Choosing Initial ART & Managing First Episode of Virologic Failure

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Outline

- Review current options for initial ART and discuss considerations for choosing between the options
- Highlight recommendations for lab monitoring after ART initiation and management of first virologic failure

HHS Guidelines, October 2018
Recommended Initial Regimens for Most People with HIV

INSTI + 2 NRTI's
Dolutegravir/Abacavir/Lamivudine[+] Dolutegravir + TAF/Emtricitabine* Dolutegravir + TDF/Emtricitabine*
Bictegravir/TAF/Emtricitabine*
Raltegravir + TAF/Emtricitabine* Raltegravir + TDF/Emtricitabine*

INSTI = integrase strand transfer inhibitor
TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate
[+]Only if HLA-B*5701 negative; caution if history of ischemic CV disease
*TAF ok with creatinine clearance as low as 30 mL/min; avoid TDF if baseline renal insufficiency

Source: HHS Adult and Adolescent Treatment Guidelines (aidsinfo.nih/gov)

HHS Guidelines, October 2018
Recommended Initial Regimens in Certain Clinical Situations

INSTI + 2 NRTI's
Elvitegravir/cobicistat/Emtricitabine/TAF
Elvitegravir/cobicistat/Emtricitabine/TDF
Boosted PI + 2 NRTI's
Darunavir (with a booster[+]) plus 2 NRTI's*
Atazanavir (with a booster[+]) plus 2 NRTI's*
NNRTI + 2 NRTI's
Efavirenz/TDF/Emtricitabine
Rilpivirine/TAF/Emtricitabine^ or Rilpivirine/TDF/Emtricitabine^
Doravirine/TDF/Lamivudine

[+]Booster can be a combined tablet with cobicistat or a separate ritonavir tablet
*NRTI combinations: TAF-emtricitabine, TDF-emtricitabine, or abacavir-lamivudine
^Rilpivirine should not be used if CD4 count <200 or HIV RNA >100,000

Source: HHS Adult and Adolescent Treatment Guidelines (aidsinfo.nih/gov)

HHS Guidelines, October 2018
Regimens to Consider When TAF, TDF, and ABC Cannot Be Used or Are Not Optimal

2-Drug Regimens that Include an Agent with High Barrier to Resistance + A Second Agent
Dolutegravir/Lamivudine
Darunavir (+ ritonavir) + Raltegravir (BID)*
Darunavir (+ ritonavir) + Lamivudine

*Only if CD4 count >200 cells/mm^3 and HIV RNA <100,000 copies/mL

Source: HHS Adult and Adolescent Treatment Guidelines (aidsinfo.nih/gov)

Key Considerations for Choosing Initial ART

- See Table 7 of Guidelines
- Key Factors:
  - CD4 count, HIV RNA
  - Starting before genotype result available
  - HLA-B*5701 (if considering abacavir)
  - Pill count/size, tolerability, food requirements
  - Comorbidities (CKD, liver disease, osteoporosis, psychiatric illness, cardiac risk, hyperlipidemia, HIV-associated dementia)
  - Pregnancy
  - Co-infections (e.g. HBV, HCV, TB)
  - Other: insurance coverage

