Virological suppression in people with HIV-1 (PWH) receiving dolutegravir/lamivudine (DTG/3TC) was high and similar across age groups despite older PWH having increased rates of comorbidities and polypharmacy (TANDEM Subgroup Analysis)

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Key Takeaways

- **Virological suppression rates were high and similar by age group (<50 years, ≥50 years, ≥65 years) and among dolutegravir/lamivudine (DTG/3TC) stable-switch PWH despite higher rates of comorbidities and polypharmacy in the older age groups**
- **While the proportion of PWH with no treatment considerations / risk factors was similar (45-52%) across age-groups, treatment considerations / risk factors became prominent with increasing age**
- **Avoidance of long-term toxicities was the biggest driver for initiating DTG/3TC in the ≥50 years cohort (reported by 32.1% of health care providers (HCPs)), while in the <50 years cohort, simplification / streamlining of treatment was most common (27.9%)**
- **This real-world analysis is consistent with clinical study data supporting DTG/3TC as an effective treatment strategy in older PWH**

Introduction

- Treatment for people with HIV-1 (PWH) continues to advance with a two-drug regimen (2DR) approach.[1]
- DTG/3TC is the only oral 2DR indicated for both treatment-naïve and virally suppressed PWH and is included as a first-line choice in HIV treatment guidelines.[2-3]
- The TANDEM study aimed to characterize real-world prescribing behaviors and treatment outcomes of DTG-based 2DRs in the US.
- Aging with HIV has unique challenges, including more comorbidities and potential for drug-drug interactions.

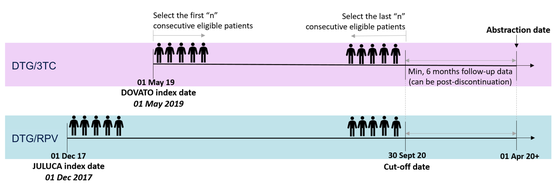
Objectives

- This TANDEM subgroup analysis examines stable-switch PWH receiving DTG/3TC by age.

Methods

- TANDEM was a US-based, retrospective chart review. Data was abstracted from medical charts of PWH (24 sites) who were initiated on DTG/3TC or dolutegravir/rilpivirine (DTG/RPV) prior to Sept/30/2020, with a minimum clinical follow-up of six months (**Figure 1**).
  - Minimum follow-up could include time post-discontinuation of either regimen.
  - Clinical characteristics, treatment history, drivers for prescribing, and post-initiation outcomes were abstracted (minimum 6-months after index date).

Figure 1. Study design (only DTG/3TC stable-switch PWH included in this analysis)



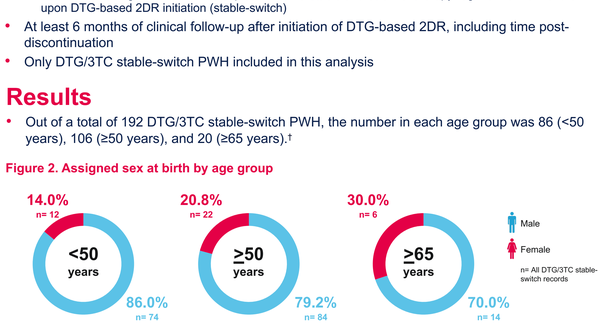
Inclusion Criteria

- ≥18 years old
- Have a diagnosis of HIV-1 infection
- Have a history of antiretroviral therapy (ART) consisting of 2DR
- One of the antiretroviral therapies must be either DTG/3TC or DTG/RPV as a single-tablet regimen (STR)
- DTG/3TC cohort:
  - Must have been initiated after 1st May 2019 (DTG/3TC approved by US Food and Drug Administration on April 8, 2019)
  - Upon initiation, PWH must have been either naïve (N) to antiretroviral therapy or virologically suppressed defined as having HIV-1 RNA <50 copies/mL, on a stable antiretroviral therapy regimen for ≥3 months upon DTG-based 2DR initiation (stable-switch)
- At least 6 months of clinical follow-up after initiation of DTG-based 2DR, including time post-discontinuation
- Only DTG/3TC stable-switch PWH included in this analysis

