Update to ART Treatment Guidelines 2020

(updated 12-18-2019):

2 Drug Regimen for Initial Therapy

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16 January 2020

Created 16 January 2020

Disclosures

No conflicts of interest or relationships to disclose

Question:

29 year old man with newly diagnosed HIV. No co-morbidities and is not on any other medications. Would you offer him a 2-drug regimen for treatment?

A. Yes

B. No

C. It depends

What stayed the same?

Recommended Initial Regimens for Most People with HIV

Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use.

INSTI plus 2 NRTIs:

Note: For individuals of childbearing potential, see Table 6b before prescribing one of these regimens.

- BIC/TAF/FTC **(AI)**
- DTG/ABC/3TC **(AI)—if HLA-B*5701 negative**
- DTG plus (TAF or TDF)[a] plus (FTC or 3TC) **(AI)**
- RAL plus (TAF or TDF)[a] plus (FTC or 3TC) (**BI** for TDF/[FTC or 3TC], **BII** for TAF/FTC)

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What's new in the guidelines?

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INSTI plus 1 NRTI:

- DTG/3TC **(AI)**, except for individuals with HIV RNA >500,000 copies/mL, HBV coinfection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available

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Rationale for 2 Drug Regimen as Initial Therapy

- **PADDLE Study** (Pilot Antiretroviral Design with Dolutegravir LamivudinE)
  - Only 20 patients, treatment naive
  - Excluded those with HIV VL > 100,000 copies/mL or any baseline resistance
  - 2 did not achieve suppression - 1 suicide, 1 failure (baseline VL 106,000)
- **ACTG A5353**
  - Phase 2 single-arm pilot study, n=120 treatment naïve
  - HIV VL baseline between 1000-500,000 copies/mL; no baseline resistance
  - 85% (102/120) virologic suppression at 48 weeks
  - One patient developed M184V and an integrase mutation

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DTG + 3TC versus DTG + TDF-FTC as Initial ART
GEMINI 1 and 2: Background

Study Design: GEMINI 1 and 2

- **Background**:
  - Two identical, double-blind, multinational, noninferiority randomized controlled trials that compared initial antiretroviral therapy (ART) of DTG + 3TC versus DTG + TDF-FTC

- **Enrollment Criteria:**
  - Treatment-naïve adults
  - HIV RNA 1,000-500,000 copies/mL
  - No NRTI, INSTI, or major PI mutations
  - No chronic HBV
  - No need for HCV therapy
  - Not pregnant or breastfeeding

DTG + 3TC
(Dual ART)
n = 716

DTG + TDF-FTC
(Triple ART)
n = 717

Primary endpoint: % with HIV RNA <50 copies/mL at 48 weeks by ITT

Source: Cahn P, et al. Lancet. 2019;393:143-55.

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DTG + 3TC versus DTG + TDF-FTC as Initial ART
GEMINI 1 and 2: Baseline Characteristics

GEMINI 1 and 2 Baseline Characteristics		
Characteristic	**DTG + 3TC** (n = 716)	**DTG + TDF-FTC** (n = 717)
Age, years, median (IQR)	32 (26-40)	33 (26-42)
Female, n (%)	113 (16)	98 (14)
White, n (%)	480 (67)	497 (69)
Black or African American, n (%)	99 (14)	76 (11)
CD4 cell count, mean (SD)	462 (219.2)	461.3 (213.1)
CD4 count ≤200 cells/mm^3, n (%)	63 (9)	55 (8)
HIV RNA (log_{10} copies/mL)	4.42 (0.66)	4.45 (0.65)
≤100,000 copies/mL, n (%)	576 (80)	564(79)
>100,000 copies/mL, n (%)	140 (20)	153 (21)

Source: Cahn P, et al. Lancet. 2019;393:143-55.

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DTG + 3TC versus DTG + TDF-FTC as Initial ART

