Elvitegravir-Cobicistat-Tenofovir DF-Emtricitabine (Stribild)

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Elvitegravir-Cobicistat-Tenofovir DF-Emtricitabine

Dose: 1 tablet once daily with food
Elvitegravir-Cobicistat-Tenofovir DF-Emtricitabine

- **Stribild Components**:  
  - Elvitegravir 150 mg  
  - Cobicistat 150 mg  
  - Emtricitabine 200 mg  
  - Tenofovir disoproxil fumarate 300 mg

- **Dosing**: 1 pill daily with food (separate ≥ 2 hours with antacids)

- **With Renal Impairment**:  
  - Do *not* initiate if CrCl <70 mL/min  
  - Discontinue if CrCl <50 mL/min

- **Pregnancy**: category B

- **Common Adverse Events (≥5%)**:  
  - Nausea, diarrhea, abnormal dreams, headache, and fatigue
## Elvitegravir-Cobicistat-Tenofovir DF-Emtricitabine
### Summary of Key Phase 3 Studies

<table>
<thead>
<tr>
<th>Trials in Treatment Naïve</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Study 102: EVG-COBI-TDF-FTC vs. EFV-TDF-FTC</td>
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<td>Study 103: EVG-COBI-TDF-FTC vs. RTV + ATV + TDF-FTC</td>
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<td>Study 128 (WAVES): EVG-COBI-TDF-FTC vs. RTV + ATV + TDF-FTC</td>
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<table>
<thead>
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<th>Switch Trials</th>
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<tbody>
<tr>
<td>Study 115 (STRATEGY PI): PI Switch to EVG-COBI-TDF-FTC</td>
<td></td>
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<tr>
<td>Study 121 (STRATEGY NNRTI): NNRTI Switch to EVG-COBI-TDF-FTC</td>
<td></td>
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<tr>
<td>Study 123: Raltegravir Switch</td>
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</tbody>
</table>

**Abbreviations**: EVG-COBI-TDF-FTC = elvitegravir-cobicistat-tenofovir DF-emtricitabine; EFV-TDF-FTC = efavirenz-tenofovir DF-emtricitabine; RTV = ritonavir; ATV = atazanavir; TDF-FTC = tenofovir DF-emtricitabine; EVG-COBI-TAF-FTC = elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine; PI = protease inhibitor; NNRTI = non-nucleoside reverse transcriptase inhibitor
Initial Therapy

Elvitegravir-Cobicistat-Tenofovir DF-Emtricitabine
Elvitegravir-Cobicistat-TDF-FTC versus Efavirenz-TDF-FTC

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

• **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 years
  - 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

Elvitegravir-Cobicistat-TDF-FTC versus Efavirenz-TDF-FTC
Study 102: Common Adverse Events

<table>
<thead>
<tr>
<th>Treatment Emergent Adverse Events in ≥ 10% of Subjects in Either Group</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†</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

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

**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.”

EVG-COBI-TDF-FTC versus ATV + RTV + TDF-FTC

Study 103
Elvitegravir-Cobicistat-TDF-FTC versus Atazanavir + Ritonavir + TDF-FTC
Study 103: Design

• **Background**: Randomized, double-blind, phase 3 trial comparing elvitegravir-cobicistat-tenofovir-emtricitabine with atazanavir + ritonavir + tenofovir DF-emtricitabine

• **Inclusion Criteria** (n = 708)
  - Antiretroviral-naïve adults
  - Age ≥18 years
  - HIV RNA ≥5,000 copies/mL
  - Any CD4 count

• **Treatment Arms**
  - Elvitegravir-Cobicistat-TDF-FTC
  - Atazanavir + RTV + TDF-FTC

Elvitegravir-Cobicistat-TDF-FTC versus Atazanavir + RTV + TDF-FTC
Study 103: Results

Week 48 Virologic Response

DeJesus E, et al. 19th IAC. 2012; Abstract TUPE43.
## Elvitegravir-Cobicistat-TDF-FTC versus Atazanavir + RTV + TDF-FTC

