GIORNATE INFETTIVOLOGICHE "LUIGI SACCO" 2019

Milano OSPEDALE LUIGI SACCO POLO UNIVERSITARIO ASST FATEBENEFRATELLI SACCO - AULA MAGNA POLO LITA

28/05/2019 - 29/05/2019

Strategie terapeutiche: regimi a due farmaci

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Disclosures

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Gilead Sciences
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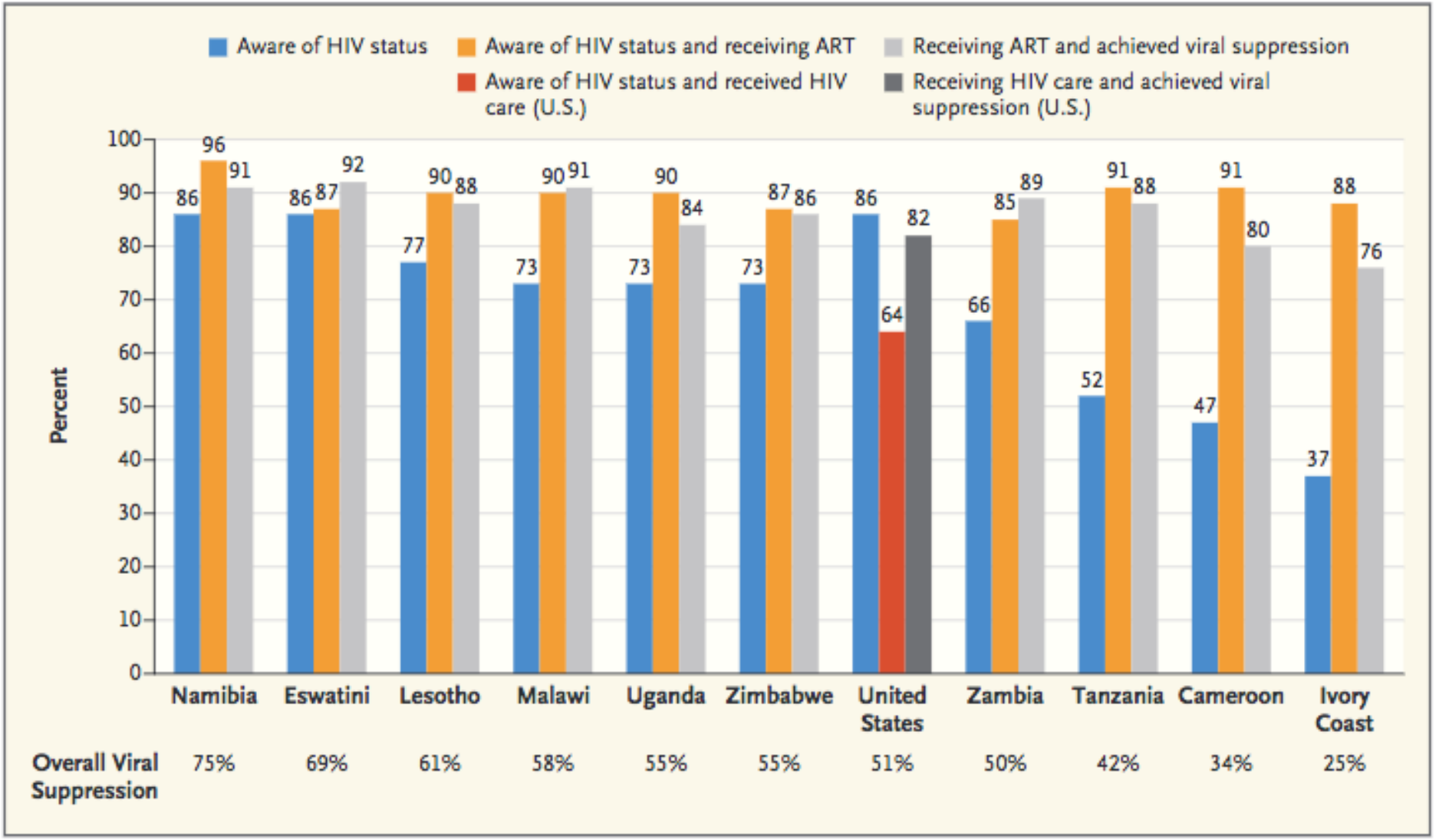
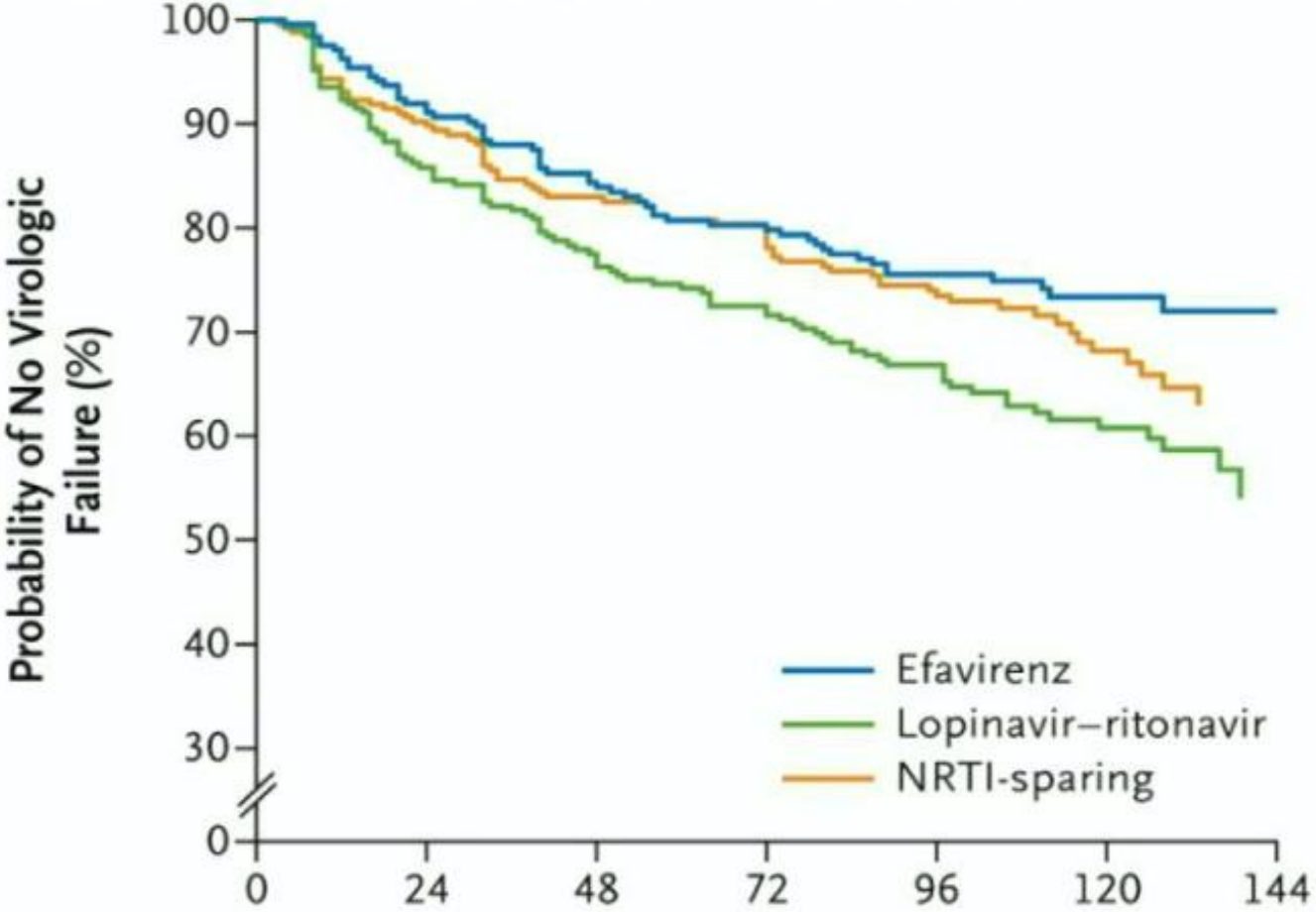
Diagnosis and Treatment Status of Persons Living with HIV in Ten African Countries and the United States



