FDA Antiviral Drugs Advisory Committee Meeting
September 5, 2007

Raltegravir
(MK-0518)

Merck Research Laboratories

Agenda

- Robert A. Fromtling, PhD
  - Introduction
- Bach-Yen Nguyen, MD
  - Raltegravir Background
  - Clinical Development Program Overview
  - Clinical Trials Results
    - Efficacy
    - Resistance
    - Safety
- Robin Isaacs, MD
  - Drug-Drug Interactions
  - Risk Management Plan
  - Conclusions

Unmet Need for Novel HIV Therapies

- In the USA in 2005, there were 1.2 million HIV positive people including 33,000 new infections and 16,300 AIDS deaths
- There is an unmet need for new therapeutic agents
  - ~10-15% of treated patients are failing therapy and have triple-class resistant HIV (Napravnik, et al. 2006)
  - Current regimens in treatment-experienced patients often have issues with safety and/or inconvenient dosing options
- Ideally, new agents should demonstrate
  - Potent efficacy
  - Favorable safety profile and dosing convenience
  - Manageable drug interactions
- Urgent need in the heavily treatment-experienced population

Raltegravir Addresses Unmet Medical Need

- Novel mechanism of action
  - First-in-class HIV integrase inhibitor with no cross-resistance with currently licensed antiretroviral agents
- In clinical trials, raltegravir demonstrated rapid, potent, and sustained antiretroviral activity in treatment-experienced patients
  - Major contribution to the new treatment paradigm
    - Undetectable viral load demonstrated in treatment-experienced patients with triple-class resistant virus
- Excellent safety profile and tolerability
- Low pill burden and convenience in dosing
  - Dosed one tablet twice daily without regard to food
  - No dose adjustment with other antiretroviral agents
- Overall favorable benefit/risk profile, particularly in treatment-experienced patients

Proposed Indication and Dosage and Administration

- Indication

  Raltegravir is indicated in combination with other antiretroviral agents for the treatment of human immunodeficiency virus (HIV-1) infection in treatment-experienced patients with evidence of HIV-1 replication despite ongoing antiretroviral therapy

- Dosage and administration

  The recommended dosage of raltegravir is 400 mg administered orally, twice daily with or without food

  Raltegravir is to be given in a combination regimen with other antiretroviral agents

Consultants

Terry Blaschke, MD	Stanford University
Susan Krown, MD	Memorial Sloan Kettering Cancer Center
Martin Markowitz, MD	Aaron Diamond AIDS Research Center
Robert Maronpot, DVM	Maronpot Consulting, Inc.
Alexander Walker, MD, DrPH	i3 Drug Safety
Lee-Jen Wei, PhD	Harvard University