Implementation of Cabotegravir and Rilpivirine Long-Acting (CAB + RPV LA): Primary Results From the CAB + RPV Implementation Study in European Locations (CARISEL)

P069

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Key Takeaways

- We present the results on the acceptability, appropriateness, and feasibility of cabotegravir + rilpivirine long-acting (CAB + RPV LA) dosed every 2 months (Q2M) from the perspective of staff participants through Month 12 of a Phase 3b hybrid type III implementation–effectiveness trial.
- Despite most participating European study sites having no prior CAB + RPV LA experience, high implementation acceptability, appropriateness, and feasibility levels were seen regardless of implementation arm.
- Some context-specific factors, such as time to reach optimal implementation, may benefit from different levels of implementation support.

Introduction

- CAB + RPV LA dosed Q2M is a recommended regimen in European and US treatment guidelines for virologically suppressed people living with HIV-1 (PLWH).[1,2]
- CAB + RPV LA reduces dosing frequency compared with daily oral antiretroviral therapy, and may help address concerns 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 examining strategies to support the implementation of CAB + RPV LA dosed Q2M across five European countries.
  - CARISEL is the first study in which all participants switched from daily oral therapy to CAB + RPV LA dosed Q2M.
  - CAB + RPV LA dosed Q2M was efficacious, with 87% of participants in CARISEL maintaining HIV-1 virologic suppression and 0.7% of participants having HIV-1 RNA ≥50 copies/mL at Month 12 (intention-to-treat exposed, Snapshot analysis).[4]
- Here, we present the results on the acceptability, appropriateness, and feasibility of CAB + RPV LA implementation support from the perspective of staff participants.

Methods

- CARISEL is an open-label, single-arm switch study that enrolled virologically suppressed PLWH to receive CAB + RPV LA dosed Q2M.
- Staff participants at 18 clinics across Belgium (n=4), France (n=6), Germany (n=2), the Netherlands (n=2), and Spain (n=4) were randomized to one of two implementation arms (Enhanced arm [Arm-E] and Standard arm [Arm-S]) to better understand the level of support needed for successful implementation (**Figure 1**; **Table 1**).
- Staff participants completed 4-item measures rated on a 1–5 Likert scale: 1 "completely disagree"; 2 "disagree"; 3 "neither agree nor disagree"; 4 "agree"; 5 "completely agree" on acceptability (AIM), appropriateness (IAM), and feasibility (FIM) of implementation and intervention.
  - An analysis of covariance (ANCOVA) was performed for the statistical analysis of change in AIM, IAM, and FIM of CAB + RPV LA.
- Qualitative data were obtained from semi-structured qualitative interviews on CAB + RPV LA implementation.
  - Interview guide topics were informed by the Exploration, Preparation, Implementation, and Sustainment (EPIS) framework[5] and Proctor outcomes.[6] The EPIS framework highlights key phrases that guide and describe the implementation process and identify common and unique factors within, and across, settings. The Proctor outcomes framework identifies key implementation outcomes that should be considered and evaluated during a study.

Table 1. Implementation Support

	Arm-E	Arm-S
Study treatment injection training (prior to first injection)	Face-to-face*	Virtual
Toolkits (patient/staff participant)	✓	✓
SWAT meeting(s)†	✓	
CQI calls (monthly)	✓	

*Four staff study participants in Arm-E received their injection training remotely rather than face-to-face due to COVID-19 restrictions. †SWAT meetings introduced CAB + RPV LA to clinic staff and discuss what might make implementation easier and/or what might make it difficult prior to first injection at the site. SWAT, skilled wrap-around team.

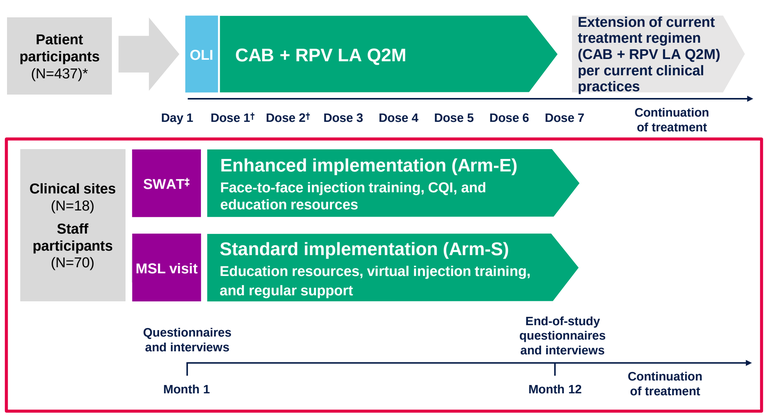
Continuous quality improvement (CQI)

- CQI is a process to support improving routine care by identifying problems, planning a solution, studying the results, and acting accordingly
- The CQI process is documented through Plan, Do, Study, and Act cycles

Two staff participants per site

Monthly calls (Month 2–Month 7)

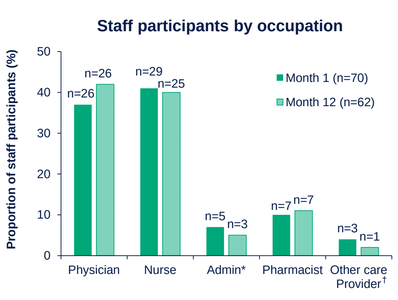
Figure 1. Study Design



*437 patient participants enrolled, 430 received CAB + RPV LA. †Dose 1 was received at Month 1, Dose 2 at Month 2, with the remaining doses Q2M thereafter. ‡Introduce CAB + RPV LA to clinic staff and discuss what might make implementation easier and/or what might make it difficult prior to first injection at the site. Meetings discussed implementation plans, how to work through challenges, as well as how to introduce CQI.
MSL, medical scientific liaison; OLI, oral lead-in.

Results

Figure 2. Baseline Characteristics



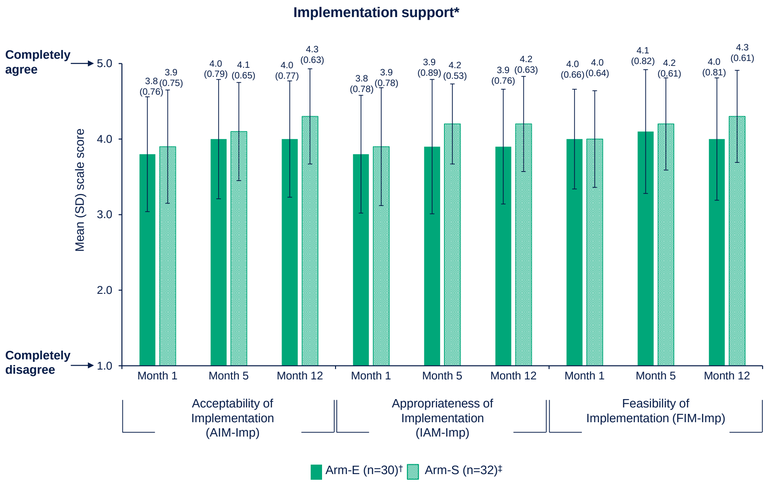
Staff participants by country

Country, n (%)	Month 1 (n=70)	Month 12‡ (n=62)
Belgium	15 (21)	13 (21)
France	25 (36)	22 (35)
Germany	8 (11)	8 (13)
The Netherlands	8 (11)	7 (11)
Spain	14 (20)	12 (19)
Arm, n (%)		
Arm-E	34 (49)	30 (48)
Arm-S	36 (51)	32 (52)

*Two of the admin staff hold a hybrid role of nurse/admin. †An error in the staff participant classification was noticed during the analysis phase: two of the "Other care provider" staff participants were physicians. ‡The primary analysis (n=60) consisted of staff participants with data at Month 1 and Month 12.

