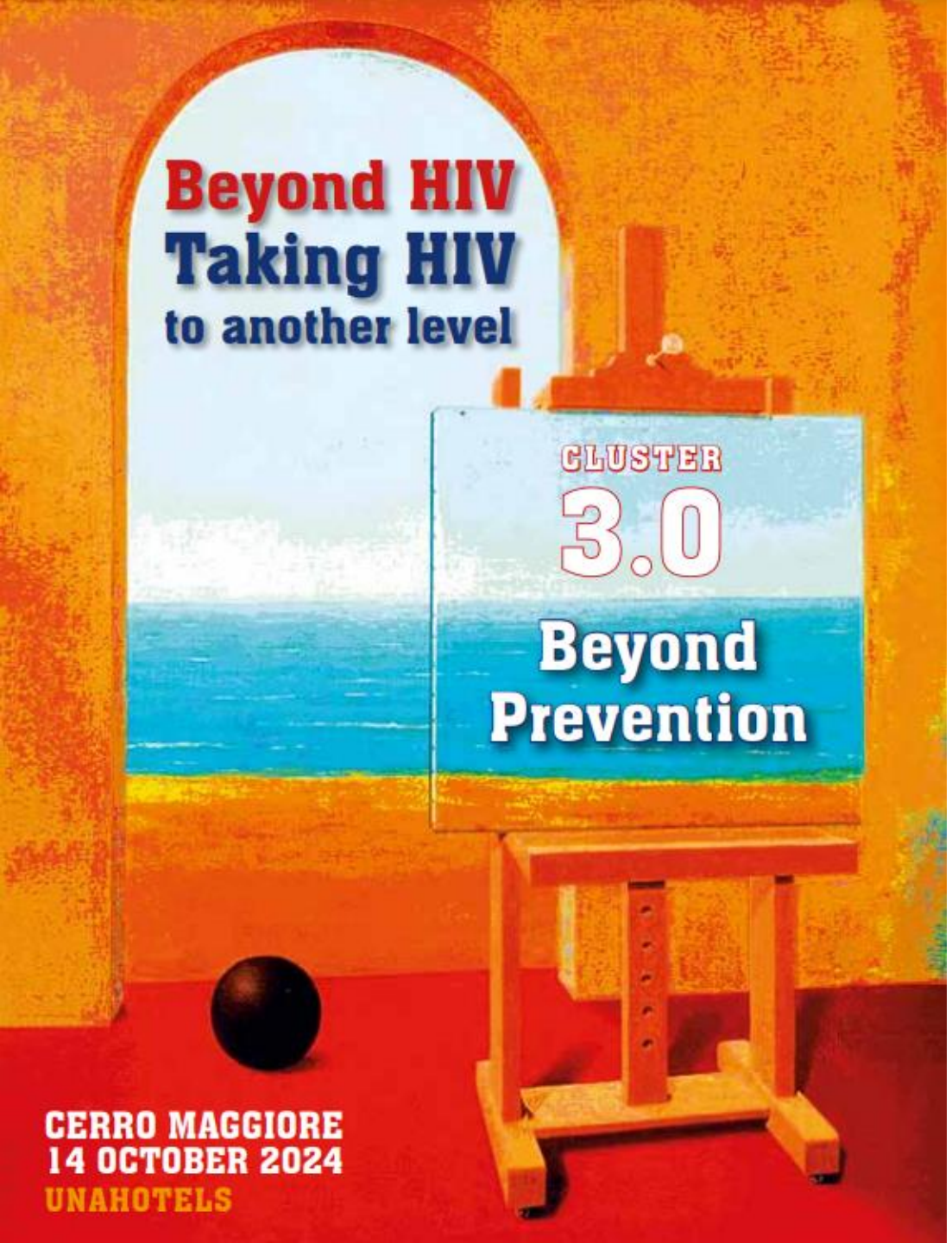
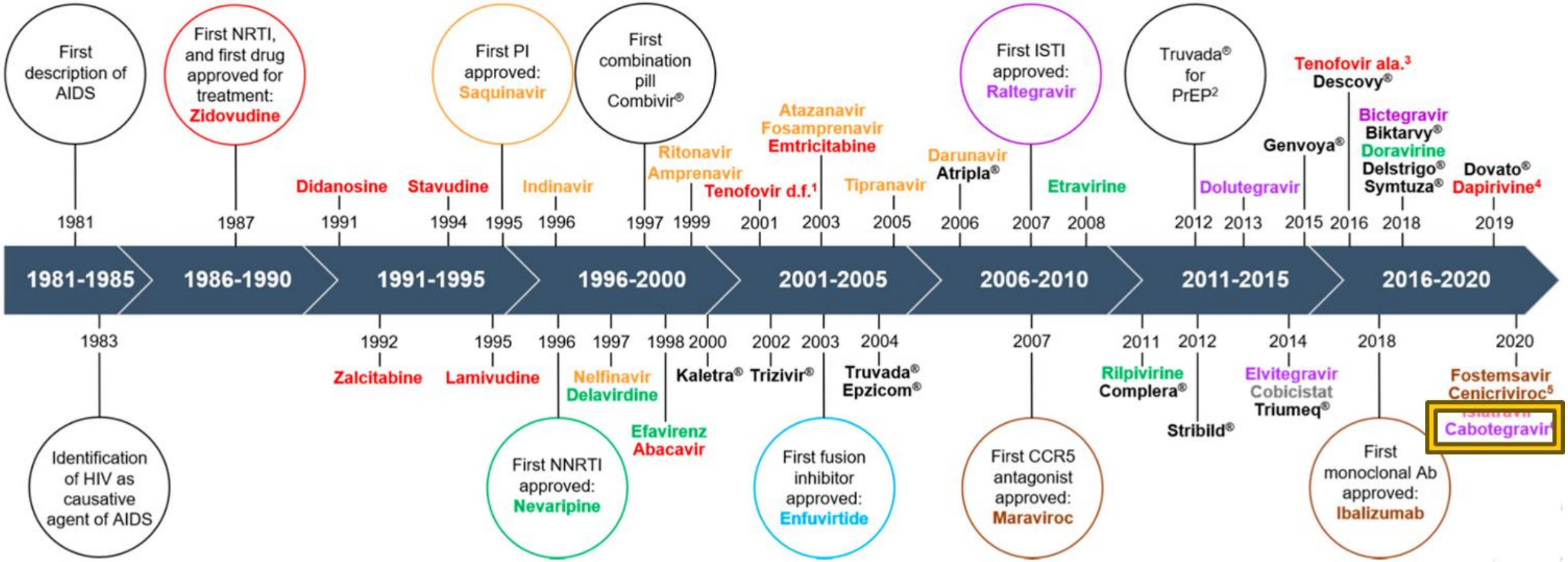


cART and stigma: the role of LA drugs

Camilla Muccini
IRCCS Ospedale San Raffaele Turro, Milan

Timeline of Antiretroviral Drug Development



Cheney L et al. Cells. 2021.

