Switching antiretroviral therapy to safer strategies based on integrase inhibitors

Dr Paddy Mallon

UCD HIV Molecular Research Group
UCD School of Medicine
paddy.mallon@ucd.ie

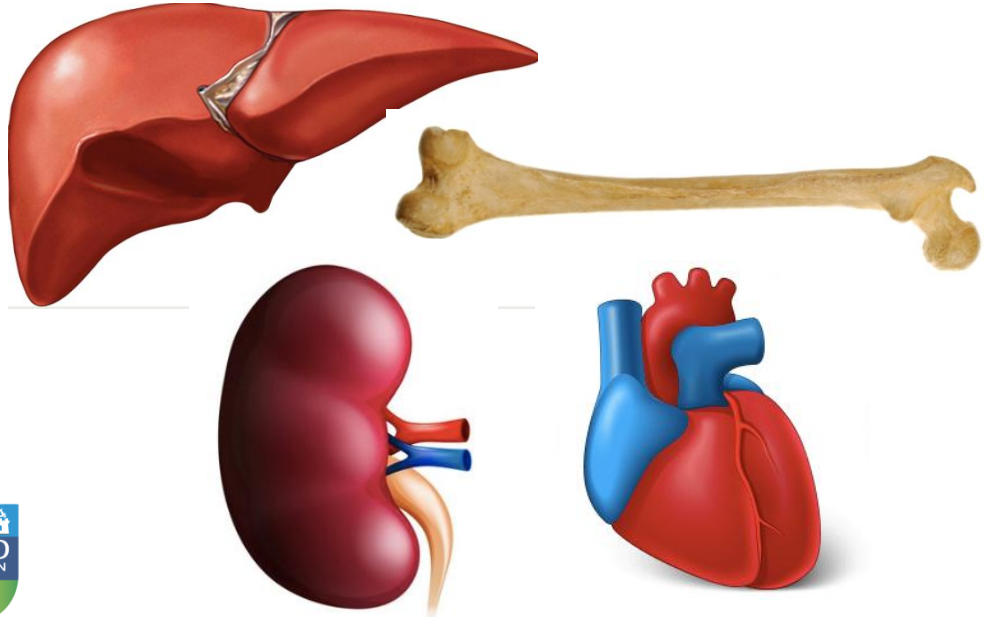
UCD School of Medicine
& Medical Science

HMRG
HIV Molecular Research Group

Scoil an Leighis agus
Eolaíocht An Leighis UCD

HMRG
HIV Molecular Research Group

WE NEED SAFER DRUGS!!



UCD DUBLIN

Reasons to switch

- To decrease polypharmacy
- To simplify dosing (food effects) / monitoring
- To reduce potential for drug-drug interactions
- To manage / avoid adverse events
- Better safety in special circumstances - pregnancy
- To decrease cost (medications, labs, clinic visits)

Reasons *NOT* to switch?

- If it ain't broke, don't fix it
- 'Threshold' of toxicity / tolerability
- Can you be sure the switch will fix the problem?
- Potential to introduce new toxicities
- Will the switch be as effective?
- Virological failure (new resistance)
- Short-term gain, long-term costs – generics

Switching to InSTI as a ‘safer’ option

Raltegravir

200mg

Elvitegravir

Stribild

Genvoya

Dolutegravir

Dolutegravir

Triumeq

*please note pictures do not represent actual size

A380

Switching to InSTI as a ‘safer’ option

Raltegravir

200mg

Elvitegravir

Stribid

Genvoya

Dolutegravir

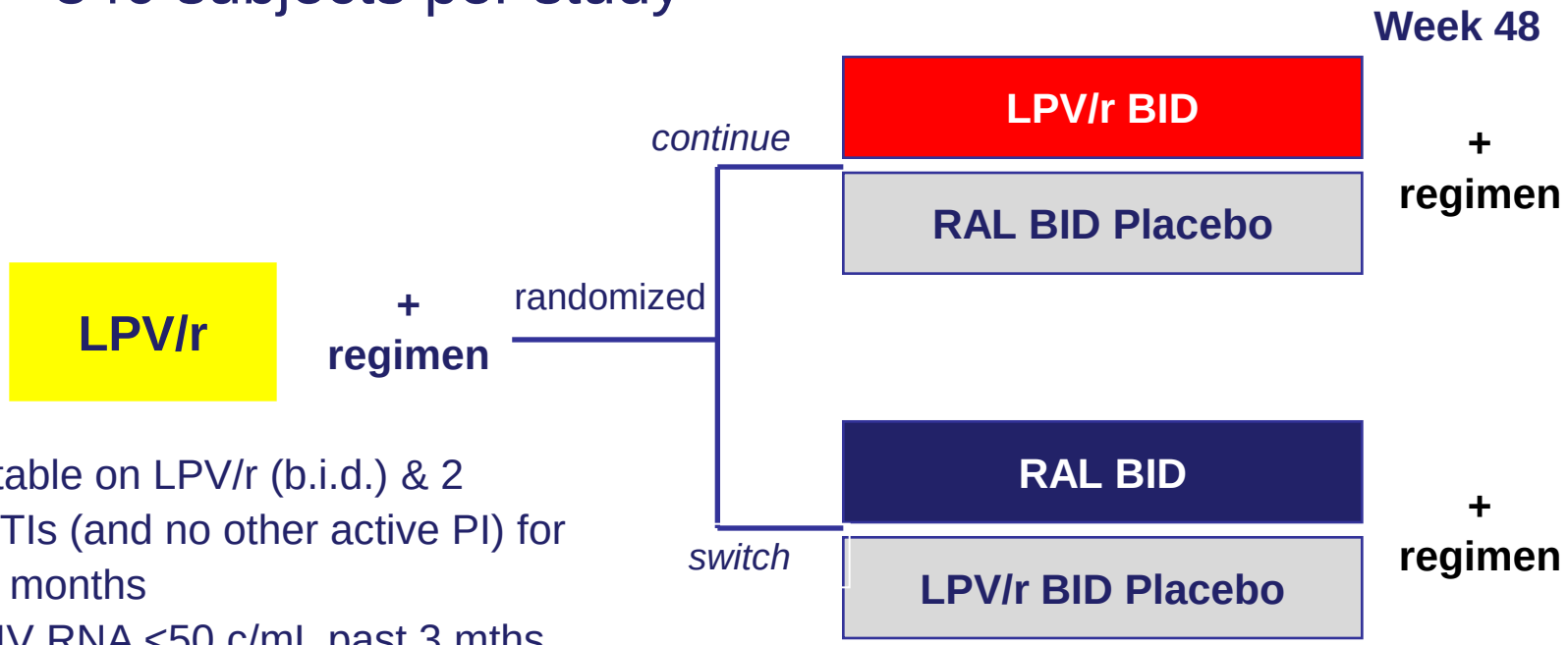
Dolutegravir

Triumeq

Switching to raltegravir

SWITCHMRK (032/033)

N= 340 subjects per study



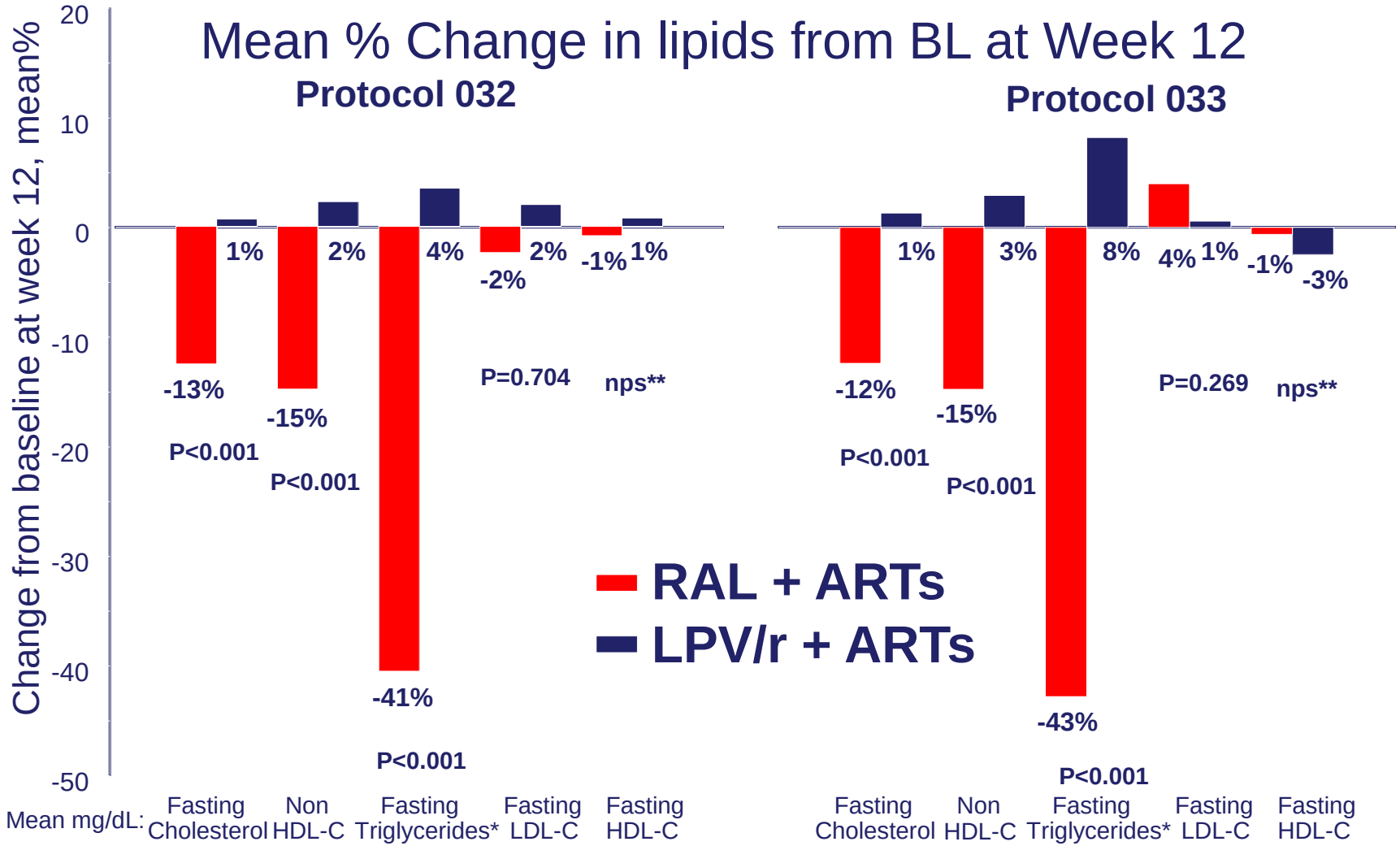
- Stable on LPV/r (b.i.d.) & 2 NRTIs (and no other active PI) for ≥ 3 months
- HIV RNA <50 c/mL past 3 mths
- Patients with prior virologic failure were not excluded
- No LLT past 12 weeks

<u>Primary endpoints:</u>
Week 12: Mean % change in lipids (Total-C, Triglycerides, non-HDL-C and LDL-C)
Week 24: Proportion with viral load <50 copies/mL by Non-completer = Failure (NC=F)

Eron J, et al. *Lancet*. 2010;375:396-407.

Switching to raltegravir

SWITCHMRK (032/033) study

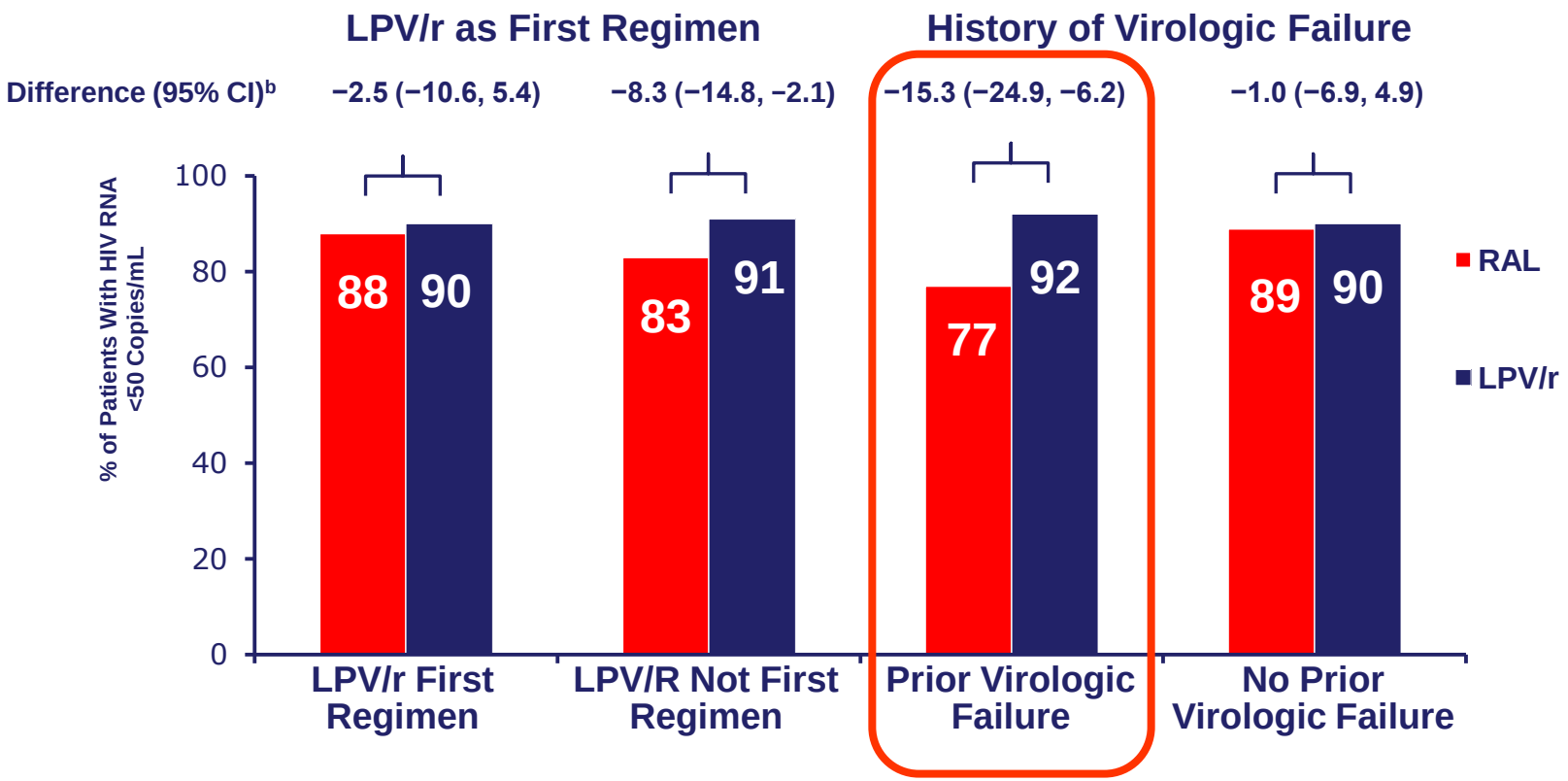


*Median Percent Change **Not prespecified for test

Eron J, et al. *Lancet*. 2010;375:396-407.

