9º Congreso SOGAISIDA
Lugo, 18 y 19 de Octubre de 2019

Futuro del Tratamiento Antirretroviral

Santiago Moreno
Hospital U. Ramón y Cajal. UAH. IRYCIS.
Madrid

1 Tratamiento Antirretroviral Actual

HIV Guidelines.

What to Start.

AIDS*info*

Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents

Clinical Review & Education

JAMA | Special Communication

Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults
2018 Recommendations of the International Antiviral Society–USA Panel

Michael S. Saag, MD; Constance A. Benson, MD; Rajesh T. Gandhi, MD; Jennifer F. Hoy, MBBS; Raphael J. Landovitz, MD; Michael J. Mugavero, MD, MHSc; Paul E. Sax, MD; Davey M. Smith, MD; Melanie A. Thompson, MD; Susan P. Buchbinder, MD; Carlos del Rio, MD; Joseph J. Eron Jr, MD; Gerd Fätkenheuer, MD; Huldrych F. Günthard, MD; Jean-Michel Molina, MD; Donna M. Jacobsen, BS; Paul A. Volberding, MD

IMPORTANCE Antiretroviral therapy (ART) is the cornerstone of prevention and management of HIV infection.

OBJECTIVE To evaluate new data and treatments and incorporate this information into updated recommendations for initiating therapy, monitoring individuals starting therapy, changing regimens, and preventing HIV infection for individuals at risk.

EVIDENCE REVIEW New evidence collected since the International Antiviral Society–USA 2016 recommendations via monthly PubMed and EMBASE literature searches up to April 2018; data presented at peer-reviewed scientific conferences. A volunteer panel of experts in HIV research and patient care considered these data and updated previous recommendations.

FINDINGS ART is recommended for virtually all HIV-infected individuals, as soon as possible after HIV diagnosis. Immediate initiation (eg, rapid start), if clinically appropriate, requires adequate staffing, specialized services, and careful selection of medical therapy. An integrase strand transfer inhibitor (InSTI) plus 2 nucleoside reverse transcriptase inhibitors (NRTIs) is generally recommended for initial therapy, with unique patient circumstances (eg, concomitant diseases and conditions, potential for pregnancy, cost) guiding the treatment choice. CD4 cell count, HIV RNA level, genotype, and other laboratory tests for general health and co-infections are recommended at specified points before and during ART. If a regimen switch is indicated, treatment history, tolerability, adherence, and drug resistance history should first be assessed; 2 or 3 active drugs are recommended for a new regimen. HIV testing is recommended at least once for anyone who has ever been sexually active and more often for individuals at ongoing risk for infection. Preexposure prophylaxis with tenofovir disoproxil fumarate/emtricitabine and appropriate monitoring is recommended for individuals at risk for HIV.

CONCLUSIONS AND RELEVANCE Advances in HIV prevention and treatment with antiretroviral drugs continue to improve clinical management and outcomes for individuals at risk for and living with HIV.

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Supplemental content
CME Quiz at jamanetwork.com/learning

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Michael S. Saag, MD, School of Medicine, University of Alabama at Birmingham, 845 19th St S, BBRB 256, Birmingham, AL 35294 (msaag@uabmc.edu).

JAMA. 2018;320(4):379-396. doi:10.1001/jama.2018.8431

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EACS European AIDS Clinical Society

GUIDELINES

Version 9.1
October 2018

English

Documento de consenso de Gesida/Plan Nacional sobre el Sida respecto al tratamiento antirretroviral en adultos infectados por el virus de la inmunodeficiencia humana

(Actualización enero 2018)

Panel de expertos de Gesida y Plan Nacional sobre el Sida

GeSIDA GRUPO DE ESTUDIO DEL SIDA-SEIMC

GOBIERNO DE ESPAÑA | MINISTERIO DE SANIDAD, SERVICIOS SOCIALES E IGUALDAD

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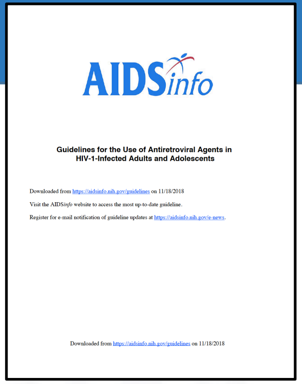


DHHS Guidelines October, Julio 2019

What to Start: Recommended regimens

- BIC/TAF/FTC **(AI)**
- DTG/ABC/3TC[a] **(AI)—if HLA-B*5701 negative**
- DTG plus tenofovir[b]/FTC[a] (**AI** for both TAF/FTC and TDF/FTC)
- RAL[c] plus tenofovir[b]/FTC[a] (**BI** for TDF/FTC, **BII** for TAF/FTC)

DHHS Guidelines. July 10, 2018.


JAMA | Special Communication

Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults

2018 Recommendations of the International Antiviral Society–USA Panel

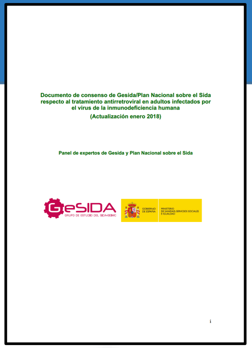
IAS-USA Panel Guidelines 2018

What to Start: Recommended regimens

Generally Recommended Initial Regimens (Listed in Alphabetic Order by InSTI Component)

- Bictegravir/TAF/emtricitabine (evidence rating AIa)[b]
- Dolutegravir/abacavir/lamivudine (evidence rating AIa)[c,d]
- Dolutegravir plus TAF/emtricitabine (evidence rating AIa)[c,e]

IAS/USA Panel Guidelines; July 2018.


Documento de consenso de Gesida/Plan Nacional sobre el Sida respecto al tratamiento antirretroviral en adultos infectados por el virus de la inmunodeficiencia humana

(Actualización enero 2018)

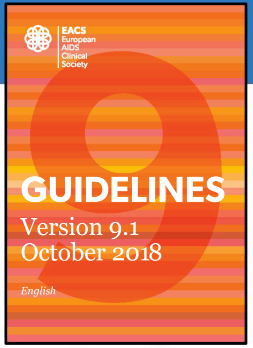
Panel de expertos de Gesida y Plan Nacional sobre el Sida

GeSIDA Guidelines 2019

What to Start: Preferred regimens

3er Fármaco	Pauta†	Comentarios‡
Preferentes. *Pautas aplicables a la mayoría de los pacientes y que en ensayos clínicos aleatorizados han mostrado una eficacia no-inferior a otras pautas también consideradas actualmente como preferentes o superior frente a otras pautas y presentan ventajas adicionales en tolerancia, toxicidad o un bajo riesgo de interacciones farmacológicas.*		
INI	BIC/FTC/TAF*	
	DTG/ABC/3TC	- ABC está contraindicado en pacientes con HLA-B*5701 positivo. - DTG no debe utilizarse en mujeres en edad fértil que no utilicen medidas anticonceptivas eficaces. - No utilizar en pacientes con hepatitis B crónica.
	DTG+FTC/TAF**	- DTG no debe utilizarse en mujeres en edad fértil que no utilicen medidas anticonceptivas eficaces.
	RAL+FTC/TAF**	- RAL puede administrarse indistintamente como 1 comprimido de 400 mg cada 12 horas, o 2 comprimidos de 600 mg (nueva formulación) cada 24 horas.

GeSIDA Guidelines 2019



EACS Guidelines 2018

What to Start: Recommended regimens

Regimen	Dosing
2 NRTIs + INSTI	
ABC/3TC/DTG[i, ii, x]	ABC/3TC/DTG 600/300/50 mg, 1 tablet qd
TAF/FTC[iii] or TDF/FTC[iii] + DTG[x]	TAF/FTC 25/200 mg, 1 tablet qd or TDF/FTC 300/200 mg, 1 tablet qd + DTG 50 mg, 1 tablet qd
TAF/FTC/BIC[xi]	TAF/FTC/BIC 25/200/50 mg, 1 tablet qd
TAF/FTC[iii] or TDF/FTC[iii] + RAL[iv]	TAF/FTC 25/200 mg, 1 tablet qd or TDF/FTC 300/200 mg, 1 tablet qd + RAL 600 mg, 2 tablets qd or + RAL 400 mg, 1 tablet bid
2 NRTIs + NNRTI	
TAF/FTC/RPV[iii] or TDF/FTC/RPV[iii]	TAF/FTC/RPV 25/200/25 mg, 1 tablet qd or TDF/FTC/RPV 300/200/25 mg, 1 tablet qd
2 NRTIs + PI/r or PI/c	
TAF/FTC[iii] or TDF/FTC[iii] + DRV/c[v] or + DRV/r[v]	TAF/FTC 10/200 mg, 1 tablet qd or TDF/FTC 300/200 mg, 1 tablet qd + DRV/c 800/150 mg, 1 tablet qd or + DRV 800 mg, 1 tablet qd + RTV 100 mg, 1 tablet qd or TAF/FTC/DRV/c 10/200/800/150 mg, 1 tablet qd

2 Futuro: Nuevos Fármacos

Antiretrovirals available in 2019 in Spain

NRTIs
- Abacavir
- Didanosine
- Emtricitabine
- Lamivudine
- Stavudine
- Tenofovir
- Zidovudine

NNRTIs
- Delavirdine
- Efavirenz
- Etravirine
- Nevirapine
- Nevirapine XR
- Rilpivirine

PIs
- Atazanavir
- Darunavir
- Fosamprenavir
- Indinavir
- Lopinavir
- Nelfinavir
- Ritonavir
- Saquinavir
- Tipranavir

INIs
- Raltegravir
- Dolutegravir
- Elvitegravir
- Bictegravir

Fusion inhibitors
- Enfuvirtide

CCR5 Inhibitors
- Maraviroc

PK Boosters
- Ritonavir
- Cobicistat

STR
- Atripla
- Eviplera
- Odefsey
- Stribild
- Genvoya
- Triumeq
- Symtuza
- Biktarvy
- Juluca

NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; PK, pharmacokinetic; STR, single tablet regimens
Adapted from http://www.aidsmeds.com/list.shtml and each product's eMC SPC available at http://www.medicines.org.uk/emc/search

Antiretrovirals available in 2019 in Spain

NRTIs
- Abacavir
- Didanosine
- Emtricitabine
- Lamivudine
- Stavudine
- Tenofovir
- Zidovudine

NNRTIs
- Delavirdine
- Efavirenz
- Etravirine
- Nevirapine
- Nevirapine XR
- Rilpivirine
- Doravirine

PIs
- Atazanavir
- Darunavir
- Fosamprenavir
- Indinavir
- Lopinavir
- Nelfinavir
- Ritonavir
- Saquinavir
- Tipranavir

INIs
- Raltegravir
- Dolutegravir
- Elvitegravir
- Bictegravir

Fusion inhibitors
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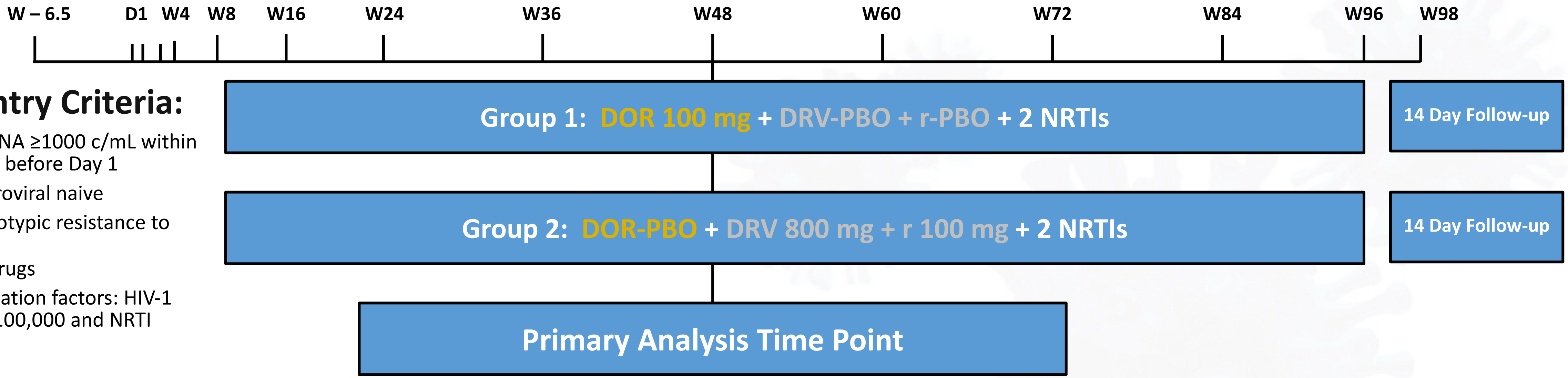
Doravirine

