Bictegravir/emtricitabina/tenofovir alafenamide: dati real-life da un centro italiano.

Bictegravir/emtricitabine/tenofovir alafenamide: Real World Data in an Italian setting.

Laura Labate[1,2], Lucia Preve[1], Lucia Taramasso[1], Elena Ricci[3], Giorgia Brucci[1,2], Sabrina Blanchi[1], Federica Centorrino[1], Matteo Bassetti[1,2], Antonio Di Biagio[1,2]

[1] IRCCS Ospedale Policlinico San Martino, Genoa, Italy.
[2] Department of Health's Sciences, University of Genoa, Italy.
[3] Fondazione ASIA Onlus, Buccinasco (MI)

Corresponding Author:

Laura Labate
Clinica di Malattie Infettive, Università degli Studi di Genova DiSSal, Via A. Pastore 1, 16132 Genova

laura.labate92@gmail.com

Keywords:
observational; HIV Infection; BIC/F/TAF; effectiveness; tolerability

Conflict of interest:
none

JHA 2023; 8(4): 80-82

DOI: 10.19198/JHA31563

Riassunto

Il ruolo della terapia antiretrovirale in singola compressa a base di Bictegravir/emtricitabina/tenofovir alafenamide (B/F/TAF) è ormai consolidato nella popolazione di soggetti che vivono con HIV, sia nei soggetti naive (TN) che già in trattamento antiretrovirale (TE).

I dati degli studi clinici randomizzati ci mostrano come questo regime abbia un'ottima efficacia e tollerabilità e la conferma ci arriva da alcuni studi osservazionali di coorte che hanno valutato efficacia, sicurezza, tollerabilità e gli esiti riferiti dai pazienti del trattamento con in persone con HIV TN o TE.

Da qui nasce il nostro studio retrospettivo che ha esaminato i dati real-life del nostro centro, l'ospedale Policlinico San Martino di Genova con l'obiettivo di valutare efficacia e tollerabilità di B/F/TAF in un'ampia coorte di soggetti che vivono con HIV, sia TN che TE, che hanno iniziato questo regime tra il 2020 e il 2022.

Abstract

Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) is an oral single-tablet regimen (STR) with the indication for the treatment -naïve (TN) and treatment-experienced (TE) people with HIV (PWH) with a limited drug interaction potential and a high barrier to resistance. We evaluated the effectiveness and tolerability of B/F/TAF in a large real-life cohort. This observational, retrospective, single-center, real-life cohort study included PWH who started B/F/TAF at our institution between 2020 and 2022. Virological success (VS) was defined as achieving an HIV-RNA <30 copies/ml six months after B/F/TAF start. We enrolled 475 PWH (48 TN, 427 TE); among the TE, 305 (71,4%) PWH had undetectable viremia at the time of initiation. After 6 months, 32 TN achieved virologic success, as did an additional 33 in TE group. CD4+ T-lymphocyte count increased, in TN group (from 353.8 to 612.8/µl). Fifty-six (11.7%) PWH discontinued treatment, only in one case due to therapeutic failure. Our data demonstrated that B/F/TAF is effective, safe, and durable for both TN and TE PWH.

Introduction

Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) is a single-tablet regimen (STR) recommended for HIV-1 antiretroviral therapy (ART) in treatment-naïve (TN) or treatment-experienced (TE) people living with HIV (PWH). (1,2) B/F/TAF has been evaluated in different randomized, double-blind, multicenter, non-inferiority trials (3,4), but few studies have assessed its effectiveness, tolerability, and safety in clinical practice (1-7). Given these premises, we analyzed the effects of B/F/TAF in our cohort.

Patients and methods

This was a retrospective cohort study conducted at Policlinico San Martino Hospital, Genoa, Italy, in which we enrolled all PWH who started a B/F/TAF-based regimen as of February 2020.

We performed a follow-up every 6 months, during which we analyzed HIV-RNA copies/mL and CD4+ T-cell lymphocyte count. The rate of change of these parameters was estimated at different time periods: 12 and 6 months before the start of B/F/TAF, at the start of B/F/TAF, and 6-12-18-24 months after starting B/F/TAF.

Data were collected from the paper and electronic medical records of the ONESYS Hospital Information System.

