An Update in the Management of HIV

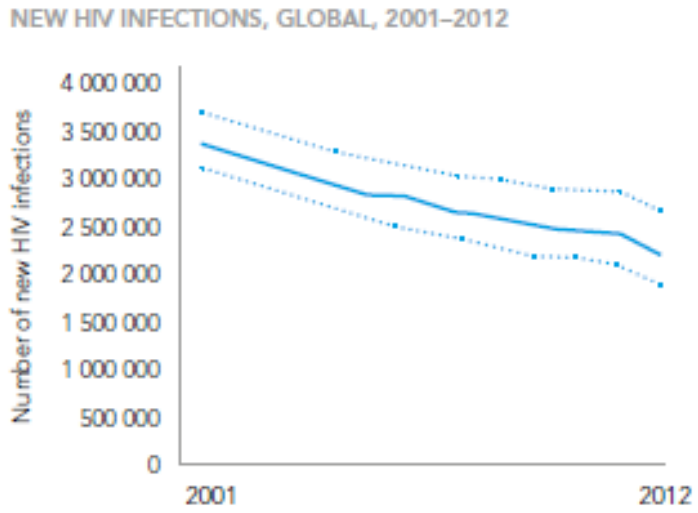
Patricia Pecora Fulco, Pharm.D., BCPS, FASHP, AAHIVP
Clinical Pharmacy Specialist in Internal Medicine/HIV
Affiliate Professor of Pharmacy
Clinical Assistant Professor of Internal Medicine/
Division of Infectious Diseases
Virginia Commonwealth University
Virginia Commonwealth University Medical Center

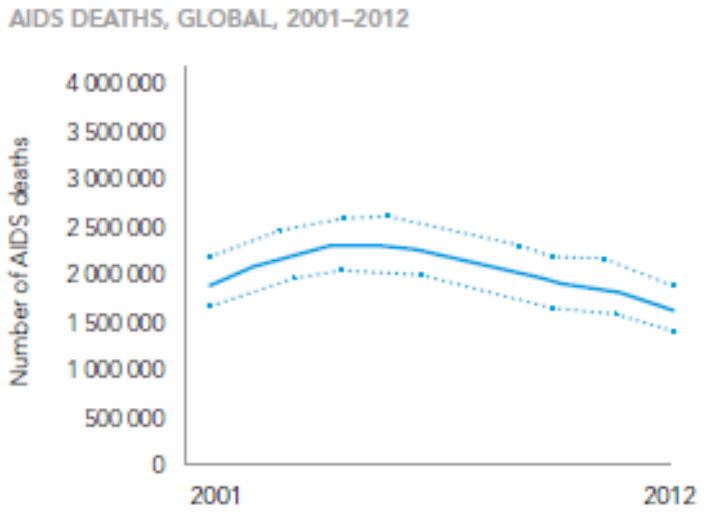
Objectives

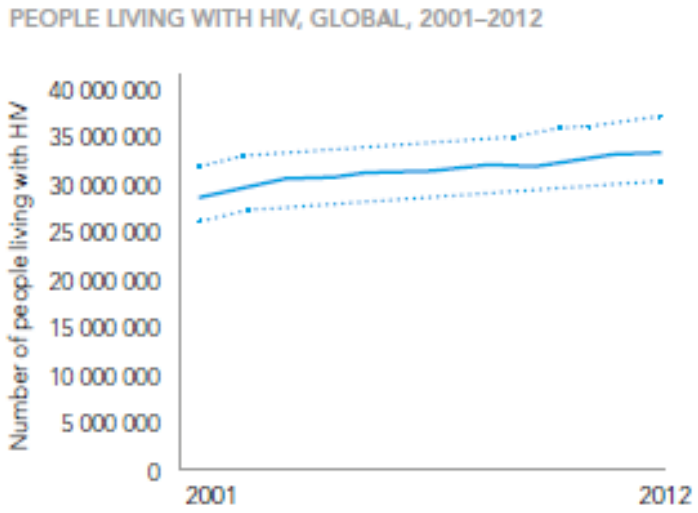
- The participant will be able to list the preferred antiretroviral regimens for the initial management of a treatment-naïve HIV positive patient.
- The participant will compare and contrast new antiretroviral therapies recently FDA approved and their clinical applicability in HIV positive patients.

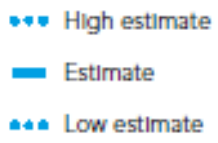
HIV Incidence and Prevalence

Global HIV Infections and AIDS Death 2001-2012









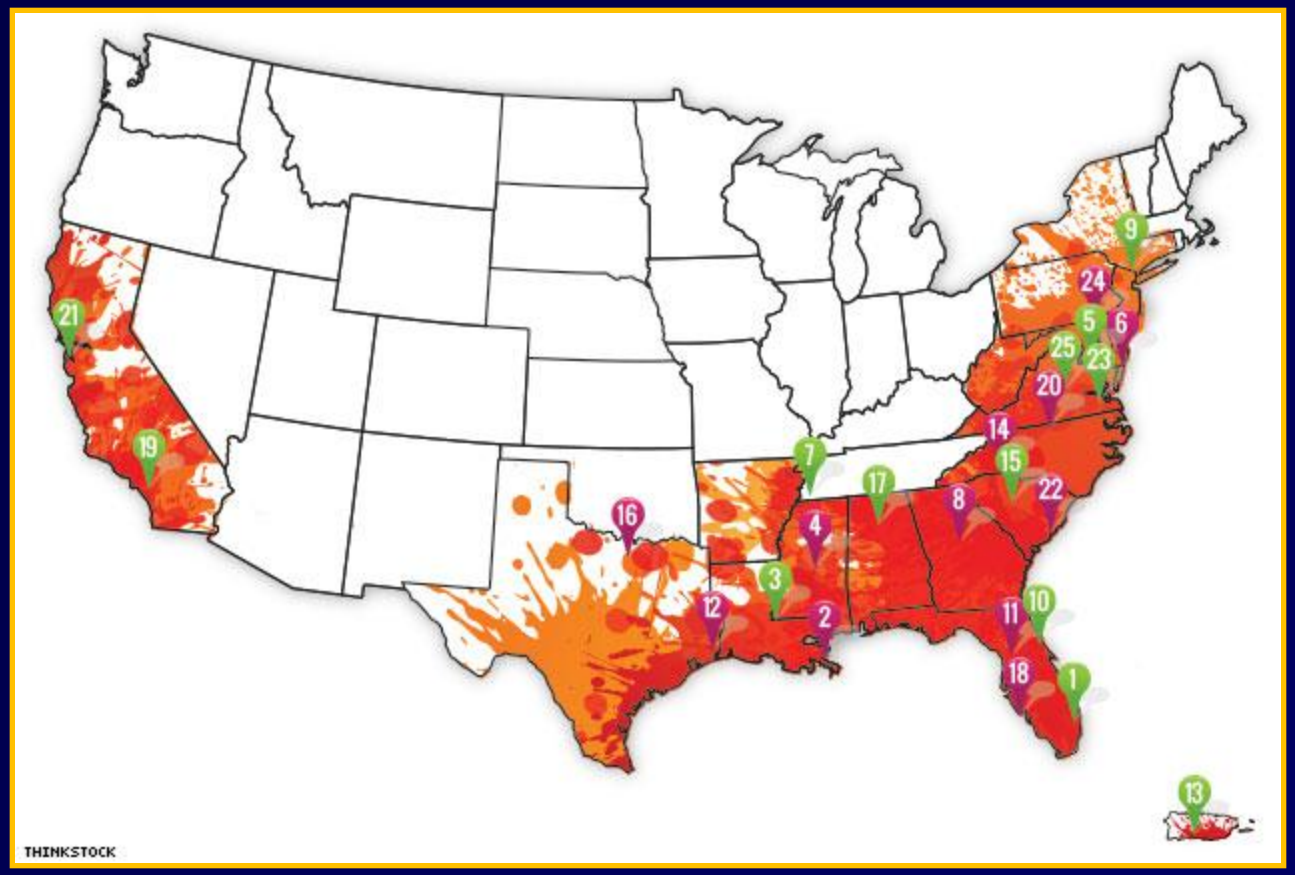
Global report: UNAIDS report on the global AIDS epidemic 2013. November 2013. www.unaids.org

Epidemiology

- CDC:
  - 1,148,200 persons are living with HIV
  - Approximately 50,000 new cases annually
- By 2015, 50% of HIV patients in the United States will be > 50 years old

The HIV and Aging Consensus Project. http://www.aahivm.org/Upload_Module/upload/HIV%20and%20Aging/Aging%20report%20working%20document%20FINAL%2012.1.pdf (accessed March 22, 2012).
Hasse B, et aL. CID 2012;53:1130-9.
N Engl J Med 2012;366:1270-3.
CDC. Estimated HIV incidence in the United States, 2007–2010. HIV Surveillance Supplemental Report 2012;17(No. 4). http://www.cdc.gov/hiv/surveillance/resources/reports/2010supp_vol17no4/. Published December 2012.

