2024 International AIDS Society Conference Review: Part 2

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No conflicts of interest or relationships to disclose.

Disclaimer

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AETC AIDS Education & Training Center Program Mountain West

HPTN 083: Performance Characteristics of HIV RNA Screening with Long-Acting Cabotegravir (CAB-LA)

- HPTN 083: phase 3 HIV PrEP trial comparing CAB-LA IM every 2 months to daily oral TDF/FTC for MSM and transgender women
  - Retrospective data: RNA tests identified HIV earlier, often prior to INSTI resistance
- Open-label extension:
  - Rapid test, Ag/Ab lab test, plus HIV RNA every study visit
  - Total 26,528 RNA screening tests for 2,619 participants
- Isolated RNA-positive cases: **n = 27**
  - **22 false positive** (median BLQ; range BLQ – 149 copies/mL)
  - 5 true positive (median 1,597 copies/mL; range 124 – 4,120 copies/mL)

*BLQ = below limit of quantification

Source: Landovitz RJ, et al. IAS 2024. Abstract OAE0406LB.

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HPTN 083: Performance Characteristics of HIV RNA Screening with Long-Acting Cabotegravir

	Positive predictive value (PPV, 95% CI)
Overall	**18.5%** (7.0%, 38.7%)
CAB-LA within prior 6 months	9.1% (1.6%, 30.6%)
No CAB-LA within prior 6 months	60% (17%, 92.7%)

- "In this preliminary analysis, a single isolated positive RNA result performed poorly for detecting HIV with CAB-LA PrEP"
- Single isolated positive RNA results were infrequent and usually false positive
  - Performance better if CAB-LA not given within past 6 months
  - Repeat HIV RNA testing was able to discriminate true from false positive

Source: Landovitz RJ, et al. IAS 2024. Abstract OAE0406LB.

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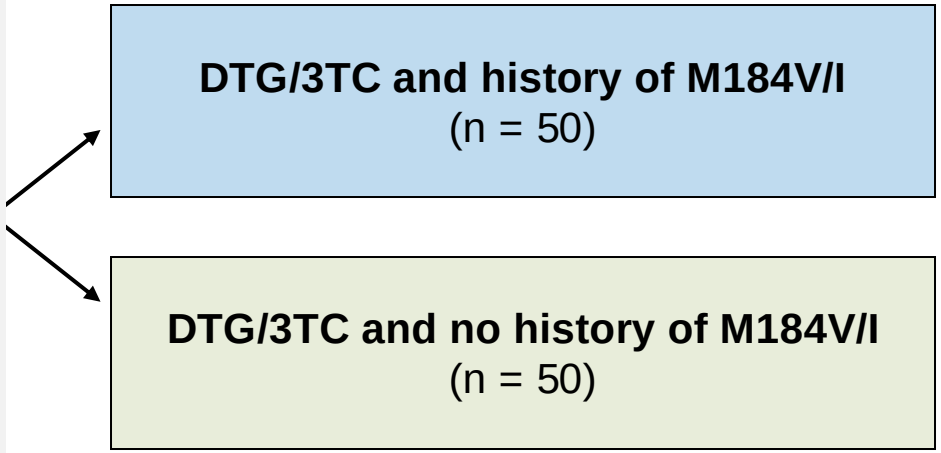
SOLAR3D: Switch to DTG/3TC with Prior Virologic Failure and M184V/I Mutation

