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

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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.