critical for a successful cure. Central to our strategy is to focus HIV-1-specific CTL on the most functionally conserved regions (not a string of epitopes and not full-length proteins) common to most HIV-1 variants, which HIV-1 typically cannot change without losing fitness. These conserved regions were defined by bioinformatics, and a bivalent mosaic was computationally designed to increase the vaccine perfect match of potential T-cell epitopes to 80% of global HIV-1 variants; if successful, the vaccine will be suitable for global deployment. Furthermore, we maximised the inclusion of protective epitopes associated with viral control in treatment-naïve HIV-1-positive individuals defined on 4 continents. These immunogens are delivered by the non-replicating simian adenovirus ChAdOx1 prime and non-replicating poxvirus MVA boost regimen, clinically proven safe and potent.

Methods The GREAT consortium has been established to build capacity for a future efficacy trial in Zambia, around Lake Victoria and in Kenya by engaging populations at documented high risk for HIV-1 infection, despite preventive interventions, by diverse clades. We will conduct a phase I/IIa clinical trial HIV-CORE 006 to assess the safety and immunogenicity of the conserved-region vaccines, in preparation for an efficacy trial in these at-risk populations.

Conclusion The aims of the GREAT consortium are to ensure that at the completion of the programme grant, the vaccine regimen will be proven safe and potent, and the sites will be prepared to launch an appropriately designed trial to prove vaccine efficacy.

OC 8510 BIOTRANSFORMATION OF PRAZIQUANTEL FOR THE PHARMACOKINETIC OPTIMISATION OF PRAZIQUANTEL USE IN MASS DRUG ADMINISTRATION AND DEVELOPMENT OF NEW PAEDIATRIC FORMULATIONS

¹Roslyn S Thelingwani*, ¹Nyasha Kapungu, ²Xueqing Li, ¹Comfort Kanji, ¹Chenai Mutiti, ³Wilma J Reinhard-Rupp, ¹Collen Masimirembwa. ¹African Institute of Biomedical Science and Technology, Harare, Zimbabwe; ²AstraZeneca, Södertälje Sweden; ³EMD Serono, Darmstadt, Germany

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Background Praziquantel (PZQ) is the only drug available for the treatment of all forms of schistosomiasis. New paediatric formulations for the active enantiomer R-PZQ and the racemate PZQ are currently under development. There is however limited drug metabolism and pharmacokinetic data on PZQ available to support these initiatives. Detailed knowledge of PZQ metabolism will enable the use of PBPK modelling to determine appropriate doses for the new formulations in paediatric patients and to predict risks for drug-drug interactions in mass drug administration.

Methods Biotransformation studies on PZQ were conducted in human liver microsomes and recombinant Cytochrome P450s (CYPs). Structure elucidation was inferred from mass spectra. Enzyme kinetic studies to determine the Michaelis-Menten kinetics, Km and Vmax, of the formation of the main metabolites and analysis of clinical samples were determined by LC-MS/MS.

Results CYP reaction phenotyping studies with HLM and r-CYPs indicate major involvement of CYP1A2, 2C19, 2D6 and 3A4/5 in the metabolism of R- and S-PZQ.

Biotransformation studies showed that PZQ is metabolised to cis-4-OH-PZQ mainly by CYP1A2 and CYP2C19. CYP3A4/5 metabolises PZQ to a mono-hydroxyl metabolite (X-OH-PZQ) whilst CYP2D6 metabolises PZQ to minor novel mono-hydroxyl metabolite (Y-OH-PZQ) both pending structural elucidation by nuclear magnetic resonance. R-PZQ was more rapidly cleared than S-PZQ with variable interindividual AUC and Cmax.

Discussion and conclusion The differential role of CYP1A2 and CYP2C19 and of CYP3A4 and CYP3A5 in the formation the 4-OH-PZQ and the novel X-OH-PZQ respectively are intriguing findings as this has not been reported before in humans. *In vitro*, cis and not trans 4-OH-PZQ formation has been observed contrary *in vivo* reports in humans which indicate trans 4-OH-PZQ as the main metabolite. The data will enable us to understand the rapid clearance of PZQ and predict potential drug-drug-gene interactions which may explain the inter-individual variability of PZQ pharmacokinetics.

OC 8526 THE RWANDA CLINICAL RESEARCH NETWORK (RWANDA-CRN): A MODEL FOR MIXED SOUTH-SOUTH AND NORTH-SOUTH COLLABORATIONS FOR CLINICAL RESEARCH CAPACITY DEVELOPMENT

Jean Pierre Musabyiman*, Clarisse Musanabaganwa, Valentine Dushimiyimana, Jean Pierre Namabajimana, Prosper Karame, Ladislav Nshimiyimana, Pacific Ndishimye. Rwanda Biomedical Center, Ministry of Health, Kigali, Rwanda

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Background Poor countries carry 90% of the global burden of disease, with access to only 10% of globally available health research funding and technical capacity. Fragile south-south collaborations hinder effective use of limited resources, career opportunities and funding to retain the insufficiently available quality scientists. The Rwanda Health System established a clinical research network involving academia, non-governmental organisations and private sector to accelerate generation of talented scientists, create enabling environment and incentives to retain scientists by establishing a local funding model.

Methods Based on a baseline assessment, potential clinical trial units were mapped and developed through adoption of a Clinical trial management training model from European Universities. The Rwandan law on Public Private Partnership was leveraged to attract and engage local and international private players in a win-win approach. So far, countries such as Kenya and Sweden were engaged in the roadmap.