- 13 of the 18 clinics (72%) had no previous CAB + RPV LA experience.
- Clinics were evenly distributed across implementation arms (Arm-E, n=9 sites; Arm-S, n=9 sites).
- 70 staff participants completed interviews and surveys at Month 1, and 62 completed them at Month 12 (**Figure 2**).

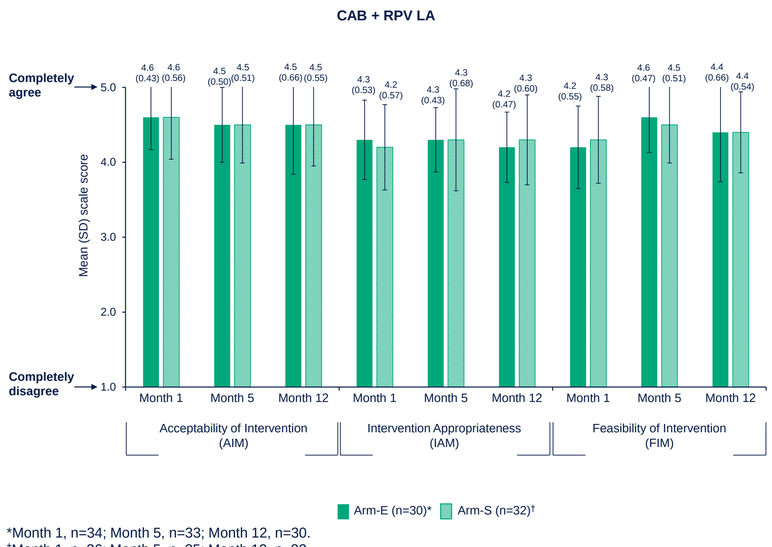
Figure 3. Staff Participant Perception of Acceptability, Appropriateness, and Feasibility of Implementation Support



*The AIM, IAM, and FIM are brief measures of acceptability, appropriateness, and feasibility. All were administered for the CAB + RPV LA (intervention) and the implementation support (noted with "-Imp").
†Month 1, n=34; Month 5, n=33; Month 12, n=30. ‡Month 1, n=36; Month 5, n=35; Month 12, n=32.
SD, standard deviation.

- Mean AIM-Imp/IAM-Imp/FIM-Imp scores remained high (≥3.8) and stable for levels of acceptability, appropriateness, and feasibility of implementation support through Month 12 (**Figure 3**).
- Implementation measure scores were similar over time, regardless of the level of support by implementation arm.
- An ANCOVA (primary analysis, n=60) controlling for provider type showed no significant difference between arms.

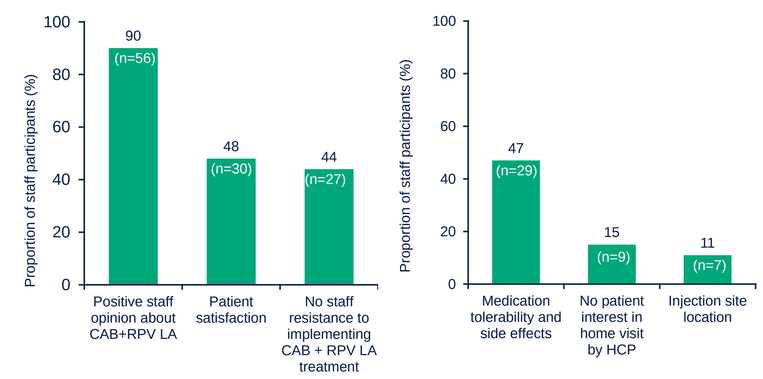
Figure 4. Staff Participant Perception of Acceptability, Appropriateness, and Feasibility of CAB + RPV LA



*Month 1, n=34; Month 5, n=33; Month 12, n=30.
†Month 1, n=36; Month 5, n=35; Month 12, n=32.

- Mean AIM/IAM/FIM scores showed high (≥4.2) and stable scores for acceptability, appropriateness, and feasibility of CAB + RPV LA over time (**Figure 4**).
- All intervention measure scores were similar, regardless of implementation arm.

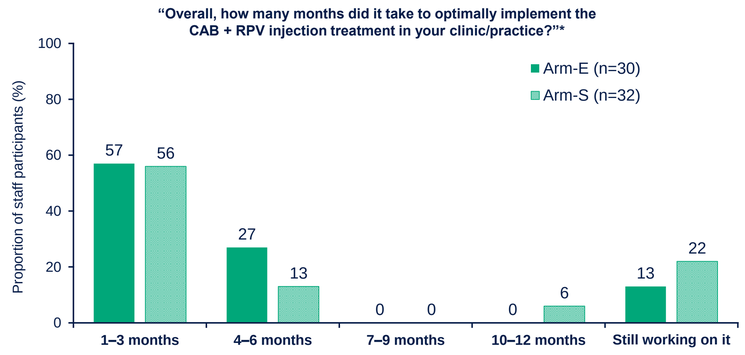
Figure 5. Staff Participant Acceptability at Month 12



*Responses were not mutually exclusive.
HCP, healthcare provider.

- 90% of staff participants reported positive opinion about CAB + RPV LA as a facilitator of acceptability (**Figure 5**).
- Data from semi-structured interviews showed that: CAB + RPV treatment attributes (e.g. reduced dosing frequency) were the strongest drivers of staff participant acceptability, patients found CAB + RPV LA appropriate (data not shown), and feasibility facilitators outnumbered barriers (data not shown).

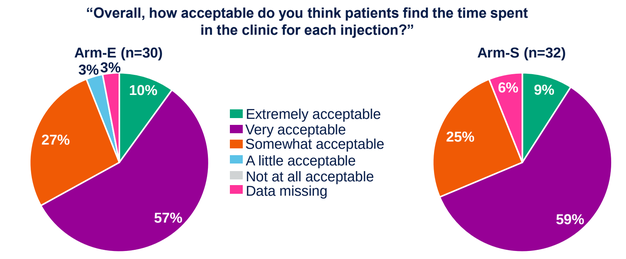
Figure 6. Implementation at Month 12



*Data missing for 1% (n=2/62) of staff participants.

- Overall, 56% (n=35/62) of staff participants reported optimal implementation within 1–3 months, with more Arm-S staff participants (22%, n=7/32) still working on implementation than Arm-E staff (13%, n=4/30) at Month 12 (**Figure 6**).

Figure 7. Time Spent in the Clinic at Month 12



- Time spent in the clinic across study visits averaged 67 minutes in Arm-E and 65 minutes in Arm-S at Month 12.
  - This question did not ask staff participants to exclude study-specific procedures, such as completing two study questionnaires and extensive laboratory tests; time spent in a routine care setting is predicted to be shorter.
- At Month 12, 68% (n=42/62) of staff participants thought the time spent in clinic was "very" or "extremely acceptable" across arms (**Figure 7**).

Conclusions

- In CARISEL, despite most participating European study sites having no prior CAB + RPV LA experience, high implementation acceptability, appropriateness, and feasibility levels were seen regardless of implementation arm.
- Time spent in the clinic was similar between Arm-E and Arm-S, with roughly two-thirds of participants in both arms finding the time spent in clinic either "very" or "extremely acceptable."
- Most staff participants reported optimal implementation within 1–3 months across both arms, with more sites in Arm-S reporting they were still working towards optimal implementation at Month 12 compared with Arm-E.
- CARISEL data show that while acceptability, appropriateness, and feasibility were comparable across arms, there may be some context-specific factors, such as time to reach optimal implementation, that may benefit from different levels of implementation support.
- CAB + RPV LA dosed Q2M was well tolerated and highly effective, with a low rate of virologic failure over 1 year across diverse participants and European clinical settings,[4] complementing the positive implementation results reported by staff participants.

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