Dovato, nuevos datos post IAS/EACS.

Alella,14 de noviembre de 2023

Boris Revollo B. MD, PhD
Germans Trias i Pujol University Hospital
Infectious Diseases Department

Salut/ Germans Trias i Pujol Hospital

Conflicts of interest

- Educational grants (HIV Unit): UAB, MAG, Primavera Sound group.
- Honoraria and travel sponsorship: Merck Sharp & Dohme, Gilead Sciences, Janssen, ViiV Healthcare.
- Co-investigator in clinical trials sponsored: Merck Sharp & Dohme, Gilead Sciences, Janssen, ViiV Healthcare
- Not a patent holder or a shareholder
- No disclosures for any family members

AGENDA

- Guidelines Update
- DTG/3TG in Treatment-Naïve “Special” People With HIV-1
- RWD reports of DTG/3TG Effectiveness in Treatment-Naive People With HIV-1 and Low TCD4+ or High Viral Load
- New data on switch treatment strategies
- Conclusions

Guidelines recommendations for Initial ART in adults. It's not only yes or no.

- **DTG/3TC preferred in all guidelines.**
- ABC starting to be removed (IAS-USA, BHIVA).
- RAL removed (IAS-USA, DHHS, GeSIDA).

Cortesía Dr. Llibre

Preferred/recommended

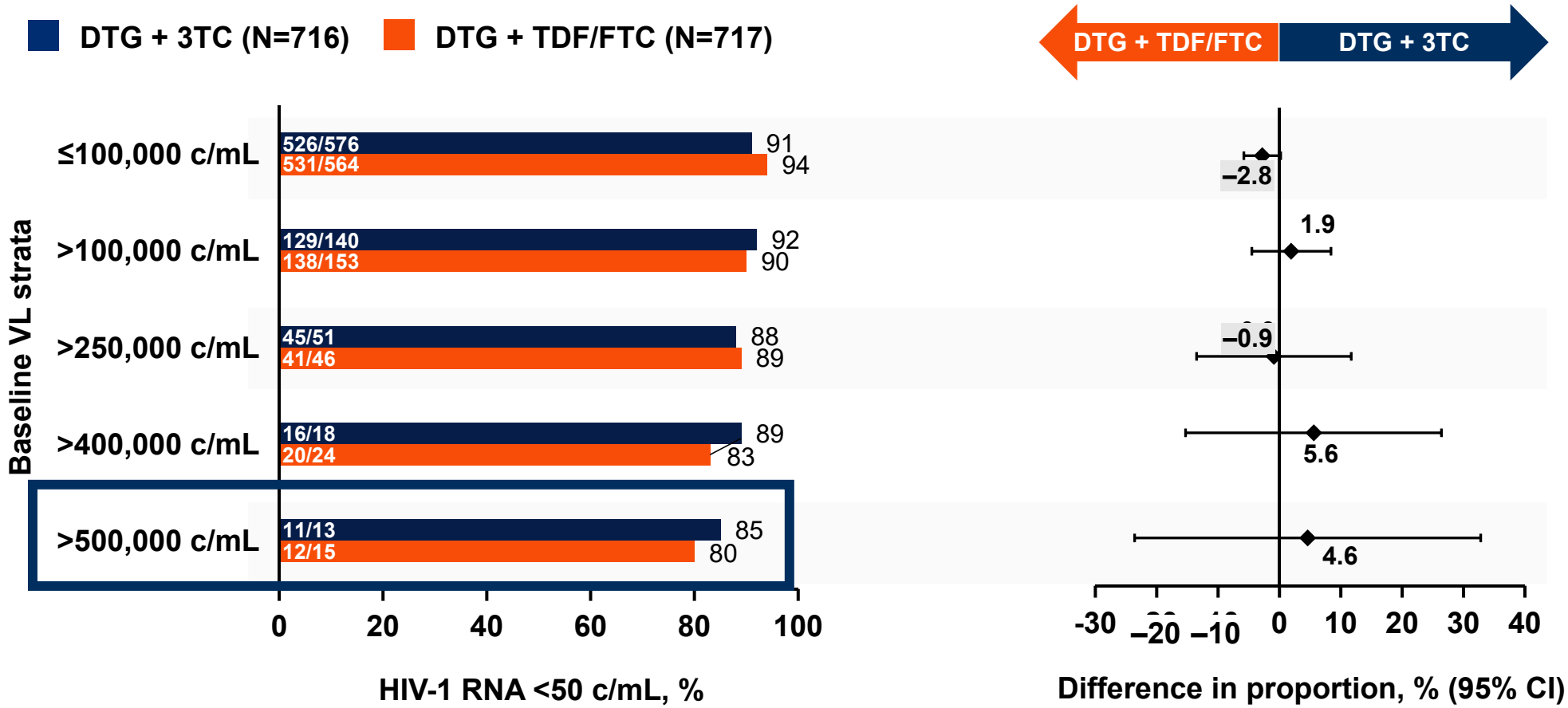
Recommended in certain clinical situations

	DHHS March 23, 2023 "Recommended for most people"	**EACS** Oct 2023 "Recommended"	**IAS-USA** Dec 2022 "Recommended"	**GESIDA** 2022 "Preferred"
DTG/3TC	HBsAg negative HIV-VL < 500,000 copies/mL **(limited data are available in patients with viral loads above > 500,000)** Not for rapid start (TDR, HBV data) Not recommended after PrEP failure (CAB or TDF/FTC)	HBsAg negative HIV-VL < 500,000 copies/mL Not recommended after PrEP failure	HBsAg negative HIV-VL < 500,000 copies/mL ~~Perhaps CD4 < 200 cells, unclear~~ Not for rapid start (TDR) or after PReP failure or IOs. ~~Close monitoring for adherence~~ Cost or safety advantages over 3DR. Not recommended during pregnacy	HBsAg negative CD4 > 200 cells Not recommended after PrEP failure
DTG/ABC/3TC	HLA-B*57:01 negative HBsAg negative	HLA-B*57:01 negative HBsAg negative	**OTHER** Concerns with ABC and increased risk AMI HLA-B*57:01 negative HBsAg negative	HLA-B*57:01 negative HBsAg negative
TAF/FTC or TDF/XTC + DTG	TDF renal and bone toxicity but better lipid profile		TDF renal and bone toxicity TAF Associated with greater weight gain	
BIC/FTC/TAF	Not recommended after CAB PrEP failure (INSTI genotiping)	Weight increase (BIC, TAF)	TAF associated with greater weight gain Not recommended during pregnacy	
TAF/FTC or TDF/XTC + RAL	**OTHER**: No STR, lower resistance barrier, higher pill		**OTHER**: Only in pregnancy	
TAF/FTC or TDF/XTC + DOR or TDF/3Tc/DOR				

EACS Guidelines 12.0. October 2023. Available at: https://www. https://www.eacsociety.org/media/guidelines-12.0.pdf. IAS-USA Guidelines. Gandhi R. JAMA 2023; 329(1):63-84. doi:10.1001/jama.2022.22246. DHHS. Available at https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/whats-new . Updated September 21, 2022. GeSIDA/PNS TAR en adultos infectados por el VIH (Actualización enero 2023). Disponible en: https://gesida-seimc.org

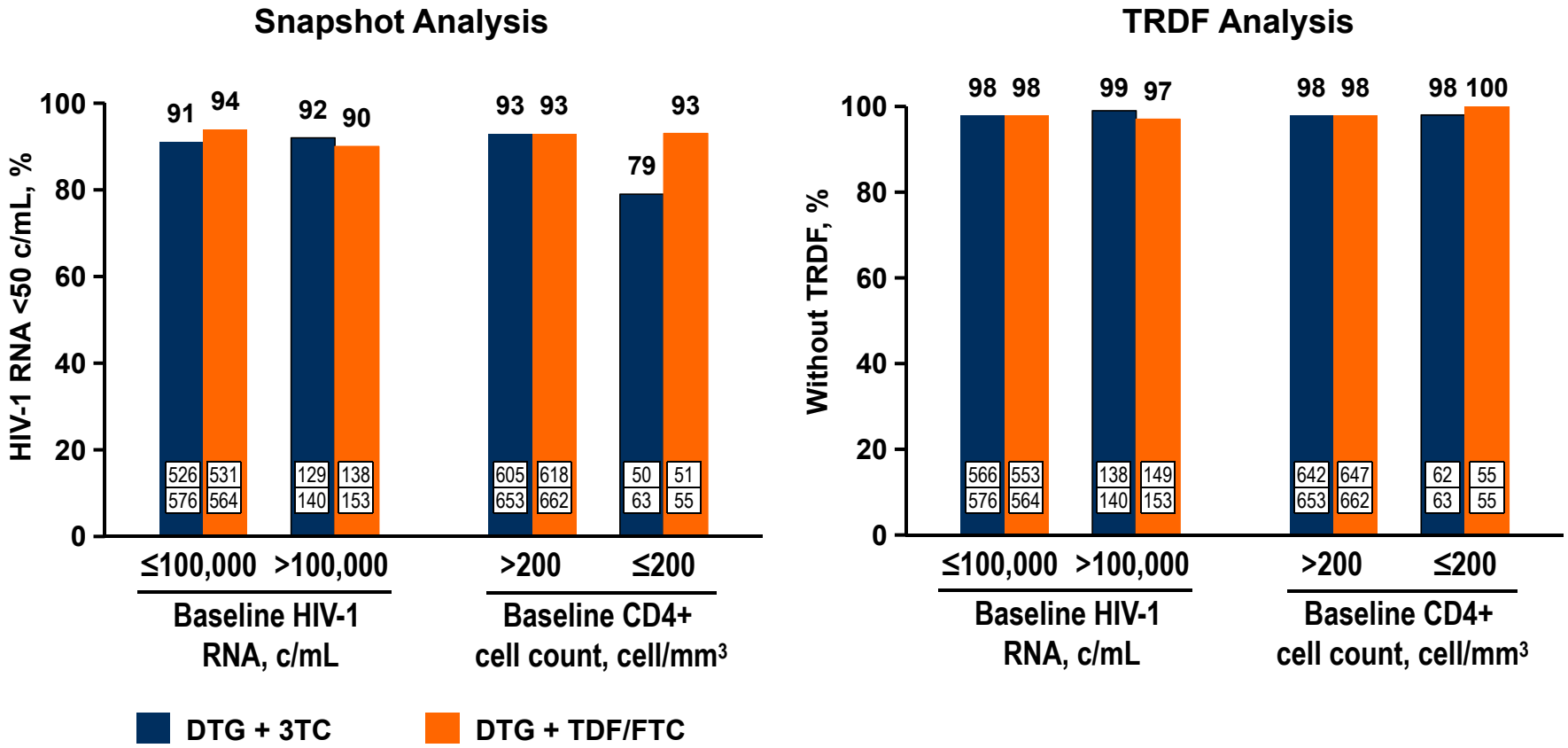
DTG + 3TC achieves virologic suppression at 48 weeks regardless of baseline viral load

GEMINI-1, GEMINI-2



Eron J, Hung C-C, Baril J-G, et al. Virologic Response by Baseline Viral Load With Dolutegravir Plus Lamivudine vs Dolutegravir Plus Tenofovir Disoproxil Fumarate/Emtricitabine Pooled Analysis. J Acquir Immune Defic Syndr. 2020 Jan.

