NORTHWEST AIDS EDUCATION AND TRAINING CENTER

AIDS 2012 Highlights

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Last Updated: August 21, 2012

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Disclosures

Dr. Ramers discloses the following relationships:

- Advisory board, speaker's bureau: Gilead Sciences

XIX meeting of the International AIDS Society
July 22-27, 2012 – Washington, DC

Conference Facts	
Total Participants	23,767
Countries Represented	183
Abstracts Submitted	12,433
Abstracts Accepted	3,837
Total Sessions	194
Abstract Sessions	110

AIDS 2012
XIX INTERNATIONAL AIDS CONFERENCE JULY 22 - 27
WASHINGTON DC USA
TURNING THE TIDE TOGETHER

First IAS Conference in the US since 1990 – San Francisco, CA

Source: Official AIDS 2012 Daily Bulletin – 27 July 2012

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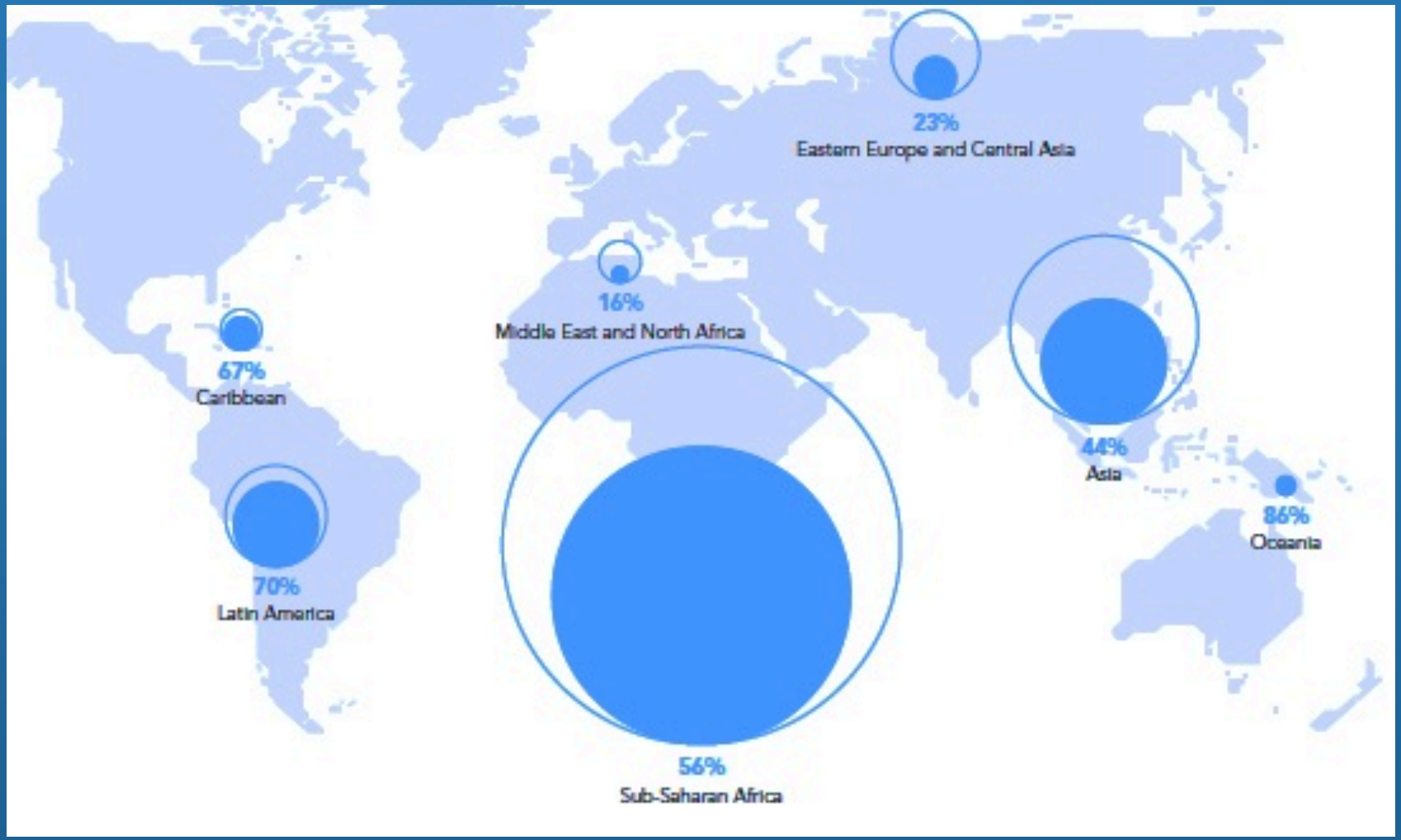
HIV EPIDEMIOLOGY

- Global WHO/UNAIDS outlook
- HIV Care Continuum in US: the ‘Leaky Cascade’

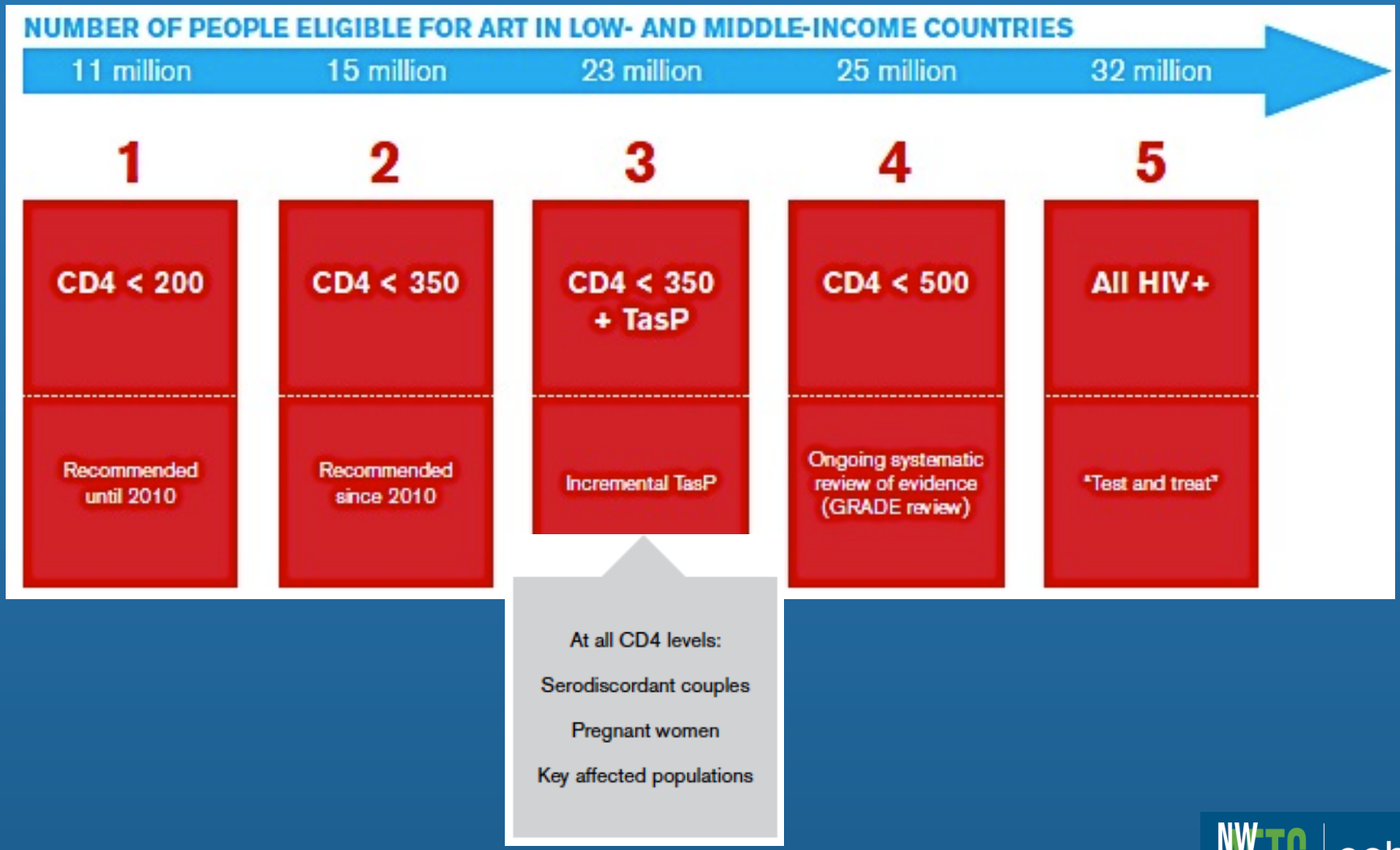
Eligibility for antiretroviral therapy versus coverage, low- and middle-income countries, by region, 2011



