LONGER-TERM (3-YEAR) EFFECTIVENESS AND SAFETY OF B/F/TAF FOR THE TREATMENT OF HIV IN THE GERMAN BICSTaR COHORT

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Introduction

BICSTaR is a prospective, ongoing, observational cohort study evaluating the effectiveness and safety of B/F/TAF in clinical practice treatment-naïve (TN) and -experienced (TE) people living with HIV (PLWH).

Originally planned as a two-year study, BICSTaR has been extended for additional 3 years to a total of 5 years in Germany, France and Canada.

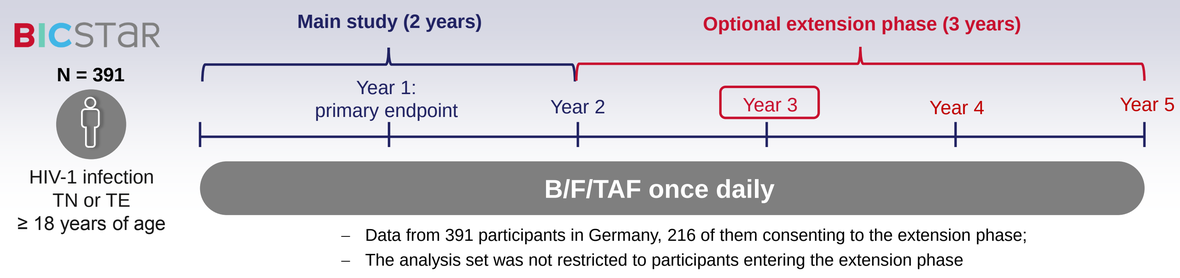
Here we present the outcomes of the German BICSTaR cohort up to year 3.

Methods

This 3-year analysis included all PLWH receiving B/F/TAF in clinical practice from 20 German sites. Data were collected from June 2018 until August 2022. Participants were included according to the SmPC (summary of product characteristics). The analysis included both PLWH that entered the extension phase and PLWH that did not.

Virological outcomes (HIV-1 RNA <50 cp/mL, loss-to-follow-up/missing/discontinued=excluded [M = E] and HIV-1 RNA <50 cp/mL, discontinued=failure [D = F] analyses), **immunological outcomes**, **B/F/TAF discontinuations**, non-serious/serious drug-related adverse events (**DRAEs/DRSAEs**) coded by MedDRA [Medical Dictionary for Regulatory Activities] terms using system organ class [SOC] and preferred terms [PT])**, and weight changes** were collected. Parametric and non-parametric statistical tests were performed to compare subgroups, as appropriate.

Study design



– Data from 391 participants in Germany, 216 of them consenting to the extension phase;
– The analysis set was not restricted to participants entering the extension phase

Participants – Baseline Characteristics

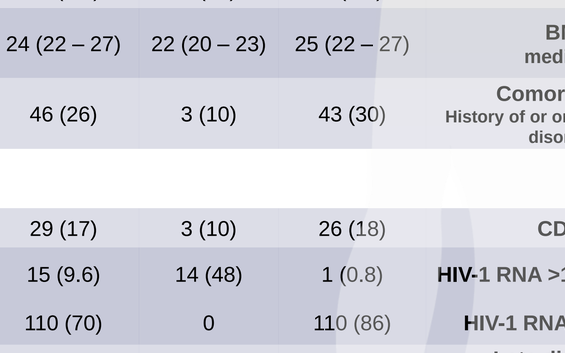
PLWH not in extension phase			Total population* N=391	PLWH in extension phase		
Overall N=175	TN N=30	TE N=145	**Baseline characteristics** *(Data as observed)*	Overall N=216	TN N=36	TE N=180
15 (9)	4 (13)	11 (8)	**Female, n (%)**	13 (6)	3 (8)	10 (6)
45 (35 – 53)	36 (30 – 48)	47 (37 – 54)	**Age at B/F/TAF initiation, years, median (Q1 – Q3)**	47 (38 – 54)	39 (30 – 47)	48 (40 – 55)
62 (35)	7 (23)	55 (38)	**Age ≥50 years, n (%)**	87 (40)	8 (22)	79 (44)
12 (6.9)	3 (10)	9 (6.2)	**Age ≥65 years, n (%)**	5 (6.9)	1 (2.8)	4 (2.2)
157 (90)	24 (80)	133 (92)	**Race: White, n (%)**	206 (95)	36 (100)	170 (94)
8 (4.6)	2 (6.7)	6 (4.1)	**Black, n (%)**	6 (2.8)	0	6 (3.3)
10 (5.7)	4 (13)	6 (4.1)	**Other, n (%)**	4 (1.9)	0	4 (2.2)
24 (22 – 27)	22 (20 – 23)	25 (22 – 27)	**BMI (kg/m²) median (Q1 – Q3)**	24 (22 – 27)	24 (22 – 27)	24 (22 – 27)
46 (26)	3 (10)	43 (30)	**Comorbidities, n (%):** History of or ongoing neuropsychiatric disorders ongoing	76 (35)	11 (31)	65 (36)
29 (17)	3 (10)	26 (18)	**CDC Stage C**	30 (14)	1 (2.8)	29 (16)
15 (9.6)	14 (48)	1 (0.8)	**HIV-1 RNA >100,000 cp/mL, n (%)**	10 (5.1)	9 (25)	1 (0.6)
110 (70)	0	110 (86)	**HIV-1 RNA <50 cp/mL, n (%)**	153 (77)	0	153 (94)
15 (54)	15 (54)	n.a.	**Late diagnosis, n (%): CD4 <350 cells/µL and/or at least one AIDS def. event**	10 (29)	10 (29)	n.a.
36 (23)	14 (52)	22 (17)	**CD4 <350 cells/µL, n (%)**	31 (16)	10 (29)	21 (13)
18 (12)	8 (30)	10 (7.9)	**CD4 <200 cells/µL, n (%)**	9 (4.6)	5 (15)	4 (2.5)
			Previous ART, n (%) – taken immediately prior to B/F/TAF			
n.a.	n.a.	87 (60)	TAF-based regimen	n.a.	n.a.	133 (74)
n.a.	n.a.	36 (25)	TDF-based regimen	n.a.	n.a.	29 (16)
n.a.	n.a.	54 (38)	Multi-tablet regimen	n.a.	n.a.	81 (45)

