HIV - terapia

Il paziente soppresso, associazioni attuali e prospettive di terapia

Sergio Lo Caputo

Malattie Infettive

Università di Foggia

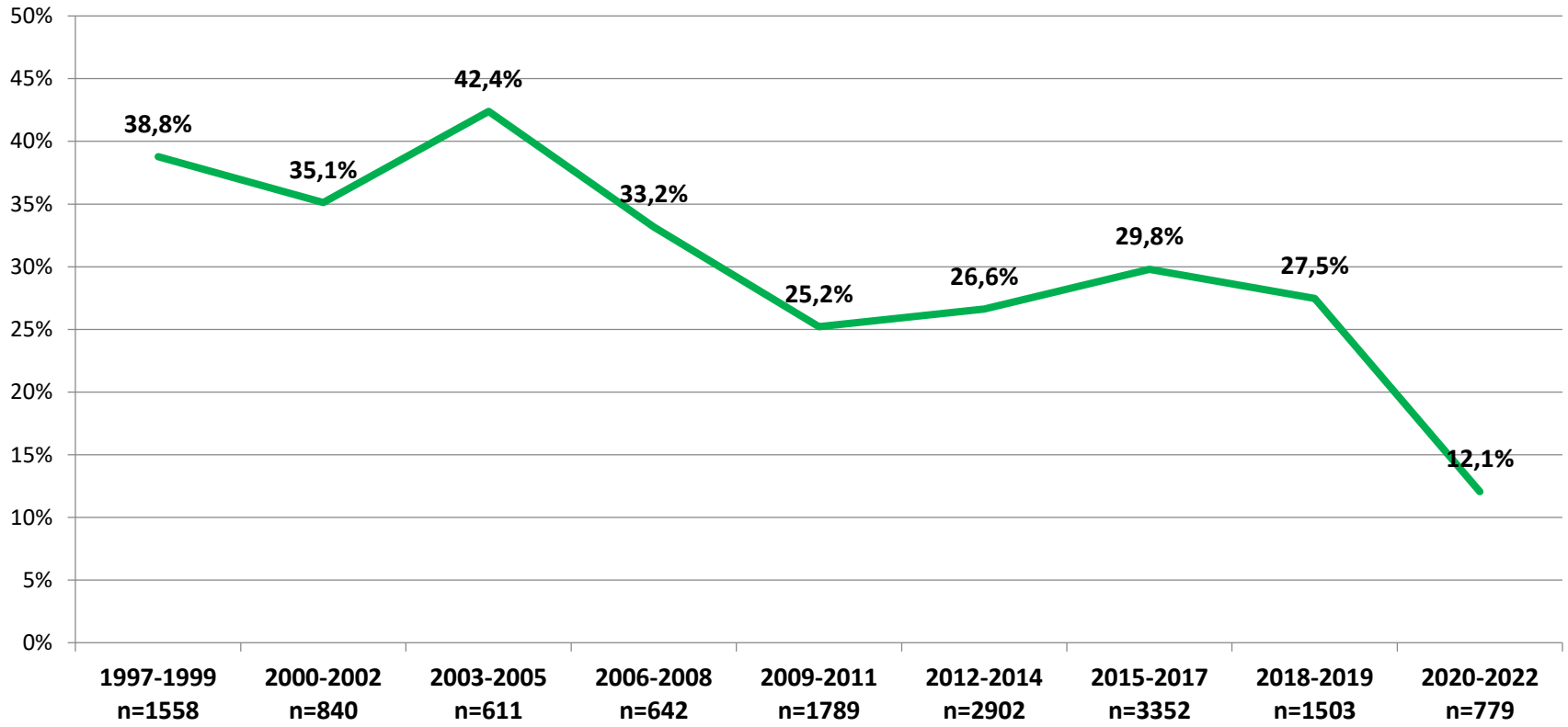
- Has been advisor for Gilead,ViiV, Janssen-Cilag, GSK, Astra Zeneca and MSD
- Had received speakers' honoraria from Gilead, ViiV, Astra Zeneca, MSD and Janssen-Cilag
- Had received support for travel meetings from Gilead, Janssen-Cilag, and ViiV
- Had received grant for research from Gilead

With actually regimens few switches are really needed

Fondazione Icona
ITALIAN COHORT NAIVE ANTIRETROVIRALS

Italian Cohort I. C. O. N. A. Naive Antiretrovirals

Proportion of patients stopping at least one drug of their first ART regimen within 1 year, according to calendar period of starting



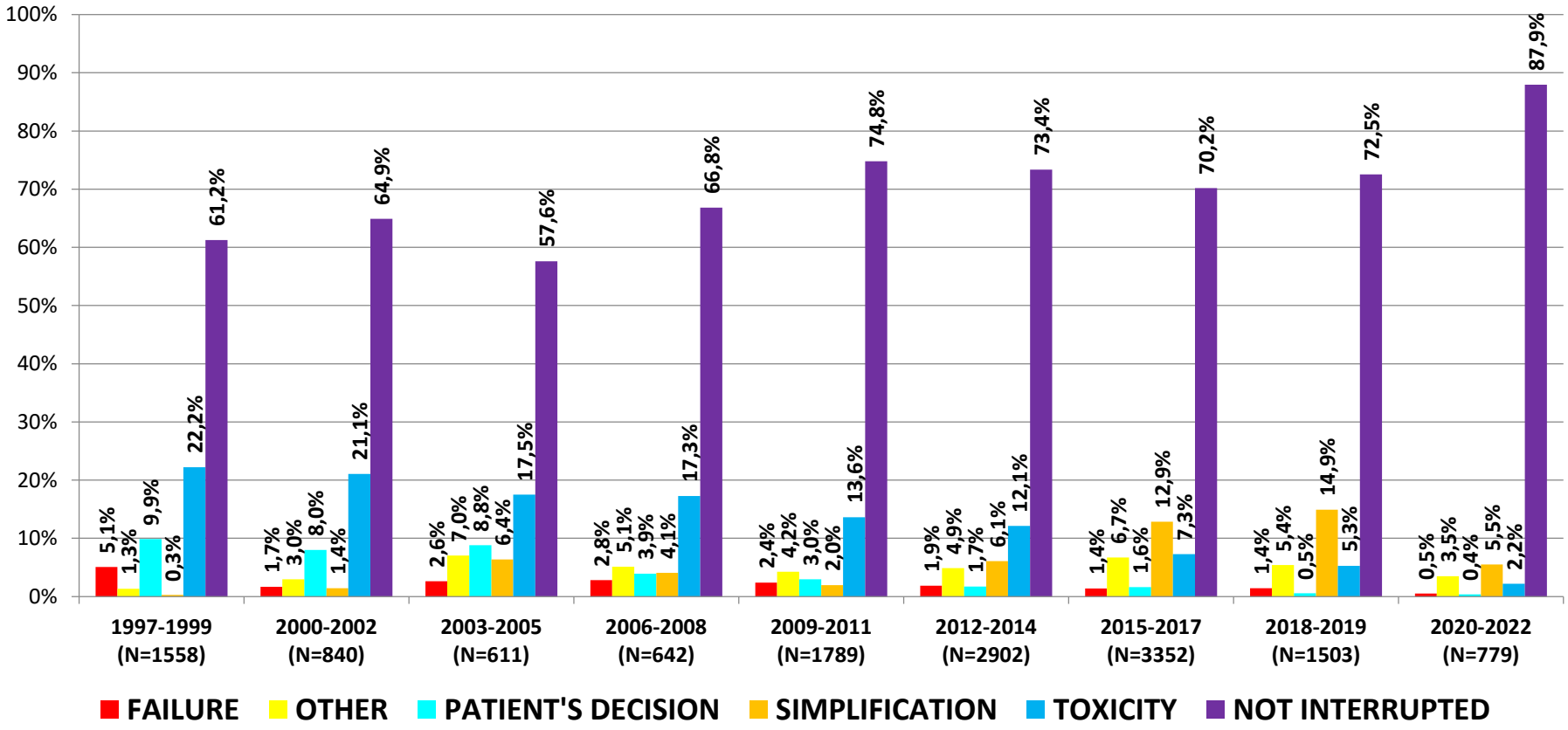
Jan 2023 Report

Fondazione Icona
ITALIAN COHORT NAIVE ANTIRETROVIRALS

Italian Cohort Naive Antiretrovirals

Reasons for stopping at least one drug of first ART regimen within 1 year, according to calendar period of starting

N = therapy startings per period



Jan 2023 Report

Definition of virologically suppressed

Clinical trials exploring switching strategies have generally defined suppression as an HIV-VL < 50 copies/mL for at least 6 months

Indications

1. **Documented toxicity** caused by one or more of the antiretrovirals included in the regimen, see Adverse Effects of ARVs and Drug Classes
2. **Prevention of long-term toxicity**, see Adverse Effects of ARVs and Drug Classes. This may include person's concerns about safety
3. **Avoidance of drug-drug interactions**, page 26. This includes ART switch when starting HCV treatment to avoid DDIs, see Drug-drug Interactions between Viral Hepatitis Drugs and ARVs
4. **Planned pregnancy or women wishing to conceive**, see Treatment of Pregnant Women Living with HIV or Women Considering Pregnancy
5. **Ageing and/or comorbidity** with a possible negative impact of drug(s) in current regimen, e.g. on CVD risk, metabolic parameters
6. **Simplification**: to reduce pill burden, adjust food restrictions, improve adherence and reduce monitoring needs
7. **Protection from HBV** infection or reactivation by including tenofovir in the regimen
8. **Regimen fortification**: Increasing the barrier to resistance of a regimen in order to prevent VF (e.g. in persons with reduced adherence)
9. **Cost reduction:** switching to the generic form of their current regimen, if available

Clinicians should always review possible adverse events or tolerability issues with current antiretroviral regimens. Just because the viremia is suppressed it should not be assumed that the person is well adapted and tolerating the current regimen

Dual therapies

In persons with suppression of HIV-VL < 50 copies/mL for the past 6 months these dual therapy strategies should only be given if there is

a) no historical resistance and
b) HBV immunity with anti-HBs antibodies (if non-immune provide HBV Vaccination, if isolated HBc antibodies see the section on Treatment and Monitoring of Persons with HBV/HIV Co-infection for details)

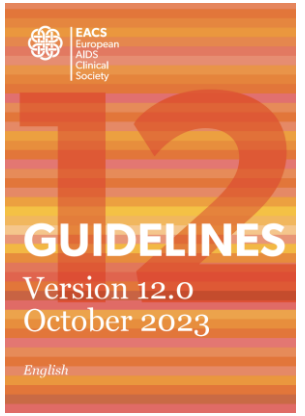
Oral dual therapies supported by large randomized clinical trials or meta-analyses:

DTG + RPV
XTC + DTG
XTC + DRV/b

In clinical trials, these strategies have not been associated with more virological rebounds than triple therapy. There were a few cases of resistance development on DTG + RPV and CAB + RPV

Long-acting intramuscular dual therapy CAB + RPV

- The use of oral lead-in (1 month) is optional
- Injections are administered every 2 months. In case of bridging, see the section on Drug-Drug Interactions after Oral and Intramuscular Administration of CAB and RPV



Strategies not recommended

a. Monotherapy
b. Dual or triple NRTIs combinations
c. Specific two-drug combination, i.e.1 NRTI + 1 NNRTI or 1 NRTI + 1 unboosted PI, 1 NRTI + RAL, MVC + RAL, PI/b + MVC, ATV/b + RAL
d. Intermittent therapy, sequential or prolonged treatment interruptions. In one open-label randomized study, 4 consecutive days a week of triple therapy was non inferior to 7 days a week, at 48 weeks in the context of close monitoring and counseling with visits every 3 months

Reasons to Consider Optimization in the setting of viral suppression

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV

Developed by the DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents – A Working Group of the Office of AIDS Research Advisory Council (OARAC)

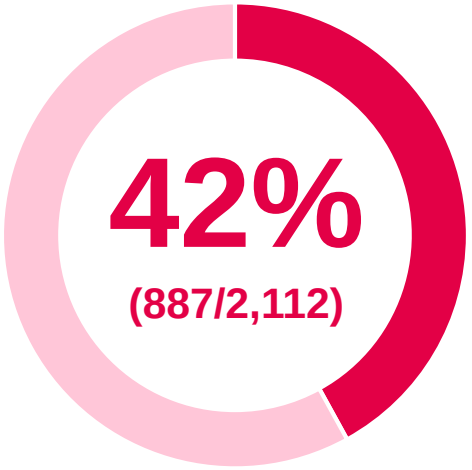
- To simplify a regimen by reducing pill burden and/or dosing frequency
- To enhance tolerability and/or decrease short- or long-term toxicity
- To prevent or mitigate drug-drug interactions
- To eliminate food or fluid requirements
- To switch to a long-acting injectable (LAI) regimen to relieve pill fatigue or to decrease potential stigma or disclosure concerns associated with taking daily oral medications
- To allow optimal use of ART during pregnancy or when pregnancy is desired or may occur
- To reduce costs

Key Considerations and Panel's Recommendations
• Advances in antiretroviral (ARV) treatment and a better understanding of HIV drug resistance have made it possible to consider switching a person with HIV from an effective regimen to an alternative regimen in some situations.
• The fundamental principle of regimen optimization is to maintain viral suppression without jeopardizing future treatment options.
• Adverse events, drug-drug or drug-food interactions, pill burden, pregnancy, cost, or the desire to simplify a regimen may prompt a regimen switch.
• It is critical to review a patient's full ARV history, including virologic responses, past ARV-associated toxicities and intolerances, and cumulative resistance test results before selecting a new ARV regimen **(AI)**.
• A long-acting ARV regimen, such as the combination of injectable cabotegravir and rilpivirine, is an optimization option for patients who are engaged with their health care, virologically suppressed on oral therapy for 3 to 6 months, and who agree to make the frequent clinic visits needed to receive the injectable drugs **(AI)**.
• Monotherapy with either a boosted protease inhibitor or an integrase strand transfer inhibitor has been associated with unacceptable rates of virologic failure and the development of resistance; therefore, monotherapy as a switch strategy **is not recommended (AI)**.
• When switching an ARV regimen in a person with hepatitis B virus (HBV)/HIV coinfection, ARV drugs that are active against HBV should be continued **(AII)**. Using lamivudine or emtricitabine as the only drug in a regimen with HBV activity **is not recommended (AII)**, because HBV resistance to these drugs can emerge. Discontinuation of HBV drugs may lead to reactivation of HBV, which may result in serious hepatocellular damage.
• Consultation with an HIV specialist is recommended when planning a regimen switch for a patient with a history of resistance to one or more drug classes **(AIII)**.
• Close monitoring to assess tolerability, viral suppression, adherence, and safety is recommended during the first 3 months after a regimen switch **(AIII)**.

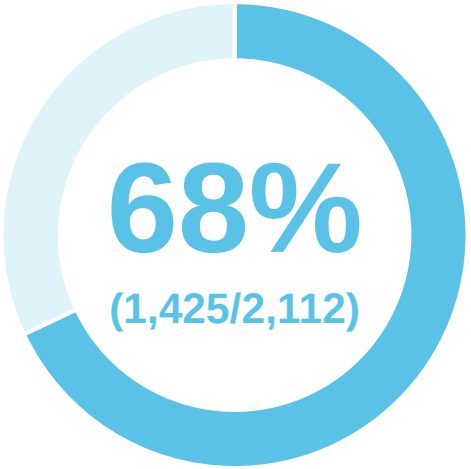
DHHS Guidelines. Dec 2022

PLHIV are Living Longer, and Long Lives Should be Healthy Lives

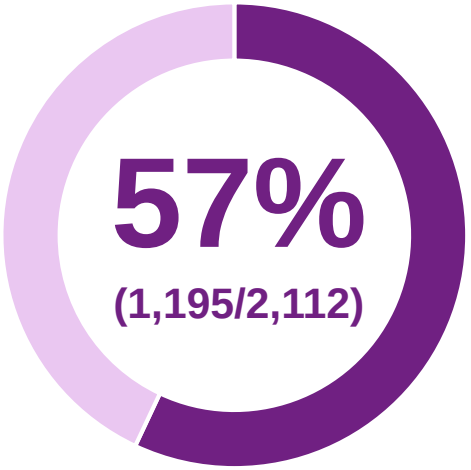
With effective ART, PLHIV are living longer, and are therefore exposed to more daily doses of ART over a lifetime of treatment.[1,2] PLHIV are concerned about long-term side effects and taking more medicines as they get older[2]



Overall prevalence of **polypharmacy** amongst PLHIV in the Positive Perspectives Study[2]



PLHIV were worried about the **long-term effects** of HIV medicines[2]



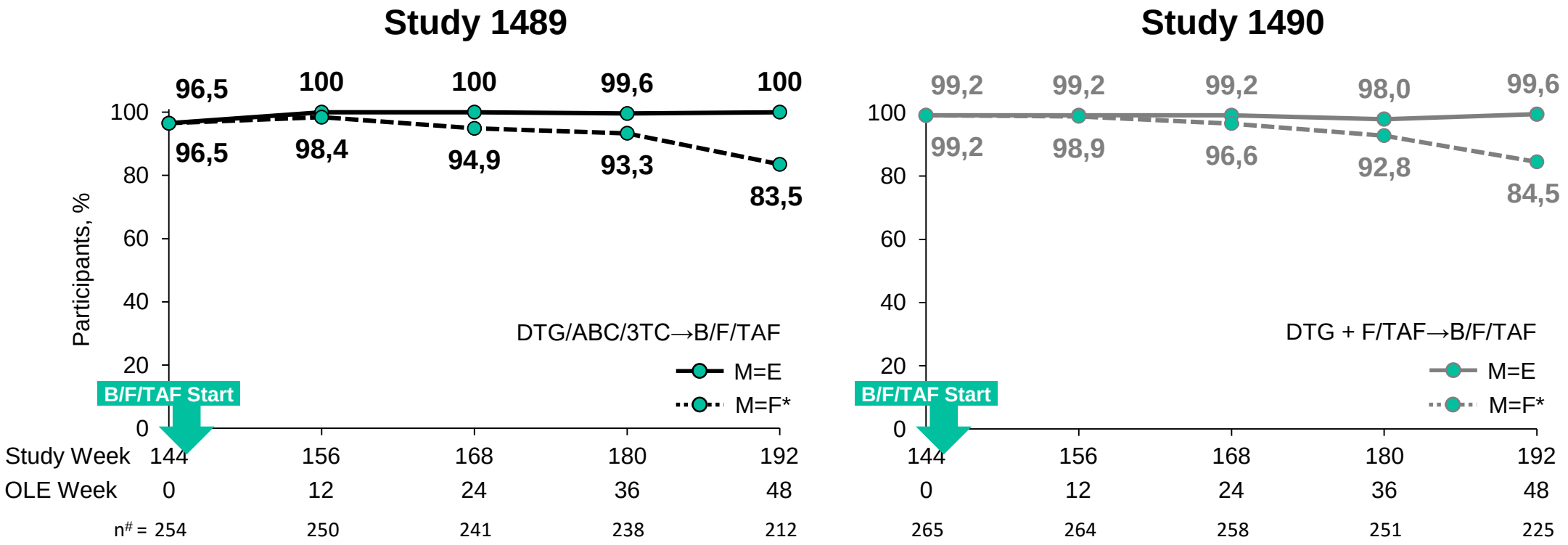
PLHIV were concerned about taking **more medicines** as they **get older[2]**

ART, antiretroviral therapy

1. WHO HIV/AIDS Fact Sheet. November 2022. Available at: https://www.who.int/news-room/fact-sheets/detail/hiv-aids. Accessed January 2023
2. Okoli C, et al. Prev Chronic Dis. 2020


3 Drugs
2 Drugs
Long Acting

Virologic Outcomes: OLE W144-W192 (HIV-1 RNA <50 c/mL)



High rates of virologic suppression were maintained after switching to B/F/TAF through W192 (OLE W48)

*There were no discontinuations due to lack of efficacy
#Participants with non missing HIV-1 RNA at each visit
M=E, missing=excluded; M=F, missing=failure.

