IAS 2019: Antiretroviral Studies

Brian R. Wood, MD
Associate Professor of Medicine
University of Washington
Mountain West AIDS Education & Training Center

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Disclosures

No conflicts of interest or relationships to disclose.

Outline

- Update on 2-drug (dual) ART
  - TANGO (DTG/3TC as maintenance ART)
  - DUALIS (Boosted DRV + DTG as maintenance ART)
  - GEMINI (DTG/3TC as initial ART)
- New antiretroviral agents
  - Fostemsavir (FTR)
  - Islatravir (ISL)

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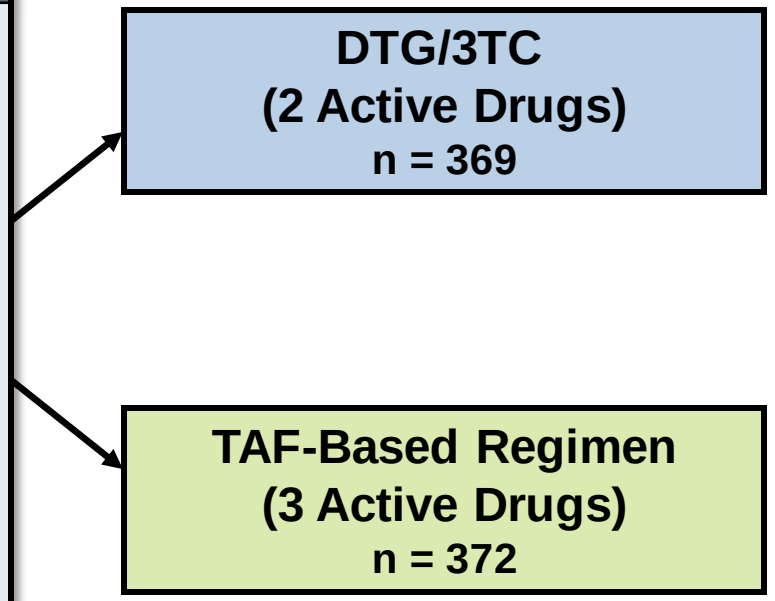
Update on Dual ART

Switch to DTG/3TC vs Continued TAF-Based 3-Drug ART
TANGO: Background

Study Design: TANGO

- **Background**:
  - Ongoing, phase 3, randomized, open label, multicenter, non-inferiority trial
- **Enrollment Criteria:**
  - Adults with HIV RNA <50 copies/mL for >6 months on stable 3-drug TAF-based ART (ok if started TDF but switched to TAF ≥3 months before screening)
  - No HBV or need for HCV treatment
  - No prior virologic failure or documented NRTI or INSTI resistance resistance



Primary endpoint: virologic response at 48 weeks by FDA snapshot

Source: van Wyk J et al. IAS July 2019, Mexico City.

Switch to DTG/3TC vs Continued TAF-Based 3-Drug ART
TANGO: Baseline Characteristics

Characteristic	DTG/3TC (n = 369)	TAF-Based 3-Drug ART (n = 372)
Age, years, median (range)	40 (20-74)	39 (18-73)
Female, n (%)	25 (7)	33 (9)
White, n (%)	296 (80)	289 (78)
Black/African American, n (%)	51 (14)	13 (3)
CD4 cell count, mean (range)	682 (133-1904)	720 (119-1810)
CD4 cell count <350, n (%)	35 (9)	30 (8)
Months on ART, median (range)	33.8 (7.1-201.2)	35.1 (7.0-160.8)
Baseline third agent class		
INSTI	289 (78)	296 (80)
NNRTI	51 (14)	48 (13)
PI	29 (8)	28 (8)

Source: van Wyk J et al. IAS July 2019, Mexico City.

