Virologic Outcomes of Individuals Prescribed Dolutegravir/Lamivudine After an Oral Antiretroviral Therapy Treatment Interruption: Findings from the OPERA Cohort

P - 1026

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Background

- Treatment interruptions (TI) are common in routine HIV care and may lead to viral rebound, creating uncertainty around optimal regimen choice upon treatment resumption
- Resumption of treatment with effective ART is critical for virologic suppression and preventing both disease progression and transmission
- Real-world evidence on DTG/3TC use following treatment interruption is limited

Objectives

To describe virologic outcomes after treatment resumption with dolutegravir/lamivudine following an oral ART treatment interruption in a large, US-based, real-world cohort

Methods

OPERA® Cohort

- Prospectively captured, routine clinical data from electronic health records in the US (124 clinics, 23 US states/territories)

Inclusion Criteria

- Adults (i.e., age ≥ 18 years) with HIV who were prescribed a complete oral ART regimen (i.e., ≥ 2 ARVs, including ≥ 1 core agent)
- Experienced ≥1 TI of > 45 days followed by treatment resumption with DTG/3TC between 01JUL2021 and 30JUN2025 (based on prescription data, not fills or usage)

Censoring Criteria

- Discontinuation of DTG/3TC
- Death
- Loss to follow-up (i.e., ≥ 12 months without clinical contact)
- Study end (31DEC2025)

Outcomes

- Demographic and clinical characteristics at time of resumption of treatment with DTG/3TC
- Suppression (i.e., VL < 200 copies/mL) at 3, 6, and 12 months (± 4 weeks) after treatment resumption with DTG/3TC
- Virologic outcomes over follow-up after treatment resumption with DTG/3TC, assessed using Kaplan-Meier methods
- Virologic outcomes of interest
  - Among individuals viremic (i.e., VL ≥ 200 c/mL) at treatment resumption: virologic suppression (i.e., VL < 200 c/mL)
  - Among individuals suppressed at treatment resumption: virologic failure (i.e., two consecutive VLs ≥ 200 c/mL or VL ≥ 200 c/mL followed by change in core agent)

Sensitivity Analysis

- Analyses repeated for TI > 60 and TI > 90 days
- Results stratified by pre-interruption regimen: DTG/3TC vs. not DTG/3TC

Results

Table 1. Demographic and clinical characteristics of individuals at treatment resumption with DTG/3TC following treatment interruption, by duration of TI[a]

Characteristic	TI > 45 days N = 700	TI > 60 days N = 617	TI > 90 days N = 480
Age, median years (IQR)	40 (32, 54)	40 (31, 54)	38 (31, 52)
Female, n (%)	131 (19)	111 (18)	89 (19)
Black race, n (%)	294 (42)	252 (41)	205 (43)
White race, n (%)	324 (46)	296 (48)	220 (46)
Hispanic ethnicity, n (%)	165 (24)	153 (25)	119 (25)
MSM, n (%)	392 (56)	345 (56)	271 (56)
People who inject drugs, n (%)	55 (8)	50 (8)	42 (9)
Years since HIV diagnosis, median (IQR)	8 (3, 15)	7 (3, 14)	7 (3, 14)
History of an AIDS-defining event, n (%)	206 (29)	172 (28)	128 (26)
Ever had syphilis infection, n (%)	313 (45)	279 (45)	225 (47)
Number of resumptions with DTG/3TC, mean (SD)[b]	1.2 (0.7)	1.2 (0.6)	1.1 (0.4)

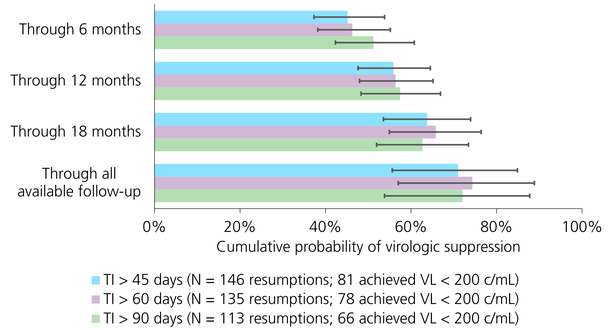
[a] Individuals with a TI > 60 days are a subset of individuals with a TI > 45 days; individuals with a TI > 90 days are a subset of each of the other groups
[b] The median duration of a treatment interruption was 114 days (IQR: 75, 217), 132 days (IQR: 88, 251), and 179 days (IQR: 120, 305) in the > 45, > 60, and > 90-day interruption groups, respectively

Table 2. Characteristics of ART regimens preceding treatment interruption & resumption with DTG/3TC, by duration of TI[a]