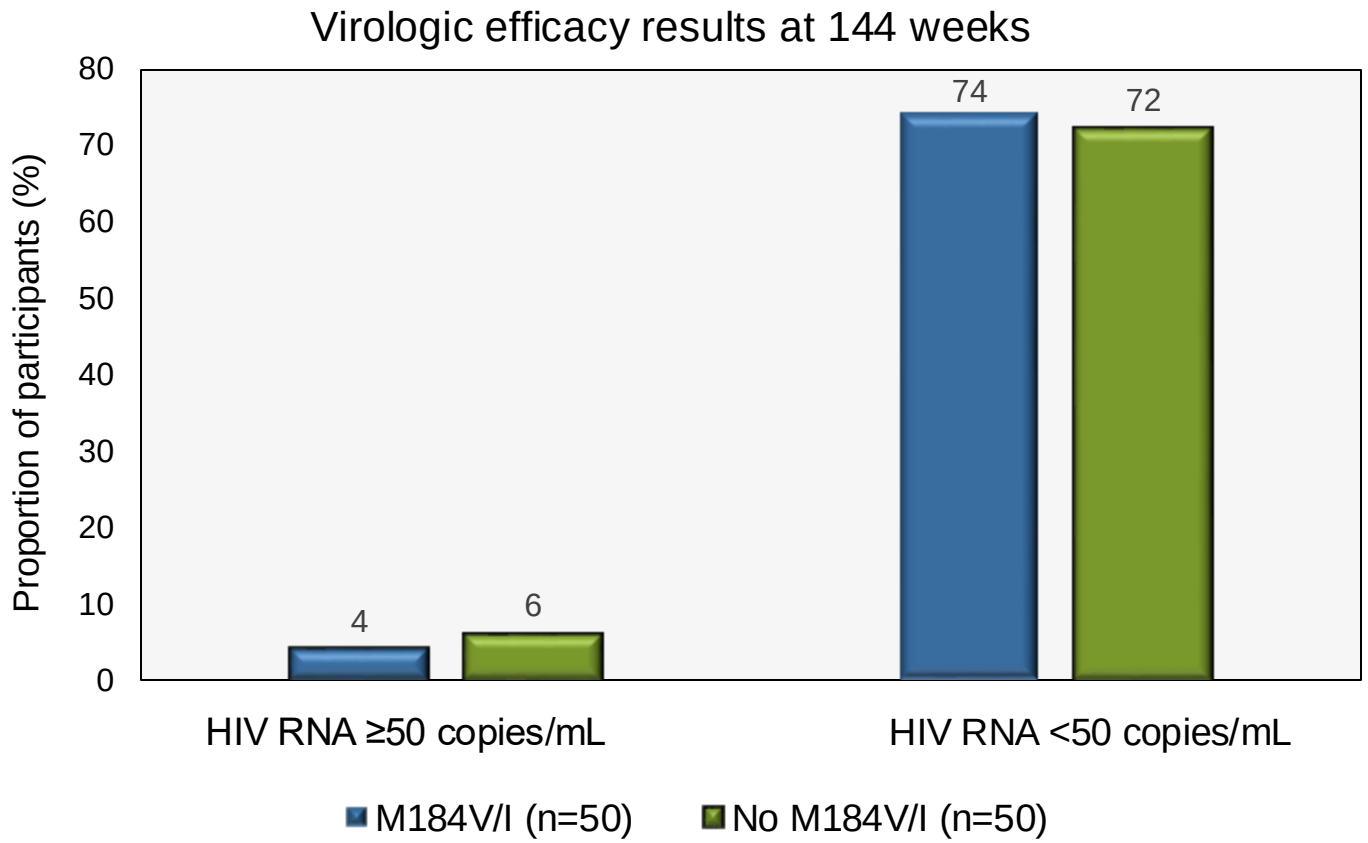
- **Design**
  - Prospective, open-label, comparative study
- **Eligibility Criteria**
  - Adults with HIV RNA <50 copies/mL for ≥6 months on any stable 2-/3-/4-drug ART
  - All with prior virologic failure and at least 2 prior ART regimens
  - No exclusion for CD4 count, INSTI experience, past NRTI resistance, M184V/I or K65R on baseline proviral genotype
- **Primary endpoint:**
  - Proportion of participants with HIV RNA >50 copies/mL at 144 weeks



At baseline: median ART duration 22.3 years, median 7 previous ART regimens, median duration viral suppression 11.8 years

Source: Blick G, et al. IAS 2024. Abstract SS0403LB.

SOLAR3D: Switch to DTG/3TC with Prior Virologic Failure and M184V/I Mutation



	M184V/I on Historical Genotype (n = 50)	No M184V/I on Historical Genotype (n = 50)
Proviral genotype	41 (82)	29 (58)
M184V/I present	15 (37)	0
M184V/I absent	26 (63)	29 (100)
All reported as: n (%)		

No difference in rate of virologic suppression, confirmed virologic failures (0 with M184V/I, 1 with no M184V/I due to adherence), incidence of viral blips

Source: Blick G, et al. IAS 2024. Abstract SS0403LB.

