To Evaluate Efficacy, Safety, Tolerability and PK of Intravenous Cipargamin in Participants With Severe Plasmodium Falciparum Malaria

Last Update: May 30, 2025

An Adaptive, Randomized, Active-controlled, Open-label, Sequential Cohort, Multicenter Study to Evaluate the Efficacy, Safety, Tolerability and Pharmacokinetics of Intravenous Cipargamin (KAE609) in Adult and Pediatric Participants With Severe Plasmodium Falciparum Malaria (KARISMA - KAE609's Role In Severe Malaria)

ClinicalTrials.gov Identifier:
NCT04675931

Novartis Reference Number:CKAE609B12201

See if you Pre-qualify

All compounds are either investigational or being studied for (a) new use(s). Efficacy and safety have not been established. There is no guarantee that they will become commercially available for the use(s) under investigation.

Study Description

The purpose of this study is to identify the safe and effective dose of intravenous cipargamin in participants with moderately severe and severe malaria.

The study also intends to evaluate clinical treatment success using a novel clinical endpoint for drug development in severe malaria.

Severe malaria is a medical emergency and is affecting primarily young children in Africa. Injectable artesunate is the standard of care for the treatment of severe malaria and is highly efficacious. However, the spread of artemisinin-resistance in Plasmodium falciparum in Asian countries poses a threat for future treatment of patients with this life-threatening disease. To mitigate this risk, there is a need of another drug in malaria endemic countries. Cipargamin treatment results in rapid clearance of parasites including artemisinin resistant parasites.

Condition
Severe Malaria
Phase
Phase2
Overall Status
Recruiting
Number of Participants
252
Start Date
Mar 07, 2022
Completion Date
Sep 26, 2025
Gender

All
Age(s)
6 Years - 100 Years (Child, Adult, Older Adult)

Interventions

Drug

Coartem

Oral Standard of Care
Drug

IV Artesunate

Parenteral artesunate is the WHO recommended first line treatment for severe malaria. Hence IV artesunate is used as comparator. Also, this will be used as rescue medication for participants where IV KAE609 is not working.
Drug

KAE609

Two doses of Intravenous Cipargamin will be evaluated in the initial phase of the study (Cohorts 1-2). These doses will cover a wider exposure range and facilitate the selection of an appropriate dose for later Cohorts 3-5.

Eligibility Criteria

Inclusion Criteria:

* Cohort 1: Participants aged ≥ 12 years with moderately severe malaria as defined in (prostration and/or repeated vomiting) without presence of other signs of severe malaria (and with high P. falciparum parasitemia (60,000-250,000 parasites per µl)

* Subsequent Cohorts 2 to 5: Participants diagnosed with severe malaria as defined in modified version of WHO criteria and P. falciparum parasite count of ≥ 5000 per µl
* Cohort 2: Participants aged ≥ 12 years
* Cohort 3: Participants aged 6 - \< 12 years
* Cohort 4: Participants aged 2 - \< 6 years
* Cohort 5: Participants aged ≥ 6 months - \< 2 years

Exclusion Criteria:

Exclusion criteria applying to all Cohorts 1 to 5:

* Mixed Plasmodium infections
* Treatment with quinine or artemisinin derivative or any other antimalarial drug or any antibiotic with known antimalarial activity within 12 hours of screening.
* Signs/symptoms of severe malnutrition in general accordance with WHO guidelines:

1. Under 18 years: \<-3 Z-scores of WHO growth standard for weight-for-height/length (in children \< 5 years)

or BMI for age (5-18 years), or very low mid-upper arm circumference (MUAC \< 115 mm in children \< 12 years, \< 160mm 12-18 years), or bilateral pitting edema
2. Over 18 years: BMI \< 16 kg/m2 or MUAC \< 160mm or bilateral pitting edema
* Known underlying illness, surgical or medical condition, which is not related to ongoing event of severe malaria and which might jeopardize the participant's health in case of participation in the study or which might alter the distribution, metabolism or excretion of study treatment. For example:

1. neurological or neurodegenerative disorders,
2. cardiac, renal, or hepatic disease, diabetes,
3. epilepsy, cerebral palsy,
4. known or suspected to be HIV-1 positive and/or receiving antiretroviral treatment
5. malignancy of any organ system (other than localized basal cell carcinoma of the skin or in situ cervical cancer), treated or untreated, within the past 5 years, regardless of whether there is evidence of local recurrence or metastases
6. known or suspected cases of active infections or concurrent febrile illness such as TB, Typhoid, COVID-19 etc.

Additional exclusion criteria are as follows:

Exclusion criteria for Cohort 1:

* ALT \> 5 x the upper limit of normal range (ULN), regardless the level of total bilirubin
* Total bilirubin is \> 3 mg/dL
* Body weight of \< 35 kg or \>75 kg

Exclusion criteria for Cohort 2:

* Body weight of \< 35 kg or \>75 kg
* Participants diagnosed as moderately severe malaria due to repeated vomiting without presence of any of the symptoms of severe malaria

Exclusion criteria for Cohorts 3 to 5:

* Body weight of \< 5 kg
* Participants diagnosed as moderately severe malaria due to repeated vomiting without presence of any of the symptoms of severe malaria

Burkina Faso

Novartis Investigative Site

Recruiting

Burkina Faso,2208,Burkina Faso

Novartis Investigative Site

Recruiting

Ouagadougou,Burkina Faso

Congo, The Democratic Republic of the

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Recruiting

Kinsasha,Democratic Republic Of Congo,Bp 7948,Congo, The Democratic Republic of the

Côte D'Ivoire

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Recruiting

Abidjan,13bp972,Côte D'Ivoire

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Recruiting

Agboville,Bp 154,Côte D'Ivoire

Gabon

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Recruiting

Lambarene,Bp 242,Gabon

Kenya

Novartis Investigative Site

Recruiting

Siaya,2300,Kenya

Mozambique

Novartis Investigative Site

Recruiting

Manhica,Maputo Province,1929,Mozambique

Nigeria

Novartis Investigative Site

Recruiting

Ilorin,240003,Nigeria

Rwanda

Novartis Investigative Site

Recruiting

Kigali,Bp 4560,Rwanda

Uganda

Novartis Investigative Site

Recruiting

Tororo,10102,Uganda

Worldwide Contacts

If the location of your choosing does not feature any contact detail, please reach out using the information below.

Novartis Pharmaceuticals

Phone: +41613241111
Email: novartis.email@novartis.com

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