# CHARACTERIZATION OF HEAVILY TREATMENT-EXPERIENCED HIV-1–INFECTED CLINICAL TRIAL PARTICIPANTS INFECTED WITH SARS-COV-2 COVID-19: FOSTEMSAVIR BRIGHTE PHASE 3 CLINICAL TRIAL


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## Introduction

- Fostemsavir (FTR), an oral prodrug of the first-in-class attachment inhibitor temsavir, is approved for the treatment of multidrug-resistant (MDR) HIV-1 infection in heavily treatment-experienced (HTE) adults who are otherwise unable to form a suppressive antiretroviral (ARV) regimen due to resistance, prior intolerance, or other safety concerns[1-4]
- In the phase 3 BRIGHTE study, in HTE adults with advanced HIV-1 disease and limited treatment options, fostemsavir plus optimized background therapy (OBT) was generally well tolerated and showed maintenance of virologic response and continuous clinically meaningful increases in CD4+ T-cell count through Week 96[1-5]
- People living with HIV-1 (PLHIV) have a higher risk of infection with SARS-CoV-2 and a higher mortality risk from COVID-19 compared with people without HIV-1[6,7]
  - Specifically, those with HIV viremia and/or low CD4+ T-cell count may be at increased risk of serious adverse outcomes[8]
- It is important to characterize outcomes of COVID-19 in PLHIV, particularly those who have other risk factors such as older age and underlying medical conditions associated with more severe COVID-19 illness

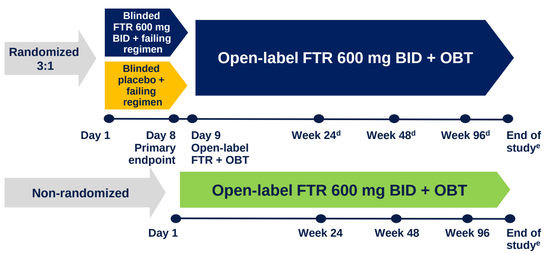
## Objective

- We describe the reported COVID-19 cases in a multinational clinical trial population of people living with MDR HIV-1 and immune suppression who are receiving FTR-based ARV therapy

## Methods

- BRIGHTE is an ongoing, multinational, phase 3 study evaluating twice-daily (BID) fostemsavir 600 mg plus OBT in HTE adults failing ARV therapy with limited treatment options (Figure)[3,4]
- At the start of the COVID-19 pandemic (December 2019), all ongoing BRIGHTE participants had achieved ≥192 weeks on FTR plus OBT
- Investigators used WHO guidelines[9] for COVID-19 diagnosis and reported exposure risk, testing results, and symptom presence
- Cases reported up to the Week 240 data cutoff (June 24, 2021) are described

### Figure. BRIGHTE Study Design




[a]Participants were enrolled at 108 investigational sites across Africa, Asia-Pacific, Europe, North America, and South America. There were no screening temsavir susceptibility criteria. [b]Fully active is based on susceptibility (current or historical resistance measures) and availability (the participant is tolerant of, eligible for, and willing to take [in the case of enfuvirtide only] the ARV). [c]Use of investigational agents as part of OBT was permitted in the Non-randomized Cohort only. [d]Measured from the start of open-label FTR 600 mg BID + OBT. [e]The study is expected to be conducted until participants can access FTR through other means.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## Results

- 371 participants were enrolled and treated in BRIGHTE, 272 in the Randomized Cohort and 99 in the Non-randomized Cohort
  - There was a high prevalence of risk factors for adverse COVID-19 outcomes (Table 1)
- 252 participants remained in BRIGHTE at the start of the pandemic, 200 in the Randomized Cohort and 52 in the Non-randomized Cohort

### Table 1. Demographics and Baseline Characteristics (Safety Population)

| Parameter, n (%)[a] | Randomized Cohort (N=272) | Non-randomized Cohort (N=99) | Total (N=371) |
|---|---|---|---|
| Sex | | | |
| Female | 71 (26) | 10 (10) | 81 (22) |
| Age | | | |
| ≥50 years | 111 (41) | 55 (56) | 166 (45) |
| Race | | | |
| African American/African heritage | 60 (22) | 23 (23) | 83 (22) |
| White | 185 (68) | 74 (75) | 259 (70) |
| History of AIDS | 231 (85) | 89 (90) | 320 (86) |
| Baseline HIV-1 RNA | | | |
| Median (range), $log_{10}$ c/mL | 4.7 (1.6-6.9) | 4.3 (1.6-6.6) | 4.6 (1.6-6.9) |
| ≥100,000 c/mL | 80 (29) | 15 (15) | 95 (26) |
| Baseline CD4+ T-cell count | | | |
| Median (range), cells/mm$^3$ | 99.5 (0-1160) | 41 (0-641) | 80 (0-1160) |
| <200 cells/mm$^3$ | 199 (73) | 79 (80) | 278 (75) |
| <20 cells/mm$^3$ | 72 (26) | 40 (40) | 112 (30) |
| Current and past medical conditions[b] | | | |
| Respiratory conditions | 134 (49) | 52 (53) | 186 (50) |
| Cardiovascular conditions | 86 (32) | 49 (49) | 135 (36) |

