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VIROLOGICAL EFFICACY OF DOLUTEGRAVIR PLUS DARUNAVIR IN MULTI-DRUG-RESISTANT HIV PATIENTS: A REAL-WORLD COHORT STUDY WITH DATA FROM THE PRESTIGIO REGISTRY

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Background: This study evaluated the virological efficacy of DTG plus DRV/b in people with 4-class drug-resistant HIV (4DR-PWH) in a real-world setting.

Materials and Methods: Retrospective study analyzing antiretroviral treatment (ART) used by adults with 4DR HIV from the PRESTIGIO Registry [1]. The ART regimes were categorized into three groups: i) DTG and DRV/b only (DTG+DRV/b); ii) DTG and DRV/b plus ≥1 additional antiretroviral drug (ARV) (DTG+DRV/b+other); iii) regimens not including the combination of DTG and DRV/b (Other). Follow-up started from the first evidence of 4DR (baseline) until death, loss to follow-up, or May 30 2024. A person can change group multiple times during follow-up. The relationship between DTG+DRV/b and virological failure (VF) was analyzed using mixed-effects logistic regression. VF was defined as ≥2 HIV-RNA determinations ≥50 copies/mL or one ≥1000 cp/mL. Regimens were classified as 0 (not failed) or 1 (failed) at each HIV-RNA measurement. Regression was adjusted for age, ART duration, number of fully active ARV, sex at birth, and nadir CD4+. Individual failure predisposition was estimated with a random intercept.

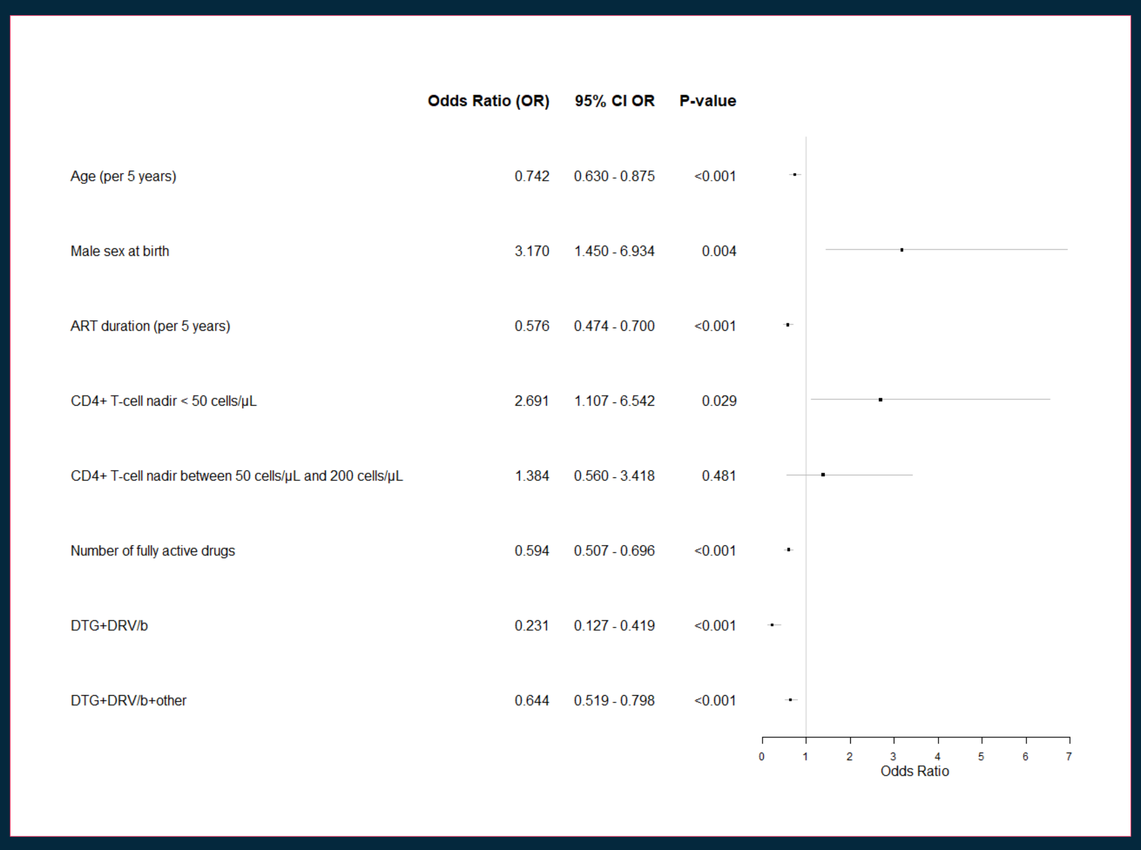
Results: We evaluated 844 regimens from 249 4DR-PWH with a median follow-up of 8.7 years (5.9–11.5). Specifically, the 844 regimens were distributed as follows: 72 (8.5%) DTG+DRV/b, 264 (31.3%) DTG+DRV/b+Other, and 508 (60.2%) Other. Overall, 60 people were exposed to DTG+DRV/b , 136 people to DTG+DRV/b+Other, and 181 to Other. In the DTG+DRV/b, the median number of fully active ARV included and the percentage of full activity of DTG and DRV/b were higher than the other groups. (table 1) Logistic analysis indicated the odds of VF is 77% and 35.9% lower with DTG+DRV/b and DTG+DRV/b+other, respectively, compared to "Other". Each fully active ARV in the regimen decreases VF odds by 40%. Older age and longer ART duration lessen the odds of VF, likely due to better HIV control over time. (Figure 1). DTG+DRV/b remains virologically effective despite the partial activity of its components in the group (DRV/b fully active in 47.2%, DTG fully active in 63.9%).
DTG and DRV/b dual therapy remains virologically effective despite the partial activity of its individual components in the group (DRV/b fully active in 47.2% of cases and DTG in 63.9%) with only 30.6% of cases showing full activity to both drugs combined. Additionally, DTG+DRV/b+other seems to be more effective than Other, even when full activity of the combination is present in just 15.5% of cases.

