



Clinical trial results:

A Phase 2 interventional, multicenter, randomized, open-label study in three age-descending cohorts to evaluate efficacy, safety and tolerability of KAF156 and Lumefantrine-SDF combination in the treatment of acute uncomplicated Plasmodium falciparum Malaria in a pediatric population

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2021-003583-27 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 28 August 2024 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 15 March 2025 |
| First version publication date | 15 March 2025 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | CKAF156A2203 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04546633 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Novartis Pharmaceuticals |
| 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 August 2024 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 28 August 2024 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of KAF156 combined with LUM- Solid dispersion formulation (SDF) compared to Coartem® (non-inferiority trial) for the treatment of uncomplicated malaria caused by *P. falciparum* in children 6 months to < 12 years.

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 | 16 February 2021 |
| 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: 59 |
| Country: Number of subjects enrolled | Congo, The Democratic Republic of the: 1 |
| Country: Number of subjects enrolled | Gabon: 92 |
| Country: Number of subjects enrolled | Mali: 132 |
| Country: Number of subjects enrolled | Côte d'Ivoire: 11 |
| Worldwide total number of subjects | 295 |
| 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) | 80 |
| Children (2-11 years) | 140 |

| | |
|---------------------------|----|
| Adolescents (12-17 years) | 75 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Participants took part in 10 investigative sites in 5 countries.

Pre-assignment

Screening details:

During pre-screening, a *P. falciparum* parasite count was obtained for all patients. Further screening assessments took place only if the outcome was in the pre-defined range ($\geq 1,000$ and $\leq 150,000$ parasites/ μL in Run-In Cohort and $\geq 1,500$ and $\leq 150,000$ parasites/ μL in Cohort 1 and Cohort 2).

Period 1

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

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | Run-in Cohort-KAF400mg/LUM240mg-QDx2-Fed |

Arm description:

KAF156-400 mg and LUM-240 mg-solid dispersion formulation (SDF), once daily (QD) for 2 days in fed condition, via oral.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Lumefantrine Solid Dispersion Formulation |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Oral powder in sachet |
| Routes of administration | Oral use |

Dosage and administration details:

Administered in combination with KAF156 once daily for 2 days in fed condition at 240mg.

| | |
|--|----------|
| 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 for 2 days in fed condition at 400mg.

| | |
|------------------|---|
| Arm title | Run-in Cohort-KAF400mg/LUM240mg-QDx2-Fasted |
|------------------|---|

Arm description:

KAF156-400 mg and LUM-240 mg-SDF once daily for 2 days in fasted condition, via oral.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Lumefantrine Solid Dispersion Formulation |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Oral powder in sachet |
| Routes of administration | Oral use |

Dosage and administration details:

Administered in combination with KAF156 once daily for 2 days in fasted condition at 240mg.

| | |
|---|---|
| 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 for 2 days in fasted condition at 400mg. | |
| Arm title | Run-in Cohort-KAF400mg/LUM480mg-QDx2-Fed |
| Arm description: | |
| KAF156-400 mg and LUM-480 mg-SDF once daily for 2 days in fed condition, via oral. | |
| Arm type | Experimental |
| Investigational medicinal product name | Lumefantrine Solid Dispersion Formulation |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Oral powder in sachet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Administered in combination with KAF156 once daily for 2 days in fed condition at 480mg. | |
| 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 for 2 days in fed condition at 400mg. | |
| Arm title | Run-in Cohort-KAF400mg/LUM480mg-QDx2-Fasted |
| Arm description: | |
| KAF156-400 mg and LUM-480 mg-SDF once daily for 2 days in fasted condition, via oral. | |
| Arm type | Experimental |
| Investigational medicinal product name | Lumefantrine Solid Dispersion Formulation |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Oral powder in sachet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Administered in combination with KAF156 once daily for 2 days in fasted condition at 480mg. | |
| 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 for 2 days in fasted condition at 400mg. | |
| Arm title | Cohort 1/2-KAF400mg/LUM480mg-QDx3 |
| Arm description: | |
| KAF156-400mg and LUM-480 mg-SDF once daily for 3 days, via oral. It was administered with a light meal and the full dose was adjusted based on patient's body weight. | |
| Arm type | Experimental |

| | |
|--|---|
| Investigational medicinal product name | Lumefantrine Solid Dispersion Formulation |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Oral powder in sachet |
| Routes of administration | Oral use |

Dosage and administration details:

Administered in combination with KAF156 once daily for 3 days with a light meal and the full dose was adjusted based on patient's body weight.

| | |
|--|----------|
| 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 for 3 days with a light meal and the full dose was adjusted based on patient's body weight.

| | |
|------------------|------------------------------------|
| Arm title | Cohort 1/2-Artemether80mg/LUM480mg |
|------------------|------------------------------------|

Arm description:

Artemether-80mg/LUM-480 mg, twice daily for 3 days, it was administered with food and the doses were based on patient's body weight as per product label.

| | |
|--|-------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Artemether80mg/LUM480mg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Dispersible tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Administered with food and the doses were based on patient's body weight as per product label, twice daily for 3 days.

| Number of subjects in period 1 | Run-in Cohort- KAF400mg/LUM240 mg-QDx2-Fed | Run-in Cohort- KAF400mg/LUM240 mg-QDx2-Fasted | Run-in Cohort- KAF400mg/LUM480 mg-QDx2-Fed |
|---------------------------------------|--|---|--|
| Started | 25 | 26 | 11 |
| Completed | 23 | 26 | 11 |
| Not completed | 2 | 0 | 0 |
| Lost to follow-up | 1 | - | - |
| Guardian decision | 1 | - | - |

| Number of subjects in period 1 | Run-in Cohort- KAF400mg/LUM480 mg-QDx2-Fasted | Cohort 1/2- KAF400mg/LUM480 mg-QDx3 | Cohort 1/2- Artemether80mg/LU M480mg |
|---------------------------------------|---|---|--|
| Started | 13 | 110 | 110 |
| Completed | 13 | 104 | 102 |
| Not completed | 0 | 6 | 8 |
| Lost to follow-up | - | 4 | 4 |
| Guardian decision | - | 2 | 4 |

