Efavirenz-Tenofovir DF-Emtricitabine (Atripla)

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Efavirenz-Tenofovir DF-Emtricitabine (Atripla)

Atripla
[uh TRIP luh]

Dose: 1 tablet once daily on an empty stomach

Efavirenz-Tenofovir DF-Emtricitabine
600 mg 300 mg 200 mg
NNRTI NRTI NRTI
Efavirenz-emtricitabine-tenofovir DF (*Atripla*)

- **Atripla Components**:  
  Efavirenz 600mg  
  Tenofovir disoproxil fumarate: 300 mg  
  Emtricitabine: 200 mg

- **Dosing**: 1 tablet once daily on empty stomach (bedtime dosing recommended to minimize side effects)

- **Pregnancy**: may cause fetal harm when administered during the first trimester of pregnancy

- **Common Adverse Events (≥ 10%)**  
  - Nausea, diarrhea, fatigue, headache, dizziness, depression, insomnia, abnormal dreams, rash
Efavirenz-Tenofovir DF-Emtricitabine
Summary of Key Studies

• Phase 3 Trials in Treatment Naïve
  - ASSERT: ABC-3TC + EFV versus TDF-FTC plus EFV
  - STUDY 934: TDF + FTC + EFV versus ZDV-3TC + EFV
  - STARTMRK: RAL + TDF- FTC versus EFV + TDF-FTC
  - ECHO: RPV + FTC-TDF versus EFV + FTC-TDF
  - STaR: RPV-FTC-TDF versus EFV-TDF-FTC
  - SINGLE: DTG + ABC-3TC versus EFV-TDF-FTC
  - STUDY 102: EVG-COBI-FTC-TDF versus EFV-TDF-FTC

• Phase 3 Switch/Simplification Trials
  - SWEET: Switch from EFV + AZT-3TC to EFV + TDF-FDC
  - STUDY 073: Simplification to EFV-FTC-TDF
  - COMET: Switch from AZT-3TC plus EFV to TDF-FTC plus EFV
  - ROCKET-1: Switch from ABC-3TC + EFV to EFV-FTC-TDF
  - ADONE: Adherence to FTC-TDF-EFV
INITIAL THERAPY

Efavirenz-Tenofovir DF-Emtricitabine
EFV + ABC-3TC versus EFV + TDF-FTC

ASSERT Trial
Efavirenz + ABC-3TC versus Efavirenz + TDF-FTC

ASSERT: Study Design

**Study Design: ASSERT Study**

- **Background**: Randomized, open label phase 3 study comparing tenofovir DF-emtricitabine plus efavirenz with zidovudine-lamivudine plus efavirenz in antiretroviral-naïve adults with HIV

- **Inclusion Criteria (n = 385)**
  - Antiretroviral-naïve adults
  - Age ≥18 years
  - HIV RNA ≥1,000 copies/mL
  - HLA-B*5701 negative
  - CrCl ≥50 mL/min
  - No AIDS conditions or HBV infection

- **Treatment Arms**
  - Efavirenz + abacavir-lamivudine
  - Efavirenz + tenofovir DF-emtricitabine

Efavirenz + ABC-3TC versus Efavirenz + TDF-FTC

ASSERT: Result

Week 48 Virologic Response (Intent-to-Treat Analysis)

Efavirenz + ABC-3TC versus Efavirenz + TDF-FTC

ASSERT: Renal Biomarkers

Week 48: Changes in Markers of Renal Tubular Function

**Interpretation**: “The study showed no difference in estimated glomerular filtration rate between the arms, however, increases in markers of tubular dysfunction were observed in the tenofovir/emtricitabine arm, the long-term consequence of which is unclear. A significant difference in efficacy favoring tenofovir/emtricitabine was observed.”
Efavirenz + ABC-3TC versus Efavirenz + TDF-FTC
ASSERT: Bone Effects

Week 48: Changes in Spine and Hip Bone Mineral Density from Baseline

Change in BMD (%)

