This document provides a short summary of this study for a general audience. You can find more information in scientific summaries of the study. Links to those summaries are provided at the end of this document.

Study names

Short Title: A study to assess the efficacy and safety of a new medicine (tafenoquine) for the treatment of malaria.

Full Scientific Title: A multi-centre, double-blind, randomised, parallel-group, active controlled study to evaluate the efficacy, safety and tolerability of tafenoquine (SB-252263, WR238605) in subjects with *Plasmodium vivax* malaria.

Study Number: 112582

Who sponsored this study?

GlaxoSmithKline (GSK)
GSK Clinical Support Help Desk
Website: www.clinicalsupporthd.gsk.com
Email: GSKClinicalSupportHD@gsk.com

General information about the clinical study

When was this study done?

The main part of this study (Part 2) started in April 2014 and ended in November 2016.

What were the reasons for conducting this study?

Malaria is a serious tropical disease spread by mosquitos. People get malaria if they are bitten by a mosquito that is infected with *Plasmodium* parasites. When an infected mosquito bites a person, the parasite is passed from the mosquito into a person's blood.

Once infected, the malaria parasites live and grow in the person's body. They feed on blood cells, causing a person to get sick. Malaria can cause high fever, chills and other flu-like symptoms. Symptoms need to be treated quickly or the person could die.

There are a number of malaria parasites. *Plasmodium vivax* (*P. vivax*) is one type of malaria-causing parasite. The *P. vivax* parasites can live in a person's liver even after he or she feels better. While in the liver, the parasites are inactive and cannot be detected. After weeks or months, the *P. vivax* parasites can return to the blood making the person sick again.

What was the main objective of this study?

The purpose of the main part (Part 2) of this study was to see how well a new malaria medicine (tafenoquine) worked in stopping *P. vivax* malaria parasites from causing malaria sickness within six months after finishing treatment to clear the initial infection (malaria-free).

Which medicines were studied?

This summary describes the results of the main part of this study (Part 2). An earlier part of the study (Part 1) helped researchers choose the appropriate dose of the new medicine. The dose selected in the earlier part was then used in the main part of the study. For more information about the earlier part of the study, see the scientific results summary on the GSK Study Register. The link is provided at the end of this document.

Patients were assigned to one of the three treatment groups by chance (randomisation):

- Chloroquine (CQ) only,
- Tafenoquine and Chloroquine (TQ+CQ),
- Primaquine and Chloroquine (PQ+CQ).

Patients in all three treatment groups received chloroquine (CQ) on days 1-3. CQ is the standard treatment to remove *P. vivax* from the blood. CQ does not treat the inactive liver stage of the malaria parasite. Some patients also received either primaquine (PQ) or tafenoquine (TQ) to clear the inactive liver stage of the parasite.

No matter what treatment group patients were in, each patient received the same number of pills (tablets or capsules) for 15 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 described below.

All patients in the study had to be at least 16 years old and tested positive for *P. vivax* infection.

Patients could not be in the study if they:

- Tested positive for more than one type of malaria.
- Were very sick due to *P. vivax* malaria.
- Had been vomiting a lot recently or had other serious health issues.
- Had taken malaria medicines in the last 30 days.

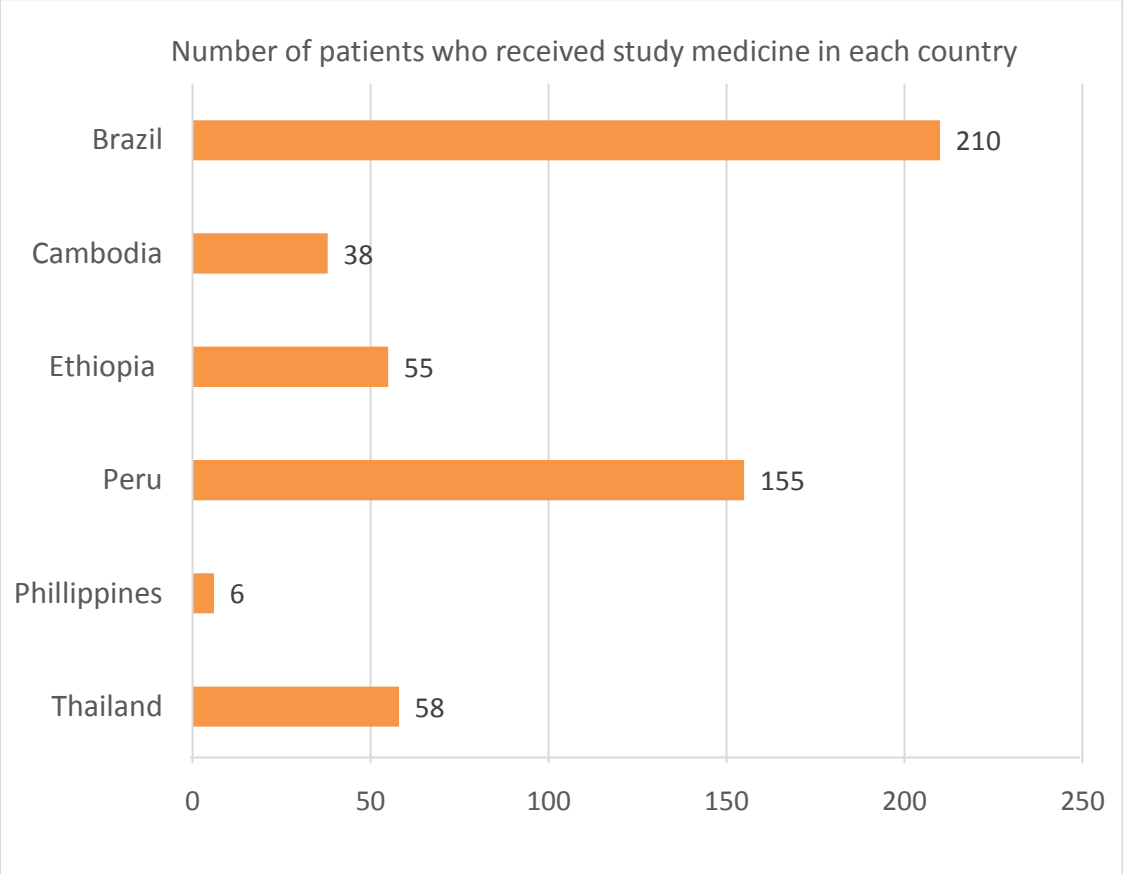
For more detailed information about the patients included in this study, see the scientific summary on ClinicalTrials.gov (link provided at the end of this document).

