The PREVENT TB Study
TB Trials Consortium Study 26

3 months of once-weekly rifapentine plus INH vs.
9 months of daily INH
for treatment of latent TB infection

Background

• Treatment of latent *M. tuberculosis* infection is a key component of TB prevention and elimination

• 9 months of isoniazid (INH) is highly efficacious, but effectiveness is diminished by low completion rates (30-60%)

• A shorter regimen is needed
  – High completion rates, effectiveness, and tolerability
Study Design

Once-weekly, directly-observed rifapentine + INH x 3 months (3HP) vs. Daily, self-administered INH x 9 months (9H)

For the treatment of latent TB infection in high-risk tuberculin skin-test reactors

Randomized, open-label
33 months of follow-up from date of enrollment
Study Doses

• **Rifapentine + INH x 3 months (3HP):** 12 doses
  – Rifapentine 900 mg
    • Graduated dosing for persons ≤ 50 kg
  – Isoniazid 15-25 mg/kg; 900 mg max.

• **Isoniazid x 9 months (9H):** 270 doses
  – Isoniazid 5-15 mg/kg; 300 mg max.

• **Vitamin B6 (pyridoxine):** 50 mg with each INH dose
Inclusion Criteria

- Persons > 2 years old who were:
  - Tuberculin skin-test (TST)-positive close contacts of a culture-confirmed TB case
  - TST-converters
    - Documented negative → positive within 2 years
  - HIV-infected with
    - Positive TST
    - Close contact to TB case regardless of TST
  - TST-positive, fibrosis on chest radiograph consistent with prior untreated TB
  - Children 2-4 years old with + TST or close contact with a culture-confirmed TB case
Exclusion Criteria

- Confirmed or suspected TB
- TB resistant to INH or rifampin in source case
- History of treatment with
  - > 14 consecutive days with a rifamycin
  - > 30 days with INH
- Prior treatment of TB or *M. tuberculosis* infection in HIV-uninfected persons
- Intolerance to INH or rifamycins
- Aspartate aminotransferase (AST) > 5x upper limit if AST determined
- Pregnant or lactating females
- HIV-1 antiretroviral therapy within 90 days of enrollment
- Weight < 10 kg
Primary Aim

• Evaluate the effectiveness of weekly 3HP vs. daily 9H

• Primary endpoint:
  - Culture-confirmed TB in persons $\geq$ 18 y.o and culture-confirmed or clinical TB in persons $<$ 18 y.o.
Secondary Aims

- Evaluate the tolerability of weekly 3HP vs. daily 9H
- Secondary endpoints:
  - Treatment completion
  - Permanent drug discontinuation for any reason
  - Drug discontinuation due to adverse drug reaction
  - Grade 3, 4, and 5 toxicity
  - Culture-confirmed or clinical TB in all persons
  - Resistance to study medications among persons developing TB
Study Design and Sample Size

• Non-inferiority study design
  – Non-inferiority margin (delta): 0.75%
• > 80% power to demonstrate that 3HP is not inferior to 9H
  – 3,200 persons per arm
• Allow for 20% loss
  – Loss to follow-up
  – Clustering of enrollments
• 4,000 persons per arm

Possible Scenarios of Observed Treatment Differences in Noninferiority Trials

Enrollment

• Enrollment began June 2001

• Enrollment ended February 15, 2008

• Follow-up ended September 30, 2010
Analysis Populations

• Enrolled before February 15, 2008
  – Completed 33 months of follow-up by September 30, 2010

• Intention-to-treat (ITT)
  – All persons enrolled in the study

• Modified intention-to-treat (MITT)
  – Enrolled in the study
  – Eligible

• Per protocol (PP)
  – All persons enrolled in the study who were eligible
  – Completed study drug within targeted time period
  – Or developed TB or died but completed ≥ 75% of expected doses prior to event
  – All follow-up time counted; did not require reaching 33 months
Effectiveness and Efficacy

• Effectiveness:
  – TB rate among all persons enrolled who were eligible for the study
    • MITT
    • Takes into account nonadherence

• Efficacy
  – TB rate among all persons who were enrolled, eligible, and completed therapy
    • PP
    • Best-case scenario regarding drug activity
Analysis Populations

• In group settings (e.g., households), participants could be placed on the same regimen as the first person in the group (cluster)
  – Only the first person in that cluster was randomized
  – The size of clusters varied by arm early in the study
  – Later, entire cluster had to be identified before randomization of first person

