17th Residential Course on Clinical Pharmacology of Antiretrovirals

January 19-21, 2022

TWO-DRUG REGIMENS FOR HIV INFECTION:
2DRs: from clinical trials to real data experiences

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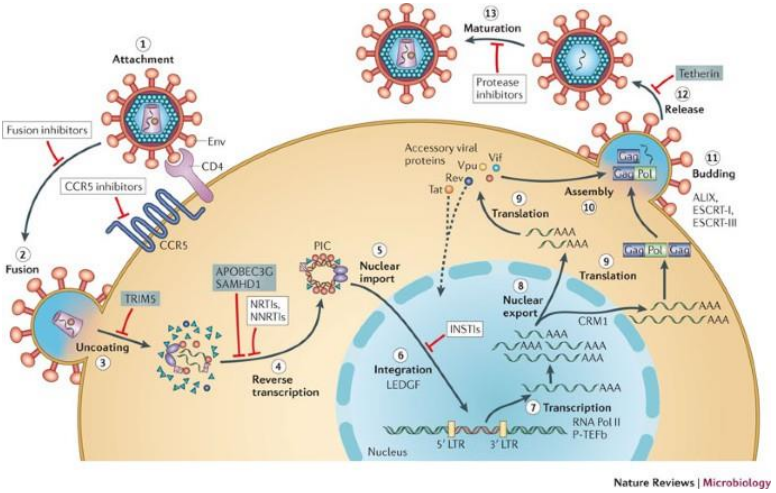


NNRTI-based
INSTI-based
bPI-based

2NRTIs + 3rd drug = HAART

NRTI: 3TC, ABC, FTC, TAF, TDF…..
AZT, d4T, ddI, ddC..

boosted PI: darunavir/r, atazanavir/r, lopinavir/r……
NNRTI: efavirenz, nevirapine, rilpivirine, doravirine
INSTI: raltegravir, elvitegravir/r, dolutegravir, bictegravir
CCR5: maraviroc

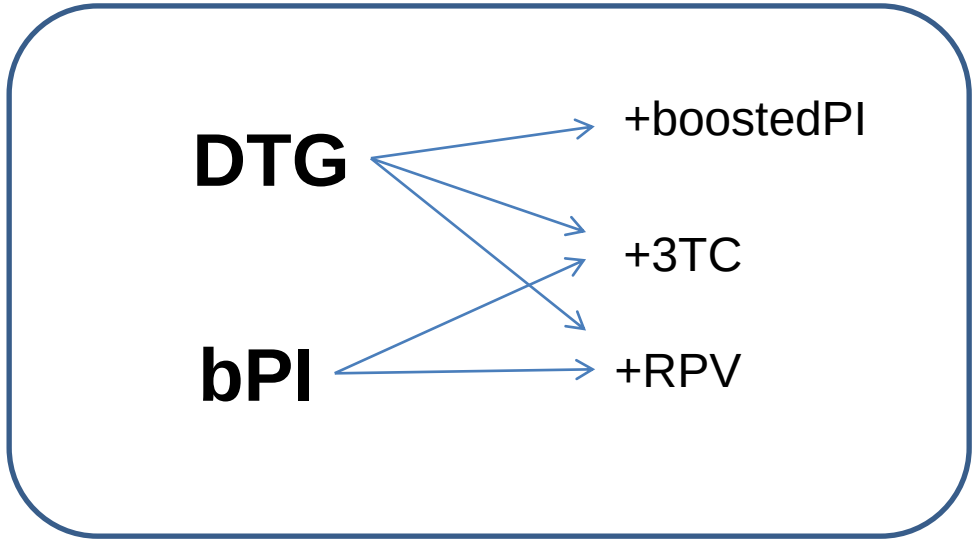
Fusion inhibitor: enfuvirtide
Attachment inhibitor: fostemsavir
mAb: ibalizumab

Exploring 2-Drug Regimens (2DRs)

Why?

Which combination?

How to compare with 3DRs?



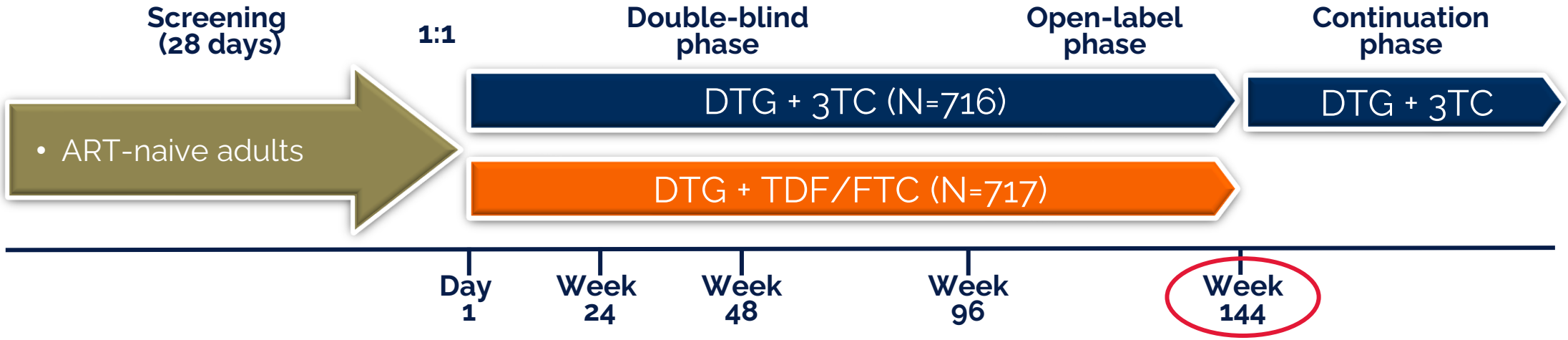
2-DRUG REGIMENS FOR HIV INFECTION

lopinavir/r + lamivudine (LOP-r + 3TC)	OLE’
atazanavir/r + lamivudine (ATV-r + RPV)	ATLAS and SALT
darunavir/r + lamivudine (DRV-r + DRV-r)	DUAL
dolutegravir + lamivudine (DTG + 3TC)	GEMINI 1&2, TANGO, SALSA
dolutegravir + rilpivirine (DTG + RPV)	SWORD 1&2
dolutegravir + darunavir-r (DTG + DRV-r)	DUALIS
darunavir/r + rilpivirine (DRV/r + RPV)	PROBE 2
cabotegravir + rilpivirine (CAB + RPV LA)	ATLAS, FLAIR, ATLAS-2M

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;65:2112-211;
5. Llibre JM et al. Lancet 2018;391:839-849; 6. Cahn P et al. IAS 2019; slides WEAB0404LB7. 7. van Wyk et al. IAS 2019; slides WEAB0403LB. 8. Llibre et al. IAS 2021; Virtual. Slides OALB0303 9. Spinner CD et al. Open Forum Infect Dis 2020; 10. Maggiolo F. et al. J Antimicrob Chemother. 2020;75:1332-1337. 11. Swindells S et al. N Engl J Med. 2020; 12. Orkin C, et al. N Engl J Med. 2020;382:1124-1135. 13 Overton ET, et al. Lancet. 2021;396:1994-2005

Dolutegravir + lamivudine (DTG+3TC)

Identically designed, randomized, double-blind, parallel-group, multicenter, non-inferiority studies



Eligibility criteria
- VL 1000-500,000 c/mL at screening
- ≤10 days of prior ART
- No major RT or PI resistance 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

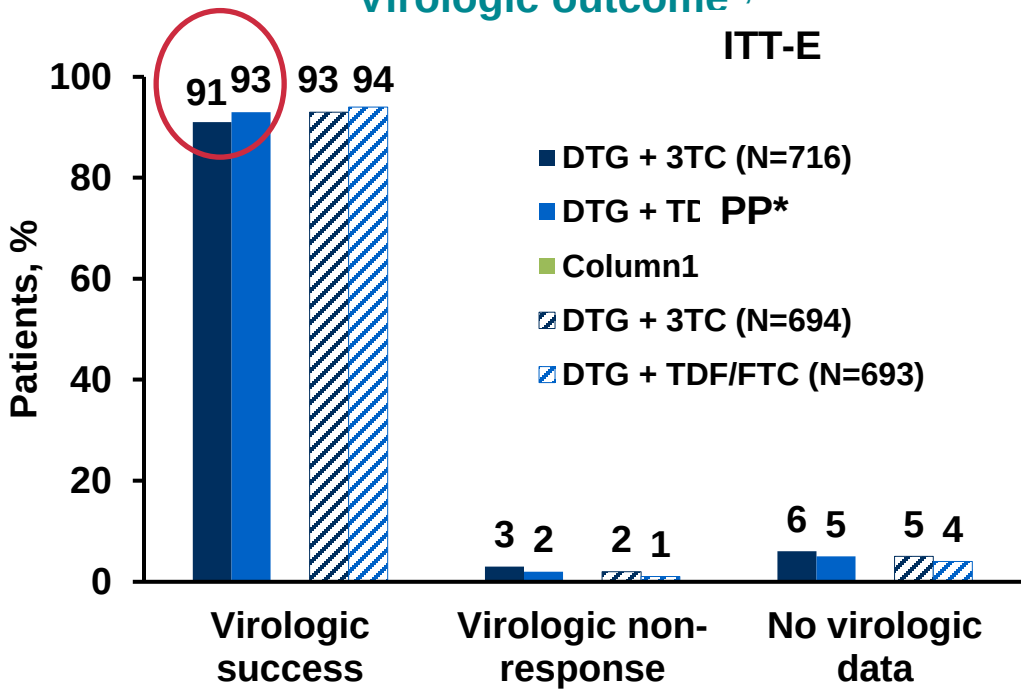
Baseline stratification factors: plasma HIV-1 RNA (≤100,000 vs >100,000 c/mL) and CD4+ cell count (≤200 vs >200 cells/mm^3).

