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The following guiding principles have been applied to the disclosure:

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- *Patient data listings will be completely removed* to protect patient privacy. Anonymized data from each patient may be made available subject to an approved research proposal. For further information please see the Patient Level Data section of the* ***GSK Clinical Study Register****.*
- *Aggregate data will be included; with any direct reference to individual patients excluded*

**Complete removal of patient data listings may mean that page numbers are no longer consecutively numbered*

Dolutegravir use and incidence of prediabetes and type 2 diabetes mellitus:

Final Study Report

Study Report: July 20, 2019

OPERA Build: December 04, 2018

Effective Date: October 07, 2019

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I have read this report and confirm that to the best of my knowledge this report accurately describes the conduct and results of study [209368].

PPD

Aug 21, 2019

Cassidy Henegar
Primary Author/ Project officer

Date

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1. Executive Summary

Background

Prevalence of T2DM among HIV-positive individuals has been estimated to be between 5-14%[1-4] in the United States and between 2-9%[4-7] in other Western countries. Incidence rates of T2DM among HIV-positive patients range from 11-47 cases/1,000 person-years in the United States[2,10-13] to 3-16 cases/1,000 person-years in other Western countries. Exposure to ART has been associated with an increased risk of incident T2DM in HIV patients, particularly when cumulative exposure is considered.[5,7,18] To date, very little research has been conducted on the association between INSTIs and potential risk of DM.

A signal evaluation for hyperglycemia and diabetes mellitus with DTG use was conducted, following a raised disproportionality (DPA) score and case reports of incident diabetes and hyperglycemia among patients taking DTG identified through routine pharmacovigilance monitoring. After evaluating clinical trial data and post-marketing data, the strength of evidence was insufficient to show a causal association between DTG and hyperglycemia or T2DM. This analysis, utilizing data from a large real-world population of treated HIV patients, will provide additional information to support the signal evaluation.

Primary Objectives

1) To assess the baseline prevalence of prediabetes and T2DM among new users of DTG, RAL, EVG/c and DRV(/r/c)
2) To assess the incidence rate of prediabetes and T2DM over follow-up among new users of DTG, RAL, EVG/c and DRV(/r/c) without prevalent prediabetes or T2DM
3) To estimate the association between core agent initiation (DTG vs. RAL, EVG/c or DRV(/r/c)) and development of T2DM among new users of DTG, RAL, EVG/c and DRV(/r/c) without prevalent prediabetes or T2DM

Secondary Objectives

1) To compare baseline patient characteristics between patients who developed T2DM and those who did not among new users of DTG, RAL, EVG/c and DRV(/r/c) without prevalent prediabetes or T2DM
2) To describe HbA1c levels and fasting glucose at core agent initiation and after 6, 12, 18 or 24 months on core agent among new users of DTG, RAL, EVG/c and DRV(/r/c) with prevalent T2DM
3) To describe HbA1c levels and fasting glucose at core agent initiation and after 6, 12, 18 or 24 months on core agent among new users of DTG, RAL, EVG/c and DRV(/r/c) with incident T2DM

Exploratory Objective

1) To compare weight gain at 6, 12, 18 or 24 months after core agent initiation between patients with and without an incident T2DM diagnosis during their follow-up, stratified by core agent, among new users of DTG, RAL, EVG/c and DRV(/r/c) without prevalent prediabetes or T2DM

Methods

Study populations

A total of four distinct study populations were identified from the OPERA Observational Database. All study populations were derived from Population 1, which included HIV-positive patients aged 13 years or older, never diagnosed with type 1 or juvenile DM, initiating DTG, RAL, EVG/c or DRV(/r/c) for the first time between 01AUG2013 and 31MAR2018, not exposed to >1 core agent of interest concurrently and with baseline viral load available. Patients were observed from their index date (core agent initiation) until the first of the following censoring events: a) discontinuation of the core agent of interest, b) loss to follow up (i.e. any 12-month period in which no clinical contact is made), c) death, d) study end (30SEP2018). Population 1 consisted of all patients meeting the inclusion criteria listed above; Population 2 consisted of patients without prevalent prediabetes or T2DM at baseline; Population 3 consisted of patients with prevalent prediabetes or T2DM at baseline; and Population 3 consisted of those in Population 2 who developed incident T2DM during follow-up. Study populations were stratified by prior ART experience at core agent initiation as ART-naïve (no history of ART and baseline HIV viral load ≥1,000 copies/mL) or ART-experienced (history of ART, or baseline HIV viral load <1,000 copies/mL). ART-experienced patients were further stratified by baseline viral load as ART-experienced/suppressed (baseline viral load <50 copies/mL) or ART-experienced/viremic (baseline viral load ≥50 copies/mL).

Outcomes definitions

Prediabetes was defined as either a diagnosis of prediabetes or two any labs indicative of prediabetes, measured at least 90 days apart (HbA1c ≥5.7% to <6.5%, fasting plasma glucose ≥100 mg/dl to <126 mg/dl (grade 1), or oral glucose tolerance test ≥140 mg/dl to <200 mg/dl. T2DM was defined as either a diagnosis of T2DM/non-insulin-dependent diabetes (NIDDM), an antidiabetic prescription, or a labe indicative of T2DM (HbA1c ≥6.5%, fasting plasma glucose ≥126 mg/dl, or oral glucose tolerance test ≥200 mg/dl).

Statistical analyses

Baseline demographic and clinical characteristics were described using medians and interquartile ranges or absolute and relative frequencies (Pop 2). Pairwise comparisons between DTG and each of the other core agent groups was evaluated by p-values calculated from Pearson Chi-Square test, Fisher's exact test or Wilcoxon Rank Sum test as appropriate. Baseline characteristics were also compared between patients who did or did not develop incident T2DM during follow-up (Pop 2)

The prevalence of prediabetes and T2DM were calculated as the proportion of patients with prediabetes or T2DM within 12 months before or on baseline (Pop 1). The incidence rates of prediabetes and T2DM over follow-up were assessed with Poisson regression, by core agent used among patients without prediabetes or T2DM at baseline (Pop 2). A Cox proportional hazards models were used to assess the presence of an association between core agent use and T2DM, adjusted for baseline age, sex, race, HCV co-infection and BMI (Pop 2).

HbA1c and fasting glucose were described categorical and as absolute and percent change from baseline to predefined follow-up times (6, 12, 18 and 24 months) among patients with prevalent prediabetes/T2DM (Pop 3) or those with incident T2DM (Pop 4).

Weight gain at 6, 12, 18 and 24 months was described as the absolute increase in BMI, as well as categorically, and compared between patients with and without incident T2DM during follow-up for each core agent (Pop 2). Inverse probability of treatment weights will be used to fit marginal structural Cox models to assess the relative hazard of incident T2DM during exposure to DTG (vs. RAL, EVG/c, and DRV(/r/c)), while accounting for potential confounding and mediation by weight gain (Pop 2).

Results

ART-NAÏVE:

Out of 29,674 patients included in Population 1, 8,489 were ART-naïve (3234 DTG, 3906 EVG/c, 241 RAL, 1108 DRV(/r/c)). Prevalence of prediabetes was lower with EVG/c (7.7%, p=0.01) but no different with RAL (8.3%, p=0.58) or DRV(/r/c) (9.1%, p=0.80), compared to DTG (9.4%) (Figure 1). Prevalence of T2DM was also lower with EVG/c (3.1%, p=0.02) but no different with RAL (6.6%, p=0.07) or DRV(/r/c) (4.2%, p=0.99), compared to DTG (4.1%).

There were 7,494 ART-naïve patients without prevalent prediabetes/T2DM in Population 2 (2,816 DTG, 3,504 EVG/c, 207 RAL, 967 DRV(/r/c)). Compared to DTG, EVG/c users were less likely to be underweight; RAL users were older, and more likely to be female, obese and HCV co-infected; DRV(/r/c) users were older, and more likely to be female, non-Hispanic Black, and HCV co-infected. There was no difference in the unadjusted incidence rate of prediabetes per 1000 person-years between DTG (IR: 23, 95% CI: 19, 28) and EVG/c (IR: 21, 95% CI: 17, 25), RAL (IR: 13, 95% CI: 4, 39) or DRV(/r/c) (IR: 20, 95% CI: 13, 29). Similarly, there was no difference in the unadjusted incidence rate of T2DM between DTG (IR: 11, 95% CI: 9, 15), EVG/c (IR: 7, 95% CI: 6, 10), RAL (IR: 13, 95% CI: 4, 40), or DRV(/r/c) (IR: 8, 95% CI: 4, 14). After adjustments for baseline age, sex, race, HCV co-infection and BMI, no statistically significant association was found between core agents and incident T2DM for EVG/c (aHR: 0.70, 95% CI: 0.47, 1.05) or DRV(/r/c) (aHR: 0.53, 95% CI: 0.26, 1.04) when compared to DTG. RAL was excluded from the model due to the small number of events in this group (n=3). Compared to patients who remained free of T2DM during follow-up, those with incident T2DM were older, and more likely to be female and overweight or obese at baseline. The absolute BMI change was larger among patient with incident T2DM at 12 months and 18 months, compared to those without incident T2DM. Pooled logistic regression with inverse probability of censoring weighting (IPCW) yielded comparable results for EVG/c (aOR: 0.76, 95% CI: 0.49, 1.12) and DRV/r/c (aOR: 0.54, 95% CI: 0.27, 1.07).

There were 995 ART-naïve patients with prevalent prediabetes/T2DM at baseline in Population 3 (418 DTG, 402 EVG/c, 34 RAL, 141 DRV(/r/c)). The absolute and percent decrease in HbA1c was greater among DRV(/r/c) users than DTG users at 12 months only. Fasting glucose was measured too infrequently to evaluate.

There were 326 ART-naïve patients with incident prediabetes/T2DM during follow-up in Population 4 (133 DTG, 155 EVG/c, 5 RAL, 33 DRV(/r/c)). HbA1c and fasting glucose were measured too infrequently evaluate.

<u>ART-experienced/suppressed</u>

There were 12,322 ART-experienced/suppressed patients in Population 1 (4,747 DTG, 5,243 EVG/c, 962 RAL, 1,370 DRV(/r/c)). Prevalence of prediabetes was lower with EVG/c (13.3%, p<0.01), RAL (11.1%, p<0.01) and DRV(/r/c) (11.5%, p<0.01), compared to DTG (17.9%). However, while the prevalence of

T2DM was also lower with EVG/c (7.7%, p<0.01), it was higher with RAL (16.8%, p<0.01) and no different with DRV(/r/c) (10.9%, p=0.53), compared to DTG (10.4%).

There were 9,704 ART-experienced/suppressed patients without prevalent prediabetes/T2DM in Population 2 (3,584 DTG, 4,281 EVG/c, 730 RAL, 1,109 DRV(/r/c)). Compared to DTG, EVG/c users were younger, and less likely to be female or HCV co-infected; RAL users were older, and more likely to be female, non-Hispanic White and HCV co-infected; DRV(/r/c) users were more likely to be female, overweight or obese, and less likely to be HCV co-infected. There was no difference in the unadjusted incidence rate of prediabetes per 1000 person-years between DTG (IR: 39, 95% CI: 35, 45) and RAL (IR: 33, 95% CI: 24, 45) or DRV(/r/c) (IR: 28, 95% CI: 21, 36), but it was lower with EVG/c (IR: 25, 95% CI: 21, 29) than DTG. However, there was no difference in the unadjusted incidence rate of T2DM between any core agents: DTG (IR: 14, 95% CI: 12, 18), EVG/c (IR: 11, 95% CI: 9, 14), RAL (IR: 18, 95% CI: 12, 28), or DRV(/r/c) (IR: 16, 95% CI: 11, 23). After adjustments for baseline age, sex, race/ethnicity, HCV co-infection and BMI, no statistically significant association was found between core agents and incident T2DM for EVG/c (aHR: 0.96, 95% CI: 0.70, 1.33), RAL (aHR: 1.17, 95% CI: 0.70, 1.96) or DRV(/r/c) (aHR: 0.90, 95% CI: 0.57, 1.42), compared to DTG. Compared to patients who remained free of T2DM during follow-up, those with incident T2DM were older, and more likely to be obese at baseline. There was no difference in absolute BMI change between patient with or without incident at any of the time points evaluated. In an inverse probability of censoring weighted pooed logistic regression analysis, there was no association between risk of T2DM and core agent when comparing EVG/c to DTG (aOR: 0.95, 95% CI: 0.68, 1.32), RAL to DTG (aOR: 0.94, 95% CI: 0.53, 1.70) and bDRV to DTG (aOR: 0.97, 95% CI: 0.61, 1.54)

There were 2,618 ART-experienced/suppressed patients with prevalent prediabetes/T2DM at baseline in Population 3 (1,163 DTG, 962 EVG/c, 232 RAL, 261 DRV(/r/c)). HbA1c and fasting glucose were measured too infrequently evaluate.

There were 616 ART-naïve patients with incident prediabetes/T2DM during follow-up in Population 4 (285 DTG, 214 EVG/c, 49 RAL, 68 DRV(/r/c)). The median absolute and percent increase in HbA1c was larger with RAL than DTG at 18 and 24 months. Fasting glucose was measured too infrequently evaluate.

ART-experienced/viremic

There were 8,863 ART-experienced/viremic patients in Population 1 (3,415 DTG, 3,633 EVG/c, 412 RAL, 1,403 DRV(/r/c)). Prevalence of prediabetes was lower with EVG/c (9.6%, p<0.01), RAL (8.5%, p<0.01) and DRV(/r/c) (11.0%, p=0.01), compared to DTG (13.6%). However, while the prevalence of T2DM was also lower with EVG/c (5.3%, p<0.01), it was higher with RAL (11.2%, p<0.01) and no different with DRV(/r/c) (8.2%, p=0.21), compared to DTG (7.1%).

There were 13,703 ART-experienced/viremic patients without prevalent prediabetes/T2DM in Population 2 (2,787 DTG, 3,140 EVG/c, 338 RAL, 1,162 DRV(/r/c)). Compared to DTG, EVG/c users were younger, and less likely to be female or HCV co-infected; RAL users were older, and more likely to be female and HCV co-infected, and less likely to be non-Hispanic Black; DRV(/r/c) users were older, and more likely to be female, non-Hispanic Black and HCV co-infected. There was no difference in the unadjusted incidence rate of prediabetes per 1000 person-years between DTG (IR: 29, 95% CI: 24, 34) and EVG/c (IR: 23, 95% CI: 20, 28), RAL (IR: 29, 95% CI: 17, 50) or DRV(/r/c) (IR: 20, 95% CI: 14, 28). There was no difference in the unadjusted incidence rate of T2DM between DTG (IR: 11, 95% CI: 8, 14) and either EVG/c (IR: 7, 95% CI: 5, 10), RAL (IR: 23, 95% CI: 13, 42), or DRV(/r/c) (IR: 6, 95% CI: 3, 10),

although it was statistically higher with RAL than with EVG/c or DRV(/r/c). No modelling was performed among ART-experienced/viremic patients. Compared to patients who remained free of T2DM during follow-up, those with incident T2DM were older and more likely to be obese at baseline. Changes in BMI, HbA1c and fasting glucose were not assessed among ART-experienced/viremic patients.

Conclusions

Among ART-naïve patients, those initiating DTG had a higher prevalence of prediabetes and T2DM at baseline. However, the risk of progressing to incident T2DM did not appear to be elevated compared to patients initiating EVG/c or DRV(/r/c) in adjusted analyses. Among ART-experienced patients, the prevalence of prediabetes was also higher with DTG than EVG/c, RAL or DRV(/r/c), but prevalence of T2DM with DTG was higher compared to EVG/c and lower compared to RAL (suppressed and viremic). However, there was no statistically significant association between DTG initiation and development of incident T2DM among ART-experienced/suppressed patients.

2. Background and Rationale

2.1. Background

Prevalence of T2DM among HIV-positive individuals has been estimated to be between 5-14%[1-4] in the United States and between 2-9%[4-7] in other Western countries. In some studies, individuals with HIV were more likely to have or develop T2DM than people not infected with HIV,[8-10] although this has not been observed in all populations. Incidence rates among HIV-positive patients vary as well, ranging from 11-47 cases/1,000 person-years in the United States[2,10-13] and 3-16 cases/1,000 person-years in other Western countries. Exposure to ART has been associated with an increased risk of incident T2DM in HIV patients, particularly when cumulative exposure is considered.[5,7,18] Protease inhibitors, as a class of drugs, have been associated with increased incidence of DM; the highest risk has been observed in patients taking indinavir.[3,14,17,19] Certain NRTIs, specifically didanosine[5,14] and stavudine,[3,5,14,19] have shown an increased risk of T2DM, while others, such as tenofovir[20] and emtricitabine,[20] have been associated with reduced risk. Some analyses have shown an increased risk of DM with lamivudine exposure, but these findings are not consistent across all studies.[3,13] To date, very little research has been conducted on the association between INSTIs and potential risk of DM.

2.2. Rationale

A signal evaluation for hyperglycemia and diabetes mellitus with DTG use was conducted, following a raised disproportionality (DPA) score and case reports of incident diabetes and hyperglycemia among patients taking DTG identified through routine pharmacovigilance monitoring. After evaluating clinical trial data and post-marketing data, the strength of evidence was insufficient to show a causal association between DTG and hyperglycemia or T2DM. This analysis, utilizing data from a large real-world population of treated HIV patients, will provide additional information to support the signal evaluation, assessing the frequency of prediabetes (persistent hyperglycemia) and T2DM among patients taking DTG, and conducting a robust assessment of DTG as a risk factor for incident T2DM.

3. Objectives

3.1. Primary Objectives

4) To assess the baseline prevalence of prediabetes and T2DM among new users of DTG, RAL, EVG/c and DRV(/r/c)
5) To assess the incidence rate of prediabetes and T2DM over follow-up among new users of DTG, RAL, EVG/c and DRV(/r/c) without prevalent prediabetes or T2DM
6) To estimate the association between core agent initiation (DTG vs. RAL, EVG/c or DRV(/r/c)) and development of T2DM among new users of DTG, RAL, EVG/c and DRV(/r/c) without prevalent prediabetes or T2DM

3.2. Secondary Objectives

4) To compare baseline patient characteristics between patients who developed T2DM and those who did not among new users of DTG, RAL, EVG/c and DRV(/r/c) without prevalent prediabetes or T2DM
5) To describe HbA1c levels and fasting glucose at core agent initiation and after 6, 12, 18 or 24 months on core agent among new users of DTG, RAL, EVG/c and DRV(/r/c) with prevalent T2DM
6) To describe HbA1c levels and fasting glucose at core agent initiation and after 6, 12, 18 or 24 months on core agent among new users of DTG, RAL, EVG/c and DRV(/r/c) with incident T2DM

3.3. Exploratory Objective

2) To compare weight gain at 6, 12, 18 or 24 months after core agent initiation between patients with and without an incident T2DM diagnosis during their follow-up, stratified by core agent, among new users of DTG, RAL, EVG/c and DRV(/r/c) without prevalent prediabetes or T2DM

4. Methodology

4.1. Study design

Study population

A total of four distinct study populations were identified from the OPERA Observational Database for analysis per the inclusion criteria defined below. All study populations are a subset of Population 1; additional inclusion criteria are color-coded (Table 1).

Eligibility period: 01AUG2013 to 31MAR2018

Baseline (index) date: Date of regimen initiation

Baseline period: The 12-month baseline period preceding the index date were used to assess patient demographic and clinical characteristics

Observation period: Patients were observed from their index date until the first of the following censoring events:

a) Discontinuation of the core agent of interest
b) Loss to follow up, defined as any 12-month period in which no clinical contact is made (cessation of continuous clinical activity)
c) Death
d) Study end (30SEP2018)

Continuous Clinical Activity

Patients failing to meet the continuous clinical activity requirement (defined as any 12-month period in which no clinical contact is made) were 12 months after their last contact. Regimen gaps in therapy of 45 days or less will be collapsed for continuity of treatment analysis.

Table 1. Inclusion criteria for the four study populations

	Population 1 (primary objective 1)	Population 2 (primary objectives 2-3, secondary objective 1)	Population 3 (secondary objective 2)	Population 4 (secondary objective 3)
Diagnosis of HIV, a positive HIV Western Blot, or a positive HIV enzyme-linked immunosorbent assay (ELISA); and a detectable HIV viral load test	X	X	X	X
At least 13 years of age at the index date	X	X	X	X
Never diagnosed with, type 1 or juvenile DM	X	X	X	X
Initiating DTG, RAL, EVG/c or DRV(/r/c) for the first time between 01AUG2013 and 31MAR2018	X	X	X	X
Not exposed to >1 core agent of interest concurrently	X	X	X	X
Baseline viral load measurement	X	X	X	X
No diagnosis of prediabetes* or T2DM** at or before core agent initiation*		X		X
Diagnosis of prediabetes or T2DM* at or before core agent initiation			X	
New diagnosis of T2DM after core agent initiation				X

* Prevalent prediabetes defined as (a) diagnosis of prediabetes or borderline diabetes mellitus, or (b) abnormal value on the last lab before or at baseline (HbA1c ≥5.7% to <6.5%, or fasting plasma glucose ≥100 mg/dl to <126 mg/dl, or oral glucose tolerance test ≥140 mg/dl to <200 mg/dl)

** Prevalent T2DM defined as (a) diagnosis of T2DM, (b) prescription of antidiabetic, or (c) abnormal value on the last lab before or at baseline (HbA1c ≥6.5%, fasting plasma glucose ≥126 mg/dl, oral glucose tolerance test ≥200 mg/dl)

4.2. Stratification by prior ART exposure

ART-naïve: patients without any history of ART prior to initiation of the core agent of interest, and with a baseline HIV viral load ≥1,000 copies/mL.

ART-experienced: patients with a history of ART prior to initiation of the core agent of interest, or with a baseline HIV viral load <1,000 copies/mL.

- ART-experienced/suppressed: baseline viral load <50 copies/mL
- ART-experienced/viremic: baseline viral load ≥50 copies/mL

4.3. Exposure definition

First exposure to a core agent of interest (DTG vs. RAL, EVG/c or DRV(/r/c)), after inclusion in the OPERA database. Among ART-experienced patients, prior exposure to other core agents of interest is allowed if it occurred prior to inclusion in the OPERA database, or if it occurred while contributing to the OPERA database, but its use was discontinued prior to 01AUG2013.

4.4. Outcomes definition

- Prediabetes, defined as either:
    a) Diagnosis of prediabetes
    b) Two labs reporting any of the following, measured at least 90 days apart: Haemoglobin A1c (HbA1c) ≥5.7% to <6.5%, Fasting plasma glucose (FPG) ≥100 mg/dl to <126 mg/dl (grade 1), or Oral glucose tolerance test (OGTT) ≥140 mg/dl to <200 mg/dl

- T2DM, defined as either:
    a) Diagnosis of T2DM/non-insulin-dependent diabetes (NIDDM)
    b) Prescription of antidiabetic
    c) Lab: HbA1c ≥6.5%, Fasting plasma glucose (FPG) ≥126 mg/dl, or Oral glucose tolerance test (OGTT) ≥200 mg/dl

- Body Mass Index (BMI):
    - Continuous: $BMI = weight/height^2$
    - Categorical
        - Underweight (BMI: <18.5)
        - Normal weight (BMI: 18.5 – 24.9)
        - Overweight (BMI: 25.0 – 29.9)
        - Obese (BMI: ≥30)

- HbA1c
  - Continuous
  - Categorical
    - Controlled: <7.0%
    - Uncontrolled: ≥7.0%

- Fasting glucose grade during follow-up
  - Continuous
  - Categorical
    - Grade 1: ≥100 mg/dl to <126 mg/dl)
    - Grade 2: 126-250 mg/dL
    - Grade 3 to 4: >250 mg/dL

4.5. Analyses

4.5.1. Baseline descriptive analyses (population 2)

Descriptive analyses will be conducted for patients prescribed a core agent of interest between 01AUG2013 and 31MAR2018. All study covariates listed in section 8.4.3. will be described; medians and interquartile ranges for continuous variables and frequencies (counts and percentages) for categorical variables will be provided. Pairwise comparisons between DTG and each of the other core agent groups will be evaluated by p-values calculated from Pearson Chi-Square test for categorical variables. Fisher's exact test will be used to compare frequencies with few events. Wilcoxon Rank Sum test will be used to calculate p-values for continuous variables.

***All descriptive analyses will be stratified by ART-naïve, ART-experienced/suppressed, and ART-experienced/viremic

4.5.2. Primary objective 1: Prevalence of prediabetes and T2DM (population 1)

The baseline prevalence of prediabetes and T2DM will both be assessed by core agent used. The prevalence and 95% confidence intervals will be calculated in each core agent group as the proportion of patients with prediabetes or T2DM within 12 months before or on baseline.

***Prevalence estimates will be stratified by ART-naïve, ART-experienced/suppressed, and ART-experienced/viremic

4.5.3. Primary objective 2: Incidence rate of prediabetes and T2DM (population 2)

The incidence rate of prediabetes and T2DM will both be assessed over follow-up by core agent used among patients without prediabetes or T2DM at baseline.

The incidence rate and 95% confidence intervals will be calculated for each core agent as the proportion of patients with a new diagnosis of prediabetes or T2DM during follow-up, out of the person-time at risk for the event (person-time free of the prediabetes and T2DM).

The proportion of new T2DM identified through a diagnosis vs. through prescription of T2DM treatment will be described and compared across core agent groups.

***Incidence estimates will be stratified by ART-naïve, ART-experienced/suppressed, and ART-experienced/viremic

4.5.4. Primary objective 3: Association between anchor agent use and incident T2DM

A time to event analysis will be conducted with multivariate Cox proportional hazards model to assess the presence of an association between core agent use and T2DM. Baseline variables included in the multivariate model were selected a priori, based on the literature, including age, sex, race, HCV co-infection, and BMI. HDL and triglyceride were not included due to missing data.

4.5.4.1. Continuous BMI and Use of Higher Order Polynomials

In considering the best approaches for handling continuous data, it is often more appropriate to model the data in continuous form rather than imposing boundaries and assessing the data in categorical form. One limitation in categorizing continuous data is that we assume that risk of the outcome is homogeneous across all values within each category. If this assumption does not hold, then residual confounding can occur and result in bias.

Including a continuous variable in the model is useful for indicating whether there is a linear dose-response relationship with the outcome variable, such that each one-unit increment in the continuous variable corresponds to a change in the outcome variable. However, we can evaluate the assumption of linearity and determine the most appropriate shape of the modeled dose-response relationship by including higher order polynomials (i.e. quadratic, cubic, etc.). If a higher order polynomial is found to be statistically significant, this suggests that the flexible form in the model, which also includes the lower order polynomial(s), better characterizes the relationship between the continuous variable and outcome. Using a flexible form that fits the data better will therefore result in a better statistical adjustment and less residual confounding.

***Cox proportional hazards model will be stratified by ART-naïve and ART-experienced/suppressed

4.5.5. Secondary objective 1: Patient factors associated with T2DM (population 2)

Descriptive analyses will be conducted to compare baseline patient characteristics between patients who develop T2DM during follow-up to those who do not. Descriptive statistics including medians and interquartile ranges will be provided for continuous variables with frequencies (counts and percentages) for categorical variables. Differences between groups will be evaluated by p-values calculated from Pearson Chi-Square test for categorical variables. Fisher's exact test will be used to compare frequencies with few events. Wilcoxon Rank Sum test will be used to calculate p-values for continuous variables.

***All descriptive analyses will be stratified by ART-naïve, ART-experienced/suppressed, and ART-experienced/viremic

4.5.6. Secondary objective 2: Description of follow-up HbA1c and fasting glucose levels among patients with prevalent T2DM (population 3)

Change in HbA1c

Both the absolute and percent change in HbA1c will be assessed between t_0 and t_n. Percent change will be calculated as:

$$\%\ change\ = 100 \times \frac{HbA1c(t_n) - HbA1c(t_0)}{HbA1c(t_0)}$$

where t_0 is the date of core agent initiation and t_n is a predefined time of follow-up (n= 6, 12, 18 and 24 months following DTG initiation).

For each follow-up duration assessed (n), the study population will be restricted to patients with a follow-up ≥ n.

Categorical HbA1c

HbA1c categories will be described as controlled (HbA1c <7.0%) or uncontrolled (HbA1c ≥7.0%). The proportion of patients in each HbA1c categorical level at baseline and at 6, 12, 18 or 24 months after core agent initiation will be compared across core agent groups. Differences between groups will be evaluated by p-values calculated from Pearson Chi-Square test for categorical variables.

For each time point assessed (6, 12, 18 or 24 months), the study population will be restricted to patients with a follow-up greater or equal to that time point.

Change in fasting glucose

Both the absolute and percent change in fasting glucose will be assessed between t_0 and t_n. Percent change will be calculated as:

$$\%\ change\ = 100 \times \frac{fasting\ glucose(t_n) - fastingglucose(t_0)}{fasting\ glucose(t_0)}$$

where t_0 is the date of core agent initiation and t_n is a predefined time of follow-up (n= 6, 12, 18 or 24 months following core agent initiation).

For each follow-up duration assessed (n), the study population will be restricted to patients with a follow-up ≥ n.

Categorical fasting glucose

Three fasting glucose categories will be described: grade 1 (≥100 mg/dl to <126 mg/dl), grade 2 (126-250 mg/dl) and grade 3 to 4 (>250 mg/dl). The proportion of patients in each fasting glucose grade at T2DM onset and at 6, 12, 18 or 24 months after T2DM onset will be compared across core agent groups. Differences between groups will be evaluated by p-values calculated from Pearson Chi-Square test for categorical variables.

For each time point assessed (6, 12, 18 or 24 months), the study population will be restricted to patients with a follow-up greater or equal to that time point.

***All descriptive analyses will be stratified by ART-naïve and ART-experienced/suppressed

4.5.7. Secondary objective 3: Description of follow-up HbA1c among patients with incident T2DM (population 4)

All analyses performed for Secondary Objective 2 will be performed among patients with incident T2DM for Secondary Objective 3.

4.5.8. Exploratory objective: weight gain (population 2)

4.5.8.1. Descriptive analysis of weight gain by incident T2DM (population 2)

Weight gain will be compared between patients with and without incident T2DM for each core agent at 6, 12, 18 and 24 months after initiation. Weight gain will be assessed continuously as the absolute increase in BMI, as well as categorically, as the proportion of patients changing categories of BMI. Pairwise comparisons will be performed using Pearson Chi-Square test or Fisher's exact test for categorical variables and Wilcoxon Rank Sum test for continuous variables.

***All descriptive analyses will be stratified by ART-naïve and ART-experienced/suppressed

4.5.8.2. Marginal structural model of time to T2DM (population 2)

Inverse probability of treatment weights will be used to fit marginal structural Cox models in order to assess the relative hazard of incident T2DM during exposure to DTG (vs. RAL, EVG/c, and DRV(/r/c))., while accounting for potential confounding and mediation of weight gain.

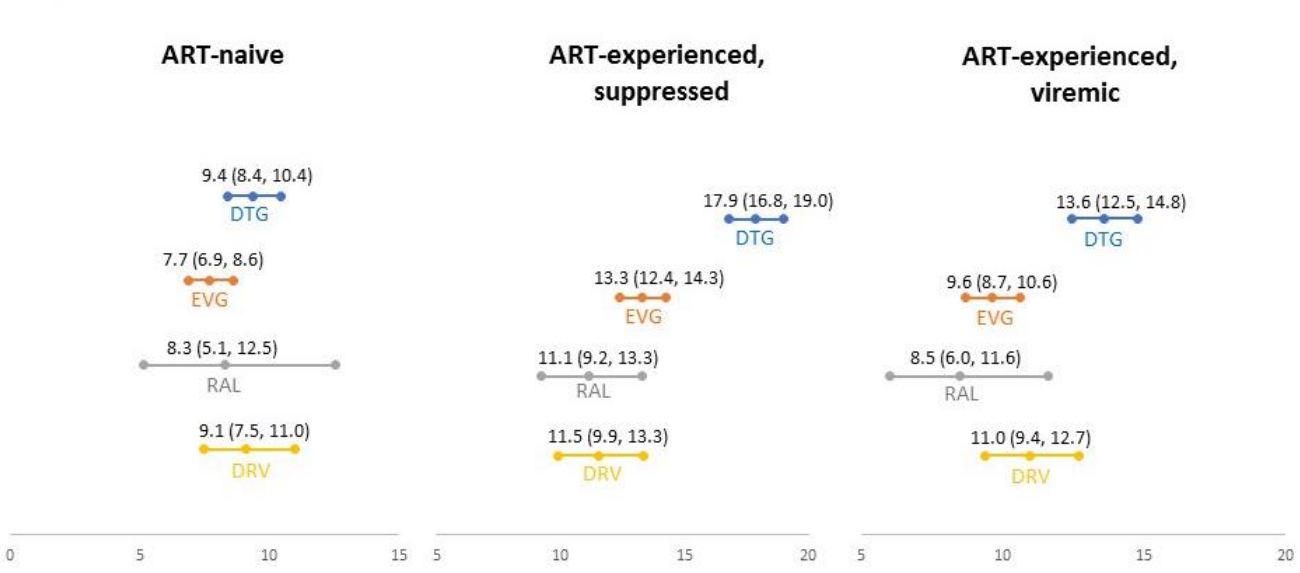
***Modeling analyses will be stratified by ART-naïve and ART-experienced/suppressed

5. Results

ART-naïve:

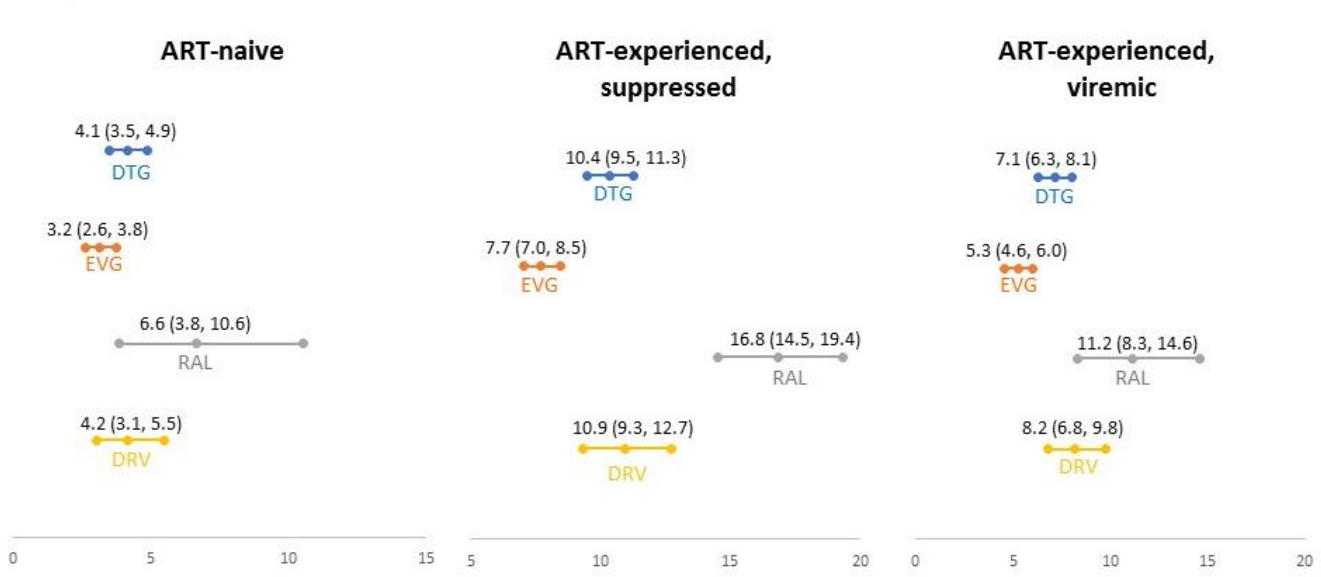
Out of 29,674 patients included in Population 1, 8,489 were ART-naïve (3234 DTG, 3906 EVG/c, 241 RAL, 1108 DRV(/r/c)). Prevalence of prediabetes was lower with EVG/c (7.7%, p=0.01) but no different with RAL (8.3%, p=0.58) or DRV(/r/c) (9.1%, p=0.80), compared to DTG (9.4%) (Figure 1).

Figure 1. Prevalence of prediabetes at baseline by core agent and ART experience



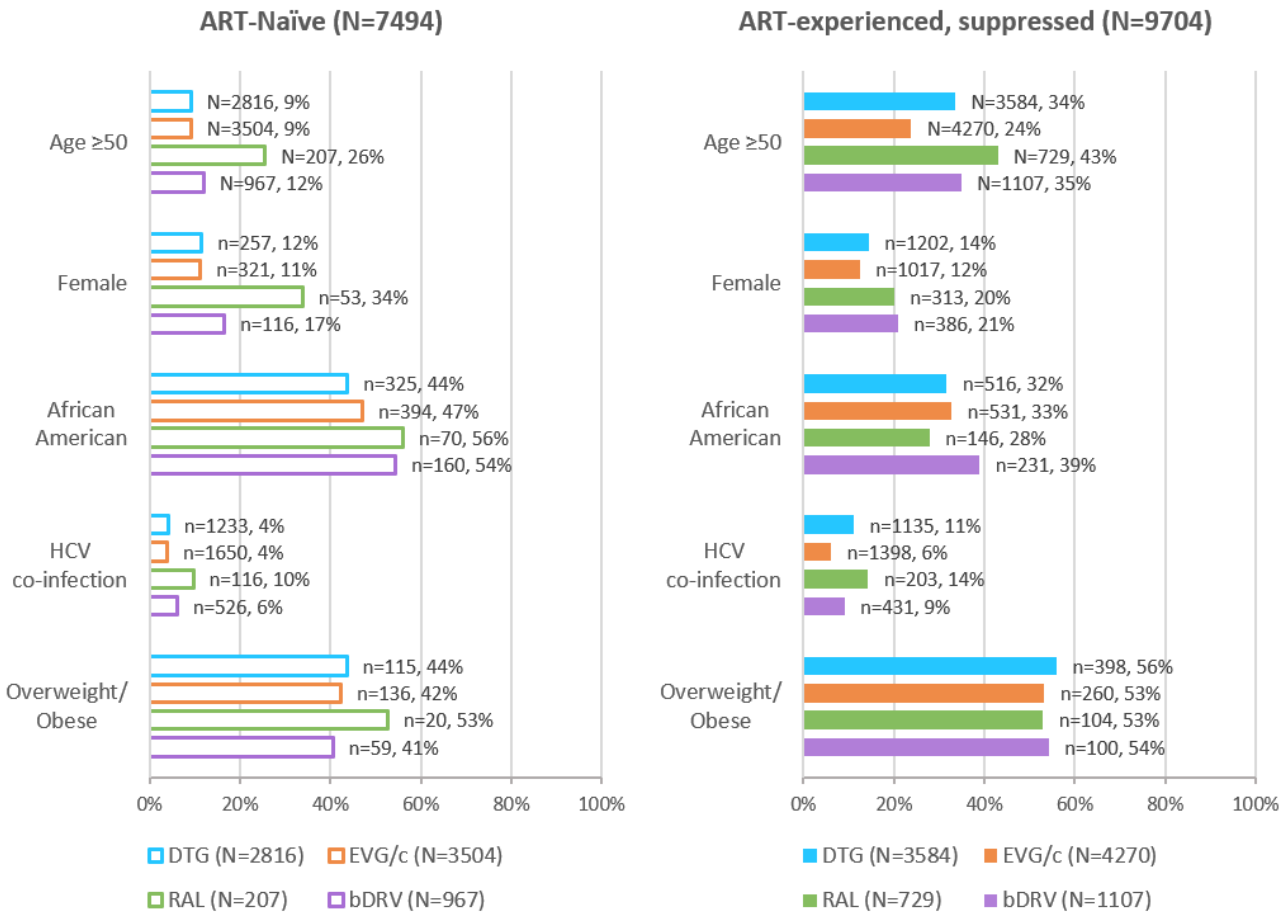
Prevalence of T2DM was also lower with EVG/c (3.1%, p=0.02) but no different with RAL (6.6%, p=0.07) or DRV(/r/c) (4.2%, p=0.99), compared to DTG (4.1%) (Figure 2).

