Two-Year Long-term Data on the Efficacy and Tolerability of Dolutegravir-Based Regimens From the Prospective Multicenter TESLA Cohort Study in ART-Naive and Pre-treated People Living With HIV in Russia

P094

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Key Takeaways

- **In the real-world TESLA study, both 2-drug and 3-drug dolutegravir (DTG)-based regimens (DBRs) showed robust effectiveness and a good safety and tolerability profile among people living with HIV-1 in Russia**
- **These findings are consistent with clinical trial results and other real-world evidence[1-3] and further support the use of 2-drug and 3-drug DBRs in people living with HIV-1**

Introduction

- Russia has one of the highest prevalences of HIV in the World Health Organization European region, with a downward trend in incidence between 2019 and 2022[4]
- In December 2023, more than 1.1 million people in Russia were living with HIV, and 58,740 new cases were registered in 2023[5]
  - The number of new HIV cases identified in 2023 was 7% lower than in 2022 (63,150)
- The 2024 Russian Federation HIV treatment guidelines recommend the initiation of DTG-based 3-drug regimens (3DRs) and 2-drug regimens (2DRs) as one of the first-line treatment options and DTG-based 2DRs as an antiretroviral therapy (ART) optimization strategy in individuals who are virologically suppressed[6]
- Here, we present results from a 24-month interim analysis of effectiveness and tolerability in people living with HIV-1 using DBRs in the prospective, real-world, 3-year TESLA study in Russia

Methods

- TESLA is a prospective, 3-year, multicenter, non-interventional, single-arm, real-world cohort study of adults living with HIV-1 initiating DBRs in Russia
- 1000 people living with HIV-1 initiating DTG, primarily as part of the 2DR DTG + lamivudine (3TC) or a DTG-based 3DR, for HIV-1 treatment were screened from 14 centers in Russia
- Participants were evaluated at routine clinical care visits until DTG discontinuation, death, loss to follow-up, or end of data collection
- The primary endpoint was the proportion of participants who discontinued DTG and reasons for discontinuation
- Secondary endpoints included virologic outcomes and change from baseline in CD4+ cell count at Month 24
  - Month 24 effectiveness analyses of DTG + 3TC and DTG-based 3DR subpopulations excluded individuals lost to follow-up or those who had a change in place of residence or were removed from dispensary registration
- Safety and tolerability assessments included incidence of adverse drug reactions (ADRs), serious adverse events (SAEs), and laboratory and clinical parameters

Results

Baseline Demographics and Clinical Characteristics

- 1000 adults living with HIV-1 were screened, and 959 were included in the 24-month full analysis set
  - Median age was 40 years, 82% had prior ART experience, and 57% were male (Table 1)
  - 27% (n=258) of participants were using DTG + 3TC and 65% (n=621) were using a DTG-based 3DR
  - 2 participants did not meet inclusion criteria, and 39 were excluded from the analysis due to non-adherence with the visit window

Table 1. Baseline Demographics and Clinical Characteristics of Participants in the TESLA Study

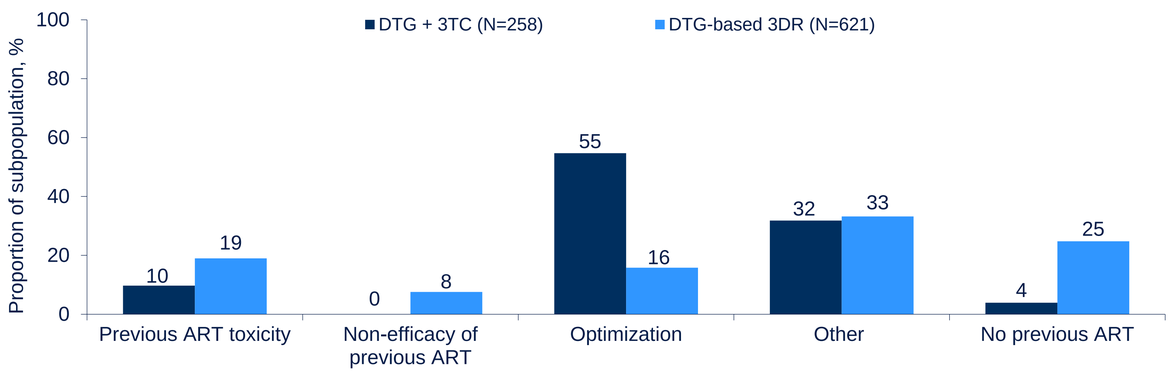
Parameter	Overall (N=959)	DTG + 3TC (N=258)[a]	DTG-based 3DR (N=621)[a]
Age, median (IQR), y	40.0 (35.0-44.0)	40.0 (35.0-45.0)	40.0 (34.0-44.0)
Female, n (%)	408 (43)	110 (43)	256 (41)
ART experience, n (%)			
Naive to ART	176 (18)	10 (4)	154 (25)
Prior ART experience	783 (82)	248 (96)	467 (75)
Virologically suppressed[b]	650 (83)	233 (94)	360 (77)
Not virologically suppressed[b]	121 (15)	14 (6)	96 (21)
No virologic data	12 (2)	1 (<1)	11 (2)
CD4+ cell count, n (%)			
<200 cells/mm^3	102 (11)	5 (2)	91 (15)
≥200 cells/mm^3	845 (88)	252 (98)	519 (84)
Data not available	12 (1)	1 (<1)	11 (2)
Weight, median (IQR), kg	71.5 (63.0-80.0)	72.0 (63.2-80.8)	71.0 (62.0-79.0)
BMI, median (IQR), kg/m^2	23.8 (21.6-26.7)	23.8 (21.5-26.8)	23.6 (21.5-26.5)

