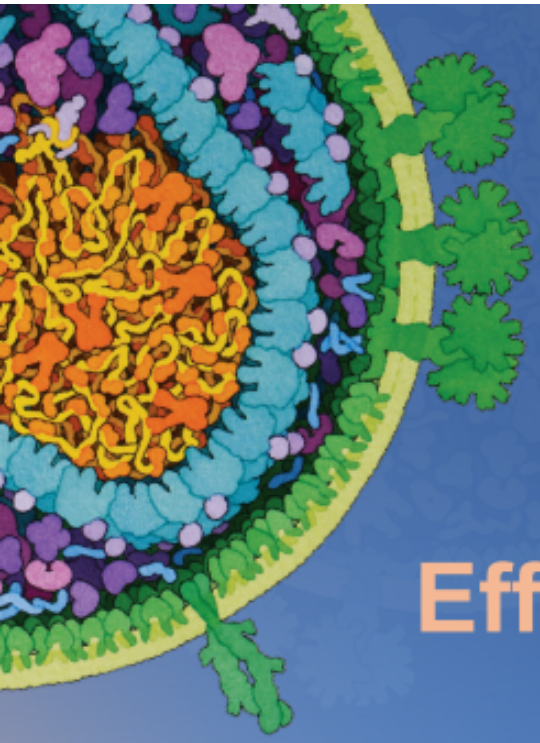

SCIENCE SPOTLIGHT™

Effects of Switch from 3DR to 2DR on Inflammatory Biomarkers

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Background

- Cumulative data support the use of several ART combinations with 2-drug regimens (2DR) in both treatment-naive and experienced patients.[1,2]
- Increased inflammation persists even during triple ART and strongly predicts adverse clinical outcomes.[3-5]
- Inflammation has been linked with virologic events that occur during ART-mediated suppression:
  - HIV RNA and p24 are likely pro-inflammatory and produced in lymphoid tissues, were many drugs are poorly distributed.[6,7]
  - Suboptimal ART adherence is associated with increased inflammation despite virologic suppression in plasma.[8,9]
- There are no data on the long-term dynamics of inflammatory biomarkers after reduction of the number of antiretrovirals.

Objective: To assess the effects of switching ART from triple therapy (TT) to 2DR on long-term trajectories of inflammatory markers.

1. European AIDS Clinical Society Guidelines. https://www.eacsociety.org/guidelines/eacs-guidelines/eacs-guidelines.html 2. DHSS Guidelines. https://aidsinfo.nih.gov/guidelines
3. Kuller et al. Plos Medicine 2008. 4. Hunt et al. JID 2014. 5. Tenorio et al. JID 2014
6. Rothenberg et al. PNAS 2015. 7. Imamichi et al. PNAS 2020. 8. Castillo-Mancilla et al. CID 2016. 9. Castillo-Mancilla et al. JIAS 2019.

Methods

Design: Nested study in the Spanish AIDS Cohort (CoRIS)

Inclusion criteria

- Patients initiating ART in CORIS between 2004-2018 with TT (2NRTI+bPI/INSTI).
- Virological suppression achieved in the first 48 weeks of ART.
- Either remained on TT or switched to 2DR (3TC+bPI, 3TC+DTG, RPV+DTG) or 1DR (LPVr or bDRV).
- At least 3 plasma samples available

Exclusion criteria

- ART initiation with regimens with <3 drugs
- Virological failure: ≥2 consecutive viral loads more than 50 copies/mL) during the first 48 weeks of ART
- AIDS conditions or serious non-AIDS events (malignancies, cardiovascular disease, end-stage liver disease, end-stage kidney disease), in the first 48 weeks of ART.

