The Analysis of Metabolic Parameters in People Living With HIV Using Dolutegravir-Based Regimens in Routine Clinical Practice in Russia

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Key Takeaways

- **24-month findings from the real-world TESLA study support a neutral effect of dolutegravir (DTG)-based regimens (DBRs) on the cardiometabolic health of people living with HIV-1**
- **The 2-drug regimen (2DR) DTG + lamivudine (3TC) was associated with a decrease in the proportion of participants with clinically significant abnormalities in lipids, supporting the benefits of a 2DR with fewer drugs**

Introduction

- The prevalence of obesity has increased globally, including among people living with HIV-1[1]
- Weight gain has been reported to be more pronounced after initiation of second-generation integrase strand transfer inhibitors (INSTIs) with tenofovir alafenamide (TAF) compared with the older antiretroviral agents efavirenz and tenofovir disoproxil fumarate (TDF)[1,2]
- Regimens containing TDF but not TAF are preferred for first-line antiretroviral therapy (ART) by Russian Federation HIV treatment guidelines[3]
- DBRs have been associated with generally favorable lipid profiles in some studies, particularly compared with boosted protease inhibitors (PIs)[4-6]
- Long-term effects of ART, including 2DRs, on the metabolic health of people living with HIV-1 require further assessment, including through real-world evidence
- We present results from a 24-month interim analysis of weight, metabolic parameters, and cardiometabolic events 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 in Russia initiating DBRs
- Metabolic health was assessed in the 24-month interim analysis in subpopulations of participants using either the 2DR DTG + 3TC or a DTG-based 3-drug regimen (3DR; DTG + 2 antiretroviral agents)
- Metabolic parameters evaluated included weight, body mass index (BMI), blood glucose, lipid parameters (triglycerides, total cholesterol, low-density-lipoprotein cholesterol [LDL-C], high-density-lipoprotein cholesterol [HDL-C]), and liver parameters (alanine aminotransferase [ALT], aspartate aminotransferase [AST])
  - Proportions of participants with clinically significant abnormalities in blood biochemistry parameters were assessed based on the expert opinion of treating physicians
- Cardiometabolic-related adverse events (AEs) including adverse drug reactions (ADRs; deemed related to DTG) and serious AEs (SAEs; regardless of relationship to DTG) were assessed

Results

Study Population

- 959 adults living with HIV-1 were included in this analysis (Table 1)
  - 258 participants were using DTG + 3TC; 96% had prior ART experience, and 4% were naive to ART
  - 621 participants were using DTG-based 3DRs; 75% had prior ART experience, and 25% were naive to ART
  - Most participants switched from a non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimen
    - 80 participants in the full analysis set were not included in the DTG + 3TC or DTG-based 3DR subpopulation analysis: 5 did not meet subpopulation inclusion criteria and 75 were excluded due to a change in ART regimen

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

Parameter	DTG + 3TC (N=258)	DTG-based 3DR (N=621)
Age, median (IQR), y	40.0 (35.0-45.0)	40.0 (34.0-44.0)
Female, n (%)	110 (43)	256 (41)
ART experience, n (%)		
Naive to ART	10 (4)	154 (25)
Previous ART	248 (96)	467 (75)
Previous NNRTI[a]	177 (71)	325 (70)
Previous PI[a]	144 (58)	272 (58)
Previous INSTI[a]	7 (3)	14 (3)
Virologically suppressed[a,b]	233 (94)	360 (77)
Not virologically suppressed[a,b]	14 (6)	96 (21)
No virologic data[a]	1 (<1)	11 (2)
Weight, median (IQR), kg	72.0 (63.2-80.8)	71.0 (62.0-79.0)
BMI, median (IQR), kg/m^2	23.8 (21.5-26.8)	23.6 (21.5-26.5)

[a]Among participants with prior ART experience. [b]Virologic suppression defined as HIV-1 RNA <250 c/mL.

Virologic Outcomes

- In the DTG + 3TC subpopulation, 90% (9/10) of participants who were naive to ART and 83% (200/240) with prior ART experience achieved HIV-1 RNA <50 c/mL at 24 months
- Proportions with HIV-1 RNA <50 c/mL in the DTG-based 3DR subpopulation were 79% (100/126) among those naive to ART and 76% (323/423) among those with prior ART experience

Weight and BMI

- At 24 months, weight was assessed in 85% (818/959) of participants overall
- Mean weight and BMI values slightly increased from baseline to 24 months in the DTG + 3TC and DTG-based 3DR subpopulations (Table 2)
- An ADR of increased weight was reported in 12% (30/258) of participants using DTG + 3TC and in 5% (33/621) of those using DTG-based 3DRs

