Continuing Medical Education Internet Symposium

ARV Therapies and Therapeutic Strategies

Reporting From

The Eleventh International Congress on Drug Therapy in HIV Infection (HIV11)

Jointly Sponsored by the Postgraduate Institute for Medicine and ViralEd, LLC.

Supported by an Unrestricted Educational Grant by Gilead Sciences Medical Affairs

CONTINUING MEDICAL EDUCATION INTERNET SYMPOSIUM

ARV THERAPIES AND THERAPEUTIC STRATEGIES

Reporting From

THE ELEVENTH INTERNATIONAL CONGRESS ON DRUG THERAPY IN HIV INFECTION (HIV11)

Jointly Sponsored by the Postgraduate Institute for Medicine and ViralEd, LLC.

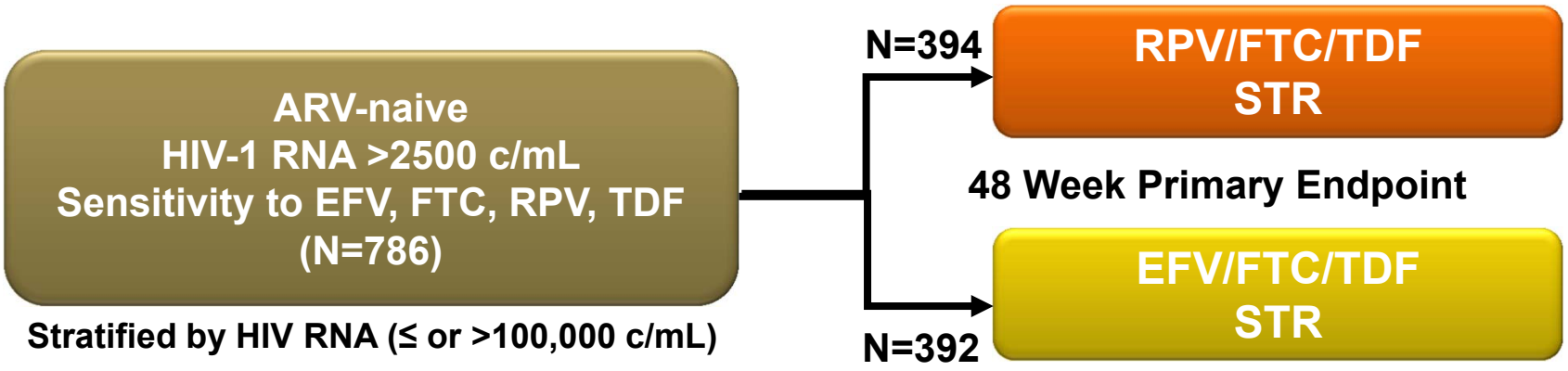
Studies in Treatment Naïve Patients

Calvin Cohen, MD

Boston, MA USA

STaR: Study Design

Multicenter, International, Randomized, Open-label, Phase 3b, 96-Week Study

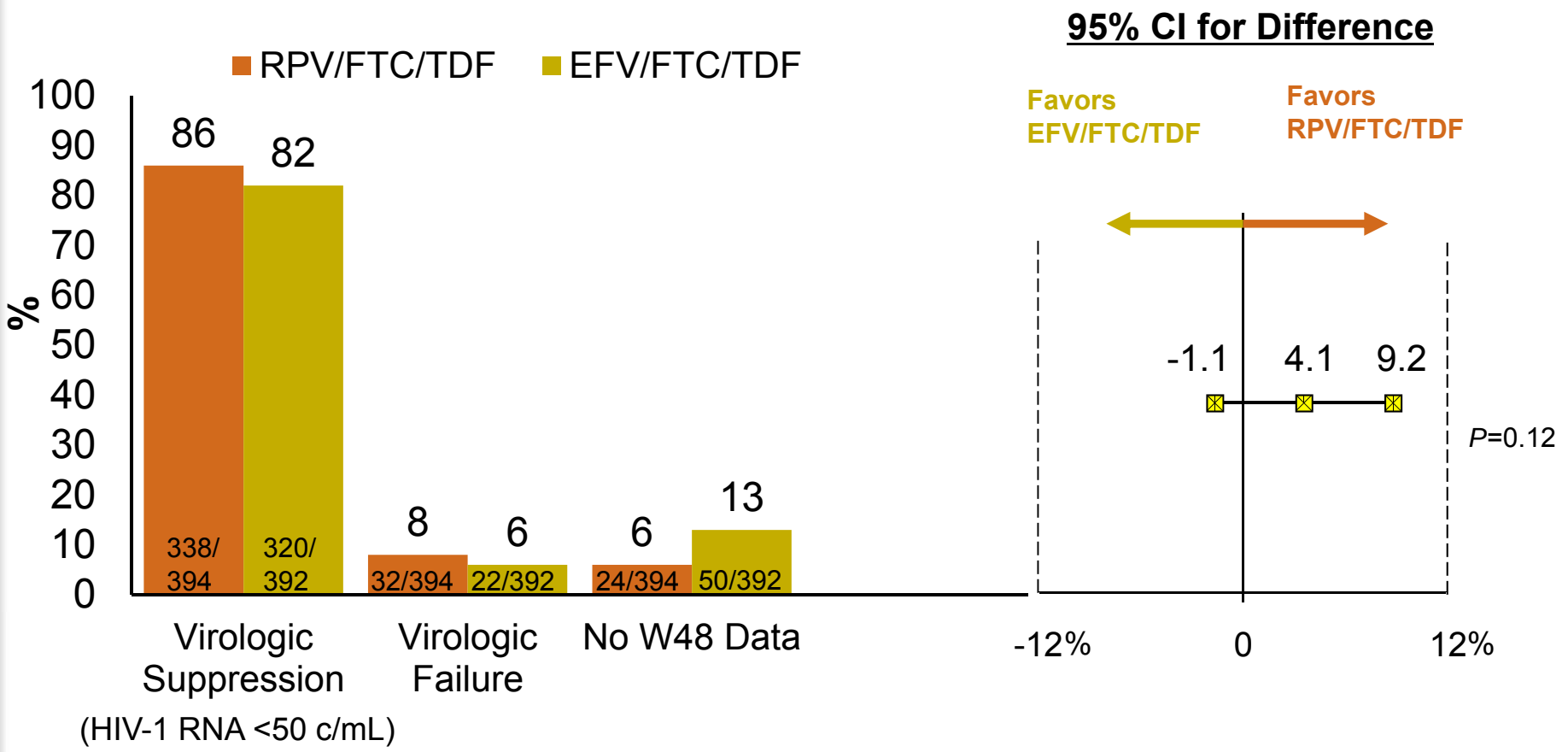


Primary endpoint: % VL <50 c/mL at Wk 48 (FDA Snapshot); 12% non-inferiority

	RPV/FTC/TDF	EFV/FTC/TDF
Median age, years (IQR)	37 (29, 45)	35 (28, 45)
Male	93%	93%
Black race	25%	24%
Latino ethnicity	15%	19%
Mean CD4 cell count, cells/mm^3 (SD)	396 (180)	385 (187)
HIV-1 RNA, $\log_{10}$ c/mL, mean (SD)	4.8 (0.7)	4.8 (0.6)

Cohen C, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O425.

STaR: Virologic Suppression and CD4 Change at Week 48

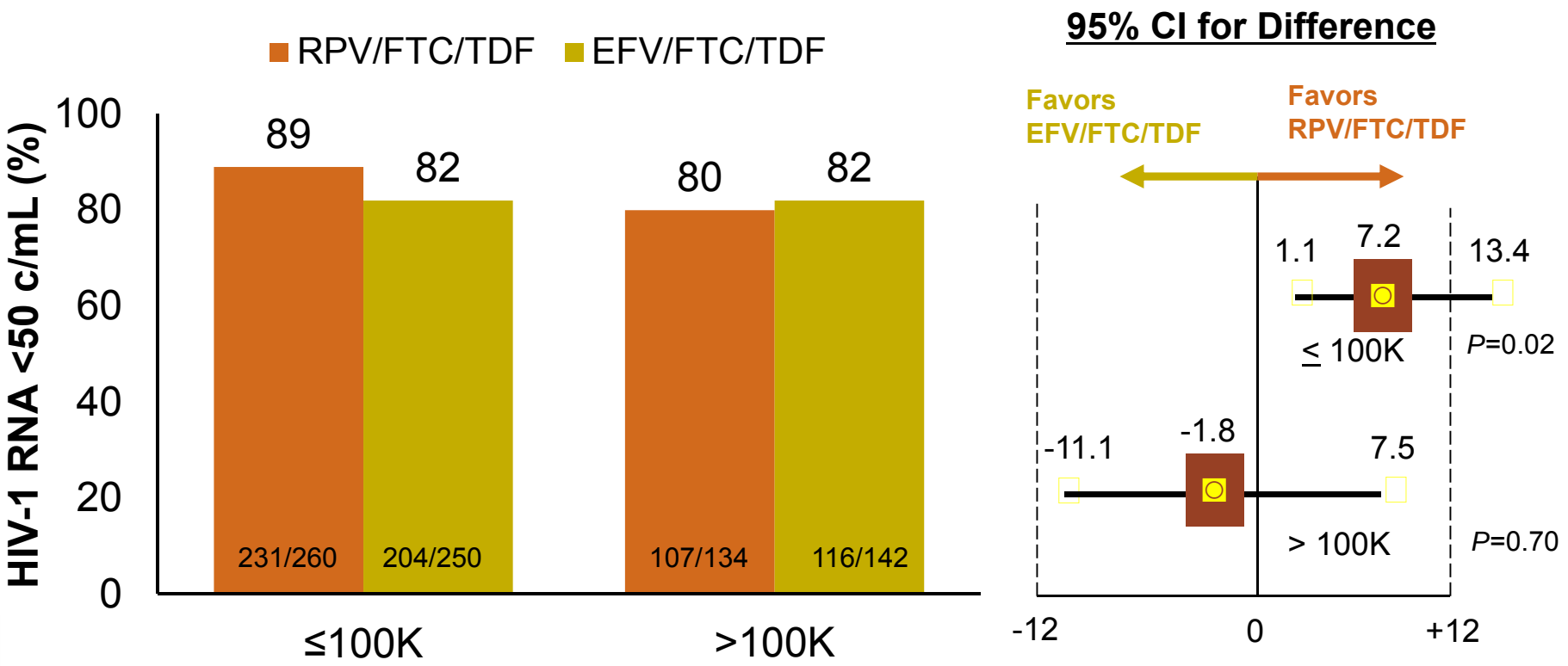


CD4 count change (cells/mm^3): RPV/FTC/TDF +200 vs. EFV/FTC/TDF +191 (*P*=0.34)

FDA Snapshot

Cohen C, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O425.

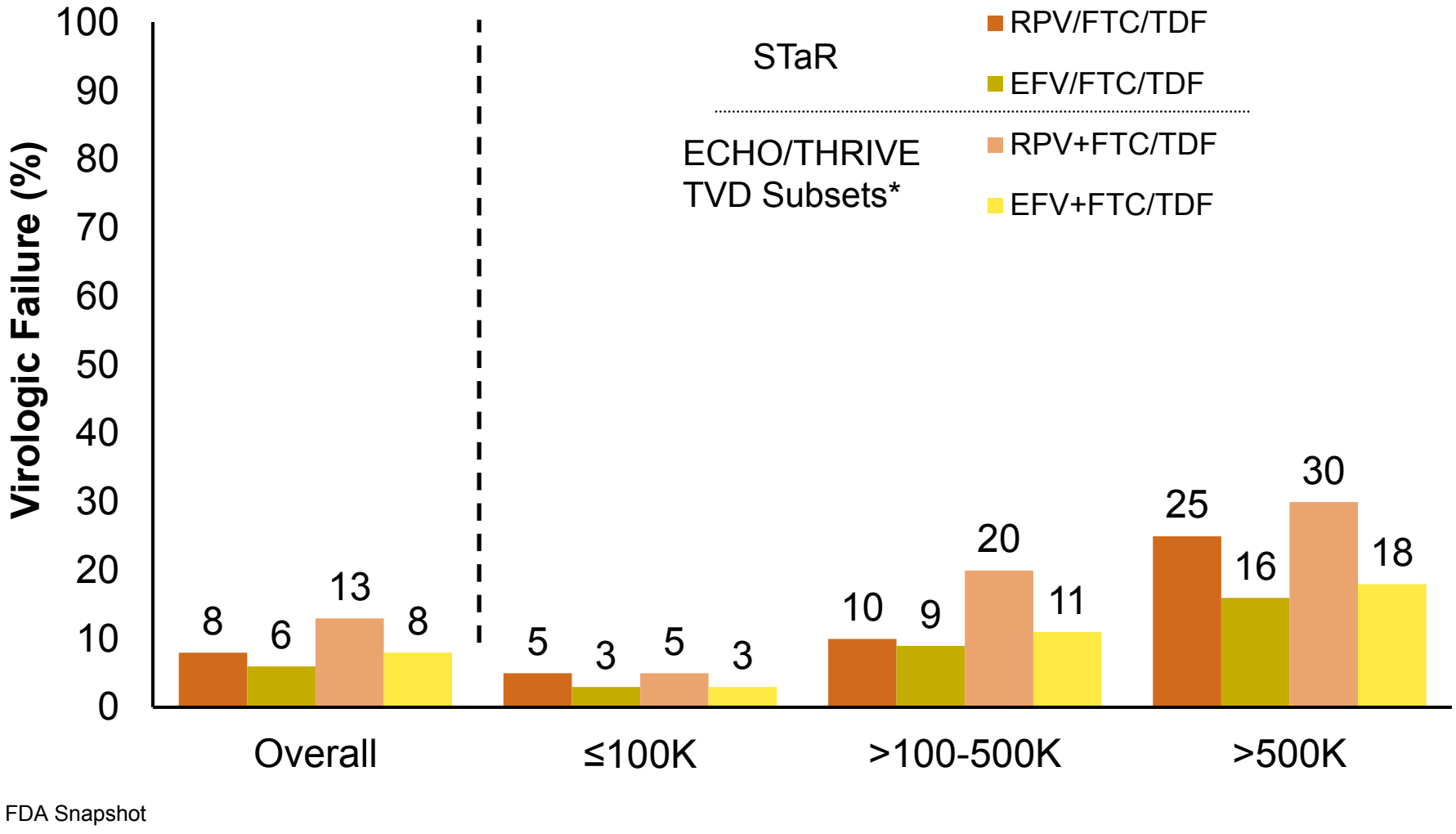
STaR: Week 48 Virologic Suppression by Baseline HIV-1 RNA



Post hoc Analysis of HIV RNA >5 Log:
>100-500K: 83% RPV, 82% EFV. >500K: 72% RPV, 80% EFV

Cohen C, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O425.

STaR & ECHO/THRIVE: Virologic Failure Overall and by Baseline HIV-1 RNA at Week 48



FDA Snapshot

Cohen C, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O425.

STaR: Resistance Analysis Through Week 48

	RPV/FTC/TDF (n=394)	EFV/FTC/TDF (n=392)
Subjects with Resistance Data	5%	2%
Subjects with Resistance to ARVs	4%	1%
Any Primary NNRTI-R	4%	1%
Key NNRTI-R	E138K/Q (2%)	K103N (0.3%)
	Y181C/I (2%)	
	K101E (1%)	
Any Primary NRTI-R	4%	0.3%
Key NRTI-R	M184V/I (4%)	M184I (0.3%)
	K65R/N (1%)	
Within Baseline (BL) HIV-1 RNA		
≤100,000 copies/mL at BL	2%	1%
>100,000–500,000 copies/mL at BL	5%	0
>500,000 copies/mL at BL	19%	4%

Cohen C, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O425.

STaR: Treatment-Emergent Adverse Events

	RPV/FTC/TDF (n=394)	EFV/FTC/TDF (n=392)	
Nervous System Events, n (%)	117 (30%)	198 (51%)	*P*< 0.001
Events >5% difference between arms			
Dizziness, vertigo, balance disorder	30 (8%)	100 (26%)	
Psychiatric Events, n (%)	62 (16%)	147 (38%)	*P*< 0.001
Events >5% difference between arms			
Abnormal Dreams	23 (6%)	96 (25%)	
D/C Due to Adverse Event (AE), n (%)	10 (2.5%)	34 (8.7%)	*P*<0.001

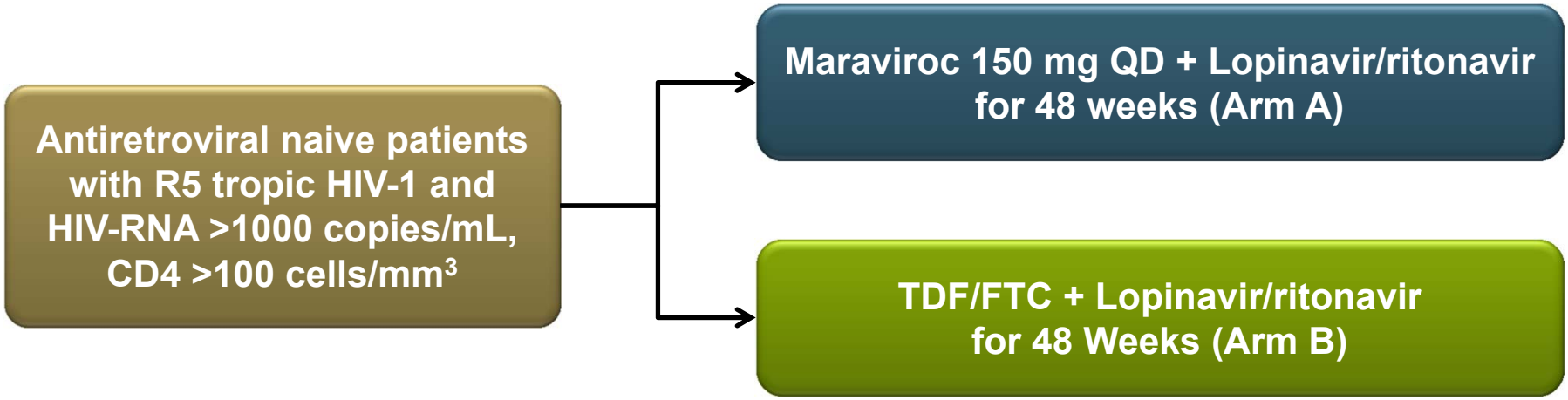
*prespecified evaluation for common adverse events, US Efavirenz Prescribing Information
† 1 (0.3%) suicide occurred in the EFV/FTC/TDF arm, day 36 of study

Cohen C, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O425.

Comparison of LPV/r with MVC or TDF/FTC

Prospective, Open-label, Multi-center, Randomized, Parallel-group, Proof-of-Principle Study

Study Design



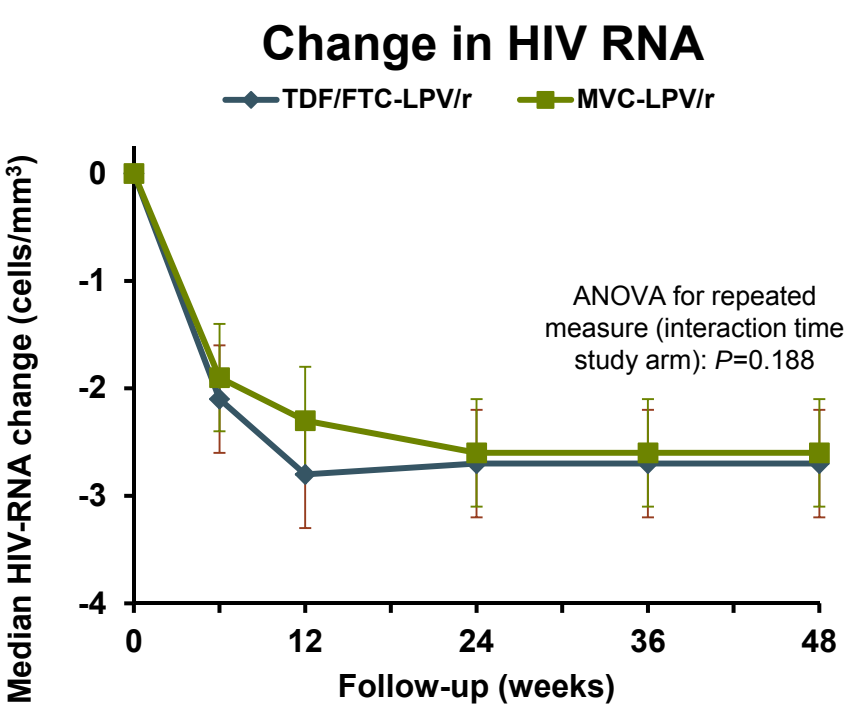
Nozza S, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. P261.

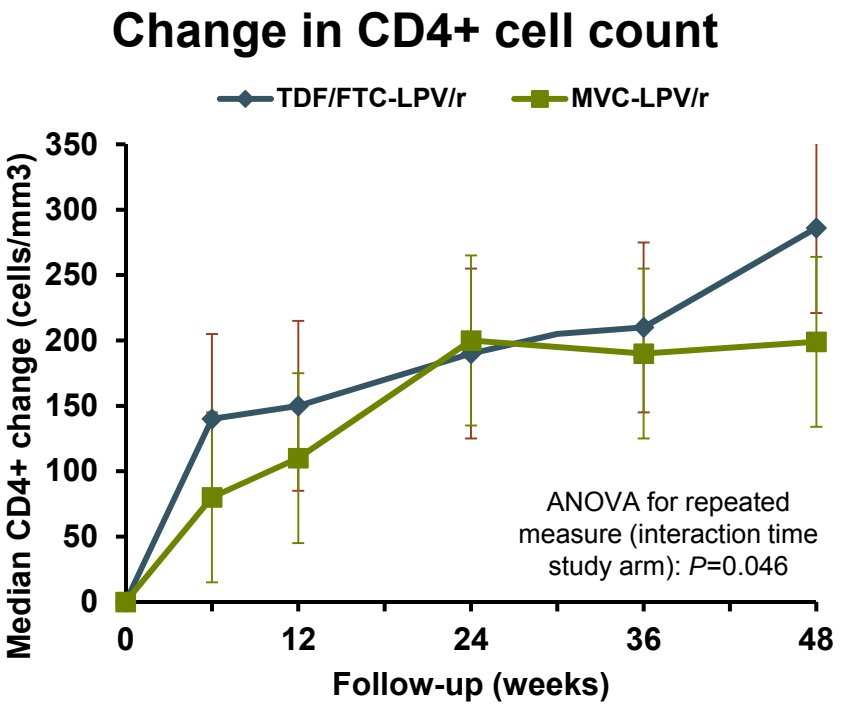
Baseline Characteristics

Baseline Characteristics	Overall (N=50)	MVC+LPV/r (N=26)	TDF/FTC+LPV/r (N=24)	*P*-value
Gender, No. (%)				
Male	48 (96%)	25 (96.2%)	23 (95.8%)	0.999
Female	2 (4%)	1 (3.8%)	1 (4.2%)	
Age at last visit, years (range)	39.1 (32.4-44)	38.9 (34.2-44)	39.4 (34.3-43.5)	0.961
Risk Factors, No.(%)				
MSM	38 (76%)	19 (73.1%)	19 (79.2%)	0.745
Heterosexual	12 (24%)	7 (26.9%)	5 (20.8%)	
HIV-infection, years (range)	2.9 (0.8-5.3)	2.9 (0.6-7.2)	2.9 (0.9-4.6)	0.459
Nadir CD4+, cells/mm^3 (range)	266 (242-315)	269 (249-321)	263 (230-308)	0.547
CD4, cells/mm^3 (range)	295 (260-369)	292 (261-359)	297 (257-373)	0.676
CD4, % (range)	18.8 (14.6-23)	19.5 (16.3-24.3)	18.8 (14.3-22.3)	0.756
CD4/CD8 (range)	0.33 (0.25-0.47)	0.35 (0.25-0.48)	0.33 (0.28-0.4)	0.793
HIV-RNA, $\log_{10}$copies/ml (range)	4.41 (3.96-4.8)	4.42 (4.07-4.84)	4.41 (3.84-4.76)	0.420

Nozza S, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. P261.

