EFFECTIVENESS OF BICTEGRAVIR/EMTRICITABINE/TENOFOVIR ALAFENAMIDE (BIC/FTC/TAF) IN ART-NAIVE PATIENTS: REAL-WORLD DATA FROM THE ICONA COHORT

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BACKGROUND

Some **key populations** among ART-naïve are characterized by sub-optimal response to ART:

53% of new HIV diagnoses in Europe are **late presenters**, usually at higher risk of clinical progression and treatment failure

Proportion of people living with HIV (PLWH) **≥50 years** at HIV diagnosis increased in recent years: older PLWH had more comorbidities, polypharmacy and are prone to drug-drug interaction

Limited RCT-based evidence is available to guide the choice of therapy for **women,** characterized by different PK of ART and higher adverse events compared to men

Despite the remarkable results in the subgroups analysis, key vulnerable population as *female*, *older PLWH* and *subjects with low CD4* are largely under **underrepresented** in BIC registrational RCT

AIM

Evaluate in real-life setting the effectiveness and tolerability of BIC/FTC/TAF in ART-Naïve focusing on specific key-populations (female, older, late presenter, advanced HIV disease)

STUDY DESIGN AND METHODS

Study Design: Observational study including ART-naïve PLWH from Icona Cohort who started BIC/FTC/TAF from Jun2016 to Dec2021.

Exposure of interest:
(1) Age (≥50 years old);
(2) Sex (Female);
(3) Late presenters (CD4<350 cell/mm3 or AIDS);
(4) Advanced HIV disease (CD4<200 cell/mm3 or AIDS);

Primary Endpoint: Time to **treatment failure** (TF) i.e. virological failure (VF: 2 HIV,RNA>200 copies/ml or 1 >1000 copies/ml >6 months from start) 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** (intention to treat); **(4)** Changes in **CD4**, **CD4/CD8** and **weight** at 12 (±3) months from start.

Statistical Analyses: Standard **survival analysis** (Kaplan-Meier curves 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

416 ART-naïve included (17.5% female, 29.8% ≥50 years, 58.2% late presenters, 40.6% Advanced HIV disease). Patients' characteristics shown in **Table1**

Table1- Patients' Characteristics

	ART-naive N=416	
Italian, n(%)	239	70.43
Ethnicity, Caucasian, n(%)	329	79.1
Gender, Female, n(%)	73	17.5
Year of BIC start, median (IQR)	2020	2020-2021
Age, years, median (IQR)	42	32,52
Age, >50 years, n(%)	124	29.81
Mode of HIV Transmission, n(%)		
Heterosexual	172	41.35
IVDU	19	4.57
MSM	188	45.19
Other/Unknown	37	8.89
HCVAb positive status, n(%)	20	4.81
HBsAg positive status, n(%)	11	2.64
AIDS, n(%)	59	14.18
CD4, cells/mmc, median (IQR)	280	87,495
CD4<200 cells/mmc, n(%)	165	39.66
CD4<350 cells/mmc, n(%)	241	57.9
CD4/CD8 ratio, median (IQR)	0.33	0.14-0.58
HIV,RNA, log_{10} copies/mL, median (IQR)	5.02	4.39-5.60
LDL cholesterol, median (IQR)	102	80,124
HDL cholesterol, median (IQR)	40	33,49
Serum glucose, median (IQR)	87	80,93
eGFR, CKD-EPI, ml/min, median (IQR)	106.4	92.2-117.5
Weight, kg, median (IQR)	70	60,78
BMI, Kg/m², median (IQR)	23	20.6-24.7
Follow-up on BIC, years, median (IQR)	0.83	0.44,1.22

Primary Endpoint TF

51 TF occurred (12.2%, 7 VF and 44 TD). The 1-year KM estimated probability of TF overall and by subgroups are shown 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	11.0% (7.9,15.1)	
Age<50 years	9.2% (6.1,13.8)	0.397
Age>=50 years	14.9% (8.9,24.3)	
Female	9.4% (4.3,19.9)	0.536
Male	11.3% (7.9,16.0)	
Non late presenters	9.4% (5.6,15.5)	0.514
Late presenters	12.1% (8.0,18.2)	
Non advanced HIV disease	8.7% (5.4,13.8)	0.263
Advanced HIV disease	14.3% (9.2,21.8)	

In the Cox regression models adjusted for confounders, none of the groups analysed had a higher risk of TF **(Table 3)**

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

	HR (95%CI)	p	AHR (95%CI)	p
Age, >=50 years (vs <50 years)[1]	1.28 (0.72,2.26)	0.398	1.36 (0.74,2.48)	0.323
Gender, male (vs. Female)[2]	1.28 (0.58,2.85)	0.537	1.37 (0.61,3.05)	0.443
Late presenters (vs. Non-late presenters)[3]	1.21 (0.68,2.12)	0.514	1.23 (0.68,2.21)	0.496
Advanced HIV disease (vs. Non-advanced)[4]	1.37 (0.78,2.39)	0.265	1.46 (0.81,2.63)	0.208

[1] adjusted for nationality and mode of HIV transmission; [2]adjusted for nationality; [3] adjusted for gender, mode of HIV transmission, HIV,RNA and nationality; [4] adjusted for gender, mode of HIV transmission, HIV,RNA and nationality

Secondary Endpoints

45 TD occurred (10.8%): 16 toxicity/intolerance (3.8%), 15 simplification (3.6%), 4 failures (1.0%), 1 patient's decision (0.2%) and 9 other reasons (2.2%).

Overall **7 VF** occurred (2.6%), 6 with a single HIV-RNA >1000 copies/ml and 1 with confirmed 2 HIV-RNA >50 copies/ml.

KM 1-yr 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	9.9% (7.0, 13.8)
Treatment Discontinuation for toxicity/intolerance	3.9% (2.3, 6.7)
Virological Failure	2.1% (0.8, 5.5)

Mean CD4 increase at 1-year was +244 cells/mmc (95%CI 216, 271; p<0.001).

Mean CD4/CD8 change was +0.09% (95%CI 0.15,0.32; p=0.476).

Weight change among 43 PLWH included was +5.2kg (95%CI 3.3,6.9; p<0.001) with greater increase for Advanced HIV diseases +7.2 kg (95%CI 4.3,10.0; p<0.001).

Table 5- Mean weight changes after 1-year

	1-yr mean weight change, kg	P-value
Overall	5.2 (3.3,6.9)	<0.001
Non late presenters	3.5 (1.5,5.5)	0.002
Late presenters	5.8 (3.3,8.3)	0.001
Non advanced disease	2.8 (0.9,4.6)	0.005
Advanced diseases	7.2 (4.3,10.0)	0.001
Female	4.1 (,1.0,9.1)	0.097
Male	5.3 (3.3,7.4)	<0.001
Age<50 yrs	4.9 (2.3,7.6)	0.008
Age>=50 yrs	5.4 (3.2,7.7)	0.001

CONCLUSIONS

- **First line therapy with BIC/FTC/TAF demonstrated high effectiveness at 1-year 11.0% TF, 2.1% VF and +244 cells CD4/mm3, including in populations usually at risk of lower response (LP and AD).**
- **TD was mainly driven by toxicity/intolerance (3.8%) and simplification (3.6%).**

Limits

- **Other key populations (e.g. migrants, PWID) have not yet been investigated**
- **Longer follow-up needed to confirm these results**

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