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Changes in LDL After Switch from TDF to TAF in the U.S.

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Background

- Since TAF was approved in the US in late 2015, switches from TDF to TAF have been common in virologically suppressed people living with HIV (PLWH)
- Compared to TDF, TAF has been associated with lower risk of bone and renal toxicity[1]
- TDF has been reported to be associated with reduction in lipid levels, including in the OPERA cohort[2]
- The long-term impact on lipids of switching from TDF to TAF remains unclear in real-world clinical practice

Objective

To assess changes in LDL over time following a switch from TDF to TAF

Methods

Study population

- Data source: OPERA database of electronic health records from 93,170 PLWH (84 clinics, 18 U.S. states/territories)
- Inclusion Criteria:
  - HIV-positive, ≥18 years of age
  - On TDF ≥4 weeks, switched directly from TDF to TAF between 5NOV2015 and 31MAR2018
  - ≥1 lipid panel while on TDF ≤6 months before switch
  - ≥1 lipid panel at any time while on TAF
- Follow-up from TDF-to-TAF switch until 1) discontinuation of TAF, 2) cessation of continuous clinical activity (patients censored 12 months after their last contact), 3) death or 4) study end (30JUN2018)

Analyses

- Predicted changes in LDL over time after switch from TDF to TAF in:
  - All PLWH included in the study (All switches)
  - PLWH without changes in ART other than the TDF-to-TAF switch (Maintained other ARVs)
- Multivariable linear regression with generalized estimating equations (GEE), autoregressive correlation structure
- Linear splines on months of TAF use (knots at 3, 9, 16 months)

Results

Figure 1. OPERA sites and HIV burden in the U.S. (CDC estimates)

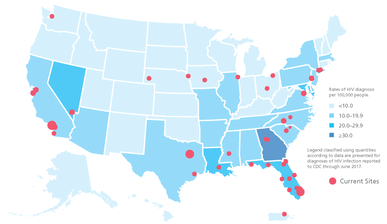
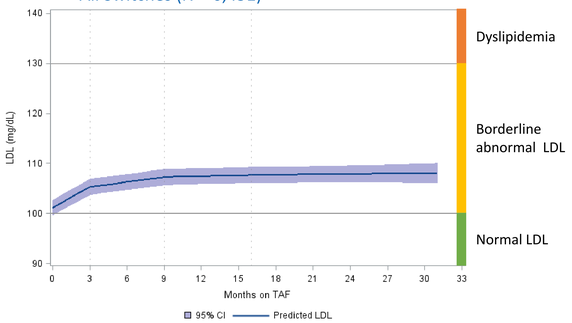


Table 1. Demographic and Clinical Characteristics at TDF-to-TAF Switch

	All switches N = 6,451	Maintained other ARVs N = 4,328
Months on TDF pre-switch, median (IQR)	29 (14, 52)	28 (14, 46)
Age, median (IQR)	48 (38, 55)	47 (37, 54)
Female, n (%)	1,010 (16)	674 (16)
HIV viral load ≥50 copies/mL, n (%)	1,103 (17)	620 (14)
PI use, n (%)	1,272 (20)	815 (19)
Boosting agent use, n (%)	4,019 (62)	2,520 (58)
Hormone use, n (%)	554 (8)	372 (9)
Statin use, n (%)	1,112 (17)	732 (17)
Non-statin lipid lowering agent use*, n (%)	425 (7)	267 (6)

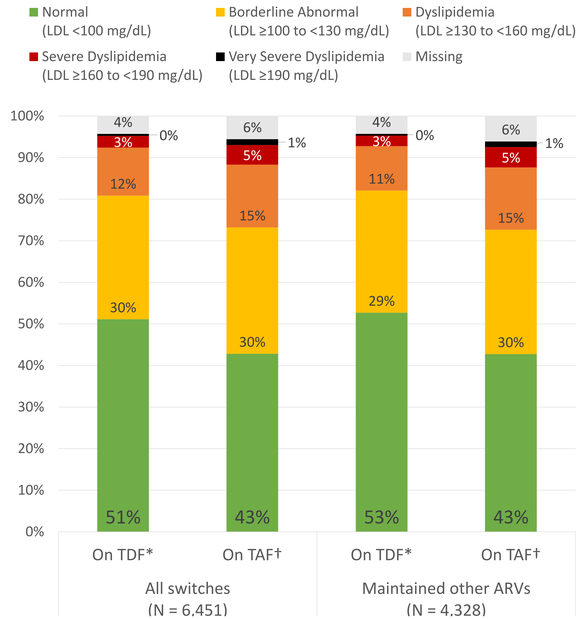
* Omega-3, fibrate, etc.

Figure 3. Adjusted Predicted LDL* Over Time After TDF-to-TAF Switch, All Switches (N = 6,451)



* Predicted LDL values over time on TAF for PLWH with specific characteristics at baseline (LDL: 98, age: 45, sex: male, months on TDF: 24) and throughout follow-up (VL: <50, hormones: none, statins: none, non-statins lipid lowering agents: none, boosting agent: none, PI: none)

Figure 2. LDL-Based NCEP ATP III Dyslipidemia Categorization Before and After TDF-to-TAF Switch



* Measured at the last lipid panel on TDF
† Measured at the first lipid panel on TAF

Table 2. Rates* of Change in LDL Over Time After TDF-to-TAF Switch (mg/dL/month)

Time after TDF-to-TAF switch	All switches N = 6,451 mg/dL/month (95% CI)	Maintained other ARVs N = 4,328 mg/dL/month (95% CI)
0-3 months	+1.40 (1.19, 1.60)	+1.72 (1.47, 1.96)
3-9 months	+0.33 (0.20, 0.46)	+0.27 (0.11, 0.42)
9-16 months	+0.06 (-0.05, 0.16)	+0.10 (-0.03, 0.23)
16+ months	+0.03 (-0.07, 0.12)	-0.00 (-0.11, 0.11)

* Estimated from a multivariable linear regression adjusted for baseline LDL, age, months on TDF and sex; time-updated HIV viral load ≥50 copies/mL, and use of hormones, statins, non-statin lipid lowering agents, PI and boosting agent

Discussion

- Switching from TDF to TAF was associated with worsening LDL in this large, diverse population of PLWH in the U.S. (Fig 1)
  - Consistent with previous TDF-to-TAF switch studies[2]
- Average predicted LDL levels increased over time after a switch from TDF to TAF (Fig 2-3, Table 2)
  - First 3 months on TAF: Statistically significant increase in LDL (1.40 mg/dL per month)
  - 3 to 9 months on TAF: Slower, statistically significant increase in LDL (0.33 mg/dL per month)
  - >9 months: No statistically significant changes in LDL over time
- Similar trends observed with all TDF-to TAF switches and when maintaining other ARVs
  - Observed LDL increases cannot be attributed to changes in other ARVs (Fig 2, Table 2)

Key Findings

- After adjusting for confounding, TDF-to-TAF switch was associated with an overall increase in LDL over the first 9 months on TAF with a plateau at higher LDL levels beyond 9 months
- No return to baseline LDL levels
- Results consistent whether or not other ARVs were maintained

References

1. Wang H, Lu X, Yang X, Xu N. The efficacy and safety of tenofovir alafenamide versus tenofovir disoproxil fumarate in antiretroviral regimens for HIV-1 therapy: Meta-analysis. Medicine 2016; 95(41): e5146-e.
2. Mallon P, Brunet L, Fusco J, et al. Changes in Lipids After a Direct Switch from TDF to TAF. In: CROI Conference on Retroviruses and Opportunistic Infections. Seattle, WA, 2019.

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