Figure 2. Prevalence of type 2 diabetes mellitus at baseline by core agent and ART experience



There were 7,494 ART-naïve patients without prevalent prediabetes/T2DM in Population 2 (2,816 DTG, 3,504 EVG/c, 207 RAL, 967 DRV(/r/c)). Compared to DTG, EVG/c users were less likely to be underweight; RAL users were older, and more likely to be female, obese and HCV co-infected; DRV(/r/c) users were older, and more likely to be female, non-Hispanic Black, and HCV co-infected (Figure 3).

Figure 3. Baseline demographic and clinical characteristics of ART-naïve and ART-experienced patients.



There was no difference in the unadjusted incidence rate of prediabetes per 1000 person-years between DTG (IR: 23, 95% CI: 19, 28) and EVG/c (IR: 21, 95% CI: 17, 25), RAL (IR: 13, 95% CI: 4, 39) or DRV(/r/c) (IR: 20, 95% CI: 13, 29) (Figure 4).

Figure 4. Incidence of prediabetes per 100 person-years by core agent and ART experience

ART-Naive

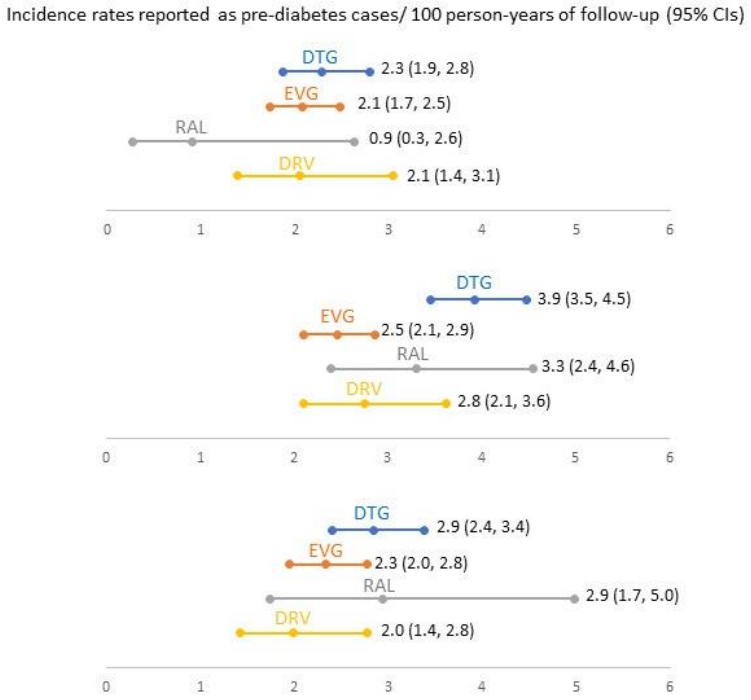
	N	# prediabetes cases	%
DTG	2816	101	3.6%
EVG	3504	125	3.6%
RAL	207	3	1.4%
DRV	967	25	2.6%

ART-Experienced, suppressed

	N	# prediabetes cases	%
DTG	3584	232	6.5%
EVG	4281	168	3.9%
RAL	730	37	5.1%
DRV	1109	51	4.6%

ART-Experienced, viremic

	N	# prediabetes cases	%
DTG	2787	131	4.7%
EVG	3140	125	4.0%
RAL	338	14	4.1%
DRV	1162	35	3.0%



Similarly, there was no difference in the unadjusted incidence rate of T2DM between DTG (IR: 11, 95% CI: 9, 15), EVG/c (IR: 7, 95% CI: 6, 10), RAL (IR: 13, 95% CI: 4, 40), or DRV(/r/c) (IR: 8, 95% CI: 4, 14) (Figure 5).

Figure 5. Incidence of T2DM per 100 person-years by core agent and ART experience

ART-Naive

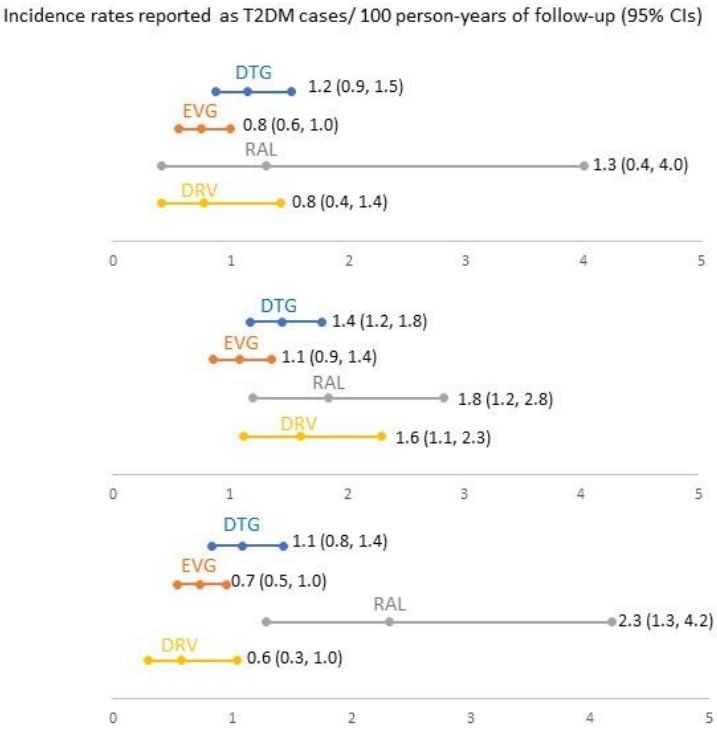
	N	# T2DM cases	%
DTG	2816	51	1.8%
EVG	3504	46	1.3%
RAL	207	3	1.4%
DRV	967	10	1.0%

ART-Experienced, suppressed

	N	# T2DM cases	%
DTG	3584	88	2.5%
EVG	4281	75	1.8%
RAL	730	21	2.9%
DRV	1109	30	2.7%

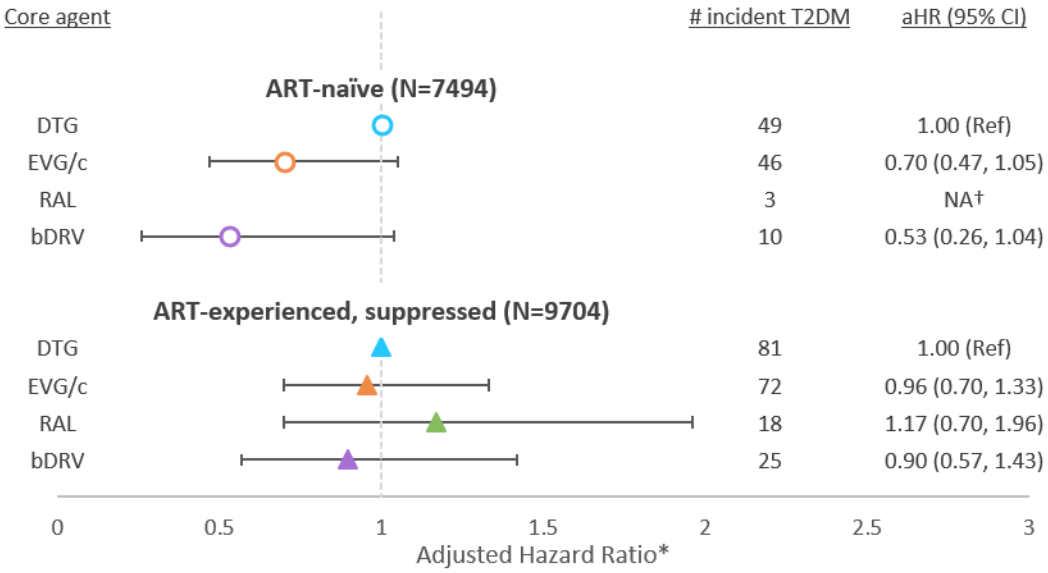
ART-Experienced, viremic

	N	# T2DM cases	%
DTG	2787	51	1.8%
EVG	3140	40	1.3%
RAL	338	11	3.3%
DRV	1162	10	0.9%



After adjustments for baseline age, sex, race, HCV co-infection and BMI, no statistically significant association was found between core agents and incident T2DM for EVG/c (aHR: 0.70, 95% CI: 0.47, 1.05) or DRV(/r/c) (aHR: 0.53, 95% CI: 0.26, 1.04) when compared to DTG (Figure 6). RAL was excluded from the model due to the small number of events in this group (n=3).

Figure 6. Adjusted hazard ratios* for the association between core agent and T2DM

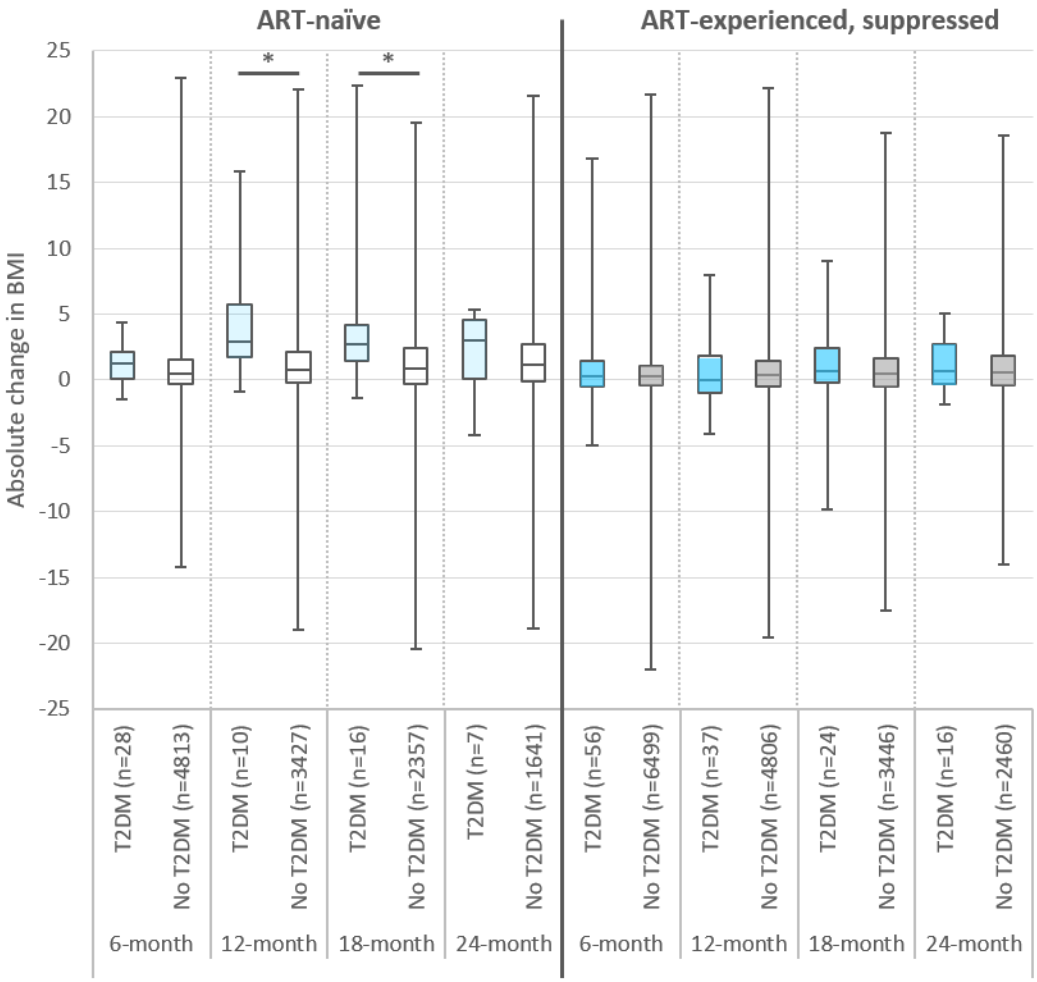


* Obtained from Cox proportional hazards models adjusted for age, sex, race/ethnicity, HCV co-infection and BMI at baseline

† RAL was not included in the ART-naïve model due to the small number of incident T2DM

Compared to patients who remained free of T2DM during follow-up, those with incident T2DM were older, and more likely to be female and overweight or obese at baseline. The absolute BMI change was larger among patient with incident T2DM at 12 months and 18 months, compared to those without incident T2DM (Figure 7).

Figure 7. 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)

Pooled logistic regression with inverse probability of censoring weighting (IPCW) yielded comparable results for EVG/c (aOR: 0.76, 95% CI: 0.49, 1.12) and DRV/r/c (aOR: 0.54, 95% CI: 0.27, 1.07).

There were 995 ART-naïve patients with prevalent prediabetes/T2DM at baseline in Population 3 (418 DTG, 402 EVG/c, 34 RAL, 141 DRV(/r/c)). The absolute and percent decrease in HbA1c was greater among DRV(/r/c) users than DTG users at 12 months only (Figure 8). Fasting glucose was measured too infrequently to evaluate.

Figure 8. Control of HbA1c over follow-up

	ART-Naive				ART-Experienced, suppressed			
	DTG	EVG	RAL	DRV	DTG	EVG	RAL	DRV
			Baseline				Baseline	
	n=373	n=359	n=28	n=128	n=1073	n=833	n=182	n=205
Uncontrolled HbA1c (≥7.0%)	48 (12.9%)	48 (13.4%)	6 (21.4%)	23 (18.0%)	164 (15.2%)	129 (13.4%)	43 (23.6%)	47 (18.0%)
			6-month				6-month	
	n=148	n=126	n=7	n=58	n=587	n=423	n=90	n=93
Uncontrolled HbA1c (≥7.0%)	39 (26.4%)	22 (17.4%)	1 (14.3%)	13 (22.4%)	144 (24.5%)	92 (21.7%)	31 (34.4%)	25 (26.8%)
			12-month				12-month	
	n=132	n=115	n=7	n=23	n=473	n=336	n=77	n=75
Uncontrolled HbA1c (≥7.0%)	33 (25.0%)	20 (17.4%)	3 (42.8%)	5 (21.7%)	109 (23.0%)	72 (21.4%)	27 (35.0%)	20 (26.7%)
			24-month				24-month	
	n=63	n=54	n=4	n=8	n=264	n=193	n=50	n=40
Uncontrolled HbA1c (≥7.0%)	15 (23.8%)	13 (24.1%)	3 (75.0%)	2 (25.0%)	62 (23.5%)	41 (21.2%)	19 (38.0%)	11 (27.5%)

There were 326 ART-naïve patients with incident prediabetes/T2DM during follow-up in Population 4 (133 DTG, 155 EVG/c, 5 RAL, 33 DRV(/r/c)). HbA1c and fasting glucose were measured too infrequently evaluate.

ART-experienced/suppressed:

There were 12,322 ART-experienced/suppressed patients in Population 1 (4,747 DTG, 5,243 EVG/c, 962 RAL, 1,370 DRV(/r/c)). Prevalence of prediabetes was lower with EVG/c (13.3%, p<0.01), RAL (11.1%, p<0.01) and DRV(/r/c) (11.5%, p<0.01), compared to DTG (17.9%) (Figure 1). However, while the prevalence of T2DM was also lower with EVG/c (7.7%, p<0.01), it was higher with RAL (16.8%, p<0.01) and no different with DRV(/r/c) (10.9%, p=0.53), compared to DTG (10.4%) (Figure 2).

There were 9,704 ART-experienced/suppressed patients without prevalent prediabetes/T2DM in Population 2 (3,584 DTG, 4,281 EVG/c, 730 RAL, 1,109 DRV(/r/c)). Compared to DTG, EVG/c users were younger, and less likely to be female or HCV co-infected; RAL users were older, and more likely to be female, non-Hispanic White and HCV co-infected; DRV(/r/c) users were more likely to be female, overweight or obese, and less likely to be HCV co-infected (Figure 3).

There was no difference in the unadjusted incidence rate of prediabetes per 1000 person-years between DTG (IR: 39, 95% CI: 35, 45) and RAL (IR: 33, 95% CI: 24, 45) or DRV(/r/c) (IR: 28, 95% CI: 21, 36), but it was lower with EVG/c (IR: 25, 95% CI: 21, 29) than DTG (Figure 4).

However, there was no difference in the unadjusted incidence rate of T2DM between any core agents: DTG (IR: 14, 95% CI: 12, 18), EVG/c (IR: 11, 95% CI: 9, 14), RAL (IR: 18, 95% CI: 12, 28), or DRV(/r/c) (IR: 16, 95% CI: 11, 23) (Figure 5).

After adjustments for baseline age, sex, race/ethnicity, HCV co-infection and BMI, no statistically significant association was found between core agents and incident T2DM for EVG/c (aHR: 0.96, 95% CI: 0.70, 1.33), RAL (aHR: 1.17, 95% CI: 0.70, 1.96) or DRV(/r/c) (aHR: 0.90, 95% CI: 0.57, 1.42), compared to DTG (Figure 6).

Compared to patients who remained free of T2DM during follow-up, those with incident T2DM were older, and more likely to be obese at baseline. There was no difference in absolute BMI change between patient with or without incident at any of the time points evaluated (Figure 7).

In an inverse probability of censoring weighted pooled logistic regression analysis, there was no association between risk of T2DM and core agent when comparing EVG/c to DTG (aOR: 0.95, 95% CI: 0.68, 1.32), RAL to DTG (aOR: 0.94, 95% CI: 0.53, 1.70) and bDRV to DTG (aOR: 0.97, 95% CI: 0.61, 1.54)

There were 2,618 ART-experienced/suppressed patients with prevalent prediabetes/T2DM at baseline in Population 3 (1,163 DTG, 962 EVG/c, 232 RAL, 261 DRV(/r/c)). HbA1c and fasting glucose were measured too infrequently evaluate (Figure 8).

There were 616 ART-naïve patients with incident prediabetes/T2DM during follow-up in Population 4 (285 DTG, 214 EVG/c, 49 RAL, 68 DRV(/r/c)). The median absolute and percent increase in HbA1c was larger with RAL than DTG at 18 and 24 months. Fasting glucose was measured too infrequently evaluate.

ART-experienced/viremic:

There were 8,863 ART-experienced/viremic patients in Population 1 (3,415 DTG, 3,633 EVG/c, 412 RAL, 1,403 DRV(/r/c)). Prevalence of prediabetes was lower with EVG/c (9.6%, p<0.01), RAL (8.5%, p<0.01) and DRV(/r/c) (11.0%, p=0.01), compared to DTG (13.6%) (Figure 1). However, while the prevalence of T2DM was also lower with EVG/c (5.3%, p<0.01), it was higher with RAL (11.2%, p<0.01) and no different with DRV(/r/c) (8.2%, p=0.21), compared to DTG (7.1%) (Figure 2).

There were 13,703 ART-experienced/viremic patients without prevalent prediabetes/T2DM in Population 2 (2,787 DTG, 3,140 EVG/c, 338 RAL, 1,162 DRV(/r/c)). Compared to DTG, EVG/c users were younger, and less likely to be female or HCV co-infected; RAL users were older, and more likely to be female and HCV co-infected, and less likely to be non-Hispanic Black; DRV(/r/c) users were older, and more likely to be female, non-Hispanic Black and HCV co-infected.

There was no difference in the unadjusted incidence rate of prediabetes per 1000 person-years between DTG (IR: 29, 95% CI: 24, 34) and EVG/c (IR: 23, 95% CI: 20, 28), RAL (IR: 29, 95% CI: 17, 50) or DRV(/r/c) (IR: 20, 95% CI: 14, 28) (Figure 4). There was no difference in the unadjusted incidence rate of T2DM between DTG (IR: 11, 95% CI: 8, 14) and either EVG/c (IR: 7, 95% CI: 5, 10), RAL (IR: 23, 95% CI: 13, 42), or DRV(/r/c) (IR: 6, 95% CI: 3, 10), although it was statistically higher with RAL than with EVG/c or DRV(/r/c) (Figure 5).

No modelling was performed among ART-experienced/viremic patients.

Compared to patients who remained free of T2DM during follow-up, those with incident T2DM were older and more likely to be obese at baseline.

Changes in BMI, HbA1c and fasting glucose were not assessed among ART-experienced/viremic patients.

6. Discussion

ART-naïve

Among 8,489 ART-naïve patients, prevalence of prediabetes was lower with EVG/c (7.7%, p=0.01) but no different with RAL (8.3%, p=0.58) or DRV(/r/c) (9.1%, p=0.80), compared to DTG (9.4%). Prevalence of T2DM was also lower with EVG/c (3.1%, p=0.02) but no different with RAL (6.6%, p=0.07) or DRV(/r/c) (4.2%, p=0.99), compared to DTG (4.1%).

Among 7,494 ART-naïve patients without prevalent prediabetes/T2DM, EVG/c users were less likely to be underweight; RAL users were older, and more likely to be female, obese and HCV co-infected; DRV(/r/c) users were older, and more likely to be female, non-Hispanic Black, and HCV co-infected, compared to DTG user. There was no difference in the unadjusted incidence rate of prediabetes per 1000 person-years between DTG (IR: 23, 95% CI: 19, 28) and EVG/c (IR: 21, 95% CI: 17, 25), RAL (IR: 13, 95% CI: 4, 39) or DRV(/r/c) (IR: 20, 95% CI: 13, 29). Similarly, there was no difference in the unadjusted incidence rate of T2DM between DTG (IR: 11, 95% CI: 9, 15), EVG/c (IR: 7, 95% CI: 6, 10), RAL (IR: 13, 95% CI: 4, 40), or DRV(/r/c) (IR: 8, 95% CI: 4, 14).

After adjustments for baseline age, sex, race, HCV co-infection and BMI, no statistically significant association was found between core agents and incident T2DM for EVG/c (aHR: 0.70, 95% CI: 0.47, 1.05) or DRV(/r/c) (aHR: 0.53, 95% CI: 0.26, 1.04) when compared to DTG. RAL was excluded from the model due to the small number of events in this group (n=3). Inverse probability of censoring weighting did not change the interpretation of results in the ART-naïve population. There appears to be a trend towards a lower risk of T2DM with EVG/c and bDRV compared to DTG. However, the results are not statistically significant, and no firm conclusion can be reached considering the small number of events observed in this population.

ART-experienced/suppressed

Among 12,322 ART-experienced/suppressed patients, the prevalence of prediabetes was lower with EVG/c (13.3%, p<0.01), RAL (11.1%, p<0.01) and DRV(/r/c) (11.5%, p<0.01), compared to DTG (17.9%). However, while the prevalence of T2DM was also lower with EVG/c (7.7%, p<0.01), it was higher with RAL (16.8%, p<0.01) and no different with DRV(/r/c) (10.9%, p=0.53), compared to DTG (10.4%).

Among 9,704 ART-experienced/suppressed patients without prevalent prediabetes/T2DM, EVG/c users were younger, and less likely to be female or HCV co-infected; RAL users were older, and more likely to be female, non-Hispanic White and HCV co-infected; DRV(/r/c) users were more likely to be female, overweight or obese, and less likely to be HCV co-infected, compared to DTG users. There was no difference in the unadjusted incidence rate of prediabetes per 1000 person-years between DTG (IR: 39, 95% CI: 35, 45) and RAL (IR: 33, 95% CI: 24, 45) or DRV(/r/c) (IR: 28, 95% CI: 21, 36), but it was lower with EVG/c (IR: 25, 95% CI: 21, 29) than DTG. However, there was no difference in the unadjusted incidence rate of T2DM between any core agents: DTG (IR: 14, 95% CI: 12, 18), EVG/c (IR: 11, 95% CI: 9, 14), RAL (IR: 18, 95% CI: 12, 28), or DRV(/r/c) (IR: 16, 95% CI: 11, 23).

After adjustments for baseline age, sex, race/ethnicity, HCV co-infection and BMI, no statistically significant association was found between core agents and incident T2DM for EVG/c (aHR: 0.96, 95% CI: 0.70, 1.33), RAL (aHR: 1.17, 95% CI: 0.70, 1.96) or DRV(/r/c) (aHR: 0.90, 95% CI: 0.57, 1.42), compared to DTG. In an analysis weighted by the inverse probability of censoring, there was no association between risk of T2DM and core agent. Differences between Cox proportional hazards and pooled logistic regression modeling results appear to

be driven by the exclusion of observations with missing covariates to create the IPCW, especially the for the RAL group, where 22% of events were excluded. Indeed, unadjusted results for EVG/c and bDRV are comparable between the two unadjusted models, but the point estimate changed for RAL. However, the interpretation of results remains unchanged across all analyses. There is no association between core agent and risk of T2DM in the ART-experienced, suppressed population.

ART-experienced/viremic

Among 8,863 ART-experienced/viremic patients, the prevalence of prediabetes was lower with EVG/c (9.6%, p<0.01), RAL (8.5%, p<0.01) and DRV(/r/c) (11.0%, p=0.01), compared to DTG (13.6%). However, while the prevalence of T2DM was also lower with EVG/c (5.3%, p<0.01), it was higher with RAL (11.2%, p<0.01) and no different with DRV(/r/c) (8.2%, p=0.21), compared to DTG (7.1%).

Among 13,703 ART-experienced/viremic patients without prevalent prediabetes/T2DM, EVG/c users were younger, and less likely to be female or HCV co-infected; RAL users were older, and more likely to be female and HCV co-infected, and less likely to be non-Hispanic Black; DRV(/r/c) users were older, and more likely to be female, non-Hispanic Black and HCV co-infected, compared to DTG users. There was no difference in the unadjusted incidence rate of prediabetes per 1000 person-years between DTG (IR: 29, 95% CI: 24, 34) and EVG/c (IR: 23, 95% CI: 20, 28), RAL (IR: 29, 95% CI: 17, 50) or DRV(/r/c) (IR: 20, 95% CI: 14, 28). There was no difference in the unadjusted incidence rate of T2DM between DTG (IR: 11, 95% CI: 8, 14) and either EVG/c (IR: 7, 95% CI: 5, 10), RAL (IR: 23, 95% CI: 13, 42), or DRV(/r/c) (IR: 6, 95% CI: 3, 10).

Conclusions

Incident T2DM was uncommon among ART naïve and ART-experienced/suppressed persons initiating DTG, EVG/c, RAL or bDRV in this large clinical population. None of the comparisons between DTG and other core agents showed statistically significant increased risk of T2DM. However, with the small number of events in the ART naive population, we cannot exclude the possibility that a difference may exist; so monitoring HgA1c remains prudent.

7. References

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Supplemental Materials: Tables

Dolutegravir use and incidence of prediabetes and type 2 diabetes mellitus:

Final Study Report

Study Report: July 20, 2019

OPERA Build: December 04, 2018

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1. Appendix: Tables for all results

1.1. Study Populations Identification

Table 1. Exploration of the study population 1

		Patients Included	%	Patients Excluded	%
1	Patients who are HIV+	94,145	.	0	.
2	Patients never diagnosed with Type1 or juvenile diabetes	93,591	99.4	554	0.6
3	Patients ever prescribed ART after first OPERA visit	82,461	88.1	11,130	11.9
4	Patients ever prescribed DTG, EVG/c, RAL, DRV/r, or DRV/c	54,994	66.7	27,467	33.3
5	Patients prescribed DTG, EVG/c, RAL, DRV/r, or DRV/c between August 1, 2013 and March 31, 2018	44,857	81.6	10,137	18.4
6	Patients were prescribed DTG, EVG/c, RAL, DRV/r, or DRV/c for the first time of the study period*	37,325	83.2	7,532	16.8
7	Patients aged 13 years and older at regimen initiation	37,321	100.0	4	0.0
8	Patients whose first regimen of interest did not include two or more of the core agents of interest	34,949	93.6	2,372	6.4
9	Patients with at least one viral load available prior to or at initiation of the regimen of interest	29,674	84.9	5,275	15.1

* Prior exposure to DTG, EVG, RAL or DRV was allowed regardless of boosting agent use if it was discontinued before August 1, 2013

Table 2. Study population 1 by ART core agent of interest and ART experience

Core Agent	N (%)	ART experience	N (%)
DTG	11,396 (38.4%)	ART-naïve	3,234 (28.4%)
		ART-experienced, stable suppressed	4,747 (41.7%)
		ART-experienced, viremic	3,415 (30.0%)
EVG/c	12,782 (43.1%)	ART-naïve	3,906 (30.6%)
		ART-experienced, stable suppressed	5,243 (41.0%)
		ART-experienced, viremic	3,633 (28.4%)
RAL	1,615 (5.4%)	ART-naïve	241 (14.9%)
		ART-experienced, stable suppressed	962 (59.6%)
		ART-experienced, viremic	412 (25.5%)
DRV/r or DRV/c	3,881 (13.1%)	ART-naïve	1,108 (28.5%)
		ART-experienced, stable suppressed	1,370 (35.3%)
		ART-experienced, viremic	1,403 (36.2%)

Table 3. Identification of the study population 2

		Patients Included	%	Patients Excluded	%
1	Patients in Population 1	29,674	.	0	.
2	Patients without prediabetes* or T2DM** prior to or at core agent initiation*	24,625	83.0	5,049	17.0

* Prevalent prediabetes defined as (a) diagnosis of prediabetes or borderline diabetes mellitus, or (b) abnormal value on the last lab before or at baseline (HbA1c ≥5.7% to <6.5%, or fasting plasma glucose ≥100 mg/dl to <126 mg/dl, or oral glucose tolerance test ≥140 mg/dl to <200 mg/dl)

** Prevalent T2DM defined as (a) diagnosis of T2DM, (b) prescription of antidiabetic, or (c) abnormal value on the last lab before or at baseline (HbA1c ≥6.5%, fasting plasma glucose ≥126 mg/dl, oral glucose tolerance test ≥200 mg/dl)

Table 4. Study population 2 by ART core agent of interest and ART experience

Core Agent	N (%)	ART experience	N (%)
DTG	9,187 (37.3%)	ART-naïve	2,816 (30.7%)
		ART-experienced, stable suppressed	3,584 (39.0%)
		ART-experienced, viremic	2,787 (30.3%)
EVG/c	10,925 (44.4%)	ART-naïve	3,504 (32.1%)
		ART-experienced, stable suppressed	4,281 (39.2%)
		ART-experienced, viremic	3,140 (28.7%)
RAL	1,275 (5.2%)	ART-naïve	207 (16.2%)
		ART-experienced, stable suppressed	730 (57.3%)
		ART-experienced, viremic	338 (26.5%)
DRV/r or DRV/c	3,238 (13.1%)	ART-naïve	967 (29.9%)
		ART-experienced, stable suppressed	1,109 (34.2%)
		ART-experienced, viremic	1,162 (35.9%)

Table 5. Identification of the study population 3

		Patients Included	%	Patients Excluded	%
1	Patients in Population 1	29,674	.	0	.
2	Patients with prediabetes* or T2DM** prior to or at core agent initiation	5,049	17.0	24,625	83.0

* Prevalent prediabetes defined as (a) diagnosis of prediabetes or borderline diabetes mellitus, or (b) abnormal value on the last lab before or at baseline (HbA1c ≥5.7% to <6.5%, or fasting plasma glucose ≥100 mg/dl to <126 mg/dl, or oral glucose tolerance test ≥140 mg/dl to <200 mg/dl)

** Prevalent T2DM defined as (a) diagnosis of T2DM, (b) prescription of antidiabetic, or (c) abnormal value on the last lab before or at baseline (HbA1c ≥6.5%, fasting plasma glucose ≥126 mg/dl, oral glucose tolerance test ≥200 mg/dl)

Table 6. Study population 3 by ART core agent of interest and ART experience

Core Agent	N (%)	ART experience	N (%)
DTG	2,209 (43.8%)	ART-naïve	418 (18.9%)
		ART-experienced, stable suppressed	1,163 (52.6%)
		ART-experienced, viremic	628 (28.4%)
EVG/c	1,857 (36.8%)	ART-naïve	402 (21.6%)
		ART-experienced, stable suppressed	962 (51.8%)
		ART-experienced, viremic	493 (26.5%)
RAL	340 (6.7%)	ART-naïve	34 (10.0%)
		ART-experienced, stable suppressed	232 (68.2%)
		ART-experienced, viremic	74 (21.8%)
DRV/r or DRV/c	643 (12.7%)	ART-naïve	141 (21.9%)
		ART-experienced, stable suppressed	261 (40.6%)
		ART-experienced, viremic	241 (37.5%)

Table 7. Identification of the study population 4

		Patients Included	%	Patients Excluded	%
1	Patients in Population 1	29,674	.	0	.
2	Patients without prediabetes or T2DM prior to or at core agent initiation	24,625	83.0	5,049	17.0
3	Patients with new prediabetes* or T2DM** after core agent initiation	1,316	5.3	23,309	94.7

*New prediabetes defined as (a) diagnosis of prediabetes or borderline diabetes mellitus, or (b) 2 abnormal labs, measured at least 90 days apart (HbA1c ≥5.7% to <6.5%, fasting plasma glucose ≥100 mg/dl to <126 mg/dl, oral glucose tolerance test ≥140 mg/dl to <200 mg/dl)

** New T2DM defined as (a) diagnosis of T2DM, (b)pPrescription of antidiabetic, or (c) abnormal lab (HbA1c ≥6.5%, fasting plasma glucose ≥126 mg/dl, oral glucose tolerance test ≥200 mg/dl)

Table 8. Study population 4 by ART core agent of interest and ART experience

Core Agent	N (%)	ART experience	N (%)
DTG	578 (43.9%)	ART-naïve	133 (23.0%)
		ART-experienced, stable suppressed	285 (49.3%)
		ART-experienced, viremic	160 (27.7%)
EVG/c	519 (39.4%)	ART-naïve	155 (29.9%)
		ART-experienced, stable suppressed	214 (41.2%)
		ART-experienced, viremic	150 (28.9%)
RAL	75 (5.7%)	ART-naïve	5 (6.7%)
		ART-experienced, stable suppressed	49 (65.3%)
		ART-experienced, viremic	21 (28.0%)
DRV/r or DRV/c	144 (10.9%)	ART-naïve	33 (22.9%)
		ART-experienced, stable suppressed	68 (47.2%)
		ART-experienced, viremic	43 (29.9%)

1.2. Primary objective 1: Prevalence of prediabetes and T2DM in Study Population 1

1.2.1. ART-Naïve Patients

Table 9. Baseline prevalence of prediabetes in ART-naïve patients (Study Population 1)

		DTG N= 3,234	EVG/c N= 3,906	DTG vs. EVG/c p-value	RAL N= 241	DTG vs. RAL p-value	DRV(r/c) N= 1,108	DTG vs. DRV(r/c) p-value
Prevalent prediabetes	n (%)	303 (9.4%)	301 (7.7%)	0.0119	20 (8.3%)	0.5809	101 (9.1%)	0.8019
	% (95% CI)	9.37 (8.39, 10.43)	7.71 (6.89, 8.59)	.	8.30 (5.14, 12.53)	.	9.12 (7.49, 10.97)	.
diagnosis only	n (%)	7 (0.2%)	11 (0.3%)	0.6423	2 (0.8%)	0.1249	3 (0.3%)	0.7222
labs only	n (%)	257 (7.9%)	267 (6.8%)	0.0731	18 (7.5%)	0.7909	91 (8.2%)	0.7782
diagnosis and labs	n (%)	39 (1.2%)	23 (0.6%)	0.0067	0 (0.0%)	0.1091	7 (0.6%)	0.1261

Table 10. Baseline prevalence of T2DM in ART-naïve patients (Study Population 1)

		DTG N= 3,234	EVG/c N= 3,906	DTG vs. EVG/c p-value	RAL N= 241	DTG vs. RAL p-value	DRV(r/c) N= 1,108	DTG vs. DRV(r/c) p-value
Prevalent T2DM	n (%)	134 (4.1%)	123 (3.1%)	0.0247	16 (6.6%)	0.0659	46 (4.2%)	0.9906
	% (95% CI)	4.14 (3.48, 4.89)	3.15 (2.62, 3.75)	.	6.64 (3.84, 10.56)	.	4.15 (3.06, 5.50)	.
diagnosis only	n (%)	21 (0.6%)	20 (0.5%)	0.5297	1 (0.4%)	1.0000	6 (0.5%)	0.8267
labs only	n (%)	10 (0.3%)	16 (0.4%)	0.5568	2 (0.8%)	0.2003	7 (0.6%)	0.1619
Antidiabetic prescription only	n (%)	9 (0.3%)	5 (0.1%)	0.1835	2 (0.8%)	0.1745	3 (0.3%)	1.0000
diagnosis and lab only	n (%)	22 (0.7%)	11 (0.3%)	0.0144	0 (0.0%)	0.3974	2 (0.2%)	0.0594
diagnosis and prescription only	n (%)	35 (1.1%)	27 (0.7%)	0.0951	4 (1.7%)	0.3437	7 (0.6%)	0.2160
Lab and prescription only	n (%)	0 (0.0%)	1 (0.0%)	1.0000	1 (0.4%)	0.0694	1 (0.1%)	0.2552
diagnosis, lab and prescription	n (%)	37 (1.1%)	43 (1.1%)	0.8629	6 (2.5%)	0.0683	20 (1.8%)	0.0953

1.2.2. ART-Experienced/Suppressed Patients

Table 11. Baseline prevalence of prediabetes in ART-experienced/suppressed patients (Study Population 1)

		DTG N= 4,747	EVG/c N= 5,243	DTG vs. EVG/c p-value	RAL N= 962	DTG vs. RAL p-value	DRV(r/c) N= 1,370	DTG vs. DRV(r/c) p-value
Prevalent prediabetes	n (%)	848 (17.9%)	698 (13.3%)	<.0001	107 (11.1%)	<.0001	158 (11.5%)	<.0001
	% (95% CI)	17.86 (16.78, 18.98)	13.31 (12.40, 14.26)	.	11.12 (9.21, 13.28)	.	11.53 (9.89, 13.34)	.
diagnosis only	n (%)	71 (1.5%)	57 (1.1%)	0.0698	6 (0.6%)	0.0325	11 (0.8%)	0.0495
labs only	n (%)	628 (13.2%)	527 (10.1%)	<.0001	96 (10.0%)	0.0057	133 (9.7%)	0.0005
diagnosis and labs	n (%)	149 (3.1%)	114 (2.2%)	0.0032	5 (0.5%)	<.0001	14 (1.0%)	<.0001

Table 12. Baseline prevalence of T2DM in ART-experienced/suppressed patients (Study Population 1)

		DTG N= 4,747	EVG/c N= 5,243	DTG vs. EVG/c p-value	RAL N= 962	DTG vs. RAL p-value	DRV(r/c) N= 1,370	DTG vs. DRV(r/c) p-value
Prevalent T2DM	n (%)	492 (10.4%)	405 (7.7%)	<.0001	162 (16.8%)	<.0001	150 (10.9%)	0.5341
	% (95% CI)	10.36 (9.51, 11.27)	7.72 (7.02, 8.48)	.	16.84 (14.53, 19.36)	.	10.95 (9.34, 12.72)	.
diagnosis only	n (%)	63 (1.3%)	47 (0.9%)	0.0394	21 (2.2%)	0.0444	19 (1.4%)	0.8656
labs only	n (%)	59 (1.2%)	72 (1.4%)	0.5673	19 (2.0%)	0.0745	32 (2.3%)	0.0032
Antidiabetic prescription only	n (%)	24 (0.5%)	22 (0.4%)	0.5564	15 (1.6%)	0.0010	4 (0.3%)	0.3703
diagnosis and lab only	n (%)	39 (0.8%)	27 (0.5%)	0.0589	10 (1.0%)	0.5040	7 (0.5%)	0.2411
diagnosis and prescription only	n (%)	79 (1.7%)	54 (1.0%)	0.0057	33 (3.4%)	0.0003	26 (1.9%)	0.5576
Lab and prescription only	n (%)	11 (0.2%)	4 (0.1%)	0.0671	2 (0.2%)	1.0000	6 (0.4%)	0.2398
diagnosis, lab and prescription	n (%)	217 (4.6%)	179 (3.4%)	0.0031	62 (6.4%)	0.0140	56 (4.1%)	0.4450

1.2.3. ART-Experienced/Viremic Patients

Table 13. Baseline prevalence of prediabetes in ART-experienced/viremic patients (Study Population 1)

		DTG N= 3,415	EVG/c N= 3,633	DTG vs. EVG/c p-value	RAL N= 412	DTG vs. RAL p-value	DRV(r/c) N= 1,403	DTG vs. DRV(r/c) p-value
Prevalent prediabetes	n (%)	464 (13.6%)	350 (9.6%)	<.0001	35 (8.5%)	0.0037	154 (11.0%)	0.0138
	% (95% CI)	13.59 (12.45, 14.78)	9.63 (8.69, 10.64)	.	8.50 (5.99, 11.62)	.	10.98 (9.39, 12.73)	.
diagnosis only	n (%)	26 (0.8%)	22 (0.6%)	0.4702	4 (1.0%)	0.5574	8 (0.6%)	0.5720
labs only	n (%)	377 (11.0%)	283 (7.8%)	<.0001	27 (6.6%)	0.0051	137 (9.8%)	0.1929
diagnosis and labs	n (%)	61 (1.8%)	45 (1.2%)	0.0630	4 (1.0%)	0.3112	9 (0.6%)	0.0020

Table 14. Baseline prevalence of prediabetes and T2DM in ART-experienced/viremic patients (Study Population 1)

		DTG N= 3,415	EVG/c N= 3,633	DTG vs. EVG/c p-value	RAL N= 412	DTG vs. RAL p-value	DRV(r/c) N= 1,403	DTG vs. DRV(r/c) p-value
Prevalent T2DM	n (%)	244 (7.1%)	191 (5.3%)	0.0010	46 (11.2%)	0.0036	115 (8.2%)	0.2066
	% (95% CI)	7.14 (6.30, 8.06)	5.26 (4.55, 6.03)	.	11.17 (8.29, 14.61)	.	8.20 (6.81, 9.76)	.
diagnosis only	n (%)	33 (1.0%)	25 (0.7%)	0.2350	3 (0.7%)	1.0000	19 (1.4%)	0.2819
labs only	n (%)	30 (0.9%)	26 (0.7%)	0.4416	6 (1.5%)	0.2511	20 (1.4%)	0.0887
Antidiabetic prescription only	n (%)	10 (0.3%)	10 (0.3%)	1.0000	2 (0.5%)	0.3762	4 (0.3%)	1.0000
diagnosis and lab only	n (%)	19 (0.6%)	9 (0.2%)	0.0563	5 (1.2%)	0.1724	11 (0.8%)	0.4196
diagnosis and prescription only	n (%)	36 (1.1%)	36 (1.0%)	0.8135	4 (1.0%)	1.0000	15 (1.1%)	1.0000
Lab and prescription only	n (%)	6 (0.2%)	3 (0.1%)	0.3302	2 (0.5%)	0.2099	1 (0.1%)	0.6812
diagnosis, lab and prescription	n (%)	110 (3.2%)	82 (2.3%)	0.0130	24 (5.8%)	0.0066	45 (3.2%)	0.9805

1.3. Baseline Characteristics of Study Population 2

1.3.1. ART-Naïve Patients

Table 15. Baseline Demographic Characteristics of ART-naïve patients (Study Population 2)

		DTG N= 2,816	EVG/c N= 3,504	DTG vs. EVG p-value	RAL N= 207	DTG vs. RAL p-value	DRV(r/c) N= 967	DTG vs. DRV(r/c) p-value
Age	Median (IQR)	30.3 (25.2, 39.6)	30.3 (25.3, 39.5)	0.9257	41.2 (30.7, 50.4)	<.0001	34.1 (27.3, 44.2)	<.0001
	13-25	836 (29.8%)	1010 (28.9%)	0.7636	25 (12.1%)	<.0001	189 (19.6%)	<.0001
	26-49	1715 (61.1%)	2160 (61.9%)	.	129 (62.3%)	.	658 (68.3%)	.
	50+	257 (9.2%)	321 (9.2%)	.	53 (25.6%)	.	116 (12.0%)	.
Sex	Male	2484 (88.2%)	3105 (88.6%)	0.5718	137 (66.2%)	<.0001	807 (83.5%)	0.0001
	Female	325 (11.5%)	394 (11.2%)	.	70 (33.8%)	.	160 (16.5%)	.
	Unknown	7 (0.2%)	5 (0.1%)	.	0 (0.0%)	.	0 (0.0%)	.
Hispanic	Black	33 (4.5%)	32 (3.8%)	0.2066	4 (16.0%)	0.0064	11 (6.2%)	0.6546
	American Indian/Alaska Native	3 (0.4%)	2 (0.2%)	.	0 (0.0%)	.	0 (0.0%)	.
	Hawaiian/Other Pacific Islander	2 (0.3%)	4 (0.5%)	.	0 (0.0%)	.	1 (0.6%)	.
	Asian	3 (0.4%)	1 (0.1%)	.	0 (0.0%)	.	1 (0.6%)	.
	White	690 (93.4%)	780 (92.6%)	.	19 (76.0%)	.	160 (90.4%)	.

