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Risk of virological failure after drug burden reduction in non-viremic people with 4-class drug-resistant HIV: data from the PRESTIGIO Registry

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Presenter Disclosure Information

No conflict of interest to disclose.

Rationale

- Individuals with 4-class drug resistant (4DR) HIV constitute a fragile population, often requiring complex antiretroviral regimens.[1]
- Antiretroviral treatment (ART) simplification, and particularly drug burden reduction (DBR), could be extremely useful in this population to limit drug toxicities and increase adherence.
- No data are available on the effect of DBR in people with 4DR HIV (4DR-PWH).

1. Galli L, et al. **Burden of Disease in PWH Harboring a Multidrug-Resistant Virus: Data From the PRESTIGIO Registry**. *Open Forum Infect Dis* 2020. doi: 10.1093/ofid/ofaa456.

Primary objective

To evaluate the risk of virological failure (VF) after DBR in 4DR-PWH on stable virological suppression (VS).

Study design

Retrospective, cohort study on 4DR-PWH on ART, with stable VS [≥2 consecutive viral loads (VLs) <50 copies/mL], enrolled in the PRESTIGIO Registry.

Methods & Statistical Analysis

- During follow-up (FU), ART regimens:
  - ✓remained unchanged
  - ✓were modified with reduction in the number of drugs or dosage (DBR)
  - ✓were modified without DBR (other switches).

- FU accrued from the second VL <50 copies/mL after evidence of 4-class drug resistance (baseline) until VF at 200 copies/mL (VF200) or the second ART switch or the last available VL measurement.

- Cumulative probabilities and risk of VF200 were estimated using the Simon-Makuch method and the Cox regression model, respectively; type of ART switch was considered as time-dependent variable.

