Programmatic Experience with the 12 Dose Isoniazid/Rifapentine in the US: The Post-marketing Project

Christine S. Ho, M.D., M.P.H.
18th Annual Conference of the Union-NAR
Boston, MA
March 1, 2014
Newest Treatment Choice for Latent Tuberculosis Infection (LTBI)

- 12 weekly doses of isoniazid and rifapentine (INH-RPT)
  - up to 900 mg Isoniazid
  - up to 900 mg Rifapentine
  - Directly Observed Therapy (DOT) only
  - Known as 3HP, INH-RPT or the 12-dose regimen

- 3 clinical trials
  - Effectiveness equal to 9 months of isoniazid (9H)
  - Higher treatment completion
  - Lower rates of hepatotoxicity
  - Prevent TB study reported some possible drug hypersensitivity reactions

- Potential to improve adherence
  - 47% of patients who start LTBI treatment (mostly 9H) do not complete
CDC Recommendations: 12-dose regimen, Dec 2011

- 12 weekly DOT doses of INH-RPT an equal alternative to 9 months of daily self-supervised INH for treating LTBI

- Use in otherwise healthy patients aged ≥12 years with a greater risk of developing TB
  - Recent contacts
  - Convertors from negative to positive on an indirect TB test
  - Those with radiographic findings of healed TB
  - HIV-infected patients who are otherwise healthy and not taking anti-retroviral medications
  - Patients unlikely to complete 9H
  - For children aged 2-11 INH-RPT can be considered on a case-by-case basis

- Vigilance for drug hypersensitivity reactions, particularly hypotension or thrombocytopenia

MMWR Dec 9, 2011
Post-marketing Project Objectives

- **Monitor patients taking the 12-dose regimen in programmatic settings**
  - Track number of patients started on regimen
  - Monitor adverse events (AE)
  - Note if certain populations, risk factors or settings are associated with AE more often

- **Assess adherence and treatment completion**

- **Assess impact of the 12-dose regimen on programs**
  - Staffing
  - Costs

- **Conduct passive surveillance for TB after 2 years**
  - TB registry match
  - Drug-resistant TB
22 volunteer sites participated in study design

13 sites contributed data

Patients treated from July 2011 – October 2013

DOT used for all sites
Participating Sites Represented Different Types of Programs

- **State TB programs**
  - Entire state - centralized programs
  - Select counties – decentralized programs
- **County programs**
- **Community providers** partnered with health department (HD)
- **Mandatory LTBI reporting** in some sites
- **Rifapentine**
  - Some programs controlled access to RPT (authorization required)
  - Some programs paid for RPT
  - Some programs ordered and provided RPT
Target Populations Differ By Sites

- Some programs offered 12-dose regimen to all latent TB infection (LTBI) patients.
- Some programs offered 12-dose regimen to select patients:
  - Contacts
  - HCW
  - Convertors
  - Class B immigrants
  - Refugees
  - Homeless
  - Immunosuppressed
  - Foreign-born university students
  - Children > 12 years old
  - Correctional facilities workers and inmates
Project Design

- **Core information collected by all sites**
  - Number of treatment starts
  - Symptom occurrence and frequency
  - Reason for LTBI treatment
  - Treatment outcome

- **Additional information about patient characteristics collected by some sites**
  - Medical history
  - Social risk factors
  - Medications
  - Laboratory results
Forms for Doses, Symptoms, and Outcomes

Final Disposition:

☐ Completed INH-RPT treatment
☐ Stopped INH-RPT treatment
☐ Lost to follow-up
☐ Died
☐ Other
☐ Adverse event
☐ Pending Completion of Alternate Regimen

Date: 

09/03/12
09/03/12
09/10/12
09/17/12

Baseline

Directly Observed Therapy (DOT) received

☐ No adverse reaction
☐ Loss of appetite
☐ Nausea or vomiting
☐ Yellow eyes or skin
☐ Diarrhea
☐ Rash/hives
☐ Fever or chills
☐ Sore muscles or joints
☐ Numbness or tingling
☐ Fatigue
☐ Dizziness/fainting
☐ Abdominal pain
☐ Treatment stopped or held (complete AE report on next page)