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

Dolutegravir + lamivudine (DTG+3TC)

GEMINI 1&2 trials

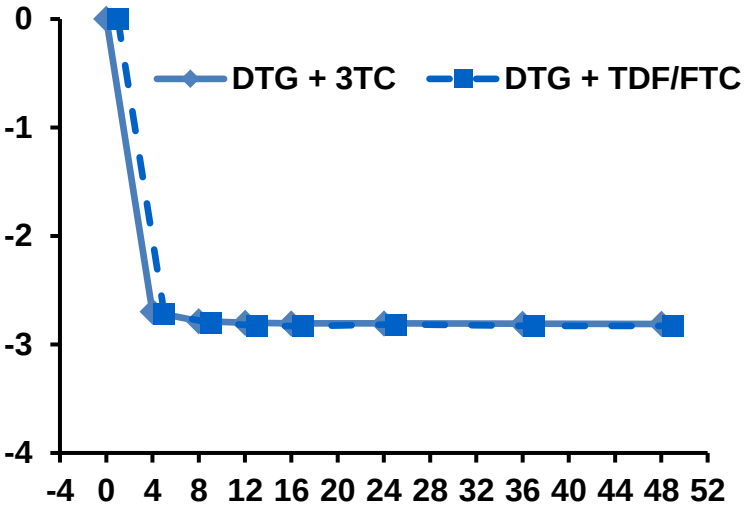
Virologic outcome[1,2]



- Data pooled from both GEMINI-1 and -2 studies
*PP population consisted of subjects in the ITT-E population except those with protocol violations that could affect assessment of antiviral activity; †Based on Cochran-Mantel-Haenszel stratified analysis adjusting for baseline stratification factors: plasma HIV-1 RNA (≤100,000 vs >100,000 c/mL) and CD4+ cell count (≤200 vs >200 cells/mm^3).[1] PP, per protocol

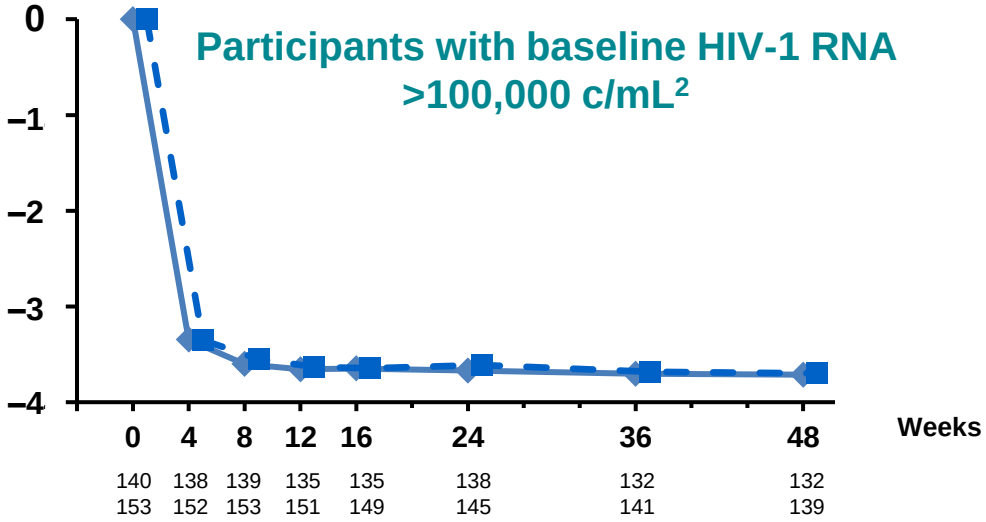
Adapted from: 1. Cahn P, et al. Lancet 2019;393:143–55
2. Cahn P, et al. IAS 2018. TUAB0106LB

Viral Load Decline by study arm



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

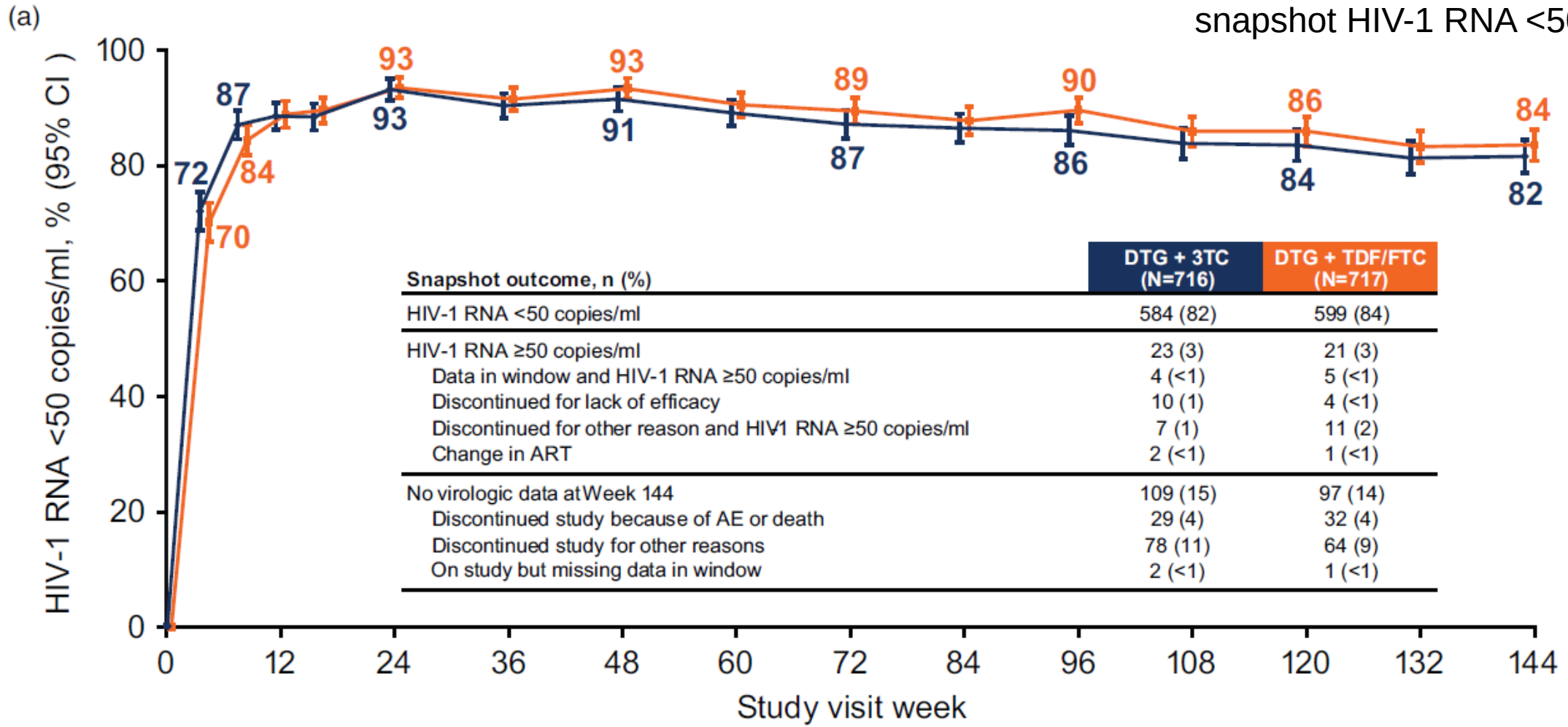
Participants with baseline HIV-1 RNA >100,000 c/mL[2]



	140	138	139	135	135	138	132	132
	153	152	153	151	149	145	141	139

Adapted from: 1. Cahn P, et al. Lancet 2019;393:143–55 plus supplementary appendix
2. Eron J, et al. HIV DART and Emerging Viruses 2018. Oral

Dolutegravir + lamivudine (DTG+3TC) in naive patients: 144-week results

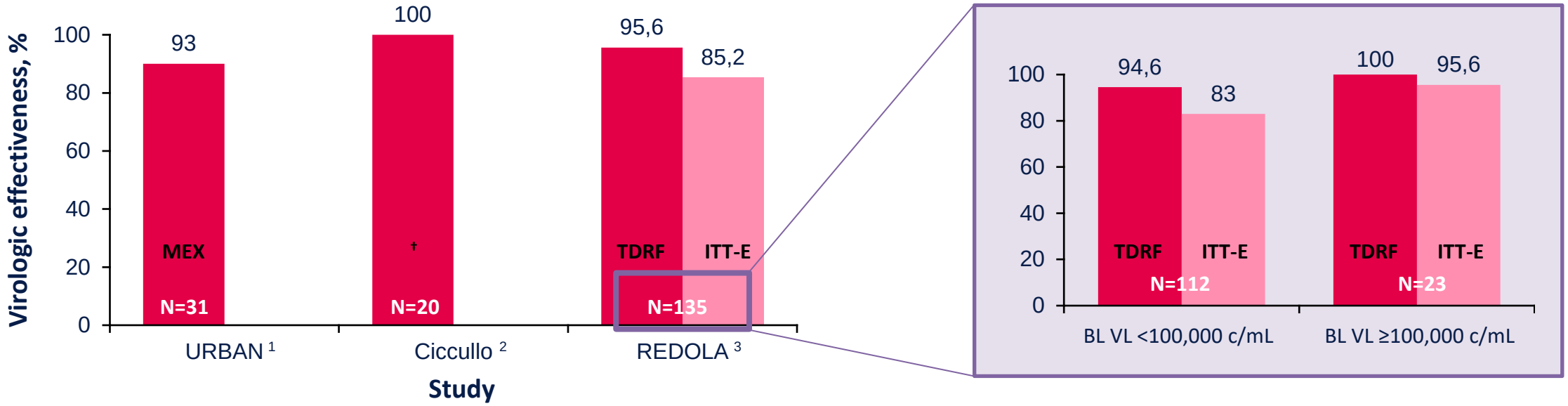


Snapshot outcome, n (%)	DTG + 3TC (N=716)	DTG + TDF/FTC (N=717)
HIV-1 RNA <50 copies/ml	584 (82)	599 (84)
HIV-1 RNA ≥50 copies/ml	23 (3)	21 (3)
Data in window and HIV-1 RNA ≥50 copies/ml	4 (<1)	5 (<1)
Discontinued for lack of efficacy	10 (1)	4 (<1)
Discontinued for other reason and HIV1 RNA ≥50 copies/ml	7 (1)	11 (2)
Change in ART	2 (<1)	1 (<1)
No virologic data atWeek 144	109 (15)	97 (14)
Discontinued study because of AE or death	29 (4)	32 (4)
Discontinued study for other reasons	78 (11)	64 (9)
On study but missing data in window	2 (<1)	1 (<1)

One DTG + 3TC participant (with no adherence) , not meeting CVW criteria, developed M184V (week 132) and R263R/K (week 144) conferring a 1.8-fold change in susceptibility to DTG.

Cahn P et al. AIDS. 2022 ;36:39-48.

