FLS SCIENCE FOSTERING LEARNING & SHARING

Update on Clinical Topics in ART Workshop
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Barcelona

Dual ART: 2DR

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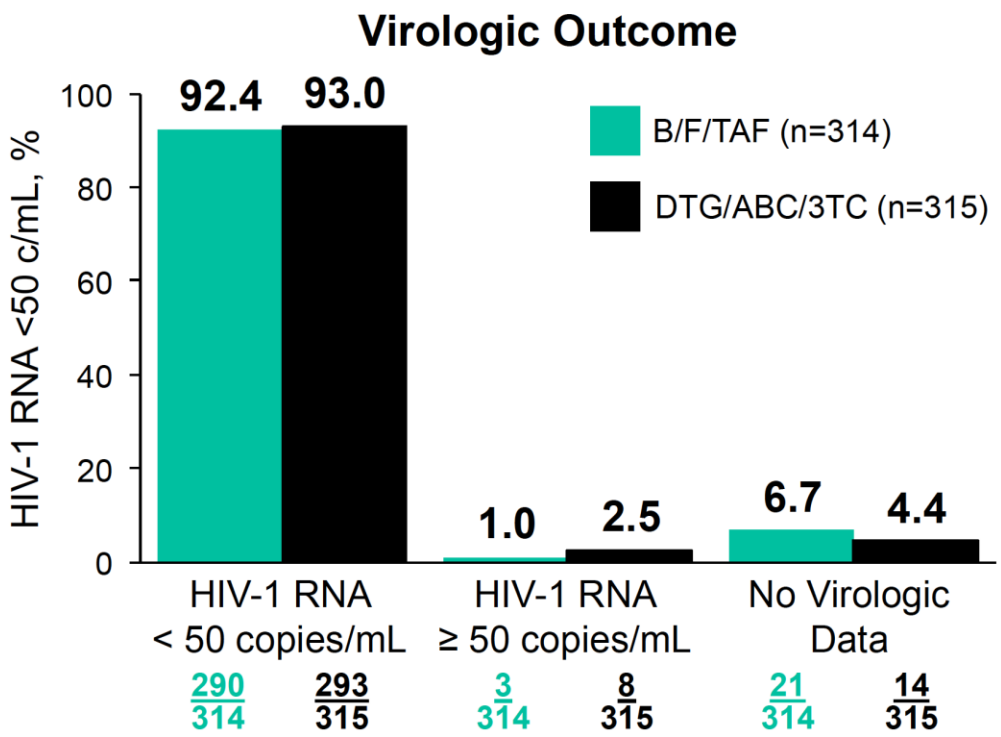
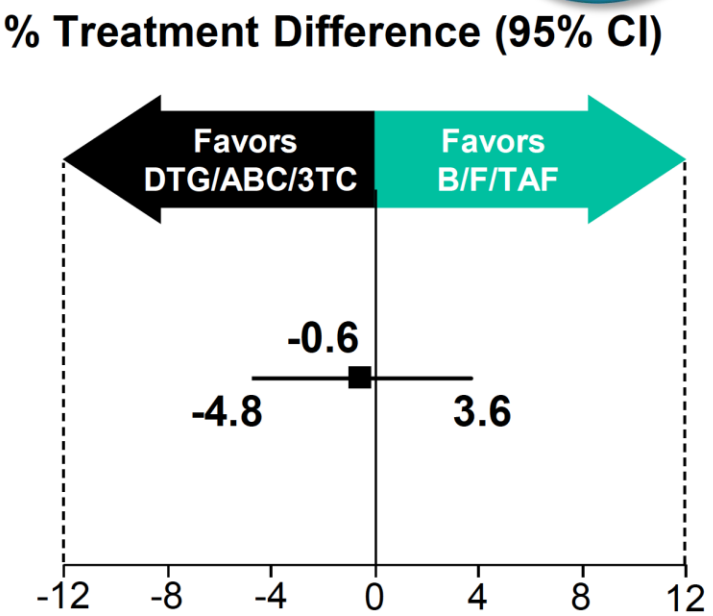
Virologic Outcome at Week 48

HIV-1 RNA < 50 copies/mL



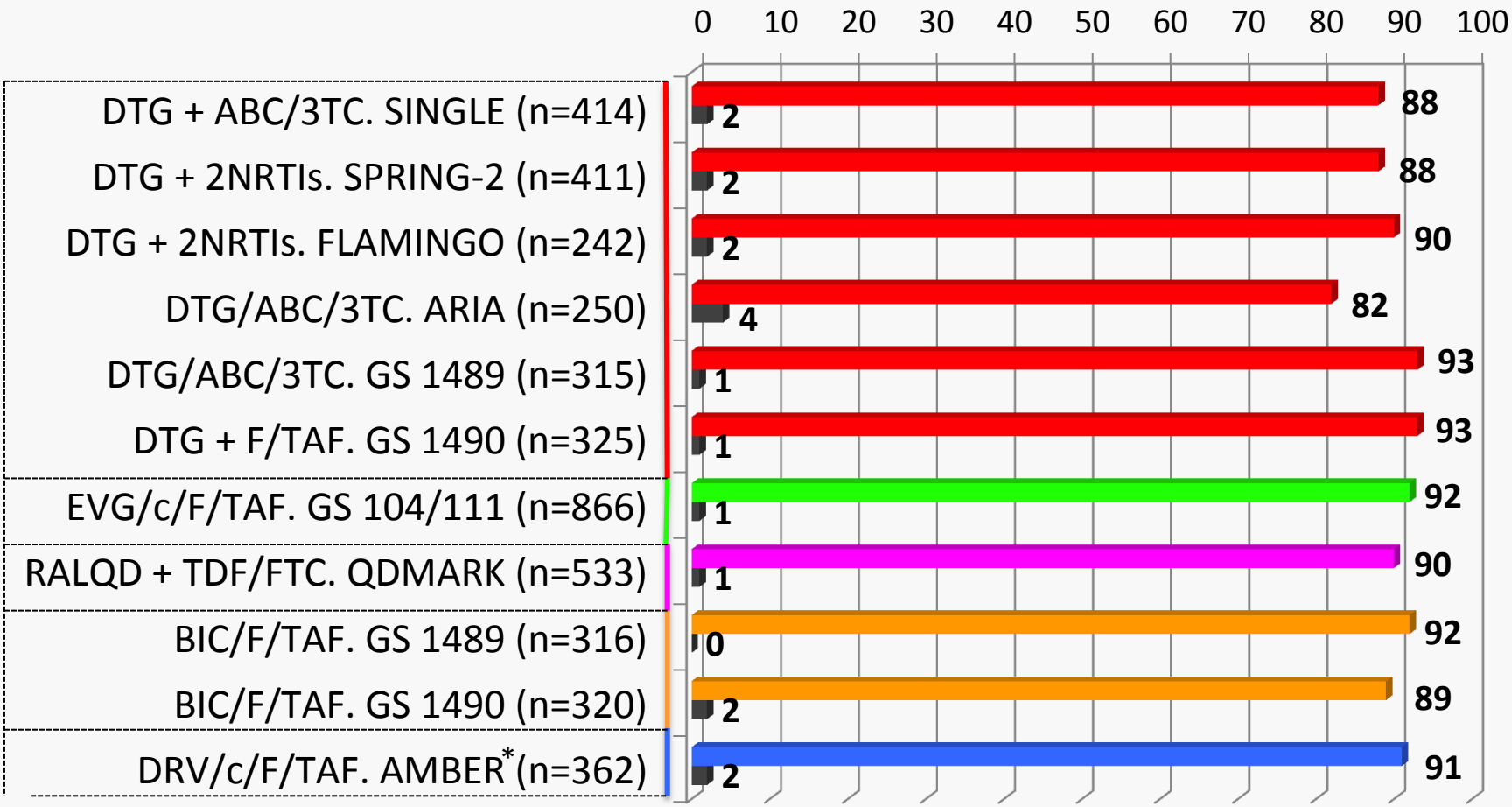


- Non-inferiority confirmed by pre-specified analyses for HIV-1 RNA < 50 copies/mL:
  - Per protocol: B/F/TAF 99.3% vs DTG/ABC/3TC 98.6% (p=0.43)
  - Missing=Failure: B/F/TAF 92.4% vs DTG/ABC/3TC 93.3% (p=0.65)
  - Missing=Excluded: B/F/TAF 99.3% vs DTG/ABC/3TC 97.7% (p=0.10)
- Mean CD4 increase from baseline at Week 48:
  - B/F/TAF +233 cells/μL vs DTG/ABC/3TC +229 cells/μL (p=0.81)

- **0 resistance**!!
- **D/C AEs**: 0 vs 1.3%
- 2 **STR**
- No PK booster

Phase 3 RCTs, newest OD Regimens, Initial ART.

Efficacy 48 weeks, VL<50 c/mL (ITT)



*Excludes CD4 ≤ 50 cells.

References in slide footnotes.

Less-drug ART regimens: NOT an unmet need.

