# Cabotegravir + Rilpivirine Long-Acting Effectiveness and Safety Outcomes by Sex at Birth, Age, and Race: A Subgroup Analysis of the CARISEL Study



Jade Ghosn[1,2], Laurent Hocqueloux[3], María José Crusells-Canales[4], Leïla Belkhir[5], Celia Jonsson-Oldenbüttel[6,7], Thomas Lutz[8], Marc van der Valk[9], Berend J. van Welzen[10], Kai Hove[11], Mounir Ait-Khaled[11], Rebecca DeMoor[12], Gilda Bontempo[13], Christine L. Latham[13], Cassidy A. Gutner[13], Supriya Iyer[14], Martin Gill[15], Ronald D'Amico[13], Jean van Wyk[11], Maggie Czarnogorski[13]

*[1]Université de Paris, INSERM UMR 1137 IAME, Paris, France; [2]Service de Maladies Infectieuses et Tropicales, AP-HP, Hôpital Bichat–Claude Bernard, Paris, France; [3]Service des Maladies Infectieuses et Tropicales, CHU d'Orléans, Orléans, France; [4]Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain; [5]AIDS Reference Center, Department of Internal Medicine, Cliniques Universitaires Saint-Luc, Université Catholique de Louvain, Brussels, Belgium; [6]MUC Research GmbH, Munich, Germany; [7]MVZ München am Goetheplatz, Munich, Germany; [8]Infektiologikum, Frankfurt, Germany; [9]Amsterdam UMC, Department of Infectious Diseases, Institute for Infection and Immunity, University of Amsterdam, Amsterdam, the Netherlands; [10]Department of Infectious Diseases, University Medical Center Utrecht, Utrecht, the Netherlands; [11]ViiV Healthcare, Brentford, United Kingdom; [12]GSK, Collegeville, PA, United States; [13]ViiV Healthcare, Durham, NC, United States; [14]GSK, Bangalore, India; [15]GSK, Brentford, United Kingdom*

## Key Takeaways

- **We present outcomes by key subgroups (sex at birth, age, and race) for people living with HIV (PWH) who received cabotegravir + rilpivirine long-acting (CAB + RPV LA) dosed every 2 months (Q2M) in the Phase 3b CARISEL implementation study.**
- **CAB + RPV LA Q2M was effective for the maintenance of virologic suppression in a diverse population of PWH across Europe, irrespective of sex at birth, age, and race.**
- **The overall rate of confirmed virologic failure (CVF) was low (0.23%), with one participant having CVF through Month 12. One participant was withdrawn following two instances of suspected virologic failure (SVF).**
- **CAB + RPV LA Q2M was well tolerated and infrequently led to withdrawal across all subgroups evaluated.**

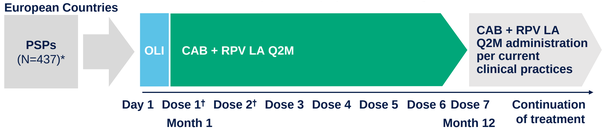
## Introduction

- CAB + RPV LA administered Q2M is the only complete LA maintenance regimen indicated for virologically suppressed PWH.[1,2]
- CAB + RPV LA reduces dosing frequency compared with daily oral antiretroviral therapy and may help address psychosocial challenges associated with oral treatment, including fear of disclosure, anxiety around medication adherence, and daily reminders of HIV status.[3]
- CAB And RPV Implementation Study in European Locations (CARISEL; NCT04399551) is a Phase 3b, multicenter, open-label, hybrid type III implementation–effectiveness trial evaluating participants switching from daily oral therapy to CAB + RPV LA dosed Q2M across five European countries (**Figure 1**).
- CAB + RPV LA dosed Q2M was efficacious and well tolerated, with 87% of participants in CARISEL maintaining HIV-1 virologic suppression, consistent with the results from four large Phase 3/3b CAB + RPV LA trials.[4–8]
- By design, the CARISEL study enrolled a diverse set of participants broadly representative of PWH in Europe.
- This *post hoc* analysis summarizes efficacy and safety outcomes by key subgroups (sex at birth, age, and race) through 12 months.