☐ Other

Date: ___/___/___
## Form for Adverse Events

### FILL OUT ONLY FOR ADVERSE EVENTS:

<table>
<thead>
<tr>
<th>Symptom Related DOSE #</th>
<th>Rx Stepped or Held</th>
<th>Date Symptom Began</th>
<th>Symptom Onset after Dose</th>
<th>Symptom Duration</th>
<th>Hospital Admission</th>
<th>Medication Re-challenge</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>□ Yes</td>
<td>09/17/12</td>
<td>□ &lt; 2 hrs</td>
<td>□ &lt; 1 day _______ hrs</td>
<td>□ Yes</td>
<td>□ INH re-challenged</td>
<td>□ Continue INH/RPT</td>
</tr>
<tr>
<td></td>
<td>□ No</td>
<td></td>
<td>□ 2 - 48hrs</td>
<td>□ &gt; 1 day _______ days</td>
<td>□ No</td>
<td>□ RPT re-challenged</td>
<td>□ Switch to INH for 6 or 9 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>□ &gt; 48hrs</td>
<td>□ Unknown</td>
<td>□ Unknown</td>
<td>□ Stopped any LTBI treatment</td>
<td>□ Unknown</td>
</tr>
<tr>
<td></td>
<td>□ Yes</td>
<td></td>
<td>□ &lt; 2 hrs</td>
<td>□ &lt; 1 day _______ hrs</td>
<td>□ Yes</td>
<td>□ INH re-challenged</td>
<td>□ Continue INH/RPT</td>
</tr>
<tr>
<td></td>
<td>□ No</td>
<td></td>
<td>□ 2 - 48hrs</td>
<td>□ &gt; 1 day _______ days</td>
<td>□ No</td>
<td>□ RPT re-challenged</td>
<td>□ Switch to RIF for 4 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>□ &gt; 48hrs</td>
<td>□ Unknown</td>
<td>□ Unknown</td>
<td>□ Stopped any LTBI Treatment</td>
<td>□ Unknown</td>
</tr>
</tbody>
</table>

Comment: Please (briefly) describe the adverse event, including symptoms, time of onset in relation to last INH-RPT dose, duration and resolution and any other factors (other medical conditions, medications). Enter comments in text box below:

Patient 01 called 9:30AM on Tuesday, September 18th 2012 complaining of diarrhea. Symptom started at approximately 9:00PM on Monday Sept 17th 2012 (12 hours after last INH-RPT dose).
Preliminary Results from 13 sites: July 2011 – October 2013
### Patient Demographics Profile

**Post-Marketing Project, 13 sites (N=2134)**

**July 2011 – October 2013**

<table>
<thead>
<tr>
<th>Patients</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>1155</td>
<td>54</td>
</tr>
<tr>
<td>Female</td>
<td>964</td>
<td>45</td>
</tr>
<tr>
<td>Missing Gender</td>
<td>15</td>
<td>0.7</td>
</tr>
<tr>
<td>Hispanic</td>
<td>397</td>
<td>19</td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>1648</td>
<td>77</td>
</tr>
<tr>
<td>Missing Ethnicity</td>
<td>89</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Race*</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>768</td>
<td>36</td>
</tr>
<tr>
<td>American Indian/Alaska Native</td>
<td>17</td>
<td>0.8</td>
</tr>
<tr>
<td>Asian</td>
<td>325</td>
<td>15</td>
</tr>
<tr>
<td>Black or African American</td>
<td>835</td>
<td>39</td>
</tr>
<tr>
<td>Native Hawaiian or Pacific Islander</td>
<td>32</td>
<td>2</td>
</tr>
<tr>
<td>Other</td>
<td>28</td>
<td>1</td>
</tr>
<tr>
<td>Unknown</td>
<td>80</td>
<td>4</td>
</tr>
<tr>
<td>Missing</td>
<td>49</td>
<td>2</td>
</tr>
</tbody>
</table>

