OA-029 PATTERNS OF MOLECULAR MARKERS OF RESISTANCE IN 'REAL LIFE' REPETITIVE DIHYDROARTEMISININ-PIPERAQUINE MALARIA TREATMENT: A MOLECULAR ANALYSIS OF THE WANECAM CLINICAL TRIAL PLATFORM OUTPUT

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Background The pharmacologic characteristic of piperaquine (PPQ), namely its very long half-life, raises concerns on the possibility of relatively rapid rise of resistance. Recent unequivocal reports from SE Asia support this worry. Due to its long half-life, conventional follow-up of up to 63 days in efficacy trials misses the low concentrations of PPQ, prone to select less sensitive parasite sub-populations. The WANECAM clinical trials included a follow-up of two years of the same patients, allowing for the first time the analysis of both, the patterns of selection upon an expected large range of PPQ concentrations and the potential effect of residual levels upon repetitive treatments.

Methods We have successfully determined a random sample of E1 (D0) 151 and 405 (E2-E10) pfcrt K76T genotypes, as well as 151 E1 (D0) and 389 (E2-E10) genotypes for the pfmdr1 E2-E10 episodes. Pfmdr1 N86Y analysis was limited by a large (>90%) prevalence of the 86N allele. Established PCR-RFLP methods were applied, with high precision band analysis being performed through image analysis software (GelEval®). Qui Square and Kruskal Wallis tests were used as applicable.

Results The present data analysis was limited to episodes with an intervening period of<180 days. Preliminary conclusions point to recurrences of pfmdr1 carrying 184Y parasites to emerge earlier as compared with 184F (D78 *vs* D89, Kruskal Wallis test, p< 0.01), corresponding to an expected difference of ca. 20 to 10 nM on PPQ blood levels. No significant differences were detected concerning pfcrt K76T.

Conclusions Long-term analysis of molecular markers throughout repetitive treatments is expected to unveil informative patterns concerning early steps of PPQ resistance development. The complete set of data will be presented and analysed in the context of the recent findings of PPQ resistance in SE Asia. Its relevance for the East African settings will be discussed.