The Importance of Individualizing HIV Care:

An Interactive Program on How to Select the Ideal Antiretroviral Therapy for Each Patient

Jointly provided by the Annenberg Center for Health Sciences at Eisenhower and ViralEd, Inc. in collaboration with Postgraduate Institute for Medicine
This activity is supported by an independent educational grant from Janssen Therapeutics, Division of Janssen Products, LP

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Welcome and Introduction

Faculty: Wilbert Jordan, MD

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Program Objectives

Upon completion of the program, participants should be better able to:

- Explain the importance of individualizing ARV therapy
- Individualize ARV therapy to improve treatment outcomes
- Employ the skills needed to gather knowledge regarding the patient and establish a trusting relationship that furthers the exchange of information between clinician and patient needed to accomplish individualization of care

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What to Start

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Which Antiretrovirals: 2015 Currently Available

NRTIs

- Abacavir
- Didanosine
- Emtricitabine
- Lamivudine
- Stavudine
- Tenofovir
- Zidovudine

NNRTIs

- Delavirdine
- Efavirenz
- Etravirine
- Nevirapine (XR)
- Rilpivirine

PIs

- Atazanavir**
- Darunavir**
- Fos-Amprenavir
- Indinavir
- Lopinavir
- Nelfinavir
- Ritonavir
- Saquinavir
- Tipranavir

PK Booster

- Cobicistat

Fusion Inhibitors

- Enfuvirtide

Entry Inhibitors

- Maraviroc

Integrase Inhibitors

- Raltegravir
- Elvitegravir*
- Dolutegravir

*Only available co-formulated with TDF/FTC; **atazanavir and darunavir available as individual drugs or co-formulated with cobicistat.

U.S. DHHS Guidelines January 2013: Four Preferred Regimens

NNRTI	**Efavirenz[1]/emtricitabine[2]/tenofovir DF[3]**
PI	**Atazanavir[4] + ritonavir + emtricitabine[2]/tenofovir DF[3]** **Darunavir + ritonavir (qd) + emtricitabine[2]/tenofovir DF[3]**
INSTI	**Raltegravir + emtricitabine[2]/tenofovir DF[3]**

- INSTI: Integrase strand transfer inhibitors.

1. Efavirenz should not be used during the first trimester of pregnancy or in women trying to conceive or not using effective and consistent contraception.
2. Lamivudine may substitute for emtricitabine or visa versa.
3. Tenofovir DF should be used with caution in patients with renal insufficiency.
4. Atazanavir + RTV should not be used in patients who require >20 mg omeprazole equivalent/day.
5. Patients with creatinine clearance >70 mL/min.
6. Patients who are HLA-B*5701 negative.

DHHS. Available at: http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf. Revision February 12, 2013.
DHHS. Available at: http://aidsinfo.nih.gov/contentfiles/AdultARV_INSTIRecommendations.pdf. Update October 30,2013.

DHHS Guidelines 10/2013 to 4/2014: What to Start: Seven Preferred Regimens

Preferred Regimens: Regimens with optimal and durable efficacy, favorable tolerability and toxicity profile, and ease of use	
NNRTI	**EFV/TDF/FTC**
Boosted PI	**ATV/r + TDF/FTC** **DRV/r (once daily) + TDF/FTC**
Integrase Inhibitor	**RAL + TDF/FTC** **EVG/cob/TDF/FTC** **DTG + TDF/FTC** **DTG + ABC/3TC**

Available at: http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf. Revision Oct 30, 2013

DHHS Guidelines May 2014: Ten Recommended Regimens

NNRTI	**Efavirenz/emtricitabine/tenofovir DF**
PI	**Atazanavir + ritonavir + emtricitabine/tenofovir DF** **Darunavir + ritonavir (QD) + emtricitabine/tenofovir DF**
INSTI	**Raltegravir + emtricitabine/tenofovir DF** **Elvitegravir/cobicistat/emtricitabine/tenofovir DF** **Dolutegravir + abacavir/lamivudine** **Dolutegravir + emtricitabine/tenofovir DF**
Additional options if the VL <5 log:	**Efavirenz + abacavir/lamivudine** **Atazanavir + ritonavir + abacavir/lamivudine** **Rilpivirine/tenofovir DF/emtricitabine (if CD4 count >200/mm^3)**

IAS-USA 2014 Guidelines Concur on All Ten Recommended Regimens

DHHS. Available at: http://aidsinfo.nih.gov/contentfiles/AdultARV_INSTIRecommendations.pdf. Update May 2014

DHHS Guidelines April 2015: Five Recommended Regimens

PI	**Darunavir/ritonavir (DRV/r) + TDF/FTC**
INSTI	**Dolutegravir/abacavir/lamivudine (DTG/ABC/3TC)** **only for patients who are HLA-B*5701 negative** **DTG + tenofovir disoproxil fumarate/emtricitabine (TDF/FTC)** **Elvitegravir/cobicistat/TDF/FTC (EVG/c/TDF/FTC)** **only for patients with pre-ART CrCl >70 mL/min** **Raltegravir (RAL) + TDF/FTC**

- On the basis of individual patient characteristics and needs, an Alternative regimen or; less frequently, an Other regimen; may in some instances be the optimal regimen for a patient.
- Given the large number of excellent options for initial therapy, selection of a regimen for a particular patient should be guided by factors such as virologic efficacy, toxicity, pill burden, dosing frequency, drug-drug interaction potential, resistance testing results, comorbid conditions, and cost.

DHHS. Available at: http://aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf. Update April 8, 2015

How Do We Choose from Among These Five Options?

Patient Characteristics:

- Pre-treatment virus resistance
- Risk of adverse events
  - Rate and type of adverse events
  - Type of evidence demonstrating the adverse event
- Other medical comorbidities
  - CV, diabetes, renal, bone, psychological, and others
- Financial Concerns
  - Patient copays, formulary restrictions, generics

Other Criteria You Use?

Criteria that ARE NOT Considered When Selecting a Regimen

- Age
  - Beyond specific co-morbidity concerns
- Gender
- Race
- Weight/BMI

Case: Mr. CQM

- Mr. M comes in to start treatment
- He is a 24 yo BM
- His last HIV negative test was two years ago, tested positive six months ago
- Medical history
  - Father had an MI at age 64-years-old
  - The patient used to smoke
  - Has been treated for STI's twice
  - CD4 488
  - HIV PCR 77,000
  - HLA B*5701 neg
  - HIV genotype - wildtype

How Do We Choose from Among These Five Options?

Drug Characteristics:

- BID vs. QD
  - Raltegravir only recommended drug that is taken BID
  - Most patients prefer qd over bid , and one pill over multiple

ACTG A5257 Study: Wk 96 Virologic Outcomes

ITT, Regardless of ART Change

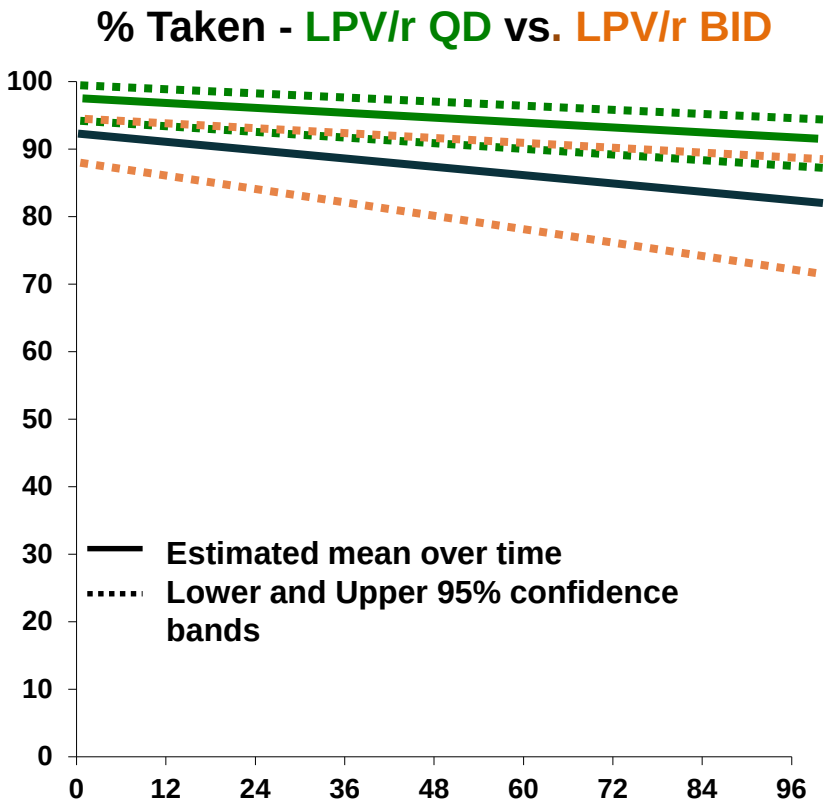
	RAL (n=603)	DRV/r (n=601)	ATV/r (n=605)
HIV RNA			
<50 copies/mL (%)	**94**	**89**	**88**
CD4 gain (cells/mm^3)	**288**	**256**	**284**
Any resistance(%)	**3**	**<1**	**1.5**

All patients received emtricitabine/tenofovir DF.

Landovitz RJ, et al. 21st CROI. Boston, 2014. Abstract 85.

Abbott 418 - Adherence by MEMS Caps: Once-daily vs. Twice-daily with the Same HAART

- **QD vs BID LPV/r + TDF / FTC**
- **Weeks 84-96:**
  - **% taken**
  - **93% vs. 81%, p=0.013**
- **Days with correct dosing:**
  - **85% vs. 65%, p<0.001**
  - **% taken on time:**
  - **76% vs. 51%, p<0.001**



Rode R, et al. 45th ICAAC; December 16–19, 2005; Washington D.C., Abstract H-522.

