Continuing Medical Education Internet Symposium

The 6th IAS Conference on Pathogenesis, Treatment and Prevention: ARV Therapies and Therapeutic Strategies

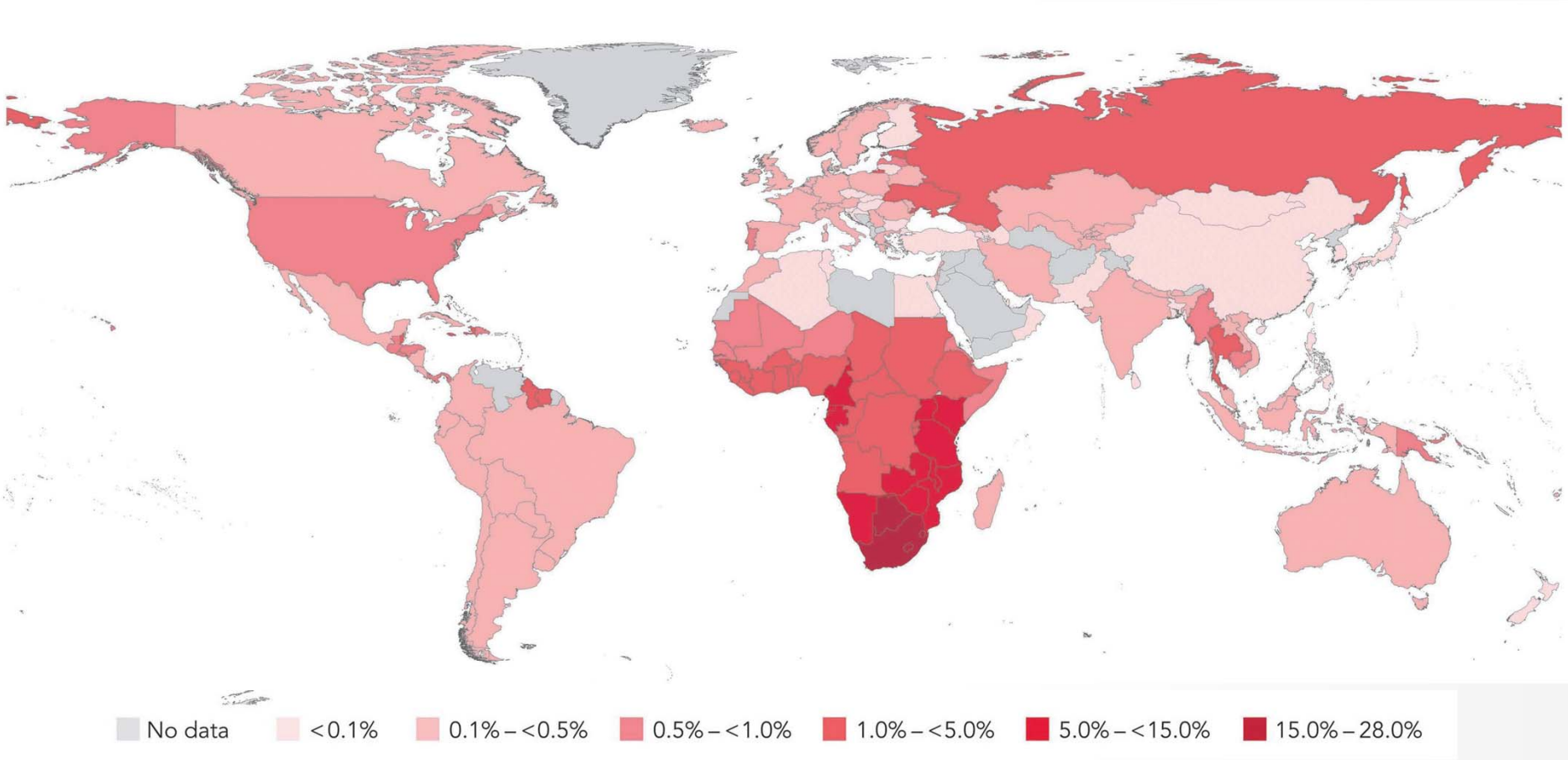
Jointly sponsored by the Postgraduate Institute for Medicine and ViralEd, LLC

Epidemiology and Prevention

David Cooper, MD
Director and Professor,
Kirby Institute
University of New South Wales Sydney Australia
Sydney, Australia

Jointly sponsored by the Postgraduate Institute for Medicine and ViralEd, LLC Supported by an educational grant from Merck & Co., Inc.

2010: A Global View of HIV Infection



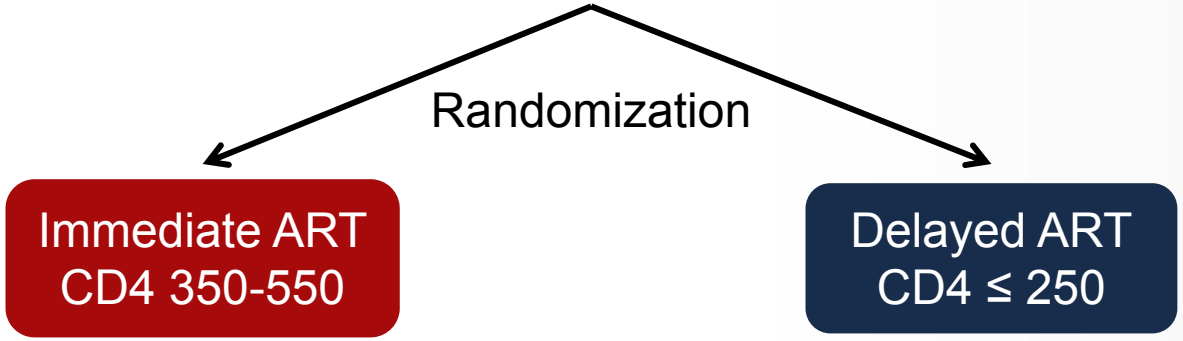
- *>33 million HIV-infected worldwide*
- *~6.5 million currently on ARV therapy*

Rome Statement for an HIV Cure: Objectives

- Recognizing the importance of developing a safe, accessible and scalable HIV cure as a therapeutic and preventive strategy against HIV infection and to help control the AIDS epidemic
- Committing to stimulating international and multidisciplinary research collaborations in the field of HIV cure research
- Encouraging other stakeholders, international leaders and organizations to contribute to accelerating HIV cure research through their own initiatives and/or by endorsing this statement and supporting the alliance that the Advisory Board is building

HPTN 052 Study Design

- 1,736 serodiscordant, sexually active, heterosexual couples randomized
- HIV-positive partner CD4 cell count between 350 and 550 cells/mm3



Primary Transmission Endpoint
Virologically-linked transmission events

Primary Clinical Endpoint
WHO stage 4 clinical events, pulmonary tuberculosis, severe bacteria infection and/or death

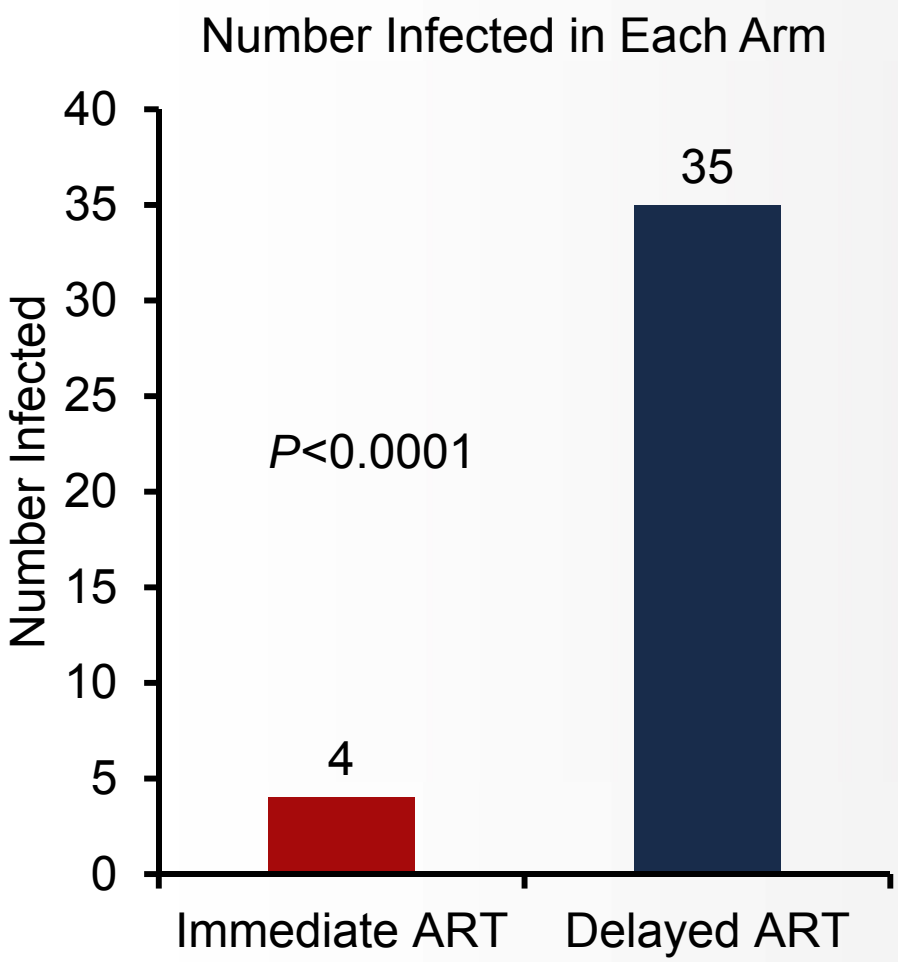
Countries: Botswana, Brazil, India, Kenya, Malawi, South Africa and Zimbabwe

HPTN 052: Baseline Characteristics

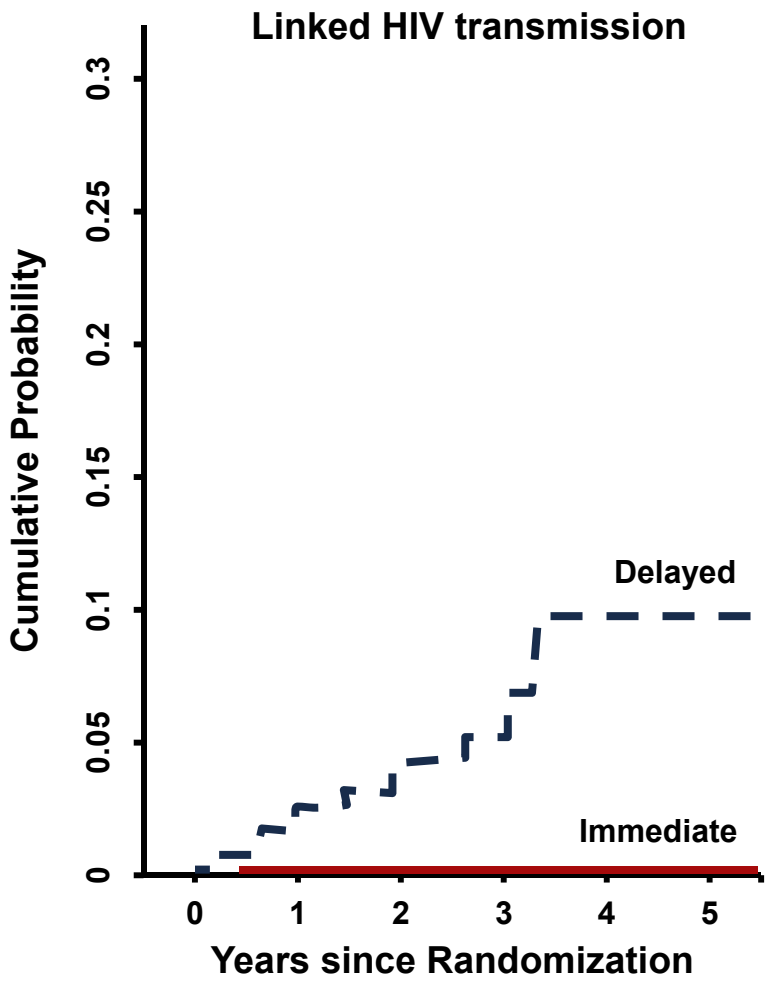
	Index		Partner	
	Immediate N = 886	Delayed N = 877	Immediate N = 893	Delayed N = 882
Female	49%	50%	49%	47%
Age (median)	33	32	32	32
Married	94%	95%	93%	94%
Any unprotected sex	6%	8%	8%	8%
CD4 (median [IQR])	442 [373-522]	428 [357-522]	---	---
HIV RNA $\log_{10}$ (median [IQR])	4.4 [3.8-4.9]	4.4 [3.9-4.9]	---	---

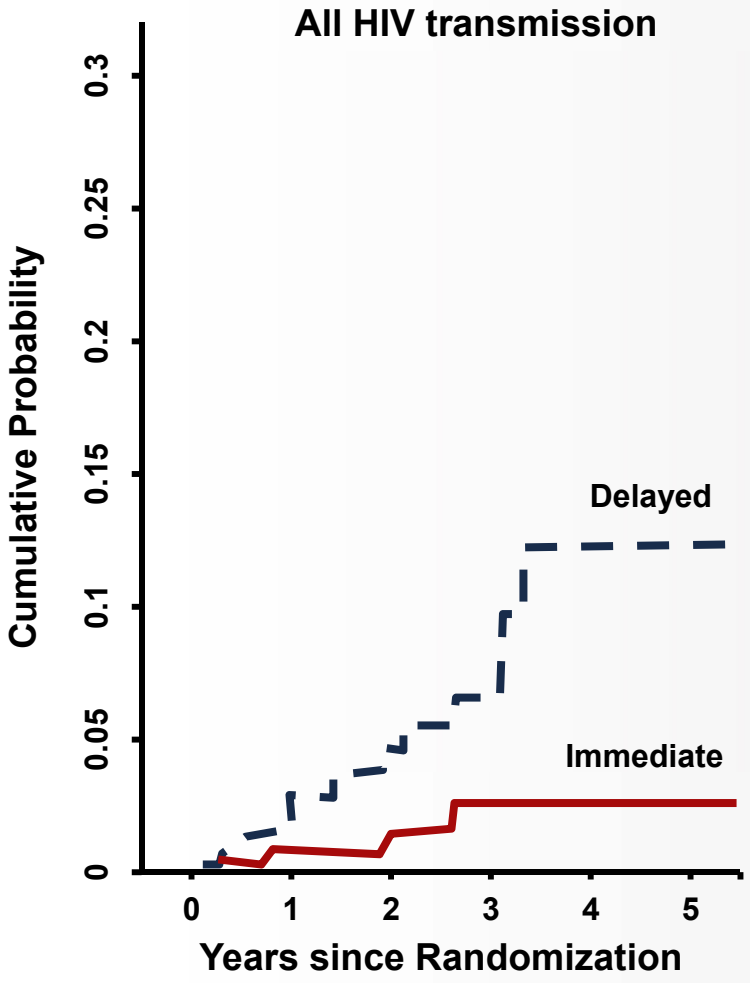
HPTN 052: Halted Early

- Study halted significantly more infections in delayed ART arm
- 96% reduction in the risk of transmission with immediate ART (*P*<0.0001)
- 27/28 infections genetically linked to HIV-positive partner occurred in Delayed Arm



HPTN 052: HIV Transmission Patterns





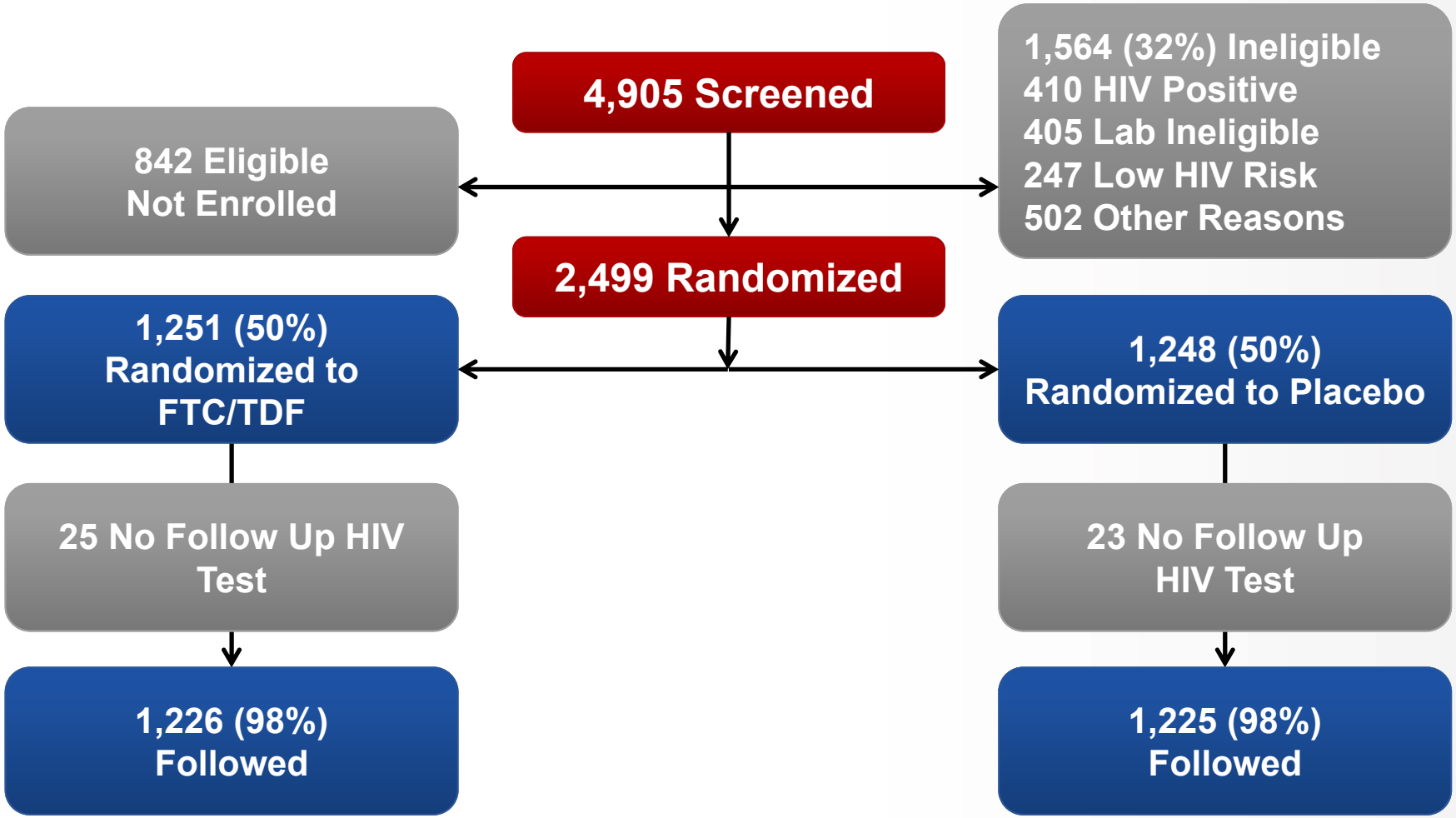
HPTN 052:
Sexual Behaviors at Baseline and Follow-up

		Immediate (N=886)		Delayed (N=876)	
		Enrollment	Follow-up	Enrollment	Follow-up
Index pregnancy		63	47	59	79
STDs*	Index	1% - 5%	0% - 3%	1% - 5%	0% - 3%
	Partner	1% - 3%	0% - 2%	1% - 2%	0% - 4%
Sexual activity**	Index	72%	62% - 74%	74%	53% - 70%
	Partner	72%	67% - 81%	73%	62% - 76%
Condom use**	Index	94%	92% - 97%	92%	92% - 100%
	Partner	92%	90% - 100%	92%	92% - 100%

*STDs include hepatitis B, syphilis, gonorrhea, and C. trachomatis
**Self-reported data

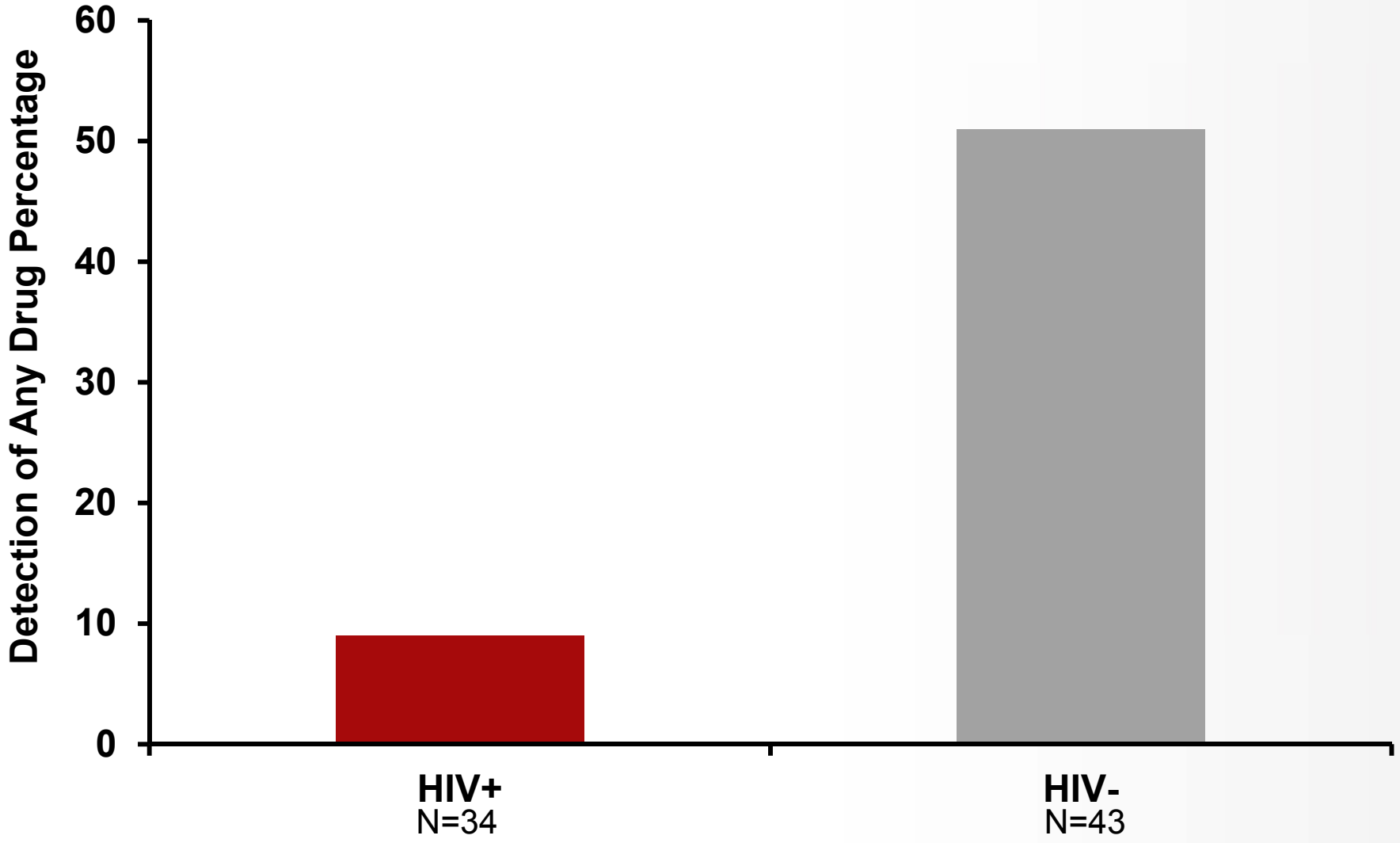
Cohen MS, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. MOAX0102.

iPrEx: Study of TDF/FTC PrEP in HIV-negative men or transgender women who have sex with men



Grant R, et al. N Engl J Med 2010;30:2587-99.