<table>
<thead>
<tr>
<th></th>
<th>EFV + ABC-3TC</th>
<th>EFV + TDF-FTC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hip</td>
<td>-1.90</td>
<td>-1.60</td>
</tr>
<tr>
<td>Lumbar Spine</td>
<td>-3.6</td>
<td>-2.40</td>
</tr>
</tbody>
</table>

Efavirenz + ABC-3TC versus Efavirenz + TDF-FTC

ASSERT: Bone Effects

Week 48: Proportion of Subjects with Decrease in BMD from Baseline

EFV + TDF + FTC versus EFV + ZDV-3TC

Study 934
Efavirenz + TDF + FTC + versus Efavirenz + ZDV-3TC

Study 934: Study Design

Study Design: STUDY 934

- Background: Randomized, open label phase 3 study comparing efavirenz plus either tenofovir DF and emtricitabine or fixed-dose zidovudine-lamivudine

- Inclusion Criteria (n = 509)
  - Antiretroviral-naïve adults
  - Age ≥18 years
  - HIV RNA ≥10,000 copies/mL
  - CD4 >50 cells/mm³
  - No AIDS conditions in prior 30 days

- Treatment Arms
  - Efavirenz + tenofovir DF + emtricitabine
  - Efavirenz + zidovudine-lamivudine

Efavirenz + TDF + FTC + versus Efavirenz + ZDV-3TC
Study 934: Result

Week 48: Virologic Response (< 400 copies/mL)

![Bar chart showing virologic response at Week 48 in the ITT Population and Excluding NNRTI-R populations.](chart.png)

**ITT Population**
- EFV + TDF + FTC: 81/206/255 (81%)
- EFV + ZDV-3TC: 70/177/254 (70%)

**Excluding NNRTI-R**
- EFV + TDF + FTC: 84/206/244 (84%)
- EFV + ZDV-3TC: 73/177/243 (73%)

Efavirenz + TDF + FTC + versus Efavirenz + ZDV-3TC
Study 934: Result

Week 48: Virologic Response (<50 copies/mL)


ITT = Intention-to-Treat; NNRTI-R = Patients with baseline NNRTI mutations.
Efavirenz + TDF + FTC + versus Efavirenz + ZDV-3TC

Study 934: Result

Week 48: Immunologic Response

Efavirenz + TDF + FTC + versus Efavirenz + ZDV-3TC

Study 934: Result

Adverse Events through 48 Weeks

Efavirenz + TDF + FTC + versus Efavirenz + ZDV-3TC

Study 934: Common Adverse Events

<table>
<thead>
<tr>
<th>Treatment Emergent Adverse Events in ≥ 5% of Subjects in Either Arm</th>
<th>EFV + TDF + FTC (n = 257)</th>
<th>EFV + ZVD-3TC (n = 254)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dizziness</td>
<td>8%</td>
<td>7%</td>
</tr>
<tr>
<td>Nausea</td>
<td>8%</td>
<td>6%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>7%</td>
<td>4%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>7%</td>
<td>6%</td>
</tr>
<tr>
<td>Depression</td>
<td>4%</td>
<td>7%</td>
</tr>
<tr>
<td>Headache</td>
<td>5%</td>
<td>4%</td>
</tr>
<tr>
<td>Rash</td>
<td>5%</td>
<td>4%</td>
</tr>
<tr>
<td>Insomnia</td>
<td>4%</td>
<td>5%</td>
</tr>
<tr>
<td>Anemia</td>
<td>&lt;1%</td>
<td>5%</td>
</tr>
</tbody>
</table>

Interpretation: “Through week 48, the combination of tenofovir DF and emtricitabine plus efavirenz fulfilled the criteria for noninferiority to a fixed dose of zidovudine and lamivudine plus efavirenz and proved superior in terms of virologic suppression, CD4 response, and adverse events resulting in discontinuation of the study drugs.”
Raltegravir + TDF-FTC versus Efavirenz + TDF-FTC

STARTMRK Trial
**Study Design: STARTMRK Study**

- **Background**: Randomized, double-blind phase 3 study comparing the safety and efficacy of raltegravir with efavirenz, in combination with co-formulated tenofovir DF and emtricitabine.