DHHS Guidelines April 2015: Five Recommended Regimens

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INSTI	**Dolutegravir/abacavir/lamivudine (DTG/ABC/3TC)** **only for patients who are HLA-B*5701 negative** **DTG + tenofovir disoproxil fumarate/emtricitabine (TDF/FTC)** **Elvitegravir/cobicistat/TDF/FTC (EVG/c/TDF/FTC)** **only for patients with pre-ART CrCl >70 mL/min** **Raltegravir (RAL) + TDF/FTC**

DHHS. Available at: http://aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf. Update April 8, 2015

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We Can Expand This

1. Atripla
2. Darunavir/rtv + Truvada (taf)
3. Complera (Odefsey)
4. Stribild (Genvoya)
5. Dolutegrivir + Truvada (taf)
6. Triumeq
7. Prezcobix + Truvada (taf)

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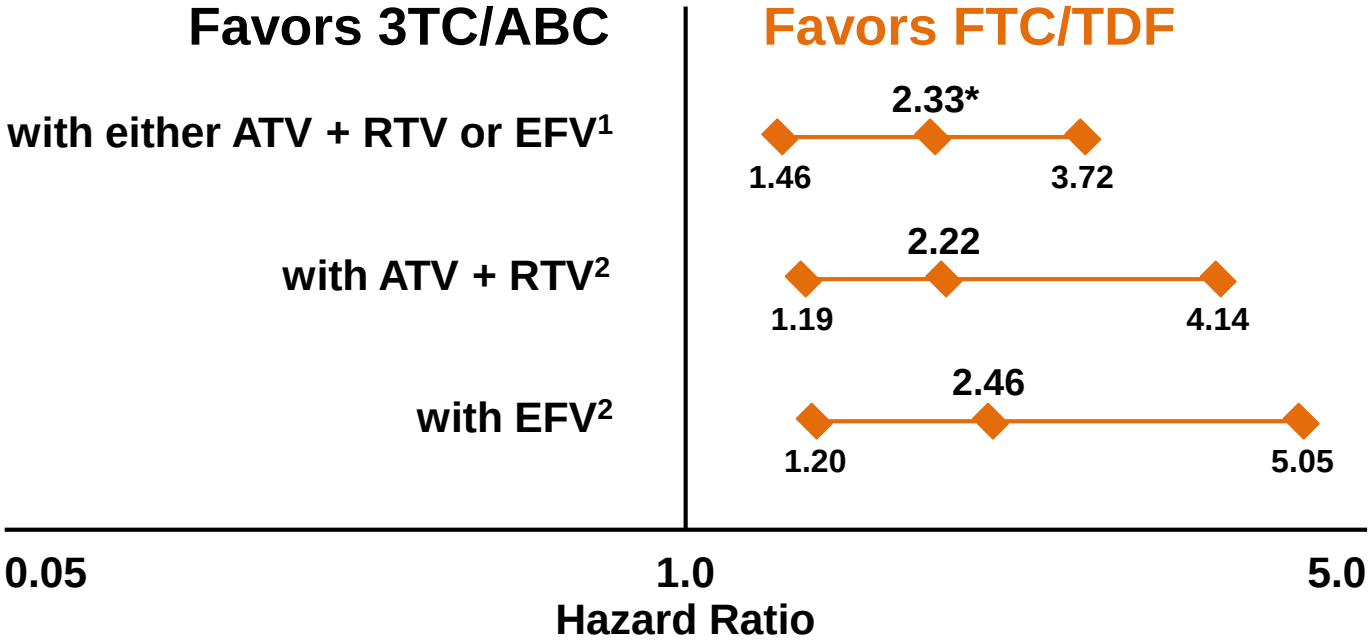
A5202: Time to Virologic Failure by Baseline Viral Load ≥100,000 copies/mL (Week 192)

Hazard Ratio (95% CI) for 3TC/ABC vs FTC/TDF



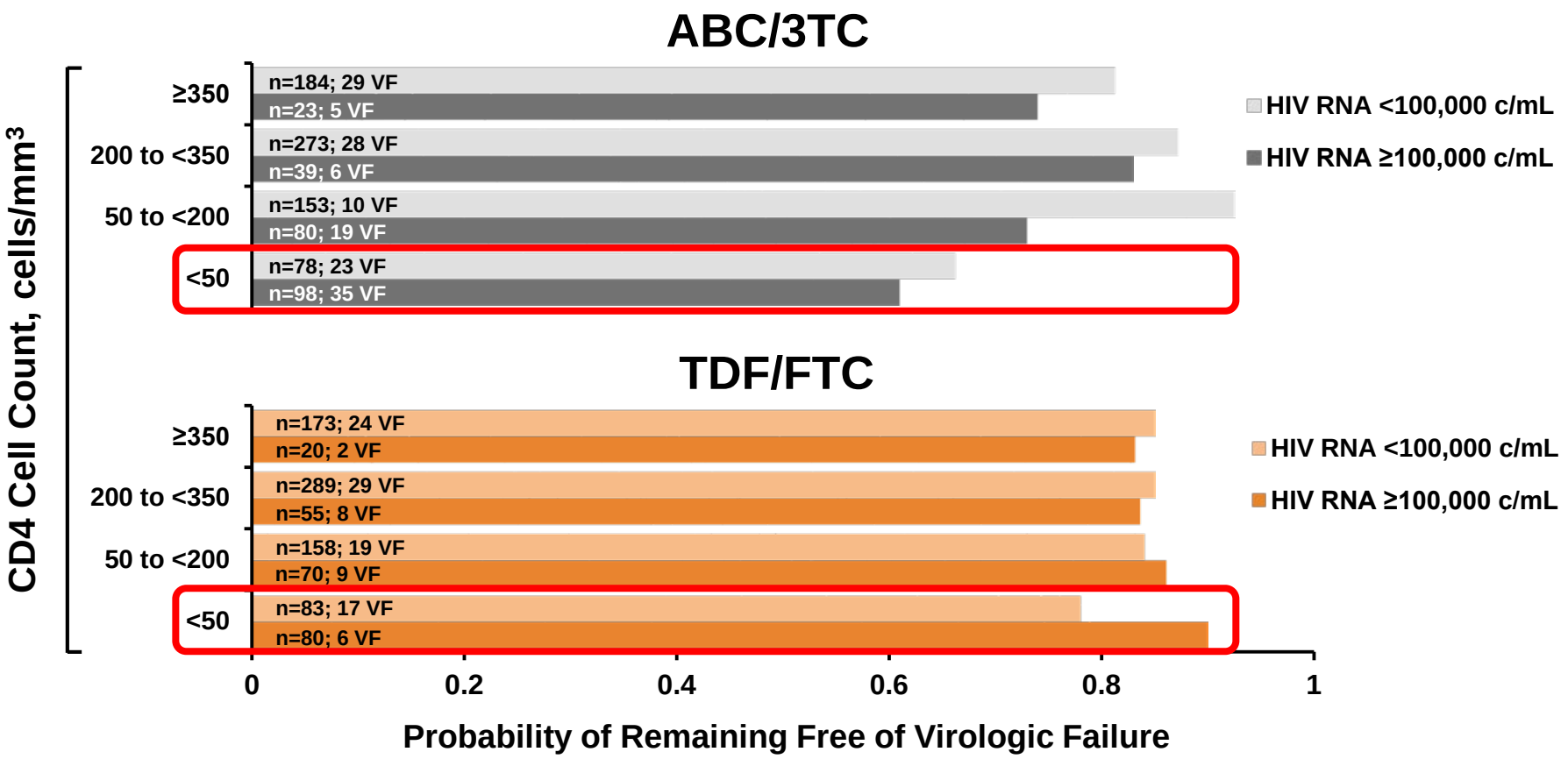
N=797; median (25th, 75th) follow-up = 60 weeks (28, 84).

DSMB discontinues the high viral load 3TC/ABC arm due to higher virologic failure with 3TC/ABC versus FTC/TDF *in HIV RNA ≥100,000 copies mL*

*Log rank test P <.001
CI, confidence interval.

1 Sax PE, et al. N Engl J Med. 2009;361:2230-2240.
2 Daar ES, et al. CROI 2010. San Francisco, CA. Oral 59LB.

A5202: Time to Virologic Failure by Baseline Viral Load and CD4 Cell Count (Week 192)



Baseline Lower CD4 Cell Count or Higher Viral Load Associated with Increased Risk of Virologic Failure with ABC/3TC

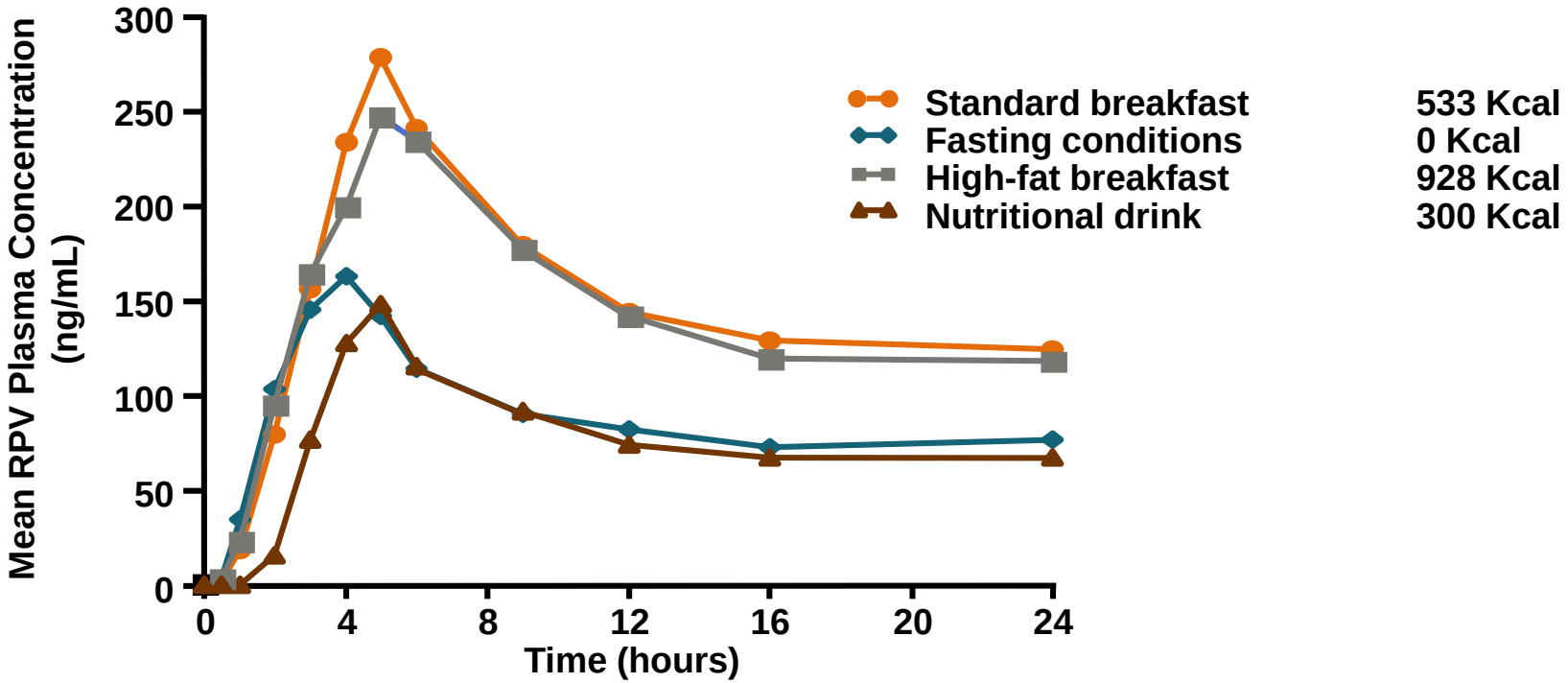
Grant P, et al. CROI 2011. Boston, MA. #535.

How Do We Choose from Among These Five Options?