Results From 2014 to date, a total of 285 scientists are trained on various clinical research components: Good Clinical Practice (28%), Research Grant writing (14%), systematic review and meta-analysis (9%) and scientific communication (8.7%). Ten Clinical Research Units and one centre for evidence-based healthcare were established. So far 13 health investigator-initiated projects in malaria, metabolic disorders and maternal health were funded through the local funding model. A process to empower six malaria sentinel sites into fully functioning clinical research sites is underway.

Conclusion The creation of strong networks of excellence for clinical research among southern academic, research

institutions and pharmaceutical and non-pharmaceutical industry is a promising strategic approach to promote sustainable clinical research capacity. The government vision is that beyond national boundaries, resource sharing and involvement of private players are key factors to mitigate the high burden of disease, nationally and regionally.

OC 8521 PRELIMINARY REPORT ON SAFETY OF CO-ADMINISTERED HUMAN HOOKWORM VACCINE CANDIDATES NA-APR-1 (M74)/ALHYDROGEL® AND NA-GST-1/ALHYDROGEL® IN GABONESE CHILDREN

¹Jeanot Fréjus Zinsou*, ¹Josiane Honpkhedji, ¹Dejon Agobe Jean Claude, ¹Bayodé R Adegbite, ¹Jean Ronald Edoa, ²Remko Van Leeuwen, ³David Diemert, ⁴Maria Elena Botazzi, ⁵Peter G Kremsner, ⁶Maria Yazdanbakhsh, ⁴Peter Hotez, ²Martin P Grobusch, ¹Ayola Akim Adegnik, ²Sophie De Vries. ¹Centre de Recherches Médicales de Lambaréné, Gabon; ²Academic Medical Center, University of Amsterdam, The Netherlands; ³George Washington University School of Medicine and Health Sciences, USA; ⁴Baylor College of Medicine and Texas Children's Hospital, USA; ⁵Institut für Tropenmedizin, Universität Tübingen, Germany; ⁶Leiden University Medical Center, The Netherlands

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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 (deltoid) 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 1.3 (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.

OC 8535 AN OVERVIEW OF RESEARCH ETHICS COMMITTEES OPERATING IN LUSOPHONE AFRICAN COUNTRIES

¹Maria Rosário Oliveira Martins*, ²João Schwalbach, ^{2,3}Esperança Severe, ⁴Antonieta Martins, ⁵Ema Candida Branco Fernandes, ⁴Isabel Ines Araujo, ⁶Helena Pereira De Melo, ²Amílcar Bernardo Tome Da Silva, ⁵Emanuel Catumbela, ³Jahit Sacarlal, ¹Jorge Seixas, ⁵Maria Chimpolo, ²Rassul Nala, ⁵Maria Tazi Nimi, ⁷Amabelia Rodrigues. ¹Global Health and Tropical Medicine Institute, Universidade NOVA de Lisboa, Portugal; ²Comité Nacional de Bioética para a Saúde de Moçambique; ³Universidade Eduardo Mondlane, Maputo, Mozambique; ⁴Universidade de Cabo Verde, Praia, Cape Verde; ⁵Faculdade de Medicina, Universidade Agostinho Neto, Comité Independente de Ética da Angola; ⁶Faculdade de Direito, Universidade Nova de Lisboa, Conselho de Ética da Universidade NOVA, Portugal; ⁷Projeto Saúde Bandim, Statens Serum Institut, Guiné-Bissau

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Background In 2017, a North-South partnership was created, to strengthen Bioethics Committees in African Lusophone African countries (LAC), by joining the forces of National and Institutional Research Ethics Committees (REC) and Universities in Angola, Cape Verde, Mozambique and Portugal. This study is part of an EDCTP2-funded project and aims to describe key RECs operating in LAC, its establishment dates and further characteristics.

Methods Document analysis and interviews with REC representatives of five LAC were conducted in April 2018. Legal documents were obtained through official national sources.

Results We identified four National Ethics Committees, created between 2000 and 2008 by ministerial or governmental decree; only S. Tomé e Príncipe does not have an established REC. In Angola, the National REC was created in 2000, and since 2007, seven Institutional Committees were implemented at faculty level. National REC in Cape Verde and Guinee-Bissau (CNES) are unique and were founded in 2007 and 2009 respectively. In Mozambique, National REC (CNBS) dates to 2002, and since 2011, 8 Institutional Committees were formed; they functioned as a network under the umbrella of CNBS. Most National REC have representatives from health professional associations, lawyers, civil society and religious communities and have regular meetings (usually monthly). The number of members ranges between 6 (CNES) and 13 (CNBS). In 2007, around 200 protocols were reviewed by CNBS and 29 by CNES. Most of the National REC members attended training activities in bioethics but at different levels.

Conclusion Few publications described REC operating in LAC; this study fills this gap by reporting historical and functional characteristics of RECs in five Lusophone African countries. Additional tools based on quantitative and qualitative approaches are being developed to assess more in-depth REC operational characteristics and to identify their needs in order to target training and capacity building initiatives underlying our project.

OC 8546 SAFETY AND IMMUNOGENICITY OF THE MALARIA VACCINE CANDIDATE BK-SE36 IN YOUNG CHILDREN LIVING IN BURKINA FASO

¹Sodiomon Sirima, ¹Alfred B Tiono, ²Sophie Houard, ¹Edith C Bougouma, ¹Sam A Coulibaly, ²Odile Leroy, ³Nirianne Palapac, ³Toshihiro Horii, ¹Issa N Ouedraogo. ¹Centre National de Recherche et de Formation sur le Paludisme, Burkina Faso; ²European Vaccine Initiative, Universitäts Klinikum Heidelberg, Germany; ³Department of Molecular Protozoology, Research Institute for Microbial Diseases, Osaka University, Japan

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Background The malaria blood stage vaccine candidate SE-36 is based on the serine repeat antigen of *Plasmodium*