

Dolutegravir-Lamivudine

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Dolutegravir-Lamivudine: Basics

- **Medication**

- Oral, once daily, fixed dose combination of dolutegravir (integrase strand transfer inhibitor) and lamivudine (nucleoside reverse transcriptase inhibitor)

- **Administration**

- Few drug-drug interactions and no food requirements
- Must rule out hepatitis B to avoid lamivudine monotherapy

- **With Renal Impairment**

- Not recommended in patients with renal impairment

- **With Hepatic Impairment**

- Not recommended in patients with severe hepatic impairment (Child-Pugh C)

- **Pregnancy**

- Insufficient data for use in pregnancy

- **Common Adverse Effects ($\geq 2\%$)**

- Headache, nausea, diarrhea, insomnia, fatigue, anxiety, and dizziness

Dolutegravir-Lamivudine

Dolutegravir

50 mg

 INSTI

Lamivudine

300 mg

 NRTI

Dose: 1 tablet once daily with or without food

Dolutegravir-Lamivudine

Initial Antiretroviral Therapy

Initial Antiretroviral Therapy

Dolutegravir-Lamivudine (2-Drug Regimen)



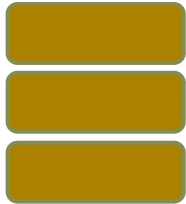
Baseline Requirements

- HIV RNA <500,000 copies/mL
- HBsAg negative
- Results from genotype known

Maintenance Antiretroviral Therapy

Initial Antiretroviral Therapy
3-Drug Regimen

Maintenance Antiretroviral Therapy
Dolutegravir-Lamivudine (2-Drug Regimen)



Requirements Prior to Switching

- HIV RNA <50 copies/mL for ≥ 6 months
- HBsAg negative
- No prior virologic failure
- No resistance to either maintenance drug

Dolutegravir-Lamivudine: Caution in Hepatitis B

Prior to prescribing DTG-3TC:

- Evaluate for active hepatitis B
 - If chronic hepatitis B is identified:
 - Avoid 3TC HBV monotherapy due to possible emergence of lamivudine-resistant HBV
 - DTG-3TC should only be used if another HBV-active agent is used
 - Discontinuation of DTG-3TC may lead to acute exacerbation
- Evaluate for immunity against hepatitis B
 - If not immune, vaccinate against hepatitis B

Dolutegravir-Lamivudine: Key Drug Interactions

- Contraindicated with dofetilide
- Dolutegravir concentrations typically decrease with:
 - Rifampin
 - Polyvalent cations
 - Some anticonvulsants
 - St. John's wort (*Hypericum perforatum*)

Dolutegravir-Lamivudine: Key Studies

Dolutegravir-Lamivudine: Key Studies

- **Treatment Naïve**
 - GEMINI 1 and 2
- **Treatment Experienced**
 - TANGO
 - SALSA

DTG + 3TC versus DTG + TDF-FTC as Initial ART

GEMINI 1 and GEMINI 2: Background

- **Background**

- Two double-blind, multinational, noninferiority, randomized, controlled trials that compared initial ART of dolutegravir plus lamivudine (DTG + 3TC) versus dolutegravir plus tenofovir-DF-emtricitabine (DTG + TDF-FTC)

- **Enrollment Criteria**

- Treatment-naïve adults
- HIV RNA 1,000-500,000 copies/mL
- No NRTI, INSTI, or major PI mutations
- No chronic HBV
- Not pregnant or breastfeeding

Dolutegravir-lamivudine
(Dual ART)