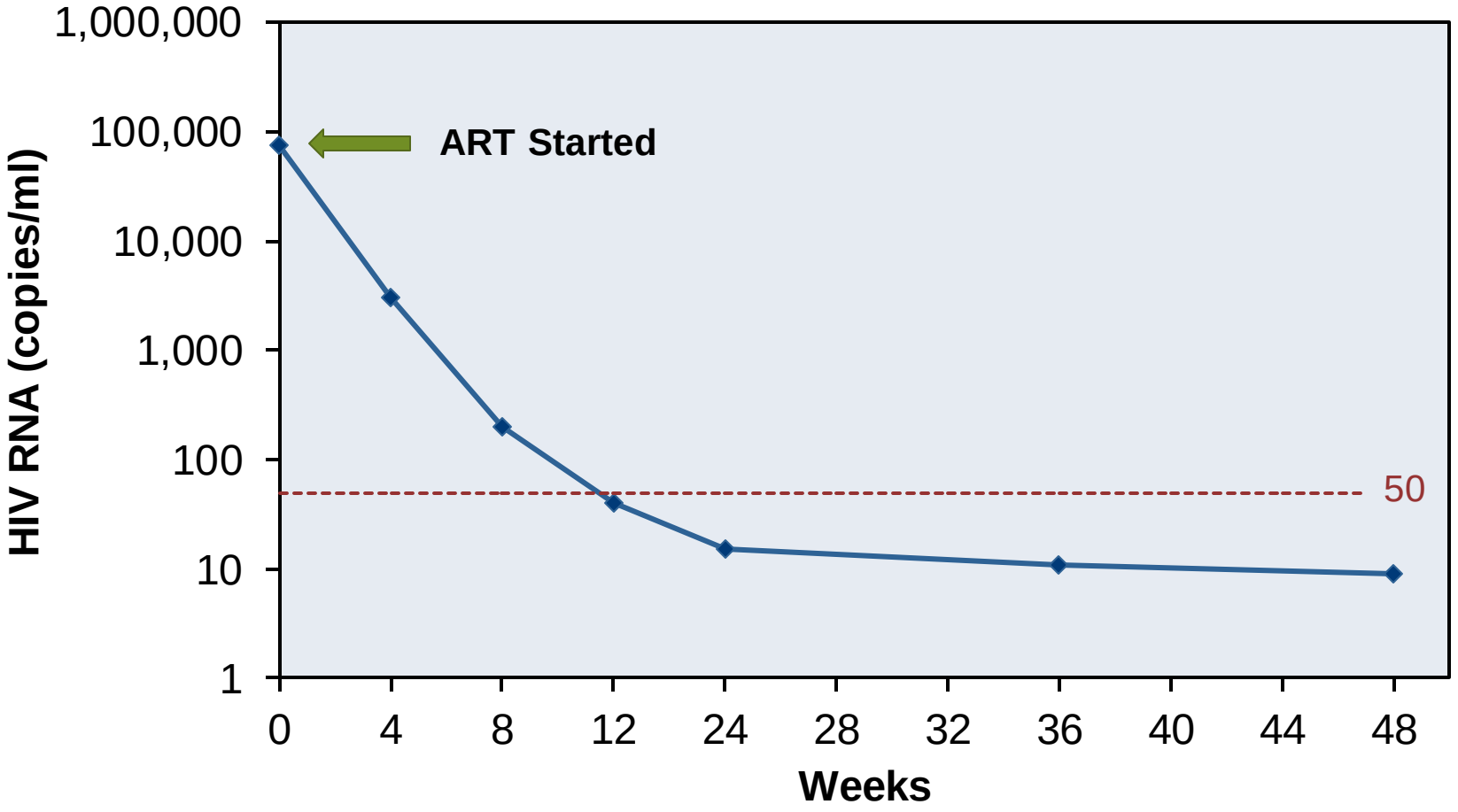
Source: HHS Adult and Adolescent Treatment Guidelines (aidsinfo.nih/gov)

Monitoring After ART Initiation

- HIV RNA checks:
  - 2 to 8 weeks after ART initiation
  - Then every 4 to 8 weeks until suppressed
  - Then every 3 to 6 months
  - Once consistently suppressed with stable immunologic status for ≥2 years, extend to every 6 months
- CD4 count checks:
  - Every 3 to 6 months during first 2 years of ART, or if viremia develops while on ART, or if CD4 count below 300
  - After 2 years on ART with suppressed viral load:
    - CD4 300-500: every 6 to 12 months
    - CD4 >500: recheck optional

Source: HHS Adult and Adolescent Treatment Guidelines (aidsinfo.nih/gov)