Gemini 1 and 2 : Pooled Outcomes at Week 48 Stratified by Baseline HIV-1 RNA and CD4+ Cell Count: Snapshot Analysis



- 2% of participants in each arm had baseline HIV-1 RNA >500,000 c/mL
- Treatment related discontinuation = failure (TRDF) population accounts for confirmed virologic withdrawal (CVW), withdrawal due to lack of efficacy, withdrawal due to treatment-related AE, and participants who met protocol-defined stopping criteria
- DTG + 3TC CD4 <200 Snapshot non-response (n=13): **1 CVW**, 3 with VL >50 in window **(2 of 3 re-suppressed),** 2 discontinued due to AE (TB, Chagas disease), 2 protocol violations, 2 lost to follow-up, 1 withdrew consent, 1 withdrew to start HCV treatment, 1 change in ART (incarcerated)
- DTG + TDF/FTC < 200 Snapshot non-response (n=4):1 investigator discretion, 1 withdrew consent, 1 lost to follow-up, 1 VL >50 (re-suppressed)

Cahn P et al. The Lancet, January 12, 2019

Gemini 1 and 2 : Confirmed Virologic Withdrawals Through Week 48: ITT-E Population

- Low rates of virologic withdrawals were observed at Week 48

	GEMINI 1		GEMINI 2		Pooled	
Variable, n (%)	**DTG + 3TC (N=356)**	**DTG + TDF/FTC (N=358)**	**DTG + 3TC (N=360)**	**DTG + TDF/FTC (N=359)**	**DTG + 3TC (N=716)**	**DTG + TDF/FTC (N=717)**
CVW	4 (1)	2 (<1)	2 (<1)	2 (<1)	6 (<1)	4 (<1)
Treatment-emergent resistance	**0**	**0**	**0**	**0**	**0**	**0**

- No treatment-emergent INSTI mutations or NRTI mutations were observed among participants who met CVW (confirmed virologic failure) criteria

Confirmed virologic withdrawal criteria is defined as a second and consecutive HIV-1 RNA value meeting virologic non-response or rebound. Virologic non-response is defined as either a decrease in plasma HIV-1 RNA of less than 1 $\log_{10}$ c/mL by Week 12 with subsequent confirmation unless plasma HIV-1 RNA is <200 c/mL, or confirmed plasma HIV-1 RNA levels ≥200 c/mL on or after Week 24. Virologic rebound is defined as confirmed rebound in plasma HIV-1 RNA levels to ≥200 c/mL after prior confirmed suppression to <200 c/mL.

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Cahn P et al. The Lancet, January 12, 2019

STAT

0 MUTACIONES DE RESISTENCIAS A 48S[1]

N=131 todos los pacientes sin test de resistencias previo[1]

1 participante cambió por M184V basal. Alcanzó ARN VIH-1 <40 c/mL a semana 7, justo antes del cambio de tratamiento[1]

0 discontinuaciones por falta de eficacia[1]

REDOLA

0 MUTACIONES DE RESISTENCIAS A 48S[2]

N=135, 97 (71,9%) pacientes sin test de resistencias previo[2]

2 pacientes discontinuaron por decisión del médico tras identificar la mutación M184V en el test basal de mutaciones de resistencias: 1 de ellos alcanzó ARN VIH-1 <50 c/mL a semana 4[2]

CORIS

0 MUTACIONES DE RESISTENCIAS
SEGUIMIENTO 2018-2021[3]

N=401, >50% (n=266) de los participantes iniciaron tratamiento en los primeros 7 días tras la primera visita[3]

Sólo 1 paciente tenía la mutación M184V en el basaL y cambió en la 1ª semana a DRV/c/FTC/TAF, alcanzando la SV a las semanas 24 y 48[3]

3 pacientes presentaron FV, todos sin mutaciones de resistencia[3]

TANDEM

0 MUTACIONES DE RESISTENCIAS
SEGUIMIENTO MEDIO 1,3 AÑOS[4,5]

N=126, 48,4% iniciaron el tratamiento con Dovato como estrategia de Test-and-treat

56,2% pacientes con >100.000 c/mL no disponían del test de resistencias[4,5]

3 (2,4%) pacientes presentaron FV[4,5]

DOLAVI

0 MUTACIONES DE RESISTENCIAS A 48S[6]

N=88 todos los pacientes iniciaron tratamiento en los primeros 7 días tras la primera visita[6]

84,1% iniciaron tratamiento en la primera visita[6]

1 paciente (1,1%) presentó FV[6]

