Study Title: Operational feasibility of appropriate radical cure of Plasmodium vivax with tafenoquine or primaquine after semi-quantitative G6PD testing in Ethiopia: a mixed methods study

Short title: N/A

Phase of the trial: N/A

CTA Number: ET-CT-0038

Protocol No. MMV_TQ_Ethiopia_20_01

Version No.3.2 **Date:** February 6, 2024

National Principal Investigator (NPI): Endalamaw Gadisa

Trial Site: AHRI; Sawla, Laska, Gambella Hospitals; Beto, Galma, Lote, Dombe, Abole, Bonga health center, village 8 and 9 health centers in Gambella, and two health posts in Abobo and Gambella Zuria woreda

Sponsor: Appropriate Technologies in Health (PATH)

Ethics Approval date: May 15, 2024

Submission Date to EFDA: April 3, 2023

EFDA Status of trial (Approval or Rejection): Approved **Date:** February 1, 2024

Study Rationale

Primaquine (PQ) and tafenoquine (TQ) can be used for the radical cure (RC) of P. vivax malaria. PQ requires a 14-day dose, compared to a single-day dose for TQ, which is likely to improve patient adherence to the treatment. However, a significant safety concern with both TQ and PQ is the high risk of acute hemolytic anemia (AHA) in individuals with glucose-6-phosphate dehydrogenase (G6PD) deficiency. WHO recommends that "the G6PD status of patients should be used to guide administration of PQ & TQ for preventing relapse. The aim of the study is to investigate whether it is operationally feasible to provide appropriate radical cure (RC) treatment after semi-quantitative G6PD testing to P. vivax patients who are eligible for RC based on the national treatment guidelines

General objective / Study aims

to investigate whether it is operationally feasible to provide appropriate radical cure (RC) treatment after semi-quantitative G6PD testing to P. vivax patients who are eligible for RC based on the national treatment guidelines.

Primary objectives

Objective: Assess adherence to a revised case management algorithm for P. vivax malaria

Outcome measures:

- Proportion of vivax patients that are correctly treated with RC based on the revised algorithm
- Proportion of HCP that adhere to the revised RC treatment algorithm

Secondary Objectives and Outcome Measures

Objective:

- Determine the capacity of the health system to safely implement radical cure treatment
- Assess the quality and effectiveness of training and supervision strategies
- Explore barriers and facilitators at the patient, provider, and facility level that mediate effective use of RC treatment with semi quantitative G6PD testing.
- Determine the costs associated with introducing semi-quantitative G6PD testing

Outcome measures:

- Proportion of non-eligible patients that receive RC treatment
- Proportion of patients experiencing AHA during follow-up period
- Proportion of AHA identified by HCP during the study follow-up visits
- HCP knowledge and skills regarding G6PD testing and radical cure treatment
- Patients and HCP perception of and experience with the new RC tools
- Total and per patient monetary cost of including G6PD testing and single dose cure from the perspective of the health system

Study Design

Prospective longitudinal and cross-sectional study

Study Population

- HCP directly involved in the management of P. vivax patients
- Patients with confirmed P. vivax infection
- Other health professionals indirectly involved in management of vivax patients (qualitative component)

Eligibility Criteria

Inclusion Criteria:

- All HCPs working in the selected facilities who are involved in the management of vivax patients
- Health Extension Workers, who have been trained on using the new tools
- Local and regional health administrators involved in the supervision of malaria service delivery in study facilities
- Persons aged 18 years and older who have been diagnosed and treated for P. vivax malaria within the past 3 months
- Caregivers of children aged less than 18 years diagnosed and treated for P. vivax within the past 3 months.
- Community leaders
- Local medical/pharmaceutical organization
- Those who provide informed consent will be enrolled in the study.

Exclusion criteria:

- Pregnant and lactating women
- Patients aged 65 years and older will be excluded from TQ administration
- Those with signs of severe infection
- Patients' treatment with artemisinin derivatives and TQ

Study Duration

15 months in total

- Stage 1: 3 months.
- Stage 2: 3 months before target interim data lock & 3 months during interim analysis
- Stage 3: 6 months

Investigational Medicinal Product

Formulation: tablet of Chloroquine (CQ), Artemether +Lumefantrine (AL), Tafenoquine and Primaquine

Dose: CQ 25 mg/kg/day for 3 days; PQ 0.25 mg/kg/day for 14 days; TQ 300mg once

Route of administration: Oral

Other interventions: N/A

Intervention

Assessment of the implementation of Oral administration of CQ 25 mg/kg/day for 3 days; PQ 0.25 mg/kg/day for 14 days; TQ 300mg once, and of G6PD status evaluation based on the national guideline

Sample size

- 40 Health care professionals
- 2,300 patients

Evaluator's Risk/Benefit Assessment:

It is implementation research that doesn't have direct risk to the patient; assessment of the program implementation could help to identify potential barriers of the program