Wafaa M. El-Sadr, NEJM 2019

2DR in the boosted PI era: ACTG 5142

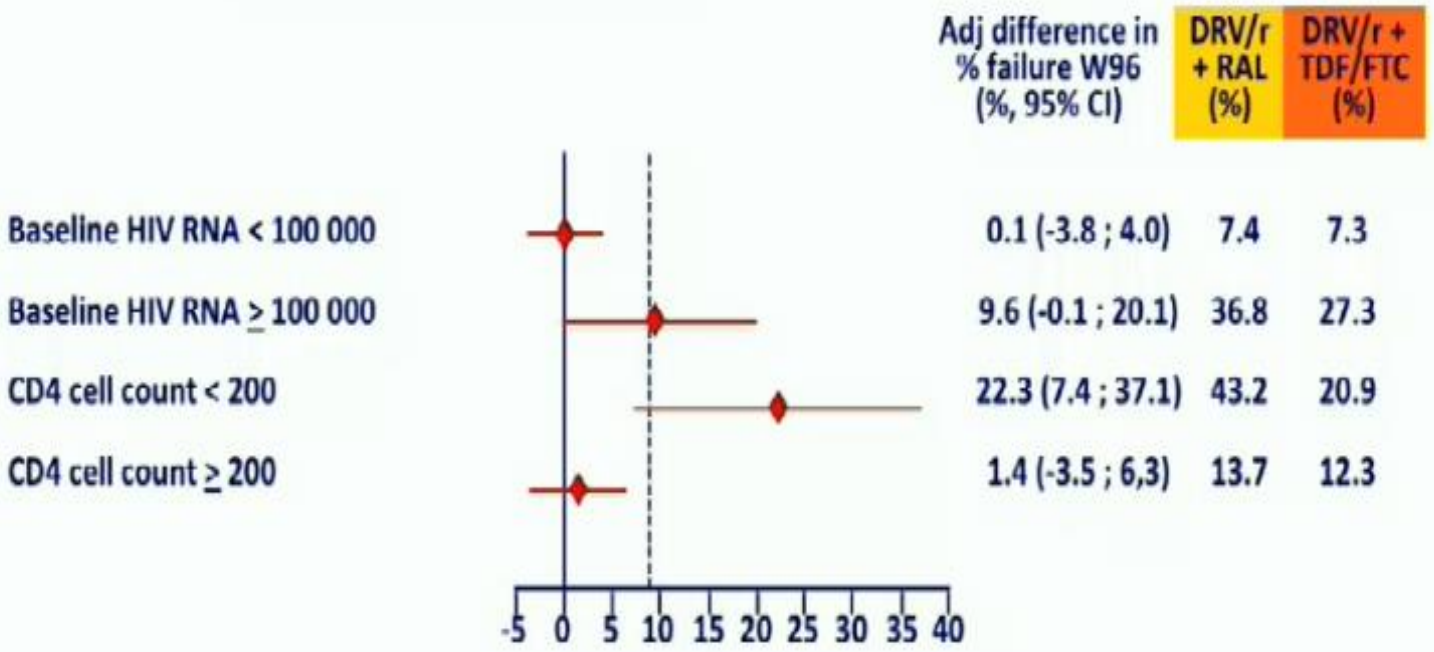


Riddler SA et al. N Engl J Med. 2008 May 15;358(20):2095-106.

2DR significantly worse for lipids and NNRTI resistance (63% vs 44%)

NEAT 001: 2DR non-inferior to 3DR at W48 primary endpoint

= VF, death, AIDS or serious non-AIDS

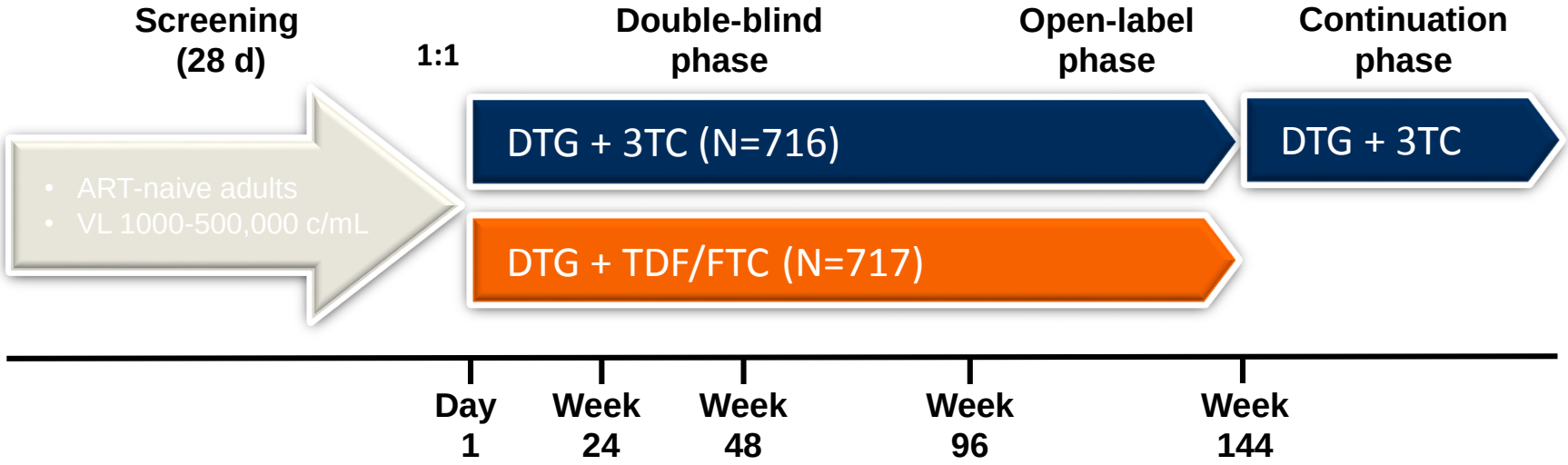


- **Resistance:**
  - No resistance in 3DR arm (n=49)
  - 27% on 2DR had INSTI RAMs, 2% PI (n=61)

Raffi F et al. Lancet 2014;384:1942-51

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

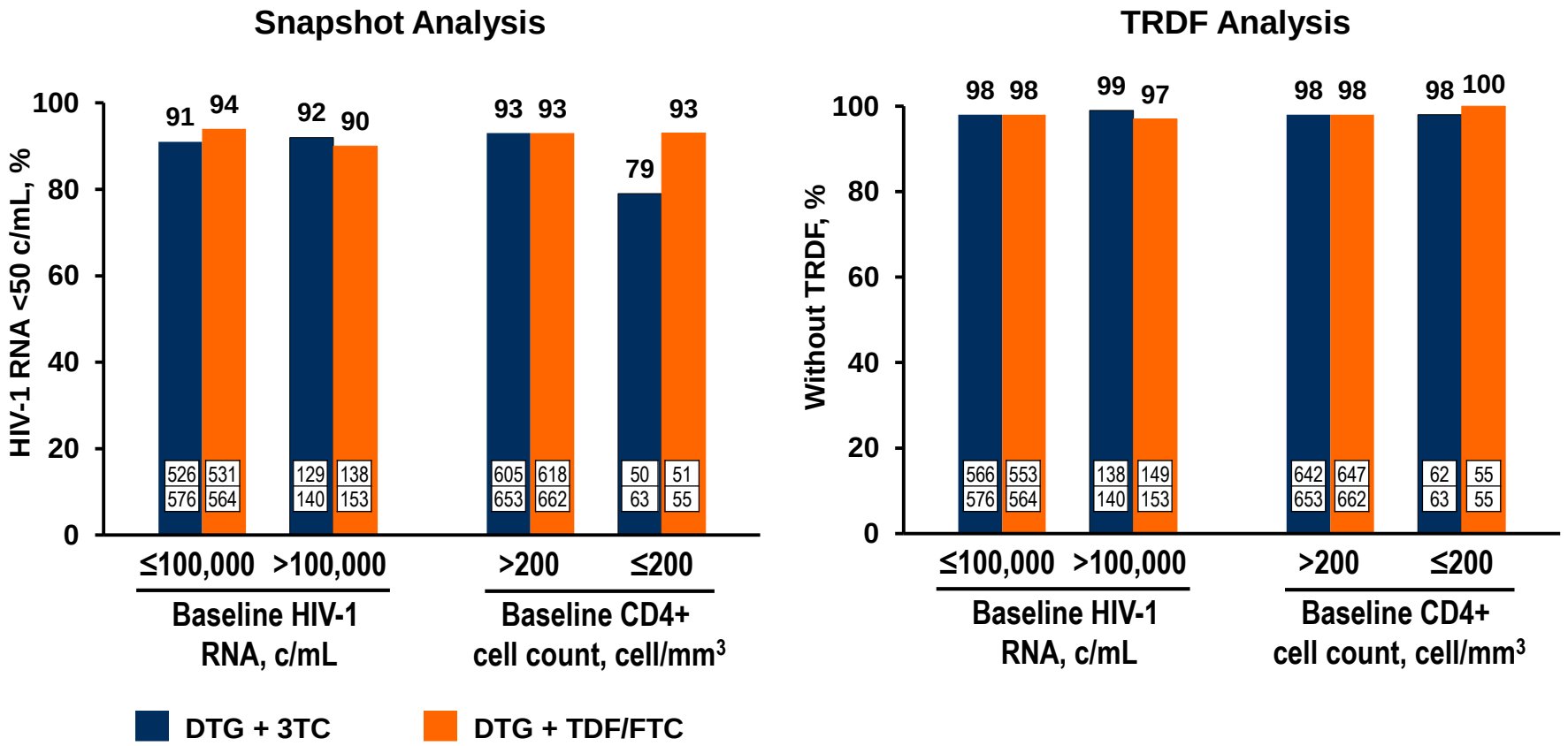
Argentina	Australia	Belgium
Canada	France	Germany
Italy	Republic of Korea	Mexico
Netherlands	Peru	Poland
Portugal	Romania	Russian Federation
South Africa	Spain	Switzerland
Taiwan	United Kingdom	United States

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.

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: ITT-E Population

- Low rates of virologic withdrawals were observed at Week 48

Variable, n (%)	GEMINI 1		GEMINI 2		Pooled	
	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 et al. AIDS 2018; Amsterdam, the Netherlands. Slides TUAB0106LB.

