Real-world Effectiveness of Dolutegravir + Lamivudine (DTG + 3TC) in Treatment-Naive People With HIV-1 and Low CD4+ Cell Count or High Viral Load at Baseline: A Systematic Literature Review

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Key Takeaway

Results from a systematic literature review (SLR) of real-world studies of treatment-naive people with HIV-1 initiating DTG + 3TC demonstrated high rates of virologic suppression (HIV-1 RNA <50 copies/mL) among individuals with high baseline viral load or baseline CD4+ cell count <200 cells/mm³ at Weeks 48 and 96

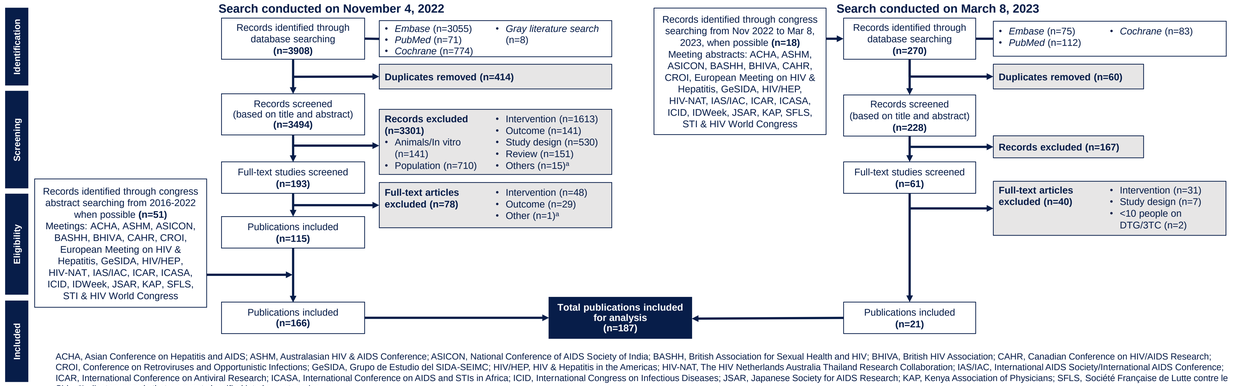
Introduction

- Treatment-naive people with HIV-1 who initiate antiretroviral therapy with high viral load or CD4+ cell count <200 cells/mm³ experience higher rates of treatment failure, morbidity, and mortality[1,2]
- In the GEMINI-1/-2 and STAT clinical trials, DTG + 3TC was effective for achieving virologic suppression among treatment-naive participants with baseline viral load ≥100,000 copies/mL
  - At Week 144 in GEMINI-1/-2, 5% (7/140) of participants had HIV-1 RNA ≥50 copies/mL (Snapshot analysis), and at Week 48 in STAT, 6% (3/51) had HIV-1 RNA ≥50 copies/mL (ITT-E missing = failure analysis)[3,4]
  - The proportion of participants with viral load ≥500,000 copies/mL at baseline who achieved HIV-1 RNA <50 copies/mL was 77% (10/13) in GEMINI-1/-2 and 89% (17/19) in STAT
- Among treatment-naive participants with low baseline CD4+ cell count, 10% (6/63) in GEMINI-1/-2 and 5% (2/37) in STAT had HIV-1 RNA ≥50 copies/mL at Week 144 or Week 48, respectively[3,4]
- To complement existing clinical trial data and support treatment decisions, we summarize data on DTG + 3TC effectiveness from studies of real-world use in treatment-naive people with HIV-1 with high viral load or low CD4+ cell count at treatment initiation

Methods

- The SLR was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Figure 1)
- Ovid MEDLINE®, Embase®, PubMed, Cochrane library, and relevant international conference proceedings were searched for studies reporting data on DTG + 3TC use in real-world populations between January 2013 and March 2023
  - The original SLR searched from January 2013 to November 4, 2022; to supplement the original SLR, an updated SLR was conducted with identical search criteria and included publications up to March 8, 2023
- Reports identified in the search were subsequently screened and only those with baseline or outcomes data for treatment-naive individuals with high baseline viral load or low baseline CD4+ cell count were retained for further analysis
- Among studies reporting virologic outcomes from the same cohort, only the report with the largest population with high viral load or low CD4+ cell count at baseline was included in the analysis to avoid overlap

