Real-World Outcomes With Long-Acting Cabotegravir Plus Rilpivirine in People With HIV-1 Aged ≥50 Years: A Systematic Literature Review

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Key Takeaways

- This systematic literature review identified 494 real-world publications reporting long-acting cabotegravir plus rilpivirine (CAB+RPV LA) use, of which 13 non-overlapping cohorts reported clinical outcomes for 4371 adults aged ≥50 years with HIV-1, a population with high baseline multimorbidity and polypharmacy
- Across publications, virologic suppression was consistently high, ranging from 89% to 100%, and virologic failure was uncommon, ranging from 0% to 2%
- Treatment persistence ranged from 69% to 89% over ≥1 year of follow-up, and safety- or tolerability-related discontinuations were low
- Adherence was consistently high across publications, and the most common reason for switching to CAB+RPV LA was comfort or quality of life (as reported in 2 publications); 1 publication reported treatment satisfaction, finding it increased over a 1-year period

Plain Language Summary

- This review looked at published data from routine clinic visits around the world to study how well long-acting cabotegravir plus rilpivirine, an HIV treatment given as injections 6 or 12 times a year, works for people with HIV-1 and aged 50 years and older
- Researchers found 13 publications with results from 4371 people across the United States, Europe, and Asia, most of whom were living with other health conditions and taking several other medicines
- The medicine kept the virus under control in the majority of people, and very few had treatment that stopped working; this was similar to how treatment works in people younger than 60 years
- Most people stayed on the injections, with 69% to 89% still using them for over a year; few stopped because of side effects, the most common being a reaction where the injection was given
- Few studies reported asking older people directly about their experiences; in the 2 studies that did ask, most people switched from daily pills to injections because the injections were more comfortable, and 1 study looked at how satisfied people were with their treatment and found that satisfaction went up after they switched to long-acting cabotegravir plus rilpivirine