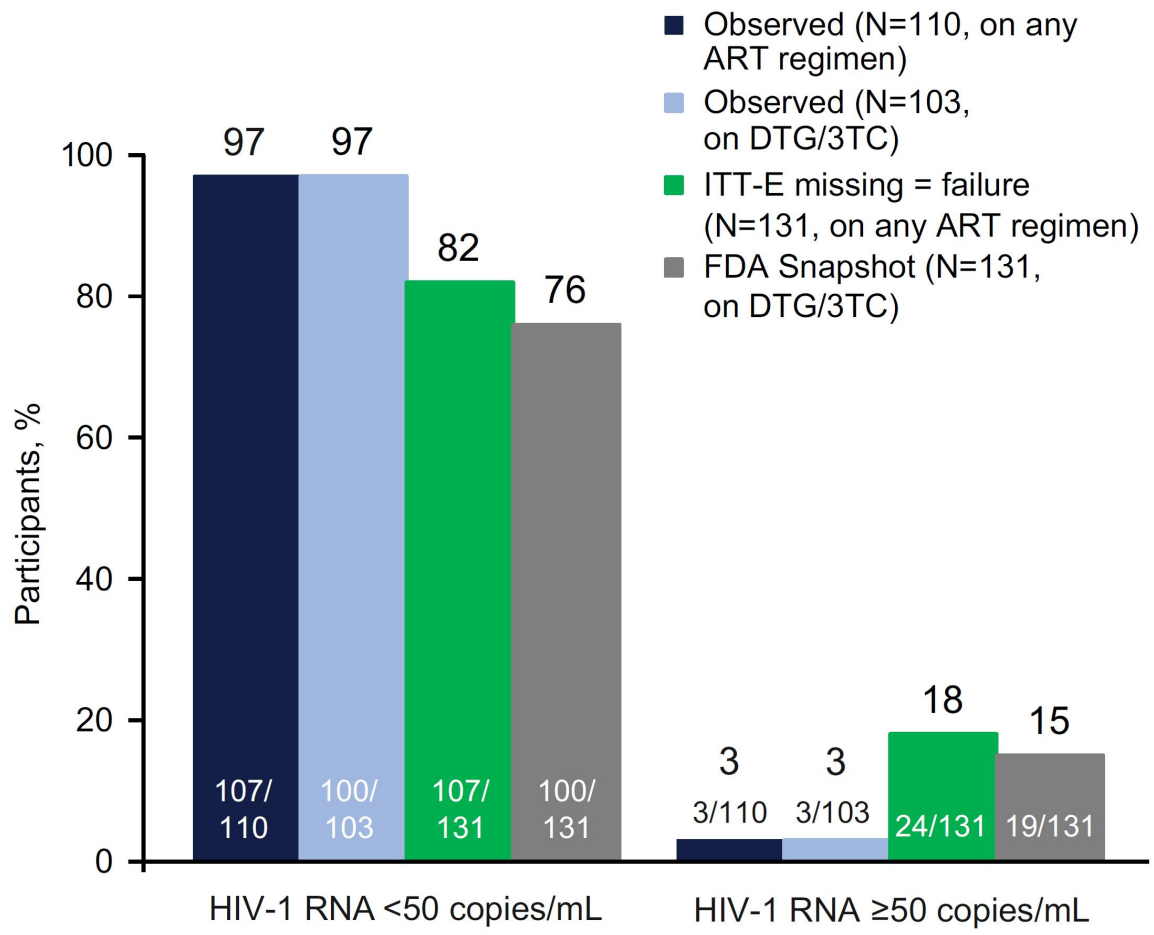
PM-ES-DLL-PPTX-230006 (v1) 09/2023

Referencias: 1. Rolle CP, Berhe M, Singh T, et al. Sustained Virologic Suppression With Dolutegravir/ Lamivudine in a Test-and-Treat Setting Through 48 Weeks. Open Forum Infect Dis. 2023 Mar 1;10(3):ofad101 **2.** Pulido F, López Bernaldo de Quiros JC, Górgolas M. 96 weeks effectiveness and tolerability of DTG+ 3TC in naive patients: The REDOLA study. Presented at: HIV Glasgow 2022; October 23-26, 2022; Glasgow, UK. Poster P059. Disponible en: https://virtual.hivglasgow.org/posters-exhibitions/posters/96-weeks-effectiveness-and-tolerability-dtg3tc-naive-patients-redola. Acceso realizado en septiemre 2023 **3.** Suárez-García I, Alejos B, Hernando V, et al. Effectiveness and tolerability of dolutegravir/lamivudine for the treatment of HIV-1 infection in clinical practice. J Antimicrob Chemother. 2023 Jun 1;78(6):1423-1432.
4. Schneider, C Burke, D Ward, et al. Real-world treatment experience of single tablet dolutegravir/lamivudine in the US: Results from the TANDEM study. AIDS 2022. Poster EPB147. Disponible en https://programme.aids2022.org/PAGMaterial/PPT/1533_9302/AIDS_2022_DTG_3TC_Poster_v9.0_15.07.22_FINAL.pdf Acceso realizado septiembre 2023 **5.** Benson P, Donovan C, Harper G, et al. Real-world Treatment Experience of Single-Tablet DOVATO (DTG/3TC) in Those Naive to Treatment With Baseline Viral Loads ≥100,000 copies/mL in the United States. Presented at IDWeek 2022; Virtual and Washington, DC. Poster 1278. Disponible en https://www.natap.org/2022/IDWeek/AGE_62.htm Acceso realizado septiembre 2023 **6.** Hidalgo-Tenorio C, Pasquau J, Vinuesa D, Ferra S, Terrón A, SanJoaquín I, Payeras A, Martínez OJ, López-Ruz MÁ, Omar M, de la Torre-Lima J, López-Lirola A, Palomares J, Blanco JR, Montero M, García-Vallecillos C. DOLAVI Real-Life Study of Dolutegravir Plus Lamivudine in Naive HIV-1 Patients (48 Weeks). Viruses. 2022 Mar 4;14(3):524

- Slim et al. IDWeek 2023; Boston, MA. Poster 1593.

DTG/3TC in a Test-and-Treat Setting

A

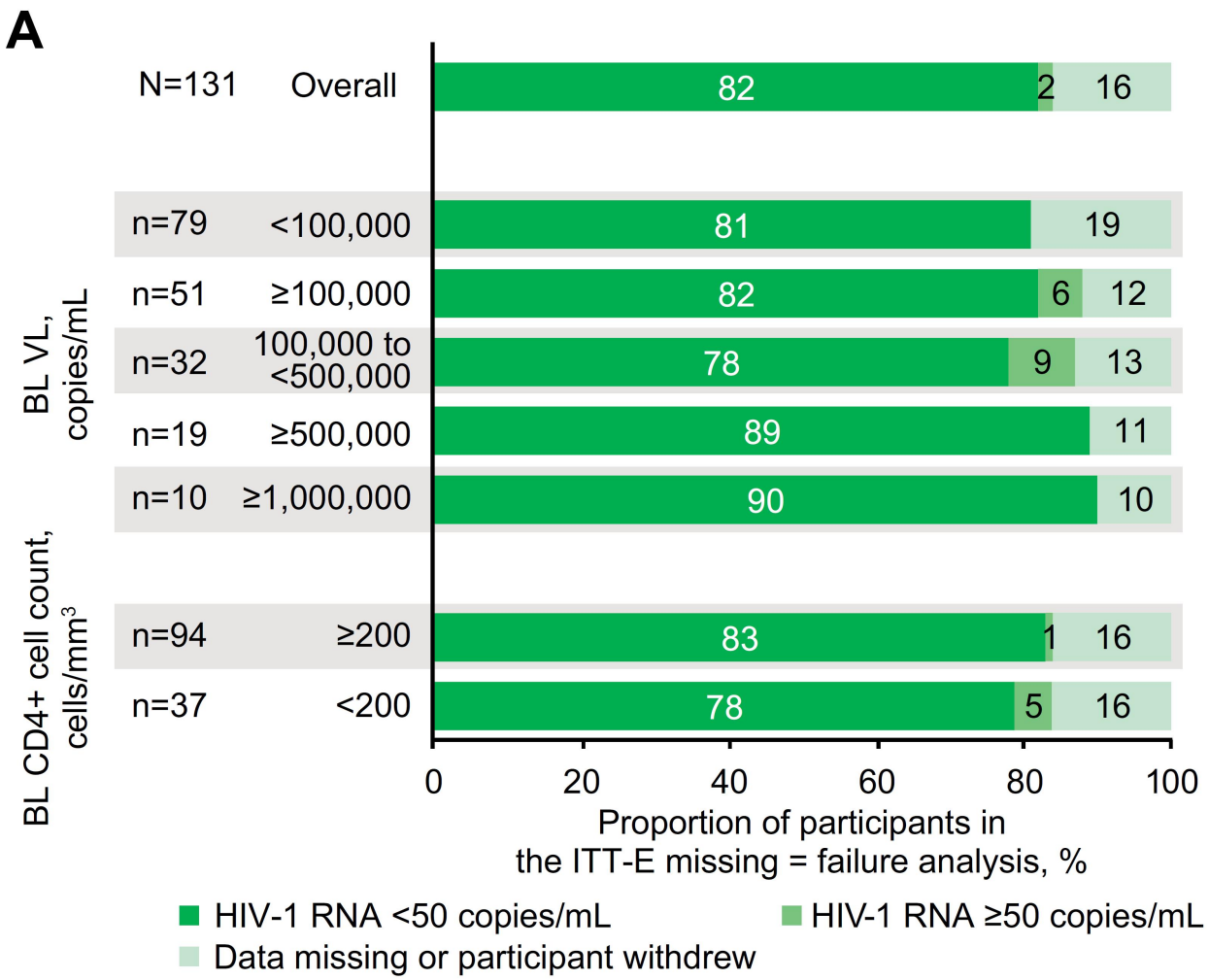


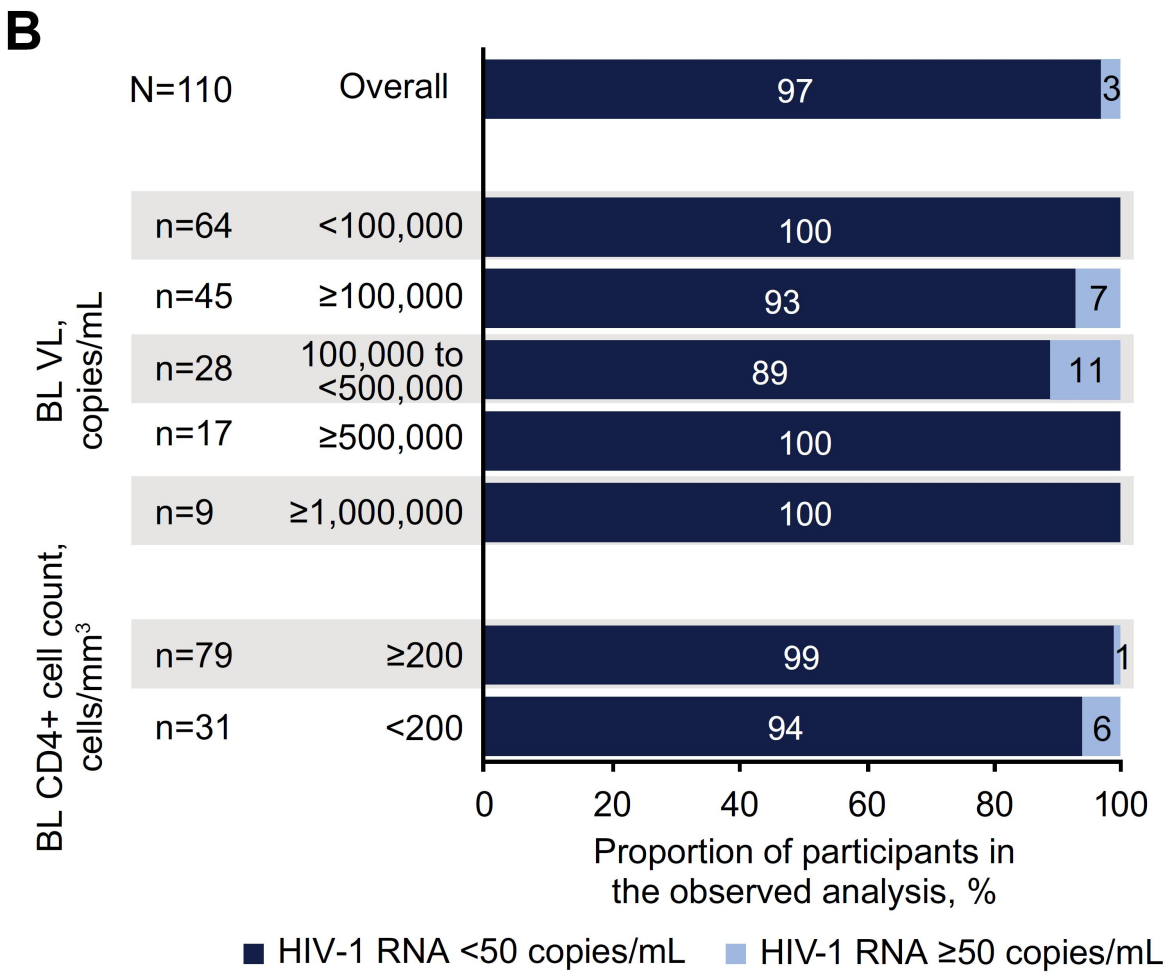
B

	DTG/3TC, n (%)
Observed analysis (N=110)	
HIV-1 RNA <50 copies/mL	**107 (97)**
On DTG/3TC	100/103 (97)
On modified ART	7/7 (100)
ITT-E missing = failure analysis (N=131)	
HIV-1 RNA <50 copies/mL	**107 (82)**
HIV-1 RNA ≥50 copies/mL	**24 (18)**
Data in window and HIV-1 RNA ≥50 copies/mL	3 (2)
On study but missing data in window	3 (2)[a]
Discontinued study due to lost to follow-up/withdrew consent	14 (11)[b]
Discontinued study for other reasons	4 (3)[c]
FDA Snapshot analysis (N=131)	
HIV-1 RNA <50 copies/mL	**100 (76)**
HIV-1 RNA ≥50 copies/mL	**19 (15)**
Data in window and HIV-1 RNA ≥50 copies/mL	3 (2)
Discontinued for lack of efficacy	0
Discontinued study for other reason and HIV-1 RNA ≥50 copies/mL	6 (5)
Change in ART	10 (8)
No virologic data	**12 (9)**