n = 716

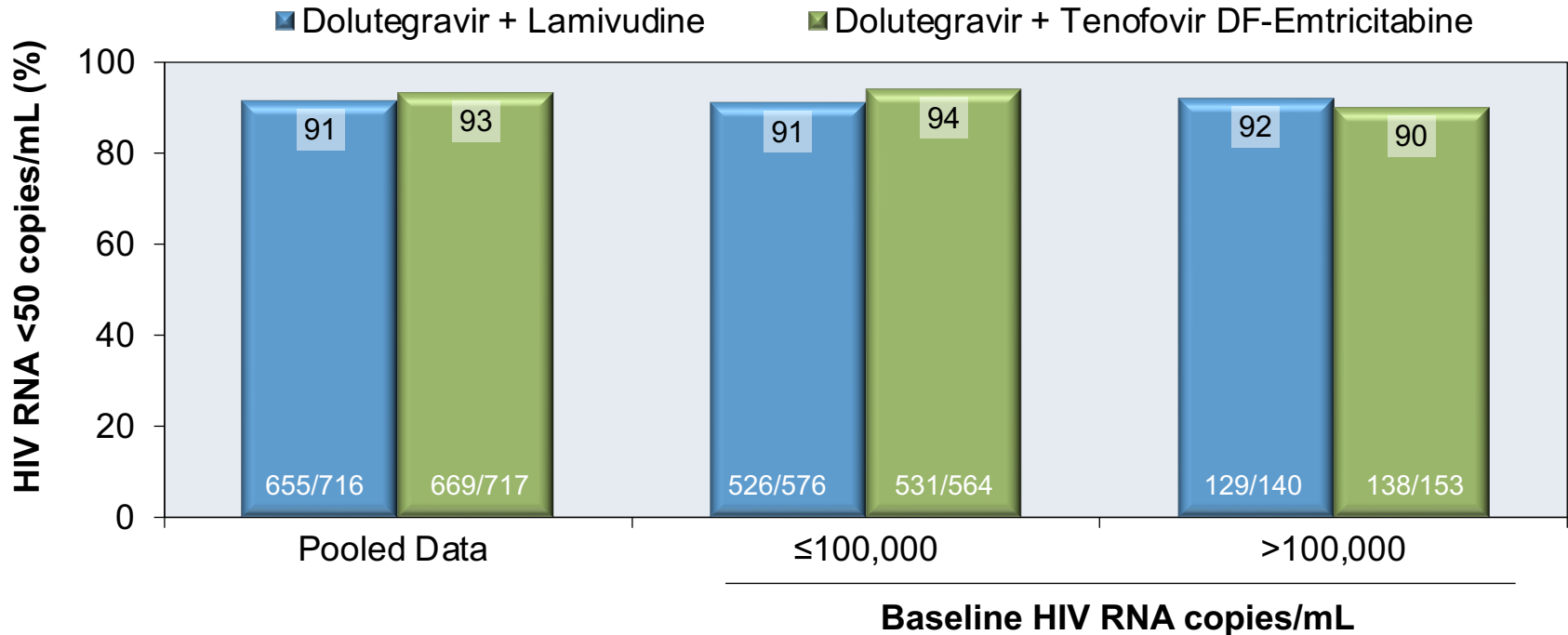
Dolutegravir + TDF-FTC
(Triple ART)

