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ARTESUNATE-MEFLOQUINE: PAST, PRESENT AND FUTURE

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Artesunate and mefloquine (AS-MQ) ranks as the most durable artemisinin-based combination treatment (ACT) for uncomplicated *Plasmodium falciparum* malaria deployed to date. In the early 1990s in Southeast Asia, home to the most drug-resistant parasites in the world, artemisinin derivatives were introduced, adding them to a failing high-dose mefloquine regimen. This brought about a remarkable and sustained improvement in efficacy[1].

In 2002, a fixed-dose combination (FDC) of AS-MQ was developed, with the aim of simplifying the dosing regimen, improving adherence to treatment and slowing the emergence of drug resistance. Clinical trials in Thailand and Myanmar have shown that reduction of the daily dose of mefloquine and coformulation of the two antimalarials also lead to improved mefloquine bioavailability and tolerability[2,3].

Despite good evidence of sustained high efficacy in Southeast Asia, mefloquine-based ACTs have not been adopted widely. Reasons for this include concerns about tolerability and safety related to repeated dosing, especially in high-transmission areas, lack of safety data in pregnancy and wide publicity of neuropsychiatric side-effects when mefloquine is used as chemoprophylaxis.

The FDC AS-MQ is now registered in Brazil where large-scale deployment combined with passive pharmacovigilance have been associated with a reduction in malaria incidence without identification of any safety concerns.

Reports of emerging artemisinin resistance from Cambodia indicate an incipient global public health disaster unless action is taken urgently. The imperative to provide ACTs only as FDCs is stronger than ever. Trials of FDC AS-MQ treatment during pregnancy and in Africa are ongoing. The combination should be considered as an alternative first-line treatment in malaria-endemic countries. The long half-life of mefloquine with the associated prolonged secondary prophylactic effect make it an attractive option for alternative malaria control strategies such as intermittent preventive therapy.

(1) Carrara VI, Zwang J et al. PLoS One 2009;4(2):e4551.
(2) Ashley EA, Lwin KM et al.Trop Med Int Health 2006;11(11):1653-60.
(3) Ashley EA, Stepniewska K et al.Antimicrob Agents Chemother 2006;50(7):2281-5.