AETC AIDS Education & Training Center Program
Southeast Regional Conference 2022

Cases from the NCCC: Testing, Long-Acting ART, and More…

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By the end of this session, participants will be able to

- *Describe what types of tele-consultation services the National Clinician Consultation Center offers*
- *Reflect on unique considerations regarding HIV testing and diagnosis in pregnancy*
- *Discuss key clinical considerations regarding "real world" use of long-acting (LA) ART informed by cases the NCCC has assisted with*

Disclosures

None

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National Clinician Consultation Center

Established in 1993 as national service/component of the Health Resources and Services Administration's Ryan White HIV/AIDS Program

Early operationalization and scale-up of distance-based consultation service and educational resource ("Warmline")

NCCC core consultants

500+ collective years of service and clinical experience in HIV, hepatitis C, and substance use

Engagement with local/regional learners as well as national landscape of clinicians and researchers

UCSF Schools of Nursing & Pharmacy; SFGH Occupational Health

UCSF Primary Care Addiction Medicine Fellowship

NorCal Kaiser HIV Fellowship

HIV residency and fellowship programs across U.S. (MA, PA, ID, NY)

AAHIVM Mentoring Program: residents/graduates from San Joaquin and UC Davis FM Residency Programs

ReproID Listserv: dynamic community forum for emerging/complex issues

Recent partnerships and collaborations

CDC & UCSF SeroPrEP Study

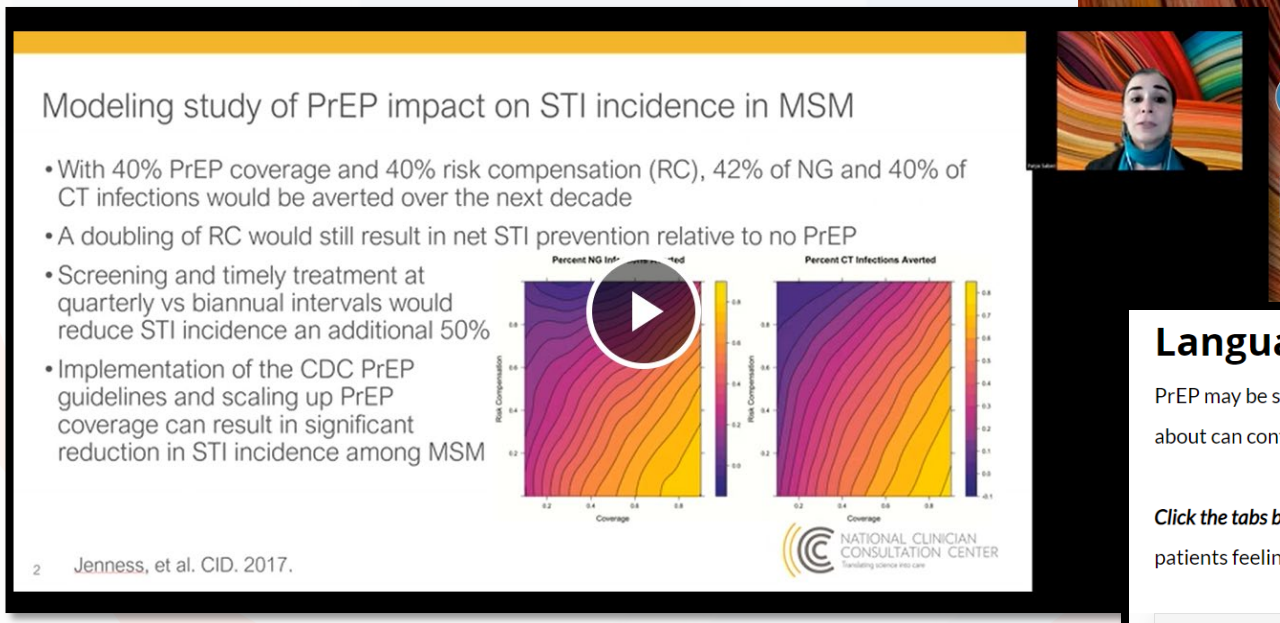
Managing PrEP Patients with Ambiguous HIV test Results

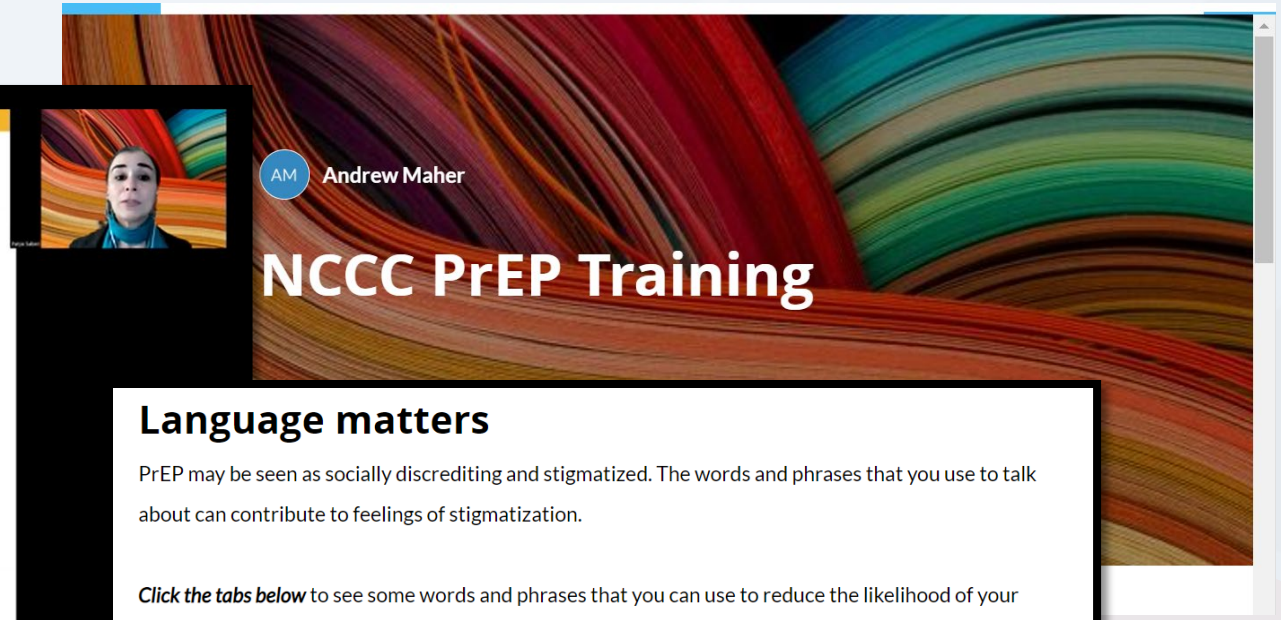
Acquiring HIV while taking daily PrEP as prescribed is very uncommon. While PrEP use has steadily increased since 2012, with more than 220,000 persons prescribed PrEP in 2018,[152] only a handful of incident HIV infections in PrEP-adherent patients have been documented in the US. However, with quarterly HIV testing of persons prescribed PrEP, there is a small but increasing number of PrEP patients with test results that are indeterminate (ambiguous) or that may be false positive.[153, 154] Use of antiretroviral PrEP medications at the time of infection can alter the dynamics of viremia and the patient's immune response and lead to ambiguous test results using standard HIV testing algorithms. For example, such patients may have positive point-of-care antibody results but negative antigen results or may have a reactive qualitative NAT test result but no virus detected by quantitative NAT testing.

