Evaluation of the Safety and Effectiveness of Tenofovir Alafenamide (TAF)-Containing Antiretroviral Therapy in HIV Positive Women

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Background

- Women represent over half the global population of people living with HIV (PLWH).
  - Less than 20% of participants in antiretroviral (ART) studies are women.[1]
- As the life expectancy of PLWH has increased, patients are more susceptible to long-term, chronic adverse effects (ADEs) of ART.
- Tenofovir disoproxil fumarate (TDF), a commonly used NRT for the treatment of HIV, is associated with an increased risk of nephrotoxicity and reduced bone mineral density (BMD).
- Tenofovir alafenamide (TAF) results in < 90% tenofovir plasma concentration and proposed reduction of ADEs compared to TDF.[2]
- Studies mainly included men and found that when compared to TDF, TAF was associated with:
  - Improved renal and BMD safety.
  - Increased weight and serum lipid levels.
  - Equivalent efficacy.

Objectives

Primary objective:

- Describe the proportion of women experiencing ADEs from TAF.

Secondary objectives:

- Describe changes in bone health, weight, renal function, and lipid profile after starting TAF compared to previous ART.
- Describe virologic suppression (HIV-1 RNA viral load < 40 copies/mL) and CD4+ cell count before and after starting TAF.
- Describe the frequency of monitoring for ADEs following initiation of TAF compared to guideline recommendations.

Methods

- **Design:** Retrospective, cohort study
- **Inclusion:** HIV positive females ≥ 12 years initiated on TAF-containing ART prior to August 31, 2019 for ≥ 30 days with adherence of ≥ 80% at BC Women's Hospital Oak Tree Clinic.
- **Adverse effects:** Naranjo score of ≥ 1 (possible) included.
- **Sample size:** N= 35 was calculated using 80% prevalence for the primary objective with 90% confidence level and 11% precision.

Results

Table 1: Participant Characteristics

	N=35
Mean age, years (± SD)	53.2 ± 10.1
Median weight, kg (± IQR)	67.4 ± 27.9
Median CD4 nadir (± IQR)	190 ± 170
Median baseline CD4+ cell count, cells/µL (± IQR)	515 ± 512
Undetectable HIV-1 viral load copies/mL, n (%)	22 (63)
ART naïve	0
Median time since diagnosis, years (± IQR)	16 ± 11.5
Pregnant, n (%)	1 (3)
Post-menopausal, n (%)	25 (71)
Current nicotine use, n (%)	11 (31)
Current alcohol use, n (%)	14 (40)
HLA B*57:01 status positive, n (%)	6 (17)
HIV resistance/reduced response, n (%)	20 (57)
Abacavir	13 (37)
Tenofovir	3 (9)
Median duration of TAF-containing regimen, years (± IQR)	1.3 ± 1.3

Table 2: Frequency and severity of ADEs.

	Frequency n (%)	Severity (n)	Naranjo Score (Median ± IQR)
Any ADE	22 (63)	N/A	N/A
New weight gain ≥ 3%	9 (26)	N/A	2 ± 3
New onset nephrotoxicity	7 (20)	N/A	1 ± 1
Nausea/Vomiting	5 (14)	Mild (5)	2 ± 2
New onset dyslipidemia	3 (9)	N/A	2 ± 0.5
Dizziness	2 (6)	Mild (3)	3 ± 1
Fatigue	2 (6)	Mild (2)	4 ± 0
Diarrhea	2 (6)	Mild (2)	3 ± 1
Depression/anxiety	2 (6)	Mild (1) Moderate (1)	1 ± 0
Abdominal pain	1 (3)	Mild (1)	1
Arthralgia	1 (3)	Mild (1)	4
Headache	1 (3)	Mild (1)	1
Leg pain	1 (3)	Mild (1)	1
≥ 2 ADEs	8 (23)	N/A	N/A
Discontinued due to ADE	1 (3)	N/A	N/A

