Durability and effectiveness of fostemsavir in heavily treatment-experienced people with HIV

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Background

- Heavily-treatment experienced people with HIV (PWH) are individuals with limited treatment options due to resistance, drug intolerance, etc.
- Fostemsavir (FTR) is a novel attachment inhibitor which binds to glycoprotein 120 (gp120) on the surface of the HIV-1 virion, preventing interaction with the human CD4 cell binding site[1,2]
- FTR is taken orally (twice daily), in combination with other antiretrovirals[1]
- FTR was approved by the FDA on 2JUL2020 for people with multidrug resistant HIV-1 who have experienced multiple therapies, and whose HIV infection cannot be successfully treated with other antiretrovirals (ARVs) because of resistance, intolerance or safety considerations[3]
- The phase III BRIGHTE trial showed a distinctive trend of increasing virologic response and CD4 cell count which was sustained through 240 weeks on FTR[4,5]

Objective

To assess the durability of FTR-containing regimens, as well as their virologic and immunologic effectiveness in routine clinical care in the US

Methods

Study Population

- OPERA cohort
  - Prospectively captured, routine clinical data from electronic health records from 96 clinics in the US (22 states, 1 US territory)
  - >145K PWH as of March 2022, representing ~14% of people with diagnosed HIV infection in the US[5]
- Inclusion criteria
  - HIV infection
  - Aged 18+
  - Prescribed FTR for the first time between 2JUL2020 and 1SEP2021
- Censoring events
  - Discontinuation of FTR
  - Death
  - Loss to follow-up (i.e., 12 months after last clinical contact)
  - Study end (i.e., 28FEB2022)

Stratification

- Suppressed: baseline VL <50 copies/mL
- Viremic: baseline VL ≥50 copies/mL)

Durability

- FTR discontinuation (changes in other ARVs allowed)

Virologic Response

- Assessed at 6 and 12 months (±3 months) after FTR start
- Viral suppression: viral load (VL) <50 copies/mL
- Virologic failure: 2 consecutive VL ≥200 copies/mL, or 1 VL ≥200 copies/mL followed by FTR discontinuation within 120 days, after suppression
- Viral blip: 1 VL ≥50 copies/mL preceded and followed by VLs <50 copies/mL

Immunologic Response

- By 6 months: ≥50 cells/μL increase from baseline CD4 count to last CD4 count within 6 months of baseline (days 1-180)
- By 12 months: ≥100 cells/μL increase from baseline CD4 count to last CD4 count within 12 months of baseline (days 1-365 days)
- By study end: Rate of change ≥ 0.278 cells/μL/day from baseline CD4 count to last CD4 count after 6 months (≥180 days after baseline)
  - Derived from a ≥100 cells/μL increase in 12 months

Results

Table 1. Demographic and clinical characteristics at FTR initiation

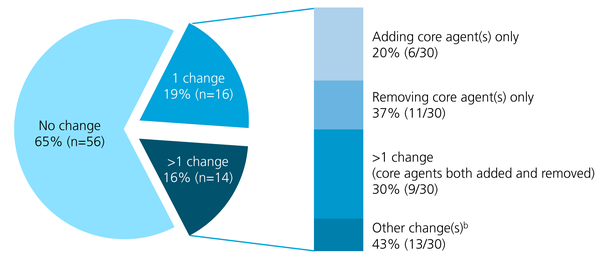
	Overall N=86	Baseline VL < 50 copies/mL N=31	Baseline VL ≥ 50 copies/mL N=55
Age (years), median (IQR)	55 (48, 60)	60 (54, 66)	52 (40, 58)
Male sex, n (%)	74 (86)	27 (87)	47 (86)
Black race, n (%)	36 (42)	≤5[a]	32 (58)
Hispanic ethnicity, n (%)	18 (21)	11 (36)	7 (13)
Years since HIV diagnosis, median (IQR)	21 (12, 30)	27 (15, 33)	18 (11, 27)
Prior exposure, n (%)			
INSTI	78 (91)	29 (94)	49 (89)
PI	70 (81)	22 (71)	48 (87)
NNRTI	58 (67)	20 (65)	38 (69)
CD4 cell count <200 cells/μL, n (%)	28 (32)	7 (22)	21 (38)
Viral load, n (%)			
<50 copies/mL	31 (36)	31 (100)	NA
≥50 to <200 copies/mL	12 (14)	NA	12 (22)
≥200 to <10,000 copies/mL	22 (26)	NA	22 (40)
≥10,000 copies/mL	21 (24)	NA	21 (38)

