In It for the Long Haul: Perspectives on Long-Acting Injectable Treatment for HIV

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- *This program is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) under grant number U1OHA30535 as part of an award totaling $4.2m. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by HRSA, HHS, or the U.S. Government. For more information, please visit HRSA.gov.*

- *"Funding for this presentation was made possible by cooperative agreement U1OHA30535 from the Health Resources and Services Administration HIV/AIDS Bureau. The views expressed do not necessarily reflect the official policies of the Department of Health and Human Services nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government. Any trade/brand names for products mentioned during this presentation are for training and identification purposes only."*

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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

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Learning Outcomes

- By the end of this session, participants will be able to:
  - Summarize the pharmacologic action and effectiveness of long-acting injectable (LAI) cabotegravir/rilpivirine (CAB/RPV) for HIV treatment
  - List at least three important patient criteria to consider when assessing appropriateness of HIV treatment with LAI CAB/RPV
  - Explain the administration process, dosing schedule, and monitoring schedule for LAI CAB/RPV
  - List positive and negative patient experiences with using LAI CAB/RPV for HIV treatment

Who is Here Today?

- In what state are you located?
- Do you work in a clinical or non-clinical setting?
- If clinical, what is your role?
- On a scale of 1-10, how much do you already know about LAI CAB/RPV?

How Long is “Long-Acting”?

- Per US DHHS HIV treatment guidelines, the term LA (long-acting) refers to any ARV that is dosed once weekly or less frequently
- Achieving LA dosing requires:
  - unique longer pharmacokinetics (such as a long half-life) OR
  - altered formulations that last longer (such as nanoparticles) OR
  - a delivery method or device that achieves sustained delivery (such as vaginal rings or subcutaneous implants)

LAI Cabotegravir/rilpivirine (CAB/RPV) Approvals Timeline

- Jan 2021: FDA approved CAB/RPV, an INSTI/NNRTI combo, as a once-monthly IM injection with a *recommended* one month daily oral lead-in phase
  - 600mg CAB/900mg RPV initiation injection
  - 400mg CAB/600mg RPV continuation injections monthly
- Feb 2022: FDA approval updated to bimonthly dosing
  - Two 600mg CAB/900mg RPV initiation injections one month apart
  - 600mg CAB/900mg RPV continuation injections bimonthly

https://www.fda.gov/drugs/human-immunodeficiency-virus-hiv/fda-approves-cabenuva-and-vocabria-treatment-hiv-1-infection

Quick Real-Life Check

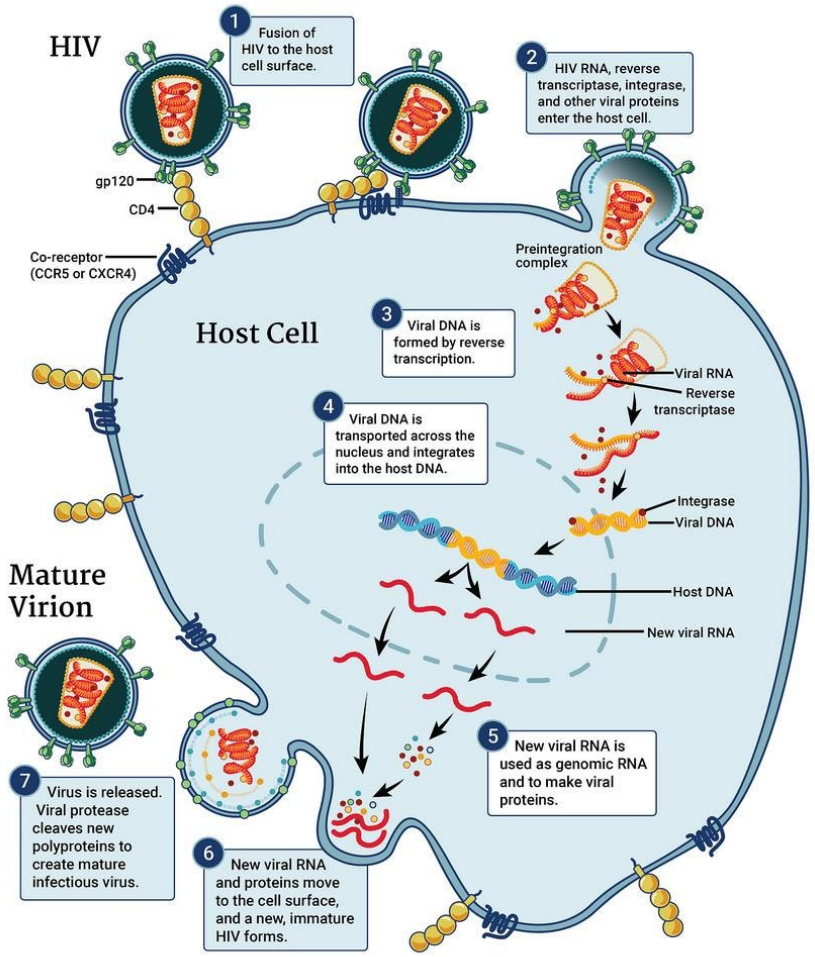
- If you work in a clinical setting and have patients using LAI CAB/RPV, what percentage of patients at your clinic utilize the 30 day oral-lead in before starting injections?

