Background Human hookworm infection is a major public health issue in tropical low and middle-income countries with severe consequences. To date, improvement of water supply, sanitation, and hygiene is the major contributor to disease control, and additional control tools are needed. Here, we assess a phase I trial of a new hookworm vaccine candidate Na-APR-1 (M74)/Alhydrogel and Na-GST-1/Alhydrogel in Gabonese school-age children.

Methods A double-blind, randomised, controlled, dose-escalation phase I clinical trial that aims to evaluate safety, reactogenicity and immunogenicity of Na-APR-1 (M74)/Alhydrogel co-administered with Na-GST-1/Alhydrogel hookworm vaccines in children aged 6 to 10 years living in hookworm-endemic area of Lambaréné, compared to the hepatitis B vaccine (ENGERIX-B). Children received three doses of assigned vaccines, delivered intramuscularly (del- toid) on Days 0, 56, and 112 or 180. Safety is measured from Day 0 through Day 14 by the occurrence of solicited injection site and systemic reactogenicity events. Clinical laboratory evaluations were performed approximately 14 days after each immunisation. Unsolicited adverse events were collected from Day 0 through approximately 1 month after each vaccination.

Results A total of 135 children were screened, and 60, aged 6 to 10 years old, were randomised into 3 groups and received 10 μg, 30 μg or 100 μg of Na-APR-1 (M74)/Alhydrogel and Na-GST-1 Alhydrogel, respectively, compared to ENGERIX-B. At baseline, the mean age of the study population was 7.4 years and the sex ratio 1:1 (male: female). From Day 0 up to Day 14 after vaccination, the main solicited adverse events were pain and swelling at injection sites with 135 (26 of grade 2 and 1 of grade 3) and 9 events, respectively. Regarding systemic adverse events, 3 occurrences of grade 1 headache were recorded. Immunogenicity analyses are underway.

Conclusion The preliminary results confirm that co-administration of the two hookworm vaccine candidates is safe and well-tolerated in Gabonese children.
Abstracts

OC 8552  
Efficacy of the ChAd63-MVC ME-TRAP VECTORED MALARIA VACCINE CANDIDATE IN 5–17 MONTHS OLD INFANTS AND CHILDREN IN BURKINA FASO

1Alfred B Tiono*, 1Issa Nebie, 2Nicholas Anagnostou, 3Sam A Coulibaly, 4Alison Lawrie, 5Edith C Bougouni, 6Alphonse Ouedraogo, 7Jean Baptiste Yaro, 8Issaata Baye, 9Rachel Roberts, 10Amidou Ouedraogo, 11Katie J Ewer, 12Nicola K Viebig, 13Amidou Diarra, 14Odile Leroy, 15Philip Bejan, 16Adrian Hill, 17Sudomann B Sirima, 18Centre National de Recherche et de Formation sur le Paludisme, Burkina Faso; 19Centre for Clinical Vaccinology and Tropical Medicine University of Oxford Churchill Hospital, UK; 20European Vaccine Initiative, Universitäts Klinikum Heidelberg, Germany

Background Heterologous prime-boost immunisation with chimpanzee adenovirus 63 (ChAd63) and Modified Vaccinia Virus Ankara (MVA)-vectored vaccines is a strategy previously shown to provide substantial protective efficacy against P. falciparum infection in a UK adult phase IIa sporozoite challenge study, and in a trial in Kenyan adults.

Methods We conducted the first phase Ib clinical trial assessing the safety, immunogenicity and efficacy of ChAd63-MVA ME-TRAP in 700 healthy malaria exposed children aged 5–17 months in a highly malaria-endemic area of Burkina Faso.

Participants were randomly assigned to received either ChAd63 ME-TRAP followed eight weeks later by MVA ME-TRAP or 2 doses of rabies vaccine. Monitoring of solicited adverse events was performed for seven days after each vaccination. Unsolicited adverse events were recorded until one month post each vaccination. Serious adverse events and malaria episodes were monitored throughout the study duration. Blood samples were collected at predefined timepoints to assess vaccine immunogenicity.

Results ChAd63-MVA ME-TRAP was shown to be safe and immunogenic, inducing high-level T cell responses [median 326 SFU/106 PBMC (95% CI 290–387)]. However, non-significant low efficacy was observed against clinical malaria during the follow-up period, with efficacy against primary endpoint estimated by proportional analysis being 10.7% (95% CI: −44.2 to 44.7%) at sixth months post MVA ME-TRAP and 3.1% (95% CI −15.0 to 18.3; p=0.72) by cox regression.

Conclusion This study has confirmed ChAd63-MVA ME-TRAP is a safe and highly immunogenic vaccine regimen in children and infants with prior exposure to malaria. No significant protective efficacy was observed in this highly endemic context.

OC 8561  
RAPAED TB: AN INNOVATIVE CHILD TB DIAGNOSTIC VALIDATION STUDY

1Laura Obirich*, 2Heather Zar, 3Steve Graham, 4Issa E Ntinginya, 5Nilesh Bhatt, 6Manriott Nliwasa, 7Elizabeth Corbett, 8Rinn Song, 9Claudia Denkinger, 10Michael Hänscher, 11Norbert Heinrich, 12University of Munich (LMU), Germany; 13Red Cross War Memorial Children’s Hospital, MRC Unit on Child and Adolescent Health Unit, Cape Town, South Africa; 14University of Melbourne, Australia; 15NIMR-Mbeya Medical Research Programme, Dar es Salam, Tanzania; 16Instituto Nacional de Saúde (INS), Maputo, Mozambique; 17Malawi College of Medicine, Blantyre, Malawi; 18London School of Hygiene and Tropical Medicine, UK; 19Oxford Vaccine Group, University of Oxford, UK; 20Foundation for Innovative New Diagnostics (FIND), Geneva, Switzerland

Background Children account for an estimated 1 million new cases of TB every year, representing roughly 7% of the total disease burden. Every year, around 2 09 000 children die from TB, half of those cases are in Africa. The main issue continues to be timely and accurate diagnosis, as treatment outcomes – even in the case of drug resistance – are significantly better than in adults.

Clinical diagnosis in the absence of laboratory confirmation is hampered by non-specificity of symptoms. Diagnostics validation studies in children are difficult – in most studies, very few of the symptomatic children achieved microbiological disease confirmation, resulting in imprecise estimates for test sensitivity.

Design/methods With the RaPaed TB study funded by EDCTP, we are preparing an improved diagnostic validation study design to improve on the traditional approach of a single-gate, double diagnostic study in the target population. The project will evaluate multiple new tests on the same patients, to determine algorithms of screening and confirmatory tests. Most novel tests in this study use non-sputum samples and are therefore more suitable for children.

Allocation of patients to standardised groups will follow the recommendations of the NIH-convened consensus panel on case definitions of paediatric TB diagnostic studies. Using an endpoint review committee will allow blinded review of those new-positive cases, plus matched controls, and determine their likelihood of disease based on clinical data including follow-up, and X-ray. This will improve the quality of evaluation of false positive vs. true positive results of new tests and therefore improve the assessment of specificity.

To improve on sensitivity assessment, the study includes partners with a high number of confirmed cases in past studies and plans to draw in cases of confirmed disease from other diagnostic facilities.

Conclusion This improved methodology will lead to more meaningful and applicable results of diagnostic validation studies.