Source: Together We Will End AIDS. UNAIDS 2012

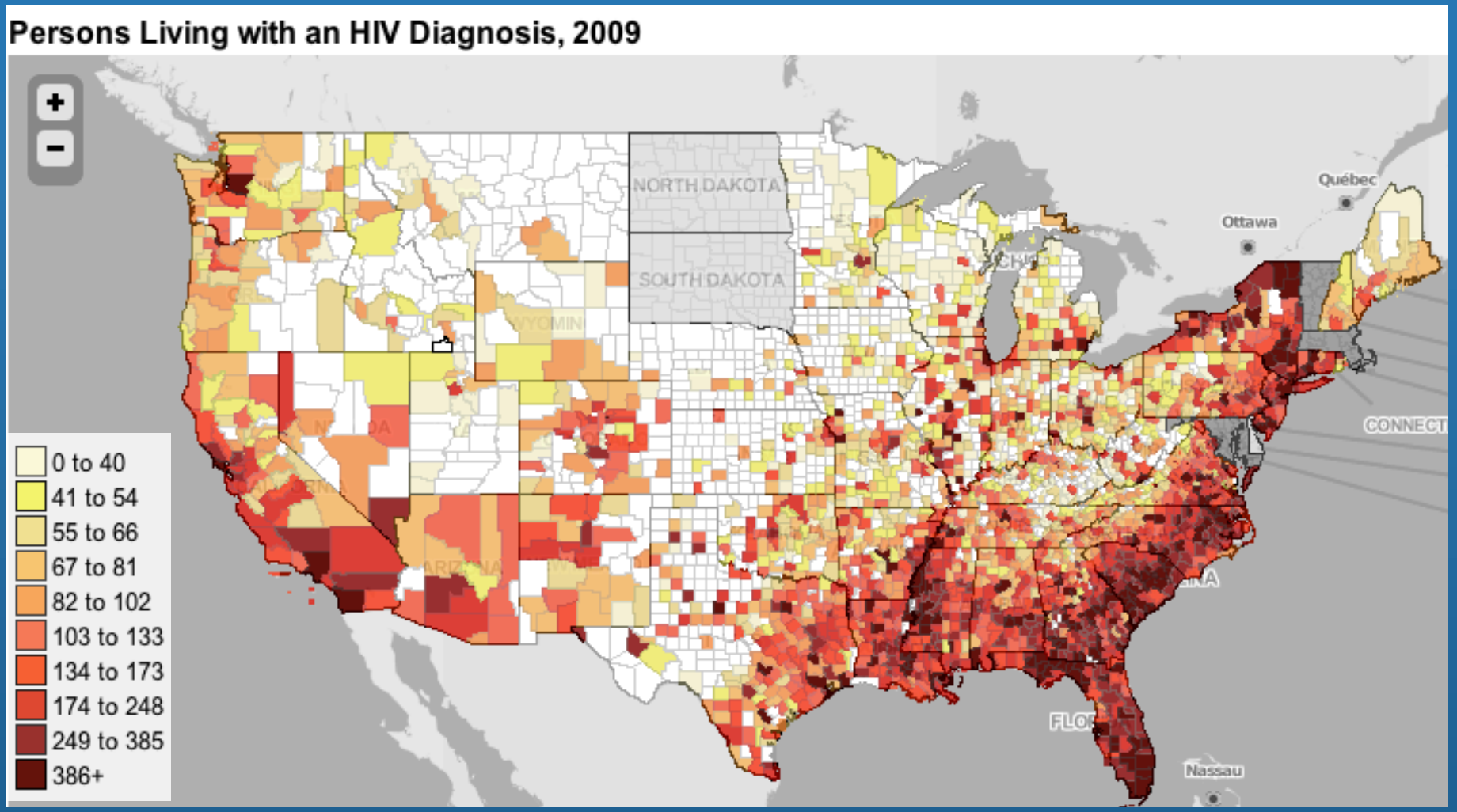
Figure 4:

Scenarios for the incremental expansion of ARV provision to treat and prevent HIV



Source: The Strategic Use of Antiretrovirals to help end the HIV Epidemic, WHO 2012

HIV Epidemic in the US - www.aidsvu.org



2009 Rate of adults/adolescents living with an HIV diagnosis per 100,000 population

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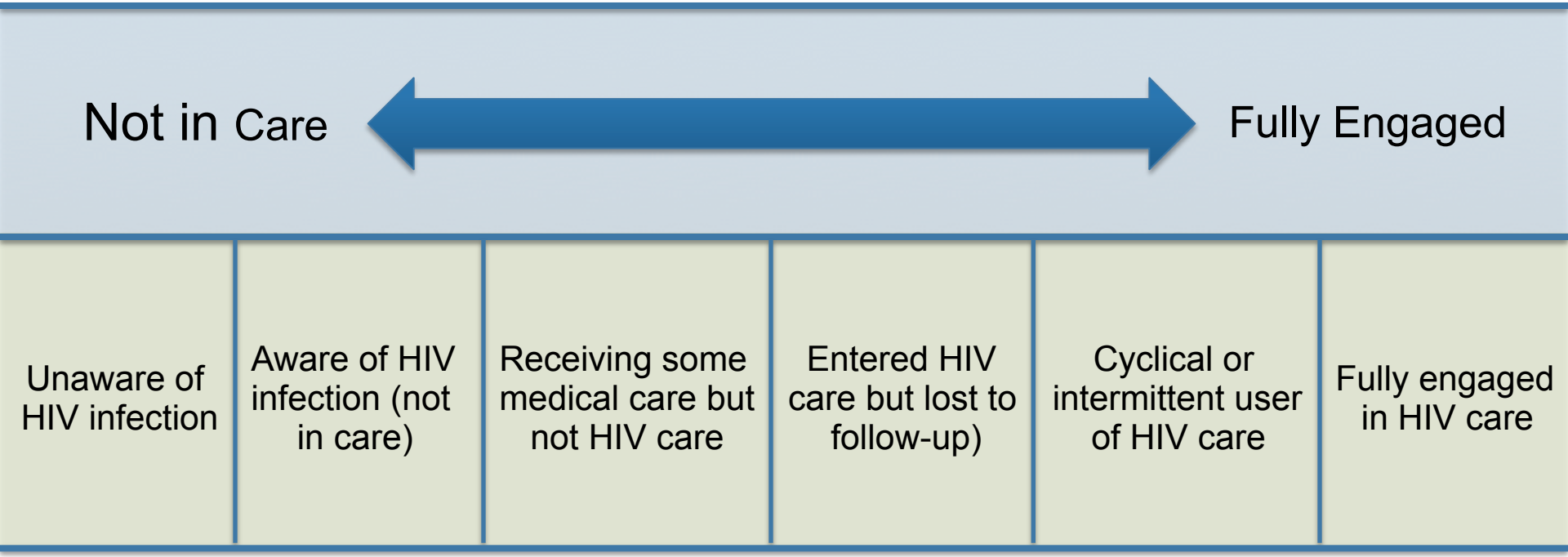
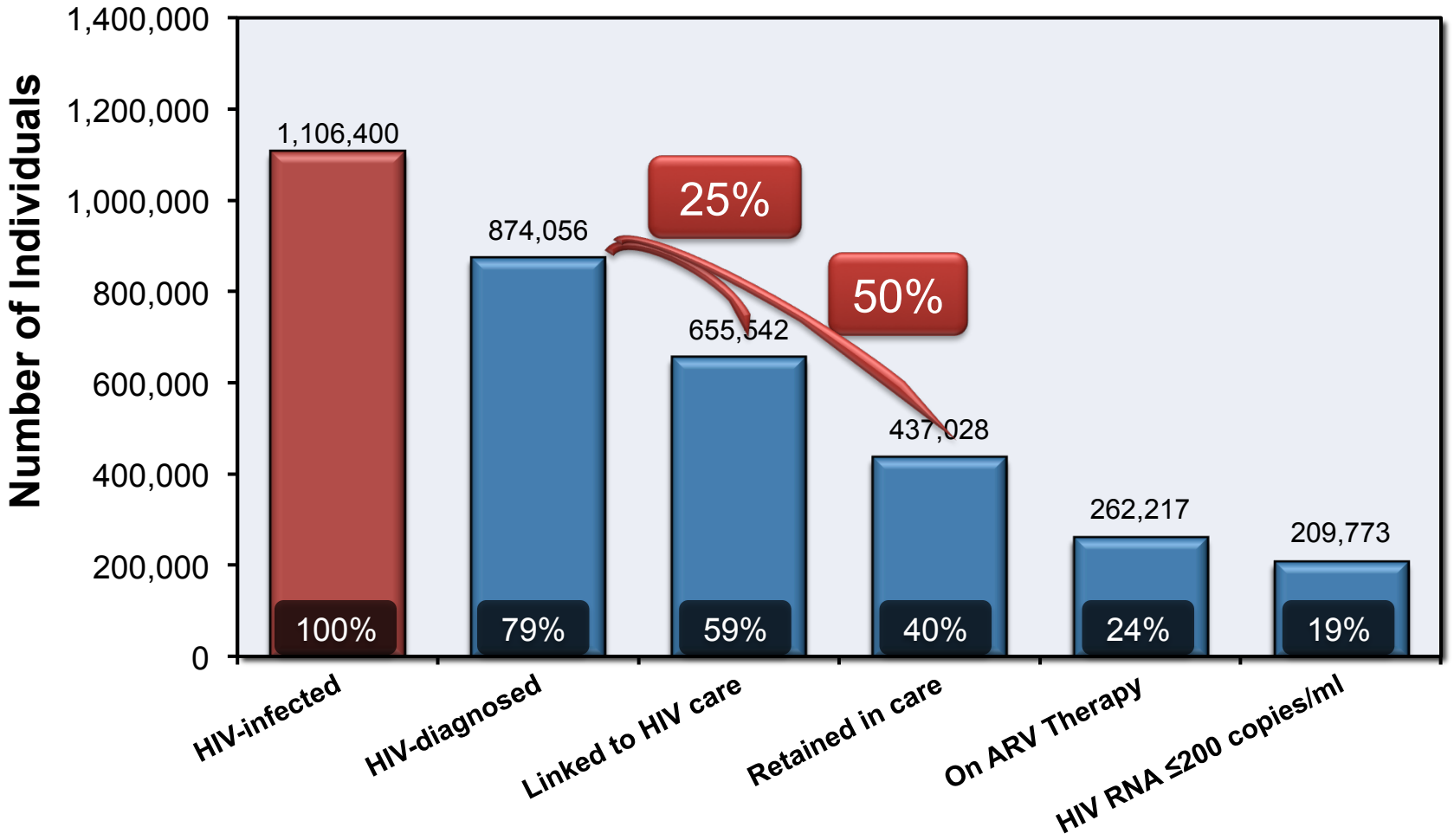
HRSA Continuum of HIV Care