• For MITT and PP populations, we therefore assessed results for:
  – All patients enrolled
  – First patient enrolled in a cluster
Analysis Populations

- Enrolled (ITT) 8,053
- Eligible (MITT) 7,731
  - 9H 3,745
  - 3HP 3,986
- Per protocol (PP) 5,858
  - 9H 2,585
  - 3HP 3,273
## Reason for Ineligibility

N=322 (of 8,053)

<table>
<thead>
<tr>
<th>Reason</th>
<th>Frequency</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source TB case resistant to INH or RIF</td>
<td>161</td>
<td>50</td>
</tr>
<tr>
<td>Source TB case culture-negative for <em>M. tuberculosis</em></td>
<td>103</td>
<td>32</td>
</tr>
<tr>
<td>Positive TST not confirmed</td>
<td>37</td>
<td>12</td>
</tr>
<tr>
<td>No susceptibility testing for index case</td>
<td>14</td>
<td>4</td>
</tr>
<tr>
<td>TB at enrollment</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>322</strong></td>
<td><strong>100%</strong></td>
</tr>
</tbody>
</table>


### Clinical and Demographic Characteristics

**MITT Population**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>9H (N=3,745)</th>
<th>3HP (N=3,986)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (median, IQR)</td>
<td>36 (25-46)</td>
<td>37 (25-47)</td>
</tr>
<tr>
<td>Male sex</td>
<td>2,004 (54)</td>
<td>2,210 (55)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>2,160 (58)</td>
<td>2,296 (58)</td>
</tr>
<tr>
<td>Black</td>
<td>947 (25)</td>
<td>978 (25)</td>
</tr>
<tr>
<td>Asian/Pac. Island</td>
<td>490 (13)</td>
<td>494 (12)</td>
</tr>
<tr>
<td>Am./Can. Indian</td>
<td>33 (1)</td>
<td>84 (2)*</td>
</tr>
<tr>
<td>Multiracial (Brazil)</td>
<td>115 (3)</td>
<td>134 (3)</td>
</tr>
<tr>
<td>Ethnicity (US/Can)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>1,442 (43)</td>
<td>1,576 (44)</td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>1,899 (57)</td>
<td>1,966 (56)</td>
</tr>
</tbody>
</table>
## Clinical and Demographic Characteristics
### MITT Population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>9H</th>
<th>3HP</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-infected</td>
<td>100 (3%)</td>
<td>105 (3%)</td>
</tr>
<tr>
<td>BMI (median, IQR)</td>
<td>27 (23-30)</td>
<td>27 (23-31)</td>
</tr>
<tr>
<td>Site of recruitment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>U.S./Canada</td>
<td>3,341 (89)</td>
<td>3,542 (89)</td>
</tr>
<tr>
<td>Brazil/Spain</td>
<td>404 (11)</td>
<td>444 (11)</td>
</tr>
<tr>
<td>Completed high school</td>
<td>2,126 (57)</td>
<td>2,269 (57)</td>
</tr>
<tr>
<td>Jail/prison ever</td>
<td>175 (5)</td>
<td>221 (6)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>390 (10)</td>
<td>424 (11)</td>
</tr>
<tr>
<td>Hx EtOH at enrollment</td>
<td>1,888 (50)</td>
<td>1,929 (48)</td>
</tr>
<tr>
<td>Hx IDU at enrollment</td>
<td>136 (4)</td>
<td>149 (4)</td>
</tr>
<tr>
<td>Current tobacco</td>
<td>1,034 (28)</td>
<td>1,112 (28)</td>
</tr>
</tbody>
</table>
## Clinical and Demographic Characteristics
### MITT Population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>9H N=3,745</th>
<th>3HP N=3,986</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indication for TLI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Close contact</td>
<td>2,609 (70)</td>
<td>2,857 (72)</td>
</tr>
<tr>
<td>Recent TST converter</td>
<td>972 (26)</td>
<td>953 (24)</td>
</tr>
<tr>
<td>HIV-infected</td>
<td>74 (2)</td>
<td>87 (2)</td>
</tr>
<tr>
<td>Fibrosis on CXR</td>
<td>90 (2)</td>
<td>89 (2)</td>
</tr>
<tr>
<td>Co-morbid liver disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCV</td>
<td>97 (3)</td>
<td>99 (3)</td>
</tr>
<tr>
<td>HBV</td>
<td>60 (2)</td>
<td>42 (1)</td>
</tr>
</tbody>
</table>
## Follow-up and Retention

<table>
<thead>
<tr>
<th>Measure</th>
<th>9H</th>
<th>3HP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Person-years of follow-up</td>
<td>9,619</td>
<td>10,327</td>
</tr>
<tr>
<td># months in study (mean)</td>
<td>30.3</td>
<td>30.7</td>
</tr>
<tr>
<td>Proportion of participants completing month 33 follow-up visit</td>
<td>86%</td>
<td>88%</td>
</tr>
</tbody>
</table>
## Event rate estimates and the non-inferiority test for A33

33 months of follow-up from time of randomization

<table>
<thead>
<tr>
<th>Population</th>
<th>study arms</th>
<th># of patients</th>
<th># TB cases</th>
<th>TB per 100 p-y</th>
<th>Cumulative TB rate (%)</th>
<th>Difference in cumulative TB rate</th>
<th>Upper bound of 95% CI of difference in cumulative TB rates*</th>
</tr>
</thead>
<tbody>
<tr>
<td>MITT</td>
<td>9H</td>
<td>3,745</td>
<td>15</td>
<td>0.16</td>
<td>0.43</td>
<td>-0.24</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>3HP</td>
<td>3,986</td>
<td>7</td>
<td>0.07</td>
<td>0.19</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Per Protocol</td>
<td>9H</td>
<td>2,585</td>
<td>8</td>
<td>0.11</td>
<td>0.32</td>
<td>-0.19</td>
<td>0.06</td>
</tr>
<tr>
<td></td>
<td>3HP</td>
<td>3,273</td>
<td>4</td>
<td>0.05</td>
<td>0.13</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* non-inferiority margin (delta) = 0.75%
Difference in TB rates between the 2 study arms, and non-inferiority "delta"
Modified Intention to Treat Population; A33 analysis
Difference in TB rates between the 2 study arms, and non-inferiority “delta”

Per Protocol Population; A33 analysis
Cumulative TB Rate
33 months from enrollment—MITT

Log-rank P-value: 0.06
Additional Analyses

- 24 months from completion of treatment
  - Similar results
- Limited to first person enrolled in cluster
  - Similar results
- Including 4 culture-negative TB cases in adults (total TB = 26) (secondary endpoint)
  - Similar results
- Sensitivity analysis of primary endpoint
  - Number of additional cases in 3HP arm required to be unable to claim non-inferiority (assuming no additional cases in 9H arm):
    - 23
Tolerability
Participants who took ≥1 dose

<table>
<thead>
<tr>
<th>Outcome</th>
<th>9H N=3,759</th>
<th>3HP N=4,040</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment completion</td>
<td>2,599 (69.0%)</td>
<td>3,327 (82.0%)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Permanent drug d/c- any reason</td>
<td>1,160 (31.0%)</td>
<td>713 (18.0%)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Permanent drug d/c- due to an adverse event</td>
<td>139 (3.7%)</td>
<td>196 (4.9%)</td>
<td>0.009</td>
</tr>
<tr>
<td>Death</td>
<td>39 (1.0%)</td>
<td>31 (0.8%)</td>
<td>0.22</td>
</tr>
</tbody>
</table>
### Reported Adverse Events
Among persons receiving ≥ 1 dose
During treatment or within 60 days of the last dose
Regardless of attribution to study drug

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>9H N=3,759</th>
<th>3HP N=4,040</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1-2</td>
<td>341 (9.0%)</td>
<td>310 (7.6%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Grade 3</td>
<td>203 (5.4%)</td>
<td>193 (4.8%)</td>
<td>0.22</td>
</tr>
<tr>
<td>Grade 4</td>
<td>43 (1.1%)</td>
<td>36 (0.9%)</td>
<td>0.27</td>
</tr>
</tbody>
</table>
### Reported Adverse Events
Among persons receiving ≥ 1 dose
During treatment or within 60 days of the last dose
Accounting for attribution to study drug

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>9H N=3,759</th>
<th>3HP N=4,040</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Related to drug</td>
<td>206 (5.5)</td>
<td>328 (8.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Rash only</td>
<td>17 (0.5)</td>
<td>35 (0.9)</td>
<td>0.02</td>
</tr>
<tr>
<td>Possible HS</td>
<td>15 (0.4)</td>
<td>158 (3.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Other</td>
<td>71 (2.0)</td>
<td>122 (3.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>Not related</td>
<td>399 (10.3)</td>
<td>220 (5.5)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