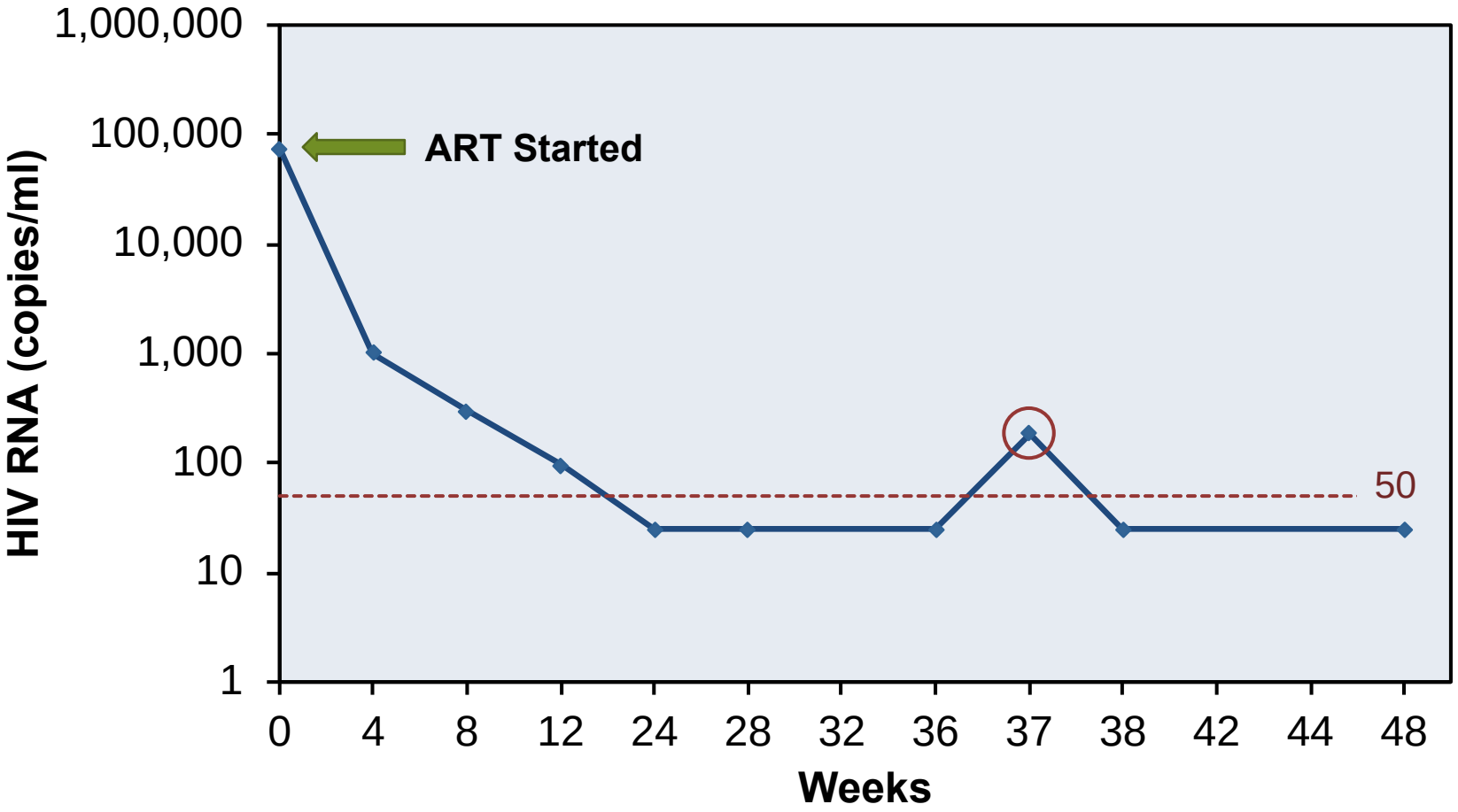
Virologic Responses on Antiretroviral Therapy
Virologic Suppression



A confirmed HIV RNA level below the limit of assay detection, usually by 3-6 months

Source: 2018 HHS Antiretroviral Therapy Guidelines. AIDS Info (www.aidsinfo.nih.gov)