CLINICIANS CAN CALL THE NATIONAL CLINICIANS CONSULTATION CENTER PREPLINE AT 855-448-7737 FOR ADVICE ABOUT INTERPRETATION OF HIV TEST RESULTS AND MANAGEMENT OF PATIENTS WHO ACQUIRE HIV INFECTION WHILE TAKING PREP MEDICATION.

https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

More than consultations – PrEP Champion Preceptorship





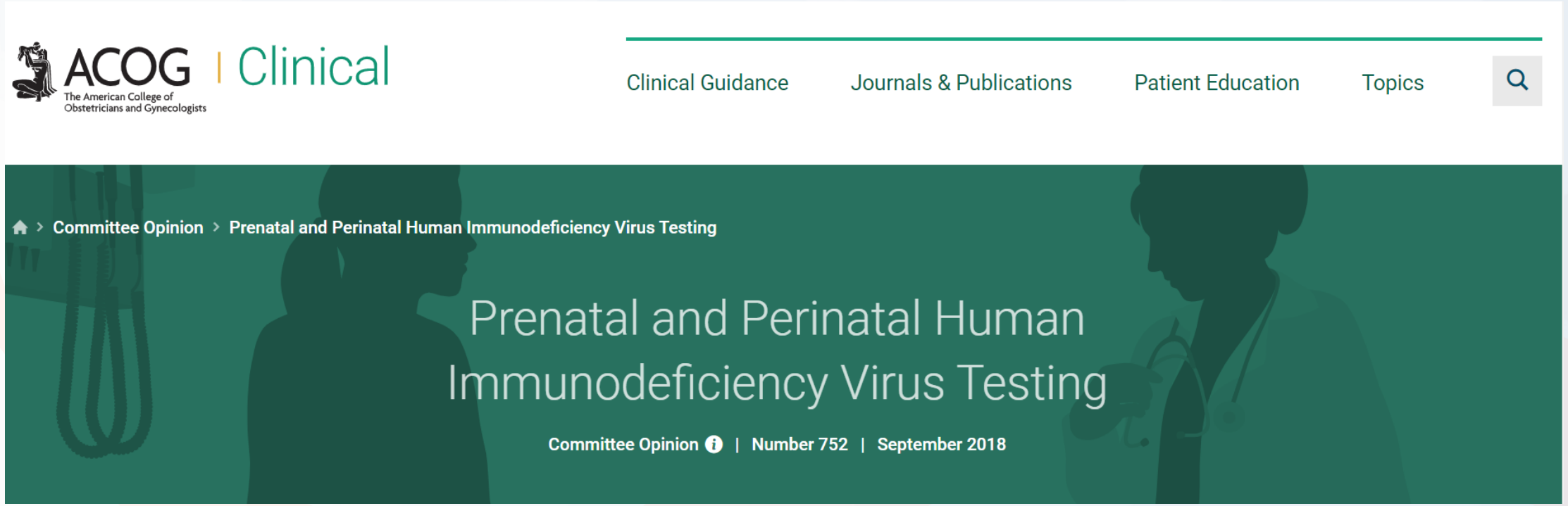
Language matters

PrEP may be seen as socially discrediting and stigmatized. The words and phrases that you use to talk about can contribute to feelings of stigmatization.

Click the tabs below to see some words and phrases that you can use to reduce the likelihood of your patients feeling stigmatized.

INSTEAD OF SAYING THS...	YOU COULD SAY ....
Sex without a condom, sex without the use of PrEP, or sex without an undetectable viral load.	**Be specific**

Case 1: HIV testing and pregnancy



August 2021

36yo at 22wks GA, conceived via IVF

Pre-IVF work-up (or early antenatal screening?): HIV negative by patient report

8/5/2021 HIV Ag/Ab reactive --> HIV-1 Ab reactive, HIV-2 Ab indeterminate

*Based on these results, started F/TDF + DTG 8/13/2021

**HIV-1 NAT subsequently resulted: not detected

8/5/2021 HBsAg screen reactive but (confirmatory) neutralization: negative

Born/raised in Ethiopia, unknown vaccine history, 1 sex partner: husband- ?testing history

What would you do?

(1) Counsel patient about elite controller status, and continue ART

(2) Obtain HIV-2 NAT

(3) Gather more clinical/laboratory history: PrEP use? COVID infection/vaccine?

(4) Call the Lab Director

(5) No idea: call the Perinatal HIV Hotline?

(6) Something else

G_1P_0 at 22wks, born/raised in Ethiopia
HIV Ag/Ab reactive, HIV-1 Ab reactive, HIV-2 Ab indeterminate

HIV-1 NAT not detected
[No copies of prior screening/testing results]

October 2021

HIV-2 NAT: not detected; repeat HIV-1 NAT: not detected (drawn after 3wks on ARVs)

[Lab Director re-ran 8/2021 samples: same results—reactive env gp41, non-reactive env gp160]

Patient requested repeat HIV and HBV screening
Works in meat factory --> read that animal exposures can cause false positive results

HIV Ag/Ab with addition of heterophile blocking reagent (HBR): non-reactive

HBsAg indeterminate; HBcAb and HBsAb both reactive

****With addition of HBR --> HBsAg non-reactive**

Confirmed partner tested negative in past; D/C ART?

Month	Weeks
0	0 - 4
1	5 - 8
2	9 - 12
3	13
Month	**Weeks**
3	14 - 17
4	18 - 21
5	22 - 25
6	26 - 27
Month	**Weeks**
6	28 - 30
7	31 - 34
8	35 - 38
9	39 - 42

Now what would you do?

(1) Discontinue ART, and check viral load in ~2 weeks (HIV-1? HIV-2? Both?)

(2) Continue ART to delivery, and try to sort things out definitively postpartum

(3) Continue ART indefinitely (patient is an elite controller): heterophile blocking reagents aren't clinically validated

(4) Something else

G_1P_0 at 31+wks
Initial screening: HIV Ag/Ab reactive, HIV-1 Ab reactive, HIV-2 Ab indeterminate
Pre-ART HIV-1 NAT not detected
With HBR: HIV Ag/Ab non-reactive
Post-ART HIV NAT not detected (both HIV-1 and HIV-2)

Rouzioux, et al. (1995) Am J Epidemiol

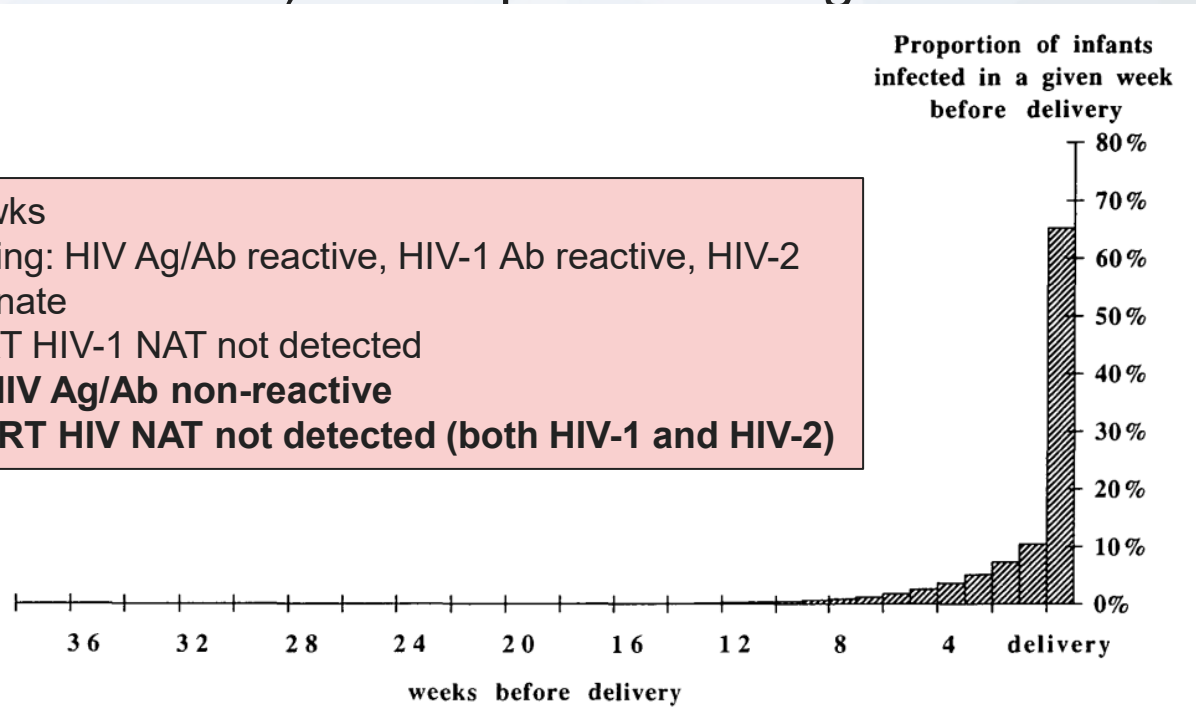


FIGURE 2. Estimated distribution of the dates of transmission.

