2DR vs. 3DR INTEGRASE INHIBITOR-BASED REGIMENS INITIATION AND CD4+/CD8+ RATIO RECOVERY

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Javier Martínez-Sanz[1], Raquel Ron[1], Elena Moreno[1], Matilde Sánchez-Conde[1], Alfonso Muriel[2,3], María Rivero[4], José Ramón Blanco[5], Enrique Bernal[6], Miguel de Zárraga[7], María José Galindo[8], Eva Poveda[9], Gloria Samperiz[10], Santiago Moreno[1], and Sergio Serrano-Villar[1], on behalf of CoRIS

[1]Department of Infectious Diseases, Hospital Ramón y Cajal, IRYCIS, Madrid, Spain. [2]Biostatistics Unit, Hospital Ramón y Cajal, Universidad de Alcalá, IRYCIS, Madrid, Spain. [3]CIBER Epidemiología y Salud Pública (CIBERESP), Spain. [4]Complejo Hospitalario de Navarra, Pamplona, Spain. [5]Hospital San Pedro, Centro de Investigación Biomédica de La Rioja (CIBIR), Logroño, Spain. [6]Hospital General Universitario Reina Sofía, Murcia, Spain. [7]Hospital San Agustín, Avilés, Spain. [8]Hospital Clínico Universitario de Valencia, Valencia, Spain. [9]Hospital Álvaro Cunqueiro, Vigo, Spain. [10]Hospital Universitario Miguel Servet, Zaragoza, Spain.

BACKGROUND

- Accumulating evidence suggests that integrase strand-transfer inhibitors (INSTI)-based initial antiretroviral therapy (ART) results in greater CD4/CD8 ratio recovery compared to other regimens.
- However, it is unknown whether the treatment initiation with INSTI-based two-drug regimens (2DR) has a different impact on the CD4/CD8 ratio recovery compared to INSTI-based 3DR.

METHODS

- We emulated a target trial to assess the effect of two different ART strategies on CD4/CD8 ratio normalization at **48 weeks** for **three different cutoffs** (0.5, 1.0 and 1.5)
- We included all subjects included in the Cohort of the Spanish HIV Research Network (CoRIS) who started 2DR with **dolutegravir (DTG) plus 3TC** or **3DR based on bictegravir or DTG**.
- For each outcome, we excluded participants who initiated ART with a CD4/CD8 ratio above the cutoff point.
- We matched each participant who started 2DR with up to four participants who received 3DR based on **age**, **sex**, **transmission category**, **educational level**, **country of origin**, **baseline HIV RNA**, **AIDS diagnosis**, and **pre-ART nadir CD4/CD8 ratio**.
- We fitted generalized estimating equation (GEE) models to allow for clustered data analysis, to assess the risk of CD4/CD8 ratio normalization at 48 (+12) weeks. Survival curves were estimated with the Kaplan–Meier method.
- Participants were censored if they changed their initial ART regimen or at the last study visit.

RESULTS

- A total of 485, 805, and 924 participants were matched for each of the three analyses (cutoffs of 0.5, 1.0, and 1.5, respectively). The distribution of covariates was similar in the three models.
- Overall, the study sample was representative of a medium-aged population (median age **37 years**) with a higher representation of **men (88%)** and a **median CD4/CD8 ratio around 0.30**.

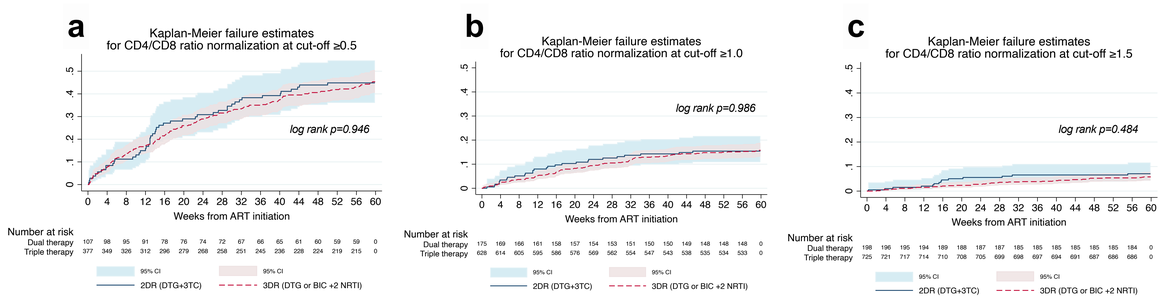
This study provides new evidence that **CD4/CD8 ratio recovery rates are similar during the first *48 weeks* after ART initiation with DTG+3TC or three-drug INSTI-based regimens.**

