LE MALATTIE INFETTIVE OGGI
COMO 12 Settembre 2019
Auditorium Ospedale Sant'Anna – ASST Lariana

Terapia antiretrovirale: regimi a due farmaci

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Disclosures

Diego Ripamonti has received advisory fees, speaker fees, travel and education from:

- *ViiV*
- *Janssen*
- *Gilead*
- *Merck*

Dual vs triple regimens

Dual regimen	Study	Design	Baseline regimen	Number of pts	Non inferiority	F-up weeks	Emergent resistance
LOP/r + 3TC [1]	OLE	switch	bPI §	1051	yes	48	1
ATV/r + 3TC [2]	SALT					96	1
ATV/r + 3TC [3]	ATLAS-M					96	---
DRV/r + 3TC [4]	DUAL					48	1
DTG + RPV [5]	SWORD 1-2	switch	any	1024	yes	48-148	….
DTG + 3TC [6]	GEMINI 1-2	naive	-	1433	yes	**96**	0
DTG + 3TC [7]	TANGO	switch	any	741	yes	**48**	0

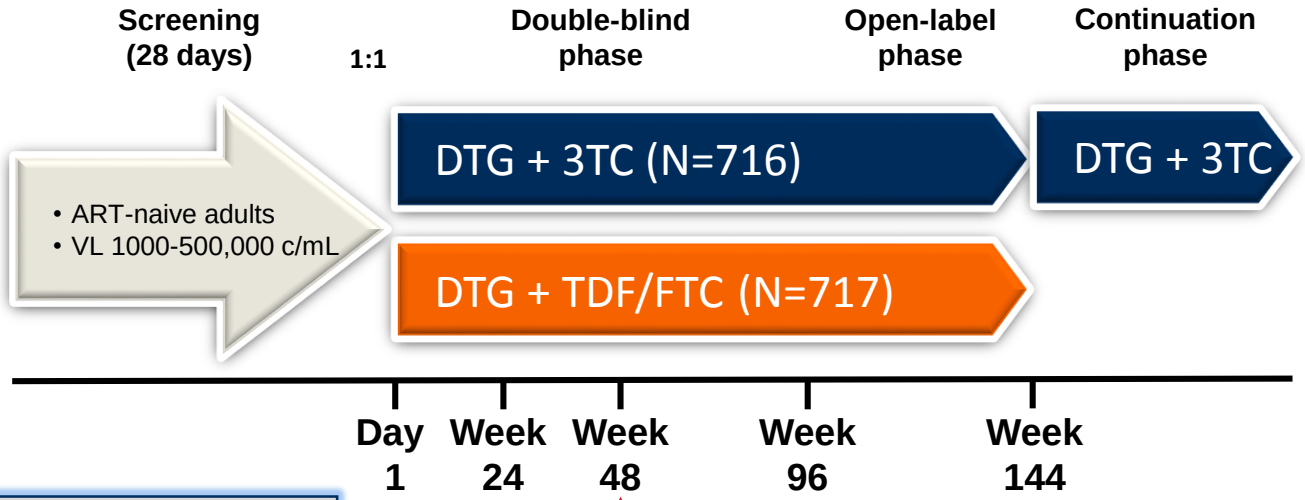
§ = 33% from NNRTI-based rx, * ABC/3TC/DTG for first 20 weeks LA: Long Acting

1. Arribas JR et al. Lancet ID 2015;
2. Perez-Molina JA et al. Lancet ID 2015;
3. Di Giambenedetto S et al. JAC 2017;
4. Pulido F. et al. CID 2017;65:2112-2118;
5. Llibre JM et al. Lancet 2018;391:839-849;
6. Cahn P et al. IAS 2019; Abs WEAB0404LB
7. van Wyk et al. IAS 2019; Abs. WEAB0403LB
8. Swindell S et al. CROI 2019, Abs 1475
9. Orkin C et al. CROI 2019, Abs 3947

GEMINI 1 & 2

GEMINI 1 -2, phase III study design

Identically designed, randomized, double-blind, parallel-group, multicenter, non-inferiority 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 vs >100,000 c/mL) and CD4+ cell count (≤200 vs >200 cells/mm^3).

[a]–10% non-inferiority margin for individual studies.

Cahn P et al. Lancet 2018; November

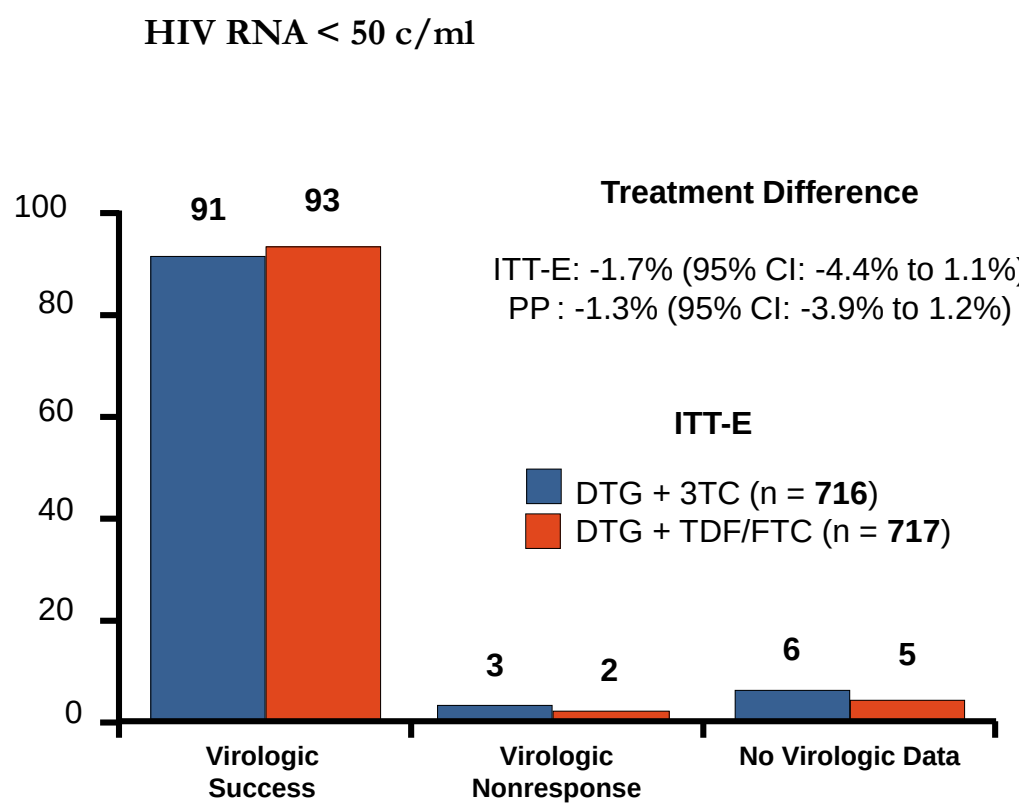
Demographic and Baseline Characteristics for the Pooled GEMINI-1 and -2 Population

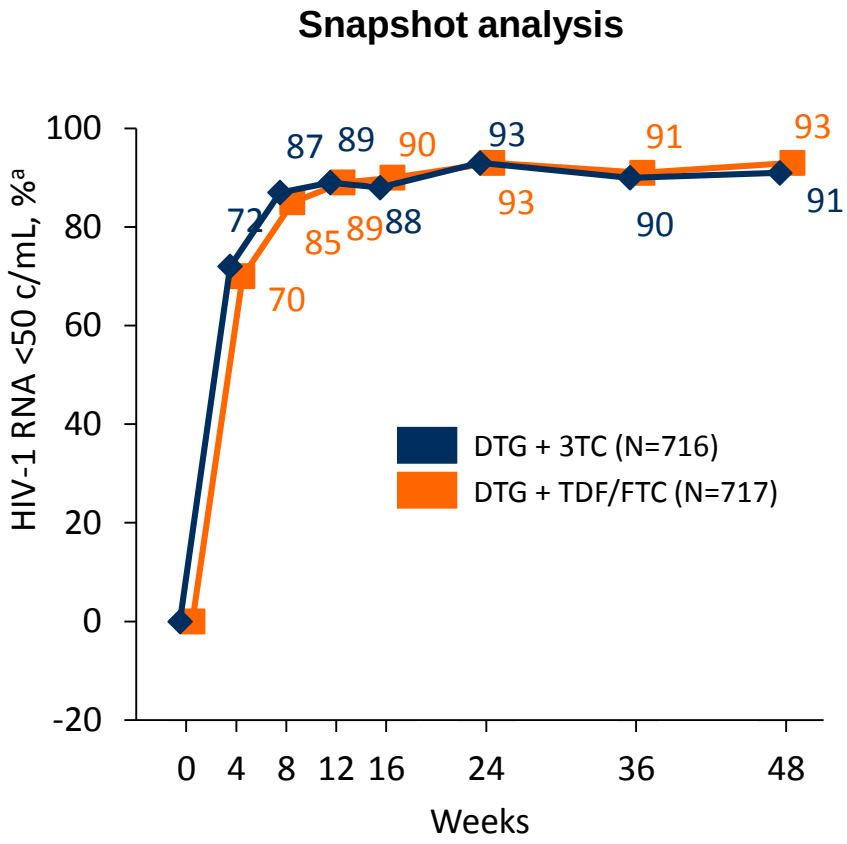
Characteristic	DTG + 3TC (N=716)	DTG + TDF/FTC (N=717)
Age, median (range), y	32.0 (18-72)	33.0 (18-70)
≥50 y, n (%)	65 (9)	80 (11)
Female, n (%)	113 (16)	98 (14)
Race, n (%)		
White	480 (67)	497 (69)
African American/African heritage	99 (14)	76 (11)
Asian	71 (10)	72 (10)
Other	66 (9)	72 (10)
Ethnicity, n (%)		
Hispanic or Latino	215 (30)	232 (32)
Not Hispanic or Latino	501 (70)	485 (68)
HIV-1 RNA, median (range), log_{10} c/mL	4.43 (1.59-6.27)	4.46 (2.11-6.37)
≤100,000	576 (80)	564 (79)
>100,000	140 (**20**)	153 (**21**)
>250,000	51 (7)	46 (6)
>400,000	18 (3)	24 (3)
>500,000[a]	13 (2)	15 (2)
CD4+ cell count, median (range), cells/mm³	427.0 (19-1399)	438.0 (19-1497)
≤200	63 (**9**)	55 (**8**)
>200	653 (91)	662 (92)

[a]Participants were required to have HIV-1 RNA ≤500,000 c/mL at screening. Other than 1 participant enrolled without meeting study entry criteria, these participants had an observed increase in HIV-1 RNA between screening and baseline.

Cahn et al. *Lancet.* 2018 [Epub ahead of print].