Table 1. Number, Duration, and Activity of antiretrovirals Included in the ART regimes analyzed.

	DTG+DRV/b (n=72)	DTG+DRV/b+ OTHER (n=264)	OTHER (n=508)
Duration of the regimen in years; Median (IQR)	4.2 (1.7-5.7)	1.3 (0.5-2.8)	1.8 (0.6-3.5)
Cumulative duration of the regimen in years	280.1	1010.1	656.9
Number of fully active drugs included at each regimen initiation; Median (IQR)	1 (1-2)	1 (0-2)	1 (0-1)
Percentage of regimens with fully activity of DRV/b at the time of its inclusion in the regimen	34 (47.2%)	70 (26.5%)	* 49 (23.7%)
Percentage of regimen with fully activity of DTG at the time of its inclusion in the regimen	46 (63.9%)	122 (46.2%)	** 89 (49.7%)
Full activity of both DRV and DTG at the time of its inclusion in the regimen	22 (30.6%)	41 (15.5%)	NA

**regimens with DRV /b in Other N=207 (40.7%)*
*** regimens with DTG in Other N=179 (35.2%)*
DRV/b: Boosted Darunavir
DTG: Dolutegravir

Figure 1 Multivariate Logistic Regression Analyzing the Relationship Between DTG+DRV/b and Virological Failure in a cohort of people with 4-class drug-resistant HIV



Variable	Odds Ratio (OR)	95% CI OR	P-value
Age (per 5 years)	0.742	0.630 - 0.875	<0.001
Male sex at birth	3.170	1.450 - 6.934	0.004
ART duration (per 5 years)	0.576	0.474 - 0.700	<0.001
CD4+ T-cell nadir < 50 cells/µL	2.691	1.107 - 6.542	0.029
CD4+ T-cell nadir between 50 cells/µL and 200 cells/µL	1.384	0.560 - 3.418	0.481
Number of fully active drugs	0.594	0.507 - 0.696	<0.001
DTG+DRV/b	0.231	0.127 - 0.419	<0.001
DTG+DRV/b+other	0.644	0.519 - 0.798	<0.001

Conclusions: Among 4DR-PWH, DTG+DRV/b is associated with a lower odd of VF even after adjusting for the number of fully active drugs. This combination is also effective when not fully active or combined with other ARVs.

REFERENCE

[1] T. Clemente et al., "Cohort profile: PRESTIGIO, an Italian prospective registry-based cohort of people with HIV-1 resistant to reverse transcriptase, protease and integrase inhibitors," BMJ Open, vol. 14, no. 2, Feb. 2024

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