- Doravirine is a novel NNRTI
- **High *in vitro* potency** vs broad panel of isolates including common NNRTI-resistant variants[4]
- **Primary metabolism by CYP3A4;** not an inducer or inhibitor[5]
- **Once daily dosing** (without regard to food)
- **No interactions expected with proton pump inhibitors**

Doravirine vs Darunavir in Naïves: Design

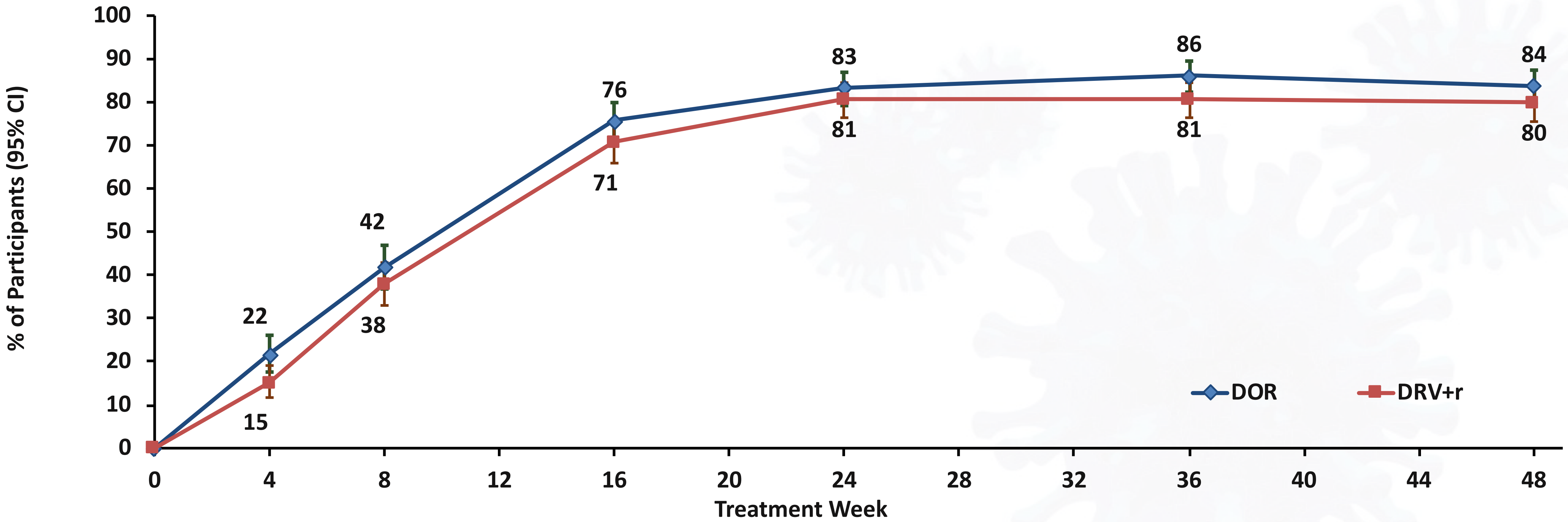


Key Entry Criteria:

- HIV-1 RNA ≥1000 c/mL within 45 days before Day 1
- Antiretroviral naive
- No genotypic resistance to any study drugs
- Stratification factors: HIV-1 RNA > 100,000 and NRTI choice

Source: Molina JM, et al. 24th CROI; Seattle, WA; February 13-16, 2017. Abst. 45LB

Doravirine vs Darunavir in Naïves: Efficacy

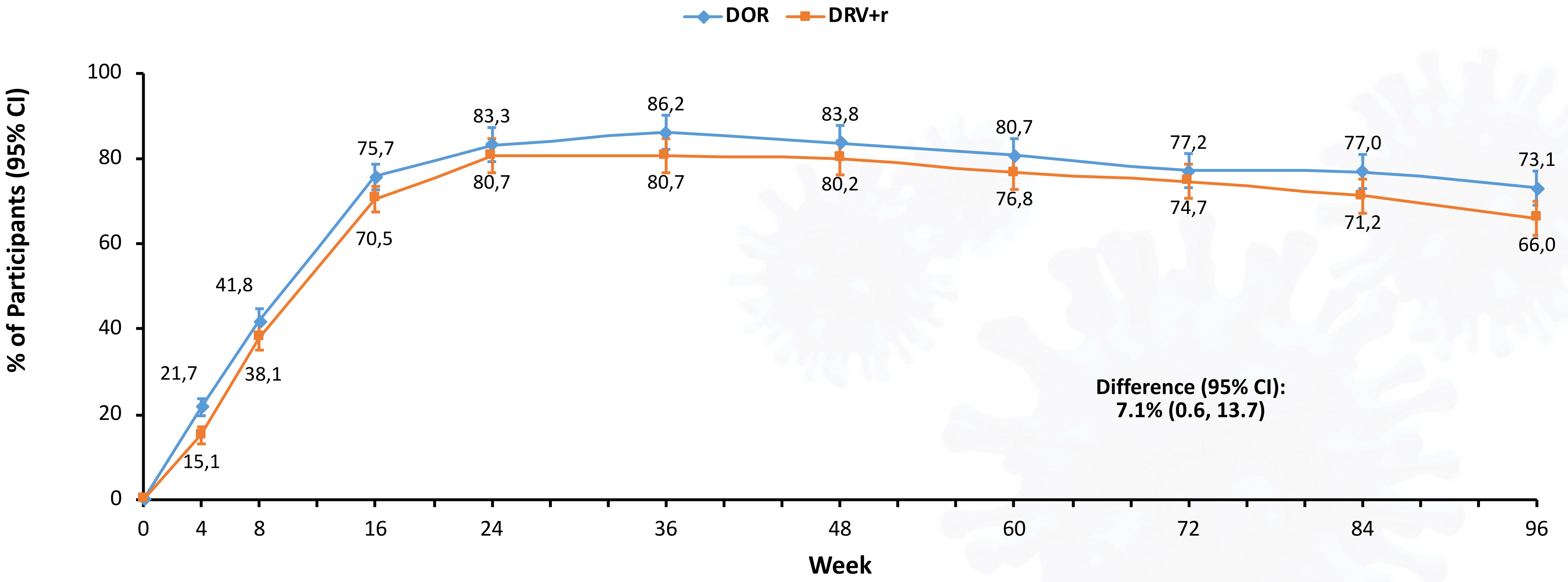


† FDA Snapshot Approach

Difference (95% CI): 3.9% (-1.6%, 9.4%)

Source: Molina JM, et al. 24th CROI; Seattle, WA; February 13-16, 2017. Abst. 45LB.

Doravirine vs Darunavir in naïve at 96 weeks



2/383 (0.5%) participants on doravirine developing resistance to any study drug

Molina JM, et al. AIDS 2018; Amsterdam, the Netherlands; July 23-27, 2018; Abst. LBPEB017

Antiretrovirals available in 2019 in Spain

NRTIs
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- Lamivudine
- Stavudine
- Tenofovir
- Zidovudine

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- Efavirenz
- Etravirine
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- Nevirapine XR
- Rilpivirine
- Doravirine

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- Enfuvirtide

CCR5 Inhibitors
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NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; PK, pharmacokinetic; STR, single tablet regimens

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- Stavudine
- Tenofovir
- Zidovudine

NNRTIs
- Delavirdine
- Efavirenz
- Etravirine
- Nevirapine
- Nevirapine XR
- Rilpivirine
- Doravirine

PIs
- Atazanavir
- Darunavir
- Fosamprenavir
- Indinavir
- Lopinavir
- Nelfinavir
- Ritonavir
- Saquinavir
- Tipranavir

INIs
- Raltegravir
- Dolutegravir
- Elvitegravir
- Bictegravir

Fusion inhibitors
- Enfuvirtide

Entry Inhibitors
- Maraviroc
- Fostemsavir
- Ibalizumab
- Pro140
- UB-421

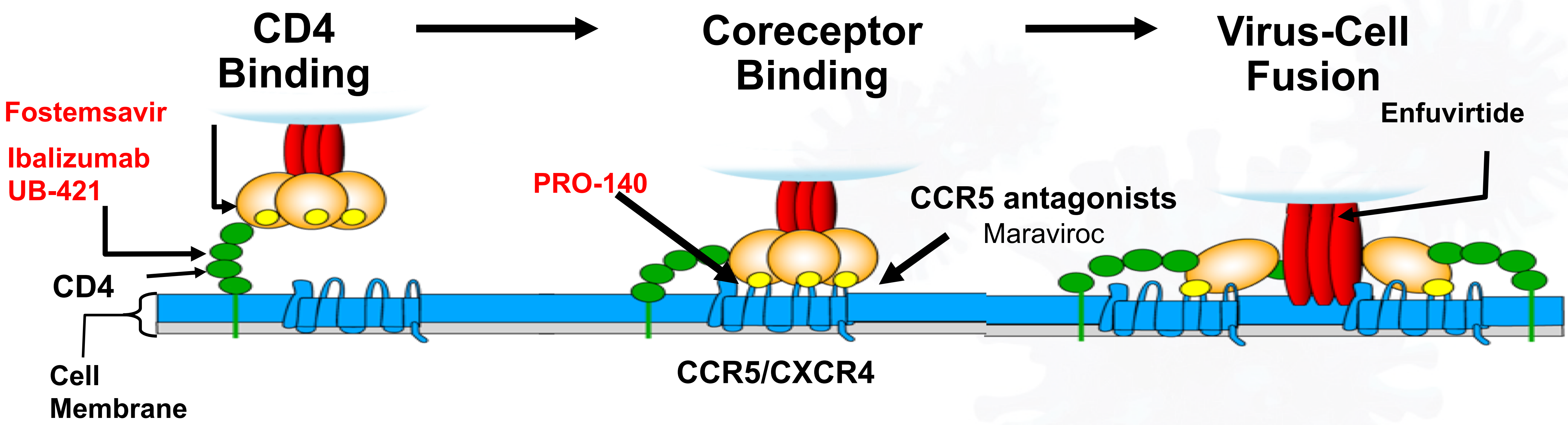
PK Boosters
- Ritonavir
- Cobicistat

STR
- Atripla
- Eviplera
- Odefsey
- Stribild
- Genvoya
- Triumeq
- Symtuza
- Biktarvy
- Juluca

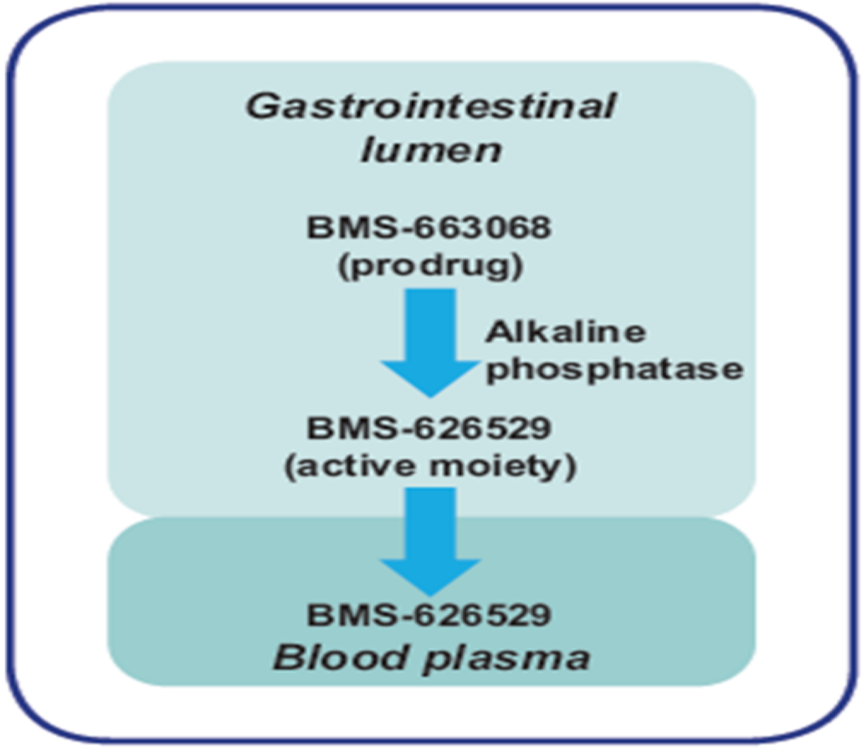
NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; PK, pharmacokinetic; STR, single tablet regimens

