Dettaglio abstract

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Title: Effectiveness of switch to bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) in virologically suppressed persons living with HIV (PLWH): 96-week data from the Icona cohort

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Abstract
Background: Real-world clinical data on BIC/FTC/TAF, especially from key-populations, are still lacking. The aim of this study is to evaluate the effectiveness of switching to BIC/FTC/TAF in ART-experienced virologically suppressed (VS) people living with HIV (PLWH), focusing on females and PLWH older than 50 years.
Methods: Observational study including ART-experienced VS PLWH from the Icona cohort who switched to BIC/FTC/TAF for the first time from Apr-2018 to Dec-2021. Primary endpoint: treatment failure (TF1) defined as virological failure (VF: 2 consecutive HIV-RNA > 200 copies/ml or 1 HIV-RNA>1000 cps/ml) or treatment discontinuation (TD) for any reason. Secondary endpoints: (i) treatment failure excluding TD for pregnancy (ii) treatment failure 2 (TF2): VF or TD only for toxicity/intolerance or for virological failure; (iii) VF in ITT and (iv) VF OT.
Standard survival analysis (Kaplan–Meier curves) were used. Unadjusted and adjusted hazard ratios (HR) of the different endpoints were estimated by means of Cox regression models for the different exposure groups: ≥50 years old and females. Sets of confounders were tailored for each of the exposure of interest.
Results: 1,233 PLWH were included (44.0% >50 years, 18.6% female). Patients' characteristics are shown on Table1.
Over a median follow-up of 125.2 weeks from BIC/FTC/TAF switch (IQR 52-88.7), 179 PLWH had TF1 (14.5%; 19 VF, 159 TD); TD due to pregnancy/planned pregnancy was observed in 8 out of 229 (3.5%) women. 56 PLWH had TF2 (4.8%; 37 TD for toxicity/failure and 19 VF); VF-ITT occurred in 23 (1.9%), VF-OT in 19 (1.6%) PLWH.
Reasons for BIC/FTC/TAF discontinuation among 159 PLWH were: 88 TD for simplifications (7.1% of total population, 55% of total discontinuations), 34 TD for toxicities/intolerance (2.6%, 21.4%), 3 TD for virological failures (0.3%, 1.9%), 3 TD for patient's decision (0.3%, 1.9%) and 31 (2.5%, 19.5%) for other reasons (including the 8 pregnancies/planned pregnancy).
The 96-week probability of TF1 estimated by KM was 10.3% (95%CI 8.7-12.2-), KM probabilities by

subgroups are shown in Table2, together with KM probabilities of TF excluding pregnancies, TF2, VF-ITT and VF-OT.
In the adjusted Cox regression models, PLWH ≥50 years did not have a different risk of TF1 compared to those <50 years (aHR 0.88, 95%CI 0.64-1.2), while females had a 42% higher risk (aHR 1.42, 95%CI 1.00-2.04) (Table3). However, after excluding 8 TD for pregnancy or planned pregnancy as events, treatment failure risk in women was comparable to that of men (aHR 1.13, 95%CI 0.77-1.68).
Neither age nor sex was associated with risk of treatment failure according to the TF2 definition.
In the Cox regression models PLWH older than 50 did not have a higher risk of VF OT and ITT, while females had a significant 2.78-fold higher risk of VF in the ITT analysis (aHR=2.78, 95%CI 1.19-6.5), witha marginally significant aHR of 2.38 (95%CI 0.91-6.2) in the OT analysis (Table 3).
Conclusions: Switching to BIC/FTC/TAF demonstrated high long-term effectiveness, including also in PLWH older than >50, consistent with data from RCTs. Higher risk of treatment failure in females is mainly related to planned or ongoing pregnancies. Reasons for higher risk of VF for females have to be further investigated.
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Table 1. Baseline demographic and clinical characteristics of the 1233 PLWH switching to BIC/FTC/TAF in the Icona cohort

