National HIV Curriculum

Fostemsavir (*Rukobia*)

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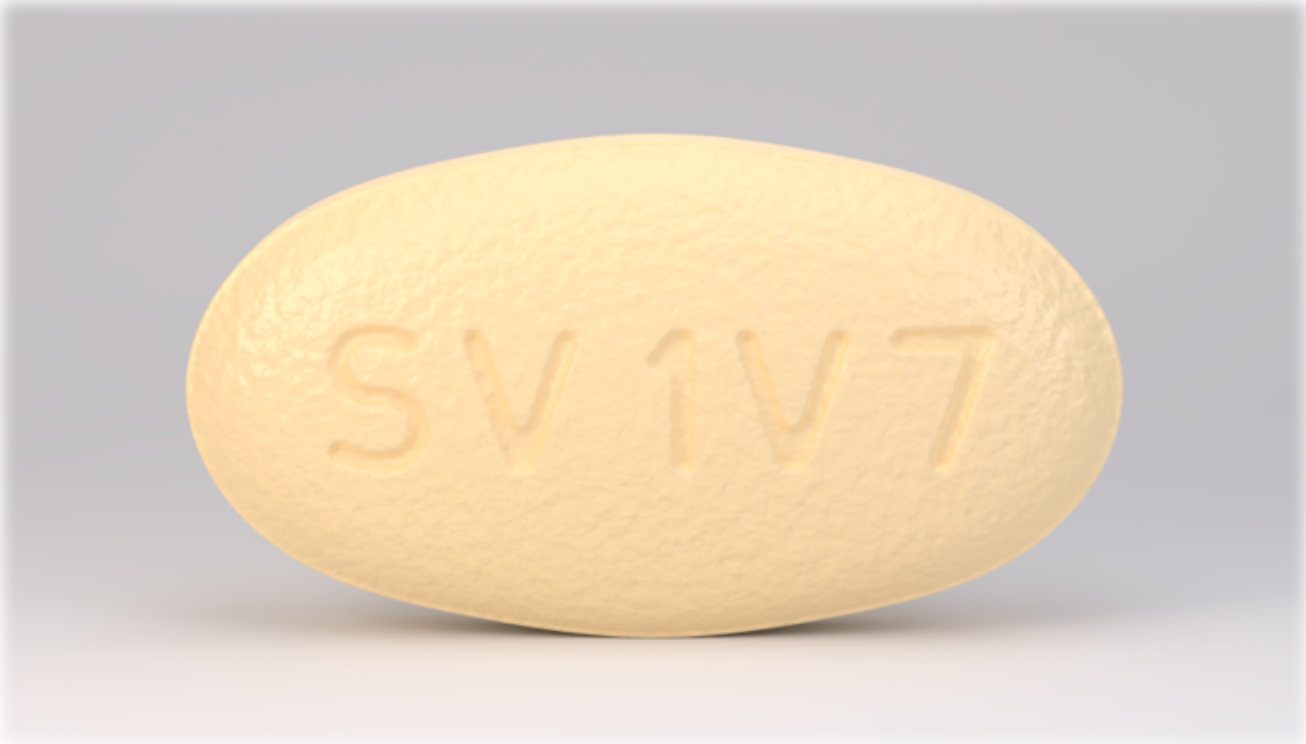
Last Updated: December 30, 2020

AETC AIDS Education & Training Center Program

Fostemsavir (*Rukobia*)

Rukobia

[rue-KOH-bee-ah]



Source: Photograph courtesy of ViiV Healthcare

Fostemsavir (*Rukobia*)

Rukobia

[rue-KOH-bee-ah]

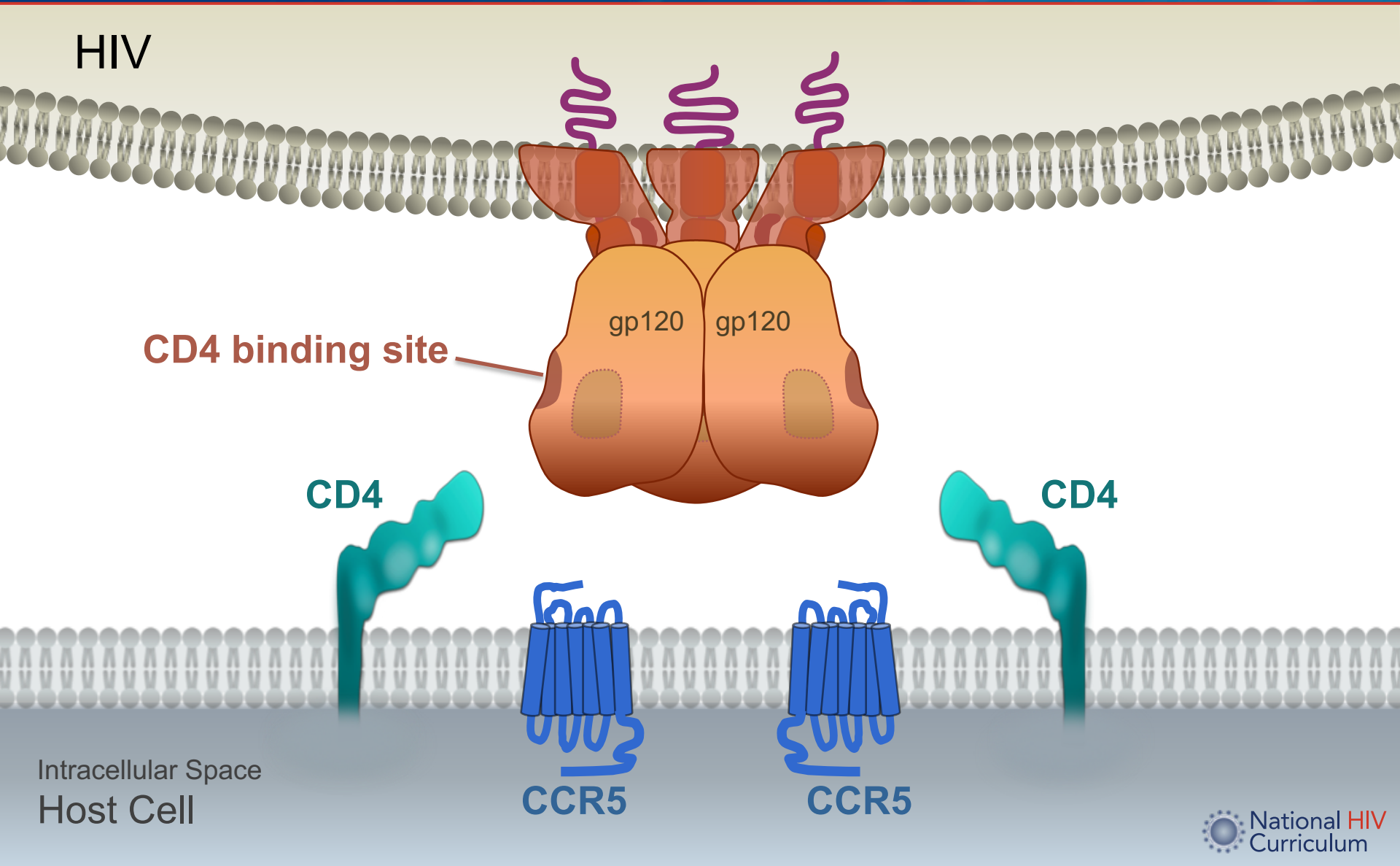
Source: Photograph courtesy of ViiV Healthcare

Fostemsavir (*Rukobia*)

