Terapia long-acting: aspetti clinici ed organizzativi

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Disclosures

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CAB-RPV LA è raccomandato nei pazienti viro-soppressi dalle principali linee guida internazionali

EACS[1]* (Oct 2022)

- In persons with suppression of HIV (VL <50 c/mL for the past 6 months), dual therapy strategies should only be given if there is **no historical resistance, and HBV immunity or concomitant HBV vaccination if non-immune**
- Dual therapies supported by large randomized clinical trials or meta-analyses include **CAB + RPV every 2-month injections**
- In clinical trials, these strategies have not been associated with more virologic rebounds than triple therapy. There were a few cases of resistance development on DTG + RPV and **CAB + RPV**

US DHHS[2]* (Jan 2022)

- CAB and RPV IM injections **can be used as an optimization strategy** **for people with HIV currently on oral ART with documented viral suppression for at least 3 to 6 months (AI) who:**
  - Have no BL resistance to either medication
  - Have no prior VF
  - Do not have active or occult HBV infection (unless also receiving an oral HBV active regimen)
  - Are not pregnant and are not planning on becoming pregnant
  - Are not receiving medication with significant drug interaction with oral (during lead-in or bridging therapy) or injectable CAB or RPV
- **Additional key considerations include switching to long-acting injectable therapy can be advantageous** in patients for a variety of reasons, including but not limited to:
  - **Reducing pill fatigue†**
  - **Disclosure concerns or stigma associated with taking daily oral medications†**
  - **To improve quality of life**

IAS[3]* (Oct 2020)

- In the setting of successful viral suppression, switching from 3DR to 2DR is an appropriate strategy to manage toxic effects, intolerance, adherence, or patient preference
  - CAB + RPV LA injectable, dosed Q4W or Q8W,‡ is included as a recommended regimen for PHIV switching therapy

Indicazioni terapeutiche

Cabotegravir-Rilpivirine (CAB-RPV) LA is indicated for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in

- Adults (≥ 18 years) who are virologically suppressed (HIVRNA < 50 cp/ml) on a stable ART regimen for the past six months
- Without present or past evidence of viral resistance to agents of the NNRTI and INI class
- With NO prior virological failure with agents of the NNRTI and INI class
- With NO HBV coinfection

CAB-RPV LA is not recommended in:

- Patients with severe hepatic impairment (Child-Pugh score C)
- Patients with severe renal impairment (estimated creatinine clearance < 30 mL/min/1.73) or end stage renal disease
- Pregnancy and breastfeeding
- Hypersensitivity to the active substance or to any of the excipients

https://www.ema.europa.eu/en/documents/product-information/rekambys-epar-product-information_it.pdf
https://www.ema.europa.eu/en/documents/product-information/vocabria-epar-product-information_it.pdf

Virological efficacy in RCTs

Phase 3/3b RCTs	Patients	Regimens	VS at w 48 (primary endpoint)
FLAIR	521 ART naive pts	Induction all pts: oral DTC/ABC/3TC x 20 w • CAB-RPV LA q4w (OLI x4 w) • DTG/ABC/3TC q24h	• LA: 93.6% • Oral: 93.3%
ATLAS	616 ART experienced, virologically suppressed pts	• CAB-RBV LA q4w (OLI x 4w) • 2NRTIs+INSTI, NNRTI or b/PI or unboosted ATV	• LA: 92.5% • Oral: 95.5%
ATLAS-2M	1045 pts who completed the 52-w ATLAS and had VL<50 cp/ml	• CAB-RPV LA q4w • CAB-RPV LA q8w	• q4w: 93% • q8w:94%

Orkin, NEJM 2020; Swindells, NEJM 2020; Overton, Lancet 2021

Indicazioni terapeutiche-2

Before starting the regimen, it should be taken into account that **a combination of at least 2 of the following baseline factors may be associated with an increased risk of virological failure**:

- Archived rilpivirine resistance mutations
- HIV-1 subtype A6/A1
- BMI ≥30 kg/m2 .

Available data suggest that **virologic failure occurs more often when these patients are treated according to the every 2 month dosing regimen** as compared to the monthly dosing regimen.
In patients with an incomplete or uncertain treatment history without pre-treatment resistance analyses, caution is warranted in the presence of either BMI ≥30 kg/m2 or HIV-1 A6/A1 subtype

https://www.ema.europa.eu/en/documents/product-information/rekambys-epar-product-information_it.pdf
https://www.ema.europa.eu/en/documents/product-information/vocabria-epar-product-information_it.pdf

Risk Factors for Virologic Failure With LA CAB + RPV: post-hoc analysis of data from ATLAS, FLAIR, and ATLAS-2M

- Confirmed VF was rare across all 3 RCTs (1%; n=17/1636)
- **Post hoc analysis of data from 13/1039 (1.25%) participants who developed CVF**

Baseline Factors Associated With CVF	OR
• RPV RAM(s) at baseline	40.36
• HIV-1 subtype A6/A1	5.92
• BMI ≥30 kg/m^2	1.13

- Among 96.7% of pts with **0/1 risk factor** for CVF, **0.4% had confirmed VF**
- **≥2 risk factors** needed for significant increase in CVF risk

- Expanded multivariate analysis of confirmed VF from **FLAIR through w124, ATLAS through w96, and ATLAS-2M through w152**
  - **Baseline RPV RAMs** and **HIV-1 subtype A6/A1 were** most significant predictive factors for confirmed VF
  - Patients with **0/1 baseline factors** had **low risk of failure**

1. Cutrell. AIDS. 2021;35:1333. 2. Orkin. HIV Glasgow 2022. Abstr O44.

Indicazioni terapeutiche-3

- The healthcare professional **should carefully select patients who agree to the required injection schedule and counsel patients about the importance of adherence to scheduled dosing visits** to help maintain viral suppression and reduce the risk of viral rebound and potential development of resistance associated with missed doses.

https://www.ema.europa.eu/en/documents/product-information/rekambys-epar-product-information_it.pdf
https://www.ema.europa.eu/en/documents/product-information/vocabria-epar-product-information_it.pdf

What are the key considerations when selecting patients who may be suitable for CAB + RPV LA?

Clinical criteria*[1,2]

- ❑ Virologically suppressed
- ❑ On a stable ARV regimen with no history of treatment failure
- ❑ No known or suspected resistance to either CAB or RPV
- ❑ No HBV coinfection

Patient interest[1–6]

- ❑ Patients interested in injectables and less-frequent dosing
- ❑ An alternative for those with challenges on daily oral therapy
- ❑ Patients who are able to adhere to and agree to required every 2-month appointments

Review of patient history

- ❑ Patients who are adherent to:
  - ✓ Oral medication
  - ✓ Lab-testing requirements
  - ✓ Appointments
- ❑ Screening out patients with behavioral health and substance abuse issues

Team approach

- ❑ Multi-disciplinary meetings are very helpful to gain the insight from multiple teams
- ❑ Allows patients to be identified from various sources

Good history of adherence to appointments was identified as a key, non-clinical factor for patient selection[1,2]

*As per local product labels

1. Vocabria EU SmPC. Jan 2022; **2.** Rekambys EU SmPC. Feb 2022
3. Derrick CB, et al. Open Forum Infect Dis 2018;5:ofy247; **4.** Williams J, et al. Nanomedicine 2013;8:1807–13
5. de los Rios P, et al. AIDS Behav 2021;25:961–72; **6.** de los Rios P, et al. Popul Med 2020;2:23

Characteristics of PLWH potential eligible for CAB + RPV LA from the ARCA Cohort

Variables	Overall population (n = 514)	Non-eligible for CAB+RPV (n = 285)	Eligible for CAB+RPV (n = 229)	p-value
Gender male, n (%)	377 (73.3)	198 (69.5)	179 (78.2)	0.034
Age (years), median (IQR)	51 (43 to 58)	54 (46 to 58)	48 (38 to 55)	<0.001
Ethnicity, n (%)				
Caucasian	314 (60.0)	169 (59.3)	145 (63.3)	0.353
Black	36 (7.0)	25 (8.7)	11 (4.8)	0.114
Other/unknown	164 (33.0)	91 (32.0)	73 (31.9)	0.597
HIV-1 subtype, n (%)				
B	382 (74.3)	225 (78.9)	157(68.6)	0.007
A[a]	19 (3.7)	6 (2.1)	13 (5.7)	0.058
CRF02_AG	43 (8.4)	24 (8.4)	19 (8.3)	1.000
CRFs_BC	18 (3.5)	2 (0.7)	16 (7.0)	<0.001
CRFs_BF	11 (2.1)	6 (2.1)	5 (2.2)	1.000
Others	41 (8.0)	22 (7.7)	19 (8.3)	0.939
HIV-1 risk factor, n (%)				
Heterosexual	212 (41.2)	118 (41.4)	94 (41.1)	0.935
MSM	121 (23.5)	57 (20.0)	64 (27.9)	0.035
Drugs injection	96 (18.7)	75 (26.3)	21 (9.2)	<0.001
Other/unknown	85 (16.5)	35 (12.3)	50 (21.8)	0.005
VL zenith (log10 copies/mL), median (IQR)	4.9 (4.0 to 5.5)	5.1 (4.4 to 5.7)	4.5 (3.1 to 5.2)	<0.001
CD4 count nadir (cells/mm^3), median (IQR)	210 (80 to 370)	170 (50 to 320)	260 (120 to 450)	<0.001
Year of HIV-1 diagnosis, median (IQR)	2008 (1995 to 2014)	2002 (1991 to 2011)	2012 (2006 to 2016)	<0.001
HCV co-infection, n (%)	65 (12.6)	53 (18.6)	12 (5.2)	<0.001
HBV co-infection, n (%)	41 (8.0)	41 (14.4)	0 (0.0)	–
First therapy (year), median (IQR)	2011 (2003 to 2016)	2007 (1997 to 2014)	2015 (2010 to 2017)	<0.001
Years from first therapy, median (IQR)	9 (4 to 17)	13 (6 to 23)	6 (3 to 10)	<0.001
Previous drug classes experienced, n (%)				
NRTI	498 (98.6)	276 (97.9)	222 (99.6)	0.14
NNRTI	315 (62.4)	194 (68.8)	121 (54.3)	<0.001
PI	349 (69.1)	227 (80.5)	122 (54.7)	<0.001
INSTI	388 (76.8)	244 (86.5)	144 (64.6)	<0.001
MVC	35 (6.9)	28 (9.9)	7 (3.1)	0.005
T20	17 (3.4)	17 (6.0)	0 (0.0)	<0.001
No. of previous therapies, median (IQR)	4 (2 to 7)	6 (3 to 11)	3 (2 to 4)	< 0.001
Therapy at last viraemia, n (%) (n = 497)				
2 NRTI + 1 INSTI	179 (36.0)	101 (36.6)	78 (35.6)	0.869
2 NRTI + 1 NNRTI	106 (21.3)	32 (11.5)	74 (33.8)	<0.001
2 NRTI + 1 PI	62 (12.5)	38 (13.7)	24 (11.0)	0.441
1 NRTI + 1 INSTI	39 (7.8)	16 (5.8)	23 (10.5)	0.074
Other	111 (22.3)	91 (32.7)	20 (9.1)	<0.001
Previous VFs, n (%)				
NNRTI	136 (26.4)	136 (47.7)	–	–
RPV	17 (3.3)	17 (6.0)	–	–
INSTI	119 (23.2)	119 (41.8)	–	–
Time from last VF (months), median (IQR)	63 (34.7 to 105.2)	62.1 (34 to 102)	64.4 (36.2 to 107.6)	0.583
At least one major RAM for INSTI, n (%)	33 (6.4)	33 (11.6)	0 (0)	–
At least one RAM for NNRTI, n (%)	168 (32.7)	168 (58.9)	0 (0)	–
At least one RAM for RPV, n (%)	104 (20.2)	104 (36.5)	0 (0)	–
CAB + RPV cumulative GSS, median (IQR)	2 (1.5 to 2)	1.5 (1 to 2)	2 (2 to 2)	<0.001