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

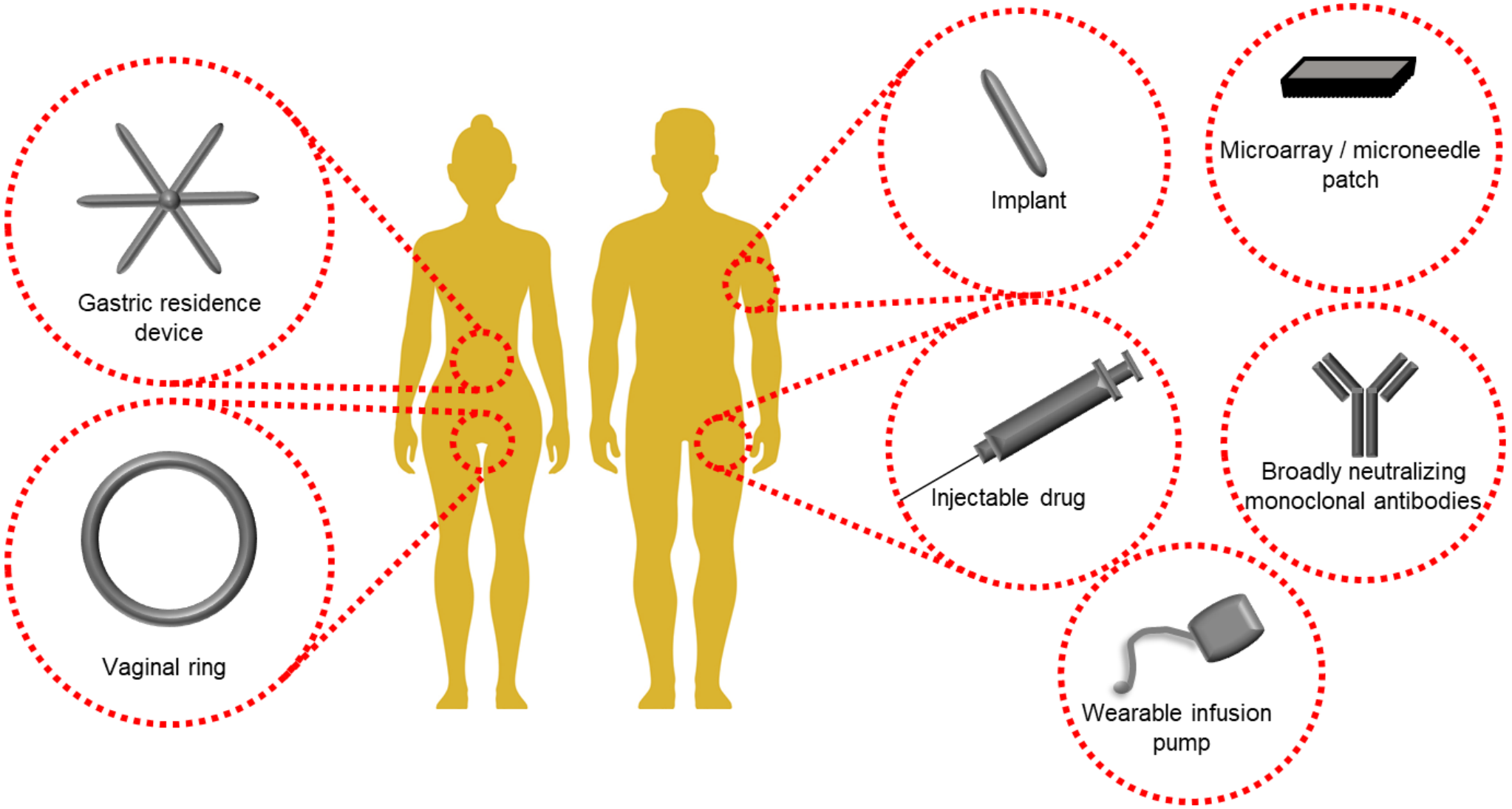
SC every 6 months

Combined with oral ARV

FDA/EMA Approved

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

Drug Delivery Systems and Long-acting Technologies



Adapted from A. Owen

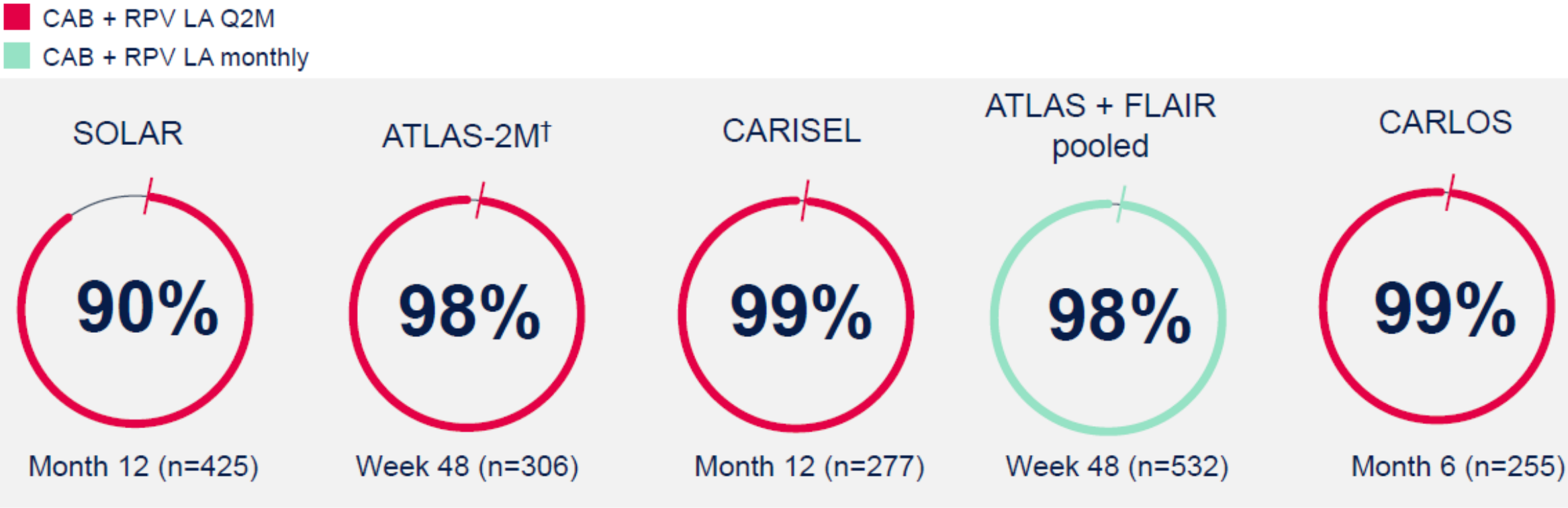
Some Long-acting Drugs in Development for HIV

DRUG	MANUFACTURER	DRUG CLASS	INDICATION	REGIMEN	ADMINISTRATION	DEVELOPMENT PHASE
ISL/DOR	Merck	NRTTI/NNRTI	VS	STR	QD, Oral	Phase III
ISL/LEN	Merck/Gilead	NRTTI/CA	VS	STR	QW, LA Oral	Phase II
LEN/BIC	Gilead	CA/InSTI	VS	STR	QD, Oral	Phase II
VH3810109	ViiV/GSK	bNAb	TBD	TBD	TBD, LA Injectable	Phase II
GS-6212	Gilead	InSTI	TBD	TBD	Q3M, LA Injectable	Phase I
GS-5894	Gilead	NNRTI	TBD	TBD	QW, LA Oral	Phase I
GS-1720	Gilead	InSTI	TBD	TBD	QW, LA Oral	Phase I
VH3739937	ViiV/GSK	MI	TBD	TBD	TBD, LA Injectable	Phase I
VH4524184	ViiV/GSK	InSTI	TBD	TBD	Q3M+, LA Injectable	Phase I

Patients’ Perspectives

Less Psychological Burden

Preference for CAB + RPV LA versus daily oral ART after up to 1 year of treatment*[1–5]



1. Ramgopal MN et al. Lancet HIV. 2023.
2. Overton ET et al. Lancet. 2021.
3. Lutz T et al. HIV Glasgow 2022.
4. Rizzardini G et al. J Acquir Immune Defic Syndr. 2020.
5. Scherzer J et al. IAS. 2023

SOLAR Study

47% (n=315) of participants from the **SOLAR** study "always" or "often" reported at least one of the following psychosocial challenges with daily oral therapy:

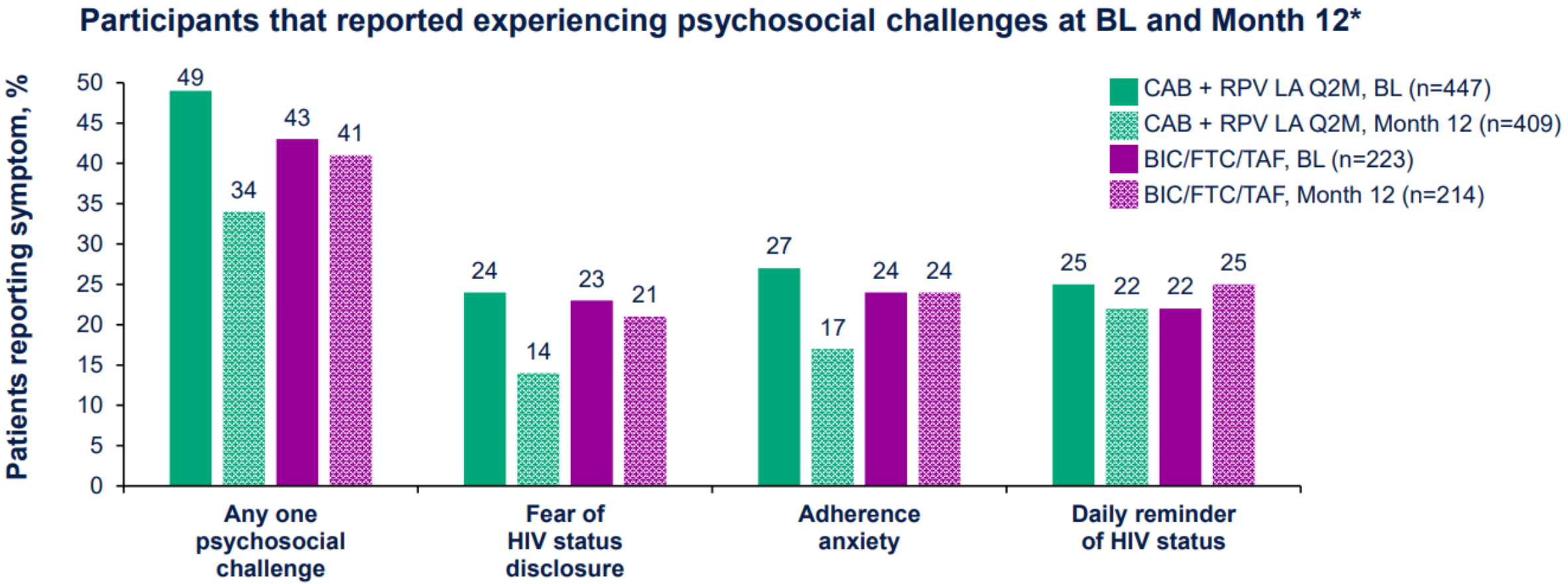
"Worried about people unintentionally discovering their HIV status" → **Fear of disclosure**

"Worried about forgetting to take their HIV medication" → **Adherence anxiety**

"Felt that taking their HIV medication was an uncomfortable reminder of their HIV status" → **Daily reminder of HIV**

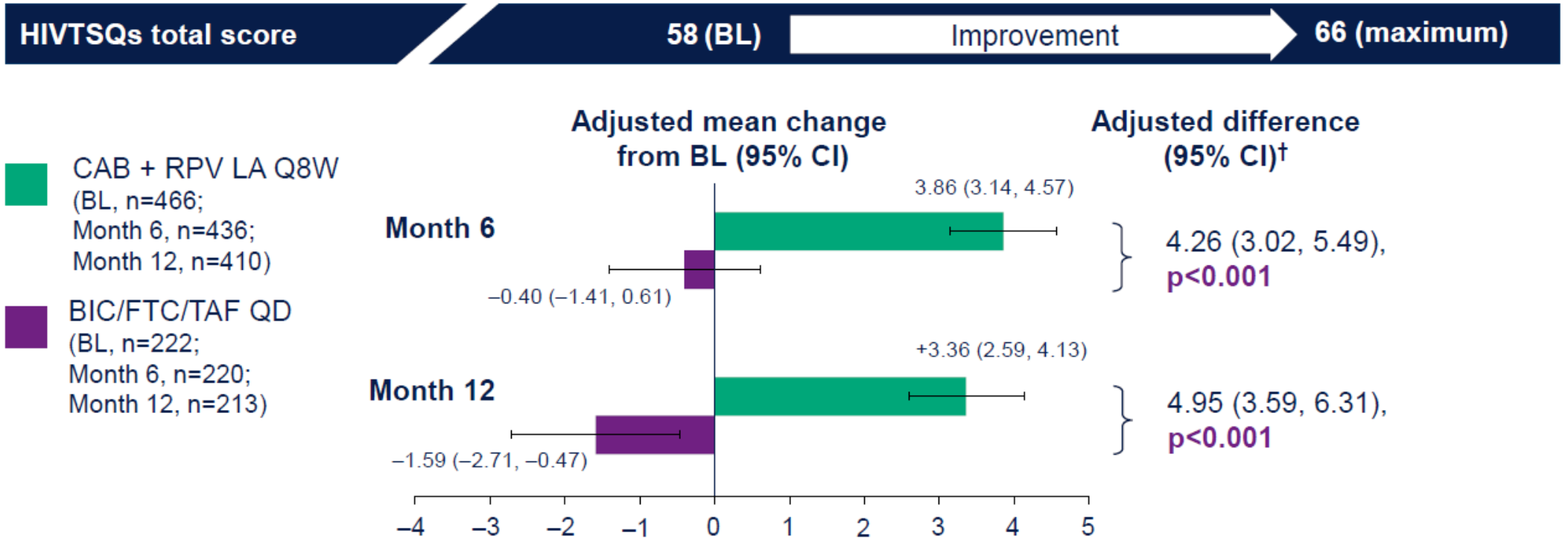
1. Ramgopal MN et al. Lancet HIV. 2023.
2. Scherzer J et al. IAS. 2023

SOLAR Study



Chounta V et al. IAS. 2023.