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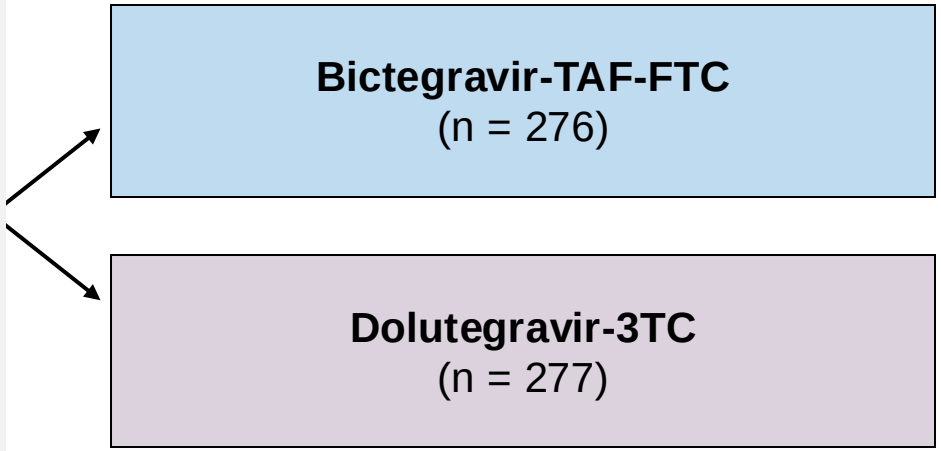
PASO DOBLE: Switch to DTG/3TC or BIC/TAF/FTC for PWH with Virologic Suppression

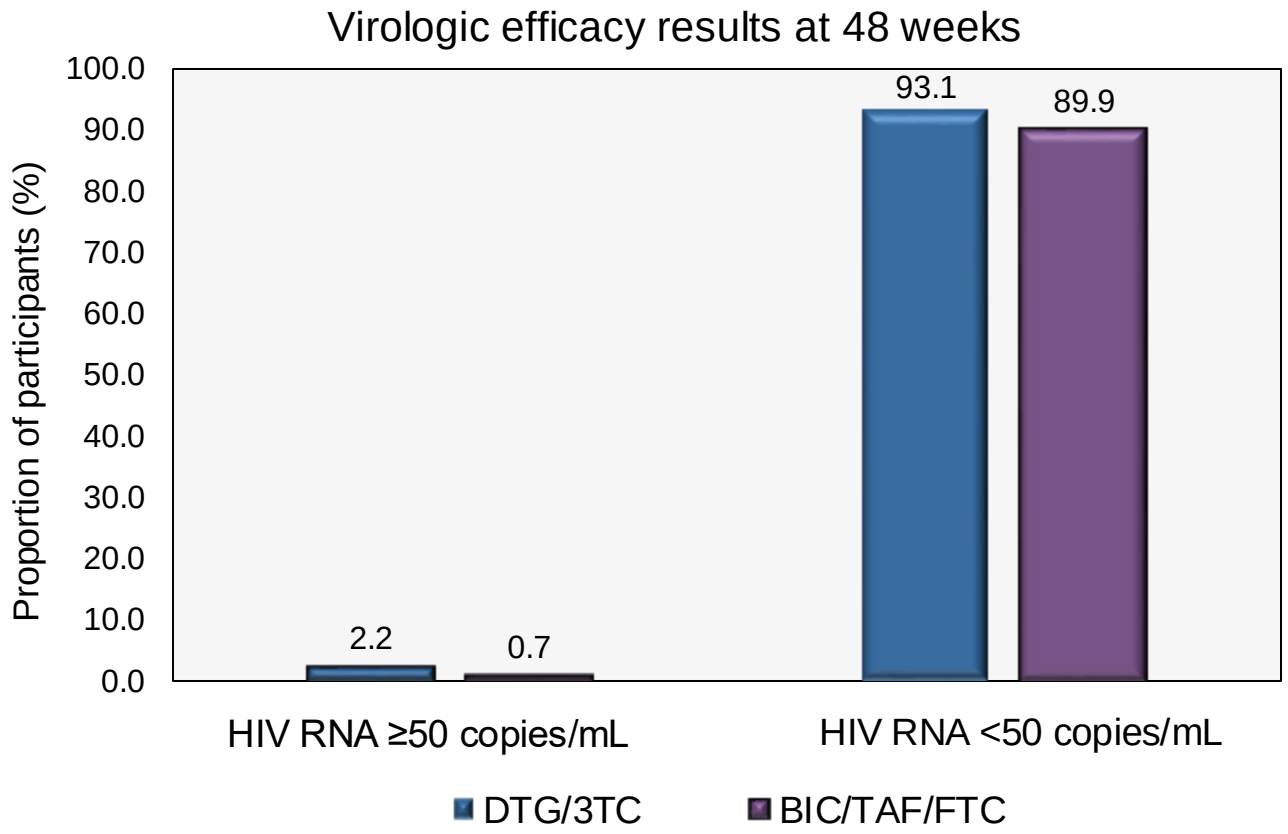
- **Design**
  - Phase 4, randomized, open-label trial conducted at 30 sites in Spain
- **Including Criteria**
  - Adults with HIV RNA <50 copies/mL for ≥6 months while taking ART containing >1 pill/day, cobicistat booster, EFV, or TDF
  - No prior virologic failure or known or suspected resistance
  - No prior dolutegravir or bictegravir
  - No hepatitis B
- **Primary endpoints:**
  - HIV RNA >50 copies/mL and weight change at 48 weeks



