Real world use of dolutegravir/lamivudine in treatment naïve people living with HIV during the COVID pandemic

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OPERA® The Longitudinal Cohort

BACKGROUND

- For years, antiretroviral therapy (ART) consisting of three-drug regimens (3DR) were the standard to treat people with HIV (PWH)[1]
- Two-drug regimens (2DR) have been introduced in recent years to potentially reduce ART toxicities and drug-drug interactions for individuals with comorbid conditions[2] while demonstrating comparable efficacy to 3DRs[3]
- Dolutegravir/lamivudine (DTG/3TC) 2DR was approved by the FDA for ART-naïve PWH in April 2019[4]
- DTG/3TC 2DR uptake in the US coincided with the COVID-19 pandemic

OBJECTIVE

To compare dolutegravir/lamivudine two-drug regimen to typical three-drug regimens among ART-naïve people with HIV initiating ART

METHODS

Study Population

- OPERA® observational cohort
  - Prospectively captured, routine clinical data from electronic health records from 96 clinics in the US (22 states, 1 US territory)
  - >140K people with HIV (PWH) as of July 2022, representing ~13% of people with diagnosed HIV infection in the US[4]
- Inclusion criteria
  - HIV-1 infection without HIV-2 infection
  - Aged 18+
  - ART-naïve
  - ART initiated between 01MAY2019 and 30APR2021 with either:
    - DTG/3TC 2DR
    - Bictegravir-based three-drug regimen (BIC 3DR)
    - DTG-based 3DR (i.e., DTG/abacavir [ABC]/3TC, DTG/tenofovir disoproxil fumarate [TDF]/emtricitabine [FTC], or DTG/tenofovir alafenamide [TAF]/FTC)
- Censoring events: study end (i.e., 31OCT2021), loss to follow-up (i.e., 12 months after last contact), death, or regimen change
- Baseline: Date of ART initiation

Outcome Definitions

- Discontinuation (D/C): A switch to another regimen or prescription gap >45 days
- Virologic failure (VF): Two consecutive viral loads (VL) ≥200 copies/mL after 24 weeks on the regimen

Analyses

- Univariate Poisson regression to estimate incidence rates (IR) and 95% confidence intervals (CI) of D/C and VF
- Cox proportional hazards marginal structural models to estimate hazard ratios (HR) and 95% CIs for the association between ART regimen and VF