*Includes Hispanic and non-Hispanic

As of 10/2013
Preliminary Data: July 2011 – October 2013, 13 Sites

2134 persons started on 12-dose regimen

23 treatment stopped:
20 Index-case resistant
2 QFT negative
1 Active TB

50 still on treatment

2061 eligible to complete treatment

1745 (85%) completed

179 (57%) discontinued with symptoms

316 (15%) discontinued

137 (43%) discontinued without symptoms

As of 10/2013
As of 10/2013
## Range of Treatment Outcomes Across Sites

<table>
<thead>
<tr>
<th>Site</th>
<th>Eligible to complete</th>
<th>Completed</th>
<th>Discontinued Total</th>
<th>Discontinued with symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range</td>
<td>18-726</td>
<td>15-606</td>
<td>1-120</td>
<td>0-80</td>
</tr>
<tr>
<td>%</td>
<td>79%-98%</td>
<td>2%-21%</td>
<td>0%-16%</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>158.5</td>
<td>134</td>
<td>11</td>
<td>14</td>
</tr>
<tr>
<td>%</td>
<td>86%</td>
<td>14%</td>
<td>7%</td>
<td></td>
</tr>
</tbody>
</table>
### Patient Completion Rates by Reasons for Treatment *

<table>
<thead>
<tr>
<th>Reason for Treatment</th>
<th>Eligible to complete</th>
<th>Completed (%)</th>
<th>Discontinued without symptoms (%)</th>
<th>Discontinued with symptoms (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Converter</td>
<td>595</td>
<td>485 (82)</td>
<td>29 (5)</td>
<td>81 (14)</td>
</tr>
<tr>
<td>Foreign-born</td>
<td>576</td>
<td>512 (89)</td>
<td>31 (5)</td>
<td>33 (6)</td>
</tr>
<tr>
<td>Contact</td>
<td>518</td>
<td>472 (91)</td>
<td>18 (4)</td>
<td>28 (5)</td>
</tr>
<tr>
<td>Correctional facility resident</td>
<td>186</td>
<td>145 (78)</td>
<td>31 (17)</td>
<td>10 (5)</td>
</tr>
<tr>
<td>Homeless</td>
<td>126</td>
<td>107 (85)</td>
<td>13 (10)</td>
<td>6 (5)</td>
</tr>
<tr>
<td>Refugee</td>
<td>74</td>
<td>59 (80)</td>
<td>2 (3)</td>
<td>13 (18)</td>
</tr>
<tr>
<td>Other</td>
<td>192</td>
<td>148 (77)</td>
<td>23 (12)</td>
<td>21 (11)</td>
</tr>
</tbody>
</table>

As of 10/2013  
*Patients could have had multiple reasons for treatment
### Homeless Contacts Receiving 12-Dose INH-RPT for LTBI Treatment, Two Post-marketing Project Sites

<table>
<thead>
<tr>
<th>Mississippi</th>
<th>Kane County, IL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All LTBI patients offered 12-dose regimen</strong></td>
<td>Carefully selected patients offered 12-dose regimen</td>
</tr>
<tr>
<td>▪ 76 homeless contacts</td>
<td>▪ 47 homeless contacts</td>
</tr>
<tr>
<td>▪ 1 still on treatment</td>
<td>▪ 46/47 (98%) completed</td>
</tr>
<tr>
<td>▪ 60/75 (80%) completed</td>
<td>▪ 1/47 (2%) discontinued with symptoms</td>
</tr>
<tr>
<td>▪ 15/75 (20%) discontinued , total</td>
<td>▪ 15/75 (20%) discontinued</td>
</tr>
<tr>
<td>▪ 3/75 (4%) discontinued with symptoms</td>
<td>▪ 3/75 (4%) discontinued with symptoms</td>
</tr>
</tbody>
</table>

As of 10/2013
Foreign-born Students Receiving 12-Dose INH-RPT for LTBI Treatment, Four Post-marketing Project Sites

<table>
<thead>
<tr>
<th>Site</th>
<th>Started</th>
<th>Eligible to complete</th>
<th>Completed</th>
<th>Discontinued, total</th>
<th>Discontinued with symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kansas</td>
<td>70</td>
<td>70</td>
<td>63 (90)</td>
<td>7 (10)</td>
<td>43 (4)</td>
</tr>
<tr>
<td>Minnesota</td>
<td>14</td>
<td>12</td>
<td>11 (92)</td>
<td>1 (8)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>San Diego</td>
<td>28</td>
<td>28</td>
<td>26 (93)</td>
<td>2 (7)</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Arkansas</td>
<td>53</td>
<td>46</td>
<td>45 (98)</td>
<td>1 (2)</td>
<td>1 (2)</td>
</tr>
</tbody>
</table>

