Organitza:

Col·laboren:

Aval científic:

Patrocina:

VII Jornada sobre aspectes rellevants de la infecció pel VIH

Maneig a l'Atenció Primària i a l'hospital

Actualització en tractament antiretroviral

Arkaitz Imaz

Servei de Malalties Infeccioses

Hospital Universitari de Bellvitge

Barcelona, 24 d'octubre de 2024

Quan iniciar el TAR

L'inici del TAR està recomanat per a totes les persones amb VIH, independentment de la xifra de CD4, tan aviat com sigui possible després del diagnòstic.

Update of recommendations on first- and second-line antiretroviral regimens. Geneva, Switzerland: World Health Organization; 2019 (WHO/CDS/HIV/19.15).; EACS Guidelines. Version 11.0. October 2021; Documento de Consenso de GeSIDA/Plan Nacional sobre el SIDA respecto al Tratamiento Antirretroviral en adultos infectados por Virus de la Inmunodeficiencia Humana (Actualización Enero 2022); Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults 2020 Recommendations of the International Antiviral Society–USA Panel. JAMA 2020 (Published online October 14, 2020.); DHHS Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV (Last updated September 1, 2022)

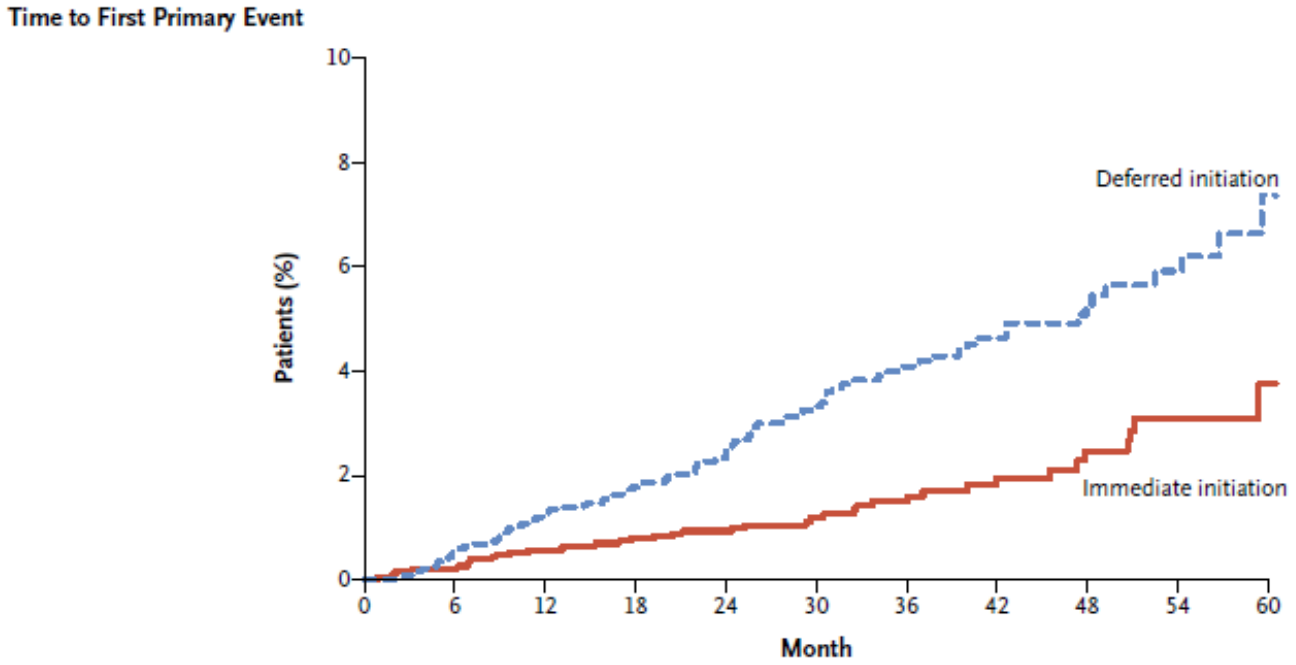
The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 AUGUST 27, 2015 VOL. 373 NO. 9

Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection

The INSIGHT START Study Group*

Immediate ART in PLWH with CD4 T cell count >500 cells/mL:

57% relative reduction in serious AIDS-related events, non-AIDS serious events and death from any cause

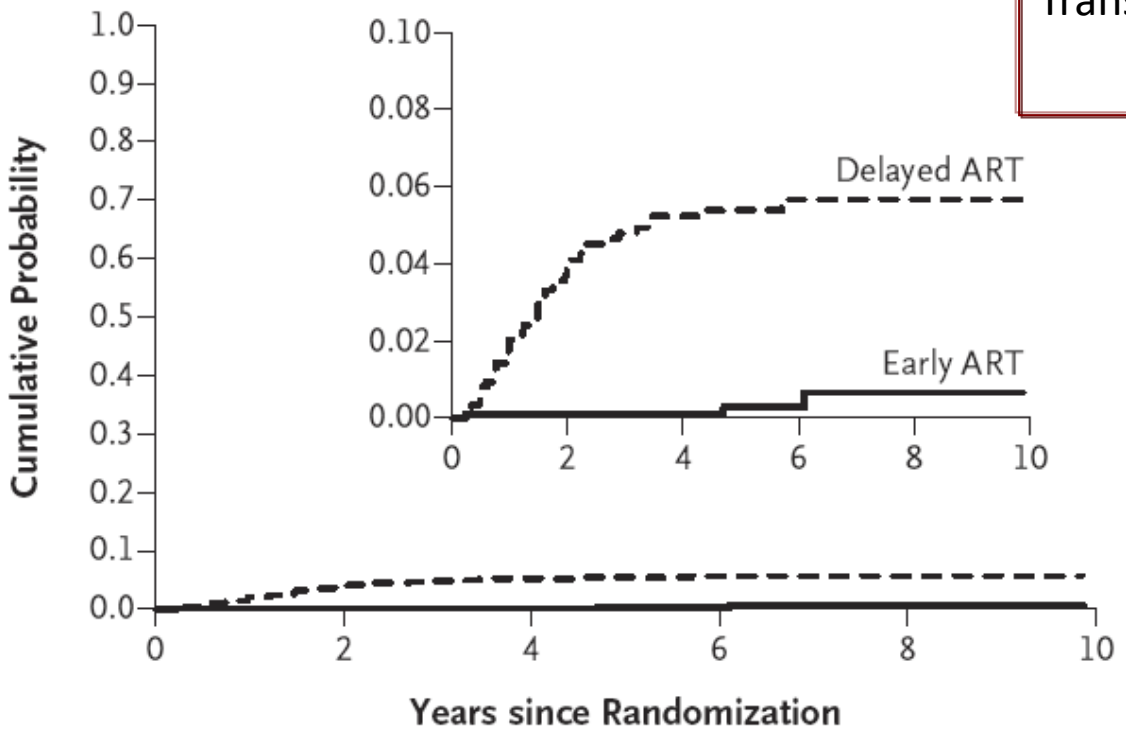


No. at Risk											
Immediate initiation	2326	2302	2279	2163	1801	1437	1031	757	541	336	110
Deferred initiation	2359	2326	2281	2135	1803	1417	1021	729	520	334	103
Estimated Percentage											
Immediate initiation		0.2	0.6	0.8	0.9	1.2	1.5	2.0	2.5	3.1	3.7
Deferred initiation		0.5	1.2	1.8	2.4	3.3	4.1	4.6	5.3	5.9	7.4

N Engl J Med 2015;373:795-807.

