AGIDEI
ASOCIACION GALLEGA PARA LA INVESTIGACION Y DOCENCIA EN ENFERMEDADES INFECCIOSAS

II Jornada de Excelencia en VIH
5 y 6 de Octubre de 2018

Biterapia óptima (con o sin análogo)
Biterapia libre de análogos
Biterapia basada en INSTI

Josep M Llibre
Infectious Diseases & "Fight AIDS" Fndn
Univ Hosp Germans Trias i Pujol
Badalona, Barcelona
jmllibre@flsida.org

FLS
www.flsida.org

Why would anyone wish something different??

- If anyone wants something different, will have to make sure that the patient is not exposed to increased risks, and the new strategy can get/prove a potential benefit.

Less-drug ART regimens: NOT an unmet need.

>90%
(>97%)

- Reduce lifelong drug exposure (sure)
- Reduce toxicity (potential)
- Reduce costs (potential)
- 3rd drug saved for future needs
- **Scientifically relevant question**

Rules to be met by less-drug regimens:

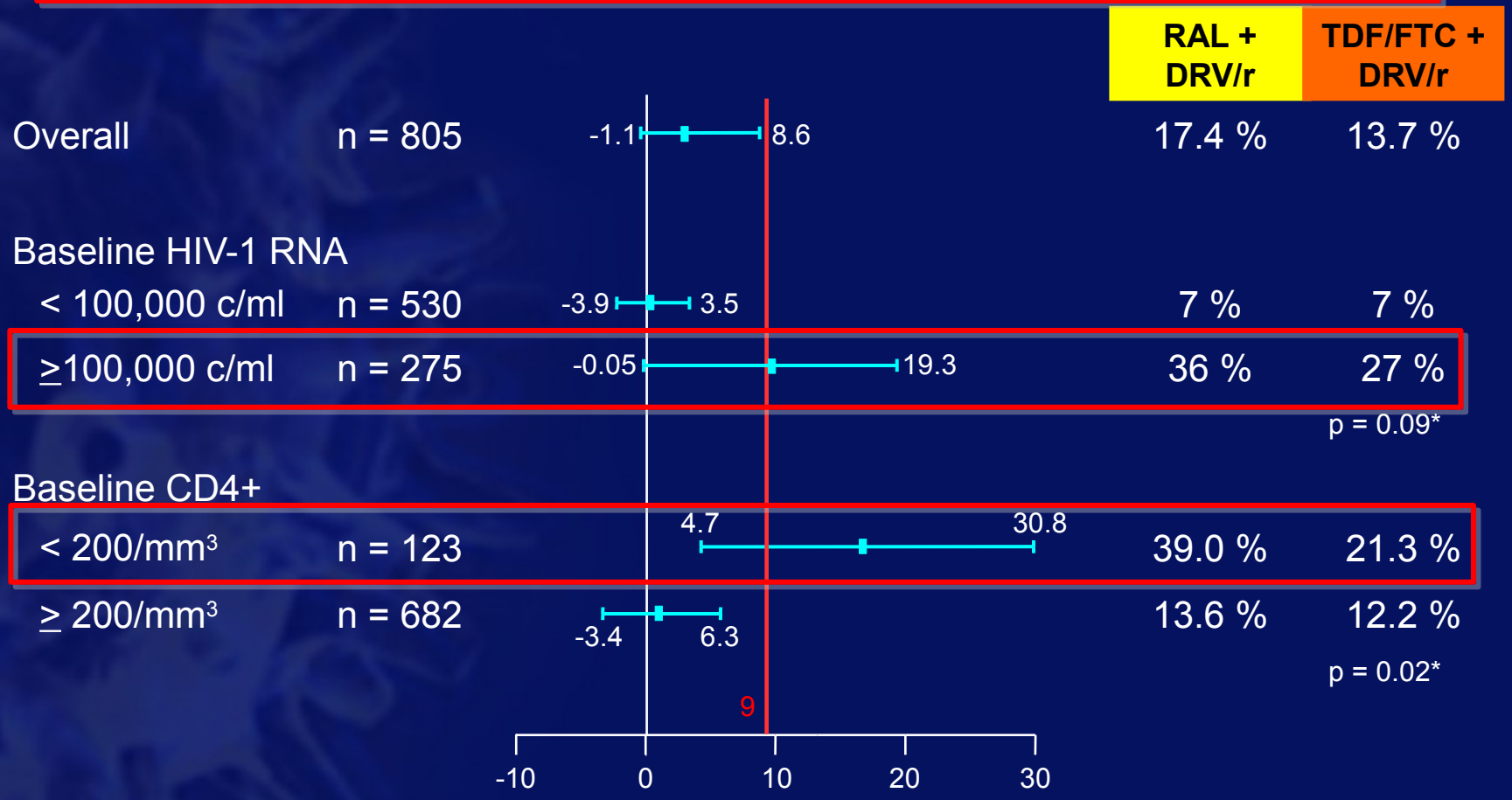
1. **Non-inferiority** against recommended/preferred regimens in fully-powered RCT (**robust data, concordant, no limitations/tricks**)
2. Include **preferred drugs**
3. Report a **benefit to the patient**
4. Be **cost-effective**

We must be very demanding and meet ethical and evidence-based standards with less than 3-DR.

RAL+DRV/r vs DRV/r+TDF/FTC, naïves. Primary endpoint

at W96 by baseline characteristics

Overall analysis: RAL + DRV/r non inferior to TDF/FTC + DRV/r



* Test for homogeneity

21st CROI, Boston, March 3-6,2014, 84LB. Lancet 2014; 384: 1942–51

Virological failureduringfollow-up and resistance data

	RAL + DRV/r n=401	TDF/FTC + DRV/r n=404
Protocol-defined virological failure (PDVF), n	66	52
Number of PDVF who met criteria for genotype testing (HIV RNA > 500 copies/ml at or after W32)	33	9
Number of patients with single unconfirmed value of HIV RNA > 500 copies/ml at or after W32 (meeting criteria for genotype testing)	3	6
Genotype done, n	28/36	13/15
Major resistance mutations, n	5	0
NRTI		
PI		
INI		

Key messages:

- ✓ **EVERYTHING MUST BE PROVEN**
- ✓ **2DR can fail when stressed** to the limit: high VL, low CD4.
- ✓ The **PI/r may not protect the 2nd drug** as well as 2NRTIs.

* 1 additional p

Protocol-define med
insufficient virc es/ml at W24
;failure to achie ≥ 50 c/ml at
any time after
Genotypic testing was carried out by local labs when patients had a single VL > 500 copies/ml at or after W32.

Optimal INSTI-based 2DR strategies

- **DTG + 3TC**, naives. PADDLE, ACTG A5353, **GEMINI 1&2**

  , switch ASPIRE, LAMIDOL, DOLAM, **TANGO**
- **DTG + RPV**, switch. **DTG/RPV**. LATTE (CAB/RPV), **SWORD 1&2**
- **LA IM CAB + RPV**, switch **LATTE 2, FLAIR, ATLAS, ATLAS2**

PADDLE. Viral Suppression at Week 48

#	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					
14	15.348	15.151	791	198	< 50	61	64	< 50					
15	23.185	23.500	4.217	192	< 50	< 50	< 50	Not do					
16	11.377	3.910	97	143	< 50	< 50	< 50	< 50					
17	39.100	25.828	1.970	460	52	< 50	< 50	< 50					
18	60.771	73.069	2.174	692	156	< 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

No RT DRMs. IN did not amplify.
VL 246 c/mL
Resuppressed w/o Tx change

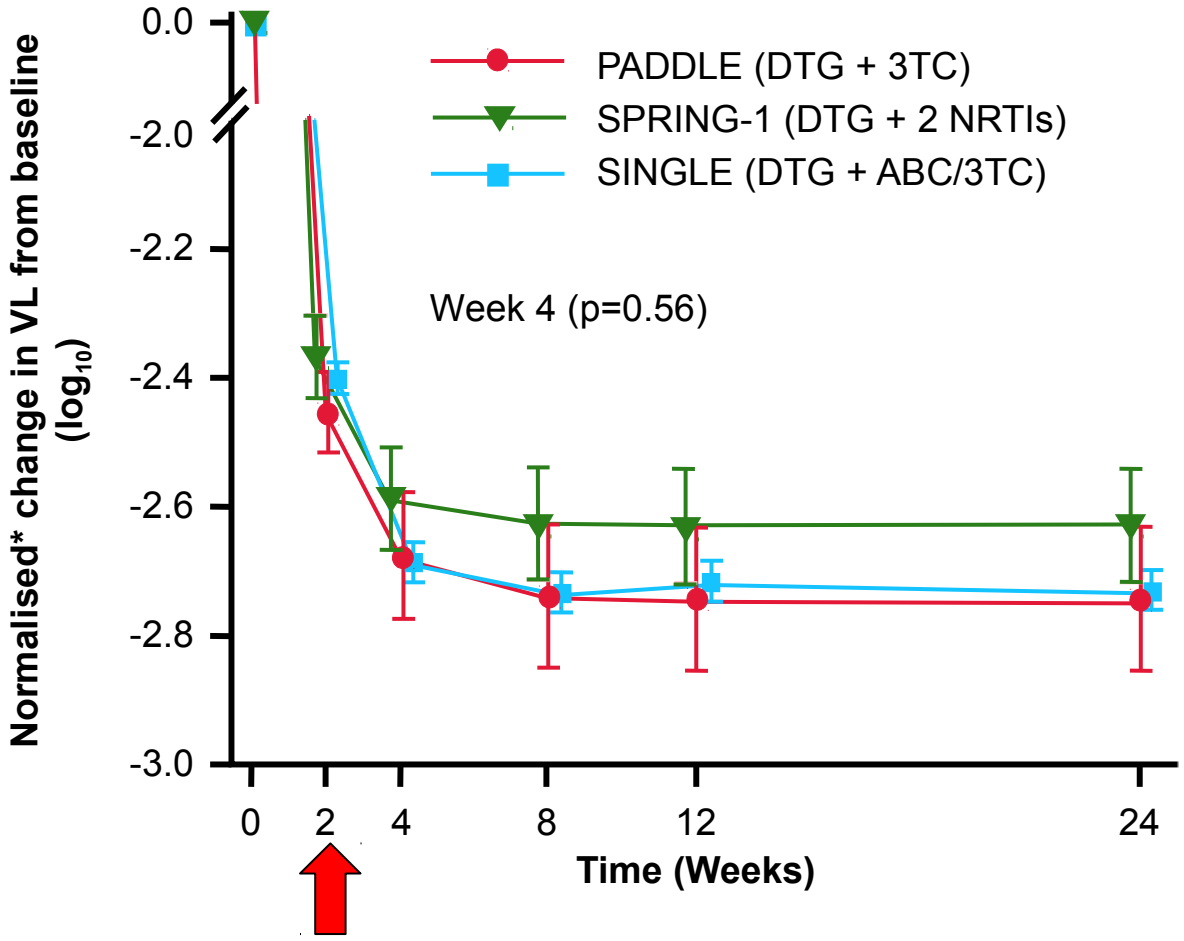
90%

Same efficacy at 96 weeks.

