Effectiveness, Safety, and Implementation Outcomes of Cabotegravir + Rilpivirine Long-Acting by Country in the Cabotegravir And Rilpivirine Implementation Study in European Locations (CARISEL)

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Key Takeaways

- **We present outcomes by country (Belgium, France, Germany, Spain, and the Netherlands) 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 demonstrated high effectiveness at Month 12, with 81–94% of participants across countries maintaining HIV-1 virologic suppression and only one participant having confirmed virologic failure (CVF) overall (0.23%).**
- **CAB + RPV LA Q2M was well tolerated and increased participant satisfaction, irrespective of country.**
- **High and comparable acceptability, appropriateness, and feasibility of CAB + RPV LA implementation was observed across all countries.**

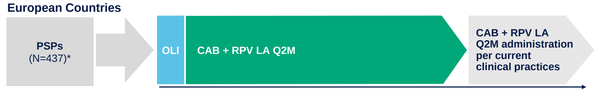
Introduction

- CAB + RPV LA administered Q2M is the only complete LA 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 daily 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 (Belgium, France, Germany, the Netherlands, and Spain).
- CAB + RPV LA dosed Q2M was efficacious and well tolerated, with 87% of participants in CARISEL maintaining HIV-1 virologic suppression at Month 12, 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, safety, and implementation outcomes by study country.

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 at screening as well as twice in the 12 months prior to 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 was primarily designed to evaluate the perceived acceptability, appropriateness, and feasibility of CAB + RPV LA implementation for staff study participants.
- Clinics with no prior experience with administering CAB + RPV LA were preferentially selected for study participation.
- For PSPs, CARISEL was designed as a single-arm, unblinded, interventional study in which all participants who fulfilled eligibility requirements were assigned to receive CAB + RPV LA Q2M (**Figure 1**).
- In this *post hoc* analysis, data from participants receiving CAB + RPV LA in CARISEL were stratified by country (Belgium, France, Germany, the Netherlands, and Spain) and are summarized descriptively.

Endpoints assessed at Month 12:

- The proportion of PSPs with plasma HIV-1 RNA ≥50 copies/mL and <50 copies/mL (FDA Snapshot algorithm).
- The incidence of CVF (two consecutive plasma HIV-1 RNA levels ≥200 copies/mL).
- Safety and tolerability.
- Treatment satisfaction (12-item HIV Treatment Satisfaction Questionnaire status version [HIVTSQs], range 0–66).
- The acceptability of intervention measure (AIM), intervention appropriateness measure (IAM), and feasibility of intervention measure (FIM) of CAB + RPV LA (1–5 Likert scale).

Results

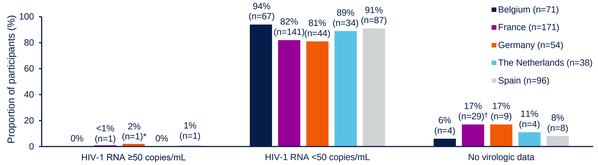
Table 1. Baseline Characteristics

- Overall, 430 participants received CAB + RPV LA (France, 40% [n=171]; Spain, 22% [n=96]; Belgium, 17% [n=71]; Germany, 13% [n=54]; the Netherlands, 9% [n=38]).
  - 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), with the remaining five participants withdrawing consent.
- 13 of 18 clinics (72%) had no experience with administering CAB + RPV LA at the start of the study.
- The median age (interquartile range [IQR]) was 44 years (37–51), 25% (n=109) were female (sex at birth), and the median body mass index (BMI) (IQR) was 25 kg/m^2 (23–28) (**Table 1**).
- At screening, 100% (n=430/430) were on nucleoside reverse transcriptase inhibitors, 73% (n=312/430) were on integrase strand transfer inhibitors, and 43% (n=186/430) were on protease inhibitors.

Parameter	CAB + RPV LA (n=430)
Age, median (IQR), years	44 (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, median (IQR), kg/m^2	25 (23–28)
≥30 kg/m^2, n (%)	56 (13)
Duration of prior ARTs (months), median (range)	96 (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; RPV, rilpivirine.

Figure 2. Virologic Response at Month 12



*Participant met the CVF criterion. †Six participants at one site in France had a missed viral load assessment at Month 12 and had HIV-1 RNA <50 copies/mL at Month 14.
CVF, confirmed virologic failure.

