HIV e farmaci long-acting: identikit del paziente da trattare

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Disclosures

- I have participated in Advisory boards for ViiV Healthcare, Gilead Sciences, Janssen Cilag, Abbvie, MSD.
- I have received research grants from ViiV Healthcare and Gilead Sciences

Identikit del paziente da trattare?

4. INFORMAZIONI CLINICHE

4.1 Indicazioni terapeutiche

[redacted] è indicato, in associazione con rilpivirina iniettabile, per il trattamento dell'infezione da virus dell'immunodeficienza umana di tipo 1 (HIV-1) negli adulti in soppressione virologica (HIV-1 RNA <50 copie/mL) con un regime antiretrovirale stabile, senza evidenza presente o passata di resistenza virale e di precedente fallimento virologico agli agenti della classe degli NNRTI e degli INI (vedere paragrafi 4.2, 4.4 e 5.1)[redacted]

Identikit del paziente da trattare?

1. Compliante, aderente, puntuale, HIV-RNA non rilevato persistentemente, no fallimenti, da molti anni in f-up ?
2. Aderenza <90%, alcuni blip viremici, con o senza fallimenti virologici, da molti anni in f-up ma sempre irregolare, attualmente <50 copie/mL da oltre 12 mesi?

Tutti e 2 i profili sono nel «bugiardino»

- Devo tenere conto ancora di qualcosa?

Patient interest

- 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

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Long-acting cabotegravir and rilpivirine for HIV-1 suppression: switch to 2-monthly dosing after 5 years of daily oral therapy

AIDS 2022, Vol 36 No 2

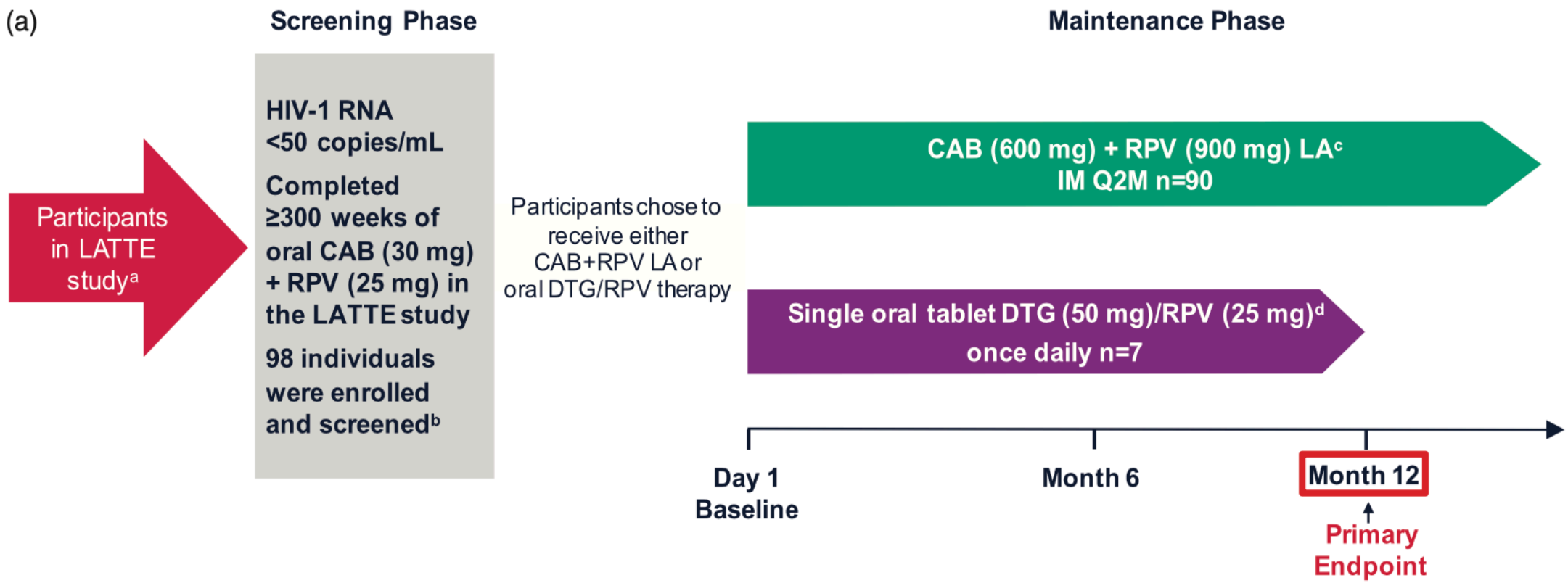

Table 1. Baseline participant characteristics.