HS: hypersensitivity reaction
Hepatotoxicity
Among persons receiving ≥ 1 dose
During treatment or within 60 days of the last dose

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>9H N=3,759</th>
<th>3HP N=4,040</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All hepatotoxicity</td>
<td>113 (3.0)</td>
<td>24 (0.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Related to drug</td>
<td>103 (2.7)</td>
<td>18 (0.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Not related</td>
<td>13 (0.4)</td>
<td>6 (0.2)</td>
<td>0.08</td>
</tr>
</tbody>
</table>
Possible Hypersensitivity
Among persons receiving ≥ 1 dose
During treatment or within 60 days of the last dose

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>9H N=3,759</th>
<th>3HP N=4,040</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All hypersensitivity reactions</td>
<td>17 (0.5)</td>
<td>152 (3.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HS reactions with treatment discontinuation</td>
<td>15 (0.4)</td>
<td>117 (2.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HS reactions w/ hypotension*</td>
<td>0</td>
<td>6 (0.15)</td>
<td></td>
</tr>
</tbody>
</table>

Systolic BP <90 mm Hg G1 n=3, G2 n=1, G3 n=2
## Risk Factor Analysis for TB

### Univariate

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Reference group</th>
<th>HR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regimen (3RPT/INH)</td>
<td>9INH</td>
<td>0.43 (0.18, 1.07)</td>
<td>0.07</td>
</tr>
<tr>
<td>Age (10 years)</td>
<td>10 years younger</td>
<td>0.87 (0.65, 1.17)</td>
<td>0.37</td>
</tr>
<tr>
<td>Male sex</td>
<td>Female</td>
<td>1.50 (0.63, 3.58)</td>
<td>0.35</td>
</tr>
<tr>
<td>Black race</td>
<td>White race</td>
<td>1.56 (0.64, 3.81)</td>
<td>0.33</td>
</tr>
<tr>
<td>HIV +</td>
<td>HIV negative</td>
<td>7.00 (2.19, 22.30)</td>
<td>0.001</td>
</tr>
<tr>
<td>BMI (1 unit)</td>
<td>1 unit lower</td>
<td>0.85 (0.78, 0.93)</td>
<td>0.0006</td>
</tr>
<tr>
<td>EtOH abuse</td>
<td>No EtOH</td>
<td>4.84 (1.58, 14.78)</td>
<td>0.006</td>
</tr>
<tr>
<td>Current smoking</td>
<td>No smoking</td>
<td>4.73 (1.98, 11.27)</td>
<td>0.0005</td>
</tr>
<tr>
<td>IDU</td>
<td>No IDU</td>
<td>1.29 (0.17, 9.59)</td>
<td>0.80</td>
</tr>
<tr>
<td>High school</td>
<td>Completed</td>
<td>1.21 (0.51, 2.85)</td>
<td>0.66</td>
</tr>
<tr>
<td>Jail/prison</td>
<td>No jail/prison</td>
<td>3.12 (0.92, 10.54)</td>
<td>0.07</td>
</tr>
<tr>
<td>Unemployed</td>
<td>Not unemployed</td>
<td>2.55 (0.94, 6.92)</td>
<td>0.07</td>
</tr>
</tbody>
</table>

No interaction between treatment arm and above variables.
## Risk Factor Analysis-for TB
### Multivariate

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Reference group</th>
<th>HR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regimen (3RPT/INH)</td>
<td>9INH</td>
<td>0.38 (0.15, 0.99)</td>
<td>0.05</td>
</tr>
<tr>
<td>Age (10 years)</td>
<td>10 years younger</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male sex</td>
<td>Female</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black race</td>
<td>White race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV +</td>
<td>HIV neg/unknown</td>
<td>4.07 (1.26, 3.16)</td>
<td>0.01</td>
</tr>
<tr>
<td>BMI (1 unit)</td>
<td>1 unit lower</td>
<td>0.81 (0.73, 0.90)</td>
<td>0.0002</td>
</tr>
<tr>
<td>EtOH abuse</td>
<td>EtOH use or none</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking-current</td>
<td>Smoke last 5 yrs/never</td>
<td>4.89 (1.90, 12.58)</td>
<td>0.001</td>
</tr>
<tr>
<td>IDU</td>
<td>No IDU</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High school</td>
<td>Completed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jail/prison</td>
<td>No jail/prison</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unemployed</td>
<td>Not unemployed</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Drug Resistance

