Key Takeaways

- The aim of the study was to describe the real-world data of DBR use in Russia.
- The use of DTG-based regimens in this real-world Russian TESLA cohort was associated with a high level of effectiveness and safety through 12 months.

Introduction

- ART-related long-term toxicities remain a topic of interest. Considering that ART is life-long, reasons for therapy discontinuation and switching regimens need further investigation in large epidemiological datasets.
- Russia has the largest HIV epidemic in Europe and Central Asia with a small downward trend in new HIV infections [1]. 5.6% of all people living with HIV (PLHIV) in Russia were infected through drug use [2].
- TESLA is the first prospective real-world data study evaluating the effectiveness and long-term safety of using DBRs in both ART-naive and experienced PLHIV in Russia, including key affected populations (including drug users: intravenous and synthetic).
- Here we present the study baseline characteristics and Month 12 outcomes.

Methods

- TESLA is a prospective, non-interventional, 3-year study of 1000 PLHIV who started taking DBRs from May to October 2020 (study initiation time) in 14 Russian centres.
- Study data was collected during visits in accordance with routine clinical practice. Each participant in the study was observed until discontinuation or suspension of DTG.
- No additional visits or procedures are mandated per protocol.
- The visits of PLHIV take place approximately every 3-6 months and allow time windows were 12 months for Month 12 full analysis set (FAS).
- PLHIV with any prior use of DTG or history of virologic failure on initial ART and virologic rebound (two consecutive measurements of viral load ≥500 cp/mL, after previously achieved suppression <250 cp/mL) were not eligible to enter the study.
- Outcomes:
  - Proportion of participants continued or switched from DTG;
  - Reasons for discontinuation;
- Time to discontinuation of DTG (estimated using Kaplan-Meier analysis);
- Proportion of participants with virologic suppression (viral load <250 cp/mL); proportion of participants with low-level viremia (viral load ≥250 cp/mL, and <500 cp/mL); proportion of participants with virologic rebound (two consecutive measurements of viral load ≥500 cp/mL, after at least 6 months of suppression <250 cp/mL).
- CD4+ cell count from baseline;
- Proportion and frequency of adverse drug reactions (ADRs) deemed related to DTG and serious adverse events (SAEs), including pregnancy outcomes, whether related or not to DTG; Reasons for management switching to DTG-based regimens at baseline (investigator reported for ART-experienced PLHIV according to the pre-specified reason or toxicity of the previous regimen and other).

Results

Study Population

- 982 PLHIV were included in the FAS for 12 months. 18 participants were not included as their data were not fully verified.
- Baseline characteristics are shown in Table 1.
- Overall, 81% were ART-experienced, 27% were on a two-drug regimen, 56% were male, median age was 40 years, median body mass index (BMI) was 24 kg/m².
- Baseline HIV-1 RNA was <250 cp/mL in 83% and CD4+ cell count was ≥200 cells/μL in 91% of ART-experienced PLHIV. 20% had viral load ≥1000 cp/mL and 77% had CD4+ counts ≥200 cells/μL, at baseline.
- Of ART-naive participants, regimen prior to switch contained an NNRTI, PI and INSTI in 57%, 47% and 2%, respectively.
- Additional subpopulations for the purpose of exploratory sub-analysis were identified: participants on DTG + lamivudine (3TC) - 3DR (n=269) and 3DR (n=708).
- 32.4% (258/797) of ART-experienced and 5.1% (11/185) of ART-naive PLHIV were included in the 3DR subgroup. 5 participants were not included in either subgroup as they did not match the criteria.
- Comorbidities (>2.5%) at baseline were detected in 645/982 (65.7%) PLHIV: Liver diseases - 38.4% (HCV - 35.3% and HBV - 2.5%); Obesity - 16.2% and metabolic disorders - 12.6%; Hypertension - 6.5%; Other viral infections - 5.8%; CVD - 3.2%; Borderline - 2.5%.

Table 1: Baseline Characteristics

<table>
<thead>
<tr>
<th>ART-experienced (n=708)</th>
<th>ART-naive (n=269)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, male, n (%)</td>
<td>458 (65.7%)</td>
</tr>
<tr>
<td>Age ≥250, n (%)</td>
<td>686 (18.8%)</td>
</tr>
<tr>
<td>Drug users, n (%)</td>
<td>121 (15.2%)</td>
</tr>
<tr>
<td>Intravenous drug users</td>
<td>120 (15.1%)</td>
</tr>
<tr>
<td>HIV-1 RNA &gt;100000 cp/mL</td>
<td>16 (2.0%)</td>
</tr>
<tr>
<td>HIV-1 RNA ≤250 cp/mL</td>
<td>660 (82.8%)</td>
</tr>
<tr>
<td>CD4+ count &lt;200 cells/μL, median (IQR)</td>
<td>429 (231 - 580)</td>
</tr>
<tr>
<td>Comorbidities &gt;2.5%</td>
<td>33 (4.1%)</td>
</tr>
</tbody>
</table>

Reasons for Administration/Switching to DBR

- Majority of investigators (73.4%) reported “other” as the main reason. Of these, 45.9% (289/585) due to regimen optimization.
- Toxicity of the previous regimen - 161/797 (20.2%)
- Ineffectiveness of the previous regimen - 51/797 (6.4%)

Reasons for Study Discontinuation

- Nine percent of PLHIV (90/982) discontinued the study; most reasons were loss of contact (6.0%), discontinuation of DTG (2.0%), n=20; 3 (1.1%) in 3DR and 17 (2.4%) in 3DR subgroups, death (0.7%) and physician’s decision (0.5%).
- Reasons for DTG discontinuation are shown in Figure 1.

Figure 1. Reasons for DTG Discontinuation

- Kaplan-Meier median estimate of the time to DTG discontinuation was not possible due to discontinuation or switch, the median time to DTG discontinuation was 12 months for the study population.
- The time to DTG discontinuation was only for the indicated participants, not for the study population. The median time to DTG discontinuation reported was only for discontinued participants, for not the study population. The median time to DTG discontinuation in 3DR subpopulation was 5.4 months for ART-naive and experienced ART-naive participants (Figure 2).

Table 2: Virological Outcomes at Month 12 by ART Regimen

<table>
<thead>
<tr>
<th>ART-experienced</th>
<th>ART-naive</th>
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<tbody>
<tr>
<td>HIV-1 RNA &lt;250 cp/mL, n (%)</td>
<td>253 (94.1%)</td>
</tr>
<tr>
<td>HIV-1 RNA &gt;250 cp/mL, n (%)</td>
<td>242 (90.0%)</td>
</tr>
<tr>
<td>Low level viremia, n (%)</td>
<td>2 (0.7%)</td>
</tr>
<tr>
<td>Non-response, n (%)</td>
<td>2 (0.7%)</td>
</tr>
<tr>
<td>Virologic rebound, n (%)</td>
<td>0</td>
</tr>
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</table>

Conclusions

- The use of DTG-based 3-drug and 2-drug regimens in this real-world Russian TESLA cohort was associated with a high level of effectiveness and safety through 12 months.
- The rate of ADRs associated with DTG was 5.5%, no new safety signals identified.
- Small weight changes reported in 4.8% with no discontinuation due to weight gain.

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