Baseline characteristics

Reporting groups

| | |
|---|---|
| Reporting group title | Run-in Cohort-KAF400mg/LUM240mg-QDx2-Fed |
| Reporting group description: KAF156-400 mg and LUM-240 mg-solid dispersion formulation (SDF), once daily (QD) for 2 days in fed condition, via oral. | |
| Reporting group title | Run-in Cohort-KAF400mg/LUM240mg-QDx2-Fasted |
| Reporting group description: KAF156-400 mg and LUM-240 mg-SDF once daily for 2 days in fasted condition, via oral. | |
| Reporting group title | Run-in Cohort-KAF400mg/LUM480mg-QDx2-Fed |
| Reporting group description: KAF156-400 mg and LUM-480 mg-SDF once daily for 2 days in fed condition, via oral. | |
| Reporting group title | Run-in Cohort-KAF400mg/LUM480mg-QDx2-Fasted |
| Reporting group description: KAF156-400 mg and LUM-480 mg-SDF once daily for 2 days in fasted condition, via oral. | |
| Reporting group title | Cohort 1/2-KAF400mg/LUM480mg-QDx3 |
| Reporting group description: KAF156-400mg and LUM-480 mg-SDF once daily for 3 days, via oral. It was administered with a light meal and the full dose was adjusted based on patient's body weight. | |
| Reporting group title | Cohort 1/2-Artemether80mg/LUM480mg |
| Reporting group description: Artemether-80mg/LUM-480 mg, twice daily for 3 days, it was administered with food and the doses were based on patient's body weight as per product label. | |

| Reporting group values | Run-in Cohort-KAF400mg/LUM240 mg-QDx2-Fed | Run-in Cohort-KAF400mg/LUM240 mg-QDx2-Fasted | Run-in Cohort-KAF400mg/LUM480 mg-QDx2-Fed |
|---|---|--|---|
| Number of subjects | 25 | 26 | 11 |
| Age Categorical Units: | | | |
| <=18 years | 25 | 26 | 11 |
| Between 18 and 65 years | 0 | 0 | 0 |
| >=65 years | 0 | 0 | 0 |
| Age Continuous Units: years | | | |
| arithmetic mean | 14.08 | 13.62 | 14.36 |
| standard deviation | ± 1.382 | ± 1.416 | ± 1.859 |
| Sex: Female, Male Units: participants | | | |
| Female | 15 | 12 | 8 |
| Male | 10 | 14 | 3 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| Black or African American | 25 | 26 | 11 |

| Reporting group values | Run-in Cohort-KAF400mg/LUM480 mg-QDx2-Fasted | Cohort 1/2-KAF400mg/LUM480 mg-QDx3 | Cohort 1/2-Artemether80mg/LUM480mg |
|------------------------|--|------------------------------------|------------------------------------|
| Number of subjects | 13 | 110 | 110 |

| | | | |
|---|---------|---------|---------|
| Age Categorical Units: | | | |
| <=18 years | 13 | 110 | 110 |
| Between 18 and 65 years | 0 | 0 | 0 |
| >=65 years | 0 | 0 | 0 |
| Age Continuous Units: years | | | |
| arithmetic mean | 14.85 | 4.86 | 4.58 |
| standard deviation | ± 1.573 | ± 3.464 | ± 3.251 |
| Sex: Female, Male Units: participants | | | |
| Female | 4 | 60 | 42 |
| Male | 9 | 50 | 68 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| Black or African American | 13 | 110 | 110 |

| | | | |
|---|-------|--|--|
| Reporting group values | Total | | |
| Number of subjects | 295 | | |
| Age Categorical Units: | | | |
| <=18 years | 295 | | |
| Between 18 and 65 years | 0 | | |
| >=65 years | 0 | | |
| Age Continuous Units: years | | | |
| arithmetic mean | - | | |
| standard deviation | - | | |
| Sex: Female, Male Units: participants | | | |
| Female | 141 | | |
| Male | 154 | | |
| Race/Ethnicity, Customized Units: Subjects | | | |
| Black or African American | 295 | | |

Subject analysis sets

| | |
|---|----------------------------------|
| Subject analysis set title | Cohort 1-KAF400mg/LUM480mg-QDx3 |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: KAF156-400mg and LUM-480 mg-SDF once daily for 3 days, via oral. It was administered with a light meal and the full dose was adjusted based on patient's body weight. Cohort 1 participants age 2 to <12 years. | |
| Subject analysis set title | Cohort 2-KAF400mg/LUM480mg-QDx3 |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: KAF156-400mg and LUM-480 mg-SDF once daily for 3 days, via oral. It was administered with a light meal and the full dose was adjusted based on patient's body weight. Cohort 2 participants ages 6 months to <2 years. | |
| Subject analysis set title | Cohort 1-Artemether80mg/LUM480mg |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Artemether-80mg/LUM-480 mg, twice daily for 3 days, it was administered with food and the doses were based on patient's body weight as per product label. Cohort 1 participants age 2 to <12 years.

| | |
|----------------------------|----------------------------------|
| Subject analysis set title | Cohort 2-Artemether80mg/LUM480mg |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Artemether-80mg/LUM-480 mg, twice daily for 3 days, it was administered with food and the doses were based on patient's body weight as per product label. Cohort 2 participants ages 6 months to <2 years.

| | |
|----------------------------|-------------------------------------|
| Subject analysis set title | Cohort 2-KAF400mg/LUM480mg-QDx3Edit |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

KAF156-400mg and LUM-480 mg-SDF once daily for 3 days, via oral. It was administered with a light meal and the full dose was adjusted based on patient's body weight. Cohort 2 participants ages 6 months to <2 years.

| | |
|----------------------------|---------------------------------|
| Subject analysis set title | Cohort 1-KAF400mg/LUM480mg-QDx3 |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

KAF156-400mg and LUM-480 mg-SDF once daily for 3 days, via oral. It was administered with a light meal and the full dose was adjusted based on patient's body weight. Cohort 1 participants age 2 to <12 years.

| | |
|----------------------------|----------------------------------|
| Subject analysis set title | Cohort 1-Artemether80mg/LUM480mg |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Artemether-80mg/LUM-480 mg, twice daily for 3 days, it was administered with food and the doses were based on patient's body weight as per product label. Cohort 1 participants age 2 to <12 years.

| | |
|----------------------------|----------------------------------|
| Subject analysis set title | Cohort 2-Artemether80mg/LUM480mg |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Artemether-80mg/LUM-480 mg, twice daily for 3 days, it was administered with food and the doses were based on patient's body weight as per product label. Cohort 2 participants ages 6 months to <2 years.

| Reporting group values | Cohort 1- KAF400mg/LUM480 mg-QDx3 | Cohort 2- KAF400mg/LUM480 mg-QDx3 | Cohort 1- Artemether80mg/LU M480mg |
|---|---|---|--|
| Number of subjects | 65 | 31 | 53 |
| Age Categorical Units: | | | |
| <=18 years | | | |
| Between 18 and 65 years | | | |
| >=65 years | | | |
| Age Continuous Units: years arithmetic mean standard deviation | ± | ± | ± |
| Sex: Female, Male Units: participants | | | |
| Female | | | |
| Male | | | |
| Race/Ethnicity, Customized Units: Subjects | | | |
| Black or African American | 65 | 31 | 53 |

| Reporting group values | Cohort 2- Artemether80mg/LU | Cohort 2- KAF400mg/LUM480 | Cohort 1- KAF400mg/LUM480 |
|------------------------|--------------------------------|------------------------------|------------------------------|
|------------------------|--------------------------------|------------------------------|------------------------------|

| | M480mg | mg-QDx3Edit | mg-QDx3 |
|---|--------|-------------|---------|
| Number of subjects | 31 | 31 | 68 |
| Age Categorical Units: | | | |
| <=18 years | | | |
| Between 18 and 65 years | | | |
| >=65 years | | | |
| Age Continuous Units: years | | | |
| arithmetic mean | | | |
| standard deviation | ± | ± | ± |
| Sex: Female, Male Units: participants | | | |
| Female | | | |
| Male | | | |
| Race/Ethnicity, Customized Units: Subjects | | | |
| Black or African American | 31 | 31 | 68 |

| Reporting group values | Cohort 1- Artemether80mg/LU M480mg | Cohort 2- Artemether80mg/LU M480mg | |
|---|--|--|--|
| Number of subjects | 65 | 35 | |
| Age Categorical Units: | | | |
| <=18 years | | | |
| Between 18 and 65 years | | | |
| >=65 years | | | |
| Age Continuous Units: years | | | |
| arithmetic mean | | | |
| standard deviation | ± | ± | |
| Sex: Female, Male Units: participants | | | |
| Female | | | |
| Male | | | |
| Race/Ethnicity, Customized Units: Subjects | | | |
| Black or African American | 65 | 35 | |

