

# Early Discontinuation of 3TC/ABC/DTG and BIC/TAF/FTC Single Tablet Regimens: a real-life multicenter cohort study

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**Objectives:** Comparing rates and reasons of early discontinuation within 24 weeks in a large cohort of HIV-1 infected patients, ART experienced with HIV-RNA level <50 copies/mL switching to BIC/TAF/FTC or DTG/3TC/ABC/ in five centers in Italy.

**Methods:** A retrospective, multicentre cohort study was carried out. Patients with plasma HIV-1 RNA <50 copies/mL switching to a STR regimen BIC/TAF/FTC or DTG/3TC/ABC/, in 5 large Italian out-patient facilities were included and followed-up 24 weeks. Major outcome was early discontinuation due to any cause (EDAC) and more specifically due to adverse events (EDAEs) or Virological Failure (VF). Study entry was the switch date starting STR, study exit the date of EDAC or loss to follow-up (FU)/death. X2/Fisher's and Wilcoxon signed rank test were used where appropriate. Kaplan-Meier for the probability of VF/EDAC/EDAEs and Cox model for regression analysis and Wald test were employed.

**Table 1. Clinical/demographic characteristics and outcome of HIV-1 infected patients, ART experienced with HIV-RNA level <50 copies/mL switching to BIC/TAF/FTC or DTG/3TC/ABC in five different centers in Italy.**

	BIC/TAF/FTC (262)		DTG/3TC/ABC (524)		P
Italian origin	221	84.3	431	82.2	0.502
Male Gender, n (%)	206	78.6	385	73.5	0.171
Age at entry, median [IQR]	54	[44-60]	51	[41-57]	0.0032
Route of HIV transmission, n (%)					0.010
• Sex	196	74.8	415	79.1	
• IVDU	36	13.7	63	12	
• Other	6	2.3	2	0.4	
• Not known	24	9.1	44	8.4	
Months of undetectable viremia, median [IQR]	51	[24-106]	42	[14-98]	0.0062
Patients with at least one comorbidity	115	43.9	117	22.3	<0.001
AIDS diagnosis, n (%)	54	20.6	86	16.4	0.147
HCV Ab positivity, n (%)	47	17.9	93	17.7	0.947
HIV RNA Zenit copies/mL Log <sub>10</sub> , median [IQR]	5.1	[4.7-5.6]	5.1	[4.6-6.0]	0.5094
Nadir CD4 (cells/mL), median [IQR]	230	[110-342]	219	[77-353]	0.6184
Years of HIV, median [IQR]	13	[5-22]	10	[4-19]	0.0081
Years of antiretroviral therapy, median [IQR]	9	[4-18]	8	[3-16]	0.0030
History of a previous virologic failure, n (%)	104	39.7	194	37.6	0.569
CD4+ T cells at baseline/μL, median [IQR]	690	[470-944]	679	[466-949]	0.6147
CD4 <350 cells/mL at baseline	33	12.6	75	14.3	0.510
Number of antiretroviral drugs before switch	7	[5-9]	5	[3-7]	<0.0001
Pre-switch Therapy					
• Mono-Therapy	2	0.8	5	0.9	0.788
• Dual-Therapy	21	8	36	6.9	0.560
• Three drug-regimen NNRTI-based	17	6.5	136	25.6	<0.001
• Three drug-regimen PI-based	12	4.5	166	31.7	<0.001
• Three drug-regimen INSTI-based	206	78.6	163	31.1	<0.001
• Other	4	1.5	18	3.4	0.126
Switch from a previous INSTI regimen	209	79.8	185	35.3	<0.0001
Switch from a previous ABC regimen	4	1.5	217	41.4	<0.0001
M184V/I mutation					0.020
• Yes	12	4.6	40	7.3	
• No	182	69.5	277	52.9	
• Unknown	68	25.9	207	39.5	
Discontinuation due to all cause	13	5.0	57	10.9	0.1970*
Discontinuation due to adverse event	7	2.7	48	9.1	0.0323*
Virologic failure	1	0.4	5	0.9	0.6276*

ART: antiretroviral therapy; IVDU: intravenous drug users; TDF: Tenofovir disoproxil fumarate; ABC: Abacavir; BIC: Bictegravir; TAF: Tenofovir alafenamide ; 3TC: Lamivudine; PI: Protease inhibitor; NNRTI: non-nucleoside reverse transcriptase inhibitors; INSTI: integrase strand transfer inhibitor

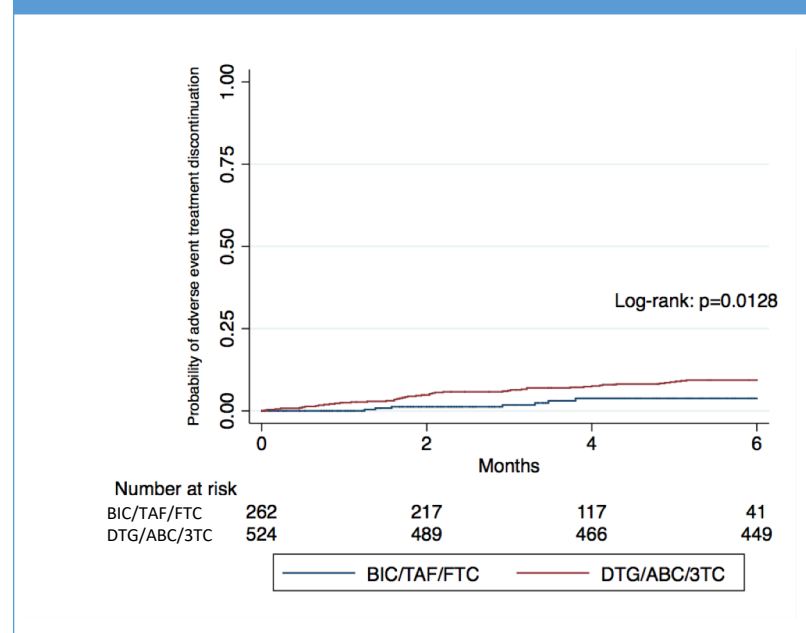
\*Wald test

**Table 2. Incidence rates (per 100-py) of virologic failure, discontinuation due to all causes and discontinuation due to treatment adverse events in HIV-1 infected patients, ART experienced with HIV-RNA level <50 copies/mL switching to BIC/TAF/FTC or to DTG/3TC/ABC in five centers in Italy**

	Discontinuation due to all causes		Discontinuation due to treatment adverse events		Discontinuation due to virologic failure	
	Incidence rate	95%CI	Incidence rate	95%CI	Incidence rate	95%CI
BIC/TAF/FTC	16.01	9.29-27.57	8.62	4.10-18.08	1.23	0.17-8.74
DTG/3TC/ABC	23.74	18.31-30.77	20.01	15.7-26.5	2.08	0.87-5.00

**Results:** We included 786 patients: 524 with DTG/3TC/ABC, 262 with BIC/TAF/FTC [Table 1]. At week 24, we observed 70 EDAC: 5 (7.1%) for VF (1 with BIC and 4 with DTG; log-rank p=0.6276), 10 for simplification, more frequently with BIC than DTG (n=5, 1.9% and n=5, 0.9%;) and 55 EDAEs, 7 (2.7%) with BIC, 48 (9.2%) with DTG). EDAEs due to neurological toxicity were similar between regimens (DTG 2.76% and BIC 0.80% (p=0.074)), gastrointestinal toxicity was more frequent in DTG (3.4% vs. 0.76%; p=0.025). No drug related AEs were serious or grade 3/4. There were no significant differences among regimens in the rates of VF and EDAC [Table 2]. The EDAEs rate was significantly higher for DTG than for BIC [20.01 x 100 py [95% 15.1-26.5] versus 8.62 x 100 py [95% 4.10-18.08], respectively [Figure 1]; The adjusted HR for EDAEs in DTG group compared to BIC was 3.28 (95%CI:1.34-7.99; p=0.009). We identified an association between age >60 years-old and switch from regimens without ABC. [Table 3].

**Figure 1. Probability of discontinuation for adverse events after 24 weeks in HIV-1 infected patients, ART experienced with HIV-RNA level <50 copies/mL switching to BIC/TAF/FTC or DTG/3TC/ABC in five different centers in Italy.**



**Conclusions:** Patients who received DTG/3TC/ABC, or BIC/TAF/FTC do not show significant differences in VF or EDAC rates. However, EDAEs within 24 week is more frequent with DTG/3TC/ABC, especially in the over-sixties and in those who come from regimens without abacavir.

**Table 9. Multivariable Cox model for discontinuation due to adverse events in HIV-1 infected patients, ART experienced with HIV-RNA level <50 copies/mL switching to BIC/TAF/FTC or DTG/3TC/ABC in five centers in Italy**

Variables	HR	95%CI	p
<b>Group</b>			
• BIC/TAF/FTC	-		
• DTG/3TC/ABC	3.28	1.34-7.99	0.009
<b>Gender</b>			
• Male	-		
• Female	1.24	0.64-2.40	0.135
• Transgender	4.80	0.57-40.1	0.147
<b>Age at entry in years</b>			
• < 40 years	-		
• 40-60 years	1.89	0.81-4.35	0.136
• > 60 years	2.85	1.08 - 7.53	0.034
<b>Risk behavior</b>			
• Heterosexual	-		
• MSM	0.67	0.31-1.44	0.306
• IVDU	1.51	0.68-3.32	0.301
• Other/ Unknown	1.12	0.44-2.87	0.798
<b>Previous AIDS event</b>			
• No	-		
• Yes	1.15	0.56-2.37	0.699
<b>Years of antiretroviral treatment</b>			
• > 11 years	-		
• 4-10 years	0.79	0.35-1.77	0.580
• ≤ 3 years	1.87	0.75-4.62	0.173
<b>CD4 baseline (cell/mm<sup>3</sup>)</b>			
• >350	-		
• <350	0.63	0.27-1.45	0.279
<b>Pre-switch regimen containing abacavir</b>			
• No	-		
• Yes	0.37	0.18-0.74	0.005
<b>Pre-switch PI boosted regimen</b>			
• No	-		
• Yes	1.10	0.62-1.96	0.736
<b>Pre-switch regimen containing INSTI</b>			
• No	-		
• Yes	0.72	0.38-1.38	0.329
<b>Previous Neuropsychiatric illness</b>			
• No	-		
• Yes	1.19	0.27-5.16	0.814
Number of previous ART regimens	1.01	0.90-1.13	0.771

\*Adjusted also for diabetes, dyslipidemia, Hypertension

ART: antiretroviral therapy; IVDU: intravenous drug users; TDF: Tenofovir disoproxil fumarate; ABC: Abacavir; BIC: Bictegravir; TAF: Tenofovir alafenamide ; 3TC: Lamivudine; PI: Protease inhibitor; NNRTI: non-nucleoside reverse transcriptase inhibitors; INSTI: integrase strand transfer inhibitor