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Real World Evidence: insights from Italian Cohorts

OC 36 Durability of Bictegravir/Emtricitabine/Tenofovir alafenamide vs Dolutegravir-based single tablet regimens in a large Cohort of experienced PWH: the BIC-LASTING study

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ABSTRACT
Background: Large real-world data about the durability of bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) vs. dolutegravir (DTG)-based single tablet regimens (STR) on treatment failure-related discontinuations are limited.
Methods: BIC-LASTING (GS-IT-380-7317, sponsored by Gilead Sciences) is a retrospective analysis on people with HIV (PWH) enrolled in the ICONA cohort who initiated BIC/FTC/TAF or a DTG-STR (both two-drug regimens-2DR- and 3DR) with HIV-RNA≤50 cp/mL after Jan-2019 (baseline). PWH of the DTG-STR group who were previously on the same non-STR regimen were excluded. Baseline characteristics were compared by treatment group. Main reasons for treatment discontinuations (TD) as reported by the treating physician were collected. The primary endpoint was time to VF/AEs-related TDs, i.e. TD due to virological failure (VF) or toxicity. VF/AEs-related TDs were compared between groups using Kaplan-Meier (KM) curves and Cox regression models adjusted for selected covariates. Secondary endpoints: time to TD regardless of the reason (including simplification) overall and after excluding the switch from abacavir (ABC)/lamivudine(3TC)/DTG to DTG/3TC.
Results: We included 4,520 PWH; 2,332 who started BIC/FTC/TAF (52%) vs. 2,188 DTG-STR (48%), mainly DTG/3TC (75%), followed by DTG/rilpivirine (18.7%) and DTG/3TC/ABC (6.2%). Median age was 48 years (interquartile range, IQR:39-56), 19% females, CD4 count of 726 cells/mm3 (528-954). NRTI backbone of the

previous regimen was the most imbalanced factor between groups (in DTG-STR mainly with ABC/3TC (50%) while only 38% used TAF/FTC, p<0.001), followed by calendar year of baseline (2021 for DTG vs 2020, p<0.001). Over a median follow-up of 39 months (22-52), 210 VF/AEs-related TDs were observed (42 VF and 168 AEs). The 2-year risk of VF/AEs-related TD was 3.7% (95% CI 2.9–4.5) with BIC/FTC/TAF vs 3.9% (3.0–4.8) with DTG-STR (p=0.164). After controlling for confounders, no evidence for a difference between the 2 groups in the primary endpoint was observed in the adjusted Cox regression model (BIC vs DTG-STR: adjusted Hazard Ratio (aHR): 0.77, 95% CI 0.55-1.07) (Table 1). For the secondary endpoint of TD for any reason, additional discontinuations were counted as events: 585 for simplification, 45 for PWH's decision and 193 for other reasons. No evidence for differences among the 2 groups was found in the risk of TD for any reason overall (BIC vs DTG-STR: aHR 0.89. 95% CI 0.76-1.04) and after excluding the switch from ABC/3TC/DTG to DTG/3TC (BIC vs DTG-STR: aHR 1.14, 95% CI 0.97-1.35) (Tables 2-3).

Conclusions: In virologically suppressed PWH, no evidence for a difference in treatment failure was observed in those switching to BIC/FTC/TAF compared to DTG based STR, including 2DR in 94% of cases. These data support the favourable long-term efficacy and safety profile of BIC/FTC/TAF in clinical practice. Immortal time bias, and the possibility of unmeasured confounding cannot be excluded.

Table 1: Hazard ratio (HR) of TD for VF/AEs by Cox regression models

	Unadjusted and adjusted HR of TD for VF or AEs			
	Unadjusted HR (95% CI)	p-value	Adjusted* HR (95% CI)	p-value
DTG-STR	1		1	
BIC/TAF/FTC	0.82 (0.63, 1.08)	0.165	0.77 (0.55, 1.07)	0.114
*adjusted for sex at birth, age, nation of birth, baseline CD4 count, HIV-RNA at zenith, HCV/HBV status, AIDS, comorbidities (CVD, diabetes, ESRD) time from HIV diagnosis, type of previous ART regimen (NRTI pair and anchor drug), number of drugs previously failed and year of starting ART;				

Table 2: Hazard ratio (HR) of TD for any cause by Cox regression models

	Unadjusted and adjusted HR of TD for any reason			
	Unadjusted HR (95% CI)	p-value	Adjusted* HR (95% CI)	p-value
DTG-STR	1		1	
BIC/TAF/FTC	0.93 (0.82, 1.05)	0.260	0.89 (0.76, 1.04)	0.153
*adjusted for sex at birth, age, nation of birth, baseline CD4 count, HIV-RNA at zenith, HCV/HBV status, AIDS, comorbidities (CVD, diabetes, ESRD) time from HIV diagnosis, type of previous ART regimen (NRTI pair and anchor drug), number of drugs previously failed and year of starting ART.				

Table 3: Hazard ratio (HR) of TD for any cause excluding switch from ABC/3TC/DTG to DTG/3TC, by Cox regression models

	Unadjusted and adjusted HR of TD for any reason (switch from ABC/3TC/DTG to DTG/3TC not counted)			
	Unadjusted HR (95% CI)	p-value	Adjusted* HR (95% CI)	p-value
DTG-STR	1		1	
BIC/TAF/FTC	1.13 (0.99, 1.28)	0.074	1.14 (0.97, 1.35)	0.107
*adjusted for sex at birth, age, nation of birth, baseline CD4 count, HIV-RNA at zenith, HCV/HBV status, AIDS, comorbidities (CVD, diabetes, ESRD) time from HIV diagnosis, type of previous ART regimen (NRTI pair and anchor drug), number of drugs previously failed and year of starting ART.				