

Speaker Abstracts

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A Controlled Human Malaria Infection study to examine naturally-acquired immunity CHMI-SIKA Study Team

Background

A high efficacy vaccine against falciparum malaria would substantially impact global health. Adults in malaria endemic areas are known to acquire clinical immunity that limits parasite growth, and to acquire antibodies to several hundred Plasmodium falciparum (Pf) antigens. We are using the controlled human malaria infection (CHMI) model with malaria-exposed volunteers to identify correlations between immune responses and parasite growth rates in vivo. In this presentation we outline the initial quantitative polymerase chain reaction (qPCR) outcomes and associations with proxies of previous exposure to malaria (i.e. residence and antibody levels to schizont extract).

Methods

We recruited adult volunteers in Kilifi (Coastal Kenya) and Ahero (Western Kenya) who were willing to give fully informed consent for participation in CHMI. We excluded volunteers with significant health problems, including HIV, and excluded volunteers with sickle-cell trait. All volunteers positive for Pf by qPCR were treated with 7 days of artesunate monotherapy prior to CHMI.

We administered 3,200 aseptic, purified, cryopreserved Pf sporozoites (Sanaria® PfSPZ Challenge [NF54]) by direct venous inoculation. Serial qPCR for the falciparum 18s rRNA gene was undertaken during the 21 days following challenge to measure parasite growth in vivo. Participants were treated with anti-malarial drugs when ≥ 500 parasites per μ l were detected, or when fever was present at lower parasite counts.

Results

122 of 161 (76%) participants developed parasitemia detectable by PCR. Of the 122 participants with parasitemia, 58 (48%) required treatment, of whom 27 were febrile. 39 participants (24%) were PCR negative throughout monitoring. Prior residence at higher malaria transmission and higher anti-schizont antibody levels were associated with lower risk of needing treatment following CHMI (HR=0.12, 95%CI 0.07 to 0.2 for residence in a moderate transmission versus low transmission area and HR=0.25, 95%CI 0.16-0.38 for increasing anti-schizont antibody concentrations).

Anti-Schizont antibody levels explained 15% of the variability in outcome in CHMI, compared with **0.8% of the variability in previous field-based cohort studies.**

Conclusion

CHMI is a powerful platform for studying host immunity to malaria. Next steps will include high throughput immunological screening of responses. We expect causal correlates to be independently and strongly associated with outcome after adjusting for the non-causal correlates (i.e. schizont antibodies and residence).