Rolle CP et al, Open Forum Infectious Diseases 1 March 2023

DTG/3TC in a Test-and-Treat Setting



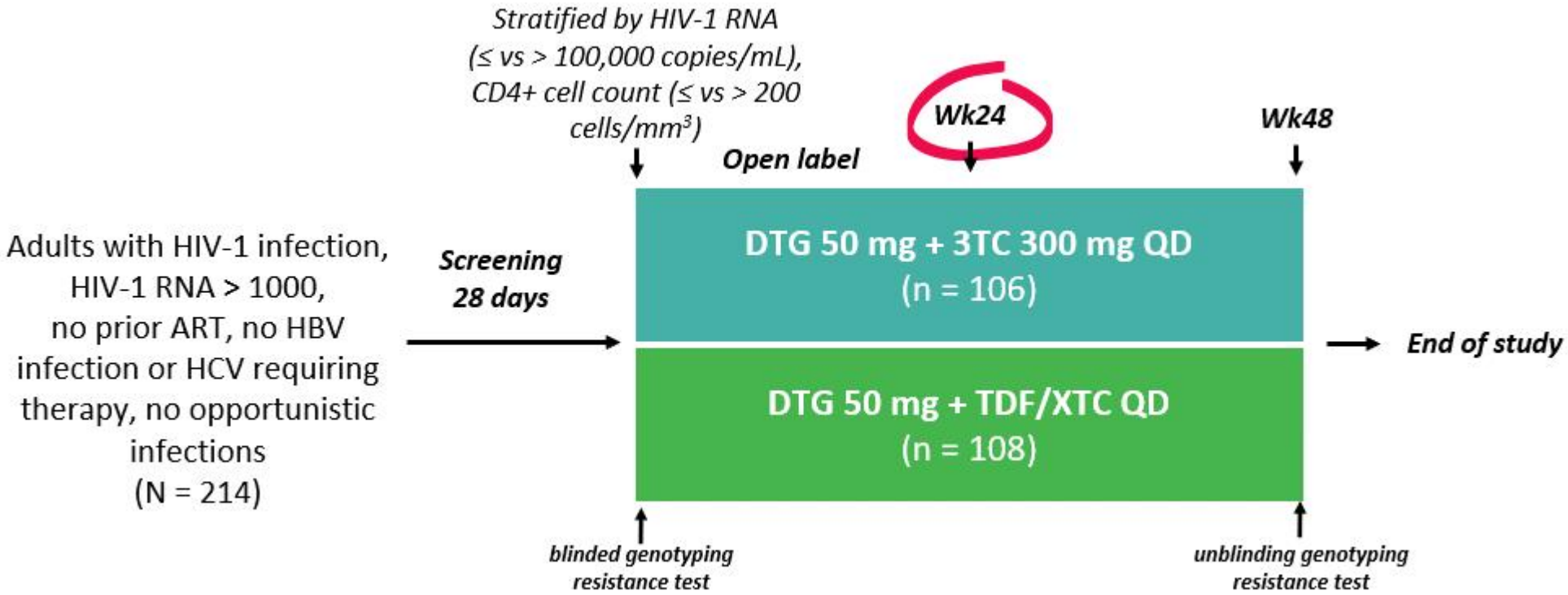


Rolle CP et al, Open Forum Infectious Diseases 1 March 2023

D2ARLING Study Design

Study Objectives

Assess the efficacy and safety of DTG+3TC in treatment-naïve PLHIV without baseline HIV-1 resistance testing



Out of 244 subjects screened, 214 were randomized to receive DTG+3TC (n=106) or DTG+TDF/XTC (n=108)

- Cordova et al. IAS 2023; Brisbane, Australia. Poster TUPEB02.

Demographics and Clinical Baseline Characteristics in the ITT-Exposed Population

- Baseline characteristics were similar between arms

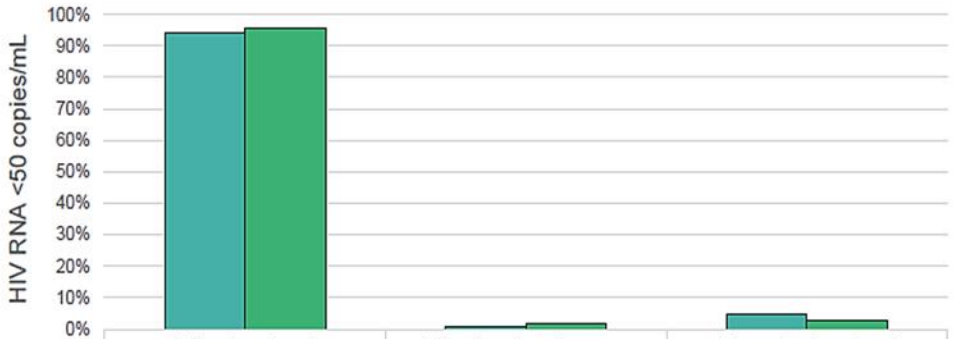
Characteristic	3TC-DTG (n=106)	XTC/TDF-DTG (n=108)	Total (N=214)
Female sex	24 (22.6%)	25 (23.1%)	49 (22.9%)
Median age, y (IQR)	31.50 (27-41)	31(26-37)	31 (26, 39)
Hispanic Latin, n (%)	106 (100%)	108 (100%)	214 (100%)
HIV-1 RNA >100000 c/mL	33 (31.1%)	33 (30.6%)	66 (30.8%)
CD4 T <200 cells/µL	21 (19.8%)	23 (21.3%)	44 (20.6%)
CDC stage C	0 (0.0%)	1 (1.0%)	1 (0.5%)

- Cordova et al. IAS 2023; Brisbane, Australia. Poster TUPEB02.

Virologic Results

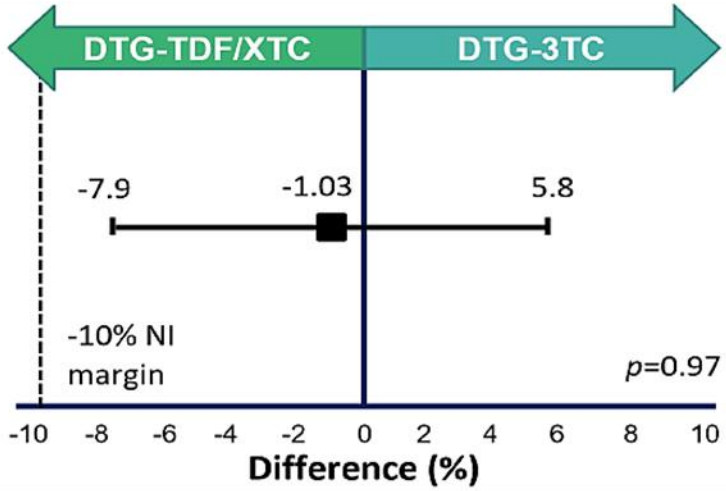
- In the ITT-exposed snapshot, 94.34% of participants on DTG+3TC arm and 95.37% on DTG+TDF/XTC arm achieved HIV-1 RNA <50 copies/mL (difference -1.03; 95% CI, 7.89% to 5.82%, p=0.97)
- One subject in the DTG+TDF/XTC arm met protocol-defined virological failure
  - No treatment-emergent mutations to any of the study drugs were observed in the virological failure genotypic resistance test

Virologic Snapshot Outcomes at Week 24 (ITT-E Population)



	Virological success	Virological non-response	No virological data
3TC-DTG	94,34%	0,94%	4,7%
DTG-XTC/TDF	95,37%	1,85%	2,8%

Adjusted Treatment Difference



Endpoint (<50 c/mL)

DTG-3TC is non-inferior to DTG-TDF/XTC (week 24)

- Cordova et al. IAS 2023; Brisbane, Australia. Poster TUPEB02.

