Isoniazid-Rifapentine for Treatment of Latent TB Infection
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Preventing Tuberculosis
• Treatment for latent TB infection is the cornerstone of the US strategy for TB elimination
• Active TB develops in 5-10% of individuals who are infected with TB
• Those with impaired cellular immunity are at higher risk for developing active TB

Latent TB Infection Therapy
• Isoniazid:
  - 9 months of treatment
• Pros:
  - Inexpensive
  - Best efficacy and safety data
    • Hepatitis in 0.1-0.6% of patients
    • About 75-80% effective
• Cons:
  - Low completion rates of 30-64%
Other LTBI Treatment Options

- Rifampin:
  - 4 months of therapy
  - to be used when contact to INH-resistant disease, INH contraindicated or is not tolerated by the patient
- Rifampin/PZA:
  - not recommended due to hepatotoxicity

PREVENT TB Trial

- Enrolled 8,053 patients
- Most participants were from the US and Canada, some from Spain and Brazil
- Participants either received 9 months of INH or a once-weekly dose of rifapentine and isoniazid for 3 months given via DOT
- Trial lasted for 10 years and participants were followed for approximately 33 months to evaluate for development of TB disease
PREVENT TB Trial

• Completion of INH-RPT was defined as 11 or 12 doses within 16 weeks
• Doses had to be separated by >72 hours to be counted

12-Weeks of once weekly INH/Rifapentine (1)

Pros:
• Shorter duration of treatment (12 doses vs. 270 doses)
• Individuals more likely to complete therapy (82% vs 69%)
• 7 cases of TB in INH-Rifapentine group vs. 15 cases in INH group
• Similar amount of adverse drug events in each group

12-Weeks of once weekly INH/Rifapentine (2)

Cons:
• More Expensive: $503 vs $237
• May have difficulty getting Rifapentine
• Trial results are applicable only in low-to-medium TB incidence countries
• Not clear how to use this regimen in special populations:
  - HIV positive
  - Children under 5
INH-RPT given as 12 weekly DOT doses is recommended as an equal alternative to 9 months of daily self-supervised INH for treating LTBI in otherwise healthy patients aged ≥ 12 years at risk for TB disease:
- recent exposure to contagious TB
- conversion of TST or IGRA
- radiographic findings of healed pulmonary TB

Choosing between INH and INH-RPT
- Feasibility of DOT
- Resources available for obtaining drugs
- Ability of the program to monitor patient
- Expectance of treatment completion based on medical/social circumstances
- Preferences of the patient and the prescribing physician

INH-RPT NOT Recommended
- Children <2 years old
- HIV-infected patients receiving HAART
- Pregnant women and women expecting to become pregnant during treatment
- Where LTBI is presumed to have INH or RIF resistance
Children

- Preferred regimen for children aged 2-11 years: 9 months of INH
- However, INH-RPT may be considered on a case-by-case basis when BOTH:
  1) completion of 9 months of therapy is unlikely
  2) the likelihood or hazard of TB is great

Dosing

Rifapentine (1)

- Longer half life than rifampin
- Orange discoloration of secretions, urine, tears
- Can stain contact lenses
- Rare adverse effects:
  - elevated liver function tests
  - thrombocytopenia
  - headache and dizziness
Rifapentine (2)

- Increases the metabolism of medications, particularly those metabolized by cytochrome P450 3A:
  - birth control
  - coumadin
  - methadone
  - glipizide, glimepiride, glyburide
  - levothyroxine

Directly-observed therapy

- DOT recommended as missed doses or altered dosing intervals can affect efficacy and safety of INH-RPT
- DOT workers need to be trained to look for adverse effects of medications and report them to clinician

Monitoring (1)

- At each encounter, patients need to be instructed to seek medical attention immediately if they have:
  - fever
  - yellow eyes (jaundice)
  - dizziness
  - rash
  - aches
  - >1 day of nausea, vomiting, weakness, abdominal pain or loss of appetite
Monitoring (2)

- Medications should be withheld while cause of symptoms is being determined
- Patients should undergo at least monthly clinical assessments, to include inquiries about side effects and a physical examination
- Laboratory tests:
  - baseline LFTS in HIV, liver disease, ETOH use, immediate post-partum period
  - repeat liver tests at subsequent visits for those with baseline abnormal tests or those at risk for liver disease