Primaquine Efficiacy and Safety for Vivax Malaria: Brazil

WWARN Vivax Primaquine Study Group. For further information go to https://www.iddo.org/wwarn/vivax-reports

05 May, 2025

Introduction

This report is a condensed version of the full report assessing the effect of primaquine dose on efficacy, safety and tolerability. This report provides an overview of the results only. For more detail please refer to the standard report.

Table 1: Studies included in this report

Author-year	Follow up (days)	Treatment arms	PQ treatment arm details	Patients available
Chamma-Siqueira-2022	168	PQ 3.5 mg/kg	Cq_Pq_3.5_7d_D17_obs	1
Llanos-Cuentas-2019	180	PQ 3.5 mg/kg	Cq_Pq_3.5_14d_D1	23
Lacerda-2019	180	No PQ, PQ 3.5 mg/kg	Cq_Pq_3.5_14d_D1	105
Ladeia-Andrade-2019	180	PQ 3.5 mg/kg	Cq_Pq_3.5_7d_D0	94
Llanos-Cuentas-2014	180	No PQ, PQ 3.5 mg/kg	Cq_Pq_3.5_14d_D1	12
Daher-2018	63	PQ 3.5 mg/kg	AsMf_Pq_3.5_7-9d_D0, Cq_Pq_3.5_7-9d_D0, AL_Pq_3.5_7-9d_D0	264
de Sena-2019	42	PQ 3.5 mg/kg	Cq_Pq_3.5_7d_D0	113
Siqueira-unpublished2024	180	PQ 7 mg/kg	Cq_Pq_7.0_14d_D0, DP_Pq_7.0_14d_D0, Cq_Pq_7.0_14d_D42	224

∗ *ACT – artemisinin-based combination treatment; As – artesunate; AL – artemether-lumefantrine; Aq – amodiaquine; Cq – chloroquine; DP – dihydroartemisinin-piperaquine; GI – gastrointestinal; Mf – mefloquine; PQ/Pq – primaquine; SP – sulfadoxine-pyrimethamine;*

Primaquine treatment code describes (schizontocidal drug)(hypnozoitocidal drug)(total primaquine dose)(duration of primaquine treatment eg 14d = 14 days)(primaquine start day)

Efficacy

Inclusion in the efficacy analysis was restricted to studies with 42 days or more follow up and patients with data on day 0 parasitaemia. In this report, the efficacy analysis includes 836 patients across 10 study sites, from 8 studies.

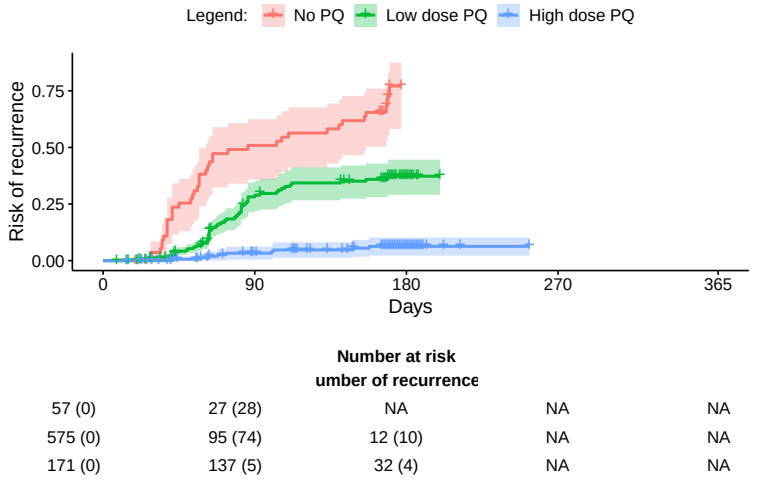

Figure 1: Kaplan-Meier figure of cumulative risk of recurrence between day 7 and day 365 for primaquine treatment category. Please interpret the results of this figure with caution as there may not always be paired treatment comparisons in the original studies contributing to these pooled results.

Low dose PQ - total primaquine 2 - <5 mg/kg;
High dose PQ - total primaquine ≥ 5 mg/kg

Haematology

The haematology analysis included 233 patients across 5 study sites, from 4 studies. The following analysis only considers the 231 patients across 4 studies with G6PD activity $\geq$ 30%.

Table 2: Summary of haematology outcomes, stratified by daily primaquine dose

	Primaquine daily dose level				
	Nil	**Low**	**Intermediate**	**High**	**Total**
	(N=58)	**(N=82)**	**(N=87)**	**(N=4)**	**(N=231)**
Drop in Haemoglobin of >25% AND Hb below 7 g/dL:					
No	58 (100.0%)	82 (100.0%)	84 (96.6%)	4 (100.0%)	228 (98.7%)
Yes	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Missing	0 (0%)	0 (0%)	3 (3.4%)	0 (0%)	3 (1.3%)
Drop in Haemoglobin of >5 g/dL from baseline OR Hb below 5 g/dL:					
No	58 (100.0%)	82 (100.0%)	83 (95.4%)	4 (100.0%)	227 (98.3%)
Yes	0 (0.0%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	1 (0.4%)
Missing	0 (0%)	0 (0%)	3 (3.4%)	0 (0%)	3 (1.3%)

The following figure provides the estimated change in haemoglobin (Hb) from day 0, for different Primiquine doses at day 2/3, adjusted for baseline haemoglobin, age, sex and day 0 parasitaemia and allowing for clustering by study site.

Care should be taken when interpreting these results, as model assumptions have not been fully assessed in this automated report format.

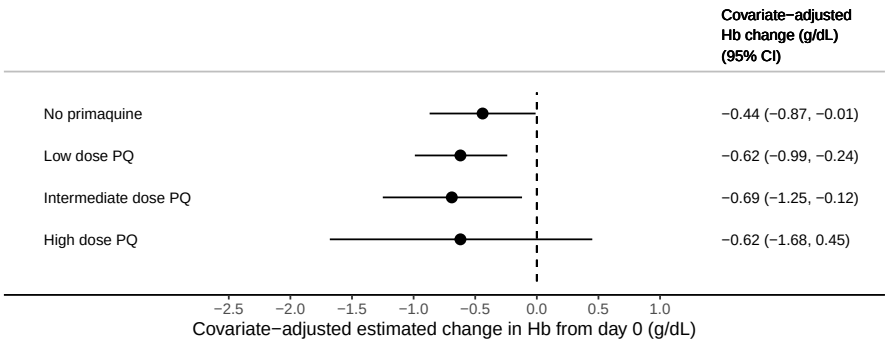

Figure 2: The covariate-adjusted estimated change in Hb from baseline to days 2-3, between primaquine daily dose groups, in patients with G6PD activity $\geq$30%.

Low dose daily primaquine (<0.375 mg/kg/day)
Intermediate dose daily primaquine ($\geq$0.375 & <0.75 mg/kg/day)
High dose daily primaquine ($\geq$0.75 mg/kg/day).