Updates in TB Preventive Therapy Guidelines

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Disclosures

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TB prevention for PLWH

• TB is the leading cause of death for PLWH worldwide

• Treating latent TB infection (LTBI) in 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 LTBI
WHO/Global Guidelines

- Updated 2018
- Screen all people with HIV for active TB
- In high-burden settings, treat LTBI if active TB excluded.
  -9H, 6H, 3HP
<table>
<thead>
<tr>
<th>Regimen</th>
<th>Medication (s)</th>
<th>Duration</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>3HR</td>
<td>Isoniazid &amp; Rifampicin</td>
<td>3 months</td>
<td>Daily</td>
</tr>
<tr>
<td>3HP</td>
<td>Isoniazid &amp; RifaPENtine</td>
<td>3 months</td>
<td>Weekly</td>
</tr>
<tr>
<td>4R</td>
<td>Rifampicin</td>
<td>4 months</td>
<td>Daily</td>
</tr>
<tr>
<td>9H</td>
<td>Isoniazid</td>
<td>9 months</td>
<td>Daily</td>
</tr>
<tr>
<td>6H</td>
<td>Isoniazid</td>
<td>6 months</td>
<td>Daily</td>
</tr>
</tbody>
</table>
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
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
  - raltegravir: OK, if RIF given daily, double dose during and for 2 weeks after end of RIF (no change if weekly RPT)

• Cobi: no RIF

• TAF: Not preferred. TDF with RIF ok. PK concerns

• PIs: RIF interacts/contraindicated with most. Lopinavir/ritonavir can be given, but must be double dose during and for 2 weeks after end of RIF
<table>
<thead>
<tr>
<th>Regimen</th>
<th>Medication(s)</th>
<th>Duration</th>
<th>ART</th>
</tr>
</thead>
<tbody>
<tr>
<td>3HR</td>
<td>Isoniazid &amp; Rifampicin</td>
<td>3M daily</td>
<td>TDF/FTC/DTG bid or TDF/FTC/EFV</td>
</tr>
<tr>
<td>3HP</td>
<td>Isoniazid &amp; RifaPENtine</td>
<td>3M weekly</td>
<td>TDF/FTC/DTG or TDF/FTC/EFV</td>
</tr>
<tr>
<td>4R</td>
<td>Rifampicin</td>
<td>4M daily</td>
<td>TDF/FTC/DTG bid or TDF/FTC/EFV</td>
</tr>
<tr>
<td>9H</td>
<td>Isoniazid</td>
<td>9M daily</td>
<td>No change to ART</td>
</tr>
<tr>
<td>6H</td>
<td>Isoniazid</td>
<td>6M</td>
<td>No change to ART</td>
</tr>
</tbody>
</table>
Evidence, but not yet guidelines:

- Noninferior to 9M INH in PLWH taking EFV-based ART
- No studies with DTG/INSTI ART
- Likely would need to switch to bid DTG

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<th>Duration</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>1HP</td>
<td>Isoniazid &amp; Rifapentine</td>
<td>1 month</td>
<td>Daily</td>
</tr>
</tbody>
</table>

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/AS279 Study Team

March 14, 2019

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