A total of 522 patients took part in the study. The table below provides the gender and ages of these patients.

	CQ only 133 patients	**TQ+CQ** 260 patients	**PQ+CQ** 129 patients
Gender - Number of patients (percent)			
Female	36 (27%)	64 (25%)	30 (23%)
Male	97 (73%)	196 (75%)	99 (77%)
Age - in years			
Range	17 to 71	15 to 79	15 to 66
Average	35	35	35

Where was this study done?

The study sites were located in six countries.



What were the overall results of the study?

For this study, malaria-free is defined as no *P. vivax* malaria parasites in the blood at six months after the parasites were originally removed with CQ treatment. Results by treatment group are shown in the following table:

	CQ only 133 patients	**TQ+CQ** 260 patients	**PQ+CQ** 129 patients
Number of patients in the study who remained malaria-free at six months	35 of 133 (26%)	155 of 260 (60%)	83 of 129 (64%)

The data from the study were analysed to compare the TQ+CQ treatment group to CQ only treatment group. At any point within the six months following the start of treatment, about three times more cases of malaria are expected for patients who received CQ only treatment than for patients who received TQ+CQ treatment. This treatment difference between the two groups was clinically and statistically significant. Statistically significant means that the difference was not likely due to chance alone.

What were the side effects?

Study doctors collect information about the safety of study medicines. Any medical events including symptoms reported by patients in the clinical study are called adverse events. These adverse events can be found in the scientific summary (see link provided at the end of this document).

The study doctors record if they think any of these events may be caused by the medicine. If the study doctor believes that the event was caused by the medicine, they record this adverse event as a possible side effect. In a clinical study these are called **adverse reactions**. A **serious adverse reaction** is an adverse reaction that is life threatening, requires hospitalisation, or results in death or permanent damage.

This plain language summary describes those side effects (adverse reactions including serious adverse reactions) recorded by study doctors. The tables below show the serious and non-serious adverse reactions reported in at least 1% or more of patients in any treatment group. Heart rhythm problem (Electrocardiogram QT prolonged) was the only serious adverse reaction, all others were non-serious.

Adverse Reactions (Serious and Non-Serious) Reported in at Least 1% of Patients in Any Treatment Group			
	CQ only 133 patients	**TQ+CQ** 260 patients	**PQ+CQ** 129 patients
Itchiness (Pruritus)	9 of 133 (7%)	3 of 260 (1%)	2 of 129 (2%)
Feeling sick (Nausea)	1 of 133 (less than 1%)	7 of 260 (3%)	3 of 129 (2%)
Being sick (Vomiting)	4 of 133 (3%)	5 of 260 (2%)	2 of 129 (2%)
Headache	2 of 133 (2%)	1 of 260 (less than 1%)	1 of 129 (less than 1%)
Higher than normal levels of a liver protein in the blood (Alanine Aminotransferase increased)	3 of 133 (2%)	5 of 260 (2%)	3 of 129 (2%)
Heart rhythm problem (Electrocardiogram QT prolonged) (serious adverse reaction)	3 of 133 (2%)	0	0
Higher than normal levels of a form of haemoglobin in the blood (Methaemoglobinaemia)	0	0	2 of 129 (2%)

*Note: A drop in haemoglobin levels was not reported as an adverse reaction in 1% or more of patients in any treatment group in this study, but it is considered an important possible safety issue with medicines like tafenoquine. In this study, a drop in haemoglobin levels was reported as an adverse event in 2% (2 out of 133) of patients in the CQ only treatment group; 5% (14 out of 260) of patients in the TQ+CQ treatment group; and 2% (2 out of 129) of patients in the PQ+CQ treatment group.

For further information about safety, including details about the adverse events that study doctors did not think were related to the study medicine, please see the scientific summaries using the links at the end of this document.

How has this study helped patients and researchers?

Information from this study may help doctors learn more about *P. vivax* malaria and its treatment. The data from this study will be used to support the approval of tafenoquine as a new medicine to prevent *P. vivax* malaria from returning after the initial infection has been treated.

Are there plans for further studies?

Other studies of tafenoquine in patients with malaria are currently ongoing. The results of these studies will also be available on the ClinicalTrials.gov website after the studies end and the results are analysed.

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 numbers associated with this study are shown below with internet links to scientific summaries and other information.

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

Organization	Study Part	Website	Study Number
United States National Institutes of Health (NIH)	Part 2	www.clinicaltrials.gov	NCT01376167
GlaxoSmithKline (GSK)	Part 1	www.gsk-clinicalstudyregister.com	112582

For readers of this document in printed form, the websites that go with the internet links above are

https://clinicaltrials.gov/ct2/show/NCT01376167?term=112582&rank=1
https://www.gsk-clinicalstudyregister.com/search/?study_ids=112582

Your doctor can help you understand more about this study and the results. 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 the 30th of July 2018. The information in this summary does not include additional information available after this date.