bictegravir/emtricitabine/tenofovir alafenamide among virologically suppressed adults-results from the 144-week observational extension phase of the DYAD study

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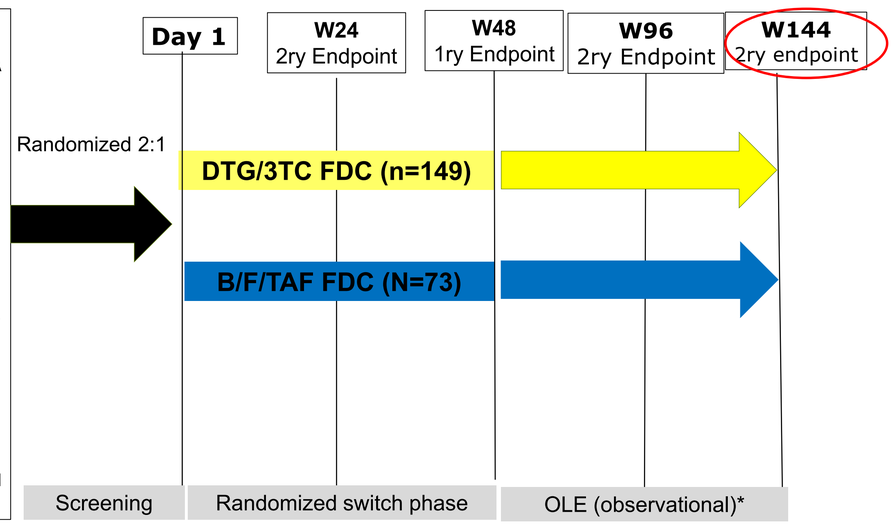
BACKGROUND

- DYAD demonstrated noninferior efficacy of switching to dolutegravir/lamivudine (DTG/3TC) vs. continuing bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) among virologically suppressed adults through Week (W) 48[1]
- In the real-world, open-label extension phase, virologic suppression and persistence were similar between treatment arms at W96, however drug-related adverse events (AEs) and discontinuations due to AEs were higher with DTG/3TC[2]
- Here, we present long-term, efficacy, safety and persistence from the observational extension phase through W144

METHODS

DYAD (NCT04585737) was an open-label randomized clinical trial of virologically suppressed adults

Eligibility criteria
- On B/F/TAF for ≥3 months
- Two documented HIV-1 RNA measurements <50 copies/mL on B/F/TAF at least 3 months apart
- No HBV infection or acute need for HCV therapy
- No history of prior virologic failure
- No suspected or documented INSTI resistance
- History of 1-2 thymidine analogue mutations (TAMs), and other reverse transcriptase substitutions allowed, with the following exceptions: History of 3 or more TAMs (M41L, D67N, K70R, L210W, T215F/Y, and K219Q/E/N/R), M184V/I, T69-insertions, or K65R/E/N



- Primary endpoint of the study was the proportion of participants with HIV-1 RNA≥50 c/mL at Week 48 using the FDA snapshot algorithm (ITT-E)
- At study exit, informed consent was obtained from participants to collect and report virologic efficacy, safety and persistence on therapy from electronic medical records through Weeks 96 and 144
- Mean change in creatinine, glomerular filtration rate, lipid parameters, weight, and BMI at Week 144 were compared between treatment groups using 2-sample t-tests.

RESULTS

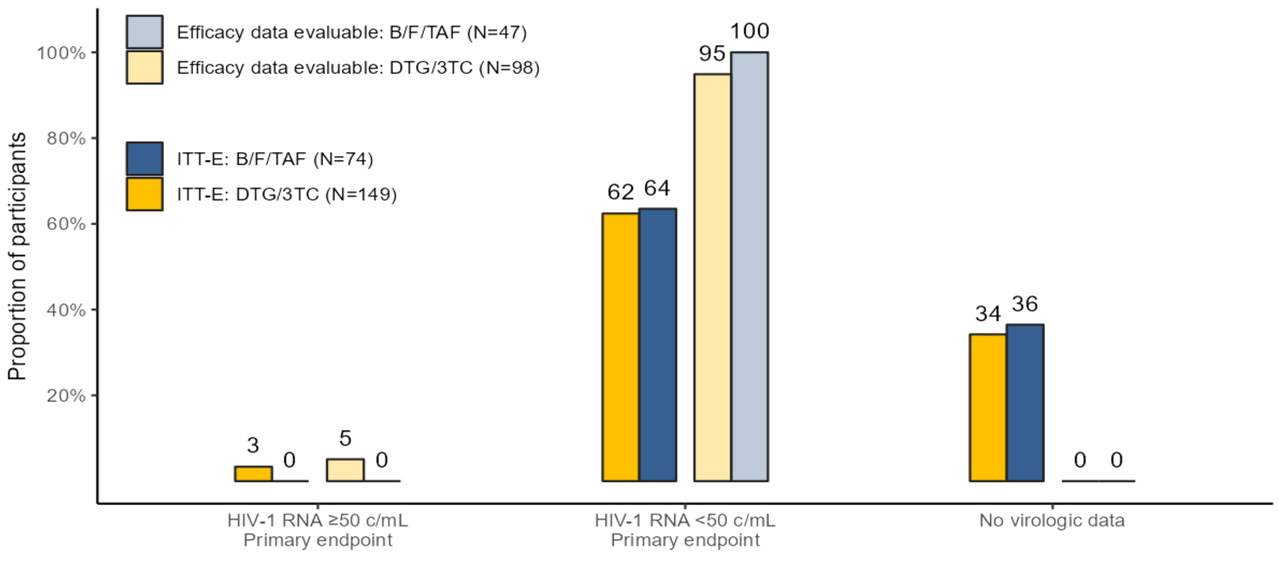
Table 1. Baseline demographic and clinical characteristics