GEMINI 1 and GEMINI 2: Week 96 Data

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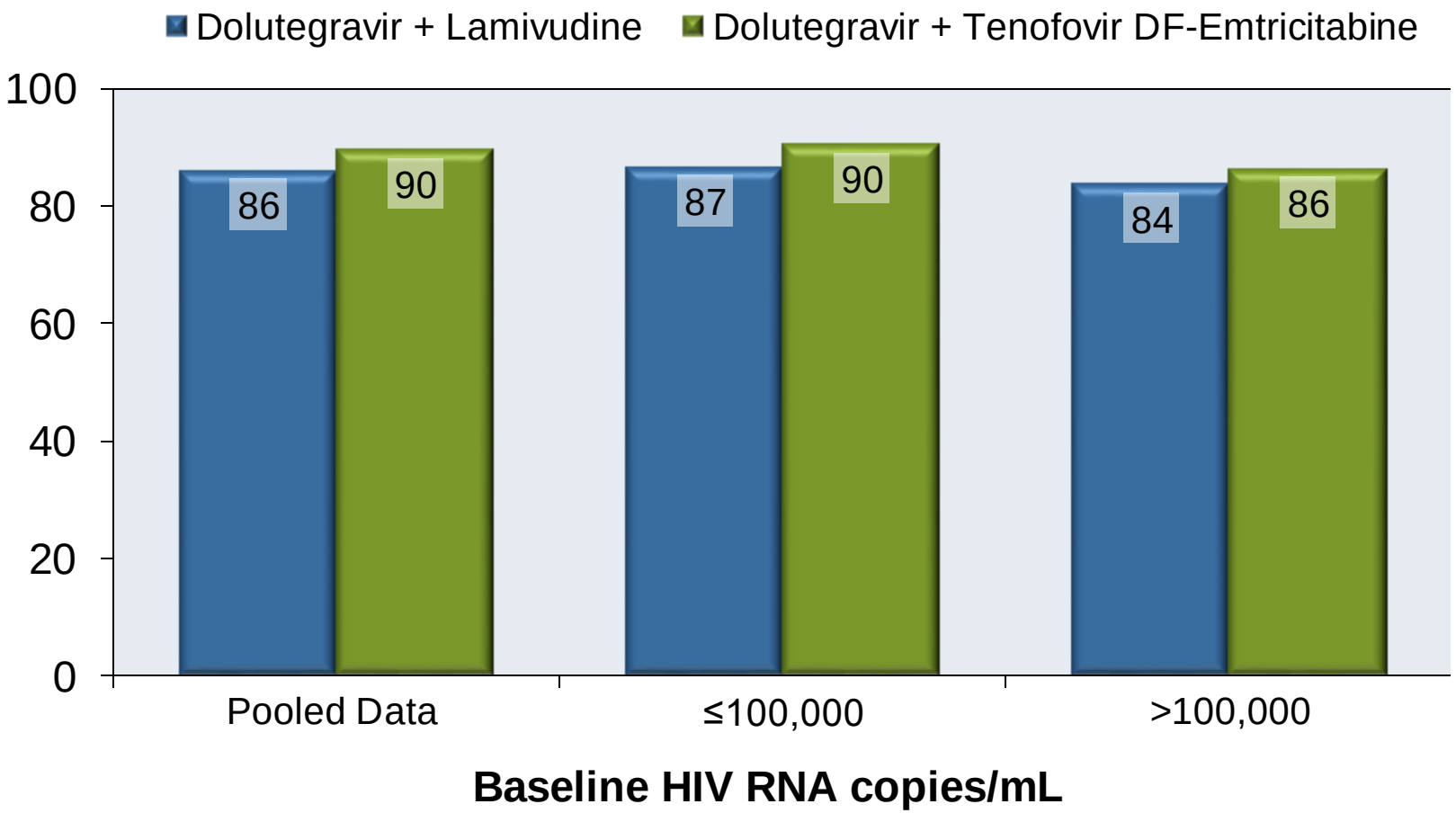
DTG + 3TC versus DTG + TDF-FTC as Initial ART
GEMINI 1 and 2: Results by Baseline HIV RNA Level

Week 96 Virologic Response (Intention-To-Treat Analysis)



Source: Cahn P, et al. J Acquir Immune Defic Syndrome. 2019 Dec 10. Epub ahead of print

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DTG + 3TC versus DTG + TDF-FTC as Initial ART
GEMINI 1 and 2: Results by Baseline CD4 Cell Count

