National HIV Curriculum

Mini-Lecture Series

Ibalizumab-uiyk

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Disclosures

Dr. Wood does not have any disclosures.

Ibalizumab-uiyk

- **Indication**
  - In combination with other antiretroviral medications for heavily treatment-experienced adults with multidrug-resistant HIV-1 failing their current antiretroviral regimen
- **Dosing (Intravenous)**
  - Loading dose: 2,000 mg IV
  - Maintenance dose: 800 mg IV every 2 weeks
- **Contraindications and Drug-Drug Interactions**
  - No major contraindications or interactions
- **Use During Pregnancy**
  - Insufficient data
- **Common Adverse Events (≥5%)**
  - Diarrhea, dizziness, nausea, rash

Source: Ibalizumab Prescribing Information

Ibalizumab-uiyk: Mechanism of Action

HIV Cell Entry
Binding to Host Cell CD4 Receptor

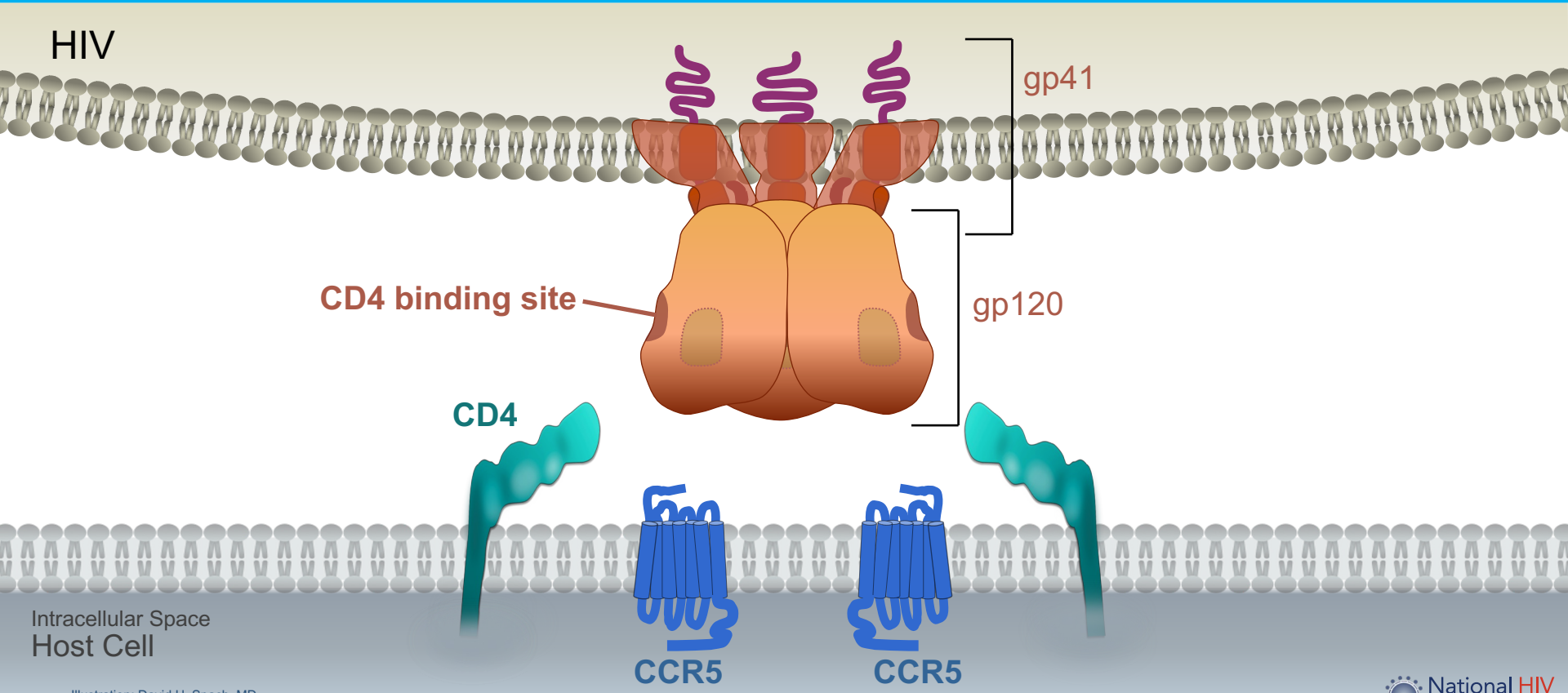

Illustration: David H. Spach, MD

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HIV Cell Entry
Binding to Host Cell CD4 Receptor

