Primaquine Efficiacy and Safety for Vivax Malaria: Asia-Pacific

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

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Introduction

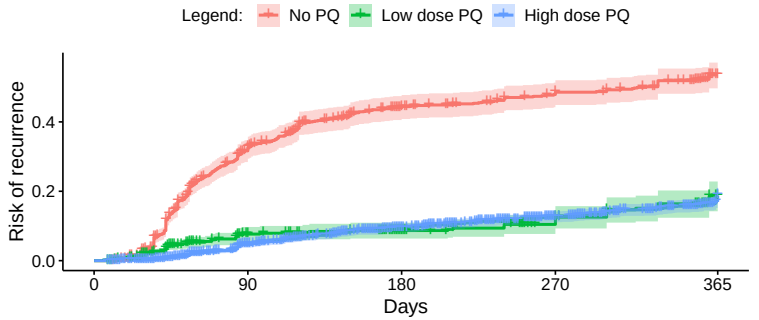
This report is a condensed version of the full report assessing the effect of primaquine dose on efficacy, safety and tolerability. This report provides an overview of the results only. For more detail please refer to the standard report.

∗ *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 5102 patients across 35 study sites, from 18 studies.



Number at risk
umber of recurrence

No PQ	996 (0)	539 (277)	365 (87)	306 (25)	159 (26)
Low dose PQ	1397 (0)	384 (64)	282 (4)	213 (10)	177 (14)
High dose PQ	2442 (0)	1812 (97)	1394 (84)	1165 (45)	215 (54)

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

Table 1: Studies included in this report

Author-year	Follow up (days)	Treatment arms	PQ treatment arm details	Patients available
Chu-2018	365	No PQ, PQ 7 mg/kg	Cq_Pq_7.0_14d_D0	420
Longley-2016	270	PQ 3.5 mg/kg	Cq_Pq_3.5_14d_D1	43
Pasaribu-2013	365	PQ 3.5 mg/kg	AsAq_Pq_3.5_14d_D0, DP_Pq_3.5_14d_D0	331
Llanos-Cuentas-2019	180	PQ 3.5 mg/kg	Cq_Pq_3.5_14d_D1	23
Taylor-2019	365	No PQ, PQ 7 mg/kg	Cq_Pq_7.0_14d_D0, Cq_Pq_7.0_7d_D0, DP_Pq_7.0_14d_D0, DP_Pq_7.0_7d_D0	1717
Poespoprodjo-2021	180	PQ 7 mg/kg	DP_Pq_7.0_14d_D2_us, DP_Pq_7.0_14d_D2_s	164
Nelwan-2015	365	PQ 7 mg/kg	DP_Pq_7.0_14d_D0	56
Lacerda-2019	180	No PQ, PQ 3.5 mg/kg	Cq_Pq_3.5_14d_D1	52
Pukrittayakamee-2010	28	PQ 3.5 mg/kg, PQ 7 mg/kg	Pq_7.0_7d_D0, Pq_3.5_7d_D0	85
Llanos-Cuentas-2014	180	No PQ, PQ 3.5 mg/kg	Cq_Pq_3.5_14d_D1	48
Hasugian-2007	84	PQ 4.2 mg/kg	AsAq_Pq_4.2_14d_D2, DP_Pq_4.2_14d_D2	115
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
Chu-2019	365	PQ 7 mg/kg	DP_Pq_7.0_7d_D0, DP_Pq_7.0_14d_D0, Cq_Pq_7.0_7d_D0, Cq_Pq_7.0_14d_D0	654
Rijal-2019	365	No PQ, PQ 3.5 mg/kg	Cq_Pq_3.5_14d_D0	206
Karunajeewa-unpub	84	No PQ, PQ 3.5 mg/kg, PQ 7 mg/kg	AL_Pq_3.5_14d_D0, AL_Pq_7.0_14d_D0	26
Saravu-2016	28	PQ 3.5 mg/kg	Cq_Pq_3.5_14d_D0	155
Ley-2016	30	PQ 3.5 mg/kg	Cq_Pq_3.5_14d_D2	55
Awab-2017	390	No PQ, PQ 3.5 mg/kg	Cq_Pq_3.5_14d_D0	544
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
Lidia-2015	42	PQ 3.5 mg/kg	Cq_Pq_3.5_14d_D0, DP_Pq_3.5_14d_D0	51

Haematology

The haematology analysis included 4329 patients across 34 study sites, from 17 studies.
The following analysis only considers the 4189 patients across 17 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=985)	(N=725)	(N=1421)	(N=1058)	(N=4189)
Drop in Haemoglobin of >25% AND Hb below 7 g/dL:					
No	780 (79.2%)	529 (73.0%)	1222 (86.0%)	1038 (98.1%)	3569 (85.2%)
Yes	1 (0.1%)	0 (0.0%)	4 (0.3%)	6 (0.6%)	11 (0.3%)
Missing	204 (20.7%)	196 (27.0%)	195 (13.7%)	14 (1.3%)	609 (14.5%)
Drop in Haemoglobin of >5 g/dL from baseline OR Hb below 5 g/dL:					
No	780 (79.2%)	529 (73.0%)	1219 (85.8%)	1037 (98.0%)	3565 (85.1%)
Yes	1 (0.1%)	0 (0.0%)	6 (0.4%)	7 (0.7%)	14 (0.3%)
Missing	204 (20.7%)	196 (27.0%)	196 (13.8%)	14 (1.3%)	610 (14.6%)

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.

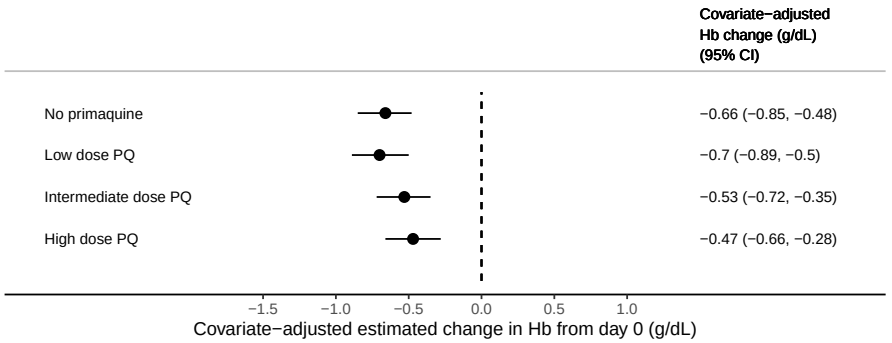


Figure 2: The covariate-adjusted estimated change in Hb from baseline to days 2-3, between primaquine daily dose groups, in patients with G6PD activity $\geq$30%.

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).