Current DHHS Treatment Guidelines for CAB/RPV

- "A long-acting ARV regimen of injectable cabotegravir (CAB) and rilpivirine (RPV) given every 1 or 2 months is an optimization option for patients who are engaged with their health care, virologically suppressed on oral therapy for 3 to 6 months, and who agree to make the frequent clinic visits needed to receive the injectable drugs " (AI)
- "Long-acting injectable CAB plus RPV is indicated in individuals with sustained (e.g., 3 to 6 months) virologic suppression (HIV-1 RNA <50 copies/mL) on a stable ARV regimen, with *no history of treatment failure*, and with *no known or suspected resistance to either CAB or RPV*."

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. 2023. Available at https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv. Accessed May 23, 2024.

CAB/RPV Mechanisms



- Cabotegravir – integrase inhibitor (INSTI)
- Rilpivirine – non-nucleotide reverse transcriptase inhibitor (NNRTI)

https://www.niaid.nih.gov/diseases-conditions/hiv-replication-cycle

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FLAIR and ATLAS – Phase 3 Trials for LAI CAB/RPV

- FLAIR – **treatment-naïve** subjects were suppressed on a dolutegravir-based regimen for 20 weeks, then randomized to monthly LAI CAB/RPV or left on their original ART
- ATLAS – **ART-experienced**, virologically suppressed subjects were randomized to monthly LAI CAB/RPV or left on their current ART
- Both trials followed subjects for 48 weeks
- In both trials, the proportion of subjects with VL > 50 copies/mL was between 1-2%, with no significant difference between groups

https://www.fda.gov/drugs/human-immunodeficiency-virus-hiv/fda-approves-cabenuva-and-vocabria-treatment-hiv-1-infection

