4-Drug Regimens versus 3-Drug Regimen

ACTG 388 Trial
**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/mm³
  - 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).

# 4-Drug Regimens versus 3-Drug Regimen

**ACTG 388: Results**

<table>
<thead>
<tr>
<th>Variable</th>
<th>IDV only (n = 168)</th>
<th>EFV + IDV (n = 168)</th>
<th>NVF + IDV (n = 168)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea (+/- vomiting)</td>
<td>15</td>
<td>7</td>
<td>19</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4</td>
<td>3</td>
<td>16</td>
</tr>
<tr>
<td>Rash</td>
<td>2</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Nephrolithiasis</td>
<td>22</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Serum bilirubin &gt;2.5x ULN</td>
<td>16</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>ANC &lt;750 cells/mm³</td>
<td>8</td>
<td>12</td>
<td>21</td>
</tr>
<tr>
<td>AST &gt;5x ULN</td>
<td>6</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td>Serum triglycerides &gt;750 mg/dL</td>
<td>7</td>
<td>12</td>
<td>8</td>
</tr>
</tbody>
</table>

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