

This document provides a short summary of this study for a general audience. You can find more information in the scientific summary of the study. A link to the summary is provided at the end of this document.

Study names

Short Title: A study to assess how well a combination of tafenoquine and dihydroartemisinin-piperaquine works and how safe it is in patients with *Plasmodium vivax* malaria.

Full Scientific Title: A double-blind, randomised, parallel group, placebo-controlled superiority study to evaluate the efficacy and safety of tafenoquine (SB-252263, WR238605) co-administered with dihydroartemisinin-piperaquine for the radical cure of *Plasmodium vivax* malaria.

Study Number: 200894

Who sponsored this study?

GlaxoSmithKline (GSK)

GSK Clinical Support Help Desk

Website: clinicalsupporthd.gsk.com/contact.html

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General information about the clinical study

When and where was this study done?

The study started in April 2018 and ended in August 2019. The study site was in Indonesia.

What was the main objective of this study?

Malaria is a serious disease spread by mosquitoes infected with Plasmodium parasites. When an infected mosquito bites a person, the parasites are passed from the mosquito into the person's blood. Malaria can cause high fever, chills, other flu-like symptoms, and low red blood cell count (anaemia).

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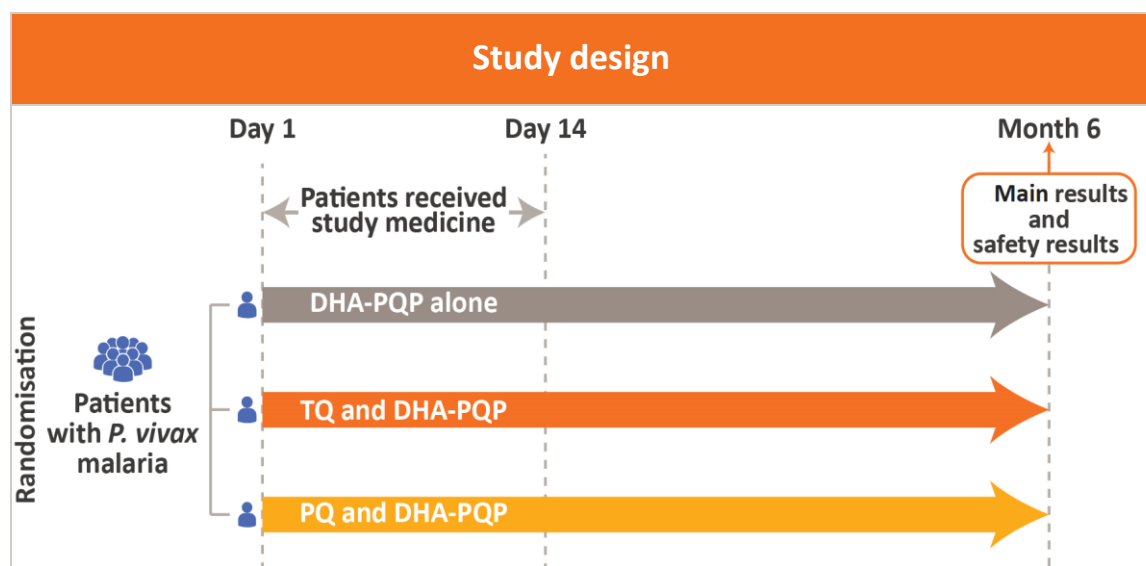
Plasmodium vivax (*P. vivax*) is a type of parasite which causes malaria. The presence of *P. vivax* parasites in the blood makes a patient feel unwell. These parasites can also hide in the patient's liver, even after the patient feels better. The *P. vivax* parasites can later come out of the liver into the blood and make the patient unwell again.

Tafenoquine (TQ), dihydroartemisinin-piperaquine (DHA-PQP), and primaquine (PQ) are medicines that are used to treat malaria. DHA-PQP treats malaria by removing *P. vivax* parasites from the blood. TQ and PQ stop further episodes of malaria by removing the parasites from the liver.

In this study, researchers compared a combination of TQ and DHA-PQP with DHA-PQP alone in men with *P. vivax* malaria. They wanted to see how well TQ worked at stopping malaria from returning within six months after treatment with DHA-PQP. Researchers also assessed the safety of TQ.

Which medicines were studied?

Patients were placed in one of the three treatment groups by chance (randomisation), as shown in the figure below.



Patients in all the three treatment groups received DHA-PQP. No matter what treatment group patients were in, each patient received the same number of tablets or capsules for 14 days. Neither patients nor study doctors knew who received which treatment. This is called a double-blind study.

Which patients were included in this study?

Studies have a list of requirements for patients who can enrol (inclusion criteria) and those who can't (exclusion criteria). For this study, the main inclusion and exclusion criteria are listed below.



