Introduction

- Tenofovir Disoproxil Fumarate – Emtricitabine (TDF-FTC), a commonly prescribed medication for pre-exposure prophylaxis (PrEP), is associated with a reduced risk of HIV infection.
- Clinical trials have shown that once daily oral PrEP with TDF-FTC reduces the risk of HIV infection in heterosexual men, transgender women, men who have sex with men, and people who inject drugs.
- There is conflicting evidence on whether or not TDF-FTC, along with the initiation of other types of anti-retroviral therapy is associated with a reduction in bone mineral density.
- Is the risk of osteopenia/osteoporosis a dose dependent phenomenon?

Objectives

- To address the risk of osteopenia or osteoporosis in a real life setting for patients on TDF-FTC therapy for PrEP.
- To address the breakthrough incidence of HIV in patients with relation to TDF-FTC adherence.

Study Definitions

- Osteopenia/Osteoporosis: DEXA scan T-score of S-1
- Proportion of Days Covered (PDC), a measure of adherence: \( \frac{\# \text{ of days supply}}{\# \text{ of follow-up days}} \times 100\% \)

Inclusion Criteria

- Kaiser Permanente Southern California members with at least 1 year of membership before the most recent treatment episode.
- Patients of 18 years of age or older on TDF-FTC therapy for PrEP between 2012 and 2020 with no prior history of bone loss.
- Must have DEXA scan during the study period.

Exclusion Criteria

- Patients who were HIV positive prior to therapy.
- Pregnant patients.
- Patients on TDF-FTC for reasons besides PrEP.
- Patients with history of T-score S-1.

Methods

- IRB approved retrospective cohort study (N = 7,698).
- Patient charts dated from January 2012 to December 2020 were extracted and reviewed using Epic/HealtheConnect electronic medical record system at Kaiser Permanente.
- POC is measured from the index date (start date of most recent PrEP episode (plus 60 days), whichever comes first.
- Age, sex, race, HIV status, T-scores from DEXA scan, proportion of days covered, diagnosis of Hepatitis B and C, diabetes mellitus, cardiovascular disease, chronic kidney disease, and hypertension, baseline eGFR value, and body mass index (BMI) were extracted from the electronic health records.
- Osteopenia/Osteoporosis was defined as any T-score ≤ -1 during the follow-up period.
- Descriptive statistics was used to compare patient characteristics between those with and without osteopenia/osteoporosis during follow-up.
- Time to the first incidence of osteopenia/osteoporosis was modeled using a Cox proportional hazards model, with PDC and other baseline patient characteristics included as covariates.
- Kaplan-Meier curve demonstrated a significant decrease in event-free rate of any osteopenia or osteoporosis in patients with PDC 90-100% to be at significant risk for osteopenia/osteoporosis (Table 2).
- When adjusted for all covariates, the adjusted HR only showed osteopenia/osteoporosis in patients with POC 90-100% to be at significant risk for osteopenia/osteoporosis (Table 2).
- No incidence of HIV infection was detected in the sample population.

Highlights

- High adherence of TDF-FTC (90% and greater) was significantly associated with an increase in the incidence of osteoporosis and osteopenia.
- TDF-FTC confers high protection against HIV infection.
- Counseling on the incidence of osteoporosis/osteopenia and routine screening should be conducted on patients initiated on TDF-FTC.
- Future studies should explore the utilization of on-demand TDF-FTC therapy for PrEP in lieu of continuous therapy to potentially mitigate the risk of serious adverse effects.

Results

- Of 7,698 patients, 217 developed osteopenia or osteoporosis (T-score ≤ -1).
- Average follow-up time for the cohort is 502.6 days.
- Patients in a PDC category of 90-100% (90.8%) were more likely to develop osteopenia/osteoporosis compared to patients in a PDC category below 90% (9.2%) (p<0.001).
- Kaplan-Meier curve demonstrated a significant decrease in event-free rate of any osteopenia or osteoporosis development in 6.5 years after the start of the most recent TDF-FTC episode in patients with POC of 90-100% (86.3%) vs. POC <90% (94.3%) (p<0.001) (Figure 1).
- Unadjusted survival analysis showed significantly higher hazard ratios for the risk of osteopenia/osteoporosis in patients with POC 90-100%, Hep B, CVD, CKD, HTN, and baseline eGFR < 90 mL/min/1.73 m² (Table 1). When adjusted for all covariates, the adjusted HR only showed patients with POC 90-100% to be at significant risk for osteopenia/osteoporosis (Table 2).
- No incidence of HIV infection was detected in the sample population.

Conclusion

- A correlational relationship between TDF-FTC adherence and incidence of osteoporosis/osteopenia was observed.
- Hepatitis B, CVD, CKD, age, baseline eGFR<90 mL/min/1.73 m² and BMI were not associated with an increase in the risk of osteopenia/osteoporosis after adjusting for other confounders.
- Obesity conveyed a protective effect on the incidence of osteopenia/osteoporosis.
- This study was able to confirm that TDF-FTC is highly effective against HIV infection even with low adherence rate patients.

References

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