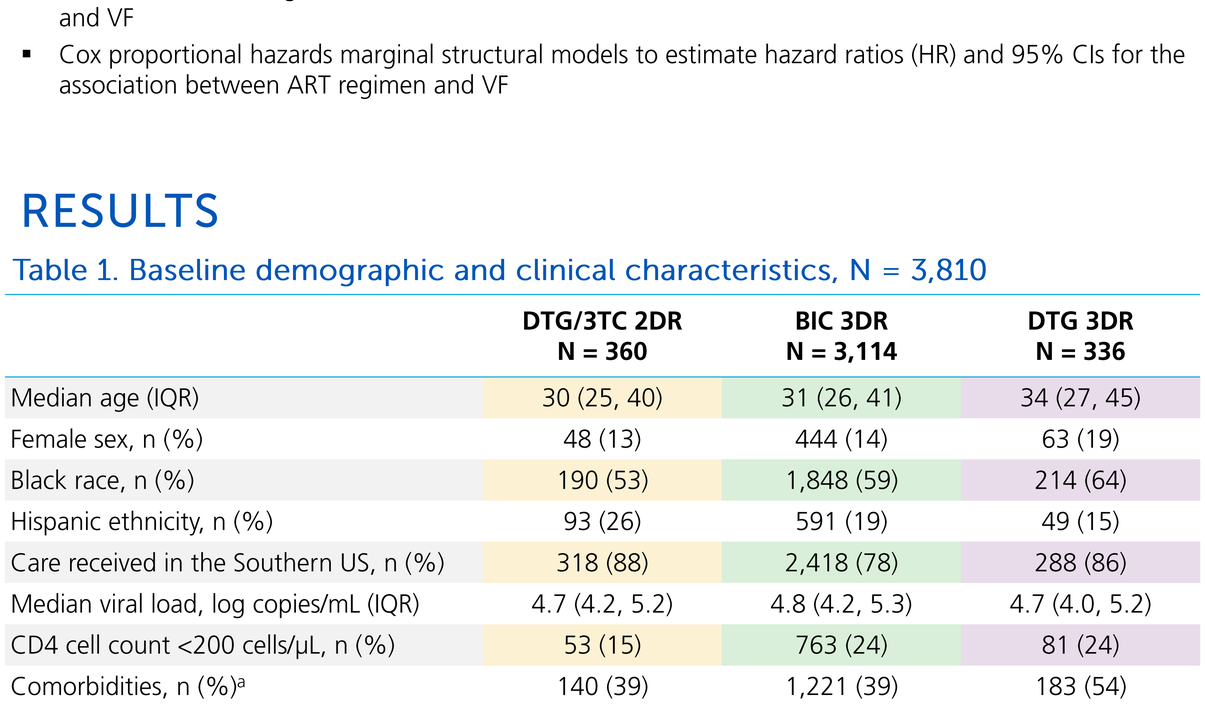
RESULTS

Table 1. Baseline demographic and clinical characteristics, N = 3,810

	DTG/3TC 2DR N = 360	BIC 3DR N = 3,114	DTG 3DR N = 336
Median age (IQR)	30 (25, 40)	31 (26, 41)	34 (27, 45)
Female sex, n (%)	48 (13)	444 (14)	63 (19)
Black race, n (%)	190 (53)	1,848 (59)	214 (64)
Hispanic ethnicity, n (%)	93 (26)	591 (19)	49 (15)
Care received in the Southern US, n (%)	318 (88)	2,418 (78)	288 (86)
Median viral load, log copies/mL (IQR)	4.7 (4.2, 5.2)	4.8 (4.2, 5.3)	4.7 (4.0, 5.2)
CD4 cell count <200 cells/μL, n (%)	53 (15)	763 (24)	81 (24)
Comorbidities, n (%)[a]	140 (39)	1,221 (39)	183 (54)

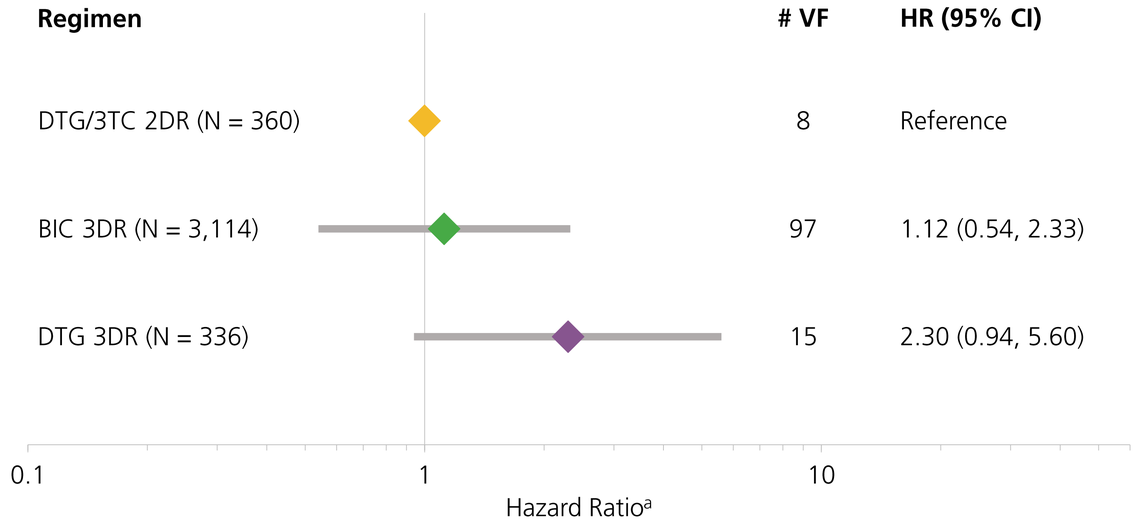
2DR, two-drug regimen; 3DR, three-drug regimen; 3TC, lamivudine; BIC, bictegravir; DTG, dolutegravir; IQR, interquartile range; N, number
[a] Any diagnosis of autoimmune disease, cardiovascular disease, invasive cancer, endocrine disorder, mental health condition, liver disease, bone disease, peripheral neuropathy, renal disease, hypertension, or substance abuse

