Two-fold increased risk of cardiovascular events in people with multidrug-resistant HIV: data from the PRESTIGIO Registry

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Introduction

- Major adverse cardiovascular events (MACEs) may contribute to the high morbidity in people with 4-class drug-resistant HIV (4DR-PWH) [1].
- Aim of this study was to explore the probability of MACEs in 4DR-PWH compared with non-4DR controls.

Study design

- Retrospective, propensity score-matched cohort study on 4DR- (cases) and non-4DR-PWH (controls), on antiretroviral therapy (ART), without previous MACEs.
- Cases were individuals with 4DR HIV from the PRESTIGIO Registry with ≥1 matched control [2].
- Controls were individuals who never developed resistance to >2 drug classes and were matched to cases in a 4:1 ratio for age (±3 years), sex-assigned-at-birth, and ART duration (±3 years).
- An index date [baseline (BL)] was assigned to each case and control: for cases, this was the date of first evidence of 4-class drug resistance; for controls, this was the index date of the corresponding case.

Table 2. Cox time-dependent multivariable analysis for first MACE

Characteristics	Category	Adjusted HR of first MACE (95%CI)	p
4DR status	Yes vs no	1.8 (1.0-3.3)	**0.039**
Age (time-dependent)	Per 5-year higher	1.2 (1.0-1.4)	0.054
Sex-assigned-at-birth	Male vs female	2.2 (0.9-5.0)	0.070
HIV load (time-dependent)	≥50 vs <50 copies/mL	2.2 (1.2-3.9)	**0.011**
CD4⁺ nadir	Per 100-cell/mm³ higher	1.0 (0.9-1.1)	0.956
BL smoking habit	Yes vs no	1.7 (1.0-3.0)	0.070
BL diabetes mellitus	Yes vs no	2.1 (1.2-4.0)	**0.015**
BL dyslipidaemia	Yes vs no	2.0 (1.0-3.9)	**0.037**
BL chronic kidney disease	Yes vs no	2.5 (0.8-7.8)	0.101
BL HCV serostatus	Positive vs negative	1.8 (1.1-3.1)	**0.030**

Conclusions

- In PWH, multidrug resistance is significantly associated with a higher incidence and risk of cardiovascular events.
- Prompt implementation of prevention strategies is mandatory in this fragile population.

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Methods

- The primary outcome was the probability of first MACE (cardiovascular death, myocardial infarction, unstable angina, stroke, transient ischemic attack, peripheral arterial ischemia, or revascularization).
- Poisson regression modelled incidence rates (IRs), 95% confidence intervals (95%CIs), and incidence rate ratios (IRRs); follow-up accrued from BL until last visit (censoring date: 12th April, 2024).
- Kaplan-Meier curves estimated cumulative probabilities of first MACE, compared using log-rank test. Predictors of first MACE assessed by multivariable stepwise Cox model, including fixed (at BL) and time-dependent covariates (with univariable p<0.100). Follow-up accrued from BL until first event or last visit.