Switching to raltegravir

SWITCHMRK (032/033) study
Virological outcomes



CI = confidence interval; LPV/r = lopinavir/ritonavir; RAL = raltegravir. [a]All patients who did not complete the study were regarded as failures.

[b]Calculated by the method of Miettinen and Nurminen. cPlus existing baseline regimen.

Eron J, et al. *Lancet*. 2010;375:396-407.

Switching to raltegravir

SPIRAL study

Study design – open labeled RCT

Study Population (N = 286)

Patients on current PI/r + at least 2 ARV

for ≥ 6 months

VL<50 cp/mL within 180 days

LPVr = 45.5%

ATVr = 36.4%

1:1 Randomization

Stratified by presence or not of lipid lowering agents

Switch to Raltegravir†
(N = 143)

Baseline

Continue with boosted PI
(N = 143)

Analysis, Week 48

*** Raltegravir 400mg BID (maintaining other antiretrovirals unchanged).**

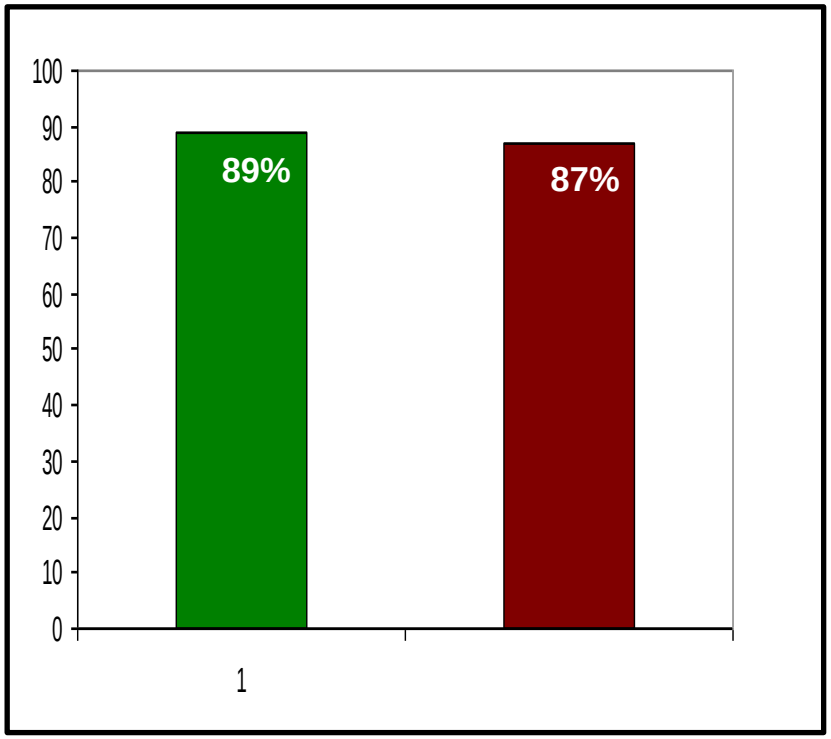
Martinez E et al. AIDS 2010Jul 17;24(11):1697-707

Switching to raltegravir

SPIRAL study
Virological outcomes[1]

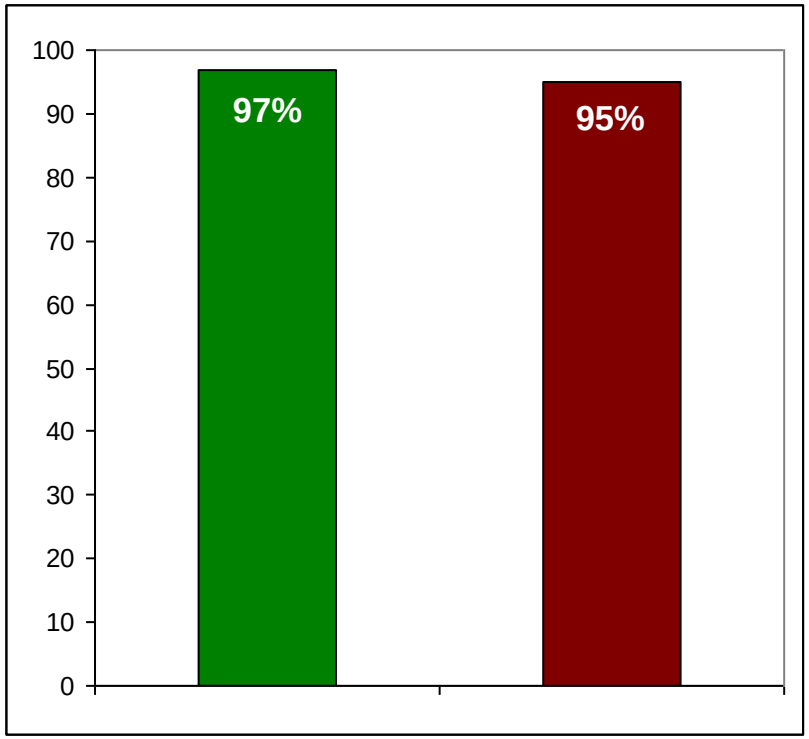
RALTEGRAVIR PI/r

Free of Treatment Failure (ITT, S=F)



Difference Estimate (95% CI) 2.6% (–5.2%, 10.6%)

Free of Virologic Failure (≥ 50 cp/mL) (OT)



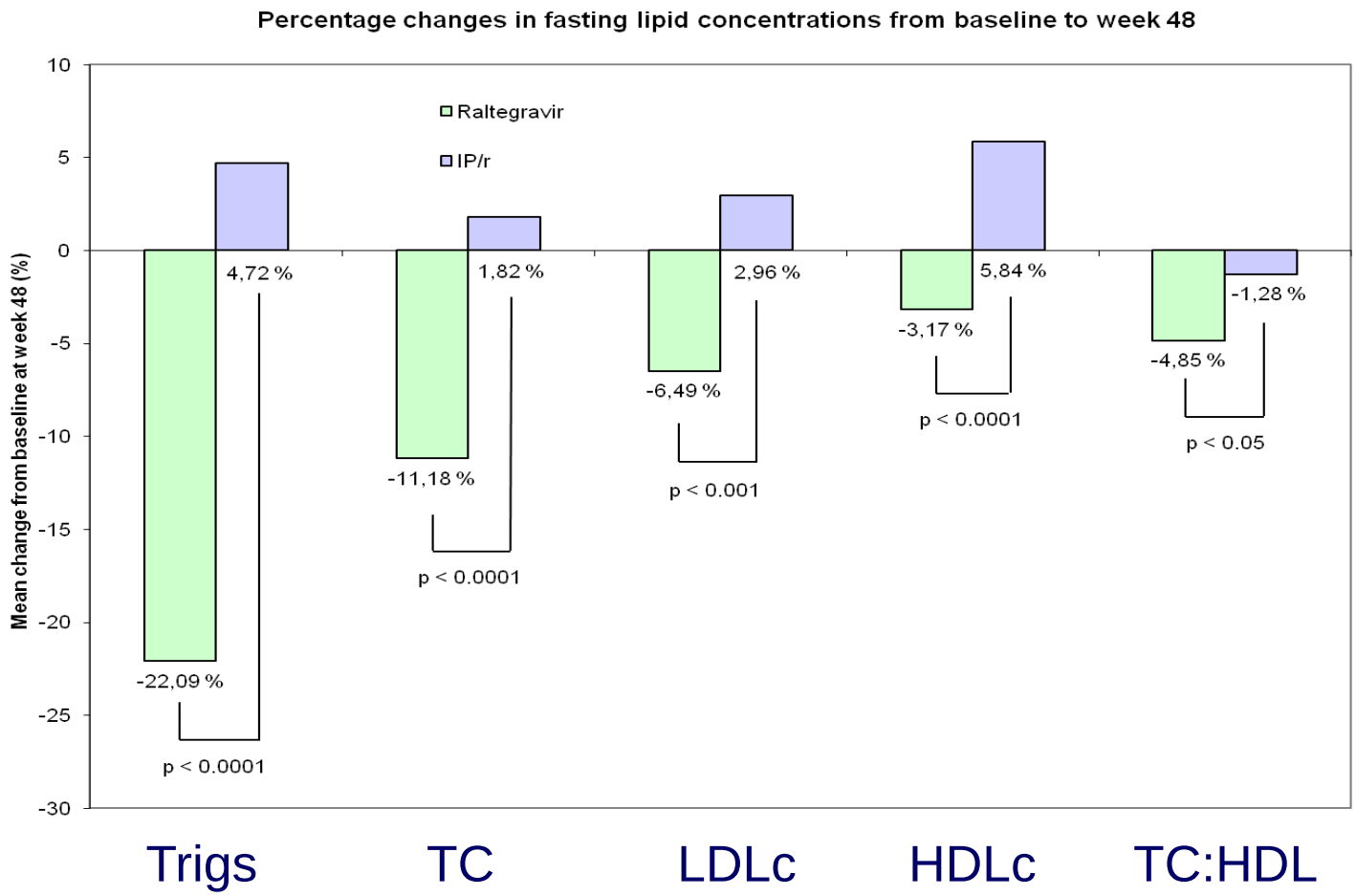
Difference Estimate (95% CI) 1.8% (–3.5%, 7.5%)

Outcomes not influenced by previous virological failures[2]

1. Martinez E et al. AIDS 2010Jul 17;24(11):1697-707, 2. Blanco JL et al. Antivir Ther. 2015;20(5):487-92

Switching to raltegravir

SPIRAL study
Changes in lipids

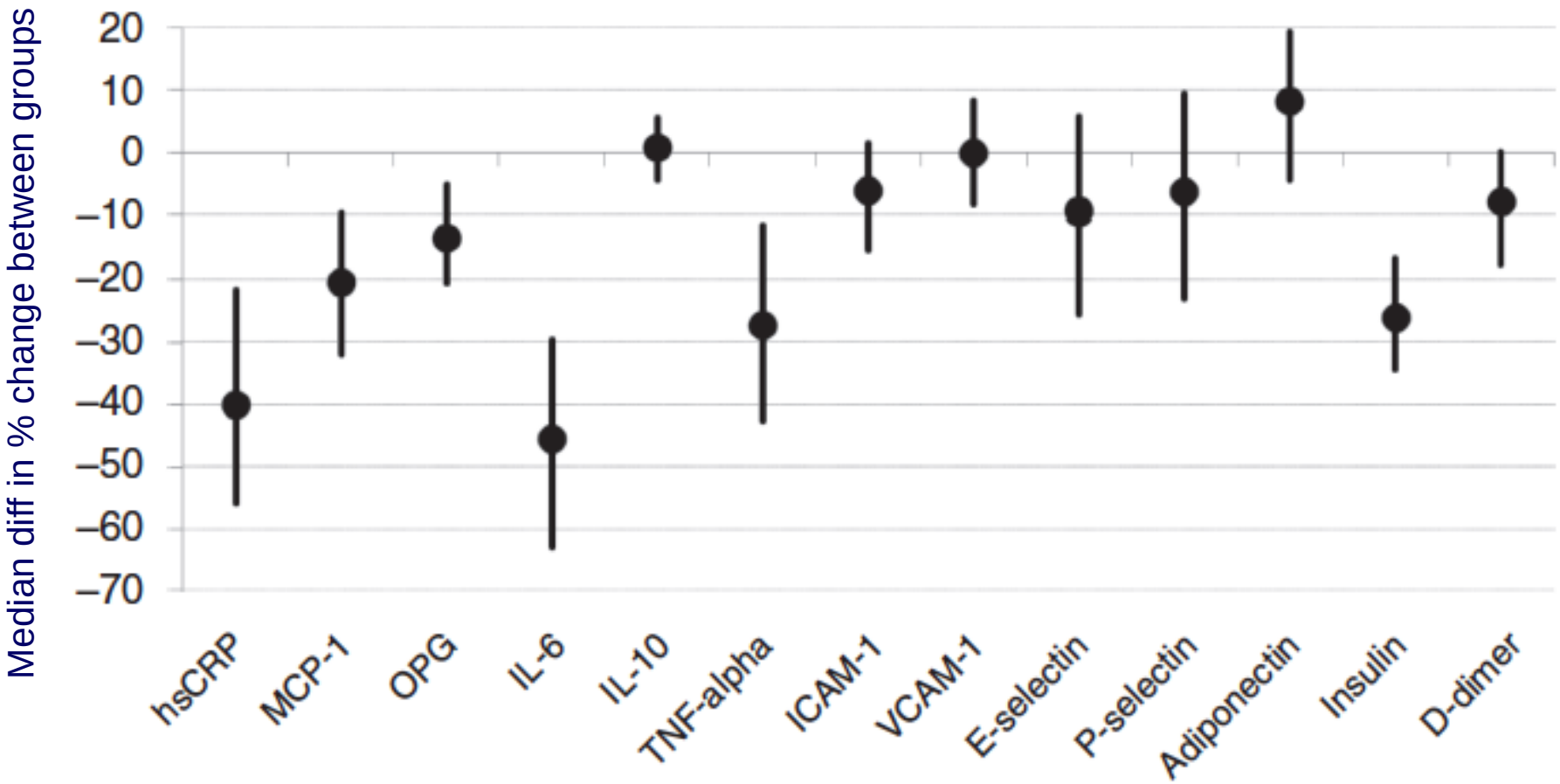


Martinez E et al. AIDS 2010Jul 17;24(11):1697-707

Switching to raltegravir

SPIRAL study

Changes in CVD and inflammatory biomarkers



Martinez E et al. AIDS. 2012 Nov 28;26(18):2315-26

Switching to raltegravir

Protocol 003
Double-blind, RCT

EFV QD vs RAL BID
96 week followup

83% RAL vs 84% EFV with HIVRNA<50c/ml @ wk96

TABLE 4. Summary of Adverse Events

	Raltegravir, 400 mg Twice a Day, (N = 160) n (%)	Efavirenz, 600 mg Every Day, (N = 38) n (%)
One or more clinical adverse events	146 (91.3)	35 (92.1)
Serious clinical adverse events	16 (10.0)	3 (7.9)
Discontinued due to clinical adverse event	2 (1.3)	1 (2.6)
Drug-related* clinical adverse events†	82 (51.3)	28 (73.7)
Diarrhea	11 (6.9)	4 (10.5)
Nausea	20 (12.5)	5 (13.2)
Vomiting	4 (2.5)	3 (7.9)
Flatulence	9 (5.6)	1 (2.6)
Dizziness	14 (8.8)	11 (28.9)
Headache	14 (8.8)	9 (23.7)
Abnormal dreams	10 (6.3)	7 (18.4)
Insomnia	13 (8.1)	4 (10.5)
Nightmares	0 (0.0)	4 (10.5)
Fatigue	8 (5.0)	2 (5.3)
Malaise	2 (1.3)	3 (7.9)
Anxiety	2 (1.3)	2 (5.3)
Lethargy	2 (1.3)	2 (5.3)
Disturbance in attention	1 (0.6)	2 (5.3)
One or more laboratory adverse events	38 (23.8)	11 (28.9)
Discontinued due to laboratory adverse event	1 (0.6)	0 (0.0)
Drug-related* laboratory adverse events†	19 (11.9)	3 (7.9)
Aspartate aminotransferase increased	7 (4.4)	2 (5.3)
Alanine aminotransferase increased	6 (3.8)	2 (5.3)