Food Requirements:

- Food required: on label for DRV/r, EVG/cob
- No concern re food: DTG, RAL

Effect of Food Type on the Mean Rilpivirine Pharmacokinetic Profile



- Taking RPV with food increases RPV exposure by 40% compared to fasting
  - Similar after a high-fat or standard breakfast.
- But – less food effect on RPV exposure for the RPV/FTC/TDF STR vs. RPV single agent:
  - Diff of Fasting vs. fed comparison: ↓16% with STR vs. ↓43% as RPV alone

FDA Label: Recommended Dose: One tablet taken once daily with food

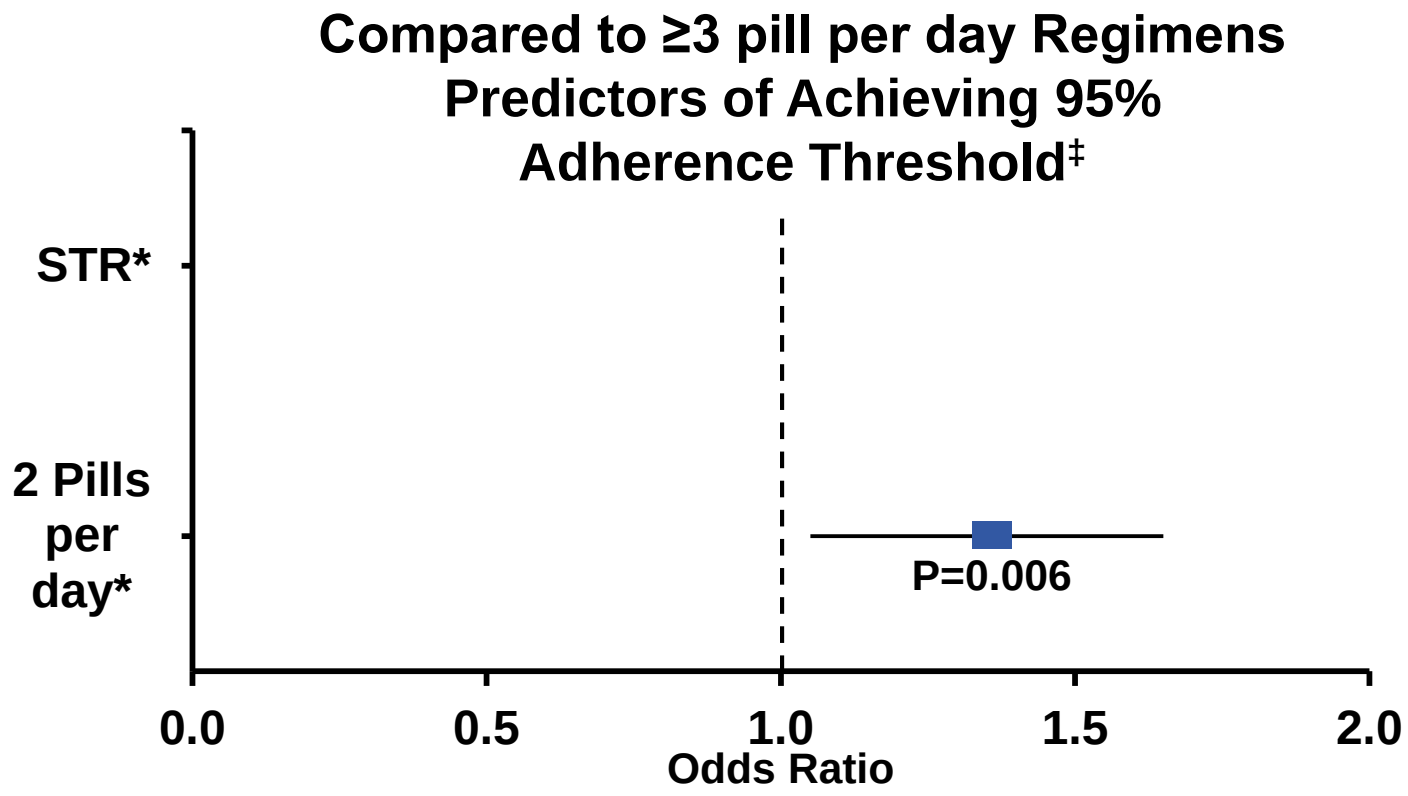
Crauwels HM, et al. IWCPHIV 2008. Abstract P32; Ramanathan S, et al. HIV-11 2012; Glasgow, UK. P068

How Do We Choose from Among These Options?

Drug Characteristics:

- BID vs. QD (or less?)
- Efficacy at any pre-treatment viral load and CD4 count
- Food requirements
- Number of pills per day (range 1-3)
- Potential drug-drug interactions
- Years of experience
- Barrier to resistance if viremic

US LifeLink Database: Predictors of Achieving ≥95% Adherence and Hospitalizations



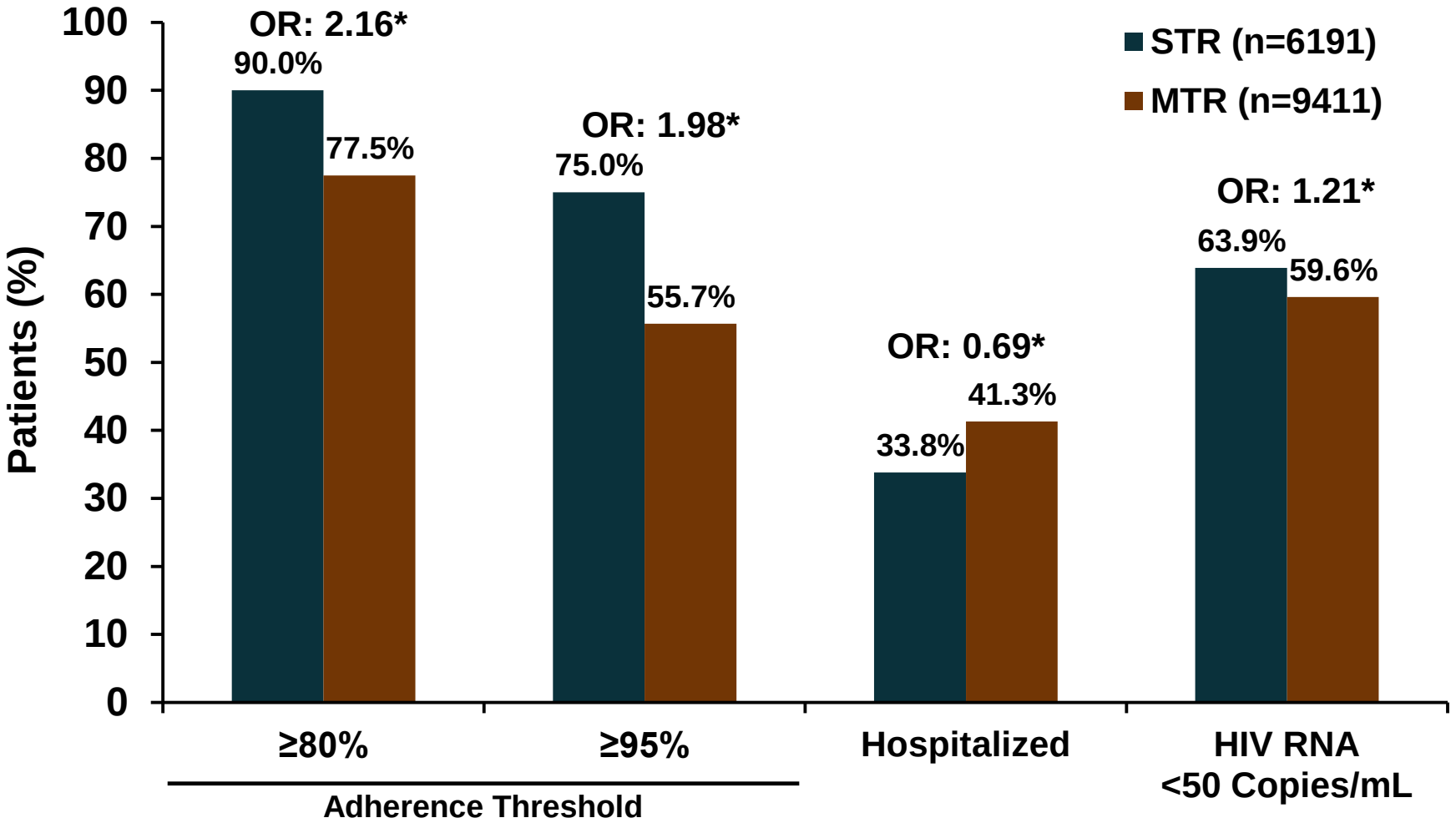
Being on the STR:

- Associated with 24% lower risk of hospitalization (p=0.003) due to improved adherence vs. other regimens

Retrospective chart analysis; N=7,073 HIV+ pts; 6/2006 – 12/2008
* vs. 3 or more pills per day regimen
‡ Multivariate Logistic Regression

Sax P, et al. HIV10 2010. Glasgow. Oral #113

ART in the VA Healthcare System: Impact on Adherence and Outcomes



STR: single-tablet regimen; MTR: multiple-tablet regimen.
*P<0.001. Odds ratios are adjusted for all baseline characteristics.

Rao G, et al. 53rd ICAAC. Denver, 2013. Abstract H-1464.

How Do We Choose from Among These Five Options?

Drug Characteristics:

- BID vs. QD (or less?)
- Efficacy at any pre-treatment viral load and CD4 count
- Food requirements
- Number of pills per day (range 1-3)
- Potential drug-drug interactions
- Years of experience
- Barrier to resistance if viremic

How Do We Choose from Among These Five Options?

- Potential drug-drug interactions
  - Fewest: RAL, DTG - though there are a few
  - DRV, EVG: inducer of CYP3A4
  - RTV, Cobi: inhibitors of CYP3A4 and other isoenzymes

  - Important role of the pharmacy /pharmacist

Indications and Usage

- DESCOVY® is a two-drug combination of emtricitabine (FTC) and tenofovir alafenamide (TAF)[a], both HIV nucleoside analog reverse transcriptase inhibitors (NRTIs)

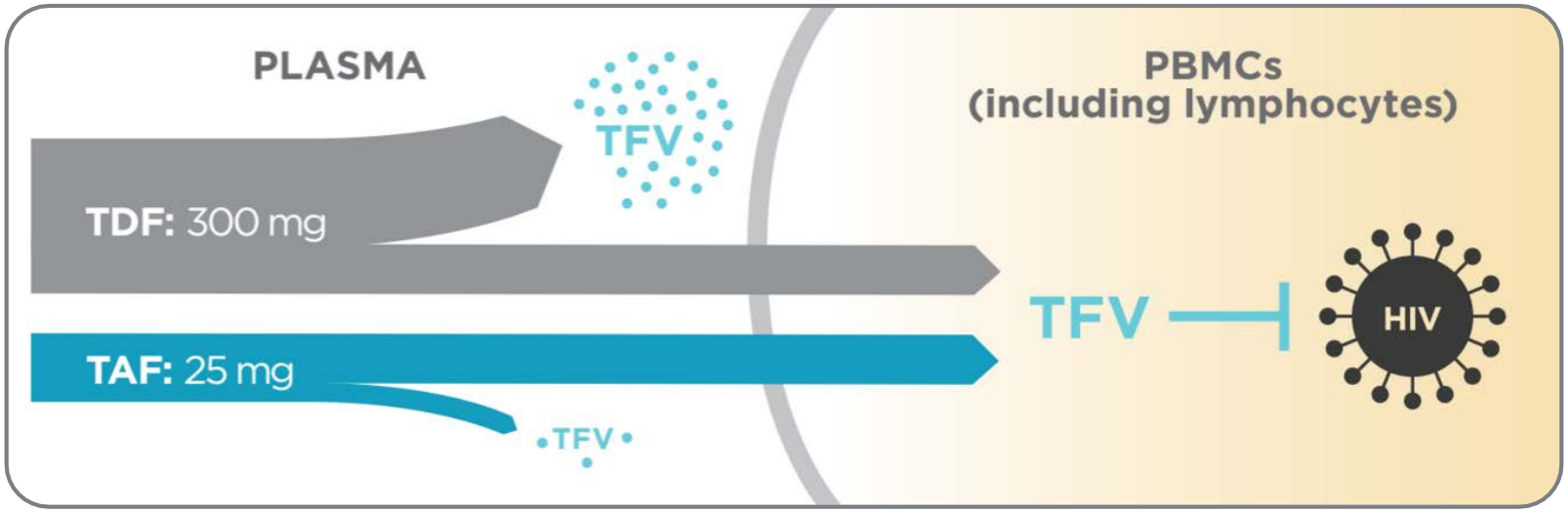
- DESCOVY is indicated, in combination with other antiretroviral agents, for the treatment of HIV-1 infection in adults and adolescent patients 12 years of age and older

- Limitations of Use
  - DESCOVY is not indicated for use as pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in adults at high risk

a. Single-agent TAF has not been approved by the U.S. Food and Drug Administration and its safety and efficacy have not been established.

