Safety, Tolerability, Immunogenicity and Efficacy of PfSPZ Vaccine versus PfSPZ-CVac in Equatoguinean Young Adults.

Vicente Urbano[1,2], Ally Olotu[1,3], Ali Hamad[1,3], Ali Mtoro[1,3], Mwajuma Chemba[1,3], Stephen R. Manock[1,4], Maximillian Mpina[1,3], Elizabeth Nyakarungu[1,3], Esther Eburi[1,5], Antonio Enrique Ngua Sama Roca[1,5], Martin Eka Ondo Mangue[1,2], Thomas Stabler[1,4], Yonas Abebe[4], Carl D. Maas[6], Mitoha Ondo'o Ayekaba[6], Salomón Nguema Owono[4], Matilde Riloha Rivas[4], Chris Schwabe[5], Julie Niemczura de Carvalho[5], Luis Segura[1,5], Wonder Phiri[1,5], Tobias Schindler[7], Elizabeth Saverino[4], Peter F. Billingsley[4], B. Kim Lee Sim[4], Claudia Daubenberger[7,8], Thomas Richie[4], Salim Abdulla[3], Stephen L. Hoffman[4]

1=Equatorial Guinea Malaria Vaccine Initiative; 2=Ministry of Health and Social Welfare; 3= Ifakara Health Institute; 4=Sanaria Inc.; 5=Medical Care Development International; 6=Marathon EG Production Ltd; 7=Swiss Tropical and Public Health Institute; 8=University of Basel.

PfSPZ Vaccine is a candidate pre-erythrocytic malaria vaccine composed of radiation-attenuated, aseptic, purified, cryopreserved *Plasmodium falciparum* (Pf) NF54 sporozoites (SPZ). In trials in the U.S. and Africa, PfSPZ Vaccine administered by direct venous inoculation (DVI) provided durable protection against heterologous strains and heterogeneous populations of Pf for at least 24 to 33 wks. A second PfSPZ-based vaccine approach – administration of low doses of non-irradiated, infectious NF54 PfSPZ (PfSPZ Challenge) under chloroquine chemoprophylaxis (PfSPZ-CVac) – protected against homologous strains of Pf in the U.S. and Europe for at least 10 wks, but had not been tested in Africa. We conducted a randomized, double blind placebo-controlled trial comparing tolerability, safety, immunogenicity and efficacy against controlled human malaria infection (CHMI) of PfSPZ Vaccine versus PfSPZ-CVac in healthy malaria-exposed Equatoguinean 18 to 35-year-old men and women. We randomized 26 subjects to receive 3 doses of $2.7x10^6$ PfSPZ (PfSPZ Vaccine) or placebo at 0, 8 and 16 wks, and 24 subjects to receive 3 doses of $1x10^5$ PfSPZ (PfSPZ Challenge) or placebo at 0, 4 and 8 wks after an oral dose of chloroquine (CQ) 600 mg base then CQ 300 mg base weekly (PfSPZ-CVac), followed in both groups by homologous CHMI at 10-13 wks post final vaccine dose. Adverse events (AEs) were solicited for 7 days and surveillance for unsolicited AEs done for 28 days after each vaccination. Monitoring for serious AEs was done throughout. Hematologic, renal and hepatic tests were done at baseline, 2 and 14 days after each vaccination, and prior to CHMI. Blood samples for humoral and cellular immunology were taken at baseline and 14 days after each vaccination. Both vaccine approaches were well-tolerated, and DVI was typically straightforward with only mild pain associated with injection. Safety, immunogenicity and efficacy data will be presented. This comparison of PfSPZ Vaccine and PfSPZ-CVac will provide more information as to which product could be used in mass vaccination programs aimed at regional elimination of malaria. (ClinicalTrials.gov number, NCT02859350)