# High virologic suppression and adherence with rare virologic failure in treatment experienced virologically suppressed individuals on Cabotegravir + Rilpivirine: results from the COMBINE-2 European cohort

P070

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## Background

- Cabotegravir (CAB) + rilpivirine (RPV) is the first complete long-acting (LA) regimen for people with HIV who are virologically suppressed (viral load [VL] <50 copies/mL) on a stable antiretroviral regimen, with no prior virologic failure or known resistance to NNRTI or INSTI classes
- Real-world evidence in routine clinical practice on the effectiveness, durability, adherence, and resistance would further evaluate the potential value of CAB+RPV LA
- This study evaluated clinical outcomes among individuals initiating CAB+RPV LA in routine clinical practice across Europe

## Objective

Assess persistence, adherence and virologic outcomes among individuals initiating CAB+RPV LA in routine clinical practice across Europe

## Methods

### Study Design

Five year-long prospective cohort study using data from NEAT ID Network between December 2020 and September 2025

### Study Population

- Treatment-experienced, virologically suppressed (HIV-1 RNA <50 copies/mL) adults (aged ≥18 years) initiating CAB+RPV LA
- No evidence of prior virological failure with agents of the NNRTI and INSTI class
- No evidence of present or past documented viral resistance to agents of the NNRTI and INSTI class

### Outcomes

- **Adherence:**
  - Number of participants that missed one or more consecutive injections without taking daily oral bridging therapy or any other oral ARV regimen while not on CAB+RPV LA regimen
  - Number of participants who received the injections more than seven days later than their scheduled injection visit

**Outcomes** (continued)

- **Regimen discontinuation:** reasons for discontinuation were collected for all participants who switched off CAB+RPV LA regimen
- **Clinical effectiveness:** assessed using viral loads (VL) assessed from the first injection through discontinuation or time of analysis
  - Proportion virologically suppressed/undetectable with VL of <50 copies/mL
  - Confirmed virologic failure: two consecutive VLs ≥200 c/mL or VL ≥200 c/mL followed by CAB+RPV LA discontinuation within 2 months (monthly dosing) or within 4 months (every 2 months dosing)
- **Resistance testing:** testing for resistance and subtype at baseline and at VF
  - During 24-month follow-up period while on CAB+RPV LA
  - During the 48 months following any switch from CAB+RPV LA with subsequent VF on new regimen during follow-up

## Results

**Table 1. Baseline Demographic and Clinical Characteristics of Individuals Initiating CAB+RPV LA**

| | Overall (N=1,022) |
|---|---|
| **Age at initiation (in years), n (%)** | |
| 18-29 | 63 (6) |
| 30-49 | 586 (57) |
| 50+ | 373 (37) |
| Median (IQR) | 45 (37-53) |
| **Sex, n (%)** | |
| Female | 155 (15) |
| Male | 867 (85) |
| **Ethnic origin, n (%)** | |
| White Caucasian | 654 (64) |
| Black | 111 (11) |
| White mixed | 74 (7) |
| Asian | 12 (1) |
| Other | 171 (17) |
| **Route of HIV infection, n (%)** | |
| MSM | 661 (65) |
| Heterosexual | 189 (19) |
| Other | 110 (11) |
| **Geographic region, n (%)** | |
| Spain | 560 (55) |
| France | 234 (23) |
| Germany | 85 (8) |
| Belgium | 53 (5) |
| Switzerland | 42 (4) |
| Netherlands | 32 (3) |
| UK | 16 (2) |
| Italy | 0 (0) |
| **CD4 Cell Count at initiation (cells/µL), n (%)** | |
| <350 | 51 (5) |
| ≥350 to <500 | 124 (12) |
| ≥500 | 846 (83) |
| Median (IQR) | 726 (558-912) |
| **Number of years since HIV diagnosis, Median (IQR)** | 10.8 (6.5-17.1) |
| **Number of years since ART initiation, Median (IQR)** | 9.3 (5.9-14.2) |
| **Body mass index (BMI, kg/m²)** | |
| <30 | 787 (77) |
| 30-34.9 | 82 (8) |
| 35-39.9 | 13 (1) |
| ≥40 | 6 (1) |
| Median (IQR) | 25.0 (22.9-27.6) |
| **History of previous use of INSTI or NNRTI-based regimen, n (%)** | |
| Yes | 982 (96) |
| **History of AIDS defining events, n (%)** | |
| Yes | 86 (8) |
| **Comorbidities, n (%)** | 155 (15) |
| HCV co-infection | 97 (10) |
| HBV co-infection | 34 (3) |
| NADM | 19 (2) |
| CVD | 13 (1) |
| CKD | 9 (1) |
| ESLD | 0 (0) |
| **Concurrent medications, n (%)** | 92 (9) |
| Atorvastatin | 40 (4) |
| Paracetamol | 31 (3) |
| Tadalafil | 11 (1) |
| Metformin | 10 (1) |
| Sildenafil | 9 (1) |
| **Last ARV regimen received prior to initiation of CAB+RPV LA, n (%)** | |
| Bictegravir/Emtricitabine/Tenofovir alafenamide | 232 (23) |
| Dolutegravir/Lamivudine | 185 (18) |
| Dolutegravir/Rilpivirine | 94 (9) |
| Rilpivirine/Emtricitabine/Tenofovir alafenamide | 83 (8) |
| Cabotegravir/Rilpivirine LA prior clinical trial | 78 (8) |
| Other | 350 (34) |
| **Previous HIV drug resistance tests, prior to initiation of CAB+RPV LA regimen, n (%)** | |
| Yes | 644 (63) |

