TRATAMIENTO ANTIRRETROVIRAL FARMACOS COMERCIALIZADOS CROI-2020

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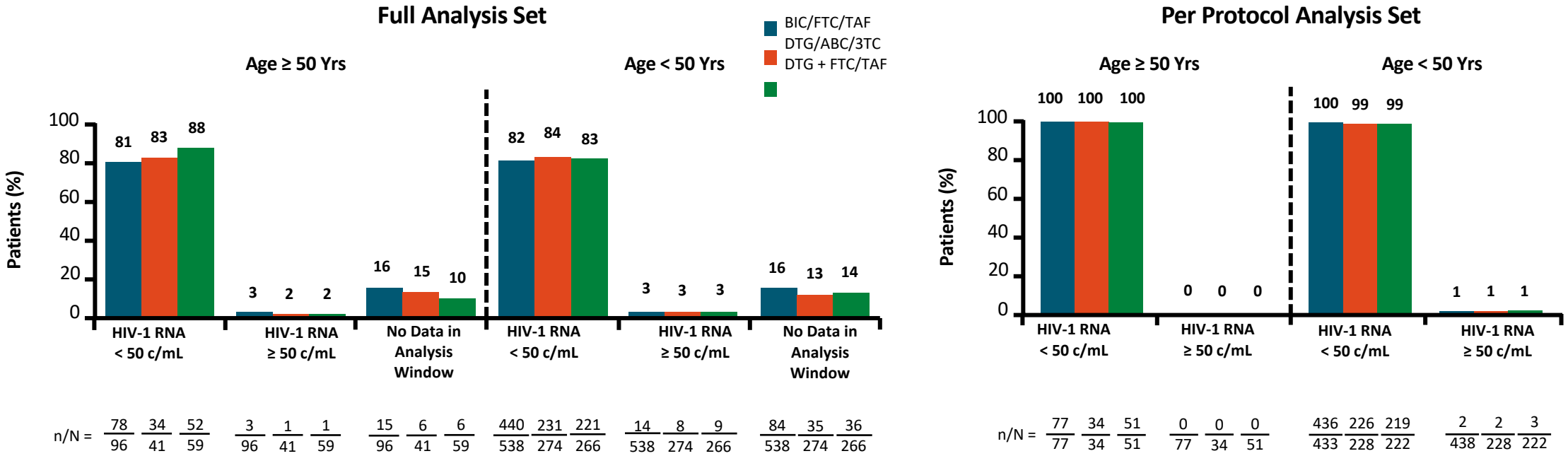
BIC/FTC/TAF IN PATIENTS ≥ 50 YRS: POOLED ANALYSIS OF STUDIES 1489 AND 1490

Virologic Outcomes at Wk 144 (FDA Snapshot)



- No resistance detected in 21 patients who met criteria for resistance testing (BIC/FTC/TAF: n = 8; DTG/ABC/3TC: n = 6; DTG + FTC/TAF: n = 7)

Source: Mills. CROI 2020. Abstr 477.

BIC/FTC/TAF IN PATIENTS ≥ 50 YRS: SAFETY OUTCOMES THROUGH WK 144

Safety Outcome	Age ≥ 50 Yrs (n = 196)			Age < 50 Yrs (n = 1078)		
	BIC/FTC/TAF (n = 96)	DTG/ABC/3TC (n = 41)	DTG + FTC/TAF (n = 59)	BIC/FTC/TAF (n = 538)	DTG/ABC/3TC (n = 274)	DTG + FTC/TAF (n = 266)
All-grade study drug-related AEs occurring In ≥ 5% patients in any group, %						
Diarrhea	4	10	3	5	3	3
Nausea	5	7	2	4	19	6
Headache	4	0	0	5	6	4
Flatulence	2	0	5	< 1	< 1	2
Hypercholesterolemia	2	0	5	< 1	0	0
Discontinuations, n (%)	2 (2)	2 (5)	4 (7)	4 (1)	3 (1)	2 (1)
Any grade 3/4 laboratory abnormality, %	26	29	27	25	25	22

- No discontinuations for renal AEs in BIC/FTC/TAF or DTG + FTC/TAF arms
- BMD changes with each treatment similar in patients aged ≥ 50 yrs vs < 50 yrs
- Lipid changes in patients aged ≥ 50 yrs similar with BIC/FTC/TAF vs comparators