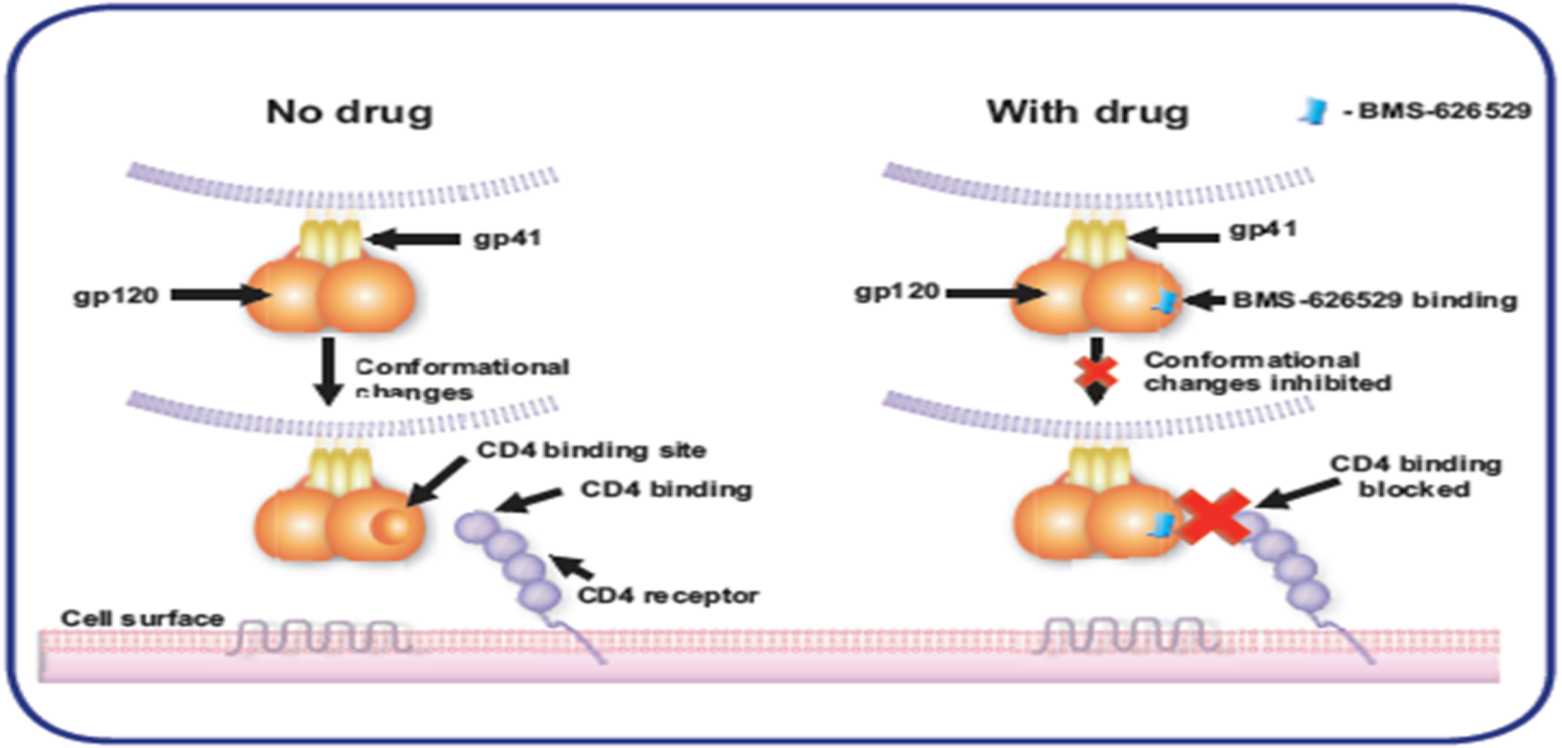
Adapted from http://www.aidsmeds.com/list.shtml and each product's eMC SPC available at http://www.medicines.org.uk/emc/search

Entry Inhibitors



Fostemsavir: Inhibidor del acoplamiento





BRIGHTE study: FOSTEMSAVIR in HIGHLY TREATMENT EXPERIENCED PATIENTS

Randomised Cohort :

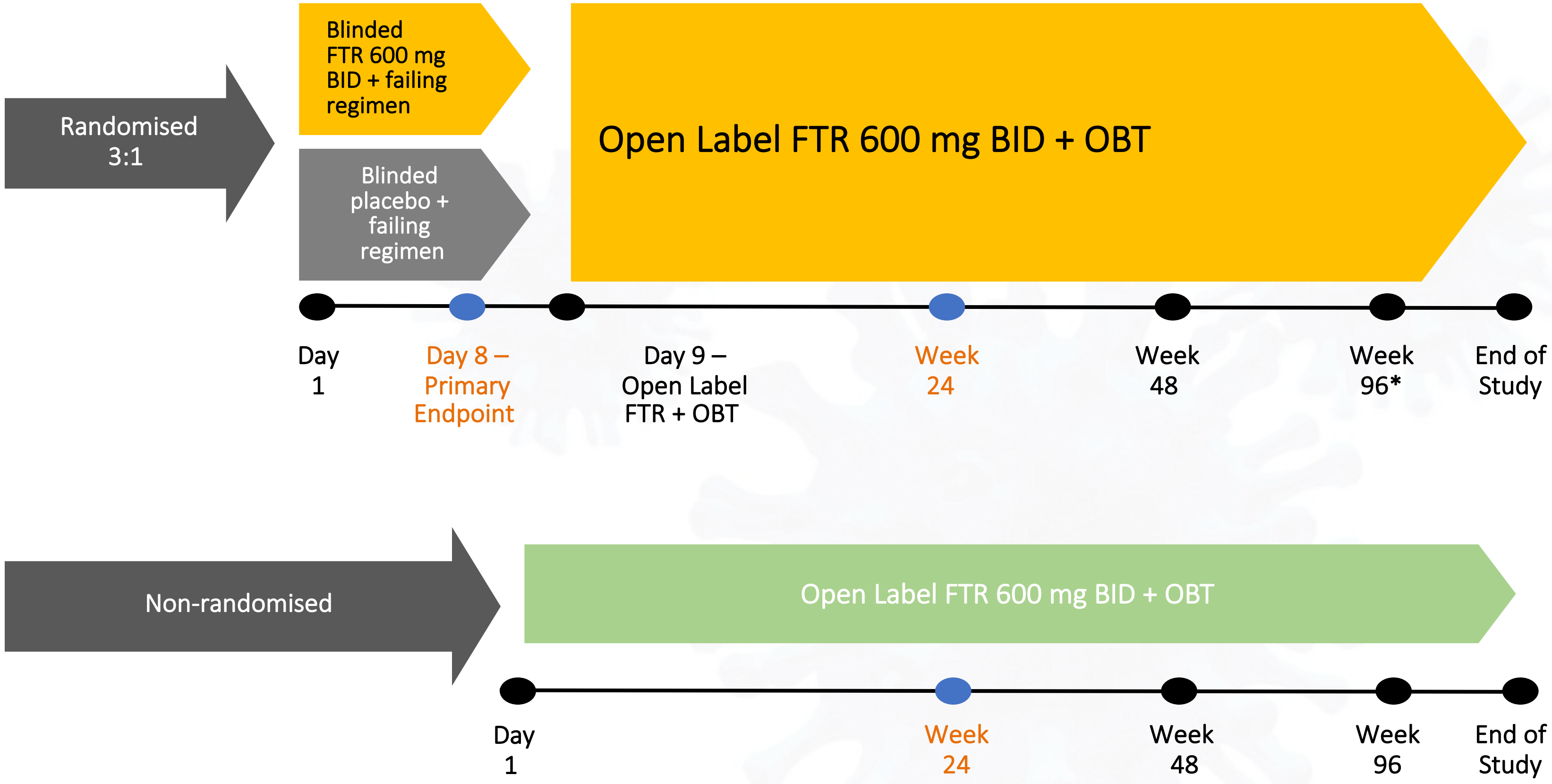
HTE participants failing current regimen with confirmed HIV-1 RNA ≥ 400 c/mL and:

- 1 or 2 ARV classes remaining
  & ≥1 fully active & available agent per class
- Unable to construct viable regimen from remaining agents

Non-randomised Cohort :

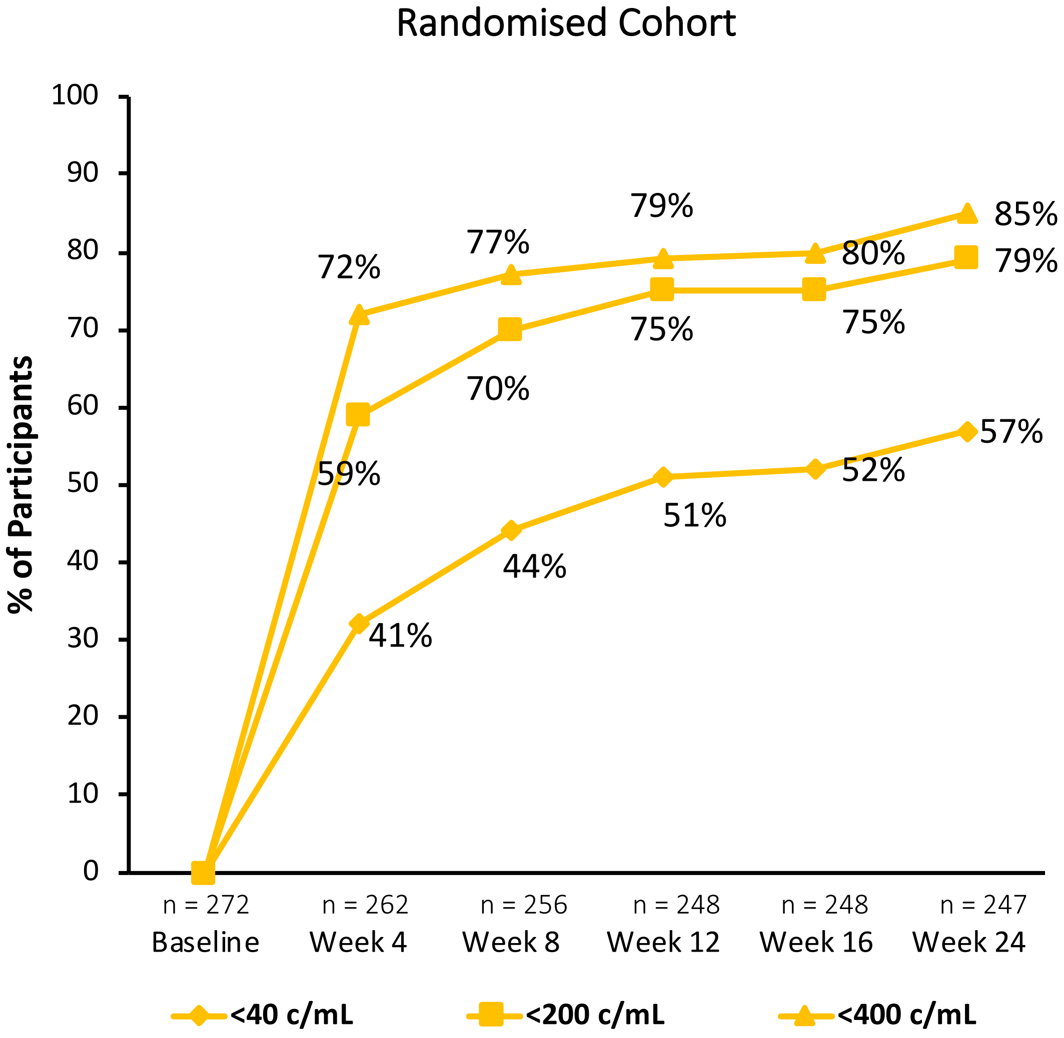
HTE participants, failing current regimen with confirmed HIV-1 RNA ≥400 c/mL and:

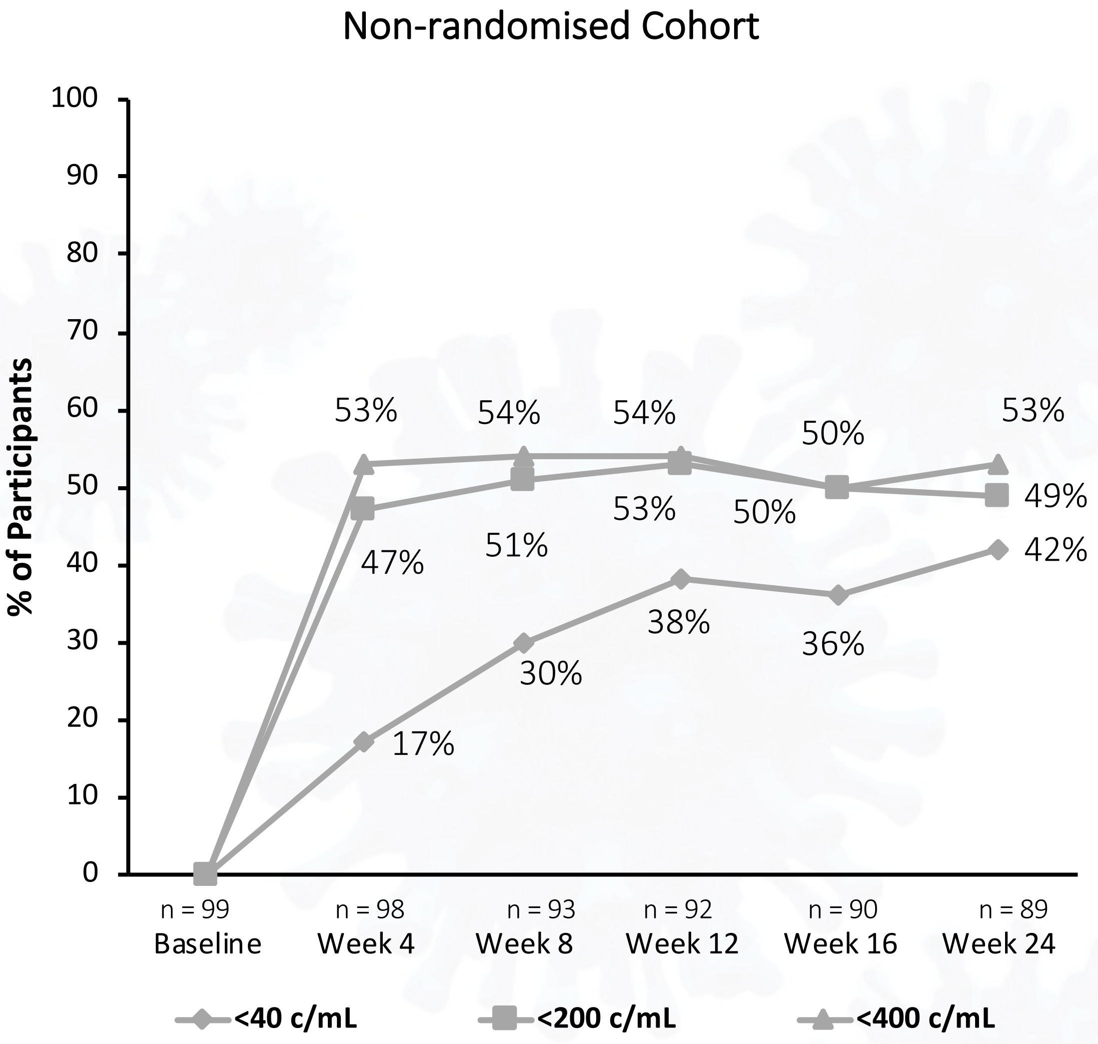
- 0 ARV classes remaining
  and no remaining fully active approved agents



Pialoux G, et al. AIDS 2018; Amsterdam, the Netherlands; July 23-27, 2018; Abst. THPEB045

BRIGHTE study: Results

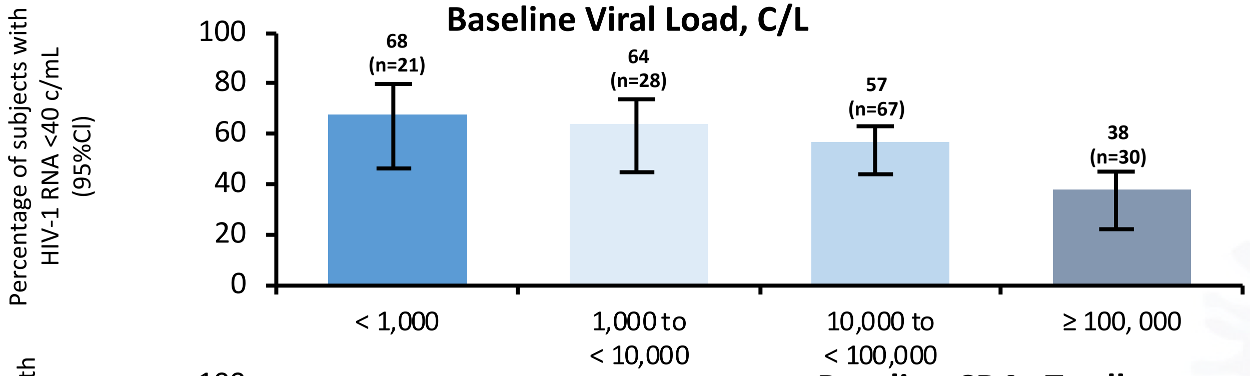


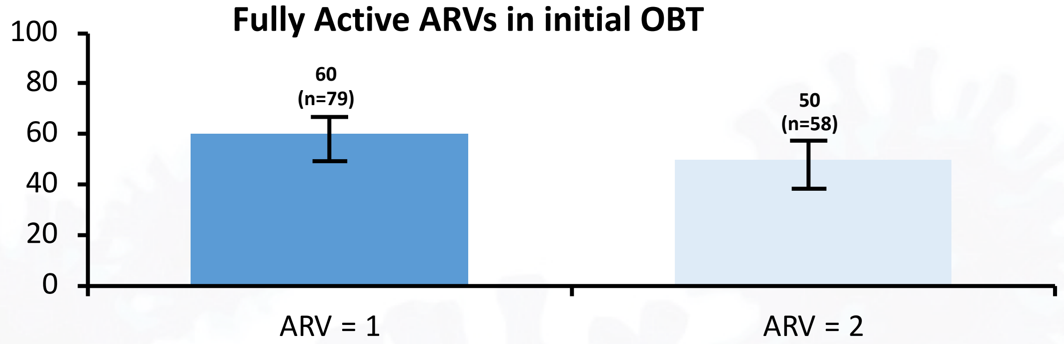


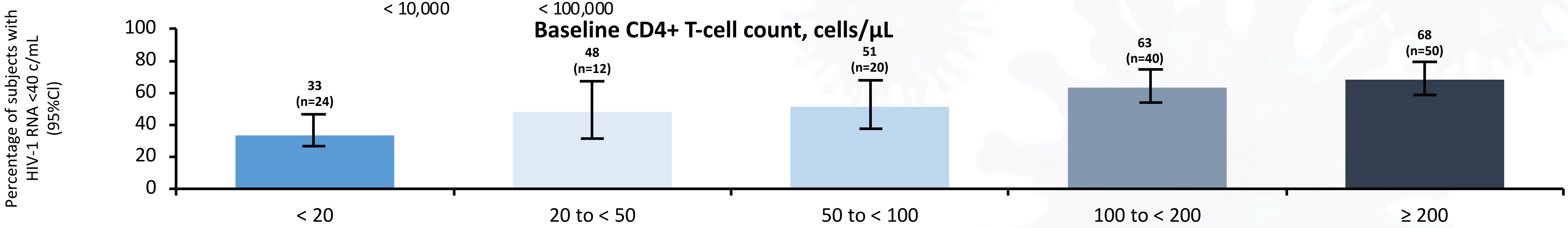
Lataillade M, et al; 16th EACS, Milan, Italy, October 25-27, 2017; Abst. PS8/5.

BRIGHTE study: Results by Baseline Characteristics

Disease Characteristics







Higher response rates:

- Participants with a baseline VL <100,000 c/mL (60%) vs baseline VL≥100,000 c/mL (38%)
- Participants with a baseline CD4+ T-cell counts of ≥50 cells/µL (63%) vs baseline CD4+ T-cell counts of <50 cells/µL (37%)

No difference in response by age, gender, race, and region subgroups

a Analysis performed using FDA Snapshot algorithm

Pialoux G, et al. AIDS 2018; Amsterdam, the Netherlands; July 23-27, 2018; Abst. THPEB045.

3 ¿Cuál es el **paradigma actual** **del TAR?**

¿Cuál es el paradigma actual del TAR?

- Tres fármacos antirretrovirales
- Diario
- Administración oral
- Una sola pastilla
- Éxito virológico 90-100%
- No desarrollo de resistencias
- Escasa toxicidad (<2% EA graves)

¿Se necesita **cambiar el paradigma** de TAR?

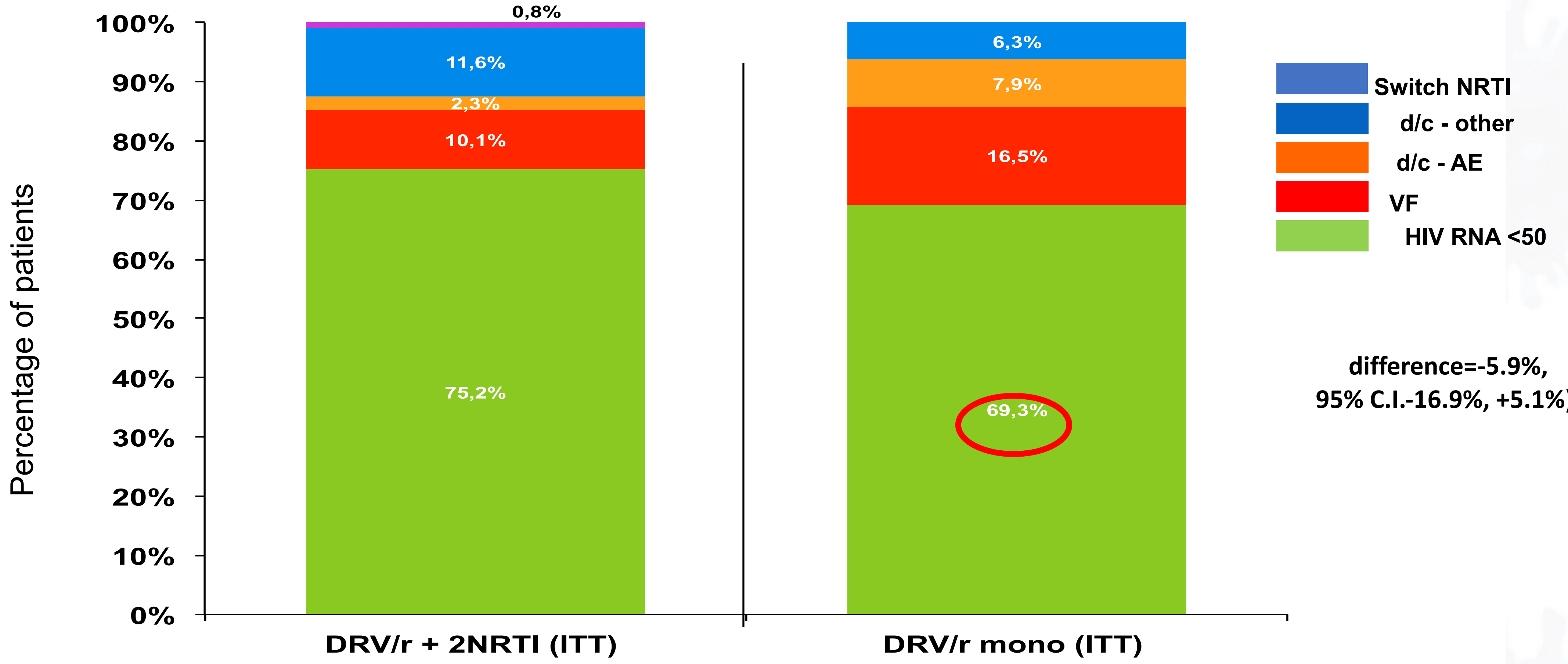
¿Se necesita cambiar el paradigma del TAR?