## Methods

### Figure 1. CARISEL Study Design

**Hybrid Type III Implementation–Effectiveness, Phase 3b, Open-Label Study Across Five European Countries**




*437 PSPs enrolled, and 430 received CAB + RPV LA. PSPs were ≥18 years of age, receiving a highly active ART regimen for ≥6 months prior to screening, had plasma HIV-1 RNA <50 copies/mL twice in the 12 months prior to and at screening, and no prior CVF. †Dose 1 was received at Month 1, Dose 2 at Month 2, with the remaining doses Q2M thereafter.
ART, antiretroviral therapy; CAB, cabotegravir; CVF, confirmed virologic failure; LA, long-acting; OLI, oral lead-in; PSP, patient study participant; Q2M, every 2 months; RPV, rilpivirine.

- The CARISEL study enrolled virologically suppressed PWH from Belgium, France, Germany, Spain, and the Netherlands to receive CAB + RPV LA dosed Q2M.
- Clinics with no prior experience with administering CAB + RPV LA were preferentially selected for study participation.
- In this *post hoc* analysis, data from participants receiving CAB + RPV LA in CARISEL were stratified by sex at birth (female and male), age (<50 and ≥50 years), and race (White, Black, Asian, and Other races) and are summarized descriptively.

**Endpoints assessed at Month 12:**

- The proportion of participants with plasma HIV-1 RNA ≥50 copies/mL and <50 copies/mL (FDA Snapshot algorithm).
- The incidence of CVF (two consecutive HIV-1 RNA ≥200 copies/mL).
- Safety and tolerability.

## Results

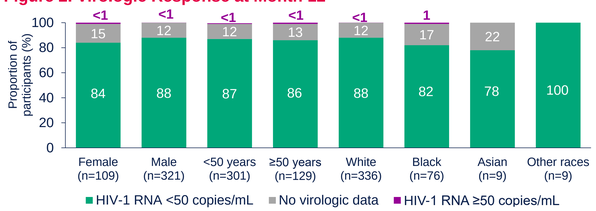
### Table 1. Baseline Characteristics

| Parameter | CAB + RPV LA Q2M (n=430) |
|---|---|
| Age (years), median (IQR) | 44.0 (37–51) |
| ≥50 years, n (%) | 129 (30) |
| Sex at birth, n (%) | |
| Female | 109 (25) |
| Male | 321 (75) |
| Race, n (%) | |
| White | 336 (78) |
| Black/African heritage | 76 (18) |
| Asian | 9 (2) |
| Other races* | 9 (2) |
| BMI (kg/m$^2$), median (IQR) | 25 (23–28) |
| ≥30 kg/m$^2$, n (%) | 56 (13) |
| Duration of prior ARTs (months), median (range) | 95.5 (10–368) |

*Other races: American Indian or Alaska Native, n=7; mixed race, n=2.
ART, antiretroviral therapy; BMI, body mass index; CAB, cabotegravir; IQR, interquartile range; LA, long-acting; Q2M, every 2 months; RPV, rilpivirine.

- Overall, 430 participants received CAB + RPV LA Q2M; 25% were female (sex at birth), 30% were aged ≥50 years, and 18% identified as Black (**Table 1**).
  - An additional seven participants were enrolled but withdrew prior to receiving study treatment, two of whom withdrew due to protocol deviation (eligibility criteria not met), and the remaining five participants withdrew consent.
- Few participants were in the Asian and Other races subgroups (both n=9).

### Figure 2. Virologic Response at Month 12




- At Month 12, rates of virologic suppression (HIV-1 RNA <50 copies/mL) with CAB + RPV LA ranged 78–100% across subgroups, and rates of non-response (HIV-1 RNA ≥50 copies/mL) ranged 0–1% (**Figure 2**).

