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The US REGAL Cohort: A Retrospective Real-world Study of the Effectiveness and Tolerability of the Antiretroviral Treatment Regimens DTG/3TC Compared to BIC/FTC/TAF in Older Persons Living with HIV

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Key Takeaways

- **The US REGAL study evaluates dolutegravir/lamivudine (DTG/3TC) and bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) in aging persons living with human immunodeficiency virus (PWH) in the US across 5 study sites.**
- **The study cohort comprises people with prior antiretroviral therapy (ART) aged ≥50 years who have been living with HIV-1 for more than a decade, with diverse comorbidities and co-medications.**
- **Only 2 virological failures (one in each group) occurred at 48 weeks. The proportion of PWH with a switch, change, or discontinuation of BIC/FTC/TAF was greater than that of DTG/3TC. However, adjusted incidence rate (IR) differences did not yield differences across treatment groups.**
- **Compared to BIC/FTC/TAF, DTG/3TC was equally effective and well tolerated in a population of older, virologically suppressed PWH.**

Introduction

- Modern ART has evolved from three-drug to two-drug regimens, including guidelines recommending DTG/3TC as initial treatment for most PWH with no prior ART treatment and as a switch option for virologically suppressed PWH. Data comparing the real-world effectiveness of the two-drug DTG/3TC and three-drug BIC/FTC/TAF are limited in older PWH.
- **Study Aim:** To assess the demographics and clinical characteristics, and compare the real-world effectiveness, tolerability, and other core outcomes of switching treatment to DTG/3TC versus BIC/FTC/TAF in older PWH

Methods

- Retrospective chart review of people with prior ART treatment, virally suppressed, with HIV diagnosis, aged ≥50 years at time of study index
- Definitions:
  - Study exposure: Treatment with either study intervention for at least 24 weeks
  - Index date: DTG/3TC or BIC/FTC/TAF initiation date
- **Primary Study Outcome:**
- Virologic Failure at 48 weeks defined as 2 consecutive HIV RNA viral loads of ≥200 copies/mL or 1 HIV RNA viral load of ≥200 copies/mL followed by core agent/regimen change within 4 months of the viral load of ≥200 copies/mL
- Demographics, clinical characteristics, and effectiveness outcomes were abstracted from clinical charts for PWH after DTG/3TC or BIC/FTC/TAF initiation and summarized using appropriate descriptive statistics.
- **Propensity score weighting**, using inverse probability of treatment weighting (IPTW), was applied in analyses of all endpoints to ensure comparability of baseline characteristics between groups.
- The propensity score model from the global study population was estimated using age at index date, gender, race/ethnicity, and region and applied to the US cohort. Variables with a p-value of <0.10 in bivariate analyses were considered as potential confounders.

Results

Table 1. Description of Demographic Characteristics at Index Date

		DTG/3TC (N=165)	BIC/FTC/TAF (N=161)
Age (years)	Mean (SD)	60.9 (7.3)	60.8 (6.4)
	Median (Q1, Q3)	59.0 (55.0, 65.0)	60.0 (57.0, 65.0)
	(Range)	(50.0, 87.0)	(50.0, 80.0)
Age >65 years	Yes	41.0 (24.9%)	36.0 (22.4%)
	No	124.0 (75.2%)	125.0 (77.6%)
Gender assigned at birth	Male	128.0 (77.6%)	120.0 (75.0%)
	Female	37.0 (22.4%)	40.0 (25.0%)

Demographics at Index Date

- 326 PWH (165 on DTG/3TC and 161 on BIC/FTC/TAF) were enrolled in the US.
- The proportion of PWH age >65 years was 24.9% for DTG/3TC and 22.4% for BIC/FTC/TAF.
- The proportion of PWH with male gender assigned at birth reported was 77.6% for DTG/3TC and 75.0% for BIC/FTC/TAF.

Table 2. Description of Clinical Characteristics at Index Date

	DTG/3TC (N=165)	BIC/FTC/TAF (N=161)
Weight (kg)		
Median (Q1, Q3)	81.3 (72.1, 92.4)	81.6 (72.1, 95.3)
Not reported (n)	19.0	24.0
Time between HIV diagnosis and index date (years)		
Median (Q1, Q3)	18.5 (11.1, 24.6)	21.8 (14.4, 27.3)
Not reported (n)	19.0	23.0
Plasma HIV viral load*		
Undetectable-Target not detected	70.0 (45.2%)	53.0 (34.4%)
Detectable but Quantifiable	19.0 (12.3%)	42.0 (27.3%)
Detectable and Unquantifiable	66.0 (42.6%)	59.0 (38.3%)
Not reported (n)	10.0	7.0
CD4 cell count (cells/mm^3)		
Median (Q1, Q3)	734.0 (523.0, 997.0)	662.8 (463.0, 897.0)
Not reported (n)	15.0	25.0
CD4/CD8 ratio		
Median (Q1, Q3)	0.9 (0.7, 1.3)	0.9 (0.6, 1.3)
Not reported (n)	56.0	38.0
BMI category (kg/m^2)		
Underweight (<18.5)	2.0 (1.4%)	1.0 (0.7%)
Healthy Weight (18.5 - <25)	44.0 (30.6%)	37.0 (27.6%)
Overweight (25.0 - <30)	54.0 (37.5%)	55.0 (41.0%)
Obesity (30 and above)	44.0 (30.6%)	41.0 (30.6%)
Not reported (n)	21.0	27.0

* Limit of detection by HIV RNA viral load assay varies by site and local laboratory

Clinical Characteristics at Index Date

- Among PWH on DTG/3TC and BIC/FTC/TAF, respectively:
  - Overweight (37.5% and 41.0%) and Obesity (30.6% in both groups) were most common
  - Median time from HIV diagnosis to index date was 18.5 and 21.8 years
  - Median CD4 count was 734.0 and 662.8 cells/mm^3

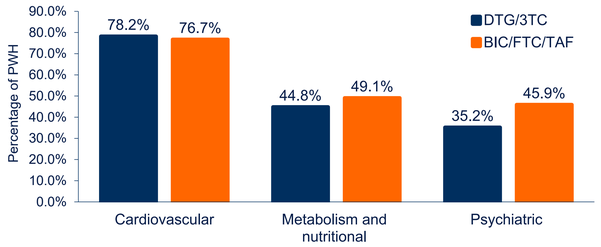
Table 3. Description of Historical Characteristics Prior to Index Date

		DTG/3TC (N=165)	BIC/FTC/TAF (N=161)
Prior Virological Failure	No	43.0 (93.5%)	43.0 (82.7%)
	Yes	3.0 (6.5%)	9.0 (17.3%)
	Not reported	143.0	136.0
Number of Prior ART regimens	Median (Q1, Q3)	2.0 (1.0, 3.0)	2.0 (1.0, 4.0)
	Not reported	125.0	111.0
Duration of Prior ART regimen (years)	Median (Q1, Q3)	6.4 (3.5, 11.7)	7.2 (3.2, 15.4)
	Not reported	119.0	109.0

Historical Characteristics Prior to Index Date

- 12 PWH experienced virological failure prior to index date and had received a median of 2.0 prior ART regimens in each treatment group.

Figure 1. Top 3 Comorbidities at Index Date

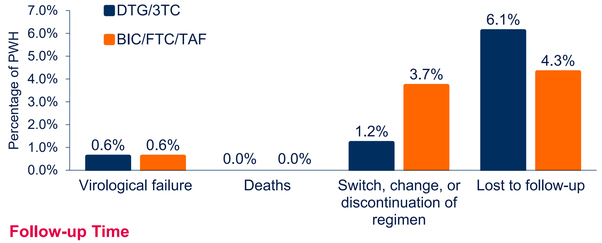


Comorbidities and Co-medications

- At the index date, 95.4% of PWH had >1 comorbidity; ≥3 comorbidities were reported in 60.0% of PWH on DTG/3TC and 67.0% on BIC/FTC/TAF.
- One or more non-ART co-medications were reported in 95.8% of PWH on DTG/3TC and 98.7% of PWH on BIC/FTC/TAF.

Endpoint Results

Figure 2. Cumulative Incidence of Study Endpoints up to 288 Weeks From Index Date



Follow-up Time

- Total follow-up was 356.6 and 435.8 person-years in the DTG/3TC and BIC/FTC/TAF groups, respectively.
- Overall, 20.0% of PWH had 240 weeks of follow-up.

