Investigational

National HIV Curriculum

Bictegravir-Tenofovir alafenamide-Emtricitabine

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

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AETC AIDS Education & Training Center Program
National Coordinating Resource Center

Investigational

Bictegravir 10-day Dose-Ranging Monotherapy

GS-US-141-1219

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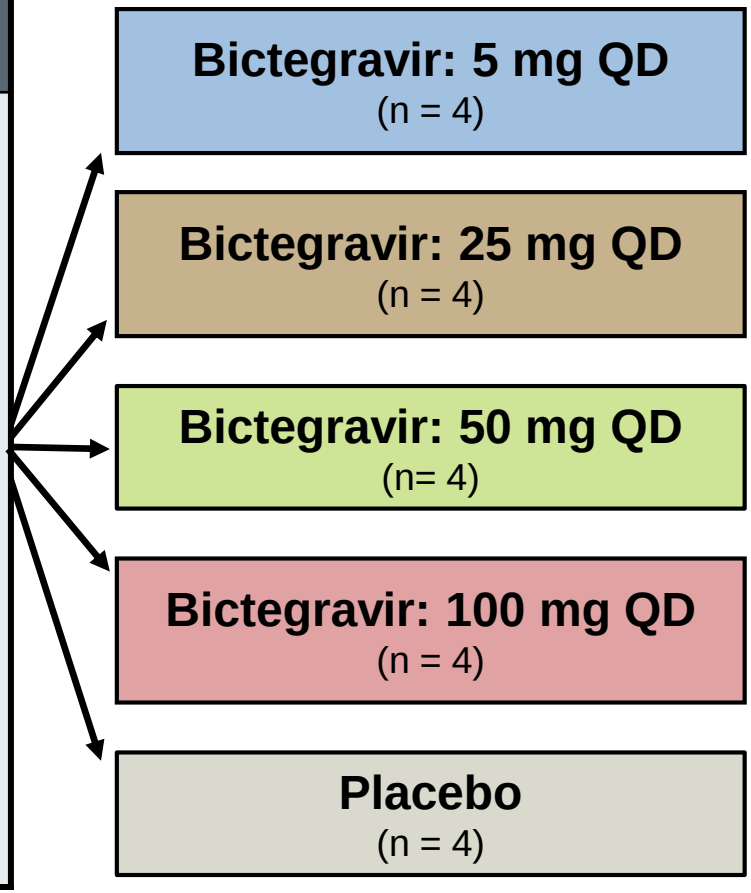
Investigational

Bictegravir 10-day Dose-Ranging Monotherapy
GS-US-141-1219: Design

GS-US-141-1219: Study Design

- **Background**: Randomized, double-blind, dose-ranging, placebo-controlled, 10-day, phase 1b study to evaluate antiviral activity, safety, and pharmacokinetics of the INSTI bictegravir
- **Inclusion Criteria (n = 20)**
  - Antiretroviral-naïve or
  - Antiretroviral-experienced but INSTI-naïve
  - Age: between 18 and 65
  - CD4 >200 cells/mm^3
  - HIV RNA between 10,000 and 400,000 copies/mL
- **Treatment Arms**
  - Bictegravir: 5, 25, 50, or 100 mg daily
  - Placebo: daily



Source: Gallant JE, et al. J Acquir Immune Defic Syndr. 2017;75:61-6.