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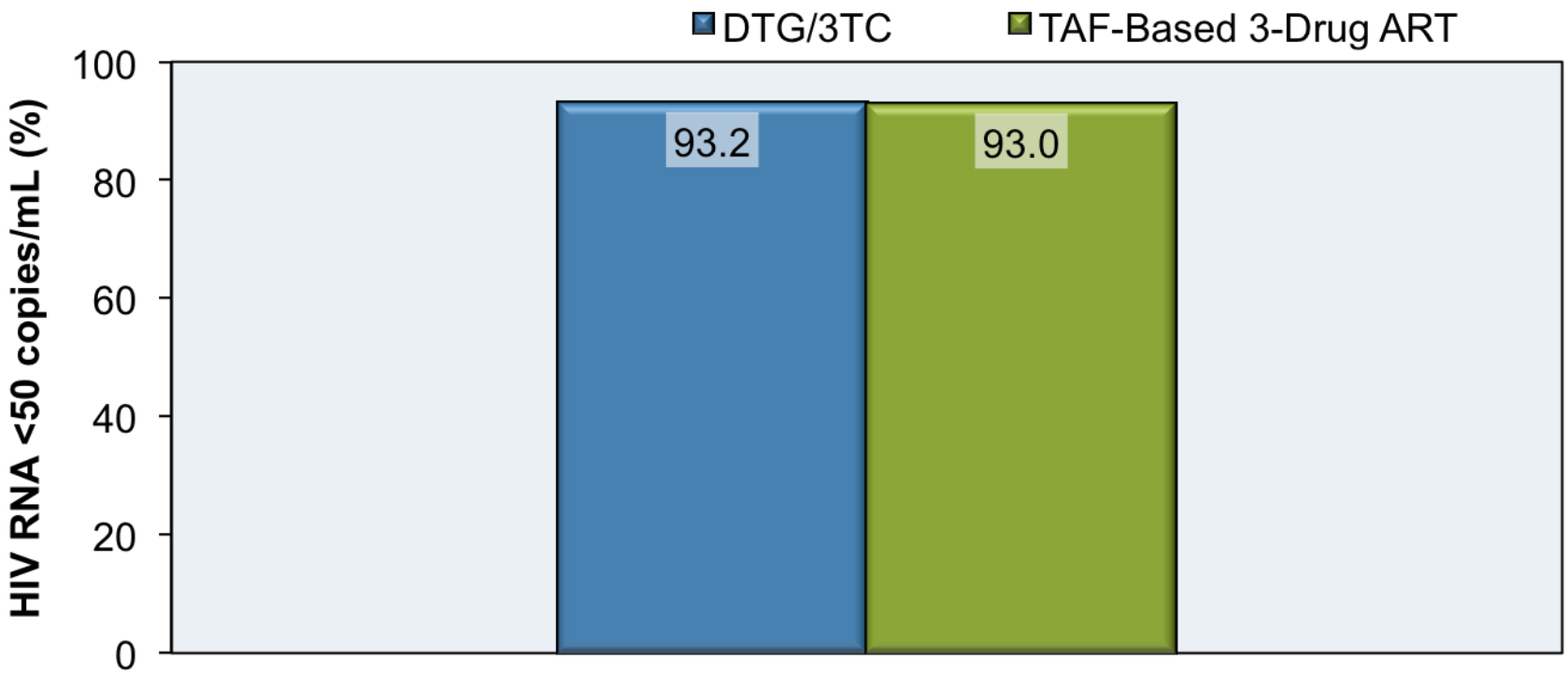
Switch to DTG/3TC vs Continued TAF-Based 3-Drug ART TANGO: Results

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



- Confirmed withdrawal for virologic failure: 0 in DTG/3TC arm, 1 in TAF-based ART arm
- No new resistance mutations occurred
- 4 with baseline M184V/I in DTG/3TC arm (by proviral genotype) suppressed at week 48

Source: van Wyk J et al. IAS July 2019, Mexico City.