[a]75 participants were included in the full analysis set but excluded from the DTG + 3TC or DTG-based 3DR subpopulations due to a change in ART regimen, and an additional 5 were excluded because they were using DTG-based 2DRs without 3TC or a DTG-based 4-drug regimen. [b]Among participants with prior ART experience. Virologic suppression defined as HIV-1 RNA <250 c/mL.

Reasons for Initiating DBRs and Discontinuations Through 24 Months

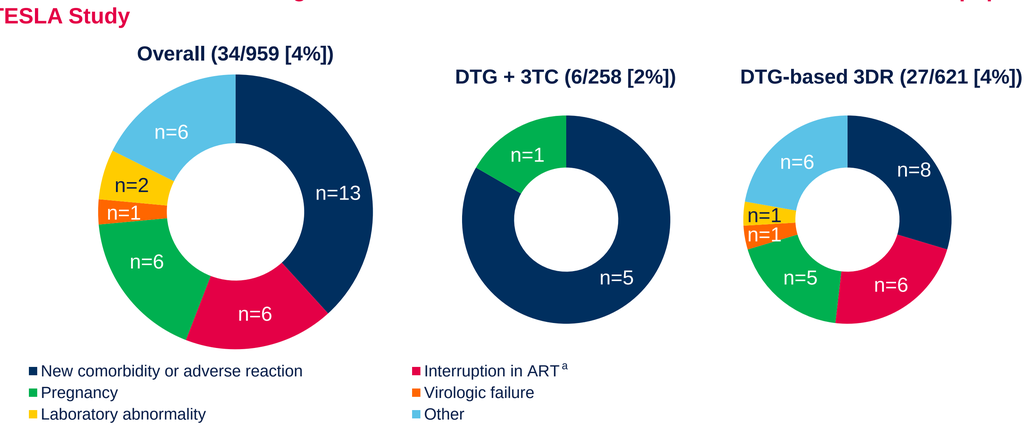
- Optimization and other reasons were the most common reasons for initiating DTG + 3TC; other reasons and previous ART toxicity were the most common reasons for initiating DTG-based 3DRs (Figure 1)

Figure 1. Reasons for Initiating DBRs in the DTG + 3TC and DTG-Based 3DR Subpopulations in the TESLA Study



- Discontinuations were rare through 24 months (DTG + 3TC subpopulation, n=6; DTG-based 3DR subpopulation, n=27; Figure 2)
  - New comorbidities or adverse reactions were the most common reasons for discontinuation

Figure 2. Reasons for Discontinuing DBRs Overall and in the DTG + 3TC and DTG-Based 3DR Subpopulations in the TESLA Study

