community, matched closely on date of birth. Vaccination status is determined from home-based records, and from clinic registers. Similar approaches were used for studies of safety outcomes.

Results We share preliminary results and discuss the challenges encountered and lessons learned about implementing a multicentre case control study for a malaria vaccine, and approaches to data collection which have proved effective, including establishing surveillance, the use of specific case definitions standardized across centres, recruiting closely age-matched community controls, and obtaining reliable information from both cases and controls on potential confounding factors which may be associated with both risk of the outcome and with access to vaccination.

Conclusion Case control studies are an efficient means of monitoring vaccine effectiveness and safety, but require care in design and implementation. The lessons learned from the malaria vaccine pilots will be useful for countries planning introduction of a malaria vaccine.

PA-718 HIV-INFECTED ADOLESCENTS HAVE ALARMINGLY LOW ADHERENCE LEVELS TO ART – A SHORT REPORT FROM TANZANIA

[1,2]Lisa Lynn ten Bergen, [2,3]Iraseni Swai, [4]Kennedy Ngowi*, [1,2,5,6]Marion Sumari-de Boer. *[1]Amsterdam Institute for Global Health and Development, The Netherlands; [2]Vrije Universiteit Amsterdam, The Netherlands; [3]UMC Amsterdam, Location AMC, The Netherlands; [4]Kilimanjaro Clinical Research Institute, United Republic of Tanzania; [5]Wageningen University and Research, The Netherlands; [6]Institute of Public Health, Kilimanjaro Christian Medical University College, Tanzania*

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Background More than eight in ten of the world's 1.65 million adolescents living with HIV live in sub-Saharan Africa. Despite the availability of antiretroviral therapy (ART), there is limited robust data on adherence to ART levels among adolescents, as this group is often neglected in HIV research.

Objective

Our study aimed to estimate and compare adherence levels, based on self-reporting, pharmacy-refill counts and electronic monitoring using a digital adherence tool (DAT) among adolescents living with HIV in Tanzania.

Methods We used three measures to assess adherence levels among adolescents aged 15 to 19 years, residing in Kilimanjaro region, in Tanzania. Median adherence levels were calculated, and optimal adherence was defined as > 95% of pills taken. Adolescents used the DAT, the Wisepill dispenser (RT2000), for one month and were followed-up with a short semi-structured exit-interview. Thereafter, adolescents were interviewed about their experiences with using the Wisepill® device.

Results Median adherence levels were respectively 100% (IQR 93 – 100%), 97% (IQR 85 – 98%) and 72% (IQR 24 – 91%), based on self-report, pharmacy-refill counts and on results from the DAT. Strikingly, out of the twenty participants, the proportion of adolescents achieving 95% pill intake were 70%, 55% and 20% of adolescents respectively.

Conclusion Even based on self-reported adherence, only less than three-quarters of adolescents achieved sufficient adherence to treatment. Therefore, interventions to improve adherence to ART regimen are urgently needed among HIV-positive adolescents, especially in resource-limited settings.

PA-727 PHYSIOLOGICALLY-BASED PHARMACOKINETIC MODELLING OF DRUG-DRUG INTERACTIONS BETWEEN RITONAVIR-BOOSTED ATAZANAVIR AND RIFAMPICIN IN PREGNANCY

[1]Shakir Atoyebi*, [1]Maiara Camotti Montanha, [2]Letisha Najjemba, [3]Catherine Orrell, [3]Lauren Jennings, [4]Henry Mugerwa, [2]Aida Kawuma, [2]Francis Ojara, [1]Marco Siccardi, [5]Paolo Denti, [1,2]Catriona Waitt. *[1]University of Liverpool, UK; [2]Infectious Diseases Institute, Makerere University College of Health Sciences, Uganda; [3]Desmond Tutu Health Foundation, Institute of Infectious Disease and Molecular Medicine and Department of Medicine, University of Cape Town, South Africa; [4]Joint Clinical Research Centre, Uganda; [5]Division of Pharmacology, Department of Medicine, University of Cape Town, South Africa*

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Background Ritonavir-boosted atazanavir (ATV/r) and rifampicin are mainstays of second-line antiretroviral and multiple anti-TB regimens, respectively. Rifampicin is a strong inducer of CYP3A4, the main enzyme involved in atazanavir metabolism, causing drug-drug interaction (DDI) in those co-infected with HIV and TB, which might be exaggerated in pregnancy. We employed physiologically-based pharmacokinetic (PBPK) modelling to investigate atazanavir pharmacokinetics during coadministration of rifampicin and ATV/r in pregnancy.

Methods A pregnancy PBPK model was developed from a published adult PBPK model by incorporating pregnancy-induced biological changes. Predicted pharmacokinetic parameters in pregnancy were validated with published clinical datasets for once daily (OD) rifampicin 600 mg and clinical data for ATV/r (300/100 mg) in pregnancy (NCT03923231). Predicted atazanavir Ctrough was compared against its protein-adjusted IC90 (14 ng/ml) when simulating the coadministration of ATV/r 300/100 mg OD and rifampicin 600 mg OD in pregnancy. Alternative dosing regimens were also explored.

Results The pregnancy model was considered validated when the absolute average fold error (AAFE) for Ctrough and AUC0–24 of ATV/r 300/100 mg OD and for Cmax and AUC0–24 for rifampicin 600 mg OD were <2, when comparing predicted vs observed data. Similarly, comparison of predicted and observed plasma concentrations of atazanavir and ritonavir in the sparse pregnancy data (NCT03923231) gave AAFE values <2. Pregnancy was predicted to increase the rifampicin DDI effect on atazanavir. For the dosing regimens of ATV/r 300/100 mg OD, ATV/r 300/200 mg OD and ATV/r 300/100 mg BD (all with rifampicin 600 mg OD), predicted atazanavir Ctrough was above 14 ng/ml in 29%, 71% and 100%; and 32%, 73% and 100% of the population in second and third trimesters, respectively.

Conclusion PBPK modelling suggests ATV/r 300/100 mg BD could maintain antiviral efficacy when co-administered with rifampicin 600 mg OD in pregnancy. Clinical studies are warranted to confirm safety and efficacy in pregnancy.

PA-728 EXPLORING THE DISPOSITION OF SELECT ARTEMISININ COMBINATION THERAPIES IN THE TREATMENT OF MALARIA AND MALARIA PARASITE KINETICS IN CHILDREN WITH SICKLE CELL DISEASE IN KENYA

Godfrey Allan Otieno*, Bernhards Ragama Ogutu. *CREATES-Strathmore University, Kenya*

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Background Children with Sickle Cell Disease (SCD) have decreased spleen function which is responsible for increased susceptibility of SCD patients to malaria and other infections.