Dolutegravir (Tivicay)

Prepared by:
Brian R. Wood, MD
David H. Spach, MD

Last Updated: January 28, 2021
Dolutegravir (Tivicay)

**Tivicay**
[TIV-eh-kay]

Dolutegravir  
50 mg

- Treatment Naïve: 50 mg once daily with or without food
- Coadministered with certain UGT1A or CYP3A inducers: 50 mg twice daily with or without food
- INSTI-experienced with certain substitutions: 50 mg twice daily with or without food
- Clinically suspected INSTI resistance: 50 mg twice daily with or without food
Dolutegravir (Tivicay)

• **Class**: integrase strand transfer inhibitor (INSTI)

• **Approval Status**: approved for persons 12 and older

• **Dose (with or without food)**:
  - Treatment Naïve: 50 mg once daily
  - Treatment Experienced, INSTI-Naive: 50 mg once daily
  - INSTI Resistant: 50 mg twice daily
  - Coadministration of Certains Inducers: 50 mg twice daily

• **Metabolism**: glucuronidation via UGT 1A1

• **Adverse Events**:
  - Small increases in serum creatinine (benign inhibition of creatinine secretion)
## Dolutegravir Recommended Dosing

### Adult Population

<table>
<thead>
<tr>
<th>Treatment-naïve or Treatment-experienced INSTI-naïve</th>
<th>Recommended Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>50 mg once daily</td>
</tr>
</tbody>
</table>

Coadministered with potent UGT1A/CYP3A inducer:
- Efavirenz
- Fosamprenavir/ritonavir
- Tipranavir/ritonavir
- Rifampin

<table>
<thead>
<tr>
<th>INSTI-experienced with certain INSTI mutations* or Clinically suspected INSTI resistance</th>
<th>50 mg twice daily</th>
</tr>
</thead>
</table>

Poor virologic response associated with Q148 Substitution plus ≥2 INSTI mutations

---

**Source:** Dolutegravir Prescribing Information
Dolutegravir
Summary of Key Studies

• Phase 2b Trials in Treatment Naïve
  - SPRING-1: Dose-ranging Dolutegravir vs. Efavirenz + 2NRTIs

• Phase 3 Trials in Treatment Naïve
  - SPRING 2: Dolutegravir + 2NRTIs vs Raltegravir + 2NRTIs
  - FLAMINGO: Dolutegravir vs. Ritonavir-boosted Darunavi
  - GS-380-1489: Dolutegravir + TAF-FTC versus Bictegravir-TAF-FTC
  - ING 116070: Dolutegravir CSF levels and virologic response in CSF

• Phase 2a Trial in Treatment Naïve & Experienced
  - ING 111521: 10-Day, dose-ranging, dolutegravir monotherapy trial
  - IMPAACT P1093: Dolutegravir in infants, children, and adolescents
Dolutegravir
Summary of Key Studies

- **Phase 2b Trials in Treatment Experienced**
  - VIKING 1 & 2: Dolutegravir 50 mg QD added to failing regimen
  - VIKING 2: Dolutegravir 50 mg BID added to failing regimen

- **Phase 3 Trials in Treatment Experienced**
  - DAWNING: Dolutegravir 50 mg QD vs. LPV-RTV in salvage regimen
  - SAILING: Dolutegravir 50 mg QD vs. Raltegravir in salvage regimen
  - VIKING 3: Dolutegravir 50 mg BID in patients with INSTI resistance
  - VIKING-4: Dolutegravir 50 mg BID in patients with INSTI resistance (with placebo-controlled 7-day monotherapy phase)

- **Phase IV Switch Studies**
  - DUALIS: Dolutegravir + boosted PI as maintenance
  - NEAT 022: CV Risk Switching from boosted PI to Dolutegravir
  - DOMONO: Dolutegravir 50 mg QD Monotherapy vs. 3-drug treatment
INITIAL THERAPY

Dolutegravir
Dolutegravir vs. Efavirenz in Antiretroviral Naive

SPRING-1 Study
Dolutegravir versus Efavirenz in ARV-Naïve
SPRING-1: Study Design

Study Design: SPRING-1

- **Background**: Dose-ranging, partially-blinded phase 2b trial in antiretroviral-naïve persons with HIV to select a dolutegravir dose for phase 3 trials.

- **Inclusion Criteria (n = 205)**
  - Age ≥18
  - Antiretroviral-naïve
  - CD4 >200 cells/mm³
  - HIV RNA >1,000 copies/mL
  - No NNRTI mutations

- **Treatment Arms**
  - Dolutegravir: 2, 10, or 50 mg daily + 2 NRTIs*
  - Efavirenz: 600 mg daily + 2 NRTIs*

*2 NRTIs = Tenofovir DF-Emtricitabine or Abacavir-Lamivudine

Dolutegravir versus Efavirenz in ARV-Naïve SPRING-1: Results

Week 48 Virologic Response (TLOVR)

<table>
<thead>
<tr>
<th>HIV RNA &lt;50 copies/mL (%)</th>
<th>Dolutegravir: 10 mg</th>
<th>Dolutegravir: 25 mg</th>
<th>Dolutegravir: 50 mg</th>
<th>Efavirenz: 600 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>48/53</td>
<td>45/51</td>
<td>46/51</td>
<td>41/50</td>
</tr>
</tbody>
</table>

Dolutegravir versus Efavirenz in ARV-Naïve SPRING-1: Results

Week 16, 24, and 48 Virologic Response (TLOVR)

![Bar chart showing virologic response at weeks 16 and 48.]