n = 717

DTG + 3TC versus DTG + TDF-FTC as Initial ART

GEMINI 1 and GEMINI 2: Results by Baseline HIV RNA Level

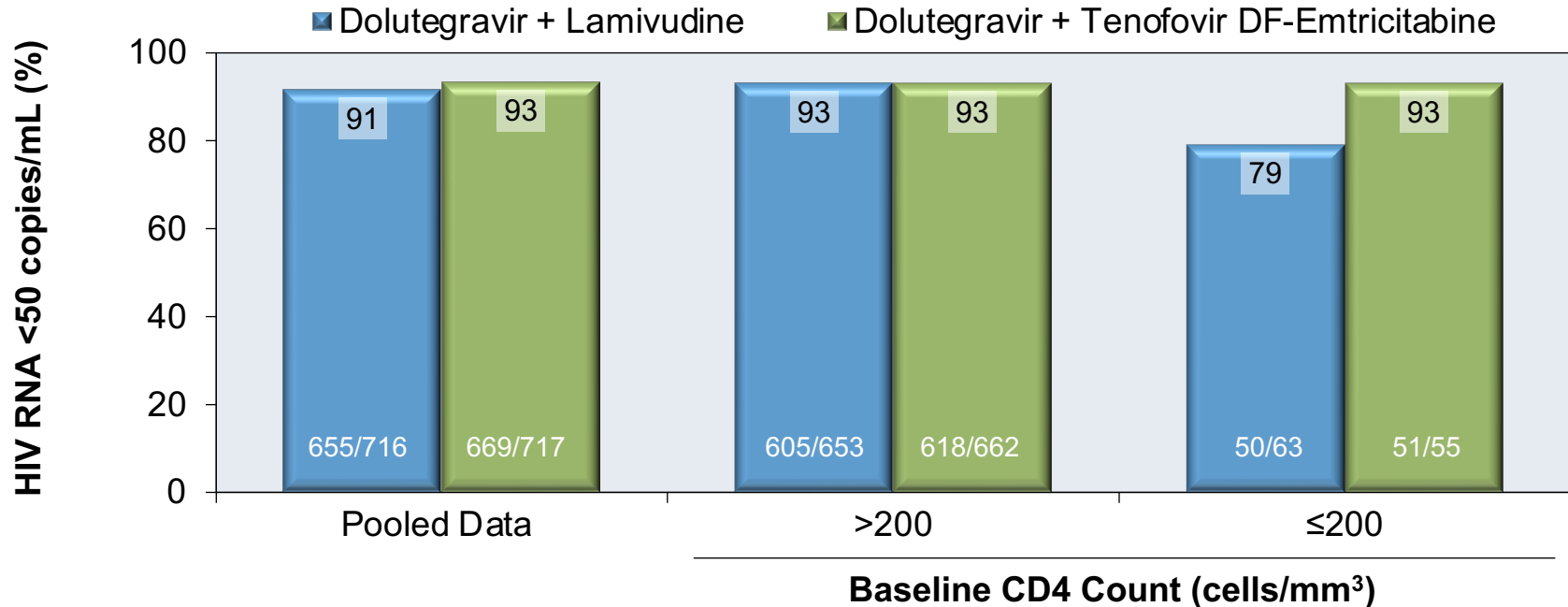
Week 48 Virologic Response (Intention-to-Treat Analysis)



DTG + 3TC versus DTG + TDF-FTC as Initial ART

GEMINI 1 and GEMINI 2: Results by Baseline HIV CD4 Cell Count

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



Switch to DTG-3TC versus Continued TAF-Based Baseline Regimen

TANGO: Design

- **Design**

- Open-label, non-inferiority trial
- Adults with suppressed HIV RNA while taking a 3- or 4-drug tenofovir alafenamide (TAF)-based regimen, randomized to switch to fixed-dose dolutegravir-lamivudine (DTG-3TC) or continue the baseline regimen

- **Inclusion Criteria**

- Adults with suppressed HIV RNA > 6 months
- No history of virologic failure
- No major NRTI mutation or any INSTI-RAM
- No Hepatitis B or C

