

Switching to dolutegravir/lamivudine two-drug regimen: durability and virologic outcomes in routine U.S. clinical care

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OPERA
The Longitudinal Cohort

Background

- Dolutegravir/lamivudine (DTG/3TC) is the second two-drug regimen approved in the US for the treatment of people with HIV (PWH)
- On 08Apr2019, the FDA expanded the indication for DTG/3TC to include ART-experienced, suppressed individuals
- DTG/3TC is indicated for
 - PWH without any known substitutions associated with resistance to the individual components
 - PWH without hepatitis B co-infection

Objective

To describe the real-world experience of virologically suppressed, ART experienced adults switching to DTG/3TC from one of three commonly prescribed traditional three-drug regimens in the US

Methods

Data Source: OPERA Cohort

- Prospectively captured, routine clinical data from electronic health records from 84 clinics in 18 US states/territories
- ~12% of people with HIV in US

Inclusion Criteria

- HIV-1 positive
- ≥13 years old
- Switch to DTG/3TC between 8APR2019 and 30APR2021
- Switched from bicitegravir/tenofovir alafenamide/emtricitabine (BIC/TAF/FTC), DTG/abacavir (ABC)/3TC or DTG+TAF/FTC
- Viral load <50 copies/ml at switch
- No known history of virologic failure or resistance

Censoring Criteria

- Any change in DTG+3TC regimen (add or remove of any antiretroviral)
- Lost to follow-up (18 months after last visit, lab, or clinic contact)
- Death
- Study end (31OCT2021)

Definitions

- Baseline: date of the first DTG/3TC prescription
- Discontinuation:
 - Switch from DTG/3TC to any other regimen (e.g., stop DTG or 3TC, and/or add another core agent or nucleoside reverse transcriptase inhibitor)
 - ART interruption
- Loss of suppression
 - First VL ≥50 copies/mL
 - First VL ≥200 copies/mL
- Confirmed virologic failure: 2 VL ≥ 200 copies/mL or discontinuation after 1 VL ≥ 200 copies/mL

Statistical Analyses

- Incidence rates assessed with univariate Poisson regression
 - Overall
 - Stratified by age, sex and race

Results

Table 1. Population characteristics at ART initiation

	Overall N = 787
Age, median years (IQR)	44 (33, 55)
Ryan White/ADAP program beneficiary, n (%)	252 (32)
CD4 cell count, median cells/μL (IQR)	738 (569, 932)
History of AIDS, n (%)	149 (19)
HBV co-infection, n (%)	19 (2)
Any comorbidity ^a actively managed in past 12 months, n (%)	422 (54)
Prior ART regimen, n (%)	
DTG/ABC/3TC	421 (54)
BIC/TAF/FTC	240 (30)
DTG + TAF/FTC	126 (16)

3TC, lamivudine; ABC, abacavir; BIC, bicitegravir; DTG, dolutegravir; FTC, emtricitabine; IQR, interquartile range; TAF, tenofovir alafenamide
^a Autoimmune Disease, Cardiovascular Disease, Invasive Cancers, Endocrine Disorders, Mental Health Disorders, Liver Disease, Bone Disorders, Peripheral Neuropathy, Renal Disease, Hypertension, Substance Abuse, COVID-19

Table 2. Duration of follow-up and confirmed virologic failure, stratified by age, sex and race

	N	Months of follow-up, Median (IQR)	Confirmed virologic failure ^a , n	Confirmed virologic failure, IR per 100 py (95% CI)
Overall	787	13.6 (8.2, 22.3)	≤5	0.43 (0.16, 1.00)
Age < 50	490	13.7 (8.8, 22.2)	≤5	0.52 (0.17, 2.00)
Age ≥ 50	297	13.5 (7.5, 22.3)	≤5	0.29 (0.04, 2.00)
Male	659	13.6 (8.3, 22.4)	≤5	0.51 (0.19, 1.00)
Female	128	13.6 (7.6, 21.3)	0	0
Black	250	13.3 (7.9, 21.3)	≤5	1.07 (0.35, 3.00)
Non-Black	537	13.3 (7.9, 21.3)	≤5	0.15 (0.02, 1.00)