- **Week 16**
  - Dolutegravir: 10 mg: 96/53
  - Dolutegravir: 25 mg: 92/51
  - Dolutegravir: 50 mg: 90/51
  - Efavirenz: 600 mg: 60/50

- **Week 48**
  - Dolutegravir: 10 mg: 91/53
  - Dolutegravir: 25 mg: 88/51
  - Dolutegravir: 50 mg: 90/51
  - Efavirenz: 600 mg: 82/50

## Dolutegravir versus Efavirenz in ARV-Naive SPRING-1: Adverse Events

<table>
<thead>
<tr>
<th>Adverse Effect</th>
<th>DTG 10 mg</th>
<th>DTG 25 mg</th>
<th>DTG 50 mg</th>
<th>DTG Subtotal</th>
<th>EFV 600 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious Adverse Events</td>
<td>3 (6%)</td>
<td>1 (2%)</td>
<td>4 (8%)</td>
<td>8 (5%)</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>7 (13%)</td>
<td>6 (12%)</td>
<td>6 (12%)</td>
<td>19 (12%)</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4 (8%)</td>
<td>3 (6%)</td>
<td>5 (10%)</td>
<td>12 (8%)</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>2 (4%)</td>
<td>0</td>
<td>3 (6%)</td>
<td>5 (3%)</td>
<td>9 (18%)</td>
</tr>
<tr>
<td>Headache</td>
<td>2 (4%)</td>
<td>4 (8%)</td>
<td>4 (8%)</td>
<td>10 (6%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>1 (2%)</td>
<td>3 (6%)</td>
<td>1 (2%)</td>
<td>5 (3%)</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>0</td>
<td>0</td>
<td>3 (6%)</td>
<td>3 (2%)</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>Abnormal Dreams</td>
<td>1 (2%)</td>
<td>0</td>
<td>0</td>
<td>1 (&lt;1%)</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>Rash</td>
<td>2 (4%)</td>
<td>0</td>
<td>0</td>
<td>2 (1%)</td>
<td>4 (8%)</td>
</tr>
</tbody>
</table>

Interpretation: “Dolutegravir was effective when given once daily without a pharmacokinetic booster and was well tolerated at all assessed doses. Our findings support the assessment of once daily 50 mg dolutegravir in phase 3 trials.”

Dolutegravir vs. Raltegravir

SPRING-2 Study
Dolutegravir versus Raltegravir
SPRING-2: Design

Study Design: SPRING-2

**Background**: Randomized, double-blind study, phase 3 trial comparing dolutegravir versus raltegravir, both with 2NRTI backbone in persons with HIV.

**Inclusion Criteria (n = 822)**
- Antiretroviral-naïve
- Age ≥18
- HIV RNA ≥1,000 copies/mL
- No active CDC AIDS condition

**Treatment Arms**
- Dolutegravir + 2NRTIs
- Raltegravir + 2NRTIs
- Fixed dose 2NRTIs* = TDF-FTC or ABC-3TC

---

**Dolutegravir**: 50 mg QD
Fixed-dose NRTI backbone*
(n = 411)

**Raltegravir**: 400 mg BID
Fixed-dose NRTI backbone*
(n = 411)

Dolutegravir versus Raltegravir
SPRING-2: Results

Week 48: Virologic Response, by Baseline HIV RNA

![Bar chart showing virologic response by baseline HIV RNA level.](chart.png)

- **HIV RNA <50 copies/mL (%):**
  - All: Dolutegravir + 2NRTIs (88/411), Raltegravir + 2NRTIs (85/411)
  - ≤100,000 copies/mL: Dolutegravir + 2NRTIs (90/297), Raltegravir + 2NRTIs (89/295)
  - >100,000 copies/mL: Dolutegravir + 2NRTIs (82/114), Raltegravir + 2NRTIs (75/116)

Dolutegravir versus Raltegravir
SPRING-2: Results

Week 48: Virologic Response, by NRTI Component

HIV RNA <50 copies/mL (%)

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Abacavir-Lamivudine</th>
<th>Tenofovir DF-Emtricitabine</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>86/333</td>
<td>87/489</td>
</tr>
<tr>
<td>Dolutegravir</td>
<td>86/169</td>
<td>89/242</td>
</tr>
<tr>
<td>Raltegravir</td>
<td>87/164</td>
<td>85/247</td>
</tr>
</tbody>
</table>

**Interpretation**: “The non-inferior efficacy and similar safety profile of dolutegravir compared with raltegravir means that if approved, combination treatment with once-daily dolutegravir and fixed-dose nucleoside reverse transcriptase inhibitors would be an effective new option for treatment of HIV-1 in treatment-naive patients.”
Dolutegravir vs. Raltegravir
SPRING-2 Study: Week 96 Data
Dolutegravir + 2NRTIs versus Raltegravir + 2NRTIs
SPRING-2 (Week 96): Results

Week 96 Virologic Response: Background Dual NRTI Therapy

**Interpretation:** “At week 96, once-daily dolutegravir was non-inferior to twice-daily raltegravir in treatment-naive, patients with HIV-1. Once-daily dosing without requirement for a pharmacokinetic booster makes dolutegravir-based therapy an attractive treatment option for HIV-1-infected treatment-naive patients.”
Dolutegravir + 2 NRTIs versus Darunavir + RTV + 2 NRTIs

FLAMINGO
Dolutegravir + 2 NRTIs versus Darunavir + RTV + 2 NRTIs

FLAMINGO: Study Design

**Study Design: FLAMINGO**

- **Background**: Randomized, open label phase 3b study comparing dolutegravir to darunavir-ritonavir with fixed-dose NRTI backbone in antiretroviral-naïve persons with HIV.

- **Inclusion Criteria (n = 484 analyzed)**
  - Antiretroviral-naïve
  - Age ≥18
  - HIV RNA ≥1,000 copies/mL
  - No active class C conditions
  - No resistance to NRTIs or protease inhibitors

- **Treatment Arms (once daily)**
  - Dolutegravir 50 mg + 2 NRTIs*
  - Darunavir 800 mg + Ritonavir 100 mg + 2 NRTIs*

*2 NRTIs = tenofovir-emtricitabine or abacavir-lamivudine (with negative HLA-B*5701 testing).