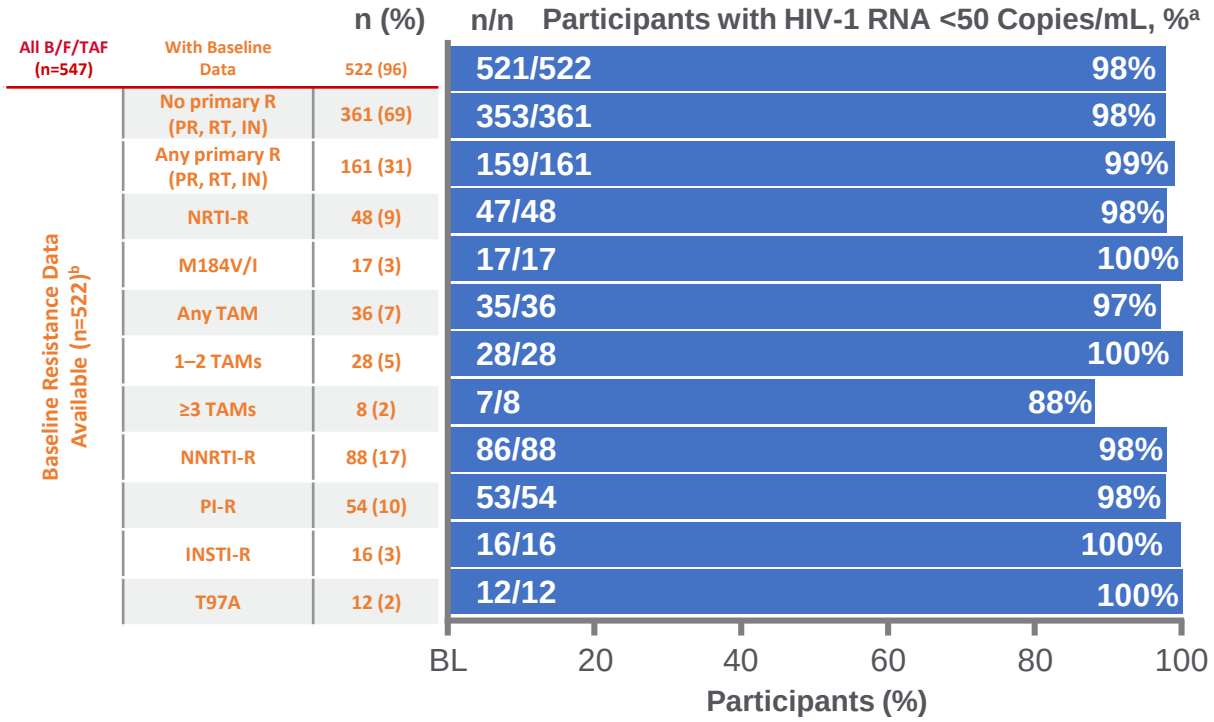
Pozniak A, et al. EACS 2021, PE2/68

‡

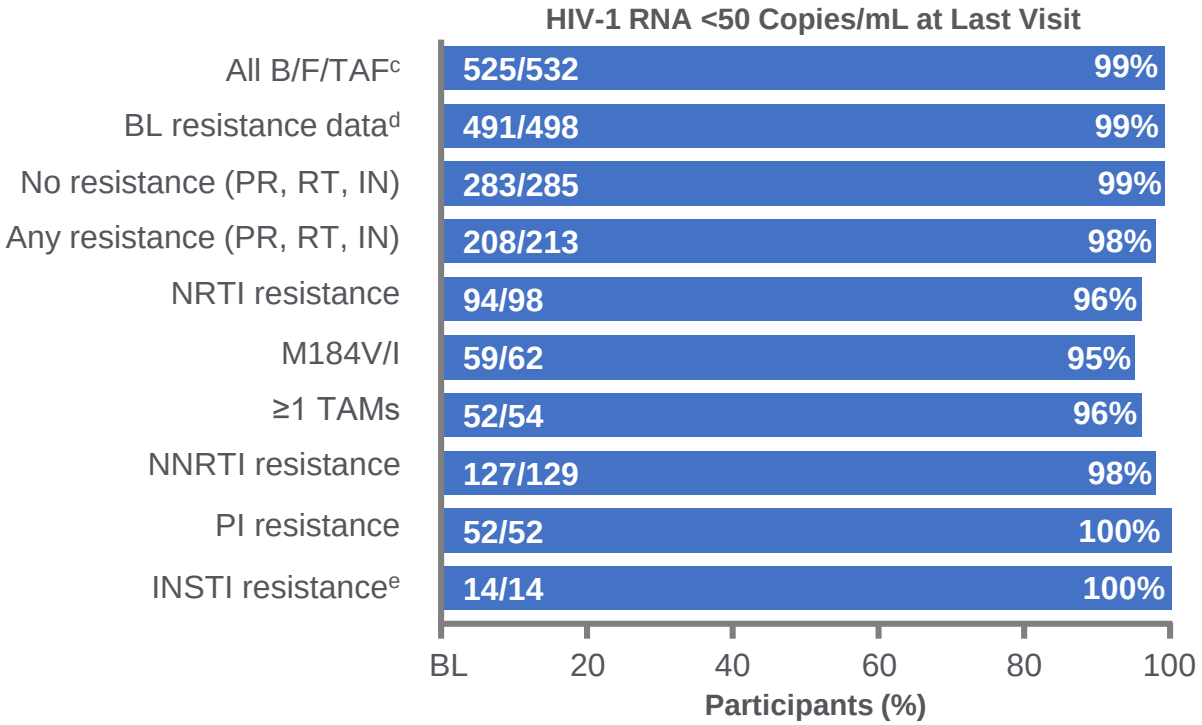
B/F/TAF Has Shown Efficacy in Patients with Baseline Resistance

In the long-term follow-up of studies 1844 and 1878 in TE PLWH switching to B/F/TAF, sustained efficacy in the presence of BL resistance and no treatment-emergent resistance has been demonstrated[1,2]

Study 1844[1,a] (follow-up through to Week 168)



Study 1878[2] (follow-up through to Week 96)



Footnotes located in speaker notes

BL: baseline; TAM: thymidine analogue mutation; TE: treatment-experienced.

1. Brar I, *et al*. IDWeek 2020 (Abstract 1028; poster presentation); 2. Rockstroh J, *et al*. Glasgow HIV 2020 (abstract P036; poster presentation).

EFFECTIVNESS OF BICTEGRAVIR/EMTRICITABINE/TENOFOVIR ALAFENAMIDE (BIC/FTC/TAF) AS SWITCH STRATEGY IN VIROLOGICALLY SUPPRESSED: REAL-WORLD DATA FROM THE ICONA COHORT

P098

A. d'Arminio Monforte[1], A. Tavelli[2], A. Cingolani[3], L. Taramasso[4], C. Mussini[5], S. Piconi[6], A. Calcagno[7], G. Orofino[8], S. Cicalini[9], A. Castagna[10], F. Ceccherini-Silberstein[11], A. Gori[12], G. Guaraldi[5], A. Antinori[9]

1 1ASST Santi Paolo e Carlo, University of Milan, Department of Health Sciences, Clinic of Infectious Diseases, Milan, Italy ; 2 Icona Foundation, Milano, Italy; 3Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Catholic University of the Sacred Heart, Department of Safety and Bioethics, Infectious Diseases Unit, Rome, Italy; 4 Ospedale Policlinico San Martino IRCCS, University of Genoa, Unit of Infectious Diseases, Genoa, Italy; 5Azienda Ospedaliero Universitaria di Modena, University of Modena and Reggio Emilia, Infectious and Tropical Diseases Unit,Modena, Italy; 6 ASST Lecco, Infectious Diseases Unit, Lecco, Italy; 7 Ospedale Amedeo di Savoia, University of Turin, Unit of Infectious Diseases, Department of Medical Sciences, Turin, Italy; 8 Ospedale Amedeo di Savoia, ASL Città di Torino, Division A of Infectious Diseases, Turin, Italy; 9 National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Clinical Deparment, HIV/AIDS Unit, Rome, Italy; 10 IRCCS San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Infectious Diseases Unit, Milan, Italy; 11University of Rome Tor Vergata, Department of Experimental Medicine, Rome, Italy; 12IRCCS Ca' Granda Ospedale Maggiore Policlinico, University of Milan, Department of Pathophysiology and Transplantation, Clinic of Infectious Diseases, Milan

HIV Drug Therapy GLASGOW 2022 | HYBRID

Evaluate the effectiveness of BIC/FTC/TAF in ART-experienced virologically suppressed (VS) people living with HIV (PLWH)

1237 PLWH included: 544 (44.0%) >50 years,
229 (18.5%) female,
95 (5.7%) switching from NNRTIs

112 TF occurred (9.1%, 14 VF and 98 TD)
The 1-year probability of TF was 4.6%

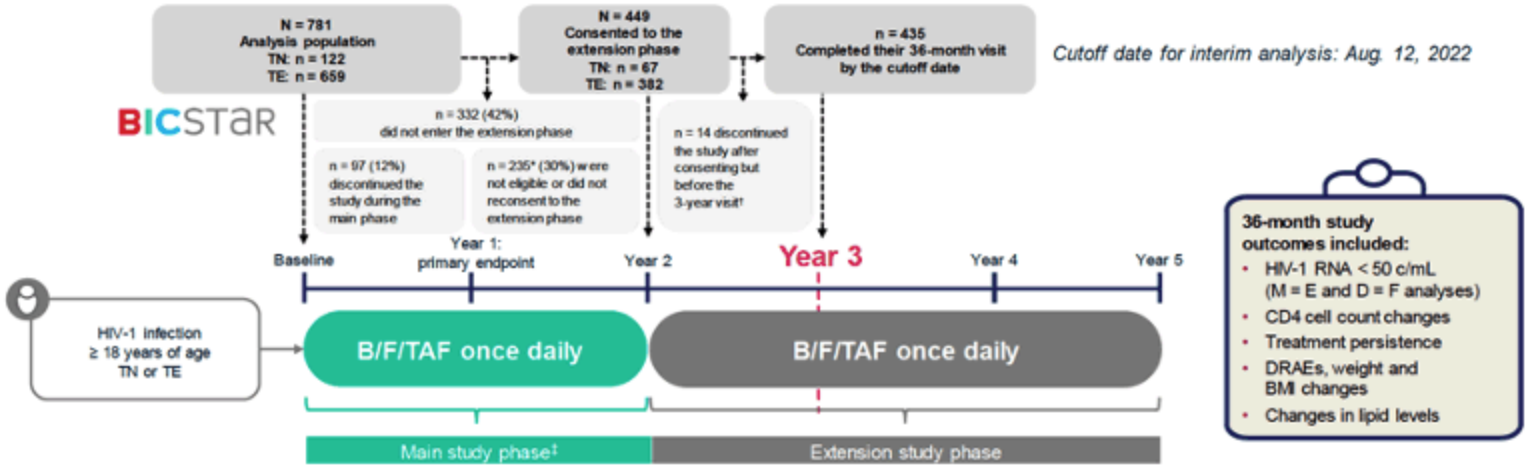
Table 3- Hazard Ratios (HR) and Adjusted HR of TF from fitting 4 Cox regression models

ART-experienced	HR (95%CI)	p	AHR (95%CI)	p
Age, >=50 years (vs <50years)[1]	0.73 (0.50-1.0)	0.103	0.75 (0.50-1.12)	0.163
Gender, Female (vs. male)[2]	1.72 (1.13-2.62)	0.011	2.01 (1.17-3.44)	0.011
Previous NNRTI-based regimen (vs non-NNRTI)[3]	0.56 (0.25-1.28)	0.172	0.63 (0.27-1.44)	0.272

After excluding 6 TD for pregnancy as events,
TF risk in Females was attenuated to aHR 1.63 (95%CI 0.93,2.90).

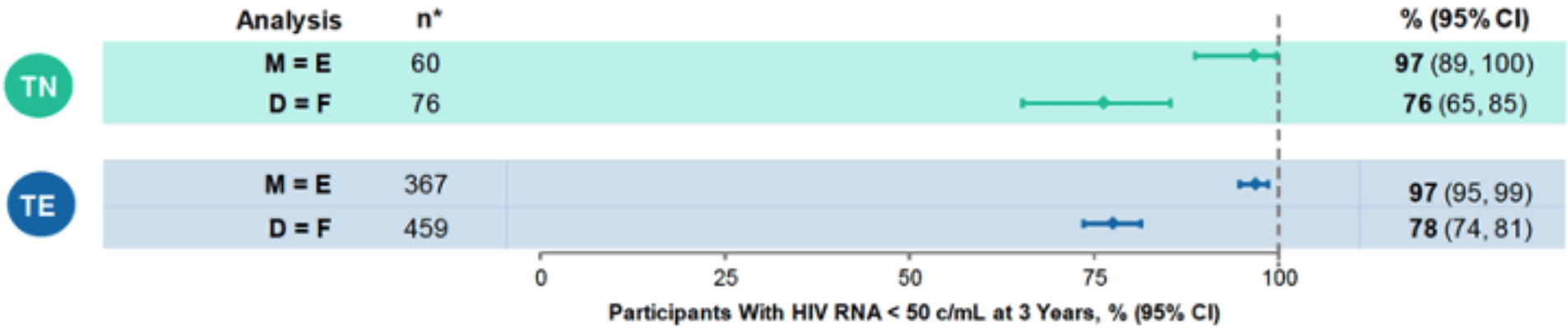
- **BIC/FTC/TAF as switch strategy demonstrated high effectiveness in real-life with 4.6% TF and 0.7% VF at 1-year.**
- **Higher risk of TF in women seems mainly related to discontinuation of BIC/FTC/TAF for pregnancy concerns.**
- **4.1% of TD at 1-year, main cause of discontinuation was simplification**

Bictegravir/Emtricitabine/Tenofovir Alafenamide (B/F/TAF) in Antiretroviral Treatment-Naïve (TN) and -Experienced (TE) People With HIV (PWH): 3-Year Effectiveness and Safety Outcomes in the BICSTaR Observational Cohort



The analysis population includes participants who had a visit at 36 months and those who discontinued the study having initiated treatment ≥ 30 months (lower bound of the 36-month visit window) prior to the data cutoff date.
*69 participants (9%) discontinued B/F/TAF but were still in the study at 24 months and 166 (21%) were eligible for the extension phase but did not reconsent; †Due to participant decision (n = 6), participant lost to follow-up (n = 5), study drug discontinuation (n = 2) and death (n = 1); ‡Participants could complete the main phase either on B/F/TAF or on an alternative ART regimen following discontinuation of B/F/TAF treatment.

Virologic Effectiveness at 3 Years (M = E and D = F Analyses)



*Number of participants with available viral load data. For D = F, denominator includes those participants discontinuing B/F/TAF prior to the visit window, and in such cases viral load was imputed as ≥ 50 c/mL. Reasons for discontinuation before the 36-month window that resulted in D = F were, n-values for TN and TE, respectively: AEs, 8 and 52; death, 2 and 7; investigator decision, 1 and 11; lack of efficacy, 0 and 5; new treatment available, 0 and 2; pregnancy, 0 and 1; participant decision, 3 and 11.

M. Sabranski et al., EACS 2023

HIV Treatment

RWE

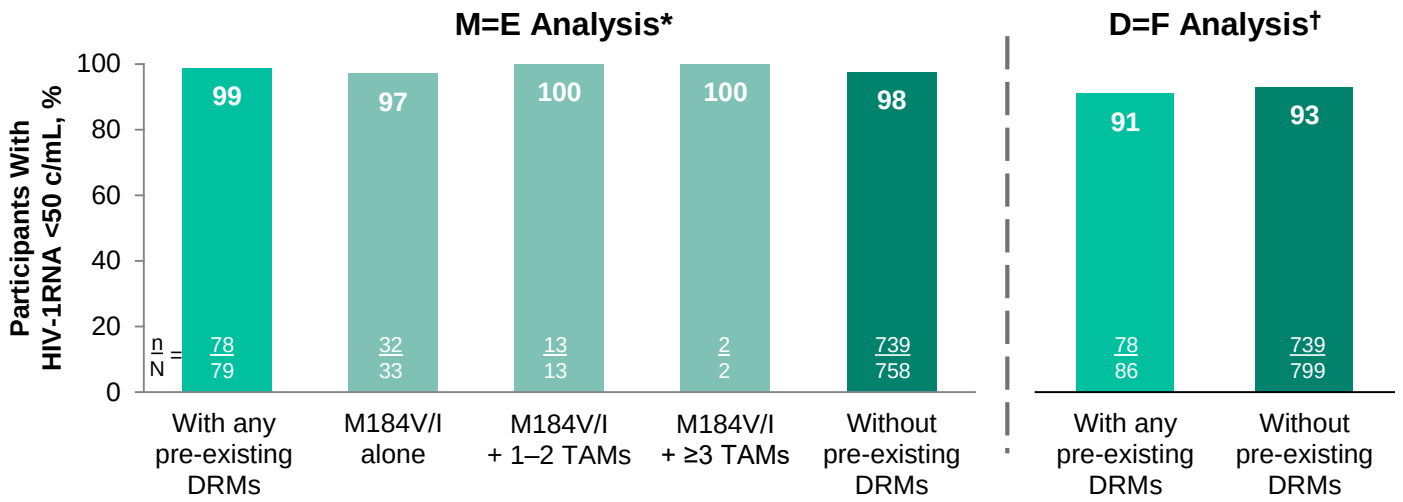
BICSTaR

VS at 12 Months in Virologically Suppressed PWH

Most Common Pre-Existing NRTI DRMs (>1% of Participants)

DRM	Participants with any pre-existing DRMs, n (%) (N=105)
M184V/I	39 (37)
M184V/I + 1–2 TAMs	14 (13)
M184V/I + ≥3 TAMs	4 (4)
T215Y/F	15 (14)
D67N	13 (12)
M41L	13 (12)
K70R/E	9 (9)
K219Q/E/N/R	8 (8)
L210W	4 (4)
>1 TAM	40 (38)

VS at Month 12



- Pre-existing DRMs were identified in **24%** of virologically suppressed participants with available data
- High levels of VS were maintained after switching to B/F/TAF, **irrespective of pre-existing DRMs**
- **No treatment-emergent DRMs** to B/F/TAF were reported

After 12 months, TE PWH initiating B/F/TAF in routine clinical practice maintained high rates of VS despite the presence of DRMs (including M184V/I)

*Denominators represent number of participants with available HIV-1 RNA data at Month 12. Of 159 participants with missing HIV-1 RNA data at Month 12, 48 had discontinued B/F/TAF or had a treatment interruption >30 days before the Month 12 analysis window, and 111 were still on B/F/TAF and had no HIV-1 RNA data in the Month 12 analysis window; †Participants who discontinued B/F/TAF or had a treatment interruption >30 days before the beginning of the 12-month analysis window were imputed as >50 c/mL. D=F, discontinuation=failure; DRM, drug resistance mutation; M=E, missing=excluded; RWE, real-world evidence; TAM, thymidine analog mutation; TE, treatment-experienced; VS, virologic suppression

Trottier B, et al. IDWeek 2023, Poster 1611

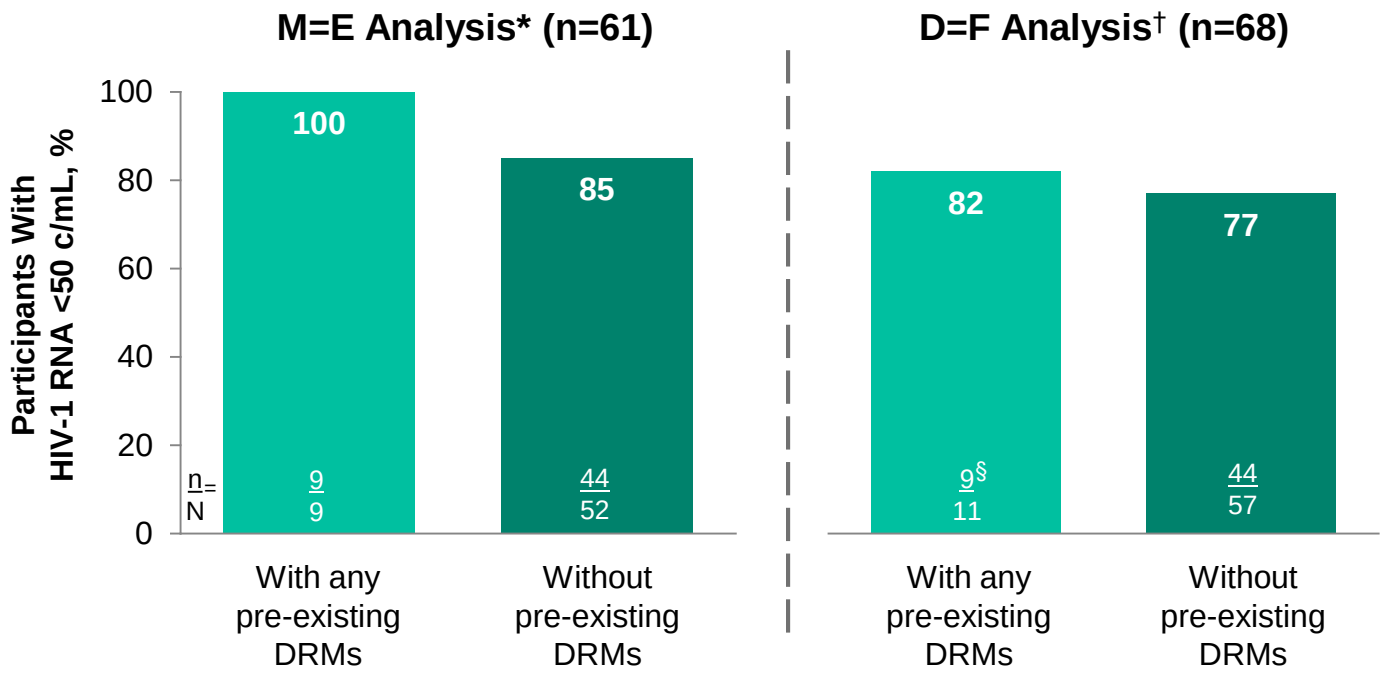
HIV Treatment

RWE

BICSTaR

VS at 12 Months in PWH With Viremia

VS at Month 12 in Participants With Viremia at Enrollment



B/F/TAF achieved high rates of VS in participants with viremia and pre-existing DRMs at enrollment

*Denominators represent number of participants with available HIV-1 RNA data at Month 12; †Participants who discontinued B/F/TAF or had a treatment interruption >30 days before the beginning of the 12-month analysis window were imputed as >50 c/mL; §Of the 11 participants with viremia at enrollment who had pre-existing DRMs, 7 had a history of prior virologic failure and 5 had ≥1 pre-existing DRM related to NRTI resistance (M184V/I, n=3, M184V/I + T215Y/F, n=1; M184V/I + D67N, K70R/E, K219Q/E/N/R, n=1)