DOLAM-500: Efficacy and safety of Dolutegravir (DTG) plus Lamivudine (3TC) in ART-naive PLWH with baseline viral load ≥500.000 copies/ml

Table1: Baseline characteristics of the patients and reasons for DTG + 3TC as first line therapy

Median age, years	**37 (21-85)**
Female %	7.2
Median (range) CD4 cells/mm³	330 (25-982)
Median (range) HIV-1 RNA copies/mL	1.023.000 (500.000- 55.549.410)
CD4/CD8 mean ±SD	0.32± 0.28
HBV/HCV coinfection	0
Underlying diseases/conditions n(%)	
Cardiovascular disease	4(7.1)
Chronic renal failure	2 (3.5)
Osteopenia/osteoporosis	4 (7.1)
Diabetes mellitus	7 (12.5)
Hypertension	9 (16.0)
Obesity	5(8.9)
Smoking	31(55.3)
Dyslipidemia	18 (26.9)
Family history of CVD	18(28.8)
Reasons of DTG+LAM therapy n(%)	
Patient's request/toxicity concern	22(42.3)
Provider's choise	14(26.9)
Osteopenia/osteoporosis	4 (7.6)
Polypharmacy/drug-drug interaction	8 (15.3)
CRF or renal function test abnormalities	4(7.6)

Table 2: Virologic outcomes at w24 and w48 in patients with baseline HIV RNA ≥ 500,000 copies/mL

Baseline HIV-1 RNA copies/mL	**N**		**W24**	**W48**
Total	56	**N**	56	38*
		HIV-1 RNA <50 copies /mL	46	35
		HIV-1 RNA ≥ 50 copies/mL	10	3
		No data	0	2**
500.000- 1.000.000	28	**N**	28	17*
		HIV-1 RNA <50 copies/mL	23	17
		HIV-1 RNA ≥ 50 copies/mL	5	0
		No data	0	1**
1.000.000 - 2.000.000	15	**N**	15	9*
		HIV-1 RNA <50 copies/mL	14	8
		HIV-1 RNA ≥ 50 copies/mL	1	1
		No data	0	0
2.000.000- 3.000.000	5	**N**	5	4*
		HIV-1 RNA <50 copies/mL	4	3
		HIV-1 RNA ≥ 50 copies/mL	1	1
		No data	0	0
>3.000.000	8	**N**	8	8
		HIV-1 RNA <50 copies/mL	5	7
		HIV-1 RNA ≥ 50 copies/mL	3	1
		No data	0	1**
Baseline CD4 (cells/mm³) mean ±SD	**N**		**W24**	**W48**
		N	56	38
375,9 ± 209.7	56	**CD4 mean ±SD**	624.1 ± 307.4	721.1 ± 339.8

Inan A et al. EACS 2023; Warsaw, Poland. Poster 190

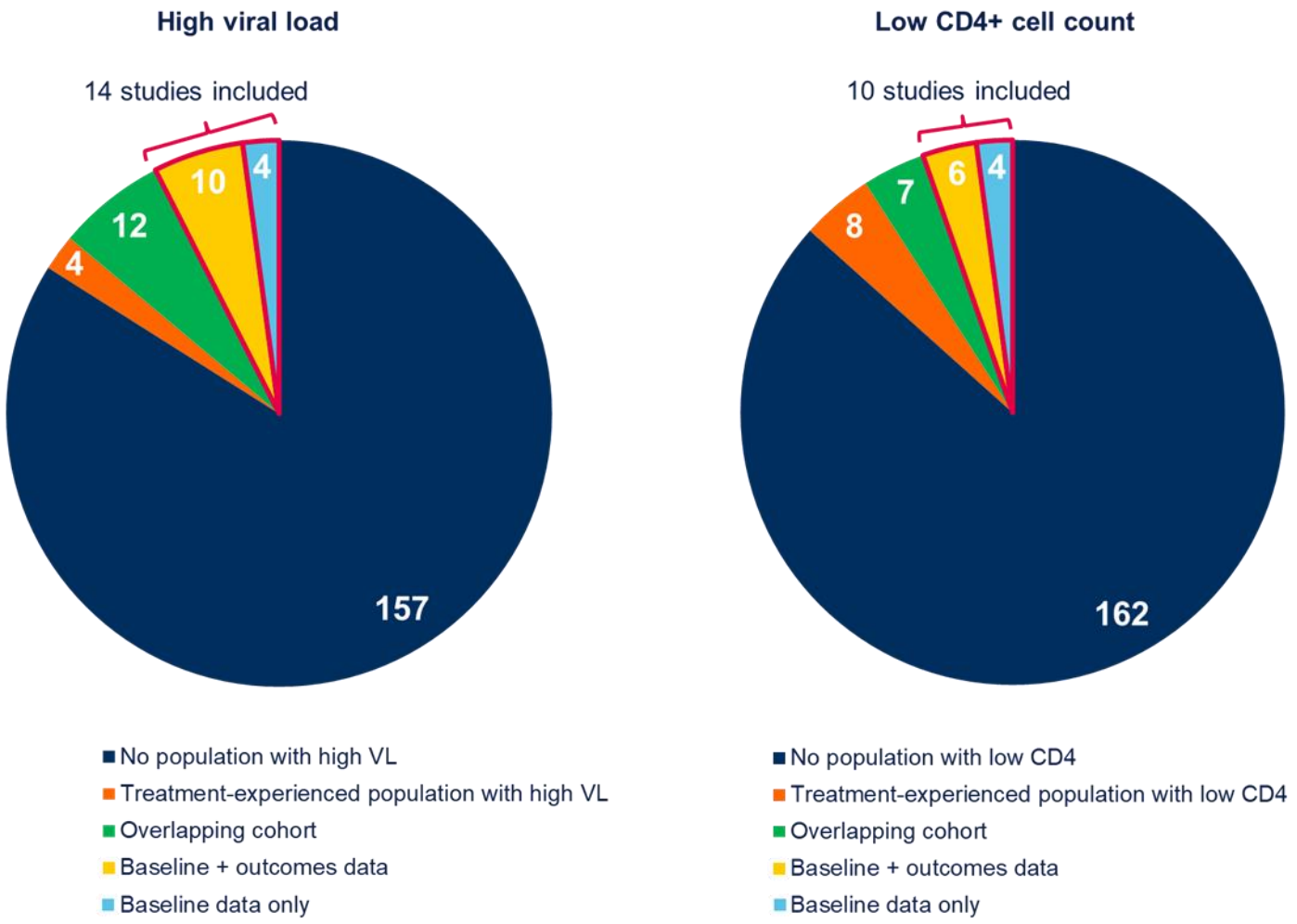
Real-world Effectiveness of Dolutegravir + Lamivudine (DTG + 3TC) in Treatment-Naive People With HIV-1 and Low CD4+ Cell Count or High Viral Load at Baseline: A Systematic Literature Review

Emilio Letang,[1] Tristan J. Barber,[2,3] Clotilde Allavena,[4] Laurent Hocqueloux,[5] José Casado,[6] Simona Di Giambenedetto,[7] Alfonso Cabello-Úbeda,[8] Antonella d'Arminio Monforte,[9] Madhusudan Kabra,[10] Julie Priest,[11] Ana Milinkovic,[10] Bryn Jones[10]

[1]ViiV Healthcare, Madrid, Spain; [2]Ian Charleson Day Centre, Royal Free London NHS Foundation Trust, London, UK; [3]Institute for Global Health, University College London, London, UK; [4]CHU Hôtel-Dieu, Nantes, France; [5]Centre Hospitalier Universitaire d'Orléans, Orléans, France; [6]Hospital Universitario Ramón y Cajal, Madrid, Spain; [7]Fondazione Policlinico Universitario Agostino Gemelli IRCCS and Università Cattolica del Sacro Cuore, Rome, Italy; [8]Fundación Jimenez Diaz University Hospital, Madrid, Spain; [9]'San Paolo' Hospital, University of Milan, Milan, Italy; [10]ViiV Healthcare, Brentford, UK; [11]ViiV Healthcare, Durham, NC, USA

Letang et al. EACS 2023; Warsaw, Poland. Poster eP.A.050.

Breakdown of Real-world Publications Reporting Data on People With HIV-1 Initiating DTG + 3TC With Viral Load ≥100,000 Copies/mL and CD4+ Cell Count <200 Cells/mm³



Letang et al. EACS 2023; Warsaw, Poland. Poster eP.A.050.

Studies With Virologic Effectiveness Data for ≥10 Treatment-Naive People With HIV-1 and Baseline Viral Load ≥100,000 Copies/mL or CD4+ Cell Count <200 Cells/mm3

- 7 and 4 studies reported the virologic effectiveness of DTG + 3TC for ≥10 treatment-naive individuals with high baseline viral load or low baseline CD4+ cell count, respectively

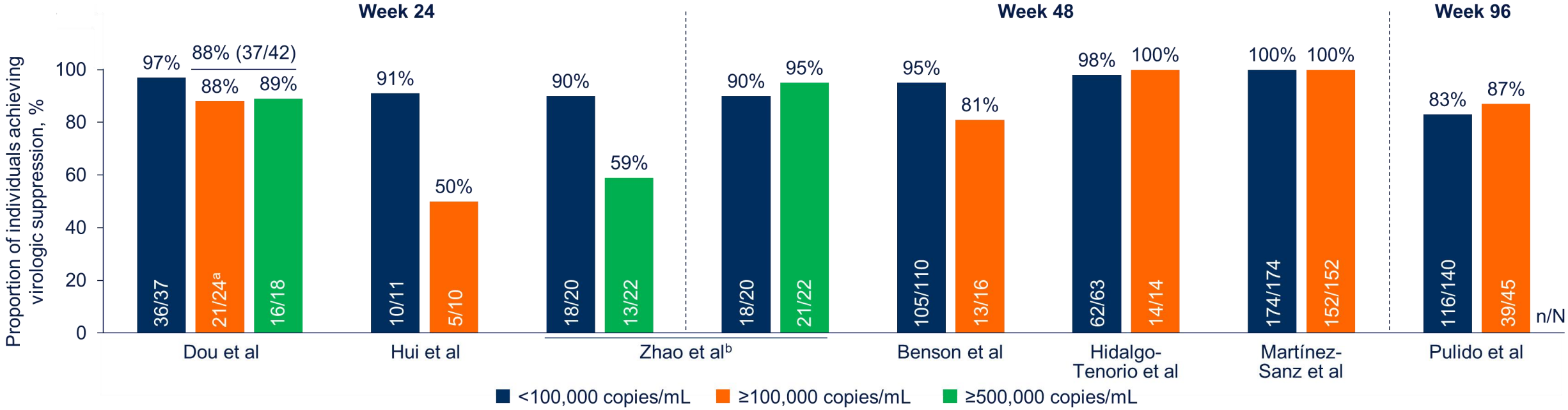
Study	Cohort or network	Country	Total DTG + 3TC cohort, N	High viral load or low CD4 cohort, n	Outcome reporting window(s)
High baseline viral load					
Dou et al[5]	—	China	96	42	Week 24
Hui et al[6]	—	China	54	34	Week 24[a]
Zhao et al[7]	—	China	42	22	Week 24 Week 48
Benson et al[8]	TANDEM	United States	126	16	Week 48
Hidalgo-Tenorio et al[9]	DOLAVI	Spain	88	17	Week 48
Martínez-Sanz et al[10]	CoRIS	Spain	326	152	Week 48
Pulido et al[11]	REDOLA	Spain	185	45	Week 96
Low baseline CD4+ cell count					
Dou et al[5]	—	China	96	51	Week 24
Yang et al[12]	—	China	36	17	Week 48
Zhao et al[7]	—	China	42	32	Week 48
Pulido et al[11]	REDOLA	Spain	185	10	Week 96

[a]Only 21 people in this cohort, 10 with high viral load, were included in the efficacy analysis.