Continuum Engagement in Care



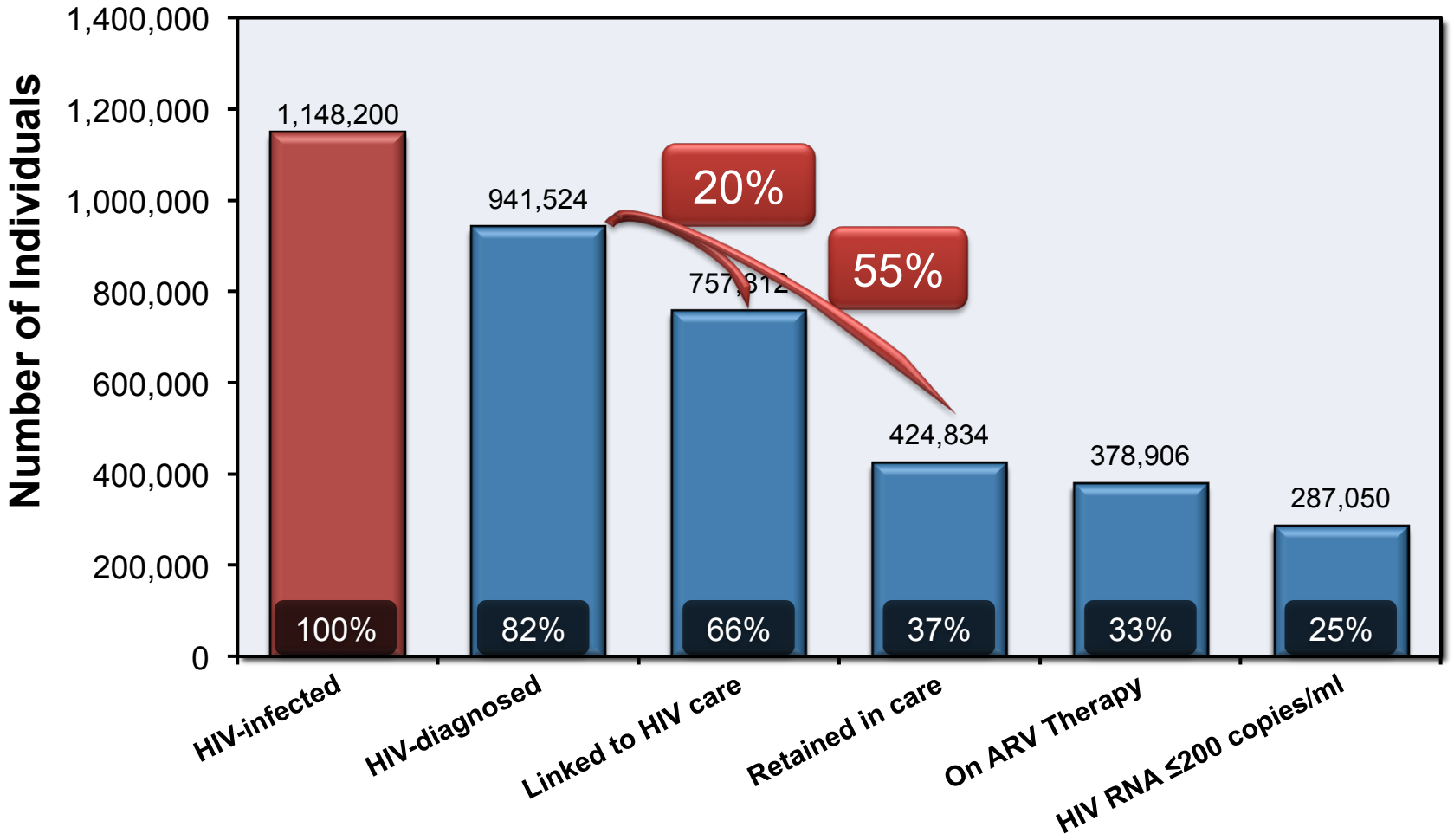
Source: Adapted from Cheever LW. Clin Infect Dis. 2007;44:1493-9.

HIV-Infected Persons Engaged in Selected Stages of the Continuum of HIV Care in United States



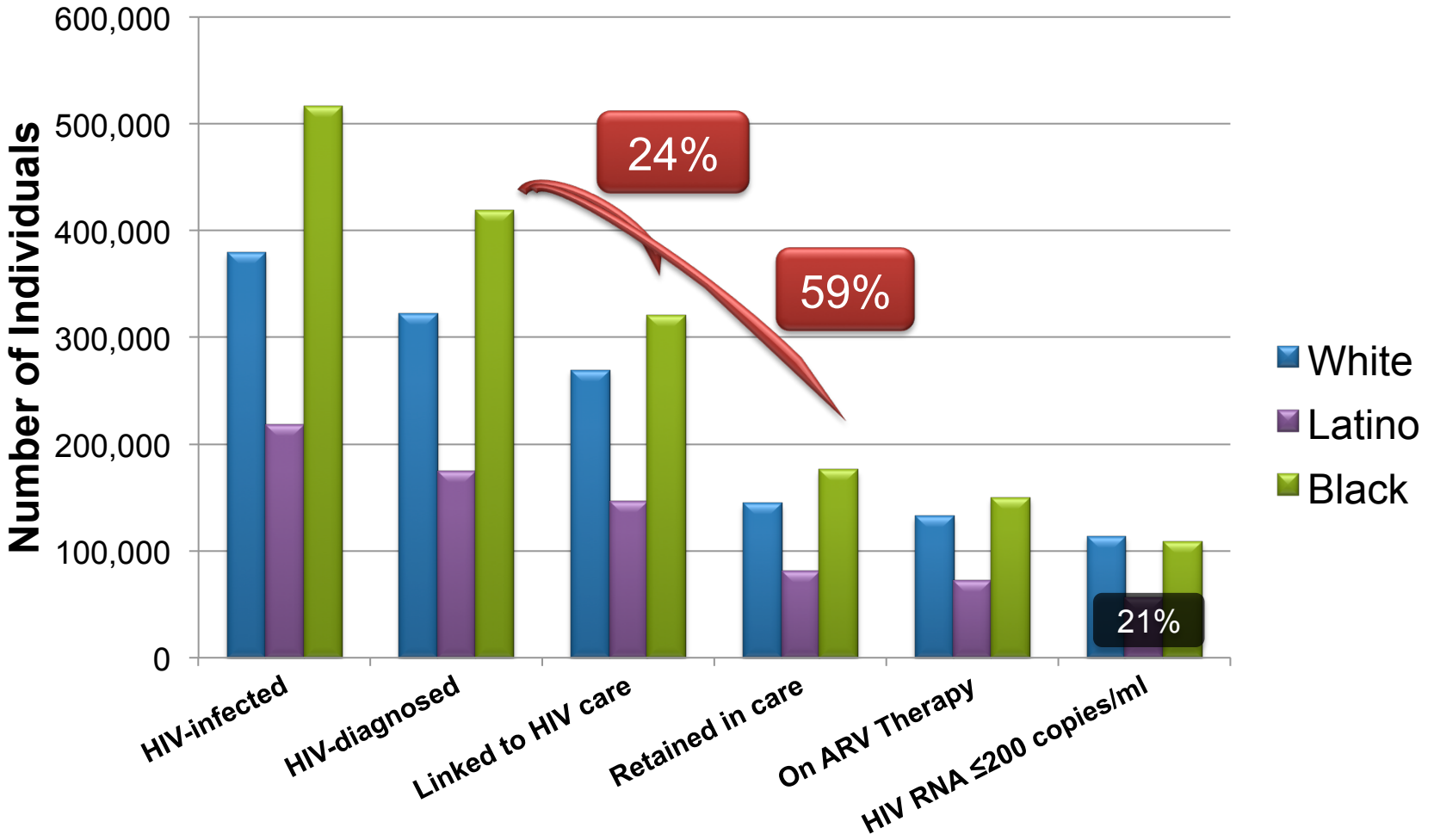
Source: Gardner EM et al Clinical Infectious Disease 2011;52(6):793-800

