Risk of Incident Hypertension with Common Antiretroviral Agent Combinations in the OPERA Cohort

Poster #823

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Background

- People with HIV have a higher likelihood of developing hypertension (HTN) compared to people without HIV (risk ratio: 1.12; 95% CI: 1.02, 1.23)[1]
- The literature on the association between modern ART and HTN is conflicting:
  - The RESPOND consortium of HIV cohorts reported a higher incidence of HTN with regimens containing an INSTI, TAF, or both compared to regimens containing neither[2]
  - In a pooled analysis of the SPRING-1, SPRING-2, SINGLE, and FLAMINGO clinical trials, the odds of incident HTN did not differ between DTG and other regimens among ART-naïve individuals without HTN[3]

Objective

To compare rates of incident hypertension across combinations of common ARVs among people with HIV in routine clinical care in the US

Methods

Study Population

- OPERA cohort: prospectively captured, routine clinical data from electronic health records in the US (260 clinics, 23 US states/territories), representing ~14% of people with HIV in the US
- Inclusion criteria
  - ≥18 years old people with HIV
  - Started a new ART regimen between 01JAN2016 and 31DEC2022
  - Baseline BP (at regimen initiation):
    - **Normal BP** (SBP < 120 mmHg, DBP < 80 mmHg)
    - **Normal/elevated BP** (SBP < 140 mmHg, DBP < 90 mmHg)
  - No HTN Dx or current antihypertensive Rx
  - ≥ 2 BP measurements during follow-up
- Censoring criteria: regimen discontinuation, loss to follow-up, death or study end (31DEC2023)

Incident HTN Definition

- First occurrence of any of the following:
  - 2 consecutive SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg
  - New HTN Dx
  - New antihypertensive Rx

Statistical Analyses

- All analyses performed among the **Normal BP** and the **Normal/Elevated BP** groups
- All analyses stratified by previous ART experience (naïve vs. experienced)
- Exposure of interest: DTG, no TAF 3DR vs. DTG/3TC 2DR or DTG, TAF 3DR or B/F/TAF or bDRV, no TAF 3DR or bDRV, TAF 3DR
- Incidence of HTN:
  - Univariate Poisson regression (IR per 100 person-years)
- Association between regimen and incident HTN
  - Multivariate Poisson regression (IRR)
  - Adjusted for baseline age (quadratic), female sex, Black race, VL (quadratic), diabetes, eGFR (quadratic), SBP (quadratic), time-updated BMI (quadratic)

Results – ART-naïve

Figure 1. ART-naïve study population by baseline BP level

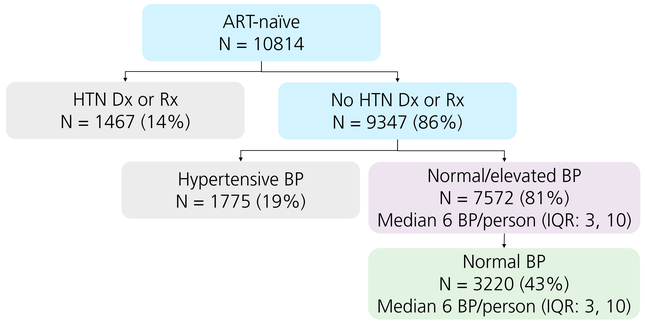
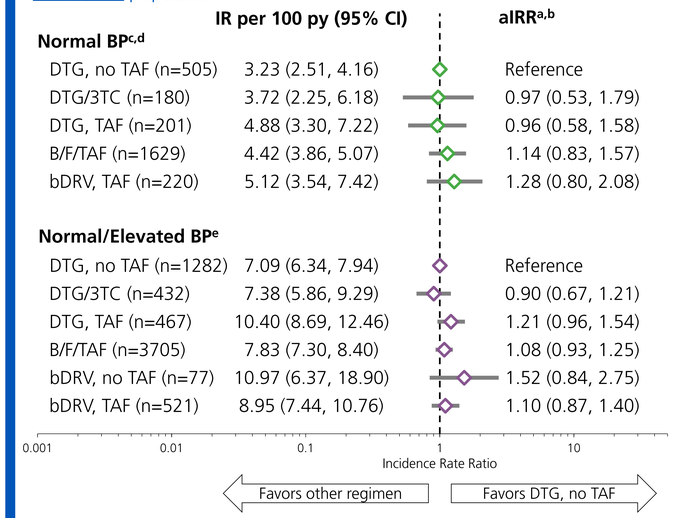