- **Regimens**

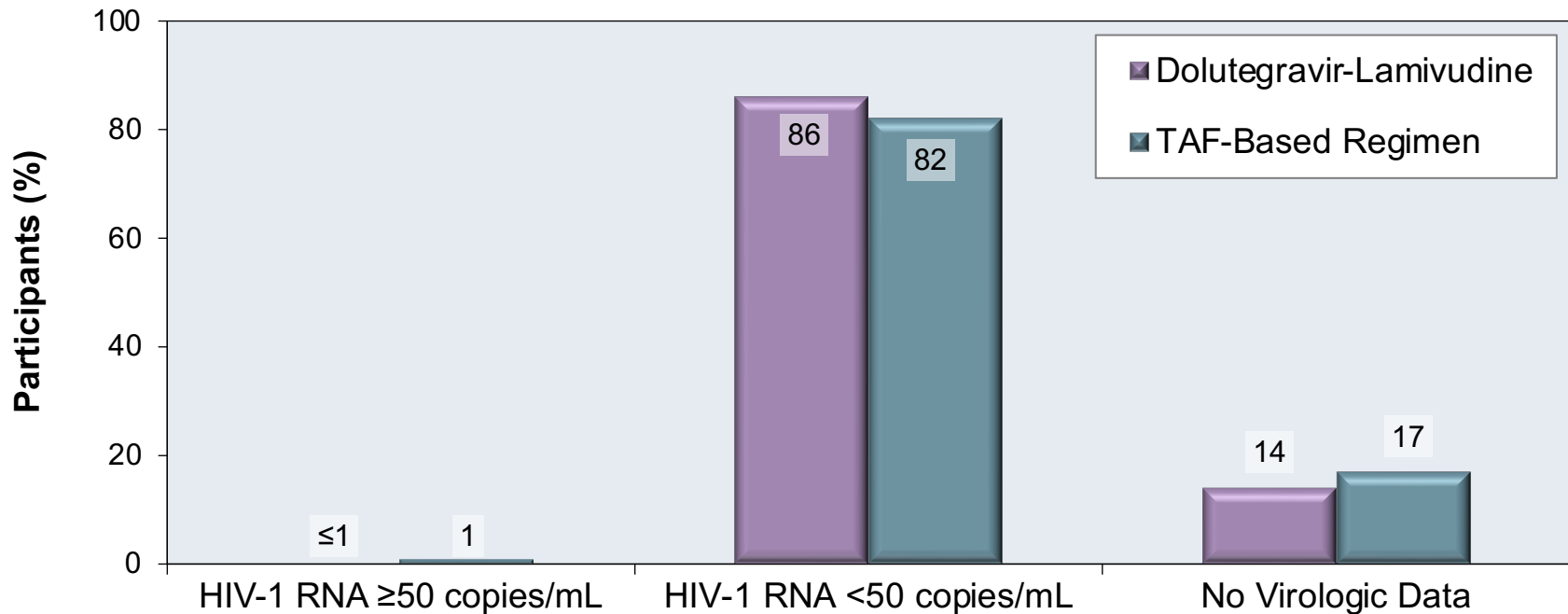
- Dolutegravir-lamivudine (50/300mg) daily
- TAF-based 3- or 4-drug baseline regimen

Switch Group
Dolutegravir-Lamivudine
(n = 369)

Continue Baseline Regimen Group
TAF-Based Regimen
(n = 372)

Switch to DTG-3TC versus Continued TAF-Based Baseline Regimen TANGO: 144 Week Results

Week 144 Virologic Response (ITT-Exposed)



Switch to DTG-3TC versus Continued 3- or 4-Drug Regimen

SALSA: Design

- **Design**

- Open-label, non-inferiority trial
- Adults with suppressed HIV RNA while taking a 3- or 4-drug regimen, randomized to switch to fixed-dose dolutegravir-lamivudine (DTG-3TC) or continue baseline regimen

- **Inclusion Criteria**

- Adults with suppressed HIV RNA \geq 6 months
- No history of virologic failure
- No major NRTI mutation or any INSTI-RAM
- No Hepatitis B or C