>90%

Could :

- Reduce lifelong drug exposure
- Reduce toxicity
- Reduce costs
- 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, no limitations**)
2. Include **preferred drugs**
3. Report a **benefit to the patient**
4. Being **cost-effective**

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

EACS European AIDS Clinical Society

Adverse Effects of ARVs and Drug Classes

Bold: Frequent effects
Red: Severe effects
Black: Neither Frequent nor Severe[i]

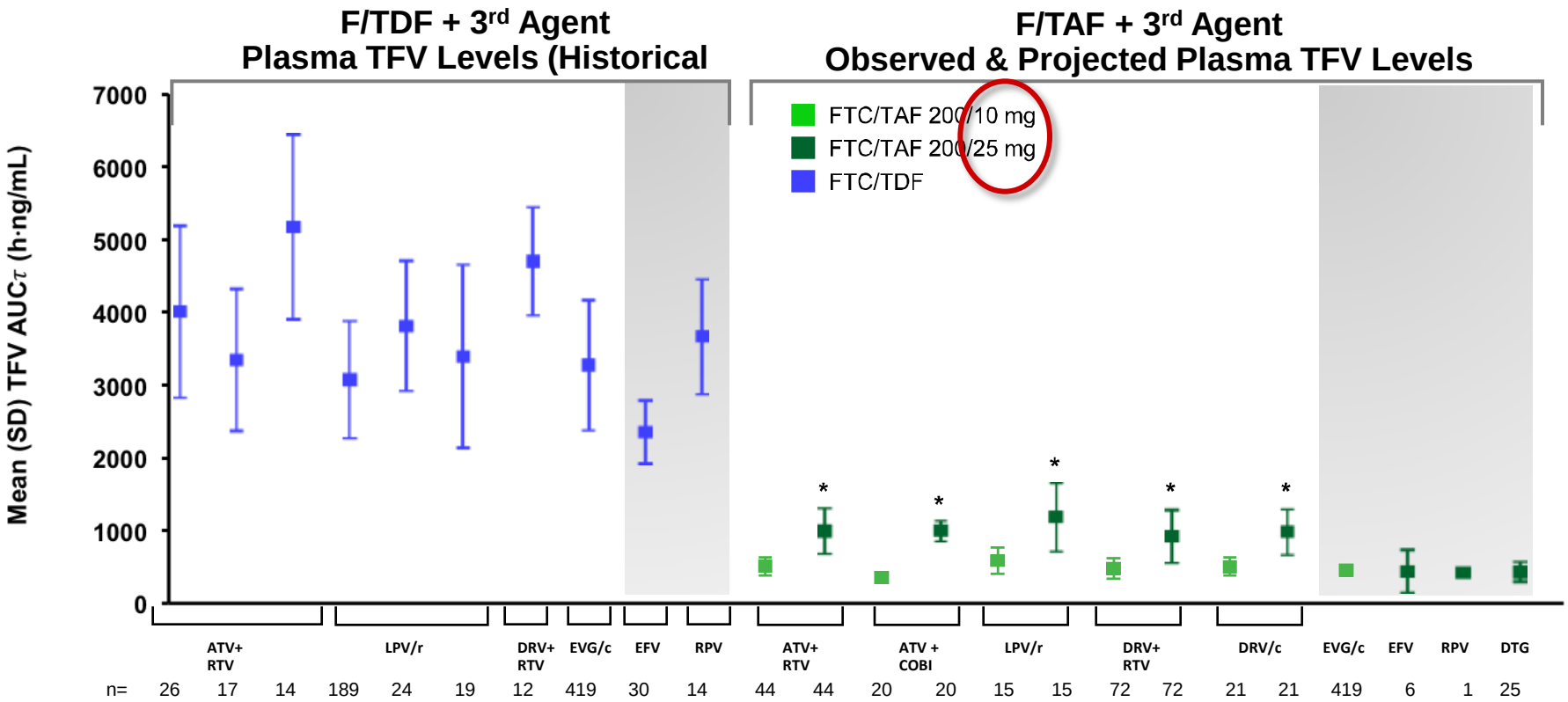
	Skin	Digestive	Liver	CV	Musculo-skeletal	Genito-urinary	Nervous	Body fat	Metabolic	Other
NRTIs										
ABC		Nausea* Diarrhoea*		IHD ?	Generic					
3TC					Generic					
FTC										
TDF[ii]					Generic					
TAF[iii]										

EACS Guidelines, version 9.0. October 2017. Available at: http://www.eacsociety.org

Study 1089: Switch from F/TDF to F/TAF at Week 48

TAF > TDF

Plasma TFV Exposures
F/TAF vs F/TDF + a 3rd Agent



*Projected TFV exposures were estimated from FTC/TAF 10 mg from Study GS-US-311-1089 with ATV+RTV, LPV+RTV, and DRV+RTV, Study GS-US-311-1388 with ATV+COBI as separate components, and Study GS-US-299-0102 with DRV+COBI as a single-tablet regimen; TFV exposures at FTC/TAF 25 mg were estimated by linear scaling of TFV exposures from TAF 10 mg

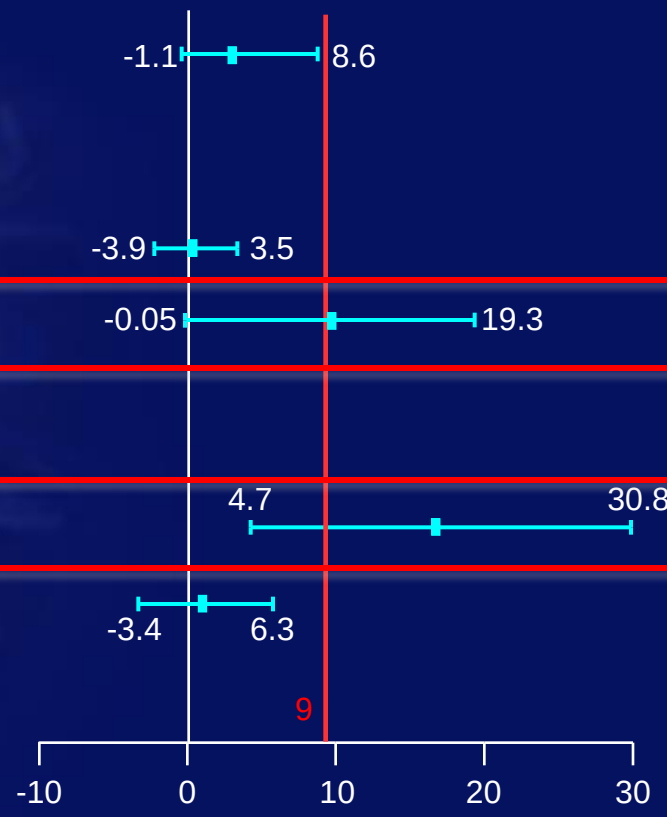
- **F/TAF relative to F/TDF results in markedly lower TFV plasma exposures**
- **Projected plasma TFV levels are 80% lower when F/TAF 25mg (compared to F/TDF) is paired with a boosted PI**

Custodio J, et al. ASM 2016. Boston, MA. #410

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

		RAL + DRV/r	TDF/FTC + DRV/r
Overall	n = 805	17.4 %	13.7 %
Baseline HIV-1 RNA			
< 100,000 c/ml	n = 530	7 %	7 %
≥100,000 c/ml	n = 275	36 %	27 %
			p = 0.09*
Baseline CD4+			
< 200/mm^3	n = 123	39.0 %	21.3 %
≥ 200/mm^3	n = 682	13.6 %	12.2 %
			p = 0.02*



Difference in estimated proportion (95% CI) RAL – TDF/FTC; adjusted

* Test for homogeneity

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:

- ✓ **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.
- ✓ No reduction in AEs.

* 1 additional p

Protocol-define ned
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.

- **Naives**

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

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

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	< 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

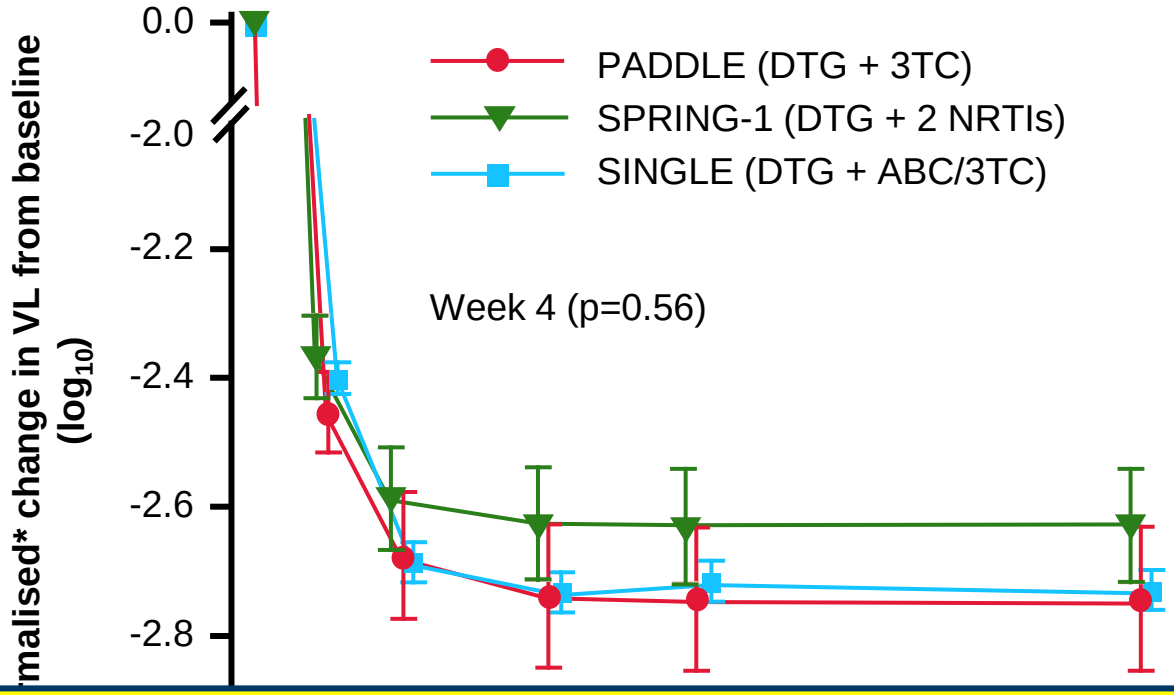
90%

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 or triple DTG regimens. Naives (<100.000 c/mL).



Phase 3 GEMINI 1 (NCT02831673) and **GEMINI 2** (NCT02831764), n≈1400, both vs DTG + TDF/FTC, fully recruited. Stay tuned. (VL ≤500.000 c/mL)

IDMC, 2^{5th} October 2017 (50% week 24): no potential issues, continue both studies.

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

ACTG A5353: DTG + 3TC naives, single arm.