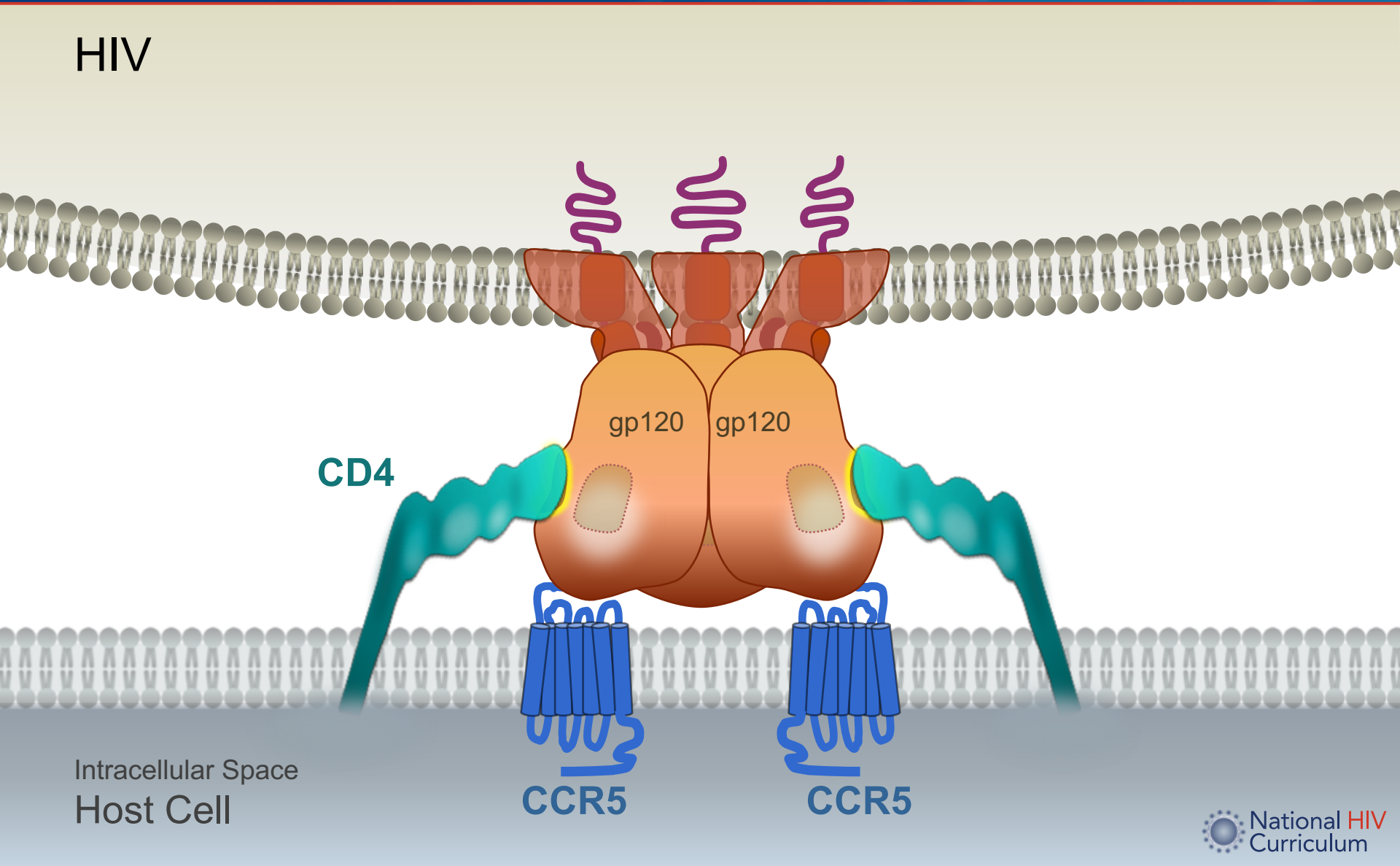
- **Indication**:
  - Heavily treatment-experienced adults with multidrug resistant
  - HIV-1 failing their current antiretroviral regimen
- **Dosing**:
  - 600 mg orally twice daily, with or without food
- **Contraindications**
  - Hypersensitivity to fostemsavir
  - Coadministration with strong cytochrome P450 (CYP) 3A inducers
- **Use During Pregnancy**
  - Insufficient data
- **Common Adverse Events (≥5%)**
  - Nausea (10%)

Source: *Rukobia* Prescribing Information

HIV Cell Entry



HIV Cell Entry
HIV gp120 Attachment to Host Cell CD4 Receptor



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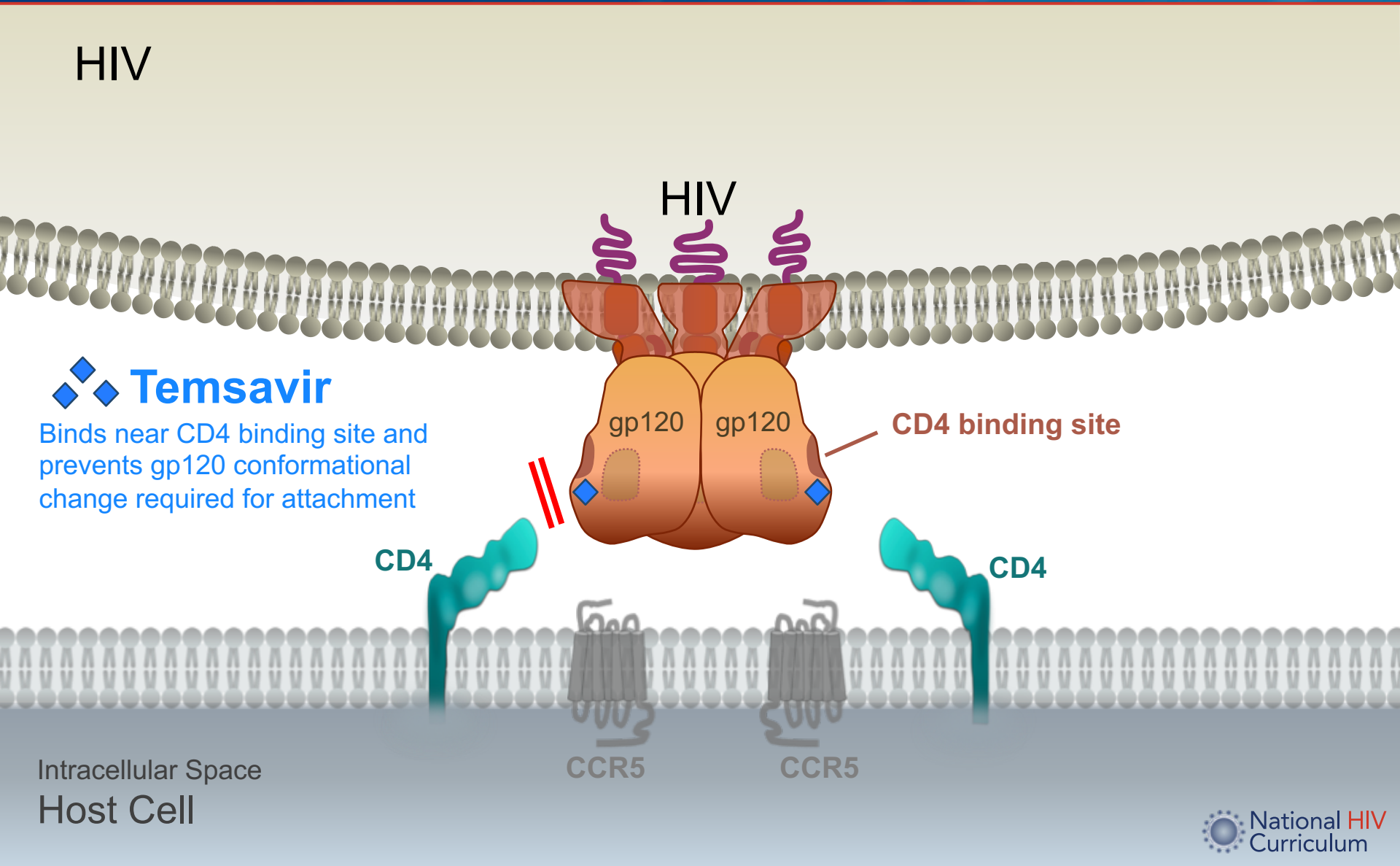
HIV Entry Inhibitors: Attachment Inhibitors
Fostemsavir—prodrug converted to Temsavir



