



Clinical trial results:

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)

Summary

EudraCT number	2020-005035-70
Trial protocol	Outside EU/EEA
Global end of trial date	20 August 2025

Results information

Result version number	v2 (current)
This version publication date	13 June 2026
First version publication date	07 March 2026
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	CKAE609B12201
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04675931
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	20 August 2025
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	20 August 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to assess the efficacy of intravenous (IV) cipargamin. Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use <https://www.novctrd.com> for complete trial results.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 March 2022
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: 46
Country: Number of subjects enrolled	Congo, The Democratic Republic of the: 19
Country: Number of subjects enrolled	Côte d'Ivoire: 106
Country: Number of subjects enrolled	Kenya: 22
Country: Number of subjects enrolled	Mozambique: 1
Country: Number of subjects enrolled	Rwanda: 47
Country: Number of subjects enrolled	Uganda: 13
Worldwide total number of subjects	254
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	40

months)	
Children (2-11 years)	154
Adolescents (12-17 years)	24
Adults (18-64 years)	36
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

316 participants were screened for the study.

Period 1

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

Blinding implementation details:

Treatment allocation, dose information, PK/AAG assessment schedule and concentration data, as well as other data that could result in systematic unblinding, were not available to the Clinical Trial Team (CTT) (particularly clinicians, trial statisticians, trial programmers) until the database was locked after IA of Cohorts 1-2. After interim database lock, the CTT was unblinded with the results, however, the blinding was continued for Cohorts 3-5 until the final database was locked.

Arms

Are arms mutually exclusive?	Yes
Arm title	IV Cipargamin 20 mg

Arm description:

Participants received intravenous cipargamin 20 mg, as a minimum of two doses every 24 hours, not exceeding 3 doses followed by oral medication (Coartem®, twice daily [b.i.d.] for 3 days).

Arm type	Experimental
Investigational medicinal product name	Cipargamin
Investigational medicinal product code	
Other name	KAE609
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Participants received intravenous cipargamin 20 mg, as a minimum of two doses every 24 hours, not exceeding 3 doses followed by oral medication (Coartem®, twice daily [b.i.d.] for 3 days).

Arm title	IV Cipargamin 40 mg
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Arm description:

Participants received intravenous cipargamin 40 mg, as a minimum of two doses every 24 hours, not exceeding 3 doses followed by oral medication (Coartem®, twice daily [b.i.d.] for 3 days).

Arm type	Experimental
Investigational medicinal product name	Cipargamin
Investigational medicinal product code	
Other name	KAE609
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Participants received intravenous cipargamin 40 mg, as a minimum of two doses every 24 hours, not exceeding 3 doses followed by oral medication (Coartem®, twice daily [b.i.d.] for 3 days).

Arm title	IV Artesunate
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Arm description:

Participants received IV artesunate according to label and followed by oral medication (Coartem® b.i.d. for 3 days).

Arm type	Active comparator
Investigational medicinal product name	Artesunate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Participants received IV artesunate according to label and followed by oral medication (Coartem® b.i.d. for 3 days).

Number of subjects in period 1^[1]	IV Cipargamin 20 mg	IV Cipargamin 40 mg	IV Artesunate
Started	20	114	117
Completed	20	114	116
Not completed	0	0	1
Lost to follow-up	-	-	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The patients randomized to IV Cipargamin 40 mg and one patient randomized to IV Artesunate discontinued the study before receiving any dose of study treatment.

Baseline characteristics

Reporting groups

Reporting group title	IV Cipargamin 20 mg
Reporting group description:	
Participants received intravenous cipargamin 20 mg, as a minimum of two doses every 24 hours, not exceeding 3 doses followed by oral medication (Coartem®, twice daily [b.i.d.] for 3 days).	
Reporting group title	IV Cipargamin 40 mg
Reporting group description:	
Participants received intravenous cipargamin 40 mg, as a minimum of two doses every 24 hours, not exceeding 3 doses followed by oral medication (Coartem®, twice daily [b.i.d.] for 3 days).	
Reporting group title	IV Artesunate
Reporting group description:	
Participants received IV artesunate according to label and followed by oral medication (Coartem® b.i.d. for 3 days).	