		DTG N= 2,816	EVG/c N= 3,504	DTG vs. EVG p-value	RAL N= 207	DTG vs. RAL p-value	DRV(r/c) N= 967	DTG vs. DRV(r/c) p-value
	Other	1 (0.1%)	6 (0.7%)	.	0 (0.0%)	.	1 (0.6%)	.
	>1 race	7 (0.9%)	17 (2.0%)	.	2 (8.0%)	.	3 (1.7%)	.
Non-Hispanic	Black	1200 (61.5%)	1618 (64.5%)	0.0407	112 (65.1%)	0.2183	515 (68.4%)	0.0068
	American Indian/Alaska Native	3 (0.2%)	7 (0.3%)	.	0 (0.0%)	.	1 (0.1%)	.
	Hawaiian/Other Pacific Islander	6 (0.3%)	2 (0.1%)	.	0 (0.0%)	.	3 (0.4%)	.
	Asian	63 (3.2%)	51 (2.0%)	.	1 (0.6%)	.	9 (1.2%)	.
	White	647 (33.2%)	795 (31.7%)	.	57 (33.1%)	.	213 (28.3%)	.
	Other	2 (0.1%)	4 (0.2%)	.	1 (0.6%)	.	2 (0.3%)	.
	>1 race	29 (1.5%)	31 (1.2%)	.	1 (0.6%)	.	10 (1.3%)	.
Race and/or ethnicity unknown	Yes	127 (4.5%)	154 (4.4%)	0.8256	10 (4.8%)	0.8303	37 (3.8%)	0.3677
Marital Status	Single	2114 (75.1%)	2548 (72.7%)	0.3665	139 (67.1%)	0.0964	712 (73.6%)	0.1081
	Married	107 (3.8%)	152 (4.3%)	.	15 (7.2%)	.	57 (5.9%)	.
	Domestic partnership	32 (1.1%)	42 (1.2%)	.	3 (1.4%)	.	10 (1.0%)	.
	Widowed	10 (0.4%)	9 (0.3%)	.	1 (0.5%)	.	6 (0.6%)	.
	Separated/divorced	57 (2.0%)	77 (2.2%)	.	6 (2.9%)	.	18 (1.9%)	.

		DTG N= 2,816	EVG/c N= 3,504	DTG vs. EVG p-value	RAL N= 207	DTG vs. RAL p-value	DRV(r/c) N= 967	DTG vs. DRV(r/c) p-value
	Unknown	496 (17.6%)	676 (19.3%)	.	43 (20.8%)	.	164 (17.0%)	.
Risk of Infection	MSM	1904 (67.6%)	2309 (65.9%)	0.1500	89 (43.0%)	<.0001	543 (56.2%)	<.0001
	Not MSM	912 (32.4%)	1195 (34.1%)	.	118 (57.0%)	.	424 (43.8%)	.
History of Syphilis	Yes	847 (30.1%)	1077 (30.7%)	0.5720	48 (23.2%)	0.0361	300 (31.0%)	0.5810
Region	Northeast	168 (6.0%)	205 (5.9%)	<.0001	19 (9.2%)	<.0001	57 (5.9%)	0.0003
	South	1668 (59.2%)	2391 (68.2%)	.	141 (68.1%)	.	643 (66.5%)	.
	Midwest	92 (3.3%)	148 (4.2%)	.	14 (6.8%)	.	18 (1.9%)	.
	West	888 (31.5%)	759 (21.7%)	.	33 (15.9%)	.	249 (25.7%)	.
	US Territories	0 (0.0%)	1 (0.0%)	.	0 (0.0%)	.	0 (0.0%)	.
Medicaid	Yes	455 (16.2%)	465 (13.3%)	0.0012	46 (22.2%)	0.0235	195 (20.2%)	0.0044
Medicare	Yes	139 (4.9%)	98 (2.8%)	<.0001	26 (12.6%)	<.0001	74 (7.7%)	0.0016
Commercial Insurance	Yes	1029 (36.5%)	1291 (36.8%)	0.8042	74 (35.7%)	0.8192	276 (28.5%)	<.0001
Cash	Yes	1336 (47.4%)	1697 (48.4%)	0.4349	107 (51.7%)	0.2376	452 (46.7%)	0.7065
ADAP/Ryan White	Yes	1152 (40.9%)	1349 (38.5%)	0.0515	68 (32.9%)	0.0226	383 (39.6%)	0.4768
Other	Yes	16 (0.6%)	31 (0.9%)	0.1845	2 (1.0%)	0.3522	5 (0.5%)	1.0000
No Payer info	Yes	332 (11.8%)	517 (14.8%)	0.0006	27 (13.0%)	0.5905	132 (13.7%)	0.1281

Table 16. Baseline Clinical Characteristics of ART-naïve patients (Study Population 2)

		DTG N= 2,816	EVG/c N= 3,504	DTG vs. EVG p-value	RAL N= 207	DTG vs. RAL p-value	DRV(r/c) N= 967	DTG vs. DRV(r/c) p-value
Hemoglobin, g/dL	Median (IQR)	14.2 (12.9, 15.2)	14.2 (13.0, 15.1)	0.7694	13.2 (11.6, 14.4)	<.0001	13.6 (12.0, 14.7)	<.0001
	Normal	2554 (90.7%)	3252 (92.8%)	0.0396	172 (83.1%)	0.0030	819 (84.7%)	<.0001
	DAIDS Grade 1 (mild)	100 (3.6%)	99 (2.8%)	.	12 (5.8%)	.	58 (6.0%)	.
	DAIDS Grade 2 (moderate)	54 (1.9%)	43 (1.2%)	.	5 (2.4%)	.	31 (3.2%)	.
	DAIDS Grade 3 (Severe)	40 (1.4%)	33 (0.9%)	.	4 (1.9%)	.	20 (2.1%)	.
	DAIDS Grade 4 (potentially life-threatening)	4 (0.1%)	4 (0.1%)	.	1 (0.5%)	.	1 (0.1%)	.
	Missing	64 (2.3%)	73 (2.1%)	.	13 (6.3%)	.	38 (3.9%)	.
Hematocrit, %	Median (IQR)	42.4 (39.1, 45.1)	42.5 (39.4, 45.0)	0.4375	40.0 (35.8, 43.2)	<.0001	40.9 (36.5, 43.8)	<.0001
	Low	521 (18.5%)	610 (17.4%)	0.6315	63 (30.4%)	<.0001	285 (29.5%)	<.0001
	Normal	2173 (77.2%)	2739 (78.2%)	.	129 (62.3%)	.	626 (64.7%)	.
	High	58 (2.1%)	80 (2.3%)	.	2 (1.0%)	.	17 (1.8%)	.
	Missing	64 (2.3%)	75 (2.1%)	.	13 (6.3%)	.	39 (4.0%)	.
VACS mortality index	Median (IQR)	20.0 (13.0, 34.0)	20.0 (13.0, 30.0)	0.1080	35.0 (23.0, 49.0)	<.0001	29.5 (17.0, 52.0)	<.0001

		DTG N= 2,816	EVG/c N= 3,504	DTG vs. EVG p-value	RAL N= 207	DTG vs. RAL p-value	DRV(r/c) N= 967	DTG vs. DRV(r/c) p-value
	0 to <15	932 (33.1%)	1185 (33.8%)	0.1877	30 (14.5%)	<.0001	184 (19.0%)	<.0001
	>=15 to <30	779 (27.7%)	1013 (28.9%)	.	41 (19.8%)	.	237 (24.5%)	.
	>=30 to <45	380 (13.5%)	413 (11.8%)	.	44 (21.3%)	.	151 (15.6%)	.
	>= 45	398 (14.1%)	464 (13.2%)	.	62 (30.0%)	.	270 (27.9%)	.
	Missing	327 (11.6%)	429 (12.2%)	.	30 (14.5%)	.	125 (12.9%)	.
BMI	Median (IQR)	24.3 (21.7, 27.8)	24.4 (21.8, 27.6)	0.9270	25.6 (22.1, 30.3)	0.0016	24.1 (21.3, 27.9)	0.2780
	Underweight	168 (6.0%)	148 (4.2%)	0.0033	15 (7.2%)	0.0001	67 (6.9%)	0.2856
	Normal weight	1327 (47.1%)	1751 (50.0%)	.	69 (33.3%)	.	466 (48.2%)	.
	Overweight	774 (27.5%)	983 (28.1%)	.	58 (28.0%)	.	247 (25.5%)	.
	Obese	454 (16.1%)	501 (14.3%)	.	51 (24.6%)	.	145 (15.0%)	.
	Missing	93 (3.3%)	121 (3.5%)	.	14 (6.8%)	.	42 (4.3%)	.
HDL, mg/dL	Median (IQR)	41.0 (33.0, 51.0)	41.0 (33.0, 50.0)	0.5070	40.0 (31.5, 48.0)	0.2030	40.0 (32.0, 49.0)	0.0771
	Normal	261 (9.3%)	260 (7.4%)	<.0001	13 (6.3%)	0.1729	78 (8.1%)	0.0124
	Borderline Abnormal	918 (32.6%)	1029 (29.4%)	.	62 (30.0%)	.	285 (29.5%)	.
	Dyslipidemia	994 (35.3%)	1132 (32.3%)	.	73 (35.3%)	.	335 (34.6%)	.
	Missing	643 (22.8%)	1083 (30.9%)	.	59 (28.5%)	.	269 (27.8%)	.

		DTG N= 2,816	EVG/c N= 3,504	DTG vs. EVG p-value	RAL N= 207	DTG vs. RAL p-value	DRV(r/c) N= 967	DTG vs. DRV(r/c) p-value
Triglycerides, mg/dL	Median (IQR)	106.0 (76.0, 155.0)	103.5 (75.0, 151.5)	0.3204	114.5 (84.0, 170.0)	0.0528	115.0 (82.0, 166.0)	0.0002
	Normal	1583 (56.2%)	1808 (51.6%)	<.0001	98 (47.3%)	0.0574	475 (49.1%)	0.0038
	Borderline Abnormal	270 (9.6%)	311 (8.9%)	.	26 (12.6%)	.	108 (11.2%)	.
	Dyslipidemia	302 (10.7%)	292 (8.3%)	.	24 (11.6%)	.	114 (11.8%)	.
	Severe Dyslipidemia	23 (0.8%)	21 (0.6%)	.	0 (0.0%)	.	7 (0.7%)	.
	Missing	638 (22.7%)	1072 (30.6%)	.	59 (28.5%)	.	263 (27.2%)	.
Any concomitant non-ART listed below	Yes	880 (31.3%)	1029 (29.4%)	0.1050	86 (41.5%)	0.0022	350 (36.2%)	0.0046
Antibiotics	Yes	474 (16.8%)	524 (15.0%)	0.0419	41 (19.8%)	0.2719	204 (21.1%)	0.0029
Direct Acting Antivirals (DAAs)	Yes	0 (0.0%)	1 (0.0%)	1.0000	0 (0.0%)	.	0 (0.0%)	.
Lipid lowering agents	Yes	52 (1.8%)	70 (2.0%)	0.6643	10 (4.8%)	0.0035	28 (2.9%)	0.0505
Non-steroidal Anti-inflammatory Agents (NSAIDS)	Yes	73 (2.6%)	85 (2.4%)	0.6734	8 (3.9%)	0.2739	34 (3.5%)	0.1350
Antidepressants	Yes	258 (9.2%)	267 (7.6%)	0.0273	31 (15.0%)	0.0060	94 (9.7%)	0.6058
Anxiolytics/Hypnotics/Sedatives	Yes	94 (3.3%)	145 (4.1%)	0.0975	22 (10.6%)	<.0001	43 (4.4%)	0.1114
Immune Modulators	Yes	145 (5.1%)	157 (4.5%)	0.2156	12 (5.8%)	0.6851	53 (5.5%)	0.6894
Number of concomitant non-ART medications listed above	0	1936 (68.8%)	2475 (70.6%)	0.0838	121 (58.5%)	<.0001	617 (63.8%)	0.0066

		DTG N= 2,816	EVG/c N= 3,504	DTG vs. EVG p-value	RAL N= 207	DTG vs. RAL p-value	DRV(r/c) N= 967	DTG vs. DRV(r/c) p-value
	1-2	812 (28.8%)	966 (27.6%)	.	69 (33.3%)	.	311 (32.2%)	.
	3-4	65 (2.3%)	56 (1.6%)	.	16 (7.7%)	.	38 (3.9%)	.
	5+	3 (0.1%)	7 (0.2%)	.	1 (0.5%)	.	1 (0.1%)	.

Table 17. Baseline Comorbidities of ART-naïve patients (Study Population 2)

		DTG N= 2,816	EVG/c N= 3,504	DTG vs. EVG p-value	RAL N= 207	DTG vs. RAL p-value	DRV(r/c) N= 967	DTG vs. DRV(r/c) p-value
Comorbidity at baseline	Any	1232 (43.8%)	1492 (42.6%)	0.3505	121 (58.5%)	<.0001	462 (47.8%)	0.0298
Cardiovascular Disease Conditions	Any	51 (1.8%)	59 (1.7%)	0.7005	7 (3.4%)	0.1119	26 (2.7%)	0.0954
	Arrhythmia	24 (0.9%)	23 (0.7%)	0.3803	3 (1.4%)	0.4267	6 (0.6%)	0.6741
	Myocardial Infarction	2 (0.1%)	4 (0.1%)	0.6983	1 (0.5%)	0.1917	2 (0.2%)	0.2712
	Angina	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.	1 (0.1%)	0.2556
	Other/Unspecified CHD	20 (0.7%)	28 (0.8%)	0.7713	3 (1.4%)	0.2056	12 (1.2%)	0.1517
	Occlusion/stenosis of precerebral arteries	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.	2 (0.2%)	0.0653

		DTG N= 2,816	EVG/c N= 3,504	DTG vs. EVG p-value	RAL N= 207	DTG vs. RAL p-value	DRV(r/c) N= 967	DTG vs. DRV(r/c) p-value
	Stroke	5 (0.2%)	7 (0.2%)	1.0000	0 (0.0%)	1.0000	5 (0.5%)	0.1366
	Transient Ischemic Attack	2 (0.1%)	2 (0.1%)	1.0000	0 (0.0%)	1.0000	0 (0.0%)	1.0000
	Other CBV	8 (0.3%)	10 (0.3%)	1.0000	1 (0.5%)	0.4723	8 (0.8%)	0.0393
	Peripheral Arterial Disease	1 (0.0%)	1 (0.0%)	1.0000	0 (0.0%)	1.0000	0 (0.0%)	1.0000
	Abdominal Aortic Aneurysm	0	0	.	0	.	0	.
Invasive Cancer	Any	48 (1.7%)	44 (1.3%)	0.1387	9 (4.3%)	0.0070	23 (2.4%)	0.1827
Endocrine Disorders (excluding T2DM)	Any	179 (6.4%)	208 (5.9%)	0.4884	19 (9.2%)	0.1132	51 (5.3%)	0.2242
	Hyperlipidemia	170 (6.0%)	186 (5.3%)	0.2117	15 (7.2%)	0.4835	48 (5.0%)	0.2166
	Hyperthyroidism	0 (0.0%)	4 (0.1%)	0.1338	1 (0.5%)	0.0685	1 (0.1%)	0.2556
	Hypothyroidism	11 (0.4%)	26 (0.7%)	0.0958	5 (2.4%)	0.0034	5 (0.5%)	0.5729
	Thyroiditis	0 (0.0%)	1 (0.0%)	1.0000	0 (0.0%)	.	0 (0.0%)	.
Mental Health Conditions	Any	410 (14.6%)	529 (15.1%)	0.5505	36 (17.4%)	0.2675	142 (14.7%)	0.9244
	Anxiety Disorders	245 (8.7%)	370 (10.6%)	0.0132	23 (11.1%)	0.2389	78 (8.1%)	0.5427
	Bipolar or Manic Disorders	90 (3.2%)	81 (2.3%)	0.0313	10 (4.8%)	0.2043	38 (3.9%)	0.2763
	Major Depressive Disorder	85 (3.0%)	85 (2.4%)	0.1478	7 (3.4%)	0.7691	26 (2.7%)	0.6001

		DTG N= 2,816	EVG/c N= 3,504	DTG vs. EVG p-value	RAL N= 207	DTG vs. RAL p-value	DRV(r/c) N= 967	DTG vs. DRV(r/c) p-value
	Schizophrenic Disorder	36 (1.3%)	24 (0.7%)	0.0184	1 (0.5%)	0.5129	16 (1.7%)	0.4231
	Dementia	5 (0.2%)	5 (0.1%)	0.7594	0 (0.0%)	1.0000	3 (0.3%)	0.4295
	Suicidality	4 (0.1%)	4 (0.1%)	1.0000	1 (0.5%)	0.2988	0 (0.0%)	0.5780
Liver Diseases	Any	208 (7.4%)	252 (7.2%)	0.7673	31 (15.0%)	<.0001	111 (11.5%)	<.0001
	Hepatitis B	94 (3.3%)	125 (3.6%)	0.6204	9 (4.3%)	0.4396	51 (5.3%)	0.0068
	Hepatitis C	115 (4.1%)	136 (3.9%)	0.6820	20 (9.7%)	0.0002	59 (6.1%)	0.0098
	Other chronic liver disease	16 (0.6%)	13 (0.4%)	0.2659	5 (2.4%)	0.0118	10 (1.0%)	0.1726
Bone Diseases	Any	1 (0.0%)	0 (0.0%)	0.4456	0 (0.0%)	1.0000	2 (0.2%)	0.1625
Peripheral Neuropathy	Any	34 (1.2%)	35 (1.0%)	0.4278	6 (2.9%)	0.0399	15 (1.6%)	0.4146
Renal Disease	Any	347 (12.3%)	421 (12.0%)	0.7099	45 (21.7%)	<.0001	151 (15.6%)	0.0090
	Renal Impairment	347 (12.3%)	421 (12.0%)	0.7099	45 (21.7%)	<.0001	151 (15.6%)	0.0090
	Moderate/Severe CKD	5 (0.2%)	3 (0.1%)	0.4795	0 (0.0%)	1.0000	1 (0.1%)	1.0000
	End Stage Renal Disease	1 (0.0%)	0 (0.0%)	0.4456	0 (0.0%)	1.0000	0 (0.0%)	1.0000
Hypertension	Any	264 (9.4%)	319 (9.1%)	0.7112	40 (19.3%)	<.0001	111 (11.5%)	0.0589
Rheumatoid Arthritis	Any	1 (0.0%)	6 (0.2%)	0.1403	0 (0.0%)	1.0000	0 (0.0%)	1.0000
Substance Abuse	Any	321 (11.4%)	337 (9.6%)	0.0212	19 (9.2%)	0.3291	133 (13.8%)	0.0519

		DTG N= 2,816	EVG/c N= 3,504	DTG vs. EVG p-value	RAL N= 207	DTG vs. RAL p-value	DRV(r/c) N= 967	DTG vs. DRV(r/c) p-value
	Alcohol Dependence	61 (2.2%)	77 (2.2%)	0.9326	6 (2.9%)	0.4897	20 (2.1%)	0.8560
	Drug Abuse	305 (10.8%)	322 (9.2%)	0.0300	19 (9.2%)	0.4583	128 (13.2%)	0.0426

Table 18. Baseline HIV-Infection Characteristics of ART-naïve patients (Study Population 2)

		DTG N= 2,816	EVG/c N= 3,504	DTG vs. EVG p-value	RAL N= 207	DTG vs. RAL p-value	DRV(r/c) N= 967	DTG vs. DRV(r/c) p-value
Months from first OPERA visit to baseline	Median (IQR)	0.7 (0.0, 1.4)	0.7 (0.0, 1.5)	0.0817	0.3 (0.0, 1.2)	<.0001	0.2 (0.0, 1.0)	<.0001
	0	740 (26.3%)	868 (24.8%)	0.1039	90 (43.5%)	<.0001	436 (45.1%)	<.0001
	>0 to 6	1759 (62.5%)	2192 (62.6%)	.	96 (46.4%)	.	435 (45.0%)	.
	>6 to 12	80 (2.8%)	106 (3.0%)	.	6 (2.9%)	.	19 (2.0%)	.
	>12 to 24	75 (2.7%)	133 (3.8%)	.	6 (2.9%)	.	29 (3.0%)	.
	>24	162 (5.8%)	205 (5.9%)	.	9 (4.3%)	.	48 (5.0%)	.
Year of study inclusion	Median (IQR)	2016.0 (2015.0, 2017.0)	2016.0 (2014.0, 2017.0)	<.0001	2015.0 (2014.0, 2017.0)	<.0001	2015.0 (2014.0, 2017.0)	<.0001
	2013	72 (2.6%)	287 (8.2%)	<.0001	41 (19.8%)	<.0001	102 (10.5%)	<.0001
	2014	339 (12.0%)	626 (17.9%)	.	52 (25.1%)	.	203 (21.0%)	.

		DTG N= 2,816	EVG/c N= 3,504	DTG vs. EVG p-value	RAL N= 207	DTG vs. RAL p-value	DRV(r/c) N= 967	DTG vs. DRV(r/c) p-value
	2015	560 (19.9%)	616 (17.6%)	.	42 (20.3%)	.	189 (19.5%)	.
	2016	730 (25.9%)	810 (23.1%)	.	19 (9.2%)	.	178 (18.4%)	.
	2017	815 (28.9%)	961 (27.4%)	.	42 (20.3%)	.	244 (25.2%)	.
	2018	300 (10.7%)	204 (5.8%)	.	11 (5.3%)	.	51 (5.3%)	.
History of AIDS-defining Illnesses	Yes	488 (17.3%)	503 (14.4%)	0.0012	53 (25.6%)	0.0027	279 (28.9%)	<.0001
HIV viral load (copies/ml)	Median (IQR)	50510.0 (16710.0, 140395.0)	45743.5 (13285.0, 131000.0)	0.0041	38100.0 (13370.0, 132000.0)	0.1307	63260.0 (17910.0, 203874.0)	0.0026
	>= 1,000 to < 10,000	481 (17.1%)	716 (20.4%)	0.0024	43 (20.8%)	0.3345	178 (18.4%)	<.0001
	>= 10,000 to < 100,000	1396 (49.6%)	1698 (48.5%)	.	102 (49.3%)	.	401 (41.5%)	.
	>= 100,000	939 (33.3%)	1090 (31.1%)	.	62 (30.0%)	.	388 (40.1%)	.
Log10 HIV viral load	Median (IQR)	4.7 (4.2, 5.1)	4.7 (4.1, 5.1)	0.0041	4.6 (4.1, 5.1)	0.1307	4.8 (4.3, 5.3)	0.0026
	>= 3 to < 4	481 (17.1%)	716 (20.4%)	0.0024	43 (20.8%)	0.3345	178 (18.4%)	<.0001
	>= 4 to < 5	1396 (49.6%)	1698 (48.5%)	.	102 (49.3%)	.	401 (41.5%)	.
	>= 5	939 (33.3%)	1090 (31.1%)	.	62 (30.0%)	.	388 (40.1%)	.
CD4 cell count (cell/µl)	Median (IQR)	372.0 (216.0, 529.0)	375.0 (219.0, 535.0)	0.2385	298.0 (134.0, 446.0)	<.0001	251.0 (90.0, 444.0)	<.0001

		DTG N= 2,816	EVG/c N= 3,504	DTG vs. EVG p-value	RAL N= 207	DTG vs. RAL p-value	DRV(r/c) N= 967	DTG vs. DRV(r/c) p-value
	>500	792 (28.1%)	1009 (28.8%)	0.5920	37 (17.9%)	0.0004	177 (18.3%)	<.0001
	>350 to <= 500	699 (24.8%)	865 (24.7%)	.	49 (23.7%)	.	160 (16.5%)	.
	>200 to <= 350	624 (22.2%)	815 (23.3%)	.	47 (22.7%)	.	221 (22.9%)	.
	>50 to <= 200	414 (14.7%)	495 (14.1%)	.	41 (19.8%)	.	206 (21.3%)	.
	<= 50	228 (8.1%)	261 (7.4%)	.	31 (15.0%)	.	177 (18.3%)	.
	Missing	59 (2.1%)	59 (1.7%)	.	2 (1.0%)	.	26 (2.7%)	.

1.3.2. ART-Experienced/suppressed Patients

Table 19. Baseline Demographic Characteristics of ART- experienced/suppressed patients (Study Population 2)

		DTG N= 3,584	EVG/c N= 4,281	DTG vs. EVG p-value	RAL N= 730	DTG vs. RAL p-value	DRV(r/c) N= 1,109	DTG vs. DRV(r/c) p-value
Age	Median (IQR)	44.4 (33.6, 52.7)	39.8 (30.8, 49.6)	<.0001	48.6 (40.2, 54.7)	<.0001	45.5 (34.8, 52.7)	0.0731
	13-25	299 (8.3%)	448 (10.5%)	<.0001	20 (2.7%)	<.0001	74 (6.7%)	0.1829
	26-49	2080 (58.1%)	2812 (65.7%)	.	397 (54.4%)	.	648 (58.5%)	.
	50+	1202 (33.6%)	1017 (23.8%)	.	313 (42.9%)	.	386 (34.8%)	.
Sex	Male	3068 (85.6%)	3748 (87.5%)	0.0090	583 (79.9%)	<.0001	876 (79.0%)	<.0001

		DTG N= 3,584	EVG/c N= 4,281	DTG vs. EVG p-value	RAL N= 730	DTG vs. RAL p-value	DRV(r/c) N= 1,109	DTG vs. DRV(r/c) p-value
	Female	516 (14.4%)	531 (12.4%)	.	146 (20.0%)	.	231 (20.8%)	.
	Unknown	0 (0.0%)	2 (0.0%)	.	1 (0.1%)	.	2 (0.2%)	.
Hispanic	Black	36 (4.1%)	35 (3.3%)	0.3359	3 (2.6%)	0.8379	14 (6.8%)	0.0556
	American Indian/Alaska Native	1 (0.1%)	3 (0.3%)	.	0 (0.0%)	.	1 (0.5%)	.
	Hawaiian/Other Pacific Islander	0 (0.0%)	3 (0.3%)	.	0 (0.0%)	.	1 (0.5%)	.
	Asian	3 (0.3%)	1 (0.1%)	.	1 (0.9%)	.	0 (0.0%)	.
	White	815 (92.4%)	992 (93.2%)	.	109 (94.8%)	.	186 (90.7%)	.
	Other	13 (1.5%)	10 (0.9%)	.	1 (0.9%)	.	3 (1.5%)	.
	>1 race	14 (1.6%)	20 (1.9%)	.	1 (0.9%)	.	0 (0.0%)	.
Non-Hispanic	Black	1099 (43.5%)	1363 (46.6%)	0.0597	200 (35.3%)	0.0123	417 (49.1%)	0.0298
	American Indian/Alaska Native	4 (0.2%)	10 (0.3%)	.	0 (0.0%)	.	3 (0.4%)	.
	Hawaiian/Other Pacific Islander	4 (0.2%)	6 (0.2%)	.	1 (0.2%)	.	1 (0.1%)	.
	Asian	66 (2.6%)	73 (2.5%)	.	14 (2.5%)	.	13 (1.5%)	.
	White	1317 (52.1%)	1441 (49.3%)	.	346 (61.1%)	.	409 (48.1%)	.
	Other	8 (0.3%)	2 (0.1%)	.	1 (0.2%)	.	0 (0.0%)	.

		DTG N= 3,584	EVG/c N= 4,281	DTG vs. EVG p-value	RAL N= 730	DTG vs. RAL p-value	DRV(r/c) N= 1,109	DTG vs. DRV(r/c) p-value
	>1 race	28 (1.1%)	27 (0.9%)	.	4 (0.7%)	.	7 (0.8%)	.
Race and/or ethnicity unknown	Yes	176 (4.9%)	295 (6.9%)	0.0002	49 (6.7%)	0.0460	54 (4.9%)	0.9554
Marital Status	Single	2515 (70.2%)	2967 (69.3%)	0.6724	454 (62.2%)	<.0001	759 (68.4%)	0.0860
	Married	275 (7.7%)	357 (8.3%)	.	79 (10.8%)	.	97 (8.7%)	.
	Domestic partnership	42 (1.2%)	64 (1.5%)	.	15 (2.1%)	.	19 (1.7%)	.
	Widowed	24 (0.7%)	24 (0.6%)	.	7 (1.0%)	.	8 (0.7%)	.
	Separated/divorced	83 (2.3%)	99 (2.3%)	.	38 (5.2%)	.	40 (3.6%)	.
	Unknown	645 (18.0%)	770 (18.0%)	.	137 (18.8%)	.	186 (16.8%)	.
Risk of Infection	MSM	2315 (64.6%)	2755 (64.4%)	0.8258	380 (52.1%)	<.0001	629 (56.7%)	<.0001
	Not MSM	1269 (35.4%)	1526 (35.6%)	.	350 (47.9%)	.	480 (43.3%)	.
History of Syphilis	Yes	1056 (29.5%)	1364 (31.9%)	0.0218	164 (22.5%)	0.0001	247 (22.3%)	<.0001
Region	Northeast	387 (10.8%)	328 (7.7%)	<.0001	94 (12.9%)	<.0001	84 (7.6%)	<.0001
	South	1728 (48.2%)	2566 (59.9%)	.	427 (58.5%)	.	690 (62.2%)	.
	Midwest	115 (3.2%)	138 (3.2%)	.	38 (5.2%)	.	46 (4.1%)	.
	West	1354 (37.8%)	1248 (29.2%)	.	171 (23.4%)	.	289 (26.1%)	.
	US Territories	0 (0.0%)	1 (0.0%)	.	0 (0.0%)	.	0 (0.0%)	.

		DTG N= 3,584	EVG/c N= 4,281	DTG vs. EVG p-value	RAL N= 730	DTG vs. RAL p-value	DRV(r/c) N= 1,109	DTG vs. DRV(r/c) p-value
Medicaid	Yes	735 (20.5%)	647 (15.1%)	<.0001	167 (22.9%)	0.1514	224 (20.2%)	0.8233
Medicare	Yes	430 (12.0%)	325 (7.6%)	<.0001	121 (16.6%)	0.0007	174 (15.7%)	0.0013
Commercial Insurance	Yes	1416 (39.5%)	1826 (42.7%)	0.0048	300 (41.1%)	0.4246	388 (35.0%)	0.0068
Cash	Yes	1907 (53.2%)	2129 (49.7%)	0.0021	398 (54.5%)	0.5172	576 (51.9%)	0.4590
ADAP/Ryan White	Yes	1028 (28.7%)	1212 (28.3%)	0.7159	132 (18.1%)	<.0001	299 (27.0%)	0.2658
Other	Yes	10 (0.3%)	21 (0.5%)	0.1512	2 (0.3%)	1.0000	1 (0.1%)	0.4762
No Payer info	Yes	461 (12.9%)	689 (16.1%)	<.0001	134 (18.4%)	<.0001	175 (15.8%)	0.0131

Table 20. Baseline Clinical Characteristics of ART- experienced/suppressed patients (Study Population 2)

		DTG N= 3,584	EVG/c N= 4,281	DTG vs. EVG p-value	RAL N= 730	DTG vs. RAL p-value	DRV(r/c) N= 1,109	DTG vs. DRV(r/c) p-value
Hemoglobin, g/dL	Median (IQR)	14.7 (13.6, 15.6)	14.7 (13.8, 15.6)	0.0687	14.6 (13.4, 15.6)	0.2042	14.3 (13.3, 15.3)	<.0001
	Normal	3451 (96.3%)	4135 (96.6%)	0.2660	683 (93.6%)	0.0008	1061 (95.7%)	0.2680
	DAIDS Grade 1 (mild)	37 (1.0%)	33 (0.8%)	.	11 (1.5%)	.	6 (0.5%)	.

		DTG N= 3,584	EVG/c N= 4,281	DTG vs. EVG p-value	RAL N= 730	DTG vs. RAL p-value	DRV(r/c) N= 1,109	DTG vs. DRV(r/c) p-value
	DAIDS Grade 2 (moderate)	14 (0.4%)	8 (0.2%)	.	5 (0.7%)	.	8 (0.7%)	.
	DAIDS Grade 3 (Severe)	13 (0.4%)	10 (0.2%)	.	0 (0.0%)	.	6 (0.5%)	.
	DAIDS Grade 4 (potentially life-threatening)	2 (0.1%)	2 (0.0%)	.	0 (0.0%)	.	1 (0.1%)	.
	Missing	67 (1.9%)	93 (2.2%)	.	31 (4.2%)	.	27 (2.4%)	.
Hematocrit, %	Median (IQR)	43.3 (40.5, 45.6)	43.7 (41.0, 46.0)	<.0001	43.3 (40.0, 45.8)	0.4998	42.6 (39.7, 45.3)	<.0001
	Low	321 (9.0%)	293 (6.8%)	0.0051	81 (11.1%)	<.0001	111 (10.0%)	0.3360
	Normal	3057 (85.3%)	3735 (87.2%)	.	574 (78.6%)	.	933 (84.1%)	.
	High	138 (3.9%)	160 (3.7%)	.	42 (5.8%)	.	37 (3.3%)	.
	Missing	68 (1.9%)	93 (2.2%)	.	33 (4.5%)	.	28 (2.5%)	.
VACS mortality index	Median (IQR)	10.0 (0.0, 20.0)	6.0 (0.0, 16.0)	<.0001	15.0 (6.0, 24.0)	<.0001	12.0 (6.0, 22.0)	<.0001
	0 to <15	2059 (57.4%)	2760 (64.5%)	<.0001	309 (42.3%)	<.0001	531 (47.9%)	<.0001
	>=15 to <30	867 (24.2%)	827 (19.3%)	.	207 (28.4%)	.	326 (29.4%)	.
	>=30 to <45	238 (6.6%)	184 (4.3%)	.	58 (7.9%)	.	90 (8.1%)	.
	>= 45	128 (3.6%)	74 (1.7%)	.	51 (7.0%)	.	46 (4.1%)	.

		DTG N= 3,584	EVG/c N= 4,281	DTG vs. EVG p-value	RAL N= 730	DTG vs. RAL p-value	DRV(r/c) N= 1,109	DTG vs. DRV(r/c) p-value
	Missing	292 (8.1%)	436 (10.2%)	.	105 (14.4%)	.	116 (10.5%)	.
BMI	Median (IQR)	25.8 (23.0, 28.8)	25.6 (23.1, 28.9)	0.8982	25.9 (23.1, 28.9)	0.3978	26.1 (23.1, 29.5)	0.0406
	Underweight	100 (2.8%)	115 (2.7%)	0.0002	22 (3.0%)	<.0001	29 (2.6%)	<.0001
	Normal weight	1348 (37.6%)	1647 (38.5%)	.	234 (32.1%)	.	396 (35.7%)	.
	Overweight	1360 (37.9%)	1510 (35.3%)	.	258 (35.3%)	.	363 (32.7%)	.
	Obese	646 (18.0%)	764 (17.8%)	.	128 (17.5%)	.	237 (21.4%)	.
	Missing	130 (3.6%)	245 (5.7%)	.	88 (12.1%)	.	84 (7.6%)	.
HDL, mg/dL	Median (IQR)	48.0 (39.0, 59.0)	48.0 (40.0, 58.0)	0.3259	45.0 (37.0, 57.0)	0.0013	47.0 (39.0, 57.0)	0.1520
	Normal	725 (20.2%)	798 (18.6%)	<.0001	120 (16.4%)	<.0001	167 (15.1%)	<.0001
	Borderline Abnormal	1522 (42.5%)	1811 (42.3%)	.	274 (37.5%)	.	468 (42.2%)	.
	Dyslipidemia	827 (23.1%)	859 (20.1%)	.	189 (25.9%)	.	239 (21.6%)	.
	Missing	510 (14.2%)	813 (19.0%)	.	147 (20.1%)	.	235 (21.2%)	.
Triglycerides, mg/dL	Median (IQR)	125.0 (84.0, 187.0)	121.0 (82.0, 178.0)	0.0204	119.0 (81.0, 188.0)	0.3400	132.0 (92.0, 190.5)	0.0061
	Normal	1914 (53.4%)	2257 (52.7%)	<.0001	380 (52.1%)	0.0003	532 (48.0%)	<.0001
	Borderline Abnormal	498 (13.9%)	562 (13.1%)	.	77 (10.5%)	.	153 (13.8%)	.