FTR, fostemsavir; HIV, human immunodeficiency virus; INSTI, integrase strand transfer inhibitor; IQR, interquartile range; μL, microliter; mL, milliliter; N, number; NA, not applicable; NNRTI, non-nucleoside reverse transcriptase inhibitors; PI, protease inhibitor; VL, viral load
[a] HIPAA requires the masking of cells with 1 to 5 individuals

Figure 1. Core agents prescribed in combination with FTR at index, N = 86

BIC, bictegravir; DRV, darunavir; DTF, dolutegravir; FTR, fostemsavir; N, number

Figure 2. Changes in the background therapy while maintaining FTR use[a], N = 86



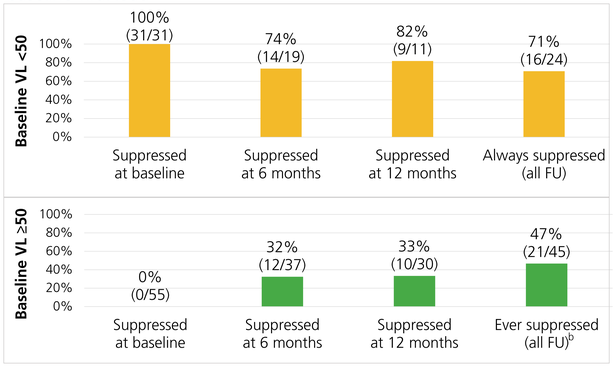
[a] From start of FTR until FTR discontinuation, death, loss to follow-up or study end
[b] Core agent switch, >1 change in which core agents are added and removed, or changes in non-nucleoside reverse transcriptase inhibitor only

Table 2. Follow-up and censoring events

	Overall N=86	Baseline VL < 50 copies/mL N=31	Baseline VL ≥ 50 copies/mL N=55
Months on FTR, median (IQR)	10.8 (6.8, 15.3)	11.1 (6.4, 14.6)	10.4 (6.8, 15.9)
Any VL over follow-up, n (%)	69 (80)	24 (77)	45 (82)
Any CD4 over follow-up, n (%)	70 (81)	24 (77)	46 (84)
Still on FTR at study end, n (%)	60 (70)	20 (64)	40 (73)
Discontinued FTR			
n (%)	17 (20)	8 (26)	9 (16)
IR per 100 person-years (95% CI)	22.1 (13.8, 35.6)	30.9 (15.5, 61.8)	17.7 (9.2, 34.0)
Died, n (%)	7 (8)	3 (10)	4 (7)
Lost to Follow Up, n (%)	≤5[a]	0 (0)	≤5[a]

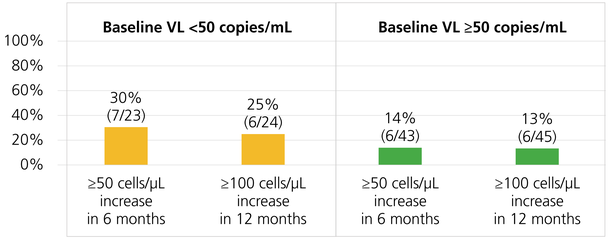
FTR, fostemsavir; CI, confidence interval; IQR, interquartile range; IR, incidence rate; mL, milliliter; N, number; VL, viral load
[a] HIPAA requires the masking of cells with 1 to 5 individuals