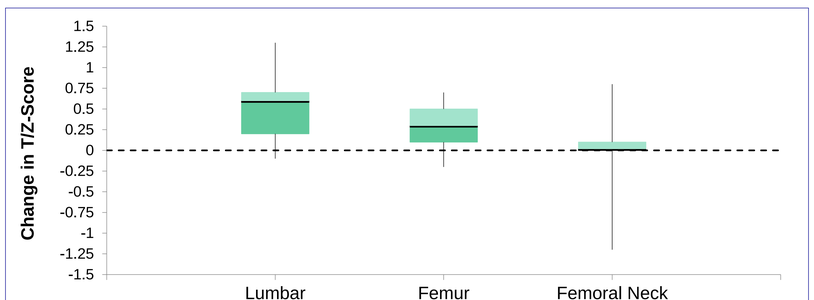

Figure 1: Change in T- and Z-score from baseline after initiating TAF (n=9).

Table 3: Change in target laboratory parameters from baseline.

Parameter	N=35
Renal function	
Median serum creatinine, µmol/L (± IQR)	2.3 ± 16.6
Median eGFR, mL/min (± IQR)	-0.5 ± 15
Median phosphate, mmol/L (± IQR)	-0.01 ± 0.23
ACR increased to ≥ 3 mg/mmol, n (%)	4 (11)
Lipid profile	
Mean total cholesterol, mmol/L (± SD)	0.6 ± 0.7
Mean triglycerides, mmol/L (± SD)	0.2 ± 0.8
Mean HDL cholesterol, mmol/L (± SD)	0.2 ± 0.3
Mean LDL cholesterol, mmol/L (± SD)	0.3 ± 0.9
Mean non-HDL cholesterol, mmol/L (± SD)	0.4 ± 0.7
Mean CD4+ cell count, cells/µL (± SD)	-4.4 ± 183.5

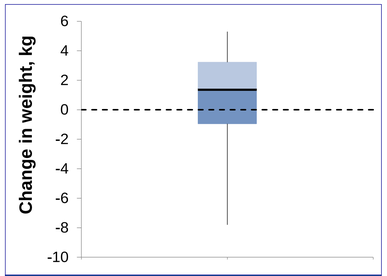

Figure 2: Change in weight from baseline after initiating TAF.

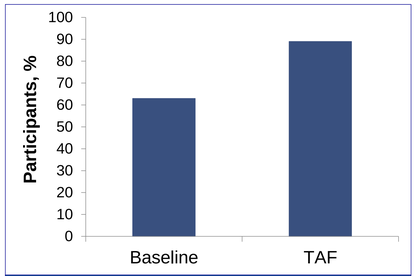

Figure 3: Undetectable HIV-1 viral load at baseline and after initiating TAF.

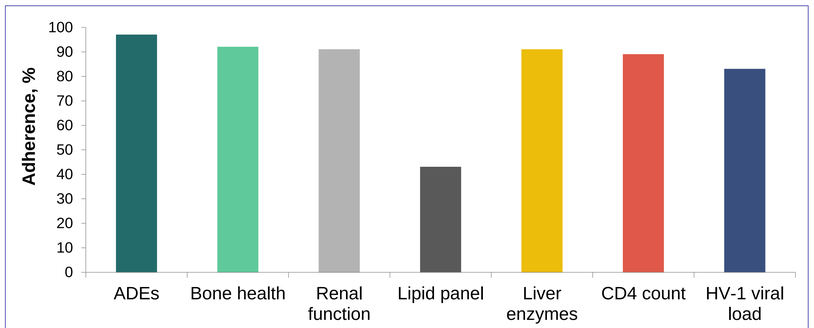

Figure 4: Monitoring safety and effectiveness to guideline recommendations.

Conclusions

- In this cohort of women, TAF was well tolerated and effective.
- No clinically significant change in bone health, renal function, lipid profile or weight from baseline was observed.
- Frequency of monitoring adhered to guideline recommendations.

References

1. Curno MJ, Rossi S, Hodges-Mameletzis I, Johnston R, Price MA, Heidari S, *et al.* A systematic review of the inclusion (or exclusion) of women in HIV research: from clinical studies of antiretrovirals and vaccines to cure strategies. J Acquir Immune Defic Syndr. 2016;71(2):181-188.
2. Dhanireddy S, Baeten JM. Tenofovir alafenamide for HIV: time to switch? Lancet Infect Dis. 2016;16(1):3-5.