Updated HIV Care Cascade in United States



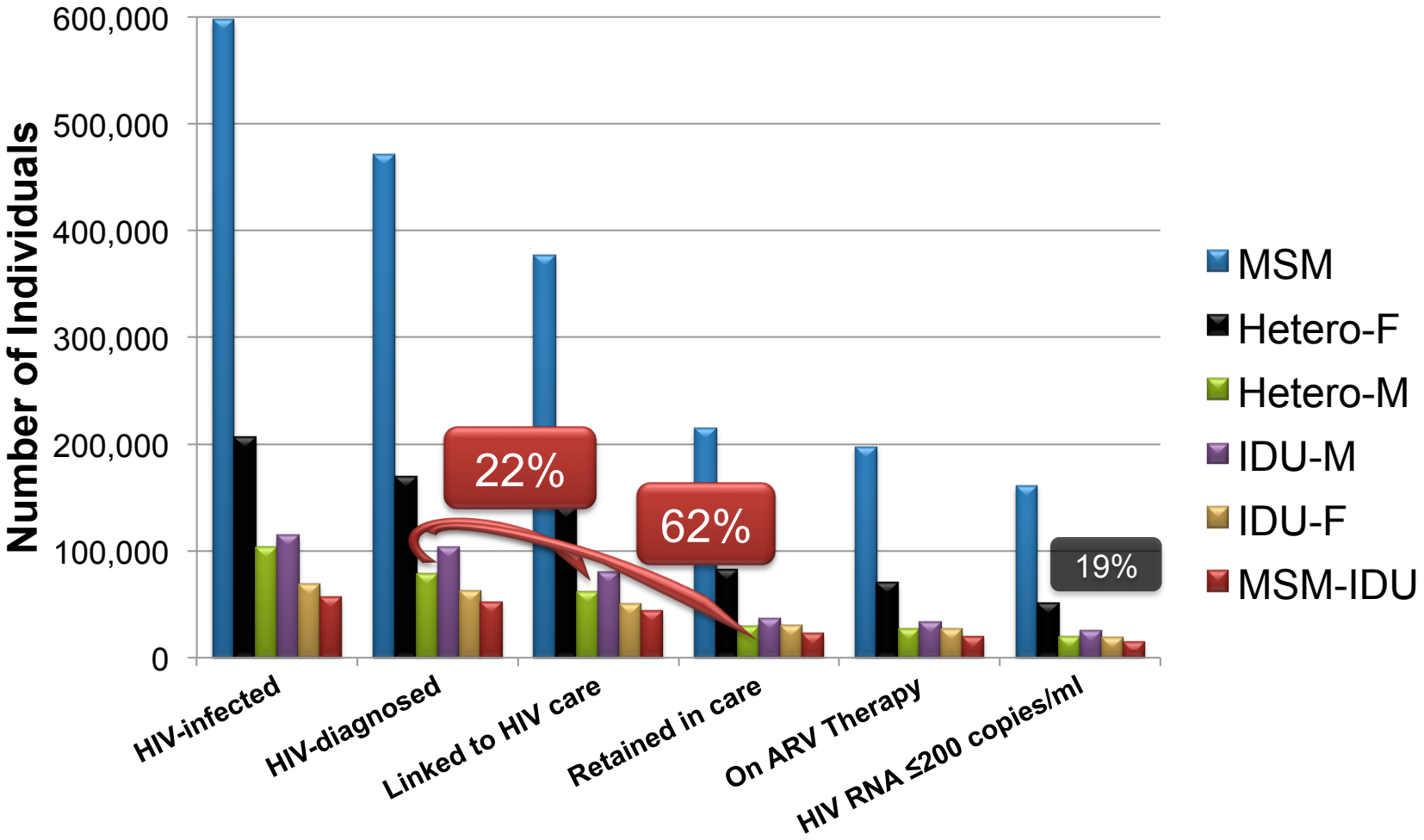
Source: Hall HI, et al XIX IAC; July 22-27, Washington DC. Abs FRLBX05

HIV Care Cascade - Breakdown by Race: Black



Source: Hall HI, et al XIX IAC; July 22-27, Washington DC. Abs FRLBX05

HIV Care Cascade - Breakdown by Risk Factor: Heterosexual Males



Source: Hall HI, et al XIX IAC; July 22-27, Washington DC. Abs FRLBX05

HIV Epidemiology - Summary

- Despite discussions of ‘cure’ research and ‘treatment as prevention’ Global HIV epidemic still massive & requires continued $, energy, human resources
- Increasing recognition of ‘Leaky Cascade’ of HIV care in the United States with racial, age, risk factor disparities
  - Lowest rates of linkage to care and viral suppression in Blacks, Heterosexual Men, and Injection Drug Users
- Overall, roughly 20-25% of individuals with HIV have a fully suppressed viral load

Anti-Retroviral Therapy

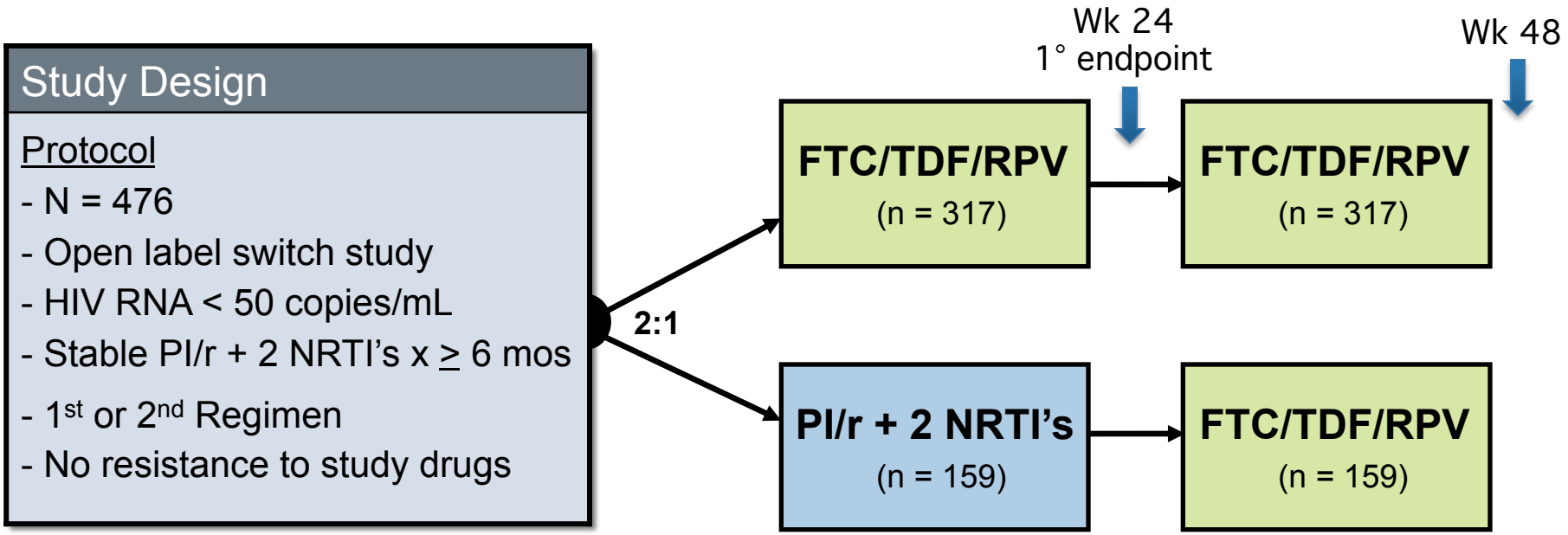
- New Agents: Rilpivirine, Dolutegravir, Cobicistat

Investigational

Switch to FTC/TDF/RPV from PI/r + 2 NRTI's
SPIRIT Study

Investigational

Switch to FTC/TDF/RPV from ritonavir-boosted PI Regimen
SPIRIT Study

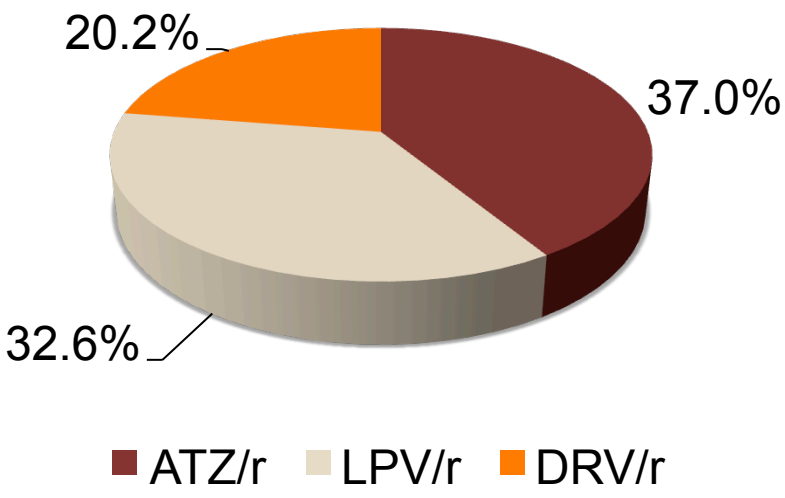


- **1° Endpoint:** Non-inferiority (12% margin) of FTC/TDF/RPV to continuation of PI/r + 2 NRTI's by FDA snapshot analysis (HIV RNA < 50 copies at 24 weeks)
- **2° Endpoints:** Lipids, safety/tolerability, change in CD4 counts