Real-world Treatment-naïve Studies* with DTG + 3TC



Endpoint	24 weeks	24 weeks	48 weeks
Effectiveness outcome of patients on treatment with DTG + 3TC at endpoint	HIV-1 RNA <50 c/mL or 50–200 c/mL with subsequent HIV-1 RNA <50 c/mL	Proportion of patients achieving virologic suppression (HIV-1 RNA <50 c/mL)	Proportion of patients achieving virologic suppression (HIV-1 RNA <50 c/mL)

*Includes studies reporting applicable effectiveness outcomes for ≥20 treatment-naïve patients receiving DTG + 3TC. Reported effectiveness outcomes vary between studies; †Study reports "all patients"; ‡When emergence of resistance-associated mutations have been reported

ITT-E, intention to treat exposed; **MEX,** missing equals excluded; **TRDF**. treatment-related discontinuations equals failure; **VL,** viral load

1. Scholten et al. EACS 2021; Virtual and London, UK. Poster PE2/52.; **2.** Ciccullo A, et al. AIDS Res Hum Retroviruses 2021;37:486–8 **3**. Cabello A, et al. IAS 2021. Poster PEB183;
4. Cahn P, et al. Lancet 2019;393:143–55 **5.** Cahn P, et al. J Acquir Immune Defic Syndr 2020;83:310–8 **6**. Rolle CP, et al. AIDS. 2021;35:1957-1965.

DOLUTEGRAVIR + LAMIVUDINE

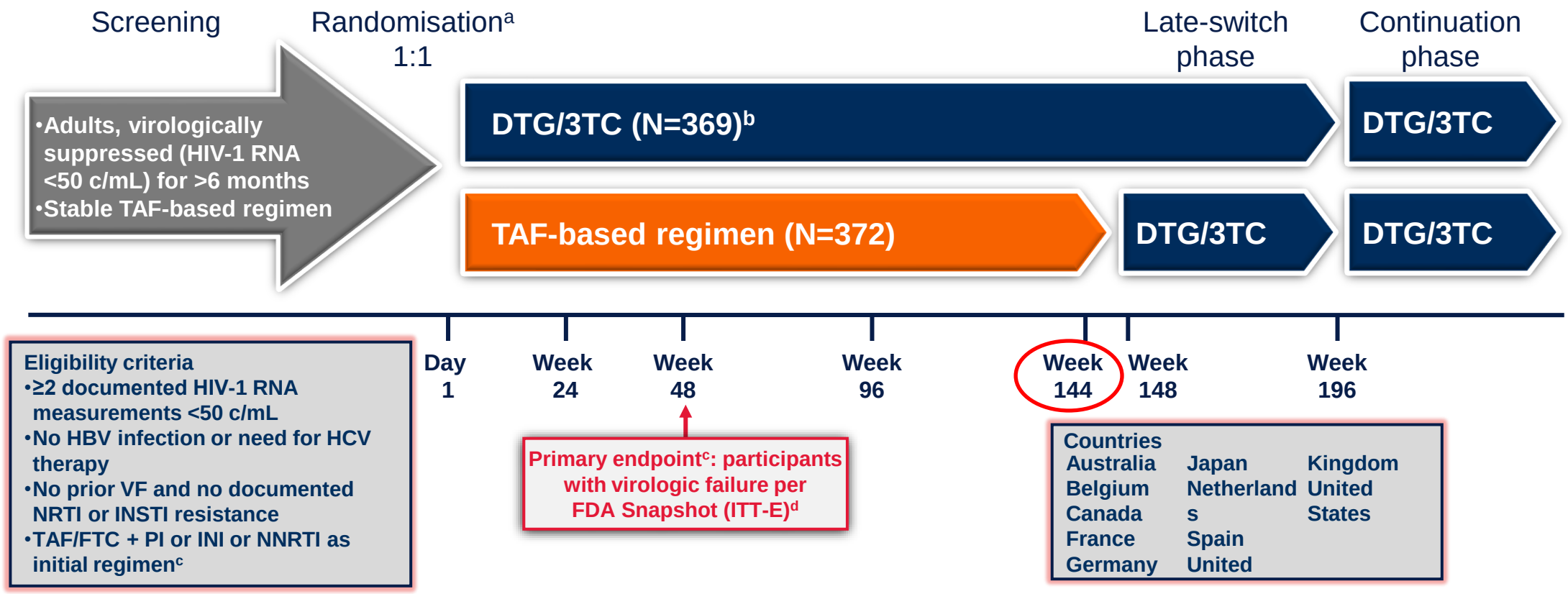
in virologically suppressed patients

Clinical trials vs Real World Evidence

Dolutegravir + lamivudine (DTG+3TC)

TANGO trial

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



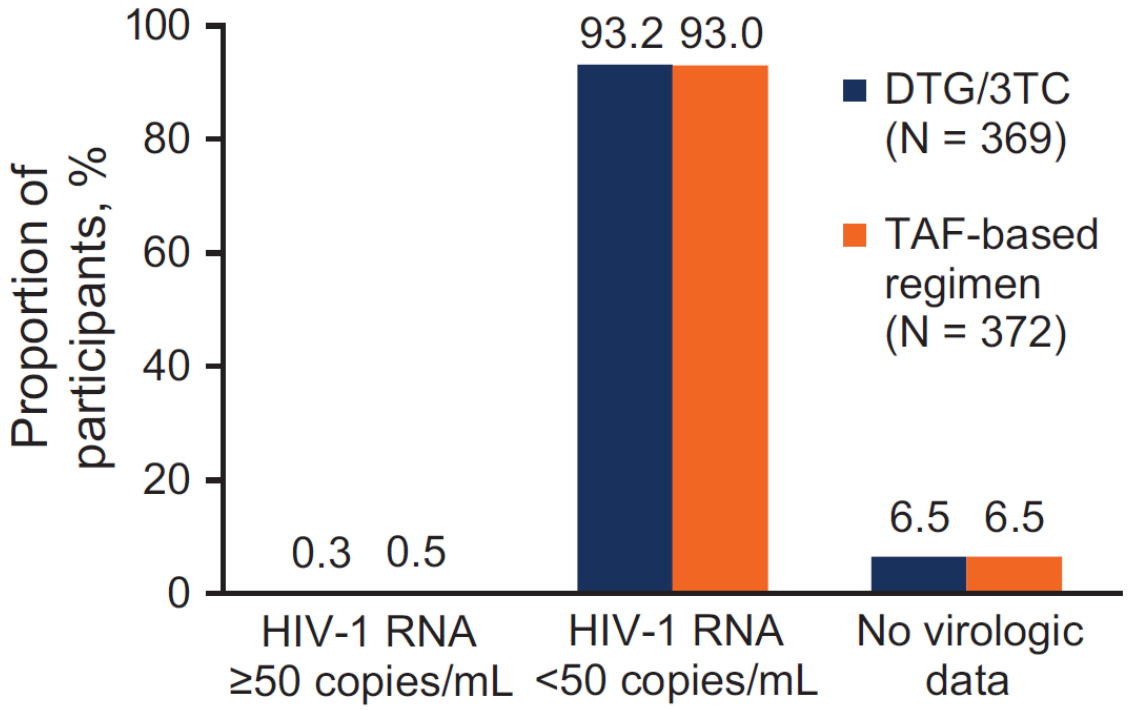
Adapted from van Wyk et al. IAS 2019; Mexico City, Mexico. Slides WEAB0403LB.

Dolutegravir + lamivudine (DTG+3TC)