Reporting group values	IV Cipargamin 20 mg	IV Cipargamin 40 mg	IV Artesunate
Number of subjects	20	114	117
Age Categorical			
Units: participants			
6 months to < 2 years	0	21	18
2 to <6 years	0	37	39
6 to <12 years	0	38	40
12 to <18 years	9	7	7
18 to <65 years	11	11	13
Age Continuous			
Units: years			
arithmetic mean	22.7	7.7	8.6
standard deviation	± 10.07	± 7.81	± 9.13
Sex: Female, Male			
Units: participants			
Female	9	49	64
Male	11	65	53
Race			
Units: Subjects			
Black or African American	20	114	117

Reporting group values	Total		
Number of subjects	251		
Age Categorical			
Units: participants			
6 months to < 2 years	39		
2 to <6 years	76		
6 to <12 years	78		
12 to <18 years	23		
18 to <65 years	35		
Age Continuous			
Units: years			
arithmetic mean			

standard deviation	-		
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Sex: Female, Male			
Units: participants			
Female	122		
Male	129		
Race			
Units: Subjects			
Black or African American	251		

End points

End points reporting groups

Reporting group title	IV Cipargamin 20 mg
Reporting group description: Participants received intravenous cipargamin 20 mg, as a minimum of two doses every 24 hours, not exceeding 3 doses followed by oral medication (Coartem®, twice daily [b.i.d.] for 3 days).	
Reporting group title	IV Cipargamin 40 mg
Reporting group description: Participants received intravenous cipargamin 40 mg, as a minimum of two doses every 24 hours, not exceeding 3 doses followed by oral medication (Coartem®, twice daily [b.i.d.] for 3 days).	
Reporting group title	IV Artesunate
Reporting group description: Participants received IV artesunate according to label and followed by oral medication (Coartem® b.i.d. for 3 days).	

Primary: Percentage of Participants Achieving at Least 90% Reduction in Plasmodium falciparum (P. falciparum) at 12 Hours

End point title	Percentage of Participants Achieving at Least 90% Reduction in Plasmodium falciparum (P. falciparum) at 12 Hours ^[1]
End point description: A blood draw was performed at each collection time point for parasitemia assessment.	
End point type	Primary
End point timeframe: 12 Hours	
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 primary outcome.	

End point values	IV Cipargamin 20 mg	IV Cipargamin 40 mg	IV Artesunate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	114	117	
Units: percentage of participants				
number (not applicable)	80.0	93.0	39.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving Clinical Success at 48 Hours

End point title	Percentage of Participants Achieving Clinical Success at 48 Hours
End point description: Clinical success was a composite endpoint based on following criteria: 1. Was participant dead or alive 2. Presence of asexual parasites (yes/no) 3. Presence of any of the key signs of severe malaria (yes/no)	

End point type	Secondary
End point timeframe:	
48 Hours	

End point values	IV Cipargamin 20 mg	IV Cipargamin 40 mg	IV Artesunate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	114	117	
Units: percentage of participants				
number (confidence interval 90%)	95.0 (78.4 to 99.7)	85.1 (78.5 to 90.3)	74.4 (66.9 to 80.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Individual Signs of Severe Malaria Over Time

End point title	Percentage of Participants With Individual Signs of Severe Malaria Over Time
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End point description:

Individual signs of severe malaria over time were monitored for the presence of the following signs of severe malaria during the entire study duration:

1. Altered consciousness - Prostration or GCS < 11 for participants > 5 years / BCS < 3 for participants =< 5 years of age
2. Renal Impairment - Serum creatinine > 3xULN or > 3 mg/dL or need for renal replacement therapy
3. Acidosis - Serum lactate > 4 mmol/L
4. Respiratory distress - present or absent
5. Severe anemia - Hb < 5 g/dl or Hb < 7g/dl in pediatric and adults respectively or need of blood transfusion
6. Jaundice - Serum bilirubin > 3 g/dl
7. Hypoglycemia- plasma glucose < 40 mg/dL

End point type	Secondary
End point timeframe:	
Baseline to Day 29	

End point values	IV Cipargamin 20 mg	IV Cipargamin 40 mg	IV Artesunate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	114	117	
Units: percentage of participants				
number (not applicable)				
Baseline, at Least One Sign	95.0	98.2	100.0	
Baseline, at Least Two Signs	35.0	43.9	45.3	
Baseline, at Least Three Signs	10.0	14.0	17.9	
Baseline, at Least Four Signs	0	3.5	10.3	
Baseline, at Least Five Signs	0	0.9	4.3	
Baseline, at Least Six Signs	0	0	0.9	

Day 29, at Least One Sign	5.0	6.2	7.0	
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Developing Hemolysis (Early and Delayed) After Treatment

End point title	Percentage of Participants Developing Hemolysis (Early and Delayed) After Treatment
End point description: Development (early and delayed) of hemolysis after treatments was defined as follows: Early Hemolytic anemia was defined as 10% or greater decrease in hemoglobin levels and an increase of lactate dehydrogenase (LDH) levels to >390 U/L, or an increase of $\geq 10\%$ above baseline occurring up to Day 8 of the study. Delayed hemolytic anemia occurred > 7 days after initiation of parenteral study drug (IV artesunate or IV cipargamin) during the study period. The event was characterized by a 10% or greater decrease in hemoglobin levels accompanied by increase of LDH levels to >390 U/L, or an increase of $\geq 10\%$ compared to the values measured at Day 8 of the study.	
End point type	Secondary
End point timeframe: Day 8 and Day 29	

End point values	IV Cipargamin 20 mg	IV Cipargamin 40 mg	IV Artesunate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	114	117	
Units: percentage of participants				
number (not applicable)				
Early Hemolysis	55.0	54.4	62.1	
Delayed Hemolysis	5.0	3.5	3.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Neurological Sequelae at Day 29

End point title	Percentage of Participants With Neurological Sequelae at Day 29
End point description: Detailed neurological examination was conducted and relevant medical history collected to assess the extent of neurological signs and symptoms at baseline and to monitor the extent of neurological sequelae in follow-up visits.	
End point type	Secondary

End point timeframe:

Day 29

End point values	IV Cipargamin 20 mg	IV Cipargamin 40 mg	IV Artesunate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	113	115	
Units: percentage of participants				
number (not applicable)				
Speech Impairment	0	0	0.9	
Hemiplegia or Hemiparesis	0	0	0.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving at Least 90% Reduction in Plasmodium falciparum (P. falciparum)

End point title	Percentage of Participants Achieving at Least 90% Reduction in Plasmodium falciparum (P. falciparum)
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End point description:

A blood draw was performed at each collection time point for parasitemia assessment.

End point type	Secondary
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End point timeframe:

24 hours and 48 hours

End point values	IV Cipargamin 20 mg	IV Cipargamin 40 mg	IV Artesunate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	114	117	
Units: percentage of participants				
number (not applicable)				
24 Hours Post-Dose	90.0	100.0	97.4	
48 Hours Post-Dose	100.0	100.0	99.1	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Parasite Clearance (PCT)

End point title	Time to Parasite Clearance (PCT)
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End point description:

Parasite clearance time (PCT) was 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 24 hours.