Primary Outcome: FDA Snapshot at Week 24

Preliminary

Any CD4, VL < 500.000 c/mL	Baseline HIV-1 RNA > 100,000 cpm N=37	Baseline HIV-1 RNA ≤ 100,000 cpm N=83	Total N=120
Virologic success	**33 (89%)**	**75 (90%)**	**108 (90%)**
HIV-1 RNA < 50 cpm [95% CI]	[75%,97%]	[82%,96%]	[83%,95%]
Virologic non-success	**3 (8%)**	**2 (2%)**	**5 (4%)**
HIV-1 RNA ≥ 50 cpm	3 (8%)	0	3
Discontinued study treatment for other reasons while HIV RNA ≥ 50**	0	2 *	2
No virologic data in window	**1 (3%)**	**6 (7%)**	**7 (6%)**
Discontinued study treatment for other reasons #	1	5	6
On study but missing data in window	0	1	1

* ***1 Virological failure**: M184V (RT), R263K (IN) (DTG plasma levels not detectable).*
*** Poor adherence; # Lost to follow-up, pregnancy*

Taiwo B. IAS Paris July 2017. #MOAB0107LB

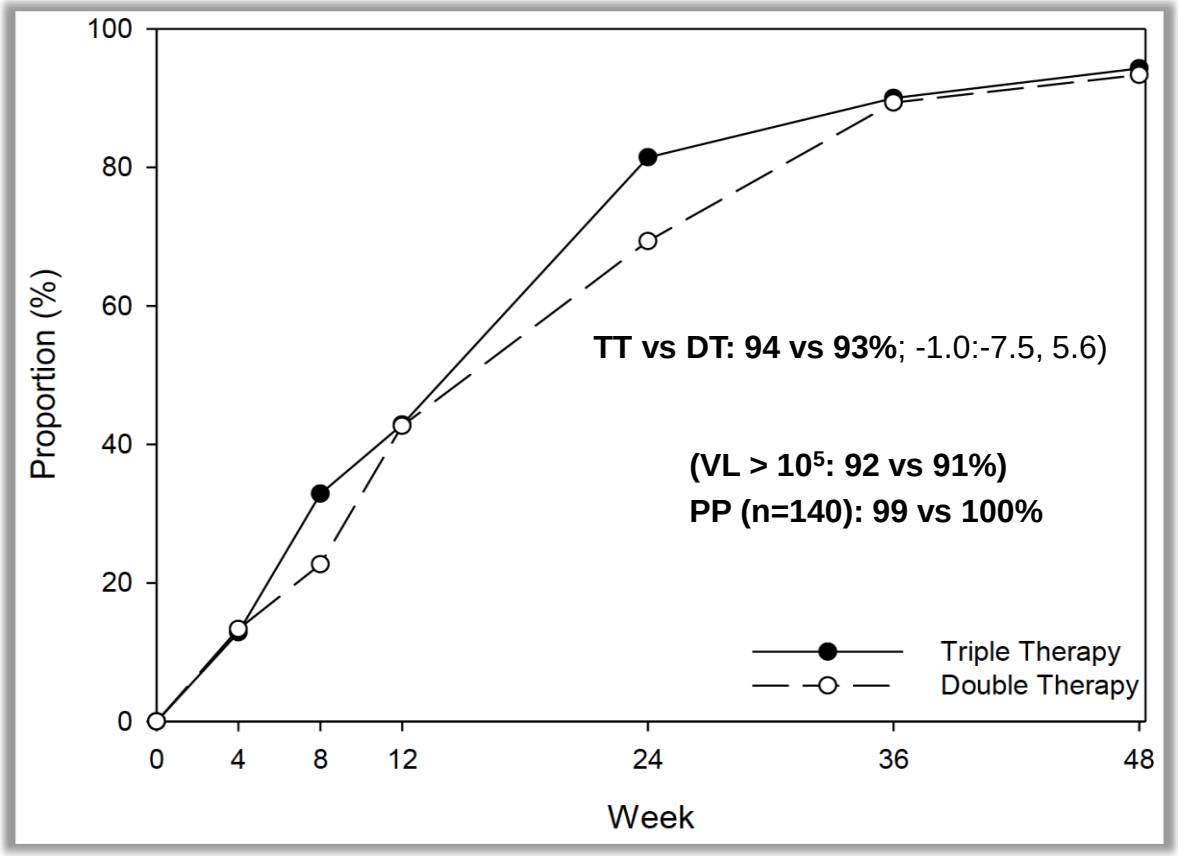
ACTG AIDS CLINICAL TRIALS GROUP

ANDES: gen DRV/r/3TC non-inf to gen DRV/r + TDF/3TC.

- N=145, naives. Open-label.
- No entry restrictions (HBsAg -).
- Stratified by VL (≤ or >10^5 c/mL)

- Median CD4 383 cells;
- % VL>10^5: 24%.

- Similar CD4 recovery.
- 1 VF (TT), no R.
- No dif AEs; D/C AEs "rare" and similar.



P Cahn. CROI 2018, Boston, MA. #489.

- **Switch**

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

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

LPV/r

OLE (n=239) [1]
LPV/r + XTC + NRTI

→ LPV/r + XTC (n=118) — non-inf
→ LPV/r + XTC+NRTI (n=121)

ATV/r

ATLAS-M (n=266) [2]
ATV/r + 2NRTIs

→ ATV/r + 3TC (n=133) — Superior!
→ ATV/r + 2NRTIs (n=133)

SALT (n=286) [3]
3rd Drug + 2NRTIs (40% ATV/r)

→ ATV/r + 3TC (n=143) — non-inf
→ ATV/r + 2NRTIs optimized (n=143)

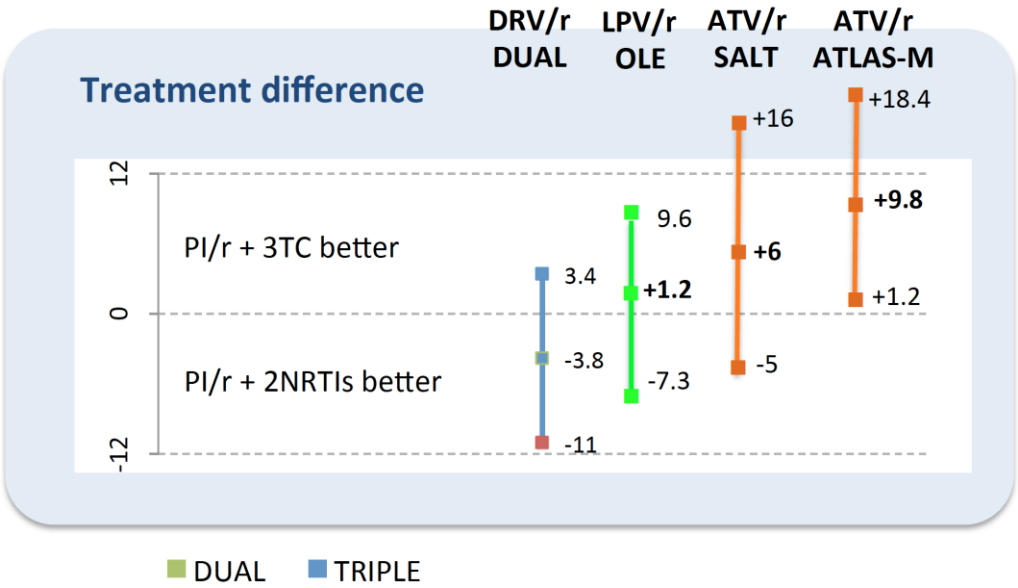
DRV/r

DUAL (n=207) [4]
DRV/r + ABC/3TC or TDF/FTC

→ DRV/r + 3TC (n=107) — non-inf
→ DRV/r + ABC/3TC or TDF/FTC (n=100)

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.

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



Δ for noninf: -12.

Ready for use

No resistance at VF.
Increased rates virol non- response (PIVOT).
CNS issues (PROTEA, Swiss cohort).

Virol failure rates (48 w HIV-RNA ≥50 cop/mL): 4% DT vs. 3.04% TT (Dif 0.9% (95%CI, -1.3% to 3.2%)*

HIV-RNA ≥50 cop/mL at week 48 Dual therapy – triple therapy (%)		Absolute risk difference, (95% CI) Non-inferiority margin: 4%
SALT		1.40 (-2.80, 5.60)

Phase 3 DUALIS (n=320), DTG QD + DRV/r 800/100 QD.
Switch from DRV/r + 2NRTIs with virol. suppression.

Recruitment completed (Germany)

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. * JA Perez-Molina. EACS Milano 2017;#PS1-1.

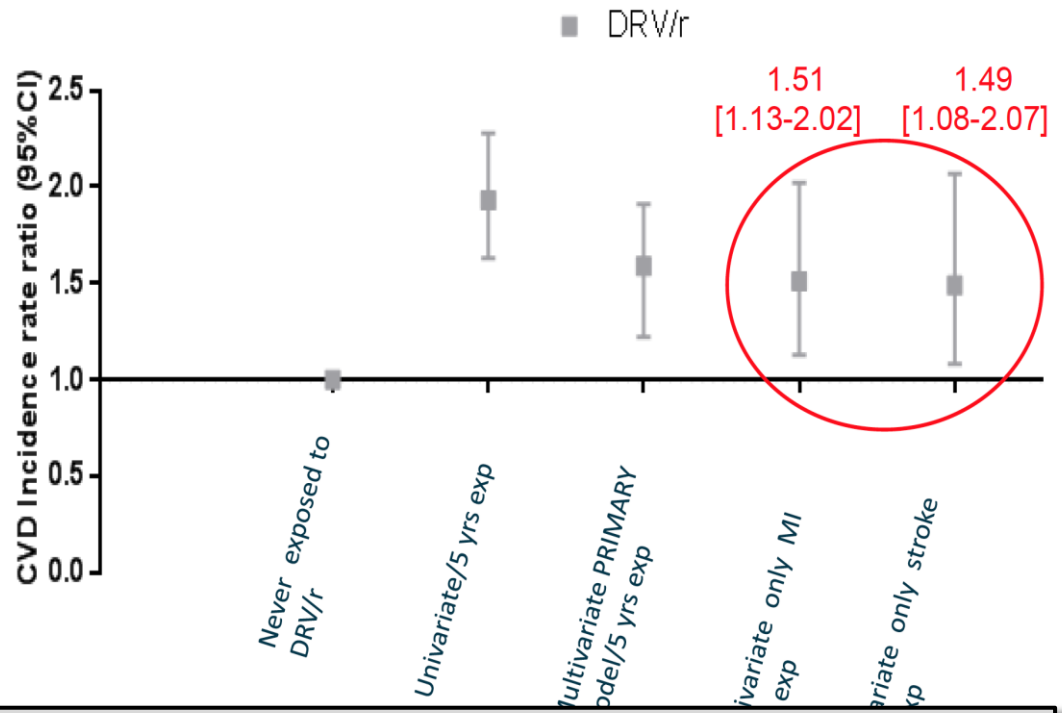
D:A:D Cohort.