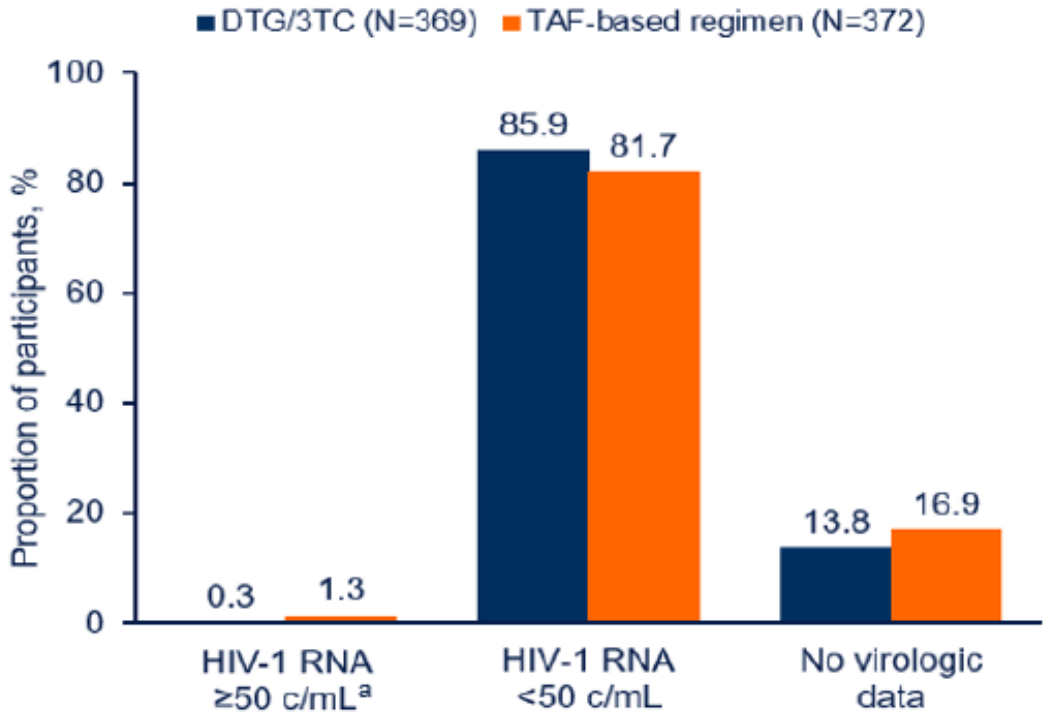
TANGO trial

No emergence of resistance

48-week data



144-week data



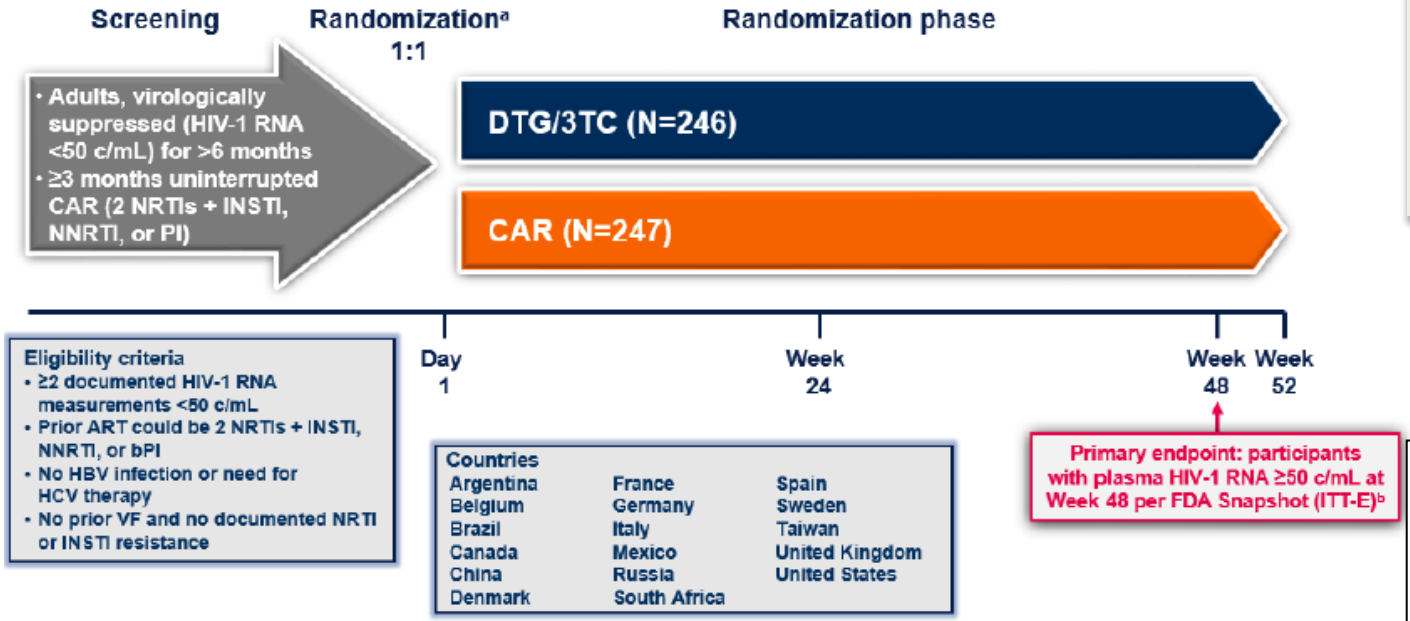
At baseline, the median **CD4+/ CD8+ cell count ratio** was 0.**95** for the DTG/3TC group and **0.96** for the TAF-based regimen group, with median changes at week 48 of **0.03** and **0.05**, respectively.

Van Wick J et al. CID 2020:71(15 October)

van Wyk et al. IAS 2021; Virtual. Poster PEB164.

SALSA trial

Dolutegravir + lamivudine (DTG+3TC)



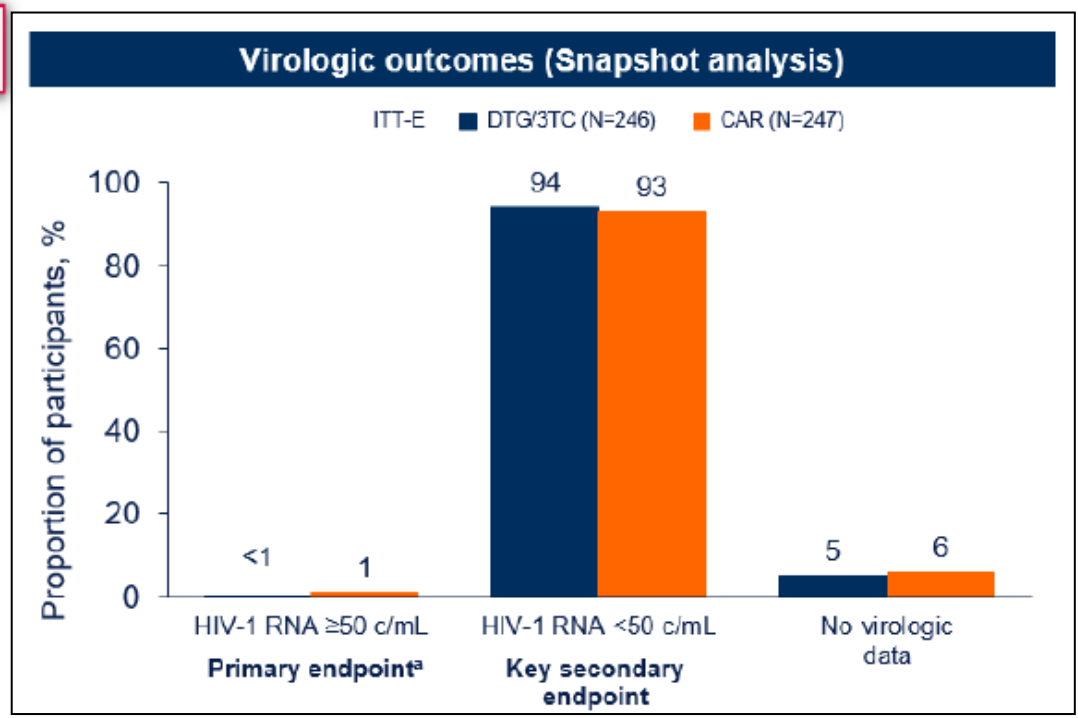
[a]Stratified by baseline third agent class (PI, INSTI, or NNRTI). [b]5% non-inferiority margin.

No emergence of resistance
(no one with CVW*)

*CVW: confirmed virological withdrawal

SALSA compared to **TANGO** trial:

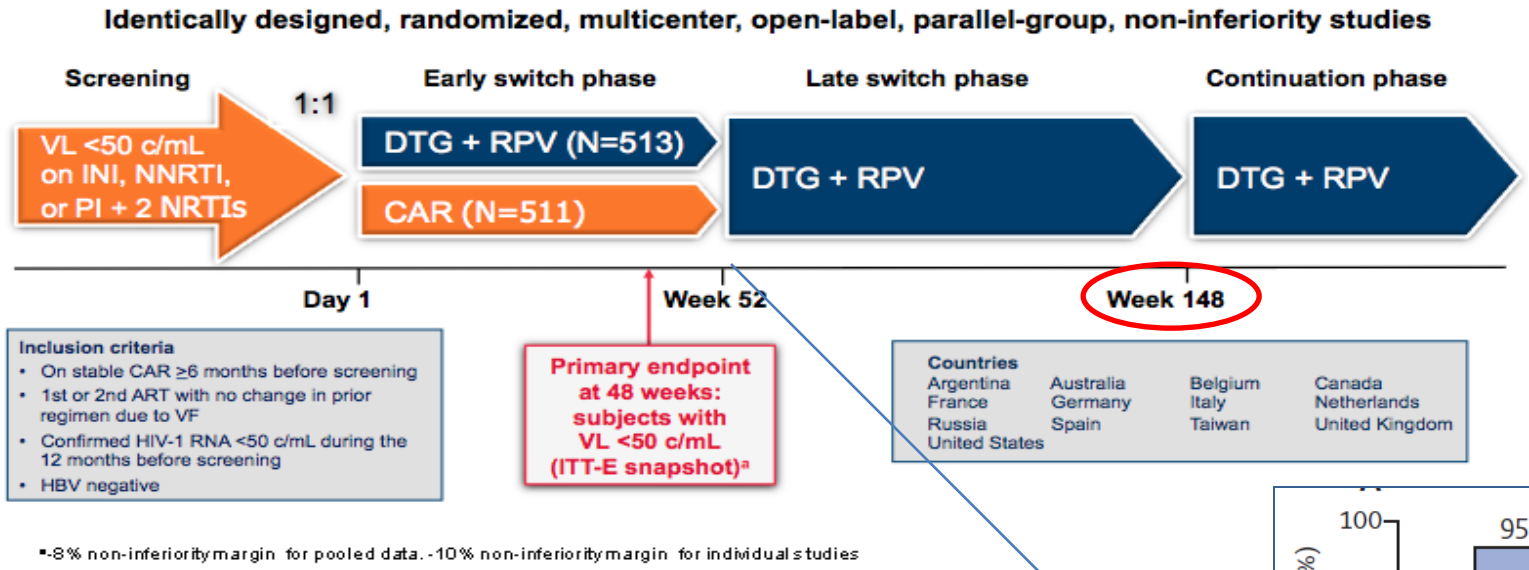
- ✓ More women (~ 44-34 vs 7%)
- ✓ More non-white (~ 40 vs 23%)
- ✓ More > 50 years (~ 40 vs 20%)

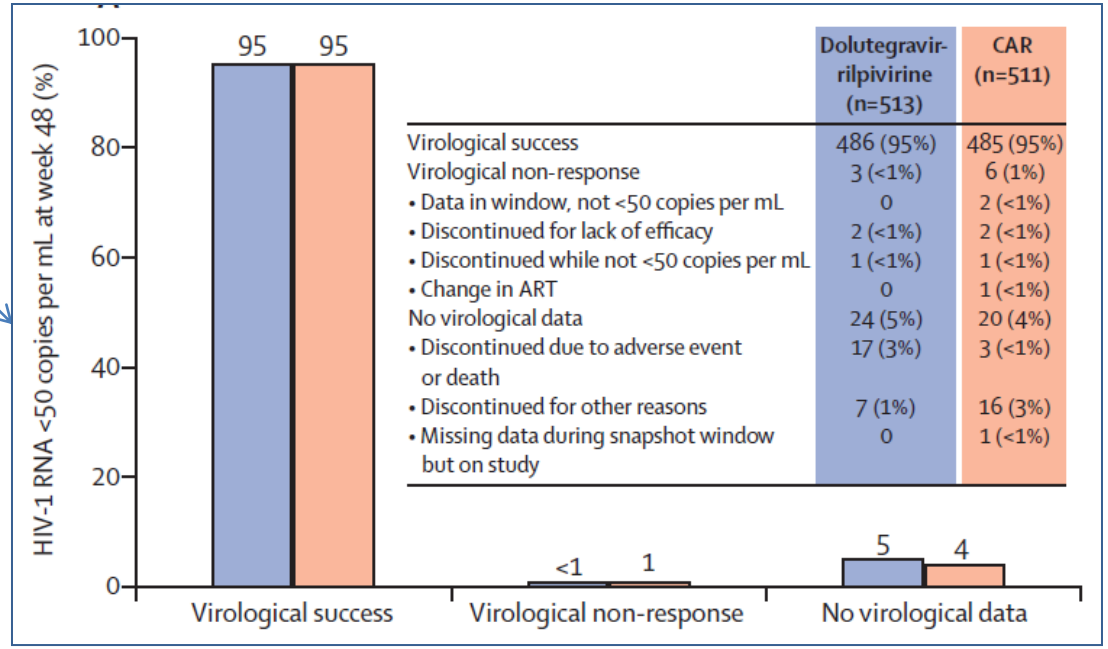


Llibre et al. IAS 2021; Virtual. Slides OALB0303

Dolutegravir + rilpivirine (DTG + RPV)

