Cabotegravir and Rilpivirine Implementation Study in European Locations (CARISEL): Examining Healthcare Staff Attitudes During a Hybrid III Implementation-Effectiveness Trial Implementing Cabotegravir + Rilpivirine Long-Acting Injectable (CAB + RPV LA) for People Living With HIV

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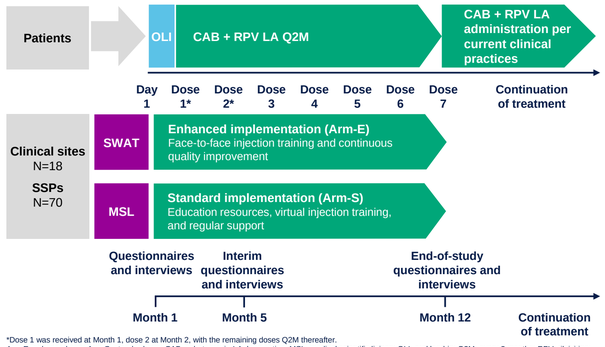
Introduction

- Cabotegravir (CAB) plus rilpivirine (RPV) is the first complete long-acting (LA) regimen recommended by treatment guidelines[1,2] for the maintenance of HIV-1 virologic suppression.
- Intramuscular CAB + RPV LA administered monthly[3–5] or every 2 months[6] may address some challenges associated with daily oral antiretroviral therapy, such as fear of inadvertent disclosure, anxiety related to staying adherent, and the daily reminder of HIV status.
- CARISEL (NCT04399551) is a Phase 3b, multicenter, open-label, hybrid type III implementation-effectiveness trial that examines the acceptability, appropriateness, and feasibility of CAB + RPV LA injections and implementation support in HIV centers across Belgium, France, Germany, the Netherlands, and Spain.
- This interim qualitative analysis summarizes staff study participant (SSP) perspectives on CAB + RPV LA implementation at Month (M)1 and M5.

Methods

- SSPs from 18 clinics across Belgium, France, Germany, the Netherlands, and Spain completed semi-structured qualitative interviews, informed by the Exploration, Preparation, Implementation, Sustainment framework,[7] on CAB + RPV LA implementation.
  - At Month 1, 70 SSPs were interviewed from five countries, 34 for Enhanced Implementation (Arm-E) and 36 for Standard Implementation (Arm-S); most were nurses or physicians, and two SSPs had hybrid nurse/administrative roles.
- Participants in CARISEL were enrolled during the SARS-CoV-2 (COVID-19) pandemic, which has disrupted healthcare service delivery globally and presents potential challenges to starting patients on this novel LA regimen.
- M1 and M5 interview transcripts were analyzed for thematic trends using ATLAS.ti, a data analysis software used for qualitative research.
- A theory-driven approach yielded a thematic analysis for outcomes categorized by the Proctor[8] implementation outcomes framework.
- CARISEL is a two-arm study with centers randomized to Arm-E and Arm-S implementation arms to understand the level of support needed for successful implementation (**Figure 1**).
- CARISEL is also a single-arm switch study for patient study participants.

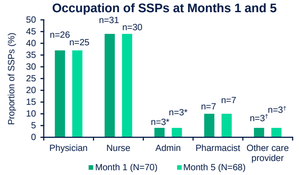
Figure 1. CARISEL Study Design



*Dose 1 was received at Month 1, dose 2 at Month 2, with the remaining doses Q2M thereafter.
Arm-E, enhanced arm; Arm-S, standard arm; CAB, cabotegravir; LA, long-acting; MSL, medical scientific liaison; OLI, oral lead-in; Q2M, every 2 months; RPV, rilpivirine; SSP, study staff participant; SWAT, skilled wrap around team.

Results

Figure 2. SSP Characteristics

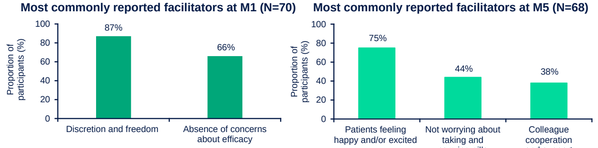


Country and arm of SSPs at Months 1 and 5		
Country, n (%)	**Month 1 (N=70)**	**Month 5 (N=68)**
Belgium	15 (21)	15 (22)
France	25 (36)	23 (34)
Germany	8 (11)	8 (12)
The Netherlands	8 (11)	8 (12)
Spain	14 (20)	14 (21)
Arm, n (%)		
Enhanced arm (Arm-E)	34 (49)	33 (49)
Standard arm (Arm-S)	36 (51)	35 (51)

*Two of the admin staff hold a hybrid role of nurse/admin. †An error in the SSP classification was noticed during the analysis phase: two of the "other care provider" SSPs were physicians. Arm-E, enhanced arm; Arm-S, standard arm; SSP, study staff participant.

- SSP characteristics are shown in **Figure 2**.

Figure 3. Acceptability



M, month.

- At M1, the discretion and freedom of CAB + RPV LA was the top facilitator of acceptability.
- At M5, 75% (n=51/68) of SSPs described that their patients felt happy and/or excited (**Figure 3**).

> *"Not having to take medication every day, having some freedom, with quite a long window of time before the next injection. That's very attractive – it means they don't have to be reminded every day that they're ill."*
> **Physician, Arm-E, France (M1)**

> *"Not having to depend on… daily pills, having to remember, not forgetting, not remembering whether or not they took it already… Patients tell us about it, how comfortable and liberated they feel… Here, we'll get them to come every 8 weeks, give them the treatment and they'll be ready to go home really quickly."*
> **Physician, Arm-S, Spain (M5)**

Table 1. Appropriateness

	Month 1	Month 5
Top facilitators	• Potential for clinic to be seen as a leader • Similarity between CAB + RPV LA and other intramuscular injections • No need to take the pills every day • More discreet treatment • Motivated and adherent patients • Increased adherence	• Clinical infrastructure (including scheduling system) • No need to think about/carry pills • Suitable for patients with difficulty taking oral medication • Appointment flexibility • More discreet treatment
Top barriers	• Patients not wanting to be injected • Patients not adherent to oral medication • Patients not wanting to change treatments • Patients medically unsuitable for treatment • Potential reorganization of scheduling system • No previous experience with cold chain storage	• Number of visits • Work-related scheduling challenges

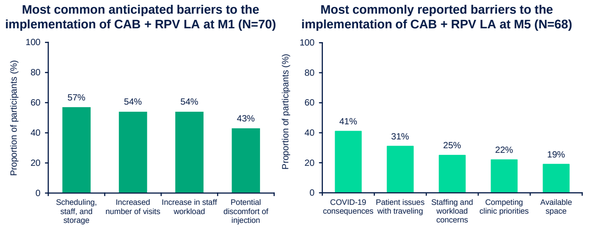
CAB, cabotegravir; LA, long-acting; RPV, rilpivirine.

- More facilitators related to appropriateness of CAB + RPV LA were reported vs. barriers (**Table 1**).
  - Both barriers and facilitators of appropriateness changed as staff gained more experience with CAB + RPV LA.

> *"It will disrupt things a bit, because it's a new method of administration so you need to totally rethink how you organize things. Yes, it's disruptive, but it's more a case of adapting than it being a problem. You need to find new methods to ensure you're dealing with the medication correctly."*
> **Physician, Arm-E, France (M1)**

> *"They're happy, liberated. They feel freer. The last one told me that each time they take their pill, that reminds them that they're sick. But now they come for an injection and then they're happy for two months. For two months, they're not sick… It frees them, yes. And also there isn't that fear that someone will discover their box of meds and ask about it. It frees them."*
> **Nurse, Arm-S, France (M5)**

Figure 4. Barriers to Feasibility



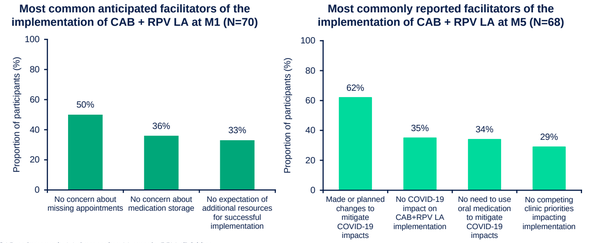
CAB, cabotegravir; LA, long-acting; M, month; RPV, rilpivirine.

- At M1, the most common anticipated implementation barriers included scheduling, staff, and storage concerns (**Figure 4**).
- At M5, as staff gained experience administering CAB + RPV LA in their clinic, staffing and workload issues became less frequently reported, with ≤25% identifying these as barriers.
- SSP-reported barriers to the feasibility of implementing CAB + RPV LA decreased from M1 to M5.

> *"It's not easier, because giving an injection is more time-consuming than writing a prescription. There is a bit more involved, but it is doable if you have practice and the right staff."*
> **Pharmacist, Arm-E, Germany (M1)**

> *"I think COVID might influence people not being very eager to come to the hospital. They're a bit scared to get to the hospital."*
> **Physician, Arm-E, the Netherlands (M5)**

Figure 5. Facilitators of Feasibility



CAB, cabotegravir; LA, long-acting; M, month; RPV, rilpivirine.

- At M1, minimal concerns about the feasibility of implementation by clinic staff were noted.
- At M5, the ease of implementing CAB + RPV LA during the COVID-19 pandemic was a facilitator for overall implementation in European clinics (**Figure 5**).

> *"It's not hard to administer. But it wouldn't be logistically feasible to have all our patients come for injectable treatments. There are limits to our capacity."*
> **Physician, Arm-S, Germany (M1)**

> *"I've not adapted at all. Since the first day of the first lockdown, we've changed nothing at all in terms of how we work. We've kept our opening hours. Even during lockdown, we were open to patients. They were able to come and get their treatment. That was the first lockdown. Since then, it's been quite easy. Patients come in the morning, that's not going to change."*
> **Pharmacist, Arm-S, France (M5)**

Figure 6. Top Five Patient Needs Met by CAB + RPV LA

Top five most frequently reported needs met at M1 (N=70)	Top five most frequently reported needs met at M5 (N=68)
1. No need to take pills every day	1. No need to think about and/or carry pills
2. Increased adherence	2. Need for discreet treatment
3. More discreet treatment	3. No need to take medication daily
4. No need to worry/think about taking the pills	4. Need for increased treatment adherence
5. No daily reminder of HIV status	5. Need for not being reminded of HIV status

CAB, cabotegravir; LA, long-acting; M, month; RPV, rilpivirine.

- At M1, SSPs reported that the elimination of daily oral therapy burden was the top need met by CAB + RPV LA (**Figure 6**).
- Overall, adherence, convenience, discretion, and decreased stigma were reasons that SSPs believed CAB + RPV LA was a good fit for their patients.

> *"There is a benefit especially for the patients who… don't take their medication very well. They forget it. There are lots of patients who forget it like two, three, four times a month. For those patients, it's very convenient that they only have to come every 2 months for an injection, and for the rest, they don't have to think about the medication anymore."*
> **Nurse, Arm-S, Belgium (M1)**

> *"The feedback we get from patients is very, very positive… The impression we get often is that it's been life changing. That's what most patients tell us. Even though some have a terrible fear of needles, they say that they've found positives, and that's what they focus on. All the benefits of the injections. So they prefer to have a bit of stress when they get the injections, but it's really changed their lives. It's very positive."*
> **Nurse, Arm-E, France (M5)**

Conclusions

- Qualitative data from SSPs showed that the elimination of worry about taking pills and daily HIV reminders, as well as increased treatment discretion, were factors supporting the need for, and benefit of, CAB + RPV LA treatment for people living with HIV.
- SSPs reported their patients were positive about taking CAB + RPV LA.
- At M1, scheduling, staffing, and storage were identified as potential concerns related to the feasibility of implementation. By M5, these were no longer reported as top concerns.
- This study began during the COVID-19 pandemic; many SSPs reported COVID-19 mitigation strategies were a facilitator for implementation.
- Qualitative interim data through M5 of the CARISEL study suggest that SSPs across five European countries find CAB + RPV LA implementation acceptable, appropriate, and feasible, even during the COVID-19 pandemic.

Acknowledgments

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