US Cities with the Highest Rates of HIV Infection



1. Miami, FL
2. New Orleans
3. Baton Rouge
4. Jackson, MS
5. Washington, D.C.
6. Baltimore–Towson, MD
7. Memphis, TN
8. Atlanta, GA
9. New York City, NY
10. Jacksonville, FL
11. Orlando, FL
12. Houston, TX
13. San Juan, Puerto Rico
14. Charlotte, NC
15. Columbia, SC
16. Dallas, TX
17. Birmingham, AL
18. Tampa, FL
19. Los Angeles, CA
20. Greensboro, NC
21. San Francisco, CA
22. Charleston, SC
23. Virginia Beach, VA
24. Philadelphia, PA
25. Richmond, VA

Patient Case

- Patient is a 32yo AAF with shortness of breath:
  - HTN
  - Protein S deficiency
  - PE
- Recent evaluations by her PCP. Most recently the patient had completed levofloxacin 750 mg daily for 5 days for CAP.
- At her most recent clinic appt, her room air saturations decreased from 97% to 86%. Home oxygen was prescribed. A few days later, the patient was febrile to 101, with worsening cough, nausea, vomiting and her saturations decreasing to 80% at home. Patient was admitted to the hospital with CXR consistent with pneumonia.

Patient Case

- HIV screening was performed and on admission, she was told she was HIV positive.

- Social History:
  - Married with three children
  - Youngest child, age 5
  - Manager of a childcare center

HIV Screening

- The USPSTF recommends that clinicians screen adolescents and adults aged 15 to 65 years for HIV infection

Moyer VA, et al. Screening for HIV: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med 2013;159:51-60. Greenwald JL, Routine rapid HIV screening in hospitals: another opportunity for hospitalists to improve care. J Hosp Med 2006;1:106-12.

HIV Screening

- Earlier diagnosis
- Antiretroviral therapy (ART) decreases the risk of sexual transmission
- ART in pregnant females reduces perinatal transmission

Moyer VA, et al. Screening for HIV: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med 2013;159:51-60.
Cohen MS, et al. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med 2013; 365:493-505.
Recommendations for use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to reduce perinatal HIV. transmission in the United States. Available at www.aidsinfo.nih.gov

Patient Case

- Labs:
- ABG: 7.48/31/72/23.3/96%
- Na 142, K 4.4, Cl 104, CO2 28, BUN 11, SCr 0.87, BG 98, Ca 9.5, AST 33, ALT 33, Alk Phos 62, T Bili 0.9, C bili 0.3, Alb 3.7
- WBC 7.9 Hgb 13.5, Hct 41.5, Plts 345
- G6PD, Quant : WNL
- INR=2.7

Patient Case

- Labs:
- BAL culture: Gomori's methenamine silver stain (+) PCP; Ziehl-Neelsen stain (-) for AFB
- HAV (-), HBV cAb (-), HBV sAg (-), HBV sAb (-)
- HCV (-), CMV IgG (+), Toxo IgG (-), RPR NR, HLA B*5701
- CD4=50 (5%), HIV PCR 484,000 copies/mL, HIV genotype E138A
- AFB BC NGTD

Patient Case

- What are the current guidelines for initiating antiretroviral therapy?

Initiating Antiretroviral Therapy In Treatment–Naïve Patients

- ART is recommended to reduce the risk of disease progression
  - CD_4 < 350 cells/mm^3 (AI)
  - CD_4 350-500 cells/mm^3 (AII)
  - CD_4 > 500 cells/mm^3 (BIII)
- ART is recommended for the prevention of HIV transmission
  - Perinatal transmission (AI)
  - Heterosexual transmission (AI)
  - Other transmission risk groups (AIII)

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. Available at http://aidsinfo.nih.gov

Antiretroviral Therapy and CD4 Responses

- Objective:
  - To identify risk factors for incomplete CD4 recovery
  - To identify associated mortality
- Inclusion:
  - Patients (age > 16 yo) with viral suppression (≤ 500 copies/mL) for > 3 years
  - CD4 count ≤ 200 cells/mm^3 at viral suppression

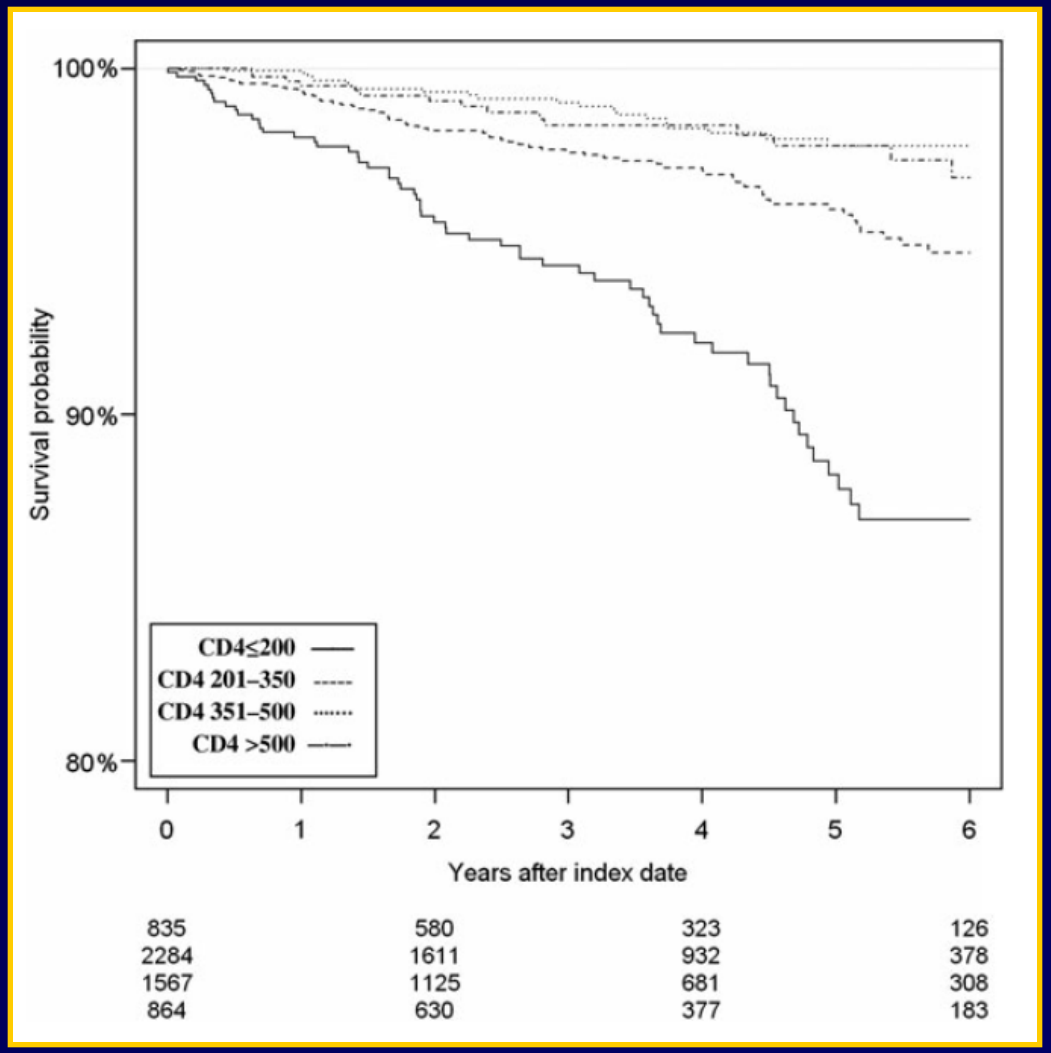
Engsig FN, et al. CID 2014;58:1312-21.

Factors Associated with Low CD4 Responses

Variable	Adjusted OR (95% CI)
Age, y	
40-49	2.04 (1.45-2.88)
≥ 50	4.01 (2.84-5.68)
Route of transmission	
Male heterosexual sex	1.50 (1.21-1.85)
Injection drug use	2.03 (1.57-2.61)
CD4 count at suppression, cells/mm^3	
≤ 25	5.21 (3.75-7.23)
26-50	4.46 (3.35-5.95)
51-100	3.73 (2.99-4.68)
101-150	2.08 (1.67-2.60)
Time from ART initiation to viral suppression, mo	
≥ 12	2.05 (1.68-2.50)

Engsig FN, et al. CID 2014;58:1312-21.

Cumulative Probability of Survival



Engsig FN, et al. CID 2014;58:1312-21.