Antiretroviral Therapy for the Prevention of HIV-1 Transmission

B Linked Partner Infections



No. at Risk

Early ART	903	808	746	697	645	569	263	95	28	26	1
Delayed ART	890	792	715	663	611	536	269	99	21	19	2

Transmission risk reduction associated to Early ART:

93%

HPTN 052 Study

Cohen MS, et al. N Engl J Med. 2016 Sep 1;375(9):830-9

Objectius del TAR

❖ **Aconseguir i mantenir la màxima supressió de la CV plasmàtica**

- Restablir la funció immunològica
- Reduir la inflamació i la activació immunològica associada al VIH
- Evitar la mortalitat i morbiditat associada al VIH, les malalties definitòries de SIDA altres malalties associades al VIH (cardiovascular, renal, hep`tica deteriorament neuro-cognitiu, neoplàsies no-SIDA, …)
- Augmentar supervivència
- Millorar la qualitat de vida
- Prevenir la transmissió

Documento de Consenso de GeSIDA/Plan Nacional sobre el SIDA respecto al Tratamiento Antirretroviral en adultos infectados por Virus de la Inmunodeficiencia Humana (Actualización Enero 2022); DHHS Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV (Accessed July 11, 2022)

Currently available Antiretroviral drugs

Entry Inhibitors

Enfuvirtide
Maraviroc

Fostemsavir
Ibalizumab

Integrase Inhibitors (InSTI)

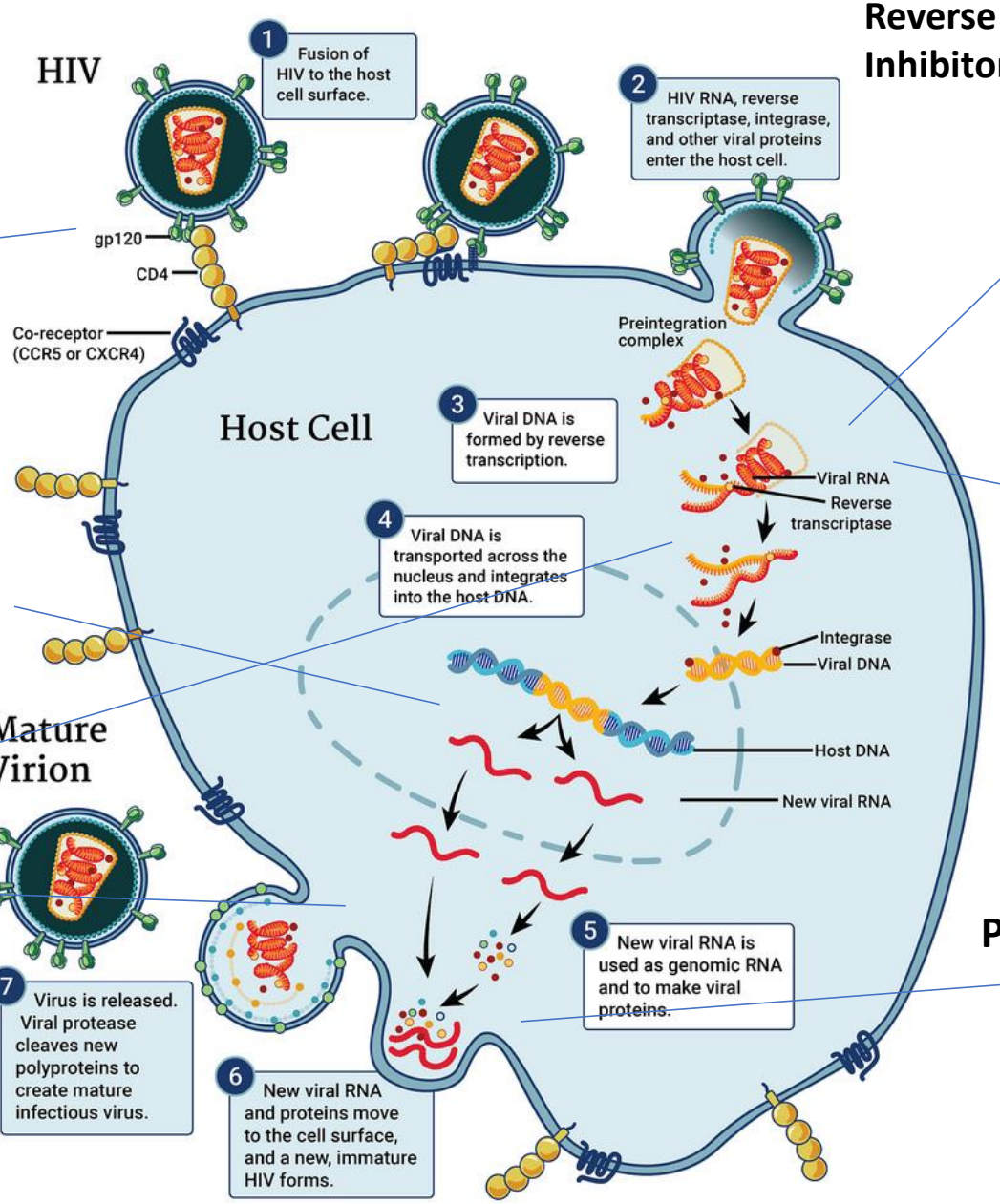
Raltegravir
Elvitegravir *
Dolutegravir *
Bictegravir *

Capside Inhibitors

Lenacapavir

* Available as fixed dose combination with other ARV in single pill

www.niaid.nih.gov/diseases-conditions/hiv-replication-cycle



Nucleo(t)side analogues Reverse Transcriptase Inhibitors (NRTI)

Tenofovir (TDF and TAF) *
Lamivudine *
Emtricitabine *
Abacavir *
Zidovudine *
Didanosine, Estavudine, Zalcitabine

Non-nucleoside Reverse Transcriptase Inhibitors (NNRTI)

Efavirenz *
Nevirapine
Etravirine
Rilpivirine *
Doravirine *

Protease Inhibitors (PI)

Indinavir
Nelfinavir
Saquinavir
(Fos)Amprenavir
Lopinavir
Atazanavir
Tipranavir
Darunavir *

Preferred first-line ART regimens for adults (2024)

World Health Organization March 2021	EACS European AIDS Clinical Society October 2023	GeSIDA January 2023	DHHS September 2024	IAS–USA International Antiviral Society–USA December 2022
INSTI + 2 NRTI DTG + 2 NRTI	**INSTI + 2 NRTI** BIC/FTC/TAF DTG/ABC/3TC or DTG+ABC/3TC (if HLA-B*5701 negative and no HBV coinfection) DTG + FTC/TAF or XTC/TDF RAL + FTC/TAF or XTC/TDF **INSTI + 1 NRTI** DTG+3TC or DTG/3TC (If HIV-1 RNA < 500,000 c/mL and HBsAg negative Not recommended after PrEP failure) **NNRTI + 2 NRTI** DOR+FTC/TAF or XTC/TDF or TDF/3TC/DOR	**INSTI + 2 NRTI** BIC/FTC/TAF (AI) ABC/3TC/DTG (AI) (not recommended if HLA-B*5701 positive or HBV coinfection) DTG + FTC/TAF (AI) **INSTI + 1 NRTI** DTG/3TC (AI) *Not recommended for individuals with CD4 count <200/uL * Not recommend for individuals with HBV coinfection *Not recommended after PrEP if the results of HIV genotypic resistance testing are not available	*For people with HIV who do not have a history of using long-acting cabotegravir (CAB-LA) as pre-exposure prophylaxis (PrEP)* **INSTI + 2 NRTI** BIC/FTC/TAF (AI) DTG + FTC/TAF (AI) or XTC/TDF (AI) **INSTI + 1 NRTI** DTG/3TC (AI) (except for individuals with HIV RNA > 500,000 c/mL, HBV coinfection, or for whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available)	**INSTI + 2 NRTI** BIC/FTC/TAF (AIa) DTG + XTC/TXF (AIa) **INSTI + 1 NRTI** DTG/3TC (AIa) (Only if HIV RNA <500 000 copies/mL and HBV coinfection not present. This regimen should not be used for rapid initiation when genotype, HIV RNA, and HBV serology results are not yet available)

