Antimicrobial resistance

OC - (8450) - ABSENCE OF MINORITY HIV-1 DRUG RESISTANT VARIANTS FOLLOWING MOTHER-TO-CHILD TRANSMISSION DOES NOT PREDICT VIROLOGIC SUCCESS TO FIRST-LINE ANTIRETROVIRAL THERAPY

Kityo, Cissy (Uganda); Rinke De Wit, Tobias (Netherlands); Nankya, Immaculate (Uganda); Balinda, Sheilla (Uganda); Sigallof, Kim (Netherlands); Ndashimye, Emmanuel (Netherlands); Mugyenyi, Peter (Uganda); Quinones-Mateu, Miguel (United States of America)

BACKGROUND: Although minority HIV-1 drug resistant HIV-1 variants may be selected under antiretroviral pressure, leading to therapy failure, their clinical significance remains controversial. This is particularly relevant in the case of prevention of mother-to-child transmission (MTCT), where transmitted drug resistance can affect treatment outcomes.

METHODOLOGY: An ultrasensitive HIV-1 genotyping assay based on deep sequencing(DEEPGEN™HIV) with a 1% mutation frequency sensitivity, was used to quantify MTCT drug resistant variants in 38 prenatally HIV-infected children experiencing (Group I, n=27) or not (Group II, n=11) virologic failure 12 months after initiating first-line antiretroviral therapy(ART) as part of a Pediatric cohort in Uganda.

RESULTS: Infants were infected with subtype A(n=20), D(n=16) or C(n=2) HIV-1 strains, distributed equally between both patients groups. Similarly, no significant difference was observed in intra-patient HIV-1 diversity among viruses obtained from Group I or II individuals at baseline. DEEPGEN™HIV was able to detect all the mutations originally detected in samples obtained from four control patients in Group II, where drug resistance was identified at baseline using Sanger sequencing, e.g., K65R (78% mutation frequency), K103N(47%), or M184V(85%). More importantly, a series of low abundance (<20% detection limit of Sanger) primary and compensatory mutations associated with resistance to PIs(D30N, Q48V), NRTIs(D67N, K219Q), or NNRTIs(L100I, K103N) were identified in both groups of patients, although just a few seem to have been selected and became majority variants after 12 or 24 months of ART.

CONCLUSIONS: DEEPGEN™HIV improves the detection of minority viral variants in infants following MTCT; however, most of the emergent HIV-1 drug resistance mutations were not present at low frequency at baseline in subjects failing ART, most likely being generated and selected following exposure to treatment. Further studies, using this or other ultrasensitive assays, are needed to better understand the transmission, dynamics and overall evolution of minority drug resistant viruses in MTCT.