Virological and Immunological Results

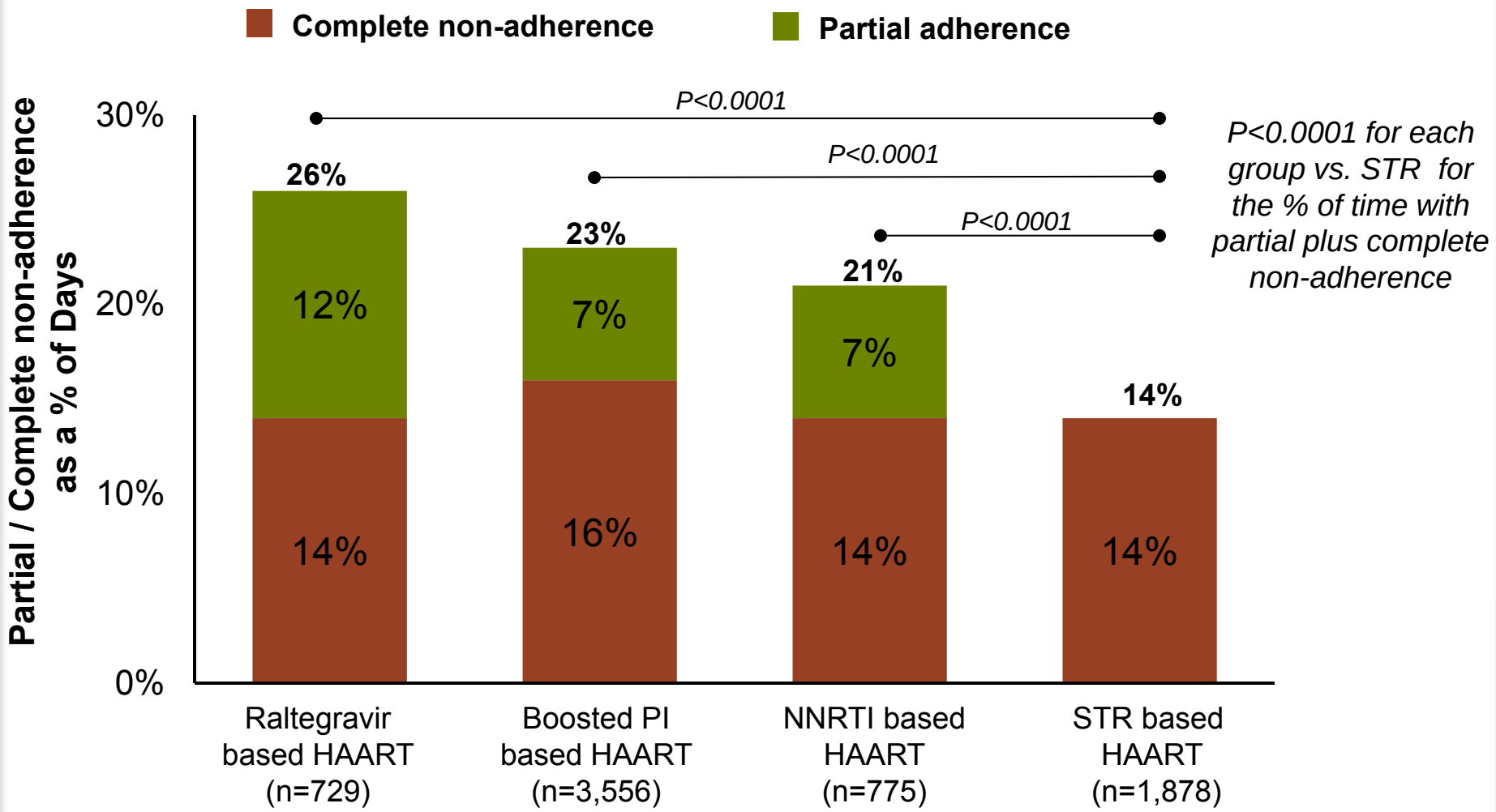




Graph Bars are IQR

Nozza S, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. P261.

Partial and Complete Non-Adherence to ART



Cohen C, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. P001.

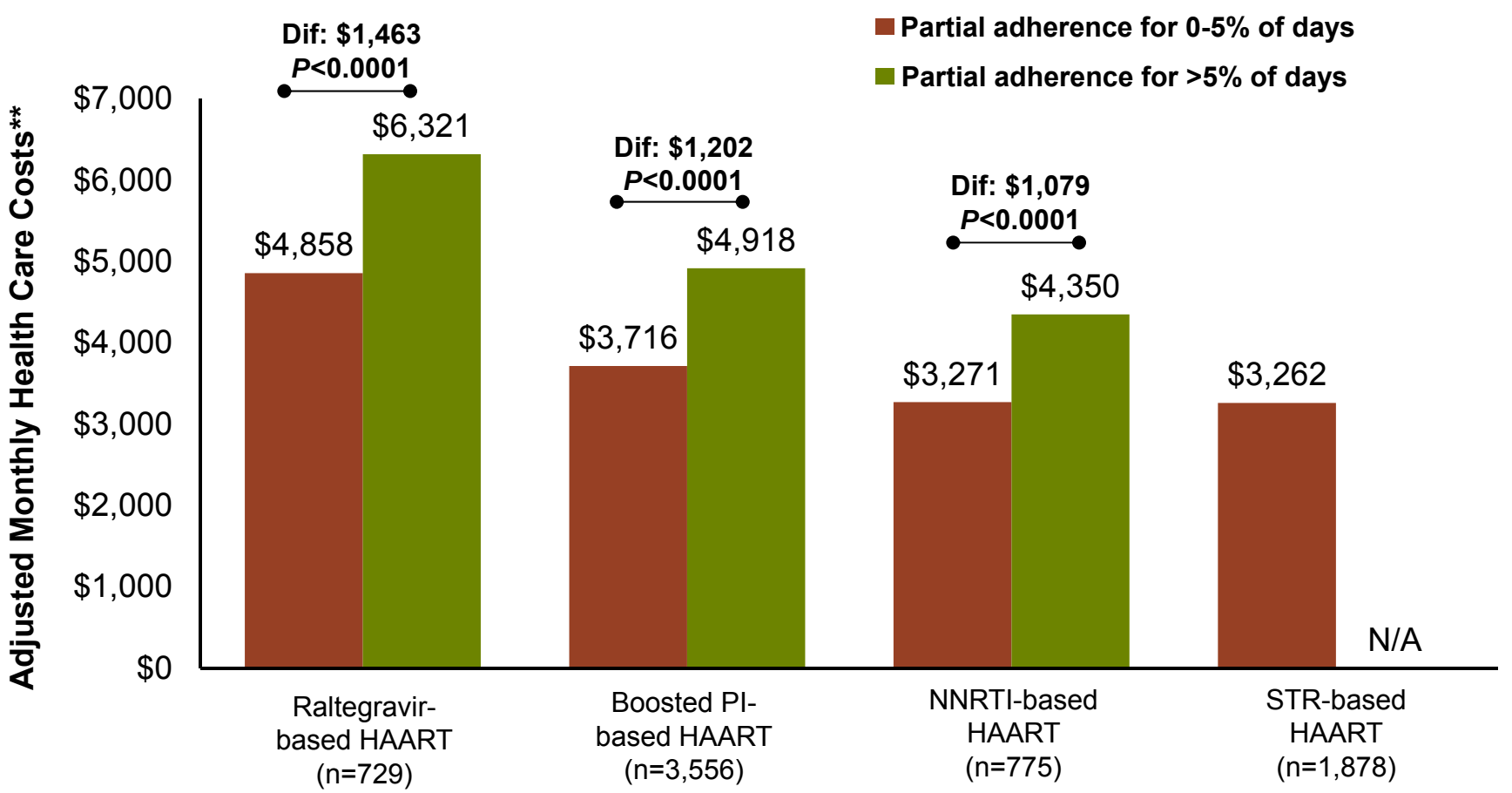
Partial and Complete Non-Adherence and Risk of Hospitalization

Variable	Odds Ratio	Lower 95% CI	Upper 95% CI	*P*-value
Partial adherence (vs. 0 to 10 days)				
10 to 20 days	1.06	0.79	1.41	0.71
20 to 30 days	1.34	1.02	1.76	0.04
30 to 40 days	1.61	1.16	2.23	0.004
40 to 50 days	1.71	1.17	2.50	0.005
Greater than 50 days	1.74	1.45	2.09	<0.0001
Complete non-adherence (vs. 0 to 10 days)				
10 to 20 days	1.25	0.99	1.57	0.055
20 to 30 days	1.45	1.14	1.84	0.002
30 to 40 days	1.48	1.15	1.89	0.002
40 to 50 days	1.84	1.43	2.36	<0.0001
Greater than 50 days	1.99	1.66	2.40	<0.0001

Additional covariates included race, gender, treatment naïve vs. experienced status, regimen length, and third component

Cohen C, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. P001.

Association of Partial Adherence and Health Care Costs Per Month



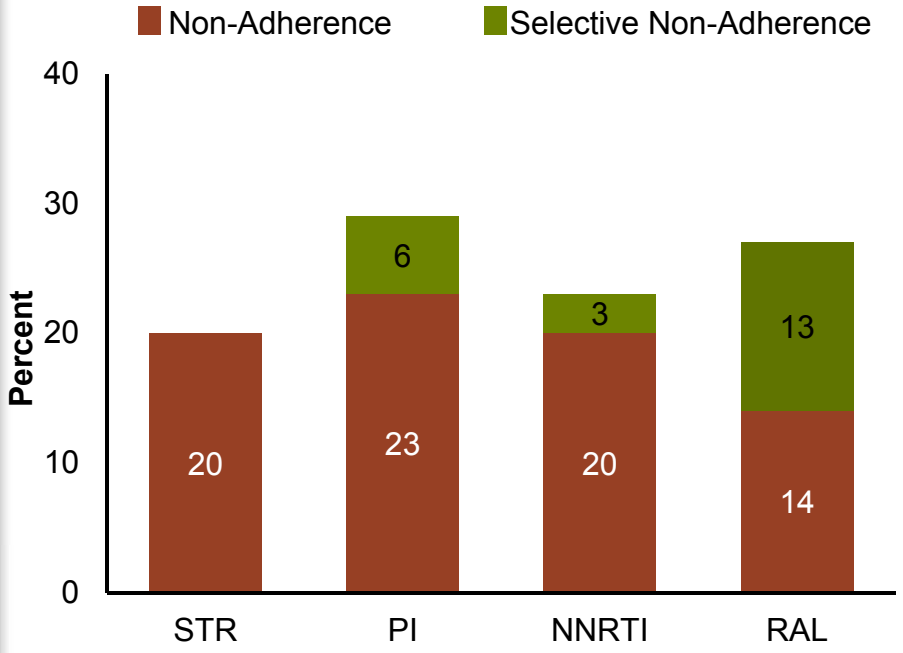
* Partial Adherence: Patients with at least 5% of days with either no NRTIs or no 3rd agents.
** Adjusted for differences between groups including complete non-adherence, treatment status at index, age, geographic location, plan and types.

Cohen C, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. P001.

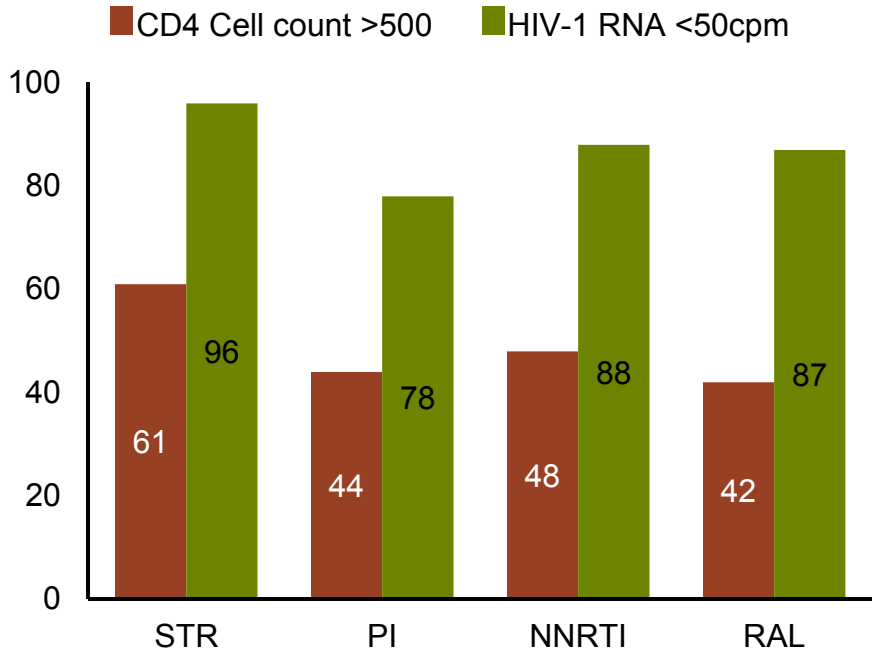
COMPACT: Adherence on Single-Tablet (STR) or Multi-Pill Regimens

Retrospective, Observational Cohort Analysis in 1,604 HIV+ Patients (2008-2010)

Non-Adherence to cART Regimens



Viral Load and CD4 at Follow-Up



Antinori A, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. P14.

Clinical Impact of Incomplete Adherence: Probability of Rebound Viremia

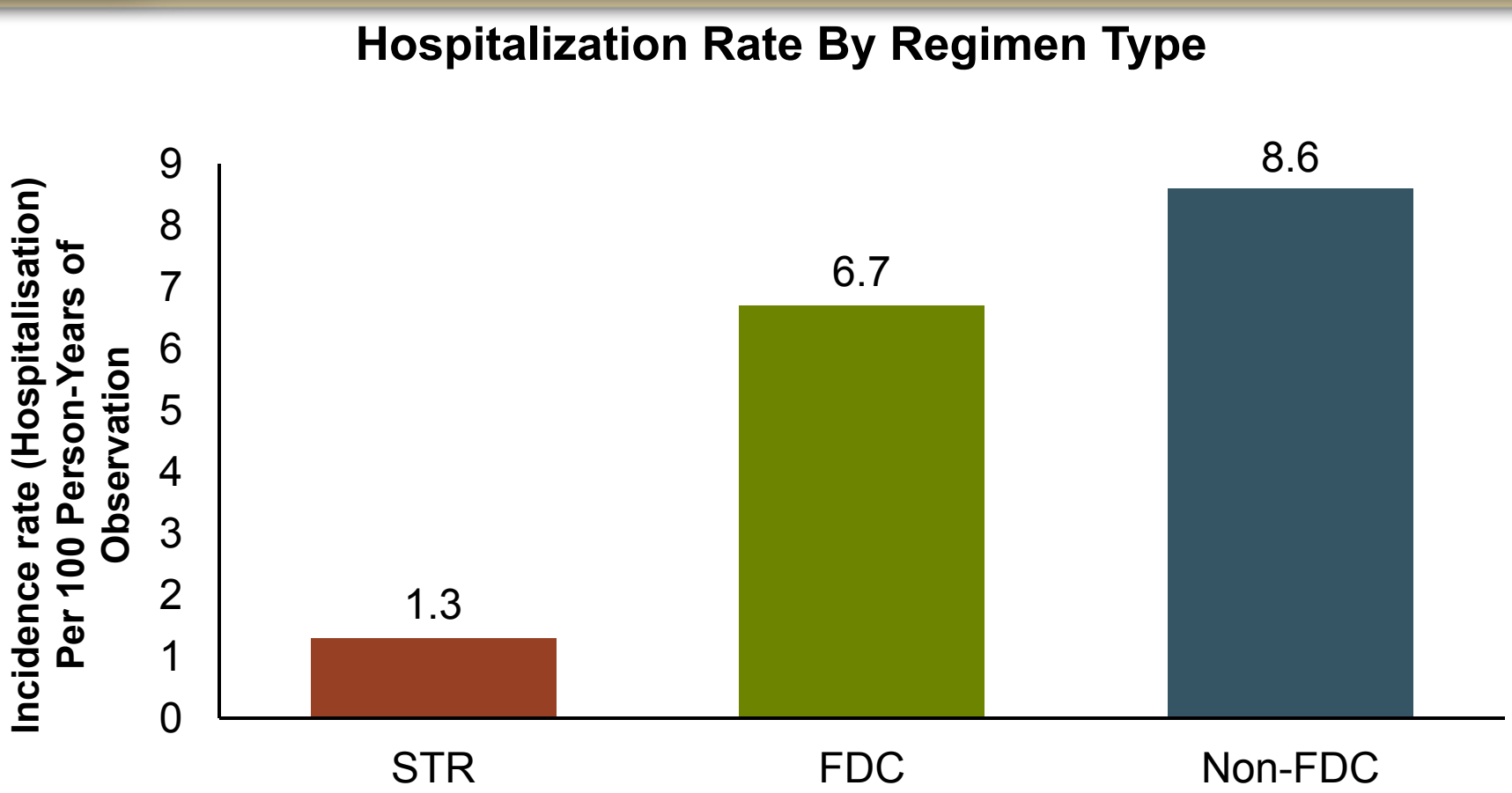
Retrospective Cohort Analysis of HIV-1+ Patients between 2001 and 2011 (n=1436)

Odds Ratio (OR) for Rebound Viremia

Variable	OR	*P*-value
Complete non-adherence	1.037	<0.001
Selective non-adherence	1.025	0.020
Regimen duration (days)	1.227	<0.001
Calendar year	0.915	0.025

Vera J, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. P5c.

Adherence: Clinical and Economic Outcomes



STR associated with a €1,330 (~$1702) reduction in annual ART + hospitalization costs vs. not being on STR

Vera J, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. P5c.

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Discussion

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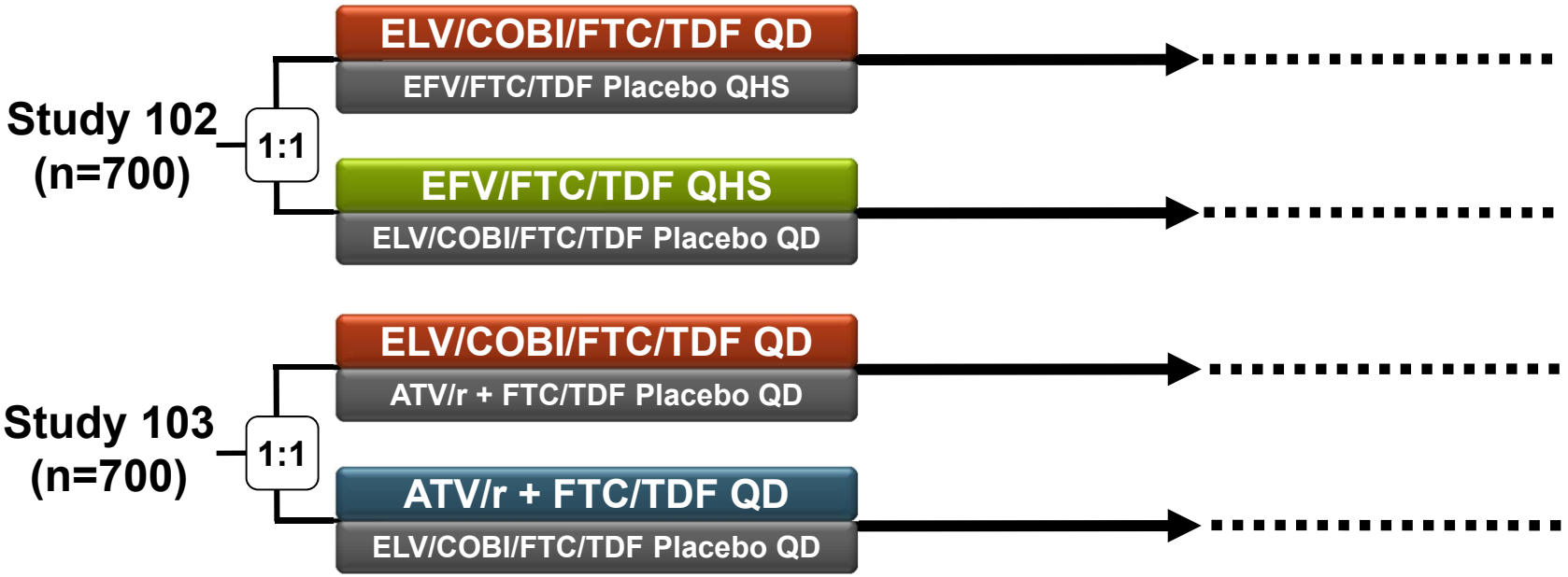
New ARVs for Treatment Naïve Patients

Andrew Zolopa, MD

Palo Alto, CA USA

Studies 102 and 103: ELV/COBI/FTC/TDF vs. EFV/FTC/TDF or ATV/r + FTC/TDF

Randomized, double-blind, double dummy, active-controlled studies
Treatment Naïve Patients with HIV-1 RNA ≥ 5000 c/mL
Any CD4 cell count, eGFR ≥ 70 mL/min



Studies to be continued blinded through Week 192

Zolopa A, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O424A. Rockstroh J, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O424AB

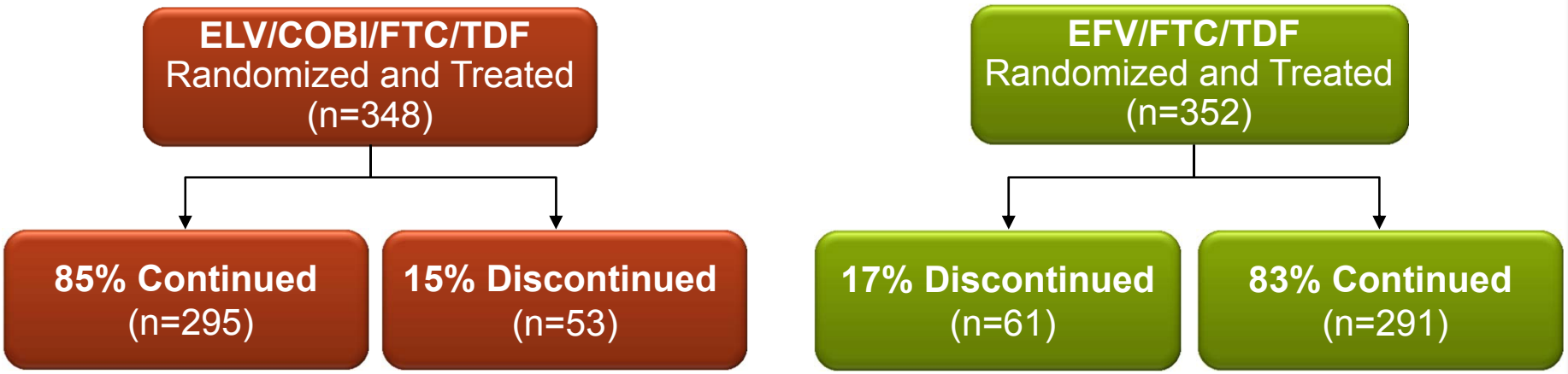
Study 102: Baseline Characteristics

Characteristic	ELV/COBI/FTC/TDF (n=348)	EFV/FTC/TDF (n=352)
Age (years), Mean	38	38
Male	88%	90%
Non-White	39%	36%
Black or African Descent	30%	26%
Asymptomatic HIV Infection	83%	84%
HBV; HCV Seropositive*	1%; 5%	3%; 4%
HIV-1 RNA (log_{10}c/mL), Median	4.75	4.78
≤100,000 c/mL	66%	67%
>100,000 c/mL	34%	33%
CD4 count (cells/µL), Mean	391	382
≤200	12%	14%
201 to≤ 350	32%	27%
>351	55%	58%
eGFR (mL/min), Median (Cockcroft Gault)	115	114

*Positive HBV surface antigen or HCV antibody

Zolopa A, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O424A.