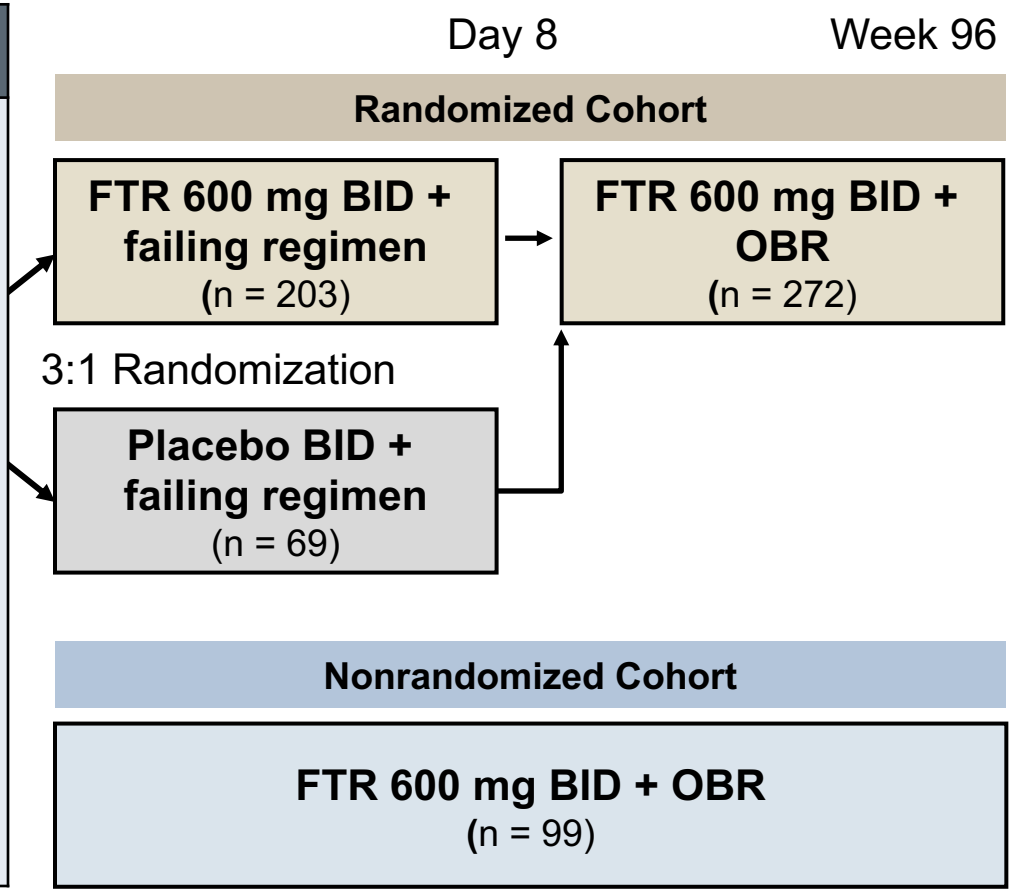
Fostemsavir in Treatment-Experienced Patients

BRIGHTE Study (Week 48 Data)

Fostemsavir (FTR) for Heavily Treatment Experienced BRIGHTE Study (Week 48): Background

Study Design: BRIGHTE

- **Background**:
  - Phase 3, randomized, multicenter, placebo-controlled, non-inferiority trial evaluating attachment inhibitor fostemsavir (FTR) in salvage ART
- **Enrollment Criteria:**
  - Highly ART-experienced adults
  - Failing current ART regimen
  - HIV RNA >400 copies/mL
  - Multiclass ART resistance
  - At least one fully active agent
  - Unable to construct viable regimen



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

Source: Kozal M, et al. N Engl J Med. 2020;382:1232-43.

Fostemsavir (FTR) for Heavily Treatment Experienced BRIGHTE Study (Week 48): Baseline Characteristics

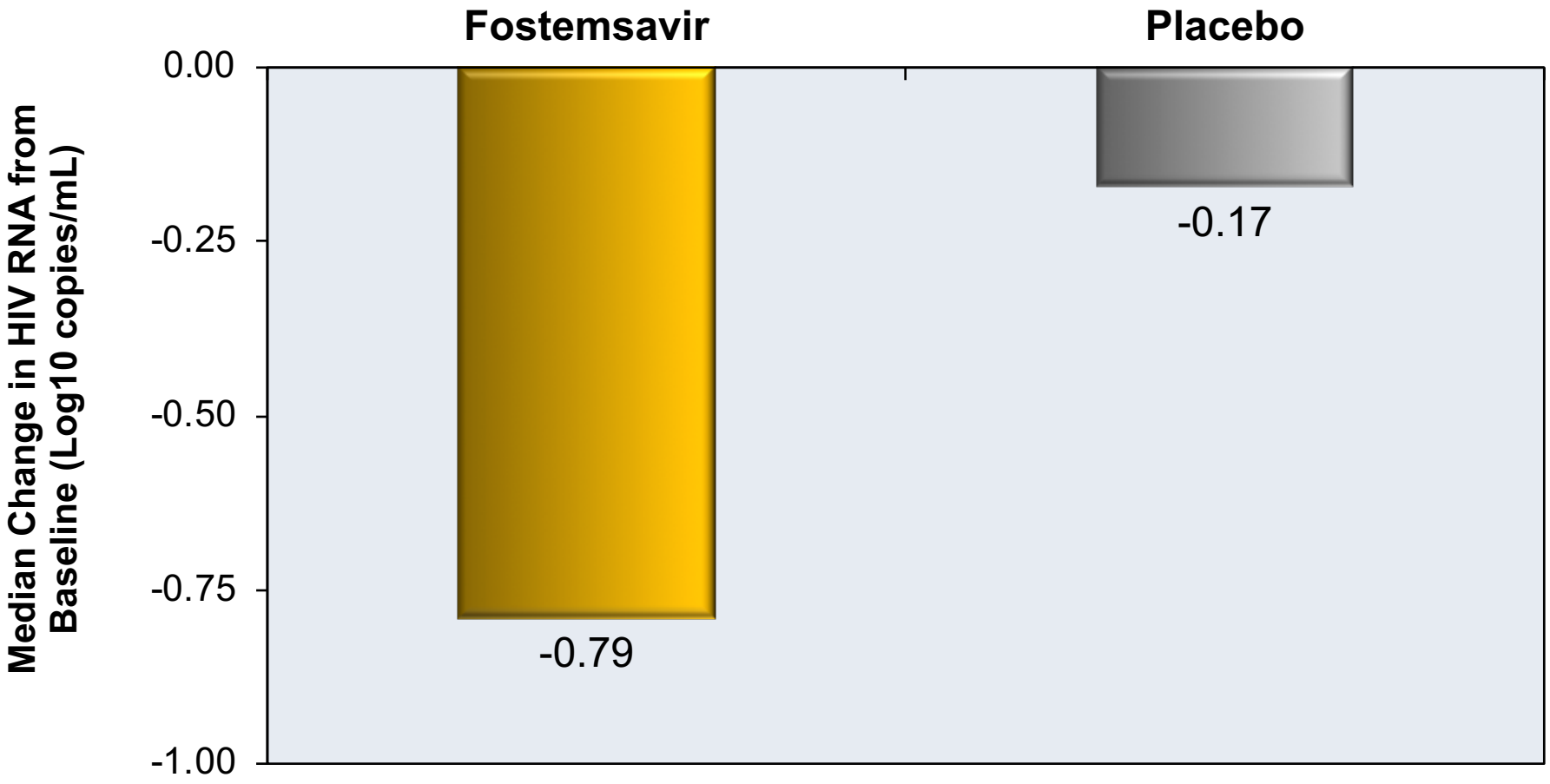
Baseline Characteristics	Randomized (n = 272)	Non-Randomized (n = 99)
Age, years, median (range)	48 (18-73)	50 (17-72)
Male sex, n (%)	200 (74)	89 (90)
White, n (%)	184 (68)	74 (74)
Black/African American, n (%)	60 (22)	23 (23)
HIV RNA 1,000-100,000 copies/mL, n (%)	161 (59)	75 (76)
HIV RNA >100,000 copies/mL, n (%)	80 (29)	15 (15)
CD4 count—cells/mm^3, median (range)	99 (0-1160)	41 (0-641)
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: dolutegravir, darunavir, tenofovir DF, etravirine, maraviroc, enfuvirtide, ibalizumab

Source: Kozal M, et al. N Engl J Med. 2020;382:1232-43.

