TB Prevention in PLHIV: Options Other Than Isoniazid

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Approaches to TB Prevention

• Primary Prevention (prevent infection)
  – Reduce exposure
  – Reduce transmission
  – Vaccination

• Secondary Prevention (prevent disease)
  – Chemoprophylaxis (IPT) or ART

• Tertiary Prevention (prevent recurrence)
  – Chemoprophylaxis or ART
Reasons to Look Beyond IPT

• IPT isn’t being used!
  – Toxicity, adherence, resistance and dogma
• IPT isn’t enough, even with HAART
• Risk of TB may rise again after completing IPT
• INH resistance
# TB Rates in HIV+ Patients With Access to ART and IPT in Rio de Janeiro

<table>
<thead>
<tr>
<th>Exposure category</th>
<th>Person-Years</th>
<th>TB cases</th>
<th>IR (per 100 PYs)</th>
<th>IRR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naïve</td>
<td>3,865</td>
<td>155</td>
<td>3.98 (3.38-4.67)</td>
<td>1.0</td>
</tr>
<tr>
<td>HAART only</td>
<td>11,627</td>
<td>221</td>
<td>1.91 (1.67-2.18)</td>
<td>0.48 (0.39-0.59)</td>
</tr>
<tr>
<td>IPT only</td>
<td>395</td>
<td>5</td>
<td>1.27 (0.41-2.95)</td>
<td>0.32 (0.10-0.76)</td>
</tr>
<tr>
<td>Both</td>
<td>1,253</td>
<td>10</td>
<td>0.80 (0.38-1.47)</td>
<td>0.20 (0.09-0.91)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>17,142</td>
<td>391</td>
<td>2.28 (2.06-2.52)</td>
<td></td>
</tr>
</tbody>
</table>

Golub et al., AIDS 2007;21:1441-8
TB Incidence in Selected Populations:
African Countries and ART Patients

- Swaziland
- Botswana
- SA Gold Mine
- HIV/ART
- ART/IPT
- SA HIV-
Durability of Protection Following TB Preventive Therapy

Mwinga et al., AIDS 1998;12:2447
What to use instead of IPT for 6-9 months?

- More INH – continuously or repetitively
- Rifampin ± INH
- Rifapentine + INH or Moxifloxacin
- PA-824
- Moxifloxacin/PZA
- TMC 207, Otsuka compound, etc.
Botswana IPT Trial Study Design

Randomized Double-Blind Placebo Controlled Trial

2,000 participants- 1,000 per study arm

Healthy
HIV+ adult

6 mo INH qd → 30 mo placebo

36 mo INH qd

CDC – BOTUSA Project
PHRU/JHU Trial of Novel TB Preventive Regimens for HIV+/PPD+ Adults in Soweto

- Patients: HIV+, PPD >5 mm, >18 y.o., CD4 >200
- Regimens
  - Rifapentine/INH weekly x 12 weeks
  - Rifampin/INH twice weekly x 12 weeks
  - INH daily indefinitely (lifelong)
  - INH daily x 6 months (control)
- Median follow up ~ 3.6 years
- Analysis planned for July 2008
### Short-Course RIF/INH for Latent TB Infection in HIV+ Patients

<table>
<thead>
<tr>
<th>Regimen</th>
<th>TB Risk/100 py</th>
</tr>
</thead>
<tbody>
<tr>
<td>INH daily x 6 m</td>
<td>1.1</td>
</tr>
<tr>
<td>INH/RIF daily x 3 m</td>
<td>1.3</td>
</tr>
</tbody>
</table>

Whalen et al.
Efficacy of RIF for the Prevention of TB in Patients with Silicosis

# UFRJ/JHU Trial of Weekly Rifapentine/INH in Household Contacts of Pulmonary TB Cases

<table>
<thead>
<tr>
<th></th>
<th>RPT/INH</th>
<th>RIF/PZA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Patients</td>
<td>206</td>
<td>193</td>
</tr>
<tr>
<td>Person-Years of Follow Up</td>
<td>564</td>
<td>522</td>
</tr>
<tr>
<td>TB Cases</td>
<td>3 (1.5%)</td>
<td>1 (0.5%)*</td>
</tr>
<tr>
<td>TB Rate (Cases/100 Person-Years)</td>
<td>0.5</td>
<td>0.2</td>
</tr>
</tbody>
</table>

*RR 2.8 (95% CI 0.3-26.8), P=0.66

Schechter et al. AJRCCM 2006
Efficacy of Daily Rifapentine and Moxi in the Mouse Model of Active TB

Rosenthal et al., PLoS Medicine 2007
CFU counts in the lungs of mice treated with PA-824 in the continuation phase

Tyagi et al, AAC (2005); 49:2289
PA-824 and Moxi Regimens in Active TB in the Mouse Model

Nueremberger et al., unpublished
Effect of Secondary Preventive Therapy in HIV+ Patients

Population: HIV+ gold miners with prior TB

Endpoint: TB Incidence

Secondary IPT rate – 5.7 cases/100 PY
No secondary IPT rate – 29.3 cases/100 PY

Relative Risk: 0.19 (0.04-0.42)

Churchyard, AIDS 2003;17:2063-70
Infection Control?
Primary Prevention of TB Infection in Resource-Poor Settings

• Earlier case detection and treatment
• Natural ventilation
• Patient/community education
• Administrative isolation with rapid evaluation for TB and MDR TB
• Personal respiratory protection
• Germicidal $uv$ radiation
Yield of Contact Investigation as a Tool for Case Detection and Earlier Treatment

- Rio de Janeiro
  - 4% of household contacts of TB cases had active disease

- Zambia/South Africa
  - 6% of households of TB case have second case detected with evaluation

Cavalcante et al., unpublished
ZAMSTAR Study, unpublished
Natural vs. Mechanical Ventilation of Hospital Rooms in Peru

PREVENT DISEASE

CARELESS
SPITTING, COUGHING, SNEEZING,
SPREAD INFLUENZA
and TUBERCULOSIS

RENSSELAER COUNTY TUBERCULOSIS ASSOCIATION, BRONY, N. Y.
Infection Control, Brazilian Style
Conclusions

• Options other than IPT
  – Rifamycins, new drugs, secondary PT

• Primary prevention
  – Case finding
  – Infection control – simple solutions can be implemented now
TB & HIV

FIND TB
TREAT TB
PREVENT TB