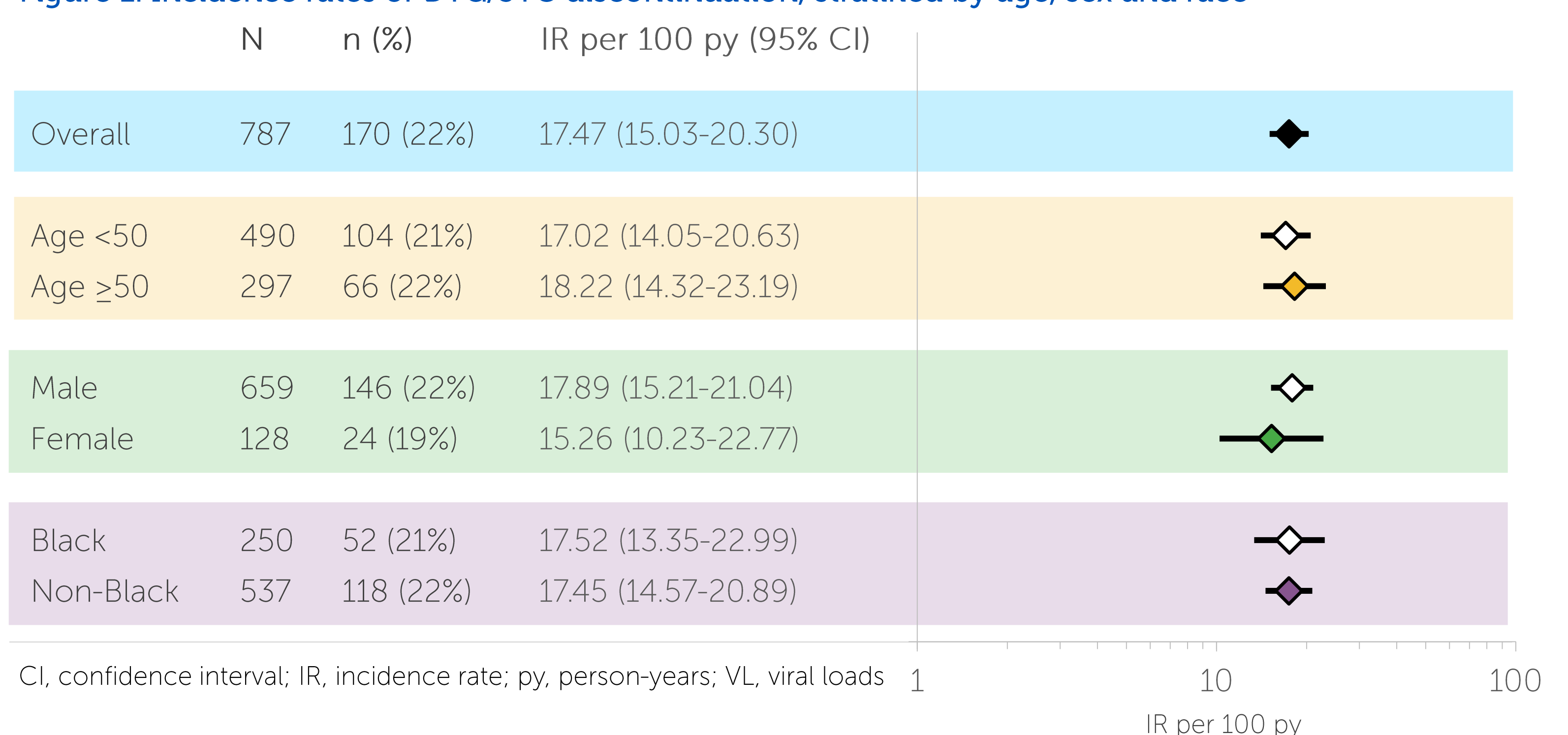
CI, confidence interval; IR, incidence rate; py, person-years
^a Masking of cells with 1 to 5 individuals is required by HIPAA (US federal law to protect sensitive patient health information)

Table 3. Reasons for discontinuation^a among discontinuers

	Discontinuers N = 170
Treatment-related reasons, n (%) (i.e., detectable VL, adverse diagnosis/side effect, lab abnormality), n (%)	6 (4)
Any other reason, n (%) (i.e., simplification, access issues, non-adherence, therapeutic gap, patient preference, provider preference)	66 (39)
None identified, n (%)	101 (59)