Letang et al. EACS 2023; Warsaw, Poland. Poster eP.A.050.

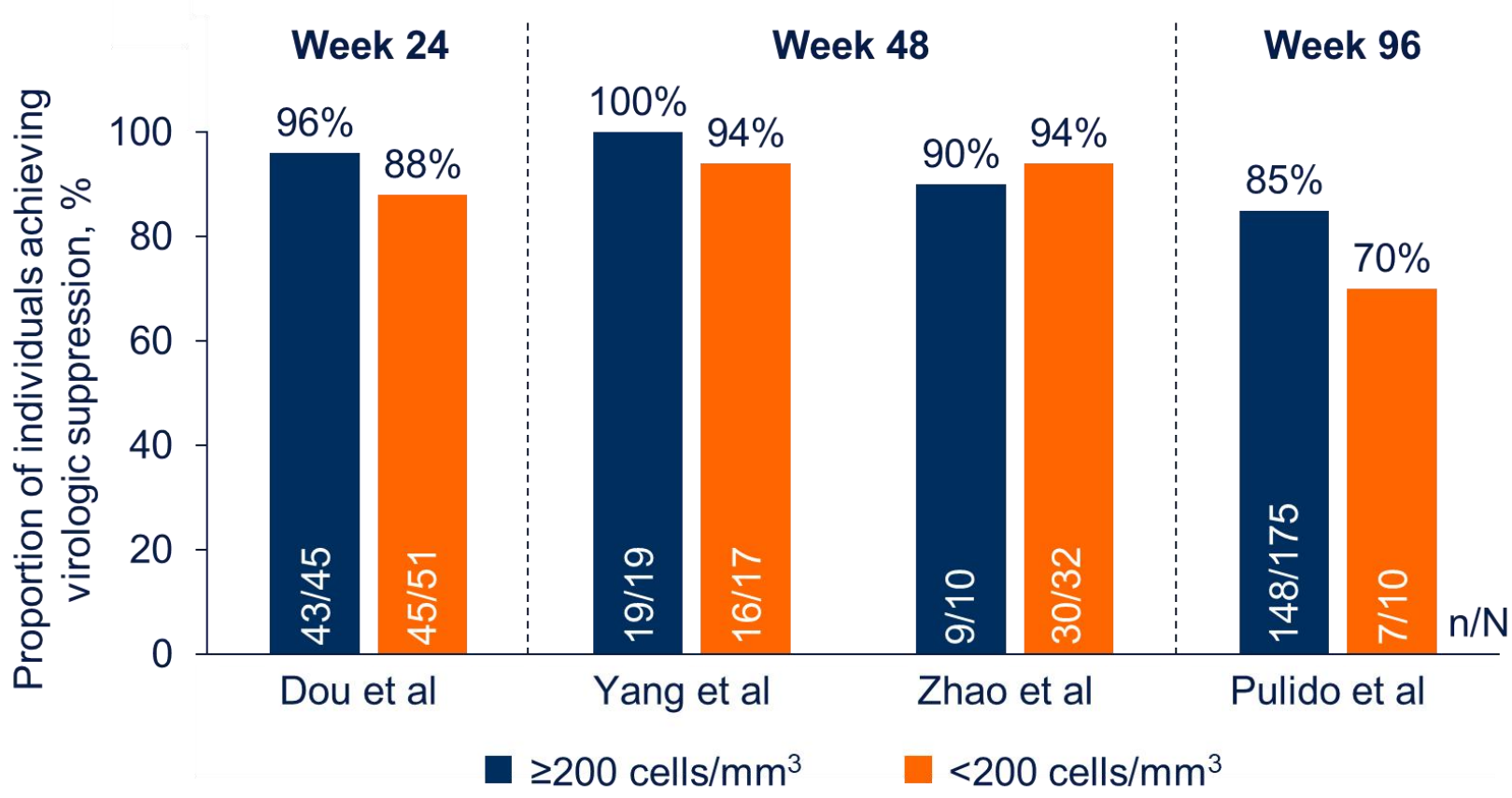
Letang et al. EACS 2023; Warsaw, Poland. Poster eP.A.050.

Proportions of Individuals With Baseline Viral Load ≥100,000 Copies/mL Achieving Virologic Suppression at Weeks 24, 48, and 96



Letang et al. EACS 2023; Warsaw, Poland. Poster eP.A.050.

Proportion of Individuals With Baseline CD4+ Cell Count <200 Cells/mm³ Achieving Virologic Suppression at Weeks 24, 48, and 96



Letang et al. EACS 2023; Warsaw, Poland. Poster eP.A.050.

Virologic Outcomes in Treatment-Naive Populations With High Baseline Viral Load

- Overall, the proportion of individuals with high baseline viral load who achieved virologic suppression was 76% (61/80) at Week 24, 97% (208/215) at Week 48, and 87% (39/45) at Week 96
- Among studies reporting data for ≥10 individuals with high baseline viral load from the same cohort, the proportion with HIV-1 RNA <50 copies/mL ranged from 50% (5/10) to 88% (37/42) at Week 24 and from 81% (13/16) to 100% (152/152) at Week 48; at Week 96, one study reported that 87% (39/45) of individuals were virologically suppressed
  - In a longitudinal cohort study following individuals with baseline viral load ≥500,000 copies/mL, the proportion achieving virologic suppression increased from 59% (13/22) at Week 24 to 95% (21/22) at Week 48
- Using inverse-variance weighting methods with a correction of 0.01% for studies with 100% suppression, the pooled proportions of individuals with high baseline viral load from studies with n ≥10 who achieved virologic suppression were 80.3% at Week 24, >99.9% at Week 48, and 87% at Week 96

Letang et al. EACS 2023; Warsaw, Poland. Poster eP.A.050.

Letang et al. EACS 2023; Warsaw, Poland. Poster eP.A.050.

Optimizing Antiretroviral Therapy in the Setting of Viral Suppression.

Preferred/recommended Recommended in certain clinical situations

- Maintain virological suppression without jeopardizing future treatment options
- It is critical to review ART history
- In the settings of existing NRTI resistance, should be included in the regimen with a fully active and high barrier drugs (DTG, BIC, boost DRV

	DHHS March 23, 2023 "Recommended for most people"	**EACS** Oct 2023 "Recommended"	**IAS-USA** Dec 2022 "Recommended"	**GESIDA** 2022 "Preferred"
DTG/3TC	HBsAg negative From TDF From NNRTI From RAL From PI	HBsAg negative HIV-VL < 500,000 copies/mL Not recommended after PrEP failure	HBsAg negative ~~HIV-VL < 500,000 copies/mL~~ Perhaps CD4 < 200 cells, unclear Not for rapid start (TDR) or after PReP failure or IOs. Close monitoring for adherence Cost or safety advantages over 3DR. Not recommended during pregnacy	AI HBsAg negative From any 3DR that contain (NNRTI, 2 NRTI, PI or INI)
DTG/RPV	HBsAg negative From TDF From NNRTI From PI	HLA-B*57:01 negative HBsAg negative	**OTHER** Concerns with ABC and increased risk AMI HLA-B*57:01 negative HBsAg negative	AI HBsAg negative
BIC/FTC/TAF **DTG/ABC/3TC***	From TDF or ABC From TDF From NNRTI From PI From RAL, EVG/c or DTG		TDF renal and bone toxicity TAF Associated with greater weight gain	AI
TAF	From TDF or ABC	Weight increase (BIC, TAF)	TAF associated with greater weight gain Not recommended during pregnacy	
DOR or RPV	From efavirenz From PI		**OTHER**: Only in pregnancy	

* **GESIDA guidelines**

EACS Guidelines 12.0. October 2023. Available at: https://www. https://www.eacsociety.org/media/guidelines-12.0.pdf. IAS-USA Guidelines. Gandhi R. JAMA 2023; 329(1):63-84. doi:10.1001/jama.2022.22246. DHHS. Available at https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/whats-new . Updated September 21, 2022. GeSIDA/PNS TAR en adultos infectados por el VIH (Actualización enero 2023). Disponible en: https://gesida-seimc.org

Switch to DOVATO in Patients Suppressed on Biktarvy (The SOUND Study), Week 48 Interim Analysis

Study Objective

To report results from the Week 48 interim analysis of the SOUND study, evaluating virologically suppressed patients on bictegravir/emtricitabine/tenofovir-alafenamide (B/F/TAF) who were switched to DTG/3TC

Inclusion criteria:

HIV VL < 50 copies/ml for ≥ 6 months

Taking B/F/TAF ≥24 weeks

No known resistance testing, no history of virological failure in prior 12 months

Primary end point:

% of patients with HIV-1 VL ≥ 50 copies/mL at week 48

Secondary end points:

At weeks 48 and 96 include: percentage of patients with HIV-1 VL < 50 copies/mL

Incidence and severity of adverse events (AEs) and laboratory abnormalities

% of subjects who discontinued treatment due to AEs

Change in baseline CD4 cell count at week 48 and 96

Retrospective pro-viral DNA testing on banked samples at baseline to compare virologic outcome (with or without M184V/I)