Gemini 1- 2: naive patients, 48-week results



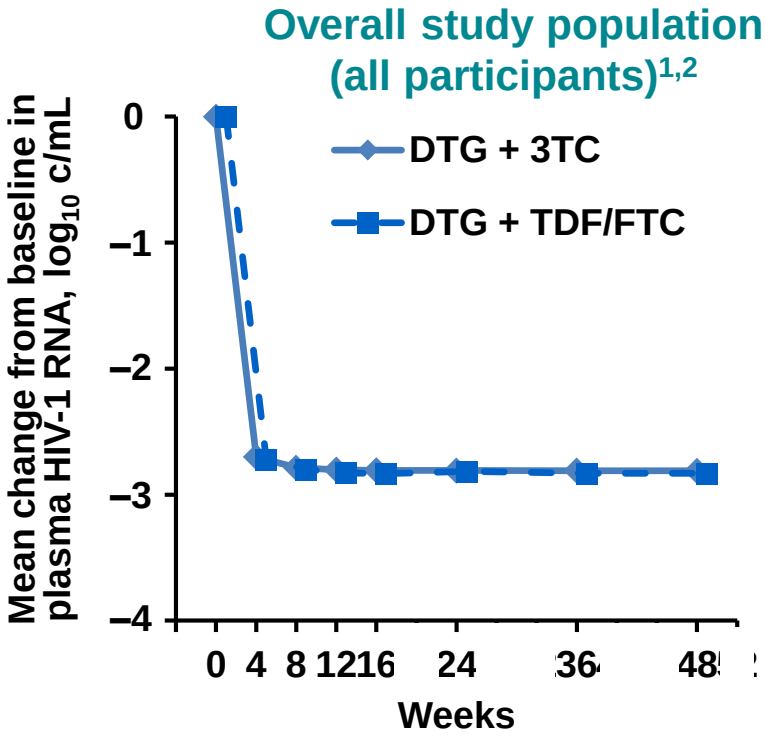


No treatment-emergent mutations

Cahn P et al. Lancet 2018; November

Eron et al. HIV DART and Emerging Viruses 2018; Miami, FL. Oral Presentation #7.

GEMINI-1 and -2: Rapid Viral Load Decline



DTG + 3TC, n	716	708	704	686	681	688	674	664
DTG + TDF/FTC, n	717	706	699	699	688	688	681	675

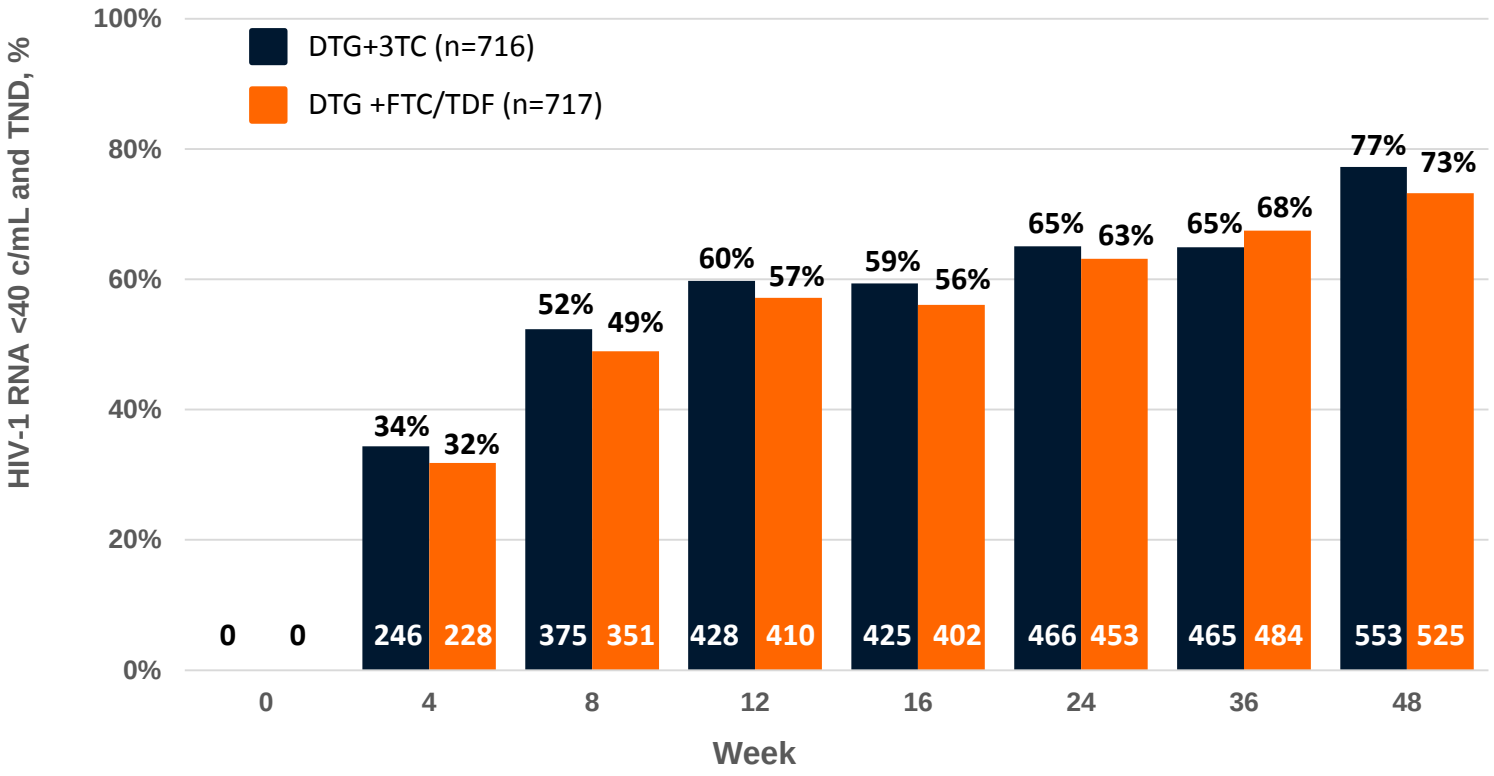
Magnitude and speed of viral load decline were similar in the DTG + 3TC and DTG + TDF/FTC arms, irrespective of baseline viral load[2]

- Pooled ITT-E population

Adapted from: **1.** Cahn P, et al. Lancet 2019;393:143–55

2. Eron J, et al. HIV DART and Emerging Viruses 2018. Oral Presentation 7

Target Non Detected (TND) for subjects with HIV RNA < 40 copies/ml by study arm

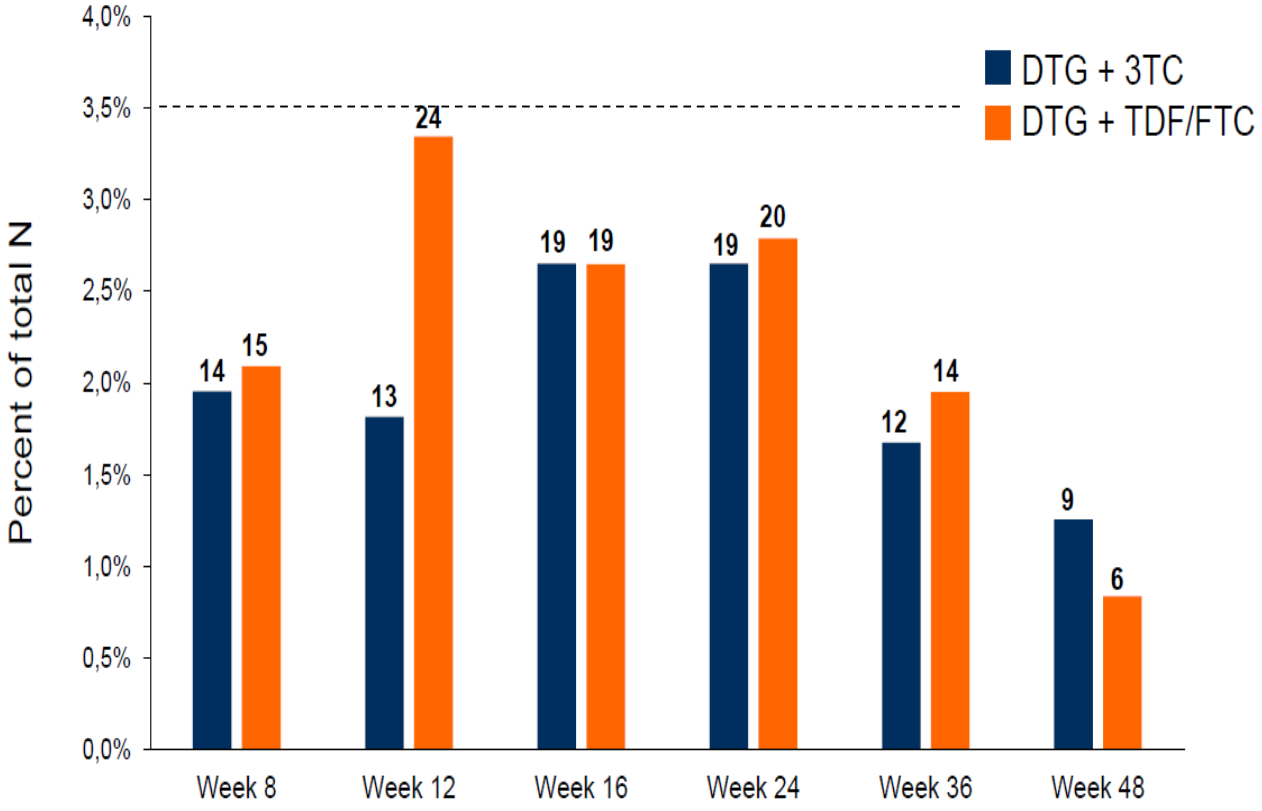


At week 48 **similar proportion** of subjects had snapshot TND in the 2DR and 3DR arms (77% [553/716] vs 73% [525/717], adjusted difference 3.8%, 95% CI -0.6%, 8.2%)