Results

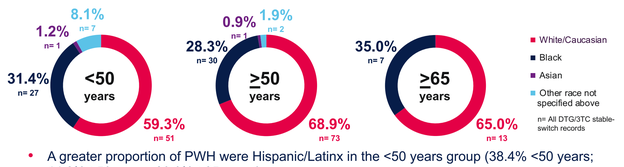
- Out of a total of 192 DTG/3TC stable-switch PWH, the number in each age group was 86 (<50 years), 106 (≥50 years), and 20 (≥65 years).†

Figure 2. Assigned sex at birth by age group



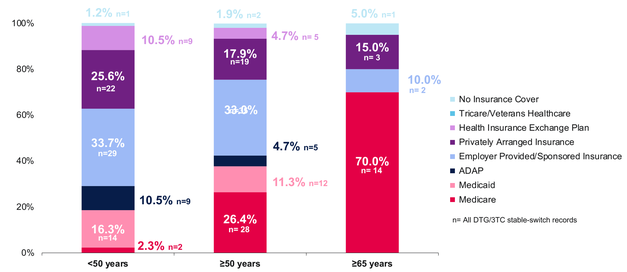
- A higher proportion of PWH in the older age groups were female sex at birth (14.0% <50 years; 20.8% ≥50 years; 30.0% ≥65 years) (**Figure 2**). Across all age groups, PWH were predominantly white / Caucasian (**Figure 3**).

Figure 3. Race by age group



- A greater proportion of PWH were Hispanic/Latinx in the <50 years group (38.4% <50 years; 14.2% ≥50 years; 20.0% ≥65 years).
- The proportion on a Medicare plan increased with age, with other types of insurance (employer-provided, privately arranged, Medicaid and the AIDS Drug Assistance Program (ADAP)) generally decreasing with age (**Figure 4**).

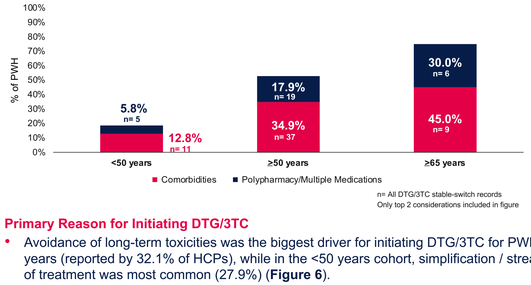
Figure 4. Insurance coverage by age group



Treatment Considerations / Risk Factors by Age

- More PWH in older age groups had reported comorbidities (12.8% <50 years; 34.9% ≥50 years; 45.0% ≥65 years) and polypharmacy (5.8% <50 years; 17.9% ≥50 years; 30.0% ≥65 years (**Figure 5**).
  - No treatment considerations / risk factors were reported for approximately half PWH in each age group (50.0% <50 years, 51.9% ≥50 years, 45.0% ≥65 years).
- PWH aged ≥50 years were more likely to have had >1 previous antiretroviral regimen (81.1%) compared to those aged <50 years (47.7%). Within the oldest sub-group of ≥65 years, the majority (55.0%) had received 3 or more regimens, and 30.0% received more than 5 ART regimens in the past before switching to DTG/3TC.

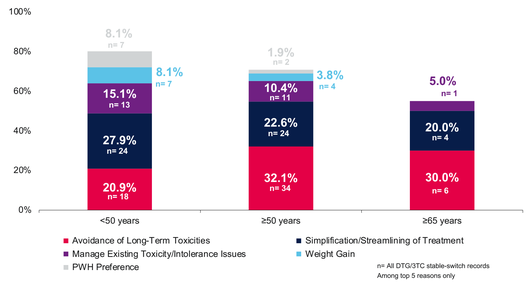
Figure 5. Highlighted treatment considerations / risk factors



Primary Reason for Initiating DTG/3TC

- Avoidance of long-term toxicities was the biggest driver for initiating DTG/3TC for PWH ≥50 years (reported by 32.1% of HCPs), while in the <50 years cohort, simplification / streamlining of treatment was most common (27.9%) (**Figure 6**).
  - DTG/3TC initiation due primarily to comorbidities other than cardiovascular disease (CVD) and chronic kidney disease (CKD) increased with age (n=1 of 86 in <50 years cohort vs. n=3 of 20 in ≥65 cohort).