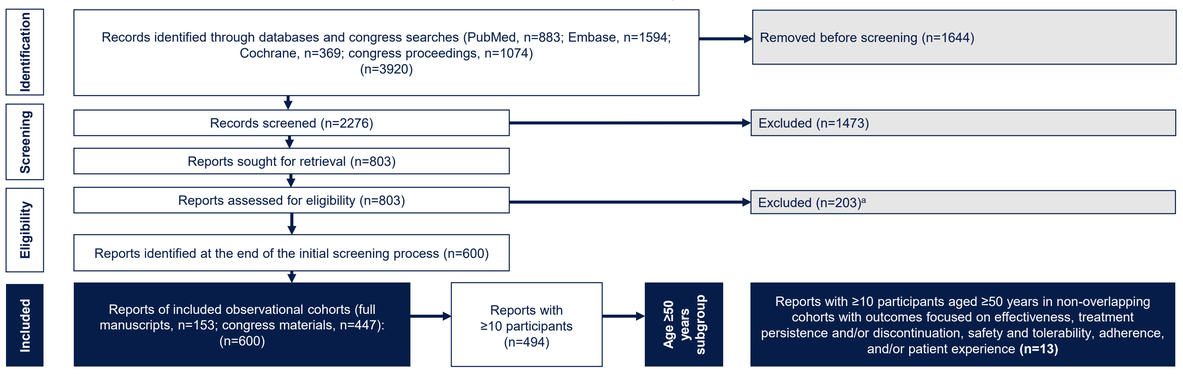
Introduction

- Driven by improvements in HIV management and the success of antiretroviral therapy (ART), over 70% of people with HIV are expected to be ≥50 years by 2030, a demographic experiencing increasing rates of multimorbidity, polypharmacy, and accelerated aging compared with the general population[1-3]
  - Guidelines recommend treatment simplification to minimize drug interactions and cumulative toxicities while maintaining virologic suppression[4-6]
- Cabotegravir (CAB) plus rilpivirine (RPV) is the first and only complete long-acting (LA) injectable regimen approved for people with HIV-1 and suppressed viral load administered 6 or 12 times a year[7-10]
  - CAB+RPV LA has a low potential for drug-drug interactions and eliminates the daily pill burden, potentially addressing some adherence concerns in older adults with HIV-1 on multiple medications[4,6-8]
- Pooled phase 3 analyses have demonstrated the efficacy and safety of CAB+RPV LA in adults aged ≥50 years with suppressed viral load,[11] with recent findings also supporting its use in adults aged ≥60 years with a high burden of comorbidities and concomitant medications[12]
- Real-world evidence (RWE) can complement these clinical trial findings by providing broader evidence on outcomes with CAB+RPV LA among older people in routine clinical practice
- Here, we present findings from a systematic literature review (SLR) of RWE studies reporting outcomes in people with HIV-1 aged ≥50 years using CAB+RPV LA

Methods

- An ongoing SLR of RWE studies reporting outcomes with CAB+RPV LA was conducted following Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines
- Literature searches were conducted in Embase®, PubMed®, and Cochrane Library databases, supplemented by manual searches of major international HIV congresses to capture both journal articles and congress presentations from January 2020 to March 2026 (Figure 1)
- Eligible RWE studies reported outcomes in ≥10 people aged ≥50 years in routine clinical practice or non-interventional settings
- Publications, defined here as peer-reviewed manuscripts and congress proceedings, were assessed for overlapping cohorts to avoid double-counting
- Clinical endpoints were synthesized descriptively

Figure 1. SLR PRISMA Flowchart



[a]Reasons for exclusion: intervention, n=50; study design, n=33; publication type, n=55; outcomes, n=36; lack of sufficient information for individuals using CAB+RPV LA, n=20; presentation was withdrawn or presumed to have been withdrawn from congress, n=4; full text was not available or encore included instead, n=2; abstract or final presentation with incomplete data, n=1; unclear if the study included individuals using CAB+RPV LA, n=1; individual in the study died from other complications soon after starting CAB+RPV LA, n=1.

Results

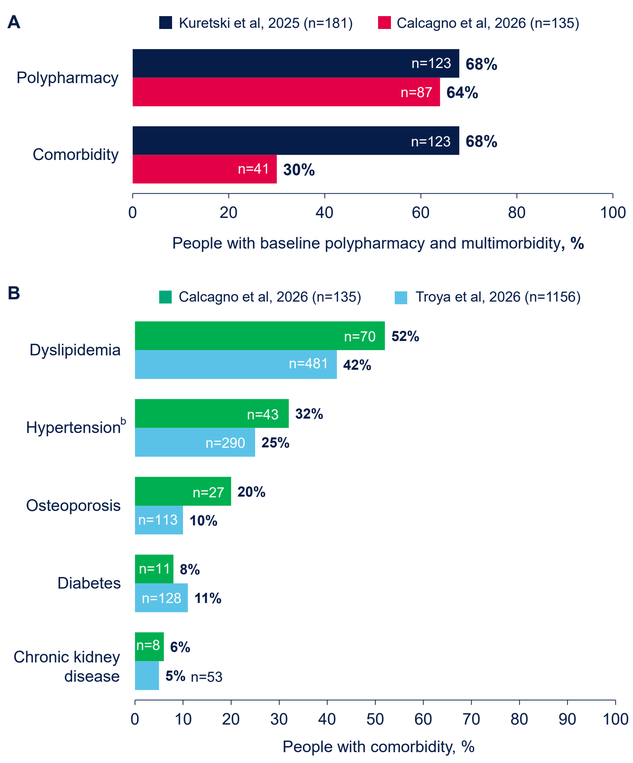
Overview of RWE Included

- The SLR identified 494 publications reporting CAB+RPV LA use in ≥10 people, representing 133 unique cohorts and 45,596 people with HIV-1
- Of these, 13 non-overlapping cohorts reported outcomes data for 12,784 people with HIV-1, of which 4371 people were aged ≥50 years and comprise this analysis[13-25]
- All publications reported the threshold for older adults as ≥50 years, except for 1, which used ≥65 years[23]
- The included cohorts represented routine clinical practice, comprising 6 cohorts from the United States[13,15-17,21,22]; 2 from Spain[20,25]; 1 each from Italy,[23] the United Kingdom,[14] Taiwan,[18] and Japan[24]; and 1 multi-country European cohort[19]

