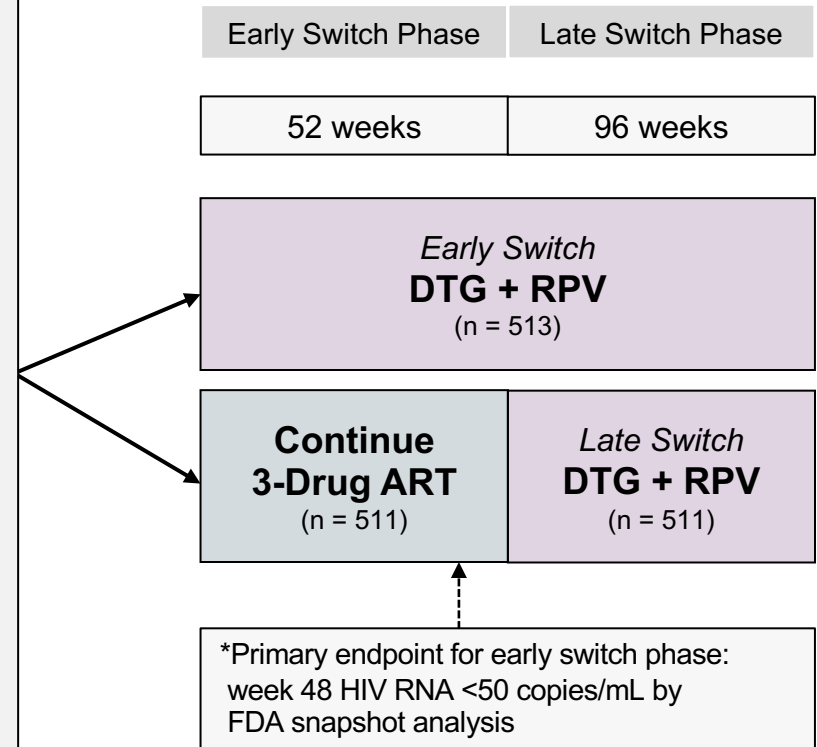Dolutegravir plus Rilpivirine as Maintenance Dual Therapy

SWORD-1 and SWORD-2

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

- **Background**: Identical, randomized, multinational, open-label, industry-sponsored, parallel-group, noninferiority studies of dolutegravir (DTG) plus rilpivirine (RPV) to maintain virologic suppression

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

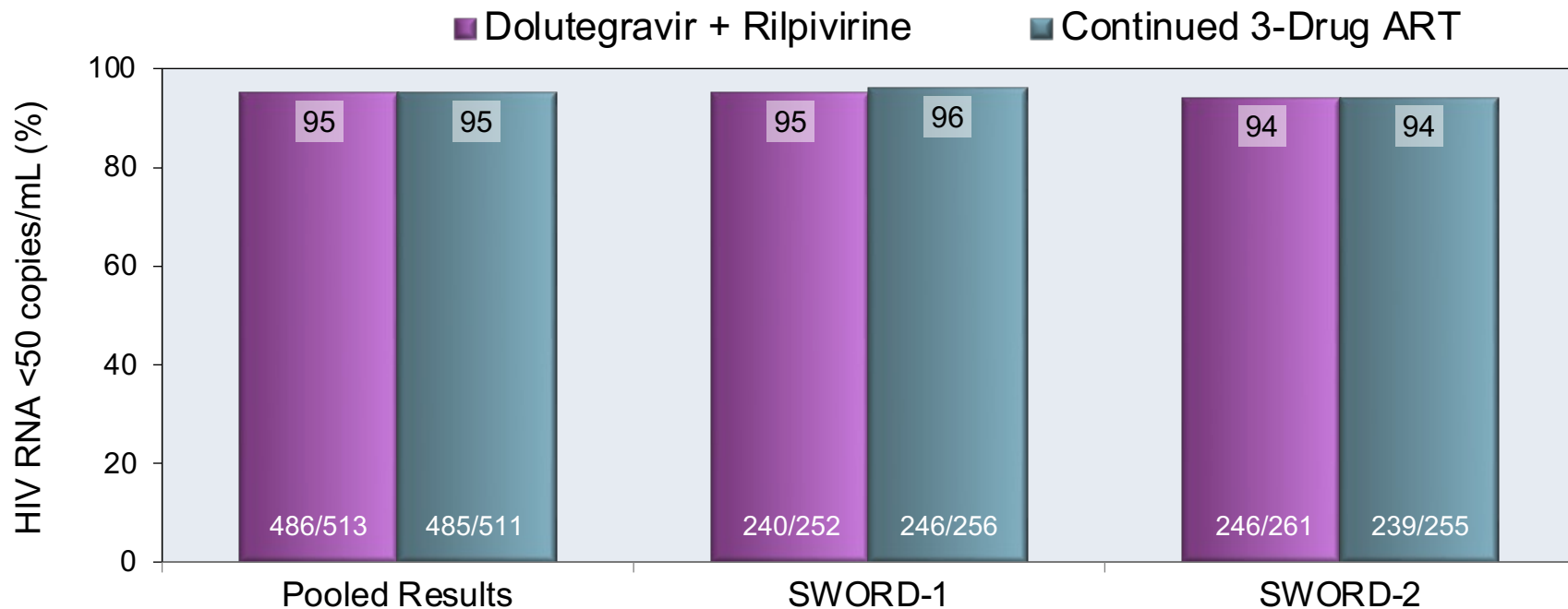- **Regimen (Once Daily):**
  - Dolutegravir 50 mg + Rilpivirine 25 mg