Patient Case

- Labs:
- BAL culture: Gomori's methenamine silver stain (+) PCP; Ziehl-Neelsen stain (-) for AFB
- HAV (-), HBV cAb (-), HBV sAg (-), HBV sAb (-)
- HCV (-), CMV IgG (+), Toxo IgG (-), RPR NR, HLA B*5701
- CD4=50 (5%), HIV PCR 484,000 copies/mL, HIV genotype E138A
- AFB BC NGTD

Patient Case

- Which antiretroviral regimens are recommended?

Recommended Antiretroviral Therapy In Treatment–Naïve Patients

Antiretroviral Class	NRTIs combinations
INSTIs	
Dolutegravir	Abacavir with Lamivudine [only if HLA-B*5701(-)] Emtricitabine with Tenofovir
Elvitegravir	Cobicistat, Emtricitabine with Tenofovir (only if CrCl > 70 mL/min)
Raltegravir	Emtricitabine with Tenofovir
PIs	
Darunavir/ritonavir	Emtricitabine with Tenofovir

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Alternative Antiretroviral Regimens for Treatment–Naïve Patients

Antiretroviral Class	NRTIs combinations
NNRTIs	
Efavirenz	Emtricitabine with Tenofovir
Rilpivirine (only if HIV PCR < 100,000 copies/mL and CD_4 > 200 cells/mm^3)	Emtricitabine with Tenofovir
PIs	
Atazanavir/cobicistat (only if CrCl > 70 mL/min)	Emtricitabine with Tenofovir
Atazanavir/ritonavir	Emtricitabine with Tenofovir
Darunavir/cobicistat (only if CrCl > 70 mL/min)	Abacavir with Lamivudine [only if HLA-B*5701(-)]
	Emtricitabine with Tenofovir
Darunavir/ritonavir	Abacavir with Lamivudine [only if HLA-B*5701(-)]

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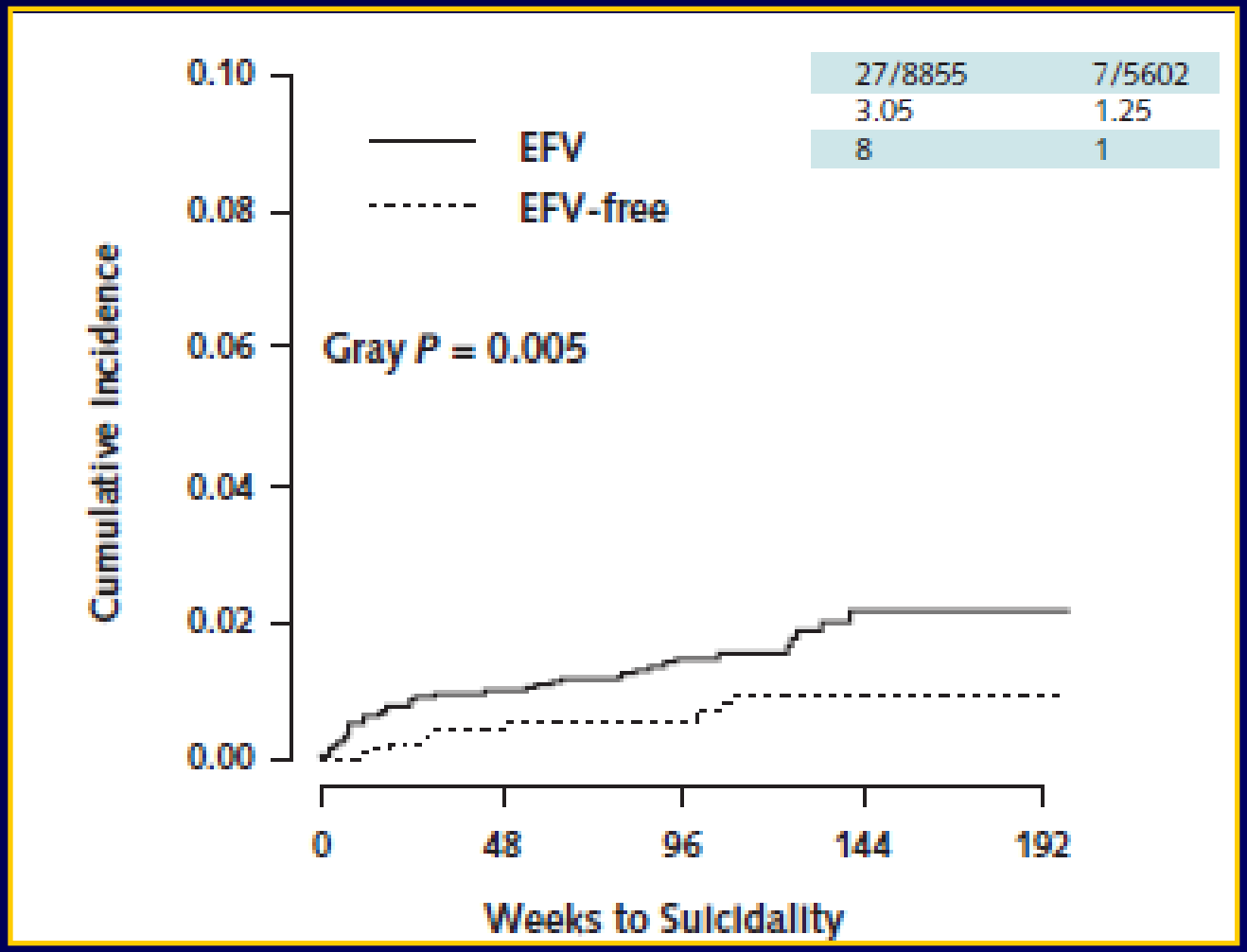
Efavirenz and CNS Dysphoria



Mollan K, et al. Ann Intern Med 2014;161:1-10.

Patient Case

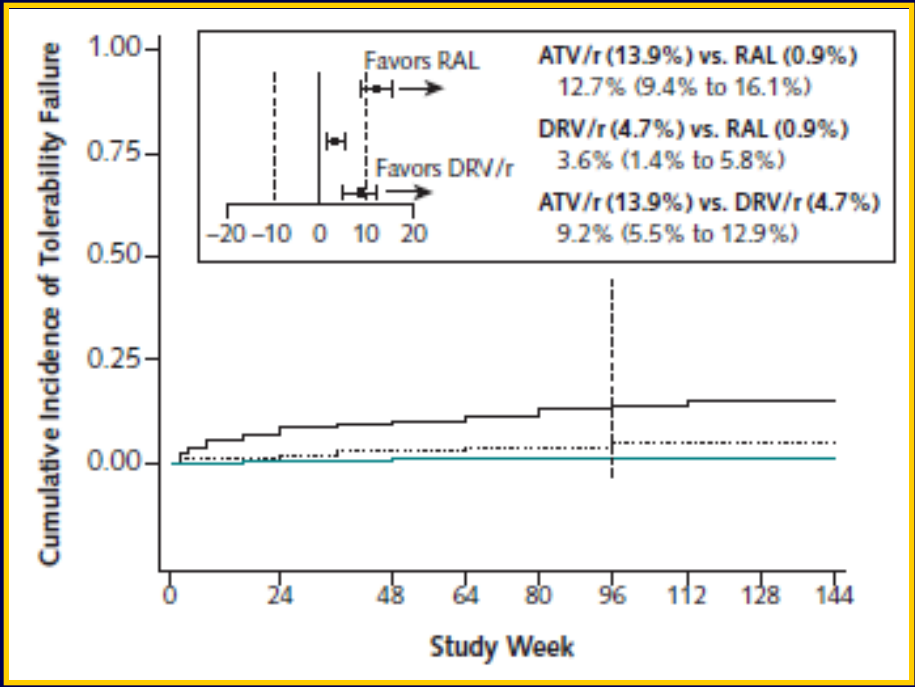
- Which antiretroviral regimens is the best for this patient?