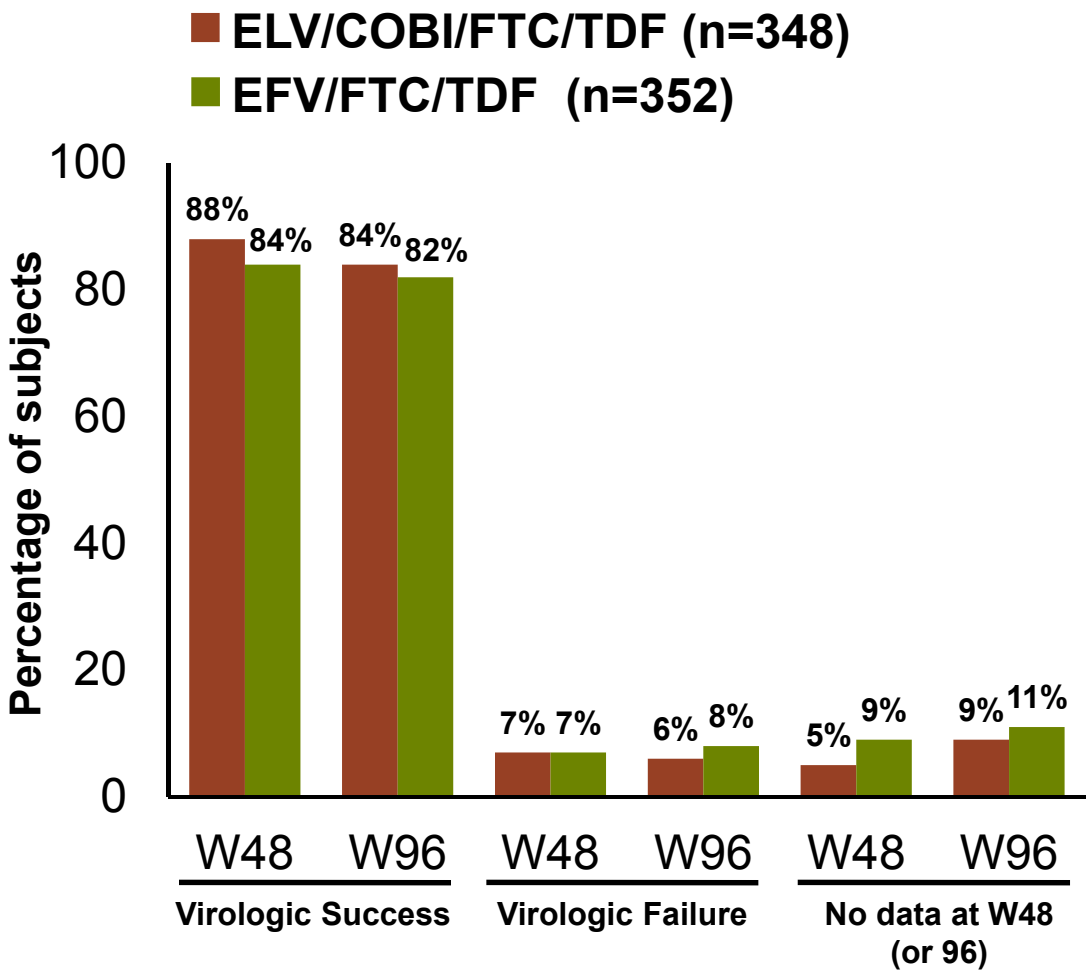
Study 102: Subject Disposition Through Week 96

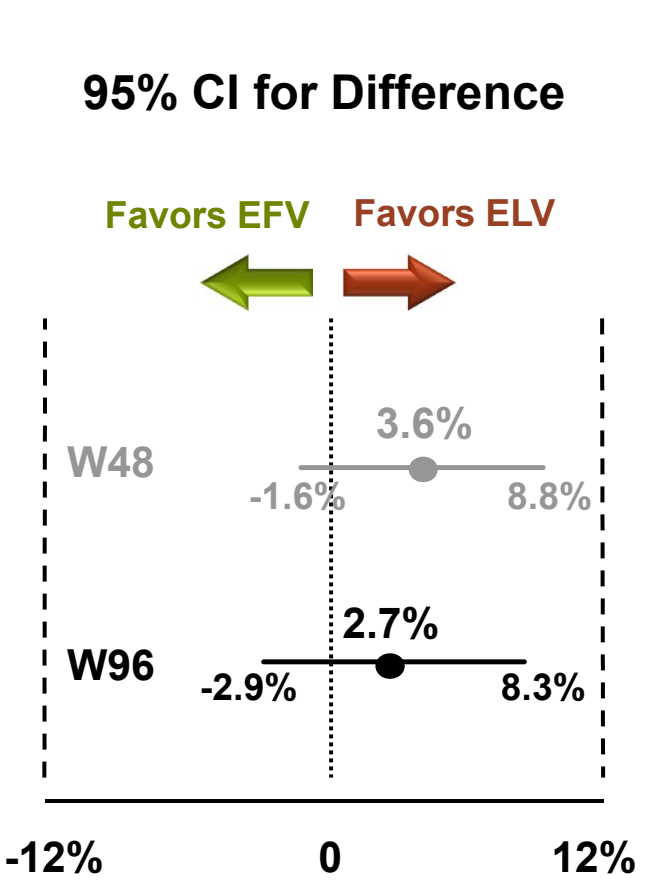


Number of Patients		
16	Adverse event	24
17	Lost to follow-up	17
6	Lack of efficacy	5
5	Non-compliance	7
3	Withdrew consent	7
2	Investigator discretion	0
1	Death	1
2	Pregnancy	0
1	Protocol violation	0

Zolopa A, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O424A.

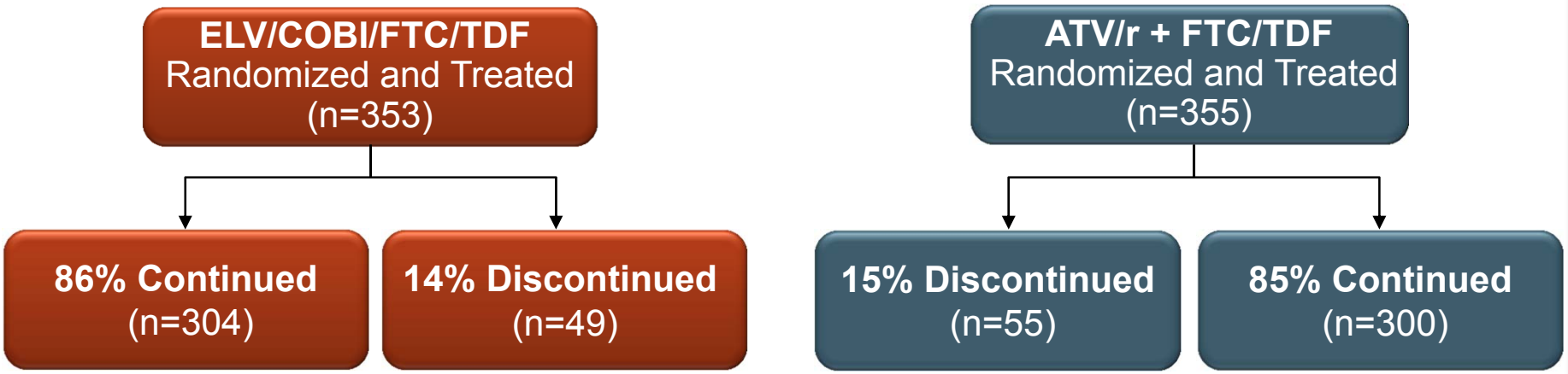
Study 102: HIV-1 RNA <50 c/mL at Weeks 48 and 96





Zolopa A, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O424A.

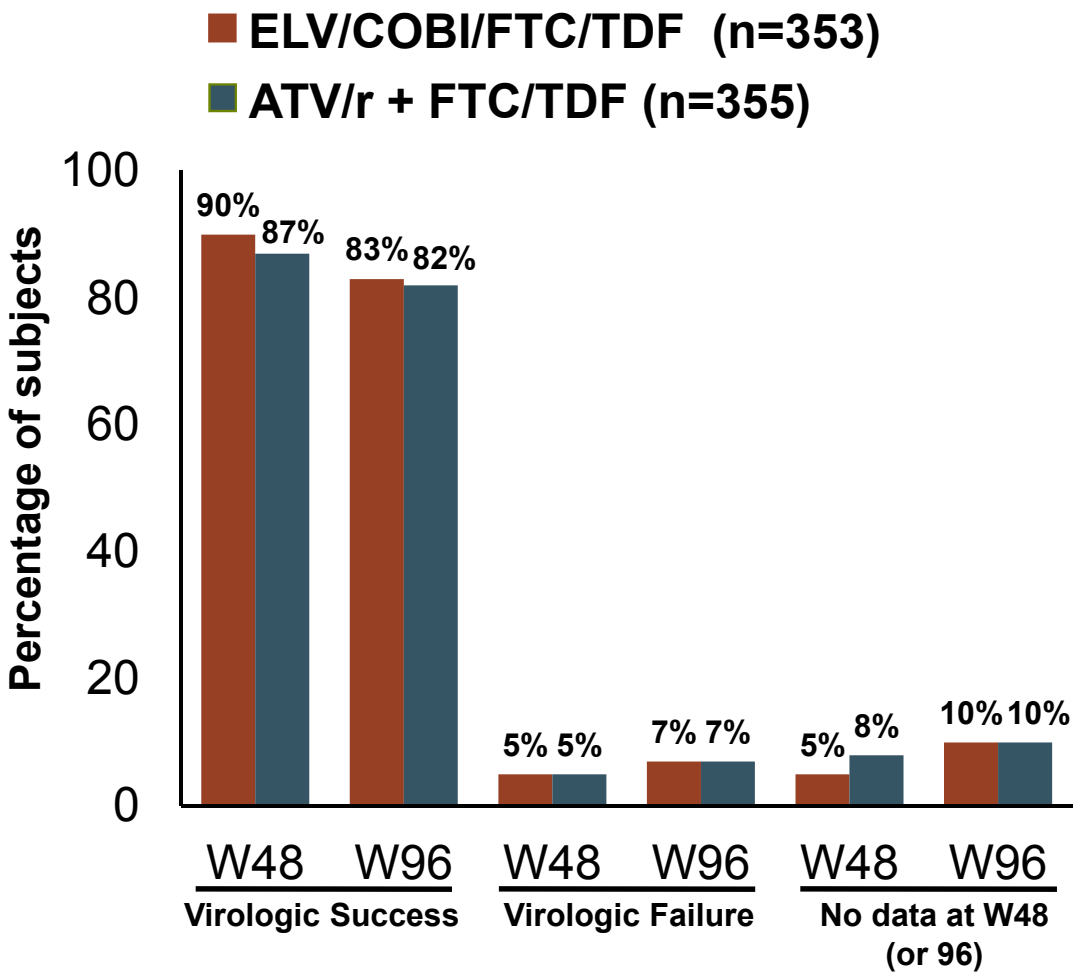
Study 103: Subject Disposition Through Week 96

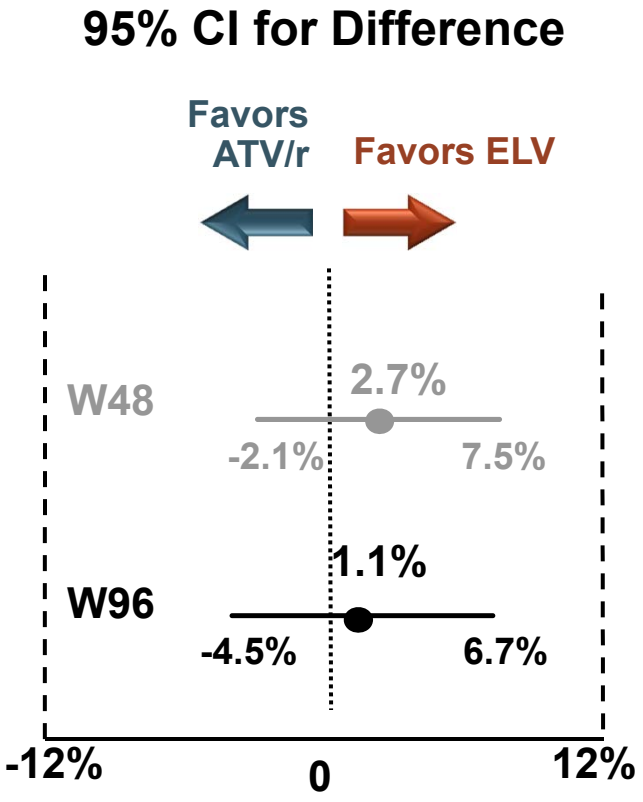


Number of Patients		
15	Adverse event	21
10	Lost to follow-up	10
4	Lack of efficacy	1
9	Non-compliance	6
3	Withdrew consent	11
4	Investigator discretion	5
3	Pregnancy	1
1	Protocol violation	0

Rockstroh J, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O424AB

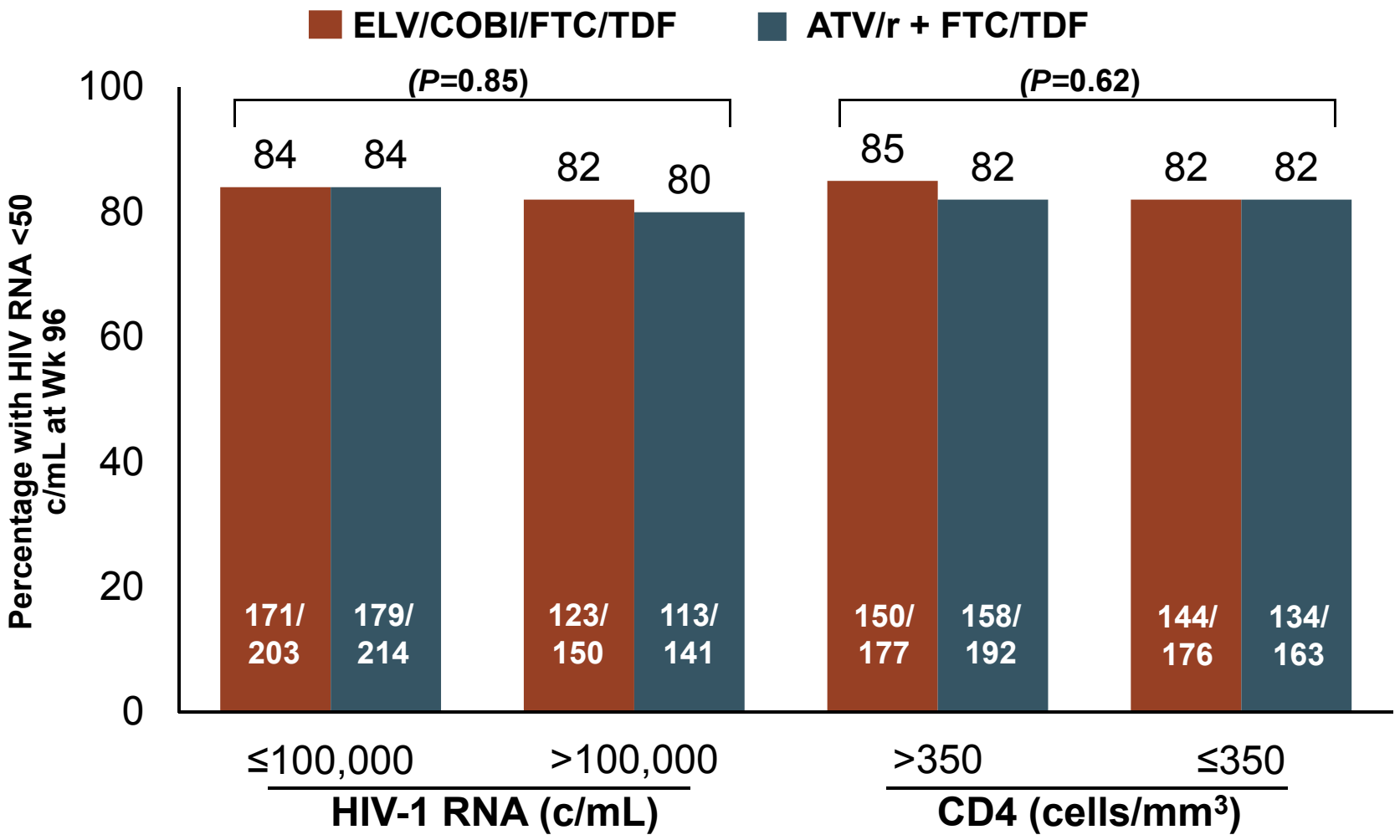
Study 103: HIV-1 RNA <50 c/mL at Weeks 48 and 96





Rockstroh J, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O424AB

Study 103: HIV RNA < 50 c/mL by Baseline HIV-1 RNA and CD4 Subgroups at Week 96



Rockstroh J, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O424AB

Study 102: Integrase, NNRTI, NRTI Resistance at Weeks 48 and 96

	ELV/COBI/FTC/TDF (n=348)			EFV/FTC/TDF (n=352)	
	W48	W96		W48	W96
Emergent Resistance, n (%)	8 (2%)	+2 (+1%)		8 (2%)	+2 (+1%)
Primary INSTI-R or NNRTI-R, n (%)	7 (2%)	+2(+1%)		8 (2%)	+2 (+1%)
E92Q	7	0	K103N	7	+2
N155H	1	+2	K101E/K	3	0
Q148R	1	0	M230L	2	0
			Y188F/H/L	1	+1
			G190A/S	1	0
Primary NRTI-R, n (%)	8 (2%)	+2(+1%)		2 (1%)	+1 (+0.3%)
M184V/I	8	+2	M184V/I	2	+1
K65R	3	+1	K65R	2	+1

Zolopa A, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O424A.

Study 102: Summary of Adverse Events at Weeks 48 and 96

	ELV/COBI/FTC/TDF (n=348)		EFV/FTC/TDF (n=352)	
	W48	W96	W48	W96
Any Grade	94%	+3%	95%	+2%
Related to study drug	46%	+2%	67%	+1%
Grade 2 to 4	55%	+9%	55%	+9%
SAE	12%	+4%	7%	+3%
AE leading to study drug DC	4%	+1%	5%	+2%
Death*, n	1	0	2	0

*Causes of death included suicide and metastatic carcinoma

Zolopa A, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O424A.

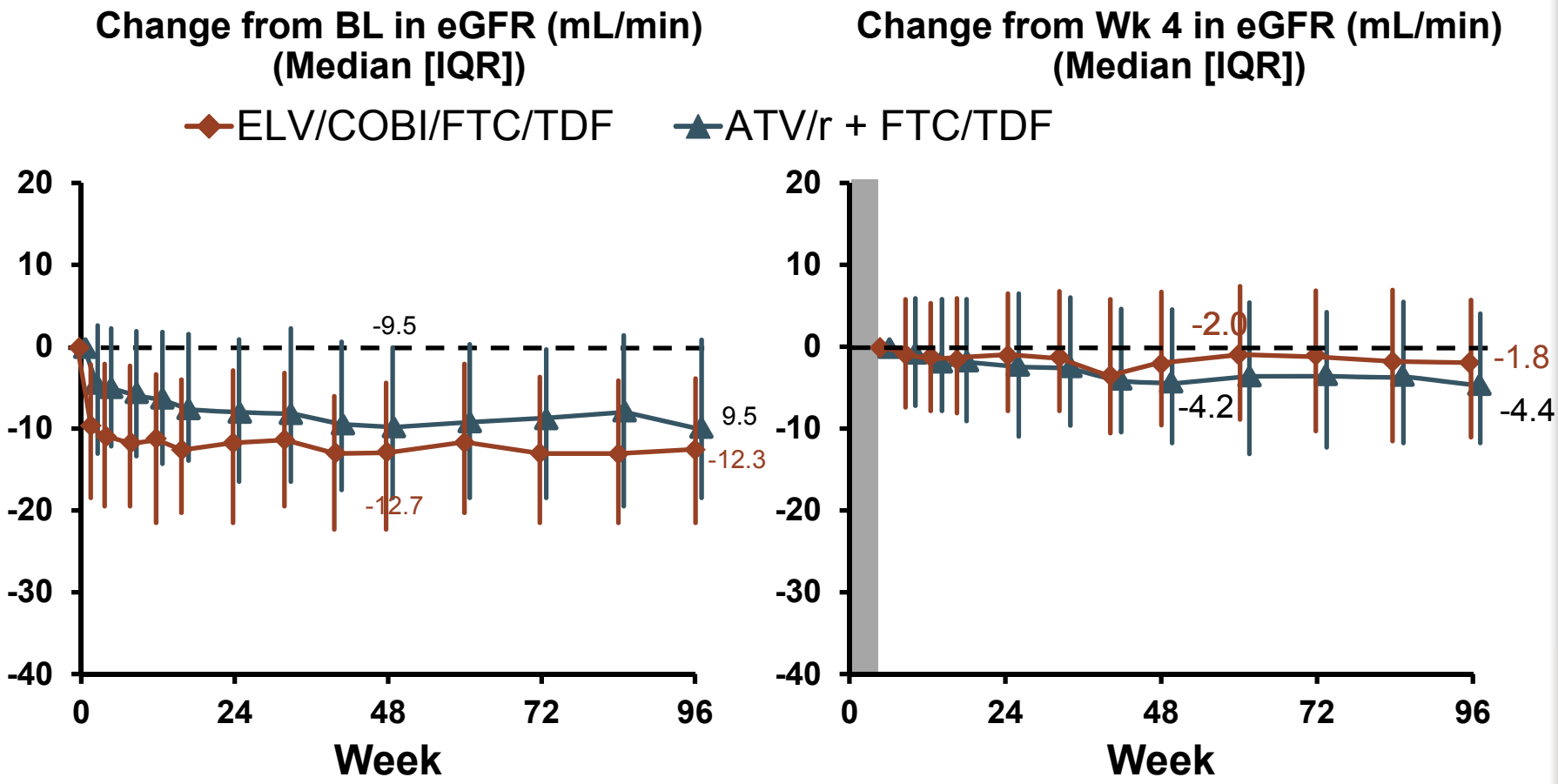
Study 102: Adverse Events Leading to Study Drug Discontinuation at Weeks 48 and 96

	ELV/COBI/FTC/TDF (n=348)		EFV/FTC/TDF (n=352)	
AE Leading to Study Drug DC	**W48**	**W96**	**W48**	**W96**
Renal events	1.4%	+0.6%	0	0
Depression	0.3%	0	0.9%	+0.3%
Fatigue	0.3%	0	0.3%	+0.3%
Abnormal dreams	0	0	0.6%	0
Anxiety	0	0	0.3%	+0.3%
Insomnia	0	0	0.3%	+0.3%
Rash events and drug hypersensitivity	0	0	1.4%	0

- Two **ELV/COBI/FTC/TDF** subjects DC due elevation in serum creatinine after Week 48
  - Both had baseline eGFR <70 mL/min and a medical history of HTN and DM
  - Creatinine improved after study drug DC in both

Zolopa A, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O424A.

