Molecular determinants of artemisinin resistance in k13 gene of plasmodium falciparum

ABSTRACT

Artemisinin-based combination therapy (ACT) is the first-line therapy in most malaria endemic countries. An impressive 47% reduction in the global mortality rate between 2000 and 2013 has been achieved by ACT and artemisinin (ART) monotherapy. However, artemisinin resistance (AR) by Plasmodium falciparum(P. falciparum) is now prevalent across south-east Asia (SEA). AR is indicated by delayed parasite clearance of more than 3 days after standard ART treatment and reduced in vitrosusceptibility. Recent work has shown association of AR with mutations in the propeller domain of the kelch gene on chromosome 13 (PF3D7_1343700, k13gene) of P. falciparum. The C580Y mutation of thek13gene is highly prevalent in Cambodia, Myanmar and eastern and western Thailand, while the F446I mutation is predominant in the China-Myanmar border regions as well as in Myanmar. AR has not reached India and Africa, where non-synonymous mutations not associated with delayed parasite clearance are present. Because the location of Myanmar is central between SEA and Africa, a country-specific strategy for Myanmar Artemisinin Resistance Containment (MARC) is necessary. Moreover, regular periodic tracking of prevalent molecular determinants such as C580Y and F446I mutations will be beneficial.