SWORD 1&2 trials



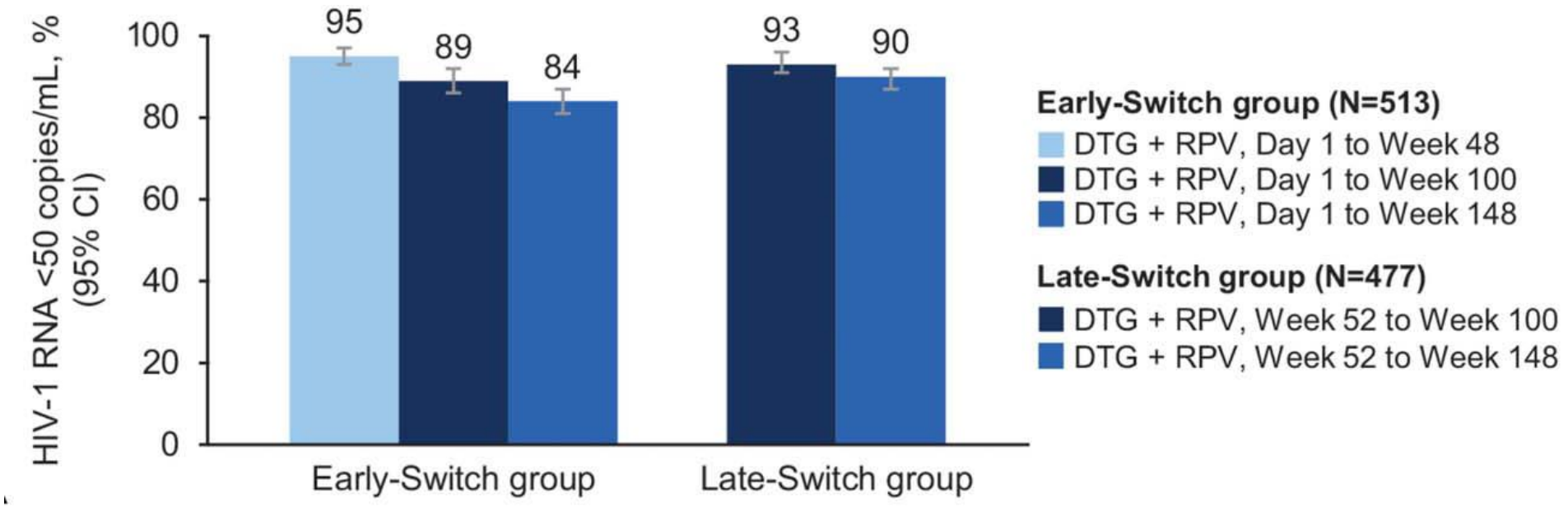


	Dolutegravir-rilpivirine (n=513)	CAR (n=511)
Virological success	486 (95%)	485 (95%)
Virological non-response	3 (<1%)	6 (1%)
• Data in window, not <50 copies per mL	0	2 (<1%)
• Discontinued for lack of efficacy	2 (<1%)	2 (<1%)
• Discontinued while not <50 copies per mL	1 (<1%)	1 (<1%)
• Change in ART	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%)

Entry criteria:
- no prior virologic failure
- no documented resistance mutations
- no HBV infection

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

SWORD 1&2: virological efficacy at week 148



Emergence of resistance?

Van Wick J et al. JAIDS 2020;85;3

SWORD 1&2: resistance data at week 148

Virological failure in **11 pts** (1%): 8 in Early switch, 3 in Late switch

			Resistance mutations[a]				
			Baseline (GenoSure)[b]		CVW		
Week of failure	Previous regimen	Viral loads, copies/mL[c]	NNRTI	INSTI	NNRTI	INSTI	Fold change in sensitivity[d]
24	EFV/TDF/FTC	88; 466; 162	None	G193E	None	G193E	DTG, 1.02
36	EFV/TDF/FTC	1,059,771; 1018; <40	None	None	K101K/E	None	RPV, 0.75
64[e]	DTG/ABC/3TC	833; 1174; <40	None	N155N/H, G163G/R	None	V151V/I	—
76[e]	ATV, ABC/3TC	162; 217; 195	V108I	L74I	Assay failed		—
88	DTG/ABC/3TC	278; 2571; 55	None	None	E138E/A	None	RPV, 1.61 DTG, 0.72
88	RPV/TDF/FTC	147; 289; 503	Sample unavailable		K103N, V179I	None	RPV, 5.24
100	EFV/TDF/FTC	651; 1105; 300	K101E, E138A	G193E	K101E, E138A, M230M/L	Assay failed	RPV, 31
100	ATV, RTV, TDF/FTC	280; 225; 154	None	None	None	None	—
112	RAL/TDF/FTC	118; 230; 324	None	E157Q, G193E, T97T/A	M230M/L	E157Q, G193E	RPV, 2 DTG, 1.47
112	DRV, RTV, TDF/FTC	148; 219; 307	Viral load below assay cutoff		Viral load below assay cutoff		—
136[e]	EFV/TDF/FTC	4294; 7247; 40,020; 3378	Assay failed		E138A, L100L/I	Assay failed	RPV, 4.14

6/990 pts

48 weeks

100 weeks

149 weeks

Van Wick J et al.JAIDS 2020;85

DOLUTEGRAVIR + RILPIVIRINE
DOLUTEGRAVIR + LAMIVUDINE

in switching strategies

Real World Evidence

Switch to 2DR in the real word

Study (year)	**Country**	**Study design** (years)	**Patients**	**Dual regimens** (pts)	**setting**
Fabbiani M et al. (2021)	**Italy** (11 centres)	Retrospective	1666	**DTG+3TC**: 332 **DTG+RPV**: 69 3DR: 1334	switch
Pierone G et al. (2020)	US and Puerto Rico	Retrospective (2017-19)	6069	**DTG/RPV**: 545 3DR: 5524	switch
Teira R et al. (2021)	Spain	Retrospective (2012-2017)	7481	3DR: 5992 2DR: 1489 (**DTG/RPV**: 293)	with and w/out virological suppression at switch
Deschanvres C. et al. (2021)	France (Dat'AIDS cohort)	Retrospective (2014-18)	1374	**DTG+xTC**: 575 **DTG+RPV**: 799	switch
Ward D et al. (2020)	US	Retrospective (2018)	278	DTG+bPI: 203 **DTG+RPV**: 75	with and w/out virological suppression at switch
Galizzi N et al. (2020)	**Italy**	Retrospective (2014-18)	374	**DTG+3TC**: 307 **DTG+RPV**: 67	switch
Ciccullo A et al. (2019)	**Italy** (7 centres)	Retrospective	416	**DTG+3TC**: 229 **DTG+RPV**: 187	switch
Palacios R et al. (2018)	Spain	Retrospective (2015-16)	104	**DTG+RPV**: 104	switch
Capetti AF et al. (2018)	**Italy** (8 centers)	Retrospective (2014-15)	132	**DTG+RPV**: 132	with and w/out virological suppression at switch
Gantner P et al. (2017)	France	Retrospective (2014-15)	152	**DTG+RPV**: 152	switch

Fabbiani M et al. HIV Med. 2021;22:843-853.
Pierrone et al. CROI 2020, P0491
Teira R, et al 2021. PLoS ONE 2021;16(4) e0249515
Deschanvres C et al. J Antimicrob Chemother. 2021 Oct 15

Galizzi N et al. Int J Antimicrob Agents. 2020;55:105893
Ward D et al. AIDS Research and Treatment 2020
Ciccullo A et al. Antivir Ther. 2019;24:63-67.

Palacios R et al. J Int Assoc Provid AIDS Care. 2018 Jan-Dec;
Capetti AF et al. Ann Pharmacother. 2018;52:740-746.
Gantner P et al. HIV Med. 2017;18:704-708

2 year outcomes of DTG/RPV in virologically suppressed HIV-infected PLHIV: Real-world data from the German JUNGLE cohort

JUNGLE is an ongoing non-interventional, 3 year, prospective, 24-center cohort study in Germany

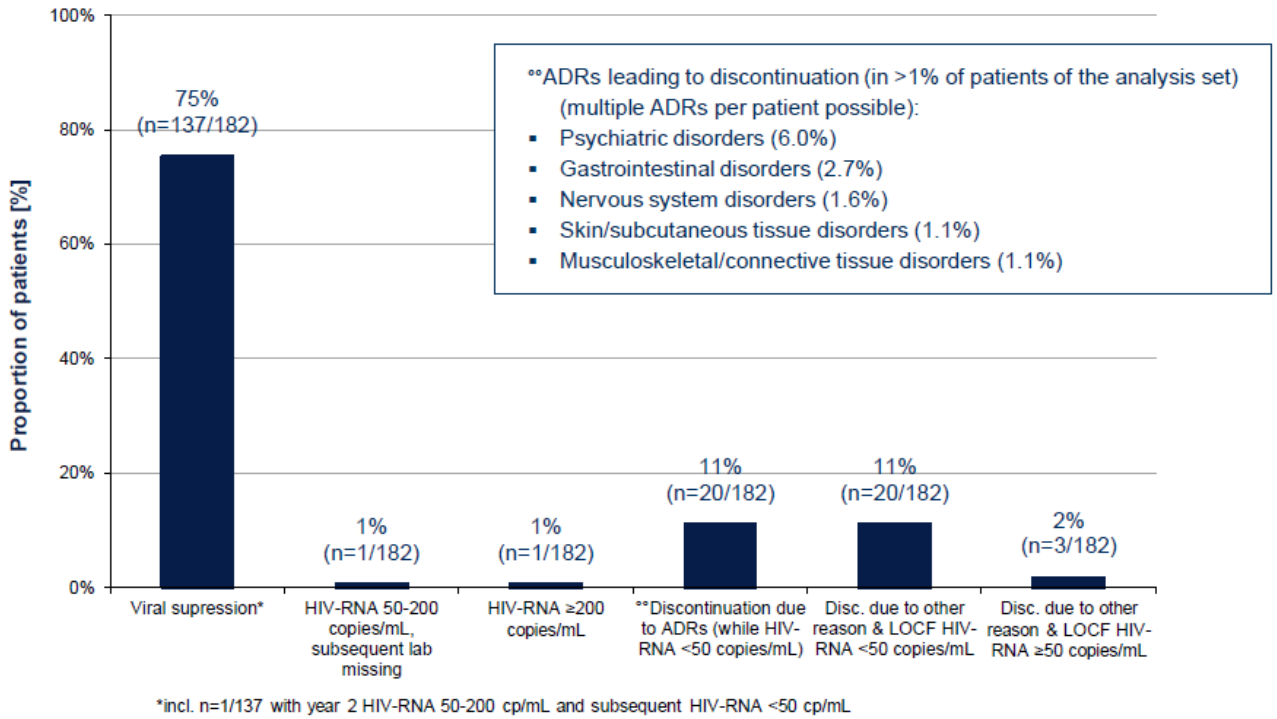
Main inclusion criteria

- Adult HIV-1 infected patients on suppressive ART for ≥6 months switched to DTG/RPV in routine clinical care
- No history of virologic failure
- No INSTI or NNRTI resistance mutations
- No hepatitis B coinfection
- No contraindication based on the SmPC (summary of product characteristics)