Characteristic	TI > 45 days N = 864 resumptions	TI > 60 days N = 738 resumptions	TI > 90 days N = 539 resumptions
Months on regimen, median (IQR)	14 (6, 28)	16 (8, 29)	17 (12, 30)
DTG/3TC, n (%)	675 (78)	578 (78)	422 (78)
Core agent, n (%)[b]			
Bictegravir (INSTI)	52 (6)	49 (7)	41 (8)
Dolutegravir (INSTI)	759 (88)	645 (87)	470 (82)
Elvitegravir (INSTI)	28 (3)	26 (4)	14 (3)
Darunavir (PI)	23 (3)	18 (2)	10 (2)
Rilpivirine (NNRTI)	19 (2)	11 (1)	10 (2)
≥2 core agent classes, n (%)	17 (2)	10 (1)	6 (1)

[a] TIs > 60 days and TIs > 90 days are subsets of TIs > 45 days
[b] No other core agent exceeded a frequency of 5

Figure 1. Cumulative probability and 95% confidence interval error bars[a] of virologic suppression over follow-up among people who were viremic at treatment resumption with DTG/3TC



[a] Cumulative probabilities were assessed using Kaplan-Meier methods; individuals were included regardless of whether VL measurements were available over follow-up

Figure 2. Proportion of VLs < 200 c/mL among people who were viremic at treatment resumption(s) with DTG/3TC, by time point

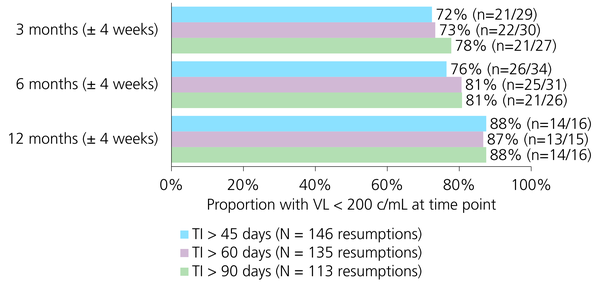
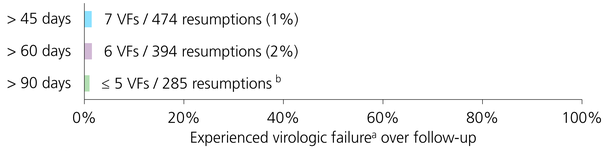


Figure 3. Proportion with virologic failure[a] among people who were suppressed at treatment resumption(s) with DTG/3TC



[a] Virologic failure: two consecutive viral loads ≥ 200 copies/mL or viral load ≥ 200 copies/mL followed by change in core agent
[b] HIPAA regulations require masking values of 1 to 5 individuals

Abbreviations

AIDS, acquired immunodeficiency syndrome; **ART**, antiretroviral therapy; **c/mL**, copies/mL; **DTG/3TC**, dolutegravir/lamivudine; **HIV**, human immunodeficiency virus; **IQR**, interquartile range; **mL**, milliliter; **MSM**, men who have sex with men; **SD**, standard deviation; **TI**, treatment interruption; **VF**, virologic failure; **VL**, viral load

Discussion

- There were 700 individuals who experienced a total of 864 TIs > 45 days followed by resumption of treatment with DTG/3TC
  - The median duration of a TI > 45 days was 114 days (IQR: 75, 217)
  - Median age was 40 years old, 19% were women, 42% were Black, 46% were White, 24% were Hispanic, and median time since HIV diagnosis was 8 years (IQR: 3, 15; Table 1)
    - Characteristics of individuals and of pre-interruption regimens were similar across TI durations
- Time on the pre-interruption regimen was slightly longer for TIs > 60 or > 90 days compared to TIs > 45 days (Table 2)
- Most (78%) TIs, regardless of duration, were also preceded by DTG/3TC (Table 2)
- After resuming treatment while viremic, most individuals were able to achieve virologic suppression over follow-up (Figure 1)
  - When VL measurements were available over follow-up, most VLs were < 200 copies/mL (Figure 2)
- After resuming treatment while virologically suppressed, virologic failure was rare over follow-up (Figure 3)
- Limitations
  - Data in OPERA reflects prescriptions, rather than use, and adherence cannot be determined; this could lead to inaccurate identification of treatment interruptions and resumptions
  - Low availability of VL measurements over follow-up
  - Only 22% of pre-interruption regimens were not DTG/3TC; outcomes were similar, regardless of pre-interruption regimen, but limited by sample size

Key Findings

- These real-world findings show that virologic suppression can be achieved or maintained following treatment resumption with DTG/3TC after oral ART treatment interruptions, including longer interruptions of more than 90 days

Acknowledgements

This research would not be possible without the generosity of people living with HIV and their OPERA caregivers. Additionally, we are grateful for the following individuals: Kristine Ferguson (SAS programming), Michael Stagner (QA), Bernie Stooks (IT/data management), Lisa Lutzi & Nicole Shaw (data architecture), and Judy Johnson & Quateka Cochran (medical terminology classification).

Support

This research was sponsored by ViiV Healthcare

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