EFFECTIVNESS OF BICTEGRAVIR/EMTRICITABINE/TENOFOVIR ALAFENAMIDE (BIC/FTC/TAF) AS SWITCH STRATEGY IN VIROLOGICALLY SUPPRESSED: REAL-WORLD DATA FROM THE ICONA COHORT

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BACKGROUND

- **BIC/FTC/TAF** co-formulation showed excellent efficacy and tolerability in randomized clinical trials as switch strategy in people living with HIV (PLWH) virologically suppressed, while in real-life setting effectiveness need to be further investigated especially among some sub-groups:
  - **Older** PLWH is a growing population among HIV, with increased levels of comorbidities, polypharmacy and drug–drug interactions.
  - Sex-related factors influence ART outcomes and wellbeing of PLWH. **Women** are historically differentially affected by ART side effects

AIM

Evaluate the effectiveness of BIC/FTC/TAF in ART-experienced virologically suppressed (VS) people living with HIV (PLWH)

STUDY DESIGN AND METHODS

Study Design: Observational study including ART-experienced VS PLWH from the Icona cohort who switched, for the first time to BIC/FTC/TAF from Apr2018 to Dec2021.

Exposure of interest:
(1) Age (≥50 years old);
(2) Sex (Female);
(3) Switching from NNRTI-based regimen

Primary Endpoint: Time to **treatment failure** (TF) i.e. virological failure (VF: 2 HIV,RNA>200 copies/ml or 1 >1000 copies/ml) or treatment discontinuation (TD) for any reason.
Secondary Endpoints: **(1)** Time to **TD** for any reason; **(2)** Time to **TD for toxicity/intolerance**; **(3)** Time to **VF** in intention to treat analysis; **(4)** Changes in **CD4**, **CD4/CD8** and **weight** at 12 (±3) months from switch.

Statistical Analyses: Standard **survival analysis** (Kaplan-Meier curves (KM) and log-rank test), the probability of different endpoints has been estimated at 1-year from BIC/FTC/TAF start according to the different exposures of interest.

Unadjusted and adjusted hazard ratios (HR) of the primary endpoint TF and of TD, TDT, TDS and VF have been estimated by fitting **Cox regression models** according to main exposures of interest

RESULTS

1237 PLWH included: 544 (44.0%) >50 years, 229 (18.5%) female, 95 (5.7%) switching from NNRTIs (of whom 47 switching from EFV). Patients' characteristics are shown in **Table1**

Table1 – Patients' Characteristics

	ART-experienced VS (N=1237)	
Italian, n(%)	1043	84.3
Ethnicity, Caucasian, n(%)	1102	89.1
Gender, Female, n(%)	229	18.5
Year of BIC start, median (IQR)	2019	2019-2020
Year cART start, median (IQR)	2015	2011-2017
Age, years, median (IQR)	47	39-55
Age, >50 years, n(%)	544	43.98
Mode of HIV Transmission, n(%)		
Heterosexual	456	36.86
IVDU	100	8.08
MSM	622	50.28
Other/Unknown	59	4.77
HCVAb positive status, n(%)	129	10.43
HBsAg positive status, n(%)	49	3.96
AIDS, n(%)	203	16.41
CD4, cells/mmc, median (IQR)	702	505-928
CD4<350 cells/mmc, n(%)	140	11.3
CD4/CD8 ratio, median(IQR)	0.87	0.59-1.22
HIV-RNA, copies/mL, median (IQR)	0.30	0.00-1.38
LDL cholesterol, median (IQR)	120	100-145
HDL cholesterol, median (IQR)	49	41-58
Triglycerides, median (IQR)	116	83-168
Serum Glucose, median (IQR)	88	81-96
eGFR, CKD-EPI, ml/min, median (IQR)	89.5	77.2-101.8
Weight, kg, median (IQR)	74	66-82
BMI, Kg/m2, median (IQR)	24.2	22.2-26.9
Follow-up on BIC, years, median (IQR)	1.37	0.97-1.67
Previous ART-regimen		
INSTI-based	1061	85.77
NNRTI-based	95	7.68
PI-based	62	5.01
Other	19	1.54

Primary Endpoint TF

112 TF occurred (9.1%, 14 VF and 98 TD). The 1-year probability of TF was 4.6% (95%CI 3.5,6.1), subgroups probabilities in **Table 2**

Table 2- KM 1-yr cumulative probability of TF overall and in the different groups

	1-yr cum. probability (95%CI)	log-rank p
Treatment Failure Overall	4.6% (3.5,6.1)	.
Age<50 years	4.8% (3.3,6.7)	0.103
Age>=50 years	4.5% (3.0,6.7)	
Female	7.5% (4.7,12.0)	0.009
Male	4.0% (2.9,5.5)	
Previous regimen NNRTIs	5.8% (2.5,13.5)	0.166
Previous regimen non-NNRTIs	4.5% (3.4,6.0)	

In the adjusted Cox regression models, age ≥50 years and NNRTI class in the previous regimen were not with a higher risk of TF, while female had a 2-fold higher risk of TF (Table 3).

Table 3- Hazard Ratios (HR) and Adjusted HR of TF from fitting 4 Cox regression models

ART-experienced	HR (95%CI)	p	AHR (95%CI)	p
Age, >=50 years (vs <50years)[1]	0.73 (0.50-1.0)	0.103	0.75 (0.50-1.12)	0.163
Gender, Female (vs. male)[2]	1.72 (1.13-2.62)	0.011	2.01 (1.17-3.44)	0.011
Previous NNRTI-based regimen (vs non-NNRTI)[3]	0.56 (0.25-1.28)	0.172	0.63 (0.27-1.44)	0.272

[1]AHR adjusted for nationality and calendar year first ART; [2]AHR adjusted for nationality; [3]adjusted for age, nationality, HDL, calendar year ART;

After excluding 6 **TD for pregnancy** as events, TF risk in Females was attenuated to **aHR 1.63** (95%CI 0.93,2.90).

Secondary Endpoints

Overall 15 VF and 100 TD (8.1%) occurred: 41 simplifications (3.3%), 30 toxicity/intolerance (2.4%), 3 failures (0.2%), 3 patient's decision (0.2%) and 23 (1.9%) other reasons (including 6 pregnancies). KM 1-yr cumulative probabilities are shown in **Table 4**.

Table 4- KM 1-yr cumulative probability of TD, TD toxicity/intolerance and VF

	1,yr cum. probability (95%CI)
Treatment Discontinuation	4.1% (3.1-5.5)
Treatment Discontinuation for toxicity/intolerance	2.6% (1.8-3.7)
Virological Failure	0.7% (0.3-1.4)

Mean CD4 increase at 1-year was +36 cells/mmc (95%CI 22,51; p<0.001)

Mean CD4/CD8 ratio change was +0.06% (95%CI 0.04,0.08; p<0.001).

Weight change at 1-year among 232 PLWH was +1.9kg (95%CI 1.1,2.7; p<0.001) with a greater increase in PLWH with previous NNRTIs regimen +2.8 kg (95%CI 0.15-5.5; p<0.001), despite not statistical significance compared to non-NNRTI based regimen (p=0.555)

CONCLUSIONS

- **BIC/FTC/TAF as switch strategy demonstrated high effectiveness in real-life with 4.6% TF and 0.7% VF at 1-year.**
- **Higher risk of TF in women seems mainly related to discontinuation of BIC/FTC/TAF for pregnancy concerns.**
- **4.1% of TD at 1-year, main cause of discontinuation was simplification**

Limits

- **These data should be confirmed with long-term follow-up**
- **Few numbers on weight at 12 (±3) months from switch**

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