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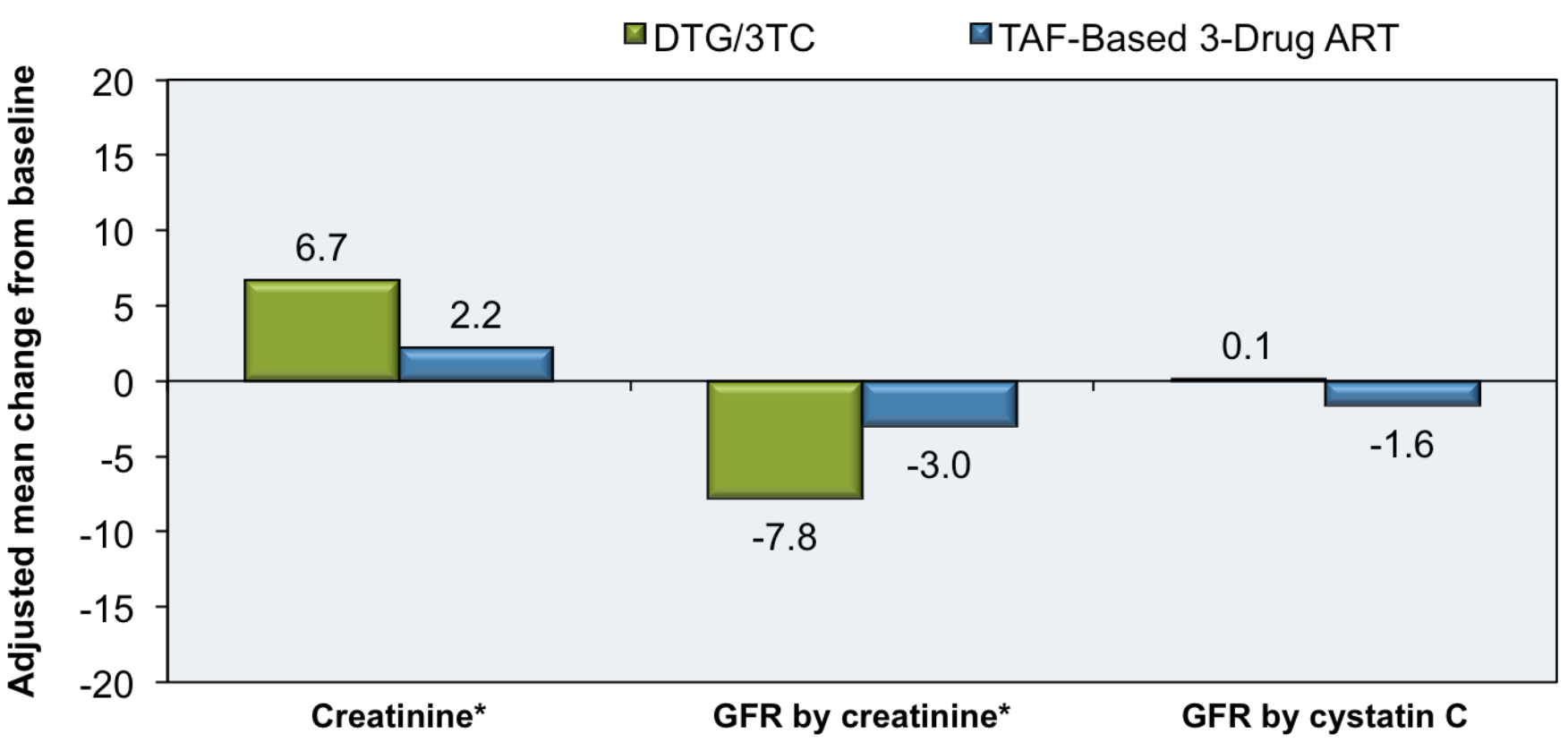
Switch to DTG/3TC vs Continued TAF-Based 3-Drug ART TANGO: Results

Week 48 Changes in Renal Function (Plasma/Serum Markers)



*Statistically significant difference

Source: van Wyk J et al. IAS July 2019, Mexico City.