DESCOVY Prescribing Information. Gilead Sciences, Inc. 2016.

The TAF Component of DESCOVY is Expected to Result in Lower Concentrations of TFV in Plasma vs a 300 mg Dose of TDF



- TAF: A novel prodrug of TFV that is metabolized to TFV by cathepsin A in PBMCs and macrophages[1]
- In 2 trials of treatment-naive adults with HIV-1 infection, a 10 mg oral dose of TAF in FTC/TAF + EVG/COBI resulted in >90% lower concentrations of TFV in plasma as compared to a 300 mg oral dose of TDF in FTC/TDF + EVG/COBI (both coadministered as an STR)[2,3]
  - In a pharmacokinetic study, the unboosted 25 mg of TAF in DESCOVY was demonstrated to be bioequivalent to the COBI-boosted 10 mg of TAF in FTC/TAF + EVG/COBI[4]
  - The concentration of TFV in plasma may differ if DESCOVY is paired with a boosted protease inhibitor[5]

COBI, cobicistat; EVG, elvitegravir; PBMC, peripheral blood mononuclear cells; STR, single tablet regimen; TFV, tenofovir

1. DESCOVY Prescribing Information. Gilead Sciences, Inc. 2016. 2. GENVOYA Prescribing Information. Gilead Sciences Inc. 2016.
3. Sax P, et al. *Lancet*. 2015;385(9987):2606-15 4. Zack J, et al. *J Bioequiv*. 2016:8;49-54. 5. Data on File. Gilead Sciences, Inc.

Concomitant Use of HIV Drugs and HCV Drugs for Treatment of HCV in HIV-Infected Adults

HIV Drugs	HCV Drugs					
	SOF	LDV/SOF	3D	SMV	RBV	PegIFN
3TC	✓	✓	✓	✓	✓	✓
ABC	✓	✓	✓	✓	✓	✓
FTC	✓	✓	✓	✓	✓	✓
TDF	✓	✓ (monitor for TDF toxicity)	✓	✓	✓	✓
ZDV	✓	✓	✓	✓	X[1]	X[1]
ATV (unboosted)	✓	✓	✓[2]	X	✓	✓
ATV/r or ATV/c	✓	✓[3]	✓[4]	X	✓	✓
DRV/r or DRV/c	✓	✓[3]	X	X	✓	✓
FPV or FPV/r	✓	✓[3]	X	X	✓	✓
LPV/r	✓	✓[3]	X	X	✓	✓

√ = ARV agents that can be used concomitantly; X = ARV agents not recommended. 3D = Ombitasvir/paritaprevir/ritonavir + dasabuvir. 1. Concomitant use of ZDV with ribavirin or pegylated interferon is not recommended given the potential for worsening neutropenia. 2. Reduce ATV dose to 300 mg and take in AM at same time as ombitasvir/paritaprevir/r plus dasabuvir. 3. If PI/r or ATV/c, DRV/c is used with TDF, ↑TDF concentrations are expected. If co-administration necessary, monitor for TDF-associated toxicities. Consider alternative HCV or ARV therapy to avoid increases in TDF exposures. If co-administration is necessary, monitor for TDF-associated adverse reactions. 4. Take ATV 300 mg in AM at same time as ombitasvir/paritaprevir/r plus dasabuvir; discontinue RTV or COBI in HIV regimen until HCV therapy completed.

aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/26/hiv-hcv

Concomitant Use of HIV Drugs and HCV Drugs for Treatment of HCV in HIV-Infected Adults (Cont'd)

HIV Drugs	HCV Drugs					
	SOF	LDV/SOF	3D	SMV	RBV	PegIFN
SQV/r	✓	✓[3]	X	X	✓	✓
TPV/r	X	X	X	X	✓	✓
EFV	✓	✓[5]	X	X	✓	✓
ETR	✓	✓	X	X	✓	✓
NVP	✓	✓	X	X	✓	✓
RVP	✓	✓	X	✓	✓	✓
DTG	✓	✓	?	✓	✓	✓
EVG/c/TDF/FTC	✓	X	X	X	✓	✓
EVG (+ PI/r without COBI)	Refer to recommendations specific to each PI/r					
RAL	✓	✓	✓	✓	✓	✓
MVC	✓	✓	X	✓	✓	✓

√ = ARV agents that can be used concomitantly; X = ARV agents not recommended; ? = Data on PK interactions with the ARV drug are unavailable or insufficient to make a recommendation. 3D = Ombitasvir/paritaprevir/ritonavir + dasabuvir. 3. If PI/r [or ATV/c, DRV/c] is used with TDF, ↑TDF concentrations are expected. If co-administration necessary, monitor for TDF-associated toxicities. Consider alternative HCV or ARV therapy to avoid increases in TDF exposures. If co-administration is necessary, monitor for TDF-associated adverse reactions. 5. If EFV used with TDF/FTC, monitor for TDF toxicity due to ↑ TDF concentrations

http://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/26/hiv-hcv

How Do We Choose from Among These Five Options?

Drug Characteristics:

- BID vs. QD (or less?)
- Efficacy at any pre-treatment viral load and CD4 count
- Food requirements
- Number of pills per day (range 1-3)
- Potential drug-drug interactions
- Years of experience
- Barrier to resistance if viremic

How Do We Choose from Among These Five Options?

Drug Characteristics:

- Barrier to resistance if viremic on treatment
  - Boosted PIs and DTG: No primary mutations to drug detected, none (very low rate) of NRTI resistance
  - **RAL, EVG/c:** NRTI mutation then InSTI resistance, at similar rates in clinical trials

How Do We Choose from Among These Five Options?

Patient Characteristics:

- Pre-treatment virus resistance
- Risk of adverse events
  - The rate of - and type of - adverse events
  - Type of evidence demonstrating the adverse event
- Other medical comorbidities
  - CV, diabetes, renal, bone, psychological, and others
- Financial Concerns
  - Patient copays, formulary restrictions, generics

How Do We Choose from Among These Five Options?

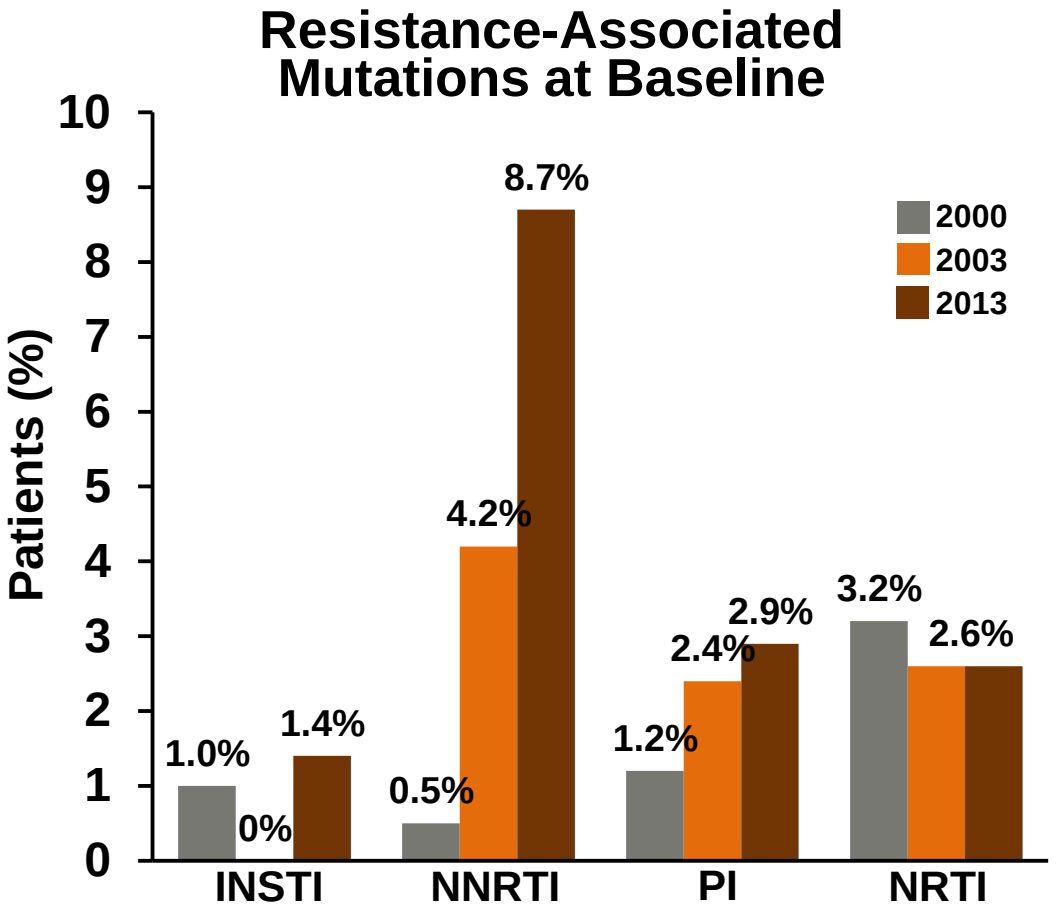
Patient Characteristics:

Pre-treatment resistance testing

- Most common – NNRTIs (K103N) (but this is no longer critical since EFV and RPV are no longer part of recommended regimens)
- Lower – NRTIs (usually TAMs)
- Few – PIs
  - Unclear impact if any on boosted PI efficacy
- Rare – Integrase