Raltegravir with Emtricitabine/Tenofovir

- Advantages:
  - No virologic or immunologic restrictions
  - Virologic efficacy comparable to boosted PI regimens with enhanced tolerability
- Disadvantages:
  - Twice daily regimen
  - Minimal drug-drug interactions (must be avoided with concurrent administration with antacids)
  - Low genetic resistance barrier

www.fda.gov
Lennox JL et al. Ann Int ern Med 2014;161:461-71.
Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. Available at http://aidsinfo.nih.gov

Initial Antiretroviral Therapy for Treatment-Naïve Patients



Variable	Treatment Group, *n*		
	ATV/r	RAL	DRV/r
Virologic failure	95	85	115
Genotype testing complete	75	65	99
Any resistance detected	9	18	4
PI resistance detected	0	0	0
NRTI-only resistance detected	8	7	3
Emtricitabine*	5	7	3
TDF†	2	0	0
TDF and emtricitabine	1	0	0
INI-only resistance detected‡	1	1	1
NRTI and INI resistance detected	0	10	0
Emtricitabine and RAL	0	7	0
Emtricitabine, TDF, and RAL	0	3	0

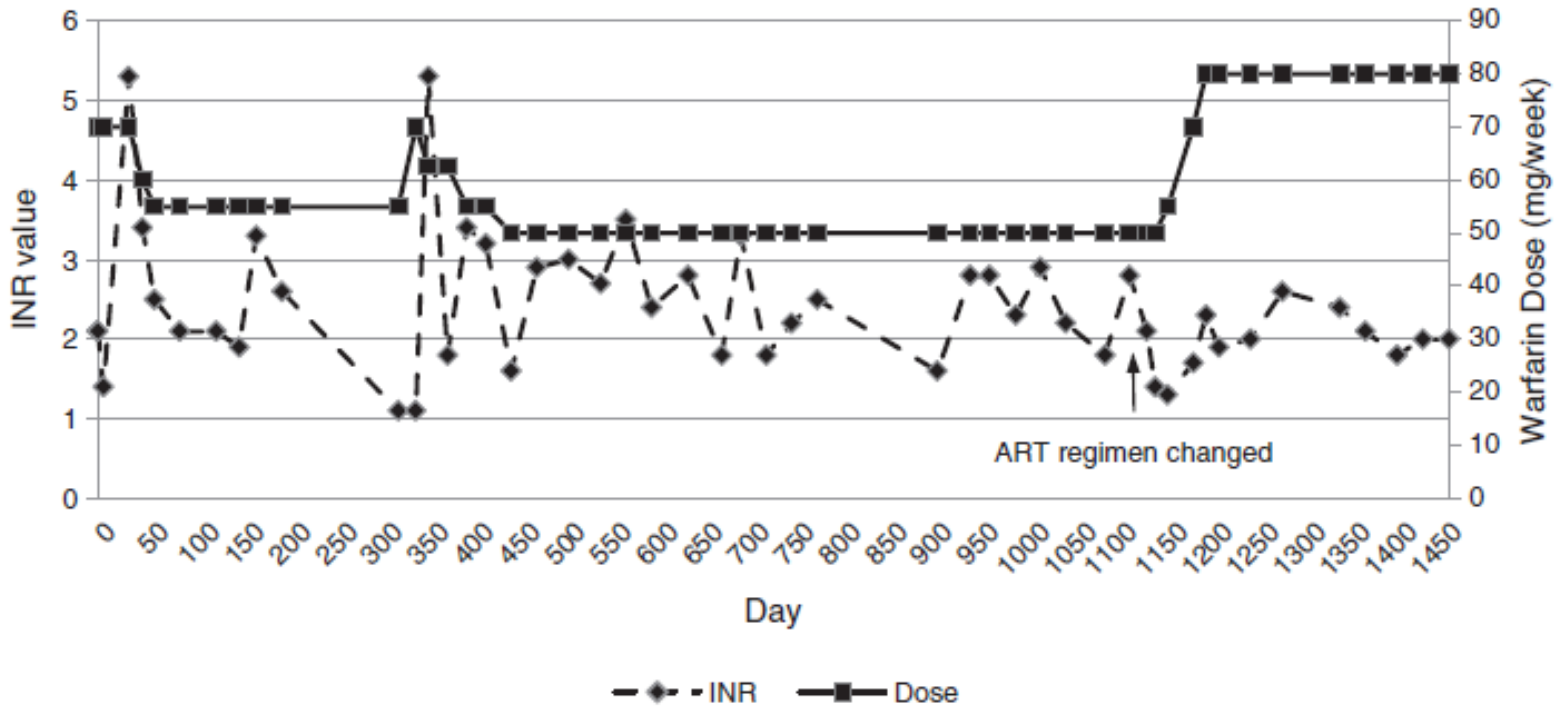
Lennox JL et al. Ann Int ern Med 2014;161:461-71.

Elvitegravir/Cobicistat/Emtricitabine/Tenofovir

- Advantages:
  - Once-daily dosing
  - No virologic or immunologic restrictions
  - Comparable to efavirenz or atazanavir-based regimens
  - Indicated now for simplification
- Disadvantages:
  - Not recommended in patients with CrCl < 70 mL/min
  - COBI inhibits tubular secretion of SCr
  - Multiple drug-drug interactions (including concurrent administration with antacids)
  - Low genetic resistance barrier

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. Available at http://aidsinfo.nih.gov

Elvitegravir/Cobicistat



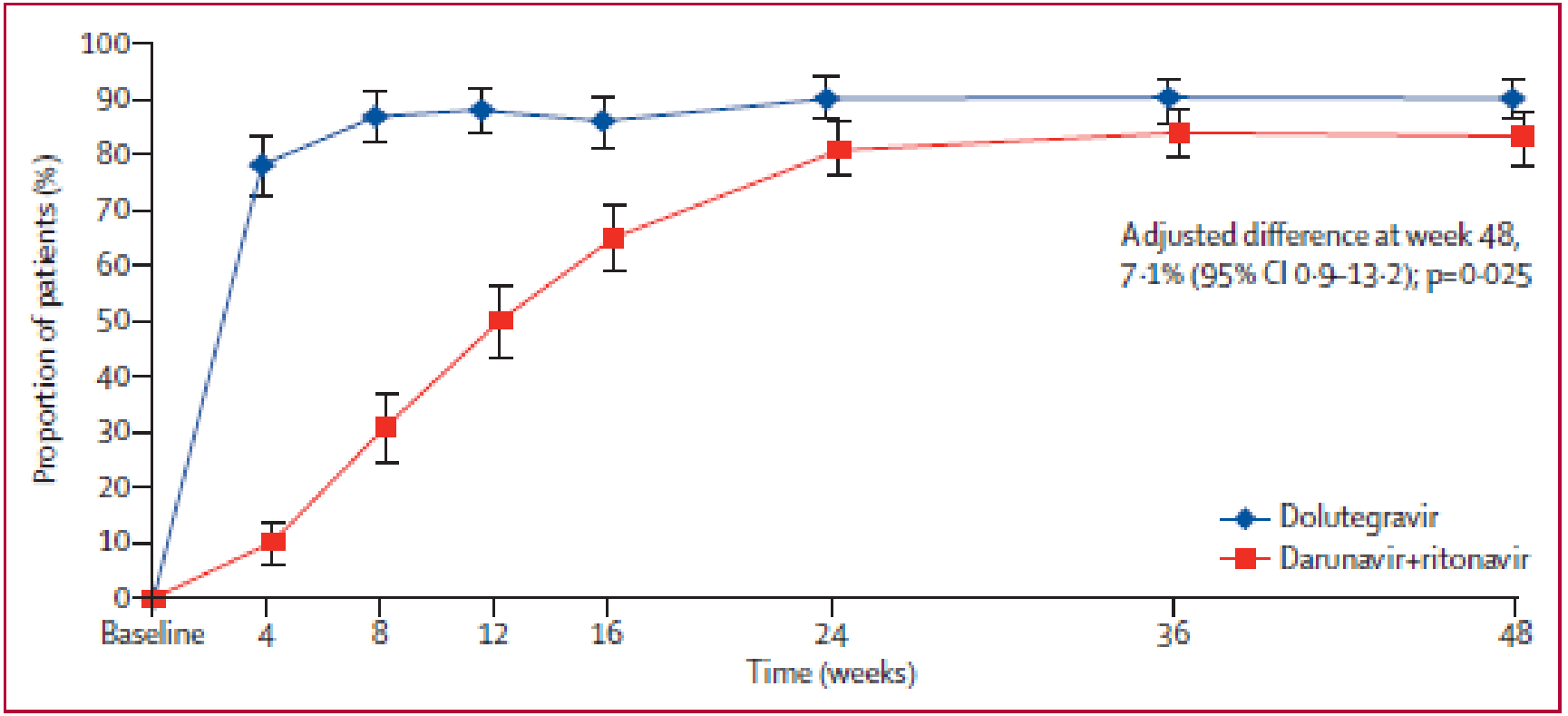
Good BL, et al. AIDS 2015;29:985-6.