Underwood M et al. CROI 2019; Poster 490

Blip Frequencies and Number by Visit

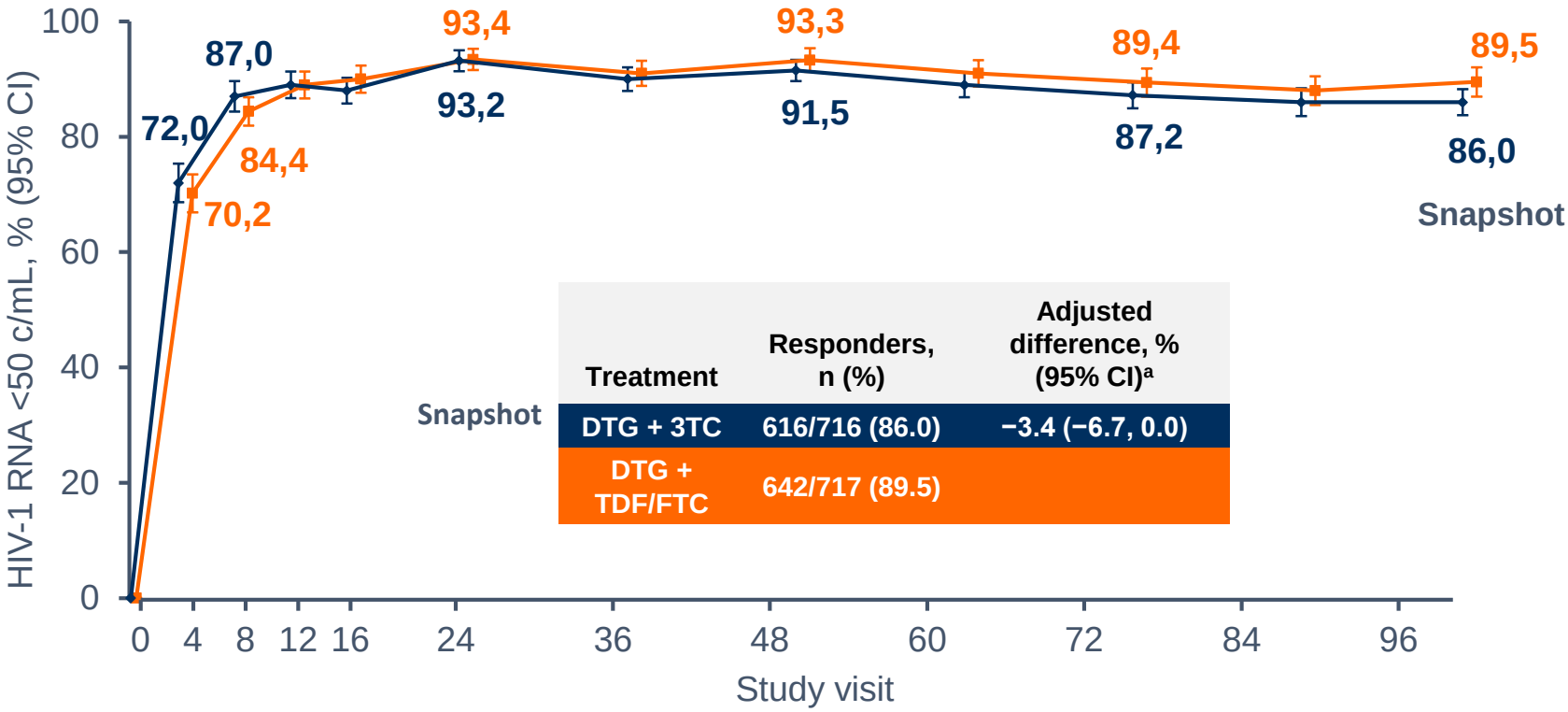
- Similar 'blip' frequencies were seen across arms



Bold numbers on chart are # of blips at given week visits. Note that individual subjects in Category 1a can have had more than one blip.

Underwood et al. IAS 2019; Mexico City, Mexico. Poster MOPEB231.

DTG + 3TC is non-inferior to DTG + TDF/FTC in snapshot HIV-1 RNA <50 c/ml at week 96



Snapshot	Treatment	Responders, n (%)	Adjusted difference, % (95% CI)[a]
	DTG + 3TC	616/716 (86.0)	−3.4 (−6.7, 0.0)
	DTG + TDF/FTC	642/717 (89.5)	

Non-inferiority criteria were met for GEMINI-1, GEMINI-2 and the pooled analysis[b]

[a]Based on Cochran-Mantel-Haenszel stratified analysis adjusting for the following baseline stratification factors: plasma HIV-1 RNA (≤100,000 vs >100,000 c/mL), CD4+ cell count (≤200 vs >200 cells/mm^3), and study (GEMINI-1 vs GEMINI-2). The upper limit of the 95% CI for the pooled analysis was 0.0007%.

[b]In **GEMINI-1**, HIV-1 RNA <50 c/mL (95% CI) was achieved in 300/356 participants (84.3% [80.5-88.1]) in the DTG + 3TC group and 320/358 (89.4% [86.2-92.6]) in the DTG + TDF/FTC group (adjusted treatment difference [95% CI], −4.9% [−9.8, 0.03]). In **GEMINI-2,** the corresponding values were 316/360 (87.8% [84.4-91.2]) and 322/359 (89.7% [86.5-92.8]), respectively (adjusted treatment difference [95% CI], −1.8% [−6.4, 2.7]).

Adapted from Cahn et al. IAS 2019; Mexico City, Mexico. Slides WEAB0404LB.

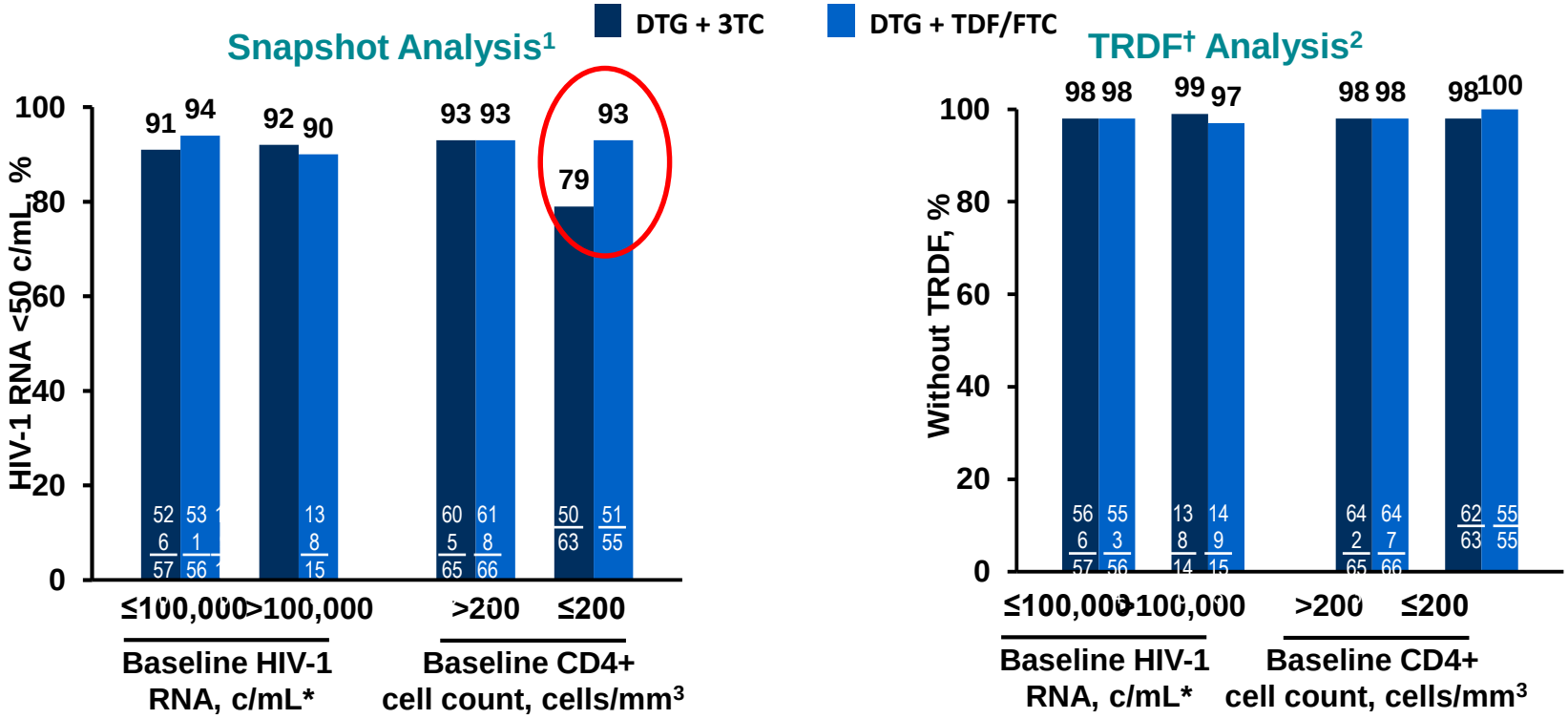
No treatment-emergent resistance was observed among participants who met Confirmed Virologic Withdrawal criteria

		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)**
Week 48	CVW	4 (1.1)	2 (0.6)	2 (0.6)	2 (0.6)	6 (0.8)	4 (0.6)
Week 96	CVW	5 (1.4)	4 (1.1)[a]	6 (1.7)	3 (0.8)	11 (1.5)	7 (1.0)[a]
	Treatment-emergent resistance	**0**	**0**	**0**	**0**	**0**	**0**

[a]One participant met the criteria for CVW at Week 12 but was not reported at the Week 48 analysis because of a laboratory reporting error identified after the Week 48 analysis.

Adapted from Cahn et al. IAS 2019; Mexico City, Mexico. Slides WEAB0404LB.

GEMINI-1 and -2:
Efficacy at Week 48 by Baseline HIV-1 RNA and CD4+ Cell Count



Response rates in subjects with baseline HIV-1 RNA >100,000 c/mL or CD4+ cell count ≤200 cells/mm³ were high and similar between arms in the TRDF analysis[2]

*2% of subjects in each arm had baseline HIV-1 RNA ≥500,000 c/mL after having <500,000 c/mL at screening[1]; †TRDF population accounts for CVW, withdrawal due to lack of efficacy, withdrawal due to treatment-related AE, and subjects who met protocol-defined stopping criteria.[2] Please see slide notes for reasons for Snapshot non-response in patients with CD4+ T cell count <200 cells/mm³
TB, tuberculosis; TRDF, treatment-related discontinuation = failure

1. Cahn P, et al. Lancet 2019;393:143–55
2. Cahn P, et al. IAS 2018. TUAB0106LB

In patients with a CD4 count ≤200, most reasons for Snapshot non response were unrelated to efficacy or treatment

- GEMINI-1 and -2: Among patients with ≤200 CD4+ T cells/mm^3 at baseline, 13 in the DTG + 3TC group and 4 in the DTG + TDF/FTC group had Snapshot non-response at Week 48

Reason for Snapshot non-response, n (%)	DTG + 3TC (n=63)	DTG + TDF/FTC (n=55)
HIV-1 RNA ≥50 c/mL*	3 (5)	1 (2)
Discontinued due to non-treatment-related AE	2 (3)	0
Protocol violation	2 (3)	0
Lost to follow up	2 (3)	1 (2)
CVW	1 (2)	0
Withdrew consent	1 (2)	1 (2)
Withdrew to start HCV treatment	1 (2)	0
Unplanned change in ART	1 (2)	0
Investigator discretion	0	1 (2)