Table 1. ART-naïve population baseline characteristics

	Normal BP N = 3220	Normal/elevated BP N = 7572
Median age (IQR)	30 (25, 38)	30 (25, 38)
Female sex, n (%)	519 (16)	953 (13)
Black race, n (%)	1710 (53)	4031 (53)
Median HIV VL (IQR)	64835 (16088, 234500)	57345 (15400, 193000)
Diabetes, n (%)	35 (1)	100 (1)
Median eGFR (IQR)	117 (104, 130)	116 (102, 129)
Median BMI (IQR)	23 (21, 26)	24 (21, 28)

Figure 2. Association between ART regimen and incident HTN in the ART-naïve population



[a] Multivariate Poisson regression adjusted for baseline age, female sex, Black race, VL, diabetes, eGFR, SBP and time-updated BMI
[b] Individuals missing BMI, race and/or eGFR data were excluded from the multivariate Poisson model (Normal BP: n = 263; Normal/Elevated BP: n = 703
[c] Individuals on bDRV, no TAF 3DR were excluded (n = 35) due to the small number of events
[d] Individuals on other ART combinations were excluded (n = 187)
[e] Individuals on other ART combinations were excluded (n = 433)

Results – ART-experienced

Figure 3. ART-experienced study population by baseline BP level

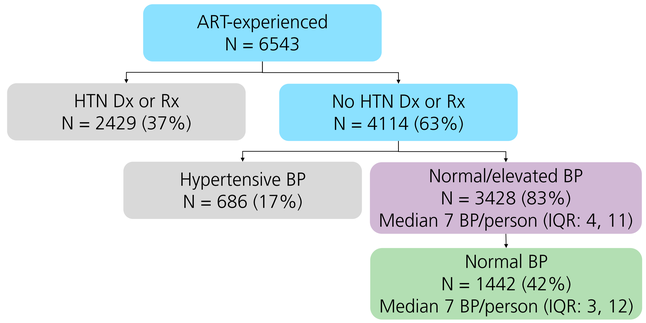
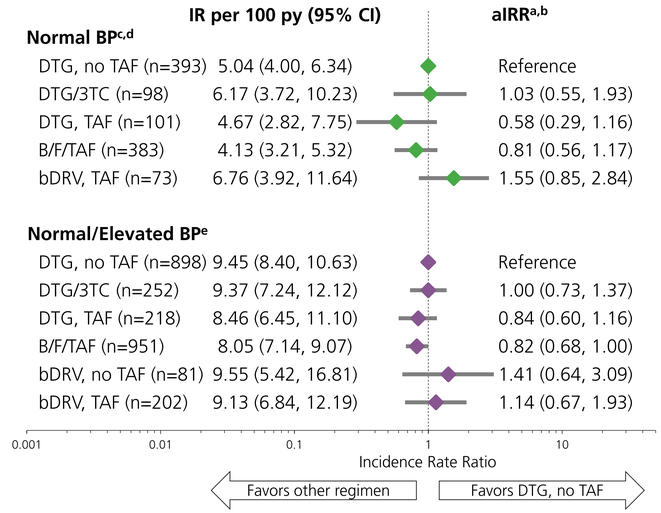


Table 2. ART-experienced population baseline characteristics

	Normal BP N = 1442	Normal/elevated BP N = 3428
Median age (IQR)	41 (32, 51)	42 (32, 51)
Female sex, n (%)	311 (22)	605 (18)
Black race, n (%)	576 (40)	1343 (39)
Median HIV VL (IQR)	20 (<20, 528)	<20 (<20, 320)
Diabetes, n (%)	63 (4)	160 (5)
Median eGFR (IQR)	102 (87, 116)	101 (85, 115)
Median BMI (IQR)	24 (22, 28)	25 (22, 29)