### Study 103: Common Adverse Events

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

<table>
<thead>
<tr>
<th></th>
<th>EVG-COBI-TDF-FTC (n = 353)</th>
<th>ATV + RTV + TDF-FTC (n= 355)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>22%</td>
<td>27%</td>
</tr>
<tr>
<td>Nausea*</td>
<td>20%</td>
<td>19%</td>
</tr>
<tr>
<td>Upper Respiratory Tract Infection</td>
<td>15%</td>
<td>16%</td>
</tr>
<tr>
<td>Headache</td>
<td>15%</td>
<td>12%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>14%</td>
<td>13%</td>
</tr>
<tr>
<td>Ocular Icterus*</td>
<td>1%</td>
<td>14%</td>
</tr>
</tbody>
</table>

* *p < 0.001

**Elvitegravir-Cobicistat-TDF-FTC versus Atazanavir + RTV + TDF-FTC**

**Study 103: Conclusions**

**Interpretation:** “This study met the primary endpoint of non-inferiority of elvitegravir/cobicistat/emtricitabine/tenofovir (EVG/COBI/FTC/TDF) to atazanavir plus ritonavir plus emtricitabine/tenofovir (ATV + RTV + FTC/TDF) and demonstrates the robust antiviral efficacy of the only integrase inhibitor-based single tablet regimen for initial HIV treatment.”

EVG-COBI-TAF-FTC versus EVG-COBI-TDF-FTC

Study 104 and Study 111
**Background:** Randomized, double-blind, phase 3 trial comparing elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine with elvitegravir-cobicistat-tenofovir DF-emtricitabine

**Inclusion Criteria (n = 1,733)**
- Antiretroviral-naïve patients
- Age >18
- HIV RNA ≥1000 copies/mL
- Any CD4 count allowed
- No AIDS conditions in prior 30 days

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

EVG-COBI-TAF-FTC versus EVG-COBI-TDF-FTC
Study 104/111: Result

Week 48 Virologic Response

Week 48 Change in Serum Creatinine from Baseline

EVG-COBI-TAF-FTC versus EVG-COBI-TDF-FTC
Study 104/111: Adverse Effects

Week 48 Changes in Quantitative Proteinuria from Baseline

Week 48 Changes in Spine and Hip Bone Mineral Density (BMD)

<table>
<thead>
<tr>
<th></th>
<th>Hip</th>
<th>Spine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tenofovir alafenamide arm</td>
<td>-1.30</td>
<td>-2.86</td>
</tr>
<tr>
<td>Tenofovir DF arm</td>
<td>-0.66</td>
<td>-2.95</td>
</tr>
</tbody>
</table>

### Week 48 Changes in Lipid Parameters

<table>
<thead>
<tr>
<th>Median Change from Baseline to Week 48</th>
<th>EVG-COBI-TAF-FTC (n = 866)</th>
<th>EVG-COBI-TDF-FTC (n = 867)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol</td>
<td>+29</td>
<td>+14</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LDL</td>
<td>+14</td>
<td>+5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HDL</td>
<td>+8</td>
<td>+4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>+19</td>
<td>+8</td>
<td>0.027</td>
</tr>
<tr>
<td>Total cholesterol:HDL ratio</td>
<td>+0.1</td>
<td>+0.1</td>
<td>0.84</td>
</tr>
</tbody>
</table>

**Interpretation**: “Through 48 weeks, more than 90% of patients given E/C/F/tenofovir alafenamide or E/C/F/tenofovir disoproxil fumarate had virological success. Renal and bone effects were significantly reduced in patients given E/C/F/tenofovir alafenamide. Although these studies do not have the power to assess clinical safety events such as renal failure and fractures, our data suggest that E/C/F/tenofovir alafenamide will have a favourable long-term renal and bone safety profile.”