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

Cahn et al. EACS 2015 Barcelona, # LBPS4/1. CROI 2016, Boston, MA: #947. AIDS 2016; Durban, South Africa. #FRAB0104LB. IAS 2017; MOPEB0287.

Comparable VL decay in dual (DTG+3TC) or triple DTG regimens. Naives (<100.000 c/mL).

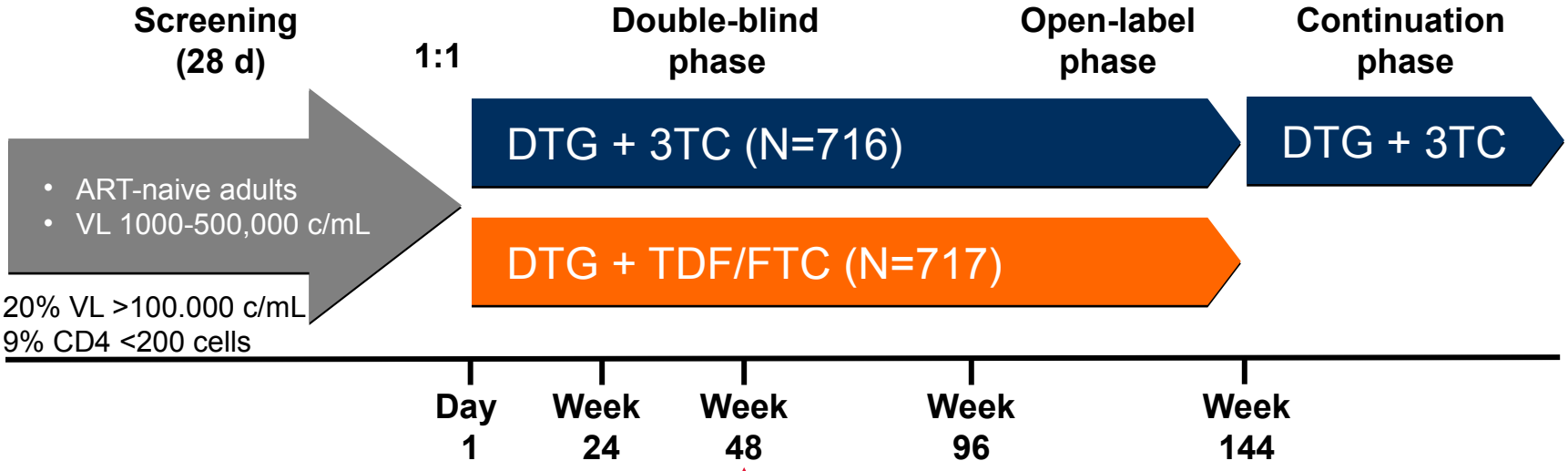


*Day 14: PADDLE Early evolution of VL (log 10) **-2.54**±0.27 (mean ± SD).

Sued O. CROI 2016, Boston, MA. #947.

GEMINI-1 and -2 Phase III Study Design

Identically designed, randomized, double-blind, parallel-group, multicenter, noninferiority studies



Eligibility criteria
- ≤10 days of prior ART
- No evidence of pre-existing viral resistance based on presence of any major resistance-associated mutation
- No HBV infection or need for HCV therapy

Primary endpoint at Week 48: participants with HIV-1 RNA <50 c/mL (ITT-E snapshot)[a]

Countries

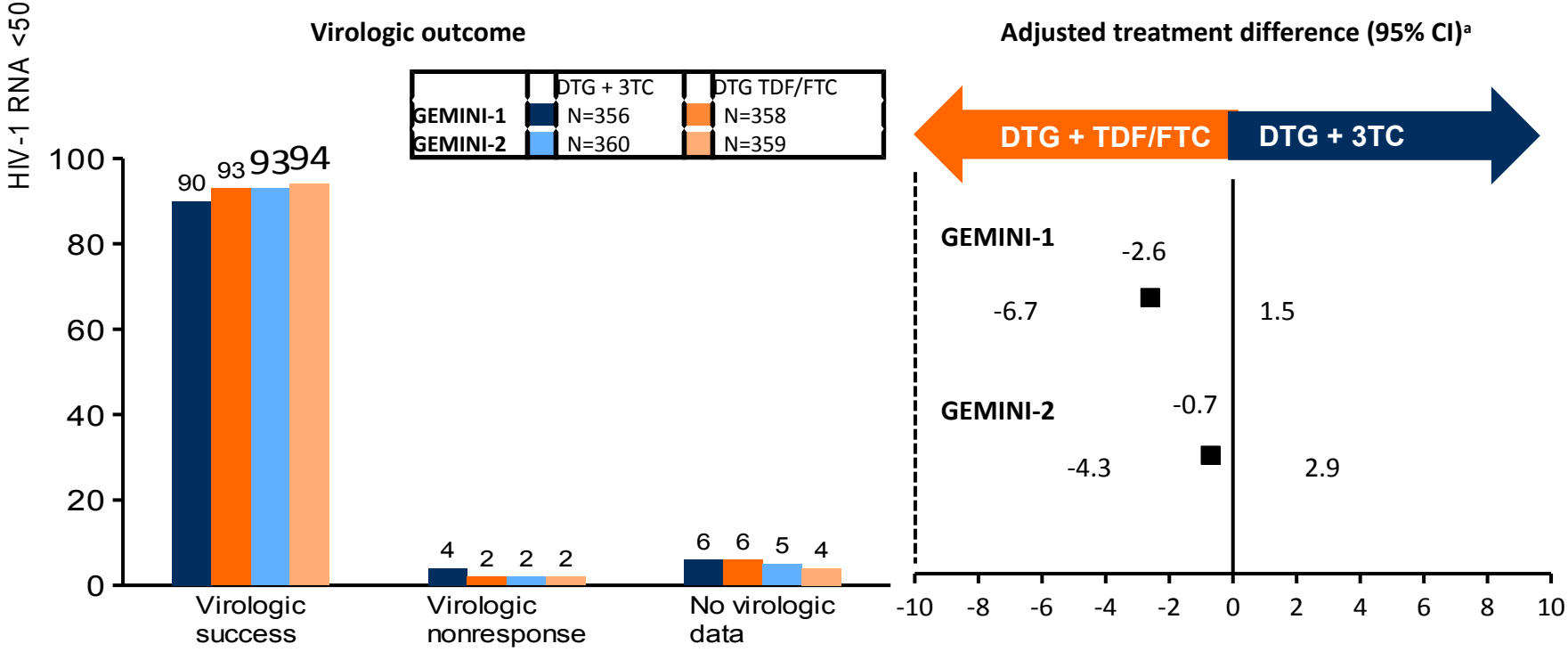
Argentina	Australia	Belgium
Canada	France	Germany
Italy	Republic of Korea	Mexico
Netherlands	Peru	Poland
Portugal	Romania	Russian Federation
South Africa	Spain	Switzerland
Taiwan	United Kingdom	United States

Baseline stratification factors: plasma HIV-1 RNA (≤100,000 c/mL vs >100,000 c/mL) CD4+ cell count (≤200 cells/mm^3 vs >200 cells/mm^3).

[a]–10% noninferiority margin for individual studies.

Cahn et al. AIDS 2018; Amsterdam, the Netherlands. Slides TUAB0106LB.

Virological Outcomes at Week 48

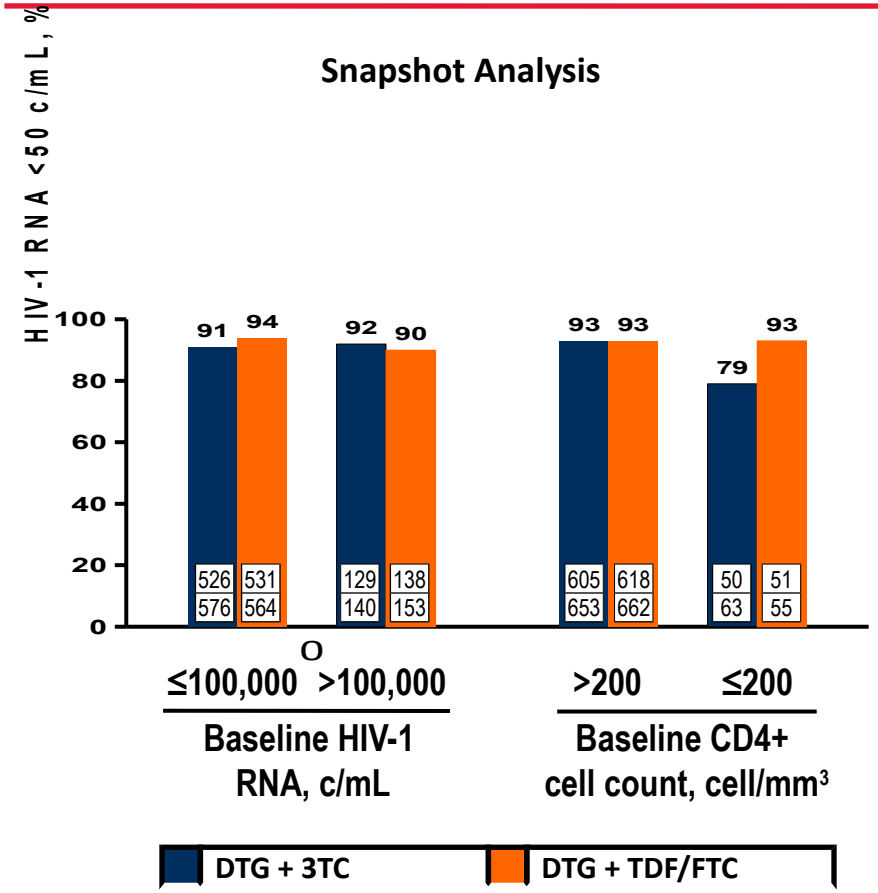


- DTG + 3TC is non-inferior to DTG + TDF/FTC with respect to proportion <50 c/mL at Week 48 (snapshot, ITT-E population) in both studies

Cahn P, et al. AIDS 2018; Amsterdam, NHL. Oral #TUAB0106LB

[a] Based on Cochran-Mantel-Haenszel stratified analysis adjusting for the following baseline stratification factors: plasma HIV-1 RNA (≤100,000 c/mL vs >100,000 c/mL) and CD4+ cell count (≤200 cells/mm^3 vs >200 cells/mm^3).