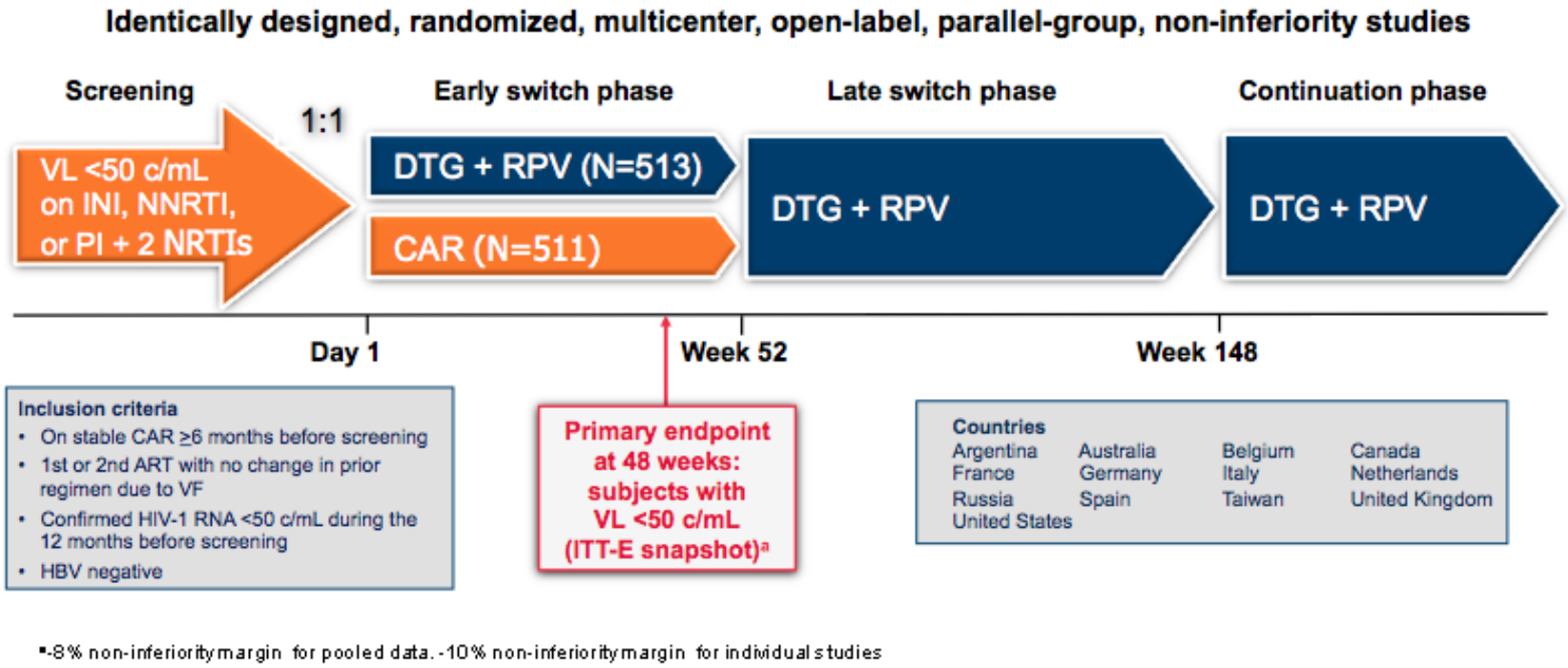
In patients with low baseline CD4 count, there were more Snapshot failures with DTG + 3TC versus DTG + TDF/FTC but most were unrelated to efficacy or treatment failure

*Two of three participants in the DTG + 3TC group and one participant in the DTG + TDF/3TC group resuppressed

Adapted from: Cahn P, et al. Lancet 2019;393:143–55

SWORD 1 & 2

SWORD 1, 2 studies



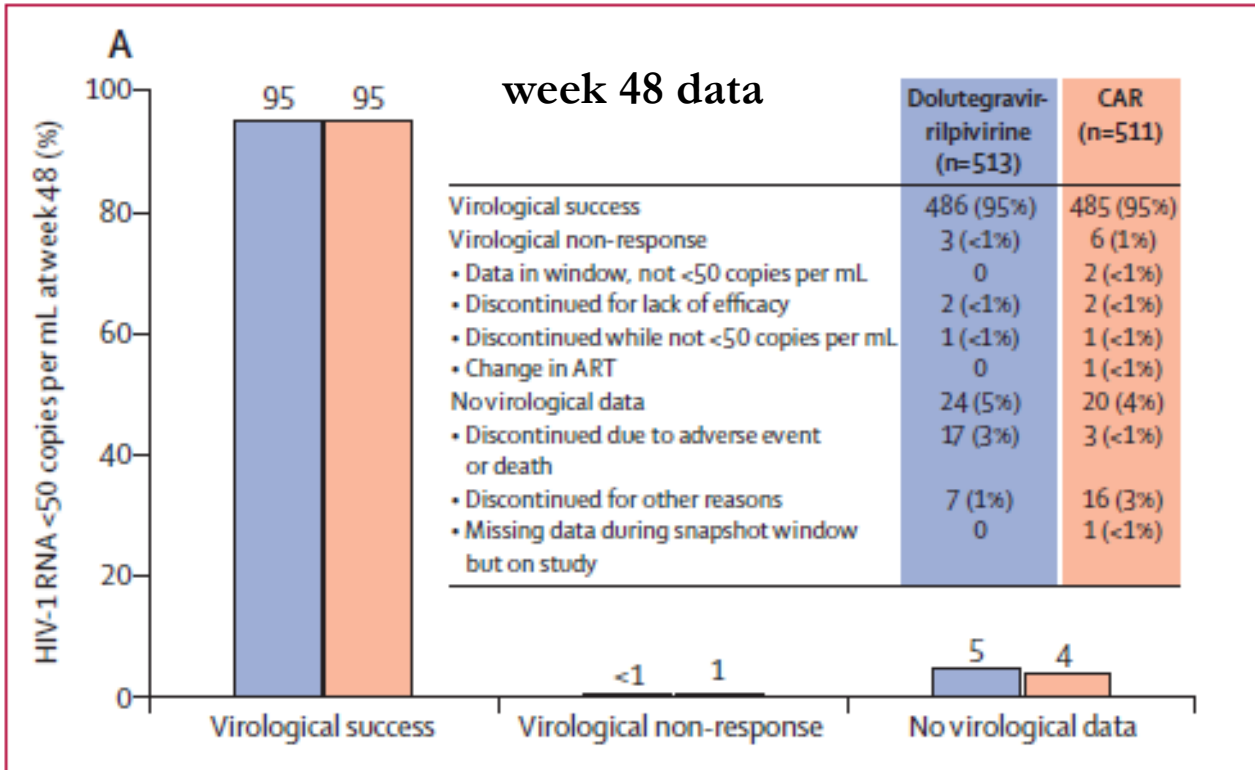
a-8% non-inferiority margin for pooled data. -10% non-inferiority margin for individual studies

Llibre JM, et al. Lancet. 2018;391:839-849

SWORD 1, 2 studies

HAART at baseline

from PI:	26%
from NNRTI:	54%
from II:	20%



week 48 data

	Dolutegravir-rilpivirine (n=513)	CAR (n=511)
Virological success	486 (95%)	485 (95%)
Virological non-response	3 (<1%)	6 (1%)
• Data in window, not <50 copies per mL	0	2 (<1%)
• Discontinued for lack of efficacy	2 (<1%)	2 (<1%)
• Discontinued while not <50 copies per mL	1 (<1%)	1 (<1%)
• Change in ART	0	1 (<1%)
No virological data	24 (5%)	20 (4%)
• Discontinued due to adverse event or death	17 (3%)	3 (<1%)
• Discontinued for other reasons	7 (1%)	16 (3%)
• Missing data during snapshot window but on study	0	1 (<1%)

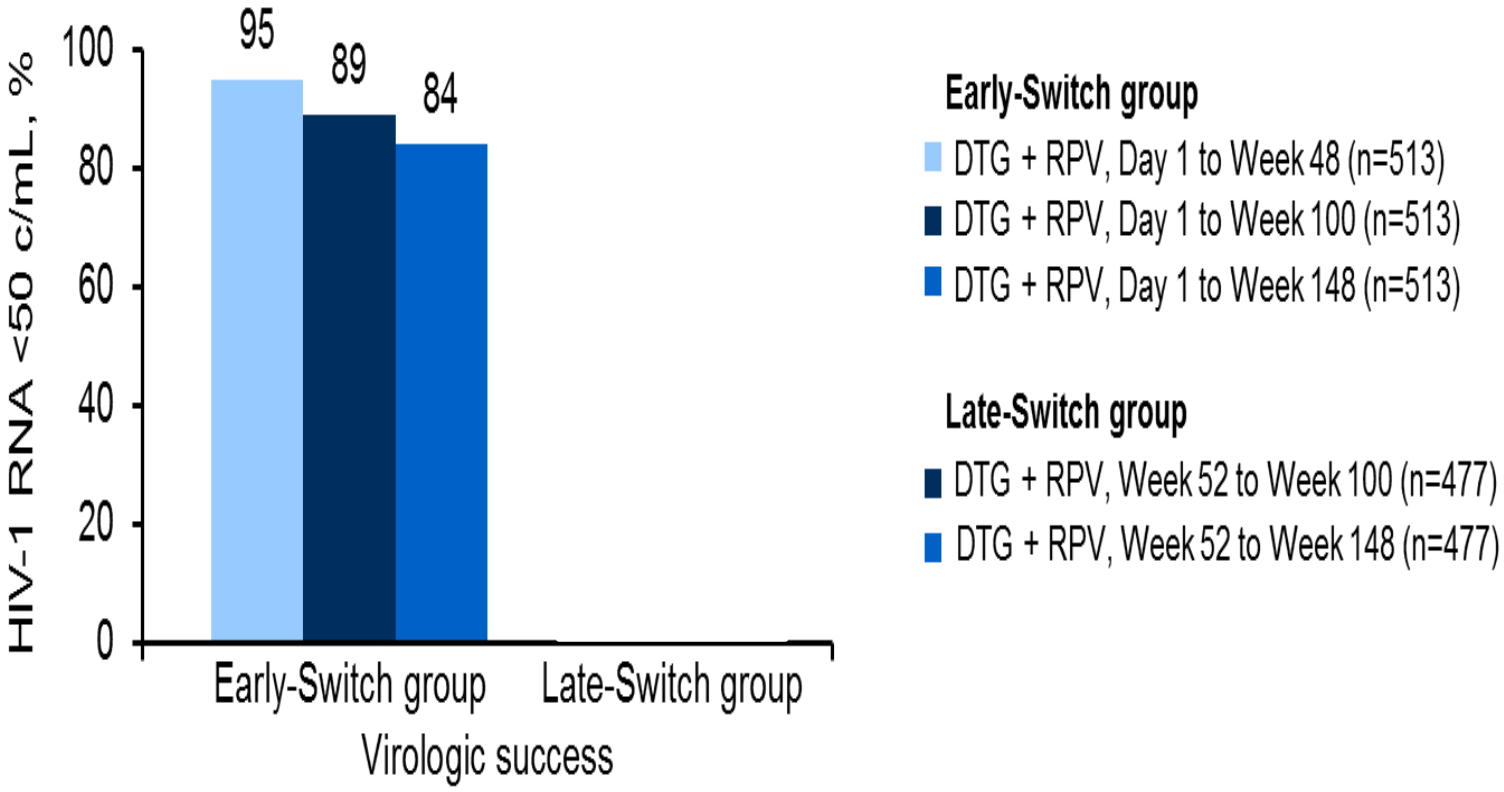
10/990 (1%) confirmed virologic withdrawals through week 100 (**NNRTI resistance** in 3/10, all from early switch arm).

