

Initial Oral ART With 2DR vs 3DR by Clinical Scenario

Scenario: Rapid Start/Test and Treat¹

2DR

- ▲ Not recommended in current guidelines
- ▲ Well supported by multiple studies
- ▲ Baseline HBV testing and HIV genotypic resistance testing required prior to use
 - Switch to 3DR if active HBV infection or NRTI (3TC) resistance
- ▲ Avoid if taking PrEP at/around time of HIV infection

3DR

- ▲ Recommended in current guidelines
- ▲ Well supported by multiple studies
- ▲ Genotypic resistance testing required if prior use of LA CAB for PrEP (for INSTI-based 3DRs)

Scenario: Advanced HIV

2DR

- ▲ Well supported by available data

3DR

- ▲ Well supported by available data and long-term use

Myth



In advanced HIV infection, 3DR achieves more rapid viral decay and shorter time to viral suppression vs 2DR

True



In DOLCE in advanced HIV (baseline CD4+ cell count ≤ 200 cells/mm³), time to viral suppression, HIV-1 RNA decay, and CD4+ cell count recovery **all similar with 2DR vs 3DR initial ART²**

Scenario: Older Age and/or Multiple Comorbidities^{3,4}

2DR

Potential pros:

- ▲ Lower DDI risk
- ▲ Avoids potential TDF-associated toxicities (bone/kidney)
- ▲ Avoids potential TAF-associated weight gain

Potential cons:

- ▲ Insufficient activity against HBV coinfection

3DR

Potential pros:

- ▲ Potential for higher DDI risk
- ▲ Risk of potential TDF-associated toxicities (bone/kidney)
- ▲ Risk of potential TAF-associated weight gain

Potential cons:

- ▲ Active against HBV coinfection

Scenario: Pregnancy⁵

DTG/3TC recommended as an alternative ART regimen in pregnancy if:

- ▲ HIV-1 RNA $\leq 500,000$ c/mL
- ▲ No active HBV coinfection
- ▲ Confirmed susceptibility to 3TC per resistance testing

Additional notes:

- ▲ If history of LA CAB PrEP use, INSTI genotypic resistance test results should also be obtained
- ▲ Not recommended for acute or recent HIV infection in pregnancy

Scenario: HIV/HBV Coinfection

- ▲ With active HBV coinfection, 2DR ART is inferior to 3DR ART because 3TC monotherapy is considered insufficient for treatment of HBV
 - A tenofovir drug (TAF or TDF) must be included in the ART regimen to confer sufficient anti-HBV activity and avoid development of HBV drug resistance

Scenario: Oral Bridging to LA ART

2DR

- ▲ Feasibility supported by data from open-label, nonrandomized phase IIIb VOLITION trial^{6,7}

3DR

- ▲ Supported by randomized, double-blind phase III trials that led to regulatory approval of LA CAB + RPV^{8,9}

US DHHS guidelines support use of oral bridge with ≥ 3 mo of sustained viral suppression before switch to LA CAB + RPV, but do not specify oral bridge regimen¹

References

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5. clinicalinfo.hiv.gov/en/guidelines/perinatal/recommendations-arv-drugs-pregnancy-what-start-art-never-received.
6. Córdova. IAS 2025. Abstr WEPEB033.
7. Rolle. CROI 2026. Abstr 525.
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Abbreviations

2DR, 2-drug regimen
3DR, 3-drug regimen
3TC, lamivudine
ART, antiretroviral therapy
DHHS, Department of Health and Human Services
DDI, drug-drug interaction
DTG, dolutegravir
INSTI, integrase strand transfer inhibitor
LA CAB, long-acting cabotegravir
NRTI, nucleoside reverse transcriptase inhibitor
PrEP, pre-exposure prophylaxis
RPV, rilpivirine
TAF, tenofovir alafenamide
TDF, tenofovir disoproxil fumarate



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