Top Practices for Implementing Cabotegravir (CAB) and Rilpivirine (RPV) Long-Acting (LA) in European Clinics

Julián Olalla[1], Cassidy Gutner[2], Miguel Pascual-Bernaldez[3], Beatriz Hernandez[3], Samia Dakhia[4], Laurence Slama[5], María José Crusells Canales[6], Thomas Lutz[7], Marc van der Valk[8], Berend van Welzen[9], Eric Florence[10], Nicola Barnes[11], Owen Cooper[11], Dina Filipenko[11], Maggie Czarnogorski[2]

[1]Hospital Costa del Sol, Marbella, Spain; [2]ViiV Healthcare, Research Triangle Park, NC, United States; [3]ViiV Healthcare, Madrid, Spain; [4]ViiV Healthcare, Brentford, United Kingdom; [5]Hôpital Hôtel-Dieu, Paris, France; [6]Hospital Clinico Lozano Blesa, Zaragoza, Spain; [7]Infektio Research, Frankfurt, Germany; [8]Department of Infectious Diseases, Amsterdam Infection and Immunity Institute, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands; [9]UMC Utrecht, Utrecht, The Netherlands; [10]Instituut voor Tropische Geneeskunde, Antwerpen, Belgium; [11]Evidera, London, United Kingdom

P008

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.
- CAB + RPV LA administered monthly[3,4] or every 2 months[5] may address some issues associated with daily oral antiretroviral therapy (ART), such as fear of inadvertent disclosure, anxiety with staying adherent and the daily reminder of HIV.
- CAB + RPV LA also represents a paradigm shift in how HIV treatment has been delivered from oral therapy.
- CAB And RPV Implementation Study in European Locations (CARISEL; NCT04399551) examines two implementation packages to support the integration of CAB + RPV LA administered every 2 months into HIV clinics across Belgium, France, Germany, the Netherlands and Spain.
- Delivery of CAB + RPV LA may present different challenges across healthcare systems. Understanding which practices support implementation from this study is important to support real-world efforts.
- The aim of this interim analysis was to identify top practices for CAB + RPV LA implementation from staff study participants (SSPs) over the first 7 months of implementation, regardless of which implementation strategy they were randomised to.

Methods

- CARISEL is a hybrid type III implementation-effectiveness, Phase 3b, two-arm study investigating the level of support needed for successful implementation of CAB + RPV LA administered every 2 months.
- The study began in September 2020 and ended in February 2022.
- COVID-19 prevalence changed throughout the study. Notably, implementation of CAB + RPV LA began during the second wave of COVID-19 in Europe (**Figure 1**).
- SSPs from 18 clinics across Belgium, France, Germany, the Netherlands and Spain were randomised to receive one of two implementation support packages (**Figures 2–4**).
- All SSPs completed quantitative assessments and qualitative interviews at Month 1 and Month 5. Two SSPs from each Arm-E site participated in continuous quality improvement (CQI) calls monthly for 6 months. Data from all three of these sources contributed to the synthesis of top implementation practices reported herein.

Figure 1. Confirmed 7-Day Average Daily COVID-19 Cases in the 5 European Countries During the CARISEL Study Period[6]