- **Inclusion Criteria (n = 569)**
  - Antiretroviral-naïve patients
  - Age ≥18 years
  - HIV RNA ≥5000 copies/mL
  - No resistance to EFV, TDF, or FTC

- **Treatment Arms**
  - Raltegravir + TDF-FTC
  - Efavirenz + TDF-FTC

Raltegravir + TDF-FTC vs. Efavirenz + TDF-FTC

STARTMRK: Result

Week 48: Virologic Response (Primary Analysis, M=F)

RALTEGRAVIR + TDF-FTC versus EFAVIRENZ + TDF-FTC

STARTMRK: Result

Week 48 Virologic Response (Observed-Failure Method)

Raltegravir versus Efavirenz in Combination Therapy
STARTMRK Trial: Results

Week 48 Virologic Response

Raltegravir + TDF-FTC vs. Efavirenz + TDF-FTC

STARTMRK: Result

Adverse Events through 48 Weeks

Raltegravir + TDF-FTC vs. Efavirenz + TDF-FTC
STARTMRK: Result

Week 48: Changes in Lipid Concentrations

### Treatment Emergent Adverse Events in >10% of Subjects in Either Arm

<table>
<thead>
<tr>
<th>Event</th>
<th>RAL+TDF-FTC (n = 281)</th>
<th>EFV+ TDF-FTC (n= 282)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dizziness</td>
<td>6%</td>
<td>34%</td>
</tr>
<tr>
<td>Headache</td>
<td>9%</td>
<td>14%</td>
</tr>
<tr>
<td>Abnormal dreams</td>
<td>7%</td>
<td>13%</td>
</tr>
<tr>
<td>Immune Reconstitution Inflammatory Syndrome (IRIS)</td>
<td>6%</td>
<td>4%</td>
</tr>
</tbody>
</table>

Interpretation: “Raltegravir-based combination treatment had rapid and potent antiretroviral activity, which was non-inferior to that of efavirenz at week 48. Raltegravir is a well tolerated alternative to efavirenz as part of a combination regimen against HIV-1 in treatment-naive patients.”

Rilpivirine + TDF-FTC versus Efavirenz + TDF-FTC

ECHO Trial
Rilpivirine + TDF-FTC versus Efavirenz + TDF-FTC

ECHO: Study Design

**Study Design: ECHO Study**

- **Background**: Randomized, double-blind, phase 3 trial comparing rilpivirine and efavirenz in combination with a fixed background regimen consisting of tenofovir DF-emtricitabine in treatment-naïve adult with HIV

- **Inclusion Criteria (n = 690)**
  - Antiretroviral-naïve adults
  - Age ≥18 years
  - HIV RNA ≥5000 copies/mL
  - No resistance to any study drugs

- **Treatment Arms**
  - Rilpivirine + Tenofovir DF-Emtricitabine
  - Efavirenz + Tenofovir DF-Emtricitabine

Rilpivirine + TDF-FTC versus Efavirenz + TDF-FTC

ECHO: Result

48 Week Virologic Response (ITT-TLOVR)

HIV RNA <50 copies/mL (%)

- Rilpivirine + TDF-FTC
- Efavirenz + TDF-FTC

Baseline HIV RNA (copies/mL)

- All
- ≤100,000
- 100,000-500,000
- >500,000

Rilpivirine + TDF-FTC versus Efavirenz + TDF-FTC

ECHO: Result

48 Week Virologic Failure and Discontinuations (ITT-TLOVR)

Rilpivirine + TDF-FTC versus Efavirenz + TDF-FTC
ECHO: Resistance Results

Incidence of NNRTI Resistance Associated Mutations (RAMs)

**Interpretation**: “Rilpivirine showed non-inferior efficacy compared with efavirenz, with a higher virological-failure rate, but a more favourable safety and tolerability profile.”