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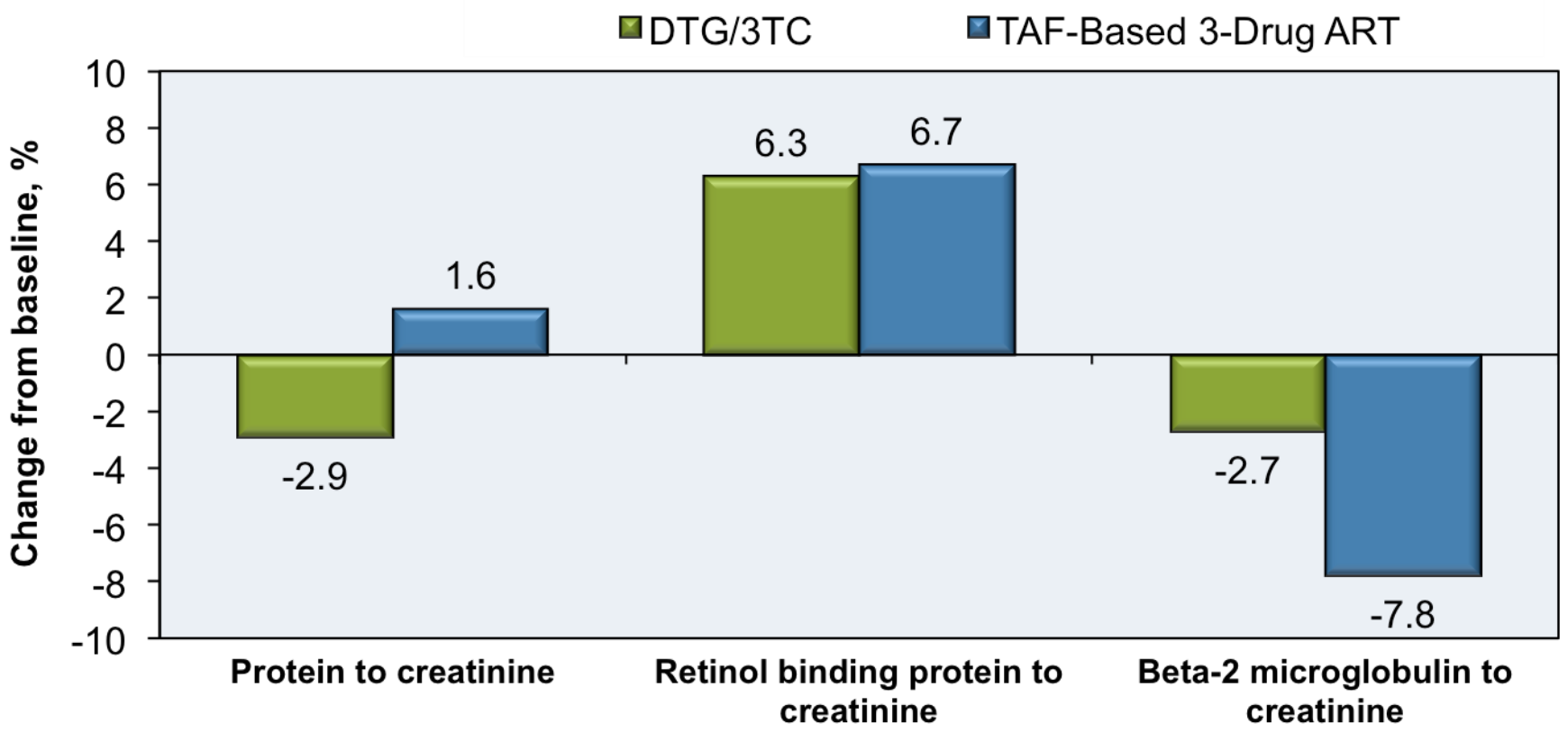
Switch to DTG/3TC vs Continued TAF-Based 3-Drug ART TANGO: Results

Week 48 Changes in Markers of Proximal Tubulopathy (Urine Tests)



Source: van Wyk J et al. IAS July 2019, Mexico City.