Tabella 8 - Numero di nuove diagnosi di infezione da HIV per numero di linfociti CD4 (< 200 e < 350 cell/µL) alla diagnosi e per regione di segnalazione (2017)

Regione	Numero di casi con CD4 riportati	Completezza del dato (% sul totale dei casi)	CD4 < 200		CD4 < 350	
			n.	%[a]	n.	%[a]
Piemonte	251	99,2	96	38,2	151	60,2
Valle d'Aosta	4	100,0	3	75,0	3	75,0
Liguria	103	96,3	43	41,7	61	59,2
Lombardia	585	86,7	219	37,4	341	58,3
Provincia Autonoma di Trento	24	100,0	8	33,3	12	50,0
Provincia Autonoma di Bolzano	15	100,0	3	20,0	5	33,3
Veneto	148	63,2	52	35,1	81	54,7
Friuli Venezia Giulia	37	92,5	18	48,6	22	59,5
Emilia-Romagna	303	100,0	105	34,7	163	53,8
Toscana	263	100,0	101	38,4	147	55,9
Umbria	58	100,0	22	37,9	30	51,7
Marche	89	97,8	35	39,3	55	61,8
Lazio	nd[b]	nd[b]	nd[b]	nd[b]	nd[b]	nd[b]
Abruzzo	62	95,4	26	41,9	44	71,0
Molise	27	100,0	11	40,7	15	55,6
Campania	224	99,1	75	33,5	120	53,6
Puglia	180	100,0	61	33,9	96	53,3
Basilicata	16	100,0	6	37,5	8	50,0
Calabria	11	100,0	2	18,2	5	45,5
Sicilia	251	90,3	67	26,7	119	47,4
Sardegna	59	96,7	25	42,4	34	57,6
Totale	**2.710**	**78,7**	**978**	**36,1**	**1.512**	**55,8**

(a) Percentuale sul numero di casi con CD4 riportati per Regione; *(b)* non disponibile

Pay attention to HBV, OI, TB, Pregnancy, Resistance…..

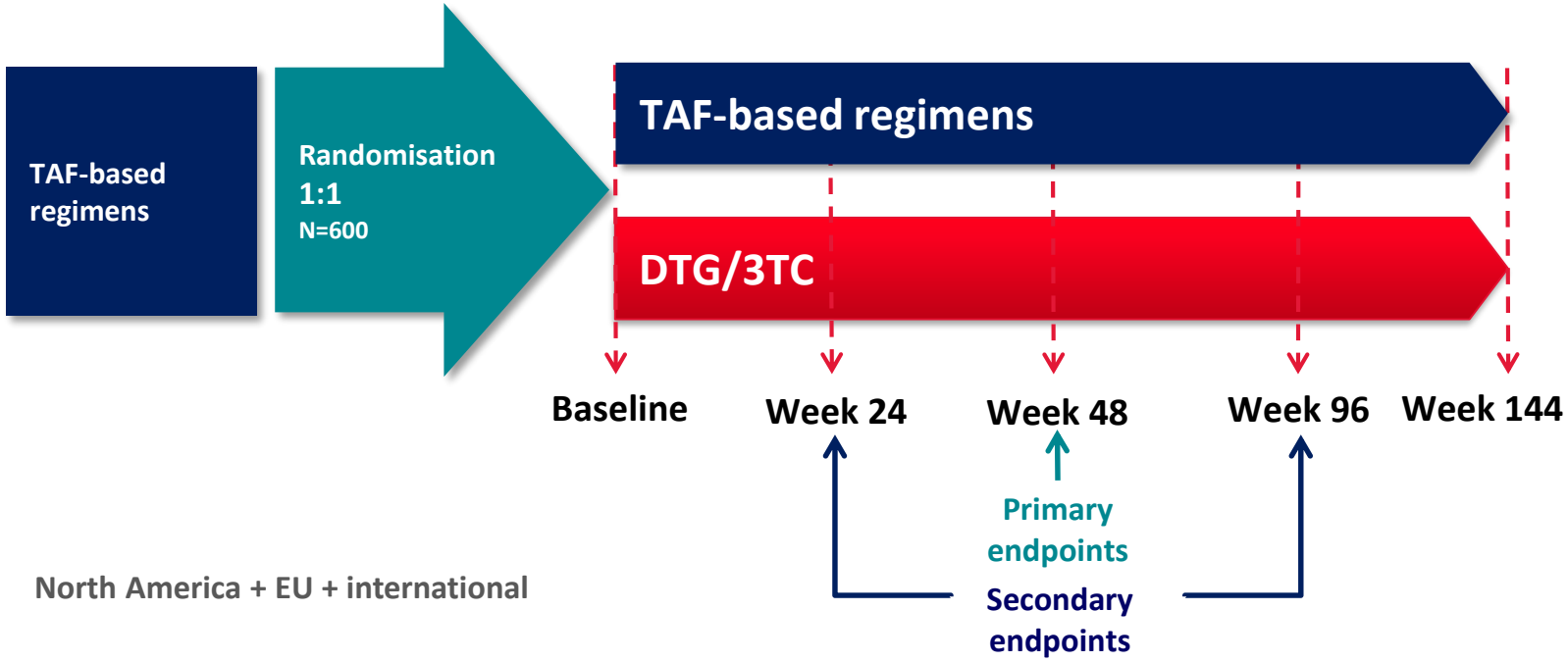
DHHS Guidelines 2018 (updated 25/10)

Recommended Initial Regimens		AI	BI	BII	CI
for Most People with HIV	INSTI+2NRTI	DTG/ABC/3TC DTG+TAF/FTC or TDF/FTC	RAL+ TDF/FTC	RAL+ TAF/FTC	
		BIC/TAF/FTC			
in Certain Clinical Situations	INSTI+2NRTI		EVG/c/TAF/FTC or TDF/FTC	RAL+ABC/3TC	
	PI+2NRTI	DRV/b+TDF/FTC	ATV/b+TAF /FTC or TDF/FTC	DRV/b+ABC/3TC	
	NNRTI+2NRTI		DOR/TDF/3TC	DOR+TAF/FTC	
			EFV/TDF/FTC or 3TC	EFV+TAF/FTC	
			RPV/TDF/FTC		
Regimens to Consider when ABC, TAF, and TDF Cannot be Used or Are Not Optimal	INSTI+NRTI		DTG+3TC		
	INSTI+PI				DRV+RAL
	PI+NRTI				DRV+3TC

Switch study (TANGO)

Phase III, randomised, multicentre, parallel-group, non-inferiority study

- Objective: To demonstrate the non-inferior antiviral activity of switching to DTG/3TC QD compared with continuation of current ARV regimen over 48 weeks in HIV-1-infected ART-experienced subjects (no previous failure)
- Primary endpoint: The proportion of participants who meet the snapshot virological failure criteria at week 48 using the ITT-E population
  - Non-inferiority margin = 4%; week 48 primary endpoint



0493 - FACTORS ASSOCIATED WITH THERAPEUTIC FAILURE OF 2 DRUG REGIMENS (DAT'AIDS COHORT)

Clotilde Allavena[1], Colin Deschanvres[1], Gilles Peytavin[2], David Rey[3], Marc-Antoine Valantin[4], Firouze Bani-Sadr[5], Olivier Robineau[6], Claudine Duvivier[7], André Cabié[8], Laurent Hocqueloux[9], Lise Cuzin[8], Véronique Joly[10], Antoine Cheret[11], Jacques Reynes[12] and the Dat'AIDS group

[1]Infectious Diseases Department, Hôpital Hôtel-Dieu, Nantes, [2] Infectious Diseases Department, APHP Bichat Claude Bernard, Paris, [3] Le Trait d'Union, HIV-infection care center, Hôpitaux Universitaires de Strasbourg, [4] Department of Infectious Diseases, AP-HP, Pitié-Salpêtrière University Hospital, Paris, [5]Infectious Diseases Department, CHU Reims, Reims, [6]Infectious Diseases Department, University hospital of Tourcoing, [7] AP-HP-Necker Hospital, Infectious Diseases Department, Necker-Pasteur Infectiology Center, Paris; Centre médical de l'Institut Pasteur, Necker-Pasteur Infectiology Center, Paris; Paris Descartes University, Sorbonne Paris Cité, EA7327, Paris; IHU Imagine, F-75015 Paris, [8]Infectious Diseases Department, CHU de Fort-de-France, Martinique, [9] Infectious Diseases Department, CHR d'Orléans, Orléans, France, [10] Infectious Diseases Department, APHP Bichat Claude Bernard, Paris, [11] Infectious Diseases Department, AP-HP Bicêtre, Paris Kremlin Bicêtre, [12] Infectious Diseases Department, CHU Montpellier, Montpellier. France.