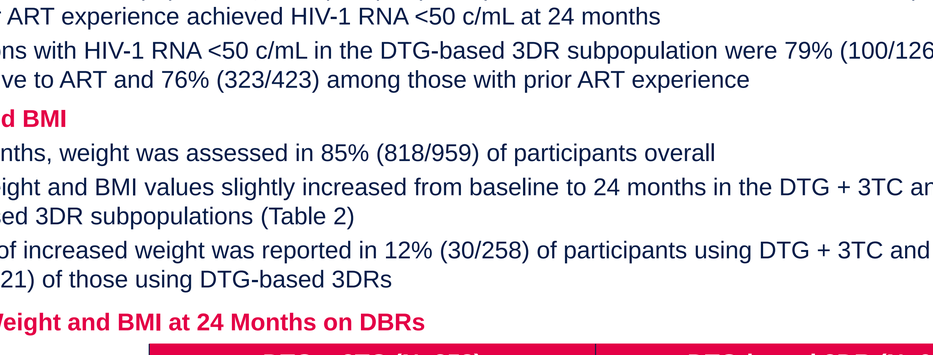
Table 2. Weight and BMI at 24 Months on DBRs

	DTG + 3TC (N=258)			DTG-based 3DR (N=621)		
Parameter	**Baseline**	**24 months**	**Mean change**	**Baseline**	**24 months**	**Mean change**
Weight, mean (SD), kg	73.1 (14.6)	75.6 (15.3)	2.8 (6.0)	71.8 (14.2)	74.1 (14.7)	1.7 (6.1)
BMI, mean (SD), kg/m^2	24.5 (4.2)	25.2 (4.2)	0.9 (2.0)	24.2 (4.1)	24.9 (4.4)	0.6 (2.0)

Metabolic-Related Biochemistry

- For blood biochemistry parameters in the overall population (N=959), 24-month data were available in 76% (n=728) of participants for blood glucose, 34% (n=327) for triglycerides, 62% (n=591) for total cholesterol, 21% (n=198) for LDL-C, 20% (n=192) for HDL-C, 82% (n=788) for ALT, and 82% (n=786) for AST
- In participants using DTG + 3TC and DTG-based 3DRs, proportions with clinically significant abnormalities in blood glucose were low at baseline and Month 24 (Figure 1)

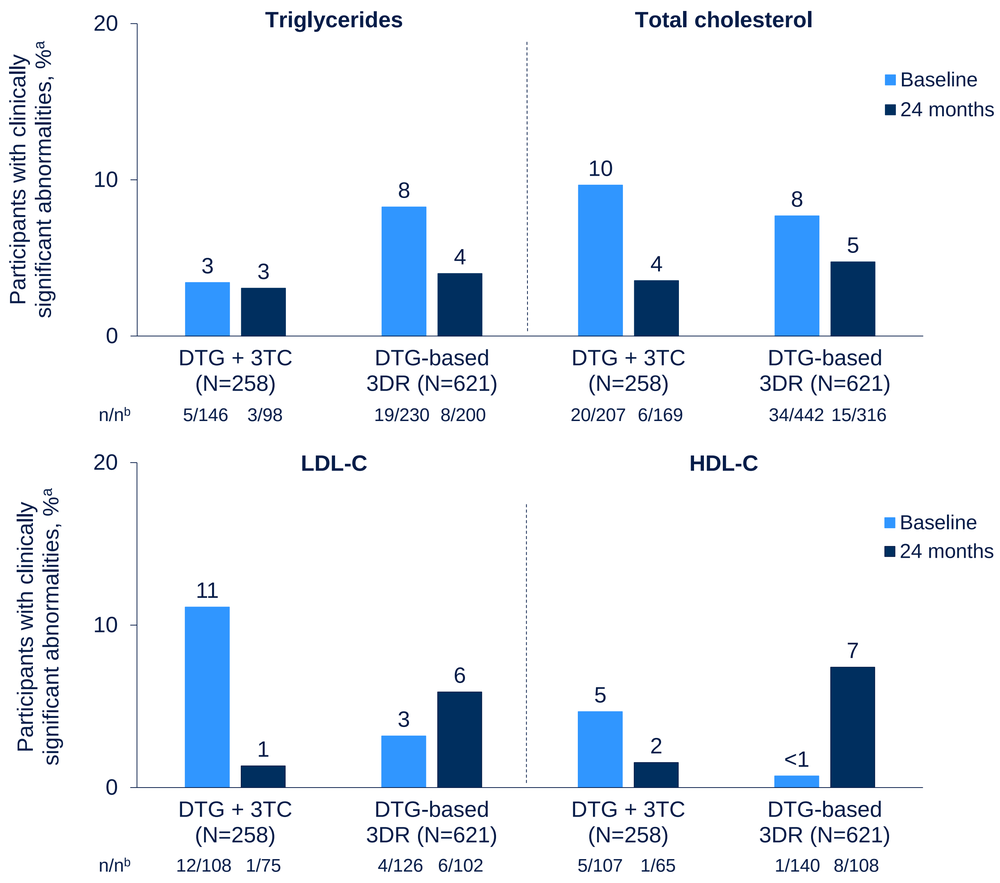
Figure 1. Proportions of Participants Using DBRs With Clinically Significant[a] Abnormalities in Blood Glucose



