Poster
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Starting or Switching to Bictegravir/Emtricitabine/ Tenofovir Alafenamide (B/F/TAF) in Clinical Practice: Pooled 12-month Results from the Global BICSTaR Study

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Background

- The **BIC**tegravir **S**ingle **Ta**blet **R**egimen (BICSTaR) study is an ongoing, multi-country, observational cohort study planned to enrol at least 1400 people living with HIV (PLWH) initiating B/F/TAF and followed for 2 years.
- We evaluated the effectiveness, safety, and tolerability of B/F/TAF in routine clinical practice in antiretroviral (ART)-naïve (TN) and ART-experienced (TE) PLWH.
- We present 12-month data from sites in Germany, Canada, France, and the Netherlands (BICSTaR Europe [GS-EU-380-4472]/ BICSTaR Canada [GS-CA-380-4574]).

Methods

- This analysis includes pooled data from 513 participants who had a baseline and Month 12 (M12) visit or who discontinued the study at the time of data cut-off (March 2020).
- M12 study outcomes included:
  - HIV-1 RNA <50 copies (cp)/mL using a Missing=Excluded (M=E) approach.
    - Missing data were excluded, such that only HIV-1 RNA data collected within the M12 time window, while on study treatment, were analysed.
  - Treatment persistence (% participants still on B/F/TAF).
  - Drug-related adverse events, weight, and body mass index (BMI) changes.
- Multivariate logistic regression analysis of risk factors associated with B/F/TAF effectiveness and relative weight increase of >5% from baseline at M12 were explored.

Results

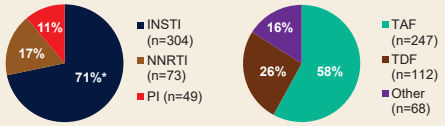
- Baseline characteristics are shown in **Table 1** and prior ART regimens in **Figure 1**.

Table 1. Baseline characteristics

		TN (n=84)	TE (n=429)
Demographics	Male, n (%)	76 (91)	392 (91)
	Age, years, median (Q1–Q3)	38 (29–48)	49 (40–56)
	Age ≥50 years, n (%)	20 (24)	209 (49)
	White, n (%)	71 (85)	387 (90)
Ongoing comorbidities	None, n (%)	41 (49)	108 (25)
	1–2, n (%)	25 (30)	168 (39)
	≥3, n (%)	18 (21)	153 (36)
	Neuropsychiatric disorder[a], n (%)	16 (19)	122 (28)
	Hyperlipidaemia, n (%)	7 (8)	87 (20)
	Hypertension, n (%)	5 (6)	87 (20)
HIV-related characteristics	HIV-1 RNA, log_{10} cp/mL, median (Q1, Q3)	4.77 (3.94, 5.18)	1.59 (1.28, 1.59)
	<50 cp/mL, n (%)	0 (0)	362/393 (92)
	>100,000 cp/mL, n (%)	30/82 (37)	2/393 (1)
	CD4 count[b], cells/µL, median (Q1, Q3)	427 (244, 581)	668 (455, 877)
	CD4 <200 cells/µL, %	21	4
	CD4 <350 cells/µL, %	38	14
	CD4/CD8 ratio, median (Q1, Q3)	0.4 (0.3, 0.6)	0.8 (0.6, 1.2)
	≥1 major mutation[c], n (%)	7 (9)	36 (9)
	PI / NNRTI / NRTI / INSTI, n (%)	2 (2) / 5 (6) / 1 (1) / 0	12 (3) / 20 (5) / 16 (4) / 0

[a]Most common neuropsychiatric disorders at baseline were insomnia (2.9%), depression (1.6%), and anxiety (1.4%).
[b]Sample size of 78 for TN and 382 for TE.
[c]A participant could have >1 mutation/substitution.
INSTI, integrase strand transfer inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleo[s/t]ide reverse transcriptase inhibitor; PI, protease inhibitor; Q, quartile.

Figure 1. Prior ART regimens (n=427)

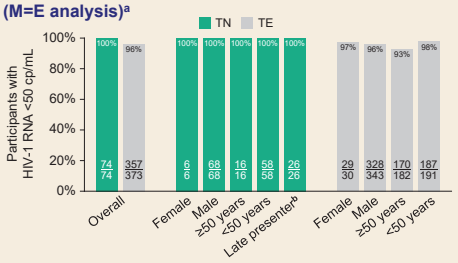


*DTG, 34%; EVG, 24%; RAL, 14%; 1 participant without third agent.
DTG, dolutegravir; EVG, elvitegravir; RAL, raltegravir; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.

- Effectiveness results are shown in **Figure 2**.
- HIV-1 RNA was <200 cp/mL in 370/373 (99%) TE participants.
  - One participant with suboptimal adherence had a viral load (VL) of 4100 cp/mL at M12 (no major resistance mutations reported).
    - VL was 240, 18,000, and 3700 cp/mL at BL, M3, and M6, respectively.
  - Two participants had VL <250 cp/mL.

Results (cont'd)

Figure 2. Effectiveness of B/F/TAF at Month 12 (M=E analysis)[a]



[a]Missing=Excluded analysis. Denominator reflects number of participants with available HIV-1 RNA data analysed within the time window.
[b]Defined as CD4 <350 cells/µL and/or ≥1 AIDS-defining event at baseline.