		DTG N= 3,584	EVG/c N= 4,281	DTG vs. EVG p-value	RAL N= 730	DTG vs. RAL p-value	DRV(r/c) N= 1,109	DTG vs. DRV(r/c) p-value
	Dyslipidemia	621 (17.3%)	604 (14.1%)	.	117 (16.0%)	.	177 (16.0%)	.
	Severe Dyslipidemia	43 (1.2%)	55 (1.3%)	.	8 (1.1%)	.	14 (1.3%)	.
	Missing	508 (14.2%)	803 (18.8%)	.	148 (20.3%)	.	233 (21.0%)	.
Any concomitant non-ART listed below	Yes	1768 (49.3%)	1689 (39.5%)	<.0001	375 (51.4%)	0.3151	498 (44.9%)	0.0100
Antibiotics	Yes	306 (8.5%)	315 (7.4%)	0.0533	57 (7.8%)	0.5174	72 (6.5%)	0.0287
Direct Acting Antivirals (DAAs)	Yes	41 (1.1%)	16 (0.4%)	<.0001	4 (0.5%)	0.2270	4 (0.4%)	0.0203
Lipid lowering agents	Yes	648 (18.1%)	524 (12.2%)	<.0001	140 (19.2%)	0.4842	156 (14.1%)	0.0019
Non-steroidal Anti-inflammatory Agents (NSAIDS)	Yes	249 (6.9%)	230 (5.4%)	0.0036	38 (5.2%)	0.0852	70 (6.3%)	0.4624
Antidepressants	Yes	740 (20.6%)	652 (15.2%)	<.0001	178 (24.4%)	0.0246	226 (20.4%)	0.8467
Anxiolytics/Hypnotics/Sedatives	Yes	540 (15.1%)	443 (10.3%)	<.0001	137 (18.8%)	0.0122	139 (12.5%)	0.0361
Immune Modulators	Yes	259 (7.2%)	269 (6.3%)	0.0961	33 (4.5%)	0.0080	64 (5.8%)	0.0943
Number of concomitant non-ART medications listed above	0	1816 (50.7%)	2592 (60.5%)	<.0001	355 (48.6%)	0.4460	611 (55.1%)	0.0067
	1-2	1378 (38.4%)	1417 (33.1%)	.	283 (38.8%)	.	413 (37.2%)	.
	3-4	314 (8.8%)	235 (5.5%)	.	77 (10.5%)	.	68 (6.1%)	.
	5+	76 (2.1%)	37 (0.9%)	.	15 (2.1%)	.	17 (1.5%)	.

Table 21. Baseline Comorbidities of ART- experienced/suppressed patients (Study Population 2)

		DTG N= 3,584	EVG/c N= 4,281	DTG vs. EVG p-value	RAL N= 730	DTG vs. RAL p-value	DRV(r/c) N= 1,109	DTG vs. DRV(r/c) p-value
Comorbidity at baseline	Any	2784 (77.7%)	2896 (67.6%)	<.0001	594 (81.4%)	0.0274	808 (72.9%)	0.0009
Cardiovascular Disease Conditions	Any	282 (7.9%)	222 (5.2%)	<.0001	78 (10.7%)	0.0121	76 (6.9%)	0.2657
	Arrhythmia	109 (3.0%)	74 (1.7%)	0.0001	23 (3.2%)	0.8757	15 (1.4%)	0.0022
	Myocardial Infarction	24 (0.7%)	13 (0.3%)	0.0182	8 (1.1%)	0.2212	11 (1.0%)	0.2757
	Angina	10 (0.3%)	6 (0.1%)	0.2119	1 (0.1%)	0.7027	3 (0.3%)	1.0000
	Other/Unspecified CHD	134 (3.7%)	101 (2.4%)	0.0003	37 (5.1%)	0.0933	47 (4.2%)	0.4506
	Occlusion/stenosis of precerebral arteries	3 (0.1%)	1 (0.0%)	0.3368	0 (0.0%)	1.0000	2 (0.2%)	0.3383
	Stroke	28 (0.8%)	24 (0.6%)	0.2292	17 (2.3%)	0.0002	7 (0.6%)	0.6118
	Transient Ischemic Attack	10 (0.3%)	7 (0.2%)	0.3324	4 (0.5%)	0.2754	2 (0.2%)	0.7431
	Other CBV	53 (1.5%)	50 (1.2%)	0.2272	19 (2.6%)	0.0307	13 (1.2%)	0.4486
	Peripheral Arterial Disease	20 (0.6%)	15 (0.4%)	0.1774	6 (0.8%)	0.4280	5 (0.5%)	0.8156
	Abdominal Aortic Aneurysm	3 (0.1%)	1 (0.0%)	0.3368	0 (0.0%)	1.0000	0 (0.0%)	1.0000
Invasive Cancer	Any	245 (6.8%)	209 (4.9%)	0.0002	50 (6.8%)	0.9896	88 (7.9%)	0.2128
Endocrine Disorders (excluding T2DM)	Any	1126 (31.4%)	1120 (26.2%)	<.0001	204 (27.9%)	0.0641	259 (23.4%)	<.0001

		DTG N= 3,584	EVG/c N= 4,281	DTG vs. EVG p-value	RAL N= 730	DTG vs. RAL p-value	DRV(r/c) N= 1,109	DTG vs. DRV(r/c) p-value
	Hyperlipidemia	1079 (30.1%)	1059 (24.7%)	<.0001	181 (24.8%)	0.0040	248 (22.4%)	<.0001
	Hyperthyroidism	17 (0.5%)	16 (0.4%)	0.6000	7 (1.0%)	0.1649	4 (0.4%)	0.7988
	Hypothyroidism	100 (2.8%)	96 (2.2%)	0.1207	30 (4.1%)	0.0574	22 (2.0%)	0.1403
	Thyroiditis	2 (0.1%)	2 (0.0%)	1.0000	0 (0.0%)	1.0000	1 (0.1%)	0.5547
Mental Health Conditions	Any	1084 (30.2%)	1041 (24.3%)	<.0001	212 (29.0%)	0.5176	266 (24.0%)	<.0001
	Anxiety Disorders	715 (19.9%)	732 (17.1%)	0.0012	119 (16.3%)	0.0229	164 (14.8%)	0.0001
	Bipolar or Manic Disorders	189 (5.3%)	155 (3.6%)	0.0004	46 (6.3%)	0.2647	50 (4.5%)	0.3113
	Major Depressive Disorder	359 (10.0%)	279 (6.5%)	<.0001	57 (7.8%)	0.0654	86 (7.8%)	0.0246
	Schizophrenic Disorder	43 (1.2%)	40 (0.9%)	0.2513	16 (2.2%)	0.0354	11 (1.0%)	0.5705
	Dementia	18 (0.5%)	9 (0.2%)	0.0327	2 (0.3%)	0.5581	1 (0.1%)	0.0607
	Suicidality	11 (0.3%)	12 (0.3%)	0.8372	3 (0.4%)	0.7179	4 (0.4%)	0.7634
Liver Diseases	Any	624 (17.4%)	505 (11.8%)	<.0001	152 (20.8%)	0.0287	183 (16.5%)	0.4831
	Hepatitis B	191 (5.3%)	199 (4.6%)	0.1660	44 (6.0%)	0.4487	85 (7.7%)	0.0039
	Hepatitis C	398 (11.1%)	260 (6.1%)	<.0001	104 (14.2%)	0.0158	100 (9.0%)	0.0485
	Other chronic liver disease	132 (3.7%)	102 (2.4%)	0.0007	20 (2.7%)	0.2077	30 (2.7%)	0.1190
Bone Diseases	Any	106 (3.0%)	68 (1.6%)	<.0001	15 (2.1%)	0.1781	16 (1.4%)	0.0056
Peripheral Neuropathy	Any	269 (7.5%)	199 (4.6%)	<.0001	60 (8.2%)	0.5079	84 (7.6%)	0.9395

		DTG N= 3,584	EVG/c N= 4,281	DTG vs. EVG p-value	RAL N= 730	DTG vs. RAL p-value	DRV(r/c) N= 1,109	DTG vs. DRV(r/c) p-value
Renal Disease	Any	1429 (39.9%)	1381 (32.3%)	<.0001	333 (45.6%)	0.0040	457 (41.2%)	0.4275
	Renal Impairment	1429 (39.9%)	1381 (32.3%)	<.0001	333 (45.6%)	0.0040	457 (41.2%)	0.4275
	Moderate/Severe CKD	109 (3.0%)	48 (1.1%)	<.0001	25 (3.4%)	0.5863	13 (1.2%)	0.0006
	End Stage Renal Disease	7 (0.2%)	2 (0.0%)	0.0891	4 (0.5%)	0.0997	3 (0.3%)	0.7090
Hypertension	Any	862 (24.1%)	825 (19.3%)	<.0001	206 (28.2%)	0.0174	220 (19.8%)	0.0036
Rheumatoid Arthritis	Any	15 (0.4%)	11 (0.3%)	0.2399	1 (0.1%)	0.4992	4 (0.4%)	1.0000
Substance Abuse	Any	521 (14.5%)	449 (10.5%)	<.0001	78 (10.7%)	0.0061	144 (13.0%)	0.1952
	Alcohol Dependence	157 (4.4%)	117 (2.7%)	<.0001	20 (2.7%)	0.0416	40 (3.6%)	0.2615
	Drug Abuse	496 (13.8%)	429 (10.0%)	<.0001	71 (9.7%)	0.0027	141 (12.7%)	0.3391

Table 22. Baseline HIV-Infection Characteristics of ART- experienced/suppressed patients (Study Population 2)

		DTG N= 3,584	EVG/c N= 4,281	DTG vs. EVG p-value	RAL N= 730	DTG vs. RAL p-value	DRV(r/c) N= 1,109	DTG vs. DRV(r/c) p-value
Months from first OPERA visit to baseline	Median (IQR)	12.2 (0.2, 54.5)	4.2 (0.0, 40.9)	<.0001	0.7 (0.0, 20.3)	<.0001	0.7 (0.0, 30.4)	<.0001
	0	855 (23.9%)	1288 (30.1%)	<.0001	298 (40.8%)	<.0001	450 (40.6%)	<.0001

		DTG N= 3,584	EVG/c N= 4,281	DTG vs. EVG p-value	RAL N= 730	DTG vs. RAL p-value	DRV(r/c) N= 1,109	DTG vs. DRV(r/c) p-value
	>0 to 6	720 (20.1%)	952 (22.2%)	.	184 (25.2%)	.	252 (22.7%)	.
	>6 to 12	213 (5.9%)	250 (5.8%)	.	31 (4.2%)	.	52 (4.7%)	.
	>12 to 24	336 (9.4%)	341 (8.0%)	.	42 (5.8%)	.	56 (5.0%)	.
	>24	1460 (40.7%)	1450 (33.9%)	.	175 (24.0%)	.	299 (27.0%)	.
Year of study inclusion	Median (IQR)	2016.0 (2015.0, 2017.0)	2016.0 (2015.0, 2017.0)	0.0079	2014.0 (2014.0, 2016.0)	<.0001	2015.0 (2014.0, 2016.0)	<.0001
	2013	108 (3.0%)	204 (4.8%)	<.0001	119 (16.3%)	<.0001	145 (13.1%)	<.0001
	2014	594 (16.6%)	562 (13.1%)	.	258 (35.3%)	.	306 (27.6%)	.
	2015	793 (22.1%)	690 (16.1%)	.	153 (21.0%)	.	214 (19.3%)	.
	2016	956 (26.7%)	1529 (35.7%)	.	103 (14.1%)	.	224 (20.2%)	.
	2017	912 (25.4%)	1032 (24.1%)	.	73 (10.0%)	.	179 (16.1%)	.
	2018	221 (6.2%)	264 (6.2%)	.	24 (3.3%)	.	41 (3.7%)	.
Prior exposure: DTG	Yes	8 (0.2%)	1 (0.0%)	0.0141	0 (0.0%)	0.3661	0 (0.0%)	0.2110
Prior exposure: EVG/c	Yes	10 (0.3%)	44 (1.0%)	<.0001	1 (0.1%)	0.7027	0 (0.0%)	0.1302
Prior exposure: RAL	Yes	29 (0.8%)	33 (0.8%)	0.8483	64 (8.8%)	<.0001	11 (1.0%)	0.5629
Prior exposure: DRV(/r/c)	Yes	34 (0.9%)	27 (0.6%)	0.1094	7 (1.0%)	0.9793	37 (3.3%)	<.0001

		DTG N= 3,584	EVG/c N= 4,281	DTG vs. EVG p-value	RAL N= 730	DTG vs. RAL p-value	DRV(r/c) N= 1,109	DTG vs. DRV(r/c) p-value
Number of classes of core agents experienced prior to baseline	1	1877 (52.4%)	1807 (42.2%)	<.0001	160 (21.9%)	<.0001	277 (25.0%)	<.0001
	2	292 (8.1%)	219 (5.1%)	.	42 (5.8%)	.	69 (6.2%)	.
	3	11 (0.3%)	20 (0.5%)	.	17 (2.3%)	.	8 (0.7%)	.
	4+	3 (0.1%)	1 (0.0%)	.	2 (0.3%)	.	1 (0.1%)	.
	Missing	1401 (39.1%)	2234 (52.2%)	.	509 (69.7%)	.	754 (68.0%)	.
History of AIDS-defining Illnesses	Yes	973 (27.1%)	844 (19.7%)	<.0001	198 (27.1%)	0.9889	313 (28.2%)	0.4830
CD4 cell count (cell/µl)	Median (IQR)	646.0 (469.0, 831.0)	646.0 (485.0, 851.0)	0.0668	610.0 (428.0, 823.0)	0.0080	578.0 (412.0, 788.0)	<.0001
	>500	2456 (68.5%)	3081 (72.0%)	0.0003	448 (61.4%)	0.0055	665 (60.0%)	<.0001
	>350 to <= 500	621 (17.3%)	732 (17.1%)	.	156 (21.4%)	.	221 (19.9%)	.
	>200 to <= 350	311 (8.7%)	309 (7.2%)	.	75 (10.3%)	.	118 (10.6%)	.
	>50 to <= 200	121 (3.4%)	97 (2.3%)	.	33 (4.5%)	.	67 (6.0%)	.
	<= 50	5 (0.1%)	8 (0.2%)	.	3 (0.4%)	.	6 (0.5%)	.
	Missing	70 (2.0%)	54 (1.3%)	.	15 (2.1%)	.	32 (2.9%)	.

1.3.3. ART-Experienced/viremic Patients

Table 23. Baseline Demographic Characteristics of ART- experienced/viremic (Study Population 2)

		DTG N= 2,787	EVG/c N= 3,140	DTG vs. EVG p-value	RAL N= 338	DTG vs. RAL p-value	DRV(r/c) N= 1,162	DTG vs. DRV(r/c) p-value
Age	Median (IQR)	36.8 (28.5, 47.9)	34.2 (27.0, 45.0)	<.0001	45.0 (35.2, 52.0)	<.0001	40.1 (30.9, 49.3)	<.0001
	13-25	439 (15.8%)	631 (20.1%)	<.0001	22 (6.5%)	<.0001	112 (9.7%)	<.0001
	26-49	1779 (64.0%)	2043 (65.1%)	.	203 (60.2%)	.	784 (67.6%)	.
	50+	562 (20.2%)	462 (14.7%)	.	112 (33.2%)	.	264 (22.8%)	.
Sex	Male	2337 (83.9%)	2713 (86.4%)	0.0015	267 (79.0%)	0.0302	919 (79.1%)	0.0003
	Female	450 (16.1%)	423 (13.5%)	.	71 (21.0%)	.	242 (20.8%)	.
	Unknown	0 (0.0%)	4 (0.1%)	.	0 (0.0%)	.	1 (0.1%)	.
Hispanic	Black	25 (3.8%)	29 (4.3%)	0.6616	3 (7.1%)	0.8446	10 (4.5%)	0.8549
	American Indian/Alaska Native	3 (0.5%)	3 (0.4%)	.	0 (0.0%)	.	0 (0.0%)	.
	Hawaiian/Other Pacific Islander	0 (0.0%)	3 (0.4%)	.	0 (0.0%)	.	0 (0.0%)	.
	Asian	1 (0.2%)	2 (0.3%)	.	0 (0.0%)	.	1 (0.5%)	.
	White	610 (93.8%)	622 (93.3%)	.	39 (92.9%)	.	206 (93.2%)	.
	Other	2 (0.3%)	1 (0.1%)	.	0 (0.0%)	.	1 (0.5%)	.
	>1 race	9 (1.4%)	7 (1.0%)	.	0 (0.0%)	.	3 (1.4%)	.

		DTG N= 2,787	EVG/c N= 3,140	DTG vs. EVG p-value	RAL N= 338	DTG vs. RAL p-value	DRV(r/c) N= 1,162	DTG vs. DRV(r/c) p-value
Non-Hispanic	Black	1233 (60.5%)	1449 (62.2%)	0.3886	140 (50.5%)	0.0306	575 (64.5%)	0.0085
	American Indian/Alaska Native	6 (0.3%)	6 (0.3%)	.	0 (0.0%)	.	3 (0.3%)	.
	Hawaiian/Other Pacific Islander	2 (0.1%)	3 (0.1%)	.	0 (0.0%)	.	3 (0.3%)	.
	Asian	41 (2.0%)	44 (1.9%)	.	5 (1.8%)	.	4 (0.4%)	.
	White	743 (36.4%)	798 (34.3%)	.	130 (46.9%)	.	300 (33.6%)	.
	Other	0 (0.0%)	0 (0.0%)	.	0 (0.0%)	.	1 (0.1%)	.
	>1 race	14 (0.7%)	28 (1.2%)	.	2 (0.7%)	.	6 (0.7%)	.
Race and/or ethnicity unknown	Yes	98 (3.5%)	145 (4.6%)	0.0328	19 (5.6%)	0.0542	49 (4.2%)	0.2893
Marital Status	Single	2065 (74.1%)	2310 (73.6%)	0.8859	234 (69.2%)	0.0600	847 (72.9%)	0.0083
	Married	129 (4.6%)	166 (5.3%)	.	26 (7.7%)	.	84 (7.2%)	.
	Domestic partnership	36 (1.3%)	43 (1.4%)	.	2 (0.6%)	.	16 (1.4%)	.
	Widowed	20 (0.7%)	19 (0.6%)	.	3 (0.9%)	.	10 (0.9%)	.
	Separated/divorced	67 (2.4%)	77 (2.5%)	.	13 (3.8%)	.	37 (3.2%)	.
	Unknown	470 (16.9%)	525 (16.7%)	.	60 (17.8%)	.	168 (14.5%)	.
Risk of Infection	MSM	1761 (63.2%)	2049 (65.3%)	0.0972	169 (50.0%)	<.0001	606 (52.2%)	<.0001

		DTG N= 2,787	EVG/c N= 3,140	DTG vs. EVG p-value	RAL N= 338	DTG vs. RAL p-value	DRV(r/c) N= 1,162	DTG vs. DRV(r/c) p-value
	Not MSM	1026 (36.8%)	1091 (34.7%)	.	169 (50.0%)	.	556 (47.8%)	.
History of Syphilis	Yes	900 (32.3%)	1040 (33.1%)	0.4976	78 (23.1%)	0.0006	388 (33.4%)	0.5024
Region	Northeast	188 (6.7%)	235 (7.5%)	<.0001	22 (6.5%)	0.6504	59 (5.1%)	0.0015
	South	1635 (58.7%)	2083 (66.3%)	.	209 (61.8%)	.	742 (63.9%)	.
	Midwest	124 (4.4%)	158 (5.0%)	.	16 (4.7%)	.	30 (2.6%)	.
	West	840 (30.1%)	664 (21.1%)	.	91 (26.9%)	.	331 (28.5%)	.
Medicaid	Yes	688 (24.7%)	549 (17.5%)	<.0001	98 (29.0%)	0.0847	300 (25.8%)	0.4544
Medicare	Yes	311 (11.2%)	193 (6.1%)	<.0001	57 (16.9%)	0.0021	152 (13.1%)	0.0871
Commercial Insurance	Yes	942 (33.8%)	1159 (36.9%)	0.0125	120 (35.5%)	0.5324	327 (28.1%)	0.0005
Cash	Yes	1440 (51.7%)	1654 (52.7%)	0.4387	202 (59.8%)	0.0049	637 (54.8%)	0.0708
ADAP/Ryan White	Yes	1010 (36.2%)	1235 (39.3%)	0.0143	102 (30.2%)	0.0279	386 (33.2%)	0.0703
Other	Yes	16 (0.6%)	21 (0.7%)	0.7418	2 (0.6%)	1.0000	9 (0.8%)	0.5099
No Payer info	Yes	244 (8.8%)	323 (10.3%)	0.0454	47 (13.9%)	0.0021	157 (13.5%)	<.0001

Table 24. Baseline Clinical Characteristics of ART- experienced/viremic (Study Population 2)

		DTG N= 2,787	EVG/c N= 3,140	DTG vs. EVG p-value	RAL N= 338	DTG vs. RAL p-value	DRV(r/c) N= 1,162	DTG vs. DRV(r/c) p-value
Hemoglobin, g/dL	Median (IQR)	14.1 (12.8, 15.1)	14.2 (13.1, 15.2)	0.0117	14.1 (12.5, 15.2)	0.3843	13.7 (12.4, 14.8)	<.0001
	Normal	2581 (92.6%)	2958 (94.2%)	0.1242	288 (85.2%)	<.0001	1048 (90.2%)	0.0691
	DAIDS Grade 1 (mild)	76 (2.7%)	70 (2.2%)	.	16 (4.7%)	.	49 (4.2%)	.
	DAIDS Grade 2 (moderate)	53 (1.9%)	39 (1.2%)	.	13 (3.8%)	.	33 (2.8%)	.
	DAIDS Grade 3 (Severe)	33 (1.2%)	27 (0.9%)	.	2 (0.6%)	.	15 (1.3%)	.
	DAIDS Grade 4 (potentially life-threatening)	1 (0.0%)	3 (0.1%)	.	1 (0.3%)	.	1 (0.1%)	.
	Missing	43 (1.5%)	43 (1.4%)	.	18 (5.3%)	.	16 (1.4%)	.
Hematocrit, %	Median (IQR)	42.2 (38.8, 44.8)	42.4 (39.3, 45.1)	0.0016	41.8 (37.8, 45.2)	0.3794	41.1 (37.5, 44.0)	<.0001
	Low	533 (19.1%)	512 (16.3%)	0.0298	76 (22.5%)	<.0001	287 (24.7%)	0.0008
	Normal	2143 (76.9%)	2494 (79.4%)	.	227 (67.2%)	.	839 (72.2%)	.
	High	65 (2.3%)	86 (2.7%)	.	17 (5.0%)	.	19 (1.6%)	.
	Missing	46 (1.7%)	48 (1.5%)	.	18 (5.3%)	.	17 (1.5%)	.
VACS mortality index	Median (IQR)	19.0 (12.0, 34.0)	17.0 (10.0, 29.0)	<.0001	20.0 (7.0, 35.5)	0.9649	23.0 (13.0, 41.0)	<.0001

		DTG N= 2,787	EVG/c N= 3,140	DTG vs. EVG p-value	RAL N= 338	DTG vs. RAL p-value	DRV(r/c) N= 1,162	DTG vs. DRV(r/c) p-value
	0 to <15	1019 (36.6%)	1279 (40.7%)	<.0001	109 (32.2%)	0.0009	321 (27.6%)	<.0001
	>=15 to <30	799 (28.7%)	883 (28.1%)	.	81 (24.0%)	.	331 (28.5%)	.
	>=30 to <45	324 (11.6%)	337 (10.7%)	.	46 (13.6%)	.	170 (14.6%)	.
	>= 45	411 (14.7%)	334 (10.6%)	.	52 (15.4%)	.	238 (20.5%)	.
	Missing	234 (8.4%)	307 (9.8%)	.	50 (14.8%)	.	102 (8.8%)	.
BMI	Median (IQR)	24.9 (22.3, 28.4)	24.9 (22.1, 28.3)	0.6993	25.1 (22.2, 28.8)	0.7925	25.0 (22.1, 28.3)	0.8199
	Underweight	114 (4.1%)	120 (3.8%)	0.8182	11 (3.3%)	0.0014	52 (4.5%)	0.0008
	Normal weight	1265 (45.4%)	1436 (45.7%)	.	143 (42.3%)	.	500 (43.0%)	.
	Overweight	873 (31.3%)	967 (30.8%)	.	108 (32.0%)	.	358 (30.8%)	.
	Obese	470 (16.9%)	530 (16.9%)	.	55 (16.3%)	.	195 (16.8%)	.
	Missing	65 (2.3%)	87 (2.8%)	.	21 (6.2%)	.	57 (4.9%)	.
HDL, mg/dL	Median (IQR)	43.0 (35.0, 54.0)	44.0 (35.0, 52.0)	0.8739	44.0 (37.0, 56.0)	0.1636	43.0 (34.0, 53.0)	0.2001
	Normal	355 (12.7%)	360 (11.5%)	0.0409	50 (14.8%)	0.0264	137 (11.8%)	0.6203
	Borderline Abnormal	1007 (36.1%)	1153 (36.7%)	.	115 (34.0%)	.	412 (35.5%)	.
	Dyslipidemia	882 (31.6%)	936 (29.8%)	.	88 (26.0%)	.	391 (33.6%)	.
	Missing	543 (19.5%)	691 (22.0%)	.	85 (25.1%)	.	222 (19.1%)	.

		DTG N= 2,787	EVG/c N= 3,140	DTG vs. EVG p-value	RAL N= 338	DTG vs. RAL p-value	DRV(r/c) N= 1,162	DTG vs. DRV(r/c) p-value
Triglycerides, mg/dL	Median (IQR)	111.5 (80.0, 166.0)	111.0 (77.0, 163.0)	0.2957	122.0 (83.0, 183.0)	0.0429	116.0 (83.5, 165.0)	0.1058
	Normal	1559 (55.9%)	1730 (55.1%)	0.1317	162 (47.9%)	0.0016	644 (55.4%)	0.9399
	Borderline Abnormal	346 (12.4%)	348 (11.1%)	.	39 (11.5%)	.	144 (12.4%)	.
	Dyslipidemia	333 (11.9%)	364 (11.6%)	.	46 (13.6%)	.	149 (12.8%)	.
	Severe Dyslipidemia	14 (0.5%)	18 (0.6%)	.	6 (1.8%)	.	7 (0.6%)	.
	Missing	535 (19.2%)	680 (21.7%)	.	85 (25.1%)	.	218 (18.8%)	.
Any concomitant non-ART listed below	Yes	1163 (41.7%)	1135 (36.1%)	<.0001	172 (50.9%)	0.0013	527 (45.4%)	0.0360
Antibiotics	Yes	453 (16.3%)	454 (14.5%)	0.0553	59 (17.5%)	0.5730	241 (20.7%)	0.0007
Direct Acting Antivirals (DAAs)	Yes	12 (0.4%)	5 (0.2%)	0.0855	0 (0.0%)	0.6310	2 (0.2%)	0.3767
Lipid lowering agents	Yes	204 (7.3%)	157 (5.0%)	0.0002	44 (13.0%)	0.0003	63 (5.4%)	0.0304
Non-steroidal Anti-inflammatory Agents (NSAIDS)	Yes	177 (6.4%)	160 (5.1%)	0.0372	22 (6.5%)	0.9106	78 (6.7%)	0.6735
Antidepressants	Yes	396 (14.2%)	375 (11.9%)	0.0096	66 (19.5%)	0.0093	185 (15.9%)	0.1664
Anxiolytics/Hypnotics/Sedatives	Yes	219 (7.9%)	195 (6.2%)	0.0130	43 (12.7%)	0.0023	85 (7.3%)	0.5597
Immune Modulators	Yes	196 (7.0%)	189 (6.0%)	0.1140	25 (7.4%)	0.8054	82 (7.1%)	0.9784
Number of concomitant non-ART medications listed above	0	1624 (58.3%)	2005 (63.9%)	<.0001	166 (49.1%)	0.0116	635 (54.6%)	0.2051

		DTG N= 2,787	EVG/c N= 3,140	DTG vs. EVG p-value	RAL N= 338	DTG vs. RAL p-value	DRV(r/c) N= 1,162	DTG vs. DRV(r/c) p-value
	1-2	968 (34.7%)	993 (31.6%)	.	143 (42.3%)	.	442 (38.0%)	.
	3-4	177 (6.4%)	118 (3.8%)	.	25 (7.4%)	.	78 (6.7%)	.
	5+	18 (0.6%)	24 (0.8%)	.	4 (1.2%)	.	7 (0.6%)	.

Table 25. Baseline Comorbidities of ART- experienced/viremic (Study Population 2)

		DTG N= 2,787	EVG/c N= 3,140	DTG vs. EVG p-value	RAL N= 338	DTG vs. RAL p-value	DRV(r/c) N= 1,162	DTG vs. DRV(r/c) p-value
Comorbidity at baseline	Any	1756 (63.0%)	1713 (54.6%)	<.0001	260 (76.9%)	<.0001	819 (70.5%)	<.0001
Cardiovascular Disease Conditions	Any	137 (4.9%)	112 (3.6%)	0.0098	31 (9.2%)	0.0011	67 (5.8%)	0.2713
	Arrhythmia	60 (2.2%)	52 (1.7%)	0.1809	5 (1.5%)	0.5451	31 (2.7%)	0.3518
	Myocardial Infarction	14 (0.5%)	7 (0.2%)	0.0814	5 (1.5%)	0.0466	5 (0.4%)	1.0000
	Angina	4 (0.1%)	1 (0.0%)	0.1941	0 (0.0%)	1.0000	2 (0.2%)	1.0000
	Other/Unspecified CHD	52 (1.9%)	34 (1.1%)	0.0119	18 (5.3%)	<.0001	27 (2.3%)	0.3491
	Occlusion/stenosis of precerebral arteries	5 (0.2%)	0 (0.0%)	0.0229	0 (0.0%)	1.0000	1 (0.1%)	0.6775

		DTG N= 2,787	EVG/c N= 3,140	DTG vs. EVG p-value	RAL N= 338	DTG vs. RAL p-value	DRV(r/c) N= 1,162	DTG vs. DRV(r/c) p-value
	Stroke	26 (0.9%)	15 (0.5%)	0.0348	7 (2.1%)	0.0532	6 (0.5%)	0.1833
	Transient Ischemic Attack	3 (0.1%)	3 (0.1%)	1.0000	0 (0.0%)	1.0000	2 (0.2%)	0.6349
	Other CBV	33 (1.2%)	24 (0.8%)	0.0984	8 (2.4%)	0.0711	14 (1.2%)	0.9563
	Peripheral Arterial Disease	9 (0.3%)	6 (0.2%)	0.4384	3 (0.9%)	0.1322	2 (0.2%)	0.5249
	Abdominal Aortic Aneurysm	0	0	.	0	.	0	.
Invasive Cancer	Any	115 (4.1%)	97 (3.1%)	0.0319	22 (6.5%)	0.0433	66 (5.7%)	0.0334
Endocrine Disorders (excluding T2DM)	Any	439 (15.8%)	405 (12.9%)	0.0017	78 (23.1%)	0.0006	179 (15.4%)	0.7843
	Hyperlipidemia	403 (14.5%)	388 (12.4%)	0.0175	73 (21.6%)	0.0006	173 (14.9%)	0.7283
	Hyperthyroidism	7 (0.3%)	5 (0.2%)	0.5655	1 (0.3%)	0.6002	0 (0.0%)	0.1134
	Hypothyroidism	46 (1.7%)	24 (0.8%)	0.0016	8 (2.4%)	0.3399	10 (0.9%)	0.0557
	Thyroiditis	0 (0.0%)	1 (0.0%)	1.0000	0 (0.0%)	.	1 (0.1%)	0.2943
Mental Health Conditions	Any	671 (24.1%)	644 (20.5%)	0.0010	103 (30.5%)	0.0101	300 (25.8%)	0.2468
	Anxiety Disorders	384 (13.8%)	405 (12.9%)	0.3194	56 (16.6%)	0.1637	163 (14.0%)	0.8363
	Bipolar or Manic Disorders	150 (5.4%)	130 (4.1%)	0.0245	24 (7.1%)	0.1932	75 (6.5%)	0.1853
	Major Depressive Disorder	228 (8.2%)	193 (6.1%)	0.0023	34 (10.1%)	0.2393	88 (7.6%)	0.5213

		DTG N= 2,787	EVG/c N= 3,140	DTG vs. EVG p-value	RAL N= 338	DTG vs. RAL p-value	DRV(r/c) N= 1,162	DTG vs. DRV(r/c) p-value
	Schizophrenic Disorder	50 (1.8%)	40 (1.3%)	0.1022	10 (3.0%)	0.1406	25 (2.2%)	0.4533
	Dementia	3 (0.1%)	4 (0.1%)	1.0000	2 (0.6%)	0.0935	2 (0.2%)	0.6349
	Suicidality	15 (0.5%)	10 (0.3%)	0.2298	2 (0.6%)	0.7054	9 (0.8%)	0.3757
Liver Diseases	Any	416 (14.9%)	341 (10.9%)	<.0001	76 (22.5%)	0.0003	242 (20.8%)	<.0001
	Hepatitis B	163 (5.8%)	147 (4.7%)	0.0440	28 (8.3%)	0.0775	96 (8.3%)	0.0052
	Hepatitis C	262 (9.4%)	183 (5.8%)	<.0001	45 (13.3%)	0.0225	152 (13.1%)	0.0006
	Other chronic liver disease	62 (2.2%)	47 (1.5%)	0.0374	13 (3.8%)	0.0658	17 (1.5%)	0.1193
Bone Diseases	Any	34 (1.2%)	14 (0.4%)	0.0012	4 (1.2%)	1.0000	10 (0.9%)	0.4063
Peripheral Neuropathy	Any	140 (5.0%)	102 (3.2%)	0.0006	25 (7.4%)	0.0654	81 (7.0%)	0.0153
Renal Disease	Any	634 (22.7%)	581 (18.5%)	<.0001	111 (32.8%)	<.0001	291 (25.0%)	0.1208
	Renal Impairment	634 (22.7%)	581 (18.5%)	<.0001	111 (32.8%)	<.0001	291 (25.0%)	0.1208
	Moderate/Severe CKD	29 (1.0%)	15 (0.5%)	0.0118	13 (3.8%)	<.0001	14 (1.2%)	0.6503
	End Stage Renal Disease	6 (0.2%)	0 (0.0%)	0.0108	2 (0.6%)	0.2114	1 (0.1%)	0.6814
Hypertension	Any	487 (17.5%)	449 (14.3%)	0.0008	85 (25.1%)	0.0006	237 (20.4%)	0.0306
Rheumatoid Arthritis	Any	12 (0.4%)	7 (0.2%)	0.1737	3 (0.9%)	0.2160	4 (0.3%)	0.7911
Substance Abuse	Any	503 (18.0%)	430 (13.7%)	<.0001	57 (16.9%)	0.5919	248 (21.3%)	0.0162

		DTG N= 2,787	EVG/c N= 3,140	DTG vs. EVG p-value	RAL N= 338	DTG vs. RAL p-value	DRV(r/c) N= 1,162	DTG vs. DRV(r/c) p-value
	Alcohol Dependence	112 (4.0%)	90 (2.9%)	0.0147	14 (4.1%)	0.9133	60 (5.2%)	0.1082
	Drug Abuse	490 (17.6%)	421 (13.4%)	<.0001	53 (15.7%)	0.3837	239 (20.6%)	0.0275

Table 26. Baseline HIV-Infection Characteristics of ART- experienced/viremic (Study Population 2)

		DTG N= 2,787	EVG/c N= 3,140	DTG vs. EVG p-value	RAL N= 338	DTG vs. RAL p-value	DRV(r/c) N= 1,162	DTG vs. DRV(r/c) p-value
Months from first OPERA visit to baseline	Median (IQR)	2.3 (0.7, 34.0)	1.8 (0.7, 26.0)	0.0001	1.8 (0.0, 41.2)	0.0234	6.7 (0.7, 46.8)	0.0144
	0	229 (8.2%)	310 (9.9%)	0.0130	90 (26.6%)	<.0001	162 (13.9%)	<.0001
	>0 to 6	1387 (49.8%)	1617 (51.5%)	.	100 (29.6%)	.	407 (35.0%)	.
	>6 to 12	157 (5.6%)	163 (5.2%)	.	21 (6.2%)	.	64 (5.5%)	.
	>12 to 24	194 (7.0%)	234 (7.5%)	.	23 (6.8%)	.	93 (8.0%)	.
	>24	820 (29.4%)	816 (26.0%)	.	104 (30.8%)	.	436 (37.5%)	.
Year of study inclusion	Median (IQR)	2016.0 (2015.0, 2017.0)	2016.0 (2014.0, 2017.0)	<.0001	2014.0 (2014.0, 2015.0)	<.0001	2015.0 (2014.0, 2016.0)	<.0001
	2013	90 (3.2%)	225 (7.2%)	<.0001	82 (24.3%)	<.0001	206 (17.7%)	<.0001

		DTG N= 2,787	EVG/c N= 3,140	DTG vs. EVG p-value	RAL N= 338	DTG vs. RAL p-value	DRV(r/c) N= 1,162	DTG vs. DRV(r/c) p-value
	2014	389 (14.0%)	565 (18.0%)	.	120 (35.5%)	.	301 (25.9%)	.
	2015	670 (24.0%)	636 (20.3%)	.	55 (16.3%)	.	215 (18.5%)	.
	2016	734 (26.3%)	804 (25.6%)	.	41 (12.1%)	.	217 (18.7%)	.
	2017	720 (25.8%)	761 (24.2%)	.	31 (9.2%)	.	191 (16.4%)	.
	2018	184 (6.6%)	149 (4.7%)	.	9 (2.7%)	.	32 (2.8%)	.
Prior exposure: DTG	Yes	7 (0.3%)	0 (0.0%)	0.0051	0 (0.0%)	1.0000	0 (0.0%)	0.1134
Prior exposure: EVG/c	Yes	8 (0.3%)	16 (0.5%)	0.2202	1 (0.3%)	1.0000	0 (0.0%)	0.1148
Prior exposure: RAL	Yes	30 (1.1%)	22 (0.7%)	0.1215	26 (7.7%)	<.0001	18 (1.5%)	0.2168
Prior exposure: DRV(/r/c)	Yes	37 (1.3%)	26 (0.8%)	0.0612	11 (3.3%)	0.0065	61 (5.2%)	<.0001
Number of classes of core agents experienced prior to baseline	1	949 (34.1%)	945 (30.1%)	<.0001	107 (31.7%)	<.0001	459 (39.5%)	<.0001
	2	157 (5.6%)	114 (3.6%)	.	31 (9.2%)	.	100 (8.6%)	.
	3	15 (0.5%)	12 (0.4%)	.	13 (3.8%)	.	7 (0.6%)	.
	4+	2 (0.1%)	0 (0.0%)	.	1 (0.3%)	.	0 (0.0%)	.

