AETC AIDS Education & Training Center Program
Mountain West

Updates on the Prevention of TB for people living with HIV

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Disclaimer

Funding for this presentation was made possible [in part, if applicable] by U1OHA29296 from the Human Resources and Services Administration HIV/AIDS Bureau. The views expressed do not necessarily reflect the official policies of the Department of Health and Human Services nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government. *Any trade/brand names for products mentioned during this presentation are for training and identification purposes only.*

Disclosures

Vir Biotechnology, Inc.

Data presented in this presentation offer a limited glimpse of health inequities that exist within a larger social context. Racism, not race, creates and perpetuates health disparities.

https://www.ama-assn.org/press-center/press-releases/new-ama-policies-recognize-race-social-not-biological-construct

TB prevention for PLWH

- TB is the leading cause of death for PLWH worldwide
- Providing TB preventive therapy (TPT) to PLWH reduces:
  - TB incidence
  - TB mortality
  - Overall mortality in excess of benefit of ART alone *(Ross JM, Lancet ID, 2021)*
- New evidence → changes in screening and treatment of TB infection

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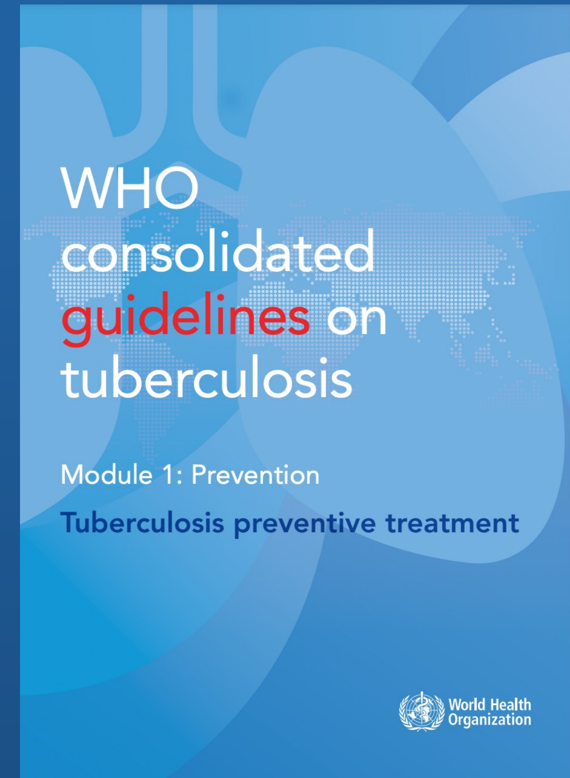
WHO/Global Guidelines

- Updated 2021
- Screen all people with HIV for active TB
- In high-burden settings, treat presumptively for TB infection if active TB excluded.
  - -6H, 3HP, (1HP)

→Pts who initiated ART outside the US may have received TPT



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US Setting – screening for TB infection (LTBI)

- Screen all people with HIV for active TB
- Screen for TB infection:
  - PPD/TST
  - IGRA (Quantiferon)
- If positive screen for LTBI→ CXR to exclude active TB
- Screen all people with HIV for TB infection
  - At entry to care/ART initiation
  - Consider re-screening if CD4<200
  - Consider re-screening if new exposure
- PLWH from TB-endemic settings
  - IGRA preferred (no BCG cross-reaction)
  - Shared decision-making if prior TB or LTBI treatment

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CDC Guidelines - 2020

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 69 / No. 1
February 14, 2020

Guidelines for the Treatment of Latent Tuberculosis Infection: Recommendations from the National Tuberculosis Controllers Association and CDC, 2020

Regimen	Medication (s)	Duration	Dosing
3HR	Isoniazid & Rifampicin	3 months	Daily
3HP	Isoniazid & RifaPENtine	3 months	Weekly
4R	Rifampicin	4 months	Daily
9H	Isoniazid	9 months	Daily
6H	Isoniazid	6 months	Daily

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LTBI treatment guidelines continued

- Rifamycin-containing regimens preferred if possible
- Short-course→Better treatment-completion rates
  - (12 weeks, 3M, 4M)
- Drug-drug interactions with rifamycins can be limiting
  - warfarin
  - hormonal contraceptives
  - antiepileptic drugs
  - glucocorticoids
  - opioids
  - antiretrovirals
- INH-only: 9M higher treatment success than 6M; 6M lower risk of hepatotoxicity. Current recommendations (2020):
  - 6M>9M

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DHHS Guidelines for OIs in PLWH (2021)

LTBI in HIV

Preferred*:

- 9H

Alternate:

- 3HP

*panel update allows 6H

Treating LTBI to Prevent TB Disease

<u>Indications</u>:

- Positive screening test[a] for LTBI, no evidence of active TB disease, and no prior history of treatment for active disease or latent TB infection **(AI)**;
- Close contact with a person with infectious TB, regardless of screening test result **(AII)**

<u>Preferred Therapy</u>:

- Isoniazid 300 mg PO daily plus pyridoxine 25–50 mg PO daily **(AI)**

Duration of Therapy:

- 9 months

<u>Alternative Therapies</u>:

- Rifapentine (see weight-based dosing below) PO once weekly plus isoniazid 15 mg/kg PO once weekly (900 mg maximum) plus pyridoxine 50 mg PO once weekly for 12 weeks **(AII)**. **Note**: Rifapentine is only recommended for patients receiving an efavirenz- or raltegravir-based ART regimen.
  - <u>Rifapentine Weekly Dose (maximum 900 mg)</u>
    - *Weighing 32.1–49.9 kg:* 750 mg
    - *Weighing ≥50.0 kg:* 900 mg
- Rifampin 600 mg PO daily for 4 months **(BI)**
- For persons exposed to drug-resistant TB, select anti-TB drugs after consultation with experts or with public health authorities **(AII)**.

https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-opportunistic-infection/mycobacterium-tuberculosis-infection-and?view=full

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TB/HIV Coinfection – DHHS panel update (6/2021)

Panel's Key Considerations and Recommendations Regarding Tuberculosis/HIV Coinfection

Key Considerations and Recommendations

- Selection of tuberculosis (TB)-preventive treatment for individuals with HIV and latent tuberculosis infection (LTBI) should be based on the individual's antiretroviral (ARV) regimen as noted below.
  - With daily isoniazid alone for 6 or 9 months, any ARV regimen can be used **(AIII)**.
  - With once-weekly isoniazid plus rifapentine for 3 months:
    - Efavirenz (EFV) 600 mg once daily or raltegravir 400 mg twice daily (in combination with either abacavir/lamivudine [ABC/3TC] or tenofovir disoproxil fumarate/emtricitabine [TDF/FTC]) can be used **(AII)**.
    - Dolutegravir (DTG) 50 mg once daily may be used for those in whom once-daily DTG is appropriate **(BII)**. This 3-month regimen **is not recommended** for patients who require twice-daily DTG therapy (e.g., those with certain integrase strand transfer inhibitors [INSTI]-associated resistance substitutions or clinically suspected INSTI resistance) **(AIII)**.
  - With once-daily isoniazid and rifapentine for 1 month:
    - EFV 600 mg once daily (in combination with either ABC/3TC or TDF/FTC) can be used without dose adjustment **(AI)**.
  - If rifampin or rifapentine is used to treat LTBI, clinicians should review Tables 24a through 24e to assess the potential for drug-drug interactions among different ARV drugs and the rifamycins **(AII).**

https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/tuberculosishiv-coinfection

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TB treatment and ART

- Rifampicin and rifapentine induce CYP450 → interaction with many antiretrovirals.
- Shared decision-making with pts to determine whether switching ART to optimize TB/LTBI treatment options is preferred, or choosing an LTBI regimen if ART options limited
- “Universal TPT:” daily INH → compatible with all ART
- “Universal ART:” Atripla (EFV+TDF+FTC) → compatible with all LTBI & TB treatment
- All other LTBI options and TB treatment likely to require some ART adjustment.

Rifampicin & Rifapentine interactions with key ARVs

- INSTIs:
  - -bictegravir: NO (rifampicin/rifapentine **contraindicated** with bictegravir – lowers concentration below therapeutic threshold)
  - -dolutegravir: OK; if RIF/RPT given daily, increase to bid DTG for 2 weeks after end of RIF.
  - -raltegravir: OK with weekly RPT (no dose adj); inferior to EFV if RIF given daily;
- Cobi (booster): no RIF
- TAF: Not preferred. PK concerns. TDF with RIF ok.
- PIs: RIF interacts/contraindicated with most (and booster). Lopinavir/ritonavir can be given, but must be double dose during and for 2 weeks after end of RIF

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ART Alphabet soup ahead

First-line ART

- INSTI + 2 NRTI
  - BIC/TAF/FTC **(AI)**[a] **(Biktarvy)**
  - DTG/ABC/3TC **(AI)—if HLA-B*5701 negative (Triumeq)**
  - DTG plus (TAF or TDF)[a] plus (FTC or 3TC) **(AI)**
    - **Dolutegravir + Truvada (TDF/FTC) or Descovy (TAF/FTC)**
- **INSTI plus 1 NRTI:**
  - DTG/3TC **(AI)**, except for individuals with HIV RNA >500,000 copies/mL, HBV coinfection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available

https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/what-start-initial-combination-regimens-antiretroviral-naive

