PYRAMAX® (PYRONARIDINE/ARTESUNATE), TABLET OR PAEDIATRIC SACHET, VERSUS COARTEM® (ARTEMETHER/LUMEFANTRINE), TABLET OR CRUSHED TABLET, IN PATIENTS WITH ACUTE UNCOMPLICATED PLASMODIUM FALCIPARUM MALARIA: RESULTS OF TWO PIVOTAL PHASE III STUDIES


1 Medicines for Malaria Venture, Geneva, Switzerland
2 Ecole de Santé Publique, Faculté de Médecine, Université de Kinshasa, Kinshasa, DRC ex, Zaire
3 Service de Parasitologie, Faculté de Médecine Université Cheikh Anta Diop, Dakar, Senegal
4 Malaria Research and Training Center, Faculté de Médecine de Pharmacie et d’Ondontostomatologie, Bamako, Mali
5 Instituto Nacional de Saude, Ministerio de Saude, Maputo, Mozambique
6 UNITID, College of Health Sciences, University of Nairobi, Nairobi, Kenya
7 Farafenni Field Station, MRC Laboratories, Fajara, Gambia
8 Ospital ng Palawan, Palawan, Philippines
9 Biomedical and Pharmaceutical Research and Development, Center National Institute of Health Research and Development, Jakarta, Indonesia
10 Komfo Anokye Teaching Hospital, Kumasi, Ghana
11 Unité de Paludologie, Institut Pasteur d’Abidjan, Abidjan, Cote D’Ivoire (Ivory Coast)
12 Medical Research Unit, Albert Schweitzer Hospital, Lambaréné, Gabon
13 Centre National de Recherche et de Formation sur le Paludisme, Ouagadougou, Burkina Faso
14 Shin Poong Pharmaceuticals, Seoul, Sth Korea

Two phase III comparative randomized, non-inferiority, multi-center clinical trials were conducted to assess the efficacy and safety of Pyramax (pyronaridine/artesunate=PA) versus Coartem (artemether/lumefantrine=AL) in patients from Africa and South-East Asia with acute uncomplicated P. falciparum malaria. The first study was carried out with PA tablets (180:60mg) in a double-blind, double-dummy design in 1272 children and adults (5-60 year-old) in 10 sites in Africa and South-East Asia. The second study was carried out with PA sachets (60:20mg) in an open-label design in 535 paediatric patients (<12 year-old; 5-25 kg) from 7 sites in Africa and South-East Asia. For the two studies, the primary efficacy endpoint was D28-PCR-corrected adequate clinical and parasitological response (ACPR). Recrudescence and re-infection rates were also assessed using Kaplan-Meier survival analysis. Safety was assessed with 12-lead ECG, clinical laboratory evaluations for hematology, biochemistry and urinalysis. In the efficacy evaluable population of the children and adults study, the PCR-corrected ACPR was 99.5% with PA and 99.2% with AL. Results demonstrate non-inferiority of PA to AL with a 5% non-inferiority margin. Kaplan-Meier survival analysis showed a lower rate of re-infection and a longer time to re-infection in the PA group than in the AL group. In the efficacy evaluable population of the paediatric study, the PCR-corrected ACPR was 97.6% with PA and 98.8% with AL. Results demonstrate non-inferiority of PA to AL using a 10% non-inferiority margin. Kaplan-Meier survival analysis did not show any difference between PA and AL. Treatments with PA or AL were well-tolerated in both studies. The adverse event profiles of PA and AL were similar with mostly mild events and no drug-related serious adverse events. These two pivotal trials comparing PA to AL demonstrated high level efficacy, safety and tolerability of the treatments in patients with uncomplicated P. falciparum malaria in Africa and South-East Asia.