		DTG N= 2,787	EVG/c N= 3,140	DTG vs. EVG p-value	RAL N= 338	DTG vs. RAL p-value	DRV(r/c) N= 1,162	DTG vs. DRV(r/c) p-value
	Missing	1664 (59.7%)	2069 (65.9%)	.	186 (55.0%)	.	596 (51.3%)	.
History of AIDS-defining Illnesses	Yes	745 (26.7%)	616 (19.6%)	<.0001	122 (36.1%)	0.0003	428 (36.8%)	<.0001
HIV viral load (copies/ml)	Median (IQR)	10772.0 (280.0, 62300.0)	13210.0 (390.0, 63720.0)	0.0537	395.0 (110.0, 22455.0)	<.0001	6400.0 (245.0, 63260.0)	0.2095
	>= 50 to < 200	588 (21.1%)	609 (19.4%)	0.2673	125 (37.0%)	<.0001	253 (21.8%)	0.0078
	>= 200 to < 1,000	401 (14.4%)	421 (13.4%)	.	85 (25.1%)	.	211 (18.2%)	.
	>= 1,000 to < 10,000	384 (13.8%)	442 (14.1%)	.	27 (8.0%)	.	154 (13.3%)	.
	>= 10,000 to < 100,000	925 (33.2%)	1108 (35.3%)	.	63 (18.6%)	.	331 (28.5%)	.
	>= 100,000	489 (17.5%)	560 (17.8%)	.	38 (11.2%)	.	213 (18.3%)	.
Log10 HIV viral load	Median (IQR)	4.0 (2.4, 4.8)	4.1 (2.6, 4.8)	0.0537	2.6 (2.0, 4.4)	<.0001	3.8 (2.4, 4.8)	0.2095
	>= 1.7 to < 2.3	501 (18.6%)	525 (17.2%)	0.3549	111 (34.3%)	<.0001	229 (20.1%)	0.0050
	>= 2.3 to < 3	401 (14.9%)	421 (13.8%)	.	85 (26.2%)	.	211 (18.5%)	.
	>= 3 to < 4	384 (14.2%)	442 (14.5%)	.	27 (8.3%)	.	154 (13.5%)	.
	>= 4 to < 5	925 (34.3%)	1108 (36.3%)	.	63 (19.4%)	.	331 (29.1%)	.
	>= 5	489 (18.1%)	560 (18.3%)	.	38 (11.7%)	.	213 (18.7%)	.

		DTG N= 2,787	EVG/c N= 3,140	DTG vs. EVG p-value	RAL N= 338	DTG vs. RAL p-value	DRV(r/c) N= 1,162	DTG vs. DRV(r/c) p-value
CD4 cell count (cell/µl)	Median (IQR)	423.0 (240.0, 612.0)	438.0 (272.0, 625.0)	0.0064	412.0 (224.0, 638.0)	0.9508	335.0 (155.0, 545.0)	<.0001
	>500	1057 (37.9%)	1255 (40.0%)	0.0040	134 (39.6%)	0.2057	340 (29.3%)	<.0001
	>350 to <= 500	609 (21.9%)	748 (23.8%)	.	57 (16.9%)	.	212 (18.2%)	.
	>200 to <= 350	529 (19.0%)	594 (18.9%)	.	65 (19.2%)	.	250 (21.5%)	.
	>50 to <= 200	389 (14.0%)	372 (11.8%)	.	53 (15.7%)	.	223 (19.2%)	.
	<= 50	174 (6.2%)	149 (4.7%)	.	22 (6.5%)	.	130 (11.2%)	.
	Missing	29 (1.0%)	22 (0.7%)	.	7 (2.1%)	.	7 (0.6%)	.

1.4. Primary Objective 2: Incidence of prediabetes and T2DM in Study Population 2

1.4.1. ART-Naïve Patients

1.4.1.1. Incident prediabetes in ART-naïve patients

Table 27. Identification of prediabetes cases among ART-naïve patients (Population 2)

	DTG N= 2,816	EVG/c N= 3,504	DTG vs. EVG p-value	RAL N= 207	DTG vs. RAL p-value	DRV(r/c) N= 967	DTG vs. DRV(r/c) p-value
Incident Prediabetes	101 (3.6%)	125 (3.6%)	1.0000	3 (1.4%)	0.1148	25 (2.6%)	0.1464
diagnosis only	24 (0.9%)	37 (1.1%)	0.4397	1 (0.5%)	1.0000	9 (0.9%)	0.8415
labs only	38 (1.3%)	44 (1.3%)	0.7390	1 (0.5%)	0.5173	8 (0.8%)	0.2361
diagnosis and labs	39 (1.4%)	44 (1.3%)	0.6583	1 (0.5%)	0.5207	8 (0.8%)	0.2377

Table 28. Incidence rates of prediabetes in ART-naïve patients (Study Population 2)

	N	# prediabetes	Person-years	IR (95% CI), per 1,000 person-years
DTG	2816	101	4369.60	23.11 (19.02, 28.09)
EVG/c	3504	125	6064.11	20.61 (17.30, 24.56)
RAL	207	3	235.59	12.73 (4.11, 39.48)
DRV/c, DRV/r	967	25	1279.97	19.53 (13.20, 28.91)
Overall	**7494**	**254**	**11949.28**	**21.26 (18.80, 24.04)**

Table 29. Incidence rates of prediabetes in ART-naïve patients (Study Population 2), excluding 346 patients missing sex and/or baseline BMI

	N	# prediabetes	Person-years	IR (95% CI), per 1,000 person-years
DTG	2683	96	4194.23	22.89 (18.74, 27.96)
EVG/c	3356	122	5859.28	20.82 (17.44, 24.86)
RAL	192	2	219.78	9.10 (2.28, 36.39)
DRV/c, DRV/r	917	25	1213.08	20.61 (13.93, 30.50)
Overall	**7148**	**245**	**11486.37**	**21.33 (18.82, 24.17)**

1.4.1.2. Incident T2DM in ART-naïve patients

Table 30. Identification of T2DM cases among ART-naïve patients (Population 2)

	DTG N= 2,816	EVG/c N= 3,504	DTG vs. EVG p-value	RAL N= 207	DTG vs. RAL p-value	DRV(r/c) N= 967	DTG vs. DRV(r/c) p-value
Incident T2DM	51 (1.8%)	46 (1.3%)	0.1225	3 (1.4%)	1.0000	10 (1.0%)	0.1049
diagnosis only	4 (0.1%)	3 (0.1%)	0.7073	0 (0.0%)	1.0000	0 (0.0%)	0.5780
lab only	15 (0.5%)	11 (0.3%)	0.2350	0 (0.0%)	0.6186	4 (0.4%)	0.7960
Antidiabetic prescription only	7 (0.2%)	6 (0.2%)	0.5816	0 (0.0%)	1.0000	1 (0.1%)	0.6884
diagnosis and lab only	8 (0.3%)	3 (0.1%)	0.0722	0 (0.0%)	1.0000	3 (0.3%)	1.0000
diagnosis and prescription only	3 (0.1%)	4 (0.1%)	1.0000	1 (0.5%)	0.2471	1 (0.1%)	1.0000
Lab and prescription only	1 (0.0%)	0 (0.0%)	0.4456	0 (0.0%)	1.0000	0 (0.0%)	1.0000
diagnosis, lab and prescription	13 (0.5%)	19 (0.5%)	0.7234	2 (1.0%)	0.2744	1 (0.1%)	0.1353

Table 31. Incidence rates of T2DM in ART-naïve patients (Study Population 2)

	N	# T2DM	Person-years	IR (95% CI), per 1,000 person-years
DTG	2816	51	4453.99	11.45 (8.70, 15.07)
EVG/c	3504	46	6170.55	7.46 (5.58, 9.95)
RAL	207	3	231.33	12.97 (4.18, 40.21)
DRV/c, DRV/r	967	10	1298.87	7.70 (4.14, 14.31)
Overall	**7494**	**110**	**12154.74**	**9.05 (7.51, 10.91)**

Table 32. Abnormal labs before discontinuation among ART-naïve patients (Study Population 2)

		DTG N= 2,816	EVG/c N= 3,504	DTG vs. EVG p-value	RAL N= 207	DTG vs. RAL p-value	DRV(r/c) N= 967	DTG vs. DRV(r/c) p-value
Core agent discontinued (no prediabetes/T2DM during follow-up)	Any	975 (34.6%)	1462 (41.7%)	<.0001	150 (72.5%)	<.0001	553 (57.2%)	<.0001
Last lab before discontinuation	Normal range*	136 (13.9%)	263 (18.0%)	0.0234	18 (12.0%)	0.8482	70 (12.7%)	0.6076
	Prediabetes range**	31 (3.2%)	38 (2.6%)	.	4 (2.7%)	.	14 (2.5%)	.
	No labs	808 (82.9%)	1161 (79.4%)	.	128 (85.3%)	.	469 (84.8%)	.

* Normal range: HbA1c <5.7%, FPG <100 mg/dl, OGTT <140 mg/dl

** Prediabetes range: HbA1c >=5.7% to <6.5%, FPG >=100 mg/dl to <126 mg/dl, OGTT >=140 mg/dl to <200 mg/dl

Table 33. Incidence rates of T2DM in ART-naïve patients (Study Population 2), excluding 346 patients missing sex and/or baseline BMI

	N	# T2DM	Person-years	IR (95% CI), per 1,000 person-years
DTG	2683	49	4277.27	11.46 (8.66, 15.16)
EVG/c	3356	46	5962.19	7.72 (5.78, 10.30)
RAL	192	3	214.40	13.99 (4.51, 43.39)
DRV/c, DRV/r	917	10	1231.98	8.12 (4.37, 15.09)
Overall	**7148**	**108**	**11685.85**	**9.24 (7.65, 11.16)**

1.4.2. ART-Experienced/Suppressed Patients

1.4.2.1. Incident prediabetes in ART-experienced/suppressed patients

Table 34. Identification of prediabetes cases among ART-experienced/suppressed patients (Population 2)

	DTG N= 3,584	EVG/c N= 4,281	DTG vs. EVG p-value	RAL N= 730	DTG vs. RAL p-value	DRV(r/c) N= 1,109	DTG vs. DRV(r/c) p-value
Incident Prediabetes	232 (6.5%)	168 (3.9%)	<.0001	37 (5.1%)	0.1525	51 (4.6%)	0.0219
diagnosis only	46 (1.3%)	47 (1.1%)	0.4482	6 (0.8%)	0.2976	13 (1.2%)	0.7714
labs only	126 (3.5%)	75 (1.8%)	<.0001	22 (3.0%)	0.4971	22 (2.0%)	0.0107
diagnosis and labs	60 (1.7%)	46 (1.1%)	0.0216	9 (1.2%)	0.3864	16 (1.4%)	0.5937

Table 35. Incidence rates of prediabetes in ART-experienced/suppressed patients (Study Population 2)

	N	# prediabetes	Person-years	IR (95% CI), per 1,000 person-years
DTG	3584	232	5896.57	39.34 (34.59, 44.75)
EVG/c	4281	168	6833.73	24.58 (21.13, 28.60)
RAL	730	37	1122.81	32.95 (23.88, 45.48)
DRV/c, DRV/r	1109	51	1847.32	27.61 (20.98, 36.33)
Overall	**9704**	**488**	**15700.44**	**31.08 (28.44, 33.97)**

Table 36. Incidence rates of prediabetes in ART-experienced/suppressed patients (Study Population 2), excluding 613 patients missing sex and/or baseline BMI

	N	# prediabetes	Person-years	IR (95% CI), per 1,000 person-years
DTG	3434	226	5703.11	39.63 (34.78, 45.15)
EVG/c	4005	161	6414.84	25.10 (21.51, 29.29)
RAL	639	32	971.90	32.93 (23.28, 46.56)
DRV/c, DRV/r	1013	47	1705.26	27.56 (20.71, 36.68)
Overall	**9091**	**466**	**14795.11**	**31.50 (28.76, 34.49)**

1.4.2.2. Incident T2DM in ART-experienced/suppressed patients

Table 37. Identification of T2DM cases among ART-experienced/suppressed patients (Population 2)

	DTG N= 3,584	EVG/c N= 4,281	DTG vs. EVG p-value	RAL N= 730	DTG vs. RAL p-value	DRV(r/c) N= 1,109	DTG vs. DRV(r/c) p-value
Incident T2DM	88 (2.5%)	75 (1.8%)	0.0292	21 (2.9%)	0.5085	30 (2.7%)	0.6424
diagnosis only	9 (0.3%)	5 (0.1%)	0.1855	1 (0.1%)	1.0000	4 (0.4%)	0.5204
lab only	27 (0.8%)	13 (0.3%)	0.0063	3 (0.4%)	0.4623	8 (0.7%)	1.0000
Antidiabetic prescription only	11 (0.3%)	8 (0.2%)	0.3575	6 (0.8%)	0.0534	2 (0.2%)	0.7450
diagnosis and lab only	12 (0.3%)	10 (0.2%)	0.4020	0 (0.0%)	0.2382	0 (0.0%)	0.0812
diagnosis and prescription only	6 (0.2%)	9 (0.2%)	0.7975	5 (0.7%)	0.0259	2 (0.2%)	1.0000
Lab and prescription only	5 (0.1%)	3 (0.1%)	0.4816	0 (0.0%)	0.5967	4 (0.4%)	0.2290
diagnosis, lab and prescription	18 (0.5%)	27 (0.6%)	0.4519	6 (0.8%)	0.2898	10 (0.9%)	0.1311

Table 38. Incidence rates of T2DM in ART-experienced/suppressed patients (Study Population 2)

	N	# T2DM	Person-years	IR (95% CI), per 1,000 person-years
DTG	3584	88	6103.35	14.42 (11.70, 17.77)
EVG/c	4281	75	6953.67	10.79 (8.60, 13.52)
RAL	730	21	1139.05	18.44 (12.02, 28.28)
DRV/c, DRV/r	1109	30	1877.13	15.98 (11.17, 22.86)
Overall	**9704**	**214**	**16073.21**	**13.31 (11.64, 15.22)**

Table 39. Abnormal labs before discontinuation among ART-experienced/suppressed patients (Population 2)

		DTG N= 3,584	EVG/c N= 4,281	DTG vs. EVG p-value	RAL N= 730	DTG vs. RAL p-value	DRV(r/c) N= 1,109	DTG vs. DRV(r/c) p-value
Core agent discontinued (no prediabetes/T2DM during follow-up)	Any	1321 (36.9%)	1768 (41.3%)	<.0001	487 (66.7%)	<.0001	599 (54.0%)	<.0001
Last lab before discontinuation	Normal range*	287 (21.7%)	315 (17.8%)	0.0095	93 (19.1%)	0.2838	114 (19.0%)	0.3805
	Prediabetes range**	47 (3.6%)	50 (2.8%)	.	23 (4.7%)	.	24 (4.0%)	.
	No labs	987 (74.7%)	1403 (79.4%)	.	371 (76.2%)	.	461 (77.0%)	.

* Normal range: HbA1c <5.7%, FPG <100 mg/dl, OGTT <140 mg/dl

** Prediabetes range: HbA1c >=5.7% to <6.5%, FPG >=100 mg/dl to <126 mg/dl, OGTT >=140 mg/dl to <200 mg/dl

Table 40. Incidence rates of T2DM in ART-experienced/suppressed patients (Study Population 2), excluding 613 patients missing sex and/or baseline BMI

	N	# T2DM	Person-years	IR (95% CI), per 1,000 person-years
DTG	3434	81	5909.35	13.71 (11.02, 17.04)
EVG/c	4005	72	6532.97	11.02 (8.75, 13.88)
RAL	639	18	996.20	18.07 (11.38, 28.68)
DRV/c, DRV/r	1013	25	1733.72	14.42 (9.74, 21.34)
Overall	**9091**	**196**	**15172.24**	**12.92 (11.23, 14.86)**

1.4.3. ART-Experienced/Viremic Patients

1.4.3.1. Incident prediabetes among ART-experienced/viremic patients

Table 41. Identification of prediabetes cases among ART-experienced/viremic patients (Population 2)

	DTG N= 2,787	EVG/c N= 3,140	DTG vs. EVG p-value	RAL N= 338	DTG vs. RAL p-value	DRV(r/c) N= 1,162	DTG vs. DRV(r/c) p-value
Incident Prediabetes	131 (4.7%)	125 (4.0%)	0.1738	14 (4.1%)	0.6449	35 (3.0%)	0.0160
diagnosis only	25 (0.9%)	37 (1.2%)	0.3083	2 (0.6%)	0.7617	13 (1.1%)	0.5915
labs only	66 (2.4%)	46 (1.5%)	0.0108	6 (1.8%)	0.4926	14 (1.2%)	0.0180
diagnosis and labs	40 (1.4%)	42 (1.3%)	0.7480	6 (1.8%)	0.6241	8 (0.7%)	0.0510

Table 42. Incidence rates of prediabetes in ART-experienced/viremic patients (Study Population 2)

	N	# prediabetes	Person-years	IR (95% CI), per 1,000 person-years
DTG	2787	131	4596.97	28.50 (24.01, 33.82)
EVG/c	3140	125	5368.47	23.28 (19.54, 27.75)
RAL	338	14	475.87	29.42 (17.42, 49.67)
DRV/c, DRV/r	1162	35	1759.81	19.89 (14.28, 27.70)
Overall	**7427**	**305**	**12201.12**	**25.00 (22.34, 27.97)**

1.4.3.2. Incident T2DM among ART-experienced/viremic patients

Table 43. Identification of T2DM cases among ART-experienced/viremic patients (Population 2)

	DTG N= 2,787	EVG/c N= 3,140	DTG vs. EVG p-value	RAL N= 338	DTG vs. RAL p-value	DRV(r/c) N= 1,162	DTG vs. DRV(r/c) p-value
Incident T2DM	51 (1.8%)	40 (1.3%)	0.0823	11 (3.3%)	0.0761	10 (0.9%)	0.0244
diagnosis only	2 (0.1%)	6 (0.2%)	0.2957	3 (0.9%)	0.0106	3 (0.3%)	0.1554
lab only	8 (0.3%)	8 (0.3%)	0.8086	2 (0.6%)	0.2956	3 (0.3%)	1.0000
Antidiabetic prescription only	6 (0.2%)	4 (0.1%)	0.5309	1 (0.3%)	0.5516	0 (0.0%)	0.1892
diagnosis and lab only	4 (0.1%)	4 (0.1%)	1.0000	1 (0.3%)	0.4360	0 (0.0%)	0.3272
diagnosis and prescription only	11 (0.4%)	4 (0.1%)	0.0663	1 (0.3%)	1.0000	0 (0.0%)	0.0408
Lab and prescription only	2 (0.1%)	1 (0.0%)	0.6040	0 (0.0%)	1.0000	1 (0.1%)	1.0000
diagnosis, lab and prescription	18 (0.6%)	13 (0.4%)	0.2790	3 (0.9%)	0.4901	3 (0.3%)	0.1535

Table 44. Incidence rates of T2DM in ART-experienced/viremic patients (Study Population 2)

	N	# T2DM	Person-years	IR (95% CI), per 1,000 person-years
DTG	2787	51	4688.45	10.88 (8.27, 14.31)
EVG/c	3140	40	5478.43	7.30 (5.36, 9.54)
RAL	338	11	473.77	23.22 (12.86, 41.93)
DRV/c, DRV/r	1162	10	1796.18	5.67 (3.00, 10.35)
Overall	**7427**	**112**	**12436.82**	**9.01 (7.48, 10.84)**

Table 45. Abnormal labs before discontinuation among ART-experienced/viremic patients (Study Population 2)

		DTG N= 2,787	EVG/c N= 3,140	DTG vs. EVG p-value	RAL N= 338	DTG vs. RAL p-value	DRV(r/c) N= 1,162	DTG vs. DRV(r/c) p-value
Core agent discontinued (no prediabetes/T2DM during follow-up)	Any	1060 (38.0%)	1324 (42.2%)	0.0012	244 (72.2%)	<.0001	712 (61.3%)	<.0001
Last lab before discontinuation	Normal range*	151 (14.2%)	192 (14.5%)	0.4197	28 (11.5%)	0.0719	109 (15.3%)	0.0890
	Prediabetes range**	32 (3.0%)	53 (4.0%)	.	14 (5.7%)	.	35 (4.9%)	.
	No labs	877 (82.7%)	1079 (81.5%)	.	202 (82.8%)	.	568 (79.8%)	.

* Normal range: HbA1c <5.7%, FPG <100 mg/dl, OGTT <140 mg/dl

** Prediabetes range: HbA1c >=5.7% to <6.5%, FPG >=100 mg/dl to <126 mg/dl, OGTT >=140 mg/dl to <200 mg/dl

1.5. Primary Objective 3: Association between core agent initiation and development of T2DM in Study Population 2

1.5.1. ART-Naïve Patients

RAL users were excluded from the ART-naïve Cox proportional hazards models due to the small number of T2DM events in this group

Figure 1. Kaplan Meier Curve for T2DM-free survival probability in ART-naïve patients (Population 2)

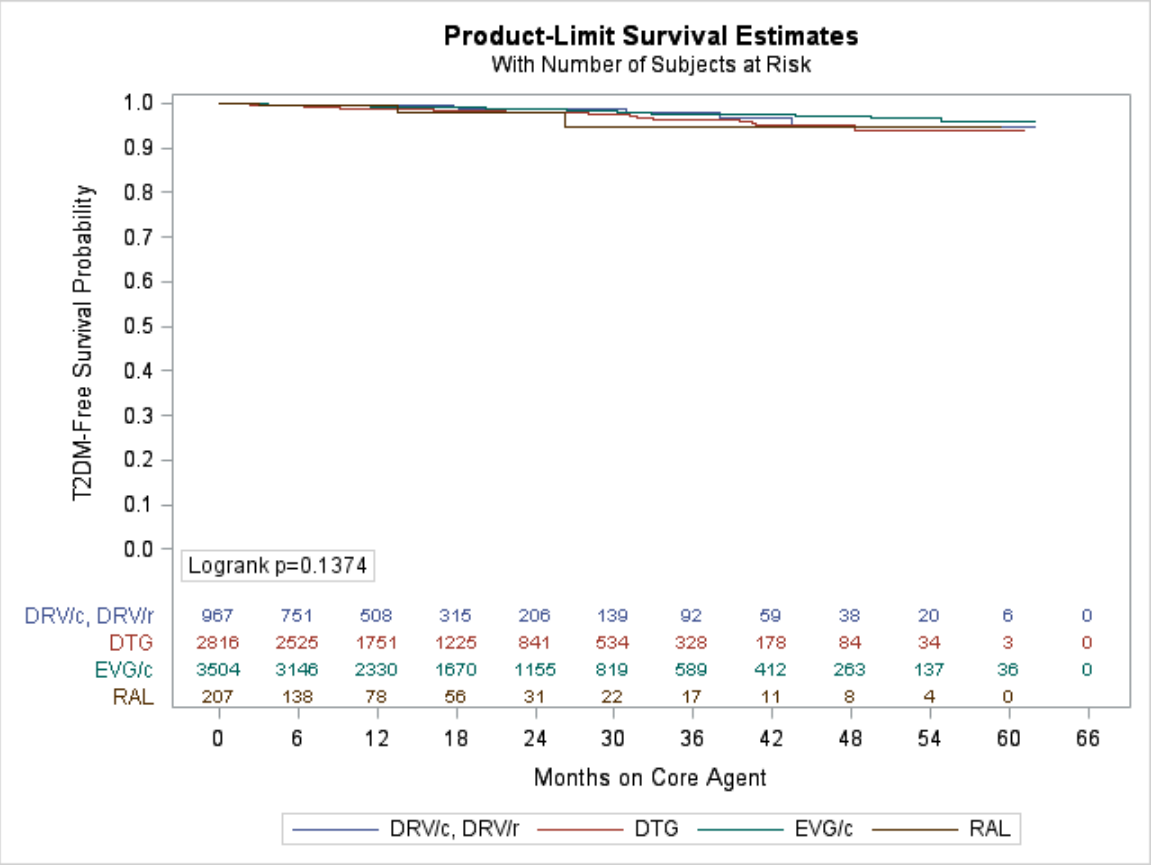

Table 46. Unadjusted and adjusted Cox proportional hazards model results in ART-naïve patients (Population 2), excluding 346 patients missing sex and/or baseline BMI

	# incident T2DM (n=105)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
DTG	49	1.00 (Ref)	1.00 (Ref)
EVG/c	46	0.66 (0.44, 0.99)	0.70 (0.47, 1.05)
DRV/c, DRV/r	10	0.71 (0.36, 1.39)	0.53 (0.26, 1.04)
Age: 13-25	9	-	1.00 (Ref)
Age: 26-49	61	-	2.59 (1.28, 5.23)
Age: 50+	35	-	9.85 (4.67, 20.78)
Female	33	-	1.98 (1.26, 3.11)
African American	59	-	1.22 (0.81, 1.83)
HCV co-infection	6	-	1.08 (0.46, 2.50)
BMI	105	-	1.42 (1.19, 1.71)
BMI^2	NA	-	1.00 (1.00, 1.00)[a]

[a] p-value <0.05

1.5.2. ART-Experienced/Suppressed Patients

Figure 2. Kaplan Meier Curve for T2DM-free survival probability in ART-experienced/suppressed patients (Population 2)

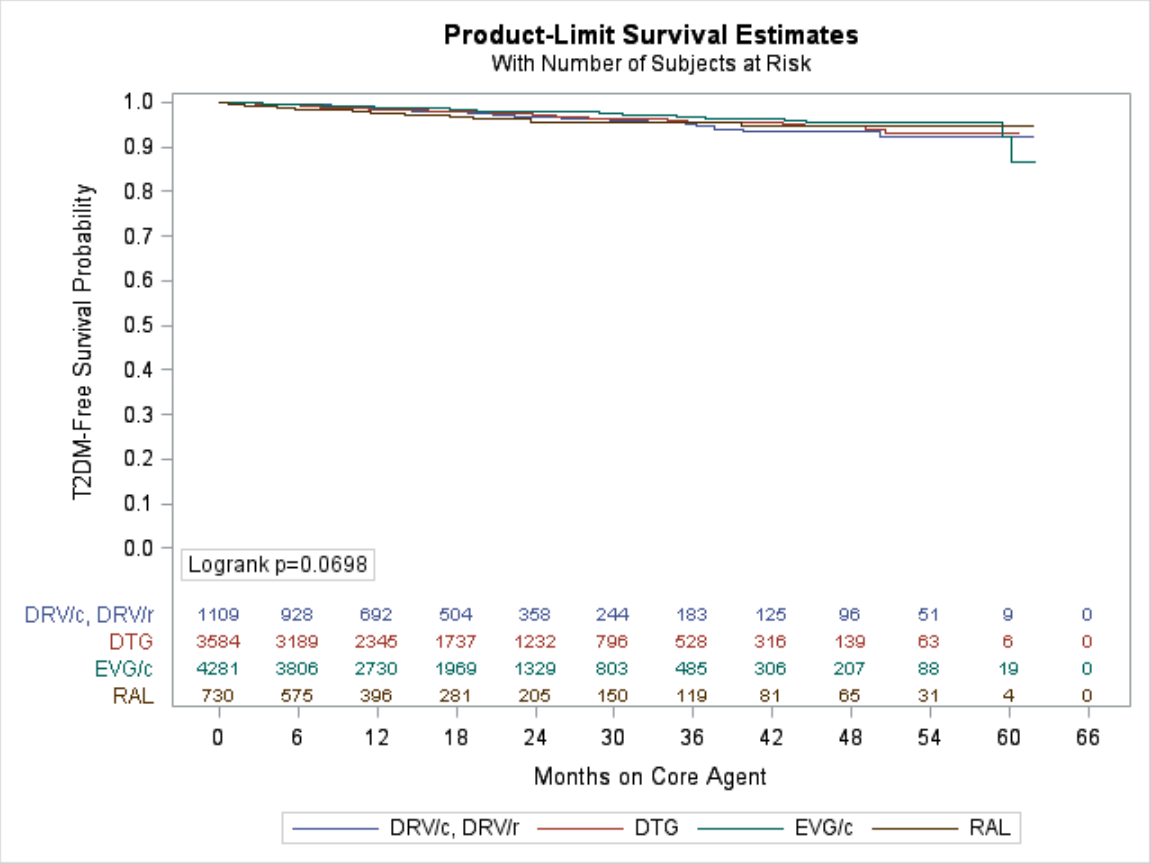

Table 47. Unadjusted and adjusted Cox proportional hazards model results ART-experienced/suppressed patients (Population 2), excluding 613 patients missing sex and/or baseline BMI

	# incident T2DM (n=196)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
DTG	81	1.00 (Ref)	1.00 (ref)
EVG/c	72	0.80 (0.58, 1.10)	1.17 (0.70, 1.96)
RAL	18	1.31 (0.79, 2.19)	0.90 (0.57, 1.42)
DRV/c, DRV/r	25	1.04 (0.66, 1.63)	3.04 (2.27, 4.07)
Age: 50+ [a]	110	-	0.78 (0.53, 1.15)
Female	37	-	1.43 (1.05, 1.93)
African American	79	-	1.36 (0.90, 2.04)
HCV co-infection	28	-	1.28 (1.16, 1.41)
BMI	195	-	1.00 (1.00, 1.00) [b]
BMI^2	-	-	0.96 (0.70, 1.33)

[a] vs. 13-46 (only 1 person aged 13-29)

[b] p-value <0.05

1.6. Secondary Objective 1: Factors associated with T2DM in Study Population 2

1.6.1. ART-Naïve Patients

Table 48. Baseline Demographic Characteristics of ART-naïve patients by follow-up T2DM (Population 2)

		Incident T2DM N= 110	No incident T2DM N= 7,384	p-value
Age	Median (IQR)	45.4 (34.9, 52.2)	30.6 (25.4, 40.3)	<.0001
	13-25	9 (8.2%)	2051 (27.9%)	<.0001
	26-49	62 (56.4%)	4600 (62.5%)	.
	50+	39 (35.5%)	708 (9.6%)	.
Sex	Male	75 (68.2%)	6458 (87.5%)	<.0001
	Female	35 (31.8%)	914 (12.4%)	.
	Unknown	0 (0.0%)	12 (0.2%)	.
Hispanic	Black	2 (9.1%)	78 (4.4%)	0.1226
	American Indian/Alaska Native	0 (0.0%)	5 (0.3%)	.

		Incident T2DM N= 110	No incident T2DM N= 7,384	p-value
	Hawaiian/Other Pacific Islander	0 (0.0%)	7 (0.4%)	.
	Asian	0 (0.0%)	5 (0.3%)	.
	White	19 (86.4%)	1630 (92.6%)	.
	Other	1 (4.5%)	7 (0.4%)	.
	>1 race	0 (0.0%)	29 (1.6%)	.
Non-Hispanic	Black	59 (68.6%)	3386 (63.9%)	0.8218
	American Indian/Alaska Native	0 (0.0%)	11 (0.2%)	.
	Hawaiian/Other Pacific Islander	0 (0.0%)	11 (0.2%)	.
	Asian	3 (3.5%)	121 (2.3%)	.
	White	24 (27.9%)	1688 (31.9%)	.
	Other	0 (0.0%)	9 (0.2%)	.
	>1 race	0 (0.0%)	71 (1.3%)	.
Race and/or ethnicity unknown	Yes	2 (1.8%)	326 (4.4%)	0.2418
Marital Status	Single	66 (60.0%)	5447 (73.8%)	<.0001
	Married	9 (8.2%)	322 (4.4%)	.
	Domestic partnership	0 (0.0%)	87 (1.2%)	.
	Widowed	2 (1.8%)	24 (0.3%)	.
	Separated/divorced	8 (7.3%)	150 (2.0%)	.
	Unknown	25 (22.7%)	1354 (18.3%)	.
Risk of Infection	MSM	52 (47.3%)	4793 (64.9%)	0.0001
	Not MSM	58 (52.7%)	2591 (35.1%)	.
History of Syphilis	Yes	13 (11.8%)	2259 (30.6%)	<.0001
Region	Northeast	12 (10.9%)	437 (5.9%)	0.2390

		Incident T2DM N= 110	No incident T2DM N= 7,384	p-value
	South	69 (62.7%)	4774 (64.7%)	.
	Midwest	5 (4.5%)	267 (3.6%)	.
	West	24 (21.8%)	1905 (25.8%)	.
	US Territories	0 (0.0%)	1 (0.0%)	.
Medicaid	Yes	23 (20.9%)	1138 (15.4%)	0.1137
Medicare	Yes	4 (3.6%)	333 (4.5%)	0.8191
Commercial Insurance	Yes	39 (35.5%)	2631 (35.6%)	0.9694
Cash	Yes	55 (50.0%)	3537 (47.9%)	0.6618
ADAP/Ryan White	Yes	40 (36.4%)	2912 (39.4%)	0.5126
Other	Yes	1 (0.9%)	53 (0.7%)	0.5513
No Payer info	Yes	17 (15.5%)	991 (13.4%)	0.5349

Table 49. Baseline Clinical Characteristics of ART-naïve patients by follow-up T2DM (Population 2)

		Incident T2DM N= 110	No incident T2DM N= 7,384	p-value
Hemoglobin, g/dL	Median (IQR)	14.0 (12.3, 15.0)	14.1 (12.8, 15.1)	0.1055
	Normal	93 (84.5%)	6704 (90.8%)	0.1537
	DAIDS Grade 1 (mild)	5 (4.5%)	264 (3.6%)	.
	DAIDS Grade 2 (moderate)	3 (2.7%)	130 (1.8%)	.
	DAIDS Grade 3 (Severe)	4 (3.6%)	93 (1.3%)	.
	DAIDS Grade 4 (potentially life-threatening)	0 (0.0%)	10 (0.1%)	.
	Missing	5 (4.5%)	183 (2.5%)	.

		Incident T2DM N= 110	No incident T2DM N= 7,384	p-value
Hematocrit, %	Median (IQR)	41.5 (37.1, 44.5)	42.3 (38.9, 44.9)	0.0467
	Low	28 (25.5%)	1451 (19.7%)	0.3857
	Normal	76 (69.1%)	5591 (75.7%)	.
	High	2 (1.8%)	155 (2.1%)	.
	Missing	4 (3.6%)	187 (2.5%)	.
VACS mortality index	Median (IQR)	27.0 (17.0, 47.0)	20.0 (13.0, 35.0)	0.0002
	0 to <15	19 (17.3%)	2312 (31.3%)	0.0111
	>=15 to <30	31 (28.2%)	2039 (27.6%)	.
	>=30 to <45	17 (15.5%)	971 (13.2%)	.
	>= 45	27 (24.5%)	1167 (15.8%)	.
	Missing	16 (14.5%)	895 (12.1%)	.
BMI	Median (IQR)	29.0 (26.1, 33.0)	24.3 (21.7, 27.6)	<.0001
	Underweight	1 (0.9%)	397 (5.4%)	<.0001
	Normal weight	18 (16.4%)	3595 (48.7%)	.
	Overweight	40 (36.4%)	2022 (27.4%)	.
	Obese	49 (44.5%)	1102 (14.9%)	.
	Missing	2 (1.8%)	268 (3.6%)	.
HDL, mg/dL	Median (IQR)	37.0 (28.0, 48.0)	41.0 (33.0, 50.0)	0.0744
	Normal	9 (8.2%)	603 (8.2%)	0.5716
	Borderline Abnormal	30 (27.3%)	2264 (30.7%)	.
	Dyslipidemia	44 (40.0%)	2490 (33.7%)	.

		Incident T2DM N= 110	No incident T2DM N= 7,384	p-value
	Missing	27 (24.5%)	2027 (27.5%)	.
Triglycerides, mg/dL	Median (IQR)	136.0 (96.0, 198.0)	106.0 (76.0, 155.0)	<.0001
	Normal	49 (44.5%)	3915 (53.0%)	0.0101
	Borderline Abnormal	16 (14.5%)	699 (9.5%)	.
	Dyslipidemia	15 (13.6%)	717 (9.7%)	.
	Severe Dyslipidemia	3 (2.7%)	48 (0.7%)	.
	Missing	27 (24.5%)	2005 (27.2%)	.
Any concomitant non-ART listed below	Yes	54 (49.1%)	2291 (31.0%)	<.0001
Antibiotics	Yes	23 (20.9%)	1220 (16.5%)	0.2195
Direct Acting Antivirals (DAAs)	Yes	0 (0.0%)	1 (0.0%)	1.0000
Lipid lowering agents	Yes	12 (10.9%)	148 (2.0%)	<.0001
Non-steroidal Anti-inflammatory Agents (NSAIDS)	Yes	9 (8.2%)	191 (2.6%)	0.0003
Antidepressants	Yes	14 (12.7%)	636 (8.6%)	0.1281
Anxiolytics/Hypnotics/Sedatives	Yes	6 (5.5%)	298 (4.0%)	0.4540
Immune Modulators	Yes	9 (8.2%)	358 (4.8%)	0.1078
Number of concomitant non-ART medications listed above	0	56 (50.9%)	5093 (69.0%)	0.0001
	1-2	47 (42.7%)	2111 (28.6%)	.
	3-4	7 (6.4%)	168 (2.3%)	.
	5+	0 (0.0%)	12 (0.2%)	.

Table 50. Baseline Comorbidities of ART-naïve patients by follow-up T2DM (Population 2)

	Incident T2DM N= 110	No incident T2DM N= 7,384	p-value
Any Comorbidity at baseline	75 (68.2%)	3232 (43.8%)	<.0001
Any Cardiovascular Disease Conditions - Any	6 (5.5%)	137 (1.9%)	0.0062
Arrhythmia	2 (1.8%)	54 (0.7%)	0.1984
Myocardial Infarction	2 (1.8%)	7 (0.1%)	0.0072
Angina	0 (0.0%)	1 (0.0%)	1.0000
Other/Unspecified CHD	4 (3.6%)	59 (0.8%)	0.0135
Occlusion/stenosis of precerebral arteries	0 (0.0%)	2 (0.0%)	1.0000
Stroke	0 (0.0%)	17 (0.2%)	1.0000
Transient Ischemic Attack	0 (0.0%)	4 (0.1%)	1.0000
Other CBV	0 (0.0%)	27 (0.4%)	1.0000
Peripheral Arterial Disease	0 (0.0%)	2 (0.0%)	1.0000
Abdominal Aortic Aneurysm	0	0	.
Invasive Cancer	1 (0.9%)	123 (1.7%)	1.0000
Endocrine Disorders (excluding T2DM)	20 (18.2%)	437 (5.9%)	<.0001
Hyperlipidemia	19 (17.3%)	400 (5.4%)	<.0001
Hyperthyroidism	0 (0.0%)	6 (0.1%)	1.0000
Hypothyroidism	2 (1.8%)	45 (0.6%)	0.1511
Thyroiditis	0 (0.0%)	1 (0.0%)	1.0000
Mental Health Conditions - Any	25 (22.7%)	1092 (14.8%)	0.0203
Anxiety Disorders	14 (12.7%)	702 (9.5%)	0.2541
Bipolar or Manic Disorders	7 (6.4%)	212 (2.9%)	0.0309
Major Depressive Disorder	5 (4.5%)	198 (2.7%)	0.2253

	Incident T2DM N= 110	No incident T2DM N= 7,384	p-value
Schizophrenic Disorder	4 (3.6%)	73 (1.0%)	0.0262
Dementia	0 (0.0%)	13 (0.2%)	1.0000
Suicidality	1 (0.9%)	8 (0.1%)	0.1247
Liver Diseases - Any	10 (9.1%)	592 (8.0%)	0.6809
Hepatitis B	2 (1.8%)	277 (3.8%)	0.4428
Hepatitis C	6 (5.5%)	324 (4.4%)	0.5883
Other chronic liver disease	2 (1.8%)	42 (0.6%)	0.1359
Bone Diseases	0 (0.0%)	3 (0.0%)	1.0000
Peripheral Neuropathy	2 (1.8%)	88 (1.2%)	0.3821
Renal Disease - Any	23 (20.9%)	941 (12.7%)	0.0111
Renal Impairment	23 (20.9%)	941 (12.7%)	0.0111
Moderate/Severe CKD	0 (0.0%)	9 (0.1%)	1.0000
End Stage Renal Disease	0 (0.0%)	1 (0.0%)	1.0000
Hypertension	39 (35.5%)	695 (9.4%)	<.0001
Rheumatoid Arthritis	0 (0.0%)	7 (0.1%)	1.0000
Substance Abuse - Any	12 (10.9%)	798 (10.8%)	0.9727
Alcohol Dependence	5 (4.5%)	159 (2.2%)	0.0931
Drug Abuse	12 (10.9%)	762 (10.3%)	0.8402

Table 51. Baseline HIV-Infection Characteristics of ART-naïve patients by follow-up T2DM (Population 2)

		Incident T2DM N= 110	No incident T2DM N= 7,384	p-value
Months from first OPERA visit to baseline	Median (IQR)	0.7 (0.2, 1.4)	0.7 (0.0, 1.4)	0.3299
	0	27 (24.5%)	2107 (28.5%)	0.5789
	>0 to 6	70 (63.6%)	4412 (59.8%)	.
	>6 to 12	1 (0.9%)	210 (2.8%)	.
	>12 to 24	4 (3.6%)	239 (3.2%)	.
	>24	8 (7.3%)	416 (5.6%)	.
Year of study inclusion	Median (IQR)	2015.0 (2014.0, 2016.0)	2016.0 (2015.0, 2017.0)	0.0044
	2013	8 (7.3%)	494 (6.7%)	0.0695
	2014	27 (24.5%)	1193 (16.2%)	.
	2015	24 (21.8%)	1383 (18.7%)	.
	2016	26 (23.6%)	1711 (23.2%)	.
	2017	19 (17.3%)	2043 (27.7%)	.
	2018	6 (5.5%)	560 (7.6%)	.
History of AIDS-defining Illnesses	Yes	23 (20.9%)	1300 (17.6%)	0.3671
HIV viral load (copies/ml)	Median (IQR)	43740.0 (10360.0, 151270.0)	48844.0 (14925.0, 141270.0)	0.3241
	>= 1,000 to < 10,000	25 (22.7%)	1393 (18.9%)	0.5840
	>= 10,000 to < 100,000	51 (46.4%)	3546 (48.0%)	.
	>= 100,000	34 (30.9%)	2445 (33.1%)	.
Log10 HIV viral load	Median (IQR)	4.6 (4.0, 5.2)	4.7 (4.2, 5.2)	0.3241
	>= 3 to < 4	25 (22.7%)	1393 (18.9%)	0.5840

		Incident T2DM N= 110	No incident T2DM N= 7,384	p-value
	>= 4 to < 5	51 (46.4%)	3546 (48.0%)	.
	>= 5	34 (30.9%)	2445 (33.1%)	.
CD4 cell count (cell/µl)	Median (IQR)	321.0 (170.0, 485.0)	358.5 (199.5, 522.5)	0.3837
	>500	26 (23.6%)	1989 (26.9%)	0.8738
	>350 to <= 500	25 (22.7%)	1748 (23.7%)	.
	>200 to <= 350	24 (21.8%)	1683 (22.8%)	.
	>50 to <= 200	21 (19.1%)	1135 (15.4%)	.
	<= 50	12 (10.9%)	685 (9.3%)	.
	Missing	2 (1.8%)	144 (2.0%)	.