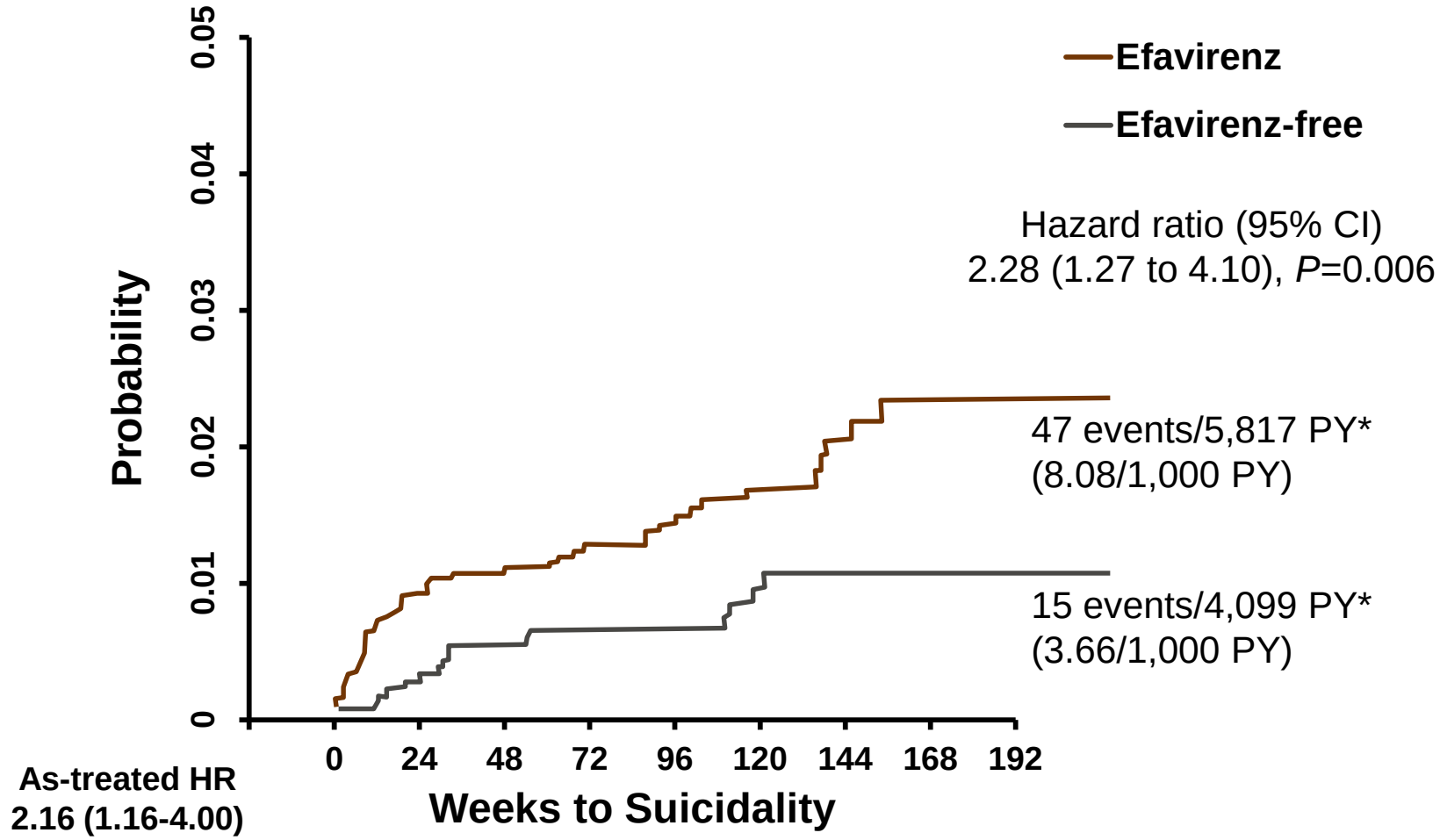
Drug Resistance Mutations in Treatment-Naïve HIV Patients (2000-2013)

- Retrospective Analysis
  - Analysis of pre-treatment samples from four phase 3 studies
    - IN sequences (n=1617)
    - PR-RT sequences (n=2531)
- Enrollment Years
  - 2000 (study 903),
  - 2003 (study 934),
  - 2013 (studies 104 and 111)



Margot NA, et al. 21st CROI. Boston, 2014. Abstract 578.

Time to Suicidality, Primary Analysis



Hazard Ratio (95% CI) 2.28 (1.27 to 4.10), P=0.006

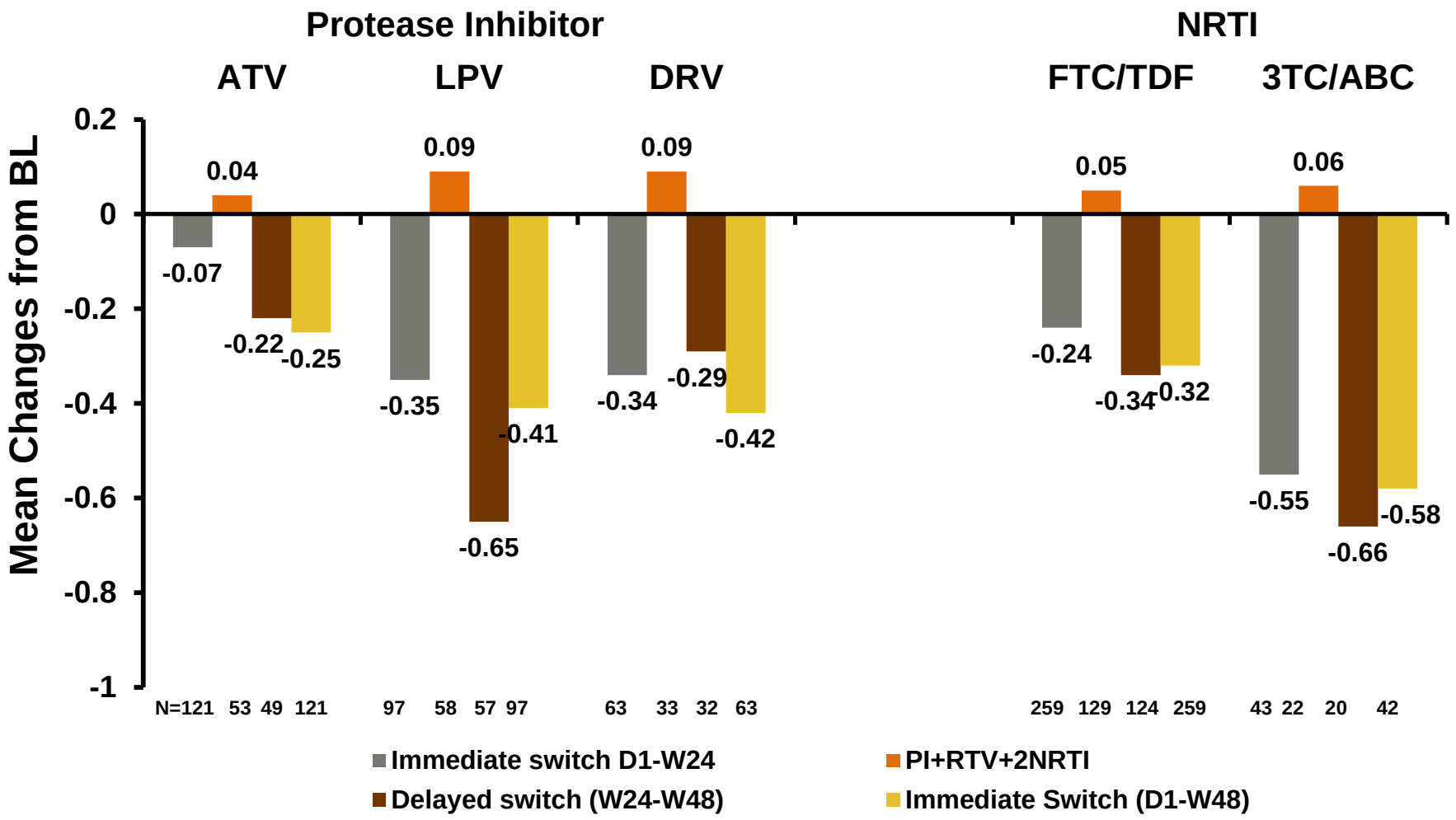
*Person Years, sum of at-risk follow-up

How Do We Choose from Among These Options?

Patient Characteristics:

- Pre-treatment resistance testing
- **Risk of Adverse Events**
  - Lab and Test Based:
    - Lipids
    - CV Risk
    - Bone Demineralization
    - Renal function
    - Inflammatory Markers

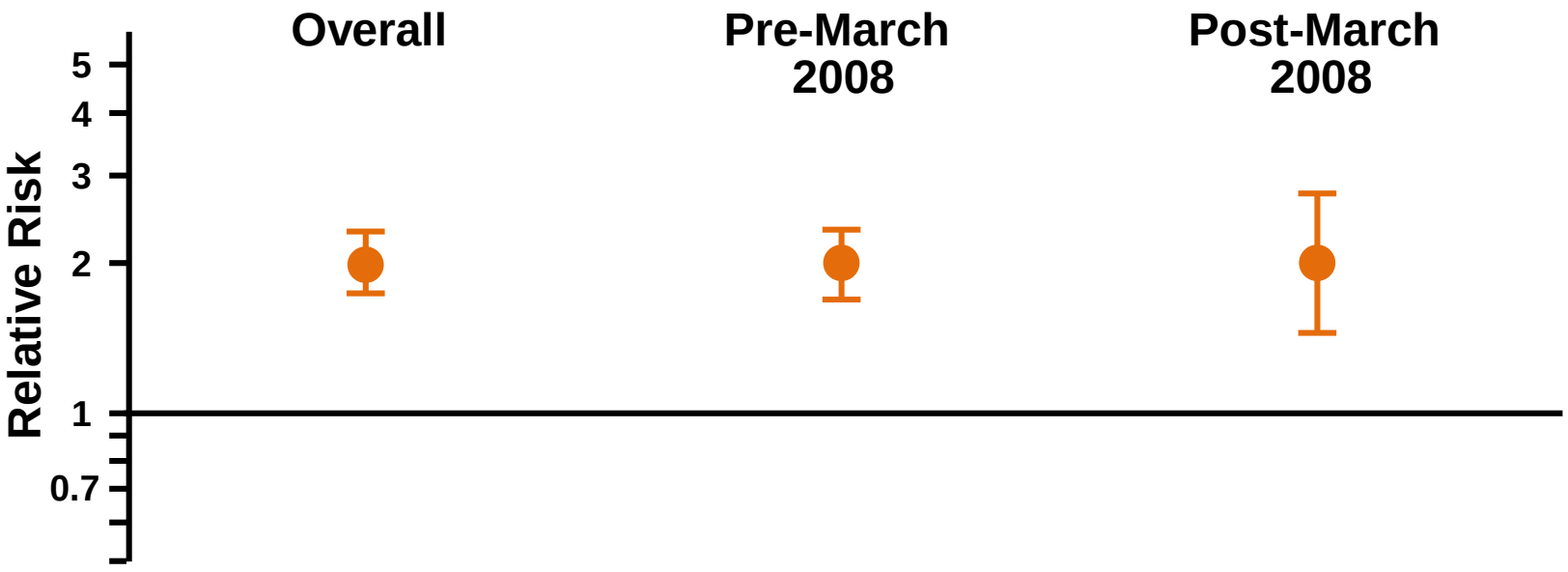
SPIRIT Change in TC:HDL Ratio by Baseline Protease Inhibitor and NRTI



Brunetta J et al. 22nd CAHR April 11-14, 2013; Vancouver, Canada; Oral O064

ABC and Risk of MI: D:A:D

- Analysis of MI risk with ABC pre and post 3/08 in D:A:D cohort
- Trend of less ABC use in high risk individuals post 3/08
- MI rates
  - Current/Recent ABC 0.47 (0.42-0.52)/1000 pt yrs of FU
  - No ABC 0.21 (0.19-0.22)/1000 pt yrs of FU
- Overall RR with ABC 1.98 (1.72-2.29): Pre 3/08 1.97, Post 3/08 1.97



Sabin C, et al. 21st CROI; Boston, MA; March 3-6, 2014. Abst. 747LB.

