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## Editorial

# Challenges in Concomitant Treatment of HIV and Tuberculosis - ②

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## EDITORIAL

HIV is among the leading infectious diseases with approximately 36.9 million HIV positive individuals globally and 1.2 million people dying from HIV-related causes annually [1]. HIV-TB co-infection is a deadly duo as concurrent treatment of HIV and TB is complicated by many factors that include drug-drug interactions [2], overlapping toxicity, non-adherence and TB-associated Immune Reconstitution Inflammatory Syndrome (IRIS) [3]. This synergistic relationship between TB and HIV influences each other's progress leaving the host more vulnerable to death [4,5]. TB is the most common opportunistic infection affecting HIV-positive individuals and leading cause of death in patients with HIV [6,7]. Parallel to it, HIV is the pre-eminent risk factor in the progression of TB infection [7] to active TB disease. On the other hand, the use of Anti-Retroviral Drugs (ARV's) in HIV patients complicates the diagnosis and treatment of active TB [8]. HIV patients with pulmonary TB are frequently sputum smear negative and up to 20% may have completely normal chest X-rays [9,10]. HIV-TB co-infected patients are exposed to increased pill burden with overlapping toxicities. ARV agents and TB drugs, particularly Isoniazid (INH), Rifampicin (RIF), and Pyrazinamide (PYZ), can cause drug-induced hepatitis. As such they are more prone to nonadherence and treatment failure with higher risk of death while under treatment for TB. Many studies have shown that mortality rate has been consistently high with as many as 50% of HIV patients dying during the first two months of TB treatment [3,11-13]. Next, drug-drug interaction mainly between ARV's and Rifamycins (Rifampin, Rifabutin and Rifapentine) is a serious problem in itself. Rifamycins trigger overexpression of hepatic cytochrome CYP 450 and Uridine Diphosphate Gluconyltransferase (UGT) 1A1 enzymes that lead to significant reduction in drug exposure and increased metabolism of ARV's [14]. The CYP3A4 isoform metabolises many drugs that include all Protease Inhibitors (PIs), Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs), Maraviroc (MVC), and HIV Integrase Inhibitors (IN) like Raltegravir while the ARV's on the other hand nullify the effects of rifamycins (Rifampin is usually replaced with Rifabutin in most HIV-TB regimens as it is a weaker inducer of cytochrome CYP P450) [15]. This undesired biological link between HIV and TB affects the distribution, progression and outcomes of both diseases that force the use of high dosage of multiple drugs with negative impact. Henceforth, the treatment for both the HIV patients infected with TB or vice-versa is a complex process that must address the selection of tailored ATD regimen and cocktail of ARV's with higher effectiveness, lower drug-drug interactions, and minimum complications related to IRIS [16]. Therefore, it is need of an hour to search for new ATD's that can address the current challenges posed by long treatment duration, emergence and world wide spread of drug resistance, LTBI treatment, co-morbidities due to coinfection with HIV [17], and other factors like diabetes [18], paediatric TB [19] and socio-economic determinants of TB [20].

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