Study 103: Changes in eGFR from Baseline and from Week 4



Rockstroh J, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O424AB

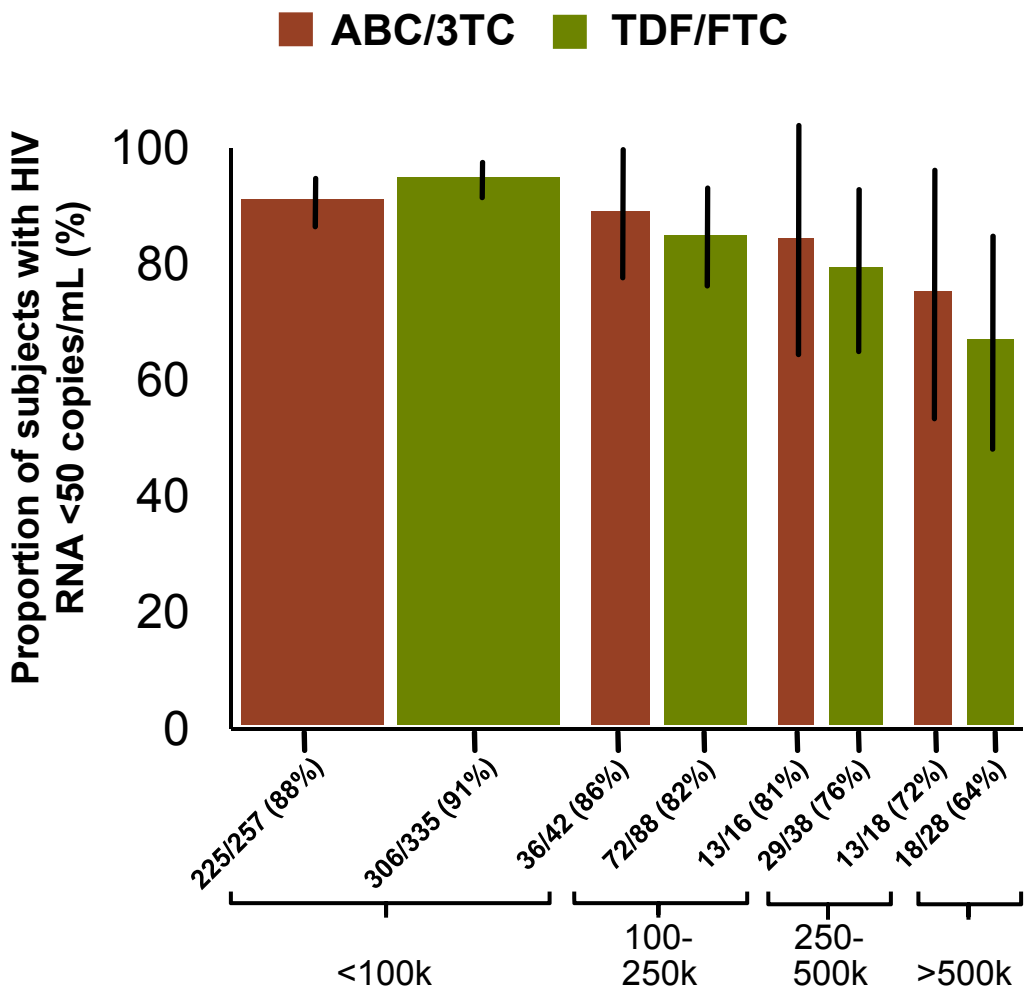
SPRING-2 and SINGLE: DTG Treatment Response by Baseline Viral Load and NRTI Backbone in Treatment-Naïve Patients

	SPRING		SINGLE	
	DTG + NRTIs (n=411)	RAL + NRTIs (n=411)	DTG + ABC/3TC (n=414)	EFV/ TDF/FTC (n=419)
Proportion of subjects at BL >100K	**28%**	**28%**	**32%**	**31%**
Week 48 <50 copies/mL, %	**88%**	**85%**	**88%**	**81%**
Difference (CI), %	2.5 (-2.2 to 7.1)		7.4 (2.5 to 12.3)	
Week 48 $CD4^+$ cell count change from BL, median (IQR)	230 (128-338)	230 (139-354)	246 (150-352)	187 (107-304)
PDVF, n(%)	**20 (5%)**	**28 (7%)**	**18 (4%)**	**17 (4%)**
RT Results at BL, PDVF	**12**	**19**	**9**	**9**
NRTI TEM mutations	0	4[a,b]	0	1 (K65K/R)
NNRTI TEM mutations	-	-	0	4[c]
INI Results at BL, PDVF	**8**	**18**	**7**	**7**
INI-r TEM substitution	0	1[a]	0[d]	0

TEM = treatment-emergent major
[a] n=1 (TDF/FTC) T97T/A, E138E/D, V151V/I, N155H + A62A/V, K65K/R, K70K/E, M184V
[b] n=1 (TDF/FTC) A62A/V, n=1 (TDF/FTC) M184M/I, n=1 (ABC/3TC) M184M/V
[c] n=1 with K101E, n=1 with K103N, n=1 with G190A, n=1 with K103N + G190A
[d] E157Q/P polymorphism detected with no significant change in IN phenotypic susceptibility

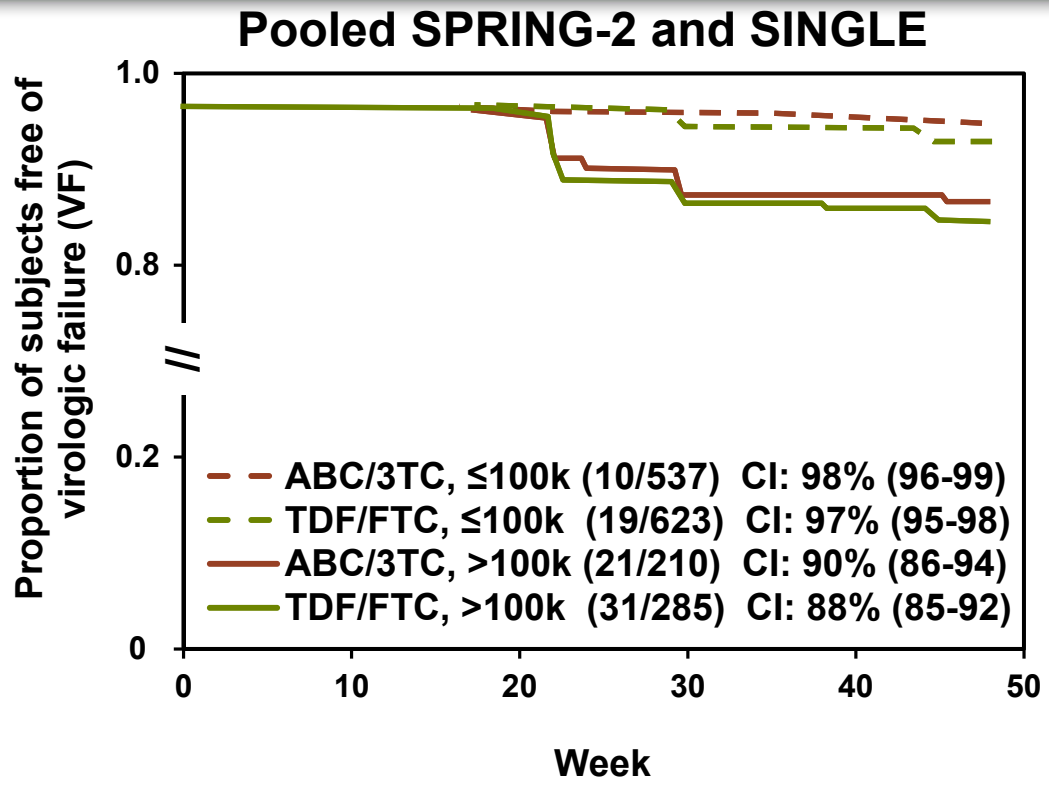
Eron J, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. P204.

SPRING-2: Primary Endpoint by NRTI and BLVL



Eron J, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. P204.

SPRING-2 and SINGLE: Time to VF by NRTI and VL



BLVL	NRTI	Events/N	KM est (CI)	BLVL	NRTI	Events/N	KM est (CI)
≤100k	ABC/3TC	10/537	98% (96-99)	>100k	ABC/3TC	21/210	90% (86-94)
	TDF/FTC	19/623	97% (95-98)		TDF/FTC	31/285	88% (85-92)

Eron Jr, J. et al. HIV11, Glasgow, UK; 11-15 November 2012; Abst. P204.

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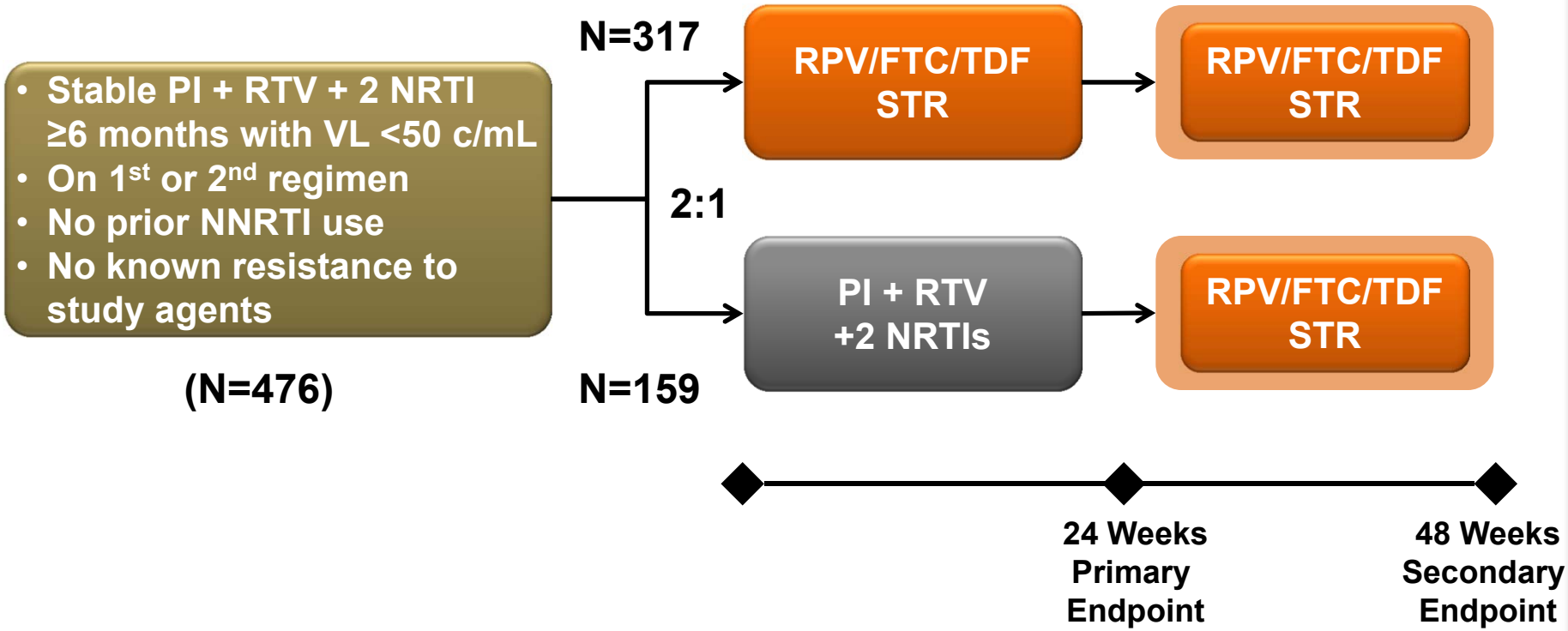
Studies in Treatment Experienced Patients

Jose R Arribas, MD

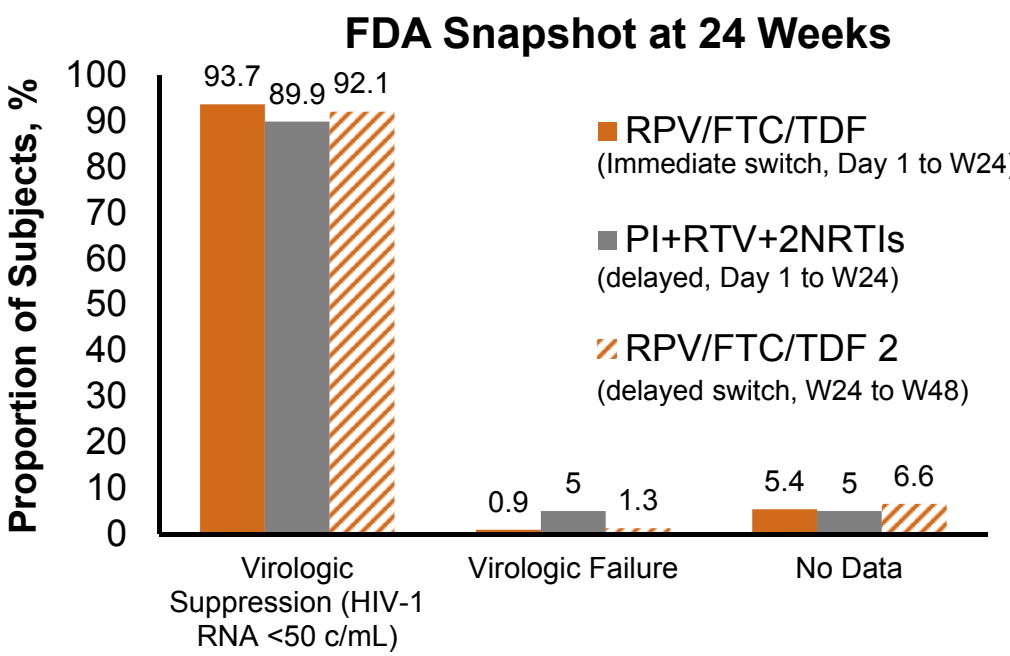
Madrid, Spain

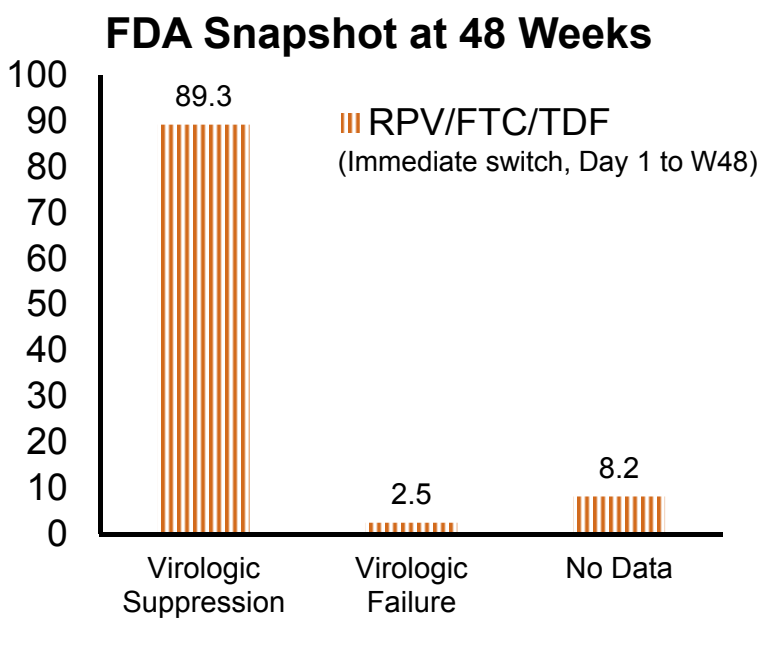
SPIRIT: Study Design



Fisher M, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. P285.

SPIRIT: Virologic Suppression at Weeks 24 and 48





- 22/24 subjects with pre-existing K103N had virological suppression

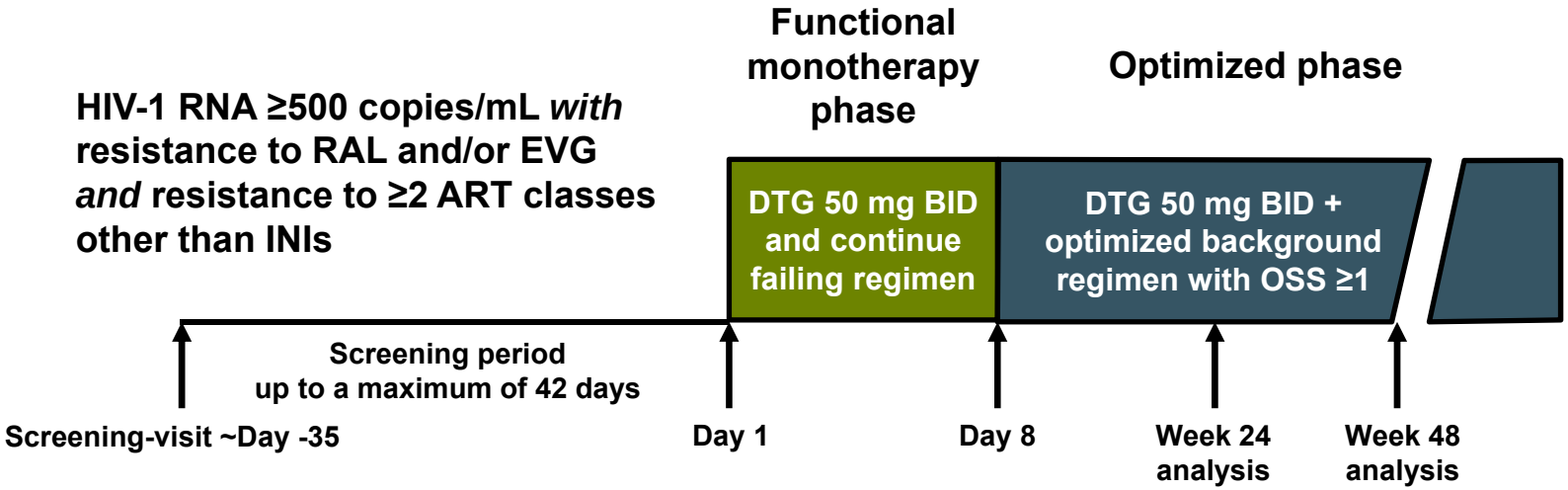
Fisher M, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. P285.

SPIRIT: RPV/FTC/TDF NNRTI and NRTI Resistance

	RPV/FTC/TDF All Subjects N=469
Subjects Analyzed for Resistance, n (% study arm)	7 (4.5%)
Subjects with Resistance to ARV Regimen, n (% study arm)	4 (0.9%)
Emergent NNRTI and NRTI Resistance Mutations by Subject	Subject 1: K103N+L100I+M184I Subject 2: M184I Subject 3: E138E/K+M184/I/V Subject 4: E138K+V108V/I+M184V

Fisher M, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. P285.

Viking 3: DTG in Patients with Integrase Inhibitor Resistance



- Extensive ARV Resistance
  - 79% had ≥2 NRTIs, 75% had ≥1 NNRTI, and 70% had ≥2 PI resistance-associated mutations; 62% had non-R5 detected
  - All had INI (RAL and/or EVG) resistance
    - 68% at screening, 32 documented resistance from prior INI failure

Nichols G, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O232.

Viking 3: Integrase Genotypic and Phenotypic Resistance at Baseline

	Q148 + ≥2	Q148 + 1	N155	Y143	≥2 Primary	Primary not detected
Subjects, n (%)	21 (11)	31 (17)	30 (18)	28 (15)	7 (4)	59 (32)
Median DTG FC	10.00	4.60	1.49	1.10	4.57	0.89
Q1	4.47	3.39	1.29	0.91	1.68	0.80
Q3	13.00	6.27	1.76	1.18	20.00	1.04
Min	2.56	0.47	0.82	0.78	1.46	0.45
Max	37.00	12.00	3.89	2.01	27.00	3.7

Nichols G, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O232.

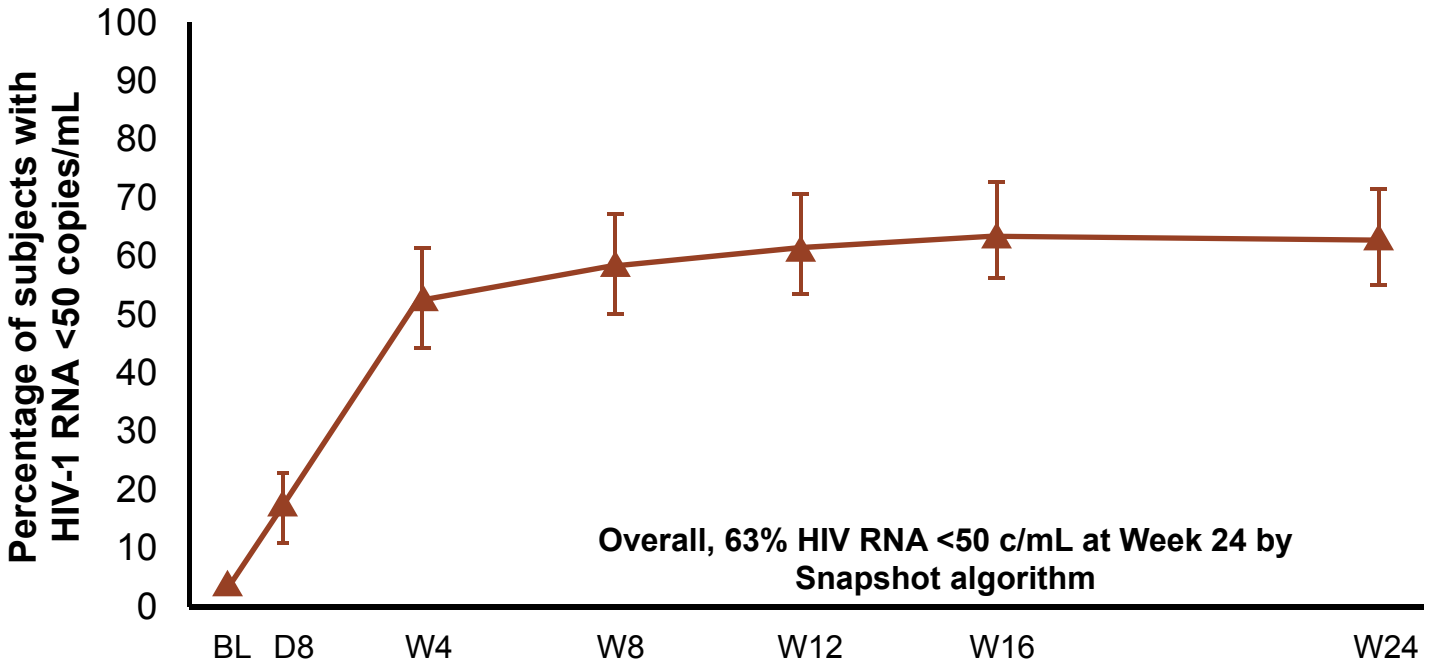
Viking 3: Day 8 Responses by Baseline Resistance

Primary INI-resistance mutations at BL	N	Mean HIV-1 RNA (log_{10}) change from BL (SD) at Day 8	% >1-log_{10} HIV-1 RNA decline or <50 copies/mL at Day 8
Total	183	-1.4 (0.61)	82%
No primary mutations	60	-1.6 (0.55)	95%
T66	1	-1.9	100%
Y143	28	-1.7 (.042)	96%
N155	33	-1.4 (0.51)	82%
≥2 Primary mutations	8	-1.4 0.76)	75%
Q148 + ≤1 Secondary mutation*	32	-1.1 (0.51)	69%
Q148 + ≥2 Secondary mutations*	21	-1.0 (0.81)	48%

* Key secondary mutations were G140A/C/S, L741, and E138A/K/T

Nichols G, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O232.

Viking 3: Efficacy

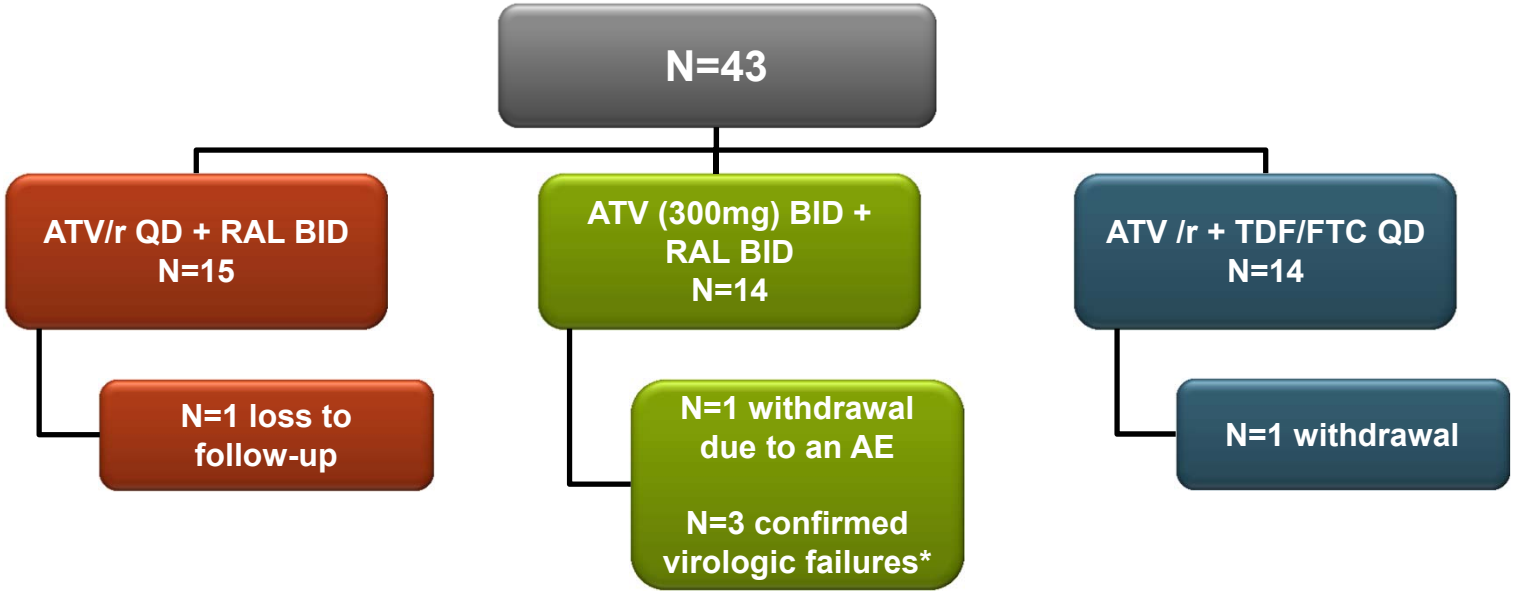


- In multivariate analyses of baseline factors of Week 24 response rates, the presence of Q148 + ≥2 mutations and increasing DTG FC were highly correlated with fewer subjects achieving <50 copies/mL ($P \leq 0.001$)
- Increasing background ART activity score did not impact response

Nichols G, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O232.