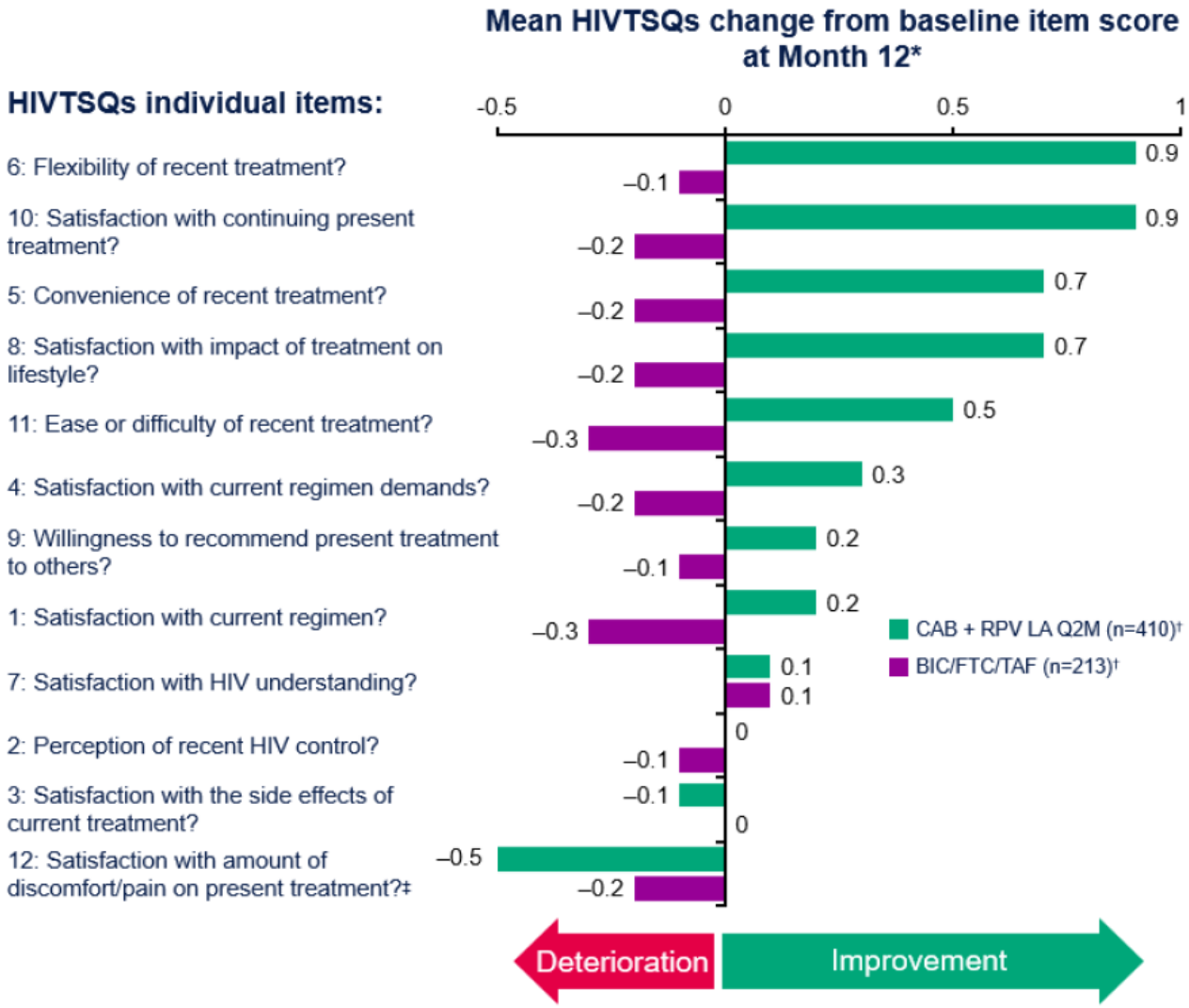
SOLAR Study



Significantly greater **increase in treatment satisfaction** from BL after switching to CAB + RPV LA Q8W compared with continuing current daily oral ART at Months 6 and 12

1. Ramgopal MN et al. Lancet HIV 2023
2. Woodcock A and Bradley C. Value Health 2006

SOLAR Study

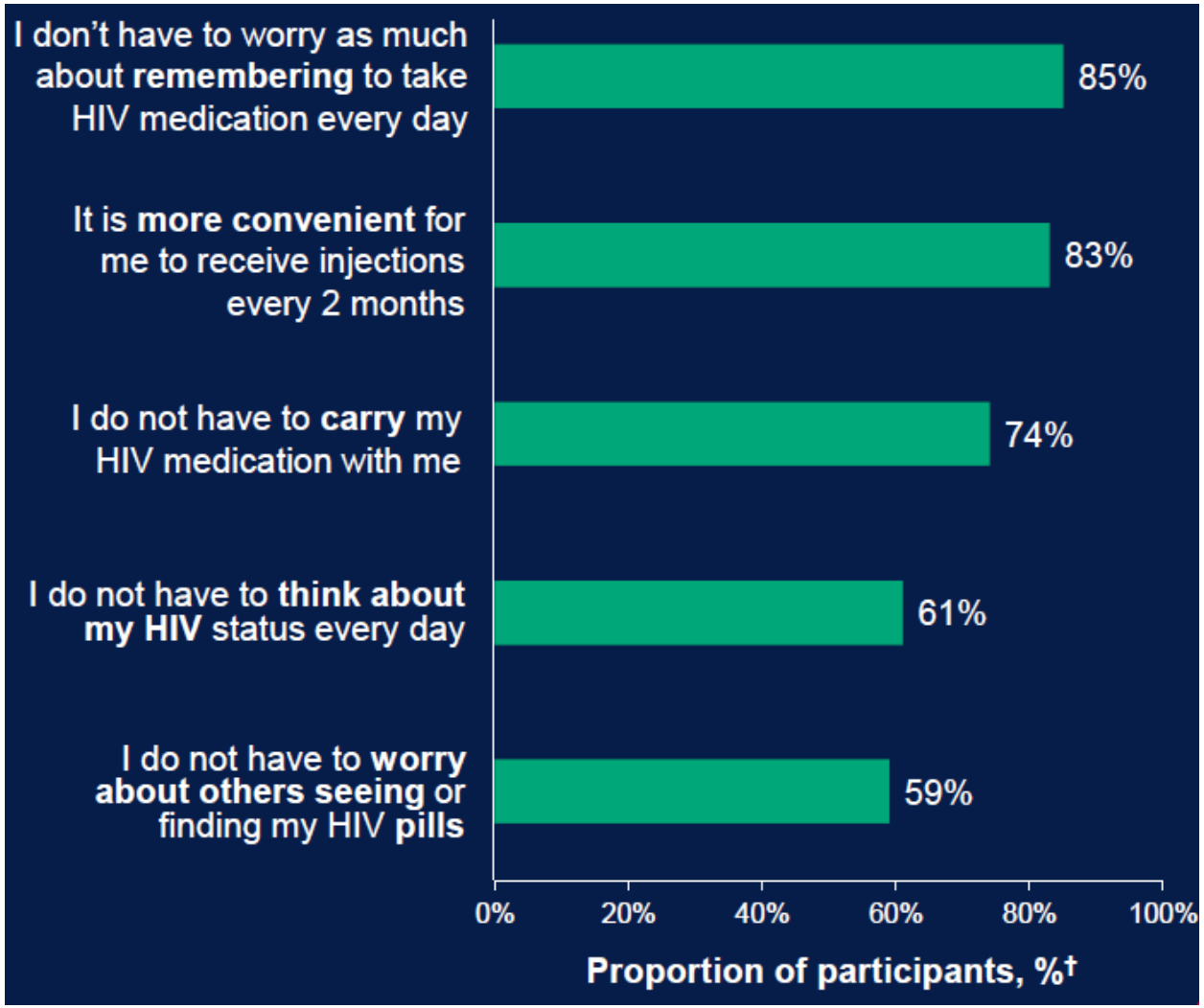


At Month 12, treatment satisfaction had improved from baseline in 9/12 individual items for CAB + RPV LA participants, with the greatest improvements observed for treatment **flexibility, satisfaction, and convenience**

Chounta V et al. IAS. 2023.

SOLAR Study

Why do they prefer long acting therapy to oral therapy?