Results consistent if:

- DRV/r first ARV regimen.
- DRV/r used with an NNRTI.
- High vs low CVR.
- Adjusted for dyslipidemia

Limitation: DRV/r dose not recorded.

Association Between CVD & Cumulative DRV/r Use;
MI (n=477) and Stroke (n= 395) Separately



Conclusion:
DRV/r (but not ATV/r) associated with a low but significant 59% gradual increase of CVD every 5 years of exposure.

Ryom L. CROI 2017, Seattle, WA. #128LB.

DTG + 3TC in switch. Summary of evidence.

- N=183 (n=154 at 48 weeks).
- Open-label, small RCT (LAMIDOL single-arm). Low number of participants.
- *Inclusion*: VL<50 c/mL >1 y (>2 y in LAMIDOL), Any triple ART. HBsAg-.
  Nadir >200 CD4 cells (DOLAM, LAMIDOL).

48 weeks, ITT, % VL<50 c/mL (data for DTG + 3TC)

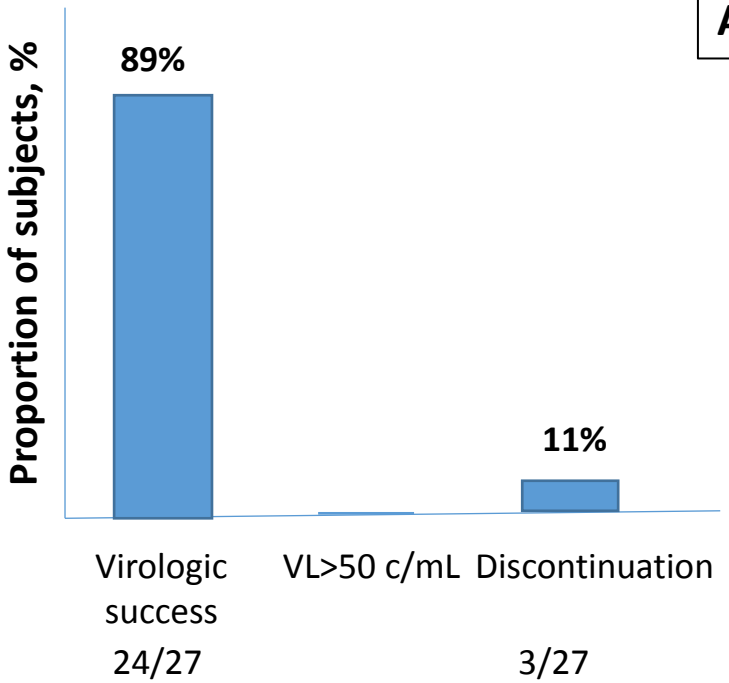
	N (n DTG+3TC)	Efficacy	D/C AEs	VF	Resistance
ANRS LAMIDOL [1]	110 (110)	**92%** vs -	3,6%	1% (3.6*)%	No
ASPIRE [2]	89 (44)	**91%** vs 89% (vs control)	2,3%	2,3%	No
DOLAM [3] *(24 weeks)*	60 (29)[&]	96% vs 100%	0 %	3,5%	No

Phase 3 TANGO RCT (ViiV 204862). n~766. Recruiting. Switch to DTG/3TC FDC from any TAF-3DR.

1. Joly V. CROI 2017, Seattle, WA. #458. 2. Taiwo B. EACS 2017. Milano, Italy. #PE8/5. 3. Martinez E. EACS 2017. Milano, Italy. #PS1/3.

DOLULAM: Switch to DTG+3TC in heavily pre-treated pts

Disposition after 96 weeks (n=27)



Any M184V prevalence (RNA or DNA): 17/27 (63%)

"Prospective cohort", single center.

At Wk 96 :

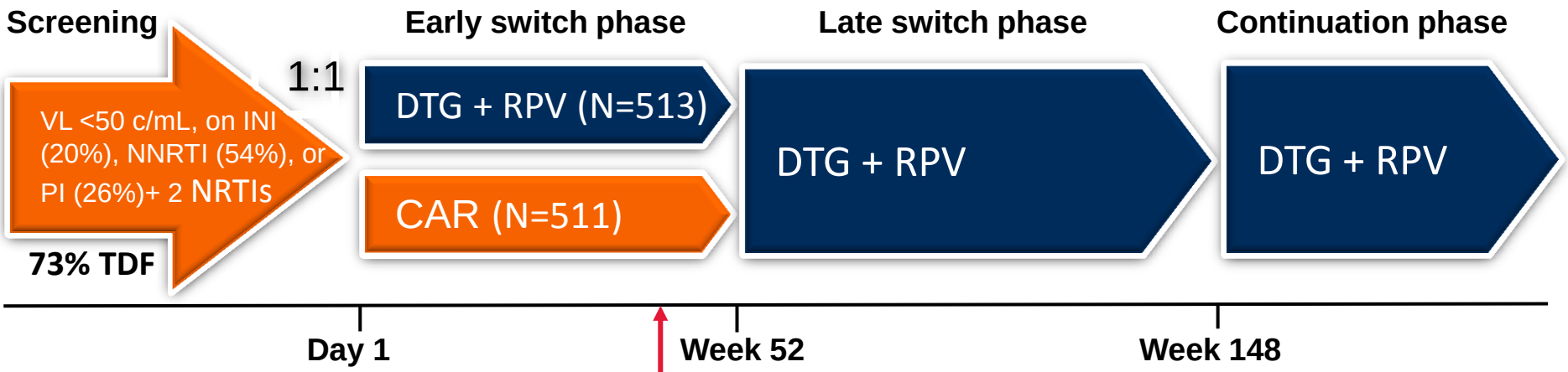
- 24/27 (89%) patients maintained VL < 50 c/mL
- All pts remained free of VF
- 2 D/C AEs at Wk 16 and 24
- 1 re-intensification at Wk 18, due to *blip* (52 c/mL).
- History of M184V/I (63%) was without deleterious impact on efficacy of DTG + 3TC through Wk 102

- **Despite the small sample size, the impressive results of this first pilot study support the concept of maintenance regimen combining DTG and 3TC in this heavily experienced population**

Reynes J. IAS 2017 Paris #MOPEB0322, #MOPEBO315.

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]

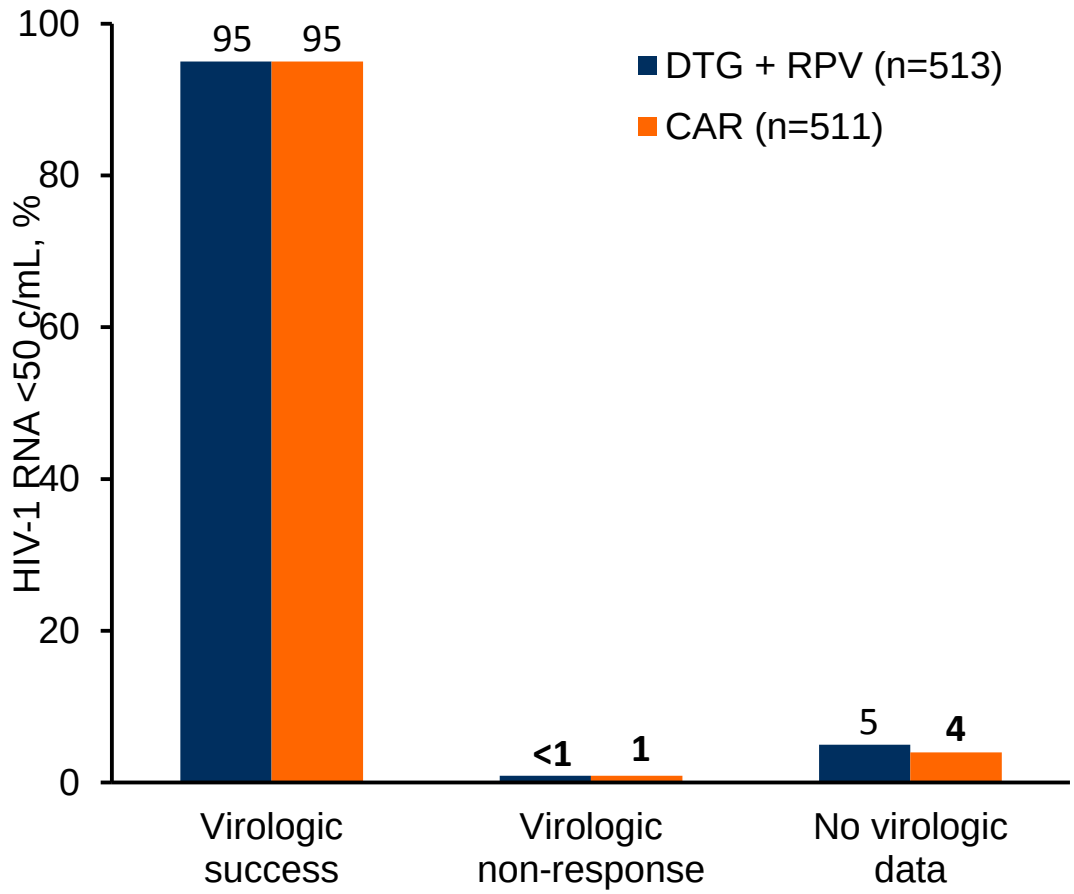
Countries
Argentina, Australia, Belgium, Canada, France, Germany, Italy, Netherlands, Russia, Spain, Taiwan, United Kingdom, United States.

[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.