December 2021

Full-term infant delivered 2hrs ago via NSVD

Sign-out from maternal HIV provider to Peds: "6wks AZT for infant and OK to breastfeed"

--> Overnight Peds advised to pump/save until able to clarify prior breastfeeding counseling/discussions and considerations

Overnight convo with Hotline: ?Role of initial infant ARVs while awaiting further info

Next day f/u: Likely interpretation of maternal testing = false positive... ? Decision to continue maternal ART to delivery, then D/C

(a) Infant testing: NAT? HIV Ag/Ab?

(b) Infant ART management?

(c) Additional maternal testing?

In an abundance of caution,

Heterophile antibodies

Endogenous Ab in human serum/plasma that may interfere with immunoassays --> false elevations of measured values

?Exposure to mice/mouse products

?Immunization, transfusion

?Autoimmune disease

?Infection (e.g., EBV)

0.17-40% prevalence[1]

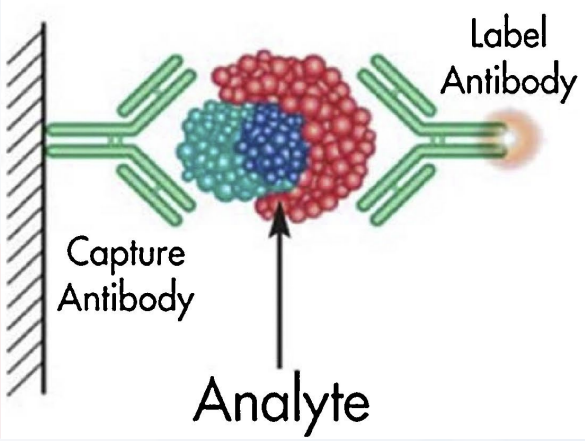
95% clinical specimens repeatedly reactive on one HIV screening platform negative when retested on different platform; *HBR pre-treatment eliminated/reduced false reactivity*

J Clin Virol. 2018 Jul;104:23-28. doi: 10.1016/j.jcv.2018.03.014. Epub 2018 Apr 12.

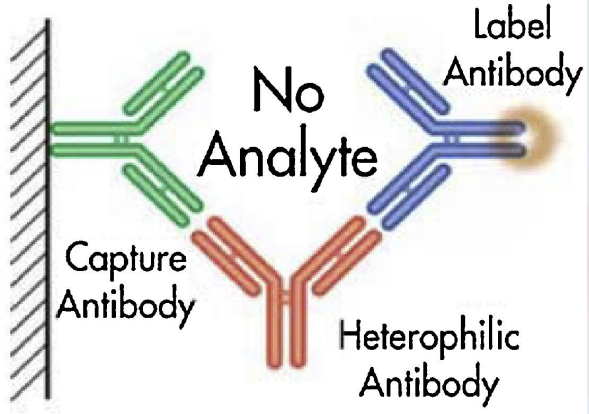
Heterophilic interference in specimens yielding false-reactive results on the Abbott 4th generation ARCHITECT HIV Ag/Ab Combo assay

S Lavoie [1], D Caswell [2], M J Gill [3], K Kadkhoda [4], C L Charlton [5], P N Levett [2], T Hatchette [6], R Garceau [7], J Maregmen [8], T Mazzulli [8], R Needle [9], K Kadivar [1], J Kim [10]

(a) True Reactive



(b) False Reactive



1. Morton A. (2014) Aust Fam Physician

Case Reports > Case Reports Hepatol. 2021 Jul 19;2021:9928098. doi: 10.1155/2021/9928098. eCollection 2021.

An Interesting Case of Isolated False-Reactive Hepatitis B Surface Antigen

Victoria Costa [1], Zhen Zhao [1], Sabrina E Racine-Brzostek [1], Gadi Lalazar [2], He S Yang [1]

77yo without history of liver disease or evident hepatitis risk factors/exposures

Diagnosed with basal cell carcinoma; pre-resection screening yielded reactive HBsAg. Rapid HIV Ab/Ag screen also reactive, but negative for HIV-1 Ab and HIV-2 Ab on differentiation assay

Serial dilutions, heterophilic Ab blocking tubes, and repeat analysis using different commercial assay all supported interpretation as initial false positive HBsAg (attributed to heterophilic Ab)

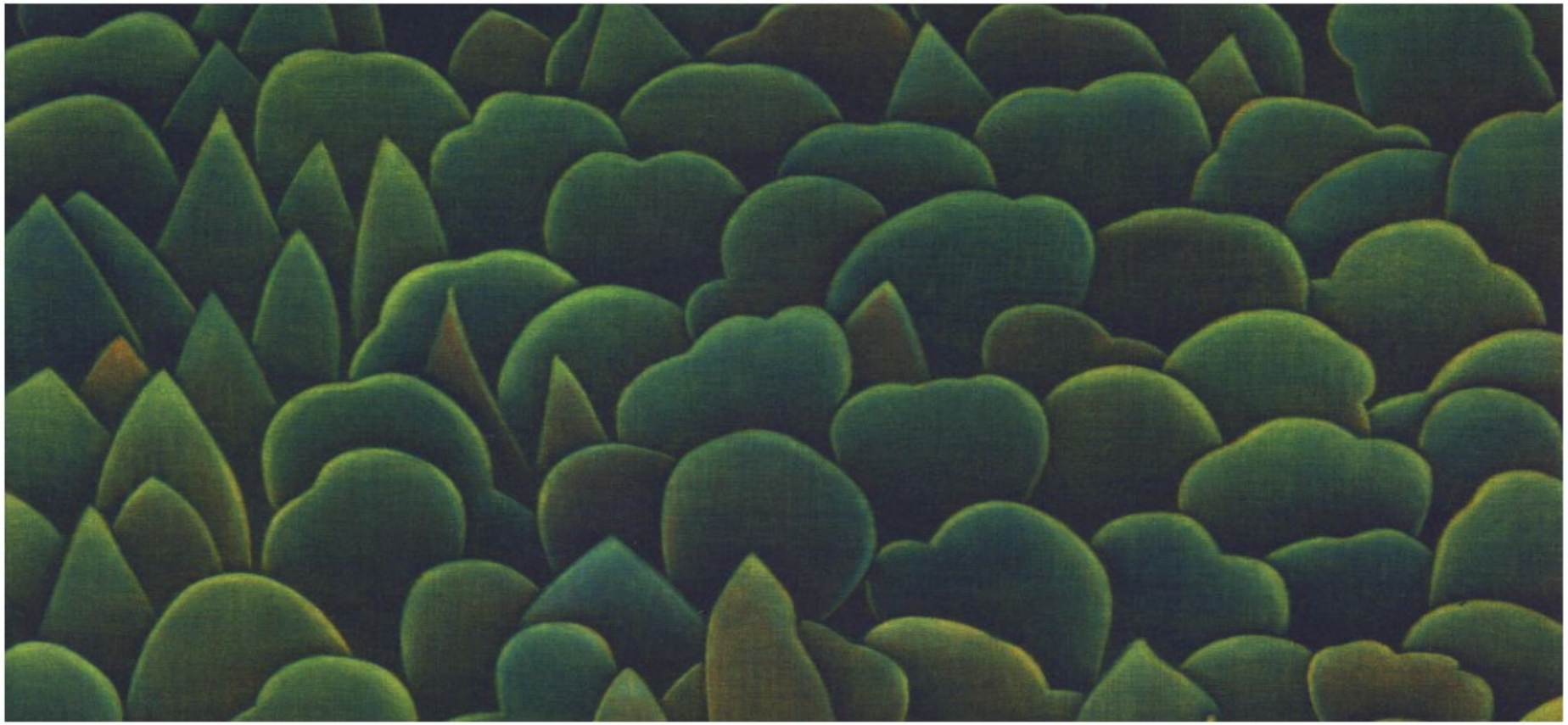
Questions?