Fostemsavir (FTR) for Heavily Treatment Experienced BRIGHTE Study (Week 48): Results

Baseline to Day 8 Change in HIV RNA Level



Source: Kozal M, et al. N Engl J Med. 2020;382:1232-43.

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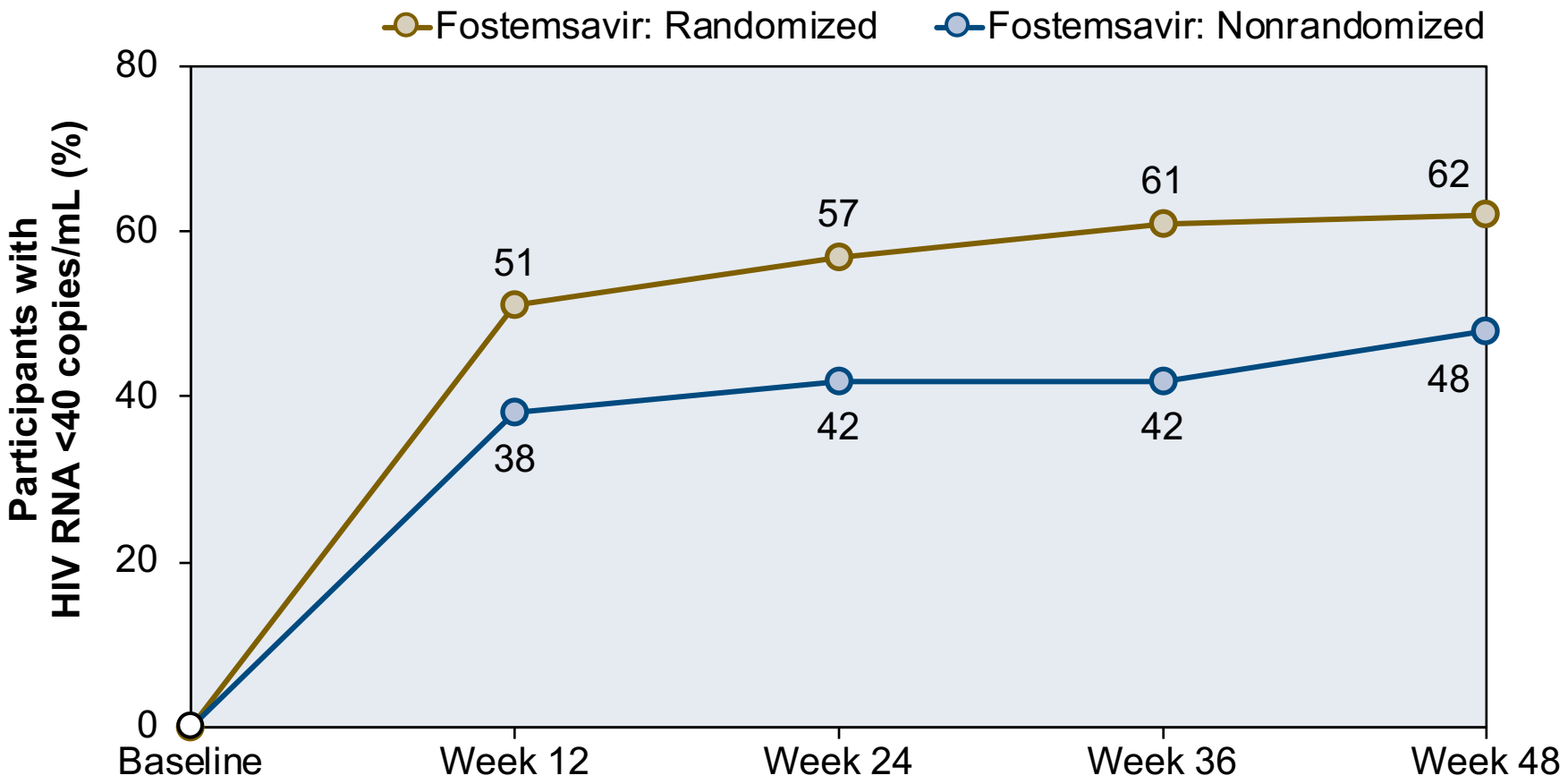
Fostemsavir (FTR) for Heavily Treatment Experienced BRIGHTE Study (Week 48): Results

Virologic Response Through Week 48 (HIV RNA <40 copies/mL)



Source: Kozal M, et al. N Engl J Med. 2020;382:1232-43.

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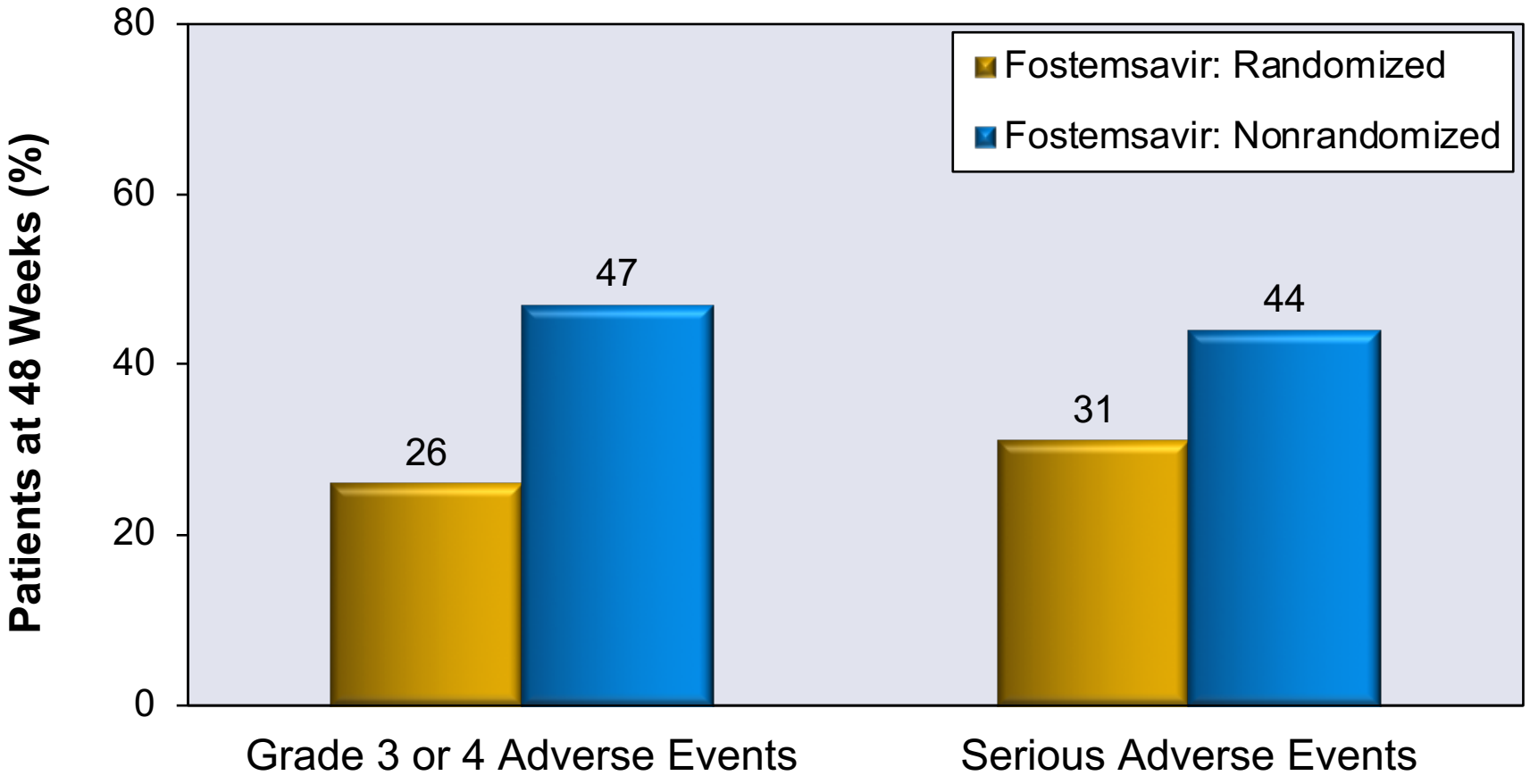
Fostemsavir (FTR) for Heavily Treatment Experienced BRIGHTE Study (Week 48): Results

Adverse Events



Source: Kozal M, et al. N Engl J Med. 2020;382:1232-43.

