National HIV Curriculum

Dolutegravir-Rilpivirine (*Juluca*)

Prepared by:

David H. Spach, MD
Brian R. Wood, MD

Last Updated: December 18, 2022

Dolutegravir-Rilpivirine

Dolutegravir-Rilpivirine

50 mg → INSTI

25 mg → NNRTI

Dose: 1 tablet once daily with a meal

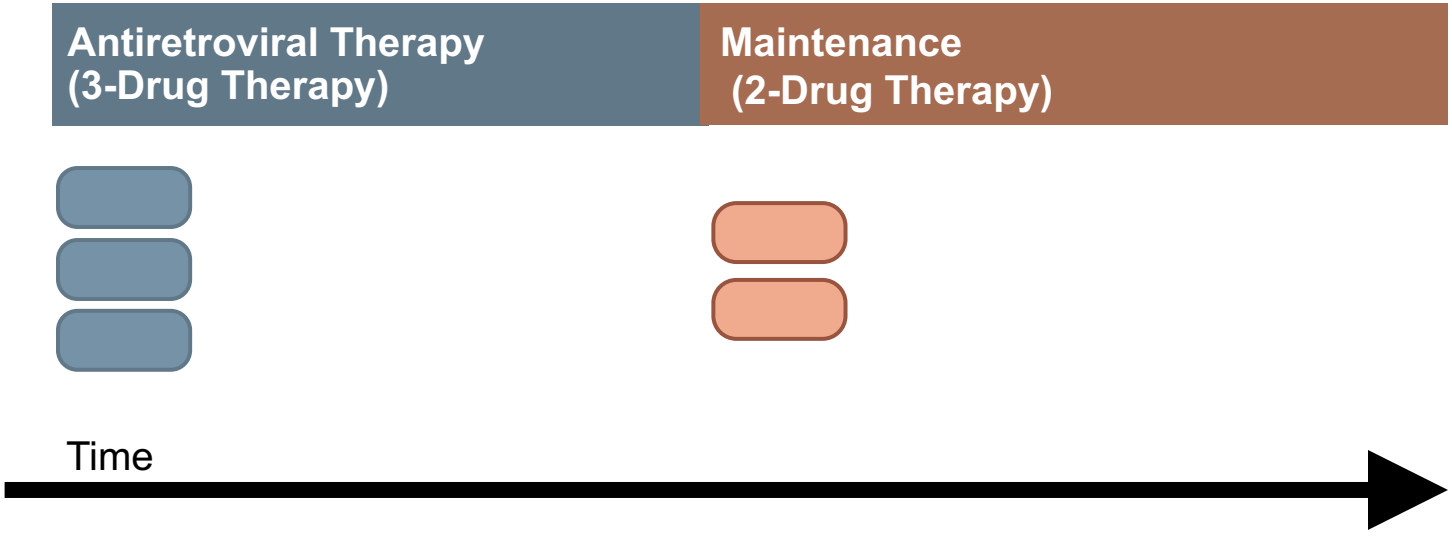
Photograph courtesy of ViiV

Dolutegravir-Rilpivirine

- **Class**
  - Dolutegravir: integrase strand transfer inhibitor (INSTI)
  - Rilpivirine: non-nucleoside reverse transcriptase inhibitor (NNRTI)
- **Indication**
  - Complete regimen to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen for at least 6 months with no history of treatment failure and no known substitutions associated with resistance to dolutegravir or rilpivirine
- **Dose (with food)**:
  - 1 tablet once daily with a meal
- **Adverse Events**: (≥2%)
  - Headache, diarrhea, nausea

Source: *Juluca* FDA prescribing information.