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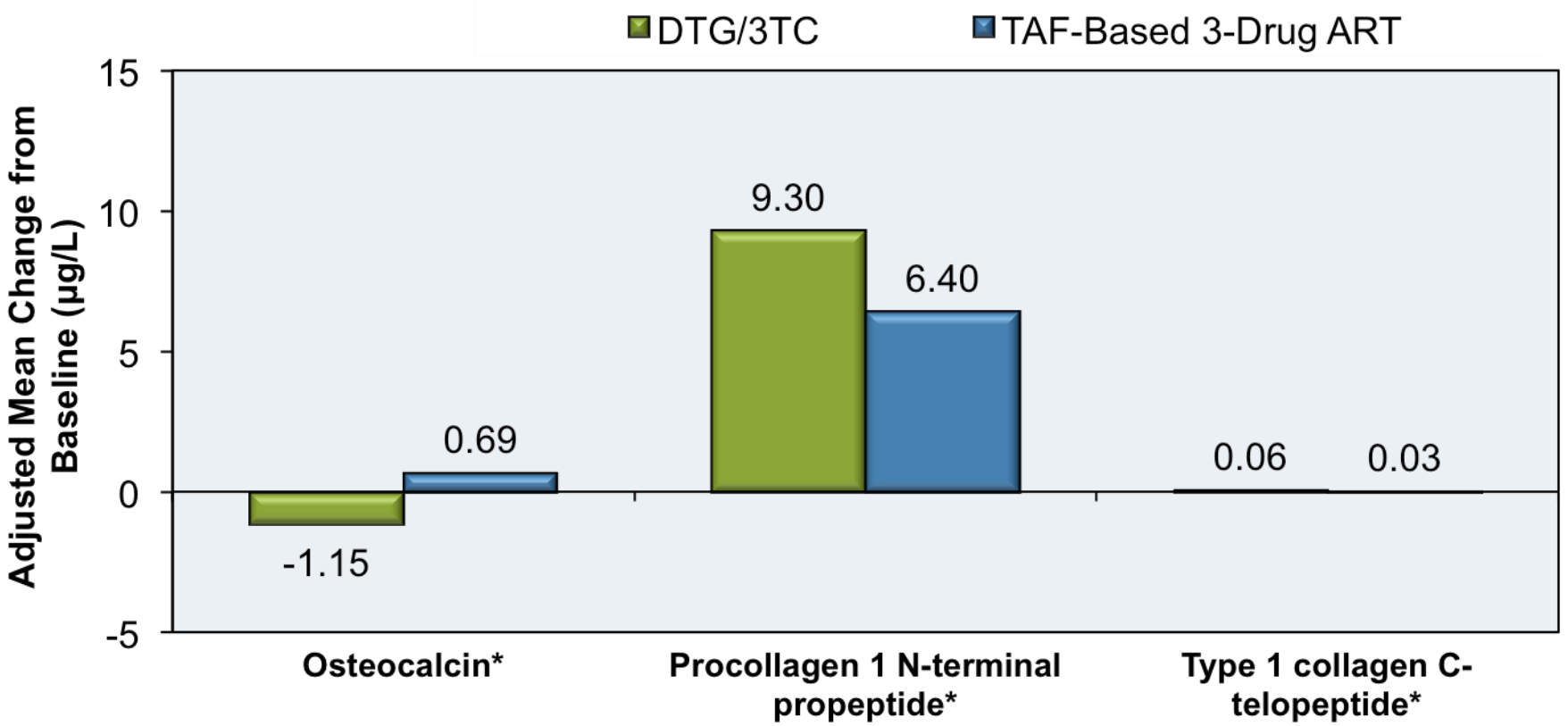
Switch to DTG/3TC vs Continued TAF-Based 3-Drug ART TANGO: Results

Week 48 Changes in Serum Bone Biomarkers



*Statistically significant difference

Source: van Wyk J et al. IAS July 2019, Mexico City.

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Switch to DTG/3TC vs Continued TAF-Based 3-Drug ART
TANGO: Conclusions

Conclusion: “These data support the use of DTG/3TC as a new robust switch option without increased risk of virologic failure or resistance and with reduced ART exposure.”

Source: van Wyk J et al. IAS July 2019, Mexico City.