Característica	Actual	Cambio	Justificación
Número de fármacos	Tres	Menos de 3	Evitar toxicidad y costes
Frecuencia	Diaria	Semanal, cada 1, 2, 3, 6 o 12 meses	Mejorar adherencia y calidad de vida
Vía de administración	Oral	No mejorable	-
Número de pastillas	Una	No mejorable	-
Tasa de éxito virológico	90-100%	No mejorable	-
Desarrollo de resistencias	0%	No mejorable	-
Efectos adversos graves	<2%	No mejorable	-

4

Cambios en el paradigma:
Reducción del
número de fármacos

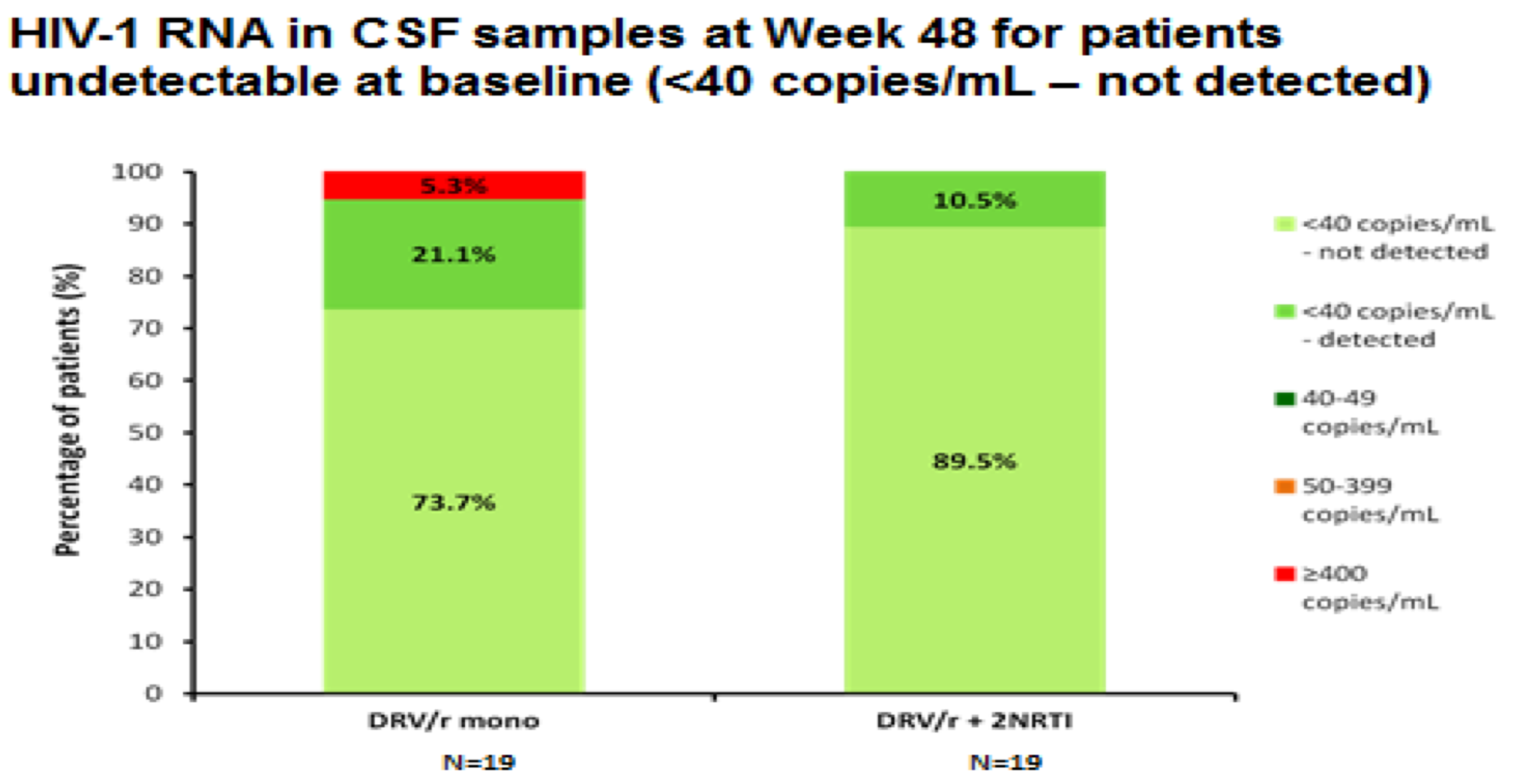
DRV-r en monoterapia no cumplió criterios de no inferioridad frente a DRV/r + 2 ITIAN (Monet, 144 sem)



difference=-5.9%,
95% C.I.-16.9%, +5.1%).

HIV Med. 2012 Aug;13(7):398-405. doi: 10.1111/j.1468-1293.2012.00989.x. Epub 2012 Mar 14.

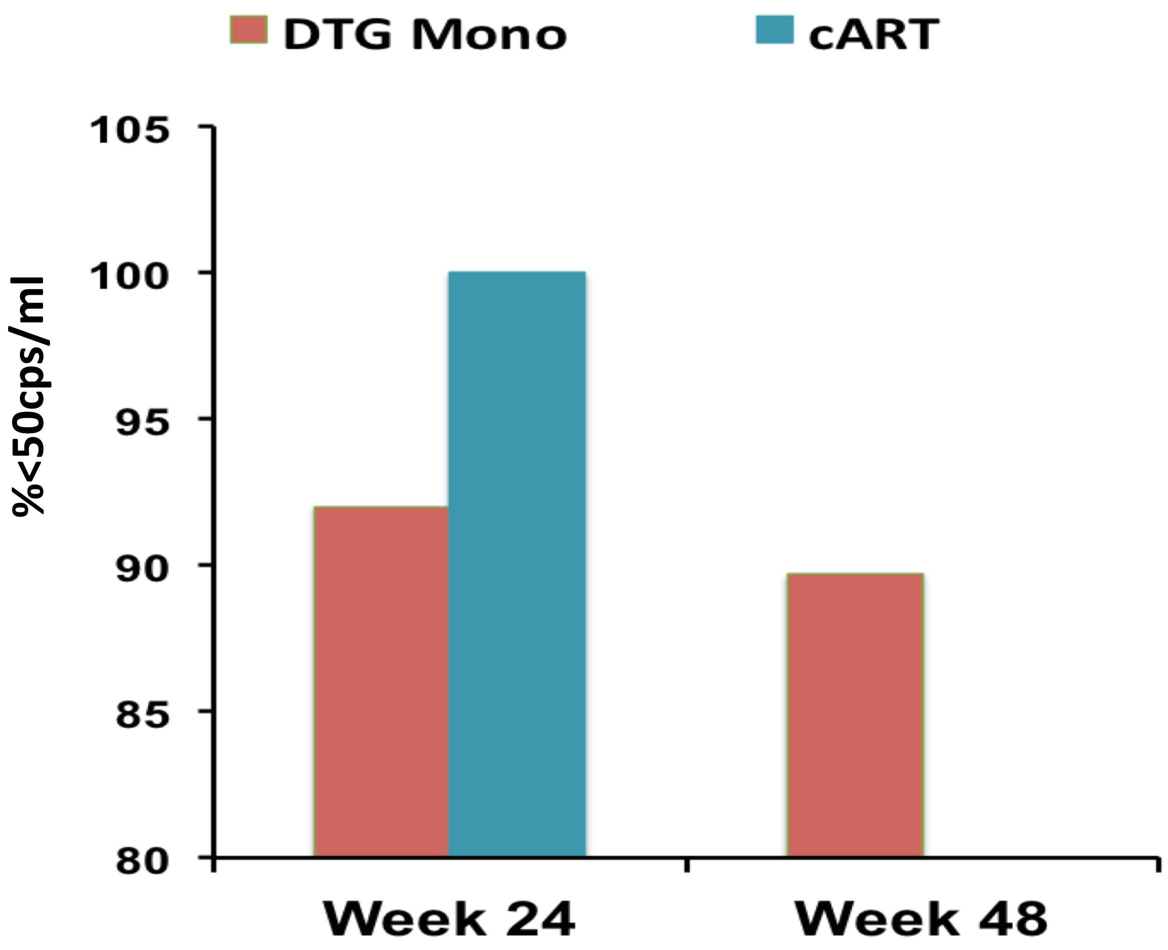
Estudio PROTEA. HIV-1 RNA in CSF samples at Week 48



There were 2 patients with HIV-1 RNA <40 copies/mL (target detected) at baseline in the CSF. Both patients had HIV RNA <40 copies/mL (target not detected) at Week 48.

Clarke A. HIV Drug Therapy Conference, Glasgow, UK, November 2014 [oral presentation: O423A]

DTG Monotherapy RCT Stopped Due to Failures



- 8/77 Monotherapy >50 by week 48
- 6/8 Genotype amplified
- 3/6 INI resistance
- 1 each 155H, 263K, 230R

- DSMB stopped study
- Authors recommend against DTG monotherapy
- Combined analysis of 3 cohorts*
  - 11/178 (6.1%) VF
  - 3.9% INI resistance
  - 148R/H (3), 155H (2), 118R (2)

Wijting I, et al. 24th CROI; Seattle, WA; February 13-16, 2017. Abst. 451LB.
*Blanco JI, et al. 24th CROI; Seattle, WA; February 13-16, 2017. Abst. 42

FV con DTG-mono

Número de pacientes controlados en las 3 cohortes: 10.440

DTG-bi-triterapia: **1.082** (10%)

Fracaso virológico
64 (6%; IC 95%: 5-7%)

No MR
64

Si MR
0

DTG-monoterapia: 122 (1,17%)

Fracaso virológico:
11 (9%; IC 95%: 6-18%)

No MR:
2

Si MR
9

82%

Valor exacto de Fisher *p=0,17*
Razón de VF mono:
1,58 (IC 95%: 0,73-3,13)

Blanco JL et al. CROI 2017. Seattle, 13-16 Febrero 2017. Abstract 42

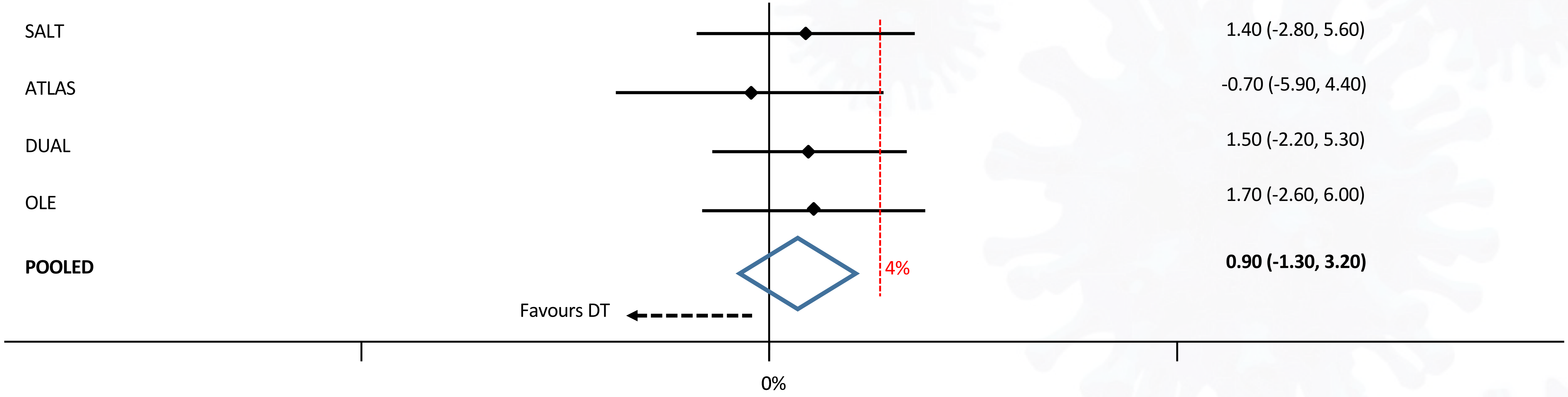
Combinations of bPI + 3TC: Switch in suppressed patients

At 48w, 4% of patients on DT vs. 3.04% on TT had HIV-RNA ≥50 cop/mL

Difference 0.9% (95%CI, -1.3% to 3.2%)