Rilpivirine-TDF-FTC versus Efavirenz-TDF-FTC

STaR Trial
Rilpivirine-TDF-FTC versus Efavirenz-TDF-FTC
STaR Study: Design

Study Design: STaR Study

- **Background**: Randomized, open label, phase 3b trial comparing safety and efficacy of two single-tablet regimens, RPV-TDF-FTC and EFV-TDF-FTC, in treatment-naïve adults with HIV

- **Inclusion Criteria (n = 786)**
  - Antiretroviral-naïve adults
  - Age ≥ 18 years
  - HIV RNA ≥ 2500 copies/mL
  - No resistance to EFV, RPV, TDF, or FTC

- **Treatment Arms**
  - Rilpivirine-tenofovir DF-emtricitabine
  - Efavirenz-tenofovir DF-emtricitabine

Rilpivirine-TDF-FTC versusEfavirenz-TDF-FTC
STaR: Result

Week 48 Virologic Response (Intent-to-Treat Analysis)

Rilpivirine-TDF-FTC versus Efavirenz-TDF-FTC

STaR: Result

48 Week Virologic Outcomes

## Treatment Emergent Adverse Events in > 5% of Subjects in Either Arm

<table>
<thead>
<tr>
<th></th>
<th>RPV-TDF-FTC (n = 392)</th>
<th>EFV-TDF-FTC (n = 394)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dizziness</td>
<td>6.6%</td>
<td>22.2%</td>
</tr>
<tr>
<td>Insomnia</td>
<td>9.6%</td>
<td>14.0%</td>
</tr>
<tr>
<td>Somnolence</td>
<td>2.5%</td>
<td>6.9%</td>
</tr>
<tr>
<td>Headache</td>
<td>12.4%</td>
<td>13.5%</td>
</tr>
<tr>
<td>Abnormal Dreams</td>
<td>5.8%</td>
<td>24.5%</td>
</tr>
<tr>
<td>Depression</td>
<td>6.6%</td>
<td>8.9%</td>
</tr>
<tr>
<td>Anxiety</td>
<td>5.1%</td>
<td>8.4%</td>
</tr>
<tr>
<td>Folliculitis</td>
<td>5.3%</td>
<td>1.0%</td>
</tr>
<tr>
<td>Rash</td>
<td>6.1%</td>
<td>12.0%</td>
</tr>
</tbody>
</table>

Conclusion: “In treatment-naive participants, RPV/FTC/TDF demonstrated noninferior efficacy and improved tolerability compared with EFV/FTC/TDF, as well as a statistically significant difference in efficacy for participants with baseline HIV-1 RNA 100,000 copies/ml or less at week 48.”

Rilpivirine-TDF-FTC versus Efavirenz-TDF-FTC
STaR Trial: Week 96 Resistance Data
Rilpivirine-TDF-FTC versus Efavirenz-TDF-FTC
STaR Study: Result

Development of Genotypic Resistance at Week 48

Rilpivirine-TDF-FTC versus Efavirenz-TDF-FTC
STaR Study: Result

Development of Resistance to Study Drugs at 48 weeks, by Viral Load

Conclusions: “Among subjects in the primary resistance associated populations (RAP), resistance development to RPV/FTC/TDF consisted of NNRTI and NRTI mutations and was more frequent than resistance development to EFV/FTC/TDF. In subjects with baseline viral load ≤ 100,000 copies/mL, resistance development was low (<2%) for both RPV/FTC/TDF and EFV/FTC/TDF arms and less frequent compared with subjects with baseline viral load >100,000 copies/mL, for RPV/FTC/TDF.”
Dolutegravir + ABC-3TC versus Efavirenz-TDF-FTC
SINGLE Study
Dolutegravir + ABC-3TC versus Efavirenz-TDF-FTC
SINGLE Study: Design