Baseline ART:
≈ 28% TAF, 35% TDF
≈ 50% NNRTI, 16.5% INSTI, 32% PI, 1% multiple

Source: Ryan P, et al. IAS 2024. Abstract OAB3606LB.

PASO DOBLE: Switch to DTG/3TC or BIC/TAF/FTC for PWH with Virologic Suppression



No difference in virologic suppression, virologic failures, viral blips, tolerability

Source: Ryan P, et al. IAS 2024. Abstract OAB3606LB.

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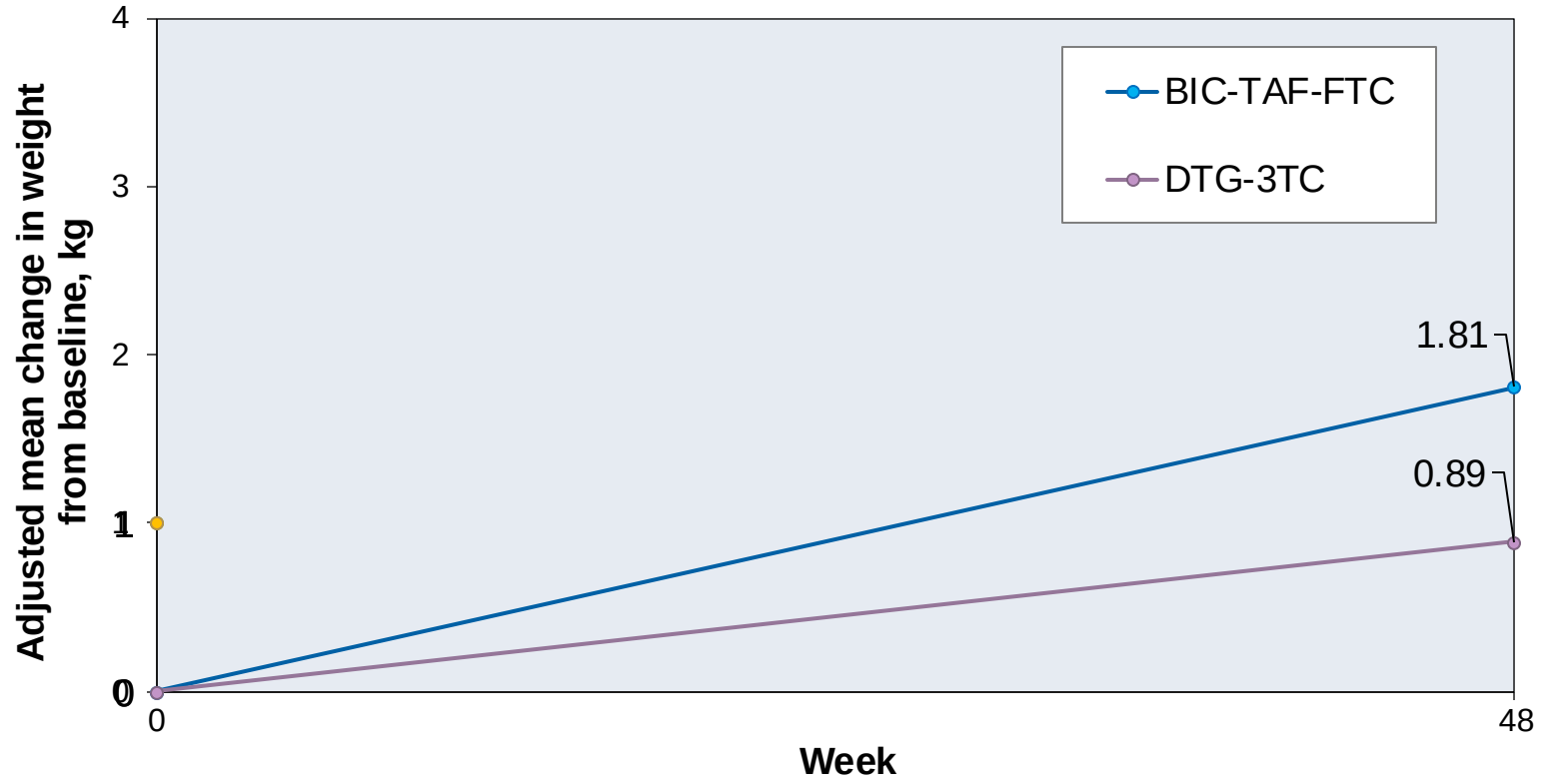
PASO DOBLE: Switch to DTG/3TC or BIC/TAF/FTC for PWH with Virologic Suppression