1.6.1. ART-Experienced/Suppressed Patients

Table 52. Baseline Demographic Characteristics of ART-experienced/suppressed patients by follow-up T2DM (Population 2)

		Incident T2DM N= 215	No incident T2DM N= 9,489	p-value
Age	Median (IQR)	50.9 (45.2, 57.0)	43.0 (32.4, 51.5)	<.0001
	13-25	1 (0.5%)	840 (8.9%)	<.0001
	26-49	94 (43.7%)	5843 (61.6%)	.
	50+	120 (55.8%)	2798 (29.5%)	.
Sex	Male	174 (80.9%)	8101 (85.4%)	0.1762
	Female	41 (19.1%)	1383 (14.6%)	.
	Unknown	0 (0.0%)	5 (0.1%)	.
Hispanic	Black	6 (10.0%)	82 (3.7%)	0.2757

		Incident T2DM N= 215	No incident T2DM N= 9,489	p-value
	American Indian/Alaska Native	0 (0.0%)	5 (0.2%)	.
	Hawaiian/Other Pacific Islander	0 (0.0%)	4 (0.2%)	.
	Asian	0 (0.0%)	5 (0.2%)	.
	White	53 (88.3%)	2049 (92.9%)	.
	Other	1 (1.7%)	26 (1.2%)	.
	>1 race	0 (0.0%)	35 (1.6%)	.
Non-Hispanic	Black	80 (53.0%)	2999 (44.7%)	0.1786
	American Indian/Alaska Native	0 (0.0%)	17 (0.3%)	.
	Hawaiian/Other Pacific Islander	0 (0.0%)	12 (0.2%)	.
	Asian	0 (0.0%)	166 (2.5%)	.
	White	71 (47.0%)	3442 (51.3%)	.
	Other	0 (0.0%)	11 (0.2%)	.
	>1 race	0 (0.0%)	66 (1.0%)	.
Race and/or ethnicity unknown	Yes	4 (1.9%)	570 (6.0%)	0.0077
Marital Status	Single	142 (66.0%)	6553 (69.1%)	0.3493
	Married	22 (10.2%)	786 (8.3%)	.
	Domestic partnership	0 (0.0%)	140 (1.5%)	.
	Widowed	2 (0.9%)	61 (0.6%)	.
	Separated/divorced	5 (2.3%)	255 (2.7%)	.
	Unknown	44 (20.5%)	1694 (17.9%)	.
Risk of Infection	MSM	132 (61.4%)	5947 (62.7%)	0.7018
	Not MSM	83 (38.6%)	3542 (37.3%)	.
History of Syphilis	Yes	50 (23.3%)	2781 (29.3%)	0.0536

		Incident T2DM N= 215	No incident T2DM N= 9,489	p-value
Region	Northeast	39 (18.1%)	854 (9.0%)	<.0001
	South	124 (57.7%)	5287 (55.7%)	.
	Midwest	7 (3.3%)	330 (3.5%)	.
	West	45 (20.9%)	3017 (31.8%)	.
	US Territories	0 (0.0%)	1 (0.0%)	.
Medicaid	Yes	48 (22.3%)	1725 (18.2%)	0.1197
Medicare	Yes	28 (13.0%)	1022 (10.8%)	0.2930
Commercial Insurance	Yes	84 (39.1%)	3846 (40.5%)	0.6660
Cash	Yes	130 (60.5%)	4880 (51.4%)	0.0087
ADAP/Ryan White	Yes	45 (20.9%)	2626 (27.7%)	0.0286
Other	Yes	0 (0.0%)	34 (0.4%)	1.0000
No Payer info	Yes	38 (17.7%)	1421 (15.0%)	0.2735

Table 53. Baseline Clinical Characteristics of ART-experienced/suppressed patients by follow-up T2DM (Population 2)

		Incident T2DM N= 215	No incident T2DM N= 9,489	p-value
Hemoglobin, g/dL	Median (IQR)	14.3 (13.2, 15.3)	14.7 (13.6, 15.6)	0.0083
	Normal	200 (93.0%)	9130 (96.2%)	0.0079
	DAIDS Grade 1 (mild)	1 (0.5%)	86 (0.9%)	.
	DAIDS Grade 2 (moderate)	1 (0.5%)	34 (0.4%)	.
	DAIDS Grade 3 (Severe)	0 (0.0%)	29 (0.3%)	.
	DAIDS Grade 4 (potentially life-threatening)	0 (0.0%)	5 (0.1%)	.
	Missing	13 (6.0%)	205 (2.2%)	.
Hematocrit, %	Median (IQR)	42.3 (39.9, 45.1)	43.5 (40.7, 45.8)	0.0052
	Low	16 (7.4%)	790 (8.3%)	0.0130
	Normal	179 (83.3%)	8120 (85.6%)	.
	High	8 (3.7%)	369 (3.9%)	.
	Missing	12 (5.6%)	210 (2.2%)	.
VACS mortality index	Median (IQR)	16.0 (10.0, 23.0)	10.0 (0.0, 18.0)	<.0001
	0 to <15	88 (40.9%)	5571 (58.7%)	<.0001
	>=15 to <30	71 (33.0%)	2156 (22.7%)	.
	>=30 to <45	22 (10.2%)	548 (5.8%)	.
	>= 45	10 (4.7%)	289 (3.0%)	.
	Missing	24 (11.2%)	925 (9.7%)	.
BMI	Median (IQR)	28.9 (26.0, 33.0)	25.7 (23.0, 28.9)	<.0001
	Underweight	6 (2.8%)	260 (2.7%)	<.0001

		Incident T2DM N= 215	No incident T2DM N= 9,489	p-value
	Normal weight	27 (12.6%)	3598 (37.9%)	.
	Overweight	82 (38.1%)	3409 (35.9%)	.
	Obese	84 (39.1%)	1691 (17.8%)	.
	Missing	16 (7.4%)	531 (5.6%)	.
HDL, mg/dL	Median (IQR)	41.0 (35.0, 52.0)	48.0 (39.0, 58.0)	<.0001
	Normal	23 (10.7%)	1787 (18.8%)	<.0001
	Borderline Abnormal	83 (38.6%)	3992 (42.1%)	.
	Dyslipidemia	79 (36.7%)	2035 (21.4%)	.
	Missing	30 (14.0%)	1675 (17.7%)	.
Triglycerides, mg/dL	Median (IQR)	166.0 (114.0, 233.0)	122.0 (84.0, 181.0)	<.0001
	Normal	76 (35.3%)	5007 (52.8%)	<.0001
	Borderline Abnormal	41 (19.1%)	1249 (13.2%)	.
	Dyslipidemia	60 (27.9%)	1459 (15.4%)	.
	Severe Dyslipidemia	8 (3.7%)	112 (1.2%)	.
	Missing	30 (14.0%)	1662 (17.5%)	.
Any concomitant non-ART listed below	Yes	133 (61.9%)	4197 (44.2%)	<.0001
Antibiotics	Yes	17 (7.9%)	733 (7.7%)	0.9212
Direct Acting Antivirals (DAAs)	Yes	5 (2.3%)	60 (0.6%)	0.0143
Lipid lowering agents	Yes	74 (34.4%)	1394 (14.7%)	<.0001
Non-steroidal Anti-inflammatory Agents (NSAIDS)	Yes	15 (7.0%)	572 (6.0%)	0.5639
Antidepressants	Yes	52 (24.2%)	1744 (18.4%)	0.0302

		Incident T2DM N= 215	No incident T2DM N= 9,489	p-value
Anxiolytics/Hypnotics/Sedatives	Yes	39 (18.1%)	1220 (12.9%)	0.0226
Immune Modulators	Yes	20 (9.3%)	605 (6.4%)	0.0839
Number of concomitant non-ART medications listed above	0	82 (38.1%)	5292 (55.8%)	<.0001
	1-2	95 (44.2%)	3396 (35.8%)	.
	3-4	25 (11.6%)	669 (7.1%)	.
	5+	13 (6.0%)	132 (1.4%)	.

Table 54. Baseline Comorbidities of ART-experienced/suppressed patients by follow-up T2DM (Population 2)

	Incident T2DM N= 215	No incident T2DM N= 9,489	p-value
Any Comorbidity at baseline	187 (87.0%)	6895 (72.7%)	<.0001
Any Cardiovascular Disease Conditions - Any	21 (9.8%)	637 (6.7%)	0.0781
Arrhythmia	2 (0.9%)	219 (2.3%)	0.2458
Myocardial Infarction	2 (0.9%)	54 (0.6%)	0.3532
Angina	0 (0.0%)	20 (0.2%)	1.0000
Other/Unspecified CHD	16 (7.4%)	303 (3.2%)	0.0006
Occlusion/stenosis of precerebral arteries	1 (0.5%)	5 (0.1%)	0.1258
Stroke	1 (0.5%)	75 (0.8%)	1.0000
Transient Ischemic Attack	1 (0.5%)	22 (0.2%)	0.4030
Other CBV	6 (2.8%)	129 (1.4%)	0.0764
Peripheral Arterial Disease	2 (0.9%)	44 (0.5%)	0.2714
Abdominal Aortic Aneurysm	0 (0.0%)	4 (0.0%)	1.0000

	Incident T2DM N= 215	No incident T2DM N= 9,489	p-value
Invasive Cancer	10 (4.7%)	582 (6.1%)	0.3692
Endocrine Disorders (excluding T2DM)	87 (40.5%)	2622 (27.6%)	<.0001
Hyperlipidemia	85 (39.5%)	2482 (26.2%)	<.0001
Hyperthyroidism	1 (0.5%)	43 (0.5%)	1.0000
Hypothyroidism	5 (2.3%)	243 (2.6%)	1.0000
Thyroiditis	0 (0.0%)	5 (0.1%)	1.0000
Mental Health Conditions - Any	67 (31.2%)	2536 (26.7%)	0.1465
Anxiety Disorders	43 (20.0%)	1687 (17.8%)	0.4000
Bipolar or Manic Disorders	15 (7.0%)	425 (4.5%)	0.0817
Major Depressive Disorder	21 (9.8%)	760 (8.0%)	0.3487
Schizophrenic Disorder	3 (1.4%)	107 (1.1%)	0.7371
Dementia	1 (0.5%)	29 (0.3%)	0.4899
Suicidality	1 (0.5%)	29 (0.3%)	0.4899
Liver Diseases - Any	51 (23.7%)	1413 (14.9%)	0.0003
Hepatitis B	13 (6.0%)	506 (5.3%)	0.6454
Hepatitis C	30 (14.0%)	832 (8.8%)	0.0082
Other chronic liver disease	15 (7.0%)	269 (2.8%)	0.0004
Bone Diseases	8 (3.7%)	197 (2.1%)	0.0972
Peripheral Neuropathy	15 (7.0%)	597 (6.3%)	0.6827
Renal Disease - Any	96 (44.7%)	3504 (36.9%)	0.0204
Renal Impairment	96 (44.7%)	3504 (36.9%)	0.0204
Moderate/Severe CKD	7 (3.3%)	188 (2.0%)	0.1878
End Stage Renal Disease	0 (0.0%)	16 (0.2%)	1.0000

	Incident T2DM N= 215	No incident T2DM N= 9,489	p-value
Hypertension	96 (44.7%)	2017 (21.3%)	<.0001
Rheumatoid Arthritis	1 (0.5%)	30 (0.3%)	0.5012
Substance Abuse - Any	27 (12.6%)	1165 (12.3%)	0.9013
Alcohol Dependence	13 (6.0%)	321 (3.4%)	0.0341
Drug Abuse	24 (11.2%)	1113 (11.7%)	0.7984

Table 55. Baseline HIV-Infection Characteristics of ART-experienced/suppressed patients by follow-up T2DM (Population 2)

		Incident T2DM N= 215	No incident T2DM N= 9,489	p-value
Months from first OPERA visit to baseline	Median (IQR)	7.2 (0.0, 43.5)	4.8 (0.0, 43.8)	0.8018
	0	63 (29.3%)	2828 (29.8%)	0.5660
	>0 to 6	39 (18.1%)	2069 (21.8%)	.
	>6 to 12	16 (7.4%)	530 (5.6%)	.
	>12 to 24	17 (7.9%)	758 (8.0%)	.
	>24	80 (37.2%)	3304 (34.8%)	.
Year of study inclusion	Median (IQR)	2015.0 (2014.0, 2016.0)	2016.0 (2015.0, 2017.0)	<.0001
	2013	20 (9.3%)	556 (5.9%)	<.0001
	2014	54 (25.1%)	1666 (17.6%)	.
	2015	54 (25.1%)	1796 (18.9%)	.
	2016	58 (27.0%)	2754 (29.0%)	.
	2017	26 (12.1%)	2170 (22.9%)	.

		Incident T2DM N= 215	No incident T2DM N= 9,489	p-value
	2018	3 (1.4%)	547 (5.8%)	.
Prior exposure: DTG	Yes	1 (0.5%)	8 (0.1%)	0.1827
Prior exposure: EVG/c	Yes	2 (0.9%)	53 (0.6%)	0.3452
Prior exposure: RAL	Yes	2 (0.9%)	135 (1.4%)	0.7719
Prior exposure: DRV(/r/c)	Yes	1 (0.5%)	104 (1.1%)	0.7322
Number of classes of core agents experienced prior to baseline	1	95 (44.2%)	4026 (42.4%)	0.1220
	2	22 (10.2%)	600 (6.3%)	.
	3	2 (0.9%)	54 (0.6%)	.
	4+	0 (0.0%)	7 (0.1%)	.
	Missing	96 (44.7%)	4802 (50.6%)	.
History of AIDS-defining Illnesses	Yes	66 (30.7%)	2262 (23.8%)	0.0199
CD4 cell count (cell/µl)	Median (IQR)	671.5 (456.0, 881.0)	637.0 (464.0, 832.0)	0.2339
	>500	146 (67.9%)	6504 (68.5%)	0.9493
	>350 to <= 500	38 (17.7%)	1692 (17.8%)	.
	>200 to <= 350	17 (7.9%)	796 (8.4%)	.
	>50 to <= 200	8 (3.7%)	310 (3.3%)	.
	<= 50	1 (0.5%)	21 (0.2%)	.
	Missing	5 (2.3%)	166 (1.7%)	.

1.6.1. ART-Experienced/Viremic Patients

Table 56. Baseline Demographic Characteristics of ART-experienced/viremic patients by follow-up T2DM (Study Population 2)

		Incident T2DM N= 112	No incident T2DM N= 7,315	p-value
Age	Median (IQR)	46.3 (38.7, 54.9)	36.4 (28.2, 47.2)	<.0001
	13-25	2 (1.8%)	1202 (16.5%)	<.0001
	26-49	63 (56.3%)	4746 (65.0%)	.
	50+	47 (42.0%)	1353 (18.5%)	.
Sex	Male	87 (77.7%)	6149 (84.1%)	0.1372
	Female	25 (22.3%)	1161 (15.9%)	.
	Unknown	0 (0.0%)	5 (0.1%)	.
Hispanic	Black	3 (13.0%)	64 (4.1%)	0.5563
	American Indian/Alaska Native	0 (0.0%)	6 (0.4%)	.
	Hawaiian/Other Pacific Islander	0 (0.0%)	3 (0.2%)	.
	Asian	0 (0.0%)	4 (0.3%)	.
	White	20 (87.0%)	1457 (93.6%)	.
	Other	0 (0.0%)	4 (0.3%)	.
	>1 race	0 (0.0%)	19 (1.2%)	.
Non-Hispanic	Black	56 (65.1%)	3341 (61.3%)	0.9373
	American Indian/Alaska Native	0 (0.0%)	15 (0.3%)	.
	Hawaiian/Other Pacific Islander	0 (0.0%)	8 (0.1%)	.
	Asian	2 (2.3%)	92 (1.7%)	.
	White	28 (32.6%)	1943 (35.7%)	.
	Other	0 (0.0%)	1 (0.0%)	.
	>1 race	0 (0.0%)	50 (0.9%)	.

		Incident T2DM N= 112	No incident T2DM N= 7,315	p-value
Race and/or ethnicity unknown	Yes	3 (2.7%)	308 (4.2%)	0.6317
Marital Status	Single	66 (58.9%)	5390 (73.7%)	0.0151
	Married	9 (8.0%)	396 (5.4%)	.
	Domestic partnership	2 (1.8%)	95 (1.3%)	.
	Widowed	2 (1.8%)	50 (0.7%)	.
	Separated/divorced	6 (5.4%)	188 (2.6%)	.
	Unknown	27 (24.1%)	1196 (16.3%)	.
Risk of Infection	MSM	59 (52.7%)	4526 (61.9%)	0.0469
	Not MSM	53 (47.3%)	2789 (38.1%)	.
History of Syphilis	Yes	29 (25.9%)	2377 (32.5%)	0.1384
Region	Northeast	11 (9.8%)	493 (6.7%)	0.5038
	South	70 (62.5%)	4599 (62.9%)	.
	Midwest	6 (5.4%)	322 (4.4%)	.
	West	25 (22.3%)	1901 (26.0%)	.
Medicaid	Yes	28 (25.0%)	1607 (22.0%)	0.4422
Medicare	Yes	20 (17.9%)	693 (9.5%)	0.0028
Commercial Insurance	Yes	47 (42.0%)	2501 (34.2%)	0.0854
Cash	Yes	70 (62.5%)	3863 (52.8%)	0.0414
ADAP/Ryan White	Yes	30 (26.8%)	2703 (37.0%)	0.0268
Other	Yes	1 (0.9%)	47 (0.6%)	0.5189
No Payer info	Yes	10 (8.9%)	761 (10.4%)	0.6116

Table 57. Baseline Clinical Characteristics of ART-experienced/viremic patients by follow-up T2DM (Study Population 2)

		Incident T2DM N= 112	No incident T2DM N= 7,315	p-value
Hemoglobin, g/dL	Median (IQR)	13.5 (12.3, 14.5)	14.1 (12.9, 15.1)	0.0013
	Normal	95 (84.8%)	6780 (92.7%)	0.0081
	DAIDS Grade 1 (mild)	4 (3.6%)	207 (2.8%)	.
	DAIDS Grade 2 (moderate)	4 (3.6%)	134 (1.8%)	.
	DAIDS Grade 3 (Severe)	4 (3.6%)	73 (1.0%)	.
	DAIDS Grade 4 (potentially life-threatening)	0 (0.0%)	6 (0.1%)	.
	Missing	5 (4.5%)	115 (1.6%)	.
Hematocrit, %	Median (IQR)	40.8 (37.4, 43.1)	42.2 (38.8, 44.8)	0.0018
	Low	25 (22.3%)	1383 (18.9%)	0.1050
	Normal	79 (70.5%)	5624 (76.9%)	.
	High	3 (2.7%)	184 (2.5%)	.
	Missing	5 (4.5%)	124 (1.7%)	.
VACS mortality index	Median (IQR)	24.0 (13.0, 45.0)	18.0 (10.0, 32.0)	0.0002
	0 to <15	28 (25.0%)	2700 (36.9%)	0.0141
	>=15 to <30	30 (26.8%)	2064 (28.2%)	.
	>=30 to <45	17 (15.2%)	860 (11.8%)	.
	>= 45	26 (23.2%)	1009 (13.8%)	.
	Missing	11 (9.8%)	682 (9.3%)	.
BMI	Median (IQR)	28.0 (24.3, 33.8)	24.9 (22.1, 28.2)	<.0001
	Underweight	2 (1.8%)	295 (4.0%)	<.0001

		Incident T2DM N= 112	No incident T2DM N= 7,315	p-value
	Normal weight	29 (25.9%)	3315 (45.3%)	.
	Overweight	38 (33.9%)	2268 (31.0%)	.
	Obese	40 (35.7%)	1210 (16.5%)	.
	Missing	3 (2.7%)	227 (3.1%)	.
HDL, mg/dL	Median (IQR)	42.0 (32.5, 50.0)	43.0 (35.0, 53.0)	0.0752
	Normal	9 (8.0%)	893 (12.2%)	0.3504
	Borderline Abnormal	42 (37.5%)	2645 (36.2%)	.
	Dyslipidemia	41 (36.6%)	2256 (30.8%)	.
	Missing	20 (17.9%)	1521 (20.8%)	.
Triglycerides, mg/dL	Median (IQR)	157.5 (106.0, 215.0)	112.0 (79.0, 164.0)	<.0001
	Normal	42 (37.5%)	4053 (55.4%)	<.0001
	Borderline Abnormal	23 (20.5%)	854 (11.7%)	.
	Dyslipidemia	26 (23.2%)	866 (11.8%)	.
	Severe Dyslipidemia	1 (0.9%)	44 (0.6%)	.
	Missing	20 (17.9%)	1498 (20.5%)	.
Any concomitant non-ART listed below	Yes	59 (52.7%)	2938 (40.2%)	0.0074
Antibiotics	Yes	18 (16.1%)	1189 (16.3%)	0.9585
Direct Acting Antivirals (DAAs)	Yes	0 (0.0%)	19 (0.3%)	1.0000
Lipid lowering agents	Yes	22 (19.6%)	446 (6.1%)	<.0001
Non-steroidal Anti-inflammatory Agents (NSAIDS)	Yes	6 (5.4%)	431 (5.9%)	0.8113
Antidepressants	Yes	26 (23.2%)	996 (13.6%)	0.0034

		Incident T2DM N= 112	No incident T2DM N= 7,315	p-value
Anxiolytics/Hypnotics/Sedatives	Yes	10 (8.9%)	532 (7.3%)	0.5037
Immune Modulators	Yes	9 (8.0%)	483 (6.6%)	0.5451
Number of concomitant non-ART medications listed above	0	53 (47.3%)	4377 (59.8%)	0.0031
	1-2	44 (39.3%)	2502 (34.2%)	.
	3-4	13 (11.6%)	385 (5.3%)	.
	5+	2 (1.8%)	51 (0.7%)	.

Table 58. Baseline Comorbidities of ART-experienced/viremic patients by follow-up T2DM (Study Population 2)

	Incident T2DM N= 112	No incident T2DM N= 7,315	p-value
Any Comorbidity at baseline	91 (81.3%)	4457 (60.9%)	<.0001
Any Cardiovascular Disease Conditions - Any	9 (8.0%)	338 (4.6%)	0.0892
Arrhythmia	3 (2.7%)	145 (2.0%)	0.4900
Myocardial Infarction	0 (0.0%)	31 (0.4%)	1.0000
Angina	0 (0.0%)	7 (0.1%)	1.0000
Other/Unspecified CHD	3 (2.7%)	128 (1.7%)	0.4507
Occlusion/stenosis of precerebral arteries	0 (0.0%)	6 (0.1%)	1.0000
Stroke	4 (3.6%)	50 (0.7%)	0.0087
Transient Ischemic Attack	0 (0.0%)	8 (0.1%)	1.0000
Other CBV	4 (3.6%)	75 (1.0%)	0.0310
Peripheral Arterial Disease	1 (0.9%)	19 (0.3%)	0.2624
Abdominal Aortic Aneurysm	0	0	.

	Incident T2DM N= 112	No incident T2DM N= 7,315	p-value
Invasive Cancer	8 (7.1%)	292 (4.0%)	0.0928
Endocrine Disorders (excluding T2DM)	32 (28.6%)	1069 (14.6%)	<.0001
Hyperlipidemia	30 (26.8%)	1007 (13.8%)	<.0001
Hyperthyroidism	0 (0.0%)	13 (0.2%)	1.0000
Hypothyroidism	4 (3.6%)	84 (1.1%)	0.0435
Thyroiditis	0 (0.0%)	2 (0.0%)	1.0000
Mental Health Conditions - Any	31 (27.7%)	1687 (23.1%)	0.2502
Anxiety Disorders	18 (16.1%)	990 (13.5%)	0.4365
Bipolar or Manic Disorders	8 (7.1%)	371 (5.1%)	0.3229
Major Depressive Disorder	8 (7.1%)	535 (7.3%)	0.9450
Schizophrenic Disorder	3 (2.7%)	122 (1.7%)	0.4389
Dementia	1 (0.9%)	10 (0.1%)	0.1540
Suicidality	0 (0.0%)	36 (0.5%)	1.0000
Liver Diseases - Any	22 (19.6%)	1053 (14.4%)	0.1172
Hepatitis B	6 (5.4%)	428 (5.9%)	0.8250
Hepatitis C	12 (10.7%)	630 (8.6%)	0.4321
Other chronic liver disease	6 (5.4%)	133 (1.8%)	0.0061
Bone Diseases	1 (0.9%)	61 (0.8%)	0.6117
Peripheral Neuropathy	12 (10.7%)	336 (4.6%)	0.0023
Renal Disease - Any	34 (30.4%)	1583 (21.6%)	0.0265
Renal Impairment	34 (30.4%)	1583 (21.6%)	0.0265
Moderate/Severe CKD	4 (3.6%)	67 (0.9%)	0.0220
End Stage Renal Disease	0 (0.0%)	9 (0.1%)	1.0000

	Incident T2DM N= 112	No incident T2DM N= 7,315	p-value
Hypertension	46 (41.1%)	1212 (16.6%)	<.0001
Rheumatoid Arthritis	1 (0.9%)	25 (0.3%)	0.3268
Substance Abuse - Any	16 (14.3%)	1222 (16.7%)	0.4953
Alcohol Dependence	7 (6.3%)	269 (3.7%)	0.1532
Drug Abuse	16 (14.3%)	1187 (16.2%)	0.5800

Table 59. Baseline HIV-Infection Characteristics of ART-experienced/viremic patients by follow-up T2DM (Study Population 2)

		Incident T2DM N= 112	No incident T2DM N= 7,315	p-value
Months from first OPERA visit to baseline	Median (IQR)	3.4 (0.7, 32.0)	2.2 (0.7, 32.5)	0.6670
	0	16 (14.3%)	775 (10.6%)	0.2536
	>0 to 6	44 (39.3%)	3467 (47.4%)	.
	>6 to 12	8 (7.1%)	397 (5.4%)	.
	>12 to 24	12 (10.7%)	532 (7.3%)	.
	>24	32 (28.6%)	2144 (29.3%)	.
Year of study inclusion	Median (IQR)	2015.0 (2014.0, 2016.0)	2016.0 (2014.0, 2017.0)	0.0007
	2013	10 (8.9%)	593 (8.1%)	0.0024
	2014	37 (33.0%)	1338 (18.3%)	.
	2015	21 (18.8%)	1555 (21.3%)	.
	2016	25 (22.3%)	1771 (24.2%)	.
	2017	16 (14.3%)	1687 (23.1%)	.

		Incident T2DM N= 112	No incident T2DM N= 7,315	p-value
	2018	3 (2.7%)	371 (5.1%)	.
Prior exposure: DTG	Yes	0 (0.0%)	7 (0.1%)	1.0000
Prior exposure: EVG/c	Yes	0 (0.0%)	25 (0.3%)	1.0000
Prior exposure: RAL	Yes	2 (1.8%)	94 (1.3%)	0.6570
Prior exposure: DRV(/r/c)	Yes	1 (0.9%)	134 (1.8%)	0.7249
Number of classes of core agents experienced prior to baseline	1	51 (45.5%)	2409 (32.9%)	0.0611
	2	7 (6.3%)	395 (5.4%)	.
	3	1 (0.9%)	46 (0.6%)	.
	4+	0 (0.0%)	3 (0.0%)	.
	Missing	53 (47.3%)	4462 (61.0%)	.
History of AIDS-defining Illnesses	Yes	38 (33.9%)	1873 (25.6%)	0.0455
HIV viral load (copies/ml)	Median (IQR)	1860.0 (180.0, 44520.0)	10370.0 (280.0, 61700.0)	0.0201
	>= 50 to < 200	35 (31.3%)	1540 (21.1%)	0.1136
	>= 200 to < 1,000	17 (15.2%)	1101 (15.1%)	.
	>= 1,000 to < 10,000	14 (12.5%)	993 (13.6%)	.
	>= 10,000 to < 100,000	29 (25.9%)	2398 (32.8%)	.
	>= 100,000	17 (15.2%)	1283 (17.5%)	.
Log10 HIV viral load	Median (IQR)	3.3 (2.3, 4.6)	4.0 (2.4, 4.8)	0.0201
	>= 1.7 to < 2.3	28 (26.7%)	1338 (18.8%)	0.3110
	>= 2.3 to < 3	17 (16.2%)	1101 (15.5%)	.
	>= 3 to < 4	14 (13.3%)	993 (14.0%)	.

		Incident T2DM N= 112	No incident T2DM N= 7,315	p-value
	>= 4 to < 5	29 (27.6%)	2398 (33.7%)	.
	>= 5	17 (16.2%)	1283 (18.0%)	.
CD4 cell count (cell/µl)	Median (IQR)	417.0 (204.0, 672.0)	417.0 (239.0, 608.0)	0.9769
	>500	43 (38.4%)	2743 (37.5%)	0.2309
	>350 to <= 500	18 (16.1%)	1608 (22.0%)	.
	>200 to <= 350	21 (18.8%)	1417 (19.4%)	.
	>50 to <= 200	19 (17.0%)	1018 (13.9%)	.
	<= 50	8 (7.1%)	467 (6.4%)	.
	Missing	3 (2.7%)	62 (0.8%)	.

1.7. Secondary Objective 2: HbA1c and fasting glucose among patients with prevalent T2DM in Study Population 3

1.7.1. ART-Naïve Patients

Table 60. Categorical HbA1c among ART-naïve patients with prevalent prediabetes or T2DM (Population 3)

		DTG N= 418	EVG/c N= 402	DTG vs. EVG p-value	RAL N= 34	DTG vs. RAL p-value	DRV(r/c) N= 141	DTG vs. DRV(r/c) p-value
Baseline (among all patients)	Total	418 (100.0%)	402 (100.0%)	.	34 (100.0%)	.	141 (100.0%)	.
	Controlled HbA1c (<7.0%)	325 (77.8%)	311 (77.4%)	0.9795	22 (64.7%)	0.2213	105 (74.5%)	0.3125
	Uncontrolled (HbA1c >=7.0%)	48 (11.5%)	48 (11.9%)	.	6 (17.6%)	.	23 (16.3%)	.
	Missing HbA1c	45 (10.8%)	43 (10.7%)	.	6 (17.6%)	.	13 (9.2%)	.
6-month* (among patients with follow-up >3m)	Total	390 (93.3%)	364 (90.5%)	0.1591	31 (91.2%)	0.7197	117 (83.0%)	0.0006
	Controlled HbA1c (<7.0%)	109 (27.9%)	104 (28.6%)	0.1382	6 (19.4%)	0.2454	21 (17.9%)	0.0861
	Uncontrolled (HbA1c >=7.0%)	39 (10.0%)	22 (6.0%)	.	1 (3.2%)	.	13 (11.1%)	.
	Missing HbA1c	242 (62.1%)	238 (65.4%)	.	24 (77.4%)	.	83 (70.9%)	.
12-month* (among patients with follow-up >9m)	Total	342 (81.8%)	327 (81.3%)	0.8608	26 (76.5%)	0.4408	88 (62.4%)	<.0001

		DTG N= 418	EVG/c N= 402	DTG vs. EVG p-value	RAL N= 34	DTG vs. RAL p-value	DRV(r/c) N= 141	DTG vs. DRV(r/c) p-value
	Controlled HbA1c (<7.0%)	99 (28.9%)	95 (29.1%)	0.2345	4 (15.4%)	0.3266	18 (20.5%)	0.1030
	Uncontrolled (HbA1c >=7.0%)	33 (9.6%)	20 (6.1%)	.	3 (11.5%)	.	5 (5.7%)	.
	Missing HbA1c	210 (61.4%)	212 (64.8%)	.	19 (73.1%)	.	65 (73.9%)	.
18-month* (among patients with follow-up >15m)	Total	224 (53.6%)	221 (55.0%)	0.6903	19 (55.9%)	0.7964	55 (39.0%)	0.0027
	Controlled HbA1c (<7.0%)	68 (30.4%)	61 (27.6%)	0.3648	3 (15.8%)	0.3454	11 (20.0%)	0.2890
	Uncontrolled (HbA1c >=7.0%)	22 (9.8%)	15 (6.8%)	.	3 (15.8%)	.	5 (9.1%)	.
	Missing HbA1c	134 (59.8%)	145 (65.6%)	.	13 (68.4%)	.	39 (70.9%)	.
24-month* (among patients with follow-up >21m)	Total	168 (40.2%)	153 (38.1%)	0.5318	13 (38.2%)	0.8229	25 (17.7%)	<.0001
	Controlled HbA1c (<7.0%)	48 (28.6%)	41 (26.8%)	0.9093	1 (7.7%)	0.0967	6 (24.0%)	0.9433
	Uncontrolled (HbA1c >=7.0%)	15 (8.9%)	13 (8.5%)	.	3 (23.1%)	.	2 (8.0%)	.
	Missing HbA1c	105 (62.5%)	99 (64.7%)	.	9 (69.2%)	.	17 (68.0%)	.

*+/- 3 months, value closest to X months

Table 61. Changes in HbA1c among ART-naïve patients with prevalent prediabetes or T2DM (Population 3)

			DTG N= 418	EVG/c N= 402	DTG vs. EVG p-value	RAL N= 34	DTG vs. RAL p-value	DRV(r/c) N= 141	DTG vs. DRV(r/c) p-value
6-month* (among patients with follow-up >3m)	HbA1c available at baseline and 6 months	N(%)	130 (31.1%)	116 (28.9%)	0.4832	7 (20.6%)	0.1996	32 (22.7%)	0.0571
	Absolute HbA1c change at 6 months from baseline	Median (IQR)	-0.2 (-0.5, 0.1)	-0.3 (-0.6, 0.0)	0.1092	-0.1 (-0.3, 0.2)	0.4251	-0.3 (-1.5, 0.0)	0.1306
	% HbA1c change at 6 months from baseline	Median (IQR)	-3.4 (-8.3, 1.8)	-5.0 (-10.0, 0.0)	0.1153	-1.0 (-4.3, 3.3)	0.3453	-5.8 (-15.1, 0.0)	0.1512
12-month* (among patients with follow-up >9m)	HbA1c available at baseline and 12 months	N(%)	115 (27.5%)	105 (26.1%)	0.6528	7 (20.6%)	0.3818	22 (15.6%)	0.0045
	Absolute HbA1c change at 12 months from baseline	Median (IQR)	-0.1 (-0.4, 0.2)	-0.3 (-0.5, 0.0)	0.0614	0.1 (-0.3, 0.2)	0.3131	-0.5 (-1.6, -0.2)	0.0093
	% HbA1c change at 12 months from baseline	Median (IQR)	-1.8 (-6.9, 3.0)	-5.0 (-8.5, 0.0)	0.0694	1.4 (-4.9, 2.9)	0.2214	-7.7 (-19.8, -3.3)	0.0085
18-month* (among patients with follow-up >15m)	HbA1c available at baseline and 18 months	N(%)	79 (18.9%)	68 (16.9%)	0.4590	6 (17.6%)	0.8574	16 (11.3%)	0.0390
	Absolute HbA1c change at 18 months from baseline	Median (IQR)	-0.2 (-0.5, 0.1)	-0.3 (-0.5, 0.0)	0.4657	0.1 (0.0, 0.3)	0.0699	-0.3 (-0.7, 0.1)	0.7880

			DTG N= 418	EVG/c N= 402	DTG vs. EVG p-value	RAL N= 34	DTG vs. RAL p-value	DRV(r/c) N= 141	DTG vs. DRV(r/c) p-value
	% HbA1c change at 18 months from baseline	Median (IQR)	-3.4 (-8.2, 1.8)	-3.8 (-8.5, 0.8)	0.5639	2.0 (0.0, 2.9)	0.0675	-3.8 (-10.9, 1.8)	0.9010
24-month* (among patients with follow-up >21m)	HbA1c available at baseline and 24 months	N(%)	55 (13.2%)	50 (12.4%)	0.8345	4 (11.8%)	1.0000	8 (5.7%)	0.0137
	Absolute HbA1c change at 24 months from baseline	Median (IQR)	-0.2 (-0.5, 0.0)	-0.1 (-0.5, 0.1)	0.5415	0.9 (-0.5, 1.4)	0.1060	-0.0 (-0.8, 0.4)	0.5765
	% HbA1c change at 24 months from baseline	Median (IQR)	-3.4 (-7.9, 0.0)	-2.5 (-6.8, 1.7)	0.5002	13.5 (-3.1, 19.6)	0.0882	-0.8 (-10.1, 6.9)	0.5084

*+/- 3 months, value closest to X months

Table 62. Categorical fasting glucose among ART-naïve patients with prevalent prediabetes or T2DM (Population 3)

		DTG N= 418	EVG/c N= 402	DTG vs. EVG p-value	RAL N= 34	DTG vs. RAL p-value	DRV(r/c) N= 141	DTG vs. DRV(r/c) p-value
Baseline (among all patients)	Total	418 (100.0%)	402 (100.0%)	.	34 (100.0%)	.	141 (100.0%)	.
	Normal fasting glucose (<100 mg/dl)	3 (0.7%)	1 (0.2%)	0.2264	0 (0.0%)	0.4238	1 (0.7%)	1.0000

		DTG N= 418	EVG/c N= 402	DTG vs. EVG p-value	RAL N= 34	DTG vs. RAL p-value	DRV(r/c) N= 141	DTG vs. DRV(r/c) p-value
	Grade 1 fasting glucose (>=100 to <126 mg/dl)	2 (0.5%)	7 (1.7%)	.	1 (2.9%)	.	1 (0.7%)	.
	Grade 2 fasting glucose (126-250 mg/dl)	1 (0.2%)	1 (0.2%)	.	0 (0.0%)	.	0 (0.0%)	.
	Missing fasting glucose	412 (98.6%)	393 (97.8%)	.	33 (97.1%)	.	139 (98.6%)	.
6-month* (among patients with follow-up >3m)	Total	390 (93.3%)	364 (90.5%)	0.1591	31 (91.2%)	0.7197	117 (83.0%)	0.0006
	Normal fasting glucose (<100 mg/dl)	0 (0.0%)	1 (0.3%)	0.4828	0 (0.0%)	.	1 (0.9%)	0.2308
	Missing fasting glucose	390 (100.0%)	363 (99.7%)	.	31 (100.0%)	.	116 (99.1%)	.
12-month* (among patients with follow-up >9m)	Total	342 (81.8%)	327 (81.3%)	0.8608	26 (76.5%)	0.4408	88 (62.4%)	<.0001
	Normal fasting glucose (<100 mg/dl)	0 (0.0%)	1 (0.3%)	0.7390	0 (0.0%)	1.0000	0 (0.0%)	1.0000
	Grade 2 fasting glucose (126-250 mg/dl)	1 (0.3%)	0 (0.0%)	.	0 (0.0%)	.	0 (0.0%)	.
	Missing fasting glucose	341 (99.7%)	326 (99.7%)	.	26 (100.0%)	.	88 (100.0%)	.
18-month* (among patients with follow-up >15m)	Total	224 (53.6%)	221 (55.0%)	0.6903	19 (55.9%)	0.7964	55 (39.0%)	0.0027

		DTG N= 418	EVG/c N= 402	DTG vs. EVG p-value	RAL N= 34	DTG vs. RAL p-value	DRV(r/c) N= 141	DTG vs. DRV(r/c) p-value
	Normal fasting glucose (<100 mg/dl)	0 (0.0%)	1 (0.5%)	0.7472	0 (0.0%)	1.0000	0 (0.0%)	1.0000
	Grade 2 fasting glucose (126-250 mg/dl)	1 (0.4%)	0 (0.0%)	.	0 (0.0%)	.	0 (0.0%)	.
	Missing fasting glucose	223 (99.6%)	220 (99.5%)	.	19 (100.0%)	.	55 (100.0%)	.
24-month* (among patients with follow-up >21m)	Total	168 (40.2%)	153 (38.1%)	0.5318	13 (38.2%)	0.8229	25 (17.7%)	<.0001
	Missing fasting glucose	168 (100.0%)	153 (100.0%)	.	13 (100.0%)	.	25 (100.0%)	.