The reported laboratory values were extracted using the MEDINFO platform (www.reteligureHIV.it). Anthropometric, anamnestic, and laboratory data were collected for each patient: weight [kg], height [cm], BMI [kg/m^2], abdominal circumference [cm], sex, age, CDC stage, smoking, lipodystrophy, cardiovascular familiarity, date of HIV diagnosis, date of initiation of first ART, previous ART regimens with Integrase strand transfer inhibitors (INSTI), nucleoside reverse transcriptase inhibitor (NRTI), non-nucleoside reverse transcriptase inhibitor (NNRTI) or protease inhibitor (PI), durability of ART regimens in months, chronic comorbidities and concomitant therapies, date of initiation of B/F/TAF therapy, and date of discontinuation for any reason.

Laboratory values considered were: HbsAg, HCV Ab, HCV-RNA, nadir CD4+ and its date, zenit HIV-RNA and its date, CD4+ T lymphocytes count, CD8+ T lymphocytes count and HIV-RNA.

This study aimed to assess the efficacy and tolerability of the B/F/TAF regimen for HIV.

Virological success has been defined as ≤30 copies/mL. T0 marked the start, and T1 was the 6-month value. We compared T0 and T1 to determine therapy-induced virological success in both experienced and naive groups.

Results

A total of 475 PWH, 427 TE, and 48 TN were included. Among the TE population, 78% had prior INSTI use (51% elvitegravir, 19% dolutegravir, and 8% raltegravir), while 10% used NRTIs, 9% PIs, and 2.8% NNRTIs. The median duration of ART in the TE group was 12.7 years. The population characteristics are shown in **Table 1**.

Among the 427 TE, 33 (8%) were detectable at the start of B/F/TAF and virological success was achieved. Among the 48 TN cases, 32 (67%) achieved virological success within the first 6 months. At month 6, six TN subjects were detectable, reducing to two by month 12. At 12 months, 430 (90%) PWH were undetectable.

Regarding the durability of the B/F/TAF regimen, 56 (11.7%) PWH discontinued treatment. Table 2 outlines the reasons for this, with 30 discontinuations due to missed follow-up.

Table 1. Patients' characteristics. TN, treatment naïve; TE, treatment experienced.

Variable	Overall	TN (48)	TE (427)
Mean age, years	49.2	38.1	50.4
Males, n (%)	319 (67)	32 (67)	287 (67)
Females, n (%)	156 (33)	16 (33)	140 (33)
Height, cm	170.3	169.2	170.4
Familiarity for cardiovascular disease	83 (17)	10 (21)	73 (17)
Current smokers	236 (50)	21 (44)	215 (50)
HbsAg positive	21 (4)	0	21 (5)
HCV-Ab positive	122 (26)	1 (2)	121 (28)
Detected HCV-RNA	11 (2)	0	11 (3)
Lipodystrophy	64 (13)	1 (2)	63 (15)
AIDS (Stage C of CDC classification)	50 (10)	6 (13)	44 (10)
Nadir CD4+ T lymphocytes/µl	257.5	339.9	247.1
Zenit HIV-RNA /ml	445516.1	939197.2	383806
Years since HIV diagnosis	14.1	0.1	15.7
Years of antiretroviral therapy	11.3	0	12.7

However, it is important to note that only one PWH experienced treatment failure, demonstrating the effectiveness of the B/F/TAF-based regimen.

Statistical analysis of the data collected using the LIFETEST procedure made it possible to construct a Kaplan–Meier curve (**Figure 1**) to examine discontinuation from the study and therefore from B/F/TAF therapy.

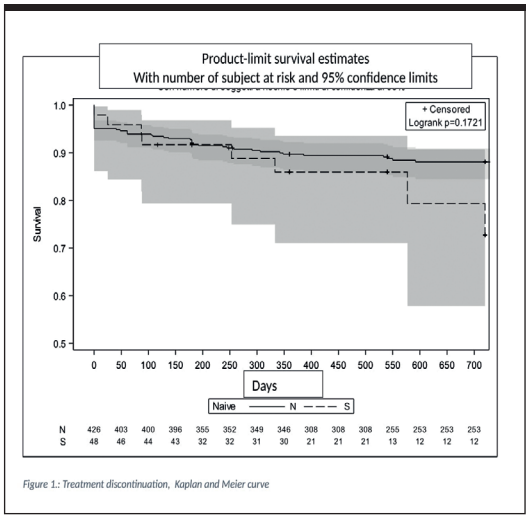

Figure 1. Durability of B/F/TAF by Kaplan - Meier estimates

Discussion

Our primary endpoint was to evaluate the effectiveness and tolerability of B/F/TAF, a once-daily fixed-dose ART regimen approved for PWH treatment.

At six months, 364 (77%) PWH achieved virological suppression, which increased to 430 (90%) at 12 months.