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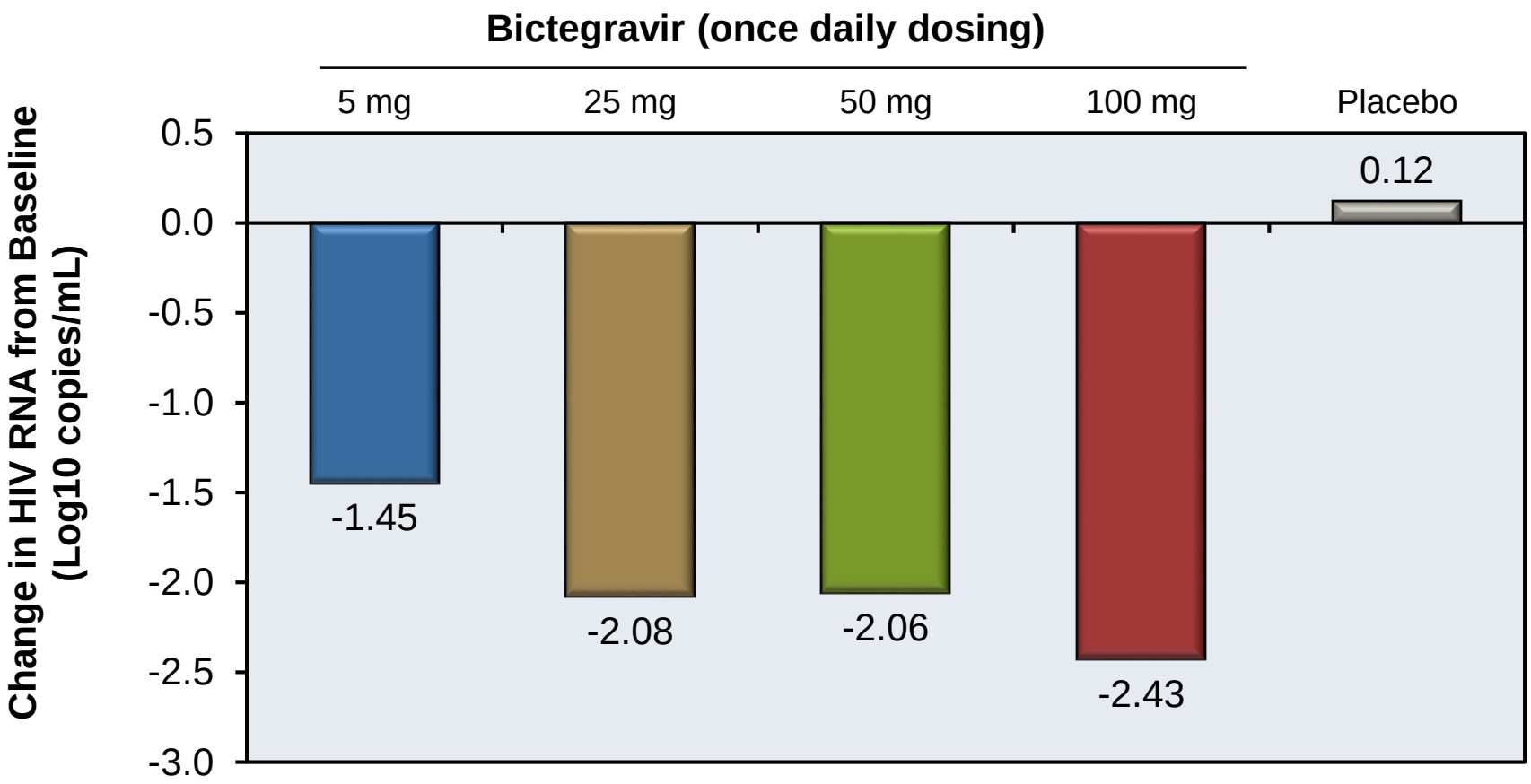
Bictegravir 10-day Dose-Ranging Monotherapy
GS-US-141-1219: Results

Baseline to Day 11: Change in Baseline HIV RNA Level



Source: Gallant JE, et al. J Acquir Immune Defic Syndr. 2017;75:61-6

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Bictegravir 10-day Dose-Ranging Monotherapy
GS-US-141-1219: Conclusions

Interpretation: “Bictegravir is a novel, potent, unboosted integrase strand transfer inhibitor (INSTI) that demonstrated rapid, dose-dependent declines in HIV-1 RNA after 10 days of monotherapy. Bictegravir was well tolerated, and displayed rapid absorption and a half-life supportive of once-daily therapy in HIV-infected subjects.”

