OA-484 IMPROVING RAPID DETECTION OF 2ND LINE DRUG RESISTANCE IN MYCOBACTERIUM TUBERCULOSIS WITH XPERT MTB/XDR AND MOLBIO 2ND LINE

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Background Rapid detection of resistance to key drugs such as fluoroquinolones (FQ) and bedaquiline (BDQ) is essential for appropriate management of multi-drug resistant tuberculosis (MDR-TB). . Molecular tests available require either infrastructures not available in peripheral laboratories in low resource countries, or do not detect resistance to BDQ. Recently, two tests have been developed: GeneXpert MTB/XDR (Cepheid, USA) detecting resistance to isoniazid (INH), FQ and ethionamide (ETH), and TrueNat XDR (Molbio Diagnostics, India) for detection of resistance to INH, FQ and BDQ.

Methods In the EDCTP-funded project (DIAMA) aimed at developing culture free approaches for diagnosis and management of MDR-TB patients, we assessed the performances of these tests in field conditions compared to phenotypic drug-susceptibility testing (pDST) and whole genome sequencing (WGS) using 1711 unique samples consecutively collected in the Sub-Saharan African region (Benin, Cameroon, DRC, Ethiopia, Guinea, Mali, Nigeria, Rwanda and Senegal).

Results Using a composite reference standard comprising pDST and WGS, Xpert-XDR showed a sensitivity of 87.3% for INH, 37.8% for ETH and 66.7% for FQ, with a respective specificity of 96.5%, 98.3% and 99.7%. For TrueNat, the sensitivity was 88.1% for INH and 47.4% for FQ, with a specificity of 85.7% for INH, 97.7% for FQ and 98.5% for BDQ.

Conclusion These tests showed promising results, particularly as screening test for detection of resistance to FQ and BDQ.

OA-490 SAFETY, REACTOGENICITY AND IMMUNOGENICITY OF MTBVAC IN NEWBORNS IN A TB ENDEMIC AREA: A PHASE 2A RANDOMIZED, DOUBLE-BLIND, DOSE-DEFINING TRIAL

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Background New safe and effective TB vaccine strategies to replace infant BCG vaccination are needed urgently. We evaluated the safety, reactogenicity and immunogenicity of three doses of the live-attenuated Mycobacterium tuberculosis (Mtb) vaccine candidate, MTBVAC, in comparison to BCG in South African newborns.

Methods Healthy infants, HIV-unexposed, BCG-naïve newborns without history of close TB contact were randomly allocated into three sequential cohorts to receive a single intradermal dose of BCG (SSI, 2.5×10^5 CFU) or MTBVAC (2.5×10^4; 2.5×10^5 CFU; or 2.5×106 CFU).

Results 228 pregnant women consented, and 99 newborns were enrolled. Seventy-eight infants across all 3 cohorts had local reactions, all rated mild, except one grade 2 erythema. Induration, swelling, and erythema was more common with increased MTBVAC dosage. Induration and swelling were more common in MTBVAC 2.5x106 than in BCG and reactogenicity in MTBVAC 2.5x105 was same as BCG. Twelve infants experienced 14 vaccine-unrelated SAEs including one death due to bronchopneumonia. Eight infants commenced TB treatment for unconfirmed pulmonary TB (BCG n=4 and MTBVAC 2.5x104 CFU n=4) and one for unconfirmed TB meningitis (BCG). MTBVAC was highly immunogenic at all 3 doses, inducing predominantly Th1-cytokine-expressing CD4 T-cells, which peaked at day 56 and waned thereafter. The 2.5×105 and 2.5×106 CFU MTBVAC doses were more immunogenic than BCG, inducing very similar response magnitudes and phenotypes. Vaccination with any MTBVAC dose resulted in QFT conversion in most infants at Day 56, but these responses waned and reverted to QFT-negative in more than half by the end of the 1-year follow-up period.

Conclusion MTBVAC appeared safe and well tolerated and immunogenic at doses between 2.5×10^4 CFU and 2.5×106 CFU in South Africans newborns. The 2.5×105 CFU MTBVAC dose was selected for the ongoing phase 3 trial in a high TB prevalence setting.

OA-498 PEDMAB1 CLINICAL TRIAL: SAFETY ASSESSMENT OF CAP256V2LS TO PREVENT BREASTMILK HIV TRANSMISSION IN HIV-1 EXPOSED UNINFECTED NEONATES

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Background Breastmilk optimizes child survival in low-middle income high HIV prevalence settings. However, breastmilk transmission of HIV-1 continues to contribute to residual vertical HIV transmission. The Phase 1 PedMAb clinical trial aims to define the optimal doses, ideal combination and timing of subcutaneous (SC) administration of two HIV-1 broadly neutralizing antibodies (bNAbs), VRC07-523LS and CAP256V2LS, separately or in combination, to prevent breastmilk transmission of HIV-1 in high incidence regions such as South Africa. The trial is being conducted at the South African Medical Research Council Chatsworth Clinical Research site and the RK Khan hospital. Here we first report the