Reasons for discontinuation	TE		TN	
	N	%	N	%
Allergy	1	0.21	1	0.21
Self-discontinuation	1	0.21	0	0
Change of center	5	1.05	0	0
Death	5	1.05	0	0
Failure	1	0.21	0	0
Pregnancy	2	0.42	0	0
Interactions with other therapies	1	0.21	1	0.21
Intolerance	2	0.42	0	0
Other pathology	2	0.42	0	0
Lost to follow-up	30	6.32	4	0.84

Table 2. Reasons of discontinuation.

TN had a higher success rate (66%) than TE (10%) within 6 months. CD4+ T-cell count consistently increased, notably within the first 6 months.

Therefore, this study highlights the efficacy of B/F/TAF in achieving virological success and boosting CD4+ T cell counts, especially during the initial treatment phase.

It should be noted that, as expected, the increase in CD4+ lymphocytes was more pronounced in TN (from 353.8 to 612.8/µl) than in TE (from 664.2 to 685.6/µl). As shown in a recent Quebec cohort study (8), INSTI-based ART appears to be better than NNRTI- and PI-based regimens for normalizing the CD4+/CD8+ ratio, a potential marker of reduced immune system activity.

The two-year drop-out rate was 11.7%, with only one case of therapeutic failure, confirming the effectiveness of this STR regimen.

Conclusion

After 24 months of analysis, B/F/TAF demonstrated its efficacy, as evidenced by the achievement and maintenance of an HIV-RNA load below 30 copies/mL in 90% of PWH and an increase in CD4+ T-lymphocyte count. In addition, the low dropout rate is evidence of good tolerability, which translates to a high level of adherence in clinical practice. ■

REFERENCES

1. Molina JM, Ward D, Brar I, Mills A, Stellbrink HJ, López-Cortés L, et al. *Switching to fixed-dose bictegravir, emtricitabine, and tenofovir alafenamide from dolutegravir plus abacavir and lamivudine in virologically suppressed adults with HIV-1: 48 week results of a randomised, double-blind, multicentre, active-controlled, phase 3, non-inferiority trial.* Lancet HIV. 2018;5(7):e357–65.

2. Havens JP, Bares SH, Lyden E, Podany AT, Scarsi KK, Fadul N, et al. *Effectiveness and Safety of Bictegravir/Emtricitabine/Tenofovir Alafenamide in Patients With HIV-1 Infection and Ongoing Substance Use Disorder: The BASE Study.* Open Forum Infect Dis. 2023;10(3):ofad080.

3. Squillace N, Ricci E, Maggi P, Taramasso L, Menzaghi B, De Socio GV, et al. *Real-life safety of Emtricitabine/Tenofovir Alafenamide/Bictegravir.* PloS One. 2023;18(8):e0289132.

4. Torralba M, Rodríguez G, González Gasca FJ, Cuadra F, Barberá J, Geijo P, et al. *Bictegravir/Emtricitabine/Tenofovir Alafenamide in a Multicentre Cohort: Real-Life Experience From Spain.* Ann Pharmacother. 2023;10600280231168852.

5. Lazzaro A, Cacciola EG, Borrazzo C, Innocenti GP, Cavallari EN, Mezzaroma I, et al. *Switching to a Bictegravir Single Tablet Regimen in Elderly People Living with HIV-1: Data Analysis from the BICTEL Cohort.* Diagn Basel Switz. 2021;12(1):76.

6. Pérez Barragán E, Guevara Maldonado MF, Mancilla Galindo J, Kammar García A, Ortiz Hernández A, Mata-Marín JA, et al. *Weight gain after 12 months of switching to bictegravir/emtricitabine/tenofovir alafenamide in virologically suppressed HIV patients.* AIDS Res Hum Retroviruses. 2023; 39(10):511-517.

7. Emond B, Rossi C, Côté-Sergent A, Dunn K, Lefebvre P, Lafeuille MH, et al. *Weight Change and Predictors of Weight Change Among Patients Initiated on Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide or Bictegravir/Emtricitabine/Tenofovir Alafenamide: A Real-World Retrospective Study.* J Health Econ Outcomes Res. 2021;8(1):88–98.

8. Sangaré MN, Baril JG, de Pokomandy A, Klein M, Thomas R, Tremblay C, et al. *CD4/CD8 Ratio Outcome According to the Class of the Third Active Drug in Antiretroviral Therapy Regimens: Results From the Quebec Human Immunodeficiency Virus Cohort Study.* Clin Infect Dis Off Publ Infect Dis Soc Am. 2023;76(11):1879–88.