As of 10/2013
Santa Clara CA Correctional Facility

- 68 inmates started
- 13 still on treatment (55 eligible to complete treatment)
- 44/55 (80%) completion rate
- 11 (20%) discontinued, total
- 1/55 (2%) discontinued with symptoms

As of 10/2013
## Number and Percentage of Patients That Started Treatment Reporting Symptoms at Least Once (N= 2134)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Reported</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any symptom</td>
<td>730</td>
<td>34</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>306</td>
<td>14</td>
</tr>
<tr>
<td>Fatigue</td>
<td>193</td>
<td>9</td>
</tr>
<tr>
<td>Sore muscles/joints</td>
<td>148</td>
<td>7</td>
</tr>
<tr>
<td>Fever/Chills</td>
<td>126</td>
<td>6</td>
</tr>
<tr>
<td>Rash/hives</td>
<td>108</td>
<td>5</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>107</td>
<td>5</td>
</tr>
<tr>
<td>Dizziness/fainting</td>
<td>102</td>
<td>5</td>
</tr>
<tr>
<td>Loss of Appetite</td>
<td>90</td>
<td>4</td>
</tr>
<tr>
<td>Numbness/tingling</td>
<td>90</td>
<td>4</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>82</td>
<td>4</td>
</tr>
<tr>
<td>Yellow eyes/skin</td>
<td>16</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>350</td>
<td>16</td>
</tr>
</tbody>
</table>

As of 10/2013  
*patients can have more than one symptom*
Number of patients that started treatment reporting symptoms at least once and treatment outcome (n=730)

179/730 (24.5%) patients with symptoms discontinued

As of 10/2013

*patients can have more than one symptom
Among 350 patients reporting “Other” reasons for stopping or interrupting treatment *

- 33 instances of headache
- 31 instances of elevation in liver transaminase levels per program
- 8 instances of cold
- 8 instances of hypotension
- 7 instances of itching
- 7 instances of angioedema
- 7 instances of shortness of breath
- 6 instances of blurred Vision

The following reasons were reported in ≤5 events:

- Chest pain
- Weight loss
- Weight gain
- Hallucinations
- Urinary tract infection
- Cough
- Bruising
- Difficulty speaking
- Menstrual irregularities
- Pregnancy
- Confusion
- Methadone withdrawal
- Red dots on chin
- Black stool
- Bumps on lips
- Hot Flashes
- Sweating/diaphoresis
- Swollen lymph nodes
- Body aches
- Tachycardia
- URI
- Flushing

As of 10/2013

*patients can have more than one reason
Number of Patients Who Had Treatment Discontinued By Program Because of Elevated Transaminase Levels, 13 Sites (N=28)

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Missing</th>
<th>ALT &lt;3xULN*</th>
<th>ALT ≥3, &lt;5xULN</th>
<th>ALT ≥5xULN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>15</td>
<td>0</td>
<td>8†</td>
<td>3†</td>
<td>4</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>13</td>
<td>2</td>
<td>5</td>
<td>2</td>
<td>4†</td>
</tr>
</tbody>
</table>

Hepatotoxicity defined as ALT 3xULN for symptomatic persons and 5xULN for asymptomatic persons = 10 cases of hepatotoxicity

*Upper limits of normal (ULN)
†one patient with underlying HCV

As of 10/13
### Adverse Events: Patients with Low Blood Pressure Without Fever

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age</th>
<th>M/F, Race</th>
<th>PMH</th>
<th>Medications</th>
<th>BP</th>
<th>Event and Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>23</td>
<td>WF</td>
<td>Obesity, migraine headache</td>
<td>Eletryptan, nadalol</td>
<td>71/46</td>
<td>Hypotensive with bradycardia while exercising due to nadalol</td>
</tr>
<tr>
<td>2</td>
<td>71</td>
<td>WM</td>
<td>HTN, gout</td>
<td>Rolpinarole, HCTZ, lisinopril, allopurinol</td>
<td>SBP 70’s</td>
<td>Hospitalized for fever, chills, hypotension, tachycardia, rash, hives, URI after 3&lt;sup&gt;rd&lt;/sup&gt; dose; recurred after 4&lt;sup&gt;th&lt;/sup&gt; dose</td>
</tr>
</tbody>
</table>
### Adverse Events: Patients with Low Blood Pressure Without Fever (2)

