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# Re-suppression regimens and outcomes after virological failure in randomised controlled trials and real-world evidence studies evaluating cabotegravir and rilpivirine (LAI CAB+RPV)

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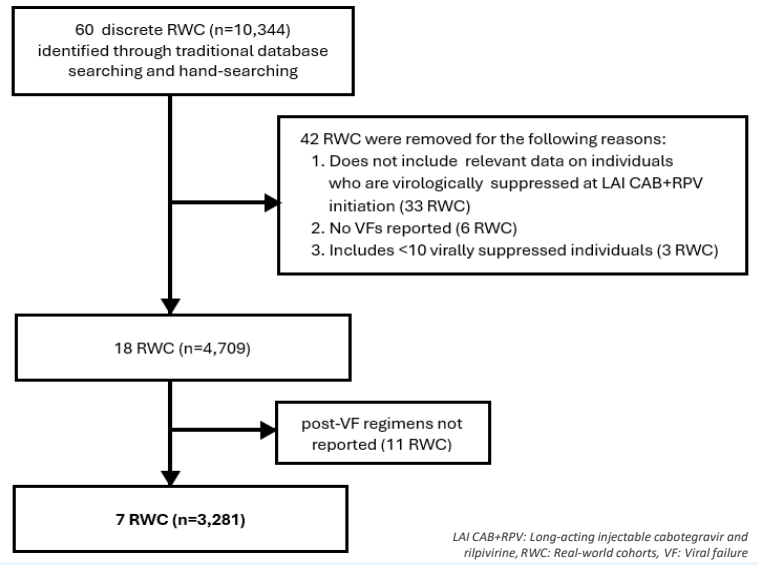
## BACKGROUND

- Efficacy of long-acting injectable (LAI) cabotegravir and rilpivirine (CAB + RPV) in virally suppressed people living with HIV is well described in clinical trials.
- However, little is known regarding re-suppression rates/outcomes after virological failure (VF) in Phase 3/3b studies and real-world cohorts (RWC).
- We present the first summary of post-VF regimen use and re-suppression outcomes from Phase 3/3b studies and RWC.

***Figure 1. Number of real-world cohorts and people living with HIV (n) included in the systematic literature review***




*LAI CAB+RPV: Long-acting injectable cabotegravir and rilpivirine, RWC: Real-world cohorts, VF: Viral failure*

## METHODS

- We performed a systematic literature review (SLR) using Pubmed, Embase, Cochrane and 23 HIV-related conferences through March 2024 to identify all RWC evaluating LAI CAB+RPV.
- We included Phase 3/3b studies evaluating LAI CAB+RPV in virologically suppressed people living with HIV.
- We described data from a sub-set of RWC that report post-VF regimens, and re-suppression outcomes (where available) among individuals who were virally suppressed at baseline (Figure 1).
- We categorised post VF-regimens as: Integrase Inhibitor (INI), Protease Inhibitor (PI), Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI), Multi-core agent (regimens composed of more than one third agent), LAI CAB+RPV, therapeutic gap.
- We report proportion with re-suppression where known.

## RESULTS

**Phase 3/3b studies:**

- 7 Phase 3/3b studies were identified. VF events occurred in 30 participants across 6 trials (ATLAS, ATLAS-2M, FLAIR, SOLAR, CARES, CARISEL; no VF events occurred in CUSTOMIZE). VF definitions used were consistent and used a confirmatory viral load (VL≥200 c/mL).
- Data on post-VF regimen and virological re-suppression was available for 28/30 participants. 26/28 participants re-suppressed (Table 1).

**Real World Cohorts:**

- 7 RWC reported post-VF regimens for individuals who were virally suppressed at LAI CAB+RPV initiation and experienced VF (Figure 1).
- In those studies, 42/50 individuals with VF had a known post-VF regimen. Re-suppression outcome was described for 33/42 individuals with a known post-VF regimen, of whom 28/33 re-suppressed. Details on post-VF regimens and re-suppression are described in Table 1.