44.5% of HIV-suppressed PLWH with available genotypic resistance testing were eligible for CAB-RPV LA

Eligibility criteria were:

- Negative HBsAg
- No resistance-associated mutations (RAMs) for NNRTIs or INISTIs
- No previous virological failure to NNRTIs and/or INSTIs

- 8% of patients were coinfected with HBV;
- 6%, 24% and 20% had at least one RAM for INSTIs, NNRTIs (excluding RPV) and RPV, respectively

Cervo A, P096, HIV Glasgow 2022

Similar proportions of PLWH were eligible for CAB-RPV LA in another cohort from a single center in Italy

Borghetti, J Med Virol 2022

Patients' interest in LA

- **84% of PLWH** in a web survey conducted by an Italian Patient Advocacy Group in the field of HIV/AIDS (Nadir Onlus) said that LA regimen would be convenient, and **69% declared that the greatest benefit would be not having to remember to take pills.**
  Rusconi S, New Microbiol 2017

- **55% of PLWH** respondents to an online nationwide cross-sectional European survey preferred to take LA-ART. Main reason for switching were **convenience of LA formulation, reduced pill burden, easier adherence and no risk of inadvertently missing a dose, freedom or feeling of normalcy**.
  Dubé K, AIDS Res Human Retrovir 2020

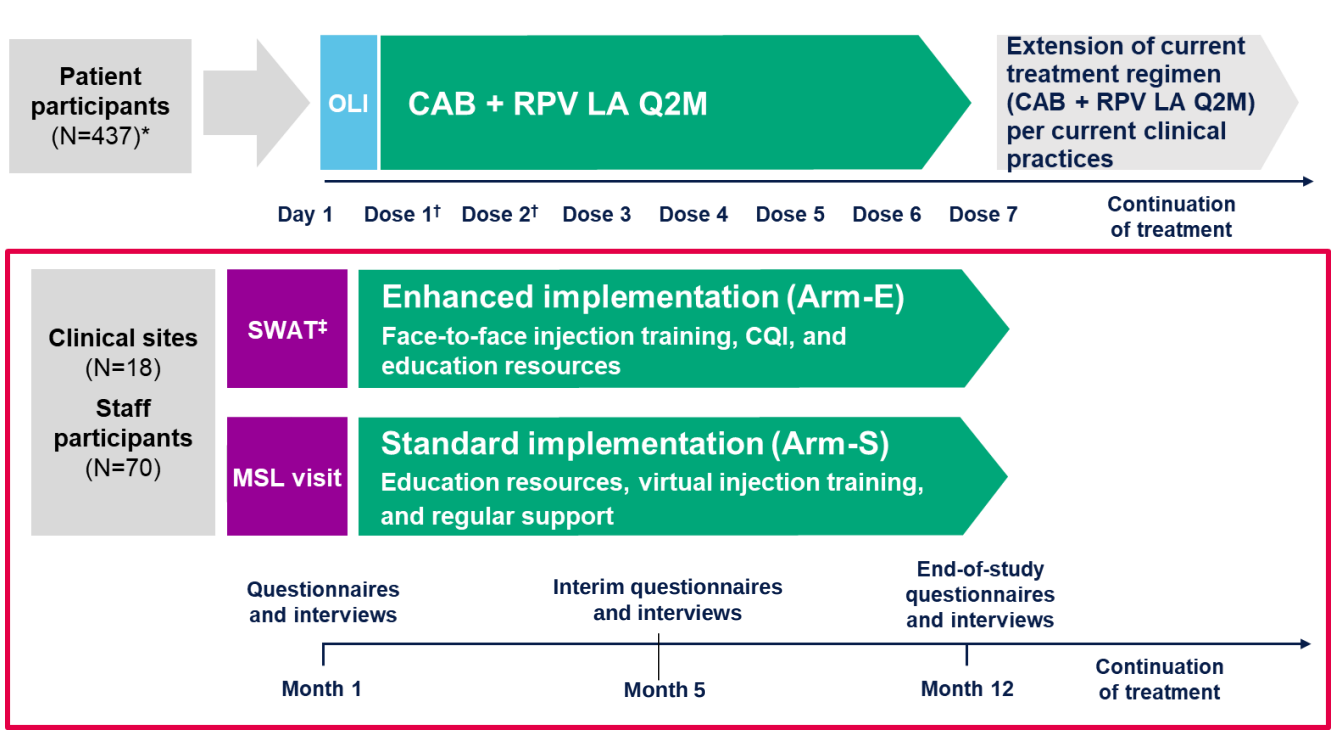
- **57% of PLWH** in an online anonymous survey conducted through the ICONA Network declared interest in LA; **they were younger ($p < 0.001$), with a higher education level ($p = 0.02$), with more recent HIV diagnosis ($p < 0.001$), afraid to disclose serostatus ($p = 0.002$)** and not fully satisfied with the ongoing ART ($p < 0.001$). Subjects interested in LA declare **higher issues in their daily organization for taking ART ($p = 0.026$)**, were more bothered by having to rely on the ART medications ($p < 0.001$) and **more frequently felt frustrated by their HIV status** ($p = 0.041$).
  Cingolani A, J Clin Med 2022

- **67% of PLWH** eligible for CAB-RPV LA expressed their interest to switch to the LA regimen in a single center in North Italy.
  Alberton F, J Med Virol 2022

- **88.8% of PLWH** in an online anonymous survey in Italy are interested in changing their actual treatment with a LA one.
  Celesia M, Medicine 2022

CARISEL: An Implementation–Effectiveness, Phase 3b, Open-Label Study in Europe

- **Study design:** CARISEL is an implementation-effectiveness trial examining strategies to support the implementation of CAB + RPV LA dosed Q2M across five European countries
- **Acceptability, appropriateness, and feasibility of CAB + RPV LA injections and implementation support** were evaluated in 18 HIV clinics in Belgium, France, Germany, the Netherlands, and Spain
- Staff participants at 18 clinics 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.



Baseline characteristics:

- **13 of the 18 clinics (72%) had no previous CAB + RPV LA experience**
- 70 staff participants (**37% Physician, 45% Nurse, 4% Administrative, 10% Pharmacist, 4% other care provider**) completed interviews and surveys at Month 1, and 62 completed them at Month 12
- Overall, 430 enrolled and treated participants were included
- A total of 379 patient participants from France (n=147), Spain (n=87), Belgium (n=68), Germany (n=43), and the Netherlands (n=34) completed the survey through Months 1–12
- Patient participants had a mean age of 44.2 years, 22% were non-White, and 27% were female (self-reported)

*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.
Arm-E, Enhanced Arm; Arm-S, Standard Arm; CAB, cabotegravir; CQI, continuous quality improvement; LA, long-acting; MSL, medical scientific liaison; OLI, oral lead-in; Q2M, every 2 months; RPV, rilpivirine; SWAT, skilled wrap-around team.

1. van Welzen et al. HIV Drug Therapy Glasgow 2022; Virtual and Glasgow, Scotland. Poster P069.
2. Lutz et al. HIV Drug Therapy Glasgow 2022; Virtual and Glasgow, Scotland. Poster P123.

CARISEL: An Implementation–Effectiveness, Phase 3b, Open-Label Study in Europe
Top Five Patient Needs Met by CAB + RPV LA as Perceived by Staff Participants

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

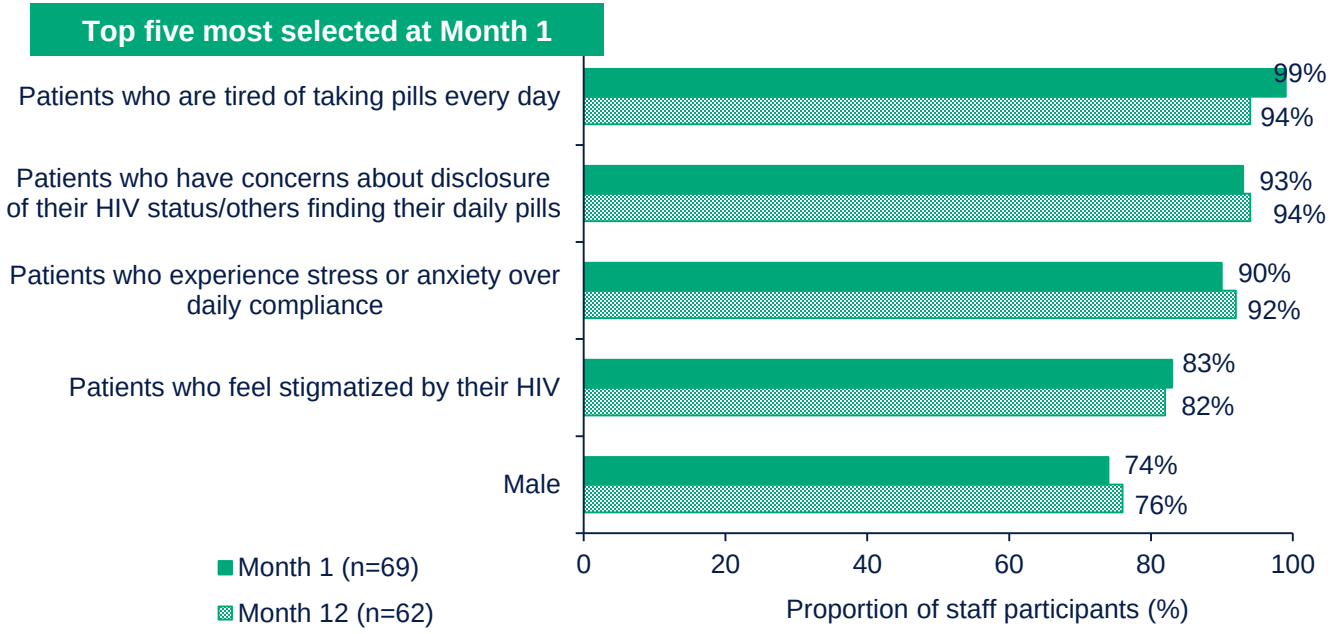
- Overall, adherence, convenience, discretion, and decreased stigma were reasons that staff participants believed CAB + RPV LA was a good fit for their patients

The elimination of the worry over taking pills, increased adherence, and more discretion were factors supporting the need and benefit of CAB + RPV LA

Gutner et al. EACS 2021; Virtual and London, UK. Poster PE2/56.

