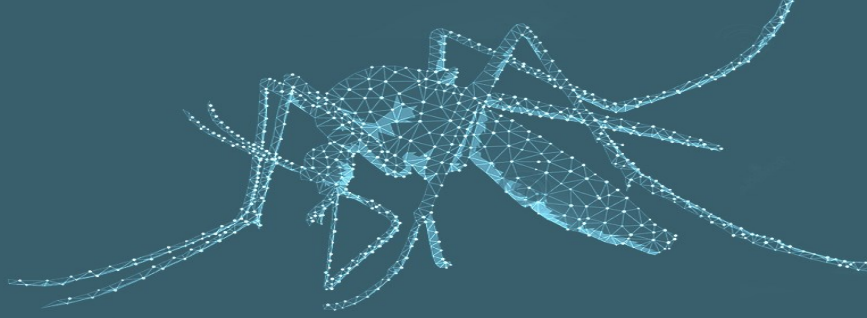
hVIVO
part of Open Orphan plc



Infectious Diseases

Malaria vaccines and treatments

Malaria is a serious and life-threatening, mosquito borne disease prevalent across much of tropical and sub-tropical Asia, South America and Sub-Saharan Africa. Due to increasing resistance to current antimalarial regimens, new drugs are required as both stand-alone and partner therapies to address a growing unmet medical need. New therapies will not only reduce mortality and disease in vulnerable populations, but also to help the move towards a greater goal of malaria elimination.

hVIVO is developing additional capability and capacity within its unique Human Challenge facilities to assist in the advancement of novel anti-malarial drug and vaccine candidates and is now able to offer a Direct Venous Inoculation (DVI), Controlled Human Malaria Infection (CHMI) model for estimations of efficacy. Results from CHMI modelling of drug and vaccine performance have shown good translation into the field.

VALIDATED MALARIA MODEL

GMP manufactured *P. falciparum* sporozoite challenge agent

(Sanaria® PfSPZ Challenge)

Sanaria® PfSPZ Challenge has been used in multiple clinical trials in the United Kingdom, United States, Europe, Australia and Africa.

As of June 2021, 1,204 volunteers have received 2,011 doses of Sanaria® PfSPZ Challenge (NF54) with no unresolved adverse events or sequelae to date.

Reported symptoms are mostly mild to moderate and include headache, fever, nausea and fatigue.

Vaccines/Prophylactics

Operational Challenges

Estimating vaccine efficacy in endemic regions is time-consuming, costly and associated with risks

- Cohort: prior history of *Plasmodium spp.* exposure unknown
- Incidence: 10-20%*
- Study size and duration: large, 1-5+ yrs
- Powering: large 'n' required for clinical efficacy (80-400+)
- Seasonality of vectored transmission

hVIVO Human Challenge Models:

Fast, Translatable Data

- Small (20-30+) cohorts with high attack rate (100%)
- Statistically meaningful estimations of vaccine efficacy
- Year-round availability of modelling
- Match study design to life stage or MoA

Primary & Secondary Endpoints:

- Time to parasitaemia
- Incidence and severity of malarial disease

Antimalarials/Therapeutics

Operational Challenges

Demonstrating efficacy of antimalarials in the field has a high barrier

- Follow-up period: 28 days and as much as 63 days after starting treatment
- Rate of cure: ≥95% (WHO) may lead to premature rejection of potentially valuable new drugs
- Resistance: wide regional variations
- Recrudescence / reinfection: drugs with no effect on liver stages may lead to bounce-back parasitaemias once drug levels fall below the MIC

hVIVO Human Challenge Models:

Fast, Predictive Data

- In-house periods of observation plus close safety monitoring of cohorts
- Monoinfection with drug-sensitive NF54 clone (no recrudescence observed)
- Consistent growth curve and time to parasitaemia
- Optimisation of treatment timing
- Triggered-dosing options (time (d) or parasitaemia threshold)
- Dose ranging studies vs Standard of Care
- Test of cure prior to discharge

Complementary Diagnostics

Operational Challenges

Negative and positive predictive values for novel diagnostics may be heavily affected by relative incidence of disease

- Baseline values are difficult to establish
- Variable parasitaemias in differing cohorts and age groups
- Circulating strain variations
- High clinical significance of missed positive or incorrect value test results
- Operation challenges e.g. standardisation of local laboratories, power etc.

hVIVO Human Challenge Models:

Fast, Reproducible Data

- Well defined sampling schedules
- Predictable and consistent parasite growth curves
- Agreed thresholds for positivity (ppmL / ppuL or Ct)
- All stages of life-cycle expressed
- Species specific data including resistance markers
- Standardised or expert laboratory services.
- Benchmark equipment and MSAs

*Adults (>15yrs), global and sub-Saharan Africa