A Real-World Observational Study on Patients With HIV Who Switched From Nevirapine + 2 Nucleoside Reverse Transcriptase Inhibitors to Dolutegravir/Lamivudine in British Columbia, Canada

Presenting author: Joseph J. de Wet
Spectrum Health, 1080 Howe Street, Suite 702
Vancouver, BC, V6Z 2T1, Canada
jossdewet@spectrum-health.net
Phone: 604-681-1080
Fax: 604-681-0244

Joseph J. de Wet,[1,2] Joann K. Ban,[3] Gustavo Verdier,[4] Juejing Ling,[5] Maria Eberg,[5] Andrean Bunko,[5] Michael McKimm[4]

[1]Spectrum Health, Vancouver, British Columbia, Canada; [2]Department of Family Practice, University of British Columbia, Vancouver, British Columbia, Canada; [3]GSK, Mississauga, Ontario, Canada; [4]ViiV Healthcare, Montréal, Québec, Canada; [5]IQVIA, Kirkland, Québec, Canada

Key Takeaways

- **We assessed real-world use of dolutegravir/lamivudine (DTG/3TC) in antiretroviral therapy (ART)-experienced, virologically suppressed Canadian patients living with HIV (PLHIV) who switched from nevirapine extended release (NVP XR) + 2 nucleoside reverse transcriptase inhibitors (NRTIs) to DTG/3TC due to market discontinuation**
- **Results showed that switching to DTG/3TC was effective and well tolerated with low metabolic impact and few discontinuations over 12 months in a group of PLHIV who had no reason to switch other than a manufacturing discontinuation**

Introduction

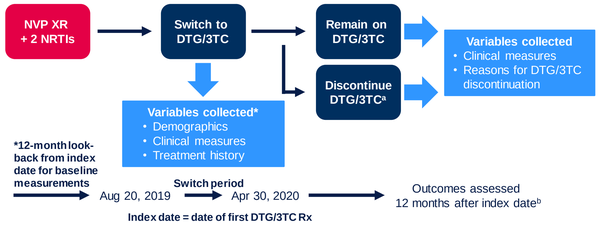
- Despite the availability of single-tablet ART regimens in recent years, some PLHIV remained on multi-tablet NVP XR + 2 NRTIs due to its excellent safety profile[1-3]
  - Discontinuation of NVP XR from the Canadian market on August 20, 2019, required switching to another ART regimen
- Fixed-dose combination DTG/3TC as a once-daily, single-tablet, 2-drug regimen is recommended as first-line therapy for ART-naive PLHIV and as a switch option for virologically suppressed PLHIV in major US and international guidelines[4-6]
- We conducted this analysis to better understand real-world use of DTG/3TC in ART-experienced, virologically suppressed Canadian PLHIV who had previously been using NVP XR + 2 NRTIs
  - Changes in weight and body mass index (BMI) were also examined given controversy concerning use of second-generation integrase strand transfer inhibitors and weight gain[7]

Methods

Study Design

- A retrospective, observational cohort study using de-identified electronic medical records from Spectrum Health in British Columbia, Canada (Figure 1)
- PLHIV were selected for inclusion based on the following criteria:
  - ≥18 years of age as of August 20, 2019
  - Virologically suppressed (HIV-1 RNA <50 c/mL)
  - Switched from NVP XR + 2 NRTIs to DTG/3TC between August 20, 2019, and April 30, 2020

Figure 1. Study Design



[a]Last viral load measurement before DTG/3TC discontinuation was used.
[b]Included a ± 6-month window to account for variability of routine care visit schedules and impact of COVID-19 pandemic.

Study Outcomes

- **Primary Endpoints:**
  - (1) proportion of PLHIV with HIV-1 RNA <50 c/mL and <200 c/mL at Month 12 and (2) CD4+ cell count at baseline and Month 12
- **Secondary Endpoints:**
  - Change in weight and BMI, number of ART regimens before switch, and proportion of PLHIV with prior virologic failure before switch
  - Virologic failure: one measurement of HIV-1 RNA ≥50 c/mL followed by a second consecutive measurement ≥200 c/mL or 2 consecutive measurements of HIV-1 RNA ≥200 c/mL on different dates with the second occurring within 90 days of the first
- **Exploratory Endpoints:**
  - Reasons for discontinuing DTG/3TC after switch, and metabolic syndrome–related variables and medication use at baseline and Month 12
- All endpoints were summarized using descriptive statistics
  - The completed analysis set was composed of all PLHIV with follow-up data in the 12-month window (6 and 18 months after index date)
  - The complete case subgroup was composed of all PLHIV with data at baseline and Month 12