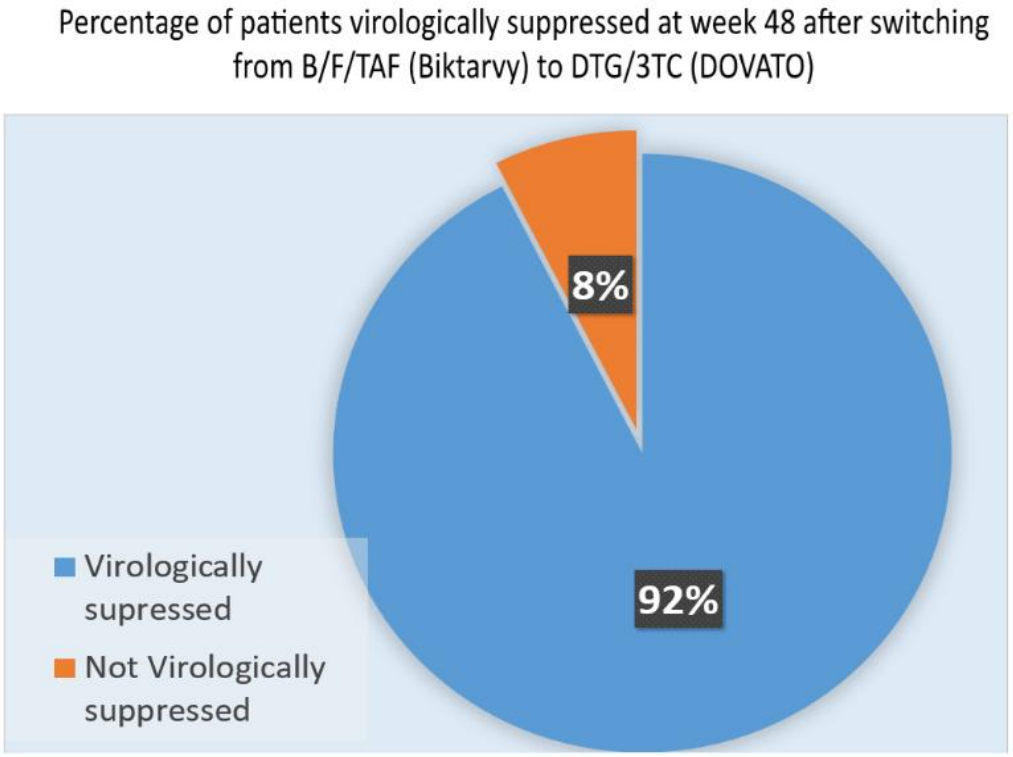
Number and type of resistance-associated mutations in virologic failure

- Slim et al. IDWeek 2023; Boston, MA. Poster 1593.

Switch to DOVATO in Patients Suppressed on Biktarvy (The SOUND Study), Week 48 Interim Analysis

Patient Characteristics	N
Sample size	40
Sex	M-22 (55%)/F-18 (45%)
Race/Ethnicity	AA – 23(57.5%) H- 12 (30%) C- 4 (10%), O-1 (2.5%)
BMI kg/m2	30.67 (range 16.97-49.55)
Median Age	58 years (range 27-81)
Median time on B/F/TAf	2.5 years(range: 1 – 3.6)
Median time since HIV diagnoses	16.0 years (range: 1.2 – 36)
Median number of prior ART regimens before study	3 (range 1 – 14)
Median baseline CD4	651 cells/mm3 (range:362-1044)
Median Nadir CD4	394 cells/mm3 (range:13-734).

AA – African American, H- Hispanic, C- Caucasian, O – Other Races/Ethnicities
M- Male, F-Female. BMI- Body Mass Index



- Slim et al. IDWeek 2023; Boston, MA. Poster 1593.

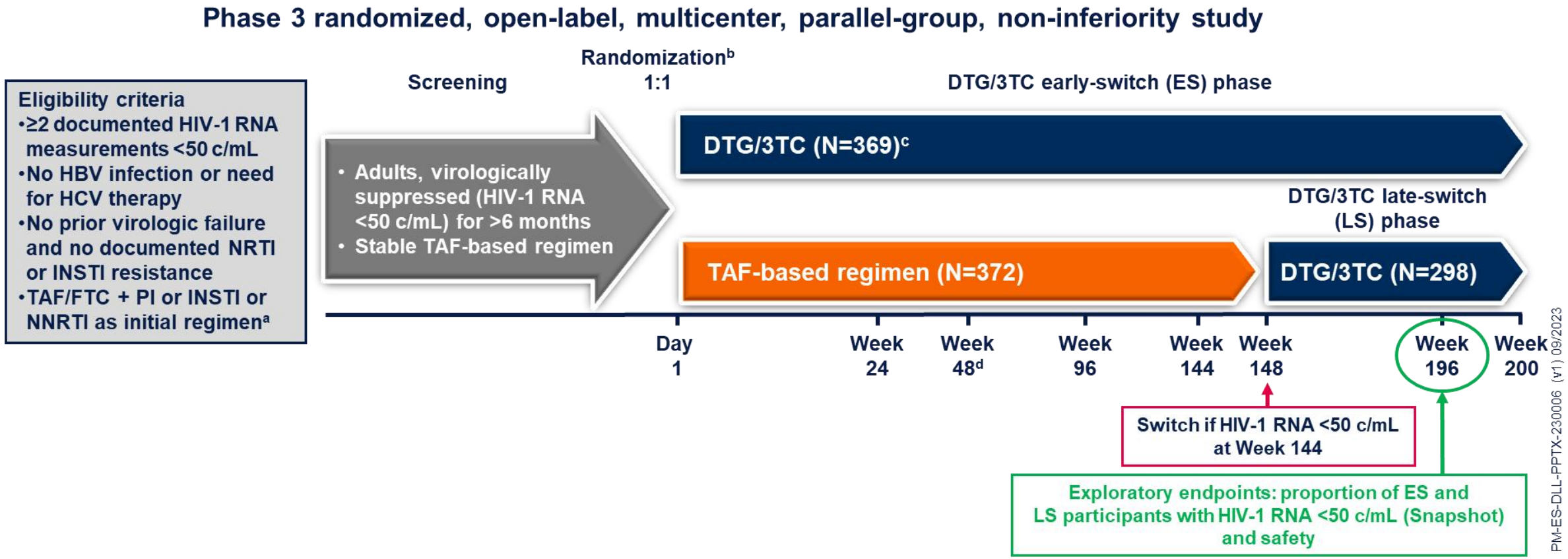
Switching to Dolutegravir/Lamivudine (DTG/3TC) Is Non-inferior to Continuing Tenofovir Alafenamide (TAF)-Based Regimens at Week 196: TANGO Subgroup Analyses

Don E. Smith,[1] Jean-Pierre Routy,[2] Stefan Scholten,[3] Julián Olalla Sierra,[4] Mounir Ait-Khaled,[5] Ruolan Wang,[6] Parminder Saggu,[7] Riya Moodley,[5] Bryn Jones[5]

[1]Albion Centre, Sydney, Australia; [2]McGill University Health Centre, Montreal, QC, Canada; [3]Praxis Hohenstaufenring, Cologne, Germany; [4]Hospital Costa del Sol, Marbella, Spain; [5]ViiV Healthcare, Brentford, UK; [6]ViiV Healthcare, Durham, NC, USA; [7]GSK, Brentford, UK

Referencia: 1. Smith D.E., Routy J.-P., Scholten S., et al. Switching to Dolutegravir/Lamivudine (DTG/3TC) is non-inferior to continuing tenofovir alafenamide (TAF)-based regimens at Week 196: TANGO subgroup analyses. Poster EPB0218. Presentado en IAS 2023, the 12th IAS Conference on HIV Science. 23–26 Julio 2023. Brisbane, Australia. Disponible en: https://www.natap.org/2023/IAS/IAS_27.htm Acceso realizado septiembre 2023

TANGO Study Design



[a]Participants with initial TDF treatment who switched to TAF ≥3 months before screening, with no changes to other drugs in their regimen, were also eligible. [b]Stratified by baseline third agent class (PI, INSTI, or NNRTI). [c]2 participants excluded who were randomized but not exposed to study drug. [d]Primary endpoint was proportion of participants with plasma HIV-1 RNA ≥50 c/mL at Week 48 (Snapshot, ITT-E), with a 4% non-inferiority margin.

Referencia: 1. Smith D.E., Routy J.-P., Scholten S., et al. Switching to Dolutegravir/Lamivudine (DTG/3TC) is non-inferior to continuing tenofovir alafenamide (TAF)-based regimens at Week 196: TANGO subgroup analyses. Poster EPB0218. Presentado en IAS 2023, the 12th IAS Conference on HIV Science. 23–26 Julio 2023. Brisbane, Australia. Disponible en: https://www.natap.org/2023/IAS/IAS_27.htm Acceso realizado septiembre 2023

Participant Demographics and Baseline Characteristics (ITT-E Population)

- At Week 196, TANGO included 369 ES group and 298 LS group participants treated with DTG/3TC for 196 and 48 weeks, respectively
- Demographics and baseline characteristics were generally balanced between the ES group and LS group
  - At the time of starting DTG/3TC, 21% of participants were aged ≥50 years in the ES group compared with 34% in the LS group (3 years after ES start)
  - LS group participants had higher CD4+ cell count at DTG/3TC start compared with the ES group

Characteristic	Early-switch DTG/3TC (N=369) Baseline (Day 1)	Late-switch DTG/3TC (N=298) Baseline (Week 148)[a]
Age, median (range), years	40 (20-74)	43 (20-76)
≥50, n (%)	79 (21)	100 (34)
Sex, female, n (%)	25 (7)	21 (7)
Race, n (%)		
White	297 (80)	235 (79)
Black or African American	50 (14)	41 (14)
Asian	13 (4)	12 (4)
Other races[b]	9 (2)	10 (3)
CD4+ cell count, mean (SD), cells/mm^3	702 (289)	751 (292)
CD4+ cell count, n (%), cells/mm^3		
<350	35 (9)	19 (6)
≥350	334 (91)	279 (94)
CDC HIV-1 classification		
Stage 1	255 (69)	202 (68)
Stage 2	94 (25)	79 (27)
Stage 3	20 (5)	17 (6)
Baseline third agent class, n (%)		
INSTI	289 (78)	242 (81)
EVG/c	243 (66)	202 (68)
NNRTI	51 (14)	33 (11)
RPV	43 (12)	30 (10)
PI	29 (8)	23 (8)
bDRV	25 (7)	22 (7)
Duration of ART before Day 1, median (range), mo	33.8 (7.1-201.2)	34.0 (7.0-160.8)
Duration of TAF before Day 1, median (range), mo	17.7 (3.6-73.7)	18.3 (3.9-71.2)

[a]Age was calculated at late-switch baseline (Week 148); all other characteristics were collected only at screening. [b]Includes American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and individuals of multiple races.