Patient Criteria to Consider Ahead of LAI CAB/RPV

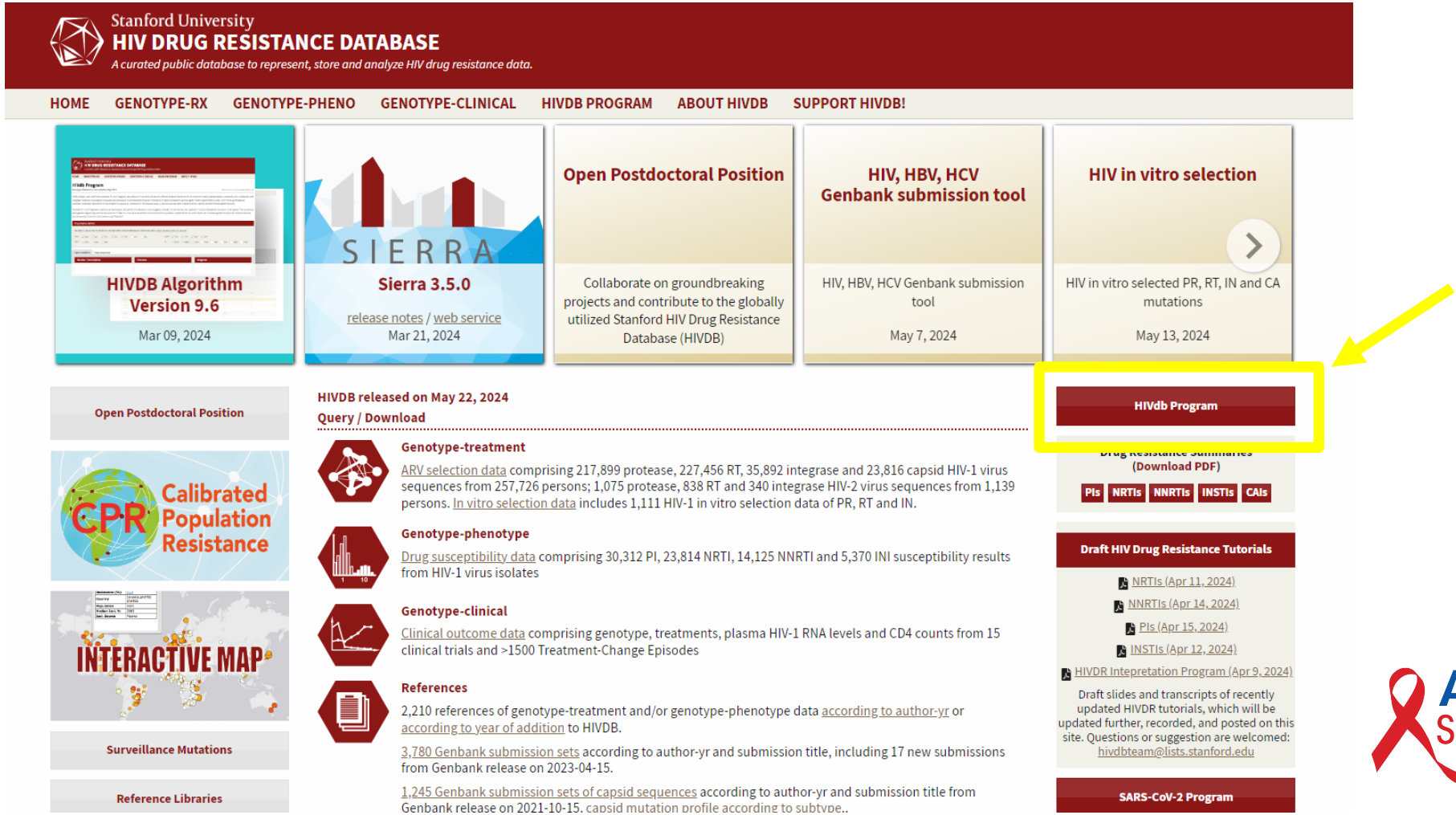
- Direct Clinical Factors
  - Pre-treatment genotype
  - History of ART adherence
  - Any known viral resistance
  - Recent VLs
  - Allergies to either CAB or RPV
  - Drug-drug interactions
  - Age (must be > 12 yo)
  - Weight (must be >/= 35 kg)
- Non-Clinical Factors
  - Patient preference for LAI
  - Patient's ability to come to clinic monthly/bimonthly
  - Acceptance of bilateral gluteal injections
  - Access to CAB/RPV - $$$

This can be a long discussion and research process!