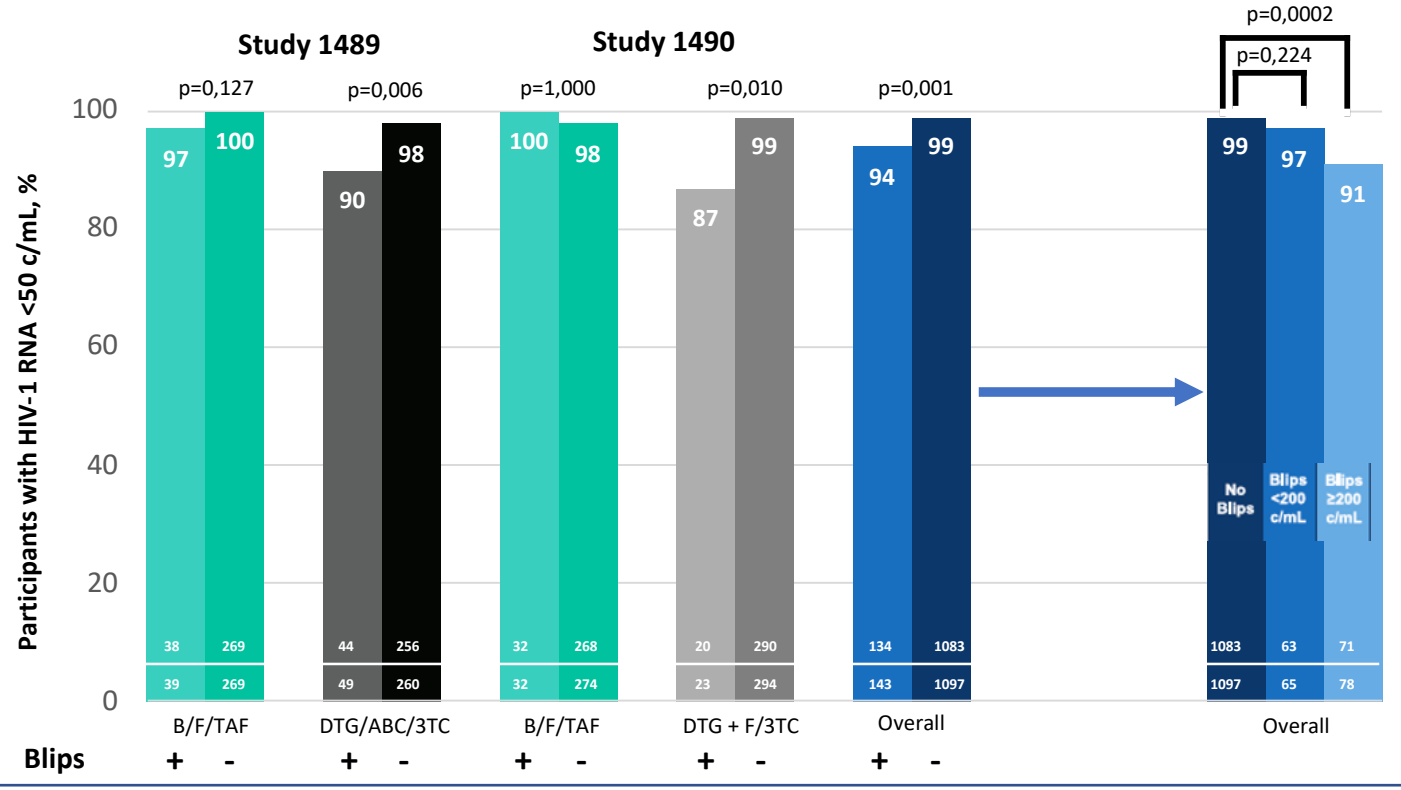
Source: Mills. CROI 2020. Abstr 477.

HIV VIRAL BLIPS IN ADULTS TREATED WITH INSTI-BASED REGIMENS THROUGH 144 WEEKS

Viral Blips through week 144

	Study 1489		Study 1490		
	B/F/TAF N=308	DTG/ABC/3TC N=309	B/F/TAF N=306	DTG + F/TAF N=317	All N=1240
Experienced Blips, % (n)	12.4% (39)	15.6% (49)	10.2% (32)	7.1% (23)	11.5% (143)