CARISEL: Staff's Perspectives

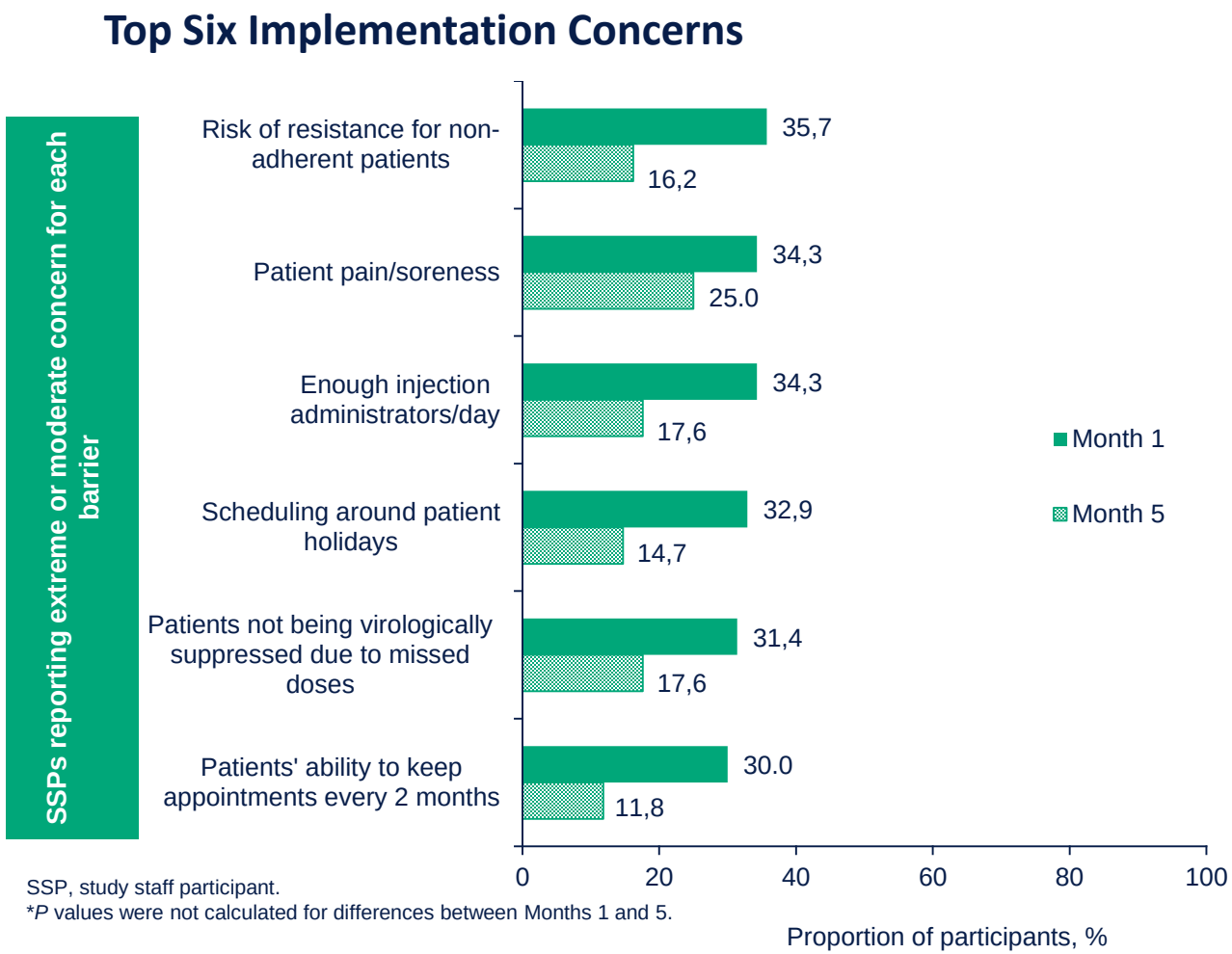
Patient Characteristics Appropriate for CAB + RPV LA Treatment



- **Feeling burdened by daily pill taking as well as having a fear of inadvertent disclosure of HIV status were highlighted as patient characteristics more appropriate for CAB + RPV LA therapy**

Slama et al. HIV Drug Therapy Glasgow 2022; Virtual and Glasgow, Scotland. Poster P116.

CARISEL: Staff's Top Concerns About Implementation

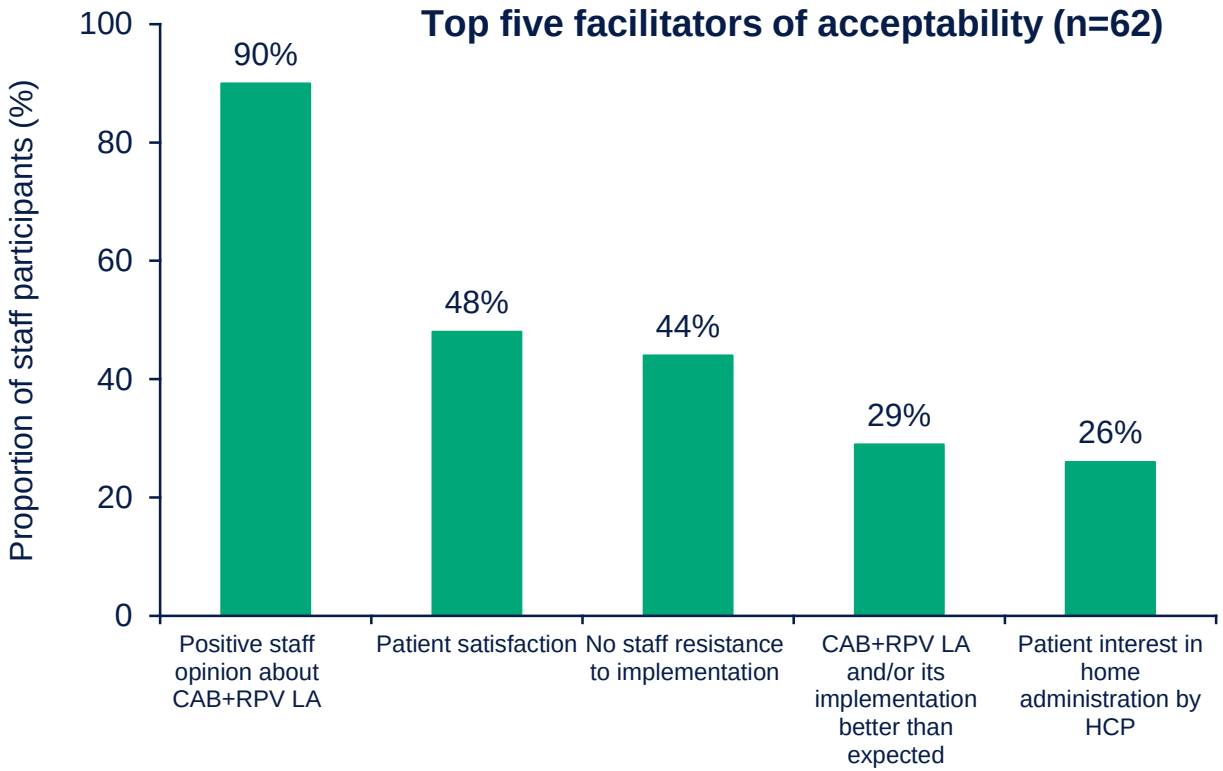


SSP, study staff participant.
**P* values were not calculated for differences between Months 1 and 5.

- **All top implementation concerns decreased from Month 1 to Month 5**

Gutner et al. EACS 2021; Virtual and London, UK. Poster PE2/36.

CARISEL: Staff's Facilitators of Acceptability



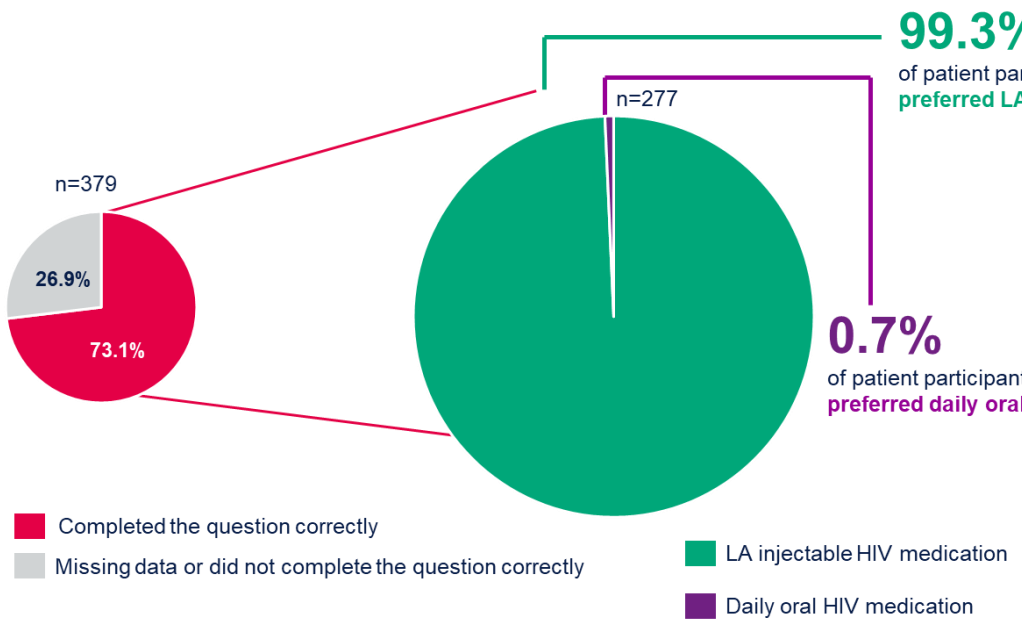
- At Month 12, qualitative data showed 90% of staff participants reported a positive opinion about CAB + RPV LA as a facilitator of acceptability

Positive staff participant opinion of CAB + RPV LA and patient satisfaction were top facilitators of acceptability of CAB + RPV LA

Slama et al. HIV Drug Therapy Glasgow 2022; Virtual and Glasgow, Scotland. Poster P116.

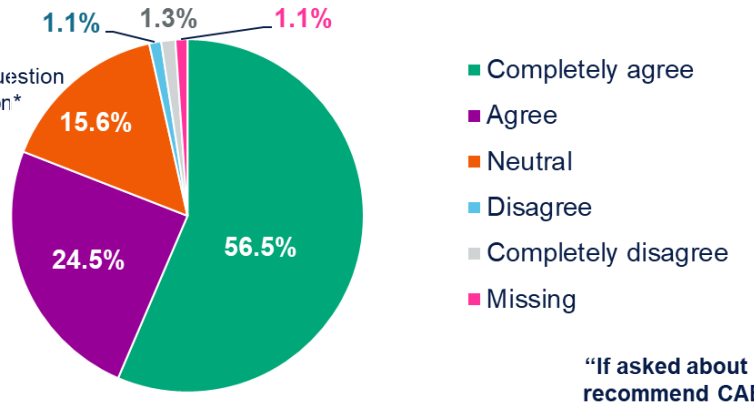
CARISEL: Perceptions From Patient Participants

"We would like you to compare your experience using the LA injectable medication with daily oral HIV medication. Please select the treatment you prefer"*



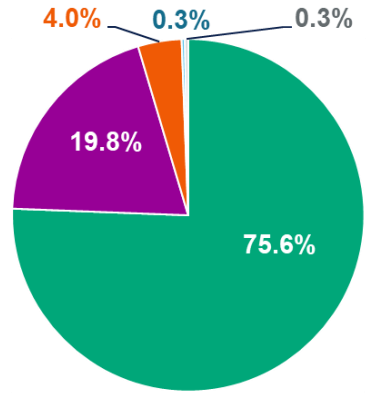
- **99% of patient participants (n=275/277) preferred CAB + RPV LA vs daily oral therapy**

"CAB + RPV LA treatment is less stigmatizing than my oral medications"



- 81% of patient participants agreed/completely agreed that CAB-RPV LA **is less stigmatizing** than daily oral therapy
- 95% of patient participants agreed/completely agreed that they **would recommend** CAB-RPV LA to other PLWH

"If asked about it or it came up in discussion, I would recommend CAB + RPV LA treatment to other PLWH"

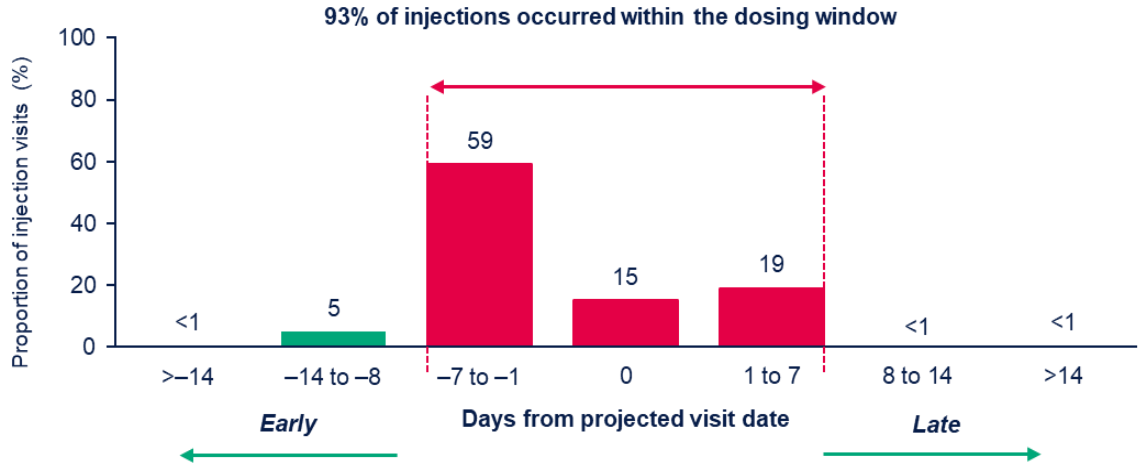


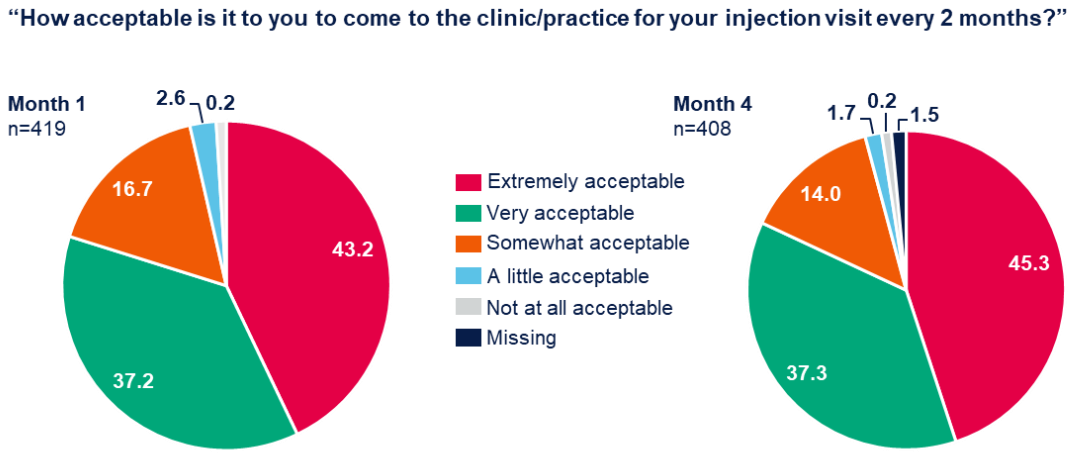
Almost all participants preferred CAB + RPV LA over oral therapy and 81% felt it was less stigmatizing than oral medications

Lutz et al. HIV Drug Therapy Glasgow 2022; Virtual and Glasgow, Scotland. Poster P123.

CARISEL: Patients – Adherence to Injection Visits

- Overall, **93% of injection visits occurred within ±7 days of the target date**
- **96.6% of patients felt it was acceptable to come to the clinic**/practice for an injection visit **every 2 months**
- Most patients felt that talking to their medical provider about the new treatment was the most helpful material/information shared at Months 1 and 4
- In total, **91.2% of patients felt "very" or "extremely positive"** about CAB-RPV LA treatment at Month 4, compared with 83.5% at Month 1

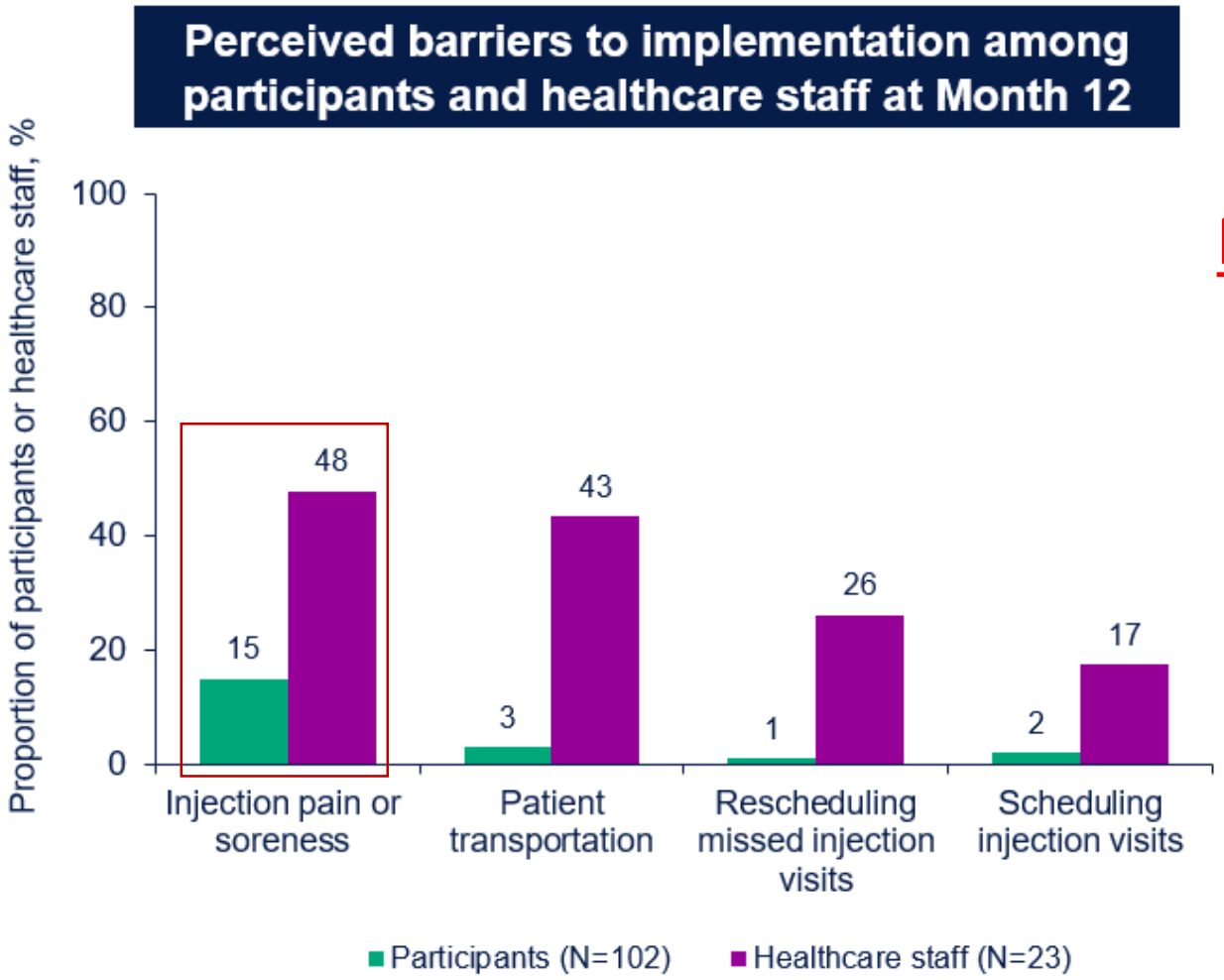




Most patients were very positive about CAB + RPV LA at Month 4 and felt that it was extremely/very acceptable to come to the clinic every 2 months for the injection visit

Hocqueloux et al. EACS 2021; Virtual and London, UK. Poster PE2/37.

CUSTOMIZE: An Implementation- Effectiveness Study Focused On Implementation of CAB + RPV LA Monthly In US HealthCare Settings



Participants Reported Fewer Concerns Compared With Healthcare Staff

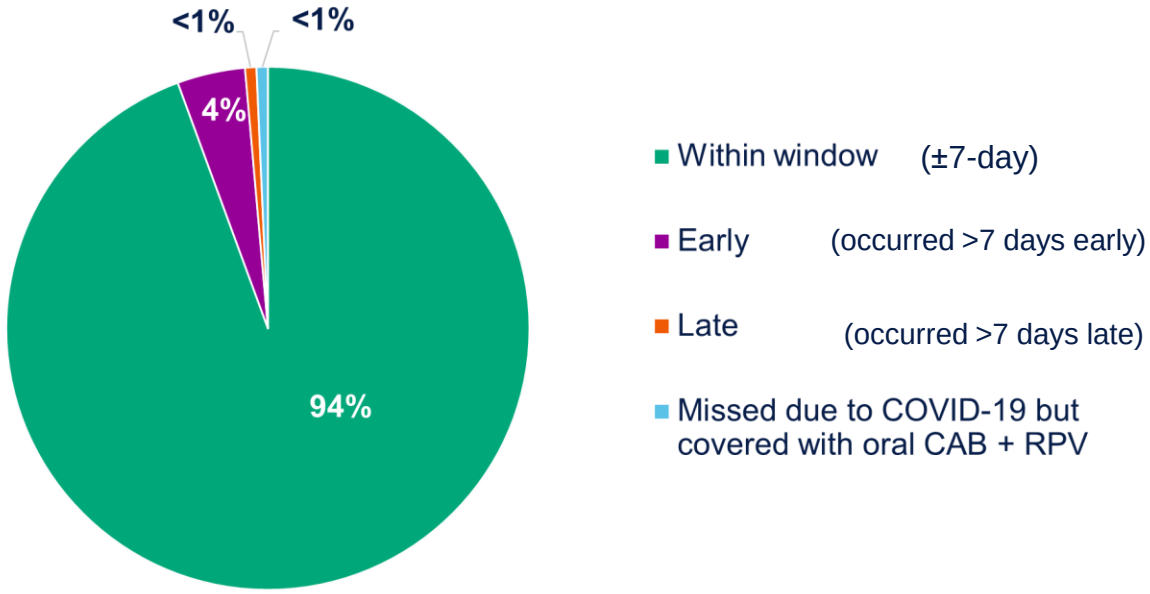
- **Participants reported fewer factors interfering with their ability to receive CAB + RPV LA injections compared with healthcare staff perceptions**
- The factor most reported as interfering with participants' ability to receive injections was injection pain or soreness (15%)

CAB, cabotegravir; LA, long-acting; RPV, rilpivirine.
Each bar represents the proportion of healthcare staff who agreed or completely agreed that the item was a barrier.

Czarnogorski et al. IAS 2021; Virtual. Slides OAD0705.

CUSTOMIZE: An Implementation- Effectiveness Study Focused On Implementation of CAB + RPV LA Monthly In US HealthCare Settings

Adherence to Treatment Window (±7-day) Through Month 12



- Monthly CAB + RPV LA was **highly effective in a diverse US population, with no confirmed virologic failures occurring after 12 months of treatment**
- Although injection site reactions were frequent, most (96%) were mild or moderate in severity, **decreased after the first injection, and few participants (2%) withdrew for injection-related reasons**
- Most injection visits (94%) occurred within the **±7-day dosing window through 12 months** of treatment, **with <1% of injection visits impacted by COVID-19**

Sinclair et al. IAS 2021; Virtual. Poster PED416.

Initiating Long-Acting Cabotegravir and Rilpivirine in a Real-world Setting: Clinical Characteristics and Switch Reasons From PLHIV and Health Care Provider Perspective in the German CARLOS Cohort

Study design: Ongoing, non-interventional, 3-year, prospective, multicenter cohort study in Germany

Outcome measures:

- Clinical characteristics were identified from medical records
- The perspectives of PLHIV and HCPs regarding CAB + RPV LA HIV treatment were assessed through surveys conducted at baseline

Study Population

- Between May and December 2021, 236 PLHIV initiated CAB + RPV LA every 2 months across 19 sites

Baseline characteristics

- 95.3% male (sex at birth), median (IQR) age 42.5 (36.0-49.5) years, 24.6% aged 50 to 65 years, 10.5% with BMI ≥30 kg/m^2, median 8.1 years on ART

Antiretroviral Treatment (ART) Prior to Switch to CAB + RPV

- The median duration on ART before switch was 8.1 years
- The most common regimens (in >10%) prior to switch were BIC/FTC/TAF (n=54/236; 22.9%), DTG/3TC (n=44; 18.6%) and RPV/FTC/TAF (*or* TDF) (n=24; 10.2%) (missing information for n=7; 3.0%)

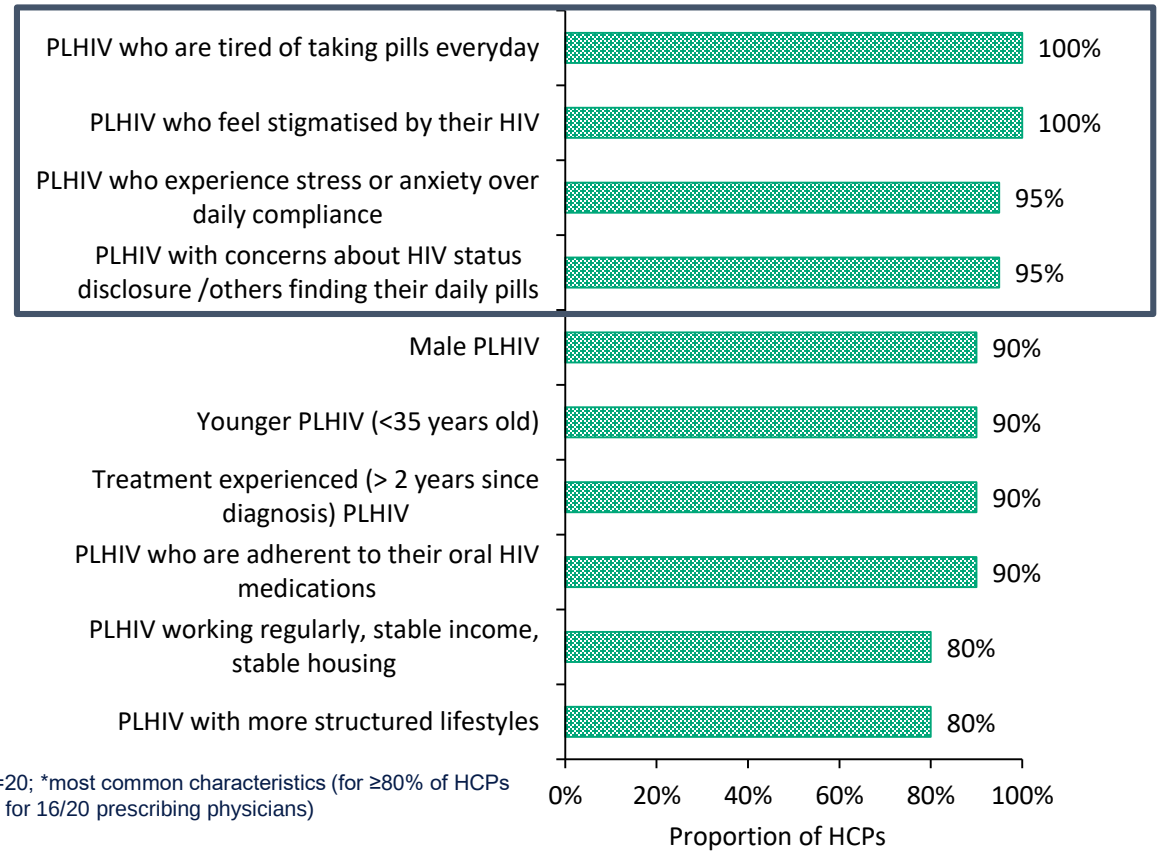
Oral Lead-in

- The majority (n=200/236; 84.7%) started with oral lead-in (OLI) therapy (once daily oral CAB + RPV) prior to the injectables.
- The median time of the OLI phase was 28 days (IQR: 27–30 days)

Wyen et al. 24th International AIDS Conference, 2022, Virtual and Montreal, Canada. Poster EPB179.

CARLOS Cohort: General Characteristics of PLHIV Suitable for CAB + RPV LA from the Health Care Provider Perspective

The most common **patient characteristics suitable for LA therapy** (for ≥80% of HCPs)



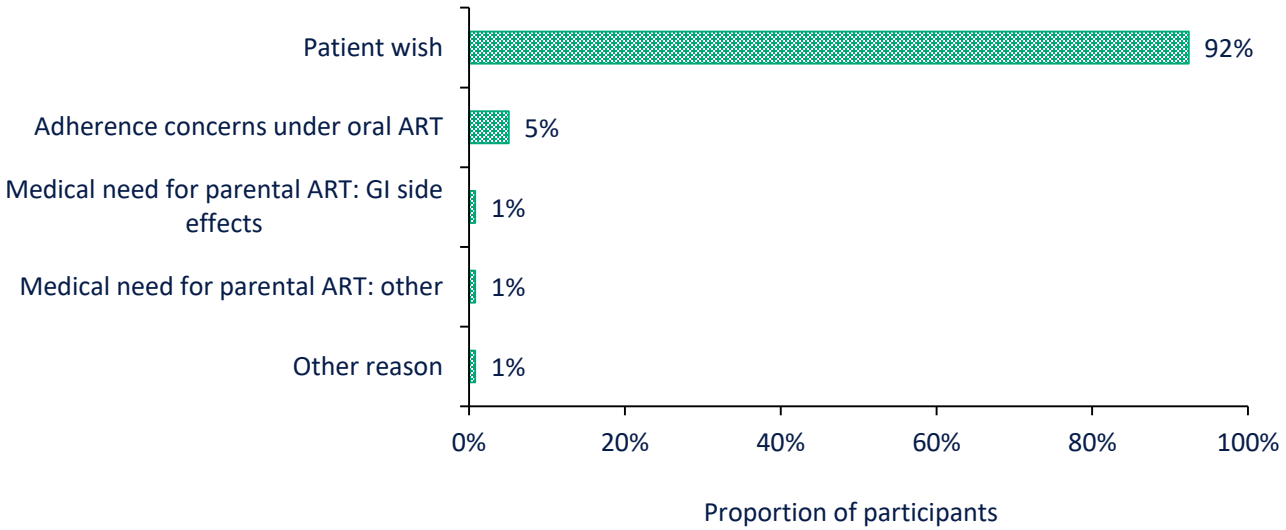
N=20; *most common characteristics (for ≥80% of HCPs ie, for 16/20 prescribing physicians)