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)	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+ cell count, median (range) cells/mm3	720.5 (214-1479)	734.5 (151-1573)
CD4⁺ cell count		
≥350 cells/mm^3, n (%)	139 (93)	70 (96)
<350 cells/mm^3, n (%)	10 (7)	3 (4)
Duration of HIV infection, 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)
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)
Baseline genotype available, n (%)	60 (40)	37 (51)
NRTI Resistance, n (%)	3 (2)	6 (8)
NNRTI Resistance, n (%)	16 (11)	13 (18)
PI Resistance, n (%)	27 (18)	16 (22)
INSTI Resistance, n (%)	1 (1)	2 (3)

Abbreviations. BMI, Body Mass Index; ART, antiretroviral therapy; HIV, human immunodeficiency virus; NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; DTG, dolutegravir; 3TC, lamivudine; B, bictegravir; F, emtricitabine; TAF, tenofovir alafenamide

At Week 48, 134 on DTG/3TC and 65 on B/F/TAF completed the study. Of these, 124 on DTG/3TC and 63 on B/F/TAF consented to participate in the observational extension phase

Figure 1. Virologic outcomes at Week 144 by FDA Snapshot Analysis



Abbreviations. B, bictegravir; F, emtricitabine; TAF, tenofovir alafenamide; DTG, dolutegravir; 3TC, lamivudine; ITT-E, intention-to-treat evaluation; c/mL, copies/mL

RESULTS cont'd

Table 2. Week 144 Study Outcome by Snapshot Analysis

	DTG/3TC (N=149) n (%)	B/F/TAF (N=73) n (%)	Adjusted treatment difference (95% CI)
HIV-1 RNA ≥ 50 c/mL	5 (3)	0 (0)	3.4% (-1.6%, 7.6%)
HIV-1 RNA < 50 c/mL	93 (62)	47 (64)	1.1% (-12.5%, 8.5%)
No virologic data	51 (34)	27 (36)	

Abbreviations. DTG, dolutegravir; 3TC, lamivudine; B, bictegravir; F, emtricitabine; TAF, tenofovir alafenamide; CI, confidence interval; c/ml, copies/mL

At Week 144, 5 (3%) on DTG/3TC and 0 (0%) on B/F/TAF had HIV-1 RNA≥50 c/mL (adjusted treatment difference 3.4%, 95% confidence interval [-1.6%, 7.6%]).

Confirmed Virologic Failures and Resistance

Through Week 144, 16 (11%) on DTG/3TC and 6 (8%) on B/F/TAF met confirmed virologic failure (CVF) criteria (defined as two consecutive HIV-1 RNA values≥50 c/mL), resistance was observed in 2 (1%) on DTG/3TC and 1 (1%) on B/F/TAF. Between Weeks 48-144, 4 on DTG/3TC experienced CVF, and there was no evidence of treatment-emergent resistance

Table 3. Persistence on DTG/3TC vs. B/F/TAF through Week 144

	DTG/3TC N (%)	B/F/TAF N (%)
Remains on therapy at Week 144	108 (72)	54 (74)
Discontinuations for any reason		
Weeks 0-48	15 (10)	8 (11)
Weeks 0-96	37 (25)	14 (19)
Weeks 0-144	41 (28)	19 (26)
Reasons for Discontinuation, Weeks 0-144		
Consent Withdrawal	11 (7.4)	6 (8)
Adverse Events	11 (7.4)	0 (0)
Lost to follow up	9 (6)	7 (10)
Change to LAI	4 (3)	2 (3)
Research Study Participation	2 (1.35)	2 (3)
Confirmed virologic failure[a]	2 (1.35)	1 (1)
Participant request	1 (0.7)	1 (1)
Low-level viremia[b]	1 (0.7)	0 (0)

[a]14 CVFs in the DTG/3TC arm remained in the study and continued DTG/3TC, 12 resuppressed on DTG/3TC and 2 continued to have low-level viremia (HIV-1 RNA<200 c/mL) through W144. 5 CVFs in the B/F/TAF arm remained in the study on B/F/TAF and all resuppressed.
[b]Participant did not meet criteria for confirmed virologic failure
Abbreviations. DTG, dolutegravir; 3TC, lamivudine; B, bictegravir; F, emtricitabine; TAF, tenofovir alafenamide; LAI, long acting injectable