Criteria for 2-Drug Maintenance Antiretroviral Therapy



- HIV RNA <50 copies/mL for ≥6 months
- No prior virologic failure
- No resistance to either maintenance drug
- No hepatitis B infection

Dolutegravir-Rilpivirine
Summary of Key Phase 3 Studies

- **Trials in Adults with Virologic Suppression**
  - SWORD 1: Dolutegravir-Rilpivirine vs. continued 3-4 drug ART
  - SWORD 2: Dolutegravir-Rilpivirine vs. continued 3-4 drug ART

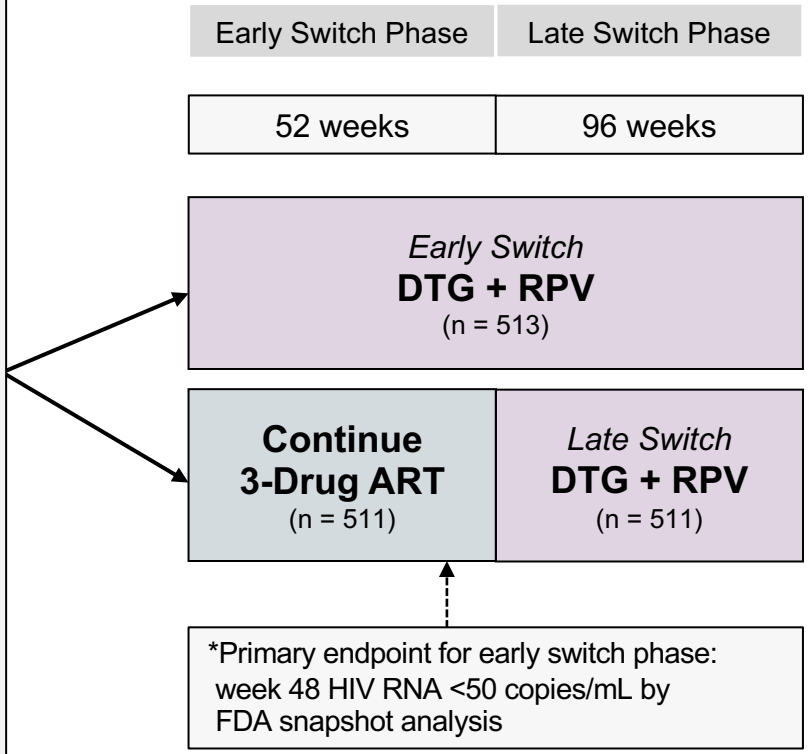
Abbreviations: ART = antiretroviral therapy

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



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

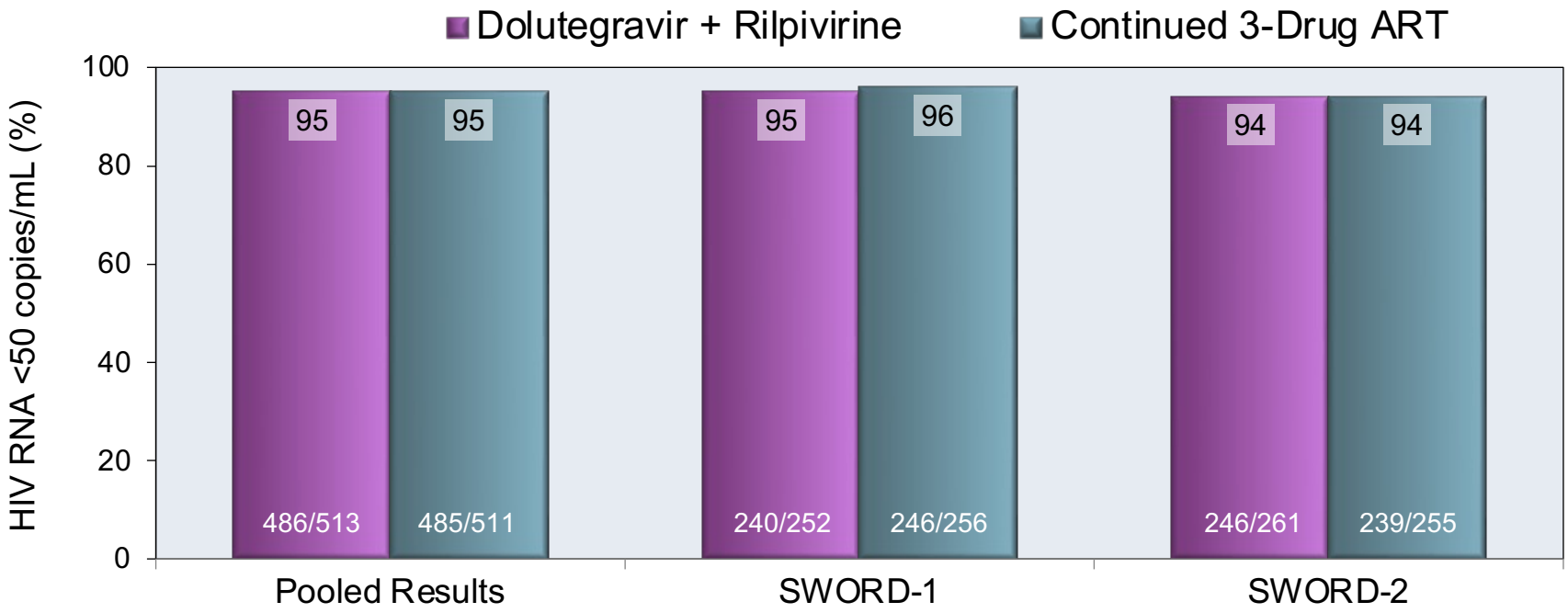
Dolutegravir plus Rilpivirine as Maintenance Dual Therapy SWORD-1 and SWORD-2: Baseline Characteristics