Pooled Outcomes at Week 48 Stratified by Baseline HIV-1 RNA and CD4+ Cell Count: Snapshot Analysis

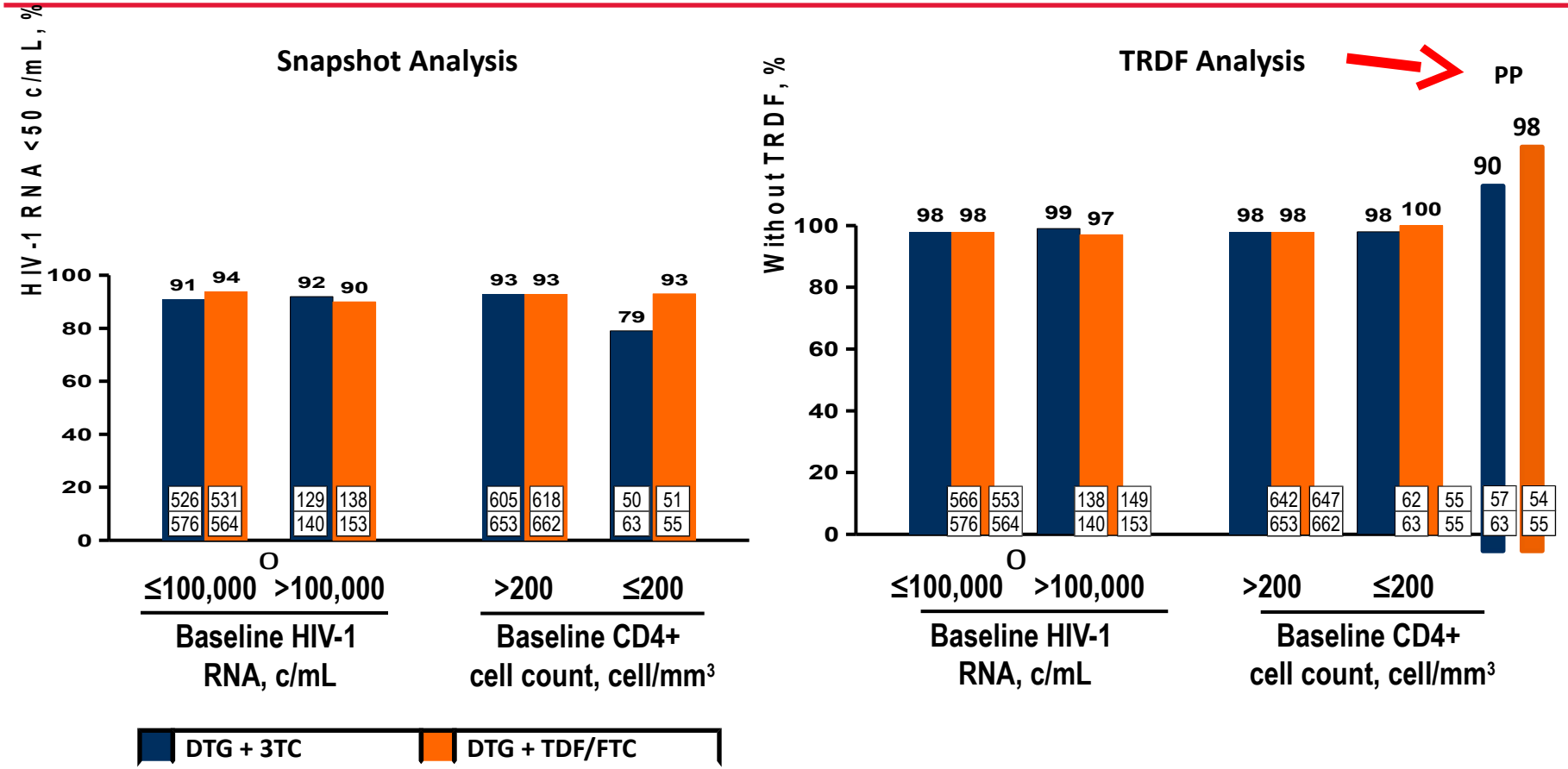


- 2% of participants in each arm had baseline HIV-1 RNA >500,000 c/mL

9% had CD4 ≤cells, and 20% had VL>100.000 c/mL.

Cahn et al. AIDS 2018; Amsterdam, the Netherlands. Slides TUAB0106LB.

Pooled Outcomes at Week 48 Stratified by Baseline HIV-1 RNA and CD4+ Cell Count: Snapshot and TRDF Analysis



- 2% of participants in each arm had baseline HIV-1 RNA >500,000 c/mL
- Treatment related discontinuation = failure (TRDF) population accounts for confirmed virologic withdrawal (CVW), withdrawal due to lack of efficacy, withdrawal due to treatment-related AE, and participants who met protocol-defined stopping criteria
- DTG + 3TC CD4 <200 Snapshot non-response (n=13): **1 CVW**, 3 with VL >50 in window **(2 of 3 re-suppressed),** 2 discontinued due to AE (TB, Chagas disease), 2 protocol violations, 2 lost to follow-up, 1 withdrew consent, 1 withdrew to start HCV treatment, 1 change in ART (incarcerated)
- DTG + TDF/FTC < 200 Snapshot non-response (n=4):1 investigator discretion, 1 withdrew consent, 1 lost to follow-up, 1 VL >50 (re-suppressed)

Cahn et al. AIDS 2018; Amsterdam, the Netherlands. Slides TUAB0106LB.

Confirmed Virologic Withdrawals Through Week 48

- Low rates of virologic withdrawals were observed at Week 48
- Genotypes were performed from W24, on the second confirmed sample if VL ≥ 200c/mL

	GEMINI 1		GEMINI 2		Pooled	
Variable, n (%)	**DTG + 3TC (N=356)**	**DTG + TDF/FTC (N=358)**	**DTG + 3TC (N=360)**	**DTG + TDF/FTC (N=359)**	**DTG + 3TC (N=716)**	**DTG + TDF/FTC (N=717)**
CVW	4 (1)	2 (<1)	2 (<1)	2 (<1)	6 (<1)	4 (<1)
Treatment-emergent resistance	**0**	**0**	**0**	**0**	**0**	**0**

- No treatment-emergent INSTI mutations or NRTI mutations were observed among participants who met CVW (confirmed virologic failure) criteria

Confirmed virologic withdrawal criteria is defined as a second and consecutive HIV-1 RNA value meeting virologic non-response or rebound. Virologic non-response is defined as either a decrease in plasma HIV-1 RNA of less than 1 $\log_{10}$ c/mL by Week 12 with subsequent confirmation unless plasma HIV-1 RNA is <200 c/mL, or confirmed plasma HIV-1 RNA levels ≥200 c/mL on or after Week 24. Virologic rebound is defined as confirmed rebound in plasma HIV-1 RNA levels to ≥200 c/mL after prior confirmed suppression to <200 c/mL.

Cahn P, et al. AIDS 2018; Amsterdam, NHL. Oral #TUAB0106LB

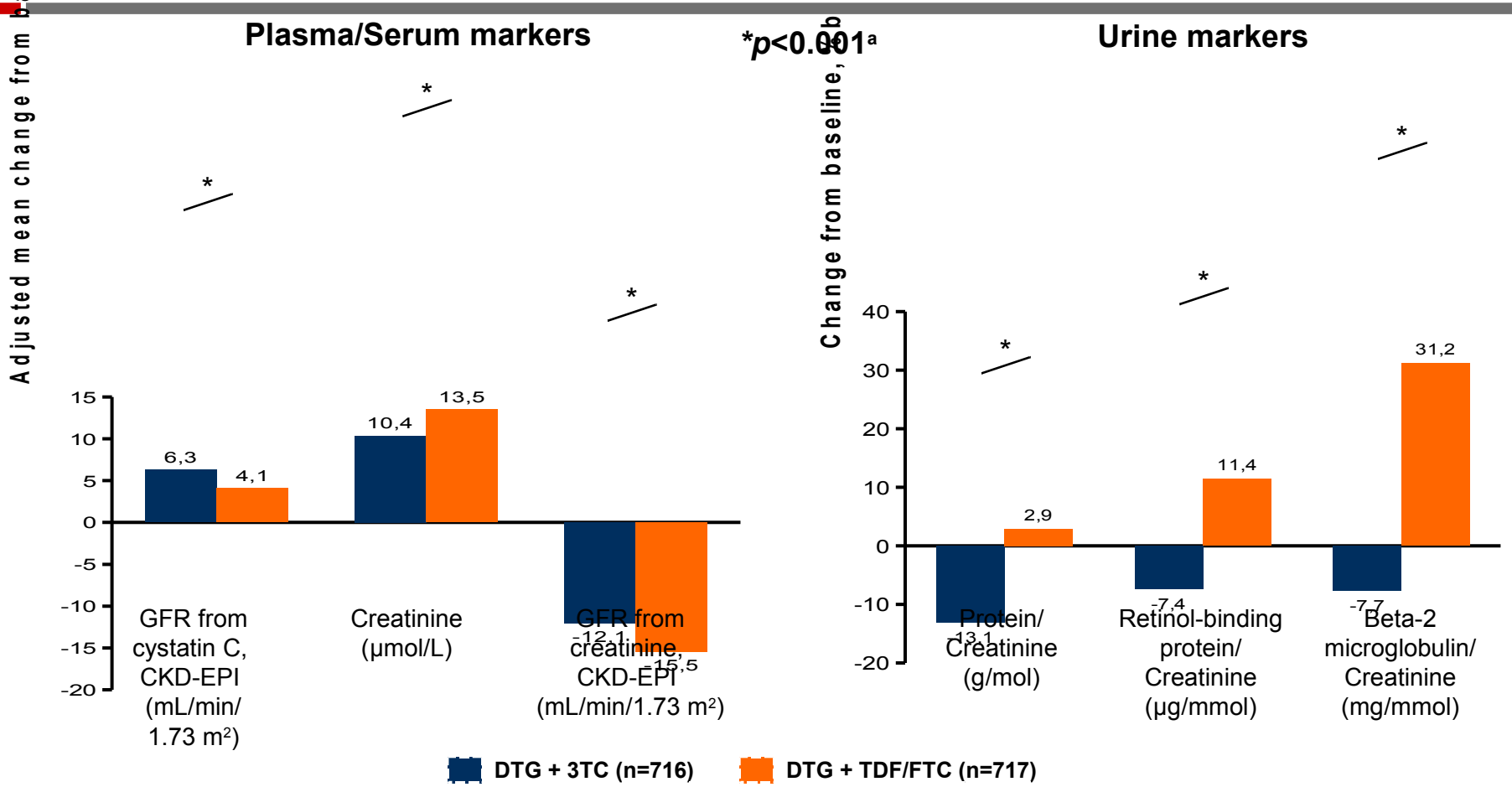
Adverse Events: Pooled ITT-E Population

n (%)	DTG + 3TC (N=716)	DTG + TDF/FTC (N=717)
Any AE	543 (76)	579 (81)
AE occurring in ≥5% of participants in either group		
Headache	71 (10)	75 (10)
Diarrhea	68 (9)	77 (11)
Nasopharyngitis	55 (8)	78 (11)
Upper respiratory tract infection	56 (8)	44 (6)
Nausea	27 (4)	53 (7)
Insomnia	27 (4)	45 (6)
Pharyngitis	36 (5)	32 (4)
Back pain	35 (5)	31 (4)
Drug-related AE	126 (18)	169 (24)
Grade 2-4 AE occurring in ≥1% of participants	42 (6)	47 (7)
Headache	8 (1)	8 (1)
AE leading to withdrawal from the study	15 (2)	16 (2)
Neuropsychiatric AEs leading to withdrawal	6 (<1) 0.8%	4 (<1) 0.6%
Any serious AE[a]	50 (7)	55 (8)

[a]2 deaths (acute myocardial infarction, n=1; Burkitt's lymphoma, n=1) in the GEMINI-2 study; both were in the DTG + 3TC group and were considered unrelated to the study drug regimen.