Markowitz M et al. JAIDS 2009; 52;:350-356

Switching to raltegravir

SPIRAL study

Tolerability outcomes

Characteristic	RALTEGRAVIR N = 142 N (%)	PI/r N = 140 N (%)
Patients with AE leading to study drug discontinuation	3 (2)	3(2)
Neuropsychiatric	2	1
Patients with Serious Adverse Event	6 (4)	5 (4)
Neuropsychiatric	3	1
Digestive	2	1
Respiratory	1	1

Martinez E et al. AIDS 2010Jul 17;24(11):1697-707

Switching to InSTI as a ‘safer’ option

Raltegravir

200mg

Stribid

Elvitegravir

Genvoya

Dolutegravir

Dolutegravir

Triumeq

Switching to Genvoya

Study 109: virologically suppressed adults switching from TDF-based regimen to Genvoya

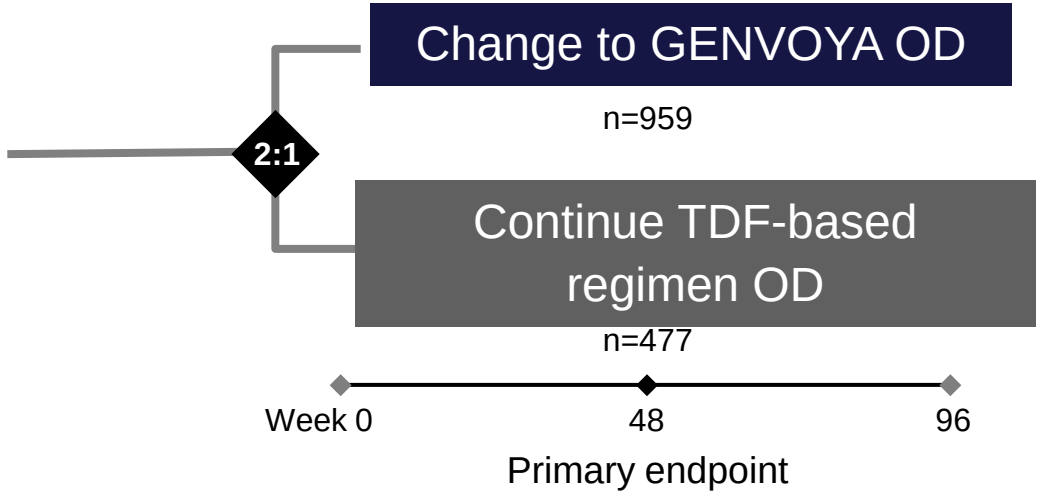
96 week, randomised, open-label, active-controlled Phase III study

Inclusion criteria:

- HIV-suppressed adults on ART (E/C/F/TDF, EFV/FTC/TDF, or boosted ATV + FTC/TDF)
- All patients were virologically suppressed* and had been on a TDF-based regimen for ≥96 weeks
  - CrCl >50 mL/min

Primary endpoint:

- Proportion with HIV-1 RNA <50 copies/mL at Week 48



E, elvitegravir; C, cobisistat; FTC, emtricitabine; TDF, tenofovir disoproxil fumarate; EFV, efavirenz; ATV, atazanavir; OD, once daily; CrCl, creatinine clearance

* Virological suppression: plasma HIV-1 RNA <50 copies/mL

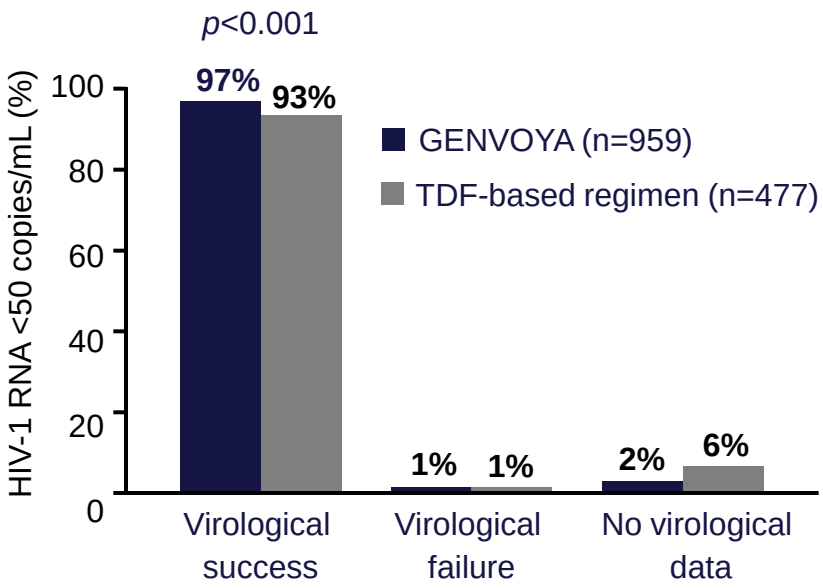
1. Mills A, et al. IAS 2015. Vancouver, Canada. Oral TUAB0102

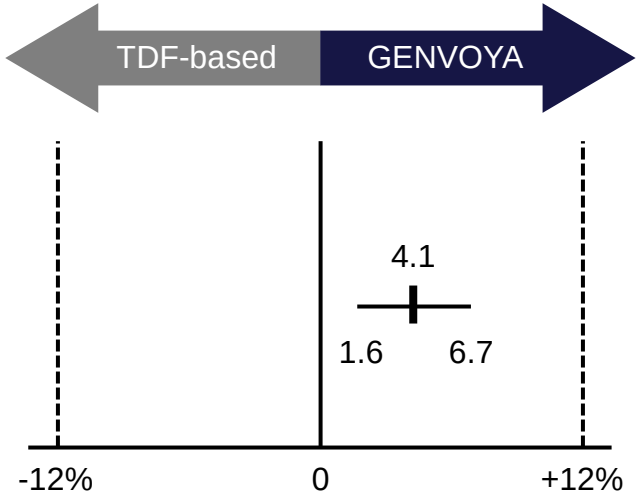
Switching to Genvoya

Study 109

Primary endpoint - switch to Genvoya non-inferior at week 48

Better virological success rates versus remaining on TDF-based regimens





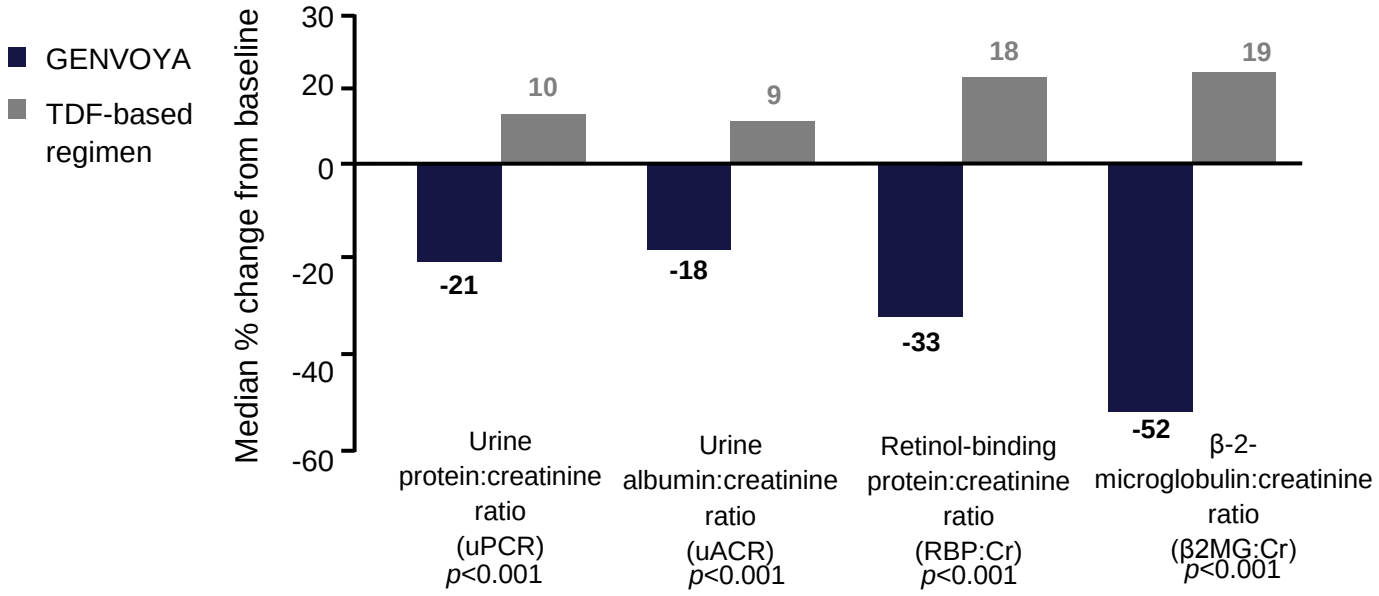
TDF, tenofovir disoproxil fumarate

1. Mills A, et al. IAS 2015. Vancouver, Canada. Oral TUAB0102

Switching to Genvoya

Study 109

Statistically significantly lower quantitative proteinuria at week 48 versus remaining on TDF-containing regimens (all P<0.001)[1]

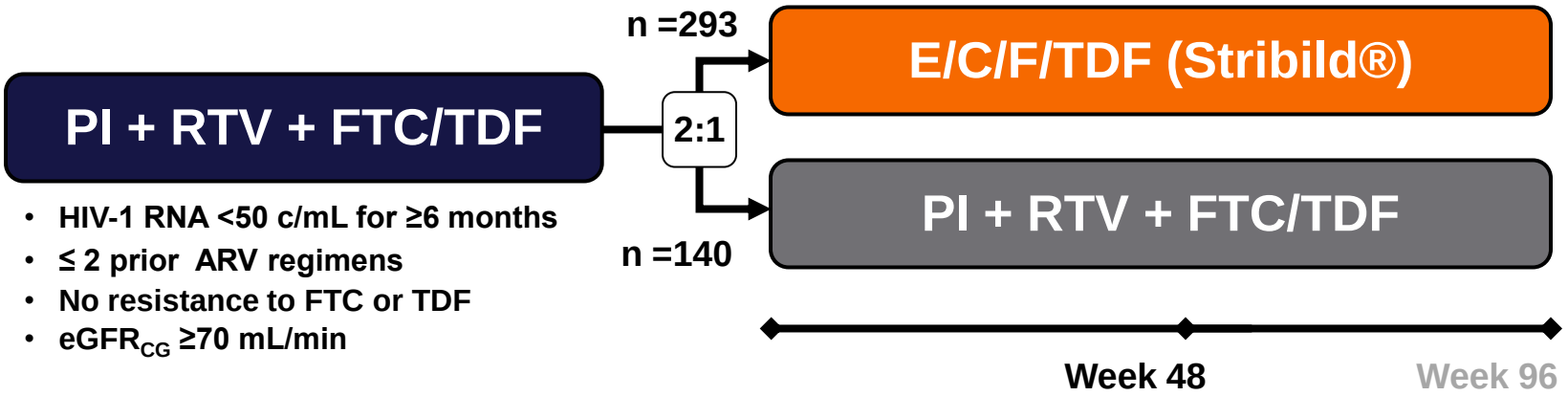


CrCl, creatinine clearance; TDF, tenofovir disoproxil fumarate

1. Mills A, et al. IAS 2015. Vancouver, Canada. Oral TUAB0102

Switching PI to Elvitegravir/c

STRATEGY PI – multicentre, randomised, open-label, 96 week study



- HIV-1 RNA <50 c/mL for ≥6 months
- ≤ 2 prior ARV regimens
- No resistance to FTC or TDF
- $eGFR_{CG}$ ≥70 mL/min

Primary endpoint: HIV-1 RNA <50 c/mL at Week 48 by Snapshot (noninferiority margin of 12%). If noninferiority is established, then superiority will be tested.