From 14,458 patients, 8,416 met these criteria

https://www.redris.es/en/web/guest/services/coris

90 patients on 3DC
60 patients on 2DC
30 patients on 1DC

Selected based on
At least 3 samples
Longer follow-up

IL-6, hsCRP
sCD14, sCD163
D-dimers
IFABP

Statistics

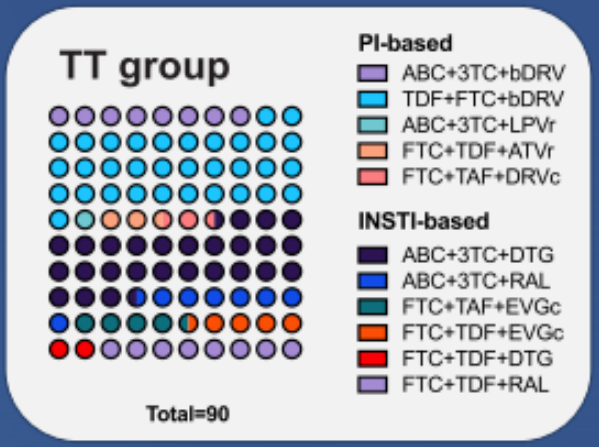
- Plasma samples measured in duplicate using comercial ELISA kits.
- Linear trajectories estimated using piecewise linear mixed models with fixed effects (interaction term biomarker concentration#time, age, sex, risk group, education level, AIDS, CD4 nadir, maximum HIV RNA, biomarker level at HIV RNA suppression).

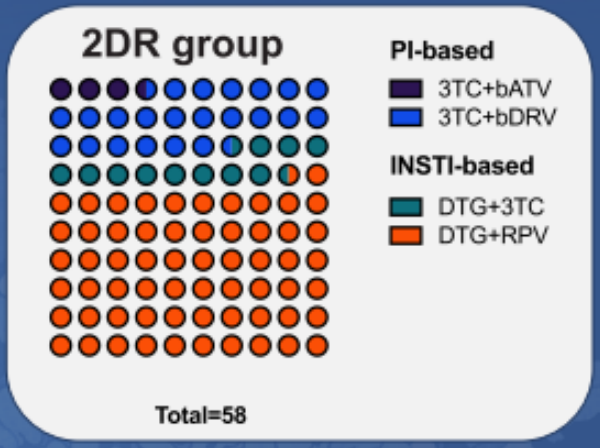
Results

General characteristics

	TT N=90	2DR N=58	p value
Age (mean, [SD])	37 (9)	40 (11)	0.227
Male, n (%)	78 (87)	50 (86)	0.936
IDU, n (%)	6 (7)	3 (6)	0.972
Spanish origin, n (%)	59 (66)	36 (62)	0.666
University education, n (%)	22 (24)	18 (31)	0.593
AIDS diagnosis, n (%)	15 (16)	8 (14)	0.769
HCV positive ever, n (%)	12 (13)	6 (10)	0.570
Maximum HIV-1 RNA (c/mL), median (IQR)	114500 (33770-344426)	93599 (36307-219000)	0.376
Time from ART initiation to virologic suppression (years), median (IQR)	0.5 (0.2-0.9)	0.5 (0.3-0.9)	0.524
Time from virologic suppression (years) to ART switch, median (IQR)	-	3.5 (1.9-5.2)	-
Nadir CD4 cell count (cells/µL), median (IQR)	300 (151-373)	259 (112-382)	0.309
Number of samples analyzed, median (min, max)	4 (3-11)	3 (3-8)	<0.001
Follow-up (years), median (IQR)	3.9 (2.5-4.7)	5.3 (3.9-6.8)	<0.001