Results

Baseline Characteristics

- 69 PLHIV who met study criteria were identified (Table 1)
- Overall, mean age was 54.2 years and 100% of the cohort were male
- Median (IQR) duration of follow-up was 17.0 (16.0-17.7) months

Table 1. Demographics and Baseline Characteristics: Completed Analysis Set

Parameter	N=69
Age, mean (SD), y	54.2 (8.5)
Sex, male, n (%)	69 (100)
≥6-month duration of HIV-1 RNA <50 c/mL before switch, n (%)	65 (94)
≥6-month duration of HIV-1 RNA <200 c/mL before switch, n (%)	69 (100)
Duration of NVP XR use before switch, median (IQR), y	5.0 (2.2-7.2)
Number of prior ART regimens before switch, n (%)	
1 prior ART regimen	69 (100)
NRTIs administered with NVP XR, n (%)	
Abacavir + lamivudine	60 (87)
Emtricitabine + tenofovir alafenamide	3 (4)
Emtricitabine + tenofovir disoproxil fumarate	6 (9)

Primary Outcomes

- 69 PLHIV completed the study; 63 remained on DTG/3TC while 6 discontinued DTG/3TC during the study period
- A high proportion of PLHIV maintained virologic suppression (defined as HIV-1 RNA <50 c/mL or <200 c/mL) at Month 12 (Figure 2)
  - Among the 6 PLHIV who discontinued DTG/3TC, 5 had HIV-1 RNA <50 c/mL while 1 had HIV-1 RNA <200 c/mL at discontinuation
- Among PLHIV with available data, mean CD4+ cell count increased between baseline and Month 12 (Figure 3)

Figure 2. Virologic Outcomes at Month 12 in the Completed Analysis Set

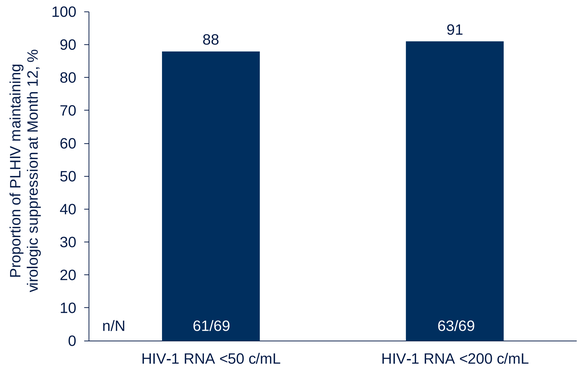
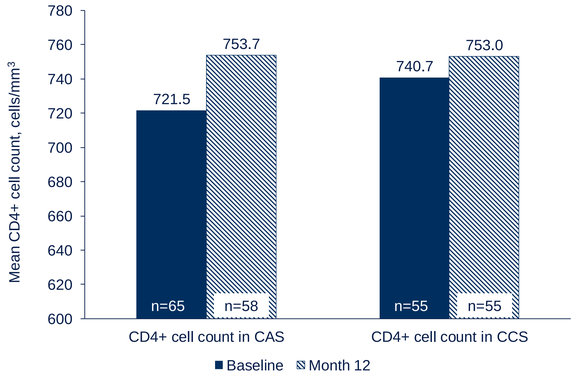


Figure 3. Mean CD4+ Cell Count at Baseline and Month 12 in the Completed Analysis Set and Complete Case Subgroup



CAS, completed analysis set (composed of all PLHIV with follow-up data in 12-month window [6 and 18 months after index date]); CCS, complete case subgroup (composed of all PLHIV with CD4+ cell count data at baseline and Month 12).