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age</th>
<th>M/F, Race</th>
<th>PMH</th>
<th>Medications</th>
<th>BP</th>
<th>Event and Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>77</td>
<td>WF</td>
<td>Hypothyroidism, arthritis, gout, depression</td>
<td>Trazadone, Pravastatin, Aspirin, Zanaflex, Meloxicam, Levoxyl, Metoclopramide, Tramadol, Omeprazole</td>
<td>70/40</td>
<td>Dizziness, fainting and low BP after 4th dose, similar previous episodes before LTBI treatment</td>
</tr>
<tr>
<td>4</td>
<td>87</td>
<td>HM</td>
<td>DM, HTN, atrial fibrillation, gout, hyperlipidemia</td>
<td>Albuterol, Allopurinol, Lisinopril, HCTZ, Budesonide, Metformin, Coumadin</td>
<td>91/60</td>
<td>N/V, fatigue, low BP after 6th dose, went to ER, not hospitalized. Meds stopped but low BP persisted, HTN meds changed</td>
</tr>
</tbody>
</table>
## Adverse Events: Patients with Low Blood Pressure With Fever

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age</th>
<th>M/F, Race</th>
<th>PMH</th>
<th>Medications</th>
<th>BP</th>
<th>Event and Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>26</td>
<td>WM</td>
<td>None</td>
<td>None</td>
<td>80/35</td>
<td>Fever without source; responded to intravenous fluids (IVF)</td>
</tr>
<tr>
<td>6</td>
<td>42</td>
<td>WF</td>
<td>Depression, Irritable bowel syndrome, seasonal allergies</td>
<td>Polycarbophil, mometasone nasal spray, citalopram</td>
<td>85/61</td>
<td>Fever without source; No pulmonary embolism by CT angiography; Responded to IVF</td>
</tr>
</tbody>
</table>
**Adverse Events: Patients with Low Blood Pressure With Fever (2)**

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age</th>
<th>M/F, Race</th>
<th>PMH</th>
<th>Medications</th>
<th>BP</th>
<th>Event and Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>58</td>
<td>WM</td>
<td>s/p PTCA for MI, HTN</td>
<td>Ezetimibe/simvastatin, ramipril, ASA</td>
<td>95/59</td>
<td>Fever without source; HTN meds held; responded to IVF</td>
</tr>
<tr>
<td>8</td>
<td>62</td>
<td>BF</td>
<td>DM, HTN</td>
<td>Aspirin, metformin, irbesartan, HCTZ, pravastatin, esomeprazole</td>
<td>100/60 79/44 (with LP)</td>
<td>Fever without source; HTN meds held; responded to IVF</td>
</tr>
</tbody>
</table>
Severe Adverse Events

- Severe AE: any patient who was hospitalized or died while on LTBI therapy (NSSAE definition)
- 17 reports of hospitalizations
  - 6 on-site CDC investigations complete
  - 10 investigations in progress
  - 1 has not been initiated
  - No deaths
  - No serious or permanent medical sequelae
- Coordination with NSSAE project under Krista Powell and Lilia Manangan
## 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>Prevent TB, Study 26</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>Completion Rate</td>
<td>82.1</td>
<td></td>
<td>1745/2061</td>
<td>84.7</td>
</tr>
</tbody>
</table>

Discontinuation rates from Prevent TB Study 26 and Post-marketing Project are not directly comparable due to differences in definition.