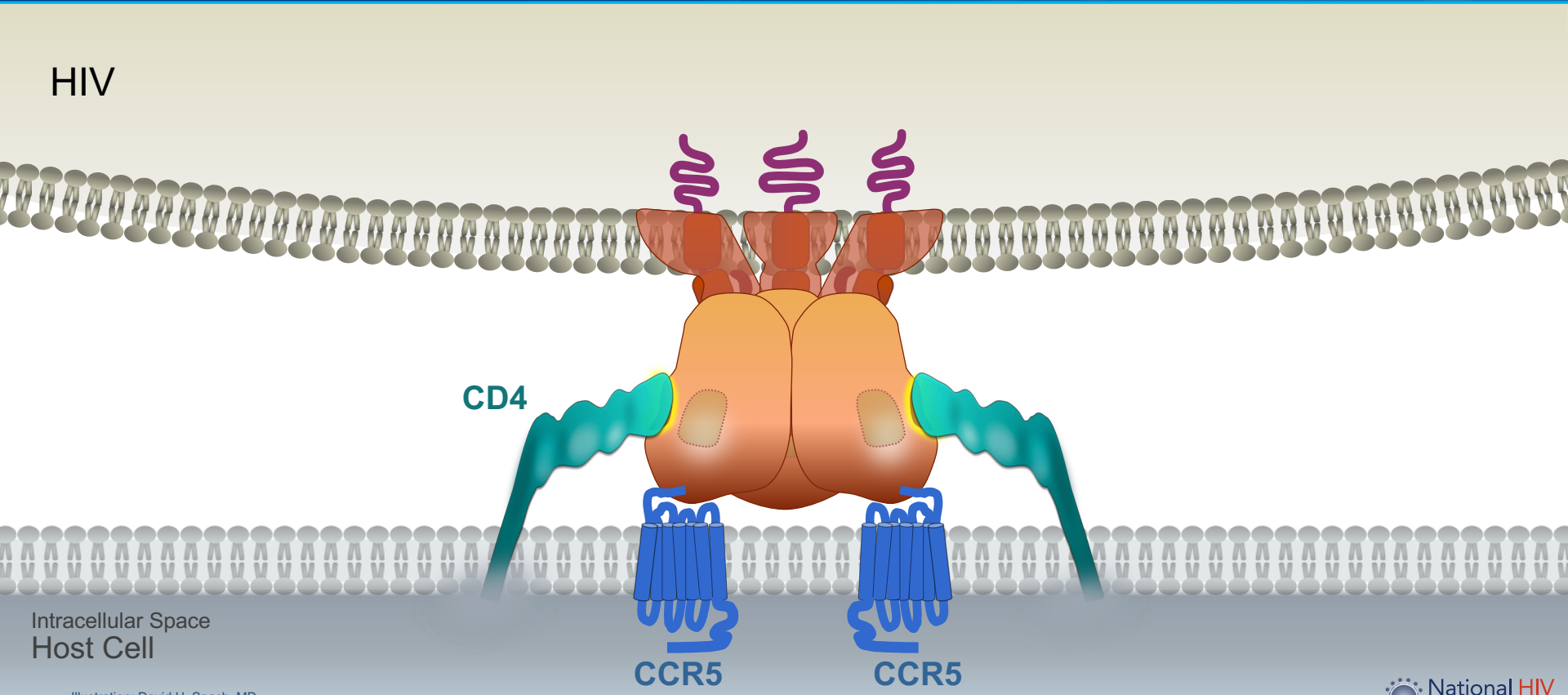

Illustration: David H. Spach, MD

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HIV Cell Entry
Binding to Host CCR5 Co-Receptor

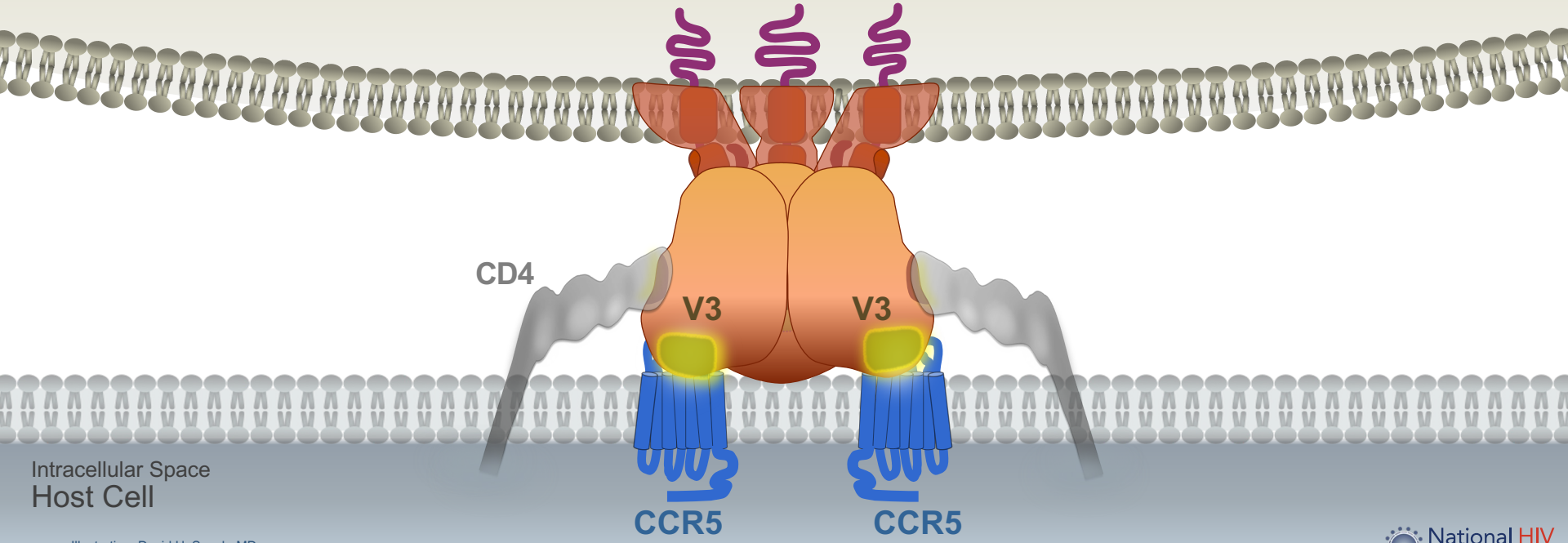

Illustration: David H. Spach, MD

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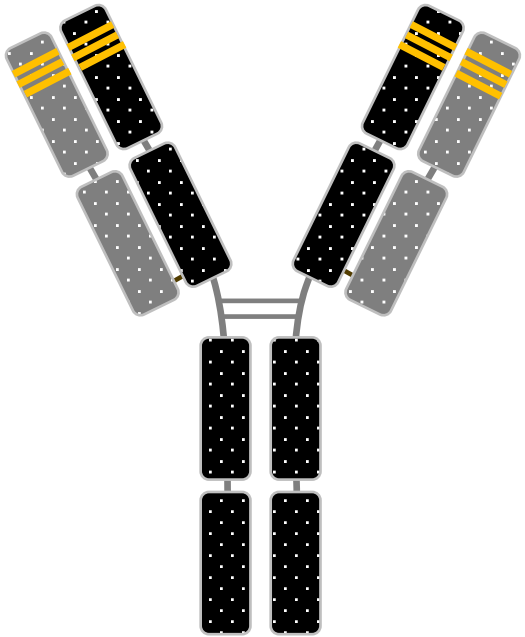

Humanized Monoclonal Antibody

Illustration: David H. Spach, MD

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Host Cell CD4 Receptor

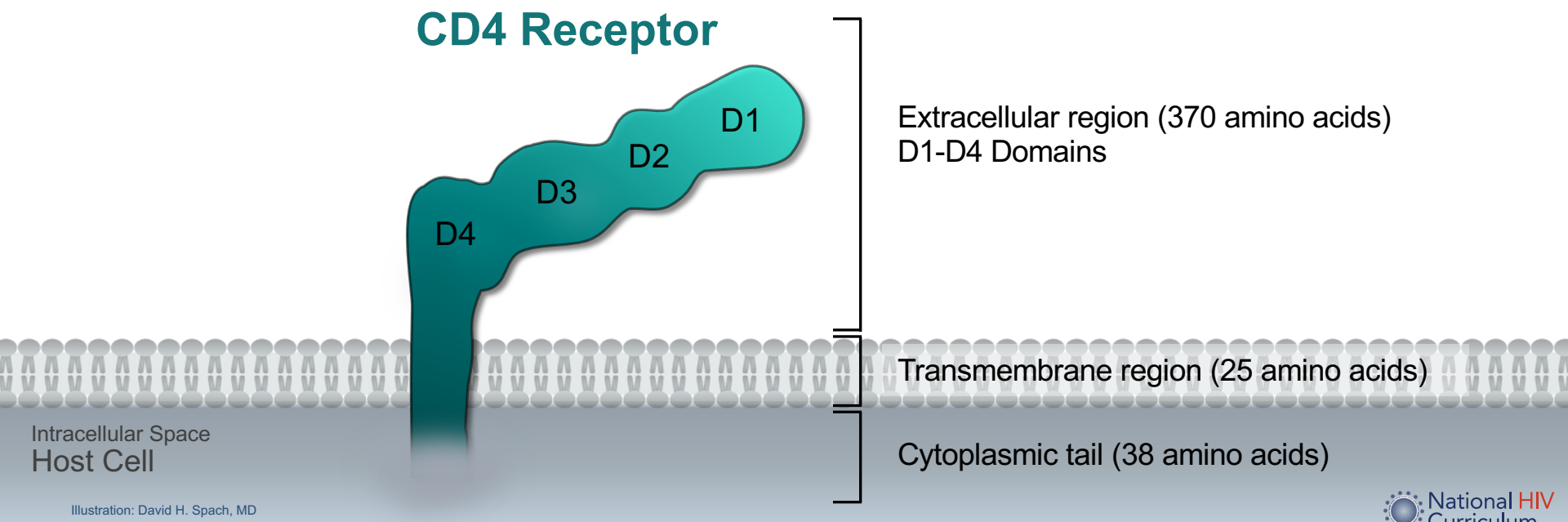

Illustration: David H. Spach, MD

Host Cell CD4 Receptor and Ibalizumab Binding

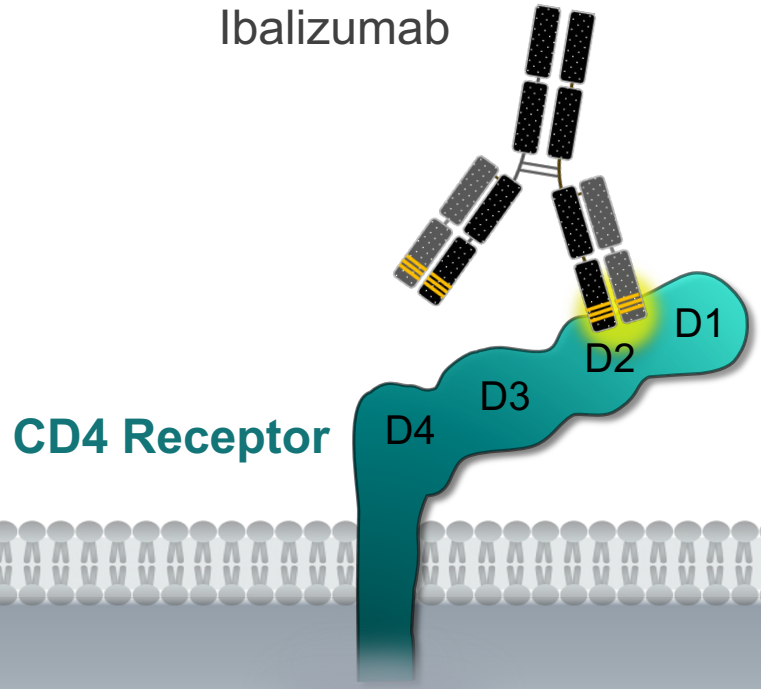

Illustration: David H. Spach, MD

Ibalizumab: CD4 Directed Post-Attachment HIV Inhibitor

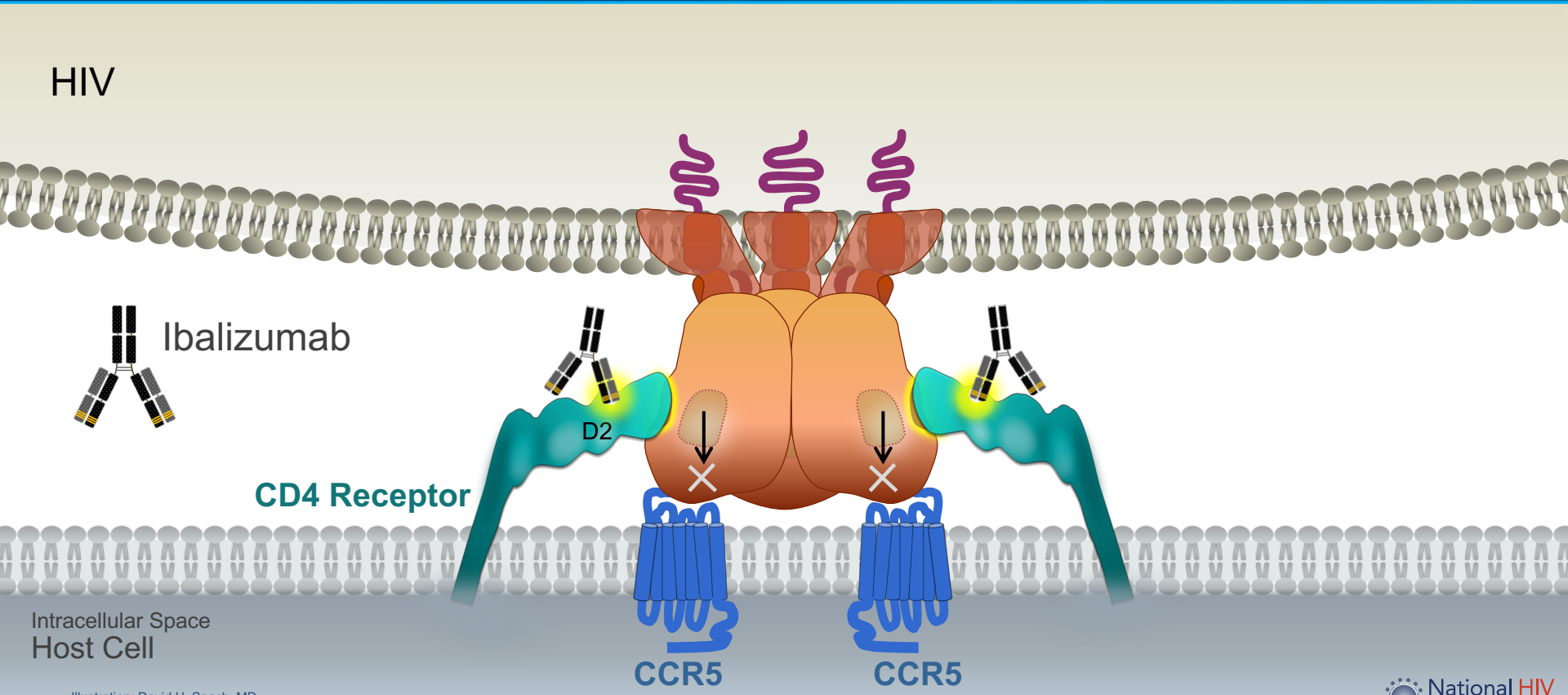

Illustration: David H. Spach, MD

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Ibalizumab for Individuals with Multidrug-Resistant HIV

TMB-301 Study

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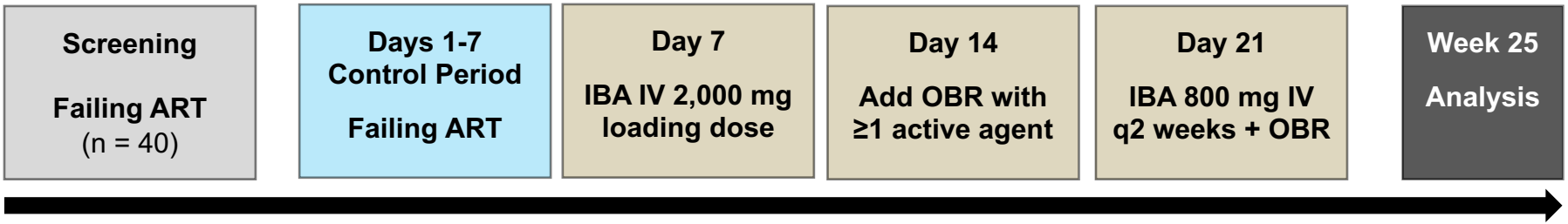
Ibalizumab (IBA) for Individuals with Multidrug-Resistant HIV
TMB-301: Study Design

- **Study design**
  - Single-arm, open label study of ibalizumab (IBA) added to optimized background regimen (OBR) for individuals with virologic failure on ART
  - Primary endpoint: proportion achieving ≥0.5 $\log_{10}$ decrease in HIV RNA 7 days after initiating IBA therapy (day 14 of study)
  - Secondary endpoints: virologic outcomes, safety, & tolerability at week 25 (after 24 weeks of IBA)
- **Inclusion Criteria**
  - Adults with HIV-1, taking ART for ≥6 months, HIV RNA >1,000 copies/mL, and ≥3 class drug resistance (but ≥1 remaining active drug)



Source: Emu B, et al. N Engl J Med. 2018;379:645-54.

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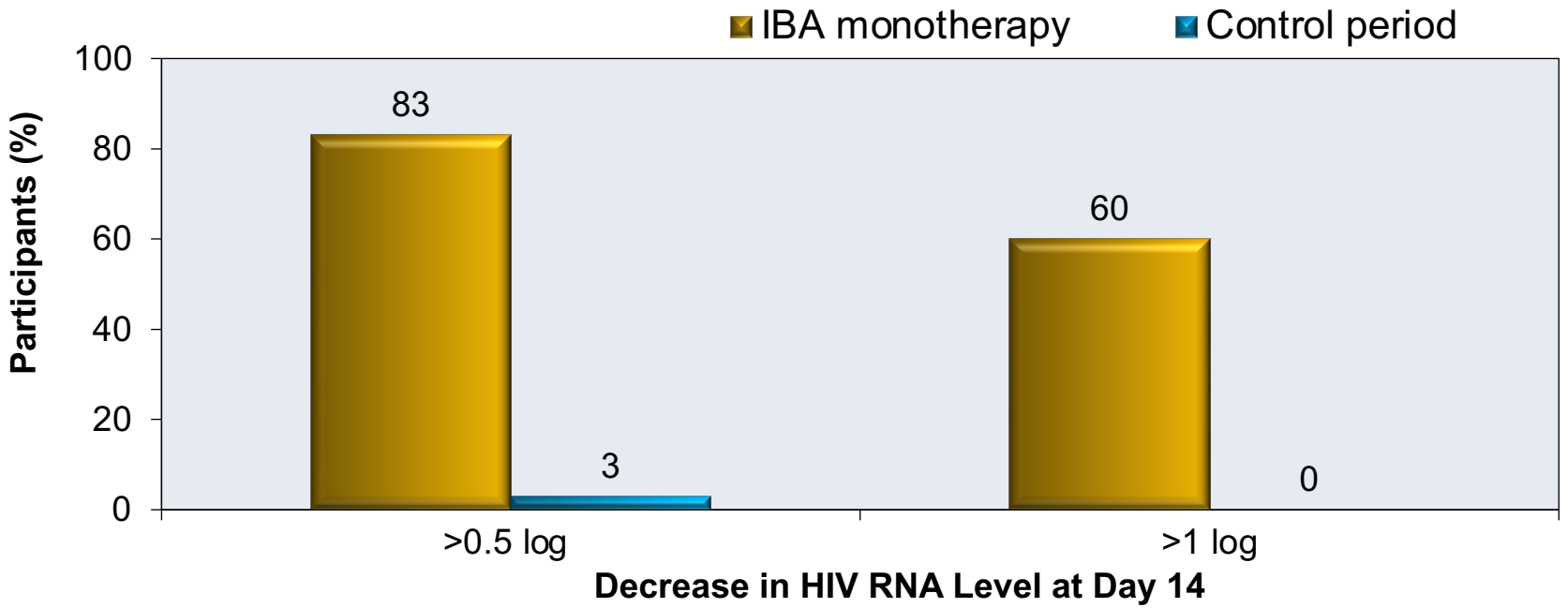
Ibalizumab (IBA) for Individuals with Multidrug-Resistant HIV
TMB-301: Study Design

Baseline Characteristics of the 40 Participants in TMB-301	
Characteristic	**Ibalizumab (n = 40)**
Median age (range)—years	53 (23-65)
Male	34 (85%)
Non-White	18 (45%)
Mean duration since HIV diagnosis—years	20 ± 8
Mean CD4 count—cells/mm^3	150 ± 182
Mean HIV RNA—copies/mL	4.5 log (31,623)
Participants with HIV RNA >100,000 copies/mL	7 (18%)

Source: Emu B, et al. N Engl J Med. 2018;379:645-54.