Source: Gallant JE, et al. J Acquir Immune Defic Syndr. 2017;75:61-6

Investigational

Bictegravir versus Dolutegravir, each with TAF-FTC

GS-US-141-1475

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Bictegravir versus Dolutegravir, each with TAF-FTC
GS-US-141-1475: Design

Study Design

- **Background**: Randomized, double-blind, placebo controlled, phase 2 study evaluating the efficacy and safety of bictegravir versus dolutegravir as part of antiretroviral therapy for treatment-naïve individuals
- **Inclusion Criteria**
  - Age ≥ 18
  - Antiretroviral-naïve
  - CD4 count >200 cells/mm^3
  - HIV RNA ≥1,000 copies/mL
  - eGFR >70 mL/min
  - Genotypic sensitivity to TAF and FTC
  - No hepatitis B or C
  - Not pregnant
  - No AIDS-defining condition within 30 days

Bictegravir 75 mg QD + TAF-FTC
(n = 65)

Dolutegravir 50 mg QD + TAF-FTC
(n = 33)

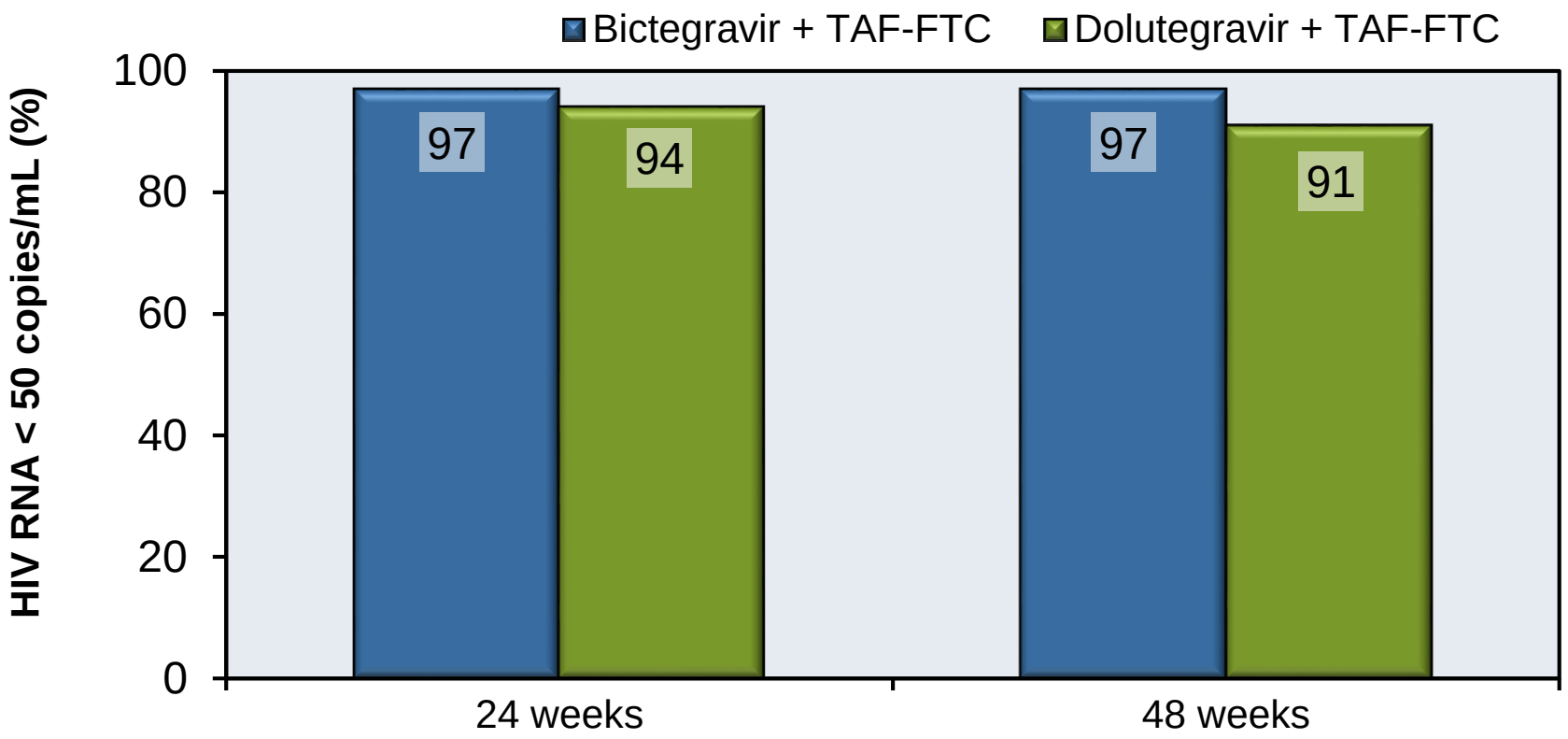
Source: Sax PE, et al. Lancet HIV. 2017;4:e154-e160.

