MEETING

Un approccio multidisciplinare alla terapia Long Acting in HIV per la sfida del futuro

Desenzano, 6 Giugno 2025

Centro Congressi Hotel Desenzano

NUOVE MODALITÀ DI SOMMINISTRAZIONE DI FARMACI LONG-ACTING: UN CAMBIO DI PARADIGMA?

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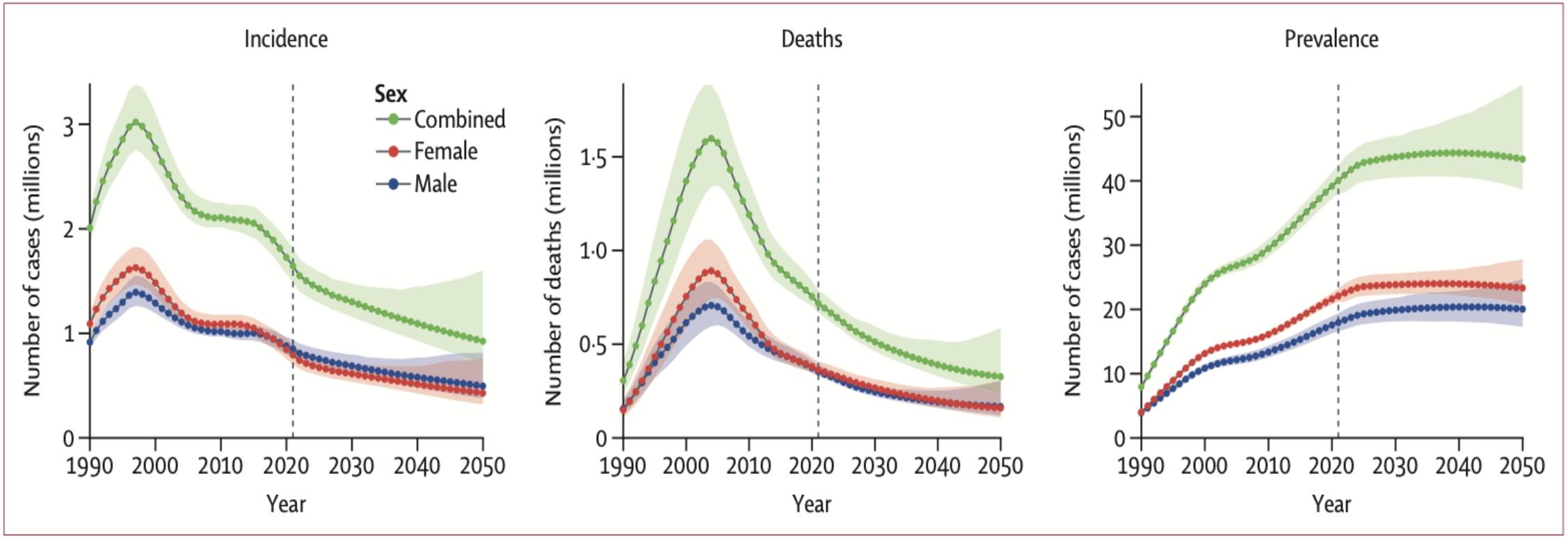
Temporal trends of HIV incidence, mortality, and prevalence counts for 1990–2050



More than 40 million people globally will continue to require lifelong ART for decades into the future

GBD 2021 HIV Collaborators, Lancet HIV 2024

MILESTONES IN HIV PREVENTION, TREATMENT AND CARE[1–8]

1982
Gay Men's Health Crisis (the first community-based AIDS service provider) is established in New York City[1]

1983
Treatment goals are focussed on preventing death and protecting healthcare professionals[2,3]

1987
First ART approved for the treatment of AIDS[1]

1991
International Council of AIDS Service Organisations is established as a network for nongovernmental and community-based organisations[1]

1995
HAART era begins[1]

2000
Durban Declaration, signed by 5,000 prominent clinicians and investigators, attests to overwhelming evidence that HIV causes AIDS, counteracting AIDS "denialism"[1]

2006
First single pill regimen approved[4]

2012
First approved daily oral regimen for PrEP[4]

2014
UNAIDS launches ambitious 90-90-90 targets to be achieved by 2020[5]

2016
U=U consensus statement issued[6]

2016
WHO updates treatment guidelines recommending treatment for all[7]

2021
First approved long-acting regimen for HIV treatment and first approved long-acting regimen for PrEP[8]

2021
UNAIDS targets for 2025 are 95-95-95[9]

Adapted from Brandt AM, et al. N Engl J Med. 2013

Prolonging life → Evolving treatment goals → Holistic health

- **ART,** antiretroviral; **HAART,** highly-active antiretroviral therapy; **PrEP,** pre-exposure prophylaxis **U=U,** Undetectable=Untransmittable; **UNAIDS,** Joint United Nations Programme on HIV/AIDS
WHO, World Health Organization

1. Brandt AM, et al. N Engl J Med. 2013;368:2149–52; **2.** HIV.gov. A timeline of HIV and AIDS. Available at: https://www.hiv.gov/hiv-basics/overview/history/hiv-and-aids-timeline. Accessed February 2022; **3.** Piot P, et al. Science. 1988;239:573–9; **4.** Tseng A, et al. Br J Clin Pharmacol. 2015;79:182–94
5. Levi J, et al. BMJ Global Health 2016;1:e000010; **6.** BHIVA. BHIVA encourages universal promotion of Undetectable=Untransmittable (U=U). Available at: https://www.bhiva.org/BHIVA-encourages-universal-promotion-of-U-U. Accessed February 2022; **7.** WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Available at: https://www.who.int/publications/i/item/9789241549684. Accessed February 2022
8. FDA news release. FDA Approves First Injectable Treatment for HIV Pre-Exposure Prevention. Available at: https://www.fda.gov/news-events/press-announcements/fda-approves-first-injectable-treatment-hiv-pre-exposure-prevention. Accessed February 2022
9. UNAIDS. 2025 AIDS targets. Available at: https://www.unaids.org/sites/default/files/2025-AIDS-Targets_en.pdf. Accessed February 2022

Seeking to end the HIV pandemic

UNAIDS targets for 2025 include:*[1]

- 95% of PLWH knowing their HIV status
- 95% of PLWH who know their status on treatment
- 95% of PLWH on treatment with suppressed viral loads

Proposed additional target for international bodies ('the 4th 90'):[2]

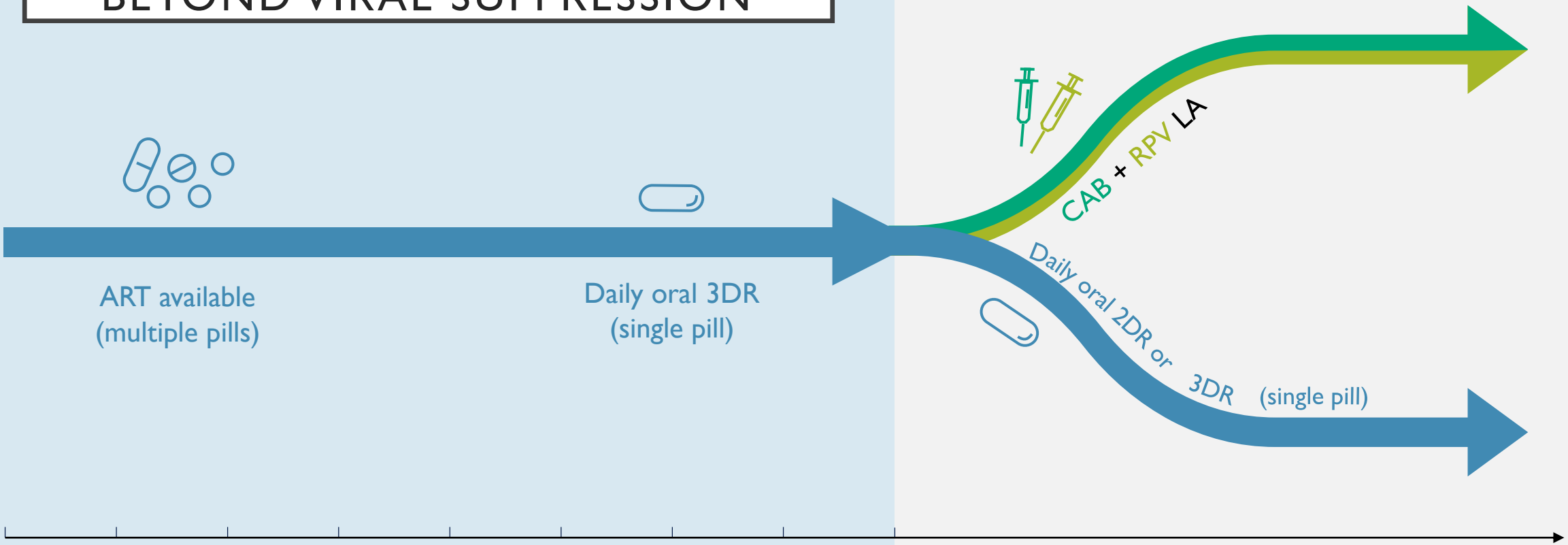
by addressing multimorbidity, HRQoL, stigma and discrimination

→ Addressing key unmet needs and improving HRQoL supports UNAIDS overall targets

*Additional targets include 95% coverage of services for eliminating vertical transmission, 95% of women accessing HIV, sexual and reproductive health services and 95% use of combination prevention[1]
HRQoL, health-related quality of life; **UNAIDS,** Joint United Nations Programme on HIV/AIDS

1. UNAIDS. 2025 AIDS Targets. Available at: https://aidstargets2025.unaids.org/ (accessed Sep 2023)
2. Lazarus JV, et al. Nat Commun 2021;12:4450

HIV TREATMENT EVOLUTION: ADDRESSING NEEDS OF PLWH BEYOND VIRAL SUPPRESSION



In the early days[1,2]

of HIV treatment, success was defined as prolonging life

As treatment evolved[2]

success became prolonging life with fewer short- and long-term side effects and more convenient dosing

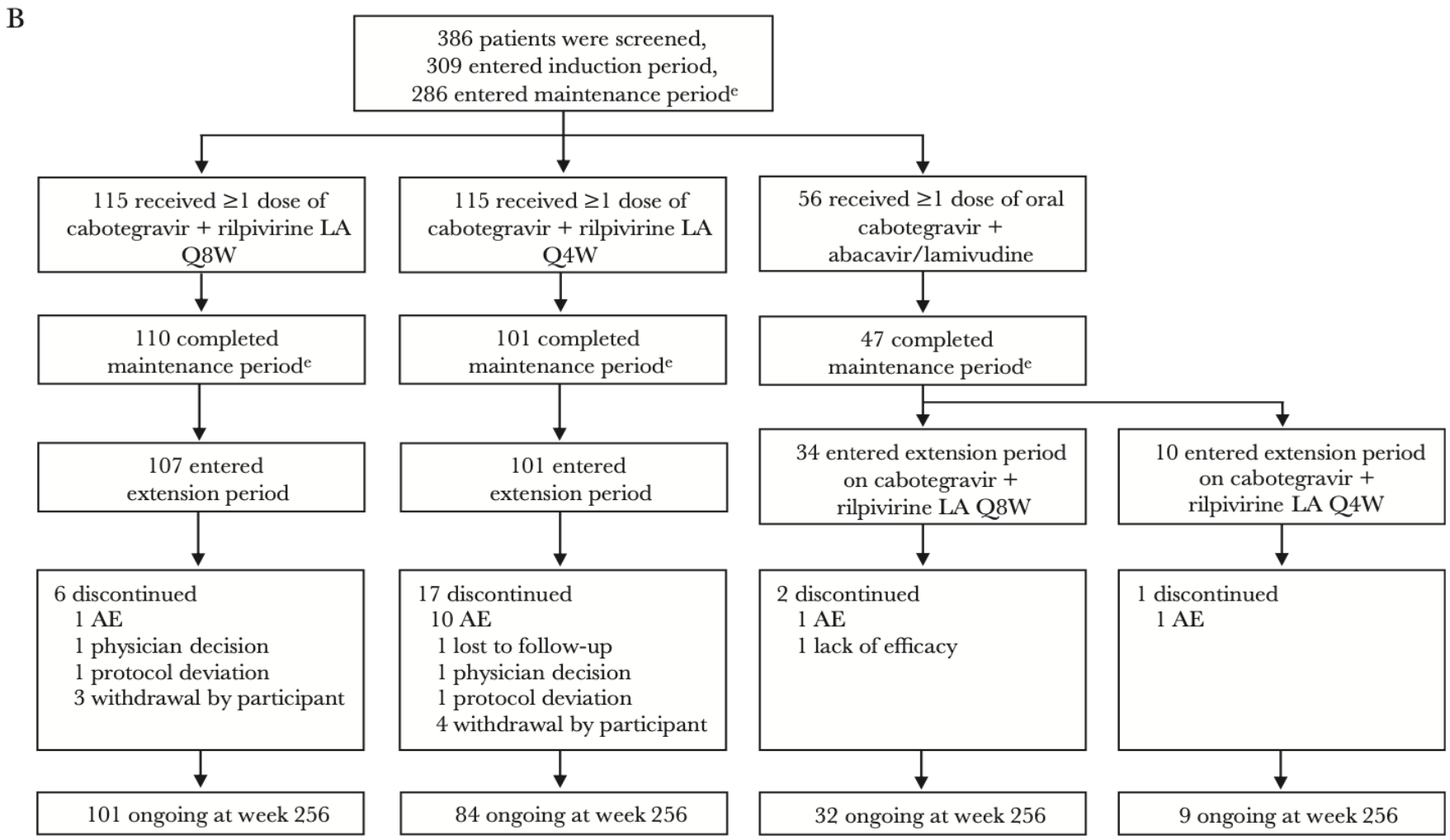
Today[3–5]

with increasing emphasis on patient-reported outcomes and PLWH engagement in care, there are clear benefits to adding QoL to the definition of success

2DR, 2-drug regimen; **3DR,** 3-drug regimen; **QoL,** quality of life

1. Fischl MA, et al. N Engl J Med 1987;317:185–91; **2.** Vella S, et al. AIDS. 2012;26:1231–41
3. Lazarus JV, et al. BMC Med 2016;14:94; **4.** DHHS Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Mar 2023; **5.** Gandhi RT, et al. JAMA 2023;329:63–84

FIVE- YEARS RESULTS OF THE LATTE 2 STUDY



Five participants had HIV-RNA > 50 copies/ml at week 256 (4 in the randomized Q8W, 1 in the extension-switch Q8 group)

The first participant developed an R269R/G integrase mixture, which did not decrease susceptibility to cabotegravir. The second participant developed treatment-emergent reverse transcriptase mutations in K103N, E138G, and K238T and integrase mutation Q148R

At week 256, 88% (n = 101) and 74% (n = 84) of participants in the randomized Q8W and Q4W groups, respectively, maintained HIV-1 RNA <50 copies/mL

GHR SMITH, OFID 2021

Long-Acting Cabotegravir and Rilpivirine Dosed Every 2 Months in Adults With Human Immunodeficiency Virus 1 Type 1 Infection: 152-Week Results From ATLAS-2M, a Randomized, Open-Label, Phase 3b, Noninferiority Study

Background. Cabotegravir (CAB) + rilpivirine (RPV) dosed intramuscularly monthly or every 2 months is a complete, long-acting (LA) regimen for the maintenance of HIV-1 virologic suppression. Here, we report the Antiretroviral Therapy Long-Acting Suppression (ATLAS)-2M study week 152 results.

Methods. ATLAS-2M is a phase 3b, randomized, multicenter study assessing the efficacy and safety of CAB+RPV LA every 8 weeks (Q8W) versus every 4 weeks (Q4W). Virologically suppressed (HIV-1 RNA <50 copies/mL) individuals were randomized to receive CAB+RPV LA Q8W or Q4W. Endpoints included the proportion of participants with plasma HIV-1 RNA ≥50 copies/mL and <50 copies/mL, incidence of confirmed virologic failure (CVF; 2 consecutive measurements ≥200 copies/mL), safety, and tolerability.

Results. A total of 1045 participants received CAB+RPV LA (Q8W, n = 522; Q4W, n = 523). CAB+RPV LA Q8W demonstrated noninferior efficacy versus Q4W dosing, with 2.7% (n = 14) and 1.0% (n = 5) of participants having HIV-1 RNA ≥50 copies/mL, respectively, with adjusted treatment difference being 1.7% (95% CI: 0.1–3.3%), meeting the 4% noninferiority threshold. At week 152, 87% of participants maintained HIV-1 RNA <50 copies/mL (Q8W, 87% [n = 456]; Q4W, 86% [n = 449]). Overall, 12 (2.3%) participants in the Q8W arm and 2 (0.4%) in the Q4W arm had CVF. Eight and 10 participants with CVF had treatment-emergent, resistance-associated mutations to RPV and integrase inhibitors, respectively. Safety profiles were comparable, with no new safety signals observed since week 48.

Conclusions. These data demonstrate virologic suppression durability with CAB+RPV LA Q8W or Q4W for ~3 years and confirm long-term efficacy, safety, and tolerability of CAB+RPV LA as a complete regimen to maintain HIV-1 virologic suppression.

Keywords. antiretroviral therapy; cabotegravir; HIV-1; long-acting; rilpivirine.

ET Overton CID 2023

Long-Acting Cabotegravir and Rilpivirine Dosed Every 2 Months in Adults With Human Immunodeficiency Virus 1 Type 1 Infection: 152-Week Results From ATLAS-2M, a Randomized, Open-Label, Phase 3b, Noninferiority Study

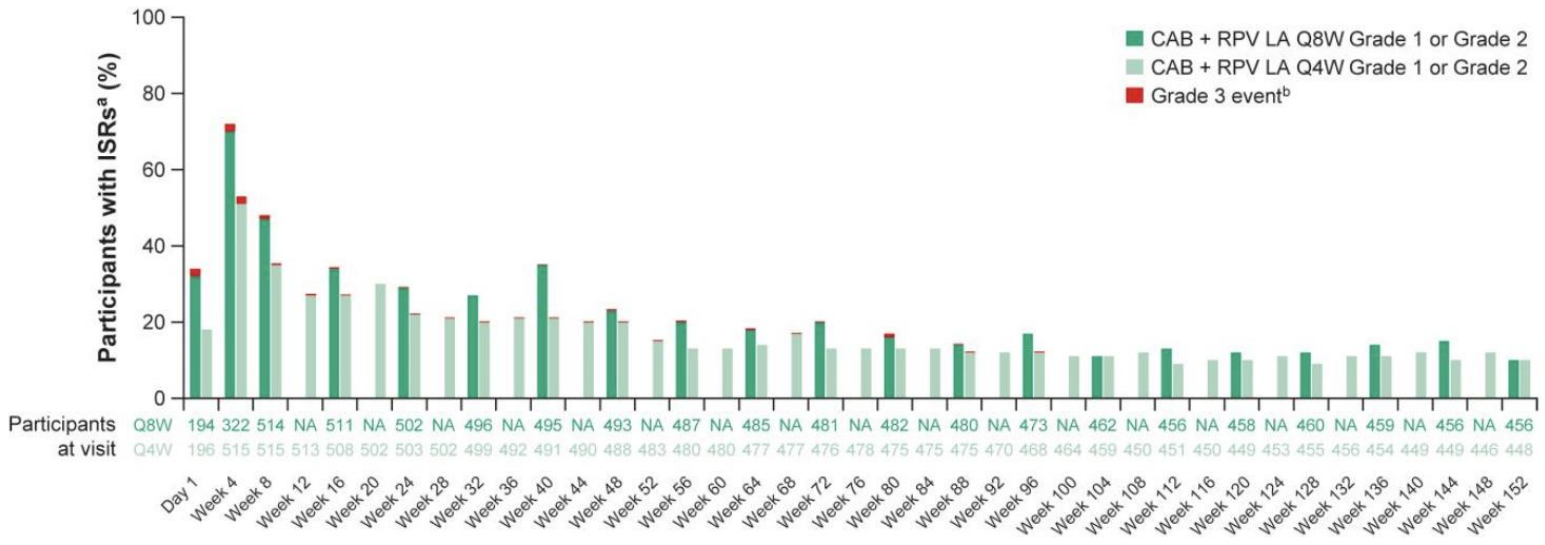
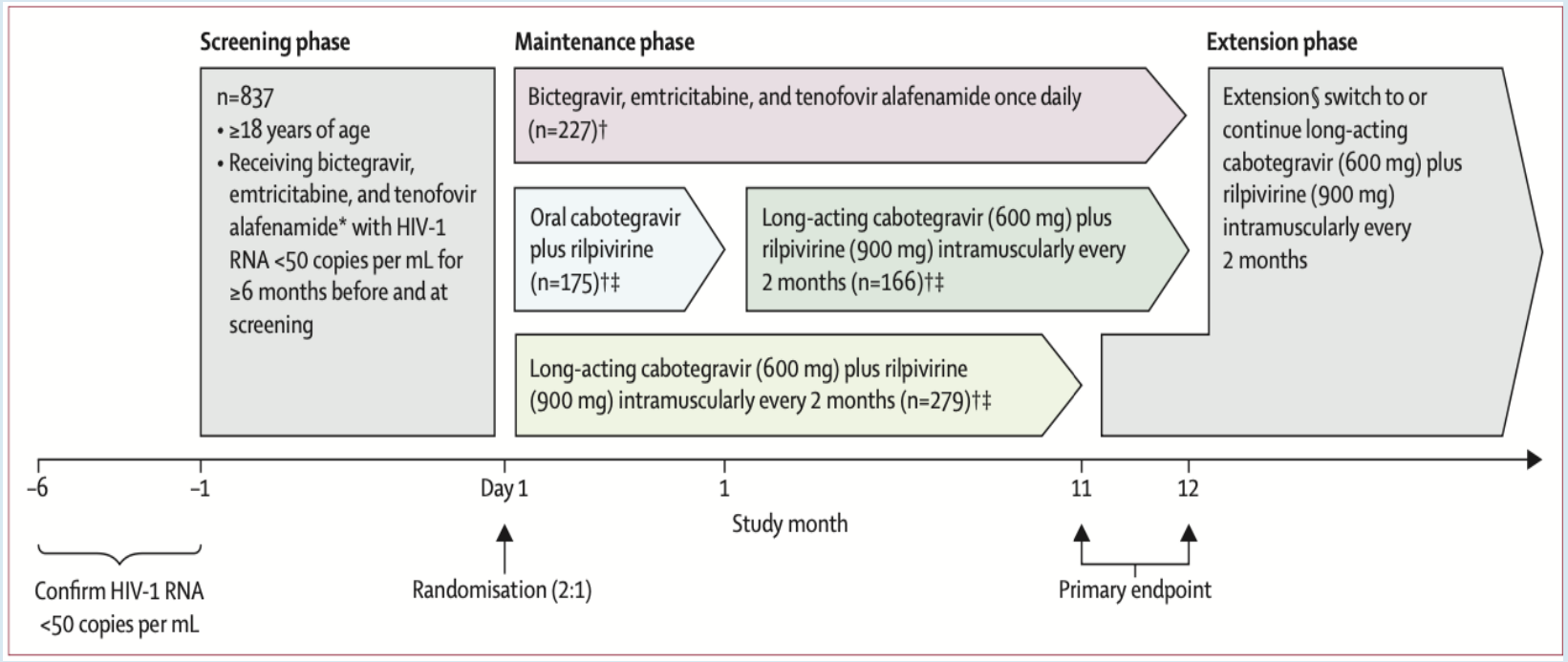


Figure 2. ISRs over time. [a]AE grade is the maximum grade reported by the participant at each visit. [b]There were no grade 4 or 5 ISRs. Abbreviations: AE, adverse event; CAB, cabotegravir; ISR, injection-site reaction; LA, long-acting; NA, not applicable; Q4W, every 4 weeks; Q8W, every 8 weeks; RPV, rilpivirine.

E Overton

Efficacy, safety, and tolerability of switching to long-acting cabotegravir plus rilpivirine versus continuing fixed-dose bictegravir, emtricitabine, and tenofovir alafenamide in virologically suppressed adults with HIV, 12-month results (SOLAR): a randomised, open-label, phase 3b, non-inferiority trial

Moti N Ramgopal, Antonella Castagna, Charles Cazanave, Vicens Diaz-Brito, Robin Dretler, Shinichi Oka, Olayemi Osiyemi, Sharon Walmsley, James Sims, Giovanni Di Perri, Kenneth Sutton, Denise Sutherland-Phillips, Alessandro Berni, Christine L Latham, Feifan Zhang, Ronald D'Amico, Miguel Pascual Bernáldez, Rodica Van Solingen-Ristea, Veerle Van Eygen, Parul Patel, Vasiliki Chounta, William R Spreen, Harmony P Garges, Kimberly Smith, Jean van Wyk



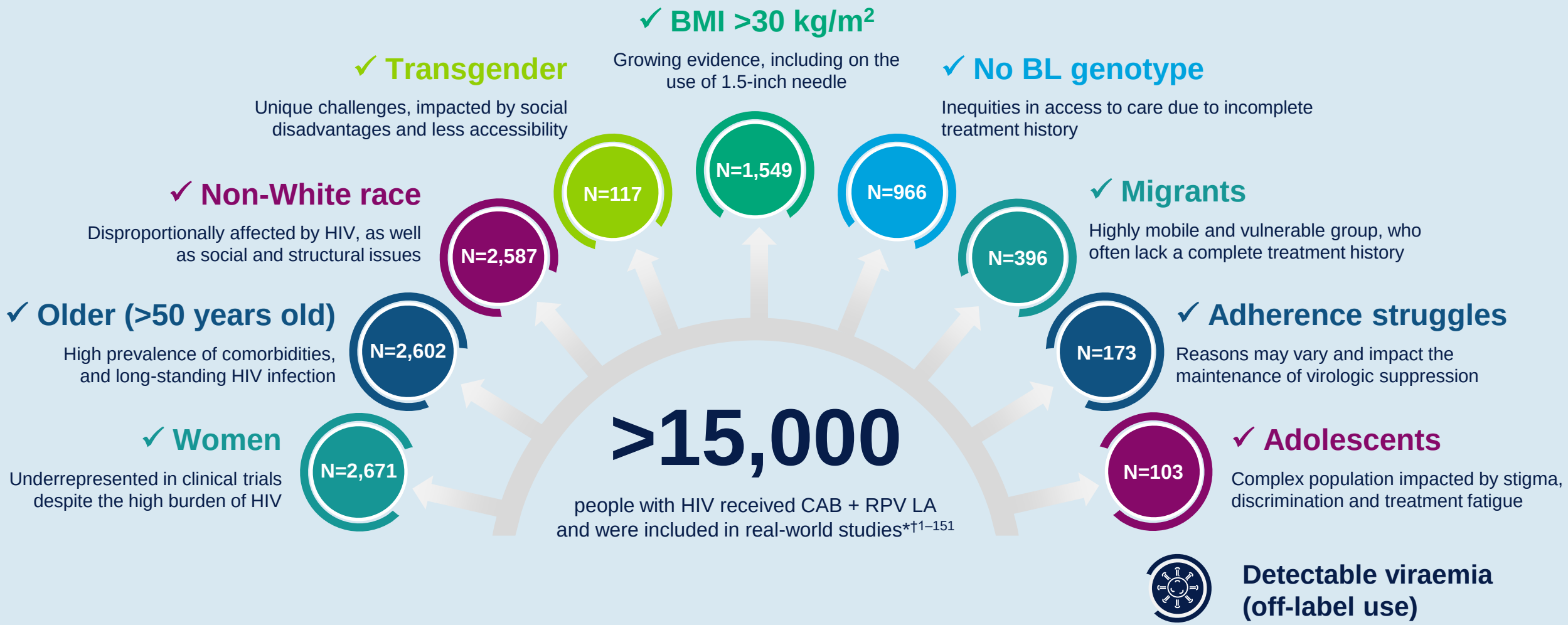
Lancet HIV 2023

SOLAR

	Long-acting cabotegravir plus rilpivirine group (n=447)	Bictegravir, emtricitabine, and tenofovir alafenamide group (n=223)	Difference in proportion* (95% CI)	Adjusted difference in proportion† (95% CI)
Modified intention-to-treat exposed analysis				
Plasma HIV-1 RNA ≥50 copies per mL (primary endpoint)‡	5 (1%)	1 (<1%)	0·7 (–0·6 to 2·0)	0·7 (–0·7 to 2·0)
Data in window not below threshold	3 (<1%)	1 (<1%)	..	..
Discontinued for other reason while not below threshold	1 (<1%)	0	..	..
Discontinued for lack of efficacy	1 (<1%)	0	..	..
No virological data	39 (9%)	15 (7%)	..	..
Discontinued study due to adverse events or death	13 (3%)	1 (<1%)	..	..
Discontinued study for other reasons	24 (5%)§	13 (6%)¶	..	..
On study but missing data in window	2 (<1%)	1 (<1%)	..	..
Plasma HIV-1 RNA <50 copies per mL (key secondary endpoint)‖	403 (90%)	207 (93%)	–2·7 (–7·0 to 1·7)	–2·7 (–7·0 to 1·7)

M. Ramgopal, Lancet HIV 2023

RWE SUPPORTS THE USE OF CAB + RPV LA IN BROAD AND DIVERSE GROUPS OF PEOPLE WITH HIV



*Supporting references for subgroup population N numbers can be found in the slide notes
†Potential overlap between real-world cohorts cannot be ruled out

See next slide for references

REAL-WORLD DATA REPORTS

RWD and implementation studies **on CAB + RPV LA** presented at CROI 2025

Study	N	Follow-up	Virologic suppression	Virologic failure	CVF definitions	VF with RAMs	D/C
OPERA[1]	2,485	Median 11 months (IQR 6-18)	**95%** (2,355/2,485)	**0.8%** (n=21/2,485)	2 consecutive **VL ≥200 c/mL** or a single **VL ≥200 c/mL** followed by treatment **discontinuation** within 4 months	NR	**17%** (n=439/2,618)[a]
TRIO[2]	928	Median 12 months (IQR 5-19)	**95%** (882/928)	**1.6%** (n=15/928)	2 consecutive **VL ≥200 c/mL** or a single **VL ≥200 c/mL** followed by treatment **discontinuation** within 4 months	**0.3%** (n=3/928)[b]	**21%** (n=254/1,198)[c]
Hospital Clínic[3]	402	Week 28	**90%** (ITT, n NR)[d]	**1.2%** (n=5/402)	2 consecutive **VL >50 c/mL**	NR	NR
UCSD[4]	465	NR	NR	**1.3%** (n=6/465)	NR	NR	**19.8%** (n=92/465)
Ward 86[5]	437	Median 553 days (IQR 253-804)	NR	**1.6%** (n=7/437)	NR	**1.6%** (n=7/437)	**15.8%** (n=69/437)
Davy-Mendez et al.[6]	111	Median 4 clinic visits (IQR 3-5)	VL <50 c/mL at BL: 96.8% VL ≥50 c/mL at BL: 76.5% (n NR)[e]	NR	NR	NR	**21.7%** (n=30/138)[f]
Dieterich et al.[7]	124	4 months	**99%** (123/124)[g]	NR	NR	NR	**5.6%** (n=7/124)
Colasanti et al.[8]	81	Median 263 days from 1st inj.	**92%** (73/79)[h]	**2.5%** (n=2/81)	NR	**2.5%** (n=2/81)	**2.5%** (n=2/81)
Short et al.[9]	23	NR	**81%** (17/21)[i]	NR	NR	NR	NR
O'Connor et al.[10]	20	11.4 patient-years	**100%** (20/20)	NR	NR	NR	**0%** (n=0/20)

Use of CAB + RPV LA in individuals with VL ≥50 c/mL, with known or suspected resistance to, or prior virologic failure with agents of the NNRTI or INI class is outside of the labeled indication

Studies from CROI 2025 including adult PWH and reporting relevant effectiveness and/or VF outcomes

[a] Discontinuation among complete initiators (n=2,618) and excluding individuals who discontinued and then reinitiated CAB+RPV LA during the study period; [b] HIV genotype at CVF was available for 5/15 individuals; [c] Discontinuation among all initiators (n=1,198) and excluding 21 individuals who discontinued and then reinitiated CAB+RPV LA and remained on CAB+RPV LA through end of follow-up; [d] 90% virologic suppression reported for women (n=29) and 90% virologic suppression reported for men (n=373); [e] At initiation of LAI ART, 117/138 (85%) were virologically suppressed, but n is not reported for the 111 individuals with sufficient follow-up in the 6 months after first injection; [f] Discontinuation among all initiators of CAB+RPV LA (n=138); [g] Virologic suppression defined as VL <200 c/mL; [h] Primary outcome of virologic suppression reported only for 79 who did not discontinue CAB+RPV LA; [i] VL at delivery only available for 21/23 women

1. Sension M, et al. CROI 2025; San Francisco, CA. Poster 674; **2.** Sax P, et al. CROI 2025; San Francisco, CA. Poster 675; **3.** González-Cordón A, et al. CROI 2025; San Francisco, CA. Poster 678; **4.** Faggiano T, et al. CROI 2025; San Francisco, CA. Poster 685; **5.** Christopoulos K, et al. CROI 2025; San Francisco, CA. Poster 683; **6.** Davy-Mendez T, et al. CROI 2025; San Francisco, CA. Poster 1339; **7.** Dieterich M, et al. CROI 2025; San Francisco, CA. Poster 1318; **8.** Colasanti J, et al. CROI 2025; San Francisco, CA. Poster 690; **9.** Short W, et al. CROI 2025; San Francisco, CA. Poster 1015; **10.** O'Connor K, et al. CROI 2025; San Francisco, CA. Poster 691

TRIO

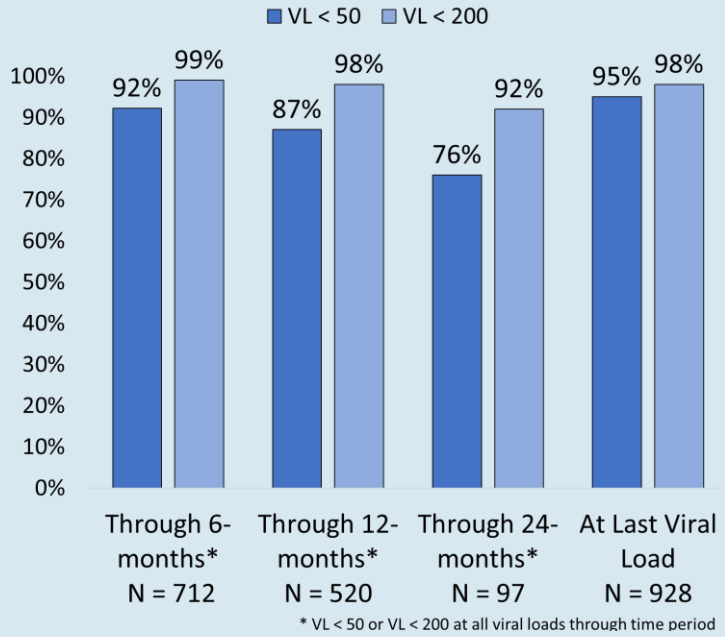
Use of CAB + RPV LA in individuals with known or suspected resistance to, or prior virologic failure with agents of the NNRTI or INI class is outside of the labeled indication

CAB+RPV LA: High effectiveness and low virologic failure rates in large US cohort

- **Study Design:** Observational cohort study utilizing prospectively collected longitudinal EMR data from Trio Health HIV Network
- 1,198 virologically suppressed individuals included with median 12 months (IQR 5-19) follow-up after the first injection
  - Median age 43 (34, 54) years, 22% female, 48% Black/African American
  - 30% with BMI 30-39 kg/m^2 and 6% ≥40 kg/m^2
  - 2% (6/314) and 19% (61/314) had INSTI and NNRTI resistance at BL, respectively
- 944 (79%) CAB+RPV LA initiators remained on the regimen, including 21 who re-initiated CAB+RPV LA and remained on it through end of follow-up
- Among the 928 individuals with ≥1 follow-up VL, 882 (95%) had VL <50 c/mL at last VL
- CVF§ among those with follow-up VL data was observed in 15 (1.6%) individuals
  - HIV genotype at CVF was available for 5/15 (33%): 2 individuals had no RAMs at VF, 2 had NNRTI RAMs and 1 had NNRTI and INSTI RAMs
  - 8/15 had >2 months follow-up on a subsequent regimen, with re-suppression observed in 6 individuals (75%)
- During study period, 89% of injections were administered without delay, with 69% of people with HIV receiving no delayed injections

Maintenance of viral suppression during follow-up on CAB+RPV LA

Median follow-up time: 12 months (IQR 5-19)



VL <50 c/mL was maintained in 95% of individuals throughout follow-up, with low (0.3%) virologic failure rates with resistance

Sax P, et al. CROI 2025; San Francisco, CA. Poster 675

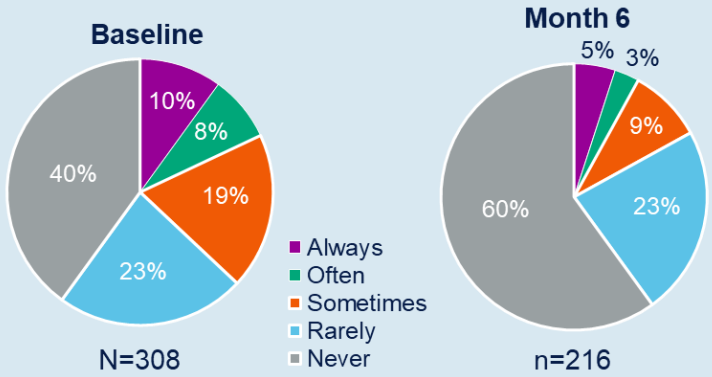
§CVF was defined as 2 consecutive VLs ≥200 c/mL or 1 VL ≥200 c/mL with discontinuation within 4 months of the last recorded injection
EHR, electronic medical record

PROS IN RWE

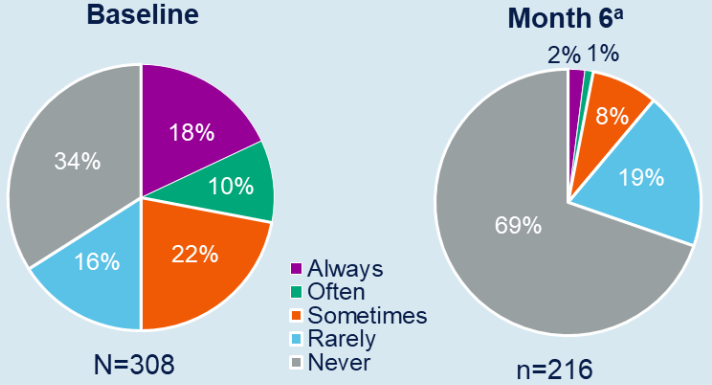
BEYOND

- 308 participants ≥18 years of age were enrolled and completed baseline surveys about reasons for initiating CAB + RPV LA, challenges with daily oral ART, ART preference, and perceived benefits of more frequent clinic visits.
- The most common HCP-reported relevant social determinants of health were comorbidities (23% [70/308]), adherence issues (19% [58/308]), and mental health issues (15% [47/308]).
- At the time of data cut-off, 217 of 308 (70%) participants had reached Month 6 follow-up and completed surveys.

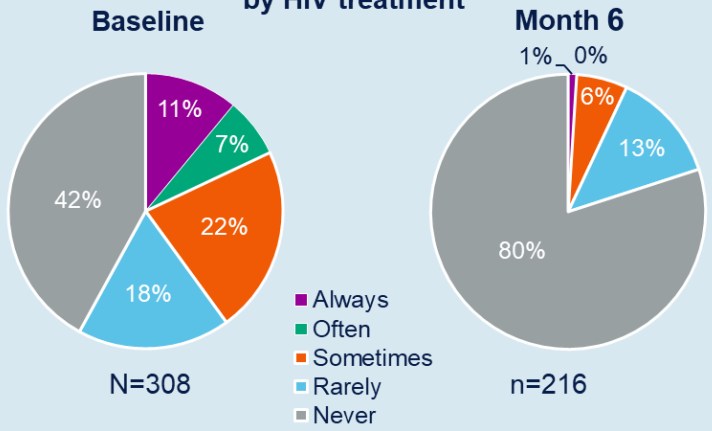
Proportion of participants worried about disclosure of HIV status



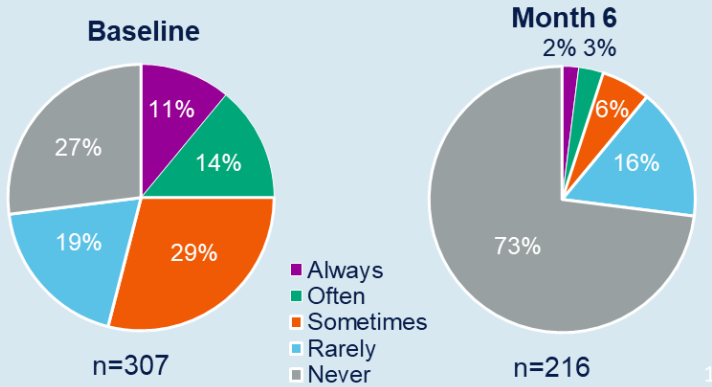
Proportion of participants feeling uncomfortably reminded of HIV status



Proportion of participants feeling stigmatized by HIV treatment



Proportion of participants worried about forgetting to take ART/missing an injection



Dandachi et al. IDWeek 2023; Boston, MA. Poster 1567.

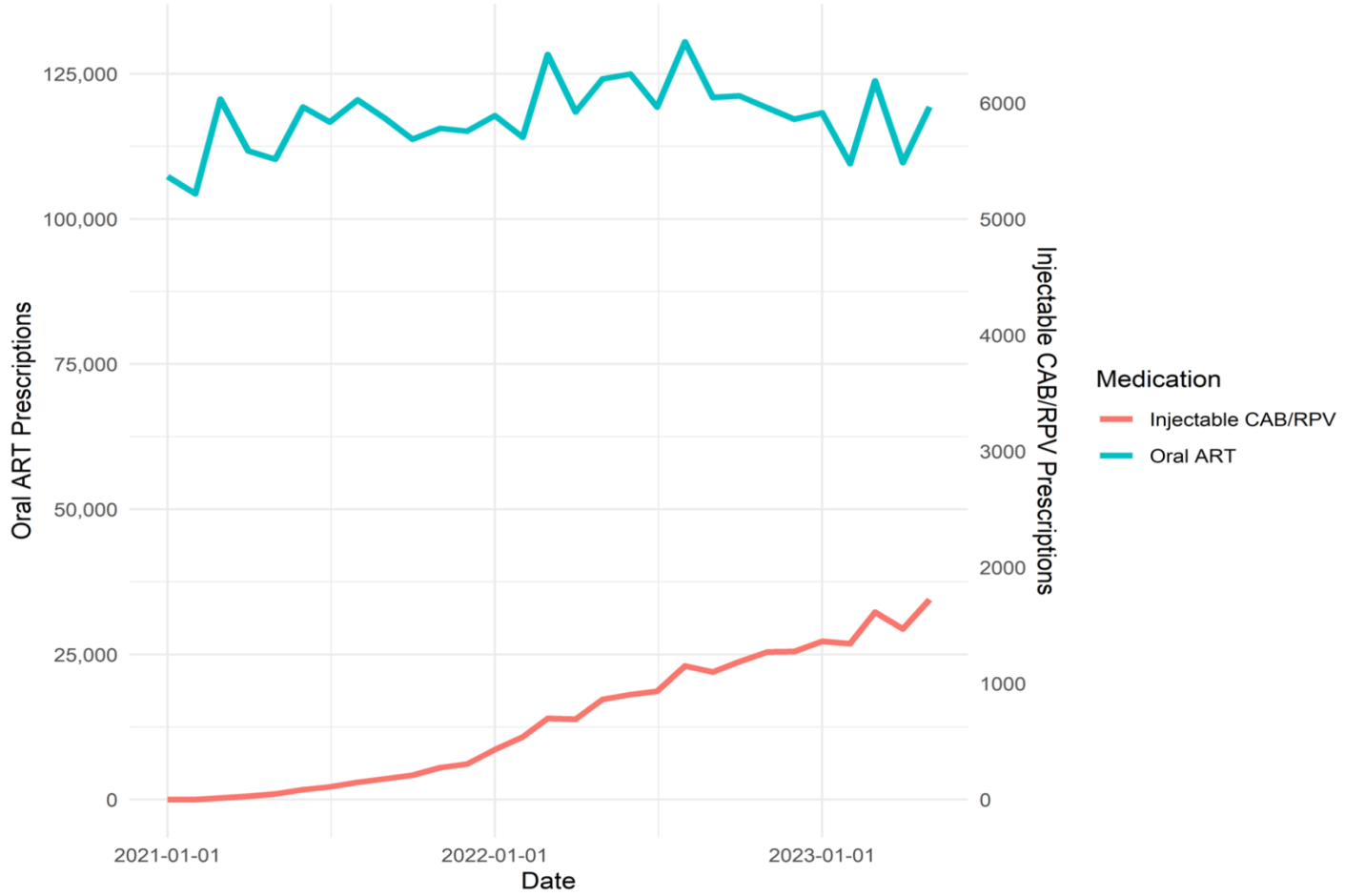
NATIONAL CENTER FOR HIV, VIRAL HEPATITIS, STD, AND TB PREVENTION

Uptake of injectable cabotegravir/rilpivirine for treatment of HIV infection in US, 2021-2023

Jesse O'Shea MD, MSc; James Patrick Henson PhD; Abigail Derton MS; Athena P. Kourtis MD, PhD, MPH; Kate Buchacz, PhD

Division of HIV Prevention, CDC, Atlanta, GA

Figure 1. Monthly number of prescriptions of oral ART and injectable cabotegravir/rilpivirine, HealthVerity Real-World Data — Longitudinal Database — United States, January 2021 through May 2023



Note: Data for June-August 2023 is omitted due to the closed claims having a 90-day lag.

CROI 2025
Poster 1337

Table 2. Characteristics of persons prescribed long-acting cabotegravir/rilpivirine, United States, January 2021 through August 2023

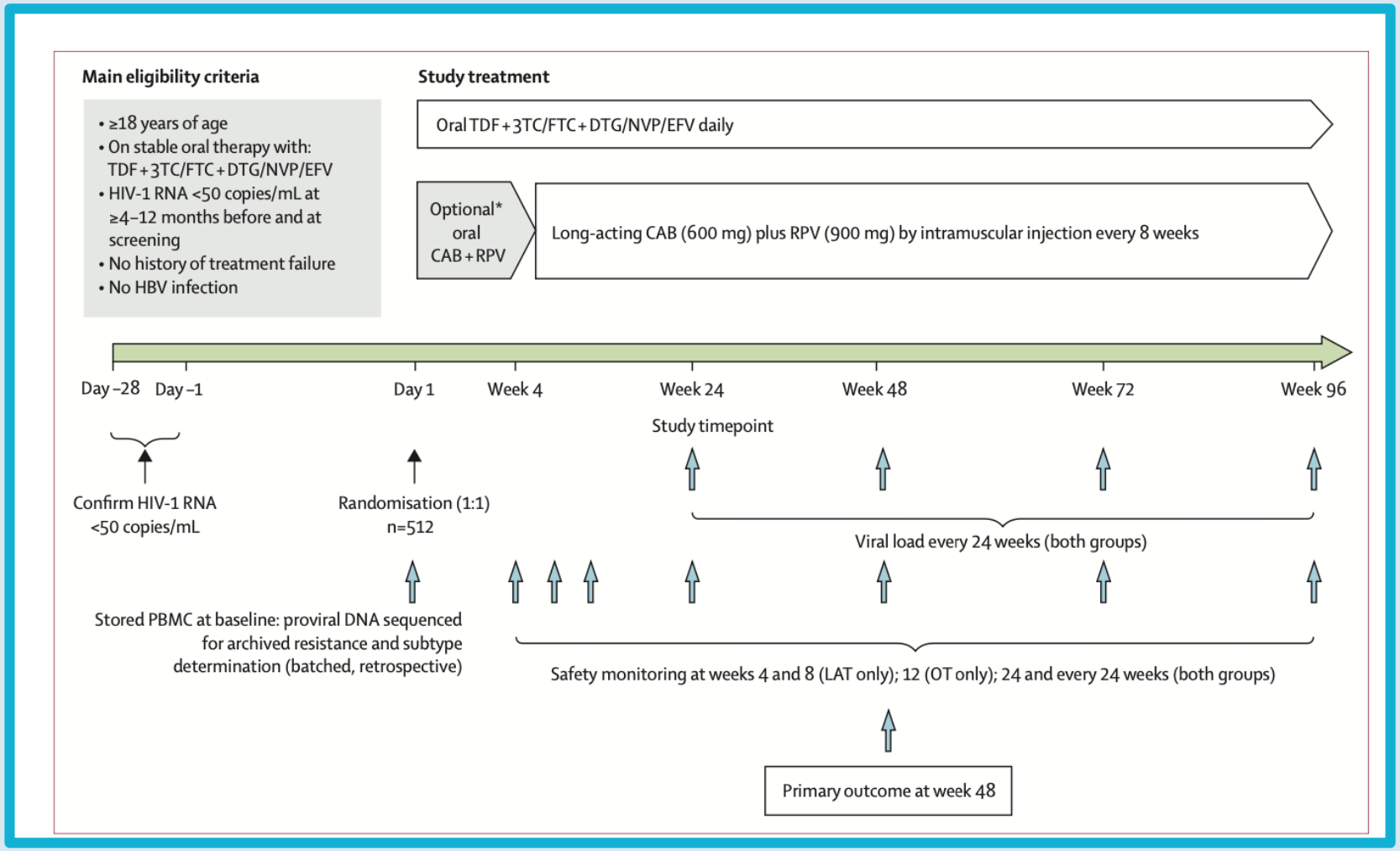
	Oral ART[a] (n = 208,196), No. (%)	Injectable CAB+RPV[b] (n =4,087), No. (%)	p[c]
Age[d]			
13-24	13,176 (6.3)	170 (4.2)	<0.001
25-34	49,649 (23.8)	1,126 (27.6)	<0.001
35-44	45,280 (21.7)	1,092 (26.7)	<0.001
45-54	40,812 (19.6)	860 (21.0)	0.02
55-64	45,068 (21.6)	654 (16.0)	<0.001
65+	13,471 (6.5)	184 (4.5)	<0.001
Patient sex[e]			
Male	156,031 (74.9)	2,890 (70.7)	<0.001
Female	52,153 (25.0)	1,197 (29.3)	<0.001
Mental health[f]	*(n = 200,758 evaluable)*	*(n = 3,965 evaluable)*	
Alcohol use disorder	22,845 (11.4)	448 (11.3)	0.87
Cannabis use disorder	20,796 (10.4)	526 (13.3)	<0.001
Cocaine use disorder	13,603 (6.8)	251 (6.3)	0.27
Opioid use disorder	16,038 (8.0)	309 (7.8)	0.65
Substance use disorder[g]	80,420 (40.1)	1,893 (47.7)	<0.001
Homelessness	10,204 (5.1)	184 (4.6)	0.21
Depression	66,865 (33.3)	1,660 (41.9)	<0.001
Anxiety	68,437 (34.1)	1,580 (39.8)	<0.001
Bipolar disorder	21,079 (10.5)	517 (13.0)	<0.001
Schizophrenia	8,119 (4.0)	149 (3.8)	0.37

Table 1. Characteristics of prescriptions oral ART and long-acting cabotegravir/rilpivirine, United States, January 2021 through August 2023

	Oral ART[a] (n = 3,469,191), No. (%)	Injectable CAB+RPV[b] (n = 21,698), No. (%)	p[c]
Prescription Year[d]			
2021	1,344,575 (38.8)	1,410 (6.5)	<0.001
2022	1,431,532 (41.3)	11,051 (50.9)	<0.001
2023 (January to August)	693,084 (20.0)	9,237 (42.6)	<0.001
Region[e]			
Midwest	395,720 (11.4)	1,970 (9.1)	<0.001
Northeast	941,101 (27.1)	7,026 (32.4)	<0.001
South	1,400,948 (40.4)	7,215 (33.3)	<0.001
West	685,373 (19.8)	5,312 (24.5)	<0.001
Puerto Rico	6,136 (0.2)	5 (0.0)	<0.001
Unknown	39,913 (1.2)	170 (0.8)	<0.001
Number of Payers[f]			
0	316,086 (9.1)	2,103 (9.7)	0.003
1	3,152,511 (90.9)	19,593 (90.3)	0.003
2	594 (0.0)	2 (0.0)	0.374
Payer Type[g] (if number of payers = 1)			
Medicaid	1,696,146 (53.8)	14,926 (76.2)	<0.001
Medicare	665 (0.0)	11 (0.1)	<0.001
Medicare Advantage	418,105 (13.3)	1,869 (9.5)	<0.001
Commercial	1,013,519 (32.1)	2,708 (13.8)	<0.001
Unknown	24,076 (0.8)	79 (0.4)	<0.001

[a] Oral ART prescriptions among patients with no CAB/RPV prescriptions and at least one oral ART prescription during the study period.
[b] CAB/RPV prescriptions among patients with at least one CAB/RPV prescription during the study period.
[c] Both χ^2 and two-sample proportion tests were used to compare characteristics of the patient populations. P values from the two-sample Z-test for proportions are shown here.
[d] Year of pharmacy prescription.
[e] Region of prescription (Midwest: IA, IL, IN, KS, MI, MN, MO, ND, NE, OH, SD, WI; Northeast: CT, MA, ME, NH, NJ, NY, PA, RI, VT; South: AL, AR, DC, DE, FL, GA, KY, LA, MD, MS, NC, OK, SC, TN, TX, VA, WV; West: AK, AZ, CA, CO, HI, ID, MT, NM, NV, OR, UT, WA, WY).
[f] Number of unique payers with pharmacy benefits within the month and year of the patient prescribed the medication.
[g] Type of payer among prescriptions with only one unique payer.

Switch to long-acting cabotegravir and rilpivirine in virologically suppressed adults with HIV in Africa (CARES): week 48 results from a randomised, multicentre, open-label, non-inferiority trial



C. Kityo, Lancet Infect Dis 2024

CARES: BASELINE CHARACTERISTICS

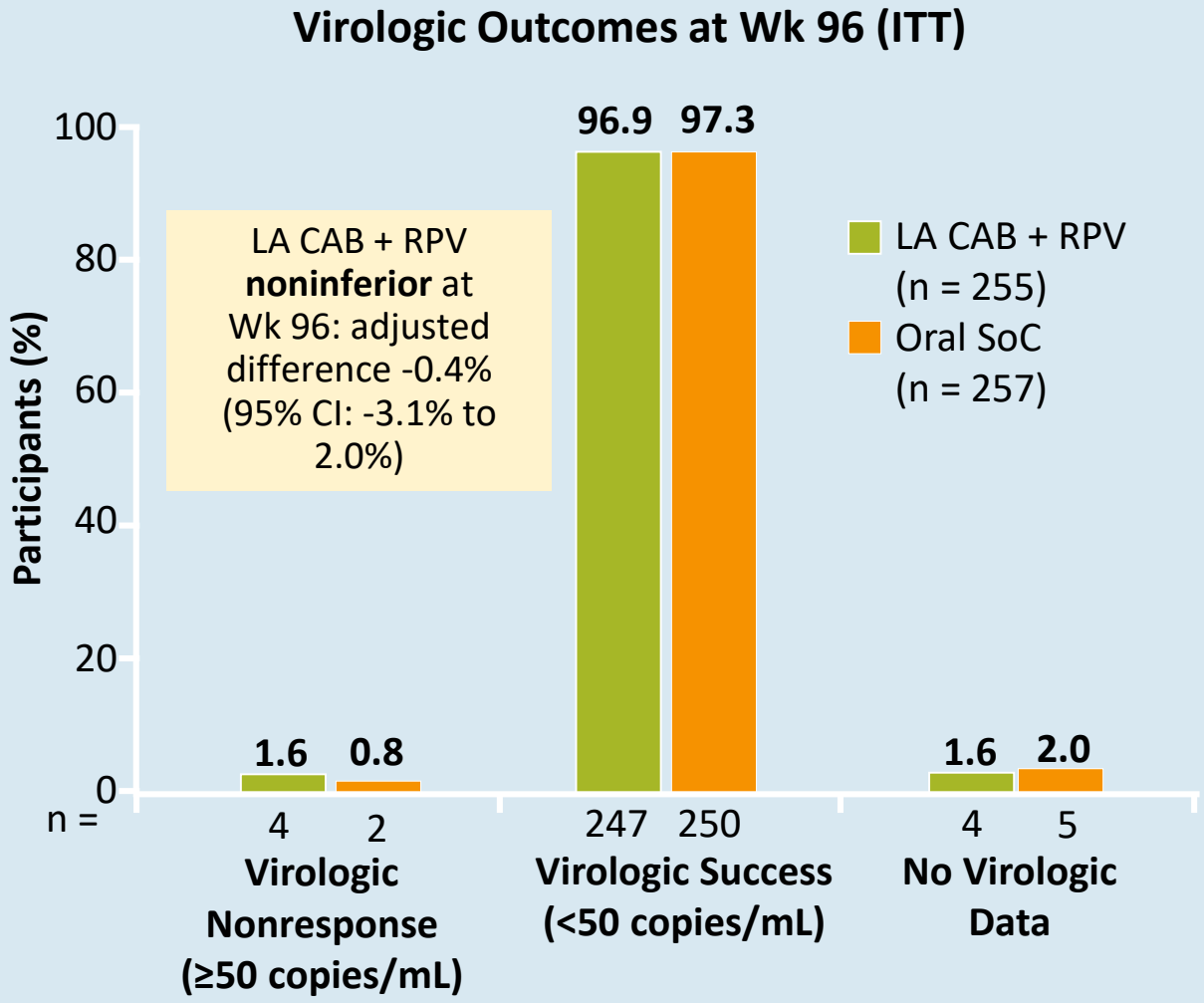
Characteristic	All Patients (N = 512)
Median age, yr (IQR)	42 (35-51)
Female, n (%)	295 (58)
BMI ≥30 kg/m^2, n (%)	108 (21)
Black race, n (%)	510 (>99)
Median time on first-line ART, yr (IQR)	8 (4-13)
Prior exposure to NNRTI, n (%)	380 (74)
INSTI regimen at screening, n (%)	471 (92)
NNRTI regimen at screening, n (%)	41 (8)
Archived proviral DNA analysis, n/n (%)	
▪ Subtype A1	236/433 (55)
▪ RPV resistance mutations	30/401 (7)
▪ RPV intermediate/high-level resistance	**12/401 (3)**
▪ CAB resistance mutations	20/202 (10)
▪ CAB intermediate/high-level resistance	**5/202 (2)**

- Baseline characteristics well balanced between groups
- Participants were enrolled without prior resistance testing
- Archived proviral DNA analysis performed at study conclusion

APOBEC-related mutations excluded in current analysis

Kityo. CROI 2025. Abstr 202. Kityo. CROI 2024. Abstr 122.

CARES: VIROLOGIC EFFICACY, INJECTION TIMING, SAFETY, TOLERABILITY, AND TREATMENT SATISFACTION AT WK 96



- 81.1% of participants (n = 206) received all scheduled injections; 97% of 3261 injections were administered on time
- Safety and tolerability:
  - SAEs: LA CAB + RPV, 5%; oral SoC, 4%
  - Grade ≥3 AEs related to study drug: 2% in both arms
- ISRs primarily grade 1/2; 1 grade 3 ISR which led to treatment discontinuation
- Treatment satisfaction improvement greater with switch to LA CAB + RPV
  - >99% preferred LA vs oral ART

At Wk 48 and 96, virologic success with LA CAB + RPV was **noninferior** to SoC oral ART

Kityo. CROI 2025. Abstr 202.

PERINATAL AND INFANT OUTCOMES AFTER BIC EXPOSURE IN PREGNANCY

N=1256

All live births to pregnant PWH

Outcomes

Rate of congenital anomalies, preterm births, low birth weights and perinatal transmission with BIC versus non-BIC ART exposure

2018–2023

Perinatal and Early Infant Outcomes

	All infants (n=1256)	BIC-exposed infants (n=161)	Non-BIC–exposed infants (n=1095)	*P* value[a]
Maternal ART adherence in pregnancy				**0.014**
Unknown, n	46	4	42	
Excellent, n (%)	1066 (88.1)	129 (82.2)	937 (89.0)	
Suboptimal, n (%)	144 (11.9)	28 (17.8)	116 (11.0)	
Maternal ART continuation at delivery, n (%)	1228/1235 (99.4)	155/158 (98.1)	1073/1077 (99.6)	**0.049**
Maternal ART continuation postpartum, n (%)	1091/1118 (97.6)	132/139 (95.0)	959/979 (98.0)	**0.031**
Congenital anomalies, n (%)	66/1208 (5.5)	8/151 (5.3)	58/1057 (5.5)	0.924
Preterm birth, n (%)	170/1241 (13.7)	31/160 (19.4)	139/1081 (12.9)	**0.025**
Low birth weight (<2500 g), n (%)	154/1230 (12.5)	27/159 (17.0)	127/1071 (11.9)	0.069
Perinatal HIV transmission, n (%)	7/1162 (0.6)	1/136 (0.7)	6/1026 (0.6)	0.583

There were no significant associations between **timing of BIC exposure** (preconception and/or during pregnancy) and **perinatal outcomes**[b]

Multivariate analysis showed **no significant increase** in odds of **preterm birth** with **BIC versus non-BIC** ART exposure:
OR: 1.39 (95% CI: 0.78–2.49); *P*=0.261

BIC exposure in pregnancy was not associated with adverse perinatal and early infant outcomes in this Canadian cohort

[a]Univariate analysis. [b]Preterm delivery, low birth weight (<2500 g), small for gestational age (birth weight <10th percentile), congenital anomalies and perinatal HIV transmission
OR, odds ratio

Wong JMH, et al. CROI 2025, Poster 997

Long-Acting Cabotegravir/Rilpivirine in Pregnancy

1015

William R. Short[1], Matty Zimmerman [2], Mariam Aziz [3] Jillian Baron[1], Phillip Bolduc[4], Eric Farmer[5], Naima Joseph[6], Stephen Kohlhoff[7], Florence Momplaisir[1], Alexander Nelson[8], Natalie Nielsen[9], Dimple Patel[10], Stephen Pagkalinawan[11], Mireya Wessolossky[4], Rachel K. Scott[12]

Table 2: Characteristics of those who started LA CAB/RPV prior to pregnancy

	N=23
Initiated LA CAB/RPV prior to pregnancy, n (%)	17 (74)
LA CAB/RPV dosing during pregnancy, n (%)	
Monthly	6 (38)
Bimonthly	11 (62)
Switched off LA CAB/RPV to oral ART during pregnancy*, n (%)	5 (29)
Gestational age at switch off LA CAB/RPV, weeks, median (IQR)	7 (6, 8)
LA CAB/RPV dose changed during pregnancy, n =12, n (%)	
No	10 (83)
Yes**	2 (17)

* Switched to TAF/FTC and DTG (3), ABC/3TC/DTG (1), 3TC/DTG to ABC/3TC/DTG (1)
** Changed from bimonthly to monthly dosing

Table 3: Characteristics of those who started LA CAB/RPV during pregnancy

	N=23
Initiated LA CAB/RPV during pregnancy, n (%)	6 (26)
LA CAB/RPV dosing during pregnancy, n (%)	
Monthly	6 (100)
Prior oral ART, n (%)	
FTC/TAF/BIC	5 (83)
FTC/TAF/BIC + DRV/c + DOR	1 (17)
Gestational age at switch to LA CAB/RPV, weeks, median (IQR)	22 (17, 28)

Not yet recruiting

CREATE - Cabotegravir & Rilpivirine Antiretroviral Therapy in Pregnancy

ClinicalTrials.gov ID NCT06336434

Sponsor National Institute of Allergy and Infectious Diseases (NIAID)

Information provided by National Institute of Allergy and Infectious Diseases (NIAID) (Responsible Party)

Last Update Posted 2024-11-20

GEPPO

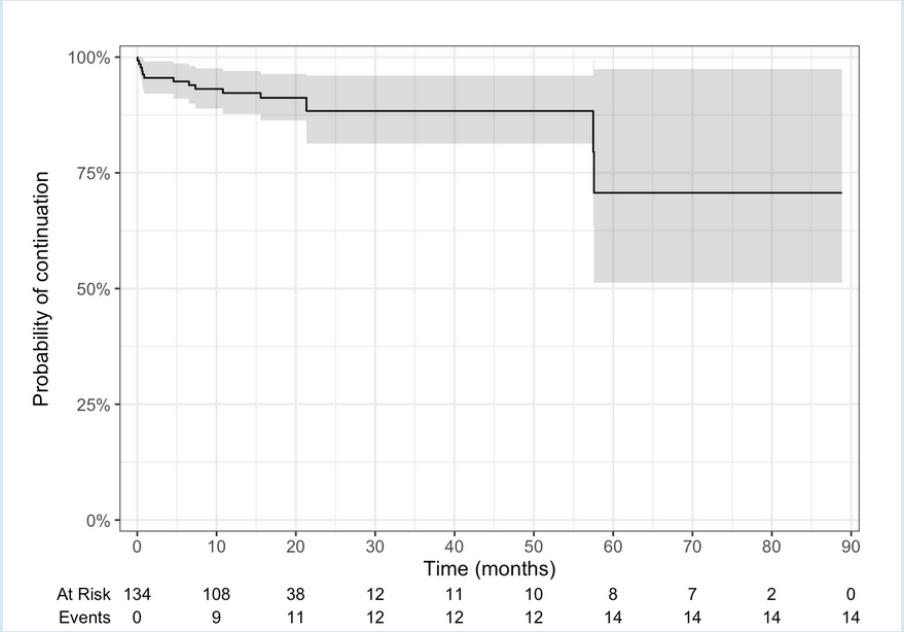
CAB+RPV LA: High effectiveness and persistence among people with HIV aged ≥65 years

- **Objective:** Assess the effectiveness and safety of CAB+RPV LA in older people with HIV in78 cluded in the GEPPO cohort

- 134 people with ≥65 years were included
  - Median age 67.9 years
  - Median 21 years of HIV infection, and 20 years on ART
  - >20% with multimorbidity (≥3 comorbidities), >60% with polypharmacy (≥5 medications other than ART)
  - 5 had history of NNRTI RAMs, 7 had A1/A6 subtype, 7 had BMI >30 kg/m^2

- **Discontinuations** (14 subjects)
  - Toxicity/ personal choice (7)
  - Other (5)
  - Death (1)

MEDIAN FOLLOW-UP	**17.6 (CI 95% 17.2-18.4) months**
LAI CAB + RPV (currently)	120 partecipants (89%)
VIROLOGICAL FAILURE	**ZERO**



No virologic failures and good tolerability profile among older people with HIV with a long ART history and high prevalence of multimorbidity and polypharmacy

Focà E, et al. ICAR 2025

Use of CAB + RPV LA in individuals with VL ≥50 c/mL, with known or suspected resistance to, or prior virologic failure with agents of the NNRTI or INI class is outside of the labeled indication

CAB+RPV LA: High effectiveness in people with HIV who have challenges adhering to daily oral ART and/or viremia at initiation

*HIV-1 RNA <200 c/mL (75% <50 c/mL); #Defined as 2 consecutive VL ≥200 c/mL or single VL ≥200 c/mL followed by treatment discontinuation (regimen change or 2 missed injections); ¶VL <200 c/mL; †VL ≤200 c/mL; ‡VL<50 c/mL

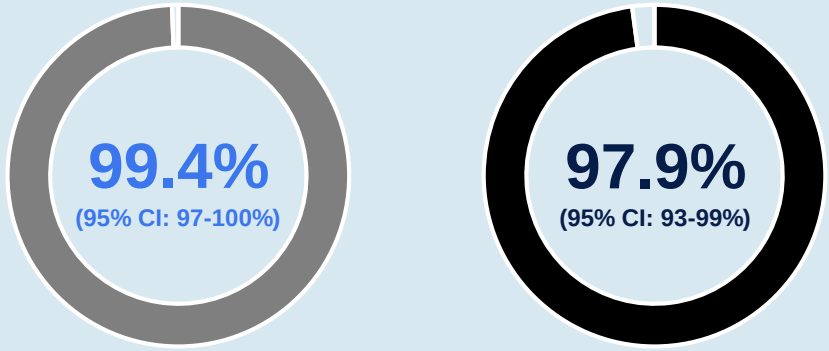
1. Hsu R, et al. IDWeek 2023; Boston, MA. Oral 1028; **2.** Dieterich M, et al. CROI 2025; San Francisco, CA. Poster 1318; **3.** Gistand N, et al. CROI 2025; San Francisco, CA. Poster 689; **4.** Colasanti J, et al. CROI 2025; San Francisco, CA. Poster 690; **5.** Elion R, et al. IDWeek 2023; Boston, MA. Poster 1592; **6.** O'Connor K, et al. CROI 2025; San Francisco, CA. Poster 691

Use of CAB + RPV LA in individuals with VL ≥50 c/mL, with known or suspected resistance to, or prior virologic failure with agents of the NNRTI or INI class is outside of the labeled indication

CAB+RPV LA: High effectiveness at W48, irrespective of virologic suppression at baseline

- **Study Design:** Retrospective study using EMR data of people with HIV who initiated CAB+RPV LA in Jan 2021 through Sep 2024 in the SPLASH program
- **Objective:** Compare and report longer-term viral suppression outcomes in those who started CAB+RPV LA with and without viremia
- 370 individuals were included in this analysis: 129 with viremia, 241 virologically suppressed
  - Median age 45 (range 21-70) years, 81.6% cisgender men, 15.1% transgender women
  - 40.8% White, 23.0% Black, 52.4% CD4+ cell count <200 cells/mm^3 - people with initial viremia were more likely to have CD4+ cell count <200 cells/mm^3 (OR = 1.22, 95% CI 1.09-1.36, p<0.001)
  - 44.3% unstable housing, 46.2% with current or past substance use - rates of current or past substance use (OR = 1.22, 95% CI 1.11-1.34, p<0.001) and unstable housing (OR = 1.11, 95% CI 1.01-1.23, p=0.031) were higher in those starting CAB+RPV LA with initial viremia
- Proportion of people maintaining/achieving virologic suppression did not significantly differ between the virologically suppressed and viremic groups at 48 weeks (p=0.61)
  - Median time to achieve virologic suppression (≤200 c/mL) in those with viremia was 32 days

Virologic suppression ≤200 c/mL at W48



Virologically suppressed at BL
N=169

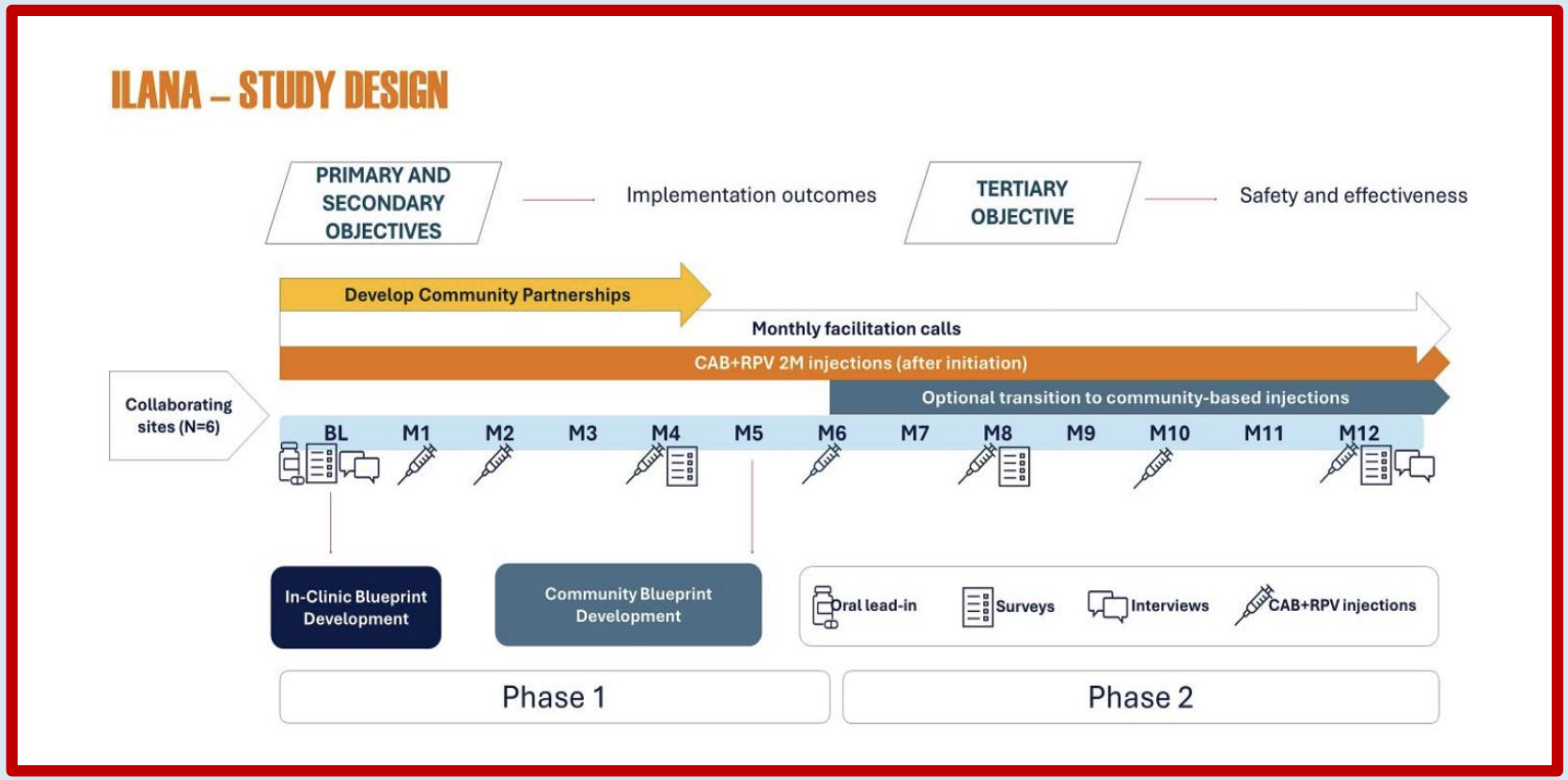
Viremic at BL
N=96

CAB+RPV LA was highly effective in a cohort of people with HIV with high rates of unstable housing, substance use and low CD4+ cell counts

Gistand N, et al. CROI 2025; San Francisco, CA. Poster 689

SPLASH, Special Programs to Stop HIV Using Long-Acting ART; **OR**, odds ratio; **BL**, baseline

Perspectives of People With Human Immunodeficiency Virus on Implementing Long-acting Cabotegravir Plus Rilpivirine in Clinics and Community Settings in the United Kingdom: Results From the Antisexist, Antiracist, Antiageist Implementing Long-acting Novel Antiretrovirals Study



Primary endpoint: proportion of participants agreeing that the injection and community setting were feasible

Perspectives of People With Human Immunodeficiency Virus on Implementing Long-acting Cabotegravir Plus Rilpivirine in Clinics and Community Settings in the United Kingdom: Results From the Antisexist, Antiracist, Antiageist Implementing Long-acting Novel Antiretrovirals Study

Community settings offered by sites included: home visits (n = 3), HIV support organizations (n = 2), and community clinic (n = 1). Of 114 participants, 54% were female, 70% racially minoritized, and 40% aged ≥50 years. A total of 27/114 chose to receive injections in community settings. FIM/AIM/IAM scores at M12 were high for the injection (79.0–87.4%) and lower for the community setting (44.2–47.4%) overall. Subgroup analyses indicated differences in scores by gender and ethnicity. Among those who attended the community, FIM/AIM/IAM scores for the community setting at M12 were high (73.1–80.8%). Concerns about stigma, inconvenience, and losing access to trusted clinicians negatively influenced perceptions of receiving injections at community settings, amongst other factors

CAB+RPV injections were considered highly feasible, acceptable, and appropriate; however, few chose community delivery. Those that chose community delivery found it highly acceptable and feasible. Further exploration of CAB + RPV delivery in alternative community sites not offered (eg, primary care, pharmacies) is warranted

Why Do People With HIV Stop Long-Acting Injectable Cabotegravir-Rilpivirine and What Happens?

0683

Katerina Christopoulos[1], Matt Hickey[1], Janet Grochowski[1], Francis Mayorga-Munoz[1], Xavier Erguera[1], Samantha Dilworth[1], Elizabeth Imbert[1], Ayesha Appa[1], Matthew Spinelli[1], Chesa Cox[1], Mary Shiels[1], Jon Oskarsson[1], Monica Gandhi[1]
[1]University of California San Francisco, San Francisco, CA, USA

Of 437 PWH initiating LA-CAB/RPV with overall median time on injections 553 days (IQR 253,804 days), 69 (16%) discontinued, of whom 47 (68%) initiated with VS and 22 (32%) with viremia

Table 1. Reasons for Discontinuation, Stratified by HIV VL at LA-CAB/RPV Initiation

Reason for Discontinuation	Overall (n=69)	HIV VL <50 copies/mL (n=47)	HIV VL ≥50 copies/mL (n=22)
Injection site pain	14	10	4
Injection site pain with other side effect/concern*	11	9	2
Other side effect/concern*	14	11	3
Residential treatment for mental health/substance use or incarceration	5	5	-
Need to come to clinic for injections	2	2	-
Allergic reaction	1	1	-
Relocation	2	2	-
Lateness leading to provider discontinuation	8	2	6
Provider discontinuation for HIV RNA blip	1	1	-
Loss to follow up	3	3	-
Virologic failure	7	1	6
Declined ART but remained in care	1	-	1

Why Do People With HIV Stop Long-Acting Injectable Cabotegravir-Rilpivirine and What Happens?

0683

Katerina Christopoulos[1], Matt Hickey[1], Janet Grochowski[1], Francis Mayorga-Munoz[1], Xavier Erguera[1], Samantha Dilworth[1], Elizabeth Imbert[1], Ayesha Appa[1], Matthew Spinelli[1], Chesa Cox[1], Mary Shiels[1], Jon Oskarsson[1], Monica Gandhi[1]
[1]University of California San Francisco, San Francisco, CA, USA

Initiated with Viremia and Developed Resistance After Discontinuation

Patient 9	VL 67,000; CD4 cell count 20; mutations: none Received 10 on-time injections; VL <200 copies/mL wk 4 and <50 wk 24; self-dc due to severe depression; genotype 18 wk later NNRTI: K101E, E138 K, Y181F/I/N, M230L
Patient 10	VL 801,000; CD4 cell count: 27; mutations: V179I. Received 5 on-time q4week injections; was 15 d late to 6th and received reloading. Presented on time for 7th injection but left without being seen, then discontinued all ART due to belief they were cured of HIV; declined all care engagement until 1 y later; VL 226,000; genotype RT E138A/K/T and Y181C; patient resumed CAB + LEN and had resuppression.
Patient 11	VL 34,000; CD4 10, mutations: M184V. Received 7 on-time q4 week injections; 14 d late to 8th injection and when came to clinic -> TAF/FTC/DRV/c due to c/f SSTI. VS observed 3 months later, then patient discontinued oral ART. Genotype 14 months after last injection: K101E, V179I, Y181Y/C. Now VS on TAF/FTC/BIC.
Patient 12	VL 114,000; CD4 50; mutations: none. Had 17 q4 week injections with 6 late, one requiring a reloading. VL 382 and switched to TAF/FTC/DRV/r due to concern for resistance. Patient disengaged from care and presented one year later with VL 12,000. Genotype K101E. Started CAB/LEN with home nursing and has VS.
Patient 13	VL 1,700; CD4 56; mutations: n/a. History of TDF/FTC/RPV use. Had 17 on-time q4week inj., then 62 d late, reloaded; on-time at 4 weeks; then reloaded at 67d late. At last injection VL 99; genotype K101E. Disengaged from care then genotype 5 months later showed NNRTI: E138K. Now suppressed on TAF/FTC/DRV/c.
Patient 14	VL 18,600; CD4 20; mutations: n/a. Had 2 on-time injections and then disengaged. Returned to clinic two years later with VL 5,000; genotype: V106VI, Y181Y/C, H221Y, I178I/M. Now suppressed on TAF/FTC/DRV/c.

*Cases shaded in blue described in Hickey et. al., CID 2024, Gandhi et. al., Annals Int Med, 2023, and Christopoulos et. al., CID 2022.

Distance to Care Measures Predict Injection Visit No-Shows Among Cabotegravir/Rilpivirine Recipients

Nimish Patel[1], Lucas Hill[2], Jeffrey Yin[2], Inma Hernandez[1], Kari Abulhosn[2], Elvia Suarez[2], Afsana Karim[2], Laura Bamford[2]

[1]University of California San Diego Skaggs School of Pharmacy and Pharmaceutical Sciences, La Jolla, USA

[2]Univerisity of California San Diego Owen Clinic, San Diego, USA

UC San Diego Health

UC San Diego SKAGGS SCHOOL OF PHARMACY AND PHARMACEUTICAL SCIENCES

Results of multivariable Cox proportional hazards regression models evaluating each DTC measure as an independent predictor of IVNS

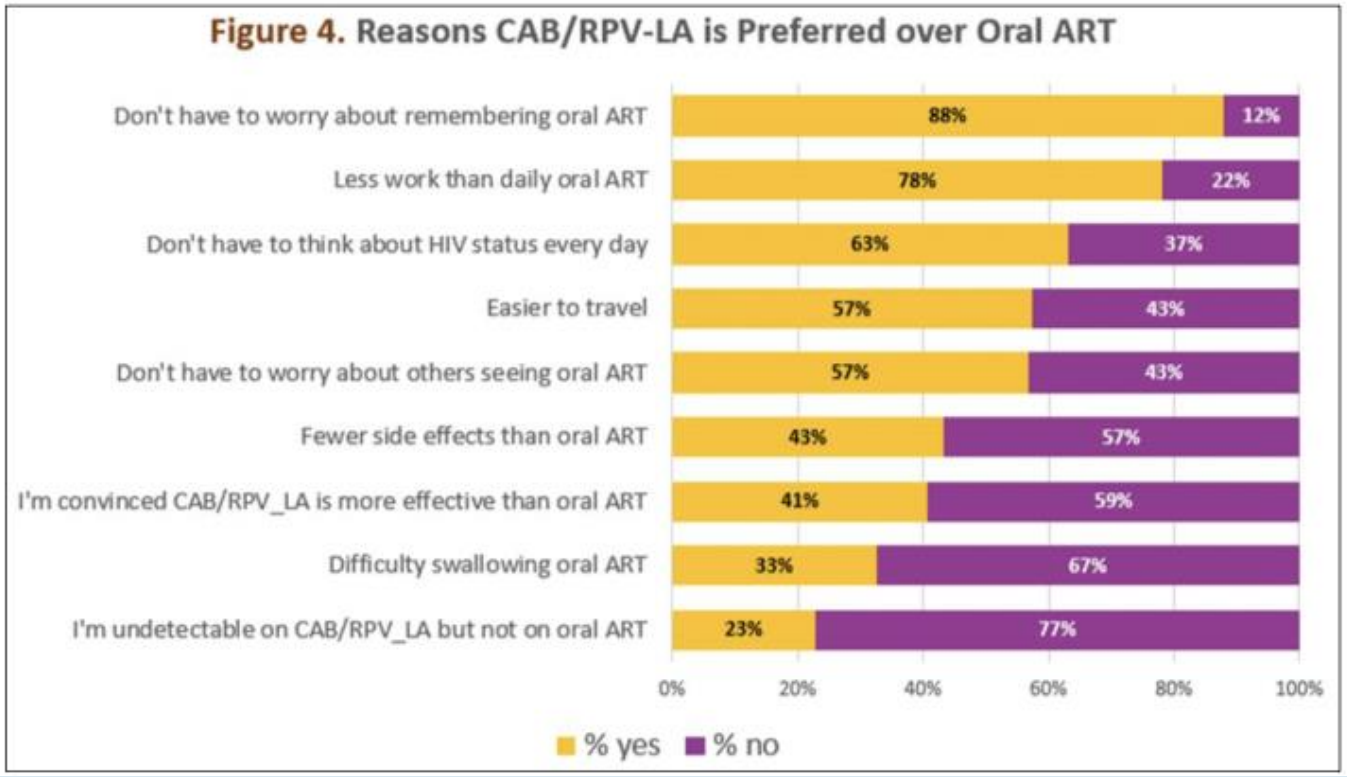
Covariate	Hazard Ratio	95% Confidence Interval	P-value
Mileage >9.2 miles	2.05	1.27 – 3.31	0.003
Driving >19 min	1.64	0.97 – 2.78	0.07
Public Transit >73 min	2.05	1.12 – 3.76	0.02
Walking >117 min	2.33	1.43 – 3.79	<0.001
Bicycling >45 min	1.88	1.18 – 3.01	0.008

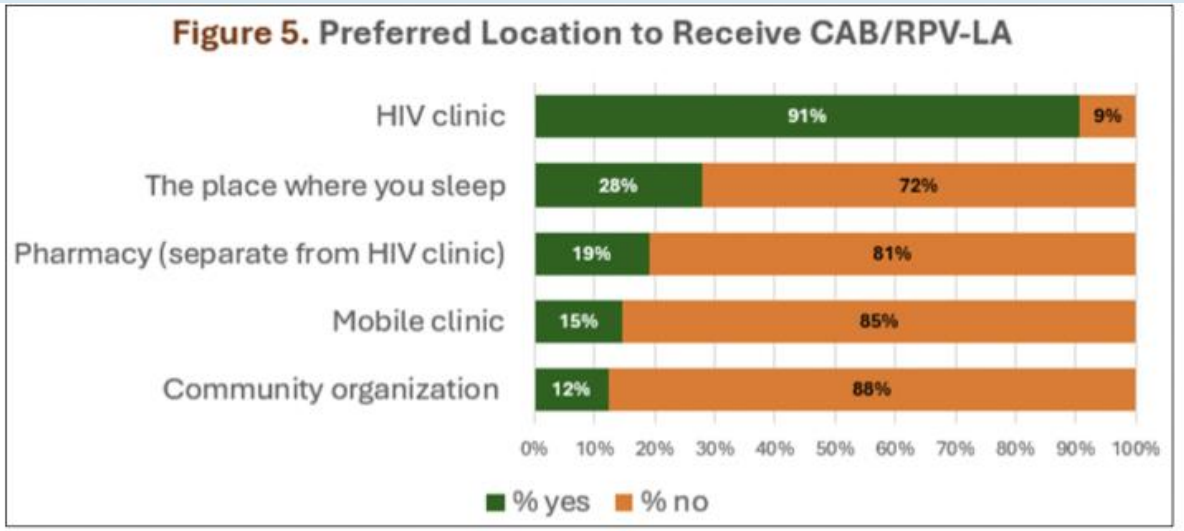
*Variables at model entry were those with a p<0.25 from previous publication by Hill et al[1]

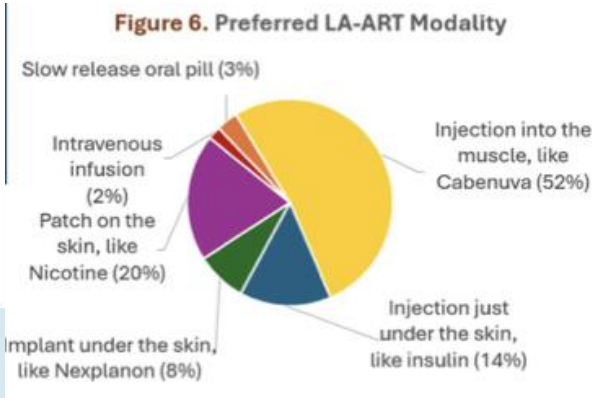
What Do Early Adopters of Long-Acting Injectable Cabotegravir-Rilpivirine Think About It?

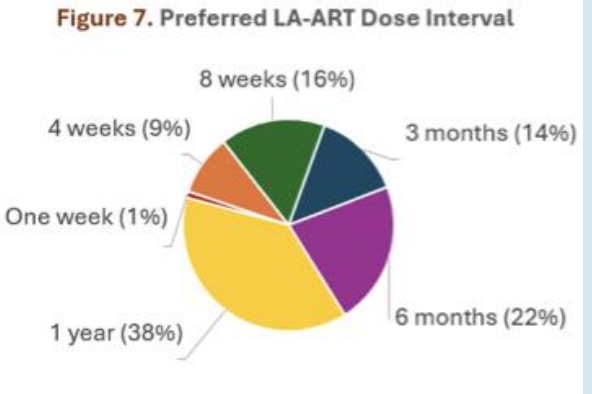
0684

Katerina Christopoulos[1], Moira McNulty[2], Lauren Collins[3,5], Matt Hickey[1], Mallory Johnson[1], Aaloke Mody[4], Kimberly Koester[1], Geoffroy Liegeon[2], Jorge Salazar[1], Samantha Dilworth[1], Sophie Plotkin[2], Kaylin Dance[3,5], Xavier Erguera[1], Elizabeth Montgomery[1,6], Jonathan Colasanti[3,5]
[1]University of California San Francisco, San Francisco, CA, USA, [2]University of Chicago, Chicago, Illinois, USA, [3]Emory University, Atlanta, Georgia, USA, [4]Washington University in St. Louis, St. Louis, Missouri, USA,
[5]Ponce de Leon Center, Grady Health System, Atlanta, Georgia, USA, [6]Research Triangle International, Berkeley, California, USA









CROI 2025

WHAT'S NEXT?

CAB-ULA
PK OF NEW ULTRA-LONG-ACTING FORMULATION

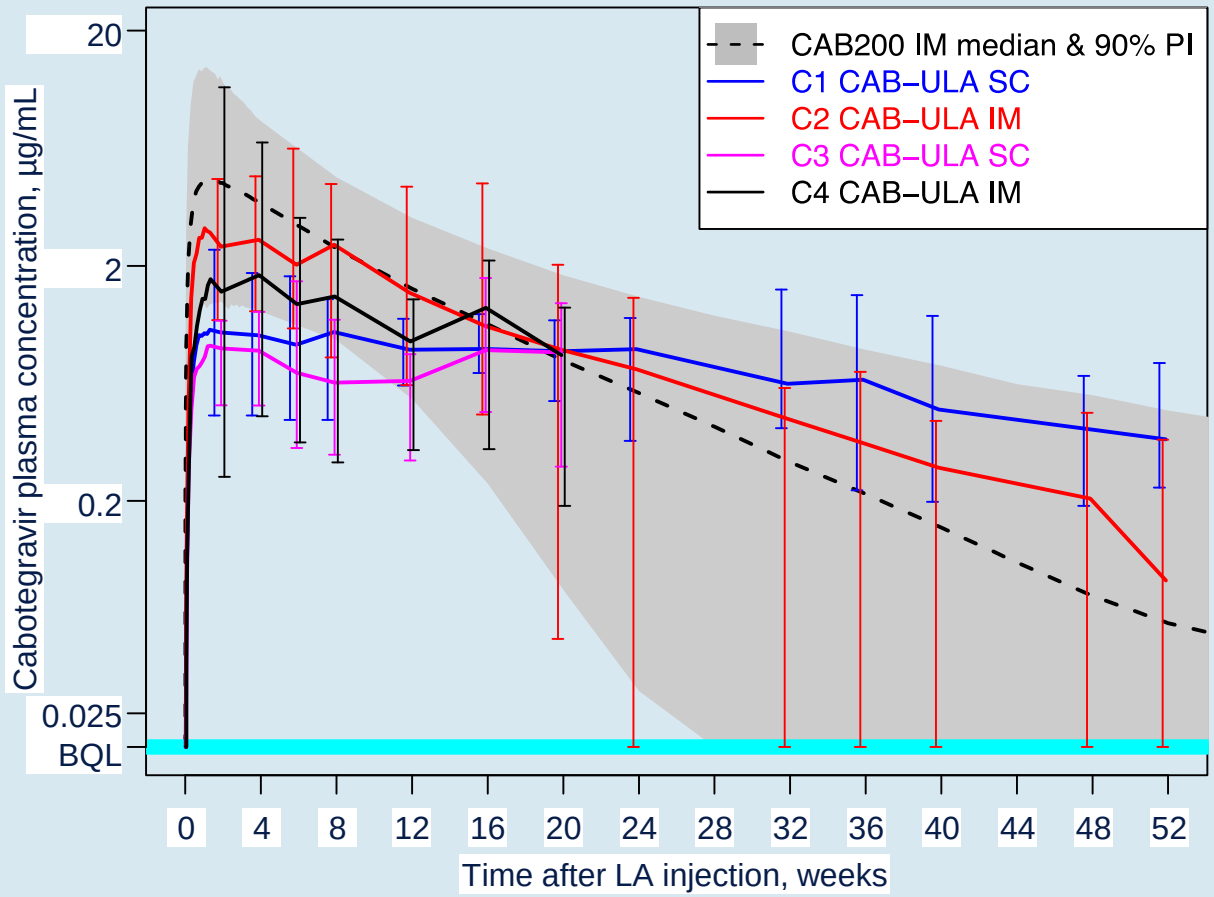
Part C: CAB-ULA

Parameter, geometric mean (%CVb)	SC C1 800 mg (2 mL) (n=8)	SC C3 1200 mg (3 mL) (n=8)	IM C2 800 mg (2 mL) (n=8)	IM C4 1200 mg (3 mL) (n=8)
Cmax, µg/mL	0.7 (35.5)	0.8 (39.0)	1.8 (53.5)	1.8 (148)
tmax, hours	570 (158)	349 (147)	298 (136)	383 (107)

CAB-ULA has slower absorption and longer $t_{1/2}$ than CAB200 IM

- PK profiles were flatter than CAB200 IM
- CAB-ULA Cmax was lower with SC than IM; both were lower than CAB200 IM[1]
- tmax was longer than CAB200 IM[1]
- **CAB-ULA $t_{1/2}$ for SC and IM was predicted to be >6x and >2x the $t_{1/2}$ of CAB200 IM, respectively[1,a]**

Observed median and range (error bar) dose-normalized to 1600 mg[b]



- BQL, below quantification limit of 0.025 µg/mL; CAB, cabotegravir; Cmax, maximum observed plasma concentration; %CVb, coefficient of variation; IM, intramuscular; n, number of participants with valid PK parameters; PI, prediction interval; PK, pharmacokinetics; SC, subcutaneous; $t_{1/2}$, terminal half-life; tmax, time to Cmax; ULA, ultra-long-acting. [a]Current follow-up time is insufficient to calculate final $t_{1/2}$ value for CAB-ULA. [b]Error bars before Week 2 are not displayed for visibility.

1. Cabenuva [prescribing information]. ViiV Healthcare; 2025.

CAB-ULA
SAFETY OF CAB-ULA

- Non-ISR drug-related AEs were infrequent
- CAB-ULA IM was better tolerated than SC
  - SC: ISRs occurred in 100% (16/16) of participants; most common SC ISRs were erythema, nodule, and pain
  - IM: ISRs occurred in 69% (22/32) of participants; most common IM ISR was pain and except for 1, all were mild (grade 1)
- CAB-ULA IM ISR profile appears comparable to established CAB200 IM ISR profile despite higher single doses of CAB-ULA

	Part C: CAB-ULA				
	SC		IM		
Parameter	C1: 800 mg (2 mL) (N=8)	C3: 1200 mg (3 mL) (N=8)	C2: 800 mg (2 mL) (N=8)	C4: 1200 mg (3 mL) (N=8)	C5: 1600 mg (3 mL) (N=16)
Any ISR, n (%)	8 (100)	8 (100)	3 (38)	8 (100)	11 (69)
Total ISR events, n	21	24	5	9	15
Maximum grade 1, n (% of ISRs)	19 (90)	22 (92)	4 (80)	9 (100)	14 (93)
Maximum grade 2, n (% of ISRs)	2 (10)	2 (8)	1 (20)	0	1 (7)
Maximum grade ≥3, n (% of ISRs)	0	0	0	0	0
Duration, median (IQR), days[a]	15 (6-41)	13 (6-21)	5 (5-8)	4 (3-5)	6 (4-8)

AE, adverse event; CAB, cabotegravir; IM, intramuscular; IQR, interquartile range; ISR, injection site reaction; SC, subcutaneous; ULA, ultra-long-acting.
[a]Only calculated for events that have resolved (C1: 15/21 [71%]; C3: 17/24 [71%]; C2: 5/5 [100%]; C4: 9/9 [100%]; C5: 12/15 [80%]).

Han et al. CROI 2024; Denver, CO. Oral Presentation 130.

CAB-ULA CONCLUSIONS

- A new CAB-ULA formulation exhibits favorable tolerability and safety, with a PK profile that supports dose intervals of ≥4 months
  - IM tolerability is encouraging at CAB-ULA doses up to 2.7x (1600 mg) the approved CAB dose
  - Additional SC evaluation is planned
- CAB-ULA has the potential for less frequent dosing and may reduce clinic visits
- CAB-ULA IM Q4M is progressing into upcoming late-stage HIV-1 PrEP and treatment studies

- CAB, cabotegravir; IM, intramuscular; PK, pharmacokinetics; PrEP, pre-exposure prophylaxis; Q4M; every 4 months; SC, subcutaneous; ULA, ultra-long-acting.

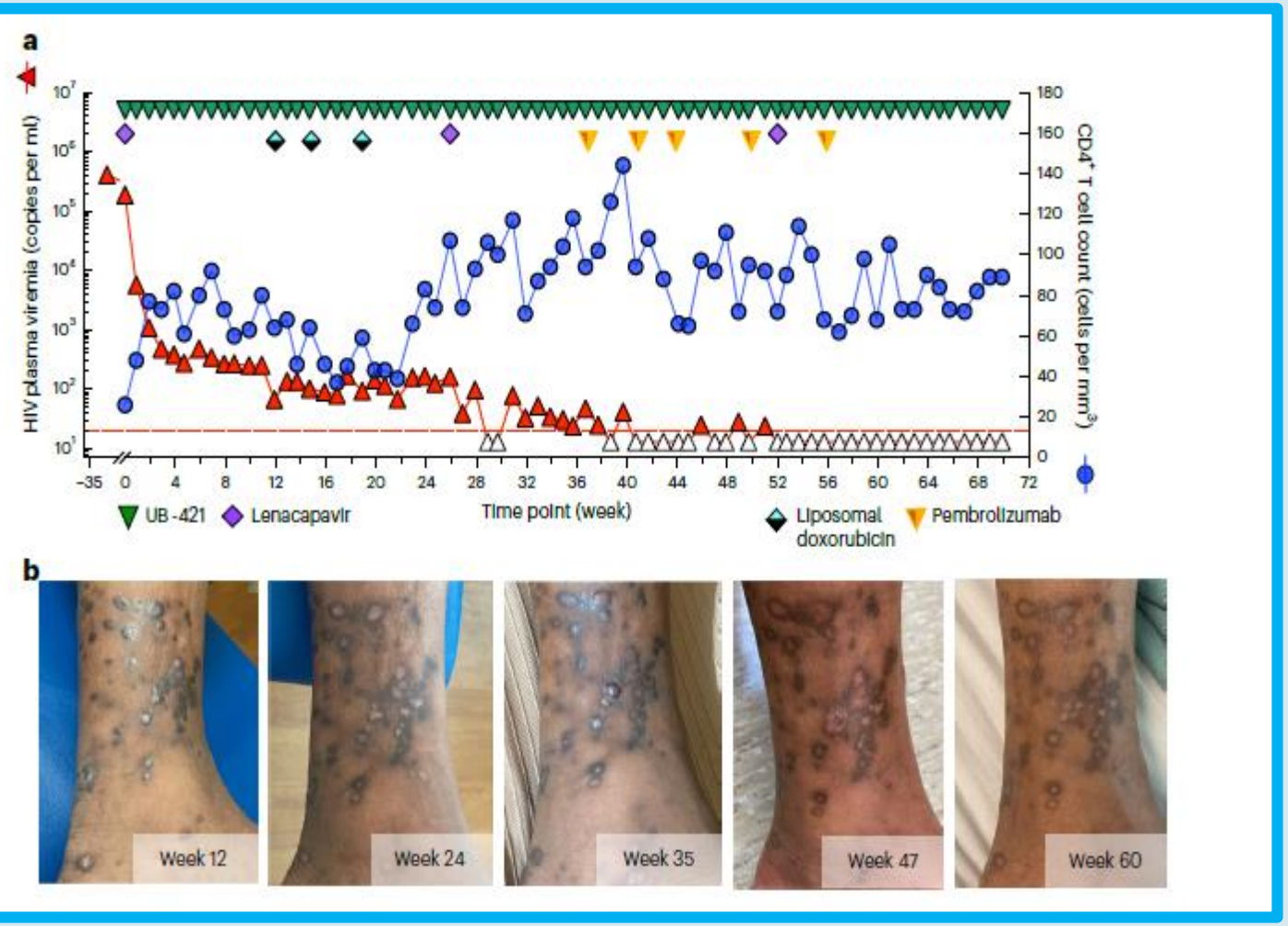
Han et al. CROI 2024; Denver, CO. Oral Presentation 130.

A NEW DEFINITION OF CURE?

- "Classic" Cure:
  - Elimination of all replication competent HIV-1 from the body
  - Substantial challenges[1,2] and difficult (impossible) to prove[3]
- "Functional" Cure:
  - Control of HIV in the absence of ART
    - Minimize potential replication events (infected cells with replication competent virus)
    - Improve immune control and potentially protect uninfected cells
  - Reduce or eliminate persistent immune activation and inflammation

1. Henrich et al. *Ann Intern Med*. 2014 Sep 2;161(5):319-27
2. Luzuriaga et al. *N Engl J Med*. 2015 Feb 19;372(8):786-8
3. Jiang et al. Litcherfeld, Yu *Nature* 2020

SUSTAINED VIROLOGIC SUPPRESSION OF MULTIDRUG-RESISTANT HIV IN AN INDIVIDUAL TREATED WITH ANTI-CD4 DOMAIN 1 ANTIBODY AND LENACAPAVIR



A 58-year-old male individual with MDR HIV and Kaposi sarcoma (KS) was treated with a new antiretroviral regimen consisting of anti-CD4 domain 1 antibody UB-421 and capsid inhibitor lenacapavir. The individual experienced delayed but sustained suppression of plasma viremia and a substantial increase in the CD4+ T cell count. A longitudinal examination of plasma HIV and infectious isolates showed no evidence of viral evolution or the emergence of UB-421- or lenacapavir-resistant viruses. The individual received three cycles of liposomal doxorubicin and five doses of anti-programmed cell death protein 1 (PD-1) monoclonal antibody pembrolizumab that resulted in improvement in KS with flattening of lesions. Our data demonstrate that combination therapy with UB-421 could provide sustained virologic suppression in people harboring MDR HIV with limited therapeutic alternatives

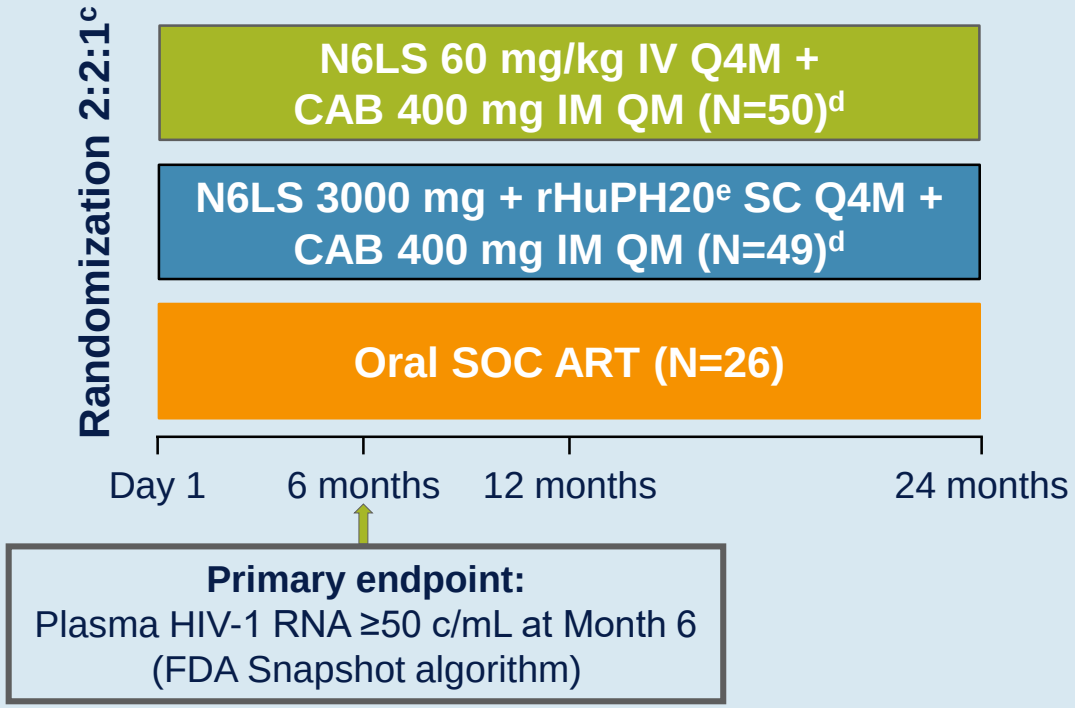
M. Ali Rai, Nat Med 2025

EMBRACE (N6LS) STUDY DESIGN

Randomized, open-label, multicenter, phase 2b study conducted at 45 sites in the United States and Puerto Rico

Key inclusion/exclusion criteria

- Aged 18-70 years
- ≥2 HIV-1 RNA measurements <50 c/mL in the 12 months before screening
- No prior ART switch due to VF
- CD4+ cell count ≥350 cells/mm^3
- On stable ART for ≥6 months
- No active HBV co-infection[a]
- Phenotypic sensitivity to N6LS (IC_{90} ≤2.0 µg/mL and MPI >98%)[b]



- ART, antiretroviral therapy; CAB, cabotegravir; FDA, US Food and Drug administration; HBcAb, hepatitis B core antibody; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; IC_{90}, 90% inhibitory concentration; IM, intramuscular; IV, intravenous; MPI, maximum percent inhibition; N6LS, VH3810109; PBMC, peripheral blood mononuclear cell; QM, every month; Q4M, every 4 months; rHuPH20, recombinant human hyaluronidase PH20; SC, subcutaneous; SOC, standard of care; VF, virologic failure.
- [a]Individuals positive for HBsAg or negative for HBsAg but positive for HBcAb with detectable HBV DNA were excluded. [b]Performed using the PhenoSense® mAb DNA assay (Monogram Biosciences, South San Francisco, CA) using PBMC samples obtained at screening. [c]Stratified by N6LS IC_{90} > or ≤1.0 µg/mL. [d]CAB 600 mg IM loading dose on Day 1. [e]rHuPH20 sourced from Halozyme Therapeutics, Inc (San Diego, CA).

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EMBRACE (N6LS) PARTICIPANT DEMOGRAPHICS AND BASELINE CHARACTERISTICS

Parameter	N6LS 60 mg/kg IV (N=50)	N6LS 3000 mg + rHuPH20 SC (N=49)	Oral SOC ART (N=26)[a]	Total (N=125)
Age, median (range), y	53 (28-69)	53 (22-67)	47 (25-68)	53 (22-69)
Male, n (%)[b]	44 (88)	39 (80)	21 (81)	104 (83)
Race, n (%)				
Asian	0	2 (4)	1 (4)	3 (2)
Black or African American	11 (22)	19 (39)	5 (19)	35 (28)
White	37 (74)	26 (53)	16 (62)	79 (63)
Ethnicity, Hispanic or Latin American, n (%)	18 (36)	21 (43)	15 (58)	54 (43)
Weight, median (range), kg	81 (60-109)	81 (58-112)	86 (57-136)	83 (57-136)
Body mass index, median (range), kg/m^2	27 (17-37)	27 (19-40)	29 (21-40)	28 (17-40)
CD4+ cell count, median (range), cells/mm^3	602 (309-1210)	759 (351-1635)	644 (307-1174)	647 (307-1635)
N6LS IC_{90} phenotypic sensitivity[c]				
Median (range), µg/mL	0.76 (0.21-1.92)	0.85 (0.12-1.97)	0.94 (0.24-1.96)	0.83 (0.12-1.97)
≤1 µg/mL, n (%)	33 (66)	28 (57)	16 (62)	77 (62)
>1 to ≤2 µg/mL, n (%)	17 (34)	21 (43)	10 (38)	48 (38)

- ART, antiretroviral therapy; IC_{90}, 90% inhibitory concentration; INSTI, integrase strand transfer inhibitor; IV, intravenous; N6LS, VH3810109; rHuPH20, recombinant human hyaluronidase PH20; SC, subcutaneous; SOC, standard of care.
- [a]23/26 (88%) participants in the oral SOC ART group were using INSTI-based regimens. [b]Sex assigned at birth. [c]All participants were sensitive to N6LS (IC_{90} ≤2.0 µg/mL) per inclusion criteria.

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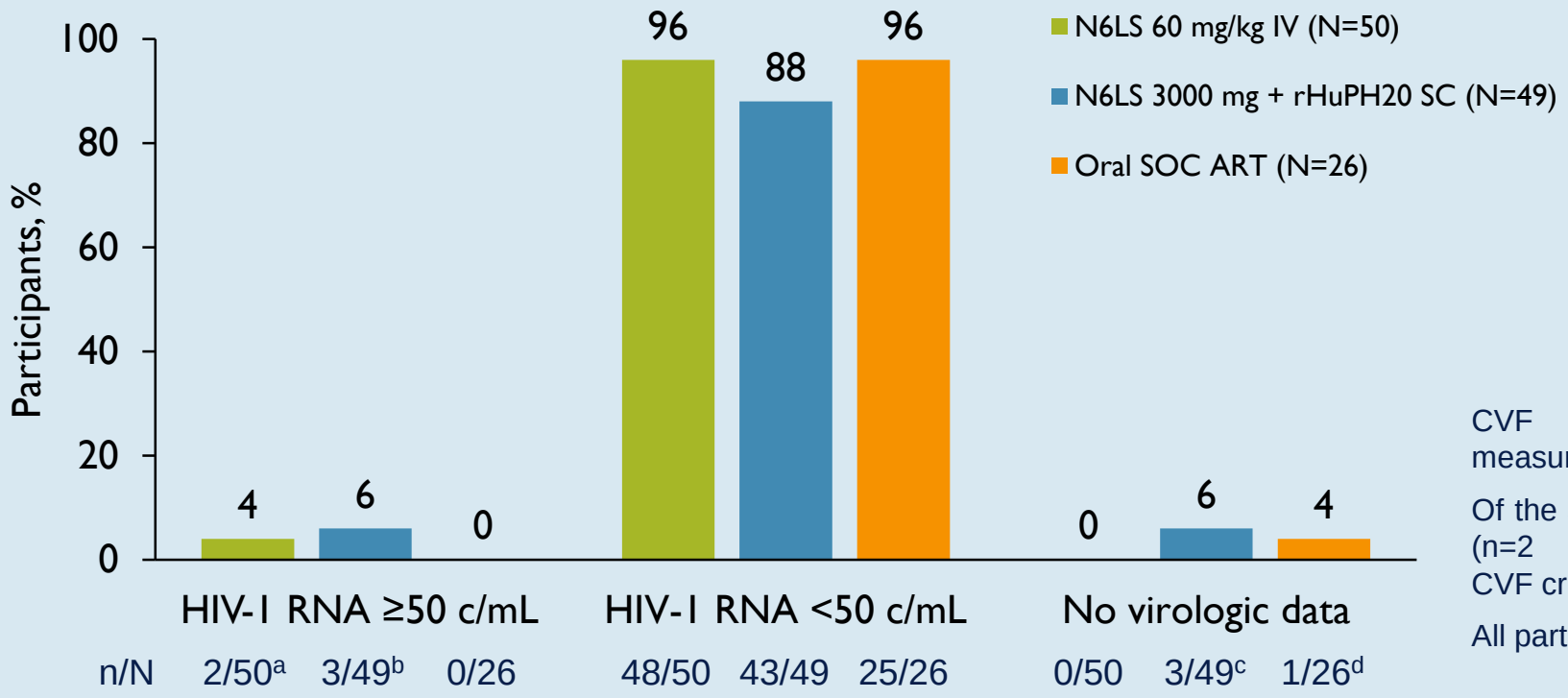
EMBRACE (N6LS)
N6LS MAINTAINED VIRAL SUPPRESSION IN A HIGH PROPORTION OF ADULTS WITH BASELINE N6LS SENSITIVITY

Efficacy at Month 6 (FDA Snapshot, FAS)



CVF was defined as 2 consecutive HIV-1 RNA measurements ≥200 c/mL

Of the 5 participants with Snapshot HIV-1 RNA ≥50 c/mL, 4 (n=2 in each N6LS group) met CVF criteria and 1 did not meet CVF criteria

All participants with CVF re-suppressed on DVR/c/FTC/TAF

No Trend Was Observed for Median Change From Baseline in CD4+ Cell Count Through Month 6

- ART, antiretroviral therapy; FAS, full analysis set; FDA, US Food and Drug Administration; IV, intravenous; N6LS, VH3810109; rHuPH20, recombinant human hyaluronidase PH20; SC, subcutaneous; SOC, standard of care.
- [a]n=1 data in window not below threshold and n=1 discontinued for lack of efficacy. [b]n=1 data in window not below threshold and n=2 discontinued for lack of efficacy. [c]n=2 discontinued due to adverse event and n=1 discontinued for other reasons (participant withdrawal). [d]n=1 discontinued for other reasons (participant withdrawal).

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EMBRACE (N6LS) SAFETY SUMMARY

Participants, n (%)	N6LS 60 mg/kg IV (N=50)	N6LS 3000 mg + rHuPH20 SC (N=49)	Oral SOC ART (N=26)
Any AE[a]	46 (92)	40 (82)	17 (65)
Grade 1-2	41 (82)	23 (47)	15 (58)
Grade 3	5 (10)	15 (31)	1 (4)
Grade 4	0	2 (4)	1 (4)
N6LS/CAB-related AEs	32 (64)	32 (65)	—
Grade 3	0	8 (16)[b]	—
Grade 4	0	0	—
Any serious AE	0	3 (6)	2 (8)
N6LS/CAB-related serious AEs	0	0	—
AEs leading to withdrawal	0	3 (6)[c]	0

- N6LS was generally well tolerated when given IV, with no AEs leading to withdrawal and no N6LS- or CAB-related serious AEs reported
- Participants receiving N6LS SC had 3 serious AEs and 3 AEs leading to withdrawal
- CAB LA QM safety and tolerability were consistent with product label

- AE, adverse event; ART, antiretroviral therapy; CAB, cabotegravir; IV, intravenous; LA, long-acting; N6LS, VH3810109; QM, every month; rHuPH20, recombinant human hyaluronidase PH20; SC, subcutaneous; SOC, standard of care.
- [a]AEs occurring in ≥10% of participants receiving N6LS IV included injection site pain, fatigue, COVID-19, increased lipase, and headache. AEs occurring in ≥10% of participants receiving N6LS SC included infusion site erythema, injection site pain, infusion site pain, infusion site induration, infusion site swelling, and injection site nodule. [b]Included infusion site erythema (n=6), infusion site swelling (n=3), infusion site induration (n=2), and injection site pain (n=1). [c]Included CAB-associated injection site pain (n=1), hepatitis B reactivation (n=1), and anxiety and depression (n=1).

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EMBRACE (N6LS) CONCLUSIONS

- N6LS administered IV or SC every 4 months in combination with monthly CAB LA maintained viral suppression in a high proportion of adults with baseline N6LS sensitivity
- N6LS resistance was detected in both participants with CVF in the IV group, and an INSTI RAM was detected in 1 of the 2 participants with CVF in the SC group
- N6LS was better tolerated after IV than SC administration
  - In the IV group, N6LS-associated ISRs were rare, all were grade 1 and resolved within 3 days, and there were no N6LS-associated grade 3 or 4 AEs or N6LS-related treatment discontinuations
- Based on these results, N6LS IV Q6M in combination with CAB LA has been selected for further evaluation in part 2 of the EMBRACE study

- AE, adverse event; CAB, cabotegravir; CVF, confirmed virologic failure; INSTI, integrase strand transfer inhibitor; ISR, infusion site reaction; IV, intravenous; LA, long-acting; N6LS, VH3810109; Q6M, every 6 months; RAM, resistance-associated mutation; SC, subcutaneous.

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TAKE HOME MESSAGES

- CAB-LA mostra un'eccellente efficacia virologica con importante miglioramento dei PROs nella RWE.
- Buona durability nei trial registrativi con interruzioni del trattamento legate a diversi fattori, tra cui le reazioni nel sito di iniezione ISR.
- L'implementazione richiede di adattare questo nuovo tipo di regime ai bisogni delle PLWH e alle risorse disponibili, con crescenti evidenze per l'applicazione a popolazioni più variegate di quelle dei trial.
- Risultati preliminari incoraggianti emergono dalla combinazione di antiretrovirali long-acting iniettabili e bNAbs per il raggiungimento di una cura funzionale.