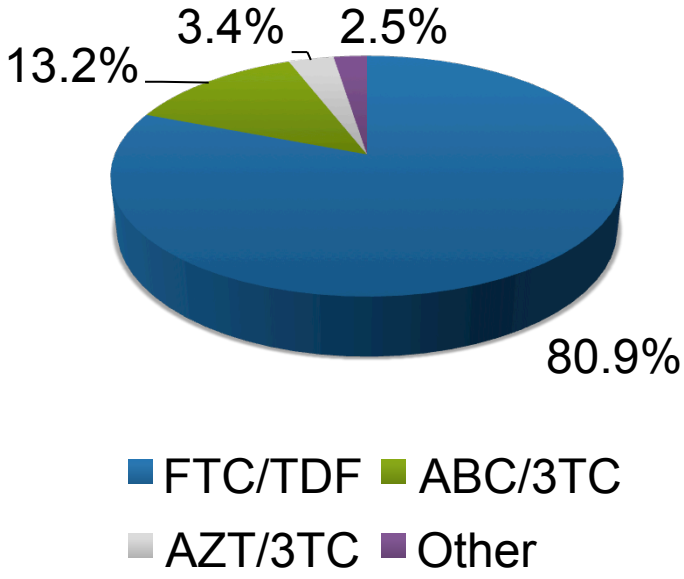
Palella F et al XIX IAC; July 22-27; Washington DC, Abs TUAB0104

Switch to FTC/TDF/RPV from ritonavir-boosted PI Regimen
SPIRIT Study

Baseline PI Regimen



Baseline NRTI Regimen

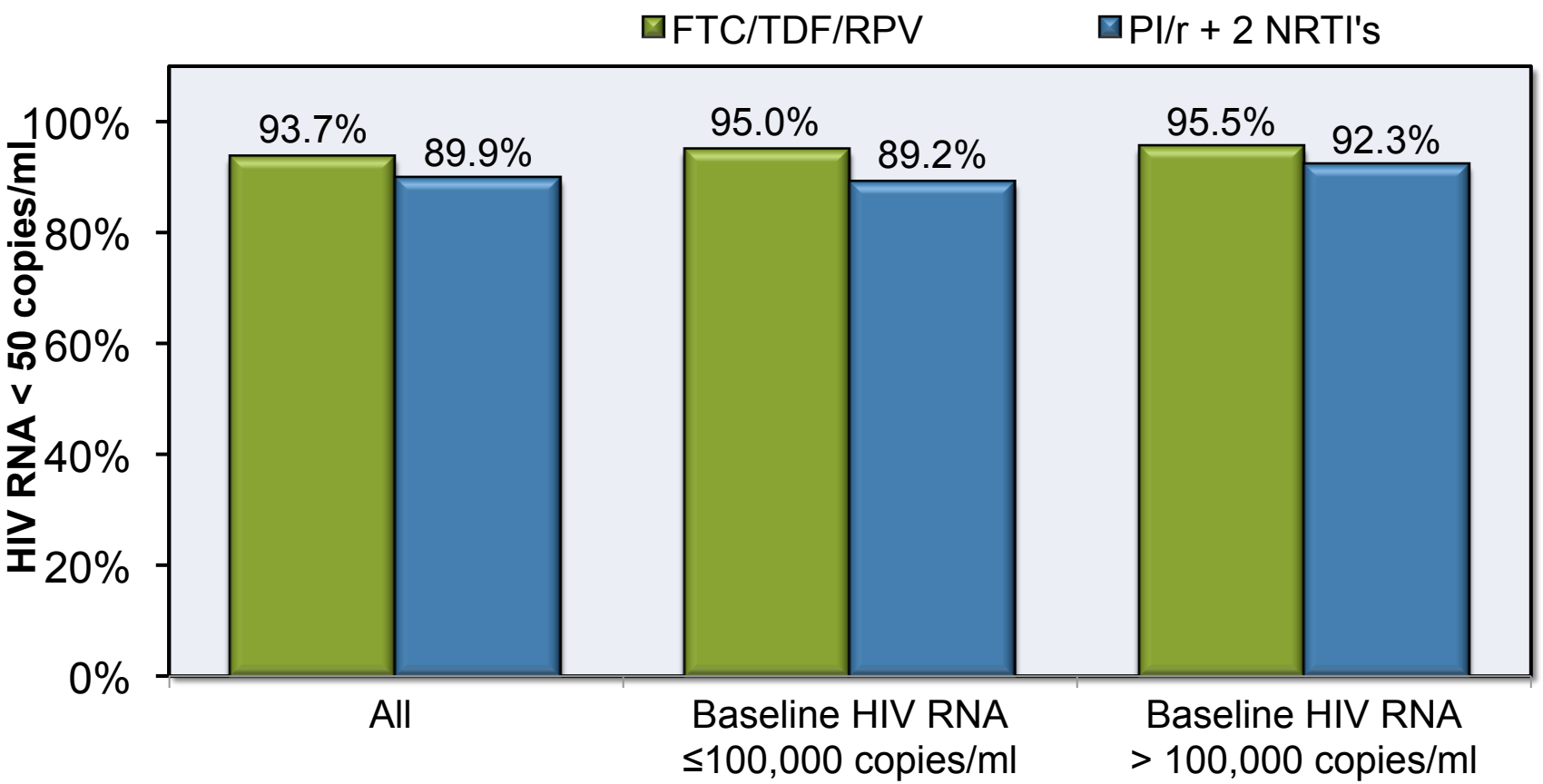


- **Baseline characteristics comparable between study arms** (Median age 42, 86-91% male, 75% white, 2.6-2.9 years since starting ART, Median CD4 576-600)

Investigational

SPIRIT Study – Main results

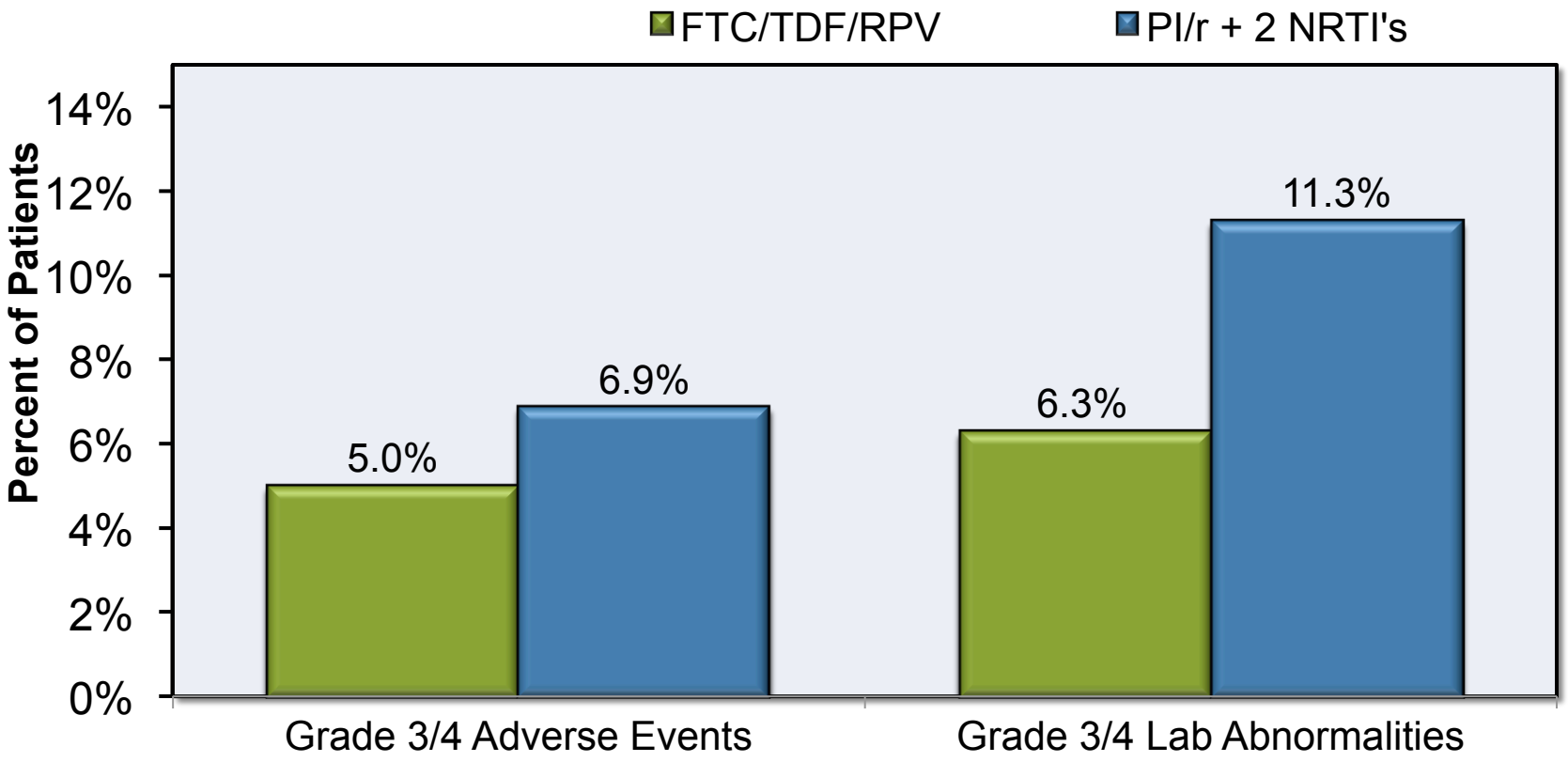
Week 24: Virologic Suppression (FDA Snapshot analysis)