Drug Detection by HIV Status in the FTC/TDF Group



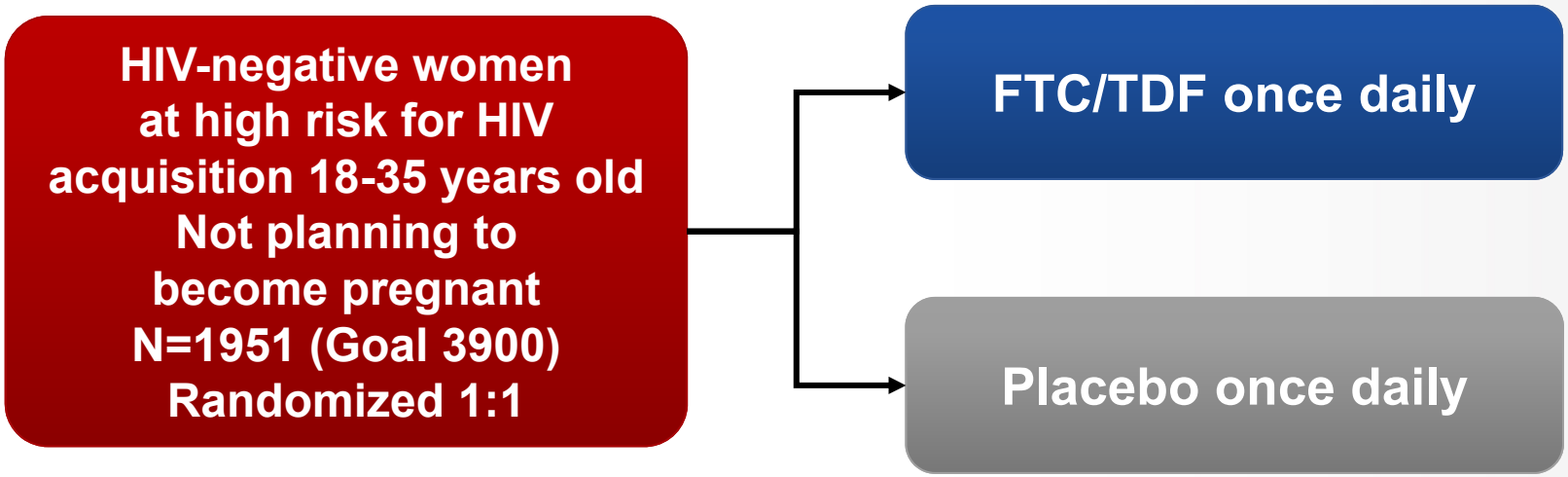
Grant R, et al. N Engl J Med 2010;30:2587-99.

HIV by Group and Drug Detection

Group	Drug Detection	HIV Infections	Incidence Density
Placebo	No	64	3.86
FTC/TDF	No	33	4.04
	Yes	3	0.35
Relative Rate Reduction		91%	

Grant R, et al. N Engl J Med 2010;30:2587-99.

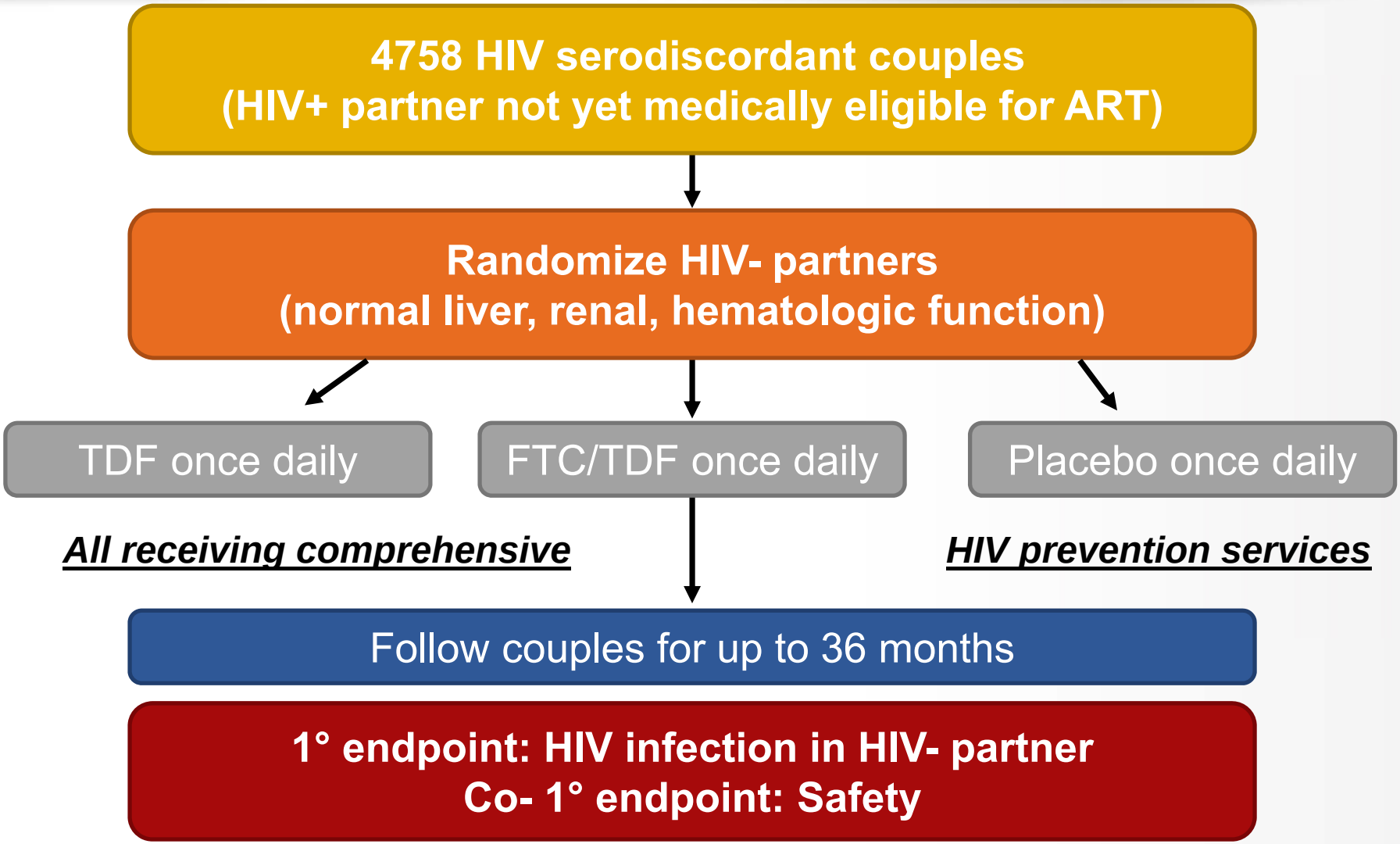
FEM-PrEP



- Study halted Feb 18, 2011
  - Incident HIV infection: ~5% per year
  - N=56 new infections occurred
  - Equal number of infections in the two study arms

FHI statement on the FEM-PrEP. Available at: www.fhi.org/en/AboutFHI/Media/Releases/FEM-PrEP_statement041811.htm. Accessed April 18, 2011.

Partners PrEP Study



Baeten J, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. MOAX0106.

Partners PrEP Study: Study Procedures

HIV- participants

- Monthly HIV & pregnancy testing
- Monthly symptom & 3-monthly laboratory safety monitoring
- Monthly provision of study medication and individualized adherence counseling, including not sharing study drug

HIV+ participants

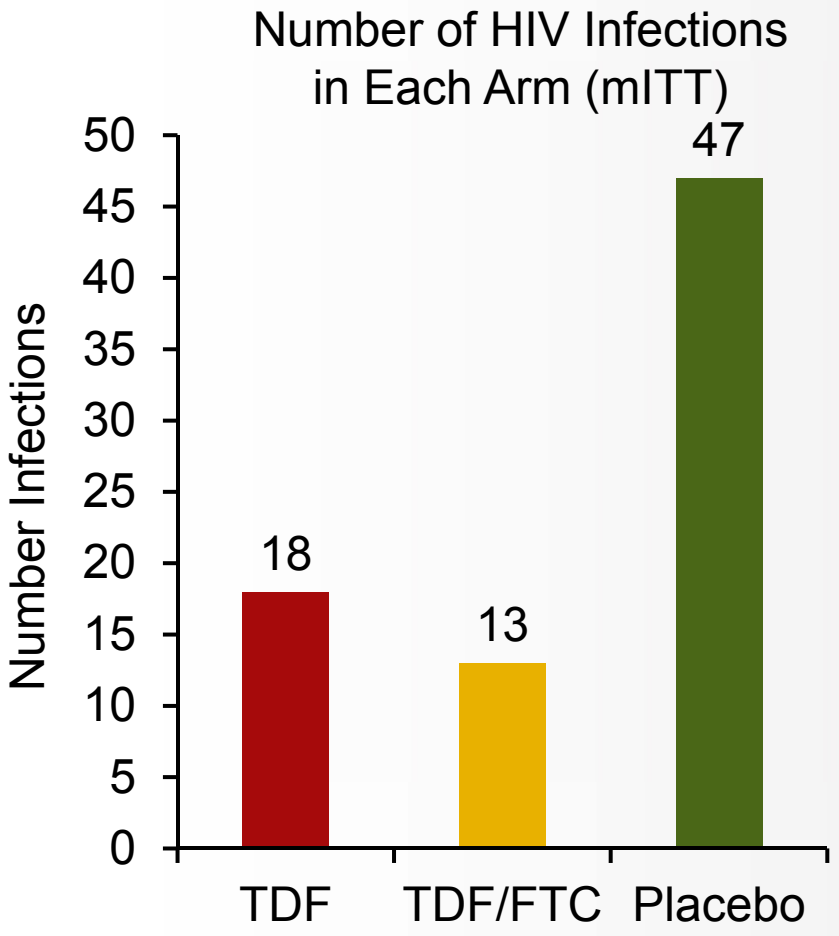
- 3-monthly visits
- 6-monthly CD4 counts
- Ongoing HIV primary care
- Active referral for ART following national guidelines

All participants: comprehensive HIV prevention package

- Risk reduction counseling (individual and couple)
- Free condoms and condom counseling
- Contraception counseling and provision
- Screening and treatment for STIs
- Counseling & referral for other HIV prevention interventions (e.g., male circumcision), per national policies

Partners PrEP Study: Results

- Based on analysis through May 31, 2011, placebo arm discontinued but those receiving study medication continued
- Significantly fewer infections with TDF and TDF/FTC than placebo,
  - TDF: 62% reduction (P=0.0003)
  - TDF/FTC: 73% reduction (*P*<0.0001)
- TDF and TDF/FTC statistically similar (*P*=0.18)



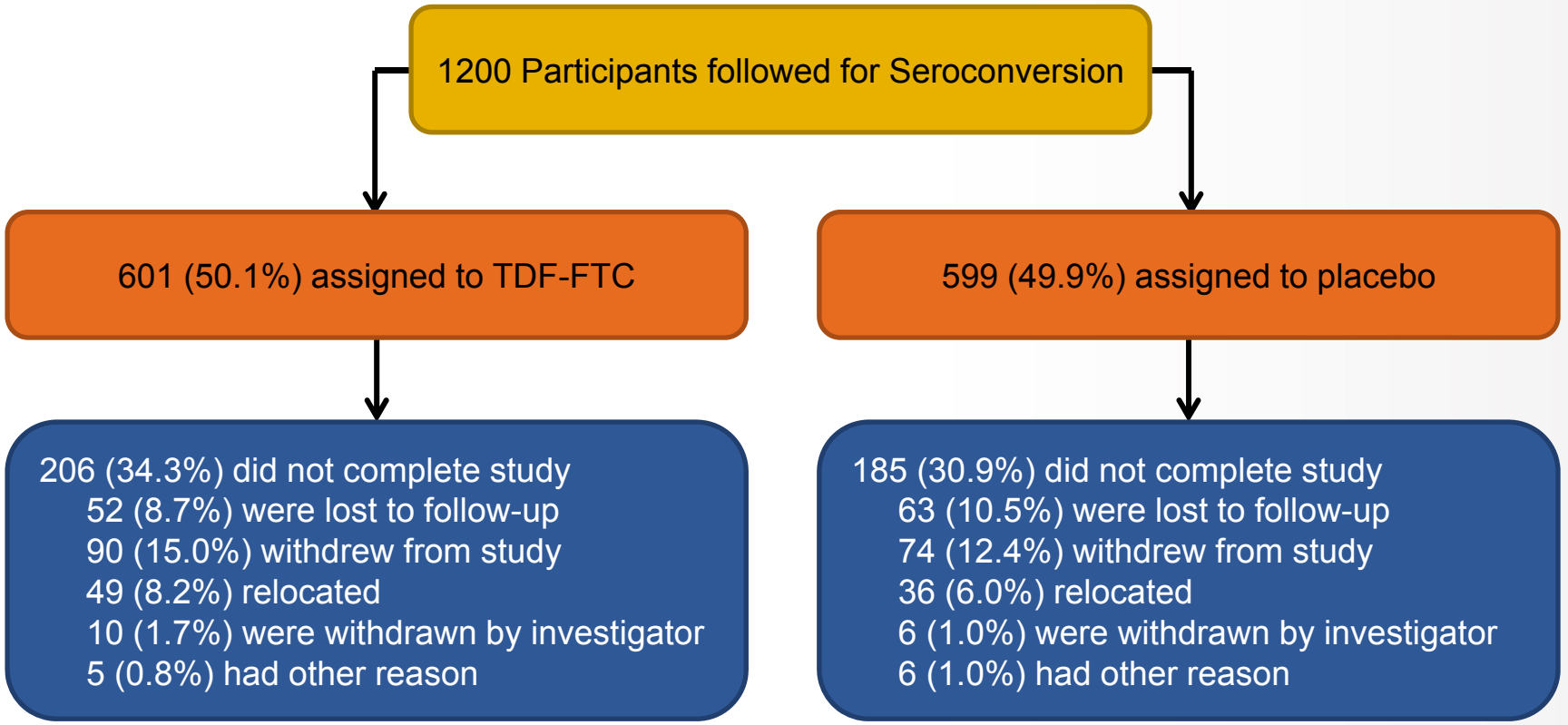
Partners PrEP Study: Summary

- TDF and FTC/TDF PrEP reduced risk of HIV acquisition in African men and women
  - Similar efficacy between TDF & FTC/TDF
- TDF and FTC/TDF PrEP safe and well-tolerated
  - Mild gastrointestinal side effects
- No evidence of change in risk behavior

Baeten J, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. MOAX0106.

TDF2 Study

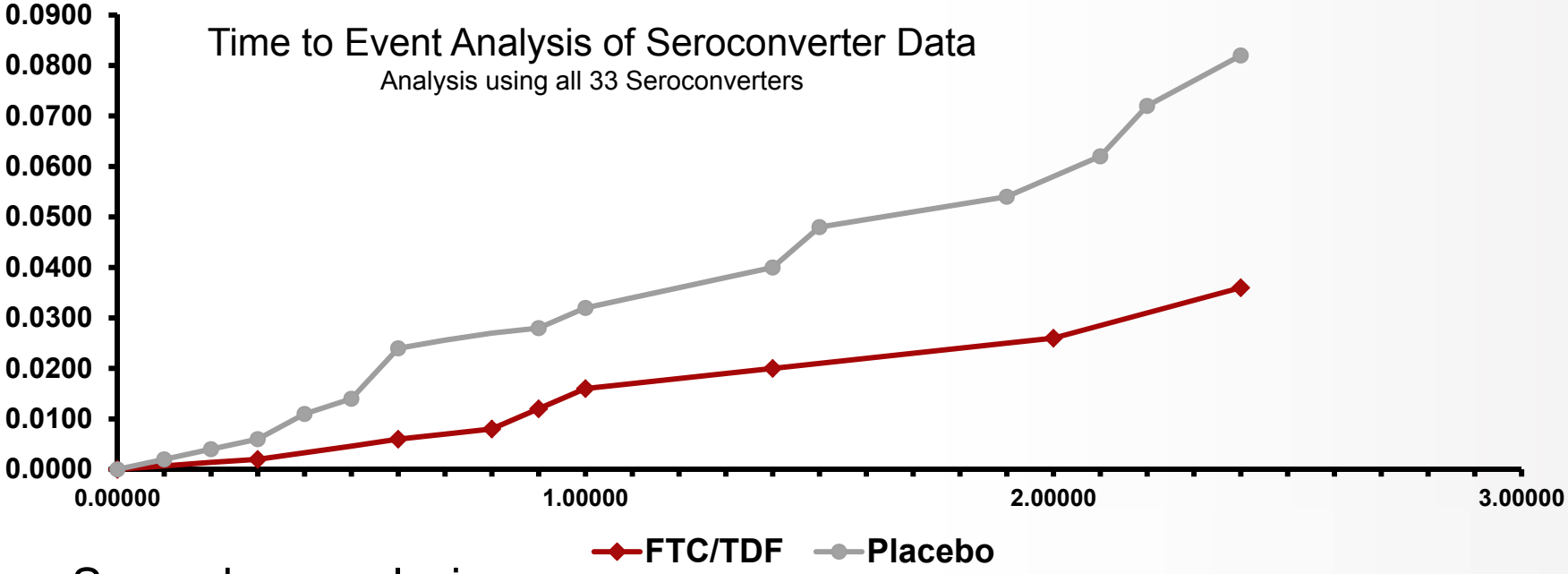
- Double-blind placebo-controlled randomized clinical trial
  - 18-39 years old, HIV-negative, sexually active within past 3 months, healthy



Thigpen MC, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. WELBC01.

TDF2: Results

- Primary analysis:
  - 9/601 treated with TDF/FTC vs. 24/599 placebo became HIV+
  - 63% reduction in infections with TDF/FTC (p=0.0133)



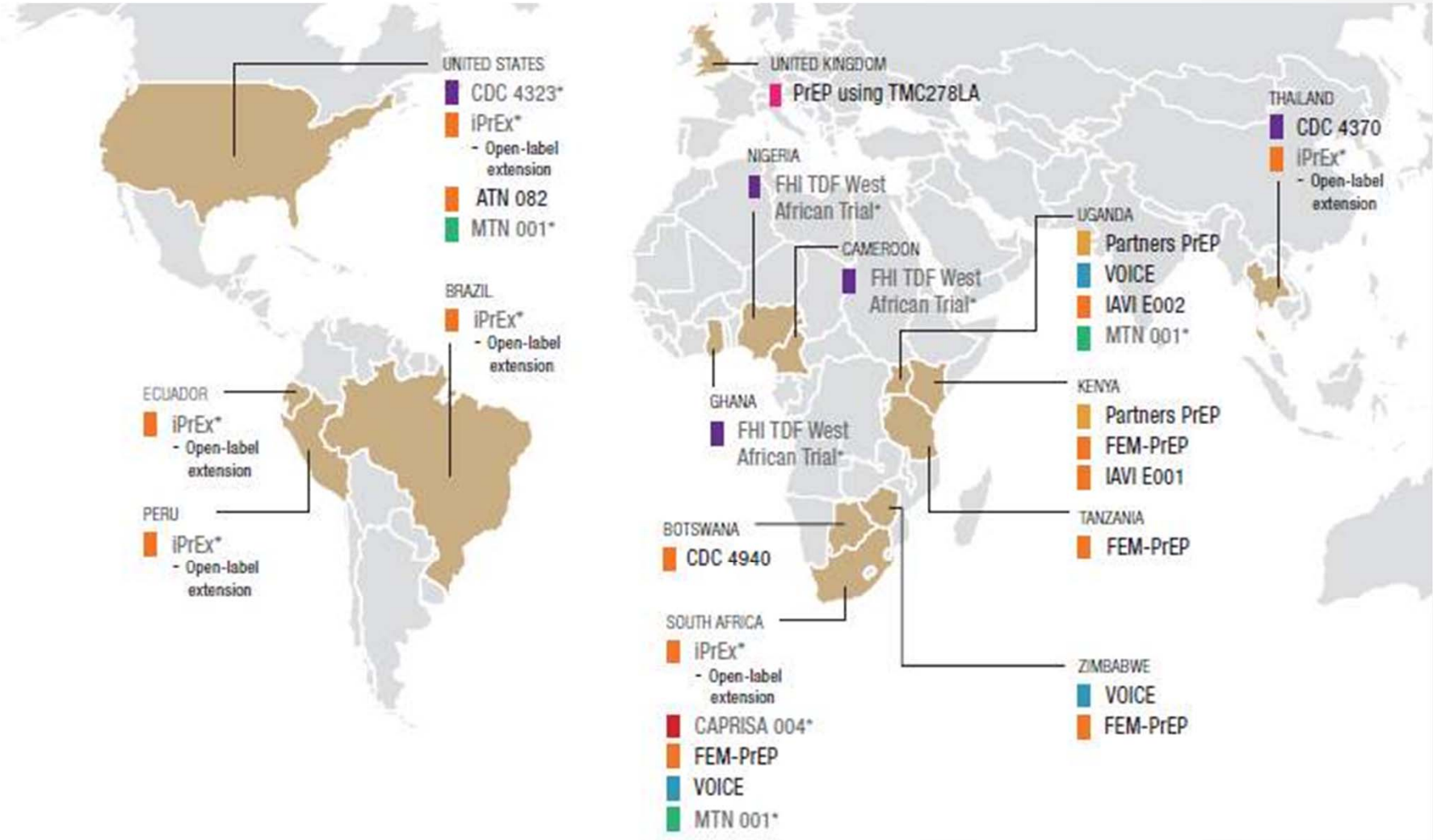
- Secondary analysis:
  - Excluding those infections in subjects who had run out of pills and who had not taken pills for >30 days, 77.9% fewer infections in people taking TDF/FTC (*P*=0.0053)

Thigpen MC, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. WELBC01.

TDF2: Conclusions

- Daily TDF-FTC effective and safe for prevention of HIV infection among heterosexual men and women
  - Study not large enough to draw definitive conclusions by gender separately
  - Increased rates of dizziness, nausea and vomiting but otherwise well tolerated
- Overall safety and efficacy findings consistent with Partners of PrEP data

Ongoing and Completed PrEP Trials



Kim S, et al. J Int AIDS Soc 2010;13:24.

Antiretroviral Therapy for Treatment Naïve Patients

Joseph J. Eron Jr.
Professor of Medicine
UNC at Chapel Hill

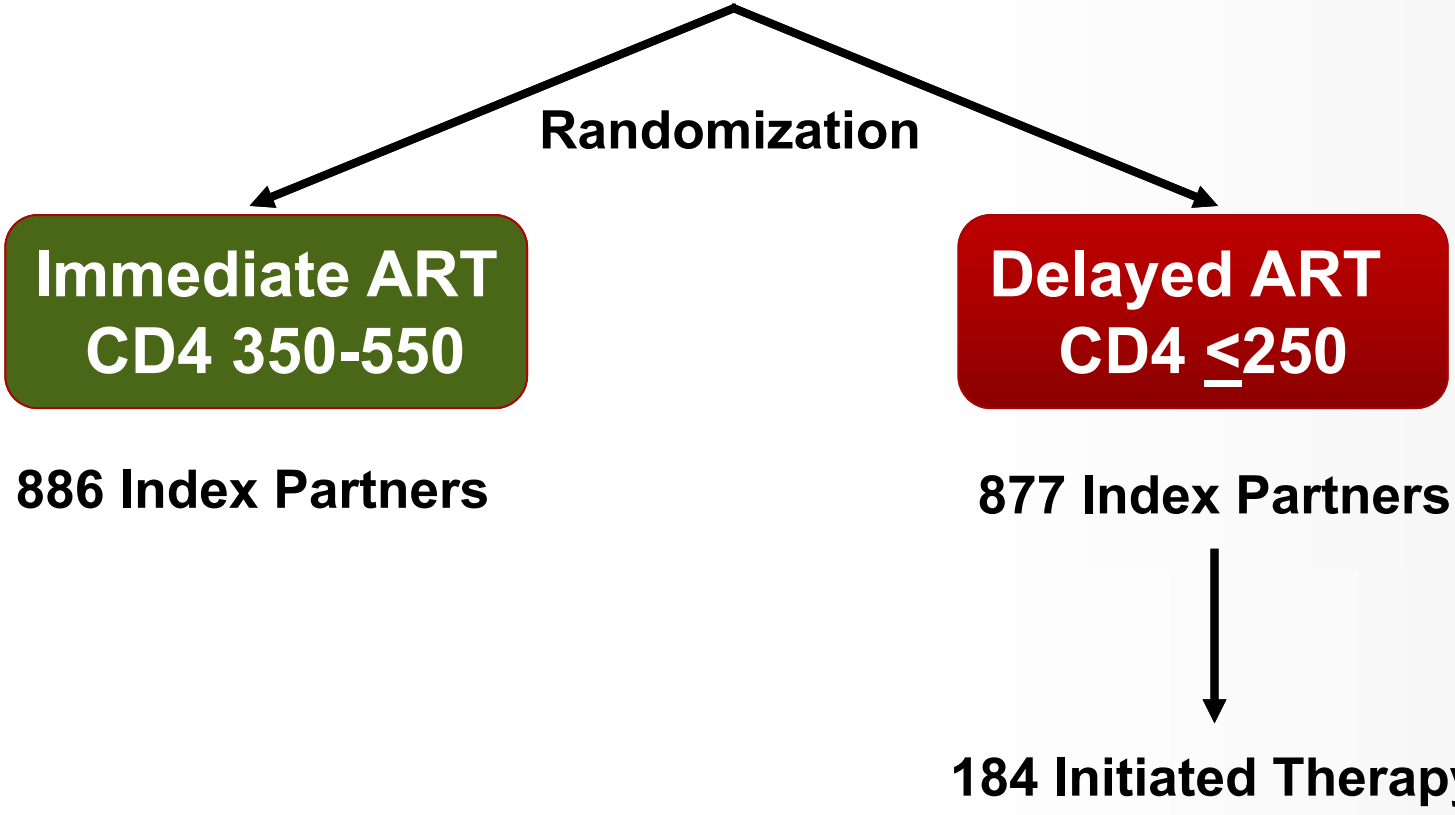
Jointly sponsored by the Postgraduate Institute for Medicine and ViralEd, LLC Supported by an educational grant from Merck & Co., Inc.