End points

End points reporting groups

| | |
|---|---|
| Reporting group title | Run-in Cohort-KAF400mg/LUM240mg-QDx2-Fed |
| Reporting group description: KAF156-400 mg and LUM-240 mg-solid dispersion formulation (SDF), once daily (QD) for 2 days in fed condition, via oral. | |
| Reporting group title | Run-in Cohort-KAF400mg/LUM240mg-QDx2-Fasted |
| Reporting group description: KAF156-400 mg and LUM-240 mg-SDF once daily for 2 days in fasted condition, via oral. | |
| Reporting group title | Run-in Cohort-KAF400mg/LUM480mg-QDx2-Fed |
| Reporting group description: KAF156-400 mg and LUM-480 mg-SDF once daily for 2 days in fed condition, via oral. | |
| Reporting group title | Run-in Cohort-KAF400mg/LUM480mg-QDx2-Fasted |
| Reporting group description: KAF156-400 mg and LUM-480 mg-SDF once daily for 2 days in fasted condition, via oral. | |
| Reporting group title | Cohort 1/2-KAF400mg/LUM480mg-QDx3 |
| Reporting group description: KAF156-400mg and LUM-480 mg-SDF once daily for 3 days, via oral. It was administered with a light meal and the full dose was adjusted based on patient's body weight. | |
| Reporting group title | Cohort 1/2-Artemether80mg/LUM480mg |
| Reporting group description: Artemether-80mg/LUM-480 mg, twice daily for 3 days, it was administered with food and the doses were based on patient's body weight as per product label. | |
| Subject analysis set title | Cohort 1-KAF400mg/LUM480mg-QDx3 |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: KAF156-400mg and LUM-480 mg-SDF once daily for 3 days, via oral. It was administered with a light meal and the full dose was adjusted based on patient's body weight. Cohort 1 participants age 2 to <12 years. | |
| Subject analysis set title | Cohort 2-KAF400mg/LUM480mg-QDx3 |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: KAF156-400mg and LUM-480 mg-SDF once daily for 3 days, via oral. It was administered with a light meal and the full dose was adjusted based on patient's body weight. Cohort 2 participants ages 6 months to <2 years. | |
| Subject analysis set title | Cohort 1-Artemether80mg/LUM480mg |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Artemether-80mg/LUM-480 mg, twice daily for 3 days, it was administered with food and the doses were based on patient's body weight as per product label. Cohort 1 participants age 2 to <12 years. | |
| Subject analysis set title | Cohort 2-Artemether80mg/LUM480mg |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Artemether-80mg/LUM-480 mg, twice daily for 3 days, it was administered with food and the doses were based on patient's body weight as per product label. Cohort 2 participants ages 6 months to <2 years. | |
| Subject analysis set title | Cohort 2-KAF400mg/LUM480mg-QDx3Edit |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: KAF156-400mg and LUM-480 mg-SDF once daily for 3 days, via oral. It was administered with a light meal and the full dose was adjusted based on patient's body weight. Cohort 2 participants ages 6 months to <2 years. | |
| Subject analysis set title | Cohort 1-KAF400mg/LUM480mg-QDx3 |

| | |
|--|----------------------------------|
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: KAF156-400mg and LUM-480 mg-SDF once daily for 3 days, via oral. It was administered with a light meal and the full dose was adjusted based on patient's body weight. Cohort 1 participants age 2 to <12 years. | |
| Subject analysis set title | Cohort 1-Artemether80mg/LUM480mg |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Artemether-80mg/LUM-480 mg, twice daily for 3 days, it was administered with food and the doses were based on patient's body weight as per product label. Cohort 1 participants age 2 to <12 years. | |
| Subject analysis set title | Cohort 2-Artemether80mg/LUM480mg |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Artemether-80mg/LUM-480 mg, twice daily for 3 days, it was administered with food and the doses were based on patient's body weight as per product label. Cohort 2 participants ages 6 months to <2 years. | |

Primary: Polymerase Chain Reaction (PCR)-corrected adequate clinical and parasitological response (ACPR) - Cohorts 1 and 2 pooled

| | |
|--|---|
| End point title | Polymerase Chain Reaction (PCR)-corrected adequate clinical and parasitological response (ACPR) - Cohorts 1 and 2 pooled ^[1] |
| End point description: PCR-corrected ACPR, defined as the absence of parasitemia(PS),was evaluated on Day29. 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 Day29 if the participant did not meet any of the criteria of early treatment failure (up to Day4), late clinical failure(Day5 to Day29) or late parasitological failure(Day8 to Day29), and had absence of PS on Day29 irrespective of axillary temperature unless the presence of PS after 7days(Day8 or later) was due to reinfection based on PCR genotyping.A presence of PS after 7days of treatment initiation was considered as a reinfection only if the PS was clear before Day8 and none of the parasite strain(s) detected on Day8 or later match with the parasite strain at baseline based on PCR genotyping.Given the age-independent symptoms of acute malaria, and to increase statistical power,the cohorts 1 and 2 were pooled. | |
| End point type | Primary |
| End point timeframe: Day 29 | |

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: This Endpoint is not analyzed for all arms

| End point values | Cohort 1/2-KAF400mg/LUM480mg-QDx3 | Cohort 1/2-Artemether80mg/LUM480mg | | |
|-----------------------------------|-----------------------------------|------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 98 | 99 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 99.0 (94.4 to 100.0) | 99.0 (94.5 to 100.0) | | |

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | PCR-ACPR |
| Comparison groups | Cohort 1/2-KAF400mg/LUM480mg-QDx3 v Cohort 1/2-Artemether80mg/LUM480mg |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 197 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.9 |
| upper limit | 2.8 |