### Table 2.Snapshot Outcomes at Month 12

| | Sex at birth | | Age (years) | | Race | | | |
|---|---|---|---|---|---|---|---|---|
| Parameter, n (%) | Female (n=109) | Male (n=321) | <50 (n=301) | ≥50 (n=129) | White (n=336) | Black (n=76) | Asian (n=9) | Other races (n=9) |
| HIV-1 RNA <50 copies/mL | 92 (84) | 281 (88) | 262 (87) | 111 (86) | 295 (88) | 62 (82) | 7 (78) | 9 (100) |
| HIV-1 RNA ≥50 copies/mL | 1 (<1) | 2 (<1) | 2 (<1) | 1 (<1) | 2 (<1) | 1 (1) | 0 | 0 |
| No virologic data | 16 (15) | 38 (12) | 37 (12) | 17 (13) | 39 (12) | 13 (17) | 2 (22) | 0 |
| Discontinued due to AE or death | 10 (9) | 30 (9) | 24 (8) | 16 (12) | 32 (10) | 7 (9) | 2 (22) | 0 |
| Discontinued for other reason | 3 (3) | 4 (1) | 6 (2) | 1 (<1) | 5 (1) | 2 (3) | 0 | 0 |
| On study but missing data in window | 3 (3) | 4 (1) | 7 (2) | 0 | 3 (<1) | 4 (5) | 0 | 0 |

AE, adverse event.

- Snapshot outcomes were comparable between subgroups; 0–22% of participants had no virologic data (**Table 2**).

### Table 3. Participants With CVF and SVF*

| Sex at birth, race, baseline BMI (kg/m$^2$), country | HIV-1 subtype at baseline | Viral load at SVF/CVF (copies/mL) | RPV RAMs observed at baseline | INI RAMs observed at baseline | RPV RAMs observed at failure‡ | INI RAMs observed at failure‡ | Phenotypic resistance (fold-change) to RPV/CAB§ |
|---|---|---|---|---|---|---|---|
| **Participant with CVF†** | | | | | | | |
| Female, White, 29, Germany | G | 214/1861 | E138A | None | E138A + M230L | None | 22.0/0.9 |
| **Participant with SVF‖** | | | | | | | |
| Male, White, 30, Spain | B | 585/NA | None | None | E138K | N155N/S¶ | 6.1/1.3 |

*Data previously presented at IAS 2022, poster EPLBB05. †Following discontinuation, the participant switched to darunavir/cobicistat/emtricitabine/tenofovir alafenamide. ‡CVF or SVF. §The CVF and SVF virus was susceptible to CAB, dolutegravir, and bictegravir. ‖Participant met the SVF criterion (HIV-1 RNA 585 copies/mL) at Month 4 but was not confirmed at the Month 4 retest. Following a second retest at Month 4, the participant met the SVF criterion (HIV-1 RNA 386 copies/mL at the time of the resistance test) and withdrew from the study, as per the principal investigator's discretion, and switched ART to darunavir/cobicistat/emtricitabine/tenofovir alafenamide. ¶N155S is an extremely rare, non-polymorphic mutation that reduces raltegravir and elvitegravir susceptibility to a lesser degree than N155H.[9]
ART, antiretroviral therapy; BMI, body mass index; CAB, cabotegravir; CVF, confirmed virologic failure; INI, integrase inhibitor; NA, not applicable; RAM, resistance-associated mutation; RPV, rilpivirine; SVF, suspected virologic failure.

- Overall, 1/430 (0.23%) participant had CVF with a viral load of 1861 copies/mL at discontinuation (Month 10); the participant was White, female (sex at birth), ≥50 years of age, and had a body mass index (BMI) of 29.3 kg/m$^2$ at baseline.
  - At failure, the RPV resistance-associated mutations (RAMs) E138A + M230L were detected; no integrase inhibitor (INI) RAMs were detected; E138A was present in baseline peripheral blood mononuclear cells (PBMCs) (**Table 3**).
  - At the time of CVF (6 weeks following the prior injection), CAB and RPV plasma concentrations were 1.5 µg/mL and 78.5 ng/mL, respectively.
- An additional participant met the SVF criterion (single HIV-1 RNA ≥200 copies/mL) twice, at Month 4 and again at last visit prior to withdrawal (Month 6); neither were confirmed upon retest; the participant was White, male (sex at birth), <50 years of age, and had a BMI of 30.4 kg/m$^2$ at baseline.
  - The RPV RAM E138K and INI RAM N155N/S were detected in the SVF sample at Month 4; no INI or RPV RAMs were present in baseline PBMCs; no pharmacokinetic data were available for this participant.