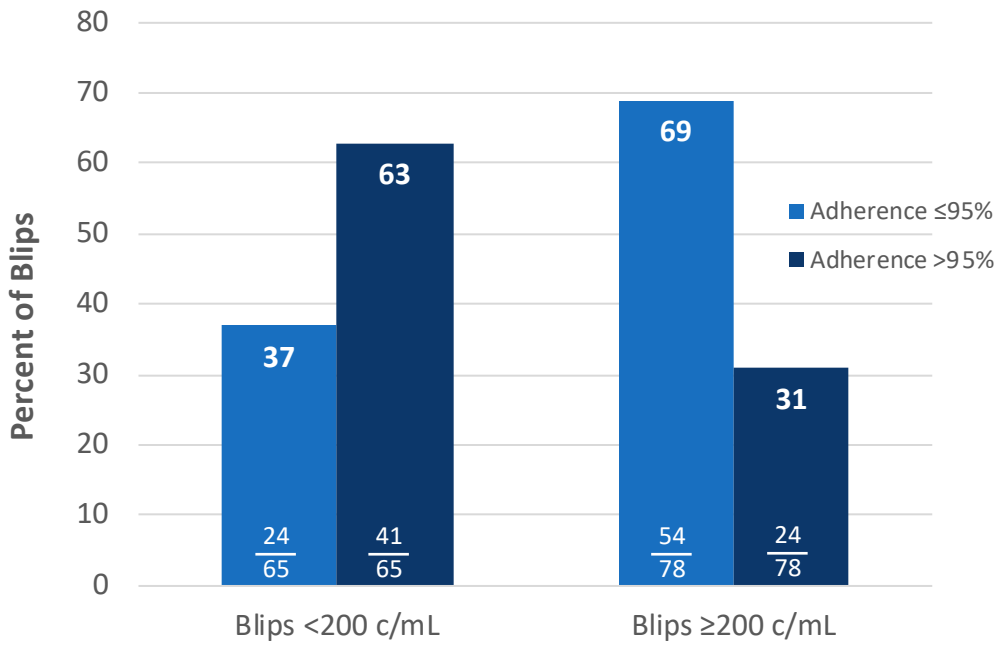
Week 144 LOCF outcomes of Participants with Blips vs. No Blips



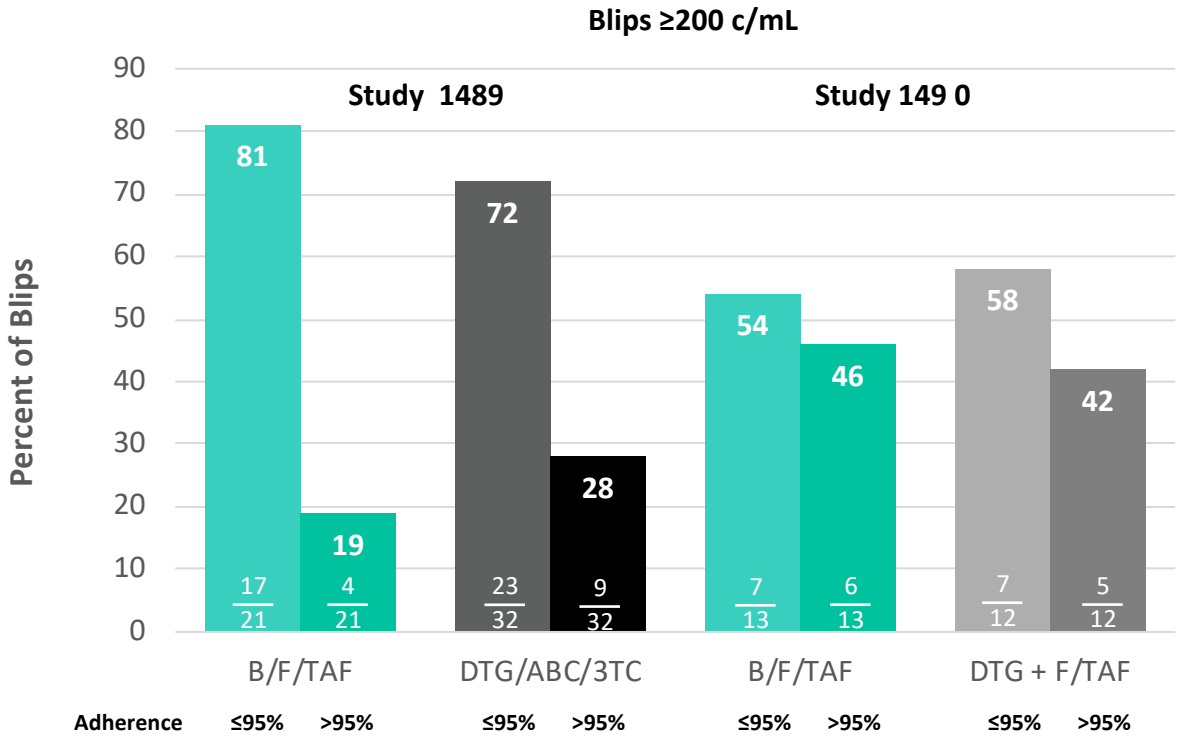
Source: Axosta et al. CROI 2020; Boston, MA. Poster 540

HIV VIRAL BLIPS IN ADULTS TREATED WITH INSTI-BASED REGIMENS THROUGH 144 WEEKS

Blips and Adherence Level



Blips ≥200 c/mL and Adherence Level



Source: Axosta et al. CROI 2020; Boston, MA. Poster 540

GEMINI-1 AND -2: CVW BY BASELINE CHARACTERISTICS

- Similar numbers of patients experienced protocol-defined CVW with DTG + 3TC vs DTG + FTC/TDF through Wk 96
  - DTG + 3TC: n = 11; DTG + FTC/TDF: n = 7
- All patients with CVW had virologic rebound, none had preceding blips (single HIV-1 RNA value ≥ 50 to < 200 copies/mL with adjacent value < 50 copies/mL)
  - 2 patients per arm had ≥ 1 HIV-1 RNA value ≥ 200 copies/mL after suppression to < 50 copies/mL

