Updated Considerations on Use of TB Preventive Therapy (TPT) Regimens with Antiretroviral Therapy (ART) (Including Dolutegravir)

Goals of Tool: Provide talking points about use of TPT with ARVs including dolutegravir

Note: This tool was developed by the TPT Unit within CDC’s Division of Global HIV and TB, and is available for adaptation by in-country teams as they see fit. Please let us know if you use it in some form, so that we can keep track of its impact and any modifications that have made it more useful in practice.
TB Preventive Therapy Regimens and ART (Including Dolutegravir)

Tuberculosis Preventive Therapy (TPT) is a priority for PEPFAR, and in 2018 a concerted effort is being made to scale-up TPT programming in all PEPFAR countries. Historically the most widely used TPT regimen has been six to nine months of isoniazid (INH), which has been shown to reduce both TB incidence and mortality among persons living with HIV (PLHIV). However, this relatively prolonged course is associated with sub-optimal completion rates.

More recently, shorter and potentially more effective TPT regimens that utilize rifapentine (RPT) have been shown to be safe and effective in PLHIV, and are associated with better completion rates. Three months of once-weekly high-dose INH (900mg) and RPT (900mg) – also known as 3HP – has been recommended by CDC for years and is included in WHO guidance. In March 2018, preliminary results from a study of daily INH (300mg) and RPT (450-600mg) for one month – also known as 1HP – demonstrated similar efficacy to nine months of INH, with fewer adverse events and better completion.

Currently, these regimens are likely cost-prohibitive in resource limited settings (~$46/course of 3HP), though this may change in the near future. However, the evidence supporting RPT-based TPT in PLHIV on ART has only been shown for those who are taking efavirenz- or raltegravir-based antiretroviral therapy; and rifampicin-based regimens are specifically not recommended by WHO for people receiving protease inhibitors or nevirapine (note, INH should also be used with caution in people receiving nevirapine, given its potential hepatotoxicity).

In addition, the transition to tenofovir/lamivudine/dolutegravir (TLD) is a priority for PEPFAR, and countries are being urged to transition many patients as quickly as possible. DTG can be safely administered together with either INH or rifampicin (RIF), although an extra dose of DTG is required with RIF to overcome the fact that RIF induces enzymes that metabolize DTG. Notably, this extra dose comes at an additional cost of $3.70 per month, which may be prohibitive on the scale intended for TPT. However, data on the safety of RPT-based regimens in the context of DTG scale up are still needed.

In 2017, researchers at the Conference on Retroviruses and Opportunistic Infections (CROI) conference presented data from a pharmacokinetic study of dolutegravir (DTG) and RPT in healthy volunteers, which was terminated following the development of severe flu-like syndrome and elevated aminotransferase levels in two of four subjects after the third INH-RPT dose. Since many PEPFAR-supported patients will be taking a DTG-based ART regimen in the near future, and given the cost and clinical concerns associated with RPT and/or RIF-based TPT, the current recommendation is to treat these patients with an INH-based TPT regimen. There is an ongoing trial investigating the safety and efficacy of RPT in PLHIV on DTG (DOLPHIN trial in IMPAACT4TB), and depending on the outcome of that study, and cost reductions in RPT, this recommendation is subject to change.