Cases involving LA ART (i.e. CAB/RPV)

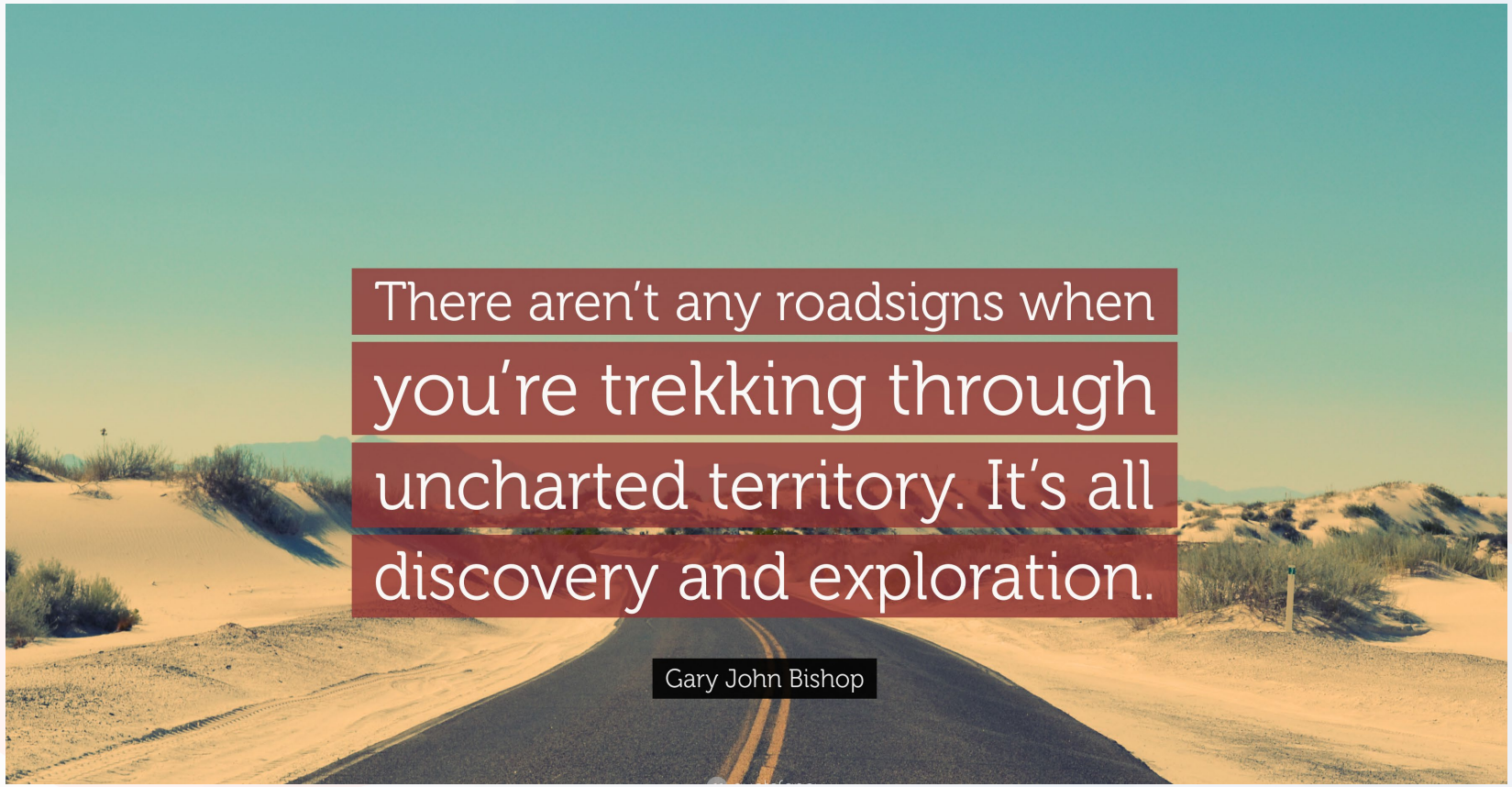
Variations on a Theme II

2 Oct — 1 Nov 2014 at the Graphic Studio Gallery in Dublin, Ireland

7 OCTOBER 2014



For each, consider: (a) eligibility and (b) continuation



CAB/RPV Case 1

49yo cis-male diagnosed with HIV ~2010

ART history: EFV/F/T (2010-2019), then EVG/c/F/TDF (2019-2021) --> suppressed for years

Expressed interest in LA ART --> July 2021 started oral CAB + RPV, then 1st injection

2 months after switch, HBV DNA 1660 IU/mL; LFTs wnl, eGFR > 60 mL/min/1.73m^2

[Prior/baseline labs: HBsAg NR, HBcAb reactive, HBsAb NR, HCV negative]

What would you do now?

(1) Not sure: call the NCCC's HIV Warmline?

(2) Go back to oral ART

(3) Continue CAB/RPV and monitor HBV (but not initiate anti-HBV therapy)

(4) Continue CAB/RPV and initiate anti-HBV therapy

(5) Something else

47yo s/p oral lead-in and initial 600/900mg CAB/RPV injxn
Now with HBV DNA 1660 IU/mL
LFTs ok
Baseline serologies: HBsAg NR, HBcAb reactive, HBsAb NR

HBV eligibility in FLAIR, ATLAS

FLAIR https://clinicaltrials.gov/ct2/show/NCT02938520	ATLAS https://www.nejm.org/doi/suppl/10.1056/NEJMoa1904398/suppl_file/nejmoa1904398_protocol.pdf
Participants positive for HBsAg excluded Participants negative for anti-HBs but positive for anti-HBc (negative HBsAg status) and positive for HBV DNA excluded Note: Participants positive for anti-HBc (negative HBsAg status) and positive for anti-HBs (past and/or current evidence) are immune to HBV and not excluded	Participants positive for HBsAg excluded Participants negative for anti-HBs but positive for anti-HBc (negative HBsAg status) and positive for HBV DNA excluded Note: Participants positive for anti-HBc (negative HBsAg status) and positive for anti-HBs (past and/or current evidence) are immune to HBV and not excluded

Open Forum Infect Dis. 2020 Sep 25;7(9):ofaa367. doi: 10.1093/ofid/ofaa367. eCollection 2020 Sep.