Dolutegravir/Abacavir/Lamivudine

- Dolutegravir 50 mg daily (N=224) or darunavir/ritonavir (N=213) once daily (with 2 NRTIs)
- Treatment-naïve patients
- VL=31,000 copies/mL
- CD_4=390-400 cells/mm^3

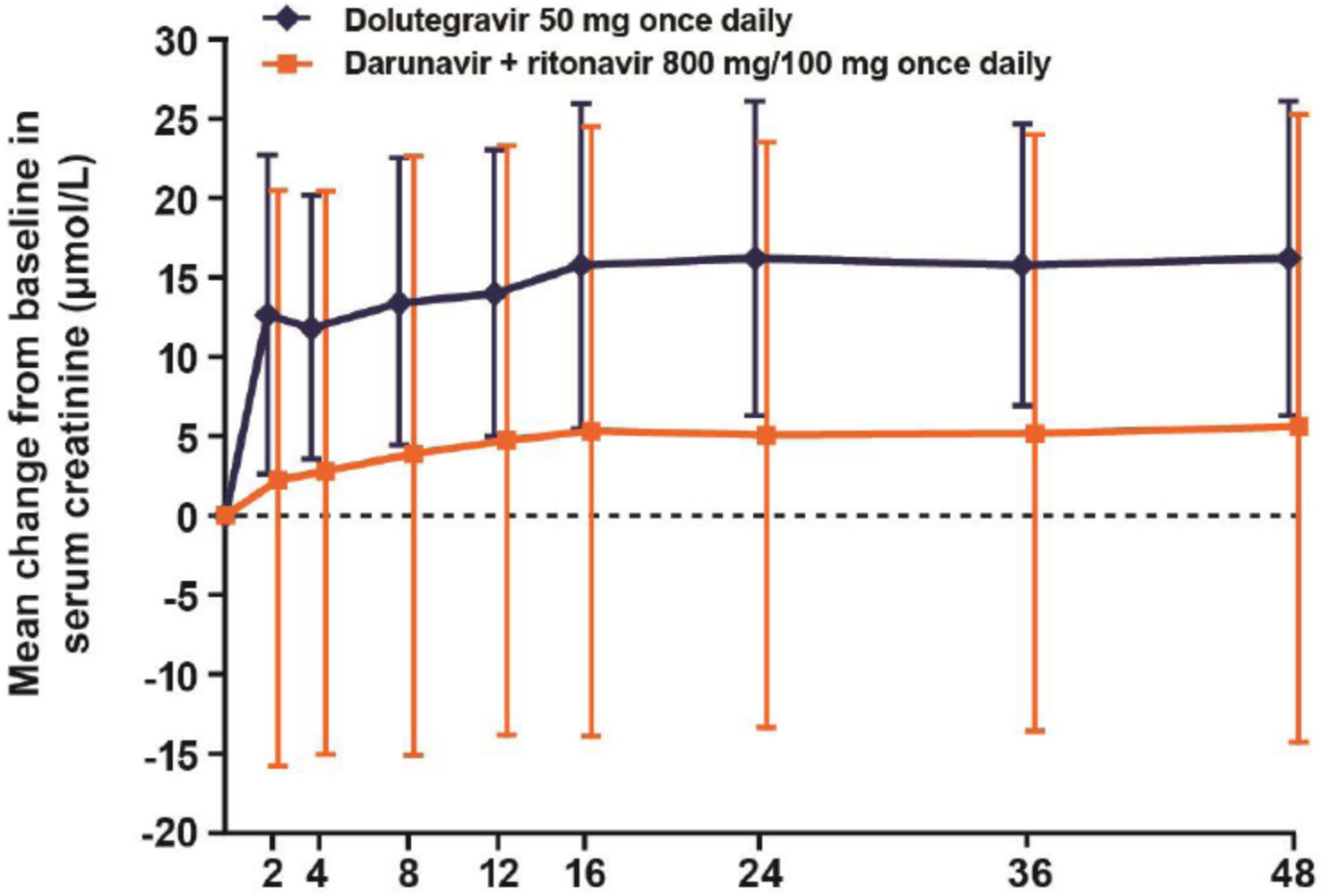
Clotet B, et al. Lancet 2014;383:2222-31.

Dolutegravir/Abacavir/Lamivudine



Clotet B, et al. Lancet 2014;383:2222-31.

Dolutegravir/Abacavir/Lamivudine



Clotet B, et al. Lancet 2014;383:2222-31.

Dolutegravir/Abacavir/Lamivudine

- Advantages:
  - Once-daily dosing
  - No virologic or immunologic restrictions
  - Virologic superiority to efavirenz or darunavir--based regimens
  - May have higher genetic resistance barrier and may be sequenced after other INSTIs
  - Minimal drug interactions
- Disadvantages:
  - Requires pre-screening with HLA-B*5701
  - DTG inhibits tubular secretion of SCr
  - Oral absorption affected concurrent administration with antacids and/or multivitamins

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. Available at http://aidsinfo.nih.gov

Dolutegravir/Abacavir/Lamivudine

Darunavir/Ritonavir/Emtricitabine/Tenofovir

- Advantages:
  - High genetic resistance barrier
  - No virologic or immunologic restrictions
  - Sustained virologic and immunologic responses
  - Well-tolerated compared to alternative boosted PI regimens
- Disadvantages:
  - Three separate tablets
  - Multiple drug interactions with co-administration with ritonavir
  - Hyperlipidemia

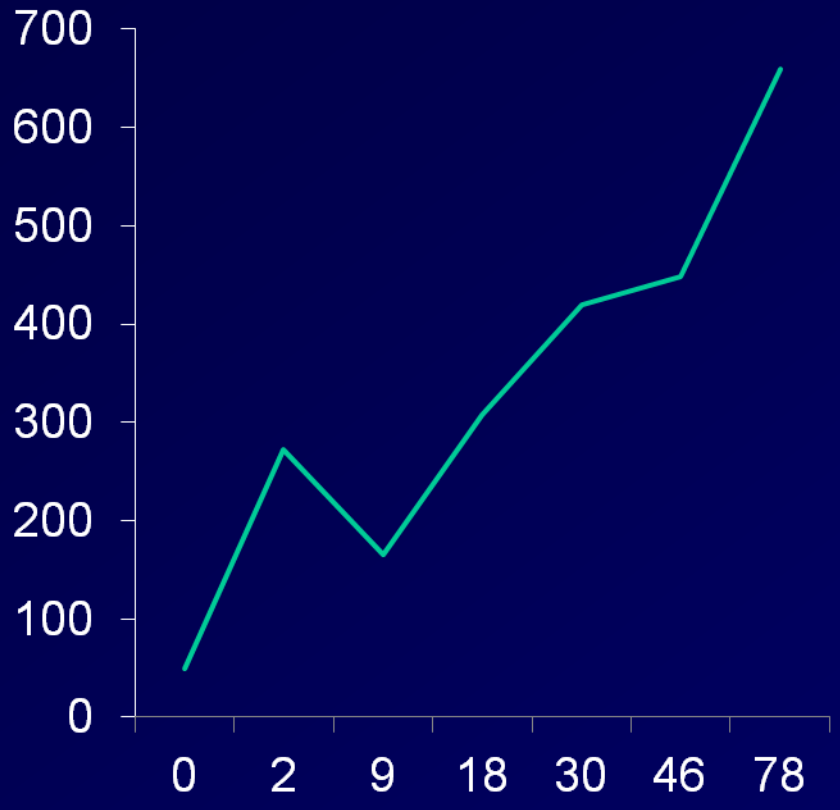
Lennox JL et al. Ann Int ern Med 2014;161:461-71.
Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. Available at http://aidsinfo.nih.gov

Patient Case

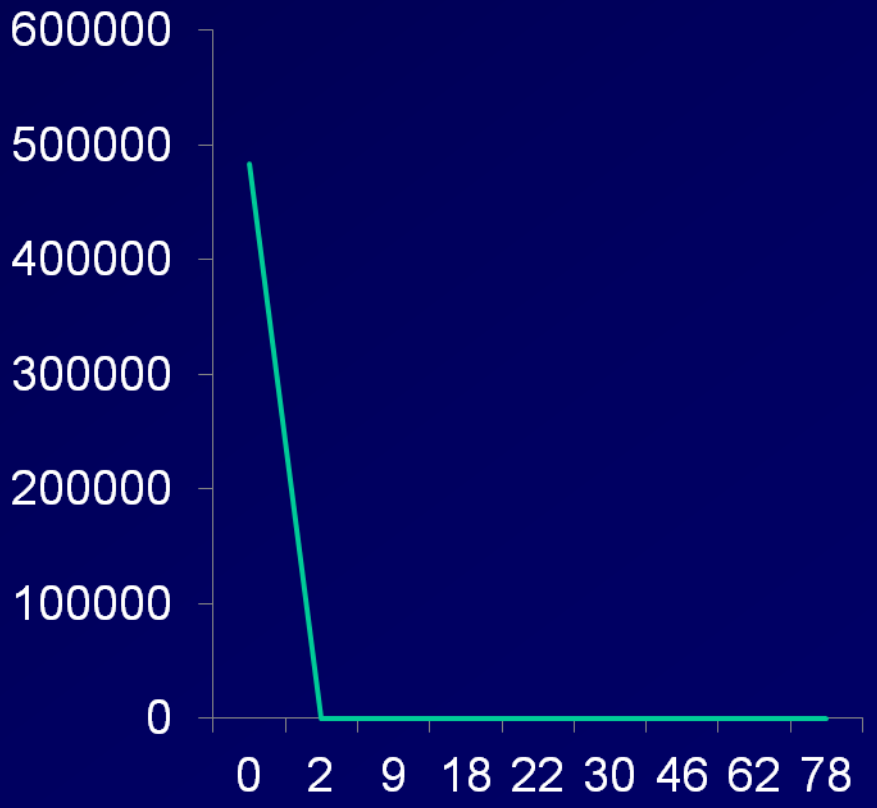
- Which antiretroviral regimens is the best for this patient?
- Raltegravir 400 mg twice daily
- Emtricitabine 200 mg/Tenofovir 300 mg once daily

