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The BICSTaR prospective cohort: Real-world effectiveness, safety and tolerability of bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) in routine clinical practice in people living with HIV (PLWH)

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Background

- Safety, efficacy, and lack of emergent resistance have been demonstrated with B/F/TAF in randomized controlled trials.[1–5]
- Bictegravir Single Tablet Regimen (BICSTaR; GS-EU-380-4472/GS-CA-380-4574) is a 2-year, multi-country, prospective, observational cohort study in antiretroviral treatment (ART)-naïve (TN) and ART-experienced (TE) PLWH initiating B/F/TAF.

Methods

- To evaluate the effectiveness, safety and tolerability of B/F/TAF in routine clinical practice using a 6-month data cut (October 2019) of BICSTaR.
- Participants with a baseline (BL) and month 6 (M6) visit, or participants who had discontinued the study at the time of the data cut-off, were included.
- Study outcomes included:
  - HIV-1 RNA <50 copies/mL (cp/mL) at M6 (the primary analysis excluded missing data, such that only HIV-1 RNA data collected within the M6 time window, while on study treatment, were analyzed); Missing=Excluded (M=E) analysis.
  - Treatment persistence (% participants still on B/F/TAF at M6).
  - Drug-related (DR) adverse events (AEs), and weight change.

Results

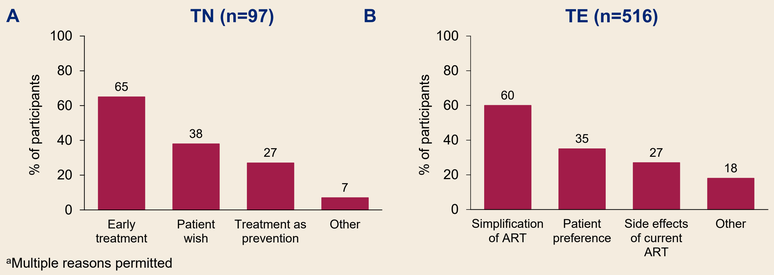
Study population

- 613 PLWH who initiated B/F/TAF after June 2018 were included in the analysis (from Germany, Canada, France, Netherlands and Ireland). **Table 1** presents the baseline characteristics.

Treatment persistence and discontinuations

- Participants primarily started B/F/TAF as early treatment, or switched to B/F/TAF for treatment simplification (**Figure 1**).
- Treatment persistence was high: 585/613 (95%) participants were still on B/F/TAF at M6 (TN, 96/97 [99%]; TE, 489/516 [95%]).
  - 28 (5%) participants (1 TN; 27 TE) discontinued B/F/TAF prior to M6 (**Table 2**).

Figure 1. Reasons[a] for (A) initiating or (B) switching to B/F/TAF



[a]Multiple reasons permitted

Table 2. Reasons for B/F/TAF discontinuation within 6 months of treatment initiation

n (%)	TN (n=97)	TE (n=516)
Lack of efficacy	—	1 (0.2)
Investigator's discretion	—	2 (0.4)
Participant decision	—	3 (0.6)
Adverse event[a]	1 (1)	21 (4)

[a]Most common AEs were: headache, n=6; nausea, n=5; fatigue, n=3; depression, n=3; sleep disorder, n=3; myalgia, n=3; rash, n=3; diarrhea, n=3; nightmare, n=2; arthralgia, n=2

References

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2. Kityo C, et al. J Acquir Immune Defic Syndr 2019; 82: 321–8
3. Molina JM, et al. Lancet HIV 2018; 5: e357–e65
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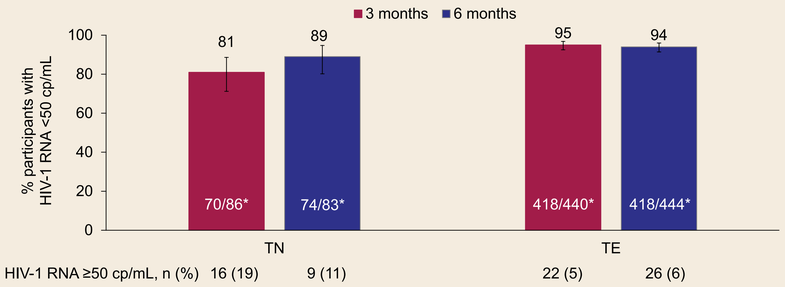
5. Wohl DA, et al. Lancet HIV 2019; 6: e355–e63.

Effectiveness

Figure 2. Participants with HIV-1 RNA <50 cp/mL at M3 and M6 (M=E analysis)



*Denominator reflects number of participants with available HIV-1 RNA data analysed within the time window

- At M6, HIV-1 RNA was <200 cp/mL in 517/527 (98%) participants (TN, 80/83 [96%]; TE, 437/444 [98%]).
- Median (Q1–Q3) CD4 cell count increased from 427 cells/μL (244–534) at BL to 672 cells/μL (480–798) at M6 in TN participants and remained stable in TE participants (BL: 670 cells/μL [457–880]; M6: 670 cells/μL [462–861]).