<table>
<thead>
<tr>
<th>Study Design: SINGLE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Background</strong>: Randomized, double-blind study, phase 3 trial comparing dolutegravir + abacavir-lamivudine with efavirenz-tenofovir DF-emtricitabine</td>
</tr>
<tr>
<td><strong>Inclusion Criteria (n = 833)</strong></td>
</tr>
<tr>
<td>- Antiretroviral-naïve adults</td>
</tr>
<tr>
<td>- Age ≥18</td>
</tr>
<tr>
<td>- HIV RNA ≥1,000 copies/mL</td>
</tr>
<tr>
<td>- No active CDC AIDS condition</td>
</tr>
<tr>
<td><strong>Treatment Arms</strong></td>
</tr>
<tr>
<td>- Dolutegravir (QD) + Abacavir-lamivudine</td>
</tr>
<tr>
<td>- Efavirenz-Tenofovir DF-Emtricitabine</td>
</tr>
</tbody>
</table>

Dolutegravir + ABC-3TC versus Efavirenz-TDF-FTC
SINGLE Study: Result

Week 48 Virologic Response (ITT Analysis)

Dolutegravir + ABC-3TC versus Efavirenz-TDF-FTC
SINGLE Study: Result

Week 48 Virologic Response (ITT Analysis)

<table>
<thead>
<tr>
<th>HIV RNA &lt;50 copies/mL (%)</th>
<th>Dolutegravir + Abacavir-Lamivudine</th>
<th>Efavirenz-Tenofovir DF-Emtricitabine</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>88/414</td>
<td>364/414</td>
</tr>
<tr>
<td>≤100,000 copies/mL</td>
<td>90/280</td>
<td>253/280</td>
</tr>
<tr>
<td>&gt;100,000 copies/mL</td>
<td>83/288</td>
<td>238/288</td>
</tr>
</tbody>
</table>

Discontinuation of therapy due to adverse events:
- Dolutegravir + Abacavir-Lamivudine: 2%
- Efavirenz-Tenofovir-Emtricitabine: 10%

Dolutegravir + ABC-3TC versus Efavirenz-TDF-FTC

SINGLE Study: Result

Mean Change from Baseline in Serum Creatinine Levels

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**Conclusions**: “Dolutegravir plus abacavir-lamivudine had a better safety profile and was more effective through 48 weeks than the regimen with efavirenz-tenofovir DF-emtricitabine.”

Elvitegravir-Cobicistat-TDF-FTC versus Efavirenz-TDF-FTC

Study 102
Elvitegravir-Cobicistat-TDF-FTC versus Efavirenz-TDF-FTC
Study 102: Design

**Study Design: Study 102**

- **Background**: Randomized, double-blind, phase 3 trial comparing elvitegravir-cobicistat-tenofovir DF-emtricitabine with efavirenz-tenofovir DF-emtricitabine

- **Inclusion Criteria (n = 700)**
  - Antiretroviral-naïve adults
  - Age ≥18
  - HIV RNA ≥5,000 copies/mL
  - No AIDS conditions in previous 30 days

- **Treatment Arms**
  - Elvitegravir-Cobicistat-TDF-FTC
  - Efavirenz-TDF-FTC

Elvitegravir-Cobicistat-TDF-FTC versus Efavirenz-TDF-FTC

Study 102: Result

Week 48 Virologic Response: Snapshot Analysis (ITT, Missing=Failure)

### Treatment Emergent Adverse Events in ≥ 10% of Subjects in Either Group

<table>
<thead>
<tr>
<th>Event</th>
<th>EVG-COBI-TDF-FTC (n = 348)</th>
<th>EFV-TDF-FTC (n = 352)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>23%</td>
<td>19%</td>
</tr>
<tr>
<td>Nausea*</td>
<td>21%</td>
<td>14%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>11%</td>
<td>13%</td>
</tr>
<tr>
<td>Upper Respiratory Tract Infection</td>
<td>14%</td>
<td>11%</td>
</tr>
<tr>
<td>Dizziness^</td>
<td>7%</td>
<td>24%</td>
</tr>
<tr>
<td>Headache</td>
<td>14%</td>
<td>10%</td>
</tr>
<tr>
<td>Abnormal Dreams^</td>
<td>15%</td>
<td>27%</td>
</tr>
<tr>
<td>Insomnia&amp;</td>
<td>9%</td>
<td>14%</td>
</tr>
<tr>
<td>Depression</td>
<td>9%</td>
<td>11%</td>
</tr>
<tr>
<td>Rash#</td>
<td>6%</td>
<td>12%</td>
</tr>
</tbody>
</table>

