1.85%)	0 / 51 (0.00%)
occurrences (all)	0	1	0
Electrocardiogram QT prolonged			
subjects affected / exposed	6 / 104 (5.77%)	9 / 54 (16.67%)	9 / 51 (17.65%)
occurrences (all)	6	9	9
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	1 / 104 (0.96%)	1 / 54 (1.85%)	0 / 51 (0.00%)
occurrences (all)	1	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 104 (12.50%)	15 / 54 (27.78%)	7 / 51 (13.73%)
occurrences (all)	16	19	8
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 104 (2.88%)	1 / 54 (1.85%)	1 / 51 (1.96%)
occurrences (all)	4	1	1
Eosinophilia			

subjects affected / exposed	1 / 104 (0.96%)	3 / 54 (5.56%)	2 / 51 (3.92%)
occurrences (all)	1	3	2
Thrombocytopenia			
subjects affected / exposed	1 / 104 (0.96%)	1 / 54 (1.85%)	5 / 51 (9.80%)
occurrences (all)	1	1	5
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	18 / 104 (17.31%)	4 / 54 (7.41%)	6 / 51 (11.76%)
occurrences (all)	18	5	6
Treatment failure			
subjects affected / exposed	0 / 104 (0.00%)	3 / 54 (5.56%)	2 / 51 (3.92%)
occurrences (all)	0	3	2
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	5 / 104 (4.81%)	2 / 54 (3.70%)	7 / 51 (13.73%)
occurrences (all)	6	2	9
Diarrhoea			
subjects affected / exposed	3 / 104 (2.88%)	1 / 54 (1.85%)	2 / 51 (3.92%)
occurrences (all)	3	1	2
Vomiting			
subjects affected / exposed	9 / 104 (8.65%)	2 / 54 (3.70%)	3 / 51 (5.88%)
occurrences (all)	9	2	3
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	10 / 104 (9.62%)	3 / 54 (5.56%)	5 / 51 (9.80%)
occurrences (all)	11	3	5
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 104 (2.88%)	0 / 54 (0.00%)	0 / 51 (0.00%)
occurrences (all)	3	0	0
Infection parasitic			
subjects affected / exposed	0 / 104 (0.00%)	1 / 54 (1.85%)	0 / 51 (0.00%)
occurrences (all)	0	1	0
Malaria			
subjects affected / exposed	25 / 104 (24.04%)	4 / 54 (7.41%)	6 / 51 (11.76%)
occurrences (all)	25	4	6

Upper respiratory tract infection			
subjects affected / exposed	12 / 104 (11.54%)	5 / 54 (9.26%)	3 / 51 (5.88%)
occurrences (all)	14	5	3

Non-serious adverse events	KAF400mg/@LUM960mg-3D	Coartem	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	59 / 97 (60.82%)	30 / 51 (58.82%)	
Investigations			
Blood phosphorus increased			
subjects affected / exposed	0 / 97 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Electrocardiogram QT prolonged			
subjects affected / exposed	9 / 97 (9.28%)	3 / 51 (5.88%)	
occurrences (all)	9	3	
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	3 / 97 (3.09%)	0 / 51 (0.00%)	
occurrences (all)	4	0	
Nervous system disorders			
Headache			
subjects affected / exposed	14 / 97 (14.43%)	7 / 51 (13.73%)	
occurrences (all)	19	7	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 97 (5.15%)	1 / 51 (1.96%)	
occurrences (all)	5	1	
Eosinophilia			
subjects affected / exposed	3 / 97 (3.09%)	0 / 51 (0.00%)	
occurrences (all)	4	0	
Thrombocytopenia			
subjects affected / exposed	0 / 97 (0.00%)	2 / 51 (3.92%)	
occurrences (all)	0	2	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	9 / 97 (9.28%)	13 / 51 (25.49%)	
occurrences (all)	9	13	
Treatment failure			

subjects affected / exposed	1 / 97 (1.03%)	2 / 51 (3.92%)	
occurrences (all)	1	2	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 97 (4.12%)	0 / 51 (0.00%)	
occurrences (all)	4	0	
Diarrhoea			
subjects affected / exposed	3 / 97 (3.09%)	0 / 51 (0.00%)	
occurrences (all)	4	0	
Vomiting			
subjects affected / exposed	8 / 97 (8.25%)	2 / 51 (3.92%)	
occurrences (all)	8	2	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 97 (6.19%)	4 / 51 (7.84%)	
occurrences (all)	6	4	
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 97 (2.06%)	0 / 51 (0.00%)	
occurrences (all)	2	0	
Infection parasitic			
subjects affected / exposed	0 / 97 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Malaria			
subjects affected / exposed	16 / 97 (16.49%)	18 / 51 (35.29%)	
occurrences (all)	17	18	
Upper respiratory tract infection			
subjects affected / exposed	12 / 97 (12.37%)	5 / 51 (9.80%)	
occurrences (all)	12	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 February 2017	PK Run-in Part was included in the amended study protocol. This first part of the study will explore the PK and safety of KAF156 given in combination with LUM-SDF to understand the impact of LUM-SDF on KAF156 exposure as victim drug.
13 April 2018	Protocol was amended to correct several errors/inconsistencies, and provide clarifications.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported