

November 2021 AIDS Clinical Conference: ART Update: New Guidelines & Medications

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.

HHS Adult and Adolescent HIV Treatment Guidelines Updated June 3rd, 2021

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV



Developed by the DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents – A Working Group of the Office of AIDS Research Advisory Council (OARAC)

How to Cite the Adult and Adolescent Guidelines:

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It is emphasized that concepts relevant to HIV management evolve rapidly. The Panel has a mechanism to update recommendations on a regular basis, and the most recent information is available on the HIVinfo Web site (<http://hivinfo.nih.gov>).

Poll

In your opinion, which is the best option for initial ART for most individuals with HIV?

- A) Bictegravir/FTC/TAF
- B) Dolutegravir + FTC/TAF
- C) Dolutegravir + FTC/TDF
- D) Dolutegravir/ABC/3TC
- E) Dolutegravir/3TC
- F) Something else

What to Start

Recommended Initial ART Options

HHS (June 2021)^{1*} Recommended for Most PWH

BIC/FTC/TAF

DTG + FTC/TAF or FTC/TDF
DTG/ABC/3TC (if B*5701 neg and no HBV)

DTG/3TC (if VL <500k, no HBV, have
baseline genotype results)

IAS-USA (October 2020)² Recommended for Most PWH

BIC/FTC/TAF

DTG + FTC/TAF or FTC/TDF

DTG/3TC (if VL <500k, no HBV, no active OI,
not rapid start, can closely monitor adherence
and VL, possibly only if CD4 >200)

**Change: moved RAL to recommended
in certain clinical situations*

*Question: would some individuals benefit
from a non-INSTI option at initiation?*

Abbreviations:

BIC – bictegravir, DTG – dolutegravir, RAL – raltegravir, ABC – abacavir, 3TC – lamivudine, FTC – emtricitabine, TDF – tenofovir disoproxil fumarate, TAF – tenofovir alafenamide, HBV - hepatitis B virus, PWH – persons with HIV

Sources:

1. HHS: clinicalinfo.hiv.gov 2. IAS-USA: ias-usa.org



What to Start

Raltegravir Removed from “Recommended for Most PWH”

- Updated data show low overall prevalence of neural tube defects (NTD) with dolutegravir (DTG)
 - DTG back to “Preferred” category for conception & pregnancy
 - No longer an indication to choose raltegravir (RAL) over DTG
- RAL has a lower barrier to resistance than DTG and BIC
- RAL regimens have higher pill burden than other options

Tsepamo Study Outcomes	Conception	
	DTG	Non-DTG
Results as of April 2020	n = 3,591	n = 19,361
NTD prevalence (95% CI)	0.19 (0.09-0.40)	0.11 (0.07-0.17)

Case #1

- 55-year-old Black cisgender man; HIV diagnosis in 2010
- Took EFV/TDF/FTC until 2016; viral loads routinely suppressed except one lapse for 6 months or so
- Switched to DTG/ABC/3TC due to depression; viral loads suppressed since
- No resistance on any historical genotypes
- Comorbidities: HTN, HLD, DM2 (A1C's range 8.0 to 10.0), osteopenia, osteoarthritis, chronic pain; no HBV
- Meds: atorvastatin, metformin, glipizide, lisinopril

Poll

How much do you worry about abacavir raising the risk of ischemic cardiovascular events?

- A) Not much
- B) A little
- C) A moderate amount
- D) A lot

Abacavir (ABC) and Cardiovascular Disease (CVD) Risk

A Brief Summary...

- No signal for CVD events in most randomized trials, but carefully selected patients with limited follow-up
- Many observational studies & systematic reviews find an association (current use, cumulative use, or recent use)
 - Concern for channeling/selection bias
- Credible mechanism? Yes: ABC causes platelet reactivity & activation; inflammatory, prothrombotic phenotype
 - Endothelial dysfunction, atherosclerotic plaque instability

Review:

Alvarez et al. AIDS 2017.

Systematic Reviews:

Dorjee K et al. Int J Animicrob Agents 2018.

Young J et al. JAIDS 2015.

Bavinger C et al. PLoS One 2013.

Mechanism:

van der Heijden WA et al. JAIDS May 2021.

O'Halloran JA et al. AIDS 2018.

Satchell CS et al. JID 2011.

Khawaja AA et al. Circ Res 2020.

Hsue P et al. AIDS 2009.



Poll

What would you recommend (ideally) for the patient?

- A) Continue DTG/ABC/3TC
- B) Switch to BIC/FTC/TAF
- C) Switch to DTG/RPV
- D) Switch to DTG/3TC
- E) Switch to IM CAB/RPV
- F) Switch to something else

DHHS Guidelines

2-Drug Maintenance ART

- Growing evidence that some 2-drug regimens are effective in maintaining virologic control in patients who initiated ART and achieved suppression with a 3-drug regimen, provided their **HIV is susceptible to both drugs** in the new regimen and they **do not have chronic hepatitis B virus (HBV)**
- *June 2021 update:* focuses long-acting injectable (LAI) intramuscular (IM) cabotegravir (CAB)/rilpivirine (RPV)

DHHS Guidelines

2-Drug Maintenance ART Options

- Dolutegravir/rilpivirine (DTG/RPV)
 - SWORD 1&2: n = 1,024, compared to TDF 3-drug regimens
 - Criteria: HIV RNA <50 for ≥ 6 months, no more than one HIV RNA 50-200 for >12 months, taking 1st or 2nd ART regimen, no history of VF, no major drug-resistance mutations, no HBV
- Dolutegravir/lamivudine (DTG/3TC)
 - TANGO: n=741, compared to TAF 3-drug regimens
 - Criteria: HIV RNA <50 for ≥ 6 months, no history of VF, no resistance to DTG or 3TC, no HBV
- Boosted PI + 3TC, boosted darunavir + DTG

POLL

How many of your patients or clients are currently receiving long-acting IM cabotegravir/rilpivirine (CAB/RPV)?

- A) 0
- B) 1-5
- C) 6-10
- D) >10

Summary of Key Studies

Cabotegravir (CAB)/Ralpivirine (RPV) Long-Acting Injectable

- Phase 2 Trials in Treatment-Naïve

- LATTE: oral CAB/RPV daily vs. EFV plus 2 NRTI's
- LATTE-2: IM CAB/RPV q1 or 2 months vs. oral CAB + ABC/3TC

- Phase 3 Trials in Treatment-Naïve

- FLAIR: IM monthly CAB/RPV vs. oral DTG/ABC/3TC

- Phase 3 Trials in Treatment-Experienced

- ATLAS: switch to monthly IM CAB/RPV vs. continue 3-drug ART
- ATLAS-2M: switch to IM CAB/RPV every 4 vs. 8 weeks

IM Cabotegravir/Rilpivirine (CAB/RPV)

FDA Indication

- **Indication**

- Replace ARV regimen in persons with HIV RNA <50
- Taking stable ARV regimen
- No history of treatment failure
- No known or suspected resistance to CAB or RPV
- No hepatitis B

IM Cabotegravir/Rilpivirine (CAB/RPV) Dosing Schedule

Oral Lead-In x 1 month (≥ 28 days)

Cabotegravir 30 mg daily +
Rilpivirine 25 mg daily

*Initiation Injections (x 1)

Cabotegravir (600 mg): 3 mL IM +
Rilpivirine (900 mg): 3 mL IM

*Continuation Injections (Monthly)

Cabotegravir (400 mg): 2 mL IM +
Rilpivirine (600 mg): 2 mL IM

*Administer injections at opposite gluteal sites (or at least 2 cm apart) and give both during the same visit.

IM Cabotegravir/Rilpivirine (CAB/RPV) Oral Therapy for Missed Injections

Oral Bridge Therapy for Planned and Unplanned Missed Injections

Time Since Last Injection	Recommendation for Oral Bridging*
<p>Planned Missed Injection</p> <ul style="list-style-type: none"> • Time from last injections is greater than 1 month + 7 days 	<ul style="list-style-type: none"> • Take daily oral therapy to replace up to 2 consecutive monthly injection visits. • Start oral therapy approximately 1 month after the last injection doses. • Continue oral therapy until the day injection dosing is restarted.
<p>Unplanned Missed Injection</p> <ul style="list-style-type: none"> • Time from last injections is greater than 1 month + 7 days 	<ul style="list-style-type: none"> • If oral therapy has not been taken, reassess patients clinically to ensure resumption of injections remains appropriate.**

*Oral therapy = cabotegravir 50 mg plus rilpivirine 25 mg, both taken once daily with food

**If >2 months since last injection and resuming LAI CAB/RPV, repeat loading dose

Note: if stopping LAI CAB/RPV, levels may remain in systemic circulation for up to 12 months; essential to start suppressive oral ART at 1 month after the last injection (missed doses may lead to resistance)

IM Cabotegravir/Rilpivirine (CAB/RPV) Outstanding Clinical Questions

FDA to rule on q8-week
dosing by 12/21/21

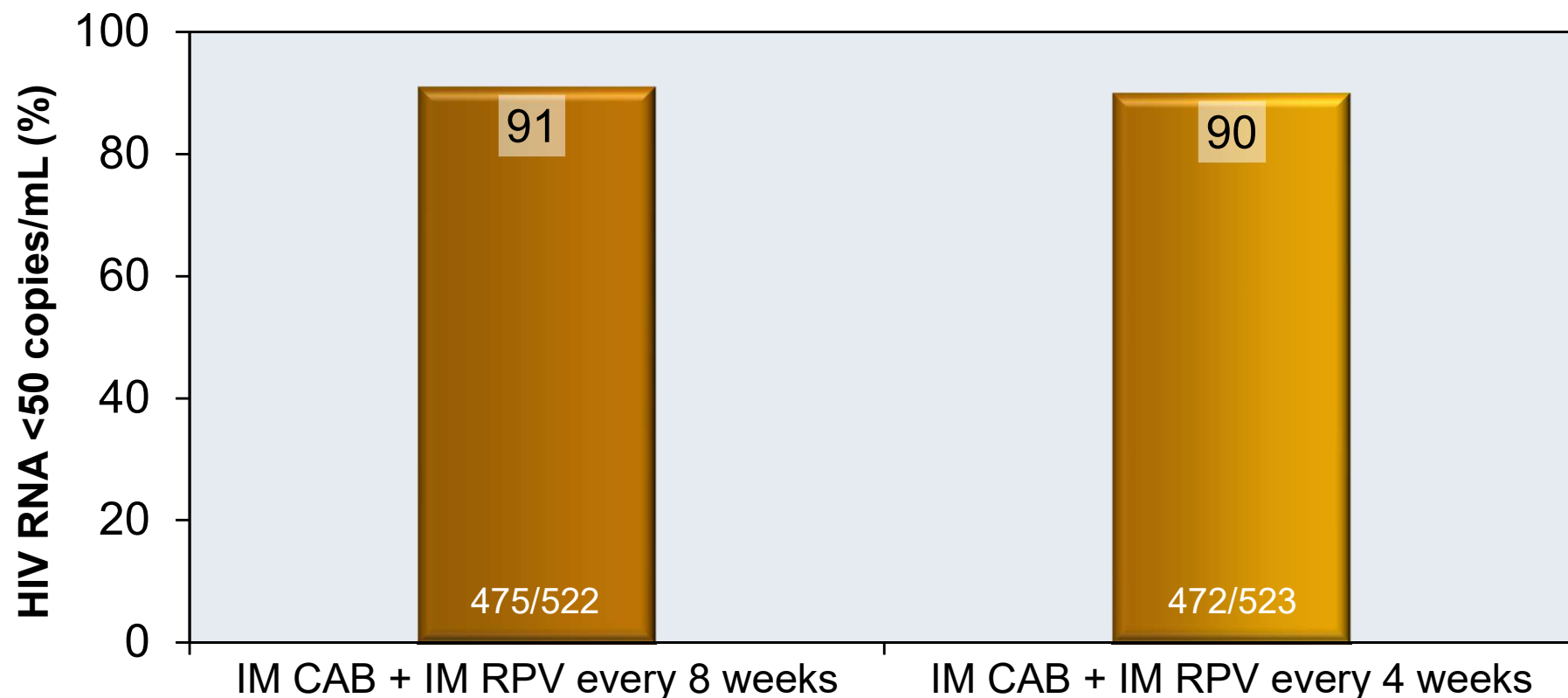
- Need to know HIV subtype or order archive genotype?
 - Predictors of virologic failure (n = 13/1,039 at 48 weeks):*
 - 1) Subtype A1/A6 virus
 - 2) ≥ 2 RPV resistance mutations
 - 3) BMI ≥ 30
 - 4) Lower RPV trough concentrations
 - 9/13 participants with VF had 2 or more risk factors
- Role for every 8-week dosing?
- Oral lead-in phase necessary?
- Risks of missed doses? Or stoppage?

*Predictors of IM CAB/RPV virologic failure: Cutrell AG et al. AIDS 2021.
Elliot E et al. EACS 2021. (Elevated BMI alone not a predictor of VF)



IM Cabotegravir/Rilpivirine Every 2 Months vs Every 1 Month ATLAS-2M Study: Results

Weeks 96: Virologic Response by FDA Snapshot Analysis



Confirmed virologic failure (CVF): 9/522 (2%) q8-week arm & 2/523 (0.4%) q4-week arm
55% of CVF cases had ≥ 2 of the predictors of VF previously described
91% of CVF cases re-suppressed on oral ART (most included boosted PI)

Source: Jaegger H et al. Lancet HIV. Oct 2021.



IM Cabotegravir/Rilpivirine “Direct-To-Inject” Open-Label Phase of FLAIR Study: Oral Lead-In Optional

- At week 100, participants in oral ART arm could choose to switch to IM CAB/RPV or withdraw (232 chose IM ART)
 - Participants could choose oral lead-in or direct-to-inject
 - 121 opted for oral lead-in (OLI), 111 direct-to-inject (DTI)
 - Comparisons made to those who continued IM CAB/RPV
- 24 weeks later, the groups had similar safety and tolerability; similar efficacy to long-term IM CAB/RPV

Case #2

- A 40-year-old African-born cisgender woman presents for follow-up in clinic
- Diagnosed with HIV in 2015; took NVP + 3TC/TDF then EFV/3TC/TDF
- Moved to US in 2019; ART switched to DTG + FTC/TAF
- Since that time, viral load routinely suppressed but has gained \approx 30 lbs.
- Comorbidities: HTN, osteoarthritis, depression

Poll

- What would you recommend for ART?
 - A) Continue dolutegravir + FTC/TAF
 - B) Switch to doravirine + FTC/TAF
 - C) Switch to dolutegravir + FTC/TDF
 - D) Switch to doravirine/3TC/TDF
 - E) Switch to dolutegravir/3TC
 - F) Switch to dolutegravir/rilpivirine
 - G) Switch to something else

Cisgender Women with HIV

HHS June 2021 Update

- New review of literature on ART-associated weight gain:
 - Clinicians should consider the possibility of weight gain in women when initiating or changing ART
 - Underlying mechanisms and impact on CVD, DM, pregnancy, and age-related comorbidities *unknown*
 - *Unclear whether switching to a non-INSTI-based regimen results in reversal of weight gain*
 - *Significant uncertainty whether INSTIs cause weight gain vs comparator drugs suppress weight gain*

CROI 2021

Weight Gain Studies: Consequences

- REPRIEVE: n=4,500, INSTI >6 months vs non-INSTI
 - INSTI: greater BMI, waist circumference, likelihood of obesity
 - *No association* with abnormal fasting glucose or LDL, metabolic syndrome, HTN

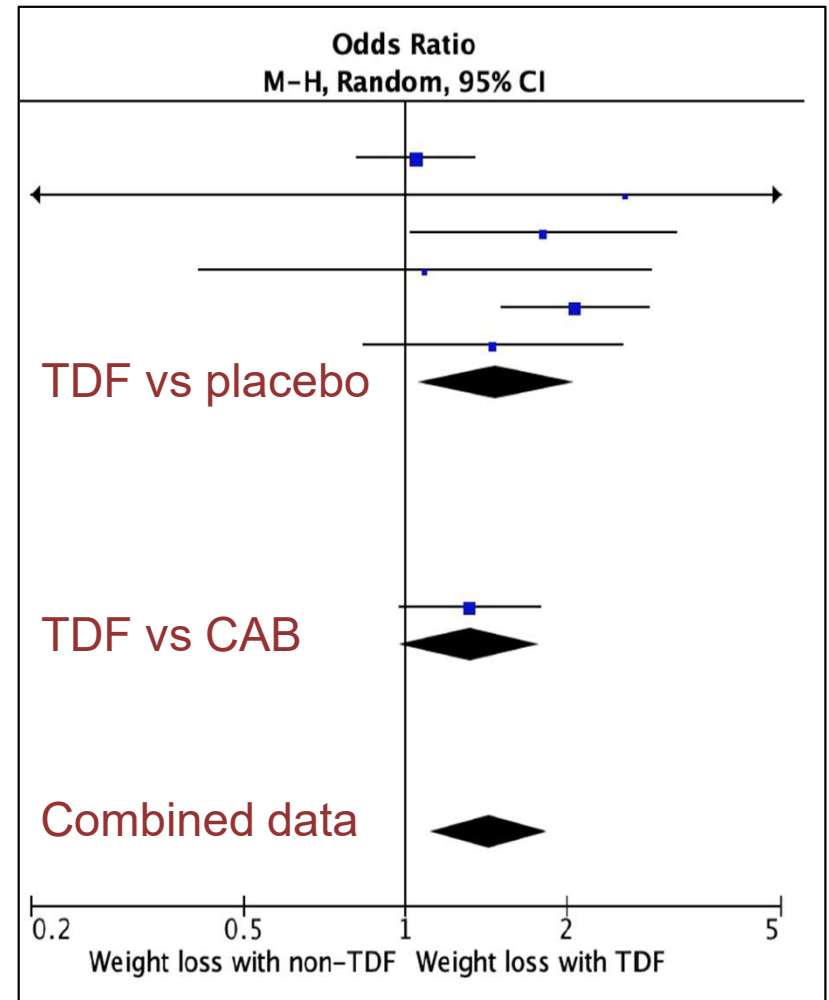
Difference in Mean	All	Female	Male
BMI (kg/m ²)	1.45 (1.03, 1.88)	2.47 (1.44, 3.49)	1.13 (0.77, 1.49)
Waist circumference (cm)	3.62 (2.51, 4.64)	5.04 (2.76, 7.32)	2.82 (1.84, 3.80)
Fasting glucose (mg/dL)	-0.019 (-0.96, 0.92)	0.47 (-1.49, 2.42)	-0.17 (-1.18, 0.83)
Fasting LDL (mg/dL)	-0.88 (-3.01, 1.25)	0.25 (-4.12, 4.51)	-0.72 (-2.93, 1.49)
Odds Ratio	All	Female	Male
Obesity	1.63 (1.39, 1.91)	1.74 (1.32, 2.29)	1.58 (1.32, 1.89)
Metabolic syndrome	0.92 (0.79, 1.07)	1.23 (0.92, 1.54)	0.91 (0.77, 1.07)
Hypertension	1.14 (0.99, 1.32)	1.08 (0.82, 1.42)	1.10 (0.94, 1.28)

- Atlanta Women's Interagency HIV Study: "Metabolomics"¹
 - 18 women with >5% body weight increase after INSTI + 15 without
 - Switch affected bioenergetic pathways that lead to insulin resistance
 - Altered mitochondrial utilization of fuels → "metabolic inflexibility," dysregulation of insulin signaling, storage of excess fat
- Mouse model: DTG, BIC, or DOR given to female mice²
 - *In vitro*:
 - DTG/BIC induce white adipocyte differentiation, lipid accumulation
 - DTG/BIC strongly affect mitochondria in brown/beige adipocytes
 - Suppress thermogenesis (estrogen-mediated pathways)
 - *In vivo*:
 - DTG inhibits oxygen consumption & energy expenditure by 15%

ID Week 2021

Systematic Review of TDF-Associated Weight Loss

- 7 PrEP trials included (total n = 19,359)
- TDF: associated with >5% weight loss when compared to placebo or CAB in persons without HIV (OR 1.44, 95% CI 1.12–1.85, p=0.005)
- TDF: greater odds of vomiting (OR 1.81, 95% CI 1.20-2.73, p <0.005); no increased odds of nausea, diarrhea, appetite loss



Weight Gain with ART

My Interpretation & Strategy

Remember ACTG 5391!

- *Consider:*
 - GEMINI: DTG/3TC vs DTG + FTC/TDF → less weight gain w/TDF¹
 - TANGO: DTG/3TC vs DTG + FTC/TAF → no difference in weight gain²
- *My interpretation:*³
 - Convincing data that TDF and EFV suppress weight
 - INSTI's, esp. DTG/BIC, can cause excess weight, insulin resistance, higher likelihood of metabolic syndrome for some individuals (not all)
 - Credible mechanisms for INSTI effects & sex differences described
 - For many, changes stabilize by 9-12 months
 - Data for reversability limited to case reports
- *My strategy:*
 - Case-by-case discussion and shared decision-making

1. Cahn P et al. JAIDS 2019. 2. Osiyemi O et al. ID Week 2021.
3. Wood BR, Huhn GD. OFID 2021.

Case #4

- 52-year-old cisgender man with longstanding HIV
- Viral load suppressed on RPV/FTC/TAF for several years
- Only prior ART: EFV/FTC/TDF
- Lapse in adherence following onset of COVID-19 pandemic
- Viral load rebound to 1,250 copies/mL
- Genotype: E138K, M184V

Poll

- Which regimen would you recommend (ideally)?
 - A) Bictegravir/FTC/TAF
 - B) Bictegravir/FTC/TAF + doravirine
 - C) Bictegravir/FTC/TAF + darunavir/cobicistat
 - D) Darunavir/cobicistat/FTC/TAF
 - E) Something else

Virologic Failure (VF)

HHS June 2021 Update

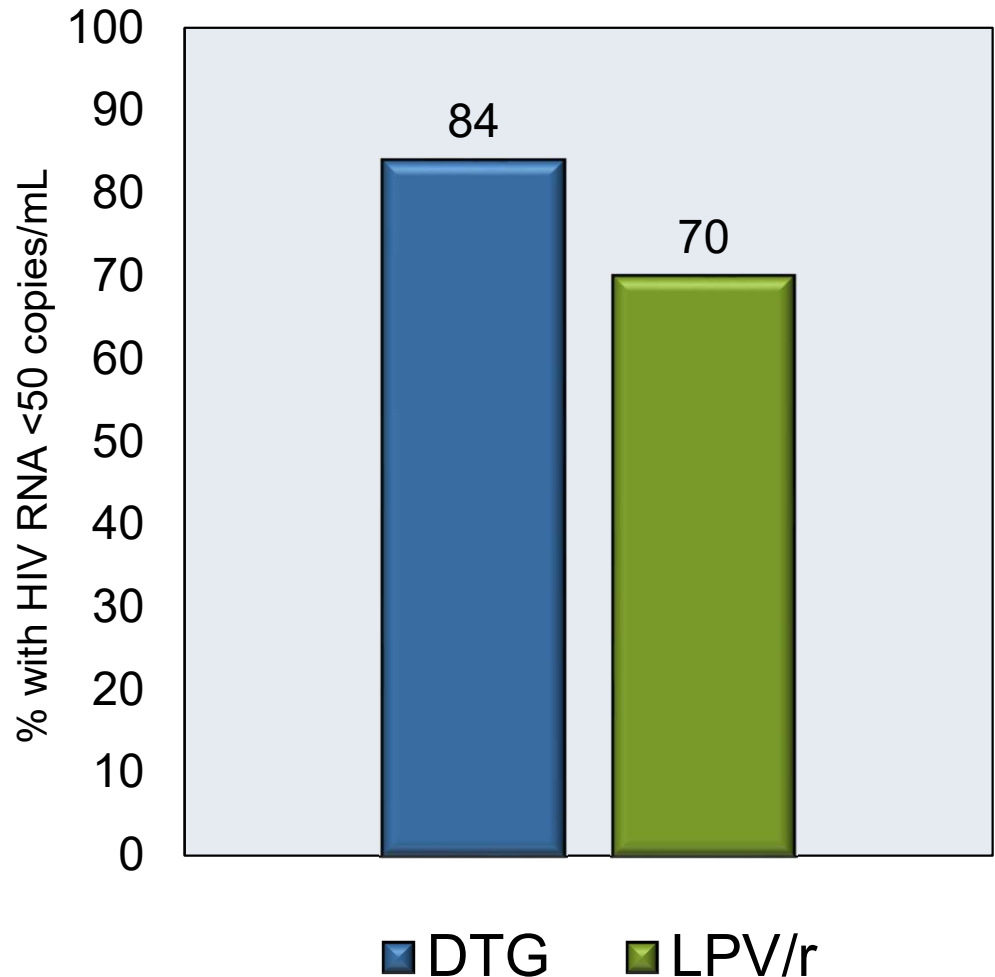
- Old language: “A new regimen should include at least two, and preferably three, fully active agents (AI)”
- **New language: “A new regimen can include two fully active drugs if at least one with a high resistance barrier is included (e.g. DTG or boosted darunavir) (AI)”**
 - Why? Accumulating clinical trial data showing that a regimen with two fully active ARV’s effectively achieves viral suppression, provided one drug has high resistance barrier
- Also added data on fostemsavir as part of salvage ART

DAWNING Study

DTG vs LPV/r after Virologic Failure on NNRTI Regimen

Overall Virologic Suppression Rate at 48 Weeks

- DTG vs LPV/r, each w/ 2 NRTI's, after VF on NNRTI regimen
- M184V/I +/- other NRTI mutations in 82% of 624 participants
- N=627; trial stopped because DTG did so well
- Regardless of M184V/I, FTC/3TC use (DTG + 1 active NRTI sufficient)
- Zero cases of VF with new resistance if baseline only M184V/I

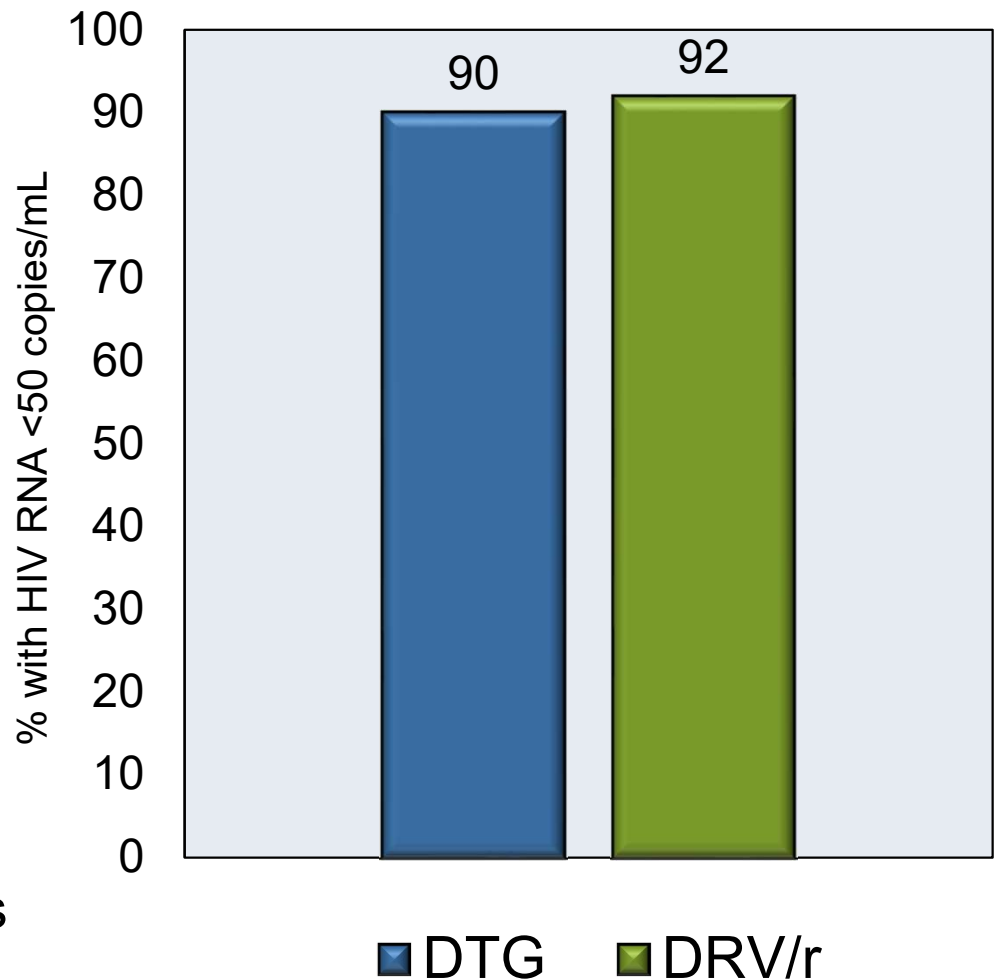


NADIA Study

DTG vs DRV/r after Virologic Failure on NNRTI Regimen

Overall Virologic Suppression Rate at 48 Weeks

- DTG vs DRV/r, each with TDF/3TC or AZT/3TC, after VF on NNRTI regimen
- N=464; 87% M184V, 50% K65R
- Similar results if: VL >100k, TDF or AZT, no predicted NRTI activity (NRTI's with zero activity added to DTG or DRV/r)
- 4 cases new INSTI RAM's w/DTG
- Supports TLD as first- and second-line ART in resource-limited settings



Additional Data for 1 High-Barrier to Resistance ARV (DTG, BIC, or boosted PI) + 1 Active ARV

- With detectable viral load:
 - GEMINI: DTG + 3TC as baseline ART
 - ANDES: DRV/rtv + 3TC as baseline ART
 - PREZENT: DRV/cobi + RPV as baseline ART
- With suppressed viral load:
 - BRAAVE 2020: switch 2:1 BIC/FTC/TAF vs cont. 3-drug ART
 - Resistance allowed, except K65R, ≥ 3 TAM's, primary INSTI
 - Baseline M184V/I in 11% (51/471), TAM's in 7% (34/471)
 - VL suppression at week 48: 95-97%

GEMINI: Cahn P et al. Lancet 2019.
ANDES: Figueroa MI et al. CROI 2018.
PREZENT: Gathe Jr J et al. IAS 2018.
BRAAVE 2020: Hagins D et al. OFID 2020.



Virologic Failure

Translating Data & Guidelines to Practical Strategy

- High-barrier agent (DTG, BIC, or boosted DRV) fully active:
 - High-barrier agent + ≥ 1 active agent sufficient
 - If high viral load, consider adding 2 active agents to DTG, BIC, or boosted DRV then drop one once suppressed
 - Examples:
 - M184V: BIC/FTC/TAF generally sufficient
 - NRTI + NNRTI resistance: DTG + DRV/cobi
- No fully active high-barrier agent:
 - Aim for 3 active drugs
 - Example:
 - NRTI, NNRTI, PI, + INSTI resistance: combine agents like fostemsavir, ibalizumab, maraviroc if R5, OBR

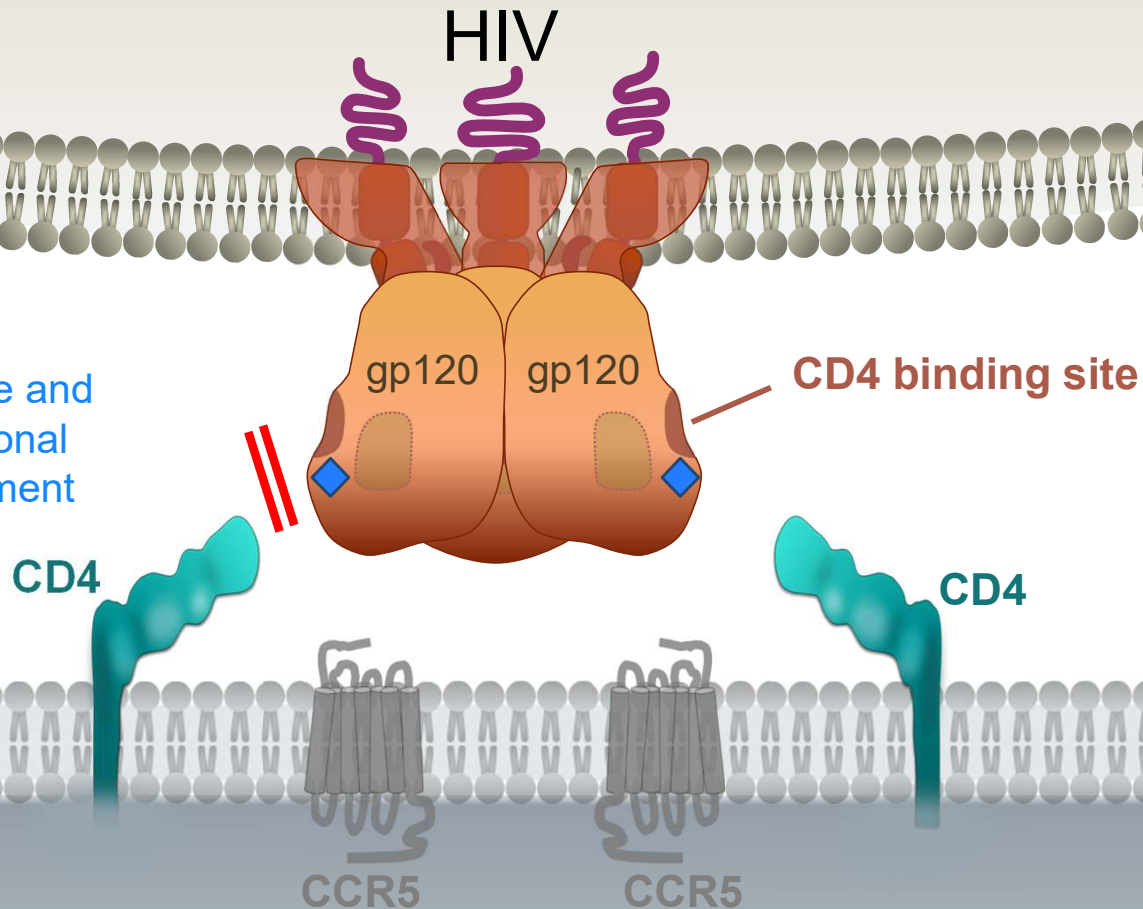
HIV Entry Inhibitors

Fostemsavir: Attachment Inhibitor (Oral, BID)

HIV

Fostemsavir

Binds near CD4 binding site and prevents gp120 conformational change required for attachment



Intracellular Space
Host Cell

HIV Entry Inhibitors

Ibalizumab: Post-Attachment Inhibitor (IV, q2 weeks)

HIV

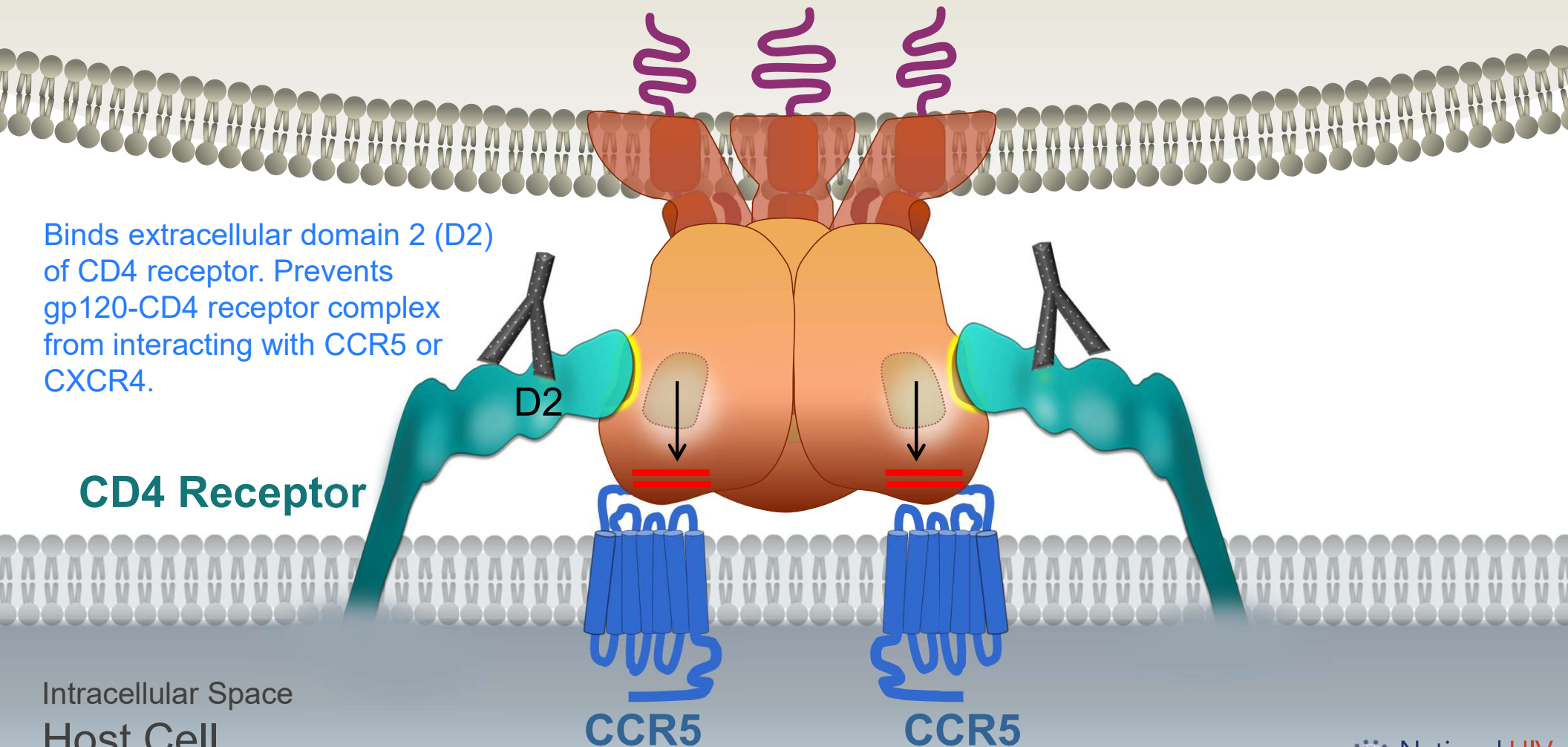
Binds extracellular domain 2 (D2) of CD4 receptor. Prevents gp120-CD4 receptor complex from interacting with CCR5 or CXCR4.

CD4 Receptor

Intracellular Space
Host Cell

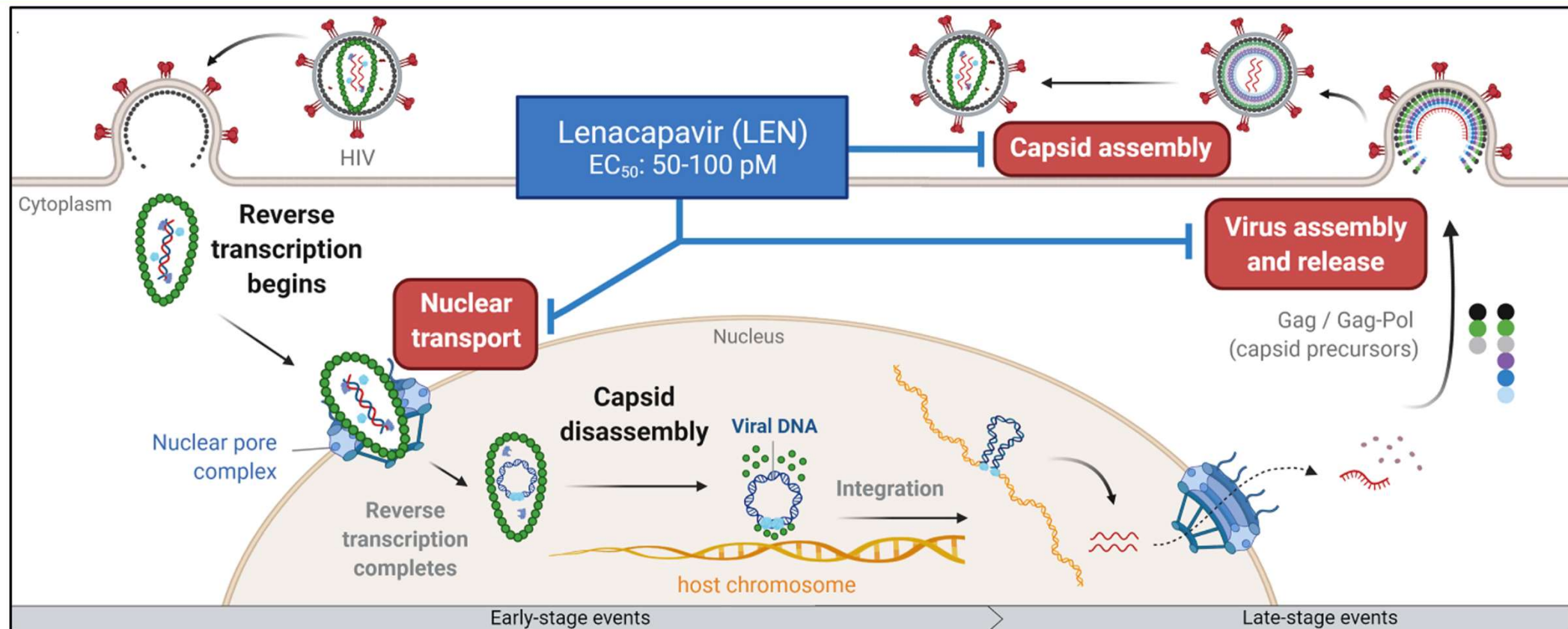
CCR5

CCR5



Lenacapavir (LEN)

Capsid Inhibitor: Mechanism of Action

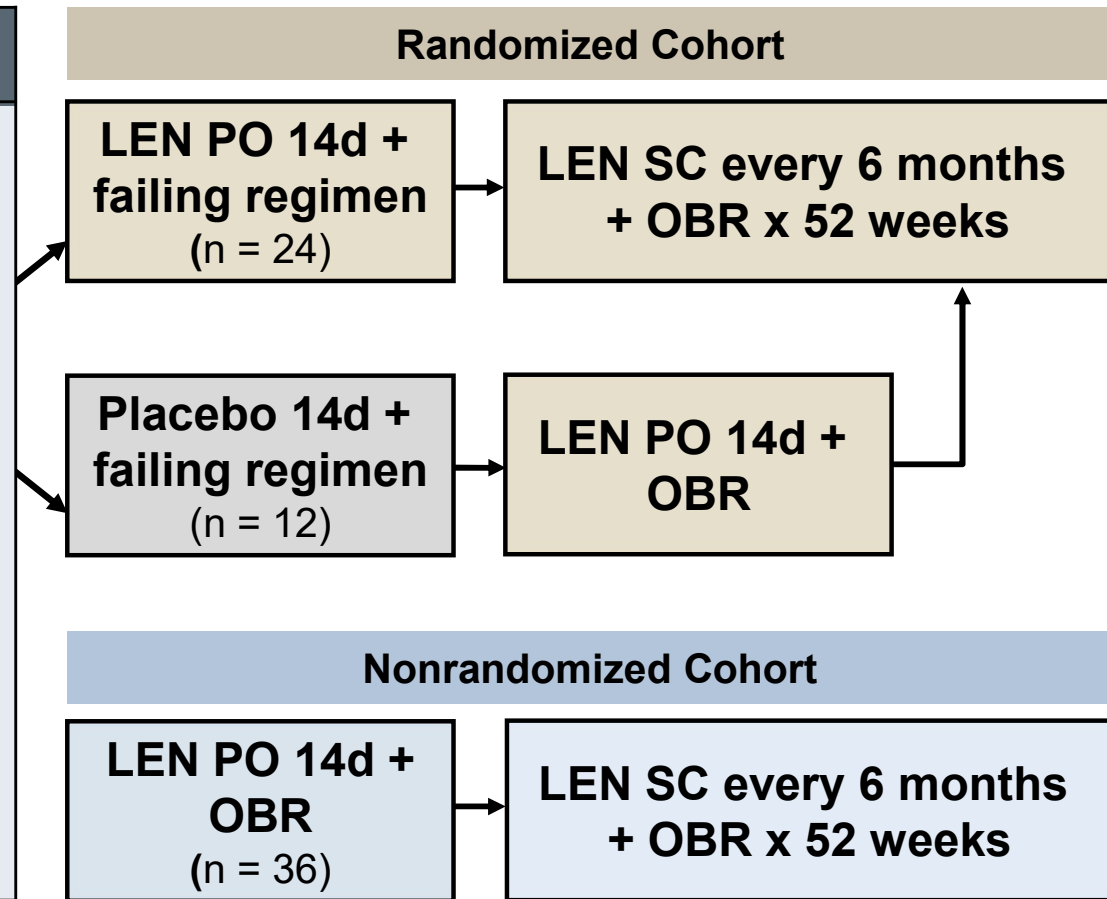


LEN binds to the HIV capsid, interferes with transport via nuclear pores, stabilizes shell and inhibits disassembly, plus distorts the capsid lattice resulting in abnormal structure that prevents viral maturation (assembly and release).

Lenacapavir (LEN) CAPELLA Study: Background

Study Design: CAPELLA

- **Background:**
 - Phase 2/3, randomized controlled trial of lenacapavir for heavily treatment-experienced individuals
- **Enrollment Criteria:**
 - Highly ART-experienced adults
 - Virologic failure on current ART
 - HIV RNA >400 copies/mL
 - Resistance to ≥ 2 agents from ≥ 3 of 4 main ARV classes
 - ≤ 2 predicted active agents

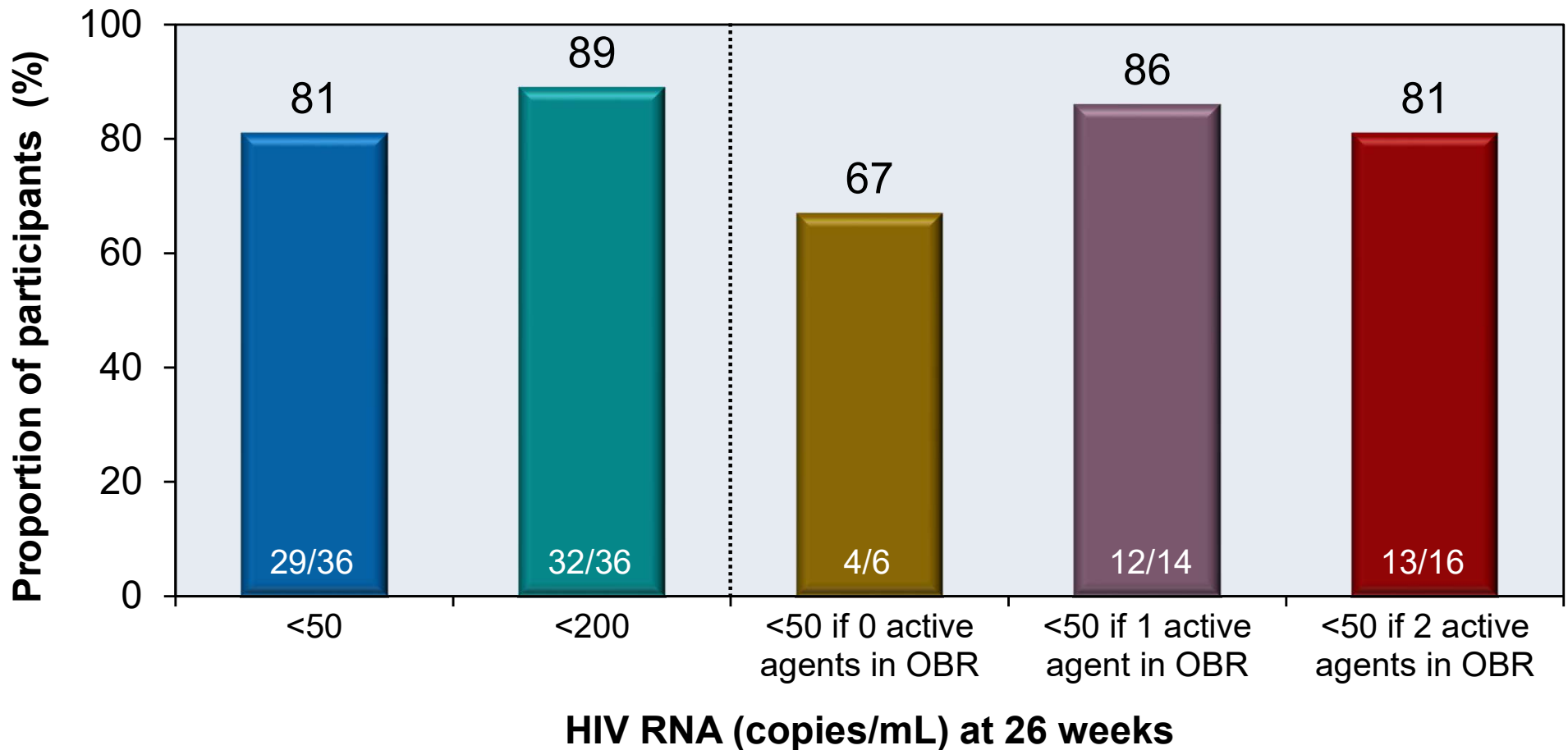


*Oral LEN for 14d = 600 mg day 1 & day 2 then 300 mg day 8; LEN SC = 927 mg (2 x 1.5 mL in abdomen)

*SC = subcutaneous; OBR = optimized background regimen

Lenacapavir (LEN) CAPELLA Study: Results

Virologic efficacy results at 26 weeks (randomized cohort only)



*4/36 (11%) developed VF with emergent capsid resistance (all functional LEN monotherapy)

Source: Molina JM et al. IAS 2021. Margot N et al. EACS 2021.



Lenacapavir (LEN)

CALIBRATE: Treatment-Naïve Trial, 28-Week Data

28-Week Results	LEN SC + FTC/TAF → LEN SC/TAF	LEN SC + FTC/TAF → LEN SC/BIC	LEN PO + FTC/TAF	BIC/FTC/TAF
N	52	53	52	25
HIV RNA <50	94	92	94	100

- Resistance developed in 1/157 (0.6%) who received LEN
 - Participant in LEN SC + FTC/TAF → LEN/BIC arm
 - Never suppressed on LEN SC + FTC/TAF; VL rise week 10
 - LEN plasma concentrations in target range
 - Plasma FTC and TFV concentrations c/w expected PK
 - M184I/V first (M184I/V week 2, capsid mutations week 4)

Islatravir (ISL)

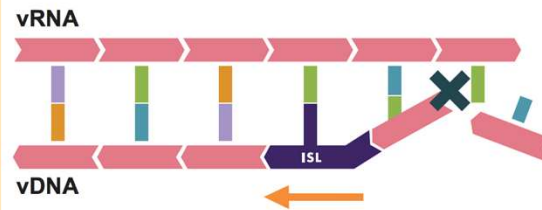
NRTTI: Mechanism of Action & Potential Advantages

Translocation Inhibition



- Translocation inhibition prevents opening of the RT nucleotide binding site
- Nucleotides cannot be incorporated into vDNA
- **Viral replication is inhibited**

Delayed Chain Termination



- ISL changes vDNA structure such that nucleotide incorporation is prevented
- As ISL is not in the RT active site, it is not susceptible to resistance-conferring mutations
- **Viral replication is inhibited**

- Active against isolates with pre-existing NRTI resistance
- Potent viral load reduction plus high barrier to resistance
- Inhibitory quotient achieved with low doses & long half-life
- Per early trial data, appears metabolically neutral

Summary of Key Treatment Studies

Islatravir (ISL) & Islatravir/Doravirine (ISL/DOR) Phase 2/3 Trials

- Treatment-Naïve

- DRIVE2SIMPLIFY: ISL/DOR/3TC → ISL/DOR vs DOR/3TC/TDF

- Treatment-Experienced

- ILLUMINATE A: switch to ISL/DOR vs cont. 3-drug ART
- ILLUMINATE B: switch to ISL/DOR vs cont. BIC/FTC/TAF
- MK-8591A-019: ISL/DOR for heavily treatment-experienced
- GS-6041: switch to weekly oral ISL + LEN vs cont. BIC/FTC/TAF

Once-daily oral ISL/DOR: phase 3

Once-weekly oral ISL/MK-8507: phase 2

Once-weekly oral ISL/LEN: phase 2

Long-acting injectable ISL/LEN: phase 1

POLL

- A 53-year-old man who takes BIC/FTC/TAF and has well-controlled HIV is diagnosed with latent tuberculosis (TB). What would you recommend for ART and for latent TB treatment, respectively?
 - A) BIC/FTC/TAF; 9 months INH with pyridoxine
 - B) DTG daily + FTC/TDF daily; 3 months INH + rifapentine weekly
 - C) DTG BID + FTC/TDF daily; 4 months rifampin daily
 - D) DTG BID + FTC/TDF daily; 3 months INH + rifampin daily
 - E) EFV/FTC/TDF daily; 1 month INH + rifapentine daily

TB-HIV Coinfection

HHS June 2021 Update

- Key update: dolutegravir (DTG) 50 mg **once daily** may be used with **once-weekly rifapentine**, provided the patient does not require twice-daily DTG dosing (meaning no confirmed or suspected DTG resistance)

CDC Recommendations Treatment of LTBI

Treatment of LTBI	“AKA”
Preferred	
Isoniazid (INH)* + Rifapentine (RPT) x 3 months (weekly)	3HP
Rifampin (RIF) x 4 months (daily)	4R
Isoniazid (INH)* + Rifampin (RIF) x 3 months (daily)	3HR
Alternative	
Isoniazid (INH)* x 6 or 9 months (daily)	6H or 9H
Abbreviation: “AKA” = Also Known As. *Give with pyridoxine	

- Avoid TAF with rifampin or rifapentine; TDF/FTC or ABC/3TC ok
- DTG daily with weekly rifapentine ok if no resistance; must be BID with rifampin
- 1HP endorsed by WHO; only studied with EFV, NVP, or no ART

Source: Centers for Disease Control and Prevention
(<https://www.cdc.gov/tb/topic/treatment/lbti.htm>)



Questions or comments?
bwood2@uw.edu

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ART Near-Future Pipeline

Compound	Class	Summary
Long-acting CAB/RPV	INSTI/ NNRTI	IM monthly approved by FDA FDA to rule on IM every 2-months dosing by 12/21/21 FDA to rule on IM CAB every 2 months for PrEP by 1/22/22 Subcutaneous CAB in phase 1
Lenacapavir (LEN)	Capsid inhibitor	CAPELLA data (tx-experienced) submitted to FDA July 2021 Combo with TAF/FTC for treatment-naïve phase 2 ongoing Combo with ISL (both oral weekly) for suppressed pts upcoming PrEP: subcutaneous every 6 months recruiting
Islatravir (ISL)	NRTTI	Switch to oral daily tablet combo with doravirine in phase 3 Oral weekly with MK-8507 in phase 2 Oral monthly for PrEP recruiting Combo with LEN upcoming PrEP: yearly implant in phase 1
MK-8507	NNRTI	Oral weekly combo with ISL ongoing in phase 2
GSK-3640254 GSK-3739937	Maturation inhibitors	254: daily oral in phase Ib 937: potential for long-acting formulation