Reason for switching:

- side effects of previous regimen (26.6%)
- switch to a single tablet (22.3%)
- reduction of N. of agents (20.2%)

Virologic outcome at 2-year follow up (188 pts)



*incl. n=1/137 with year 2 HIV-RNA 50-200 cp/mL and subsequent HIV-RNA <50 cp/mL

Overall, 11% of individuals discontinued DTG/RPV due to ADRs, with only 1% in the 2nd year.

No patient was discontinued for virologic reasons, and no resistance test during follow-up was performed.

Ummard-Berger K et al. EACS 2021. Poster PE2/2

Dolutegravir-based dual maintenance regimens combined with lamivudine/emtricitabine or rilpivirine: risk of virological failure in a real-life setting

Dat'AIDS cohort study

Previous virological failure: 43.8% and 19.8% for DTG/RPV and DTG/XTC group, respectively.
More than 5 lines of therapy: 58.7% and 37.6%, for DTG/RPV and DTG/XTC group, respectively.

2D-Regimen	Number	Follow Up months	Virolog. Failure (%)	Discontinuation for VF	New resistance at failure
DTG+ xTC	575	19 (IQR: 11-31)	15 (2.6%)	6/15	0
DTG+ RPV	799	20 (IQR: 11-31)	30 (3.8%)	17/30	2

Table 3. Description of genotypes at virological failure with NRTI-, NNRTI- or INSTI-associated resistance mutations

					Resistance mutations			
					historical genotype		genotype at VF	
n	Second regimen	Time to VF	History of VF	Plasma HIV RNA at VF (copies/mL)	NRTI or NNRTI	INSTI	NRTI or NNRTI	INSTI
1	rilpivirine	W75	NNRTI	68, 133	K103H/N/S/T	none	K103H/N/S/T	none
2	rilpivirine	W6	no	531	none	none	E138K	none
3	rilpivirine	W32	no	142, 189[a]	none	none	K101E, E138K	N155H
4	rilpivirine	W86	no	474	not available	none	E138A	none
5	rilpivirine	W34	no	52 310	E138K	none	E138A, L100I	L74I[c]
6	rilpivirine	W5	no	109, 109	K103H/N/S/T	none	K103H/N/S/T	none
7	xTC	W29	NRTI	66, 59[b]	M184V	none	M184V	none

Deschanvres C et al. J Antimicrob Chemother. 2021;15

A comparison between two dolutegravir-based 2D regimens as switch strategies in a multicentre cohort of HIV-1-infected patients

Multicenter cohort in 7 Italian centers, switch in pts with HIV RNA below 50 copies/ml

Regimen	Number	PYFU	Discontinuation	Virolog. Failure (week 48)	Resistance
DTG+3TC	229	344,4	30	10	0
DTG+RPV	187	371,9	13	5	1 (181C, 138Q)

The 2 groups were different for: NRTI mutations, time on viral suppression, previous virological failure, years on ARVs, rate of HCV Ab

At week 48, the estimated probability of remaining on the same regimen was for DTG+3TC: 89,0 %
and for DTG+RPV: 96.1%, log-rank 0.015) .
After adjusting for potential confounders, treatment group was not associated with treatment discontinuation.

Ciccullo A et al. Antivir Ther. 2019;24:63-67.

2-Drug Regimen comparable to 3-Drug Regimens up to 18 months in a real-world settings.

OPERA The Longitudinal Cohort

Table 1. Baseline demographic and clinical characteristics

Characteristic n (%)	DTG/RPV (n=545)	3-DR (n=5,524)	p-value
Age ≥50 years	298 (54.7%)	2,258 (40.9%)	<.0001
Female sex	97 (17.8%)	1,078 (19.5%)	0.5199
Black race	177 (32.5%)	2,445 (44.3%)	<.0001
Hispanic ethnicity	163 (29.9%)	1,139 (20.6%)	<.0001
Care in Southern US	350 (64.2%)	3,146 (57.0%)	<.0001
Hx of AIDS	146 (26.8%)	1,565 (28.3%)	0.4453
CD4 Count >500 cells/ µL	424 (77.8%)	3,959 (71.7%)	0.0178
Hx of Syphilis	164 (30.1%)	1,895 (34.3%)	0.0475
Any Comorbidity	475 (87.2%)	4,416 (79.9%)	<.0001

Figure 1. Distribution of core agents in the 3-DR group*

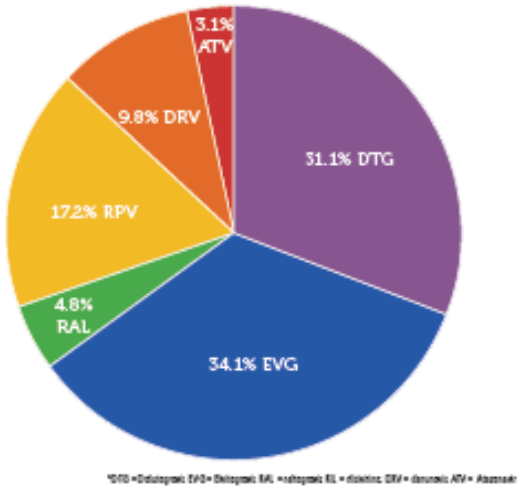


Figure 2. Unadjusted cumulative probability of discontinuation of 2-DR versus 3-DR

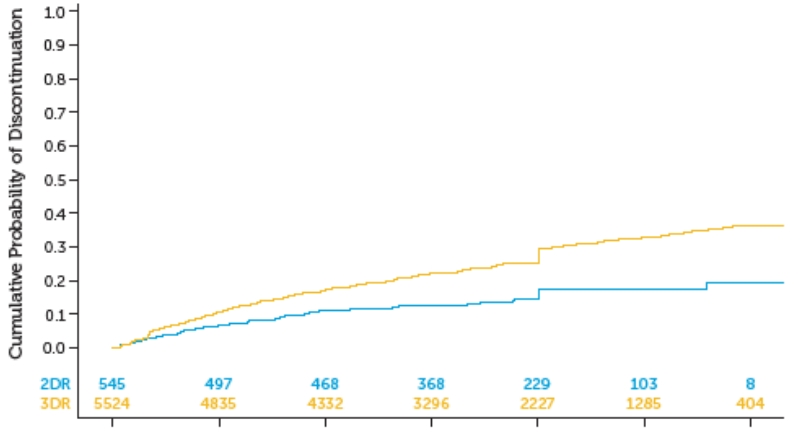


Figure 3. Unadjusted cumulative probability of virologic failure of 2-DR versus 3-DR

