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BRIEF REPORT

Short-term Adverse Events With BIC/FTC/TAF: Postmarketing Study

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Bictegravir (BIC)/emtricitabine (FTC)/tenofovir alafenamide (TAF) was Food and Drug Administration approved in February 2018. The paucity of real-world data prompted this retrospective, observational evaluation of discontinuation rates, adverse effects, and virologic control. In a Southern US, predominantly African American overweight population, we found optimal virologic control and low discontinuation rates, with 4% discontinuing BIC/FTC/TAF due to rash, low platelets, loss of appetite, and insomnia.

Keywords. adverse events; antiretroviral therapy; bictegravir; drug reaction; rash.

Bictegravir (BIC)/emtricitabine (FTC)/tenofovir alafenamide (TAF) was Food and Drug Administration (FDA) approved on February 7, 2018 [1]. Currently, there are no published postmarketing data for this antiretroviral therapy (ART). The purpose of this study was to assess 1-year postmarketing safety and tolerability of BIC/FTC/TAF. Our primary objective was to assess the prevalence of adverse events in patients taking BIC/FTC/TAF. Our secondary objectives included identifying demographic trends of patients transitioned to BIC/FTC/TAF in an open clinical setting at provider discretion and characterizing discontinuation rates and virologic control of patients placed on BIC/FTC/TAF.

METHODS

This retrospective, observational, pharmacoepidemiologic study of BIC/FTC/TAF was conducted 1 year after FDA approval. It included HIV-infected individuals seen at the University of South Carolina Immunology Center between February 2018 and March 2019 who were started on or switched to BIC/FTC/TAF. Individuals were excluded if they had not started BIC/FTC/TAF at least 3 months before the time data were collected or if they had been on BIC/FTC/TAF at any time before the aforementioned window of data collection. Notably, individuals were not excluded for a lack of follow-up visits or follow-up labs. Those under the age of 18 were excluded. Baseline demographics and serial laboratory data including HIV viral load, CD4 count, serum creatinine, aspartate aminotransferase, alanine transaminase, and creatinine phosophokinase were collected. Drug discontinuation and treatment-related adverse events (AEs) were determined by provider clinic visit notes and/or documented phone conversations with patients as well as patient pharmacy documentation. Of note, all AEs were documented when there was not a clear alternative etiology noted by the clinician including prior dermatological history or if the clinician specifically documented that the AE was attributed to BIC/FTC/TAF.

RESULTS

A total of 201 patients started on BIC/FTC/TAF between February 2018 and March 2019 were randomly selected and reviewed. The majority of individuals were African American (137, 68%) males (132, 65%), with a mean age (range) of 46 (20–76) years. Four patients were transgender. One hundred thirty-five (67%) had a BMI of ≥25 kg/m^2, and 77 (38%) had a BMI of ≥30 kg/m^2. Most patients were treatment experienced (181, 90%), with the plurality of those having previously been on elvitegravir/cobicistat/tenofovir alafenamide/emtricitabine (84 of 181, 46%). The duration of time on ART before changing therapies was not obtained. At baseline, 146 of the patients on ART (72.6% of all individuals) had virological suppression (VS; <200 copies/mL), with a mean CD4 count (range) of 529 (<35–1573) cells/mm^3. Average follow-up was 96 days with a median of 71 days. Only 1 patient who had prior VS was found on follow-up to have a viral load above 200. Of the 55 treatment-experienced individuals who were not virologically suppressed, 36 (65%) achieved VS, with another 14 (25%) of those 55 having no follow-up viral load measurements within the study period to assess.