The most common reasons for DTG/3TC discontinuation were adverse events (AEs) (11/41, (27%)) and consent withdrawal (11/41, (27%)), whereas B/F/TAF discontinuation was most commonly due to lost to follow-up (7/19, (37%))

AEs, n (%)	DTG/3TC N=149	B/F/TAF N=73
Participants reporting drug-related AEs		
Weeks 0-24	31 (21)	1 (1)
Weeks 0-96	42 (28)	4 (5)
Weeks 0-144	49 (33)	8 (11)
Drug-related AEs, Weeks 0-144 (occurring in ≥2%)		
Nausea	8 (5.3)	1 (1)
Fatigue	6 (4)	0 (0)
Diarrhea	6 (4)	0 (0)
Headaches	5 (3)	0 (0)
Insomnia	7 (4.7)	2 (3)
Weight gain	6 (4)	1 (1)
Worsening depression	4 (3)	1 (1)
Light-headedness	3 (2)	0 (0)
Elevated serum creatinine	3 (2)	1 (1)
Drug-related AEs leading to withdrawal		
Weeks 0-24	6 (4)	0 (0)
Weeks 0-96	11 (7)	0 (0)
Weeks 0-144	11 (7)[a]	0 (0)
Any SAEs, Weeks 0-144	13 (9)[b]	4 (5)
Drug-Related SAEs, Weeks 0-24	1 (0.7)	0 (0)
Drug-Related SAEs, Weeks 0-96	1 (0.7)	0 (0)
Drug-Related SAEs, Weeks 0-144	1 (0.7)	0 (0)

Abbreviations. AEs, adverse events; DTG, dolutegravir; 3TC, lamivudine; B, bictegravir; F, emtricitabine; TAF, tenofovir alafenamide; SAEs, serious adverse events
[a]AEs leading to withdrawal included neuropsychiatric complaints (7), weight gain (2), pancreatitis (1) and nausea (1)
[b]Includes one drug-related SAE in the DTG/3TC arm (pancreatitis), all other SAEs unrelated to drug and no fatal SAEs were observed

Table 5. Mean change from baseline in renal and metabolic parameters at Week 144

Parameter and Timepoint	DTG/3TC N=149	B/F/TAF N=73	Between group difference (95% CI)	P-value
Creatinine, mg/dL Week 144 Change (Mean ± SD)	0.03 ± 0.13	0.04 ± 0.13	-0.01 (-0.06 ; 0.04)	0.652
eGFR, mL/min Week 144 Change (Mean ± SD)	-3.84 ± 12.95	0.51 ± 15.2	-4.35 (-9.47 ; 0.78)	0.095
Total Cholesterol, mg/dL Week 144 Change (Mean ± SD)	-9.2 ± 34.23	-3.02 ± 27.73	-6.18 (-17.31 ; 4.96)	0.274
LDL Cholesterol, mg/dL Week 144 Change (Mean ± SD)	-8.39 ± 31.27	-5.22 ± 21.58	-3.17 (-12.7 ; 6.35)	0.511
HDL Cholesterol, mg/dL Week 144 Change (Mean ± SD)	-0.06 ± 7.07	0.18 ± 9.33	-0.24 (-3.42 ; 2.94)	0.881
Triglycerides, mg/dL Week 144 Change (Mean ± SD)	-3.12 ± 84.9	13.38 ± 81.63	-16.5 (-47.07 ; 14.07)	0.287
Total Cholesterol:HDL ratio Week 144 Change (Mean ± SD)	-0.3 ± 0.92	-0.22 ± 0.77	-0.08 (-0.47 ; 0.31)	0.692
Weight, kg Week 144 Change (Mean ± SD)	-1.67 ± 6.73	-1.85 ± 7.66	0.18 (-2.48 ; 2.84)	0.895
BMI, kg/m² Week 144 Change (Mean ± SD)	-0.97 ± 2.51	-1.11 ± 2.54	0.14 (-0.78 ; 1.05)	0.766

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

At Week 144, no significant differences in mean change from baseline in creatinine, lipid parameters, weight, and BMI were observed between treatment groups.

CONCLUSIONS

- In the 144-week DYAD observational extension phase, there was similar virologic efficacy among those switching to DTG/3TC vs. continuing B/F/TAF
- Three additional participants in the DTG/3TC arm experienced CVF between Weeks 96-144 and none had any treatment-emergent resistance
- Persistence was similar between treatment arms, however drug-related AEs continued to be higher with DTG/3TC

References
[1]Rolle CP et al. Open Forum Infect Dis. 2024 Sep 26;11(10):ofae560.
[2]Rolle CP et al. Poster P-348. IDWeek 2025, Atlanta, GA.

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