Introduction

• Fostametrix (FTI) is a produg of temsavir (TMR), a first-in-class, investigational attachment inhibitor being developed for heavily treatment-experienced (HTE) adults living with HIV-1 infection who are unable to form a viable combination ARV regimen out of remaining fully active agents.1,2

• TMR binds to HIV-1 gp120, prevents viral attachment and entry into host CD4+ T cells and other immune cells (Figure 1).1,2

• BRIGHTE (NCT02362503) is an ongoing Phase 3 study investigating the efficacy and safety of FTI plus optimized background therapy (OBT) in HTE individuals who were failing their current regimen (confirmed HIV RNA <400 copies/mL).1,2

• As previously reported, for the Randomized Cohort (RC), through Week 96, FTR + OBT demonstrated:
  - Superior virologic suppression to <40 c/mL following PDVF through Week 96 was achieved in 27% of participants meeting PDVF criteria.4
  - Among participants with PDVF, 52% in the RC and 25% in the NRC had no emergent gp120 substitutions of interest.

• There were higher rates of PDVF in NRC subjects with TMR IC50 FC >100 (relative risk [RR] 2.5; 95% CI 1.3–4.8) compared with 100–1000 (RR 1.4; 95% CI 1.0–1.9) and 20 to <100 (RR 1.3; 95% CI 0.9–1.8) relative to <20.

• Baseline and emergent virologic results are presented among participants experiencing protocol-defined virologic failure (PDVF) through 96 weeks of FTR-based therapy in the BRIGHTE study (Figure 3).

• A clinical cut-off for FTR has not yet been determined.

Methods

• Genotypic and phenotypic resistance testing was carried out by Monogram Biosciences for all participants at Screening, and at the time of virologic failure for participants meeting PDVF criteria.

• TMR IC50 FC were determined from baseline genotypes and at week 24, 48, and 96.

• For each TMR IC50 FC ≤3, baseline and emergent TMR IC50 FC were determined from baseline genotypes and at week 24, 48, and 96.

• Population sequencing of the entire gp160 envelope gene was carried out, and the presence of substitutions of interest was recorded.5

• Baseline Genotype and Phenotype

• At Baseline, gp120 substitutions of interest were present in 46% of participants in the RC and 42% of participants in the Non-Randomized Cohort (NRC).

• TMR IC50 FC was ≤100 in 22% of participants, and >1000 in 44% of participants in the RC. In the NRC, TMR IC50 FC was ≤100 in 32% of participants, and >1000 in 31% of participants.

• Baseline and emergent genotypic and phenotypic results in HIV-1-infected adults living with HIV-1 infection who were failing their current regimen (confirmed HIV RNA <400 copies/mL) are presented in this study.

• Conclusions

Baseline and Emergent Genotypic and Phenotypic Results in HIV-1-Infected, Heavily Treatment-Experienced (HTE) Participants Meeting Protocol-Defined Virologic Failure (PDVF) Criteria Through Week 96 of the Fostametsavr (FTI) Phase 3 BRIGHTE Study

P. Ackerman1, M. Garthland2, S. Chabria3, F. Mannino1, L. Garside4, R. Kustra5, A. Clark6, A. Pierce7, M. Krystal1, C. Llamas1, M. Lalatied1

1ViiV Healthcare, Bradford, United States, 2ViiV Healthcare, Research Triangle Park, United States, 3GlassSmithKline, Upper Providence, United States, 4GlassSmithKline, London, United Kingdom, 5ViiV Healthcare, London, United Kingdom

Table 1. Treatment-Emergent Genotypic Changes Among Participants Meeting PDVF Criteria at Week 96

Table 2. Treatment-Emergent Changes in TMR Susceptibility Among Participants Meeting PDVF Criteria at Week 96

Figure 5. PDVF Through Week 96 for Randomized and Non-Randomized Cohorts by Baseline gp120 Substitutions of Interest (A and B), TMR IC50 FC (C and D), CD4+ T Cell Count (E and F), HIV-1 Viral Load (G and H)

Figure 1. Mechanism of Action of TMR

Figure 2. 3D Ribbon Structure of gp120 with TMR

Figure 3. Study Design

Figure 4. (A) Baseline gp120 Substitutions of Interest; (B) Baseline TMR IC50 FC

Figure 5. PDVF through Week 96 for randomised and non-randomised cohorts by baseline gp120 substitutions of interest (A and B), TMR IC50 FC (C and D), CD4+ T cell count (E and F), HIV-1 viral load (G and H).