

Post-marketing INH-RPT Project Objectives

Monitor for adverse events with 3 month INH-RPT in non-research settings

- Track number of patients started on regimen
- Note if certain populations, risk factors or settings are associated with adverse effects (AE) more often

Assess compliance and treatment completion

Assess impact of INH-RPT on programs

- Staffing
- Costs

Match patients with TB registry at 2 years

- Observational measurement of effectiveness
- Surveillance for drug-resistant TB after LTBI treatment

Post-Marketing Surveillance Project Sites

- 18 sites using the regimen, 22 sites contributed to project design and forms
- DOT used for all sites
- Project period: January 2012 through December 2013
- Original target: 4000 patients
- Fewer patients started on INH-RPT due to —staff shortages, drug-resistant TB outbreaks, drug shortages, unable to get state approval of regimen, and waiting to get local IRB approval



(dated 5/24/2013)

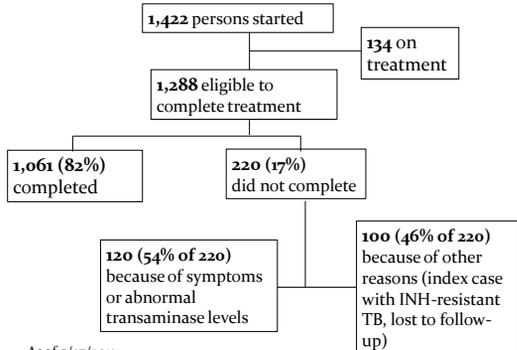
Findings to Date Preliminary Results

Snapshot Through May 27, 2013



As of 5/27/2013

Snapshot to Date: May 27, 2013, from 17 Sites



As of 5/27/2013

Severe Adverse Events

Severe AE: any patient who was hospitalized or died while on LTBI therapy (NSSAE definition)

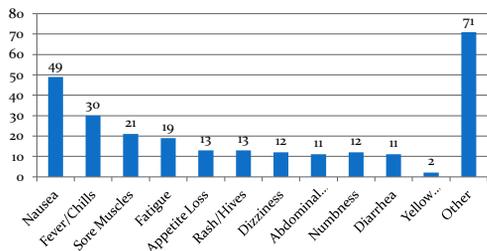
14 reports of hospitalizations

- 6 on-site CDC investigations complete
- 4 investigations in progress
- 4 have not been initiated
- No deaths
- No serious or permanent medical sequelae

Coordination with national NSSAE project under Krista Powell and Lilia Manangan

Patients Who Interrupted or Discontinued INH-RPT Due to Adverse Events by Symptom*, 7 Sites (n=1,183)

129 patients had 135 instances of stopping or interrupting treatment due to symptoms



As of 7/17/2013

*patients can have more than one symptom

"Other" Reasons Reported for Patients Who Interrupted or Discontinued INH-RPT, 7 Sites (n=1,183)

71 "other" reasons among 135 instances of stopping or interrupting treatment because of symptoms*

- > 15 instances of headache
- > 19 instances of elevation in liver transaminase levels
- > 3 pregnancies
- > The following reasons were reported in ≤2 events:

- Swollen lips
- Swollen tongue
- Difficulty breathing
- Menstrual irregularities
- Blurred vision
- Dry mouth
- Platelet drop from 212 to 85
- Gastrointestinal bleeding
- Hip pain
- Change in taste sensation
- Body ache NOS
- Muscle tightness
- Low blood pressure
- Blood pressure NOS
- Swollen lymph nodes
- Eye Pain
- Weakness
- Itching
- Chest pain
- Confusion

As of 7/17/2013

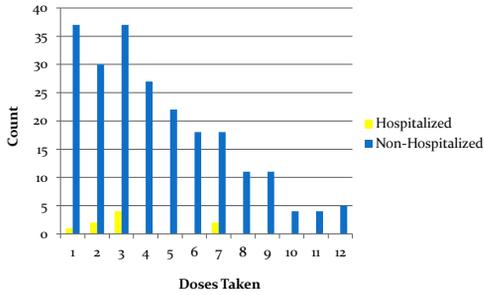
*patients can have more than one reason

Characteristics of AEs Associated with Interruption or Discontinuation of 12-dose INH-RPT, 7 sites (n=234)

	Non-severe (n=225)	%	Severe (n=9)	%
Symptom onset <2 hrs.	61	27	0	0
2-48 hrs.	104	46	5	56
>48 hrs.	27	12	1	11
Unknown onset	33	15	3	33
Duration <24 hrs.	58	26	5	56
Duration >24 hrs.	107	48	1	11
Unknown duration	60	27	3	33

As of 5/27/2013

Number of Doses Associated with Interruption or Discontinuation of 12-dose INH-RPT, 7 sites (n= 234)





Location Specific Findings



Homeless Contacts Receiving 12-Dose INH-RPT for LTBI Treatment, Two Post-marketing Project Sites

- Mississippi – 48 homeless contacts**
 - 39 (81%) completed treatment
 - 9 (18%) did not complete INH-RPT
 - > 1 (2%) because of an adverse event
- Kane County – 35 homeless contacts**
 - 11 (31%) still in treatment
 - 24 completed (of 24 eligible to complete)
 - None stopped or lost to follow-up

As of 5/27/2013

Virginia's Experience During the Post-marketing Project Symptoms for Which Treatment Stopped

- Six patients stopped treatment due to adverse events
- Reported symptoms for stoppage included:
 - Rash/hives – 4 patients
 - Nausea/vomiting – 3 patients
 - Appetite loss – 1 patient
 - Diarrhea - 1 patient
 - Abdominal pain - 1 patient
 - Sore muscles - 1 patient

*patients can have more than one symptom

Summary

- Initial field experience is similar to treatment trial experiences
- High completions rates, notably in difficult populations
- Rashes and nausea most common reasons for stopping
- No deaths or severe organ damage detected nationally
 - No deaths or hospitalizations in Virginia

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