Dolutegravir + 2 NRTIs versus Darunavir + RTV + 2 NRTIs

FLAMINGO: Results

Week 48 Virologic Response, by Baseline HIV RNA Level

Dolutegravir + 2 NRTIs versus Darunavir + RTV + 2 NRTIs

FLAMINGO: Results

48 Week Virologic Outcomes (Modified Intent-to-Treat Analysis)

Dolutegravir + 2 NRTIs versus Darunavir + RTV + 2 NRTIs
FLAMINGO: Results

Week 48 Virologic Response, by Background Dual NRTI Therapy

Dolutegravir + 2 NRTIs versus Darunavir + RTV + 2 NRTIs
FLAMINGO: Common Adverse Events

<table>
<thead>
<tr>
<th>Treatment Emergent Adverse Events in ≥ 5% of Subjects in Either Arm</th>
<th>DTG + 2 NRTIs (n = 242)</th>
<th>DRV + RTV + 2 NRTIs (n= 242)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dizziness</td>
<td>17%</td>
<td>29%</td>
</tr>
<tr>
<td>Nausea</td>
<td>16%</td>
<td>18%</td>
</tr>
<tr>
<td>Headache</td>
<td>15%</td>
<td>10%</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>9%</td>
<td>8%</td>
</tr>
<tr>
<td>Upper respiratory infection</td>
<td>5%</td>
<td>10%</td>
</tr>
<tr>
<td>Insomnia</td>
<td>7%</td>
<td>6%</td>
</tr>
<tr>
<td>Cough</td>
<td>5%</td>
<td>7%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>6%</td>
<td>6%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>6%</td>
<td>5%</td>
</tr>
</tbody>
</table>

Dolutegravir + 2 NRTIs versus Darunavir + RTV + 2 NRTIs
FLAMINGO: Common Adverse Events (continued)

<table>
<thead>
<tr>
<th>Treatment Emergent Adverse Events in ≥ 5% of Subjects in Either Arm</th>
<th>DTG + 2 NRTIs (n = 242)</th>
<th>DRV + RTV + 2 NRTIs (n = 242)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyrexia</td>
<td>5%</td>
<td>6%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>6%</td>
<td>5%</td>
</tr>
<tr>
<td>Rash</td>
<td>4%</td>
<td>6%</td>
</tr>
<tr>
<td>Back Pain</td>
<td>4%</td>
<td>5%</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>3%</td>
<td>5%</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>2%</td>
<td>5%</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>2%</td>
<td>5%</td>
</tr>
<tr>
<td>Depression</td>
<td>5%</td>
<td>2%</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>2%</td>
<td>5%</td>
</tr>
</tbody>
</table>

Interpretation: “Once-daily dolutegravir was superior to once-daily darunavir plus ritonavir. Once-daily dolutegravir in combination with fixed-dose NRTIs represents an effective new treatment option for HIV-1-infected, treatment-naive patients.”

Dolutegravir + ABC-3TC and CSF HIV-1 RNA Levels

ING116070 Study
Dolutegravir + ABC-3TC and Impact on CSF HIV RNA Levels
ING116070 Study: Design

**Study Design: ING116070**

- **Background**: Single arm, phase 3b, open-label, multi-center trial to evaluate the distribution and antiviral activity of dolutegravir + abacavir-lamivudine in CSF in persons with HIV.

- **Inclusion Criteria** (n = 13)
  - Antiretroviral-naïve
  - Age ≥18 years
  - HIV RNA ≥5,000 copies/mL
  - CD4 count ≥200 cells/mm³
  - No active CDC AIDS condition (except KS)

- **Treatment Arm** (n = 12)
  - Dolutegravir (QD) + Abacavir-lamivudine

### CSF Findings in Patients on Dolutegravir + Abacavir-Lamivudine

<table>
<thead>
<tr>
<th>Cerebrospinal Fluid (CSF) Parameter</th>
<th>Week 2</th>
<th>Week 16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean CSF DTG Concentration total, ng/mL</td>
<td>16.2</td>
<td>12.6</td>
</tr>
<tr>
<td>CSF/Total Plasma Ratio for DTG Concentration</td>
<td>0.47</td>
<td>0.55</td>
</tr>
<tr>
<td>CSF HIV-1 RNA &lt;50 copies/mL</td>
<td>11/12 (92%)</td>
<td>11/11 (100%)</td>
</tr>
<tr>
<td>CSF HIV-1 RNA &lt;2 copies/mL</td>
<td>ND</td>
<td>11/12 (92%)</td>
</tr>
</tbody>
</table>

Conclusions: “The dolutegravir concentrations in CSF were similar to unbound plasma concentrations and exceeded the in vitro 50% inhibitory concentration for wild-type HIV (0.2 ng/mL), suggesting that dolutegravir achieves therapeutic concentrations in the central nervous system. The HIV-1 RNA reductions were similar in CSF and plasma.”
TREATMENT-NAÏVE AND TREATMENT EXPERIENCED

Dolutegravir
Dolutegravir 10-Day, Dose-Ranging, Monotherapy Study

ING111521
Dolutegravir Dose-Ranging Monotherapy
ING111521 Study: Design

Study Design: ING111521

- **Background**: Randomized, double-blind, dose-ranging, 10-day, phase 2a study to evaluate antiviral activity, safety, and pharmacokinetics and pharmacodynamics of dolutegravir in persons with HIV.

- **Inclusion Criteria** (n = 35)
  - Antiretroviral-naïve and antiretroviral-experienced
  - Integrase strand transfer inhibitor-naïve
  - Age ≥18 and ≤65 years
  - CD4 ≥100 cells/mm³
  - HIV RNA ≥5,000 copies/mL
  - No AIDS conditions

- **Treatment Arms**
  - Dolutegravir 2, 10, or 50 mg daily, or placebo

Dolutegravir Dose-Ranging Monotherapy
ING111521 Study: Results

Baseline to Day 11: Change in Baseline HIV RNA Level

Dolutegravir Dose-Ranging Monotherapy
ING111521 Study: Results

Baseline to Day 11: Patients with Suppressed Viral Load at Nadir

Conclusion: “Dolutegravir demonstrated potent antiviral activity, good short-term tolerability, low pharmacokinetic variability, and a predictable pharmacokinetics/pharmacodynamics relationship, which support once daily dosing without a pharmacokinetic booster in integrase-naive patients in future studies.”
Dolutegravir in Treatment-Experienced Adolescents

IMPAACT P1093
Dolutegravir in Treatment-Experienced Adolescents

IMPAACT P1093: Study Design

Study Design: IMPAACT P1093

**Background**: Open-label, non-randomized phase I/II study treatment-experienced adolescents with HIV

**Inclusion Criteria (n = 23)**
- Age 12 to <18 years of age
- Antiretroviral-experienced
- Naïve to integrase inhibitors
- HIV RNA >1,000 copies/mL
- Genotype showing sensitivity to at least one other active antiretroviral agent