Early Switch Phase	Late Switch Phase
52 weeks	96 weeks

Early Switch
DTG + RPV
(n = 513)

Continue 3-Drug ART (n = 511) | **Late Switch DTG + RPV** (n = 511)

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

Source: Llibre JM, et al. Lancet. 2018;39:839-49.

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

Baseline Characteristic	DTG + RPV (n = 513)	3-Drug ART (n = 511)
Age, mean (range)	43 (21-79)	43 (22-76)
Age ≥50 years	147 (29%)	142 (28%)
Female	120 (23%)	108 (21%)
Race, non-White	92 (18%)	111 (22%)
CD4 count, median (cells/mm^3)	611	638
Baseline PI	133 (26%)	136 (27%)
Baseline NNRTI	275 (54%)	278 (54%)
Baseline INSTI	105 (20%)	97 (19%)
Baseline Tenofovir DF	374 (73%)	359 (70%)
Prior ART duration (median)	51 months	53 months

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Dolutegravir plus Rilpivirine as Maintenance Dual Therapy SWORD-1 and SWORD-2: Pooled Results at Week 48

Week 48 Virologic Response

Legend: Dolutegravir + Rilpivirine; Continued 3-Drug ART

Y-axis: HIV RNA <50 copies/mL (%)

Pooled Results: 95 (486/513), 95 (485/511)
SWORD-1: 95 (240/252), 96 (246/256)
SWORD-2: 94 (246/261), 94 (239/255)

Source: Llibre JM, et al. Lancet. 2018;39:839-49.

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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)

Legend: ■ Dolutegravir + Rilpivirine   ■ Continued 3-Drug ART

Y-axis: HIV RNA <50 copies/mL (%), scale 0–100

- Dolutegravir + Rilpivirine: 95 (486/513)
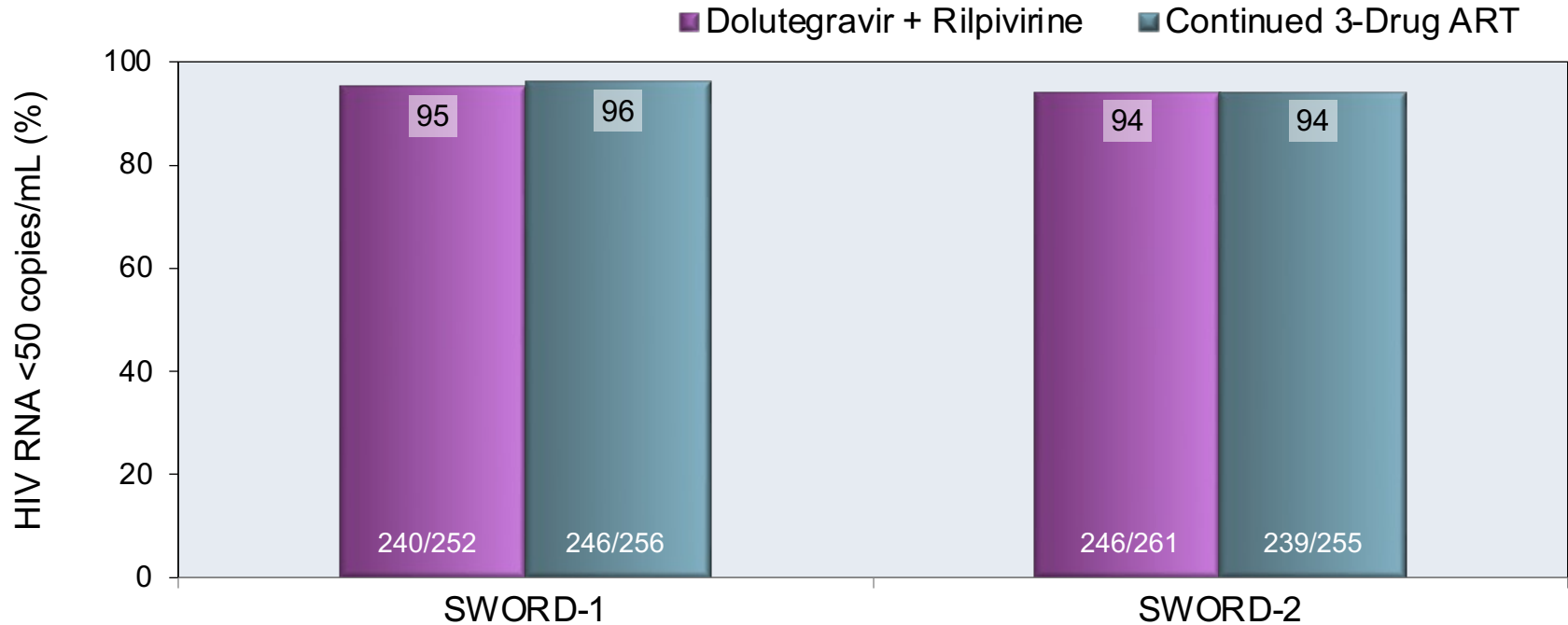- Continued 3-Drug ART: 95 (485/511)
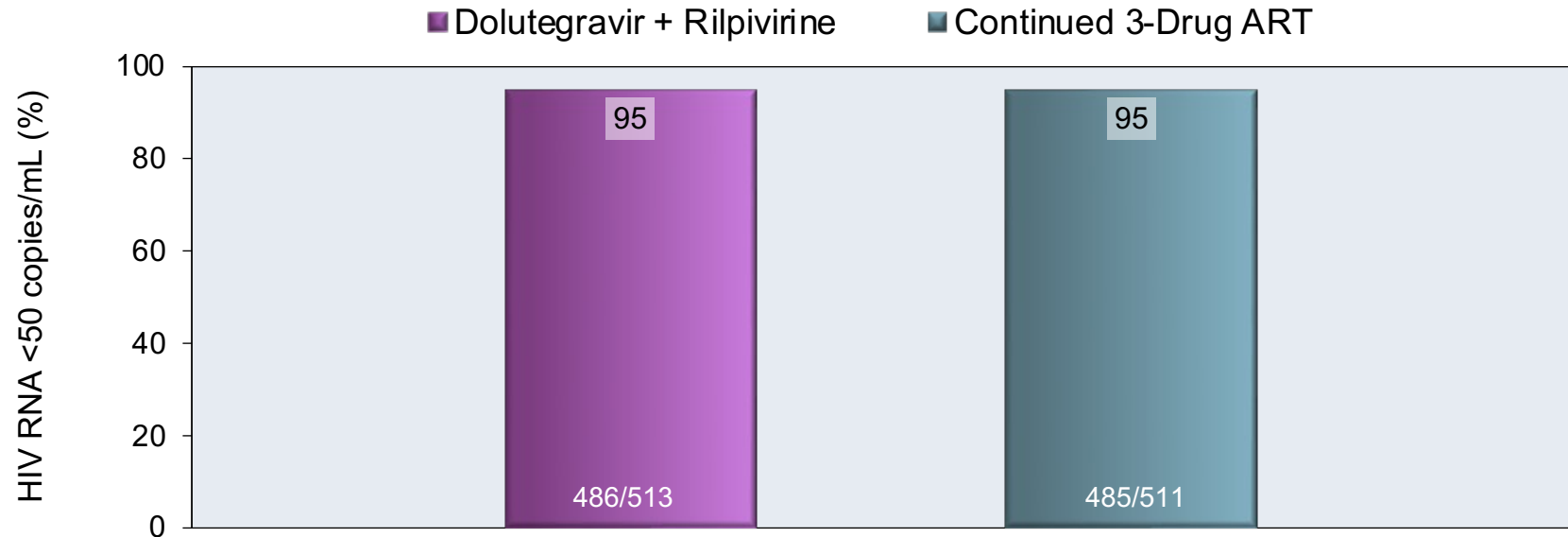
- Confirmed virologic withdrawal: 2 (<1%) in each arm
- One NNRTI resistance mutation (K101K/E) detected in DTG + RPV arm
- No integrase resistance occurred

Source: Llibre JM, et al. Lancet. 2018;39:839-49.

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Dolutegravir plus Rilpivirine as Maintenance Dual Therapy SWORD-1 and SWORD-2: Results at Week 48

Week 48 Virologic Response by SWORD-1 and SWORD-2

■ Dolutegravir + Rilpivirine ■ Continued 3-Drug ART

HIV RNA <50 copies/mL (%)

SWORD-1: Dolutegravir + Rilpivirine 95 (240/252); Continued 3-Drug ART 96 (246/256)

SWORD-2: Dolutegravir + Rilpivirine 94 (246/261); Continued 3-Drug ART 94 (239/255)

Source: Llibre JM, et al. Lancet. 2018;39:839-49.
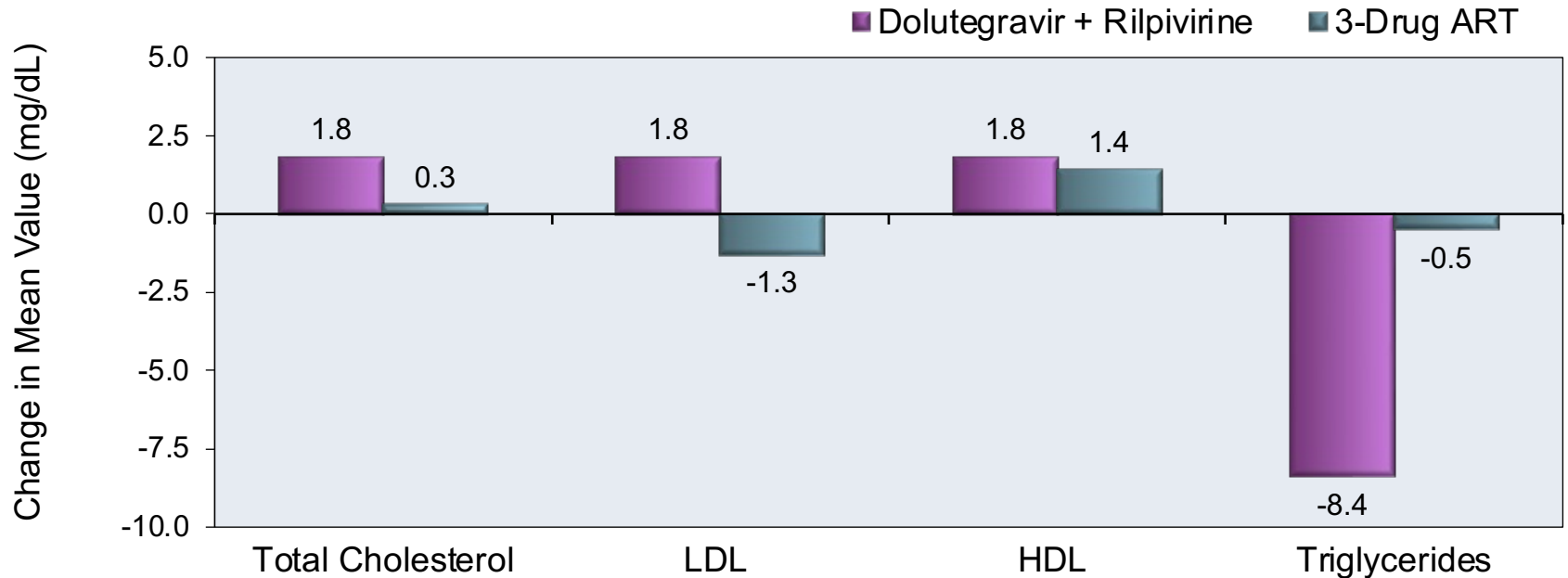
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Dolutegravir plus Rilpivirine as Maintenance Dual Therapy SWORD-1 and SWORD-2: Pooled Results at Week 48

| SWORD 1 & 2 Pooled Results: 48-Week Adverse Events (AE)		
	DTG + RPV (n = 513)	**3-Drug ART** (n = 511)
Any AE	395 (77%)	364 (71%)
Drug-related serious AE	4 (1%)	1 (<1%)
Grade 1 drug-related AE	247 (48%)	244 (48%)
Grade 2 drug-related AE	116 (23%)	116 (20%)
Grade 3 drug-related AE	27 (5%)	17 (3%)
Grade 4 drug-related AE	5 (1%)	3 (1%)
AE leading to study withdrawal	17 (3%)	3 (1%)
CNS AE leading to study withdrawal	9 (2%)	1 (<1%)

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Dolutegravir plus Rilpivirine as Maintenance Dual Therapy SWORD-1 and SWORD-2: Pooled Results at Week 48

Week 48: Change in Plasma Lipids from Baseline

Legend: ■ Dolutegravir + Rilpivirine   ■ 3-Drug ART

Y-axis: Change in Mean Value (mg/dL), scale from -10.0 to 5.0

- Total Cholesterol: 1.8 (Dolutegravir + Rilpivirine), 0.3 (3-Drug ART)
- LDL: 1.8 (Dolutegravir + Rilpivirine), -1.3 (3-Drug ART)
- HDL: 1.8 (Dolutegravir + Rilpivirine), 1.4 (3-Drug ART)
- Triglycerides: -8.4 (Dolutegravir + Rilpivirine), -0.5 (3-Drug ART)

Source: Llibre JM, et al. Lancet. 2018;39:839-49.

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Dolutegravir plus Rilpivirine as Maintenance Dual Therapy SWORD-1 and SWORD-2: Pooled Results at Week 48

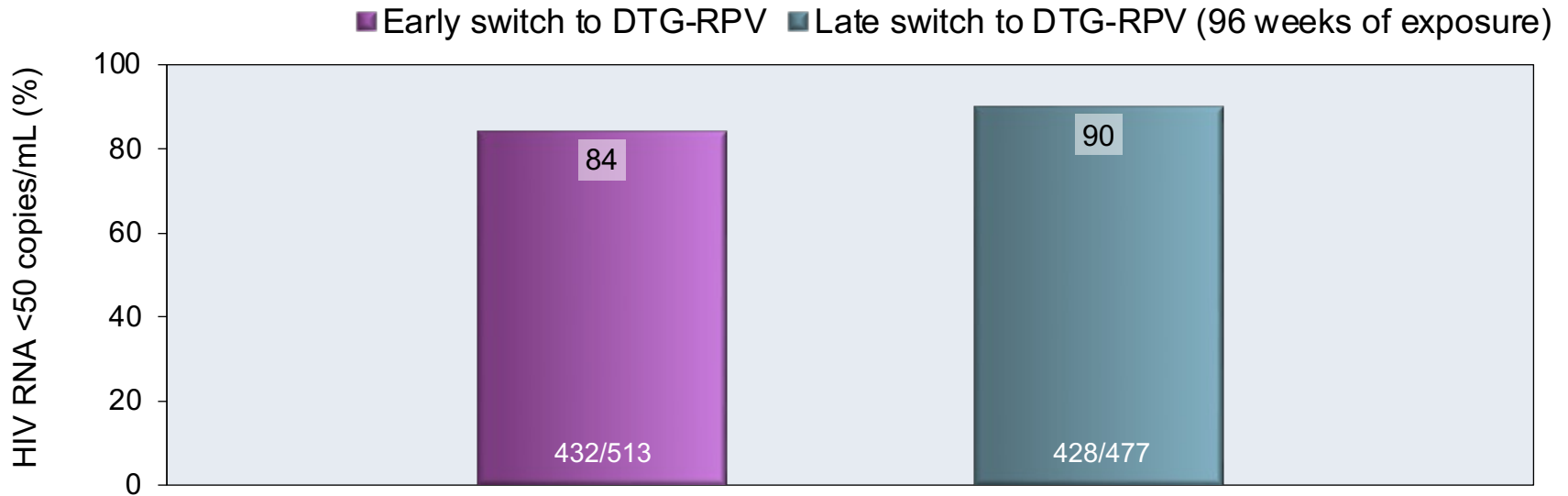## Week 48: Change in Bone Biomarkers from Baseline