No changes in **lipid levels** (total cholesterol, LDL-C, HDL-C, triglycerides, tot cholesterol:HDL-C ratio) or atherogenesis and **inflammation** biomarkers at week 100 vs baseline in either group.

Early switch group maintained improvements in markers of **renal tubular** function (urine RBP/creatinine ratio, urine β2-M/creatinine ratio) from baseline to wk 48 and wk 100.

Aboud M et al. AIDS 2018. Abs THPEB047. Llibre JM et al. Lancet. 2018;391:839-849.

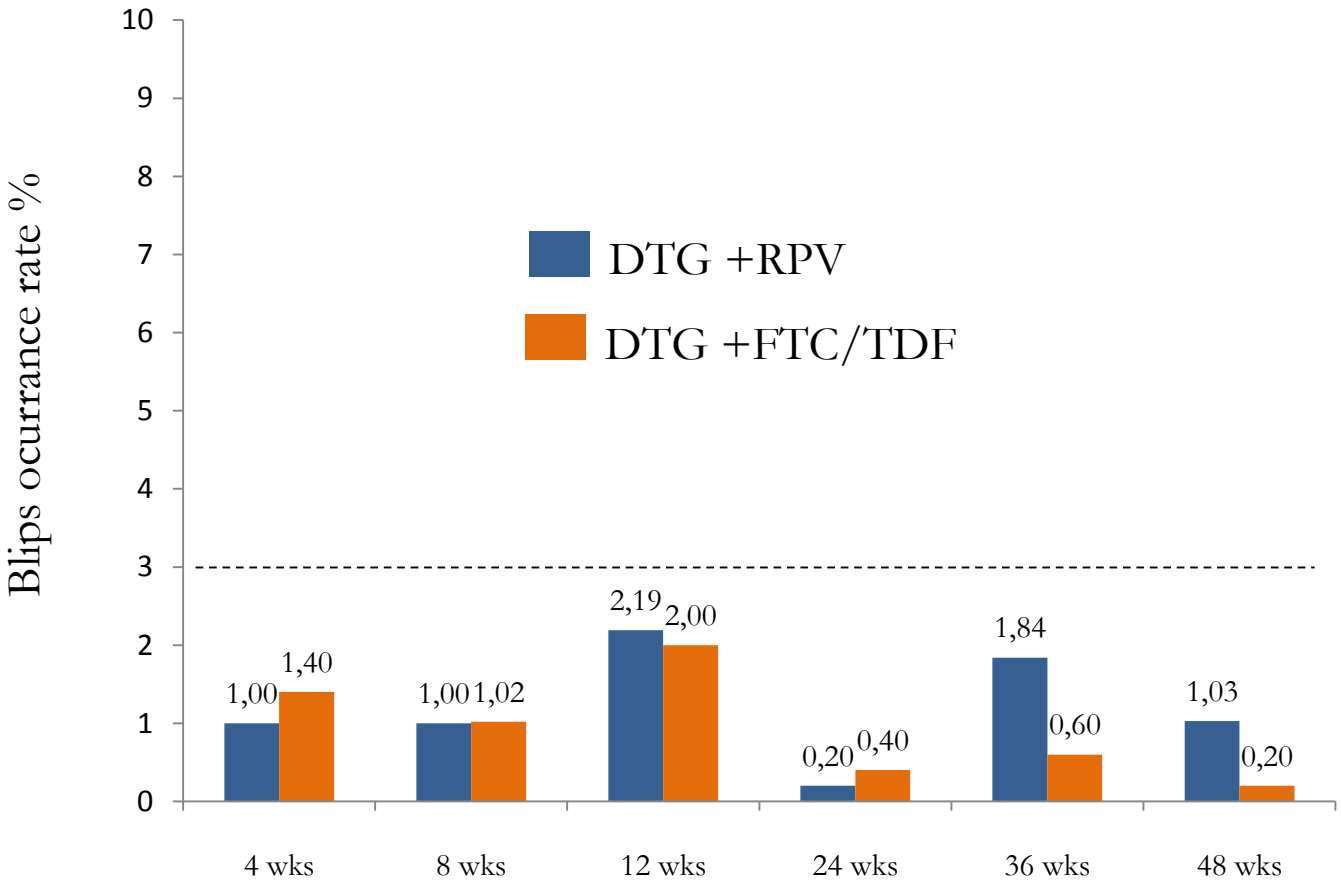
SWORD 1&2: 149 weeks



Adapted from: van Wyk et al. BHIVA 2019; Bournemouth, UK. Poster P008.

Viral blips in SWORD 1-2 studies

Rates of blips (HIV RNA >50 c/ml) by through week 48



Viral blips were not associated to CVW

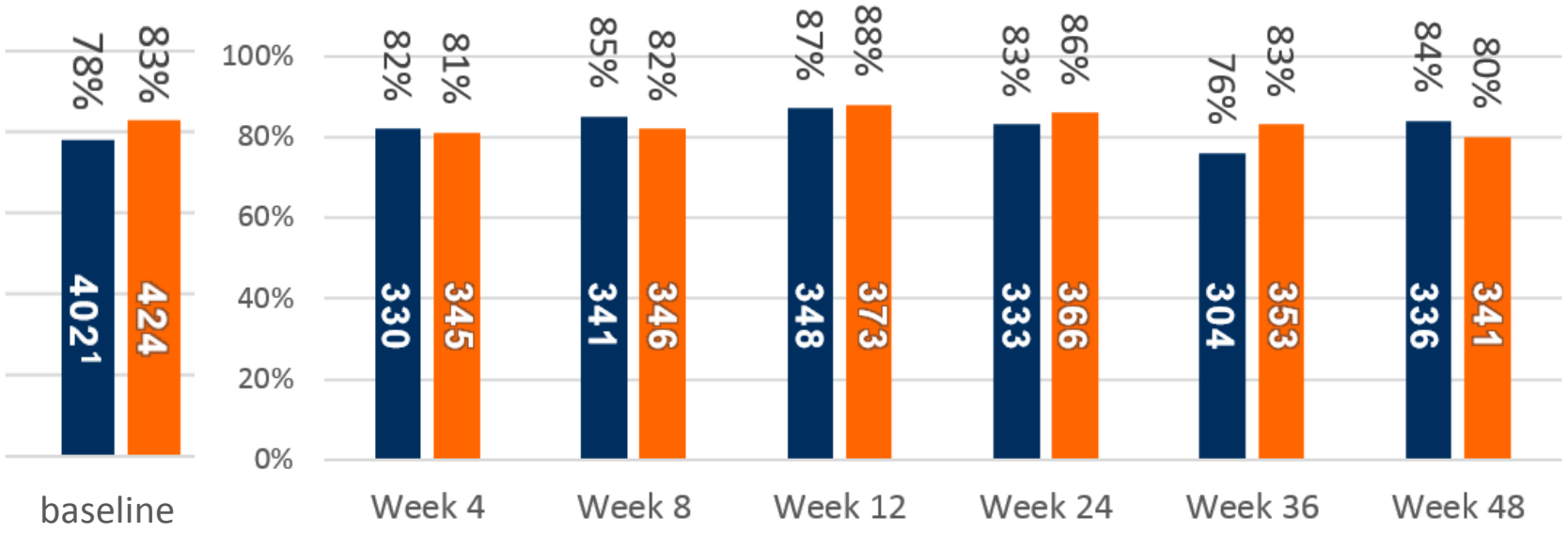
Wang R et al. HIV Drug therapy 2018, Glasgow UK; Poster 313.

Comparison of Viral Replication Below 50 c/mL

Abbott HIV-1 Realtime Assay generates qualitative data for VL <40 c/mL

- HIV-1 RNA present → **TD** (target detected)
- HIV-1 RNA not present → **TND** (target not detected)

Proportions of patients with TND



Underwood M et al. HIV Drug Therapy 2018, Glasgow UK; Poster 311.

CVW & Resistance overall Results trough week 149

In 6 pts/990

Week of failure	Previous regimen	Viral loads, copies/mL[c]	Resistance mutations[a]		Fold change
			Baseline (GenoSure[d])	Confirmed virologic withdrawal	
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[b,e]	DTG/ABC/3TC	833; 1174; <50	NNRTI: none INSTI: N155N/H, G163G/R	NNRTI: none INSTI V151V/I	———
Week 76[b]	ATV, ABC/3TC	79; 162; 217	NNRTI: V108I INSTI: L74I	No result (sample failed testing)	———
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[e]	RPV/TDF/FTC	147; 289, 503	Samples not collected	NNRTI: K103N**, V179I♦ INSTI: none	RPV, 5.24 DTG, 1.6
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	———
Week 112	DRV, RTV, TDF/FTC	118, 230, 324	NNRTI: none INSTI: E157Q, G193E, T97T/A	NNRTI: M230M/L INSTI: E157Q, G193E	RPV, 2 DTG, 1.47
Week 112	EFV/TDF/FTC	148, 219, 307	Test not performed due to low VL	Test not performed due to low VL	———
Week 136[b]	RAL/ABC/3TC	4,294, 7247	No result (sample failed testing)	NNRTI: E138A, L100L/I INSTI: -	RPV, 4.14

**K103N is not typically associated with RPV, and the Stanford HIVdb RPV resistance score = zero (scale zero to 60 max).

♦V179I is a polymorphic mutation that is frequently selected in patients receiving ETR and RPV. However, it has little, if any, effect on NNRTI susceptibility