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Alternate initial regimens

- **INSTI plus 2 NRTIs:**
  - EVG/c/(TAF or TDF)a/FTC **(BI)**[b] **(Genvoya/Stribild)**
  - RAL plus (TAF or TDF)[a] plus (FTC or 3TC) **(BI for TDF/[FTC or 3TC], BII for TAF/FTC)**
- **Boosted PI plus 2 NRTIs:** In general, boosted DRV is preferred over boosted ATV
  - (DRV/c[b] or DRV/r) plus (TAF or TDF)[c] plus (FTC or 3TC) **(AI)**[b]
  - (ATV/c[b] or ATV/r) plus (TAF or TDF)[c] plus (FTC or 3TC) **(BI)**[b]
  - (DRV/c[b] or DRV/r) plus ABC/3TC —**if HLA-B*5701 negative (BII)**[b]
- **NNRTI plus 2 NRTIs:**
  - DOR/TDF[c]/3TC **(BI)** or DOR plus TAF[c]/FTC **(BIII)** **(Delstrigo: DOR+TDF+3TC)**
  - EFV plus (TAF or TDF)[c] plus (FTC or 3TC) **(Atripla: EFV+TDF+FTC)**
    - EFV 600 mg plus TDF plus (FTC or 3TC) **(BI)**
    - EFV 400 mg/TDF/3TC **(BI)**
    - EFV 600 mg plus TAF/FTC **(BII)**
  - RPV/(TAF or TDF)[c]/FTC **(BII for TAF and BI for TDF)—if HIV RNA <100,000 copies/mL and CD4 count >200 cells/mm^3** (Odefsey/Complera)

https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/what-start-initial-combination-regimens-antiretroviral-naive

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TPT and ART

Regimen	Medication (s)	Duration	ART
3HR	Isoniazid & Rifampicin	3M daily	TDF/FTC/**DTG bid** or TDF/FTC/EFV
3HP	Isoniazid & RifaPENtine	3M weekly	TDF/FTC/DTG or TDF/FTC/EFV
4R	Rifampicin	4M daily	TDF/FTC/**DTG bid** or TDF/FTC/EFV
9H	Isoniazid	9M daily	No change to ART
6H	Isoniazid	6M	No change to ART

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Alternative regimen (DHHS Guidelines Panel):

ORIGINAL ARTICLE

One Month of Rifapentine plus Isoniazid to Prevent HIV-Related Tuberculosis

Susan Swindells, M.B., B.S., Ritesh Ramchandani, Ph.D., Amita Gupta, M.D., Constance A. Benson, M.D., Jorge Leon-Cruz, M.S., Noluthando Mwelase, M.B., Ch.B., Marc A. Jean Juste, M.D., Javier R. Lama, M.D., M.P.H., Javier Valencia, M.D., Ayotunde Omoz-Oarhe, M.D., Khuanchai Supparatpinyo, M.D., Gaerolwe Masheto, M.D., et al., for the BRIEF TB/A5279 Study Team*

March 14, 2019
N Engl J Med 2019; 380:1001-1011
DOI: 10.1056/NEJMoa1806808

Regimen	Medication (s)	Duration	Dosing
1HP	Isoniazid & RifaPENtine	1 month	Daily

- Noninferior to 9M INH in PLWH taking EFV-based ART (e.g. Atripla)
- No studies with DTG/INSTI ART
- Likely would need to switch to bid DTG

https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/tuberculosishiv-coinfection?view=full

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Considerations for switching ART

- Switching ART is a **vulnerable time for loss of virologic control** → can pt be supported to maintain good adherence with the switch? How complicated is the switch?
  - Descovy (TAF/FTC) to Truvada (TDF/FTC) is an “invisible switch,” probably straightforward to pt
  - 1 pill daily (e.g. Biktarvy)→ 1 pill bid + 1 pill daily (e.g. DTG+Truvada) is more complicated, is there a 1 pill option?
  - 2-week ”tail” can be hard to understand (for increased DTG or LPV/r dosing)
- If pt highly treatment-experienced or not suppressed, may have limited ART options. INSTI (DTG)-containing regimens are most potent at suppressing VL
- What are **priorities to pt** in terms of longer duration of LTBI treatment vs. shorter duration? ART is for life.

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Considerations for choosing TPT

- National shortage of rifapentine (Priftin) → 3HP/1HP options limited.

Presentation	Availability and Estimated Shortage Duration	Related Information	Shortage Reason (per FDASIA)
Rifapentine (Piftin) Tablets, 150 mg (NDC 0088-2102-24)	Intermittent supply		Demand increase for the drug

- Lab monitoring: CMP at baseline, LFTs periodically, LFTs with any GI/liver symptoms
- Adherence support: consider DOT/VOT for 3HP, but not longer mandatory.
- UW: eConsult ID (Epic order eConsult Infectious Diseases) for advice with TPT selection

Cases I

- 29yo man with newly diagnosed HIV, was started on Biktarvy (BIC/TAF/FTC). QFT+. Medication adherence a concern, strong preference for 1-pill ART regimen. What are your options for LTBI treatment?
  - Keep Biktarvy → 6-9M INH daily
  - Switch to Atripla → any LTBI treatment (switch back to Biktarvy after LTBI treatment complete)

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Acknowledgement

This Mountain West AIDS Education and Training (MWAETC) program is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of an award totaling $3,098,654 with 0% financed with non-governmental sources.

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