EVG-COBI-TDF-FTC versus ATV + RTV + TDF-FTC in Women

Study 128 (WAVES)
**EVG-COBI-TDF-FTC versus ATV + RTV + TDF-FTC (in Women) WAVES Study: Design**

- **Background**: Randomized, double-blind, phase 3 trial comparing elvitegravir-cobicistat-tenofovir-emtricitabine with atazanavir + ritonavir + tenofovir DF-emtricitabine in women.

- **Inclusion Criteria** (n = 575)
  - Antiretroviral-naïve women
  - Age ≥18 years
  - HIV RNA ≥500 copies/mL
  - Any CD4 count

- **Treatment Arms**
  - Elvitegravir-Cobicistat-TDF-FTC
  - Atazanavir + Ritonavir + TDF-FTC

EVG-COBI-TDF-FTC versus ATV + RTV + TDF-FTC (in Women)
WAVES Study: Result

Week 48 Virologic Response

EVG-COBI-TDF-FTC versus ATV + RTV + TDF-FTC (in Women)
WAVES Study: Result

Week 48 Virologic Response

**Table: Treatment Emergent Adverse Events in ≥ 10% of Subjects in Either Group**

<table>
<thead>
<tr>
<th>Event</th>
<th>EVG-COBI-TDF-FTC (n = 289)</th>
<th>ATV + RTV + TDF-FTC (n = 286)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>16%</td>
<td>15%</td>
</tr>
<tr>
<td>Upper Respiratory Tract Infection</td>
<td>16%</td>
<td>15%</td>
</tr>
<tr>
<td>Malaria</td>
<td>11%</td>
<td>8%</td>
</tr>
<tr>
<td>Nausea</td>
<td>15%</td>
<td>14%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>10%</td>
<td>6%</td>
</tr>
<tr>
<td>Jaundice</td>
<td>&lt;1%</td>
<td>11%</td>
</tr>
<tr>
<td>Icterus</td>
<td>&lt;1%</td>
<td>12%</td>
</tr>
</tbody>
</table>

Interpretation: “WAVES shows that clinical trials of ART regimens in global and diverse populations of treatment-naive women are possible. The findings support guidelines recommending integrase inhibitor based regimens in first-line antiretroviral therapy.”

Elvitegravir-Cobicistat-Tenofovir DF-Emtricitabine

Switch Studies
Switch from PI-Based Regimen to EVG-COBI-TDF-FTC

Study 115 (STRATEGY-PI)
Switch from PI-Based Regimen to EVG-COBI-TDF-FTC
STRATEGY-PI: Design

**Background**: Open-label, randomized, phase 3b trial comparing switch to elvitegravir-cobicistat-tenofovir DF-emtricitabine versus continuation of baseline regimen of ritonavir + PI + tenofovir DF-emtricitabine

**Inclusion Criteria** (n = 433)
- HIV RNA <50 copies/mL on ART for ≥6 months
- Baseline regimen of RTV + PI + TDF-FTC
- No prior virologic failure
- No resistance to TDF or FTC
- CrCl ≥70 mL/min

**Treatment Arms**
- EVG-COBI-TDF-FTC (Switch group)
- Remain on RTV + PI + TDF-FTC (No switch group)

*NOTE*: 3 participants from switch group and 1 from no switch group were excluded from study after screening for protocol violations.

Switch from PI-Based Regimen to EVG-COBI-TDF-FTC
STRATEGY-PI: Result

Week 48 Virologic Response

Interpretation: “Coformulated elvitegravir, cobicistat, emtricitabine, and tenofovir might be a useful regimen simplification option for virologically suppressed adults with HIV taking a multi-tablet ritonavir-boosted protease inhibitor regimen.”
Switch from NNRTI-Based Regimen to EVG-COBI-TDF-FTC

Study 121 (STRATEGY-NNRTI)
Switch from NNRTI-Based Regimen to EVG-COBI-TDF-FTC

STRATEGY-NNRTI: Design

**Background**: Open-label, randomized, phase 3b trial comparing switch to elvitegravir-cobicistat-tenofovir DF-emtricitabine versus continuation of baseline regimen of NNRTI + TDF-FTC