Viral Resistance

- Due diligence to gather all existing genotypes, an accurate ART history, and all available viral load results is needed
- Transmitted drug resistance (TDR) may be as high as 14%
- NNRTIs are the most common class for TDR
- Consider additional tools to confirm viral susceptibility to CAB/RPV past the initial genotype interpretation

Stanford's HIV Drug Resistance Database: https://hivdb.stanford.edu/



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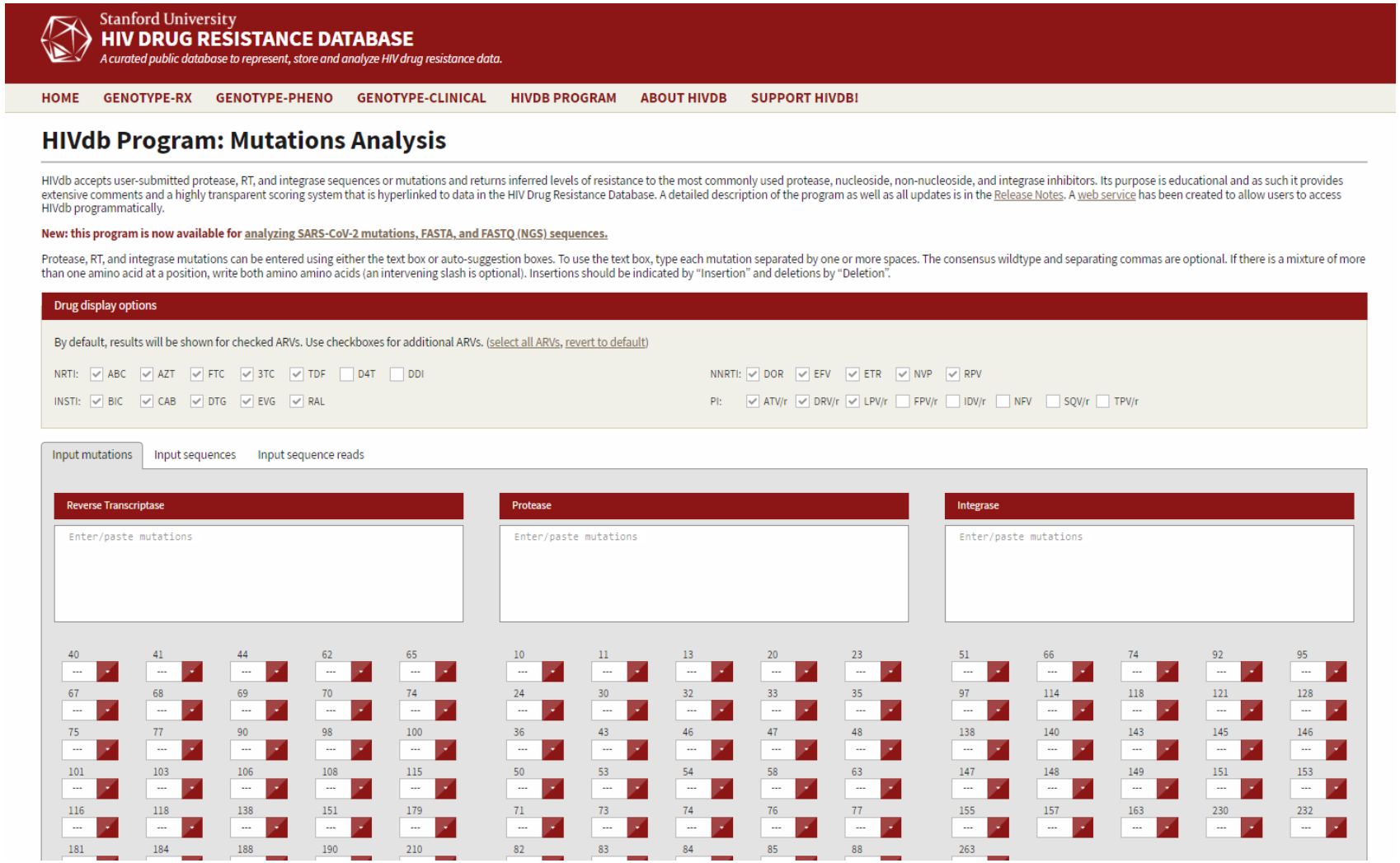
Mutations Analysis Tool