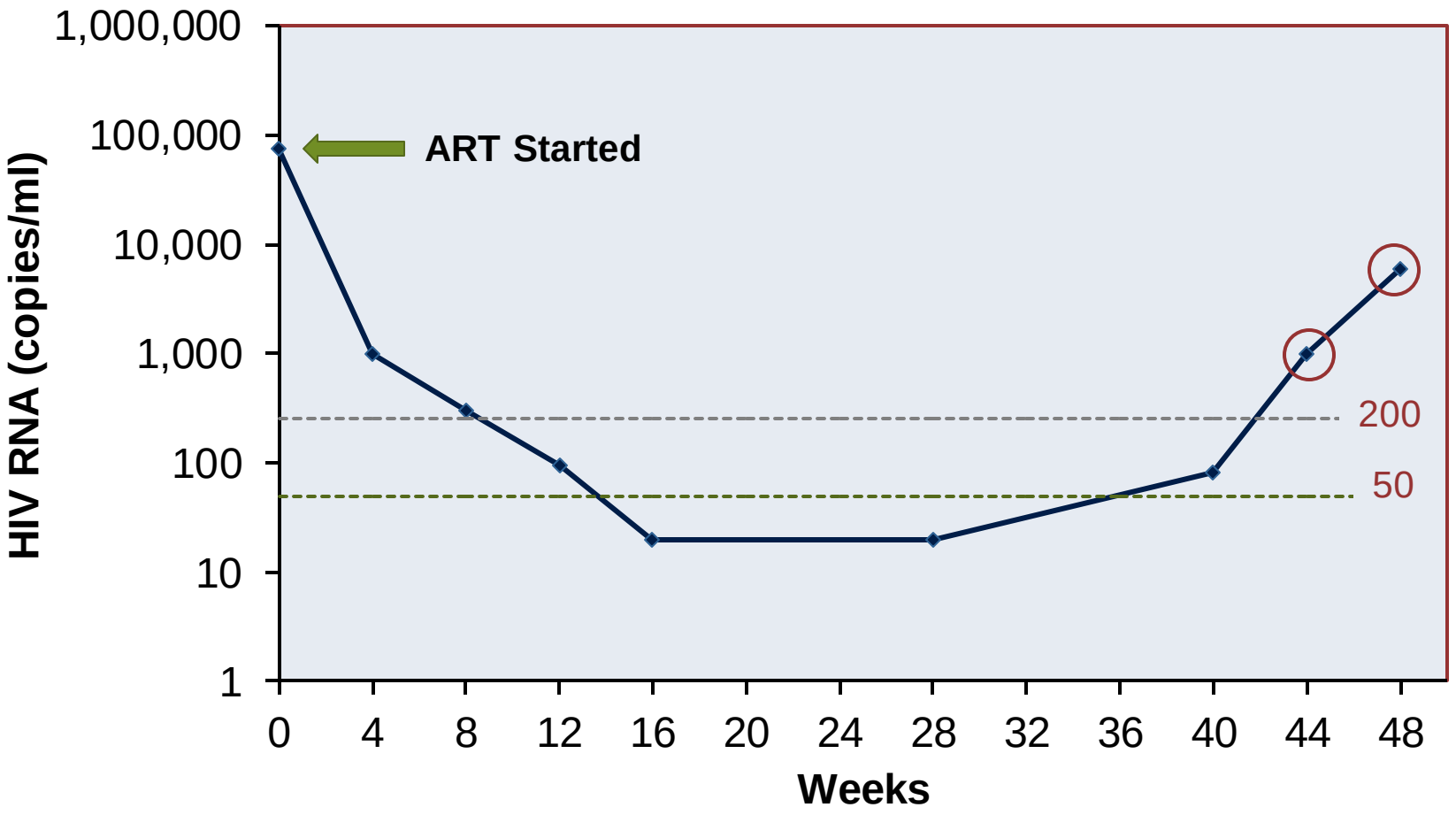
Virologic Responses on Antiretroviral Therapy
Isolated Virologic Blip



After virologic suppression, an isolated detectable HIV RNA level followed by return to virologic suppression

Source: 2018 HHS Antiretroviral Therapy Guidelines. AIDS Info (www.aidsinfo.nih.gov)

Virologic Responses on Antiretroviral Therapy
Virologic Rebound/Failure



Confirmed detectable HIV RNA (to >200 copies/mL) after virologic suppression

Source: 2018 HHS Antiretroviral Therapy Guidelines. AIDS Info (www.aidsinfo.nih.gov)

Management of First Virologic Failure

- Send genotype resistance test (+ integrase genotype if on INSTI)
  - Ideally send while on failing regimen or within 4 weeks of stopping
- Assess barriers to adherence, reasons for missed doses, drug-drug interactions, OTC's, tolerability, etc.
- Continue ART while awaiting results vs stop vs empiric switch?
  - Case-by-case decision depending on likelihood of resistance
- With resistance results, aim for new regimen with 3 active agents
  - 2 active agents acceptable if one of them has high barrier to resistance (dolutegravir, bictegravir, or boosted darunavir)

Source: 2018 HHS Antiretroviral Therapy Guidelines. AIDS Info (www.aidsinfo.nih.gov)

Example 1

- Woman in her 50's with HIV, multiple medical comorbidities, & barriers to adherence
- Transitioned from EFV/TDF/FTC to BIC/TAF/FTC
- HIV RNA levels not detected on multiple checks, then 8,196 copies/mL on a routine check
- Called back for repeat HIV RNA, genotype (including integrase), discussion of adherence barriers
- Continued BIC/TAF/FTC while awaiting results; no resistance detected; achieved suppression again on same

Example 2

- Man in his 40's whose HIV was suppressed on RPV/TDF/FTC, then multiple missed visits
- Lots of outreach and finally got labs; HIV RNA 9,476 copies
- Repeat HIV RNA 13,150 copies/mL; genotype sent
- ART stopped while awaiting genotype
- Genotype result: NRTI: M184V, K70KE; NNRTI: K101E, Y188L, H221HY (all new since baseline genotype)
- New regimen: TAF/FTC + DRV/cobi + DTG

Example 3

- Man in his 50's taking ABC + 3TC + NVP-XR
- Reports adherence, but HIV RNA increased from routinely not detected to 17,800 copies; 22,730 on recheck
- Genotype sent
- Regimen empirically changed: TAF/FTC + DRV/cobi + DTG
- Genotype result: NRTI: M184V, L74V, M41L, L210RW, T215Y; NNRTI: H221HY, K103N, Y181C
- Continuing that new regimen