Resuppression and resistance after confirmed virologic failure among women on CAB+RPV LA in the OPERA Cohort

TUPEB129

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OPERA® The Longitudinal Cohort

Background

CAB+RPV LA

- The first and only complete LA ART regimen in the US
  - Injections once a month or every 2 months
  - Indicated for ART-experienced individuals with VL < 50 c/mL
- Has demonstrated high efficacy in clinical trials and high effectiveness in real-world studies
- Convenient; potential for improved adherence
- Reduced pill burden, stigma, and other psychosocial concerns
- Minimized disruption of daily responsibilities
- May be a good option for women, who represent > 50% of people with HIV worldwide (~20% of people with HIV in the US)

Objective

To assess baseline characteristics, resistance profiles, and viral resuppression in women following confirmed virologic failure on CAB+RPV LA in the OPERA Cohort

Methods

OPERA Cohort

- Prospectively captured, routine clinical data from electronic health records in the US (101 clinics, 23 US states/territories), representing ~14% of PWH in the US (~11% of women with HIV in the US)

Inclusion Criteria

- Cisgender and transgender women living with HIV, regardless of VL
- Aged ≥ 18 years
- ART-experienced
- Received ≥ 1 CAB+RPV LA injection from 21JAN2021-31AUG2023
- Received both initiation injections ≤ 67 days apart
- Had ≥ 1 viral load (VL) available between 21JAN2021-29FEB2024
- Experienced CVF between 21JAN2021-29FEB2024
  - Defined as 2 consecutive VLs ≥ 200 c/mL, or 1 VL ≥ 200 c/mL followed by discontinuation (67 [Q1M] or 127 [Q2M] days without injection)
  - Women who in initiated CAB+RPV LA with VL ≥ 50 c/mL had to suppress to VL < 50 c/mL before meeting the definition for CVF

Outcomes (assessed through 08APR2026)

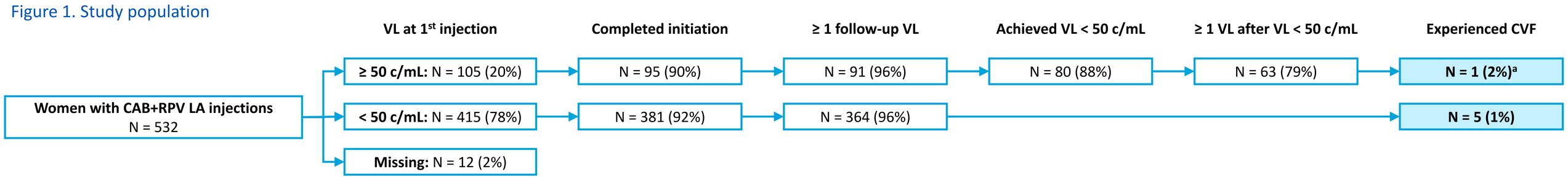
- Prior regimen and duration
- VL and BMI at initiation
- Adherence to CAB+RPV LA dosing schedule
  - On-time (Q1M: ≤ 37 days; Q2M: ≤ 67 days)
  - Late (Q1M: 38-67 days; Q2M: 68-127 days)
- Resistance tests before and after CVF
- Resuppression to VL < 50 c/mL after CVF
- Regimen when resuppressed

Abbreviations

ABC, abacavir; **ART**, antiretroviral; **BIC**, bictegravir; **BID**, twice a day; **BMI**, body mass index; **c**, cobicistat; **c/mL**, copies per milliliter; **CAB+RPV**, cabotegravir + rilpivirine; **CVF**, confirmed virologic failure; **DTG**, dolutegravir; **DRV**, darunavir; **EVG**, elvitegravir; **FTC**, emtricitabine; **FTR**, fostemsavir; **HIV**, human immunodeficiency virus; **INI**, integrase inhibitor; **inj.**, injection; **kg**, kilograms; **LA,** long-acting; **LEN**, lenacapavir; **m**, meter; **NNRTI**, non-nucleoside reverse transcriptase inhibitor; **Q1M**, monthly dosing schedule; **Q2M**, every 2 months dosing schedule; **RAL**, raltegravir; **TAF**, tenofovir alafenamide; **US**, United States; **VL**, viral load; **3TC**, lamivudine