Secondary: PCR-corrected and uncorrected Adequate Clinical and Parasitological Response (ACPR)

| | |
|---|---|
| End point title | PCR-corrected and uncorrected Adequate Clinical and Parasitological Response (ACPR) |
| End point description: | |
| <p>PCR-corrected ACPR, defined as the absence of parasitemia, was evaluated. Microscopic species identification was confirmed and determined by polymerase chain reaction (PCR) genotyping methods to establish malaria recrudescence/reinfection.</p> <p>A participant was considered as PCR-corrected ACPR if the participant did not meet any of the criteria of early treatment failure, late clinical failure or late parasitological failure and had absence of parasitemia on Days 15, 29 or 43 irrespective of axillary temperature unless the presence of parasitemia after 7 days was due to reinfection based on PCR. A presence of parasitemia after 7 days of treatment initiation was considered as a reinfection only if the parasitemia 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. Given the age-independent symptoms of acute malaria, and to increase statistical power, the cohorts 1 and 2 were pooled (cohort 1/2).</p> | |
| End point type | Secondary |
| End point timeframe: | |
| Corrected ACPR: Day 15, Day 43; Uncorrected ACPR: Day 15, Day 29 and Day 43 | |

| End point values | Run-in Cohort-KAF400mg/LU M240mg-QDx2-Fed | Run-in Cohort-KAF400mg/LU M240mg-QDx2-Fasted | Run-in Cohort-KAF400mg/LU M480mg-QDx2-Fed | Run-in Cohort-KAF400mg/LU M480mg-QDx2-Fasted |
|-----------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 11 | 22 | 8 | 13 |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Day 15-corrected ACPR | 100.0 (71.5 to 100.0) | 100.0 (84.6 to 100.0) | 100.0 (63.1 to 100.0) | 100.0 (75.3 to 100.0) |
| Day 43-corrected ACPR | 100.0 (71.5 to 100.0) | 100.0 (84.6 to 100.0) | 87.5 (47.3 to 99.7) | 92.3 (64.0 to 99.8) |
| Day 15-uncorrected ACPR | 100.0 (71.5 to 100.0) | 100.0 (84.6 to 100.0) | 100.0 (63.1 to 100.0) | 100.0 (75.3 to 100.0) |
| Day 29-uncorrected ACPR | 90.9 (58.7 to 99.8) | 95.5 (77.2 to 99.9) | 87.5 (47.3 to 99.7) | 100.0 (75.3 to 100.0) |
| Day 43-uncorrected ACPR | 81.8 (48.2 to 97.7) | 86.4 (65.1 to 97.1) | 62.5 (24.5 to 91.5) | 76.9 (46.2 to 95.0) |

| End point values | Cohort 1/2- KAF400mg/LU M480mg-QDx3 | Cohort 1/2- Artemether80 mg/LUM480mg | | |
|-----------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 98 | 99 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Day 15-corrected ACPR | 100.0 (96.3 to 100.0) | 100.0 (96.3 to 100.0) | | |
| Day 43-corrected ACPR | 94.9 (88.5 to 98.3) | 96.0 (90.0 to 98.9) | | |
| Day 15-uncorrected ACPR | 100.0 (96.3 to 100.0) | 100.0 (96.3 to 100.0) | | |
| Day 29-uncorrected ACPR | 96.9 (91.3 to 99.4) | 94.9 (88.6 to 98.3) | | |
| Day 43-uncorrected ACPR | 85.7 (77.2 to 92.0) | 85.9 (77.4 to 92.0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: PCR-corrected Adequate Clinical and Parasitological Response (ACPR) - Run-in Cohort

| | |
|-----------------|--|
| End point title | PCR-corrected Adequate Clinical and Parasitological Response (ACPR) - Run-in Cohort ^[2] |
|-----------------|--|

End point description:

PCR-corrected ACPR, defined as the absence of parasitemia, was evaluated on Day 29. Microscopic species identification was confirmed and determined by polymerase chain reaction (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 (ETF) (up to Day 4), late clinical failure (LCF) (Day 5 to Day 29) or late parasitological failure (LPF) (Day 8 to Day 29), and had absence of parasitaemia on Day 29 irrespective of axillary temperature unless the presence of parasitaemia after 7 days (Day 8 or later) was due to reinfection based on PCR genotyping. 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 match with the parasite strain at baseline based on PCR genotyping.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

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: This Endpoint is not analyzed for all arms

| End point values | Run-in Cohort-KAF400mg/LU M240mg-QDx2-Fed | Run-in Cohort-KAF400mg/LU M240mg-QDx2-Fasted | Run-in Cohort-KAF400mg/LU M480mg-QDx2-Fed | Run-in Cohort-KAF400mg/LU M480mg-QDx2-Fasted |
|-----------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 11 | 22 | 8 | 13 |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 100.0 (71.5 to 100.0) | 100.0 (84.6 to 100.0) | 100.0 (63.1 to 100.0) | 100.0 (75.3 to 100.0) |

Statistical analyses

No statistical analyses for this end point

Secondary: Parasite Clearance Time (PCT)

| | |
|---|-------------------------------|
| End point title | Parasite Clearance Time (PCT) |
| End point description: | |
| PCT 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. PCT is based on uncorrected parasite counts. PCT was calculated using the Kaplan-Meier method. Given the age-independent symptoms of acute malaria, and to increase statistical power, the cohorts 1 and 2 were pooled (cohort 1/2). | |
| End point type | Secondary |
| End point timeframe: | |
| up to 43 days | |

| End point values | Run-in Cohort-KAF400mg/LU M240mg-QDx2-Fed | Run-in Cohort-KAF400mg/LU M240mg-QDx2-Fasted | Run-in Cohort-KAF400mg/LU M480mg-QDx2-Fed | Run-in Cohort-KAF400mg/LU M480mg-QDx2-Fasted |
|----------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 25 | 26 | 11 | 13 |
| Units: hours | | | | |
| median (confidence interval 95%) | 48.1 (36.1 to 48.2) | 36.2 (36.0 to 71.9) | 48.0 (36.0 to 48.2) | 48.0 (24.0 to 48.2) |

| End point values | Cohort 1/2-KAF400mg/LU M480mg-QDx3 | Cohort 1/2-Artemether80 mg/LUM480mg | | |
|----------------------------------|------------------------------------|-------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 110 | 110 | | |
| Units: hours | | | | |
| median (confidence interval 95%) | 47.5 (36.2 to 47.8) | 35.9 (35.6 to 36.0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Fever clearance Times (FCT)

| | |
|---|-----------------------------|
| End point title | Fever clearance Times (FCT) |
| End point description: FCT 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. FCT was calculated using the Kaplan-Meier method. Participants who received any antimalarial medication (including rescue medication) before fever clearance are censored at the first use of antimalarial medication. Participants without fever clearance are censored at the time of last fever assessment. Given the age-independent symptoms of acute malaria, and to increase statistical power, the cohorts 1 and 2 were pooled (cohort 1/2). Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'. | |
| End point type | Secondary |
| End point timeframe: up to 43 days | |

| End point values | Run-in Cohort-KAF400mg/LU M240mg-QDx2-Fed | Run-in Cohort-KAF400mg/LU M240mg-QDx2-Fasted | Run-in Cohort-KAF400mg/LU M480mg-QDx2-Fed | Run-in Cohort-KAF400mg/LU M480mg-QDx2-Fasted |
|----------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 5 | 3 | 2 |
| Units: hours | | | | |
| median (confidence interval 95%) | 23.5 (23.3 to 999) | 23.9 (23.6 to 999) | 23.8 (23.7 to 999) | 27.1 (23.9 to 999) |