RESULTS

Baseline characteristics	CD4/CD8 ratio >0.5		CD4/CD8 ratio >1.0		CD4/CD8 ratio >1.5	
	DTG + 3TC (n=108)	Triple therapy (n=377)	DTG + 3TC (n=176)	Triple therapy (n=629)	DTG + 3TC (n=198)	Triple therapy (n=726)
Age, median (IQR)	37 (30, 46)	36 (29, 43)	37 (30, 46)	36 (29, 44)	37 (31, 45)	37 (30, 44)
Gender, male, n (%)	92 (85)	332 (88)	153 (87)	558 (89)	174 (88)	645 (89)
Mode of transmission, n (%)						
MSM	73 (68)	273 (72)	120 (68)	462 (73)	136 (69)	528 (73)
Other	35 (32)	104 (28)	56 (32)	167 (27)	62 (31)	198 (27)
Origin, n (%)						
Spain	51 (47)	175 (46)	84 (48)	299 (48)	100 (51)	363 (50)
Latin America	41 (38)	150 (40)	61 (35)	231 (37)	68 (34)	260 (36)
Western Europe	7 (6)	25 (7)	15 (9)	55 (9)	16 (8)	57 (8)
Africa	7 (7)	19 (5)	14 (8)	37 (6)	12 (7)	38 (5)
Other	2 (2)	8 (2)	2 (1)	7 (1)	2 (1)	8 (1)
AIDS diagnosis, n (%)	19 (18)	56 (15)	28 (16)	82 (13)	27 (14)	88 (12)
Nadir CD4/CD8 ratio, median (IQR)	0.26 (0.16, 0.39)	0.27 (0.16, 0.40)	0.32 (0.19, 0.50)	0.33 (0.19, 0.50)	0.35 (0.20, 0.53)	0.35 (0.21, 0.53)
HIV RNA >100.000 copies/µL, n (%)	59 (55)	214 (57)	87 (49)	302 (48)	94 (47)	344 (47)
INSTI						
Dolutegravir	-	300 (80)	-	508 (81)	-	562 (77)
Bictegravir	-	77 (20)	-	121 (19)	-	164 (23)
NRTI backbone						
ABC + 3TC	-	200 (53)	-	346 (55)	-	397 (55)
TDF + FTC	-	82 (22)	-	130 (21)	-	131 (18)
TAF + FTC	-	95 (25)	-	153 (24)	-	198 (27)

Abbreviations: 3TC, lamivudine; ABC, abacavir; ART, antiretroviral therapy; FTC, emtricitabine; IDU, injecting drug use; INSTI, integrase strand transfer inhibitor; MSM, men who have sex with men; NRTI, nucleoside reverse transcriptase inhibitor; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.

Kaplan-Meier survival estimates for CD4/CD8 ratio normalization at 0.5, 1, and 1.5 cutoffs in participants with 2DR and 3DR



Abbreviations: 2DR, two-drug regimens; 3DR, three-drug regimens; BIC, bictegravir; DTG, dolutegravir; NRTI, nucleoside reverse transcriptase inhibitor.

RESULTS

- At week 48, **45% of participants achieved a CD4/CD8 ratio >0.5**, **15% achieved a ratio >1.0**, and **6% achieved a ratio >1.5**. There were **no differences between 2DR and 3DR** in the incidence ratio of CD4/CD8 ratio normalization at 0.5, 1.0 and 1.5 cut-offs.

Generalized estimating equation (GEE) models for ratio normalization at 48 weeks

ART group	OR	95% CI	p
CD4/CD8 ratio > 0.5			
DTG + 3TC	Ref.	-	-
DTG or BIC + 2 NRTI	1.00	0.67, 1.50	0.985
CD4/CD8 ratio > 1.0			
DTG + 3TC	Ref.	-	-
DTG or BIC + 2 NRTI	1.03	0.68, 1.58	0.871
CD4/CD8 ratio > 1.5			
DTG + 3TC	Ref.	-	-
DTG or BIC + 2 NRTI	0.86	0.48, 1.54	0.612

Abbreviations: 3TC, lamivudine; BIC, bictegravir; CI, confidence interval; DTG, dolutegravir; NRTI, nucleoside reverse transcriptase inhibitor; OR, odds ratio; Ref, reference category.

CONCLUSIONS

- In this observational study of a prospective cohort of ART-naïve, HIV-infected individuals, we found similar CD4/CD8 ratio recovery rates at 48 weeks between 2DR with DTG plus 3TC and 3DR based on DTG or BIC, measured at three different cutoff points (0.5, 1 and 1.5).
- Next studies should address the potential long-term differences between these strategies.

• ADDITIONAL KEY INFORMATION

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Author Contact Information

Javier Martínez-Sanz, MD, PhD
Department of Infectious Diseases, Hospital Universitario Ramón y Cajal, IRYCIS
Madrid, Spain

javier.martinez.sanz@salud.madrid.org

@JMartinezSanz