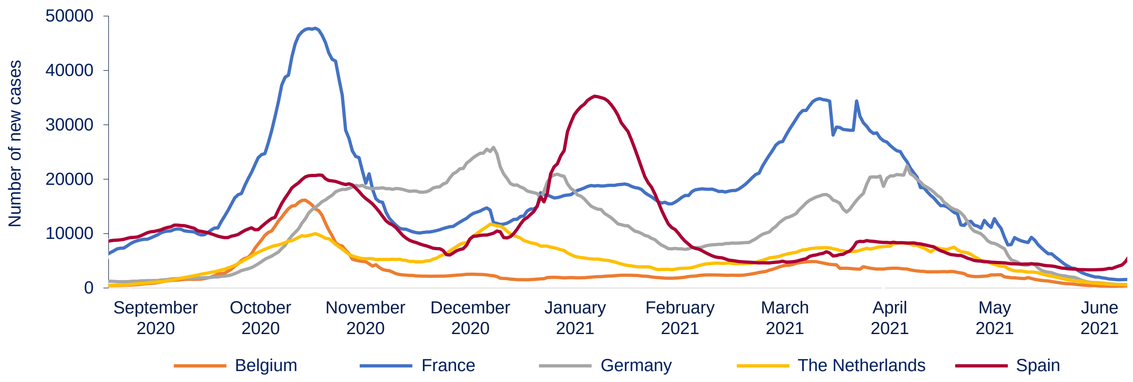
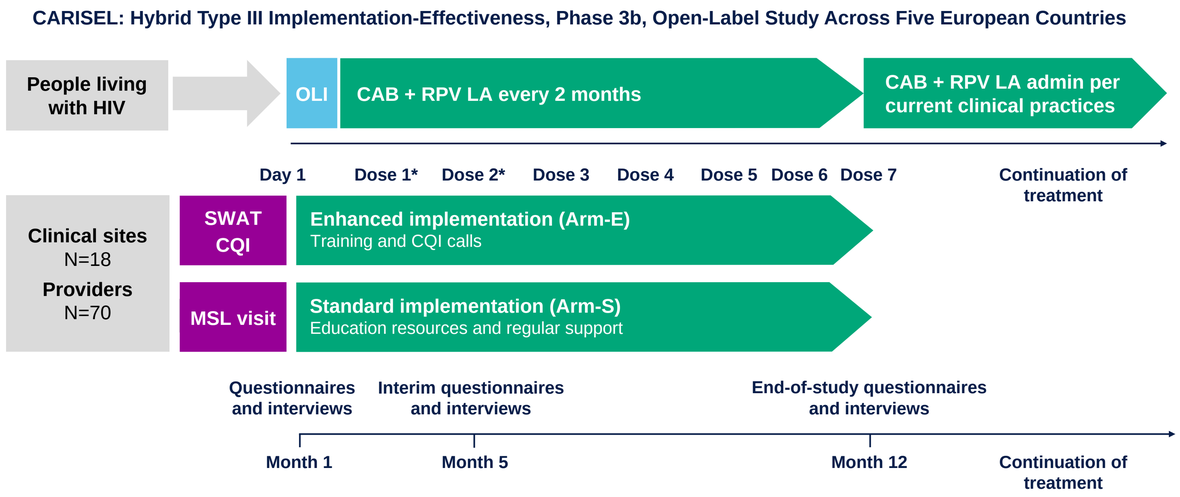


Figure 2. Study Design



*Dose 1 was received at Month 1, Dose 2 at Month 2, with the remaining doses every 2 months thereafter.
MSL, medical scientific liaison; OLI, oral lead-in; SWAT, skilled wrap around team.

Figure 3. Arm-E and Arm-S Components

	Arm-E	Arm-S*
Study treatment injection trainings (prior to first injection)†	✓	✓
Toolkits (patient/SSP)	✓	✓
SWAT meeting(s)	✓	
CQI calls (monthly)	✓	

*Meetings with MSLs could occur as needed in accordance with general support provided when a new treatment is available.
†Arm-E training was face-to-face and Arm-S training was virtual.

Figure 4. Arm-E Implementation Support

What Is Needed, In What Context, To Best Support Implementation?

SWAT MEETING(S):

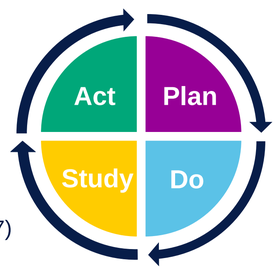
- Identify and discuss what might make implementation easier and/or what might make it difficult prior to first injection at the site.
- Discuss a plan to work through challenges.
- Ask questions about implementation and CAB + RPV LA.
- Introduce CQI calls.

CONTINUOUS QUALITY IMPROVEMENT:

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

Two staff participants per site

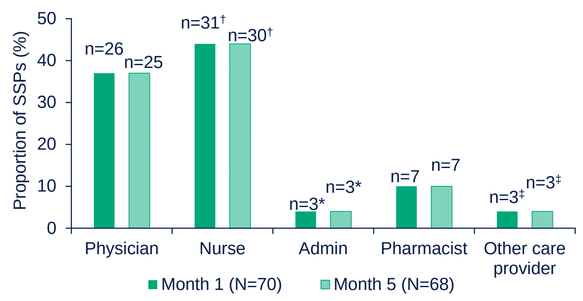
Monthly calls (Month 2–Month 7)



Results

Figure 5. SSP Characteristics*

SSPs by occupation



SSPs by country and study arm§

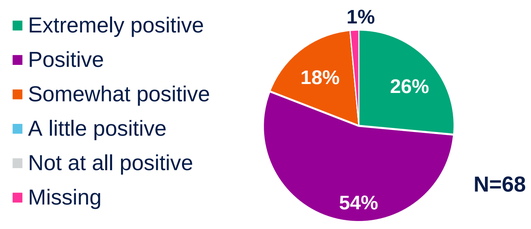
Country, n (%)	Month 1 (N=70)	Month 5 (N=68)
Belgium	15 (21.4)	15 (22.1)
France	25 (35.7)	23 (33.8)
Germany	8 (11.4)	8 (11.8)
The Netherlands	8 (11.4)	8 (11.8)
Spain	14 (20.0)	14 (20.6)
Arm, n (%)		
Enhanced arm (Arm-E)	34 (48.6)	33 (48.5)
Standard arm (Arm-S)	36 (51.4)	35 (51.5)

*Two SSPs left the study after Month 1 due to long-term leave (n=1) and termination of employment (n=1).
†Two of the nurse 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.
§Percentages are rounded to one decimal place and therefore may not equal 100%.

- SSPs who responded at Month 1 (N=70) and Month 5 (N=68) included physicians, nurses, pharmacists, administrators and other care providers (**Figure 5**).

Figure 6. Overall View of Implementation of CAB + RPV LA

- At the interim (Month 5), 81% of SSPs felt positive or extremely positive about implementation of CAB + RPV LA in their clinic (**Figure 6**).



Top Practices

- Trends emerged across sites about clinic processes during the first few months of implementation.
- Practices associated with excellence in delivery across all countries included:

Top Practice	Key Findings
Creating an implementation plan	Each clinic undertook planning activities to support implementation in their clinics, although, when directly asked, not all identified formally creating an implementation plan at the start of the study.
Educating clinic staff on clinical efficacy	Staff having a strong understanding of the CAB + RPV LA clinical efficacy early in implementation was important.
Training staff on injection administration and management of potential pain/discomfort post-injection	Information from CQI calls highlighted that injection training, in person or virtual, was key for injectors.

Figure 7. SSP Top Practice Recommendations

Clinical efficacy

- Obtain training on clinical efficacy and comparison to oral ART
- Obtain education about the importance of the dosing window

Injection education

- Obtain training on intramuscular injections
- Obtain education on potential anticipated pain and discomfort with early injections
- Ensure patients are aware that any pain and discomfort are expected to decrease over time to alleviate concerns

Implementation planning*

- Create a plan for how medication gets to the clinic (medication delivered to clinic by staff versus patient)
- Assess the potential impact of medication collection on appointment time
- Assess the potential impact of pharmacy hours on injection appointments
- Identify injectors and how many are needed to provide sick and holiday coverage
- Identify the ideal number of injections/day
- Identify space for the injection administration
- Identify process for vial differentiation

*When directly asked, many felt that a planning phase has not been needed, yet were able to articulate their plans.

- The majority (67%) of SSPs across both arms expressed satisfaction with overall training, noting that injection training, in person or virtual, was key for injectors new to gluteal intramuscular injections.

Conclusions

- Data from the CARISEL study suggest that top practices appear to be successful at supporting SSPs' ability to implement treatment efficiently across both enhanced and standard support.
- SSPs identified several top implementation practices within the first 7 months of every 2 month CAB + RPV LA implementation in the CARISEL study.
- While some practices were context specific, there were several common top practices across sites, including: education about CAB + RPV LA clinical efficacy, education around administering injections and pain/discomfort after injection, and implementation planning.
- SSP data highlighted that pain/discomfort decreased with subsequent dosing, and communicating this to patients at treatment initiation may be helpful when incorporating CAB + RPV LA into practice.
- The top implementation practices can be used as a guide for clinics starting to implement CAB + RPV LA. Notably, these top practices supported implementation during the COVID-19 pandemic, highlighting the ability to successfully incorporate CAB + RPV LA even during a time when clinic resources may be limited.

CARISEL: Acknowledgements

The authors thank everyone who has contributed to the CARISEL study, including all study 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 Daniel Williams of Scimentum (Nucleus Global), with funding provided by ViiV Healthcare.

References

1. U.S. Department of Health and Human Services. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. 2021. Available from: https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/whats-new-guidelines. Accessed March 2022.
2. Saag MS, et al. *JAMA*. 2020;324(16):1651–1669.
3. Swindells S, et al. *N Engl J Med*. 2020;382(12):1112–1123.
4. Orkin C, et al. *N Engl J Med*. 2020;382(12):1124–1135.
5. Overton ET, et al. *Lancet*. 2020;396(10267):1994–2005.
6. WHO COVID-19 Dashboard. Geneva: World Health Organization, 2022. Available from: https://covid19.who.int. Accessed March 2022.

BHIVA Spring Conference 2022; April 20-22, 2022; Manchester, UK