| End point values | Cohort 1/2-KAF400mg/LU M480mg-QDx3 | Cohort 1/2-Artemether80 mg/LUM480mg | | |
|----------------------------------|------------------------------------|-------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 33 | 36 | | |
| Units: hours | | | | |
| median (confidence interval 95%) | 23.9 (23.4 to 24.3) | 23.7 (23.5 to 23.9) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Early Treatment Failure (ETF)

| | |
|--|--|
| End point title | Percentage Early Treatment Failure (ETF) |
| End point description: Participants were defined as early treatment failures (ETFs) if they developed danger signs or severe malaria on Day 2, Day 3, or Day 4 in the presence of parasitemia, parasitemia on Day 3 with a count higher than the Day 1 count irrespective of axillary temperature, parasitemia on Day 4 with axillary temperature $\geq 37.5^{\circ}\text{C}$, or parasitemia on Day 4 with a count equal to or more than 25% of the count on Day 1. Given the age-independent symptoms of acute malaria, and to increase statistical power, the | |

cohorts 1 and 2 were pooled (cohort 1/2).

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From Day 1 to Day 4 | |

| End point values | Run-in Cohort-KAF400mg/LU M240mg-QDx2-Fed | Run-in Cohort-KAF400mg/LU M240mg-QDx2-Fasted | Run-in Cohort-KAF400mg/LU M480mg-QDx2-Fed | Run-in Cohort-KAF400mg/LU M480mg-QDx2-Fasted |
|-----------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 24 | 26 | 11 | 13 |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 0.0 (0.0 to 14.3) | 0.0 (0.0 to 13.2) | 0.0 (0.0 to 28.5) | 0.0 (0.0 to 24.7) |

| End point values | Cohort 1/2-KAF400mg/LU M480mg-QDx3 | Cohort 1/2-Artemether80 mg/LUM480mg | | |
|-----------------------------------|------------------------------------|-------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 108 | 110 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 0.0 (0.0 to 3.4) | 0.0 (0.0 to 3.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Late Clinical Failure (LCF)

| | |
|--|--|
| End point title | Percentage Late Clinical Failure (LCF) |
| End point description: | |
| Participants were defined as late clinical failures (LCFs) if they developed danger signs or severe malaria on any day from Day 5 to Day 43 in the presence of parasitemia without previously meeting any of the criteria of ETF, or if they had parasitemia and an axillary temperature of $\geq 37.5^{\circ}\text{C}$ on any day from Day 5 to Day 43 without previously meeting any of the criteria of ETF. Given the age-independent symptoms of acute malaria, and to increase statistical power, the cohorts 1 and 2 were pooled (cohort 1/2). | |
| End point type | Secondary |
| End point timeframe: | |
| Day 5 to Day 43 | |

| End point values | Run-in Cohort-KAF400mg/LU M240mg-QDx2-Fed | Run-in Cohort-KAF400mg/LU M240mg-QDx2-Fasted | Run-in Cohort-KAF400mg/LU M480mg-QDx2-Fed | Run-in Cohort-KAF400mg/LU M480mg-QDx2-Fasted |
|-----------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 23 | 26 | 11 | 13 |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 8.7 (1.1 to 28.0) | 0.0 (0.0 to 13.2) | 0.0 (0.0 to 28.5) | 7.7 (0.2 to 36.0) |

| End point values | Cohort 1/2-KAF400mg/LU M480mg-QDx3 | Cohort 1/2-Artemether80 mg/LUM480mg | | |
|-----------------------------------|------------------------------------|-------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 104 | 102 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 8.7 (4.0 to 15.8) | 3.9 (1.1 to 9.7) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Late Parasitological Failure (LPF)

| | |
|--|---|
| End point title | Percentage Late Parasitological Failure (LPF) |
| End point description: | |
| Participants were defined as late parasitological failures (LPFs) if they had parasitemia on any day from Day 8 to Day 43 and an axillary temperature < 37.5°C without previously meeting any of the criteria of ETF or LCF. Given the age-independent symptoms of acute malaria, and to increase statistical power, the cohorts 1 and 2 were pooled (cohort 1/2). | |
| End point type | Secondary |
| End point timeframe: | |
| Day 8 to Day 43 | |

| End point values | Run-in Cohort-KAF400mg/LU M240mg-QDx2-Fed | Run-in Cohort-KAF400mg/LU M240mg-QDx2-Fasted | Run-in Cohort-KAF400mg/LU M480mg-QDx2-Fed | Run-in Cohort-KAF400mg/LU M480mg-QDx2-Fasted |
|-----------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 21 | 26 | 11 | 12 |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 19.0 (5.5 to 41.9) | 19.2 (6.6 to 39.4) | 54.5 (23.4 to 83.3) | 16.7 (2.1 to 48.4) |

| End point values | Cohort 1/2-KAF400mg/LU | Cohort 1/2-Artemether80 | | |
|------------------|------------------------|-------------------------|--|--|
|------------------|------------------------|-------------------------|--|--|

| | M480mg-QDx3 | mg/LUM480mg | | |
|-----------------------------------|-------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 95 | 98 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 4.2 (1.2 to 10.4) | 11.2 (5.7 to 19.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with recrudescence events

| | |
|-----------------|--|
| End point title | Number of participants with recrudescence events |
|-----------------|--|

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. Given the age-independent symptoms of acute malaria, and to increase statistical power, the cohorts 1 and 2 were pooled (cohort 1/2).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 15, Day 29 and Day 43

| End point values | Run-in Cohort-KAF400mg/LU M240mg-QDx2-Fed | Run-in Cohort-KAF400mg/LU M240mg-QDx2-Fasted | Run-in Cohort-KAF400mg/LU M480mg-QDx2-Fed | Run-in Cohort-KAF400mg/LU M480mg-QDx2-Fasted |
|-----------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 25 | 26 | 11 | 13 |
| Units: participants | | | | |
| Day 15 | 0 | 0 | 0 | 0 |
| Day 29 | 1 | 0 | 0 | 0 |
| Day 43 | 1 | 0 | 0 | 1 |

| End point values | Cohort 1/2-KAF400mg/LU M480mg-QDx3 | Cohort 1/2-Artemether80 mg/LUM480mg | | |
|-----------------------------|------------------------------------|-------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 110 | 110 | | |
| Units: participants | | | | |
| Day 15 | 0 | 0 | | |
| Day 29 | 1 | 1 | | |
| Day 43 | 1 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with new infections events

| | |
|-----------------|---|
| End point title | Number of participants with new infections events |
|-----------------|---|