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

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

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

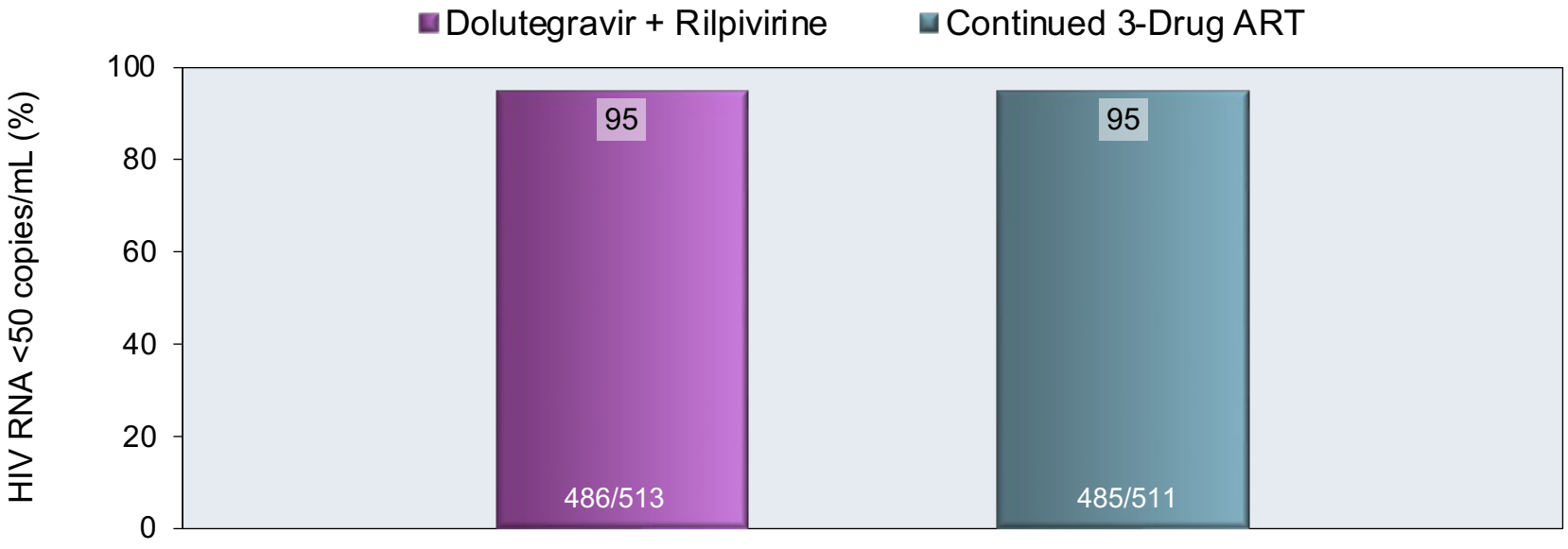
Week 48 Virologic Response



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

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)