*Information on the total population and further detail information see supplement; n.a., not applicable

Results – Effectiveness

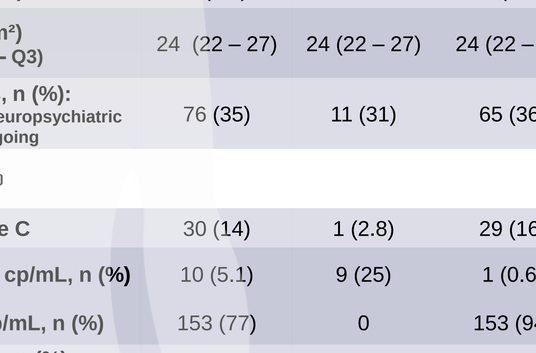
Virological Effectiveness

HIV-1 RNA <50 cp/mL (M = E analysis)



n/N (TN)	0/65	47/55	58/58	52/54	32/33
n/N (TE)	263/290	253/275	264/276	225/243	170/175

HIV-1 RNA <50 cp/mL (D = F analysis)



n/N (TN)	0/66	47/56	58/62	52/61	32/41
n/N (TE)	263/325	253/288	264/305	225/294	170/231

No treatment-emergent resistance to the components of B/F/TAF was documented through 3 years.

Overall, in 6 participants HIV-1 RNA level was ≥50 cp/mL at year 3.

Abbreviations: M = E, lost-to-follow-up/missing/discontinued = excluded (only participants with available HIV-1 RNA levels)
D = F, B/F/TAF discontinued for any reason = failure, BL = baseline; M = month

Immunological Effectiveness

	N=	Baseline CD4 cell count, cells/µL*	N=	3 years CD4 cell count, cells/µL*	N=	Baseline CD4/CD8 ratio*	N=	3 years CD4/CD8 ratio*
TN: mean (SD) median (Q1 – Q3)	61	468 (311) 437 (249 – 607)	33	866 (315) 879 (666 – 1009)	59	0.40 (0.25) 0.31 (0.22 – 0.54)	33	1.21 (0.76) 1.0 (0.75 – 1.40)
TE: mean (SD) median (Q1 – Q3)	290	714 (346) 699 (467 – 911)	165	814 (362) 772 (583 – 989)	259	0.90 (0.52) 0.8 (0.59 – 1.10)	156	1.02 (0.52) 0.96 (0.65 – 1.27)

* Data as observed

Increases in median CD4 cell counts and CD4/CD8 ratio were observed.

Results – Discontinuations

Discontinuations up to year 3

B/F/TAF discontinuations

N, %	TN (N=66)	TE (N=325)
B/F/TAF discontinuation	7 (10.6)	61 (18.8)
Reason for discontinuation:		
DRAE[1]	5 (7.6)	29 (8.9)
Pregnancy	0	1 (0.3)
Lack of efficacy	0	4 (1.2)
Participant decision	1 (1.5)	7 (2.2)
Investigator discretion	0	5 (1.5)
Death†	0	6 (1.8)
New treatment available	0	3 (0.9)
AE without drug relation	1 (1.5)	6 (1.8)

[1]DRAEs leading to discontinuation [MedDRA SOC terms (count of events, incl. PT terms)]:
- **TN**: Investigations (3, all weight increase), psychiatric disorder (1), general disorders and administration site conditions (1)
- **TE**: Investigations (11, incl. weight increase 9), psychiatric disorder (11, incl. depression 5), gastrointestinal disorder (7), general disorders and administration site conditions (4), infections and infestations (3), skin and subcutaneous tissue disorders (4), musculoskeletal and connective tissue disorders (2), nervous system disorders (2)

† Deaths were not related to B/F/TAF

Time to discontinuation

Median (Q1 – Q3)

n = 7	n = 61
12.6 (8.5 – 20.3) months	9.2 (4.0 – 14.8) months

Through 3 years of follow-up, 37 (9.5%) participants discontinued B/F/TAF due to DRAE (TN: 5/66, 7.6%; TE: 32[1]/325, 9.8%).

[1] In 3/32 participants another reason than DRAE for discontinuation was documented.

4 of 61 TE participants discontinued B/F/TAF prior to 3 years due to reasons related to effectiveness.
(last HIV-1 RNA values prior to/at discontinuation were 57 cp/mL (disc. after 298 days),131 cp/mL (275 days), 148 cp/mL (211 days), and 740 cp/mL (119 days)).

Results – Safety

Drug-related adverse events

Number (%) of participants

	Overall N=391	TN N=66	TE N=325
DRAEs	67 (17%)	13 (20%)	54 (17%)
DRSAEs[1]	2 (<1%)	0 (0%)	2 (< 1%)

Number of events

	Overall (N=391)	TN (N=66)	TE (N=325)
DRAEs	97	16	81
DRSAEs[1]	2	0	2
Most common DRAEs (≥4 events): N_{events} $(\%)_{participants}$			
Weight increase	18 (4.6)	5 (1.3)	13 (3.3)
Depression	10 (2.6)	1 (1.5)	9 (2.8)
Fatigue	7 (1.8)	1 (1.5)	6 (1.8)
Diarrhoea	5 (1.3)	0	5 (1.5)
Nausea	5 (1.3)	1 (1.5)	4 (1.2)
Pruritus	4 (1.0)	1 (1.5)	3 (<1)
Arthralgia	4 (1.0)	0	4 (1.2)
Flatulence	4 (1.0)	0	4 (1.2)

[1] DRSAEs (Serious drug-related adverse events) in two participants were depression (PT-term)

Weight – at baseline and at 3 years

Weight, kg *Median values (Q1 – Q3)*

	Baseline	3 years	Change from baseline
TN All pts with available data	N=57: 70 (65 – 82)	N=18: 76 (67 – 84)	
TN Pts with data at BL AND and 3 years	N=18: 74 (68 – 82)	N=18: 76 (67 – 84)	N=18: 2.5 (-1.0 – 6.5)
TE All pts with available data	N=268: 78 (69 – 88)	N=132: 81 (70 – 89)	
TE Pts with data at BL AND and 3 years	N=111: 78 (67 – 87)	N=111: 79 (69 – 88)	N=111: 2.1 (-0.4 – 5.0)
TE-TAF All pts with available data	N=181: 80 (69 – 89)	N=100: 82 (70 – 90)	
TE-TAF Pts with data at BL AND and 3 years	N=83: 78 (66 – 87)	N=83: 79 (68 – 87)	N=83: 2.0 (-0.6 – 5.0)
TE-TDF All pts with available data	N=51: 78 (67 – 85)	N=18: 78 (68 – 89)	
TE-TDF Pts with data at BL AND and 3 years	N=15: 74 (64 – 86)	N=15: 74 (65 – 89)	N=15: 2.8 (-0.4 – 5.2)

TE pts with TAF-based regimen prior to B/F/TAF

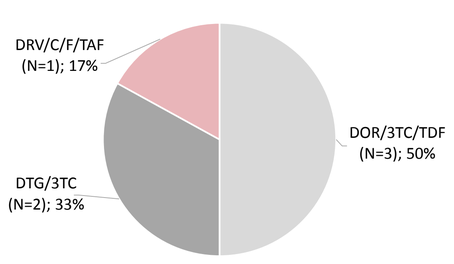
TE pts with TDF-based regimen prior to B/F/TAF

Data as observed at timepoints (based on frequency of weight measurements in clinical routine)

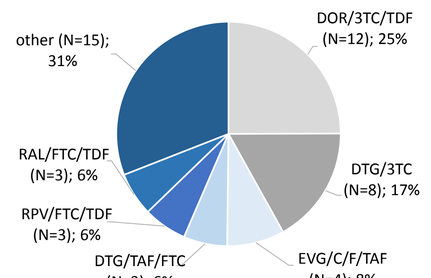
Antiretroviral therapy after discontinuation of B/F/TAF

Follow-up ART was available in 54 participants (6 TN and 48 TE).
Most common regimens (n≥3) are depicted below.

ART regimens in TN participants (N=6)



ART regimens in TE participants (N=48)



Conclusions

- This 3-year analysis of the German BICSTaR cohort demonstrated high virologic and immunological effectiveness of B/F/TAF in TN and TE PLWH in routine clinical practice.
- There was no evidence of resistance to the components of B/F/TAF.
- No new safety signals were detected during 3 years of observation, with <10% discontinuations due to drug-related AEs.

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Disclosures
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