Advanced HIV infection in the US: immune response to ART initiation

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OPERA® The Longitudinal Cohort

Background

- Advanced HIV is defined as first presentation to care with a CD4 cell count <200 cells/µL and/or with an AIDS-defining event (ADE)[1]
  - Up to 20% of individuals newly diagnosed with HIV in the US have advanced HIV infection[2]
  - Associated with increased risks of HIV clinical progression, morbidity, mortality, poor long-term retention in care, and HIV transmission
- Few studies focus on advanced HIV treatment options
- Among people with advanced HIV In the OPERA cohort in the US[3]
  - Regimen discontinuation/modification were less likely with bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) than boosted darunavir (bDRV), dolutegravir (DTG) or elvitegravir/cobicistat (EVG/c)
  - Viral suppression was more likely with B/F/TAF than with bDRV

Objective

To assess CD4 cell count and CD4:CD8 ratio recovery across regimens, among people with advanced HIV initiating common ART regimens in the US

Methods

Data Source: OPERA Cohort

- Prospectively captured, routine clinical data from electronic health records at 84 clinics in 18 US states/territories
- ~12% of people with HIV in US

Inclusion Criteria:

- ART-naïve
- ≥18 years old
- CD4 <200 cells/µL
- eGFR ≥ 30 mL/min/1.73m^2
- ≥1 CD4 cell count and HIV viral load after ART initiation
- Initiated ART between 01JAN2018 and 31DEC2020 with:
  - B/F/TAF
  - bDRV three-drug regimen (3DR)
  - Dolutegravir (DTG) 3DR
  - Elvitegravir/cobicistat (EVG/c) 3DR

Censoring Criteria:

- Discontinuation (i.e., add/drop/switch core agent or > 45-day gap)
- 12 months after last clinical contact
- Death
- Study end (i.e., 30SEP2021)

Statistical Analyses

- Time to CD4 ≥200 cells/µL
  - Cox proportional hazards models
  - Inverse probability of treatment weights (IPTW): age (quadratic), CD4 cell count (quadratic), log10 viral load, eGFR (quadratic), sex, Black race, ADAP/Ryan White payer, ADE history, any concomitant comorbidities
  - Sensitivity Analysis: restricted to people initiating ART with a single tablet regimen (STR)
- Average changes in CD4:CD8 ratio over time since ART initiation
  - Linear mixed model, random intercept
  - Restricted cubic splines on time; knots at 2, 6, 12 and 24 months
  - Inverse probability of treatment weights (IPTW):age (quadratic), CD4 cell count (quadratic), log10 viral load, eGFR (quadratic), days between baseline CD4:CD8 ratio measurement and index (quadratic), sex, Black race, ADAP/Ryan White payer, ADE history, any concomitant comorbidities, interaction between race and ADE history