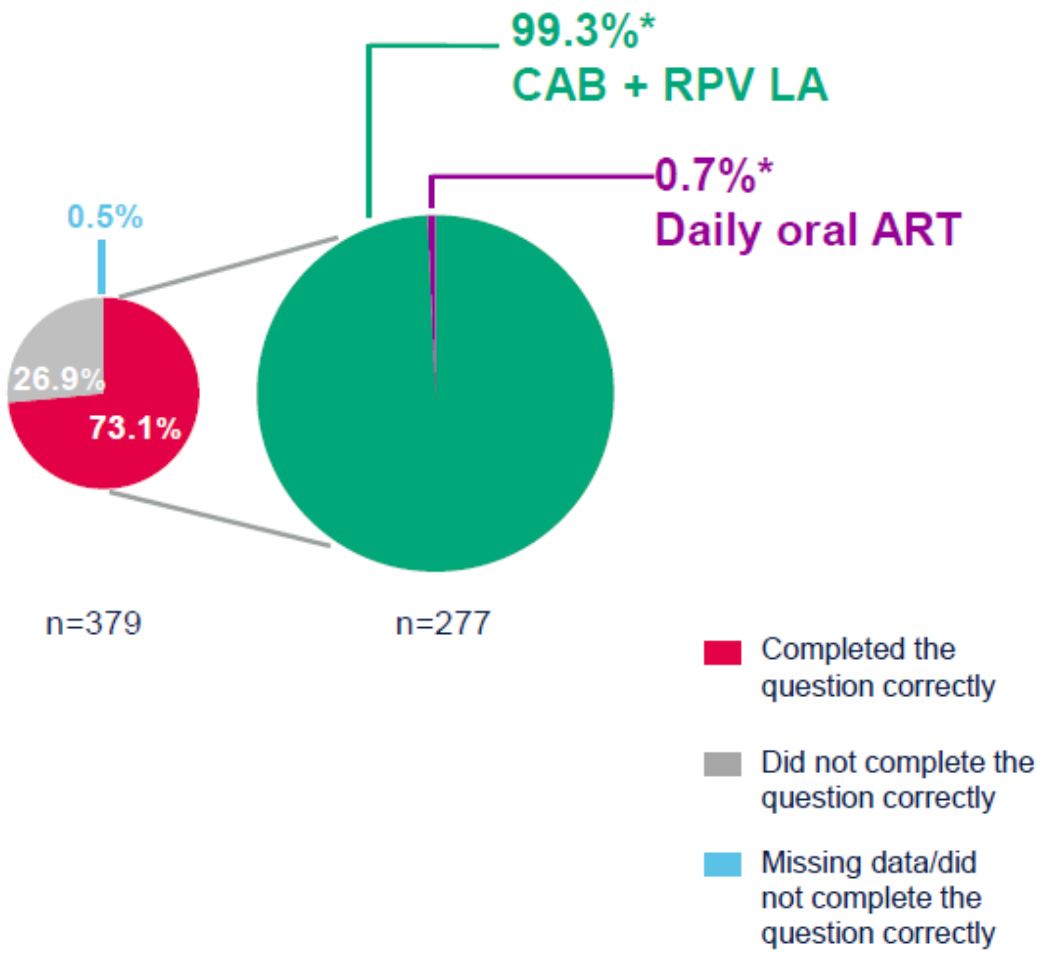


Ramgopal MN et al. Lancet HIV 2023

CARISEL Study

- **Phase III study, single-arm, open-label study** designed to evaluate acceptability, sustainability and satisfaction with implementation of a CAB + RPV LA regimen by PLHIV and their HCPs

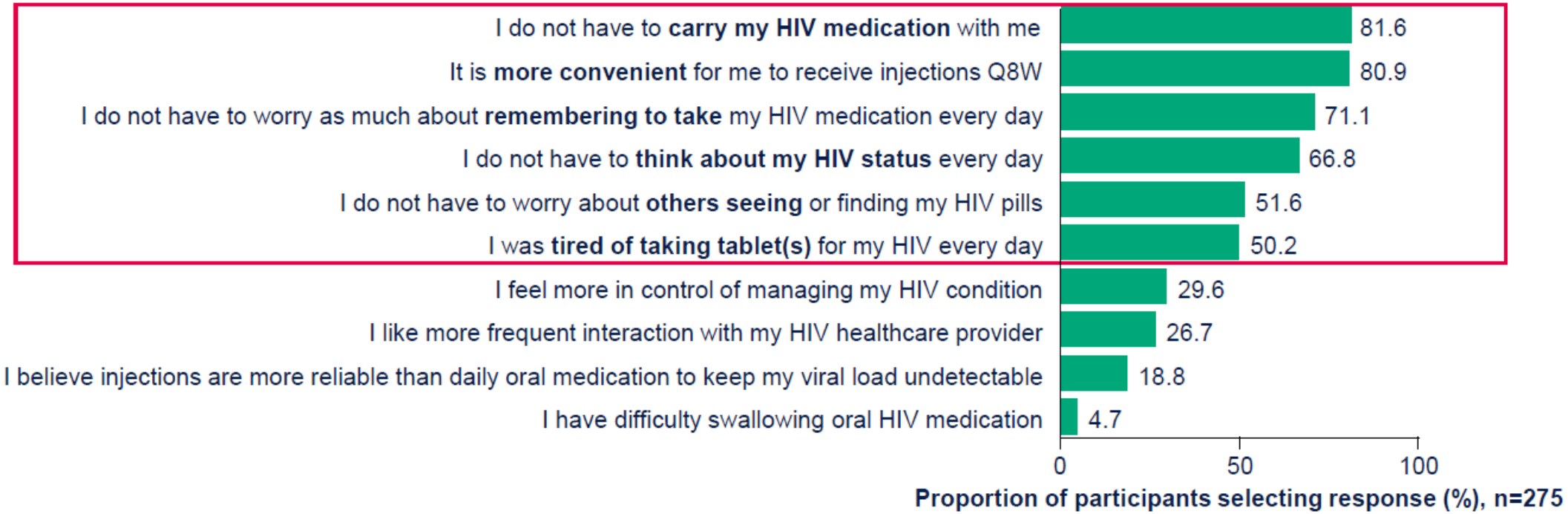
- **430** participants, who had been treated with daily oral ART for at least six months, received CAB + RPV LA treatment



Lutz T, et al. HIV Glasgow 2022

CARISEL Study

Reasons for preference

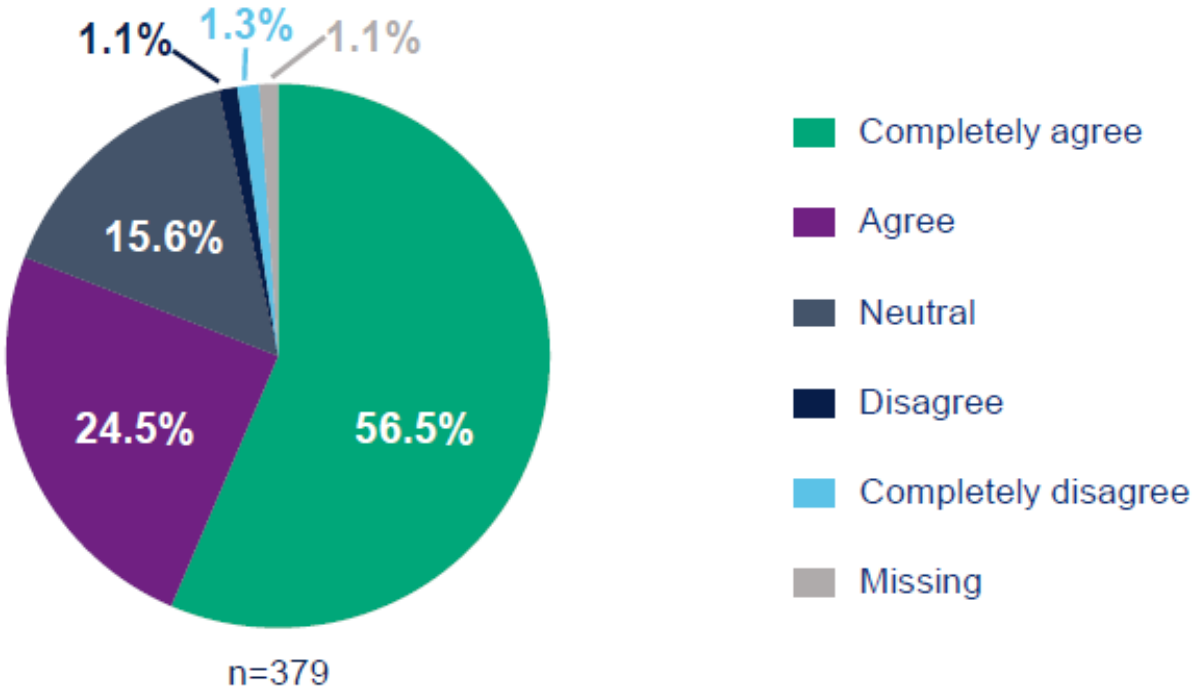


The most frequent reasons for preferring CAB + RPV LA were fewer worries about forgetting medication, less burden of taking daily medication and **fewer worries about stigma**

