Real-world Treatment Experience of Single-tablet Dolutegravir/Lamivudine in those Naïve to Treatment with Baseline Viral Loads ≥100,000 copies/mL the United States

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Key Takeaways

- **TANDEM aimed to characterize real-world prescribing behaviors and treatment outcomes of DTG-based 2DR in the United States (US).**
- **Here we describe demographics, clinical characteristics and outcomes of treatment naïve PLWH with high baseline VLs (≥100,000 copies/ mL) who initiated DTG/3TC.**
- **Out of the 16 PLWH with high baseline VLs, 13 experienced sustained virological suppression (<50 copies/mL) with no treatment discontinuations after a median follow-up time of >1 year on DTG/3TC.**
- **Data supports results from phase 3 clinical trials demonstrating DTG/3TC is an effective, well tolerated regimen when used in real-world settings in treatment-naïve PLWH with baseline VLs >100k, including >250k.**

Introduction

- Treatment for people living with human immunodeficiency virus (HIV)-1 (PLWH) continues to advance with a two-drug regimen (2DR) approach [1].
- Dolutegravir/ lamivudine (DTG/3TC) is indicated as a 2DR for both treatment naïve and virally suppressed PLWH [2].
- This approach is supported by a strong recommendation (AI*) from the DHHS Clinical Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV among PLWH with baseline VLs <500,000 copies/mL [3].
- The GEMINI and STAT trials demonstrated similarly high efficacy in treatment naïve PLWH across baseline VL strata ≥100,000 and <100,000 copies/mL.
- Though small in number, participants with baseline VLs ≥500,000 copies/mL include 13 and 19 participants from GEMINI and STAT respectively [4-5].
- Here we describe outcomes of treatment-naïve PLWH initiated on DTG/3TC with baseline viral loads of ≥100,000 copies/mL from TANDEM (n=16 out of 126); primary results have been presented previously [6-7].

Methods

- TANDEM was a US-based, retrospective chart review. 24 sites abstracted clinical characteristic, treatment history, and post-initiation outcomes data from medical charts of PLWH who were initiated on DTG/3TC or DTG/RPV.
- Analyses were descriptive and no formal hypotheses were tested.
- Missing data were not imputed. Descriptive analyses were performed in IBM® SPSS® Data Collection Survey Reporter v7.5 software.
- Time to event outcomes were calculated using Kaplan-Meier estimators conducted in StataCorp, 2015. Stata statistical software: Release 16 (College Station, TX, StataCorp LP).

Inclusion Criteria

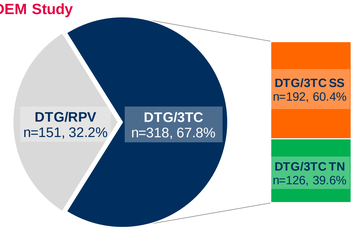
- ≥18 years old;
- Have a diagnosis of HIV-1 infection;
- Have a history of antiretroviral therapy (ART) consisting of the 2DR DTG/3TC or DTG/RPV as a single-tablet regimen (STR);
- DTG/3TC cohort:
  - Must have been initiated on or after 1st May 2019 and before 30th September 2020;
  - Upon initiation, PLWH must have been either treatment naïve [TN] to ART or virologically suppressed (i.e. stable switch [SS]) defined as having HIV-1 RNA <50 copies/mL, on a stable ART regimen for ≥3 months upon DTG-based 2DR initiation.
- Have at least 6 months of clinical follow-up after initiation of DTG-based 2DR which could include time post-discontinuation of either regimen.

*Rating for Recommendations = Strong (A) / Rating of Evidence = Data from randomized controlled trials (I)

Results

- From an overall sample of 469 PLWH, 151 received DTG/RPV and 318 received DTG/3TC, of whom 126 were TN and 192 were SS **(Figure 1)**.
  - Of the TN population (n=126), 58 had known baseline VLs available at DTG/3TC initiation. 9 had values 100,000-250,000 copies/mL while 7 were >250,000 copies/mL. Of these 7, four had VLs ≥500,000 copies/mL.
- Demographics of the sub-cohort of TN PLWH with baseline VLs ≥100,000 copies/mL are described in **Table 1**.
- Overall, the most common reasons for DTG/3TC initiation in those with baseline VLs 100,000−250k copies/mL were PLWH preference (n=2), convenience (n=2) and weight gain (n=2). For those with baseline VLs >250k copies/mL, PLWH preference (n=3), avoidance of long-term toxicities (n=2) and convenience (n=1) were most important **(Figure 2)**.