Secondary endpoint: Safety and tolerability at Week 48 & 96

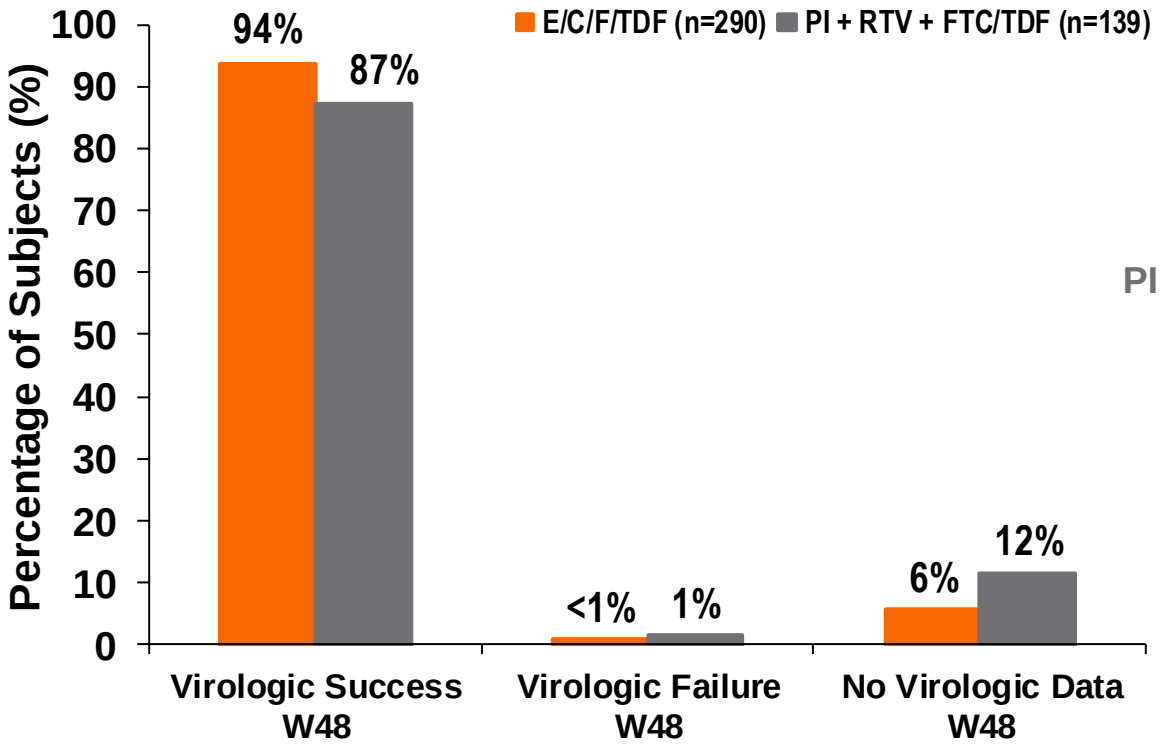
Other endpoints: Patient reported outcomes*

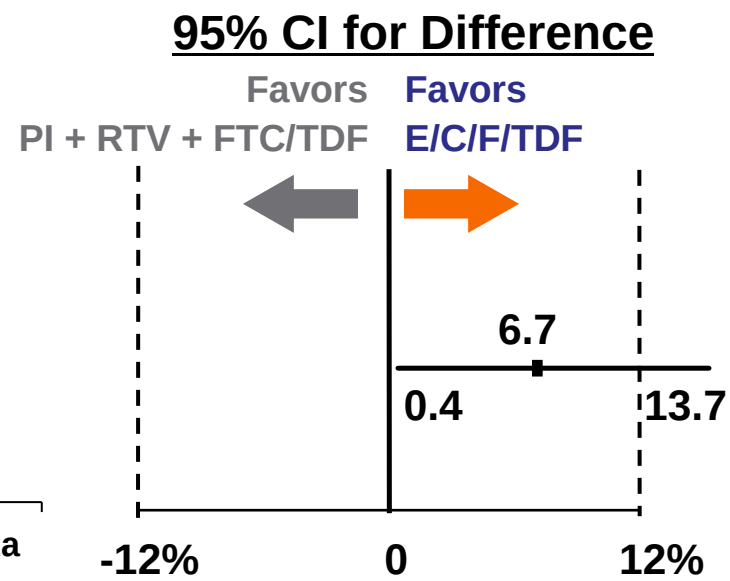
*HIV Symptom Index and HIV Treatment Satisfaction questionnaires
E/C/F/TDF: single-tablet regimen elvitegravir 150mg, cobicistat 150mg, emtricitabine 200mg, tenofovir DF 300mg; Stribild®
PI + RTV + FTC/TDF: ritonavir-boosted protease inhibitor and emtricitabine/tenofovir DF
Study GS-US-236-0115 is registered with ClinicalTrials.gov, number NCT01475838.

Arribas J et al. CROI 2014. Abstract 551LB

Switching PI to Elvitegravir/c

STRATEGY PI – primary endpoint: HIVRNA <50 cps/ml





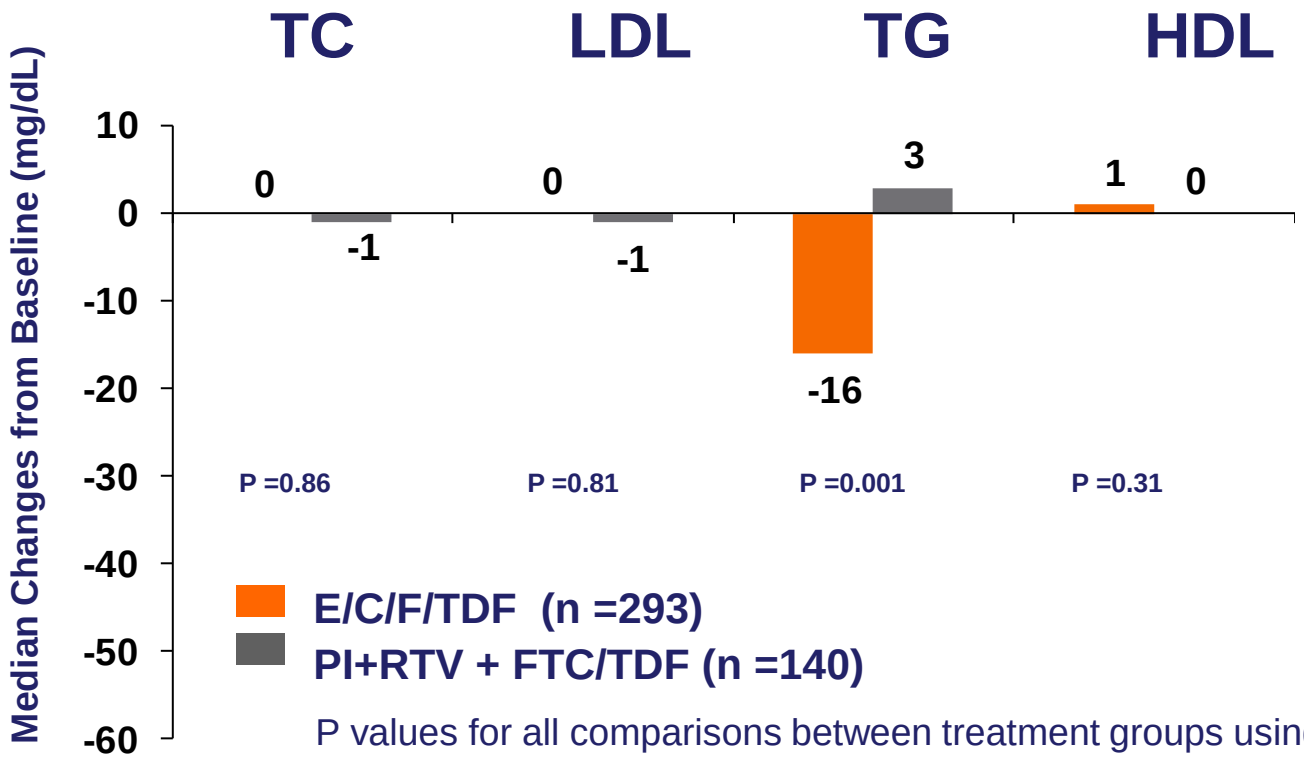
Prespecified sequential testing
Statistical superiority
(p = 0.025)

Full analysis set excluded subjects with protocol-prohibited mutations on historical genotype and those not on PI at randomization.

Arribas J et al. CROI 2014. Abstract 551LB

Switching PI to Elvitegravir/c

STRATEGY PI – change in fasting lipids



P values for all comparisons between treatment groups using ANOVA or Wilcoxon Rank Sum were not significant except for TG (p <0.001)

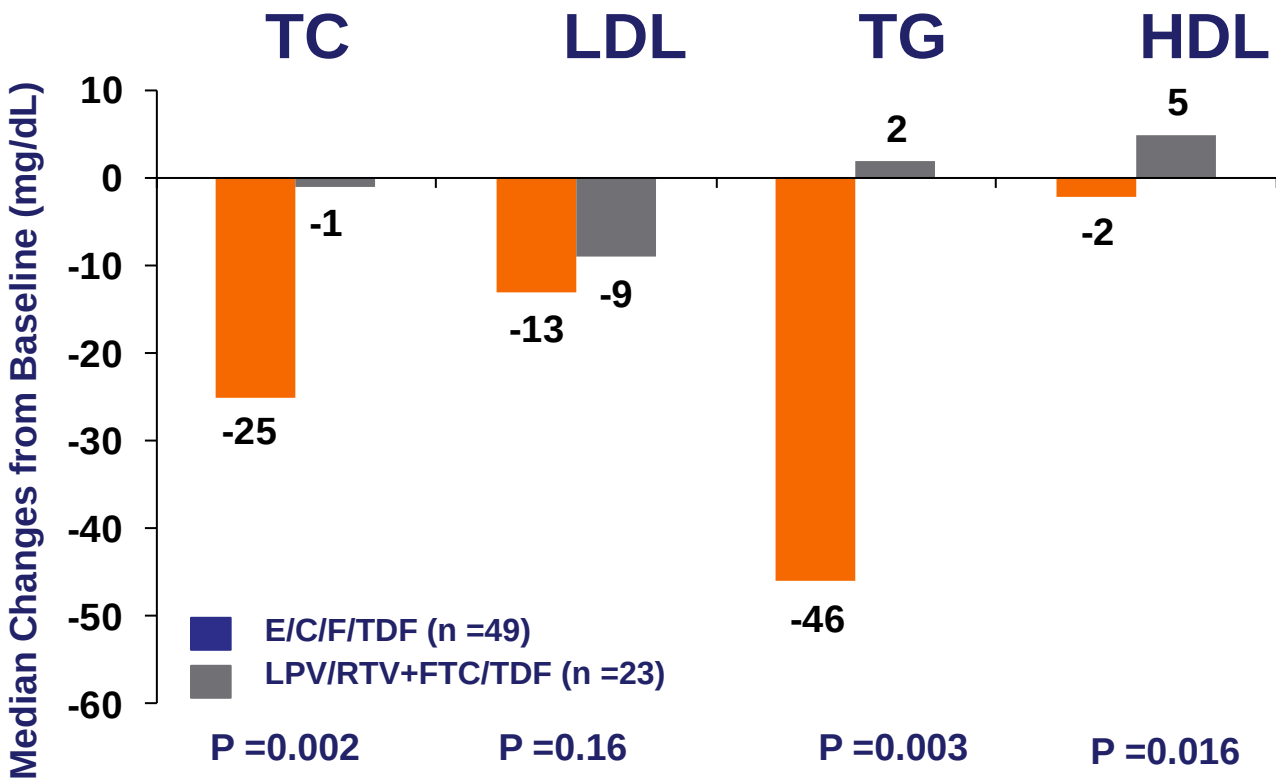
Changes from baseline in total cholesterol/HDL ratios were not statistically significant.

Decreases from baseline in triglycerides at Week 48 after switching to E/C/F/TDF

1. Mills A, et al. IAS 2015. Vancouver, Canada. Oral TUAB0102

Switching PI to Elvitegravir/c

STRATEGY PI – change in fasting lipids with switch from LPVr



P values for all comparisons between treatment groups using Wilcoxon Rank Sum test

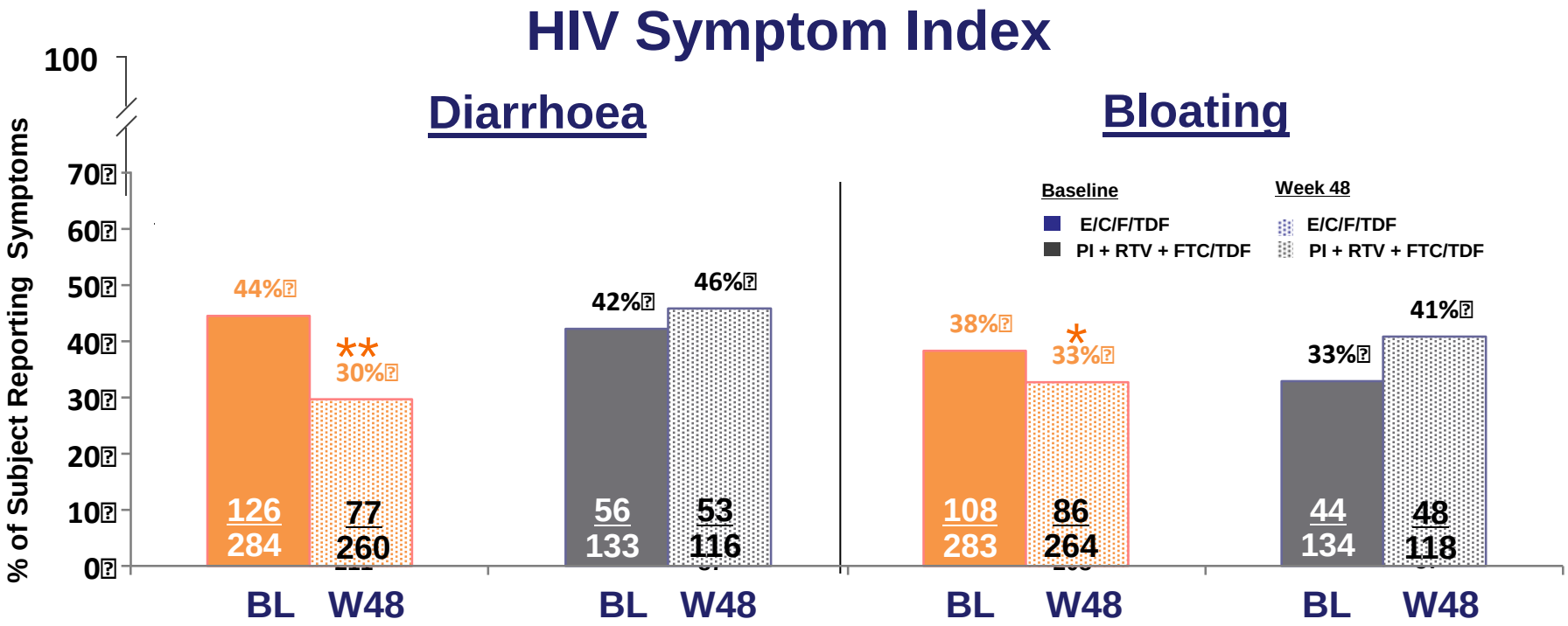
Changes from baseline in total cholesterol/HDL ratios were not statistically significant.