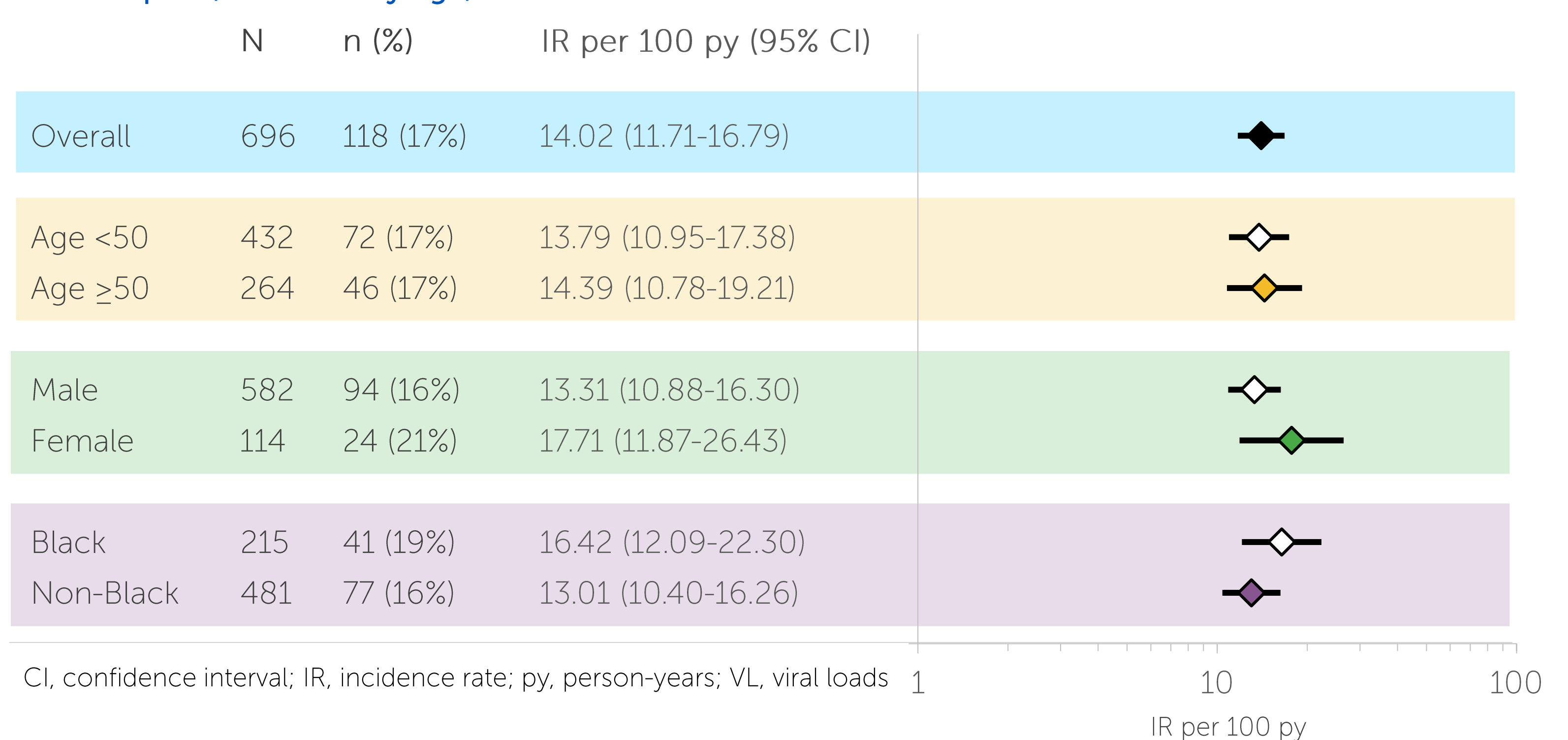
^a Reasons are not mutually exclusive

Figure 1. Incidence rates of DTG/3TC discontinuation, stratified by age, sex and race