48 weeks

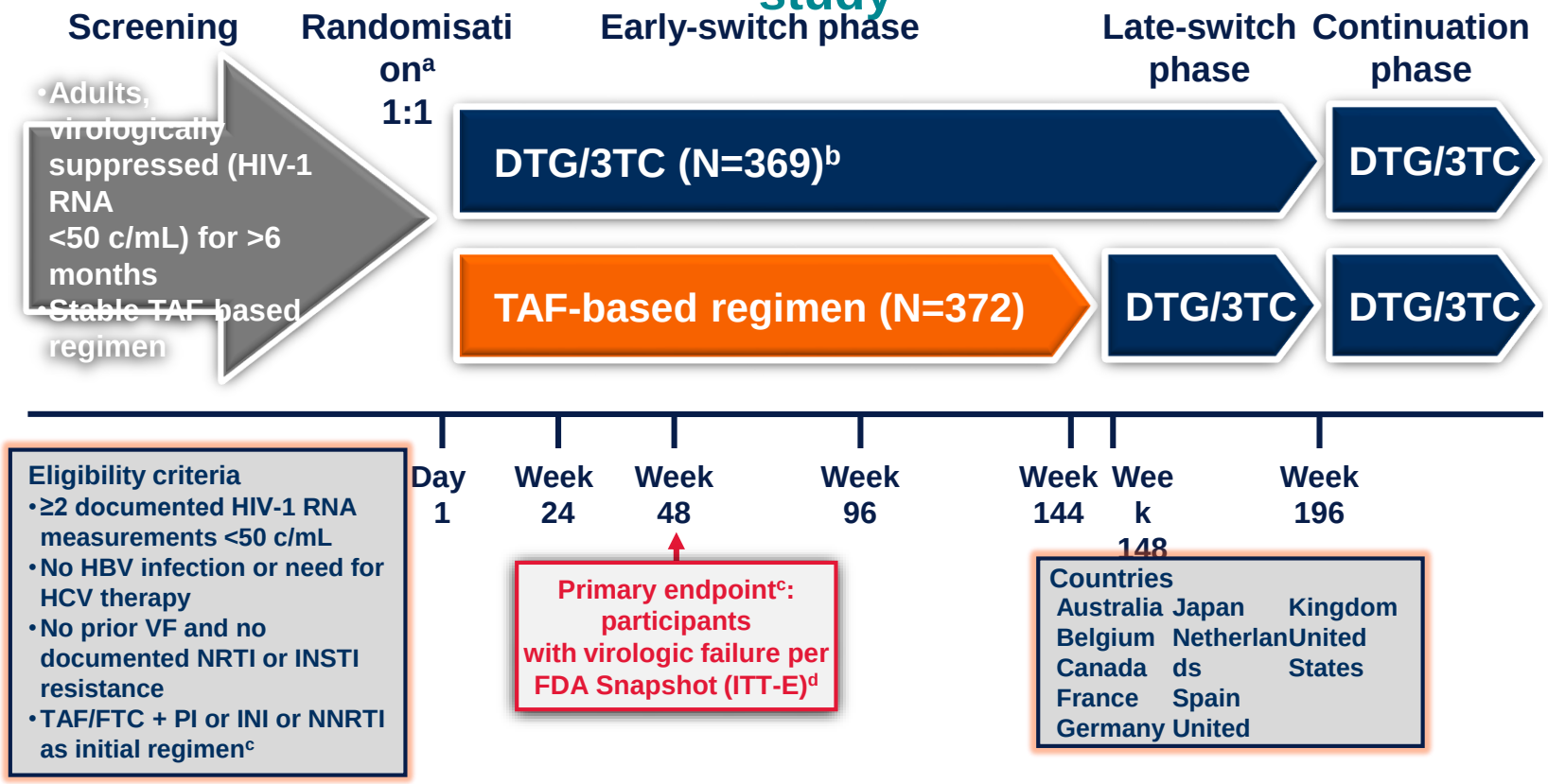
100 weeks

149 weeks

TANGO

TANGO: Phase III Study Design

Randomised, open-label, multicentre, parallel-group, non-inferiority study



[a]Stratified by baseline third agent class (PI, INI, or NNRTI). [b]Two patients excluded who were randomized but not exposed to study drug. [c]Participants with initial TDF treatment who switched to TAF ≥3 months before screening, with no changes to other drugs in their regimen, were also eligible. [d]4% non-inferiority margin. [e]Includes participants who changed a background therapy component or discontinued study treatment for lack of efficacy before Week 48, or who had HIV-1 RNA ≥50 c/mL in the 48-week window.

Adapted from van Wyk et al. IAS 2019; Mexico City, Mexico. Slides WEAB0403LB.

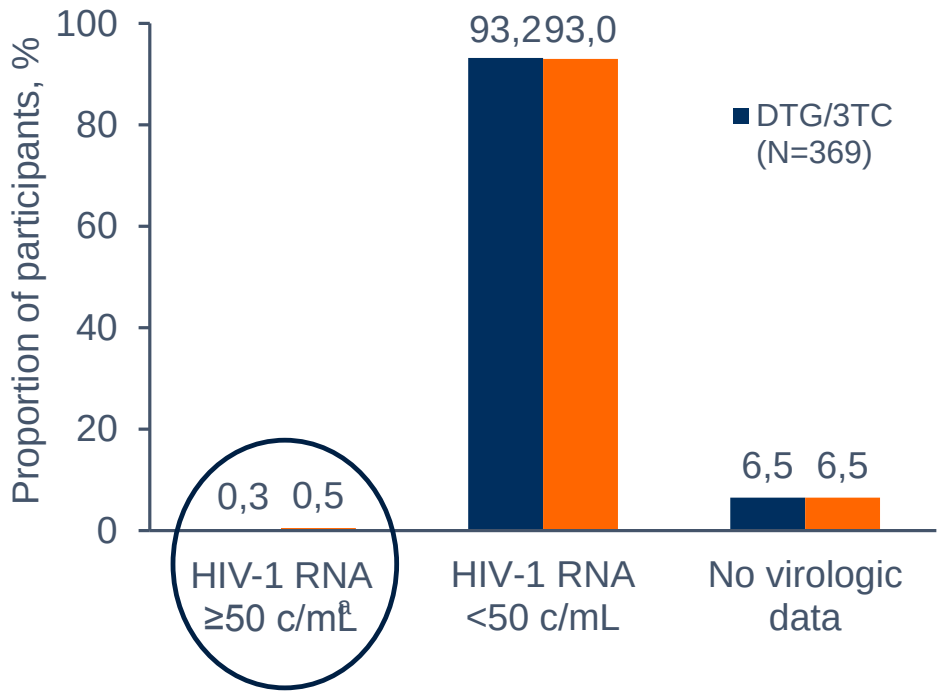
Demographic and baseline characteristics for the TANGO study ITT=E population

Characteristic, n (%)	DTG/3TC (N=369)	TAF-based regimen (N=372)
Age, median (range), y	**40 (20-74)**	**39 (18-73)**
≥50 y	79 (21)	92 (25)
Female	**25 (7)**	**33 (9)**
Race		
African American/African Heritage	51 (14)	58 (16)
Asian	13 (4)	13 (3)
White	296 (80)	289 (78)
Other	9 (2)	12 (3)
Ethnicity		
Hispanic or Latino	70 (19)	66 (18)
Not Hispanic or Latino	299 (81)	306 (82)

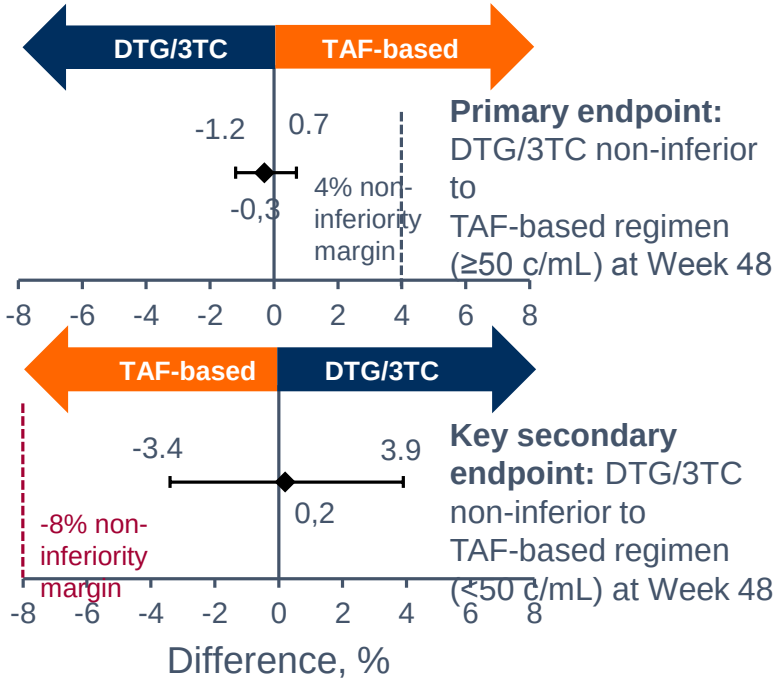
Adapted from van Wyk et al. IAS 2019; Mexico City, Mexico. Slides WEAB0403LB.

DTG/3TC is non-inferior to a TAF-based regimen at 48 weeks in TANGO study

Virologic outcomes



Adjusted treatment difference (95% CI)[b]



- In the per-protocol population, 0/352 participants in the DTG/3TC group and 2/358 participants in the TAF-based regimen group had HIV-1 RNA ≥50 c/mL at Week 48 (adjusted difference, −0.6; 95% CI, −1.3 to 0.2)[b]

[a]Primary endpoint (Snapshot virologic non-response, ITT-E). [b]Based on Cochran-Mantel-Haenszel stratified analysis adjusting for baseline third agent class.

Adapted from van Wyk et al. IAS 2019; Mexico City, Mexico. Slides WEAB0403LB.

No Confirmed Virologic Withdrawals with DTG/3TC in TANGO through 48 weeks

n (%)	DTG/3TC (N=369)	TAF-based regimen (N=372)
Confirmed virologic withdrawal (CVW)[a]	0	1 (<1)[b]
Observed resistance mutation at failure[c]	0	0

[a]One assessment with HIV-1 RNA ≥200 c/mL after Day 1 with an immediately prior HIV-1 RNA ≥50 c/mL.
[b]Treatment interrupted before suspected virologic withdrawal (VL, 38,042 c/mL) and resumed 3 weeks before VL retest (297 c/mL).
[c]Plasma HIV-1 RNA resistance genotype at failure is compared with baseline PBMC pro-viral resistance genotype.

Adapted from van Wyk et al. IAS 2019; Mexico City, Mexico. Slides WEAB0403LB.

Ongoing and randomized 2DR studies

Experimental 2DR	Switch studies vs cARV
DRV/c 800/150 mg + RPV 25mg	Studio **PROBE-2** (160 pts)
DRV/r 800/100 mg + DTG 50 mg	Studio **DUALIS** (320 pts)

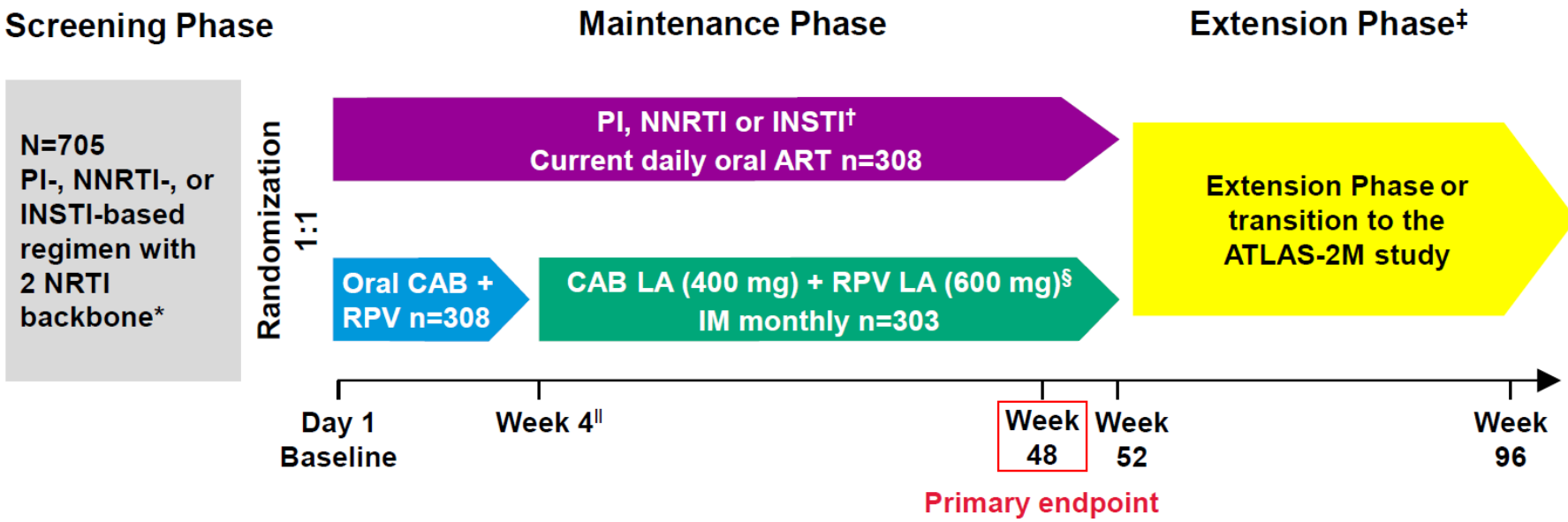
Cabotegravir LA + RPV LA (i.m. injections)