D=F, discontinuation=failure; DRM, drug resistance mutation; M=E, missing=excluded; RWE, real-world evidence; VS, virologic suppression

Trottier B, et al. IDWeek 2023, Poster 1611

VS by Adherence Category Through Week 144

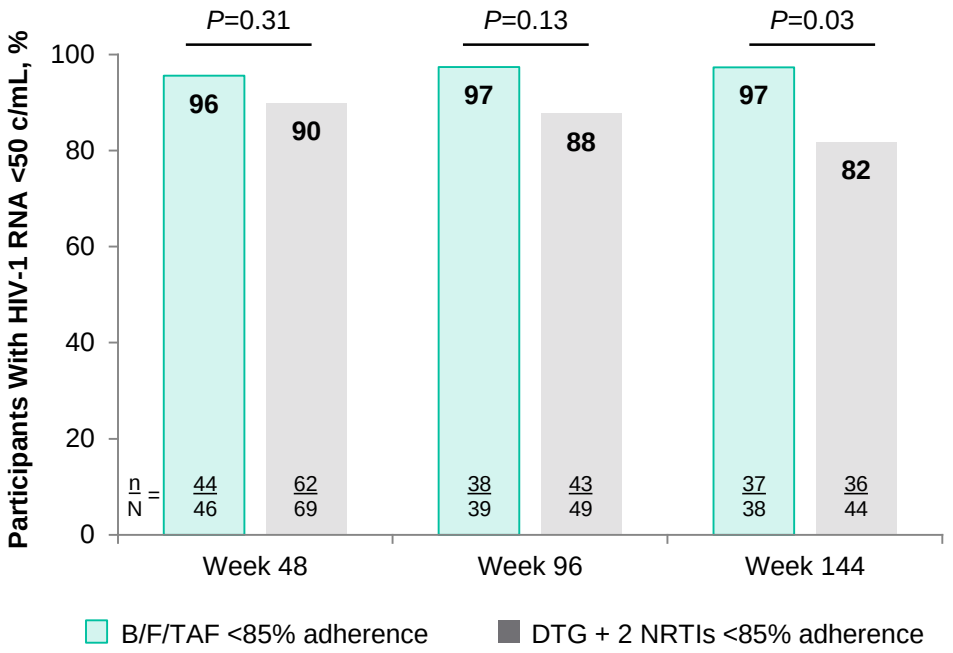
Overall, VS was high for both treatment groups through all timepoints*

The proportion of PWH with VS in each adherence category at **Weeks 48, 96 and 144**:

	B/F/TAF	DTG + 2 NRTIs	
High adherence	99%	99%	Week 48
	99%	98%	Week 96
	99%	98%	Week 144
Intermediate adherence	98%	98%	Week 48
	99%	96%	Week 96
	99%	96%	Week 144
Low adherence	96%	90%	Week 48
	97%	88%†	Week 96
	97%§	82%†	Week 144

HIV-1 RNA <50 c/mL in Participants With Low Adherence (<85%)¶

(last available on-treatment HIV-1 RNA value using LOCF imputation)



Postbaseline Resistance Analysis

B/F/TAF

- No participants had treatment-emergent resistance

DTG + 2 NRTIs

- Two participants on DTG/ABC/3TC had HIV-1 RNA ≥200 c/mL at their last visit (blinded phase)
  - Both had emergent M184V and resuppressed on open-label B/F/TAF

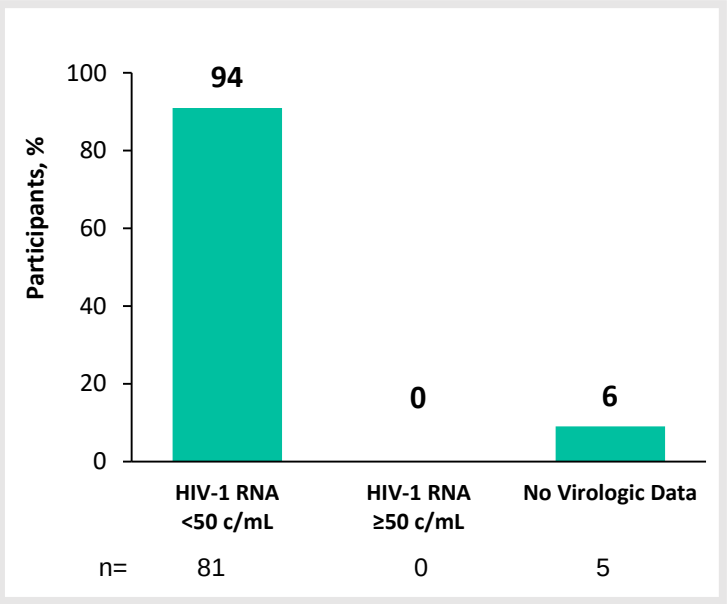
Participants on B/F/TAF had similarly high levels of VS regardless of adherence category, in contrast to those on DTG + 2 NRTIs. At Week 144, VS was significantly lower among participants with low adherence receiving DTG + 2 NRTIs than in those on B/F/TAF

*When assessed for all adherence groups combined; †Participants on DTG + 2 NRTIs with low adherence had significantly lower VS than those with intermediate or high adherence; §VS was significantly greater with B/F/TAF than DTG + 2 NRTIs (*P*=0.03) among participants with low adherence at Week 144; ¶Week 48: Studies 1489, 1490, 4458, 1844 and 4030; Week 96: Studies 1489, 1490 and 4458; Week 144: Studies 1489 and 1490. TN, treatment-naïve; VS, virologic suppression

Andreatta K, et al. IDWeek 2023, Poster 1561

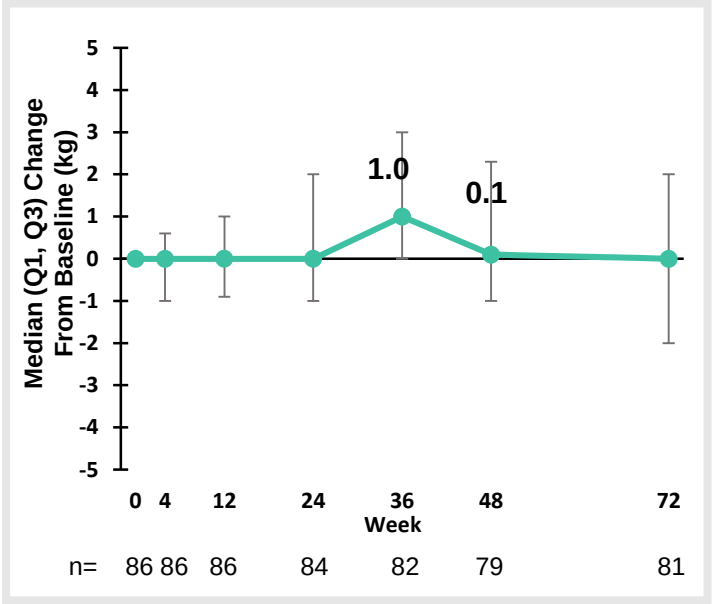
Efficacy, Weight Change and Safety through Week 72

Efficacy



- No treatment emergent resistance to any of the regimen components

Weight Change



- No change from baseline in median weight

Safety

Adverse Events, % (n)	B/F/TAF n = 86
Study drug-related AEs (grades 2, 3 or 4)	4.7% (4)
Study drug-related AEs (grades 3 or 4)	2.3% (2)
Any study drug-related serious AE	0
AE leading to study drug discontinuation	4.7% (4)
Drug-related	2.3% (2)*
Renal AEs leading to study drug discontinuation	0
Death	2†

*1) abdominal discomfort (grade 2), 2) irritability and sleep disorder (grade 4)

†1) 77 yo male with pre-existing depressive disorder led to suicide via a benzodiazepine overdose (study day 427), 2) 72 yo male developed and succumbed to pneumonia secondary to COVID-19 infection (study day 672); Neither death study drug-related

B/F/TAF was highly effective with no virologic failure and no treatment emergent resistance and well-tolerated in virologically suppressed adults ≥65 years through W72

AE, adverse event

Maggiolo F, et al. HIV Drug Therapy 2020. Glasgow. P038

Durability of Dolutegravir-Based Regimens: A 5-Year Prospective Observational Study

Lucia Taramasso, MD, PhD,[1,j] Andrea De Vito, MD,[2] Elena Delfina Ricci, PhD,[3] Giancarlo Orofino, MD,[4] Nicola Squillace, MD,[5] Barbara Menzaghi, MD,[6] Chiara Molteni, MD,[7] Roberto Gulminetti, MD,[8] Giuseppe Vittorio De Socio, MD, PhD,[9] Giovanni Francesco Pellicanò, MD,[10] Eleonora Sarchi, MD,[11] Benedetto Maurizio Celesia, MD,[12] Leonardo Calza, MD,[13] Stefano Rusconi, MD,[14] Laura Valsecchi, MD,[15] Canio Vito Martinelli, MD,[16] Antonio Cascio, MD, PhD,[17] Paolo Maggi, MD,[18] Francesca Vichi, MD,[19] Goffredo Angioni, MD,[20] Giuliana Guadagnino, MD,[21] Giovanni Cenderello, MD,[22] Chiara Dentone, MD, PhD,[1] Alessandra Bandera, MD, PhD,[23] Katia Falasca, MD, PhD,[24] Paolo Bonfanti, MD,[5] Antonio Di Biagio, MD,[25] and Giordano Madeddu, MD,[2] on Behalf of the CISAI Study Group*

- from July 2014 until November 2020
- 963 PLWH
- high DTG durability
- low rate of virological failures
- Dual therapies seemed protective toward AEs

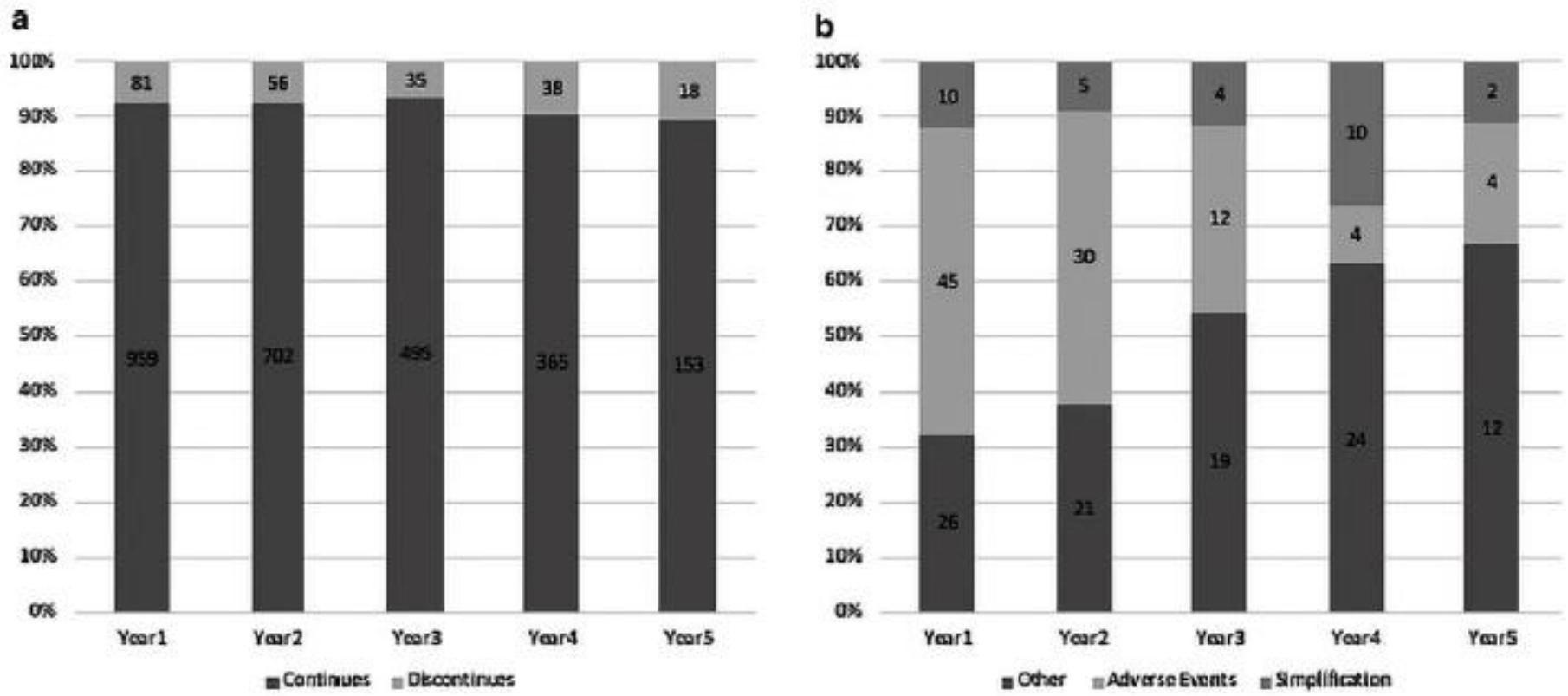


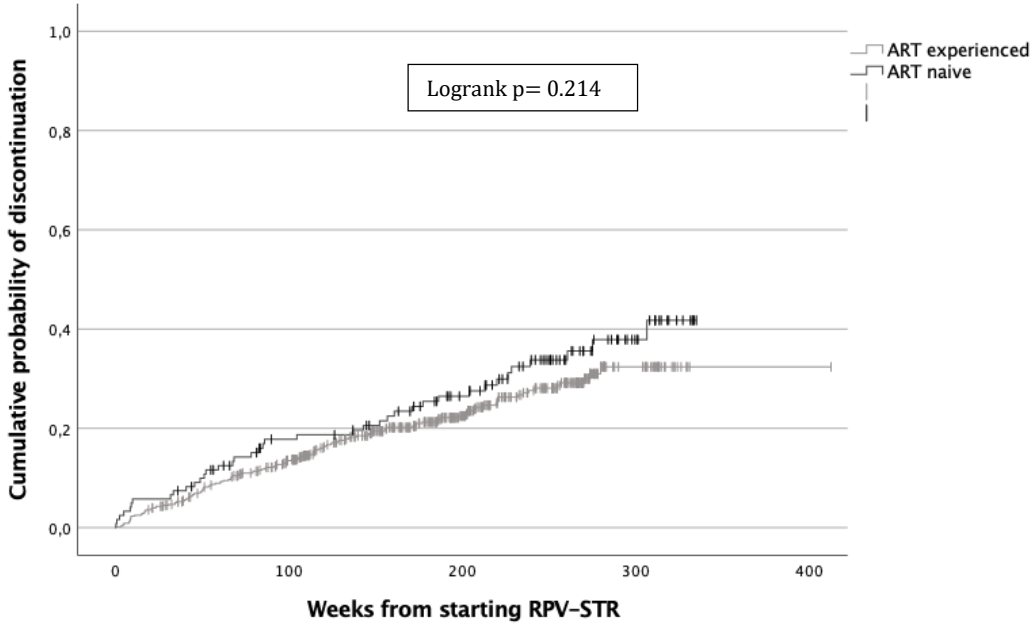
FIG. 1. Dolutegravir discontinuations over time for any cause (**a**) and according to reason of discontinuation (**b**) in the 5 years of follow-up.

AIDS PATIENT CARE and STDs
Volume 35, Number 9, 2021

DOI: 10.1089/apc.2021.0089

Long-term effectiveness of rilpivirine-based single tablet regimens in a seven-year, two centers observational cohort of people living with HIV.

Taramasso L, Lo Caputo S, Magnasco L, Briano F, Poliseno MC, Bruno SR, Ferrara S, Pincino R, Sarteschi G, Beltramini S, Sasso E, Mora S, Giacomini M, Bassetti M, Di Biagio A.



684 PLWH were enrolled.
Mean duration of RPV-STR treatment was 192.5 the incidence of discontinuation was 7.7 per 100 person-year.
The estimated proportions of discontinuation after 48 and 96 weeks were 5.6% and 13.4% respectively.
Causes of discontinuation
loss to follow up (30%), side effects (15%), ART optimization (14%), virological failure (12%), death or transfer to another center (9%), low adherence (7%), drug interactions (6%), simplification to dual therapy (3%) and unknown (3%).

AIDS Res Hum Retroviruses. 2022 Feb 16

Long-term effectiveness of rilpivirine-based single tablet regimens in a seven-year, two centers observational cohort of people living with HIV.

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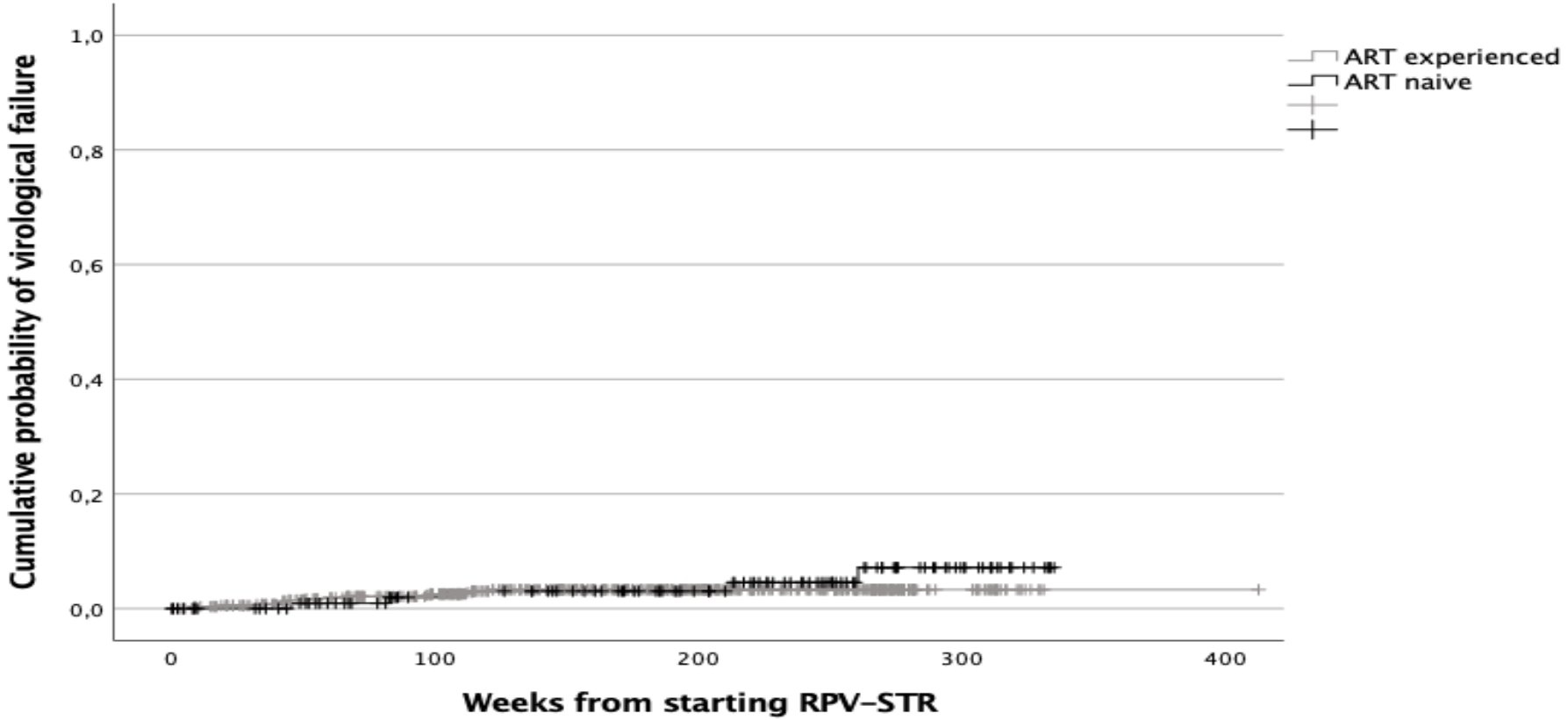
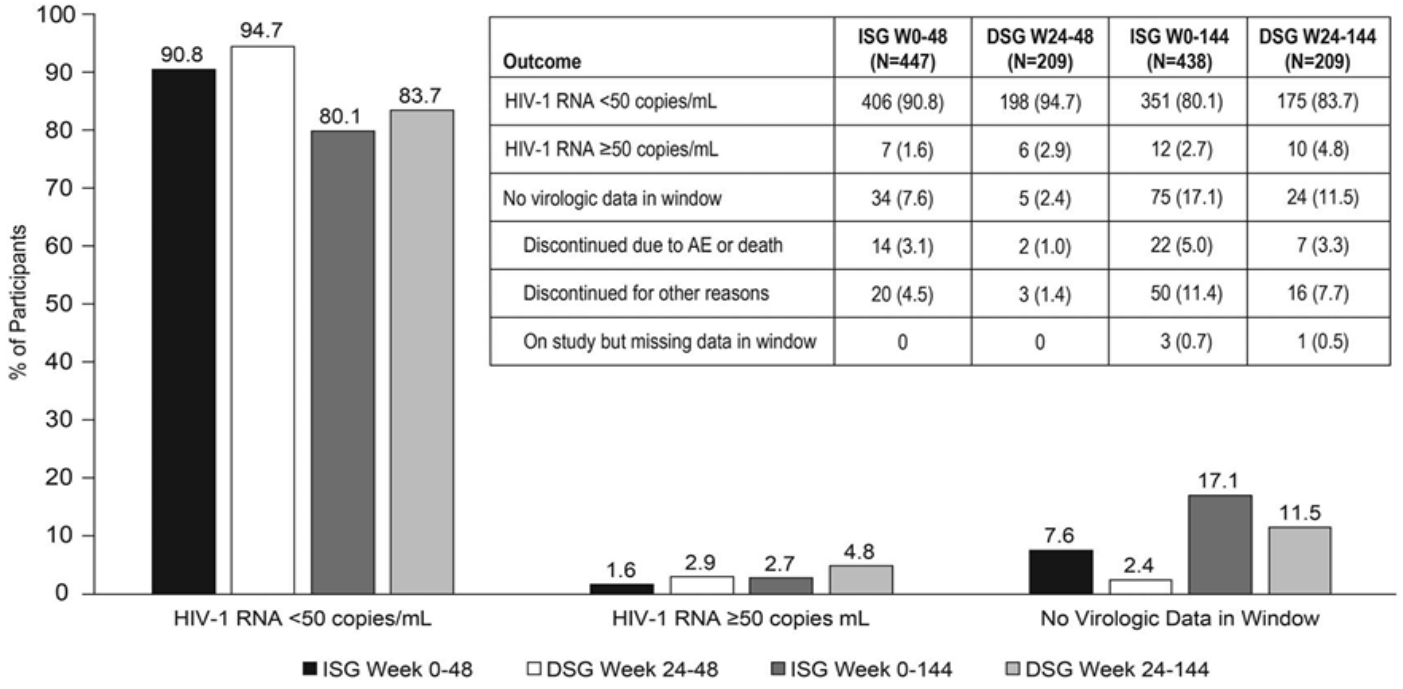