**Treatment Arms**
- Dolutegravir monotherapy, then dolutegravir with optimized background regimen

**Stage I**
Intensive PK group n=10

<table>
<thead>
<tr>
<th>Functional monotherapy or monotherapy phase</th>
<th>Optimize therapy continuation phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>48 week DTG + OBR</td>
<td></td>
</tr>
</tbody>
</table>

- Day 1
- Day 5-10 Intensive PK visit
- Week 48

**Stage II**: opens after dose/safety criteria met in stage I; n=13

- DTG and OBR from day 1

Dolutegravir in Treatment-Experienced Adolescents
IMPAACT P1093: Results

Week 48: Virologic Response

Virologic Suppression (%)

HIV <400 copies/mL

74

17/23

HIV <50 copies/mL

61

14/23

Virologic Suppression Threshold

Dolutegravir in Treatment-Experienced Adolescents
IMPAACT P1093: Results

Week 48: Patient-Reported Adherence

**Conclusions**: “Dolutegravir achieved target PK exposures in adolescents. Dolutegravir was safe and well tolerated, providing good virologic efficacy through week 48.”
Dolutegravir
Dolutegravir versus Lopinavir-Ritonavir in Second-Line Treatment
DAWNING
Dolutegravir vs Lopinavir-Ritonavir in Second-Line Treatment

DAWNING: Study Design

**Study Design: DAWNING**

- **Background:** Randomized, open-label, multinational, non-inferiority phase 3b trial comparing dolutegravir to boosted lopinavir, each with optimized background regimen (OBR) after failure of NNRTI-based first-line ART

- **Inclusion Criteria**
  - Antiretroviral-experienced adults
  - Virologic failure on NNRTI plus 2 NRTI’s
  - HIV RNA ≥400 copies/mL at 2 consecutive visits
  - INSTI and PI-naïve
  - ≥1 active NRTI available based on genotype
  - HBV and HCV allowed

- **Treatment Arms**
  - Dolutegravir 50 mg daily + investigator-selected OBR (including at least 1 active NRTI)
  - Lopinavir + ritonavir* + investigator-selected OBR (including at least 1 active NRTI)

---


*Once-daily lopinavir 800 mg + ritonavir 200 mg or twice daily lopinavir 400 mg + 100 mg, based on investigator discretion
Dolutegravir vs Lopinavir-Ritonavir in Second-Line Treatment

DAWNING: Baseline Characteristics

<table>
<thead>
<tr>
<th>Baseline Characteristics in DAWNING Study</th>
<th>DTG + OBR (n = 312)</th>
<th>LPV-RTV + OBR (n = 312)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean</td>
<td>37.5</td>
<td>38.7</td>
</tr>
<tr>
<td>Women, n, %</td>
<td>116 (37%)</td>
<td>103 (33%)</td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td>105 (34%)</td>
<td>109 (35%)</td>
</tr>
<tr>
<td>African American or African</td>
<td>130 (42%)</td>
<td>112 (36%)</td>
</tr>
<tr>
<td>Viral hepatitis (HBV, HCV, or both)</td>
<td>35 (11%)</td>
<td>38 (12%)</td>
</tr>
<tr>
<td>WHO category C (AIDS)</td>
<td>107 (34%)</td>
<td>95 (30%)</td>
</tr>
<tr>
<td>Mean HIV RNA, log_{10} copies/mL</td>
<td>4.2</td>
<td>4.2</td>
</tr>
<tr>
<td>HIV RNA &gt;100,000 copies/mL</td>
<td>70 (22%)</td>
<td>63 (20%)</td>
</tr>
<tr>
<td>CD4 count &lt;200 cells/mm³</td>
<td>166 (53%)</td>
<td>151 (48%)</td>
</tr>
</tbody>
</table>

### Dolutegravir vs Lopinavir-Ritonavir in Second-Line Treatment

**DAWNING: Previous ART History**

<table>
<thead>
<tr>
<th>Previous Antiretroviral History in DAWNING Study</th>
<th>DTG + OBR (n = 312)</th>
<th>LPV-RTV + OBR (n = 312)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration prior ART, median, weeks</td>
<td>86.4</td>
<td>90.9</td>
</tr>
<tr>
<td>Previous NNRTI therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Efavirenz</td>
<td>242 (78%)</td>
<td>242 (78%)</td>
</tr>
<tr>
<td>Nevirapine</td>
<td>70 (22%)</td>
<td>69 (22%)</td>
</tr>
<tr>
<td>Previous NRTI therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tenofovir DF</td>
<td>181 (58%)</td>
<td>186 (60%)</td>
</tr>
<tr>
<td>Zidovudine</td>
<td>89 (29%)</td>
<td>89 (29%)</td>
</tr>
<tr>
<td>Stavudine</td>
<td>15 (5%)</td>
<td>9 (3%)</td>
</tr>
<tr>
<td>Lamivudine or emtricitabine</td>
<td>311 (99%)</td>
<td>310 (99%)</td>
</tr>
</tbody>
</table>

## Dolutegravir vs Lopinavir-Ritonavir in Second-Line Treatment

### DAWNING: Optimized Background Regimens

<table>
<thead>
<tr>
<th>Optimized background regimens (OBRs) in DAWNING Study Second-Line ART</th>
<th>DTG + OBR (n = 312)</th>
<th>LPV-RTV + OBR (n = 312)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRTIs in second-line regimen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zidovudine plus lamivudine</td>
<td>132 (42%)</td>
<td>121 (39%)</td>
</tr>
<tr>
<td>Tenofovir DF plus lamivudine or emtricitabine</td>
<td>128 (41%)</td>
<td>134 (43%)</td>
</tr>
<tr>
<td>Tenofovir DF plus zidovudine</td>
<td>36 (12%)</td>
<td>41 (13%)</td>
</tr>
<tr>
<td>Abacavir plus lamivudine</td>
<td>7 (2%)</td>
<td>7 (2%)</td>
</tr>
<tr>
<td>Stanford genotype susceptibility score in background ART</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 to &lt;1</td>
<td>30 (10%)</td>
<td>36 (12%)</td>
</tr>
<tr>
<td>1 to &lt;2</td>
<td>223 (71%)</td>
<td>212 (68%)</td>
</tr>
<tr>
<td>2</td>
<td>61 (20%)</td>
<td>64 (21%)</td>
</tr>
<tr>
<td>&gt;2</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Dolutegravir vs Lopinavir-Ritonavir in Second-Line Treatment