Among TB cases

<table>
<thead>
<tr>
<th></th>
<th>9H N=12</th>
<th>3HP N=7</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>INH resistant</strong></td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td><strong>Rifampin resistant</strong></td>
<td>0</td>
<td>1*</td>
</tr>
</tbody>
</table>

*M. bovis* in an HIV-infected person who completed therapy late due to treatment interruptions
# Causes of Death by Arm

<table>
<thead>
<tr>
<th>Category</th>
<th>Arm A (N/%)</th>
<th>Arm B (N/%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant neoplasms (cancer)</td>
<td>15/38.46</td>
<td>8/25.81</td>
</tr>
<tr>
<td>Intentional injuries</td>
<td>6/15.38</td>
<td>1/3.23</td>
</tr>
<tr>
<td>Diseases of heart</td>
<td>4/10.26</td>
<td>8/25.81</td>
</tr>
<tr>
<td>Unintentional injuries</td>
<td>3/7.69</td>
<td>3/9.68</td>
</tr>
<tr>
<td>Chronic liver disease or cirrhosis</td>
<td>2/5.13</td>
<td>4/12.9</td>
</tr>
<tr>
<td>Hypertension (with or w/o renal disease)</td>
<td>2/5.13</td>
<td>1/3.23</td>
</tr>
<tr>
<td>AIDS</td>
<td>1/2.56</td>
<td>1/3.23</td>
</tr>
<tr>
<td>Cerebrovascular diseases</td>
<td>1/2.56</td>
<td>4/12.9</td>
</tr>
<tr>
<td>Chronic lower respiratory diseases</td>
<td>1/2.56</td>
<td>0/0</td>
</tr>
<tr>
<td>Chronic pancreatitis</td>
<td>1/2.56</td>
<td>0/0</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1/2.56</td>
<td>0/0</td>
</tr>
<tr>
<td>Septicemia</td>
<td>1/2.56</td>
<td>1/3.23</td>
</tr>
<tr>
<td>Unknown</td>
<td>1/2.56</td>
<td>0/0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>39</strong></td>
<td><strong>31</strong></td>
</tr>
</tbody>
</table>
Limitations

• Few HIV-infected participants
  – Enrollment of this population was extended to December 2010
  – Tolerability and effectiveness data pending

• Complete tolerability assessment in young children also pending
  – Enrollment of children 2-11 years old extended to December 2010
Conclusions
The PREVENT TB Study
TB Trials Consortium Study 26

• The effectiveness of 3HP was not inferior to 9H
  – 3HP was at least as effective as 9H
    • The 3HP TB rate was approximately half that of 9H

• The 3HP completion rate was significantly higher than 9H
  – 82% vs. 69%

• 3HP was safe relative to 9H
  – Lower rates of:
    • Any adverse event
    • Hepatotoxicity attributable to study drug
Conclusions
The PREVENT TB Study
TB Trials Consortium Study 26

• Permanent drug discontinuation due to adverse event was higher in 3HP
  – 4.7% vs. 3.6%

• Rates of any adverse event attributable to study drug also higher in 3HP
  – 8.1% vs. 5.5%
  – This relationship also seen with rash, possible hypersensitivity

• Rates of grade 3 and 4 toxicity did not differ by arm

• Rates of death low (~ 1%) in both arms
Interpretation

• The higher rates of 3HP drug discontinuation due to an adverse event and adverse event attributable to study drug could be related to:
  – Worse tolerability of 3HP
  – More frequent interaction with study personnel
    • Weekly in 3HP vs. monthly in 9H
  – Open-label design with novel regimen
    • participants and investigators
Potential Impact on TB Control

- 3HP is an alternative to 9H for treatment of latent *M. tuberculosis* infection in persons at high-risk for progression to TB
- Higher completion rates for treatment of LTBI
- 3HP as effective as 9H in this clinical trial
  - 3HP could be more effective than 9H in operational settings, particularly if 3HP is given under direct observation and 9H completion rates are 30-60%
  - Greater effectiveness → more TB prevented
Dissemination of Results

Uptake of Regimen

• CDC recommendation/guidelines
  – After publication of paper
• ATS/CDC/IDSA guidelines
  – Process starting now
  – May require >2 years to finalize
• Availability of rifapentine
• Ability of TB programs to implement DOT
• Monitoring for adverse events
  – Past history of isoniazid, rifampin + pyrazinamide
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  – HIV
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  – PK
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  – HIV
• Andy Vernon, Ken Castro
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