Use of *Dovato* in 'Test and Treat' Strategy

Summary

- The STAT study assessed *Dovato* (dolutegravir/lamivudine [DTG/3TC]) as a first-line regimen in a 'test-and-treat' model of care in the United States [1]:
  - Among all patients, 102/131 (78%) achieved HIV-1 RNA <50 copies/mL at Week 24 (Intention-to-treat–exposed [ITT-E] missing = failure analysis), irrespective of antiretroviral therapy (ART).
  - Low rates of grade 2-5 drug-related adverse events (AEs, 2%) and serious AEs (2%). One patient discontinued DTG/3TC due to an adverse event.
- The TANDEM study is a real-world evidence cohort in the United States (US) that characterizes prescribing behaviors and treatment outcomes of DTG/3TC.[2]
  - In a subgroup of test and treat patients, 57 (93.4%) achieved virologic suppression and 1 discontinuing DTG/3TC at data cut-off.
- Important safety information and boxed warning(s) can be found in the Prescribing Information link and can also be accessed at Our HIV Medicines.

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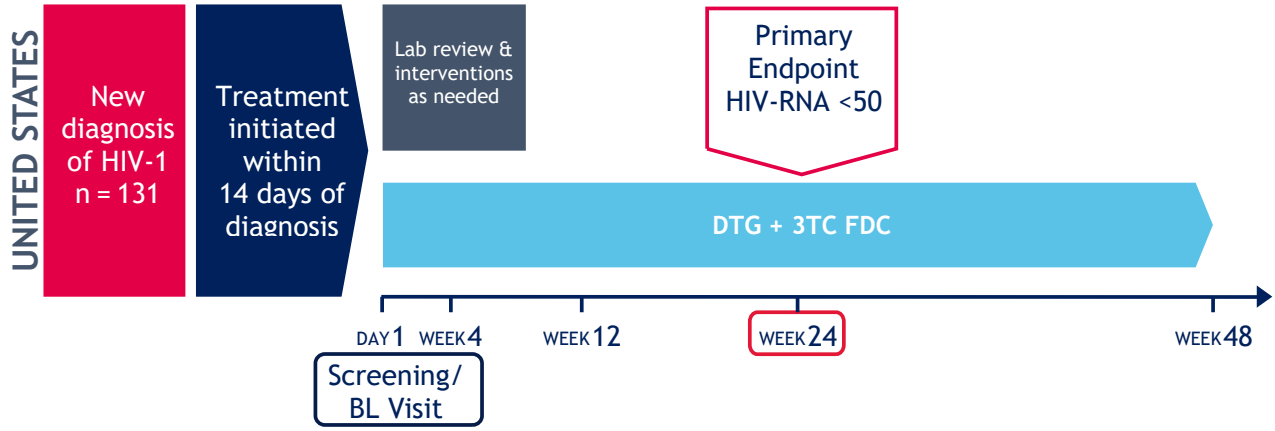
STAT STUDY[1]

The STAT study (ClinicalTrials.gov, NCT03945981) is a phase 3b, multicenter, open-label, single-arm, pilot study assessing the feasibility, efficacy, and safety of using DTG/3TC as a first-line regimen in a 'test-and-treat' model of care in the United States.

Figure 1. STAT Study Design[1]



Eligible participants were ART-naïve adults aged ≥18 years diagnosed with HIV within 14 days of study entry for whom laboratory results were not available at baseline. DTG/3TC treatment was adjusted if baseline testing indicated HBV co-infection, genotypic resistance to DTG or 3TC, or creatinine clearance <30 mL/min/1.73 m², or as required during the study, and all participants with treatment adjustments remained on study. The primary endpoint was the proportion of participants with HIV-RNA <50 copies/mL at Week 24, regardless of ART regimen (ITT-E, missing=failure). Participants with HIV-1 RNA ≥50 copies/mL at Week 24 or with no HIV-1 RNA assessment at Week 24 due to early discontinuation or still on study but with missing data are classified as HIV-1 RNA ≥50 copies/mL. Other key efficacy analyses are defined and summarized below.

- Observed Analysis: Proportion of participants with plasma HIV-1 RNA <50 copies/mL, regardless of ART regimen, among those with available HIV-1 RNA at Week 24
- FDA Snapshot Analysis: Proportion of all participants with plasma HIV-1 RNA <50 copies/mL at Week 24 still taking DTG/3TC

Baseline characteristics and demographics were similar between study arms.

