Patient-Reported Outcomes among virally suppressed people living with HIV switching to dolutegravir/lamivudine vs. continuing bictegravir/emtricitabine/tenofovir alafenamide from the randomized DYAD study

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BACKGROUND

- We previously demonstrated noninferior efficacy of switching to dolutegravir/lamivudine (DTG/3TC) vs. continuing bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) among stably suppressed adults through Week (W) 48 in the DYAD study however, more drug-related adverse events (AEs) and withdrawals due to AEs occurred in the DTG/3TC arm[1]
- Though safety findings from DYAD provide useful information about tolerability, additional data from patient-reported outcome (PRO) measures would be valuable to provide further insight on the impact of this switch on health-related quality of life, treatment satisfaction and HIV/antiretroviral (ART)-related symptoms
- Here, we present changes in patient-reported outcomes (PROs) through W48 among those switching to DTG/3TC vs. continuing B/F/TAF

METHODS

- DYAD (NCT 04585737) was a Phase IV randomized, open-label, noninferiority study designed to evaluate the efficacy and safety of switching to DTG/3TC compared with continuing B/F/TAF among virologically suppressed adults with HIV-1
- DYAD utilized PRO measures to evaluate HIV and ART-related symptom burden (HIV-SI), treatment satisfaction (HIVTSQ/c) and willingness to switch at baseline, W24 and W48
- The HIV Symptoms Index Distress Module (HIV-SI) is a validated PRO instrument to evaluate the burden of 20 symptoms commonly associated with HIV infection or its treatment. DYAD participants were asked to rate their experiences with each of the 20 symptoms in the past month using a 5-point, Likert scale
- Treatment satisfaction was assessed using the validated 12-item HIV Treatment Satisfaction Questionnaire (HIVTSQ) at Day 1 and the subsequent change version (HIVTSQc) at W24 and W48. The HIVTSQs asked patients to rank their response on a 6-point Likert scale from 6 (very satisfied) to 0 (very dissatisfied) while the HIVTSQc asked patients to rank their response from 3 (much more satisfied now) to -3 (much less satisfied now)
- The willingness to switch survey was a single-question survey with seven response options only administered to those switched to DTG/3TC at baseline
- HIV-SI responses were dichotomized into bothersome (scores of 2 ,3, or 4) vs. not bothersome (scores of 0 or 1) and compared across time by treatment group using Chi-squared testing
- Changes from baseline in HIV-SI and HIVTSQ/c scores were compared between treatment groups with ANCOVA models adjusted for baseline score, gender, age, race/ethnicity, duration of HIV infection, duration of antiretroviral use and prior duration of B/F/TAF
- The frequency reporting each reason for willingness to switch was summarized using descriptive statistics

RESULTS

Table 1. Baseline demographic and clinical characteristics

Characteristic	DTG/3TC N=149	B/F/TAF N=73
Age		
Median (range), y	49 (24-73)	51 (20-73)
Age≥50 y, n (%)	74 (50)	44 (60)
Sex		
Female, n (%)	24 (16)	12 (16)
Race		
Caucasian, n (%)	102 (68)	54 (74)
Black, n (%)	44 (30)	18 (25)
Asian, n (%)	1 (1)	0 (0)
Other, n (%)	2 (1)	1 (1)
Ethnicity		
Hispanic/Latino, n (%)	43 (29)	22 (30)
Not Hispanic/Latino, n (%)	106 (71)	51 (70)
BMI, median (range), kg/m²	29.8 (18.8-56.6)	29.5 (20-49.8)
Weight, median (range), kg	90.4 (53.1-171.9)	88.5 (59.1-123.5)
CD4⁺ T-cell count, median (range), cells/mm³	720.5 (214-1479)	734.5 (151-1573)
≥350 cells/mm³, n (%)	139 (93)	70 (96)
<350 cells/mm³, n (%)	10 (7)	3 (4)
Duration of HIV infection prior to Day 1, median (range), years	13 (1-36)	14 (1-36)
Duration of ART prior to Day 1, median (range), years	12 (1-32)	9.5 (1-27)
Duration of B/F/TAF prior to Day 1, median (range), years	2 (0.5-7.5)	2.5 (0.5-7.5)
Number of ART regimens prior to Day 1	3 (1-9)	3 (1-10)
Current Insurance Coverage		
Private, n (%)	132 (89)	59 (81)
Medicaid, n (%)	5 (3)	2 (3)
Medicare, n (%)	12 (8)	10 (13)
Ryan White, n (%)	0 (0)	2 (3)

Abbreviations. BMI, Body Mass Index; ART, antiretroviral therapy; HIV, human immunodeficiency virus; DTG, dolutegravir; 3TC, lamivudine; B, bictegravir; F, emtricitabine; TAF, tenofovir alafenamide

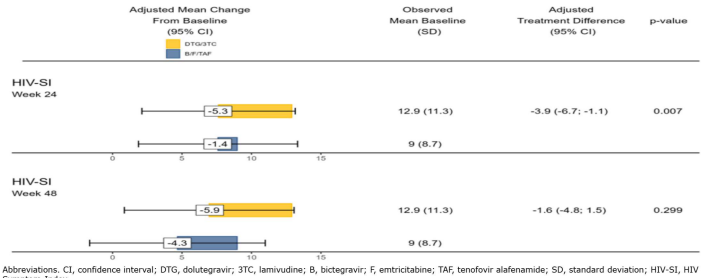
Table 2. Frequency of bothersome HIV symptoms by treatment and study visit