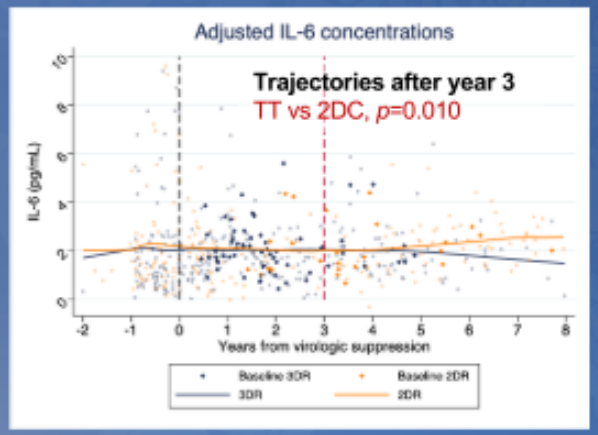
ART distribution in each group

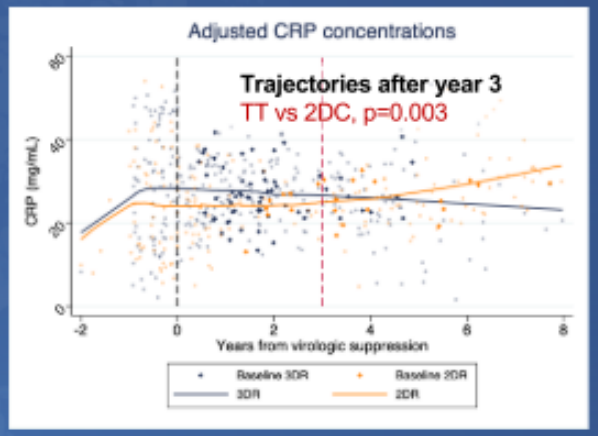


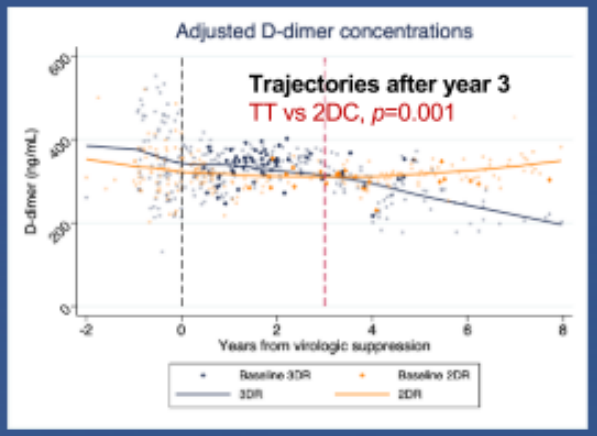


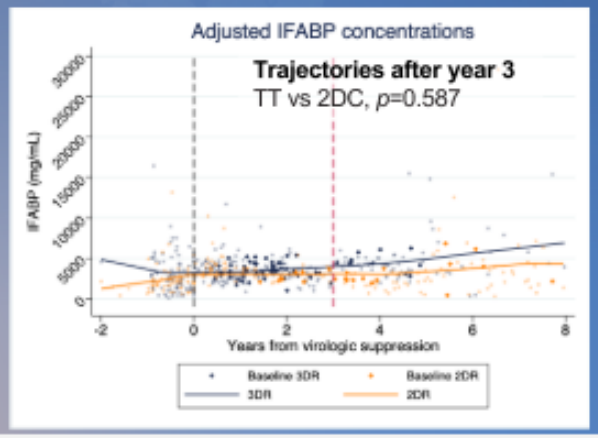
Results

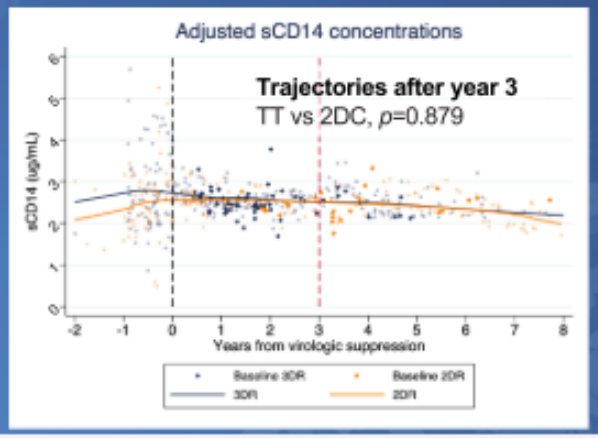
Adjusted Piecewise Linear Mixed Models

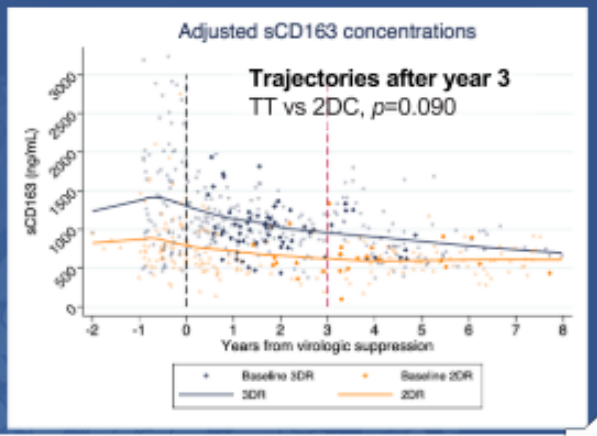








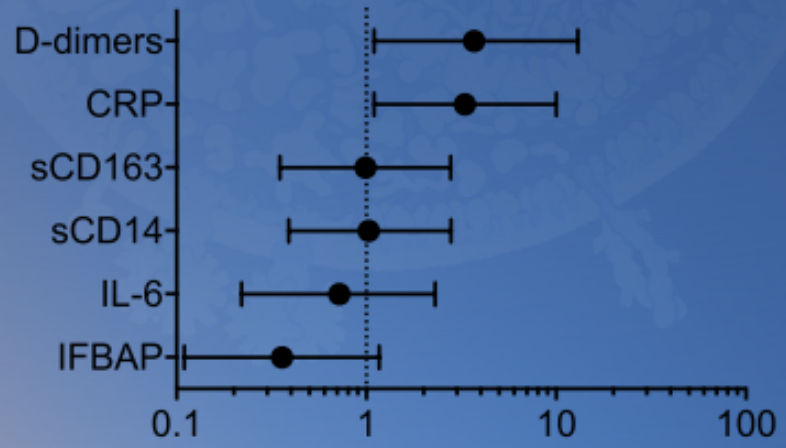




Baseline: for 3DR represents the the second sample after the HIV RNA suppression time point; for 2DR represents the first sample after switch to 2DR.
Linear trajectories estimated using **piecewise linear mixed models** with fixed effects (interaction term biomarker concentration#time, adjusted for age, sex, risk group, education level, AIDS, CD4 nadir, maximum HIV RNA, biomarker level at HIV RNA suppression).

Results

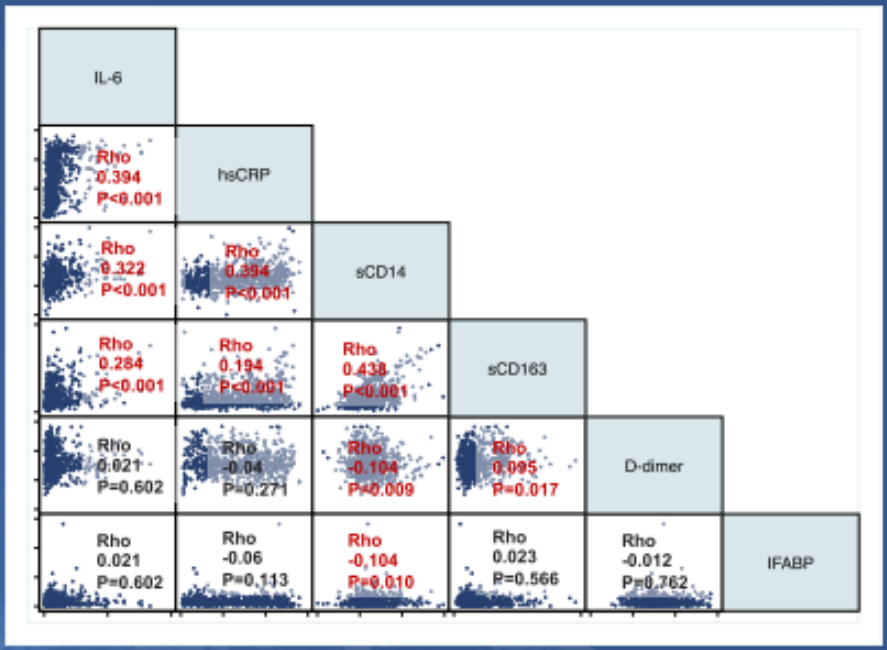
Multivariate Logistic regression: changes during follow-up TT (ref.) vs. 2DR



Adjusted Odds ratio for Quartile increase

Adjusted for age, sex, risk group, education level, AIDS, CD4 nadir, maximum HIV RNA, biomarker level at HIV RNA suppression, years of follow-up

Crossed-correlations between inflammatory biomarkers



CONCLUSIONS

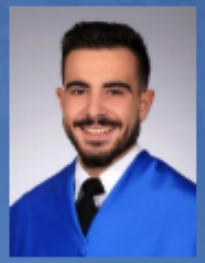
- In this observational study in virally suppressed individuals, maintaining 3DR was associated with a more favourable long-term anti-inflammatory profile than switching to 2DR.
- The potential clinical implications of these findings on the development of non-AIDS events deserve further investigation.

Limitations

- Unmeasured confounding (ART adherence) could have affected the inflammatory markers measured.
- Immortal time bias, lack of control for informative censoring

Acknowledgments


Mª Rosa López-Huertas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ENFERMEDADES INFECCIOSAS
H.U. RAMÓN Y CAJAL

To all patients and their families, who make scientific progress posible.