PM-ES-DLL-PPTX-230006 (v1) 09/2023

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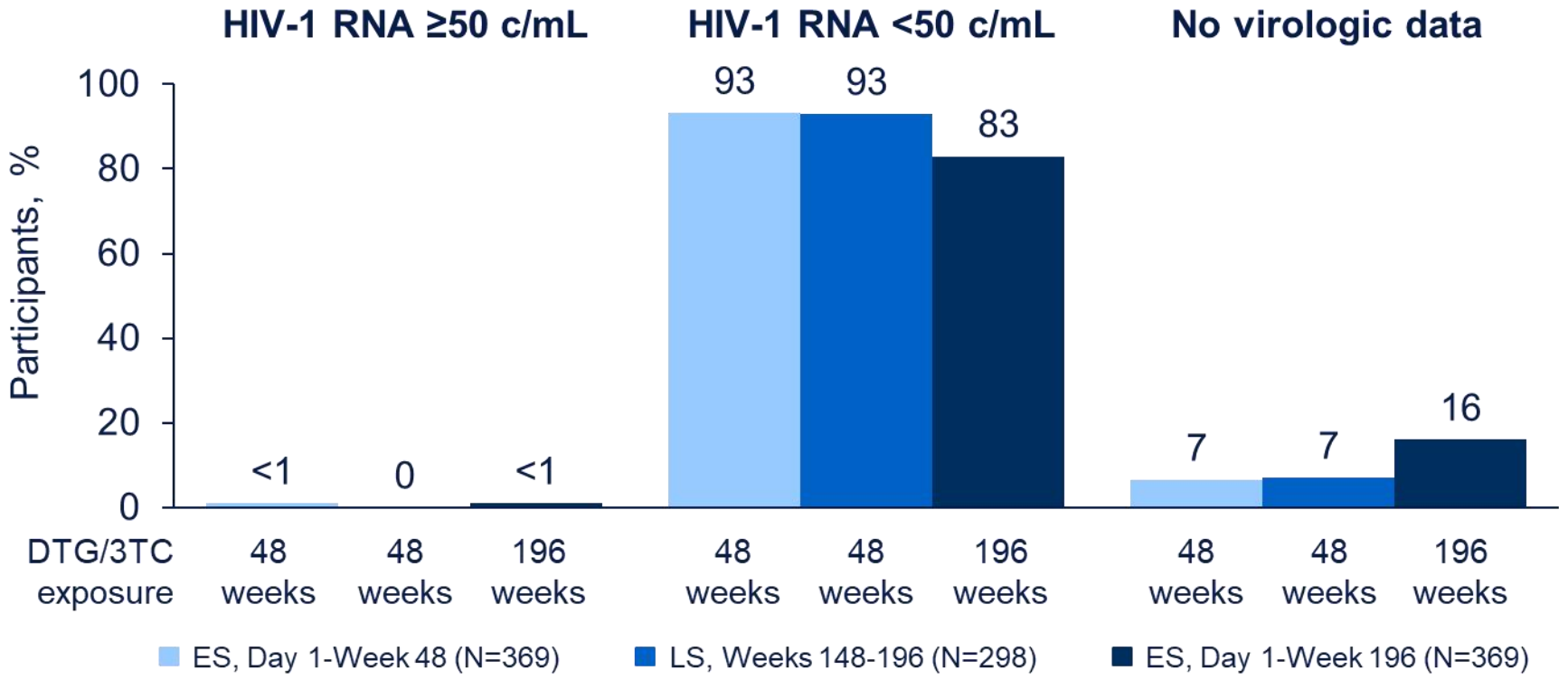
Overall Efficacy Results at Week 196 (Snapshot, ITT-E Population)

- Few ES participants (3/369 [<1%]; 95% CI, 0.0%-1.7%) and 0/298 (95% CI, 0.0%-0.0%) LS participants had HIV-1 RNA ≥50 c/mL in the overall population at Week 196 by Snapshot analysis (ITT-E)
- Confirmed virologic withdrawal criteria were met by 1/369 (<1%) ES participant and no LS participants through Week 196, with no resistance observed



PM-ES-DLL-PPTX-230006 (v1) 09/2023

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Conclusions TANGO

- Virologic efficacy and safety results by demographic, baseline disease characteristics, and baseline third agent class subgroups were consistent with overall results at Week 196
  - At 48 weeks post-switch to DTG/3TC, virologic response rates were similar between subgroups of participants who switched on Day 1 and corresponding subgroups of participants who switched at Week 148,[1] demonstrating the reproducibility of DTG/3TC efficacy after switch from 3- or 4-drug TAF-based regimens
- These results support that switching to DTG/3TC from TAF-based regimens effectively maintains virologic suppression across different demographic and baseline characteristics subgroups at 48 and 196 weeks

1. Ait-Khaled et al. EACS 2019; Basel, Switzerland. Slides PS7/2.

Referencia: 1. Smith D.E., Routy J.-P., Scholten S., et al. Switching to Dolutegravir/Lamivudine (DTG/3TC) is non-inferior to continuing tenofovir alafenamide (TAF)-based regimens at Week 196: TANGO subgroup analyses. Poster EPB0218. Presentado en IAS 2023, the 12th IAS Conference on HIV Science. 23–26 Julio 2023. Brisbane, Australia. Disponible en: https://www.natap.org/2023/IAS/IAS_27.htm Acceso realizado septiembre 2023

Real-world data shows similar efficacy of DTG/3TC versus BIC/FTC/TAF

	Study	Regimen	Timepoint	Safety/tolerability/other	VL <50 c/mL	Conclusions	
ART-experienced	**Tordi et al. Italy[1]**	DTG/3TC n=110	Median 19.6 Months	93.6% remaining on ART 4 (3.6%) discontinued due to AEs	99.1%	**Similar good effectiveness and safety profile** in virologically suppressed patients switching to DTG/3TC or BIC/FTC/TAF Low rates of VF (1.8% DTG vs 0.9% BIC)	**Durable and robust efficacy of DTG/3TC**
		BIC/FTC/TAF n=214	Median 27.5 Months	90.2% remaining on ART 5 (2.3%) discontinued due to AEs	97.2%		
	Cheng et al. Taiwan[2]	DTG/3TC n=512	Week 48	No difference in body weight, TC, HDL, LDL, TG and TC/HDL ratio between groups	97%	The proportion of patients with VL <50 c/mL was **higher for DTG/3TC vs BIC/FTC/TAF** (p<0.01) DTG/3TC was effective and **metabolically neutral** in patients with suppressed VL and those without history of VF	**Neutral impact of DTG/3TC on lipid parameters**
		BIC/FTC/TAF n=506			90%		
	Troya et al. Spain[3]	DTG/3TC n=1,032	Week 48	CD4/CD8 ratio increase by 0.04 CD8⁺ T-cell decrease by -10.5	97.5%	**Similar high rates of virologic control** and **low VF rates** with **no resistance** mutations observed in any treatment group **Increase in CD4⁺** T-cell count in all groups and **similar CD4/CD8 ratio increases** in the DTG/3TC and BIC/FTC/TAF groups	**Similar efficacy and immune recovery with DTG/3TC vs BIC/FTC/TAF**
		DTG/RPV n=760		CD4/CD8 ratio increase by 0.02	94.2%		
		BIC/FTC/TAF n=1,967		CD4/CD8 ratio increase by 0.05 CD8⁺ T-cell decrease by -25.5	95.6%		
	Farinacci et al. Italy[4]	DTG/3TC n=50 DOR/3TC/TDF n=47 BIC/FTC/TAF n=50	Week 48	2 discontinued due to treatment intensification and patient choice 2 discontinued: skin rash and other toxicity 2 discontinued: GI toxicity and simplification	100%	All regimens were **effective and well tolerated** **Improvements in CD4/CD8 ratio with DTG/3TC and DOR/3TC/TDF vs BIC/FTC/TAF** **Reduction in TG with DTG/3TC and DOR/3TC/TDF vs BIC/FTC/TAF**	**High rates of suppression, and improved immune recovery and lipid profile with DTG/3TC**
ART-naïve	**Long China[5]**	DTG + 3TC n=126	Week 48	Median weight increase 1.7 kg BMI increase 0.6 kg/m² CrCl decreased 20 mL/min	88%	Both regimens showed **high tolerability** in ART-naïve patients, with no difference in efficacy **BIC/FTC/TAF** was associated with **increased risk of weight gain** and renal function parameters vs DTG/3TC	**Additional weight gain with INI + TAF**
		BIC/FTC/TAF n=104		Median weight increase 4.0kg BMI increase 1.4 kg/m² CrCl decreased 10 mL/min	89%		

1. Tordi S, et al. EACS 2023; Warsaw, Poland. ePA052; **2.** Cheng CY, et al. EACS 2023; Warsaw, Poland. ePA023
3. Troya J, et al. EACS 2023; Warsaw, Poland. TBC; **4.** Farinacci D, et al. EACS 2023; Warsaw, Poland. ePA038 **5.** Long H. EACS 2023; Warsaw, Poland. ePA051


Muchas gracias….