

# Primaquine Efficacy 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.

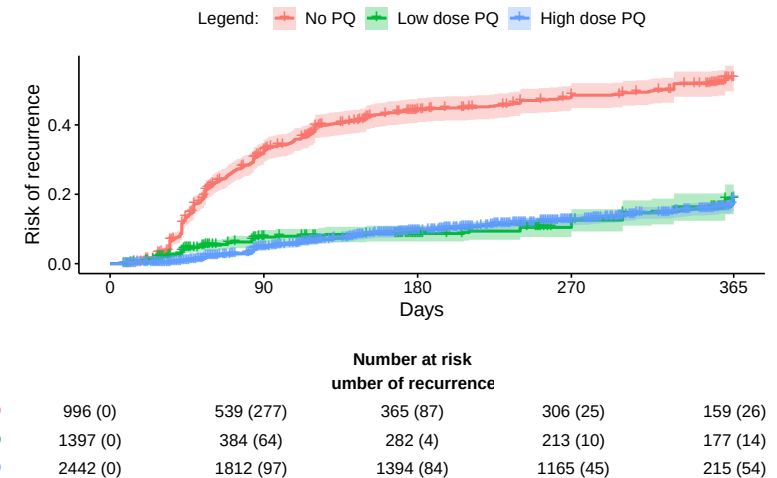


Figure 1: Kaplan-Meier figure of cumulative risk of recurrence between day 7 and day 365 for primaquine treatment category. Please interpret the results of this figure with caution as there may not always be paired treatment comparisons in the original studies contributing to these pooled results.

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

High dose PQ - total primaquine  $\geq$  5 mg/kg

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 |             |              |              | Total        |
|------------------------------------------------------------------|-----------------------------|-------------|--------------|--------------|--------------|
|                                                                  | Nil                         | Low         | Intermediate | High         |              |
|                                                                  | (N=985)                     | (N=725)     | (N=1421)     | (N=1058)     |              |
| 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 primaquine 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.

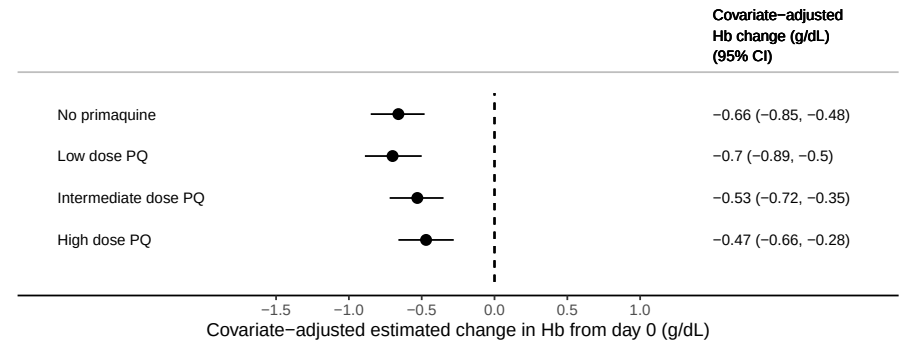


Figure 2: The covariate-adjusted estimated change in Hb from baseline to days 2-3, between primaquine daily dose groups, in patients with G6PD activity  $\geq 30\%$ .

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).