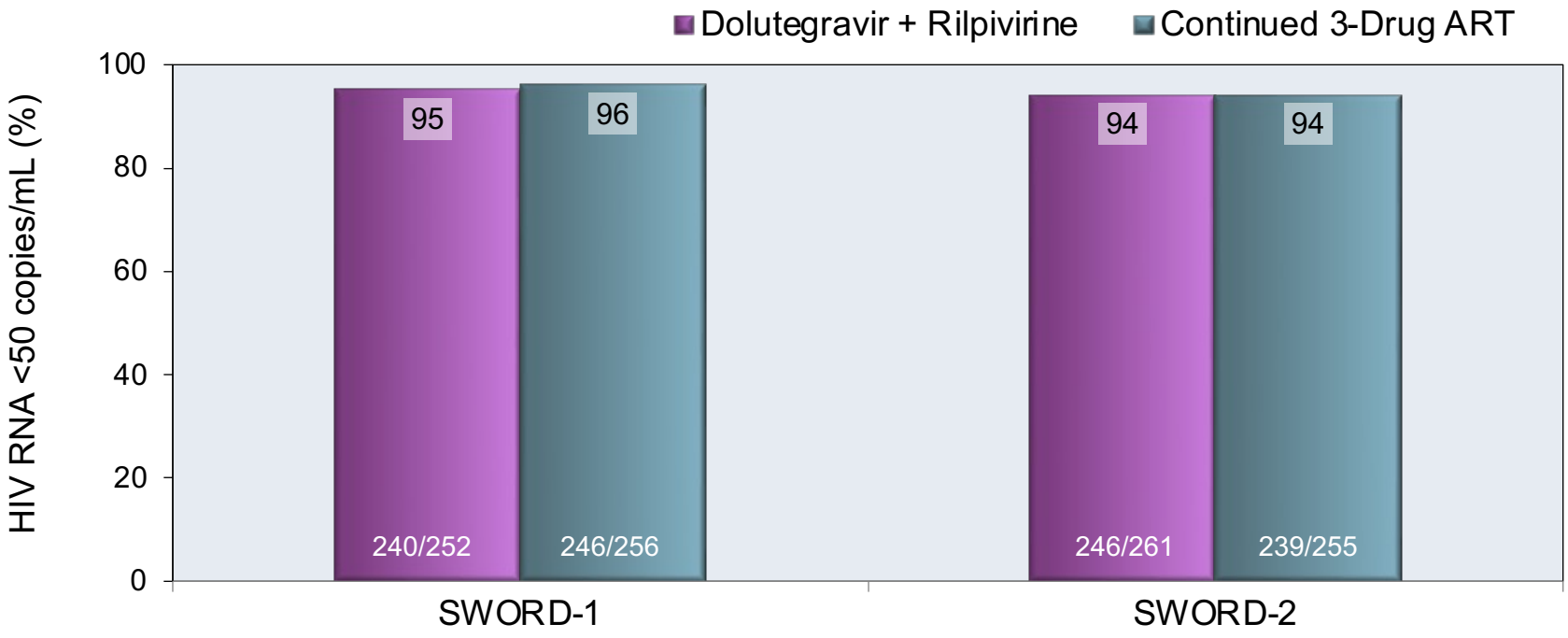


- Confirmed virologic withdrawal: 2 (<1%) in each arm
- One NNRTI resistance mutation (K101K/E) detected in DTG + RPV arm
- No integrase resistance occurred

