Elvitegravir-Cobicistat-Tenofovir alafenamide-Emtricitabine (Genvoya)

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Elvitegravir-Cobicistat-Tenofovir Alafenamide-Emtricitabine

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

- **Genvoya Components**
  - Elvitegravir 150 mg
  - Cobicistat 150 mg
  - Tenofovir alafenamide 10 mg
  - Emtricitabine 200 mg

- **Dosing:** 1 pill daily with food

- **With Renal Impairment:** Do not initiate if CrCl <30 mL/min

- **Pregnancy:** insufficient data

- **Common Adverse Events (≥5%):** Nausea (10%), diarrhea (7%), headache (6%), and fatigue (5%)

Source: Elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine. Prescribing Information.
Elvitegravir-Cobicistat-Tenofovir alafenamide-Emtricitabine
Summary of Key Phase 3 Studies

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**Abbreviations:**
- EVG-COBI-TAF-FTC = elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine;
- EVG-COBI-TDF-FTC = elvitegravir-cobicistat-tenofovir DF-emtricitabine;
- TDF = tenofovir DF;
- TAF = tenofovir alafenamide;
- DRV = darunavir
Elvitegravir-Cobicistat-Tenofovir Alafenamide-Emtricitabine

Trials in Treatment-Naïve Adults
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 (Intent-to-Treat Analysis)

<table>
<thead>
<tr>
<th>Baseline HIV RNA</th>
<th>EVG-COBI-TAF-FTC</th>
<th>EVG-COBI-TDF-FTC</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>800/866</td>
<td>784/867</td>
</tr>
<tr>
<td>≤100,000 copies/mL</td>
<td>629/670</td>
<td>610/672</td>
</tr>
<tr>
<td>&gt;100,000 copies/mL</td>
<td>171/196</td>
<td>174/195</td>
</tr>
</tbody>
</table>

HIV RNA <50 copies/mL (%)

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)

- **Hip**
  - Tenofovir alafenamide arm: -1.30%
  - Tenofovir DF arm: -2.86%

- **Spine**
  - Tenofovir alafenamide arm: -0.66%
  - Tenofovir DF arm: -2.95%

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

#### Study 104/111: Adverse Effects

#### 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.”

Elvitegravir-Cobicistat-Tenofovir Alafenamide-Emtricitabine

Switch Studies in Special Populations
Elvitegravir-Cobicistat-TAF-FTC in Renal Impairment

Study 112
Elvitegravir-Cobicistat-TAF-FTC in Renal Impairment Study 112: Design

**Background**: Open-label, single-arm, phase 3 trial evaluating switching to once-daily elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine from baseline ART*

**Inclusion Criteria** (n = 242)
- HIV RNA < 50 copies/mL for ≥6 months
- eGFR stable at 30-69 mL/min ≥3 months
- CD4 ≥50 cells/mm3
- No new AIDS conditions in past 30 days
- No resistance to EVG, FTC, or TDF

**Treatment Arms**
- Switch to EVG-COBI-TAF-FTC

*Baseline ART*

NRTIs: Tenofovir DF 65%, Abacavir 22%, Other NRTI 7%, No NRTI 5%
Third Agent: PI 44%, NNRTI 42%, INSTI 24%, CCR5 Antagonist 3%

Elvitegravir-Cobicistat-TAF-FTC in Renal Impairment
Study 112: Result

Week 48 Virologic Response

Elvitegravir-Cobicistat-TAF-FTC in Renal Impairment Study 112: Subgroup Analysis Result

Change in Estimated GFR* from Baseline to Weeks 24 and 48

*GFR estimated by Cockcroft Gault

Elvitegravir-Cobicistat-TAF-FTC in Renal Impairment Study 112: Result

Week 48: Changes in General Proteinuria

Median Change in Proteinuria (mg/g)

<table>
<thead>
<tr>
<th>Proteinuria (UPCR)</th>
<th>Baseline</th>
<th>Week 48</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>161</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Albuminuria (UACR)</th>
<th>Baseline</th>
<th>Week 48</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>29</td>
<td>10</td>
</tr>
</tbody>
</table>

Elvitegravir-Cobicistat-TAF-FTC in Renal Impairment Study 112: Result

Week 48: Changes in Tubular Proteinuria

Elvitegravir-Cobicistat-TAF-FTC in Renal Impairment Study 112: Result

Week 48: Changes in Bone Mineral Density (BMD)