Figure 1. PRISMA Diagram



ACHA, Asian Conference on Hepatitis and AIDS; ASHM, Australasian HIV & AIDS Conference; ASICON, National Conference of AIDS Society of India; BASHH, British Association for Sexual Health and HIV; BHIVA, British HIV Association; CAHR, Canadian Conference on HIV/AIDS Research; CROI, Conference on Retroviruses and Opportunistic Infections; GeSIDA, Grupo de Estudio del SIDA-SEIMC; HIV/HEP, HIV & Hepatitis in the Americas; HIV-NAT, The HIV Netherlands Australia Thailand Research Collaboration; IAS/IAC, International AIDS Society/International AIDS Conference; ICAR, International Conference on Antiviral Research; ICASA, International Conference on AIDS and STIs in Africa; ICID, International Congress on Infectious Diseases; JSAR, Japanese Society for AIDS Research; KAP, Kenya Association of Physicians; SFLS, Société Française de Lutte contre le Sida. [a]Indicates records that were not classified into key categories.

Results

Cohorts and Participants

- The SLR identified 187 publications representing 146 studies related to 67 cohorts and including 36,313 people with HIV-1 using DTG + 3TC
- 14 non-overlapping cohorts included baseline and/or outcomes data for treatment-naive people initiating therapy with DTG + 3TC with viral load ≥100,000 copies/mL (n=502; Figure 2A)
  - In total, 30 publications reported on people with high viral load, 4 of which included only treatment-experienced populations and 12 of which were duplicate cohorts with fewer individuals
- 10 publications reported data for non-overlapping cohorts of treatment-naive people with baseline CD4+ cell count <200 cells/mm³ (n=215; Figure 2B)
  - Overall, 25 reports included people with HIV-1 and low CD4+ cell count at DTG + 3TC initiation, 8 of which included treatment-experienced populations and 7 of which were from duplicate cohorts

Figure 2. Breakdown of Real-world Publications Reporting Data on People With HIV-1 Initiating DTG + 3TC With (A) Viral Load ≥100,000 Copies/mL and (B) CD4+ Cell Count <200 Cells/mm³

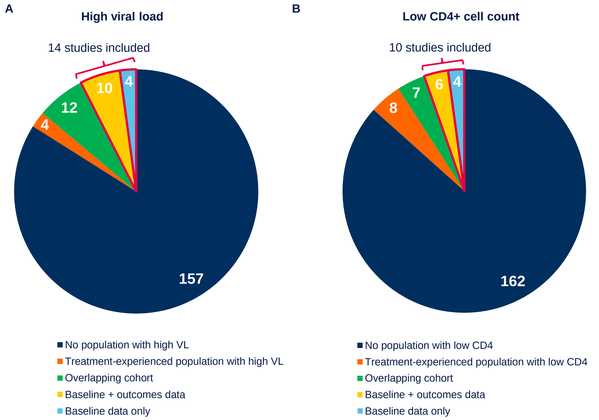
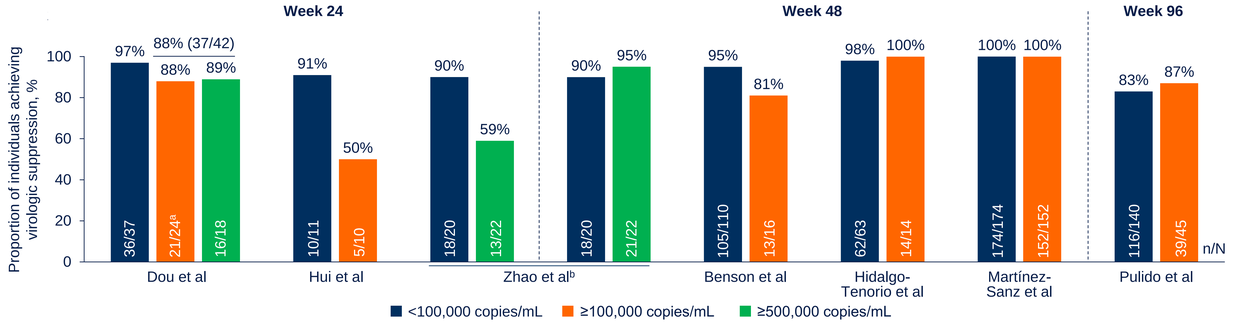


Figure 3. Proportions of Individuals With Baseline Viral Load ≥100,000 Copies/mL Achieving Virologic Suppression at Weeks 24, 48, and 96



Studies shown are limited to those with n ≥10 people with high baseline viral load. [a]Viral load ≥100,000 to <500,000 copies/mL. [b]Non–high viral load group <500,000 copies/mL.