HPTN 052: When To Start Therapy

- HPTN 052
  - HIV infected individual in a discordant relationship with CD4 cell between 350-550 cells/mm^3
    - Immediate therapy vs. delay until CD4 < 250 cells/mm^3 or WHO IV event
- Primary Endpoints
  - Death, WHO Stage 4 clinical event, pulmonary TB or severe bacterial infection
  - All events underwent blinded independent review using standardized criteria
- The primary clinical endpoint
  - Time to first primary clinical event, including death

HPTN 052: Study Design

HIV-infected Subjects with CD4 350 to 550 cells/mm^3
Serodiscordant Couples



HPTN 052: ART Regimens

	Immediate Arm	Delayed Arm
N Initiating ART	886	184
EFV + AZT/3TC	72%	70%
ATV + AZT/3TC	10%	7%
EFV + FTC/TDF	9%	11%
LPV/r + AZT/3TC	7%	2%
Other	2%	10%

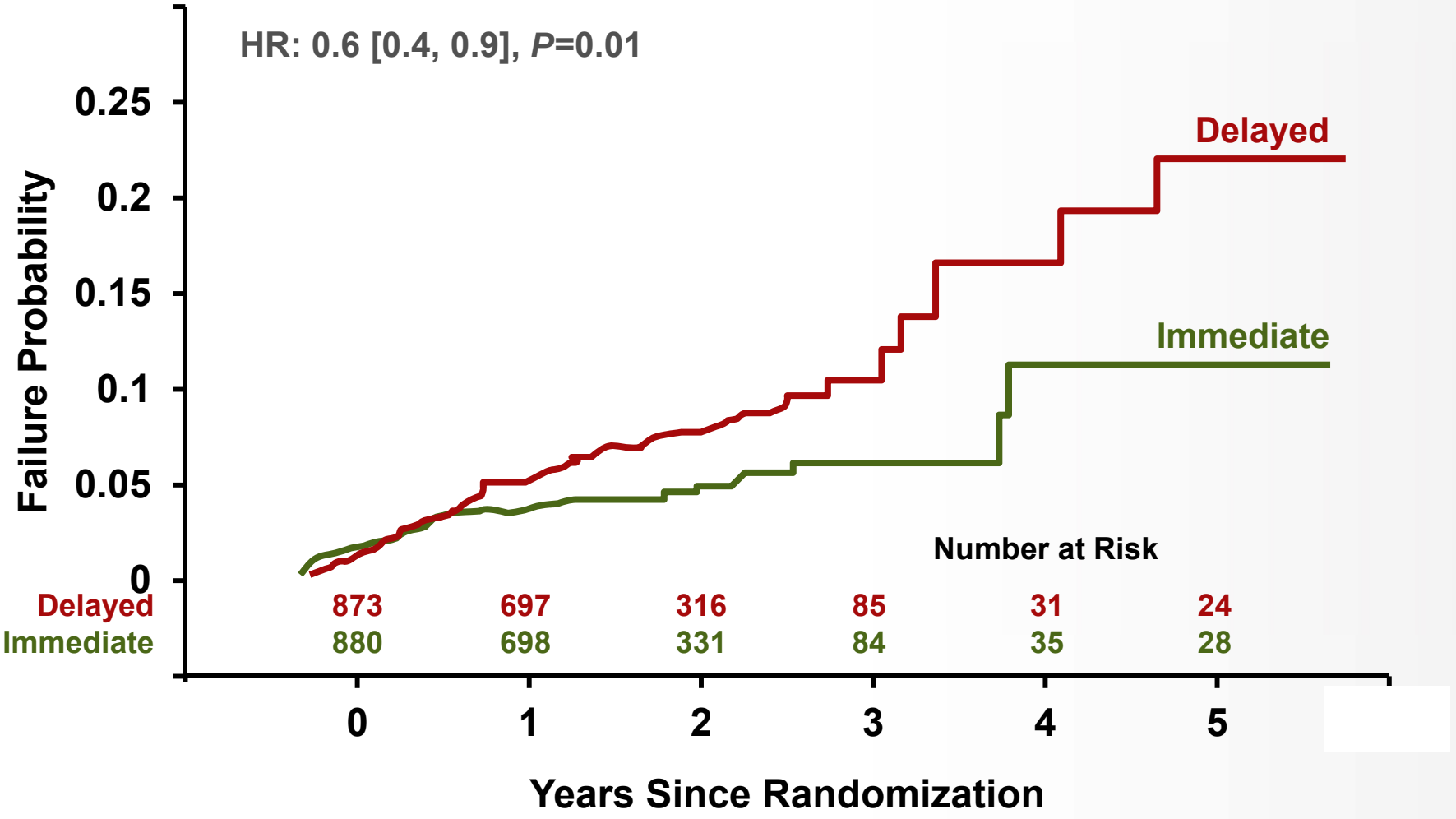
Cohen MS, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. MOAX0102.

HPTN 052: Primary Results

- Median follow-up: 1.7 years
- 105 individuals experienced at least one primary clinical event
  - 40 immediate arm
  - 65 delayed arm

Study Arm	Follow-up	Incidence /100 PY [95% CI]
Immediate	1662 PY	2.4 [1.7 – 3.3]
Delayed	1641 PY	4.0 [3.1 - 5.0]

HPTN 052: Time to First Primary Clinical Event



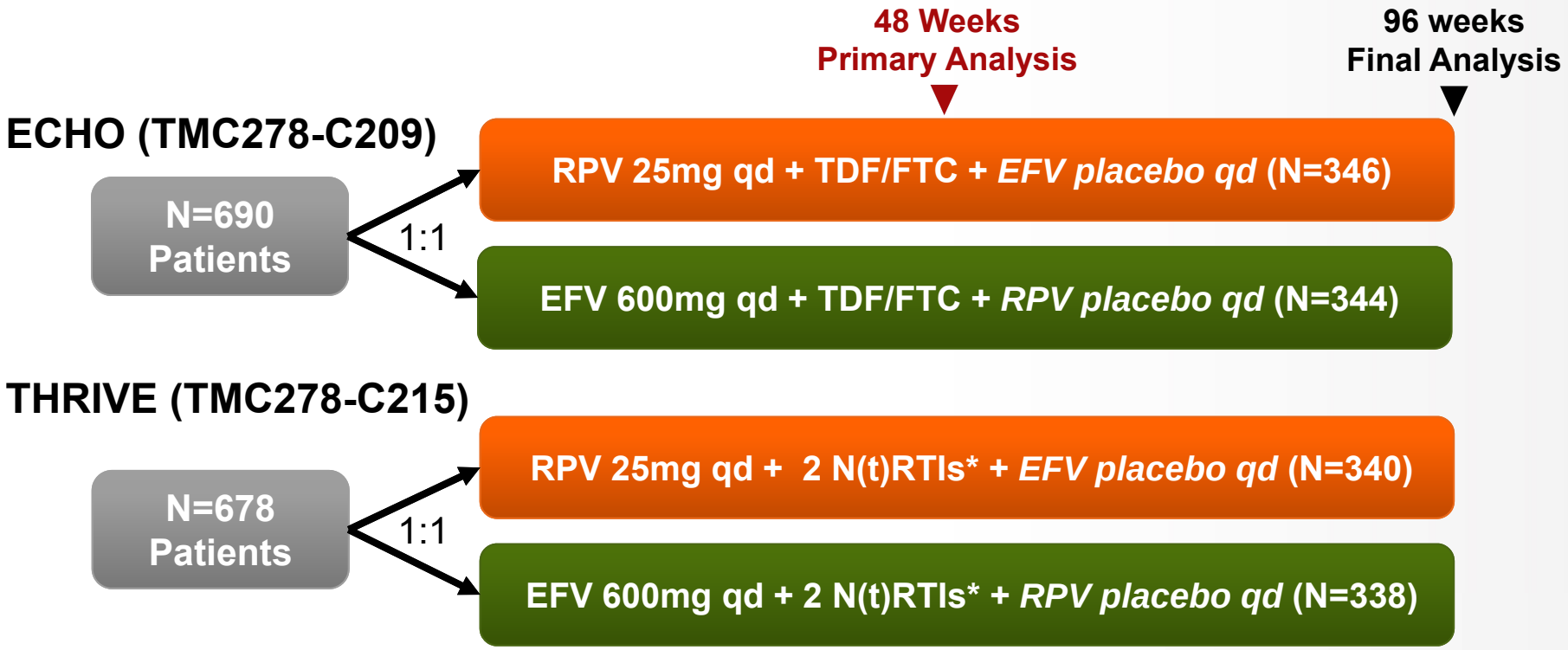
Cohen MS, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. MOAX0102.

HPTN 052: All Primary Clinical Events (N=129)

- 17 subjects experienced >1 clinical event

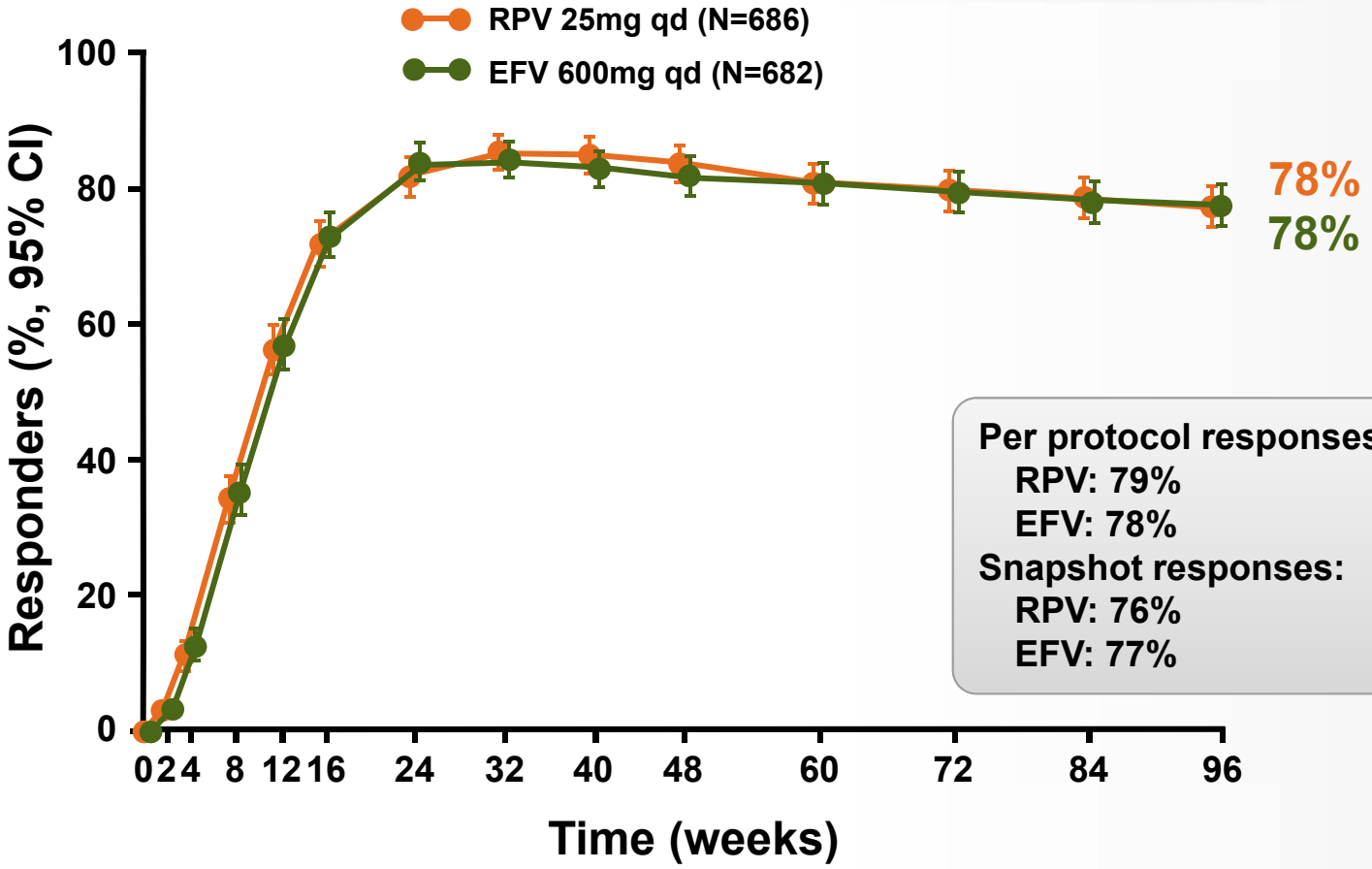
	Immediate	Delayed
Total (N=129)	53	76
Tuberculosis	17	33
Severe bacterial infection	16	11
Death	10	13
Chronic herpes simplex	3	7
Bacterial pneumonia (recurrent)	2	2
Esophageal candidiasis	2	2
Cervical carcinoma	0	2
Kaposi's sarcoma	1	1
Wasting syndrome	0	2
Other	2	3

ECHO and THRIVE Double-blind Study Designs



*Investigator's choice: TDF/FTC; AZT/3TC; ABC/3TC

Pooled ECHO and THRIVE: VL <50 copies/mL over 96 weeks (ITT-TLOVR)

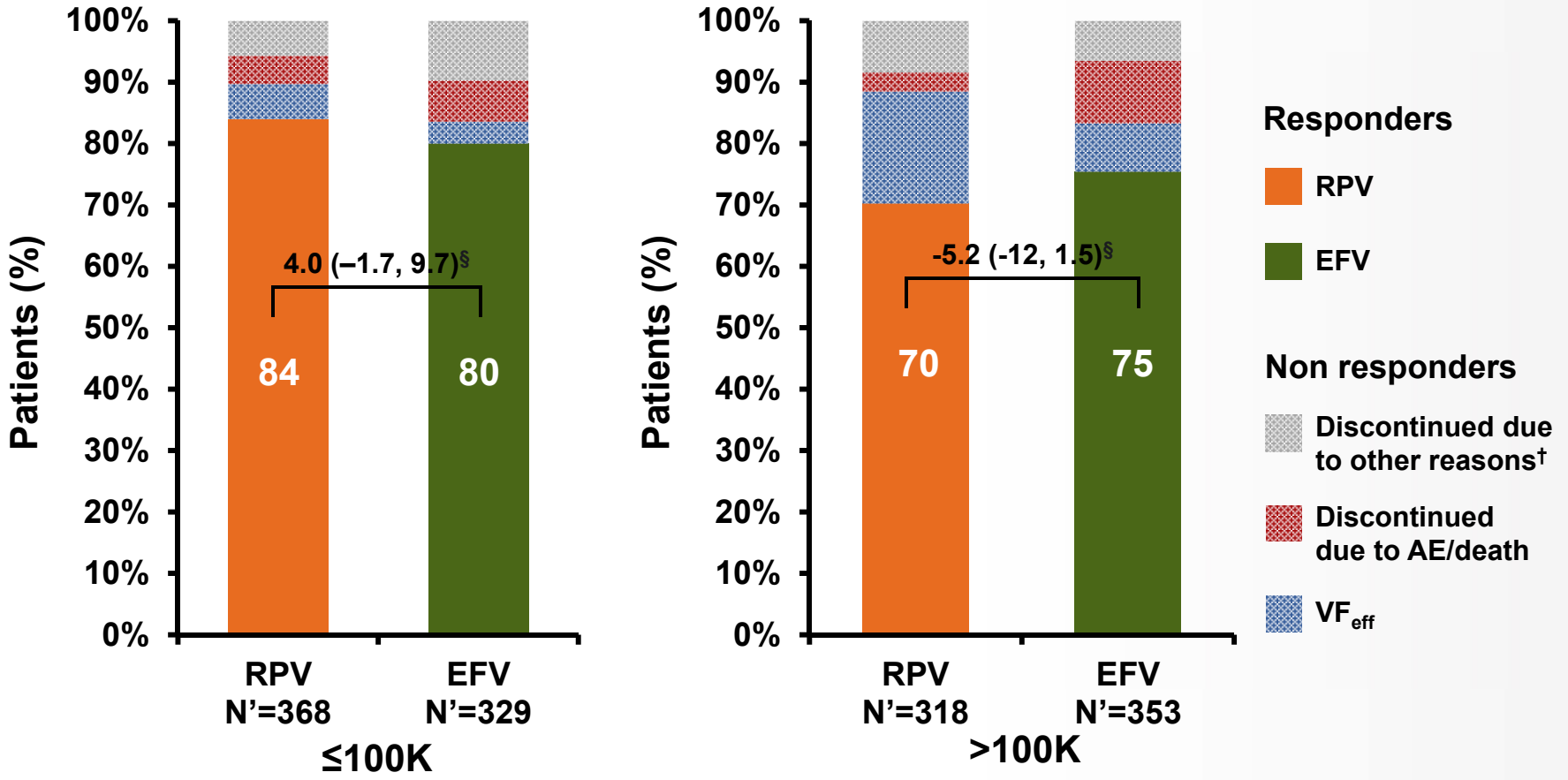


Per protocol responses:
- RPV: 79%
- EFV: 78%

Snapshot responses:
- RPV: 76%
- EFV: 77%

- **Mean change in CD4 cell count from baseline at Week 48 (NC=F): RPV: +228 vs. EFV: +219 cells/mm^3**

Pooled ECHO and THRIVE: ITT-TLOVR Outcome at Week 96 by Baseline VL



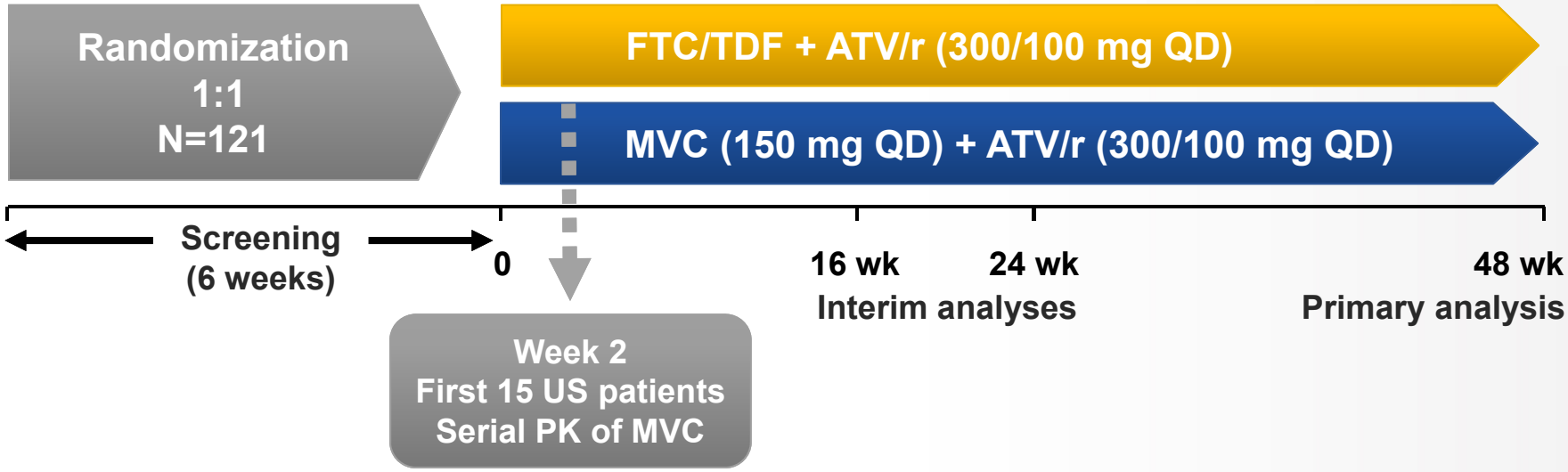
- Responses by baseline CD4 cell count were: ≥200 cells/mm^3: RPV 82% vs. EFV 79%, ≥50–<200 cells/mm^3: RPV 71% vs. EFV 75% and <50 cells/mm^3: RPV 56% vs. EFV 69%

Pooled ECHO and THRIVE: VF in the Resistance Analysis

VF_{res}, n (%)	RPV N=686	EFV N=682
VF_{res} (all)	96 (14.0)	52 (7.6)
Rebounder	52 (8)	34 (5)
Never suppressed	44 (6)	18 (3)
VF_{res} (up to week 48)	73 (11)	36 (5)
Rebounder	29 (4)	18 (3)
Never suppressed	44 (6)	18 (3)
VF_{res} (after Week 48 and up to Week 96)	22 (3)	16 (2)
Rebounder	21 (3)	15 (2)
Never suppressed	1 (0.1)	1 (0.1)

Cohen C, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. TULBPE032.