HCP perspective on PLHIV most suitable for CAB + RPV LA injections included PLHIV who experienced challenges with daily oral therapy

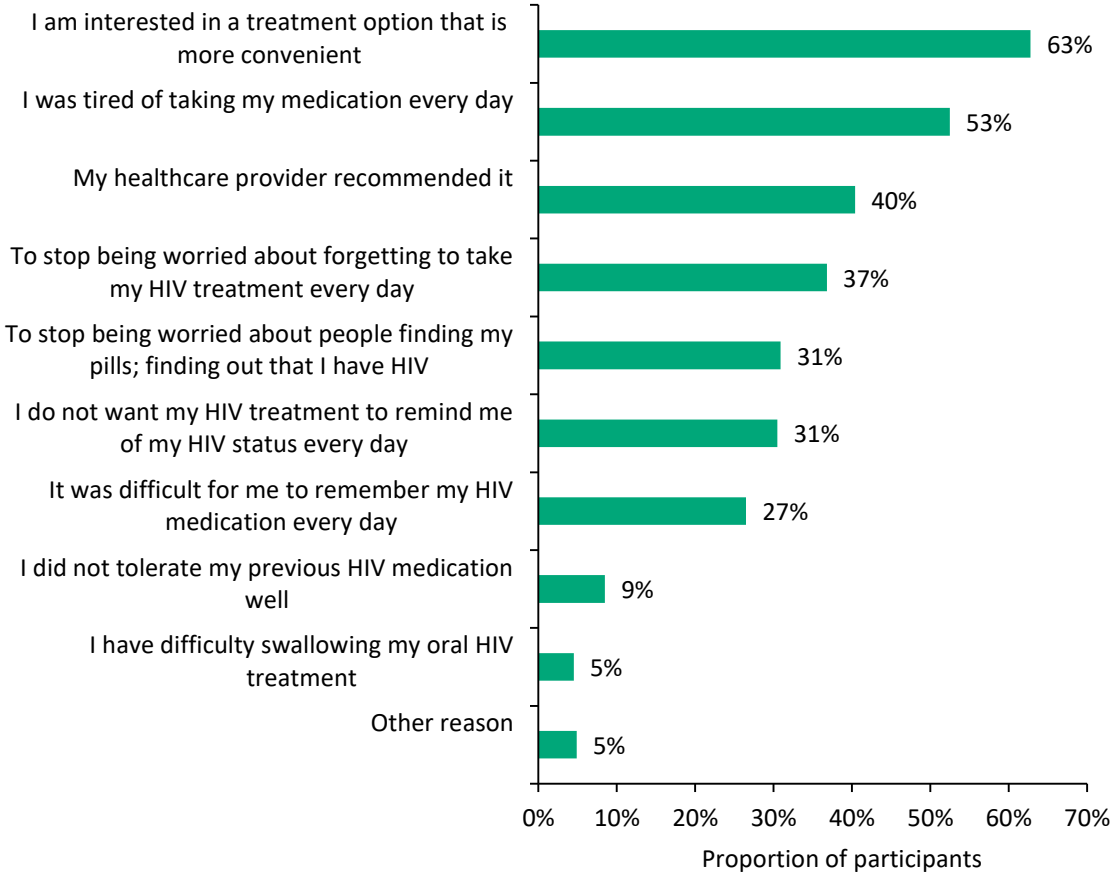
Wyen et al. AIDS 2022; Virtual and Montreal, Canada. Poster EPB179.

CARLOS Cohort: Reasons for Switching to CAB + RPV LA

HCP reason for switching N=236



PLWH reason for switching (multiple responses) N=223

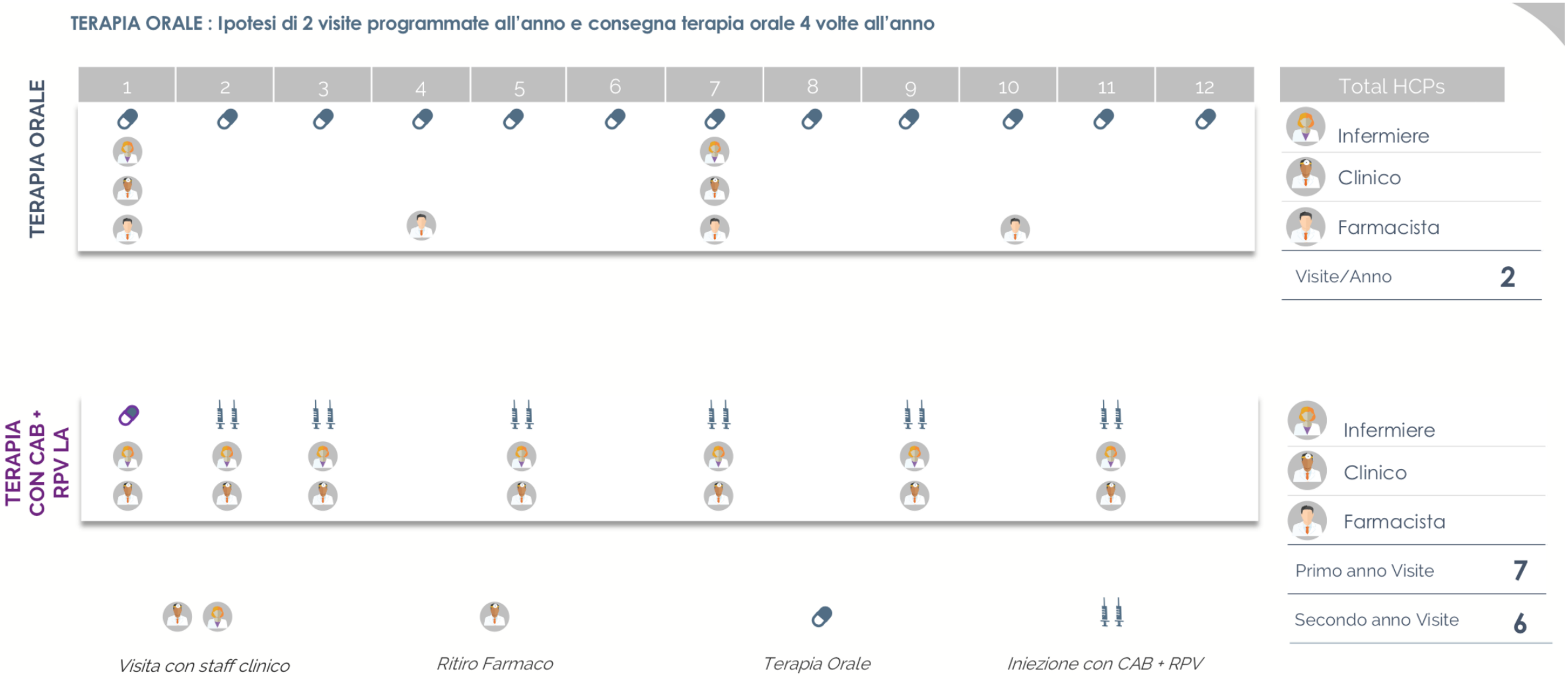


- From the **HCP perspective**, the main reason for switching to CAB-RPV LA was “patient wish”
- **Among PLHIV**, “convenience” and “pill fatigue” were the most often cited reasons for choosing CAB-RPV LA

Wyen et al. AIDS 2022; Virtual and Montreal, Canada. Poster EPB179.

Aspetti organizzativi

Cosa cambia nell'organizzazione della terapia LA rispetto alla terapia orale?



Operational Planning for Clinics

Time

≥30 min appts:

- Time to administer injections
- 10-min observation post injection
- Scheduling of next appts
- Questionnaires

Staff

- Who will administer injections?
- Will training be needed?
- Will designated staff be needed for appt reminders and/or follow-up for missed appts

Space

- Exam rooms needed for injections
- Will longer clinic hours be needed for higher patient visit volume?
- Have kit on hand for managing potential HSR

Elementi chiave nella gestione della terapia con CAB-RPV LA

ORGANIZZAZIONE DELL'AMBULATORIO

- Capacità del centro di accogliere il paziente ogni 2 mesi
- Personale infermieristico per la somministrazione di iniezioni
- Pianificazione degli appuntamenti e promemoria per i pazienti

LOGISTICA E GESTIONE DEL FARMACO

- Conoscenza dei requisiti di refrigerazione/catena del freddo della rilpivirina
- Spazi adeguati per lo stoccaggio di cabotegravir + rilpivirina (anche al di fuori della farmacia)

INFORMAZIONE AL PERSONALE INFERMIERISTICO E PAZIENTE

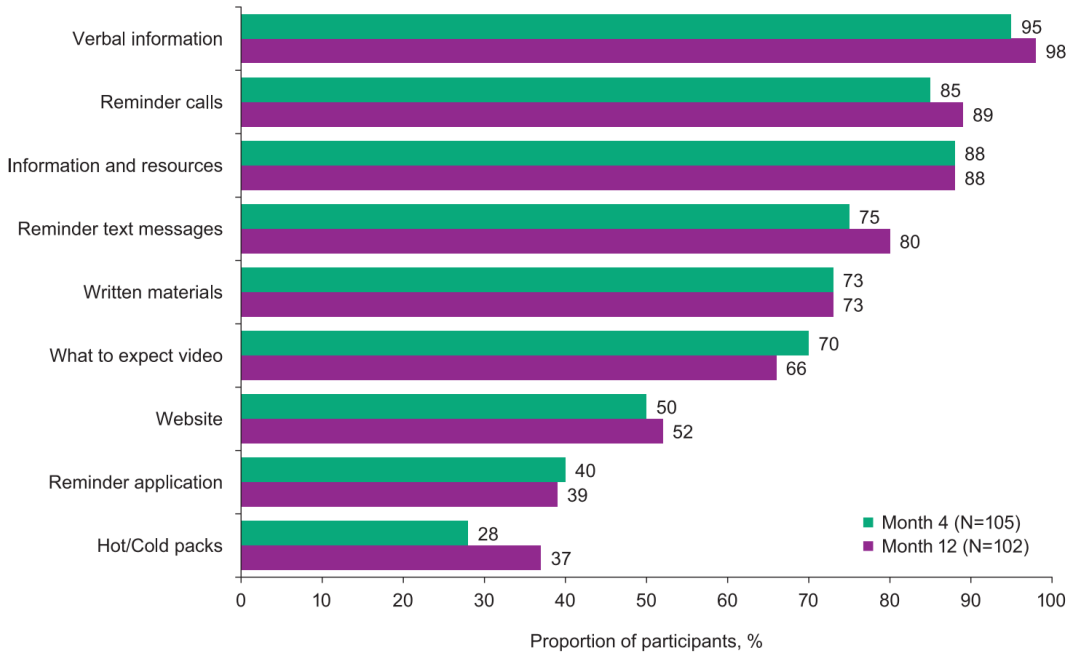
- Informazione agli infermieri sulla modalità di somministrazione
- Informazione al paziente sullo schema terapeutico e sulla compliance

Il recall dei pazienti

Key Implementation Strategies for Supporting Patient Adherence

- Good communication about dosing window
- Effective appointment reminder systems
- Designated staff for appointment tracking

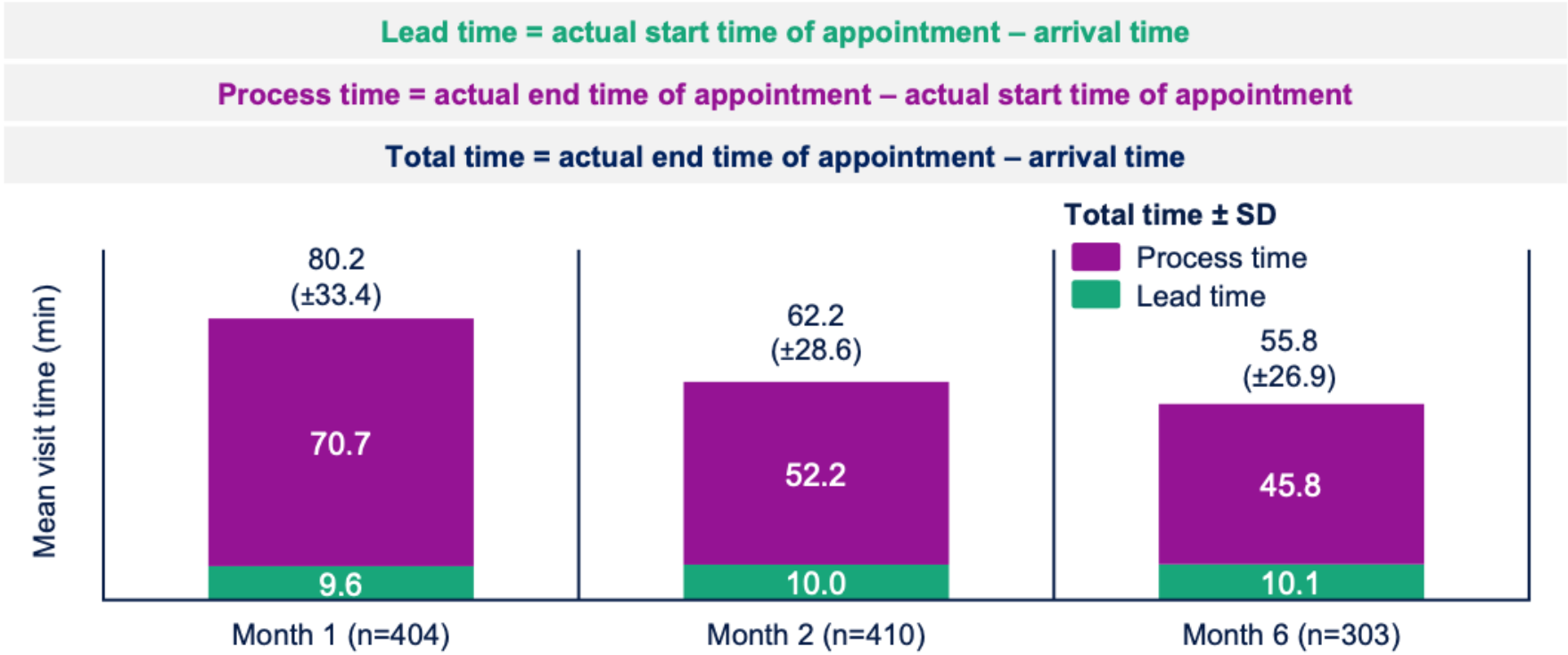
Customize trial



- Nel nostro centro, il paziente riceve una telefonata da parte dello staff infermieristico come promemoria del suo appuntamento 24 ore prima.

Czarnogorski, IAS 2021. Abstr OAD0705; Garris, J Int AIDS Soc 2022

CARISEL study: implementation-effectiveness study of CAB-RPV in EU



A 30.4% (24.4-minute) reduction in mean appointment duration was observed from Month 1 to Month 6, which was mostly driven by a decrease in process time.

- **Similar results observed in the CUSTOMIZE study where the median (IQR) total time spent in clinic (wait time plus exam room time) decreased from 57 (47-70) min for the first injection visit to 35 (25-49) minutes at month 5 and 34 (27-44) minutes at month 11**

Hocqueloux, EACS 2021. Abstr PE2/37
Sinclair, IAS 2021. PED416.

L'offerta dell'iniezione fuori dall'ambulatorio: prospettive future

Observational Study

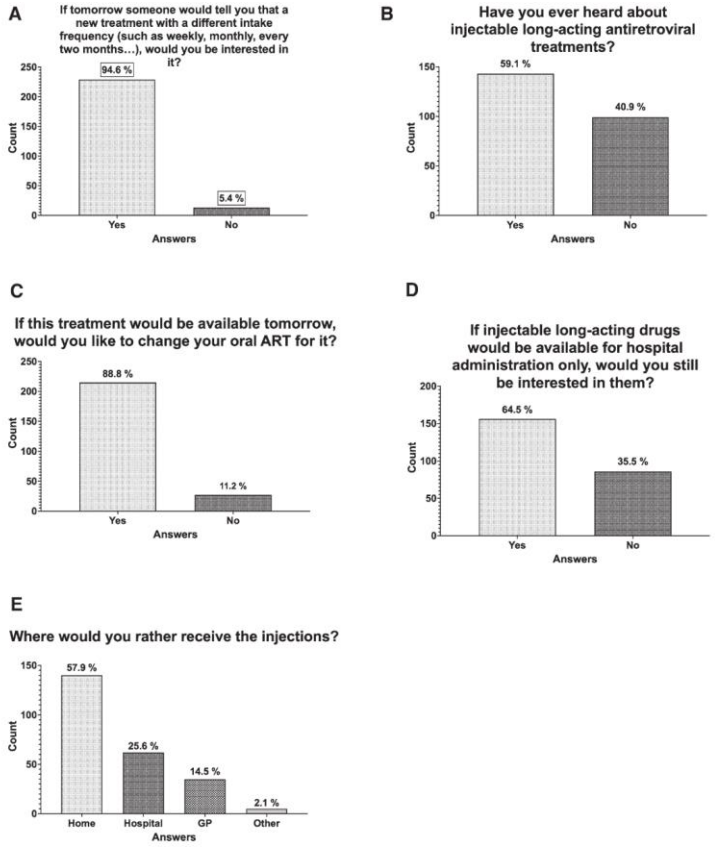
Medicine

OPEN

Long-acting drugs: people's expectations and physicians' preparedness. Are we readying to manage it? An Italian survey

Marta Celesia, DEC[a], Vittoria Moscatt, MD[b,c], Alessandra Tzannis, DEC, PhD[a], Michele Trezzi, MD[d], Emanuele Focà, MD, PhD[e], Margherita Errico[f], Paola Cinque, MD, PhD[g], Silvia Nozza, MD, PhD[g], Antonella Cingolani, MD, PhD[h], Manuela Ceccarelli, MD[b,i,*], Benedetto M. Celesia, MD, PhD[l], and for the LAI Italian Survey Research Group

Survey su 242 pazienti



Clinical Infectious Diseases

SUPPLEMENT ARTICLE

IDSA Infectious Diseases Society of America · hivma hiv medicine association · OXFORD

Barriers to Uptake of Long-Acting Antiretroviral Products for Treatment and Prevention of Human Immunodeficiency Virus (HIV) in High-Income Countries

Stanley E. Cooper, Joshua Rosenblatt, and Roy M. Gulick

Studies of alternative delivery and implementation strategies are currently underway and aim to address some of these barriers

Implementation Trials	
NCT03856580	Alternative CAB-LA injection strategies in transgender women evaluating self-injection and injection by a healthcare provider at "drop-in clinics"
NCT04001803	Qualitative Hybrid III implementation study to identify and evaluate strategies for successful implementation of CAB/RPV-LA
NCT04399551	Hybrid type III trial evaluating implementation strategies through continuous quality improvement for CAB/RPV-LA
NCT04863261	Scheduling CAB/RPV-LA alerts in the retention & huddle modules of the CHORUS App
NCT04973254	Hybrid implementation-effectiveness study evaluating CAB/RPV-LA administration outside of the standard doctor's office/clinic in community partner spaces
NCT04982445	GLACIER (Giving Long Acting CABENUVA in an Infusion centER)—Administration of CAB/RPV-LA in infusion centers

Celesia M, Medicine (United States) 2022; Cooper S, Clin Infect Dis 2022

Zone d'ombra nella terapia con CAB + RPV LA

- **Selezione del paziente**
  - «Understudied population»
    - Popolazioni vulnerabili e marginalizzate
    - Pazienti anziani/adolescenti
    - Pazienti con comorbidità (IRC grave, insufficienza epatica grave)
    - Pazienti con viremia rilevabile per aderenza subottimale alla ART
    - Pazienti con resistenza ad altra classe di farmaci (NRTI)
    - Pazienti con controindicazione assoluta a terapia con PIs
- **Sviluppo di resistenza**
  - Futuri regimi terapeutici in caso di sviluppo di resistenza alle due classi di farmaci durante la terapia con CAB + RPV LA
- **Monitoraggio dopo lo switch a CAB + RPV LA**
  - Secondo pratica clinica?
  - Necessario un monitoraggio virologico più stretto?
  - Drug-drug interactions (DDIs)
  - Utilizzo del TDM
- **Gestione del viral rebound/viral blip durante la terapia con CAB + RPV LA**
  - Quando fare il GRT?
- **Aspetti «pratici»**
  - Conservazione/refrigerazione dei farmaci
  - Training del personale per la corretta somministrazione intramuscolo-
  - Pazienti con alto BMI: lunghezza dell'ago. Guida ecografica?
  - Gestione delle reazioni nel sito di iniezione
  - Bridging non pianificato (emergency bridging pack per ogni paziente?)
  - Reminder degli appuntamenti

Conclusioni

- CAB-RPV LA è un'opzione efficace e offre alcuni vantaggi chiave rispetto alle attuali opzioni ART orali nelle PLWH virologicamente soppresse.
- Un'alta percentuale di PLWH è interessata a cambiare il proprio trattamento attuale con uno LA.
- Il venir meno della preoccupazione per l'assunzione della terapia orale e del rammentare quotidianamente la propria HIV positività, nonché una maggiore discrezione del trattamento, sono fattori a sostegno della necessità e del beneficio del trattamento CAB-RPV LA nelle PLWH.
- L'introduzione di questi nuovi farmaci potrebbe rappresentare un'opportunità per ridurre le «pilll fatigue», sentirsi liberi dall'ansia di mantenere l'aderenza e ridurre lo stigma sociale.
- E’ necessario che la terapia LA sia accessibile alle PLWH che potrebbero trarne maggior beneficio, compresi gli adolescenti, le persone con barriere all'aderenza ai farmaci e le persone in contesti con risorse limitate.
- L'organizzazione degli ambulatori per l'HIV dovrà essere riadattata per fornire l’opzione della terapia LA alle PLWH che vorranno usufruirne.

Switching to LA CAB + RPV Without an Oral Lead-in

- **FLAIR extension study**
  - Participants receiving DTG/ABC/3TC achieving virologic suppression (HIV-1 RNA <50 c/mL) could switch to monthly LA CAB + RPV at Wk 100
  - They could start with (n = 121) or without (n = 111) oral CAB + RPV lead-in
  - There were **no differences in safety or efficacy** outcomes at 24 wk
  - As of March 2022, oral lead-in **is optional**

Orkin. Lancet HIV. 2021;8:e668.

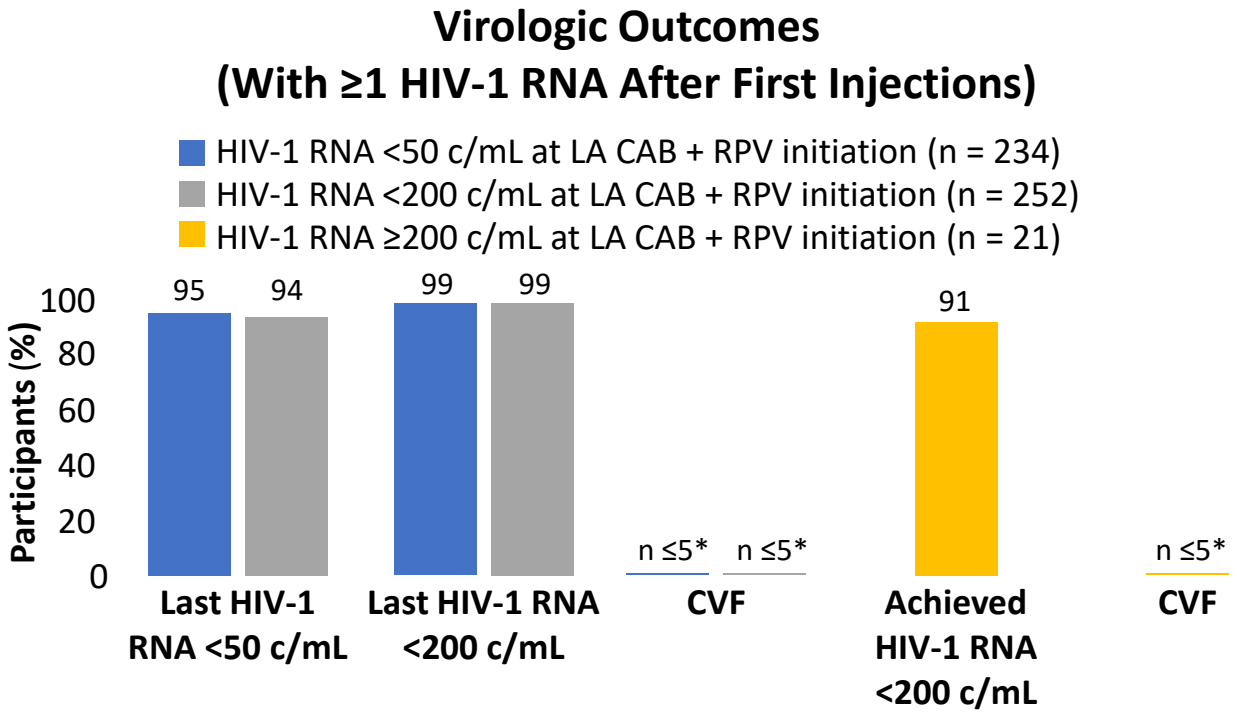
Real-world Effectiveness of Long-Acting CAB + RPV in the First Year in the US OPERA Cohort

- **LA CAB + RPV was highly effective in US OPERA cohort of PWH virologically suppressed at regimen initiation and in a small number of PLWH unsuppressed at initiation (last HIV-1 RNA <200 c/mL in 99% of PLWH).**

Characteristic	Suppressed (<200 copies/mL) (n = 348)	Viremic (≥200 copies/mL) (n = 28)	Undetectable (<50 copies/mL) (n = 321)	Detectable (≥50 copies/mL) (n = 55)
Median age, yr (IQR)	40 (32-52)	36 (29-44)	40 (32-52)	38 (31-45)
▪ **18-25**	14 (4)	≤5*	13 (4)	≤5*
▪ **26-49**	235 (68)	24 (86)	217 (68)	42 (76)
▪ **50+**	99 (28)	≤5*	91 (28)	10 (18)
Female gender, n (%)	49 (14)	15 (54)	45 (14)	19 (34)
Race, n (%)				
▪ **Black**	128 (37)	27 (79)	117 (36)	33 (60)
▪ **White**	185 (53)	6 (21)	171 (53)	20 (36)
▪ **Other/unknown**	35 (10)	0	33 (10)	≤5*
Hispanic ethnicity, n %	100 (29)	≤5*	95 (30)	8 (14)
Median yr from HIV diagnosis (IQR)	7 (4-14)	10 (5-16)	7 (4-14)	8 (4-17)
Yr of ART Initiation, n (%)				
▪ **Prior to or during 2015**	121 (35)	8 (29)	113 (35)	16 (29)
▪ **2016-2018**	109 (31)	11 (39)	97 (30)	23 (42)
▪ **During or after 2019**	118 (34)	9 (32)	111 (35)	16 (29)
AIDS-defining illness, n (%)	76 (22)	6 (21)	64 (20)	18 (33)
Median log viral load (IQR)	1.3 (1.3-1.3)	4.2 (3.1-4.8)	1.3 (1.3-1.3)	2.3 (1.9-4.2)
Median CD4+ cell count (IQR)	651 (471-865)	477 (260-689)	658 (480-871)	539 (333-696)
Median BMI (IQR)	27 (24-31)	27 (22-29)	28 (24-31)	27 (22-30)

Sension. IDWeek 2022. Abstr 1582.

LA CAB + RPV Effectiveness in the OPERA Cohort: Virologic Outcomes and Therapy Duration



*Exact number/% for ≤5 observations can not be specified because of HIPAA rules.

Duration of LA IM CAB + RPV Use	Outcome
HIV-1 RNA <200 c/mL at initiation	**(n = 348)**
▪ Still receiving LA regimen at end of follow-up, %	89
▪ Median follow up, mo (IQR)	3.4 (2.2-6.0)
HIV-1 RNA ≥200 c/mL at initiation	**(n = 28)**
▪ Still receiving LA regimen at end of follow-up, %	89
▪ Median follow up, mo (IQR)	4.4 (2.1-8.5)

CVF, confirmed virologic failure

- **LA CAB + RPV was highly effective in US cohort of PWH virologically suppressed at regimen initiation and in a small number of PWH unsuppressed at initiation**

Sension. IDWeek 2022. Abstr 1582.

LA CAB + RPV in Patients Without Virologic Suppression at Initiation

- Observational study of PWH in San Francisco with challenges adhering to oral ART who were started on LA CAB + RPV monthly[1]
- Of 132 patients referred, 39 received ≥2 follow-up injections:
  - **24 with viral suppression** at time of initiation of LA ART
    - **All maintained suppression**
  - **15 without viral suppression** at time of initiation of LA ART
    - **12 (80%) achieved viral suppression**

- US OPERA cohort: 145,398 PWH[2]
  - Analysis of those receiving first-time LA CAB + RPV Jan 2021 - Feb 2022 with follow-up through Mar 15, 2022

Baseline HIV-1 RNA at First Injections (All Treatment Experienced), n (%)	PWH (N = 383)
HIV-1 RNA <50 c/mL	321 (84)
HIV-1 RNA ≥50 to <200 c/mL	27 (7)
HIV-1 RNA ≥200 c/mL	28 (7)
No baseline HIV-1 RNA	7 (2)

- Of those with ≥1 VL after first injection, **19/21 (91%) with HIV-1 RNA ≥200 c/mL** at initiation **achieved HIV-1 RNA <200 c/mL**

1. Christopoulos. Clin Infect Dis. 2022;ciac631. 2. Sension. IDWeek 2022. Abstr 1582.

Sunlenca (lenacapavir) iniettabile, in associazione con altri antiretrovirali, è indicato per il trattamento degli adulti con infezione da HIV-1 multifarmaco-resistente per i quali non è possibile instaurare un regime antivirale soppressivo alternativo

Tabella 1: Regime di trattamento raccomandato per Sunlenca: schema di dosaggio iniziale e di mantenimento

Giorno di trattamento	
	Dose di Sunlenca: inizio
giorno 1	600 mg per via orale (2 compresse da 300 mg)
giorno 2	600 mg per via orale (2 compresse da 300 mg)
giorno 8	300 mg per via orale (1 compressa da 300 mg)
giorno 15	927 mg mediante iniezione sottocutanea (2 iniezioni da 1,5 mL[a])
	Dose di Sunlenca: mantenimento
Ogni 6 mesi (26 settimane)[b] +/-2 settimane	927 mg mediante iniezione sottocutanea (2 iniezioni da 1,5 mL[a])

a Due iniezioni in due sedi diverse nell'addome.
b Dalla data dell'ultima iniezione.

Se il trattamento con Sunlenca viene interrotto, è essenziale adottare un regime antiretrovirale alternativo totalmente soppressivo, se possibile, non oltre 28 settimane dopo l'ultima iniezione di Sunlenca

http://www.ema.europa.eu.