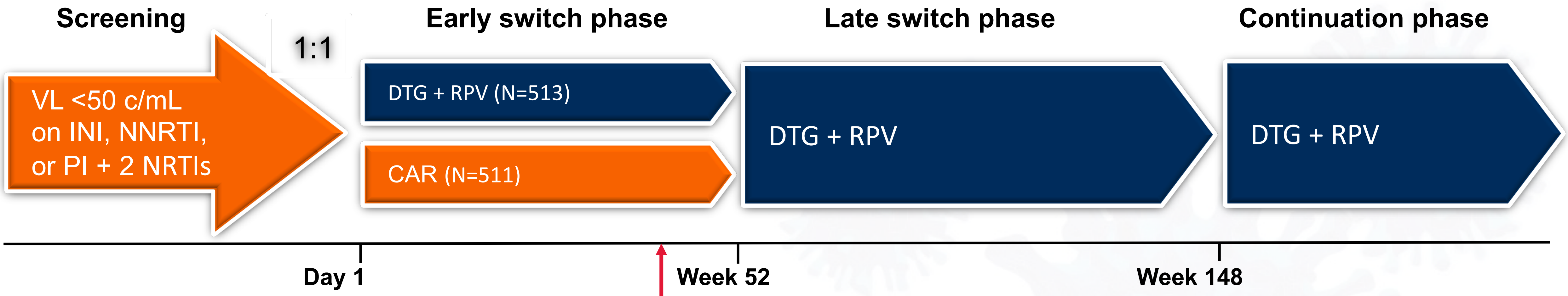
HIV-RNA ≥50 cop/mL at week 48
Dual therapy – triple therapy (%)

Absolute risk difference, (95% CI)
Non-inferiority margin: 4%



Pérez-Molina JA et al. PS1-1. 16th European AIDS Conference. Milan 2017

SWORD-1 and SWORD-2 Phase III Study Design



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]

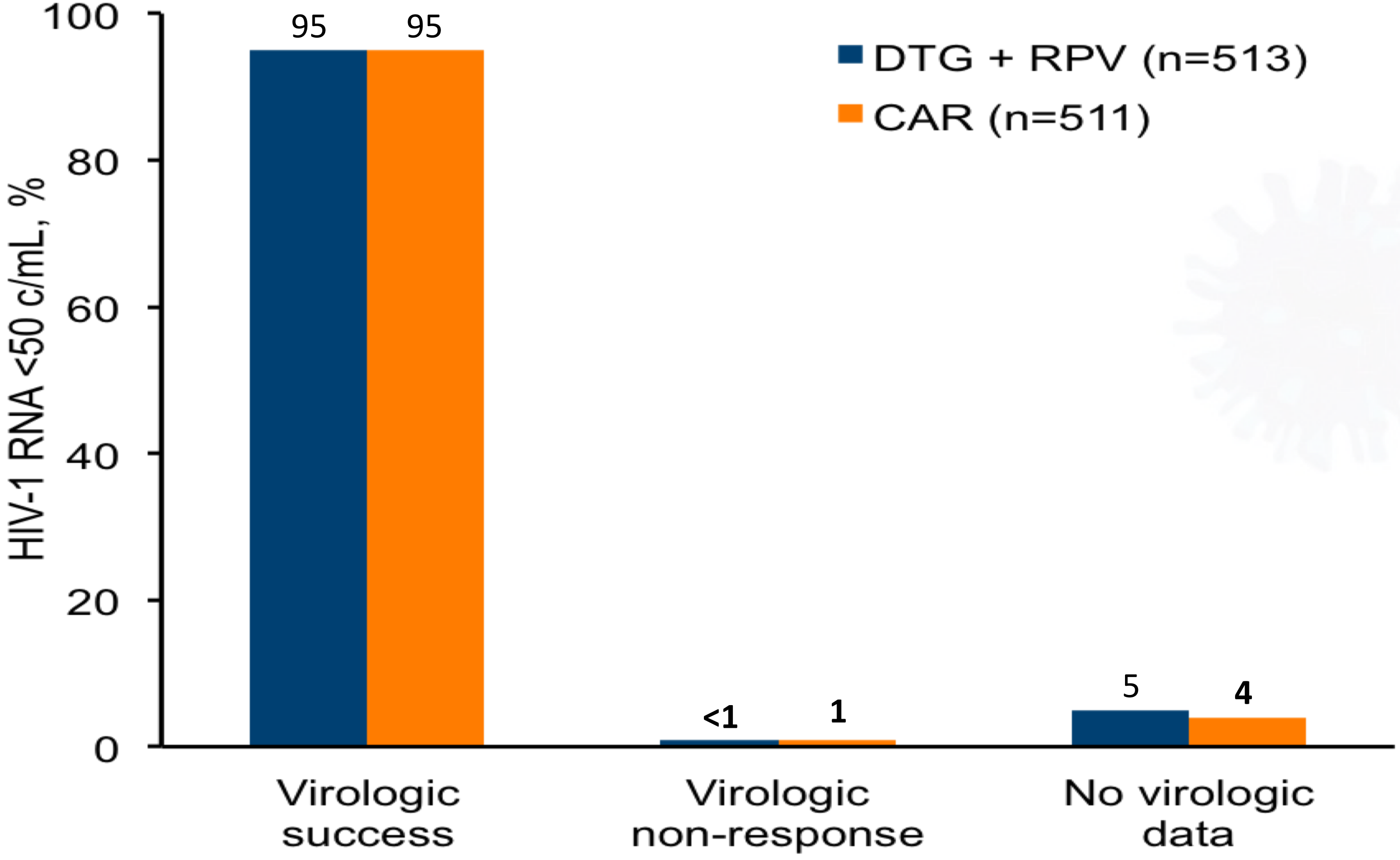
Countries

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

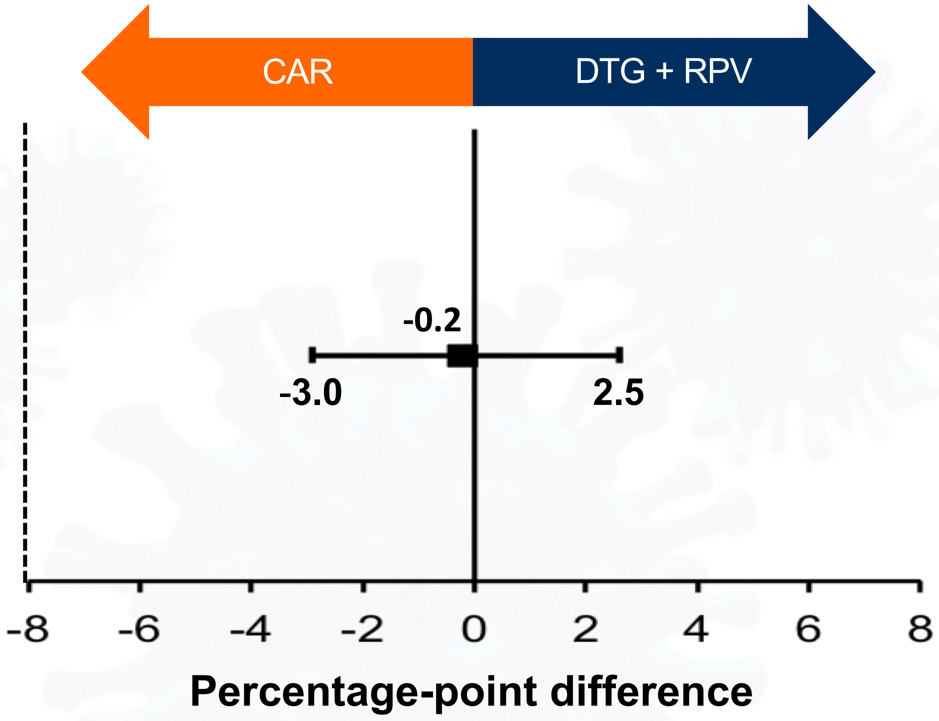
Llibre et al. CROI 2017; Seattle, WA. Abstract 44LB

Snapshot Outcomes at Week 48 (Pooled)

Virologic outcomes



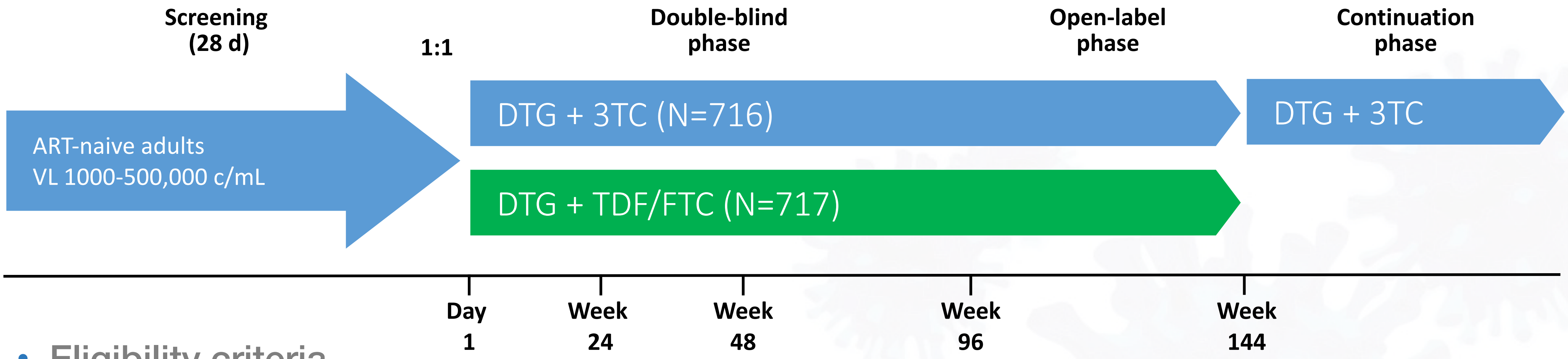
Adjusted treatment difference (95% CI)[a]



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

Llibre et al. CROI 2017; Seattle, WA. Abstract 44LB

GEMINI 1 and 2: Study design

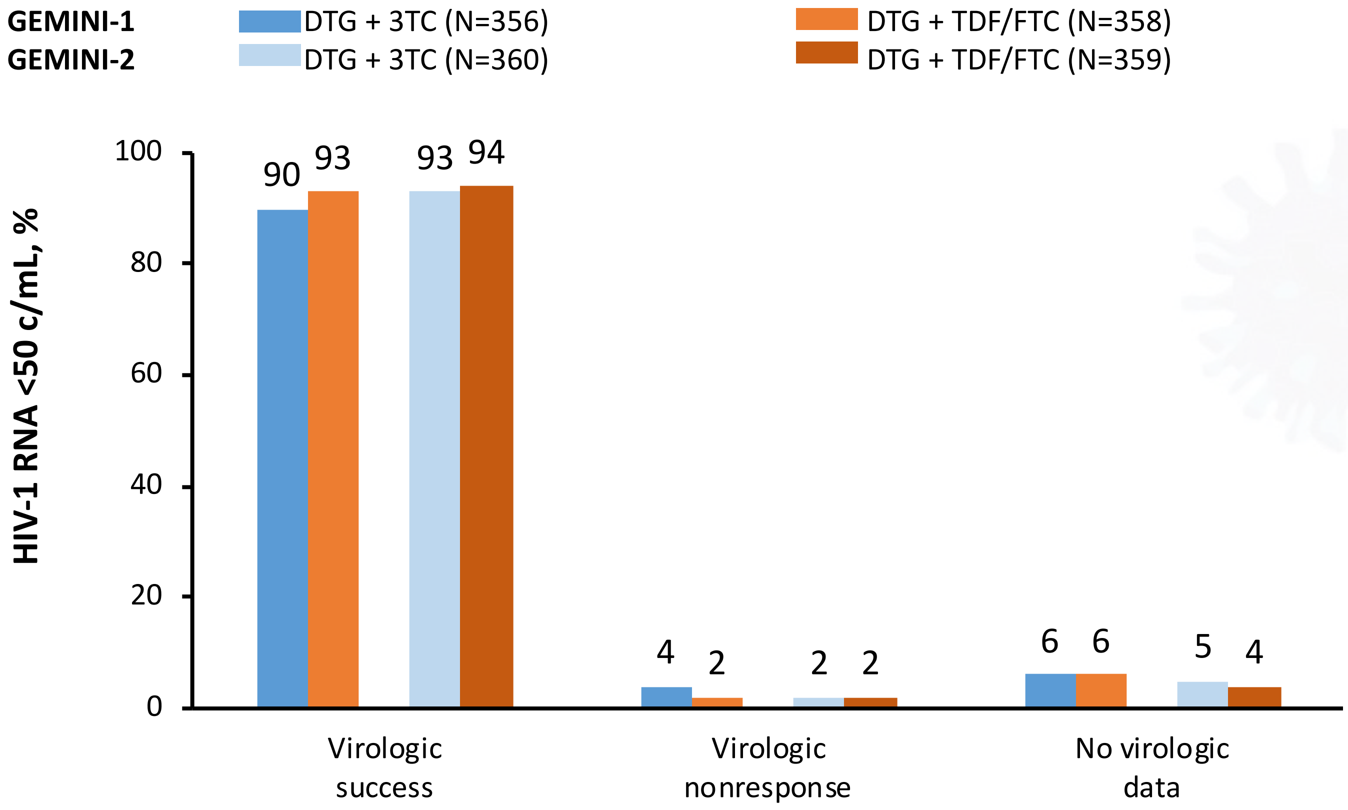


- Eligibility criteria
  - ≤10 days of prior ART
  - No evidence of pre-existing viral resistance based on presence of any major resistance-associated mutation
  - No HBV infection or need for HCV therapy