[a]Unless otherwise specified. [b]Conditions associated with adverse COVID-19 outcomes.[10]

- By June 2021, confirmed SARS-CoV-2 infection (by positive PCR test) had been reported for 18 participants (15 in the Randomized Cohort, 3 in the Non-randomized Cohort)
  - Severity was grade 1 through 3
  - All cases resolved without reported sequelae, and there were no reports of post–COVID-19 syndrome (although this was not specifically queried)
  - 7 of these 18 participants were hospitalized with COVID-19 (Table 2)
    - All 7 participants were in the Randomized Cohort
    - Most recent CD4+ T-cell counts before COVID-19 diagnosis ranged from 164 to 1641 cells/mm$^3$, and 5 of the 7 participants were virologically suppressed before COVID-19 diagnosis (HIV-1 RNA <40 c/mL)
    - Median event duration was 19 days (range, 15-43), and all 7 participants recovered
    - Treatments for COVID-19 often included prophylactic anticoagulants and supplemental oxygen; no changes were made to any ARV regimen
  - The remaining 11 of 18 participants with confirmed COVID-19 were managed as outpatients
- 4 more participants had suspected COVID-19, but no confirmatory PCR test was reported
- 3 more participants had suspected COVID-19, but negative PCR test results were reported

## Conclusions

- In the multicenter, international, phase 3 BRIGHTE study, <10% of participants had confirmed COVID-19 despite multiple risk factors and advanced HIV
  - Among 252 participants, there were 18 confirmed and 4 unconfirmed cases of COVID-19, with no deaths or reported persistent sequelae
  - In addition, 3 suspected cases had subsequent negative tests
- The lack of deaths and absence of persistent symptoms related to COVID-19 in the BRIGHTE study are reassuring
  - We hypothesize that COVID-19–related adverse outcomes may have been mitigated by improvements in immune function during the course of the study

### Table 2. Characteristics of the 7 Participants Hospitalized With COVID-19

| Demographics, baseline characteristics | Participant (Randomized Cohort) | | | | | | |
|---|---|---|---|---|---|---|---|
| | 00376 | 00631 | 00626 | 00312 | 00524 | 00449[a] | 00305 |
| Age, years | 54 | 47 | 38 | 71 | 55 | 55 | 62 |
| Sex | Female | Male | Male | Male | Male | Female | Male |
| Race | Black | Other | White | Black | Other | White | White |
| Country | Brazil | Peru | Argentina | Belgium | Brazil | Brazil | Argentina |
| CD4+ T-cell count, cells/mm$^3$ | 75 | 196 | 131 | 207 | 7 | 368 | 222 |
| HIV-1 RNA, c/mL | 82,270 | 25,694 | 373,289 | 2395 | 112,343 | 54,925 | 346,054 |
| **COVID-19 clinical characteristics** | | | | | | | |
| Positive test date | 15 Apr 2020 | 20 May 2020 | 07 Jul 2020 | 26 Oct 2020 | 12 Feb 2021 | 09 Mar 2021 | 31 Mar 2021 |
| Event duration, days | 16 | 19 | 19 | 15 | 17 | 43 | 22 |
| Severity | Grade 3 | Grade 3 | Grade 2 | Grade 3 | Grade 3 | Grade 2 | Grade 3 |
| Outcome | Recovered | Recovered | Recovered | Recovered | Recovered | Recovered | Recovered |
| Relevant medical history or known exposure risks | Diabetes, systemic arterial hypertension, no known exposure | Systemic arterial hypertension, obesity, recent exposure in community | Smoker, no known exposure | Chronic renal failure/dialysis, recent visit to healthcare facility | Systemic arterial hypertension, recent exposure in community | Asthma, recent exposure in community + visit to healthcare facility | No known exposure |
| Pre–COVID-19 CD4+ T-cell count, cells/mm$^3$ | 823 | 293 | 876 | 310 | 563 | 1641 | 164 |
| Pre–COVID-19 HIV-1 RNA, c/mL | <40 | <40 | <40 | <40 | 117 | <40 | 419,183 |
| Reported COVID-19 treatment | Ceftriaxone IV, azithromycin, oseltamivir, cefuroxime, enoxaparin, supplemental oxygen via nasal catheter | Orphenadrine, acetaminophen, enoxaparin, albuterol, ipratropium | Enoxaparin, omeprazole | Dexamethasone, enoxaparin, aspirin, tramadol, movicol, furosemide, bilastine, darbepoetin alfa, valproic acid, potassium, sodium bicarbonate, calcium carbonate, supplemental oxygen via nasal canula | Ceftriaxone, ciprofloxacin, dexamethasone, enoxaparin, loperamide, oxygen support | Dexamethasone, oxygen support | Blood transfusion, ampicillin/sulbactam, budesonide inhaler, ipratropium inhalation |

[a]1 hospitalized participant had reported symptomatic COVID-19 for 43 days.