An exploratory study to verify the safe and reproduceable use of aseptic purified cryopreserved Plasmodium falciparum sporozoites for the induction of controlled human malaria infection in healthy malaria-naïve adults at hVIVO medical research unit.

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Controlled human malaria infection (CHMI) studies involving the introduction of malaria parasites into healthy volunteers have been successfully employed in the investigation of new antimalarial drugs, vaccine candidates and diagnostic assays. Here we describe the initiation of CHMI studies at a new site in London, to facilitate research on parasite biology and host responses in a UK cohort.

In a proof-of-principle, pilot study, we challenged two malaria naive, healthy human subjects with ~3,200 aseptic purified cryopreserved *Plasmodium falciparum* Sporozoites (PfSPZ Sanaria®) by direct venous inoculation (DVI) on Day 1. Subjects remained as in-patients within the hVIVO Ltd clinical research unit for 48 hours post-inoculation (Day 3) after which they were followed up as outpatients and underwent daily monitoring from Day 7 until proven negative by quantitative polymerase chain reaction, targeting the 18S rRNA gene (18S-qPCR). Testing was carried out at United Kingdom Health safety agency (UKHSA) malaria reference laboratory at the London School of Hygiene and Tropical Medicine (LSHTM). Volunteers were rescued with a 3-day course of artemether-lumefantrine within 24 hours of reaching 18S-qPCR threshold ≥250 parasites/mL. Volunteers were exempted from daily clinic visits and were deemed to have achieved 'test of cure' following two consecutive negative 18S-qPCR signals. Safety assessments comprised clinical and laboratory monitoring of vital signs, adverse events and biochemical markers.

One female and one male volunteer were successfully inoculated with PfSPZ Sanaria®. Parasitological and clinical histories of both participants will be presented. There were no severe or serious adverse events and no evidence of *P. falciparum* recrudescence.

hVIVO Ltd and LSHTM have safely and successfully conducted a CHMI study in London. The model can now be used to better understand and develop new interventions against the *P. falciparum* parasite.