*+/- 3 months, value closest to X months

Table 63. Changes in fasting glucose among ART-naïve patients with prevalent prediabetes or T2DM (Population 3)

			DTG N= 418	EVG/c N= 402	DTG vs. EVG p-value	RAL N= 34	DTG vs. RAL p-value	DRV(r/c) N= 141	DTG vs. DRV(r/c) p-value
6-month* (among patients with follow-up >3m)	Fasting glucose available at baseline and 6 months	N(%)	0 (0.0%)	1 (0.2%)	0.4902	0 (0.0%)	.	1 (0.7%)	0.2522

			DTG N= 418	EVG/c N= 402	DTG vs. EVG p-value	RAL N= 34	DTG vs. RAL p-value	DRV(r/c) N= 141	DTG vs. DRV(r/c) p-value
	Absolute fasting glucose change at 6 months from baseline	Median (IQR)		-43.0 (-43.0, -43.0)	.		.	-19.0 (-19.0, -19.0)	.
	% fasting glucose change at 6 months from baseline	Median (IQR)		-30.3 (-30.3, -30.3)	.		.	-17.0 (-17.0, -17.0)	.
12-month* (among patients with follow-up >9m)	Fasting glucose available at baseline and 12 months	N(%)	0 (0.0%)	1 (0.2%)	0.4902	0 (0.0%)	.	0 (0.0%)	.
	Absolute fasting glucose change at 12 months from baseline	Median (IQR)		-44.0 (-44.0, -44.0)	.		.		.
	% fasting glucose change at 12 months from baseline	Median (IQR)		-31.0 (-31.0, -31.0)	.		.		.
18-month* (among patients with follow-up >15m)	Fasting glucose available at baseline and 18 months	N(%)	0 (0.0%)	1 (0.2%)	0.4902	0 (0.0%)	.	0 (0.0%)	.
	Absolute fasting glucose change at 18 months from baseline	Median (IQR)		-47.0 (-47.0, -47.0)	.		.		.
	% fasting glucose change at 18 months from baseline	Median (IQR)		-33.1 (-33.1, -33.1)	.		.		.

			DTG N= 418	EVG/c N= 402	DTG vs. EVG p-value	RAL N= 34	DTG vs. RAL p-value	DRV(r/c) N= 141	DTG vs. DRV(r/c) p-value
24-month* (among patients with follow-up >21m)	Fasting glucose available at baseline and 24 months		0	0	.	0	.	0	.
	Absolute fasting glucose change at 24 months from baseline	Median (IQR)			.		.		.
	% fasting glucose change at 24 months from baseline	Median (IQR)			.		.		.

*+/- 3 months, value closest to X months

1.7.2. ART-Experienced/Suppressed Patients

Table 64. Categorical HbA1c among ART-experienced/suppressed patients with prevalent prediabetes or T2DM (Population 3)

		DTG N= 1,163	EVG/c N= 962	DTG vs. EVG p-value	RAL N= 232	DTG vs. RAL p-value	DRV(r/c) N= 261	DTG vs. DRV(r/c) p-value
Baseline (among all patients)	Total	1163 (100.0%)	962 (100.0%)	.	232 (100.0%)	.	261 (100.0%)	.
	Controlled HbA1c (<7.0%)	909 (78.2%)	731 (76.0%)	0.0712	139 (59.9%)	<.0001	158 (60.5%)	<.0001

		DTG N= 1,163	EVG/c N= 962	DTG vs. EVG p-value	RAL N= 232	DTG vs. RAL p-value	DRV(r/c) N= 261	DTG vs. DRV(r/c) p-value
	Uncontrolled (HbA1c >=7.0%)	164 (14.1%)	129 (13.4%)	.	43 (18.5%)	.	47 (18.0%)	.
	Missing HbA1c	90 (7.7%)	102 (10.6%)	.	50 (21.6%)	.	56 (21.5%)	.
6-month* (among patients with follow-up >3m)	Total	1076 (92.5%)	878 (91.3%)	0.2913	206 (88.8%)	0.0575	228 (87.4%)	0.0067
	Controlled HbA1c (<7.0%)	443 (41.2%)	331 (37.7%)	0.0116	59 (28.6%)	0.0030	68 (29.8%)	0.0007
	Uncontrolled (HbA1c >=7.0%)	144 (13.4%)	92 (10.5%)	.	31 (15.0%)	.	25 (11.0%)	.
	Missing HbA1c	489 (45.4%)	455 (51.8%)	.	116 (56.3%)	.	135 (59.2%)	.
12-month* (among patients with follow-up >9m)	Total	935 (80.4%)	738 (76.7%)	0.0391	175 (75.4%)	0.0868	189 (72.4%)	0.0043
	Controlled HbA1c (<7.0%)	364 (38.9%)	264 (35.8%)	0.1044	50 (28.6%)	0.0270	55 (29.1%)	0.0194
	Uncontrolled (HbA1c >=7.0%)	109 (11.7%)	72 (9.8%)	.	27 (15.4%)	.	20 (10.6%)	.
	Missing HbA1c	462 (49.4%)	402 (54.5%)	.	98 (56.0%)	.	114 (60.3%)	.
18-month* (among patients with follow-up >15m)	Total	704 (60.5%)	545 (56.7%)	0.0705	121 (52.2%)	0.0178	140 (53.6%)	0.0405

		DTG N= 1,163	EVG/c N= 962	DTG vs. EVG p-value	RAL N= 232	DTG vs. RAL p-value	DRV(r/c) N= 261	DTG vs. DRV(r/c) p-value
	Controlled HbA1c (<7.0%)	267 (37.9%)	204 (37.4%)	0.5318	36 (29.8%)	0.2209	42 (30.0%)	0.0119
	Uncontrolled (HbA1c >=7.0%)	88 (12.5%)	58 (10.6%)	.	18 (14.9%)	.	10 (7.1%)	.
	Missing HbA1c	349 (49.6%)	283 (51.9%)	.	67 (55.4%)	.	88 (62.9%)	.
24-month* (among patients with follow-up >21m)	Total	534 (45.9%)	393 (40.9%)	0.0191	99 (42.7%)	0.3649	103 (39.5%)	0.0581
	Controlled HbA1c (<7.0%)	202 (37.8%)	152 (38.7%)	0.8478	31 (31.3%)	0.0938	29 (28.2%)	0.1256
	Uncontrolled (HbA1c >=7.0%)	62 (11.6%)	41 (10.4%)	.	19 (19.2%)	.	11 (10.7%)	.
	Missing HbA1c	270 (50.6%)	200 (50.9%)	.	49 (49.5%)	.	63 (61.2%)	.

*+/- 3 months, value closest to X months

Table 65. Changes in HbA1c among ART-experienced/suppressed patients with prevalent prediabetes or T2DM (Population 3)

			DTG N= 1,163	EVG/c N= 962	DTG vs. EVG p-value	RAL N= 232	DTG vs. RAL p-value	DRV(r/c) N= 261	DTG vs. DRV(r/c) p-value
6-month* (among patients with follow-up >3m)	HbA1c available at baseline and 6 months	N(%)	560 (48.2%)	405 (42.1%)	0.0053	82 (35.3%)	0.0004	85 (32.6%)	<.0001
	Absolute HbA1c change at 6 months from baseline	Median (IQR)	0.0 (-0.3, 0.3)	0.0 (-0.3, 0.3)	0.3797	0.1 (-0.3, 0.4)	0.7112	-0.1 (-0.2, 0.2)	0.3483
	% HbA1c change at 6 months from baseline	Median (IQR)	0.0 (-3.7, 5.4)	0.0 (-5.0, 4.9)	0.3467	1.6 (-3.6, 5.3)	0.5297	-1.6 (-3.5, 3.4)	0.3013
12-month* (among patients with follow-up >9m)	HbA1c available at baseline and 12 months	N(%)	457 (39.3%)	320 (33.3%)	0.0041	70 (30.2%)	0.0089	70 (26.8%)	0.0002
	Absolute HbA1c change at 12 months from baseline	Median (IQR)	0.0 (-0.3, 0.3)	-0.1 (-0.3, 0.2)	0.0627	0.0 (-0.3, 0.5)	0.8102	0.0 (-0.2, 0.4)	0.3333
	% HbA1c change at 12 months from baseline	Median (IQR)	0.0 (-5.0, 5.1)	-1.6 (-5.3, 3.5)	0.0477	0.0 (-4.7, 7.7)	0.6013	0.0 (-3.5, 7.1)	0.3760
18-month* (among patients with follow-up >15m)	HbA1c available at baseline and 18 months	N(%)	338 (29.1%)	252 (26.2%)	0.1418	47 (20.3%)	0.0062	47 (18.0%)	0.0003
	Absolute HbA1c change at 18 months from baseline	Median (IQR)	-0.1 (-0.4, 0.3)	-0.1 (-0.4, 0.3)	0.2595	0.2 (-0.4, 1.0)	0.1023	0.0 (-0.3, 0.5)	0.3256

			DTG N= 1,163	EVG/c N= 962	DTG vs. EVG p-value	RAL N= 232	DTG vs. RAL p-value	DRV(r/c) N= 261	DTG vs. DRV(r/c) p-value
	% HbA1c change at 18 months from baseline	Median (IQR)	-1.6 (-6.2, 5.3)	-1.7 (-6.8, 4.4)	0.2661	3.5 (-6.0, 14.5)	0.0651	0.0 (-3.5, 8.5)	0.2911
24-month* (among patients with follow-up >21m)	HbA1c available at baseline and 24 months	N(%)	249 (21.4%)	184 (19.1%)	0.1934	46 (19.8%)	0.5899	39 (14.9%)	0.0187
	Absolute HbA1c change at 24 months from baseline	Median (IQR)	0.0 (-0.4, 0.4)	0.0 (-0.3, 0.3)	0.9328	0.1 (-0.4, 0.8)	0.3662	-0.1 (-0.4, 0.4)	0.9266
	% HbA1c change at 24 months from baseline	Median (IQR)	0.0 (-5.6, 6.6)	0.0 (-5.2, 5.2)	0.9557	1.7 (-5.5, 13.0)	0.3078	-1.6 (-7.0, 6.9)	0.8588

*+/- 3 months, value closest to X months

Table 66. Categorical fasting glucose among ART-experienced/suppressed patients with prevalent prediabetes or T2DM (Population 3)

		DTG N= 1,163	EVG/c N= 962	DTG vs. EVG p-value	RAL N= 232	DTG vs. RAL p-value	DRV(r/c) N= 261	DTG vs. DRV(r/c) p-value
Baseline (among all patients)	Total	1163 (100.0%)	962 (100.0%)	.	232 (100.0%)	.	261 (100.0%)	.
	Normal fasting glucose (<100 mg/dl)	64 (5.5%)	40 (4.2%)	0.4326	14 (6.0%)	0.3724	25 (9.6%)	0.0012

		DTG N= 1,163	EVG/c N= 962	DTG vs. EVG p-value	RAL N= 232	DTG vs. RAL p-value	DRV(r/c) N= 261	DTG vs. DRV(r/c) p-value
	Grade 1 fasting glucose (>=100 to <126 mg/dl)	62 (5.3%)	64 (6.7%)	.	12 (5.2%)	.	21 (8.0%)	.
	Grade 2 fasting glucose (126-250 mg/dl)	18 (1.5%)	17 (1.8%)	.	8 (3.4%)	.	10 (3.8%)	.
	Grade 3 fasting glucose (>250 mg/dl)	3 (0.3%)	3 (0.3%)	.	0 (0.0%)	.	2 (0.8%)	.
	Missing fasting glucose	1016 (87.4%)	838 (87.1%)	.	198 (85.3%)	.	203 (77.8%)	.
6-month* (among patients with follow-up >3m)	Total	1076 (92.5%)	878 (91.3%)	0.2913	206 (88.8%)	0.0575	228 (87.4%)	0.0067
	Normal fasting glucose (<100 mg/dl)	3 (0.3%)	4 (0.5%)	0.7100	5 (2.4%)	0.0001	8 (3.5%)	<.0001
	Grade 1 fasting glucose (>=100 to <126 mg/dl)	3 (0.3%)	1 (0.1%)	.	4 (1.9%)	.	2 (0.9%)	.
	Grade 2 fasting glucose (126-250 mg/dl)	2 (0.2%)	3 (0.3%)	.	0 (0.0%)	.	1 (0.4%)	.
	Grade 3 fasting glucose (>250 mg/dl)	0 (0.0%)	0 (0.0%)	.	1 (0.5%)	.	0 (0.0%)	.
	Missing fasting glucose	1068 (99.3%)	870 (99.1%)	.	196 (95.1%)	.	217 (95.2%)	.
12-month* (among patients with follow-up >9m)	Total	935 (80.4%)	738 (76.7%)	0.0391	175 (75.4%)	0.0868	189 (72.4%)	0.0043

		DTG N= 1,163	EVG/c N= 962	DTG vs. EVG p-value	RAL N= 232	DTG vs. RAL p-value	DRV(r/c) N= 261	DTG vs. DRV(r/c) p-value
	Normal fasting glucose (<100 mg/dl)	0 (0.0%)	3 (0.4%)	0.2618	0 (0.0%)	1.0000	0 (0.0%)	0.6024
	Grade 1 fasting glucose (>=100 to <126 mg/dl)	3 (0.3%)	2 (0.3%)	.	0 (0.0%)	.	1 (0.5%)	.
	Grade 2 fasting glucose (126-250 mg/dl)	1 (0.1%)	1 (0.1%)	.	0 (0.0%)	.	0 (0.0%)	.
	Missing fasting glucose	931 (99.6%)	732 (99.2%)	.	175 (100.0%)	.	188 (99.5%)	.
18-month* (among patients with follow-up >15m)	Total	704 (60.5%)	545 (56.7%)	0.0705	121 (52.2%)	0.0178	140 (53.6%)	0.0405
	Normal fasting glucose (<100 mg/dl)	1 (0.1%)	3 (0.6%)	0.1456	0 (0.0%)	1.0000	2 (1.4%)	0.0345
	Grade 1 fasting glucose (>=100 to <126 mg/dl)	0 (0.0%)	1 (0.2%)	.	0 (0.0%)	.	1 (0.7%)	.
	Grade 2 fasting glucose (126-250 mg/dl)	3 (0.4%)	0 (0.0%)	.	0 (0.0%)	.	0 (0.0%)	.
	Missing fasting glucose	700 (99.4%)	541 (99.3%)	.	121 (100.0%)	.	137 (97.9%)	.
24-month* (among patients with follow-up >21m)	Total	534 (45.9%)	393 (40.9%)	0.0191	99 (42.7%)	0.3649	103 (39.5%)	0.0581
	Normal fasting glucose (<100 mg/dl)	2 (0.4%)	0 (0.0%)	0.7057	0 (0.0%)	1.0000	0 (0.0%)	1.0000

		DTG N= 1,163	EVG/c N= 962	DTG vs. EVG p-value	RAL N= 232	DTG vs. RAL p-value	DRV(r/c) N= 261	DTG vs. DRV(r/c) p-value
	Grade 1 fasting glucose (>=100 to <126 mg/dl)	2 (0.4%)	1 (0.3%)	.	0 (0.0%)	.	0 (0.0%)	.
	Grade 2 fasting glucose (126-250 mg/dl)	1 (0.2%)	0 (0.0%)	.	0 (0.0%)	.	0 (0.0%)	.
	Missing fasting glucose	529 (99.1%)	392 (99.7%)	.	99 (100.0%)	.	103 (100.0%)	.

*+/- 3 months, value closest to X months

Table 67. Changes in fasting glucose among ART-experienced/suppressed patients with prevalent prediabetes or T2DM (Population 3)

			DTG N= 1,163	EVG/c N= 962	DTG vs. EVG p-value	RAL N= 232	DTG vs. RAL p-value	DRV(r/c) N= 261	DTG vs. DRV(r/c) p-value
6-month* (among patients with follow-up >3m)	Fasting glucose available at baseline and 6 months	N(%)	6 (0.5%)	6 (0.6%)	0.7413	10 (4.3%)	<.0001	11 (4.2%)	<.0001
	Absolute fasting glucose change at 6 months from baseline	Median (IQR)	0.0 (-31.0, 23.0)	-6.0 (-12.0, 5.0)	0.6884	1.5 (-16.0, 6.0)	1.0000	-3.0 (-7.0, 10.0)	1.0000
	% fasting glucose change at 6 months from baseline	Median (IQR)	0.0 (-19.3, 24.0)	-4.8 (-11.3, 5.6)	0.6884	1.7 (-14.2, 6.3)	1.0000	-3.3 (-7.4, 8.8)	0.7249

			DTG N= 1,163	EVG/c N= 962	DTG vs. EVG p-value	RAL N= 232	DTG vs. RAL p-value	DRV(r/c) N= 261	DTG vs. DRV(r/c) p-value
12-month* (among patients with follow-up >9m)	Fasting glucose available at baseline and 12 months	N(%)	4 (0.3%)	6 (0.6%)	0.3629	0 (0.0%)	1.0000	0 (0.0%)	1.0000
	Absolute fasting glucose change at 12 months from baseline	Median (IQR)	-14.0 (-50.0, 18.0)	-22.0 (-33.0, 1.0)	1.0000		.		.
	% fasting glucose change at 12 months from baseline	Median (IQR)	-9.5 (-31.8, 15.9)	-16.9 (-23.9, 0.9)	0.9151		.		.
18-month* (among patients with follow-up >15m)	Fasting glucose available at baseline and 18 months	N(%)	4 (0.3%)	4 (0.4%)	1.0000	0 (0.0%)	1.0000	1 (0.4%)	1.0000
	Absolute fasting glucose change at 18 months from baseline	Median (IQR)	-3.5 (-15.0, 9.5)	-27.0 (-57.0, -5.0)	0.3123		.	15.0 (15.0, 15.0)	0.7237
	% fasting glucose change at 18 months from baseline	Median (IQR)	-1.9 (-9.7, 5.0)	-21.0 (-35.4, -4.4)	0.3123		.	19.2 (19.2, 19.2)	0.2888
24-month* (among patients with follow-up >21m)	Fasting glucose available at baseline and 24 months	N(%)	3 (0.3%)	1 (0.1%)	0.6313	0 (0.0%)	1.0000	0 (0.0%)	1.0000
	Absolute fasting glucose change at 24 months from baseline	Median (IQR)	-28.0 (-39.0, 7.0)	-3.0 (-3.0, -3.0)	1.0000		.		.

			DTG N= 1,163	EVG/c N= 962	DTG vs. EVG p-value	RAL N= 232	DTG vs. RAL p-value	DRV(r/c) N= 261	DTG vs. DRV(r/c) p-value
	% fasting glucose change at 24 months from baseline	Median (IQR)	-18.3 (-19.2, 7.9)	-2.8 (-2.8, -2.8)	1.0000		.		.

*+/- 3 months, value closest to X months

1.8. Secondary Objective 3: HbA1c and fasting glucose among patients with incident T2DM in Study Population 4

1.8.1. ART-Naïve Patients

Table 68. Categorical HbA1c among ART-naïve patients with incident prediabetes or T2DM (Population 4)

		DTG N= 133	EVG/c N= 155	DTG vs. EVG p-value	RAL N= 5	DTG vs. RAL p-value	DRV(r/c) N= 33	DTG vs. DRV(r/c) p-value
Baseline (among all patients)	Total	133 (100.0%)	155 (100.0%)	.	5 (100.0%)	.	33 (100.0%)	.
	Controlled HbA1c (<7.0%)	17 (12.8%)	15 (9.7%)	0.4544	1 (20.0%)	0.5083	3 (9.1%)	0.7674
	Missing HbA1c	116 (87.2%)	140 (90.3%)	.	4 (80.0%)	.	30 (90.9%)	.
6-month* (among patients with follow-up >3m)	Total	133 (100.0%)	155 (100.0%)	.	5 (100.0%)	.	33 (100.0%)	.

		DTG N= 133	EVG/c N= 155	DTG vs. EVG p-value	RAL N= 5	DTG vs. RAL p-value	DRV(r/c) N= 33	DTG vs. DRV(r/c) p-value
	Controlled HbA1c (<7.0%)	59 (44.4%)	64 (41.3%)	0.8025	1 (20.0%)	0.4840	13 (39.4%)	0.5753
	Uncontrolled (HbA1c >=7.0%)	5 (3.8%)	5 (3.2%)	.	0 (0.0%)	.	0 (0.0%)	.
	Missing HbA1c	69 (51.9%)	86 (55.5%)	.	4 (80.0%)	.	20 (60.6%)	.
12-month* (among patients with follow-up >9m)	Total	123 (92.5%)	153 (98.7%)	0.0144	5 (100.0%)	1.0000	31 (93.9%)	1.0000
	Controlled HbA1c (<7.0%)	61 (49.6%)	74 (48.4%)	0.2930	1 (20.0%)	0.3905	12 (38.7%)	0.4537
	Uncontrolled (HbA1c >=7.0%)	1 (0.8%)	6 (3.9%)	.	0 (0.0%)	.	0 (0.0%)	.
	Missing HbA1c	61 (49.6%)	73 (47.7%)	.	4 (80.0%)	.	19 (61.3%)	.
18-month* (among patients with follow-up >15m)	Total	114 (85.7%)	140 (90.3%)	0.2727	5 (100.0%)	1.0000	27 (81.8%)	0.5901
	Controlled HbA1c (<7.0%)	65 (57.0%)	60 (42.9%)	0.0701	2 (40.0%)	0.6787	10 (37.0%)	0.0645
	Uncontrolled (HbA1c >=7.0%)	2 (1.8%)	5 (3.6%)	.	0 (0.0%)	.	2 (7.4%)	.
	Missing HbA1c	47 (41.2%)	75 (53.6%)	.	3 (60.0%)	.	15 (55.6%)	.

		DTG N= 133	EVG/c N= 155	DTG vs. EVG p-value	RAL N= 5	DTG vs. RAL p-value	DRV(r/c) N= 33	DTG vs. DRV(r/c) p-value
24-month* (among patients with follow-up >21m)	Total	97 (72.9%)	115 (74.2%)	0.8934	5 (100.0%)	0.3262	21 (63.6%)	0.2923
	Controlled HbA1c (<7.0%)	47 (48.5%)	54 (47.0%)	0.9704	1 (20.0%)	0.4802	8 (38.1%)	0.4307
	Uncontrolled (HbA1c >=7.0%)	4 (4.1%)	5 (4.3%)	.	0 (0.0%)	.	0 (0.0%)	.
	Missing HbA1c	46 (47.4%)	56 (48.7%)	.	4 (80.0%)	.	13 (61.9%)	.

*+/- 3 months, value closest to X months

Table 69. Changes in HbA1c among ART-naïve patients with incident prediabetes or T2DM (Population 4)

			DTG N= 133	EVG/c N= 155	DTG vs. EVG p-value	RAL N= 5	DTG vs. RAL p-value	DRV(r/c) N= 33	DTG vs. DRV(r/c) p-value
6-month* (among patients with follow-up >3m)	HbA1c available at baseline and 6 months	N(%)	9 (6.8%)	9 (5.8%)	0.8096	0 (0.0%)	1.0000	1 (3.0%)	0.6885
	Absolute HbA1c change at 6 months from baseline	Median (IQR)	0.2 (0.1, 0.3)	0.2 (0.1, 0.4)	0.7544		.	0.4 (0.4, 0.4)	0.3768

			DTG N= 133	EVG/c N= 155	DTG vs. EVG p-value	RAL N= 5	DTG vs. RAL p-value	DRV(r/c) N= 33	DTG vs. DRV(r/c) p-value
	% HbA1c change at 6 months from baseline	Median (IQR)	3.6 (1.8, 5.6)	3.6 (1.9, 7.3)	0.7561		.	7.1 (7.1, 7.1)	0.3768
12-month* (among patients with follow-up >9m)	HbA1c available at baseline and 12 months	N(%)	10 (7.5%)	8 (5.2%)	0.4691	0 (0.0%)	1.0000	1 (3.0%)	0.6949
	Absolute HbA1c change at 12 months from baseline	Median (IQR)	-0.0 (-0.2, 0.1)	0.3 (-0.0, 0.3)	0.2446		.	-0.2 (-0.2, -0.2)	0.6329
	% HbA1c change at 12 months from baseline	Median (IQR)	-0.9 (-3.6, 1.8)	4.8 (-1.0, 5.5)	0.3728		.	-3.6 (-3.6, -3.6)	0.6337
18-month* (among patients with follow-up >15m)	HbA1c available at baseline and 18 months	N(%)	11 (8.3%)	7 (4.5%)	0.2261	0 (0.0%)	1.0000	2 (6.1%)	1.0000
	Absolute HbA1c change at 18 months from baseline	Median (IQR)	0.3 (0.0, 1.0)	0.1 (-0.1, 0.3)	0.4676		.	1.5 (0.1, 2.9)	0.4285
	% HbA1c change at 18 months from baseline	Median (IQR)	5.4 (0.0, 20.4)	1.8 (-1.8, 5.8)	0.5252		.	27.3 (1.8, 52.7)	0.5532
24-month* (among patients with follow-up >21m)	HbA1c available at baseline and 24 months	N(%)	8 (6.0%)	3 (1.9%)	0.1199	0 (0.0%)	1.0000	1 (3.0%)	0.6895
	Absolute HbA1c change at 24 months from baseline	Median (IQR)	0.4 (0.3, 1.1)	0.1 (-0.6, 105.6)	0.6090		.	0.7 (0.7, 0.7)	0.5596

			DTG N= 133	EVG/c N= 155	DTG vs. EVG p-value	RAL N= 5	DTG vs. RAL p-value	DRV(r/c) N= 33	DTG vs. DRV(r/c) p-value
	% HbA1c change at 24 months from baseline	Median (IQR)	6.4 (4.5, 23.9)	1.8 (-12.0, 1955.6)	0.6098		.	12.7 (12.7, 12.7)	0.5613

*+/- 3 months, value closest to X months

Table 70. Categorical fasting glucose among ART-naïve patients with incident prediabetes or T2DM (Population 4)

		DTG N= 133	EVG/c N= 155	DTG vs. EVG p-value	RAL N= 5	DTG vs. RAL p-value	DRV(r/c) N= 33	DTG vs. DRV(r/c) p-value
Baseline (among all patients)	Total	133 (100.0%)	155 (100.0%)	.	5 (100.0%)	.	33 (100.0%)	.
	Normal fasting glucose (<100 mg/dl)	1 (0.8%)	0 (0.0%)	0.4618	0 (0.0%)	1.0000	0 (0.0%)	1.0000
	Missing fasting glucose	132 (99.2%)	155 (100.0%)	.	5 (100.0%)	.	33 (100.0%)	.
6-month* (among patients with follow-up >3m)	Total	133 (100.0%)	155 (100.0%)	.	5 (100.0%)	.	33 (100.0%)	.
	Missing fasting glucose	133 (100.0%)	155 (100.0%)	.	5 (100.0%)	.	33 (100.0%)	.
12-month* (among patients with follow-up >9m)	Total	123 (92.5%)	153 (98.7%)	0.0144	5 (100.0%)	1.0000	31 (93.9%)	1.0000

		DTG N= 133	EVG/c N= 155	DTG vs. EVG p-value	RAL N= 5	DTG vs. RAL p-value	DRV(r/c) N= 33	DTG vs. DRV(r/c) p-value
	Normal fasting glucose (<100 mg/dl)	0 (0.0%)	1 (0.7%)	1.0000	0 (0.0%)	.	0 (0.0%)	.
	Missing fasting glucose	123 (100.0%)	152 (99.3%)	.	5 (100.0%)	.	31 (100.0%)	.
18-month* (among patients with follow-up >15m)	Total	114 (85.7%)	140 (90.3%)	0.2727	5 (100.0%)	1.0000	27 (81.8%)	0.5901
	Missing fasting glucose	114 (100.0%)	140 (100.0%)	.	5 (100.0%)	.	27 (100.0%)	.
24-month* (among patients with follow-up >21m)	Total	97 (72.9%)	115 (74.2%)	0.8934	5 (100.0%)	0.3262	21 (63.6%)	0.2923
	Normal fasting glucose (<100 mg/dl)	0 (0.0%)	1 (0.9%)	1.0000	0 (0.0%)	.	0 (0.0%)	.
	Missing fasting glucose	97 (100.0%)	114 (99.1%)	.	5 (100.0%)	.	21 (100.0%)	.

*+/- 3 months, value closest to X months

Table 71. Changes in fasting glucose among ART-naïve patients with incident prediabetes or T2DM (Population 4)

			DTG N= 133	EVG/c N= 155	DTG vs. EVG p-value	RAL N= 5	DTG vs. RAL p-value	DRV(r/c) N= 33	DTG vs. DRV(r/c) p-value
6-month* (among patients with follow-up >3m)	Fasting glucose available at baseline and 6 months		0	0	.	0	.	0	.
	Absolute fasting glucose change at 6 months from baseline	Median (IQR)			.		.		.
	% fasting glucose change at 6 months from baseline	Median (IQR)			.		.		.
12-month* (among patients with follow-up >9m)	Fasting glucose available at baseline and 12 months		0	0	.	0	.	0	.
	Absolute fasting glucose change at 12 months from baseline	Median (IQR)			.		.		.
	% fasting glucose change at 12 months from baseline	Median (IQR)			.		.		.
18-month* (among patients with follow-up >15m)	Fasting glucose available at baseline and 18 months		0	0	.	0	.	0	.
	Absolute fasting glucose change at 18 months from baseline	Median (IQR)			.		.		.
	% fasting glucose change at 18 months from baseline	Median (IQR)			.		.		.
24-month* (among patients with follow-up >21m)	Fasting glucose available at baseline and 24 months		0	0	.	0	.	0	.

			DTG N= 133	EVG/c N= 155	DTG vs. EVG p-value	RAL N= 5	DTG vs. RAL p-value	DRV(r/c) N= 33	DTG vs. DRV(r/c) p-value
	Absolute fasting glucose change at 24 months from baseline	Median (IQR)			.		.		.
	% fasting glucose change at 24 months from baseline	Median (IQR)			.		.		.

*+/- 3 months, value closest to X months

1.8.2. ART-Experienced/Suppressed Patients

Table 72. Categorical HbA1c among ART-experienced/suppressed patients with incident prediabetes or T2DM (Population 4)

		DTG N= 285	EVG/c N= 214	DTG vs. EVG p-value	RAL N= 49	DTG vs. RAL p-value	DRV(r/c) N= 68	DTG vs. DRV(r/c) p-value
Baseline (among all patients)	Total	285 (100.0%)	214 (100.0%)	.	49 (100.0%)	.	68 (100.0%)	.
	Controlled HbA1c (<7.0%)	123 (43.2%)	50 (23.4%)	<.0001	7 (14.3%)	0.0001	10 (14.7%)	<.0001
	Missing HbA1c	162 (56.8%)	164 (76.6%)	.	42 (85.7%)	.	58 (85.3%)	.
6-month* (among patients with follow-up >3m)	Total	284 (99.6%)	213 (99.5%)	1.0000	49 (100.0%)	1.0000	68 (100.0%)	1.0000

		DTG N= 285	EVG/c N= 214	DTG vs. EVG p-value	RAL N= 49	DTG vs. RAL p-value	DRV(r/c) N= 68	DTG vs. DRV(r/c) p-value
	Controlled HbA1c (<7.0%)	127 (44.7%)	81 (38.0%)	0.3056	15 (30.6%)	0.0410	16 (23.5%)	0.0014
	Uncontrolled (HbA1c >=7.0%)	12 (4.2%)	9 (4.2%)	.	0 (0.0%)	.	1 (1.5%)	.
	Missing HbA1c	145 (51.1%)	123 (57.7%)	.	34 (69.4%)	.	51 (75.0%)	.
12-month* (among patients with follow-up >9m)	Total	279 (97.9%)	207 (96.7%)	0.5718	45 (91.8%)	0.0439	67 (98.5%)	1.0000
	Controlled HbA1c (<7.0%)	149 (53.4%)	93 (44.9%)	0.0683	23 (51.1%)	0.8812	27 (40.3%)	0.0066
	Uncontrolled (HbA1c >=7.0%)	5 (1.8%)	9 (4.3%)	.	0 (0.0%)	.	6 (9.0%)	.
	Missing HbA1c	125 (44.8%)	105 (50.7%)	.	22 (48.9%)	.	34 (50.7%)	.
18-month* (among patients with follow-up >15m)	Total	251 (88.1%)	189 (88.3%)	0.9324	39 (79.6%)	0.1050	62 (91.2%)	0.4678
	Controlled HbA1c (<7.0%)	141 (56.2%)	88 (46.6%)	0.1183	20 (51.3%)	0.7424	20 (32.3%)	0.0002
	Uncontrolled (HbA1c >=7.0%)	6 (2.4%)	4 (2.1%)	.	1 (2.6%)	.	7 (11.3%)	.
	Missing HbA1c	104 (41.4%)	97 (51.3%)	.	18 (46.2%)	.	35 (56.5%)	.

		DTG N= 285	EVG/c N= 214	DTG vs. EVG p-value	RAL N= 49	DTG vs. RAL p-value	DRV(r/c) N= 68	DTG vs. DRV(r/c) p-value
24-month* (among patients with follow-up >21m)	Total	221 (77.5%)	169 (79.0%)	0.7024	38 (77.6%)	0.9991	55 (80.9%)	0.5492
	Controlled HbA1c (<7.0%)	119 (53.8%)	83 (49.1%)	0.3830	16 (42.1%)	0.3126	23 (41.8%)	0.2154
	Uncontrolled (HbA1c >=7.0%)	3 (1.4%)	5 (3.0%)	.	0 (0.0%)	.	1 (1.8%)	.
	Missing HbA1c	99 (44.8%)	81 (47.9%)	.	22 (57.9%)	.	31 (56.4%)	.

*+/- 3 months, value closest to X months

Table 73. Changes in HbA1c among ART-experienced/suppressed patients with incident prediabetes or T2DM (Population 4)

			DTG N= 285	EVG/c N= 214	DTG vs. EVG p-value	RAL N= 49	DTG vs. RAL p-value	DRV(r/c) N= 68	DTG vs. DRV(r/c) p-value
6-month* (among patients with follow-up >3m)	HbA1c available at baseline and 6 months	N(%)	68 (23.9%)	34 (15.9%)	0.0330	1 (2.0%)	<.0001	5 (7.4%)	0.0015
	Absolute HbA1c change at 6 months from baseline	Median (IQR)	0.2 (0.1, 0.5)	0.3 (0.1, 0.5)	0.8615	0.3 (0.3, 0.3)	0.8402	0.3 (0.2, 0.3)	0.6930

			DTG N= 285	EVG/c N= 214	DTG vs. EVG p-value	RAL N= 49	DTG vs. RAL p-value	DRV(r/c) N= 68	DTG vs. DRV(r/c) p-value
	% HbA1c change at 6 months from baseline	Median (IQR)	3.7 (1.8, 9.9)	5.4 (1.8, 9.4)	0.8367	5.6 (5.6, 5.6)	0.7628	5.4 (3.6, 5.6)	0.7929
12-month* (among patients with follow-up >9m)	HbA1c available at baseline and 12 months	N(%)	69 (24.2%)	30 (14.0%)	0.0046	3 (6.1%)	0.0041	6 (8.8%)	0.0047
	Absolute HbA1c change at 12 months from baseline	Median (IQR)	0.2 (0.1, 0.4)	0.4 (0.2, 0.6)	0.3998	0.4 (0.0, 1.1)	0.7123	0.6 (0.0, 6.3)	0.2887
	% HbA1c change at 12 months from baseline	Median (IQR)	3.6 (1.8, 7.5)	6.4 (3.6, 11.1)	0.2508	7.4 (0.0, 26.8)	0.5525	9.8 (0.0, 121.2)	0.3370
18-month* (among patients with follow-up >15m)	HbA1c available at baseline and 18 months	N(%)	61 (21.4%)	23 (10.7%)	0.0016	3 (6.1%)	0.0101	3 (4.4%)	0.0007
	Absolute HbA1c change at 18 months from baseline	Median (IQR)	0.2 (0.1, 0.4)	0.4 (0.1, 0.5)	0.2906	0.8 (0.4, 1.2)	0.0367	0.6 (0.2, 2.3)	0.1509
	% HbA1c change at 18 months from baseline	Median (IQR)	3.8 (1.8, 7.1)	7.3 (1.8, 9.3)	0.2132	19.5 (7.4, 22.6)	0.0203	10.7 (3.6, 43.4)	0.1570
24-month* (among patients with follow-up >21m)	HbA1c available at baseline and 24 months	N(%)	51 (17.9%)	19 (8.9%)	0.0041	4 (8.2%)	0.0985	3 (4.4%)	0.0043
	Absolute HbA1c change at 24 months from baseline	Median (IQR)	0.2 (0.0, 0.5)	0.2 (0.1, 0.5)	0.6806	0.6 (0.4, 0.7)	0.0287	0.4 (0.2, 0.8)	0.1766

			DTG N= 285	EVG/c N= 214	DTG vs. EVG p-value	RAL N= 49	DTG vs. RAL p-value	DRV(r/c) N= 68	DTG vs. DRV(r/c) p-value
	% HbA1c change at 24 months from baseline	Median (IQR)	3.6 (0.0, 8.9)	3.8 (1.8, 8.9)	0.5210	12.6 (8.9, 14.0)	0.0168	7.1 (3.6, 15.1)	0.1844

*+/- 3 months, value closest to X months

Table 74. Categorical fasting glucose among ART-experienced/suppressed patients with incident prediabetes or T2DM (Population 4)

		DTG N= 285	EVG/c N= 214	DTG vs. EVG p-value	RAL N= 49	DTG vs. RAL p-value	DRV(r/c) N= 68	DTG vs. DRV(r/c) p-value
Baseline (among all patients)	Total	285 (100.0%)	214 (100.0%)	.	49 (100.0%)	.	68 (100.0%)	.
	Normal fasting glucose (<100 mg/dl)	12 (4.2%)	7 (3.3%)	0.6438	4 (8.2%)	0.2685	2 (2.9%)	1.0000
	Missing fasting glucose	273 (95.8%)	207 (96.7%)	.	45 (91.8%)	.	66 (97.1%)	.
6-month* (among patients with follow-up >3m)	Total	284 (99.6%)	213 (99.5%)	1.0000	49 (100.0%)	1.0000	68 (100.0%)	1.0000
	Normal fasting glucose (<100 mg/dl)	2 (0.7%)	2 (0.9%)	0.8364	0 (0.0%)	0.5512	2 (2.9%)	0.1731
	Grade 1 fasting glucose (>=100 to <126 mg/dl)	2 (0.7%)	1 (0.5%)	.	1 (2.0%)	.	1 (1.5%)	.