Fostemsavir (FTR) for Heavily Treatment Experienced BRIGHTE Study (Week 48): Conclusion

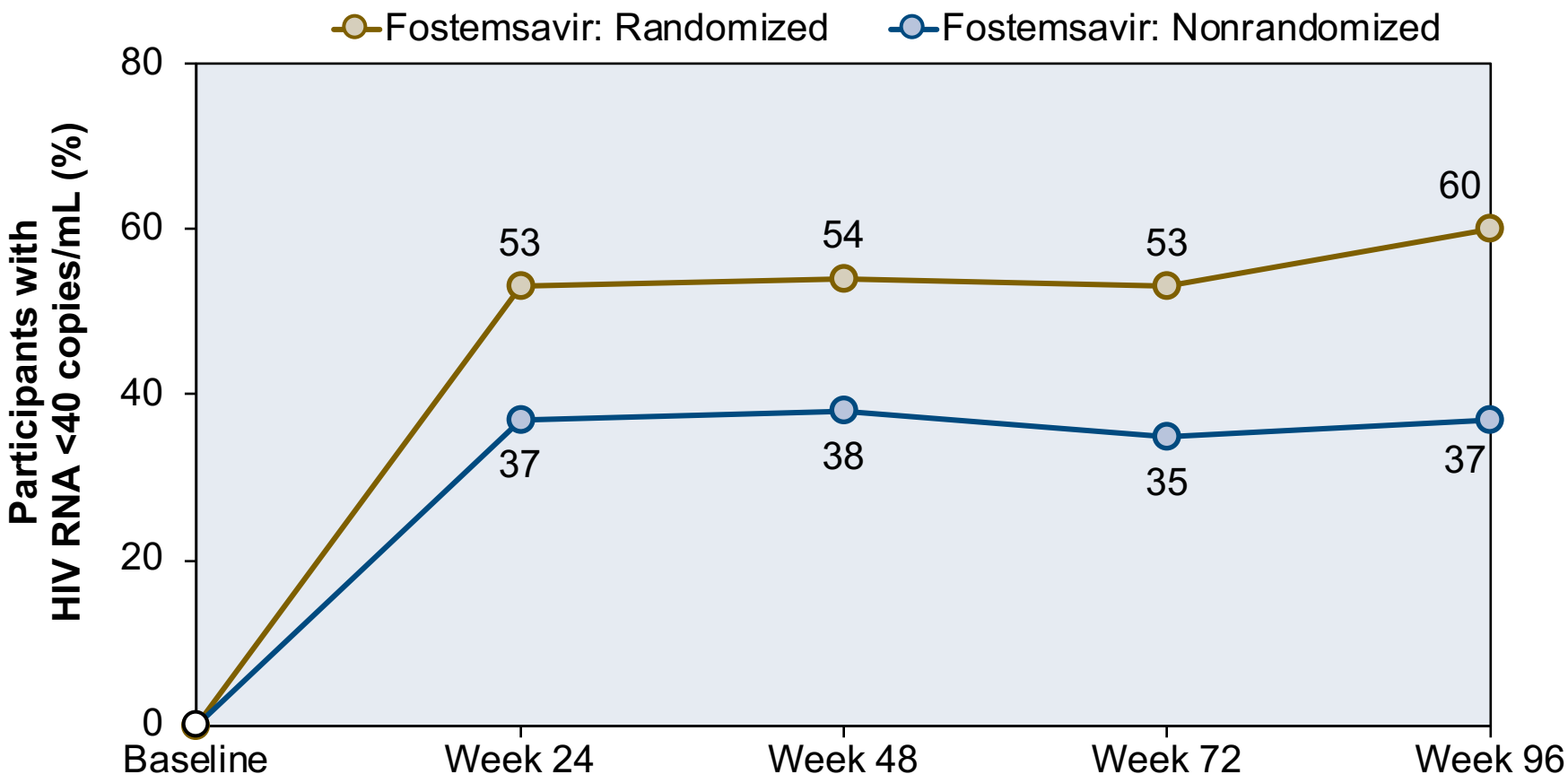
Conclusion: “In patients with multidrug-resistant HIV-1 infection with limited therapy options, those who received fostemsavir had a significantly greater decrease in the HIV-1 RNA level than those who received placebo during the first 8 days. Efficacy was sustained through 48 weeks.”

Source: Kozal M, et al. N Engl J Med. 2020;382:1232-43.

Fostemsavir in Treatment-Experienced Patients
BRIGHTE Study (Week 96 Data)

Fostemsavir (FTR) for Heavily Treatment Experienced BRIGHTE Study (Week 96): Results

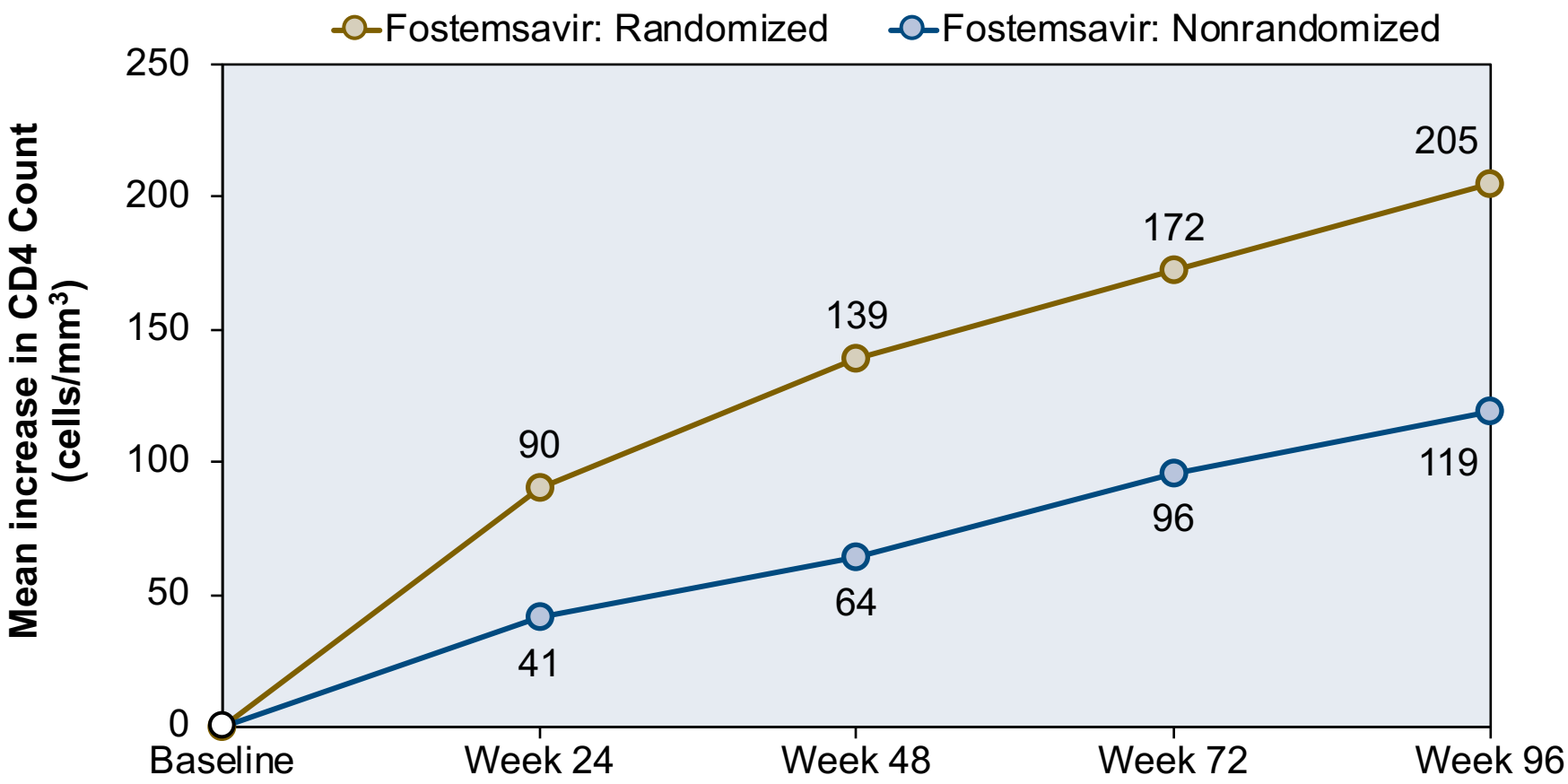
Virologic Response Through Week 96 (HIV RNA <40 copies/mL)



