National HIV Curriculum

Dolutegravir-Rilpivirine

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Dolutegravir-Rilpivirine: Basics

- **Medication**
  - Oral, once daily, fixed dose combination of dolutegravir (integrase strand transfer inhibitor) and rilpivirine (non-nucleoside reverse transcriptase inhibitor)
- **Administration**
  - Many drug-drug interactions and food requirements
- **With Renal Impairment**
  - No dose adjustment necessary in patients with renal impairment
- **With Hepatic Impairment**
  - Has not been studied in patients with severe hepatic impairment (Child-Pugh C)
- **Pregnancy**
  - Avoid use in pregnancy
- **Common Adverse Effects** (≥2%)
  - Diarrhea, headache, nausea

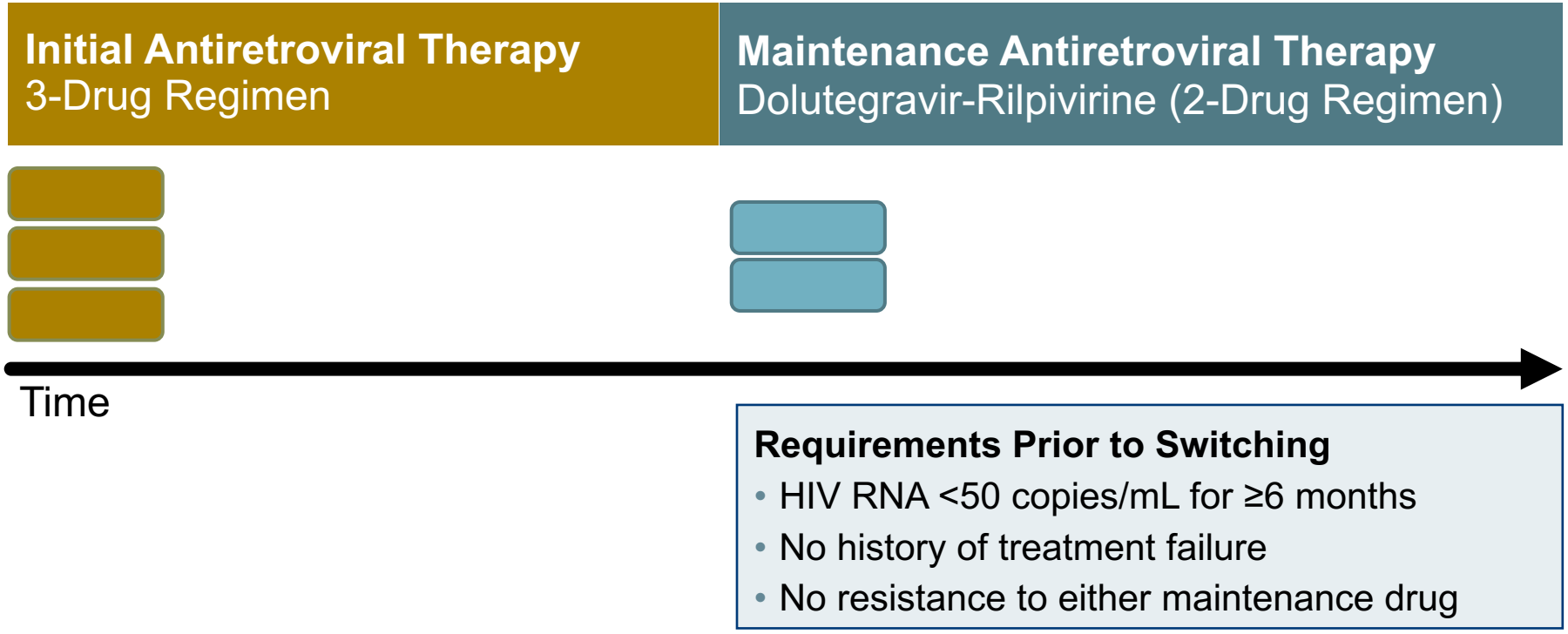
Source: Dolutegravir-Rilpivirine Prescribing Information.

Dolutegravir-Rilpivirine

Dolutegravir	Rilpivirine
50 mg	25 mg
INSTI	NNRTI

Dose: 1 tablet once daily with food

Dolutegravir-Rilpivirine
Maintenance Antiretroviral Therapy



Dolutegravir-Rilpivirine: Key Drug Interactions

- Contraindicated with dofetilide
- Dolutegravir concentrations typically **decrease** with:
  - Rifampin and rifapentine
  - Polyvalent cations
  - Some anticonvulsants
  - St. John's wort (*Hypericum perforatum*)
- Rilpivirine concentrations typically **decrease** with:
  - Rifampin and rifapentine
  - Some anticonvulsants
  - St. John's wort (*Hypericum perforatum*)
  - Proton pump inhibitors and H2 blockers

Source: Dolutegravir-Rilpivirine Prescribing Information.