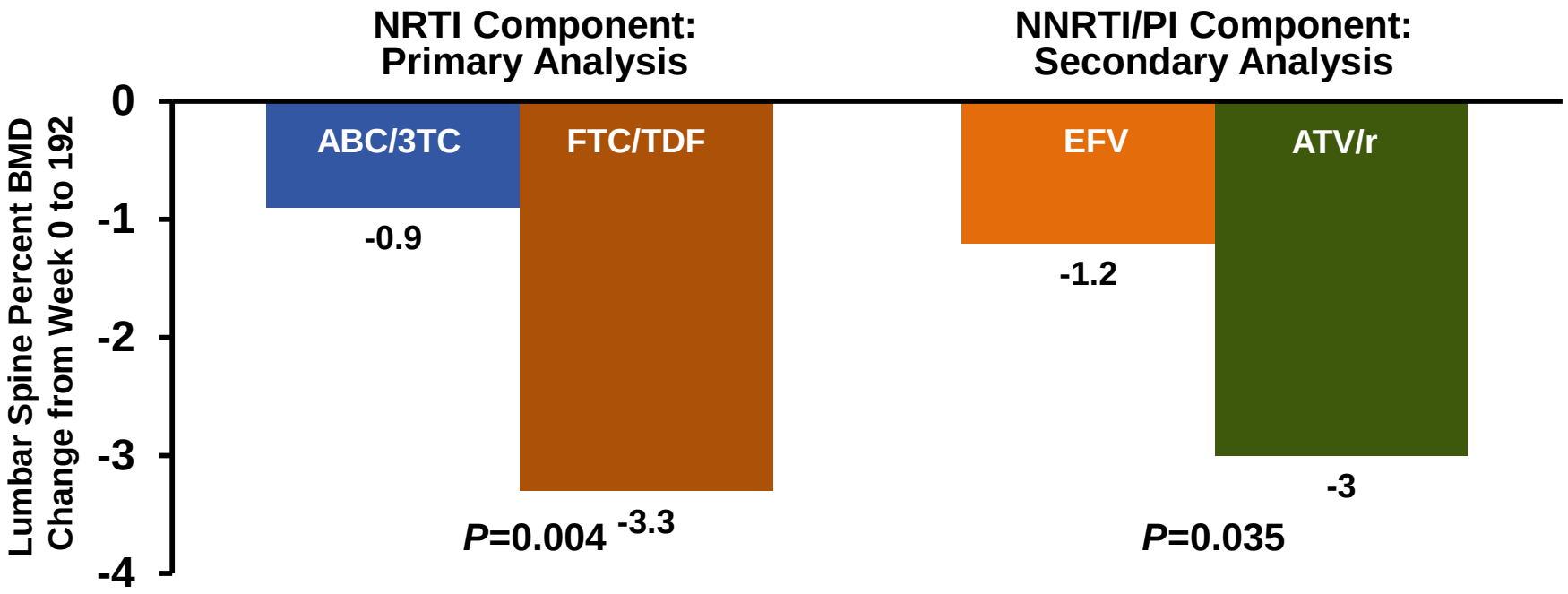
ABC Association with MI: FDA Meta-analysis

FDA Completed Trial-level Meta-analysis of 26 Completed RCTs of ABC in Adults, with N >50 Subjects

Studies	Events/Subjects		Risk Difference (95% CI)	Odds Ratio (95% CI)
	ABC	Non-ABC		
GSK	6/2341	9/2367	-0.11% (-0.43%, 0.21%)	0.70 (0.25, 2.00)
NIH	12/1985	9/1610	0.03% (-0.45%, 0.51%)	1.08 (0.43, 2.61)
Academic	6/702	4/863	0.31% (-0.53%, 1.16%)	1.60 (0.46, 5.62)
Overall	24/5028	22/4840	0.008% (-0.26%, 0.27%)	1.02 (0.56, 1.84)

Ding X, et al. CROI 2011. Boston. #808. 2. De Pablo C, et al. CROI 2011. Boston. #815.

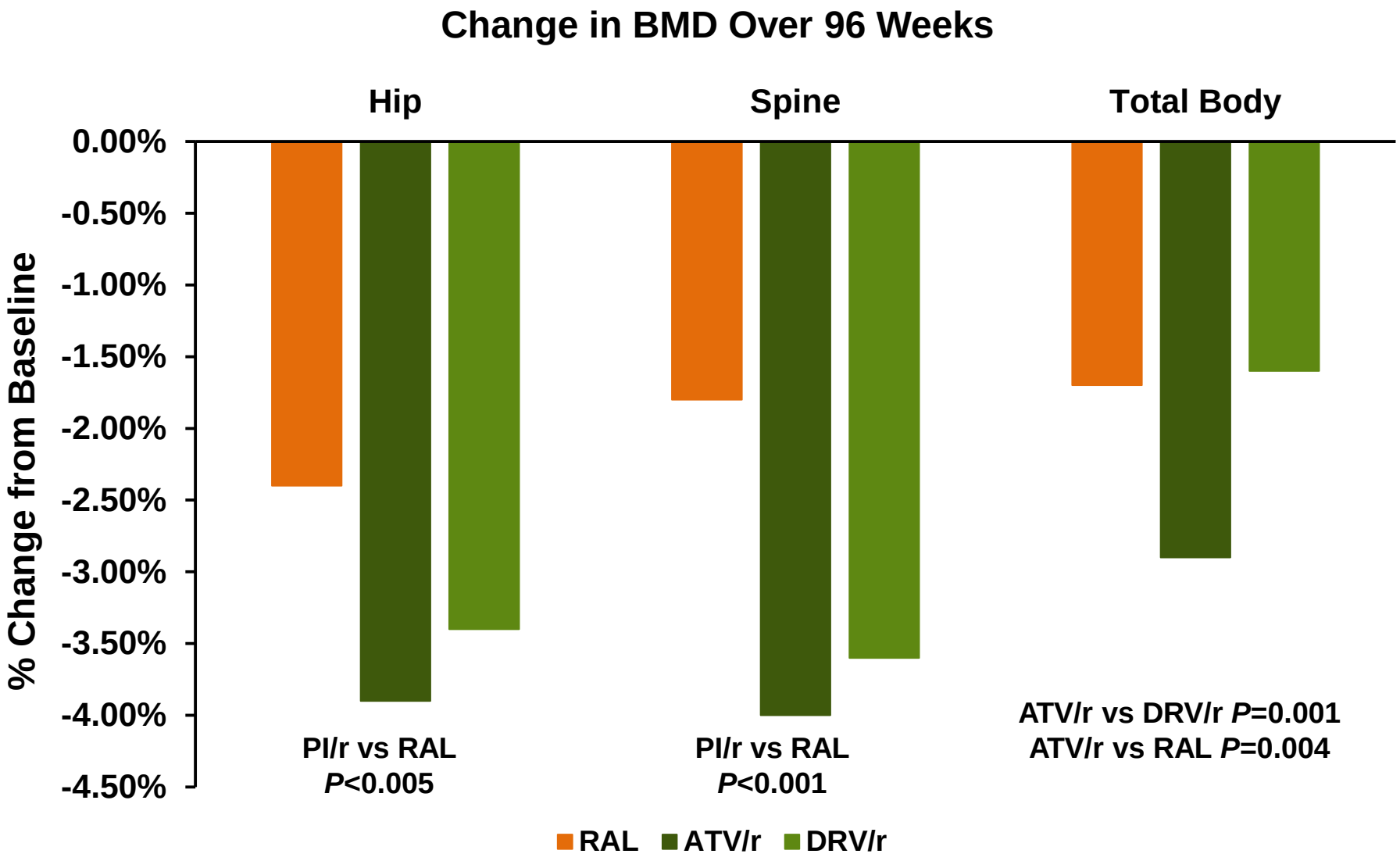
A5224s:
Mean Percent Change in Lumbar Spine Bone Mineral Density



- Hip BMD: Significantly greater percent decline with FTC/TDF than ABC/3TC; not significant for NNRTI/PI
- No significant difference in fracture rate between arms

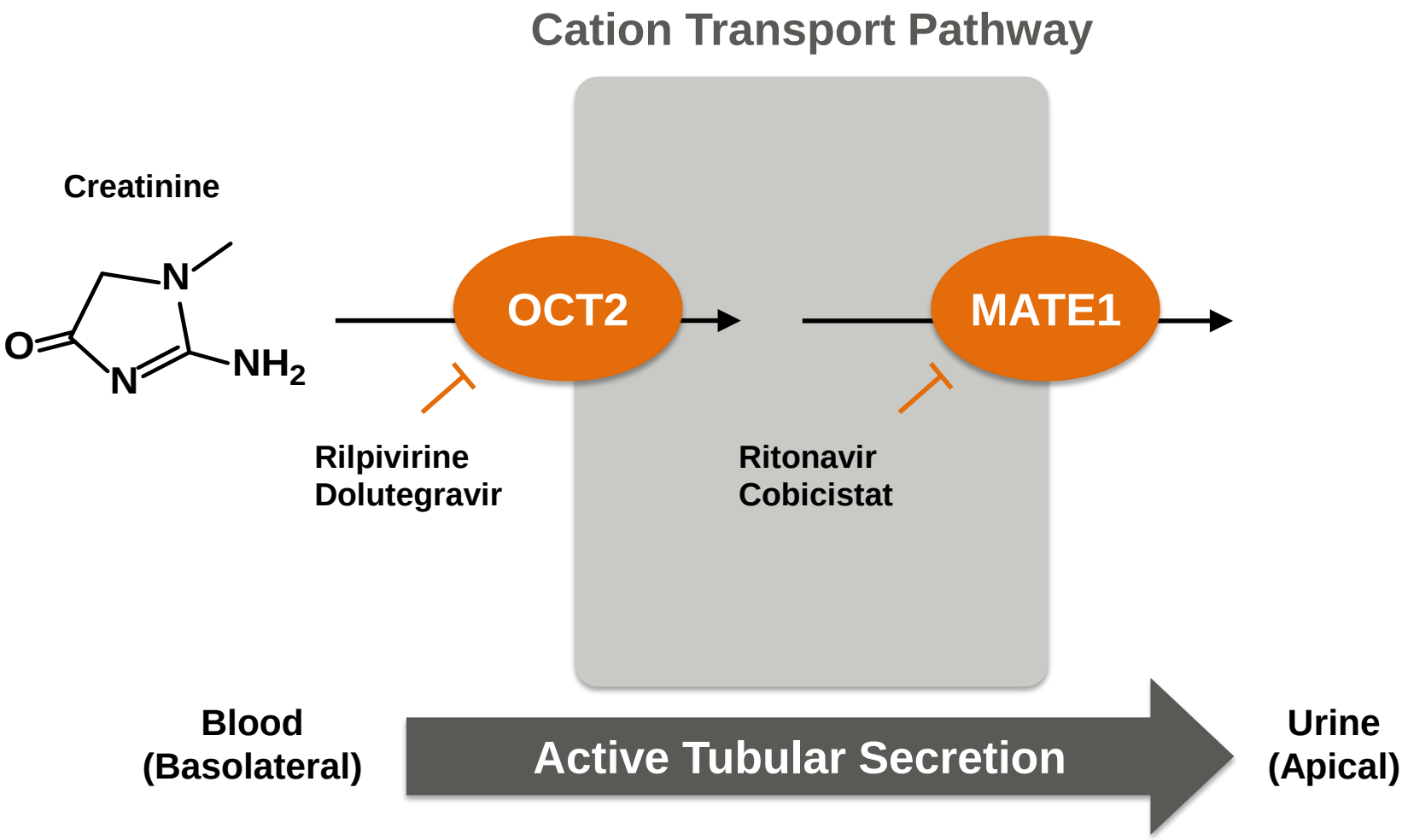
McComsey, G, et al. CROI 2010, 106LB.