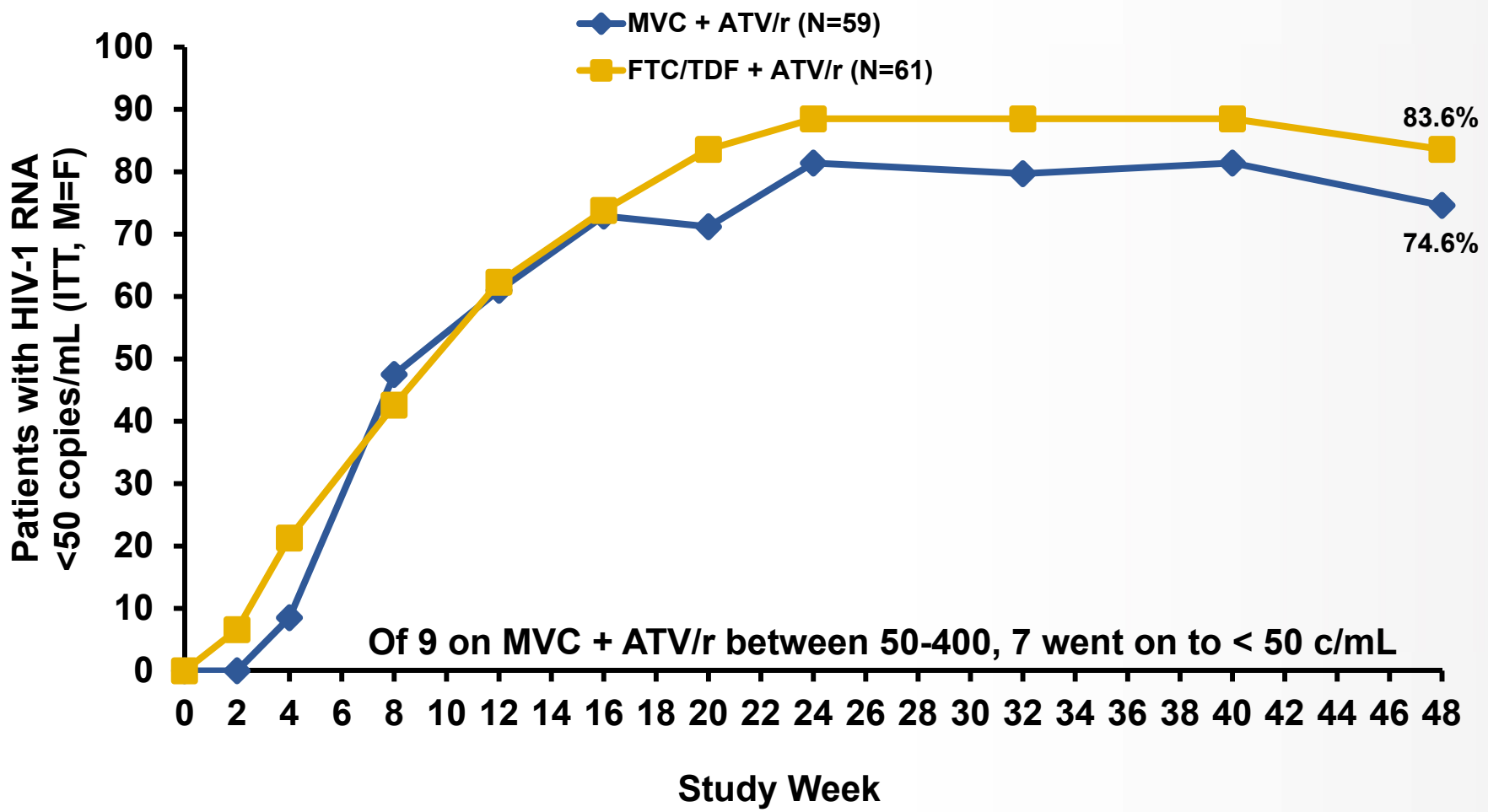
FTC/TDF vs. MVC: Open-label, 48-week Phase 2b Pilot Study



Patient Eligibility Criteria

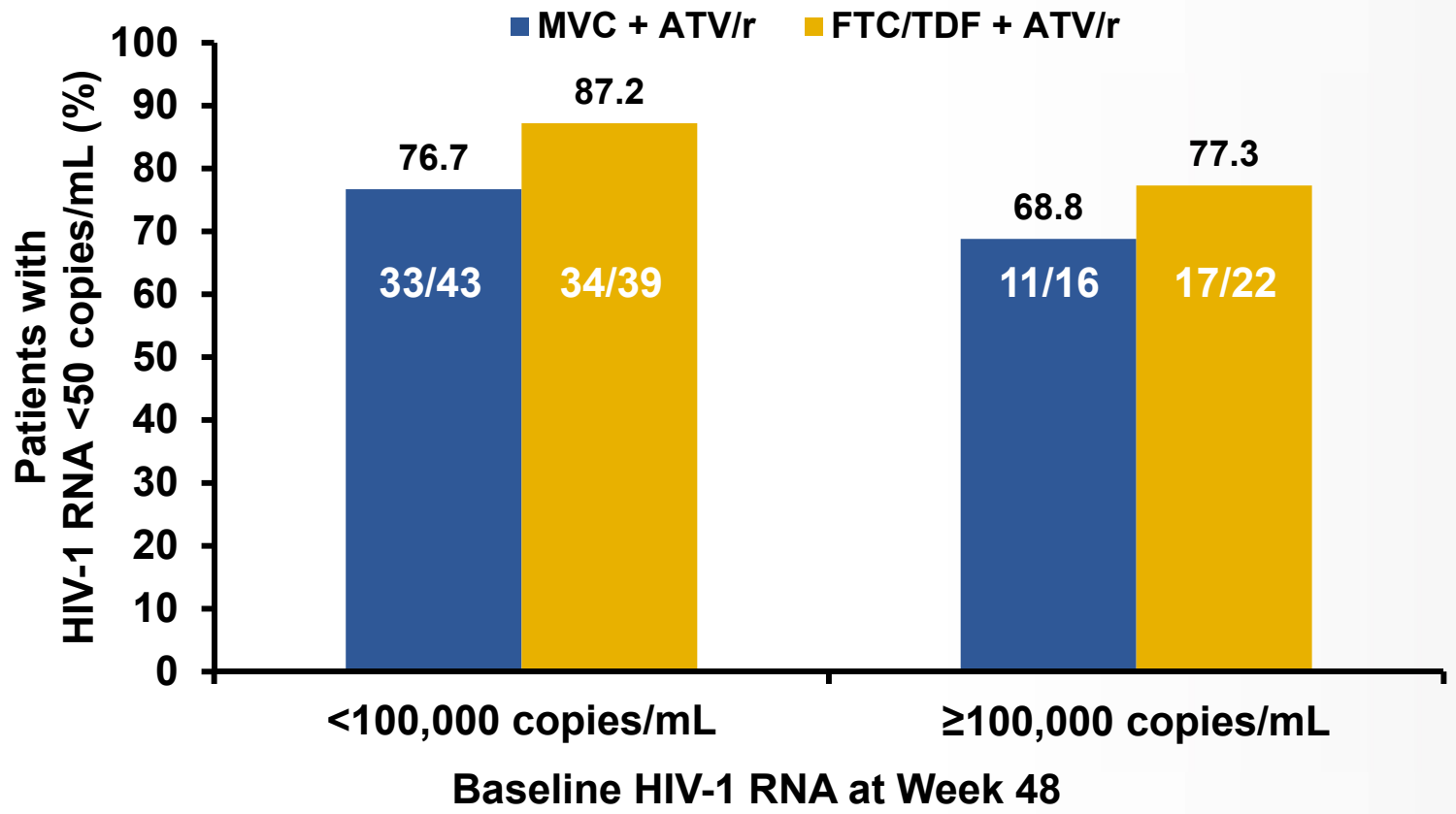
- R5 HIV (ESTA) at screening
- ≥16 years of age
- HIV-1 RNA ≥1000 copies/mL
- CD4 ≥100 cells/mm^3
- No evidence of resistance to ATV/r, TDF, or FTC

FTC/TDF vs. MVC: HIV-1 RNA <50 copies/mL at Week 48



Portsmouth S, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. TUAB0103.

FTC/TDF vs. MVC: HIV-1 RNA <50 copies/mL at Week 48 According to Baseline Viral Load



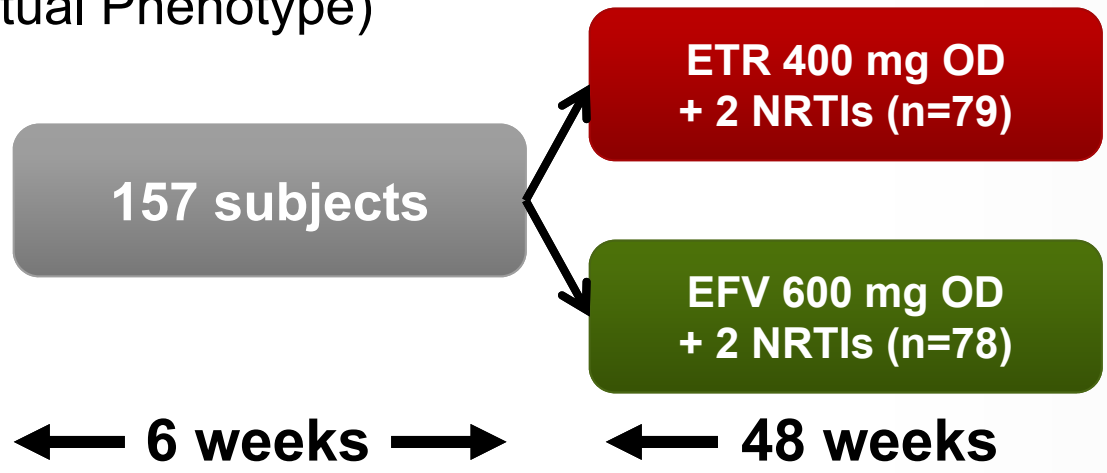
- No resistance or tropism change
- Greater Incidence of hyperbilirubinemia in MVC plus ATV/r arm

Intent-to-treat. Missing=failure

SENSE: Trial Design

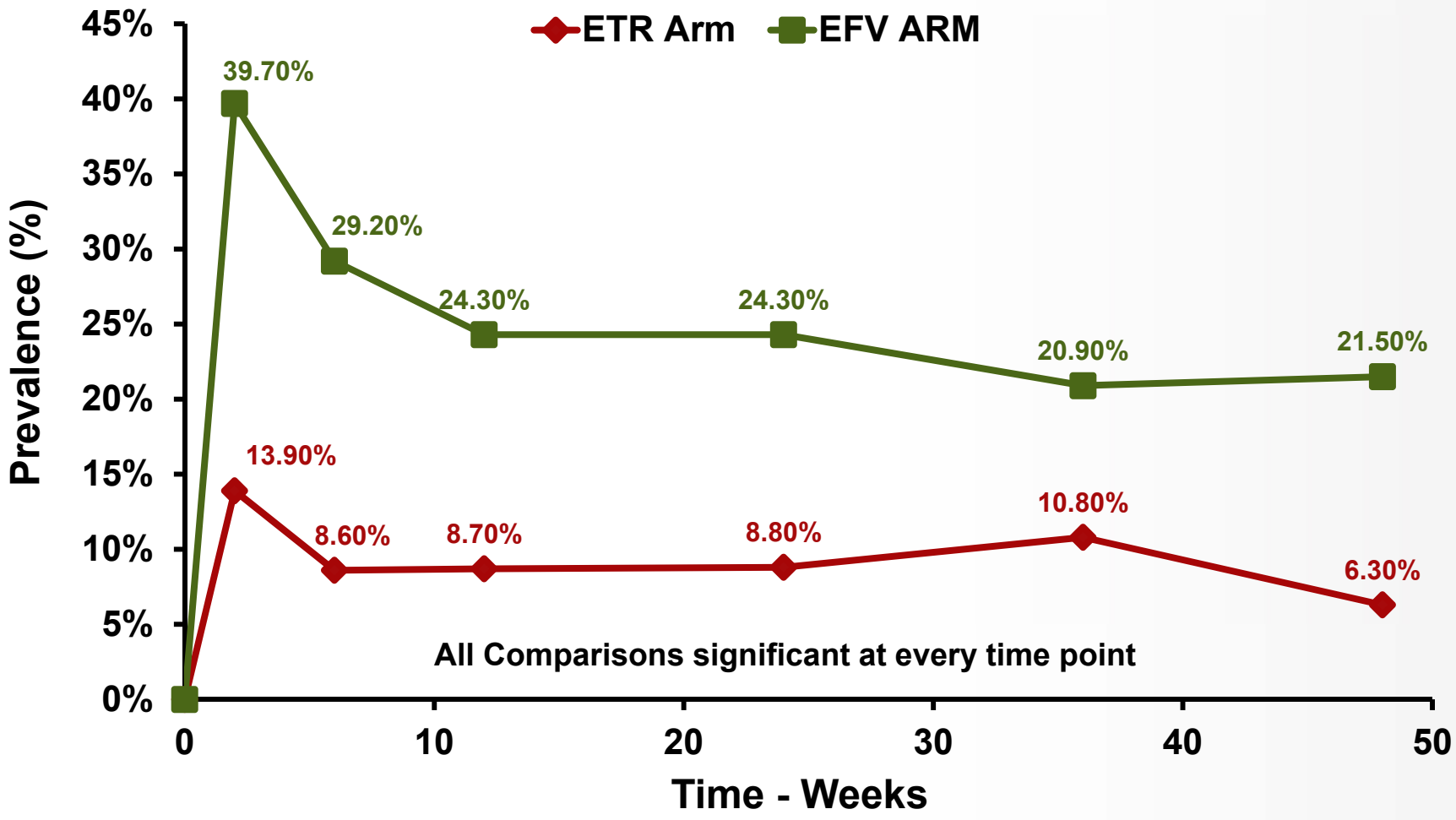
Treatment naïve, HIV RNA >5,000 copies/mL

- No genotypic mutations to NRTIs, NNRTIs or PIs (Bennett lists)
- Predicted Phenotypic sensitivity to NNRTIs and selected NRTIs (Virtual Phenotype)



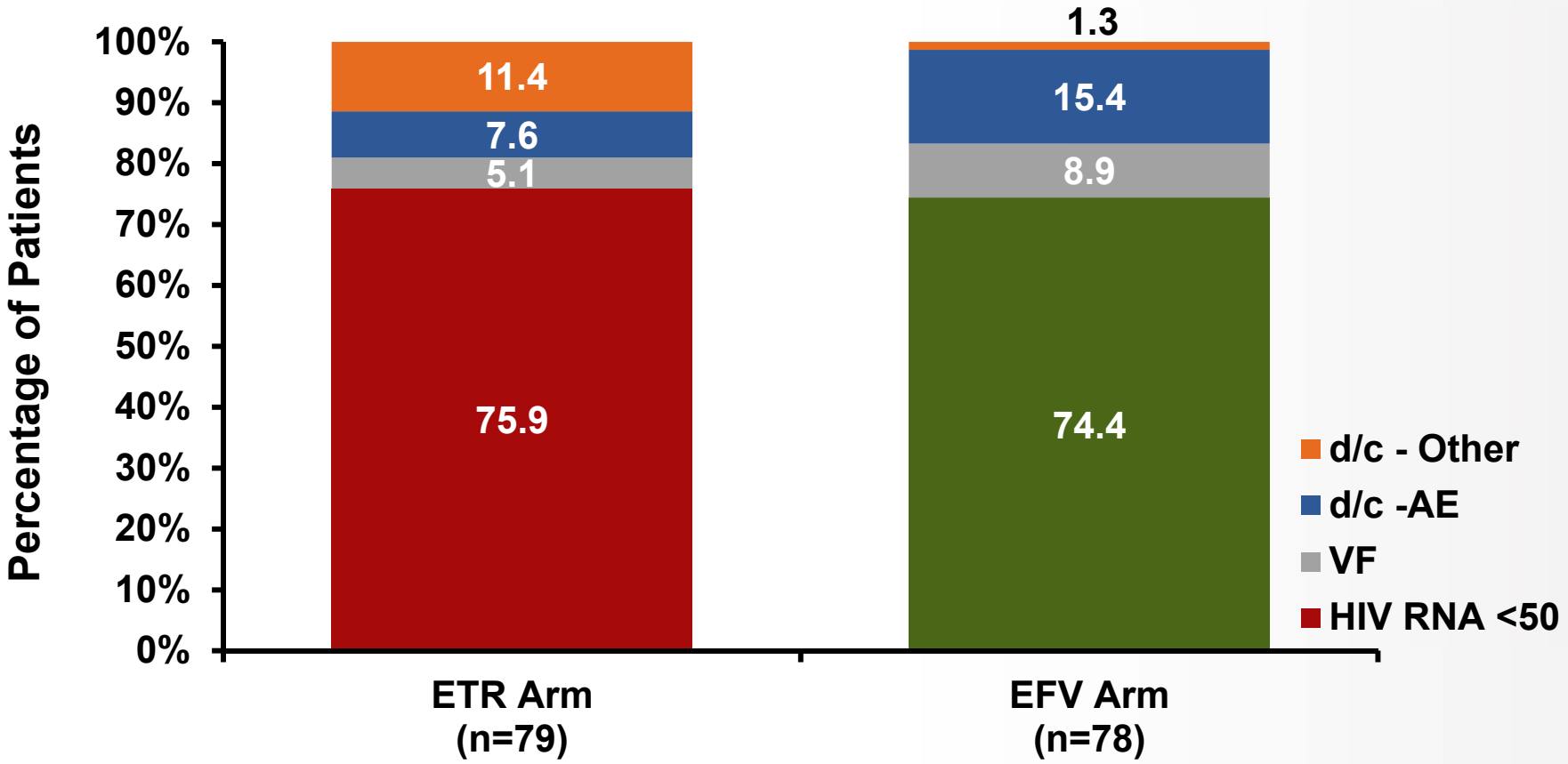
- Double-blinded, active controlled to Week 48
- Two investigator-selected NRTIs (AZT+3TC; ABC+3TC; TDF+FTC)
- Primary endpoint: neuropsychiatric adverse events up to Week 12

SENSE: Grade 1 - 4 Drug-related Neuropsychiatric AE Prevalence (ITT)

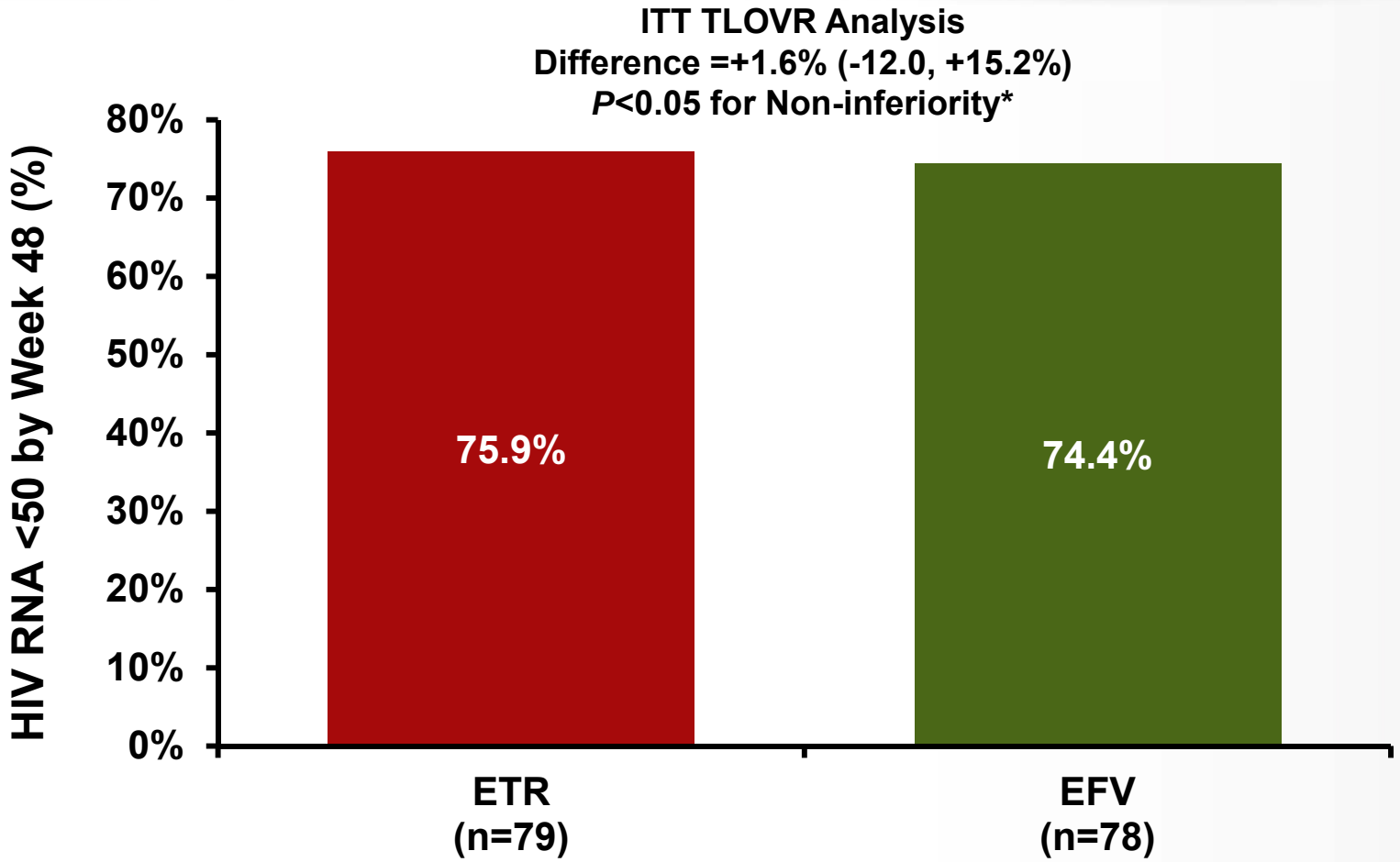


Rockstroh J, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. TULBPE025.

SENSE: Summary Efficacy at Week 48 (ITT TLOVR) – by Type of Response (%)

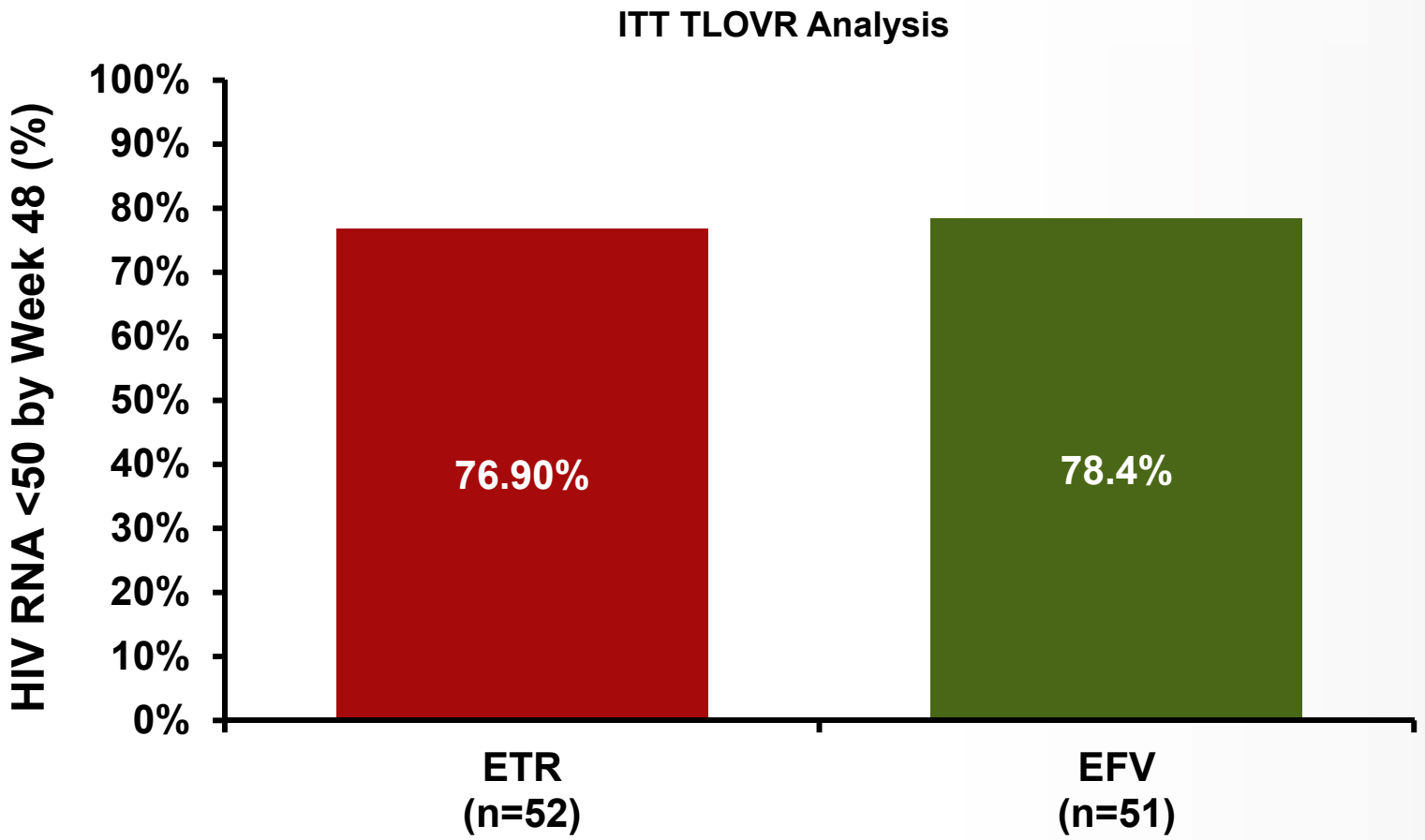


SENSE: HIV RNA <50 copies/mL at Week 48 - All Patients Randomized and Treated



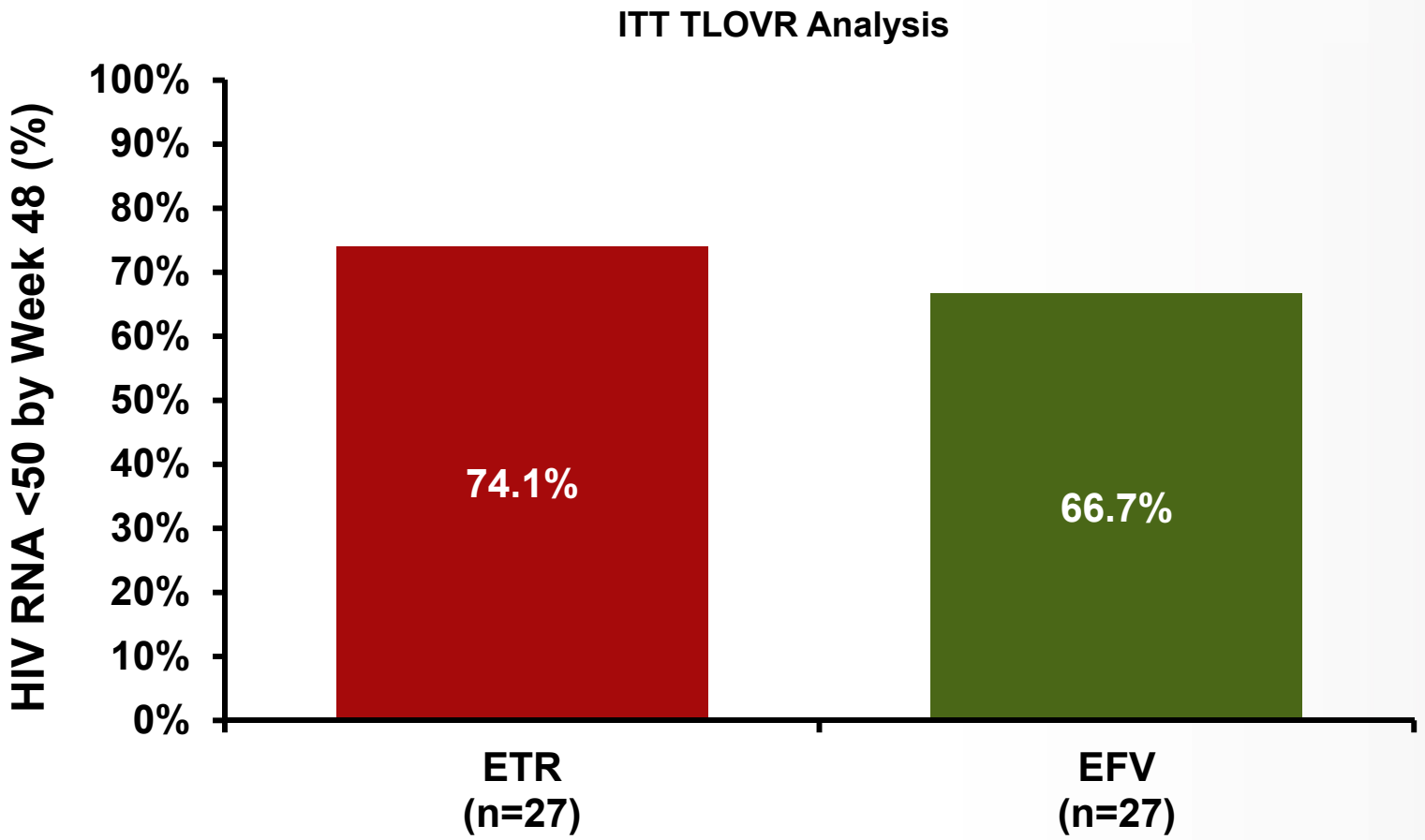
Rockstroh J, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. TULBPE025.