AIDS Res Hum Retroviruses. 2022 Feb 16

DRIVE-SHIFT Week 144

Virologic Outcomes after switch to DOR/3TC/TDF (FDA Snapshot approach)

- 9 patients in the ISG who completed the base study but did not enter the extension, were excluded from the Week 144 analysis
- By the OF approach, 96.7% of the ISG (351/363) and 94.6% of the DSG (175/185) maintained VL <50 copies/ml



Outcome	ISG W0-48 (N=447)	DSG W24-48 (N=209)	ISG W0-144 (N=438)	DSG W24-144 (N=209)
HIV-1 RNA <50 copies/mL	406 (90.8)	198 (94.7)	351 (80.1)	175 (83.7)
HIV-1 RNA ≥50 copies/mL	7 (1.6)	6 (2.9)	12 (2.7)	10 (4.8)
No virologic data in window	34 (7.6)	5 (2.4)	75 (17.1)	24 (11.5)
Discontinued due to AE or death	14 (3.1)	2 (1.0)	22 (5.0)	7 (3.3)
Discontinued for other reasons	20 (4.5)	3 (1.4)	50 (11.4)	16 (7.7)
On study but missing data in window	0	0	3 (0.7)	1 (0.5)

ISG, Immediate Switch Group, DSG, Delayed Switch Group, FDA, Food and Drug Administration

Kumar P, Johnson M, Molina JM, et al. Switching to DOR/3TC/TDF Maintains HIV-1 Virologic Suppression Through Week 144 in the DRIVE-SHIFT Trial. J Acquir Immune Defic Syndr. 2021;87(2):801-805. Brief Report: Switching to DOR/3TC/TDF Maintains HIV-1 Virologic Suppression Through Week 144 in the DRIVE-SHIFT Trial - PubMed (nih.gov)

Liver enzymes levels, metabolic and renal profile modifications after switching from TDF to TAF- based regimens among ART experienced PLWH in the ICONA cohort

M. Poliseno, S. Lo Caputo, A. Tavelli, R. Gagliardini, L. Gazzola, A. Saracino, T. A. Santantonio, M. Puoti, S. Cicalini, A. Antinori, A. d'Arminio Monforte, A. Cozzi-Lepri

Results (1/4)

- **2,911** patients met the inclusion criteria, **81%** males, median age **45** (IQR 37-53) years

- Hepatitis coinfection at baseline was reported in **346** subjects (12%)

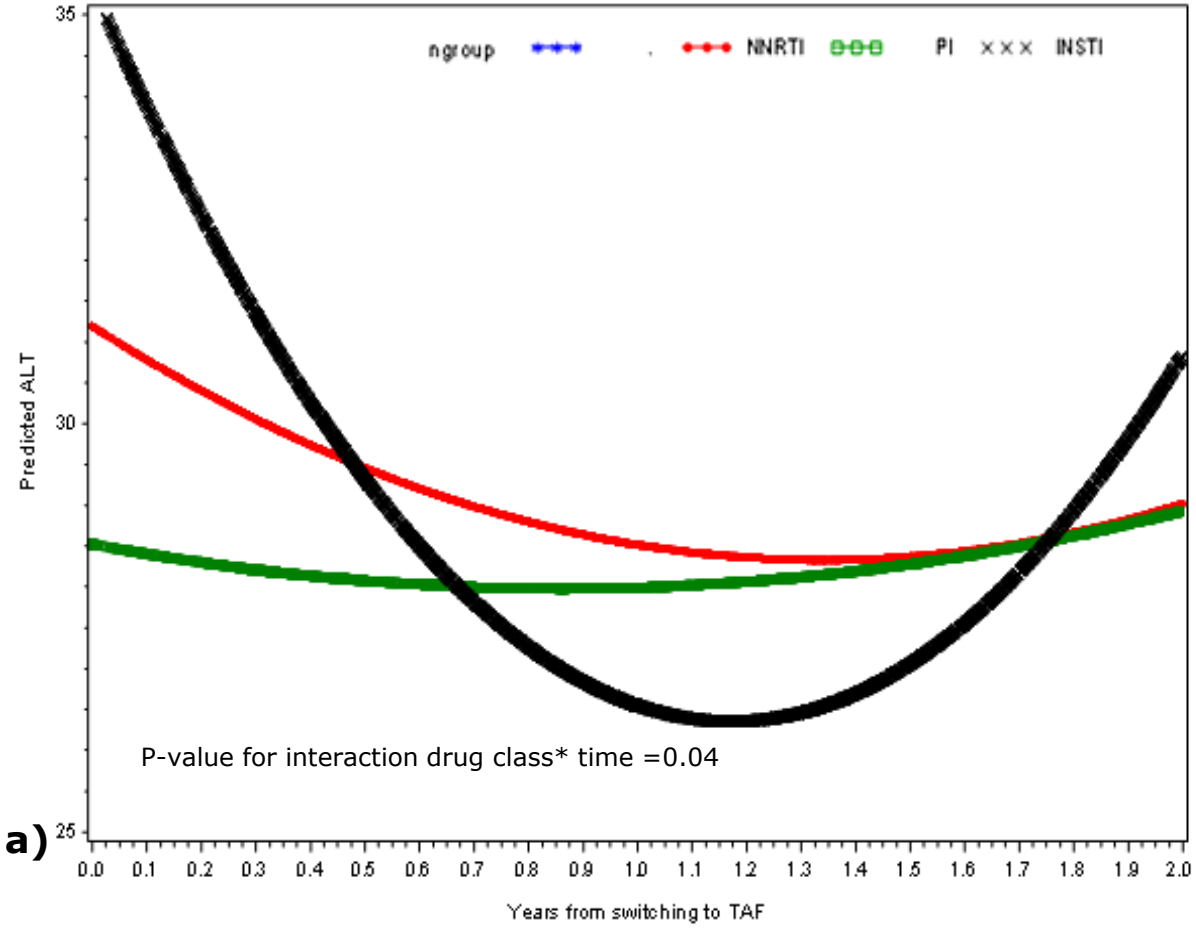
- **44** patients (1.5%) had clinically significant LEE at the moment of switch

- Median follow up of **42** (IQR 34-47) months

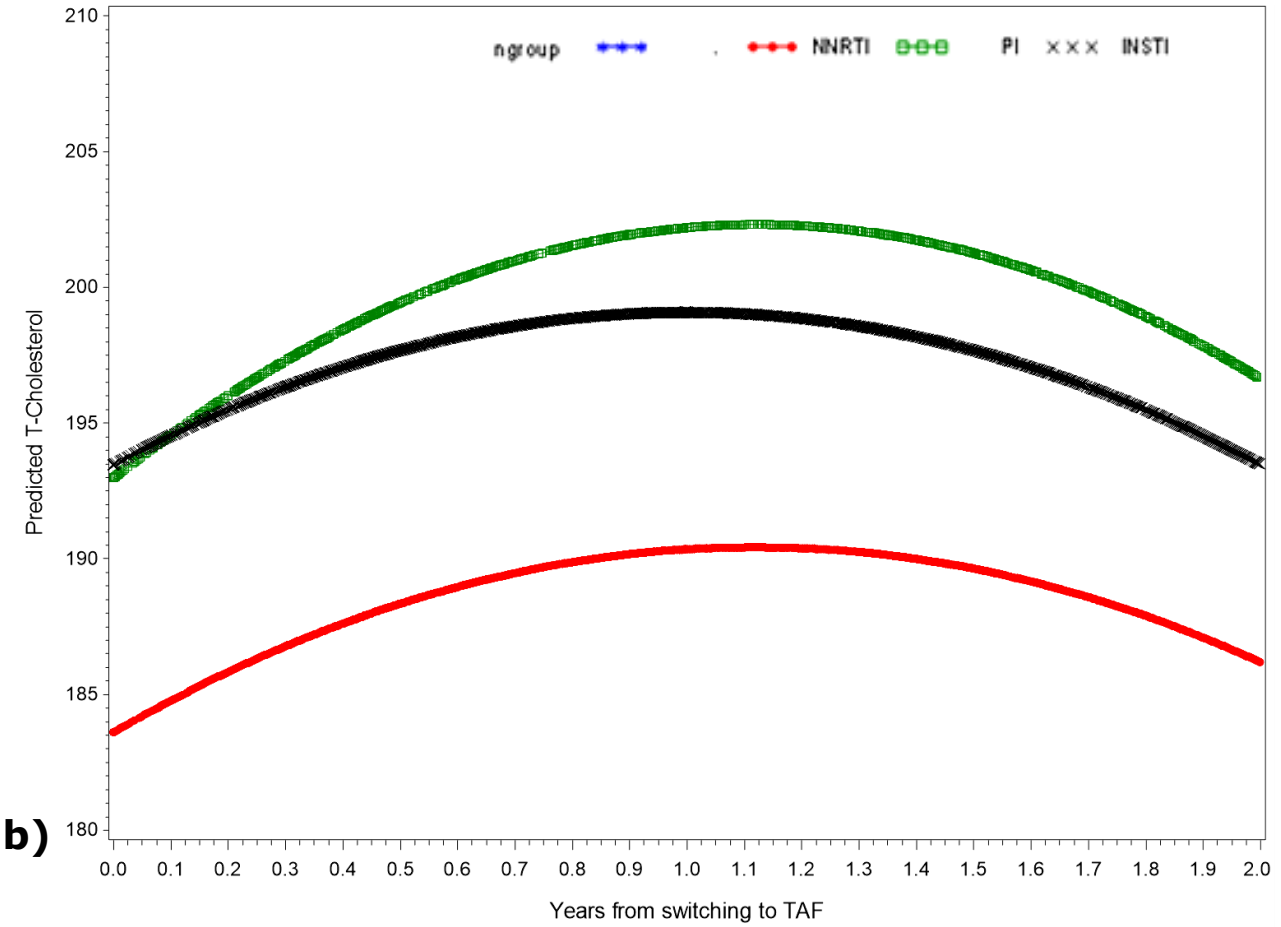
Characteristics	Anchor drug in TAF/FTC-regimen				
	NNRTI	PI/r	INSTI	p-value*	Total
	N= 1337	N= 469	N= 1105		N= 2911
Gender, n(%)				0.561	
Female	249 (18.6%)	98 (20.9%)	213 (19.3%)		560 (19.2%)
CVD diagnosis, n(%)				0.053	
Yes	16 (1.2%)	3 (0.6%)	23 (2.1%)		42 (1.4%)
Hepatitis co-infection*, n(%)				0.006	
No	1059 (79.2%)	367 (78.3%)	845 (76.5%)		2271 (78.0%)
Yes	159 (11.9%)	66 (14.1%)	121 (11.0%)		346 (11.9%)
Not tested	119 (8.9%)	36 (7.7%)	139 (12.6%)		294 (10.1%)
Age, years				0.130	
Median (IQR)	45 (37, 52)	46 (38, 53)	45 (37, 53)		45 (37, 53)
Diabetes, n(%)				0.240	
Yes	53 (4.0%)	16 (3.4%)	56 (5.1%)		125 (4.3%)
Smoking, n(%)				0.013	
No	678 (50.7%)	227 (48.4%)	568 (51.4%)		1473 (50.6%)
Yes	567 (42.4%)	202 (43.1%)	422 (38.2%)		1191 (40.9%)
Unknown	92 (6.9%)	40 (8.5%)	115 (10.4%)		247 (8.5%)
Use of statins, n(%)				0.114	
Yes	140 (10.5%)	35 (7.5%)	119 (10.8%)		294 (10.1%)
Use of blood pressure lowering drugs, n(%)				0.004	
Yes	141 (10.5%)	29 (6.2%)	129 (11.7%)		299 (10.3%)
egfr (CKD_Epi formula), ml/min/1.73m²				0.008	
Median (IQR)	89.16 (76.86, 101.2)	91.26 (78.69, 104.2)	88.00 (75.47, 100.9)		88.90 (76.65, 101.6)
Follow-up, months				<.001	
Median (IQR)	41 (32, 45)	42 (32, 47)	44 (36, 49)		42 (34, 47)
Metabolic profile					
Blood glucose, mg/dL					
Median (IQR)	87 (80, 94)	86 (80, 94)	87 (81, 95)	0.277	87 (80, 94)
Total cholesterol, mg/dL					
Median (IQR)	173 (149, 198)	184 (159, 209)	182 (157, 205)	<.001	177 (153, 202)
HDL cholesterol, mg/dL					
Median (IQR)	46 (38, 55)	45 (38, 54)	46 (38, 54)	0.512	45 (38, 54)
LDL cholesterol					
Median (IQR)	130 (106, 155)	134 (108, 159)	130 (109, 156)	0.865	130 (108, 156)
Tryglicerides					
Median (IQR)	177 (124, 271)	200 (145, 296)	182 (127, 268)	<.001	182 (128, 274)
Tot chol/HDL ratio					
Median (IQR)	3.8 (3.0, 4.5)	4.1 (3.2, 5.0)	3.9 (3.2, 4.9)	<.001	3.9 (3.1, 4.7)
LEE&					
Yes	17 (1.3%)	5 (1.1%)	22 (2.0%)	0.241	44 (1.5%)

Results (4/4)

Figure 1. Predictions of ALT (**Fig.1 a)**) and Total Cholesterol (**Fig. 1 b)**) changes after switch to TAF from fitting a quadratic mixed model, stratified by class of anchor drug used in the TAF-based regimen.



a)

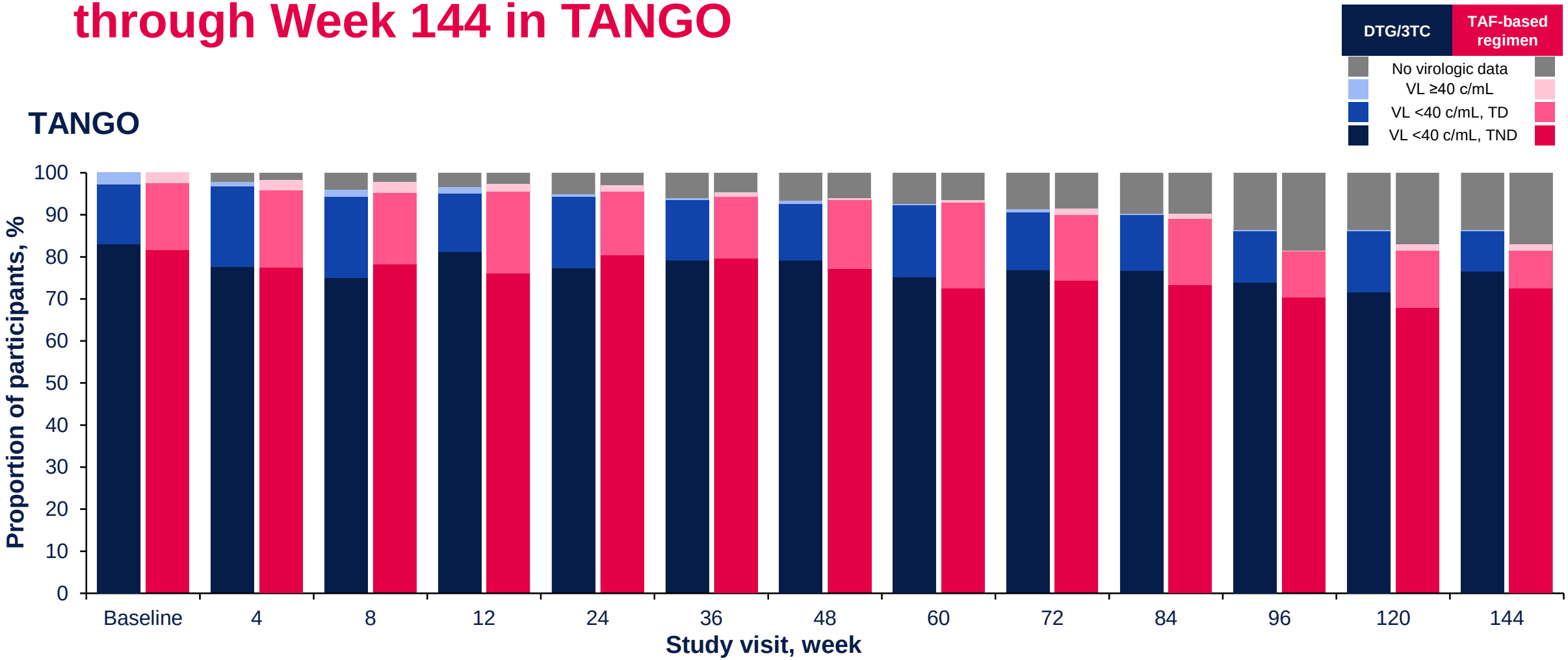


b)

NNRTI: Non Nucleosidic Reverse Trascriptase Inibhitors; *PI:* Protease Inibhitors; *INSTI*: Integrase Strand Transfer Inhibitors


3 Drugs
2 Drugs
Long Acting

Switch to DTG/3TC in Virologically Suppressed Participants Maintained High Levels of Virologic Suppression through Week 144 in TANGO



The proportion of participants with VL <40 c/mL and TND per visit through Week 144 was high and comparable in both treatment arms

Note: denominator n at each visit is number of participants with available VL data within the visit window

Wang R, et al. CROI 2022. Poster 484

TANGO Study: Robust Immunologic Improvements Observed in the Early-Switch and Late-Switch DTG/3TC Groups

DTG/3TC immunologic outcomes at Weeks 48 and 196

Mean (SD) change from BL*	Early-switch DTG/3TC (N=369)†	Late-switch DTG/3TC (N=298)‡
CD4⁺ cell count, cells/mm³		
After 48 weeks on DTG/3TC	+29.2 (179.5)	+64.8 (201.3)
After 196 weeks on DTG/3TC	+65.7 (210.6)	—
CD4⁺/CD8⁺ ratio		
After 48 weeks on DTG/3TC	+0.039 (0.204)	+0.041 (0.204)
After 196 weeks on DTG/3TC	+0.113 (0.277)	—

*ES baseline is Day 1, LS BL is Week 148. ES/LS BL values reported are actual values; †In the ES group, for CD4⁺ cell count and CD4⁺/CD8⁺ ratio, respectively, n=369 and n=366 at BL, n=344 and n=342 after 48 weeks and n=306 and n=304 after 196 weeks; ‡In the LS group, for CD4⁺ cell count and CD4⁺/CD8⁺ ratio, n=298 at LS BL and n=272 after 48 weeks

In TANGO, Overall Rates of AEs Were Comparable Between Treatment Groups Through Week 144

n (%)	DTG/3TC (N=369)	TAF-based regimen (N=371)
Any AE	336 (91)	335 (90)
Drug-related AEs	55 (15)	18 (5)
Drug-related AEs, Week 48 to Week 144*	12 (4)	13 (4)
AEs leading to study withdrawal	23 (6)	7 (2)
AEs leading to study withdrawal, Week 48 to 144*	9 (3)	5 (1)
Serious AEs	57 (15)	44 (12)
Metabolism and nutrition disorders		
Weight increased	17 (5)	19 (5)
Hyperlipidemia	7 (2)	7 (2)
Weight decreased	3 (<1)	4 (1)
Impaired glucose tolerance	1 (<1)	2 (<1)
Type 1 diabetes	1 (<1)	0
Type 2 diabetes	2 (<1)	1 (<1)

The rate of drug-related AEs with DTG/3TC was as expected in a switch study, with initial increased incidence after switch, followed by similar rates between treatment groups from Week 48 to Week 144

*N=342 for both groups

Osiyemi O, et al. Clin Infect Dis 2022;75:975–86

OAB0202

DTG/3TC è un regime ARV non indicato in pazienti con resistenza nota o sospetta verso la classe degli inibitori dell'integrasi o verso lamivudina