Comorbidity and Polypharmacy Burden at Baseline

- 4 publications reported baseline concomitant medication use and/or multimorbidity[16,20,23,25]
  - 2 publications (316 people aged ≥50 years) specifically reported polypharmacy and multimorbidity[16,23] (Figure 2A) and 2 (1291 people aged ≥50 years) reported rates of common comorbidities in older adults with HIV-1 (Figure 2B)[20,23]
  - 2 publications (1382 people aged ≥50 years), which included both people aged <50 and ≥50 years, reported higher baseline rates of comorbidities or greater use of concomitant medications among people aged ≥50 years[20,25]

Figure 2. Baseline (A) Polypharmacy and Multimorbidity,[a] and (B) Comorbidity Prevalence in People Aged ≥50 Years

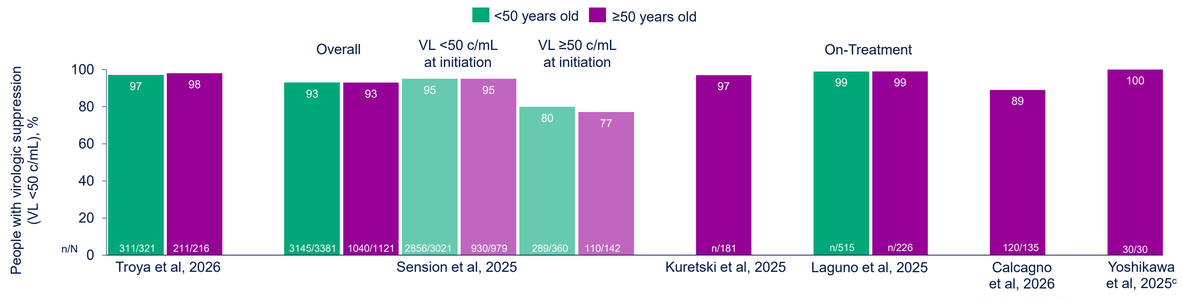


[a]Baseline polypharmacy was defined as ≥5 concomitant medications, excluding ART in both publications; multimorbidity definitions varied between studies (≥2-3 non-communicable diseases).[b]Osteoporosis included osteopenia in Troya et al, 2026.

Effectiveness

- 8 publications reported effectiveness outcomes in 3124 people aged ≥50 years,[16-18,20,22-25] with 6 reporting virologic suppression[16,20,22-25] and 7 reporting virologic failure[16-18,20,22,23,25] in 3037 and 3094 people aged ≥50 years, respectively
- Overall, high virologic suppression rates were reported in people with HIV-1 aged ≥50 years across publications, with rates from 89% to 99%[16,20,22-25]
  - 3 publications demonstrated similar virologic suppression rates in people aged ≥50 vs <50 years (Figure 3)[20,22,25]
- Virologic failure was infrequent across publications, with 28 cases reported, and rates ranging from 0% to 2% in people aged ≥50 years (Table 1)[16-18,20,22,23,25]; 3 publications (222 people aged ≥50 years) reported no individuals aged ≥50 years experienced virologic failure[17,18,23]
  - No significant differences in virologic failure rates were observed between people aged ≥60 years and <60 years (odds ratio: 0.39 [0.01-2.49])[20]
  - Data on virologic failure with resistance were limited, with only 2 publications (1337 people aged ≥50 years) reporting rates of virologic failure with resistance from <1% to 2% in people aged ≥50 years[16,20]
  - 1 publication (1156 people aged ≥50 years)[20] reported 83% (5/6) of people switched to cobicistat-boosted darunavir plus emtricitabine and tenofovir alafenamide after experiencing virologic failure, with 50% (3/6) re-suppressing at the time of data cut-off[26]