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Additional Dual ART Studies

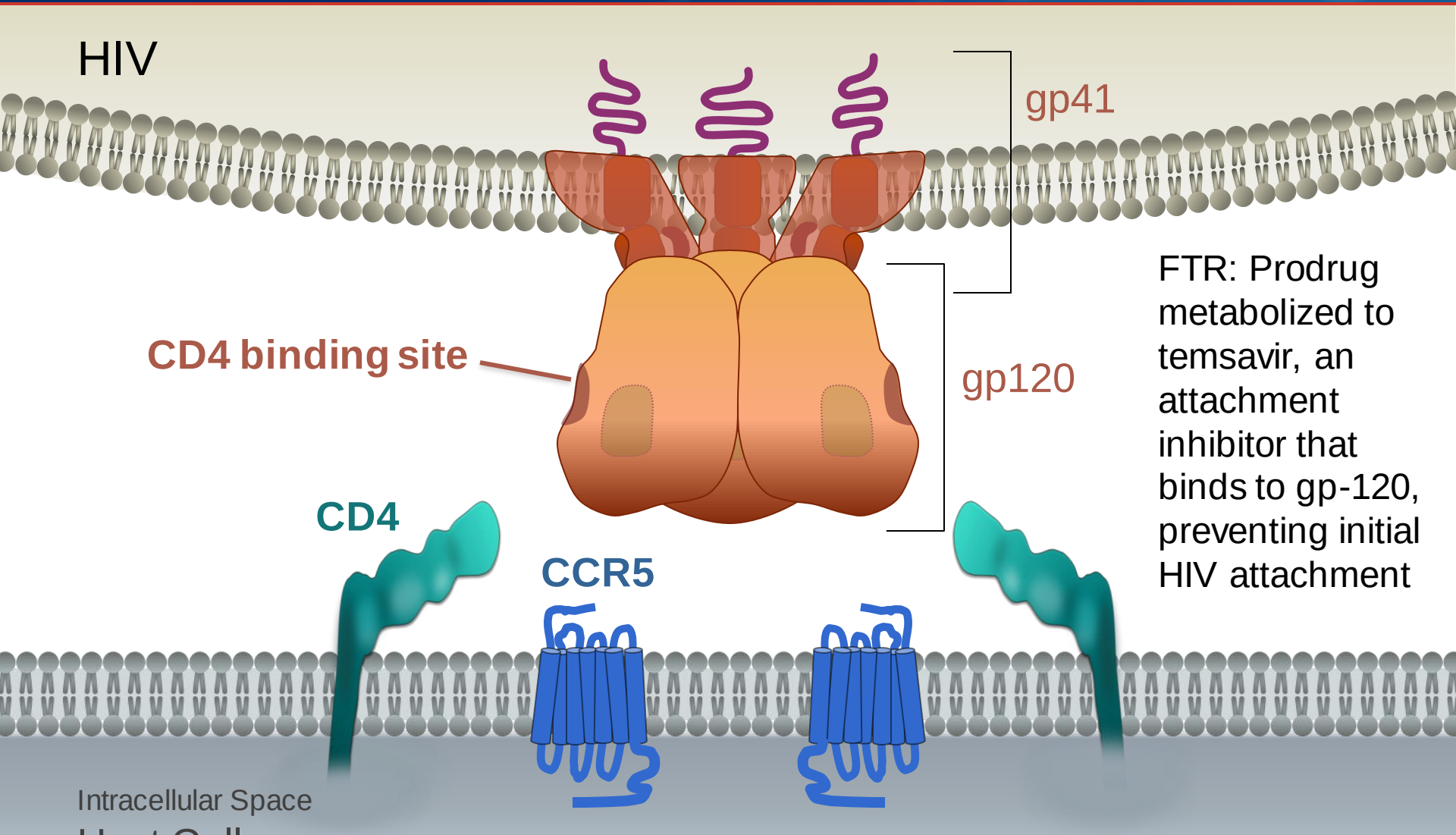
- DUALIS:[1]
  - Stable on boosted darunavir (bDRV) + 2 NRTI's with HIV RNA <50 copies/mL (one blip ok) and no HBV
  - Randomized to continue (n=132) vs switch to bDRV + DTG (n=131)
  - Proportion with HIV RNA <50 copies/mL non-inferior at 48 weeks

- GEMINI[2,3]
  - DTG/3TC vs DTG + TDF/FTC as initial ART; non-inferior at 96 weeks
  - Change in renal and bone biomarkers favors DTG/3TC
  - No resistance in 2-drug arm to date; similar frequency of viral blips

