Introduction

- Integrase strand transfer inhibitors (INSTIs) are recommended internationally in treatment guidelines for patients with HIV-1 infection, and the class is recognised for its potency and safety.
- Two INSTIs—dolutegravir (DTG) and raltegravir—have safety warnings for potential hepatotoxicity.
- Bictegravir (B) is an unboosted INSTI coformulated with emtricitabine (FTC; F) and tenofovir alafenamide (TAF).
- The single-tablet regimen B/F/TAF is a guideline-recommended regimen, with demonstrated long-term safety, efficacy, and a high barrier to resistance, and few potential drug-drug interactions.
- B/F/TAF is approved for treatment-naive patients and suppressed patients switching therapy, including those with HIV-1 and hepatitis B virus (HBV) coinfection.

Objective

- To assess the hepatic safety profile of B/F/TAF from two Phase 3 studies of treatment-naive participants over 96 wk.

Methods

Study Designs

- Data for participants taking B/F/TAF were pooled from 2 randomised, double-blind, phase 3 studies.

Study 1489
- Study goals: evaluate the hepatic safety profile of B/F/TAF from a Phase 3 study of treatment-naive patients with HIV-1 infection.
- Participants: 650 participants (B/F/TAF n=330; placebo n=320).
- Key inclusion criteria: asymptomatic HIV infection, CD4 count <200 cells/μL, HIV-1 RNA >100,000 copies/mL, Hispanic/Latino ethnicity.
- Key exclusion criteria: concurrent use of other antiretrovirals, current or recent treatment with INSTIs, hepatitis B or C coinfection.

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Baseline Characteristics

- Median age: 32 (18–71) years.
- Male: 89%.
- Race/ethnicity: 24% Hispanic/Latino.
- Median HIV-1 RNA, log10 copies/mL (IQR) 4.42 (4.00–4.88).

Overall Safety Through Week 96

- Participants, % (n): 91 (4, 23).
- Any Grade AE: 13 (1, 9).
- Grade 3 or 4 AE: 1 (1, 8).
- Study drug-related AE: 1 (1, 7).
- AE leading to study drug discontinuation: 1 (0).
- Death: 1 (0).

Conclusions

- There were no study drug-related hepatobiliary serious AEs or clinical AEs among 634 treatment-naive participants taking B/F/TAF in two Phase 3 studies with >1183 patient-years of follow-up.
- Three participants had transient liver-related laboratory abnormalities reported as AEs, which resolved while on B/F/TAF.
- There were no treatment discontinuations due to either hepatobiliary AEs or abnormal liver function tests.
- No participant had drug-induced liver injury.
- Grade 3 or 4 liver function test abnormalities were transient and resolved while continuing B/F/TAF.
- B/F/TAF was safe in participants with HBV or HCV coinfection and effective at suppressing HBV viremia.
- B/F/TAF provides a well-tolerated and effective treatment for HIV infection without evidence of hepatotoxicity.