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

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



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

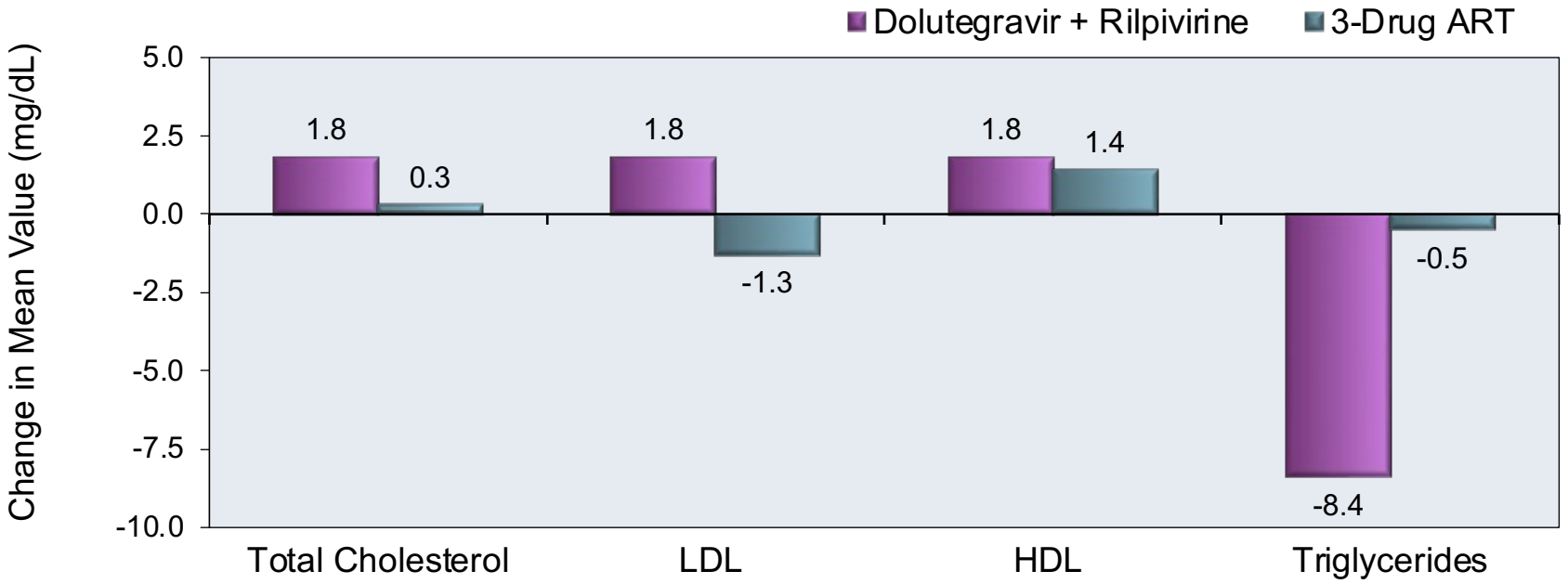
Dolutegravir plus Rilpivirine as Maintenance Dual Therapy
SWORD-1 and SWORD-2: Pooled Results at Week 48

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%)

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

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

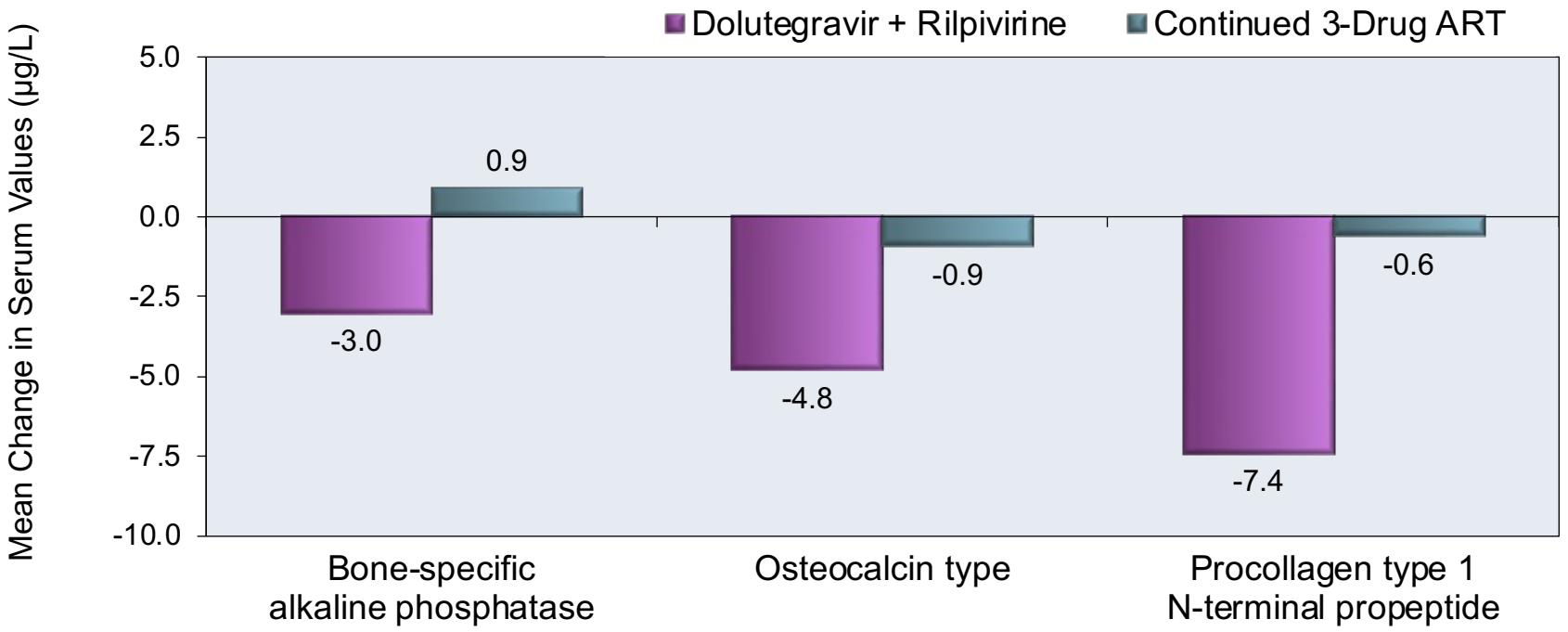
Week 48: Change in Plasma Lipids from Baseline



