Treatment of TB Infection

Marcos Burgos, MD
May 12, 2015

TB for Community Providers
May 12, 2015
Phoenix, Arizona

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- No conflict of interests
- No relevant financial relationships with any commercial companies pertaining to this educational activity
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Marcos Burgos, M.D.
Medical Director Tuberculosis control Program, New Mexico Department of Health
Associate Professor University of New Mexico, Division of Infectious Diseases
President Elect National Society of Tuberculosis Clinicians

Objectives

• Discuss guidelines for treatment of TB infection in an adult patient
• Discuss guidelines for treatment of TB infection in pediatric patients.
• Short course regimen for LTBI
• Discuss the effect to treatment duration on completion rates
• Standard treatment lengths and problems with adherence
Latent TB Infection (LTBI)

LTBI is the presence of dormant or latent *M. tuberculosis* organisms (tubercle bacilli) without clinical symptoms or radiographic or bacteriologic evidence of TB disease

Case # 1

- 52 year old white male with uncontrolled DM, US born, homeless
- History of IVDU
- Exposed to an active TB case in a homeless shelter 2 months before
- Denies fever, chills, cough, weight loss
- TST = 8 mm
Case # 1, cont.

Questions
1. What are the patient risk factors for TB infection or disease?
2. What is the appropriate management for this patient?

Evaluation of Persons with TB Infection

Person has a positive test for TB infection
TB disease ruled out
Consider for LTBI treatment

Person accepts and is able to receive treatment of LTBI
Develop a plan of treatment with patient to ensure adherence

If person refuses or is unable to receive treatment for LTBI, educate patient about the signs and symptoms of TB disease
follow-up TST or IGRA and serial chest radiographs are unnecessary
Case # 1 cont.

• As a contact of an active TB case, 5 mm of induration is considered positive

Targeted TB Testing and Treatment of Latent TB Infection

• For more than 3 decades, treatment of latent TB infection (LTBI) has been an essential component of TB prevention and control in the United States

• An important goal of TB control is finding and treating persons with LTBI at high risk for developing active disease

• Targeted TB testing is used to focus on groups at the highest risk for developing TB disease

• Treatment of LTBI substantially reduces the risk that persons infected with *M. tuberculosis* will progress to TB disease.
Targeted TB Testing

- Essential TB prevention and control strategy
- Emphasizes detection of persons with LTBI who has the heights risk of developing active disease for treatment
- De-emphasizes testing of groups that are not at high risk for TB
- Can help reduce the waste of resources and prevent inappropriate treatment

History of Recommendations for LTBI Treatment in United States

- 1965: Treatment of LTBI 12 months of INH for tuberculin skin test (TST) converters, and young children
- 1967: Expanded to include all TST positive reactors ($\geq 10$ mm)
- 1977: Treatment recommended for persons $\leq 35$ years of age
- 1994: 6 - 12 months INH
- 1998: Two months of rifampin (RIF) plus pyrazinamide (PZA) for HIV-infected patients
- 2000: Four month regimen of RIF and 2-month regimen of RIF and PZA recommended as options. Latter not recommended
- 2000: 9 months of INH
- 2011: 12-doses (3 months) of isoniazid (INH) and rifapentine (RPT)
How much Isoniazid is needed for Prevention of Tuberculosis?

Isoniazid prophylaxis in Alaska

- 6 months of Preventive treatment does not give optimal protection
- More than 12 months no added protection
- Optimal Protection 9-10 months


Persons at High Risk for Developing TB Disease

- Those with increased likelihood of exposure to persons with TB disease
- Those with clinical conditions that increase their risk for progressing from LTBI to TB disease
Increased Risk of Exposure to Persons with TB Disease

- Close contacts to person with infectious TB
- Residents and employees of high-risk congregate settings
- Recent immigrants from TB-endemic regions of the world (within 5 years of arrival to the United States)

Increased Risk for Progression to TB Disease

- HIV-infected persons
- Those with a history of prior, untreated TB or fibrotic lesions on chest radiograph
- Children ≤ 5 years with a positive TST
- Those receiving TNF-α antagonists for treatment of rheumatoid arthritis or Crohn’s disease
- Underweight or malnourished persons
- Injection drug users

CDC. November 2011
Increased Risk for Progression to TB Disease: Medical Conditions

