PAVE in Brazil: Evidence to inform Public Policies

About PAVE

The Partnership for Vivax Elimination (PAVE) is led by Medicines for Malaria Venture (MMV) and PATH, two international non-profit organizations, and funded by multiple partners, including the Bill & Melinda Gates Foundation. The initiative is a multisectoral consortium of National Malaria Programmes (NMPs), researchers, funders, and other organizations working to eliminate *P. vivax* malaria and support countries in achieving their elimination goals through:

- ☑ working with NMPs to identify optimal radical cure tool options and strategies for their given local contexts;
- ☑ generating and disseminating high-quality evidence on *P. vivax* radical cure case management to inform policy decisions and guide implementation;
- ☑ advancing the development of quality-assured medicines and diagnostics for *P. vivax*.

PAVE in Brazil: How it all started

The Amazon region of Brazil accounts for 99% of malaria cases in the country with *P. vivax* as the predominant species of malaria. One of the main challenges to malaria control in Brazil is poor adherence to radical cure, leading to relapses and ongoing transmission. Accessing remote populations, notably indigenous communities is another major challenge.

In this context, several international actors partnered with Brazilian scientific institutions in the clinical development of tafenoquine (TQ) and the quantitative G6PD test. Researchers from the Dr. Heitor Vieira Dourado Tropical Medicine Foundation (FMT-HVD) and the Rondônia Tropical Medicine Research Center (CEPEM) participated in phase III studies of the drug and in the clinical validation of the test. A single-dose drug that can be used safely would represent a major step towards improving the effectiveness of malaria treatment and supporting the country's elimination efforts.

Anvisa, the Brazilian regulatory agency, approved the STANDARD™ quantitative G6PD test in 2018 and TQ, the single dose cure for *P. vivax* patients aged 16 and over in 2019. Following these approvals, the priority was to assess the feasibility of using these technologies by healthcare professionals in routine care. The Tafenoquine Roll-out Study (TRuST) was implemented, in 2021 and 2022, in partnership between the Ministry of Health (MoH) and MMV - with financial support from the Bill & Melinda Gates Foundation and other international funders.

Improving access to malaria treatment: TQ and G6PD testing in the SUS

EVIDENCE GENERATION

TRuST was the first real-world observational study to assess the feasibility of providing malaria relapse prevention treatment with tafenoquine or primaquine based on quantitative G6PD test result. It was carried out in two phases.

Timeline

2017
PAVE trip to Brazil for discussions with MoH on operational research to assess feasibility of TQ and G6PD testing before radical cure at different levels of the health system.

2018
SD Biosensor STANDARDTM G6PD test approved by National Health Regulatory Authority (Anvisa).

2019
Anvisa approves single-dose tafenoquine in combination with chloroquine for the radical cure of *P. vivax* in patients 16 years old and over, becoming the first malaria endemic country to register the drug.

2021
MMV and the Ministry of Health sign a Memorandum of Understanding to enable the start of TRuST study.

2021
Fiocruz begins Budget Impact Analysis study on TQ and G6PD testing.

The first phase started in September 2021 in nine higher- and medium-level health facilities in Manaus and Porto Velho, in the Amazon region. In February 2022, the study was expanded to 40 lower-level facilities in the same municipalities. The last patient was recruited into the study on 31st August 2022.

Beyond the TRuST study, MMV supported two complementary studies: a qualitative study linked to TRuST (QualiTRuST) on the perceptions of patients and health professionals regarding the G6PD test and single-dose TQ; and a cost-effectiveness analysis, led by the Menzies School of Health Research. The PAVE consortium supported a budget impact analysis, which was developed by Fiocruz.

In December 2022, a comprehensive dossier with all the evidence generated prepared in partnership with the PAVE consortium was sent by the Ministry of Health's Malaria Program to the National Commission for the Incorporation of Technologies (CONITEC) requesting the incorporation of single-dose TQ and the quantitative G6PD test into the nacional health system (SUS).

INCORPORATION

On June 6, 2023, CONITEC approved the incorporation of tafenoquine for radical cure of malaria caused by *P. vivax*, in patients 16 years of age or older, and of the quantitative G6PD test into SUS. The decision to adopt these tools was based on the evidence of safety and efficacy obtained in randomized clinical trials; from real-world data from the first and second interim analysis of the TRuST study; as well as the results of the qualitative study (QualiTRuST) and the cost-effectiveness and budget impact analyses. With this decision, Brazil became the first malaria-endemic country to adopt the G6PD test and single-dose tafenoquine for the treatment of *P. vivax* malaria.

NEXT STEPS

The incorporation of these tools into SUS represents a significant change in the treatment of patients with vivax malaria in Brazil. Now, *P. vivax* patients will have access to shorter and more effective treatment, thanks to increased treatment adherence, helping to reduce relapses and reduce the transmission of the disease. In addition, access to G6PD testing will help identify patients at risk of hemolysis with tafenoquine or primaquine. These innovations will play a key role in achieving the objectives set out in the Brazilian malaria elimination plan, as well as the global goal of eliminating the disease by 2035.

The Brazilian MoH is engaged in developing and implementing a strategy to scale up the use of the new treatment in the Brazilian Amazon Region in partnership with the TRuST and PAVE teams, among other malaria community stakeholders in the country.

TRuST is the largest experience of tafenoquine use in a real-world setting. The TRuST experience and lessons learnt can benefit other countries aiming to introduce the new tools to support the elimination of *P. vivax* malaria. TRuST results have been presented to relevant global malaria stakeholders, including the Pan American Health Organization (PAHO) and World Health Organization (WHO), and will be presented to other endemic countries' National Malaria Programs, as well as at the Annual Meeting of the American Society of Tropical Medicine and Hygiene (ASTMH).

2022
The Ministry of Health presents the TRuST consolidated evidence to CONITEC in December, as one of several inputs to inform a high-level policy decision on the potential incorporation of tafenoquine and G6PD testing into SUS.

2023
Brazil adopts single-dose tafenoquine and G6PD test for the treatment of *P. vivax* malaria in SUS.

2023
Brazil becomes the first malaria-endemic country to register single-dose tafenoquine for children with relapsing malaria.

MMV Medicines for Malaria Venture

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