Figure 6. Primary reason for switching to DTG/3TC



Most recent CD4+ cell count before DTG/3TC initiation

- The most recent CD4+ cell count was collected before DTG/3TC initiation (**Table 1**).

Table 1. CD4+ cell count immediately prior to DTG/3TC initiation, n (cells/mm3)

N= All DTG/3TC stable-switch records	<50 years n=85	≥50 years n=104	≥65 years n=19
Mean	750.2	716.2	756.9
Median (IQR)	743.0 (547.5-914.0)	644.5 (483.8-842.8)	653.0 (456.0-851.0)
StdDev	±298.46	±357.84	±387.66

Data unavailable for n=1 in <50 years, n=2 in >=50 years and n=1 in >=65 year sub-groups

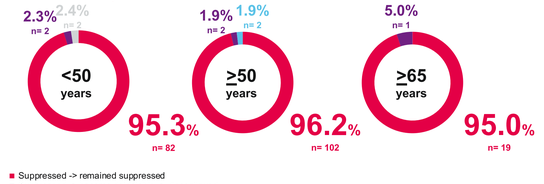
Drug Resistance Testing prior to DTG/3TC initiation

- For the stable-switch cohort, the majority of HCPs indicated that no resistance testing was performed upon initiation of DTG/3TC across age cohorts (85-91%).

Virologic Status at Abstraction Date by Age

- The proportion of PWH that remained virologically suppressed at abstraction date (minimum 6-months after stable-switch to DTG/3TC) was nearly identical across age groups (**Figure 8**).
  - Three PWH with nucleoside/nucleotide reverse transcriptase inhibitor (NRTI) resistance at baseline remained suppressed.

Figure 8. Virologic status at abstraction date (minimum 6-months after stable-switch to DTG/3TC)



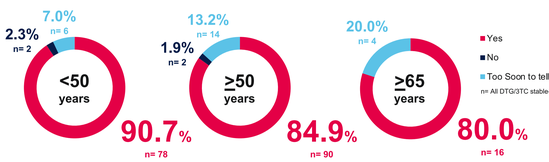
Discontinuation of DTG/3TC at Abstraction Date by Age

- Regardless of age, a very small number of DTG/3TC stable-switch PWH (n=3) had discontinued the regimen at the point of data abstraction. Discontinuation rates were therefore very low for all age groups, with 95-99% remaining on DTG/3TC.
- All three PWH who discontinued were ≥50 years. Median time to discontinuation was 29.6 weeks, from the point of DTG/3TC initiation. Reasons for discontinuation were toxicity / intolerance to DTG/3TC (n=1), PWH preference (n=1) and concerns about weight gain (n=1).

Health Outcomes at Abstraction Date by Age

- Desired health outcomes (in the opinion of the HCP) were achieved in 80% or more of PWH across age groups (**Figure 9**).

Figure 9. In HCPs opinion, did the DTG/3TC regimen achieve the desired health outcome(s) that motivated its use?



Limitations

- The retrospective nature of the analysis implies a selection bias and the number of patients included in the subgroups did not allow for formal statistical testing.

Conclusions

- Virological suppression rates were high and similar by age group among DTG/3TC stable-switch PWH despite higher rates of comorbidities and polypharmacy in the older age groups.
- Avoidance of long-term toxicities was the primary reason for switching to DTG/3TC for PWH ≥50 years.
- This real-world analysis is consistent with clinical study data supporting DTG/3TC as an effective treatment strategy in older PWH.

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.** Panel on Antiretroviral Guidelines for Adults and Adolescents. *Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV*. January 18, 2023.

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

† ≥50 years and ≥65 years were not mutually exclusive groups