Update of recommendations on first- and second-line antiretroviral regimens. Geneva, Switzerland: World Health Organization; 2019 (WHO/CDS/HIV/19.15).; EACS Guidelines. Version 12.0 October 2023; Documento de Consenso de GeSIDA/División de Control de VIH, ITS, Hepatitis virales y Tuberculosis del Ministerio de Sanidad respecto al Tratamiento Antirretroviral en adultos infectados por Virus de la Inmunodeficiencia Humana (Actualización Enero 2023); Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults: 2022 Recommendations of the International Antiviral Society–USA Panel. JAMA. 2022 Dec 1. doi: 10.1001/jama.2022.22246. Epub ahead of print. PMID: 36454551; DHHS Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV (Last updated September 1, 2022)

- Inhibidors de Integrasa
- TAF
- Nous ITINN (Rilpivirina, Doravirina)

- Tenofovir DF
- Abacavir

- Efavirenz/Nevirapina

- Inhibidors de proteasa (Darunavir)

Inhibidors de la Integrasa

- Pautes amb InSTI considerades actualment preferents coma tractament inicial a totes les Guies de TAR .
- Alts percentatges de supressió de CV, descens de CV més ràpid que altres classes de ARV.
- Bon perfil de toxicitat
- Baix risc d'interaccions farmacològiques (RAL, DTG, BIC)
- Alta barrera a la resistència (DTG, BIC)

Update of recommendations on first- and second-line antiretroviral regimens. Geneva, Switzerland: World Health Organization; 2019 (WHO/CDS/HIV/19.15).; EACS Guidelines. Version 10.1. October 2020;– Documento de Consenso de GeSIDA/Plan Nacional sobre el SIDA respecto al Tratamiento Antirretroviral en adultos infectados por Virus de la Inmunodeficiencia Humana (Actualización Julio 2020); Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults 2020 Recommendations of the International Antiviral Society–USA Panel. JAMA 2020 (Published online October 14, 2020.); DHHS Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV (Last updated December 18, 2019)

Tenofovir Alafenamida (TAF)

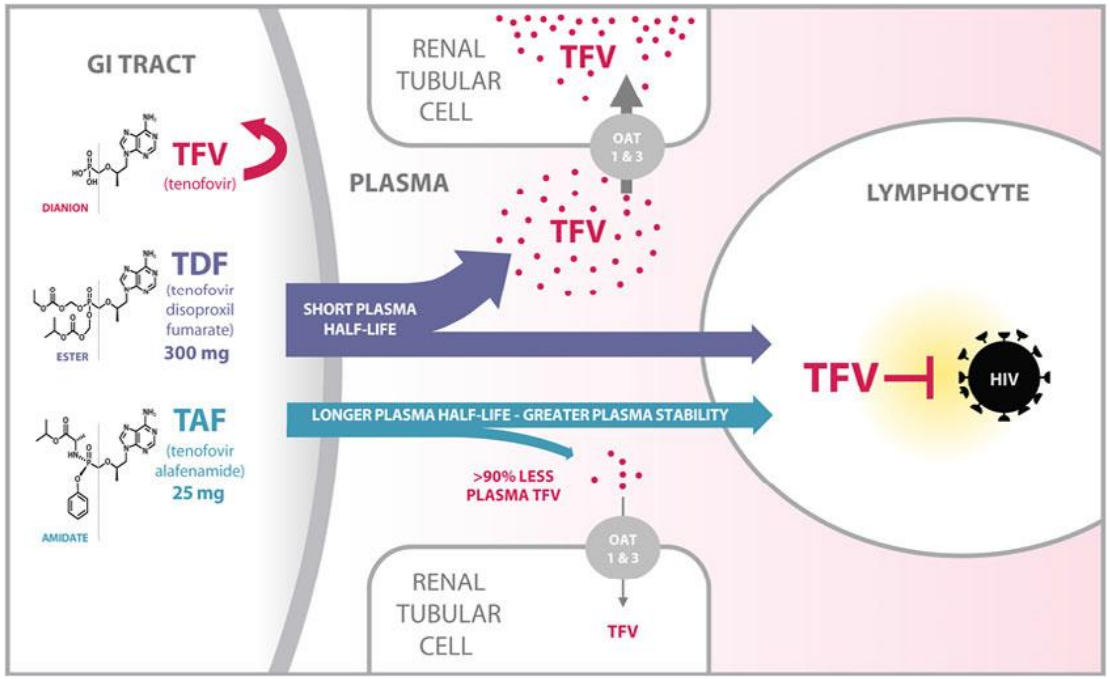
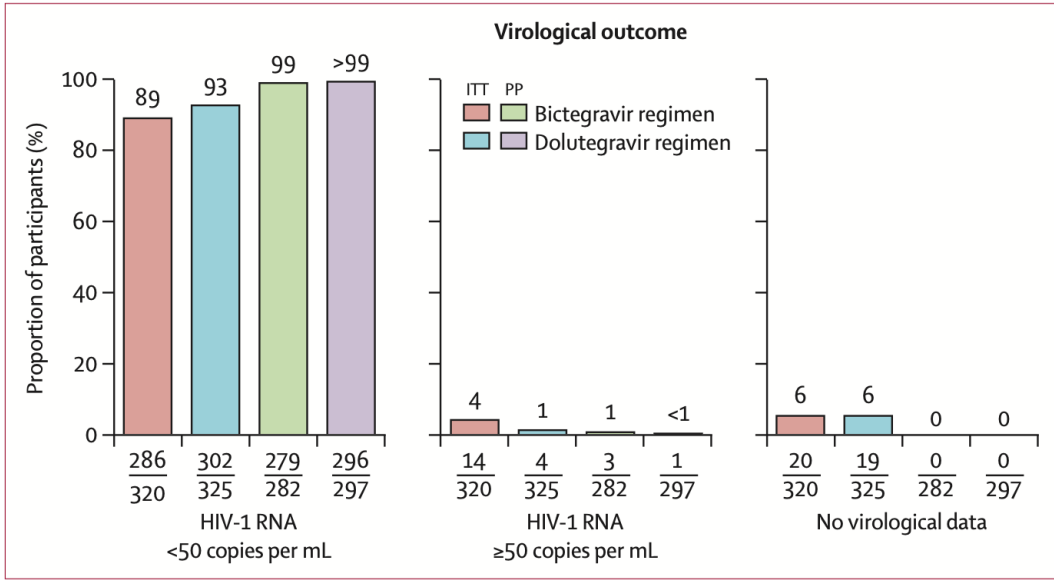


Table 1
In vitro activity and stability of TFV and its prodrugs TDF and TAF.