1. Cahn P, et al. AIDS 2018. Amsterdam, NL. Oral #TUAB0106LB

Change in Renal Biomarkers at Week 48: Pooled ITT-E Population



- [a]Estimated mean change from baseline at Week 48 in each arm calculated from ANCOVA model adjusting for: study, treatment, baseline plasma HIV-1 RNA, baseline CD4+ cell count, age, sex, race, presence of diabetes mellitus, presence of hypertension, and baseline biomarker value. Multiple imputed dataset (missing at random). [b]Estimated from geometric mean ratio for baseline and Week 48.

- More favorable change in bone biomarkers (p<0.001)

1. Cahn P, et al. AIDS 2018. Amsterdam, NL. Oral #TUAB0106LB

Data from all DTG_{mono} studies

Data from DOMONO and MONCAY RCTs, and cohorts:

New INSTI resistance can emerge in:

- Subjects previously exposed to INSTI but no VF recorded.
- Subjects not previously exposed to any INSTI.
- Beyond 24 weeks of VL suppression on DTG + 3TC.
- Severe INSTI resistance pathways can be selected straight (N155H, G140X, Q148X), never seen in triple DTG or BIC regimens.

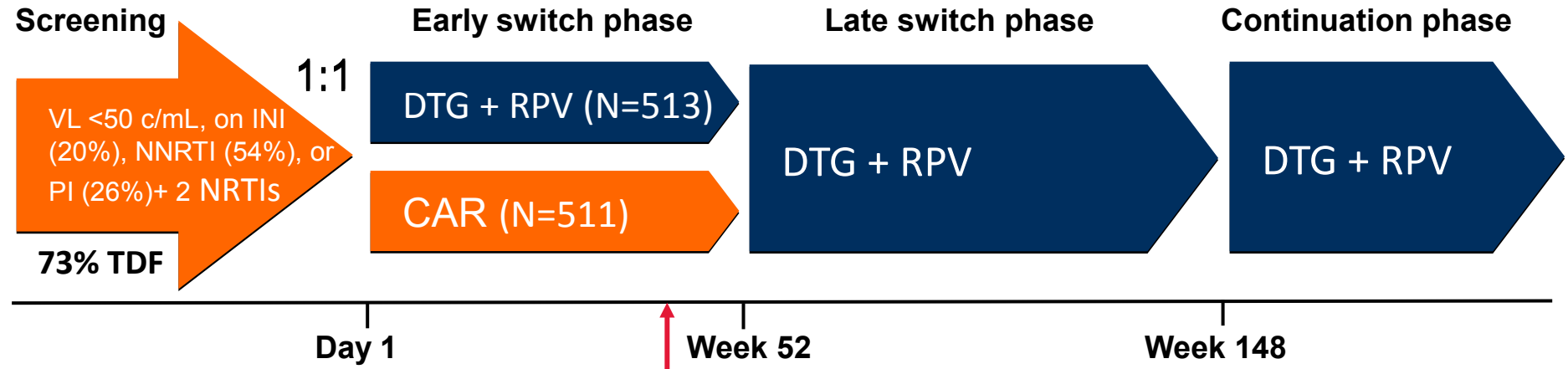
What else would you need to implement DTG + 3TC in initial ART in your practice?

- Longer follow-up, 2-3 y (DTG_{mono} threat).
- More RCTs showing same result in naives.
- Data comparing 2DR to TAF-preferred triple-drug STRs (Ongoing RCT in switch (TANGO).
- Data in real-life practice (irregular adherence).
- Co-formulation (DTG/3TC) to avoid covert monoterapy.

EMA approved 24 may 2018

SWORD-1 and SWORD-2 Phase III Study Design

Identically designed, randomized, multicenter, open-label, parallel-group, non-inferiority studies



Inclusion criteria
- On stable CAR ≥6 months before screening
- 1st or 2nd ART with no change in prior regimen due to VF
- Confirmed HIV-1 RNA <50 c/mL during the 12 months before screening
- HBV negative

Primary endpoint at 48 weeks: subjects with VL <50 c/mL (ITT-E snapshot)[a]

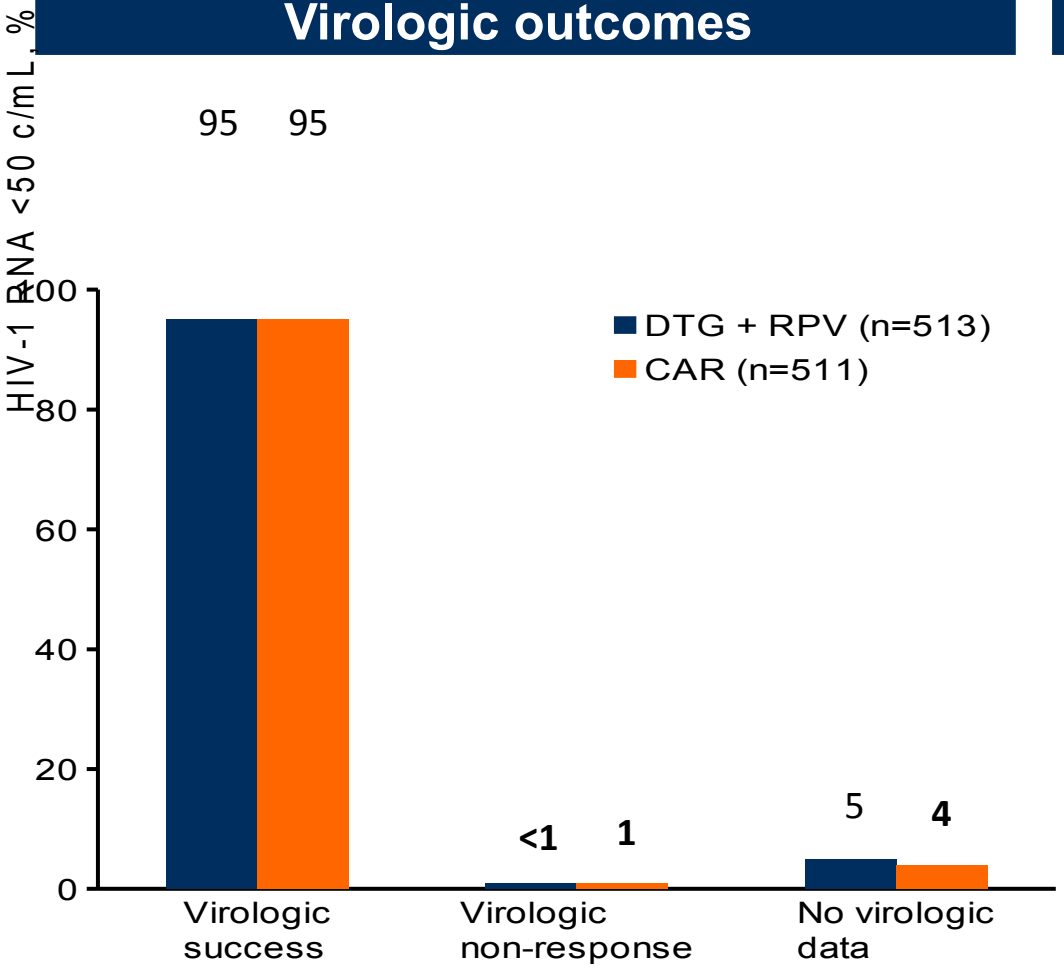
Countries
Argentina, Australia, Belgium, Canada, France, Germany, Italy, Netherlands, Russia, Spain, Taiwan, United Kingdom, United States.

[a]-8% non-inferiority margin for pooled data. -10% non-inferiority margin for individual studies

Llibre JM. CROI 2017; Seattle, WA. #44LB. The Lancet 2018;391(10123): 839–849.

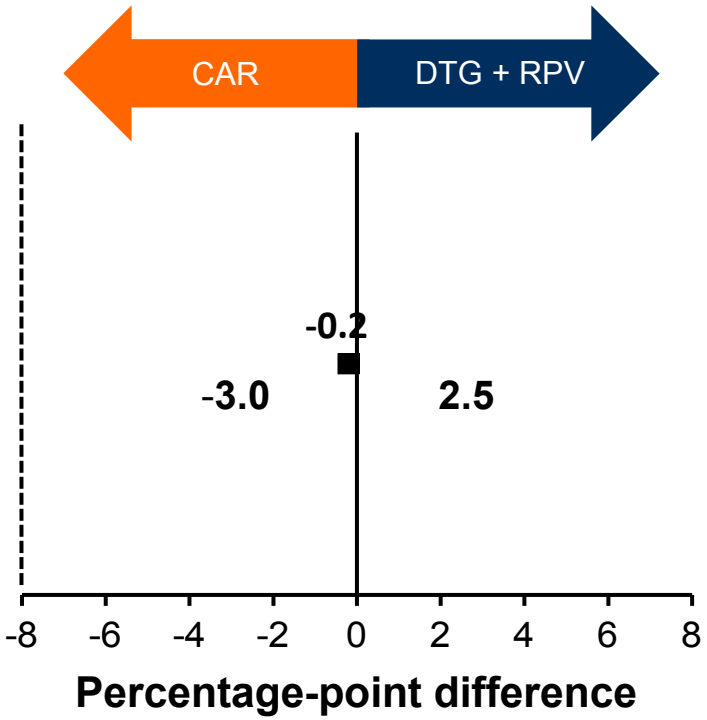
Snapshot Outcomes at Week 48 (Pooled)

Virologic outcomes



[a]Adjusted for age and baseline 3rd agent.