CVW by Baseline Subgroup, % (n/N)	DTG + 3TC	DTG + FTC/TDF
Baseline CD4+ cell count		
▪ ≤ 200 cells/mm^3	4.8 (3/63)	3.6 (2/55)
▪ > 200 cells/mm^3	1.2 (8/653)	0.8 (5/662)
Baseline HIV-1 RNA		
▪ ≤ 100,000 copies/mL	1.0 (6/576)	0.7 (4/564)
▪ > 100,000 copies/mL	3.6 (5/140)	2.0 (3/153)

Source: Underwood. CROI 2020. Abstr 483.

GEMINI-1 AND -2: CVW IN PATIENTS RECEIVING DTG + 3TC

Participant	HIV-1 Subtype	BL CD4+, cells/mm^2	CVW Visit	BL HIV-1 RNA, c/mL	SVW HIV-1 RNA, c/mL	CVW HIV-1 RNA, c/mL	WD HIV-1 RNA, c/mL	Adherence/ TI
A	BF	212	Wk 16	124,492	6648	56,435	95	Unknown
B	B	284	Wk 24	50,263	348	206	96	Adherent
C	B	529	Wk 24	17,232	461	251	59	Unknown
D	B	213	Wk 24	96,277	451	9602	67	TI
E	F	19	Wk 24	368,439	212	376	362	Adherent
F	B	414	Wk 48	37,701	43,908	38,457	ND	Unknown*
G	B	567	Wk 60	7654	3972	3131	1513	Nonadherent
H	B	347	Wk 60	101,671	703	85,556	ND	TI
I	B	50	Wk 72	63,817	422	2154	115	Nonadherent
J	B	74	Wk 72	112,812	61,076	87,794	671	Nonadherent
K	B	317	Wk 96	341,818	396	726	280	Nonadherent

*Patient developed serious adverse event (psychosis).

Source: Underwood. CROI 2020. Abstr 483.

GEMINI-1 AND -2: CVW IN PATIENTS RECEIVING DTG + FTC/TDF

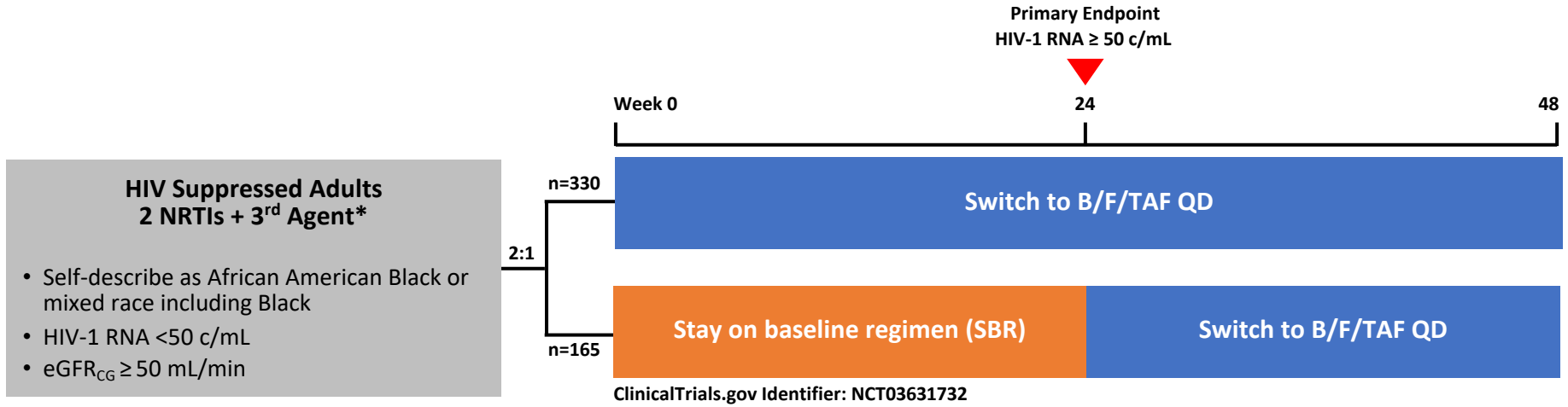
Participant	HIV-1 Subtype	BL CD4+, cells/mm^2	CVW Visit	BL HIV-1 RNA, c/mL	SVW HIV-1 RNA, c/mL	CVW HIV-1 RNA, c/mL	WD HIV-1 RNA, c/mL	Adherence/ TI
L*	B	22	Wk 12	136,753	393	276	NA	Unknown
M	B	226	Wk 24	10,930	1136	809	647	Unknown
N	B	251	Wk 24	76,325	569	362	46	Unknown
O	B	201	Wk 24	156,701	213	1559	97	Unknown
P	B	602	Wk 48	1568	8384	3653	3011	Unknown
Q	B	253	Wk 72	66,881	254	232	121	Unknown
R	B	144	Wk 96	28,905	30,316	7793	ND	Nonadherent

*Patient met criteria for WD at Wk 16 but remained on study with HIV-1 RNA suppression due to reporting error.