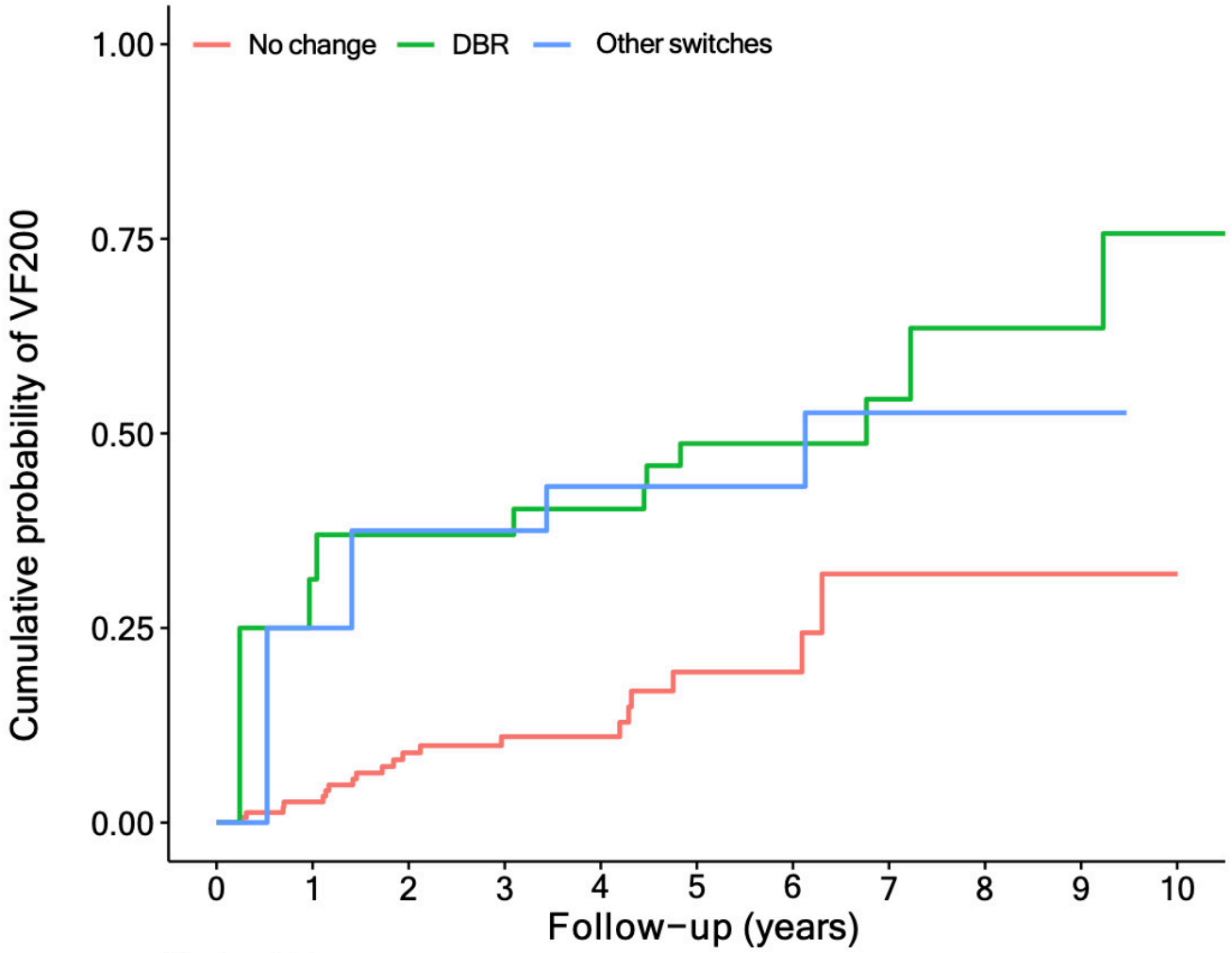
Baseline characteristics

Baseline characteristics	Overall (n=166)	No ART change (n=87)	Drug burden reduction (n=51)	Other ART switches (n=28)	p§
Age (years), ***median (IQR)***	51.3 (46.8-56.3)	52.7 (47.1-57.2)	50.2 (46.1-56.5)	50.4 (47.8-54.8)	0.48
Female sex, ***n (%)***	47 (28.3%)	23 (26.4%)	17 (33.3%)	7 (25.0%)	0.63
ART duration (years), ***median (IQR)***	19.9 (16.0-23.0)	21.3 (16.5-23.9)	19.8 (15.7-21.8)	19.0 (16.2-21.1)	0.07
CD4⁺ T-cell count (cells/µL), ***median (IQR)***	496 (326-728)	522 (396-744)	440 (266-656)	527 (336-780)	0.17
CD4⁺/CD8⁺ ratio, ***median (IQR)***	0.48 (0.31-0.71)	0.49 (0.32-0.73)	0.48 (0.32-0.60)	0.54 (0.27-0.83)	0.52
CD4⁺ T-cell nadir (cells/µL), ***median (IQR)***	115 (27-201)	70 (23-174)	102 (15-199)	167 (77-237)	0.08
Number of ongoing antiretrovirals, ***median (IQR)***	3 (3-4)	3 (2-4)	3 (3-4.5)	3 (3-4)	**0.01**
NRTI-containing regimens, ***n (%)***	78 (47.0%)	35 (40.2%)	28 (54.9%)	15 (53.6%)	0.19
NNRTI-containing regimens, ***n (%)***	57 (34.3%)	29 (33.3%)	19 (37.3%)	9 (32.1%)	0.86
PI-containing regimens, ***n (%)***	146 (88.0%)	76 (87.4%)	46 (90.2%)	24 (85.7%)	0.81
INSTI-containing regimens, ***n (%)***	147 (88.6%)	79 (90.8%)	45 (88.2%)	23 (82.1%)	0.45
Entry inhibitor (MVC / T20 / FTR / IBA)-containing regimens, ***n (%)***	57 (34.3%)	24 (27.6%)	23 (45.1%)	10 (35.7%)	0.11
Genotypic susceptibility score, ***median (IQR)***	2.0 (1.5-2.5)	2.0 (1.5-2.5)	2.0 (1.5-2.5)	2.0 (1.5-2.0)	0.48

§by Kruskal-Wallis test (continuous variables) or chi-square test (categorical variables).

Time to and risk of VF200

During a median FU of 3.8 (IQR=2.3-5.6) years, 34/166 (20.5%) individuals had VF200.



	Unadjusted Hazard ratio (95%CI)	P-value
DBR vs No change	2.20 (0.89-5.44)	0.08
DBR vs Other switches	1.19 (0.37-3.81)	0.76
Other switches vs No change	1.84 (0.54-6.24)	0.32

Multivariable Cox regression: BL factors predicting risk of VF200

Characteristics	Category	Adjusted Hazard ratio of VF200 (95% confidence interval)	p-value
Type of ART switch§	DBR vs No change	1.95 (0.74-5.15)	0.17
	Other ART switches vs No change	1.95 (0.55-6.95)	0.30
Biological sex	Female versus Male	0.67 (0.27-1.67)	0.39
Age	Per 1-year older	0.96 (0.91-1.01)	0.08
ART duration	Per 1-year higher	0.97 (0.92-1.02)	0.28
$CD4^+/CD8^+$ ratio	Per 0.1-unit higher	0.84 (0.71-0.99)	**0.04**
GSS	Per 1-unit higher	1.05 (0.64-1.73)	0.85

§ time-dependent variable

Conclusions

- Drug burden reduction showed a potential impact on the risk of VF ≥200 copies/mL in suppressed 4DR-PWH.

- The risk of failure was also increased by a low baseline $CD4^+/CD8^+$ ratio.

- Given the urgent need to simplify the complex regimens of the fragile population with a multidrug-resistant virus and the availability of new options, new tools to predict the virological safety of reducing drug burden should be investigated.

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