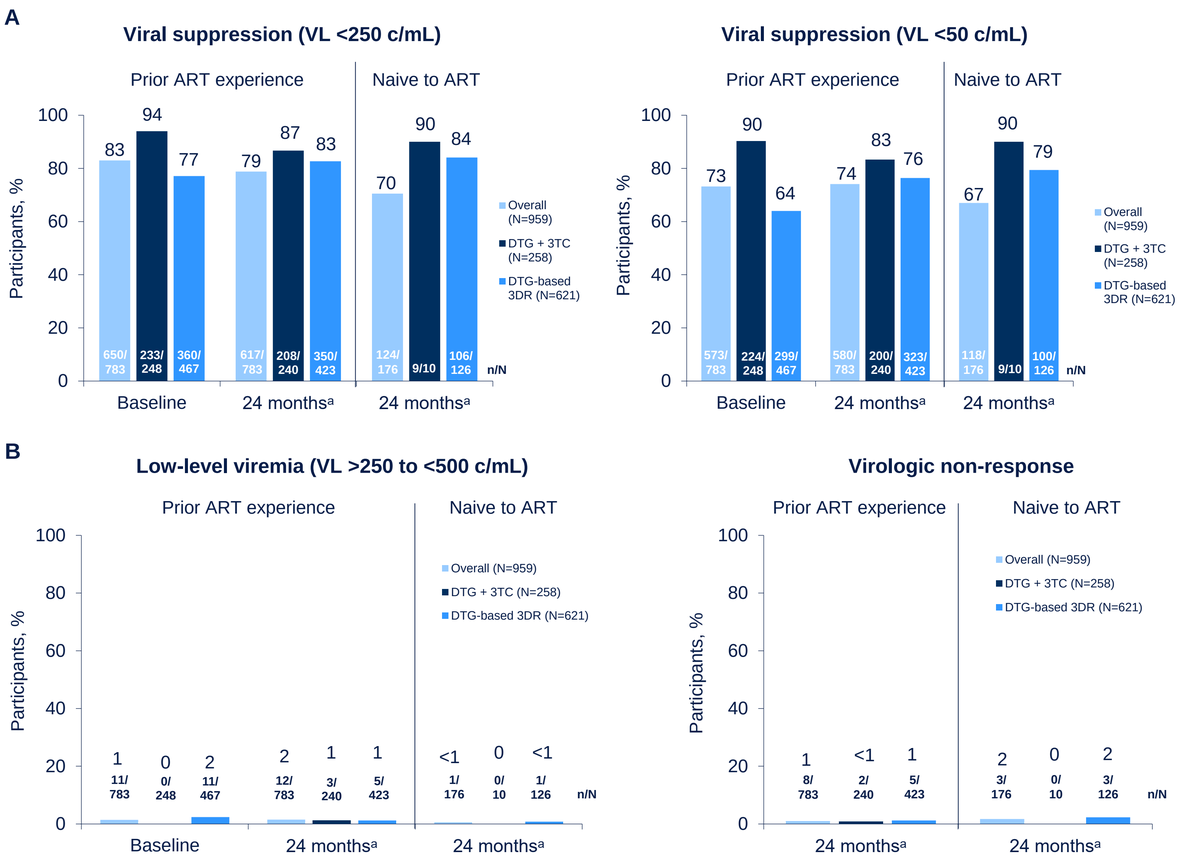


[a]Defined as ART interruption for ≥45 days.

Effectiveness at 24 Months

- At 24 months in the DTG + 3TC subpopulation, 87% (208/240) of participants with prior ART experience had viral load (VL) <250 c/mL and 83% (200/240) had VL <50 c/mL; 90% (9/10) of participants naive to ART had VL <50 c/mL
- In the DTG-based 3DR subpopulation with prior ART experience, the proportion of participants with VL <250 c/mL increased from 77% (360/467) at baseline to 83% (350/423) at Month 24, and the proportion with VL <50 c/mL increased from 64% (299/467) to 76% (323/423); 84% (106/126) of participants naive to ART had VL <250 c/mL at 24 months (Figure 3A)
- Few participants had low-level viremia (VL >250 to <500 c/mL) or virologic non-response (Figure 3B)
  - <1% (1/126) of participants naive to ART and <1% (3/423) of those with prior ART experience in the DTG-based 3DR subpopulation had virologic rebound