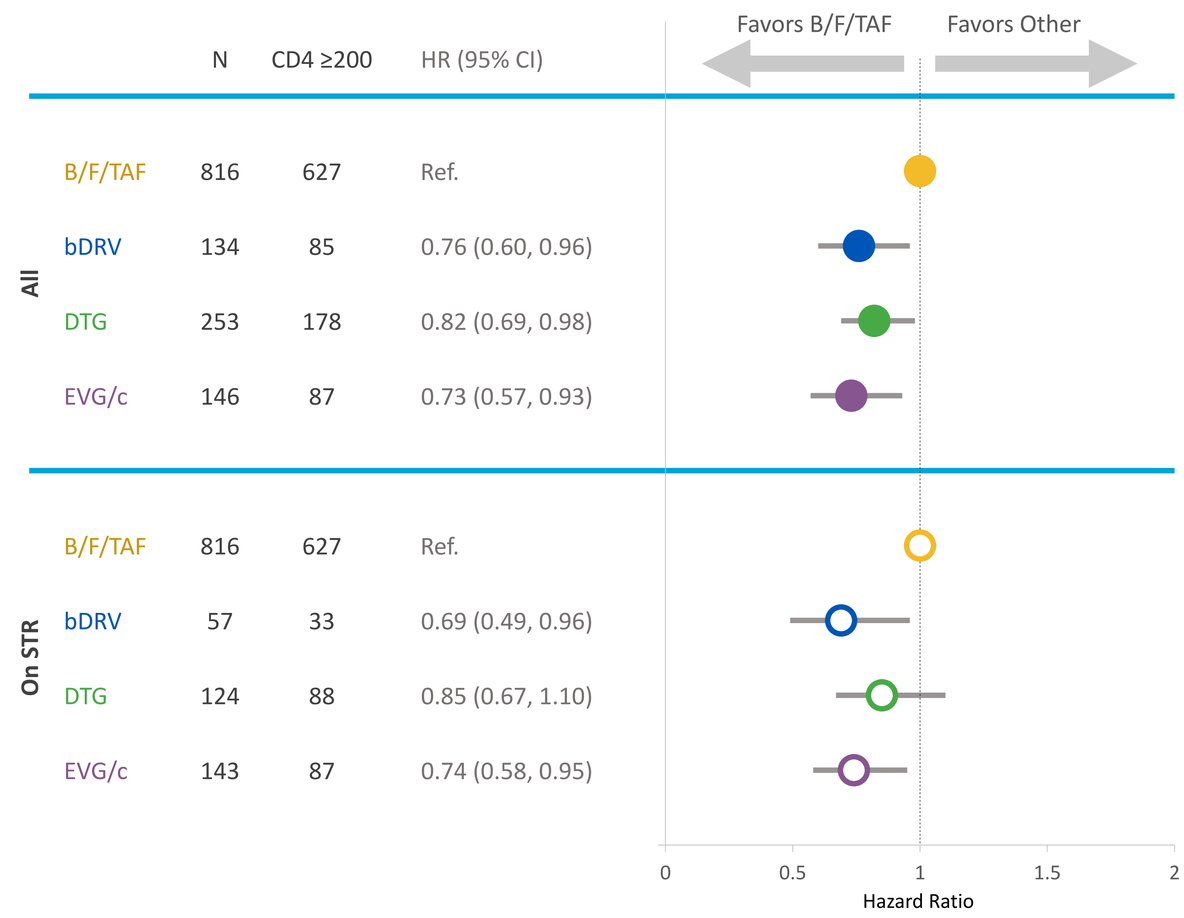
Results

Table 1. Population characteristics at ART initiation

	B/F/TAF N=816	bDRV N=134	DTG N=253	EVG/c N=146
Age, median years (IQR)	36 (29, 46)	34 (27, 46)	37 (28, 47)	36 (28, 44)
Female, n (%)	156 (19)	29 (22)	43 (17)	29 (20)
Black Race, n (%)	505 (62)	84 (63)	167 (66)	98 (67)
Ryan White/ADAP, n (%)	310 (38)	76 (57)*	134 (53)*	65 (45)
CD4 cell count, median cells/µL (IQR)	78 (29, 147)	94 (36, 145)	83 (35, 149)	84 (24, 150)
Log10 HIV viral load, median (IQR)	5.3 (4.9, 5.7)	5.4 (4.7, 5.6)	5.3 (4.8, 5.7)	5.2 (4.7, 5.6)
History of AIDS, n (%)	326 (40)	52 (39)	128 (51)*	68 (47)
Any comorbidity[a], n (%)	383 (47)	68 (51)	144 (57)*	80 (55)
eGFR, median mL/min/1.73m^2 (IQR)	114 (98, 128)	111 (98, 126)	112 (97, 126)	110 (91, 129)

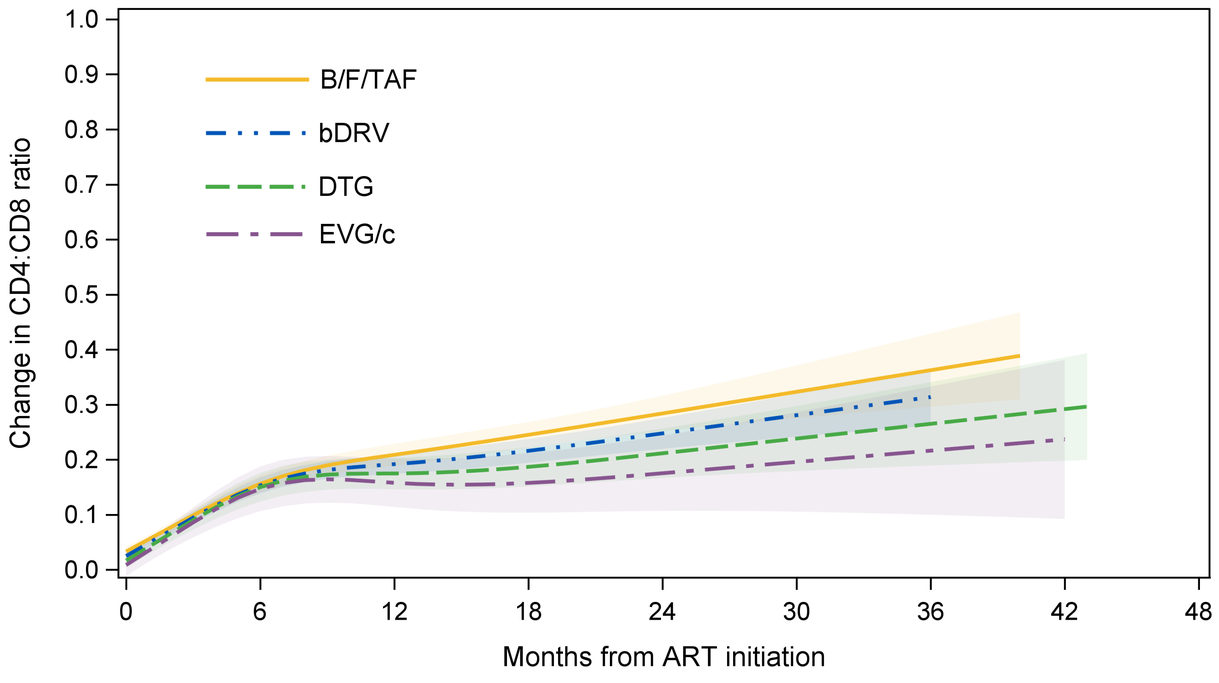
ART, antiretroviral therapy; bDRV, boosted darunavir; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; DTG, dolutegravir; eGFR, estimated glomerular filtration rate; EVG/c, elvitegravir/cobicistat; IQR, interquartile range
* p-value <0.05 for the comparison with B/F/TAF
[a] Cardiovascular disease, hypertension, diabetes mellitus, dyslipidemia, thyroid disease, mental health conditions, liver diseases, bone disorders, renal disease, rheumatoid arthritis, substance abuse

