RESIST-TB

Research Excellence to Stop TB Resistance

Testimony to the FDA Anti-Infective Drugs Advisory Committee, June 3, 2009

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RESIST-TB

An organization of concerned patients, physicians, research scientists and other stakeholders

Mission: To promote and conduct clinical research to cure and prevent drug-resistant Tuberculosis throughout the world
RESIST-TB: Promoting Clinical Trials for Drug-Resistant TB

- Workshop on Clinical Trials for DR-TB, held in Cambridge, MA, USA (June, 2008)
- Website: http://www.resisttb.org
- Support from WHO, CDC, IUATLD, Treatment Action Group, Partners in Health, Médecins Sans Frontières
Outline of Presentation

• The urgent need for new drugs for MDR-TB
• Predicting the outcome of MDR-TB treatment
• Expanding access to new drugs while avoiding creation of XDR-TB
• Developing regimens for HIV-infected and HIV-uninfected persons with MDR-TB
• Developing regimens for children with MDR-TB
• Developing regimens to prevent MDR-TB disease in contacts
The urgent need for new drugs for MDR-TB

- Half a million new cases of MDR-TB every year
- Less than 20,000 receive effective treatment
- 1 to 1.5 million cases persist, untreated, every year
- Of those receiving treatment, only 60% are cured
- No new drug classes in 30 years
- Current regimens have substantial toxicity
- Accelerated approval process for new MDR-TB drugs is justified
Predicting the outcome of MDR-TB treatment

• Sputum culture conversion is a direct reflection of drug efficacy
• Culture conversion correlates with symptomatic improvement (fever, chills, weight loss)
• Failure to convert sputum always predicts clinical failure
• When culture conversion occurs but the patient is not cured, this is often the result of toxicity or nonadherence
• Accelerated approval for new MDR-TB drugs should be granted on the basis of culture conversion as evidence of clinical benefit
Expanding access to new drugs while avoiding creation of XDR-TB

- Use of a single new drug without effective companion drugs could lead to widespread resistance to a new agent
- 18 (21%) of 87 patients being treated for MDR-TB developed XDR-TB (NEJM 2008;359:2398-2400)
- Accelerated approval for new MDR-TB drugs should require clinical trials to establish optimal companion drugs and duration of therapy
Developing regimens for HIV-infected and HIV-uninfected persons with MDR-TB

• As many as 30% of MDR-TB patients may have HIV co-infection
• HIV/MDR-TB co-infected patients have poorer treatment outcomes
• Different treatment regimens may be needed for HIV/MDR-TB co-infected patients
• Accelerated approval for new MDR-TB drugs should require clinical trials to establish optimal therapy for HIV co-infected patients
Developing regimens for children with MDR-TB

- The number of children with MDR-TB is underestimated and likely substantial
- Children will need prompt access to new drugs for MDR-TB
- Such access will require pediatric formulations and PK studies to establish pediatric dosing
- Accelerated approval for new MDR-TB drugs should require pediatric formulations and PK studies
Developing regimens for contacts of patients with MDR-TB

- Patients with MDR-TB infect at least 8-10 contacts
- 10% of HIV-uninfected and 50-80% of HIV-infected contacts with MDR-TB infection will progress to disease
- Even a single new MDR-TB drug may be able to prevent this progression
- Accelerated approval for new MDR-TB drugs should require contact prevention trials
Conclusions

• Accelerated approval is appropriate for MDR-TB indications and should be based on culture conversion

• Accelerated approval should require:
  – Trials to establish optimal regimen and duration
  – Trials to establish optimal therapy in HIV-infection
  – Pediatric formulations
  – Trials to establish pediatric PK
  – Trials of prevention in contacts