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 for persons with HIV.

**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

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

**STARTMRK: Result**

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

![Bar graph showing virologic response at week 48.](image)

- **Raltegravir + TDF-FTC**: 86% (241/281)
- **Efavirenz + TDF-FTC**: 82% (230/282)

Raltegravir + TDF-FTC versus Efavirenz + TDF-FTC

STARTMRK: Result

Week 48 Virologic Response (Observed-Failure Method)

<table>
<thead>
<tr>
<th>Baseline HIV RNA Level</th>
<th>Raltegravir + TDF-FTC</th>
<th>Efavirenz + TDF-FTC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>92/241/263</td>
<td>89/230/258</td>
</tr>
<tr>
<td>≤100,000 copies/mL</td>
<td>93/111/120</td>
<td>89/114/128</td>
</tr>
<tr>
<td>&gt;100,000 copies/mL</td>
<td>91/130/143</td>
<td>89/116/130</td>
</tr>
</tbody>
</table>

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>Adverse 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.”
Raltegravir + TDF-FTC versus Efavirenz + TDF-FTC

STARTMRK Trial: 156 Week Data
Raltegravir versus Efavirenz in Combination Therapy

STARTMRK: Results at Week 156

Week 156: Virologic Response (Observed Failure Method)

**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)

<table>
<thead>
<tr>
<th>Baseline HIV RNA level</th>
<th>Efavirenz + TDF-FTC</th>
<th>Raltegravir + TDF-FTC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>81/279</td>
<td>89/279</td>
</tr>
<tr>
<td>≤100,000 copies/mL</td>
<td>80/102</td>
<td>92/98</td>
</tr>
<tr>
<td>&gt;100,000 copies/mL</td>
<td>91/110</td>
<td>106/124</td>
</tr>
</tbody>
</table>

**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.”

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