### Table 4. Safety Summary Through Month 12

| | Sex at birth | | Age (years) | | Race | | | |
|---|---|---|---|---|---|---|---|---|
| Parameter, n (%) | Female (n=109) | Male (n=321) | <50 (n=301) | ≥50 (n=129) | White (n=336) | Black (n=76) | Asian (n=9) | Other races (n=9) |
| Any AEs* | 105 (96) | 314 (98) | 294 (98) | 125 (97) | 331 (99) | 71 (93) | 8 (89) | 9 (100) |
| Any Grade ≥3 | 12 (11) | 37 (12) | 36 (12) | 13 (10) | 37 (11) | 9 (12) | 3 (33) | 0 |
| Drug-related AEs | 98 (90) | 291 (91) | 276 (92) | 113 (88) | 308 (92) | 64 (84) | 8 (89) | 9 (100) |
| Excluding ISRs | 41 (38) | 115 (36) | 105 (35) | 51 (40) | 131 (39) | 17 (22) | 5 (56) | 3 (33) |
| Grade ≥3 | 5 (5) | 20 (6) | 17 (6) | 8 (6) | 19 (6) | 5 (7) | 1 (11) | 0 |
| AEs leading to treatment withdrawal | 10 (9) | 32 (10) | 26 (9) | 16 (12) | 32 (10) | 7 (9) | 3 (33) | 0 |
| SAEs† | 4 (4) | 11 (3) | 11 (4) | 4 (3) | 12 (4) | 1 (1) | 2 (22) | 0 |
| Drug related excluding ISRs‡ | 0 | 1 (<1) | 1 (<1) | 0 | 0 | 0 | 1 (11) | 0 |

*All AEs include ISRs unless specified. †None of the SAEs were fatal. ‡Suicidal ideation, n=1.
AE, adverse event; ISR, injection site reaction; SAE, serious adverse event.

- Safety profiles were comparable between subgroups (**Table 4**).
- Excluding injection site reactions (ISRs), drug-related adverse events (AEs) occurred in 36% (n=156/430) of participants, ranging from 22 to 56% across subgroups.
- No fatal AEs occurred in any subgroup.

### Table 5. ISR Summary Through Month 12

| | Sex at birth | | Age (years) | | Race | | | |
|---|---|---|---|---|---|---|---|---|
| Parameter | Female (n=109) | Male (n=321) | <50 (n=301) | ≥50 (n=129) | White (n=336) | Black (n=76) | Asian (n=9) | Other races (n=9) |
| Participants with injections, n (%) | 107 (98) | 316 (98) | 294 (98) | 129 (100) | 332 (99) | 75 (99) | 7 (78) | 9 (100) |
| Number of injections, n | 1514 | 4330 | 4090 | 1754 | 4590 | 1024 | 94 | 136 |
| ISR events, n* | 505 | 1353 | 1412 | 446 | 1453 | 337 | 19 | 49 |
| Pain, n (% of injections) | 395 (26) | 1138 (26) | 1148 (28) | 385 (22) | 1210 (26) | 275 (27) | 18 (19) | 30 (22) |
| Induration, n (% of injections) | 38 (3) | 36 (<1) | 59 (1) | 15 (<1) | 50 (1) | 19 (2) | 0 | 5 (4) |
| Discomfort, n (% of injections) | 12 (<1) | 82 (2) | 77 (2) | 17 (1) | 85 (2) | 1 (<1) | 1 (1) | 7 (5) |
| Nodule, n (% of injections) | 28 (2) | 29 (<1) | 46 (1) | 11 (<1) | 33 (<1) | 21 (2) | 0 | 3 (2) |
| Swelling, n (% of injections) | 7 (<1) | 30 (<1) | 30 (<1) | 7 (<1) | 25 (<1) | 10 (1) | 0 | 2 (1) |
| Grade 3, n (% of ISR events)† | 8 (2) | 22 (2) | 19 (1) | 11 (2) | 22 (2) | 8 (2) | 0 | 0 |
| Median duration (IQR), days | 3 (2–7) | 3 (2–5) | 3 (2–6) | 3 (2–5) | 3 (2–5) | 4 (3–7) | 3 (2–4) | 3 (2–4) |
| Participant withdrawal due to injection-related reasons, n (% of participants with injections)‡ | 7 (7) | 18 (6) | 13 (4) | 12 (9) | 19 (6) | 6 (8) | 0 | 0 |