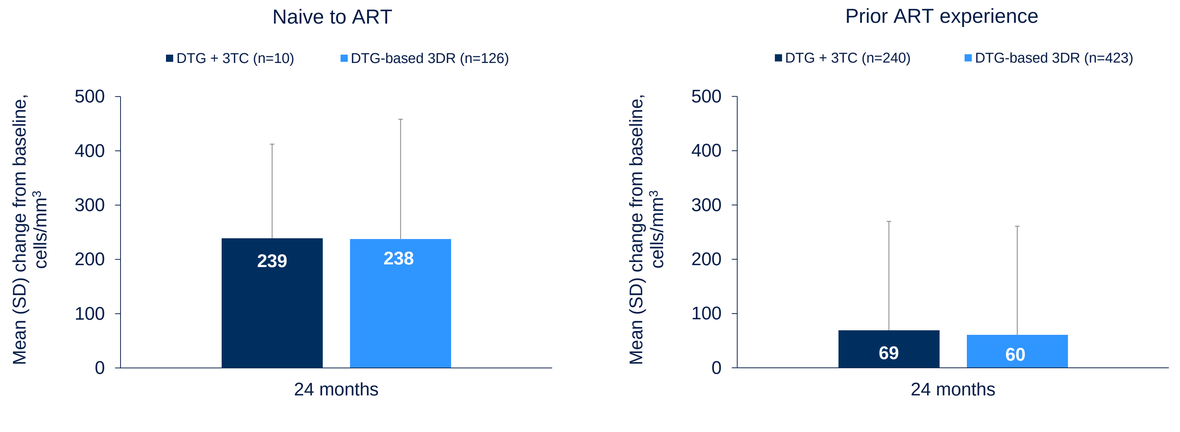
Figure 3. Proportions of Participants With (A) Virologic Suppression and (B) Low-Level Viremia or Virologic Non-response at 24 Months



[a]Month 24 analysis for DTG + 3TC and DTG-based 3DR subpopulations exclude persons lost from contact or who had a change in place of residence or were removed from dispensary registration.

- CD4+ cell count increased in both subpopulations (Figure 4)

Figure 4. Mean Change in CD4+ Cell Count From Baseline to 24 Months



Safety

- Overall, 147 ADRs/SAEs were recorded in 118 (12%) of 959 participants through 24 months (Table 2)
  - 85 ADRs/SAEs in 80 (8%) participants were deemed related to DTG; the most common DTG-related ADRs were increased weight (7%), psychiatric disorders (<1%), and nervous system disorders (<1%)
  - 19 ADRs/SAEs resulted in discontinuation of DTG in 16 (2%) participants
- In the DTG + 3TC subpopulation, 35 DTG-related ADRs/SAEs occurred in 13% (34/258) of participants, and in the DTG-based 3DR subpopulation, 42 DTG-related ADRs/SAEs occurred in 6% (40/621) of participants

Table 2. Proportions of Participants With ADRs or SAEs Through 24 Months

Participants, n (%)	Overall (N=959)	DTG + 3TC (N=258)	DTG-based 3DR (N=621)
Any ADR or SAE	118 (12)	38 (15)	70 (11)
DTG-related ADR or SAE	80 (8)	34 (13)	40 (6)
DTG-related SAE[a]	4 (<1)	3 (1)	1 (<1)
ADR or SAE leading to discontinuation or interruption[b]	16 (2)	6 (2)	9 (1)
Any SAE	43 (4)	8 (3)	31 (5)

[a]1 DTG-related SAE each of myocarditis, autoimmune hepatitis, and cerebrovascular accident in the DTG + 3TC subpopulation; 1 DTG-related SAE of epilepsy in the DTG-based 3DR subpopulation. [b]Defined as ART interruption for ≥45 days.

Conclusions

- Use of DBRs in real-life settings in the Russian TESLA cohort was associated with high effectiveness and a good safety profile for 24 months, including among those using the 2DR DTG + 3TC
- The rate of DTG-related ADRs/SAEs was 8%, and no new safety signals were identified
- Effectiveness and safety data are consistent with clinical trial data and real-world evidence, reinforcing the durability, safety, and tolerability of DBRs, including the 2DR DTG + 3TC[1-3]
- Data on cardiometabolic outcomes with the use of DBRs in the TESLA study are presented in Poster P108

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References: 1. Osiyemi et al. *Clin Infect Dis*. 2022;75:975-986. **2.** Llibre et al. *Clin Infect Dis*. 2023;76:720-729. **3.** Henegar et al. *Viruses*. 2023;15:2426. **4.** World Health Organization. https://www.ecdc.europa.eu/en/publications-data/hivaids-surveillance-europe-2023-2022-data. Accessed October 3, 2024. **5.** Federal Scientific and Methodological Center for AIDS Prevention and Control, Rospotrebnadzor 2024. http://www.hivrussia.info/dannye-po-vich-infektsii-v-rossii/. Accessed October 7, 2024. **6.** National Clinical Guidelines: HIV Infection in Adults. Ministry of Health of the Russian Federation; Moscow, Russia: 2024. https://cr.minzdrav.gov.ru/recomend/79_2. Accessed October 7, 2024.

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