		DTG N= 285	EVG/c N= 214	DTG vs. EVG p-value	RAL N= 49	DTG vs. RAL p-value	DRV(r/c) N= 68	DTG vs. DRV(r/c) p-value
	Grade 3 fasting glucose (>250 mg/dl)	0 (0.0%)	1 (0.5%)	.	0 (0.0%)	.	0 (0.0%)	.
	Missing fasting glucose	280 (98.6%)	209 (98.1%)	.	48 (98.0%)	.	65 (95.6%)	.
12-month* (among patients with follow-up >9m)	Total	279 (97.9%)	207 (96.7%)	0.5718	45 (91.8%)	0.0439	67 (98.5%)	1.0000
	Normal fasting glucose (<100 mg/dl)	2 (0.7%)	1 (0.5%)	0.8979	0 (0.0%)	1.0000	2 (3.0%)	0.1740
	Grade 1 fasting glucose (>=100 to <126 mg/dl)	2 (0.7%)	1 (0.5%)	.	0 (0.0%)	.	1 (1.5%)	.
	Grade 3 fasting glucose (>250 mg/dl)	0 (0.0%)	1 (0.5%)	.	0 (0.0%)	.	0 (0.0%)	.
	Missing fasting glucose	275 (98.6%)	204 (98.6%)	.	45 (100.0%)	.	64 (95.5%)	.
18-month* (among patients with follow-up >15m)	Total	251 (88.1%)	189 (88.3%)	0.9324	39 (79.6%)	0.1050	62 (91.2%)	0.4678
	Normal fasting glucose (<100 mg/dl)	6 (2.4%)	0 (0.0%)	0.0646	1 (2.6%)	1.0000	1 (1.6%)	0.4504
	Grade 1 fasting glucose (>=100 to <126 mg/dl)	1 (0.4%)	1 (0.5%)	.	0 (0.0%)	.	1 (1.6%)	.
	Missing fasting glucose	244 (97.2%)	188 (99.5%)	.	38 (97.4%)	.	60 (96.8%)	.

		DTG N= 285	EVG/c N= 214	DTG vs. EVG p-value	RAL N= 49	DTG vs. RAL p-value	DRV(r/c) N= 68	DTG vs. DRV(r/c) p-value
24-month* (among patients with follow-up >21m)	Total	221 (77.5%)	169 (79.0%)	0.7024	38 (77.6%)	0.9991	55 (80.9%)	0.5492
	Normal fasting glucose (<100 mg/dl)	1 (0.5%)	1 (0.6%)	0.7576	0 (0.0%)	1.0000	1 (1.8%)	0.2605
	Grade 1 fasting glucose (>=100 to <126 mg/dl)	2 (0.9%)	0 (0.0%)	.	0 (0.0%)	.	1 (1.8%)	.
	Missing fasting glucose	218 (98.6%)	168 (99.4%)	.	38 (100.0%)	.	53 (96.4%)	.

*+/- 3 months, value closest to X months

Table 75. Changes in fasting glucose among ART-experienced/suppressed patients with incident prediabetes or T2DM (Population 4)

			DTG N= 285	EVG/c N= 214	DTG vs. EVG p-value	RAL N= 49	DTG vs. RAL p-value	DRV(r/c) N= 68	DTG vs. DRV(r/c) p-value
6-month* (among patients with follow-up >3m)	Fasting glucose available at baseline and 6 months	N(%)	3 (1.1%)	4 (1.9%)	0.4689	1 (2.0%)	0.4715	2 (2.9%)	0.2470
	Absolute fasting glucose change at 6 months from baseline	Median (IQR)	28.0 (-4.0, 32.0)	10.5 (-10.5, 103.5)	0.8597	9.0 (9.0, 9.0)	1.0000	-1.5 (-9.0, 6.0)	0.3865

			DTG N= 285	EVG/c N= 214	DTG vs. EVG p-value	RAL N= 49	DTG vs. RAL p-value	DRV(r/c) N= 68	DTG vs. DRV(r/c) p-value
	% fasting glucose change at 6 months from baseline	Median (IQR)	31.8 (-4.7, 51.6)	10.9 (-11.1, 110.8)	0.8597	9.2 (9.2, 9.2)	1.0000	-1.6 (-9.8, 6.6)	0.3865
12-month* (among patients with follow-up >9m)	Fasting glucose available at baseline and 12 months	N(%)	3 (1.1%)	2 (0.9%)	1.0000	0 (0.0%)	1.0000	2 (2.9%)	0.2470
	Absolute fasting glucose change at 12 months from baseline	Median (IQR)	19.0 (1.0, 25.0)	114.0 (0.0, 228.0)	1.0000		.	6.0 (-5.0, 17.0)	0.3865
	% fasting glucose change at 12 months from baseline	Median (IQR)	28.4 (1.2, 30.6)	122.6 (0.0, 245.2)	1.0000		.	6.5 (-5.5, 18.5)	0.3865
18-month* (among patients with follow-up >15m)	Fasting glucose available at baseline and 18 months	N(%)	3 (1.1%)	1 (0.5%)	0.6386	0 (0.0%)	1.0000	2 (2.9%)	0.2470
	Absolute fasting glucose change at 18 months from baseline	Median (IQR)	24.0 (8.0, 27.0)	13.0 (13.0, 13.0)	1.0000		.	11.5 (-3.0, 26.0)	0.7728
	% fasting glucose change at 18 months from baseline	Median (IQR)	27.3 (9.3, 43.5)	14.3 (14.3, 14.3)	1.0000		.	12.7 (-3.3, 28.6)	0.7728
24-month* (among patients with follow-up >21m)	Fasting glucose available at baseline and 24 months	N(%)	3 (1.1%)	0 (0.0%)	0.2637	0 (0.0%)	1.0000	2 (2.9%)	0.2470

			DTG N= 285	EVG/c N= 214	DTG vs. EVG p-value	RAL N= 49	DTG vs. RAL p-value	DRV(r/c) N= 68	DTG vs. DRV(r/c) p-value
	Absolute fasting glucose change at 24 months from baseline	Median (IQR)	29.0 (10.0, 38.0)		.		.	13.0 (-4.0, 30.0)	0.7728
	% fasting glucose change at 24 months from baseline	Median (IQR)	33.0 (11.6, 61.3)		.		.	14.3 (-4.3, 33.0)	0.7728

*+/- 3 months, value closest to X months

1.9. Exploratory Objective: Description of weight gain in Study Population 2

1.9.1. ART-Naïve Patients

Table 76. Categorical changes in BMI at 6 months of follow-up by incident T2DM among ART-naïve patients (Population 2)

Baseline BMI	N	Follow-up BMI (6 months*)	Incident T2DM	No incident T2DM	p-value
Total		**Total**	**30 (100.0%)**	**6855 (100.0%)**	**.**
Underweight (<18.5)	279	Total	1	278	
		Underweight (<18.5)	1 (100.0%)	94 (33.8%)	0.6308
		Normal Weight (18.5 – 24.9)	0	103 (37.1%)	.
		Overweight (25.0-29.9)	0	2 (0.7%)	.
		Obese (>=30)	0	3 (1.1%)	.
		Missing	0	76 (27.3%)	.
Normal weight (18.5 – 24.9)	3337	Total	5	3332	
		Underweight (<18.5)	0	29 (0.9%)	0.0902
		Normal Weight (18.5 – 24.9)	2 (40.0%)	1938 (58.2%)	.
		Overweight (25.0-29.9)	3 (60.0%)	427 (12.8%)	.
		Obese (>=30)	0	20 (0.6%)	.
		Outside of plausible range (<10 or >50)	0	2 (0.1%)	.
		Missing	0	916 (27.5%)	.
Overweight (25.0 – 29.9)	1912	Total	8	1904	
		Underweight (<18.5)	0	1 (0.1%)	0.2342
		Normal Weight (18.5 – 24.9)	0	120 (6.3%)	.
		Overweight (25.0-29.9)	6 (75.0%)	1128 (59.2%)	.

Baseline BMI	N	Follow-up BMI (6 months*)	Incident T2DM	No incident T2DM	p-value
		Obese (>=30)	2 (25.0%)	201 (10.6%)	.
		Outside of plausible range (<10 or >50)	0	5 (0.3%)	.
		Missing	0	449 (23.6%)	.
Obese (>=30)	1026	Total	14	1012	
		Normal Weight (18.5 – 24.9)	0	8 (0.8%)	0.1474
		Overweight (25.0-29.9)	0	59 (5.8%)	.
		Obese (>=30)	14 (100.0%)	680 (67.2%)	.
		Outside of plausible range (<10 or >50)	0	12 (1.2%)	.
		Missing	0	253 (25.0%)	.
Outside of plausible range (<10 or >50)	90	NA	NA	NA	.
Missing	241	NA	NA	NA	.

*Between >3 and >=9 months, BMI value closest to 6 months

Table 77. Categorical changes in BMI at 12 months of follow-up by incident T2DM among ART-naïve patients (Population 2)

Baseline BMI	N	Follow-up BMI (12 months*)	Incident T2DM	No incident T2DM	p-value
Total		**Total**	**10 (100.0%)**	**5836 (100.0%)**	**.**
Underweight (<18.5)	231	Total	0	231	
		Underweight (<18.5)	0	64 (27.7%)	.
		Normal Weight (18.5 – 24.9)	0	70 (30.3%)	.
		Overweight (25.0-29.9)	0	7 (3.0%)	.

Baseline BMI	N	Follow-up BMI (12 months*)	Incident T2DM	No incident T2DM	p-value
		Obese (>=30)	0	3 (1.3%)	.
		Missing	0	87 (37.7%)	.
Normal weight (18.5 – 24.9)	2875	Total	1	2874	
		Underweight (<18.5)	0	20 (0.7%)	0.1558
		Normal Weight (18.5 – 24.9)	0	1279 (44.5%)	.
		Overweight (25.0-29.9)	1 (100.0%)	390 (13.6%)	.
		Obese (>=30)	0	34 (1.2%)	.
		Outside of plausible range (<10 or >50)	0	3 (0.1%)	.
		Missing	0	1148 (39.9%)	.
Overweight (25.0 – 29.9)	1618	Total	4	1614	
		Normal Weight (18.5 – 24.9)	0	113 (7.0%)	0.1204
		Overweight (25.0-29.9)	2 (50.0%)	715 (44.3%)	.
		Obese (>=30)	2 (50.0%)	206 (12.8%)	.
		Missing	0	580 (35.9%)	.
Obese (>=30)	850	Total	5	745	
		Underweight (<18.5)	0	1 (0.1%)	0.2836
		Normal Weight (18.5 – 24.9)	0	5 (0.6%)	.
		Overweight (25.0-29.9)	0	46 (5.4%)	.
		Obese (>=30)	5 (100.0%)	474 (56.1%)	.
		Outside of plausible range (<10 or >50)	0	9 (1.1%)	.
		Missing	0	310 (36.7%)	.

Baseline BMI	N	Follow-up BMI (12 months*)	Incident T2DM	No incident T2DM	p-value
Outside of plausible range (<10 or >50)	77	NA	NA	NA	.
Missing	195	NA	NA	NA	.

*Between >9 and >=15 months, BMI value closest to 12 months

Table 78. Categorical changes in BMI at 18 months of follow-up by incident T2DM among ART-naïve patients (Population 2)

Baseline BMI	N	Follow-up BMI (18 months*)	Incident T2DM	No incident T2DM	p-value
Total		**Total**	**16 (100.0%)**	**3909 (100.0%)**	**.**
Underweight (<18.5)	149	Total	0	149	
		Underweight (<18.5)	0	37 (24.8%)	.
		Normal Weight (18.5 – 24.9)	0	48 (32.2%)	.
		Overweight (25.0-29.9)	0	3 (2.0%)	.
		Obese (>=30)	0	1 (0.7%)	.
		Missing	0	60 (40.3%)	.
Normal weight (18.5 – 24.9)	1917	Total	2	1915	
		Underweight (<18.5)	0	16 (0.8%)	0.3078
		Normal Weight (18.5 – 24.9)	1 (50.0%)	859 (44.9%)	.
		Overweight (25.0-29.9)	1 (50.0%)	273 (14.3%)	.
		Obese (>=30)	0	30 (1.6%)	.
		Outside of plausible range (<10 or >50)	0	2 (0.1%)	.
		Missing	0	735 (38.4%)	.
Overweight (25.0 – 29.9)	1097	Total	9	1088	
		Underweight (<18.5)	0	1 (0.1%)	0.0424
		Normal Weight (18.5 – 24.9)	0	77 (7.1%)	.

Baseline BMI	N	Follow-up BMI (18 months*)	Incident T2DM	No incident T2DM	p-value
		Overweight (25.0-29.9)	5 (55.6%)	482 (44.3%)	.
		Obese (>=30)	4 (44.4%)	168 (15.4%)	.
		Outside of plausible range (<10 or >50)	0	1 (0.1%)	.
		Missing	0	359 (33.0%)	.
Obese (>=30)	604	Total	5	599	
		Underweight (<18.5)	0	1 (0.2%)	0.2141
		Normal Weight (18.5 – 24.9)	0	4 (0.7%)	.
		Overweight (25.0-29.9)	0	44 (7.3%)	.
		Obese (>=30)	5 (100.0%)	313 (52.3%)	.
		Outside of plausible range (<10 or >50)	0	6 (1.0%)	.
		Missing	0	231 (38.6%)	.
Outside of plausible range (<10 or >50)	53	NA	NA	NA	.
Missing	105	NA	NA	NA	.

*Between >15 and >=21 months, BMI value closest to 18 months

Table 79. Categorical changes in BMI at 24 months of follow-up by incident T2DM among ART-naïve patients (Population 2)

Baseline BMI	N	Follow-up BMI (24 months*)	Incident T2DM	No incident T2DM	p-value
Total		**Total**	**8 (100.0%)**	**2704 (100.0%)**	**.**
Underweight (<18.5)	102	Total	0	102	
		Underweight (<18.5)	0	24 (23.5%)	.
		Normal Weight (18.5 – 24.9)	0	43 (42.2%)	.

Baseline BMI	N	Follow-up BMI (24 months*)	Incident T2DM	No incident T2DM	p-value
		Overweight (25.0-29.9)	0	2 (2.0%)	.
		Obese (>=30)	0	1 (1.0%)	.
		Missing	0	32 (31.4%)	.
Normal weight (18.5 – 24.9)	1337	Total	3	1334	
		Underweight (<18.5)	0	14 (1.0%)	0.6011
		Normal Weight (18.5 – 24.9)	1 (33.3%)	568 (42.6%)	.
		Overweight (25.0-29.9)	1 (33.3%)	200 (15.0%)	.
		Obese (>=30)	0	37 (2.8%)	.
		Outside of plausible range (<10 or >50)	0	1 (0.1%)	.
		Missing	1 (33.3%)	514 (38.5%)	.
Overweight (25.0 – 29.9)	759	Total	2	757	
		Normal Weight (18.5 – 24.9)	0	55 (7.3%)	0.7153
		Overweight (25.0-29.9)	2 (100.0%)	313 (41.3%)	.
		Obese (>=30)	0	127 (16.8%)	.
		Outside of plausible range (<10 or >50)	0	2 (0.3%)	.
		Missing	0	260 (34.3%)	.
Obese (>=30)	410	Total	3	407	
		Underweight (<18.5)	0	2 (0.5%)	0.4469
		Normal Weight (18.5 – 24.9)	0	2 (0.5%)	.
		Overweight (25.0-29.9)	0	24 (5.9%)	.
		Obese (>=30)	3 (100.0%)	229 (56.3%)	.

Baseline BMI	N	Follow-up BMI (24 months*)	Incident T2DM	No incident T2DM	p-value
		Outside of plausible range (<10 or >50)	0	5 (1.2%)	.
		Missing	0	145 (35.6%)	.
Outside of plausible range (<10 or >50)	38	NA	NA	NA	.
Missing	66	NA	NA	NA	.

*Between >21 and >=27 months, BMI value closest to 24 months

Table 80. Absolute changes in BMI by incident T2DM among ART-naïve patients (Population 2)

		Incident T2DM	No incident T2DM	p-value
6-month follow-up*	BMI available and between >=10 and <=50 (baseline & 6-months)	28	4813	
	Absolute BMI change from baseline to 6-months Median (IQR)	1.3 (0.1, 2.1)	0.5 (-0.3, 1.5)	0.0611
12-month follow-up*	BMI available and between >=10 and <=50 (baseline & 12-months)	10	3427	
	Absolute BMI change from baseline to 12-months Median (IQR)	2.9 (1.7, 5.7)	0.8 (-0.2, 2.1)	0.0129
18-month follow-up*	BMI available and between >=10 and <=50 (baseline & 18-months)	16	2357 (	
	Absolute BMI change from baseline to 18-months Median (IQR)	2.7 (1.4, 4.2)	0.9 (-0.3, 2.4)	0.0037
24-month follow-up*	BMI available and between >=10 and <=50 (baseline & 24-months)	7	1641	
	Absolute BMI change from baseline to 24-months Median (IQR)	3.0 (0.1, 4.6)	1.2 (-0.1, 2.7)	0.4604

* +/- 3 months, BMI value closest to X months

1.9.1. ART-Experienced/Suppressed Patients

Table 81. Categorical changes in BMI at 6 months of follow-up by incident T2DM among ART-experienced/suppressed patients (Population 2)

Baseline BMI	N	Follow-up BMI (6 months*)	Incident T2DM	No incident T2DM	p-value
Total		**Total**	**62 (100.0%)**	**8899 (100.0%)**	**.**
Underweight (<18.5)	176	Total	2	174	
		Underweight (<18.5)	1 (50.0%)	77 (44.3%)	1.0000
		Normal Weight (18.5 – 24.9)	1 (50.0%)	55 (31.6%)	.
		Overweight (25.0-29.9)	0	4 (2.3%)	.
		Outside of plausible range (<10 or >50)	0	1 (0.6%)	.
		Missing	0	37 (21.3%)	.
Normal weight (18.5 – 24.9)	3366	Total	8	3358	
		Underweight (<18.5)	1 (12.5%)	35 (1.0%)	0.0172
		Normal Weight (18.5 – 24.9)	4 (50.0%)	2166 (64.5%)	.
		Overweight (25.0-29.9)	3 (37.5%)	381 (11.3%)	.
		Obese (>=30)	0	3 (0.1%)	.
		Outside of plausible range (<10 or >50)	0	4 (0.1%)	.
		Missing	0	769 (22.9%)	.
Overweight (25.0 – 29.9)	3219	Total	22	3197	
		Underweight (<18.5)	0	4 (0.1%)	0.0213
		Normal Weight (18.5 – 24.9)	0	209 (6.5%)	.
		Overweight (25.0-29.9)	15 (68.2%)	2089 (65.3%)	.

Baseline BMI	N	Follow-up BMI (6 months*)	Incident T2DM	No incident T2DM	p-value
		Obese (>=30)	6 (27.3%)	252 (7.9%)	.
		Outside of plausible range (<10 or >50)	0	5 (0.2%)	.
		Missing	1 (4.5%)	638 (20.0%)	.
Obese (>=30)	1601	Total	25	1576	
		Underweight (<18.5)	0	1 (0.1%)	0.0200
		Normal Weight (18.5 – 24.9)	0	9 (0.6%)	.
		Overweight (25.0-29.9)	5 (20.0%)	134 (8.5%)	.
		Obese (>=30)	20 (80.0%)	1080 (68.5%)	.
		Outside of plausible range (<10 or >50)	0	10 (0.6%)	.
		Missing	0	342 (21.7%)	.
Outside of plausible range (<10 or >50)	100	NA	NA	NA	.
Missing	499	NA	NA	NA	.

*Between >3 and >=9 months, BMI value closest to 6 months

Table 82. Categorical changes in BMI at 12 months of follow-up by incident T2DM among ART-experienced/suppressed patients (Population 2)

Baseline BMI	N	Follow-up BMI (12 months*)	Incident T2DM	No incident T2DM	p-value
Total		**Total**	**45 (100.0%)**	**7597 (100.0%)**	**.**
Underweight (<18.5)	155	Total	0	155	
		Underweight (<18.5)	0	46 (29.7%)	.
		Normal Weight (18.5 – 24.9)	0	49 (31.6%)	.
		Overweight (25.0-29.9)	0	6 (3.9%)	.

Baseline BMI	N	Follow-up BMI (12 months*)	Incident T2DM	No incident T2DM	p-value
		Missing	0	54 (34.8%)	.
Normal weight (18.5 – 24.9)	2895	Total	7	2888	
		Underweight (<18.5)	1 (14.3%)	26 (0.9%)	0.0444
		Normal Weight (18.5 – 24.9)	5 (71.4%)	1517 (52.5%)	.
		Overweight (25.0-29.9)	1 (14.3%)	375 (13.0%)	.
		Obese (>=30)	0	8 (0.3%)	.
		Outside of plausible range (<10 or >50)	0	4 (0.1%)	.
		Missing	0	958 (33.2%)	.
Overweight (25.0 – 29.9)	2739	Total	15	2724	
		Underweight (<18.5)	0	1 (0.0%)	0.0006
		Normal Weight (18.5 – 24.9)	0	191 (7.0%)	.
		Overweight (25.0-29.9)	8 (53.3%)	1464 (53.7%)	.
		Obese (>=30)	5 (33.3%)	241 (8.8%)	.
		Outside of plausible range (<10 or >50)	1 (6.7%)	2 (0.1%)	.
		Missing	1 (6.7%)	825 (30.3%)	.
Obese (>=30)	1358	Total	17	1341	
		Underweight (<18.5)	0	1 (0.1%)	0.0127
		Normal Weight (18.5 – 24.9)	0	14 (1.0%)	.
		Overweight (25.0-29.9)	3 (17.6%)	102 (7.6%)	.
		Obese (>=30)	14 (82.4%)	765 (57.0%)	.
		Outside of plausible range (<10 or >50)	0	8 (0.6%)	.

Baseline BMI	N	Follow-up BMI (12 months*)	Incident T2DM	No incident T2DM	p-value
		Missing	0	451 (33.6%)	.
Outside of plausible range (<10 or >50)	80	NA	NA	NA	.
Missing	415	NA	NA	NA	.

*Between >9 and >=15 months, BMI value closest to 12 months

Table 83. Categorical changes in BMI at 18 months of follow-up by incident T2DM among ART-experienced/suppressed patients (Population 2)

Baseline BMI	N	Follow-up BMI (18 months*)	Incident T2DM	No incident T2DM	p-value
Total		**Total**	**27 (100.0%)**	**5274 (100.0%)**	**.**
Underweight (<18.5)	113	Total	0	113	
		Underweight (<18.5)	0	33 (29.2%)	.
		Normal Weight (18.5 – 24.9)	0	41 (36.3%)	.
		Overweight (25.0-29.9)	0	4 (3.5%)	.
		Obese (>=30)	0	1 (0.9%)	.
		Missing	0	34 (30.1%)	.
Normal weight (18.5 – 24.9)	2010	Total	2	2009	
		Underweight (<18.5)	0	13 (0.6%)	0.0108
		Normal Weight (18.5 – 24.9)	1 (50.0%)	1087 (54.1%)	.
		Overweight (25.0-29.9)	0	283 (14.1%)	.
		Obese (>=30)	1 (50.0%)	5 (0.2%)	.
		Outside of plausible range (<10 or >50)	0	3 (0.1%)	.
		Missing	0	617 (30.7%)	.
Overweight (25.0 – 29.9)	1952	Total	12	1940	
		Normal Weight (18.5 – 24.9)	1 (8.3%)	146 (7.5%)	0.0648
		Overweight (25.0-29.9)	9 (75.0%)	1021 (52.6%)	.
		Obese (>=30)	2 (16.7%)	201 (10.4%)	.
		Outside of plausible range (<10 or >50)	0	1 (0.1%)	.
		Missing	0	571 (29.4%)	.

Baseline BMI	N	Follow-up BMI (18 months*)	Incident T2DM	No incident T2DM	p-value
Obese (>=30)	908	Total	11	897	
		Normal Weight (18.5 – 24.9)	1 (9.1%)	13 (1.4%)	0.0021
		Overweight (25.0-29.9)	0	88 (9.8%)	.
		Obese (>=30)	9 (81.8%)	510 (56.9%)	.
		Outside of plausible range (<10 or >50)	1 (9.1%)	3 (0.3%)	.
		Missing	0	283 (31.5%)	.
Outside of plausible range (<10 or >50)	53	NA	NA	NA	.
Missing	265	NA	NA	NA	.

*Between >15 and >=21 months, BMI value closest to 18 months

Table 84. Categorical changes in BMI at 24 months of follow-up by incident T2DM among ART-experienced/suppressed patients (Population 2)

Baseline BMI	N	Follow-up BMI (24 months*)	Incident T2DM	No incident T2DM	p-value
Total		**Total**	**17 (100.0%)**	**3779 (100.0%)**	**.**
Underweight (<18.5)	76	Total	0	76	
		Underweight (<18.5)	0	17 (22.4%)	.
		Normal Weight (18.5 – 24.9)	0	22 (28.9%)	.
		Overweight (25.0-29.9)	0	3 (3.9%)	.
		Missing	0	34 (44.7%)	.
Normal weight (18.5 – 24.9)	1478	Total	4	1474	
		Underweight (<18.5)	0	12 (0.8%)	0.1617
		Normal Weight (18.5 – 24.9)	2 (50.0%)	760 (51.6%)	.

Baseline BMI	N	Follow-up BMI (24 months*)	Incident T2DM	No incident T2DM	p-value
		Overweight (25.0-29.9)	2 (50.0%)	247 (16.8%)	.
		Obese (>=30)	0	7 (0.5%)	.
		Outside of plausible range (<10 or >50)	0	3 (0.2%)	.
		Missing	0	445 (30.2%)	.
Overweight (25.0 – 29.9)	1414	Total	9	1405	
		Underweight (<18.5)	0	3 (0.2%)	0.0870
		Normal Weight (18.5 – 24.9)	2 (22.2%)	101 (7.2%)	.
		Overweight (25.0-29.9)	6 (66.7%)	731 (52.0%)	.
		Obese (>=30)	1 (11.1%)	153 (10.9%)	.
		Outside of plausible range (<10 or >50)	0	1 (0.1%)	.
		Missing	0	416 (29.6%)	.
Obese (>=30)	609	Total	3	606	
		Normal Weight (18.5 – 24.9)	0	8 (1.3%)	0.6755
		Overweight (25.0-29.9)	0	49 (8.1%)	.
		Obese (>=30)	3 (100.0%)	347 (57.3%)	.
		Outside of plausible range (<10 or >50)	0	3 (0.5%)	.
		Missing	0	199 (32.8%)	.
Outside of plausible range (<10 or >50)	36	NA	NA	NA	.
Missing	183	NA	NA	NA	.

*Between >21 and >=27 months, BMI value closest to 24 months

Table 85. Absolute changes in BMI by incident T2DM among ART-experienced/suppressed patients (Population 2)

		Incident T2DM	No incident T2DM	p-value
6-month follow-up*	BMI available and between >=10 and <=50 (baseline & 6-months)	56	6499	
	Absolute BMI change from baseline to 6-months Median (IQR)	0.3 (-0.5, 1.4)	0.3 (-0.4, 1.1)	0.6258
12-month follow-up*	BMI available and between >=10 and <=50 (baseline & 12-months)	37	4806	
	Absolute BMI change from baseline to 12-months Median (IQR)	0.0 (-1.0, 1.8)	0.4 (-0.5, 1.4)	0.4802
18-month follow-up*	BMI available and between >=10 and <=50 (baseline & 18-months)	24	3446	
	Absolute BMI change from baseline to 18-months Median (IQR)	0.7 (-0.2, 2.4)	0.5 (-0.5, 1.6)	0.3330
24-month follow-up*	BMI available and between >=10 and <=50 (baseline & 24-months)	16	2460	
	Absolute BMI change from baseline to 24-months Median (IQR)	0.7 (-0.3, 2.7)	0.6 (-0.4, 1.8)	0.5644

*+/- 3 months, BMI value closest to X months

1.10. Exploratory Objective: Marginal structural model for time to T2DM adjusted for weight gain in Study Population 2

Inverse probability of treatment weights (IPTW) could not be performed due to the multinomial nature of the exposure in this study. Numerous attempts were made to create stabilized weights with a mean of 1 and a reasonable range. However, all our attempts resulted in very extreme weights.

There are many issues related to IPTW for multinomial treatments.[21] Proposed solutions to these issues are complex; would require a significant time investment to understand and implement; and have not reached consensus in the literature as to the best approach. [21] Therefore, we have decided to focus on

inverse probability of censoring weights (IPCW), because the greatest concern was that patients may discontinue DTG due to weight gain, and subsequently T2DM would not be observed. This concern could be alleviated with IPCW.

1.10.1. ART-naïve

Selected stabilized IPCW:

- Numerator: core agent, baseline age, sex, race/ethnicity (Black and/or Hispanic), baseline CD4 cell count, baseline HCV co-infection, VACS>=30, interaction between core agent and VAC>=30
- Denominator: covariates in numerator + time-updated viral load, time-updated BMI, time-updated systemic steroid use for >=14 days in the past 60-90 months
- Pooled logistic regression modeled by including months of follow-up (restricted cubic splines) in both the numerator and denominator models
- Mean IPCW (range): 0.999 (0.126 to 22.673); median: 1.001

In the naïve population, several attempts were made to create stabilized IPCW that would allow a good balance of all covariates, including restricted cubic splines for continuous variables and interaction terms between core agent and other covariates. While most attempted models provided a good balance of covariances (standardized difference between -5% and 5%), none provided adequate balance for treatment core agents (Figure 1).

Figure 3. Standardized difference in covariate between censored and uncensored observations, ART-naïve population

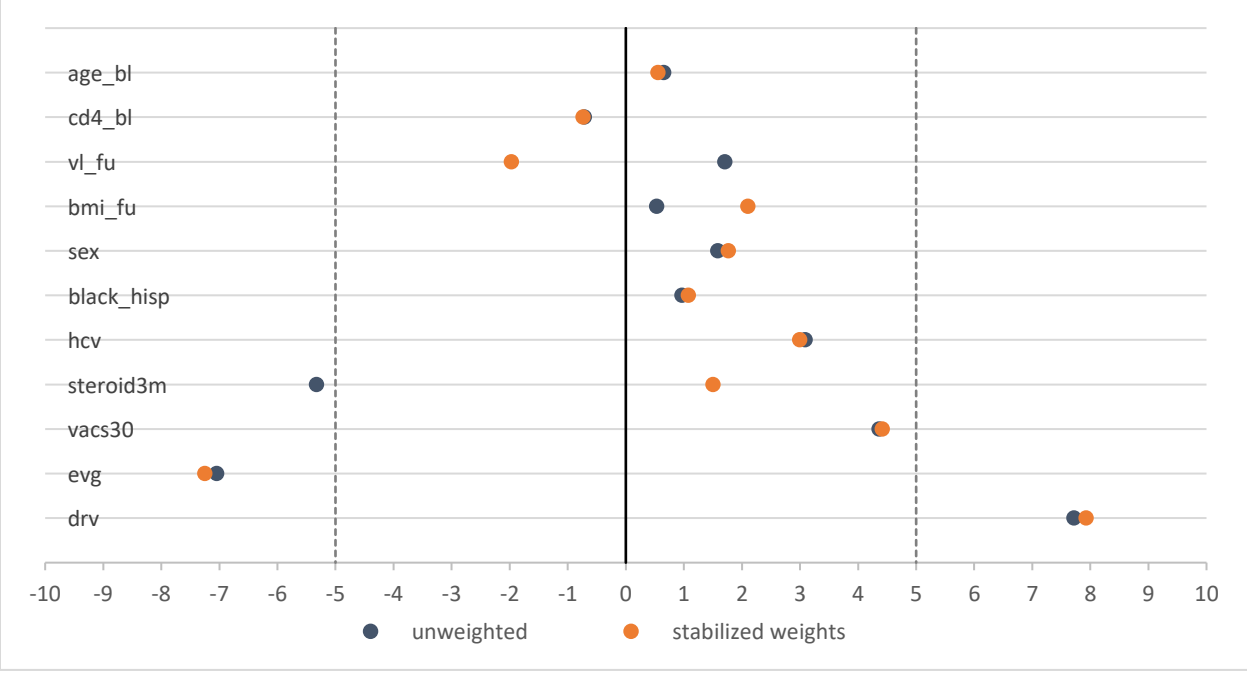

Table 86. Unadjusted and adjusted association between core agent and T2DM in ART-naïve patients using Cox Proportional Hazards Models, baseline covariates (Results included in the abstract)

	# T2DM events (n=108)	Unadjusted HR (95% CI)	Adjusted* HR (95% CI)
DTG	49	1.00 (Ref)	1.00 (Ref)
EVG/c	46	0.66 (0.44, 0.99)	0.70 (0.47, 1.05)
bDRV	10	0.71 (0.36, 1.39)	0.53 (0.26, 1.04)

* Adjusted for baseline age, sex, race, HCV co-infection, BMI

Table 87. Unadjusted and adjusted association between core agent and T2DM in ART-naïve patients using Pooled Logistic Regression with and without IPCW, time-updated covariates

	# T2DM events (n=93)	Unadjusted OR (95% CI)	Unadjusted, IPCW OR (95% CI)	Adjusted* OR (95% CI)	Adjusted*, IPCW OR (95% CI)
DTG	44	1.00	1.00	1.00	1.00
EVG/c	39	0.66 (0.44, 0.99)	0.67 (0.45, 1.01)	0.73 (0.49, 1.10)	0.76 (0.49, 1.12)
bDRV	10	0.71 (0.36, 1.39)	0.72 (0.37, 1.42)	0.52 (0.26, 1.05)	0.54 (0.27, 1.07)

* Adjusted for baseline age, sex, race, CD4 cell count, HCV, and time-updated BMI, systemic steroid (>14 days)

1.10.2. ART-experienced, suppressed

Selected stabilized IPCW:

- Numerator: core agent, baseline age, sex, race/ethnicity (Black and/or Hispanic), baseline CD4 cell count, baseline HCV co-infection, VACS>=30, any prior exposure to core agents of interest, history of AIDS
- Denominator: covariates in numerator + time-updated viral load, time-updated BMI, time-updated systemic steroid use for >=14 days in the past 60-90 months
- Pooled logistic regression modeled by including months of follow-up (restricted cubic splines) in both the numerator and denominator models
- Mean IPCW (range): 0.999 (0.321 to 1.469); median: 1.005

In the ART-experienced, suppressed population, stabilized IPCW allowing a good balance of all covariates were constructed (Figure 2). However, because more variables were required to create the IPCW, the number of T2DM events is lower and unadjusted pooled logistic regression results do not align perfectly with the Cox proportional hazards model results. None of the results from any of the modeling achieved significance.

Figure 4. Standardized difference in covariate between censored and uncensored observations, ART-experienced, suppressed population

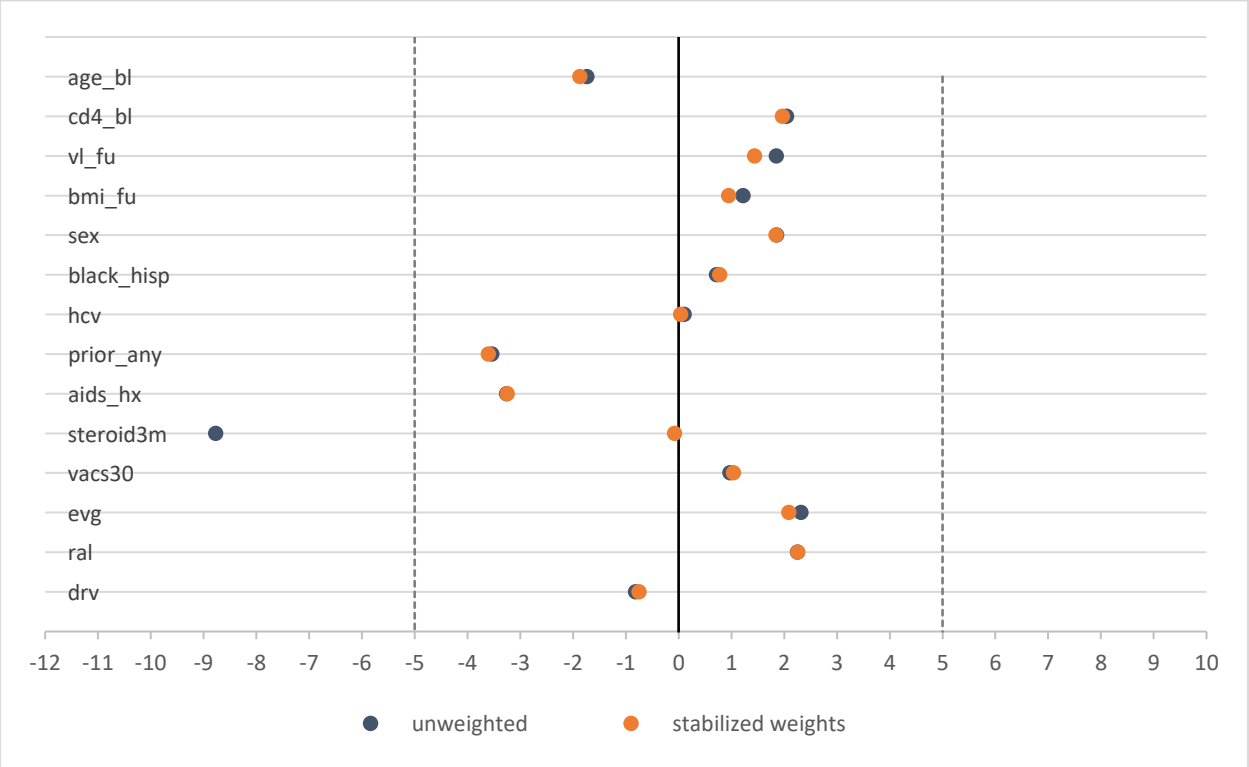

Table 88. Unadjusted and adjusted association between core agent and T2DM in ART-experienced, suppressed patients using Cox Proportional Hazards Models, baseline covariates (Results included in the abstract)

	# T2DM events (n=196)	Unadjusted HR (95% CI)	Adjusted* HR (95% CI)
DTG	81	1.00 (Ref)	1.00 (Ref)
EVG/c	72	0.80 (0.58, 1.10)	0.96 (0.70, 1.33)
RAL	18	1.31 (0.79, 2.19)	1.17 (0.70, 1.96)
bDRV	25	1.04 (0.66, 1.63)	0.90 (0.57, 1.42)

* Adjusted for BASELINE age, sex, race, HCV co-infection, BMI

Table 89. Unadjusted and adjusted association between core agent and T2DM in ART-experienced, suppressed patients using Pooled Logistic Regression with and without IPCW, time-updated covariates

	# T2DM events (n=185)	Unadjusted OR (95% CI)	Unadjusted, IPCW OR (95% CI)	Adjusted* OR (95% CI)	Adjusted*, IPCW OR (95% CI)
DTG	80	1.00	1.00	1.00	1.00
EVG/c	67	0.76 (0.55, 1.05)	0.75 (0.54, 1.04)	0.96 (0.69, 1.33)	0.95 (0.68, 1.32)
RAL	14	1.07 (0.60, 1.90)	1.07 (0.61, 1.91)	0.94 (0.52, 1.69)	0.94 (0.53, 1.70)
bDRV	24	1.02 (0.64, 1.61)	1.03 (0.65, 1.63)	0.96 (0.60, 1.53)	0.97 (0.61, 1.54)

* Adjusted for BASELINE age, sex, race, CD4 cell count, HCV, prior exposure to core agents of interest, AIDS history, and TIME-UPDATED BMI, systemic steroid (>14 days)