ID Week 2024: Updates on Long Acting Injectables

Jehan Budak, MD
Assistant Professor
Division of Infectious Diseases
University of Washington

Last Updated: 7 Nov 2024

Disclaimer

Funding for this presentation was made possible by U1OHA29296 from the Human 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.

AETC AIDS Education & Training Center Program Mountain West

Disclosures

No conflicts of interest or relationships to disclose.

Outline

1. LAI CAB-RPV Failures

2. Outcomes from people with adherence difficulties

3. LAI CAB-RPV + LEN

MWAETC

LAI CAB-RPV Failures at Henry Ford Health

MWAETC

Background

- ATLAS, FLAIR, and ATLAS-2M studies demonstrated efficacy of LAI CAB-RPV and led to FDA approval for those with viral suppression (VS)[1,2]

- Virologic failures (VF) in ATLAS-2M occurred at a rate of 2.3% q8w vs 0.4% q4w[2]

- Although virologic failure was rare, when VF occurred, it was accompanied by NNRTI-R and INSTI-R[2]

1-Orkin C et al, NEJM, 2020. 2-Overton ET et al, CID, 2023

MWAETC

Method

- Retrospective cohort study August 2021 to March 2023

- PWH ≥ 18 years at Henry Ford Health
  - Suppressed on ART for ≥ 6 months with
  - 12-month VLs available after starting LAI CAB-RPV

- Outcomes
  - Virologic Failure – HIV RNA ≥ 30 copies/mL on 2 occasions 4 weeks apart
  - CAB-RPV Failure – Regimen stopped after ≥ 1 dose

Results

- 58 PWH started CAB-RPV
  - 49/50 had virologic data at 12 months and achieved viral suppression

- Clinical Characteristics
  - Mostly middle-age Black men
  - 52% had a BMI ≥ 30 and specifically, 21% had BMI ≥ 35
  - Mean number of years with HIV: 17

- 5 individuals discontinued LAI CAB-RPV
  - 2 due to injection site reactions (ISR)
  - 3 due to virologic failure

Yared N et al, ID Week 2024.

MWAETC

Results: RAMs in Individuals with Virologic Failure

Table 2. NNRTI and INSTI DRMs in Patients Experiencing VF on CAR

Patient	Pre-Treatment GTs*		Post-Treatment GTs*	
	NNRTI DRMs	INSTI DRMs	NNRTI DRMs	INSTI DRMs
1	Not performed	Not performed	8/28/23 GT E138K (8.5%), M230I 12/22/23 GT E138 E/K M230L	8/28/23 GT E92K Q146R 12/22/23 GT None
2	Not performed	Not performed	1/26/23 GT Y188L V106I	1/26/23 GT E138K Q148K
3	None	G140R (1.2%)	6/13/23 GT E138K	6/13/23 GT Q148R

What do these RAMs mean?

NNRTI	INSTI
1 – RPV score 75	1 – minimal decrease to CAB
2 – RPV score 65	2 – CAB score 75, BIC/DTG score 50
3– RPV score 45	3– CAB score 60, BIC/DTG score 25

Yared N et al, ID Week 2024.

MWAETC

Summary: Abstract #1

- In a retrospective cohort at Henry Ford Health of 58 virally suppressed PWH starting LAI CAB-RPV, 49 had viral suppression at 12 months
  - 5/58 (8.6%) had discontinued LAI CAB-RPV

- Of those who discontinued treatment, 3 had virologic failure with treatment emergent resistance and high level NNRTI and INSTI RAMs
  - One patient developed VF with a pre-existing G140R despite on-time injections

An aside on the G140R: Per Stanford Resistance Database, a nonpolymorphic mutation that can reduce CAB susceptibility up to 7-fold (CAB score 60)

Yared N et al, ID Week 2024.

MWAETC

Outcomes from the Owen Clinic in PWH with Adherence Difficulties

Background

- Adherence to a daily, lifelong medication is difficult
  - At least 50% of individuals with HIV in the US have adherence difficulties[1]

- LATITUDE Study (first clinical trial in persons with adherence difficulties) showed LAI CAB-RPV q4w was superior to oral standard of care, leading the DSMB to halt randomization and offer switch to LAI CAB-RPV to all patients[2]

- ART Guidelines (IAS-USA and HHS) updated to reflect this
  - [HHS] “Panel recommends the use of LA CAB/RPV on a case-by-case basis in select individuals with persistent virologic failure despite intensive adherence support on oral ART, who have no evidence of resistance to CAB or RPV, and with shared decision-making between providers and people with HIV (CIII).”