Lutz T, et al. HIV Glasgow 2022

CARISEL Study

Perception of stigma



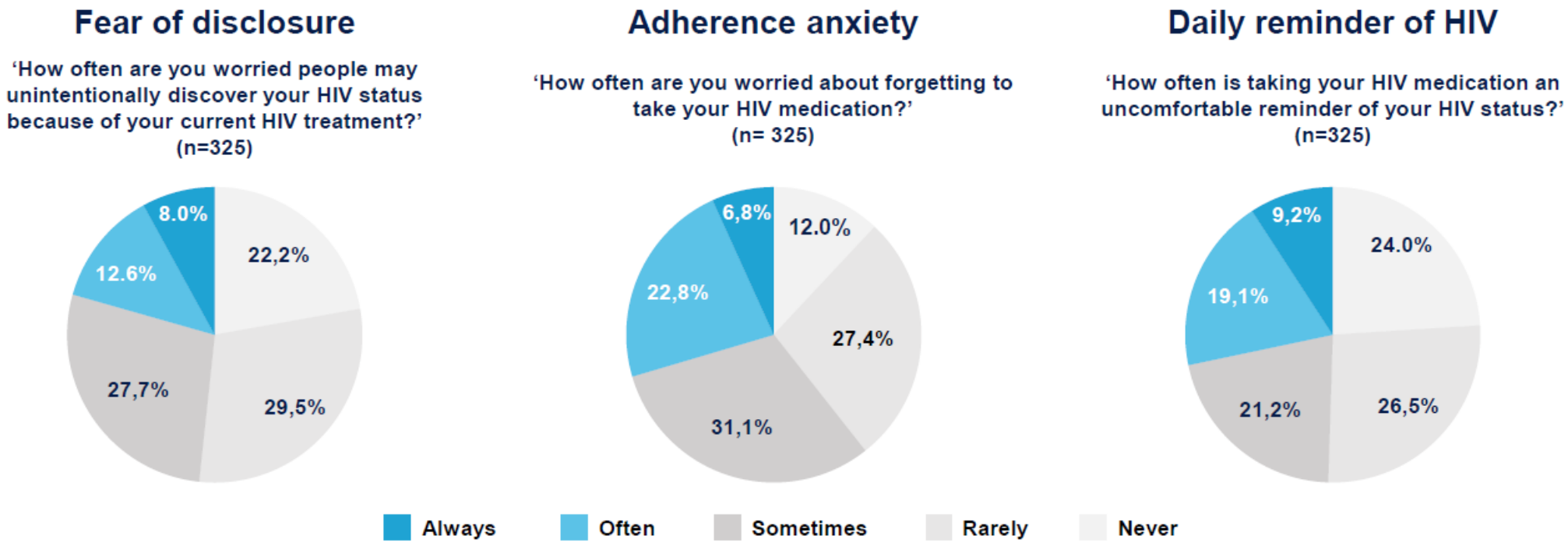
81% of patients agreed or completely agreed that CAB + RPV LA was **less stigmatizing** than oral medication

Lutz T, et al. HIV Glasgow 2022

CARLOS Study

- The prospective CARLOS cohort was initiated to generate real-world evidence describing the effectiveness, adherence and experience of participants on CAB + RPV LA in **routine clinical care in Germany**

- CARLOS is a non-interventional, **3-year multicentre** cohort study including PLHIV who switched from suppressive daily oral ART to CAB + RPV LA dosed Q2M, in accordance with the label

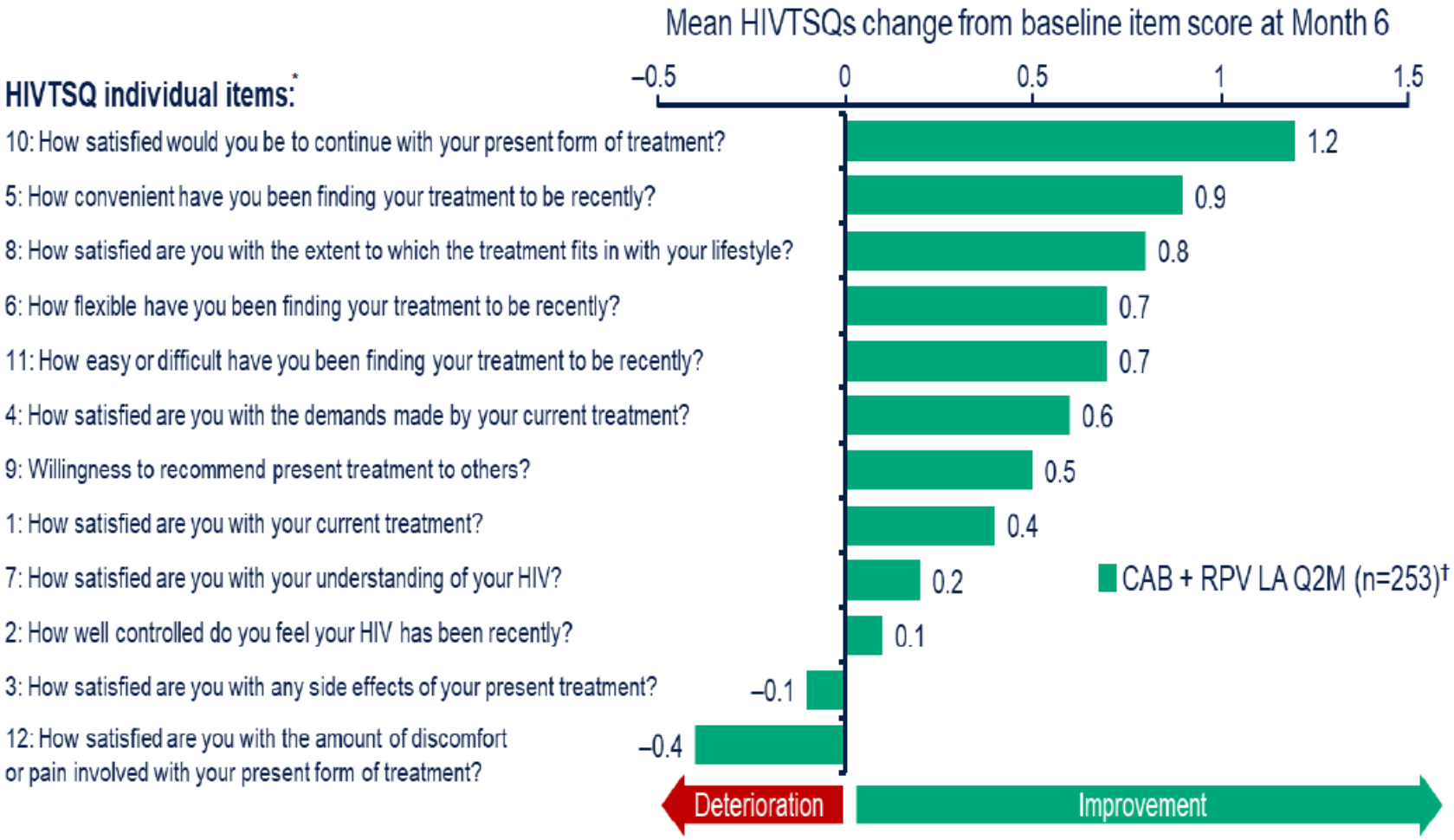


Overall, **49%** of participants reported always/often experiencing **at least one psychosocial challenge with daily oral ART at BL**

Scherzer J, et al. IAS 2023

CARLOS Study

Reasons for preference



Most participants preferred CAB + RPV LA over daily oral ART, primarily for reasons relating to **convenience and fewer concerns about adherence**

Scherzer J, et al. IAS 2023

ILANA Study

- **Multicentre, phase IV study** that evaluated feasibility and acceptability of CAB + RPV LA administration at NHS HIV clinics and community settings in PLHIV receiving the regimen as part of their routine clinical care