Decreases from baseline in TC, TGs, and HDL at Week 48 after switching from LPV/RTV to E/C/F/TDF

1. Mills A, et al. IAS 2015. Vancouver, Canada. Oral TUAB0102

Switching PI to Elvitegravir/c

STRATEGY PI – patient reported outcomes



- Subjects who switched to E/C/F/TDF from PI + RTV + FTC/TDF had
  - Lower rates of diarrhea and bloating at Week 48 compared to baseline
  - Higher treatment satisfaction scores at Week 24 (mean: 23 vs. 15, p <0.001)^

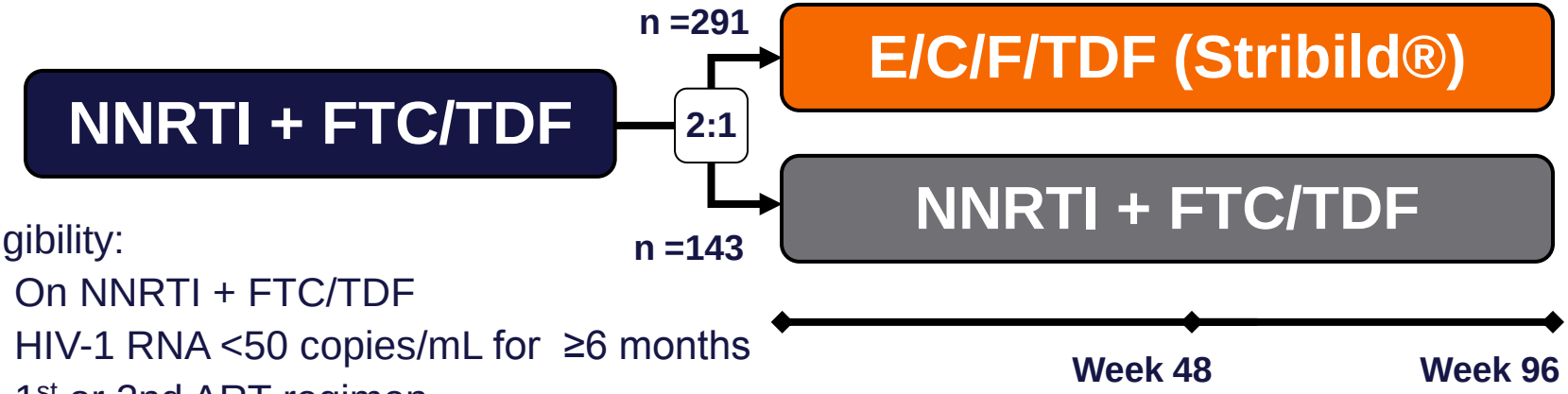
*P <0.04 & **P <0.001 (comparison with baseline within each treatment group). Decreases noted at week 4 & sustained to week 48.
P <0.001, diarrhea & P=0.019, bloating (comparison of changes from baseline at week 48 between treatment group).
^ HIV Treatment Satisfaction questionnaire, score range: -30 to 30

Arribas J et al. CROI 2014. Abstract 551LB

Switching NNRTI to Elvitegravir/c

STRATEGY-NNRTI

Study design



Eligibility:

- On NNRTI + FTC/TDF
- HIV-1 RNA <50 copies/mL for ≥6 months
- 1st or 2nd ART regimen
- No history of virological failure or resistance to FTC or TDF
- $eGFR_{CG}$ ≥70 mL/min

Primary endpoint: HIV-1 RNA <50 c/mL at Week 48 by Snapshot (noninferiority margin of 12%)

Secondary endpoint: Safety and tolerability at Week 48 & 96

ClinicalTrials.gov, number NCT01495702

Pozniak A et al. CROI 2014 Abstract #553LB

Switching NNRTI to Elvitegravir/c

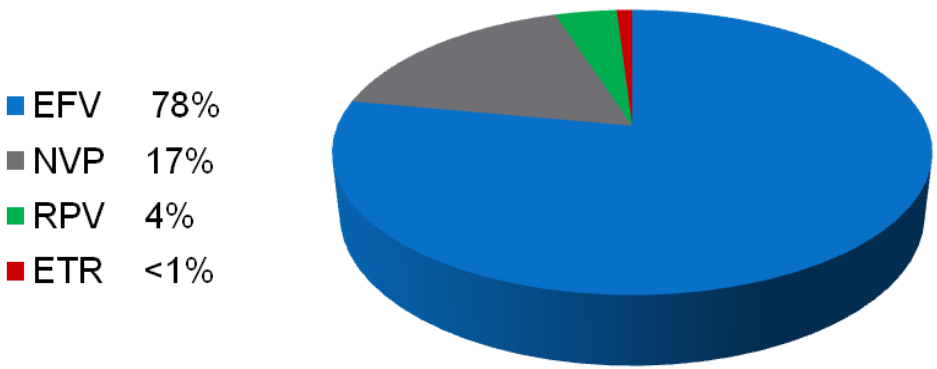
STRATEGY-NNRTI

Previous ART regimens

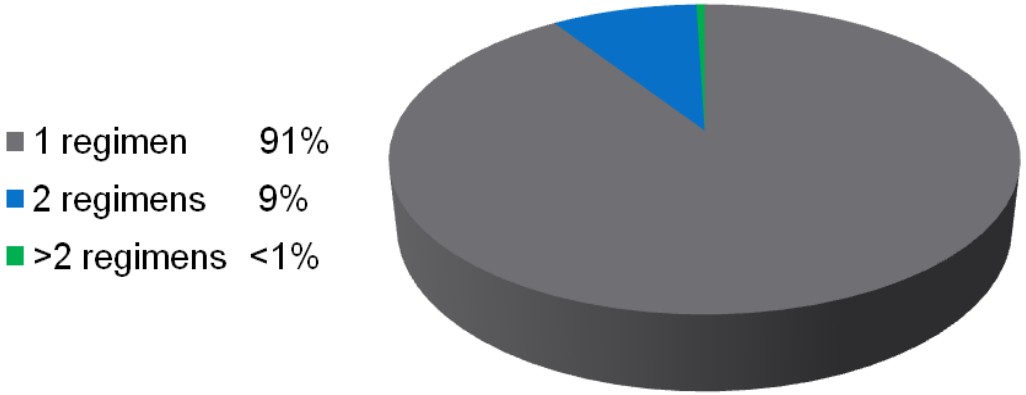
Single Tablet Regimen (n =338; 78%)
Atripla (n =322; 74%)
Eviplera (n =16; 4%)

Reasons to enrol:	(n=434)
Simplification	**48%**
Long-term toxicity concerns	**20%**
Current tolerability issues	**14%**

NNRTI at Randomization (n =434)



Number of Prior Regimens (n =434)



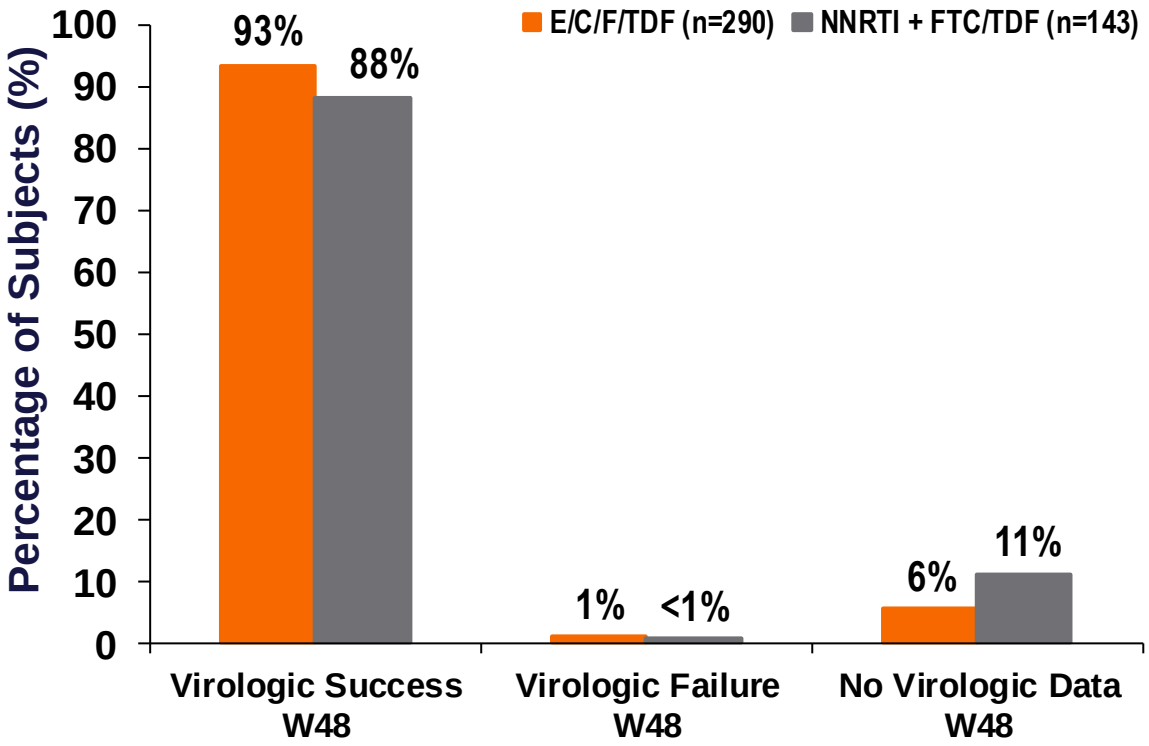
EFV, efavirenz; ETR, etravirine; NNRTI, non-nucleoside reverse transcriptase inhibitors; NVP, nevirapine; RPV, rilpivirine

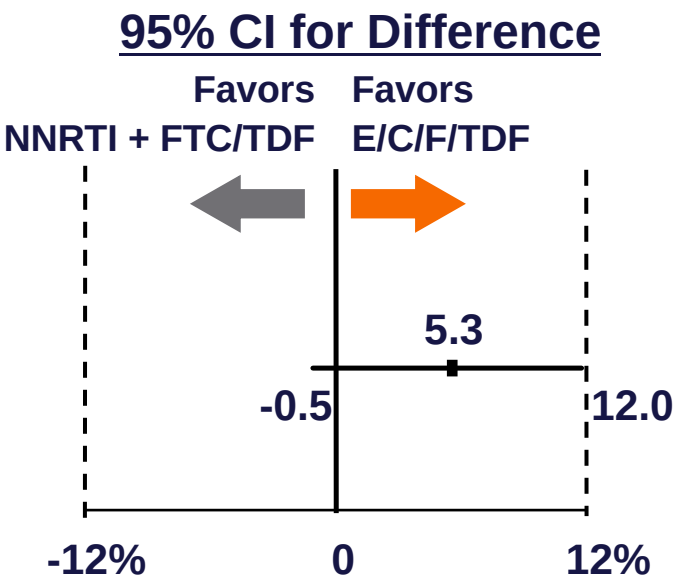
Pozniak A et al. CROI 2014 Abstract #553LB

Switching NNRTI to Elvitegravir/c

STRATEGY-NNRTI

Primary endpoint: HIV RNA<50 cps/ml





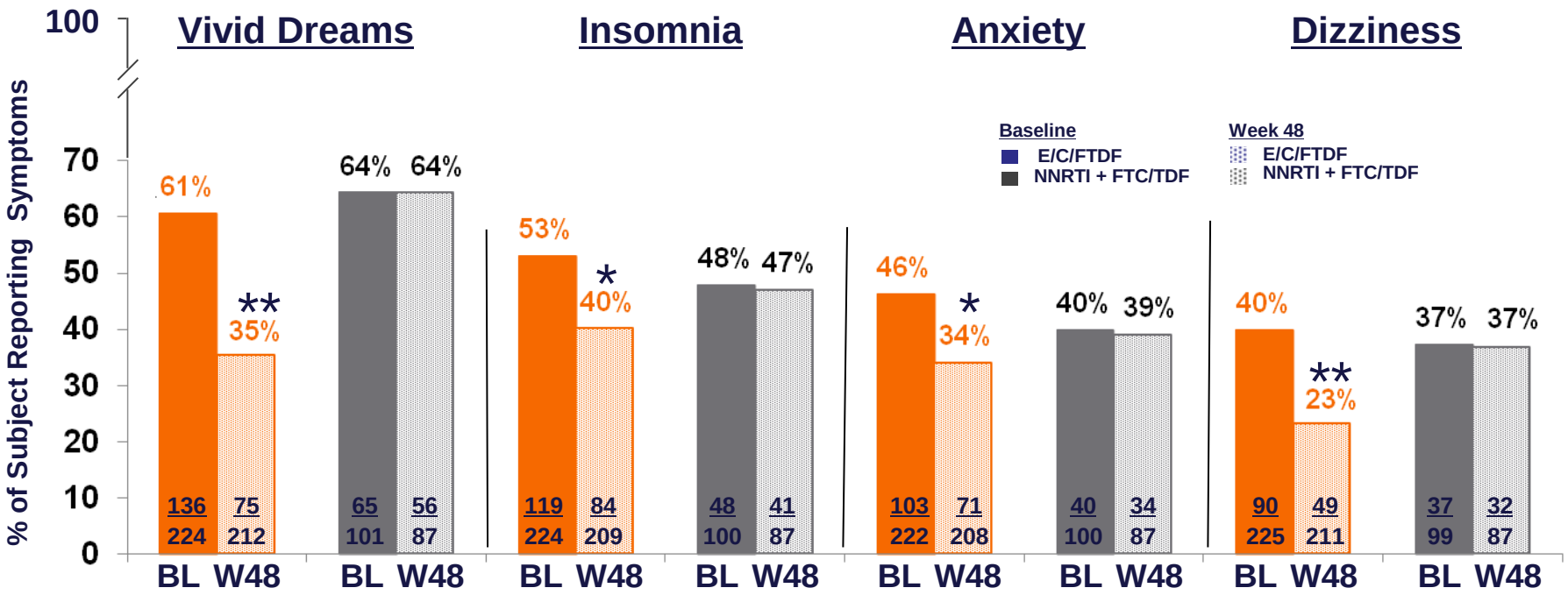
CD4 Cell Count (cells/mm³)	Baseline (mean)	ΔWeek 48 (mean)	P-value (Δ W48 - BL)
E/C/F/TDF	586	+56	<0.001
NNRTI + FTC/TDF	593	+58	<0.001

Pozniak A et al. CROI 2014 Abstract #553LB

Switching NNRTI to Elvitegravir/c

STRATEGY-NNRTI

Patient-reported outcomes – EFV subgroup group analysis



Higher treatment satisfaction scores at Week 24 (mean: 21 vs. 14, p <0.001)^

* P <0.01 & **P <0.001 (comparison with baseline within treatment group).