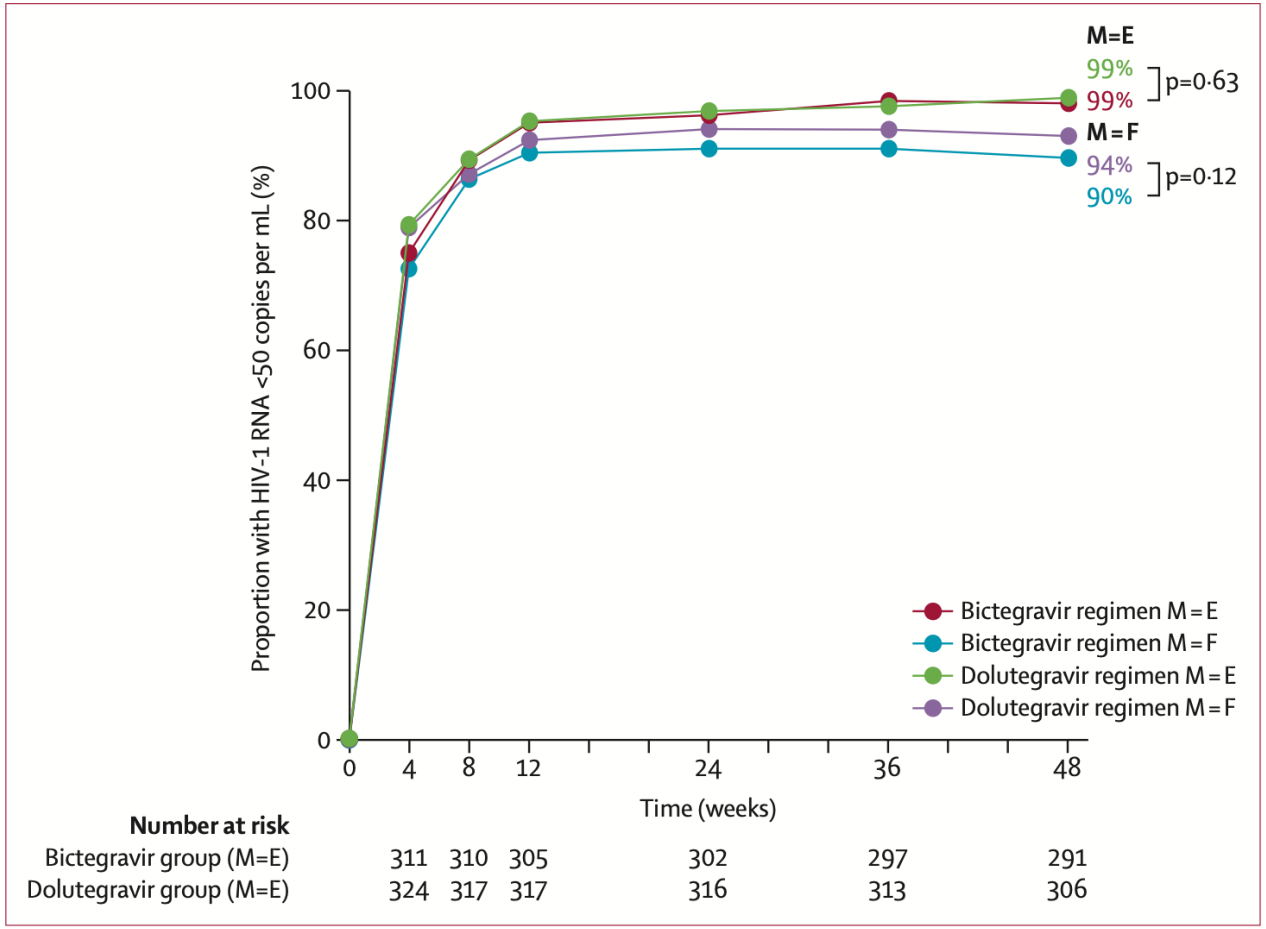
	TFV	TDF	TAF
EC_{50} HIV-1 (μM)	5.0	0.05	0.005
Half-life (min)	stable	0.41	90

Antela A, et al. HIV Med. 2016;17 Suppl 2:4-16; Lee WA, et al. Antimicrob Agents Chemother. 2005;49:1898-906. Ruane PJ, et al J Acquir Immune Defic Syndr. 2013;63:449-55.
Ray AS, et al. Antiviral Research. 2016; 125:63-70

BIC/FTC/TAF vs DTG+FTC/TAF

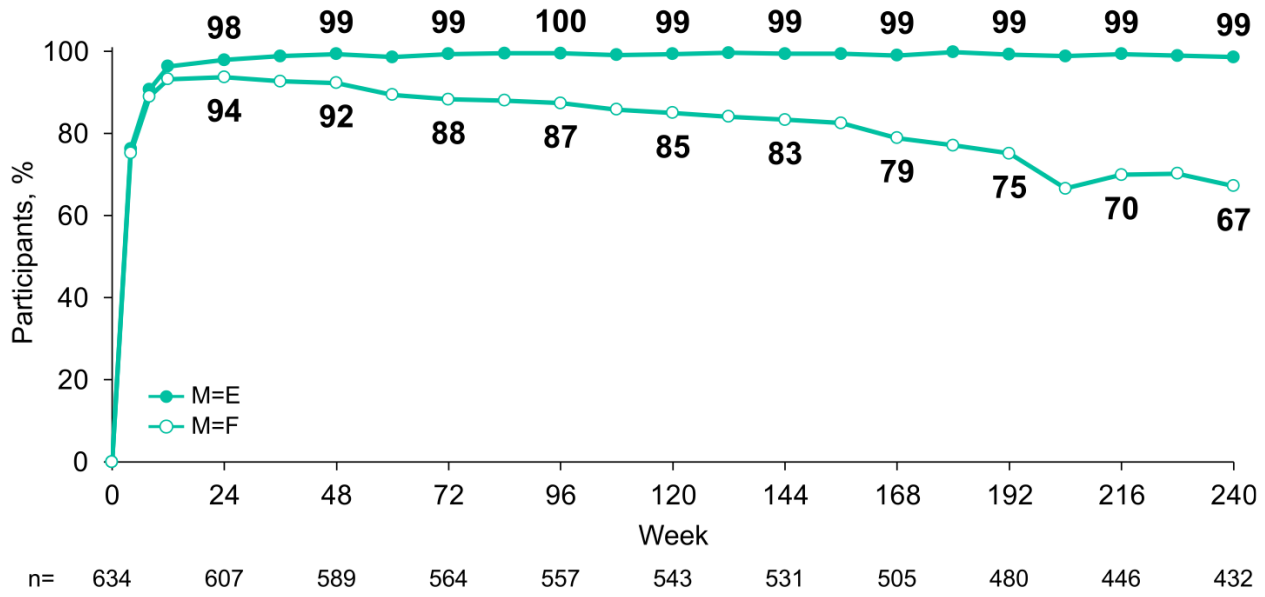


No treatment-emergent resistance to any study drug was observed



Sax PE, et al. Lancet 2017; 390: 2073–82

BIC/FTC/TAF. Resultats assaigs clínics als 5 anys



Study-drug related serious AE 5 (0.8%)

Any study-drug related AE leading to discontinuation 5 (0.8)

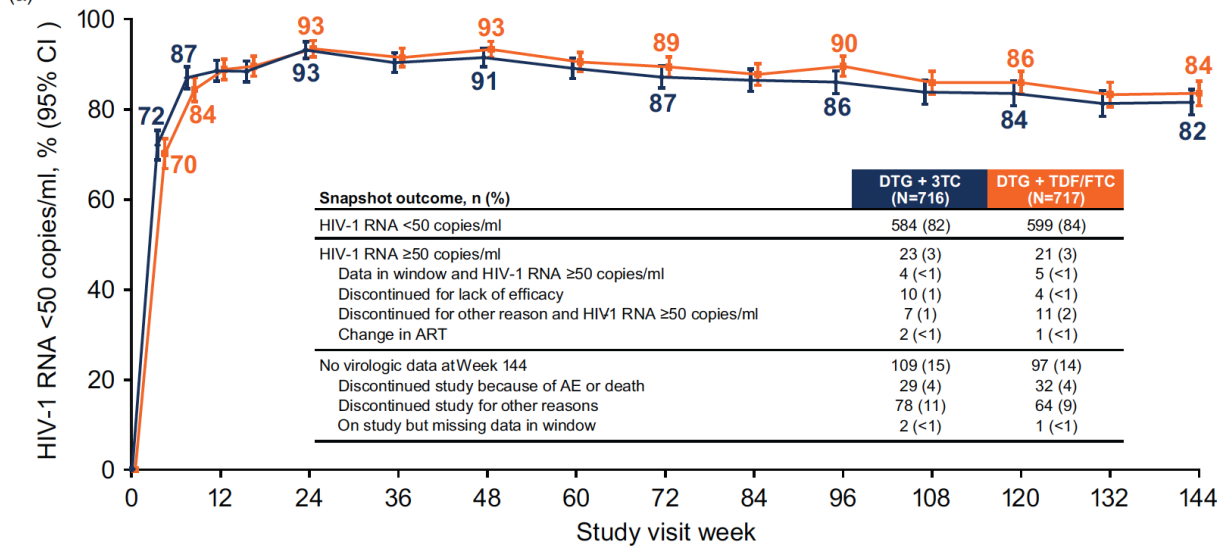
Virological Failure:
9 participants met criteria for resistance testing
0 resistance to any component of B/F/TAF