ATV BID + RAL vs. ATV/r + RAL vs. ATV/r + TDF/FTC

CD4 ≥ 200
Undetectable HIV RNA for 6 months
Stable on ATV/r + TDF/FTC x 90 days
Raltegravir naïve



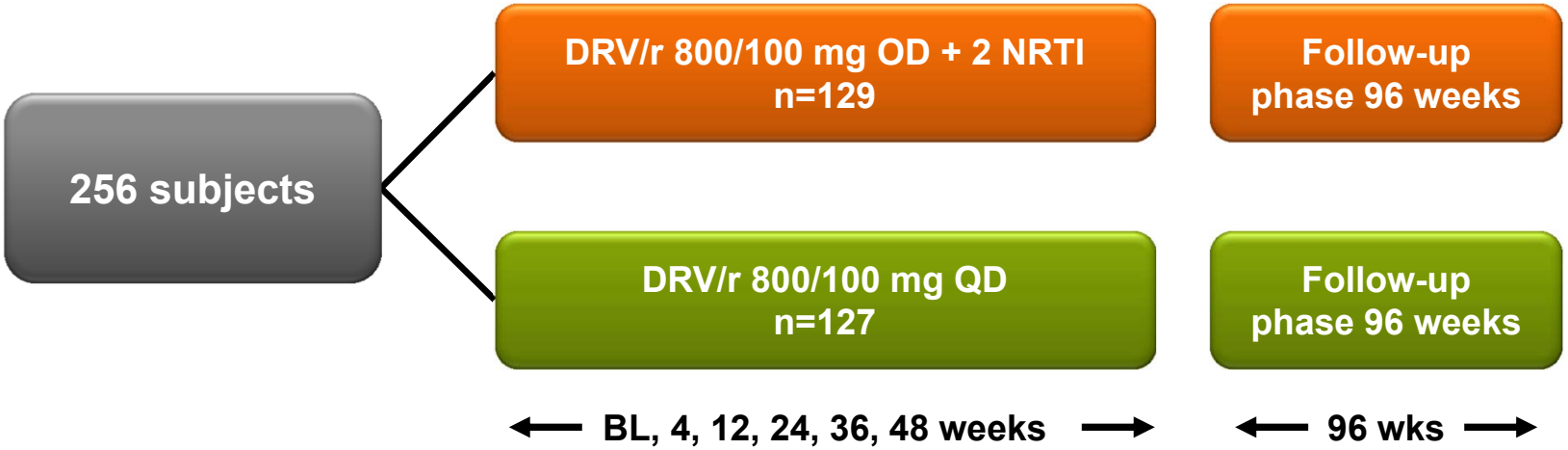
ATV BID + RAL BID:
CD4 count change was significantly less than Control
More neurologic and musculoskeletal adverse events

*No resistance development

Cohen C, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. P286.

MONET: Study Design

- Inclusion: taking 2 NRTI + either NNRTI or boosted PI at screening (stratified)
- HIV RNA <50 copies/mL for at least 6 months, no prior use of darunavir (DRV)
- No history of virological failure



- Primary Endpoint at Week 48: HIV RNA <50 copies/mL (TLOVR).
  Intent to Treat, Switch = Failure

Arribas J, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. P301.

MONET: HIV RNA <50 copies/mL at Week 144 by HCV Status and Baseline HIV RNA

HCV	BL HIV RNA	DRV/r	DRV/r + 2NRTI
HCV -	<5 c/mL	66/84=79%	67/90=74%
HCV-	>5 c/mL	12/19=63%	19/24=79%
HCV+	<5 c/mL	9/19=47%	9/10=90%
HCV+	>5 c/mL	1/5=20%	2/5=40%

Arribas J, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. P301.

PI Monotherapy and Neurocognitive Impairment

Study Design

Cross-sectional 4/11-6/12

- HIV+ patients receiving:
  - ✓ 2 N(t)RTIs + LPV/r or DRV/r
  - ✓ LPV/r or DRV/r alone
- HIV-RNA <50 (≥1yr)
- Patients with confounders excluded

DRV/r or LPV/r + 2 N(t)RTIs (n=95)

DRV/r or LPV/r (n=96)

48 weeks

Objectives

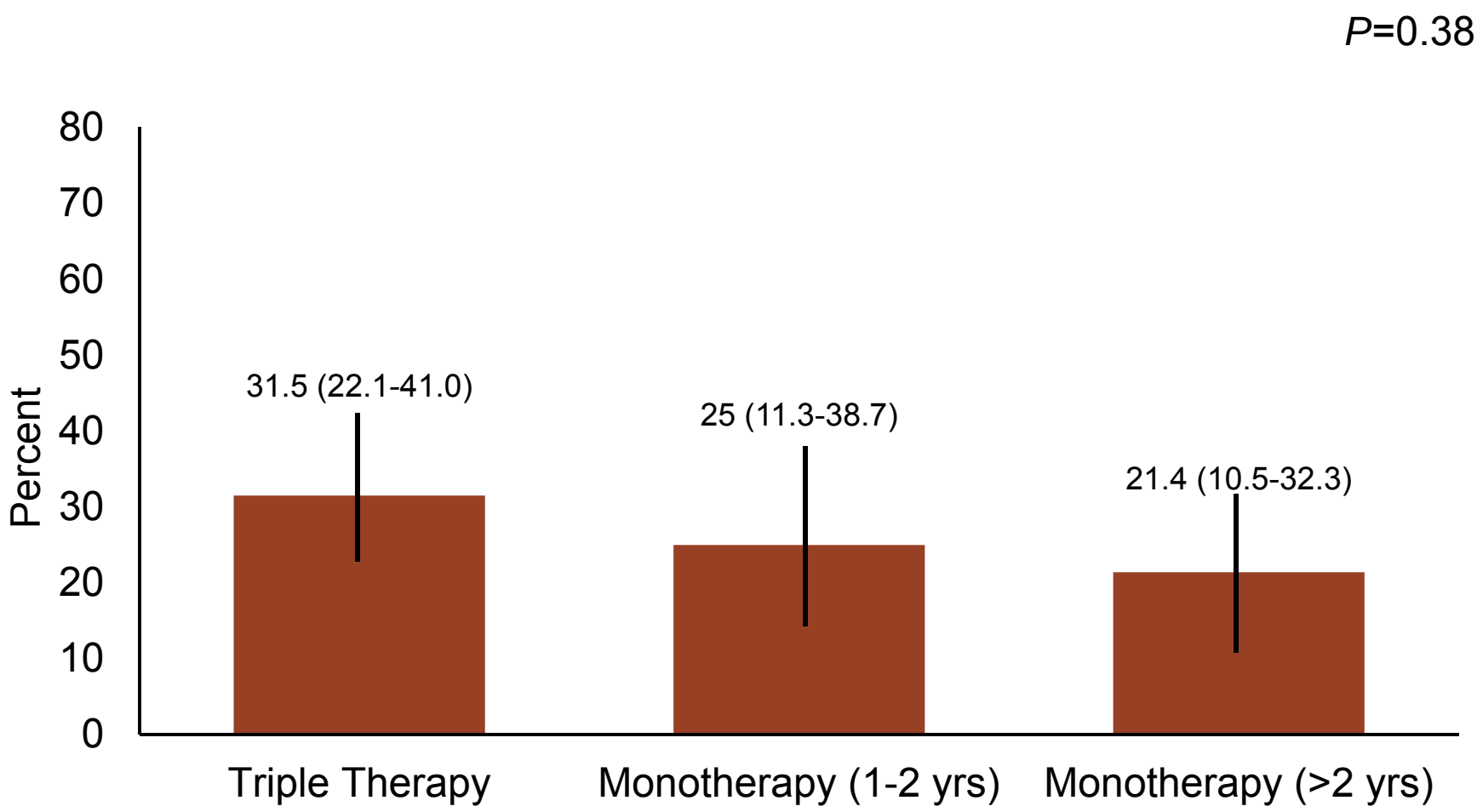
- Prevalence of NCI
- Is MT a risk factor for NCI?
- CSF Viral escape
- Biomarkers of NCI
- Evolution of NCI (48 wks)

Procedures (baseline & 48 week)

- Neurocognitive assessment
- Blood tests
- CSF & MRI (only if neurocognitively impaired)

Arribas J, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O333.

PI Monotherapy and Neurocognitive Impairment



All asymptomatic/mild by self report

Arribas J, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O333.

PI Monotherapy and Neurocognitive Impairment

Model	Confounders Included	MT (1-2 years)	MT (>2 years)
Crude	-	0.72 (031-1.67)	0.59 (0.27-1.28)
Step 1	Total duration of ART	0.94 (0.39-2.31)	0.60 (0.26-1.39)
Step 2	Years of education	0.77 (0.29-1.99)	0.43 (0.17-1.07)
Step 3	Ethnicity	0.99 (0.37-2.65)	0.51 (0.20-1.33)
Step 4	Transmission route	1.07 (0.39-2.94)	0.41 (0.15-1.13)
Step 5	HOMA index	0.85 (0.29-2.50)	0.40 (0.14-1.15)
Final Model		**0.85 (0.29-2.50)**	**0.40 (0.14-1.15)**

Arribas J, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O333.

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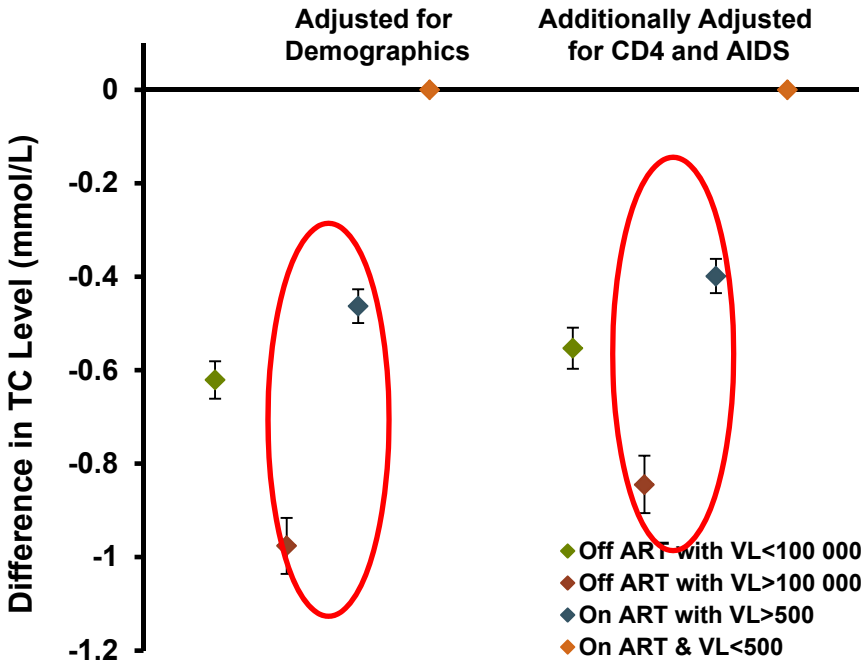
Adverse Effects

Graeme Moyle, MD

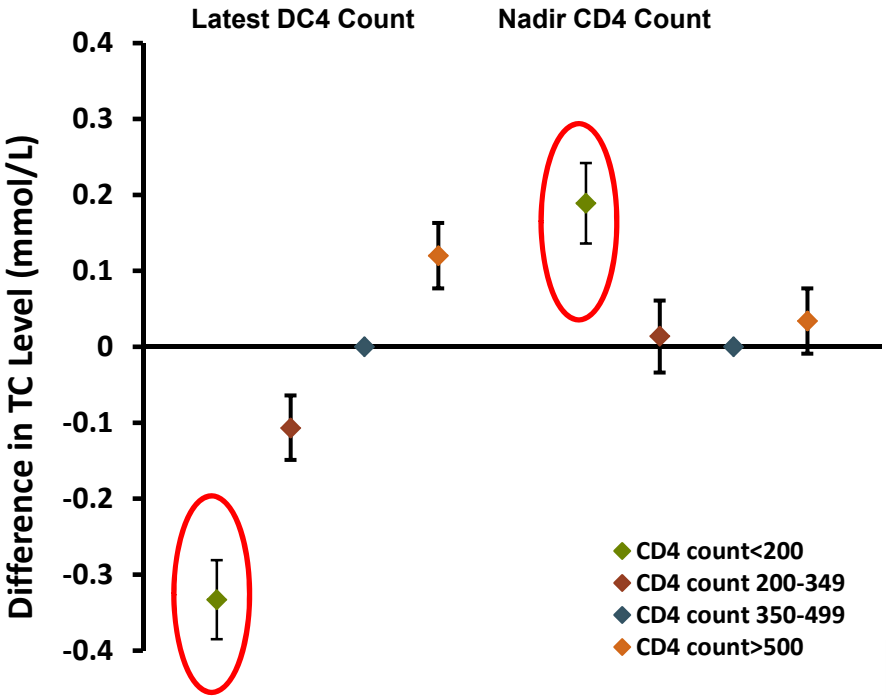
London, UK

D:A:D: Impact of ART, Viremia and Immunosuppression on TC

Impact of ART and Latest VL on TC



Impact of Immunosuppression on TC

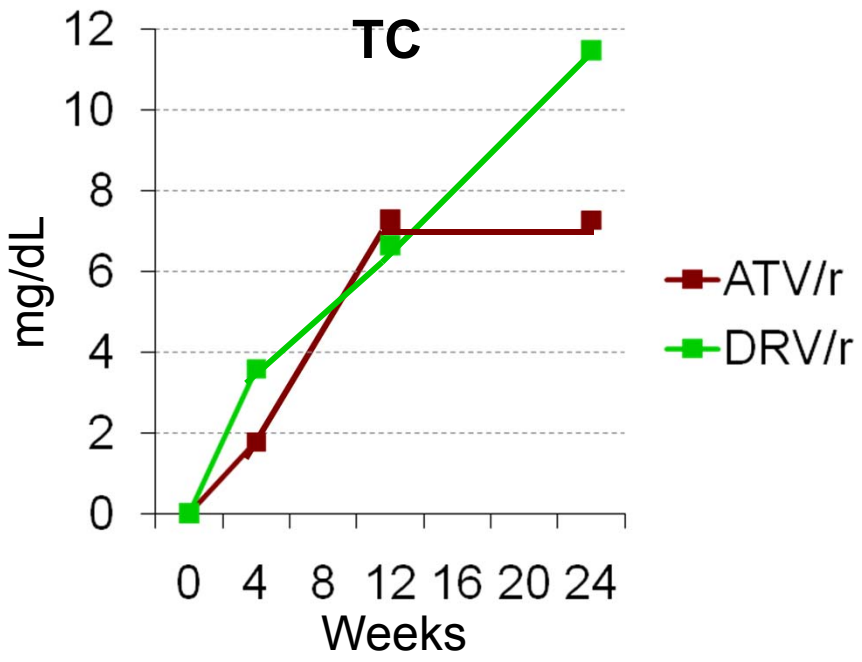


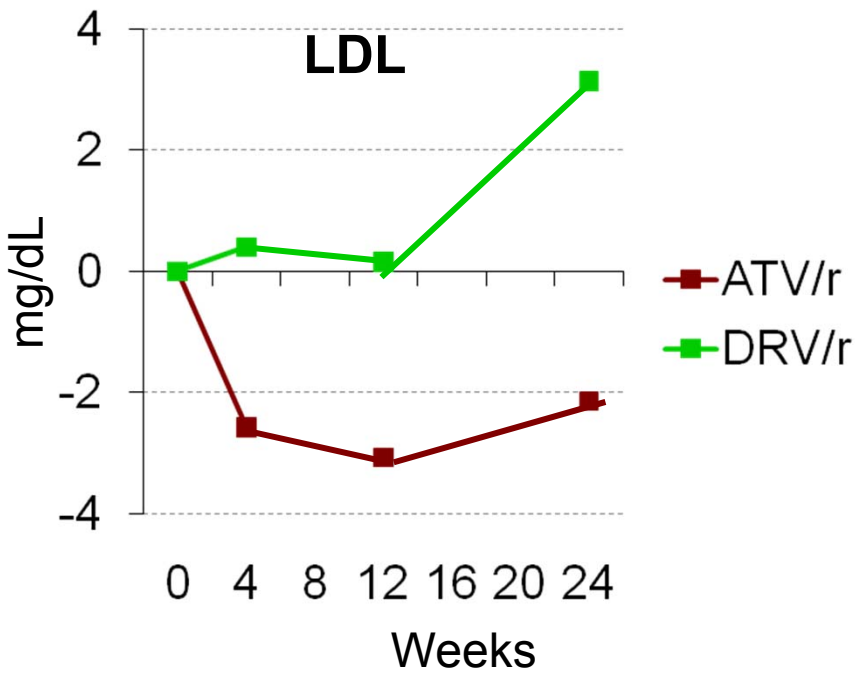
Number of TC measurement (N=45 169)

Models included adjustment for: Age, Body mass index (BMI) , Use of lipid lowering drugs , Gender, Smoking, Hepatitis-C co-infection, Mode of infection, Family history of CVD, Cohort, Ethnicity, Diabetes, Year of D:A:D entry, Prior AIDS

Kamara D, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. P034.

ATADAR: 24-Week Lipid Changes





24-w estimated difference ATV/r minus DRV/r

-4.21 (-12.11 to +3.69), *P*=0.7503

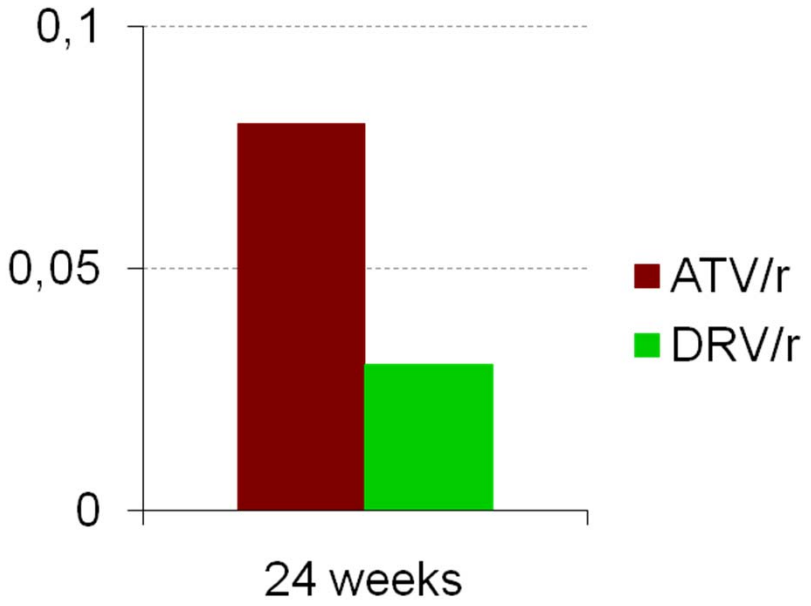
24-w estimated difference ATV/r minus DRV/r

-5.28 (-11.87 to +1.32), *P*=0.1160

Martinez E, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O423.

ATADAR: 24-Week HOMA-IR and eGFR Change

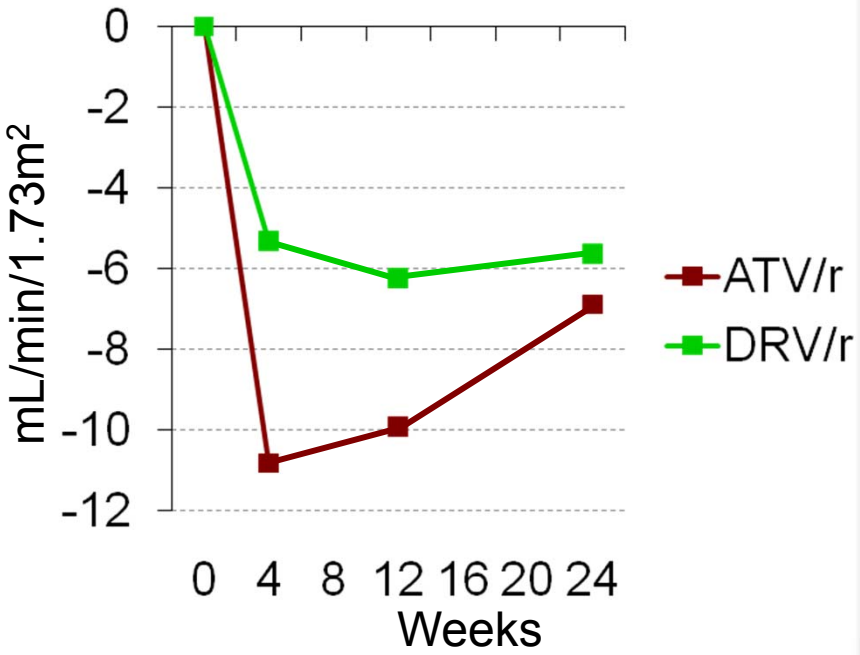
HOMA IR



24-w estimated difference ATV/r minus DRV/r

+0.53 (-0.65 to +1.70), *P*=0.3785

MDRD eGFR

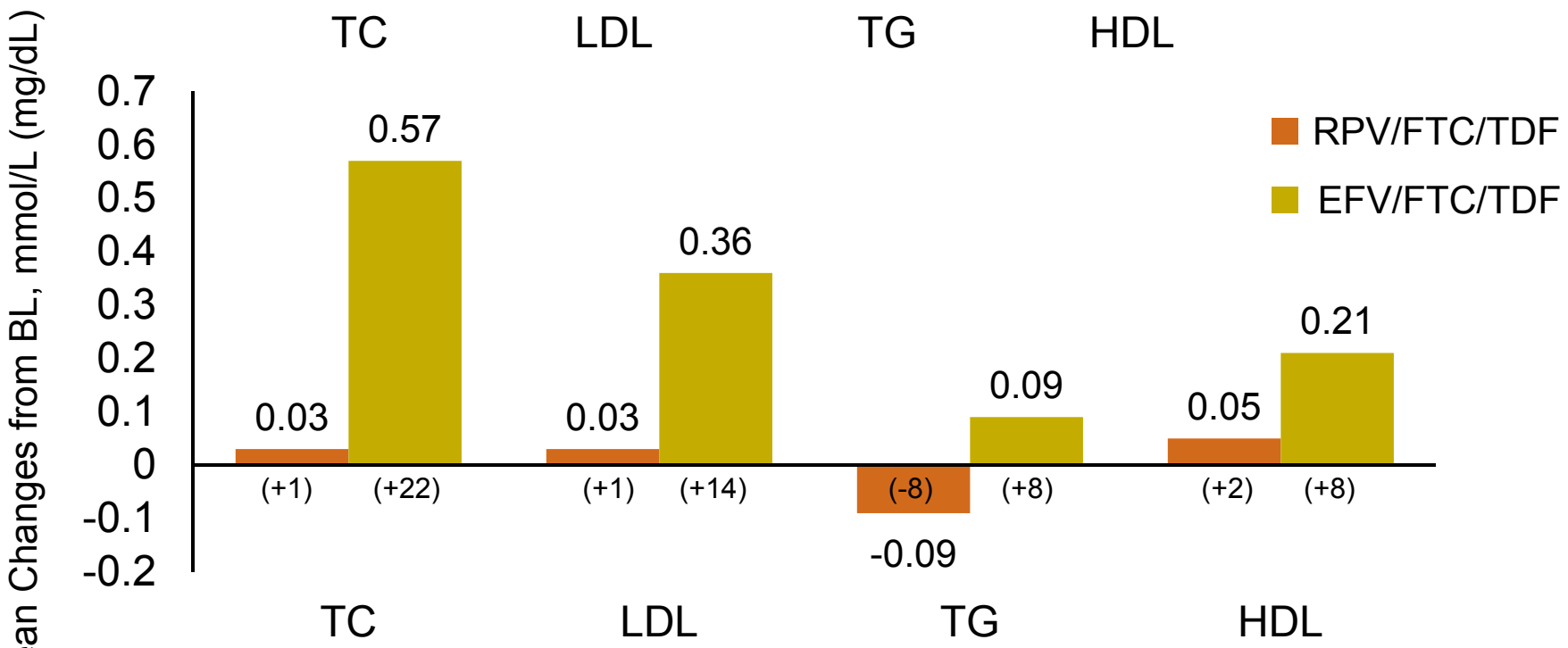


24-w estimated difference ATV/r minus DRV/r

-1.25 (-6.92 to +4.43), *P*=0.6652

Martinez E, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O423.