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

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.

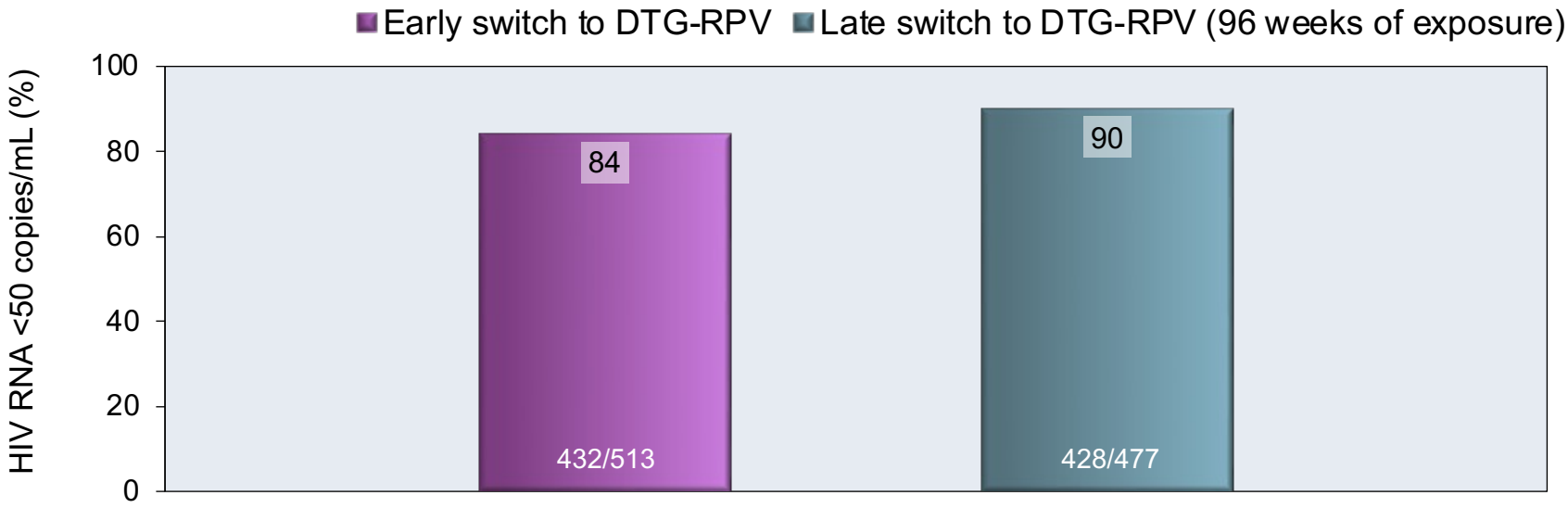
Dolutegravir plus Rilpivirine as Maintenance Dual Therapy SWORD-1 and SWORD-2: 48-Week Data Conclusion

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.”

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

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)



- 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.

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.”

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

Acknowledgments

The **National HIV Curriculum** is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of a financial assistance award totaling $1,021,448 with 0% financed with non-governmental sources. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by HRSA, HHS, or the U.S. Government. For more information, please visit HRSA.gov. This project is led by the University of Washington's Infectious Diseases Education and Assessment (IDEA) Program.

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