BONE AND RENAL OUTCOMES IN VIROLOGICALLY CONTROLLED ADOLESCENTS SWITCHING TO TDF

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BACKGROUND

- Tenofovir disoproxil fumarate (TDF) is included in first line regimens for adolescents living with HIV (ALWH), however associated bone and renal toxicity are concerning.
- TDF used in combination for treatment-naïve ALWH or those with treatment failure is associated with decreased bone mass.
- Whether switching to TDF causes decreased bone accrual or bone loss in virologically controlled ALWH is not well established.

METHODS

- We recruited 50 adolescents that were switched from abacavir (ABC)-based to TDF-based efavirenz regimen.
- Eligibility criteria included:
  - 15 – 20 years
  - Tanner stage ≥ 4
  - Weight ≥ 40 kg
  - Viral load (VL) < 100 copies/ml
  - No evidence of kidney or liver disease
- The following were measured at enrolment (switch) and week 24 after switch to TDF:

Bone Parameters

- Lumbar Spine (LS) and Total Body (TB) bone mineral content (BMC) and bone mineral density (BMD) by dual energy xray absorptiometry
- Bone formation (P1NP) and resorption (CTX) markers

Renal Parameters

- Serum creatinine
- eGFR by Revised Schwartz Equation (2009)
- Urine protein/creatinine ratio
- Fractional excretion of phosphate
- Urine β2-microglobulin (B2M)/creatinine ratio

- Change in LS and TB BMD and Z-scores at 24 weeks and eGFR were assessed by paired t-tests, stratified by sex.

Switch to TDF in virologically controlled adolescents with HIV did not result in clinically significant changes in BMD, bone turnover or renal markers.

However, female adolescents with HIV may require closer BMD monitoring.

RESULTS

Demographics at Switch

- All perinatally HIV-infected; 48% M; 52% F.
- Mean age (range): 15.8 (15-19.9) overall; 15.8 (15-19.9) for M; 15.7 (15.0-17.9) for F.
- All currently on ART, median duration of 11.4 years.
- 6 (12%) had prior AIDS-defining illness.
- Median CD4 count: 732 cells/mm^3 (IQR: 540-990).
- 38 (76%) had a VL <50 copies/ml.
- 3 (6%) thin by WHO BMI-for-age charts.
- 5 (10%) overweight by WHO BMI-for-age charts.

24-week results: Bone Parameters

- 47/50 participants had 24-week DXA results.
- 15/47 (32%) had no change or decreased LS BMD after switch; with a mean change of -1.6%. 14/15 (93%) of these participants were female.
- Overall, a greater proportion of females than males had either no change or decreased LS BMD (58% vs. 4%, p<0.0001).
- No significant changes in CTX or P1NP were observed.

24-week results: Renal Parameters

- Statistically significant increase in serum creatinine from 46.2 to 50.7 µmol/L (p<0.0001).
- Statistically significant decrease in eGFR from 132.2 to 120.4 mL/min (p=0.0003).

Table 1: BMD, renal function, and bone turnover measurements at switch and week 24 after switch to TDF

Measurement	Switch, Mean (SD)	24 Weeks, Mean (SD)	P-value (paired t-test)	Change (SD)
LS BMD Z-score	-1.22 (1.36)	-1.24 (1.30)	0.48	-0.03 (0.25)
TB BMD Z-score	-1.02 (1.09)	-0.99 (1.08)	0.50	0.02 (0.24)
Serum creatinine (µmol/L)	46.2 (10.2)	50.7 (10.2)	<0.0001	4.5 (6.4)
eGFR (mL/min)	132.2 (29.3)	120.4 (25.3)	0.0003	-11.9 (21.6)
CTX (ng/ml)	1.12 (0.72)	1.09 (0.74)	0.64	-0.03 (0.46)
P1NP (ng/ml)	165.0 (83.8)	158.2 (82.5)	0.40	-6.8 (56.6)

CONCLUSIONS

- South African ALWH switching from ABC to TDF experienced no overall change in BMD, but had decreases in eGFR that were statistically, but not clinically significant.
- However, 32% of adolescents had either no change or decrease in LS BMD, at an age when bone acquisition is critical. The majority of cases (93%) occurred in women.
- Female adolescents living with HIV may require closer BMD monitoring when switching to TDF-containing regimens.

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