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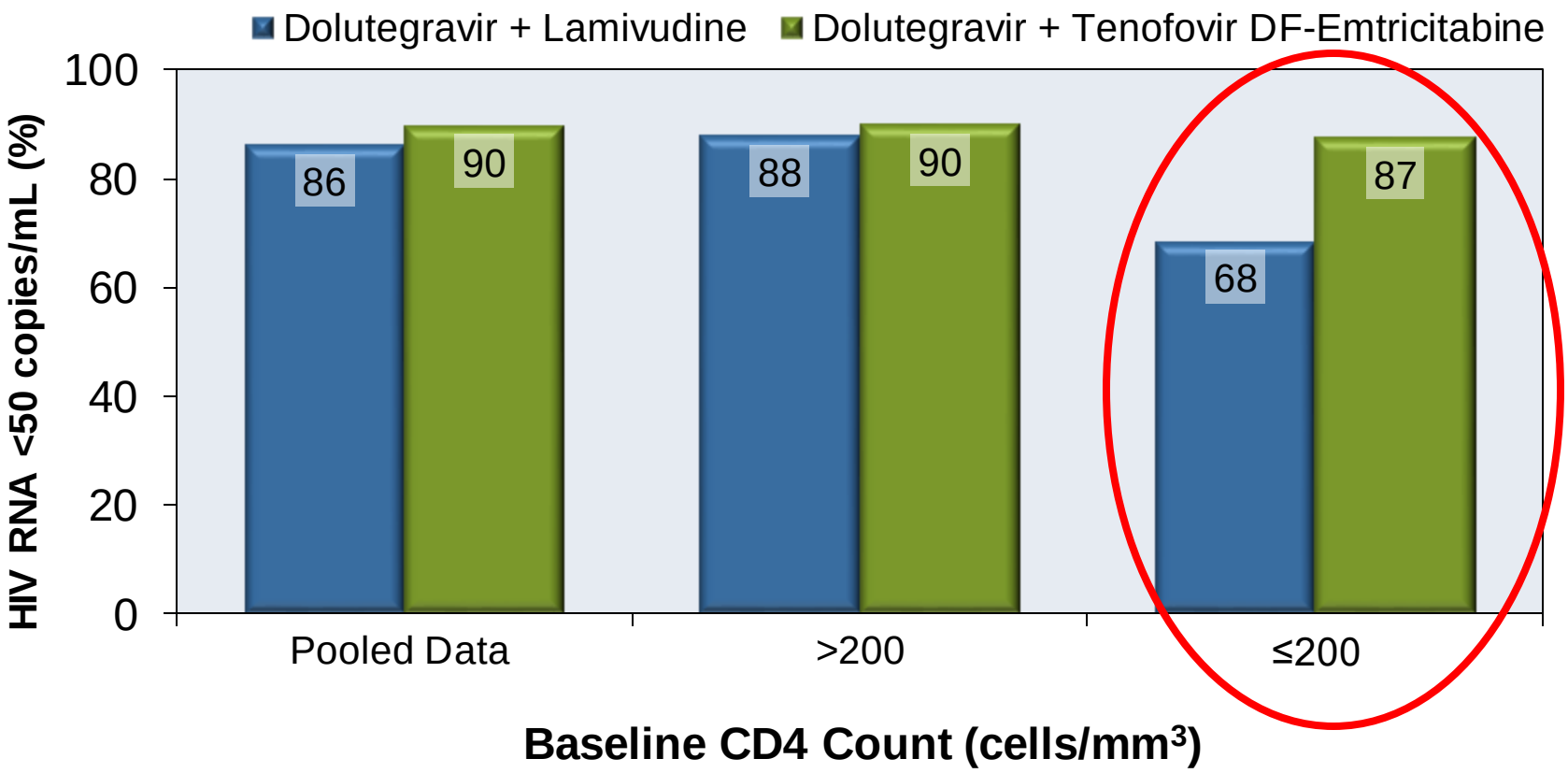

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DTG + 3TC versus DTG + TDF-FTC as Initial ART
GEMINI 1 and 2: Week 96 Conclusion

Conclusion: “Dolutegravir + lamivudine demonstrated long-term, non-inferior efficacy vs dolutegravir + tenofovir disoproxil fumarate/emtricitabine without increased risk of treatment emergent resistance, supporting its use in treatment-naive HIV-1–infected individuals.”

Source: Cahn P, et al. J Acquir Immune Defic Syndrome. 2019 Dec 10. Epub ahead of print

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Observational “Real-World” Data

- VACH Study
  - Retrospective cohort study in Spain
  - Endpoints:
    - Time to discontinuation due to failure
    - Risk of discontinuation due to failure
    - Time to discontinue due to adverse events
    - Risk of adverse events

Observational "Real-World" Data

	INSTI-based Triple Therapy	DTG+3TC or DTG+RPV	p-value
Age (years), Mean (SD)	48.1 (10.7)	52.0 (10.3)	<0.0001
Gender, % Female	23.4	28.7	0.0020
AIDS dx, % yes	23.2	26.7	0.0264
CD4 count, % > 350 cells/mm^3	81.8	82.9	0.4527
Viral load, % <50 copies/mL	81	90.2	<0.0001
Duration of ART regimens (years), mean (SD)	12.0 (8.4)	14.9 (8.1)	<0.0001
# of previous ART regimens, Mean (SD)	5.3 (3.6)	7.4 (4.6)	<0.0001
# of previous virologic failures, Mean (SD)	1.1 (2.4)	1.5 (2.9)	<0.0001
HCV, % yes	32.6	35.4	0.1323