Acute Hepatitis B Infection After a Switch to Long-Acting Cabotegravir and Rilpivirine

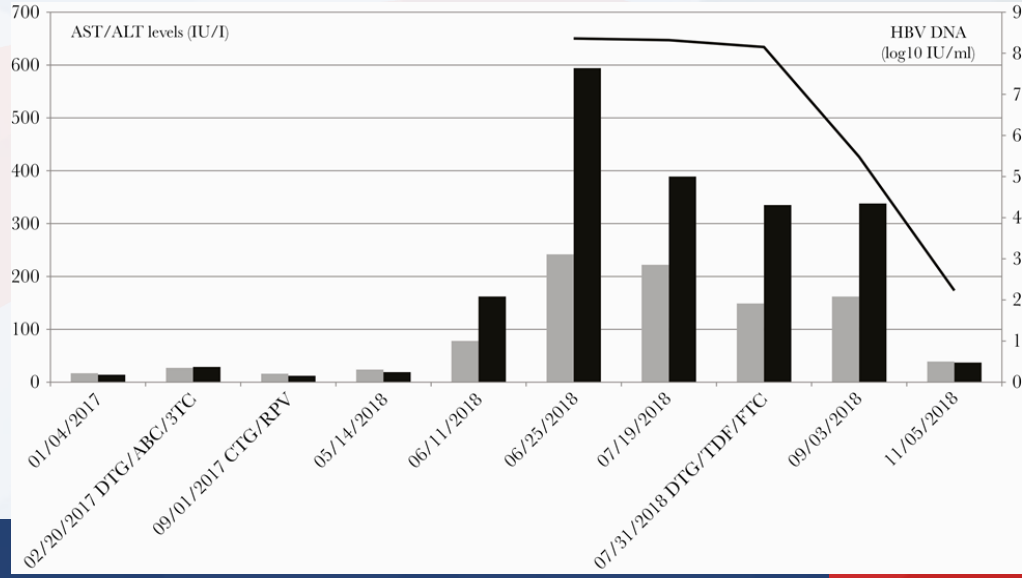
Claire Pintado [1], Constance Delaugerre [2], Jean-Michel Molina [1]

FLAIR screening: negative HBsAg, negative HBcAb, negative HBsAb; no h/o HBV vax

2 out of 3 doses of HBV series received prior to randomization to LAI arm: started 4wk oral lead-in then transitioned to monthly LA CAB/RPV

At 9mo f/u visit, increased AST & ALT noted (no symptoms, no IDU, but + interim STIs)

Diagnosed with acute HBV based on positive HBsAg, positive HBcAb IgM, positive HBeAg, and HBV DNA 229,000,000 IU/mL (negative HBsAb, negative HBeAb)



Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV

The information in the brief version is excerpted directly from the full-text guidelines. The brief version is a compilation of the tables and boxed recommendations.

Hepatitis B Virus

Diagnosis

The Centers for Disease Control and Prevention, the United States Preventive Services Taskforce, and the American Association for the Study of Liver Disease (AASLD) recommend testing patients with HIV infection for chronic HBV.[9,16,17] Initial testing should include serologic testing for surface antigen (HBsAg), hepatitis B core antibody (anti-HBc total), and hepatitis B surface antibody (anti-HBs) **(AI)**. In acute infection, HBsAg can be detected 4 weeks (range 1–9 weeks) after exposure and anti-HBc immunoglobulin M is usually detectable at the onset of symptoms.

Chronic HBV infection is defined as persistent HBsAg detected on 2 occasions at least 6 months apart.[9] Patients with chronic HBV infection should be further tested for HBV e-antigen (HBeAg), antibody to HBeAg (anti-HBe), and HBV DNA. Active disease, which can be HBeAg-negative or HBeAg-positive, can be distinguished from inactive disease by the presence of serum HBV DNA and persistent or fluctuating alanine transaminase (ALT) elevations.[3] Patients whose past infection has resolved are HBsAg-negative with positive anti-HBs and/or anti-HBc, although covalently closed circular DNA (cccDNA) may remain in hepatocyte nuclei.[3,18] With cccDNA in hepatocyte nuclei, a patient with severe immune suppression, such as seen with rituximab therapy or after stem cell transplant, may become serum HBsAg-positive again with HBV viremia.[19,20]

The presence of an isolated anti-HBc test result usually signifies infection with HBV in the past with subsequent loss of anti-HBs and occurs in 7% to 19% of patients with HIV infection.[21-25] Incidence of HBV viremia in patients with HIV infection and isolated anti-HBc ranges from 1% to 36%.[21,23,26-28] The clinical significance of isolated anti-HBc is unknown[21,25,28-30] but in individuals with HIV infection, it may indicate chronic or, more likely, resolved HBV infection.[24,31,32] In a low-prevalence country such as the United States, isolated anti-HBc may also represent a false-positive result.[24,31,33,34] Patients with HIV infection have a higher frequency of isolated anti-HBc, particularly those with underlying HCV coinfection.[24,35,36]

CAB/RPV Case 2

29yo cis-male diagnosed with HIV 2016. Baseline GRT: No significant DRMs (some polymorphisms/clinically insignificant substitutions --> no resistance predicted)

Started EVG/c/F/TAF and remained suppressed except for single VL = 41 copies/mL (late 2019) --> offered BIC/F/T and resuppressed; no GRT pursued

Fall 2021: Expressed interest in CAB/RPV and oral lead-in started 11/2/2021 --> seen 11/30/2021 for initiation injection

VL drawn at 1st injection = 137 c/mL

Most recent VL prior to transition 10/5/2021 was "*detected < 20*" (was on BIC/F/T then; no concern for gap prior to oral lead-in)

BMI 26.5 | Subtype B

What would you do?

December 2021: LLV at initiation dose LAI

29yo cisM diagnosed with HIV 2016. Baseline GRT: No significant DRMs (some polymorphisms/clinically insignificant substitutions --> no ARV resistance predicted)

Started EVG/c/F/TAF and remained suppressed except for single VL = 41 c/mL (late 2019) --> offered BIC/F/T and resuppressed; no GRT pursued

Fall 2021: Expressed interest in CAB/RPV and OLI started 11/2/2021 --> seen 11/30/2021 for IM initiation dose

VL drawn at 1st injection = 137 c/mL

Most recent VL prior to transition 10/5/2021 = detected < 20 (was on BIC/F/T then; no concern for gap prior to OLI)

BMI 26.5 | Subtype B

Was this person eligible for transition to CAB/RPV?

Would you have done anything different with transition to CAB/RPV?

Repeat VL came back < 20 c/mL

Possible explanation: pt did not consistently take RPV with food --> will proceed with next IM dose (~2wks)

FLAIR

Eligibility for the Maintenance Phase

- Participants with an undetectable HIV-1 RNA (<50 c/mL) at the Week (-4) visit are eligible to enter the Maintenance Phase.
- A single repeat HIV-1 RNA test to determine eligibility may be allowed ONLY after consultation with the medical monitor.
- Participants with HIV-1 RNA ≥400 c/mL at Week (-4) are not eligible to enter the Maintenance Phase, will not be allowed a repeat to determine eligibility, and will therefore be withdrawn from the study.

Result of HIV-1 RNA at Week (-4)	Action
<50 c/mL	Begin maintenance phase at day 1.
≥50 c/mL but <400 c/mL	Single repeat allowed only after consultation and approval from medical monitor.
Single repeat <50 c/mL	Begin maintenance phase at day 1.
Single repeat ≥50 c/mL	Cannot begin maintenance phase and must be withdrawn from study; complete withdrawal visit instead of day 1.
≥400 c/mL	Cannot begin maintenance phase and must be withdrawn from study; complete withdrawal visit instead of day 1.

Supplement to: Orkin C, Arasteh K, Górgolas Hernández-Mora M, et al. Long-acting cabotegravir and rilpivirine after oral induction for HIV-1 infection. N Engl J Med 2020;382:1124-35.

