A systematic literature review was performed to summarize effectiveness outcomes reported from real-world evidence (RWE) studies in which people with HIV (PWH) with baseline characteristics that were not consistent with inclusion criteria for the dolutegravir and lamivudine (DTG + 3TC) phase 3 clinical development program randomized controlled trials (RCTs) either initiated or switched to DTG + 3TC.

### Key Takeaways

- **Introduction:**
  - Phase 3 clinical development program RCTs demonstrated durable efficacy in both treatment-naïve (GEMINI-1, 2) and virologically suppressed switch (TANGO, SALSA) participants.
  - Eligibility criteria for these RCTs included:
    - No history of or any major nucleoside reverse transcriptase inhibitor or integrase inhibitor–associated mutations
    - No baseline hepatitis B (HBV) co-infection or need for hepatitis C (HCV) therapy
    - Viral load (VL) ≤5000 copies/mL for ~6 months (TANGO, SALSA).
    - In the GEMINI studies, although participants had ≤5000 copies/mL at screening (GEMINI-1) or ≤50 copies/mL at treatment initiation.
  - RCTs conducted under controlled settings with a population that is not always representative of the population at risk; real-world studies can be used to better understand how DTG + 3TC performs in populations that include PWH whose characteristics would have prevented them from participating in RCTs.
  - This is a follow-up to a previous systematic literature review of real-world data that supported this overall high effectiveness, safety, and durability of DTG + 3TC observed in clinical trials.
  - We summarized studies of RWE for DTG + 3TC use in PWH with baseline characteristics not consistent with clinical development program RCT inclusion criteria.

- **Methods:**
  - Conducted a systematic literature review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement.
  - RWE studies that reported on DTG + 3TC use in PWH were retrieved from Ovid MEDLINE®, Embase®, PubMed, Cochrane library, and relevant international conference proceedings from January 2013 to February 2022 (Figure 1).
  - Studies with ≥10 PWH with baseline characteristics that would exclude them from phase 3 clinical development program RCTs, case reports, reviews, editorials, and preclinical studies were excluded.

- **Results:**
  - This review includes 122 publications from 103 RWE studies of 44 unique cohorts (Figure 2). The total number of people who initiated or switched to DTG + 3TC was 6034 (Table 1).
  - Of the 6034 PWH receiving DTG + 3TC, 61% were based in Southern Europe (Italy, Spain, Portugal; n=3484), 4.4% in Western Europe (France and Germany; n=130) 5.8% each in Northern Europe (UK; n=588) and Canada (n=588), 2% each in the United States (n=161) and Brazil (n=220), 1% in China (n=96), and 1% in Turkey (n=124). The remaining 9% were from mixed regions in Europe (n=782). Of the 44 real-world cohorts, represented by 85 unique studies (17 unique publications), included 1 study that reported ≥100 PWH whose baseline characteristics were not consistent with clinical development program RCT inclusion criteria. Only 8 unique studies were summarized in Figure 3 (4 RCTs that were reported in <6 months and clinical outcomes reported in ≥12 months were excluded).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Reported outcomes</th>
<th>Total</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous VF</td>
<td>7</td>
<td>103</td>
<td>1134</td>
</tr>
<tr>
<td>Evidence of BL resistance</td>
<td>6</td>
<td>103</td>
<td>253</td>
</tr>
<tr>
<td>Evidence of HBV</td>
<td>6</td>
<td>103</td>
<td>168</td>
</tr>
<tr>
<td>Evidence of HCV</td>
<td>3</td>
<td>103</td>
<td>431</td>
</tr>
</tbody>
</table>

- **Conclusions:**
  - In real-world cohorts reflective of routine clinical practice, DTG + 3TC has been used by PWH with broad baseline characteristics.
  - Outcomes from these RWE subgroups reinforce the clinical effectiveness of DTG + 3TC and further inform its application in routine clinical practice.
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