The European 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

ePP115

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Key Takeaways

- The European (EU) REGAL study evaluates dolutegravir/lamivudine (DTG/3TC) and bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) in aging persons living with HIV-1 (PWH) in Germany, Spain, and France.
- The study cohort comprises people with prior antiretroviral therapy (ART) aged ≥50 years who have been living with HIV for decades with diverse comorbidities and co-medications.
- No virological failures occurred during follow-up. 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 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 PWH who are virologically suppressed.

Purpose

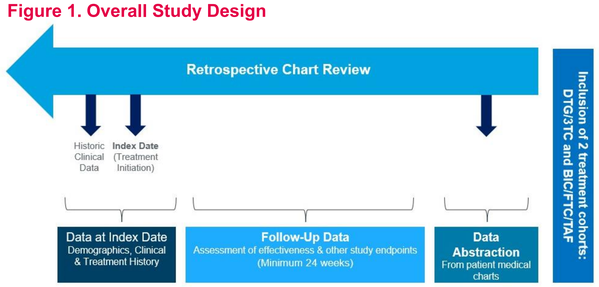
- The United Nations Programme on human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (UNAIDS) estimated that the proportion of PWH aged ≥50 years in 2020 was 21.0% and is projected to rise to 73.0% by 2030[1].
- The proportion of PWH with multiple comorbidities increases with age. PWH have concerns about the cumulative effects of long-term ART[2].
- Awareness among healthcare providers and older adults on the additional needs of treating older PWH is warranted[3], including the management of age-related comorbidities and increased likelihood of polypharmacy and drug-drug interactions.
- Modern ART has evolved from three-drug to two-drug regimens, including guidelines recommending DTG/3TC both for initial treatment and as a switch option for PWH with prior ART treatment.
- Data comparing the real-world effectiveness of the two-drug DTG/3TC and three-drug BIC/FTC/TAF is 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

Study Design

- Retrospective chart review of PWH with prior ART treatment, virological suppression, aged ≥50 years at time of DTG/3TC or BIC/FTC/TAF initiation, who have at least 24 weeks of follow-up (Figure 1).
- As part of the global REGAL study across the United States, EU, and Asia, the study population comprised PWH from France (2 sites), Germany (3 sites), and Spain (3 sites).
- Definitions:
  - Study exposure: Treatment for HIV with either DTG/3TC or BIC/FTC/TAF 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 ribonucleic acid (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 EU cohort.

Figure 1. Overall Study Design



Results

Table 1. Description of Demographic Characteristics at Index Date

	DTG/3TC (N=241)	BIC/FTC/TAF (N=201)
Age (years)		
Mean (SD)	60.0 (7.0)	59.3 (6.3)
Median (Q1, Q3)	59.0 (55.0, 64.0)	58.0 (55.0, 63.0)
(Range)	(50.0, 84.0)	(50.0, 80.0)
Age >65 years		
Yes	47.0 (19.5%)	33.0 (16.4%)
No	194.0 (80.5%)	168.0 (83.6%)
Gender assigned at birth		
Male	195.0 (80.9%)	172.0 (85.6%)
Female	46.0 (19.1%)	29.0 (14.4%)
Gender identity at index		
Male	196.0 (81.3%)	170.0 (85.0%)
Female	45.0 (18.7%)	30.0 (15.0%)
Not reported (n)	0.0	1.0
Country		
Germany	78.0 (32.4%)	62.0 (30.8%)
Spain	98.0 (40.7%)	91.0 (45.3%)
France	65.0 (27.0%)	48.0 (23.9%)

Demographics at Index Date

- 442 PWH (241 on DTG/3TC and 201 on BIC/FTC/TAF) were enrolled across France (113), Germany (140), and Spain (189).
- The proportion of PWH age >65 years was 19.5% for DTG/3TC and 16.4% for BIC/FTC/TAF.
- The proportion of PWH with Male gender assigned at birth reported was 80.9% for DTG/3TC and 85.6% for BIC/FTC/TAF.

Table 2. Description of Clinical Characteristics at Index Date

	DTG/3TC (N=241)	BIC/FTC/TAF (N=201)
Weight (kg)		
Median (Q1, Q3)	73.6 (64.0, 84.0)	77.8 (65.6, 88.3)
Not reported (n)	83.0	65.0
Time between HIV diagnosis and index date (years)		
Median (Q1, Q3)	20.0 (13.1, 27.5)	22.1 (14.7, 27.1)
Not reported (n)	11.0	5.0
Plasma HIV viral load*		
Undetectable-Target not detected	193.0 (84.6%)	152.0 (77.6%)
Detectable but Unquantifiable	6.0 (2.6%)	19.0 (9.7%)
Detectable and Quantifiable	29.0 (12.7%)	25.0 (12.8%)
Not reported (n)	13.0	5.0
CD4 cell count (cells/mm^3)		
Median (Q1, Q3)	692.0 (531.0, 904.0)	676.0 (522.0, 889.0)
Not reported (n)	36.0	20.0
CD4/CD8 ratio		
Median (Q1, Q3)	0.8 (0.6, 1.3)	0.9 (0.6, 1.2)
Not reported (n)	39.0	22.0
BMI category (kg/m^2)		
Underweight (<18.5)	5.0 (3.3%)	5.0 (3.8%)
Healthy Weight (18.5 - <25.0)	68.0 (45.0%)	55.0 (41.4%)
Overweight (25.0 - <30.0)	58.0 (38.4%)	53.0 (39.8%)
Obese (30.0 and above)	20.0 (13.2%)	20.0 (15.0%)
Not reported (n)	90.0	68.0

* Limit of detection by HIV-1 RNA viral load assay used varies by site and local laboratory

Clinical Characteristics at Index Date

- Among PWH on DTG/3TC and BIC/FTC/TAF, respectively:
  - Healthy weight (45.0% and 41.4%) and Overweight (38.4% and 39.8%) were most common.
  - Median time from HIV diagnosis to index date was 20.0 and 22.1 years.
  - Median CD4 count was 692 and 676 cells/mm^3 .

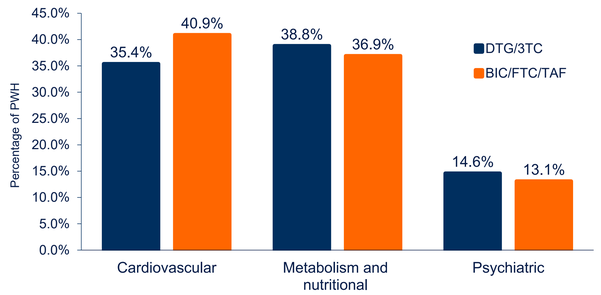
Table 3. Description of Historical Characteristics Prior to Index Date

	DTG/3TC (N=241)	BIC/FTC/TAF (N=201)
Prior Virological Failure		
No	206.0 (91.2%)	169.0 (89.4%)
Yes	20.0 (8.8%)	20.0 (10.6%)
Not reported (n)	15.0	12.0
Number of Prior ART regimens		
Median (Q1, Q3)	4.0 (2.0, 7.0)	5.0 (3.0, 7.0)
Not reported (n)	5.0	4.0
Duration of Prior ART regimens (years)		
Median (Q1, Q3)	16.6 (9.2, 22.7)	19.1 (12.5, 23.3)
Not reported (n)	11.0	9.0

Historical Characteristics Prior to Index Date

- In each treatment group, 20 PWH had experienced virological failure prior to index date (DTG/3TC: 8.8%; BIC/FTC/TAF: 10.6%).
- PWH had received a median of 4.0 and 5.0 prior ART regimens in the DTG/3TC and BIC/FTC/TAF groups, respectively.

Figure 2. Top 3 Comorbidities at Index Date

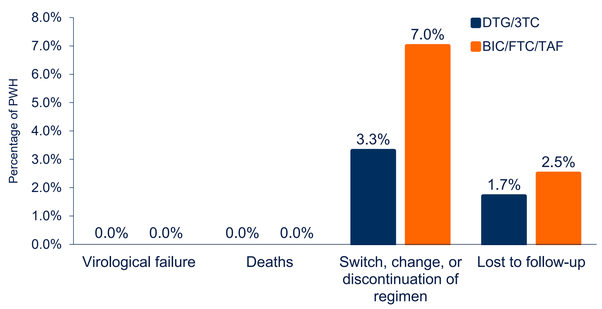


Comorbidities and Co-medications

- At the index date, approximately 75% of PWH in both treatment groups had >1 comorbidity; ≥3 comorbidities were reported in 23.8% of PWH on DTG/3TC and 27.3% on BIC/FTC/TAF.
- One or more non-ART co-medications were reported in 81.3% of PWH on DTG/3TC and 73.8% of PWH on BIC/FTC/TAF.

Endpoint Results

Figure 3. Cumulative Incidence of Study Endpoints up to 288 Weeks From Index Date



Follow-up Time

- Total follow-up was 711 and 610 person-years in the DTG/3TC and BIC/FTC/TAF groups, respectively.
- Overall, 40.0% of PWH had 192 weeks of follow-up.

Table 4. Study Outcomes by Follow-up Visit

Wk		DTG/3TC (N=241)	BIC/FTC/TAF (N=201)
24	n (%)	241.0 (100.0%)	201.0 (100.0%)
	Virological failure	0.0 (0.0%)	0.0 (0.0%)
	Switch, change, or discontinuation	1.0 (0.4%)	0.0 (0.0%)
	Lost to follow-up	0.0 (0.0%)	0.0 (0.0%)
	End of follow-up/study	0.0 (0.0%)	0.0 (0.0%)
48	n (%)	240.0 (99.6%)	201.0 (100.0%)
	Virological failure	0.0 (0.0%)	0.0 (0.0%)
	Switch, change, or discontinuation	1.0 (0.4%)	4.0 (2.0%)
	Lost to follow-up	1.0 (0.4%)	0.0 (0.0%)
	End of follow-up/study	4.0 (1.7%)	9.0 (4.5%)
	Other/Not reported	1.0 (0.4%)	1.0 (0.5%)
96	n (%)	233.0 (96.7%)	187.0 (93.0%)
	Virological failure	0.0 (0.0%)	0.0 (0.0%)
	Switch, change, or discontinuation	4.0 (1.7%)	6.0 (3.2%)
	Lost to follow-up	1.0 (0.4%)	0.0 (0.0%)
	End of follow-up/study	21.0 (9.0%)	16.0 (8.6%)
	Other/Not reported	8.0 (3.4%)	4.0 (2.1%)
144	n (%)	199.0 (82.6%)	161.0 (80.1%)
	Virological failure	0.0 (0.0%)	0.0 (0.0%)
	Switch, change, or discontinuation	1.0 (0.5%)	1.0 (0.6%)
	Lost to follow-up	2.0 (1.0%)	0.0 (0.0%)
	End of follow-up/study	22.0 (11.1%)	24.0 (14.9%)
	Other/Not reported	11.0 (5.5%)	6.0 (3.7%)
192	n (%)	163.0 (67.6%)	130.0 (64.7%)
	Virological failure	0.0 (0.0%)	0.0 (0.0%)
	Switch, change, or discontinuation	0.0 (0.0%)	2.0 (1.5%)
	Lost to follow-up	0.0 (0.0%)	1.0 (0.8%)
	End of follow-up/study	50.0 (30.7%)	36.0 (27.7%)
	Other/Not reported	18.0 (11.0%)	9.0 (6.9%)

Study Outcomes

- No virological failure was reported at 48 weeks or until end of study in either group.
- Switch, changes, or discontinuation of the regimen was observed in 7 (2.9%) PWH on DTG/3TC and 13 (6.5%) PWH on BIC/FTC/TAF up to 192 weeks of follow-up.
- Overall, both regimens were well tolerated and had low rates of discontinuation. The incidence rate 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. No significant different was observed between either endpoint.

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 EU who had a significant burden of age-related comorbidities and co-medications maintained long-term viral suppression after switching to two-drug DTG/3TC.
- No virological failure was observed across all study timepoints.
- 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.

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

References: 1. Smit M, et al. *Lancet Infect Dis*. 2015;15:810–8 **2.** Young B, et al. *Open Forum Infect Dis*. 2017;4 (Suppl 1):S431–2 **3.** Courlet P, et al. *Open Forum Infect Dis*. 2019;6:ofz531

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