- A particular focus on **women, racially minoritised people and older PWH**

- **Semi-structured qualitative interviews** with 14 patients and 13 HCPs

- Most BL interviews took place prior to first injection

- At BL, CAB + RPV LA was highly acceptable to patients and HCPs

ILANA Study

BARRIERS

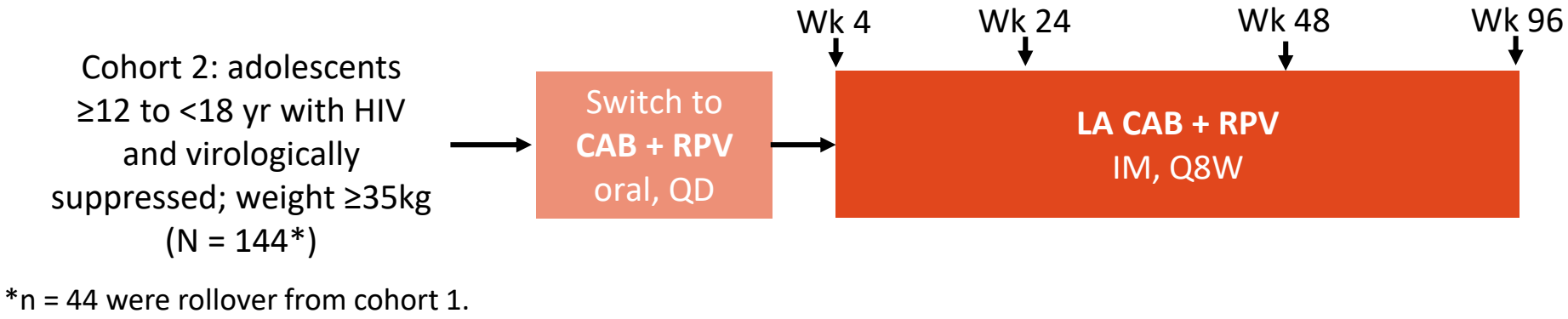
- Potential side effects and pain
- Potential for drug resistance

FACILITATORS

- Relief from pill fatigue and daily reminder of HIV
- Discrete nature of injections
- Convenience of injection schedule
- Benefits outweigh discomfort
- Confidence in effectiveness of CAB + RPV LA

1. Hayes R, et al. Spring BHIVA 2023
2. Hayes R, et al. IAS 2023

IMPAACT 2017/MOCHA Study



*n = 44 were rollover from cohort 1.

- Wk 48 virologic success per FDA snapshot: 97.2%
  - All with Wk 48 assessment (n = 140) had HIV-1 RNA <50 c/mL
- **No cases of CVF** (2 consecutive HIV-1 RNA ≥200 c/mL)
- Median predose CAB and RPV concentrations at Wk 48 approximated those in adults and were above respective protein-adjusted IC_{90}

All 140 participants who responded to Wk 48 Preference Questionnaire **preferred LA injections** to daily oral treatment

Guar et al. AIDS. 2024

Potential for Improved Adherence

- ✓ Ward 86 HIV Clinic in San Francisco serves publicly insured patients with high rates of mental illness, substance use, unstable housing
- ✓ Demonstration project for long-acting CAB/RPV
- ✓ Inclusion criteria:

-No RPV or INSTI mutations

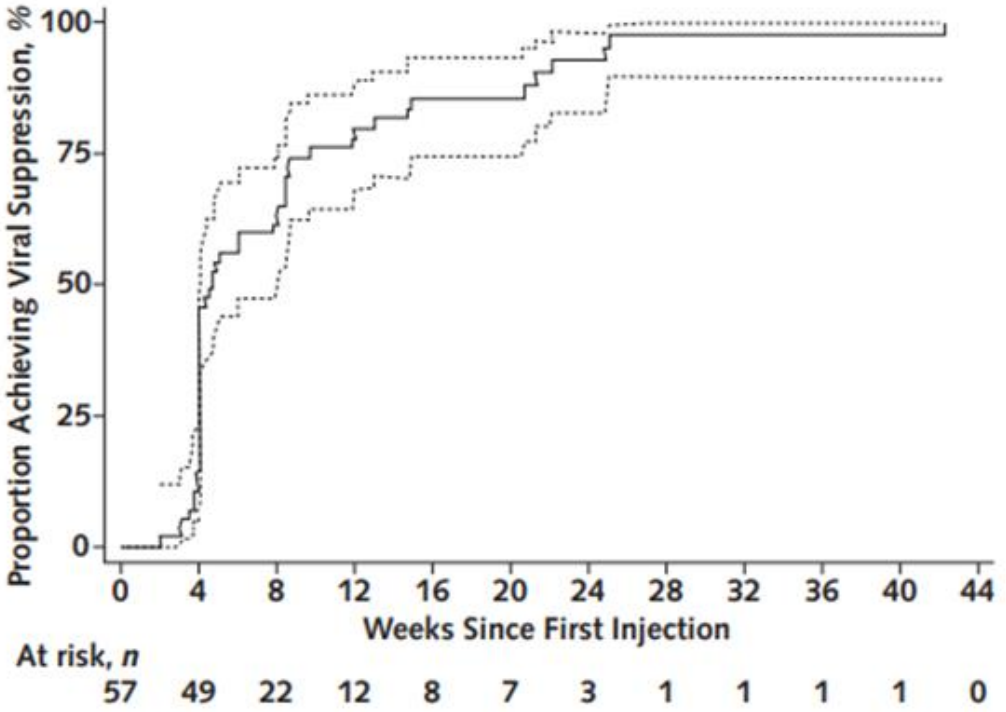
-Express willingness to come to clinic q4 weeks

Characteristic	Patients With Viremia (*n* = 57)	Patients With Virologic Suppression (*n* = 76)	Overall Sample (*n* = 133)
Median age (range), *y*	48.0 (25.0-68.0)	44.5 (29.0-68.0)	46.0 (25.0-68.0)
Gender, *n (%)*			
Cisgender man	51 (89.5)	66 (86.8)	117 (88.0)
Cisgender woman	5 (8.8)	6 (7.9)	11 (8.3)
Transgender woman	1 (1.8)	4 (5.3)	5 (3.8)
Race/ethnicity, *n (%)*			
Black	13 (22.8)	8 (10.5)	21 (15.8)
Latino/Latina	18 (31.6)	25 (32.9)	43 (32.3)
White	23 (40.4)	27 (35.5)	50 (37.6)
Multiracial/other	3 (5.3)	16 (21.1)	19 (14.3)
Housing status, *n (%)*†			
Experiencing homelessness	6 (10.5)	3 (4.0)	9 (6.8)
Unstable	24 (42.1)	23 (30.3)	47 (35.3)
Stable	27 (47.4)	50 (65.8)	77 (57.9)
Insurance, *n (%)*			
Medicare, Medicaid, or both	55 (96.5)	73 (96.1)	128 (96.2)
ADAP	2 (3.5)	3 (4.0)	5 (3.9)
Current stimulant use, *n (%)*†	28 (49.1)	17 (22.4)	45 (33.8)
Mean $\log_{10}$ viral load (SD)	4.21 (1.30)	NA	NA
Median CD4 cell count (IQR), × 10^9 *cells/L*‡	0.215 (0.075-0.402)	0.615 (0.395-0.818)	0.422 (0.219-0.749)

Gandhi M et al. Annals of Internal Medicine. 2023.