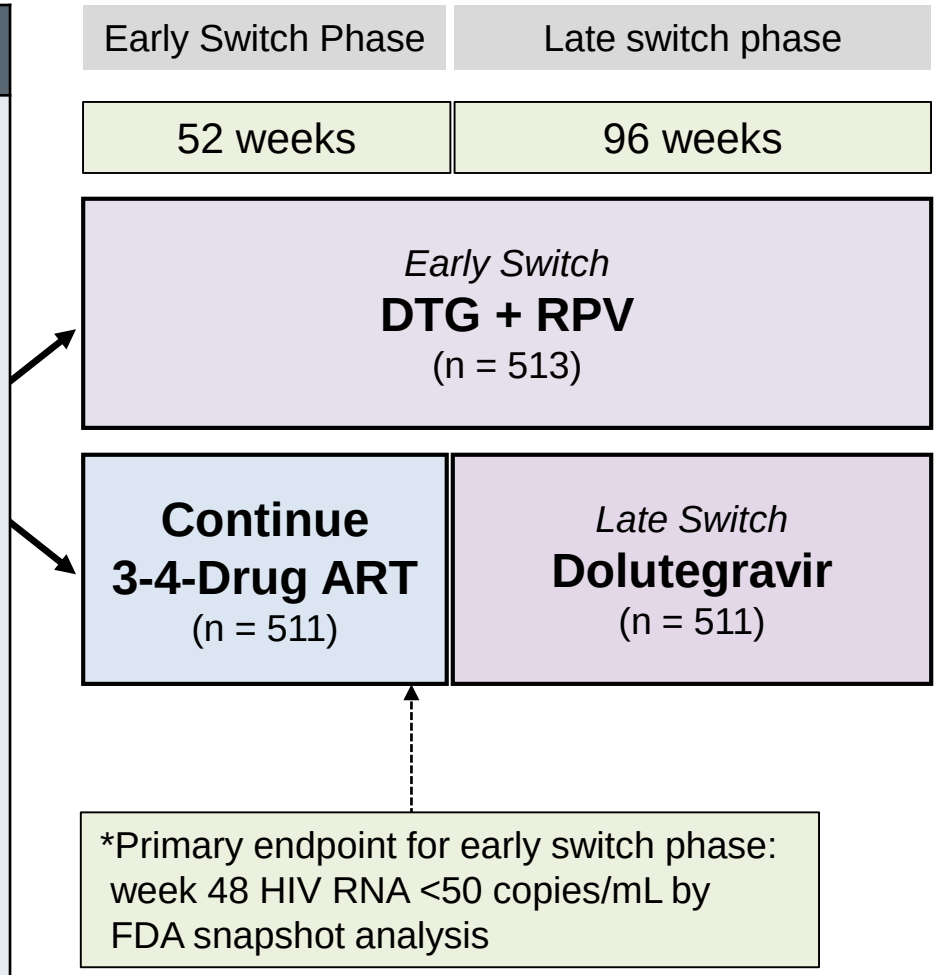
n (%) or median (IQR)	DTG/RPV n=974	DTG/xTC n=677	DRV/RAL n=604	DRV/xTC n=360	RAL/ETR n=869	2-DR n=3484
2-DR discontinuation	**215 (22)**	**127(18.7)**	**326(53.9)**	**192(53.3)**	**318(36.5)**	**1178 (33.8)**
Time on 2-DR before discontinuation (mo.)	5 [2, 13]	4 [2, 10]	15 [6, 31]	10 [3, 25]	14 [4, 26]	10 [3, 23]
Virologic failure	**18 (1.8)**	**12 (1.7)**	**37 (6.1)**	**10 (2.7)**	**45 (5.1)**	**122 (3.5)**
Adverse event	**114 (11.7)**	**59 (8.7)**	**101 (16.7)**	**52 (14.4)**	**91 (10.4)**	**417 (12)**
CNS symptom	43 (4.4)	24 (3.5)	12 (2.0)	9 (2.5)	20 (2.3)	108 (3.1)
GI disturbance	11 (1.1)	10 (1.5)	20 (3;3)	17 (4.7)	12 (1.4)	70 (2.0)
Lipodytrophy	4 (0.4)	(0)	14 (2.3)	3 (0.8)	9 (1.0)	30 (0.9)
Dyslipidemia	(0)	(0)	12 (2.0)	10 (2.8)	1 (0.1)	23 (0.7)
Cutaneous symptom	5 (0.5)	3 (0.4)	4 (0.7)	(0)	9 (1.0)	21 (0.6)
Renal impairment	3 (0.3)	2 (0.3)	3 (0.5)	2 (0.6)	(0)	10 (0.3)
Other AE	48 (4.9)	20 (3.0)	36 (6.0)	11 (3.1)	40 (4.6)	155 (4.4)
Simplification	**8 (0.8)**	**13 (1.9)**	**101 (16.7)**	**51 (14.2)**	**72 (8.3)**	**245 (7.0)**
Miscellanous	**75 (7.7)**	**43 (6.4)**	**87 (14.4)**	**79 (21.9)**	**110 (12.7)**	**394 (11.3)**

Table 2 - *Rate and reasons for treatment discontinuations*

Dolutegravir plus Rilpivirine as Maintenance Dual Therapy
SWORD-1 and SWORD-2: Design

Study Design: SWORD-1 and Sword-2

- **Background**: Identical randomized, multinational, open-label, industry-sponsored, parallel-group, non-inferiority studies of dolutegravir plus rilpivirine to maintain virologic suppression
- **Inclusion Criteria:**
  - Age ≥18 years of age
  - On stable 3-4 drug ART ≥6 months
  - No history of virologic failure
  - No resistance to DTG or RPV
  - 1st or 2nd regimen
  - HIV RNA <50 copies/mL in prior 12 months
  - HIV RNA <50 copies/mL at screening
  - No HBV co-infection
- Regimen (Once daily)
  - Dolutegravir 50 mg + Rilpivirine 25 mg



Source: Llibre JM et al. Abstract 44LB. CROI 2017. Seattle, WA.

Attribute	CAB LA	RPV LA
		
Drug concentration	200 mg/mL	300 mg/mL
Refrigeration/stability	No; store up to 30°C 24 months	Yes; store at 2–8°C 36 months (>8–25°C for ≤24 hours)
Protect from light	No	Yes
Dose – monthly	400 mg (2 mL)	600 mg (2 mL)
Dose – bimonthly	600 mg (3 mL)	900 mg (3 mL)
Dosage instructions/needle gauge	HCP administration Gluteal IM 23 G	HCP administration Gluteal IM 23 G
$t_{1/2}$ with single dose (range or SD)	~40 days (25–54 days)	44–61 days (±24 days)
Drug interactions	Low liability as perpetrator or victim	Low liability as perpetrator; victim of CYP3A4 induction/inhibition

CARLA Plasma and CSF HIV-1 RNA

Antiviral activity	Abbott real-time assay HIV-1 RNA <50 c/mL n/N (%)		SuperLow assay HIV-1 RNA <2 c/mL n/N (%)	
	Q8W (N=15)	Q4W (N=3)	Q8W (N=15)	Q4W (N=3)
Plasma HIV-1 RNA on Day 8	15/15 (100)	3/3 (100)	9/15[a] (60)	3/3 (100)
CSF HIV-1 RNA on Day 8	13/13[b] (100)	3/3 (100)	12/13[b,c] (92)	3/3 (100)

All patients maintained high rates of virologic suppression in plasma and CSF

CSF, cerebrospinal fluid; Q4W, every 4 wk; Q8W, every 8 wk.

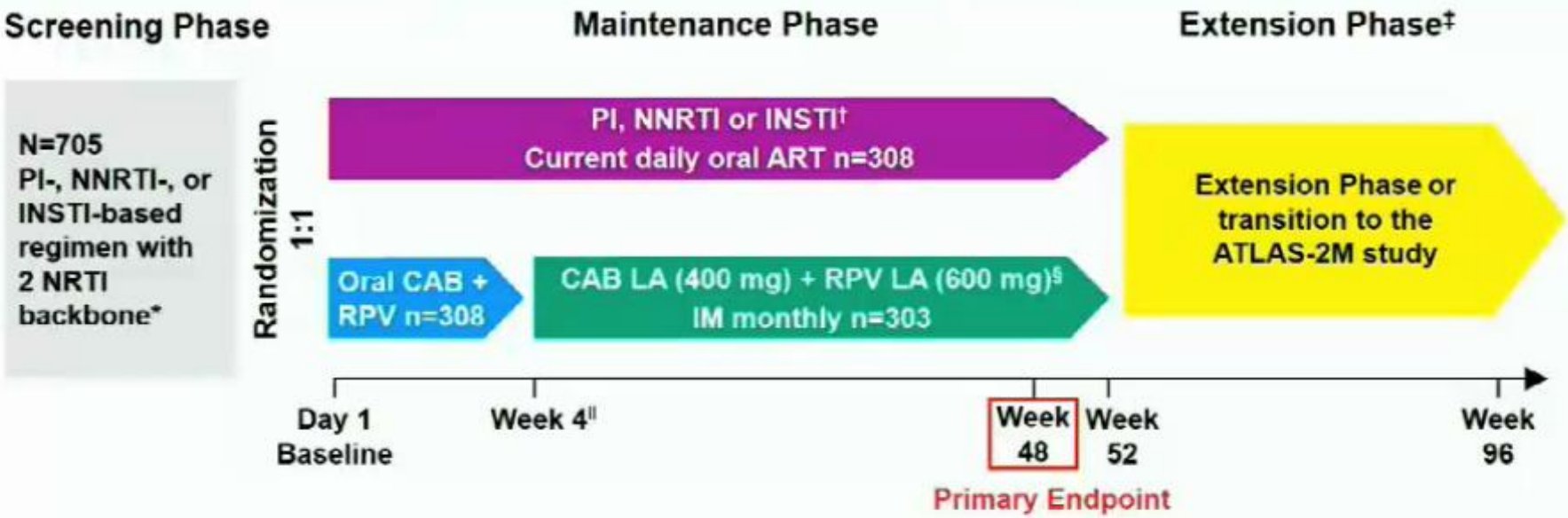
[a]Actual HIV-1 RNA levels in plasma on Day 8 for the 6 participants who were not <2 c/mL**: 3, 5, 5, 10, 15, and 42 c/mL**.

[b]N=13, failed to collect CSF for 2 participants.

[c]All except 1 participant in the Q8W arm had CSF viral load <2 c/mL. This participant had CSF HIV-1 RNA of 2 c/mL and plasma HIV-1 RNA of <2 c/mL.

Letendre et al. HIV Glasgow; Glasgow, UK. Oral O346.

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



ART, antiretroviral therapy; CAB, cabotegravir; CAR, current antiretroviral; IM, intramuscular; INSTI, integrase strand transfer inhibitor; LA, long acting; NNRTI, non nucleoside reverse transcriptase inhibitor; NRTI, nucleoside RTI; PI, protease inhibitor; RPV, rilpivirine; VL, viral load.
*Uninterrupted ART 6 months and VL <50 c/mL at Screening, 2× VL <50 c/mL ≤12 months; †INSTI-based regimen capped at 40% of enrollment; Triumeq excluded from study; ‡Optional switch to CAB LA + RPV LA at Week 52 for those on CAR, §Participants who withdraw/complete IM CAB LA + RPV LA must complete 52 weeks of follow-up; ‖Participants received an initial loading dose of CAB LA (600 mg) and RPV LA (900 mg) at Week 4b. From Week 8 onwards, participants received CAB LA (400 mg) + RPV LA (600 mg) injections every 4 weeks

Swindells S, et al. CROI 2019; Seattle, WA. Abstract 1476.

ATLAS – Baseline Characteristics: ITT-E Population

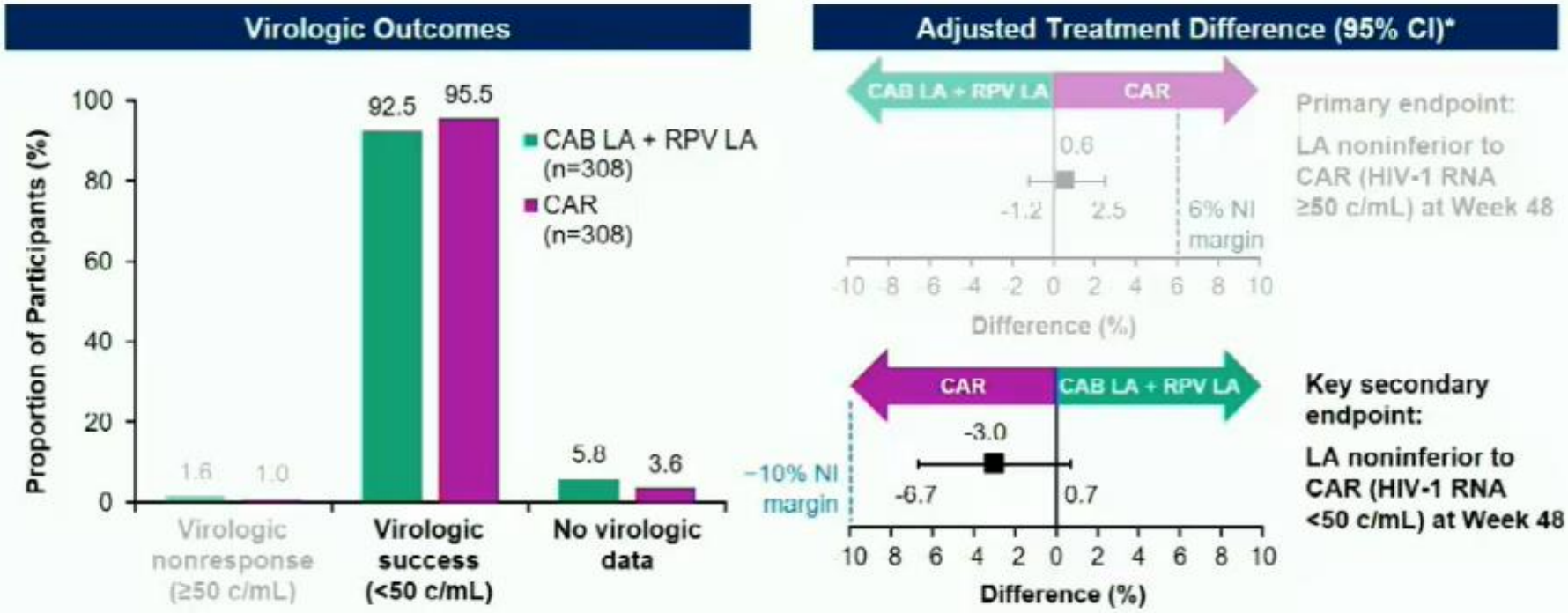
Parameter	CAB LA + RPV LA N=308	CAR N=308	Total N=616
Median age (range) – year	40 (21–74)	43 (18–82)	42 (18–82)
Age ≥50 years – n (%)	66 (21)	96 (31)	162 (26)
Female – n (%)	99 (32)	104 (34)	203 (33)
Race – n (%)			
White	214 (69)	207 (67)	421 (68)
Black or African American	62 (20)	77 (25)	139 (23)
Other	32 (10)	24 (8)	56 (9)
Median body mass index (range) – kg/m^2	26 (15–51)	26 (18–58)	26 (15–58)
Median CD4+ cell count (range) – cells/mm^3	654 (185–1903)	653 (150–2543)	653 (150–2543)
Median duration of prior ART (range) – year	4 (1–19)	4 (1–21)	4 (1–21)
Baseline third ART agent class – n (%)*			
NNRTI	155 (50)	155 (50)	310 (50)
INSTI	102 (33)	99 (32)	201 (33)
PI	51 (17)	54 (18)	105 (17)

3TC, lamivudine; ABC, abacavir; ART, antiretroviral therapy; CAB, cabotegravir; CAR, current antiretroviral; FTC, emtricitabine; INSTI, integrase strand transfer inhibitor; ITT-E, intention-to-treat exposed; LA, long-acting; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; RPV, rilpivirine; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.

*Common backbone regimens included: FTC/TDF (LA 60% vs CAR 56%), FTC/TAF (LA 16% vs CAR 17%), ABC/3TC (LA 13% vs CAR 13%)

Swindells S, et al. CROI 2019; Seattle, WA. Abstract 1476.

ATLAS Virologic Snapshot Outcomes at Week 48 for ITT-E: Noninferiority Achieved for Primary and Secondary Endpoints



CAB, cabotegravir; CAR, current antiretroviral; CI, confidence interval; ITT-E, intention-to-treat exposed; LA, long-acting; NI, noninferiority; RPV, rilpivirine.
*Adjusted for sex and baseline third agent class

Swindells S, et al. CROI 2019; Seattle, WA. Abstract 1476.

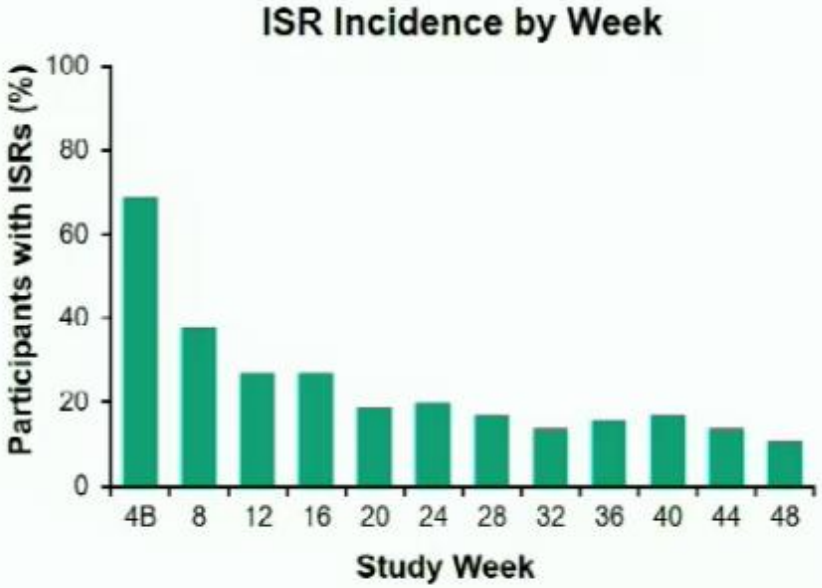
ATLAS Snapshot Outcomes at Week 48 for ITT-E

n (%)	CAB LA + RPV LA N=308	CAR N=308
HIV-1 RNA <50 copies/mL	**285 (92.5)**	**294 (95.5)**
HIV-1 RNA ≥50 copies/mL	**5 (1.6)**	**3 (1.0)**
Data in window not below threshold	1 (0.3)	1 (0.3)
Discontinued for lack of efficacy	3 (1.0)	2 (0.6)
Discontinued for other reason while not below threshold	1 (0.3)	0
No virologic data	**18 (5.8)**	**11 (3.6)**
Discontinued due to AE*	11 (3.6)	4 (1.3)
Discontinued due to death†	0	1 (0.3)
Discontinued for other reasons†	7 (2.3)	6 (1.9)

AE, adverse event; CAB, cabotegravir; CAR, current antiretroviral; ISR, injection site reaction; ITT-E, intention-to-treat exposed; LA, long-acting; RPV, rilpivirine.
*Discontinued due to AEs: LA arm (n) – ISR (3), hepatitis A (2), acute hepatitis B (1), acute hepatitis C (1), headache (1), depression suicidal (1), memory impairment (1), diarrhea/nausea/headache (1); CAR arm (n) – colitis (1), blood creatinine increased (1), renal impairment (1), anxiety disorder/depression/suicidal ideation (1); †Death: methamphetamine overdose (1); ‡Other reasons for discontinuation included: LA arm (n): pregnancy (4), lost to follow up (1), non-compliance with treatment (1), and relocation (1); CAR arm: pregnancy (1), lost to follow up (1), and withdrawal by participant due to frequency of visits (4)

Swindells S, et al. CROI 2019; Seattle, WA. Abstract 1476.