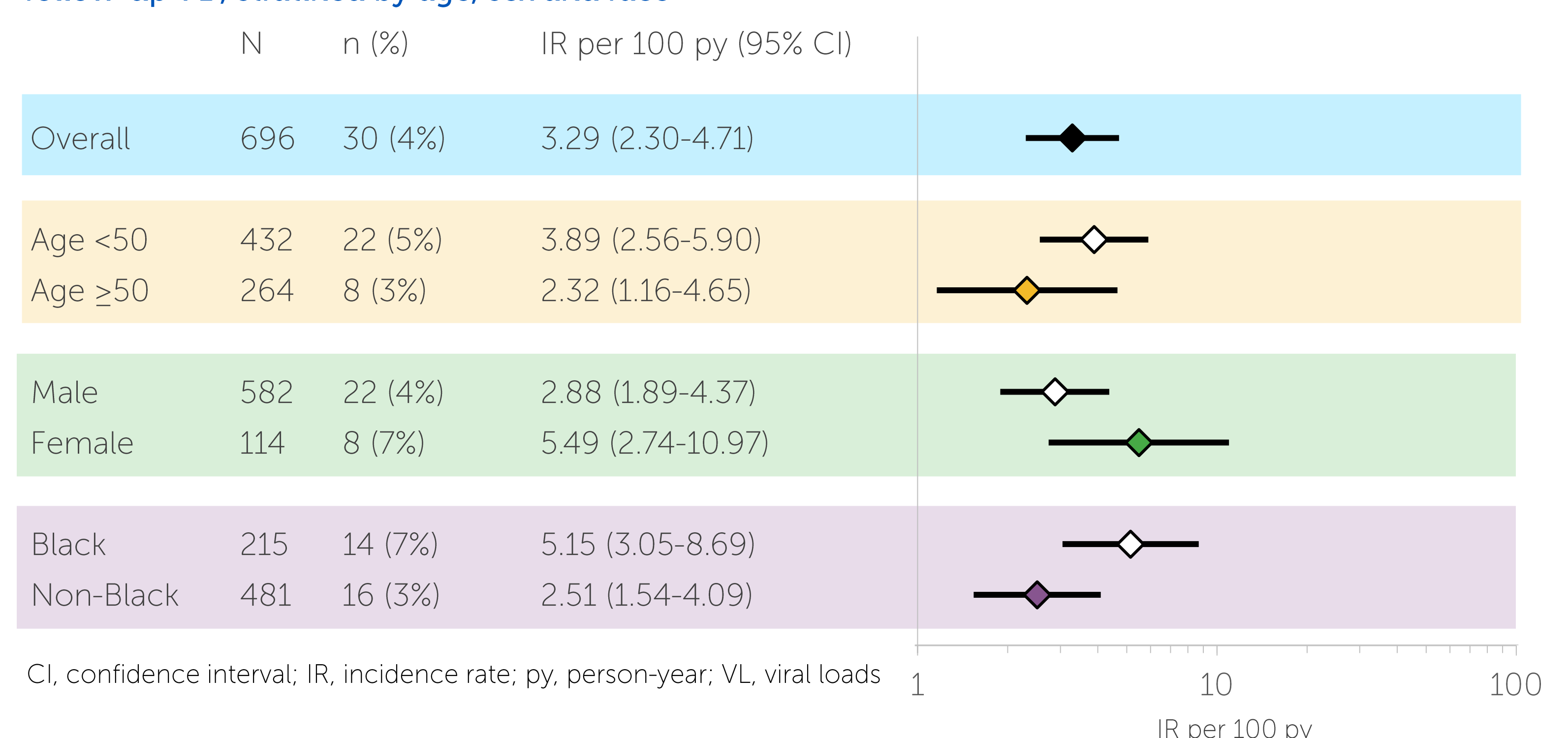
CI, confidence interval; IR, incidence rate; py, person-years; VL, viral loads

Figure 2. Incidence rates of loss of suppression (first VL ≥50 copies/mL) among individuals with ≥1 follow-up VL, stratified by age, sex and race



CI, confidence interval; IR, incidence rate; py, person-years; VL, viral loads

Figure 3. Incidence rates of loss of suppression (first VL ≥200 copies/mL) among individuals with ≥1 follow-up VL, stratified by age, sex and race



CI, confidence interval; IR, incidence rate; py, person-year; VL, viral loads

Discussion

- Among virally suppressed adults, switching to DTG/3TC was observed to be:
 - Virologically effective, with low rates of loss of viral suppression (≥200 copies/mL) and rare virologic failure events
 - Well tolerated, with few discontinuations linked to treatment-related events
- The absence of differences across strata of age, sex and race suggests that all groups were able to take DTG/3TC with equal success
- Generalizability is limited by the narrow inclusion criteria

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Key Findings

DTG/3TC was observed to be an effective and well tolerated treatment option among virologically undetectable ART-experienced PWH

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