Sax PE, et al. eClinicalMedicine 2023;59: 101991

Dual ART as first-line therapy: DTG+ 3TC

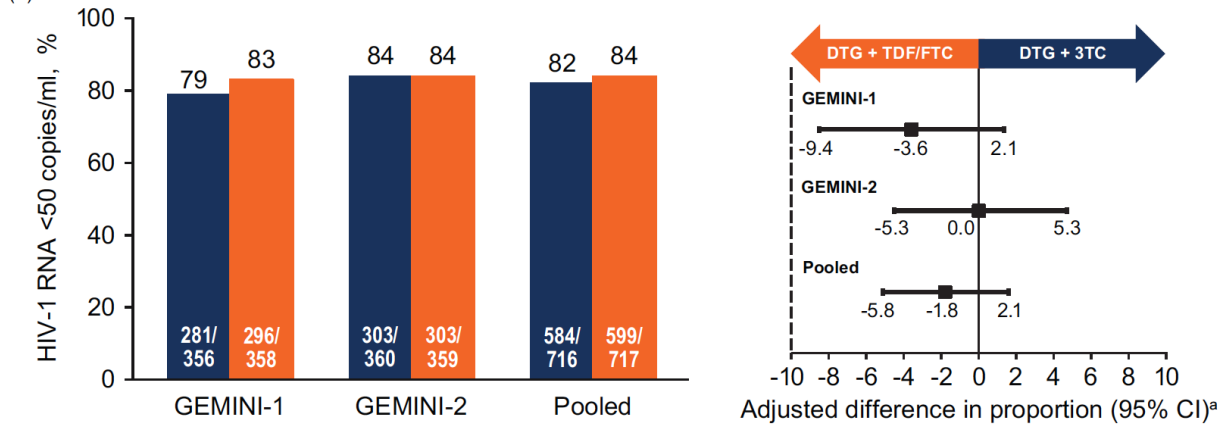
GEMINI I & II
Phase III RCT

(a)



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 at Week 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)

(b)



Cahn P, et al. AIDS 2022, 36:39–48

DTG/3TC com a TAR inicial. Potencials Limitacions

- Conifecció per VHB
- Resistència basal
- Diagnòstic de VIH durant PrEP

EACS Guidelines. Version 11.0. October 2021; Documento de Consenso de GeSIDA/Plan Nacional sobre el SIDA respecto al Tratamiento Antirretroviral en adultos infectados por Virus de la Inmunodeficiencia Humana (Actualización Enero 2022); Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults 2020 Recommendations of the International Antiviral Society–USA Panel. JAMA 2020 (Published online October 14, 2020.); DHHS Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV (Last updated September 1, 2022)

Clinical Infectious Diseases
MAJOR ARTICLE

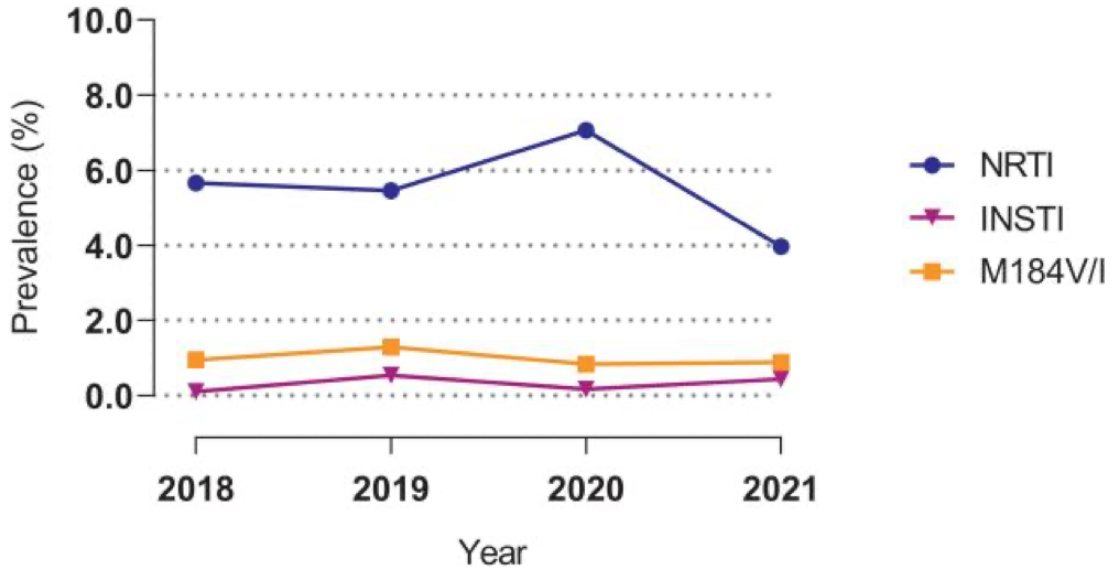
Transmitted Drug Resistance to Integrase-Based First-Line Human Immunodeficiency Virus Antiretroviral Regimens in Mediterranean Europe

France, Greece, Italy, Portugal, and Spain

2018–2021

N=2705 PWH, 72% men, median age 37 years

43.7% non-B subtypes.



Salazar A, et al. Clin Infect Dis. 2023 May 3;76(9):1628-1635.

Integrase Strand Transfer Inhibitor and Nucleoside/Nucleotide Reverse Transcriptase Inhibitor Clinically Relevant Resistance to First-Line Drugs, (as Defined by the Stanford Algorithm v9.1)

Integrase Strand Transfer Inhibitor	n (%)	95%CI
Raltegravir	62 (2.29)	1.76%–2.93%
Elvitegravir	62 (2.29)	1.76%–2.93%
Dolutegravir	4 (0.15)	.04%–.38%
Bictegravir	4 (0.15)	.04%–0.38%
Total	63 (2.33)	1.80%–2.97%
Nucleoside/Nucleotide Reverse Transcriptase Inhibitor		
Tenofovir alafenamide	24 (0.89)	.57%–1.32%
Abacavir	47 (1.74)	1.28%–2.31%
Lamivudine/Emtricitabine	29 (1.07)	.72%–1.53%
Total	47 (1.74)	1.28%–2.31%

Abbreviation: CI, confidence interval.

JOURNAL ARTICLE ACCEPTED MANUSCRIPT EDITOR'S CHOICE

HIV-1 Incidence, Adherence, and Drug Resistance in Individuals Taking Daily Emtricitabine/Tenofovir Disoproxil Fumarate for HIV-1 Pre-Exposure Prophylaxis: Pooled Analysis From 72 Global Studies

IN THIS ANALYSIS

72 pooled studies conducted across 28 countries, between June 2011 and September 2019

Total of **17,274** participants

STUDY INTERVENTION

Emtricitabine/tenofovir disoproxil fumarate (F/TDF) for HIV-1 pre-exposure prophylaxis (PrEP)

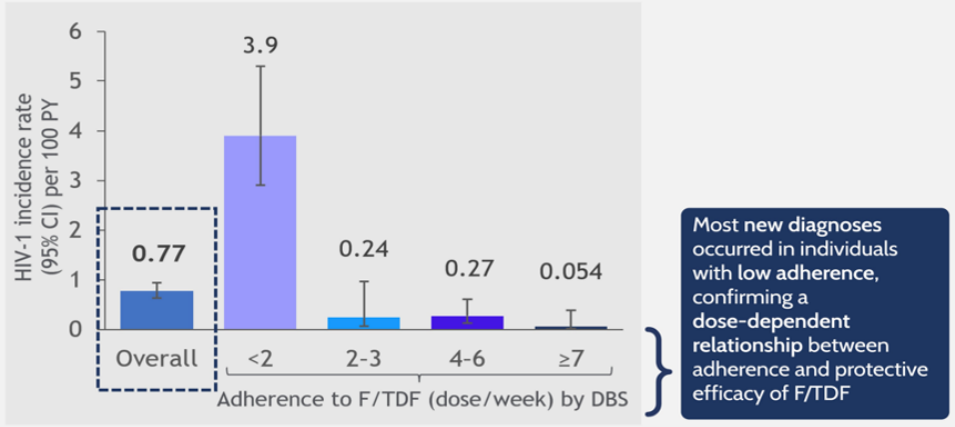
OBJECTIVES

To evaluate **HIV-1 incidence**, **drug resistance**, **adherence**, and **bone** and **renal safety** in diverse settings

