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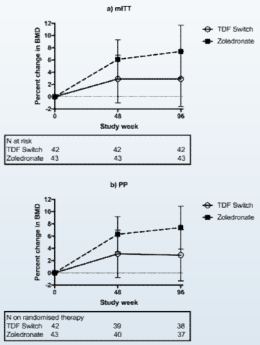
Greater Bone Turnover Marker Decline with Zoledronic Acid than with TDF Switching

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Introduction

- **Zoledronic acid (ZOL) 5mg annually was more effective than switching tenofovir disoproxil fumarate (TDF) at increasing bone mineral density (BMD) over 96 weeks in HIV+ adults with low bone mass (IAS 2017)**
- **The relative effects of ZOL vs. TDF-switching on plasma bone turnover markers (BTMs) are unknown**
- **Also unclear if TDF causes bone loss by reducing bone formation or increasing bone resorption**



Methods

- **BTMs measured** were plasma
  - C-terminal telopeptide of type 1 collagen (CTX), a marker of bone resorption
  - procollagen type 1 N propeptide (P1NP), a marker of bone formation
- Percent changes in CTX and P1NP were compared in the per-protocol population at
  - Weeks 4, 12, 24, 48 and 96 with a Wilcoxon test
  - over all follow-up with Generalised Estimating Equation (GEE)
- We also determined whether BTM changes at Week 12 across both groups combined predicted hip and spine BMD changes at Week 96 (Pearson's correlation coefficient)

Results

BTM changes

- **Median percent decreases in both BTMs were significantly greater with ZOL than with TDF-switch through Week 96 by GEE and at each time point (all p<0.001; see *Figure*) e.g., at Week 48 the median (IQR) changes for ZOL vs. TDF-switch groups were:**

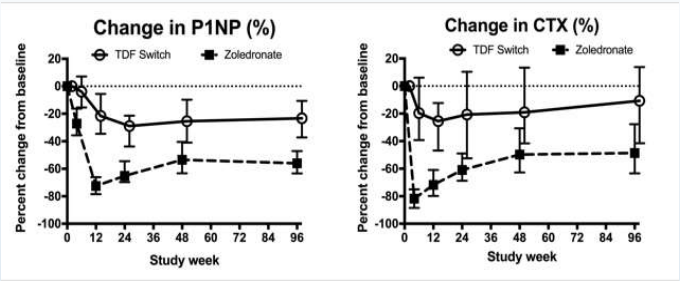
Intervention	P1NP	CTX
ZOL (n=41)	-54% (-41%, -63%)	-50% (-31%, -63%)
TDF switch (n=42)	-25% (-10%, -41%)	-19% (+13%, -42%)

Correlation of BTM changes and BMD changes

- **P1NP decreases at Week 12 were more strongly correlated with increases in BMD at Week 96 than the decreases in CTX**

Region	P1NP	CTX
Spine	r^2=-0.44; p<0.001	r^2=-0.36; p=0.001
Hip	r^2 =-0.45; p<0.001	r^2=-0.23; p=0.051

- **In subjects who switched TDF, the Wk-4 decrease in CTX was -19.7% (IQR -39.2%, +6.1%) but the change for P1NP was only -4.0% (-15.4%, +7.1%)**



Conclusions

- **ZOL resulted in larger decreases in markers of bone turnover than did TDF-switching**
- **Declining bone turnover with TDF-switch suggests that TDF reduces BMD by increasing bone turnover**
- **Early changes in P1NP predicted BMD changes at 96 weeks with both ZOL and TDF-switching**
- **Following TDF switch, CTX reductions (bone resorption) tended to precede P1NP reductions (bone formation)**

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