HIV Drug Development in Treatment-Naïve Patients

FDA/Jeff Murray Perspective

Treatment-Naïve Studies

- Need new options. Why?
  - Small margin to improve on efficacy
  - Provide alternatives for safety/tolerability
  - Improve on drug interactions (use with TB drugs etc.)
- FDA does not reject “me-too” products. Why?
  - Regulations do not prohibit “me-too” products
  - Competition in market place
  - Strengthens drug supplies
- More data required for Naïve population
  - Success of current options changed risk-benefit equation

Treatment-Naïve Patients: Role in Development

- Phase 2a (7-10 day) dose-ranging studies
  - Determine exposure-response and safety
  - Resistance issues dictate duration of monotherapy, if appropriate at all
- Phase 2b studies, multiple doses as part of HAART (24++weeks)
- Phase 3 studies supporting treatment naïve indication (48 weeks)
  - Efficacy determination clear at 48 weeks, longer term data valuable for characterization of safety

Naïve Population: Dose Finding

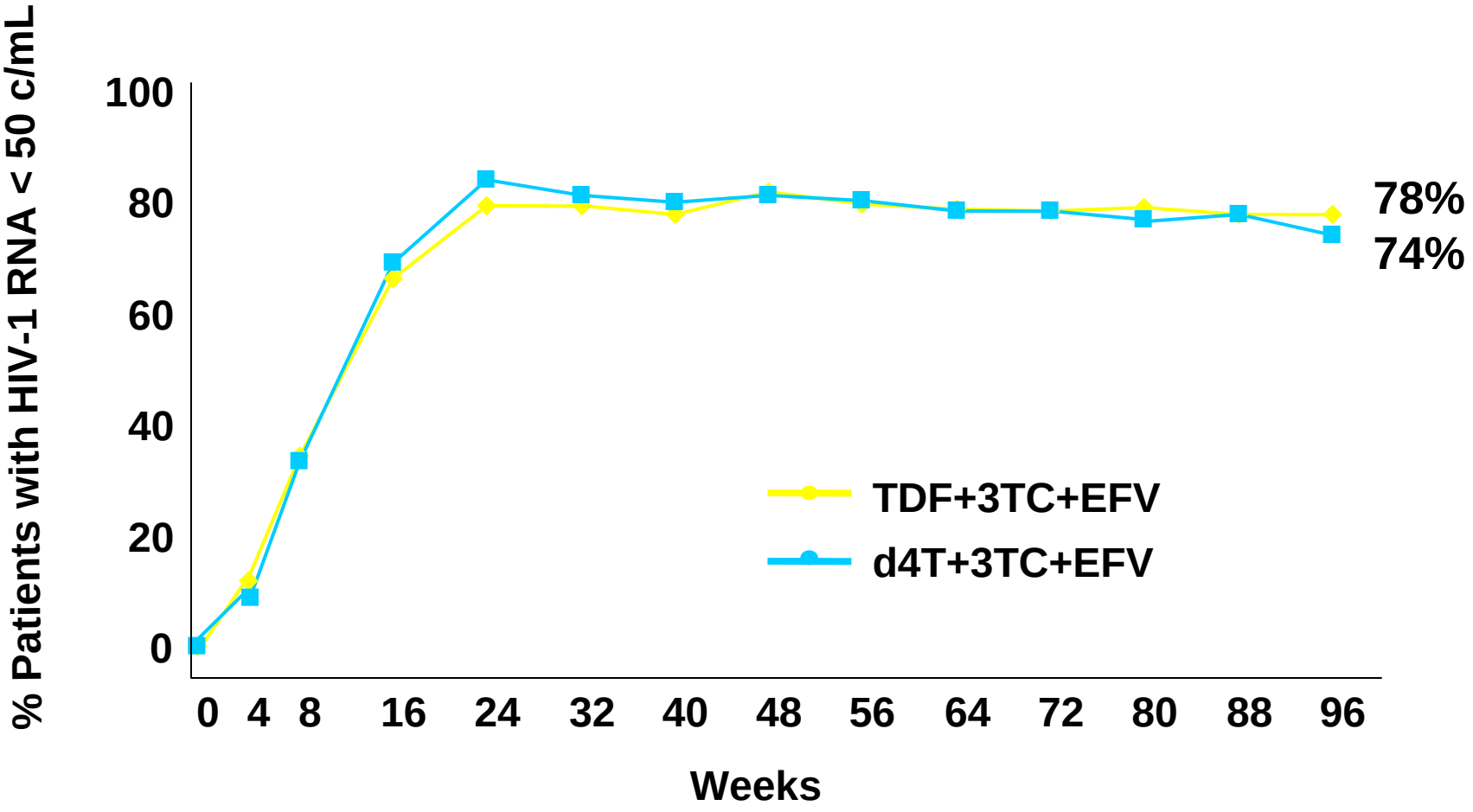
- Best population for discriminating efficacy among doses??
- Maraviroc Development Example:
  - In the Two Treatment Experienced Studies QD dosing and BID dosing similar overall
  - Differences in doses seen only in subgroups (increased HIV-RNA, decreased CD4)
  - Treatment Naïve study—differences in QD and BID arm noticed early; QD arm stopped at 16-week planned interim analysis

Dose Finding in Treatment-Naïves: Potential Benefits

- Reason for expecting dose discrimination
  - Naïve: expected standard efficacy
  - Less variable background (2 NRTIs)
  - Less variability = less noise; easier to detect treatment differences
- Different dose may be effective
- Less Risk to Participants
  - If naïve patient develops resistance-plenty of remaining options
  - Treatment experienced—fewer options left—greater risk of having no alternative treatments

Study 903: Virologic Response

Intent to Treat (Missing=Failure)



Staszewski, 10th CROI 2003, abstract 564b