Of the 201 total patients, 18 (8.9%) patients reported AEs for a total of 19 events (9 rash, 2 dizziness, 1 nausea/vomiting, 1 headache, 1 diarrhea, 1 loss of appetite, 1 weight gain, 1 fatigue, 1 insomnia, 1 thrombocytopenia) (Figure 1). Eleven (5%) patients discontinued therapy, 10 due to AEs (7 rash, 1 insomnia and loss of appetite, 1 thrombocytopenia, and 1 feeling unwell). Time to discontinuation was a mean of 70 days with a range of 6 to 159 days. Of the 9 patients reporting rash, 7 discontinued BIC/FTC/TAF. Of the 3 individuals where more specific information about the rash was recorded, rash was reported to be truncal and/or facial. All 3 described rash as maculopapular and pruritic. One patient

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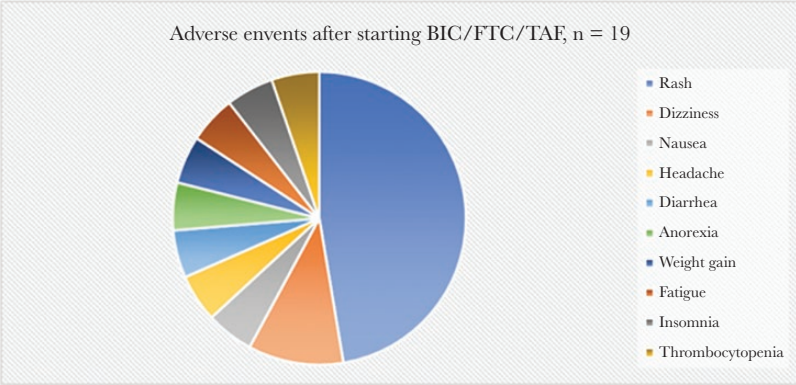

Figure 1. Adverse events after starting BIC/FTC/TAF. Abbreviations: BIC/FTC/TAF, bictegravir/emtricitabine/tenofovir alafenamide.

reported resolution of the rash within a week after stopping BIC/FTC/TAF. One patient who had high AST/ALT at baseline had an increase from 129/243 U/L to 234/394 U/L, respectively. This patient also had rash and angioedema attributed to BIC/FTC/TAF, for which it was stopped; subsequent AST/ALT was not seen at time of data collection. No other laboratory abnormalities were reported.

DISCUSSION

In a Southern US, predominantly African American overweight population, our results demonstrate low discontinuation rates associated with BIC/FTC/TAF, with rash being the predominant cause. Overall, 5% discontinued BIC/FTC/TAF due to AEs compared with <2% as reported in the package insert. This appeared to be driven mostly by rash, with 4.5% reporting rash compared with <2% reported in the package insert. Unfortunately, due to de-identification without specific coding for details, only half of patients complaining of rash had further information recorded. Given that patients were not excluded for lacking follow-up appointments, the sensitivity of detecting adverse events including rash is potentially limited. A review of the literature does not show other reports of increased rash with BIC/FTC/TAF. Of note, most studies reviewed, including those performed for prevalence in the package insert, had both a lower number and lower proportion of African American individuals on this therapy compared with our population [2–5]. It is unclear whether racial demographics and associated physiologic predispositions are contributing, but is worth considering given findings with earlier antiretrovirals. Experience with efavirenz, for instance, found a difference in metabolism by race accounting for more postmarketing central nervous system side effects than seen in the initial FDA approval studies [6]. Similarly, HLA-B*5701 sensitivity to abacavir has been noted to be a trend in people of Northern European decent in postmarketing studies [7].

This study was limited by its small study size with follow-up data not available on all patients, its retrospective approach, its lack of a comparison group, and restriction to 1 study site.

Ongoing postmarketing evaluation is important for early recognition of unexpected adverse outcomes and to further assess tolerability of ART in real-world use and in heterogeneous populations. Longer-term examination of individuals who remain on therapy will be important to help elucidate further adverse events leading to discontinuations such as weight gain. This study of individuals predominantly of African ancestry switched to BIC/FTC/TAF revealed overall good tolerability with a low rate of discontinuations, but a slightly higher-than-anticipated rate of rash leading to discontinuation—a finding deserving of further prospective study in larger groups.

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