Other Planned Studies: AS-MQ in India e Asia

Dr. Isabela Ribeiro

ASMQ Study - India

Drugs for Neglected Diseases Initiative
Indian Council of Medical Research (ICMR)

Principal Investigators: A. P. Dash and Neena Valecha

- Site PIs: Dr. N. G. Dubhashi, Goa Medical College, Goa
  Dr. P. C. Bhattacharya, Down Town Hospital, Guwahati
- Co-Is: Dr. Ashwani Kumar, NIMR, Field Station, Goa
  Dr. VasDav, NIMR, Field Station, Sonapur, Assam
  Dr. Hema Joshi, NIMR, Delhi
  Dr. Aprup Das, NIMR, Delhi

ASMQ Study - India

Assessment of efficacy, safety and population pharmacokinetics of ASAMQ in the treatment of acute uncomplicated *P. falciparum* malaria in India

ASMQ Study - India

Primary Objective:

– To evaluate the clinical and parasitological efficacy of ASMQ in adult patients with uncomplicated *falciparum* malaria, by determining the proportion of patients achieving a negative parasitemia without recrudescence by 63 days (cure rate)

ASMQ Study - India

Secondary Objectives:

- To measure the parasite reduction ratio at 48h of treatment, parasite clearance time, fever clearance time, gametocyte carriage
- To evaluate cure rate at 28 days
- To evaluate the population-pharmacokinetics of ASMQ in adult patients in India
- To evaluate the incidence of adverse events

- To collect information to enable the Ministry of Health to make informed decisions about the possible need for updating of the current national anti-malarial treatment guidelines.

Study Design

– Open-label, prospective, **single-arm**, **population PK** clinical trial

- Sample size: 84 patients
  - Anticipated failure rate around 5%.
  - 95% confidence interval with 5% precision level, we estimate that a total of 84 patients will need to be recruited
  - Adjustment of 15% for losses to follow-up

Study Design
Entry Criteria

Inclusion Criteria :

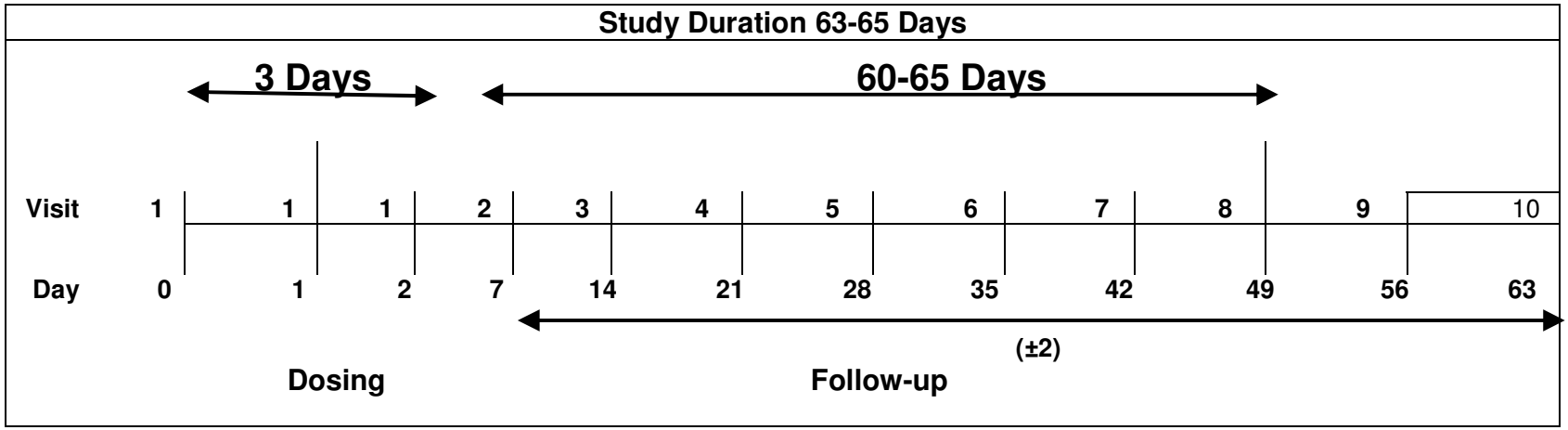
- **Age ≥ 18yrs of age**
- Acute uncomplicated *P. falciparum* mono-infection confirmed by:
  - **Axillary temperature ≥37.5°** C **and,**
    Positive microscopy of *P. falciparum* with parasite density between **1,000 and 100,000** asexual parasites/µl
- Consent from parent/guardian