Elvitegravir-Cobicistat-TAF-FTC in Renal Impairment
Study 112: Result

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

Spine

- 4% Loss ≥3%
- 37% Gain or loss <3%
- 59% ≥ 3% gain

Hip

- 6% Loss ≥3%
- 22% Gain or loss <3%
- 72% ≥ 3% gain

Interpretation: “Switch to E/C/F/TAF was associated with minimal change in GFR. Proteinuria, albuminuria and bone mineral density significantly improved. These data support the efficacy and safety of once daily E/C/F/TAF in HIV+ patients with mild or moderate renal impairment without dose adjustment.”
Elvitegravir-Cobicistat-TAF-FTC in Hepatitis B Coinfection

Study 1249
Elvitegravir-Cobicistat-TAF-FTC in HIV/HBV Coinfection Study 1249: Design

- **Background**: Open-label, single-arm, phase 3b trial evaluating switching to once-daily elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine in adults with HIV and HBV

- **Inclusion Criteria** (n = 72)
  - Adults with HIV and chronic HBV
  - HIV RNA <50 copies/mL for ≥6 months
  - Stable ART regimen for ≥4 months
  - CD4 ≥200 cells/mm³
  - CrCl ≥50 mL/min, ALT ≤10x ULN
  - No cirrhosis, HCC, HCV, hepatitis D

- **Treatment Arms**
  - Switch to EVG-COBI-TAF-FTC

Elvitegravir-Cobicistat-TAF-FTC in HIV/HBV Coinfection
Study 1249: Result

HIV Efficacy at Weeks 24 and 48

Elvitegravir-Cobicistat-TAF-FTC in HIV/HBV Coinfection Study 1249: Result

HBV Efficacy at Weeks 24 and 48, Missing = Failure

<table>
<thead>
<tr>
<th></th>
<th>Week 24</th>
<th>Week 48</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV DNA &lt;29 IU/mL</td>
<td>86</td>
<td>92</td>
</tr>
<tr>
<td>HBV DNA ≥29 IU/mL</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Data Missing</td>
<td>4</td>
<td>6</td>
</tr>
</tbody>
</table>

Elvitegravir-Cobicistat-TAF-FTC in HIV/HBV Coinfection Study 1249: Subgroup Analysis Result

ALT Measurement at Weeks 24 and 48

<table>
<thead>
<tr>
<th></th>
<th>Baseline ALT &gt;ULN</th>
<th>Baseline ALT normal</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Week 24</strong></td>
<td>5/10 (50%)</td>
<td>54/62 (87%)</td>
</tr>
<tr>
<td><strong>Week 48</strong></td>
<td>4/10 (40%)</td>
<td>57/62 (92%)</td>
</tr>
</tbody>
</table>

Changes in General Proteinuria at Weeks 24 and 48 from Baseline

Elvitegravir-Cobicistat-TAF-FTC in HIV/HBV Coinfection
Study 1249: Result

Changes in Tubular Proteinuria at Weeks 24 and 48 from Baseline

- RBP:Cr = retinol binding protein:creatinine ratio
- β2M:Cr = beta-2 microalbumin:creatinine ratio

Interpretation: “In this first study in HIV/HBV-coinfected participants with suppressed HIV infection, E/C/F/TAF was effective against HIV and HBV, well tolerated, and demonstrated improvements in renal and bone safety consistent with the clinical profile of TAF. These data support the use of E/C/F/TAF in treating HIV/HBV coinfections.”
Switch from TDF-based ART to Elvitegravir-Cobicistat-TAF-FTC

Study 109
Switch to Elvitegravir-Cobicistat-TAF-FTC
Study 109: Design

- **Background**: Open-label, randomized, phase 3 trial comparing switch to EVG-COBI-TAF-FTC versus continuation of baseline regimen of TDF-based ART

- **Inclusion Criteria** (n = 1443)
  - HIV RNA < 50 copies/mL on ART for ≥96 weeks
  - CrCl >50 mL/min
  - 1 of 4 baseline TDF-containing ART regimens:
    - EVG-COBI-TDF-FTC (n=459)
    - EFV-TDF-FTC (n=376)
    - ATV + RTV + TDF-FTC (n=385)
    - ATV-COBI + TDF-FTC (n=216)

- **Treatment Arms**
  - EVG-COBI-TAF-FTC (Switch group)
  - Remain on TDF-based ART (No switch group)

*NOTE*: Between randomization and study onset, 4 participants withdrew consent, 2 withdrew by investigator discretion, and 1 was lost to follow-up.

Switch to Elvitegravir-Cobicistat-TAF-FTC
Study 109: Subgroup Analysis Result

Week 48 Virologic Response, by Baseline Regimen

Switch to Elvitegravir-Cobicistat-TAF-FTC
Study 109: Result

Week 48: Changes in Bone Mineral Density (BMD)

Switch to Elvitegravir-Cobicistat-TAF-FTC
Study 109: Result

Week 48: Changes in Quantitative Proteinuria from Baseline

Switch to Elvitegravir-Cobicistat-TAF-FTC Study 109: Result

Week 48: Change in Plasma Lipids from Baseline

Interpretation: “Switching to a tenofovir alafenamide-containing regimen from one containing tenofovir disoproxil fumarate was non-inferior for maintenance of viral suppression and led to improved bone mineral density and renal function. Longer term follow-up is needed to better understand the clinical impact of these changes.”