ATLAS study: switch

FLAIR study: naïve (ABC/3TC/DTG)

LONG-ACTING CABOTEGRAVIR + RILPIVIRINE FOR MAINTENANCE THERAPY: **ATLAS** WEEK 48 RESULTS

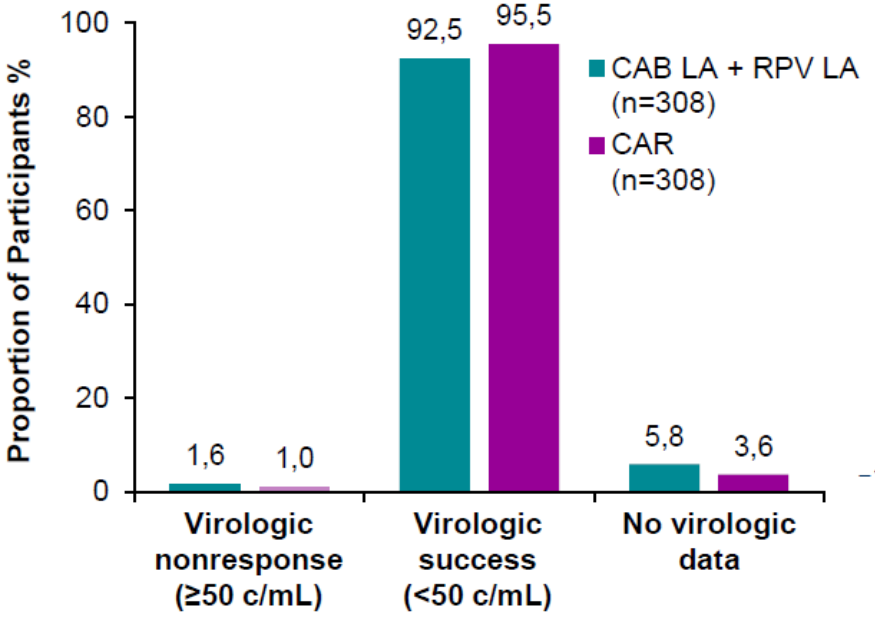
ATLAS Study Design: Randomized, Multicenter, International, Open-Label, Noninferiority Study in Adults with Virologic Suppression (Ongoing)



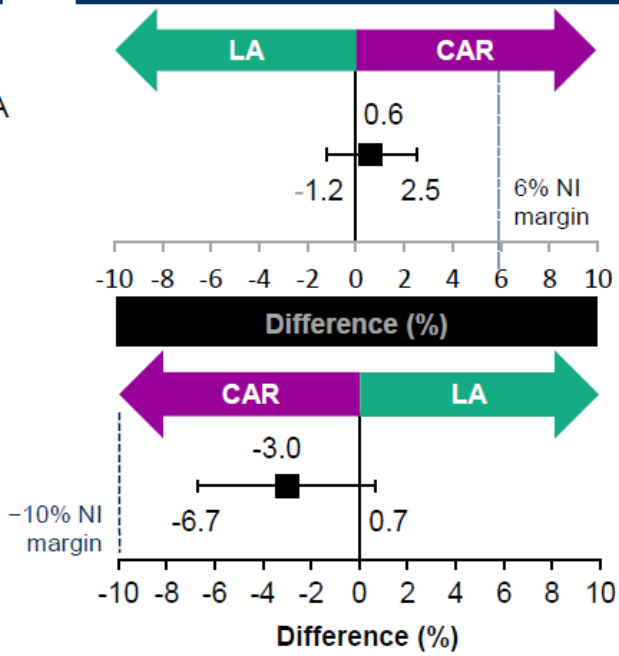
Swindells S, et al. *CROI 2019*; Seattle, WA. Abstract 1475.

ATLAS: WEEK 48 RESULTS

Virologic outcomes



Adjusted treatment difference (95% CI)*



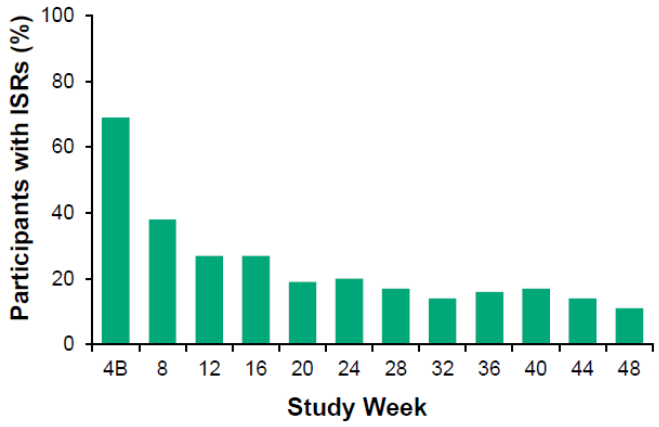
Primary endpoint:

LA noninferior to CAR (HIV-1 RNA ≥50 c/mL) at Week 48

Key secondary endpoint:

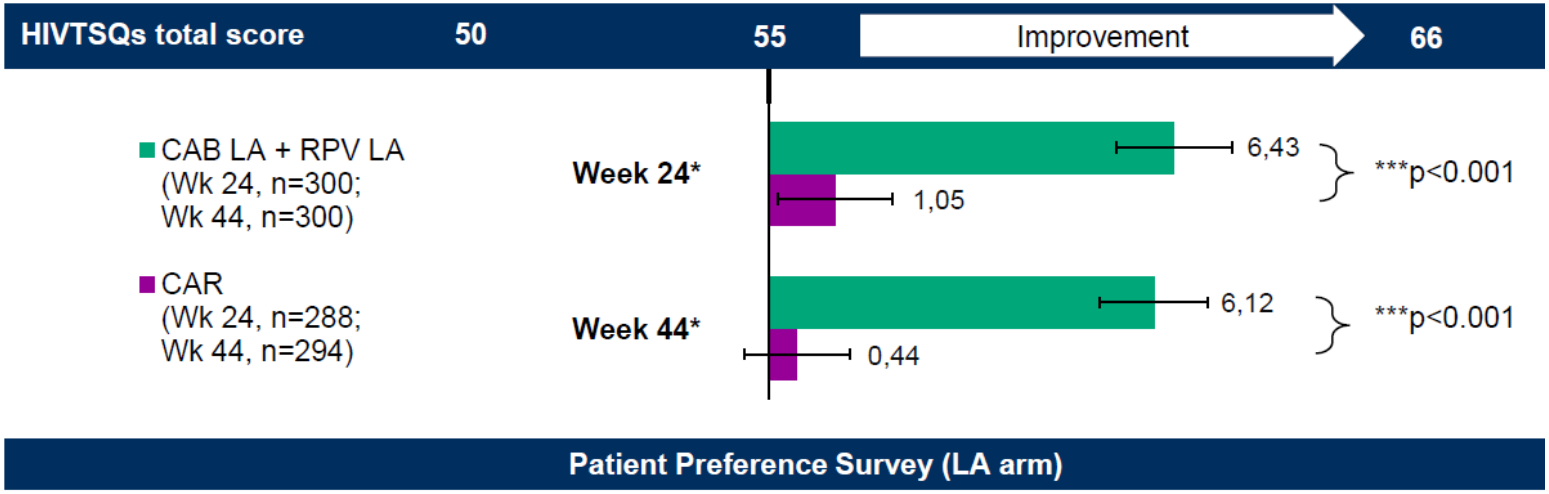
LA noninferior to CAR (HIV-1 RNA <50 c/mL) at Week 48

ISR Incidence by Week



Swindells S, et al. *CROI 2019*; Seattle, WA. Abstract 1475.

ATLAS: WEEK 48 RESULTS



Patient Preference Survey (LA arm)

Single-item question on participants' preference at Week 48

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ATLAS: Confirmed Virologic Failure: CAB LA + RPV LA Arm

CVF definition: *2 consecutive Plasma HIV-1 RNA Levels ≥200 c/mL (after prior suppression to <200 c/mL) through Wk 48*

Gender, Country, HIV-1 Subtype	Previous CAR	Baseline RAMs (PBMC/HIV-1 DNA; Day 1)		SVF Timepoint	Viral Load at SVF/CVF (c/mL)	SVF Timepoint RAMs (HIV-1 RNA)		Drug Sensitivity at SVF (Fold Change)
		RT	INSTI*			RT	INSTI	
F, Russia A	3TC, AZT, LPV/r	E138E/A	L74I	Week 8	79,166 / 25,745	E138A	L74I	**RPV (2.4)** CAB (0.8) DTG (0.9)
F, France AG	3TC, AZT, NVP to 3TC, ABC, NVP	V108V/I E138K	None	Week 12	695 / 258	V108I E138K	None	**RPV (3.7)** CAB (1.2) DTG (1.0)
M, Russia A1	FTC, RAL, TDF to ABC, EFV, 3TC	None	L74I	Week 24	544 / 1841	E138E/K	N155H L74I	**RPV (6.5)** **CAB (2.7)** DTG (1.2)

- Plasma CAB and RPV concentrations at the time of failure were below the population means but within the range for the large majority of individuals who maintained virologic suppression