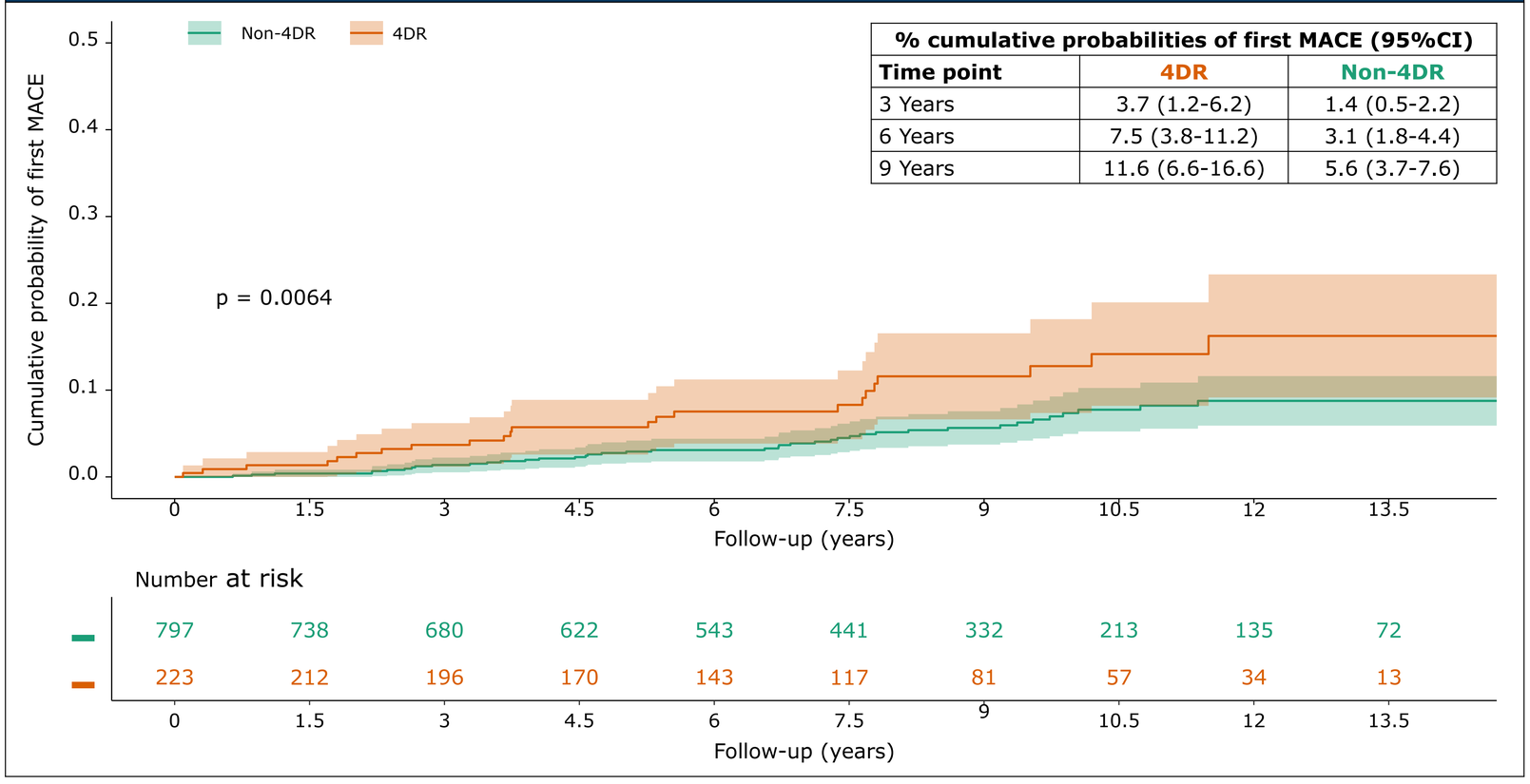
Results

- Overall, 223 4DR- and 797 non-4DR-PWH included (Table 1).
- During a median follow-up of 8.2 (interquartile range=5.4-11.1) years [1833 person-years-of-follow-up (PY)], 23/223 (10.3%) 4DR-PWH developed 29 incident MACEs: IR=1.6 (95%CI=1.1-2.3)/100 PY.
- During a median follow-up of 8.4 (5.2-11.0) years (6450 PY), 42/797 (5.3%) non-4DR controls developed 45 incident MACEs: IR=0.7 (95%CI=0.5-0.9)/100 PY; IRR (4DR/non-4DR)=2.3 (95%CI=1.4-3.6); p<0.001.
- Cumulative probabilities of first incident MACE were higher in 4DR- compared to non-4DR-PWH (Figure 1).
- After adjusting for confounders, a higher risk of MACEs was associated with 4DR status (Table 2).

Table 1. Characteristics of 4DR- and non-4DR-PWH included in the analysis.

	Overall (n=1020)	4DR-PWH (n=223)	Non-4DR-PWH (n=797)	p
Age at BL (years)	50.1 (45.4-54.5)	50.0 (44.4-54.9)	50.3 (45.6-54.5)	0.590
Male sex-assigned-at-birth	754 (73.9%)	163 (73.1%)	591 (74.2%)	0.816
ART duration at BL (years)	17.8 (14.5-21.3)	18.2 (14.5-21.2)	17.7 (14.5-21.3)	0.517
BL HIV load (copies/mL)	<20 (<1-85)	1512 (133-19802)	<1 (<1-39)	**<0.001**
BL CD4⁺/CD8⁺ ratio	0.64 (0.39-0.97)	0.37 (0.21-0.62)	0.71 (0.46-1.04)	**<0.001**
CD4⁺ T-cell nadir (cells/mm³)	188 (74-307)	96 (23-187)	216 (102-333)	**<0.001**
Current or former smoking at BL	653 (64.0%)	136 (61.0%)	517 (64.9%)	0.323
BL diabetes mellitus	101 (9.9%)	17 (7.6%)	84 (10.5%)	0.245
BL arterial hypertension	228 (22.4%)	44 (19.7%)	184 (23.1%)	0.331
BL dyslipidaemia	694 (68.0%)	148 (66.4%)	546 (68.5%)	0.600
BL chronic kidney disease	51 (5.0%)	10 (4.5%)	41 (5.1%)	0.816
Positive HCV serostatus at BL	391 (38.3%)	71 (31.8%)	320 (40.2%)	**0.029**
Positive HBsAg at BL	73 (7.2%)	15 (6.7%)	58 (7.3%)	0.871

Figure 1. Kaplan-Meier curves for probabilities of the first MACE in 4DR- (orange line) and non-4DR-PWH (green line).



% cumulative probabilities of first MACE (95%CI)		
Time point	**4DR**	**Non-4DR**
3 Years	3.7 (1.2-6.2)	1.4 (0.5-2.2)
6 Years	7.5 (3.8-11.2)	3.1 (1.8-4.4)
9 Years	11.6 (6.6-16.6)	5.6 (3.7-7.6)

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