- Resistance analysis found no evidence of treatment-emergent genotypic or phenotypic resistance following CVW in either treatment arm
- HIV-1 RNA levels decreased ≥ 2-fold between CVW and withdrawal time points in 8/9 patients in DTG + 3TC arm and 3/5 patients in DTG + FTC/TDF arm with CVW, possibly indicating return to adherence following nonadherence/TI

Source: Underwood. CROI 2020. Abstr 483.

PREEXISTING RESISTANCE AND B/F/TAF SWITCH EFFICACY IN AFRICAN AMERICANS



Resistance Criteria

Excluded	Included
NRTI-R: K65R/N/R, T69 insertions, ≥3 TAMs	NRTI-R: M184V/I, 1-2 TAMs, other substitutions
Primary INSTI-R	NNRTI-R
	PI-R

*Suppressed on regimen for ≥6 months; Allowed 3rd agents any FDA-approved INSTI except BIC, any FDA-approved PI, maraviroc, or NNRTI except ETR

Source: Andreatta K, et al. 27th CROI; Boston, MA; March 8-11, 2020. Abst. 509.

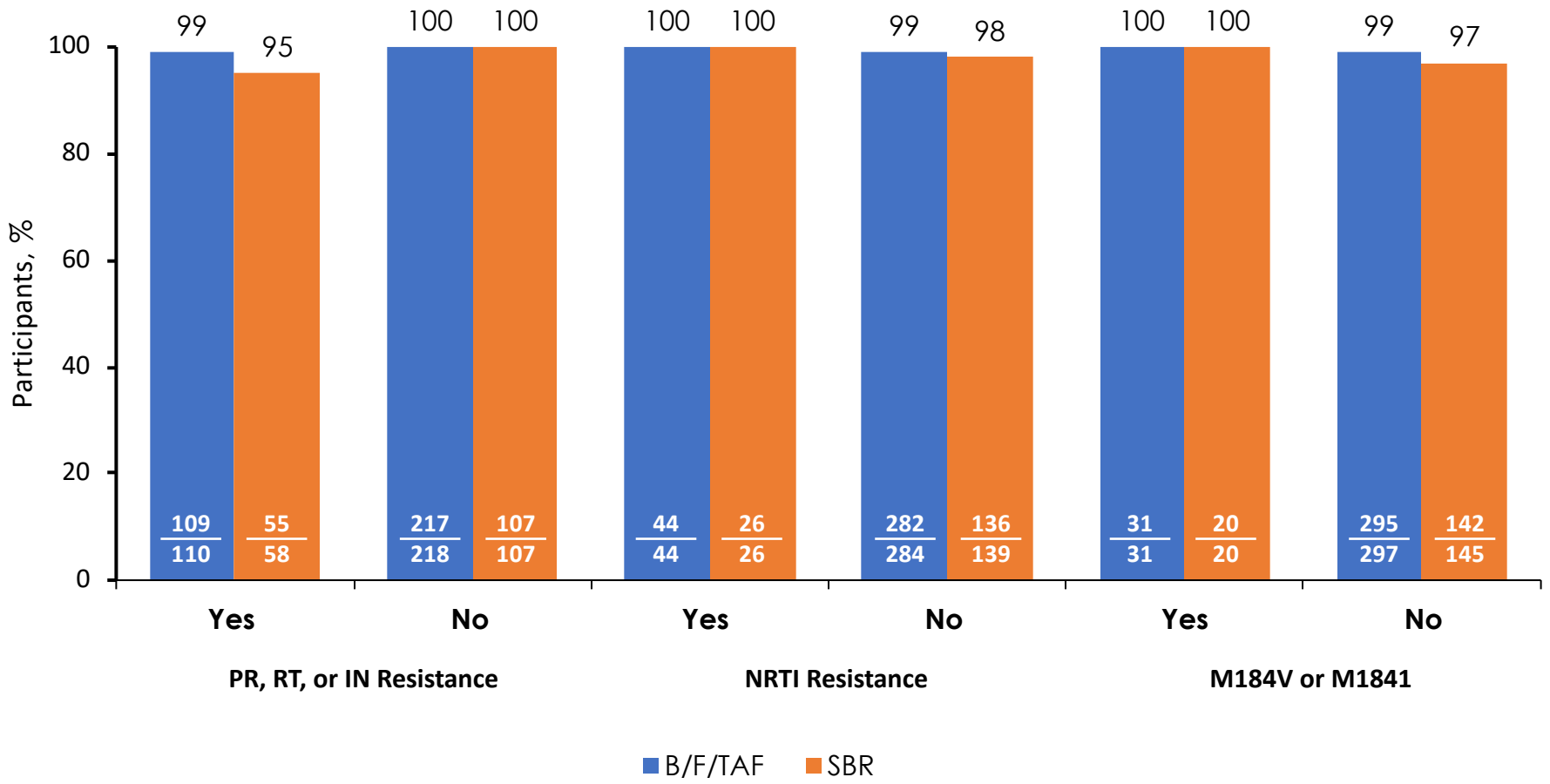
PREEXISTING RESISTANCE SUBSTITUTIONS

Resistance Category	Proportion of Participants, % (n) B/F/TAF n= 330	SBR n=165
NRTI-R	13% (44)	16% (26)
K65R	1% (2)[a]	1% (1)[a]
M184V/I	9% (31)	12% (20)
Any TAM	6% (20)	8% (14)
1-2 TAMs	5% (18)	5% (8)
≥ 3 TAMs	1% (2)	4% (6)
Other (K70E, L74I/V, Y115F. Q151M	2% (7)	3% (5)
NNRTI-R	21% (70)	19% (32)
K103N/S	10% (33)	12% (20)
Rilpivirine associated[b]	9% (29)	7% (12)
PI-R	11% (36)	15% (25)
Atazanavir or darunavir associated[c]	2% (6)	3% (5)
Primary InSTI-R	2% (8)	2% (3)
T66A	0	1% (1)
E92G	1% (2)	1% (1)
Y143C/H	1% (3)[d]	0.7% (1)
Q148H/K/R	1% (3)[d]	0
Secondary INSTI-R	45% (149)	47% (78)
M50I	21% (69)	22% (36)
T97A	3% (10)	1% (1)
S119P/R/T	21% (70)	20% (33)
E157K/Q	8% (26)	10% (16)