Palella F et al XIX IAC; July 22-27; Washington DC, Abs TUAB0104

Investigational

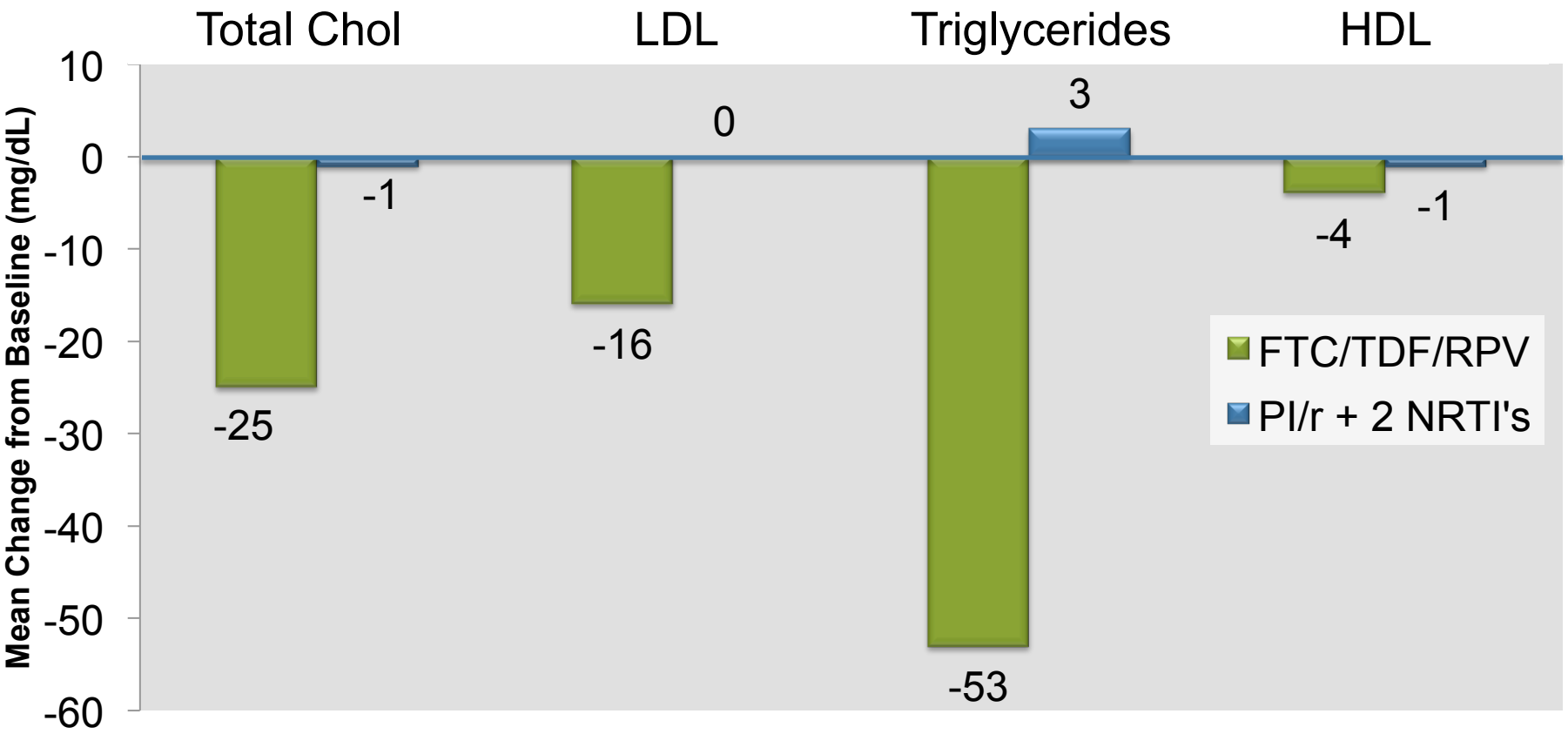
SPIRIT Study – Safety results



- Lower incidence of adverse events and lab abnormalities in FTC/TDF/RPV group
- CrCl slightly lower in FTC/TDF/RPV group (105.4 mL/min vs 108.9 mL/min)

Investigational

SPIRIT Study – Lipids



- Switch to FTC/TDF/RPV significantly improved 10-year Framingham risk score vs. continuation of PI/r + 2 NRTI's

Palella F et al XIX IAC; July 22-27; Washington DC, Abs TUAB0104

Investigational

Dolutegravir vs. Raltegravir
SPRING-2 Study

Investigational

Dolutegravir vs. Raltegravir
SPRING-2 Study: Design

Study Design

Protocol
- N = 822
- Phase 3, multi-center, Randomized, Double-blind, double-dummy trial
- Antiretroviral naïve
- HIV RNA ≥ 1,000 copies/ml
- No evidence of viral resistance
- Stratified by VL and backbone NRTI

1:1

***DTG + RAL(p) BID + 2 NRTI's** (n = 411)

Wk 48 1° endpoint

***DTG + RAL(p) BID + 2 NRTI's** (n = 411)

Wk 96

^DTG(p) + RAL BID + 2 NRTI's (n = 411)

- **1° Endpoint:** Non-inferiority (10% margin) of DTG to RAL by FDA snapshot analysis (HIV RNA < 50 copies at 48 weeks)
- **2° Endpoints:** virologic failure at 24 weeks, safety, tolerability, resistance data on virologic failures

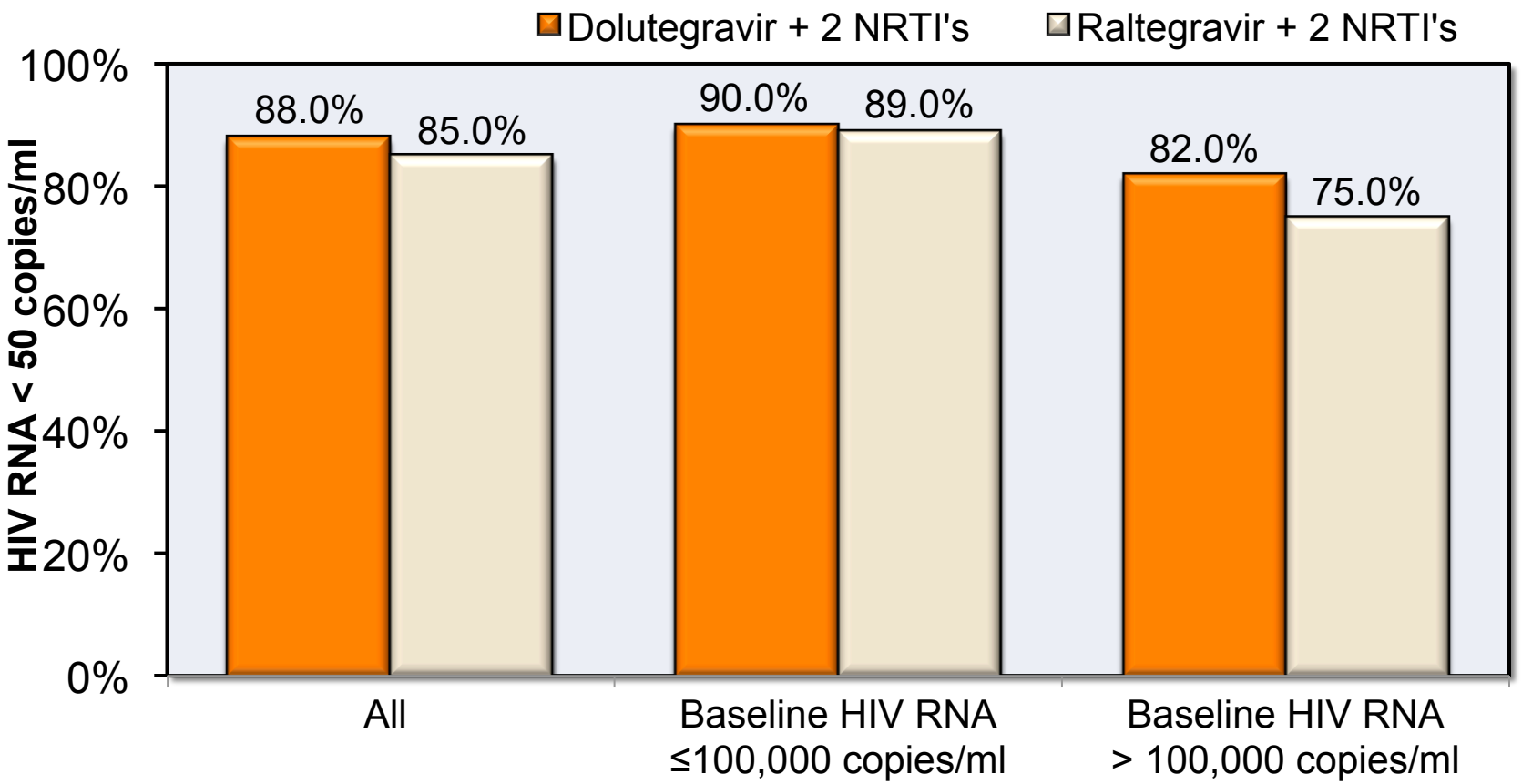
*Dolutegravir (50 mg QD); NRTI's = ABC/3TC or FTC/TDF

^Raltegravir (400 mg BID); NRTI's = ABC/3TC or FTC/TDF

Investigational

Dolutegravir vs. Raltegravir
SPRING-2: Results

Week 48: VL < 50 copies/mL (FDA Snapshot Analysis)