Potential for Improved Adherence

- ✓ 97.5% virological suppression rate median 26 weeks
- ✓ 74% on-time injections
- ✓ In those with suppression, 100% remained undetectable
- ✓ Among viremic PWH, all suppressed but 2 with early virological failure
- ✓ Current cohort virological failure rate 1.5% similar to that across clinical trials (1.4%) by 48 weeks

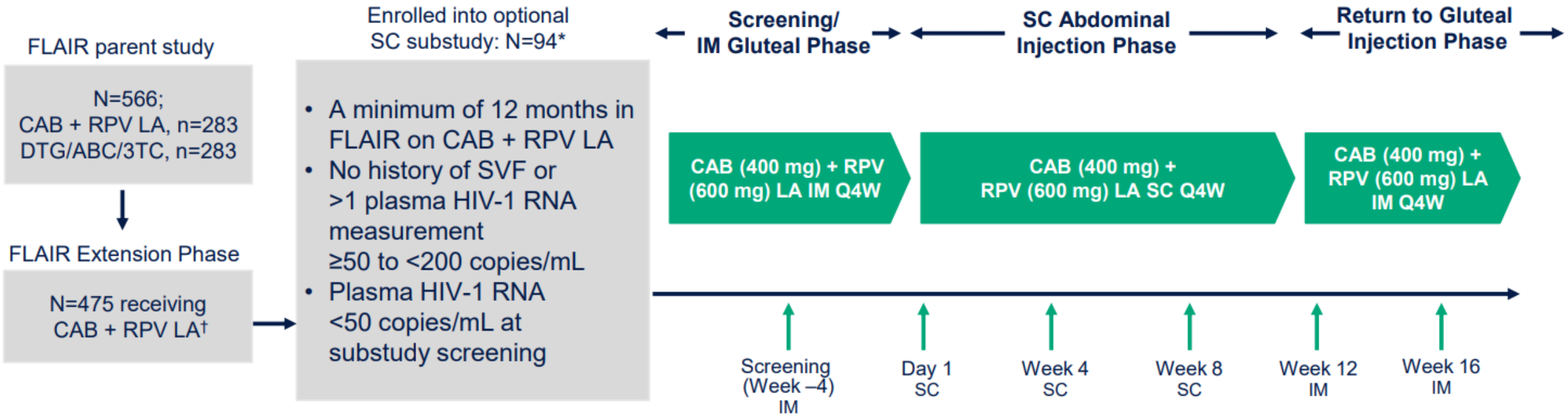


The dashed lines indicate the 95% CI.

Gandhi M et al. Annals of Internal Medicine. 2023.

Subcutaneous Administration

FLAIR SC Substudy Design



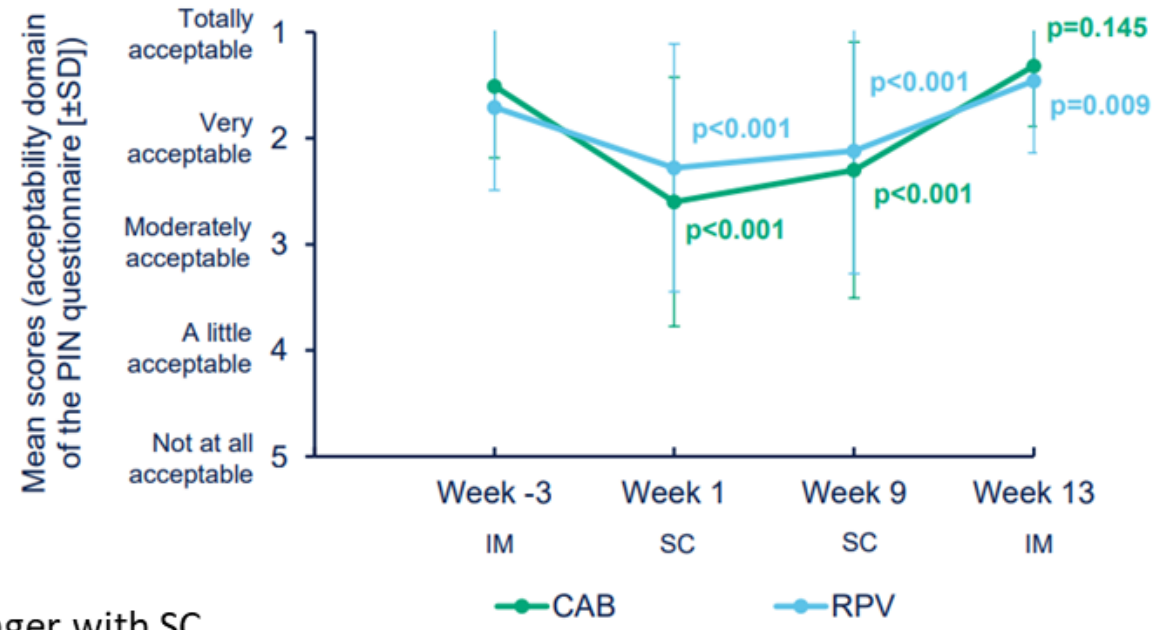
D'Amico R et al. AIDS. 2024.

Subcutaneous Administration

Injection Site Reactions

Parameter	CAB + RPV LA (n=93)
Number of injections, n	542
ISR events, n*	816
Pain, n (% of injections)	260 (48)
Nodule, n (% of injections)	183 (34)
Erythema, n (% of injections)	142 (26)
Induration, n (% of injections)	66 (12)
Swelling, n (% of injections)	66 (12)
Grade 3, n (% of ISR events)†	17 (2)
Median duration, days (IQR)	10 (4, 29)
Participant withdrawal due to injection-related reasons, n (% of participants with injections)‡	5 (5)

Acceptability of ISRs

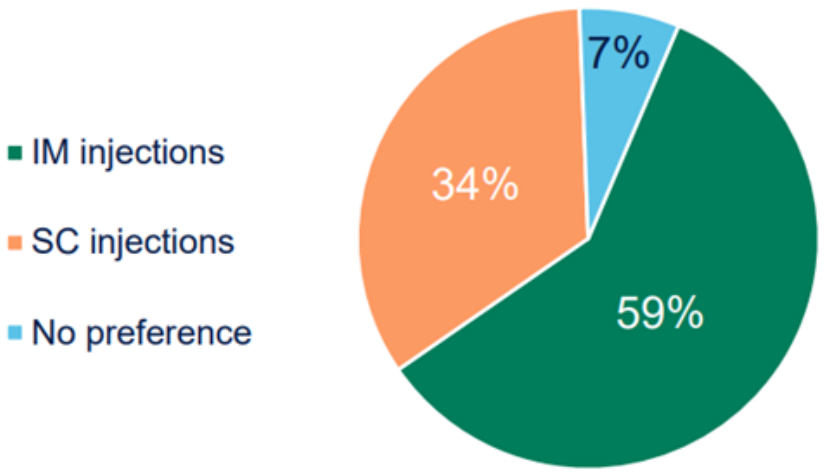


✓ The median duration of nodule, induration, and erythema ISRs was longer with SC injections vs. IM injections (39 vs. 9 days, 33 vs. 26 days, and 11 vs. 4 days, respectively)

D'Amico R et al. AIDS. 2024.

Subcutaneous Administration

"Which injection site do you prefer"
(1 week following 3rd SC injection)
(n=85)



Common reasons given for preference

IM injections:
- Less injection site swelling (58%, n=29/50), nodules (58%, n=29/50), and pain (54%, n=27/50)

SC injections:
- Convenience (86%, n=25/29) and injections not interfering with daily activities (59%, n=17/29)

✓ SC injections led to a higher incidence and longer duration of ISRs, resulting in lower acceptability of, and satisfaction with, SC injections compared with IM injections

✓ **Further development of this treatment regimen for SC self-administration will not be pursued**

D'Amico R et al. AIDS. 2024.

Take-home Messages

- ✓ Long-acting drugs for HIV treatment may reduce the psychological burden of HIV
- ✓ Long-acting therapy may be considered a valid strategy for those with adherence issues
- ✓ One of the reasons why long-acting therapy is preferred to oral therapy is because it is less stigmatising

Thanks for your attention!

Department of Infectious Diseases, IRCCS San Raffele Scientific Institute