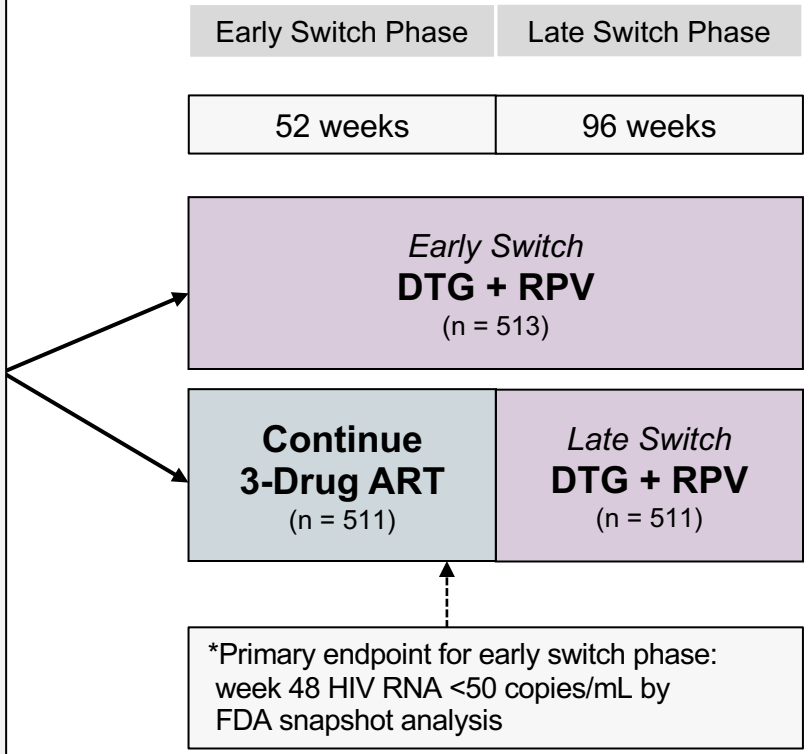
Dolutegravir-Rilpivirine: Key Studies

Dolutegravir-Rilpivirine: Key Studies

- **Treatment Naïve**
  - None
- **Treatment Experienced**
  - SWORD-1 & SWORD-2

DTG + RPV 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 INSTI, NRTI, NNRTI, or PI
  - 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.

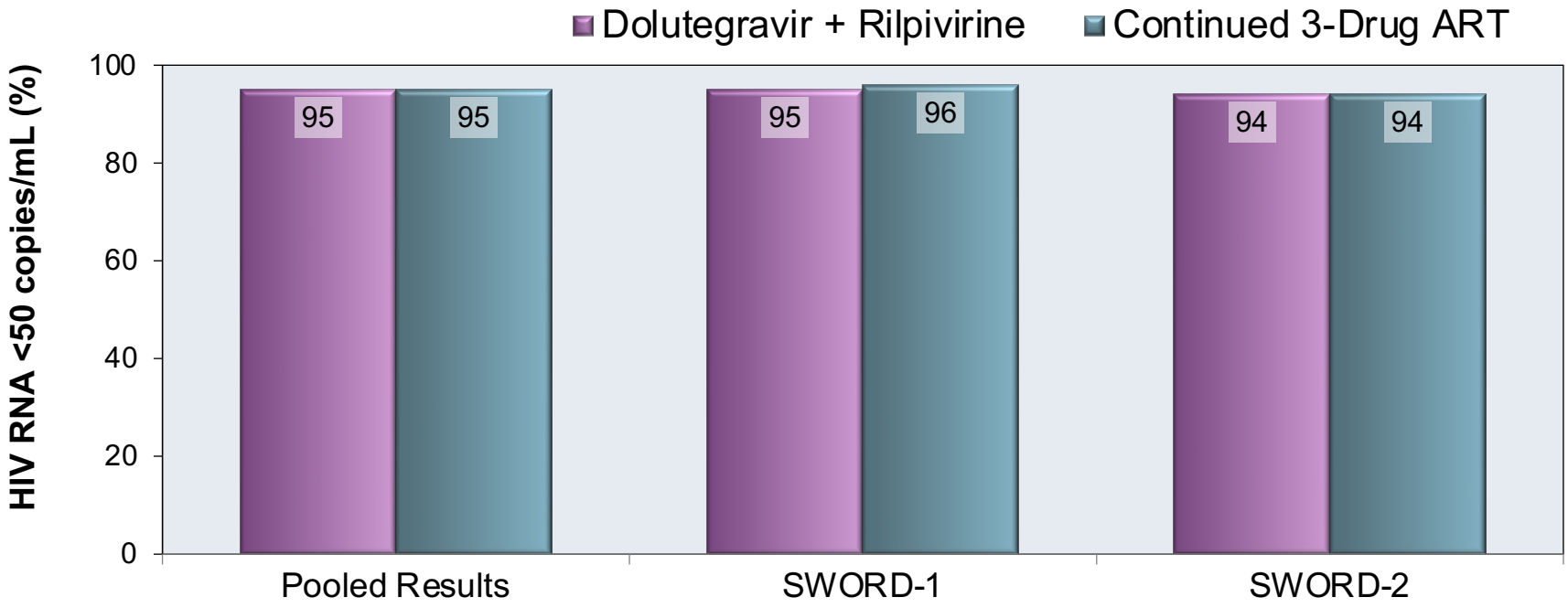
DTG + RPV as Maintenance Dual Therapy
SWORD-1 and SWORD-2: Patient Characteristics

Baseline Characteristic	DTG + RPV (n = 513)	3-Drug ART (n = 511)
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.

DTG + RPV 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-Rilpivirine: Treatment Emergent Resistance

- **In SWORD-1 and SWORD-2**
  - After 148 weeks
    - 11 on the DTG-RPV met confirmed virologic withdrawal
      - 8 in early switch arm, 3 in late switch arm
  - Viral resistance testing performed in 11 participants
    - NNRTI resistance mutations: K101E, E138A, K103N, V179I, M230L, L100I
    - INSTI resistance mutations: None

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

Dolutegravir-Rilpivirine: Summary

- Oral, once-daily pill available as a fixed dose combination
- Must be taken with food (because of rilpivirine component)
- Well-tolerated, but with many drug-drug interactions
- Exercise caution when administering medications that decrease concentrations of dolutegravir or rilpivirine
- Should only be used in virally suppressed PWH with no prior history of virologic failure and no major mutations to any ART class
- Treatment emergent resistance can develop

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