*Defined as ALT 3xULN for symptomatic persons and 5xULN for asymptomatic persons

As of 10/2013
Strengths and Limitations

- **Strengths**
  - Diverse types of programs and target populations participated in the project, findings are representative of many settings
  - All patients reporting any symptoms while discontinuing treatment were counted, probably overestimating the rate of AE due to the 12-dose regimen

- **Limitations**
  - Sites had different protocols for eliciting symptoms from patients at weekly doses
  - Symptoms were recorded exactly as patients reported them; we did not define subjective terms such as dizziness/fainting etc.
Conclusions

- The 12-dose post-marketing project experience is similar to treatment trial experiences.
- The overall completion rate is 85% and consistent across sites. Completion rates remain high in difficult to treat populations.
- No deaths (or severe organ damage detected).
Conclusions (2)

- Nausea was the most commonly reported symptom and reason for stopping
- Most patients (>75%) that reported symptoms completed treatment
- In patients with hypotension
  - Co-morbidities and concomitant medication were present in 4 patients without fever
  - Hypotension quickly resolved with intravenous fluids in 4 patients with fever
- States are encouraged to report SAEs to CDC (e-mail: LTBIdrugevents@cdc.gov)
Next Steps

- Identify demographic and medical risk factors associated with treatment completion and discontinuation
- Analyze demographic and medical risk factors associated with symptoms
- Review concomitant medications and association with symptoms

**CDC work in progress**

- iAdhere (Study 33 - directly observed vs. self administered therapy)
- Prevent TB Study Study 26 manuscripts (pediatric, HIV, systemic drug reactions)
Acknowledgments

- INH-RPT Post-implementation Workgroup
  - Naveen Patil, Leonard Mukasa, Asween Marco
  - Rose Sales
  - Mike Holcombe, Risa Webb
  - Tammy McKenna, Yolanda Jacobs
  - Jon Warkentin
  - Jane Moore
  - Ann Davis, Carla Chee, Brad McKinney, Maria Galvis
  - Elaine Darnell, Arlene Ryndak
  - Dick Brostrom
  - Diana Fortune, Marco Burgos
  - Dean Tsukiyama, Deb Sodt
  - Neha Shah, Julie Higashi, Marisa Moore, Kim Fields
  - Mark Lobato, Lynn Sosa
  - Patricia Townsend
  - Garrett Hunt, Shu-Hua Wang
  - Phil Griffin
  - Dee Pritschet

- Lorna Will
- Margaret Oxtoby
- Narita Masa
- Sara Burr, Sherri Wheeler
- Kevin Winthrop, Heidi Behm

- CDC Field Services and Evaluation Branch
  - Amy Sandul
  - Bunie Nwana
  - Vern Green
  - Gail Grant
  - Mark Miner
  - John Jereb, Sundari Mase, Terry Chorba, Brian Baker
  - Victor Balaban
  - Vincent Fears, Derrick Felix, Andy Heetderks, Dan Ruggiero, Dawn Tuckey, Awal Khan, Lakshmy Menon

- Clinical Research Branch
  - Suzanne Marks
  - Andy Vernon
  - Elsa Villarino
  - Ruth Moro
  - Andrey Borisov
  - Stefan Goldberg
  - Nigel Scott

