Population-Pharmacokinetics of the Artesunate-Mefloquine (ASMQ) Fixed Dose Combination for the Treatment of Uncomplicated Falciparum Malaria in African children

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Background
- WHO recommends fixed-dose artemisin-based combinations therapies (ACTs) to treat uncomplicated Plasmodium falciparum malaria.
- In Africa, there is limited data available on the artesunate-mefloquine (ASMQ) fixed-dose combination (FDC) and no data on MQ pharmacokinetics in children.

Methods
- A randomized clinical study evaluating the efficacy and safety of artesunate-mefloquine vs artemether-lumefantrine combinations is being conducted in children under 5 years of age in Kenya, Tanzania and Burkina Faso.
- The Laboratory participates in the WorldWide Antimalarial Resistance Network (WWARN) where our Laboratory performs well.
- The Laboratory is involved in the External Quality Control program for antimalarial drugs organized by the WorldWide Antimalarial Resistance Network (WWARN) where our Laboratory performs well.

Data
- A total of 216 MQ samples were collected from 48 Kenyan children with Plasmodium falciparum malaria.

Data analysis
- The analysis was performed using the NONMEM® (non-linear mixed effect modelling) program
- A two-compartment model with first-order absorption and elimination best describes mefloquine pharmacokinetics.
- Estimated parameters were: systemic clearance (CL), intercompartmental clearance (Q), volumes of distribution of the central and peripheral compartment (Vc and Vp) and absorption rate constant (Ka).
- Interpatient variability (IIV) was associated with CL, Vc and Ka.

Conclusions
- MQ pharmacokinetics present large inter-patient variability in children treated with fixed dose regimen.
- Clearance and volume of distribution of MQ in children is lower than in adult patients of African, Caucasian or Asian origin, but the terminal elimination half-life and mean absorption time are of similar magnitude.
- These results will be further analyzed in light of efficacy and tolerance data.