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. Given the age-independent symptoms of acute malaria, and to increase statistical power, the cohorts 1 and 2 were pooled (cohort 1/2).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 15, Day 29 and Day 43

| End point values | Run-in Cohort-KAF400mg/LU M240mg-QDx2-Fed | Run-in Cohort-KAF400mg/LU M240mg-QDx2-Fasted | Run-in Cohort-KAF400mg/LU M480mg-QDx2-Fed | Run-in Cohort-KAF400mg/LU M480mg-QDx2-Fasted |
|-----------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 25 | 26 | 11 | 13 |
| Units: participants | | | | |
| Day 15 | 0 | 0 | 0 | 0 |
| Day 29 | 1 | 0 | 2 | 0 |
| Day 43 | 3 | 3 | 3 | 2 |

| End point values | Cohort 1/2-KAF400mg/LU M480mg-QDx3 | Cohort 1/2-Artemether80 mg/LUM480mg | | |
|-----------------------------|------------------------------------|-------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 110 | 110 | | |
| Units: participants | | | | |
| Day 15 | 0 | 0 | | |
| Day 29 | 3 | 4 | | |
| Day 43 | 7 | 5 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with treatment emergent adverse events (AEs) and serious adverse events (SAEs)

| | |
|-----------------|---|
| End point title | Number of participants with treatment emergent adverse events (AEs) and serious adverse events (SAEs) |
|-----------------|---|

End point description:

Number of participants with treatment emergent adverse events (any AE regardless of seriousness), and SAEs. Given the age-independent symptoms of acute malaria, and to increase statistical power, the

cohorts 1 and 2 were pooled (cohort 1/2).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Adverse events were reported from first dose of study treatment until end of study treatment up to a maximum duration of approximately 43 days.

| End point values | Run-in Cohort-KAF400mg/LU M240mg-QDx2-Fed | Run-in Cohort-KAF400mg/LU M240mg-QDx2-Fasted | Run-in Cohort-KAF400mg/LU M480mg-QDx2-Fed | Run-in Cohort-KAF400mg/LU M480mg-QDx2-Fasted |
|-----------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 25 | 26 | 11 | 13 |
| Units: participants | | | | |
| Adverse Events | 15 | 13 | 10 | 9 |
| Serious Adverse Events | 1 | 0 | 0 | 1 |

| End point values | Cohort 1/2-KAF400mg/LU M480mg-QDx3 | Cohort 1/2-Artemether80 mg/LUM480mg | | |
|-----------------------------|------------------------------------|-------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 110 | 110 | | |
| Units: participants | | | | |
| Adverse Events | 74 | 61 | | |
| Serious Adverse Events | 0 | 4 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: KAF156 and Lumefantrine (LUM) Cmax

| | |
|-----------------|---|
| End point title | KAF156 and Lumefantrine (LUM) Cmax ^[3] |
|-----------------|---|

End point description:

Cmax is the maximum observed plasma concentration following drug administration. PK parameters are calculated from plasma concentration-time data using non-compartmental methods. Analyte KAF156 is not applicable for Artemether80mg/LUM480mg arm. Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Run-in Cohort:Pre-dose,1,3,4,5,6,8,24,25,27,28,29,30,32,48,72,168 hours; PK sampling 6-12 years: 3,6,24,48,51,54,72,168 hours; 6 months -< 6 years: 24,48,51,54,72,168 hours; Coartem arm:24,48,68,168 hours.

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: PK Endpoint not analyzed for participants on placebo

| End point values | Run-in Cohort-KAF400mg/LU M240mg-QDx2-Fed | Run-in Cohort-KAF400mg/LU M240mg-QDx2-Fasted | Run-in Cohort-KAF400mg/LU M480mg-QDx2-Fed | Run-in Cohort-KAF400mg/LU M480mg-QDx2-Fasted |
|---|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 11 | 23 | 8 | 13 |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| KAF156 | 1520 (± 27.1) | 1460 (± 26.5) | 1610 (± 17.7) | 1320 (± 24.6) |
| LUM | 11600 (± 59.1) | 7850 (± 64.4) | 25900 (± 51.1) | 10900 (± 86.7) |

| End point values | Cohort 1-KAF400mg/LU M480mg-QDx3 | Cohort 2-KAF400mg/LU M480mg-QDx3 | Cohort 1-Artemether80 mg/LUM480mg | Cohort 2-Artemether80 mg/LUM480mg |
|---|----------------------------------|----------------------------------|-----------------------------------|-----------------------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 65 | 31 | 53 | 31 |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| KAF156 | 1240 (± 60.4) | 741 (± 56.6) | 999 (± 999) | 999 (± 999) |
| LUM | 21300 (± 52.5) | 9020 (± 135.5) | 6510 (± 63.3) | 3300 (± 142) |

Statistical analyses

No statistical analyses for this end point

Secondary: KAF156 and Lumefantrine Area under plasma concentration-time curve from time zero to the last measurable concentration sampling time (AUClast)

| | |
|-----------------|---|
| End point title | KAF156 and Lumefantrine Area under plasma concentration-time curve from time zero to the last measurable concentration sampling time (AUClast) ^[4] |
|-----------------|---|

End point description:

AUC is the area under the plasma concentration-time curve. PK parameters were calculated from plasma concentration-time data using non-compartmental methods. For Cohort 1/2 - Artemether80mg/LUM480mg arms enough plasma samples were not collected to calculate AUC parameters.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Run-in Cohort: Pre-dose, 1, 3, 4, 5, 6, 8, 24, 25, 27, 28, 29, 30, 32, 48, 72, 168 hours; PK sampling 6-12 years: 3, 6, 24, 48, 51, 54, 72, 168 hours; 6 months - < 6 years: 24, 48, 51, 54, 72, 168 hours; Coartem arm: 24, 48, 68, 168 hours.

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: PK Endpoint not analyzed for participants on placebo

| End point values | Run-in Cohort-KAF400mg/LU M240mg-QDx2-Fed | Run-in Cohort-KAF400mg/LU M240mg-QDx2-Fasted | Run-in Cohort-KAF400mg/LU M480mg-QDx2-Fed | Run-in Cohort-KAF400mg/LU M480mg-QDx2-Fasted |
|---|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 11 | 23 | 8 | 13 |
| Units: h*ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| KAF156 | 45900 (± 21.2) | 44100 (± 30.7) | 53000 (± 29.1) | 44000 (± 27.4) |
| LUM | 389000 (± 60.4) | 207000 (± 86.5) | 934000 (± 49.7) | 342000 (± 80.3) |

| End point values | Cohort 1-KAF400mg/LU M480mg-QDx3 | Cohort 2-KAF400mg/LU M480mg-QDx3Edit | | |
|---|----------------------------------|--------------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 65 | 31 | | |
| Units: h*ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| KAF156 | 44100 (± 66.8) | 25600 (± 71.6) | | |
| LUM | 970000 (± 59.6) | 383000 (± 182.1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: KAF156 and Lumefantrine time to reach the maximum plasma concentration after drug administration (Tmax)

| | |
|-----------------|--|
| End point title | KAF156 and Lumefantrine time to reach the maximum plasma concentration after drug administration (Tmax) ^[5] |
|-----------------|--|

End point description:

Tmax is the time to reach maximum plasma concentration following drug administration. PK parameters are calculated from plasma concentration-time data using non-compartmental methods. For Cohort 1/2 -Artemether80mg/LUM480mg arms enough plasma samples were not collected to calculate Tmax parameter.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Run-in Cohort:Pre-dose,1,3,4,5,6,8,24,25,27,28,29,30,32,48,72,168 hours; PK sampling 6-12 years: 3,6,24,48,51,54,72,168 hours; 6 months -< 6 years: 24,48,51,54,72,168 hours; Coartem arm:24,48,68,168 hours.