Results

Figure 1. Study population



[a] 1 additional woman (#4 in the abstract and in Table 1 below) appeared to have suppressed after initiating CAB+RPV LA and was categorized as having experienced CVF in the abstract. However, further investigation of the EHR revealed an erroneous VL < 50 c/mL. After correcting this VL, this woman was not eligible to meet CVF criteria

Table 1. Summary of resistance among women who experienced CVF on CAB+RPV LA in OPERA

Legend: Before CAB+RPV LA | During CAB+RPV LA | After CAB+RPV LA

Woman (HIV subtype)	BMI at start (day measured)	VL at start (day measured)	Prior ART (duration)	Resistance testing prior to CAB+RPV LA	CAB+RPV LA – duration, dosing (adherence)	CVF (timing)	Resistance testing at/after CVF	Subsequent ART (duration)	Resuppression (timing)
#1 (subtype C)	25 kg/m² (Day -55)	20 c/mL (Day -69)	EVG/c/FTC/TAF (15 months)	Day -55: GenoSure Archive (multiple polymorphisms; pan-sensitive to NNRTIs, INIs) Day -4196: Phenosense (partial resistance to NNRTIs except RPV) Day -2452: GenoSure MG (partial resistance to NNRTIs except RPV) Day -36: GenoSure Archive (partial resistance to NNRTIs except RPV; pan-sensitive to INIs)	Day 0-999: CAB+RPV LA Q2M (16/17 inj. on time; 14th inj. 6 days late)	Day 32: VL = 380 c/mL Day 49: VL = 240 c/mL (1.6 months to CVF)	Day 57: GenoSure Archive (multiple polymorphisms; pan-sensitive to NNRTIs, INIs)	Remained on CAB+RPV LA (2.7 years total)	Day 217: VL = 20 c/mL (5.5 months after CVF)
#2 (subtype B)	50 kg/m² (Day -14)	< 20 c/mL (Day -36)	BIC/FTC/TAF (15 months)	Day 0-157: CAB+RPV LA Q1M (5/5 inj. on time) Day 158-242: CAB+RPV LA Q2M (2/2 inj. on time)	Day 214: VL = 7,960 c/mL Day 224: VL = 6,320 c/mL (7.4 months to CVF)	Day 224: GenoSure PRIme (**pan-resistance[a] to NNRTIs, INIs**)	DRV/c/ FTC/TAF (2.1 years)	Day 311: VL = 30 c/mL (2.9 months after CVF)
#3 (subtype unknown)	37 kg/m² (Day -169)	30 c/mL (Day -27)	BIC/FTC/TAF (3.8 years)	Day -1068: GenoSure Archive (insufficient sample)	Day 0-408: CAB+RPV LA Q2M (4/6 inj. on time; 5th inj. missed [131 days after 4th inj.]; 6th inj. a late reinitiation [26 days late])	Day 148: VL = 330 c/mL Day 276: > 127 days without inj. due to insurance denial (9.1 months to CVF)	No resistance tests performed	BIC/FTC/TAF (2.6 years)	Day 451: VL < 20 c/mL (5.8 months after CVF)
#4[b]	--	--	--	--	--	--	--	--	--
#5 (subtype B)	28 kg/m² (Day -57)	< 20 c/mL (Day -57)	BIC/FTC/TAF (6.3 months)	Day -393: Genosure Archive (pan-sensitive to NNRTIs, INIs)	Day 0-468: Alternating Q1M and Q2M dosing (7/9 inj. on time; 3rd inj. 30 days late; 5th inj. 25 days late)	Day 393: VL = 270 c/mL Day 465: VL = 240 c/mL (15.3 months to CVF)	Day 398: GenoSure Prime (multiple polymorphisms; pan-sensitive to NNRTIs, INIs)	DRV/c/ FTC/TAF + DOR (5 months) DRV/c/ FTC/TAF + DOR + LEN (21 days) DRV/c/ FTC/TAF + LEN (2.2 years)	Day 1066: VL = 30 c/mL (19.8 months after CVF, on DRV/c/ FTC/TAF + LEN)
#6 (subtype B)	36 kg/m² (Day -141)	< 20 c/mL (Day -69)	DTG/ABC/3TC (5.7 years)	No resistance tests performed	Day 0-272: CAB+RPV LA Q1M (7/8 inj. on time; 6th inj. 10 days late) Day 273-588: CAB+RPV LA Q2M (5/6 inj. on time; 14th inj. 1 day late)	Day 573: VL = 12,000 c/mL Day 587: VL = 7,300 c/mL (19.3 months to CVF)	Day 573: Genosure Archive (**pan-resistance[a] to NNRTIs; resistance to RAL, EVG, CAB; partial resistance to BIC, DTG**)	DRV/c + FTR (3.1 years)	Day 680: VL < 20 c/mL (3.1 months after CVF)
#7 (subtype unknown)	30 kg/m² (Day 0)	160 c/mL (Day 0)	DRV/c + DTG BID (4.0 years)	Day -645 & Day -127: GenoSure Archive (multiple polymorphisms; pan-sensitive to NNRTIs, INIs)	Day 0-208: CAB+RPV LA Q1M (7/7 inj. on time) Day 209-455: CAB+RPV LA Q2M (5/5 inj. on time)	Day 454: VL = 38,600 c/mL Day 455: discontinuation (15.0 months to CVF)	Day 470: GenoSure PRIme (**pan-resistance[a] to NNRTIs; resistance to RAL, EVG, CAB; partial resistance to BIC, DTG**)	DRV/c/ FTC/TAF (4.7 months) DRV/c + FTR + LEN (1.6 years)	Day 649: VL < 20 (6.3 months after CVF, on DRV/c + FTR + LEN)
Overall Summary	**4/6** initiated with BMI ≥ 30 kg/m²	**1/6** initiated with VL ≥ 50 c/mL	**3/6** on BIC/FTC/TAF prior to CAB+RPV LA	**2/6** had no resistance test results prior to CAB+RPV LA **3/6** pan-sensitive to NNRTIs and INIs prior to CAB+RPV LA **1/6** had partial resistance to NNRTIs except RPV	**58/65** injections on time; late/missed injections occurred after detectable VLs	**4/6** had 2 consecutive VLs ≥ 200 c/mL **2/6** had 1 VL ≥ 200 c/mL + discontinuation Median **12 months** to CVF	**3/6** developed resistance **1/6** had no resistance tests results at/after CVF	**1/6** remained on CAB+RPV LA **4/6** switched to a DRV-based regimen **1/6** switched to BIC/FTC/TAF	**6/6** resuppressed after CVF Median **6 months** to resuppression