- At Month 12, rates of virologic non-response (HIV-1 RNA ≥50 copies/mL) and suppression (HIV-1 RNA <50 copies/mL) with CAB + RPV LA ranged 0–2% and 81–94%, respectively, across countries (**Figure 2**).
- Overall, one participant (0.23%) in Germany met the CVF criterion with a viral load of 1861 copies/mL at discontinuation (Month 10).[4]
- An additional participant in Spain met the SVF criterion (HIV-1 RNA ≥200 copies/mL) at Month 4 and again at last visit prior to withdrawal (Month 6); neither were confirmed upon retest.

Table 2. Snapshot Outcomes at Month 12

Parameter, n (%)	CAB + RPV LA (n=430)				
	Belgium (n=71)	France (n=171)	Germany (n=54)	The Netherlands (n=38)	Spain (n=96)
HIV-1 RNA <50 copies/mL	67 (94)	141 (82)	44 (81)	34 (89)	87 (91)
HIV-1 RNA ≥50 copies/mL	0	1 (<1)	1 (2)*	0	1 (1)
No virologic data	4 (6)	29 (17)	9 (17)	4 (11)	8 (8)
Discontinued due to AE or death†	3 (4)	19 (11)	8 (15)	4 (11)	6 (6)
Discontinued for other reason	0	4 (2)	1 (2)	0	2 (2)
On study but missing data in window	1 (1)	6 (4)	0	0	0

*Participant met the CVF criterion. †No Grade 5 AEs or deaths were reported.
AE, adverse event; CAB, cabotegravir; CVF, confirmed virologic failure; LA, long-acting; RPV, rilpivirine.

- At the Month 12 Snapshot, 6–17% of participants were classified as having no virologic data across countries (**Table 2**).

Table 3. Safety Summary Through Month 12

Parameter, n (%)	CAB + RPV LA (n=430)				
	Belgium (n=71)	France (n=171)	Germany (n=54)	The Netherlands (n=38)	Spain (n=96)
Any AE*	70 (99)	164 (96)	53 (98)	36 (95)	96 (100)
Drug related	68 (96)	153 (89)	50 (93)	33 (87)	85 (89)
Excluding ISRs	34 (48)	69 (40)	6 (11)	17 (45)	30 (31)
Any Grade ≥3 drug-related AE	1 (1)	18 (11)	1 (2)	2 (5)	3 (3)
Excluding ISRs	1 (1)	6 (4)	0	2 (5)	1 (1)
AEs leading to withdrawal†	4 (6)	19 (11)	9 (17)	4 (11)	6 (6)
Drug related excluding ISRs	2 (3)	13 (8)	2 (4)	3 (8)	1 (1)
Any serious AE	4 (6)	4 (2)	4 (7)	0	3 (3)
Drug-related excluding ISRs	0	1 (<1)‡	0	0	0

*No Grade 5 AEs or deaths were reported. One Grade 4 drug-related AE (suicidal ideation) was reported. †Treatment withdrawal. ‡Suicidal ideation, n=1.
AE, adverse event; CAB, cabotegravir; ISR, injection site reaction; LA, long-acting; RPV, rilpivirine.

- Drug-related Grade ≥3 adverse events (AEs) occurred in ≤5% of participants across all countries except France (11% [n=18/171]), which was largely driven by injection site reactions (ISRs) (n=12) (**Table 3**).
- AEs leading to treatment withdrawal ranged 6–17% across countries.