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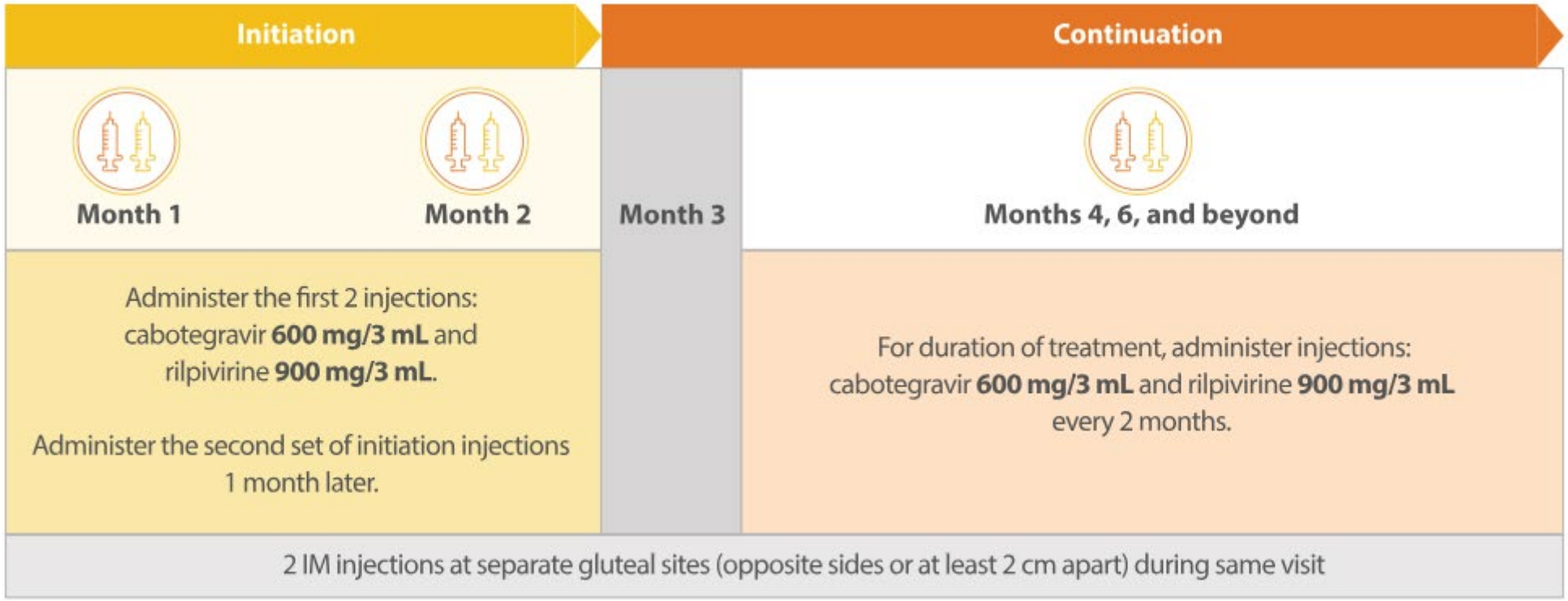
Obtaining LAI CAB/RPV for Patients

- Multiple options to obtain the medication, depending on insurance coverage
- LAI CAB/RPV may be covered under pharmacy or medical benefits
- Ordering through a specialty pharmacy for delivery to the clinic is common
  - Patients come to clinic for injections by clinic staff
- Alternative Sites for Administration (ASAs)
- Good resources exist for help with prior authorizations and copay support for patients

LAI CAB/RPV Every Other Month Dosing Schedule



Initiate injections on the last day of current oral ART or the oral lead-in if used