Pozniak A et al. CROI 2014 Abstract #553LB

Use of Genvoya in renal dysfunction

Study 112 - phase III, 96-week, single-arm, open-label study of virologically suppressed adults with mild to moderate renal dysfunction switching to GENVOYA[1]

Inclusion criteria:

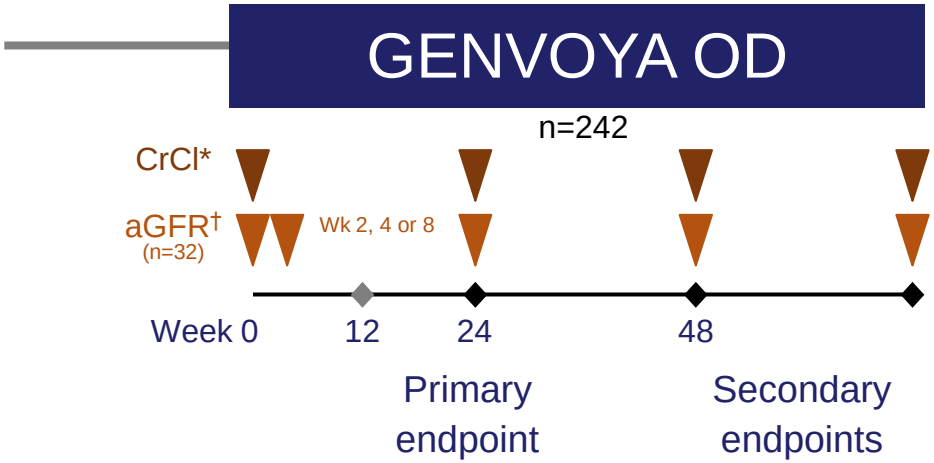
– HIV-suppressed adults with renal impairment (CrCl 30–69 mL/min)

– HIV-1 RNA <50 copies/mL for ≥6 months

– CD4 ≥50 cells/mm^3

Primary endpoint:

– Change from baseline in CrCl at Week 24**



*Creatinine clearance (CrCl) measured using the Cockcroft-Gault formula in all patients

†Actual GFR measured using iohexol plasma clearance in a subset of patients at 3 time points: baseline; Week 2, 4 or 8; and Week 24

**Median (Q1, Q3) change in CrCl from baseline to Week 24 was -0.4 (-4.8, 4.5) mL/min

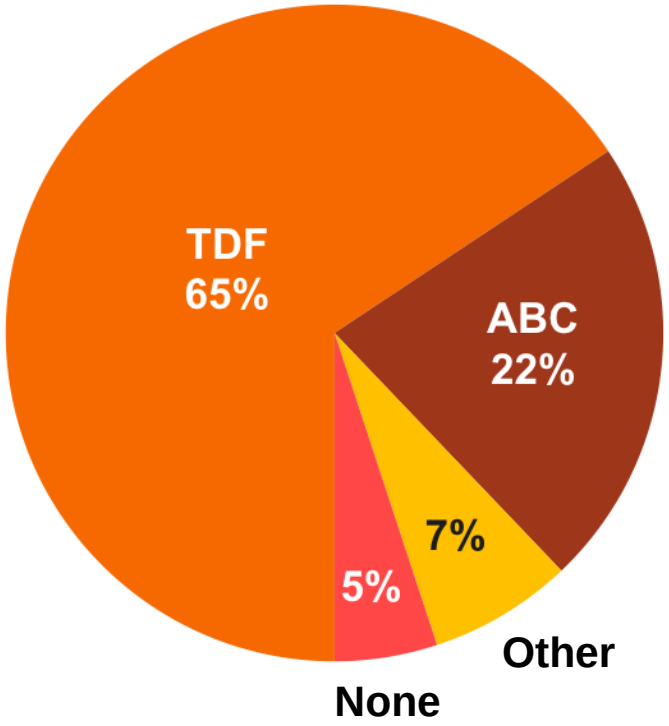
TDF, tenofovir disoproxil fumarate; OD, once daily; CrCl, creatinine clearance; aGFR, actual glomerular filtration rate

1. Pozniak A, et al. CROI 2015. Seattle, WA, USA. Poster 795

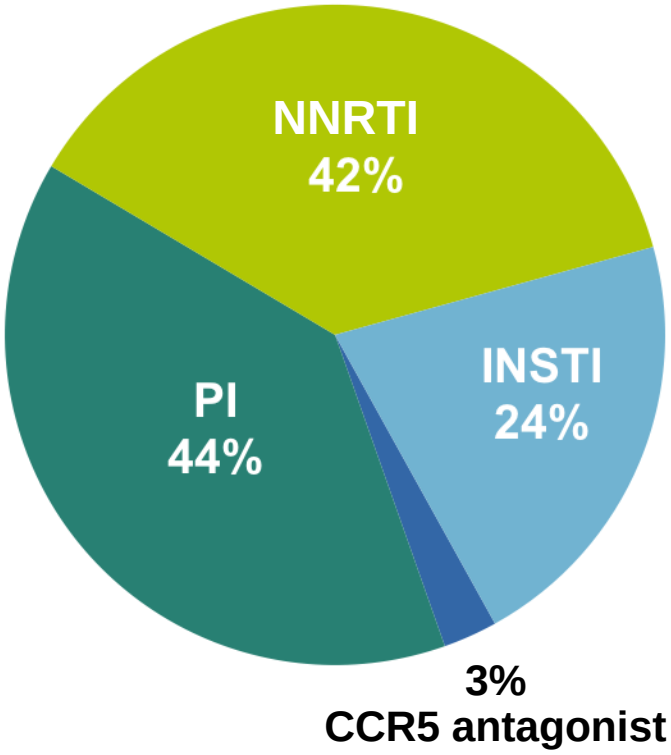
Use of Genvoya in renal dysfunction

Antiretroviral Treatment Prior to Switching to E/C/F/TAF

NRTIs



3rd Agent*



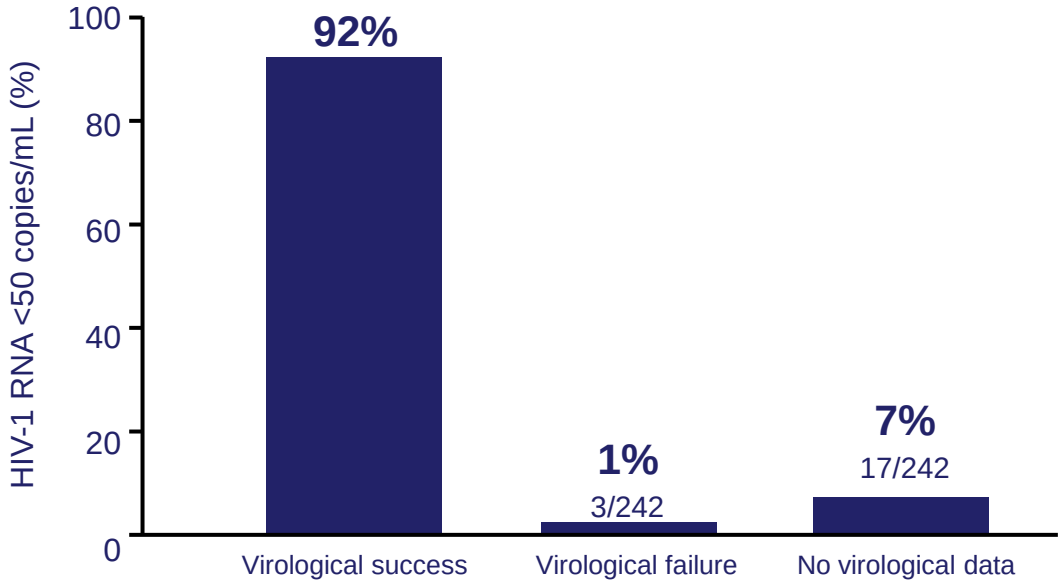
- *Some regimens included >1 3rd agent; therefore, total >100%. ABC, abacavir; CCR5, C-C chemokine receptor type 5; INSTI, integrase strand transfer inhibitor; NNRTI, non-nucleoside reverse-transcriptase inhibitor; NRTI, nucleoside reverse-transcriptase inhibitor; PI, protease inhibitor.

Post F et al. CROI 2016. Abstract #680.

Use of Genvoya in renal dysfunction

Primary endpoint change from baseline in CrCl at week 24

Genvoya maintains high rates of virological suppression at week 48



*Median (Q1, Q3) change in CrCl from baseline to Week 24 was -0.4 (-4.8, 4.5) mL/min

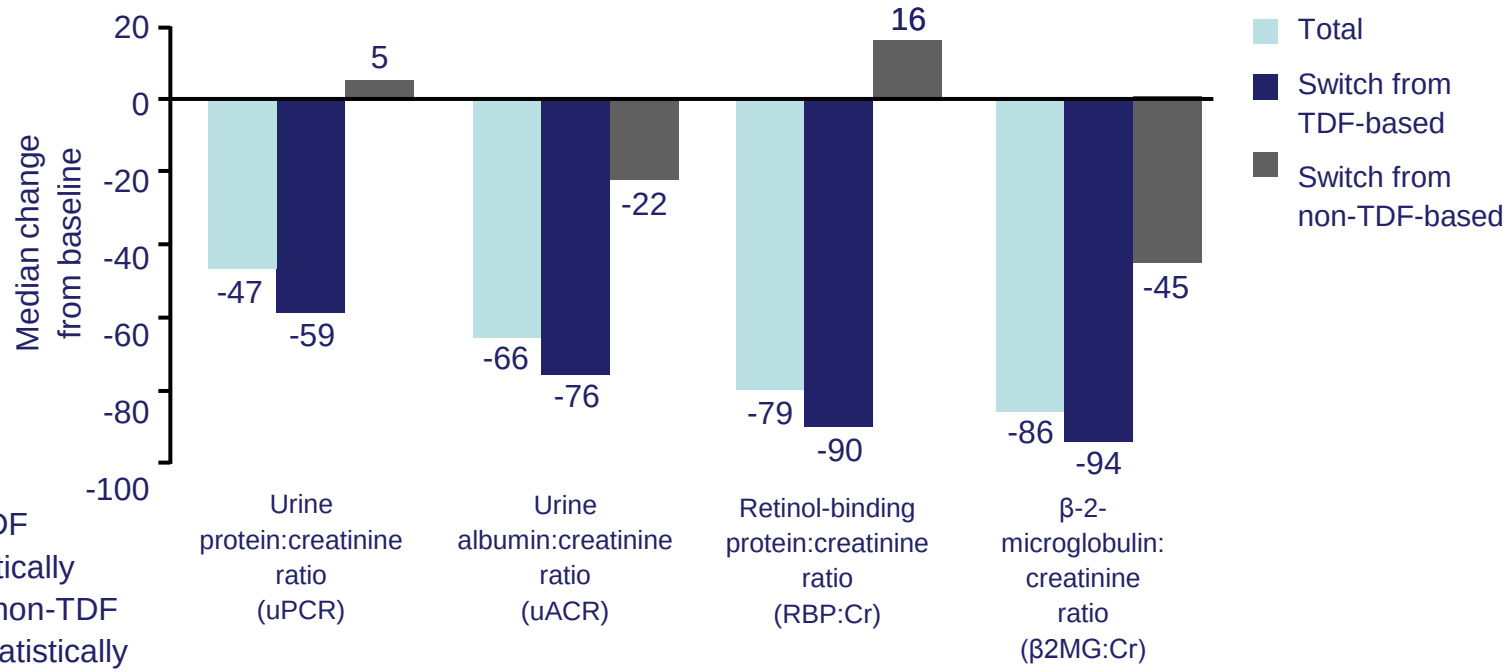
CrCl, creatinine clearance

1. Pozniak A, et al. CROI 2015. Seattle, WA, USA. Poster 795

Use of Genvoya in renal dysfunction

Statistically significant improvements in markers of renal tubular function at week 48

Improvements most notable in those switching from TDF-based ART



All total and TDF changes statistically significant; all non-TDF changes not statistically significant

* at 48 weeks in Study 112

CrCl, creatinine clearance; TDF, tenofovir disoproxil fumarate

1. Gupta SK, et al. IAS 2015. Vancouver, Canada. Oral TUAB0103

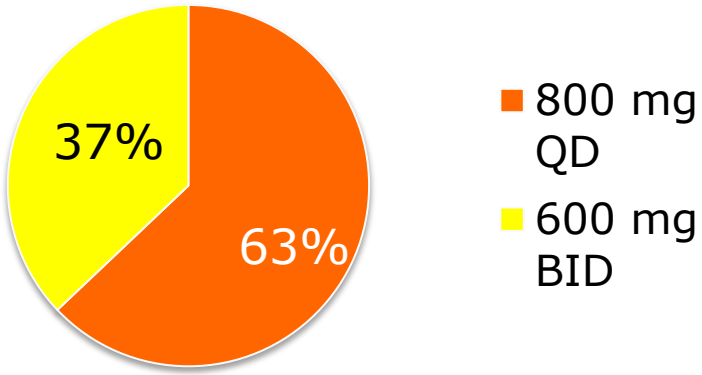
Elvitegravir/c in treatment failure

HIV Patient Population	Study	N	Regimens and Specifics
Treatment-Naive Adults	292-0104	867	E/C/F/TAF vs. E/C/F/TDF
Treatment-Naive Adults	292-0111	866	E/C/F/TAF vs. E/C/F/TDF
Treatment-Naive Adolescents	292-0106	50	E/C/F/TAF 12-17 years
Virologically-Suppressed with ≥ 2 class historical resistance	**292-0119**	**135**	**E/C/F/TAF + DRV vs. BR + DRV**
Virologically-Suppressed	292-0109	1436	E/C/F/TAF vs. F/TDF +3rd ARV
Renal Impairment (mild to moderate)	292-0112	248	E/C/F/TAF eGFR 30-68 mL/min
HIV-1/HBV co-infected	292-1249	75	E/C/F/TAF

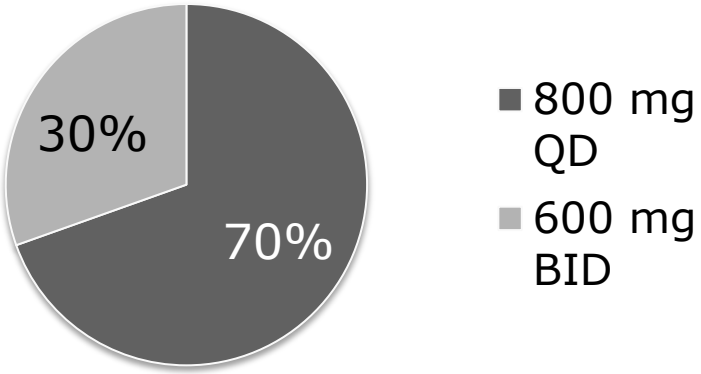
Callebaut et al. HIV Drug Therapy 2016. Abstract #0123

