

Tipranavir NDA 21-814



Antiviral Drugs Advisory Committee
May 19, 2005

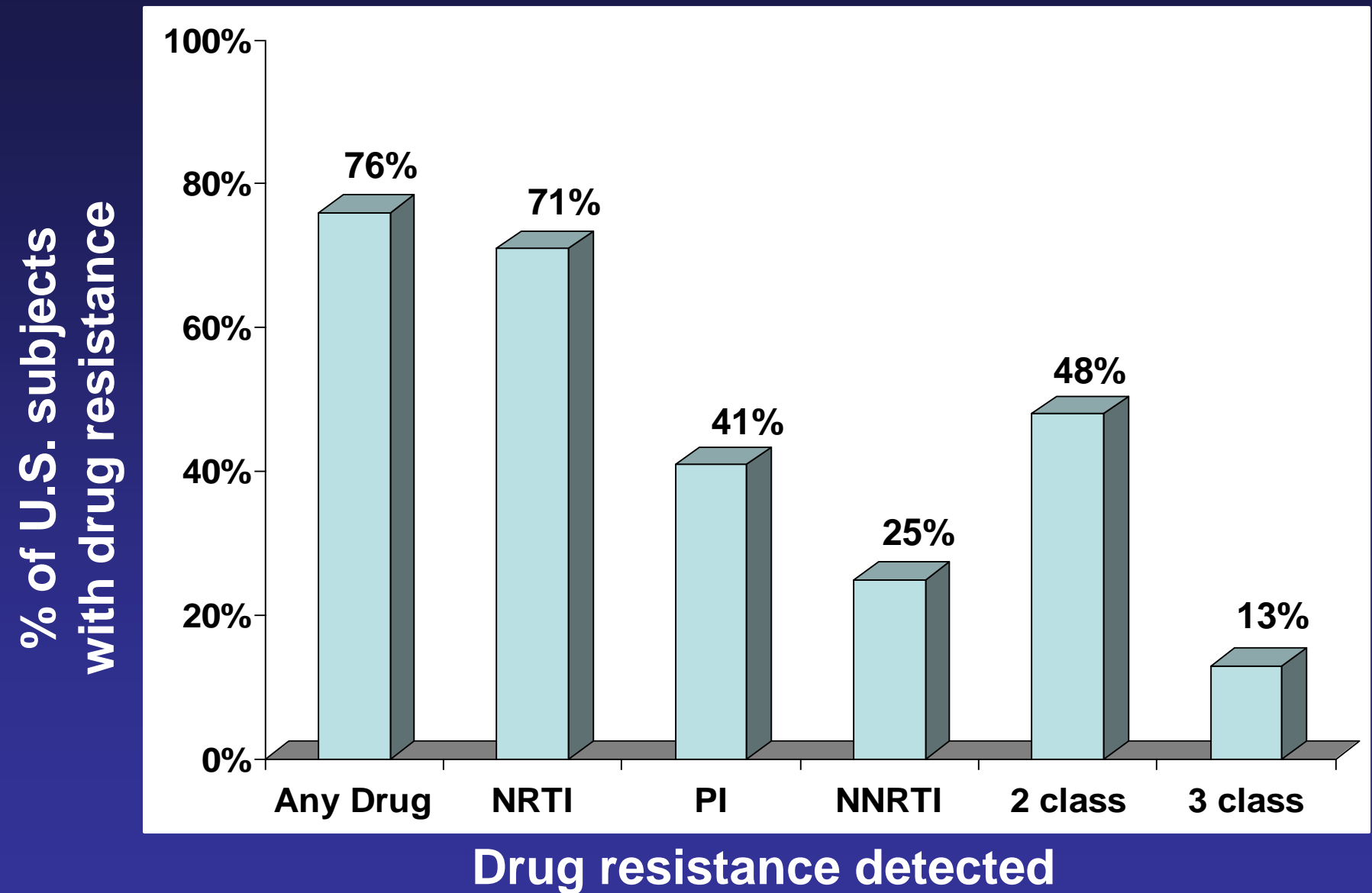
HIV Drug Resistance

- Different patient populations
 - Naïve subjects harboring resistant virus
 - Limited or Intermediate prior treatment with resistance
 - **Extensive prior treatment with resistance with limited treatment options**

HIV Drug Resistance in the U.S.

