In vivo study to monitor the sensitivity of Plasmodium falciparum and other species to Pyronaridine-artesunate and Artemether-lumefantrine in Niger.

Introduction: The emergence and spread of antimalarial drug resistance has been a major hurdle in clinical management of malaria, and therefore, Artemisinin-based combination therapies (ACT) have become the corner stone for falciparum malaria treatment worldwide. The Country of Niger recommended Artemether-Lumefantrine and Artesunate-Pyronaridine as first ACT of the treatment of uncomplicated malaria without contributing the clinical development of these combinations. The West the African Network of clinical trial of anti-malarial drug (WANECAM-II), aimed this study to monitor the *in vivo* responses and PCR-adjusted adequate clinical and parasitological responses (ACPR) as an update of the therapeutic responses.

Methods: From November 2019 to December 2020, we performed a randomized, open-label, longitudinal, and controlled phase 4 clinical trial at Koira-Tegui in Niamey, Niger. A freely given informed consent was obtained from adult patients and children aged from 6 months and older with microscopically confirmed *Plasmodium falciparum and/or other species* malaria (1000 to 200 000 parasites per µL of blood). After controlling for inclusion and exclusion criteria, eligible participants were randomized to receive either AL (Coartem®) or AP (Pyramax®). Microscopy and filter papers were collected from day0 to day42 according to WHO 2000 to evaluate clinical and parasitological responses of the treatment and for molecular correction of parasitological failures. Appropriates statistical analysis were performed and p-value less than 0.05 was considered as statistically significant.

Result: During the study period, we randomized 123 and 117 eligible participants to AL and AP groups respectively. Of the total 240 participants, female patients represented 59% while under 5 years old were 32%. The median ages were 6 years in AL group and 8 years in AP. The two groups were comparable for sex and age groups. There was a significant statistical difference of PCR-unadjusted ACPR between AL and AP on day28 (82% *versus* 97% respectively; p=0.0003) and day42 (77% *versus* 90% respectively; p=0.0119,). PCR corrections are ongoing, and the ACPR-adjusted results will be provided at the forum. After treatment initiation, the proportion of parasites clearances at 12 hours was comparable between AL and AP (p=0.1197), but significantly higher in AP group compared to AL group at 36 hours, 48 hours, and 72 hours ($p<0.05$) even if similar at 60 hours.