- Median CD4 change (Q1, Q3) at M12 in TN and TE were +242 (119, 453) and +22 (−71, 11) cells/µL, respectively.
- Median CD4/CD8 ratio changes (Q1, Q3) at M12 in TN and TE were +0.3 (0.2, 0.4) and +0.03 (−0.13, 0.12), respectively.
- Having a neuropsychiatric disorder at baseline (n=140) was associated with not achieving viral suppression at M12 (VL <50 cp/mL); adjusted odds ratio 0.26 (95% confidence interval 0.09–0.73; p=0.01).
  - Multivariate logistic regression model included the following covariates: gender, age, baseline CDC stage, ongoing neuropsychiatric disorders, ongoing metabolic syndrome, and number of comorbidities/coinfections per patient ongoing at B/F/TAF initiation.
- Outcomes in participants with evidence of pre-existing genotype resistance-associated mutations at baseline are shown in **Table 2**.
- No major resistance substitutions to the components of B/F/TAF emerged.

Table 2. Virologic outcomes in participants with evidence of pre-existing genotype resistance-associated mutations at baseline

Baseline mutation	N (%)	TN or TE	Viraemic at BL, n (%)	HIV-1 RNA <50 cp/mL at M12, n (%)
M184V/I[a]	8 (1.6)	TE	0 (0)	8 (100)
K65R	1 (0.2)	TN	1 (100)	1 (100)

[a]Alone or in combination with ≥1 TAMs; TAMs included M41L (n=1) and D67N (n=2)
TAM, thymidine analogue mutation.

- Persistence is shown in **Figure 3** and reasons for discontinuation in **Table 3**.

Figure 3. Persistence of B/F/TAF at Month 12

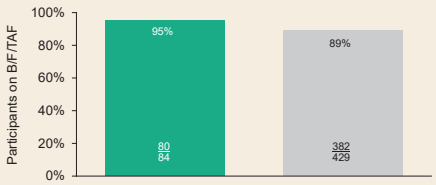


Table 3. Reasons for B/F/TAF discontinuations to M12

Discontinuations, n (%)	TN (n=84)	TE (n=429)
Any discontinuations	**4 (4.7)**	**47 (11.0)**
Pregnancy	0	1 (0.2)
Participant decision	0	3 (0.7)
Death[a]	0	3 (0.7)
Lack of efficacy	0	3 (0.7)
Investigator's discretion	0	4 (0.9)
AE[b]	4 (4.7)	33 (7.7)

[a]Deaths were unrelated to B/F/TAF and included sepsis (n=1), brain metastasis (n=1), and unknown reason (n=1).
[b]Most common AEs that led to discontinuation were fatigue (TN, n=1; TE, n=5), weight increase (TN, n=1; TE, n=5), and depression (TE, n=4).
AE, adverse event.

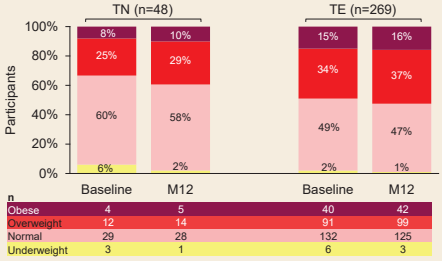
- Drug-related AEs are reported in **Table 4**.
- Serious DRAEs were rare (0.4%; n=2 cases of depression in TE participants).
  - Both led to B/F/TAF discontinuation (1 had prior history of depression).
- No discontinuations due to renal, hepatic, or bone DRAEs.
- Change in World Health Organization BMI category is shown in **Figure 4**.
- Median (Q1–Q3) BMI change at M12: TN +0.8 kg/m^2 (0.1 to 1.9); TE +0.3 kg/m^2 (−0.3 to 1.0).
- Median (Q1–Q3) weight change at M12: TN +2.5 kg (0.5 to 6.3);TE +0.9 kg (−1.0 to 3.0).
- In a multivariate analysis, no risk factors were identified that were with a relative weight increase of >5% from baseline at M12.
  - Multivariate logistic regression model including covariates gender, age, baseline BMI, comorbidities, and regimen prior to B/F/TAF initiation.

Table 4. DRAEs reported in ≥1% of all participants

n (%)	All (n=513)	TN (n=84)	TE (n=429)
Any DRAE	**76 (15)**	**12 (14)**	**64 (15)**
Nausea	1 (1.4)	1 (1.2)	6 (1.4)
Diarrhoea	6 (1.2)	0	6 (1.4)
Depression	8 (1.6)	1 (1.2)	7 (1.6)
Weight increased	14 (2.7)	2 (2)	12 (3)
Fatigue	8 (1.6)	1 (1.2)	7 (1.6)
DRAE discontinuations[a]	**32 (6.2)**	**3 (3.6)**	**29 (6.8)**

[a]Most common DRAEs that led to discontinuation were fatigue (TN, n=1; TE, n=5), weight increase TN, n=1; TE, n=5), and depression (TE, n=4).

Figure 4. BMI categories at baseline and M12[a,b]



[a]Subset of participants with baseline and M12 BMI data were included.
[b]BMI category according to the World Health Organization (underweight <18.5 kg/m^2; normal, 18.5–24.9 kg/m^2; overweight, 25.0–29.9 kg/m^2; obese, ≥30 kg/m^2).

Conclusions

- B/F/TAF use in this real-world clinical cohort was associated with high prevalence of effectiveness in PLWH regardless of gender, older age, or low CD4 count.
- B/F/TAF showed high persistence and was well tolerated, with no discontinuations due to drug-related renal, hepatic, or bone events.
- A few participants with pre-existing NRTI (M184V/I) maintained virologic suppression when switched to B/F/TAF.
- No resistance-associated mutations emerged to the components of B/F/TAF.
- These data support the real-world effectiveness, safety, and persistence of B/F/TAF in treatment-naïve and treatment-experienced PLWH who were characterised by a high prevalence of comorbidities at baseline.

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Disclosures

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