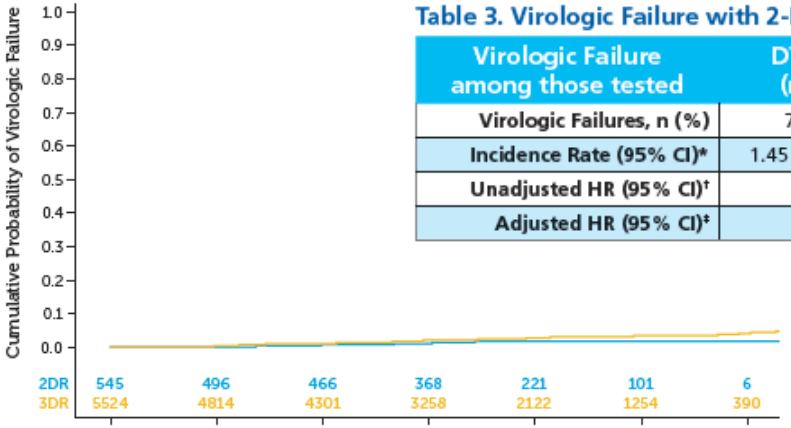


Table 3. Virologic Failure with 2-DR versus 3-DR

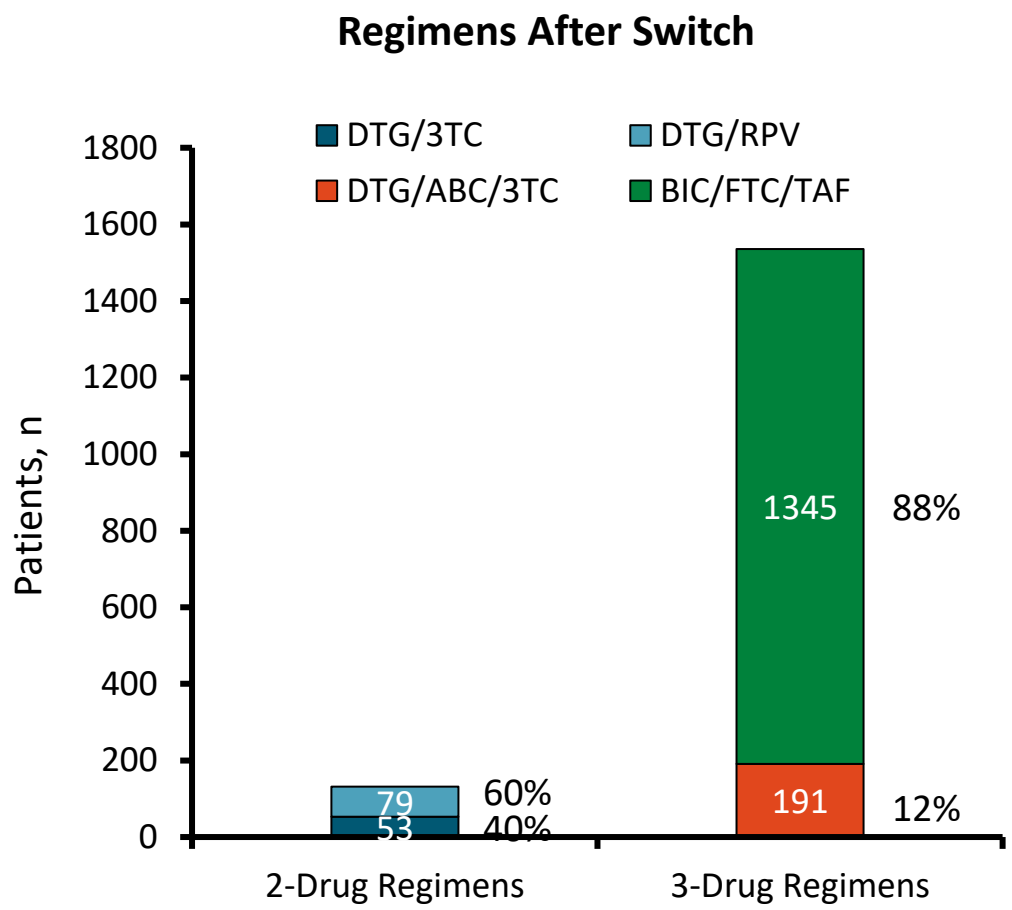
Virologic Failure among those tested	DTG/RPV (n=545)	3-DR (n=5,524)	p-value
Virologic Failures, n (%)	7 (1.4%)	124 (2.8%)	0.0823
Incidence Rate (95% CI)*	1.45 (0.69, 3.03)	2.63 (2.21, 3.14)	0.1422
Unadjusted HR (95% CI)†	1.0	1.38 (0.43, 4.43)	0.1279
Adjusted HR (95% CI)‡	1.0	1.32 (0.61, 2.90)	0.4813

*per 100 person-years
†HR=Hazard Ratio
‡HR adjusted for age, sex, race, ethnicity, region, CD4 cell count, history of comorbidities

Pierone G et al. CROI 2021; Poster 0491

Virologic Failure Among Treatment-Experienced, Suppressed PWH Switching to 2-Drug or 3-Drug Regimens

- Retrospective observational study using EMR data from Trio Health HIV Research Network for cohort of ~60,000 PWH in United States
- Study population (N = 1668)
  - ≥18 yr at date of switch
  - Treatment-experienced with known previous regimen
  - Switch to 2-drug regimen (DTG/RPV, DTG/3TC), or frequently used 3-drug STRs started after Nov 2017, with dispensing data
  - Virally suppressed (<**200** c/mL) at switch (-12 to +1 mo)
- Objective: evaluate risk of virologic failure (2 consecutive HIV-1 RNA measures >200 c/mL)



Sax. IDWeek 2021. Abstr 77.

Slide credit: clinicaloptions.com

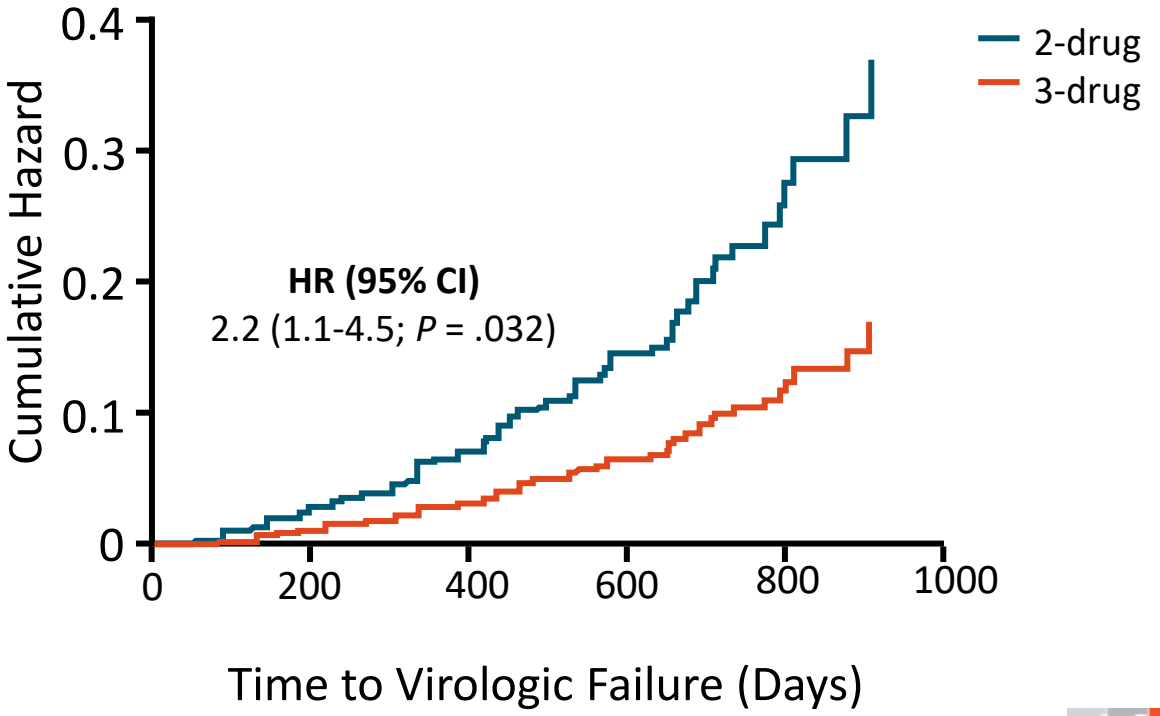
Switch to 2-Drug or 3-Drug Regimens: Time to Virologic Failure

Results influenced by:

- ✓ Patients receiving 2-drug regimens differed from those in CTs
- ✓ Poor adherence to medications
- ✓ Multiple patient factors (eg, resistance data) were unknown

Adjusted Analysis

- Risk of virologic failure higher with 2- vs 3-drug STRs after adjusting for race, gender, age, and baseline eGFR; adjusting for CD4+ cell count not feasible



Sax. IDWeek 2021. Abstr 77.

Modified from Slide credit: clinicaloptions.com

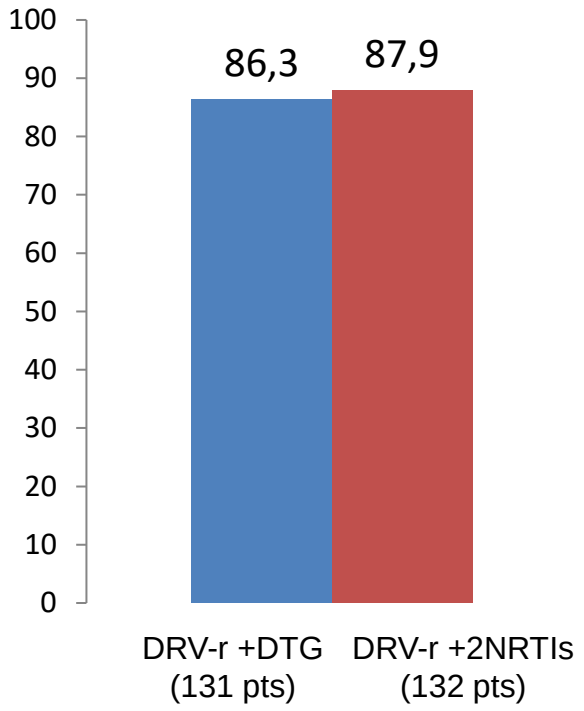
Boosted PI + (X)

DARUNAVIR-R + DOLUTEGRAVIR
DARUNAVIR-R + RILPIVIRINE
in virologically suppressed patients

RANDOMIZED TRIALS

Darunavir-r + DTG

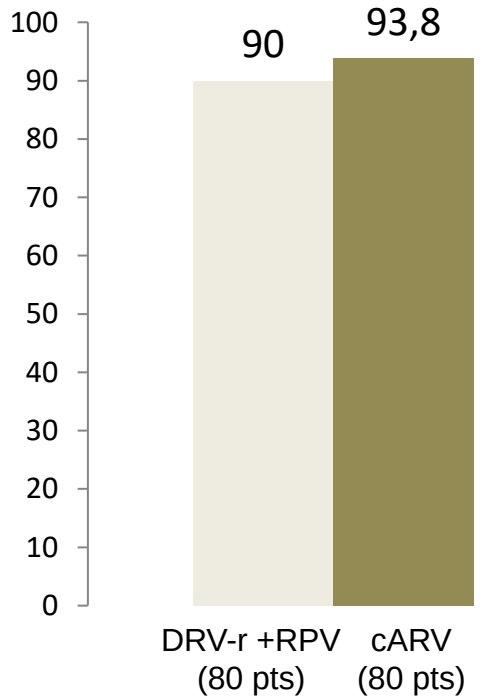
48-week data, randomized, switch trial (DUALIS), HIV RNA < 50 c/ml



No emergence of resistance

Darunavir-r + RPV

24-week data, randomized, switch trial (PROBE-2), HIV RNA < 50 c/ml



Spinner CD et al. Open Forum Infect Dis 2020;7:ofaa356

Maggiolo F et al. J Antimicrob Chemother. 2020;75:1332-1337.