Elvitegravir/c in treatment failure

E/C/F/TAF + DRV (N=89)



BR (N=46)



Response at Week 48 per prior DRV dose, n (%)	E/C/F/TAF + DRV (n=89)		BR (n=46)	
	600 mg BID	800 mg QD	600 mg BID	800 mg QD
Virologic Success	33 (100)	51 (91)	11 (78.6)	24 (75)
No Virologic Data	0	3 (5.4)	2 (14.3)	4 (12.5)
Virologic Failure	0	2 (3.6)	1 (7.1)	4 (12.5)

Virologic suppression was similar within each arm, regardless of the DRV dosage
However, E/C/F/TAF+DRV was statistically superior to staying on the Baseline Regimen

Callebaut et al. HIV Drug Therapy 2016. Abstract #0123

Switching to InSTI as a ‘safer’ option

Raltegravir

200mg

Stribid

Elvitegravir

Genvoya

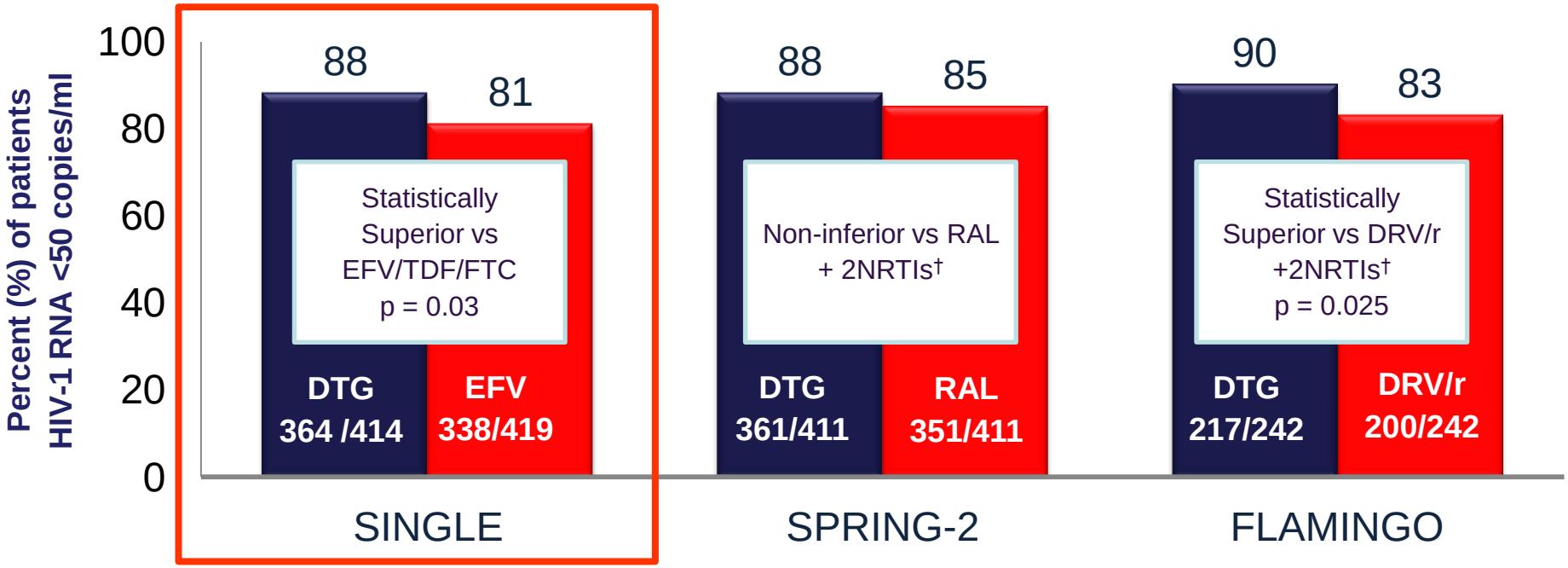
Dolutegravir

Dolutegravir

Triumeq

Dolutegravir – efficacy

DTG Phase III Clinical Trials in ART-Naïve subjects FDA Snapshot (48-Week Data; Primary Endpoint)



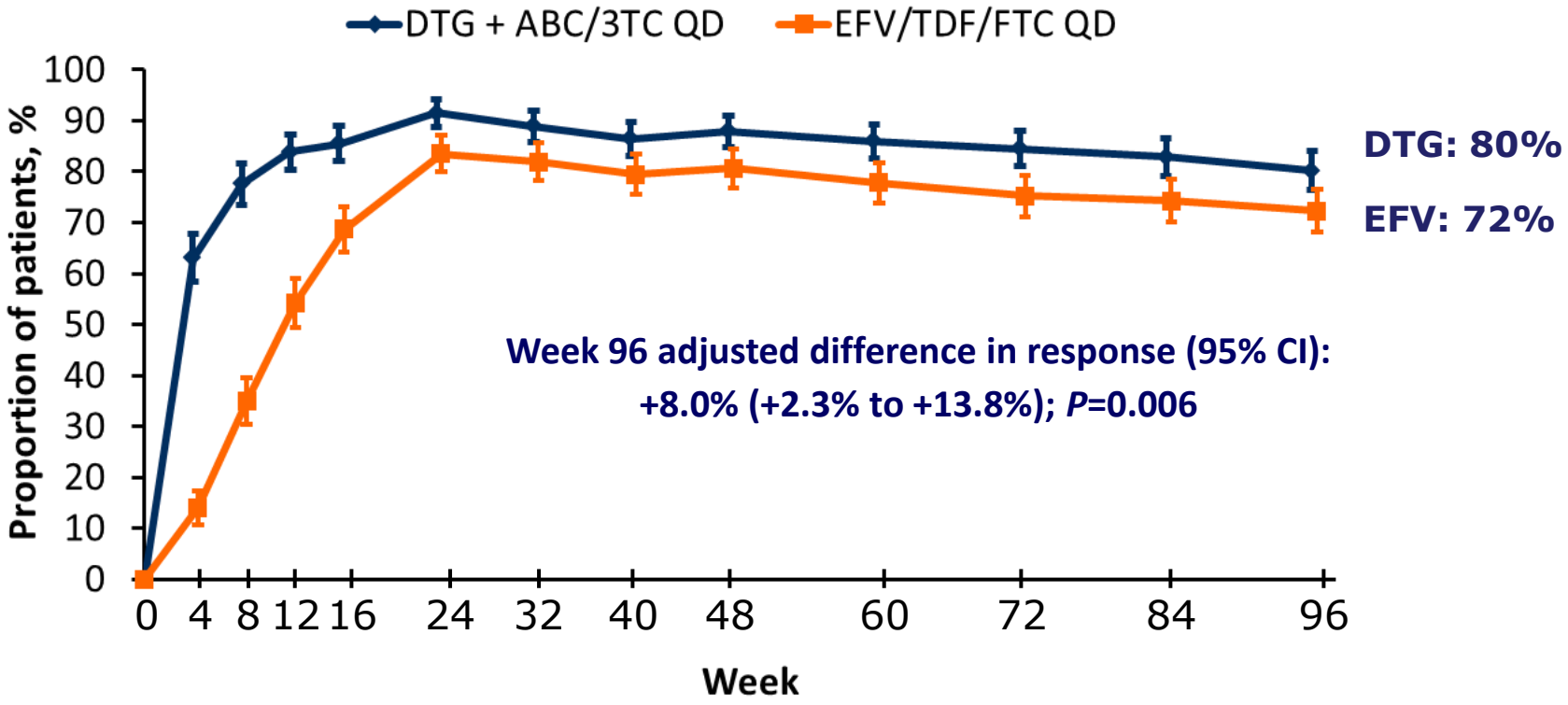
- In SINGLE, 414 patients received DTG +ABC/3TC.[1]
- In SPRING-2, on Day 1 in the DTG arm, 242 and 169 patients received TDF/FTC or ABC/3TC, respectively; in the RAL arm 247 and 164 patients received TDF/FTC and ABC/3TC, respectively.[2]
- In FLAMINGO, on Day 1 in the DTG arm, 163 and 79 patients received TDF/FTC or ABC/3TC, respectively; in the DRV/r arm 162 and 80 patients received TDF/FTC and ABC/3TC, respectively.[3]

1. Walmsley S, et al. N Engl J Med 2013;369:1807–18; 2. Raffi F, et al. Lancet 2013;381:735–43; 3. Clotet B, et al. Lancet 2014;383:2222–31;

Dolutegravir – efficacy

SINGLE Study

Virologic Suppression (HIV-1 RNA <50 c/mL; FDA Snapshot)



Higher responses on DTG + ABC/3TC vs EFV/TDF/FTC driven by withdrawals due to AEs (3% vs 11%, respectively)

Walmsley et al. CROI 2014; Boston, MA. Poster 337.

Dolutegravir – efficacy

SINGLE Study

Virologic Suppression (HIV-1 RNA <50 c/mL; FDA Snapshot)

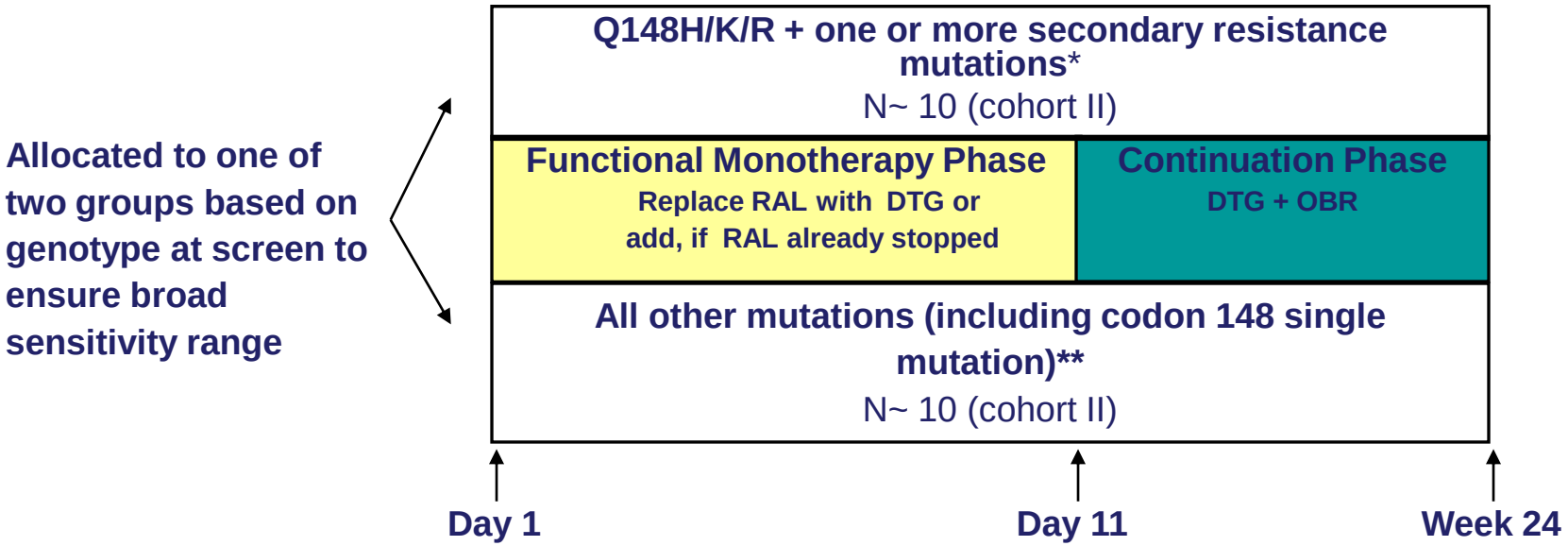
Adverse event	DTG + ABC/3TC QD (n=414)	EFV/TDF/FTC QD (n=419)
Treatment-related	**184 (44%)**	**282 (67%)**
Preferred term ≥10% in either arm		
Dizziness	29 (7%)	139 (33%)
Abnormal dreams	27 (7%)	66 (16%)
Nausea	44 (11%)	49 (12%)
Insomnia	41 (10%)	25 (6%)
Treatment-related Grades 2-4 (≥5% in either arm)	**58 (14%)**	**116 (28%)**
Dizziness	2 (<1%)	21 (5%)

Walmsley et al. CROI 2014; Boston, MA. Poster 337.