SENSE: HIV RNA <50 copies/mL at Week 48 - Baseline HIV RNA ≤100,000 copies/mL



Rockstroh J, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. TULBPE025.

SENSE: HIV RNA <50 copies/mL at Week 48 - Baseline HIV RNA >100,000 copies/mL



Rockstroh J, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. TULBPE025.

SENSE: "Virological Failures" by TLOVR

- Etravirine (n=4)
  - No resistance mutations
- Efavirenz (n=7)
  - 3/7 with Resistance
    - **V106I + M184I**
    - **K103N**
    - **K103N + P225H + M184V**

Rockstroh J, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. TULBPE025.

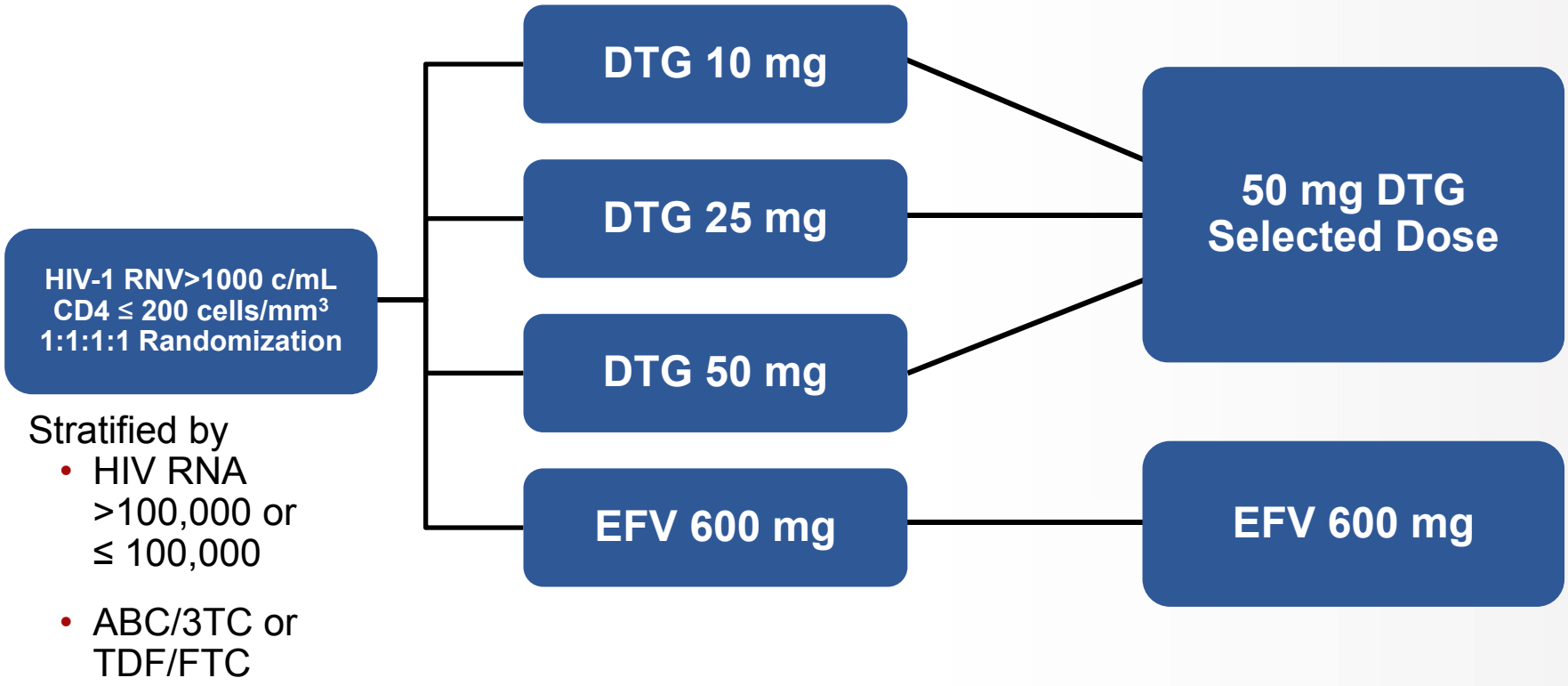
Treatment-Experienced Patients and New Therapies

Jose Arribas, MD
HIV Research Director, HIV Unit
Hospital de La Paz
Madrid, Spain

Jointly sponsored by the Postgraduate Institute for Medicine and ViralEd, LLC Supported by an educational grant from Merck & Co., Inc.

Dolutegravir in ARV-Naïve Patients

- Phase IIb dose-ranging trial, partially blinded (N~200)
- All arms included 2 NRTIs given once-daily



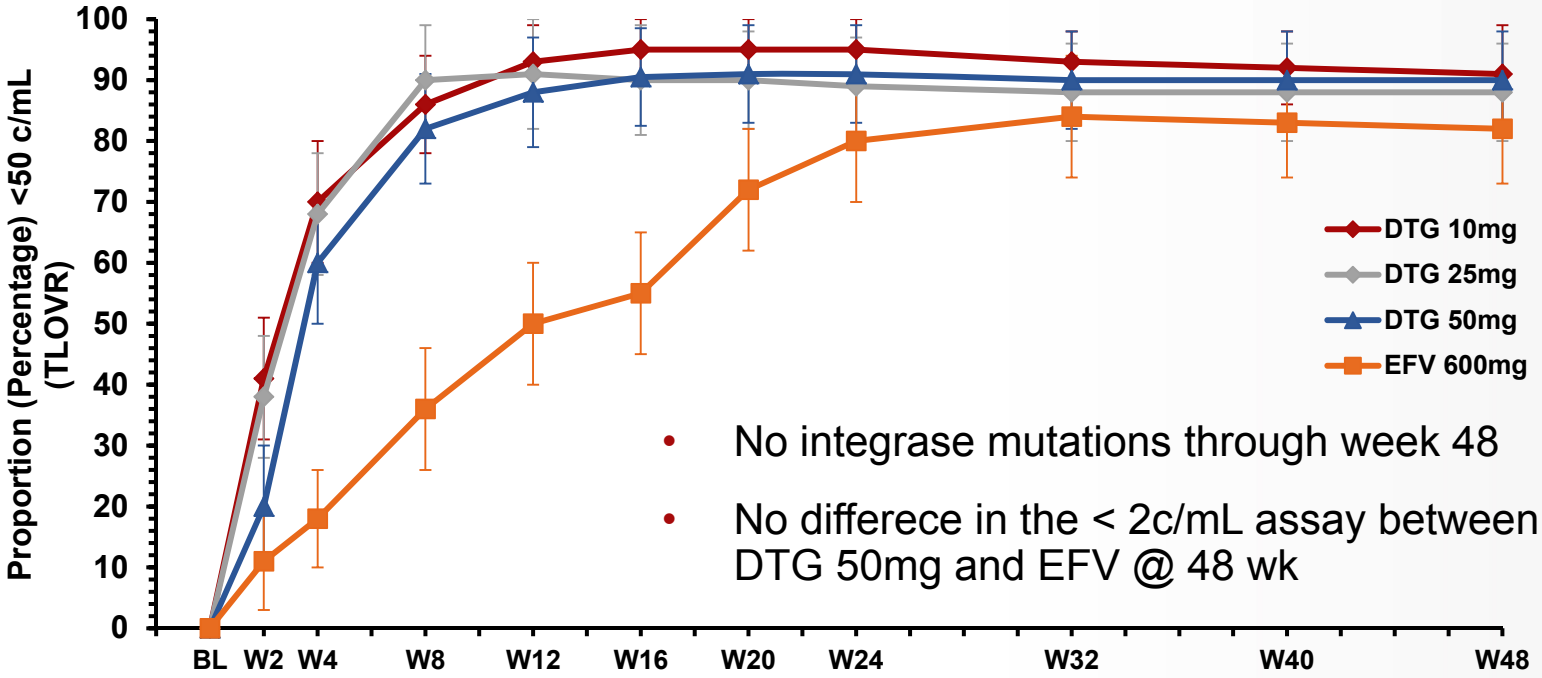
Stratified by
- HIV RNA >100,000 or ≤ 100,000
- ABC/3TC or TDF/FTC

Dolutegravir in ARV-Naïve Patients: Baseline characteristics

	DTG 10mg (N=53)	DTG 25mg (N=51)	DTG 50mg (N=51)	EFV 600mg (N=50)	Total (N=205)
Baseline HIV-1 RNA					
Mean (log_{10} c/mL)	4.42	4.38	4.58	4.46	4.46
>100,000 c/mL	11 (21%)	10 (20%)	12 (24%)	11 (22%)	44 (21%)
Baseline CD4+ (cells/mm^3)					
Mean	309.4	333.8	327.2	327.5	324.3
<350	36 (68%)	29 (57%)	35 (69%)	30 (60%)	130 (63%)
Investigator-selected NRTIs					
TDF/FTC	36 (68%)	34 (67%)	34 (67%)	34 (68%)	138 (67%)
ABC/3TC	17 (32%)	17 (33%)	17 (33%)	16 (32%)	67 (33%)

Van Lunzen J, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. TUAB0102.

Dolutegravir in ARV-Naïve Patients: Results at 48 Weeks



Outcome	DTG 10mg (N=53)	DTG 25mg (N=51)	DTG 50mg (N=51)	EFV 600mg (N=50)
Responder	48 (91%)	45 (88%)	46 (90%)	41 (82%)
Reason for non-response (virologic)				
Rebound or virologic non-response	4 (8%)	3 (6%)	2 (4%)	3 (6%)
Never suppressed through Week 48	0	0	1 (2%)	1 (2%)

Van Lunzen J, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. TUAB0102.

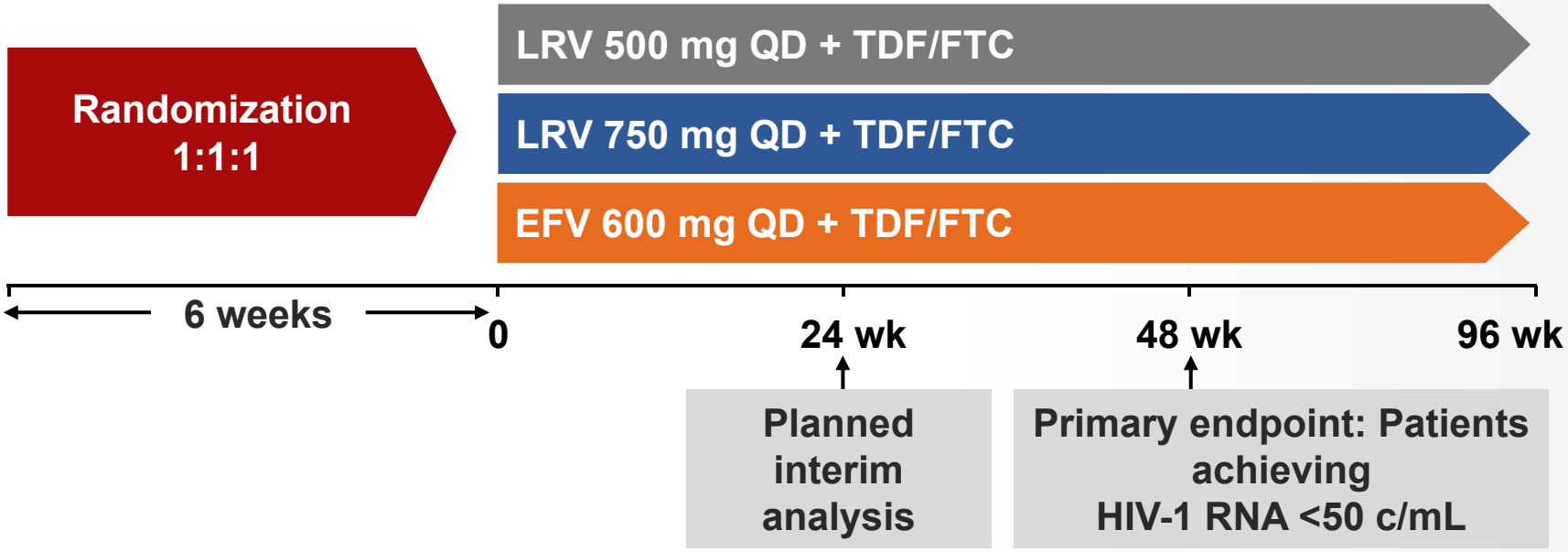
Dolutegravir in ARV-Naïve Patients: Adverse Events and Safety

- Small changes in serum creatinine (0.1-0.15 mg/dL) were observed
  - Observed with both NRTI backbones, did not progress over time
  - No effect of DTG on GFR (as measured by iohexol clearance)
  - In vitro and clinical data are consistent with inhibition of the renal transporter responsive for tubular secretion of creatinine
- Lower Impact on Plasma Lipids than EFV but no difference in TC/HDL

	DTG 10mg (N=53)	DTG 25mg (N=51)	DTG 50mg (N=51)	DTG Subtotal (N=155)	EFV 600mg (N=50)
Grade 2-4 Drug Related (all)	5 (9%)	4 (8%)	4 (8%)	13 (8%)	10 (20%)
Gastrointestinal	1 (2%)	1 (2%)	1 (2%)	3 (2%)	2 (4%)
Psychiatric disorders	0	0	0	0	3 (6%)
Metabolic disorders	0	3 68%)	1 (2%)	4 (3%)	0
Skin disorders	0	0	0	0	2 (4%)
Infections	2 (4%)	0)	0	2 (1%)	0
General disorders	1 (2%)	0	1 (2%)	2 (1%)	1 (2%)
Serious Adverse Events (all)	3 (6%)	1 (2%)	4 (8%)	8 (5%)	4 (8%)
AEs Leading to Discontinuation	0	1 (2%)	1 (2%)	2 (1%)	4 (8%)

Van Lunzen J, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. TUAB0102.

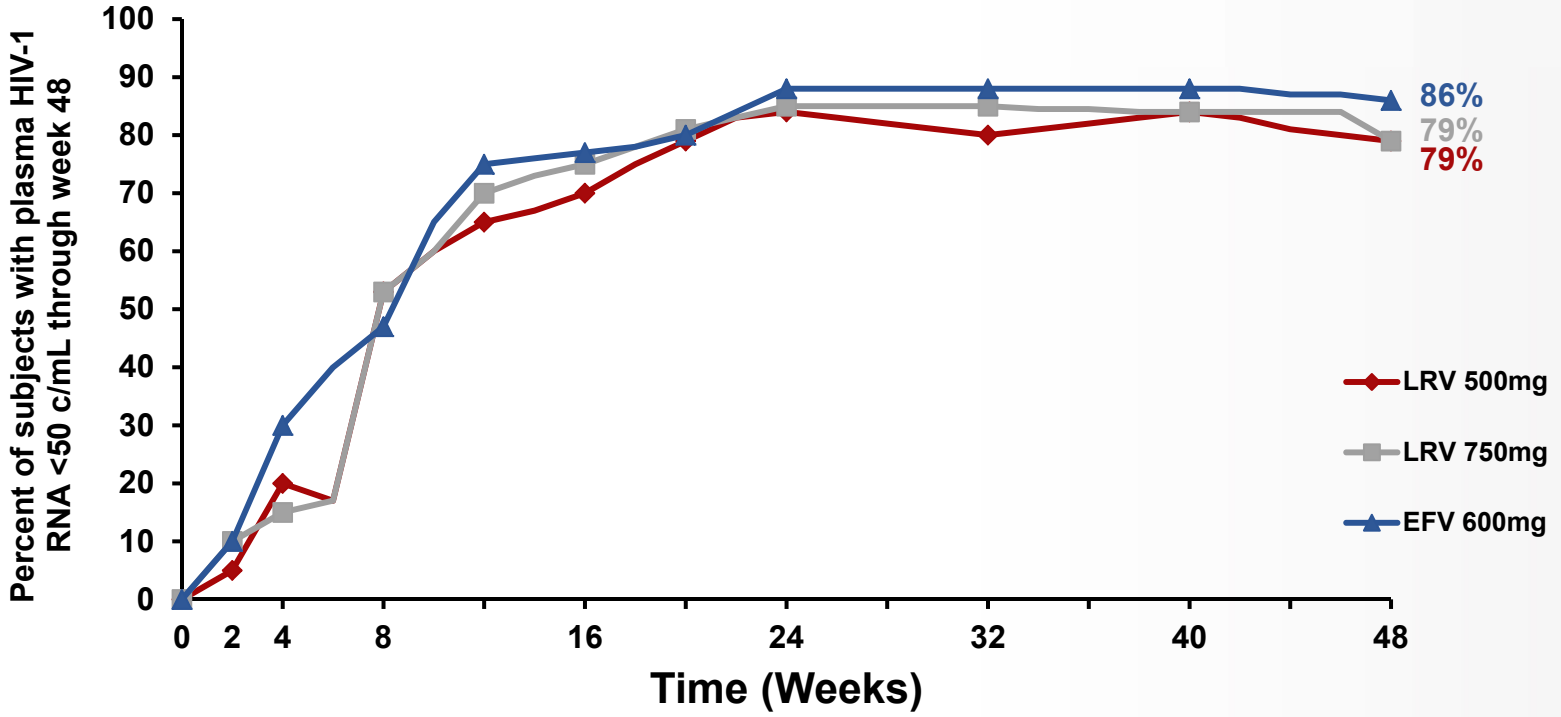
Lersivirine: Phase 2b Trial in Treatment-naïve Patients



- Randomized, double-blind, comparative study
- Selection criteria
  - ARV naïve
  - HIV-1 RNA ≥1,000 c/mL
  - CD4+ >200 cells/mm^3
  - No RT mutations by standard genotyping
- Stratified by viral load (<100,000 or ≥100,000 c/mL) & geographic region (A & B)

Vernazza P, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. TUAB0101.

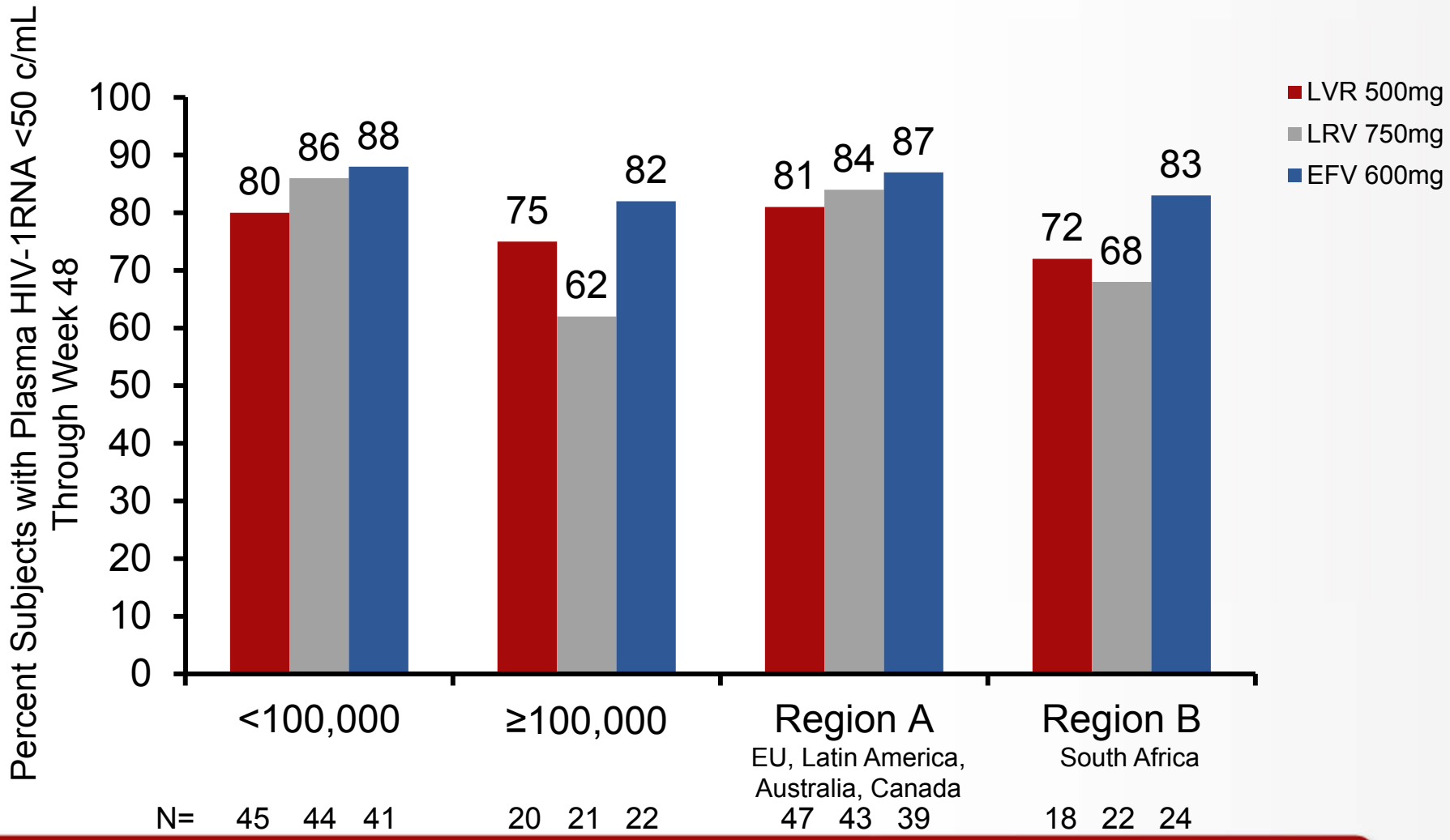
Lersivirine: Results



Treatment	N	n	%	Difference (%)	SE Diff (%)	80% CI-Lower (%)	80% CI-Upper (%)
LRV 500mg QD	65	51	79	-9	7	-18.1	0.8
LRV 750mg QD	65	51	79	-8	7	-17.0	1.2
EFV 600mg QD	63	54	86	NA	NA	NA	NA

Vernazza P, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. TUAB0101.