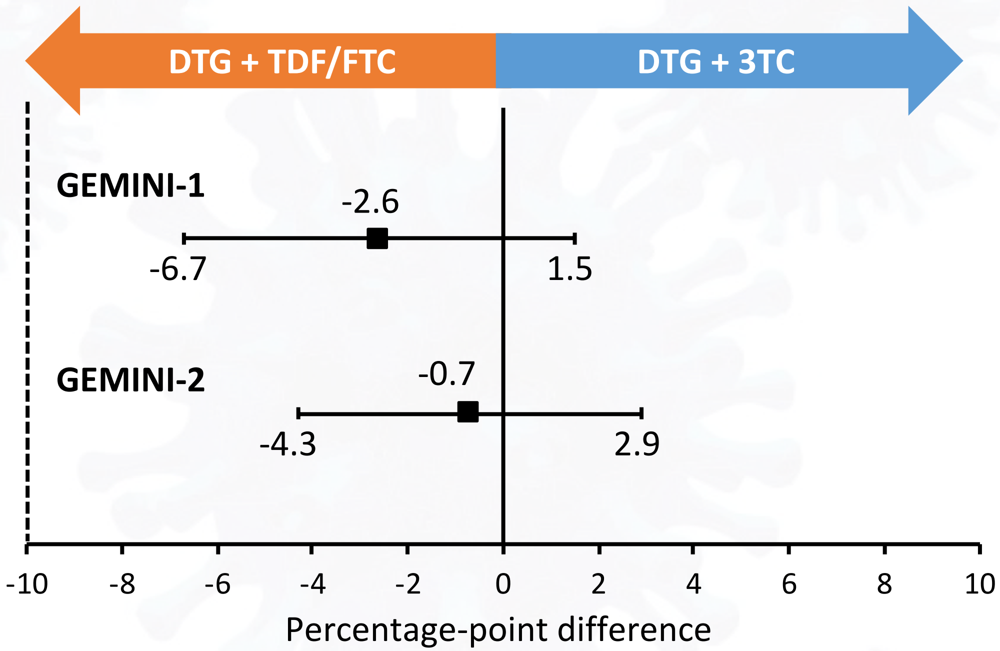
Cahn P, et al. AIDS 2018; Amsterdam, the Netherlands; July 23-27, 2018; Abst. TUAB0106LB.

GEMINI 1 and 2: Snapshot Outcomes at Week 48

Virologic outcome

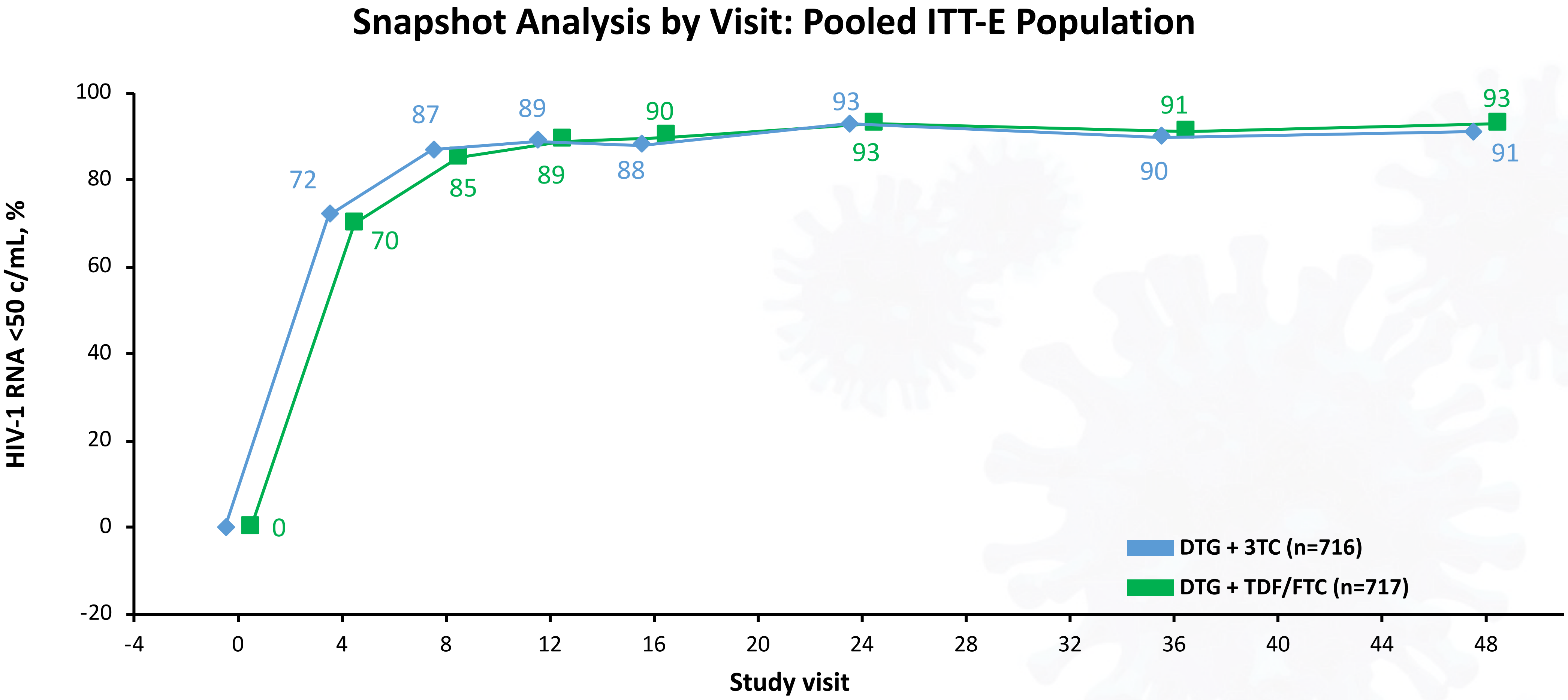


Adjusted treatment difference (95% CI)



Cahn P, et al. AIDS 2018; Amsterdam, the Netherlands; July 23-27, 2018; Abst. TUAB0106LB.

GEMINI 1 and 2: Results



Cahn P, et al. AIDS 2018; Amsterdam, the Netherlands; July 23-27, 2018; Abst. TUAB0106LB.

Disminución del número de fármacos

Aspectos Positivos y Negativos de los Regímenes de Dos Fármacos

Aspectos Positivos

- Eficacia similar al estándar
- No aumenta el riesgo de resistencias?
- Menor toxicidad a largo plazo?
- Menor coste

Aspectos Negativos

- Eficacia a largo plazo?
- No administrables en ciertas situaciones (tuberculosis, hepatitis B, embarazo)
- Impacto sobre la transmisión?
- Impacto sobre la inflamación y comorbilidades?

¿Cambios en el paradigma del TAR?

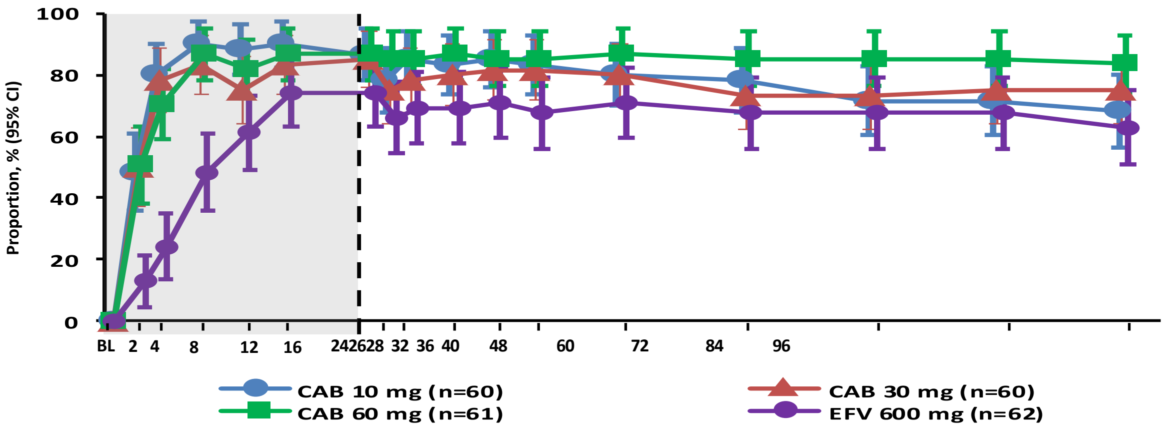
5

Cambios en el paradigma:
Reducción de la **frecuencia de dosis**

Cabotegravir + Rilpivirine as Long-Acting Maintenance Therapy: ATLAS and FLAIR 48 week

Background

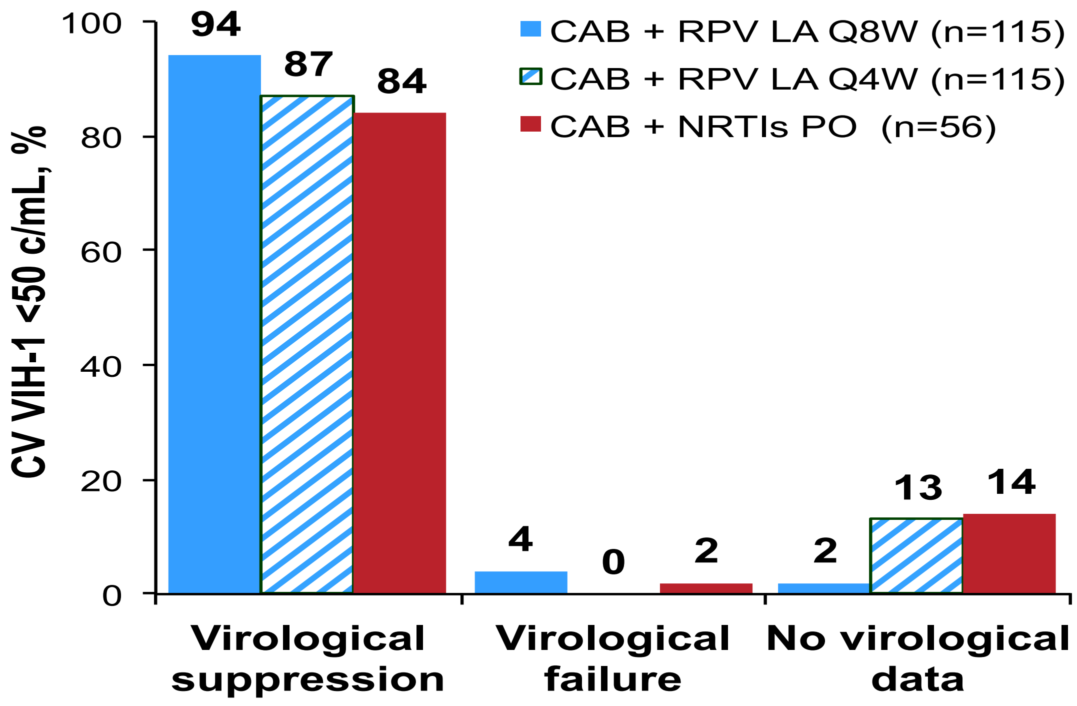
- **CAB** is an HIV-1 integrase inhibitor
  - Oral 30 mg tablet (t½, ~40 hours)
  - **LA nanosuspension 200 mg/mL (t½, ~20-40 days)**
- **RPV** is an HIV-1 NNRTI
  - Oral 25 mg tablet (t½, ~50 hours)
  - **LA nanosuspension 300 mg/mL (t½, ~30-90 days)**
- **Oral 2-drug CAB + RPV proof of efficacy through Week 96 in LATTE-1**



