

Longitudinal comparison of combination antimalarial therapies in Ugandan children: evaluation of safety, tolerability and efficacy

Submission date
16/05/2005

Recruitment status
No longer recruiting

☐ Prospectively registered

☐ Protocol

Registration date
10/06/2005

Overall study status
Completed

☐ Statistical analysis plan

☒ Results

Last Edited
09/08/2010

Condition category
Infections and Infestations

☐ Individual participant data

Plain English summary of protocol

Not provided at time of registration

Contact information

Type(s)

Scientific

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Additional identifiers

Study information

Scientific Title

Study objectives

We will test the hypothesis that the malaria treatment incidence density (number of treatments for malaria per time at risk) will differ among patients randomised to our three treatment groups (amodiaquine and sulfadoxine-pyrimethamine versus amodiaquine and artesunate versus artemether-lumefantrine).

Ethics approval required

Old ethics approval format

Ethics approval(s)

Not provided at time of registration

Primary study design

Interventional

Study design

Randomised controlled trial

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Uncomplicated falciparum malaria

Interventions

Amodiaquine plus sulfadoxine-pyrimethamine versus amodiaquine plus artesunate versus artemether-lumefantrine

Intervention Type

Drug

Phase

Not Specified

Drug/device/biological/vaccine name(s)

Amodiaquine, sulfadoxine-pyrimethamine, artesunate, artemether-lumefantrine

Primary outcome(s)

The effect of antimalarial drug therapy can be measured both in terms of drug efficacy (risk of true treatment failure) and post-treatment prophylactic effect (risk of new infection). To best reflect the overall impact of therapy, our primary outcome measurement will be the treatment incidence density (treatments per time at risk) for each treatment arm. To eliminate the period not influenced by study drugs, treatment count will exclude the first episode.

Follow-up time will be from the first episode to the end of the study. Treatment count will include both first-line treatments with study drugs and second-line treatments with quinine following study drug failure. It will be assumed that participants will not be at risk for repeat therapy for 14 days after treatment with quinine, for which resistance has not been reported, so this time will be excluded when calculating total time at risk.

Key secondary outcome(s)

1. Drug efficacy:

We will examine the efficacy of the different treatment groups using each episode of malaria treated with a study drug as the unit of analysis. We will examine the risk for repeat treatment as a function of time. Short-term (14-day) assessments of treatment efficacy will provide a standard analysis that will be useful for comparisons with other studies.

1.1. Specific short-term outcomes to be assessed will include:

1.1.1. Clinical and parasitological outcome

1.1.2. Rates of fever and parasite clearance

1.1.3. Change in hemoglobin level from day zero to 14

1.1.4. Presence of gametocytes following treatment

1.1.5. Safety and tolerability of study medications

1.2. Long-term (beyond 14-day) outcomes will be:

1.2.1. Risk of recrudescence

1.2.2. Risk of new infection using Kaplan-Meier product limit estimates of risk at various time intervals (i.e. four, six, and eight weeks after initiation of therapy)

In the analysis of long-term outcomes, molecular genotyping will be used to distinguish recrudescence (true treatment failure) from new infections.

2. Safety and tolerability:

All adverse events will be catalogued based on their frequency, severity, and relationship to study medication using standardised protocols. These indices of safety and tolerability among treatment groups will be compared using each episode of malaria treated with a study drug as the unit of analysis.

3. Other long-term outcomes that will be assessed will include:

3.1. Incidence of asymptomatic parasitemia

3.2. Change in haemoglobin level over time

3.3. Perceived tolerability of study medications among subjects and care givers

3.4. Drug costs (comparison of total cost per patient)

Completion date

20/04/2007

Eligibility

Key inclusion criteria

1. Aged one to ten years

2. Agreement to come to the study clinic for any febrile episode or other illness

3. Agreement to avoid medications administered outside the study

4. Willingness of parents or guardians to provide informed consent

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Child

Lower age limit

1 Years

Upper age limit

10 Years

Sex

All

Key exclusion criteria

1. History (obtained from the parent/guardian) of any known serious chronic disease requiring frequent medical care (e.g. Acquired Immune Deficiency Syndrome [AIDS], sickle cell disease, malignancy)
2. Intention to move from Kampala during the follow-up period
3. History (obtained from the parent/guardian) of serious side effects to study medications or sulfa drugs
4. Weight less than 10 kg
5. Severe malnutrition defined as weight-for-height or height-for-age Z-score less than -3
6. Homozygous haemoglobin SS (sickle cell) result by haemoglobin electrophoresis
7. Life-threatening screening laboratory value in the absence of malaria:
 - 7.1. Absolute neutrophil count: less than 250/mm³
 - 7.2. Hemoglobin: less than 5.0 g/dl
 - 7.3. Platelet count: less than 25,000/mm³
 - 7.4. Creatinine: less than two years: more than 1.5 mg/dl, more than two years: more than 2.0 mg/dl
 - 7.5. Alanine transaminase (ALT): more than 15.0 x Upper Limit of Normal (ULN)
 - 7.6. Bilirubin: more than 7.5 x ULN

Date of first enrolment

01/11/2004

Date of final enrolment

20/04/2007

Locations

Countries of recruitment

Uganda

United States of America

Study participating centre

San Francisco General Hospital

San Francisco

United States of America

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Sponsor information

Organisation

National Institutes of Health (NIH) - National Institute of Allergy and Infectious Diseases (NIAID) (USA)

ROR

<https://ror.org/043z4tv69>

Funder(s)**Funder type**

Government

Funder Name

The National Institute of Allergy and Infectious Diseases (NIAID) (USA)

Results and Publications**Individual participant data (IPD) sharing plan****IPD sharing plan summary**

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	23/05/2007		Yes	No
Results article	results	30/07/2010		Yes	No