Pharmacy and Poisons Board
Online clinical trials
Submitted Application : (ECCT/17/08/02)

Protocol No:	**ECCT/17/08/02**	Date of Protocol:	**01-05-2017**

Abstract of Study:

Malaria in pregnancy has devastating consequences for mother and foetus. WHO recommends intermittent preventive treatment in pregnancy (IPTp) with sulphadoxine-pyrimethamine (SP) for asymptomatic women, but high-level SP resistance threatens its efficacy. Over the last decade, several IPTp trials showed that neither amodiaquine, mefloquine, nor chloroquine-azithromycin are suitable replacements for SP because of their poor tolerability as IPTp. Furthermore, intermittent screening for malaria and treatment with artemisinin-based combination therapies has recently shown to be non-superior to IPTp-SP even in areas with very high SP resistance. Thus, there is an ever urgent need to find alternative drugs for IPTp.

Dihydroartemisinin-piperaquine (DP) has the potential to replace SP for IPTp. Exploratory trials from Kenya and Uganda showed that IPTp-DP was more effective than SP in reducing malaria infection (Incidence Rate Ratio [IRR]=0.32) and clinical malaria (IRR=0.16), but these preliminary trials were not powered to assess birth outcomes. WHO, in July 2015, recommended that definitive multi-centre trials are needed before IPTp-DP can be considered for policy.
Sexually transmitted and reproductive tract infections (STIs/RTIs) also cause poor birth outcomes and are highly prevalent in East and Southern Africa, and similar to malaria, remain mostly asymptomatic, and therefore undetected and untreated. We will therefore determine whether combining DP with azithromycin, a broad spectrum antibiotic active against STIs/RTIs, can further improve birth outcomes, potentially paving the way for integrated control strategies for malaria and curable sexually transmitted and reproductive tract co-infections.

This is a multi-national, individually-randomized, 3-arm, partially-placebo controlled superiority trial comparing the efficacy, safety and tolerance of IPTp-SP (control) versus IPTp-DP, alone or combined with azithromycin (0.5 gr/daily for 3 days) to adverse effects of malaria and curable STIs/RTIs in 4,680 women in 10 sites in high SP resistance areas in Kenya, Malawi, and Tanzania. The study is powered (90%, alpha=0.025) to detect a 25% reduction (RR=0.75) in 'adverse pregnancy outcomes' (composite of foetal loss, small-for-gestational age, low birthweight, preterm, or neonatal death). The project includes cardiac monitoring for safety, assessment of antimalarial druge and macrolide resistance, nutritional outcomes, and the impact of SP and AZ on vaginal and intestinal microbiota, and health economics.

Study Title:

IPTp with dihydroartemisinin-piperaquine and azithromycin for malaria, sexually transmitted and reproductive tract infections in pregnancy in high sulphadoxine-pyrimethamine resistance areas in Kenya, Malawi and Tanzania: an international multi-centre 3-arm placebo-controlled trial