End point type	Secondary
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End point timeframe:

Up to 72 hours

End point values	IV Cipargamin 20 mg	IV Cipargamin 40 mg	IV Artesunate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	113	116	
Units: hours				
median (confidence interval 95%)	21.1 (18.0 to 24.8)	18.0 (12.2 to 18.2)	36.0 (30.0 to 36.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Parasite Clearance Estimator (PCE) Slope Half-life

End point title	Parasite Clearance Estimator (PCE) Slope Half-life
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End point description:

Slope half-life (hours) for parasite clearance was calculated for each patient using the WWARN (World Wide Antimalarial Resistance Network) Parasite Clearance Estimator.

End point type	Secondary
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End point timeframe:

Up to 72 hours

End point values	IV Cipargamin 20 mg	IV Cipargamin 40 mg	IV Artesunate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	108	114	
Units: hours				
median (full range (min-max))	1.63 (0.22 to 3.61)	1.10 (0.27 to 10.03)	2.21 (0.65 to 10.75)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Fever Clearance (FCT)

End point title	Time to Fever Clearance (FCT)
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End point description:

Fever clearance time (FCT) was 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.

End point type	Secondary
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End point timeframe:

Up to 72 hours

End point values	IV Cipargamin 20 mg	IV Cipargamin 40 mg	IV Artesunate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	28	39	
Units: hours				
median (confidence interval 95%)	6.2 (6.1 to 18.0)	6.1 (0.6 to 11.7)	17.8 (6.1 to 18.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: P. falciparum Parasite Reduction Ratios (PRR) at 12, 24 and 48 Hours

End point title	P. falciparum Parasite Reduction Ratios (PRR) at 12, 24 and 48 Hours
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End point description:

PRR was defined as the ratio of asexual parasite at baseline divided by asexual parasite at post-baseline. If the asexual parasite count at post-baseline was 0, the half value of detection limit was used to calculate the ratio.

End point type	Secondary
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End point timeframe:

12 hours, 24 hours, and 48 hours

End point values	IV Cipargamin 20 mg	IV Cipargamin 40 mg	IV Artesunate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	114	116	
Units: ratio				
median (full range (min-max))				
12 Hours n=20,114,116	203.2 (1.4 to 8737.4)	1347.8 (2.4 to 48092.3)	7.5 (1.0 to 9582.8)	
24 Hours n=20,114,116	3772.6 (4.8 to 18744.9)	4092.5 (25.1 to 48092.3)	560.6 (4.7 to 25525.9)	
48 Hours n=20,113,116	6220.5 (560.6 to 31097.8)	7175.1 (292.0 to 51495.5)	5509.1 (58.1 to 72470.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Recrudescence and Reinfection

End point title	Percentage of Participants With Recrudescence and Reinfection
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End point description:

Recrudescence was defined as appearance of asexual parasites after clearance of initial infection with a genotype identical to that of parasites present at baseline. Reinfection was defined as appearance of asexual parasites after clearance of initial infection with a genotype different from those parasites present at baseline. Reinfection and Recrudescence were confirmed by polymerase chain reaction (PCR) analysis.

End point type	Secondary
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End point timeframe:

Day 29

End point values	IV Cipargamin 20 mg	IV Cipargamin 40 mg	IV Artesunate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	112	114	
Units: percentage of participants				
number (not applicable)				
Recrudescence	0	2.7	1.8	
Reinfection	0	8.0	7.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Switch to Oral Therapy

End point title	Time to Switch to Oral Therapy
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End point description:

Time to switch participants from IV therapy to Coartem (standard of drug for oral therapy) was analyzed.

End point type	Secondary
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End point timeframe:

Day 3 to Day 29

End point values	IV Cipargamin 20 mg	IV Cipargamin 40 mg	IV Artesunate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	114	117	
Units: hours				
median (confidence interval 95%)	43.9 (41.6 to 46.9)	43.3 (42.3 to 44.2)	44.4 (43.6 to 44.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Recover From Prostration

End point title	Time to Recover From Prostration
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End point description:

To assess recovery of participants as measured by time to recovery from prostration compared to baseline.

