

Efficacy of artemether-lumefantrine for the treatment of uncomplicated *Plasmodium falciparum* malaria in Klouekanmey and Djougou, Republic of Benin

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In 2008, artemether-lumefantrine (AL) was introduced as first-line treatment for uncomplicated *Plasmodium falciparum* malaria in Benin. Following the World Health Organization recommendation to regularly monitor antimalarial efficacy, we conducted an efficacy study of AL for uncomplicated *P. falciparum* malaria in Klouekanmey and Djougou. Febrile patients 6-59 months old with *P. falciparum* monoinfection and 2,000-200,000 parasites/ μ l were treated with a 3-day course of AL. Clinical and parasitological response was monitored for 28 days. We differentiated recrudescence from reinfection using microsatellite genotyping and calculated uncorrected and corrected adequate clinical and parasitological response (ACPR) rates. We performed molecular analyses for *PfK13* propeller and *Pfmdr1* gene mutations, associated with artemisinin and lumefantrine resistance, respectively. In Klouekanmey, among the 115 patients who completed follow-up, 2 (1.7%) infections occurred on Days 21 and 25, yielding an uncorrected ACPR of 98.3% (95% confidence interval [CI]= 93.9-99.8). In Djougou, among 120 patients with complete follow-up, there was 1 (0.8%) early treatment failure (signs of severe malaria on Day 1) and 11 (9.2%) infections identified from Day 21 to 28, uncorrected ACPR of 90.0% (95% CI= 83.2-94.7). None of the recurrent infections in Klouekanmey and one in Djougou were classified as recrudescence by genotyping; microsatellite-corrected ACPRs of 100.0% (95% CI= 96.8-100.0) and 98.2% (95% CI= 93.6-99.8), respectively. No *PfK13* gene mutations were observed at enrollment. Considering mutant and mixed (mutant and wild type) *Pfmdr1* alleles, we observed prevalence of 11.2% and 58.9% for the 86Y and 184F mutations, respectively. AL remains efficacious for falciparum malaria in these two sites in Benin; however, we found a high frequency of the *Pfmdr1* Y184F mutant allele. Our study also revealed high incidence of recurrent infections in Djougou during the 28-day follow-up, highlighting the importance of considering clinical,

parasitological, and molecular data together to adequately estimate treatment efficacy and drug resistance.