Source: Lataillade M, et al. Lancet HIV. 2020;7:e740-51.

Fostemsavir (FTR) for Heavily Treatment Experienced BRIGHTE Study (Week 96): Results

Mean Change in CD4 T-Cell Count Through Week 96



Source: Lataillade M, et al. Lancet HIV. 2020;7:e740-51.

Fostemsavir (FTR) for Heavily Treatment Experienced BRIGHTE Study (Week 96): Results

Adverse Events (AEs)	Randomized (n = 272)	Non-Randomized (n = 99)
Any AE, n (%)	249 (92)	98 (99)
Drug-related grade 2-4 AEs, n (%)	57 (21)	22 (22)
Nausea	9 (3)	5 (5)
Diarrhea	6 (2)	3 (3)
Headache	6 (2)	1 (1)
Vomiting	4 (1)	2 (2)
Fatigue	3 (1)	2 (2)
Asthenia	2 (<1)	2 (2)
Drug-related AE leading to discontinuation, n (%)	7 (3)	7 (3)
Drug-related serious AE, n (%)	9 (3)	3 (30)

Source: Lataillade M, et al. Lancet HIV. 2020;7:e740-51.

Fostemsavir (FTR) for Heavily Treatment Experienced BRIGHTE Study (Week 96): Conclusion

Interpretation: “In heavily treatment-experienced individuals with advanced HIV-1 disease and limited treatment options, fostemsavir-based antiretroviral regimens were generally well tolerated and showed a distinctive trend of increasing virological and immunological response rates through 96 weeks; these findings support fostemsavir as a treatment option for this vulnerable population.”

Source: Lataillade M, et al. Lancet HIV. 2020;7(11):e740-51.

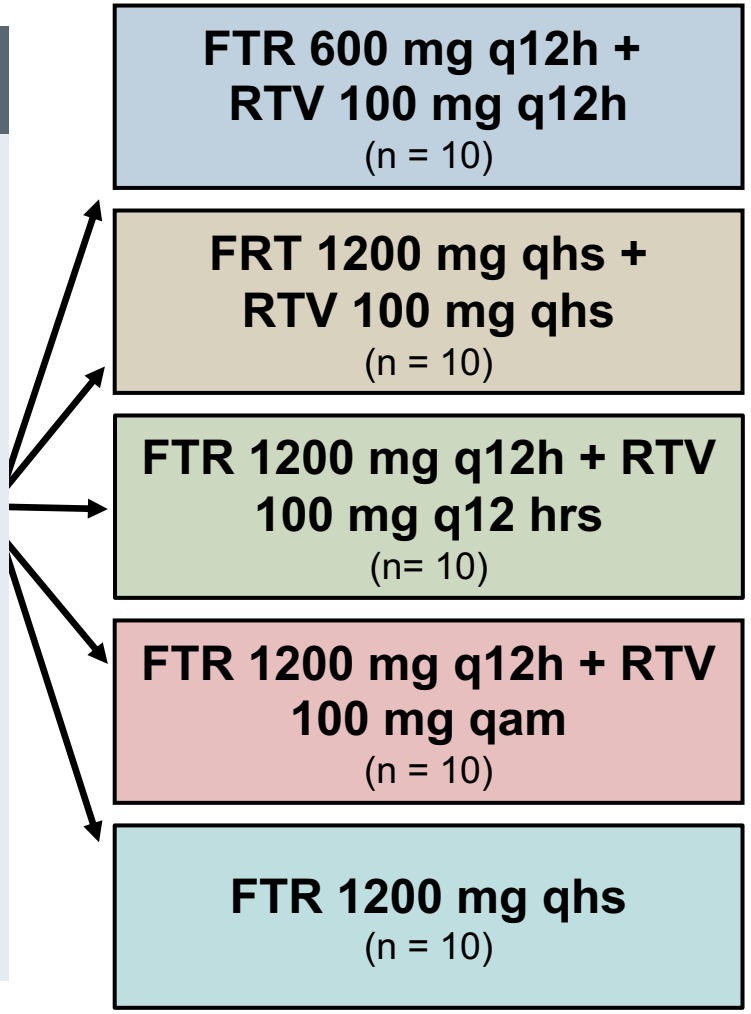
Fostemsavir (BMS-663068) Dose-Ranging Study

AI438-006 Study

Fostemsavir (BMS-663068) Dose-Ranging Study AI438-011: Results

GS-US-141-1219: Study Design

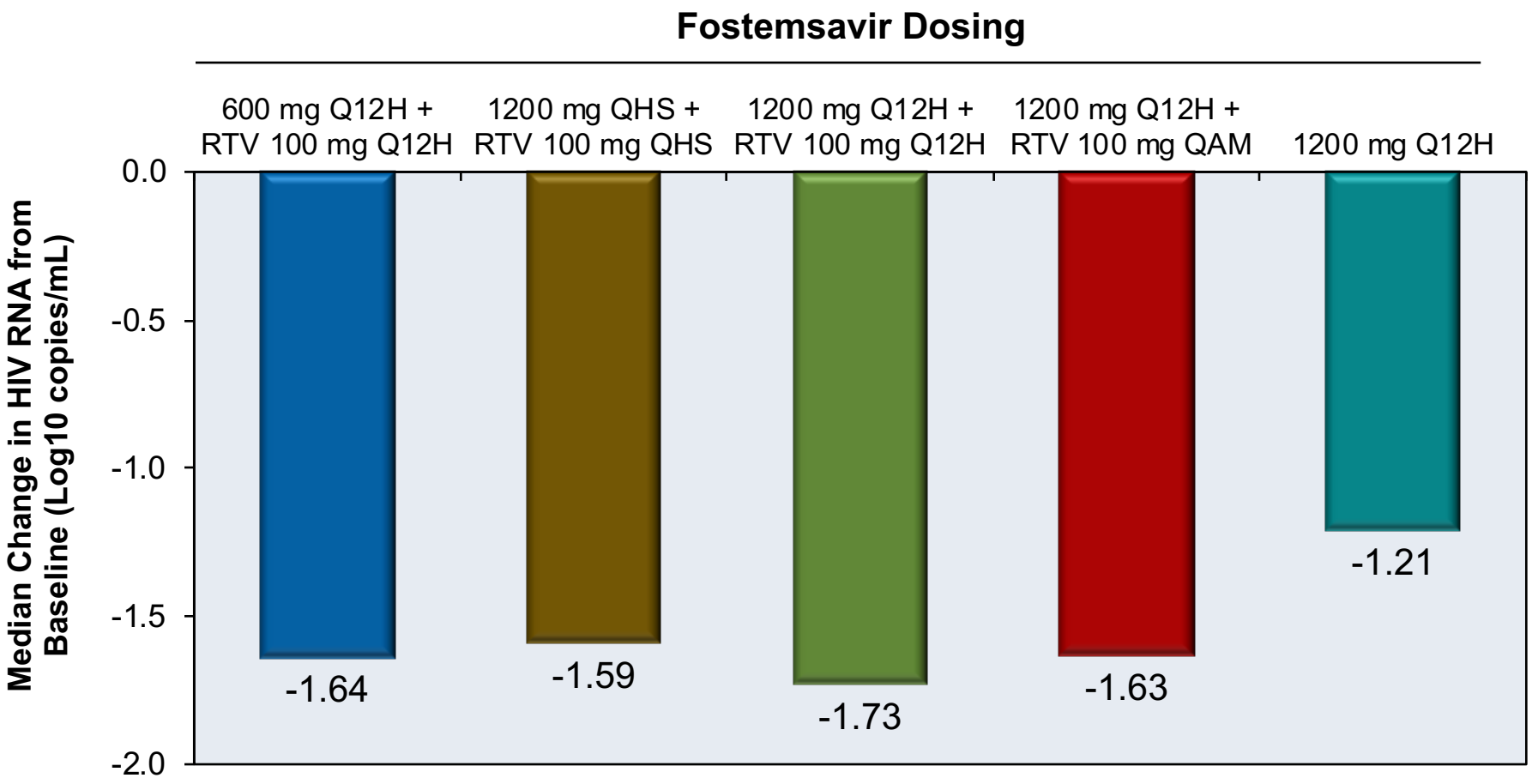
- **Background**: Randomized, open-label, multiple-dose, parallel phase IIa study
- **Inclusion Criteria (n = 50)**
  - Adults with subtype B HIV-1
  - Treatment-naïve or experienced,
  - If treatment experienced, off ART ≥8 weeks
  - HIV RNA >5,000 copies/mL
  - CD4 count ≥200 cells/mm^3
  - Not pregnant; no hepatitis B or C
  - No prior exposure to an HIV attachment inhibitor
- **Treatment Arms**
  - 8 days of fostemsavir (BMS-663068) +/- ritonavir
  - Participants randomized to various dosing arms