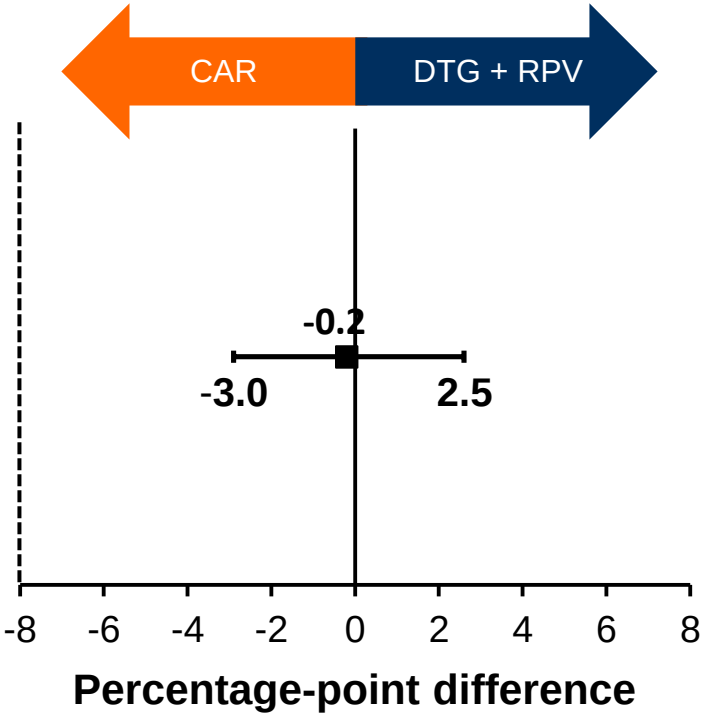
Snapshot Outcomes at Week 48 (Pooled)

Virologic outcomes



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

Adjusted treatment difference (95% CI)[a]

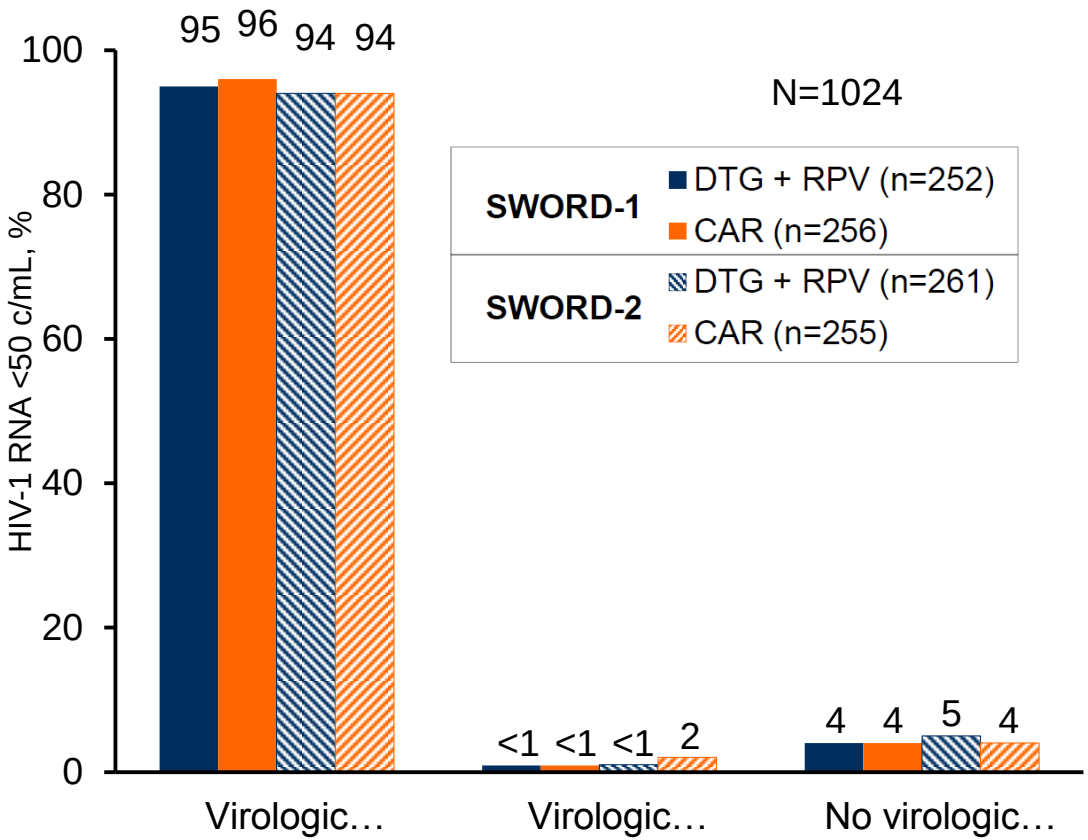


DTG + RPV is **non-inferior** to CAR with respect to snapshot in the ITT-E population (<50 c/mL) at Week 48

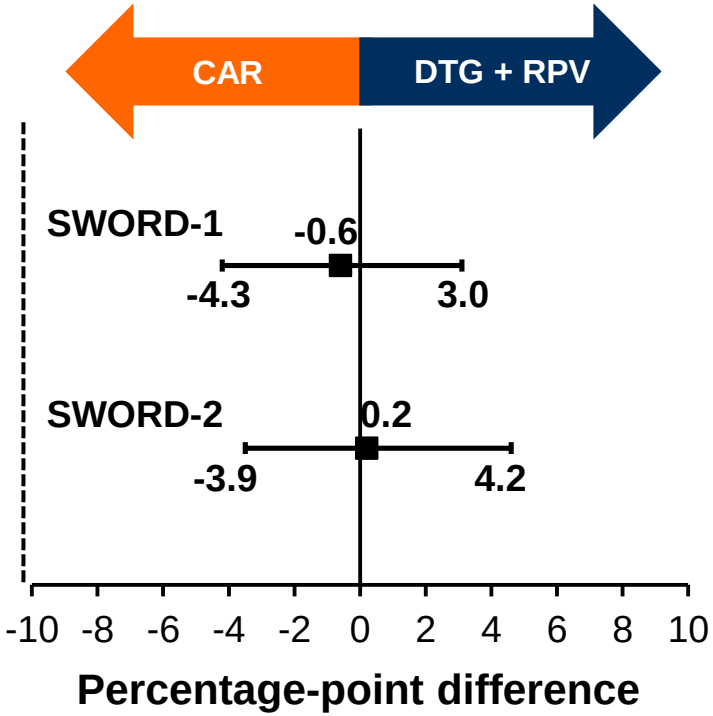
Llibre JM. CROI 2017; Seattle, WA. #44LB. The Lancet 2018;391(10123): 839–849.

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

Virologic outcomes



Adjusted treatment differences (95% CI)[a]



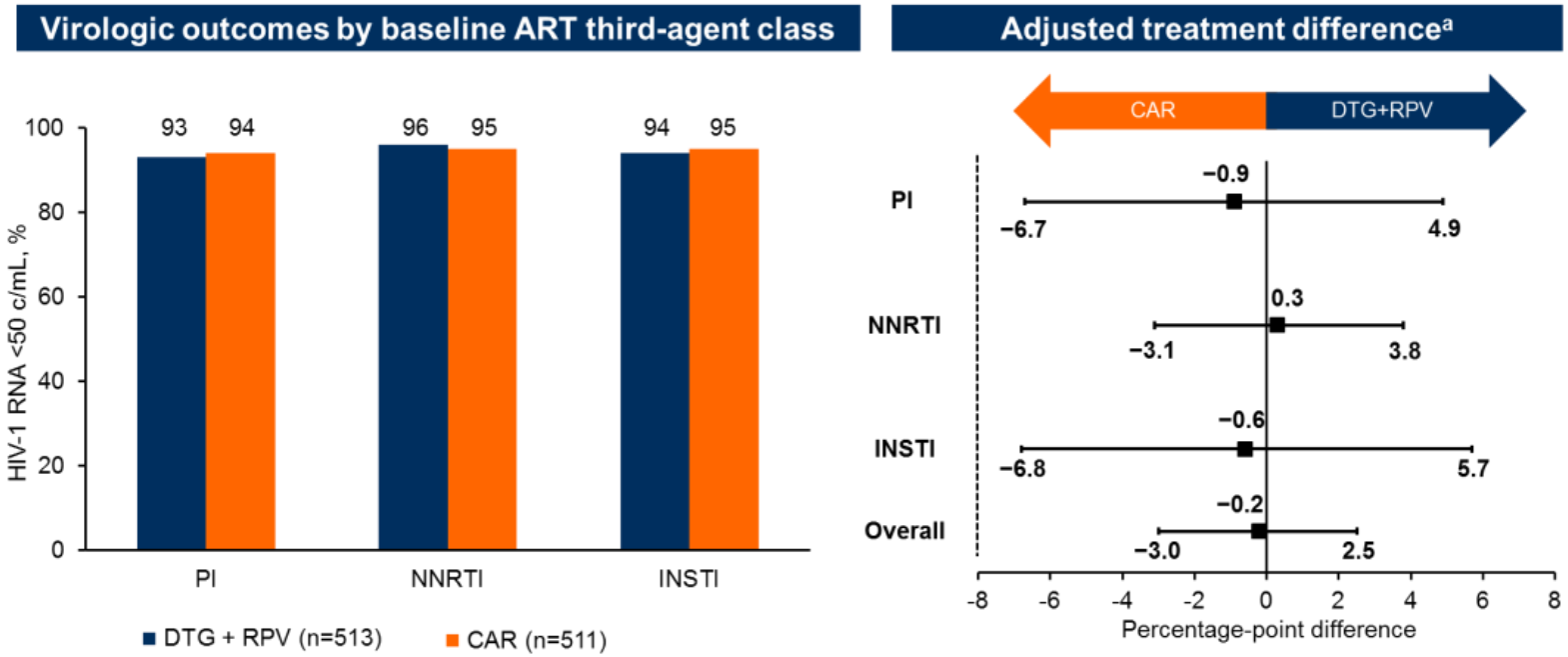
DTG + RPV is **non-inferior** to CAR with respect to snapshot in the ITT-E population (<50 c/mL) at Week 48 in both studies

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

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

Orkin C et al. EACS 2017, Milan, Italy. BPD1/5

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)

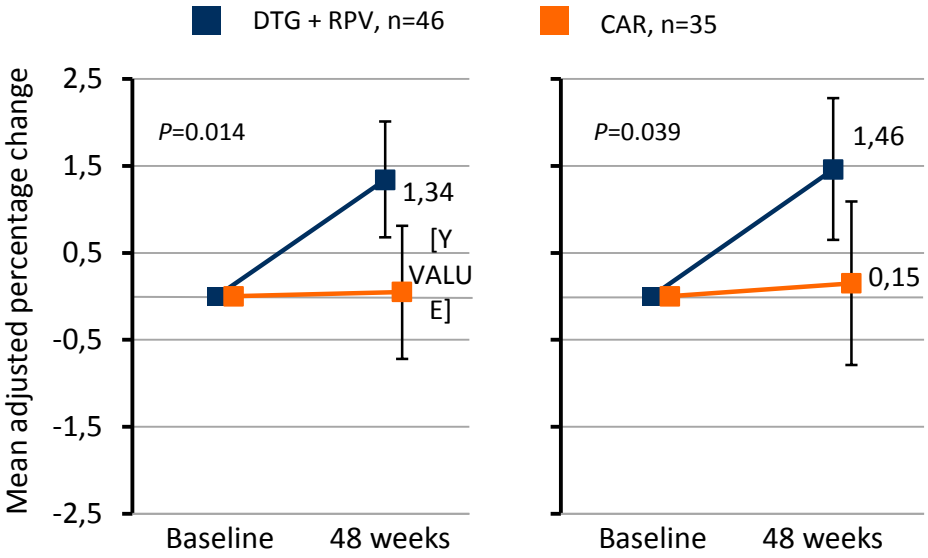
[1] Two deaths in the study, both unrelated to study drug. DTG+RPV Kaposi's Sarcoma (N=1), CAR Lung cancer (N=1)

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

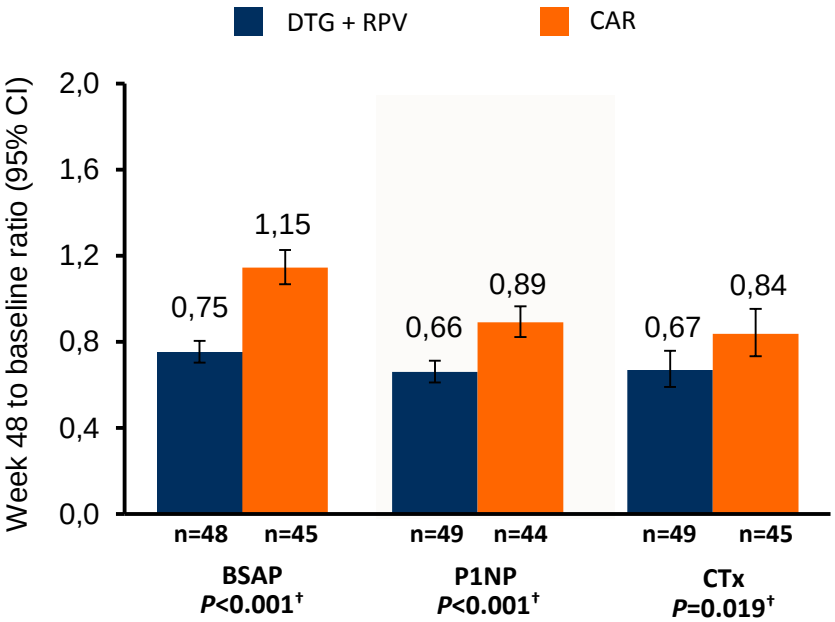
Llibre JM. CROI 2017; Seattle, WA. #44LB. The Lancet 2018;391(10123): 839–849.

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.

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

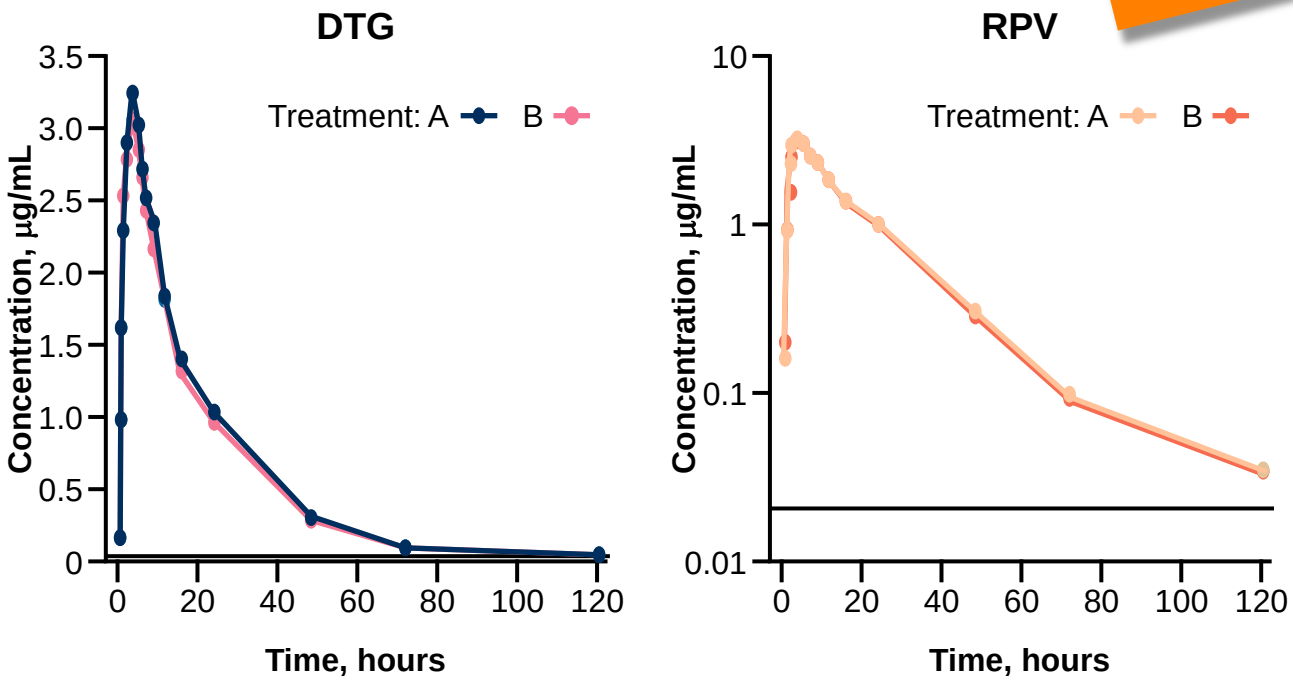
Bioequivalence Study: DTG/RPV FDC vs DTG + RPV

Median DTG and RPV Plasma Concentration-Time Plot

Ready for use

Treatment A: FDC DTG/RPV 50 mg/25 mg;

Treatment B: DTG 50 mg plus RPV 25 mg



- Open-label, crossover study. N=113 healthy subjects.

FDA approved, 21 Nov 2017. Juluca®. Smallest ever FDC single tablet**.**
EMA CHMP positive opinion 23 March 2018.

Mehta R, et al. Intl Workshop Clin Pharmacol 2017. Poster 25

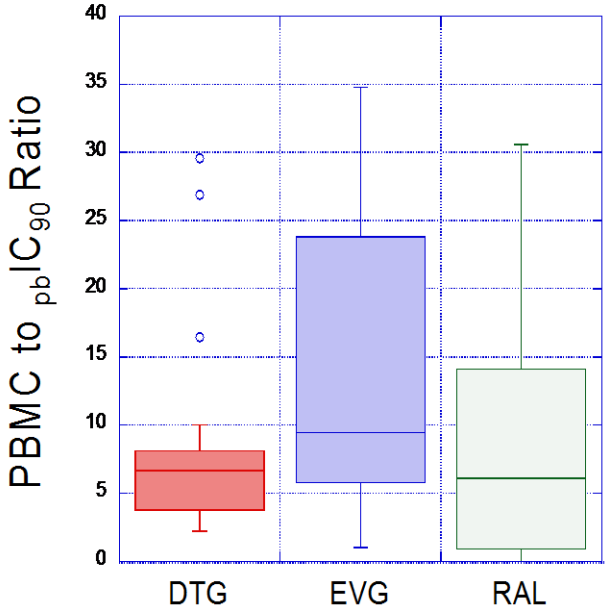
MONET 144 weeks, cohort DRV/m.
No difference in inflammation or HIV reservoir mono vs triple.

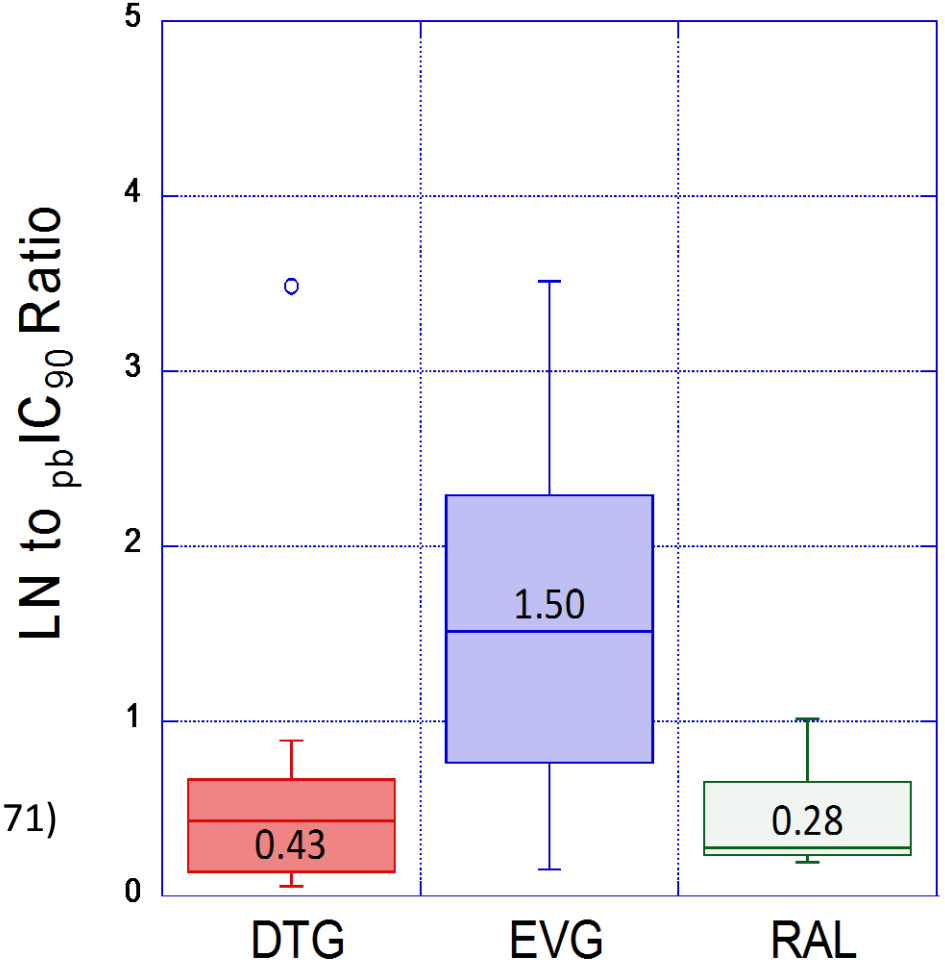
- **Mean HIV DNA levels** correlated with HIV RNA levels: mean HIV DNA was:
  - **2.48 $\log_{10}$** copies for samples with HIV RNA **<5** copies/mL
  - **2.72 $\log_{10}$** copies for samples with HIV RNA **5-50** copies/mL
  - **2.82 $\log_{10}$** copies for samples with HIV RNA **>50** copies/mL

