Elvitegravir-Cobicistat-Tenofovir alafenamide-Emtricitabine (Genvoya)

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Elvitegravir-Cobicistat-Tenofovir Alafenamide-Emtricitabine (Genvoya)

**Genvoya**
[jen-VOY-uh]

Elvitegravir-Cobicistat-Tenofovir alafenamide-Emtricitabine

150 mg  150 mg  10 mg  200 mg
INSTI  Booster  NRTI  NRTI

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

- **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%)
Elvitegravir-Cobicistat-Tenofovir alafenamide-Emtricitabine
Summary of Key Studies

• Phase 2 Trials in Treatment Naïve Adults
  - GS-292-0102: EVG-COBI-TAF-FTC vs. EVG-COBI-TDF-FTC

• Phase 2 Trials in Treatment Naïve Adolescents
  - Study 106: EVG-COBI-TAF-FTC

• Phase 3 Trials in Treatment Naïve Adults
  - GS-292-104 and 0111: EVG-COBI-TAF-FTC vs. EVG-COBI-TDF-FTC

• Phase 3 Switch Trials in Special Populations
  - STUDY 112: EVG-COBI-TAF-FTC in Renal Impairment
  - STUDY 1249: EVG-COBI-TAF-FTC in Hepatitis B coinfection

• Phase 3 Switch/Simplification Trials
  - STUDY 109: Switch from TDF-based regimens to TAF-based regimen
  - STUDY 119: Simplification to EVG-COBI-TAF-FTC plus DRV
INITIAL THERAPY

Elvitegravir-Cobicistat-Tenofovir Alafenamide-Emtricitabine
EVG-COBI-TAF-FTC versus EVG-COBI-TDF-FTC
GS-292-0102 Phase 2 Study
Study Design: GS-292-0102

**Background:** Randomized, double-blind, phase 2 trial comparing elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine with elvitegravir-cobicistat-tenofovir DF-emtricitabine

**Inclusion Criteria (n = 171 randomized)**
- Antiretroviral-naïve adults
- Age ≥18
- HIV RNA ≥5000 copies/mL
- CD4 count >50 cells/mm³
- Estimated GFR ≥70 mL/min
- No AIDS conditions in prior 30 days
- Excluded if coinfected with HBV or HCV

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

Week 24 and 48 Virologic Response (Snapshot Analysis)

**Conclusions**: “Treatment-naive patients given the STR that contained either TAF or TDF achieved a high rate of virologic success. Compared with those receiving TDF, patients on E/C/F/TAF experienced significantly smaller changes in estimated creatinine clearance, renal tubular proteinuria, and bone mineral density.”

EVG-COBI-TAF-FTC versus EVG-COBI-TDF-FTC
GS-292-0104 and GS-292-0111 Study
EVG-COBI-TAF-FTC versus EVG-COBI-TDF-FTC
GS-292-0104 and GS-292 0111 Study: Design

Study Design: GS-292-0104 & GS-292-0111

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

• **Inclusion Criteria (n = 1733)**
  - 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

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

Week 48: Change in Serum Creatinine from Baseline

Week 48: Changes in Quantitative Proteinuria

Week 48: Changes in Spine and Hip Bone Mineral Density

- **Spine**:
  - Tenofovir alafenamide arm: -1.30
  - Tenofovir DF arm: -2.86

- **Hip**:
  - Tenofovir alafenamide arm: -0.66
  - Tenofovir DF arm: -2.95

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

**GS-292-0104 and GS-292 0111 Study: 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-TAF-FTC in Adolescents

Study 106
Elvitegravir-Cobicistat-TAF-FTC in Treatment Naïve Adolescents Study 106: Design

<table>
<thead>
<tr>
<th>Study Design: Study 106</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Background</strong>: Open-label, single arm phase 2/3 trial evaluating safety and efficacy of once-daily elvitegravir-cobicistat-tenofovir alafenamide-emtricitabine in treatment-naïve adolescents with HIV</td>
</tr>
<tr>
<td><strong>Inclusion Criteria</strong> (n = 50)</td>
</tr>
<tr>
<td>- Treatment-naïve adolescents with HIV</td>
</tr>
<tr>
<td>- Adolescents aged 12-18 yrs, ≥ 35kg</td>
</tr>
<tr>
<td>- HIV RNA ≥1000 copies/mL</td>
</tr>
<tr>
<td>- CD4 count ≥100 cells/mm³</td>
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<tr>
<td>- GFR ≥90 mL/min</td>
</tr>
<tr>
<td>- No resistance to EVG, FTC, or TDF</td>
</tr>
<tr>
<td><strong>Treatment Arms</strong></td>
</tr>
<tr>
<td>- EVG-COBI-TAF-FTC</td>
</tr>
</tbody>
</table>

Elvitegravir-Cobicistat-TAF-FTC in Treatment Naïve Adolescents
Study 106: Result

Week 48 Virologic Response

Elvitegravir-Cobicistat-TAF-FTC in Treatment Naïve Adolescents
Study 106: Result

Week 48: Changes in Quantitative Proteinuria

<table>
<thead>
<tr>
<th>Tubular Proteinuria</th>
<th>Median % Change from Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proteinuria (UPCR)</td>
<td>-27.0</td>
</tr>
<tr>
<td>RBP/Cr</td>
<td>-21.6</td>
</tr>
<tr>
<td>β2M/Cr</td>
<td>-29.4</td>
</tr>
</tbody>
</table>

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

Elvitegravir-Cobicistat-TAF-FTC in Treatment Naïve Adolescents
Study 106: Result

Week 48: Changes in Spine and Total Body Bone Mineral Density

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

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>EVG-COBI-TAF-FTC (n = 50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>20%</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>12%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>10%</td>
</tr>
<tr>
<td>Upper Abdominal Pain</td>
<td>6%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>6%</td>
</tr>
<tr>
<td>Somnolence</td>
<td>6%</td>
</tr>
</tbody>
</table>

**Interpretation**: “The elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide regimen was well tolerated and achieved component plasma pharmacokinetic exposures similar to those in adults. Although non-comparative with a small sample size, these data support the use of this regimen in HIV-infected adolescents and its timely assessment in younger children.”