ATLAS

Exclusion Criteria

Deviations from exclusion criteria are not allowed because they can potentially jeopardize the scientific integrity of the study, regulatory acceptability, or participant safety. Therefore, adherence to the criteria as specified in the protocol is essential. A participant will not be eligible for inclusion in this study if any of the following criteria apply:

Exclusionary criteria prior to screening or day 1

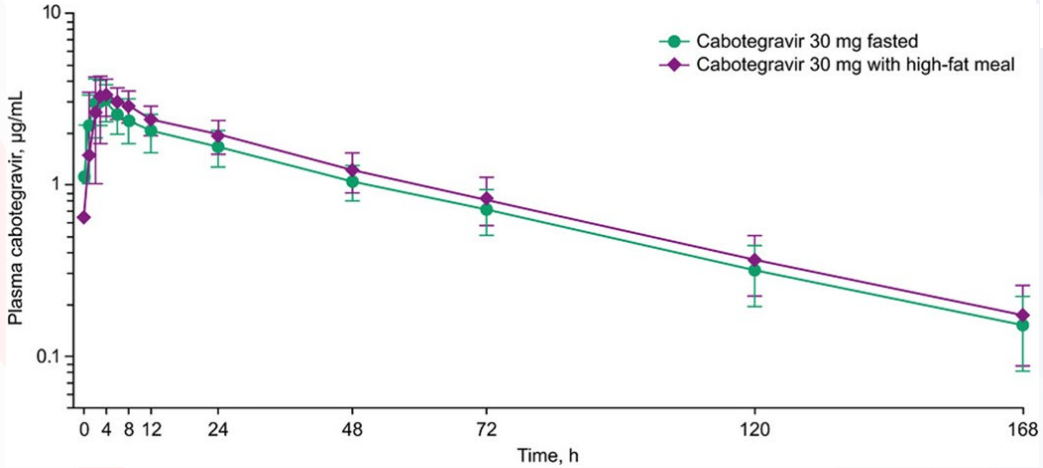
1. Within 6 months prior to screening and after confirmed suppression to <50 copies/mL on current ART regimen, any plasma HIV-1 RNA measurement ≥50 copies/mL.
2. Within the 6- to 12-month window prior to screening and after confirmed suppression to <50 copies/mL, any plasma HIV-1 RNA measurement >200 copies/mL, or two or more plasma HIV-1 RNA measurements ≥50 copies/mL.
3. Any drug holiday during the window between initiating first HIV ART and 6 months prior to screening, except for brief periods (less than 1 month) where all ART was stopped due to tolerability and/or safety concerns.
4. Any switch to a second-line regimen, defined as change of a single drug or multiple drugs simultaneously, due to virologic failure to therapy (defined as a confirmed plasma HIV-1 RNA

Supplement to: Swindells S, Andrade-Villanueva J-F, Richmond GJ, et al. Long-acting cabotegravir and rilpivirine for maintenance of HIV-1 suppression. N Engl J Med 2020;382:1112-23.

Clinical Trial > Clin Pharmacol Drug Dev. 2019 May;8(4):443-448. doi: 10.1002/cpdd.620. Epub 2018 Sep 19.

Effect of a High-Fat Meal on the Pharmacokinetics of the HIV Integrase Inhibitor Cabotegravir

Parul Patel [1], Susan L Ford [2], Yu Lou [3], Kalpana Bakshi [4], Allan R Tenorio [1], Zhiping Zhang [3], Rennan Pan [4], William Spreen [1]



Clinical Trial > J Clin Pharmacol. 2013 Aug;53(8):834-40. doi: 10.1002/jcph.107. Epub 2013 May 30.

Impact of food and different meal types on the pharmacokinetics of rilpivirine

Herta M Crauwels [1], Rolf P G van Heeswijk, Annemie Buelens, Marita Stevens, Katia Boven, Richard M W Hoetelmans

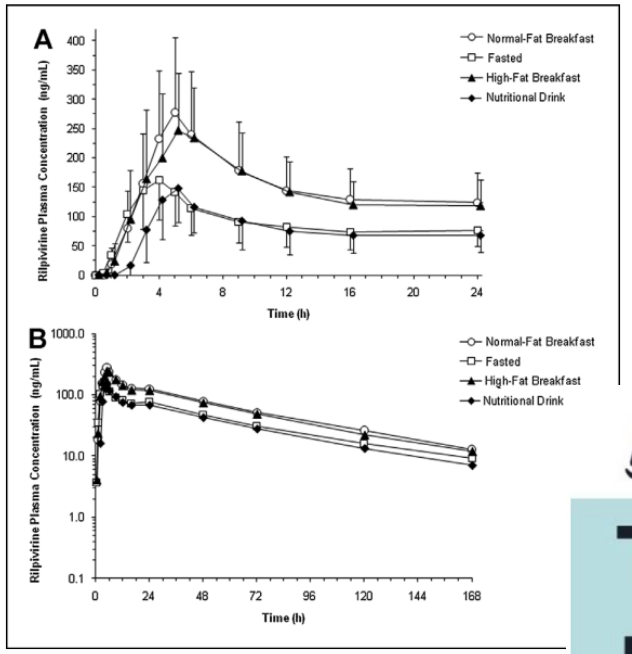


Figure 1. Mean (standard deviation) plasma concentration profiles of rilpivirine administered with a normal-fat breakfast, fasting conditions, with a high-fat breakfast, and with a protein-rich drink. Panel A shows profiles up to 24 hours after dosing (linear scale); Panel B shows profiles across entire sampling period of 168 hours (log scale).

Don't forget to

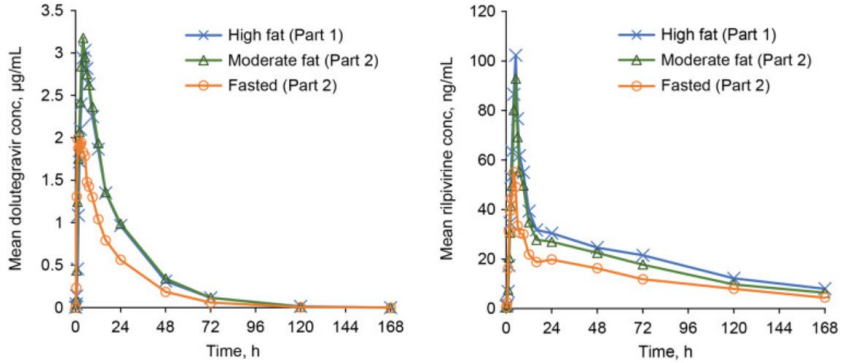
THANK A PHARMACIST

Clin Pharmacol. 2020 Jun 8;12:49-52. doi: 10.2147/CPAA.S250751. eCollection 2020.

The Effect of Moderate- and High-Fat Meals on the Bioavailability of Dolutegravir/Rilpivirine Fixed-Dose Combination Tablet

Rashmi Mehta [1], Joseph Piscitelli [2], Allen Wolstenholme [3], Caifeng Fu [4], Herta Crauwels [5], Brian Wynne [6], Kimberly Adkison [7]

Figure 1



Mean plasma concentration–time profile of dolutegravir (left) and rilpivirine (right) following a single oral dose of dolutegravir/rilpivirine fixed-dose combination tablet (Formulation AM) in healthy subjects.

Don't forget to

THANK A PHARMACIST

CAB/RPV Case 3

23yo cis-male diagnosed with HIV 12/2020, then referred to caller

Baseline: CD4 59 (5%) cells/mm^3; VL 46,400 copies/mL

GRT: pan-sensitive - V245E

Initiated BIC/F/T, and follow-up VL = 50 copies/mL after 1 month

Visit 3/25/2021 (telehealth) --> ordered labs, VL = undetectable

Early 6/2021 (in-person) --> ordered labs, but pt did not get them drawn

CAB/RPV Case 3 (cont'd)

Oral lead-in started shortly thereafter and patient next seen 7/9/2021 for 1st injection

Rec'd maintenance injections on time early Aug, Sept, Oct

VL drawn 10/4/2021 = 70 copies/mL

Rec'd subsequent maintenance injections on time Nov, Dec, Jan

VL drawn 2/1/2022 up to 890 copies/mL --> repeat 2/8/2022: 450 copies/mL **(lab auto-cancelled GRT)**

However, by 2/22/2022 VL up to 1600, with GRT showing K101E, L74M, E138E/K, G140S, Q148R

BMI 33 (1.5" needle used for all doses) | Subtype B

Drug resistance interpretation: RT

NRTI Mutations:	None
NNRTI Mutations:	K101E
RT Other Mutations:	None

Nucleoside Reverse Transcriptase Inhibitors	
abacavir (ABC)	Susceptible
zidovudine (AZT)	Susceptible
emtricitabine (FTC)	Susceptible
lamivudine (3TC)	Susceptible
tenofovir (TDF)	Susceptible

Non-nucleoside Reverse Transcriptase Inhibitors	
doravirine (DOR)	Low-Level Resistance
efavirenz (EFV)	Low-Level Resistance
etravirine (ETR)	Low-Level Resistance
nevirapine (NVP)	Intermediate Resistance
rilpivirine (RPV)	Intermediate Resistance

https://hivdb.stanford.edu/hivdb/by-patterns/

Drug resistance interpretation: IN

INSTI Major Mutations:	E138EK · G140S · Q148R
INSTI Accessory Mutations:	None
IN Other Mutations:	L74M

Integrase Strand Transfer Inhibitors	
bictegravir (BIC)	High-Level Resistance
cabotegravir (CAB)	High-Level Resistance
dolutegravir (DTG)	High-Level Resistance
elvitegravir (EVG)	High-Level Resistance
raltegravir (RAL)	High-Level Resistance

What would you do?