1. Spinner CD et al. 2. Cahn P et al. 3. Underwood M et al. All at IAS July 2019, Mexico City.

New Antiretroviral Agents

Fostemsavir (FTR): Attachment Inhibitor
Mechanism of Action

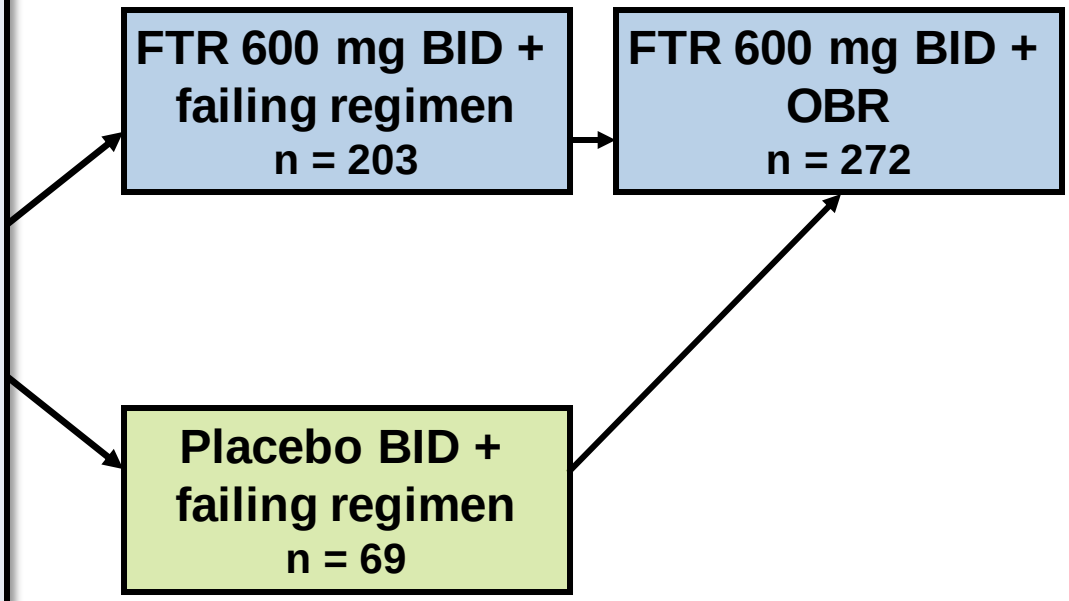


FTR: Prodrug metabolized to temsavir, an attachment inhibitor that binds to gp-120, preventing initial HIV attachment

Fostemsavir (FTR) for Heavily Treatment Experienced BRIGHTE Study: Background

Study Design: BRIGHTE

- **Background**:
  - Ongoing, phase 3, randomized, placebo-controlled, multicenter, non-inferiority trial
- **Enrollment Criteria:**
  - Highly treatment-experienced adults failing current regimen (HIV RNA >400 copies/mL)
  - Multiclass ART resistance, but at least one fully active agent
  - Unable to construct viable regimen from remaining agents



*Also a cohort with 0 remaining active agents; all given FTR 600 mg BID + OBR (n=99)
*OBR = optimized background regimen

Source: Lataillade M et al, IAS July 2019, Mexico City.

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Fostemsavir (FTR) for Heavily Treatment Experienced BRIGHTE Study: Baseline Characteristics

Baseline Characteristics	Randomized Cohort (n = 272)	Non-Randomized (n = 99)
Age, years, median (range)	48 (18-73)	50 (17-72)
Female, n (%)	72 (16)	10 (10)
White, n (%)	185 (68)	74 (75)
Black/African American, n (%)	60 (22)	23 (23)
HIV RNA 1,000 to 100,000, n (%)	161 (59)	236 (64)
HIV RNA >100,000, n (%)	80 (29)	95 (26)
CD4 count, median (IQR)	99 (15-203)	41 (6-161)
2 fully active agents in OBR, %	42	0
1 fully active agent in OBR, %	52	19
0 fully active agents in OBR, %	6	81

*Most common ARV's in OBR: DTG, DRV, TDF, ETR, MVC, ENF, IBA

Source: Lataillade M et al, IAS July 2019, Mexico City.