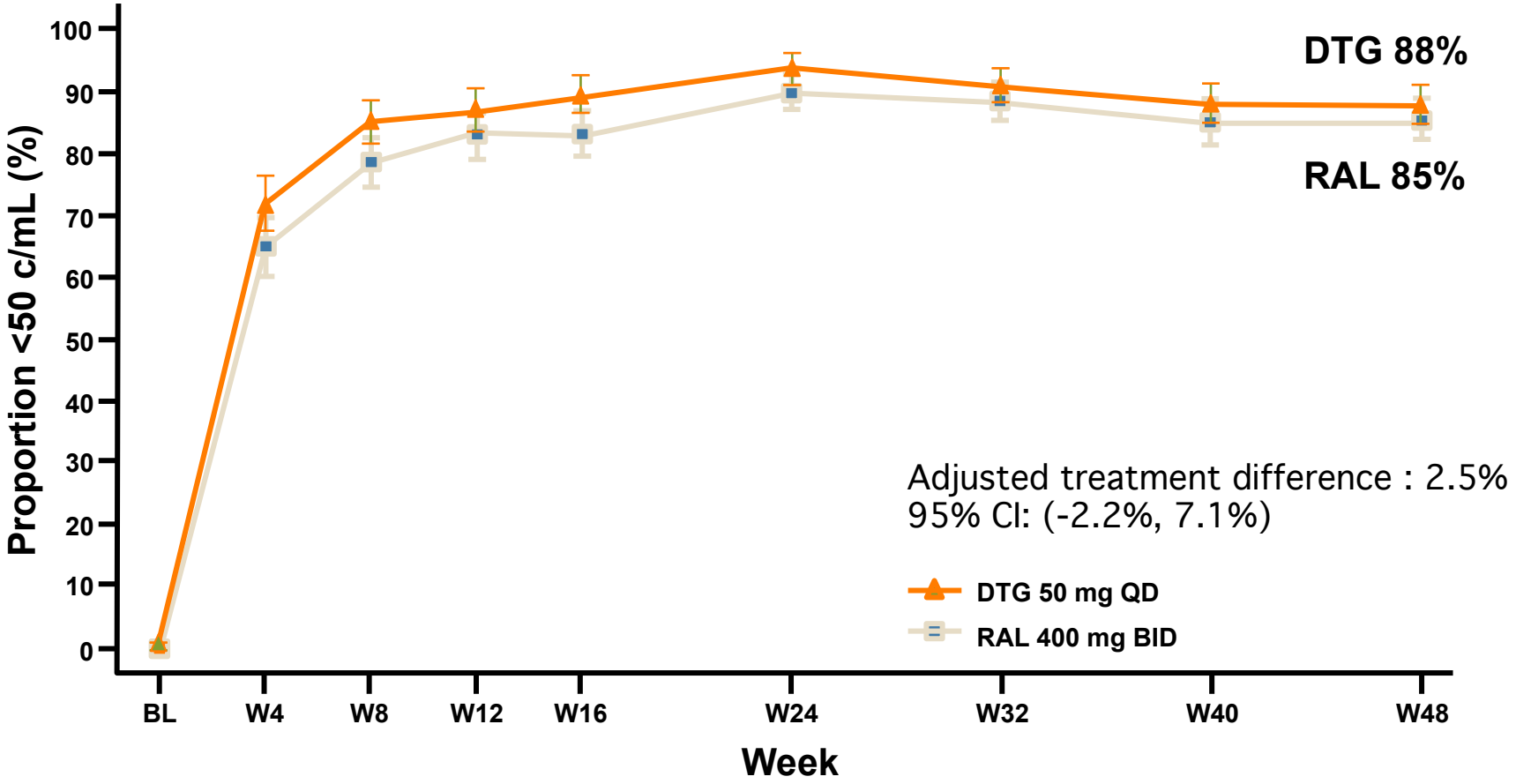


- Adjusted Treatment Difference = 2.5% (95% CI -2.2% to 7.1%)

Raffi F et al XIX IAC; July 22-27; Washington DC, Abs THLBB04

Investigational

Dolutegravir vs. Raltegravir
SPRING-2: Results

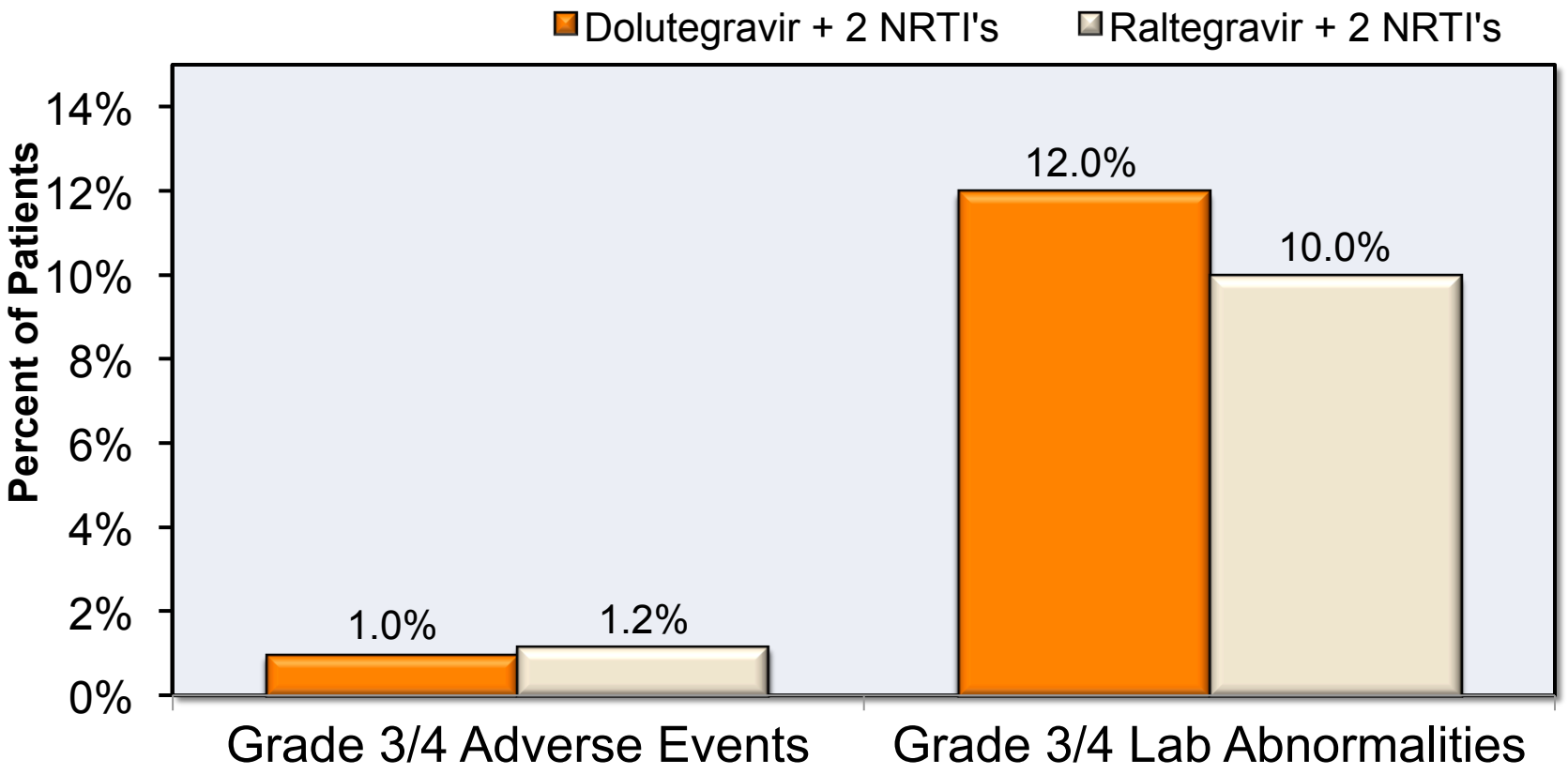


- No evidence of Integrase or NRTI resistance in DTG arm
- In RAL arm, 1 patient with Integrase and 4 with NRTI resistance
- Median CD4 increase 230 cells/mm^3 in both groups

Raffi F, et al. 19th IAC; Washington, DC; July 22-27, 2012; Abst. THLBB04.

Investigational

Dolutegravir vs. Raltegravir
SPRING-2: Results



- Low adverse event rate for both arms
- Minimal effect on T Chol (DTG = +3.9 mg/dL, RAL = +7.7 mg/dL)
- CrCl slightly lower in DTG group (-15.5 mL/min vs -5.4 mL/min)

Palella F et al XIX IAC; July 22-27; Washington DC, Abs TUAB0104

Investigational

Cobicistat vs. Ritonavir:
Study 114

Investigational

Cobicistat vs. Ritonavir (with Atazanavir + FTC/TDF) Study 114: Design

Study Design

Protocol

- N = 700
- Double-blind, double-dummy, randomized, controlled phase 3 trial
- Antiretroviral naive
- No baseline NRTI, NNRTI, or PI mutations
- HIV RNA ≥ 5,000 copies/ml
- eGFR ≥ 70 mL/min
- Stratified by VL > or < 100,000 c/mL

Wk 48
1° endpoint

***ATZ + COBI + FTC/TDF + RTV(p)**
(n = 350)

^ATZ + RTV + FTC/TDF + COBI (p)
(n = 350)