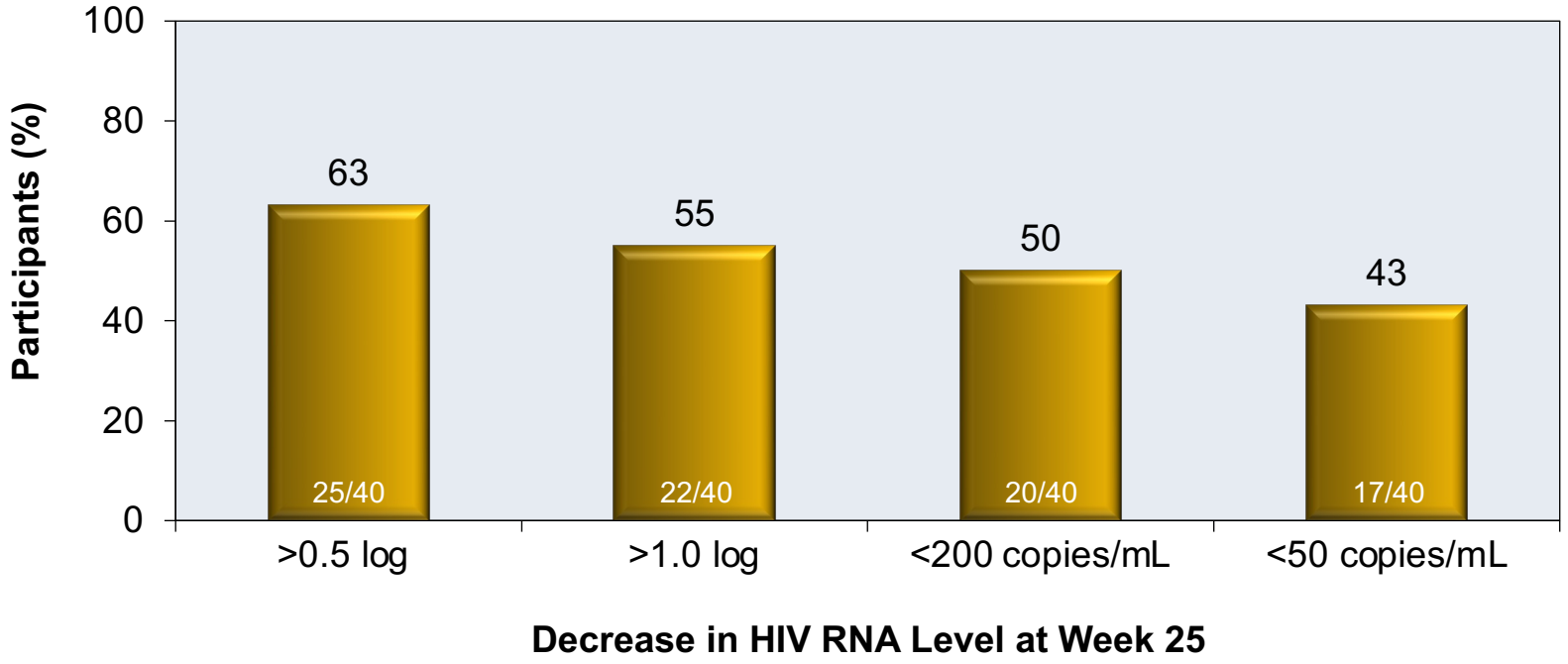
Ibalizumab (IBA) for Individuals with Multidrug-Resistant HIV
TMB-301: Efficacy at Day 14



IBA monotherapy = after 7 days of IBA added to failing ART (functional monotherapy)
Control period = after 7 days of baseline failing ART prior to adding ibalizumab

Source: Emu B, et al. N Engl J Med. 2018;379:645-54.

Ibalizumab (IBA) for Individuals with Multidrug-Resistant HIV
TMB-301: Efficacy at Week 25