STaR: Changes from Baseline to Week 48 in Fasting Lipids



P<0.001 for all comparisons between treatment groups using ANOVA

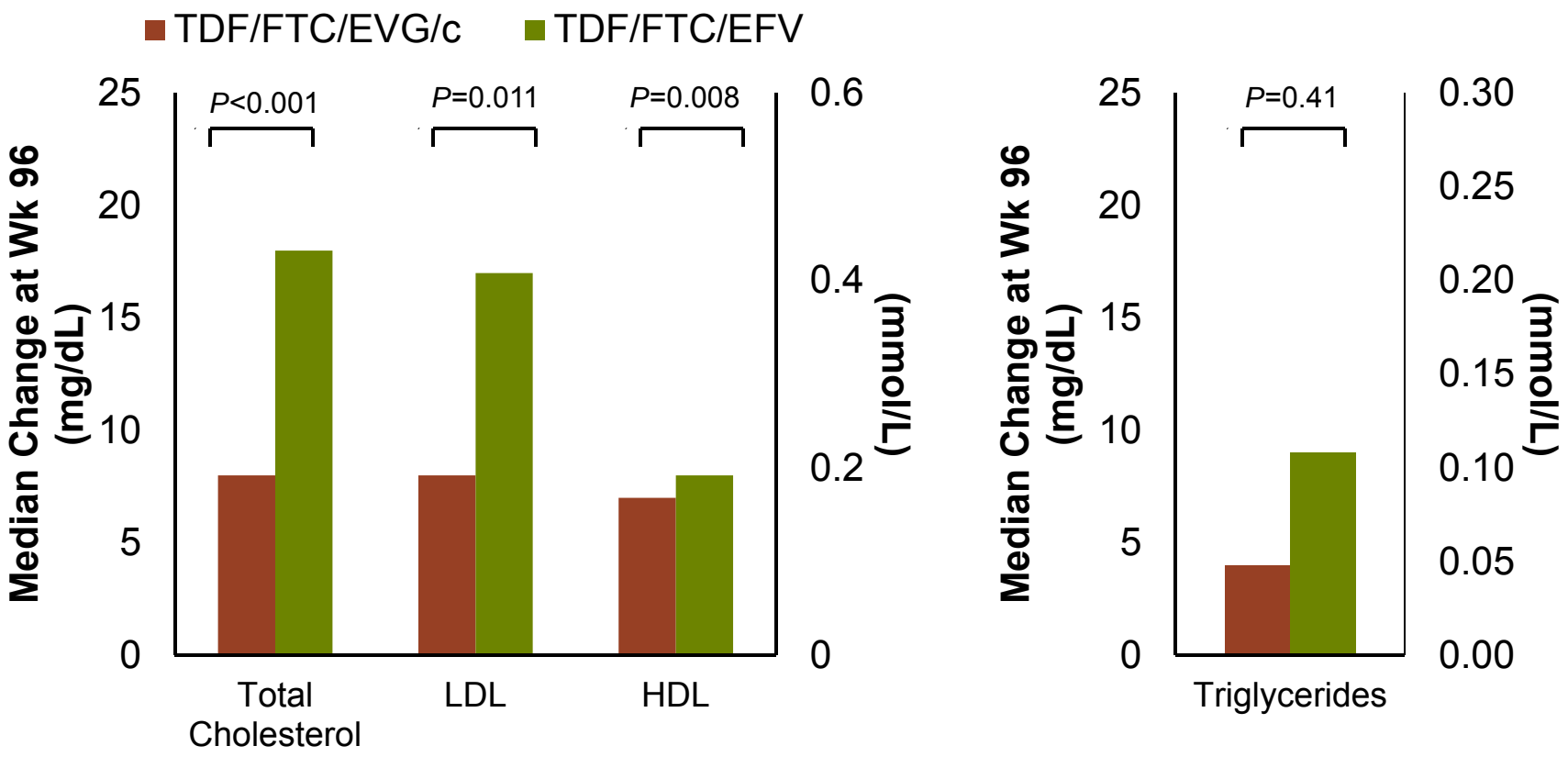
	TC		LDL		TG		HDL	
Mean Baseline Values, mmol/L	4.24	4.22	2.69	2.66	1.37	1.46	1.14	1.14

Change in TC:HDL at Week 48 was -0.2 in both arms

TC - total cholesterol, LDL - low-density lipoprotein, TG - triglycerides, HDL - high-density lipoprotein

Cohen C, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O425.

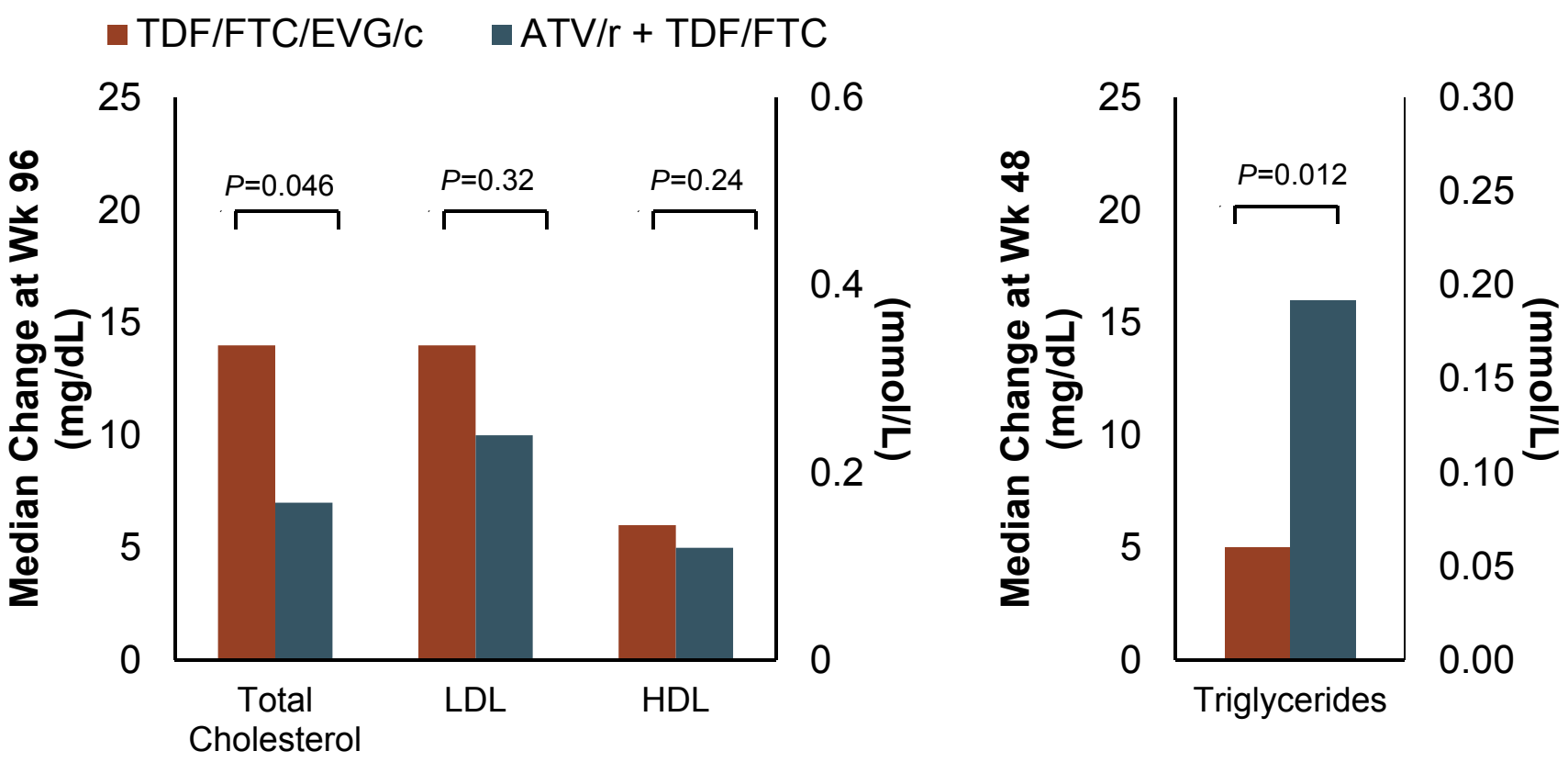
Study 102: Change from Baseline in Fasting Lipids at Week 96



No difference in change in TC to HDL ratio at Week 48 or 96

Zolopa A, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O424A.

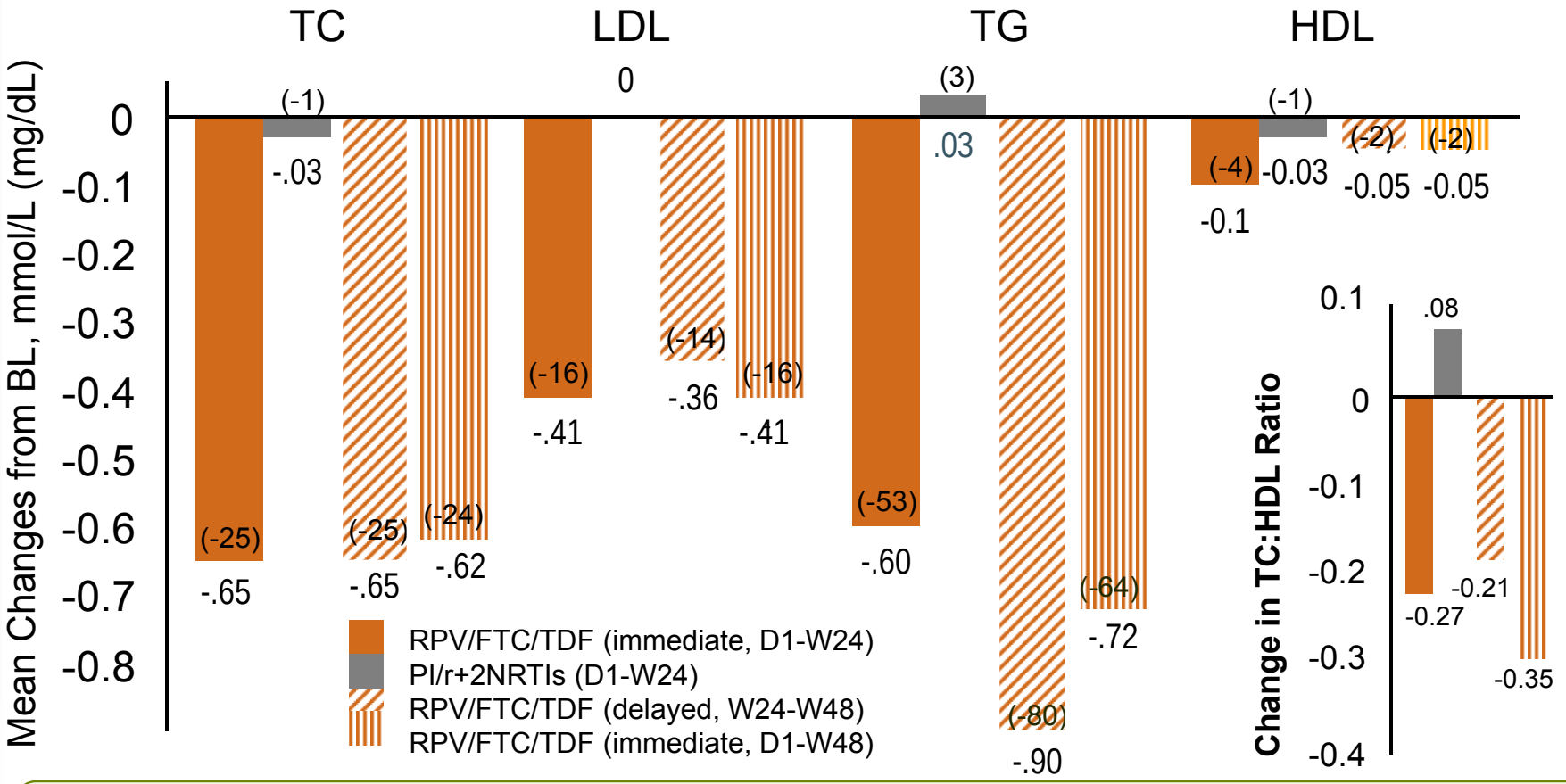
Study 103: Change from Baseline in Fasting Lipids at Week 96



No difference in change in TC to HDL ratio at Week 48 or 96

Rockstroh J, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O424B.

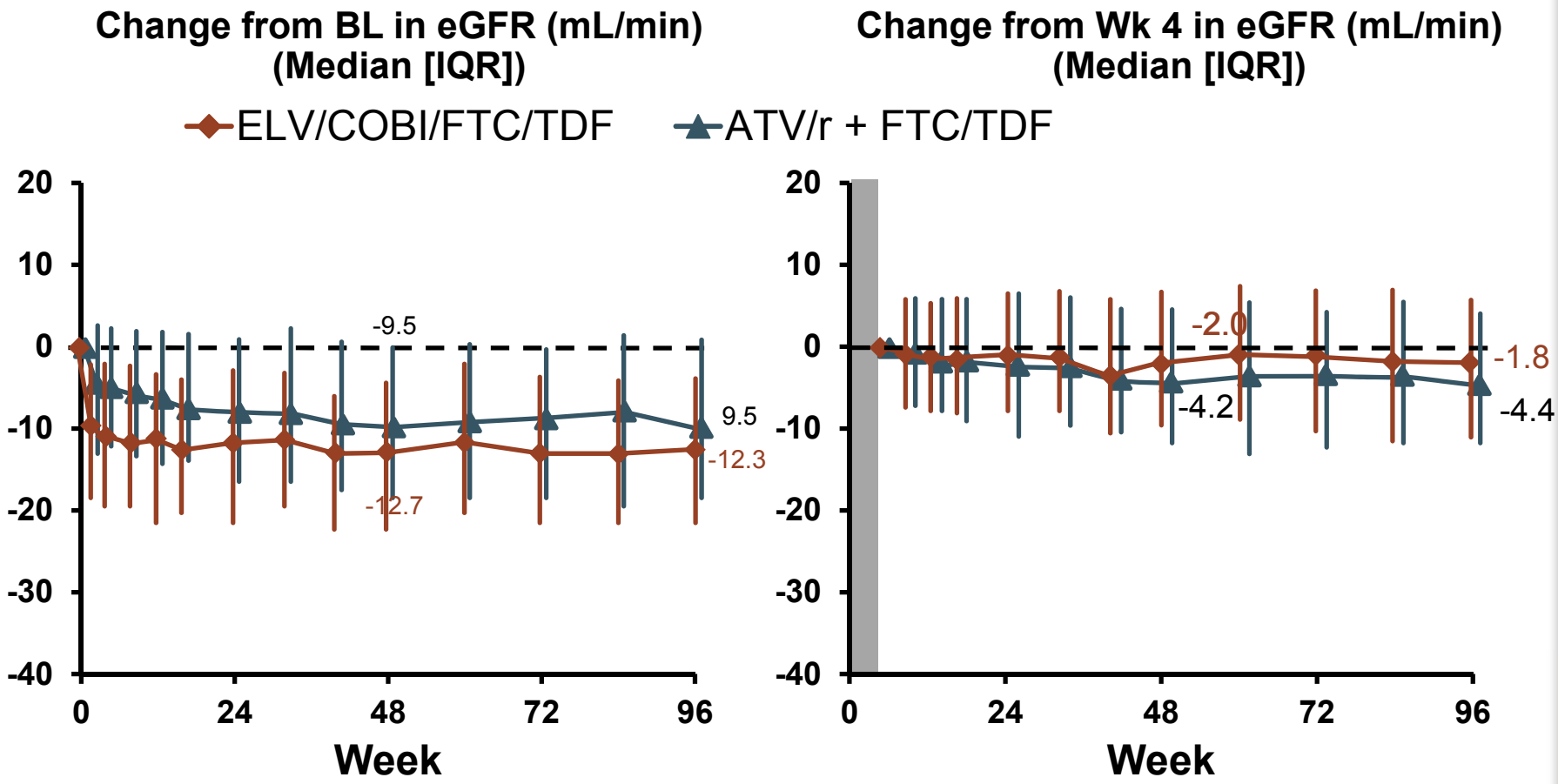
SPIRIT: Changes from Baseline in Fasting Lipids



Switching to RPV/FTC/TDF resulted in improvement in fasting lipids, including TC, LDL, TGs, and TC:HDL ratio at Week 24 and maintained through Week 48

Fisher M, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. P285.

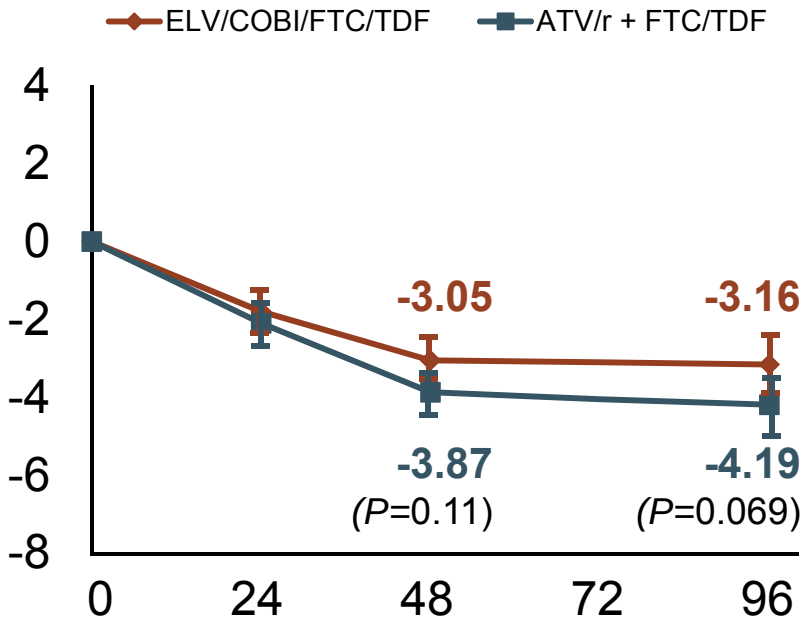
Study 103: Changes in eGFR from Baseline and from Week 4



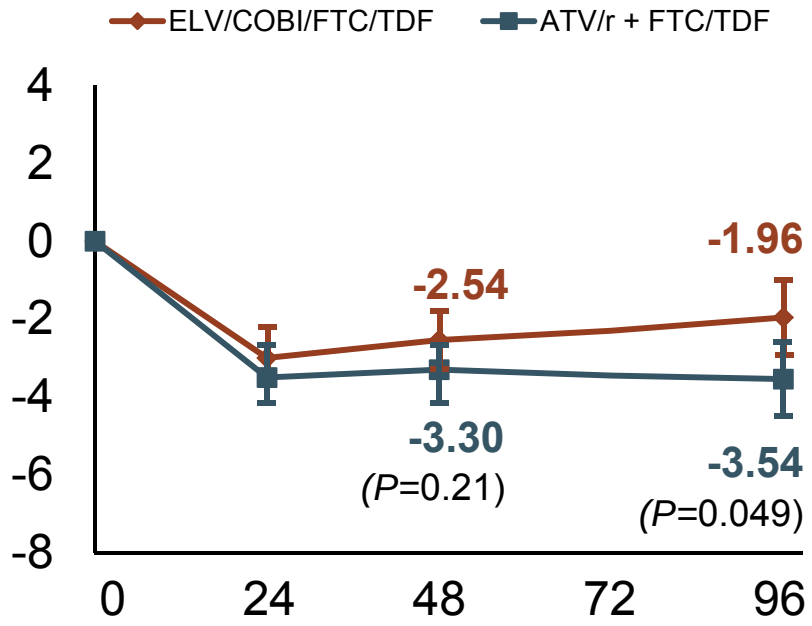
Rockstroh J, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O424AB

Study 103: Changes in Bone Mineral Density

Change in Hip BMD (%)
Mean (95% CI)

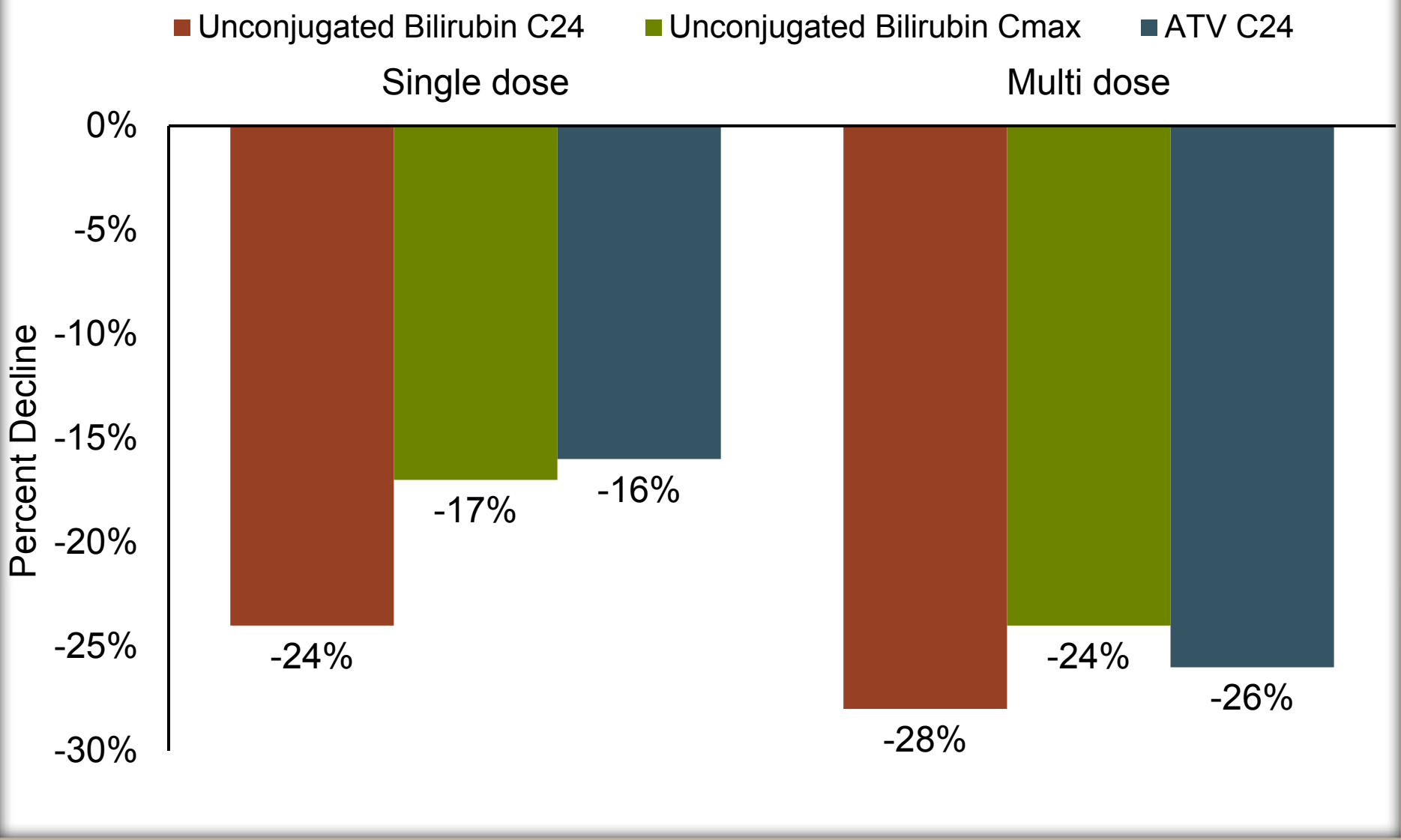


Change in Spine BMD (%)
Mean (95% CI)



	ELV/COBI/FTC/TDF (n=353)		ATV/r + FTC/TDF (n=355)	
	W48	**W96**	**W48**	**W96**
Fracture events, (n)	3 (1%)	+1 (+0.3%)	6 (2%)	+8 (+2%)

Effect of ZNSO4 on Unconjugated Bilirubin in Persons on Atazanavir



Jackson A, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. P40.

