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ARV drugs from prevention to treatment

OC 69 Risk of developing low-level viral rebound (LLVR) among people with HIV (PWH) with current HIV-RNA≤50 copies/mL receiving 2DR vs 3DR: a case control study

Authors
A. Vergori[1], A. Cervo[2], A. Roen[3], R. Gagliardini[1], T. Clemente[4], V. Mazzotta[1], E. Quiros-Roldan[5], M.C. Poliseno[6], L. Sarmati[7], F. Ceccherini-Silberstein[8], F. Maggiolo[9], C. Mussini[2], C.F. Perno[10], A. Antinori[1], A. Cozzi-Lepri[3], On Behalf Of The ICONA Foundation Study Group

Affiliation
[1]Clinical Infectious Diseases Department, Viral Immunodeficiency Unit, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy, [2]Infectious Diseases Clinic, University Hospital of Modena, Modena, Italy, [3]Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME), Institute for Global Health, University College London, London, United Kingdom, [4]Infectious Diseases, Vita-Salute San Raffaele University, Milan, Italy, [5]Division of Infectious and Tropical Medicine, ASST Spedali Civili, Brescia, Brescia, Italy, [6]Clinic of Infectious Diseases, Department of Precision and Regenerative Medicine and Jonian Area (DiMePreJ), A.O.U.C. Policlinic di Bari, Bari, Italy, [7]Clinical Infectious Diseases, Department of System Medicine, Tor Vergata University, Policlinico Tor Vergata of Rome, Rome, Italy, [8]Department of Experimental Medicine, University of Rome 'Tor Vergata', Rome, Italy, [9]Infectious diseases' specialist Freelance, None, Fabro, Italy, [10]IRCCS Bambino Gesù Pediatric Hospital, Rome, Italy

ABSTRACT
Background: Low-level viremia may indicate residual replication and is potentially linked to an increased risk of virologic failure, serious non-AIDS events and all-cause mortality. It can be persistent or occurs after sustained viral suppression (low-level viral rebound, LLVR). The risk of developing LLVR after achieving viral load suppression under dual-drug regimens (2DR) compared to triple regimens (3DR) is yet to be fully understood.
Methods: PWH enrolled in the Icona Foundation Study cohort with virological suppression (≥2 consecutive HIV-RNA≤50copies/ml over 6 months) after NOV/2014 (baseline, BL) were included. Follow-up of PWH in the cohort accrued from BL and was censored at time of viral rebound (HIV-RNA>200 copies/ml) or last available HIV-RNA. It is a 1:3 case-control study nested within the cohort and matched on previous gaps in care (>12 months between visits) and number of regimens failed. Cases were PWH experiencing LLVR (2 consecutive HIV-RNA 51-199 copies/ml or 1 HIV-RNA 51-199 copies/ml followed by ART change within 30 days) after BL. Controls were PWH who, after the same time from baseline to the date of LLVR of the matched case (index date), still had HIV-RNA≤50 copies/ml. The main exposure of interest was the type of regimen received prior to index date [2DR (DTG/3TC, DTG/RPV, DTG/DOR, CAB/RPV) vs. 3DR (DTG/BIC or RPV/DOR or boosted DRV or ATV + TXF/XTC)]. The association between regimen received (2DR vs. 3DR) and risk of LLVR was evaluated using a conditional logistic regression. Confounding factors were identified a priori (see Figure for full description of the confounder sets) and sensitivity analyses were conducted using alternative definitions for the cases and for the exposure of interest.
Results: 1,023 PWH included: 254 with LLVR and 769 matched controls. N=72 (28%) cases were currently receiving 2DR compared to N=229 (29%) controls. Overall, 19% were females, 78% were born in Italy, median age was 43 (Interquartile range, IQR 34-51), CD4 count 586/mm3(380, 819) and calendar year of baseline was 2015 (2015-2020). Younger participants, MSM and those with higher education were more likely to currently use 2DR vs. 3DR regimens; PWH starting 3DR were older and with a lower nadir than 2DR, which were also more common in more recent years compared to 3DR (Table 1). Among those receiving a 2DR, 82% were on DTG/3TC, and 12% were on a RPV-based regimen. Among those using 3DR, 33% were on RPV+TXF/XTC followed by 20% BIC+TXF/XTC and 18% DRV/cobi+TXF/XTC. After adjusting for confounding, evidence was inconclusive, although our data could rule out a >80% higher risk of LLVR with 2DR vs. 3DR [OR = 1.21 95% CI (0.82, 1.79)]; results were similar in sensitivity analyses (Figure 1).
Conclusion: Our analysis appeared to be underpowered for the comparison at stake. However, importantly, we can exclude with 95% confidence that in PWH who achieved HIV-RNA≤50copies/ml the use of 2DR can increase the risk of LLVR by >90% when compared to 3DR.