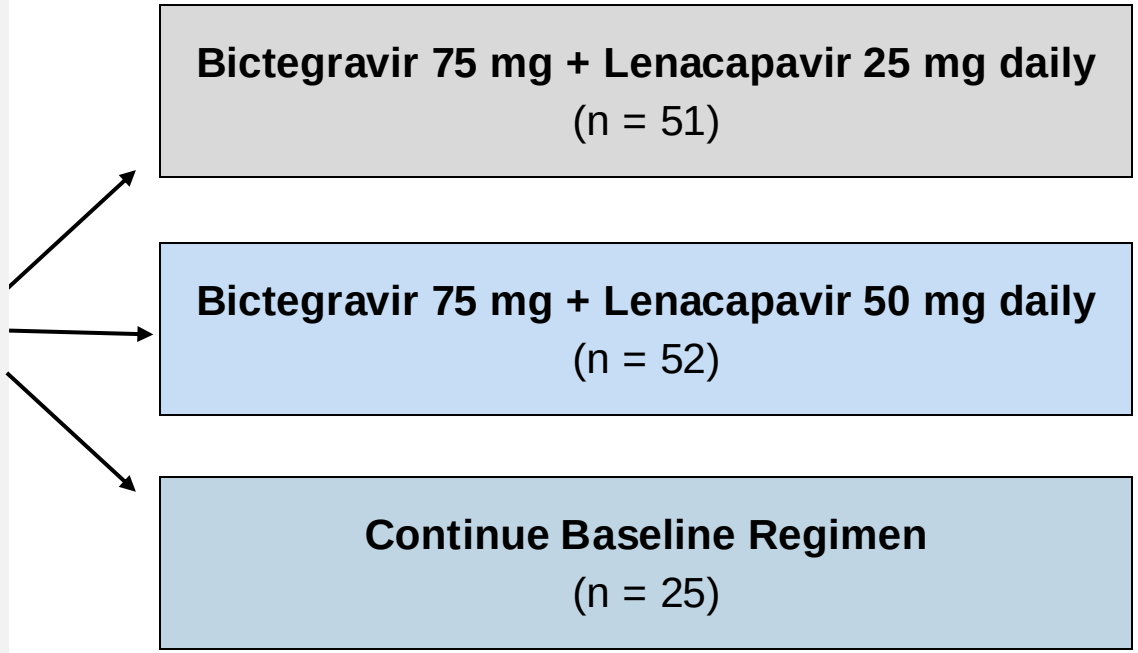


- BIC/TAF/FTC group: proportion with >5% body weight increase varied by pre-switch ARVs (most prevalent with TDF, followed by ABC, and heavily influenced by EFV)
- DTG/3TC group: proportion with >5% body weight increase similar irrespective of pre-switch ARVs

Source: Ryan P, et al. IAS 2024. Abstract OAB3606LB.