Elvitegravir-Cobicistat-TAF-FTC in Renal Impairment

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

**Study Design: Study 112**

- **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%

*Baseline ART

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

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

Week 48: Changes in Tubular Proteinurina

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

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

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.”

SWITCH STUDIES

Elvitegravir-Cobicistat-Tenofovir Alafenamide-Emtricitabine
Elvitegravir-Cobicistat-TAF-FTC in Hepatitis B Coinfection

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

Study Design: Study 1249

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

- **Inclusion Criteria (n = 72)**
  - HIV-infected adults with 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

**Study Week:** 0 24 48

**Baseline ART** (n = 72) → **EVG-COBI-TAF-FTC** (n = 72)

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

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

ALT Measurement at Weeks 24 and 48

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

Changes in General Proteinuria at Weeks 24 and 48

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

Changes in Tubular Proteinuria at Weeks 24 and 48

Median % Change 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 to Elvitegravir-Cobicistat-TAF-FTC

Study 109
# Switch to Elvitegravir-Cobicistat-TAF-FTC

## Study 109: Design

<table>
<thead>
<tr>
<th>Study Design: Study 109</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Background:</strong> Open-label, randomized study, Phase 3 trial comparing switch to EVG-COBI-TAF-FTC versus continuation of baseline regimen of TDF-based ART</td>
</tr>
<tr>
<td><strong>Inclusion Criteria (n = 1443)</strong></td>
</tr>
<tr>
<td>- HIV RNA &lt; 50 copies/mL on ART for ≥96 weeks</td>
</tr>
<tr>
<td>- CrCl &gt;50 mL/min</td>
</tr>
<tr>
<td>- 1 of 4 baseline TDF-containing ART regimens:</td>
</tr>
<tr>
<td>(a) EVG-COBI-TDF-FTC (n=459)</td>
</tr>
<tr>
<td>(b) EFV-TDF-FTC (n=376)</td>
</tr>
<tr>
<td>(c) ATV + RTV + TDF-FTC (n=385)</td>
</tr>
<tr>
<td>(d) ATV-COBI + TDF-FTC (n=216)</td>
</tr>
<tr>
<td><strong>Treatment Arms</strong></td>
</tr>
<tr>
<td>- EVG-COBI-TAF-FTC (Switch group)</td>
</tr>
<tr>
<td>- Remain on TDF-based ART (No switch group)</td>
</tr>
</tbody>
</table>

*NOTE:* Between randomization and start of study, 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)

![Bar chart showing mean change in BMD.]

- **Hip**
  - EVG-COBI-TAF-FTC (Switch): 1.47%
  - Tenofovir DF-Based ART (No Switch): -0.34%

- **Spine**
  - EVG-COBI-TAF-FTC (Switch): 1.56%
  - Tenofovir DF-Based ART (No Switch): -0.44%

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

Week 48: Changes in Quantitative Proteinuria

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

Week 48: Change in Plasma Lipids from Baseline

<table>
<thead>
<tr>
<th>Lipid</th>
<th>EVG-COBI-TAF-FTC (Switch)</th>
<th>Tenofovir DF-Based ART (No Switch)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Cholesterol</td>
<td>+20</td>
<td>-2</td>
</tr>
<tr>
<td>LDL</td>
<td>+9</td>
<td>-2</td>
</tr>
<tr>
<td>HDL</td>
<td>+2</td>
<td>-1</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>+11</td>
<td>-2</td>
</tr>
</tbody>
</table>

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**

<table>
<thead>
<tr>
<th>Study Design: Study 119</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Background:</strong> Open-label, randomized Phase 3 trial comparing simplification to EVG-COBI-TAF-FTC plus darunavir versus continuation of baseline salvage ART regimen containing darunavir</td>
</tr>
<tr>
<td><strong>Inclusion Criteria (n = 135)</strong></td>
</tr>
<tr>
<td>HIV RNA &lt;50 copies/mL on DRV-containing regimen</td>
</tr>
<tr>
<td>On regimen for ≥4 months</td>
</tr>
<tr>
<td>At least 2 prior regimen failures and ≥2-class DRMs</td>
</tr>
<tr>
<td>No DRV RAMs, no INSTI resistance, ≤3 TAMs, no Q151M or T69ins</td>
</tr>
<tr>
<td><strong>Treatment Arms</strong></td>
</tr>
<tr>
<td>EVG-COBI-TAF-FTC + DRV (Switch group)</td>
</tr>
<tr>
<td>Remain on baseline ART (No switch group)</td>
</tr>
</tbody>
</table>

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*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>&gt;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)

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

**Proteinuria (UPCR)**
- EVG-COBI-TAF-FTC + DRV: -27.0%
- Baseline ART Regimens: -25.0%

**RBP:Cr**
- EVG-COBI-TAF-FTC + DRV: -17.0%
- Baseline ART Regimens: -29.0%

**β2M:Cr**
- EVG-COBI-TAF-FTC + DRV: -29.0%
- Baseline ART Regimens: 13.0%

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.”

Acknowledgment

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