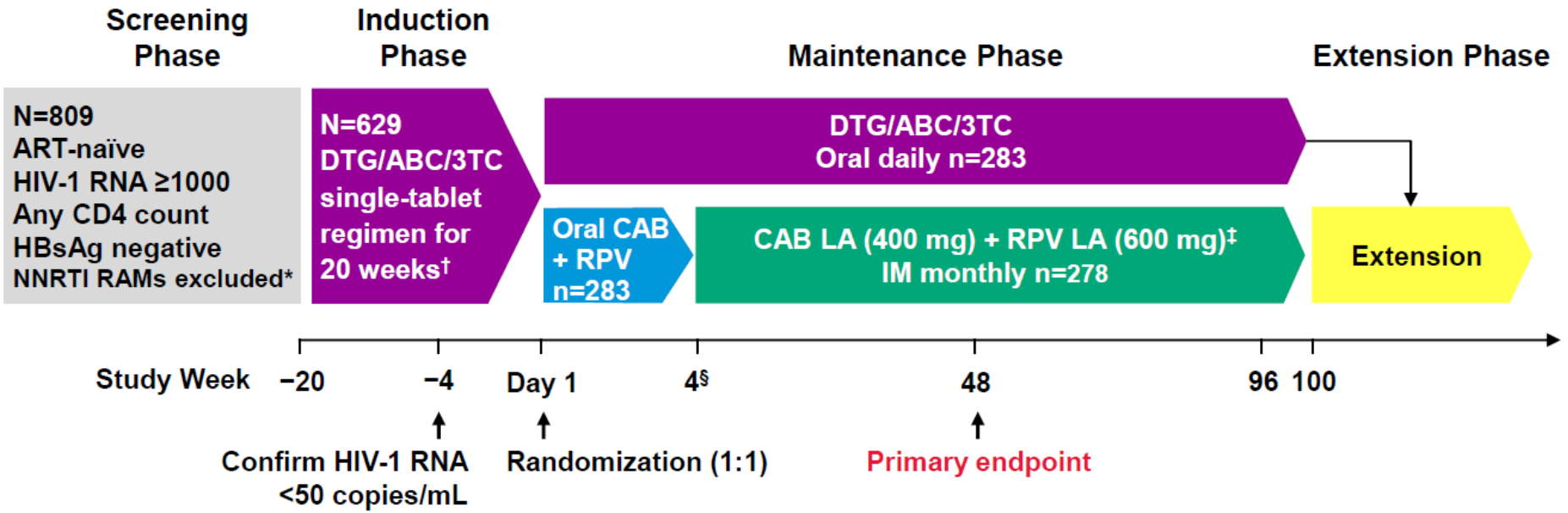
3TC, lamivudine; ABC, abacavir; AZT, azidothymidine; CAB, cabotegravir; CAR, current ART; CVF, confirmed virologic failure; DTG, dolutegravir; EFV, efavirenz; FTC, emtricitabine; INSTI, integrase strand transfer inhibitor; LA, long-acting; LPV, lopinavir; NVP, nevirapine; PBMC, peripheral blood mononuclear cell; r, ritonavir; RAL, raltegravir; RAM, resistance-associated mutation; RPV, rilpivirine; RT, reverse transcriptase; SVF, suspected virologic failure; TDF, tenofovir disoproxil fumarate.

*L74I is not considered an INSTI RAM by IAS-US guidelines and has no impact on CAB activity.

Swindells S, et al. *CROI 2019*; Seattle, WA. Abstract 1475.

LONG-ACTING CABOTEGRAVIR + RILPIVIRINE FOR HIV MAINTENANCE: **FLAIR** WEEK 48 RESULTS

FLAIR Study Design: Randomized, Multicenter, International, Open-label, Noninferiority Study in ART-Naïve Adults (Ongoing)



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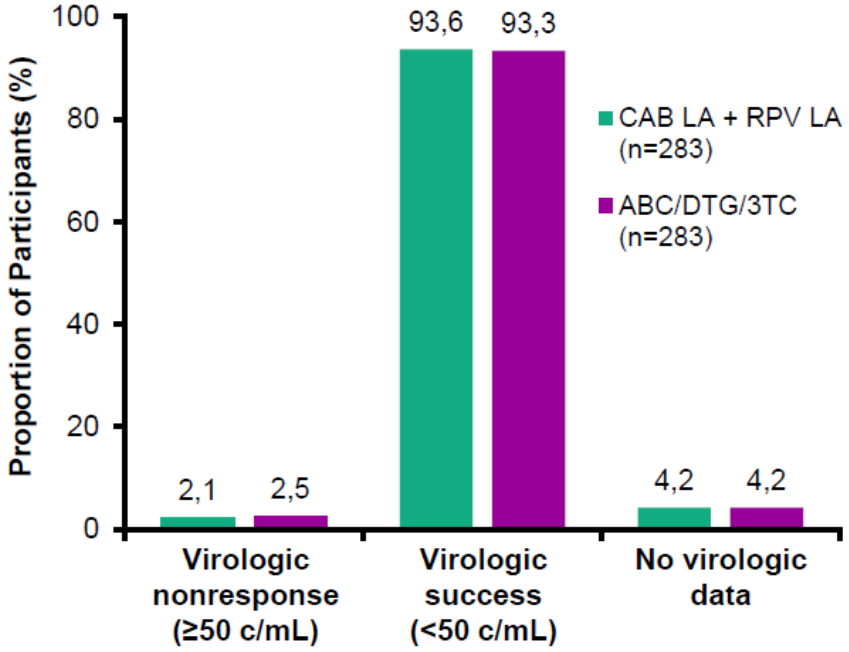
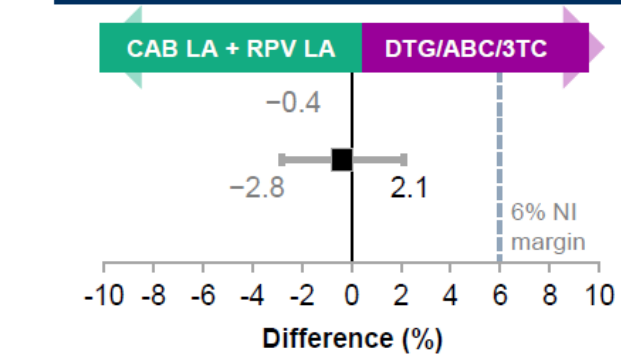
FLAIR WEEK 48 RESULTS

Virologic outcomes

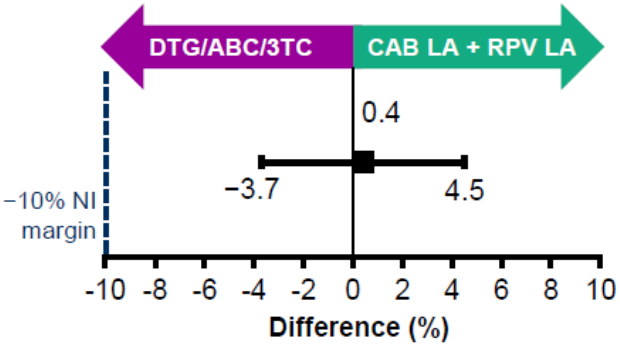


Adjusted treatment difference (95% CI)*



Primary endpoint:

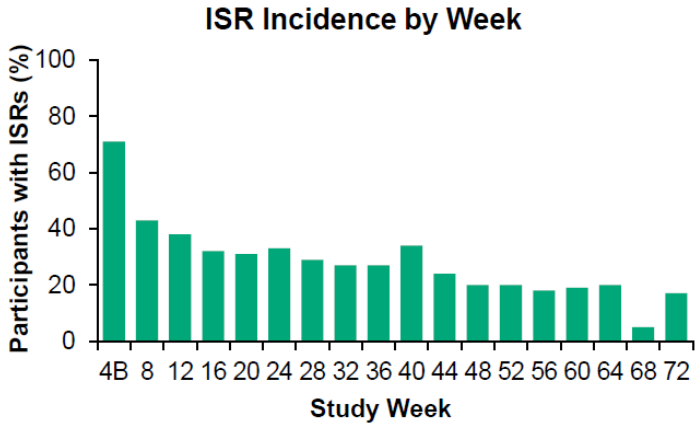
LA noninferior to DTG/ABC/3TC (≥50 c/mL) at Week 48



Key secondary endpoint:

LA noninferior to DTG/ABC/3TC (<50 c/mL) at Week 48

ISR Incidence by Week



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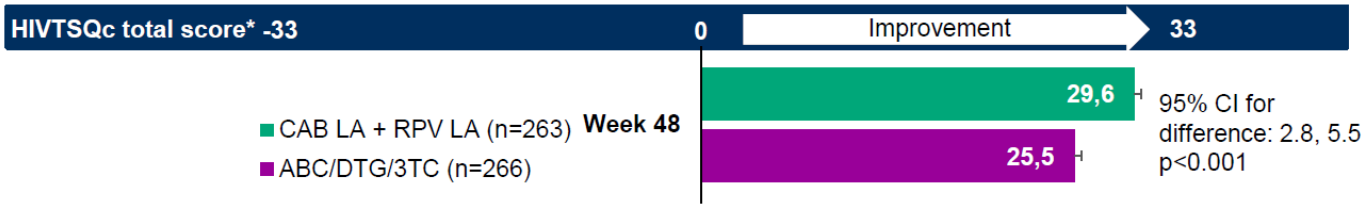
FLAIR: WEEK 48 RESULTS



- Change in satisfaction with current treatment vs induction phase treatment was significantly higher for LA vs DTG/ABC/3TC

Patient Preference Survey

Single-item question on participants' preference at Week 48:

- ITT-E population: 91% (257/283) preferred LA; 1% (2/283) preferred daily oral therapy
  - Responding participants: 99% (257/259) preferred the LA regimen over previous oral therapy

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FLAIR: Confirmed Virologic Failures: CAB LA + RPV LA Arm

Gender, Country, HIV-1 Subtype, VL	Baseline RAMs		SVF Timepoint	Viral Load at SVF/CVF (c/mL)	SVF Timepoint RAMs (HIV-1 RNA)		Drug Sensitivity at SVF (Fold Change)
	NNRTI	INSTI*			NNRTI	INSTI	
F, Russia A1, 54K	None	L74I	Week 20	373 / 456	E138E/A/K/T	L74I, Q148R	**RPV (7.1)** **CAB (5.2)** DTG (1.0)
M, Russia A1, 23K	None	L74I	Week 28	287 / 299	K101E	L74I, G140R	**RPV (2.6)** **CAB (6.7)** DTG (2.2)
F, Russia A1, 20K	None	L74I	Week 48	488 / 440	E138K	L74I, Q148R	RPV (1.0) **CAB (9.4)** DTG (1.1)

- Plasma CAB and RPV concentrations at the time of failure were below the population means but within the range for the large majority of individuals who maintained virologic suppression
- 3 participants in the DTG/ABC/3TC arm had CVF at Weeks 8, 12, and 16, respectively; no drug resistance mutations were selected

3TC, lamivudine; ABC, abacavir; CAB, cabotegravir; CVF, confirmed virologic failure; DTG, dolutegravir; INSTI, integrase strand transfer inhibitor; LA, long-acting; NNRTI, non-nucleoside RTI; RAM, resistance-associated mutation; RPV, rilpivirine; VF, virologic failure. *L74I is not considered an INSTI RAM by IAS-US guidelines and has no impact on CAB activity.

Orkin C, et al. *CROI 2019*; Seattle, WA. Abstract 3947.

Who may benefit?

- **No HBV coinfection**
- **No previous resistance**
  - ✓ No M184V (for 3TC)
  - ✓ No NNRTI resistance (for RPV)
  - ✓ No integrase resisntance (DTG)
  - ✓ No if uncertain past history

Food & antacids for RPV-based regimens

Grazie per l’attenzione