Simplification to EVG-COBI-TAF-FTC plus Darunavir

Study 119
Simplification to EVG-COBI-TAF-FTC plus DRV
Study 119: Design

**Background**: Open-label, randomized, phase 3 trial comparing simplification to EVG-COBI-TAF-FTC plus darunavir versus continuation of baseline salvage ART regimen containing darunavir

**Inclusion Criteria** (n = 135)
- HIV RNA <50 copies/mL on DRV-containing regimen
- On regimen for ≥4 months
- At least 2 prior regimen failures and ≥2-class DRMs
- No DRV RAMs, no INSTI resistance, ≤3 TAMs, no Q151M or T69 insertion

**Treatment Arms**
- EVG-COBI-TAF-FTC + DRV (Switch group)
- Remain on baseline ART (No switch group)

*Abbreviations*: RAM = resistance associated mutation, INSTI = integrase strand transfer inhibitor, TAM’s = thymidine analogue mutations

### Simplification to EVG-COBI-TAF-FTC plus DRV

Study 119: Design

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>EVG-COBI-TAF-FTC + DRV (n = 89)</th>
<th>Baseline Regimen (n = 46)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, years</td>
<td>49</td>
<td>47</td>
</tr>
<tr>
<td>Male</td>
<td>82</td>
<td>61</td>
</tr>
<tr>
<td>Black (or African descent)</td>
<td>39</td>
<td>57</td>
</tr>
<tr>
<td>Median CD4 count, cells/mL</td>
<td>519</td>
<td>518</td>
</tr>
<tr>
<td>Median eGFR, mL/min (Cockroft-Gault)</td>
<td>99</td>
<td>100</td>
</tr>
<tr>
<td>Median # pills per day in ART regimen</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>≥6 pills per day in ART regimen, %</td>
<td>40</td>
<td>37</td>
</tr>
<tr>
<td>At least BID dosing, %</td>
<td>65</td>
<td>65</td>
</tr>
<tr>
<td>Tenofovir, %</td>
<td>61</td>
<td>54</td>
</tr>
<tr>
<td>Raltegravir, %</td>
<td>56</td>
<td>50</td>
</tr>
<tr>
<td>2 class / 3 class resistance, %</td>
<td>70 / 26</td>
<td>74 / 20</td>
</tr>
<tr>
<td>M184V/I / K65R, %</td>
<td>85 / 20</td>
<td>78 / 30</td>
</tr>
<tr>
<td>NNRTI resistance / PI resistance</td>
<td>89 / 38</td>
<td>87 / 28</td>
</tr>
</tbody>
</table>

Simplification to EVG-COBI-TAF-FTC plus DRV
Study 119: Results

Week 24 and 48: Virologic Response (Full analysis set)

![Graph showing virologic response](chart)

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

- **Week 24**
  - EVG-COBI-TAF-FTC + DRV: 97/86/89
  - Baseline ART: 91/42/46

- **Week 48**
  - EVG-COBI-TAF-FTC + DRV: 94/84/89
  - Baseline ART: 76/35/46

Simplification to EVG-COBI-TAF-FTC plus DRV
Study 119: Results

Week 24 and 48: Medication Adherence

Simplification to EVG-COBI-TAF-FTC plus DRV
Study 119: Result

Week 48: Urine Protein-to-Creatinine Ratios from Baseline

Median Change in Protein-to-Creatinine Ratios (%)

<table>
<thead>
<tr>
<th>Tubular Proteinuria</th>
<th>EVG-COBI-TAF-FTC + DRV</th>
<th>Baseline ART Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proteinurin (UPCR)</td>
<td>-27.0</td>
<td>-25.0</td>
</tr>
<tr>
<td>RBP:Cr</td>
<td>-17.0</td>
<td>-14.0</td>
</tr>
<tr>
<td>β2M:Cr</td>
<td>-29.0</td>
<td>-13.0</td>
</tr>
</tbody>
</table>

Abbreviations: RBP:Cr = retinol binding protein:creatinine ratio; β2M:Cr = beta-2 microalbumin:creatinine ratio

Conclusions: “This study demonstrated that regimen simplification from a 5-tablet regimen to the 2-tablet, once-daily combination of E/C/F/TAF plus DRV has durable maintenance of virologic suppression and improvements in specific markers of renal safety. Such a strategy may lead to greater adherence and improved quality of life.”

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