A Multivariate Analysis of the Phase 3 BRIGHTE Trial, Through Week 24, to Identify Predictors of Virologic Response to Fostemsavir in Heavily Treatment-Experienced People Living With HIV

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Key Takeaways
- Fostemsavir (FTR) demonstrated efficacy and safety in heavily treatment-experienced (HTE) people with multidrug-resistant HIV-1 in the phase 3 BRIGHTE study; here, we evaluated parameters associated with virologic response.
- Virologic response to FTR functional monotherapy or treatment with FTR + optimized background therapy (OBT) in the Randomized Cohort (RC); participants with 1-2 fully active agents available was significantly associated with well-established factors such as baseline CD4+ cell count, baseline log10 HIV-1 RNA, and temsavir (TMR) concentration.
- Overall, baseline parameters associated with virologic response to FTR were not predictive of protocol-defined virologic failure (PDVF) with emergent changes through Week 24.

Introduction
- FTR is approved for the treatment of multidrug-resistant HIV-1 in HTE adults who are otherwise unable to form a suppressive antiretroviral (ARV) regimen because of resistance, intolerance, or safety concerns.
- In the ongoing phase 3 BRIGHTE study, FTR + OBT demonstrated durable virologic responses and clinically meaningful improvements in CD4+ T-cell count and CD4+CD8+ ratio through 240 weeks in HTE adults with HIV-1.
- Understanding the predictors of virologic outcomes is important for prescribers when considering use of FTR.

Objective
- To evaluate parameters associated with virologic outcomes through Week 24 in the phase 3 BRIGHTE study (goal: hoc analysis).

Methods
- BRIGHTE is an ongoing phase 3 study evaluating twice-daily (BID) FTR 600 mg + OBT in HTE adults failing ARV therapy with limited treatment options (Figure 1).

Results

Parameters Associated With Day 8 Virologic Outcomes in FTR-Treated Participants in the RC
- At Day 8, 65% (131/203) of participants in the RC receiving FTR functional monotherapy achieved a decrease of >0.5 log10 HIV-1 RNA.
- In the ITT-6 population, parameters significantly associated with a decrease of >0.5 log10 HIV-1 RNA at Day 8 included higher baseline CD4+ cell count and higher baseline HIV-1 RNA (Figure 2).
- In the stable virological subpopulation (participants with no loss of treatment to their failing regimen), parameters significantly associated with a decrease of >0.5 log10 HIV-1 RNA at Day 8 included higher baseline CD4+ cell count and higher HIV-1 RNA, and TMR Day 8 CYM.
- Presence of most relevant g120 substitutions (S375H/MV/Y, M432L, M434K) was significantly associated with lower odds of >5.0 log10 HIV-1 RNA decrease in HIV-1 RNA stable subpopulation.

Parameters Associated With PDVF With Emergent Changes
- Among evaluable participants at Week 24, 8% (22/263) and 25% (24/98) of participants in the RC and NRC, respectively, had PDVF with emergent genotypic or phenotypic changes to FTR or OBT.
- In the RC, higher baseline CD4+ cell count was significantly associated with lower odds of PDVF with emergent changes at Week 24 (Figure 4).
- In the NRC, higher baseline viral load was significantly associated with lower odds of PDVF with emergent changes.

Table 1. Parameters Investigated in Multivariate Analyses

- Table 2. Association Between Identified Baseline Parameters and PDVF With Treatment-Emergent Genotypic or Phenotypic Changes at Week 24

Conclusions
- Virologic response to FTR functional monotherapy or treatment with FTR + OBT in RC participants was significantly associated with well-established factors such as baseline CD4+ cell count, baseline log10 HIV-1 RNA, and temsavir (TMR) concentration.
- Relevant baseline g120 substitutions were significantly associated with reduced response to FTR functional monotherapy at Day 8 but not with virologic response to FTR + OBT at 24 weeks.
- Overall, the presence of baseline parameters associated with virologic response to FTR was not predictive of PDVF with emergent changes in HTE people with multidrug-resistant HIV-1 in the RC or NRC of the BRIGHTE study.

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