ARTISTRY-1: Switch to Daily Oral BIC + Daily Oral LEN for PWH Taking Complex ART Regimens

- **Background**: Phase 2/3, open-label, randomized trial
- **Inclusion Criteria**
  - Adults with HIV RNA <50 copies/mL for at least 6 months while taking a complex ART regimen*
  - No prior lenacapavir exposure or bictegravir resistance
  - No hepatitis B
  - eGFR above 15 mL/min
- **Participants:**
  - Median age 60, 79% male, 41.4% taking ART twice daily, 27.3% taking ≥5 pills per day, 72% taking a PI, resistance in INSTI/NNRTI/NRTI/PI classes: 0%/52%/64%/36%
- **Primary Outcome:**
  - Virologic efficacy at 48 weeks



*Complex ART regimen: boosted PI or NNRTI + ≥1 other ARV from a class other than NRTI, or a combination requiring ≥2 pills daily or ≥once-daily dosing, or regimen with a parenteral ARV

Source: Mounzer K, et al. IAS 2024. Abstract OAB2602.

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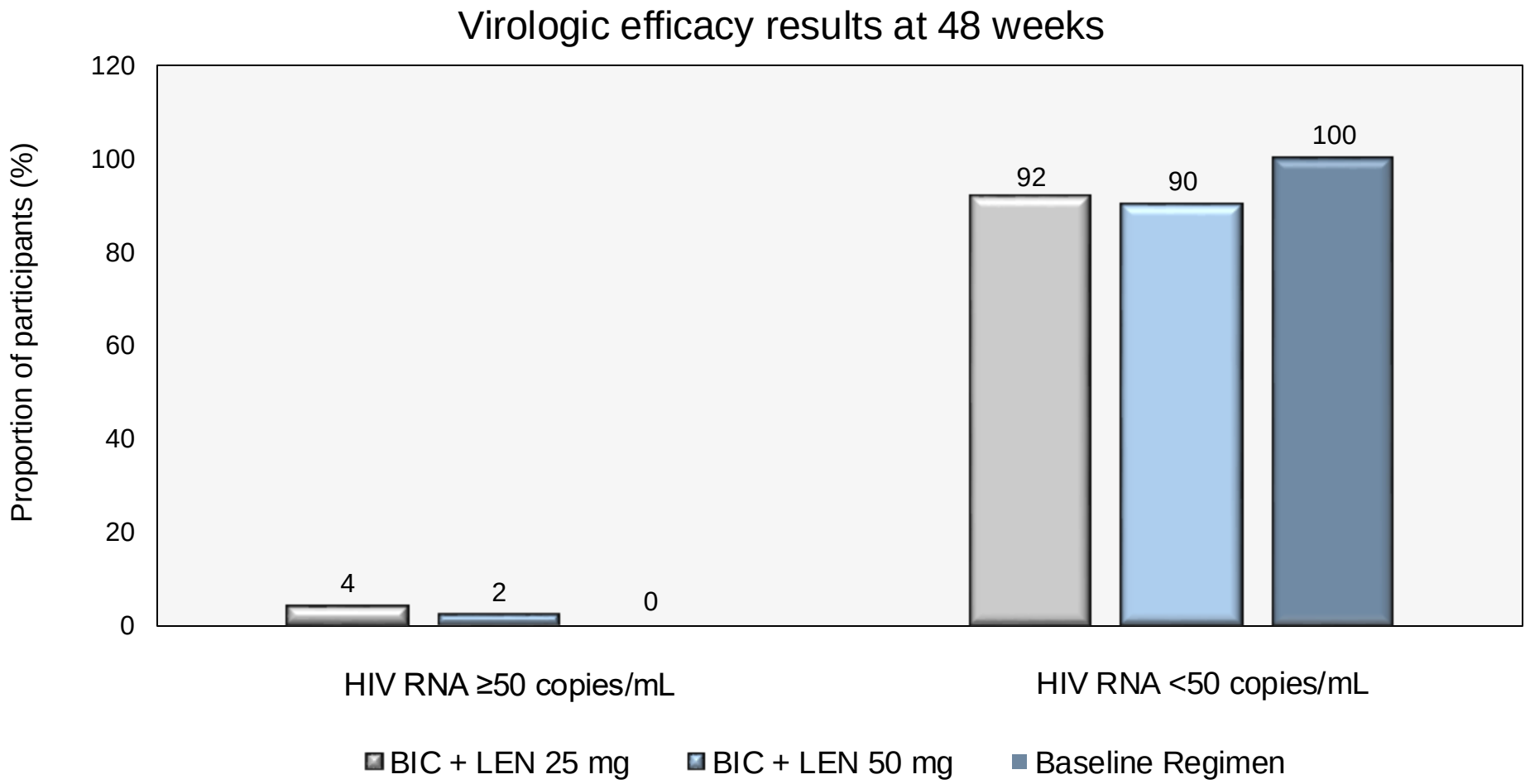

