

Primaquine Efficacy and Safety for Vivax Malaria: Cambodia, Malaysia, Myanmar, Philippines, Vietnam

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

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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.

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 1013 patients across 9 study sites, from 6 studies.

Table 1: Studies included in this report

Author-year	Follow up (days)	Treatment arms	PQ treatment arm details	Patients available
Llanos-Cuentas-2019	180	PQ 3.5 mg/kg	Cq_Pq_3.5_14d_D1	15
Taylor-2019	365	No PQ, PQ 7 mg/kg	Cq_Pq_7.0_14d_D0, Cq_Pq_7.0_7d_D0	324
Lacerda-2019	180	No PQ, PQ 3.5 mg/kg	Cq_Pq_3.5_14d_D1	22
Barber-2013	42	No PQ	Cq_Pq_D2, Cq_Pq_D1, AL_Pq_D2, AL_Pq_D5, AL_Pq_D1, AL_Pq_D3, Cq_Pq_D3	39
Grigg-2018	230	No PQ	Cq_Pq_D1, Cq_Pq_D3, Cq_Pq_D4, AsMf_Pq_D1, Cq_Pq_D2, AL_Pq_D5, AL_Pq_D1, Cq_Pq_D5	26
Yuan-2015	42	PQ 3 mg/kg	Cq_Pq_3.0_8d_D0	588

* *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)

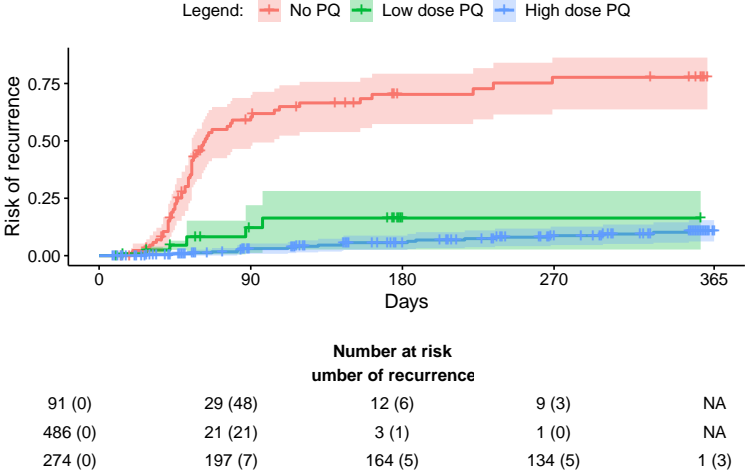


Figure 1: Kaplan-Meier figure of cumulative risk of recurrence between day 7 and day 365 for primaquine treatment category. Please interpret the results of this figure with caution as there may not always be paired treatment comparisons in the original studies contributing to these pooled results.

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

Haematology

The haematology analysis included 388 patients across 8 study sites, from 5 studies. The following analysis only considers the 383 patients across 5 studies with G6PD activity $\geq 30\%$.

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

	Primaquine daily dose level				Total
	Nil	Low	Intermediate	High	
	(N=98)	(N=28)	(N=132)	(N=125)	(N=383)
Drop in Haemoglobin of >25% AND Hb below 7 g/dL:					
No	95 (96.9%)	28 (100.0%)	130 (98.5%)	125 (100.0%)	378 (98.7%)
Yes	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Missing	3 (3.1%)	0 (0%)	2 (1.5%)	0 (0%)	5 (1.3%)
Drop in Haemoglobin of >5 g/dL from baseline OR Hb below 5 g/dL:					
No	95 (96.9%)	28 (100.0%)	130 (98.5%)	125 (100.0%)	378 (98.7%)
Yes	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Missing	3 (3.1%)	0 (0%)	2 (1.5%)	0 (0%)	5 (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.

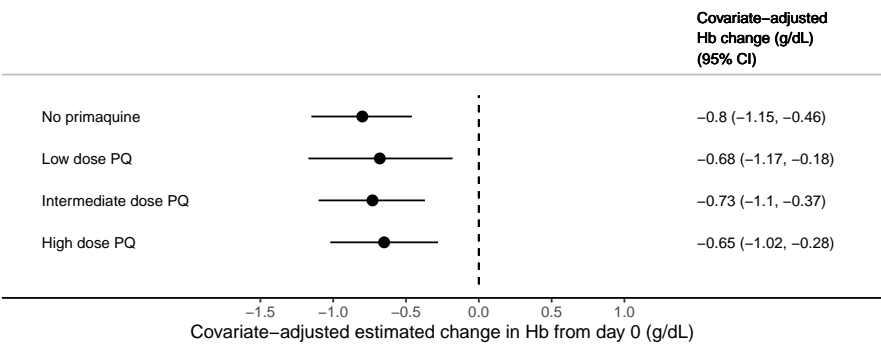


Figure 2: The covariate-adjusted estimated change in Hb from baseline to days 2-3, between primaquine daily dose groups, in patients with G6PD activity $\geq 30\%$.

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