ATLAS Injection Site Reactions



Event	CAB LA + RPV LA N=308
Participants receiving injections, n	303
Injections given, n	6978
ISR events, n (%)	1460 (20.9)
Pain	1208 (82.7)
Nodule	54 (3.7)
Induration	54 (3.7)
Swelling	48 (3.3)
Grade 3 ISR pain	20 (1.7)
Median duration of ISRs, days	3
Participants with ISR leading to withdrawal, n (%)	4 (1.3)

- The majority (99%,1439/1460) of ISRs were grade 1–2 and most (88%) resolved within ≤7 days

CAB, cabotegravir; IM, intramuscular; ISR, injection site reaction; LA, long-acting; RPV, rilpivirine.
Bars represent incidence of onset ISRs relative to the most recent IM injection visit

Swindells S, et al. CROI 2019; Seattle, WA. Abstract 1476.

ATLAS Confirmed Virologic Failure: CAR Arm

Sex, Country, HIV-1 Subtype	Study CAR	SVF Timepoint	Viral Load at SVF/CVF (c/mL)	SVF timepoint RAMs (HIV-1 RNA)		Baseline RAMs (PBMC/HIV-1 DNA; Day 1)	
				RT	INSTI	RT	INSTI
M, Russia, A1	EFV, 3TC, AZT	Week 20	1295 / 9727	M184V G190S	L74I	M184M/I	L74I
M, USA, B	EVG/c, FTC, TAF	Week 20	339 / 264	None	None	None	None
F, USA, B	EVG/c, FTC, TDF	Week 32	524 / 815	M184I	None	None	None
M, USA, B	EVG/c, FTC, TDF	Week 40	392 / 512	M230M/I	None	None	None

3TC, lamivudine; AZT, azidothymidine; c, cobicistat; CAR, current antiretroviral; CVF, confirmed virologic failure; EFV, efavirenz; EVG, elvitegravir; FTC, emtricitabine; INSTI, integrase strand transfer inhibitor; PBMC, peripheral blood mononuclear cell; RAM, resistance-associated mutation; RT, reverse transcriptase; SVF, suspected virologic failure; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.

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

ATLAS Confirmed Virologic Failure: CAB LA + RPV LA Arm

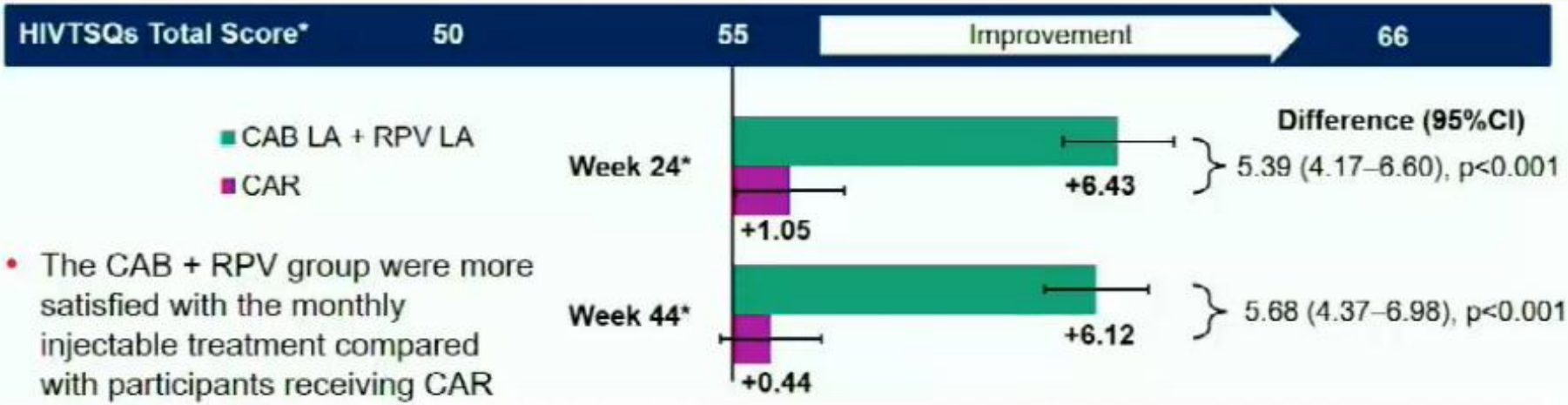
Sex, Country, HIV-1 Subtype	Previous CAR	SVF Timepoint	Viral Load at SVF/CVF (c/mL)	SVF Timepoint RAMs (HIV-1 RNA)		Drug Sensitivity at SVF† (Fold Change)
				RT	INSTI*	
F, Russia, A/A1	3TC, AZT, LPV/r	Week 8	79,166 / 25,745	E138A	L74I	**RPV (2.4)** CAB (0.8) DTG (0.9)
F, France, AG	3TC, AZT, NVP to 3TC, ABC, NVP	Week 12	695 / 258	V108I E138K	None	**RPV (3.7)** CAB (1.2) DTG (1.0)
M, Russia, A/A1	FTC, RAL, TDF to ABC, EFV, 3TC	Week 20	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 antiretroviral; 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.
†Monogram biological /clinical cutoffs are: RPV=2.0, CAB=2.5, and DTG=4.0.

Swindells S, et al. CROI 2019; Seattle, WA. Abstract 147b.

ATLAS: High Participant Satisfaction (HIVTSQs) and Preference for Injectable Therapy



- The CAB + RPV group were more satisfied with the monthly injectable treatment compared with participants receiving CAR

Patient Preference Survey (LA Arm)

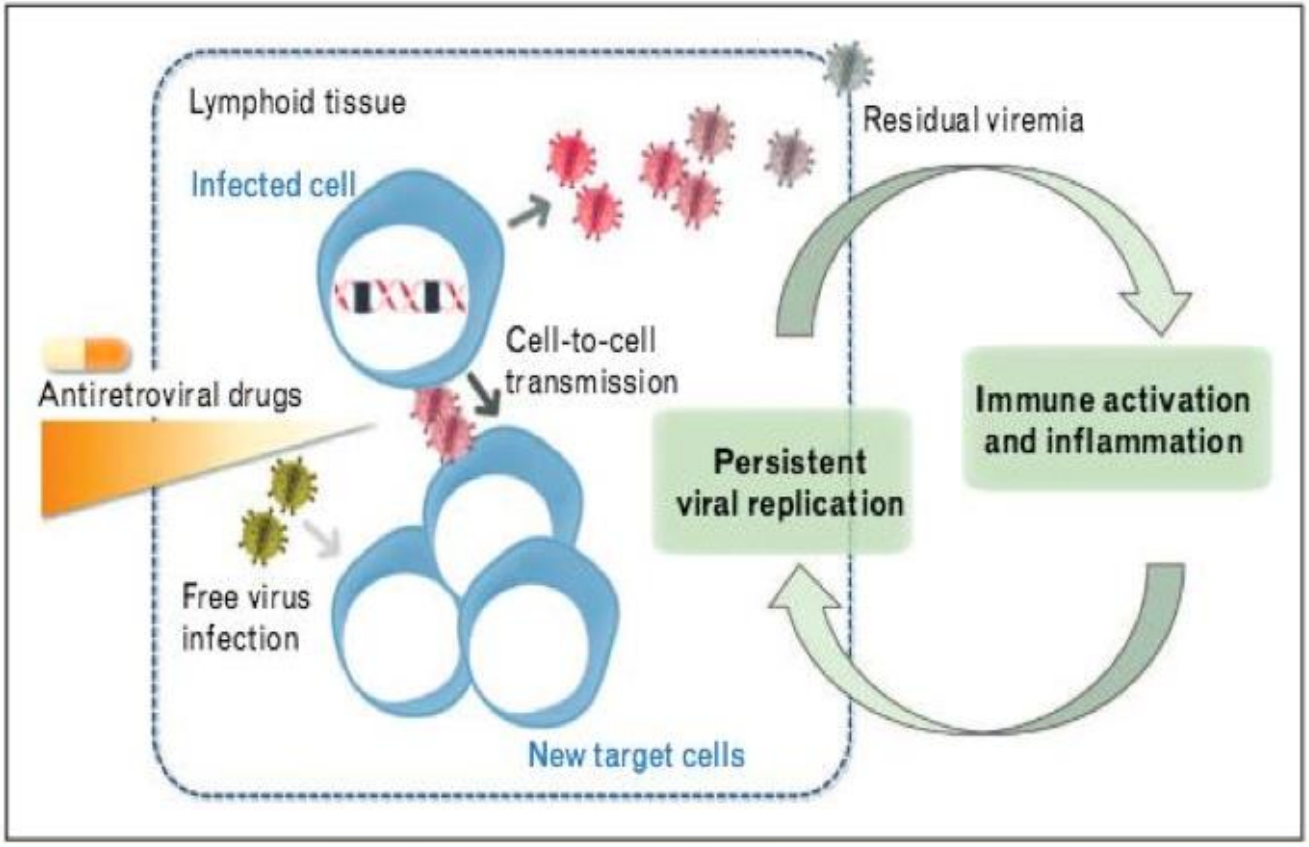
Single-item question on participants' preference at Week 48

