4-Drug Regimens versus 3-Drug Regimen

ACTG 388 Trial

4-Drug Regimens versus 3-Drug Regimen
ACTG 388: Study Design

Study Design: ACTG 388

- **Background**: Randomized, controlled, phase 3 trial comparing the activity, safety, and tolerability of two different 4-drug regimens with a 3-drug regimen in advanced HIV disease
- **Inclusion Criteria (n = 517)**
  - Prior ART: only ZDV, d4T, DDI, ddC
  - CD4 ≤200 cells/mm^3
  - HIV RNA ≥80,000 copies/mL
  - No resistance to NRTIs or PIs
- **Treatment Arms**
  - IDV 800 mg TID + ZDV-3TC BID
  - EFV 600 mg QD + IDV 800 mg TID + ZDV-3TC BID
  - NFV 1250 mg BID + IDV 1000 mg BID + ZDV-3TC BID

Indinavir Group
Indinavir + Zidovudine-Lamivudine
(n = 168)

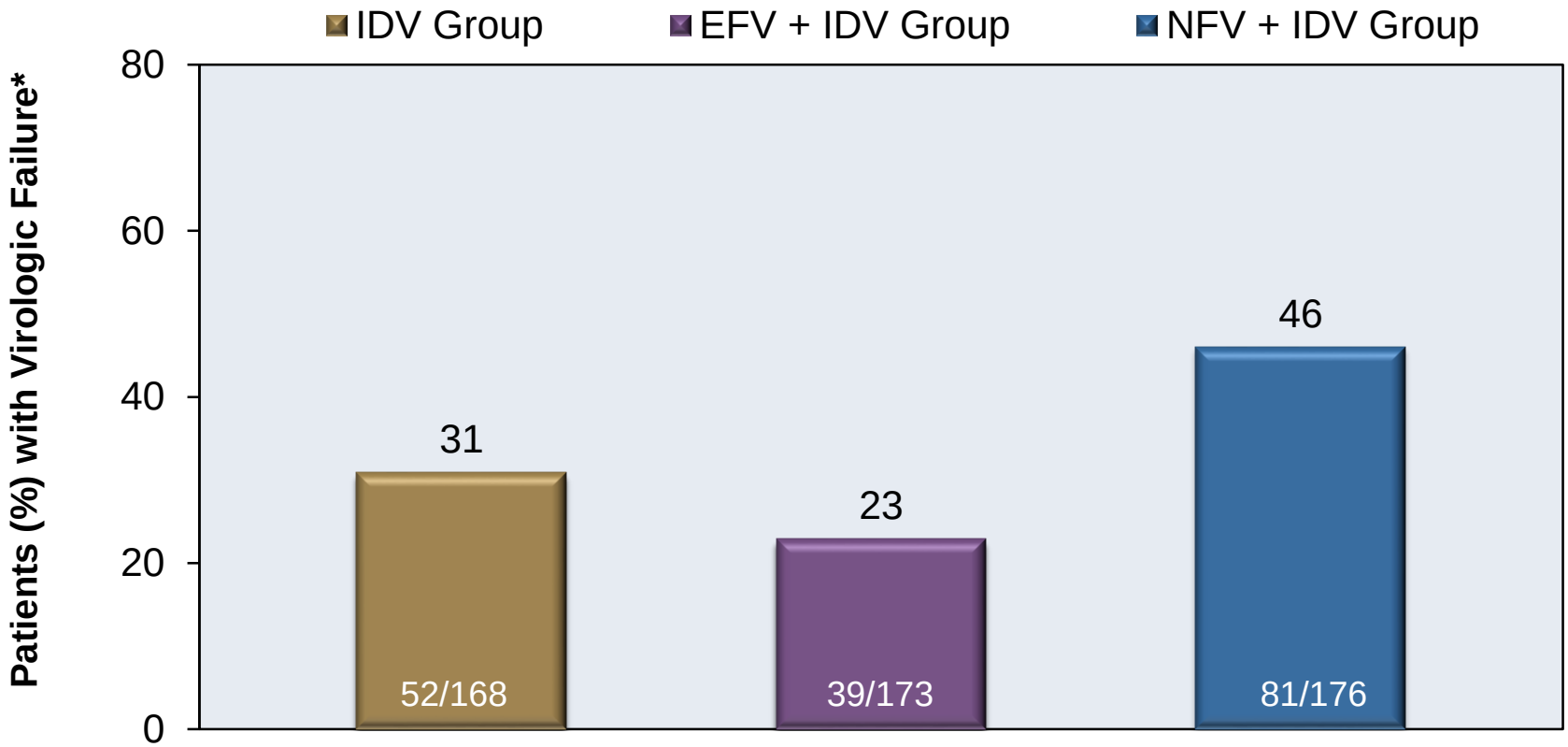
Efavirenz + Indinavir Group
Efavirenz + Indinavir + Zidovudine-Lamivudine
(n = 173)

Nelfinavir + Indinavir Group
Nelfinavir + Indinavir + Zidovudine-Lamivudine
(n = 176)

Source: Fischl MA, et al. J Infect Dis. 2003;188:625-34.

4-Drug Regimens versus 3-Drug Regimen
ACTG 388: Results

Week 48: Virologic Failure



*Virologic failure = confirmed increase in HIV-1 RNA level greater than baseline or nadir values, failure to achieve HIV RNA <200 copies by week 24, or relapse (2 consecutive HIV-1 RNA levels ≥200 copies/mL after confirmed virologic response (HIV-1 RNA levels <200 copies/mL).

Source: Fischl MA, et al. J Infect Dis. 2003;188(5):625-34.

4-Drug Regimens versus 3-Drug Regimen
ACTG 388: Results

Clinical Toxicity and Laboratory Abnormalities			
Variable	**IDV only** (n = 168)	**EFV + IDV** (n = 168)	**NVF + IDV** (n = 168)
Nausea (+/- vomiting)	15	7	19
Diarrhea	4	3	16
Rash	2	7	3
Nephrolithiasis	22	5	8
Serum bilirubin >2.5x ULN	16	0	8
ANC <750 cells/mm^3	8	12	21
AST >5x ULN	6	11	8
Serum triglycerides >750 mg/dL	7	12	8

Source: Fischl MA, et al. J Infect Dis. 2003;188:625-34.

4-Drug Regimens versus 3-Drug Regimen
ACTG 388: Conclusions

Conclusions: "A 4-drug regimen containing efavirenz plus indinavir resulted in a superior virologic response, whereas one containing nelfinavir plus indinavir resulted in an inferior response and a greater likelihood of toxicity."

Source: Fischl MA, et al. J Infect Dis. 2003;188:625-34.

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