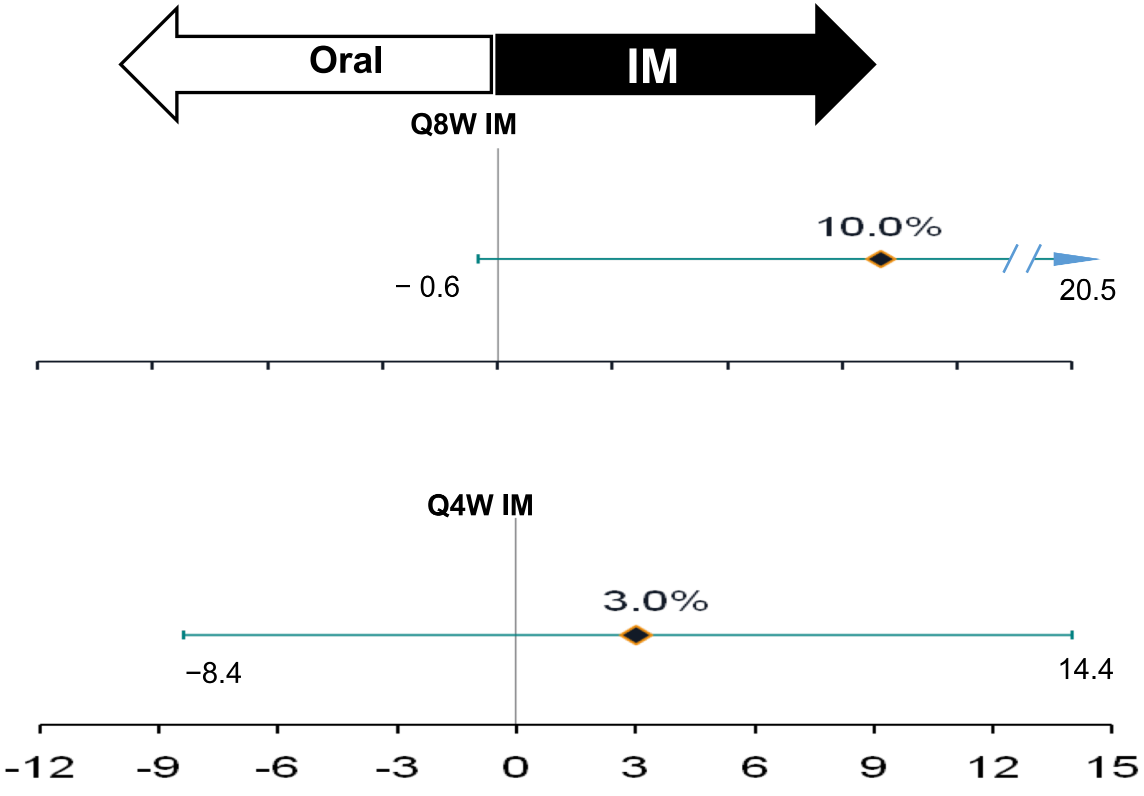
Margolis et al. CROI 2016; Boston, MA. Abstract 31LB.

LATTE-2 : Efficacy at week 96 (ITT-ME Snapshot)

Virological Response



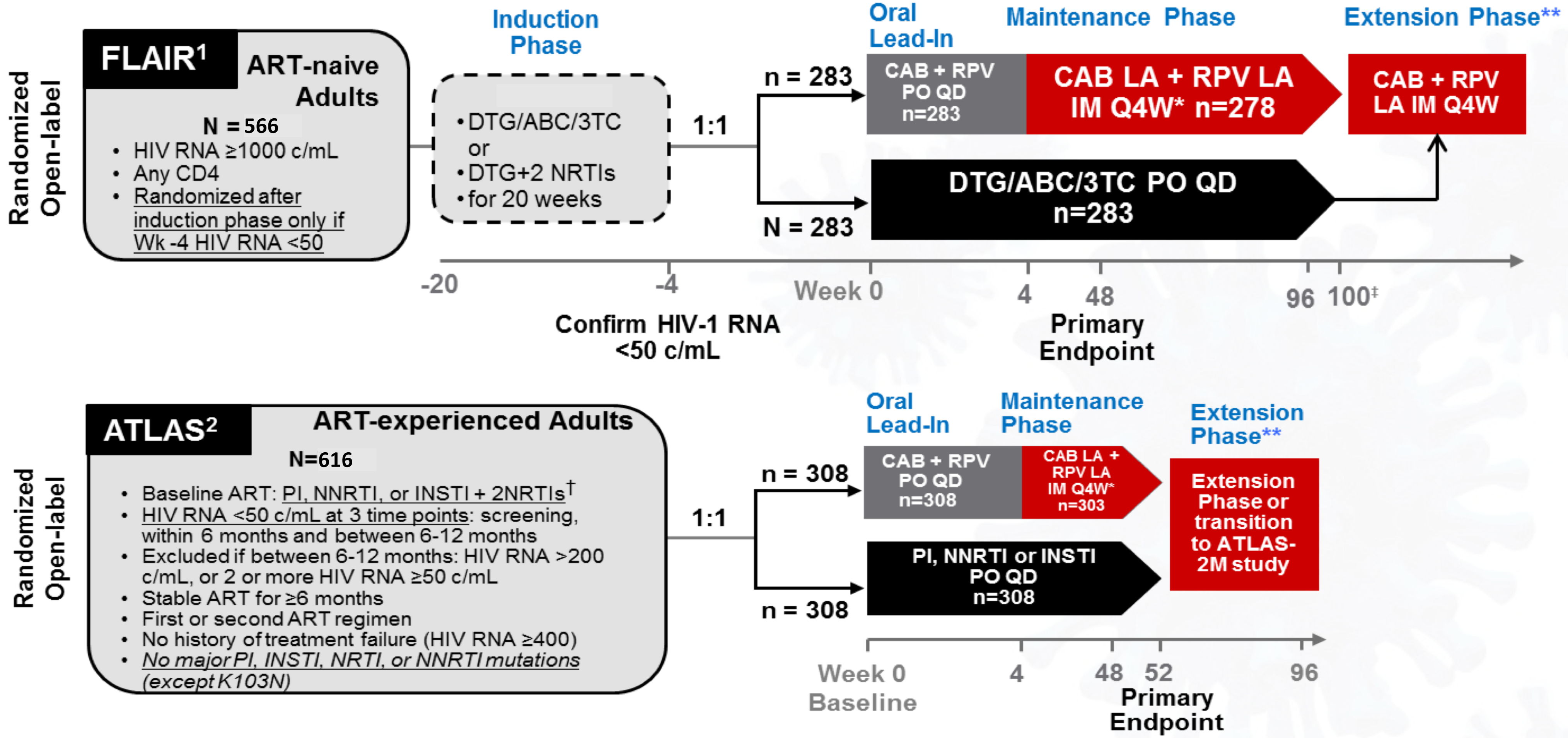
Differences in treatment (IC 95%)



Margolis DA. Lancet. 2017;390:1499-1510.

Cabotegravir + Rilpivirine Long Acting Injection

Evaluation of noninferior antiviral activity of monthly IM injection CAB LA + RPV LA vs continuing CAR



* Each drug is 2mL injection; FLAIR loading dose of CAB LA 600mg and RPV LA 900mg then CAB LA 400mg and RPV LA 600mg thereafter; ** Optional switch to CAB LA + RPV LA at week 52 for those on CAR
‡ Switch to investigational regimen for subjects randomized to comparator arm; 4-week oral lead-in optional in FLAIR and mandatory in ATLAS; † INSTI based regimen excludes DTG/ABC/3TC; INSTI therapy capped at ~40%; IM: Intramuscular; CAB: Cabotegravir; RPV: Rilpivirine; LA: long acting; CAR: current antiretroviral; SVF: suspected virologic failure

[1]Orkin C, et al. CROI 2019. Seattle, WA. Oral 140LB; [2]Swindells S, et al. CROI 2019. Seattle, WA. Oral 139

Cabotegravir + Rilpivirine Long Acting Injection

FLAIR[1]

Efficacy

	CAB LA + RPV LA	DTG/ABC/3TC	Dif (95% CI)
Primary endpoint ǂ % HIV-1 RNA≥ 50 cps/mL	2.1	2.5	-0.4 (-2.8 to 2.1)
Secondary endpoint % HIV-1 RNA< 50 cps/mL	93.6	93.3	0.4 (-3.3 to 4.5)

Safety

Adverse Events, % (excluding ISRs)	CAB LA + RPV LA	DTG/ABC/3TC
Any AE (≥10%)	87	80
Any Drug-related AEs (≥3%)	28	10
AEs leading to withdrawal	3	1
ISR events, %	28.6	-
ISRs leading to withdrawal	<1±	-

ATLAS[2]

Efficacy

	CAB LA + RPV LA	CAR	Diff (95% CI)
Primary endpoint ǂ % HIV-1 RNA≥ 50 cps/mL	1.6	1.0	0.6 (-1.2 to 2.5)
Secondary endpoint % HIV-1 RNA< 50 cps/mL	92.5	95.5	-3,0 (-6.7 to 0.7)

Safety

Adverse Events, % (excluding ISRs)	CAB LA + RPV LA	CAR
Any AE (≥10%)	86	71
Any Drug-related AEs (≥3%)	29	3
AEs leading to withdrawal	3	2
ISR events, %	20,9	-
ISRs leading to withdrawal	1,3	-

Long acting CAB + RPV was non-inferior and meet the primary and secondary endpoint in ATLAS and FLAIR studies with a numerically higher rates of AEs observed

CAB: Cabotegravir; RPV: Rilpivirine; LA: long acting; CAR: current antiretroviral; ISR: injection site reaction; ǂ6% noninferiority margin; ±2 pts withdrawal due to ISR pain, two additional due to injection intolerability

[1]Orkin C, et al. CROI 2019. Seattle, WA. Oral 140LB; [2]Swindells S, et al. CROI 2019. Seattle, WA. Oral 139

Cabotegravir + Rilpivirine Long Acting Injection

Virologic failures and risk of resistance in ATLAS and FLAIR Studies

- ATLAS: 1 out of 3 virologic failures resulted in two-class treatment emergent resistance.

Sex, Country, HIV-1 subtype	SVF Timepoint	SVF Timepoint RAMs (HIV-1 RNA)		Sensitivity at SVF (FC)
		NNRTI	INSTI†	
F, Russia, A/A1	Week 8	E138A*	L74I*	**RPV (2.4)** CAB (0.8) DTG (0.9)
F, France, AG	Week 12	V108I* E138K*	None	**RPV (3.7)** CAB (1.2) DTG (1.0)
M, Russia, A/A1	Week 20	**E138E/K**	**N155H** L74I*	**RPV (6.5)** **CAB (2.7)** DTG (1.2)

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

- FLAIR: 3 out of 3 virologic failures resulted in two-class treatment emergent resistance.

Sex, Country, HIV-1 subtype, Virologic Load (Baseline)	SVF Timepoint	SVF Timepoint RAMs (HIV-1 RNA)		Sensitivity at SVF (FC)
		NNRTI	INSTI†	
F, Russia, A1, 54K	Week 20	**E138 E/A/K/T**	L74I*, **Q148R**	**RPV (7.1)** **CAB (5.2)** DTG (1.0)
M, Russia, A1, 23K	Week 28	**K101E**	L74I*, **G140R**	**RPV (2.6)** **CAB (6.7)** DTG (2.2)
F, Russia, A1, 20K	Week 48	**E138K**	L74I*, **Q148R**	RPV (1.0) **CAB (9.4)** DTG (1.1)

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

Although virologic failure was less than 1%, treatment emergent resistance was observed in 33% and 100% of VFs in ATLAS and FLAIR studies, respectively

CAB: Cabotegravir; RPV: Rilpivirine; LA: long acting; CAR: current antiretrovirals; SVF: suspected virologic failure; FC: fold change

Swindells S, et al. CROI 2019. Seattle, WA. Oral 139; Orkin C, et al. CROI 2019. Seattle, WA. Oral 140LB

Disminución del número de dosis

Aspectos Positivos y Negativos de los Regímenes de Acción Prolongada

Aspectos Positivos

- Mayor comodidad para el paciente
- Disminución del estigma
- Mejora de la adherencia?

Aspectos Negativos

- Administración parenteral
- Modelos asistenciales diferentes
- Cansancio de las inyecciones?
- Posibilidad de pérdida de dosis

Conclusiones

- El tratamiento antirretroviral actual ha alcanzado cotas de excelencia en todas sus características
- Hay buenas perspectivas con nuevos fármacos de viejas y nuevas familias que llenarán algunas lagunas del tratamiento antirretroviral todavía existentes
- Hay un estrecho margen de mejora con posibilidad de reducción en el número de fármacos y reducción en la frecuencia de administración
- Los datos disponibles muestran la viabilidad de estos cambios, aunque algunos aspectos precisan confirmación