Figure 1. TANDEM Study

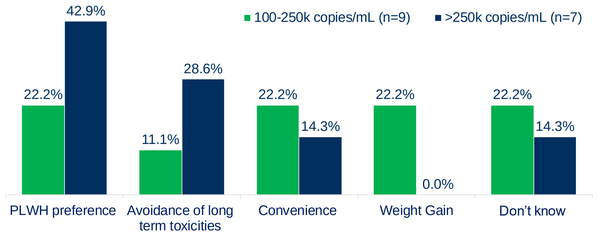


Abbreviations: TN = Treatment naïve to ART upon DTG/3TC initiation; SS = Virologically suppressed (i.e. stable switch) with HIV-RNA <50 copies/mL, on a stable ART regimen for ≥3 months upon DTG/3TC initiation

Table 1. Baseline Demographics

	100-250k copies/mL (n=9)	>250k copies/mL (n=7)
Age (years)		
Median (Interquartile range, (IQR))	34.0 (30.5, 46.5)	33.0 (26.0, 50.0)
Assigned Sex at Birth, n (%)		
Male	7 (77.8)	7 (100.0)
Current Gender Identity, n (%)		
Cis-male	7 (77.8)	6 (85.7)
Cis-female	2 (22.2)	0 (0.0)
Trans-female	0 (0.0)	1 (14.3)
Race, n (%)		
White/ Caucasian	4 (44.4)	4 (57.1)
Black	4 (44.4)	2 (28.6)
Mixed race	0 (0.0)	1 (14.3)
Not specified	1 (11.1)	0 (0.0)
Ethnicity, n (%)		
Hispanic / Latinx	4 (44.4)	2 (28.6)
Current Insurance Coverage, n (%)		
Employer provided/ sponsored insurance	3 (33.3)	2 (28.6)
Privately arranged insurance	1 (11.1)	4 (57.1)
Medicaid	4 (44.4)	1 (14.3)
AIDS Drug Assistance Program (ADAP)	1 (11.1)	0 (0.0)

Figure 2. HCP Reasons for Initiating DTG/3TC for High Baseline Viral Load



Clinical Characteristics & Virological Outcomes

- Clinical characteristics are described in **Table 2**.
- Baseline drug resistance testing was performed in 43.8% of PLWH with baseline VLs ≥100k copies/mL. Resistance-associated mutations were detected in 1 person (6.3%).

Table 2. Baseline Clinical Characteristics & Virologic Outcomes

	100-250k copies/mL (n=9)	>250k copies/mL (n=7)
Laboratory values prior to DTG/3TC initiation		
Median HIV viral load, copies/mL (IQR)	192,000 (147,619, 215,000)	722,422 (278,000, 2,680,017)
Median CD4 cell count, cells/mm^3 (IQR)	312 (43.5, 584)	114 (29, 481)
Viral suppression status on DTG/3TC, n (%)	**n=9**	**n=7**
Became virally suppressed[1]	**8 (88.9)**	**6 (85.7)**
No data available / Information unknown	1 (11.1)	1 (14.3)
Time to viral suppression from DTG/3TC initiation, n	**n=8**	**n=6**
Median Weeks (IQR)	11.2 (6.2, 30.0)	20.6 (10.5, 32.4)
Rebound status following viral suppression, n (%)	**n=8**	**n=6**
Remained virally suppressed	8 (100.0)	5 (83.3)
Rebounded[2]	0 (0.0)	1 (16.7)
Time from viral suppression to rebound, n	**n=0**	**n=1**
Median Weeks (IQR)	-	18.1 (18.1, 18.1)
Ongoing DTG/3TC[3], n (%)	**9 (100.0)**	**7 (100.0)**
Median time on DTG/3TC ongoing (years)	1.2 (0.8, 1.8)	1.0 (0.7, 1.1)
Drug Resistance Testing Performed at DTG/3TC initiation, n (%)	**n=9**	**n=7**
No resistance testing performed	3 (33.3)	5 (71.4)
Resistance testing performed; resistance detected[4]	1 (11.1)	0 (0.0)
Resistance testing performed; no resistance detected	4 (44.4)	2 (28.6)
Information unknown	1 (11.1)	0 (0.0)

