

Crusade against Malaria

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What's New

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► *Korean J Parasitol. 2010;48(2):179-82*

Appropriate time for primaquine treatment to reduce Plasmodium falciparum transmission in hypoendemic areas.

Artemisinin-combination therapies (ACT) for falciparum malaria reduce gametocyte carriage, and therefore reduce transmission. Artemisinin derivatives will act against only young gametocytes whereas primaquine acts on mature gametocytes which are present usually in the circulation at the time when the patient presents for treatment. Both artemisinin derivatives and primaquine have short half-lives, less than 1 hr and 7 hr, respectively. Therefore, asexual parasites or young gametocytes remain after completed ACT. A single dose of primaquine (0.50-0.75 mg base/kg) at the end of ACT can kill only mature gametocytes but cannot kill young gametocytes (if present). Remaining asexual forms after completion of ACT course, e.g., artesunate-mefloquine for 3 days, may develop to mature gametocytes 7-15 days later. Thus, an additional dose of primaquine (0.50-0.75 mg base/kg) given 2 weeks after ACT completion may be beneficial for killing remaining mature gametocytes and contribute to more interruption of Plasmodium falciparum transmission than giving only 1 single dose of primaquine just after completing ACT.

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► *Antimicrob Agents Chemother. 2010 Jun 14.*

New fixed dose artesunate/mefloquine for treating multidrug resistant Plasmodium falciparum in adults - a comparative phase IIb safety and pharmacokinetic study with standard dose non-fixed artesunate plus mefloquine.

A new fixed dose artesunate (AS)/mefloquine (MQ) was assessed in adults, hospitalized for 28 days, with uncomplicated, drug resistant falciparum malaria. Patients (n=25/arm) were treated with: (i) two fixed dose tablets (AS/MQ arm: AS 100 mg/MQ 200 mg/tablet) daily for 3 days (D0, 1, 2) or (ii) non fixed AS (AS+MQ arm: 4 mg/kg/d x 3d) + MQ (15 mg/kg D1, and 10 mg/kg D2), dosed by weight. Clinical, laboratory, ECG adverse events (AEs), efficacy, pharmacokinetic parameters were assessed over 28 days. Both regimens were well tolerated. No AEs were drug related. Two serious AEs, malaria induced hypotension occurring in the AS/MQ arm, necessitated rescue treatment. There were no significant changes in hematology, biochemistry, PR and QRS intervals. For all patients, mean Fridericia corrected QT intervals were significantly ($p < 0.0027$) prolonged on D3 (407 ms) and D7 (399 ms) vs. D0 (389 ms) in parallel with significant ($p < 0.0003$) falls in heart rates [67 (D3), 73 (D7), 83 (D0) beats/minute]. Fixed-non fixed formulations were bioequivalent for MQ but not for AS and DHA. One AS/MQ patient developed a new infection on D28; his D28 plasma MQ concentration was 503.8 ng/mL. Fixed dose AS/MQ was well tolerated, had broadly similar PK profiles to non fixed AS+MQ and is a suitable replacement.

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