Source: Mounzer K, et al. IAS 2024. Abstract OAB2602.

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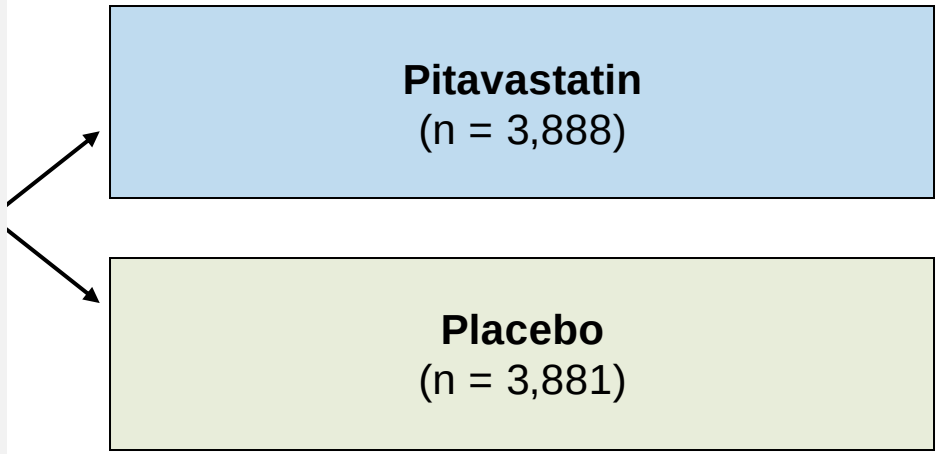
REPRIEVE: Abacavir Exposure Status and Risk of Major Adverse Cardiovascular Events (MACE)