**Inclusion Criteria** (n = 439)
- HIV RNA <50 copies/mL on ART for ≥6 months
- Baseline regimen of NNRTI + TDF-FTC
- No prior virologic failure
- No resistance to TDF or FTC
- CrCl ≥70 mL/min

**Treatment Arms**
- EVG-COBI-FTC-TDF (Switch group)
- Remain on NNRTI + FTC-TDF (No switch group)

*NOTE: 2 participants from switch group and 4 participants from no-switch group were excluded from the study after screening (2 protocol violation, 1 non-adherence, 3 withdrew consent)

Switch from NNRTI-Based Regimen to EVG-COBI-TDF-FTC
STRATEGY-NNRTI: Results

Week 48 Virologic Response

Switch from NNRTI-Based Regimen to EVG-COBI-TDF-FTC
STRATEGY-NNRTI: Results

Week 48 Virologic Response, Subgroup Analysis, by Baseline NNRTI Regimen

<table>
<thead>
<tr>
<th>HIV RNA &lt;50 copies/mL (%)</th>
<th>Efavirenz</th>
<th>Nevirapine or Rilpivirine</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVG-COBI-TDF-FTC (Switch)</td>
<td>93/214</td>
<td>97/57</td>
</tr>
<tr>
<td>NNRTI + TDF-FTC (No switch)</td>
<td>86/91</td>
<td>95/35</td>
</tr>
</tbody>
</table>

Switch from NNRTI-Based Regimen to EVG-COBI-TDF-FTC STRATEGY-NNRTI: Results

Week 48 Virologic Response, Subgroup Analysis, by Baseline NNRTI Regimen

Switch from NNRTI-Based Regimen to EVG-COBI-TDF-FTC
STRATEGY-NNRTI: Conclusions

**Interpretation:** “Coformulated elvitegravir, cobicistat, emtricitabine, and tenofovir seems to be efficacious and well tolerated in virologically suppressed adults with HIV and might be a suitable alternative for patients on an NNRTI with emtricitabine and tenofovir regimen considering a regimen modification or simplification.”

Switch to Elvitegravir-Cobicistat-Tenofovir DF-Emtricitabine

Study 123
Switch to Elvitegravir-Cobicistat-Tenofovir DF-Emtricitabine
Study 123: Study Design

• **Background:** Open-label, randomized phase 3b trial evaluating switching to once-daily elvitegravir-cobicistat-tenofovir DF-emtricitabine from twice daily raltegravir plus tenofovir DF-emtricitabine

• **Inclusion Criteria** (n = 48)
  - HIV RNA <50 copies/mL
  - On RAL+ TDF-FTC for ≥6 months
  - Not taking any other ART
  - No new AIDS-defining conditions

• **Treatment Arms**
  - Switch to EVG-COBI-TDF-FTC

Switch to Elvitegravir-Cobicistat-Tenofovir DF-Emtricitabine Study 123: Results

Virologic Response After Switch to EVG-COBI-TDF-FTC

Switch to Elvitegravir-Cobicistat-Tenofovir DF-Emtricitabine
Study 123: Common Adverse Events

<table>
<thead>
<tr>
<th>Adverse Event (treatment emergent)</th>
<th>Switched to EVG-COBI-TDF-FTC (n = 48)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper Respiratory Tract Infection</td>
<td>21%</td>
</tr>
<tr>
<td>Insomnia</td>
<td>13%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>10%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>10%</td>
</tr>
<tr>
<td>Anxiety</td>
<td>10%</td>
</tr>
</tbody>
</table>

Conclusion: “All participants switching to 1 tablet once-a-day elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate (Stribild) from a twice-daily raltegravir + emtricitabine/tenofovir disoproxil fumarate regimen remained virologically suppressed. Stribild was well tolerated. Switching to Stribild may be a viable option for virologically suppressed patients wanting to simplify from a twice-daily raltegravir-containing regimen.”
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