DAWNING: Baseline NRTI Resistance

<table>
<thead>
<tr>
<th>Baseline NRTI Resistance-Associated Mutations in DAWNING Study</th>
<th>DTG + OBR (n = 312)</th>
<th>LPV-RTV + OBR (n = 312)</th>
</tr>
</thead>
<tbody>
<tr>
<td>K65R</td>
<td>95 (30%)</td>
<td>92 (29%)</td>
</tr>
<tr>
<td>K70E</td>
<td>33 (11%)</td>
<td>37 (12%)</td>
</tr>
<tr>
<td>M184I/V only</td>
<td>77 (25%)</td>
<td>85 (27%)</td>
</tr>
<tr>
<td>M184I/V plus any other NRTI mutation</td>
<td>184 (59%)</td>
<td>167 (54%)</td>
</tr>
<tr>
<td>TAM's</td>
<td>71 (23%)</td>
<td>81 (26%)</td>
</tr>
<tr>
<td>Other major NRTI mutation</td>
<td>90 (29%)</td>
<td>88 (28%)</td>
</tr>
</tbody>
</table>

Dolutegravir vs Lopinavir-Ritonavir in Second-Line Treatment
DAWNING: Results

Virologic Suppression Rate at 48 Weeks by Baseline Viral Load


*Statistically superior
Dolutegravir vs Lopinavir-Ritonavir in Second-Line Treatment

DAWNING: Results

Virologic Suppression Rate at 48 Weeks by Baseline CD4 Count

<table>
<thead>
<tr>
<th>Baseline CD4 count (cells/mm$^3$)</th>
<th>DTG + OBR (%)</th>
<th>LPV/r + OBR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;350</td>
<td>89*</td>
<td>70</td>
</tr>
<tr>
<td>200-350</td>
<td>86*</td>
<td>74</td>
</tr>
<tr>
<td>&lt;200</td>
<td>80*</td>
<td>69</td>
</tr>
</tbody>
</table>

*Statistically superior

Dolutegravir vs Lopinavir-Ritonavir in Second-Line Treatment

DAWNING: Results

Median Days to Viral Suppression

*Statistically superior

Dolutegravir vs Lopinavir-Ritonavir in Second-Line Treatment
DAWNING: Adverse Events

<table>
<thead>
<tr>
<th>Treatment-Related Adverse Events (AEs) in DAWNING Study</th>
<th>DTG + OBR (n = 312)</th>
<th>LPV-RTV + OBR (n = 312)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE</td>
<td>50 (16%)</td>
<td>119 (38%)</td>
</tr>
<tr>
<td>Grade 2-4 AE</td>
<td>11 (4%)</td>
<td>44 (14%)</td>
</tr>
<tr>
<td>AEs that occurred in ≥ 2% of participants in either group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>1 (&lt;1%)</td>
<td>23 (7%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>0</td>
<td>6 (2%)</td>
</tr>
</tbody>
</table>

Interpretation: “When administered with two NRTIs, dolutegravir was superior to ritonavir-boosted lopinavir at 48 weeks and can be considered a suitable option for second-line treatment.”
Dolutegravir in Patients with Raltegravir-Resistant HIV

VIKING (Cohorts I & II)
Dolutegravir in Patients with Raltegravir Resistance

VIKING Study (Cohorts I & II): Study Design

**Functional Monotherapy Phase**

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 11</th>
<th>Week 24</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cohort I</strong>: Dolutegravir: 50 mg QD</td>
<td><strong>Cohort I</strong>: Dolutegravir: 50 mg QD + OBR</td>
<td><strong>Cohort II</strong>: Dolutegravir: 50 mg BID + OBR</td>
</tr>
<tr>
<td><strong>Cohort II</strong>: Dolutegravir: 50 mg BID</td>
<td><strong>Cohort II</strong>: Dolutegravir: 50 mg BID + OBR</td>
<td></td>
</tr>
</tbody>
</table>

**Continuation Phase**

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 11</th>
<th>Week 24</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cohort I</strong>: Dolutegravir: 50 mg QD</td>
<td><strong>Cohort I</strong>: Dolutegravir: 50 mg QD + OBR</td>
<td><strong>Cohort II</strong>: Dolutegravir: 50 mg BID + OBR</td>
</tr>
<tr>
<td><strong>Cohort II</strong>: Dolutegravir: 50 mg BID</td>
<td><strong>Cohort II</strong>: Dolutegravir: 50 mg BID + OBR</td>
<td></td>
</tr>
</tbody>
</table>

**Study Design: VIKING**

- **Background**: Single-arm, phase 2b trial evaluating efficacy of once daily or twice daily dolutegravir in patients with integrase resistance

- **Inclusion Criteria (n=51)**
  - Age ≥18 years
  - HIV RNA >1,000 copies/mL
  - Documented resistance ≥3 ARV classes, including integrase inhibitors

- **Treatment Arms**
  - Cohort I*: dolutegravir 50 mg once daily
  - Cohort II*: dolutegravir 50 mg twice daily

*Failing regimen continued during day 1-10, then replaced with OBR through week 24

Dolutegravir in Patients with Raltegravir Resistance
VIKING Study (Cohorts I & II): Results

Week 24 Virologic Response

Conclusion: “Dolutegravir 50 mg twice daily with an optimized background provided greater and more durable benefit than the once-daily regimen. These data are the first clinical demonstration of the activity of any integrase inhibitor in subjects with HIV-1 resistant to raltegravir.”