Figure 3. Virologic Suppression in People Using CAB+RPV LA by Age Group



IQR, interquartile range; NR, not reported; VL, viral load. [a]Individuals were grouped into people aged <50 and ≥50 years in Troya et al, Kuretski et al, Laguno et al, and Yoshikawa et al; people aged 18-49 and ≥50 years in Sension et al; and people aged ≥65 years for Calcagno et al. Younger age groups are shown for context, where reported by individual publications; between-group comparison was not an objective of this review. [b]Reflects median (IQR) time on CAB+RPV LA for complete initiators aged 18-49 years (N=3567) was 15 (8-25) months, for complete initiators aged 50-64 years (N=979) was 19 (11-28) months, and for complete initiators aged ≥65 years (N=202) was 18 (9-30) months. Median (IQR) follow-up time for complete initiators with VL <50 c/mL at initiation (N=4153) was 16 (9-26) months and for complete initiators with VL ≥50 c/mL at initiation (N=516) was 15 (8-26) months. [c]Yoshikawa et al reported that all participants in the overall effectiveness population had a suppressed viral load (117/117). Age-stratified effectiveness outcomes were not reported. Of 121 participants enrolled, 30 were aged ≥50 years; the ages of the 4 participants excluded from the effectiveness population were not reported. [d]Follow-up time reported for the overall cohort, including people aged ≥50 years.

Table 1. Virologic Failure and Related Outcomes in People Aged ≥50 Years Using CAB+RPV LA

Publication	People aged ≥50 years/overall cohort, n/N (%)	Follow-up time	Virologic failure definition	Virologic failure, n/N (%)	RAMs at virologic failure, n/N (%), details/no/NR	Historic RAMs among virologic failure, yes, n/N (%), details/no/NR	Post–virologic failure regimen, n/N (%)	Re-suppression post–virologic failure, n/N (%)
Kuretski et al, 2025[16]	181/181 (100)	NR	NR	3/181 (2)	3/181 (2) RPV: 2 CAB/RPV: 1	NR	NR	NR
Bhayani et al, 2025[17]	47/100 (47)	2 years[a]	NR	0/47 (0)	NR	NR	NR	NR
Cheng et al, 2025[18]	40/229 (18)	13 months[a]	2 consecutive VLs >200 c/mL	0/40 (0)	NR	NR	NR	NR
Troya et al, 2026[20,b]	1156/3145 (37)	Median (IQR), months: 50-59 years: 14 (9-19); 60-69 years: 15 (9-19); 70-79 years: 11 (5-15); ≥80 years: 9 (3-16)[c]	2 consecutive VLs ≥200 c/mL or a single value >500 c/mL	6/1156 (1)	4/1156 (<1) NNRTI: 3 INSTI: 3	1/6 (17) NNRTI: 1	DRV/c/FTC/TAF: 5/6 (83) DTG/3TC+DOR: 1/6 (17)	3/6 (50)
Sension et al, 2025[22]	1309/5264 (25)	Median (IQR), months: 50-64 years: 19 (11-28) ≥65 years: 18 (9-30)[e]	2 consecutive VLs ≥200 c/mL or discontinuation preceded by 1 VL ≥200 c/mL	11-16[d]/1309 (1)	NR	NR	NR	NR
Calcagno et al, 2026[23,f]	135/135 (100)	Median (95% CI): 17.4 (1.0-76.0) months	NR	0/135 (0)	NR	NR	NR	NR
Laguno et al, 2025[25]	226/741 (30)	52 weeks[a]	2 consecutive VLs ≥50 c/mL	3/226 (1)	NR	NR	NR	NR