FINDINGS

1 HIV-1 incidence rate

Overall **HIV-1 incidence rate** was low; of 17,274 individuals, 101 acquired HIV-1



Most new diagnoses occurred in individuals with **low adherence**, confirming a **dose-dependent relationship** between adherence and protective efficacy of F/TDF

CI, confidence interval; DBS, dried blood spots; F/TDF, emtricitabine/tenofovir disoproxil fumarate; PY, person-years

2 F/TDF resistance

Mutations associated with emtricitabine and/or TDF resistance were detected in n=22 (0.13%) participants

In some participants with available resistance data, the presence of mutations associated with resistance to other HIV-1 drugs suggests transmission of resistant virus

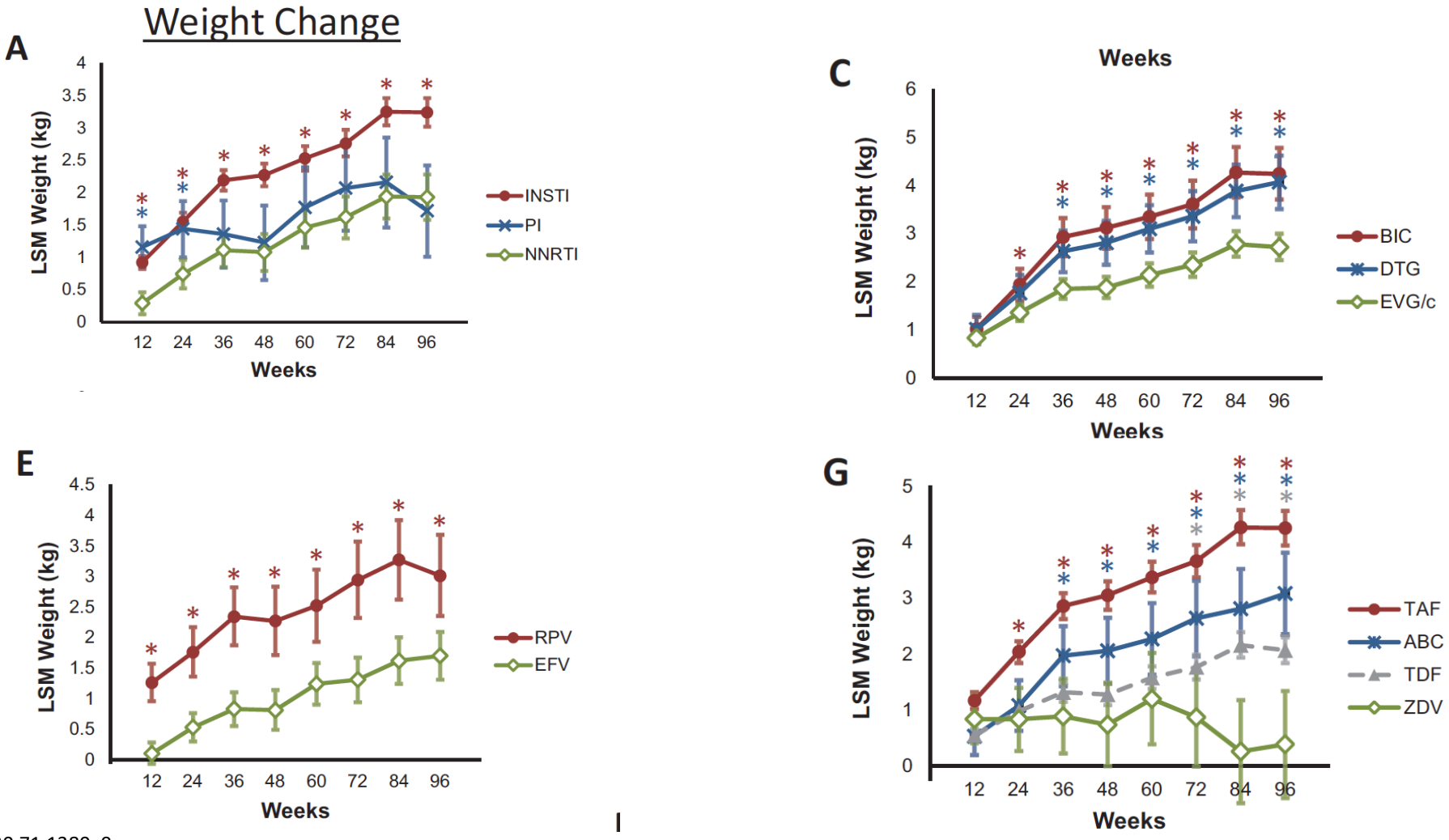
In some participants, resistance was suspected due to unrecognized baseline HIV-1 infections

Landovitz RJ, et al.Clin Infect Dis. 2024 Mar 14:ciae143. doi: 10.1093/cid/ciae143. Epub ahead of print.

Per què continuar investigant en TAR

- El TAR s'ha de mantenir sense interrupció i (actualment) tota la vida
- Reduir toxicitat
- Millorar adherència
- Hi ha persones amb opcions de tractament reduïdes per resistència o toxicitat de tractaments previs
- Millorar qualitat de vida

Augment de pes associat als inhibidors de integrasa



Sax P, et al. Clin Infect Dis 2020;71:1380–9

Augment de pes associat als inhibidors de integrasa

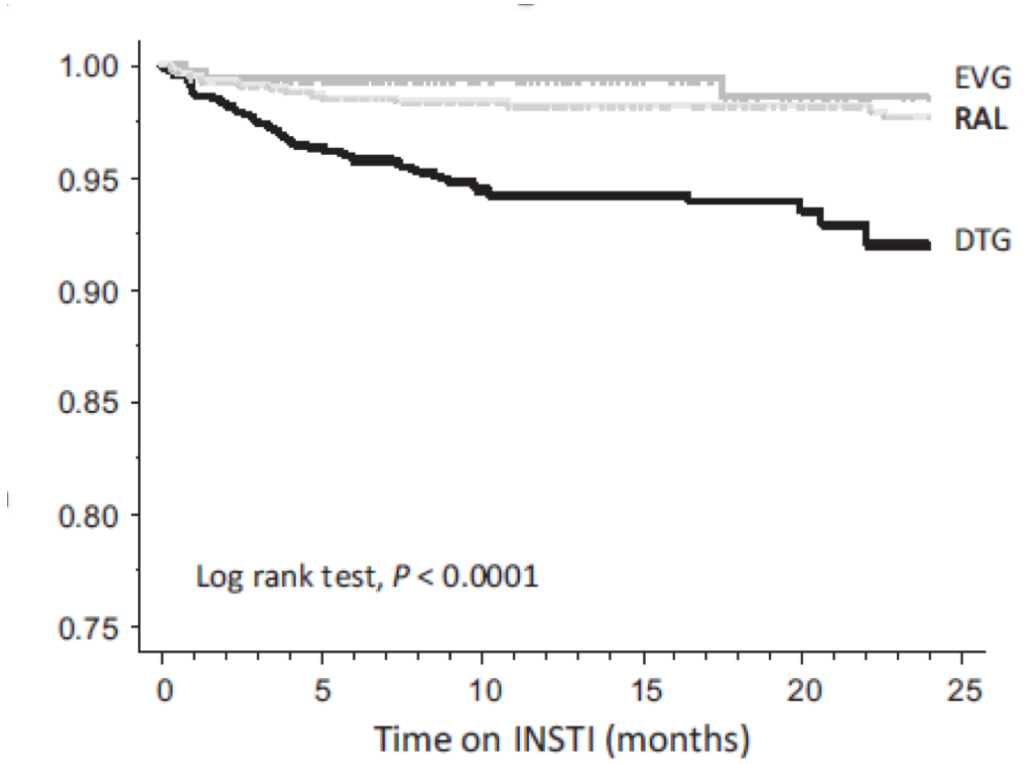
Variable	OR	(95% CI)	*P* Value
CD4 count (<200 vs ≥200 cells/all)	4.36	(3.6–5.27)	<.001
HIV RNA (>100K vs ≤100K copies/mL)	1.98	(1.65–2.37)	<.001
BMI			
Normal vs overweight	1.54	(1.27–1.87)	<.001
Normal vs obese	1.66	(1.29–2.15)	<.001
Sex (female vs male)	1.54	(1.21–1.96)	<.001
Race (black vs non-black)	1.32	(1.10–1.59)	.003
Third ART agent			
BIC/DTG vs EFV	1.82	(1.24–2.66)	.002
EVG/c vs EFV	1.36	(1.04–1.78)	.026
RPV vs EFV	1.51	(1.03–2.20)	.035
ATV/r vs EFV	0.92	(.59–1.45)	.73
NRTI			
TAF vs ZDV	1.75	(1.04–2.95)	.034
TDF vs ZDV	1.19	(.76–1.87)	.44
ABC vs ZDV	0.93	(.47–1.8)	.82
TAF vs ABC	1.9	(1.25–2.88)	.003
TDF vs ABC	1.29	(.79–2.11)	.31
TAF vs TDF	1.47	(1.14–1.90)	.003