Source: Nettles RE, et al. Ray N, et al. J Infect Dis. 2012;206:1002-11.

Fostemsavir (BMS-663068) Dose-Ranging Study AI438-011: Results

Baseline to Day 8: Change in Baseline HIV RNA Level



Source: Nettles RE, et al. Ray N, et al. J Infect Dis. 2012;206:1002-11.

Fostemsavir (BMS-663068) Dose-Ranging Study AI438-011: Conclusions

Interpretation: "Administration of BMS-663068 for 8 days with or without ritonavir resulted in substantial declines in plasma HIV-1 RNA levels and was generally well tolerated. Longer-term clinical trials of BMS-663068 as part of combination antiretroviral therapy are warranted."

Source: Nettles RE, et al. Ray N, et al. J Infect Dis. 2012;206:1002-11.

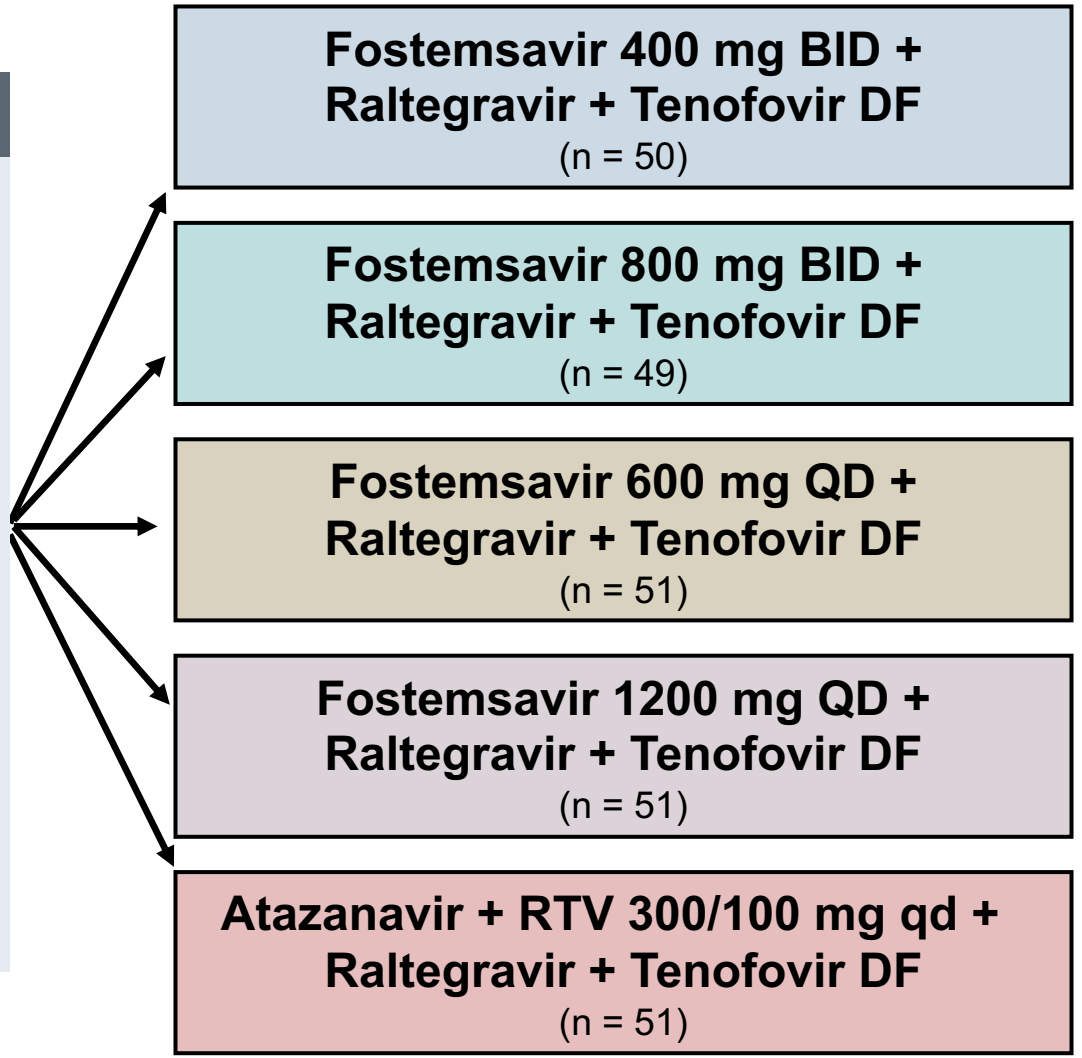
Fostemsavir in Treatment-Experienced Patients