Patient Case

CD4 (cells/mm^3)



HIV PCR (copies/mL)



HIV Monitoring

Recommendations on the Indications and Frequency of Viral Load and CD4 Count Monitoring

Clinical Scenario	Viral Load Monitoring	CD4 Count Monitoring
Before initiating ART	At entry into care (AIII)	At entry into care (AIII)
After initiating ART	2-8 weeks after ART initiation (AIII); then, every 4-8 weeks until VL suppressed	3 months after ART initiation (AIII)
The first 2 years of ART	Every 3-4 months (AIII)	Every 3-6 months (BII)
After 2 years of ART (VL consistently suppressed, CD4 consistently 300-500 cells/mm^3)	May extend to every 6 months for patients with consistent viral suppression for ≥ 2 years (AIII)	Every 12 months (BII)
After 2 years of ART (VL consistently suppressed, CD4 consistently >500 cells/mm^3)		Optional (CIII)

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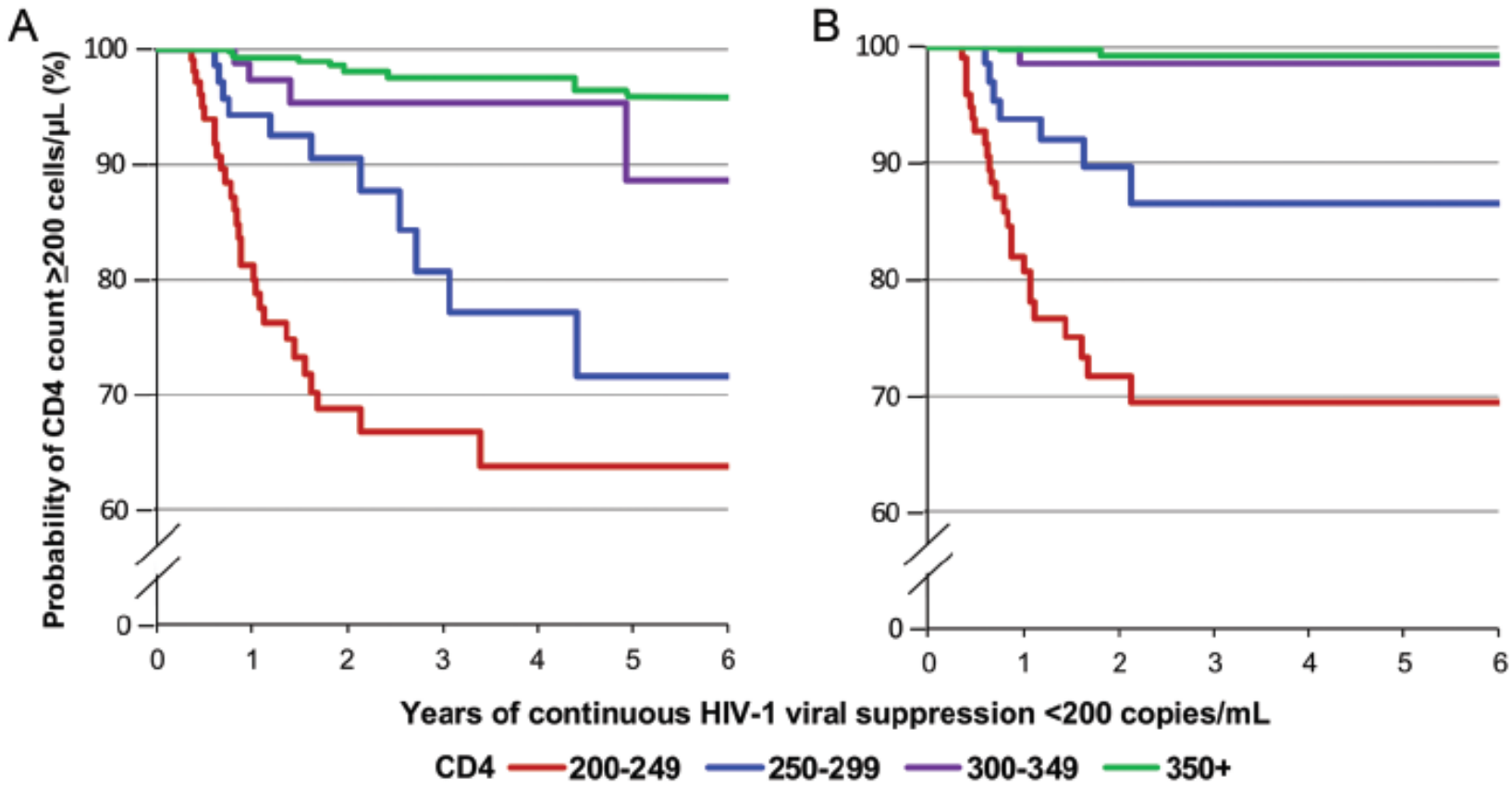
Kaplan-Meier Esimates of Probability of Maintaining CD4 > 200 cells/mm^3



Gale HB, et al. CID 2013;56:1340-3.

CD4 Monitoring

	Annual Costs[a]		Lifetime Costs[a]			
			Projected for LE of 22 Years		Projected for LE of 34 Years	
	CD4 Test Cost		CD4 Test Cost		CD4 Test Cost	
Frequency, mo	$38	$67	$38	$67	$38	$67
Every 3	41.0	72.4	902.9	1591.9	1395.4	2460.2
Every 6[b]	20.5	36.2	451.4	796.0	697.7	1230.1
Every 12	10.3	18.1	225.7	398.0	348.8	615.1

Hyle EP, Sax PE, Walensky RP. JAMA Intern Med 2013;173:1746-8.

Patient Case

- Patient is a 55yo AAM
  - HIV (2009)
  - Macular degeneration (Legally blind)
  - Schizophrenia
  - HTN
  - Hyperlipidemia

Patient Case

- Medications:
  - Atazanavir 300 mg once daily
  - Ritonavir 100 mg once daily
  - Abacavir 600 mg/lamivudine 300 mg once daily
  - Amlodipine 10 mg once daily
  - Metoprolol 50 mg twice daily
  - Hydrochlorothiazide 25 mg once daily
  - Pravastatin 40 mg once daily
  - Fluphenazine 5 mg twice daily
  - Benztropine 1 mg twice daily
  - Trazodone 50 mg once daily

Patient Case

- CD4=486 (18%)
- HIV PCR= < 20 copies/mL

Patient Case

- Admitted to the hospital with new diagnosis of diabetes mellitus
- HgbA1C=14%

Laboratory Test	Timepoint/Frequency of Testing								
	Entry into Care	Follow Up Before Initiation of ART	ART Initiation or Modification[b]	Follow-Up 2 to 8 Weeks After ART Initiation or Modification	Every 3 to 6 Months	Every 6 Months	Every 12 Months	Treatment Failure	Clinically Indicated
Hepatitis B Serology[f]	√		√ May repeat if HBsAg (-) and HBsAb (-) at baseline						√
Hepatitis C Serology, with Confirmation of Positive Results	√								√
Basic Chemistry[g,h]	√	√ Every 6–12 months	√	√	√				√
ALT, AST, T. bilirubin	√	√ Every 6–12 months	√	√	√				√
CBC with Differential	√	√ Every 3–6 months	√	√ If on ZDV	√				√
Fasting Lipid Profile	√	√ If normal, annually	√	√ Consider 4–8 weeks after starting new ART regimen that affects lipids		√ If abnormal at last measure-ment	√ If normal at last measurement		√
Fasting Glucose or Hemoglobin A1C	√	√ If normal, annually	√		√ If abnormal at last measure-ment		√ If normal at last measurement		√

Diabetes Mellitus (DM) Among HIV-infected Adults in Care in the United States, 2009-2010