March 2022: LLV during maintenance LAI

23yo cisM diagnosed with HIV 12/2020, then referred to caller

Baseline: CD4 59 (5%) cells/mm^3; VL 46,400 c/mL | GRT: pan-sensitive - V245E

Initiated BIC/F/T, and follow-up VL = 50 c/mL after 1 month
Visit 3/25/2021 (telehealth) --> ordered labs, VL = UD
Early 6/2021 (in-person) --> ordered labs, but pt did not get them drawn

OLI started shortly thereafter, pt next seen 7/9/2021 for 1st IM dose
Rec'd maintenance injections on time early Aug, Sept, Oct
VL drawn 10/4/2021 = 70 c/mL --> Rec'd maintenance injections Nov, Dec, Jan

2/1/2022 VL = 890 --> 2/8/2022 VL down to 450 (lab auto-cancelled GRT)

2/22/2022 VL = 1600, with GRT showing K101E, L74M, E138E/K, G140S, Q148R

BMI 33 (1.5" needle used for all doses) | Subtype B

Was this person eligible for transition to CAB/RPV?

Would you have done anything different with CAB/RPV management?

AIDS. 2021 Jul 15;35(9):1333-1342. doi: 10.1097/QAD.0000000000002883.

Exploring predictors of HIV-1 virologic failure to long-acting cabotegravir and rilpivirine: a multivariable analysis

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Table 3

Week 48 outcomes by presence of key baseline factors of rilpivirine resistance-associated mutation(s), HIV-1 subtype A6/A1 and BMI at least 30 kg/m^2.

Baseline factors	Virologic success[a] *n* (%)	CVF[b] *n* (%)
None of the three factors	694/732 (94.8)	3/732 (0.41)
Any one of the three baseline factors	261/272 (96.0)	1/272 (0.37)
HIV-1 subtype A6/A1 alone	90/95 (94.7)	1/95 (1.1)
BMI ≥30 kg/m^2 alone	147/153 (96.1)	0/153 (0)
RPV RAM(s) alone	24/24 (100)	0/24 (0)
At least two of the three baseline factors	25/35 (71.4)	9/35 (25.7)
RPV RAM(s) + HIV-1 subtype A6/A1	2/3 (66.7)	1/3 (33.3)
RPV RAM(s) + BMI ≥30 kg/m^2	7/10 (70.0)	3/10 (30.0)
HIV-1 subtype A6/A1 + BMI ≥30 kg/m^2	16/21 (76.2)	4/21 (19.0)
All three baseline factors	0/1 (0)	1/1 (100)
TOTAL	980/1039 (94.3)	13/1039 (1.25)
[95% CI (exact method)]	(92.74–95.65)	(0.67–2.13)

CI, confidence interval; CVF, confirmed virologic failure; RAM, resistance-associated mutation; RPV, rilpivirine.

[a]Based on the FDA Snapshot algorithm of HIV-1 RNA <50 copies/ml.

[b]Defined as two consecutive measurements of HIV-1 RNA ≥200 copies/ml.

Possible explanations?

March 2022: LLV during maintenance LAI

23yo cisM diagnosed with HIV 12/2020, then referred to caller

Baseline: CD4 59 (5%) cells/mm^3; VL 46,400 c/mL | GRT: pan-sensitive - V245E

Initiated BIC/F/T, and follow-up VL = 50 c/mL after 1 month
Visit 3/25/2021 (telehealth) --> ordered labs, VL = UD
Early 6/2021 (in-person) --> ordered labs, but pt did not get them drawn

OLI started shortly thereafter, pt next seen 7/9/2021 for 1st IM dose
Rec'd maintenance injections on time early Aug, Sept, Oct
VL drawn 10/4/2021 = 70 c/mL --> Rec'd maintenance injections Nov, Dec, Jan

2/1/2022 VL = 890 --> 2/8/2022 VL down to 450 (lab auto-cancelled GRT)

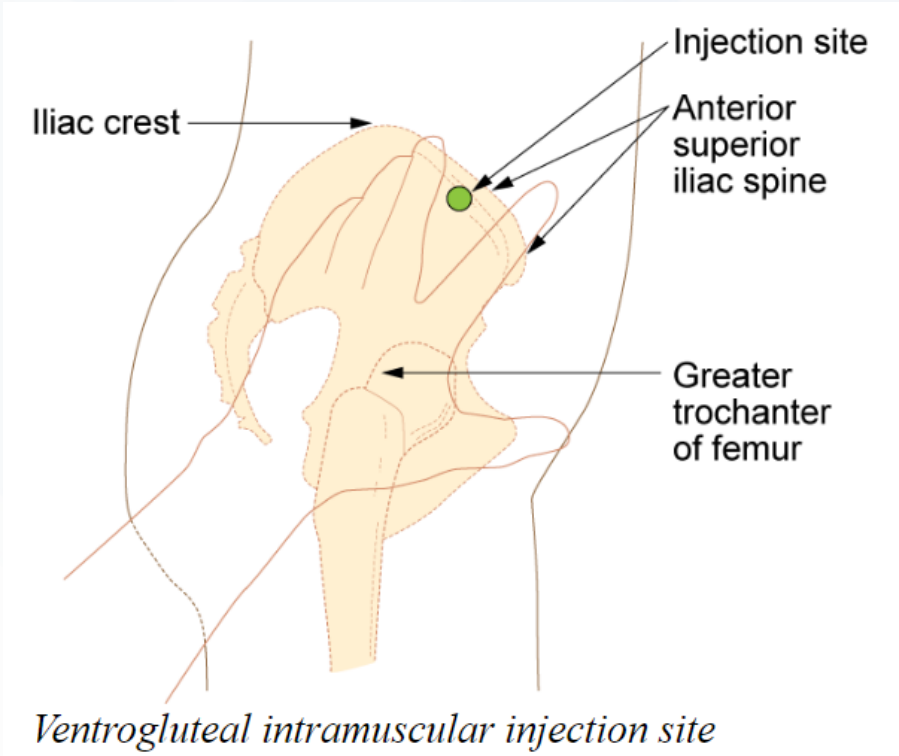
2/22/2022 VL = 1600, with GRT showing K101E, L74M, E138E/K, G140S, Q148R

BMI 33 (1.5" needle used for all doses) | Subtype B

Archived RAMs?

2" needle?

Other thoughts?



Ventrogluteal intramuscular injection site

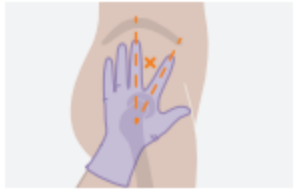
https://opentextbc.ca/clinicalskills/chapter/6-8-iv-push-medications-and-saline-lock-flush/

https://assets.gskstatic.com/pharma/us/viiv/Cabenuva-Dosing-Administration-Guide.pdf

Instructions for use: Injection

e 2022

12 Prepare the injection site[2]



- Injections must be administered to the gluteal sites
- Select from the following areas for the injection:
  - Ventrogluteal, as shown (recommended) or dorsogluteal (upper outer quadrant)

Note: For gluteal intramuscular use only.

Do not inject intravenously.