Sax P, et al. Clin Infect Dis 2020;71:1380–9

Efectes Adversos neuro-psiquiàtrics dels Inhibidors de Integrasa

Retrospective analysis of PLWH initiating INSTI from two large Clinics in Germany (2007-2016)

	Dolutegravir	Elvitegravir	Raltegravir
All AEs leading to discontinuation over entire follow-up period			
Renal [% (*n*)]	0.2 (2)	3.5 (10)	0.0 (0)
Gastrointestinal [% (*n*)]	0.7 (7)	2.8 (8)	0.9 (6)
Hepatic [% (*n*)]	0.1 (1)	0.0 (0)	0.1 (1)
Skin [% (*n*)]	0.3 (3)	0.7 (2)	0.1 (1)
Other [% (*n*)]	0.5 (5)	1.4 (4)	0.9 (6)
Neuropsychiatric [% (*n*)]	5.0 (49)	1.0 (3)	2.1 (14)
Neuropsychiatric adverse events*			
Insomnia, sleep disturbances	36	2	4
Poor concentration, slow thinking	8	0	0
Dizzyness	13	1	3
Headache, paraesthesia	16	1	6
Depression	7	0	1

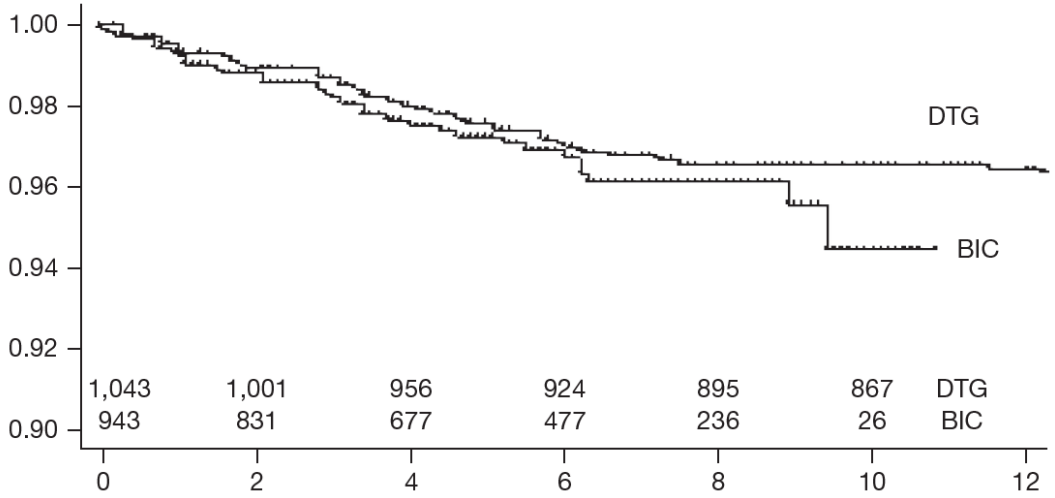


Hoffmann C, et al. HIV Med. 2017 ;18:56-63

Efectes Adversos neuro-psiquiàtrics dels Inhibidors de Integrassa

Table 1. Numbers and characteristics of patients initiated on BIC/F/TAF and the proportion of patients with any AE or with NPAEs leading to drug discontinuation

	All patients	Patients discontinuing BIC/F/TAF due to	
		Any AE	NPAEs
All patients	943	5.3 (50)	3.3 (31)
Subcentre ICH-S, % (*n*)	456	8.6 (39)	5.9 (27)
Subcentre ICH-G, % (*n*)	487	2.3 (11)	0.8 (4)
Gender, ethnicity, age, CD4⁺ T-cells			
Male, % (*n*)	852	5.5 (47)	3.4 (29)
Female gender, % (*n*)	76	3.9 (3)	2.6 (2)
Transgender/diverse, % (*n*)	15	0.0 (0)	0.0 (0)
Caucasian origin, % (*n*)	805	5.6 (45)	3.4 (27)
Median age, years (range)	50.2 (19.2–85.7)	50.2 (32.1–80.3)	50.4 (32.1–64.3)
Older age >60 years, % (*n*)	151	4.6 (7)	2.6 (4)
Median CD4⁺ T-cells/µl (range)	667 (0–1,981)	643 (113–1,575)	625 (227–1,575)
Treatment line			
First-line, % (*n*)	62	3.2 (2)	3.2 (2)
TE, % (*n*)	881	5.4 (48)	3.3 (29)
TE, HIV RNA <50 copies/ml, % (*n*)	826	5.1 (42)	3.3 (27)
TE, HIV RNA >50 copies/ml, % (*n*)	55	9.1 (5)	3.6 (2)
Prior DTG exposure			
None	496	4.8 (24)	3.0 (15)
Exposure without AEs	392	4.6 (18)	2.8 (11)
Discontinuation due to NPAEs	35	17.1 (6)	11.4 (4)
Discontinuation due to other AEs	20	10.0 (2)	5.0 (1)
Neuropsychiatric diagnoses			
Major depression	184	9.8 (18)	6.5 (12)
Other psychiatric disorders[a]	58	8.6 (5)	1.7 (1)
None	701	3.9 (27)	2.6 (18)