Prior M184V/I and Multiple Prior Virological Failures Have No Impact on the Efficacy of Switching HIV+ Adults to DTG/3TC Through 96Wks in SOLAR-3D

IAS 2023

23-26 July 2023

IAS 2023, the 12th IAS Conference on HIV Science

G.BLICK[1], E. CERRETA[1], G. MANCINI[1], A. COSENZA[1], L. FANG[2]

[1]Health Care Advocates International, Stratford CT USA

[2]Pharstat, Raleigh, NC USA

HEALTH CARE ADVOCATES INTERNATIONAL

IAS 2023
23-26 July 2023
IAS 2023, the 12th IAS Conference on HIV Science

BASELINE CHARACTERISTICS

Baseline Characteristic	All Patients (n = 100)	Historical M184V/I Resistance (n = 50)	No Historical M184V/I Resistance (n = 50)	*P* Value
Median Age, yrs (IQR)	58 (51-64)	61 (56-66)	55 (47-61)	<0.001
Cis-/Trans-Gender Female, n (%)	15 (15)	11 (22)	4 (8)	0.050
Median Time Since HIV Diagnosis, yrs (IQR)	25.3 (15.0-29.5)	28.4 (25.1-30.0)	15.5 (9.8-26.7)	<0.001
Median CD4 Nadir cell/mm3 (IQR)	190 (64-278)	160 (45-225)	225 (88-359)	0.006
History CD4<200, n (%)	53 (53)	33 (66)	20 (40)	0.009
Median ART Duration, yrs(IQR)	22.3 (14.3-25.7)	24.6 (22.0-28.1)	15.2 (8.8-22.6)	<0.001
Median Previous ART regimens, n(IQR)	7 (4-10)	9 (7-13)	4 (2-5)	<0.001
Median Duration of HIV-RNA suppression, yrs (IQR)	11.8 (8.2-14.6)	12.8 (10.2-14.4)	8.9 (4.4-14.7)	0.019

There were no significant differences observed for Age at time of HIV diagnosis, Race, HBV/HCV, Median highest PCR or History PCR>100,000c/mL

Blick et al. IAS 2023, #OAB0202

DTG/3TC è un regime ARV non indicato in pazienti con resistenza nota o sospetta verso la classe degli inibitori dell'integrasi o verso lamivudina

IAS 2023
23-26 July 2023
IAS 2023, the 12th IAS Conference on HIV Science

BASELINE ART AND PROVIRAL MUTATIONS

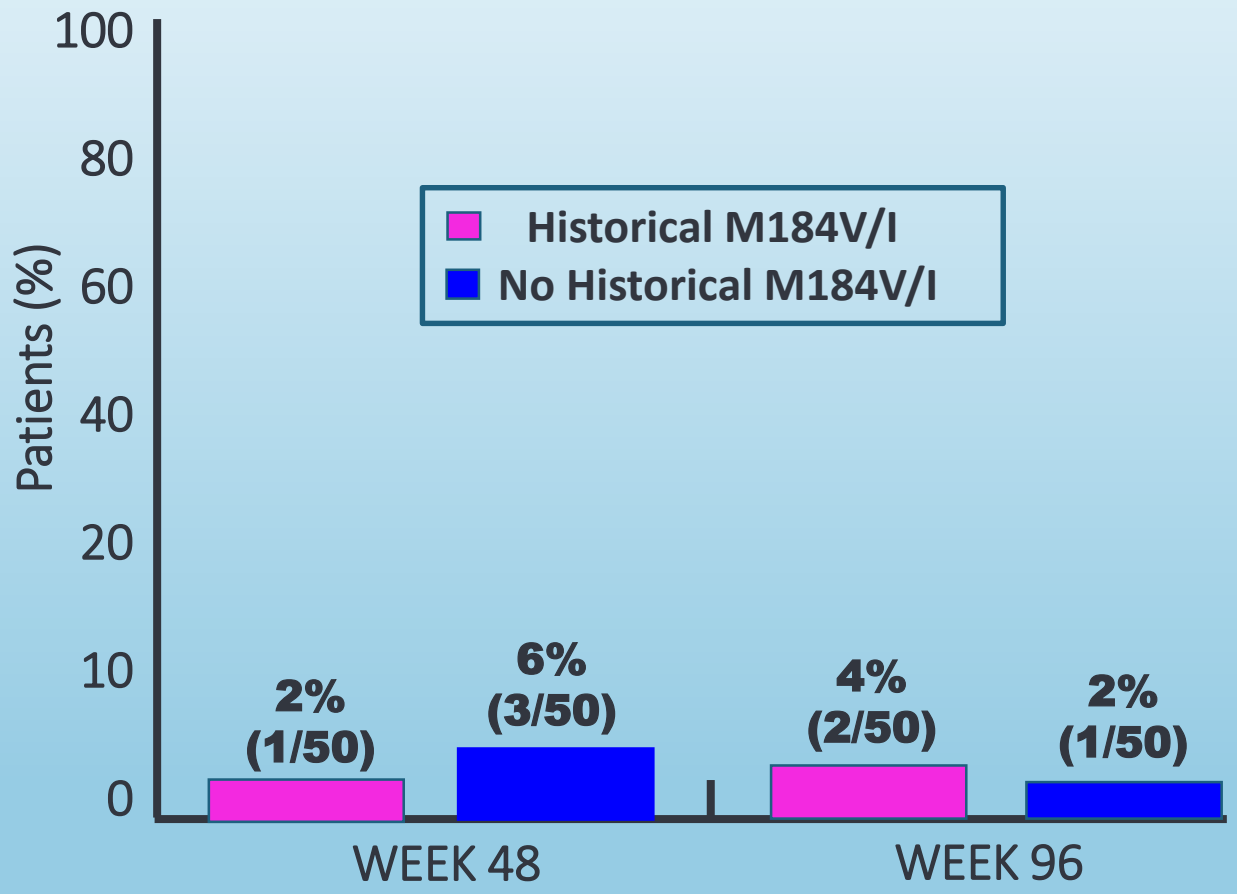
Baseline ART	All Patients (n=100)	Historical M184V/I (n=50)	No Historical M184V/I (n=50)
ART Regimen, n (%):			
• **2 NRTIs + INSTI:**	**58 (58)**	**30 (60)**	**28 (56)**
❖ TAF/FTC/BTG	4 (4)	3 (6)	1 (2)
❖ ABC/3TC/DTG	51 (51)	26 (52)	25 (50)
❖ TDF or TAF/FTC + DTG	3 (3)	1 (2)	2 (4)
• **2DR (NNRTI + INSTI):**			
❖ RPV/DTG	**21 (21)**	**12 (24)**	**9 (18)**
• **2 NRTIs + boosted INSTI:**			
❖ TAF/FTC/EVG/c	**6 (6)**	**0**	**6 (12)**
Historical GT vs Proviral DNA NGS			
M184V/I on Historical GT, n (%):	50 (50)	50 (100)	0
Proviral DNA by NGS, n (%):	70 (70)	41 (82)	29 (58)
• **M184V/I present**	15 (21)	**15 (37)**	0
• **M184V/I absent**	55 (79)	**26 (63)**	29 (100)
• K65R present	1 (1)	1 (2)	0
• K65R present with Q151M	1 (1)	0	1

NGS = Next-Generation Sequence; Performed by Quest Diagnostics; Resistance-associated mutations present in 10% or more of viral species sequenced are reported

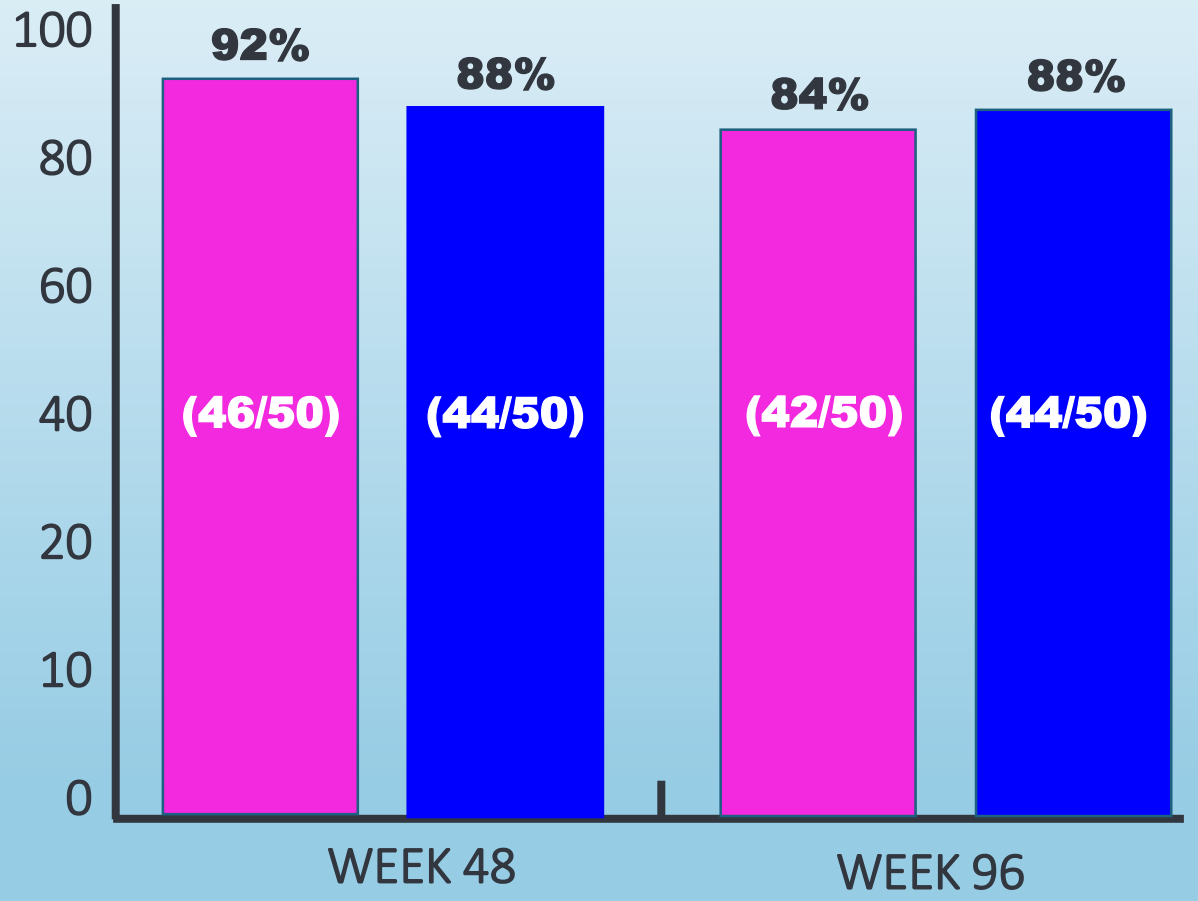
Blick et al. IAS 2023, #OAB0202

IAS 2023
23-26 July 2023
IAS 2023, the 12th IAS Conference on HIV Science

VIROLOGIC OUTCOMES:
Primary & Secondary Endpoints, Wks 48 & 96, ITT-E



PRIMARY ENDPOINT
PCR ≥ 50 c/mL by FDA Snapshot



SECONDARY ENDPOINT
PCR < 50 c/mL by FDA Snapshot

Blick et al. IAS 2023, #OAB0202

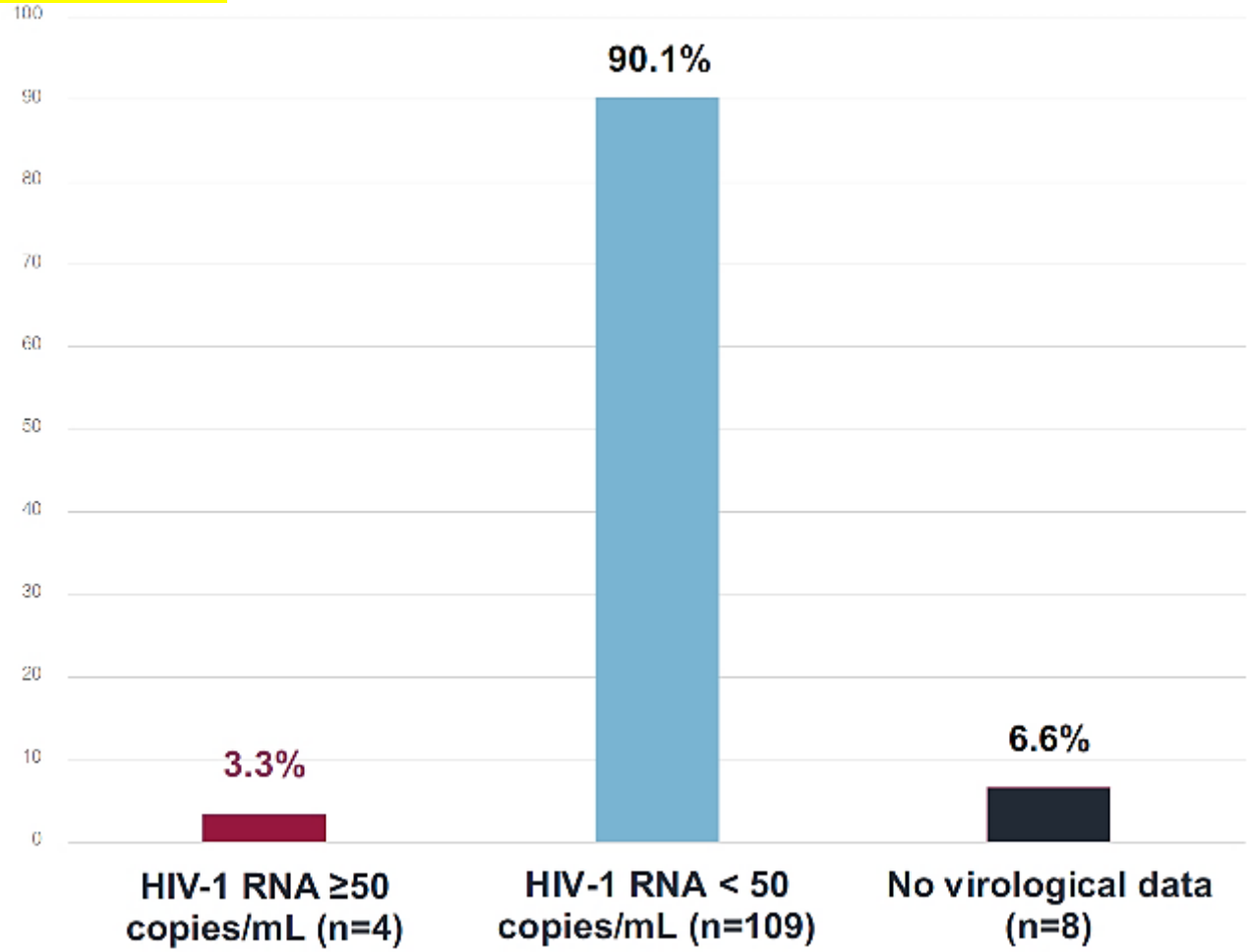
Virologic Outcomes of Lamivudine/Dolutegravir in Virologically Suppressed Persons With Expected or Confirmed Resistance to Lamivudine (VOLVER Clinical Trial-GESIDA 11820)

	All (n=121)
HIV-1 RNA < 50 copies/mL	**109 (90.1%)**
HIV-1 RNA ≥50 copies/mL	**4 (3.3%)**
HIV-1 RNA ≥50 copies/mL in W48 window	0 (0)
Discontinuation due to Lack of Efficacy	2 (1.65%)
Discontinuation for other reasons and Last VL ≥50 copies/mL	2 (1.65%) *
No virologic data at week 48	**8 (6.6%)**
Discontinuation Due to an Adverse Event (AE)	3 (2.48%)
Discontinuation for other reasons and Last VL<50 copies/mL	5 (4.13%)**

***Discontinuation for other reasons and Last VL ≥50 copies/mL:**
- 1 Lost to follow-up
- 1 adverse event and VL at study withdrawal 90 copies/mL

****Discontinuation for other reasons and Last VL<50 copies/mL:**
- 1 Lost to follow-up
- 1 protocol deviation (M184V in proviral DNA at screening)
- 2 investigator criteria (1 lung cancer, 1 M184V detected in plasma population genotyping at transient rebound, suppressed while still on DTG/3TC not fulfilling criteria for PVW/CVW but switched to DTG+DRV/c)
- 1 consent withdrawal

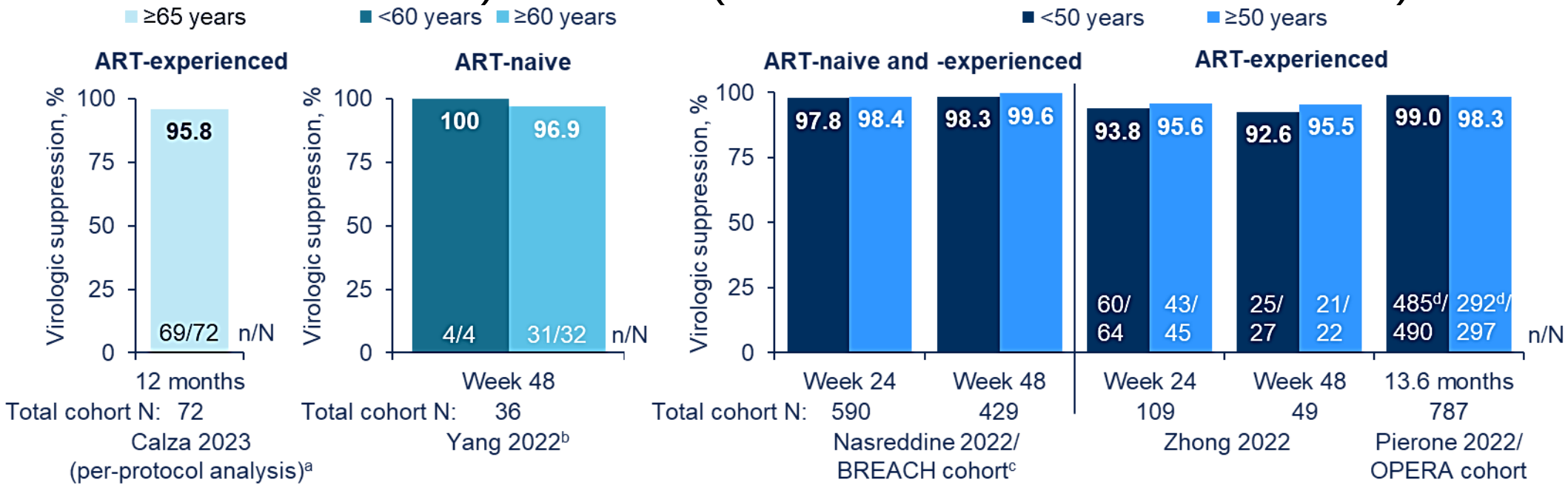
Efficacy at 48 Weeks FDA- Snapshot ITT-e



De Miguel et al. EACS 2023; Warsaw, Poland. Poster eP.A.097.

DTG + 3TC Effectiveness Outcomes Reported in People With HIV-1 Aged <50 and ≥50 Years From Lead RWE Publications With Reported Baseline Data

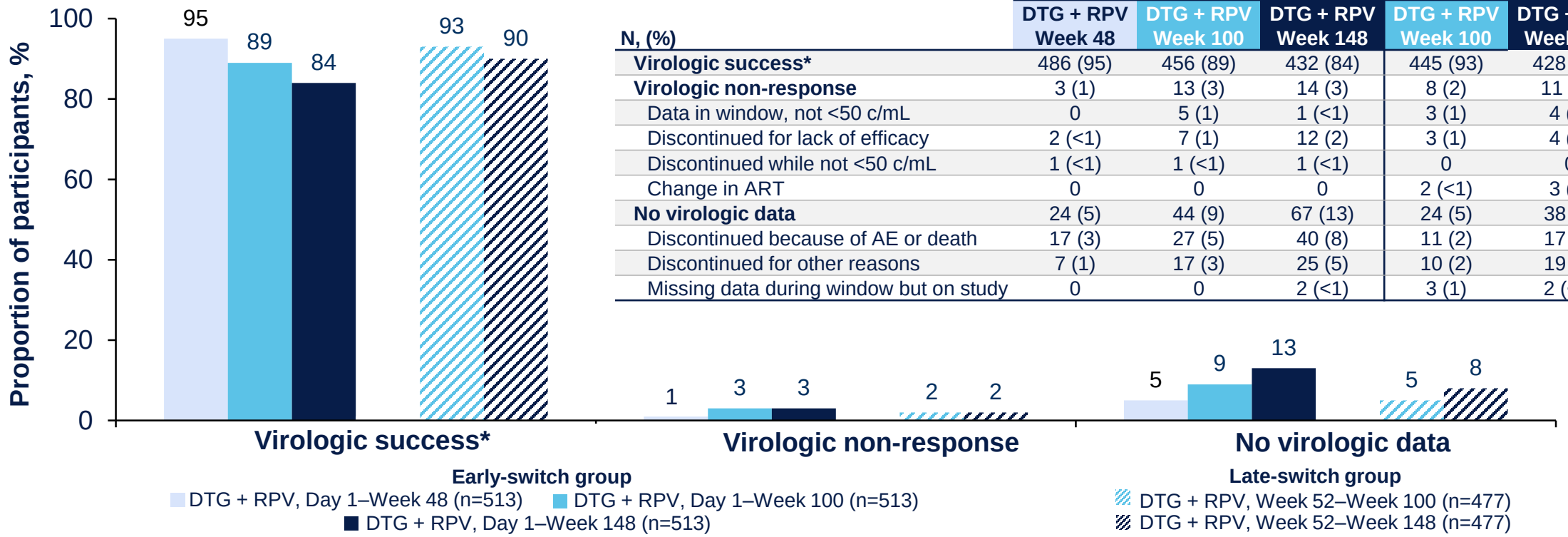
- High virologic suppression rates were reported in individuals aged ≥50 years across both ART-naive and ART-experienced populations, from 88.9% (defined as HIV-1 RNA <20 c/mL) to 99.6% (defined as HIV-1 RNA <50 c/mL)



[a]Intention-to-treat analysis: 64/72 (88.9%). [b]Virologic suppression in the ART-experienced population was reported as a proportion of the entire cohort, 84/86 (97.7%). [c]n/N not reported. [d]Assumption based on the maximum possible value of ≤5 individuals reported to have met virologic failure criteria.

