Efficacy and Safety of Dolutegravir/Lamivudine (DTG/3TC) in Antiretroviral Therapy (ART)-Naive Adolescents Living With HIV-1: DANCE Study Week 96 Results

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Key Takeaways

- **Efficacy and safety of first-line once-daily dolutegravir/lamivudine (DTG/3TC) were evaluated in ART-naive adolescents living with HIV-1 at Week 96 in the DANCE study**
- **DTG/3TC demonstrated sustained efficacy, safety, and high barrier to resistance in treatment-naive adolescents, supporting its use as first-line ART in this population**

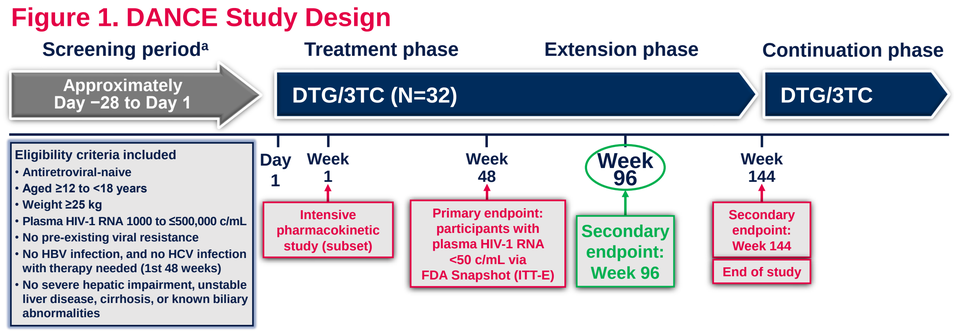
Introduction

- Adolescents living with HIV-1 are an underserved and vulnerable population expected to experience greater challenges with long-term treatment adherence compared with adults[1-4]
- The 2-drug regimen DTG/3TC is globally recommended for adults with HIV-1 as initial ART[5] and is indicated in adults and adolescents aged ≥12 years and weighing ≥40 kg in the European Union[6]
- DTG/3TC has demonstrated robust and durable efficacy as initial ART in studies in adults for up to 144 weeks (GEMINI-1/-2)[7] and in adolescents for up to 48 weeks (DANCE)[8]
- The DANCE study aims to provide additional data for DTG/3TC use as initial ART and to utilize pharmacokinetic exposure matching for extrapolation of efficacy in suppressed-switch settings for adolescents weighing ≥25 kg
- Here, we present the efficacy and safety of DTG/3TC in ART-naive adolescents living with HIV-1 through Week 96 in the DANCE study

Methods

- DANCE is an ongoing phase 3b, single-arm, multicenter, open-label study evaluating once-daily, fixed-dose combination (FDC) DTG/3TC (50 mg/300 mg) as initial ART for adolescents aged ≥12 to <18 years and weighing ≥25 kg, with HIV-1 RNA 1000 to ≤500,000 c/mL (Figure 1)
  - A total of 9 centers participated from Thailand, Kenya, and South Africa

Figure 1. DANCE Study Design



ITT-E, intention-to-treat exposed. [a]Re-testing of an exclusionary laboratory result (except for exclusionary HIV-1 resistance) was allowed during the screening window (did not require re-screening). In cases of central laboratory assay failure or shipment failure, the screening period could be extended to 35 days to accommodate sample analysis and reporting (with approval of the medical monitor).

- The primary endpoint assessed proportion of participants achieving HIV-1 RNA <50 c/mL (Snapshot, ITT-E) at Week 48
- Secondary endpoints assessed proportion of participants with HIV-1 RNA <50 c/mL (Snapshot, ITT-E), safety, and tolerability at Week 96
  - Both the ITT-E and safety populations consisted of all participants who received at least 1 dose of study drug
  - 1 study site closed due to Good Clinical Practice (GCP) non-compliance before Week 96; a sensitivity analysis was performed excluding these participants from the ITT-E population as the ITT-E sensitivity population
- Participants meeting confirmed virologic withdrawal (CVW) criteria (consecutive HIV-1 RNA measurements ≥200 c/mL) underwent viral resistance testing
- 95% CIs were calculated using exact Clopper-Pearson method

Results

Participants

- 32 participants were enrolled and received at least 1 dose of study drug (Table 1)
  - Most participants had baseline HIV-1 RNA 10,000 to <100,000 c/mL (15/32; 47%) or 100,000 to <500,000 c/mL (9/32; 28%)