ACTG 5257:
Bone Mineral Density at 96 Weeks



Brown T, et al. 21st CROI; Boston, MA; March 3-6, 2014. Abst. 779.

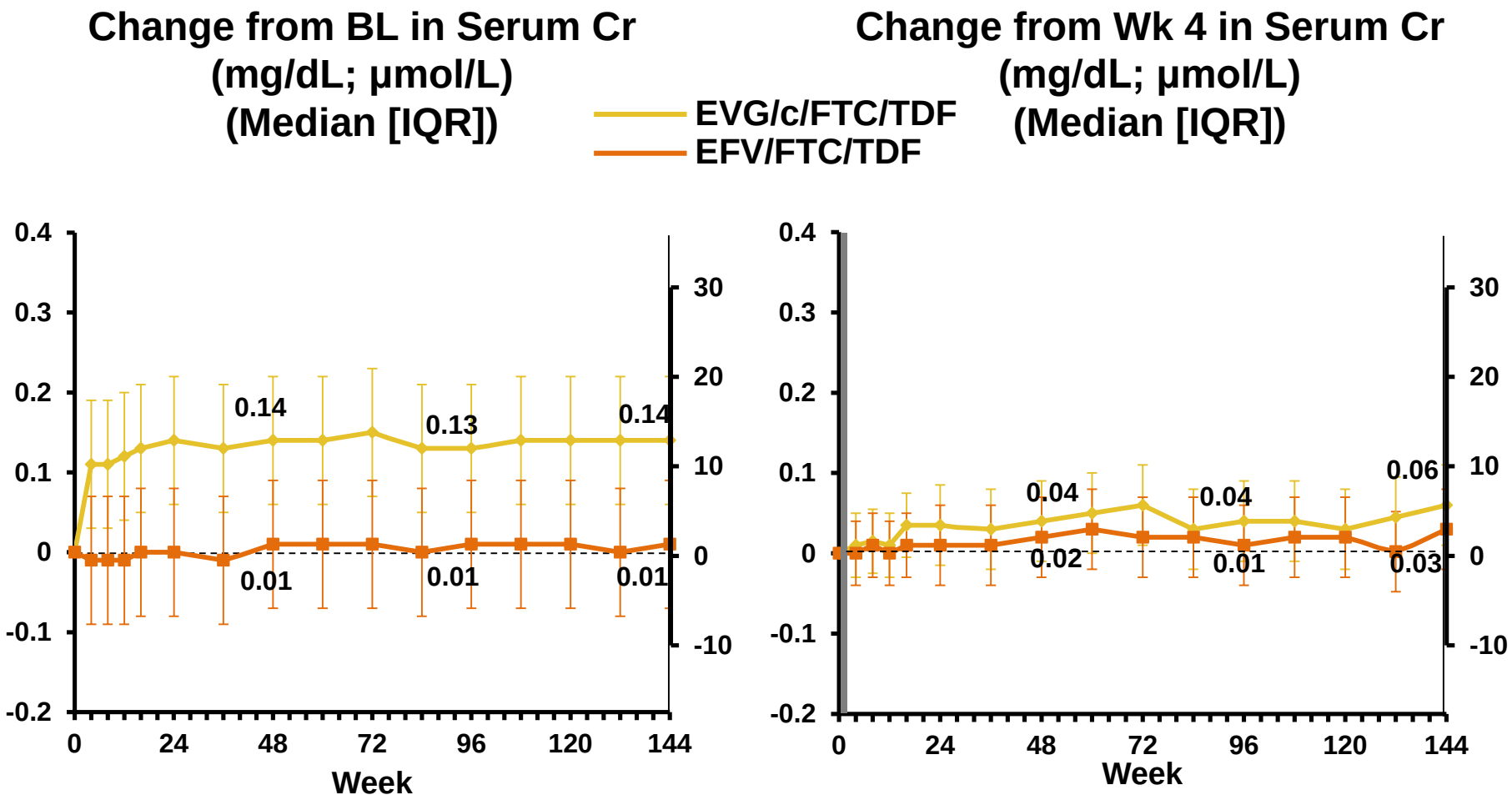
Effects on Creatinine Tubular Transporter: Inhibiting Creatinine Secretion



OCT2 = organic cation transporter 2
MATE1 = multidrug and toxin extrusion transporter 1

Benson, P, et al. 52nd ICAAC 2012.

Study 102: Week 144 Changes in Serum Cr from Baseline and from Week 4



Cohen C, et al. 14th EACS; Brussels, Belgium; October 16-19, 2013. Abst. PE7/13.

How Do We Choose from Among These Five Options?

Patient Characteristics:

- Pre-treatment virus resistance
- Risk of adverse events
  - The rate and type of adverse events
  - Type of evidence demonstrating the adverse event
- Other medical comorbidities
  - CV, diabetes, renal, bone, psychological, and others
- Financial concerns
  - Patient copays, formulary restrictions, generics

Economics: Antiretroviral Drugs Available in U.S. as a Generic Formulation

- Abacavir
- Didanosine
- Lamivudine
- Nevirapine
- Stavudine
- Zidovudine
- Zidovudine/lamivudine

Case: Mr. CQM

- Mr. M comes in to start treatment
- He is a 24 yo
- His last HIV negative test was two years ago, tested positive six months ago

- Your choice?

- What if :
- 1) He tested HLA +
- 2) Had a PCR > 200,000
- 3) Impressed you as being not to adherent
- 4) CD4 > 200, PCR 88,000
- 5) Was starting Hep C therapy
- 6 Was starting Hep C therapy and his CD4 44

How Do We Choose from Among These Five Options?

Summary

- Very little difference in virologic efficacy in pre-defined populations
- Fewer pills, once daily have advantages
  - Some studies show advantage of tolerability over these
- Know your patients – make the choice together
  - Lifestyle
  - What will they tolerate
  - Co-morbidities
  - Drug-drug interaction
  - Does cost effect their options
  - Issues with stigma
- Early follow-up to assess if the choice was right

The Importance of Individualizing HIV Care:

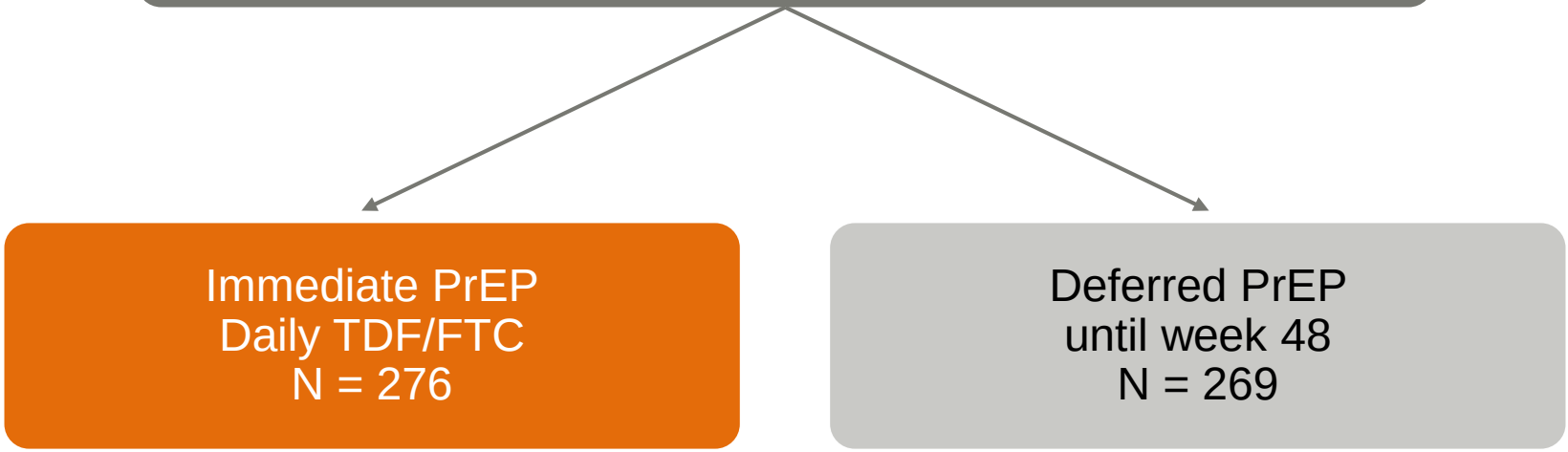
An Interactive Program on How to Select the Ideal Antiretroviral Therapy for Each Patient

PrEP

Jointly provided by the Annenberg Center for Health Sciences at Eisenhower and ViralEd, Inc. in collaboration with Postgraduate Institute for Medicine
This activity is supported by an independent educational grant from Janssen Therapeutics, Division of Janssen Products, LP

PROUD: Open-Label PrEP Trial

- **HIV negative, MSM engaging in unprotected anal intercourse in past 90 days in London, UK**
- **Willing to take a pill a day**
- **No contraindication to use of TDF/FTC**



- Follow-up at 3 month intervals
- Post-exposure prophylaxis provided

McCormack S, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 22LB.