	MMP Adjusted prevalence [CI]	NHANES Adjusted prevalence [CI]	aPR [CI]*
Total	11.6 [10.1 - 13.4]	8.2 [7.2 - 9.3]	1.42 [1.18 - 1.70]
Sex at birth			
Male	11.2 [9.9 - 12.6]	9.1 [7.5 - 10.9]	1.24 [1.00 - 1.53]
Female	12.0 [9.9 - 14.5]	7.4 [6.5 - 8.5]	1.61 [1.28 - 2.03]
Race/ethnicity			
White (non-Hispanic)	10.9 [9.2 - 13.0]	6.6 [5.4 - 8.1]	1.65 [1.27 - 2.15]
Black (non-Hispanic)	13.1 [11.3 - 15.1]	11.9 [9.7 - 14.5]	1.10 [0.87 - 1.40]
Hispanic	13.3 [11.0 - 16.0]	11.4 [9.5 - 13.7]	1.17 [0.90 - 1.51]
Other	13.3 [9.9 - 17.6]	14.6 [11.2 - 18.8]	0.91 [0.62 - 1.33]
Age in years			
20-44	6.2 [5.1 - 7.4]	2.3 [1.7 - 3.1]	2.70 [1.90 - 3.83]
45-60	13.0 [11.2 - 15.0]	9.5 [7.7 - 11.7]	1.37 [1.06 - 1.76]
≥ 60	21.5 [18.1 - 25.4]	19.7 [17.0 - 22.7]	1.09 [0.88 - 1.36]

Hernandez-Romieu AC, et al. Conference on Retroviruses and Opportunistic Infections (Poster 789). February 23-26, 2015. Seattle, WA.

Patient Case

- Follow up labs included:
- HgbA1C = 5%
- CD4=640 (16%), HIV PCR < 20 copies/mL

Patient Case

- Renal Colic CT:
- Moderate hydronephrosis. Findings may be related to a recently passed calculus.
- Multiple gallstones within the gallbladder without evidence of acute cholecystitis.

Patient Case

- Medications:
  - Atazanavir 300 mg once daily
  - Ritonavir 100 mg once daily
  - Abacavir 600 mg/lamivudine 300 mg once daily
  - Amlodipine 10 mg once daily
  - Metoprolol 50 mg twice daily
  - Hydrochlorothiazide 25 mg once daily
  - Pravastatin 40 mg once daily
  - Fluphenazine 5 mg twice daily
  - Benztropine 1 mg twice daily
  - Trazodone 50 mg once daily
  - Metformin 1000 mg twice daily

Antiretroviral Toxicities

ARV Agent(s)	Advantages	Disadvantages
ATV/r	• Once-daily dosing • Higher genetic barrier to resistance than NNRTIs, EVG, and RAL • PI resistance at the time of treatment failure uncommon with RTV-boosted PIs	• Commonly causes indirect hyperbilirubinemia, which may manifest as scleral icterus or jaundice. • Food requirement • Absorption depends on food and low gastric pH (see Table 18a for interactions with H2 antagonists, antacids, and PPIs). • Nephrolithiasis, cholelithiasis, nephrotoxicity • GI adverse effects • CYP3A4 inhibitors and substrates: potential for drug interactions (see Tables 17 and 18a)

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Patient Case

- Medications:
  - Dolutegravir 50 mg/Abacavir 600 mg/lamivudine 300 mg once daily (Triumeq)
  - Amlodipine 10 mg once daily
  - Metoprolol 50 mg twice daily
  - Hydrochlorothiazide 25 mg once daily
  - Pravastatin 40 mg once daily
  - Fluphenazine 5 mg twice daily
  - Benztropine 1 mg twice daily
  - Trazodone 50 mg once daily
  - Metformin 1000 mg twice daily

Patient Case

Metformin	↑Metformin	Consider metformin dose reductions when coadministered with TRIUMEQ.

Medications:

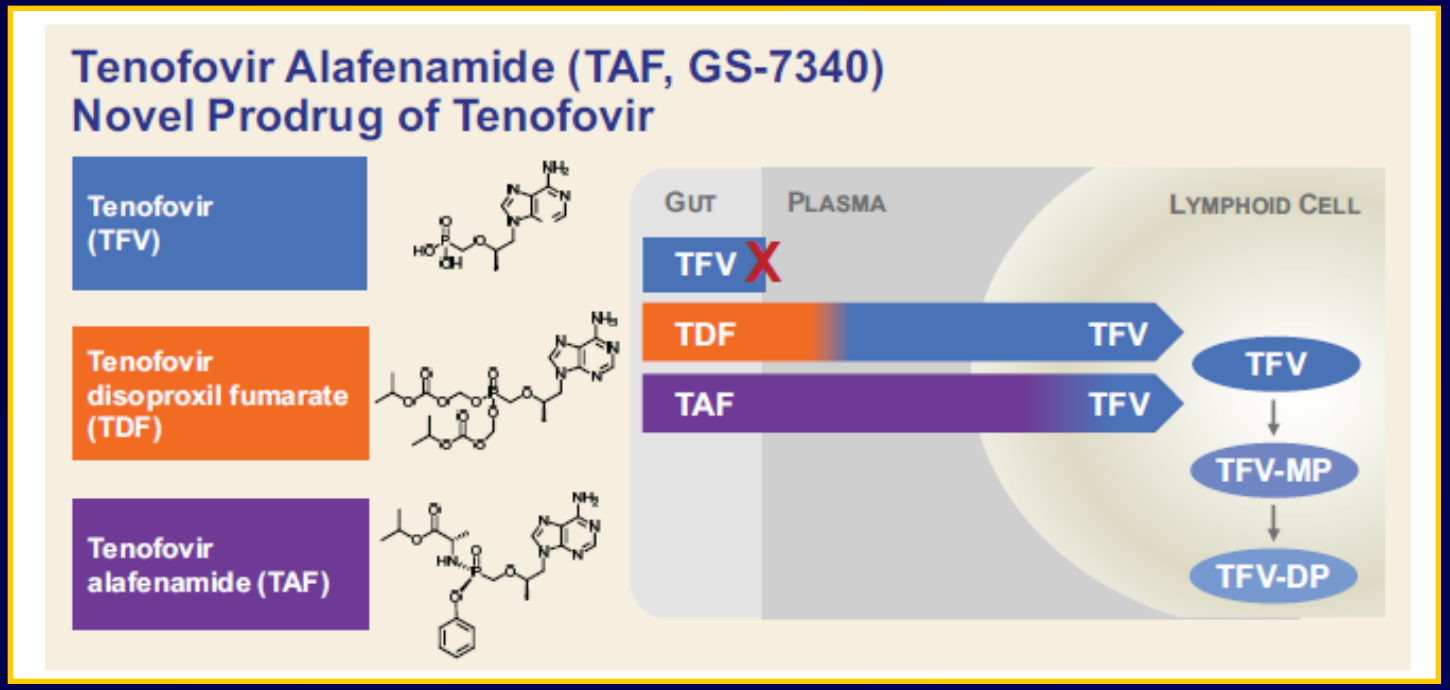
- Dolutegravir 50 mg/Abacavir 600 mg/lamivudine 300 mg once daily (Triumeq)
- Metformin 1000 mg twice daily

Metformin and Dolutegravir

Plasma Metformin PK Parameter	GLS mean Metformin Alone (Period 1)	Metformin + DTG (Period 2)	GLS mean ratio (90% CI) Metformin + DTG vs. Metformin Alone
Cohort 1 (DTG 50 mg QD)	n = 15	n = 14	
Cmax (μg/mL)	0.932	1.55	1.66 (1.53, 1.81)
AUC(0-τ) (hr*μg/mL)	6.83	12.2	1.79 (1.65, 1.93)
Cohort 2 (DTG 50 mg BID)	n = 15	n = 14	
Cmax (μg/mL)	0.845	1.878	2.11 (1.91, 2.33)
AUC(0-τ) (hr*μg/mL)	6.49	15.9	2.45 (2.25, 2.66)

Zong J, et al. J Int AIDS Soc 2014;Nov 2;17(4 Suppl 3).