<table>
<thead>
<tr>
<th>Disease</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Silicosis</td>
<td>30</td>
</tr>
<tr>
<td>Jejunoilial bypass</td>
<td>27 - 63</td>
</tr>
<tr>
<td>Solid organ transplantation</td>
<td>37</td>
</tr>
<tr>
<td>Head or Neck Cancer</td>
<td>16</td>
</tr>
<tr>
<td>Renal failure</td>
<td>10 - 25</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>2 - 4</td>
</tr>
<tr>
<td>Gastrectomy</td>
<td>2 - 5</td>
</tr>
</tbody>
</table>

ATS-CDC. AJRCCM 2000; 161:S221-S247

Evaluation of Persons with TB Infection

Person has a positive test for TB infection

TB disease ruled out

Consider for LTBI treatment

Person accepts and is able to receive treatment of LTBI

Develop a plan of treatment with patient to ensure adherence

If person refuses or is unable to receive treatment for LTBI, educate patient about the signs and symptoms of TB disease

Follow-up TST or IGRA and serial chest radiographs are unnecessary
When Considering Initiating Treatment for TB Infection

- Rule out TB disease by history, physical examination, chest radiography and, when indicated, bacteriologic studies

- Determine prior history of treatment for LTBI or TB disease

- Assess risks and benefits of treatment

Case # 1, cont.

- No symptoms, normal CXR
- No prior history of TB treatment
- HIV negative
### Treatment Regimens for Latent TB Infection

<table>
<thead>
<tr>
<th>Drug(s)</th>
<th>Duration</th>
<th>Interval</th>
<th>Minimum Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td>9 months</td>
<td>Daily</td>
<td>270</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Twice weekly</td>
<td>76</td>
</tr>
<tr>
<td></td>
<td>6 months</td>
<td>Daily</td>
<td>180</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Twice weekly</td>
<td>52</td>
</tr>
<tr>
<td>Isoniazid &amp; Rifapentine</td>
<td>3 months</td>
<td>Once weekly</td>
<td>12</td>
</tr>
<tr>
<td>Rifampin</td>
<td>4 months</td>
<td>Daily</td>
<td>120</td>
</tr>
</tbody>
</table>

### Latent TB Infection Treatment: Isoniazid Based Regimens

- 9-month regimen of isoniazid (INH) is one of the preferred regimens
  - 6-month regimen is less effective but may be used if unable to complete 9 months
- May be given daily or intermittently (twice weekly)
- Use directly observed therapy (DOT) for intermittent regimen
- Preferred regimen for children 2-11 years of age*
## Latent TB Infection Treatment: Isoniazid Based Regimens

<table>
<thead>
<tr>
<th>Regimen Type</th>
<th>Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>INH daily for 9 months</td>
<td>270 doses within 12 months</td>
</tr>
<tr>
<td>INH twice/week for 9 months</td>
<td>76 doses within 12 months</td>
</tr>
<tr>
<td>INH daily for 6 months</td>
<td>180 doses within 9 months</td>
</tr>
<tr>
<td>INH twice/week for 6 months</td>
<td>52 doses within 9 months</td>
</tr>
</tbody>
</table>

## Latent TB Infection Treatment: Rifampin Based Regimens

- Rifampin (RIF) given daily for 4 months is an acceptable alternative when treatment with INH or 3HP is not feasible.
- In situations where RIF cannot be used (e.g., HIV-infected persons receiving protease inhibitors), rifabutin may be substituted.
- RIF daily for 4 months - 120 doses within 6 months
Three Months of Rifapentine and Isoniazid for Latent Tuberculosis Infection


3HP vs. 9 month INH

<table>
<thead>
<tr>
<th>Outcome</th>
<th>9H N=3,745</th>
<th>3HP N=3,986</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment completion</td>
<td>2,585 (69.0%)</td>
<td>3,362 (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>624 (18.0%)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Permanent drug d/c- due to an adverse event</td>
<td>135 (3.6%)</td>
<td>188 (4.7%)</td>
<td>0.004</td>
</tr>
<tr>
<td>Death</td>
<td>39 (1.0%)</td>
<td>31 (0.8%)</td>
<td>0.22</td>
</tr>
</tbody>
</table>

Cumulative TB Rate
33 months from enrollment—MITT

![Graph showing cumulative tuberculosis rate over time from enrollment]

Log-rank P-value: 0.06

Recommendations for Use of an Isoniazid-Rifapentine Regimen with Direct Observation to Treat Latent Mycobacterium tuberculosis Infection

Preventing tuberculosis (TB) by treating latent *Mycobacterium tuberculosis* infection (LTBI) is a cornerstone of the U.S. strategy for TB elimination (1,2). Three randomized controlled trials have shown that a new combination regimen of isoniazid (INH) and rifapentine (RPT) administered weekly for 12 weeks as directly observed therapy (DOT) is as effective for preventing TB as other regimens and is more likely to be completed than the U.S. standard regimen of 9 months of INH daily without DOT (2–5). This report provides CDC recommendations for using the INH-RPT regimen. The new regimen is recommended as an equal alternative to the 9-month INH regimen for otherwise healthy patients aged ≥12 years who have LTBI and factors that are predictive of TB developing (e.g., recent exposure to contagious TB). The new regimen also can be considered for other categories of patients when it offers practical advantages. Although the INH-RPT regimen was well tolerated in treatment trials, monitoring for adverse effects is recommended. Severe adverse effects should be reported to the Food and Drug Administration (FDA) and CDC.

**Background**

Its long plasma half-life enables infrequent dosing, which can increase DOT convenience and thus adherence. Most RIF-resistant isolates also are resistant to RPT.

**Methods**

In April 2011, CDC convened a panel of 23 consultants, each of whom had demonstrated TB-specific expertise in at least one of the following: diagnosis, treatment, prevention, nursing case management, public health programs, surveillance, epidemiology, clinical research, pulmonology, infectious diseases, pediatrics, mycobacteriology, health communication and education, migrant worker health, patient advocacy, and health economics. The panel reviewed findings from all three INH-RPT clinical trials that had been completed (3–5), interviewed the investigators in charge of the largest trial (5), and summarized the discussions of all evidence and opinions. Each recommendation for use of INH-RPT was listed according to the quality of the evidence. High quality evidence came from randomized clinical trials that included the patient categories for which the recommendation was made. The three clinical trials of the INH-RPT regimen were limited by...
Latent TB Infection Treatment: Isoniazid & Rifapentine Based Regimens

- 3-month regimen of INH and RPT is an option equal to 9-month INH regimen for treating LTBI in certain groups, such as otherwise healthy people, 12 years of age and older, who were recently in contact with infectious TB or who had tuberculin skin test conversions or positive blood test for TB
- Must use directly observed therapy (DOT)
- Completion of therapy is based on the total number of doses administered, not on duration alone

*MMWR. Recommendations for Use of an Isoniazid-Rifapentine Regimen with Direct Observation to Treat Latent Mycobacterium tuberculosis Infection
http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6048a3.htm?s_cid=mm6048a3_w

Latent TB Infection Treatment: Isoniazid & Rifapentine Based Regimens

- Not recommended for children younger than 12 years of age, HIV-infected people taking antiretroviral therapy, pregnant women, or women expecting to be pregnant within the 12-week regimen
- INH and RPT once a week for 3 months - 12 doses within 4 months
Completion of Therapy

Completion of therapy is based on the total number of doses administered, not on duration alone.

Summary of CDC Recommendations

• 3HP equal alternative to 9H
  – Contacts
  – Recent converters
  – Old healed TB
• Adults and children > 12 years of age
• HIV if healthy and not on ARVs
• Should not be used in pregnant women
• Should be given by DOT
Case # 1, cont.

- Normal CXR,
- No prior history of TB treatment
- HIV negative
- Patient started on INH for LTBI
- Lost to follow up after the second month of treatment

Latent TB Infection Treatment: HIV-Infected Persons

- Consult an expert in managing HIV and TB
- INH daily for 9-mo, rather than 6-mo, is optimal: 270 doses within 12 months
- Rifampin is generally contraindicated for persons taking protease inhibitors or delavirdine
- Rifabutin with dose adjustments can sometimes be substituted for Rifampin
- INH/RPT regimen not recommended for HIV-infected people taking antiretroviral therapy
3HP treatment for latent TB in HIV individuals

• HIV is the strongest risk factor for progressing from latent *M. tuberculosis* infection to active tuberculosis

• 9 months of daily INH is efficacious, but has low completion rates, limiting its effectiveness
  – Most common adverse effect: hepatotoxicity

3HP for latent TB among individuals with HIV

• 3 months of once-weekly rifapentine 900 mg + INH 900 mg under direct observation (3HP) (PREVENT TB study)
  – Higher treatment completion rate than 9H

• Only 3% of study participants were HIV+
  – Enrollment of HIV+ persons was extended to adequately assess tolerability in this population

Tolerability 3HP among HIV infected individuals

<table>
<thead>
<tr>
<th>Outcome</th>
<th>9H N=193</th>
<th>3HP N=201</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment completion</td>
<td>125(65%)</td>
<td>178(89%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Permanent drug d/c-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any reason</td>
<td>68(35%)</td>
<td>23(11%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Permanent drug d/c-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Due to an adverse event</td>
<td>8(4%)</td>
<td>7(4%)</td>
<td>0.8</td>
</tr>
<tr>
<td>Death</td>
<td>4(2%)</td>
<td>2(1%)</td>
<td>0.44</td>
</tr>
</tbody>
</table>

T Sterling, 19th International AIDS Conference
Abstract no. MOAB0302

3HP treatment for Latent TB for HIV individuals

- Among HIV-infected persons with high CD4 counts and not on antiretroviral therapy, 3HP had higher treatment completion rates and was better tolerated than 9H for treatment of latent *M. tuberculosis* infection
- 9H was less well-tolerated in HIV-infected than non HIV infected individuals
- 3HP was at least as well-tolerated in HIV-infected than HIV-uninfected persons

T Sterling, 19th International AIDS Conference
Abstract no. MOAB0302
Limitations

• Sample size relatively small
  – Though sufficient for tolerability assessment
• Patients could not receive antiretroviral therapy for first 90 days after enrollment
  – Drug interactions with rifapentine not well-characterized
  – Limited the number of eligible participants

T Sterling, 2014; 19th International AIDS Conference Abstract no. MOAB0302

Latent TB in Children

• Most children with LTBI have been infected recently
• Children and adolescents are at higher risk for progression to TB disease
• Why treat with INH children < 5 years of age exposed to TB?
  – Very high rate of development of active disease
  – Takes up to 3 months for skin test to turn positive
  – 10 - 20% of TB disease can be prevented
Preventive treatment recommended after exposure:

Household contact to a known infectious person:

- Children less than 5 years of age
- Immunosuppressed patients
- Patients on tumor necrosis factor-alpha blockers
- May prevent progression to disease during window period
- May stop INH if 2nd TST is negative < 5mm in immunocompetent patients

TB Prevention Treatment

- Isoniazid main stay of therapy
  - 10 – 15 mg/kg daily dose if given by family
  - 20 – 30 mg/kg twice weekly if given by DOH
  - Duration 9 months

- Alternative: rifampin for 6 months
  - If person around child with TB is known to have INH resistant disease or if child is INH-intolerant
3HP in children

• A study among 1058 children ages 2 to 17 years demonstrated that directly observed treatment with 3HP was as effective as nine months of INH alone for prevention of tuberculosis

• Treatment related adverse events were uncommon and similar with the two regimens

• Directly observed treatment with INH-RPT is a reasonable regimen for children aged 2 to 17 years when the circumstances make completion of nine months of daily INH difficult

• Last CDC guidelines 2011, 3HP is only approved for children 12 years or older

Villarino ME, JAMA Pediatr 2015; 169:247

Considerations for Treating LTBI in Children

• Use INH suspension only in children <5 KG
• Compliance with INH is low, consider shorter regimens
• Use DOPT for recent contacts, infants, immune compromised
• When not tolerating treatment the problem is usually the parents
• Routine LFTs not necessary
Latent TB Infection Treatment: Fibrotic Lesions

- Fibrotic Lesions Suggesting Previous TB Should be treated for LTBI if they have
  - A positive TST reaction (at least 5 mm) or IGRA result
  - No symptoms of infectious TB disease
  - No history of treatment for TB disease
- Treat only after active disease excluded with sputum testing
- Acceptable regimens include
  - 9 months of INH
  - 4 months of RIF (with or without INH)
  - 3 months of INH and RPT (12-dose regimen)

Management of Patient Who Missed Doses

- Extend or re-start treatment if interruptions were frequent or prolonged enough to preclude completion
- When treatment has been interrupted for more than 2 months, patient should be examined to rule out TB disease
- Recommend and arrange for DOT as needed
Clinical Monitoring: for adverse drug reactions

Instruct patient to report:
- Fever
- Headache
- Rash
- Anorexia, nausea, vomiting, or abdominal pain in right upper quadrant
- Fatigue or weakness
- Dark urine
- Persistent numbness in hands or feet

Clinical Monitoring: Follow up visits

Monthly review of symptoms:
- Rationale for treatment
- Adherence with therapy
- Symptoms of adverse drug reactions
- Plans to continue treatment
Hepatitis due to Isoniazid:

- Incidence of hepatitis in persons taking INH is as low as 0.1%
- Hepatitis risk increases with age
  - Uncommon in persons < 20 years old
  - Nearly 2% in persons 50 to 64 years old
- Risk increases with underlying liver disease or heavy alcohol consumption

Hepatitis due to Isoniazid:

- Asymptomatic elevation of hepatic enzymes seen in 10%-20% of people taking INH
  - Levels usually return to normal after completion of therapy
- Discontinue treatment if transaminase level exceeds 3 times the upper limit of normal if patient has symptoms of hepatotoxicity, and 5 times the upper limit of normal if patient is asymptomatic
Rates of Hepatotoxicity in the 3HP Trial

<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>


Severe Isoniazid Liver Injuries among Individuals Treated for LTBI, U.S., 2004-2008

“Medical Providers should emphasized to patients that INH treatment should be stopped immediately upon the earliest onset of symptoms (e.g. excess fatigue, nausea, vomiting, abdominal pain, or jaundice), even before clinical evaluation is conducted and that initial symptoms might be subtle and might not include jaundice”

MMWR 2010; 59(08); 224-229
Laboratory Monitoring:

Baseline labs are not necessary except for individuals with:
- HIV infection
- History of liver disease
- Regular alcohol use
- Pregnancy or in early postpartum period

Laboratory Monitoring:

Repeat laboratory monitoring if patient has:
- Abnormal baseline results
- Current or recent pregnancy
- High risk for adverse reactions
- Symptoms of adverse reaction
- Liver enlargement or tenderness during examination
Systemic Drug Reactions (SDR) with Rifapentine plus Isoniazid for Treatment of Latent Tuberculosis Infection

- SDR and Flu-like syndrome have been reported with weekly rifapentine plus isoniazid for 3 months (3HP)
- Among 7,552 persons 138/3,893 (3.5%) had a SDR with 3HP vs. 15/3,659 (0.4%) with 9H (P<0.001)
- Of those with SDR in the 3HP arm, 87(63%) had flu-like syndrome and 23(17%) had cutaneous reactions and 13/3,893 (0.3%) had severe reactions
- Severe SDR were associated with white race/ethnicity and receipt of concomitant non-study medications.
- 3HP associated reactions were rare and the underlying mechanism is unclear.


Case # 1 cont.

- A year later patient admitted with pneumonia to a community hospital
- He was treated for CAP and discharge to homeless shelter
- 2 months later homeless clinic send patient to us for evaluation because of persistent cough
Case # 1 cont.

- CXR demonstrated right upper lobe cavity
- HbA1C 14, HIV neg
- Sputum's smear positive 2+, NAAT test positive for MTB complex
- Patient started on 4 drugs
- Drug susceptibility report susceptible to all 4 drugs

Case # 1, cont.

- The patient management was individualized to incorporate measures that facilitate his adherence to treatment with a patient-centered approach
  - DOT
  - social service support
  - treatment incentives and enablers,
  - housing assistance
  - referral for treatment of substance abuse,
  - comanagement of comorbidities with PCP
The clinical reality of TB Screening & treatment cascade among, HIV positive, New York City

Completed LTBI—41%

The clinical reality of TB screening & treatment cascade among HIV positive, Spain

Completed LTBI—57%
The clinical reality of TB screening & treatment cascade among contacts of AFB smear + cases

Completed LTBI treatment 53%

Int J Tuberc Lung Dis. 2014: 18(4)

The clinical Reality of LTBI Screening Cascade of Care for Contacts of Known Infectious TB Cases

Completed LTBI treatment 49%

US TB Contact Investigations: AFB+, 2010 ARPE

Slide provided by Dr. Randall Reves
The clinical reality of TB screening cascade in the community

- Missing data:
  - Who are the individuals at risk in the community?
  - Who is getting LTBI testing?
  - Of those that are tested, who is positive (LTBI not a reportable condition)
  - How many of those positive for LTBI are referred for evaluation
  - How many are referred for treatment?
  - How many complete treatment
  - Of those not treated, how many developed active TB?