[a] Resistant to all drugs in the class
[b] Not eligible to meet CVF criteria

Discussion

Key Findings

- CVF was rare in this large real-world cohort of women on CAB+RPV LA (6 of 427)
- All 6 women successfully resuppressed with a subsequent regimen after CVF (including 1 on CAB+RPV LA)
- However, 3 of 6 women had INI and NNRTI resistance at CVF (including 1 who initiated with a VL ≥ 50 c/mL). All 3 were mostly adherent to the injection schedule, had a BMI ≥ 30 kg/m², and resuppressed on a DRV-based regimen
  - 2 of 3 had emergent resistance; 1 had unclear resistance development
- These findings reinforce the durability and effectiveness of CAB+RPV LA in women and underscore the potential for effective management following CAB+RPV LA failure

Strengths

- Large population of > 500 women receiving CAB+RPV LA
  - Regionally diverse representation of women with HIV in the US
- Real world data captured through electronic health records
- In-depth investigation of 6 women who experienced CVF, including resistance tests performed up to 11 years prior to initiation

Limitations

- Only 6 women experienced virologic failure, which hindered the ability to assess predictors of failure
- 2 of 6 women did not have resistance test results available prior to initiating CAB+RPV LA
- 1 woman did not have resistance tests performed at or after experiencing CVF
- Several gaps between VL assessments in the EHR
- Several women with high BMI; needle sizes not documented

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