Adjusted treatment difference (95% CI)[a]

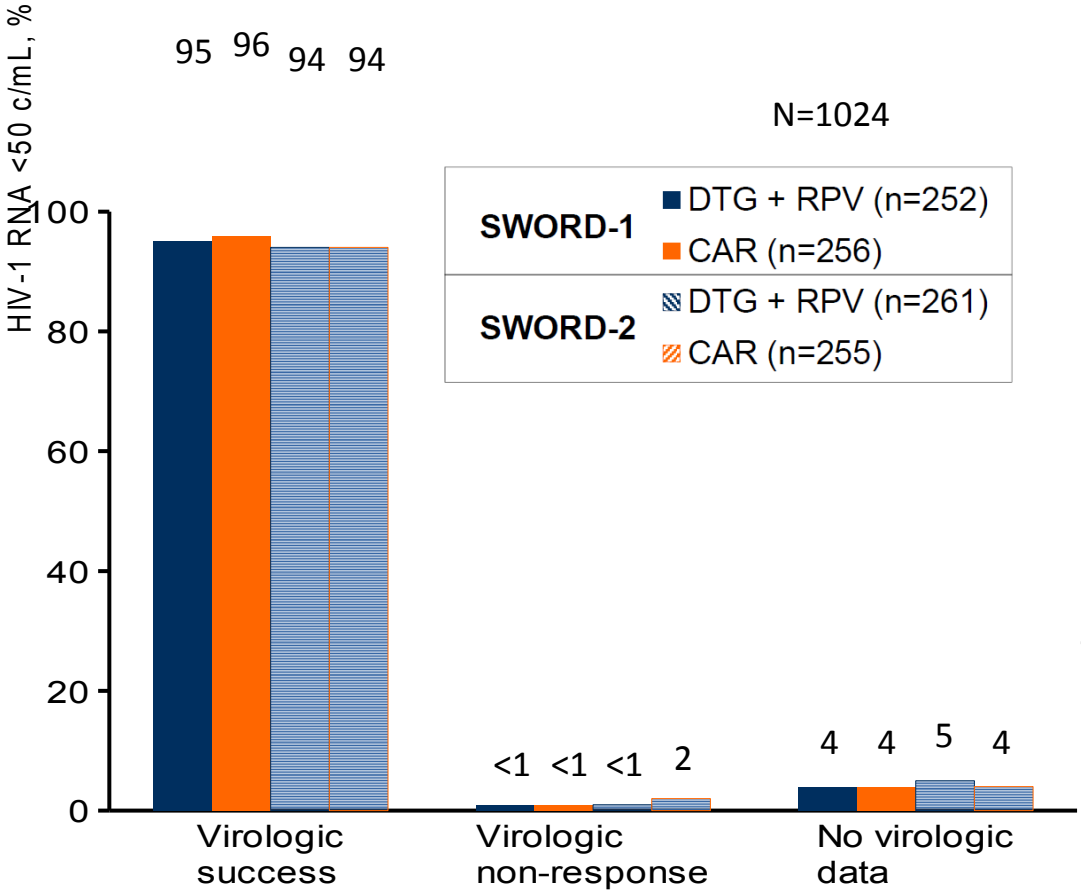


DTG + RPV is **non-inferior** to CAR with respect to snapshot in the ITT-E population (<50 c/mL) at Week 48

Llibre JM. CROI 2017; Seattle, WA. #44LB. The Lancet 2018;391(10123): 839–849.

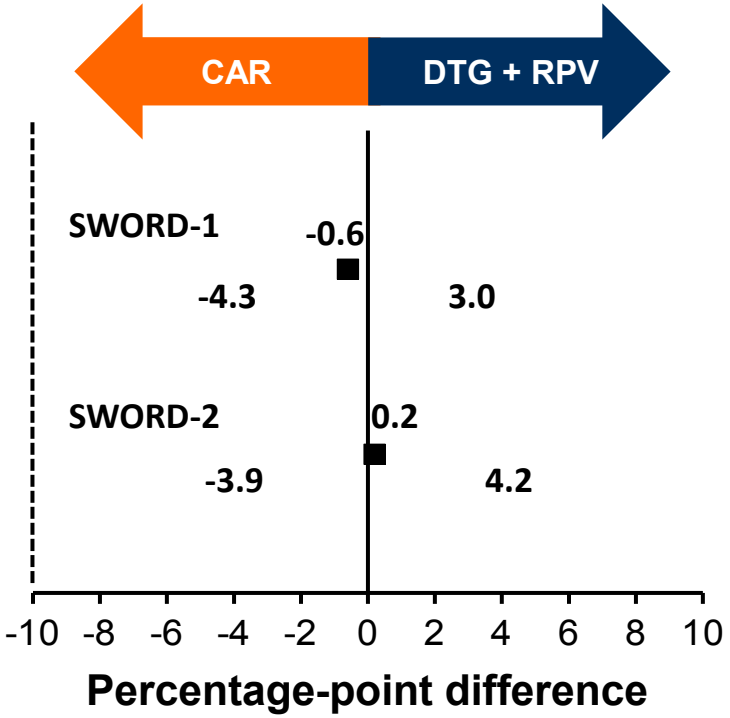
Snapshot Outcomes, Week 48 (SWORD-1&2)

Virologic outcomes



[a]Adjusted for age and baseline 3rd agent.

Adjusted treatment differences (95% CI)[a]

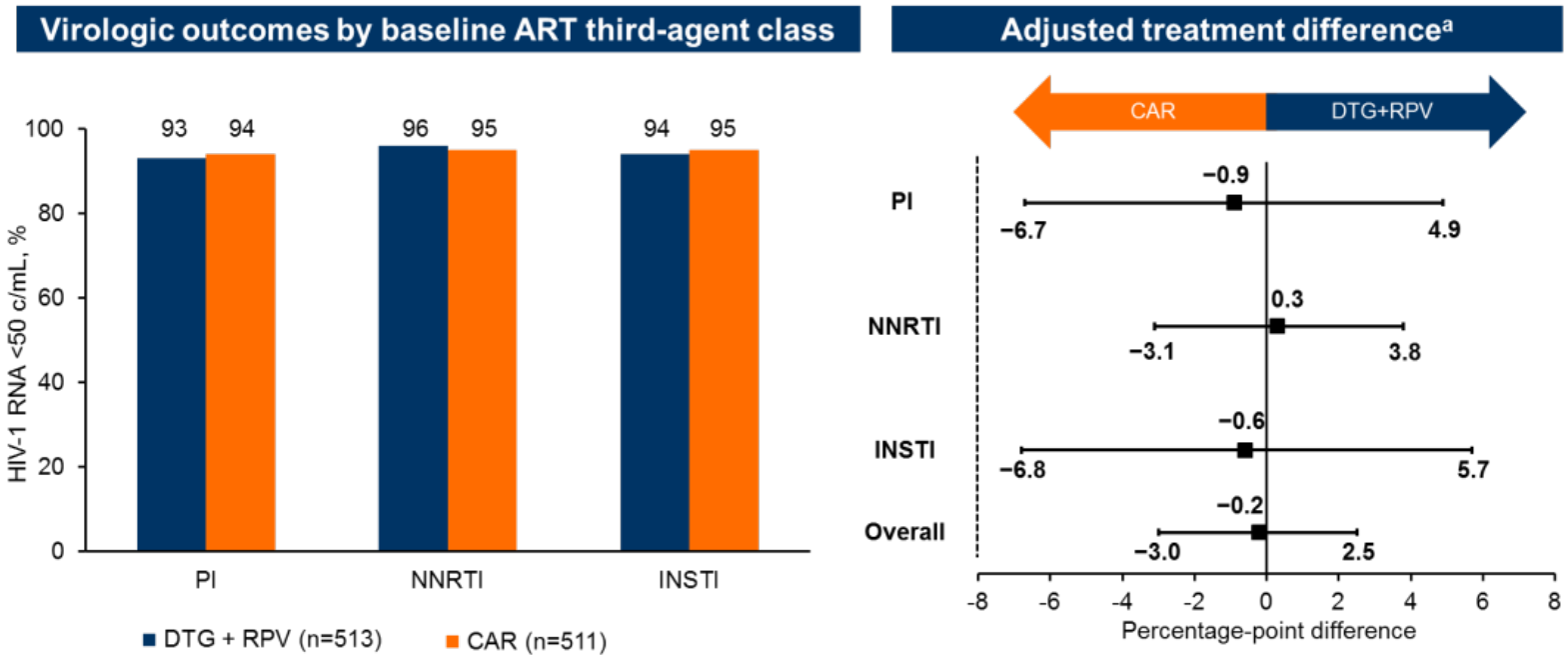


DTG + RPV is **non-inferior** to CAR with respect to snapshot in the ITT-E population (<50 c/mL) at Week 48 in both studies

Llibre JM. CROI 2017; Seattle, WA. #44LB. The Lancet 2018;391(10123): 839–849.

SWORD-1 and -2 pooled analysis:
Sub-group analysis by BL 3rd agent (stratified at randomisation) and geography

Efficacy



- At Week 48, 95% of participants maintained VL <50 c/mL in both groups of the pooled SWORD-1 and SWORD-2 analysis (adjusted treatment difference, –0.2%; 95% CI, –3.0 to 2.5)
- Subgroup analyses by baseline third-agent class gave consistent virologic efficacy results to support overall findings with no marked differences (test of homogeneity for treatment difference, P=0.930)
- Subgroup analyses of virologic outcomes were consistent across various regions
  - North America: DTG+RPV, 91/99 (92%); CAR, 86/93 (92%)
  - Europe: DTG+RPV, 298/314 (95%); CAR, 295/310 (95%)
  - Other regions: DTG+RPV, 97/100 (97%); CAR, 100/108 (93%)

[a]Error bars show 95% CI Treatment difference for the overall population is adjusted for age and BL third-class. Treatment difference between each class is unadjusted

Snapshot Outcomes at Week 48

	DTG + RPV n=513 n (%)	CAR n=511 n (%)
Virologic success	486 (95)	485 (95)
Virologic non-response	3 (<1)	6 (1)
Data in window not <50 c/mL	**0**	2 (<1)
Discontinued for lack of efficacy	2 (<1)	2 (<1)
Discontinued while VL not <50 c/mL	1 (<1)	1 (<1)
Change in ART	0	1 (<1)
No virologic data	24 (5)	20 (4)
Discontinued due to AE or death[1]	17 (3)	3 (<1)
CNS AEs leading to withdrawal	9 (2)	1 (<1)
Discontinued for other reasons	7 (1)	16 (3)
Missing data during window but on study	0	1 (<1)

[1] Two deaths in the study, both unrelated to study drug. DTG+RPV Kaposi's Sarcoma (N=1), CAR Lung cancer (N=1)

1 VF (DTG+RPV) with RT DRM K101K/E, resuppressed with DTG+RPV. No IN DRMs.

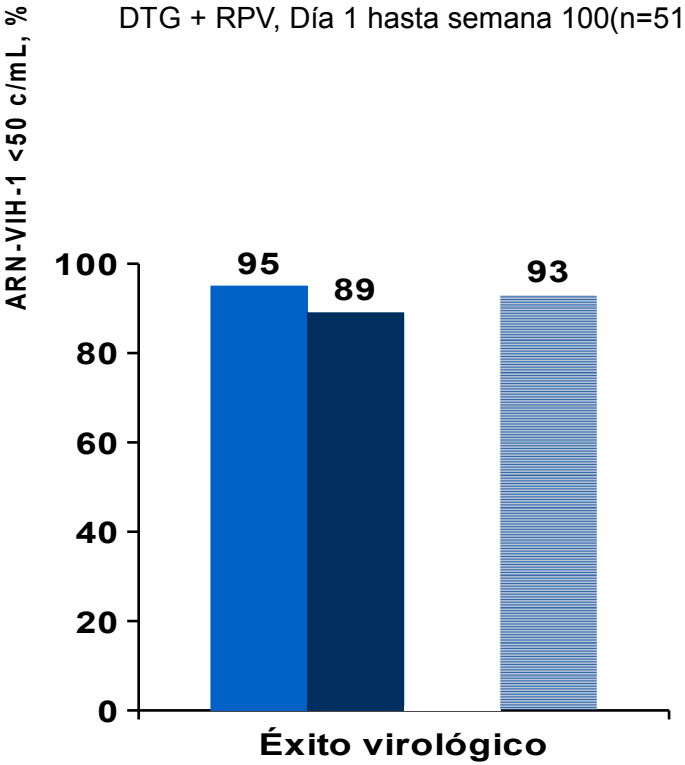
Llibre JM. CROI 2017; Seattle, WA. #44LB. The Lancet 2018;391(10123): 839–849.