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: PK Endpoint not analyzed for participants on placebo

| End point values | Run-in Cohort-KAF400mg/LU M240mg-QDx2-Fed | Run-in Cohort-KAF400mg/LU M240mg-QDx2-Fasted | Run-in Cohort-KAF400mg/LU M480mg-QDx2-Fed | Run-in Cohort-KAF400mg/LU M480mg-QDx2-Fasted |
|-------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 11 | 23 | 8 | 13 |
| Units: hours | | | | |
| median (full range (min-max)) | | | | |
| KAF156 | 3.92 (2.65 to 7.93) | 3.58 (1.35 to 5.88) | 4.46 (3.87 to 5.97) | 4.18 (2.85 to 7.98) |
| LUM | 7.67 (4.02 to 8.12) | 7.7 (0.967 to 8.23) | 7.02 (5.9 to 24.1) | 6.05 (5.05 to 24.2) |

| End point values | Cohort 1-KAF400mg/LU M480mg-QDx3 | Cohort 2-KAF400mg/LU M480mg-QDx3 | | |
|-------------------------------|----------------------------------|----------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 65 | 31 | | |
| Units: hours | | | | |
| median (full range (min-max)) | | | | |
| KAF156 | 3.03 (0 to 23.5) | 2.95 (0 to 23.5) | | |
| LUM | 5.97 (0 to 23.9) | 6.02 (0 to 24.4) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: KAF156 and Lumefantrine plasma drug concentration 168 hours post first dose administration (C168h)

| | |
|-----------------|---|
| End point title | KAF156 and Lumefantrine plasma drug concentration 168 hours post first dose administration (C168h) ^[6] |
|-----------------|---|

End point description:

C168h is the plasma concentration at 168h post first dose administration. PK parameters are calculated from plasma concentration-time data using non-compartmental methods. Analyte KAF156 is not applicable for Artemether80mg/LUM480mg arm. Due to EudraCT system limitations, data fields in the table cannot contain letters (eg. NA indicating 'not applicable'). Therefore, not applicable values are indicated as '999'.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

at 168 hours

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: PK Endpoint not analyzed for participants on placebo

| End point values | Run-in Cohort- KAF400mg/LU M240mg- QDx2-Fed | Run-in Cohort- KAF400mg/LU M240mg- QDx2-Fasted | Run-in Cohort- KAF400mg/LU M480mg- QDx2-Fed | Run-in Cohort- KAF400mg/LU M480mg- QDx2-Fasted |
|---|--|---|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 11 | 23 | 8 | 13 |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| KAF156 | 23.9 (± 38.7) | 21.8 (± 62.5) | 14.9 (± 62.7) | 25.3 (± 55.9) |
| LUM | 429 (± 50.1) | 189 (± 106.1) | 679 (± 36.5) | 332 (± 73.5) |

| End point values | Cohort 2- KAF400mg/LU M480mg-QDx3 | Cohort 1- KAF400mg/LU M480mg-QDx3 | Cohort 1- Artemether80 mg/LUM480mg | Cohort 2- Artemether80 mg/LUM480mg |
|---|---|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 31 | 68 | 65 | 35 |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| KAF156 | 11 (± 87.5) | 24.8 (± 120.8) | 999 (± 999) | 999 (± 999) |
| LUM | 574 (± 135.8) | 1320 (± 92.4) | 438 (± 80.9) | 297 (± 89.1) |

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 up to a maximum duration of approximately 43 days.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 27.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|----------------------------|
| Reporting group title | KAF400mg/LUM240mg-QDx2-Fed |
|-----------------------|----------------------------|

Reporting group description:

KAF400mg/LUM240mg-QDx2-Fed

| | |
|-----------------------|---------|
| Reporting group title | Coartem |
|-----------------------|---------|

Reporting group description:

Coartem

| | |
|-----------------------|-------------------------------|
| Reporting group title | KAF400mg/LUM480mg-QDx2-Fasted |
|-----------------------|-------------------------------|

Reporting group description:

KAF400mg/LUM480mg-QDx2-Fasted

| | |
|-----------------------|------------------------|
| Reporting group title | KAF400mg/LUM480mg-QDx3 |
|-----------------------|------------------------|

Reporting group description:

KAF400mg/LUM480mg-QDx3

| | |
|-----------------------|-------------------------------|
| Reporting group title | KAF400mg/LUM240mg-QDx2-Fasted |
|-----------------------|-------------------------------|

Reporting group description:

KAF400mg/LUM240mg-QDx2-Fasted

| | |
|-----------------------|----------------------------|
| Reporting group title | KAF400mg/LUM480mg-QDx2-Fed |
|-----------------------|----------------------------|

Reporting group description:

KAF400mg/LUM480mg-QDx2-Fed

| Serious adverse events | KAF400mg/LUM240mg-QDx2-Fed | Coartem | KAF400mg/LUM480mg-QDx2-Fasted |
|---|----------------------------|-----------------|-------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | 4 / 110 (3.64%) | 1 / 13 (7.69%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Investigations | | | |
| Liver function test increased | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 2 / 110 (1.82%) | 0 / 13 (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 |
| Blood bilirubin increased | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 1 / 25 (4.00%) | 1 / 110 (0.91%) | 1 / 13 (7.69%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 25 (0.00%) | 1 / 110 (0.91%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | KAF400mg/LUM480 mg-QDx3 | KAF400mg/LUM240 mg-QDx2-Fasted | KAF400mg/LUM480 mg-QDx2-Fed |
|---|-------------------------|--------------------------------|-----------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 110 (0.00%) | 0 / 26 (0.00%) | 0 / 11 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Investigations | | | |
| Liver function test increased | | | |
| subjects affected / exposed | 0 / 110 (0.00%) | 0 / 26 (0.00%) | 0 / 11 (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 bilirubin increased | | | |
| subjects affected / exposed | 0 / 110 (0.00%) | 0 / 26 (0.00%) | 0 / 11 (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 | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 110 (0.00%) | 0 / 26 (0.00%) | 0 / 11 (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 |