DTG + RPV Has Demonstrated Durable Efficacy in Virologically Suppressed Participants Through 148 Weeks[1,2]

SWORD-1 and -2



	Early-switch group (n=513)			Late-switch group (n=477)	
N, (%)	DTG + RPV Week 48	DTG + RPV Week 100	DTG + RPV Week 148	DTG + RPV Week 100	DTG + RPV Week 148
Virologic success*	486 (95)	456 (89)	432 (84)	445 (93)	428 (90)
Virologic non-response	3 (1)	13 (3)	14 (3)	8 (2)	11 (2)
Data in window, not <50 c/mL	0	5 (1)	1 (<1)	3 (1)	4 (1)
Discontinued for lack of efficacy	2 (<1)	7 (1)	12 (2)	3 (1)	4 (1)
Discontinued while not <50 c/mL	1 (<1)	1 (<1)	1 (<1)	0	0
Change in ART	0	0	0	2 (<1)	3 (1)
No virologic data	24 (5)	44 (9)	67 (13)	24 (5)	38 (8)
Discontinued because of AE or death	17 (3)	27 (5)	40 (8)	11 (2)	17 (4)
Discontinued for other reasons	7 (1)	17 (3)	25 (5)	10 (2)	19 (4)
Missing data during window but on study	0	0	2 (<1)	3 (1)	2 (<1)

- The incidence of CVWs remained low through Week 148 (11/990; 1%).
  - No INI RAMS were observed and few NNRTI RAMs were detected with DTG + RPV

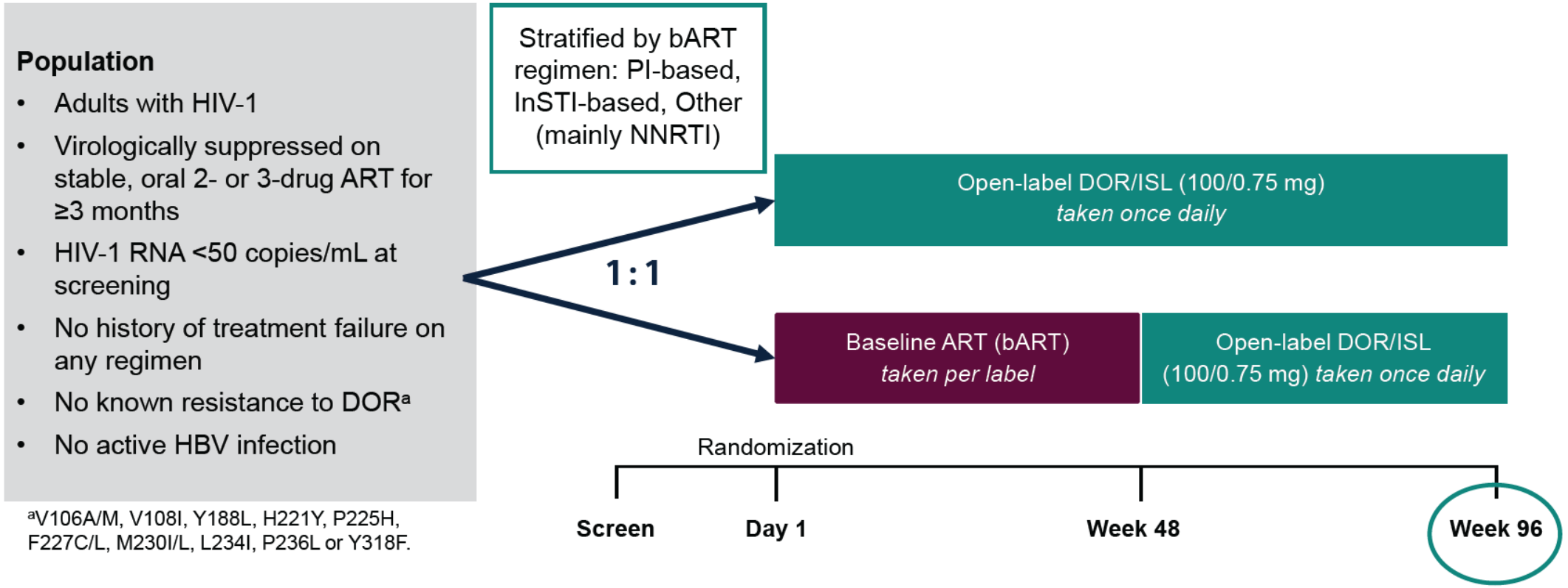
DTG + RPV demonstrated durable antiviral efficacy through 148 weeks of treatment in the early-switch group

*Defined as HIV-1 RNA <50 c/mL (FDA Snapshot)

1. van Wyk J, et al. BHIVA 2019. Poster P008
2. van Wyk J, et al. J Acquir Immune Defic Syndr 2020;85:325–30

Switch to Fixed-dose Doravirine (100 mg) with Islatravir (0.75 mg) Once Daily in Adults with HIV-1 Virologically Suppressed on Antiretroviral Therapy: Week 96 Results of a Randomized, Open-label, Phase 3 Trial

Amendment: Increased frequency of monitoring for CD4+ T-cell counts to every 12 weeks; implemented discontinuation criteria for protocol-defined decreases (eg, ≥30% reduction) in CD4+ T-cell and/or total lymphocyte counts

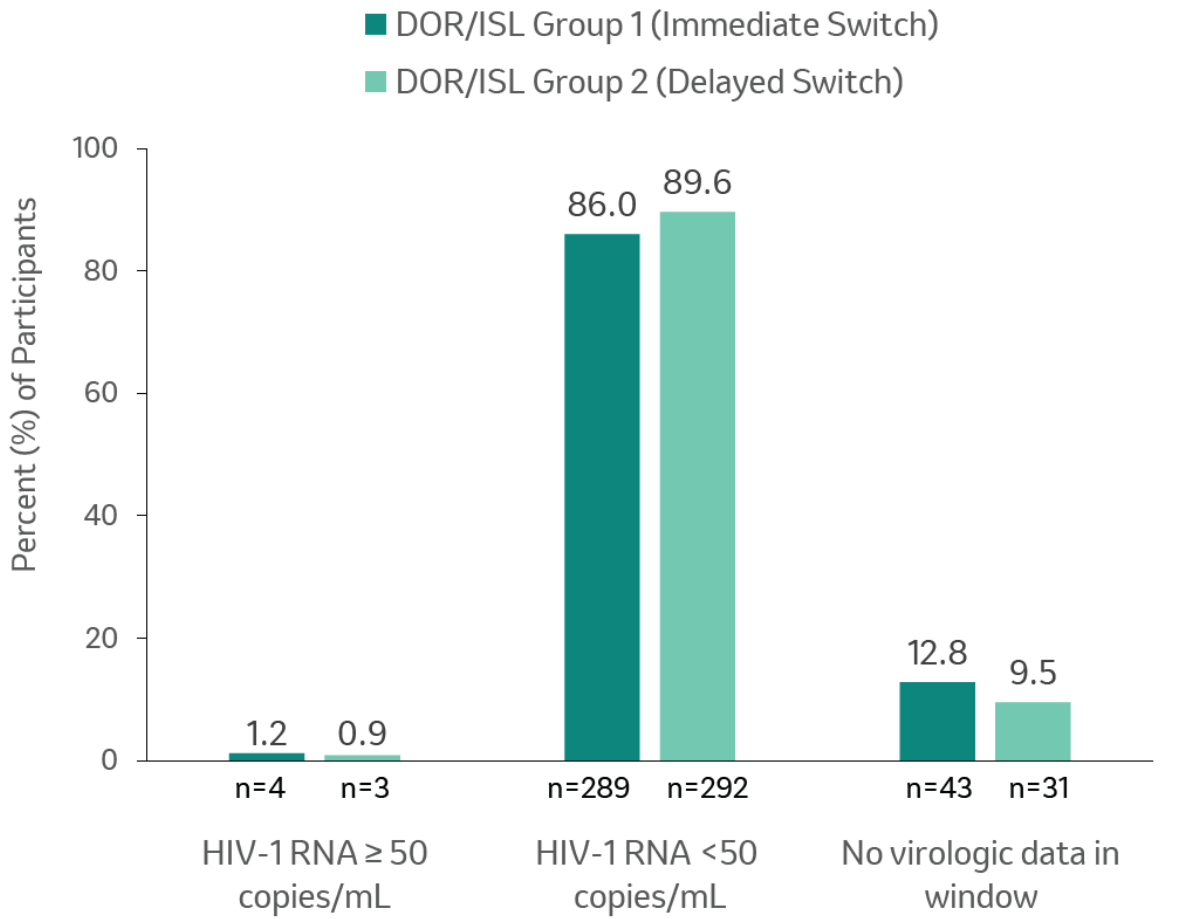


[a]V106A/M, V108I, Y188L, H221Y, P225H, F227C/L, M230I/L, L234I, P236L or Y318F.

MSD

Virologic Outcomes, Week 96 (FDA Snapshot Approach)

- Virologic suppression was maintained through week 96 after switch to DOR/ISL on day 1 (Group 1) or at week 48 (Group 2)
  - HIV-1 RNA ≥50 c/mL in 1.2% and 0.9%, respectively
- No confirmed viremia (HIV-1 RNA ≥200 c/mL) in either group
- Using the Observed Failure approach, 96.5% (275/285) and 94.3% (282/299), respectively, had HIV-1 RNA <50 c/mL at week 96



Molina MK-8591A Switch to DOR w/ISL 96wk EACS 2023

MSD

Lymphocyte and CD4+ T-cell Count Adverse Events

n (%) of participants with:	Week 0 to 48		Week 48 to 96	
	Group 1: DOR/ISL N=336	Group 2: bART N=336	Group 1:DOR/ISL N=322	Group 2: DOR/ISL N=326
Total lymphocyte count decreased[a]	0	0	63 (19.6)	44 (13.5)
Treatment-related[b] AE	0	0	47 (14.6)	28 (8.6)
Discontinuation due to AE	0	0	7 (2.2)	6 (1.8)
Serious AE	0	0	0	0
CD4+ T-cell count decreased[a]	2 (0.6)	0	40 (12.4)	37 (11.3)
Treatment-related[b] AE	1 (0.3)	0	25 (7.8)	24 (7.4)
Discontinuation due to AE	0	0	6 (1.9)	3 (0.9)
Serious AE	0	0	0	0

[a]Increased frequency of monitoring and specific criteria for reporting lymphocyte and/or CD4+ T-cell declines were implemented after week 48 by protocol amendment.
[b]Considered by the investigator to be related to the study drug.
Molina MK-8591A Switch to DOR w/ISL 96wk EACS 2023


3 Drugs
2 Drugs
Long Acting

5/588 (0.9%) of cases experienced virological failure

2 failed with INI & NNRTI mutations

Patient #1. INI: 155H RT: 101E+138K+230L

Patient #2: INI 138K+148R RT: 101E+138K

1,593 patients with >1 clinical visit

588 cases; 1,005 controls

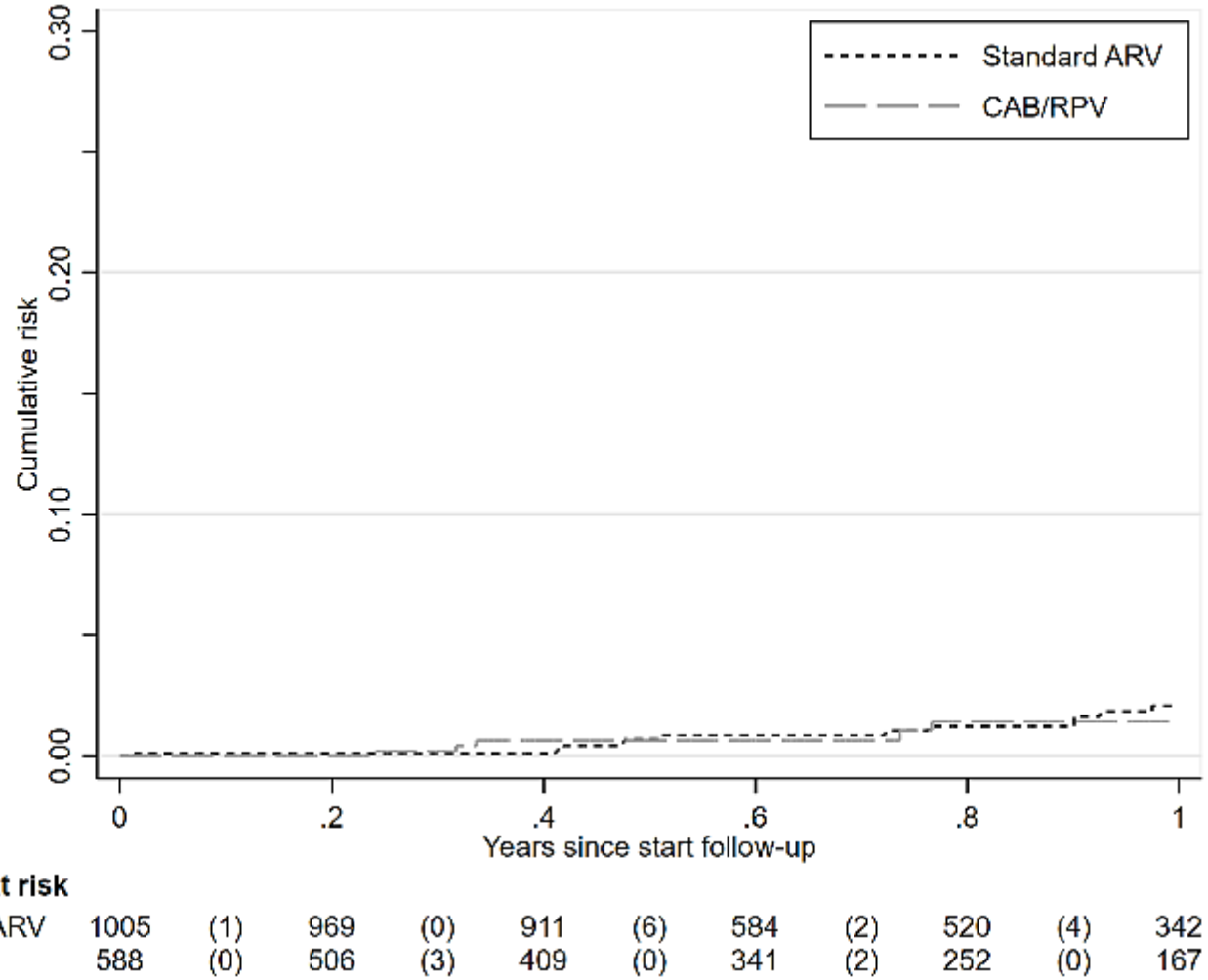
Median follow-up time 0.8 years [IQR 0.5-1.1]

58 (9%) discontinued long-acting CAB/RPV

- Restricted mean survival time cases: 0.763
- Restricted mean survival time controls: 0.763

- **No difference**
  - **Difference between mean survival time=0.000, p=0.977**

Effectiveness of Long-Acting Injectable Cabotegravir and Rilpivirine for the Treatment of HIV-1: Results From the Dutch ATHENA National Observational Cohort



Jongen et al. EACS 2023; Warsaw, Poland. Slides PS8.O3.

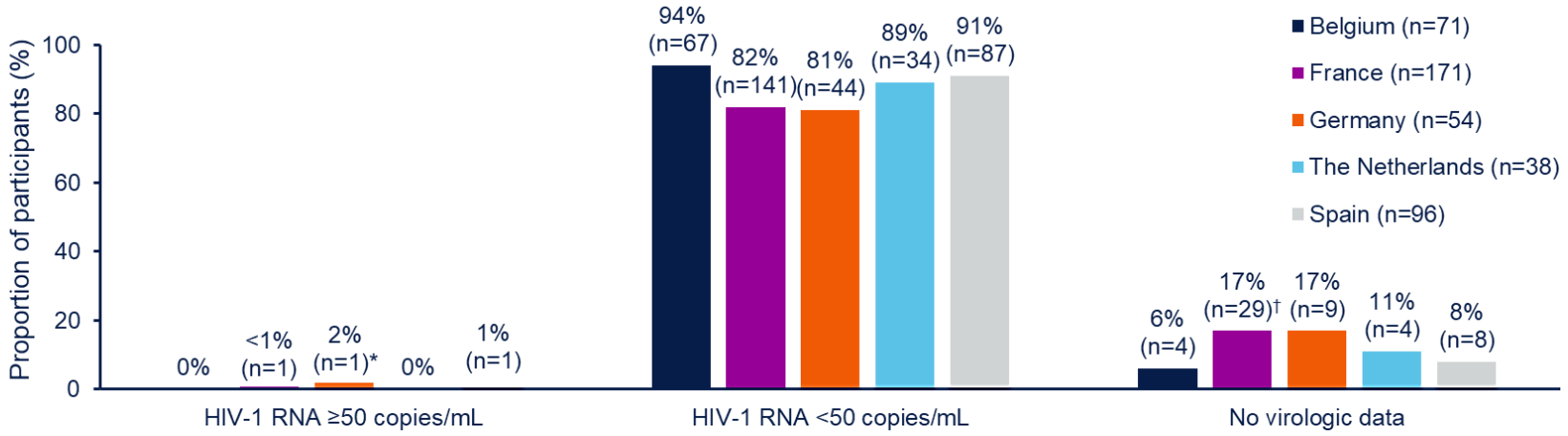
CARISEL Study Design

- The CARISEL study was primarily designed to evaluate the perceived acceptability, appropriateness, and feasibility of CAB + RPV LA implementation for staff study participants
- Clinics with no prior experience with administering CAB + RPV LA were preferentially selected for study participation
- For PSPs, CARISEL was designed as a single-arm, unblinded, interventional study in which all participants who fulfilled eligibility requirements were assigned to receive CAB + RPV LA Q2M
- In this *post hoc* analysis, data from participants receiving CAB + RPV LA in CARISEL were stratified by country (Belgium, France, Germany, the Netherlands, and Spain) and are summarized descriptively

*437 PSPs enrolled, and 430 received CAB + RPV LA. PSPs were ≥18 years of age, receiving a highly active ART regimen for ≥6 months prior to screening, had plasma HIV-1 RNA <50 copies/mL at screening as well as twice in the 12 months prior to screening, and no prior CVF. †Dose 1 was received at Month 1, Dose 2 at Month 2, with the remaining doses Q2M thereafter.
ART, antiretroviral therapy; CAB, cabotegravir; CVF, confirmed virologic failure; LA, long-acting; OLI, oral lead-in; PSP, patient study participant; Q2M, every 2 months; RPV, rilpivirine.