*A single injection could result in more than one ISR. The five most common ISRs overall are listed. †There were no Grade 4 or Grade 5 ISRs. ‡Includes participants who discontinued due to ISR AEs, and an additional participant who withdrew from the study citing injection intolerability.
AE, adverse event; IQR, interquartile range; ISR, injection site reaction.

- ISR profiles were comparable across subgroups (**Table 5**).
- Most ISRs were Grade 1 or 2 (98–100%) in severity, with a median duration of 3–4 days, and few participants discontinued due to injection-related reasons across subgroups (0–9%).

## Conclusions

- CAB + RPV LA Q2M was efficacious for the maintenance of virologic suppression across a diverse population of PWH in Europe, irrespective of sex at birth, age, and race.
- CVF was infrequent, with one participant (0.23%) meeting the criterion at Month 10.
  - An additional participant met the SVF criterion at Month 4 and prior to withdrawal at Month 6.
- Across subgroups, CAB + RPV LA Q2M was well tolerated, with most ISRs being mild to moderate in severity, short in duration (median, 3–4 days), and infrequently leading to withdrawal.
- This analysis was limited by the small sample size of certain subgroups, which limits some of the conclusions that can be drawn.

**Acknowledgments:** The CARISEL study was funded by ViiV Healthcare. The authors thank everyone who has contributed to the CARISEL study, including all patient participants and their families, and the CARISEL clinical investigators and their staff, in Belgium, France, Germany, the Netherlands, and Spain. Editorial assistance was provided by Poppy Mashilo of Scimentum (Nucleus Global), with funding provided by ViiV Healthcare.

**References: 1.** Gandhi RT, et al. *JAMA*. 2023;329(1):63–84. **2.** European Medicines Agency. Vocabria Product Information. Available from: https://www.ema.europa.eu/en/documents/product-information/vocabria-epar-product-information_en.pdf. Accessed September 2023. **3.** De Los Rios P, et al. *Open Forum Infect Dis*. 2019;6(Suppl. 2):S481. **4.** Jonsson-Oldenbüttel C, et al. IAS 2022 (Poster EPLBB05). **5.** Orkin C, et al. *N Engl J Med*. 2020;382(12):1124–1135. **6.** Overton ET, et al. *Lancet*. 2021;396(10267):1994–2005. **7.** Swindells S, et al. *N Engl J Med*. 2020;382(12):1112–1123. **8.** Ramgopal MN, et al. *Lancet HIV*. 2023;10(9):e566-e577. **9.** Stanford University. HIV Drug Resistance Database. INSTI Resistance Notes. September 2022. Available from: https://hivdb.stanford.edu/dr-summary/resistance-notes/INSTI/. Accessed September 2023.



Presenting author: Kai Hove; kai.x.hove@viivhealthcare.com

**This content was acquired following an unsolicited medical information enquiry by a healthcare professional. Always consult the product information for your country, before prescribing a ViiV medicine. ViiV does not recommend the use of our medicines outside the terms of their licence. In some cases, the scientific Information requested and downloaded may relate to the use of our medicine(s) outside of their license.**