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

| Non-serious adverse events | KAF400mg/LUM240 mg-QDx2-Fed | Coartem | KAF400mg/LUM480 mg-QDx2-Fasted |
|---|-----------------------------|-------------------|--------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 12 / 25 (48.00%) | 55 / 110 (50.00%) | 9 / 13 (69.23%) |
| Investigations | | | |

| | | | |
|--|----------------------|-------------------------|----------------------|
| Bilirubin conjugated increased subjects affected / exposed occurrences (all) | 0 / 25 (0.00%) 0 | 0 / 110 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Blood alkaline phosphatase increased subjects affected / exposed occurrences (all) | 0 / 25 (0.00%) 0 | 0 / 110 (0.00%) 0 | 1 / 13 (7.69%) 1 |
| Blood bilirubin increased subjects affected / exposed occurrences (all) | 2 / 25 (8.00%) 2 | 0 / 110 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Electrocardiogram QT prolonged subjects affected / exposed occurrences (all) | 3 / 25 (12.00%) 3 | 6 / 110 (5.45%) 6 | 1 / 13 (7.69%) 1 |
| Heart rate decreased subjects affected / exposed occurrences (all) | 0 / 25 (0.00%) 0 | 0 / 110 (0.00%) 0 | 1 / 13 (7.69%) 1 |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 2 / 25 (8.00%) 2 | 1 / 110 (0.91%) 1 | 3 / 13 (23.08%) 3 |
| Blood and lymphatic system disorders Thrombocytopenia subjects affected / exposed occurrences (all) | 0 / 25 (0.00%) 0 | 1 / 110 (0.91%) 1 | 1 / 13 (7.69%) 1 |
| Anaemia subjects affected / exposed occurrences (all) | 0 / 25 (0.00%) 0 | 6 / 110 (5.45%) 6 | 1 / 13 (7.69%) 1 |
| General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all) | 2 / 25 (8.00%) 2 | 12 / 110 (10.91%) 12 | 3 / 13 (23.08%) 3 |
| Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 1 | 0 / 110 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Diarrhoea | | | |

| | | | |
|--|----------------------|-------------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 25 (0.00%) 0 | 3 / 110 (2.73%) 3 | 1 / 13 (7.69%) 1 |
| Nausea subjects affected / exposed occurrences (all) | 0 / 25 (0.00%) 0 | 0 / 110 (0.00%) 0 | 2 / 13 (15.38%) 2 |
| Toothache subjects affected / exposed occurrences (all) | 0 / 25 (0.00%) 0 | 0 / 110 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Vomiting subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 1 | 12 / 110 (10.91%) 12 | 0 / 13 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 0 / 25 (0.00%) 0 | 4 / 110 (3.64%) 4 | 1 / 13 (7.69%) 1 |
| Skin and subcutaneous tissue disorders Urticaria subjects affected / exposed occurrences (all) | 0 / 25 (0.00%) 0 | 0 / 110 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Infections and infestations Furuncle subjects affected / exposed occurrences (all) | 0 / 25 (0.00%) 0 | 0 / 110 (0.00%) 0 | 1 / 13 (7.69%) 1 |
| Conjunctivitis subjects affected / exposed occurrences (all) | 0 / 25 (0.00%) 0 | 0 / 110 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Malaria subjects affected / exposed occurrences (all) | 6 / 25 (24.00%) 6 | 15 / 110 (13.64%) 15 | 3 / 13 (23.08%) 3 |
| Schistosomiasis subjects affected / exposed occurrences (all) | 0 / 25 (0.00%) 0 | 1 / 110 (0.91%) 1 | 1 / 13 (7.69%) 1 |
| Metabolism and nutrition disorders Hypokalaemia subjects affected / exposed occurrences (all) | 1 / 25 (4.00%) 1 | 16 / 110 (14.55%) 19 | 0 / 13 (0.00%) 0 |

| Non-serious adverse events | KAF400mg/LUM480 mg-QDx3 | KAF400mg/LUM240 mg-QDx2-Fasted | KAF400mg/LUM480 mg-QDx2-Fed |
|---|----------------------------|-----------------------------------|--------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 69 / 110 (62.73%) | 12 / 26 (46.15%) | 10 / 11 (90.91%) |
| Investigations | | | |
| Bilirubin conjugated increased | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | 0 / 26 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 0 | 1 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 0 / 110 (0.00%) | 1 / 26 (3.85%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | 0 / 26 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 18 / 110 (16.36%) | 1 / 26 (3.85%) | 4 / 11 (36.36%) |
| occurrences (all) | 18 | 1 | 6 |
| Heart rate decreased | | | |
| subjects affected / exposed | 0 / 110 (0.00%) | 0 / 26 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | 0 / 26 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 2 / 110 (1.82%) | 0 / 26 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Anaemia | | | |
| subjects affected / exposed | 5 / 110 (4.55%) | 1 / 26 (3.85%) | 1 / 11 (9.09%) |
| occurrences (all) | 5 | 1 | 1 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 16 / 110 (14.55%) | 1 / 26 (3.85%) | 2 / 11 (18.18%) |
| occurrences (all) | 16 | 1 | 2 |
| Gastrointestinal disorders | | | |

| | | | |
|--|-------------------------|----------------------|----------------------|
| Abdominal pain upper subjects affected / exposed occurrences (all) | 0 / 110 (0.00%) 0 | 2 / 26 (7.69%) 2 | 0 / 11 (0.00%) 0 |
| Diarrhoea subjects affected / exposed occurrences (all) | 2 / 110 (1.82%) 2 | 0 / 26 (0.00%) 0 | 1 / 11 (9.09%) 1 |
| Nausea subjects affected / exposed occurrences (all) | 0 / 110 (0.00%) 0 | 0 / 26 (0.00%) 0 | 0 / 11 (0.00%) 0 |
| Toothache subjects affected / exposed occurrences (all) | 0 / 110 (0.00%) 0 | 0 / 26 (0.00%) 0 | 1 / 11 (9.09%) 1 |
| Vomiting subjects affected / exposed occurrences (all) | 32 / 110 (29.09%) 32 | 2 / 26 (7.69%) 2 | 1 / 11 (9.09%) 1 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 6 / 110 (5.45%) 6 | 1 / 26 (3.85%) 1 | 0 / 11 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Urticaria subjects affected / exposed occurrences (all) | 0 / 110 (0.00%) 0 | 0 / 26 (0.00%) 0 | 1 / 11 (9.09%) 1 |
| Infections and infestations Furuncle subjects affected / exposed occurrences (all) | 0 / 110 (0.00%) 0 | 0 / 26 (0.00%) 0 | 0 / 11 (0.00%) 0 |
| Conjunctivitis subjects affected / exposed occurrences (all) | 0 / 110 (0.00%) 0 | 0 / 26 (0.00%) 0 | 1 / 11 (9.09%) 1 |
| Malaria subjects affected / exposed occurrences (all) | 13 / 110 (11.82%) 13 | 5 / 26 (19.23%) 6 | 6 / 11 (54.55%) 7 |
| Schistosomiasis subjects affected / exposed occurrences (all) | 0 / 110 (0.00%) 0 | 0 / 26 (0.00%) 0 | 1 / 11 (9.09%) 1 |

| | | | |
|------------------------------------|-------------------|----------------|----------------|
| Metabolism and nutrition disorders | | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 27 / 110 (24.55%) | 1 / 26 (3.85%) | 0 / 11 (0.00%) |
| occurrences (all) | 29 | 1 | 0 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|--------------|---|
| 29 July 2021 | Changes have been implemented due to the availability of data from another ongoing study (CKAF156A2202). The changes are related to safety and efficacy data of KAF156 combined with LUM-SDF in pediatric patients (2 to <12 years of age). |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported