Update on the Tafenoquine Roll-out STudy (TRuST), April 2023

Context

The Amazon region of Brazil accounts for 99% of malaria cases in the country with *P. vivax* as the predominant form of malaria. The disease has considerable economic and social impact, perpetuating cycles of poverty.

One of the main challenges to malaria control in Brazil is poor adherence to radical cure, leading to relapses and continued transmission. Accessing remote populations, notably indigenous communities is another major challenge.

Where it all started

Two leading malaria researchers and their associated institutes in Brazil Dr. Marcus Lacerda from Dr. Heitor Vieira Dourado Tropical Medicine Foundation (FMT-HVD) and Dr. Dhelio Pereira, Tropical Medicine Research Centre of Rondônia (CEPEM)[1], played a pivotal role in the clinical development programme for tafenoquine (a single-dose radical cure whose development was co-led by GSK and MMV). The Ministry of Health (MoH) in Brazil followed the development programme closely and before the drug was registered in the country, they recognized the potential of a single-dose cure to improve the effectiveness of malaria treatment and support elimination efforts.

Their key concern was whether it would be feasible for health workers, at different levels of the vast network of malaria services, to perform the quantitative point-of-care G6PD test and provide tafenoquine (or primaquine) based on the test results. The Gates Foundation also recognised the importance of generating this evidence and funded MMV to sponsor feasibility studies with the Brazilian and Thai Ministries of Health.

This led to the first real-world study, known as the Tafenoquine Roll-oUt Study (TRuST), which was launched in Brazil in September 2021. The study, co-sponsored by the Brazilian MoH and MMV, was led by Dr. Marcus Lacerda and Dr. Dhelio Pereira. Global Health Strategies (GHS) Brazil have played a pivotal role supporting the TRuST team.

TRuST, a real-world observational study to assess the feasibility of providing appropriate relapse-prevention treatment with tafenoquine or primaquine based on G6PD test results, was rolled out in a phased manner. The first phase started in September 2021 and was conducted in nine higher- and medium-level health facilities in Manaus and Porto Velho, in the Amazon region[2]. In February 2022, the study was expanded to 40 lower-level facilities in the same municipalities. Enrolment finished in August 2022, and in December 2022 a comprehensive dossier was submitted to CONITEC requesting the incorporation of single-dose TQ and the STANDARD™ G6PD test into the national health system (SUS).

Key results: New tools can be appropriately incorporated within the health services

The primary objective of TRuST was to investigate whether patients with *P. vivax* aged ≥16 years were treated with tafenoquine according to the appropriate level of G6PD enzyme activity.

[1] In Amazonas and Rondônia, respectively.

[2] An estimated 5% of the population in this region is G6PD-deficient. (Dombrowski JG et al. “G6PD deficiency alleles in a malaria-endemic region in the Western Brazilian Amazon” Malaria Journal 16, 253 (2017) http://doi. org/10.1186/s12936-017-1889-6).

First and second interim analysis

- 100% of patients were appropriately treated (or not treated) with tafenoquine based on G6PD enzyme activity in the first interim analysis (n=505) and 99.6% in the second interim analysis (n=3,087)
- The results were comparable at high/medium complexity units (99.6%) and low complexity units (99.7%).

QualiTRuST, a qualitative research study, was conducted to assess the acceptability of and experience with quantitative G6PD testing and tafenoquine among health professionals and patients within the framework of TRuST at higher- and lower-level facilities in the study municipalities.

QualiTRuST Key findings

- Patients and most health professionals appreciated the reduction in the number of tablets to be taken and the shorter duration of treatment.
- With practice, health professionals were able to overcome initial difficulties in using the point-of-care, quantitative G6PD test.

What's next: CONITEC recommended incorporation of TQ and quantitative G6PD testing into health system

On 29th March 2023, CONITEC reviewed the consolidated results from the TRuST first and second interim analyses, the QualiTRuST study, and a cost-effectiveness and a budget impact analysis and recommended the incorporation of the tools in the national health system. CONITEC praised the TRuST team on the conduct of a real-world study, and the robust reports that were presented. The CONITEC decision is open to public consultation in Brazil for 20 days and a definitive decision on incorporation of G6PD testing and tafenoquine is expected in early May 2023.

Ripple Effects

TRuST was envisioned as a driver of best practice and experience exchange. In Peru, a feasibility study led by MMV and UPCH is now underway with funding from Unitaid. Ahead of study start, the MoH in Peru has put single-dose TQ on their Essential Medicines List (EML)[3], and is using the feasibility study to answer the question of how best to incorporate the new tools, having already decided to adopt them within the public health system. The TRuST team travelled to Lima to train the Peru team in November 2022. In this way TRuST is allowing other vivax-endemic countries to leapfrog ahead with policy change and roll-out. The Thai Ministry of Public Health (MoPH) is sponsoring a similar study, 'ARCTIC' (Assessing Radical Cure Treatment In routine Care), with MMV's support in two provinces (Mae Hong Son, near that Myanmar border and Yala, in Southern Thailand). The Thai MoPH is also interested in incorporating TQ, starting at the hospital level in 2023.

[3] https://www.gob.pe/institucion/minsa/normas-legales/3971682-247-2023-minsa