Risk factors for treatment default in close contacts with LTBI

- LTBI treatment regimens completion rates

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Completed Treatment (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>INH alone 9 months</td>
<td>57</td>
</tr>
<tr>
<td>4 months Rifampin</td>
<td>71</td>
</tr>
<tr>
<td>3 months INH = RIF</td>
<td>74</td>
</tr>
</tbody>
</table>

- Reasons for not completing treatment

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lost to follow up</td>
<td>46</td>
</tr>
<tr>
<td>Non-adherence</td>
<td>25</td>
</tr>
<tr>
<td>Refused treatment</td>
<td>8</td>
</tr>
<tr>
<td>Side effects</td>
<td>4</td>
</tr>
</tbody>
</table>

Int J Tuberc Lung Dis. 2014: 18(4)
Patient-centered care for LTBI

- If we are to improve LTBI completion rates we need patient-centered care management strategy to maximize the likelihood of completion of therapy
- Each patient's management plan should be individualized to incorporate measures that facilitate adherence to treatment
  - social service support,
  - treatment incentives and enablers,
  - housing assistance
  - referral for treatment of substance abuse,
  - comanagement of comorbidities with other providers

Three Months of Rifapentine and Isoniazid for Latent Tuberculosis Infection

Preliminary Comparison Between TBTC Prevent TB Study and Post-marketing Project for Treatment Discontinuation Rates by Reason, 17 Sites

<table>
<thead>
<tr>
<th></th>
<th>PreventTB, Study26 (MITT)</th>
<th>%</th>
<th>Post-marketing Project</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatotoxicity*</td>
<td>18/4040</td>
<td>0.4</td>
<td>10/2134</td>
<td>0.5</td>
</tr>
<tr>
<td>Hospitalizations</td>
<td>56/3986</td>
<td>1.4</td>
<td>17/2134</td>
<td>0.8</td>
</tr>
<tr>
<td>Death</td>
<td>4/3986</td>
<td>0.1</td>
<td>0/2134</td>
<td>0</td>
</tr>
<tr>
<td>CompletionRate</td>
<td>82.1</td>
<td></td>
<td>1745/2061</td>
<td>84.7</td>
</tr>
</tbody>
</table>

Presented 18th Annual Conference of the Union-NAR, Boston, MA. March 1, 2014

LTBI treatment 3HP Vs. 9 months INH

- Patients treated for LTBI with 9 months of INH are significantly less likely to complete treatment
- 3HP studies demonstrate high completions rates, even in difficult populations
- Initial field experience with 3HP is similar to treatment trial experiences
- 12-dose INH-RPT is being adopted in the U.S.
3HP a new tool to increase LTBI treatment completion rates?

- It is thought that the completion rates of 3HP versus 9 months of INH are significantly better because 3HP is given for only 3 months
- Another important component is the use of DOT, the most important component of a patient-centered approach for the treatment of TB
- Could we get the same results on 3HP without DOT?
- Results of iAdhere in the next 6 months (Study 33 - directly observed vs. self administered 3HP)

Summary:

- For every patient:
  - Assess TB risk factors
  - If risk is present, perform TST or IGRA
  - If TST or IGRA is positive, rule out TB disease
  - If TB disease is ruled out, consider treatment for LTBI
  - Consider a regimen that will help the patient ensure completion
Additional Resources

- Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection *MMWR* 2000; 49 (No. RR-6)  
  [http://www.cdc.gov/mmwr/preview/mmwrhtml/rr4906a1.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/rr4906a1.htm)

- Recommendations for Use of an Isoniazid–Rifapentine Regimen with Direct Observation to Treat Latent *Mycobacterium tuberculosis* Infection  
  [http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6048a3.htm?s_cid=mm6048a3_w](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6048a3.htm?s_cid=mm6048a3_w)

- CDC TB Website - [http://www.cdc.gov/tb](http://www.cdc.gov/tb)

- Latent Tuberculosis Infection: A Guide for Primary Health Care Providers  

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Additional Resources

- CDC’s Morbidity and Mortality Weekly Report  

- American Thoracic Society  
  [http://www.thoracic.org/statements/](http://www.thoracic.org/statements/)