* p < 0.016; ^ p < 0.001; & p < 0.031; # p = 0.009

**Interpretation**: This study met the primary endpoint of non-inferiority of elvitegravir/cobicistat/emtricitabine/tenofovir (EVG/COBI/TDF/FTC) to efavirenz/emtricitabine/tenofovir (EFV/TDF/FTC) and demonstrates the robust antiviral efficacy of the only integrase inhibitor-based single tablet regimen for initial HIV treatment, irrespective of viral load.

SWITCH STUDIES

Efavirenz-Tenofovir DF-Emtricitabine
Switch from Efavirenz + ZDV-3TC to Efavirenz + TDF-FTC

SWEET Trial
Switch to Efavirenz + TDF-FTC
SWEET: Design

Study Design: SWEET Study

- **Background**: Randomized, controlled, open label phase 3 trial evaluating a simplification strategy for patients suppressed on efavirenz-based ART by switching from twice-daily zidovudine-lamivudine to once-daily tenofovir DF-emtricitabine in adults with HIV

- **Inclusion Criteria (n = 234)**
  - Age ≥18 years
  - On EFV + ZDV-3TC for >6 months
  - No resistance to study drugs
  - HIV RNA <400 copies/mL for ≥3 months and HIV RNA <50 copies/mL on 2 occasions

- **Treatment Arms**
  - Efavirenz + TDF-FTC
  - Efavirenz + ZDV-3TC

**Switch arm**
Efavirenz + TDF-FTC QD  
(n = 117)

**Maintain arm**
Efavirenz QD + ZDV-3TC BID  
(n = 117)

Switch to Efavirenz + TDF-FTC
SWEET: Result

Week 48 Virologic Response (ITT Analysis, M=F)

Switch to Efavirenz + TDF-FTC

SWEET: Result

Week 48: Patients with Change in Absolute Hemoglobin from Baseline

Switch to Efavirenz + TDF-FTC

SWEET: Result

Week 24: Change in Limb Fat from Baseline

Switch to Efavirenz + TDF-FTC

SWEET: Result

Week 24: Change in Plasma Lipids from Baseline

<table>
<thead>
<tr>
<th></th>
<th>EFV + TDF-FTC (switch arm)</th>
<th>EFV + ZDV-3TC (maintain arm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Cholesterol</td>
<td>-0.39</td>
<td>-0.06</td>
</tr>
<tr>
<td>HDL</td>
<td>-0.03 -0.02</td>
<td>-0.10 -0.09</td>
</tr>
<tr>
<td>LDL</td>
<td>-0.24</td>
<td>0.05</td>
</tr>
<tr>
<td>Triglycerides</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Change in Median Value (mmol/L)

Switch to Efavirenz + TDF-FTC
SWEET: Result

Week 24: Change in Plasma Lipids, by Baseline Cholesterol (Treated Analysis)

<table>
<thead>
<tr>
<th>Baseline Cholesterol Category (NCEP)</th>
<th>Median Change from Baseline (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 5.2 mmol/L (desirable)</td>
<td>-0.30</td>
</tr>
<tr>
<td>5.2-6.3 mmol/L (borderline)</td>
<td>-0.35</td>
</tr>
<tr>
<td>≥6.3 mmol/L (high)</td>
<td>-0.44</td>
</tr>
</tbody>
</table>