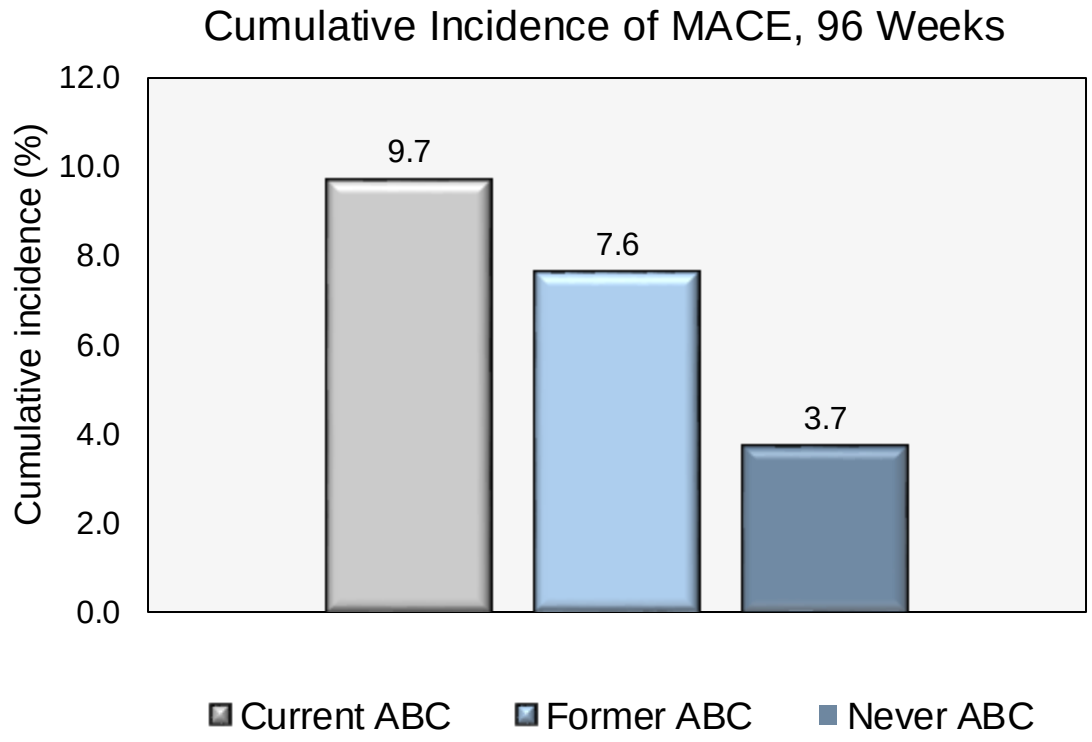
- **Design**
  - Phase 3, randomized controlled trial
- **Including Criteria**
  - PWH taking stable ART
  - 40 to 75 years of age
  - Low-to-moderate risk of atherosclerotic CVD
- **New Analysis:**
  - Compare risk of MACE with current abacavir exposure, prior abacavir exposure, or no abacavir exposure
  - Abacavir exposure: 13% current (median 1.5 years), 9% former (median 3.0 years), 78% never



Source: Fichtenbaum CJ, et al. IAS 2024. Abstract OAB3406LB.

REPRIEVE: Abacavir Exposure Status and Risk of Major Adverse Cardiovascular Events (MACE)

- Principal result: abacavir exposure (versus none) associated with higher incidence of MACE
- Adjusted hazard ratio (95% CI):
  - Former use: **1.50** (1.04, 2.15)
  - Current use: **1.42** (1.00, 2.00)
- No association with current or former use of TDF, AZT, D4T, or PI



Source: Fichtenbaum CJ, et al. IAS 2024. Abstract OAB3406LB.

7th Reported HIV Sustained Remission ("Cure") Case: The "Next Berlin Patient"

- White male, born in 1964, HIV diagnosis 2009
  - Sample from 2014: **heterozygous CCR5 wild type/delta 32 mutation**
- No ART until 4/2015, then raltegravir + ABC/3TC
- Acute myeloid leukemia (AML) diagnosis 4/2015
  - **Stem cell transplant 10/2015 from heterozygous CCR5 wild type/delta 32 donor**
- ART interrupted 2018
- **HIV remission >5.5 years**
  - No detectable HIV DNA or viral outgrowth
  - Waning HIV-specific antibody and T cell immunity

Characteristics of 7 "cure" cases:
- 4 homozygous delta 32 donors
- 1 heterozygous donor
- 1 wild type stem cells
- 1 mix of homozygous & wild type
- 4 intensive conditioning chemo
- 2 severe graft versus host disease

Source: Gaebler, et al. IAS 2024. Abstract SS0402LB.

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Key Take-Home Points

- Isolated positive HIV RNA infrequent with LA-CAB PrEP; repeat it if occurs
- Switch to DTG/3TC effective in the setting of M184V/I
- Switch to BIC/TAF/FTC and DTG/3TC similar virologic efficacy; weight gain greater with BIC/TAF/FTC, but dependent on pre-switch regimen
- Daily oral BIC + LEN promising as switch strategy for individuals with heavy treatment experience and complex ART regimen
- Current or former abacavir exposure indeed contribute to risk of MACE
- New case of sustained HIV remission following stem cell transplant suggests CCR5 delta 32 homozygous donor not always necessary

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