Table 1. Participant Demographics and Baseline Characteristics: ITT-E Population

Parameter	DTG/3TC FDC (N=32)
Age, median (range), y	17 (13-17)
Sex, female, n (%)	11 (34)
Race, n (%)	
Asian	19 (59)
Black	13 (41)
Ethnicity, not Hispanic or Latin American, n (%)	32 (100)
BMI, median (range), kg/m^2	19.96 (14.47-31.07)
Baseline HIV-1 RNA, median (range), $\log_{10}$ c/mL	4.59 (2.61-5.64)
≥100,000 c/mL	9 (28)
Baseline CD4+ cell count, median (range), cells/mm^3	373 (20-1122)
HBV and HCV positive test results, n (%)[a]	
B only	0
C only	1 (3)
B and C	0
CDC category, n (%)[b]	
Stage 1	9 (28)
Stage 2	21 (66)
Stage 3	2 (6)
Factors in HIV acquisition, n (%)[c]	
Horizontal transmission	25 (83)
Vertical/Perinatal transmission	5 (17)
HIV subtype, n (%)	
A	3 (9)
A1	3 (9)
AE	19 (59)
C	4 (13)
Other[d]	3 (9)

[a]Borderline HCV classified as HCV. [b]Assessed according to CDC Classification System for HIV Infection in Adults/WHO Clinical Staging System of HIV/AIDS for Adults and Adolescents. [c]Participants could have more than 1 HIV acquisition factor; percentages based on number of participants with known HIV acquisition factors (N=30). [d]Includes A2, D, and complex.

- By Week 96, 11 participants had withdrawn from study
  - Primary reasons listed for withdrawal were adverse event (AE; n=2, Weeks 24 and 96), lack of efficacy/CVW (n=1, Week 96), protocol violation/pregnancy (n=1, Week 60), site closure (n=5), and withdrew consent (n=2, Weeks 16 and 48)

Virologic and Immunologic Outcomes at Week 96

- 1 site closed due to GCP non-compliance, resulting in 7 participants being withdrawn from study (5 due to site closure, 1 due to pregnancy, and 1 due to withdrawal of consent)
  - All 7 participants had missing Week 96 virology data and were imputed as treatment failures in the "no virologic data" category (Snapshot, ITT-E)
- To provide more reliable estimates for efficacy outcomes, a sensitivity analysis (ITT-E sensitivity population) was performed to exclude all participants from the closed site (Table 2)
- At Week 96, HIV-1 RNA <50 c/mL (Snapshot) results were
  - ITT-E population: 22/32 (69%; 95% CI, 50%-84%)
  - ITT-E sensitivity population: 22/25 (88%; 95% CI, 69%-97%)

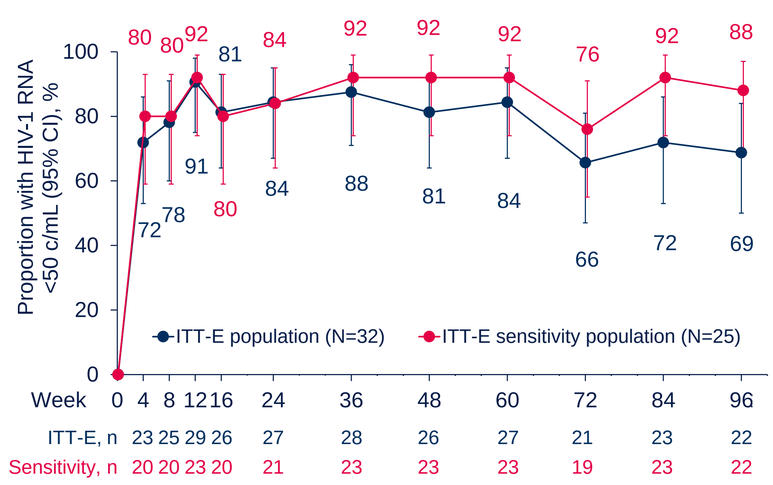
Table 2. Summary of Virologic Outcomes at Week 96: Snapshot Analysis

Outcome, n (%)	DTG/3TC FDC ITT-E population (N=32)	DTG/3TC FDC ITT-E sensitivity population (N=25)
HIV-1 RNA <50 c/mL	22 (69)	**22 (88)**
HIV-1 RNA ≥50 c/mL	3 (9)	**2 (8)**
Data in window not below threshold	1 (3)	**1 (4)**
Discontinued for other reason while not below threshold[a]	2 (6)	**1 (4)**
No virologic data	7 (22)	**1 (4)**
Discontinued due to AE or death[b]	1 (3)	**1 (4)**
Discontinued study for other reasons[c]	6 (19)	**0**

[a]1 participant withdrew consent within the Week 16 analysis window with last on-treatment viral load ≥50 c/mL at Week 12; the other participant withdrew consent due to travel burden at Week 48 with last on-treatment viral load 405,654 c/mL. [b]1 participant withdrew from study within the Week 24 analysis window due to decreased glomerular filtration rate, with HIV-1 RNA <50 c/mL at all on-treatment visits from Week 4 and at a follow-up visit 13 days after last dose. [c]Participants were from the site closed before Week 96 for GCP-related concerns (not necessarily as the primary reason for withdrawal); 2 participants had HIV-1 RNA <50 c/mL at all on-treatment visits from Week 4, 2 had HIV-1 RNA <50 c/mL at all on-treatment visits from Week 8, 1 had HIV-1 RNA <50 c/mL from Weeks 4-12 and re-suppressed with final on-treatment measurement at Week 60, and 1 withdrew due to pregnancy within the Week 60 analysis window with last on-treatment viral load <50 c/mL at Week 60.

