Dolutegravir plus Rilpivirine as Maintenance Dual Therapy

SWORD-1 and SWORD-2
Dolutegravir plus Rilpivirine as Maintenance Dual Therapy
SWORD-1 and SWORD-2: Design

**Study Design: SWORD-1 and Sword-2**

- **Background**: Identical randomized, multinational, open-label, industry-sponsored, parallel-group, non-inferiority studies of dolutegravir plus rilpivirine to maintain virologic suppression.

- **Inclusion Criteria**:
  - Age ≥18 years of age
  - On stable 3-4 drug ART ≥6 months
  - No history of virologic failure
  - No resistance to DTG or RPV
  - 1st or 2nd regimen
  - HIV RNA <50 copies/mL in prior 12 months
  - HIV RNA <50 copies/mL at screening
  - No HBV co-infection

- **Regimen (Once daily)**
  - Dolutegravir 50 mg + Rilpivirine 25 mg

**Early Switch Phase**
- 52 weeks
- **Early Switch**
  - DTG + RPV
  - (n = 513)

**Late switch phase**
- 96 weeks
- **Late Switch**
  - Dolutegravir
  - (n = 511)

**Continue 3-4-Drug ART**
- 511 participants

*Primary endpoint for early switch phase: week 48 HIV RNA <50 copies/mL by FDA snapshot analysis*

# Dolutegravir plus Rilpivirine as Maintenance Dual Therapy

**SWORD-1 and SWORD-2: Baseline Characteristics**

<table>
<thead>
<tr>
<th>Baseline Characteristic</th>
<th>DTG + RPV (n=513)</th>
<th>3 or 4-Drug ART (n=511)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean)</td>
<td>43</td>
<td>43</td>
</tr>
<tr>
<td>Age &gt;50 years</td>
<td>147 (29%)</td>
<td>142 (28%)</td>
</tr>
<tr>
<td>Female</td>
<td>120 (23%)</td>
<td>108 (21%)</td>
</tr>
<tr>
<td>Race, non-white</td>
<td>92 (18%)</td>
<td>111 (22%)</td>
</tr>
<tr>
<td>CD4 count (median)</td>
<td>611</td>
<td>638</td>
</tr>
<tr>
<td>Baseline PI</td>
<td>133 (26%)</td>
<td>136 (27%)</td>
</tr>
<tr>
<td>Baseline NNRTI</td>
<td>275 (54%)</td>
<td>278 (54%)</td>
</tr>
<tr>
<td>Baseline INSTI</td>
<td>105 (20%)</td>
<td>97 (19%)</td>
</tr>
<tr>
<td>Baseline TDF</td>
<td>374 (73%)</td>
<td>359 (70%)</td>
</tr>
<tr>
<td>ART duration (median)</td>
<td>51 months</td>
<td>53 months</td>
</tr>
</tbody>
</table>

**Source:** Llibre JM et al. Abstract 44LB. CROI 2017. Seattle, WA.
Dolutegravir plus Rilpivirine as Maintenance Dual Therapy SWORD-1 and SWORD-2: Pooled Results at Week 48

Week 48 Virologic Response (by FDA Snapshot Analysis)

- Confirmed virologic withdrawal: 2 (<1%) in each arm
- One NNRTI resistance mutation (K101K/E) detected in DTG + RPV arm
- No integrase resistance occurred

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SWORD-1 and SWORD-2: Pooled Results at Week 48

### SWORD 1&2 Pooled Results: 48-Week Adverse Events (AE)

<table>
<thead>
<tr>
<th></th>
<th>DTG + RPV (n = 513)</th>
<th>3 or 4-Drug ART (n = 511)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE</td>
<td>395 (77%)</td>
<td>364 (71%)</td>
</tr>
<tr>
<td>Any serious AE</td>
<td>27 (5%)</td>
<td>21 (4%)</td>
</tr>
<tr>
<td>Grade 1-2 drug-related AE</td>
<td>89 (17%)</td>
<td>8 (2%)</td>
</tr>
<tr>
<td>Grade 3-4 drug-related AE</td>
<td>8 (2%)</td>
<td>1 (&lt;1%)</td>
</tr>
<tr>
<td>AE leading to study withdrawal</td>
<td>21 (4%)</td>
<td>3 (&lt;1%)</td>
</tr>
<tr>
<td>CNS AE leading to study withdrawal</td>
<td>9 (2%)</td>
<td>1 (&lt;1%)</td>
</tr>
</tbody>
</table>

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SWORD-1 and SWORD-2: Pooled Results at Week 48

Week 48: Change in Plasma Lipids from Baseline

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SWORD-1 and SWORD-2: Pooled Results at Week 48

Week 48: Change in Bone Biomarkers from Baseline

![Graph showing change in bone biomarkers from baseline for Dolutegravir + Rilpivirine and Continued 3 or 4-drug ART.]

- Bone-specific alkaline phosphatase: 
  - Dolutegravir + Rilpivirine: -3.0
  - Continued 3 or 4-drug ART: 0.9

- Osteocalcin: 
  - Dolutegravir + Rilpivirine: -4.8
  - Continued 3 or 4-drug ART: -0.9

- Procollagen 1 N-terminal propeptide: 
  - Dolutegravir + Rilpivirine: -7.4
  - Continued 3 or 4-drug ART: -0.6

Conclusion: “A switch to a novel, once daily [2-drug regimen] of dolutegravir plus rilpivirine demonstrated high efficacy and was non-inferior to the continuation of [current ART] in virologically suppressed HIV-1-infected adults. The safety profiles of both dolutegravir and rilpivirine were consistent with the respective labels. A dolutegravir plus rilpivirine [2-drug regimen] offers the potential for reduction in cumulative ART exposure, without an increased risk of virologic failure.”
Acknowledgment

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The content in this slide set does not represent the official views of the U.S. Department of Health and Human Services, Health Resources & Services Administration.