SWORD 1&2. Eficacia Virológica

RNA-VIH-1<50 c/mL a 48 y 100 semanas

Grupo de *switch* temprano
DTG + RPV, Día 1 hasta semana 48 (n=513)[1]
DTG + RPV, Día 1 hasta semana 100(n=513)

Grupo de *switch* tardío
DTG + RPV, semana 52 a semana 100 (n=477)



	Grupo *switch* temprano		Grupo *switch* tardío
	DTG+ RPV Semana 48[1]	DTG + RPV Semana 100	DTG + RPV Semana 100
Éxito virológico	486 (95)	456 (89)	444 (93)
Sin respuesta virológica	3 (<1)	13 (3)	10 (2)
Datos en ventana, no <50 copias/mL	0	5 (<1)	3 (<1)
Discontinuaciones por falta de eficacia	2 (<1)	7 (1)	3 (<1)
Discontinuaciones mientras CV no <50 copias/mL	1 (<1)	1 (<1)	0
Cambio de TAR	0	0	4 (<1)
Sin datos virológicos	24 (5)	44 (9)	23 (5)
Discontinuaciones por EAs o muerte	17 (3)	27 (5)	11 (2)
Discontinuaciones por otros motivos[a]	7 (1)	17 (3)	9 (2)
Sin de datos en la ventana pero sí en el estudio	0	0	3 (<1)

aLas discontinuaciones por otros motivos mientras estaba en tratamiento con DTG + RPV fueron pérdida de seguimiento, n=3; desviación del protocolo, n=5 (uso de medicación prohibida, n=3; embarazo, n=2); retirada de consentimiento, n=18 (pacientes reubicados, n=5; carga de viaje, n=2; otros, n=9); criterio del investigador, n=2.

- Tras 100 semanas de tratamiento, DTG + RPV continuó siendo eficaz en el grupo de *switch* temprano.
- La eficacia virológica en el grupo del *switch* tardío a 100 sem fue comparable a la del *switch* temprano a 48 sem[1]

ESP/DTGP/0041/18a 07/2018

1. Llibre et al. *Lancet*. 2018;391:839-849.

Aboud M et al. AIDS 2018; Amsterdam, the Netherlands. Slides [THPEB047]

Adaptado de Aboud M, Orkin C, Podzamczer D, et al. Durable suppression 2 years after switch to DTG + RPV 2-drug regimen: SWORD-1 and -2 studies. Presented at: International AIDS Conference; July 23-27, 2018; Amsterdam, Netherlands.THPEB047. Disponible en: http://programme.aids2018.org/Search/Search?search=thpeb047

SWORD 1&2. 96 weeks.

DTG + RPV Resistance: 3/990 (0.3%)

Table 1. DTG + RPV: Low Rates of CVW Through Week 100

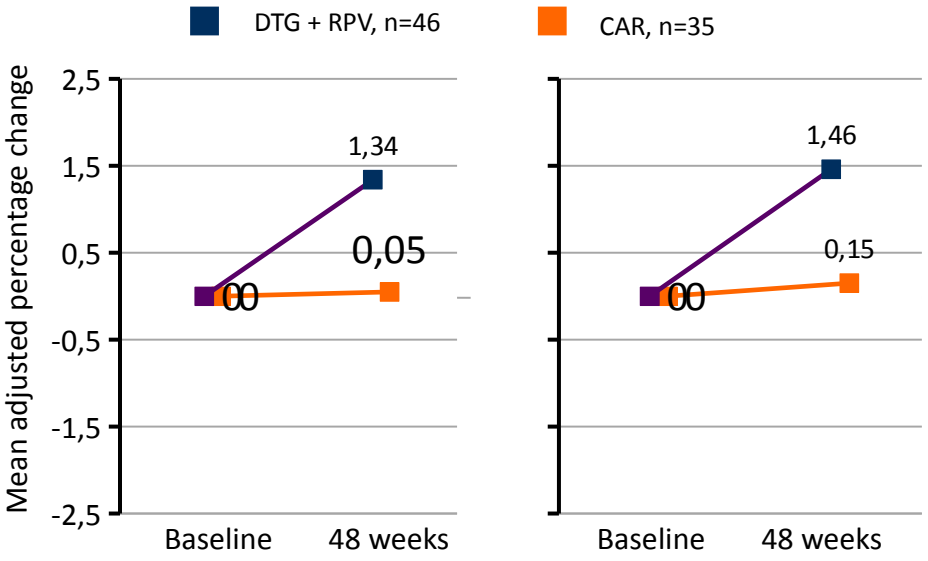
Week of failure	Previous regimen	Viral loads, copies/mL[b]	Resistance mutations[a]		Fold change
			Baseline (GenoSure[c])	CVW	
Week 24	EFV/TDF/FTC	88; 466	NNRTI: none INSTI: G193E	NNRTI: none INSTI: G193E	DTG, 1.02
Week 36	EFV/TDF/FTC	1,059,771; 1018; <50	NNRTI: none INSTI: none	NNRTI: K101K/E INSTI: none	RPV, 1.21
Week 64[d]	DTG/ABC/3TC	833; 1174; <50	NNRTI: none INSTI: N155N/H, G163G/R	INSTI resistance test failed	———
Week 76[d]	ATV, ABC/3TC	79; 162; 217	———	Test not performed[e]	———
Week 88	DTG/ABC/3TC	278; 2571; 55	NNRTI: none INSTI: none	NNRTI: E138E/A INSTI: none	RPV, 1.61 DTG, 0.72
Week 88	RPV/TDF/FTC	147; 289	———	Test not performed[e]	———
Week 100	EFV/TDF/FTC	651; 1105; 300	NNRTI: K101E, E138A INSTI: G193E	NNRTI: K101E, E138A, M230M/L INSTI resistance test failed	RPV, 31
Week 100	ATV, RTV, TDF/FTC	280; 225; 154	NNRTI: none INSTI: none	NNRTI: none INSTI: none	———

[a]Shading represents participants with treatment-emergent NNRTI resistance–associated mutations. [b]Underlined value denotes viral load when participant met virologic withdrawal. [c]HIV-1 baseline resistance testing was performed on integrated HIV-1 proviral DNA using GenoSure Archive® assay (Monogram Biosciences, South San Francisco, CA). On-study resistance testing used standard plasma-based genotypic and phenotypic resistance testing. [d]Participants in the late-switch group. [e]Resistance testing not performed because of low viral load.

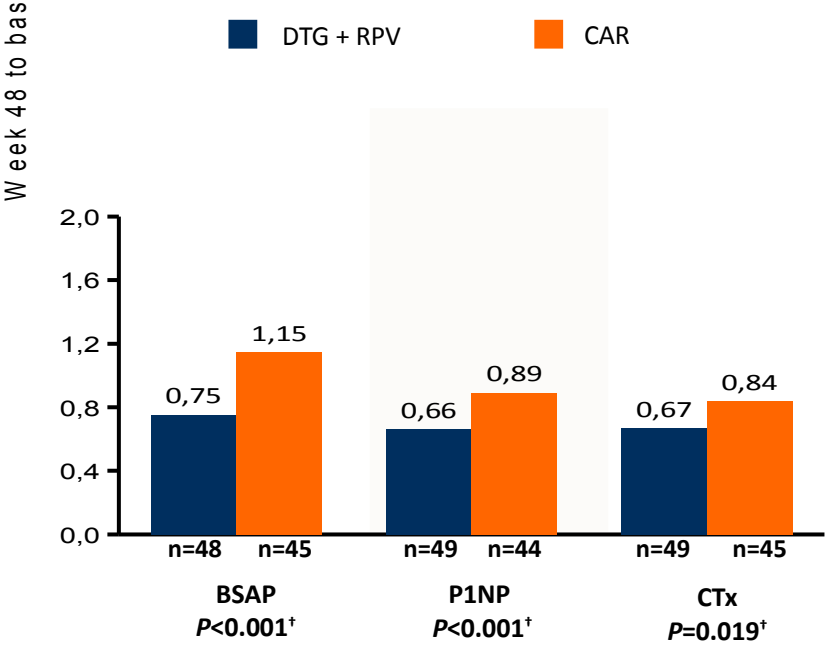
M Aboud. IAS Amsterdam 2018. #THPEB047

Change in BMD and Bone Markers at Week 48

Adjusted Change From Baseline in Total Hip and Lumbar Spine BMD (g/cm²) at Week 48*



Adjusted Week 48 to Baseline Ratio in Bone Markers



- Subgroup of N=102 subjects treated with TDF.
- Changes in total hip and lumbar spine BMD were consistent across subgroups (ie, age, sex, BMI, baseline third-agent class (NNRTI, PI or INSTI)

BSAP, bone-specific alkaline phosphatase; CTx, type-1 collagen cross-linked C-telopeptide; P1NP, procollagen type 1 N-propeptide.

*BMD *P* values are from an ANCOVA model adjusted for baseline BMD, age, and b BMI. †Biomarker *P* values show comparisons between DTG + RPV and CAR at Week 48 for each marker, adjusted for third-agent class, age, sex, BMI, smoking status, and biomarker level. Statistical model uses log-transformed data.

McComsey et al. IAS 2017; Paris, France. Poster TUPDB0205LB. AIDS 2018; DOI: 10.1097/QAD.0000000000001725

SWORD-1 and SWORD-2: DTG + RPV biomarker analysis

Atherogenesis and inflammation biomarkers – change from BL to Week 48 (pooled SWORD data)

Biomarker	DTG + RPV	CAR	Dif. DTG+RPV vs CAR
Inflammation			
C-RP	0.11	0.47	-0.36
IL-6	0.04	-0.12	0.16
Hypercoagulability			
D-dimer	-0.01	-0.05	0.04
Macrophage activation			
sCD163	58	54	4
Monocyte activation			
sCD14	419	778	**-359**
Endothelial dysfunction			
sVCAM	-2.43	63.57	**-66**
Fatty acid metabolism			
FABP2	-2.13	-1.47	-0.66

C-RP, C-reactive protein; FABP2, fatty acid binding protein-2; sCD14, soluble cluster of differentiation 14; sCD163, soluble cluster of differentiation 163; sVCAM-1, soluble vascular adhesion

Orkin C, et al. EACS 2017, Milan, Italy, BPD2/10

PLOS ONE

2016;11(10):e0164753

RESEARCH ARTICLE

Switch to Dolutegravir plus Rilpivirine Dual Therapy in cART-Experienced Subjects: An Observational Cohort

Amedeo F. Capetti[1]*, Gaetana Sterrantino[2], Maria Vittoria Cossu[1], GianCarlo Orofino[3], Giorgio Barbarini[4], Giuseppe V. De Socio[5], Simona Di Giambenedetto[6], Antonio Di Biagio[7], Benedetto M. Celesia[8], Barbara Argenteri[1], Giuliano Rizzardini[1,9]