***Table 1. Post-VF regimens used and re-suppression post-VF***

| Study | Study country/ countries | Follow-up time | Dosing | VF definition | N | VF, n (%) | Post VF regimen available n/N | Post VF regimen | Re-suppression n/N, (%) |
|---|---|---|---|---|---|---|---|---|---|
| **Phase 3/3b studies** | | | | | | | | | |
| ATLAS-2M | Australia, Argentina, Canada, France, Germany, Italy, Mexico, Russia, South Africa, South Korea, Spain, Sweden, USA | 152 Weeks | Q1M and Q2M | 2 VL ≥200 c/mL | 1,045 | 14 (1.3) | 14/14 | 2 INI-based<br>12 PI-based | 13/14 (92.8) |
| SOLAR | Australia, Austria, Belgium, Canada, France, Germany, Ireland, Italy, Japan, Netherlands, Spain, Switzerland, UK, USA | 12 Months | Q2M | 2 VL ≥200 c/mL | 454 | 3 (0.7) | 3/3 | 2 INI-based<br>1 PI-based | 3/3 (100) |
| CARISEL | Spain, France, Germany, Netherlands, Belgium | 12 Months | Q2M | 2 VL ≥200 c/mL | 437 | 2 (0.5) | 2/2 | 2 PI-based | 2/2 (100) |
| FLAIR | Canada, France, Germany, Italy, Japan, Netherlands, Russia, South Africa, Spain, UK, USA | 124 Weeks | Q1M | 2 VL ≥200 c/mL | 283 | 5 (1.8) | 4/5* | 2 PI-based<br>1 INI-based<br>1 NNRTI-based | 3/4 (75) |
| FLAIR open label extension | | 24 Weeks | | | 232 | 1 (0.4) | 1/1 | 1 PI-based | 1/1 (100) |
| CARES | Uganda, Kenya, South Africa | 12 Months | Q2M | 2 VL ≥200 c/mL | 255 | 2 (0.8) | 1/2** | 1 INI-based | 1/1 (100) |
| ATLAS | Argentina, Australia, Canada, France, Germany, Italy, Mexico, Russia, South Africa, South Korea, Spain, Sweden, USA | 48 Weeks | Q1M | 2 VL ≥200 c/mL | 252 | 3 (1.2) | 3/3 | 3 PI-based | 3/3 (100) |
| **Real-world cohorts** | | | | | | | | | |
| Hsu et al. 2024 OPERA (1) | USA | NR | Q1M and Q2M | 2 VL ≥200 c/mL or 1 VL ≥200 c/mL + discontinuation | 1,293 | 25 (1.9) | 25/25 | 10 INI-based<br>10 LAI CAB+RPV<br>4 Multi-core agents<br>1 Therapeutic gap | 15/19 (78.9)<br>Only 19 with available FU data |
| Deschanvres et al., 2023 (Dat'AIDS cohort) (2) | France | 196 Days (median) | Q2M | 2 VL >50 c/mL or 1 VL >200 c/mL | 1134 | 14 (1.2) | 6/14 | 6 LAI CAB+RPV | 5/6 (83) |
| Jongen et al., 2023*** (ATHENA cohort) (3) | Netherlands | 0.8 Years (median) | Q2M | >200 c/mL | 588 | 5 (0.9) | 5/5 | 1 LAI CAB+RPV<br>1 INI-based<br>3 PI-based | 4/4 (100)<br>Only 4 with available FU data |
| Pozniak et al., 2023 (COMBINE-2 C2C) (4) | Switzerland, Germany, France, Spain, Netherlands | 5.2 Months (median) | Q2M | 2 VL>200 c/mL or 1 VL>200c/mL + discontinuation | 89 | 1 (1.1) | 1/1 | 1 PI-based | 0/0 (0) No FU data available |
| Liegeon et al., 2024 (5) | USA | 8 Months (median) | Q1M and Q2M | NR | 78 | 1 (1.3) | 1/1 | 1 PI-based | 1/1 (100) |
| Shankaran et al., 2024 (6) | USA | NR | NR | 2 VL >200 c/mL | 75 | 3 (4) | 3/3 | 3 PI-based | 3/3 (100) |
| Masich et al., 2023 (7) | USA | 12 Months | NR | NR (Viral rebound: >200 c/ml) | 24 | 1 (4.2) | 1/1 | 1 INI-based | 0/0 (0) No FU data available |

*Abbreviations: FU: Follow-up, INI: Integrase Inhibitor, LAI CAB+RPV: long-acting injectable cabotegravir and rilpivirine, NR: Not reported, NNRTI: Non-Nucleoside Reverse Transcriptase Inhibitor, PI: Protease Inhibitor, Q1M: monthly, Q2M: 2-monthly, RAMs: resistance-associated mutations, VL: Viral load, VF: Viral failure*

*1 participant had CAB+RPV OLI interrupted at W4 (false-positive pregnancy test) and never received an injection; ** 1 participant was lost to FU due to an HIV-unrelated death;

***Information on the ATHENA cohort was also extracted from van Welzen et al., 2024 (8)

## LIMITATIONS

Limitations include data availability and heterogeneity in cohort size, definitions of VF, duration of follow-up, and lack of resistance data at baseline.

## CONCLUSIONS

We summarised post-VF regimen use and re-suppression outcomes in Phase 3/3b studies and real-world cohorts evaluating LAI CAB+RPV. In Phase 3/3b studies, PI-based post-VF regimens were used most frequently, whereas in RWC, continuation of LAI CAB+RPV was most common. This difference could potentially be explained by the various VF definitions used in RWC. Evidence on re-suppression outcomes is scant in RWC so far.

**References: 1.** Hsu RK, et al. CROI 2024. Poster 623 **2.** Deschanvres C, et al. EACS 2023. Poster MeP.T2.01 **3.** Jongen V, et al. EACS 2023. Oral PS8.01 **4.** Pozniak A, et al. EACS 2023. Poster eP.A.039 **5.** Liegeon G, et al. CROI 2024. Poster 1236 **6.** Shankaran S, et al. CROI 2024. Poster 686 **7.** Masich AM, et al. AIDS 2023;37:1641–2 **8.** van Welzen BJ, et al. Clin Infect Dis 2024;ciae016



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