- 7 and 4 studies reported the virologic effectiveness of DTG + 3TC for ≥10 treatment-naive individuals with high baseline viral load or low baseline CD4+ cell count, respectively (Table)

Table. Studies With Virologic Effectiveness Data for ≥10 Treatment-Naive People With HIV-1 and Baseline Viral Load ≥100,000 Copies/mL or CD4+ Cell Count <200 Cells/mm³

Study	Cohort or network	Country	Total DTG + 3TC cohort, N	High viral load or low CD4 cohort, n	Outcome reporting window(s)
High baseline viral load					
Dou et al[5]	—	China	96	42	Week 24
Hui et al[6]	—	China	54	34	Week 24[a]
Zhao et al[7]	—	China	42	22	Week 24 Week 48
Benson et al[8]	TANDEM	United States	126	16	Week 48
Hidalgo-Tenorio et al[9]	DOLAVI	Spain	88	17	Week 48
Martínez-Sanz et al[10]	CoRIS	Spain	326	152	Week 48
Pulido et al[11]	REDOLA	Spain	185	45	Week 96
Low baseline CD4+ cell count					
Dou et al[5]	—	China	96	51	Week 24
Yang et al[12]	—	China	36	17	Week 48
Zhao et al[7]	—	China	42	32	Week 48
Pulido et al[11]	REDOLA	Spain	185	10	Week 96

[a]Only 21 people in this cohort, 10 with high viral load, were included in the efficacy analysis.

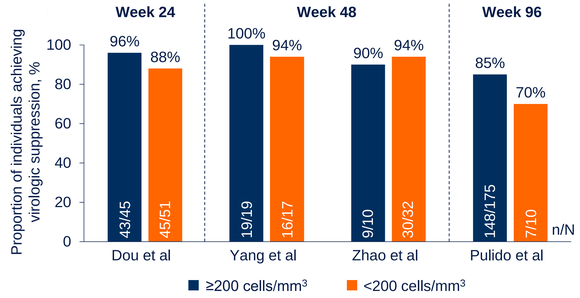
Virologic Outcomes in Treatment-Naive Populations With High Baseline Viral Load

- Overall, the proportion of individuals with high baseline viral load who achieved virologic suppression was 76% (61/80) at Week 24, 97% (208/215) at Week 48, and 87% (39/45) at Week 96
- Among studies reporting data for ≥10 individuals with high baseline viral load from the same cohort, the proportion with HIV-1 RNA <50 copies/mL ranged from 50% (5/10) to 88% (37/42) at Week 24 and from 81% (13/16) to 100% (152/152) at Week 48; at Week 96, one study reported that 87% (39/45) of individuals were virologically suppressed (Figure 3)
  - In a longitudinal cohort study following individuals with baseline viral load ≥500,000 copies/mL, the proportion achieving virologic suppression increased from 59% (13/22) at Week 24 to 95% (21/22) at Week 48
- Using inverse-variance weighting methods with a correction of 0.01% for studies with 100% suppression, the pooled proportions of individuals with high baseline viral load from studies with n ≥10 who achieved virologic suppression were 80.3% at Week 24, >99.9% at Week 48, and 87% at Week 96

Virologic Outcomes in Treatment-Naive Populations With Low Baseline CD4+ Cell Count

- Overall, 86% (54/63) of people with baseline CD4+ cell count <200 cells/mm³ were virologically suppressed at Week 24, 94% (46/49) at Week 48, and 70% (7/10) at Week 96
- Among the studies reporting outcomes for ≥10 individuals with low baseline CD4+ cell count, 88% (45/51) achieved HIV-1 RNA <50 copies/mL at Week 24, 94% (30/32 and 16/17) at Week 48, and 70% (7/10) at Week 96 (Figure 4)
- Using inverse-variance weighting methods, the pooled proportions of individuals with low baseline CD4+ cell count from studies with n ≥10 who achieved virologic suppression were 88% at Week 24, 93.9% at Week 48, and 70% at Week 96

Figure 4. Proportion of Individuals With Baseline CD4+ Cell Count <200 Cells/mm³ Achieving Virologic Suppression at Weeks 24, 48, and 96



Studies shown are limited to those with n ≥10 people with low baseline CD4+ cell count.

Conclusions

- Consistent with clinical trial data, real-world evidence from treatment-naive people with HIV-1 initiating DTG + 3TC shows high rates of virologic suppression regardless of viral load or CD4+ cell count at baseline
- The DOLCE clinical trial (ClinicalTrials.gov, NCT04880395) is an ongoing study that will provide additional efficacy data on DTG + 3TC in these subpopulations

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