Source: Andreatta K, et al. 27th CROI; Boston, MA; March 8-11, 2020. Abst. 509.

Source: Andreatta K, et al. 27th CROI; Boston, MA; March 8-11, 2020. Abst. 509.

HIV-1 RNA < 50 C/ML BY LOCF



Source: Andreatta K, et al. 27th CROI; Boston, MA; March 8-11, 2020. Abst. 509.

ASSESSING THE VIROLOGIC IMPACT OF ARCHIVED RESISTANCE IN AN HIV-1 SWITCH STUDY TANGO THROUGH WEEK 48

Table 1. Prevalence of Archived Resistance and the Most Frequent Substitutions by Drug Class at Baseline in PRAP*,†

Resistance class	DTG/3TC (N=322)	TAF-based regimen (N=321)	Total (N=643)
No major RAMs	241 (75%)	235 (73%)	476 (74%)
Any major RAMs	81 (25%)	86 (27%)	167 (26%)
Major NRTI associated	25 (8%)	17 (5%)	42 (7%)
Any TAM[a]	9 (3%)	5 (2%)	14 (2%)
A62V	5 (2%)	3 (<1%)	8 (1%)
M184V/I[b]	4 (1%)	3 (<1%)	7 (1%)
K65N/R[c]	0	2 (<1%)	2 (<1%)
Others[d]	7 (1%)	4 (1%)	11 (2%)
Major NNRTI associated	38 (12%)	52 (16%)	90 (14%)
K103N	12 (4%)	17 (5%)	29 (5%)
E138A/K	14 (4%)	13 (4%)	27 (4%)
V108I	5 (2%)	7 (2%)	12 (2%)
Others[e]	8 (2%)	19 (6%)	27 (4%)
Major PI associated	23 (7%)	20 (6%)	43 (7%)
M46I	8 (2%)	7 (2%)	15 (2%)
D30N	5 (2%)	2 (<1%)	7 (1%)
Others[f]	12 (4%)	12 (4%)	24 (4%)
Pre-specified INSTI substitutions	84 (26%)	85 (26%)	169 (26%)
Major INSTI associated	3 (<1%)	5 (1%)	8 (1%)
Q148Q/R	2 (<1%)	1 (<1%)	3 (<1%)
Y143Y/H	0	2 (<1%)	2 (<1%)
Y143Y/C	1 (<1%)	0	1 (<1%)
R263R/K	0	2 (<1%)	2 (<1%)
Other pre-specified INSTI substitutions	83 (25%)	82 (25%)	165 (26%)
G193E	34 (11%)	30 (9%)	64 (10%)
L74I	16 (5%)	24 (7%)	40 (6%)
V151I	12 (4%)	13 (4%)	25 (4%)
E157Q	9 (3%)	6 (2%)	15 (2%)
E138D	4 (1%)	4 (1%)	8 (1%)
T97A	5 (2%)	3 (<1%)	8 (1%)
L74M	3 (<1%)	4 (1%)	7 (1%)
Others[g]	12 (4%)	7 (2%)	19 (3%)