Virologic Response at Month 12

- At Month 12, rates of virologic non-response (HIV-1 RNA ≥50 copies/mL) and suppression (HIV-1 RNA <50 copies/mL) with CAB + RPV LA ranged 0–2% and 81–94%, respectively, across countries
- Overall, one participant (0.23%) in Germany met the CVF criterion with a viral load of 1861 copies/mL at discontinuation (Month 10)[1]
- An additional participant in Spain met the SVF criterion (HIV-1 RNA ≥200 copies/mL) at Month 4 and again at last visit prior to withdrawal (Month 6); neither were confirmed upon retest

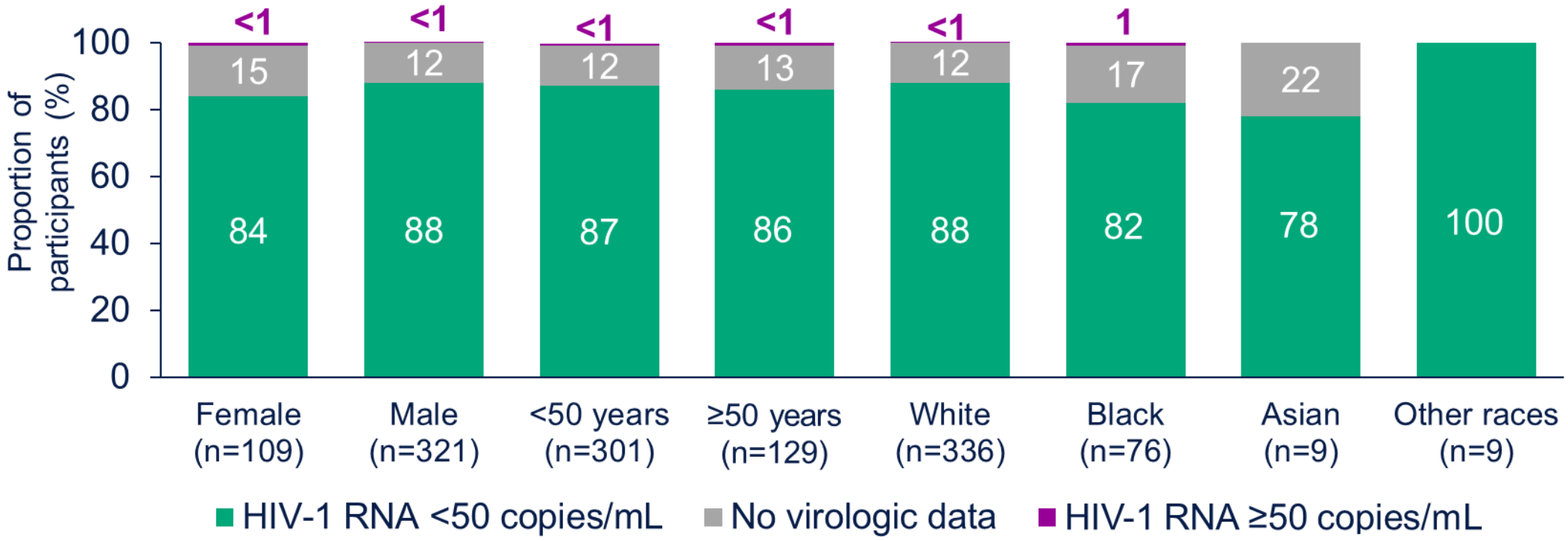


*Participant met the CVF criterion. †Six participants at one site in France had a missed viral load assessment at Month 12 and had HIV-1 RNA <50 copies/mL at Month 14.
CVF, confirmed virologic failure.

1. Jonsson-Oldenbüttel et al. IAS 2022; Virtual and Montreal, Canada; Poster EPLBB05.

Virologic Response at Month 12

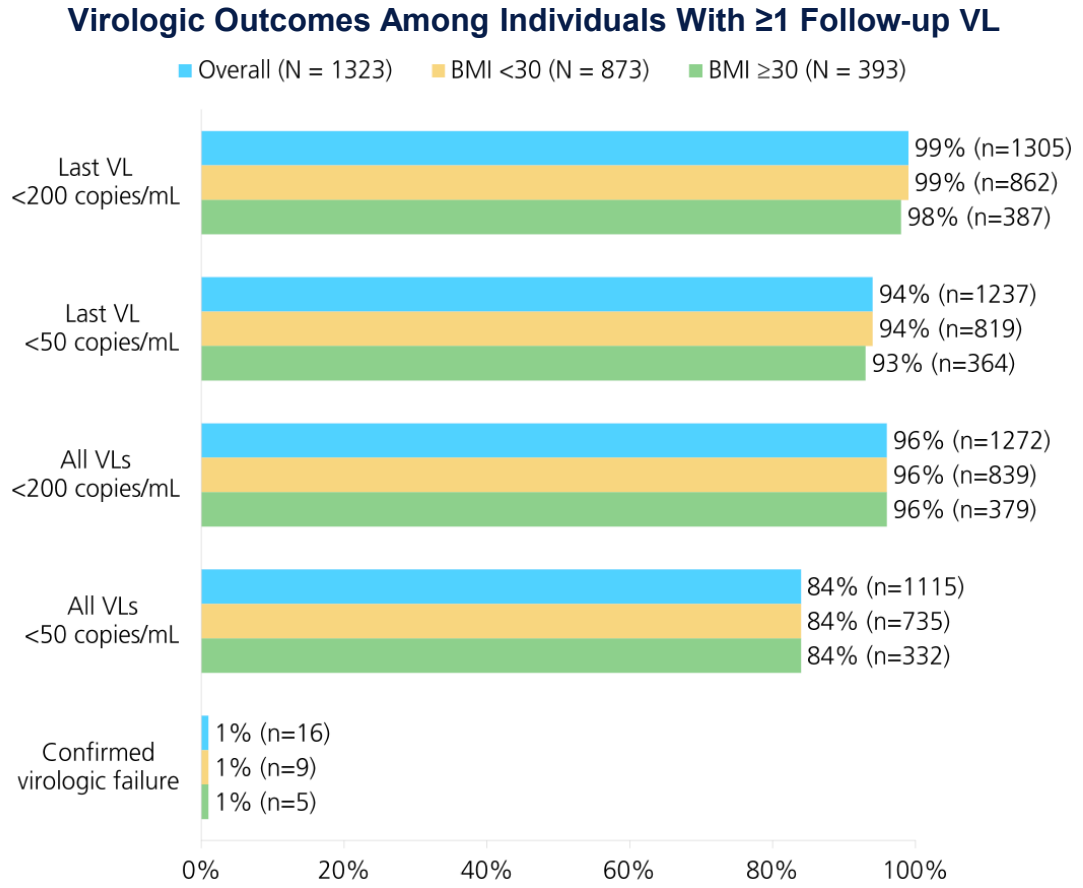
- At Month 12, rates of virologic suppression (HIV-1 RNA <50 copies/mL) with CAB + RPV LA ranged 78–100% across subgroups, and rates of non-response (HIV-1 RNA ≥50 copies/mL) ranged 0–1%



Ghosn et al. EACS 2023; Warsaw, Poland. Poster eP.A.100.

Real-world Effectiveness of CAB + RPV LA in Virologically Suppressed Individuals: 2 Years of Data From the OPERA® Cohort (cont)

- In this large cohort, CAB + RPV LA was effective at controlling HIV
- 96% (1272/1323) maintained VL <200 copies/mL throughout follow-up
- 94% (1237/1323) had VL <50 copies/mL at the end of follow-up
- Virologic outcomes were comparable between individuals with BMI <30 and ≥30 kg/m^2



BMI, body mass index; CAB, cabotegravir; HIPAA, Health Insurance Portability and Accountability Act; LA, long-acting; RPV, rilpivirine; VL, viral load.
[a]Includes 72 individuals without a baseline BMI who were excluded from the stratified analysis. [b]HIPAA privacy requirements preclude the reporting of 5 or fewer observations in any cell.

VL <200 copies/mL was maintained in 96% of individuals throughout follow-up and virological outcomes were comparable regardless of BMI

Sension et al. IDWeek 2023; Boston, MA. Poster 1608.

Real-world Utilization and Effectiveness of CAB + RPV LA Among People With HIV and Detectable VL at Initiation: Trio Cohort Study

- **Study design:** Observational, prospective cohort study
- Adults who received ≥1 CAB + RPV LA injection through July 2023 with a recorded VL ≥50 copies/mL at initiation were identified from the Trio Health HIV Network
- Among 315 individuals with CAB + RPV LA injections, 32 (10%) had VL ≥50 copies/mL at initiation
  - Results were stratified by VL ≥50 and ≥200 copies/mL at CAB + RPV LA initiation
- Historical HIV genotype results were available for 16/32 (50%) individuals
  - 1 individual had low-level resistance to CAB and had a follow-up VL <50 copies/mL
  - 5 individuals had NNRTI mutations, 1 with low-level resistance to RPV, all with follow-up VL <200 copies/mL

CAB, cabotegravir; IQR, interquartile range; LA, long-acting; NNRTI, non-nucleoside reverse transcriptase inhibitor; RPV, rilpivirine; VL, viral load.

Virologic Outcomes by VL at CAB + RPV LA Initiation

n (%) unless specified	VL ≥50 copies/mL at initiation (N=32)	VL 50–199 copies/mL at initiation (N=18)	VL ≥200 copies/mL at initiation (N=14)
Median follow-up, months (IQR)	5 (3, 8)	5 (3, 10)	5 (4,7)
On CAB + RPV at end of follow-up	31 (97)	18 (100)	13 (93)
≥1 VL test after CAB + RPV injection	24 (75)	14 (78)	10 (71)
Last recorded VL			
<50 copies/mL	19/24 (79)	11/14 (79)	8/10 (80)
<200 copies/mL	21/24 (88)	13/14 (93)	8/10 (80)
≥200 copies/mL	3/24 (12)	1*/14 (7)	2**/10 (20)

*Last VL 205; 1 injection administered. **(1) Baseline VL 2138, last VL 1148; 3 injections administered. (2) Baseline VL 616, last VL 3715; 1 injection administered.

- At time of analysis, 31/32 (97%) individuals remained on CAB + RPV LA with a median follow-up of 5 months (IQR, 3-8)
- 24 (75%) individuals had a follow-up VL
- Of those, last recorded VL before end of follow-up was <50 copies/mL in 19 individuals (79%), <200 copies/mL in 21 (88%), and 3 (12%) with VL >200 copies/mL

These data show high rates of virologic suppression in individuals who received CAB + RPV LA with ≥50 copies/mL at initiation

Use of CAB + RPV LA in individuals who are not virologically suppressed (HIV-1 RNA <50 copies/mL) is outside of the labelled indication

Elion et al. IDWeek 2023; Boston, MA. Poster 1592.

Uptake and Discontinuation of the Long-Acting Duo in the Swiss HIV Cohort Study: Preliminary Analysis on Cabotegravir + Rilpivirine

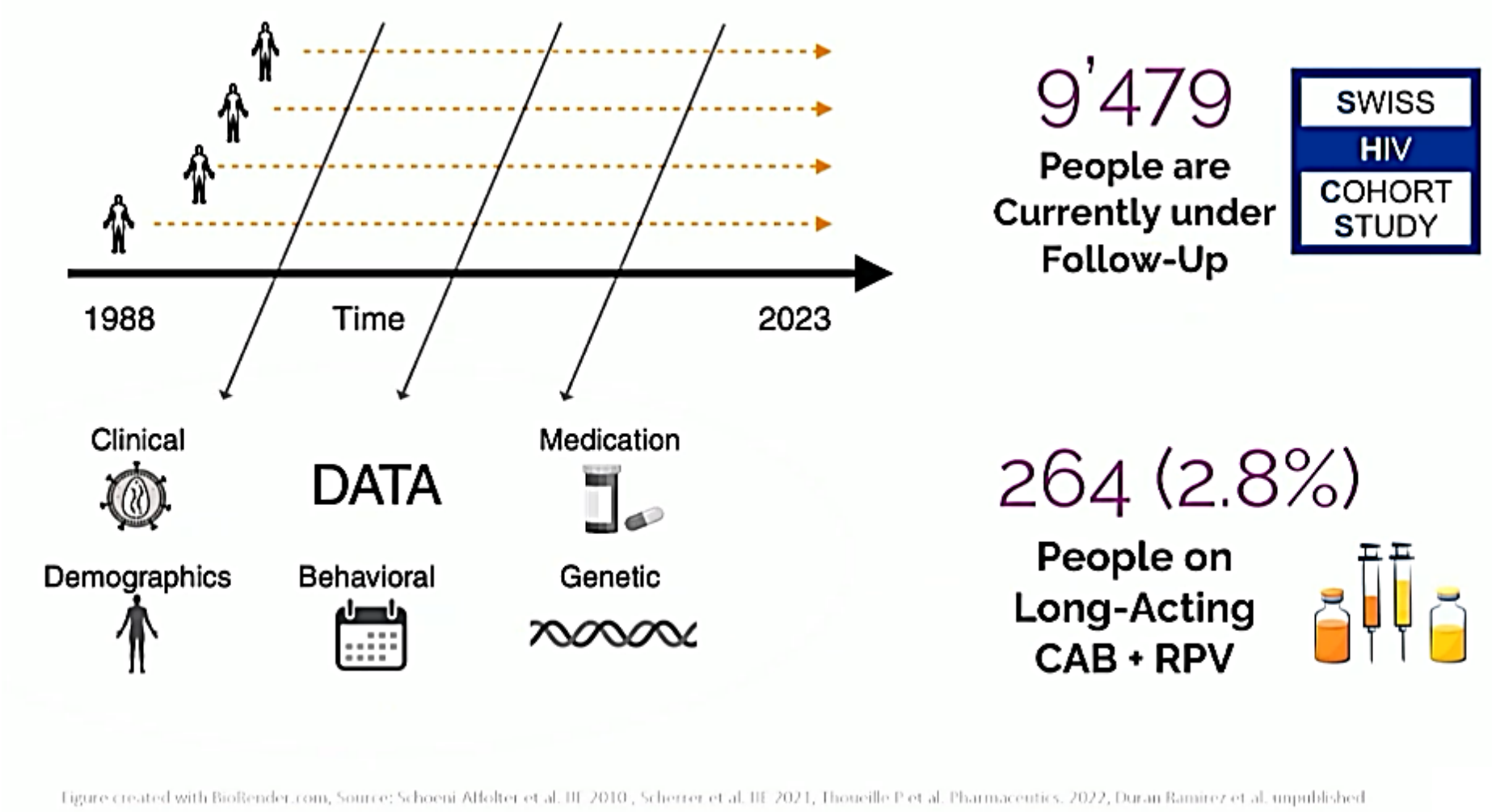
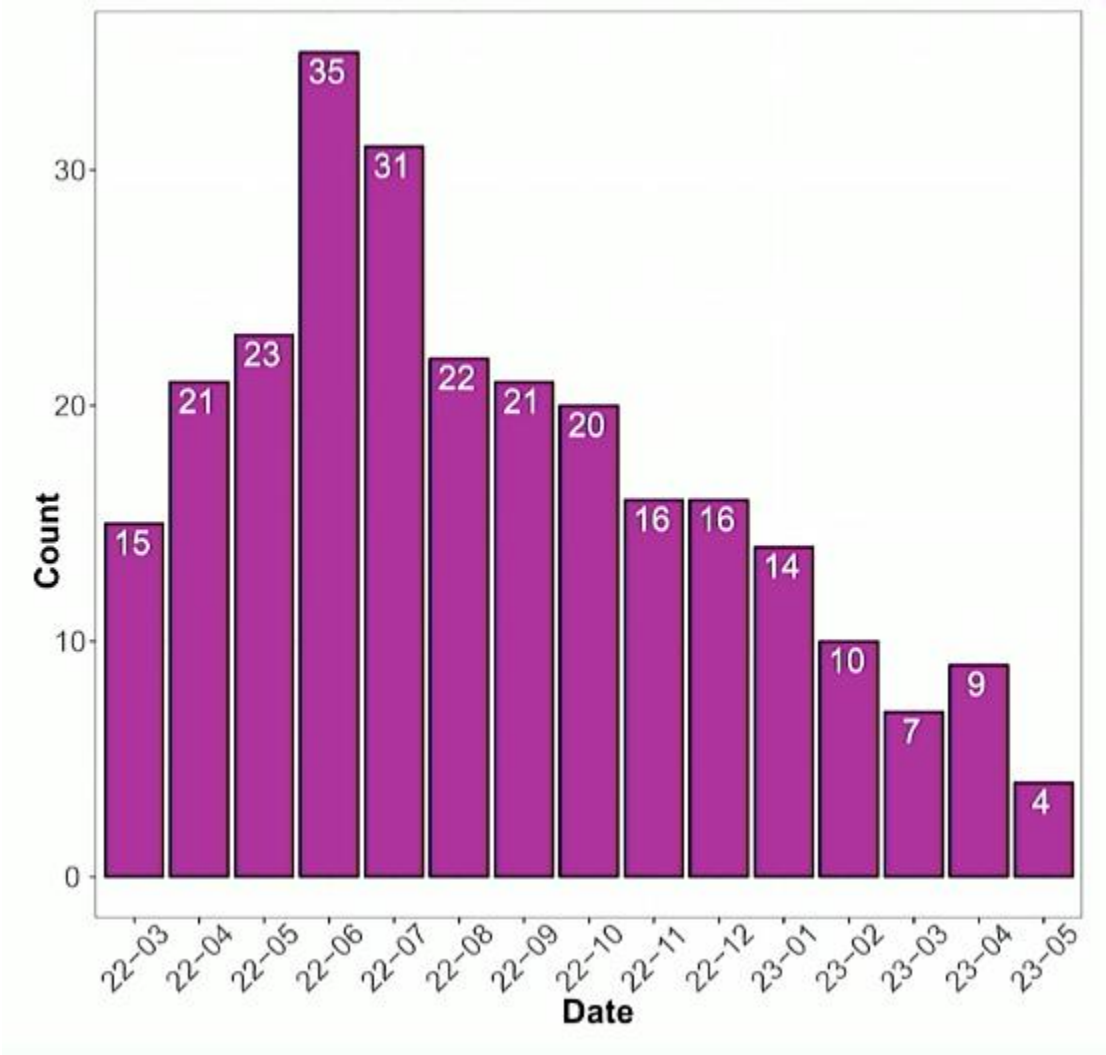


Figure created with BioRender.com, Source: Schoeni Affolter et al. IE 2010, Scherrer et al. IE 2021, Thouaille P et al. Pharmaceutics. 2022, Duran Ramirez et al. unpublished

[[Note: Data not able to be fully verified from source photo.]]

Initial Peak and Decline of Uptake



Reason for Uptake:
EACS Poster Yonas, Martin et al. Who wants to switch to injectable?

12 participant initiated within clinical trials. Due to the bi-annual Swiss HIV Cohort Study visit schedule, data may be suspect to delay by up to 6 months.

Conclusions

A Small Proportion Initiated Long-Acting CAB+RPV

264 (2.8%) 

Middle-aged White Men who have Sex with Men

216 (82%) ♂

Low Number of Long-Acting CAB+RPV Discontinuation for Diverse Reasons

8 (3.0%) 

Duran Ramirez et al. EACS 2023; Warsaw, Poland. Slides PS8.O2.

SOLAR Study Design and Baseline Characteristics

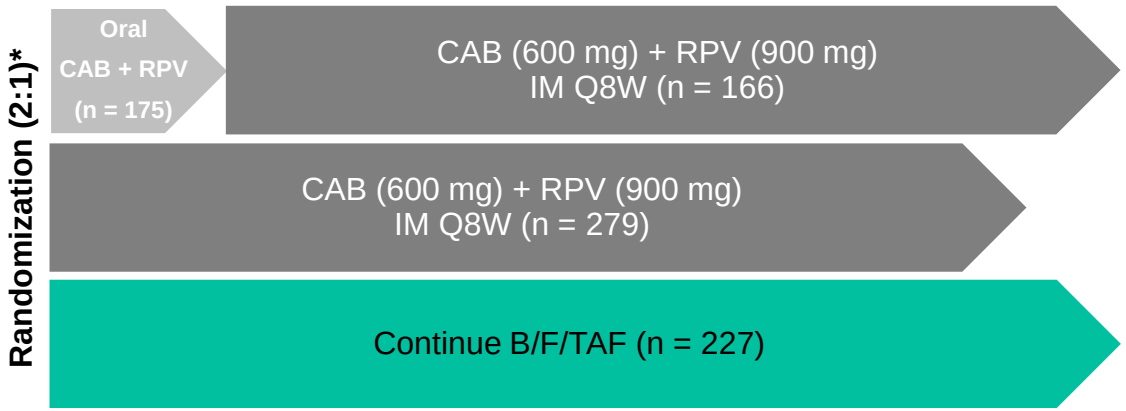
Design: Phase 3b, Randomized, Multicenter, Parallel-Group, Open-Label Study

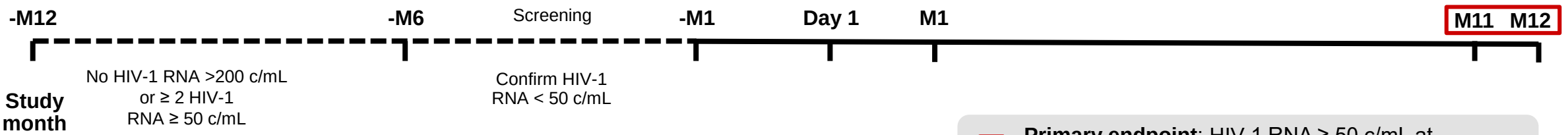
Screening

- Age ≥ 18 years
- On uninterrupted B/F/TAF for ≥ 6 months with VL < 50 c/mL
- B/F/TAF as first or second regimen
- No history of non–INSTI-based regimen use
- No resistance to B/F/TAF or CAB + RPV components
- No HBV co-infection
- No moderate to severe hepatic impairment and eGFR ≥ 30mL/min
- No conditions that may interfere with injections

N = 837

Maintenance





Primary endpoint: HIV-1 RNA ≥ 50 c/mL at Month 11/12 (FDA Snapshot; 4% NI margins)

*Participants randomized to the CAB + RPV treatment group were offered an optional oral lead-in; the decision was determined by the participants following informed consent discussions with the investigator. M, month; NI, noninferiority; Q8W, every 8 weeks; VL, viral load