Figure 1. Incidence rate of confirmed virologic failure over follow-up



2DR, two-drug regimen; 3DR, three-drug regimen; 3TC, lamivudine; BIC, bictegravir; DTG, dolutegravir; N, number

Figure 2. Association[a] between regimen and confirmed virologic failure[b]



2DR, two-drug regimen; 3DR, three-drug regimen; 3TC, lamivudine; BIC, bictegravir; CI, confidence interval; DTG, dolutegravir; HR, hazard ratio; N, number; VF, virologic failure
[a] Marginal structural model with inverse probability of treatment weights controlled for baseline age (quadratic), female, Black race, Hispanic ethnicity, Southern US, log10 viral load, comorbidities; CD4 count was included as a covariate (128 observations excluded due to missing; 4 BIC virologic failures were excluded)
[b] Defined as two consecutive viral loads ≥200 copies/mL after 24 weeks

Table 2. Duration of follow-up and regimen discontinuation

	DTG/3TC 2DR N = 360	BIC 3DR N = 3,114	DTG 3DR N = 336
Median months of follow-up (IQR)	15.0 (8.9-21.5)	15.8 (11.0-23.2)	14.6 (9.9-22.9)
Regimen discontinuation			
n (%)	69 (19)	370 (12)	121 (36)
IR per 100 person-years (95% CI)	14.9 (11.8, 18.9)	8.5 (7.7, 9.4)	27.9 (23.4, 33.4)
Type of regimen discontinuation, among discontinuers			
Switch to another regimen, n (%)	52 (75)	139 (38)	68 (56)
Prescription gap >45 days, n (%)	17 (25)	231 (62)	53 (44)
Median gap days (IQR)	75 (43, 99)	65 (34, 139)	63 (34, 116)
Resumed index regimen after >45-day gap, n (%)	6 (35)	75 (32)	12 (23)
Viral load at discontinuation			
≥1 VL ≤30 days before discontinuation, n (%)	20 (29)	81 (22)	24 (20)
Last VL <200 copies/mL, n (%)	13 (65)	44 (54)	14 (58)

2DR, two-drug regimen; 3DR, three-drug regimen; 3TC, lamivudine; BIC, bictegravir; CI, confidence interval; DTG, dolutegravir; IQR, interquartile range; IR, incidence rate; VL, viral load

DISCUSSION

- Among ART-naive PWH in the US, baseline characteristics varied across groups (e.g., higher likelihood of comorbidities with DTG 3DR, lower likelihood of low CD4 count with DTG/3TC 2DR; **Table 1**)
- Rates of confirmed virologic failure were low across regimens (**Figure 1**); risk of failure was similar between DTG/3TC 2DR and BIC 3DR (**Figure 2**)
- 25% to 62% of the discontinuations were gaps in prescriptions >45 days
  - Gaps in prescription were less common with DTG/3TC 2DR
  - 23% to 35% returned to the initial regimen after the gap
  - Such ART prescription patterns may be an anomaly of the COVID-19 pandemic

KEY FINDINGS

Among ART-naïve PWH:

- Virologic failure was uncommon with DTG/3TC 2DR, BIC 3DR or DTG 3DR
- Many discontinuation were, in fact, gaps in prescriptions; ~1/3 resumed the initial regimen

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ACKNOWLEDGEMENTS

This research would not be possible without the generosity of people living with HIV and their OPERA® caregivers. Additionally, we are grateful for the following individuals: Lito Torres (SAS programming), Robin Beckerman (QA), Bernie Stooks (Data Management), Lisa Lutzi (Database Architecture), and Judy Johnson (Medical Terminology Classification).

SUPPORT

The research was sponsored by ViiV Healthcare

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