Boosted PI + (X) in clinical practice

Study	**Design**	**Study arm** (N. of pts)	Historical genotype resistance	**Follow up** weeks	**HIV RNA < 50 c/ml** (%)	**New resistance mutations (VF)**
Navarro J [1] **(**DARIL study)	retrospective, any viral load	DRV/r **+ RPV** (84)	In 41 pts: NRTI: 87% NNRTI: 44% PI: 23%, II: 7%	48 wks	87.7	0 (4 VF)
Castagna [2] (DAU study)	retrospective **switch**	uATV + DTG (151)	?	median: 62 wks	90	0 (2 VF)
Jabłonowska [3]	retrospective, any viral load	DRV/r + DTG (76)	?	48 wks	92	0 (1 VF)
Capetti A [4]	retrospective, any viral load	DRV/r + DTG (130)	118 with resistance to 1–5 ARV classes.	96 wks	95	0 (2 VF)
Hawkins KL [5]	retrospective, any viral load	DRV/r + DTG (65)	DRV primary mutations: 8%	median: 419 days	94	0 (0 VF)
Navarro J [6]	retrospective, **switch**	DRV/r + DTG (50)	In 41 pts: NRTI: 93.2% NNRTI: 72.7% PI: 15%	median: 25 mos	98	0 (1 VF)
Vizcarra P [7]	retrospective, **switch**	DRV/r + DTG (51)	NRTI: mean 1.2 NNRTI: mean 2.4 PI: mean 3.5	48 wks	90	0 (0 VF)

1. Navarro J et al. 2020; 2 Castagna et al. AIDS 2019; 3. Jabłonowska E et al Plos One 2018; 4. Capetti A et al. HIV Clin Trials 2018; 5. Hawkins KL et al. Antivir Ther. 2019; 5. Navarro J et al. Pharmacotherapy. 2019; Vizcarra P et al. Antivir Ther 2019

LONG ACTING for HIV therapy

CABOTEGRAVIR + RILPIVIRINE **LA**

in virologically suppressed patients

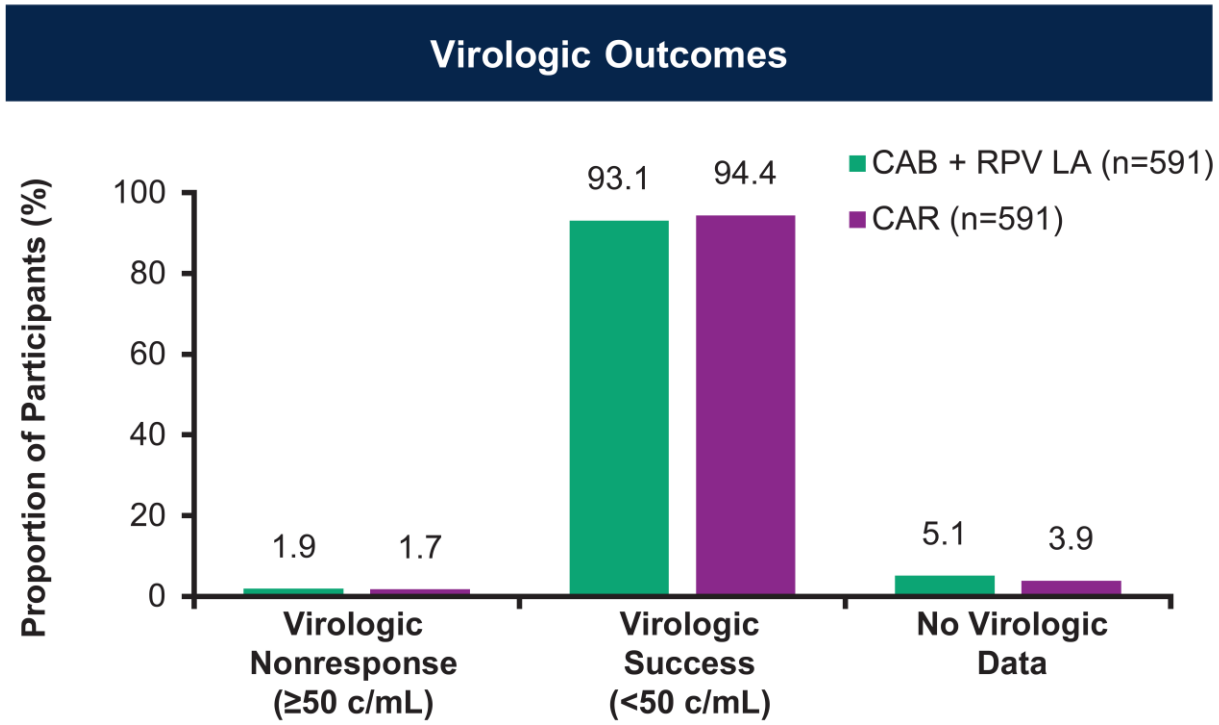
RANDOMIZED TRIALS

Cabotegravir + rilpivirine (CAB + RPV LA)

Some failure with mutations
for RPV and CAB

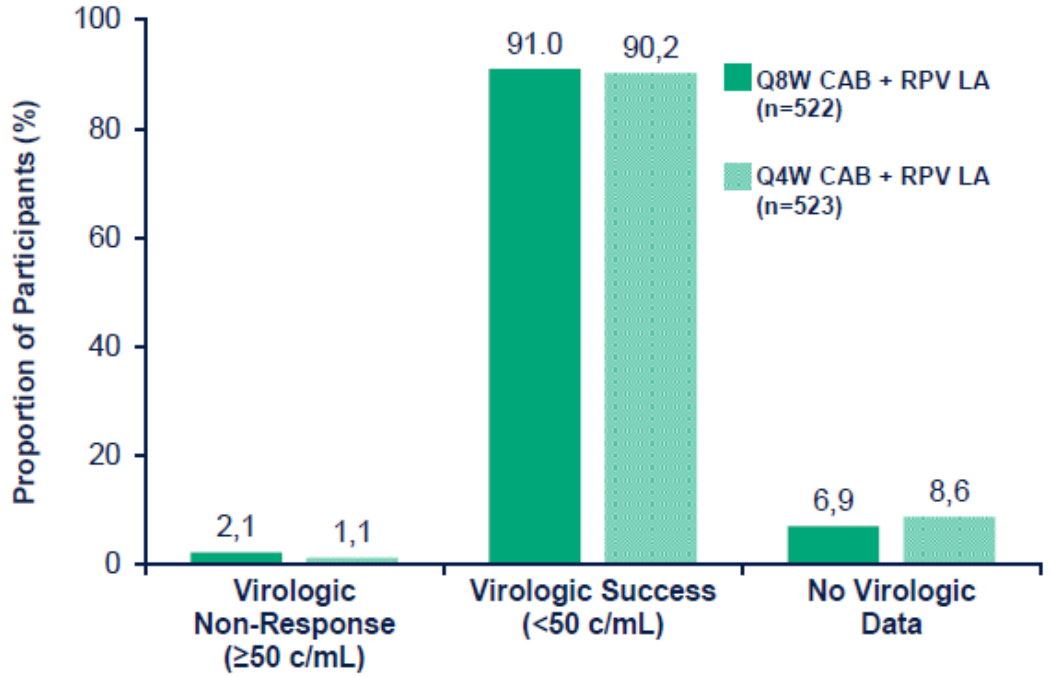
ATLAS and FLAIR Pooled data at week 48

A



Overton et al. IAS 2019; Mexico City, Mexico. Poster MOPEB257.

ATLAS-2M at week 96



Jaeger et al. CROI 2021. Science Spotlight 1753.

Real-World Implementation of LAI-CAB/RPV: Patient Characteristics and Program Success

- 42 patients referred for LAI-ART pilot
  - 74% (35/42) met clinical eligibility criteria
    - **Only 8** patients (19%) initiated LAI-CAB/RPV, with median of 35 (IQR: 20-67) days from writing of prescription to first dose of LAI-CAB/RPV
    - To date, drug access only successful for patients with commercial **health insurance coverage**
  - 26% (7/42) deemed **ineligible**
    - Due to evidence of possible RPV resistance (n = 5), possible hypersensitivity to RPV (n = 1), or HIV-1 nonsuppression (n = 1)
- Authors conclude that LAI-ART implementation challenged by substantial human resources to attain drug, delayed treatment initiation due to insurance denials, and patient ineligibility largely due to potential RPV resistance

Characteristics at Referral	N = 42
Median age, yrs	41
Male, %	83
Black, %	76
Median CD4+ cell count, cells/mm^3	583
Median time HIV-1 RNA <200 c/mL, days	1427
Payer source, %	
▪ Commercial	26
▪ Medicare	19
▪ Medicaid	10
▪ ADAP	45

Collins. ID Week 2021. Abstr 887.

Slide credit: clinicaloptions.com

Thanks for the attention

2-drug regimens era in HIV therapy

Experimental dual regimen	Study	Design	Baseline regimen	Number of pts	Follow-up weeks	Emergent resistance
LOP/r + 3TC [1]	OLE				48	1
ATV/r + 3TC [2]	SALT	switch	bPI	**1051**	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	149	6
DTG + 3TC [6]	GEMINI 1-2	naive	-	1433	144	0
DTG + 3TC [7]	TANGO	switch	any, TAF-based	741	144	0
DTG + 3TC [8]	SALSA	switch	any	503	48	0
DTG + DRV-r [9]	DUALIS	switch	DRV-r based	263	48	0
DRV-r + RPV [10]	PROBE2	switch	any	160	24	0
CAB + RPV (LA)	ATLAS[11]	switch	any	618	48	3
	FLAIR[12]	switch	ABC/3TC/DTG	629	48	3
	ATLAS-2M[13]	switch	ATLAS[11]	1045	96	8

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;65:2112-211;
5. Llibre JM et al. Lancet 2018;391:839-849; 6. Cahn P et al. IAS 2019; slides WEAB0404LB7. 7. van Wyk et al. IAS 2019; slides WEAB0403LB. 8. Llibre et al. IAS 2021; Virtual. Slides OALB0303 9. Spinner CD et al. Open Forum Infect Dis 2020; 10. Maggiolo F. et al. J Antimicrob Chemother. 2020;75:1332-1337. 11. Swindells S et al. N Engl J Med. 2020; 12. Orkin C, et al. N Engl J Med. 2020;382:1124-1135. 13 Overton ET, et al. Lancet. 2021;396:1994-2005

HIV Treatment Guidelines 2021

	naive	switch				
	DTG+3TC*	DTG+3TC	DTG+RPV	bPI+3TC	bDRV+RPV	CAB/RPV LA
EACS				boosted DRV		
IAS USA					-	
DHHS					-	

***** Except for individuals :

- ✓ with pre-treatment HIV RNA >500,000 copies/mL;
- ✓ who are known to have active hepatitis B virus (HBV) coinfection;
- ✓ who will initiate ART before results of HIV genotype testing for reverse transcriptase or HBV testing are available.

EACS: https://www.eacsociety.org/guidelines/eacs-guidelines/eacs-guidelines.html
DHHS: https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/whats-new-guidelines
IAS USA: https://www.iasusa.org/resources/guidelines