*PRAP: proviral resistance analysis population is described in the Methods section

Table 2. Virologic Outcomes by Archived Resistance Category Through Week 48 Using Last On-Treatment HIV-1 RNA in PRAP*

Baseline resistance class	% of participants with last available on-treatment HIV-1 RNA <50 c/mL	
	DTG/3TC (N=322)	TAF-based regimen (N=321)
Overall participants	100% (322/322)	>99% (319/321)
Any major RAMs	100% (81/81)	100% (86/86)
No major RAMs	100% (241/241)	>99% (233/235)
Any major NRTI RAMs	100% (25/25)	100% (17/17)
No major NRTI RAMs	100% (297/297)	>99% (302/304)
Any major INSTI RAMs	100% (3/3)	100% (5/5)
No major INSTI RAMs	100% (319/319)	>99% (314/316)
Any pre-specified INSTI substitutions	100% (84/84)	100% (85/85)
No pre-specified INSTI substitutions	100% (238/238)	>99% (234/236)
Any major NNRTI RAMs	100% (38/38)	100% (52/52)
No major NNRTI RAMs	100% (284/284)	>99% (267/269)
Any major PI RAMs	100% (23/23)	100% (20/20)
No major PI RAMs	100% (299/299)	>99% (299/301)

*PRAP is described in the Methods section

Wang et al. CROI 2020; Boston, MA. Poster 489.

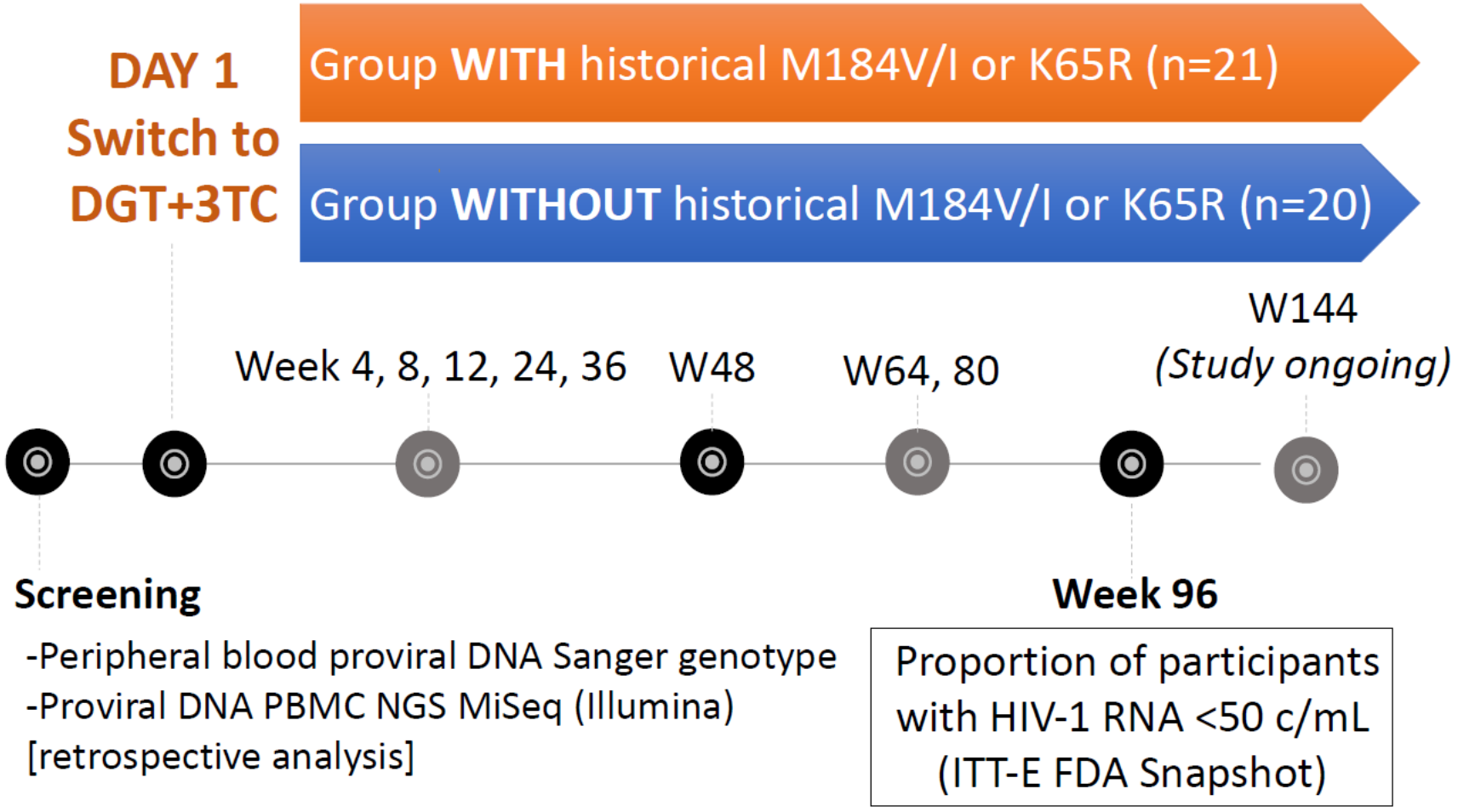
ART-PRO Trial
Long-Term DTG+3TC Switch Efficacy in Patients With Archived 3TC Resistance