Table 1. Select Baseline Characteristics, STAT Study[1]

Characteristic	DTG/3TC (N=131)
Age, median (range), years	31 (18-63)
≥50 years, n (%)	20 (15)
Cisgender female, n (%)	10 (8)
Transgender female, n (%)	1 (<1)
Ethnicity, n (%)	
Hispanic/Latino	38 (29)
Not Hispanic/Latino	93 (71)
Race, n (%)	
Black/African American	61 (47)
White	65 (50)
Other	5 (4)
Time to enrollment since diagnosis, median (range), days	5 (0-15)
HIV-1 RNA, median (range), copies/mL, n (%)[a,b]	63,056 (<40 to 68,706,840)[c]
<100,000	79 (60)
100,000 to <500,000	32 (24)
500,000 to <1,000,000	9 (7)
≥1,000,000	10 (8)
CD4+ cell count, median (range), cells/mm[3b]	389.0 (<20 to 1466)[d]
<200, n (%)	37 (28)
HBV co-infection, n (%)[b,e]	7 (5)
M184V resistance mutation, n (%)[b]	1 (<1)

[a]1 (<1%) participant had missing plasma HIV-1 RNA results at Baseline. [b]Baseline resistance was identified at Week 4, and HIV-1 viral load, CD4+ cell count, and HBV co-infection were identified at Week 1 from samples taken at Baseline. [c]Lower limit of quantification is <40. [d]Lower limit of quantification is <20. [e]2 patients with HBV co-infection remained on DTG/3TC.

DTG = dolutegravir; 3TC = lamivudine; HBV = hepatitis B virus.

The primary endpoint: ITT-E missing = failure analysis, 78% of all patients achieved HIV-1 RNA <50 copies/mL at Week 24, irrespective of ART (Table 2).

Table 2. Summary of Virologic Outcomes at Week 24 and 48[1,3]

	Week 24 DTG/3TC, n/N (%)	Week 48 DTG/3TC, n/N (%)
ITT-E missing = failure analysis		
HIV-1 RNA <50 c/mL	102/131 (78)	107/131 (82)
HIV-1 RNA ≥50 c/mL	29/131 (22)	24/131 (18)
Data in window and HIV-1 RNA ≥50 c/mL	9/131 (7)	3/131 (2)
On study but missing data in window	5/131 (4)[a]	3/131 (2)[d]
Discontinued study due to lost to follow-up/withdrew consent	12/131 (9)[b]	14/131 (11)[e]
Discontinued study for other reasons	3/131 (2)[c]	4/131 (3)[f]
Observed analysis		
HIV-1 RNA <50 c/mL	102/111 (92)	107/110 (97)
On DTG/3TC	97/111 (87)	100/107 (93)
On modified ART	5/111 (5)	7/107 (7)
FDA Snapshot analysis		
HIV-1 RNA <50 c/mL	97/131 (74)	100/131 (76)
HIV-1 RNA ≥50 c/mL	23/131 (18)	19/131 (15)
Data in window and HIV-1 RNA ≥50 c/mL	9/131 (7)	3/131 (2)
Discontinued for lack of efficacy	0	0

Discontinued study for other reason and HIV-1 RNA ≥50 c/mL	6/131 (5)	6/131 (5)
Change in ART	8/131 (6)	10/131 (8)
No virologic data	11/131 (8)	12/131 (9)

[a]3 participants missed HIV-1 RNA assessment at Week 24 due to COVID-19. [b]7 due to lost to follow-up; 5 withdrew consent (3 relocations, 1 incarceration, 1 no sub-reason). [c]3 due to physician decision (2 HIV negative, 1 did not show up to several scheduled appointments). [d]1 participant missed HIV-1 RNA assessment at Week 48 due to COVID-19. [e]8 due to lost to follow-up; 6 withdrew consent (3 relocations, 2 incarcerations, 1 no sub-reason). [f]All due to physician decision (2 HIV negative, 2 did not show up to several scheduled appointments).

3TC = lamivudine; DTG = dolutegravir.

All participants with available data who had an ART adjustment and remained on study at Week 48 had HIV-1 RNA <50 c/mL (Table 3).

Table 3. Participants Who Switched From DTG/3TC at Any Time Point by Week 48[3]

Reason for switch	Visit window	Modified ART	Plasma HIV-1 RNA at Week 24
Baseline HBV	Week 1	DTG/3TC + TAF	<40 c/mL
Baseline HBV	Week 1	BIC/FTC/TAF	NA[a]
Baseline HBV	Week 4	DTG + TDF/FTC	<40 c/mL
Baseline HBV	Week 4	BIC/FTC/TAF or DTG + TDF/FTC[b]	49 c/mL
Decision by participant or proxy	Week 4	BIC/FTC/TAF	NA[c]
Baseline HBV	Week 8	DTG/3TC + TAF	<40 c/mL
Baseline M184V	Week 8	DTG/RPV	NA[d]
Adverse event (rash)	Week 12; Week 12	COBI/DRV/FTC/TAF; BIC/FTC/TAF[e]	<40 c/mL
Decision by participant or proxy	Week 24	BIC/FTC/TAF	<40 c/mL
Pregnancy	Week 24	DTG/ABC/3TC	327 c/mL; <40 c/mL
Participants who switched after Week 48 HIV-1 RNA assessment			
Lack of efficacy	Week 48	DTG + 3TC[f]	223 c/mL; 182 c/mL; 831 c/mL
Non-adherence	Post-Week 48	Off treatment[g]	NA