13 Remove the cap[2]

- Fold the needle guard away from the needle
- Pull off the injection needle cap

14 Remove extra liquid from the syringe[2]

- Hold the syringe with the needle pointing up
- Press the plunger to the appropriate volume to remove extra liquid and any air bubbles

Note: Clean the injection site with an alcohol wipe. Allow the skin to air dry before continuing.

Figure 14 represents a 2-mL continuation injection. A 3-mL initiation injection is also available.

15 Stretch the skin[2]

- Use the z-track injection technique to minimize medicine leakage from the injection site
- Firmly drag the skin covering the injection site, displacing it by about an inch (2.5 cm)
- Keep it held in this position for the injection

16 Insert the needle[2]

- Insert the needle to its full depth, or deep enough to reach the muscle

17 Inject the dose of medicine[2]

- Still holding the skin stretched—slowly press the plunger all the way down
- Ensure the syringe is empty
- Withdraw the needle and release the stretched skin immediately

International AIDS Conference 2022

Pharmacokinetics and Tolerability of Cabotegravir and Rilpivirine Long-Acting Intramuscular Injections to the Vastus Lateralis (Lateral Thigh) Muscles of Healthy Adult Participants

AIDS 2022 July 29 - Aug 1 Montreal

Kelong Han1, Jafar Sadik Shaik1, Herta Crauwels2, Claudia Leemereise3, Gilda Bontempo4, Beta Win5, Ciara Seal1, Rebecca DeMoor1, Ojesh Upadhyay1, Vasiliki Chounta6, William R. Spreen4, Susan L. Ford7
1GlaxoSmithKline, Collegeville, PA, United States; 2Janssen Research & Development, Beerse, Belgium; 3GlaxoSmithKline, Amersfoort, the Netherlands; 4ViiV Healthcare, Research Triangle Park, NC, United States; 5GlaxoSmithKline, Stevenage, United Kingdom; 6ViiV Healthcare, Brentford, United Kingdom; 7GlaxoSmithKline, Research Triangle Park, NC, United States.

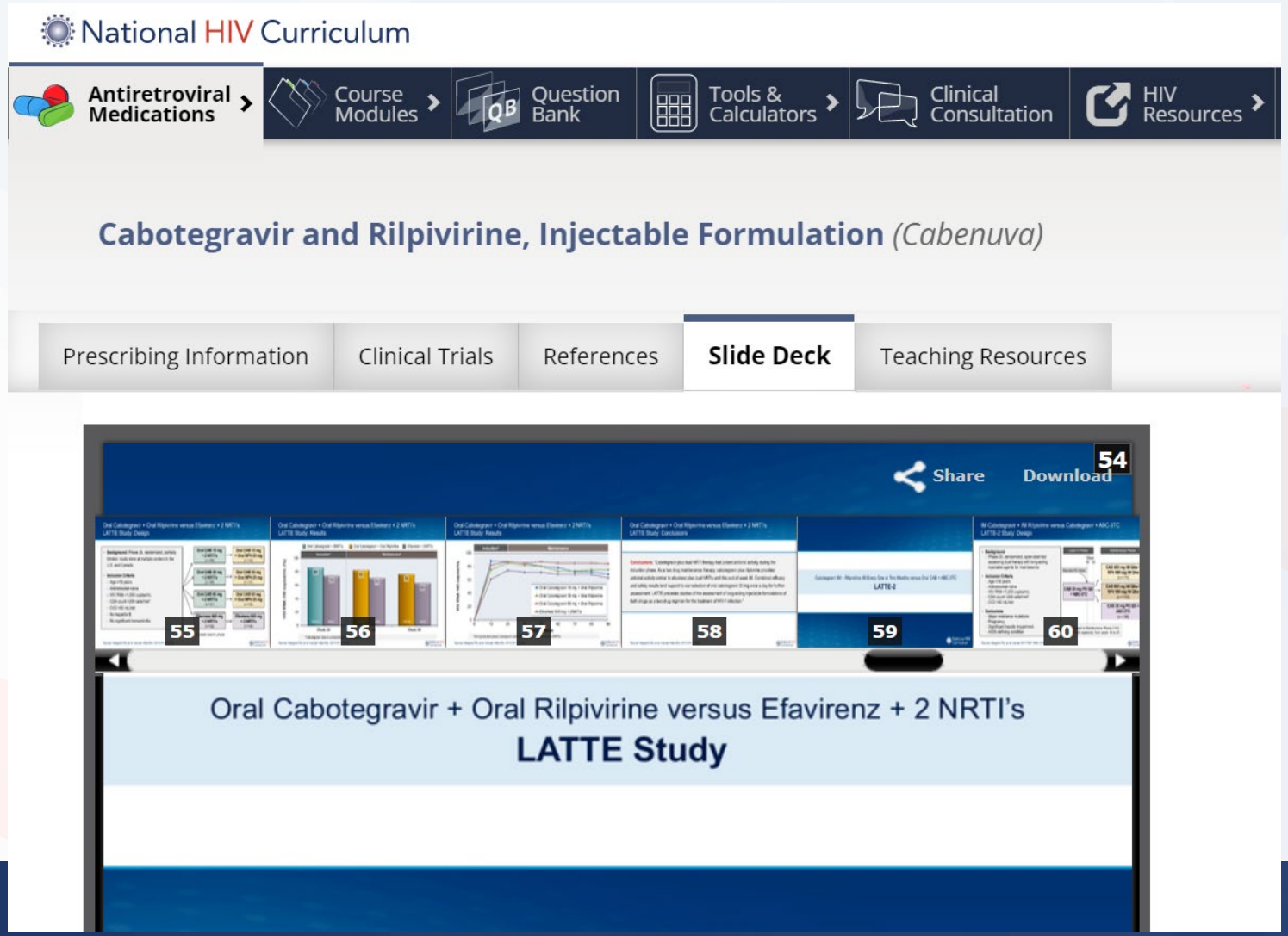
- **CAB and RPV IM injections into lateral thigh muscle were well tolerated, with mostly mild-to-moderate injection site reactions (ISRs), and showed plasma PK profiles that support further evaluation of thigh IM injections in target populations.**

Conclusions

- CAB and RPV IM injections into lateral thigh muscle resulted in plasma PK profiles that support further evaluation of thigh IM injections in target populations.
- The safety and tolerability profiles of CAB and RPV LA IM injections to the *lateral thigh* muscle were acceptable, with most ISRs reported as mild to moderate in severity.

Program number EPB176 (abs # 9906)

New CAB/RPV content from the National HIV Curriculum



THANK YOU! Questions?

For more information about the NCCC please visit: nccc.ucsf.edu

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Translating science into care

The National Clinician Consultation Center is a free telephone advice service for clinicians, by clinicians. Go to **nccc.ucsf.edu** for more information.

HIV/AIDS Warmline **800-933-3413**	HIV treatment, ARV management, complications, and co-morbidities
Perinatal HIV Hotline **888-448-8765**	Pregnancy, breastfeeding and HIV
Hepatitis C Warmline **844-HEP-INFO/** **844-437-4636**	HCV testing, staging, monitoring, treatment
Substance Use Warmline **855-300-3595**	Substance use evaluation and management
PrEPline **855-HIV-PrEP**	HIV Pre-exposure prophylaxis
PEPline **888-448-4911**	Occupational & non-occupational exposure management

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AETC Program National Centers and HIV Curriculum

- **National Coordinating Resource Center –** serves as the central web –based repository for AETC Program training and capacity building resources; its website includes a free virtual library with training and technical assistance materials, a program directory, and a calendar of trainings and other events. Learn more: https://aidsetc.org/
- **National Clinician Consultation Center –** provides free, peer-to-peer, expert advice for health professionals on HIV prevention, care, and treatment and related topics. Learn more: https://nccc/ucsf.edu
- **National HIV Curriculum –** provides ongoing, up –to-date HIV training and information for health professionals through a free, web –based curriculum; also provides free CME credits, CNE contact hours, CE contact hours, and maintenance of certification credits. Learn more: www.hiv.uw.edu