End point type	Secondary
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End point timeframe:

Day 1 to Day 29

End point values	IV Cipargamin 20 mg	IV Cipargamin 40 mg	IV Artesunate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	109	116	
Units: hours				
median (confidence interval 95%)	18.2 (12.3 to 24.4)	12.4 (12.1 to 18.2)	18.3 (17.8 to 23.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Discharge From Hospital

End point title	Time to Discharge From Hospital
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End point description:

End point type	Secondary
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End point timeframe:

Day 3 to Day 29

End point values	IV Cipargamin 20 mg	IV Cipargamin 40 mg	IV Artesunate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	114	116	
Units: hours				
median (confidence interval 95%)	73.2 (73.0 to 73.6)	73.1 (72.9 to 73.2)	73.1 (72.9 to 73.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Observed Maximum Plasma Concentration (Cmax) of IV Cipargamin

End point title	Observed Maximum Plasma Concentration (Cmax) of IV Cipargamin ^[2]
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End point description:

Blood samples were collected for pharmacokinetics characterization. Cmax is the maximum (peak) observed plasma concentration of cipargamin after dose administration. Cmax was listed and summarized using descriptive statistics.

End point type	Secondary
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End point timeframe:

Day 1 - Day 8

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: Data are reported for applicable reporting groups.

End point values	IV Cipargamin 20 mg	IV Cipargamin 40 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	55		
Units: ng/mL				
geometric mean (confidence interval 90%)				
Dose 1 n=18,55	1350 (1150 to 1570)	3230 (2870 to 3630)		
Dose 2 n=20,55	1390 (1150 to 1690)	3420 (3020 to 3880)		
Dose 3 n=3,1	1160 (553 to 2430)	2720 (999 to 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Adverse Events or Serious Adverse Events, or Who Died

End point title	Number of Participants With Adverse Events or Serious Adverse Events, or Who Died
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End point description:

Adverse events (AEs) and serious adverse events (SAEs) were collected from first dosing. Death routine laboratory assessments were assessed up to last follow-up visit or until the event had resolved to baseline grade or better, or the event was assessed stable by the investigator, or the participant was lost to follow-up or withdrew consent.

End point type Secondary

End point timeframe:

Day 1 to Day 29

End point values	IV Cipargamin 20 mg	IV Cipargamin 40 mg	IV Artesunate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	114	117	
Units: participants				
AEs	12	79	73	
SAEs	0	5	4	
Deaths	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Time of Maximum Observed Drug Concentration Occurrence (Tmax) of IV Cipargamin

End point title Time of Maximum Observed Drug Concentration Occurrence (Tmax) of IV Cipargamin^[3]

End point description:

Blood samples were collected for pharmacokinetics characterization. Tmax was listed and summarized using descriptive statistics. Time to reach maximum observed plasma concentration of cipargamin after dose administration.

End point type Secondary

End point timeframe:

Day 1 - Day 8

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: Data are reported for applicable reporting groups.

End point values	IV Cipargamin 20 mg	IV Cipargamin 40 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	55		
Units: hours				
geometric mean (confidence interval 90%)				
Dose 1 n=18,55	0.099 (0.073 to 0.135)	0.106 (0.089 to 0.125)		
Dose 2 n=20,55	0.221 (0.133 to 0.366)	0.158 (0.116 to 0.216)		

Dose 3 n=3,1	0.141 (0.007 to 2.79)	0.05 (-999 to 999)		
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Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Serum Concentration-time Curve From Time Zero to the Time of Last Quantifiable Concentration (AUClast) of IV Cipargamin

End point title	Area Under the Serum Concentration-time Curve From Time Zero to the Time of Last Quantifiable Concentration (AUClast) of IV Cipargamin ^[4]
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End point description:

Blood samples were collected for pharmacokinetics characterization. AUClast was listed and summarized using descriptive statistics.

End point type	Secondary
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End point timeframe:

Day 1 - Day 8

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: Data are reported for applicable reporting groups.

