Report of the HIV/TB Research meeting held in conjunction with the 20th Conference on Retroviruses and Opportunistic Infections (CROI 2013)

The World Health Organization and the Consortium to Respond Effectively to the AIDS/TB Epidemic (CREATE) convened their 7th CROI-affiliated HIV/TB research meeting on behalf of the TB/HIV Working Group of the Stop TB Partnership in Atlanta, Georgia USA on 3 March, 2013. The meeting discussed critical knowledge and research gaps on TB prevention among children and adults and drug interactions between new TB drugs and ART. Attended by some 100 participants, the meeting was convened by Dr Haileyesus Getahun of WHO and co-chaired by Dr Diane Havlir of UCSF and Chair of the Global TB/HIV Working Group and Dr Richard Chaisson, of Johns Hopkins and Director of CREATE.

Charles Mitchell of University of Miami presented on the reasons behind the contrasting results from two clinical trials (Zar et al and Madhi et al) on the use of isoniazid preventive therapy (IPT) among children in South Africa (link to presentation). The differences in coverage of ART and lack of exposure to TB disease are the likely explanations for the contrasting results, which was further underlined by Mark Cotton of Stellenbosch University who participated as an investigator in both trials.

Tim Sterling of Vanderbilt University presented results on the use of 3HP (3 months Rifapentine and Isoniazid once weekly) for people living with HIV showing higher treatment completion rates and better tolerance than 9 months of isoniazid (INH) administered daily (link to presentation). 3HP was at least as well-tolerated in HIV-infected as in HIV negatives. Although increased risk of selection for rifampicin resistance was observed in the 3HP group, the numbers were too few for a conclusion. Susan Swindells of the University of Nebraska commented on the presentation and described the ongoing ultra-short clinical trial comparing rifapentine and INH daily for 1 month with 9 months of INH (link to presentation). She emphasized the general challenge of lack of clarity on how long patients should be monitored for, for the development of disease after the completion of a trial.

Kelly Dooley of John Hopkins University presented on the drug interactions of new TB drugs and ART (link to presentation). She concluded that Efavirenz reduces bedaquiline concentrations by 20-50% and PA-824 concentrations by about 30% while Delamanid appears to have lower metabolic drug interaction risk and Sutezolid has not been tested in PK studies with ARVs. Gary Maartens of Cape Town University commented on Dr Dooley’s presentation and reiterated that Efavirenz is the future of TB and HIV co-treatment and its interactions with new TB drugs need to be addressed in earnest.
Key TB/HIV Coverage at the 20th Conference on Retroviruses and Opportunistic Infections

At the main CROI conference this year there was a record number of abstracts including late breakers on TB and one full day of TB discussions as well as increased mainstreaming of TB discussions in all the critical areas of HIV care including basic science. Below is a summary of the most salient findings from key studies presented during the conference:

An autopsy study that was conducted among adults who died at home in a South African setting showed that TB was found in 34% of the cadavers (Martinson et al). Similarly an autopsy study conducted in Kenya among adult HIV positives who died after receiving a median 10 months of ART found TB in 52% of cadavers (Some et al). A prospective study that was conducted among who had died from HIV within 3 months of ART initiation found out that 21% had concurrent TB disease (Mutevedzi et al).

An IPT randomized clinical trial conducted among 1329 people living with receiving ART in South Africa showed that the benefits of a 12 months IPT are significantly higher among TST and IGRA negatives (Rangaka et al).

A study conducted among TST-positive people living with HIV in Brazil showed that the protection of IPT taken for 6 months lasted up to 86 months after cessation of administering the IPT after an initial spike of TB incidence between 6 and 12 months. It was postulated that the lack of sterilization of latent infection by a 6 month Isoniazid dose was the cause of this initial spike (Golub et al).

A study conducted among 539 infants who received ART and were followed for up to 4 years showed no TB prevention effect of ART among the children (Zeldow et al).

Contrasting results were presented about the use of Urine LAM with a sensitivity of 25% among PLHIV from Uganda with a median CD4 count of 180 (Drain et al) and a sensitivity of 69% among PLHIV from South Africa with a median CD4 count of 116 (van Rie et al).

Results of the RIFAQUIN trial, which compared 2 arms (Arm 1: 2EHRZ intensive phase followed by 2 months of twice weekly Moxifloxacin and Rifapentine and Arm 2: 2ERZ and Moxifloxacin for the intensive phase followed by 4 months of once weekly Moxifloxacin and Rifapentine) with a control arm of standard treatment were presented. The 4 months regimen (Arm 1) was inferior to the standard treatment while the 6 month regimen (Arm 2) was non-inferior to the standard treatment (Jindani et al).

A poster co-authored by WHO’s M. Zignol, D. Falzon and H. Getahun on the increasing magnitude and linkage of HIV and MDR-TB was presented and discussed during the conference. The poster calls for basic and clinical research to explore any possible causal relationship and explanation.