Table 1. Baseline characteristics and comorbidities/comedications

Demographics	TN (n=97)	TE (n=516)
Male sex, n (%)	87 (90)	465 (90)
Age, years, median (Q1–Q3)	38 (29–48)	49 (39–56)
Age ≥50 years, n (%)	23 (24)	242 (47)
Weight, kg, median (Q1–Q3)	70 (63–82)[a]	77 (68–87)[b]
Race, n (%)		
White	76 (78)	446 (86)
Black	8 (8)	31 (6)
HIV-related characteristics	**TN (n=97)**	**TE (n=516)**
Prior ART regimen, n (%)[c]		
INSTI / NNRTI / PI	—	354 (69) / 84 (16) / 64 (12)
TAF-based	—	264 (51)
DTG-based	—	171 (33)
TDF-based	—	160 (31)
Number of previous ART regimens, median (Q1–Q3)	—	2 (1–4)
Time from diagnosis to B/F/TAF, median (Q1–Q3)	15.5 days (7–46)	—
HIV-1 RNA, $\log_{10}$ cp/mL, median (Q1–Q3)	4.7 (3.9–5.2)[d]	1.6 (1.3–1.6)[e]
HIV-1 RNA >100,000 cp/mL, n (%)	33 (35)	3 (0.6)
HIV-1 RNA <50 cp/mL, n (%)	1 (1)	431 (92)
CD4 count, cells/μL, median (Q1–Q3)	427 (244–534)[f]	670 (457–880)[g]
CD4 <200 cells/μL, n (%)	20 (22)[f]	18 (3)[g]
CD4 <350 cells/μL and/or CDC Stage C, n (%)	35 (39)	—
CDC Stage C (AIDS), n (%)	8 (8)[h]	69 (14)[i]
History of virological failure, n (%)	—	45 (9)
Available genotype test at baseline, n (%)	60 (62)	251 (49)
At least one ART-related mutation/substitution[j], n (%)	29 (32)[k]	155 (31)[l]
PI	21 (22)	124 (24)
NNRTI	16 (17)	66 (13)
NRTI	2 (2)	55 (11)
INSTI	5 (6)	7 (2)
Ongoing comorbidities/comedication, n (%)	**TN (n=97)**	**TE (n=516)**
Any comorbidity	50 (52)	384 (75)
0	47 (49)	130 (25)
1–3	37 (38)	272 (53)
≥4	13 (13)	112 (22)
Category[c] (in ≥10% participants)		
Neuropsychiatric	15 (16)	135 (26)
Hypertension	7 (7)	103 (20)
Hyperlipidemia	7 (7)	103 (20)
Infections	13 (13)	62 (12)
Gastrointestinal disorder	9 (9)	61 (12)
Cardiovascular	6 (6)	55 (11)
Any comedication received	42 (46)	311 (61)

[a]n=84; [b]n=449; [c]Participants may be counted more than once; [d]n=95; [e]n=469; [f]n=89; [g]n=449; [h]n=96; [i]n=507; [j]A participant could have more than one mutation/substitution (the majority were 'other' secondary mutations in n=139 [PI], n=61 [NNRTI], n=42 [NRTI], n=11 [INSTI]); [k]n=60; [l]n=251; CDC, Center for Disease Control and Prevention; DTG, dolutegravir; INSTI, integrase strand transfer inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleos(t)ide reverse transcriptase inhibitor; PI, protease inhibitor; Q, quartile; TDF, tenofovir disoproxil fumarate

Table 3. Virologic outcomes in participants with evidence of pre-existing resistance-associated mutations at baseline

BL mutation	Class	n (%)	TN or TE	Viremic at BL, n/N	Outcome HIV-1 RNA <50 cp/mL, n (%)
M184V/I[a]	NRTI	14 (2)	TE	0/14	13 (93)[b] (M6)
K65R	NRTI	1 (0.2)	TN	1/1	1 (100)[c] (M12)
G140S	INSTI	1 (0.2)	TE	0/1	1 (100) (M6)

[a]Alone or in combination with one or more thymidine analog mutation; [b]One participant had missing HIV-1 RNA at M6; [c]Missing viral load at M6

- At M6, 20 participants had an available post-BL genotype test.
  - No major resistance substitutions to the components of B/F/TAF emerged.

Safety

- 52% (55% TN, 52% TE) and 5% (9% TN, 5% TE) of participants reported an AE or serious AE (SAE), respectively.
- DRAEs (**Table 4**) and DRSAEs were reported in 67 (11%) and 3 (0.5%) participants, respectively.
  - DRSAEs: depression (n=2 [1 with a prior history]) and nausea (n=1) (B/F/TAF discontinued in each case).
- DRAEs led to B/F/TAF discontinuation in 19 (3%) participants.
  - Related to ≥1 psychiatric symptom in 9/19 (of whom 5 had a prior history of neuropsychiatric symptoms).
- There were no B/F/TAF discontinuations due to renal or bone DRAEs.
- Of 398 participants with weight data at BL and M6, the median (Q1, Q3) weight change from baseline was +3.0 kg (0.0, 6.0) in TN and +0.6 kg (−0.8, 2.6) in TE participants.
  - DR weight gain (>5 kg) led to B/F/TAF discontinuation in 1 TE participant.

Table 4. DRAEs reported in ≥1% of participants

n (%)	All Participants N=613	TN N=97	TE N=516
Diarrhea	7 (1)	0	7 (1)
Nausea	7 (1)	1 (1)	6 (1)
Depression	8 (1)	1 (1)	7 (1)
Weight increased	11 (2)	2 (2)	9 (2)
Fatigue	7 (1)	1 (1)	6 (1)

Conclusions

- A large proportion of participants achieved HIV-1 RNA <50 cp/mL at M6 with no emergence of major mutations that resulted in resistance to B/F/TAF.
- There were few B/F/TAF discontinuations overall and no discontinuations due to drug-related renal or bone events.
- These early data support the real-world effectiveness, safety and persistence of B/F/TAF in treatment-naïve and treatment-experienced PLWH who were characterized by a high prevalence of comorbidities at baseline.

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Disclosures

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