- ITT-E population: 86% (266/308) preferred LA; 2% (7/308) preferred daily oral therapy
  - **Responding participants: 97% (266/273) preferred the LA regimen over previous oral therapy**

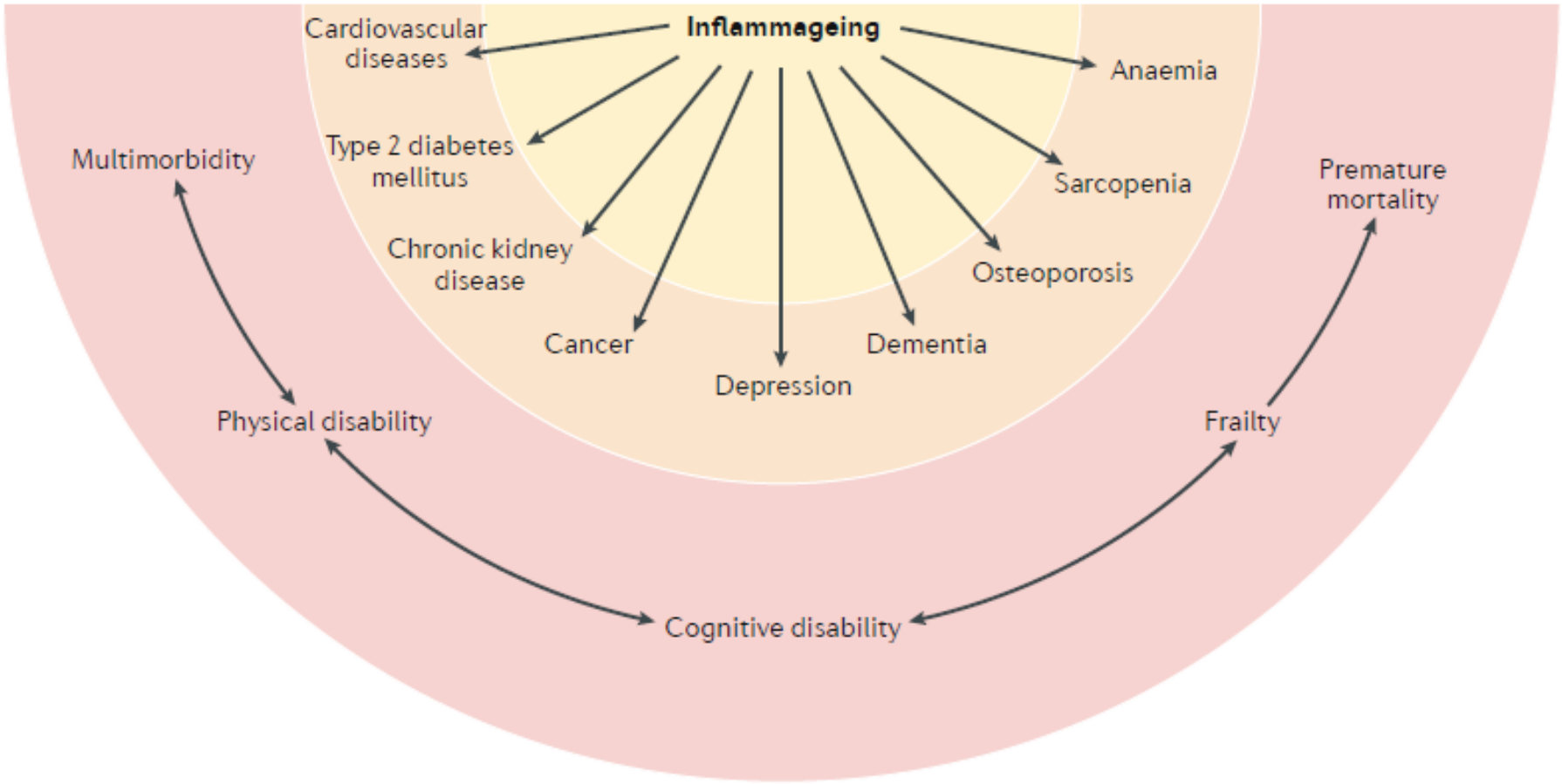
CAB, cabotegravir; CAR, current antiretroviral; HIVTSQs, HIV Treatment Satisfaction Questionnaire (Status); ITT-E, intention-to-treat exposed; LA, long-acting; RPV, rilpivirine.

*Adjusted mean change from baseline; adjusted for baseline score, sex, age, race, and baseline third agent class. Error bars show 95% confidence interval. n=300 for CAB + RPV at Week 24 and n=300 at Week 48; n=288 for CAR at Week 24 and n=294 at Week 48.

Swindells S, et al. CROI 2019; Seattle, WA. Abstract 1476.


Lymphoid tissue
Residual viremia
Infected cell
Cell-to-cell transmission
Antiretroviral drugs
Immune activation and inflammation
Persistent viral replication
Free virus infection
New target cells

Inflammageing is a risk factor for multiple chronic diseases

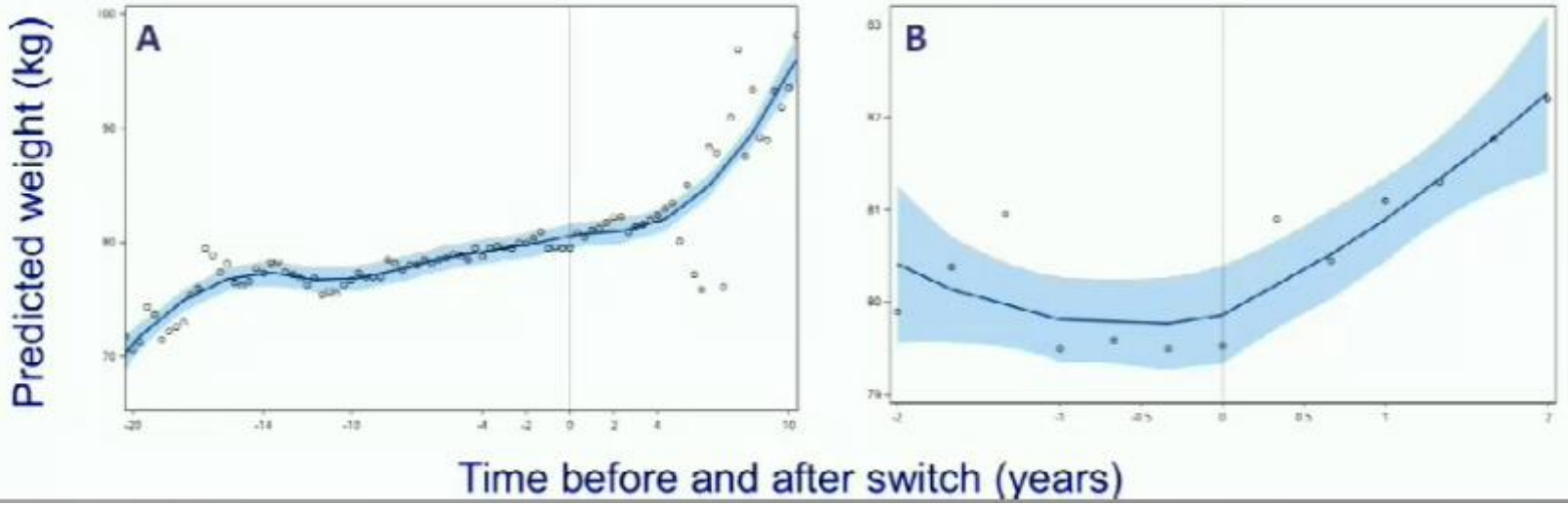


Ferrucci F, NrC, 2018

Results I

972 adults switched to INSTI at median 7.8 years after parent trial entry. 691 had suppressed HIV-1 RNA at time of switch:

- -82% male, 45% non-white
- -Median age 51 years, $CD4^+$ T cell count 610 cells/μL, and BMI 26 kg/m^2
- -63% switched from PI, 35% from NNRTI
- -289 switched to RAL, 204 to EVG and 198 to DTG (median follow-up 1.8 years)



JA LADE, CROI 2019

Sensitive virological markers

TND = target not detected

Suppressed switch studies

- ASPIRE: RCT cART vs DTG/3TC
  - No change by single copy assay at W24 or W48
- SWORD 1 & 2
  - Target not detected analysis

84% DTG-RPV
80% Control group

First line studies

- ACTG 5353: single arm DTG/3TC
  - Viral decay similar to DTG-3DR in SPRING-1 & SINGLE
- GEMINI
  - Same viral decay & time to suppression overall & >100k

Taiwo B et al. Glasgow; 2018 O213.
Li J et al Abstract O145, Glasgow 2018
Underwood M et al. Glasgow 2018
Eron et al. HIV DART and Emerging Viruses 2018. O7