Dolutegravir versus Raltegravir in Treatment Experienced

SAILING Study
Dolutegravir versus Raltegravir in Treatment Experienced SAILING: Study Design

Study Design: SAILING

• **Background:** Randomized, double-blind, active-control phase 3 trial evaluating efficacy, safety, and emergent resistance with dolutegravir versus raltegravir in antiretroviral-experienced, integrase inhibitor-naïve patients with at least 2-class resistance

• **Inclusion Criteria** (n = 715)
  - Age ≥18
  - Resistance to ≥2 ARV classes
  - Integrase inhibitor-naïve
  - 2 consecutive HIV RNA ≥400 copies/mL (unless >1000 copies/mL at screening)

• **Treatment Arms**
  - Dolutegravir + up to 2 background ARTs
  - Raltegravir + up to 2 background ARTs

Dolutegravir versus Raltegravir in Treatment Experienced
SAILING: Results

Week 48 Virologic Response, By Baseline HIV RNA Level

Dolutegravir versus Raltegravir in Treatment-Experienced
SAILING: Results

Week 48 Virologic Failure

Dolutegravir versus Raltegravir in Treatment Experienced SAILING Study: Conclusion

**Interpretation**: “Once-daily dolutegravir, in combination with up to two other antiretroviral drugs, is well tolerated with greater virological effect compared with twice-daily raltegravir in this treatment-experienced patient group.”

Dolutegravir in Patients with Integrase-Resistant HIV

VIKING-3
Dolutegravir in Patients with Integrase Inhibitor Resistance

VIKING-3: Study Design

**Day 1**
- **Functional Monotherapy Phase**
  - Dolutegravir: 50 mg BID

**Day 7**
- **Continuation Phase**
  - Dolutegravir: 50 mg BID + OBR

**Study Design: VIKING-3**

- **Background**: Single arm, open-label, phase 3 trial to determine the efficacy of twice daily dolutegravir in patients with integrase resistance

- **Inclusion Criteria (n=183)**
  - Age ≥18
  - Antiretroviral experienced, resistance to raltegravir and/or elvitegravir
  - Resistance to 2 classes of ARVs (in addition to integrase resistance)
  - HIV RNA ≥500 copies/mL
  - At least one fully active drug for optimized background regimen
  - Dolutegravir naïve

- **Treatment arm**: Dolutegravir 50 mg twice daily, with OBR added on day 7

Dolutegravir in Patients with Integrase Inhibitor Resistance

VIKING-3: Results

24 Week Virologic Response, by Baseline HIV RNA Level

Dolutegravir in Patients with Integrase Inhibitor Resistance

VIKING-3: Results

24 Week Virologic Response, by Baseline Genotype


*Included primary INI-resistance mutations N155H, Y143C/H/R, T66A or E92Q or only historical evidence of resistance

^Secondary mutations from G140A/C/S, E138A/K/T or L74I.
Dolutegravir in Patients with Integrase Inhibitor Resistance

VIKING-3: Results

24 Week Virologic Response, by Baseline Phenotype

Conclusions: “Dolutegravir 50 mg BID-based therapy was effective in this highly treatment-experienced population with integrase inhibitor-resistant virus.”

Dolutegravir in Patients with Integrase-Resistant HIV

VIKING-4
### Study Design: VIKING-4

**Background:** Single-arm, open-label, phase 3 trial to evaluate short-term antiviral efficacy of dolutegravir in persons with HIV who have integrase resistance.

**Inclusion Criteria**
- Age ≥18 years old
- ARV experienced, dolutegravir naïve,
- Documented Resistance to ≥3 ARV classes, including raltegravir or elvitegravir
- HIV RNA ≥1,000 copies/mL

**Treatment Arms (n = 30 randomized)**
- Day 0 to 7: Dolutegravir: 50 mg BID or Placebo
- Day 8 to Week 24: Dolutegravir 50 mg BID + optimized background regimen

---

**Day 1**

<table>
<thead>
<tr>
<th>Functional Monotherapy Phase</th>
<th>Continuation Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dolutegravir:</strong> 50 mg BID or Placebo</td>
<td><strong>Dolutegravir:</strong> 50 mg BID + OBR</td>
</tr>
</tbody>
</table>

**Day 8**

- Week 48

---

Dolutegravir in Patients with Integrase Inhibitor Resistance

VIKING-4: Results

Baseline to Day 8: Change in Viral Load (in Functional Monotherapy Phase)

Dolutegravir in Patients with Integrase Inhibitor Resistance

VIKING-4: Results

Week 24 and 48 Virologic Response in Dolutegravir-Treated Patients

Viral Suppression Threshold

<table>
<thead>
<tr>
<th>HIV RNA &lt; 400 copies/mL</th>
<th>Week 24</th>
<th>Week 48</th>
</tr>
</thead>
<tbody>
<tr>
<td>14/27</td>
<td>57</td>
<td>20/24</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HIV RNA &lt; 50 copies/mL</th>
<th>Week 24</th>
<th>Week 48</th>
</tr>
</thead>
<tbody>
<tr>
<td>11/27</td>
<td>47</td>
<td>18/24</td>
</tr>
</tbody>
</table>

Dolutegravir in Patients with Integrase Inhibitor Resistance

VIKING-4: Results

Week 24 Virologic Response, by Baseline Genotype

HIV RNA <50 copies/mL (%)

- Overall: 47%
  - 14/30
- No Q148 Mutation*: 64%
  - 9/14
- Q148 + 1 Mutation^: 33%
  - 4/12
- Q148 + ≥2 Mutations^: 25%
  - 1/4

Baseline Dolutegravir Fold Change (Phenotype)

*Included primary INI-resistance mutations N155H, Y143C/H/R, T66A or E92Q or historical evidence of resistance
^Secondary mutations from G140A/C/S, E138A/K/T and L74I.

Dolutegravir in Patients with Integrase Inhibitor Resistance

**VIKING-4: Results**

Week 48 Virologic Response, by Baseline Genotype

<table>
<thead>
<tr>
<th>HIV RNA &lt;50 copies/mL (%)</th>
<th>Overall</th>
<th>No Q148 Mutation*</th>
<th>Q148 + 1 Mutation^</th>
<th>Q148 + ≥2 Mutations^</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV RNA &lt;50 copies/mL (%)</td>
<td>40</td>
<td>57</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Baseline Dolutegravir Fold Change (Phenotype)</td>
<td>11/30</td>
<td>8/14</td>
<td>3/12</td>
<td>1/4</td>
</tr>
</tbody>
</table>

*Included primary INI-resistance mutations N155H, Y143C/H/R, T66A or E92Q or historical evidence of resistance
^Secondary mutations from G140A/C/S, E138A/K/T and L74I.

