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
- HIV RNA ≥ 5000 copies/mL
- No resistance to EFV, TDF, or FTC

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

### Study Design

<table>
<thead>
<tr>
<th>Arm</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raltegravir BID + TDF-FTC QD</td>
<td>(n = 281)</td>
</tr>
<tr>
<td>Efavirenz + TDF-FTC QD</td>
<td>(n = 282)</td>
</tr>
</tbody>
</table>

Raltegravir + TDF-FTC versus Efavirenz + TDF-FTC

STARTMRK: Results

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

Raltegravir + TDF-FTC versus Efavirenz + TDF-FTC
STARTMRK: Results

Week 48: Virologic Response (Observed-Failure Method)

Raltegravir + TDF-FTC versus Efavirenz + TDF-FTC

STARTMRK: Results

Week 48: Virologic Response

**HIV RNA < 50 copies/mL (%)**

![Graph showing virologic response over time with Raltegravir + TDF-FTC and Efavirenz + TDF-FTC compared.]

Raltegravir + TDF-FTC versus Efavirenz + TDF-FTC

STARTMRK: Results

Adverse Events through 48 Weeks

Raltegravir + TDF-FTC versus Efavirenz + TDF-FTC

STARTMRK: Results

Week 48: Changes in Lipid Concentrations

<table>
<thead>
<tr>
<th></th>
<th>Mean Change from Baseline (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Cholesterol</td>
<td>0.55 (-0.16)</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>1.82 (0.23)</td>
</tr>
<tr>
<td>HDL</td>
<td>2.08 (0.56)</td>
</tr>
<tr>
<td>LDL</td>
<td>0.33 (0.89)</td>
</tr>
</tbody>
</table>

### Raltegravir + TDF-FTC versus Efavirenz + TDF-FTC

**STARTMRK: Common Adverse Events**

<table>
<thead>
<tr>
<th>Treatment Emergent Adverse Events in &gt; 10% of Subjects in Either Arm</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>

Raltegravir + TDF-FTC versus Efavirenz + TDF-FTC
STARTMRK: Conclusions

**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.”

Raltegravir + TDF-FTC versus Efavirenz + TDF-FTC

STARTMRK Trial: 156 Week Data
Week 156: Virologic Response (Observed Failure Method)

- **Overall**: 85% (192/227) for Efavirenz + TDF-FTC, 89% (212/237) for Raltegravir + TDF-FTC.
- **≤ 100,000 copies/mL**: 84% (93/111) for Efavirenz + TDF-FTC, 94% (99/105) for Raltegravir + TDF-FTC.
- **> 100,000 copies/mL**: 85% (99/116) for Efavirenz + TDF-FTC, 86% (113/132) for Raltegravir + TDF-FTC.

Conclusions: “When combined with tenofovir/emtricitabine in treatment-naive patients, raltegravir produced durable viral suppression and immune restoration that was at least equivalent to efavirenz through 156 weeks of therapy. Both regimens were well tolerated, but raltegravir was associated with fewer drug-related clinical adverse events and smaller elevations in lipid levels.”
Raltegravir + TDF-FTC versus Efavirenz + TDF-FTC

STARTMRK Trial: 240 Week Data
Week 240: Virologic Response (Observed Failure Method)

Conclusions: “In this exploratory analysis of combination therapy with tenofovir/emtricitabine in treatment-naïve patients at week 240, vRNA suppression rates and increases in baseline CD4 counts were significantly higher in raltegravir than efavirenz recipients. Over the entire study, fewer patients experienced neuropsychiatric and drug-related adverse events in the raltegravir group than in the efavirenz group. Based on better virologic and immunologic outcomes after 240 weeks, raltegravir/tenofovir/emtricitabine seemed to have superior efficacy compared with efavirenz/tenofovir/emtricitabine.”
The National HIV Curriculum is an AIDS Education and Training Center (AETC) Program resource funded by the United States Health Resources and Services Administration. The project is led by the University of Washington and the AETC National Coordinating Resource Center.

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