Gametocytocidal and Transmission-blocking Efficacy of PQ in Combination With AL and TQ in Combination With SPAQ in Mali

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON23822

Source
NTR

Brief title
NECTAR3

Health condition

Malaria

Sponsors and support

Primary sponsor: London School of Hygiene and Tropical Medicine
Source(s) of monetary or material Support: Bill & Melinda Gates Foundation

Intervention

Outcome measures

Primary outcome

1. Change in mosquito infection rate assessed through membrane feeding assays (day 2 and

day 7)
Within person percent change (presented as percent reduction) in mosquito infection rate in infectious individuals from baseline (day 0, pre-treatment) to day 2 post treatment in the AL and AL-PQ arms, and day 7 post-treatment in the SPAQ and SPAQ-TQ.

[Time Frame: 3 days (days 0, 2 and 7): 7 day span]

Secondary outcome

2. Change in mosquito infection rate assessed through membrane feeding assays (all timepoints)
Within person percent change (presented as percent reduction) in mosquito infection rate from baseline to all feeding time-points, with comparison within and between arms.

[Time Frame: 7 days (day 0, day 2, day 5, day 7, day 14, day 21, day 28): 28 day span]

3. Mosquito infection rate assessed through membrane feeding assays
Mosquito infection rate at all feeding time-points, with comparison within treatment arms compared to baseline, and between arms.

[Time Frame: 7 days (day 0, day 2, day 5, day 7, day 14, day 21, day 28): 28 day span]

4. Human infectivity to locally reared mosquitoes assessed through membrane feeding assays
Infectivity to mosquitoes at all feeding time-points, with comparison within treatment arms compared to baseline, and between arms.

[Time Frame: 7 days (day 0, day 2, day 5, day 7, day 14, day 21, day 28): 28 day span]

5.Mosquito infection density assessed through membrane feeding assays
Oocyst intensity (in all/all infected mosquitoes) at all feeding time-points, with comparison within treatment arms compared to baseline, and between arms.

[Time Frame: 7 days (day 0, day 2, day 5, day 7, day 14, day 21, day 28): 28 day span]

6. Gametocyte infectivity
Infectiousness to mosquitoes for a given gametocyte density (measured as mosquito infection rate/gametocyte) at all feeding time-points, with comparison within treatment arms compared to baseline, and between arms.

[Time Frame: 7 days (day 0, day 2, day 5, day 7, day 14, day 21, day 28): 28 day span]

7. Asexual/sexual stage parasite prevalence
Male and female gametocyte prevalence at all time-points, determined by microscopy or molecular assays, with comparison within treatment arms compared to baseline, and between arms.

Asexual and total parasite prevalence at all time-points, determined by microscopy or

molecular assays, with comparison within treatment arms compared to baseline, and between arms.

[Time Frame: 7 days (day 0, day 2, day 5, day 7, day 14, day 21, day 28): 28 day span]

8. Asexual/sexual stage parasite density
Male and female gametocyte density at all time-points, determined by microscopy or molecular assays, with comparison within treatment arms compared to baseline, and between arms.

Asexual and total parasite density at all time-points, determined by microscopy or molecular assays, with comparison within treatment arms compared to baseline, and between arms.

[Time Frame: 7 days (day 0, day 2, day 5, day 7, day 14, day 21, day 28): 28 day span]

9. Sexual stage parasite sex ratio
Male and female gametocyte sex ratio (proportion male) at all time-points, determined by microscopy or molecular assays, with comparison within treatment arms compared to baseline, and between arms.

[Time Frame: 7 days (day 0, day 2, day 5, day 7, day 14, day 21, day 28): 28 day span]

10. Sexual stage parasite circulation time
Gametocyte circulation time (cumulative), determined by microscopy or molecular assays, compared within and between treatment arms.

[Time Frame: 7 days (day 0, day 2, day 5, day 7, day 14, day 21, day 28): 28 day span]

11. Sexual stage parasite area under the curve (AUC)
Gametocyte area under the curve (cumulative), determined by microscopy or molecular assays, compared within and between treatment arms.

[Time Frame: 7 days (day 0, day 2, day 5, day 7, day 14, day 21, day 28): 28 day span]

12. Haemoglobin density
Haemoglobin density (g/dL) at all time-points, with comparison within treatment arms compared to baseline, and between arms.

[Time Frame: 8 days (day 0, day 1, day 2, day 5, day 7, day 14, day 21, day 28): 28 day span]

13. Change in haemoglobin density
Within person percent change (presented as percent reduction) in haemoglobin density (g/dL) from baseline to all time-points, with comparison within and between arms.