- Patients with **HIV RNA consistently below 50 copies/mL** during the trial had **lower mean HIV DNA levels** (2.38 $\log_{10}$ copies in DRV/r arm, 2.51 $\log_{10}$ copies in the triple arm) compared with patients who had at least one HIV RNA >50 during the trial (2.75 $\log_{10}$ copies in DRV/r arm, 2.84 $\log_{10}$ copies in DRV/r + 2NRTI arm).
- **No differences in IL-6, D-dimer, fibrinogen or hs-CRP** between arms.
- **No difference in prevalence of residual viremia** (1 copy/mL, nested PCR), or with LPV/r (<3 c/mL) if VL<50 c/mL (OK Study*).

JR Arribas. JAC 2012. M Estebanez. BMC Infectious Diseases 2014, 14:379. AM Geretti. 10th Eur Meeting on HIV & Hep Treat Strat & Drug Res 2012. #O-06. * JE Mckinnon. AIDS 2006, 20:2331–2335.

Inhibitory Quotients for INSTIs in LN MNCs



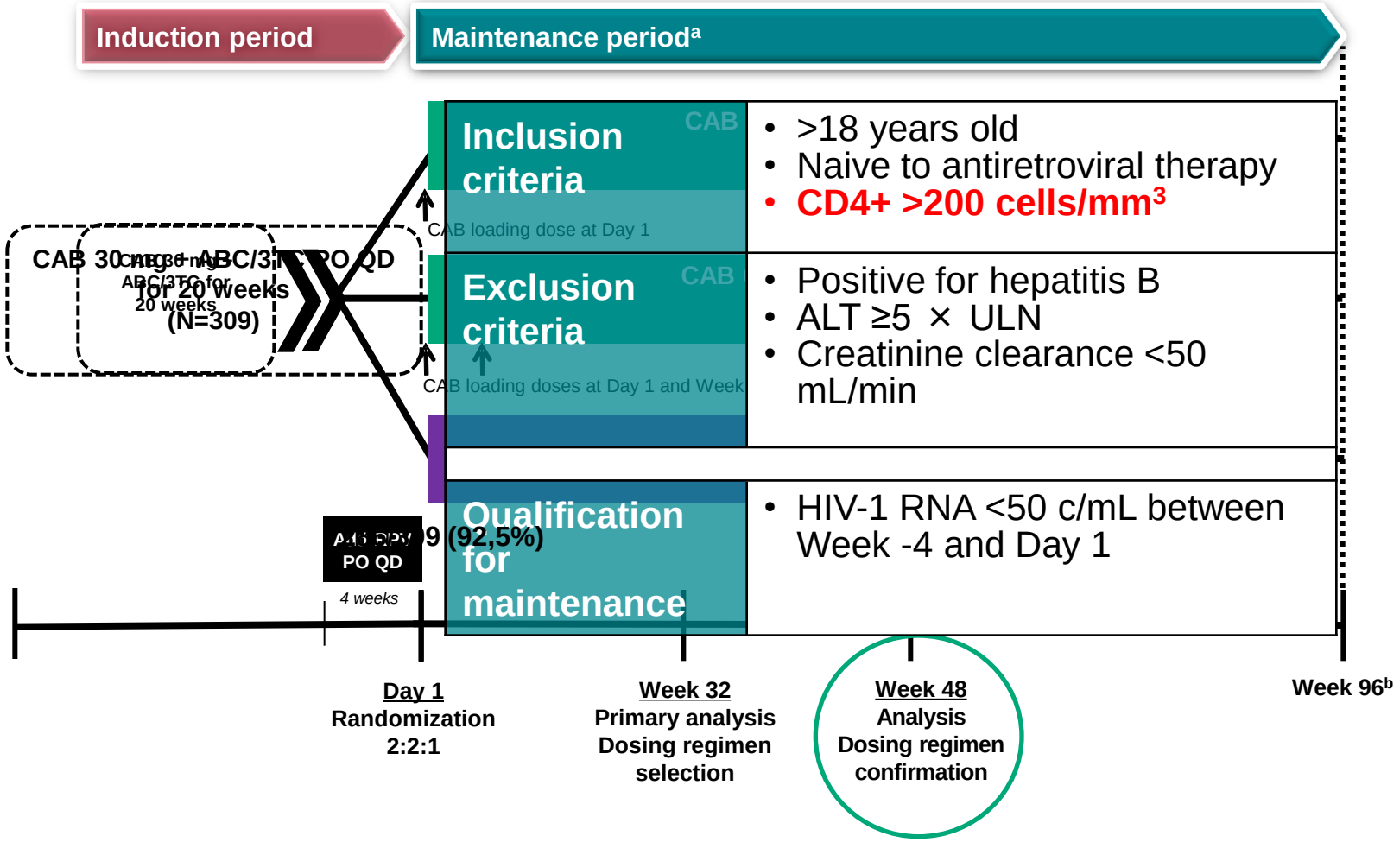


44 HIV subjects. N=11 n=17 n=6

IQ in rectal MNCs : DTG 0.62 (EVG 14.4, RAL 2.71)
All 3 INSTIs have IQ>6 in plasma PBMCs.

CV Fletcher. CROI 20187; Boston, MA. #27.

LATTE-2 Study Design (Phase 2)



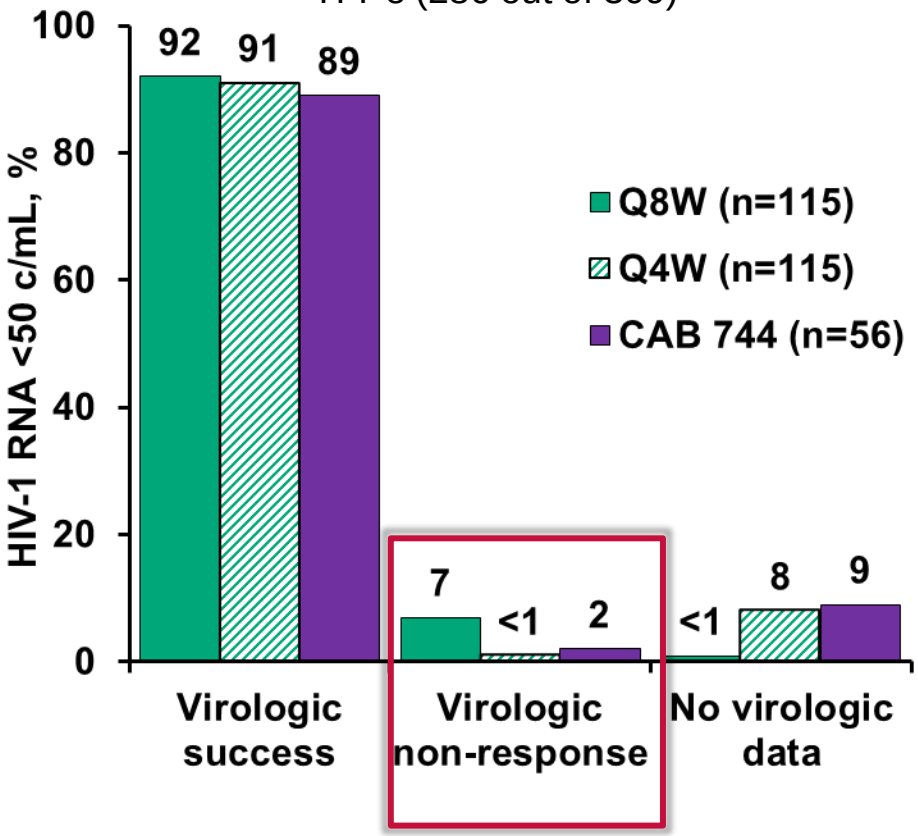
ABC/3TC, abacavir/lamivudine; ALT, alanine aminotransferase; IM, intramuscular; PO, orally; QD, once daily; Q4W, every 4 weeks; Q8W, every 8 weeks; ULN, upper limit of normal. [a]Subjects who withdrew after at least 1 IM dose entered the long-term follow-up period. [b]Subjects can elect to enter Q4W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