DOL switch – treatment experienced

VIKING Study desigm

- Current or historic RAL-failures with evidence of RAL resistance
- At least 3 ART-class resistant (including INI)
- Subjects received DTG 50mg QD (Cohort I) and 50mg BID (Cohort II)
- Cohort II subjects should have ≥1 fully active ART in OBR

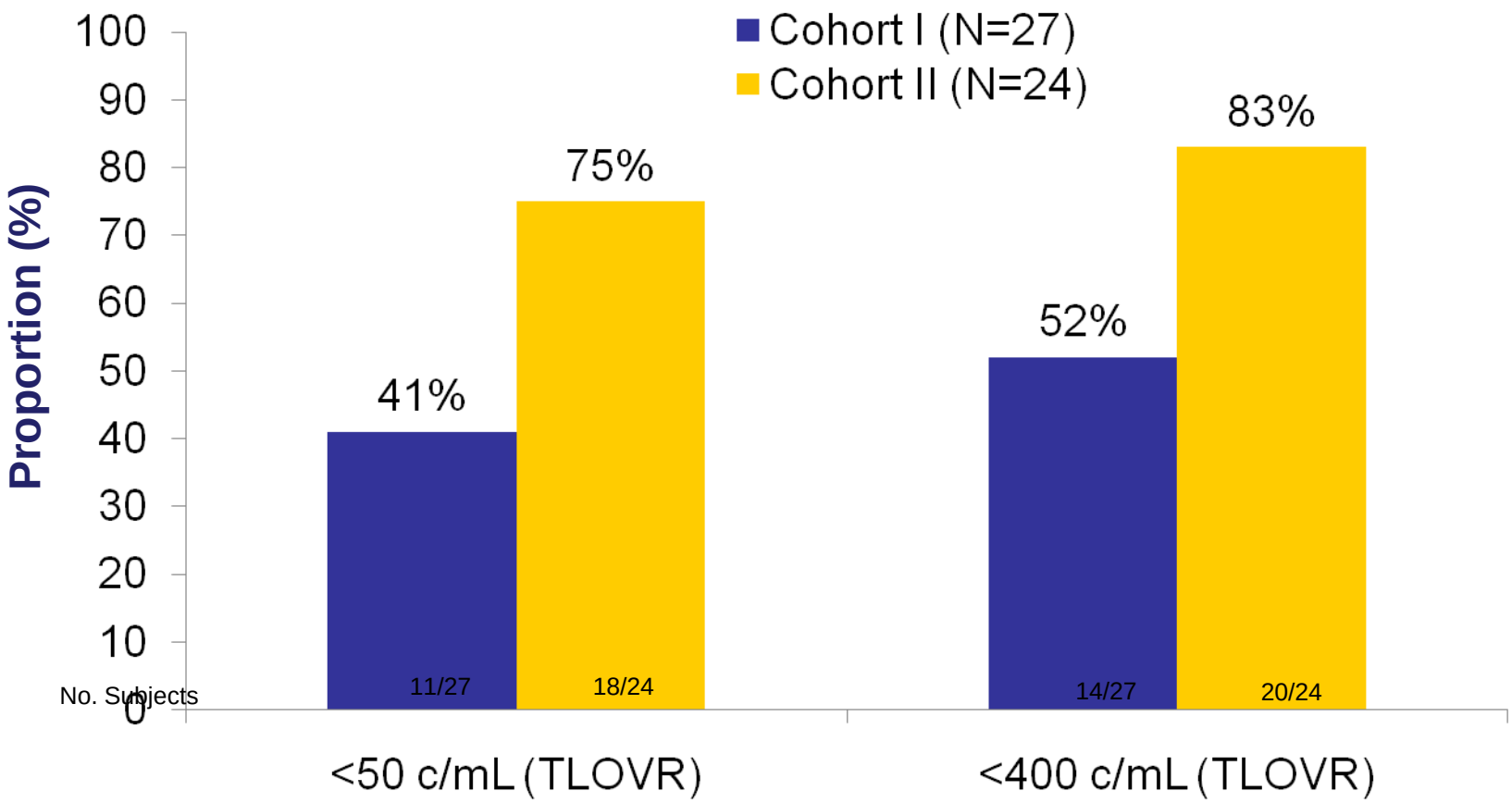


*Q148H/K/R plus changes in L74 and/or E138 and/or G140
**N155H and Y143H pathways or Q148H/K/R single mutants

Soriano V et al. 13th EACS 2011

DOL switch – treatment experienced

VIKING Study – virological responses with RAL resistance



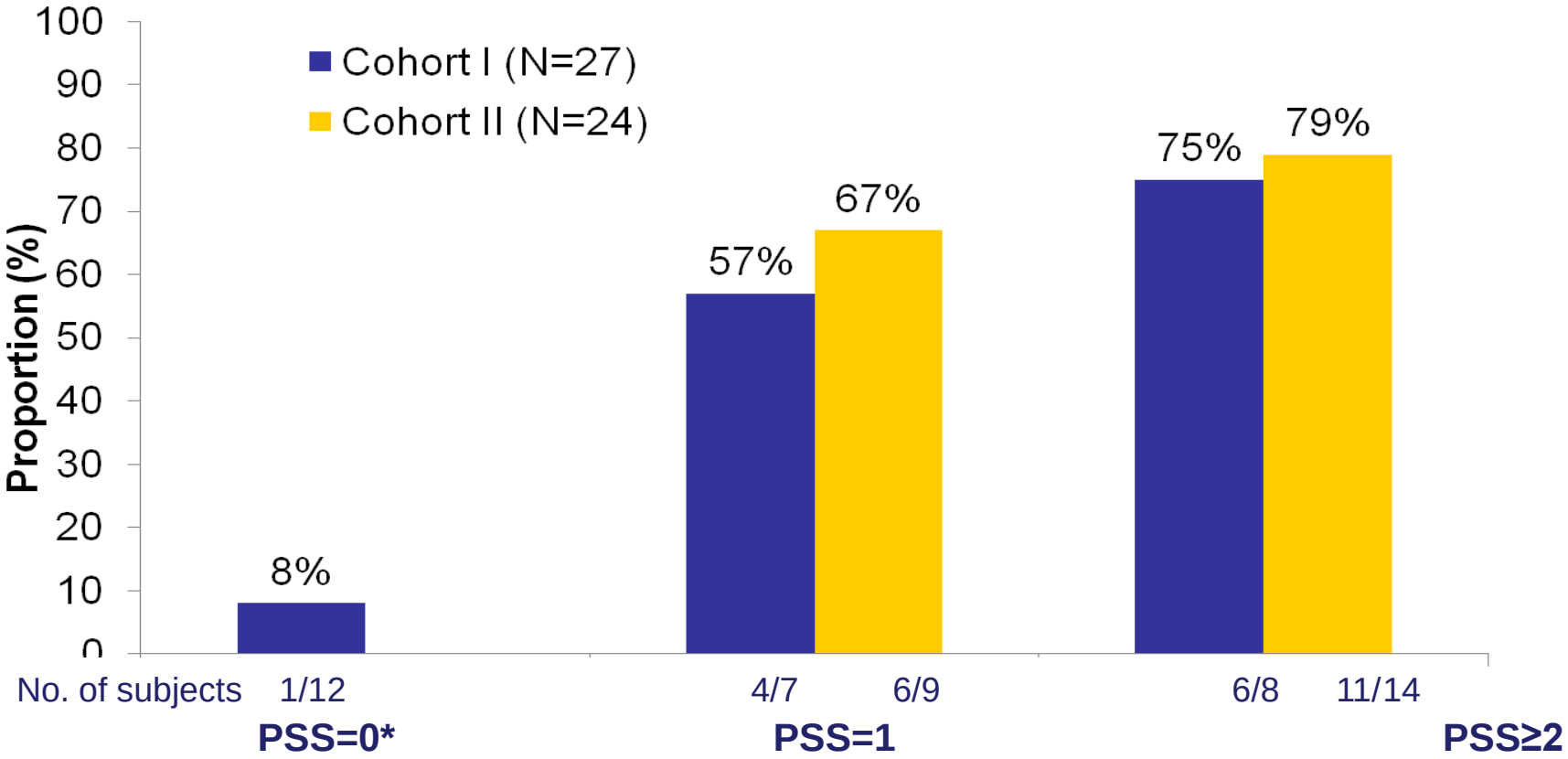
In an exploratory analysis* through Week 24, 11% and 38% of subjects receiving DTG 50 mg QD and BID respectively achieved <2 c/mL

*Modified BioMerieux EasyQ HIV-1 SuperLow assay (lower limit of detection 2 c/mL)

Soriano V et al. 13th EACS 2011

DOL switch – treatment experienced

VIKING Study –responses by OBR activity



***: 1 subject in Cohort II with PSS=0.5 responded**

Baseline PSS of OBR

Increasing background drug activity remained as independent predictor of virologic response at Week 24 after adjusting for other variables

Soriano V et al. 13th EACS 2011

Dolutegravir / 3TC as a treatment option

PADDLE (***P***ilot ***A***ntiretroviral ***D***esign with ***D***olutegravir ***L***amivudin***E***)

Phase IV, pilot, open-label, single arm exploratory trial

ARV- naïve patients,
≥18 years
HIV-1 RNA
>5,000 copies/mL and ≤100,000 copies/mL
CD4 count ≥200 cells/mL
HB(s)Ag negative
(n= 20)

→

1st cohort (n= 10)

DTG 50 mg QD
3TC 300 mg QD

→

2nd cohort (n= 10)

DTG 50 mg QD
3TC 300 mg QD

Second cohort enrolled after confirming success of first cohort at week 8

Viral load was measured at baseline, days 2,4,7,10, and weeks 2,3,4,6,8,12, 24, 36 and 48*

** 96 week extension ongoing*

Cahn P et al. IAS 2016. Abstract FRAB0104LB

Dolutegravir / 3TC as a treatment option

#	SCR	BSL	DAY 4	DAY 7	W.2	W.3	W.4	W.6	W.8	W.12	W.24	W.36	W.48
1	5.584	10.909	383	101	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
2	8.887	10.233	318	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
3	67.335	**151.569**	1.565	1.178	97	53	< 50	< 50	< 50	< 50	< 50	< 50	< 50
4	99.291	**148.370**	3.303	432	178	55	< 50	< 50	< 50	< 50	< 50	< 50	< 50
5	34.362	20.544	1.292	570	107	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
6	16.024	14.499	1.634	162	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
7	37.604	18.597	819	61	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
8	25.071	24.368	1.377	Not done	105	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
9	14.707	10.832	516	202	< 50	< 50	< 50	< 50	< 50	< 50	< 50	SAE	
10	10.679	7.978	318	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
11	50.089	**273.676**	68.129	3.880	784	290	288	147	< 50	< 50	< 50	< 50	< 50
12	13.508	64.103	3.296	135	351	84	67	< 50	< 50	< 50	< 50	< 50	< 50
13	28.093	33.829	26.343	539	61	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
14	15.348	15.151	791	198	< 50	61	64	< 50	< 50	< 50	< 50	< 50	< 50
15	23.185	23.500	4.217	192	< 50	< 50	< 50	Not done	< 50	< 50	< 50	< 50	< 50
16	11.377	3.910	97	143	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
17	39.100	25.828	1.970	460	52	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
18	60.771	73.069	2.174	692	156	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50
19	82.803	**106.320**	2.902	897	168	76	< 50	< 50	< 50	< 50	< 50	PDVF	
20	5.190	7.368	147	56	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50	< 50

CD4 increase: Median (IQR) : 267 (180-462)

Cahn P et al. IAS 2016. Abstract FRAB0104LB

Dolutegravir and tolerability

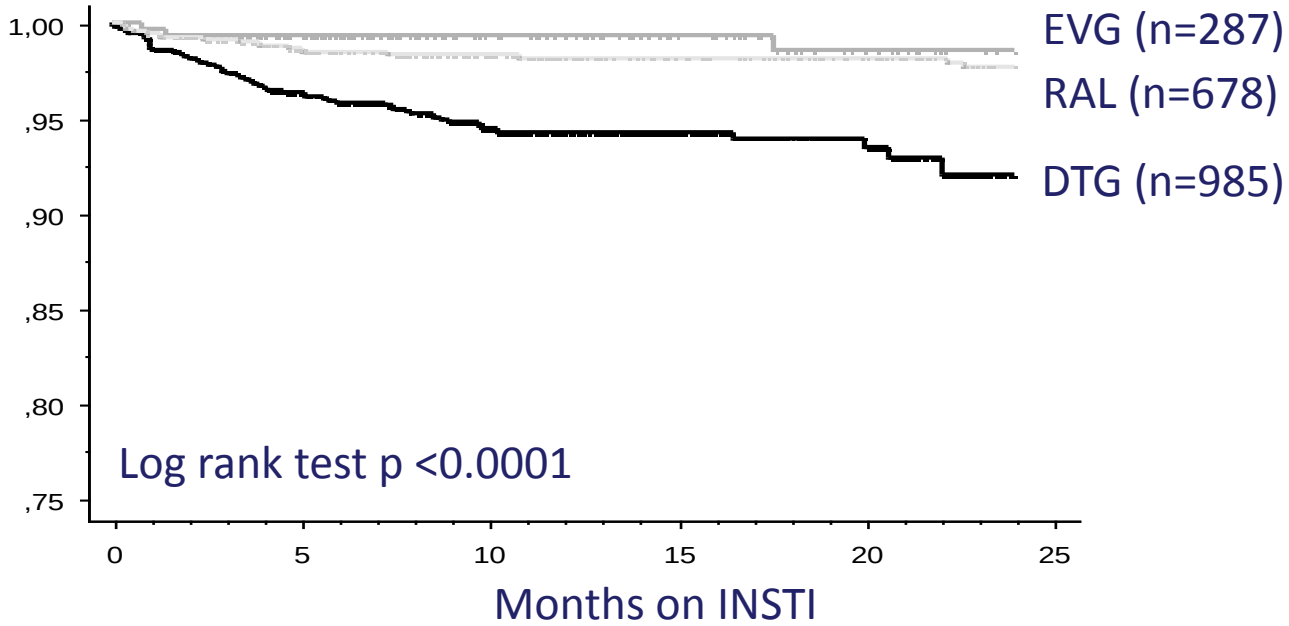
	Dolutegravir	Elvitegravir	Raltegravir
Exposures on INSTI analysed, n	985	287	678
Median Follow up per exposure, months (range)	11.5 (0-25.4)	16.0 (0.4-33.4)	36.3 (0.2-107.3)
Alive and on INSTI at time of data cut,% (n)	91.0 % (896)	83.3 % (239)	54.0 % (366)
Death while on INSTI,% (n)	0.9 % (9)	0.3 % (1)	4.7 % (32)
Reasons for discontinuation of INSTI (per exposure) over entire follow-up period			
ART Simplification, % (n)	1.0 % (10)	2.8 % (8)	31.3 % (212)
Virological failure, % (n)	0.1 % (1)	1.7 % (5)	4.7 % (32)
Other reasons, % (n)	0.2 % (2)	2.4 % (7)	1.5 % (8)
Discontinuation due to AEs (any) total, % (n)	**6.8 % (67)**	**9.4 % (27)**	**4.1 % (28)**

Sabranski et al. HIV Drug Therapy, 2016. Abstract

Dolutegravir and tolerability

Discontinuation due to neuropsychiatric AEs

	Dolutegravir n=985	Elvitegravir n=287	Raltegravir n=678
Neuropsychiatric % (n)	5.0 % (49)	1.0 % (3)	2.1 % (14)
Insomnia, sleep disturbances	36	2	4
Poor concentration, slow thinking	8	0	0
Dizzyness	13	1	3
Headache, paraesthesia	16	1	6
Depression	7	0	1



Sabranski et al. HIV Drug Therapy, 2016. Abstract

Switching for safety…what to know.

- Know your patient!!!
  - Know the treatment history
  - Is there transmitted / archived resistance?
  - How is there adherence?
- Have a reason for switch
  - Set your goals!
- Only switch in the setting of virological suppression
- Closely follow patients after switch
- Be aware of the consequences of getting it wrong!
  - Resistance can be a *disaster!*

HMRG
HIV Molecular Research Group

THANK YOU!

Paddy.mallon@ucd.ie
@HIVTox

UCD DUBLIN