	ART-experienced virologically controlled (N=1233)	
Italian, n(%)	1039	84.3
Race, White, n(%)	1098	89
Sex, Female, n(%)	229	18.6
Year of BIC start, median (IQR)	2019	2019-2020
Year HIV diagnosis, median (IQR)	2013	2008-2016
Year ART start, median (IQR)	2015	2011-2017
Age, years, median (IQR)	47	39-55
Age, >50 years, n(%)	542	44.0
Italian Geo Zone, n(%)		
Northern	786	62.9
Central	374	30.2
Southern/Islands	92	7.5
Mode of HIV Transmission, n(%)		
Heterosexual	455	36.9
IVDU	100	8.1
MSM	620	50.3
Other/Unknown	58	4.7
HCV Ab positive status, n(%)	129	10.5
HBsAg positive status, n(%)	49	3.96
Smoker, Yes, n(%)	525	42.6
CDC C-stage, n(%)	204	16.5
CD4, cells/mm^3, median (IQR)	703	505-933
Nadir CD4, cells/mm^3, median (IQR)	290	150-425
Total cholesterol, median (IQR)	194	170-218
LDL cholesterol, median (IQR)	122	101-145
HDL cholesterol, median (IQR)	49	41-59
Triglycerides, median (IQR)	117	83-169
eGFR, CKD-EPI, ml/min, median (IQR)	89.2	77.3-101.8
Weight, kg, median (IQR)	74	66-82
BMI, kg/m^2, median (IQR)	24.2	22.2-26.9
Diabetes diagnosis, n(%)	69	5.6
CVD diagnosis, n(%)	21	1.7
NADM diagnosis, n(%)	40	3.2
CKD diagnosis, n(%)	169	13.7
ESLD diagnosis, n(%)	3	0.2
Follow-up, years, median (IQR)	2.41	1.6-2.8
At least 48-weeks follow-up	1155	96.7
At least 96-weeks follow-up	970	78.7
Previous ART-regimen		
INSTI-based	1058	85.8
NNRTI-based	95	7.7
PI-based	62	5
Other	18	1.5
Years from first VS, median (IQR)	4.4	2.5-7.5

Table 2. Kaplan-Meier estimated 48- and 94-weeks probability of TF1, TF1 excluding pregnancies, TF2 and VF, overall and in the different groups for primary-endpoint in virologically suppressed ART-experienced patients switching to BIC/FTC/TAF

	48-weeks probability	95%CI	96-weeks probability	95%CI
TF1 (overall)	**3.9%**	**3.0-5.2**	**10.3%**	**8.7-12.2**
<50 years	4.3%	3.0-6.2	11.8%	9.5-14.6
>=50 years	3.4%	3.0-6.2	8.5%	6.3-11.3
Female	7.1%	4.4-11.3	15.2%	11.0-20.8
Male	3.2%	2.2-4.5	9.2%	7.5-11.3
TF1 excluding pregnancies (overall)	**3.5%**	**2.6-4.7**	**9.7%**	**8.1-11.6**
TF2 (overall)	**2.3%**	**1.6-3.3**	**4.1%**	**3.1-5.4**
VF200 ITT (overall)	**0.7%**	**0.3-1.4**	**1.5%**	**0.9-2.4**
VF200 OT (overall)	**0.50%**	**0.2-1.1**	**1.2%**	**0.7-2.0**

Table 3. Hazard ratios (HR) and Adjusted hazard ratios (AHR) of TF1, TF excluding pregnancies, TF2 and VF from fitting different Cox regression models in the different subgroups of interest for ART-experienced virologically suppressed PLWH switching to BIC/FTC/TAF

	TF1 (VF or TD any reason)					
	HR	**95%CI**	**p**	**AHR**	**95%CI**	**p**
Age, >=50 years (vs <50years)[1]	0.85	0.63-1.1	0.27	0.88	0.64-1.2	0.428
Gender, Female (vs. male)[2]	1.44	1.01-2.1	0.042	1.43	1-2	0.052
	TF1 excluding pregnancies					
	HR	**95%CI**	**P**	**AHR**	**95%CI**	**p**
Age, >=50 years (vs <50years)[1]	0.91	0.67-1.24	0.559	0.94	0.69-1.30	0.748
Gender, Female (vs. male)[2]	1.16	0.78-1.70	0.461	1.13	0.77-1.68	0.523
	TF2 (VF or TD tox/intolereance or TD viral failure)					
	HR	**95%CI**	**p**	**AHR**	**95%CI**	**p**
Age, >=50 years (vs <50years)[1]	1.01	0.59-1.7	0.970	1.02	0.59-1.80	0.920
Gender, Female (vs. male)[2]	1.40	0.75-2.60	0.287	1.27	0.68-2.40	0.454
	VF (ITT)					
	HR	**95%CI**	**p**	**AHR**	**95%CI**	**p**
Age, >=50 years (vs <50years)[1]	0.67	0.29-1.6	0.369	1.00	0.41-2.5	1.000
Gender, Female (vs. male)[2]	3.48	1.53-7.9	0.003	2.78	1.19-6.5	**0.019**
	VF (OT)					
	HR	**95%CI**	**P**	**AHR**	**95%CI**	**P**
Age, >=50 years (vs <50years)[1]	0.73	0.29-11.87	0.522	0.94	0.35-2.50	0.909
Gender, Female (vs. male)[2]	2.64	1.04-6.7	0.041	2.38	0.91-6.23	0.077

[1] AHR adjusted for nationality and calendar year first cART; [2] AHR adjusted for nationality and age