Table 1. Comparison of case/control status and of baseline characteristics stratified by 2DR vs 3DR.

		2DR N=301	3DR N=722	Overall N=1023	P-value
Control, n(%)		229 (76.1)	540(74.8)	769 (75.2)	0.664
Case, n(%)		72 (23.9)	182 (25.2)	254(24.8)	
Female, n(%)		49 (16.3)	140(19.4)	189(18.5)	0.243
HIV transmission risk group, n(%)	PWID	30 (10)	61(8.4)	91(8.9)	0.241
	heterosex	109(36.2)	298(41.3)	407(39.8)	
	MSM	149 (49.5)	320(44.3)	469(45.8)	
	other/unknown	13(4.3)	43(6)	56(5.5)	
Italian (vs non Italian), n(%)		238 (79.1)	562(77.8)	800(78.2)	0.664
Education, n(%)	Primary School	15(5)	33(4.6)	48(4.7)	0.424
	Secondary School	127(42.2)	336(46.5)	463(45.3)	
	College/University	42 (14)	78(10.8)	120(11.7)	
	missing	117(38.9)	275(38.1)	392(38.3)	
Age, median (IQR)		41(33,50)	44(35,52)	43(34,51)	0.013
Age, n(%)	>30	48(15.9)	71(9.8)	119(11.6)	0.062
	30-39	90(29.9)	205(28.4)	295(28.8)	
	40-49	86(28.6)	214(29.6)	300(29.3)	
	50-59	54(17.9)	165(22.9)	219(21.4)	
	60-69	19(6.3)	51(7.1)	70(6.8)	
	70+	4 (1.3)	16(2.2)	20(2)	
AIDS at baseline, n(%)		51(16.9)	120(16.6)	171(16.7)	0.900
Previous gap in care >18 months, n(%)		69(22.9)	171(23.7)	240(23.5)	0.794
Drug class, n(%)	INSTI	223(74.1)	225(31.2)	448(43.8)	<0.0001
	NNRTI	28(9.3)	263(36.2)	291(28.4)	
	PI	33(11)	233(32.3))	266(26)	
	Mixed	17(5.6)	1(0.1)	18(1.8)	
Duration of most recent HIV-RNA suppression, median (IQR)		9.4 (5.2,16.2)	11.3(6.1,25.9)	10.8(5.8,23)	0.002
CD4 nadir, median (IQR)		316(141,470)	271(118,416)	284(123,440)	0.021
CD4 baseline, median (IQR)		586(405,858)	586(275,796)	586(380,819)	0.433
CD8 baseline, median (IQR)		891(656,1230)	850(643,1126)	860(643,1159)	0.044
CD4/CD8 ratio baseline, median (IQR)		0.7(0.4, 1)	0.7(0.4,1)	0.7(0.4,1)	
Duration of ART (months), median (IQR)		44(26, 72)	44(21,82)	44(23,78)	0.644
Year at baseline, median (IQR)		2018(2016,2020)	2016(2015,2020)	2017(2015,2020)	<.0001

Abbreviations: PWID, people who inject drugs; MSM, men who have sex with men; LLV, low level viral rebound; ART, antiretroviral therapy, IQR, interquartile range.

Figure 1. Odd Ratios for developing low level viral rebound (LLVR) on 2DR vs 3DR after adjusting for confounding from fitting seven separate conditional logistic regression models