Poster #341

Risk of type-2 diabetes mellitus after initiating integrase and protease inhibitors in individuals living with HIV in the United States

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Background

- People living with HIV (PLWH) on antiretroviral therapy (ART) have a higher prevalence and incidence of type 2 diabetes mellitus (T2DM) than HIV negative individuals[1]
- T2DM incidence rates among PLWH range from 4 to 36 cases per 1,000 person-years[2]
- Protease inhibitors (PI) and nucleoside reverse transcriptase (NRTI) may be associated with an increased risk of T2DM[2]
- Limited data exist on the risk of T2DM with the use of integrase inhibitors

OBJECTIVE

To assess the risk of incident T2DM after initiation of DTG, EVG/c, RAL or bDRV in a large real-world population of PLWH in care in the US

Methods

Study population

- OPERA cohort
  - » Prospectively captured, routine clinical data from electronic health records in the US (84 clinics, 17 states, 1 US territory)
  - » ~7% of PLWH in care in the US
- Inclusion criteria
  - » HIV positive, ≥13 years of age
  - » Initiating DTG, RAL, EVG/c or bDRV for the first time between 01Aug2013 and 31Mar2018
  - » Exposed to only 1 core agent of interest
  - » Either ART-naïve or ART-experienced suppressed
  - » No prevalent T1DM, prediabetes or T2DM
- Observation period from core agent initiation until the first censoring event:
  - » Core agent discontinuation
  - » ≥ 12 months without contact
  - » Death
  - » Study end (30Sep2018)

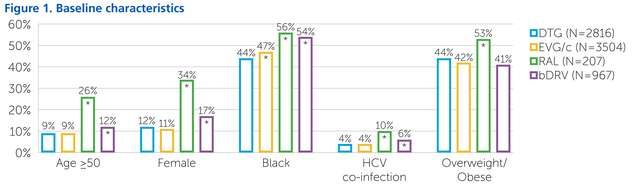
Statistical analyses

- T2DM incidence rates (IR)
  - » T2DM defined as a diagnosis of T2DM, and/or prescription of antidiabetic drug, and/or HbA1C > 6.5%
  - » Poisson regression
- Association between core agents and incident T2DM
  - » Multivariate Cox proportional hazards regression
  - » Adjusted for baseline age, sex, race, HCV co-infection and BMI
- Median (IQR) absolute BMI change from baseline
  - » Evaluated at 6, 12, 18, and 24 months, ±3 months
  - » Compared between PLWH who developed incident T2DM or not
  - » Among PLWH with weight measurement both at baseline and the time point of interest
- Stratification by ART experience
  - » ART-naïve PLWH: no known history of ART and baseline HIV viral load ≥1,000 copies/mL
  - » ART-experienced suppressed PLWH: baseline viral load <50 copies/mL with or without known history of ART

Results:

ART-Naïve PLWH (N=7494)

Figure 1. Baseline characteristics



*p-value <0.05 for the comparison with DTG

Figure 2. Incidence rates of T2DM per 1,000 person-years (95% CI)

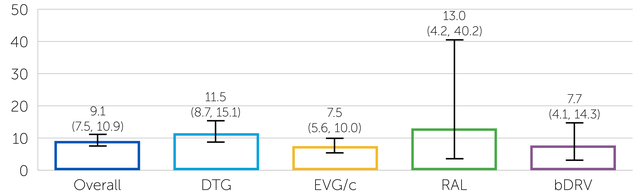
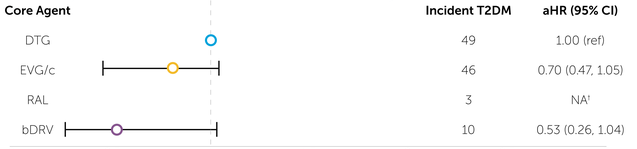
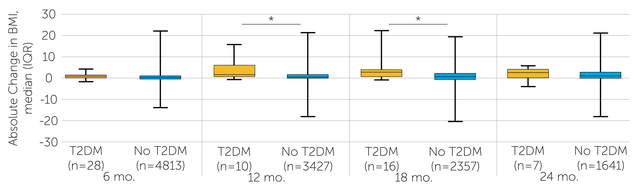


Figure 3. Adjusted hazard ratios* for the association between core agent and T2DM



*Obtained from Cox proportional hazards models adjusted for baseline age, sex, race/ethnicity, HCV co-infection and BMI
†RAL excluded from model due to the small number of incident T2DM