Efficacy by screening plasma HIV-1 RNA and geographic region (ITT, NC=F)



Vernazza P, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. TUAB0101.

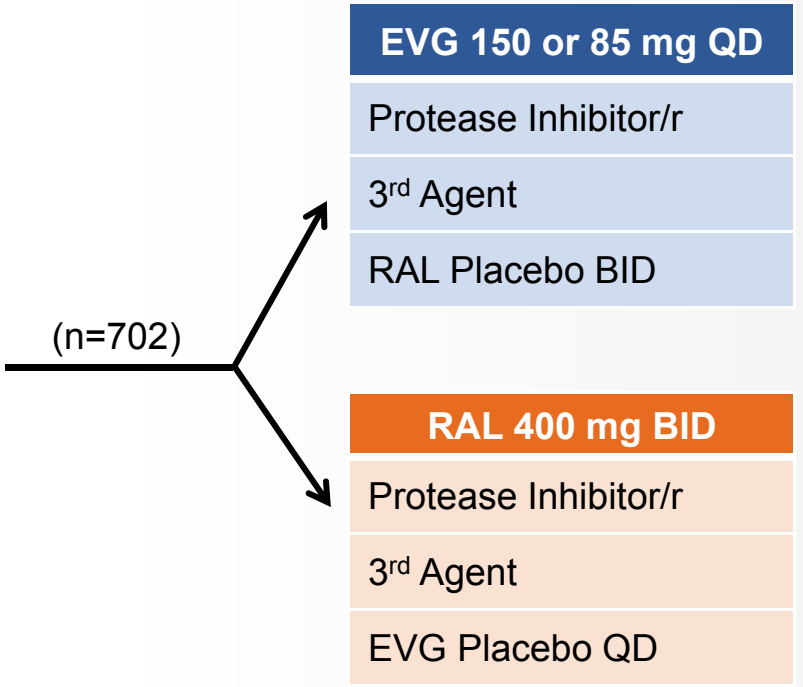
Lersivirine: Select Adverse Events

Number of Subjects with AE, n (%)	LRV 500 mg N = 65	LRV 750 mg N = 65	EFV 600 mg N = 63
Nausea	15 (23)	27 (42)	8 (13)
Headache	15 (23)	11 (17)	9 (14)
Abnormal dreams	5 (8)	5 (8)	12 (19)
Dizziness	5 (8)	4 (6)	13 (21)
Rash*	3 (5)	1 (2)	7 (11)
Abdominal pain	2 (3)	6 (9)	7 (11)
Vomiting	2 (3)	10 (15)	9 (14)
Diarrhea	10 (15)	10 (15)	10 (16)
Insomnia	5 (8)	9 (14)	5 (8)

Vernazza P, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. TUAB0101.

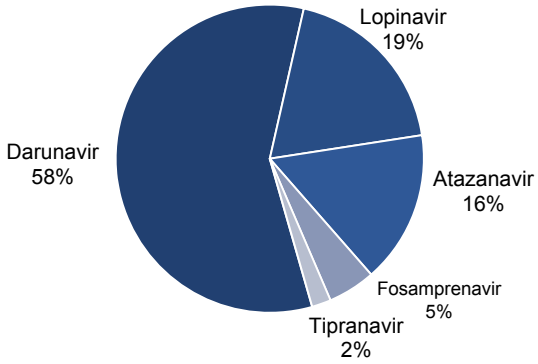
Elvitegravir vs. Raltegravir in Treatment-Experienced Patients

- 96-week randomized (1:1), double-blind, double-dummy
- Treatment-experienced patients
- Background regimen (BR) based on resistance testing:
  - 2nd Agent: fully active PI/r
  - 3rd Agent: NRTI, ETR, MVC, T-20
  - If M184V/I, may add 3TC or FTC
- Primary Endpoint: HIV-1 RNA < 50 copies/mL through 48 weeks TLOVR
- Non Inferiority Study with lower limit 95% CI at -10%

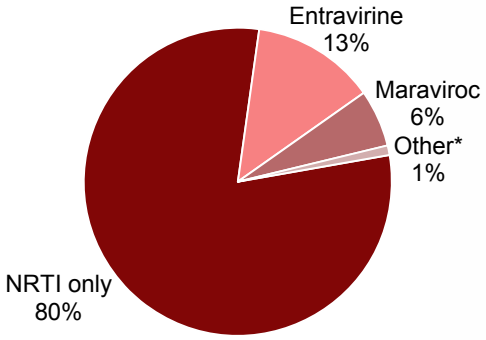


Elvitegravir vs. Raltegravir: Baseline Characteristics

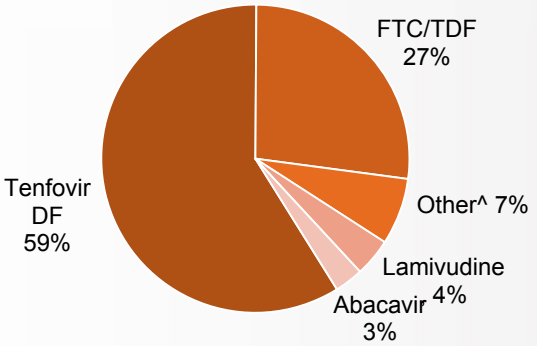
PI/r



3rd Agent



NRTI 3rd Agent



Characteristic	EVG (n = 351)	RAL (n = 351)
HIV RNA (log_{10} copies mL), Median	4.35	4.42
HIV RNA VL ≥ 100,000	26%	26%
CD4 count (cells/mm^3), Mean	259	264
CD4 count <200 cells/mm^3	44%	45%
Baseline Resistance Mutations		
NRTI	69%	68%
NNRTI	63%	60%
Primary PI	31%	34%
Two or more classes	64%	60%

Other*: T-20, T-20+TDF, ETR+NRTI
Other^: 3TC/ABC, 3TC/ZDV, Zidovudine, Didanosine, Emtricitabine

Elvitegravir vs. Raltegravir: Results

Treatment Outcome, %	EVG (n=351)	RAL (n=351)	Prop Diff (95% CI)
Responder	**59%**	**58%**	**1.1% (-6.0 – 8.2)**
Per Protocol Analysis	75%	73%	1.4% (-5.9 – 8.6)
Virologic Failure	20%	22%	
Rebound	11%	16%	
Never Suppressed	8%	5%	
Switched background regimen	1%	1%	
Any NRTI-R	14%	19%	
Any PI-R	7%	4%	
Any Integrase-R	27%	21%	
T66I/A	12%	0%	
E92Q	8%	1%	
T971	5%	4%	
Y143R/H/C	0%	1%	
S147G	5%	0%	
Q148R/H	5%	6%	
N155H	5%	13%	

Molina JM, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. WELBB05.

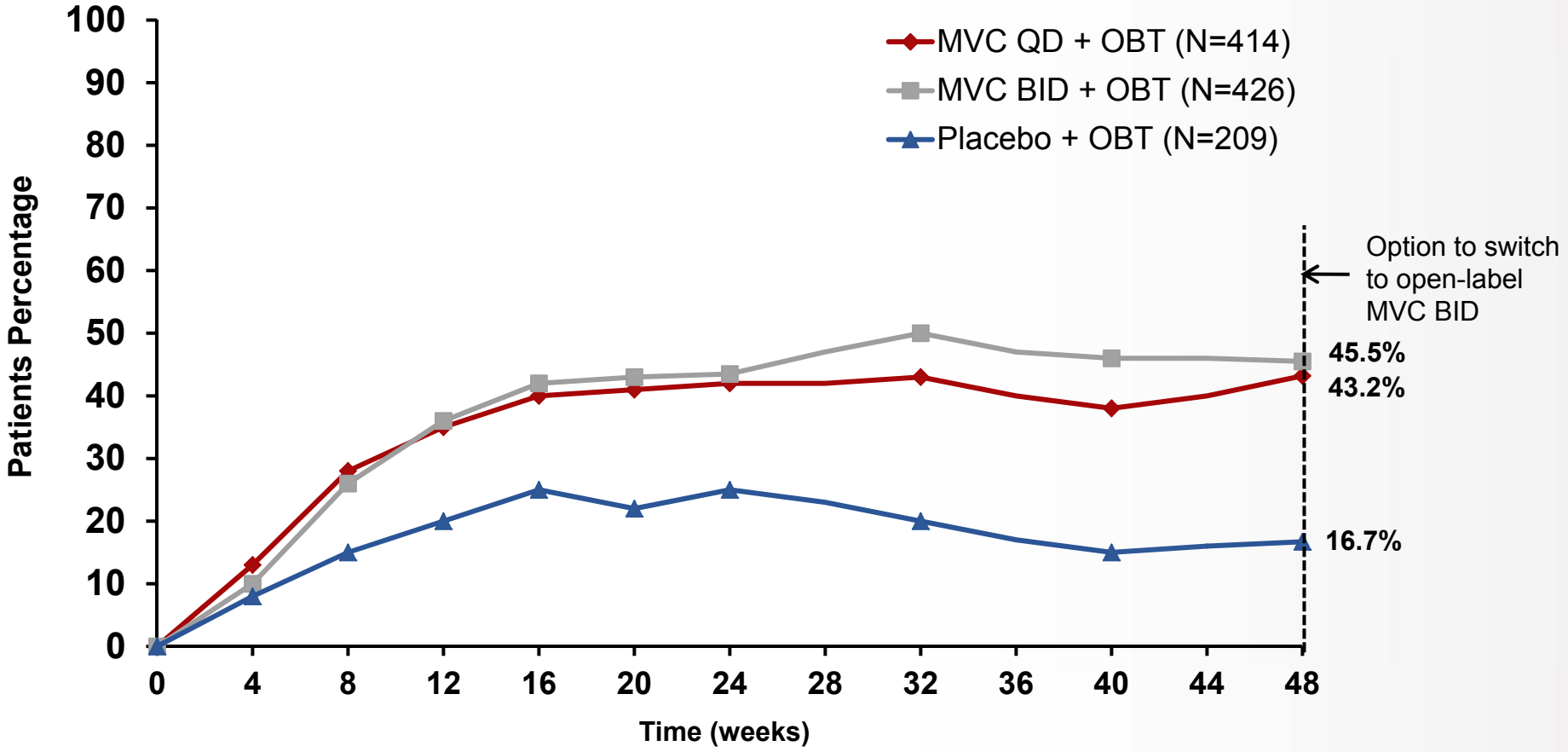
Elvitegravir vs. Raltegravir: Safety

Adverse Events (treatment Emergent)	EVG (n=354)	RAL (n=351)
Any	88%	87%
Lead to Study Drug Discontinuation	3%	4%
Grade 3 or 4	19%	22%
Serious Adverse Events (SAE)	16%	21%
Deaths (n)	1	8
Diarrhea	12%	7%
GGT	3%	6%
ALT	2%	5%
AST	1%	5%

P <0.05

Molina JM, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. WELBB05.

Maraviroc plus bPI: Subanalysis of Motivate 1 & 2

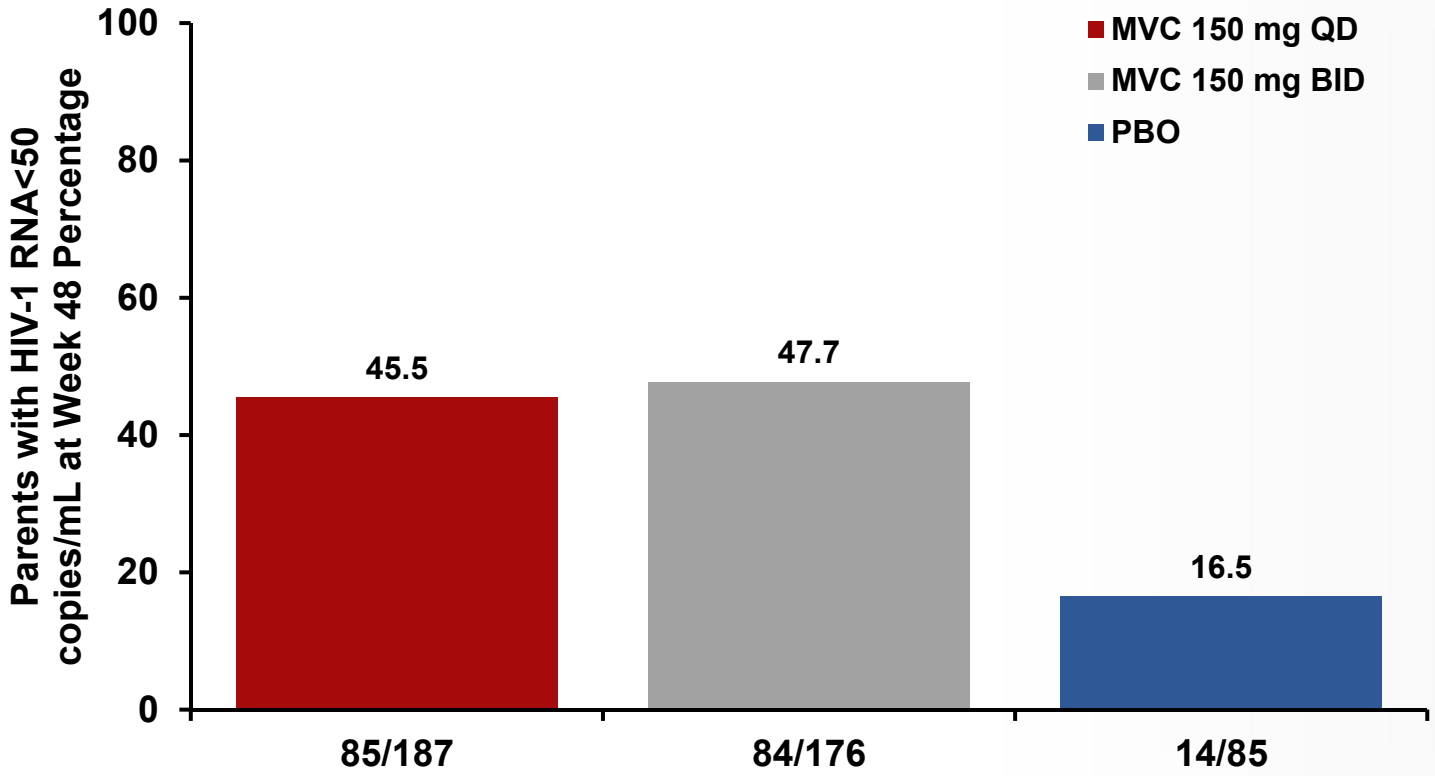


- Current analysis restricted to R5 by ESTA & bPI (fAMP excluded) and MVC 150 QD or BID

*P<0.0001 vs placebo

Taylor S, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. TUAB0106.

Maraviroc plus bPI: Results

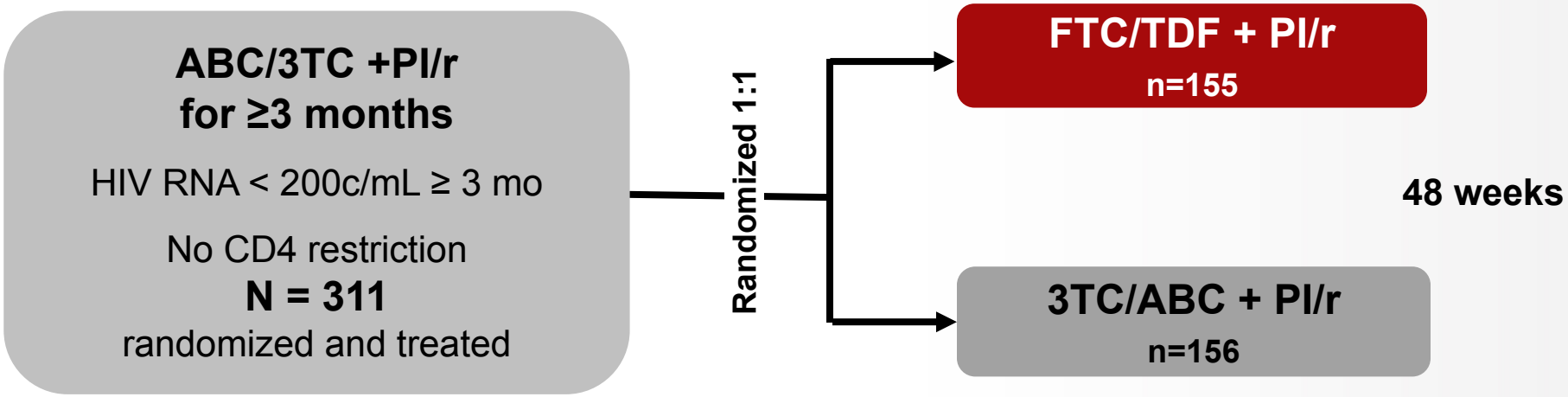


- Similar results in patients with HIV RNA >100,000 copies/mL or CD4 < 50 cells/mm^3 at screening or by number of active drugs in background regimen at baseline (wOBTss < or ≥ 1)

Taylor S, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. TUAB0106.

SWIFT: Study Design

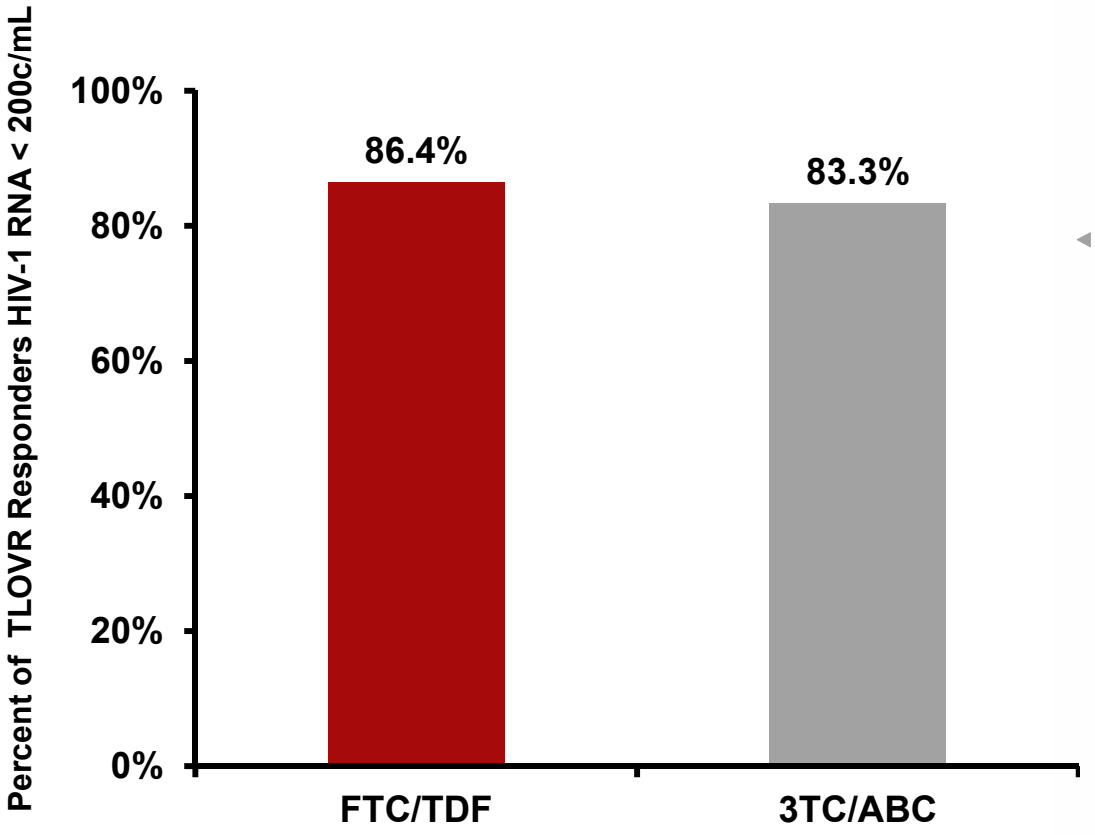
Prospective, open-label, multicenter study

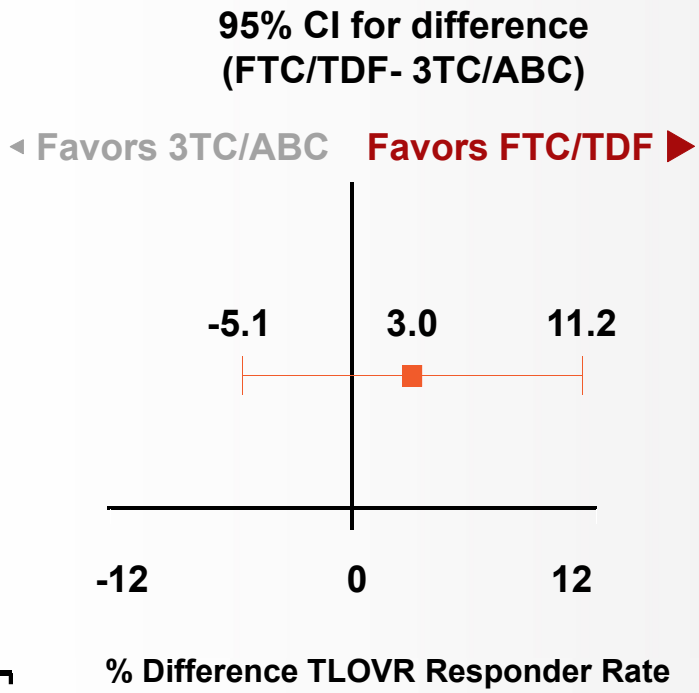


	LPV/r	ATV+RTV	FPV+RTV 100mg	FPV+RTV 200mg	DRV+RTV
FTC/TDF	48/311 (15%)	62/311 (20%)	22/311 (7%)	12/311 (4%)	9/311 (3%)
3TC/ABC	53/311 (17%)	60/311 (19%)	12/311 (4%)	19/311 (6%)	11/311 (4%)

Campo R, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. WELBB03.