Figure 4. Association between ART regimen and incident HTN in the ART-experienced population



[a] Multivariate Poisson regression adjusted for baseline age, female sex, Black race, VL, diabetes, eGFR, SBP and time-updated BMI
[b] Individuals missing BMI, race, and/or eGFR data were excluded from the multivariate Poisson model (Normal BP: n = 148; Normal/Elevated BP: n = 472
[c] Individuals on bDRV, no TAF 3DR (n = 49)were excluded due to the small number of events
[d] Individuals on other ART combinations were excluded (n = 197)
[e] Individuals on other ART combinations were excluded (n = 442)

Abbreviations: 2DR, two-drug regimen; 3DR, three-drug regimen; 3TC, lamivudine; ART, antiretroviral therapy; ARV, antiretroviral; bDRV; boosted darunavir; B/F/TAF, bictegravir/emtricitanine/tenofovir alafenamide; BMI, body mass index; BP, blood pressureCI, confidence interval; DBP, diastolic BP; DTG, dolutegravir; Dx, diagnosis; eGFR, estimated glomerular filtration rate; HTN, hypertension; INSTI, integrase strand-transfer inhibitor; IQR, interquartile range; IR, incidence rate; IRR, incidence rate ratio; N, number; py, person-years; Rx, prescription; SBP, systolic blood pressure; TAF, tenofovir alafenamide; VL, viral load

Discussion

- In this large US cohort, prevalent HTN Dx, antihypertensive Rx, or BP indicative of HTN was common in people with HIV
  - 30% at ART initiation (**Fig 1**)
  - 48% at regimen switch (**Fig 3**)
- ART-experienced individuals tended to be older and were less likely to be Black, but more likely to be women or to have diabetes compared to ART-naïve individuals (**Tables 1-2**)
- People with **normal/elevated BP** were slightly less likely to be women than those with **normal BP** (**Tables 1-2**)
- Incidence rates of HTN nearly doubled in those with **normal/elevated BP** compared to those with **normal BP** for both ART-naïve (**Fig 2**) and ART-experienced individuals (**Fig 4**)
- There was no statistically significant association between regimen and rate of HTN, regardless of baseline BP in ART-naïve (**Fig 2**) or ART-experienced individuals (**Fig 4**).
  - The important differences between the ART-naïve and experienced populations likely impacted the variation in point estimates observed
- Study strengths
  - Large real-world cohort of routine clinical care data
  - Large study population, including 11,000 people with **normal/elevated BP** and 4,662 people with **normal BP**
  - Stratification by prior ART experience and adjustment for potential confounders, including time-updated BMI, to minimize the risk of bias
- Study limitations
  - Exclusion of ART-naïve individuals on bDRV/no TAF from modelling due to the small number of events
  - Complete case analysis excluding individuals with missing covariates
  - No information on lifestyle factors affecting HTN (diet, exercise)

Key Findings

Among commonly used modern ART regimens, specific antiretroviral combinations do not appear to be a driving factor in the development of HTN in this large and diverse cohort of people with HIV in the US

References

1. Davis, et al. Association between HIV infection and hypertension: a global systematic review and meta-analysis of cross-sectional studies. *BMC Medicine* 2021.
2. Byonanebye, et al. Incidence of hypertension in people with HIV who are treated with integrase inhibitors versus other antiretroviral regimens in the RESPOND cohort consortium. *HIV Medicine* 2022.
3. Patel, et al. Evaluation of incident hypertension and blood pressure changes among people living with HIV-1 (PLWH) receiving dolutegravir (DTG)-based regimens or comparator antiretroviral therapy (CAR) in randomized clinical trials through 96 weeks[abstract LBEPB12]. *IAS* 2023.

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