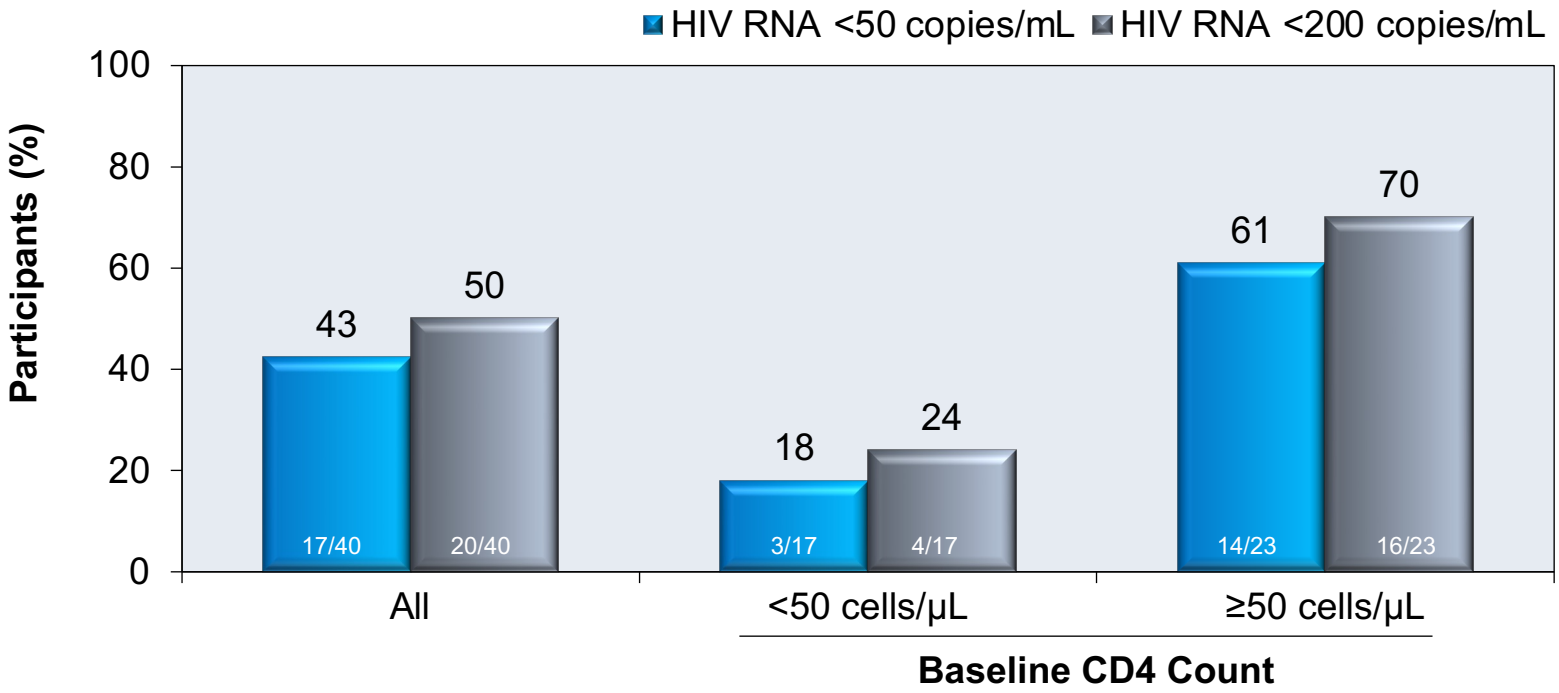


IBA added at day 7. Optimized background regimen (OBR) added at day 14. Above results are after 24 weeks of IBA.

Source: Emu B, et al. N Engl J Med. 2018;379:645-54.

Ibalizumab (IBA) for Individuals with Multidrug-Resistant HIV
TMB-301: Efficacy at Week 25, by Baseline CD4 Cell Count

Week 25 Virologic Response (Intention-to-Treat Analysis)



Source: Emu B, et al. N Engl J Med. 2018;379:645-54.

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Ibalizumab (IBA) for Individuals with Multidrug-Resistant HIV
TMB-301: Adverse Events

Adverse Events (AEs)	Participants (n = 40)
Any AE, n (%)	32 (80)
Related to IBA	7 (18)
Leading to stoppage of IBA	5 (13)
Reported by ≥10% of participants	
Diarrhea	8 (20)
Dizziness	5 (13)
Fatigue	5 (13)
Nausea	5 (13)
Pyrexia	5 (13)
Rash	5 (13)
Vomiting	4 (10)
Lymphadenopathy	4 (10)
Nasopharyngitis	4 (10)

Source: Emu B, et al. N Engl J Med. 2018;379:645-54.

Ibalizumab (IBA)
Resistance Testing & Cross Resistance

- IBA can be used regardless of HIV-1 tropism
- Standard genotype testing will not give IBA resistance information
- Decreased susceptibility to IBA has been observed in subjects experiencing virologic failure, and may be associated with genetic changes in the V5 loop of gp120, though the clinical significance is unclear and activity of other antiretrovirals is not affected
- IBA does not have known *in vitro* cross resistance with other antiretrovirals, including other entry inhibitors
- No CD4 polymorphisms affect IBA activity and use of IBA does not impact CD4 function

Source: *Trogarzo* Prescribing Information

Ibalizumab (IBA)
Summary

- Intravenous entry inhibitor that binds to host CD4 receptor
- Used as part of salvage antiretroviral therapy for individuals with multidrug-resistant HIV-1, typically with virologic failure on oral antiretrovirals and few antiretroviral options
- Typically combined with at least one other active antiretroviral agent and optimized background regimen
- Generally well-tolerated with no drug-drug interactions
- Resistance may develop but is rare and testing is not yet available

Acknowledgment

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AETC AIDS Education & Training Center Program

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