c, cobicistat; CVF, confirmed virological failure; DOR, doravirine; DRV, darunavir; FTC, emtricitabine; HIPAA, Health Insurance Portability and Accountability Act; INSTI, integrase strand transfer inhibitor; IQR, interquartile range; NNRTI, non-nucleoside reverse transcriptase inhibitor; NR, not reported; RAM, resistance-associated mutation; TAF, tenofovir alafenamide; 3TC, lamivudine; VL, viral load. [a]Follow-up time reported for the overall cohort, including people aged ≥50 years. [b]RAMs at virologic failure, historic RAMs, post–virologic failure regimen, and re-suppression post–virologic failure data from Buzón-Martín et al. *J Antimicrob Chemother*. 2025; 80:3438-3451. [c]Reflects time on CAB+RPV LA. [d]11 reported to have CVF among people who had VL <50 c/mL at initiation and were aged 50-64 years and ≤5 individuals with virologic failure among people who had VL ≥50 c/mL at initiation and were aged ≥65 years (HIPAA regulations required masking of values of 1 to 5 individuals). [e]Reflects median (IQR) time on CAB+RPV LA for complete initiators. [f]Reports cohort aged ≥65 years only.

Treatment Persistence and/or Discontinuation

- 6 publications (3190 people aged ≥50 years) reported treatment persistence and/or discontinuation outcomes, indicating that most individuals remained on CAB+RPV LA during follow-up and that safety- or tolerability-related discontinuations were generally low (Table 2)[16,20-23,25]
  - Treatment persistence was reported in 4 publications (1853 people aged ≥50 years), with 69% to 89% of individuals remaining on CAB+RPV LA over a median of 12 to 19 months[21-23,25]
  - 5 publications (1881 people aged ≥50 years) described CAB+RPV LA discontinuation rates ranged from 3% to 45% over a 9- to 17-month period, depending on the publication[16,20,21,23,25]
    - In 3 publications (1472 people aged ≥50 years), discontinuations due to safety or tolerability were generally low, with injection site reactions being a common contributor (1%-9%)[16,20,23]

Table 2. CAB+RPV LA Treatment Persistence and Discontinuation

Publication	People aged ≥50 years/overall cohort, n/N (%)	Follow-up time	Persistence rate, n/N (%)	Discontinuation rate, n/N (%)	Other persistence/discontinuation-related outcomes
Kuretski et al, 2025[16]	181/181 (100)	NR	NR	81/181 (45)	• Discontinuations were primarily driven by relocation (43%) rather than safety or tolerability concerns

Troya et al, 2026[20]	1156/3145 (37)	Median (IQR), months:
		50-59 years: 14.0 (8.5-19.1)
		60-69 years: 15.0 (9.1-19.1)
		70-79 years: 11.0 (4.8-15.4)
		≥80 years: 9.0 (2.6-15.6)[a]
			NR	73/1156 (6)	• Permanent discontinuations were 8% (29/370) vs 6% (170/2775) for ≥60 years vs <60 years (OR [95% CI] 1.30 [0.83, 1.98]; *P*=0.211)
					  • Time to permanent D/C was 5.0 and 8.7 months, respectively (*P*=0.077)
					  • Per survival analysis, statistically significant differences were not observed between age groups for any cause of definitive treatment discontinuations[b]

Christopoulos et al, 2025[21]	183/438 (42)	NR	158/183 (86)	25/183 (14)	NR
Sension et al, 2025[22]	1309/5264 (25)[c]	Median (IQR), months: 50-64 years: 19 (11-28) ≥65 years: 18 (9-30)[d]	906/1181 (77)	NR	NR
Calcagno et al, 2026[23]	135/135 (100)[e]	Median (95% CI): 17.4 (1.0-76.0) months	120/135 (89)	15/135 (11)	• The main reasons for interruptions were toxicity or intolerance (including ISRs, myalgia, and fever), participants' choice, or others
Laguno et al, 2025[25]	226/741 (30)	52 weeks[f]	157/226 (69)	n/226 (3)	• No differences between age groups in CAB+RPV LA interruptions

AE, adverse event; D/C, discontinuation; IQR, interquartile range; ISR, injection site reaction; NR, not reported; OR, odds ratio. [a]Reflects time on CAB+RPV LA. [b]Including systemic AEs (*P*=0.136), virologic failure (*P*=0.349), local ISRs (*P*=0.883), or other reasons (*P*=0.234). [c]Complete initiators alive and active in care at time of analysis were 1181/4748 (25%). [d]Reflects cumulative time on CAB+RPV LA. [e]Threshold reported was ≥65 years. [f]Follow-up time reported for the overall cohort, including people aged ≥50 years.