HCV, Hepatitis C virus; HBV, Hepatitis B virus; NADM, Non-AIDS Defining Malignancy; CVD, Cardiovascular disease; CKD, Chronic kidney disease; ESLD, End-stage liver disease

### Adherence:

- 963 individuals (94%) received all injections on-time (within ±7 days of target injection date)
  - 16 individuals (2%) missed injections but received oral bridging
- 37 individuals (4%) had a delayed dose with median delay of 15 days (IQR: 10-20)
  - None of these individuals had VF during follow-up
- 8 individuals (1%) missed injections
  - 7 participants missed 1 injection and 1 participant missed 2 injections
  - None of these individuals had VF during follow-up

### Persistence/Discontinuation:

- At the time of analysis, 885 individuals (87%) remained on CAB+RPV with median follow-up of 23 months (IQR: 21.2, 23.6)
- 137 individuals (13%) discontinued CAB+RPV LA
  - 88 (64%) continue to have follow-up visits
- Top reasons for discontinuation include:
  - Individual decision (3.3%)
  - Loss to follow-up (1.8%)
  - Injection site reaction (1.4%)

### Virologic Effectiveness:

- Among 1,007 individuals with follow-up VLs:
  - Last VL measured was <50 copies/mL in 986 (98%) individuals
  - All follow-up VLs were <50 copies/mL in 917 (91%) individuals.
- Seven individuals (0.7%) had CVF after initiation
  - All were adherent to CAB+RPV LA regimen
  - Baseline resistance information was not available for any of these individuals
  - At failure, 3 individuals had NNRTI/INSTI resistance mutations, 3 individuals had no resistance mutation detected, and 1 individual had no resistance information available
  - All resuppressed after switch to PI (n=5) or INSTI-based (n=2) regimen
  - Five individuals had BMI <30 kg/m², BMI was unknown in the other 2 individuals

**Table 2: Virologic Outcomes Among Individuals Initiating CAB+RPV LA Regimen**

| | | Overall (N=1,022) |
|---|---|---|
| Duration of follow-up | Median months (IQR) | 23.0 (21.2, 23.6) |
| On CAB+RPV LA at end of follow-up | n (%) | 885 (87) |
| ≥1 VL after first injection | n (%) | 1,007 (99) |
| | Last VL <50 copies/mL, n (%) | 986/1,007 (98) |
| | All VLs <50 copies/mL, n (%) | 917/1,007 (91) |
| | VL <50 copies/mL at month 6, n (%) | 963/1,002 (96) |
| | VL <50 copies/mL at month 12, n (%) | 910/967 (94) |
| | VL <50 copies/mL at month 24, n (%) | 160/181 (88) |
| | Confirmed virologic failure, n (%) | 7/1,007 (0.7) |

- Resistance mutations observed among those with CVF
  - The first individual: NNRTI mutation (V179I), low-level resistance to rilpivirine (E138A) and potential low-level resistance to lopinavir and atazanavir (M46I, M36I, L63P, I64L, V77I, I93L)
  - The second individual: NNRTI mutations (K101E, E138G and G190S), INSTI mutations (L74M, Q148R and T97A) and NRTI mutations (D67N, K70R and K219E)
  - The third individual: NNRTI mutation (E138K) and INSTI mutation (N155H)
- Of 776 individuals with BMI <30 kg/m2 and follow-up VLs, 761 (98%) had last measured VL <50 copies/mL
- Of 101 individuals with BMI ≥30 kg/m2 and follow-up VLs, 99 (98%) had last measured VL <50 copies/mL

### Strengths

- Real-world experience with CAB+RPV LA among individuals with virologic suppression individuals
- Large, prospective cohort of PLWH from clinical sites across seven countries in Europe with long follow-up

### Limitations

- NEAT ID provides routine clinical care data that may be subject to confounding by indication
- The high proportion of White Caucasian males limits the generalizability of the study findings

## Key Findings

- CAB+RPV LA regimen demonstrated high rates of virologic suppression, high persistence and strong adherence among people with virologic suppression at initiation in Europe
- Confirmed virologic failure was rare, with few individuals having NNRTI or INSTI mutations at failure and all individuals suppressed after switching regimens
- Virologic suppression were similar across BMI categories
- These findings reinforce CAB+RPV LA as a highly effective and durable treatment strategy in routine clinical practice

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