**Background** Currently, five artemisinin combination therapies (ACTs) are recommended by WHO for treatment of uncomplicated malaria in Africa. While artemisinin derivatives have a short half-life, the partner drugs give rise to differing durations of post-treatment prophylaxis. The pharmacokinetic and pharmacodynamic properties of drug regimens have implications for the public health benefit of the drugs. The development of new antimalarials is ongoing. The objective of this work is to evaluate the prophylactic effect of artesunate-pyronaridine (Pyramax) and dihydroartemisinin-piperaquine (Furartesim) vs artemether-lumefantrine (AR_L) and artesunate-amodiaquine (ASAQ), respectively in Bougoula Hameau.

**Methods** Through the phase IIIb/IV clinical trial of the West African Network of clinical trial of antimalarial drugs (WANECAM) in Bougoula Hameau (Mali) from January 2012 to December 2013, we evaluated the median time of occurrence for the second and third episodes of malaria on patients aged from 6 months to above. After the first randomisation, any other subsequent episodes of malaria as treated by the same ACT initially taken. Treatment failure before day 28 was treated by quinine.

**Results** Whilst 448 patients were randomised to receive DHA (224) vs ASAQ (224), 428 received PA (214) vs AR_L (214). The median time to second and third episodes of malaria were 116 days and 60.5 with PA versus 82.5 and 56.0 for AR_L, respectively. Otherwise, we found 118 and 98 vs 82.5 and 60 days as median time to second and third episode for DHA-PQP vs AS/AQ, respectively. DHA-PQP highly prolonged the median time to second and third episode as compared to ASAQ (p=0.003 and p<0.001, respectively).

**Conclusions** The ACTs artesunate-pyronaridine and dihydroartemisinin-piperaquine significantly prolonged the median time to second and third episode of malaria as compared to artemether-lumefantrine and artesunate-amodiaquine, respectively.