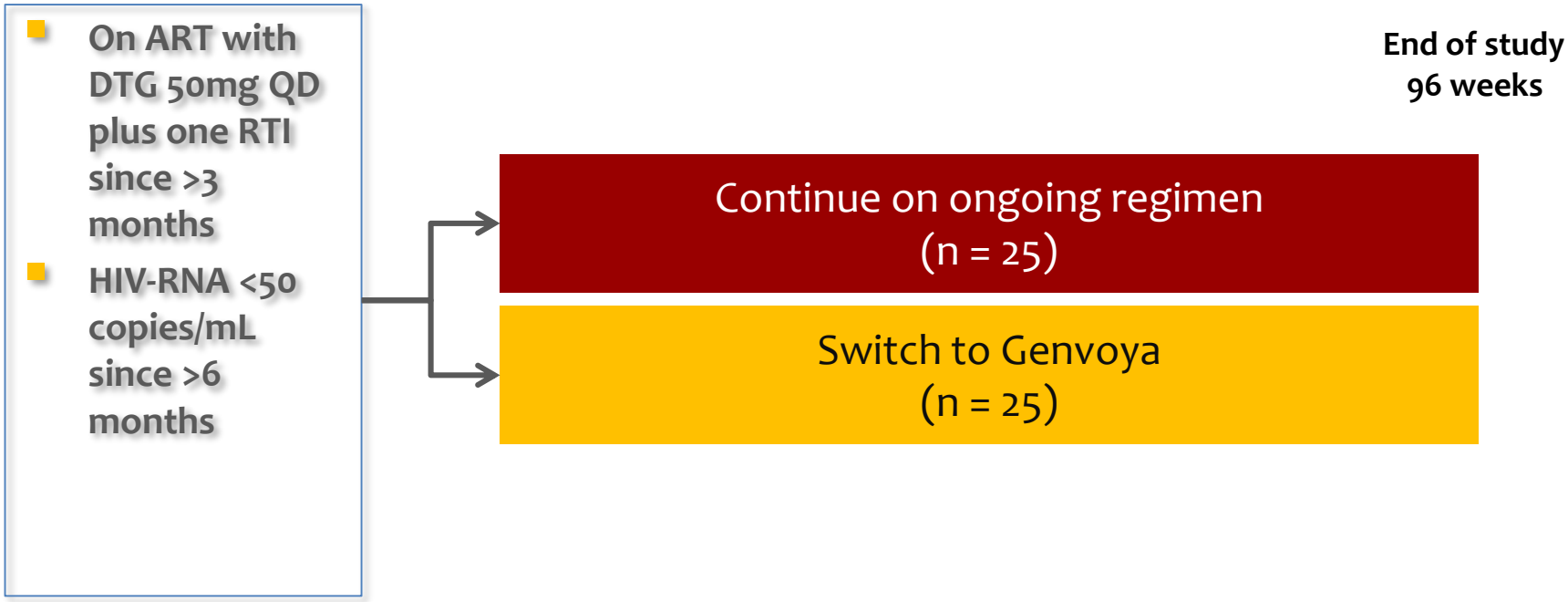
Immune activation & inflammation

- **NEAT-001 :**
  - DRV/r + RAL vs DRV/r + TDF/FTC first line
  - **No difference** in inflammatory biomarkers
- **Italian triple to DTG + 3TC switch cohort:**
  - No increase in immune activation, most VL stayed <3
- **GARDEL & ANDES:**
  - CD4/8 ratio on 2DR same as 3DR over 48 weeks

Bernardino JI et al. CROI 2015, abstract 766
Maggiolo F et al. Poster 104, Glasgow 2018
Figueroa MI et al. CROI 2019; poster 0492

Be One Study Design

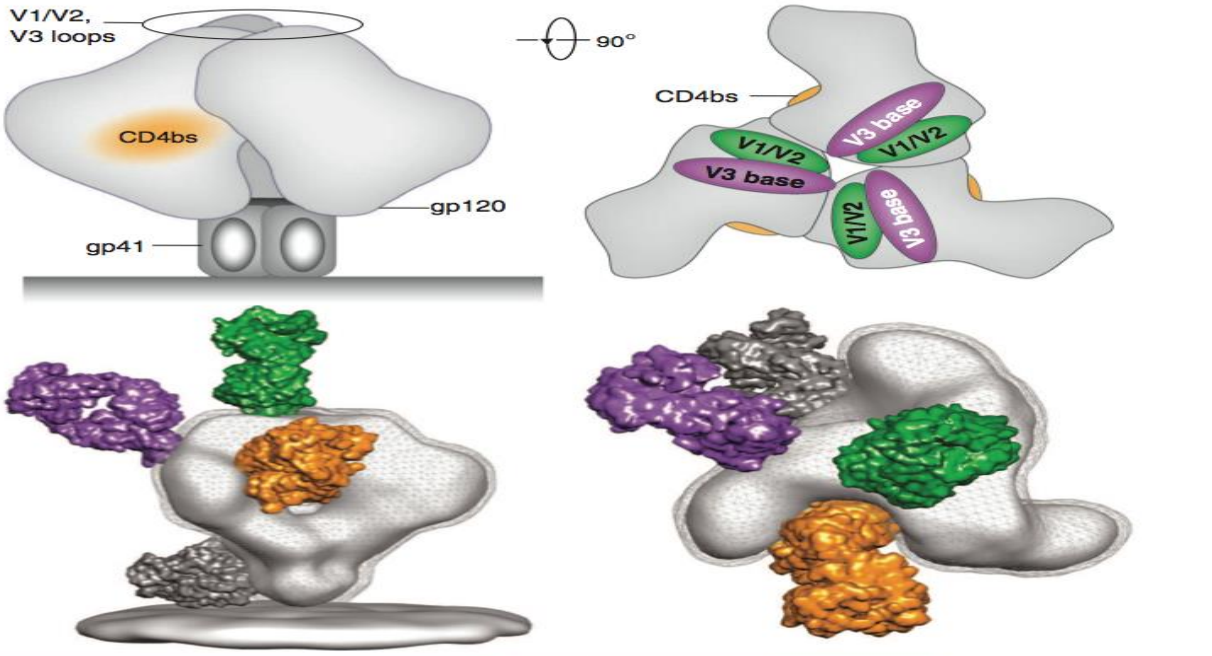
Randomized, single-center, open-label, 96-week superiority study.



Primary end-point

Proportion of subjects with no residual viremia through 48 weeks of follow-up

Antibody target sites on the HIV-1 envelope spike



CD4 binding site		Glycan-V3	V1/V2 loop	gp41	Others
b12	1NC9	PGT121-PGT123	PG9/PG16	4E10	8ANC195
HJ16	12A12, 12A21	10-1074	PGT141–145	2F5	2G12
NIH45-46, 45-46^{G54W}	8ANC131, 8ANC134	PGT125-128,130,131	CH01-CH04	10E8	3BC176/
VRC01-03, VRC06	CH30-CH34	PGT135-137		HK20	3BC315
3BNC117, 3BNC60	VRC23	VRC24		Z13	
VRC-PG04	CH103				

Each of the monomer units of the trimer composing the envelope spike is composed of a gp120 and gp41 trans- membrane protein.
The four best-characterized broadly neutralizing target sites are highlighted and include the CD4-binding site (orange), the glycan-associated epitopes on the base of the V3 loop (purple), the V1/V2 loop (green), and on gp41 (gray).

Klein F, Science 2013

A phase Ib trial

Two bnAbs better than one

VRC family[8]
(VRC01LS, VRC07, VRC07-523LS, 10E8VLS, N6LS …)
bNAbs against gp120
For prevention or treatment

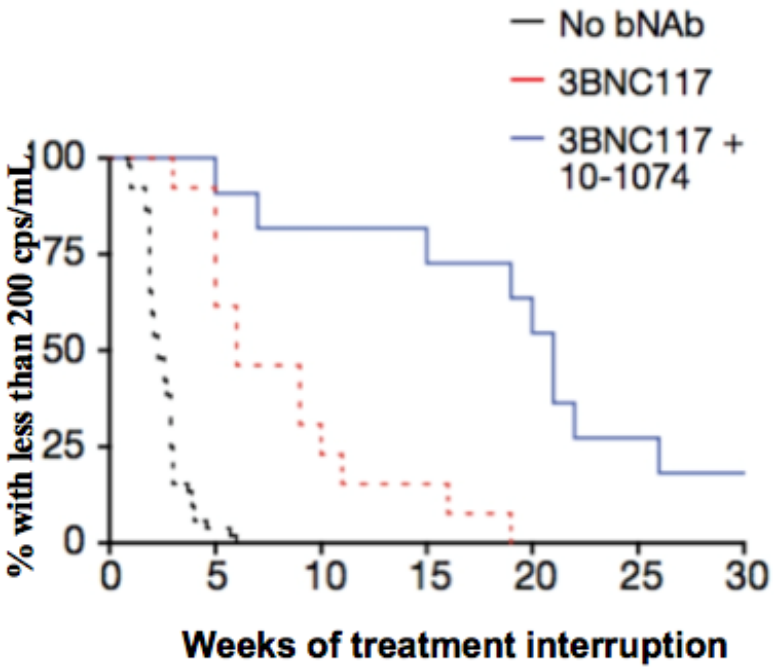
10-1074(LS) + 3BNC117(LS)[14]
bNAbs against gp120
For prevention or treatment
Rockefeller; NIH

PGDM1400 + PGT121
bNAbs against gp120
For prevention or treatment
IAVI

GS-9722[13]
bNAb against gp120
Gilead

- Phase Ib clinical trial (n=9)
  - Three injections at 0,3 and 6 weeks of two potent broadly neutralizing antibodies that target independant sites on the HIV-1 envelope spike

The combination of the antiHIV-1 monoclonal Abs 3BCN117 and 10-1074 maintains viral suppression several weeks in the absence of ART



Mendoza P et al, Nature Research, 27 September 2018 (Vol 561)

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