- **Rosa de Miguel**,[1] David Rial,[2] Lourdes Domínguez-Domínguez,[2] Rocio Montejano,[1] Andrés Esteban-Cantos,[1] Otilia Bisbal,[2] Natalia Stella-Ascariz,[1] Paula Aranguren,[2] Mónica García-Álvarez,[2] Belen Alejos,[3] Maria Lagarde,[2] Jose I. Bernardino,[1] Federico Pulido,[2] Jose R. Arribas,[1] for the ART-PRO, PI16/00837-PI16/00678 study group

[1]Hospital La Paz Institute for Health Research, Madrid, Spain; [2]Hospital Universitario 12 de Octubre, Madrid, Spain; [3]Institute of Health Carlos III, Madrid, Spain

STUDY DESIGN

Pilot, single-arm, phase IIa, open label clinical trial conducted at 2 sites



Source: de Miguel et al. CROI 2020; Boston, MA. Poster 485.

INCLUSION AND EXCLUSION CRITERIA

- CD4> 350 cells/µL and VL < 50 c/mL for 12 months (1 blip allowed)
- Stable ART for 3 months
- FTC or 3TC in past/present treatment
- INSTI naïve

- M184V/I or K65R in baseline proviral DNA Sanger genotype
- HBAgS+
- Pregnant/women wishing to conceive

Source: de Miguel et al. CROI 2020; Boston, MA. Poster 485.

STUDY POPULATION (CONT)

STUDY POPULATION	Historical 3TC resistance (n=21)	No historical 3TC resistance (n=20)
Baseline proviral DNA analysis		
M184V (Sanger genotype)♀	2 (9.5)	0 (0)
M184V/I detected by NGS, n (%)		
>20% *	7 (33)	1 (5)
>5% *	14 (66.7)	3 (15)
>1% *	20 (95.2)	7 (35)
K65R/E/N detected by NGS, n (%)		
>20%	1 (4.8)	0 (0)
>5%	2 (9.5)	0 (0)
>1%	3 (14.3)	0 (0)

♀ Protocol violations

*$p < 0.05$

Source: de Miguel et al. CROI 2020; Boston, MA. Poster 485.

RESULTS

- In this pilot trial, DTG+3TC was effective at 96 weeks in maintaining long-term virologic control despite history of 3TC resistance and presence of archived 3TC mutations detected by NGS
- No case of virologic failure occurred after 2 years of follow-up

WEEK 96 RESULTS (FDA-SNAPSHOT):	Historical 3TC resistance (n=21)	No historical 3TC resistance (n=20)
HIV-1 RNA ≤50 copies/mL	**18 (85.7)**	**19 (95)**
Virologic failure or HIV-1 RNA ≥50 copies/mL	**0 (0)**	**0 (0)**
No virologic data at Week 96	**3 (14.3)**	**1 (5)**
Discontinuation due to an adverse event	1 (4.8)	0 (0)
Discontinuation for other reasons and last available HIV-1 RNA <50 copies/mL	2 (9.5) *(Protocol Violation)*	1 (5) *(Declined to continue study)*

Source: de Miguel et al. CROI 2020; Boston, MA. Poster 485.

MENSAJES CLAVE

- B/F/TAF: similares resultados en > y < de 50 años
- Frecuencia de blips similar con DTG y BIC. Blips > 200 relacionados con adherencia < 95%.
- Retiradas por rebote virológico confirmado similares entre DTG-3TC y DTG+TDF/FTC en GEMINI. No Desarrollo de resistencias. Adherencia principal determinante?
- Resistencia archivada en DNA proviral sin impacto en B/F/TAF y DTG-3TC (piloto)
- Resistencia a 3TC archivada no detectada por DNA proviral sin impacto en la terapia con DTG-3TC a 96 semanas en el studio piloto ART-PRO