The 9th meeting on HIV/TB research in conjunction with CROI 2015 was organised by the World Health Organisation (WHO) in Seattle, USA on February 23, 2015. The meeting was convened by Haileyesus Getahun and Meg Doherty of WHO and chaired by Richard Chaisson of John Hopkins University and Constance Benson of University of California, San Diego. The meeting was opened with remarks from Eric Goosby, the UN Special Envoy on Tuberculosis, who briefly shared his plans to support the advancement of TB research which is now included as one of the three pillars of the WHO’s new End TB Strategy.

The objective of the meeting was to discuss and promote high level scientific interchange on ideas and updates about ongoing clinical trials on empirical TB treatment for preventing early mortality in people living with HIV and assess their eventual impact on policy change. The meeting also discussed the prospect of using rifamycins for prevention of tuberculosis in resource limited settings with high TB and HIV prevalence.

Haileyesus Getahun of the Global TB Programme of WHO presented a summary of ongoing trials on empirical TB treatment for people living with HIV in resource constrained settings. He reminded the meeting participants that clinical trials of empirical TB treatment to prevent early mortality of people living with HIV were identified as a priority research question in one of earlier CROI affiliated WHO TB/HIV research meetings. He pointed out the lack of a standard definition for empirical TB treatment and presented the versions used for the clinical trials and in the existing WHO guidelines. He concluded that key policy and programme questions on empirical TB treatment as an intervention to prevent early mortality among people living with HIV are being addressed by the ongoing trials. However, he noted a critical gap in generating evidence to inform the existing empirical TB recommendation of the WHO that was based on expert opinion. The recommendation encourages clinicians in peripheral health facilities in HIV prevalent settings to initiate TB treatment early in patients with serious illness thought to be due to extrapulmonary TB prior to clinical investigations.

Salim Abdool Karim of CAPRISA at the University of Kwa-Zulu Natal, South Africa, provided commentary on the topic emphasising the need for novel approaches to prevent TB particularly during the first three months after initiation of ART. He reiterated the need to concomitantly address the challenges of programme implementation, provided positive results are generated from the trials. He also urged using actual data from the trials to inform a modelling exercise that can identify numbers needed to treat to prevent mortality and incident TB. Participants of the meeting identified the lack of involvement of children in the clinical trials as a gap that needs to be addressed. Similarly, a systematic approach that can guide clinical decisions on when to stop empirical TB treatment was noted as an important gap in the clinical and programmatic implementation of the intervention that deserves attention.
There was a call for investigators of the trials to make preliminary results of these ongoing trials available as soon as possible to inform the ongoing revision of WHO guidelines for HIV associated TB.

Gary Maartens of University of Cape Town (link to presentation) reviewed the evidence around the use of rifamycins and provided perspective on the prospect of their use for TB prevention among people living with HIV in resource limited settings. He noted rifamycin regimens are not more effective than IPT. While the shorter duration of rifamycin containing regimens is an advantage over long term isoniazid, he argued that duration of preventive therapy is not an important advantage in people on ART. He also argued against the feasibility of direct observation of treatment, which has been done with weekly isoniazid rifapentine, in high burden countries. Drug-drug interactions with ART and rifamycins are a barrier for their wider use in people on ART. He suggested that a trial of the combination of isoniazid with rifabutin needs to be prioritised as it can address some of these drug interaction concerns with ART. He also said missing a few doses of a shorter duration of treatment (e.g. weekly dose of a 3 month regimen) may have more serious consequences compared to missing a higher proportion of the dose (e.g. 20% of doses) of isoniazid given for 6-12 months. He further noted most of the existing evidence about preventive treatment for people living with HIV dates back to the pre-ART era and underlined the importance of better understanding and generation of evidence of TB prevention in people using ART.

José Miró of the University of Barcelona (link to presentation) provided commentary on the topic emphasising the overall role of ART to prevent TB in people living with HIV. He further reiterated the importance of generating more evidence on TB prevention among people living with HIV receiving ART, particularly on the use of intermittent dosage of shorter regimens with self-administration in settings with high TB and HIV transmission. He also supported the suggestion of Gary Maartens to perform trials with INH and rifabutin, a combination that can be given to patients taking lopinavir-ritonavir or other boosted protease inhibitor regimens.

The meeting participants expressed concern about the progress of overall implementation of isoniazid preventive therapy and underlined the importance of novel strategies and approaches to scale up TB prevention among people living with HIV. Clinical and operational research that uses existing drugs creatively (e.g. intermittent therapy) in people living with HIV receiving ART are deemed to be critical.