Dettaglio abstract

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Title: Selected comorbidities and the risk of ART switch in the context of HIV-RNA suppressed to ≤50 copies/mL

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Abstract
Background: Although HIV-associated mortality has been greatly reduced by ART, the incidence of deaths due to non-communicable diseases remains high in PLWH. Clinical decisions regarding whether to modify ART regimens in the context of a HIV-RNA≤50 copies/mL may be guided by current ART and the development of specific comorbidities.
Methods: Cohort data analysis of the risk of ART switch (RTS) in PLWH of the Icona Foundation Study with a stable VL≤50 copies/mL according to the development in course of follow-up of a set of a priori chosen co-morbidities (i.e. becoming overweight (OW, BMI>26), developing dyslipidaemia (DP), kidney disease (KD, eGFR<60) and diabetes mellitus (DM)). At the time of their first ever episode of >6 months with VL≤50 copies/mL after January 2017 (baseline) participants had to be free from the comorbidity of interest. After baseline they were followed-up until they developed the event (if there was a ART switch) or their follow-up was censored (if ART remained unchanged or if VL went >50 copies/mL). Four separate standard Cox regression models with baseline confounders were fitted (one for each of the time-varying exposures, see footnote of the Table for exact specifications). Models were repeated after stratification by anchor drug class received at the beginning of the episode.
Results: In the model with diabetes as the time-varying exposure, we included 1,146 PLWH with a median (IQR) age of 41 (32-50) years, 18% females, 51% MSM, 60% of foreign nationality with a median of 642 (447-869) CD4 count at baseline. Estimated incidence of RTS was 0.29 (95% CI: 0.27-0.31) per 100 person-years of follow-up. The Table shows unadjusted and adjusted hazard ratios (HR) of RTS from fitting the four separate models. In the main analysis controlling for confounders, DM was the only co-morbidity associated with an increased risk of RTS (approximately 6-fold higher risk in exposed vs. unexposed, although not significant p=0.15). For DP, there was weak evidence that the risk varied by anchor drug class received at baseline (interaction p=0.31), with participants receiving PIs , however, showing a higher risk of RTS (aHR=2.23, 95% CI:1.02-4.87) vs. inconclusive results in the overall analysis (aHR=1.12, 95% CI:0.87-1.45, p=0.39, Table). Finally, there was no evidence that BMI had a different prognostic role in predicting RTS after restricting to participants currently receiving INSTI-based regimens (interaction p=0.60).
Conclusions: Overall, modern regimens appeared to be relatively safe and well tolerated with low incidence of RTS even in participants with co-morbidities. Among the conditions evaluated, only the development of DM (and of DP in those receiving PIs) appeared to be associated with a greater risk of modification of participants’ ART regimen composition in the setting of VL≤50 copies/mL. The analysis, which is slightly underpowered, needs to be repeated when a larger number of RTS cumulates.
Analysis sponsored by Gilead Srl

Table. Hazard Ratios of switching therapy from fitting a Cox regression analysis

	Hazard Ratio (95% CI) p-value	
	Unadjusted	**Adjusted**
Becoming diabetic		
No	1.00	1.00
Yes	3.84 (0.32, 46.48)	6.04[1] (0.52, 70.31)
	0.290	0.151
Developing dyslipidaemia (all)		
No	1.00	1.00
Yes	1.09 (0.86, 1.39)	1.12[2] (0.87, 1.45)
	0.473	0.388
Developing dyslipidaemia (PI-based)		
No	1.00	1.00
Yes	2.17 (1.18, 4.00)	2.23[2] (1.02, 4.87)
Experiencing a eGFR <60 (all)		
No	1.00	1.00
Yes	0.71 (0.42, 1.19)	0.78[3] (0.45, 1.34)
	0.194	0.360
BMI from <25 to 26+ (all)		
No	1.00	1.00
Yes	0.79 (0.46, 1.34)	0.75 (0.43, 1.31)
	0.383	0.318
BMI from <25 to 26+ (INSTI-based)		
No	1.00	1.00
Yes	0.95 (0.49, 1.83)	0.91 (0.47, 1.78)

[1]Adjusted for year of baseline, age, dyslipidaemia, obesity and nationality
[2]Adjusted for year of baseline, age, sex, obesity, alcohol use and nationality
[3]Adjusted for year of baseline, age, diabetes and sex
[4]Adjusted for year of baseline, age, sex and nationality

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