RANDOMIZED, CONTROLLED, DOUBLE-BLIND TRIAL OF DAILY ORAL AZITHROMYCIN IN ADULTS FOR THE PROPHYLAXIS OF *PLASMODIUM VIVAX* MALARIA IN WESTERN THAILAND


We assessed the prophylactic efficacy of azithromycin (250 mg/day) against malaria in 276 adults in western Thailand in a randomized, double-blind, placebo-controlled trial. After antimalarial suppressive treatment, volunteers were randomized in a 2:1 ratio to either the azithromycin or placebo, respectively. Study medication was given for an average of 74 days. The azithromycin group (n = 179) had five endpoint parasitemias (1 *Plasmodium vivax* and 4 *P. falciparum*), and the placebo group (n = 97) had 28 endpoint parasitemias (21 *P. vivax*, 5 *P. falciparum*, and 2 mixed infections). Adverse events and compliance and withdrawal rates were similar in both groups. The protective efficacy (PE) of azithromycin was 98% for *P. vivax* (95% confidence interval [CI] = 88–100%). There were too few cases to reliably estimate the efficacy of azithromycin for *P. falciparum* (PE = 71%, 95% CI = –14–94%). We conclude that daily azithromycin was safe, well-tolerated, and had a high efficacy for the prevention of *P. vivax* malaria.


A RANDOMIZED, DOUBLE BLINDED STUDY OF THE EFFICACY AND SAFETY OF TAFENOQUINE MONOTHERAPY FOR THE TREATMENT OF *PLASMODIUM VIVAX* IN ADULTS


**Background:** Tafenoquine is an 8-aminoquinoline antimalarial drug with demonstrated efficacy as a relapse prevention agent for the treatment *Plasmodium vivax* malaria following chloroquine administration. Although tafenoquine also possesses significant blood schizonticidal activity, no formal studies have been undertaken to assess the efficacy of tafenoquine as a single agent for clearance of both *Plasmodium vivax* asexual blood stages and hypnozoites.

**Methods:** In order to assess the safety and efficacy of tafenoquine as a single agent for the treatment of *Plasmodium vivax* malaria, 70 patients were randomized (2:1) to receive either tafenoquine (400 mg daily for three consecutive days) vs. conventional therapy (1500 mg chloroquine over three days followed by 14 days of 15 mg primaquine daily) in a double blinded, double dummy randomized trial. Adequate clinical response (ACR) was defined as clearance of parasitemia by Day 7 (treatment initiated on Day 0) and confirmed parasitological clearance throughout the follow-up period (Day 28). Thereafter subjects were followed for an additional three months to assess *Plasmodium vivax* relapse rates.
**Results:** A total of 65 subjects (tafenoquine n=43; chloroquine/primaquine n=22) were in the per protocol population and therefore evaluable for the primary analysis of ACR. For tafenoquine, 93% (40 of 43) and for chloroquine/primaquine, 100% (22 of 22) of subjects had an adequate clinical response. Three tafenoquine subjects still had low level parasitemias on Day 7, and therefore did not meet criteria for ACR. However, all 3 subjects cleared their parasitemia by Day 8 without the need for repeated or rescue therapy. Of the subjects achieving ACR, a total of 55 subjects (tafenoquine n=35; chloroquine/primaquine n=20) were evaluable for per protocol analyses of relapse rates throughout the follow-up period (Days 30-120). Relapse efficacy was 100% (35/35) in the tafenoquine arm vs. 95% (19/20) in the chloroquine/primaquine arm. The study has been completed and analysis of the efficacy and safety data is in progress. Complete efficacy and safety results will be presented.

**Conclusion:** This study demonstrates the potential utility of tafenoquine as treatment for both exo-erythrocytic and erythrocytic stages of *Plasmodium vivax* malaria.


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**RECENT ANTIMALARIAL TREATMENT AMONG KENYAN ADULTS PRESENTING TO CLINICS WITH POSITIVE MALARIA SMEARS**

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Antimalarial resistance is a growing problem in Kenya. From January 2003 - December 2004, 474 subjects enrolled in a study of antimalarial resistance across Kenya. Subjects were referred by hospitals in coastal Malindi (107), semi-arid Isiolo (135), Lake Victoria basin Kisumu (123), and Alupe on the Ugandan border (109). We examine recent antimalarial use among these smear-positive patients. Patients found by the hospital laboratory to have a positive malaria smear were referred to our study. After obtaining informed consent, the project laboratory technician repeated a malaria smear. If positive, the subject was enrolled, self-reported data and samples were collected, and the subject was treated per local standard of care. Self-reported data includes demographics, recent previous malaria diagnosis (within 6 weeks) and recent antimalarial treatment. Of the subjects, 49% were female and 51% male. Mean age was 12.3 years, with 69% younger than 18 years. 48% reported treatment for malaria in the past 6 weeks. Recent antimalarial use varied significantly among sites: Isiolo 72%, Alupe 50%, Malindi 36% and Kisumu 30% (p < 0.001). Neither sex nor age was associated with prior treatment (p = 0.760, P = 0.845). Among previously treated subjects, 24% of subjects self-treated or were treated by a pharmacist, 72% by a Ministry facility, and 4% by a private clinic. Treatment in the formal vs. informal setting was not influenced by sex or age (p = 0.177, p = 0.387), but varied among the sites (p = 0.006), with percentages treated in the formal sector highest in Alupe (93%) and lowest in Malindi (55%). Fansidar was the most commonly used antimalarial (47% of those treated), followed byquine (20%) and amodiaquine (14%). Although not legally available, 3% reported chloroquine use. That almost half of all malaria smear positive patients had taken antimalarials in the past 6 weeks suggests high levels of treatment failure or reinfection. That neither sex nor age significantly influenced recent history of treatment for malaria is surprising. Treatment being most common in Isiolo, where malaria is mesoendemic rather than endemic, may reflect the lack of partial immunity.