[Time Frame: 8 days (day 0, day 1, day 2, day 5, day 7, day 14, day 21, day 28): 28 day span]

14. Methaemoglobin density

Methaemoglobin density (g/dL) at all time-points, with comparison within treatment arms compared to baseline, and between arms.

[Time Frame: 8 days (day 0, day 1, day 2, day 5, day 7, day 14, day 21, day 28)]

15. Change in methaemoglobin density
Within person percent change (presented as percent reduction) in methaemoglobin density (g/dL) from baseline to all time-points, with comparison within and between arms.

[Time Frame: 8 days (day 0, day 1, day 2, day 5, day 7, day 14, day 21, day 28): 28 day span]

16. Incidence of adverse events
The frequency and prevalence of adverse events (all AE's, treatment related AE's, and haematological AE's) observed up to and including day 2, 7, and 14 post-treatment, and at all timepoints.

[Time Frame: 8 days (day 0, day 1, day 2, day 5, day 7, day 14, day 21, day 28): 28 day span]

Study description

Background summary

The purpose of this study is to compare the gametocytocidal and transmission reducing activity of artemether-lumefantrine (AL) with and without a single dose of 0.25mg/kg primaquine (PQ) and sulfadoxine-pyrimethamine with amodiaquine (SPAQ) with and without single dose of 1.66mg/kg tafenoquine (TQ). Outcome measures will include infectivity to mosquitoes at 2, 5 and 7 days after treatment, gametocyte density throughout follow-up, and safety measures including haemoglobin density and the frequency of adverse events.

Study objective

Compare the gametocytocidal and transmission reducing activity of artemether-lumefantrine (AL) with and without a single dose of 0.25mg/kg primaquine (PQ) and sulfadoxine-pyrimethamine with amodiaquine (SPAQ) with and without single dose of 1.66mg/kg tafenoquine (TQ).

Study design

day 0, day 1, day 2, day 5, day 7, day 14, day 21, day 28

Intervention

Artemether-lumefantrine (20/80 mg artemether and 120/480 mg lumefantrine), Primaquine Phosphate (0.25mg/kg), Sulphadoxine-pyrimethamine with amodiaquine (500mg sulfadoxine and 25mg pyrimethamine and 150mg amodiaquine), Tafenoquine (1.66mg/kg)

Contacts

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Eligibility criteria

Inclusion criteria

- Age ≥ 10 years and ≤ 50 years
- G6PD-normal defined by Carestart rapid diagnostic test or the OSMMR2000 G6PD qualitative test
- Absence of symptomatic falciparum malaria, defined by fever on enrolment
- Presence of P. falciparum gametocytes on thick blood film at a density >16 gametocytes/µL (i.e. ≥ gametocytes recorded in the thick film against 500 white blood cells)
- Absence of other non-P. falciparum species on blood film
- Hemoglobin ≥ 10 g/dL
- Individuals weighing < = 80 kg
- No evidence of acute severe or chronic disease
- Written, informed consent

Exclusion criteria

- Women who are pregnant or lactating (tested at baseline). Urine and/or serum pregnancy testing (β-hCG) will be used.
- Detection of a non-P. falciparum species by microscopy
- Previous reaction to study drugs / known allergy to study drugs
- Signs of severe malaria, including hyperparasitemia (defined as asexual parasitemia >

100,000 parasites / µL)
- Signs of acute or chronic illness, including hepatitis
- The use of other medication (except for paracetamol and/or aspirin)
- Use of antimalarial drugs over the past 7 days (as reported by the participant)
- Clinically significant illness (intercurrent illness e.g., pneumonia, pre-existing condition e.g., renal disease, malignancy or conditions that may affect absorption of study medication e.g., severe diarrhea or any signs of malnutrition as defined clinically)
- Signs of hepatic injury (such as nausea and/or abdominal pain associated with jaundice) or known severe liver disease (i.e., decompensated cirrhosis, Child Pugh stage B or C)
- Signs, symptoms or known renal impairment
- Clinically significant abnormal laboratory values as determined by history, physical examination or routine blood chemistries and hematology values (laboratory guideline values for exclusion are hemoglobin < 10 g/dL, platelets < 50,000/µl, White Blood - Cell count (WBC) < 2000/µl, serum creatinine >2.0mg/dL, or ALT or AST more than 3 times the upper limit of normal for age.
- Blood transfusion in the last 90 days.
- Consistent with the long half-life of tafenoquine, effective contraception should be continued for 5 half-lives (3 months) after the end of treatment.
- History of psychiatric disorders

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-10-2021
Enrollment:	80
Type:	Actual

IPD sharing statement

Plan to share IPD: No

Ethics review

Positive opinion

Date:	08-10-2021
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL9777
Other	LSHTM Research Ethics Committee : 26257

Study results