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

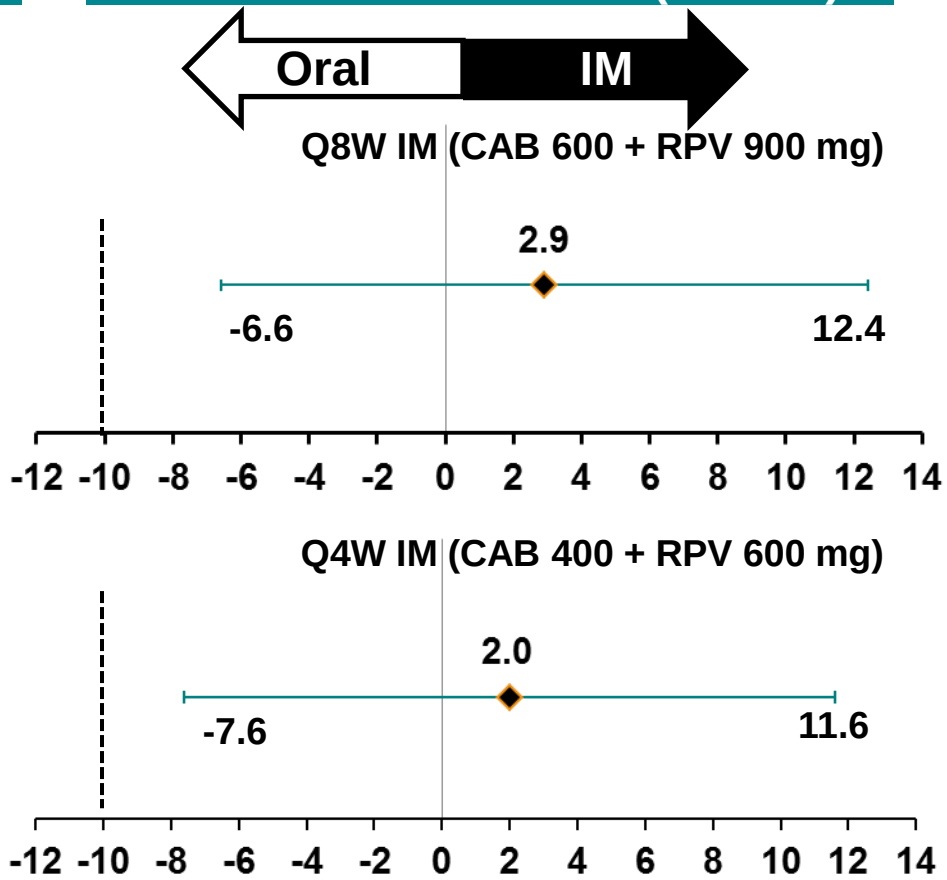
LATTE 2. HIV-1 RNA <50 c/mL at Week 48 ITT-ME (Snapshot)

Virologic outcomes

ITT-e (286 out of 309)



Treatment differences (95% CI)

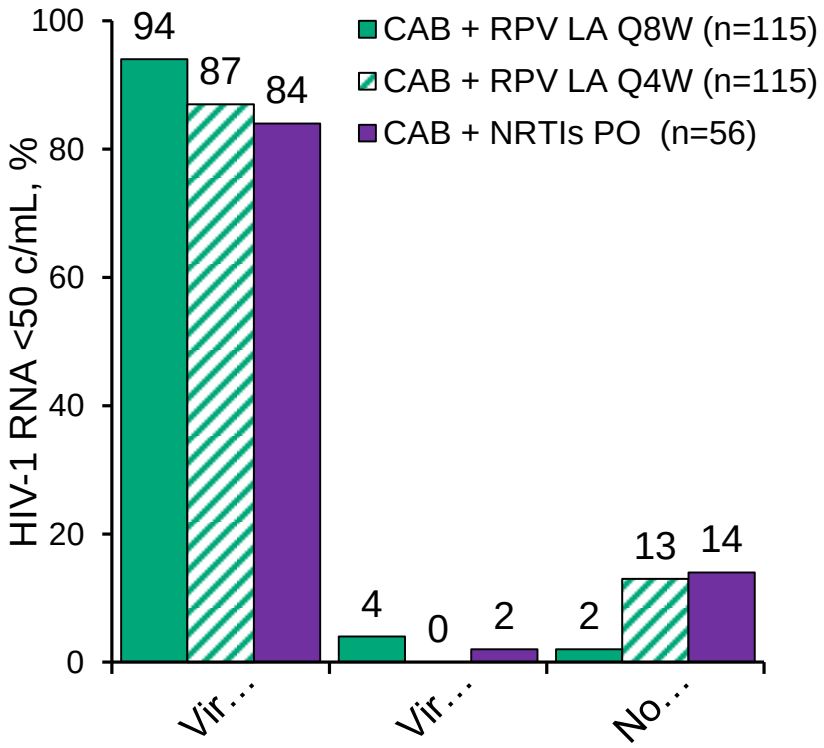


1/2 VF Q8W: NNRTI—**K103N, E138G, and K238T** (FC RPV=3.3; ETR=1.9); INI—**Q148R** (FC CAB=5.1; DTG=1.38)

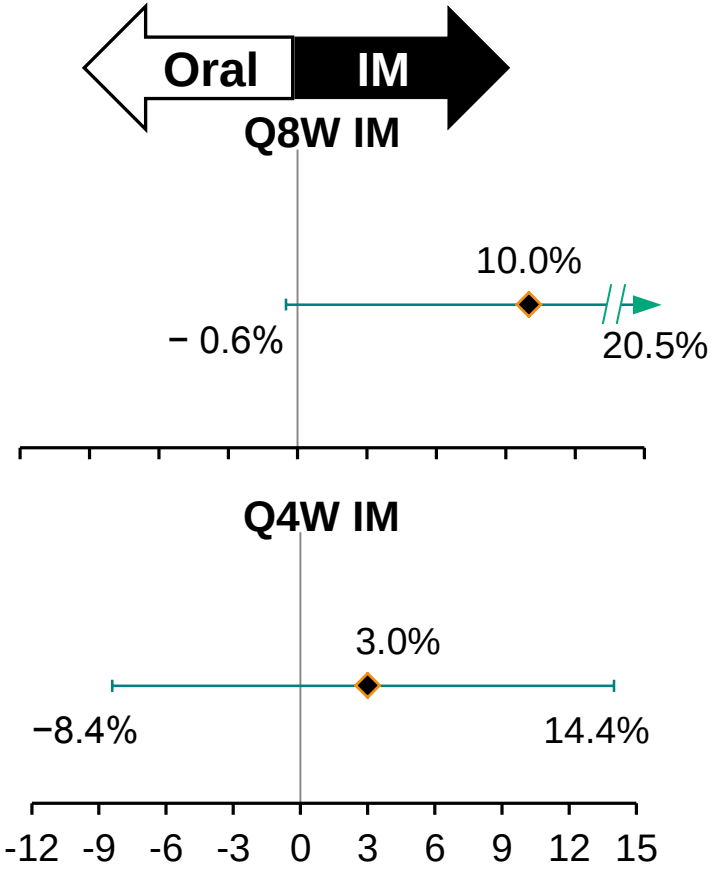
LATTE 2. Comparable Response Across Arms

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

Virologic outcomes



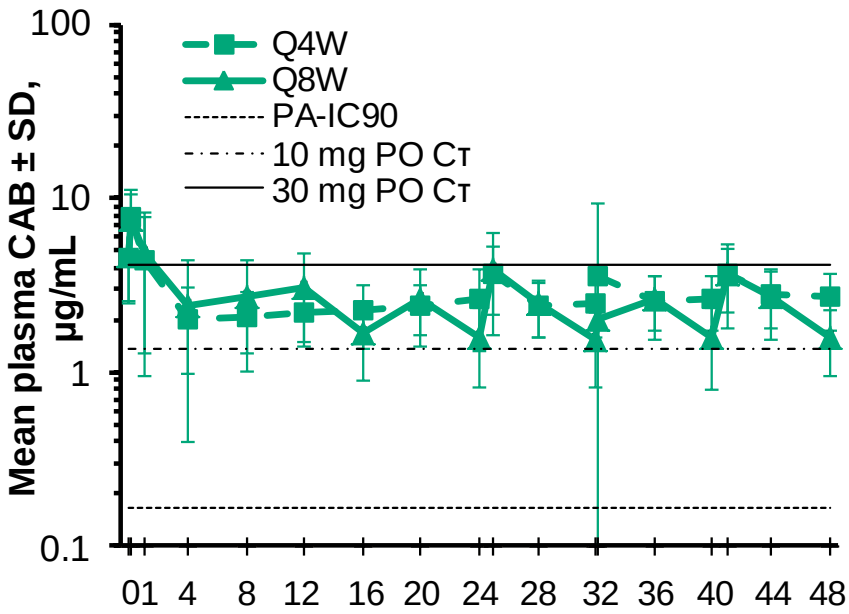
Treatment differences (95% CI)

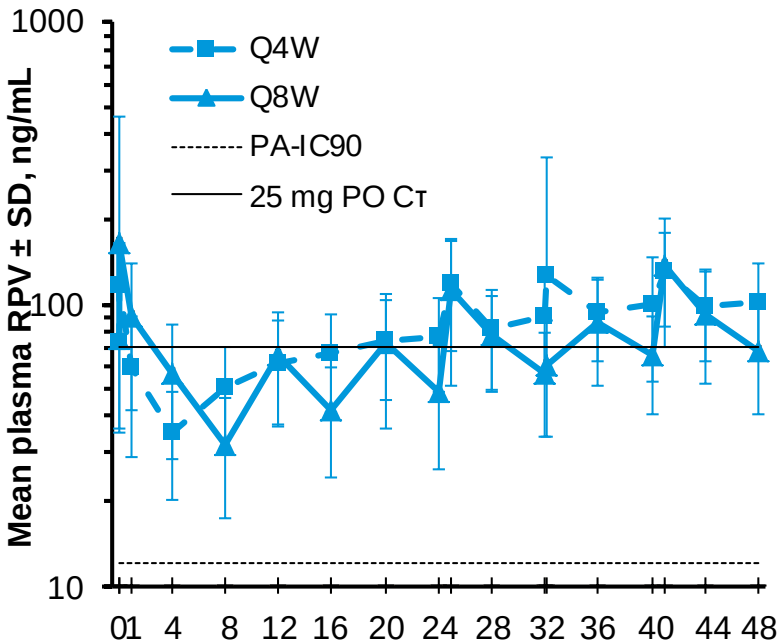


ITT-ME, intent-to-treat maintenance exposed; LA, long acting; Q4W, every 4 weeks; Q8W, every 8 weeks.

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.

- **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** is a promising regimen in late-stage development.
- **LA-CAB + LA-RPV IM** every 1 or 2 months is a promising regimen in late-stage development.
- Other DRV/b-based strategies with preliminary data (DRV/r + 3TC in naives, DRV/c + DTG, DRV/c + RPV) not ready for clinical use yet.

- **We must be <u>very demanding</u> and meet ethical and evidence-based standards with less than 3-DR**.

Stay tuned!


DANGER !
Please do not
walk beyond this
point without an
escort