End point values	IV Cipargamin 20 mg	IV Cipargamin 40 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	55		
Units: h*ng/mL				
geometric mean (confidence interval 90%)				
Dose 1 n=18,55	8150 (6930 to 9580)	18800 (16900 to 21000)		
Dose 2 n=19,55	19100 (16100 to 22800)	38700 (34700 to 43100)		
Dose 3 n=3,1	18600 (6330 to 54400)	40400 (999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration Time Curve From Time Zero (Pre-dose) Extrapolated to Infinite Time (AUCinf) of IV Cipargamin

End point title	Area Under the Concentration Time Curve From Time Zero (Pre-dose) Extrapolated to Infinite Time (AUCinf) of IV Cipargamin ^[5]
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End point description:

Blood samples were collected for pharmacokinetics characterization. AUC(0-inf) post last dose was listed and summarized using descriptive statistics.

End point type	Secondary
End point timeframe:	
Day 1 - Day 8	
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: Data are reported for applicable reporting groups.	

End point values	IV Cipargamin 20 mg	IV Cipargamin 40 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	53		
Units: h*ng/mL				
geometric mean (confidence interval 90%)				
Dose 1 n=0,0	999 (999 to 999)	999 (999 to 999)		
Dose 2 n=15,53	21300 (18000 to 25200)	40000 (36000 to 44500)		
Dose 3 n=3,1	18800 (6360 to 55500)	40400 (999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-time Curve From the Time 0 to 24 hours (AUC0-24hours) of IV Cipargamin

End point title	Area Under the Plasma Concentration-time Curve From the Time 0 to 24 hours (AUC0-24hours) of IV Cipargamin ^[6]
End point description:	
Blood samples were collected for pharmacokinetics characterization. AUC(0-24h) was listed and summarized using descriptive statistics.	
End point type	Secondary
End point timeframe:	
Day 1 - Day 8	
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: Data are reported for applicable reporting groups.	

End point values	IV Cipargamin 20 mg	IV Cipargamin 40 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	55		
Units: h*ng/mL				
geometric mean (confidence interval 90%)				
Dose 1 n=18,55	8170 (6950 to 9590)	19200 (17300 to 21300)		
Dose 2 n=19,54	11900 (10700 to 13200)	28500 (25900 to 31400)		

Dose 3 n=3,1	10100 (5800 to 17600)	26500 (999 to 99999)		
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Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Elimination Half Life (T1/2) of IV Cipargamin

End point title	Terminal Elimination Half Life (T1/2) of IV Cipargamin ^[7]
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End point description:

Blood samples were collected for pharmacokinetics characterization. The half-life post last dose was summarized using descriptive statistics.

End point type	Secondary
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End point timeframe:

Day 1 - Day 8

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: Data are reported for applicable reporting groups.

End point values	IV Cipargamin 20 mg	IV Cipargamin 40 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	53		
Units: hours				
geometric mean (confidence interval 90%)				
Dose 1 n=0,0	999 (999 to 999)	999 (999 to 999)		
Dose 2 n=15,53	18 (15.7 to 20.7)	11.6 (10.6 to 12.6)		
Dose 3 n=3,1	16.2 (8.35 to 31.4)	10.8 (-999 to 999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Total Systemic Clearance for Intravenous Administration (CL) of IV Cipargamin

End point title	Total Systemic Clearance for Intravenous Administration (CL) of IV Cipargamin ^[8]
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End point description:

Blood samples were collected for pharmacokinetics characterization. CL post last dose was summarized using descriptive statistics.

End point type	Secondary
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End point timeframe:

Day 1 - Day 8

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: Data are reported for applicable reporting groups.