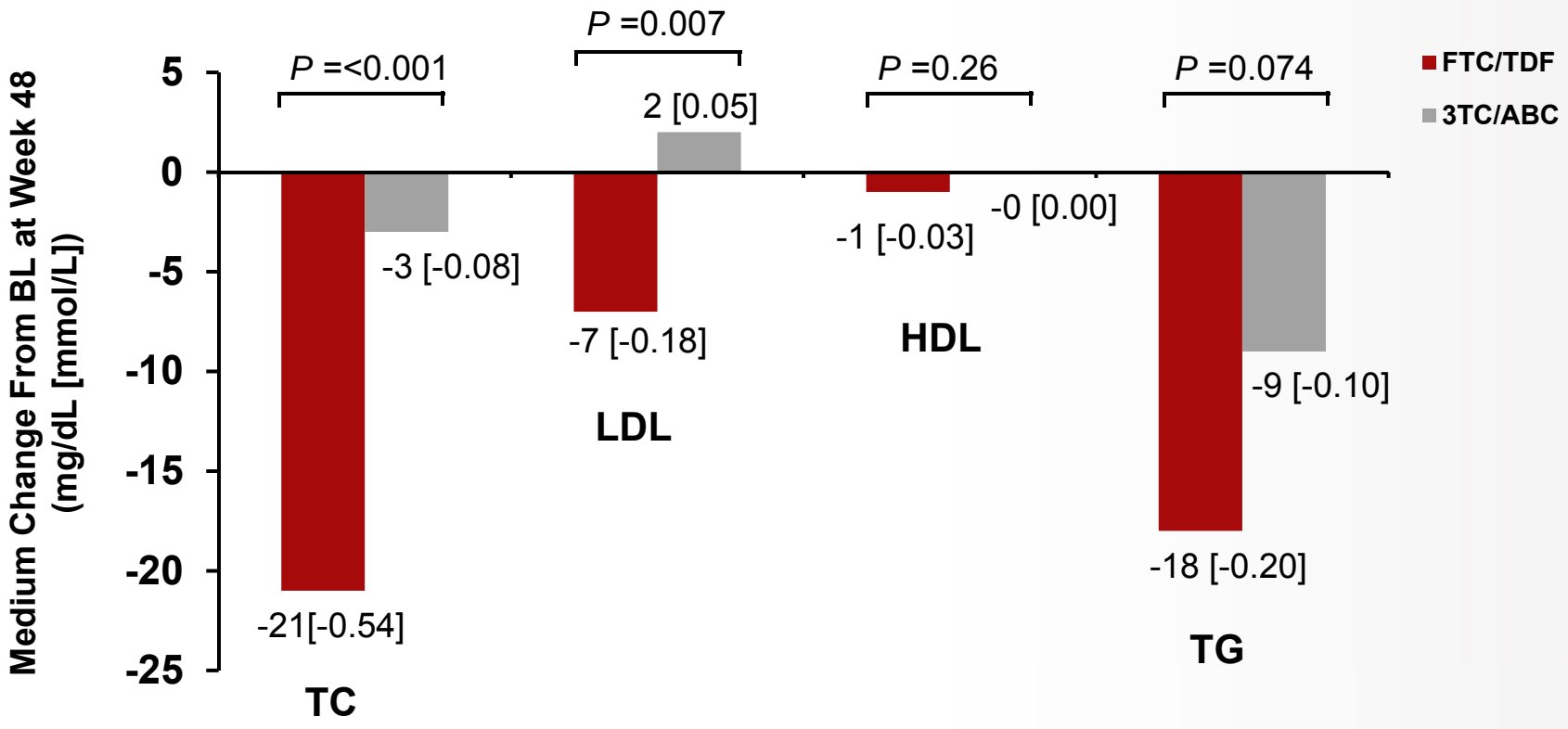
SWIFT: Results Through Week 48





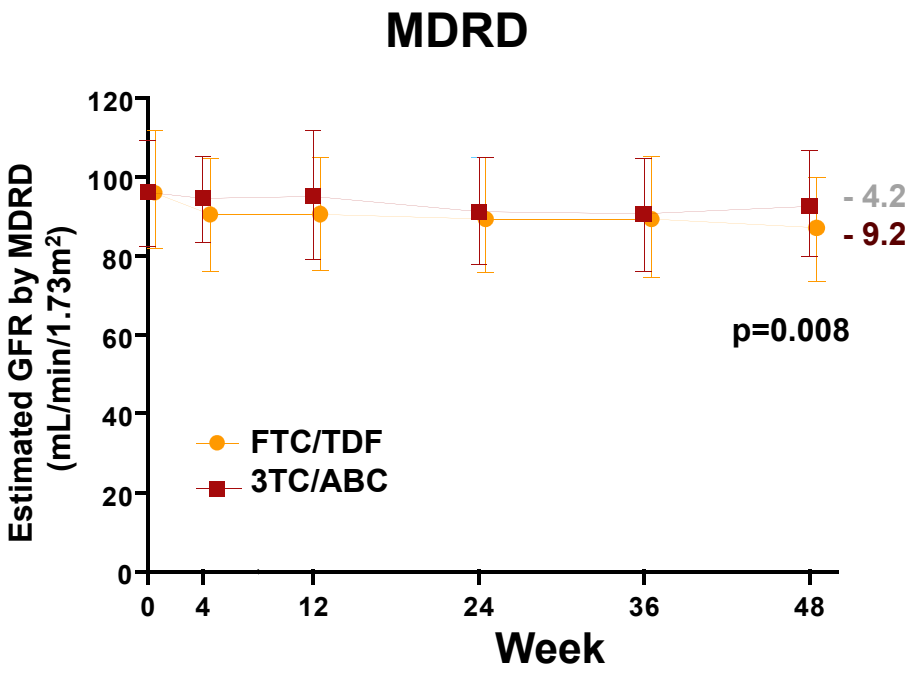
Virologic failure (>200c/mL): 3 TDF/FTC, 11 ABC/3TC

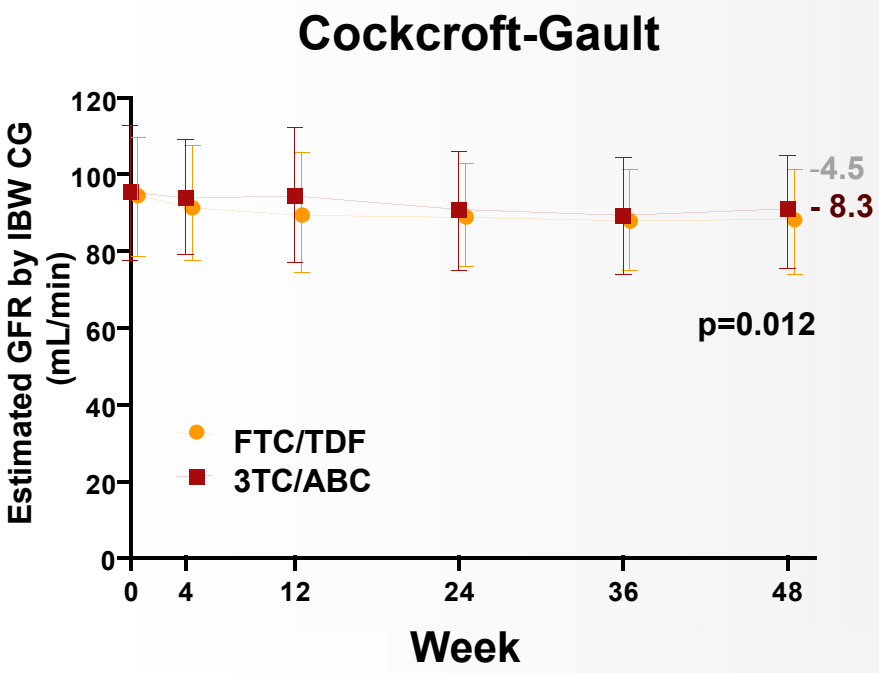
SWIFT: Fasting Lipids
Change from Baseline at Week 48



No significant difference between groups in total cholesterol/HDL ratio at Week 48

SWIFT: eGFR through 48 Weeks



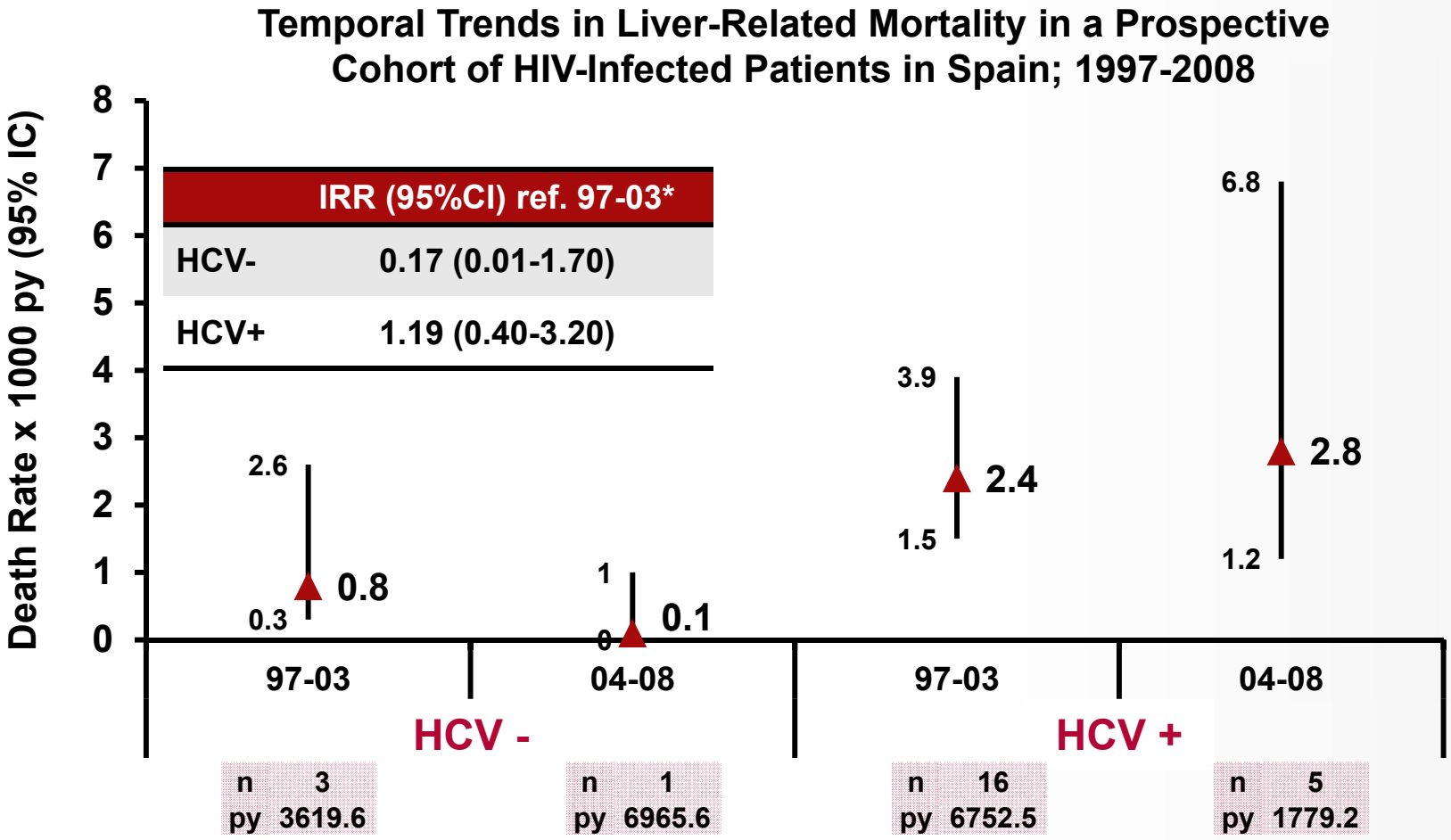


Management

Jürgen Rockstroh, MD
Professor, University of Bonn
Bonn, Germany

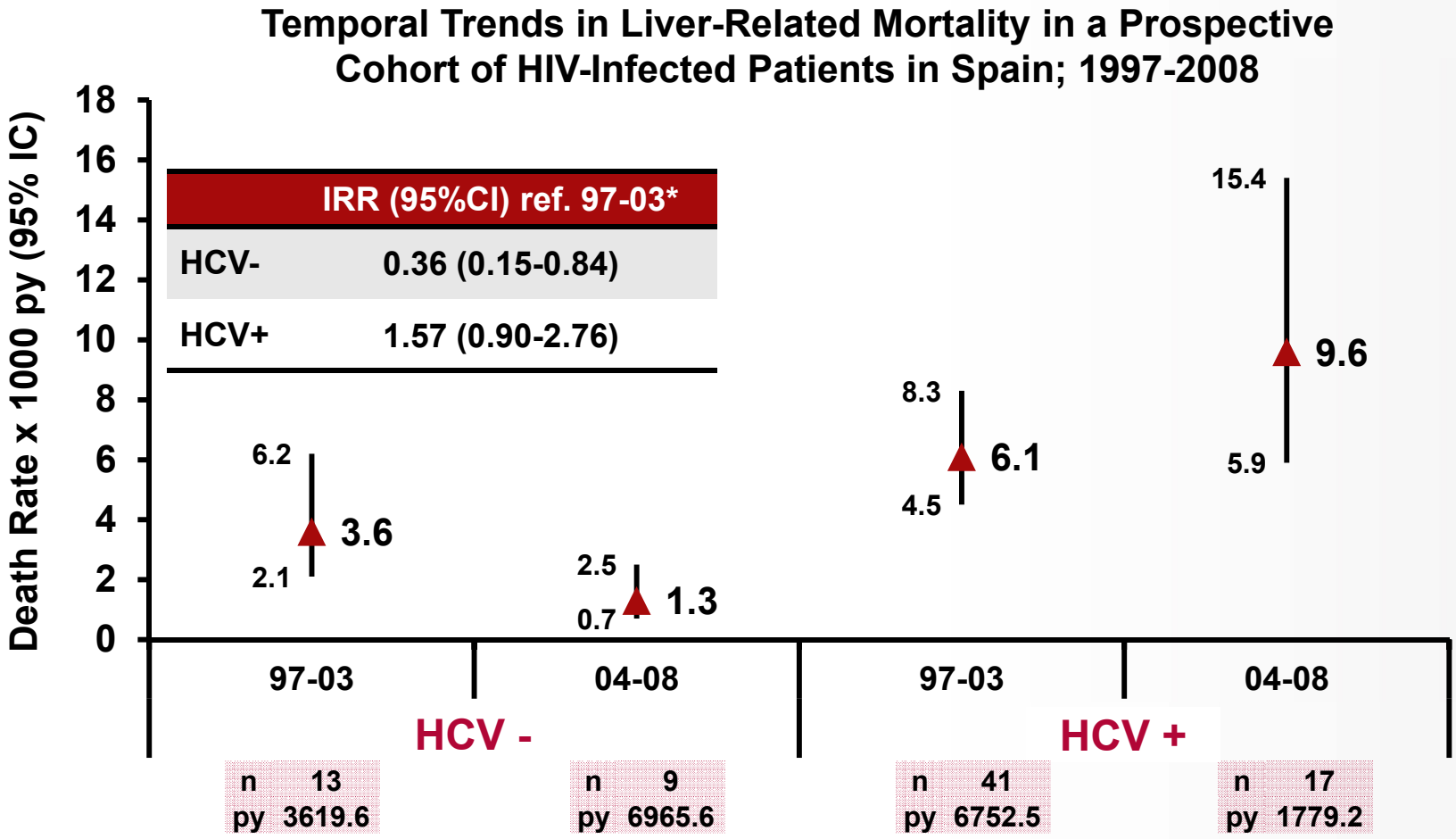
Jointly sponsored by the Postgraduate Institute for Medicine and ViralEd, LLC Supported by an educational grant from Merck & Co., Inc.

Liver-related Death Rates Stratified by HCV-status and Period



*Crude incidence rate ratio (and 95% CI) of death in period 2004-08 taking death rates in 1997-03 as reference

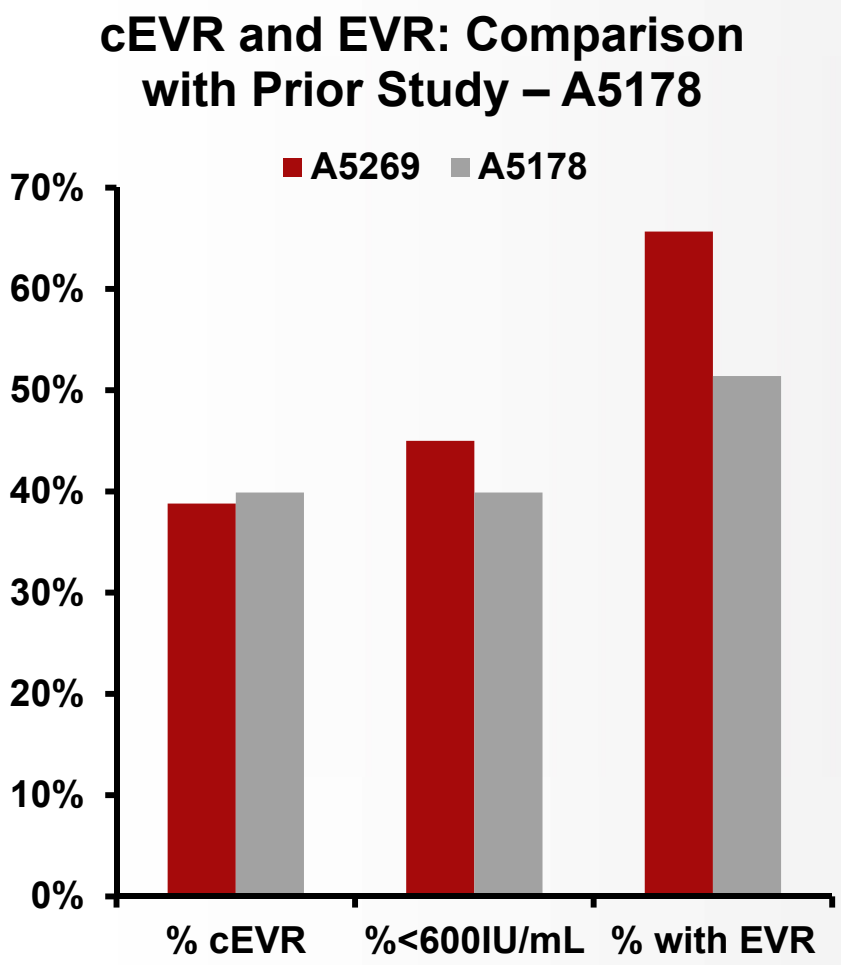
Non–liver-related Non–AIDS-related Death Rates Stratified by HCV-status and Period



*Crude incidence rate ratio (and 95% CI) of death in period 2004-08 taking death rates in 1997-03 as reference

Nitazoxanide Increases Rate of Early Virologic Response When Added to peg-IFN + RBV for HCV Genotype 1 Infection: A5269

- Single arm open label study with historical comparison
- Nitazoxanide 500 mg BID x 4 wks, then add Peg-IFNα-2a + RBV 1000 – 1200 mg QD
- **68 Subjects Enrolled**:
  - 78% men, 48% AA
  - 91% on ART
  - 73% HIV RNA <detectable
- **Response Rates**:
  - RVR – 10.4%
  - cEVR – 38.8%
  - EVR – 65.7%
- **GI Toxicity:** Diarrhea, nausea, vomiting most common
- **Conclusion**: Nitazoxanide can potentiate the effects of IFN+RBV compared to historical populations



Predictors of SVR with Boceprevir-Containing Regimens
Results from the SPRINT-2 and RESPOND-2 Studies (HCV GT 1 Monoinfection)

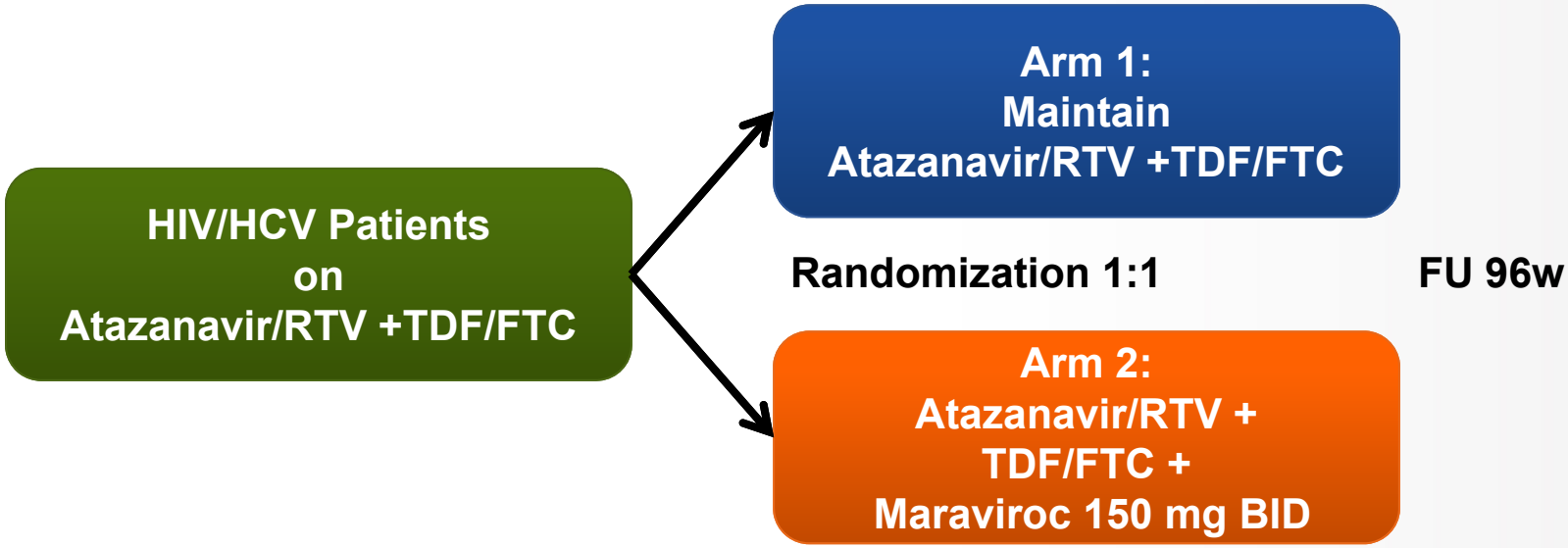
Multiple Stepwise Logistic Regression Model of Predictors of SVR Including Treatment Week 4 Response as an Effect

SPRINT-2: Effect	Odds Ratio (95% CI)	p-value
BOC/PR48 vs PR48	7.0 (4.1, 12.0)	<0.0001
BOC/RGT vs PR48	6.0 (3.5, 10.2)	<0.0001
Baseline HCV-RNA; ≤400,000 vs >400,000 IU/mL	5.8 (1.9, 17.5)	0.002
Log decline in HCV-RNA at TW 4 (continuous variable)	2.6 (2.1, 3.0)	<0.0001
Genotype: 1b/others vs 1a	2.3 (1.5, 3.6)	<0.001
BMI: 25-30 kg/m^2 vs >30 kg/m^2	2.3 (1.4, 3.9)	0.002
BMI: ≤25 kg/m^2 vs >30 kg/m^2	1.9 (1.1, 3.3)	0.02
RESPOND-2: Effect	**Odds Ratio (95% CI)**	**p-value**
BOC/PR48 vs PR48	11.4 (4.6-28.0)	<0.0001
BOC/RGT vs PR48	7.9 (3.3-18.9)	<0.0001
Previous Response: Relapser vs Nonresponder	2.2 (1.2-4.3)	0.01
Log decline in HCV-RNA at TW 4 (continuous variable)	1.8 (1.3-2.4)	<0.0001
BMI: ≤25 kg/m^2 vs >30 kg/m^2	3.4 (1.4-8.2)	0.01

Only covariates remaining significant at α=0.05 after adjustment for the other variables were retained in the model as shown in the table.
In both studies, IL-28B was no longer an important predictor of SVR when lead-in response was considered.