[a]Subjective assessment of clinically significant deviations based on the expert opinion of treating physicians. [b]Number of participants with clinically significant abnormalities over number of participants with data available at each time point.

- In the DTG + 3TC subpopulation, proportions of participants with clinically significant lipid abnormalities generally decreased from baseline to Month 24 (Figure 2)
- In the DTG-based 3DR subpopulation, proportions with triglyceride and total cholesterol abnormalities decreased, but proportions with LDL-C and HDL-C abnormalities increased

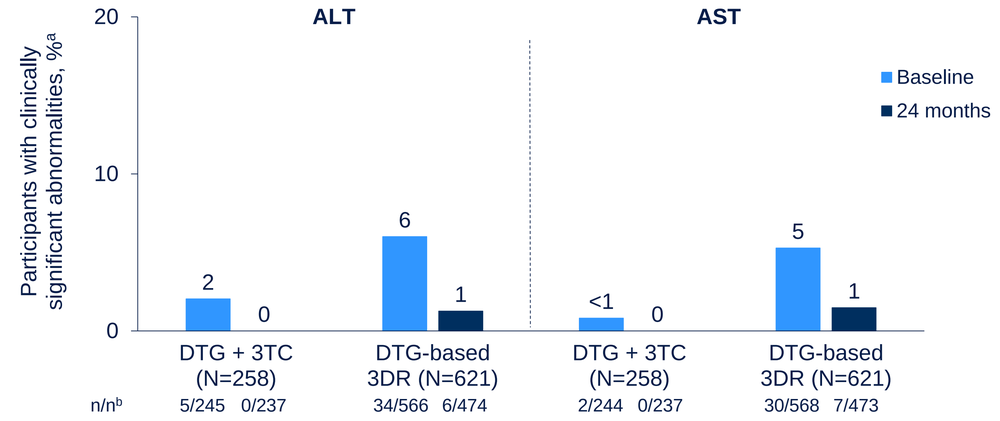
Figure 2. Proportions of Participants Using DBRs With Clinically Significant[a] Abnormalities in Lipid Parameters



[a]Subjective assessment of clinically significant deviations based on the expert opinion of treating physicians. [b]Number of participants with clinically significant abnormalities over number of participants with data available at each time point.

- Proportions of participants with clinically significant abnormalities in liver parameters (ALT and AST) decreased from baseline to Month 24 in both the DTG + 3TC and DTG-based 3DR subpopulations (Figure 3)

Figure 3. Proportions of Participants Using DBRs With Clinically Significant[a] Abnormalities in ALT and AST



[a]Subjective assessment of clinically significant deviations based on the expert opinion of treating physicians. [b]Number of participants with clinically significant abnormalities over number of participants with data available at each time point.

Cardiovascular or Metabolic ADRs/SAEs

- In the DTG + 3TC subpopulation, 1 (<1%) participant had myocarditis; in the DTG-based 3DR subpopulation, 1 (<1%) participant each had acute left ventricular failure, cardiopulmonary failure, diabetes mellitus, diabetic ketoacidosis, deep vein thrombosis, shock, and hypertensive crisis

Conclusions

- Weight gain with use of DBRs through 2 years in the TESLA study was small and should be discussed within the context of an obesogenic environment[7]
  - Most participants switched from NNRTIs, and TDF-containing ART is preferred in Russian Federation HIV treatment guidelines.[3] Therefore, the small weight gain associated with DBRs may be related to pre-switch regimen, with greater weight gain expected after switching from NNRTIs or TDF, both of which have been associated with weight-suppressing effects[1,8]
- In TESLA, lipid profiles generally improved among participants using DTG + 3TC
- Improvements in lipid profiles after switching to DTG + 3TC are consistent with clinical trial and real-world data, which have shown improvements after switch from tenofovir alafenamide–based 3- or 4-drug regimens to DTG-based 2DRs[6,9]
- Data on the efficacy and safety of DBRs in the TESLA study are presented in Poster P094

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