1-Benson C et al, AIDS Behav, 2020. 2-Rana AI et al, CROI 2024 #212. 3-HHS ART Guideline Update, September 2024.

MWAETC

Method

- Retrospective observational study at the Owen Clinic in San Diego of 63 PWH with adherence challenges started on LAI CAB-RPV November 2021-September 2023

- Adherence challenges defined as HIV RNA ≥ 200 copies/mL in prior 12 months AND
  - Poor response to oral ART
  - Loss to follow up

- Outcome
  - Discontinuation or
  - Virologic Failure

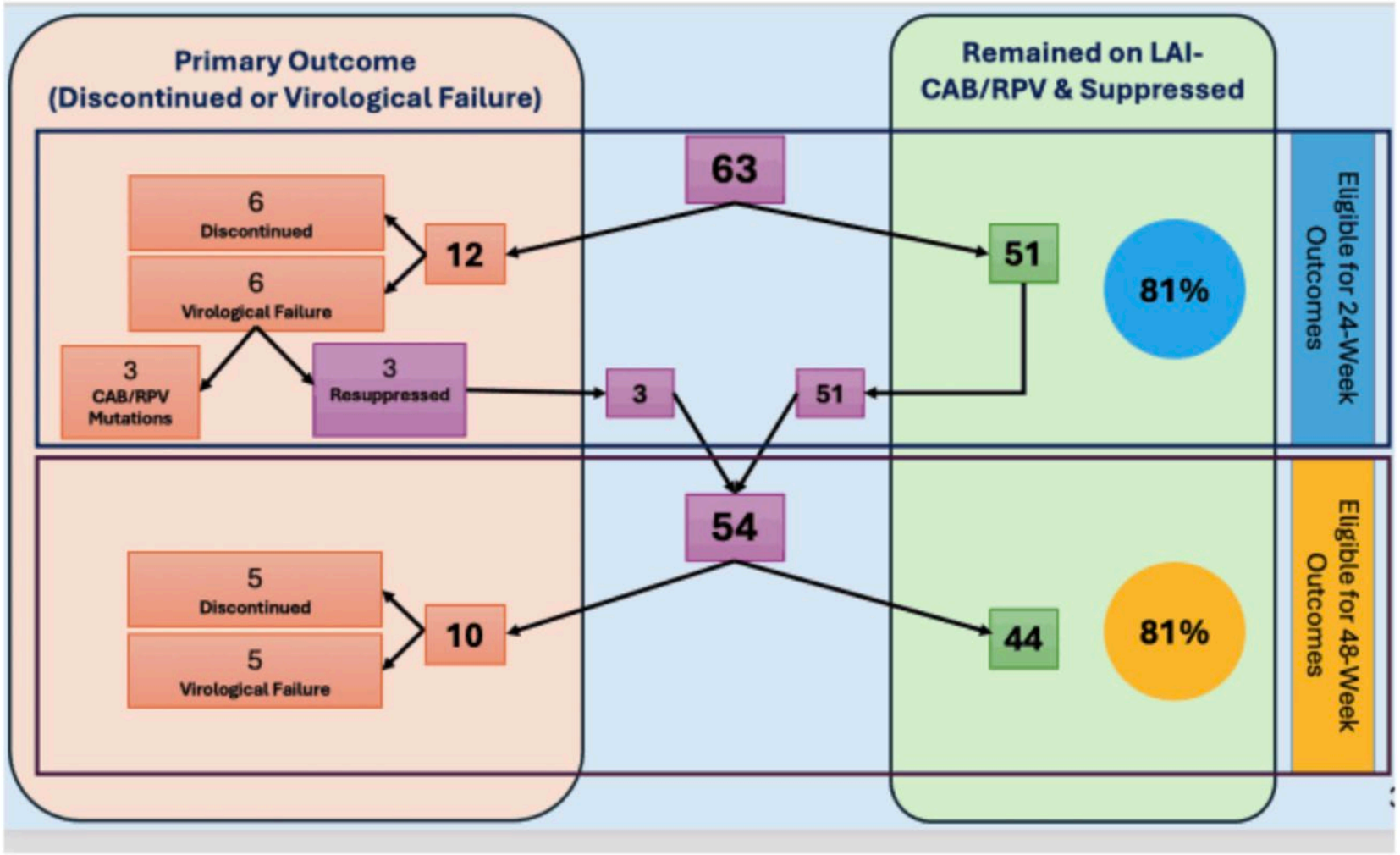
Results: Clinical Characteristics

- Of 63 PWH eligible for 24w outcomes & 54 eligible for 48w outcomes
  - Mostly middle-age White men
  - Social History
    - ~40% with any IDU history
    - ~40% with active substance use (predominantly methamphetamines)
    - 57% with any neuropsychiatric disorder
  - Insurance status
    - 65% with Medicaid
  - HIV History
    - Median years since HIV diagnosis: 13-14
    - ~40% with VL ≥ 50 copies/mL at initiation
    - 11% with VL ≥ 10,000 copies/mL

Hastie E et al, ID Week 2024.

MWAETC

Results cont.



Hastie E et al, ID Week 2024.

Results: Outcomes

- Logistics
  - ~14% with oral lead in
  - ~95% on q8w injections
  - ~15% with late injections
- Outcomes of 63 PWH
  - At 24w, 51 still on therapy with VS & at 48w, 44 still on therapy with VS
  - In total, 19 people at the end of therapy either stopped or had VF
    - 8 total with VF
    - 11 total with discontinuation
      - Of the 6 who stopped by 24w: 3 LTFU, 2 due to patient preference, 1 unrelated death
- In multiple logistic regression, two patient characteristics were associated with failure
  - Low baseline CD4 count
  - Substance use

Hastie E et al, ID Week 2024.

MWAETC

Summary: Abstract #2

- In a retrospective cohort at the Owen Clinic of 63 PWH with adherence challenges, a majority of PWH maintained VS 48w after starting LAI CAB-RPV
- Only low baseline CD4 and active substance use were associated with LAI CAB-RPV failure
- Nine individuals had virologic failure, and 11 individuals discontinued therapy