Switch to Efavirenz + TDF-FTC
SWEET: Result

Week 48: Change in Plasma Lipids from Baseline

<table>
<thead>
<tr>
<th></th>
<th>EFV + TDF-FTC (switch arm)</th>
<th>EFV + ZDV-3TC (maintain arm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Cholesterol</td>
<td>-0.22</td>
<td>-0.06</td>
</tr>
<tr>
<td>HDL</td>
<td>0.04</td>
<td>0.01</td>
</tr>
<tr>
<td>LDL</td>
<td>0.14</td>
<td>0.04</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>-0.17</td>
<td>-0.14</td>
</tr>
</tbody>
</table>

Interpretation: “Switching from zidovudine/lamivudine to tenofovir disoproxil fumarate/emtricitabine in persons on efavirenz therapy maintains virological control, establishes a once-daily regimen, results in improvements in hemoglobin and key lipid parameters, and preserves and restores limb fat relative to continuation of zidovudine/lamivudine.”

Simplification to Efavirenz-TDF-FTC

STUDY 073
Simplification to Efavirenz-TDF-FTC Study 073: Design

**Study Design: Study 073**

- **Background**: Randomized, controlled, open label phase 3 trial evaluating a simplification strategy for patients suppressed on baseline ART by switching to a single-tablet regimen of efavirenz-tenofovir DF-emtricitabine once daily.

- **Inclusion Criteria (n = 300)**
  - Age ≥18 years
  - HIV RNA ≤200 copies/mL for ≥3 months
  - No new AIDS-defining conditions in past 30 days
  - On 1st ART regimen or viral suppression on previous protease inhibitor-based therapy at time of prior therapy switch

- **Treatment Arms**
  - Switch arm: Efavirenz-tenofovir DF-emtricitabine
  - Stay arm: maintain baseline ART

**Switch arm**
Efavirenz-TDF-FTC QD (n = 203)

**Maintain arm**
Stay on Baseline ART (n = 97)

Simplification to Efavirenz-TDF-FTC
Study 073: Result

Week 48 Virologic Response by RNA Threshold

Simplification to Efavirenz-TDF-FTC
Study 073: Subgroup Analysis Result

Week 48 Virologic Response, by Baseline Regimen (ITT Analysis, NC=F)

Interpretation: “Simplification to EFV/FTC/TDF maintained high and comparable rates of virologic suppression versus stay on baseline regimen (SBR) through 48 weeks.”
Switch from EFV + ZDV-3TC versus EFV + TDF-FTC
COMET Trial
Switch from Efavirenz + AZT-3TC to Efavirenz + TDF-FTC

COMET: Study Design

**Study Design: COMET Study**

- **Background**: Prospective, single-arm 24-week phase 4 switch study evaluating of switching from twice daily zidovudine-lamivudine to once daily tenofovir DF-emtricitabine in virologically suppressed patients on efavirenz

- **Inclusion Criteria (n = 402)**
  - Age ≥18 years
  - On EFV + ZDV-3TC for ≥8 weeks
  - HIV RNA <400 copies/mL
  - CrCl ≥ 50 mL/min

- **Treatment (Switch) Arm**
  - Efavirenz-tenofovir DF-emtricitabine

Switch from Efavirenz + AZT-3TC to Efavirenz + TDF-FTC

COMET: Result

Week 24: Virologic Response

Virologic Suppression (%)

Virologic Suppression Threshold

Switch from Efavirenz + AZT-3TC to Efavirenz + TDF-FTC

COMET: Result

Week 24: Immunologic Response

Switch from Efavirenz + AZT-3TC to Efavirenz + TDF-FTC

COMET: Result

Week 24: Patient-Reported Outcomes

Switch from Efavirenz + AZT-3TC to Efavirenz + TDF-FTC

COMET: Conclusions

**Interpretation:** “Patients switched to EFV + TDF/FTC maintained virologic suppression and the regimen was well tolerated. Patients reported increased satisfaction with treatment and fewer were bothered by side effects.”