- Treatment-experienced subject cohort with VL > 500 copies/ml from HIV Cost and Service Utilization Study (Richman, et al, AIDS, 2004)
- Overall resistance was 76%
- 2-class resistance = 48%
- 3-class resistance = 13%

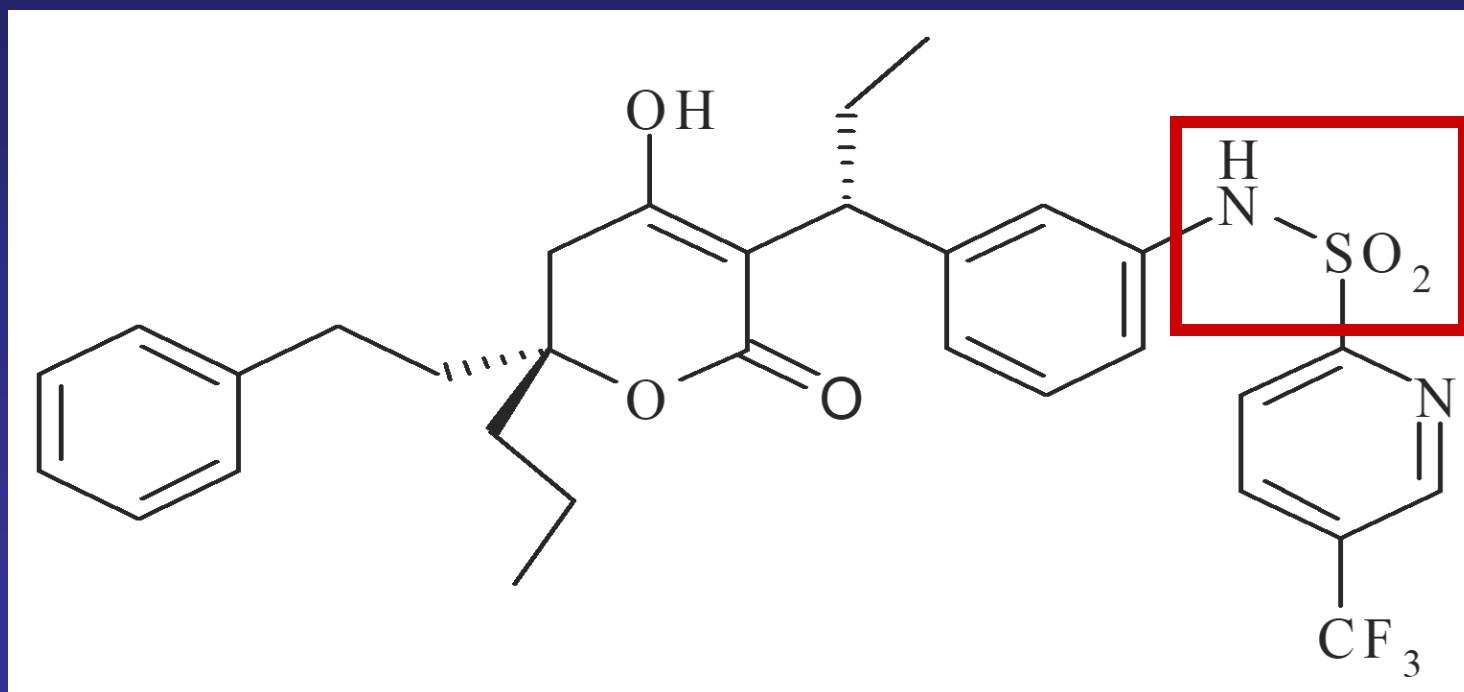
Prevalence of Estimated HIV Drug Resistance



Current State of Therapy for Patients with Limited Treatment Options

- Enfuvirtide(T-20)
 - Traditional approval 2004
- Drugs in antiviral pipeline
- Tipranavir
 - 2 key studies in a highly treatment experienced population

Tipranavir



Tipranavir/r: Trial Design

- Resist 1 and Resist 2
 - Open label
 - TPV/r + OBR vs CPI/r + OBR
 - Amended protocol allowed patients with PI resistant virus to receive a PI-based regimen
 - Analyzed as superiority trials
 - Escape clause @ week 8 to allow subjects with VF to receive TPV in 1182.17
 - Loss of control arm @ week 8

Tipranavir/r: Patient Population

- Highly treatment experienced
 - 3 class experienced
 - Median number of 12 prior antiretroviral drugs
 - Prior T-20 use in 12%
 - Baseline resistance
 - 97% of isolates resistant to at least 1 PI
 - 95% of isolates resistant to at least 1 NRTI
 - 75% of isolates resistant to at least 1 NNRTI

Tipranavir/r: FDA Presentation

- Efficacy evaluation
- Resistance evaluation
- Exposure-response data
- Drug-drug interactions
 - CYP 3A inhibitor
 - PgP inducer
- Safety profile
 - Hepatotoxicity
 - Rash
 - Hyperlipidemia
- Summary

NDA 21-814 Review Team

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