[a]Participant on study but missing data in window. Participant had HIV-1 RNA <40 c/mL at Week 36. [b]Participant participates in another double-blind clinical trial with a tenofovir-based regimen; switched to either BIC/FTC/TAF or FTC/TDF + DTG. [c]Participant withdrew consent after switch from DTG/3TC. [d]Participant had HIV-1 RNA 18,752 c/mL at baseline, <40 c/mL on Day 47, switched to DTG/RPV on Day 49, and had last HIV-1 RNA 54 c/mL on Day 57; participant withdrew consent (due to relocation) on Day 106 (Week 12). [e]Participant switched ART twice. [f]Participant switched to BIC/FTC/TAF post-Week 48 HIV-1 RNA assessment (after the 831 c/mL assessment); HIV-1 RNA was 51 c/mL at last follow-up visit. [g]Participant stopped DTG/3TC due to non-adherence and re-started DTG/3TC ~4 months later; last HIV-1 RNA was 104 c/mL at last follow-up visit on modified ART.

3TC = lamivudine; ABC = abacavir; BIC = bictegravir; COBI = cobicistat; DTG = dolutegravir; DRV = darunavir; FTC = emtricitabine; HBV = hepatitis B Virus; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

There were low rates of grade 2-5 drug-related AEs (2%) and serious AEs (2%) reported in the study (see Table 4).

Table 4. AEs Reported with DTG/3TC Treatment in STAT at Week 48[3]

Characteristic, n (%)	DTG/3TC (N=131)
Any AE	100 (76)
AEs occurring in ≥7% of patients	
Headache	12 (9)
Diarrhea	10 (8)
Depression	9 (7)
Nausea	9 (7)
Drug-related AEs	10 (8)
Grade 2-5 AEs	3 (2)[a]
AEs leading to discontinuation of DTG/3TC	1 (<1)[b]
Any SAE	2 (2)[c]

[a]All AEs were grade 2. [b]1 AE leading to discontinuation of DTG/3TC occurred (rash). The event resolved. [c]2 SAEs occurred (cellulitis, streptococcal bacteremia). No fatal SAEs occurred. AEs were coded using MedDRA v23.1.

3TC = lamivudine; AE = adverse event; DTG = dolutegravir.

TANDEM STUDY

The TANDEM study was a retrospective chart review of 24 sites throughout the US designed to describe real-world prescribing behaviors and treatment outcomes of DTG 2 drug-based regimens (2DR).[4] Out of a total population of 469 patients, 318 received DTG/3TC, of whom 126 were treatment-naïve and 192 were virologically suppressed (HIV-1 RNA <50 copies/mL) on a stable ART regimen for ≥3 months upon DTG-based 2DR initiation (SS). Patients had to have at least 6 months of clinical follow-up after initiation of DTG/3TC.

Approximately half (61/126) of the treatment naïve patients received DTG/3TC within a test and treat approach.[2] Relevant treatment considerations differed between the test and treat group and non-test and treat with the main consideration in the test and treat group identified as limited access to healthcare; whereas comorbidities were the main consideration for the non-test and treat group.

At data cut-off, 57 (93.4%) of the test and treat group achieved virologic suppression, 3 (4.9%) did not, and 1 (1.6%) was still unknown; in the non-test and treat group, 59 (95.2%) achieved virologic suppression.[2] Of the 3 individuals in the test and treat group who did not achieve viral suppression, 2 remained on DTG/3TC and 1 was switched to BIC/FTC/TAF. Virologic rebound occurred in 6 patients in the treatment naïve cohort, with 1 of these occurring in the test and treat group. See table 5 for additional virologic outcomes.

Table 5. Virologic Outcomes in the TANDEM Study[2]

	Test & Treat (n = 61)	Non-Test & Treat (n = 62)
Time to virologic suppression following DTG/3TC initiation (weeks)		
Median (IQR)	9.7 (5.8, 17.7)	10.7 (5.4, 19.3)
Time since virological suppression observed (weeks)		
Median (IQR)	59.9 (33.3, 79.3)	48.5 (29.8, 77.6)
% sustaining viral suppression to 24 weeks[a]	48 (78.7)	45 (72.6)
Discontinuation Status, n (%)		
Discontinued DTG/3TC[b]	1 (1.6)	0 (0.0)
Ongoing DTG/3TC	60 (98.4)	60 (96.8)
Unknown/lost to follow-up	0 (0.0)	2 (3.2)

3TC = lamivudine; DTG = dolutegravir; IQR = interquartile range.

[a] All had at least 24 weeks of clinical follow-up post-initiation of DTG/3TC; n=3 test and treat and n=7 non test and treat patients had remained virologically suppressed to data abstraction but had not yet reached 24 weeks suppressed; [b] Primary reason for the n=1 discontinuation was due to 'persistent low-level viremia or viral blips'.

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