FEASIBILITY, EFFICACY, AND SAFETY OF USING DOLUTEGRAVIR/LAMIVUDINE (DTG/3TC) AS A FIRST-LINE REGIMEN IN A TEST-AND-TREAT SETTING FOR NEWLY DIAGNOSED PEOPLE LIVING WITH HIV (PLWH): THE STAT STUDY

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Introduction

- Rapid initiation of antiretroviral therapy (ART) increases ART uptake, improves virologic suppression rates, and reduces onward HIV transmission[1-3]
- Dolutegravir (DTG)/Lamivudine (3TC) is indicated for treatment-naive people living with HIV (PLWH)
- Questions remain about its use in a test-and-treat setting due to potential transmitted resistance and baseline (BL) hepatitis B virus (HBV) co-infection
  - Globally, the estimated prevalence of transmitted M184V mutations is 1%[4]
  - Although 3TC has activity against HBV infection, it is not recommended for use as monotherapy because of the risk of developing resistance[5]
- The STAT study (ClinicalTrials.gov, NCT03945981) is a phase IIIb, 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

Methods

- Eligible participants were ART-naive adults aged ≥18 years diagnosed with HIV within 14 days of study entry for whom laboratory results were not available at BL
- DTG/3TC treatment was adjusted if BL testing indicated HBV co-infection, genotypic resistance to DTG or 3TC, or creatinine clearance <30 mL/min/1.73 m^2, or as required during the study, and all participants with treatment adjustments remained on study
- Key efficacy analyses
  - **Observed:** Proportion of participants with plasma HIV-1 RNA <50 c/mL, regardless of ART regimen, among those with available HIV-1 RNA at Week 24
  - **Intention-to-treat–exposed (ITT-E) missing = failure:** Proportion of **all** participants with plasma HIV-1 RNA <50 c/mL at Week 24, regardless of ART regimen
    - Participants with HIV-1 RNA ≥50 c/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 c/mL
  - **FDA Snapshot:** Proportion of **all** participants with plasma HIV-1 RNA <50 c/mL at Week 24 still taking DTG/3TC
- Safety of DTG/3TC was assessed as incidence and severity of adverse events (AEs), drug-related AEs, discontinuation of DTG/3TC due to AEs, and laboratory abnormalities

Results

Participant Characteristics

- Overall, 131 participants were enrolled in the study across 16 sites (Table 1)
- Through Week 24, DTG/3TC treatment was adjusted in 8 participants; 15 (11%) participants discontinued study before Week 24 (Table 2)
  - 2 participants met the inclusion criteria for 2 positive HIV tests and enrolled in the study, but later they were found to be HIV negative and withdrew from study

Table 1. Selected Baseline Demographics and Participant Characteristics (ITT-E Population)

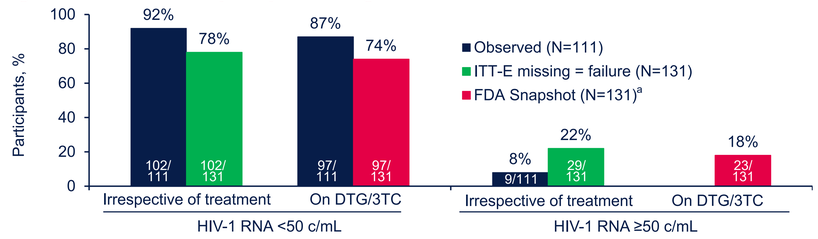
Characteristic	DTG/3TC (N=131)
Age, median (range), years	31 (18-63)
≥50 years, n (%)	20 (15)
Cisgender female, n (%)	10 (8)
Transgender female, n (%)	1 (<1)
Ethnicity, n (%)	
Hispanic/Latino	38 (29)
Not Hispanic/Latino	93 (71)
Race, n (%)	
Black/African American	61 (47)
White	65 (50)
Other	5 (4)
Time to enrollment since diagnosis, median (range), days	5 (0-15)
HIV-1 RNA, median (range), c/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^3[b]	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 BL. [b]BL 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 BL. [c]Lower limit of quantification is <40. [d]Lower limit of quantification is <20. [e]2 participants with HBV co-infection remained on DTG/3TC.

Virologic Outcomes at Week 24

- Per observed analysis, among participants with available HIV-1 RNA assessment at Week 24 (N=111), 92% achieved HIV-1 RNA <50 c/mL (Figure 1 and Table 2) and 98% achieved HIV-1 RNA <200 c/mL at Week 24, irrespective of ART
  - 87% achieved HIV-1 RNA <50 c/mL on DTG/3TC without a modified ART regimen
- Per ITT-E missing = failure analysis, among all participants, 78% achieved HIV-1 RNA <50 c/mL at Week 24, irrespective of ART (Figure 1 and Table 2)
- ITT-E suppression rates were driven by non-virologic factors (ie, high withdrawal rate)
- At Week 24, median $\log_{10}$ decrease from BL in plasma HIV-1 RNA on any ART was 3.2 $\log_{10}$ c/mL (n=110)
- Per FDA Snapshot analysis, among all participants, 74% achieved HIV-1 RNA <50 c/mL at Week 24 and were still on DTG/3TC (Figure 1 and Table 2)
- Most participants with very high viral load at BL (>1,000,000 c/mL) achieved HIV-1 RNA <50 c/mL by Week 24 (Figure 2)
- No treatment-emergent HIV or HBV resistance-associated mutations were detected