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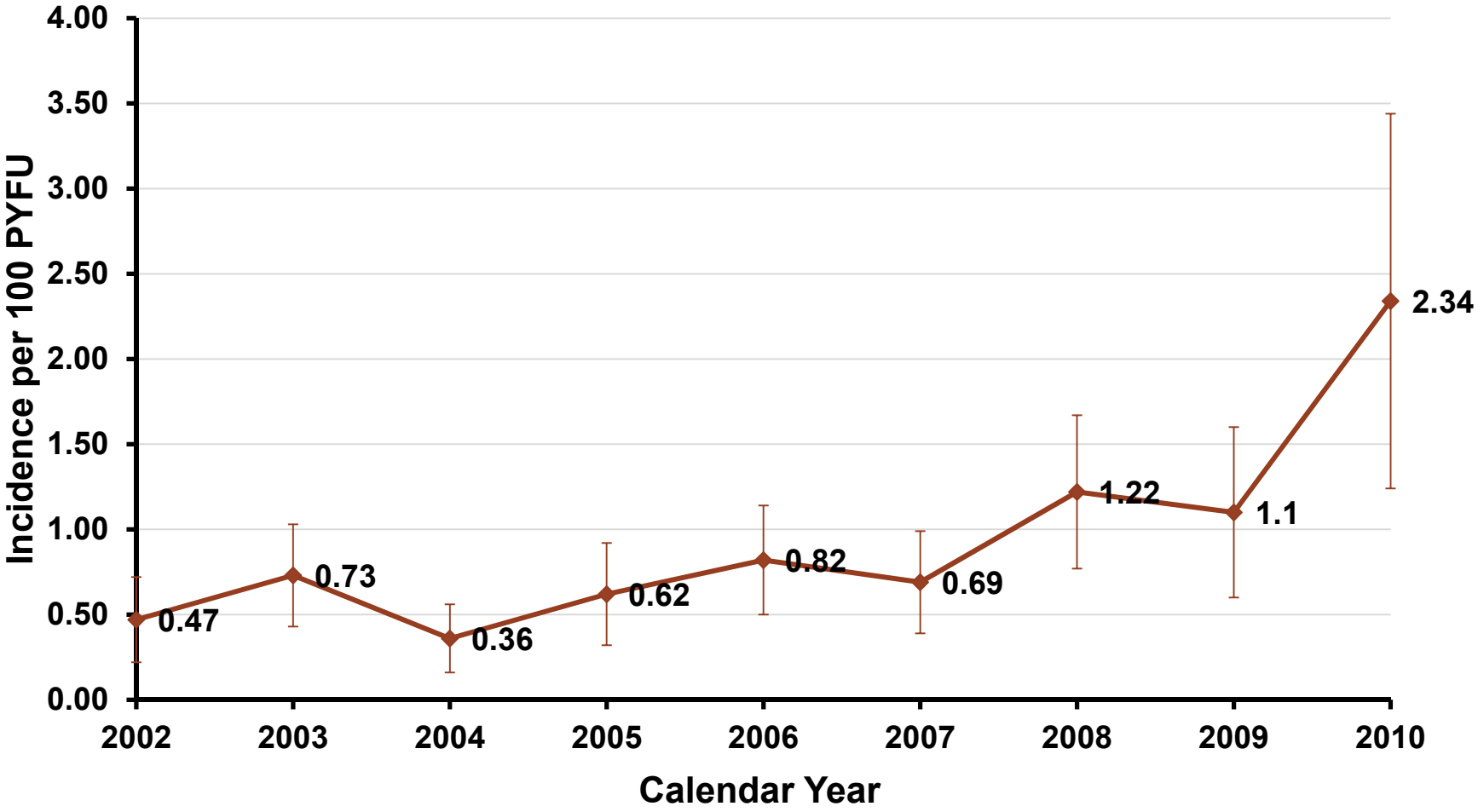
Hepatitis

Jürgen Rockstroh, MD

Bonn, Germany

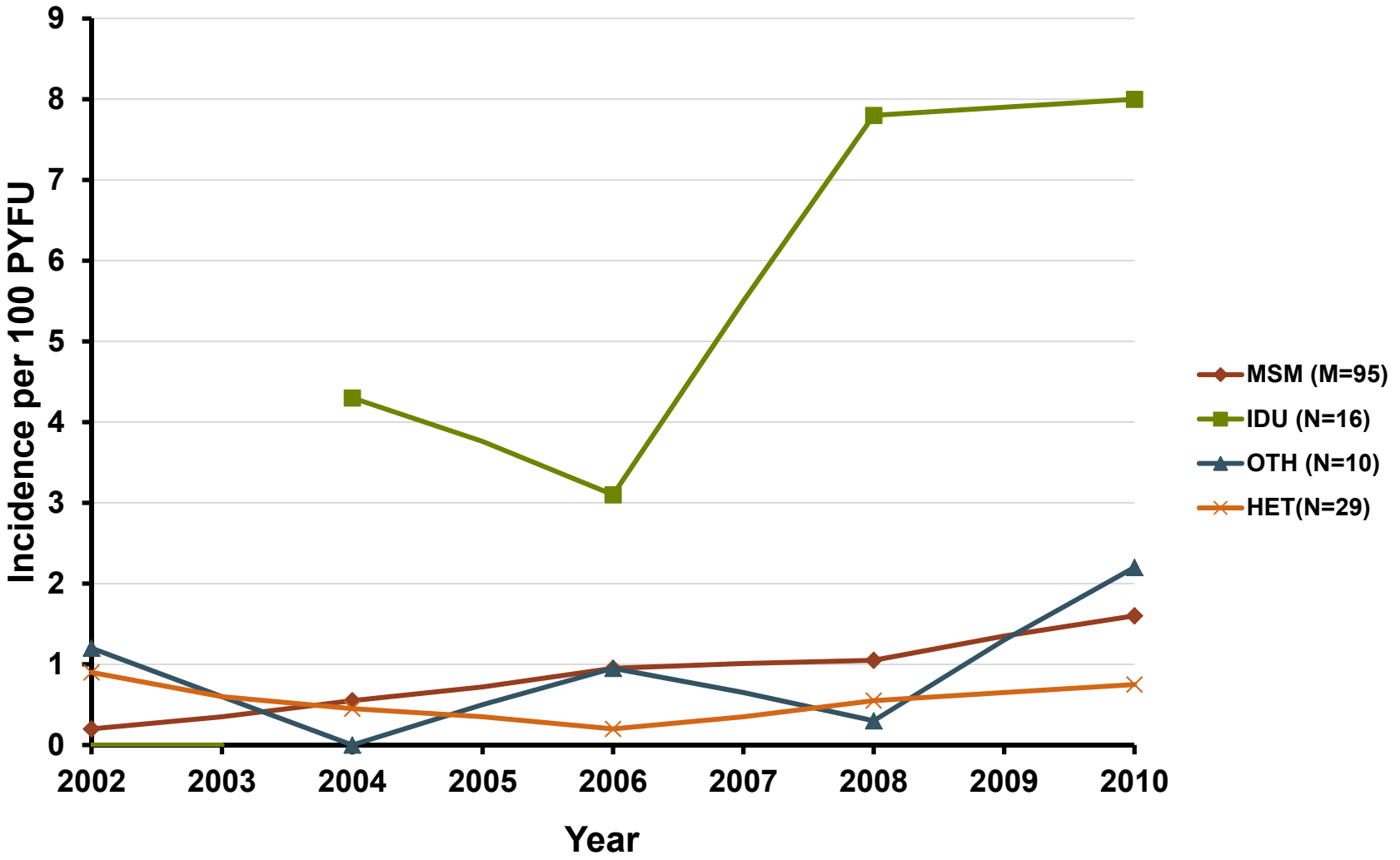
Incidence of Acute HCV by Calendar Year



Unadjusted Incidence Rate Ratio (IRR): 1.25 (1.17 – 1.34; *P*<0.0001)

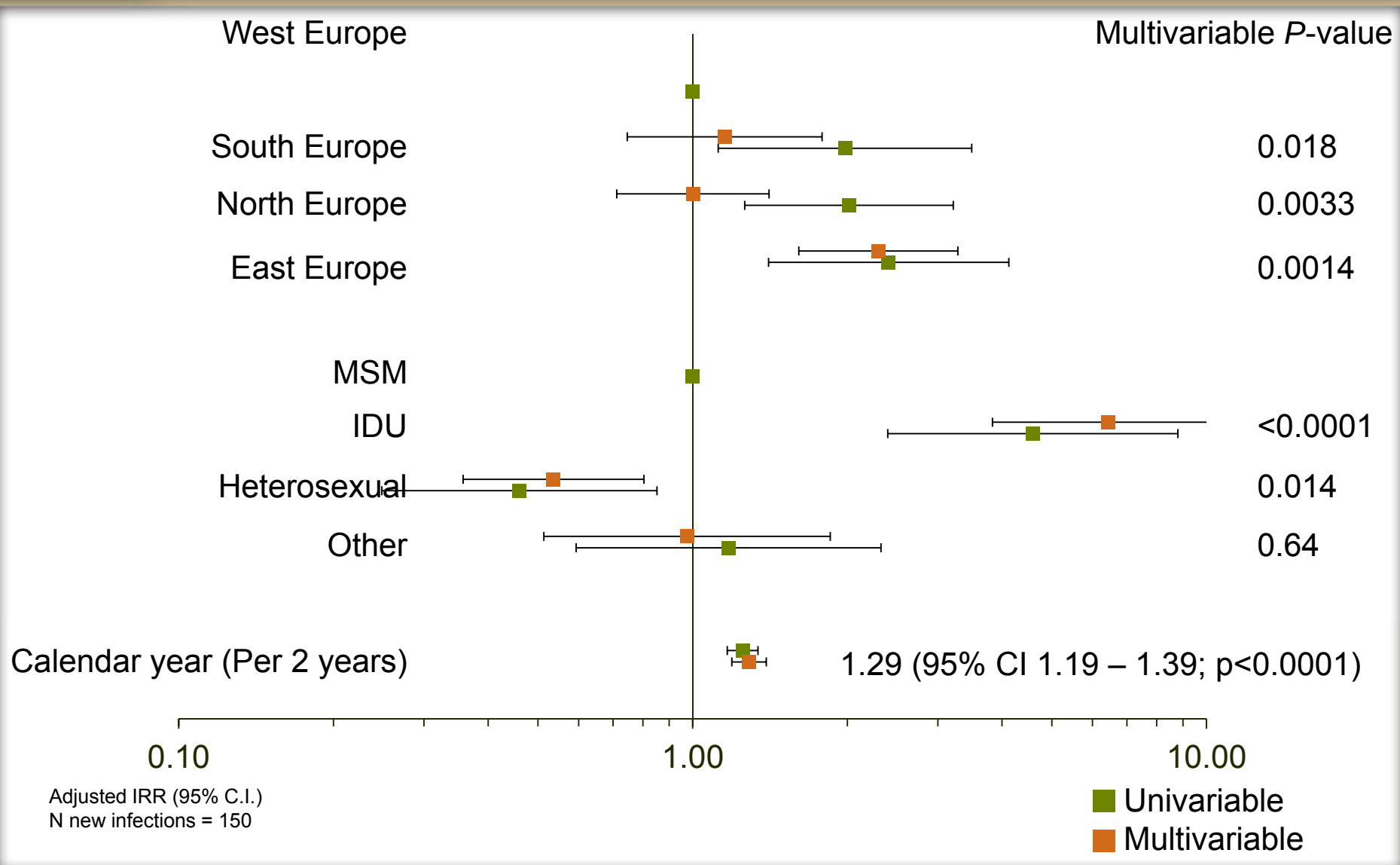
Kirk O, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O242.

Incidence of Acute HCV by Risk Group



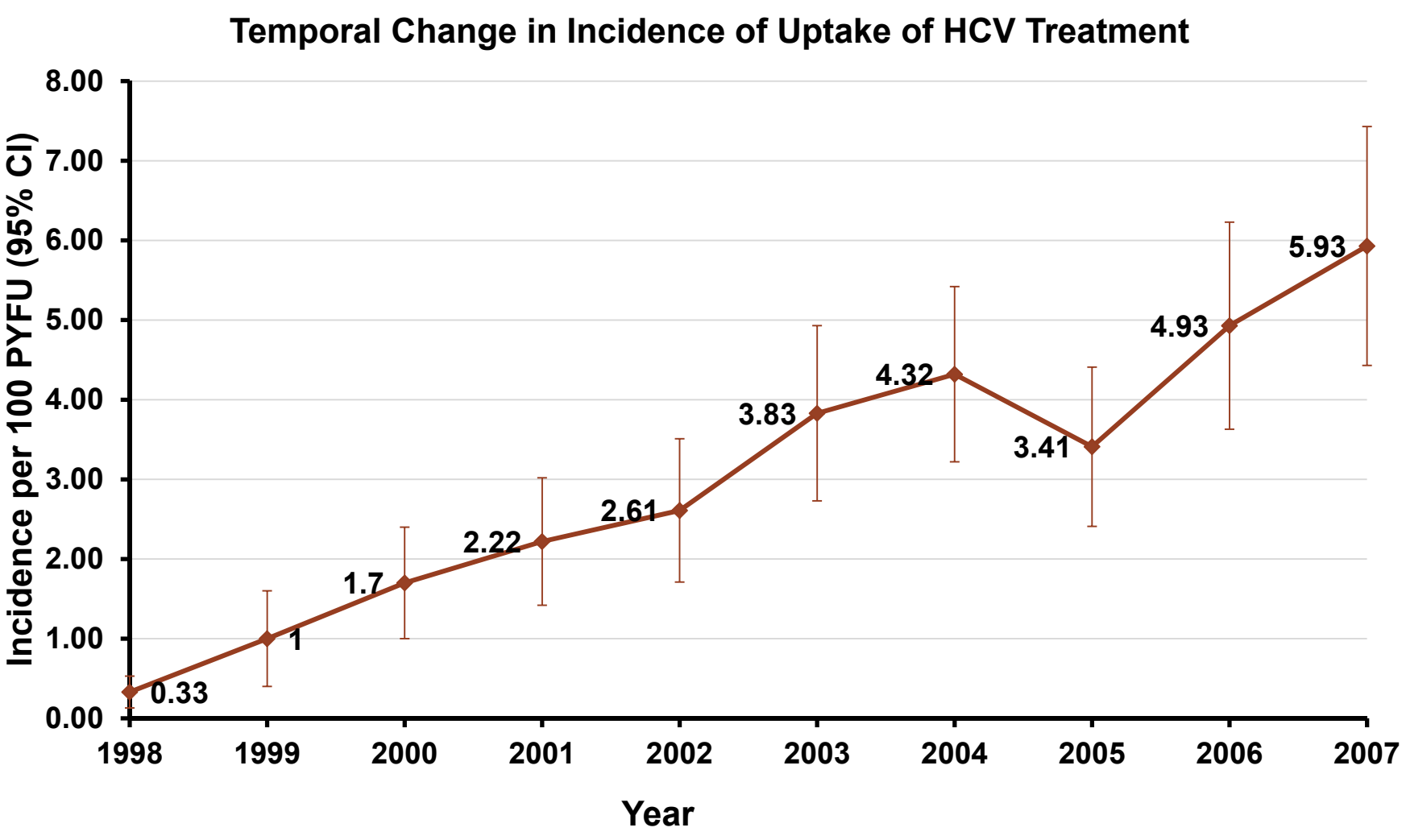
Kirk O, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O242.

Factors Associated with Acute HCV Infection



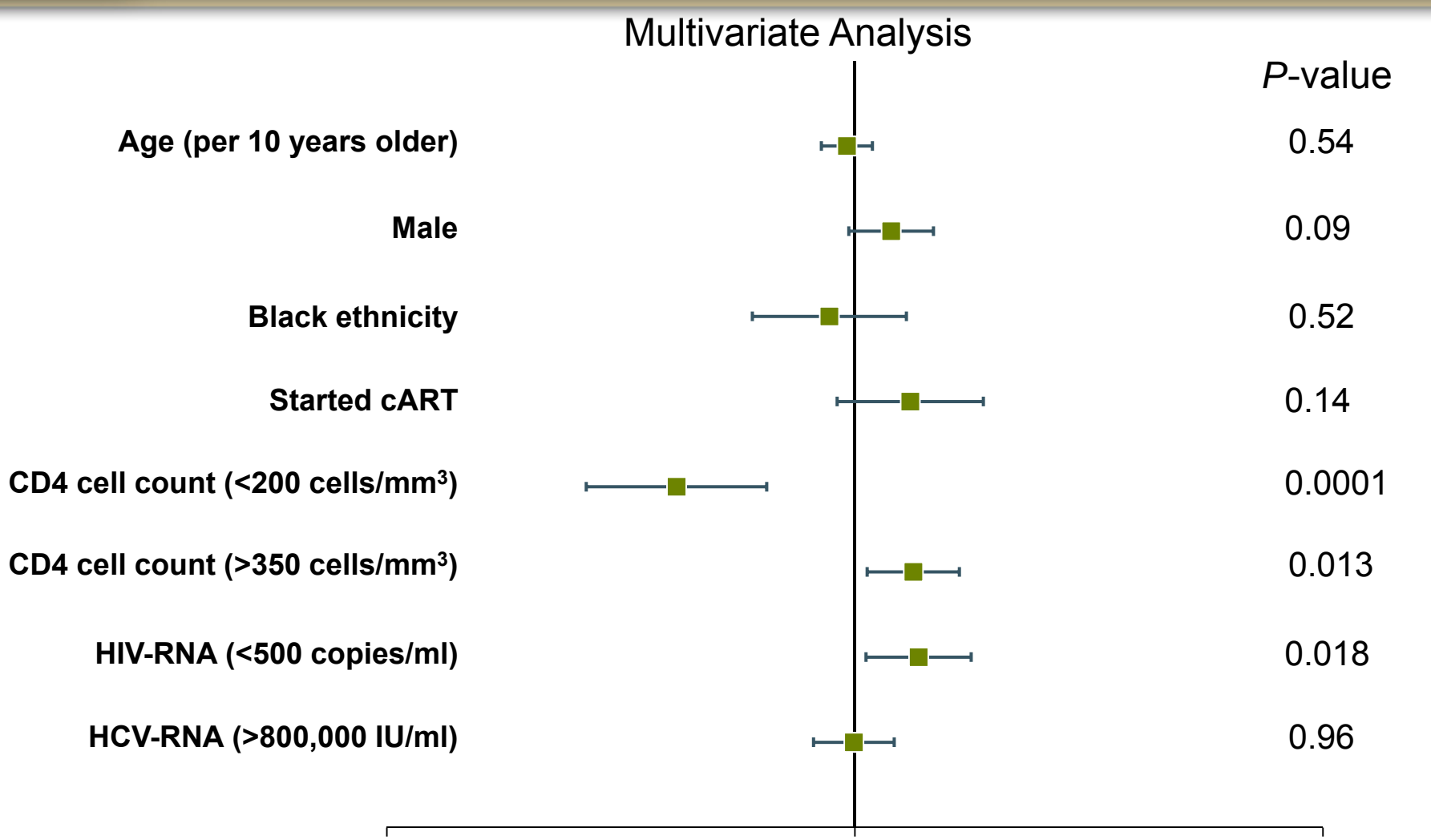
Kirk O, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O242.

Incidence of HCV Treatment Uptake



Grint D, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O243.

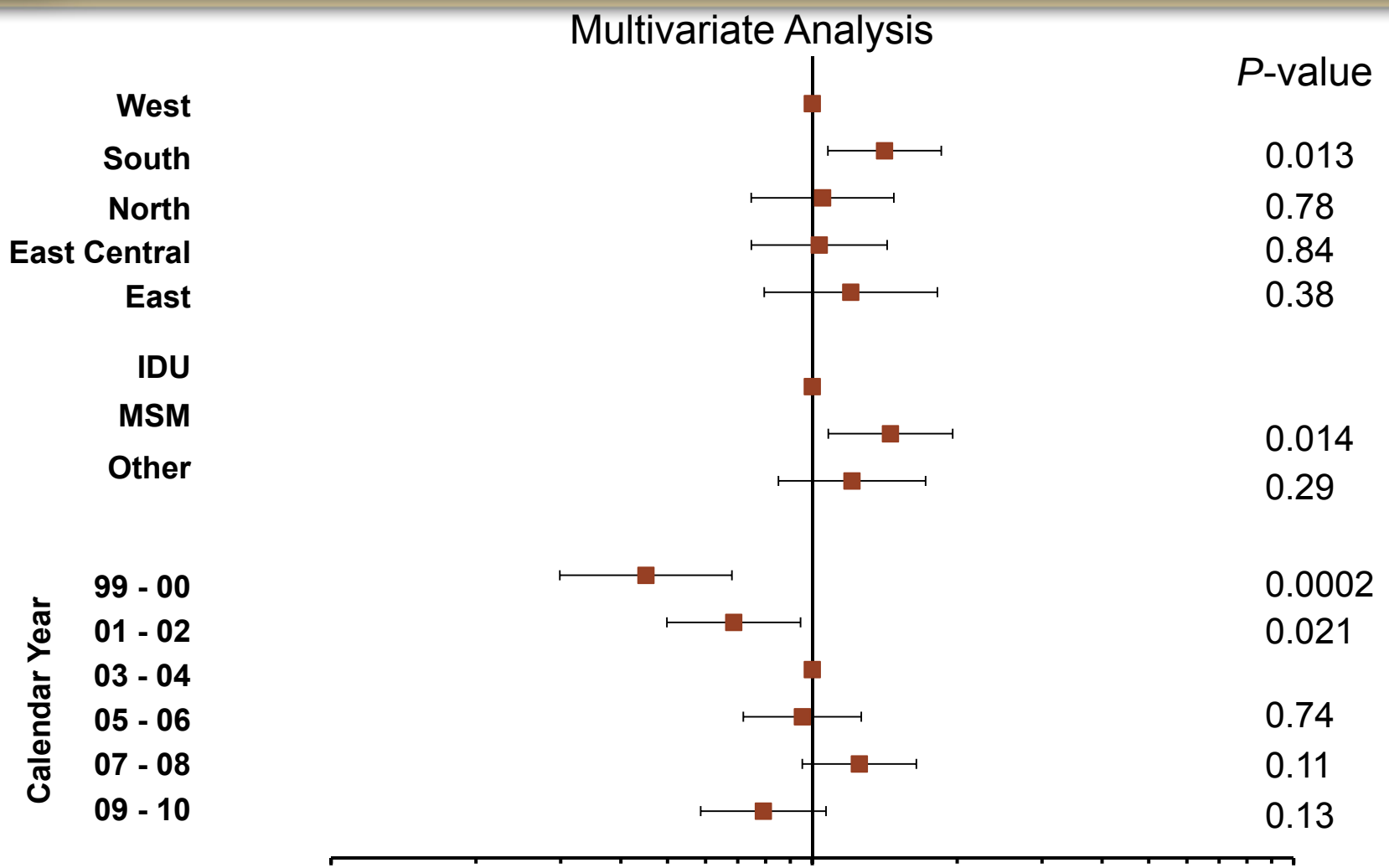
Factors Associated with HCV Treatment Uptake



IRR (95% C.I.)
N treated with interferon = 504

Grint D, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O243.

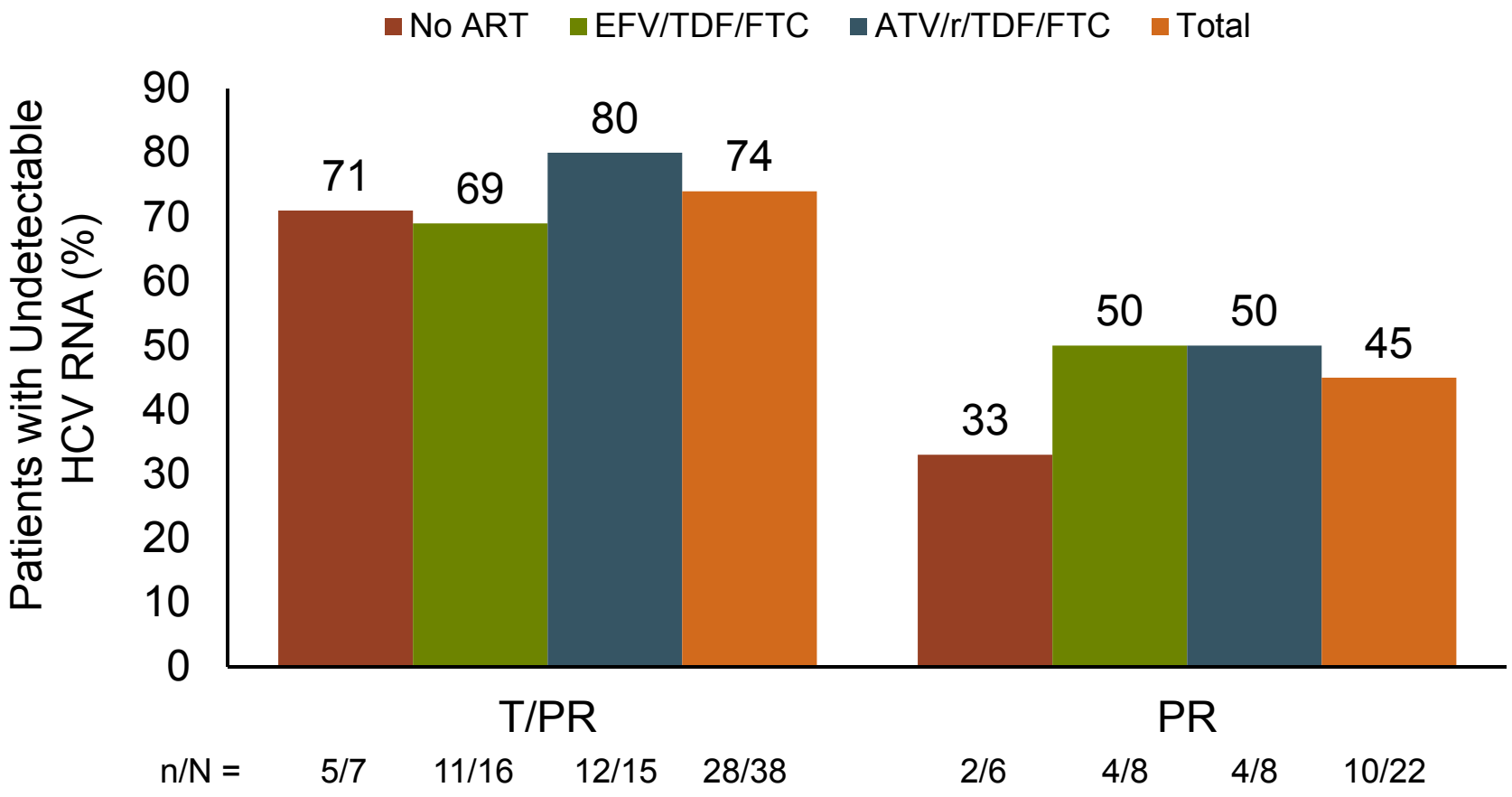
Factors Associated with HCV Treatment Uptake



IRR (95% C.I.)
N treated with interferon = 504
*Model additionally adjusted for HCV genotype + HBsAg status

Grint D, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O243.

