Fostemsavir use in the OPERA cohort: immunologic and virologic response

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OPERA® The Longitudinal Cohort

Background

- Fostemsavir (FTR): novel attachment inhibitor to be used in combination with other antiretrovirals (ARV)
  - Approved by the FDA on 2JUL2020
  - For heavily treatment-experienced (HTE) adults with multi-drug resistant HIV-1 infection who are failing their current ARV regimen due to resistance, intolerance, or safety considerations

Objective

To describe the real-world immunologic and virologic response among individuals starting a new FTR-containing regimen in the US-based OPERA cohort

Methods

Study Population

- OPERA cohort
  - Prospectively captured, routine clinical data from electronic health records in the US
  - ~14% of people with HIV in care in the US[1] (N=155,307)
- Inclusion criteria
  - HIV-1 positive
  - ≥18 years of age
  - Started FTR for the first time between 2JUL2020 and 1SEP2022
- Censoring events
  - FTR discontinuation
  - Death
  - Loss to follow-up
  - Study end (28FEB2023)

Analyses

- Assessment windows
  - 6 months: 91-270 days after FTR start (used measurement closest to 180 days)
  - 12 months: 271-455 days after FTR start (used measurement closest to 365 days)
- Virologic suppression
  - Viral load (VL) <50 copies/mL
  - Frequency and proportion
- Changes in CD4 cell count and CD4%
  - Difference between follow-up value and value at FTR start
  - Median and interquartile range (IQR)
  - Mean and standard deviation (SD)
- Stratification
  - Virologically suppressed & high CD4 cell count (baseline VL <50 copies/mL & CD4 ≥350 cells/μL)
  - Virologically suppressed & low CD4 cell count (baseline VL <50 copies/mL & CD4 <350 cells/μL)
  - Viremic & high CD4 cell count (baseline VL ≥50 copies/mL & CD4 ≥350 cells/μL)
  - Viremic & low CD4 cell count (baseline VL ≥50 copies/mL & CD4 <350 cells/μL)

Results

Table 1. Demographic and clinical characteristics at fostemsavir start

	Suppressed & High CD4 (VL <50, CD4 ≥350)	Suppressed & Low CD4 (VL <50, CD4 <350)	Viremic & High CD4 (VL ≥50, CD4 ≥350)	Viremic & Low CD4 (VL ≥50, CD4 <350)
N	**37**	**29**	**55**	**61**
Years since HIV diagnosis, n (%)	27.4 (21.2, 32.5)	17.8 (6.3, 31.4)	21.4 (9.4, 28.9)	17.4 (5.7, 24.2)
Age, median (IQR)	58 (55, 62)	56 (52, 63)	52 (48, 59)	49 (37, 57)
Female, n (%)	≤5 (≤14%)[a]	7 (24%)	15 (27%)	14 (23%)
Black race, n (%)	7 (19%)	≤5 (≤17%)[a]	23 (42%)	34 (56%)
Hispanic ethnicity, n (%)	11 (30%)	9 (31%)	≤5 (≤9%)[a]	13 (21%)
Viral load, median copies/mL (IQR)	<50	<50	216 (90, 1580)	9240 (330, 88200)
CD4 cell count (cells/μL)				
Median (IQR)	581 (453, 745)	186 (139, 257)	515 (404, 703)	110 (56, 234)
≥500, n (%)	24 (65%)	0 (0%)	31 (56%)	0 (0%)
CD4 percent				
Median (IQR)	28 (24, 39)	14 (9, 21)	25 (20, 32)	9 (4, 15)
≥29%, n (%)	18 (49%)	≤5 (≤17%)[a]	16 (29%)	0 (0%)
≥14% to <29%, n (%)	19 (51%)	13 (45%)	38 (69%)	18 (30%)
<14%, n (%)	0 (0%)	14 (48%)	≤5 (≤9%)[a]	43 (70%)
FTR added to existing regimen, n (%)	16 (43%)	22 (76%)	32 (58%)	36 (59%)

μL, microliter; IQR, interquartile range; mL, milliliters; N, number; VL, viral load
[a] HIPAA regulations require the masking of cells with 1 to 5 individuals

Table 2. Study follow-up

	Suppressed & High CD4 (VL <50, CD4 ≥350)	Suppressed & Low CD4 (VL <50, CD4 <350)	Viremic & High CD4 (VL ≥50, CD4 ≥350)	Viremic & Low CD4 (VL ≥50, CD4 <350)
N	**37**	**29**	**55**	**61**
Months on FTR, median (IQR)	12 (8, 16)	11 (6, 18)	12 (8, 17)	12 (9, 22)
Still on FTR at 6 months, n (%)	31 (84%)	23 (79%)	48 (87%)	54 (88%)
Still on FTR at 12 months, n (%)	18 (49%)	10 (34%)	28 (51%)	31 (51)

IQR, interquartile range; mL, milliliters; N, number; VL, viral load

Table 3. Virologic outcomes

	Suppressed & High CD4 (VL <50, CD4 ≥350)	Suppressed & Low CD4 (VL <50, CD4 <350)	Viremic & High CD4 (VL ≥50, CD4 ≥350)	Viremic & Low CD4 (VL ≥50, CD4 <350)
6 months, N [a]	**29**	**20**	**40**	**39**
Viral load <50 copies/mL, n (%)	24 (83%)	18 (90%)	19 (48%)	12 (31%)
Median viral load change (IQR)	NA	NA	-100 (-745, -10)	-240 (-114, 713)
12-months, N [b]	**14**	**11**	**29**	**30**
Viral load <50 copies/mL, n (%)	9 (64%)	11 (100%)	15 (52%)	10 (33%)
Median viral load change (IQR)	NA	NA	-90 (-790, -20)	-335 (-14031, 2330)