Investigational

Bictegravir versus Dolutegravir, each with TAF-FTC

GS-US-141-1475: Results

Week 24 and 48: Virologic Response by FDA Snapshot Analysis



Source: Sax PE, et al. Lancet HIV. 2017;4:e154-e160.

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Bictegravir versus Dolutegravir, each with TAF-FTC
GS-US-141-1475: Adverse Effects

Most frequent adverse events in either study group		
	Bictegravir + TAF-FTC (n = 65)	**Dolutegravir + TAF-FTC** (n = 33)
Any adverse event	55 (85%)	22 (67%)
Diarrhea	8 (12%)	4 (12%)
Nausea	5 (8%)	4 (12%)
Arthralgia	4 (6%)	2 (6%)
Fatigue	4 (6%)	2 (6%)
Headache	5 (8%)	1 (3%)
No serious treatment-related adverse events occurred in either arm. 1 participant (with history of atopic dermatitis) in the bictegravir arm discontinued due to urticaria.		

Source: Sax PE, et al. Lancet HIV. 2017;4:e154-e160.

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Bictegravir versus Dolutegravir, each with TAF-FTC
GS-US-141-1475: Laboratory Abnormalities

Most frequent laboratory abnormalities in either study group		
	Bictegravir + TAF-FTC (n = 65)	**Dolutegravir + TAF-FTC** (n = 33)
Any laboratory abnormality	28 (44%)	15 (47%)
Creatinine kinase elevation	8 (13%)	3 (9%)
AST elevation	6 (9%)	1 (3%)
Fasting glucose elevation	5 (8%)	4 (13%)
ALT elevation	4 (6%)	0 (0%)
LDL elevation	4 (6%)	3 (9%)
Amylase elevation	3 (5%)	2 (6%)
Median decrease from baseline in estimated creatinine clearance: 7.0 mL/min in the bictegravir arm and 11.3 mL/min in the dolutegravir arm.		

Source: Sax PE, et al. Lancet HIV. 2017;4:e154-e160.

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Bictegravir versus Dolutegravir, each with TAF-FTC
GS-US-141-1475: Virologic Rebound and Resistance

Participants with Viral Rebound Meeting Protocol-Defined Criteria for Genotype Resistance Testing		
	Study arm	**Resistance detected**
Participant 1	Bictegravir + TAF-FTC	None
Participant 2	Dolutegravir + TAF-FTC	None
Participant 3	Dolutegravir + TAF-FTC	T97A*
*This participant discontinued the study at week 48 due to non-adherence.		

Source: Sax PE, et al. Lancet HIV. 2017;4:e154-e160.

Investigational

Bictegravir versus Dolutegravir, each with TAF-FTC
GS-US-141-1475: Conclusions

Interpretation: “Bictegravir plus emtricitabine and tenofovir alafenamide and dolutegravir plus emtricitabine and tenofovir alafenamide both showed high efficacy up to 24 weeks. Both treatments were well tolerated. Administration of bictegravir, a novel, potent, once-daily INSTI designed to improve on existing INSTI options with the backbone of emtricitabine and tenofovir alafenamide, might provide an advantage to patients.”

Source: Sax PE, et al. Lancet HIV. 2017;4:e154-e160.

Acknowledgment

The **National HIV Curriculum** is an AIDS Education and Training Center (AETC) Program resource funded by the United States Health Resources and Services Administration. The project is led by the University of Washington and the AETC National Coordinating Resource Center.

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