Adherence

- 5 publications (2355 people aged ≥50 years) reported adherence outcomes with varying definitions; adherence to CAB+RPV LA injections was consistently high across publications (Table 3)[13,15,16,19,20]

Table 3. Adherence in People Aged ≥50 Years Using CAB+RPV LA

Publication	People aged ≥50 years/overall cohort, n/N (%)	Follow-up time	Outcomes
Garris et al, 2023[13]	415/947 (44)	Median: 9.3 months[a]	74% (306/415) of people maintained a proportion of days covered ≥90%
Do et al, 2025[15]	526/1226 (43)	NR	• 9% (45/526) of people dropped out before completing the first 2 initiation injections • 24% (124/526) of people missed their scheduled injections post-initiation • 68% (357/526) of people followed their injection schedule, including planned oral bridging therapy every 2 months or once monthly
Kuretski et al, 2025[16]	181/181 (100)	NR	99% (n/1988) injections administered on-time
Peters et al, 2025[19]	77/142 (54)	Median (IQR): 323 (204-466) days[a,b]	0% (0/77) of people missed any injections
Troya et al, 2026[20,c]	1156/3145 (37)	Median (IQR), months: 50-59 years: 14.0 (8.5-19.1) 60-69 years: 15.0 (9.1-19.1) 70-79 years: 11.0 (4.8-15.4) ≥80 years: 9.0 (2.6-15.6)[b]	99% (1102/1113) of people with ≥90% adherence

IQR, interquartile range; NR, not reported. [a]Follow-up time reported for the overall cohort, including people aged ≥50 years. [b]Reflects time on CAB+RPV LA. [c]Adherence outcomes were reported for n=1113 evaluable participants out of the total enrolled cohort aged ≥50 years (N=1156).

Patient Experience

- 3 publications (1428 people aged ≥50 years) reported patient experience[14,20,25]
  - 2 publications (1382 people aged ≥50 years) reported that the most common reason for switching was comfort; other common reasons (≥20% of participants) included patient request, regimen simplification, and interest in new therapeutic options[20,25]
  - 1 publication (46 people aged ≥50 years) found an increase in treatment satisfaction with CAB+RPV LA after 12 months (baseline median [interquartile range] HIV Treatment Status Questionnaire: 59 [48-66]; Month 12: 61.5 [54-66]); treatment satisfaction difference from baseline to Month 12 was not significantly different between older and younger populations (*P*=0.21)[14]
  - 1 publication (226 people aged ≥50 years) reported that people with HIV-1 aged ≥50 years had significantly better pain tolerance and pain perception at baseline than those aged <50 years (*P*=0.007)[25]

Conclusions

- Across 13 real-world publications, CAB+RPV LA use in people aged ≥50 years with highly prevalent multimorbidity and polypharmacy was effective and associated with rare and heterogeneously defined virologic failures (<2%)
- Treatment persistence and adherence were consistently high across studies, with a low rate of safety-related discontinuations
- In publications assessing patient experience, reported findings included comfort and/or quality of life as primary drivers for switching to CAB+RPV LA, as well as increased treatment satisfaction over 12 months post-switch
- Overall, these findings support the real-world effectiveness, tolerability, and persistence of CAB+RPV LA among people aged ≥50 years, including those with multimorbidity and polypharmacy; however, further evidence is needed to better characterize patient experience and longer-term outcomes in this growing population

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