Study 110: SVR at post-treatment week 24 (SVR24)



*Prior to Week 24 visit, 1 patient in this cohort was lost to follow up. SVR24 was imputed based on SVR12 for this patient.

Sulkowski M, et al. 63rd AASLD; Boston, MA; November 9-13, 2012; Abst. 54.

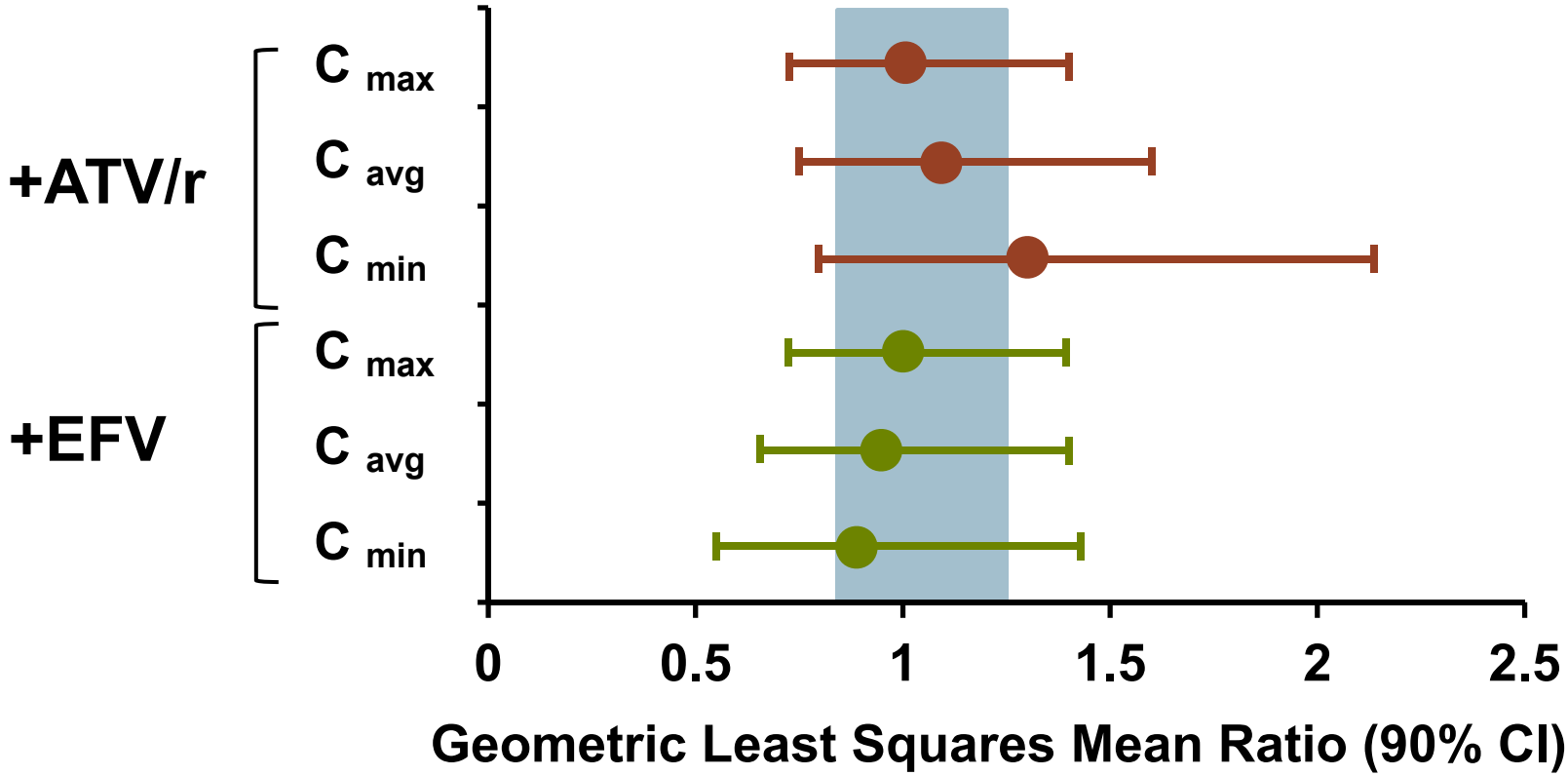
Study 110: Events of Special Interest: Overall Treatment Phase

n (%)	T/PR N=38	PR N=22
Severe rash	0 (0)	0 (0)
Mild and moderate rash	13 (34)	5 (23)
Any anemia (hemoglobin <10g/dL)	7 (18)	4 (18)
Severe anemia (hemoglobin 7.0-8.9 g/dL or decrease from baseline ≥4.5 g/dL)	11 (29)	5 (23)
Use of erythropoietin stimulating agent	3 (8)	1 (5)
Blood transfusions	4 (11)	1 (5)
Discontinuation due to AE	3 (8)	0 (0)

- No HIV breakthrough; CD4 counts declined in T/PR and PR groups; CD4% unchanged
  - 3 T/PR patients discontinued due to adverse event (3 T/PR)

Sulkowski M, et al. 63rd AASLD; Boston, MA; November 9-13, 2012; Abst. 54.

Study 110: Telaprevir Concentrations Similar Among Patients With and Without ART



ATV/r: N=13
EFV: N=15
EFV = efavirenz-based ART regimen; ATV = atazanavir/ritonavir-based ART regimen; CI = Confidence interval.
Shaded rectangle indicated the no-effect range of the geometric least squares mean ration (GLSMRs)
http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM292362.pdf

Sulkowski M, et al. 63rd AASLD; Boston, MA; November 9-13, 2012; Abst. 54.

New Treatment Options for HIV/HCV Genotype 1 Patients: EACS Guidelines

- With first pilot studies in HIV/HCV-coinfected subjects demonstrating significant higher SVR12 rates with triple therapy compared to dual therapy HCV protease inhibitor based therapy with either boceprevir or telaprevir is now the new standard of treatment in HCV genotype 1 infection in HIV-infected individuals where available.
- Although shorter treatment durations of triple therapy have been demonstrated to be very efficacious in HCV monoinfected subjects with rapid virological response this data so far is not available for HIV/HCV coinfected subjects.

EACS Guidelines, September 2012, Version 7.0.

Rockstorh J, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O241.

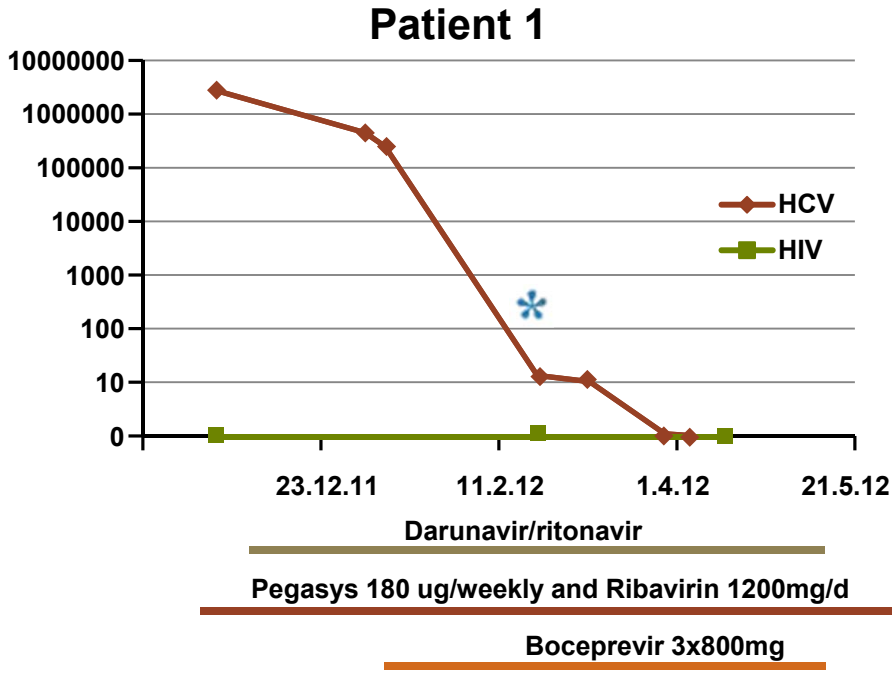
Summary of key DAA and ARV DDI recommendations

	TVR	BOC
ATV/r	Monitoring for hyperbilirubinemia recommended	Consider on a case by case basis if deemed necessary
DRV/r/, FPV/r LPV/r	Not recommended	Not recommended
EFV	Increase TVR to 1250 mg q8h	Not recommended
ETR	No dose adjustment needed	No dose adjustment needed
RPV	No dose adjustment needed	No data
RAL	No dose adjustment needed	No dose adjustment needed
TDF	Increased monitoring is warranted	No dose adjustment needed

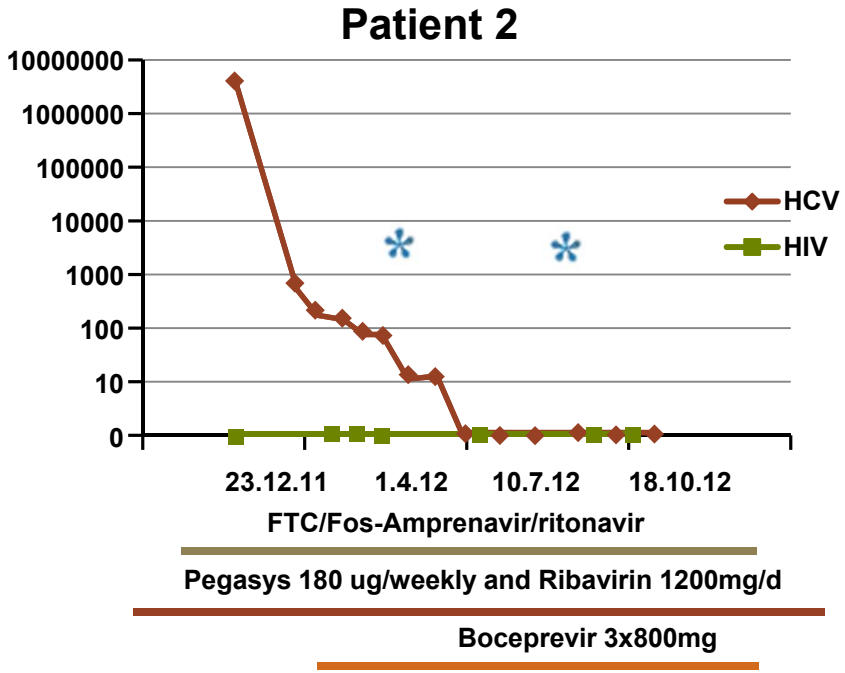
Telaprevir EU SmPC; Boceprevir EU SmPC Kakuda TN, et al. IWCPHT 2012. Abs O-18
Rockstorh J, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. O241.

Boceprevir in Combination With HIV Protease Inhibitors in Patients with Advanced Fibrosis: Altered Drug-drug interactions?

- Patient 1: Liver disease had progressed to liver cirrhosis confirmed in FibroScan with a liver stiffness of 34 kPa
- Patient 2: Liver stiffness was 32 kPa suggestive of liver cirrhosis



Amprenavir trough concentration (reference trough concentration 750-2500 ng/ml)
13.03.2012: 1699 ng/ml
06.08.2012: 1422 ng/ml

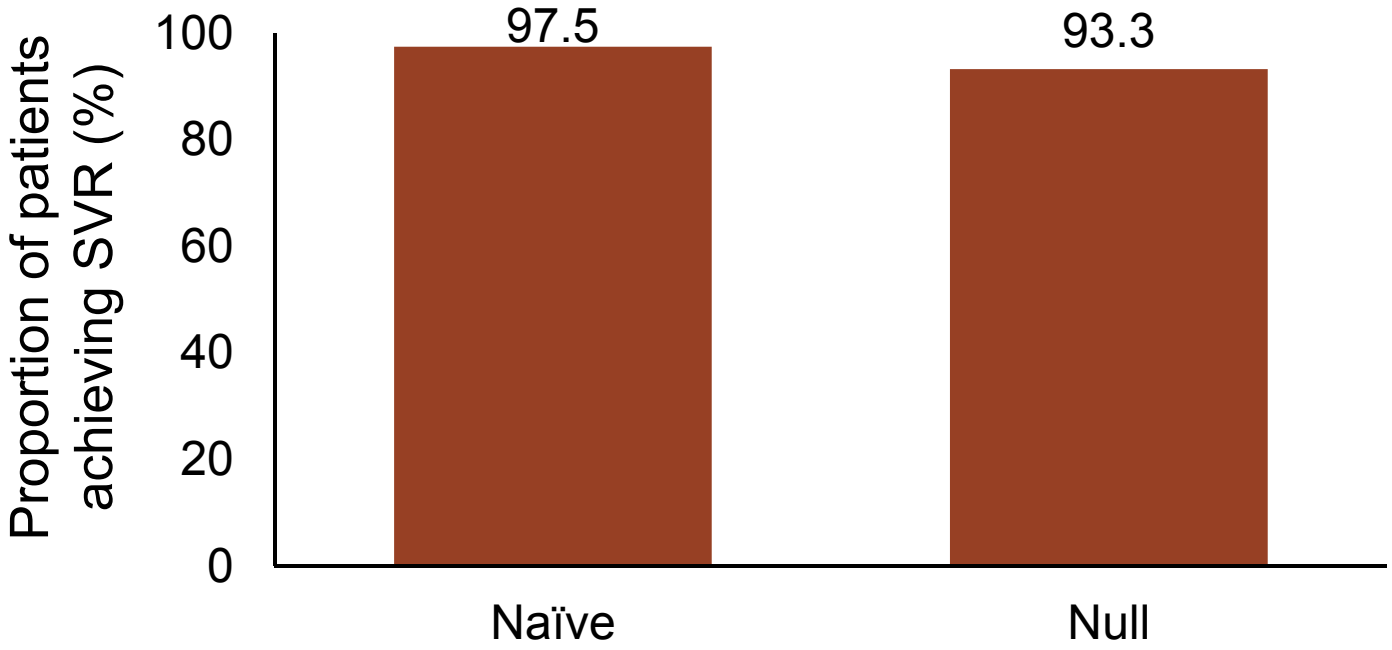


Darunavir trough concentration (reference trough concentration 2400-4600 ng/ml): 3777 ng/ml

Schwarze-Zander C, et al. HIV11; Glasgow, Scotland; November 11-15, 2012; Abst. P130.

Interferon-sparing regimens for HCV infection

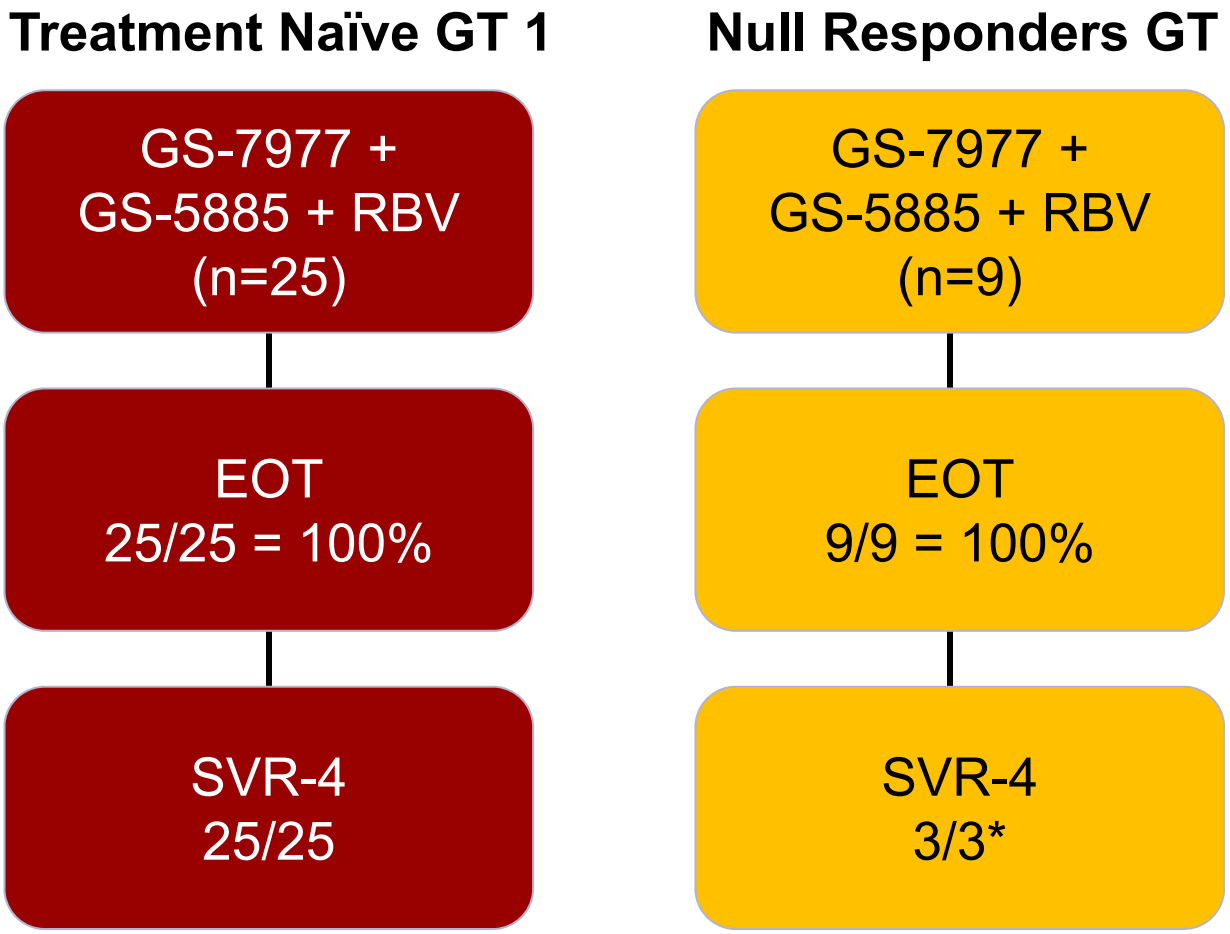
- SVR at Week 12 of interferon sparing regimen of ABT-450/r*, ABT-267, ABT-333 and ribavirin in HCV genotype 1 naïve patients and prior null-responders



*ABT-450 is a HCV protease inhibitor (dosed with ritonavir 100mg, ABT-450/r), ABT-267 is a NS5A inhibitor and ABT-333 is a non-nucleoside NS5B inhibitor

Kowdley K, et al. 63rd AASLD; Boston, MA; November 9-13, 2012; Abst. LB-1.

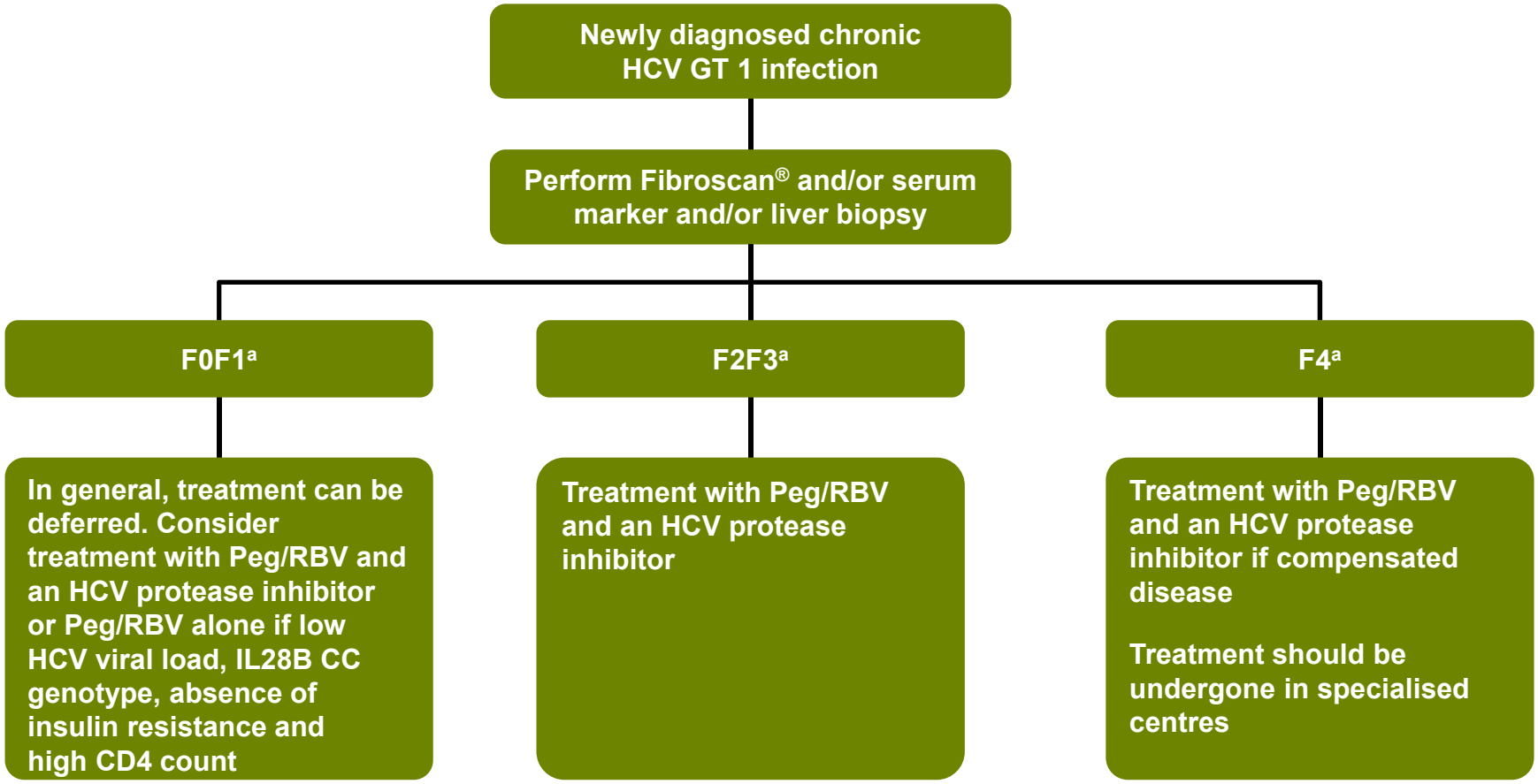
GS-5885 (NS5A-inhibitor) + GS-7977 (nucleotide) + RBV (12w): Efficacy



*6 pending

Gane E, et al. 63rd AASLD; Boston, MA; November 9-13, 2012; Abst. 229.

Management of newly diagnosed HIV-HCV coinfected genotype-1 patients



aMetavir fibrosis score: F0=no fibrosis; F1= portal fibrosis, no septae; F2= portal fibrosis, few septae, F3=bridging fibrosis, F4=cirrhosis; Peg, pegylated interferon; RBV, ribavirin

Ingiliz P, Rockstroh J. Liver International 2012 EACS guidelines, version November 2012

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