Hastie E et al, ID Week 2024.

MWAETC

LAI CAB-RPV + LEN in Mississippi

MWAETC

Background

- Lenacapavir (LEN) is a capsid inhibitor administered subcutaneously every 6 months for MDR HIV, informed by the CAPELLA Study[1]

- CAPELLA 156 Week Data: LEN, when combined with an optimized background regimen (OBR), led to high and sustained VS in heavily treatment experienced PWH[2]

- A case series of 34 patients from 4 clinics using off-label LEN and CAB +/- RPV demonstrated 94% viral suppression[3]

1-Segal-Maurer S et al, NEJM, 2022. 2-Ogbuagu O et al, ID Week 2024. 3-Gandhi M et al, CROI 2024, #629.

MWAETC

Method and Results

- Nine patients at University of Mississippi Medical Center with either NNRTI-R or INSTI-R were prescribed q2 month IM CAB-RPV (without oral lead in) and SC LEN q 6 months
- Clinical Characteristics
  - Mean HIV RNA 36,251 copies/mL (range 36-251,000)
  - Resistance History
    - Every patient had RPV RAMs
    - One patient had INSTI RAMs (N155H, T97A), conferring CAB score 30
- Outcomes, with follow up ranging from 24-36 weeks
  - All maintained VL < 200 copies/mL
  - Patients with CD4 < 200 cells/mm^3 demonstrated 208% increase
  - No treatment emergent resistance was seen

Brock JB et al, ID Week 2024.

MWAETC

Conclusions

1. The majority of PWH on LAI CAB-RPV in clinical practice are maintaining or achieving viral suppression, including in individuals with adherence challenges.

2. Discontinuation rates and virologic failure rates are higher in these cohorts than those seen in registrational trials.

3. The combination of Lenacapavir with LAI CAB and/or RPV appears efficacious, though we need more robust data to confirm if CAB and/or RPV is a sufficient OBR.

Yared N et al, ID Week 2024. Hastie E et al, ID Week 2024. Brock JB et al, ID Week 2024.

MWAETC

Acknowledgment

This Mountain West AIDS Education and Training (MWAETC) program is 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 $3,333,289 with 0% financed with non-governmental sources.

AETC AIDS Education & Training Center Program Mountain West