Exclusion Criteria :

- **Severe/complicated malaria**, requiring parenteral treatment according to the World Health Organization Criteria 2000
- Inability to tolerate oral medication
- **Mixed plasmodium infection**
- Presence of febrile conditions caused by diseases other than malaria.
- Known history of hypersensitivity, allergic or serious adverse reactions to Mefloquine, Quinine, Quinidine, Artesunate or other Artemisinins.
- History of use of any other anti-malarial agent within 2 weeks prior to start of the study.

Study Design
Schedule of Evaluation

Overall study design



Study Design

- Primary efficacy endpoint:
  - Cure Rate as determined by PCR-corrected adequate clinical and parasitological response (ACPR) on Day 63. Treatment success or failures will be classified according to WHO Guidelines 2005.
- Pharmacokinetic parameters:
  - Population pharmacokinetic parameters for artesunate (AS), dihidroartemisinin (DHA), and mefloquine (MQ)

ASMQ Study - Myanmar

- Investigators:
  - Frank Smithuis
  - Ohn Phe
  - Saw Lwin
  - Nick White

- Partnership:
  - Medecins sans Frontieres
  - Faculty of Tropical Medicine, Mahidol University
  - Centre for Tropical Medicine, Nuffield Department of Clinical Medicine
  - Disease Control, Department of Health, Myanmar

ASMQ Study - Myanmar

- General Objective:

Identify the most effective and appropriate artemisinin-based combination treatment for uncomplicated falciparum malaria in Myanmar.

Comparison of the effectiveness of the current 1st line treatment Artesunate and Mefloquine with 4 alternatives: ASMQ (fixed-dose), Artemether-Lumefantrine, Dihydroartemisinine-piperaquine and ASAQ (Artesunate-Amodiaquine)

ASMQ Study - Myanmar

Primary objective:

1. To compare the **clinical and parasitological effectiveness of unsupervised treatment** with **AS+MQ (loose tablets), ASMQ (fixed-dose), Artemether-Lumefantrine, Dihydroartemisinine-piperaquine and ASAQ (Artesunate-Amodiaquine)** as assessed by clinical cure and parasitological clearance on day 63-post treatment.

Secondary objectives:

1. To observe regional differences in effectiveness.
2. To compare the drugs in terms of safety and tolerability in adults and children.
3. To compare the drugs in their effect on post treatment gametocyte carriage (transmission potential).
4. To compare the drugs in their post treatment prophylactic effects
5. To compare acceptability of the different regimens

Study Design

– Open-label, prospective, **comparative, effectiveness** clinical trial

- Sample size: 800 patients
  - **160 patients in the 5 study arms**
  - Estimated cure rate of 95%
  - 5% precision
  - Effectiveness equivalence with a maximum allowable difference of 10%
  - 90% power and 95% confidence, and one sided alpha 0.025
  - Drop out rate of up to 20%.

Study Design
Entry Criteria

Inclusion Criteria :

- Age > 6 months
- Weight ≥ 5 kg
- Acute uncomplicated *P. falciparum* mono-infection confirmed by:
  - Positive microscopy of *P. falciparum* with parasite density between 500 and 200,000 asexual parasites/µl
- Consent from parent/guardian

Exclusion Criteria :

- Severe/complicated malaria, requiring parenteral treatment according to the World Health Organization Criteria 2000
- Inability to tolerate oral medication
- Mixed plasmodium infection.
- Presence of febrile conditions caused by diseases other than malaria.
- Known history of hypersensitivity, allergic or serious adverse reactions to Mefloquine, Quinine, Quinidine, Artesunate or other Artemisinins.
- History of use of any other anti-malarial agent within 2 weeks prior to start of the study.

Study Design

- Study endpoint: point at which a patient will no longer be followed-up within the context of the effectiveness assessment, because a valid effectiveness outcome has been reached (early treatment failure, late treatment failure, or adequate response, as defined below).

- Primary efficacy endpoint:
  - Cure Rate as determined by PCR-corrected adequate clinical and parasitological response (ACPR) on Day 63. Treatment success or failures will be classified according to WHO Guidelines 2005.