Source: Llibre JM, et al. Lancet. 2018;39:839-49.
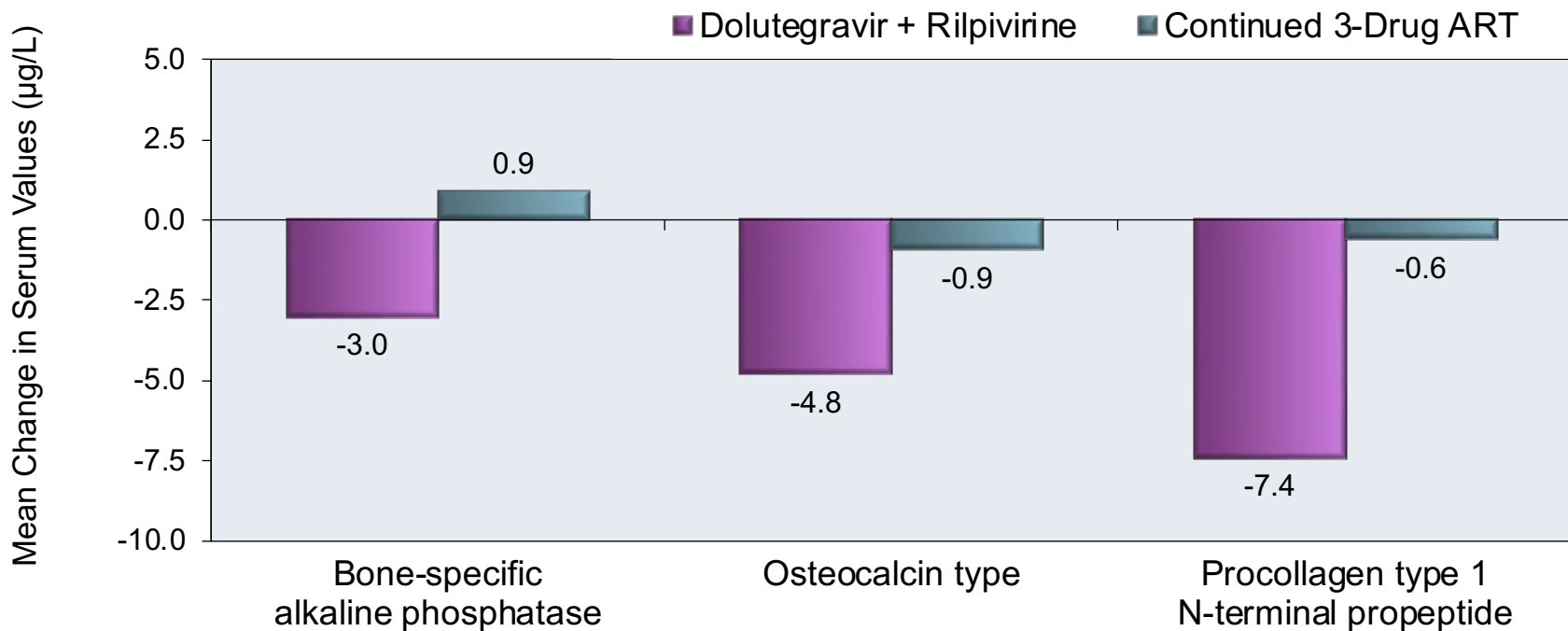
Dolutegravir plus Rilpivirine as Maintenance Dual Therapy
SWORD-1 and SWORD-2: 48-Week Data Conclusion

Interpretation: "Dolutegravir-rilpivirine was noninferior to current antiretroviral therapy regimen over 48 weeks in participants with HIV suppression and showed a safety profile consistent with its components. Results support the use of this two-drug regimen to maintain HIV suppression."

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Dolutegravir plus Rilpivirine as Maintenance Dual Therapy SWORD-1 and SWORD-2: Pooled Results at Week 148

Week 148 Virologic Response (by FDA Snapshot Analysis)

Legend: ■ Early switch to DTG-RPV ■ Late switch to DTG-RPV (96 weeks of exposure)

Y-axis: HIV RNA <50 copies/mL (%)

- Early switch to DTG-RPV: 84 (432/513)
- Late switch to DTG-RPV (96 weeks of exposure): 90 (428/477)

- 1% of all participants (n = 11) met criteria for confirmed virologic withdrawal through week 148
- NNRTI resistance-associated mutations detected in 6 total participants (<1%); no INSTI mutations identified
- Improvement in bone biomarkers observed; improvement in renal biomarkers occurred for those who switched off TDF

Source: van Wyk J, et al. J Acquir Immun Defic Syndr. 2020;85(3):325-330.

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Dolutegravir plus Rilpivirine as Maintenance Dual Therapy
SWORD-1 and SWORD-2: 148-Week Data Conclusion

Interpretation: "Switching to the 2-drug regimen dolutegravir plus rilpivirine maintained virologic suppression for a high proportion of participants through 3 years, with low rates of virologic failure and a well-tolerated safety profile."

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