- **Regimens**

- Dolutegravir-lamivudine (50/300mg) daily
- 3- or 4-drug baseline regimen

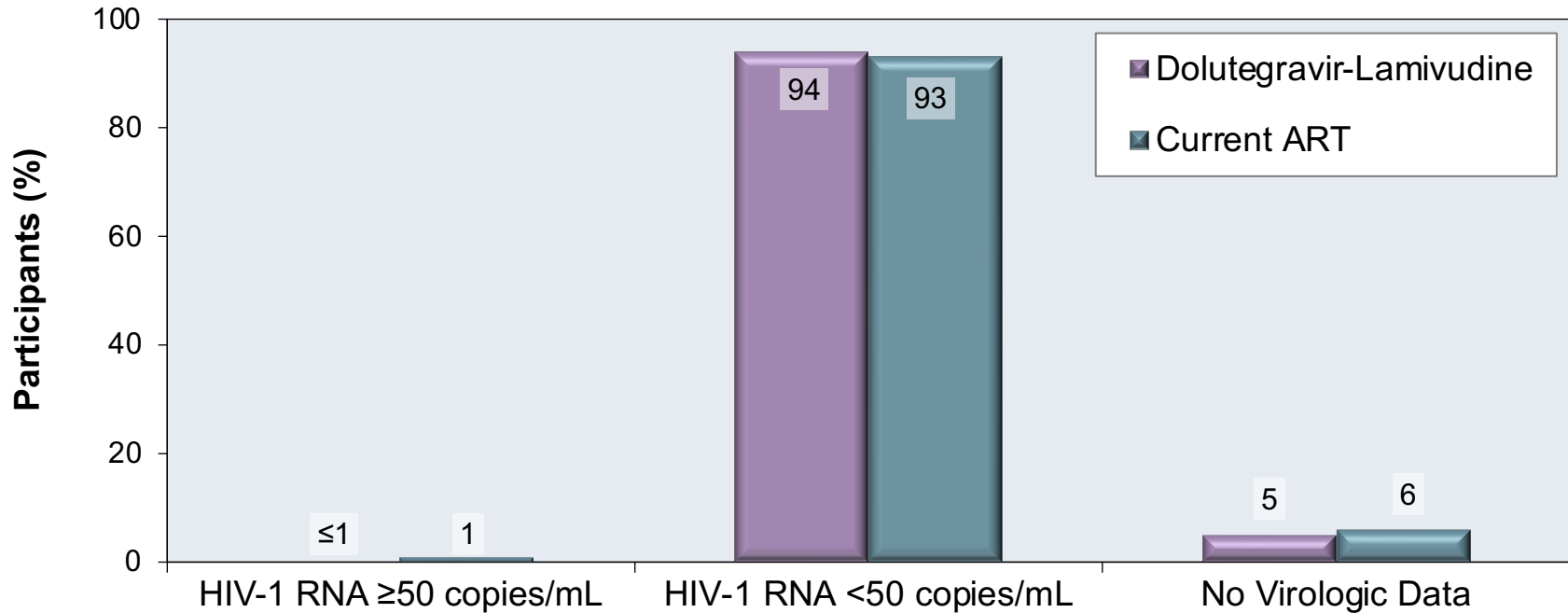
Switch Group
Dolutegravir-Lamivudine
(n = 246)

Continue Baseline Regimen Group
3- or 4-Drug Regimen
(n = 247)

Switch to DTG-3TC versus Continued 3- or 4-Drug Regimen

SALSA: 48 Week Results

Week 48 Virologic Response ITT-Exposed (Snapshot Analysis)



Summary of Dolutegravir + Lamivudine Trials

Study	Population	Outcome
GEMINI 1 and 2 ¹	Treatment-Naïve	DTG-3TC is non-inferior to Dolutegravir + 2 NRTIs, in PWH with HIV RNA <500,000 copies/mL and CD4 cell count >200 cells/mm ³
TANGO ²	Treatment-Experienced	DTG-3TC is non-inferior to 3- or 4-drug TAF-based regimen
SALSA ³	Treatment-Experienced	DTG-3TC is non-inferior to 3- or 4-drug baseline regimen

Source

¹Cahn P, et al. Lancet. 2019; 393:143-55.

Osiyemi O, et al. Clin Infect Dis. 2022;75:975-86.

³Libre JM, et al. Clin Infect Dis. 2022; Mar 2. Online ahead of print.

Dolutegravir-Lamivudine: Treatment-Emergent Resistance

- In GEMINI-1 and 2, TANGO, and SALSA, rare virologic failure occurred and no treatment emergent resistance was seen¹⁻³

Source

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²Osiyemi O, et al. Clin Infect Dis. 2022;75:975-86..

³Libre JM, et al. Clin Infect Dis. 2022; Mar 2. Online ahead of print.

Dolutegravir-Lamivudine: Summary

- Oral, once-daily pill available as a fixed dose combination
- Well-tolerated with few drug-drug interactions
- Exercise caution when administering a medication that decreases concentrations of dolutegravir
- Two-drug option for treatment-naïve PWH, without hepatitis B, with a CD4 cell count >200 cells/mm³ and HIV RNA $<500,000$ copies/mL
- Two-drug option treatment-experienced virally suppressed PWH, without hepatitis B, with no prior history of virologic failure and no major NRTI mutations or any INSTI RAMs

Acknowledgments

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