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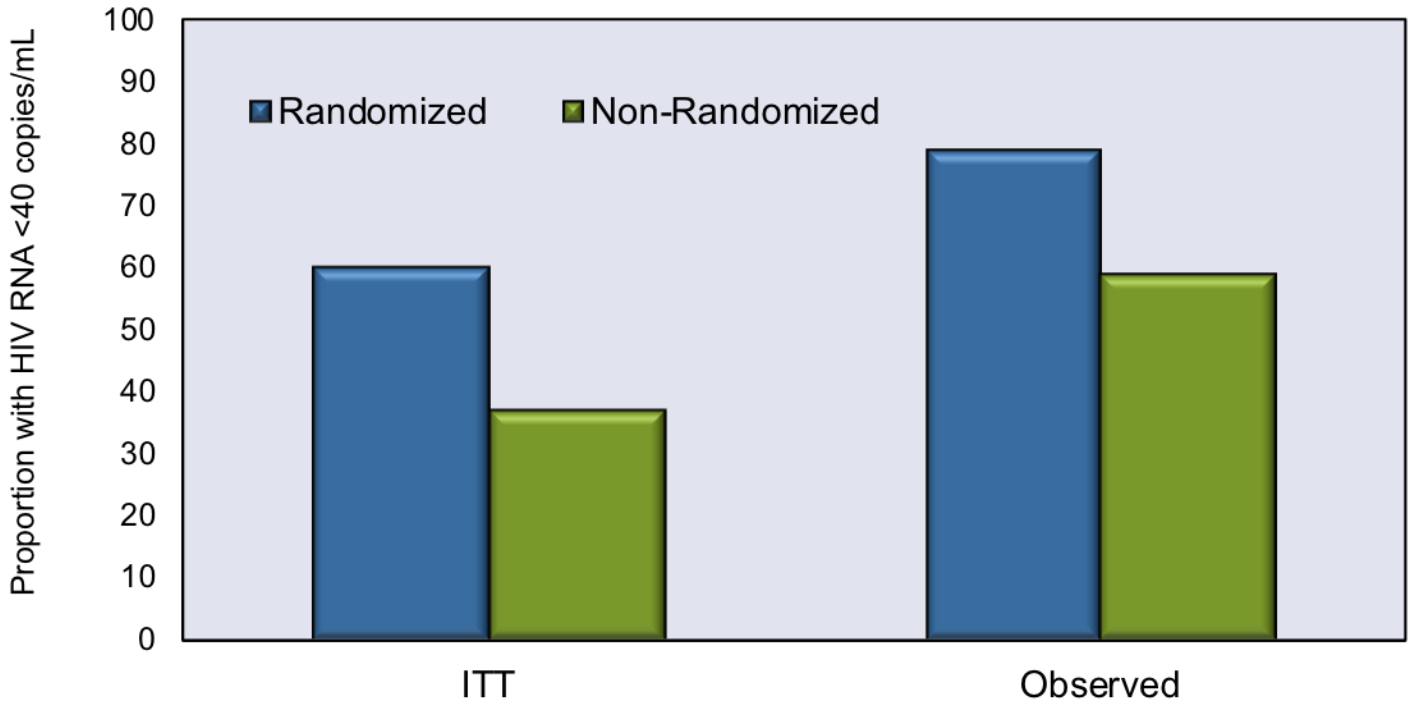
Fostemsavir (FTR) for Heavily Treatment Experienced BRIGHTE Study: Results

Virologic efficacy results at 96 weeks



*Median CD4 count increase: 206 cells/mL (randomized cohort); 119 (non-randomized)
*Adverse events reported by >2% of participants: nausea, diarrhea, headache

Source: Lataillade M et al, IAS July 2019, Mexico City.

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Fostemsavir (FTR) for Heavily Treatment Experienced BRIGHTE Study: Conclusion

Conclusion: “Results support continued development of FTR as an important treatment option for heavily treatment experienced people living with multidrug resistant HIV.”

Source: Lataillade M et al, IAS July 2019, Mexico City.

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MK-8591 (*Islatravir, ISL*)
Overview

- Novel mechanism: nucleoside reverse transcriptase translocation inhibitor (NRTTI)
  - Prevents nucleotide binding and incorporation into the DNA chain, resulting in immediate chain termination
  - Prevents nucleotide incorporation in the event of translocation
- Potent, high barrier to resistance, active with some NRTI resistance mutations
- Long intracellular half life (120 hours in healthy volunteers)
- Potential flexible dosing and novel delivery methods

Sources: 1. Molina JM et al. 2. Matthews R et al. IAS July 2019, Mexico City.

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MK-8591 (*Islatravir, ISL*) Studies at IAS

- DRIVE2SIMPLIFY: ISL + DOR + 3TC for initial ART (n=79)[1]
  - Compared to DOR/TDF/3TC for 24 weeks (n=24)
  - At 24 weeks, those receiving ISL narrow to ISL + DOR
  - At 48 weeks, well tolerated with no VF; comparable efficacy

- Drug-eluting polymer implant for 12 weeks in 12 healthy volunteers (subdermal, similar to Nexplanon)[2]
  - Generally well tolerated, no stoppage due to AE, some mild erythema and induration at site
  - Potential for a once-yearly PrEP implant!

1. Molina JM et al. 2. Matthews R et al. IAS July 2019, Mexico City.
Image from nytimes.com

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AETC AIDS Education & Training Center Program Mountain West