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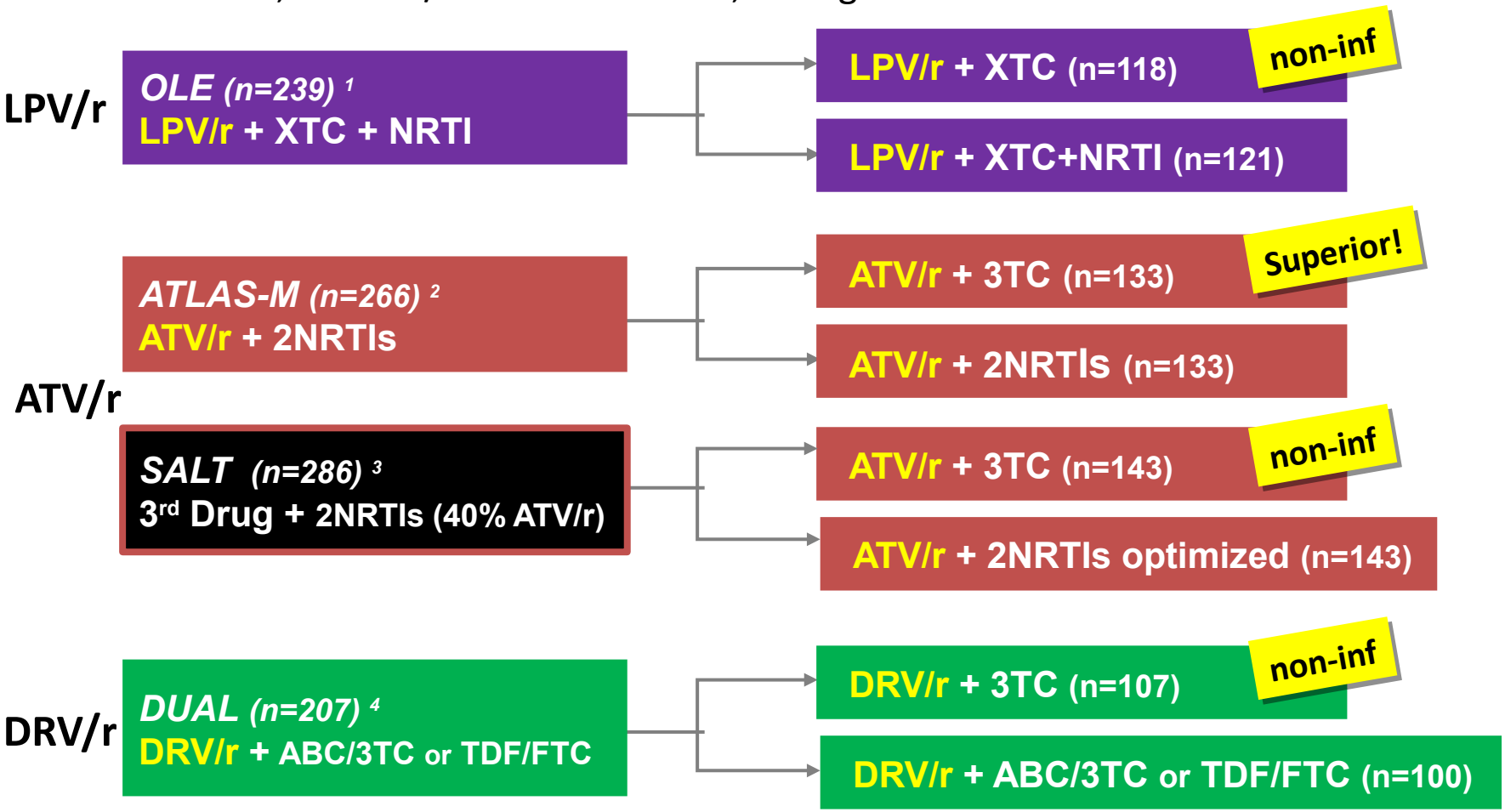
Dolutegravir and rilpivirine for the maintenance treatment of virologically suppressed HIV-1 infection

Jose L. Casado, Marta Monsalvo, Aurora M. Rojo, María Fontecha & Miguel A. Rodriguez-Sagrado

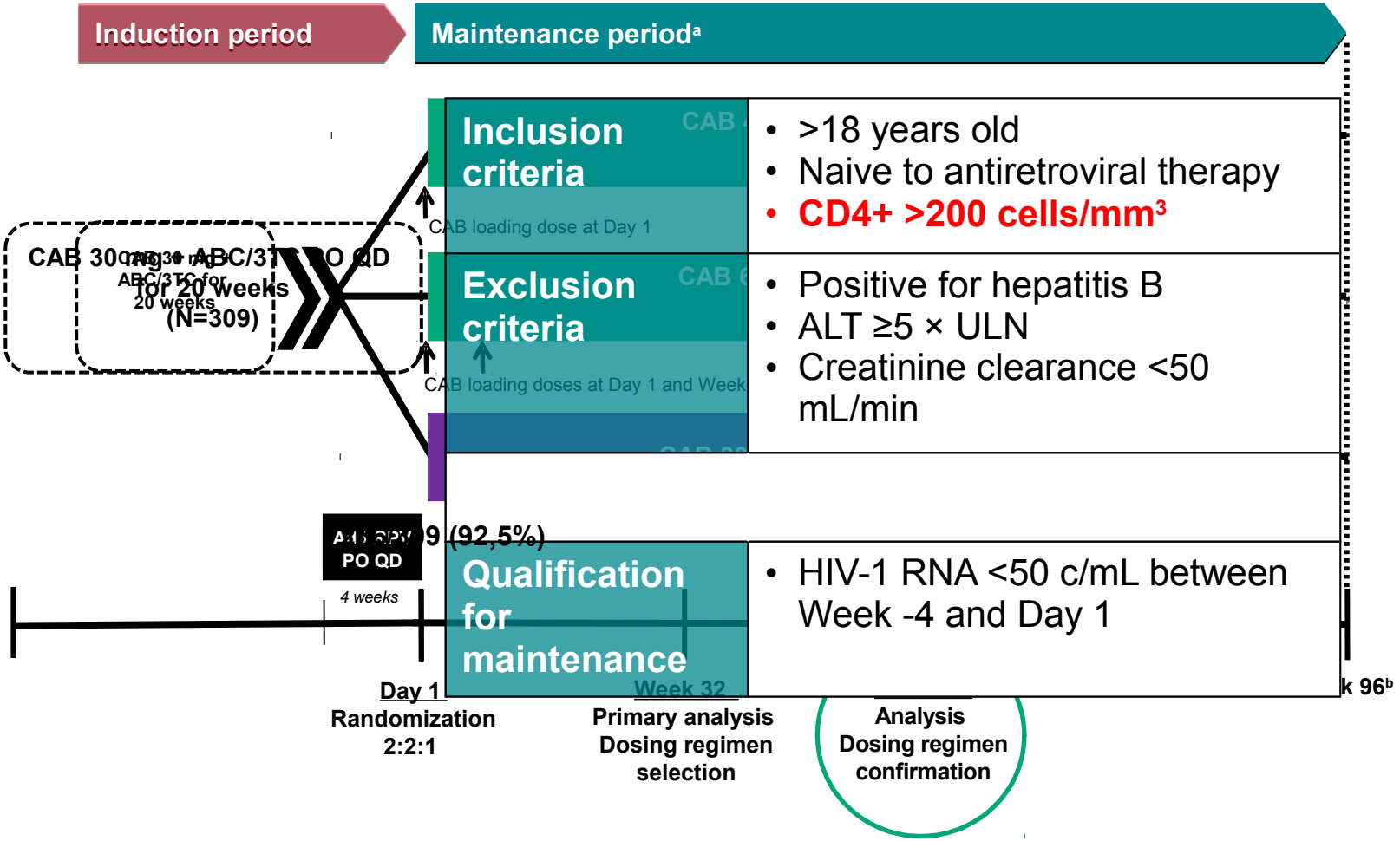
PI/r + 3TC in Switch. Summary of evidence.

- **N=998**, VL<50 c/mL for ≥6 months, HBsAg -.



1. JR Arribas. Lancet Infect Dis 2015;15: 785–92. 2. SD Giambenedetto. J Antimicrob Chemother 2017;72:1162-1171. 3. JA Perez-Molina. Lancet Infect 2015;15:775-784. 4. F Pulido. Clin Infect Dis 2017: doi 10.1093/CID/cx734.

LATTE-2 Study Design (Phase 2)

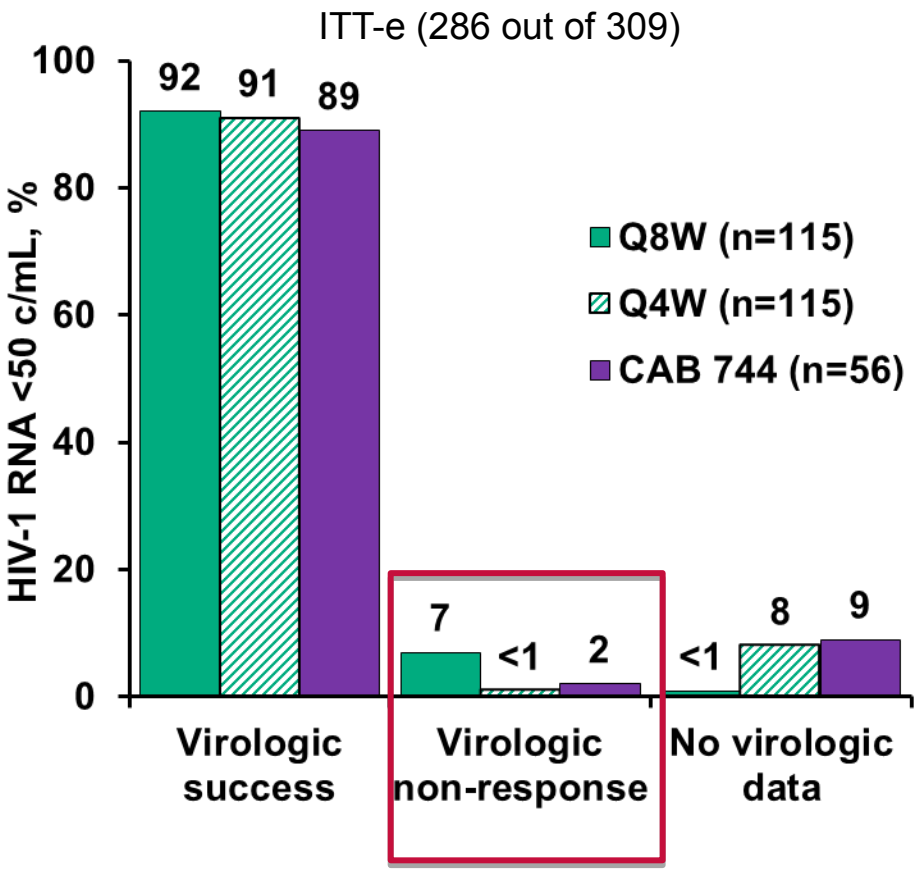


ABC/3TC, abacavir/lamivudine; ALT, alanine aminotransferase; IM, intramuscular; PO, orally; QD, once daily; Q4W, every 4 weeks; Q8W, every 8 weeks; ULN, upper limit of normal. [a]Subjects who withdrew after at least 1 IM dose entered the long-term follow-up period. [b]Subjects can elect to enter Q4W and Q8W LA Extension Phase beyond Week 96.