Figure 3. Virologic suppression (i.e., VL <50 copies/mL) over follow-up, by baseline viral load[a]



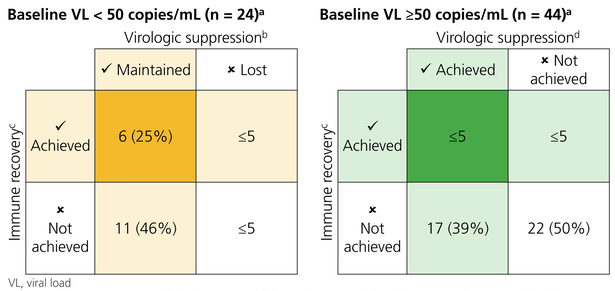
FU, follow-up; mL, millimeter; VL, viral load
[a] Among PWH with a viral load measured within 3 months before or after the follow-up timepoint of interest
[b] Any VL <50 copies/mL at any point during all of follow-up

Figure 4. Immune response[a] over follow-up, by baseline viral load[b]



Mo, months; VL, viral load
[a] Rate of change ≥ 0.278 cells/μL/day from baseline CD4 count to last CD4 count after 6 months (≥180 days after baseline)
[b] Among PWH with a baseline CD4 and a follow-up CD4 in the first 6 or 12 months on FTR

Figure 5. Discordance of virologic and immunologic response[a]



VL, viral load
[a] Among PWH with a baseline CD4, ≥1 follow-up CD4 and ≥1 follow-up VL; [b] **Maintained**: All follow-up VL <50 copies/mL, **Lost**: Any follow-up VL ≥50 copies/mL; [c] **Achieved**: CD4 increase ≥0.278 cells/μL/day from baseline to last CD4 count (≥180 days after baseline), **Not achieved**: CD4 increase <0.278 cells/μL/day from baseline to last CD4 count; [d] **Achieved**: Any follow-up VL <50 copies/mL, **Not achieved**: All follow-up VL ≥50 copies/mL

Discussion

- In routine clinical care in the US, the population receiving a prescription for FTR was heterogenous, varying substantially by baseline viral load (Table 1)
- FTR-containing regimens were durable, with most PWH remaining on FTR at study end (Table 2)
- 1/3 experienced changes in the background therapy prescribed with FTR during the study period (Figure 2)
- Over the entire study period, most PWH with a baseline VL <50 copies/mL remained suppressed throughout follow-up, and half of those with a baseline VL ≥50 copies/mL achieved suppression (Figure 3)
  - Virologic failure or blips were observed in ≤5/19 suppressed PWH with ≥2 VL and ≤5/10 viremic PWH with ≥2 VL after suppression (not shown)
- By 12 months of FTR use, CD4 recovery (i.e., CD4 cell increase ≥100 cells/μL) was achieved by 25% of PWH with a baseline VL <50 copies/mL and 13% of those with a baseline VL ≥50 copies/mL (Figure 4)
- 25% of PWH with a baseline VL <50 copies/mL achieved CD4 recovery while maintaining virologic suppression; 11% of those with a baseline VL ≥50 copies/mL achieved CD4 recovery regardless of virologic suppression achievement (Figure 5)
- Limitations
  - Adherence, resistance and reasons for discontinuation were not available or incomplete in the electronic health records
  - Follow-up was limited in this early evaluation of real-world FTR use in the COVID-19 era
    - 20% had no viral load and/or CD4 cell count (Table 2)
    - Only 61% of suppressed and 18% of viremic PWH had sufficient data to assess virologic failure and blips
    - Additional follow-up time will provide a more robust assessment

Key Findings

Among PWH initiating FTR in routine care in the US:

- Most maintained FTR use throughout the study period; over a third had background therapy changes while on FTR
- Favorable virologic and immunologic responses were observed in PWH with a baseline VL <50 copies/mL, though responses were more modest in PWH with a baseline VL ≥50 copies/mL

References

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