Parameter	IM CAB+RPV LA Q2M arm $n=90$	Oral DTG/RPV QD arm $n=7$	Total $N=97$
Age, median (range) years	41 (25–63)	53 (30–62)	41 (25–63)
Age ≥50 years, *n* (%)	16 (18)	4 (57)	20 (21)
Female (sex at birth), *n* (%)	2 (2)	0	2 (2)
Female (self-reported sex), *n* (%)	3 (3)	0	3 (3)
Race, *n* (%)			
White	63 (70)	4 (57)	67 (69)
Black or African–American	21 (23)	3 (43)	24 (25)
Other	6 (7)	0	6 (6)
BMI, median (range) kg/m^2	27 (19–48)	27 (24–31)	27 (19–48)
$CD4^+$ cell count, median (range) cells/μl	851 (376–1593)	779 (595–1050)	842 (376–1593)

Table 1 was presented previously at IDWeek; October 21–25, 2020; Virtual; Oral. CAB, cabotegravir; DTG, dolutegravir; IM, intramuscular; LA, long-acting; QD, once daily; Q2M, every 2 months; RPV, rilpivirine.

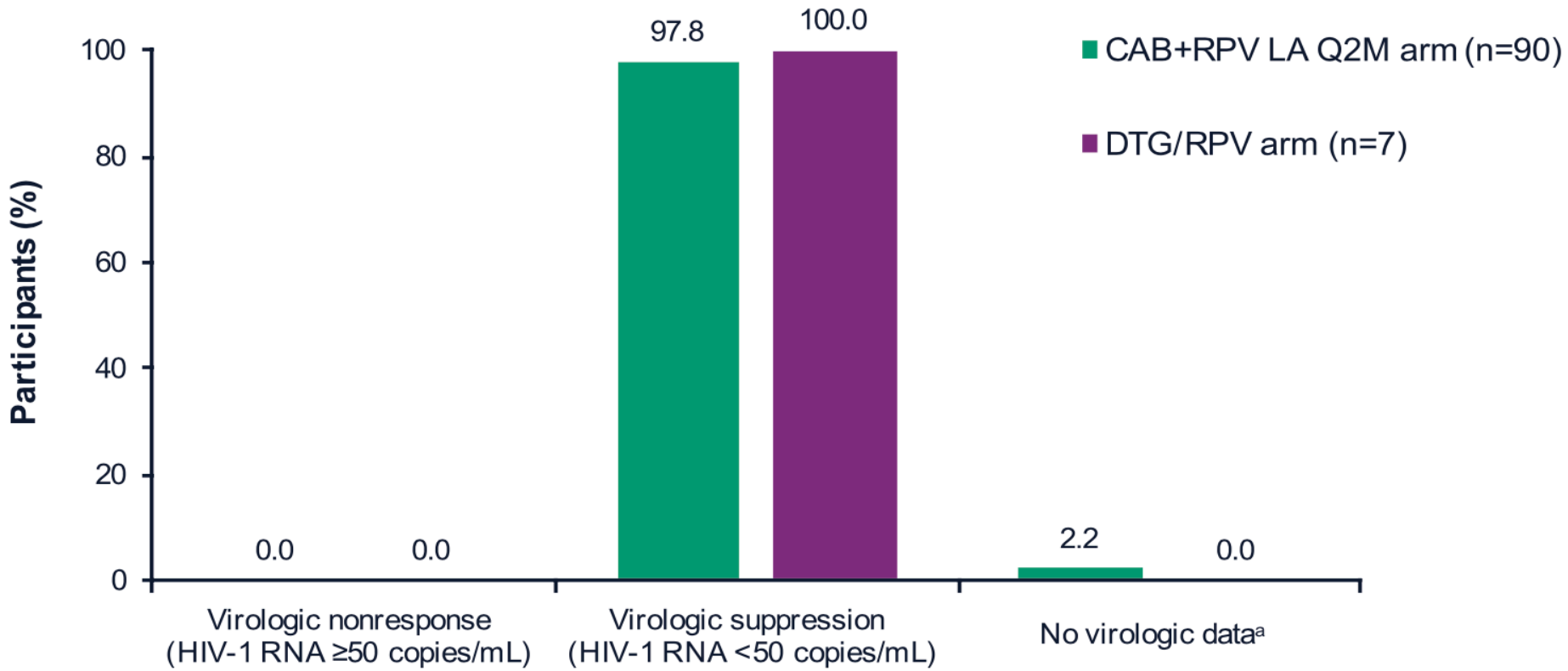

Fig. 2. Efficacy outcomes at Month 12. [a]Two (2%) participants in the LA arm had no virologic data at Month 12; one discontinued treatment due to an AE and the other was lost to follow-up. Figure 2 was presented previously at IDWeek; October 21–25, 2020; Virtual; Oral. AE, adverse event; CAB, cabotegravir; DTG, dolutegravir; LA, long-acting; Q2M, every 2 months; RPV, rilpivirine.