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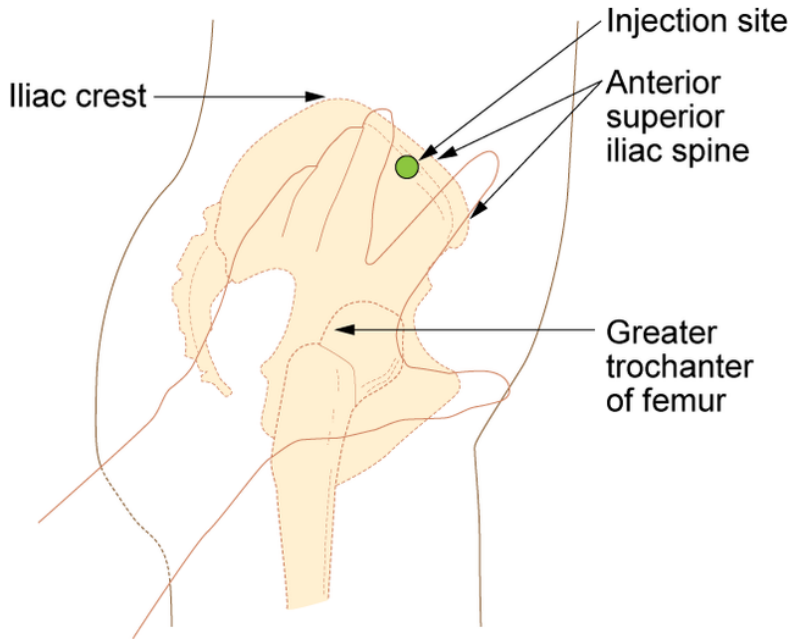
What About Missed Injections?

- Ideally, injections will be given the same date every other month
- When necessary, a +/- 7 day window is acceptable – the “dosing window”
- After an adjusted injection within the dosing window, return to the target date
- For missed injections > 7 days but < 30 days, resume q2 month injections
- For missed injections > 30 days, restart with two injections one month apart, then resume q2 month injections

LAI CAB/RPV Administration

- The package labeling recommends two intramuscular ventrogluteal injections (on opposite sides or >/= 2 cm apart) during the same visit.
- The ventrogluteal site is recommended and a longer needle length (not included in the dosing kit) may be required for patients with higher BMI.
- Kits are stored in the refrigerator
- Allow vials to sit at room temperature at least 15 minutes, for up to six hours
- Shake vials to create a uniform suspension
- Inject within two hours of pulling into syringes



https://commons.wikimedia.org

Monitoring Once Started on LAI CAB/RPV

- Because this is currently approved for switch therapy, no change in frequency of viral load monitoring is required
  - Some providers may prefer checking viral loads q3-4 months for a period of time, while patient is new to LAI CAB/RPV
- In patients with severe renal impairment, monitor more closely for adverse events
- Hepatotoxicity is possible – monitor LFTs periodically
- Injection site reactions (ISRs) are the most common adverse reaction

What Do Patients Think?

- Long-term studies and anecdotal evidence from clinicians demonstrate overall tolerability and satisfaction of LAI CAB/RPV
- Few cases of patients choosing to switch back to oral ART
- But let's hear from an expert on the patient experience!

On the Horizon…

Now, the IAS-USA guidelines panel has issued updated recommendations for use of LA CAB/RPV in PLWHIV **without virologic suppression** who meet the following additional criteria:

- Inability to take oral ART consistently despite optimal clinical support
- High risk for HIV disease progression (CD4 <200 cells/µL or history of AIDS-defining illness)
- No known resistance mutations to CAB or RPV
- Access to intensive clinical follow-up and case management

Sax PE et al. Updated treatment recommendation on use of cabotegravir and rilpivirine for people with HIV from the IAS-USA Guidelines Panel. *JAMA* 2024 Mar 1; [e-pub]. (https://doi.org/10.1001/jama.2024.2985.)

Thank You!

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