

Myanmar (n=12; 15% of studies: nine in vivo, one in vitro and one molecular; the MARC reviews unpublished findings)

- Direct evidence of artemisinin resistance is lacking, although preliminary in vitro data from southern Myanmar suggests emerging tolerance to AL and DHQ [7]
- In published in vivo studies, ACTs remain highly efficacious (clinical failure rates below 3%) [60-63]
- MQ monotherapy is less effective in clinical trials, with higher 42-day failure rates than ACT. [62] In vitro resistance to MQ appears to be highest near the border with Thailand [64]
- Molecular studies are limited. A single study from Laiza Township, Kachin State found all *P. falciparum* isolates carried the mutant K76T allele (CVIET); all isolates harboured a single copy of *pfmdr1* [39]

Western Thailand (n=41; 50% studies)

- Genetically-determined resistance to ART, measured by average parasite clearance time and the proportion slow-clearing infections during ART treatment, was recently confirmed in western Thailand [1]
- Clinical efficacy of MAS3, the standard first line treatment for uncomplicated *P. falciparum* infections, remains high but has declined slightly since 1995 [65]
- Resistance to MQ monotherapy emerged shortly after introduction in 1985 [66]. Introduction of MAS3 may have slowed or reversed the decline in clinical efficacy of MQ [67]
- *pfmdr1* amplification is associated with resistance to MQ, ART monotherapy, and MAS combination therapy. [9, 10] The prevalence of *pfmdr1* amplification has increased since 1996, [9, 10, 13, 65, 68-70] but does not appear to explain increasing tolerance to ACTs over time [1, 65]
- CQ resistance is widespread and multiple studies document fixation of the *pfcr* K76T mutation. [9, 13, 68, 71].

Yunnan Province, China (n=6, 7% of studies)

- Unpublished studies suggest low-level clinical resistance to ART monotherapy has emerged in southern Yunnan Province [7], with two- to three-fold increases in resistance parameters between 1988 and 1999. [72]
- In western Yunnan, in vitro resistance to CQ decreased from 100% in 1982 to 83% in 2003 [73], although in 2006 40% of infections exhibited in vivo resistance to CQ. [73] 90-92% of isolates carry the *pfcr* K76T mutation [40, 74]
- A single study reported *Pfmdr1* amplification in 9.4% of isolates from southern Yunnan in 2004 [40]

Northeast India (n=11, 13% of studies)

- Resistance to MQ is rare [75] and ACT appears to be nearly 100% clinically effective [76]
- CQ resistance is prevalent in north-east India, with high treatment failure rates observed in states bordering Myanmar: 60% in Mizoram, 29% in Nagaland, 80% in border districts of Arunachal Pradesh
- *pfcr* K76T mutations are at fixation. [77] Both CVIET and SVMNT haplotypes are prevalent [78]
- The literature review found no published studies on *pfmdr1* amplification in this region

Eastern Bangladesh (n=10, 12% of studies)

- MAS and AL remain highly efficacious in the Chittagong Hill Tracts, an area bordering Rakhine State, Myanmar, with 42-day PCR-corrected efficacy rates of 100% and 97%, respectively [79]
- *P. falciparum* isolates from the Chittagong Hill Tracts were more susceptible to CQ and ART in vitro compared to isolates from the Thai-Myanmar and Thai-Cambodia borders [80]
- CQ resistance is well established [79, 81] and over 95% of isolates carry the *pfcr* K76T mutation [82]
- The literature review found no published studies on *pfmdr1* amplification in this region