Tenofovir Alafenamide (TAF)



Tenofovir (TFV): Rapid metabolism in the plasma after oral administration

Tenofovir disoproxil fumarate (TDF) is well-absorbed and rapidly converted to TFV in plasma (renal/bone effects)

TAF is stable in plasma and not converted to TFV until intracellularly

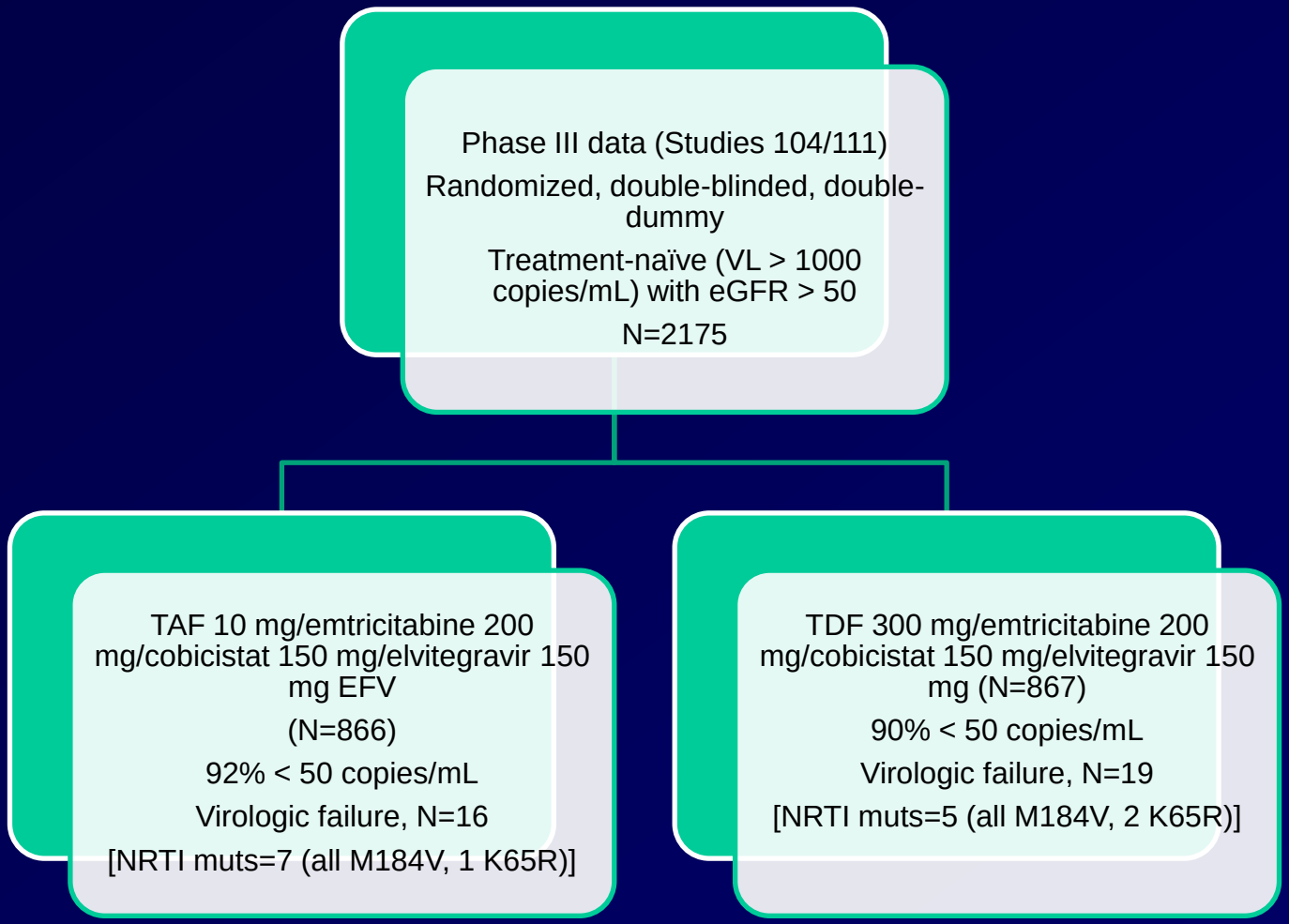
Sax PE, et al. J Acquir Immune Defic Syndr 2014;67:52-8.
Sax PE. Oral abstract (143LB). CROI 2015. Feb 23-26, 2015. Seattle, WA
Wohl D. Oral abstract (113LB). CROI 2015. Feb 23-26, 2015. Seattle, WA.
Pozniak A. Poster presentation (795) CROI 2015. Feb 23-26, 2015. Seattle, WA

Tenofovir Alafenamide (TAF) in a Single Tablet Regimen

- TFV plasma exposure is 90% lower while maintaining a high antiviral activity intracellularly (4-fold higher concentrations)
- TDF 300 mg ≈ TAF 25 mg
  - Cobicistat increases the bioavailability of TAF by approximately 2.2-fold
  - Via the inhibition of P-glycoprotein intestinal secretion, the 10 mg dose of TAF delivered by E/C/F/TAF STR is equivalent to the 25-mg dose of TAF

Sax PE, et al. J Acquir Immune Defic Syndr 2014;67:52-8. Wohl D. Oral abstract (113LB). CROI 2015. Feb 23-26, 2015. Seattle, WA.

Tenofovir Alafenamide (TAF) in a Single Tablet Regimen



Wohl D. Oral abstract (113LB). CROI 2015. Feb 23-26, 2015. Seattle, WA.
Sax PE, et al. Lancet 2015; (Published online April 16, 2015).

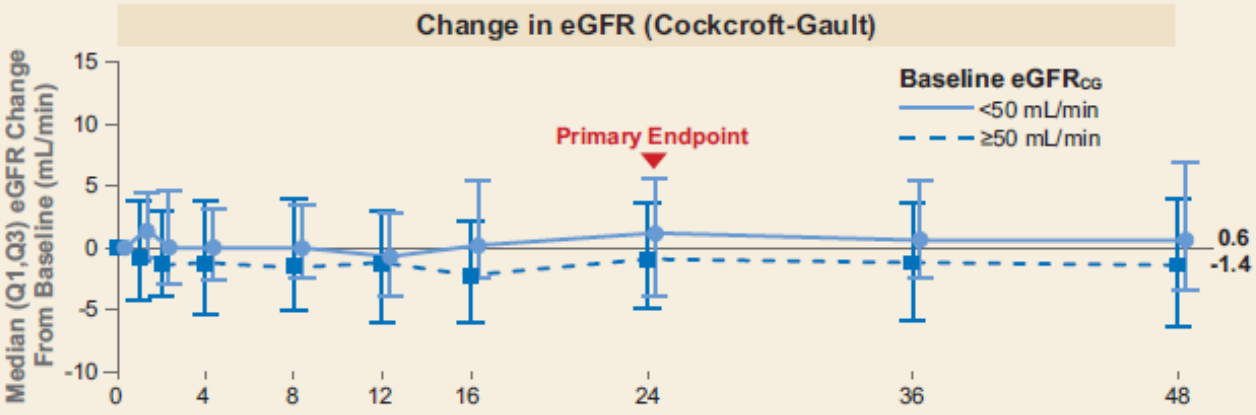
Tenofovir Alafenamide (TAF) in a Single Tablet Regimen

- Renal (week 48)—changes with cobicistat occurred at week 2
  - TAF -6.6 mL/min (N=0 for DCs)
  - TDF -11.2 mL/min (rise of SCr by 0.8mg/dL) (N=4 for DCs)
  - No cases of Fanconi's ; (N=1) of subclinical tubulopathy
  - TAF—hypophosphatemia (N=3); glucosuria (N=0); proteinuria (N=2)
  - TDF—hypophosphatemia (N=4); glucosuria (N=2); proteinuria (N=2)
- Bone (week 48) (DEXA at baseline, 24, 48)
- 1% fractures in both groups (no fragility fractures)
- Spine
  - TAF: -1.30
  - TDF: -2.86
- Hip
  - TAF: -0.66
  - TDF: -2.95

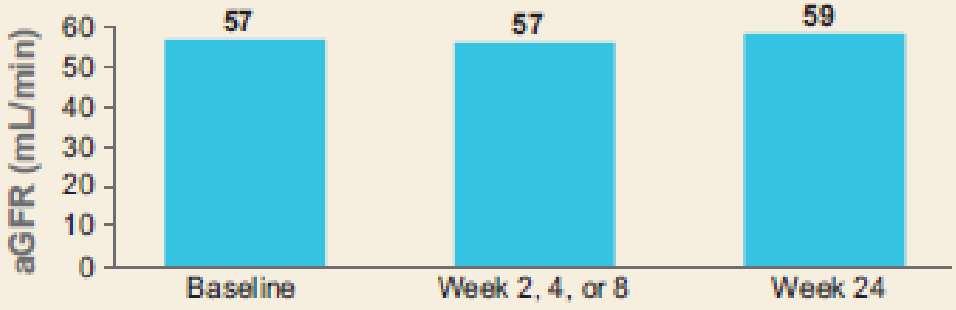
Sax PE. Oral abstract (143LB). CROI 2015. Feb 23-26, 2015. Seattle, WA.
Sax PE. Lancet 2015 (Published online April 15, 2015).

Tenofovir Alafenamide (TAF) in a Single Tablet Regimen

Change in eGFR From Baseline to Week 48



Actual GFR by Iohexol Clearance (n=32)



	GLSM Ratio (%)	90% CI
Week 2, 4, or 8 vs baseline	99	94, 104
Week 24 vs baseline	103	97, 109

CI, confidence interval; GLSM, geometric least squares mean.

Pozniak A. Poster presentation (795) CROI 2015. Feb 23-26, 2015. Seattle, WA.

Questions