

## Therapeutic efficacies of two different ACT and their relation to K13 mutations in sentinel sites of Myanmar

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Artemisinin Combination Treatment (ACT) is the first line for *Plasmodium falciparum* malaria, recommended by World Health Organization (WHO) and used globally. Artemisinin resistant *P. falciparum* was reported in Cambodia, and now confirmed in several Greater Mekong Subregion (GMS) countries. Although ACT efficacy remains high in many parts of malaria endemic world, it is progressively declining in Cambodia, raising a great concern regionally and globally. Recently mutations in *P. falciparum* Kelch propeller gene, commonly known as K13, were shown to be associated with artemisinin resistance in Cambodia and specific regions of GMS. These mutations are expected to predict clinical efficacy of ACT, and assessment of K13 mutations was recommended by the WHO, as part of studies to routinely monitor therapeutic efficacy of ACTs at the country level. Following the WHO recommendation, three prospective, multi-center, open-label clinical studies were conducted in 2013-2015 to assess the efficacy of artemether-lumefantrine (AL) and dihydroartemisinin-piperaquine (DHA-PIP). Each study drug was assessed in three sentinel sites in Myanmar: Buthidaung in Rakhine State (Western Myanmar), Myitkyina in Kachin State (Northern Myanmar), and Mu-se in Shan State (Northern-eastern Myanmar). A total of 293 participants acutely ill with mono-infection with *P. falciparum* were recruited, treated and monitored for 28 days, and assessed for safety and clinical and parasitological efficacy of the study drugs. Overall, both drugs were well tolerated. The PCR-corrected ACPR (Adequate Clinical Parasitological Response) to AL was 100%, 93% and 96% in Buthidaung, Myitkyina and Mu-se respectively, and to DHA-PIP was 100% in all the three sentinel sites. The K13 gene was successfully sequenced in all 293 participants (46.4%). K13 F446I mutation was detected in 56.7% (55/97) in Mu-se and 61.1% (58/95) in Myitkyina. The study reported the prevalence of K13 mutation together with therapeutic efficacy of different combinations of ACT.