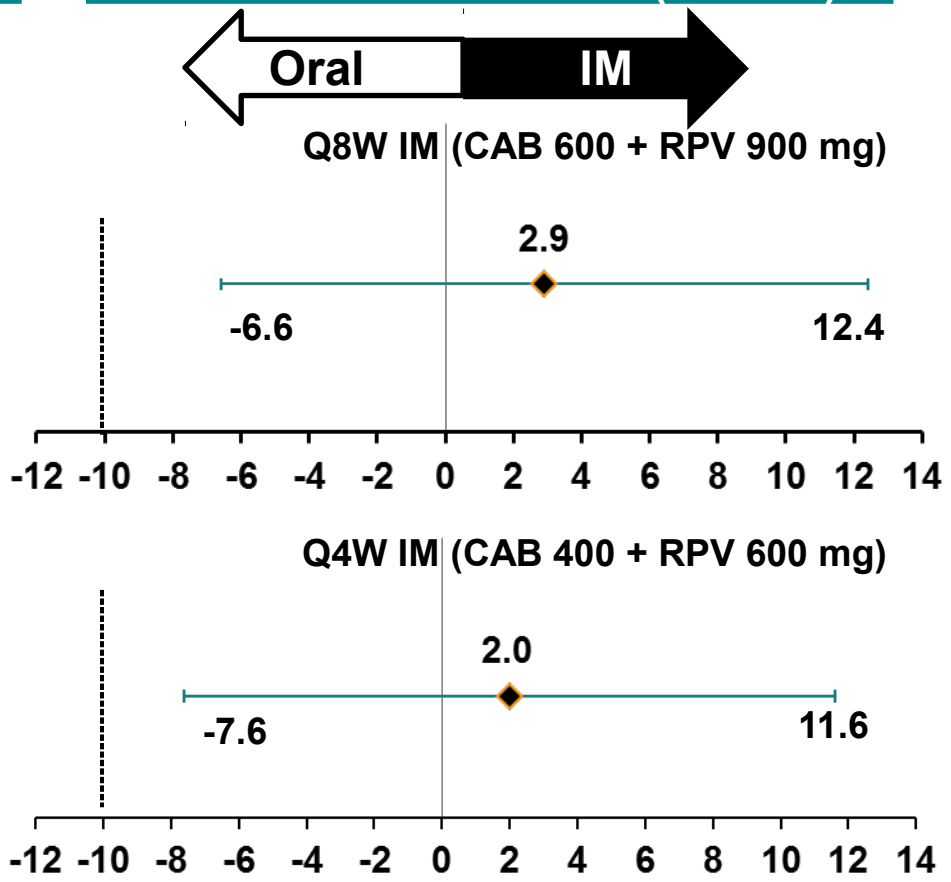
Margolis et al. AIDS 2016; Durban, South Africa. Abstract THAB0206LB.

LATTE 2. HIV-1 RNA <50 c/mL at Week 48 ITT-ME (Snapshot)

Virologic outcomes



Treatment differences (95% CI)

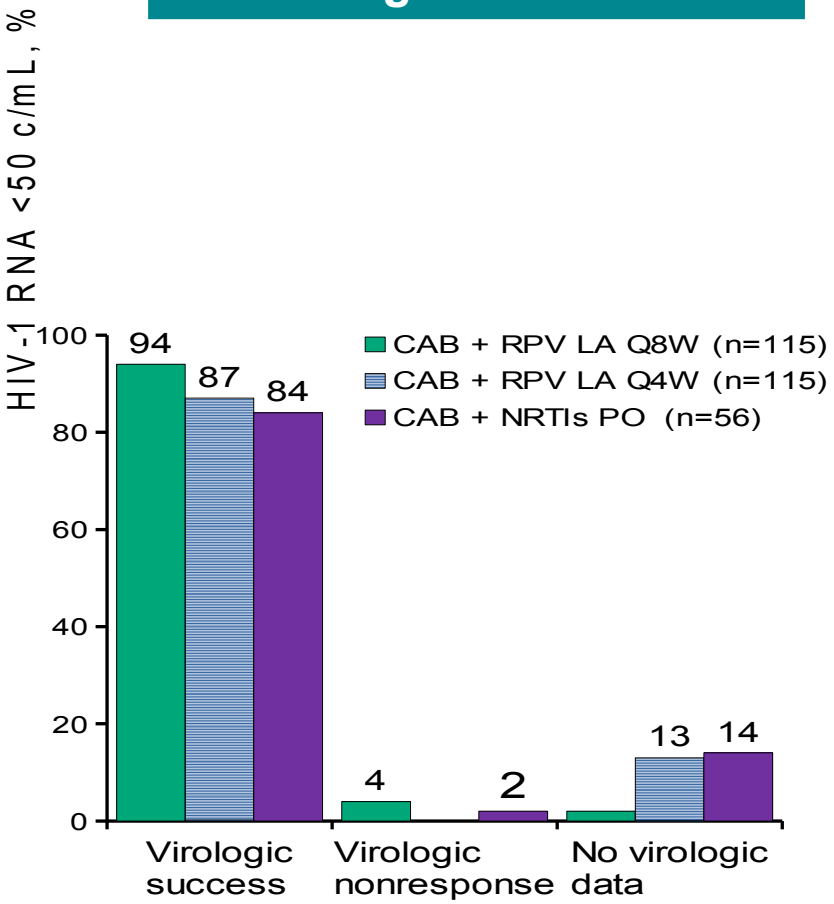


1/2 VF Q8W: NNRTI—**K103N, E138G, and K238T** (FC RPV=3.3; ETR=1.9); INI—**Q148R** (FC CAB=5.1; DTG=1.38)

LATTE 2. Comparable Response Across Arms

Week 96 HIV-1 RNA <50 c/mL by Snapshot (ITT-ME)

Virologic outcomes

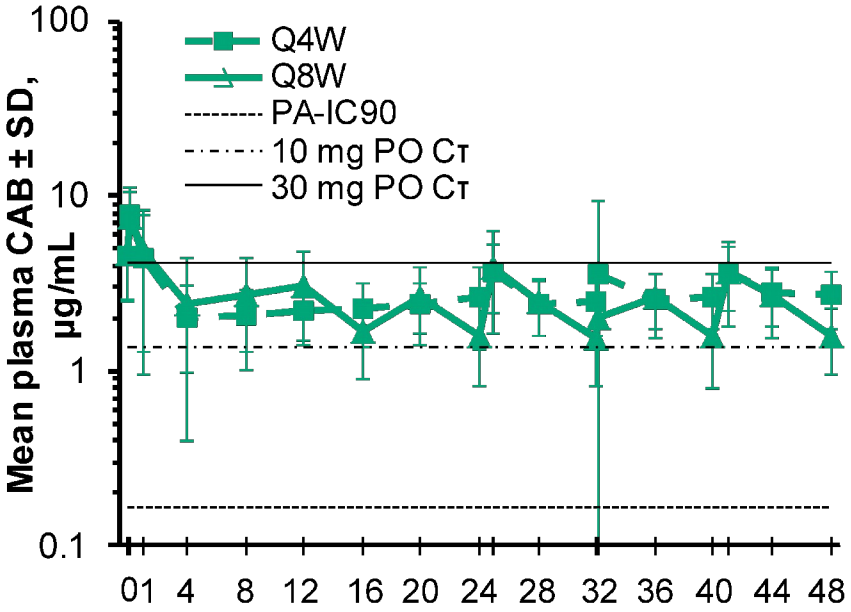


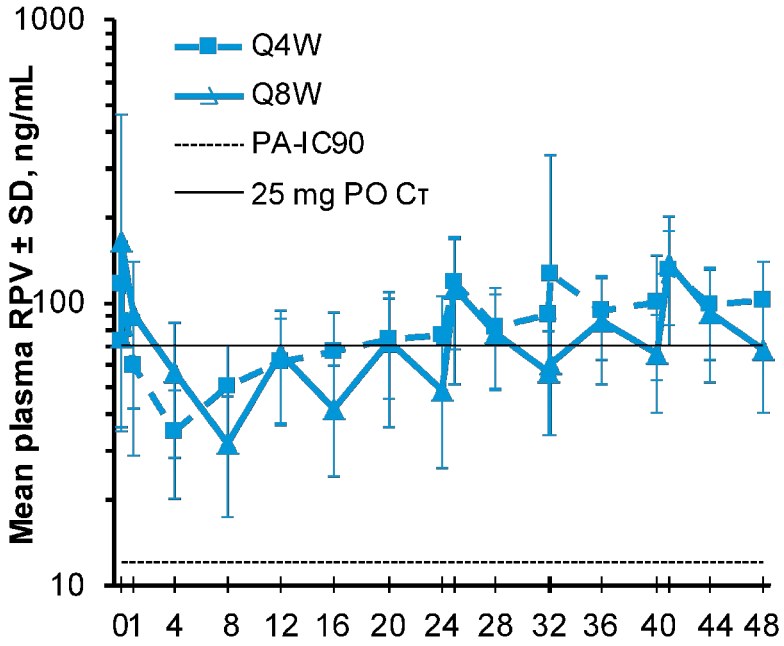
Treatment differences (95% CI)

ITT-ME, intent-to-treat maintenance exposed; LA, long acting; Q4W, every 4 weeks; Q8W, every 8 weeks.

Eron et al. IAS 2017; Paris, France. MOAX0205LB.

LATTE 2. PK of CAB + RPV Q4W and Q8W.





Phase 3 FLAIR (NCT02938520), CAB-LA + RPV-LA Q4 wk, fully recruited, vs DTG/ABC/3TC in **naives**. N=570. Stay tuned.

Phase 3 ATLAS (NCT02951052), n=570. **Switch** from any triple ART (2NRTIs + 3rd drug) to CAB LA + RPV LA Q4 wk (fully recruited).

Phase 3 ATLAS 2M (HERCULES), n=1020. Switch from any triple ART to CAB LA +RPV LA Q4 or Q8 wk (fully recruted)

Margolis et al. AIDS 2016; Durban, South Africa. Abstract THAB0206LB.

2-DR regimens. Conclusions.

Stay tuned!

- **DTG/RPV FDC** meets all the requirements to be used in switch from any triple-drug regimen.
- **DRV/b** or **ATV/b + 3TC** meet the requirements to be used in switch <u>from triple-drug DRV- or ATV-based</u> regimens.

- **DTG/3TC FDC meets all the requirements** in initial ART (VL<500.000, CD4 >200 cells).
- **LA CAB + RPV IM** every 1 or 2 months is a promising regimen in late-stage development.
- The only **benefit to the patient** proven so far with 2DR is not related with that particular strategy, but with avoiding TDF. The same benefit can be obtained with TAF in preferred triple-drug regimens, taking no risks.

"If U don't need an additional drug, don't take it"