Secondary Outcomes

- All 69 PLHIV had only 1 prior ART regimen (NVP XR + 2 NRTIs) before switch
- No PLHIV experienced virologic failure in the 12 months before index date
- Among PLHIV with data at baseline and Month 12, median change from baseline in weight and BMI was small (Table 2)

Exploratory Outcomes

- No discontinuations were due to virologic reasons: 6 (9%) PLHIV discontinued DTG/3TC, all for tolerability reasons (fatigue, n=2; weight gain, n=2; insomnia, n=1; nausea, n=1)
- There were no substantial differences in use of prescriptions for management of weight, diabetes, blood pressure, or lipids at Month 12 compared with baseline
- Changes from baseline in other exploratory metabolic variables were small and inconsistent (Table 2)

Table 2. Weight, BMI, and Metabolic Syndrome–Related Variables at Baseline and Month 12: As Observed[a]

Parameter	Baseline (N=69)	Month 12 (± 6 months) (N=69)
Weight, kg		
CAS, median (IQR) [n]	80.0 (74.0-91.0) [63]	81.0 (73.0-89.5) [37]
CCS, median (IQR) [n]	78.8 (74.0-88.0) [34]	80.5 (72.6-89.5) [34]
Change from BL, median (IQR)	1.8 (−1.5, 3.7)	
BMI, kg/m^2		
CAS, median (IQR) [n]	26.5 (23.9-29.4) [41]	27.0 (24.5-29.4) [27]
CCS, median (IQR) [n]	26.0 (23.8-28.3) [25]	27.0 (24.5-28.6) [25]
Change from BL, median (IQR)	0.8 (−0.3, 1.4)	
>10% increase in weight, n/N (%)	—	1/34 (3)
Metabolic syndrome–related variables, CAS		
Triglycerides >1.7 mmol/L, n/N (%)	21/62 (34)	17/53 (32)
HDL cholesterol <1.03 mmol/L, n/N (%)	5/63 (8)	10/59 (17)
Blood pressure >130/85 mm Hg, n/N (%)	6/31 (19)	2/24 (8)
HbA_{1c} >5.7%, n/N (%)	7/35 (20)	9/24 (38)[b]
Diagnosis of type 2 diabetes, n/N (%)	2/69 (3)	5/69 (7)

BL, baseline; CAS, completed analysis set (composed of all PLHIV with follow-up data in 12-month window [6 and 18 months after index date]); CCS, complete case subgroup (composed of all PLHIV with data at baseline and Month 12).
[a]Missing data were removed in percentage calculation for categorical variables in the table.
[b]4 of the 9 PLHIV with HbA_{1c} >5.7% at Month 12 had HbA_{1c} >5.7% at baseline; 3 PLHIV with HbA_{1c} >5.7% at Month 12 did not have baseline data, while 2 PLHIV shifted from HbA_{1c} <5.7% at baseline to HbA_{1c} >5.7% at Month 12.

Conclusions

- Results indicate that 12 months after switching from NVP XR + 2 NRTIs to DTG/3TC, most PLHIV maintained virologic suppression and had improved CD4+ cell counts with few treatment discontinuations, and there was no virologic failure or development of resistance
  - All PLHIV who remained on DTG/3TC until study end maintained HIV-1 RNA <200 c/mL
  - The use of NVP, which is associated with increases in HDL cholesterol, likely led to the increased prevalence of low HDL cholesterol 12 months after switch[1-3]
- Findings support the real-world effectiveness and low metabolic impact of DTG/3TC after switching from a 3-drug regimen in a group of PLHIV who had no reason to switch other than a manufacturing discontinuation
- Results are also consistent with results from the phase 3 TANGO[8] and SALSA[9] studies and with real-world studies on DTG/3TC use[10]

Acknowledgments: This study was funded by ViiV Healthcare. Editorial assistance and graphic design support for this poster were provided under the direction of the authors by MedThink SciCom and funded by ViiV Healthcare.

References: **1.** Reekie et al. *HIV Med*. 2011;12:259-268. **2.** Rodríguez-Arrondo et al. *Curr HIV Res*. 2009;7:526-532. **3.** Tiraboschi et al. *HIV Res Clin Pract*. 2019;20:151-155. **4.** Panel on Antiretroviral Guidelines for Adults and Adolescents. https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv. Accessed August 17, 2022. **5.** European AIDS Clinical Society. https://www.eacsociety.org/media/final2021eacsguidelinesv11.0_oct2021.pdf. Accessed August 17, 2022. **6.** Saag et al. *JAMA*. 2020;324:1651-1669. **7.** Sax et al. *Clin Infect Dis*. 2020;71:1379-1389. **8.** van Wyk et al. *Clin Infect Dis*. 2022 [Epub ahead of print]. **9.** Llibre et al. *Clin Infect Dis*. 2022 [Epub ahead of print]. **10.** Patel et al. *Infect Dis Ther*. 2021;10:2051-2070.