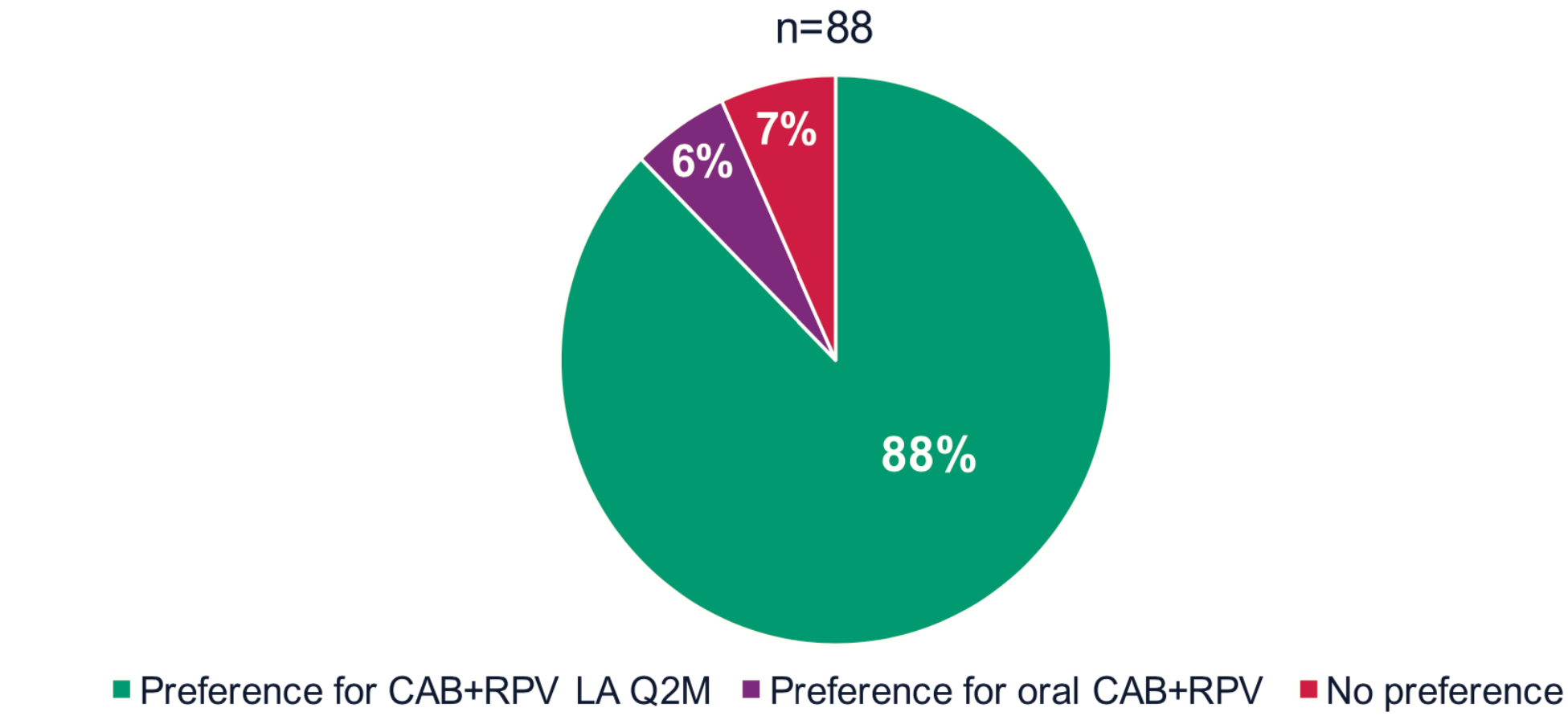

Fig. 3. Treatment preference at Month 12 for participants receiving CAB+RPV LA Q2M. Figure 3 was presented previously at IDWeek; October 21–25, 2020; Virtual; Oral. CAB, cabotegravir; LA, long-acting; Q2M, every 2 months; RPV, rilpivirine.

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RISPOSTA: SI

La mia esperienza in questo setting

1. **Compliante, aderente, puntuale, HIV-RNA non rilevata persistentemente, no fallimenti, da molti anni in f-up**

Terapia iniettiva.

GD [redacted]

martedì 21 giugno 2022, 12:09

A: Di Biagio Antonio

Buongiorno grande Prof!
Come sai sono in contatto con altre persone HIV + e sono venuto a sapere a Settembre a Verona iniziano con la terapia per iniezione. Ne ho parlato con la Dott.ssa Alessandrini la quale si è segnata il mio nome da sottoporti xché pare sia tu che tiri le fila per l introduzione di questo nuovo metodo. Ti chiedo, ovviamente se è possibile e se lo ritieni opportuno, di essere annoverato fra gli "iniettabili". La Dottoressa ha detto che assumendo Odefsey (la famosa Fedora nell ambiente) potrei essere fra i beneficiari della nuova metodica in quanto [redacted] contiene già un molecola che regolarmente assumo.
Vedi tu vosa fare e, per un informazione completa, sono coperto dalle pastiglie sino alla fine del mese di Laglio.
Grazie per un tuo cenno e saluti.
Doc
[redacted]

P.s. se pensi che ti possa servire per effettuare controlli/test ti prego di approfittare di me come meglio lo ritieni opportuno. Credimi lo faccio volentieri anche considerando il debito che ho nei vostri confronti.

15 giorni dopo

A: Di Biagio Antonio

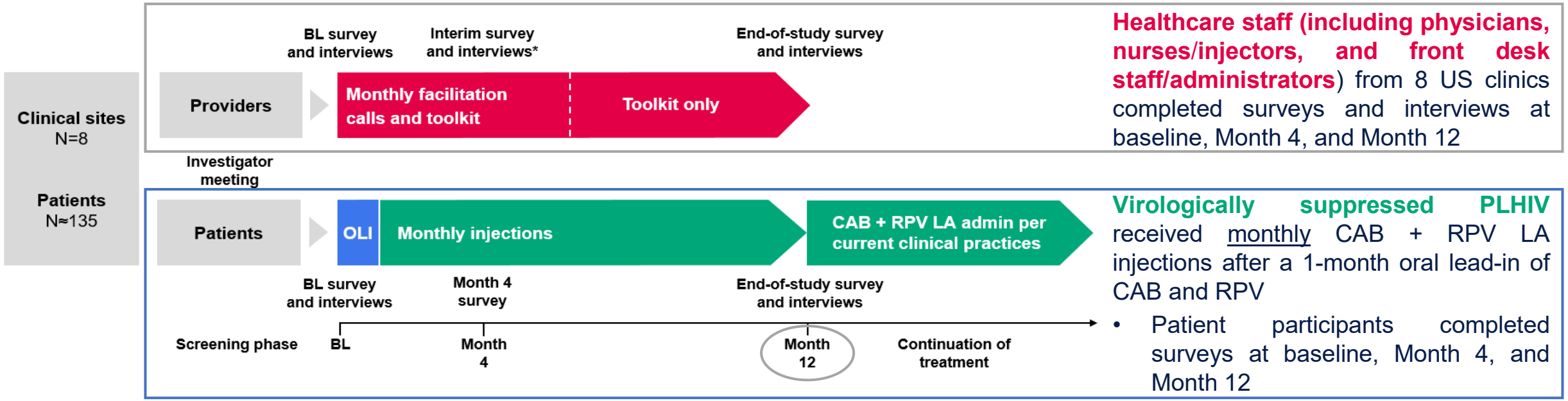
Buongiorno grande Prof!
Per quanto concerne la terapia tutto bene, solo un lieve fastidio alla gamba dove è stata iniettata da parte pastosa (tipo penicillina di una volta). Nessun effetto collaterale (un attacco lieve di emicrania ma nel cambio stagionale mi succede e curata con due banali vivin c).
L unica cosa da segnalare è che con le pastiglie avevi una gestualità metodica che ti dava appagamento psicologico (prendo pastiglia tengo a bada Hiv) con l iniezione questo appagamento nn c è più e ogni volta devo pensare "se me lo ha detto Di Biagio funziona ".
Come mi hai chiesto ho sospeso l assunzione degli aminoacidi suggeritimi dal personal trainer per supportare la muscolatura.
Ho scaricato la app che mi hai segnalato e, credo e spero, di aver fatto tutto quanto richiesto su Policlinico San Martino....se hai opportunità di controllare se tutto è corretto così nel caso correggo.
Ci vediamo il 28 ottobre per la seconda dose.
Saluti.

Ma quando non è più il singolo?

Cosa abbiamo imparato dalla pratica clinica?

CUSTOMIZE study design

CUSTOMIZE is a phase IIIb, **hybrid III**§ implementation-effectiveness study that examined barriers to, facilitators of, and effective strategies for successful implementation of the **monthly** CAB + RPV LA injectable regimen in US[1,2] clinical practice settings



Healthcare staff (including physicians, nurses/injectors, and front desk staff/administrators) from 8 US clinics completed surveys and interviews at baseline, Month 4, and Month 12

Virologically suppressed PLHIV received monthly CAB + RPV LA injections after a 1-month oral lead-in of CAB and RPV

- Patient participants completed surveys at baseline, Month 4, and Month 12

§ Hybrid type III means 80% implementation outcomes + 20% effectiveness outcomes

*Interim analysis will be conducted approximately after the 4th monthly facilitation call interim interviews have been completed with site staff. Completed Month 4 surveys from patient will also be included
BL, baseline

1. CUSTOMIZE (209493). Available at: https://clinicaltrials.gov/ct2/show/NCT04001803 (accessed Dec 2020)
2. Czarnogorski M, et al. AIDS 2020. Poster LBPEE42

NP-IT-CBR-PPT-220018

CUSTOMIZE: to inform the clinic and patient journey for implementation of monthly CAB + RPV LA

CUSTOMIZE[1,2]

US

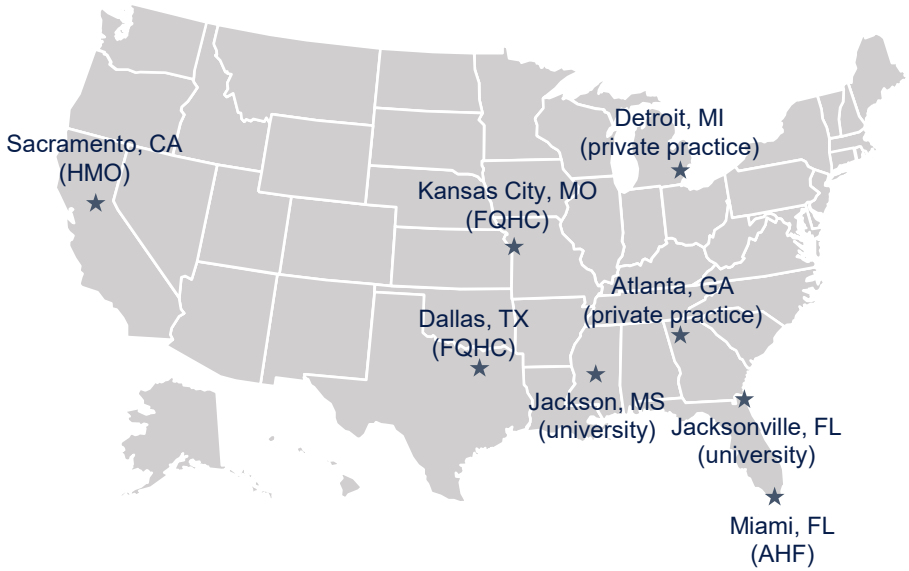
Clinical sites
8

Patients
~135

Staff
24

Sites/staff to receive a toolkit* and monthly facilitation calls

Sites allowed to choose how they will implement CAB + RPV LA delivery in their clinical settings



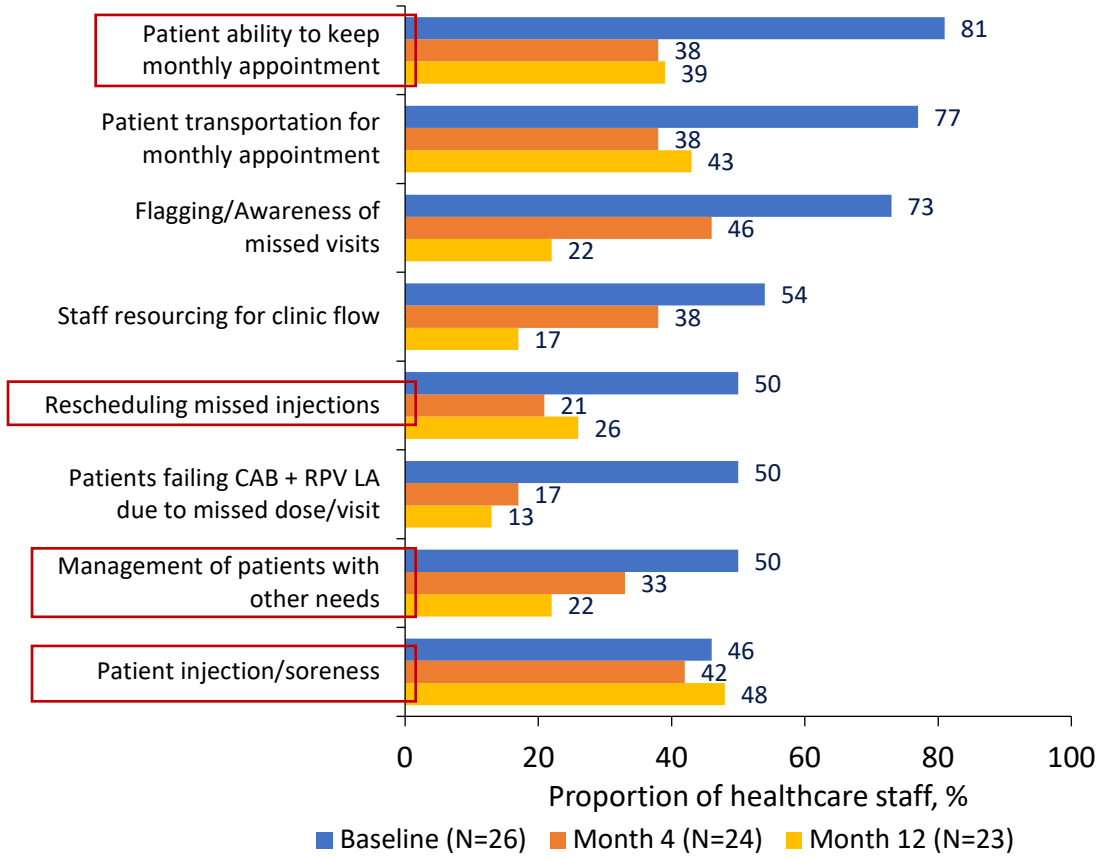
Healthcare staff and participants enrolled in CUSTOMIZE were from **5 different clinic types** in 8 cities across the United States

*CUSTOMIZE toolkit consists of CAB + RPV LA factsheet and injection video and web-based treatment planner for HCPs; hot and cold packs, injection flash card, FAQ, and 'What to expect' video for patients; patient reminder system for both HCPs and patients
CQI, continuous quality improvement, **SDM,** services delivery meeting; **US,** United States

