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Incidence of hypertension in PLWH receiving INSTI versus other third drug ART regimens in the RESPOND cohort

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Introduction

- The impact of contemporary antiretroviral therapy (ART) on hypertension incidence is not well described. We compared the incidence of hypertension in people with HIV (PLWH) receiving integrase inhibitors (INSTIs) versus non-nucleoside reverse transcriptase inhibitors (NNRTIs) or boosted protease inhibitors (PIs) within RESPOND.

Methods

- RESPOND is a consortium of 17 observational cohorts and 32,000 PLWH in Europe and Australia. [The RESPOND Study group 2020, Microorganisms 2020]
- Eligible participants were ≥18 years, without hypertension, initiating or switching to a three-drug regimen containing two NRTIs plus an ARV-class they were naïve to at baseline (INSTI or PI or NNRTI).
- Hypertension was defined as two consecutive systolic blood pressures (SBP) ≥140 mmHg and/or diastolic blood pressure (DBP) ≥90 mmHg or initiation of antihypertensives.
- Poisson regression was used to determine adjusted incidence rate ratios (aIRR) of hypertension for INSTIs versus NNRTIs and PIs, overall and stratified by baseline ART status.
- Individuals were followed until a hypertension event occurred, switched from the third ARV drug, last blood pressure, or 01/01/2020, whichever occurred first.

Results

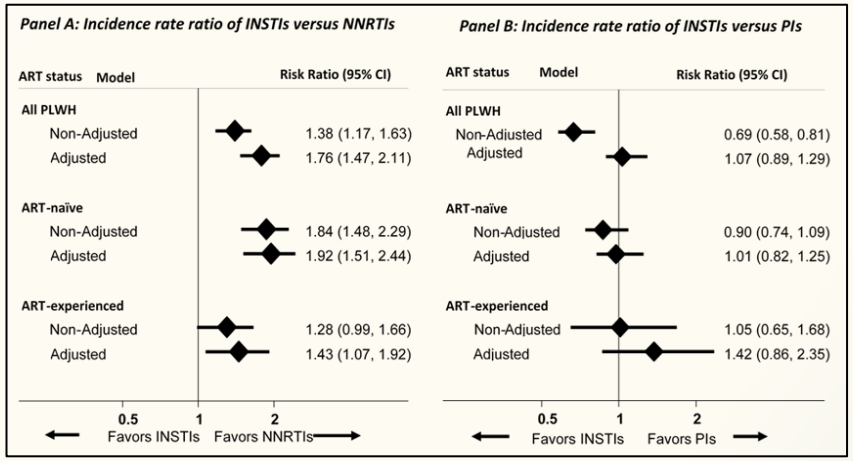
- Overall, 4606 PLWH were eligible, 68.7% of whom initiated INSTIs (DTG=1929, EVG/c=777, RAL=458), 17.5% initiated NNRTIs (RPV=487, EFV=320), and 13.8% initiated PIs (ATV/b=174, DRV/b=461).
- The median (IQR) baseline age 43.4 (34.9–50.9) years (Table 1). Baseline SBP and DBP did not differ according to ART regimens. Participants on INSTI were older, with lower HIV RNA.

Table 1: Demographics and clinical characteristics at baseline

Variable		INSTIs (n=3164; 68.7%)		NNRTIs (n=807; 17.5%)		PIs (635;13.8%)	
Gender	Male	2,284	72.2	610	75.6	485	76.4
Ethnicity	White	2,186	69.1	569	70.5	431	67.9
ART-naïve at baseline		1,074	33.9	502	62.2	544	85.7
NRTI backbone	TAF/FTC	614	19.4	43	5.3	17	2.7
	TDF/XTC	1,374	43.4	705	87.3	508	80
	ABC/3TC	1,153	36.4	31	3.8	92	14.5
	Other*	23	0.7	28	3.5	18	2.8
		Median (IQR)	**Number (%) missing**	**Median (IQR)**	**Number (%) missing**	**Median (IQR)**	**Number (%) missing**
Age (years)		45(36,51)	0(0)	39(33,47)	0(0)	36(30,45)	0(0)
Baseline CD4 (cells/µL)		560(370,767)	0(0)	474(330,652)	0(0)	344(181,529)	0(0)
HIV RNA (copies/mL)		39(19,9492)	0(0)	525(33,2500)	0(0)	2290(861,165546)	0(0)
BMI(Kg/M^2)		23.4(21.1,25.7)	391(12.4)	23.4(21.3,25.7)	123(15.2)	22.6(20.8,24.9)	106(16.7)
SBP (mmHg)		121.0(113,130)	0(0)	120(113,130)	0(0)	120(112,130)	0(0)
DBP (mmHg)		78.0(70.0,82.0)	0(0)	77.0(70.0,81.0)	0(0)	78.0(70.0,83.0)	0(0)
BP measures (per year)		2(2,3)	0(0)	2(1,3)	0(0)	2(2,3)	0(0)
5-year CVD score		2.2(1.0,4.0)	576(18.2)	1.5(0.7,3.0)	200(24.8)	1.2(0.5,2.7)	210(33.1)

Note: TAF-Tenofovir Alafenamide; FTC-Emtricitabine; TDF-tenofovir disoproxil fumarate ; XTC-emtricitabine or lamivudine; Other regimens include Zidovudine and Stavudine based regimens; CVD-cardiovascular disease

Figure 1: Incidence rate ratio of hypertension in PLWH (overall and by ART status) receiving INSTIs versus NNRTI (panel A) or PIs (panel B).



The final model adjusted for NRTI backbone, age, ethnicity, sex, mode of transmission, calendar year, estimated glomerular filtration rate, smoking, body mass index , diabetes mellitus, prior AIDS, CVD, HBV and HCV status, HIV RNA, nadir, and baseline CD4 counts, time since HIV diagnosis, baseline BP and lipid levels, lipid-lowering therapy, and prior ART exposure at baseline .

Results continued:

- During follow-up, 1058 PLWH (23.0%) developed hypertension during 8380.4 person-years of follow-up (incidence rate [IR] 126.2 per 1000 person-years; 95% confidence intervals [CI], 118.9–134.1).
- PLWH receiving an INSTI had a 76% higher incidence of hypertension than those receiving NNRTI (aIRR 1.76, 95% CI 1.47 – 2.11). The incidence of hypertension was similar between INSTIs and PIs (aIRR 1.07, 95% CI 0.89 – 1.29).
- The association between ART class and hypertension did not differ according to gender (interaction P=0.737) or age (interaction P=0.732).
- The results were consistent in the separate analyses for PLWH ART-experienced and ART naïve PLWH (Figure 1).
- The results also remained consistent after adjustment for baseline D:A:D cardiovascular risk scores and when a six-month washout period was considered for ART-experienced PLWH.

Limitations

- This was a cohort analysis and confounding by indication and channelling bias cannot be excluded.
- The analysis was not powered for individual antiretroviral drug comparisons.

Conclusion:

- Within RESPOND, hypertension was more common with use of INSTIs than with NNRTIs but similar to PIs in both ART-naïve and ART-experienced participants.

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- The RESPOND Study Group: **https://www.chip.dk/Studies/RESPOND/Study-Group**