- Surveillance, Epidemiology and Outbreak Branch
  - Tom Navin
  - Krista Powell

- Data Management and Surveillance Branch
  - Jose Becerra
  - Lon Gross
  - Chad Heilig
<table>
<thead>
<tr>
<th>Basic</th>
<th>Standard</th>
<th>Comprehensive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Georgia</td>
<td>California</td>
<td>Arkansas</td>
</tr>
<tr>
<td>Kane County, Illinois</td>
<td>Connecticut</td>
<td>Mississippi</td>
</tr>
<tr>
<td>Ohio-Columbus Department of Health</td>
<td>Hawaii</td>
<td>New Mexico</td>
</tr>
<tr>
<td>Virginia</td>
<td>Minnesota</td>
<td>Nevada</td>
</tr>
<tr>
<td></td>
<td></td>
<td>South Carolina</td>
</tr>
</tbody>
</table>
## Number and Percentage of Patients Who Reported Symptoms More than Once, of Those Starting Treatment (N= 2134)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Ever Reported</th>
<th>%</th>
<th>Reported more than once</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea/Vomiting</td>
<td>306</td>
<td>14</td>
<td>148</td>
<td>7</td>
</tr>
<tr>
<td>Fatigue</td>
<td>193</td>
<td>9</td>
<td>86</td>
<td>4</td>
</tr>
<tr>
<td>Sore muscles/joints</td>
<td>148</td>
<td>7</td>
<td>70</td>
<td>3</td>
</tr>
<tr>
<td>Fever/Chills</td>
<td>126</td>
<td>6</td>
<td>41</td>
<td>2</td>
</tr>
<tr>
<td>Rash/hives</td>
<td>108</td>
<td>5</td>
<td>34</td>
<td>2</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>107</td>
<td>5</td>
<td>35</td>
<td>2</td>
</tr>
<tr>
<td>Dizziness/fainting</td>
<td>102</td>
<td>5</td>
<td>36</td>
<td>2</td>
</tr>
<tr>
<td>Loss of Appetite</td>
<td>90</td>
<td>4</td>
<td>27</td>
<td>1</td>
</tr>
<tr>
<td>Numbness/tingling</td>
<td>90</td>
<td>4</td>
<td>31</td>
<td>1</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>82</td>
<td>4</td>
<td>26</td>
<td>1</td>
</tr>
<tr>
<td>Yellow eyes/skin</td>
<td>16</td>
<td>1</td>
<td>2</td>
<td>0.1</td>
</tr>
<tr>
<td>Other</td>
<td>350</td>
<td>16</td>
<td>135</td>
<td>6</td>
</tr>
</tbody>
</table>

*patients could have had more than one symptom*
## Characteristics of Adverse Events Associated with Interruption or Discontinuation of 12-dose INH-RPT, 13 sites (n=245)

<table>
<thead>
<tr>
<th></th>
<th>Unknown (n=8)</th>
<th>Non-Severe (n=211)</th>
<th>%</th>
<th>ED* (n=9)</th>
<th>%</th>
<th>Hospitalized (n=17)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom onset</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2 hrs.</td>
<td>-</td>
<td>36</td>
<td>17</td>
<td>1</td>
<td>13</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>2-48 hrs.</td>
<td>2</td>
<td>94</td>
<td>45</td>
<td>5</td>
<td>63</td>
<td>8</td>
<td>47</td>
</tr>
<tr>
<td>&gt;48 hrs.</td>
<td>6</td>
<td>30</td>
<td>14</td>
<td>1</td>
<td>13</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Unknown</td>
<td>-</td>
<td>51</td>
<td>24</td>
<td>2</td>
<td>13</td>
<td>6</td>
<td>35</td>
</tr>
<tr>
<td>Duration &lt;24 hrs.</td>
<td>-</td>
<td>32</td>
<td>15</td>
<td>1</td>
<td>13</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Duration &gt;24 hrs.</td>
<td>-</td>
<td>108</td>
<td>49</td>
<td>6</td>
<td>75</td>
<td>8</td>
<td>47</td>
</tr>
<tr>
<td>Unknown</td>
<td>8</td>
<td>71</td>
<td>36</td>
<td>2</td>
<td>13</td>
<td>9</td>
<td>53</td>
</tr>
</tbody>
</table>

As of 10/2013  *ED=Emergency Department
Number of Doses Associated with Interruption or Discontinuation of 12-dose INH-RPT, 7 sites (n=245)
3HP Economic Evaluation
Preliminary Results from Arkansas and Georgia

- Conducted at 2 sites to help determine whether the INH-RPT regimen is a cost-effective alternative to the 9 mos. INH regimen and under what circumstances

- In Arkansas
  - Only clinic-based DOT, 100% English speaking patients
  - Nurse visits cost the same for INH-RPT and INH, 12 for INH-RPT vs. 9 for INH ($109.95 vs. $86.52)
  - INH-RPT costs more for meds ($125.85 vs. $97.08)
  - Overall, INH-RPT costs more than INH($424.41 vs. $325.74)

- In Georgia
  - Delivery DOT, translators used for 25% of patients
  - Monthly physician visits and regular lab draws for INH-RPT and INH
  - 4 physician visits for INH-RPT and 10 physician visits for INH translates into higher staff time costs for INH ($366.12 vs. $520.87)
  - Overall, INH-RPT costs less than INH ($882.56 vs. $1427.90)

- Completion rates and adverse events not yet accounted for