Dolutegravir in Patients with Integrase Inhibitor Resistance

VIKING-4: Results

Week 24 Virologic Response, by Baseline Phenotype*

<table>
<thead>
<tr>
<th>Baseline Dolutegravir Fold Change on Phenotype</th>
<th>HIV RNA &lt;50 copies/mL (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>47</td>
</tr>
<tr>
<td>0 to 2.5</td>
<td>55</td>
</tr>
<tr>
<td>&gt; 2.5 to 4</td>
<td>60</td>
</tr>
<tr>
<td>&gt; 4 to 8</td>
<td>22</td>
</tr>
<tr>
<td>&gt; 10 to 20</td>
<td>1/2</td>
</tr>
<tr>
<td>&gt; 20</td>
<td>1/2</td>
</tr>
</tbody>
</table>

*Missing phenotypic resistance data on 1 subject

Week 48 Virologic Response, by Baseline Phenotype

<table>
<thead>
<tr>
<th>Baseline Dolutegravir Fold Change on Phenotype</th>
<th>HIV RNA &lt;50 copies/mL (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>40</td>
</tr>
<tr>
<td>0 to 2.5</td>
<td>45</td>
</tr>
<tr>
<td>&gt; 2.5 to 4</td>
<td>60</td>
</tr>
<tr>
<td>&gt; 4 to 8</td>
<td>11</td>
</tr>
<tr>
<td>&gt; 10 to 20</td>
<td>50</td>
</tr>
<tr>
<td>&gt; 20</td>
<td>50</td>
</tr>
</tbody>
</table>

*Missing phenotypic resistance data on 1 subject

Conclusions: “The observed day 8 antiviral activity in this highly treatment-experienced population with INI-resistant HIV-1 was attributable to dolutegravir. Longer-term efficacy (after considering baseline ART resistance) and safety during the open-label phase were in-line with the results of the larger VIKING-3 study.”

SWITCH STUDIES

Dolutegravir
Dolutegravir + Boosted-Darunavir as Maintenance Therapy

DUALIS
Switch to Boosted DRV + DTG vs Continue Boosted DRV + 2 NRTI’s

DUALIS: Background


Study Design: DUALIS

• **Background:**
  - Randomized, open label, multicenter phase 3 non-inferiority trial comparing a switch to boosted darunavir + dolutegravir to continued boosted darunavir + 2 NRTIs

• **Enrollment Criteria:**
  - Age ≥18 years
  - HIV RNA <50 copies/mL for >6 months
  - Taking boosted darunavir + 2 NRTI’s
  - One HIV RNA level >200 copies/mL within past 6 months allowed, as long as subsequently returned to <50 copies/mL
  - Estimated GFR >50 mL/min
  - No active hepatitis B, AIDS-defining condition, or severe hepatis impairment

Switch Regimen

**Boosted darunavir + dolutegravir**
(n = 131)

Maintain Regimen

**Boosted darunavir + 2 NRTIs**
(n = 132)

Primary endpoint: virologic response at 48 weeks by FDA snapshot
Switch to Boosted DRV + DTG vs Continue Boosted DRV + 2 NRTI’s

DUALIS: Baseline Characteristics


<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Boosted DRV + DTG (n = 131)</th>
<th>Boosted DRV + 2 NRTI’s (n = 132)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, median (IQR)</td>
<td>47 (39-55)</td>
<td>48 (40-53)</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>115 (88)</td>
<td>122 (92)</td>
</tr>
<tr>
<td>White, n (%)</td>
<td>118 (90)</td>
<td>118 (89)</td>
</tr>
<tr>
<td>MSM, n (%)</td>
<td>90 (69)</td>
<td>92 (70)</td>
</tr>
<tr>
<td>eGFR, median (IQR), mL/min</td>
<td>92 (70-104)</td>
<td>92 (81-106)</td>
</tr>
<tr>
<td>Baseline CD4, median (IQR)</td>
<td>609 (401-818)</td>
<td>585 (453-823)</td>
</tr>
<tr>
<td>NRTIs at baseline, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tenofovir-DF-emtricitabine</td>
<td>110 (84)</td>
<td>94 (71)</td>
</tr>
<tr>
<td>Tenofovir-alafenamide-emtricitabine</td>
<td>11 (8)</td>
<td>13 (10)</td>
</tr>
<tr>
<td>Abacavir-lamivudine</td>
<td>9 (7)</td>
<td>23 (17)</td>
</tr>
</tbody>
</table>
Switch to Boosted DRV + DTG vs Continue Boosted DRV + 2 NRTI’s

DUALIS: Results

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

Switch to Boosted DRV + DTG vs Continue Boosted DRV + 2 NRTI’s

DUALIS: Results

Week 48 Changes in Serum Lipid Parameters

Conclusions: “Switching to dolutegravir plus boosted darunavir was noninferior to continuing 2 nucleoside reverse transcriptase inhibitors plus boosted darunavir in subjects already treated with 2 nucleoside reverse transcriptase inhibitors plus boosted darunavir.”
Switch from Boosted PI to Dolutegravir

NEAT 022
Switching from a Boosted PI to Dolutegravir
NEAT 022: Design

Study Design

• **Background:** Randomized, open-label, multicenter trial in Europe evaluating the impact of switching from a boosted PI to dolutegravir in virologically suppressed persons with older age or elevated cardiovascular risk.