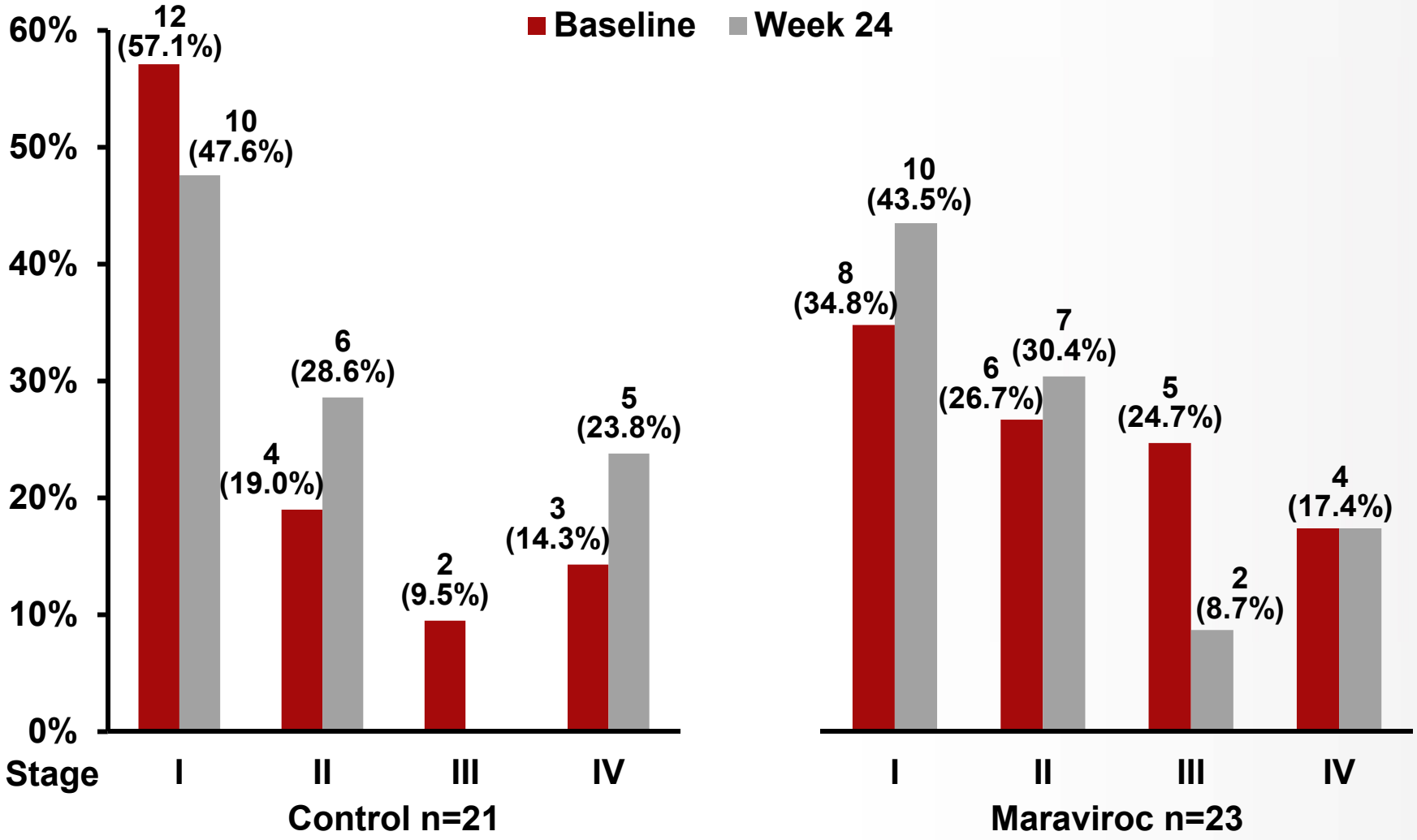
Is CCR5 Inhibition Beneficial for Further Liver Fibrosis Progression in HIV/HCV Coinfected Individuals?

- Phase III, proof of concept, prospective, open label, randomized, controlled trial
- HIV/HCV co-infected subject with undetectable HIV-RNA (< 50 copies/ml)



* Safety analysis of the intervention was planned on the first 60 patients enrolled before continuing enrolment in the study

Change of LS Stage from Baseline to Week 24

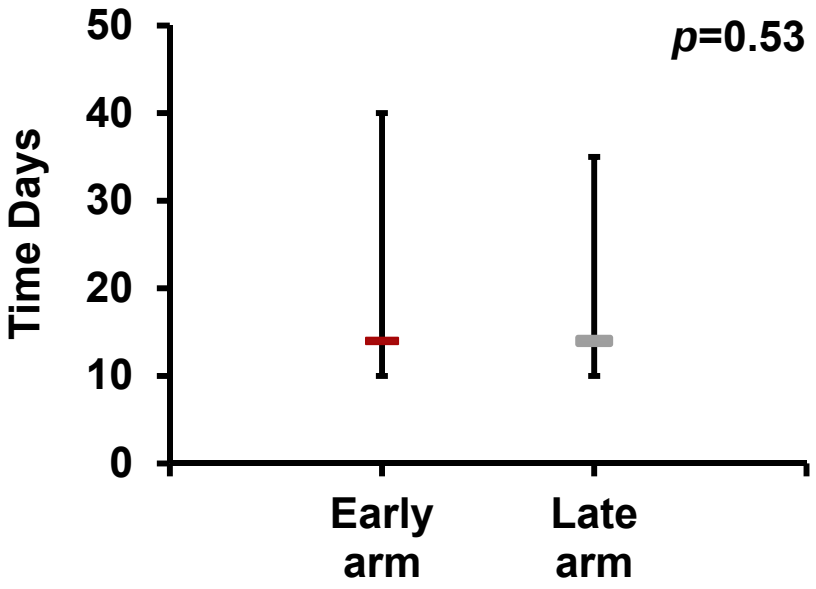


Nasta P, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. WEAB0105.

Incidence & Timing of TB-IRIS in the CAMELIA Study

- TB-IRIS occurred in 155/661 patients (26%)
- Incidence: 3.16 per 100 persons-months (95% CI, 2.7 to 3.7)
- Double the risk of developing TB-IRIS (HR 2.23) when ART initiated at 2 weeks

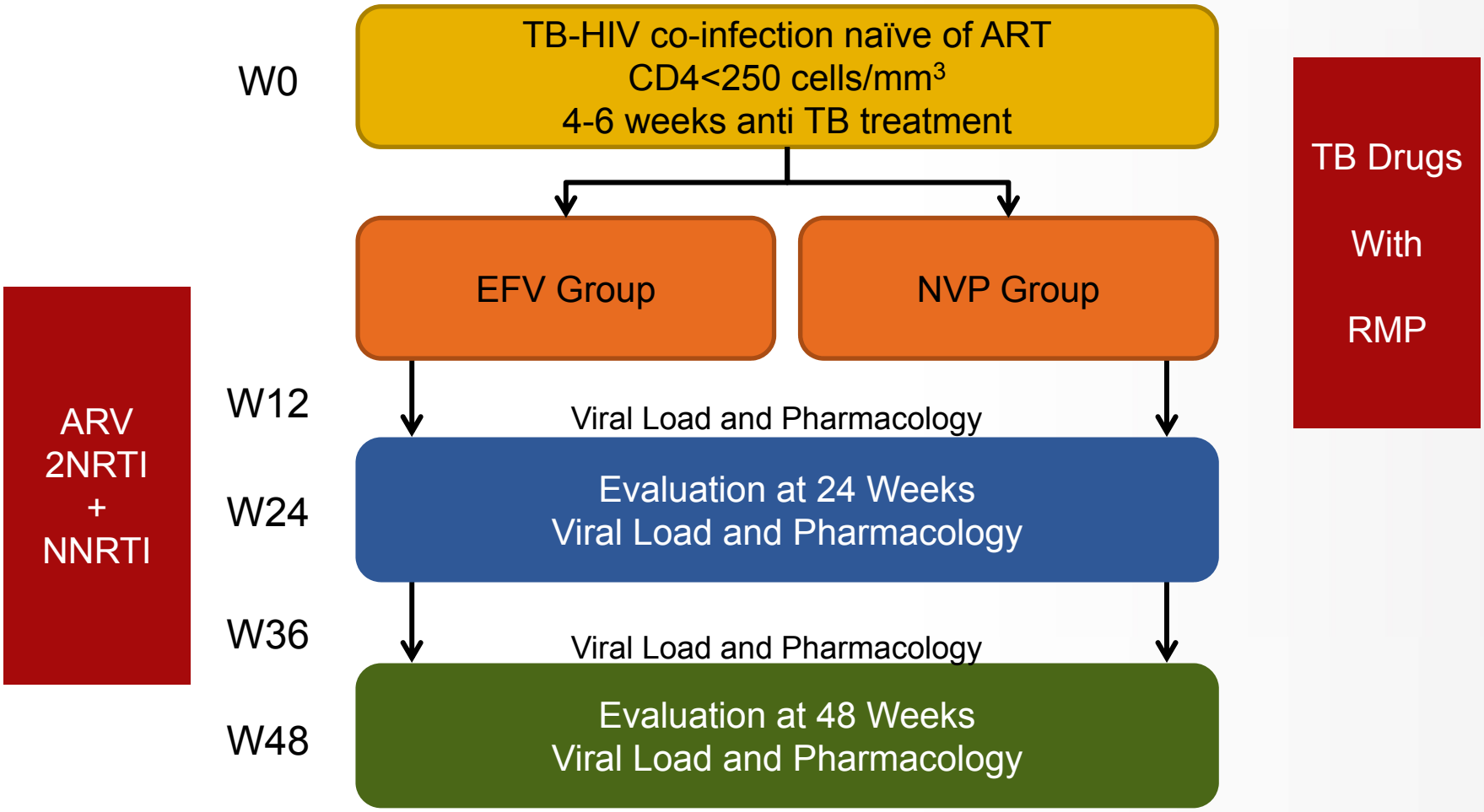
Median time (IQR) of Occurrence



Treatment and Outcome	
Treatment During IRIS	
▪ None	39
▪ Non Steroidal Anti-Inflammatory Drugs	57
▪ Corticosteroids	59
Median time from TB-IRIS to treatment, days	5
IQR	1–14
Outcome	
▪ Cured	148
▪ TB-IRIS Related Death	6
▪ Withdrawal During TB-IRIS	1

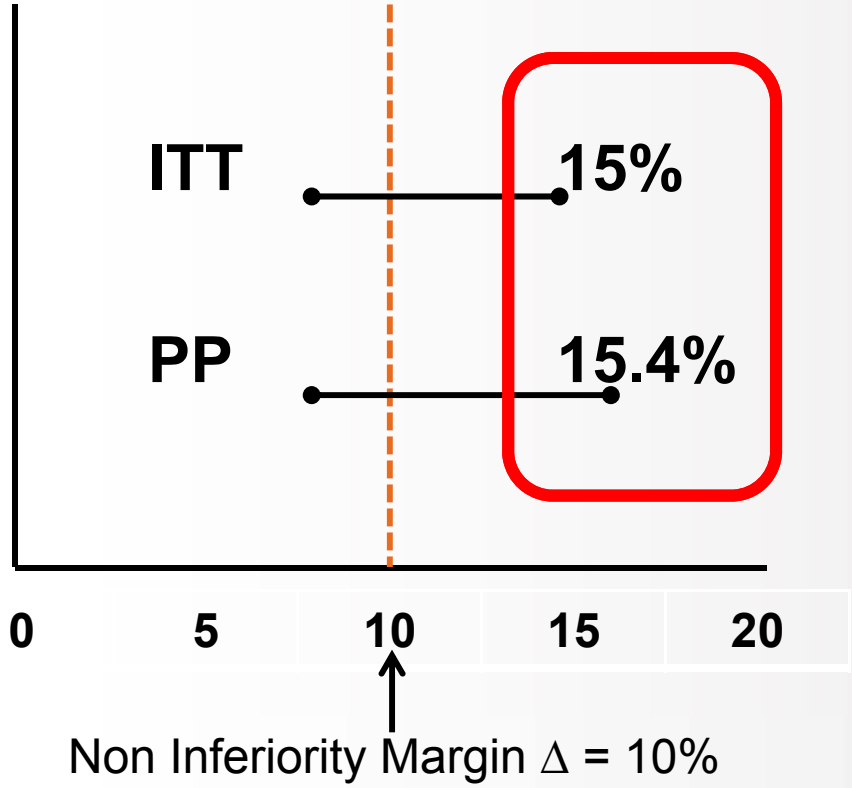
Laureillard D, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. WEAX00104.

CARINEMO-ANRS 12146

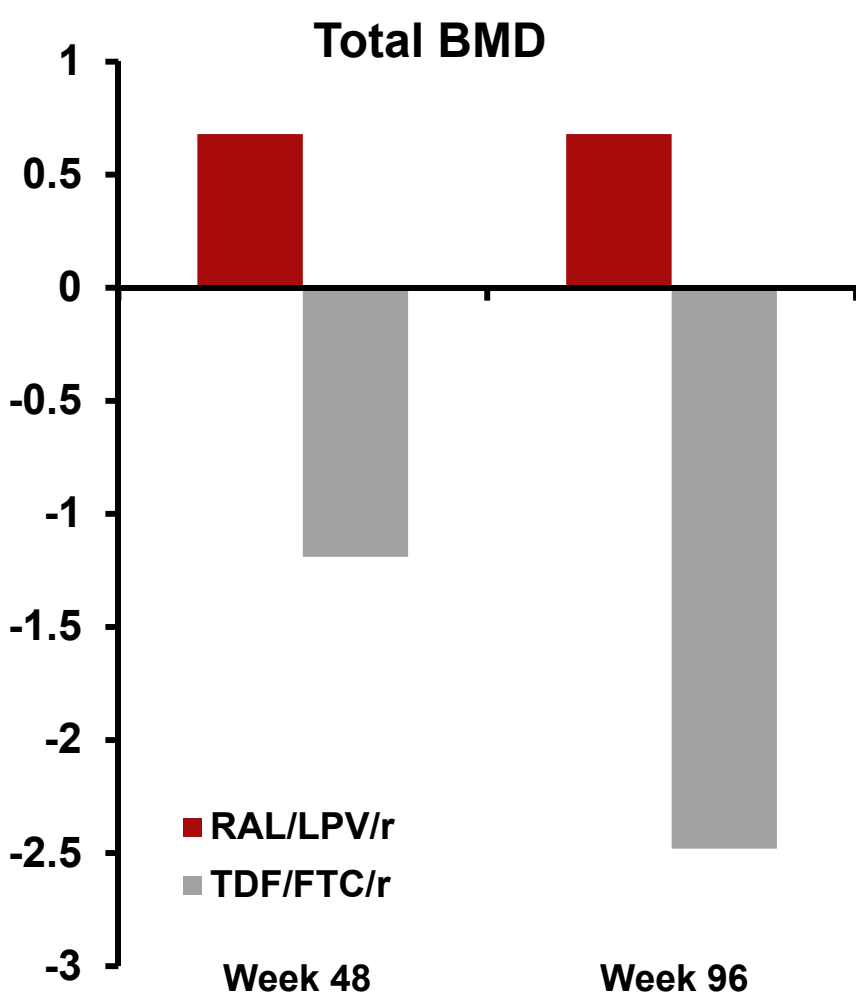


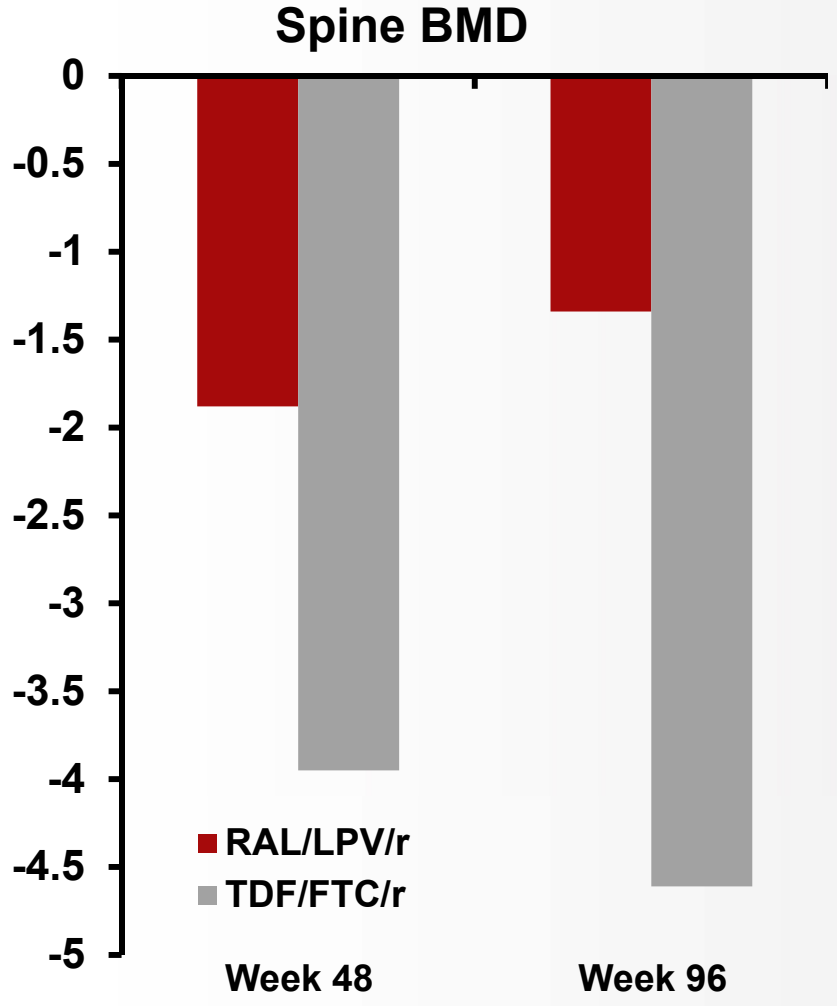
CARINEMO-ANRS 12146

EFV	-	NVP	= Δ
68.4%	-	60%	= 8.4%
(195/285)		(171/285)	
78.9%	-	70%	= 8.9%
(194/246)		(170/243)	



Progress:
BMD Changes by LPV/r + RAL or TDF/FTC





Qaqish RB, et al. ADRC 2011. Abstract O09
Bedimo R, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. TULBPE021

Antiretroviral Exposure and Risk of Osteoporotic Fractures: HAART Era

Veterans Affairs' Clinical Case Registry

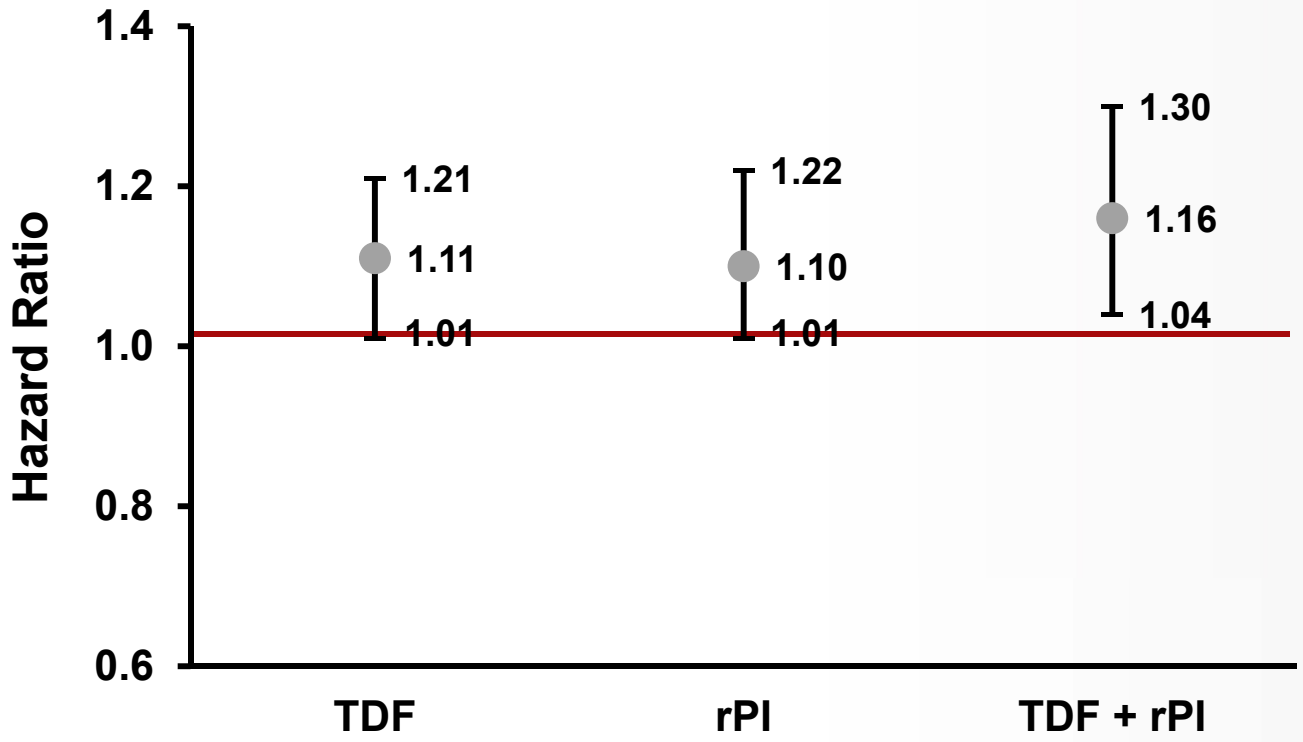
Drug or Drug Category	PY of Exposure	Hazard Ratio per Year of Exposure (95% Confidence Interval; p value)		
		Univariate Analysis	Multi-variable Model 1	Multi-variable Model 2
Tenofovir (TDF)	**38,009**	**1.16 (1.08-1.24; <0.0001)**	**1.13 (1.05-1.21; 0.001)**	**1.12 (1.03-1.21; 0.011)**
Abacavir (ABC)	18,885	0.99 (0.92-1.07; 0.842)	0.96 (0.88-1.04; 0.313)	0.95 (0.87 -1.03; 0.194)
AZT or D4T	68,376	1.02 (0.97-1.06; 0.489)	0.98 (0.93-1.02; 0.289)	0.99 (0.94-1.04; 0.600)
Boosted PI (rPI)	**32,109**	**1.11 (1.05-1.18; 0.001)**	**1.08 (1.01-1.15; 0.026)**	**1.05 (0.97-1.13; 0.237)**
NNRTI	48,943	1.01 (0.96-1.06; 0.771)	0.98 (0.93-1.03; 0.409)	0.98 (0.92-1.03; 0.386)

MV Model 1: Controlling for CKD, age, race, tobacco use, diabetes and BMI;
MV Model 2: Controlling for Model 1 variables + concomitant exposure to other ARVs.

Bedimo R, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. TULBPE021

Interaction Between TDF and PI Exposure for OF Risk: HAART Era

- Concomitant exposure to both TDF and rPI associated with a greater OF risk than exposure to either TDF without rPI or rPI without TDF



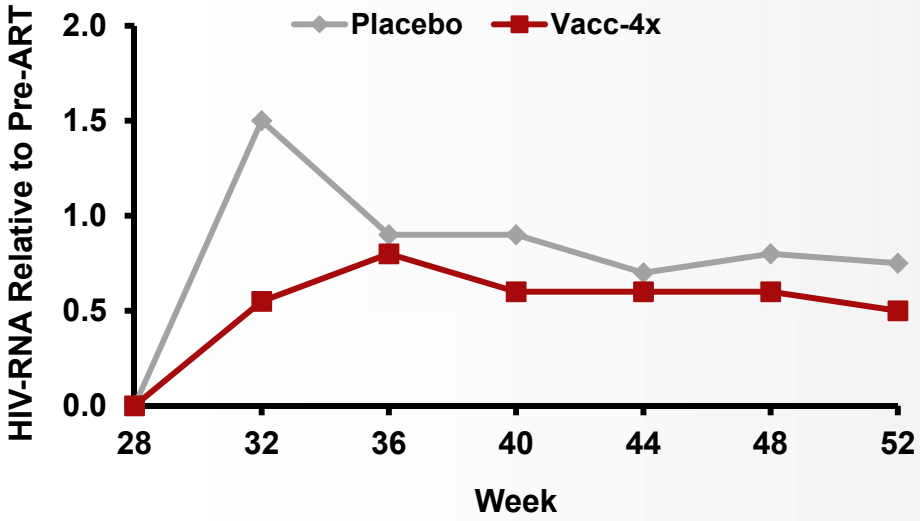
Therapeutic Vaccines – Maybe Possible

- Vacc-4x is peptide vaccine with highly conserved and immunogenic p24 domains
- **Design:** Vacc-4x or placebo (2:1) at weeks 1, 2, 3, 4, 16, 18 with analytical STI at week 28 for up to 24 weeks
  - Treatment resumed for fall in CD4+ count to <350 cells/mm^3
- **Results:**
  - 135 enrolled (92 Vacc-4x, 43 PLC)
  - Vacc-4x safe and well tolerated
- **Conclusion:**
  More effective control of HIV following vaccination

Difference in viral load at week 52:

- 44 Vacc-4x and 18 PLC off ART
- HIV RNA 0.55 $\log_{10}$ c/mL lower in Vacc-4x recipients (p=0.0003)

Trend in Viral Load Set Point Following Treatment Interruption



Rockstroh J, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. TULBPE028

Continuing Medical Education Internet Symposium

The 6th IAS Conference on Pathogenesis, Treatment and Prevention: ARV Therapies and Therapeutic Strategies

Jointly sponsored by the Postgraduate Institute for Medicine and ViralEd, LLC