

# DIHYDROARTEMISININ-PIPERAQUINE: AN UPDATE

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Dihydroartemisinin-piperaquine (DHAPQ) is a new and extremely promising artemisinin-based combination recently added by the World Health Organization to the recommended list of treatments for uncomplicated *Plasmodium falciparum* malaria. DHAPQ is about to be registered with international regulatory authorities such as the European Medicines Agency, and a formulation produced according to good manufacturing practices should be available soon. Piperaquine is characterized by a slow absorption, long mean terminal elimination half-life and large mean volume distribution. However, children, compared to the population mean profile, tend to have a smaller central volume of distribution, a shorter distribution half-life and a more rapid fall in early piperaquine plasma concentrations, suggesting that an increase of the weight-adjusted dosage in children may be required. In addition, the oral bioavailability of piperaquine improves when given with a high-fat meal, although this does not necessarily translate into a higher efficacy. Several clinical trials have repeatedly shown that DHAPQ is safe and efficacious<sup>1</sup>, with the only exception of one recently carried out in Papua New Guinea<sup>2</sup>. Patients treated with DHAPQ may have a higher rate of person/gametocyte/weeks, although it is unclear whether this translates in a higher infectiousness to biting anophelines. A large trial (NCT00393679) comparing DHAPQ with artemether-lumefantrine (AL) and artesunate-amodiaquine (ASAQ) has been recently completed. Between July, 2007, and December, 2008, more than 4,000 African children aged 6-59 months with uncomplicated *P. falciparum* malaria were recruited and followed up. Preliminary results indicate that DHAPQ efficacy is similar to that of artesunate-amodiaquine (ASAQ) and artemether lumefantrine (AL), and above 95% at day 28. A clinical trial comparing DHAPQ, ASAQ, AL and artesunate-mefloquine (ASMQ) for the treatment of women in the second or third trimester of pregnancy with malaria is about to start in four African countries, i.e. Burkina Faso, Ghana, Malawi and Zambia. Results are expected for 2013.

1. Bassat Q, Mulenga M, Tinto H, Piola P, Borrmann S, Menéndez C, Nambozi M, Valéa I, Nabasumba C, Sasi P, Bacchieri A, Corsi M, Ubben D, Talisuna A, D'Alessandro U. Dihydroartemisinin-piperaquine and artemether-lumefantrine for treating uncomplicated malaria in African children: a randomised, noninferiority trial. *PLoS One*. 2009 Nov 17;4(11).
2. Karunajeewa HA, Mueller I, Senn M, et al. A Trial of Combination Antimalarial Therapies in Children from Papua New Guinea. *N Engl J Med* 2008; 359: 2545-2557.