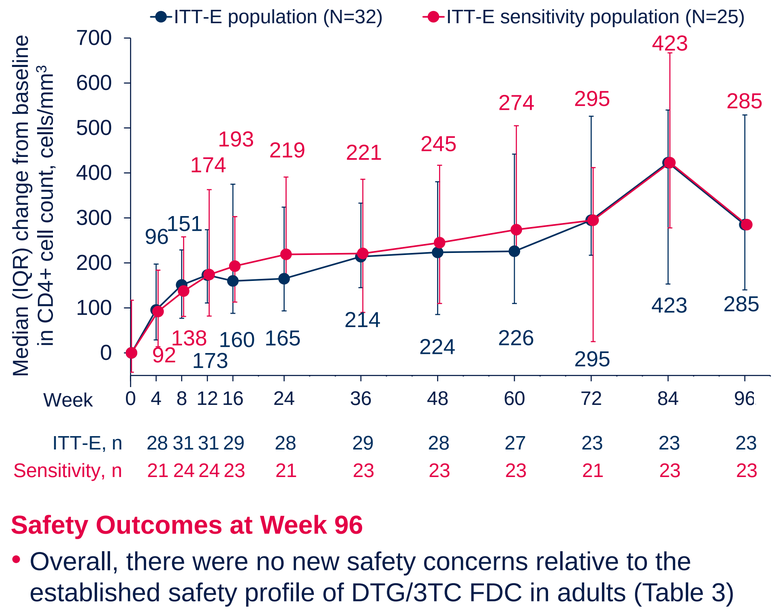
- A high proportion of participants achieved and maintained HIV-1 RNA <50 c/mL by Snapshot analysis to Week 96 (Figure 2)

Figure 2. Proportion (95% CI) With Snapshot HIV-1 RNA <50 c/mL at Each Study Visit, by Population



- 1 participant had confirmed virologic withdrawal (CVW) at Week 72 (HIV-1 RNA 3752 c/mL, confirmed 4 weeks later at 210 c/mL)
  - Samples drawn at suspected virologic withdrawal (SVW) failed to amplify; as a result, no genotypic or phenotypic data were available for the SVW time point, and no findings of treatment-emergent mutations were observed through Week 96
  - Baseline genotypic and phenotypic testing showed no evidence of pre-existing NRTI or INSTI resistance
  - The participant remained on study drug and achieved HIV-1 RNA <50 c/mL at Weeks 84 and 96
- Median (IQR) CD4+ cell count at baseline (371.5 [270.0-507.5] cells/mm^3) increased by 285.0 (140.0-529.0) cells/mm^3 to 682.0 (499.0-863.0) cells/mm^3 at Week 96 (Figure 3)

Figure 3. Change From Baseline in CD4+ Cell Count at Each Study Visit, by Population



Safety Outcomes at Week 96

- Overall, there were no new safety concerns relative to the established safety profile of DTG/3TC FDC in adults (Table 3)
- Most (27/32; 84%) participants experienced AEs that were maximum grade 1 or 2
- 1 participant developed a stage 3 HIV-1–associated condition 137 days after first dose of study drug (grade 2 pulmonary tuberculosis)
  - This participant achieved and maintained virologic suppression from Week 4 onward
- Of the 4 serious AEs reported in 3/32 (9%) participants, none were related to study drug
- No deaths were reported during the study

Table 3. Summary of AEs Reported Through Week 96: Safety Population

Participants, n (%)	DTG/3TC FDC (N=32)
Any AE	29 (91)
AEs occurring in ≥3 participants	
Nasopharyngitis	7 (22)
Upper respiratory tract infection	5 (16)
COVID-19	4 (13)
Cough	3 (9)
Folliculitis	3 (9)
Headache	3 (9)
Tonsillitis	3 (9)
Drug-related AEs[a]	1 (3)
Grade 2-5 AEs	21 (66)
Drug-related grade 2-5 AEs[a]	1 (3)
AEs leading to study withdrawal[a,b]	2 (6)
Drug-related AEs leading to study withdrawal[a]	1 (3)
Any serious AE[c]	3 (9)
Drug-related serious AEs	0

[a]Grade 3 decreased glomerular filtration rate (n=1). [b]Grade 2 depression and suicidal ideation (n=1). [c]Anal abscess (n=1), orchitis (n=1), and post-operative wound complication serious AE after vulvovaginal wart removal in participant with vulvovaginal warts serious AE (n=1).

Conclusions

- DTG/3TC was well tolerated, demonstrated high efficacy, and had a high barrier to resistance in ART-naive adolescents with HIV-1 through Week 96
- These results, in combination with well-established data in adults, support DTG/3TC as a first-line ART option in adolescents to achieve and maintain virologic suppression

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