PROUD: HIV Incidence

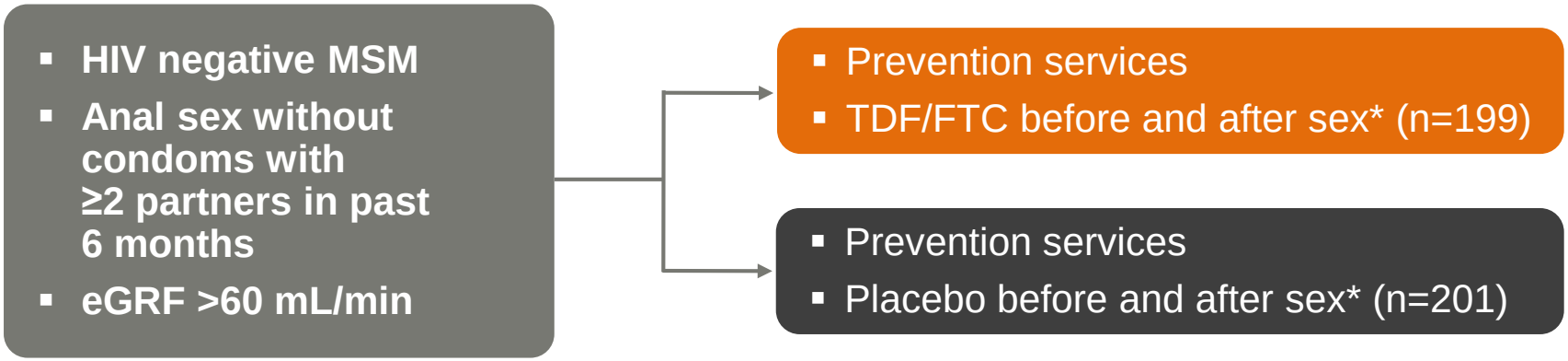
Group	No. of Infections	Follow-Up (PY)	Incidence (Per 100 PY)	90% CI
Overall	22	453	4.9	3.4 – 6.8
Immediate	3	239	1.3	0.4 – 3.0
Deferred	19	214	8.9	6.0 – 12.7

- **Efficacy** = **86%** (90% CI: 58 – 96%)
- **P value** = 0.0002
- **Rate Difference** = 7.6 (90% CI: 4.1 – 11.2)
- **Number Needed to Treat** = **13** (90% CI: 9 – 25)

McCormack S, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 22LB.

Ipergay: “On-Demand” PrEP Study Design

- Double blind, randomized placebo controlled trial to prevent HIV infection in France and Canada

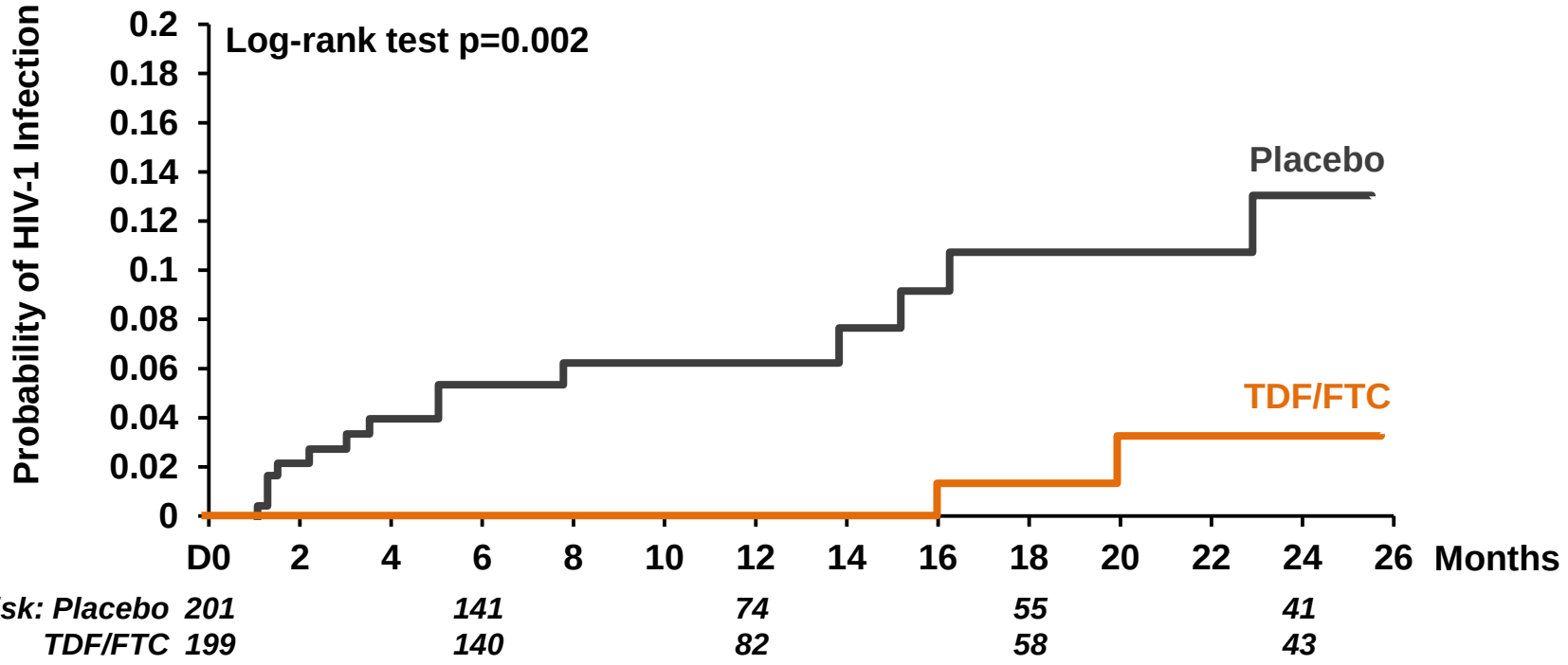


- Follow-up visits: month 1, 2, and every 2 months thereafter
- Endpoint driven study – with 64 infections there is 80% power to detect 50% reduction in infection rate in active arm
- Expected incidence 3/100 PY with placebo

* Two tablets 2-24 hours before sex; 1 tablet 24 hours later; 1 table 48 hours later

Molina JM, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 23LB.

Ipergay: Time to HIV Infection



- Infections: Placebo: 14 (incidence: 6.6 per 100 PY)
  TDF/FTC: 2 (incidence: 0.94 per 100 PY)
- Relative Reduction: 86% (95% CI: 40–99%, p=0.002)
- Number needed to treat for one year to prevent one infection: 18

Molina JM, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 23LB.

Partners Demo: PrEP & ART for Discordant Couples

Population

- Heterosexual discordant couples not using ART or PrEP in Kenya & Uganda
- At high risk for HIV transmission based on risk scoring tool

Intervention

- ART per national guidelines – treat all seropositive partners in discordant relationship
- PrEP – open label TDF/FTC until positive partner on therapy for 6 months as a ‘bridge’ to ART

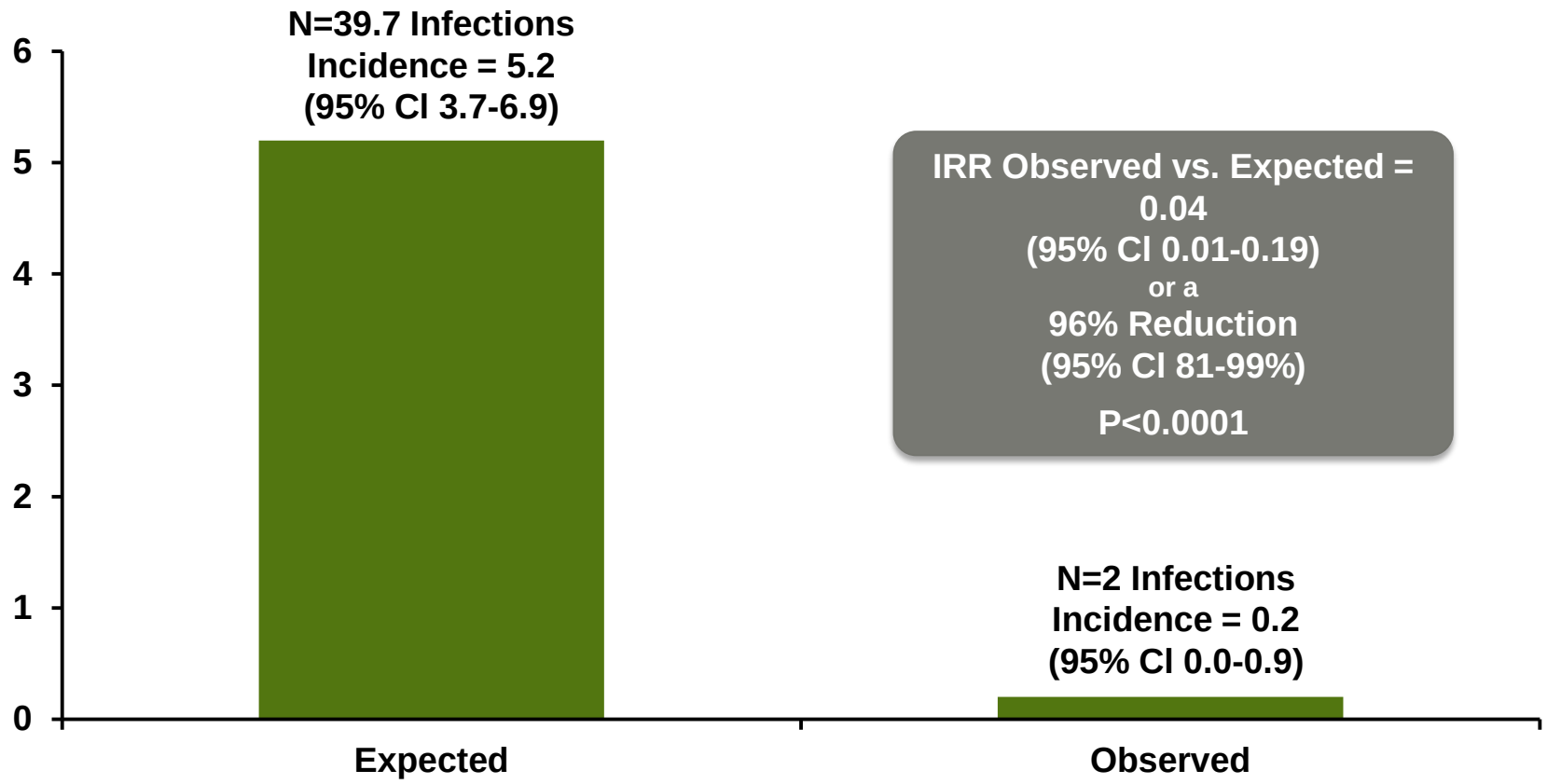
Comparison

- Counterfactual simulation model, using bootstrapping data from Partner’s PrEP Study with matching risk scores and follow-up

Baeten J, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 24.

Partners Demo: HIV Incidence

- 858 person years of follow-up
- 95% uptake of PrEP and 80% on ART



Baeten J, et al. 22nd CROI; Seattle, WA; February 23-26, 2015. Abst. 24.

What is PrEP ?

1. Truvada once daily

2. Note: taf (tenofovir alafenamide or Descovy is NOT PrEP)

What else to Consider ?

1. Test for HIV ab beforehand
2. Test for Hep B
3. If being treated for Hep B you may need to amend treatment…contact the other treating physician
4. Draw creatinine or CrCl > 60
5. Give 3 months supply at most
6. Re-evaluate in 3 months

Who Needs Prep ?

1. MSM's
2. MtF Transgenders
3. Sex workers
4. Female partners of MSM's

Physician comfort

1. Patient does not need to disclose their sexuality…if they ask for it…explain what it is…if they still want it…prescribe it !!

2. Who covers:
   a, Most private insurances
   b. Public health offices in different locals
   c. Medicaid
   d. Medicare ??

Questions