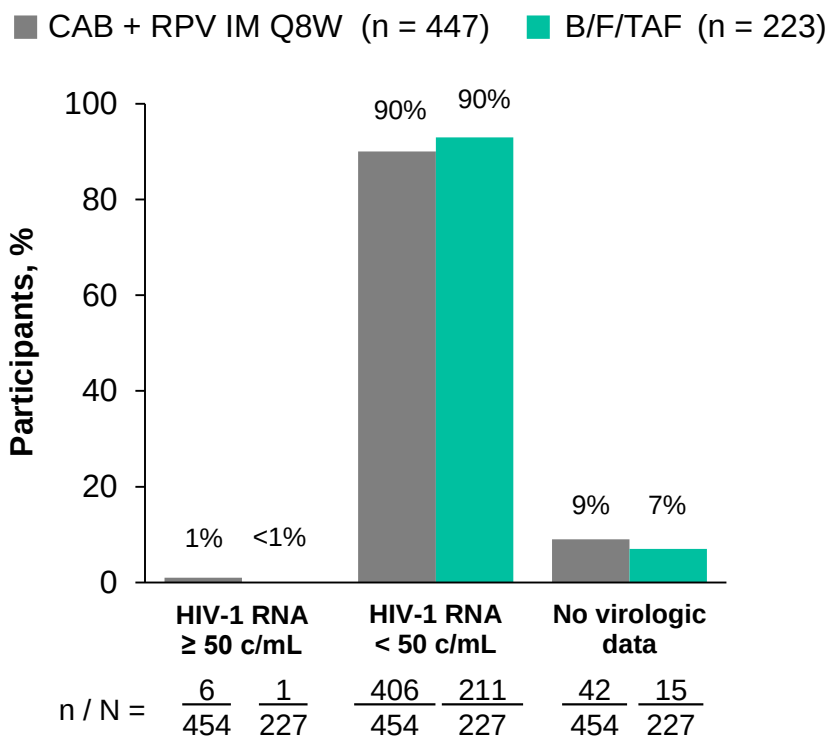
Ramgopal MN, et al. CROI 2023, Oral 191

Baseline Characteristics and Virologic Outcome at Month 12

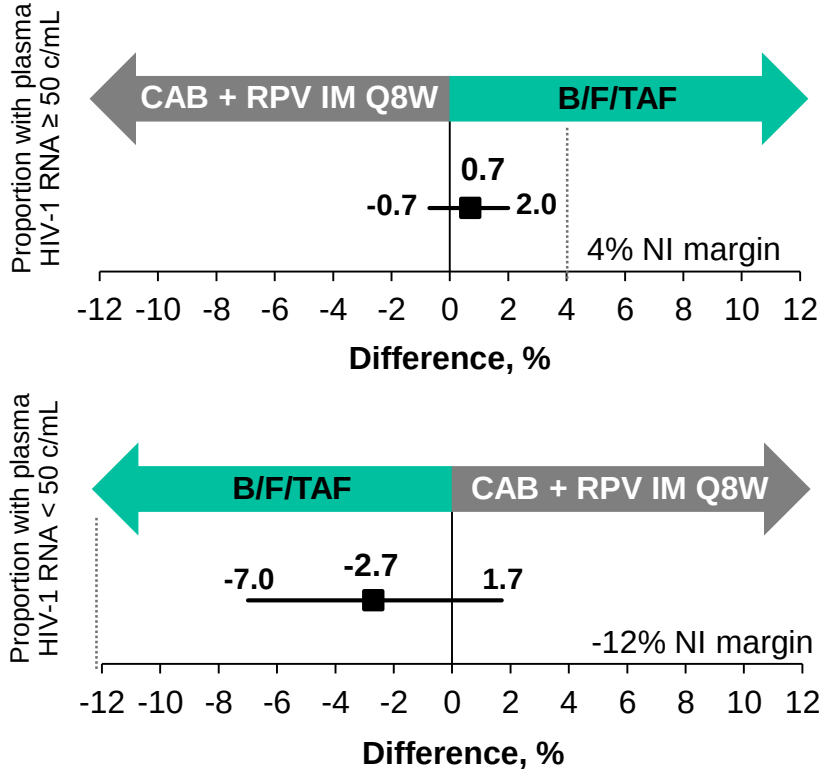
Baseline Characteristics

	CAB + RPV Q8W (n = 447)	B/F/TAF (n = 223)
Age, years, median (range)	37 (18–74)	37 (18–66)
Female sex at birth, n (%)	77 (17)	41 (18)
Race		
White	307 (69)	156 (70)
Black	95 (21)	49 (22)
BMI, kg/m^2, median (IQR)	26 (23–29)	25 (23–30)

Virologic Outcomes (mITT-E Population*,†)



Adjusted Treatment Differences (95% CI)



At M12, noninferiority was established

(1% with HIV-1 RNA >/= 50 copies/mL on CAB+RPV IM Q8W vs. <1% with B/F/TAF)

*At Month 12, CAB + RPV was noninferior to B/F/TAF in the mITT-E, ITT-E and per-protocol populations. ITT-E: 89% (n = 406/454) and 93% (n = 211/227) of participants receiving CAB + RPV and B/F/TAF demonstrated virologic success (HIV RNA < 50 c/mL); 1% (n = 6/454) and < 1% (n = 1/227) of participants receiving CAB + RPV and B/F/TAF showed virologic nonresponse (HIV ≥ 50 c/mL); †mITT-E excluded 11 participants due to protocol deviations. (m)ITT-E, (modified) intent-to-treat–exposed; Q8W, every 8 weeks

Ramgopal MN, et al. CROI 2023, Oral 191

Confirmed VF and Resistance at Month 12

Participants With CVF in the CAB + RPV Q8W Group

Sex, BMI (kg/m^2), country, HIV subtype	VL at SVF, c/mL	Month at SVF	Baseline RAMs		On-treatment RAMs SVF timepoint		Post-CVF regimen
			NNRTI	INSTI	NNRTI	INSTI	
M, ≥ 30, U.S., C*	3,797	3	N/A	N/A	**E138E/K + Y181Y/C**	None	Resuppressed on B/F/TAF[2]
M, < 30, Italy, B	1,327	6	None	None	**M230L**	**Q148R**	Resuppressed on DRV/c/F/TAF
M, < 30, Spain, AE	6,348	11	None	G140G/R	**K101E**	**G118R**	Resuppressed on B/F/TAF → DRV/c/F/TAF

All 3 cases of CVF were in the CAB + RPV group and all developed treatment-emergent resistance (2 with INSTI resistance); no participant on B/F/TAF developed CVF or resistance

*Participant in the ITT-E population.

Red bolded text indicates treatment emergent RAMs

CVF, confirmed virologic failure (two consecutive measurements of HIV-1 RNA > 200 c/mL); ITT-E, intent-to-treat–exposed; N/A, not applicable; Q8W, every 8 weeks; SVF, suspected VF; VL, viral load

1 Ramgopal MN, et al. CROI 2023, Oral 191; 2. Personal communication with the investigator

Safety at Month 12

Safety at Month 12 (excluding ISRs)

Event, n (%)	CAB + RPV Q8W (n = 447)	B/F/TAF (n = 223)
Any AE	349 (77)	172 (76)
Drug-related	90 (20)	2 (< 1)
AEs leading to withdrawal	16 (4)	2 (< 1)
Drug-related	9 (2)	0
Any serious AEs	21 (5)	15 (7)
Drug-related	3 (< 1)	0

Safety at Month 12 (including ISRs)

- **Drug-related AEs (including ISRs)[1]**
  - 72% CAB + RPV vs. < 1% B/F/TAF
- **In the CAB + RPV group:[2-3]**
  - Most common drug-related AEs: ISRs (70%)[2], pyrexia (3%)[3], headache (2%)[3], fatigue (2%)[3] and diarrhea (2%)[3]
  - 11 participants (2%) discontinued due to ISRs[3]
- **No clinically relevant changes in metabolic syndrome or insulin resistance between groups at Month 12[4]**

Drug-related AEs and AEs leading to withdrawal were higher in CAB + RPV study group

ISR, injection-site reaction; Q8W, every 8 weeks

1. Ramgopal MN, et al. CROI 2023, Abstract 191; 2. SOLAR: New Findings, Viiv Healthcare, https://cabenuvahcp.com/content/dam/cf-viiv/cabenuva-hcp/master/pdfs/cabenuva_new_findings.pdf Accessed March 10, 2023;
3. Ramgopal MN, et al. CROI 2023, Oral 191; 4. Tan DHS, et al. CROI 2023, Oral 146

Multivariable CAB+ RPV LA Pooled CVFs Analysis

A combination of at least two baseline factors contributed including RPV RAMs, subtype A6/A1 or BMI ≥30 kg/m2

Study	ID	CAB PK† ≤Q1	RPV PK† ≤Q1	Subtype A6/A1	Baseline IN L74I‡	Baseline INSTI mutation	Baseline RPV RAM	Baseline NNRTI RAM	Female at birth	BMI ≥30	Q8W
ATLAS-2M	1	√	√		√	√	√	√	√	√	√
ATLAS-2M	2	√	√	√	√				√	√	√
ATLAS	3	√	√	√	√		√		√		
ATLAS	4	√	√				√	√	√	√	
FLAIR	5	√	√	√	√			√		√	
FLAIR	6	√	√	√	√				√	√	
FLAIR	7	√	√	√	√				√	√	
ATLAS-2M	8			√	√		√	√	√	√	√
ATLAS-2M	9	√	√								
ATLAS	10		√	√	√						
ATLAS-2M	11						√	√		√	√
ATLAS-2M	12		√								√
ATLAS-2M	13							√			
ATLAS-2M	**14**				√		√	√			√

No single baseline factor alone was predictive of failure (0/24 participants with baseline archived RPV RAMs as the only factor, had CVF).

*13 of 17 participants who met the CVF criterion were CAB + RPV naive at study entry and received at least one dose of CAB + RPV LA.
†CAB and RPV PK refer to Week 8 trough concentrations (4 weeks following first injection).
‡Baseline L74I IN polymorphism excluding M mixtures.
BMI, body mass index (kg/m²); CAB, cabotegravir; CVF, confirmed virologic failure; IN, integrase; INSTI, integrase strand transfer inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PK, pharmacokinetic; Q1, 1st quartile; Q8W, every 8 weeks; RAM, resistance-associated mutation; RPV, rilpivirine.

Margolis et al. HIV Glasgow 2020

LEN + bNAbs

‡

LEN With bNAbs Teropavimab and Zinlirvimab in PLWH (GS-US-536-5816)

N = 21

VS PLWH, aged ≥ 18 years

Outcomes

Primary: Safety and tolerability

Secondary: HIV-1 RNA < 50 and ≥ 50 c/mL at Week 26 (FDA Snapshot); PK

2021–present (ongoing)

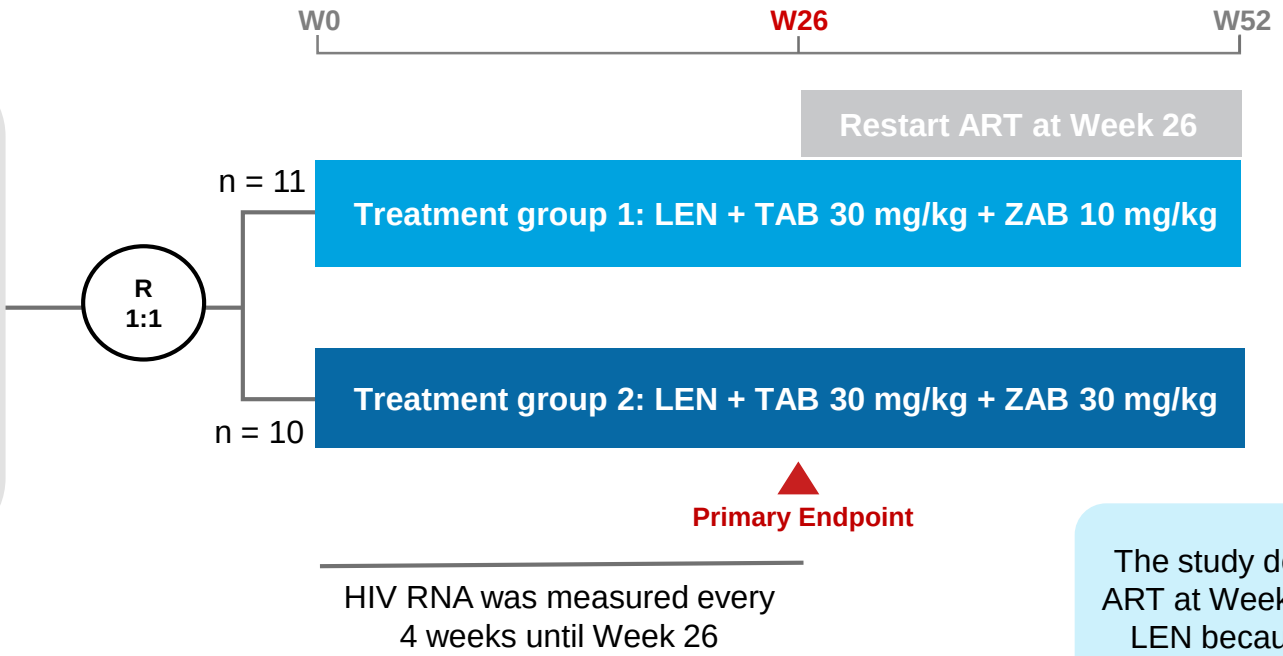
Adults living with HIV-1

VS ≥ 18 months*

Met susceptibility criteria for TAB and ZAB†

CD4 at entry ≥ 500 cells/μL

CD4 nadir ≥ 350 cells/μL



Dosing	Day 1	Day 2
LEN oral 600 mg		
LEN SC 927 mg		–
TAB IV 30 mg/kg		–
ZAB IV 10 mg/kg or 30 mg/kg		–

The study design was amended to have participants restart ART at Week 26 after the FDA clinical hold on investigational LEN because of compatibility issue with borosilicate vials

*Previous virologic failure was allowed as long as participants were VS for ≥ 18 months prior to screening

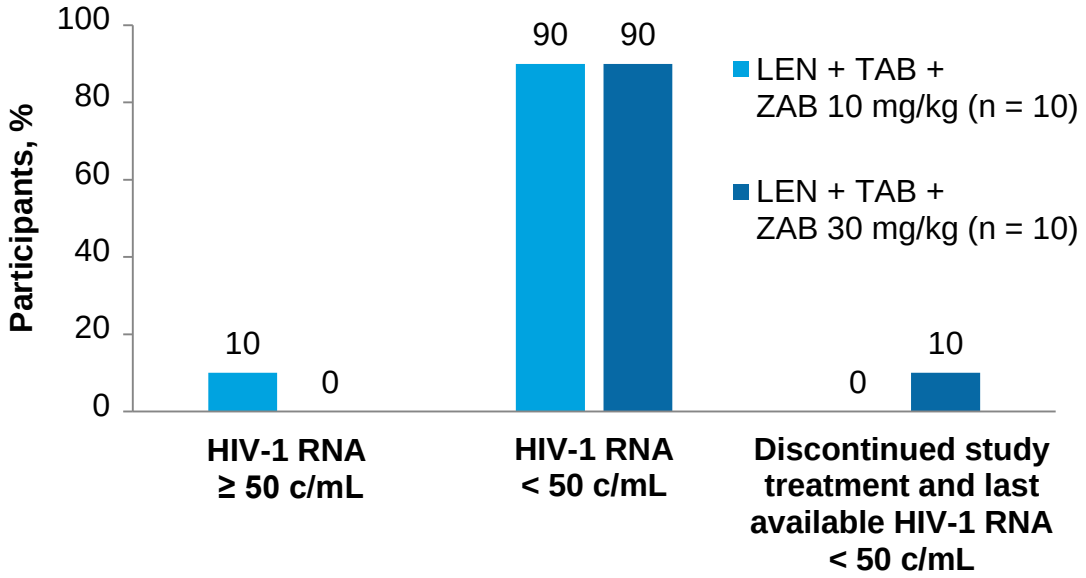
†Susceptibility defined as IC_{90} ≤ 2 μg/mL to each antibody by PhenoSense mAb Assay (Monogram Biosciences)

bNAb, broadly neutralizing antibody; IC_{90}, 90% inhibitory concentration; PK, pharmacokinetics; R, randomized; TAB, teropavimab; VS, virologically suppressed; W, Week; ZAB, zinlirvimab

Eron J, et al. CROI 2023, Oral 193

Week 26: Efficacy and Safety

Virologic Outcomes at Week 26



- One participant withdrew at Week 12 with HIV-1 RNA < 50 c/mL
- One participant had a confirmed virologic rebound at Week 16
- CD4 cell counts remained stable over the course of the study period

Safety and Tolerability

- There were no SAEs, no Grade 4 AEs and no AEs that led to study treatment discontinuation
- There were two Grade 3 AEs:
  - One injection-site cellulitis on Day 1, which resolved with antibiotics
  - One injection-site erythema on Day 3, which resolved without intervention by Day 10
- AEs occurring in ≥ 3 participants:
  - Injection-site pain
  - Erythema
  - Nodule
  - Induration
  - Mass
  - COVID-19
  - Upper respiratory tract infection

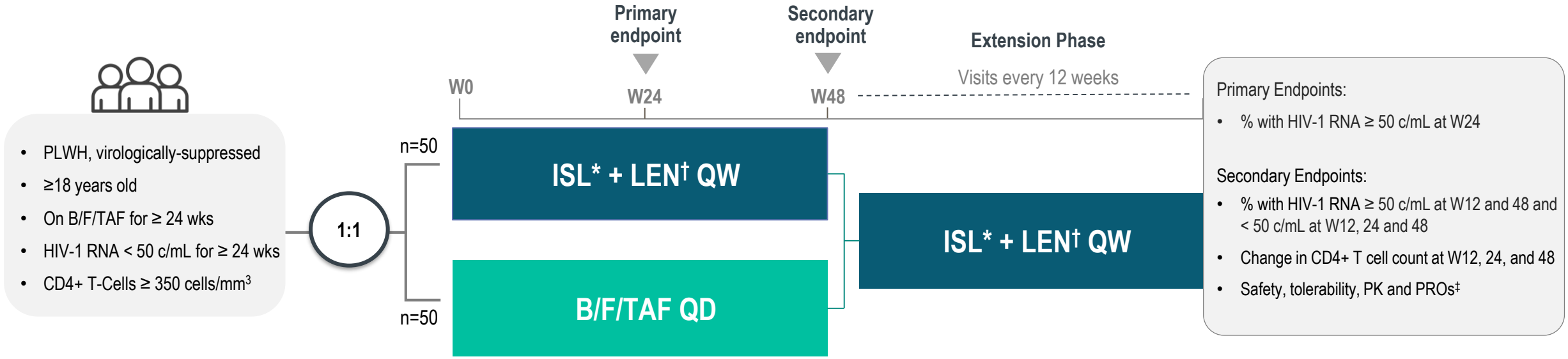
Combination of the bNAbs TAB and ZAB with LEN can sustain VS for 6 months in selected PLWH; Gilead has announced a planned Phase 2 study of LEN + TAB + ZAB in VS PLWH

bNAb, broadly neutralizing antibody; TAB, teropavimab; VS, virologically suppressed/virologic suppression; ZAB, zinlirvimab

Eron J, et al. CROI 2023, Oral 193

ISL + LEN Long-Acting Oral Weekly in PLWH who are Virologically-Suppressed

Phase 2, randomized, open-label, active-controlled, multicenter study to evaluate safety, efficacy, and PK of ISL + LEN in PLWH who are virologically suppressed (N=100)#



*ISL dosing: Day 1: 2 mg [2 × 1 mg capsule]; Day 8 and every week thereafter: 2mg [2 x 1 mg capsule]
†LEN dosing: Day 1: 600 mg [2 × 300 mg tablets]; Day 2: 600 mg [2 × 300 mg tablets]; Day 8 and every week thereafter: 300 mg [1 x 300 mg tablet]
Study design, inclusion criteria, and endpoints depicted for Cohort 2
‡ PROs are exploratory endpoints

B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; ISL, islatravir; LAO, long-acting oral; LEN, lenacapavir; Ph2, Phase 2; PK, pharmacokinetics; PLWH, people living with HIV; PROs, patient reported outcomes; QD, daily; QW, every week; VS, virologically suppressed; W, week; wks, weeks

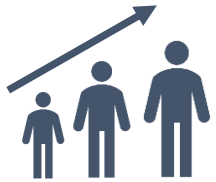
Study design Footnotes

Clinicaltrials.gov URL: https://clinicaltrials.gov/ct2/show/NCT05052996?term=lenacapavir&draw=1&rank=5. Accessed January 03, 2023
Data on file

MSD

A person-centred approach is key for the care of people living with HIV[1-5]

Several factors should be considered by people living with HIV and their HCP when initiating or switching ART:[1–5]



Age

Sex

Pregnancy

Medical history

Lifestyle

Drug use

Laboratory evaluations

Comorbidities

Drug-drug interactions

Regimen tolerability

Preference

Readiness

Socio-economic background

Mental and physical health

Taking a person-centred approach can help people living with HIV better understand the challenges ahead and enable them and their HCP to take the necessary steps to achieve long-term good health[3]

ART, antiretroviral therapy; HCP, healthcare professional; HIV, human immunodeficiency virus.

1. Lazarus JV, *et al. BMC Med.* 2016;14:94; **2.** Lazarus JV, *et al. Nat Commun*. 2021;12(1):4450; **3.** HIV Practice. From Patient Education to Patient Empowerment. Available at: www.hivpractice.com/From-Patient-Education-to-Patient-Empowerment/ (Last Accessed: July 2022); **4.** DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents. 2021. Available at: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/archive/AdultandAdolescentGL_2021_08_16.pdf (Last Accessed: July 2022); **5.** EACS guidelines. Version 11.0. 2021. Available at: https://www.eacsociety.org/media/final2021eacsguidelinesv11.0_oct2021.pdf (Last Accessed: July 2022).