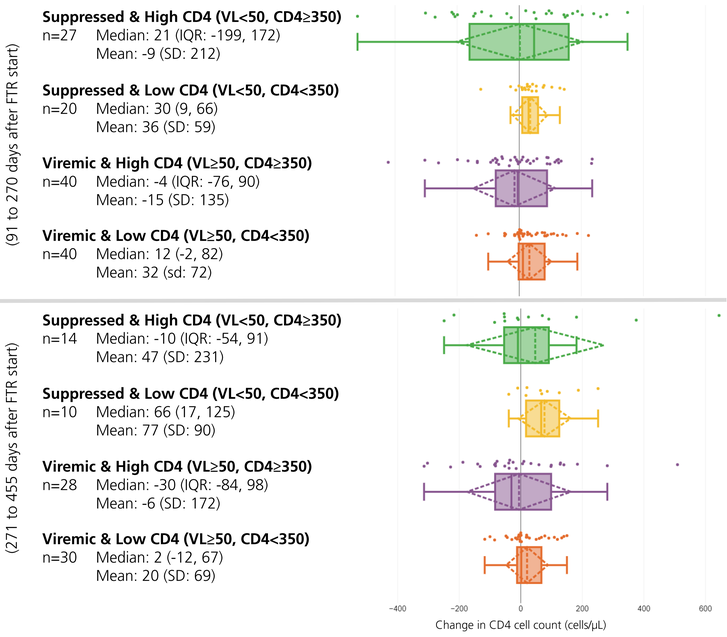
IQR, interquartile range; mL, milliliters; N, number; VL, viral load
[a] Measured 91 to 270 days after FTR start
[b] Measured 271 to 455 days after FTR start

Table 4. Immunologic outcomes

	Suppressed & High CD4 (VL <50, CD4 ≥350)	Suppressed & Low CD4 (VL <50, CD4 <350)	Viremic & High CD4 (VL ≥50, CD4 ≥350)	Viremic & Low CD4 (VL ≥50, CD4 <350)
6 months, N	**27**	**20**	**40**	**40**
CD4 ≥500 cells/μL, n (%)	16 (59%)	0 (0%)	23 (58%)	0 (0%)
CD4% ≥29%	13 (48%)	≤5 (≤25%)[a]	15 (38%)	0 (0%)
Median CD4% change (IQR)	-0.7 (-4.0, 3.0)	1.0 (-0.3, 2.8)	1.1 (-3.2, 3.7)	0.0 (-1.0, 2.7)
Mean CD4% change (SD)	-1.1 (5.4)	1.3 (2.6)	0.6 (5.3)	0.6 (3.3)
12-months, N	**14**	**10**	**28**	**30**
CD4 ≥500 cells/μL, n (%)	7 (50%)	≤5 (≤50%)[a]	12 (43%)	0 (0%)
CD4% ≥29%	6 (43%)	≤5 (≤50%)[a]	9 (32%)	0 (0%)
Median CD4% change (IQR)	0.0 (-2.4, 4.6)	1.9 (1.3, 3.9)	0.5 (-1.2, 3.4)	0.1 (-1.3, 2.8)
Mean CD4% change (SD)	-0.2 (5.7)	2.5 (1.7)	0.8 (4.7)	0.8 (3.7)

IQR, interquartile range; mL, milliliters; N, number; VL, viral load
[a] Measured 91 to 270 days after FTR start
[b] Measured 271 to 455 days after FTR start

Figure 1. Change in CD4 cell count (cells/μL)[a]



FTR, fostemsavir; IQR, interquartile range; N, number; SD, standard deviation
Dots represent the datapoints; boxes (solid lines) represent the first quartile, median and third quartile; whiskers represent the data range, excluding outliers; diamonds (dashed lines) represent the mean and standard deviation
[a] Among individuals with a measurement during the window of assessment

Discussion

- Between 2JUL2020 and 1SEP2022, 182 individuals started an FTR-containing regimen in the US OPERA cohort (**Table 1**)
  - 64% were viremic at start, of whom 53% had a CD4 cell count <350 cells/μL
  - 36% were suppressed at start, of whom 44% had a CD4 cell count <350 cells/μL
- Virologic response (**Table 3**)
  - Virologic control was maintained in most suppressed individuals, regardless of CD4 count
  - Virologic suppression was achieved by less than half of viremic individuals
- Immunologic response **(Table 4, Fig 1)**
  - Suppressed individuals with low CD4 had the largest median and mean increases in CD4 count and CD4 percent
  - Regardless of viral load, those with high CD4 counts at start experienced the greatest variability in immunologic response compared to those with low CD4 counts, although 56-65% already had a CD4 count ≥500 cells/μL at FTR start
- Strengths
  - Large cohort representative of routine HIV care in the US
  - Stratification by viral load and CD4 count at start helps better understand the role of FTR in different clinical scenarios
- Limitations
  - Timepoint analysis leading to reduced sample sizes because the timing of lab assessments in routine clinical care is variable
  - Large assessment windows give the same weight to viral loads or CD4 counts measured up to 6 months apart
  - Limited number of sequential viral load tests prevented the assessment of virologic failure and blips
  - No information on adherence or resistance available

Key Findings

In routine clinical care in the US:

- Virologic response was maintained in suppressed individuals regardless of CD4 cell count at FTR start
- Virologic response was low in viremic individuals
- Individuals with a low baseline CD4 cell count experienced the greatest immunologic gains on FTR

References

1. Centers for Disease Control and Prevention. HIV Surveillance Report, 2021; vol. 34. https://www.cdc.gov/hiv/library/reports/hiv-surveillance.html. Published May 2023. Accessed 23MAY2023.

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