Efficacy and safety of Triple ACTs compared to conventional ACTs for the treatment of uncomplicated malaria: preliminary results of the DeTACT trial in Niger

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Introduction
Artemisinin-based combination therapies (ACTs) have made a major contribution to substantial reductions in malaria morbidity and mortality worldwide over the past decade. However, future benefits are threatened by the recent emergence of resistance to artemisinin and related drugs in Asia and Africa. This study aims to evaluate alternative treatments using combinations of existing drugs.

Methodology
Multicenter, partially blinded, randomized, controlled, non-inferiority trial comparing the efficacy, tolerability and safety of artemisinin-based triple therapies (artemether-lumefantrine+amodiaquine, artesunate-mefloquine+piperazine) and ACTs (artemether-lumefantrine+placebo, artesunate-mefloquine+placebo) conducted in Maradi, Niger. 432 participants aged 6 months to 12 years with acute, uncomplicated P. falciparum monoinfection were randomized into 4 arms, hospitalized for 72 hours and followed as outpatients for 9 weeks. Blood analyses of efficacy, safety, pharmacokinetics, pharmacodynamics and electrocardiograms were performed.

Preliminary results
A better post-treatment prophylactic effect with TACT than with CTA. No differences in fever disappearance and parasite clearance between CTA and TACT. More vomiting recorded with TACT. Liver and kidney parameters comparable between arms. No cardiac safety issues noted. No signs of artemisinin resistance were found at the Niger study site. Further results are awaited on PCR-corrected efficacy, pharmacokinetics, pharmacodynamics, and those of the other study sites.

Conclusion
The loss of efficacy of first-line ACTs compromises malaria control and elimination efforts. A major concern for Africa, which bears most of the global malaria burden. Different response strategies need to be explored.

Upcoming results of PCR-corrected efficacy, the other pharmacokinetic analyses and results from other sites are likely to provide further evidence of the efficacy of TACTs in addressing artemisinin resistance.