Figure 1. Results of Efficacy Analyses: Virologic Outcomes at Week 24



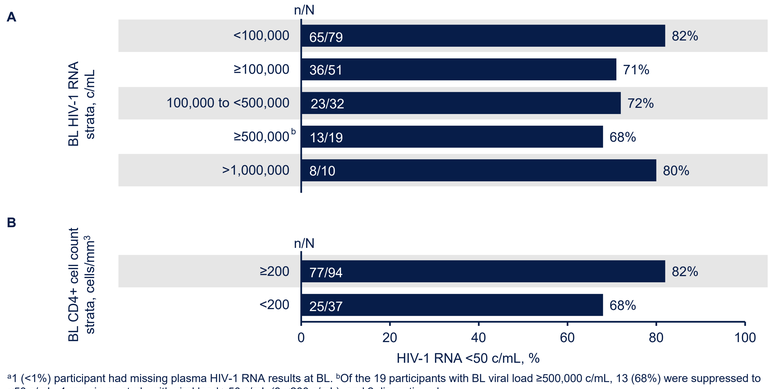
[a]11 (8%) of 131 participants had no virologic data at Week 24.

Table 2. Summary of Virologic Outcomes at Week 24

	DTG/3TC, n/N (%)
Observed analysis	
HIV-1 RNA <50 c/mL	102/111 (92)
On DTG/3TC	97/111 (87)
On modified ART	5/111 (5)
ITT-E missing = failure analysis	
HIV-1 RNA <50 c/mL	**102/131 (78)**
HIV-1 RNA ≥50 c/mL	**29/131 (22)**
Data in window and HIV-1 RNA ≥50 c/mL	9/131 (7)
On study but missing data in window	5/131 (4)[a]
Discontinued study due to lost to follow-up/withdrew consent	12/131 (9)[b]
Discontinued study for other reasons	3/131 (2)[c]
FDA Snapshot analysis	
HIV-1 RNA <50 c/mL	**97/131 (74)**
HIV-1 RNA ≥50 c/mL	**23/131 (18)**
Data in window and HIV-1 RNA ≥50 c/mL	9/131 (7)
Discontinued for lack of efficacy	0
Discontinued study for other reason and HIV-1 RNA ≥50 c/mL	6/131 (5)
Change in ART	8/131 (6)
No virologic data	**11/131 (8)**

[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).

Figure 2. Proportion of Participants With Plasma HIV-1 RNA <50 c/mL at Week 24 by BL (A) HIV-1 RNA[a] and (B) CD4+ Cell Count (ITT-E Missing = Failure Analysis)



[a]1 (<1%) participant had missing plasma HIV-1 RNA results at BL. [b]Of the 19 participants with BL viral load ≥500,000 c/mL, 13 (68%) were suppressed to <50 c/mL, 4 remain on study with viral load >50 c/mL (3 <200 c/mL), and 2 discontinued.

- All participants with available data who had an ART adjustment and remained on study at Week 24 had HIV-1 RNA <50 c/mL (Table 3)

Table 3. Participants Who Switched From DTG/3TC at Any Time Point by Week 24

Reason for switch	Visit window	Modified ART	Plasma HIV-1 RNA at Week 24
BL HBV	Week 1	DTG/3TC + TAF	<40 c/mL
BL HBV	Week 1	BIC/FTC/TAF	NA[a]
BL HBV	Week 4	DTG + TDF/FTC	<40 c/mL
BL 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]
BL HBV	Week 8	DTG/3TC + TAF	<40 c/mL
BL M184V	Week 8	DTG/RPV	NA[d]
AE (rash)	Week 12; Week 12	COBI/DRV/FTC/TAF; BIC/FTC/TAF[e]	<40 c/mL

[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 Biktarvy or Truvada + Tivicay. [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.

Safety

- DTG/3TC was well tolerated, with low rates of grade 2-5 drug-related AEs (2%) and serious AEs (2%; Table 4)
- Median (IQR) percent change from BL in weight was 5.2% (1.4%-8.4%) with DTG/3TC at Week 24
- Absolute median increase in weight was 4.6 kg

Table 4. AEs Reported Under Treatment With DTG/3TC

Characteristic, n (%)	DTG/3TC (N=131)
Any AE	85 (65)
AEs occurring in >5% of participants	
Headache	10 (8)
Diarrhea	8 (6)
Fatigue	8 (6)
Drug-related AEs	9 (7)
Grade 2-5 AEs	2 (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 v23.0.

Conclusions

- These data demonstrate the feasibility and safety of using DTG/3TC as a first-line regimen in a test-and-treat (rapid ART) setting
- Among participants with available HIV-1 RNA assessment at Week 24, 92% achieved HIV-1 RNA <50 c/mL
- Few participants required modification to their ART regimen due to BL resistance or HBV co-infection; therefore, appropriate therapy adjustments in the presence of BL resistance or HBV co-infection can be performed safely via routine clinical care and careful follow-up care after rapid initiation of DTG/3TC

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