Indonesian men were included in the study if they:

- Were at least 18 years old.
- Tested positive for *P. vivax* infection.
- Had normal levels of a protein (G6PD) in their red blood cells.



Men were excluded from the study if they:

- Were unwell due to severe *P. vivax* malaria.
- Had been vomiting a lot recently or had other serious health issues.
- Had haemoglobin (protein in the red blood cells that carries oxygen to all parts of the body) level of less than eight grams per decilitre at the start of study.
- Had taken medicines to treat malaria within a month before starting the study.
- Had any other disease(s) or were taking other medicine(s) that the study doctor thought would affect the results of the study.

Overall, 150 men received at least one dose of the study medicine. The average age was 29 years. The youngest patient was 21 years old and the oldest patient was 49 years old.

For more detailed information about the patients included in this study, see the scientific results summary (a link to the summary is provided at the end of this document).

What were the main results of the study?

For this study, malaria-free is defined as no *P. vivax* parasites in the blood for six months after the parasites were removed with DHA-PQP treatment.

The main objective of the study was a comparison between the TQ and DHA-PQP group and the DHA-PQP alone group. Researchers compared the number of patients who remained malaria-free for six months after the start of DHA-PQP treatment.

Results are shown in the table below.

Patients who remained malaria-free for six months after the start of DHA-PQP treatment			
	DHA-PQP alone 50 patients	TQ and DHA-PQP 50 patients	PQ and DHA-PQP 50 patients
Number of patients (percent) who remained malaria-free	6 (12%)	11 (22%)	26 (52%)

Six months after receiving treatment, more patients in the TQ and DHA-PQP group remained malaria-free compared with patients in the DHA-PQP alone group. However, the number of patients in the PQ and DHA-PQP group who remained malaria-free was higher compared with the other groups.

More information about the study results is available in the scientific results summary (a link to the summary is provided at the end of this document).

What were the side effects?

Unwanted medical events (adverse events) can happen to people when they receive a medicine. Study doctors record these events. A summary of these events can be found in the scientific results summary (a link to the summary is provided at the end of this document).

If the study doctor thinks that the event was caused by the study medicine, they record this as a possible side effect (adverse reaction).

In this summary, “side effects” refer to those events that the study doctor thinks may have been caused by the study medicine. The side effects in this summary may be different to those in the Informed Consent or other documents related to the study medicine.

The table below shows the number of patients (percent) with serious side effects reported during the study.

Number of patients (percent) with serious side effects			
	DHA-PQP alone 50 patients	TQ and DHA-PQP 50 patients	PQ and DHA-PQP 50 patients
Abnormally high blood pressure	0	0	1 (2%)
Heart rhythm problem	1 (2%)	0	0

The table below shows the number of patients (percent) with non-serious side effects that were reported by 4% or more of patients in any treatment group.

Number of patients (percent) with non-serious side effects reported by 4% or more of patients			
	DHA-PQP alone 50 patients	TQ and DHA-PQP 50 patients	PQ and DHA-PQP 50 patients
Vomiting	1 (2%)	3 (6%)	0
Weakness	3 (6%)	1 (2%)	1 (2%)
Diarrhoea	2 (4%)	2 (4%)	1 (2%)
Headache	2 (4%)	2 (4%)	1 (2%)
Indigestion	0	0	2 (4%)
Pain in stomach	0	0	2 (4%)

How has this study helped patients and researchers?

The study showed that more patients in the TQ and DHA-PQP group compared with the DHA-PQP alone group remained malaria-free for six months after treating the initial malaria. This difference was not big enough for researchers to conclude that a

combination of TQ and DHA-PQP was better than DHA-PQP alone in treating Indonesian men with *P. vivax* malaria. No serious side effects were reported by patients who received TQ. Non-serious side effects reported during this study were similar to those expected with TQ.

Are there plans for further studies?

Other studies on TQ in patients with malaria have been conducted and more are underway.

Where can I find more information about this study?

Clinical studies have unique study numbers that are included in publications and other information about the study. The unique study number associated with this study is shown below with an internet link to the scientific summary and other information.

The scientific summary includes more details about the requirements for study enrolment, the study visit schedule, results from other endpoints, and more detailed information about adverse events.

Organisation and Website	Study Number
United States National Institutes of Health (NIH) (www.clinicaltrials.gov)	NCT02802501 ¹

Your doctor can help you understand more about this study and the results. Speak to your doctor about the treatment options available in your country. You should not make changes to your care based on the results of this or any single study. Keep taking your current treatment unless instructed by your doctor.

We would like to thank the patients who contributed to this study. The results of this study will help answer scientific questions about treating patients with *P. vivax* malaria.

The content for this document was finalised by GSK on 23rd of July 2020. The information in this summary does not include additional information available after this date.

¹<https://clinicaltrials.gov/ct2/show/study/NCT02802501>