AI438-011 Study

Fostemsavir in Treatment-Experienced Patients
AI438-011: 24 Week Results

Study Design

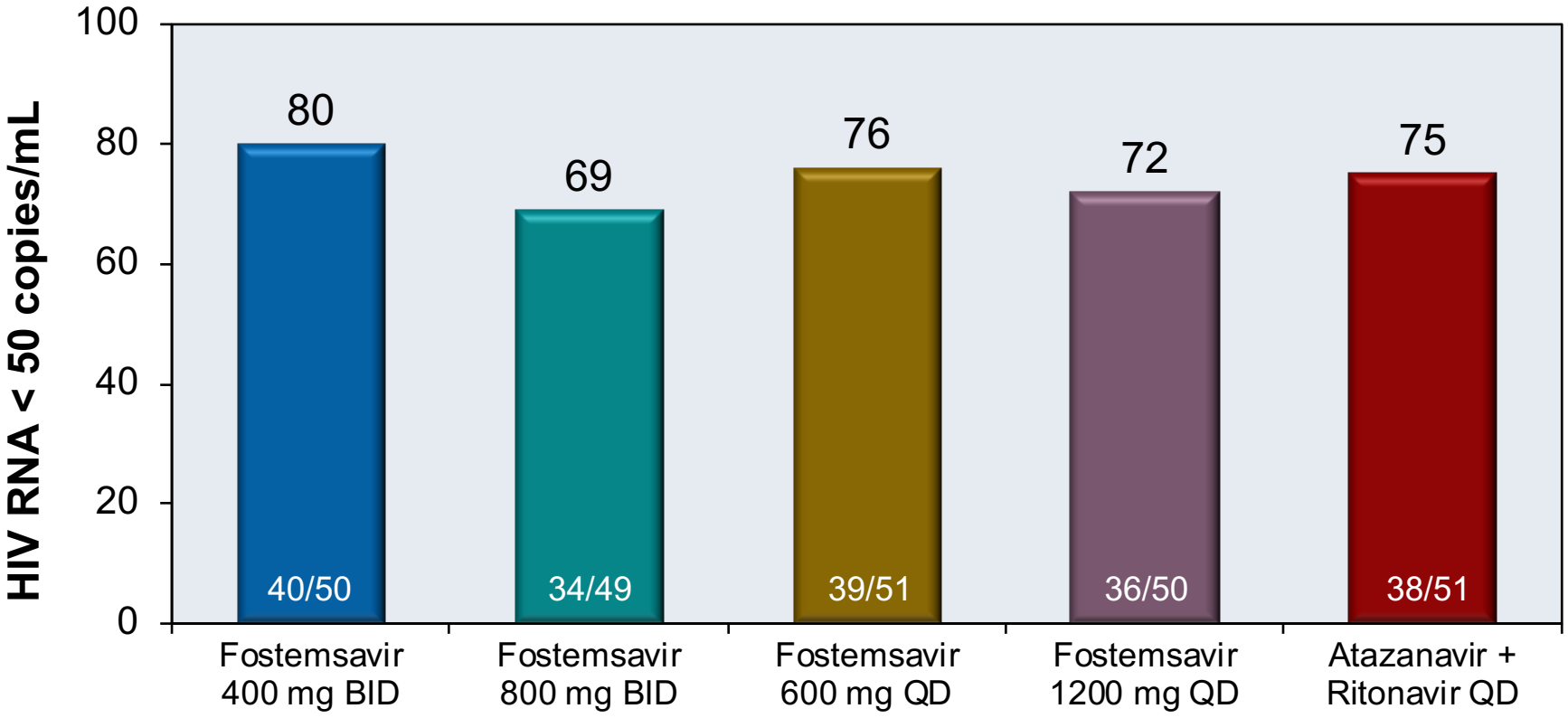
- Randomized, international, active controlled, phase 2b study comparing different doses of fostemsavir in treatment experienced with ART failure
- HIV RNA ≥1,000 copies/ml
- CD4 ≥50 cells/mm^3
- HIV susceptible to:
  - Raltegravir
  - Tenofovir
  - Temsavir



Source: Lalezari JP, et al. Lancet HIV. 2015;2:e427-37.

Fostemsavir in Treatment-Experienced Patients
AI438-011: 24 Week Results

Proportion with HIV RNA <50 copies/mL at 24 weeks (FDA snapshot analysis)



All regimens given in combination with a backbone of raltegravir + tenofovir DF

Source: Lalezari JP, et al. Lancet HIV. 2015;2:e427-37.

Fostemsavir in Treatment-Experienced Patients
AI438-011: 24 Week Conclusions

Interpretation: “In a comparison with ritonavir-boosted atazanavir, efficacy and safety of BMS-663068 up to the week 24 analysis support continued development of BMS-663068, which is being assessed in a phase 3 trial in heavily treatment-experienced individuals.”

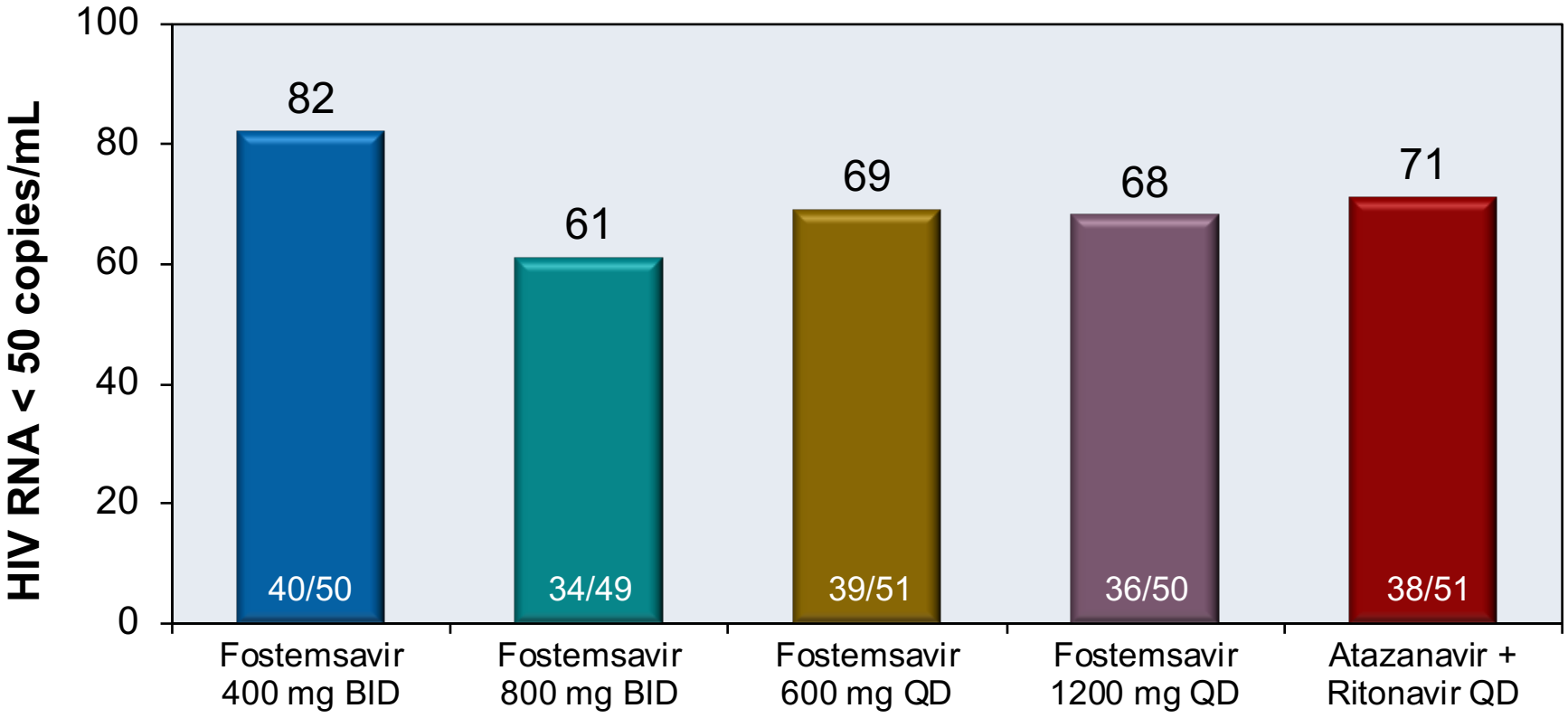
Source: Lalezari JP, et al. Lancet HIV. 2015;2:e427-37.

Fostemsavir in Treatment-Experienced Patients

AI438-011 Study: Week 48 Results

Fostemsavir in Treatment-Experienced Patients
AI438-011: 48 Week Results

Proportion with HIV RNA <50 copies/mL at 48 weeks (FDA snapshot analysis)



All regimens given in combination with a backbone of raltegravir + tenofovir DF

Source: Thompson M et al. Antivir Ther. 2017;22:215-23.

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Fostemsavir in Treatment-Experienced Patients
AI438-011: 48 Week Conclusions

Interpretation: “Through week 48, fostemsavir continued to be well tolerated and showed similar efficacy to ATV/r. These results support the ongoing Phase III trial in heavily treatment-experienced adults with limited therapeutic options (≤2 classes of active antiretrovirals remaining).”

Source: Thompson M et al. Antivir Ther. 2017;22:215-23.

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.

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