• **Inclusion Criteria**
  - Age ≥50 years or Framingham 10-year estimated cardiovascular event risk >10%
  - HIV RNA <50 copies/mL for ≥24 weeks
  - On 2 NRTI’s + boosted PI
  - No prior virologic failure and no genotypic resistance mutations

48 weeks (primary endpoint), after which all participants switch to DTG + 2 NRTI’s

### NEAT 022: Baseline Regimens

<table>
<thead>
<tr>
<th>NRTI Backbone</th>
<th>DTG + 2 NRTI’s (n = 205)</th>
<th>PI/r + 2 NRTI’s (n = 210)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tenofovir DF-Lamivudine</td>
<td>134 (65.4%)</td>
<td>135 (64.3%)</td>
</tr>
<tr>
<td>Abacavir-Lamivudine</td>
<td>63 (30.7%)</td>
<td>67 (31.9%)</td>
</tr>
<tr>
<td>Other</td>
<td>8 (3.9%)</td>
<td>8 (3.8%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Boosted PI</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Darunavir + ritonavir</td>
<td>105 (51.5%)</td>
<td>107 (51.0%)</td>
</tr>
<tr>
<td>Atazanavir + ritonavir</td>
<td>77 (37.7%)</td>
<td>74 (35.2%)</td>
</tr>
<tr>
<td>Other</td>
<td>22 (10.7%)</td>
<td>29 (13.8%)</td>
</tr>
</tbody>
</table>

Switching from a Boosted PI to Dolutegravir
NEAT 022: Results

Week 48: Virologic Response by FDA Snapshot Analysis (ITT)

![Graph showing virologic response at Week 48](image)

- **Dolutegravir + 2 NRTI's**: 93.1% (191/205)
- **Ritonavir-Boosted PI + 2 NRTI's**: 95.2% (200/210)

Switching from a Boosted PI to Dolutegravir
NEAT 022: Results

Mean Percentage Change in Lipids at 48 Weeks

Interpretation: “Switching to a dolutegravir regimen in virologically suppressed HIV type 1 patients with high cardiovascular disease risk was noninferior, and significantly improved lipid profiles.”

Dolutegravir as Maintenance Monotherapy
DOMONO
Dolutegravir as Maintenance Monotherapy
DOMONO: Design

**Study Design: DOMONO**

- **Background**: Randomized, open-label, phase 2, non-inferiority trial conducted at 2 centers in Netherlands to determine if dolutegravir monotherapy is noninferior to combination antiretroviral therapy in maintaining viral suppression.

- **Inclusion Criteria**:
  - Age ≥18 years old
  - On 3-drug ART
  - HIV RNA <50 copies/mL for ≥6 months
  - HIV RNA zenith <100,000 copies/mL
  - CD4 count nadir >200 cells/mm$^3$
  - No baseline HIV drug resistance
  - No history of virologic failure
  - No HBV co-infection

- **Dolutegravir Regimen**
  - Dolutegravir 50 mg once daily

**Immediate Switch to Monotherapy**
- **Dolutegravir**
  - (n = 51)

**Continue 3-Drug ART**
- (n = 53)

**Delayed Monotherapy**
- **Dolutegravir**
  - (n = 47)
  - 6/53 did not switch

**Separate Control Group**
- **3-Drug ART**
  - (n = 152)

# Dolutegravir as Maintenance Monotherapy

**DOMONO: Baseline Characteristics**

<table>
<thead>
<tr>
<th>Baseline Characteristic</th>
<th>Immediate Switch to DTG Monotherapy (n = 51)</th>
<th>Delayed Switch to DTG Monotherapy (n = 53)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (median, years)</td>
<td>46</td>
<td>45</td>
</tr>
<tr>
<td>Male, %</td>
<td>47</td>
<td>48</td>
</tr>
<tr>
<td>MSM, %</td>
<td>80</td>
<td>77</td>
</tr>
<tr>
<td>Caucasian ethnicity, %</td>
<td>86</td>
<td>79</td>
</tr>
<tr>
<td>On TDF before switch, %</td>
<td>86</td>
<td>85</td>
</tr>
<tr>
<td>On NNRTI + 2 NRTI’s before switch, %</td>
<td>80</td>
<td>81</td>
</tr>
<tr>
<td>On PI + 2 NRTI’s before switch, %</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>On INSTI + 2 NRTI’s before switch, %</td>
<td>14</td>
<td>17</td>
</tr>
<tr>
<td>Receiving a STR before switch, %</td>
<td>63</td>
<td>77</td>
</tr>
<tr>
<td>Time on ART (median, months)</td>
<td>35</td>
<td>43</td>
</tr>
<tr>
<td>HIV RNA zenith (median, copies/mL)</td>
<td>29,300</td>
<td>44,877</td>
</tr>
<tr>
<td>CD4 T-cell nadir (median, cells/mm³)</td>
<td>320</td>
<td>380</td>
</tr>
</tbody>
</table>

**Source:** Wijting I, et al. Lancet HIV. 2017;4;e547-54.
Dolutegravir as Maintenance Monotherapy
DOMONO: 24-Week Results

Week 24 Virologic Suppression

![Graph showing virologic suppression at Week 24 for Dolutegravir Monotherapy and 3-Drug ART.](image)

- **Dolutegravir Monotherapy (n=50*)**
  - 49/50 (98%)

- **3-Drug ART (n=53)**
  - 53/53 (100%)

*One of 51 participants in the immediate DTG switch arm discontinued treatment after 12 weeks because of disturbed sleep (HIV RNA <50 copies/mL at the time).

Dolutegravir as Maintenance Monotherapy
DOMONO: 48-Week Results

Week 48 Virologic Suppression (Entire Study Population)

- Study stopped early; 8 virologic failures in dolutegravir arm, 3 with INSTI resistance (N155H, R263K, S230R)
- RNA at failure 678–4,990 copies/mL with one exception (71,600 copies/mL); all reported >95% adherence and all suppressed with re-initiation of cART

**Interpretation:** “Dolutegravir monotherapy was non-inferior to combination ART at 24 weeks. However, virological failure continued to occur thereafter and led to dolutegravir resistance. Dolutegravir should not be used as maintenance monotherapy.”

**Source:** Wijting I, et al. Lancet HIV. 2017;4;e547-54.
Acknowledgment

The National HIV Curriculum is an AIDS Education and Training Center (AETC) Program supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of an award totaling $800,000 with 0% financed with non-governmental sources. This project is led by the University of Washington’s Infectious Diseases Education and Assessment (IDEA) Program.

The content in this presentation are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by HRSA, HHS, or the U.S. Government.