Table 4. Study Outcomes by Follow-up Visit

Wk		DTG/3TC (N=165)	BIC/FTC/TAF (N=161)	Wk		DTG/3TC (N=165)	BIC/FTC/TAF (N=161)
24	n (%)	165.0 (100.0%)	161.0 (100.0%)	144	n (%)	91.0 (55.2%)	113.0 (70.2%)
	VF	0.0 (0.0%)	0.0 (0.0%)		VF	0.0 (0.0%)	0.0 (0.0%)
	S/C/D	0.0 (0.0%)	0.0 (0.0%)		S/C/D	0.0 (0.0%)	2.0 (1.8%)
	LTFU	0.0 (0.0%)	0.0 (0.0%)		LTFU	2.0 (2.2%)	0.0 (0.0%)
	EOS	0.0 (0.0%)	0.0 (0.0%)		EOS	38 (41.8%)	28 (24.8%)
48	n (%)	165.0 (100.0%)	161.0 (100.0%)	192	n (%)	51 (30.9%)	83 (51.6%)
	VF	1.0 (0.6%)	1.0 (0.6%)		VF	0.0 (0.0%)	0.0 (0.0%)
	S/C/D	3.0 (1.8%)	2.0 (1.2%)		S/C/D	1.0 (2.0%)	2.0 (2.4%)
	LTFU	2.0 (1.2%)	0.0 (0.0%)		LTFU	1.0 (2.0%)	0.0 (0.0%)
	EOS	21.0 (12.7%)	7.0 (21.1%)		EOS	31.0 (60.8%)	34.0 (41.0%)
96	n (%)	138.0 (83.6%)	151.0 (93.8%)				
	VF	0.0 (0.0%)	0.0 (0.0%)				
	S/C/D	0.0 (0.0%)	2.0 (1.3%)				
	LTFU	4.0 (2.9%)	2.0 (1.3%)				
	EOS	42.0 (30.4%)	34.0 (22.5%)				
	Other	1.0 (0.72%)	0.0 (0.0%)				

- EOS: End of follow-up/study
- LTFU: Lost to follow-up
- S/C/D: Switch, change, discontinuation
- VF: Virological failure

Study Outcomes

- 2 virological failures were reported, one for each group, with no resistance reported.
- Switch, changes, or discontinuation of the regimen was observed in 4.0 (2.4%) PWH on DTG/3TC and 8.0 (5.0%) PWH on BIC/FTC/TAF up to 192 weeks of follow-up.
- At 48 weeks, the incidence rate (IR) (95% CI) of VF was 0.63 (0.01, 1.50) among PWH on DTG/3TC and 0.68 (0.01, 1.61) per 100 person-years among PWH on BIC/FTC/TAF. No significant difference was observed across groups (IR difference of -0.05 (-2.2, 2.0).
- The end of study IR (95% CI) of VF was 0.26 (0.01, 0.61) among PWH on DTG/3TC and 0.23 (0.00, 0.53) per 100 person-years among PWH on BIC/FTC/TAF. No significant difference was observed across groups (IR difference of 0.03 [-0.7, 0.8]).
- The end of study IR difference (95% CI) for tolerability and discontinuation between DTG/3TC compared to BIC/FTC/TAF was 0.05 (-1.83, 2.04) and 1.71 (-0.99, 4.58) per 100 person-years, respectively.

Limitations

- Certain endpoints with a high number of missing values due to the retrospective nature of the study should be interpreted with caution.

Conclusions

- As compared to BIC/FTC/TAF, older PWH in the US who had a significant burden of age-related comorbidities and co-medications maintained long-term viral suppression without resistance after switching to two-drug DTG/3TC.
- Only 2 virological failures were observed in the total cohort (one in each group).
- Both DTG/3TC and BIC/FTC/TAF were well tolerated, with minimal switches, regimen changes, and discontinuations reported.
- Using a two-drug regimen such as DTG/3TC provides high effectiveness in older adults while using fewer medications than three-drug regimens.

For global REGAL data, please see Poster P-357.

Thank you to all of the investigators and participants who contributed to the REGAL study.

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