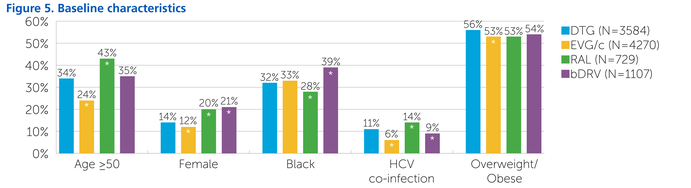
Figure 4. Overall changes in BMI from baseline to specific time points during follow-up†



*p-value <0.05
†Among those with a BMI measured both at baseline and at the time point of interest (±3 months)

ART-Experienced Suppressed PLWH (N=9704)

Figure 5. Baseline characteristics



*p-value <0.05 for the comparison with DTG

Figure 6. Incidence rates of T2DM per 1,000 person-years (95% CI)

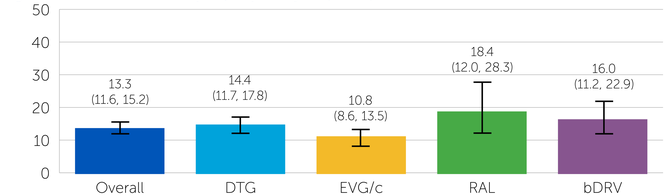
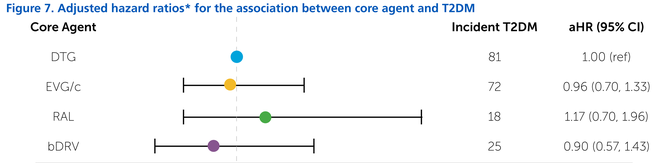
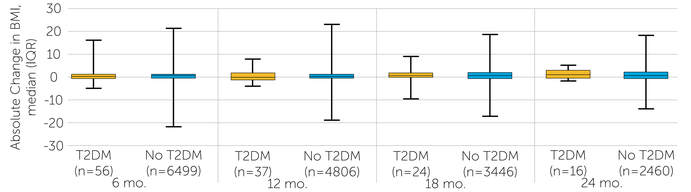


Figure 7. Adjusted hazard ratios* for the association between core agent and T2DM



*Obtained from Cox proportional hazards models adjusted for baseline age, sex, race/ethnicity, HCV co-infection and BMI

Figure 8. Overall changes in BMI from baseline to specific time points during follow-up†



*p-value <0.05 for the comparison with DTG
†Among those with a BMI measured both at baseline and at the time point of interest (±3 months)

Discussion

- Incident T2DM was uncommon among ART-naïve and ART-experienced suppressed PLWH
- No statistically significant difference in T2DM risk between DTG and other core agents in ART-naïve or ART-experienced suppressed PLWH
- Among ART-naïve PLWH, those who developed T2DM tended to have gained more weight than those without T2DM, although median absolute weight change was small in both groups, ranging from +0.5 to +3.0 kg/m²
- Among ART-experienced suppressed PLWH, the magnitude of weight gain appeared comparable in those who developed T2DM and those who didn't
- Limitations
  - » Due to the small number of incident T2DM event in ART-naïve PLWH, differential risk cannot be excluded
  - » Impact of weight gain after ART initiation on risk of T2DM remains to be assessed
  - » RAL prescription was less common in the US during the study period, resulting in small sample sizes and a reduced likelihood of observing rare events

KEY FINDINGS

- No association between T2DM risk and core agent initiation was observed in ART-naïve and ART-experienced suppressed PLWH
- Cannot exclude possible differential risk in ART-naïve PLWH due to low T2DM incidence; monitoring HbA1c remains prudent

References

1. Maseko TS, Masuku SK. The Effect of HIV and ART on the Development of Hypertension and Type 2 Diabetes Mellitus. Journal of Diabetes and Metabolism 2017; 8(3): 1000732.
2. Nigatu T, Oldenburg B, Elliott J, Setswe G, Woldegiorgis MA. The incidence of cardiovascular disease, cancer and type 2 diabetes comorbidities in HIV infection: A systematic review. Journal of Nursing Education and Practice 2013; 3(7): 58-67.

Acknowledgements

This research would not be possible without the generosity of people living with HIV and their OPERA caregivers. Additionally, we are grateful for the following individuals: Robin Beckerman (SAS programming), Jeff Briney (QA), Bernie Stooks (Database Arch & Mgmt), Judy Johnson (Med Terminology Classification), Rodney Mood (Site Support), & Antonin Fusco (Poster Design).

Support

This research was sponsored by ViiV Healthcare.

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