Figure 1. Association between regimens and reaching a CD4 cell count ≥200 cells/µL[a], among all people with advanced HIV or those initiating a single tablet regimen



bDRV, boosted darunavir; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; DTG, dolutegravir; EVG/c, elvitegravir/cobicistat
[a] Cox proportional hazards model, inverse probability of treatment weights (baseline age, CD4 cell count, log10 viral load, eGFR, sex, Black race, ADAP/Ryan White, AIDS history, any comorbidities)

Figure 2. Changes in CD4:CD8 ratio over time on ART[a] in the subset of the population with CD4:CD8 ratio measurements



ART, antiretroviral therapy; bDRV, boosted darunavir; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; DTG, dolutegravir; EVG/c, elvitegravir/cobicistat
[a] Predicted values from linear mixed model, restricted cubic splines on time (knots: 2, 6, 12, 24), inverse probability of treatment weights; reference: male, 40 years old, non-Black, no comorbidity, no AIDs history, no ADAP/Ryan White coverage, baseline CD4 cell count: 86 cells/µL, log10 viral load: 5, baseline CD4:CD8 ratio measured on index day

Table 3. Predicted change[a] in CD4:CD8 ratio from baseline in the subset of the population with CD4:CD8 ratio measurements

	N	Follow-up months Median (IQR)	6-month predicted CD4:CD8 ratio change Δ (95% CI)[a]	24-month predicted CD4:CD8 ratio change Δ (95% CI)[a]
B/F/TAF	606	21.8 (14.2, 30.2)	+ 0.16 (0.14, 0.17)	+0.28 (0.25, 0.32)
bDRV	101	19.0 (10.0, 27.0)	+0.15 (0.14, 0.17)	+0.25 (0.22, 0.28)
DTG	131	24.5 (13.6, 36.3)	+0.15 (0.12, 0.18)	+0.21 (0.17, 0.26)
EVG/c	119	20.3 (10.8, 33.2)	+0.15 (0.11, 0.19)	+0.18 (0.11, 0.24)

Δ, delta (change); bDRV, boosted darunavir; B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; CI, confidence interval; DTG, dolutegravir; EVG/c, elvitegravir/cobicistat; IQR, interquartile range
[a] Cox proportional hazards model, in[a] Predicted values from linear mixed model, restricted cubic splines on time (knots: 2, 6, 12, 24), inverse probability of treatment weights (baseline age, CD4 cell count, log10 viral load, eGFR, sex, Black race, ADAP/Ryan White, AIDS history, any comorbidities)
[b] Discontinuation is defined as 3rd agent change or >45 days without ART

Discussion

- Among individuals with advanced HIV infection at ART initiation, B/F/TAF was associated with an increased likelihood of CD4 cell count recovery to levels >200 cells/µL, compared to bDRV 3DR, DTG 3DR, and EVG/c 3DR
- Similar patterns were observed among individuals initiating ART with a STR
- No difference was observed in CD4:CD8 ratio changes over time across groups
- CD4:CD8 ratio normalization was rare with all regimens

Key Findings

Among individuals with advanced HIV:

- B/F/TAF was associated with a higher hazard of CD4 cell count recovery compared to bDRV 3DR, DTG 3DR, and EVG 3DR
- No difference in CD4:CD8 ratio recovery was observed

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