Participants reporting symptom, %	Baseline		Week 24		Week 48	
	DTG/3TC	B/F/TAF	DTG/3TC	B/F/TAF	DTG/3TC	B/F/TAF
Fatigue/loss of energy	40	28	24	30	30	20
Fever/chills/sweats	4	7	2	8	9	2
Dizzy/lightheadedness	**14**	**3**	5	9	8	8
Pain/numbness/tingling in hands/feet	26	29	14	21	18	17
Trouble remembering	25	19	18	22	19	22
Nausea/vomiting	5	7	2	3	3	6
Diarrhea/loose bowels	14	7	7	8	**10**	**0**
Sad/down/depressed	28	23	15	10	17	9
Nervous/anxious	27	25	20	18	17	11
Difficulty sleeping	42	30	28	25	29	25
Skin problems/rash/itching	13	15	15	15	14	6
Coughing/trouble breathing	14	7	7	9	9	6
Headaches	19	11	**16**	**6**	13	9
Loss of appetite	10	4	3	2	3	2
Bloating/pain/gas in stomach	29	19	13	12	14	9
Muscle aches/joint pain	33	30	23	24	25	25
Problems with sex	28	17	17	12	19	9
Changes in body composition	48	34	21	21	21	22
Weight loss/wasting	19	10	10	9	8	8
Hair loss/changes	16	11	8	10	8	9

Bolded characters are for significantly different percentages between treatment groups (p<0.05)
Abbreviations. DTG, dolutegravir; 3TC, lamivudine; B, bictegravir; F, emtricitabine; TAF, tenofovir alafenamide

At W24, 16% on DTG/3TC reported headache as bothersome compared to 6% on B/F/TAF (p=0.04), however, at W48 there was no significant difference in headache. At W48, 10% on DTG/3TC reported diarrhea as bothersome compared to 0% on B/F/TAF (p=0.01), however, there was no significant difference in diarrhea at W24. There were no other significant differences in bothersome symptoms through W48.

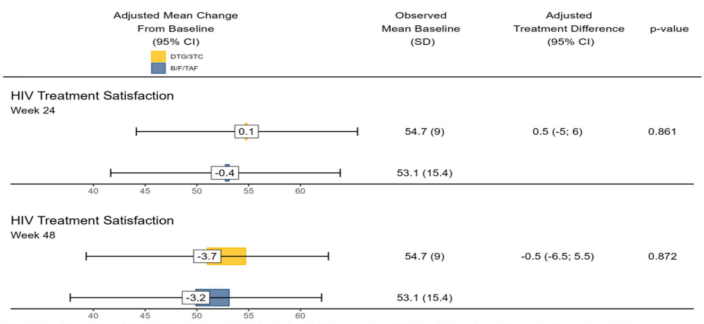
Figure 1. Mean change in HIV-SI symptom score through Week 48



Abbreviations. CI, confidence interval; DTG, dolutegravir; 3TC, lamivudine; B, bictegravir; F, emtricitabine; TAF, tenofovir alafenamide; SD, standard deviation; HIV-SI, HIV Symptom-Index

At Weeks 24 and 48, there were larger declines in total HIV-SI symptom score in the DTG/3TC arm compared to those continuing B/F/TAF, however the differences by treatment arm were not statistically significant.

Figure 2. Mean change in HIV treatment satisfaction score through Week 48



Abbreviations. CI, confidence interval; DTG, dolutegravir; 3TC, lamivudine; B, bictegravir; F, emtricitabine; TAF, tenofovir alafenamide; SD, standard deviation

At Weeks 24 and 48, there were small changes in total HIV treatment satisfaction score that did not differ significantly by study arm. There were no significant differences by study arm for changes in any of the individual treatment satisfaction score items through Week 48.

RESULTS cont'd

Table 3. Results from baseline willingness to switch survey in the DTG/3TC arm

Participants reporting reason, n (%)	DTG/3TC N=134
Side effects with the current regimen	8 (6)
Concern about the long-term effects of the current regimen	31 (23)
Adherence issues with the current regimen	0 (0)
Interested in research of new HIV therapies	114 (85)
Provider request to participate in study	80 (60)
Cost of current HIV drug	3 (2)
Other	12 (9)

Abbreviations. DTG, dolutegravir; 3TC, lamivudine

At baseline, top reasons for willingness to switch among those on DTG/3TC were interest in research of new HIV therapies (85%), physician request to participate in the study (60%) and concerns about long-term effects of current regimen (23).

LIMITATIONS

- The DYAD study enrolled stably suppressed participants on a single-tablet-regimen hence generalizability of these PRO data should be done with caution
- Though DYAD enrolled a diverse population, these results are not generalizable to many underrepresented groups as the majority of study participants were male and white
- We note that HIV is a chronic disease requiring lifelong treatment hence PRO data collected through Week 48 may not adequately capture an individual's long-term experience with HIV treatment

CONCLUSIONS

- Through Week 48, participants in both treatment arms reported lower HIV/ART-related symptom burden and declines in symptom score were higher in the DTG/3TC arm though this was not statistically significant
- At Week 24, 16% on DTG/3TC reported headache as bothersome compared to 6% on B/F/TAF (p=0.04), however, at Week 48 there was no significant difference in headache. At W48, 10% on DTG/3TC reported diarrhea as bothersome compared to 0% on B/F/TAF (p=0.01), however, there was no significant difference in diarrhea at Week 24. There were no other significant differences in bothersome symptoms through Week 48.
- There were small reductions in HIV treatment satisfaction score that were not significantly different by study arm
- These data are the first describing PRO outcomes from a randomized clinical trial of DTG/3TC and B/F/TAF and support DTG/3TC as a robust switch option with comparable symptom burden and treatment satisfaction to modern 3-drug integrase inhibitor-based regimens.

References
[1]Rolle et al. Open Forum Infect Dis. 2024 Sep 26;11(10):ofae560

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