End point values	IV Cipargamin 20 mg	IV Cipargamin 40 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	53		
Units: L/h				
geometric mean (confidence interval 90%)				
Dose 1 n=0,0	999 (999 to 999)	999 (999 to 999)		
Dose 2 n=15,53	0.939 (0.793 to 1.11)	0.66 (0.576 to 0.755)		
Dose 3 n=3,1	1.06 (0.36 to 3.15)	0.99 (-999 to 999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Volume of Distribution During the Terminal Phase Following Intravenous Elimination (V_z) of IV Cipargamin

End point title	Volume of Distribution During the Terminal Phase Following Intravenous Elimination (V _z) of IV Cipargamin ^[9]
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End point description:

Blood samples were collected for pharmacokinetics characterization. V_z post last dose was listed and summarized using descriptive statistics.

End point type	Secondary
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End point timeframe:

Day 1 - Day 8

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: Data are reported for applicable reporting groups.

End point values	IV Cipargamin 20 mg	IV Cipargamin 40 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	53		
Units: liters				
geometric mean (confidence interval 90%)				
Dose 1 n=0,0	999 (999 to 999)	999 (999 to 999)		
Dose 2 n=15,53	24.5 (21.2 to 28.2)	11 (9.34 to 13)		
Dose 3 n=3,1	24.9 (15 to 41.1)	15.5 (-999 to 999)		

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 29 days post treatment, up to a maximum duration of 36 days.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	28.0
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Reporting groups

Reporting group title	IV Cipargamin 20mg
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Reporting group description:

IV Cipargamin 20mg

Reporting group title	Total
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Reporting group description:

Total

Reporting group title	IV Artesunate
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Reporting group description:

IV Artesunate

Reporting group title	IV Cipargamin 40mg
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Reporting group description:

IV Cipargamin 40mg

Serious adverse events	IV Cipargamin 20mg	Total	IV Artesunate
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	9 / 251 (3.59%)	4 / 117 (3.42%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Haemoglobin decreased			
subjects affected / exposed	0 / 20 (0.00%)	1 / 251 (0.40%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Quadriparesis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 251 (0.40%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			

subjects affected / exposed	0 / 20 (0.00%)	1 / 251 (0.40%)	0 / 117 (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			
Thrombocytopenia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 251 (0.40%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	0 / 20 (0.00%)	3 / 251 (1.20%)	2 / 117 (1.71%)
occurrences causally related to treatment / all	0 / 0	1 / 3	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 20 (0.00%)	1 / 251 (0.40%)	0 / 117 (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
Infections and infestations			
Malaria			
subjects affected / exposed	0 / 20 (0.00%)	2 / 251 (0.80%)	0 / 117 (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
Serious adverse events			
IV Cipargamin 40mg			
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 114 (4.39%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Investigations			
Haemoglobin decreased			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Quadripareisis			

subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	1 / 114 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 114 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anaemia			
subjects affected / exposed	1 / 114 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	1 / 114 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Malaria			
subjects affected / exposed	2 / 114 (1.75%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	IV Cipargamin 20mg	Total	IV Artesunate
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 20 (35.00%)	114 / 251 (45.42%)	50 / 117 (42.74%)
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed occurrences (all)	5 / 20 (25.00%) 5	80 / 251 (31.87%) 81	35 / 117 (29.91%) 36
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2	5 / 251 (1.99%) 5	2 / 117 (1.71%) 2
Infections and infestations Malaria subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Rhinitis subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0 0 / 20 (0.00%) 0 1 / 20 (5.00%) 1	28 / 251 (11.16%) 28 12 / 251 (4.78%) 12 12 / 251 (4.78%) 12	12 / 117 (10.26%) 12 5 / 117 (4.27%) 5 4 / 117 (3.42%) 4

Non-serious adverse events	IV Cipargamin 40mg		
Total subjects affected by non-serious adverse events subjects affected / exposed	57 / 114 (50.00%)		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	40 / 114 (35.09%) 40		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	1 / 114 (0.88%) 1		
Infections and infestations Malaria subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Rhinitis	16 / 114 (14.04%) 16 7 / 114 (6.14%) 7		

subjects affected / exposed	7 / 114 (6.14%)		
occurrences (all)	7		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com for complete trial results.

Notes: