

Real life data of 2-drug therapy: CAB-RPV Long Acting

Camilla Muccini, MD, PhD
IRCCS Ospedale San Raffaele



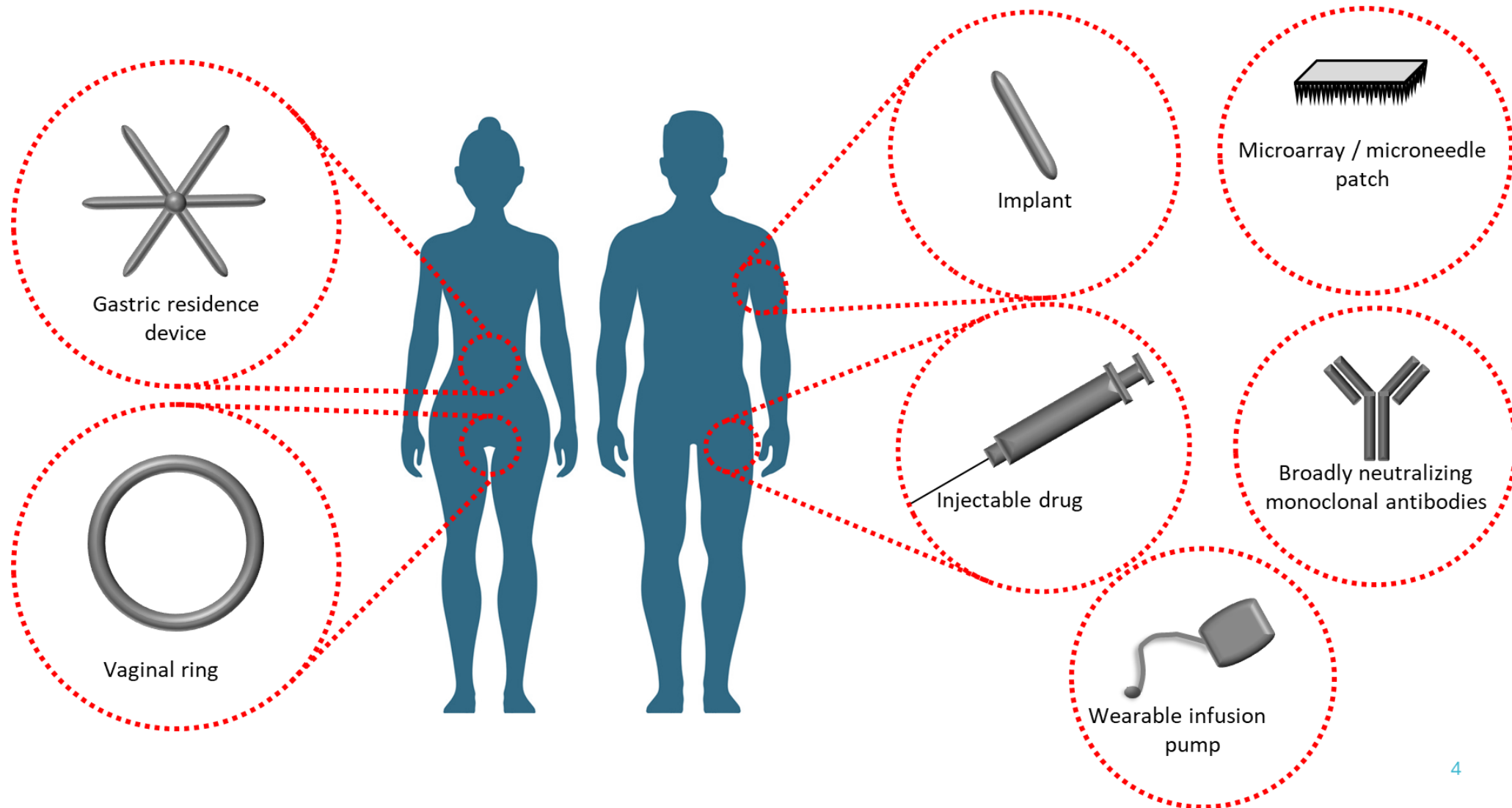
**THE WHYS AND
THE WHEREFORES
IN HIV THERAPY**

Bergamo, April 14, 2025
NH Bergamo

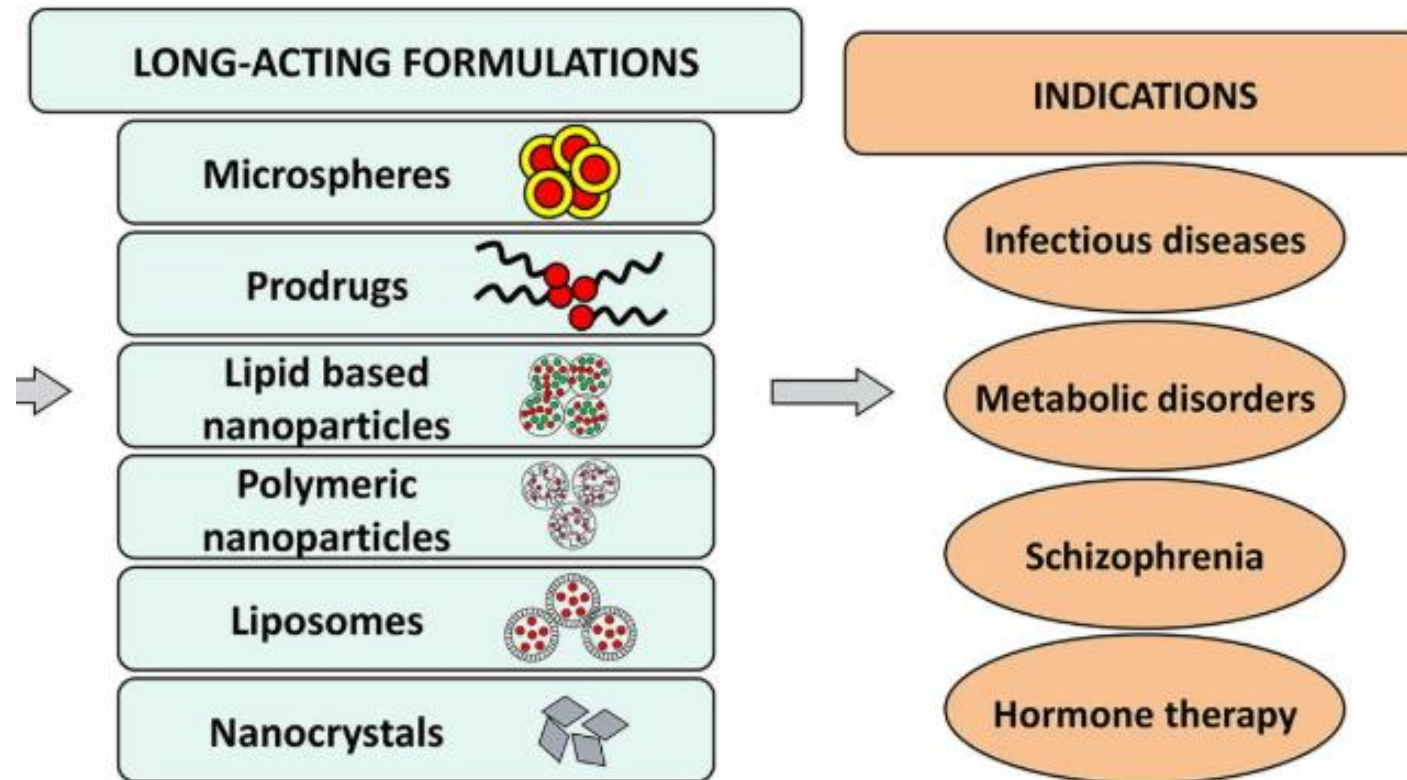
Disclosure

- I received speaking fees from ViiV Healthcare and Gilead

Drug Delivery Systems and Long-acting Technologies



Long-acting Formulations and Indications



Long-acting Drugs Approved for HIV

LA- Cabotegravir + Rilpivirine

IM, every 4 or 8 weeks
with/with out OLI

FDA/EMA Approved

Jan 2021; ART /4 weeks

Feb 1, 2022: ART /8 weeks

Switch with undetectable VL

Lenacapavir

SC every 6 months
Combined with oral ARV

FDA/EMA Approved

Dec 2022: Twice-yearly treatment
for PLH multi-drug resistant HIV

What's Happening in Clinical Practice?

RCT vs. **RWE**



**Randomized
Controlled Trial**



**Real World
Evidence**

CAB/RPV Effectiveness in the OPERA Cohort

Demographic and Clinical Characteristics at CAB+RPV LA Initiation (n= 2858)

	Individuals with ≥ 1 injection
Age, median years (IQR)	39 (31, 51)
Female, n (%)	448 (16%)
Black race, n (%) ^a	1,199 (42%)
Hispanic ethnicity, n (%) ^a	853 (30%)
Married or domestic partner, n (%) ^a	486 (17%)
Injection drug use, n (%)	86 (3%)
MSM, n (%)	1,619 (57%)
Care in Southern US, n (%)	1,577 (55%)
Payer, n (%) ^b	
Medicare	342 (12%)
Medicaid	945 (33%)
Commercial Insurance	1,954 (68%)
Ryan White/ADAP	900 (31%)
Cash	85 (3%)
Other Payer	

	Individuals with ≥ 1 injection
Years since HIV diagnosis, median (IQR)	6 (2, 13)
History of AIDS-defining illnesses, n (%)	680 (24%)
BMI, median kg/m ² (IQR) ^a	27 (24, 31)
VACS Index, median (IQR) ^a	10 (0, 18)
≥ 1 comorbidity, n (%) ^c	2,208 (77%)
Co-infections (ever), n (%)	
Hepatitis B	74 (3%)
Hepatitis C	193 (7%)
Syphilis	1,337 (47%)
CD4 cell count, median cells/μL (IQR) ^a	698 (519, 912)
Prior core agent class, n (%) ^a	
INSTI	2,227 (78%)
PI	109 (4%)
NNRTI	197 (7%)
≥ 2 core agents	207 (7%)
Other	≤ 5 ^b

CAB/RPV Effectiveness in the OPERA Cohort

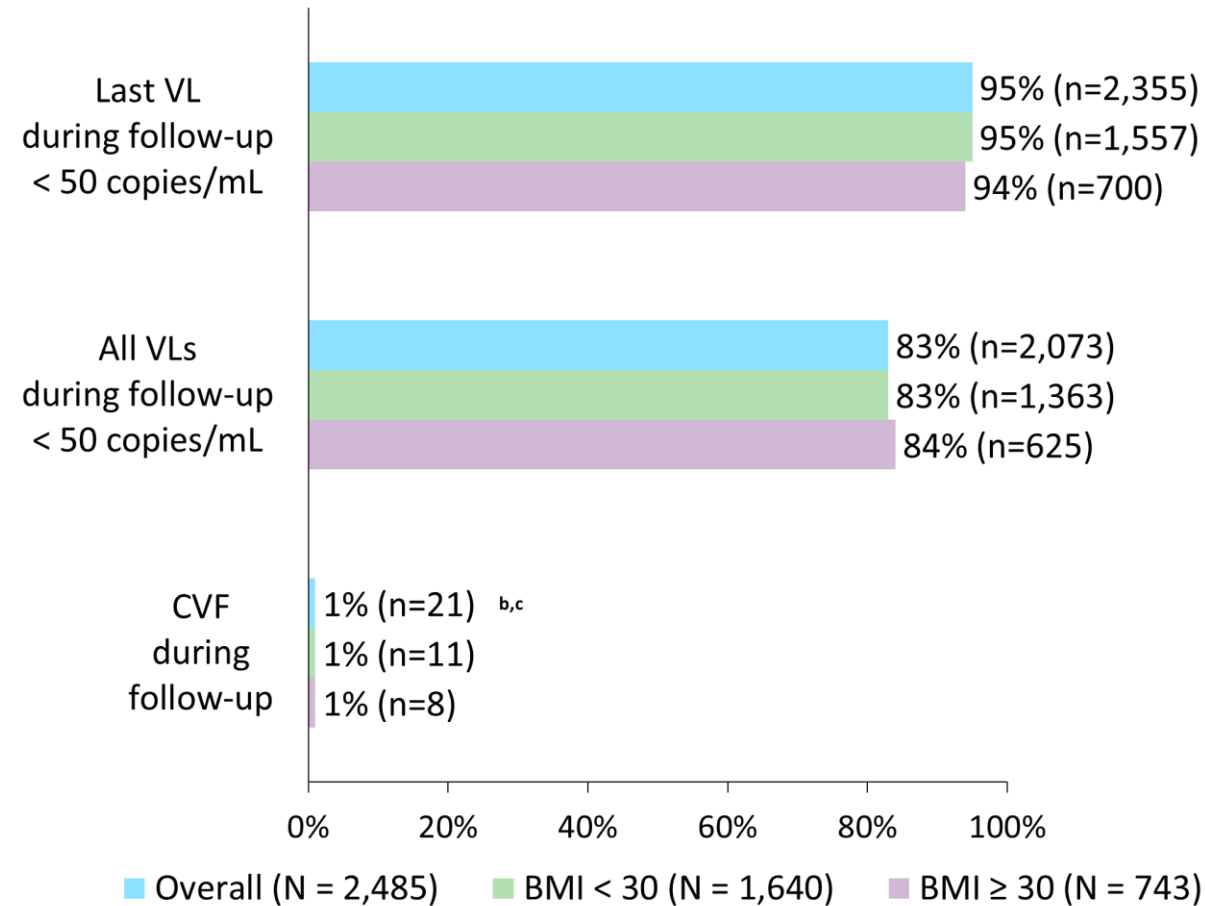
Persistence and Adherence

	Complete initiators
Months of follow-up, median (IQR)	11 (6, 18)
Receiving CAB+RPV LA at time of analysis, n (%) ^a	2,179 (83%)
Received 2 nd initiation injection on-time	2,188 (84%)
Individuals with ≥ 1 maintenance injection, n (%)	2,360
Received all maintenance injections on-time	1,475 (62%)
≥ 1 delayed maintenance injections, n (%)	711 (30%)
≥ 1 missed maintenance injections, n (%)	279 (12%)

- ✓ 2618 individuals (92%) were followed for a median of 11 months
- ✓ Most individuals received their 2nd initiation injection on-time and over half received all maintenance injections on-time
- ✓ While 38% of individuals did not receive all maintenance injections on time , ART coverage between injections with oral bridging could not be assessed

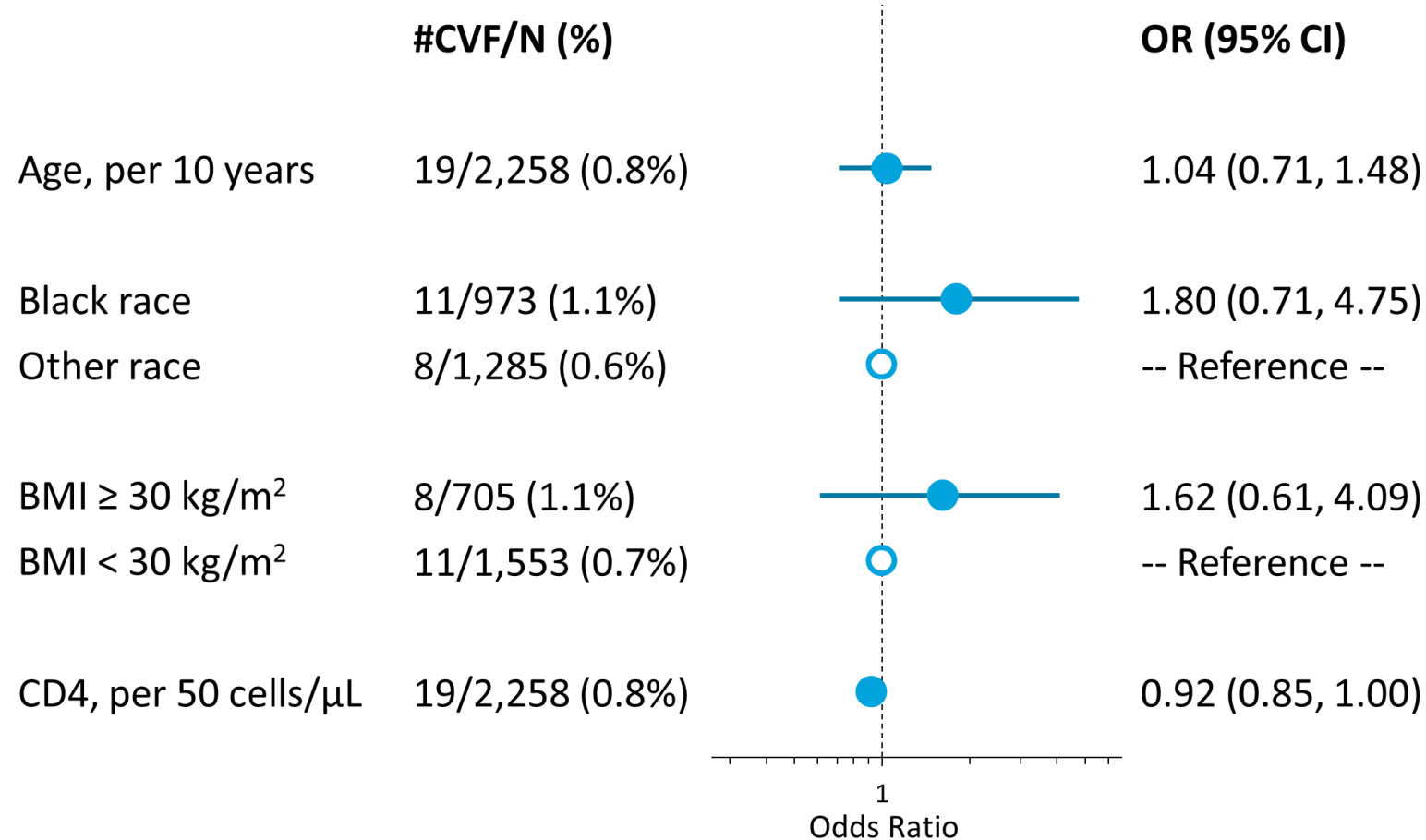
CAB/RPV Effectiveness in the OPERA Cohort

Virologic outcomes overall and stratified by BMI at initiation



CAB/RPV Effectiveness in the OPERA Cohort

Factors associated with CVF



CAB/RPV Effectiveness in the TRIO Health US Cohort

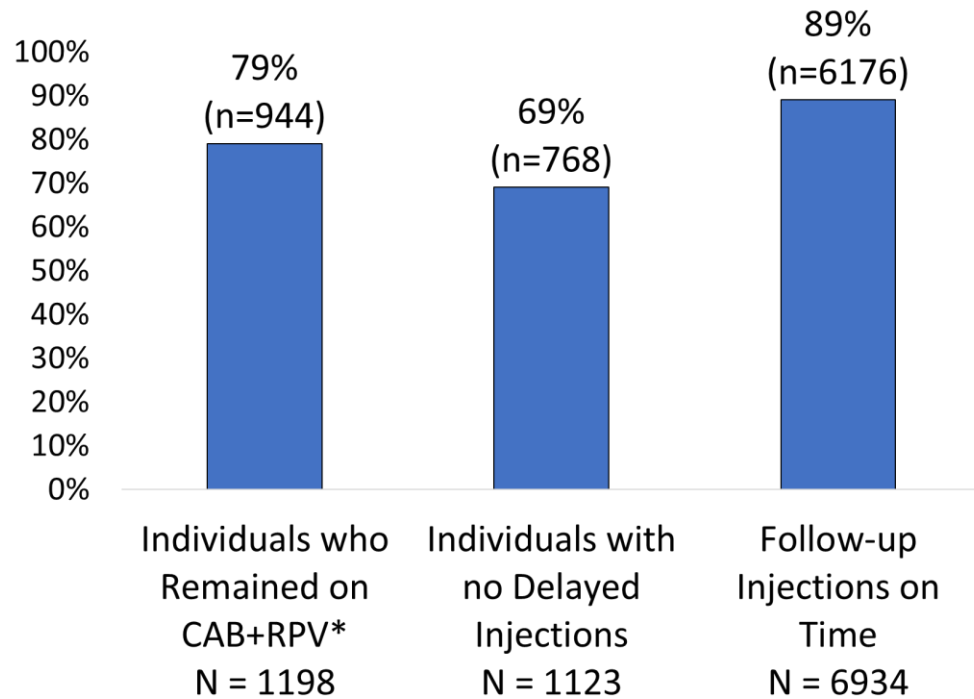
Baseline characteristics

	N (%) or Median (IQR)	All Initiators n=1198	With Viral Failure N=15
Follow-up	Months Follow-up in EMR	11 (5, 18)	13 (7, 18)
	>12 months Follow-up	549 (46)	8 (53)
	>24 months Follow-up	101 (8)	3 (20)
Gender	Age at Start	43 (34, 54)	49 (36, 52)
	Male	921 (77)	6 (40)
	Female	269 (22)	8 (53)
Race	Another or Unknown Gender	8 (1)	1 (7)
	White	500 (42)	4 (27)
	Black or African American	573 (48)	9 (60)
Payer	Another or Unknown Race	125 (10)	2 (13)
	Hispanic Ethnicity	244 (20)	1 (7)
	Commercial Payer	622 (52)	12 (80)
	Medicare/Medicaid Payer	330 (28)	2 (13)
	Other or Unknown Payer	246 (21)	1 (7)

BMI	Years since HIV Diagnosis	4 (1, 8)	3 (1, 4)
	Body mass index (BMI kg/m ²)	28 (24, 32)	31 (26, 37)
	Obese I (BMI 30-39)	357 (30)	5 (33)
CD4	Obese II (BMI ≥40)	68 (6)	3 (20)
	Absolute CD4 (cells/μL)	677 (488, 882)	657 (430, 833)
	Nadir CD4 (cells/μL)	437 (284, 631)	321 (194, 480)
Baseline resistance	INSTI	6/314 (2)	0/3 (0)
	CAB	2/314 (<1)	0/3 (0)
	NNRTI	61/314 (19)	0/3 (0)
	RPV	15/314 (5)	0/3 (0)
	Both CAB and RPV	1/314 (<1)	0/3 (0)

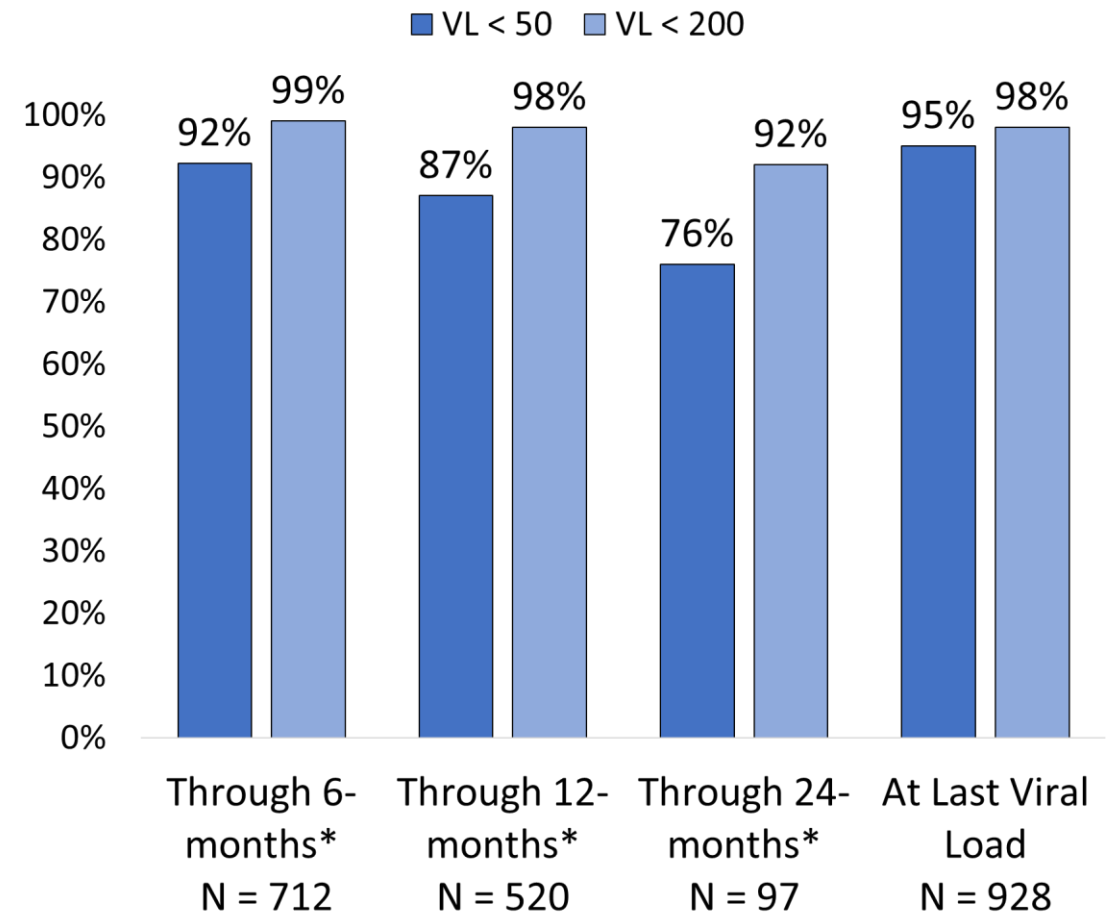
Outcomes in CAB/RPV in TRIO Health US Cohort

Adherence to and durability of CAB/RPV regimen



* Includes 21 who re-initiated CAB+RPV and remained on CAB+RPV through end of follow-up

Maintenance of viral suppression on CAB/RPV



* VL < 50 or VL < 200 at all viral loads through time period

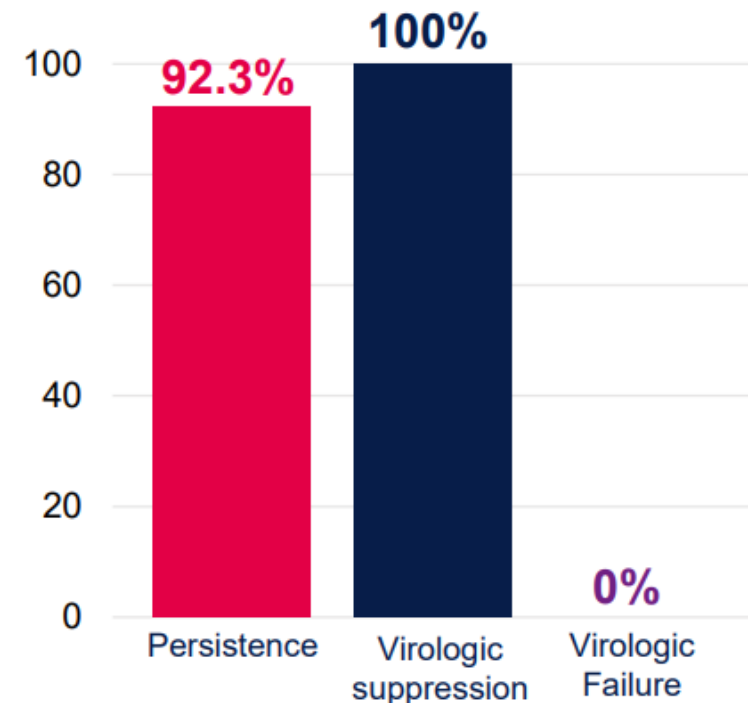
Real-life Data from the GEPPPO Cohort

Baseline characteristics

	N or median	Percentage or IQR
Age (years)	66.7	65-70
Male sex at birth	59	75.9%
Body Mass Index, BMI (Kg/m ²)	24.8	23.6-27.3
Years of HIV infection	20	14.0-28.5
Years of antiretroviral treatment	19	13.0-22.0
HIV RNA at baseline		
<20 copies/mL	70	89.7%
20-50 copies/mL	1	1.3%
>50 copies/mL	3	3.8%
Not available (6 mm window)	4	5.1%
Nadir CD4 cell count: n/mm3	270	105-410
Multimorbidity	48	61.9%
Polipharmacy	25	31.9%

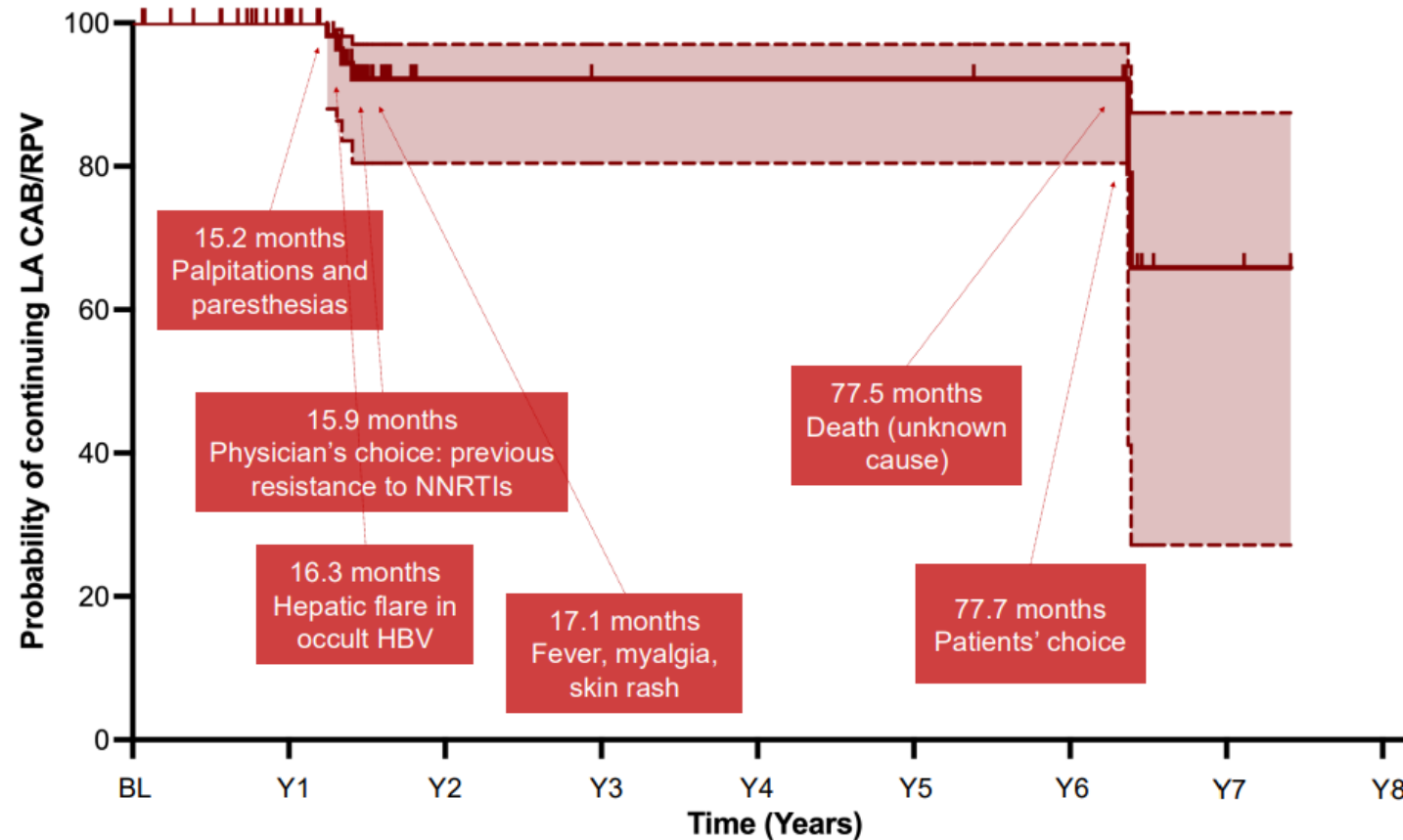
Persistence and virologic outcomes, n=78

Median follow-up time: 17.29 months (CI 95%: 16.74-17.60)



Real-life Data from the GEPPPO Cohort

Reasons for discontinuation in 6 participants



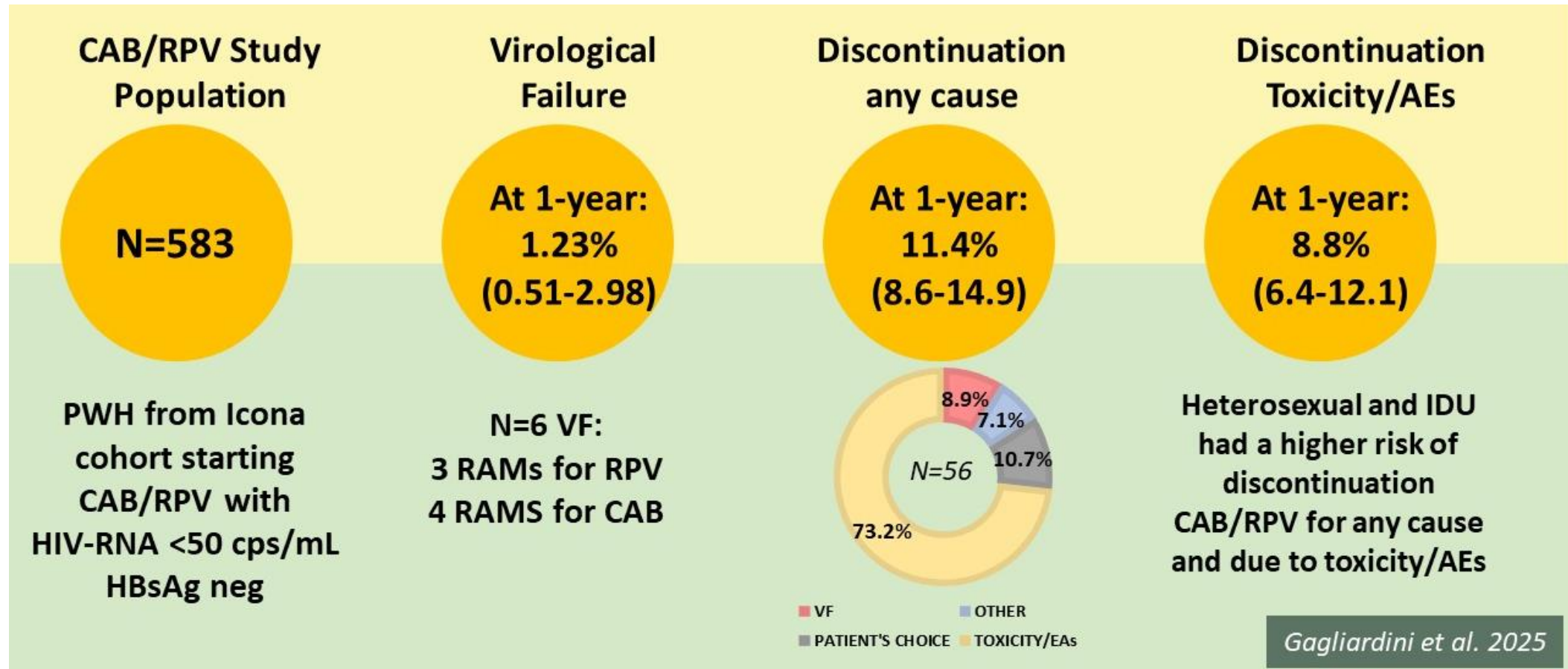
Real-life Data from the ICONA Cohort



Baseline characteristics

Female sex, n(%)	57 (11.3%)	ART exposure, years, median (IQR)	7.3 (4.4-10.2)
Italian nationality, n (%)	452 (88.7%)	Previous AIDS event, n (%)	42 (8.3%)
Mode of HIV transmission, n(%)		HBcAb positive, n (%)	79 (19.8%)
Heterosex	129 (25.5%)	HCVAb positive, n(%)	35 (7.2%)
IDU	9 (1.8%)	ART line, median (IQR)	4 [3-5]
MSM	344 (68.%)	GRT RT pre-CAB/RPV, n (%)	415 (82.0%)
BMI, median (IQR)	24.4 (22.7-26.8)	RPV fully susceptible, n(%)	405 (97.6%)
BMI > 30, n(%)	39 (7.7%)	GRT INSTI pre-CAB/RPV, n (%)	231 (45.7%)
CD4 at BL, median (IQR)	766 [590-959]	CAB fully susceptible, n (%)	231 (100%)
CD4 at nadir, median (IQR)	387 (243-532)	HIV subtype, n(%)	
CD4< 200 at nadir, n(%)	98 (19.4%)	A1	7 (1.4%)
Age, median (IQR)	46 [37-54]	B	280 (55.3%)
Age > 50 ys	165 (32.6%)		
Years of viral suppression, median (IQR)	7.0 (3.7-9.6)		

Real-life Data from the ICONA Cohort



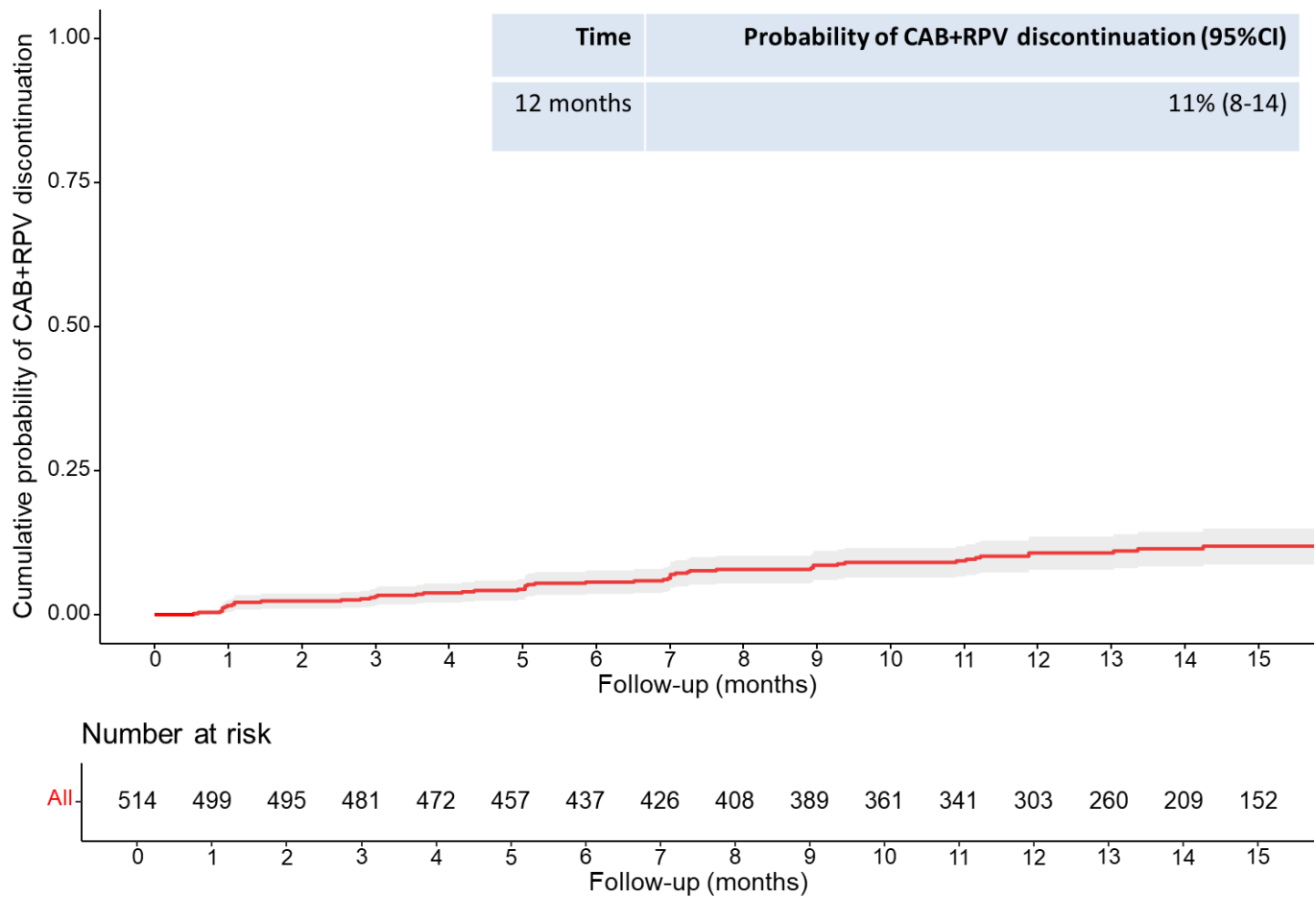
Real-life Data from the SCohoLART Study

Baseline characteristics

	N=514
Age, median (IQR)	49 (40-56)
Male, n (%)	467 (90.9)
HIV risk factor:	
Men who have sex with men, n (%)	364 (70.8)
Heterosexuals, n (%)	58 (11.3)
People who inject drugs, n (%)	11 (2.1)
Other, n (%)	81 (15.8)
Years from HIV diagnosis, median (IQR)	14.0 (8.8-20.5)
Years of ART, median (IQR)	11.4 (7.9-17.4)
CD4+ (cells/ μ L) , median (IQR)	794 (602-994)
Nadir CD4+ (cells/ μ L):	
>200 cells/ μ L, n (%)	389 (76.4)
$\leq$ 200 cells/ μ L, n (%)	120 (23.6)
CD8+ (cells/ μ L) , median (IQR)	850 (643-1114)
Years of the ART regimen in use at CAB+RPV switch, median (IQR)	3.4 (2.2-5.4)
Type of ART regimen in use at CAB+RPV switch:	
2 NRTI + 1 PI, n (%)	14 (2.8)
2 NRTI + 1 NNRTI, n (%)	124 (24.6)
2 NRTI + 1 INSTI, n (%)	179 (35.5)
2-drug regimen, n (%)	175 (34.7)
PI-monotherapy, n (%)	5 (1.0)
Other, n (%)	7 (1.4)

Real-life Data from the SCohoLART Study

Probability of treatment discontinuation



Real-life Data from the SCohoLART Study

Reasons of treatment discontinuation

	N=52
Death*, n (%)	1 (1.9)
Hypersensitivity reaction/allergy, n (%)	2 (3.8)
Injection site reaction, n (%)	15 (28.8)
Participant's wish/decision, n (%)	5 (9.6)
Gastrointestinal tract toxicity, n (%)	3 (5.8)
Central nervous system toxicity, n (%)	4 (7.7)
Other toxicity, n (%)**	10 (19.2)
Virological failure, n (%)	4 (7.7)
Other causes, n (%)***	8 (15.4)

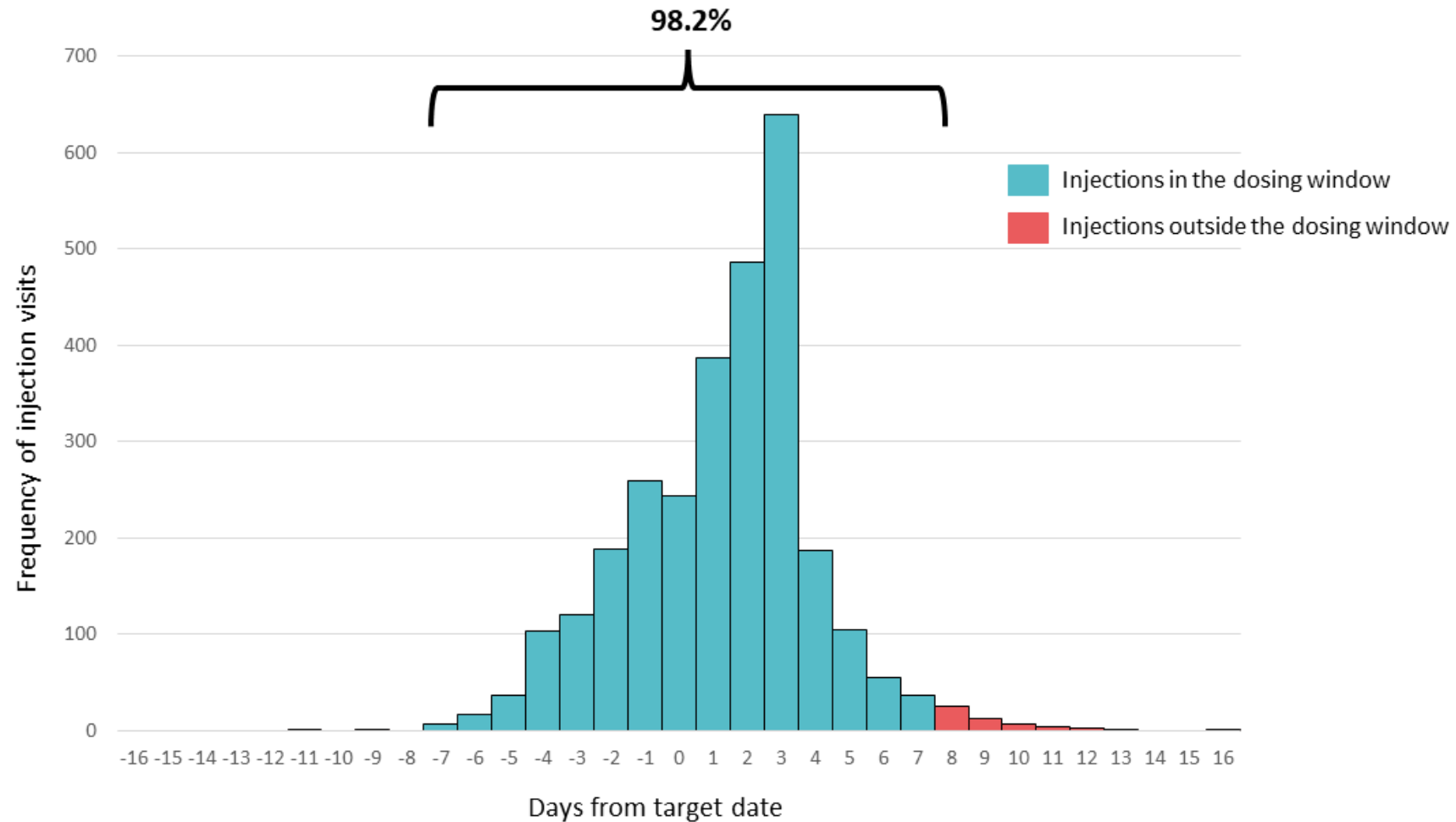
* One participant died from complications secondary to a metastatic biliopancreatic adenocarcinoma

** Other toxicity included: 3 pyrexia, 2 fatigue, 2 joint stiffness, 2 weight gain, 1 polyarthralgia

*** Other causes included: 2 personal commitments incompatible with injection visits, 1 transfer to another country, 1 HBV reactivation, 1 pregnancy, 1 viral blip, 1 enrollment in another study protocol, 1 chemotherapy-induced thrombocytopenia

Real-life Data from the SCohoLART Study

Probability of treatment discontinuation



WARD 86

Baseline characteristics

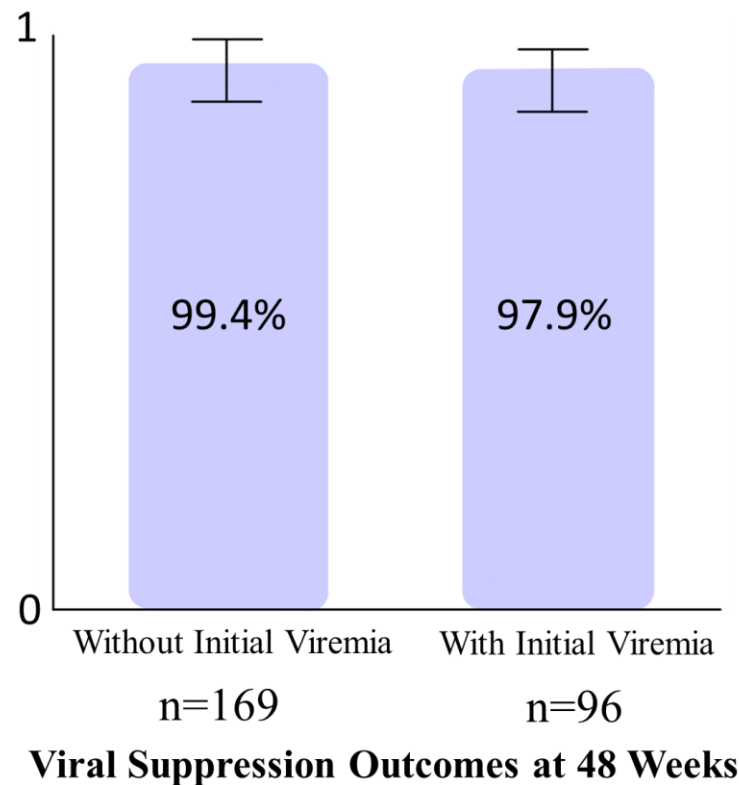
- ✓ The Ward 86 HIV Clinic in San Francisco serves publicly-insured PWH with high rates of substance use and housing insecurity

	Suppressed (N=241)	Viremic (N=129)	Overall (N=370)
Age at referral (years)			
Mean (SD)	45.6 (12.3)	47.5 (10.1)	46.3 (11.6)
Median [Min, Max]	44.0 [21.0, 70.0]	48.0 [25.0, 67.0]	45.0 [21.0, 70.0]
Race			
White	95 (39.4%)	56 (43.4%)	151 (40.8%)
American Indian	9 (3.7%)	3 (2.3%)	12 (3.2%)
Asian	23 (9.5%)	6 (4.7%)	29 (7.8%)
Black	53 (22.0%)	32 (24.8%)	85 (23.0%)
Multi-racial	4 (1.7%)	3 (2.3%)	7 (1.9%)
Other	51 (21.2%)	27 (20.9%)	78 (21.1%)
Missing	6 (2.5%)	2 (1.6%)	8 (2.2%)
Gender			
Cisgender man	191 (79.3%)	111 (86.0%)	302 (81.6%)
Nonbinary	6 (2.5%)	1 (0.8%)	7 (1.9%)
Other	1 (0.4%)	1 (0.8%)	2 (0.5%)
Transgender woman	42 (17.4%)	14 (10.9%)	56 (15.1%)
Missing	1 (0.4%)	2 (1.6%)	3 (0.8%)
Housing			
Housing unstable (SRO, shelter, outdoors, vehicle)	97 (40.2%)	67 (51.9%)	164 (44.3%)
Stable (rent or own)	144 (59.8%)	62 (48.1%)	206 (55.7%)
CD4 count at CAB+RPV initiation			
CD4 >= 200	88 (36.5%)	30 (23.3%)	118 (31.9%)
CD4 < 200	106 (44.0%)	88 (68.2%)	194 (52.4%)
Missing	47 (19.5%)	11 (8.5%)	58 (15.7%)
Substance use			
No current or past substance use	148 (61.4%)	51 (39.5%)	199 (53.8%)
Current or past substance use	93 (38.6%)	78 (60.5%)	171 (46.2%)



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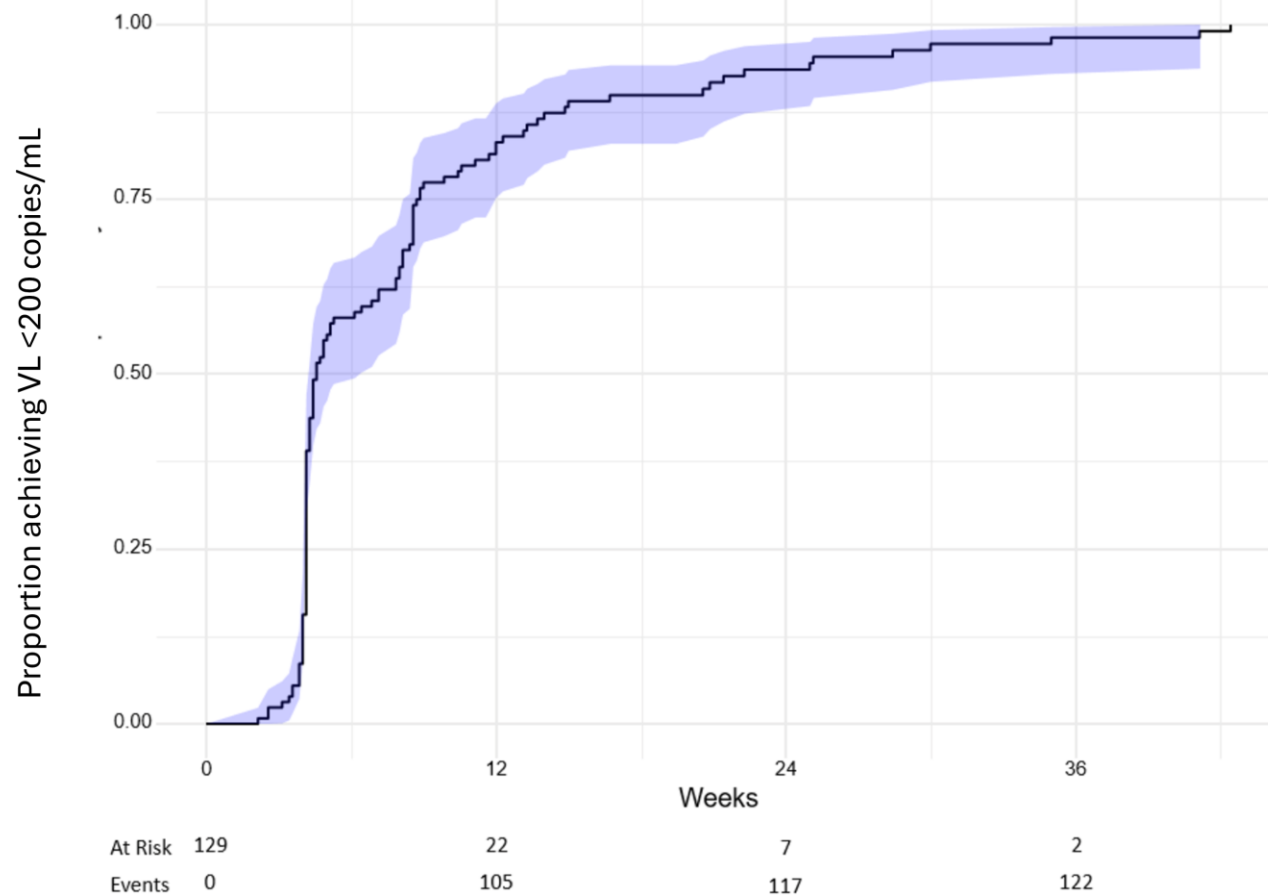
Figure 1. Viral Suppression outcomes at 48 weeks in those who started LA ART with and without viremia at baseline with at least 48 weeks of observation (n=265)



At 48 weeks, of the 265 sufficient follow-up: **99.4%** of those who started with VS remained suppressed (168/169; 95% CI=97-100%) ; **97.9%** of those with initial viremia achieved VS (94/96; 95% CI=93-99%)

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Figure 2. Kaplan-Meier Curve for PWH who initiated LA ART (cabotegravir/rilpivirine) with viremia (HIV RNA ≥ 30 copies/ml).



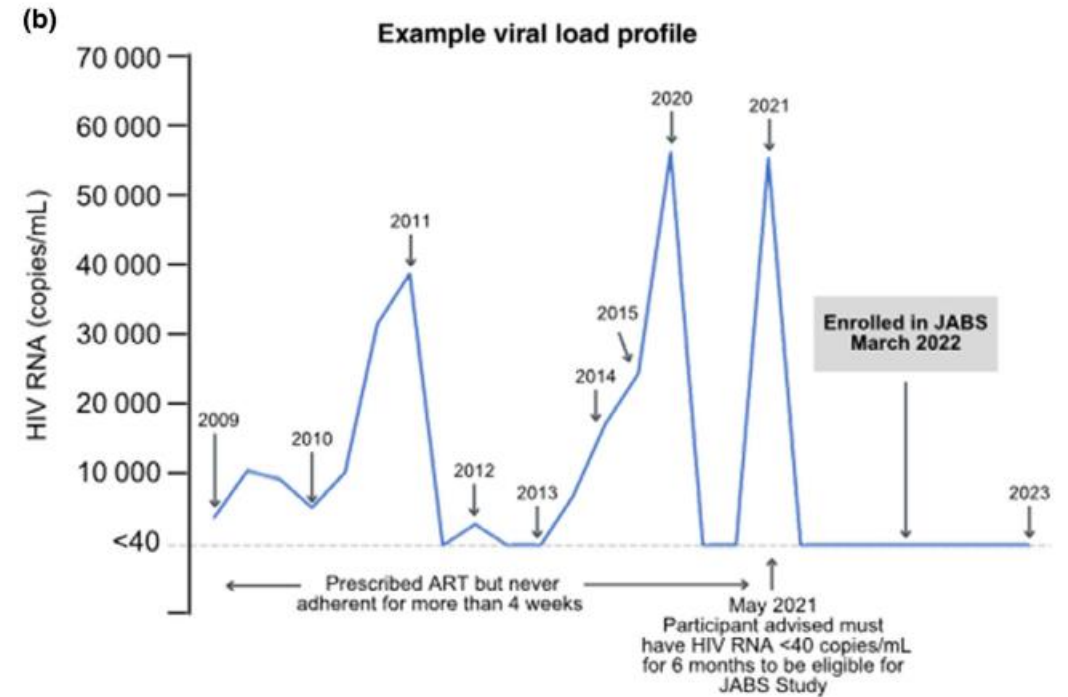
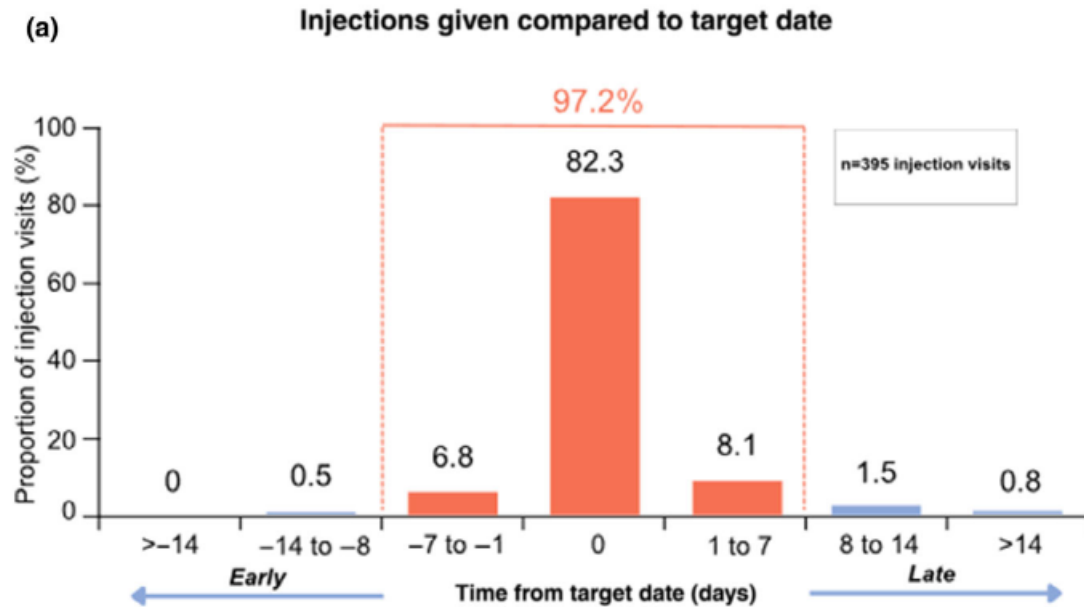
Median time to achieve VS (≤ 200 copies/ml) in those with viremia was **32 days** (95% CI 30-45)

JABS Study

Variables	Values
Patients (<i>n</i>)	60
Male birth sex	51 (85)
Age (years)	40 (36–47)
BMI	26 (23.4–28.7)
ATSI identifying	1 (1.7)
Country of birth	
Australia	26 (43.3)
African country	13 (21.7)
Other	21 (35)
First language	
English	45 (75)
Other	15 (25)
Time since HIV diagnosis (years)	8 (4–13)
Time since commencing treatment (years)	7 (4–11)
ART regimen at baseline	
BIC/FTC/TAF	25 (41.7)
E/C/FTC/TAF	15 (25)
DTG/ABC/3TC	11 (18.3)
DTG/3TC	3 (5)
RPV/FTC/TAF	3 (5)
Other	3 (5)

Historical non-adherence (VL >200 copies/mL)	10 (17)
Complexity scores	
Total score	24 (0–39)
Social isolation	30 (50)
Mental health/AOD issues	18 (30)
Financial instability	8 (13.3)
CMA	7 (11.7)
Cognitive/neurological issues	5 (8.3)
Polypharmacy (>5 medications)	4 (6.7)
Physical comorbidities	1 (1.7)
Hepatitis C and/or cancer	0 (0)
Regular GP	35 (58.3)
Formal supports (public health, mental health, or community case management)	6 (10)

JABS Study



No virological failures over a period of 12 months

Conclusions

- ✓ Efficacy and safety of long-acting regimen are confirmed by data from clinical practice
- ✓ Long-acting therapy may be also considered a valid strategy for those with adherence issues
- ✓ Longer-term real world data are needed to evaluate the CAB/RPV regime over time
- ✓ The future of research on the treatment of HIV infection is directed towards the long-acting strategy



Thanks for your attention!