Switch from EFV plus ABC-3TC to EFV-TDF-FTC

ROCKET-1 Trial
Switch from EFV + ABC-3TC to EFV-TDF-FTC

ROCKET-1: Design

Study Design: ROCKET Study

- **Background**: Randomized, open label, phase 4 trial to assess the effect on lipid profile of switching from EFV plus ABC-3TC to EFV-TDF-FTC in hypercholesterolemic adults with HIV

- **Inclusion Criteria** (n = 157)
  - Age >18 years
  - On EFV plus ABC-3TC for ≥3 months
  - HIV RNA <50 copies/mL
  - Total cholesterol >200 mg/dL x 2 consecutive tests (at least 4 weeks apart)
  - No resistance to study drugs

- **Treatment Arms**
  - Efavirenz-tenofovir DF-emtricitabine
  - Efavirenz plus abacavir-lamivudine x 12 weeks, then efavirenz-tenofovir DF-emtricitabine

Switch from EFV + ABC-3TC to EFV-TDF-FTC

ROCKET-1: Result

Week 12: Virologic Response (Intent-to-Treat Analysis)

Switch from EFV + ABC-3TC to EFV-TDF-FTC

ROCKET-1: Result

Week 12: Changes in Lipid Fractions (Treated Analysis Set)

Baseline for Delayed switch arm was reset at week 12 (prior to switch to EFV-TDF-FTC)

Switch from EFV + ABC-3TC to EFV-TDF-FTC
ROCKET-1: Result

Fasting Total Cholesterol by NCEP Thresholds

<table>
<thead>
<tr>
<th>Threshold</th>
<th>Week 12</th>
<th>Week 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5.2 mmol/L (desirable)</td>
<td>65</td>
<td>32</td>
</tr>
<tr>
<td>5.2-6.2 mmol/L (borderline)</td>
<td>29</td>
<td>43</td>
</tr>
<tr>
<td>&gt;6.2 mmol/L (above goal)</td>
<td>25</td>
<td>42</td>
</tr>
</tbody>
</table>

Patients (%)

Baseline

Week 12

Week 24

Patients in Immediate Switch Arm

Switch from EFV + ABC-3TC to EFV-TDF-FTC
ROCKET-1: Result

Fasting Total Cholesterol by NCEP Thresholds

Switch from EFV + ABC-3TC to EFV-TDF-FTC
ROCKET-1: Result

Fasting Total Cholesterol by NCEP Thresholds

Switch from EFV + ABC-3TC to EFV-FTC-TDF

ROCKET-1: Conclusions

**Interpretation:** “Switching from ABC/3TC+EFV to EFV/FTC/TDF in persons with hypercholesterolemia maintains virological control and significantly improves key lipid parameters.”

Simplification to Efavirenz-Tenofovir DF-Emtricitabine
ADONE Trial
Simplification to Efavirenz-Tenofovir DF-Emtricitabine
ADONE: Study Design

Study Design: ADONE Study

- **Background:** Prospective, comparative, open-label study evaluating the advantages of switching to one-pill-once a day with efavirenz-tenofovir DF-emtricitabine

- **Inclusion Criteria (n = 212)**
  - Stable on ART with EFV + TDF + FTC (or 3TC)
  - HIV RNA <50 copies/mL

- **Treatment (Switch) Arm**
  - Efavirenz-Tenofovir DF-Emtricitabine

Simplification to Efavirenz-Tenofovir DF-Emtricitabine
ADONE: Result

Week 48 Virologic Response (ITT Analysis, M=F)

Simplification to Efavirenz-Tenofovir DF-Emtricitabine
ADONE: Result

Week 48 CD4 Cell Count Response

Simplification to Efavirenz-Tenofovir DF-Emtricitabine
ADONE: Result

Improvement in Adherence Following Switch to One-Pill-Once-A-Day

Interpretation: “By substituting a one-pill once-a-day HAART, we observed an improvement of both adherence and QoL while maintaining high virologic and immunologic efficacy. HAART simplicity is an added value that favors adherence and may improve long-term success.”
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