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

1. CUSTOMIZE (209493). Available at: https://clinicaltrials.gov/ct2/show/NCT04001803 (accessed Dec 2020)

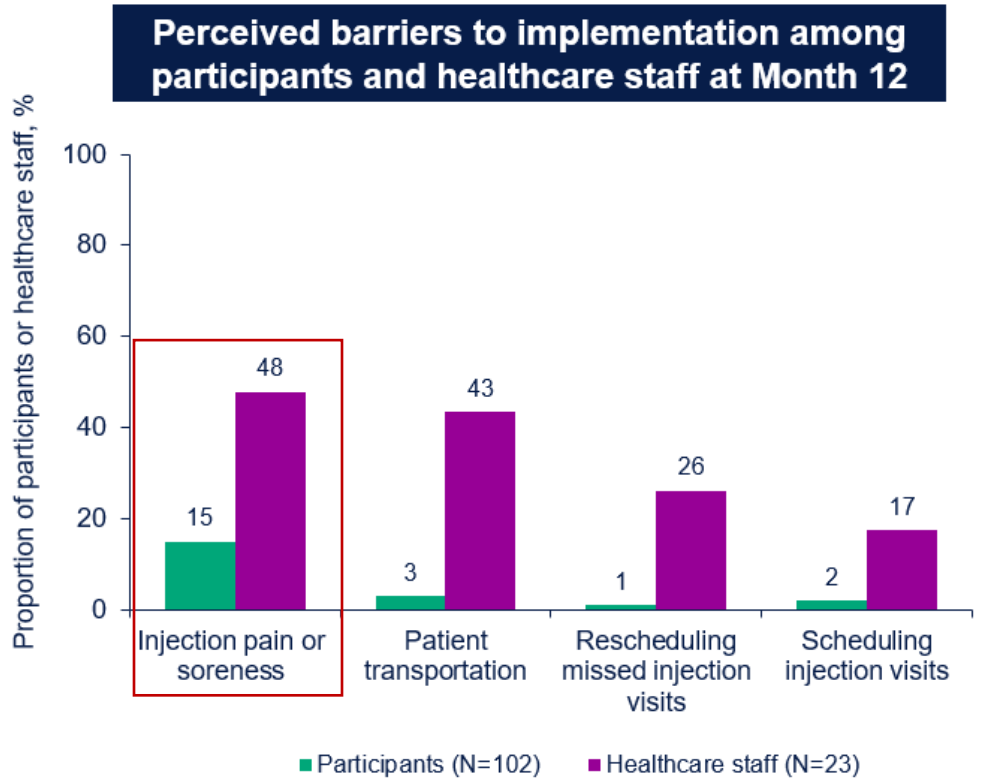
Perceived Barriers to Implementation Among Healthcare Staff Decreased over time



As perceived by healthcare staff, **all barriers to implementation substantially decreased by Month 12 except for patient injection/soreness**

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.

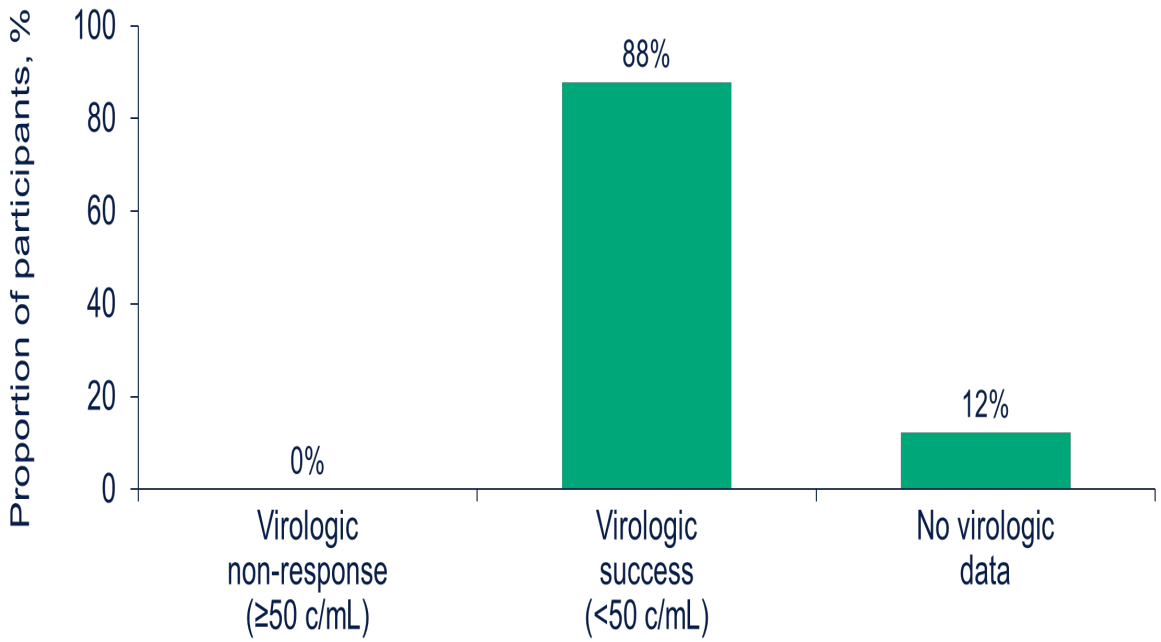
Participants Reported Fewer Concerns Compared With Healthcare Staff



- **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%)

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

Virologic Outcomes at Month 12 (FDA Snapshot Algorithm)



Outcome, n (%)	CAB + RPV LA Q1M (N=115)
HIV-1 RNA <50 c/mL	101 (88)
HIV-1 RNA ≥50 c/mL	0
No virologic data	14 (12)
Discontinued due to AE or death	5 (4)[a]
Discontinued for other reasons	8 (7)[b]
On study but missing data in window	1 (1)[c]

Q1M, every 1 month. [a]One death was reported due to diabetic ketoacidosis and drug abuse (both unrelated to study treatment). [b]Reasons include withdrawn consent (n=4), protocol deviation (n=3), and physician decision (n=1). [c]Due to COVID-19.

Virologic Outcomes

- **At Month 12, 88% (101/115) of participants maintained virologic suppression (HIV-1 RNA <50 c/mL), and no participants had HIV-1 RNA ≥50 c/mL**
  - 1 participant with missing data in the Month 12 window, due to COVID-19, maintained HIV-1 RNA <50 c/mL at all visits through Month 10 and remained undetectable at an unscheduled visit at Month 13
- **No confirmed virologic failures** (2 consecutive HIV-1 RNA measurements ≥200 c/mL) occurred through Month 12

- Sinclair et al. IAS 2021 PED416

SUPERARE LA DIFFIDENZA DEGLI OPERATORI

Identikit del paziente da trattare?

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2. **Aderenza <90%, alcuni blip viremici, con o senza fallimenti virologici, da molti anni in f-up ma NON sempre regolare, attualmente <50 copie/mL da oltre 12 mesi?**

Teoria

Journal of *Personalized Medicine*

MDPI

Article

Could Long-Acting Cabotegravir-Rilpivirine Be the Future for All People Living with HIV? Response Based on Genotype Resistance Test from a Multicenter Italian Cohort

Andrea De Vito [1,*], Annarita Botta [2], Marco Berruti [3,4], Valeria Castelli [5,6], Vincenzo Lai [7], Chiara Cassol [8,9], Alessandro Lanari [8,9], Giulia Stella [8,9], Adrian Shallvari [10,11], Antonia Bezenchek [10,11] and Antonio Di Biagio [4]

Received: 25 December 2021
Accepted: 26 January 2022
Published: 31 January 2022

Results

- **Overall, of the 4103 patients currently on follow-up in the ARCA database,**
- **1883 PWH were selected. Furthermore, we excluded people having NNRTI or INSTI mutations**
- **Therefore, 1641 (39.9%) patients met the eligibility criteria for treatment with long- acting CAB/RPV.**

PRATICA

Received: 18 March 2022 | Accepted: 12 July 2022

DOI: 10.1111/hiv.13370

ORIGINAL ARTICLE

Compassionate use of long-acting cabotegravir plus rilpivirine for people living with HIV-1 in need of parenteral antiretroviral therapy

Ronald D'Amico[1] | Santiago Cenoz Gomis[2] | Riya Moodley[3] | Rodica Van Solingen-Ristea[4] | Bryan Baugh[5] | Erika Van Landuyt[4] | Veerle Van Eygen[4] | Sherene Min[1] | Amy Cutrell[1] | Caroline Foster[6] | Daniella Chilton[7] | Sabine D. Allard[8] | Annemiek Ruiter[3]

Request programmes supported by ViiV Healthcare (for cabotegravir) and Janssen (for rilpivirine)

HIV MEDICINE, 2022

TABLE 1 Demographics and clinical characteristics at start of compassionate use programme

Characteristic	N = 35
Female at birth	20 (57)
Perinatally infected	11 (31)
Age, y	36 (20–67)
Body mass index, kg/m^2	21 (16–38)
Current AIDS diagnosis	23 (66)
No. of regimens before compassionate use	4 (1–10)
HIV-1 RNA ≥50 copies/mL	28 (80)
≥50 to 10 000	9
>10 000 to 50 000	4
>50 000 to 100 000	4
>100 000	11
CD4+ cell count, cells/mm^3	100 (3–918)
Initiation of injections without oral lead-in	12 (34)
Primary reason for compassionate use request, n	
Psychological[a]	15
Physical challenges[b]	8
Malabsorption	6
Dysphagia	3
Limited cognitive skills	3

Note: Data are presented as n (%) or median (range) unless otherwise indicated.

[a]Includes issues with swallowing pills, pill fatigue, chronic poor oral adherence, and stigma.

[b]Includes chronic diarrhoea, incarcerated ventral hernia, severe malnutrition, severe mucositis, pancreatic insufficiency, intractable or

35 totali
20 donne
11 MTCT
23 AIDS

PRIMA MOTIVAZIONE:
Psicologica

28/35 entrati con HIV RNA >50 copie/mL

11 di questi con HIV RNA >100.000 copie/mL

TABLE 2 Incomplete virological responses leading to withdrawal

Description and reason for CU[a]	• 60–69 years • BMI 32.5 kg/m^2 • Extensive small bowel resection	• 30–39 years • BMI 20.5 kg/m^2 • History of non-adherence due to trauma	• 40–49 years • BMI 35 kg/m^2 • Non-adherence (cognitive impairment)	• 30–39 years • BMI 26 kg/m^2 • Chronic oral non-adherence	• 40–49 years • BMI 26 kg/m^2 • Pancreatic insufficiency	• 30–39 years • BMI 25 kg/m^2 • Pill phobia	• 20–29 years • BMI 34.6 kg/m^2 • Poor adherence (cognitive impairment)
VL at CU start	<40 copies/mL	61 600 copies/mL	32 000 copies/mL	116 311 copies/mL	77 578 copies/mL	205 000 copies/mL	1 639 794 copies/mL
CD4+ cell count at CU start	749 cells/mm^3	53 cells/mm^3	177 cells/mm^3	20 cells/mm^3	45 cells/mm^3	50 cells/mm^3	8 cells/mm^3
Time of VF/discontinuation	After 19th injection	After 11th injection	After 10th injection	After 7th injection	After 4th injection	After 1st maintenance injection	After 2nd injection
VL at VF/discontinuation	VL blip (55 copies/mL) with no change in adherence; repeat VL <40 copies/mL	Not available	799 copies/mL	37 594 copies/mL	7190 copies/mL	186 972 copies/mL	66 000 copies/mL
Mutations at CU start	None	RT: M184V, K219E, E138G	RT: K238K/R, E138G	RT: V118I/V, V179I, R211K IN: E138D	None	RT: K103N	RT: K103N, M184V, T215Y
Mutations at VF/discontinuation	IN: G118G/R	RT: E138E/K	RT: E138G, M230L IN: Q148R, N155H	RT: E138G, Y181I IN: M50M/I, E138D, E157E/Q	RT: K101E IN: E13 8E/K, Q148R, G163E	RT: K101E, Y181Y/C	RT: Y181C, K219N
CAB LA + RPV LA regimen	Discontinued CAB LA + RPV LA; changed to double-dosed DRV/r + TAF/FTC	• No oral lead-in, LA dosing initiated with detectable viremia • Did not achieve VL <50 copies/mL	• No oral lead-in • VL <50 copies/mL 4 weeks after first injection and remained <50 copies/mL for up to 5 months	• No oral lead-in, LA dosing initiated with detectable viremia • Did not achieve VL <50 copies/mL	• No oral lead-in, LA dosing initiated with detectable viremia • Did not achieve VL <50 copies/mL	VL <50 copies/mL after 4-wk oral lead-in	• VL 512 000 copies/mL after 4 weeks oral lead-in • Did not achieve VL <50 copies/mL

SOLO 16 (35%) HIVRNA <50 copie/mL

Esperienza nei primi PLWHIV-CMIGE

- Uomo, 60aa, MSM, diagnosi 2012, NNRTI-STR, HIV RNA <50 copie/ml da oltre 10 anni, CD4+ >500 cell/mmc
- Donna di 40aa, diagnosi Marzo 2020, INSTI-STR
- Uomo di 34 aa, MTCT, NNRTI-STR, HIV RNA <50 copie/ml da oltre 20 anni, CD4+ >500 cell/mmc
- Donna di 52aa, madre del 3, NNRTI-STR, HIV RNA <50 copie/ml da oltre 20 anni, CD4+ >500 cell/mmc
- Donna di 46aa, NNRTI-STR, HIV RNA <50 copie/ml da oltre 10 anni, CD4+ >500 cell/mmc
- Donna, di 39 aa, diagnosi 2012, NNRTI-STR, HIV RNA <50 copie/ml da oltre 10 anni, CD4+ >500 cell/mmc
- Uomo, di 55aa, diagnosi 2011, NNRTI-STR, HIV RNA <50 copie/ml da oltre 10 anni, CD4+ >500 cell/mmc
- Uomo di 45aa, MSM, diagnosi 2008, DTG/RPV, HIV RNA <50 copie/ml da oltre 10 anni, CD4+ >500 cell/mmc

Identikit del paziente da trattare?

- Rispettare indicazioni
- Discutere con tutti i PLH eleggibili
- Superare ostacoli team medico-infermiere

www.reteligureHIV.it

GENOVA SANREMO

FAST TRACK CITIES

LIGURIA HIV NETWORK

www.reteligurehiv.it

OSPEDALE POLICLINICO SAN MARTINO
Sistema Sanitario Regione Liguria
Istituto di Ricovero e Cura a Carattere Scientifico per l'Oncologia

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