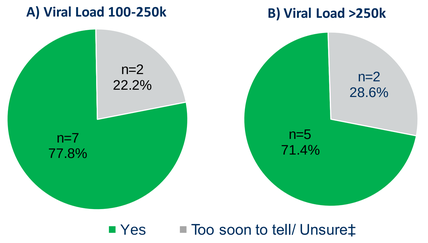
[1] Viral suppression defined as a HIV-1 viral load of <50 copies/mL
[2] Rebound defined as two consecutive viral load measurements of ≥200 copies/mL after viral suppression (<50 copies/mL).
[3] At the time of data abstraction, excludes PLWH lost to follow-up or treatment status unknown.
[4] Both NNRTI and PI resistance was detected in this N=1 PLWH, with detected mutations 'Not otherwise specified' for both types of resistance.

- For those with baseline VLs between 100−250k copies/mL, median CD4+ count was 312 cells/mm^3.
  - 8/9 PLWH became virally suppressed (HIV-1 viral load <50 copies/mL) while receiving DTG/3TC and 1 had missing data.
- For those with baseline VLs >250k, median CD4 count was 114 cells/mm^3.
  - 6/7 became virally suppressed while receiving DTG/3TC and 1 had missing data.
  - Of these six, 1 experienced virological rebound yet remained on DTG/3TC.
    - This 1 PLWH had no resistance testing performed at DTG/3TC initiation.
- Median time to viral suppression following DTG/3TC initiation was 11.2 and 20.6 weeks in the 100-250k and >250k sub-cohorts respectively.

Desired Health Outcomes

- Treating physicians were asked in their opinion 'what was the primary reason for initiating DTG/3TC' and then if the 'desired health outcome(s) that motivated DTG/3TC use' had been achieved for each PLWH†.
  - The desired health outcome was achieved in 7/9 of PLWH with baseline VLs 100-250k copies/mL and 5/7 with baseline VLs >250k copies/mL **(Figure 3)**.
- All PLWH with high baseline VLs (16/16) remained on DTG/3TC, at point of data abstraction, for a median duration of 1.2 and 1.0 years in the 100-250k and >250k sub-cohorts respectively.

Figure 3. Desired Health Outcomes Achieved† that Motivated DTG/3TC Use, According to the HCP Perspective



†'In your opinion, did their most recent DTG-based 2DR achieve the desired health outcome(s) that motivated its use? (e.g., treatment was simplified, intolerability ceased or avoided, drug-drug interactions (DDI) were avoided, exposure during pregnancy avoided, adherence improved, etc.)'
‡ For example, data not available in the medical records or insufficient follow-up to establish the treatment effect.

Limitations

- The small sample size (n=16) may limit extrapolation of these results to a broader population.
- This was a retrospective chart review therefore data may be missing or incomplete.
- TANDEM captured treatment outcomes up to and including virological rebound only; thus, there is no knowledge of outcomes post-rebound in the 1 PLWH who rebounded.
- Data from TN Test and Treat (T&T) users of DTG/3TC observed in TANDEM are not included in this sub-cohort due to the lack of baseline VL. This population could have potentially contributed to the overall sub-cohort size.
  - Findings from this T&T sub-cohort can be found in Poster 1279 at ID Week 2022.

Conclusions

- Outcomes were explored of a subset of PLWH in TANDEM who initiated onto DTG/3TC with high baseline VLs >100k.
- Out of the 16 PLWH with high baseline VLs, 13 experienced sustained virological suppression with no treatment discontinuations.
- TANDEM supports results from phase 3 clinical trials demonstrating DTG/3TC is an effective and well tolerated regimen when used in real-world settings in treatment-naïve PLWH with baseline VLs >100k, including >250k.

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References: 1. Waters, L. and Church, H., *Curr. Opin. Infect. Dis.*, 2020; 33(1): 28-33. **2.** van Wyk, J. *et al.*, *Clin. Infect. Dis.* 2020;71(8):1920-1929. **3.** US Departments of Health and Human Services. *Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV.* Accessed March 2, 2022. **4.** Cahn, P. *et al.*, *J. Aqcuir. Immune. Defic. Syndr.* 2020;8(8):310-318. **5.** Rolle, C.P., *et al.*, *AIDS, 2021;35(12):1957-1965.* **6.** Schneider, S. *et al.*, IAS Conference 2022, Montreal; Poster # EPB147. **7.** Blick, G. *et al.*, AMCP Nexus Conference 2022, National Harbor, MD.