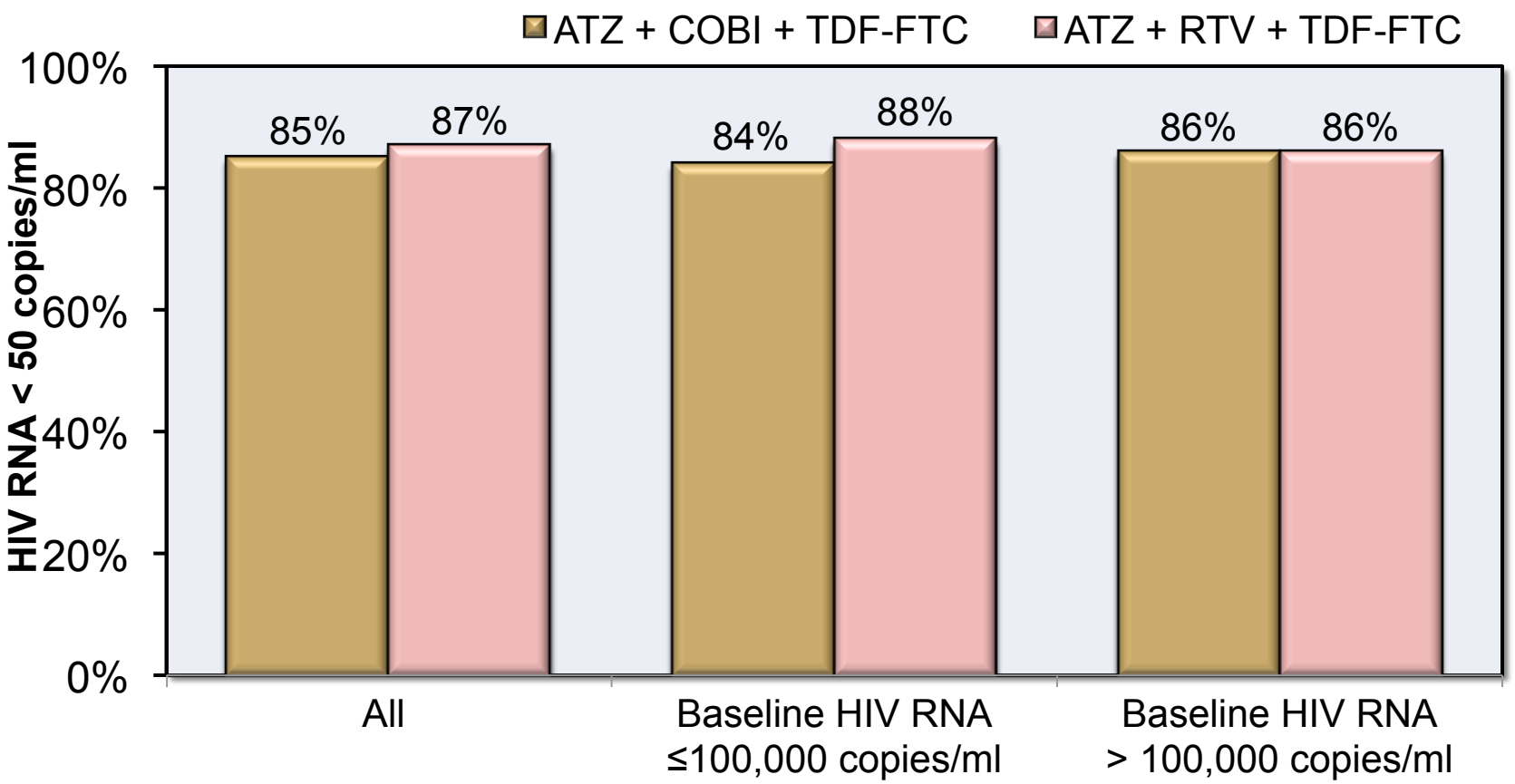
- **1° Endpoint:** Non-inferiority (12% margin) of COBI to RTV by FDA snapshot analysis (HIV RNA < 50 copies at 48 weeks)
- **2° Endpoints:** Safety, Tolerability, Pharmacokinetics

Investigational

Cobicistat vs. Ritonavir (with Atazanavir + FTC/TDF)

Study 114: Design

Week 48: Virologic Success (VL < 50 FDA Snapshot)



- Cobicistat non-inferior to Ritonavir at 48 weeks

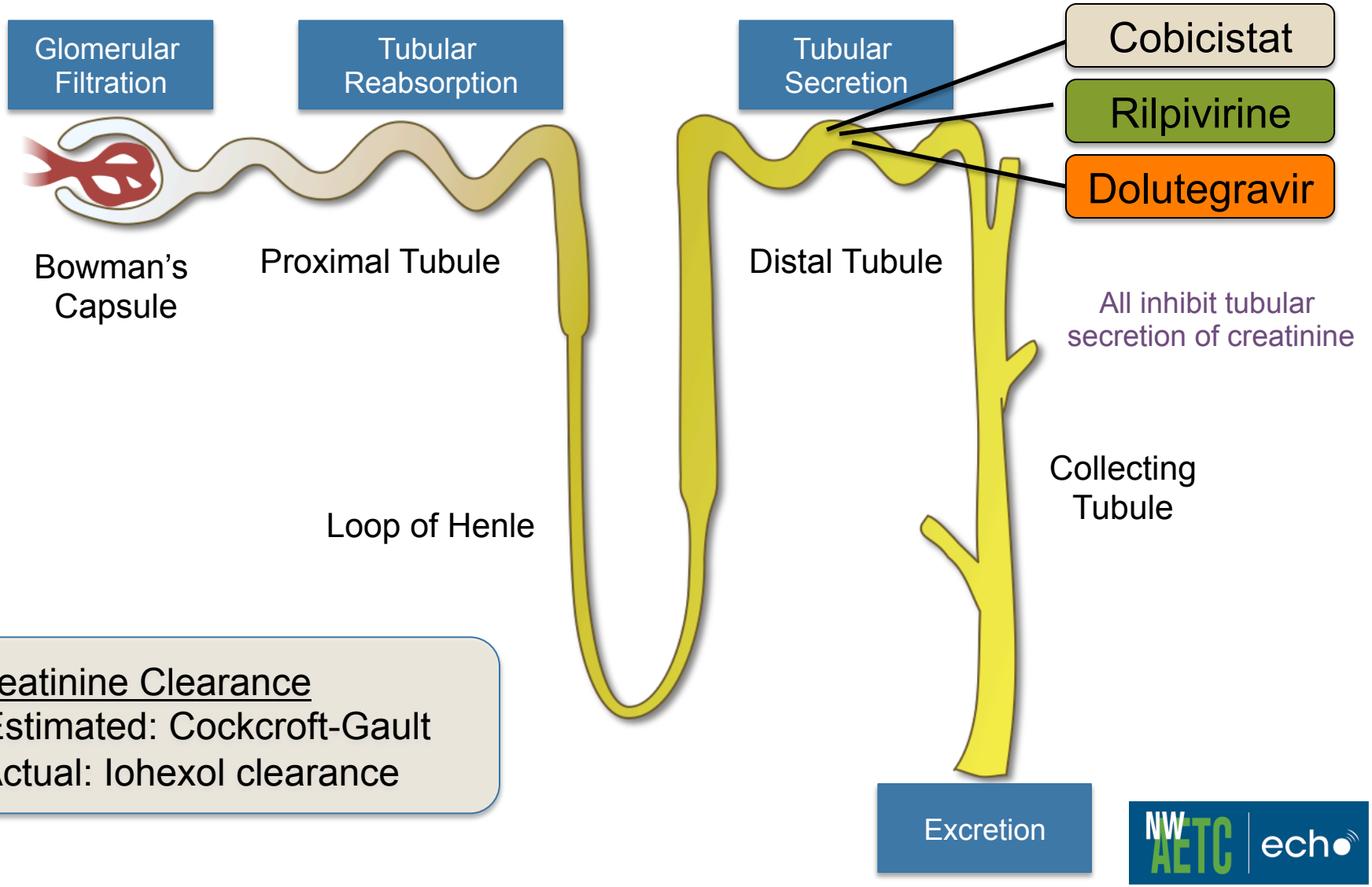
Gallant J et al XIX IAC; July 22-27; Washington DC, Abs TUAB0103

Cobicistat vs. Ritonavir (with Atazanavir + FTC/TDF)
Study 114: Adverse Events & Discontinuation

AE's ≥ 10% subjects in either group	ATZ + COBI (n = 344)	ATZ + RTV (n = 348)
Bilirubin-related	41%	36%
Nausea	18%	16%
Diarrhea	15%	20%
Headache	11%	16%
Nasopharyngitis	11%	15%
Upper Respiratory Infection	10%	8%
Discontinuation due to AE (n)	**7.3% (25)**	**7.2% (25)**
• Bilirubin-related	3.5% (12)	3.2% (11)
• Renal Abnormalities	1.7% (6)	1.4% (5)
• Rash	0.3% (1)	0.6% (2)
• Allergic Dermatitis	0.6% (2)	0

Gallant J et al XIX IAC; July 22-27; Washington DC, Abs TUAB0103

Effect of new ARV's on Creatinine Clearance



Creatinine Clearance
- Estimated: Cockcroft-Gault
- Actual: Iohexol clearance

New Anti-retroviral Agents - Summary

- FTC/TDF/RPV (Complera) FDA approved for treatment naïve patients, and emerging data in context of switch from FTC/TDF/EFV and PI/r + 2 NRTI's
  - At 24 weeks, VL >100,000 and prior K103N don't seem to affect
- Dolutegravir is a novel QD unboosted Integrase-inhibitor that appears to be well-tolerated and non-inferior to Raltegravir
- Cobicistat, a novel pharmacologic enhancer (selective CYP3A4 inhibitor) appears to be non-inferior to Ritonavir when used with Atazanavir and FTC/TDF

Questions?