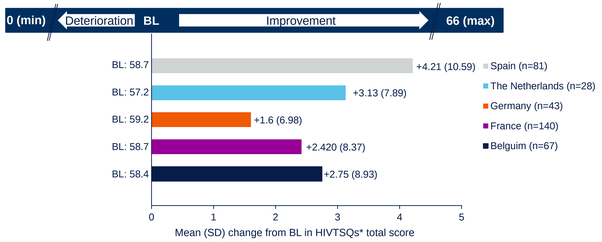
Table 4. ISR Summary Through Month 12

Parameter	CAB + RPV LA (n=430)				
	Belgium (n=71)	France (n=171)	Germany (n=54)	The Netherlands (n=38)	Spain (n=96)
Participants with injections, n (%)	70 (99)	167 (98)	53 (98)	37 (97)	96 (100)
Number of injections	982	2258	670	496	1438
ISR events, n*	447	700	202	142	367
Pain, n (% of injections)	325 (33)	601 (27)	161 (24)	129 (26)	317 (22)
Discomfort, n (% of injections)	63 (6)	8 (<1)	8 (1)	5 (1)	10 (<1)
Induration, n (% of injections)	27 (3)	30 (1)	7 (1)	0	10 (<1)
Nodule, n (% of injections)	9 (<1)	41 (2)	0	1 (<1)	6 (<1)
Swelling, n (% of injections)	9 (<1)	6 (<1)	15 (2)	7 (1)	0
Grade 3, n (% of ISR events)†	0	24 (3)	1 (<1)	1 (<1)	4 (1)
Median duration (IQR), days	3 (2–4)	4 (3–7)	4 (2–6)	3 (2–6)	3 (2–6)
Participant withdrawal due to injection-related reasons, n (% of participants with injections)‡	2 (3)	7 (4)	8 (15)	2 (5)	6 (6)

*A single injection could result in more than one ISR. The five most common ISRs overall are listed. †There were no Grade 4 or 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; CAB, cabotegravir; IQR, interquartile range; ISR, injection site reaction; LA, long-acting; RPV, rilpivirine.

- Most ISRs were Grade 1 or 2 (97–100%) in severity, with a median duration of 3–4 days (**Table 4**).
- Discontinuations due to injection-related reasons ranged 3–15% across countries, with over half occurring due to injection site pain (56% [n=14/25]).

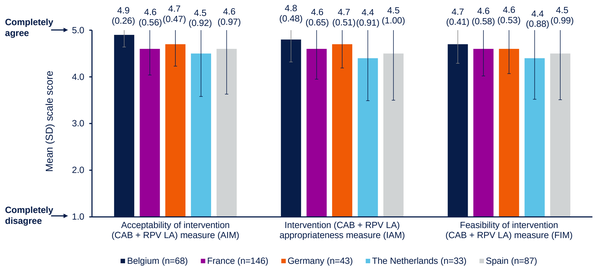
Figure 3. Change in Treatment Satisfaction Score* at Month 12



*HIVTSQs: 12-item version.[9] Range per item is 0–6: 0 = "very dissatisfied" and 6 = "very satisfied." Total score = sum of items 1–11; item 12 is not included in total score. Range for total score is 0–66; positive changes indicate improvement.
BL, baseline; HIVTSQs, HIV Treatment Satisfaction Questionnaire status version; SD, standard deviation.

- Mean HIVTSQs total scores at baseline (57.2–59.2) were high across all countries, with numerical increases at Month 12 (+1.60 to +4.21) (**Figure 3**), which were comparable to the overall mean change in HIVTSQs (+2.84).[10]

Figure 4. Acceptability, Appropriateness, and Feasibility* of CAB + RPV LA Q2M at Month 12



*Acceptability, appropriateness, and feasibility measures are rated on a 1–5 Likert scale: 1 = "completely disagree"; 2 = "disagree"; 3 = "neither agree nor disagree"; 4 = "agree"; 5 = "completely agree." †Belgium feasibility of intervention, n=67.
AIM, acceptability of intervention measure; CAB, cabotegravir; FIM, feasibility of intervention measure; IAM, intervention appropriateness measure; LA, long-acting; Q2M, every 2 months; RPV, rilpivirine; SD, standard deviation.

- At Month 12, participants found CAB + RPV LA treatment highly acceptable, appropriate, and feasible across countries (mean AIM/IAM/FIM scores ≥4.5/4.4/4.4) (**Figure 4**).

Conclusions

- Across diverse European clinical settings and participants with varied implementation setups, CAB + RPV LA dosed Q2M demonstrated high effectiveness at Month 12, with 81–94% of participants across countries maintaining HIV-1 virologic suppression and only one participant meeting the CVF criterion overall (0.23%).
- CAB + RPV LA was well tolerated across all countries, with pain being the most commonly reported ISR; ISRs were mostly Grade 1 or 2 and short-lived (median 3–4 days).
- Participant satisfaction with CAB + RPV LA was high at baseline (57.2/66–59.2/66) and improved across every country (+1.60 to +4.21).
- High and comparable levels of acceptability, appropriateness, and feasibility of CAB + RPV LA were observed across all countries.
- These data support CAB + RPV LA as a complete regimen for the maintenance of virologic suppression in PWH across diverse European healthcare settings.

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