Tiera R et al. EACS 2019 PS8/5

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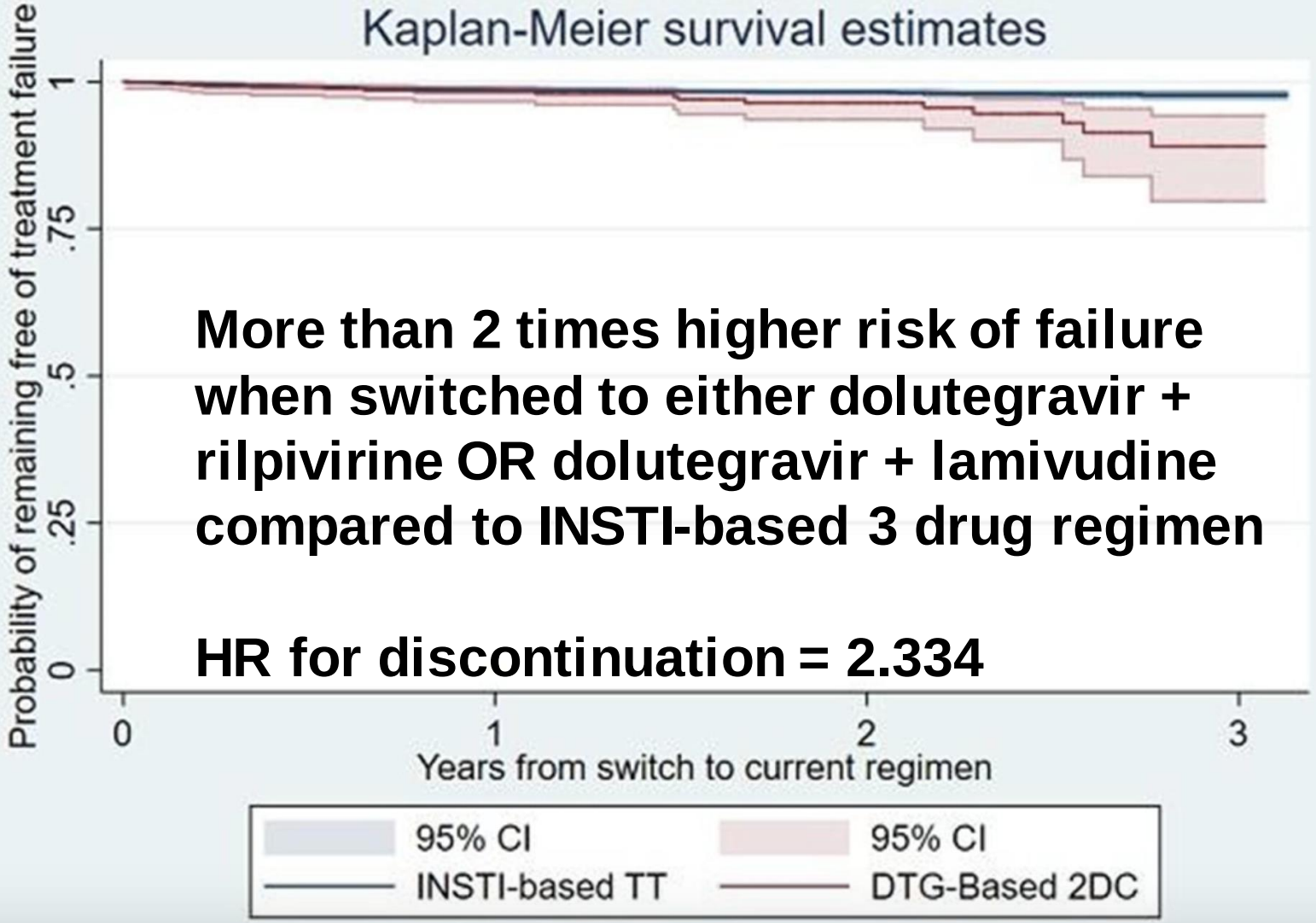
Observational ”Real-World” Data



More than 2 times higher risk of failure when switched to either dolutegravir + rilpivirine OR dolutegravir + lamivudine compared to INSTI-based 3 drug regimen

HR for discontinuation = 2.334

Tiera R et al. EACS 2019 PS8/5

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Questions?

Acknowledgment

The Mountain West AIDS Education and Training (MWAETC) program is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of an award totaling $2,972,660 with 0% financed with non-governmental sources.

The content in this presentation 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.

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- **HIV/AIDS Management (Warmline)** 1-800-933-3413
  M-F, 6am - 5pm PST
- **PEPline** 1-888-HIV-4911
  Every day, 6am - 6pm PST
- **PrEPline** 1-855-HIV-PrEP
  M-F, 8am - 3pm PST
- **Perinatal HIV Hotline** 1-888-HIV-8765
  24/7

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