Gehan-Breslow-Wilkoxon test. P=0.36

Hoffmann C, et al. Antivir Ther. 2020;25:83-90

Interaccions farmacològiques amb ARV

Inhibidors CYP3A4

IP/p

Ritonavir
Cobicistat

Inductors CYP3A4

EFV
NVP
ETR

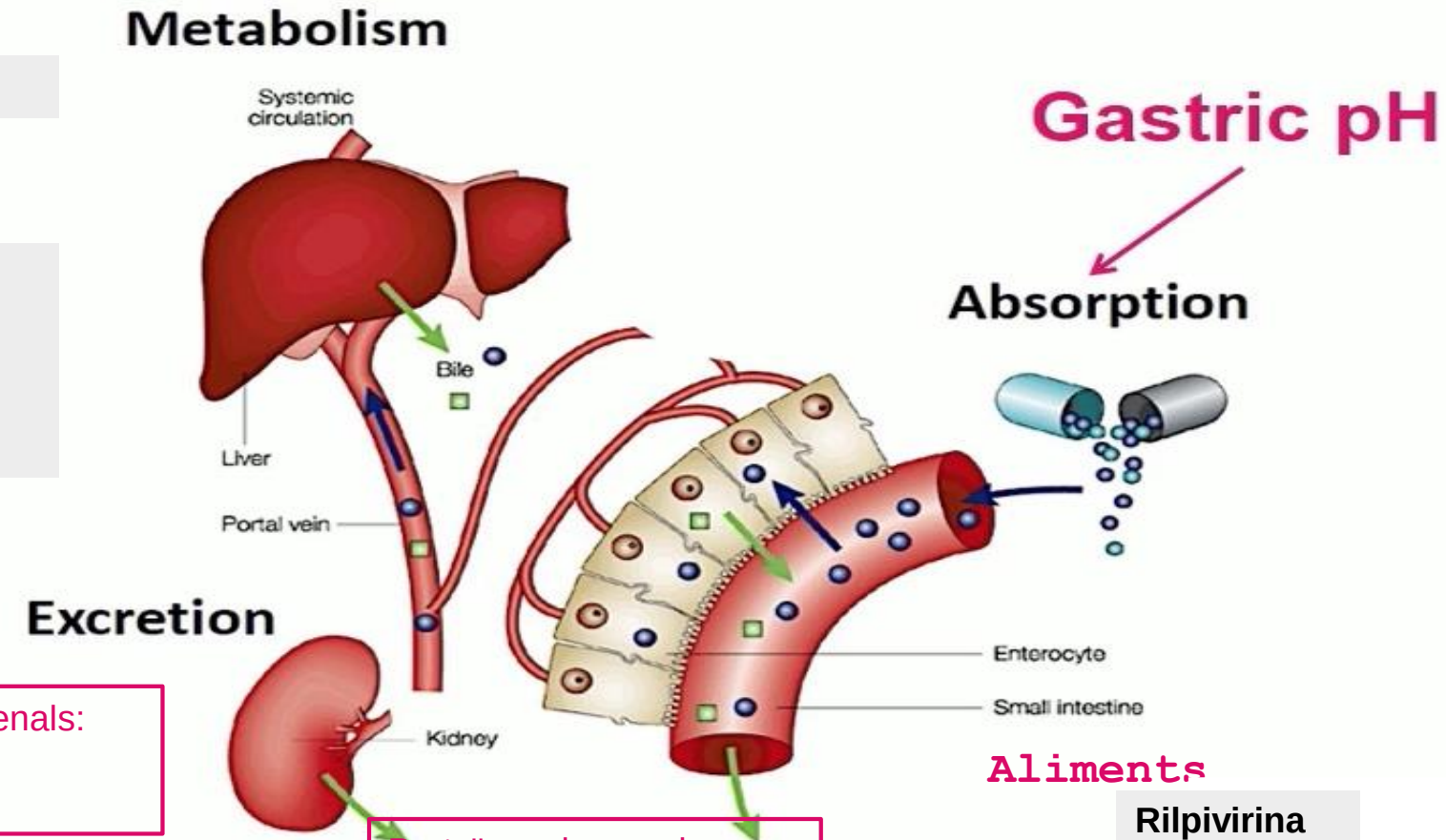
UGT1A1

Inhibidors de integrasa

CYP3A4

Inhibidors de Proteasa
ITINN
EVG/c

(Inhibidors de Integrasa 2ªG)



Transportadors renals:
- **OCT2**
- **MATE1**

DTG, BIC

Proteïnes de membrana
Glicoproteina P

TAF

Rilpivirina

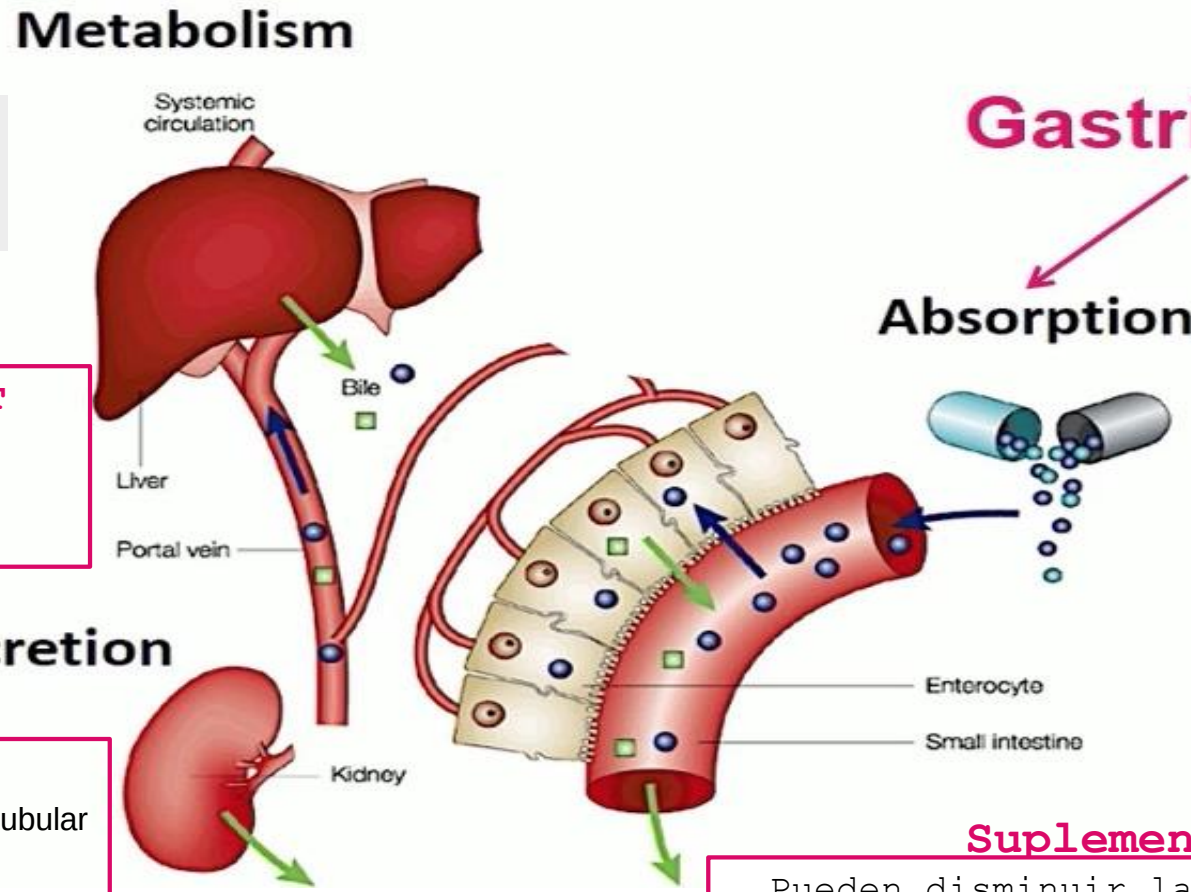
Suplements minerals

Inhibidors de integrasa

Interaccions farmacològiques amb Inhibidors de Integrassa

UGT1A1
BIC y DTG, en mucho menor grado, por **CYP3A4.**

Inductores potentes de CYPs, UGT y Trasportadores de fármacos, disminuyen concentraciones
Requiere aumentar dosis



DTG, BIC inhiben transportadores renales:
- **OCT2** (organic cationic transporter 2), secreción tubular de algunos fármacos y de Cr (**aumento de Cr** sin trascendencia renal)
- **MATE1** implicado en la eliminación de Metformina

Aumenta la concentración de Metformina (monitorizar si insuficiencia renal)

Suplementos minerales

Pueden disminuir la absorción.
se debe administrar:
2h ante o 6 h después de estos productos.

Canvis de TAR en PVIH amb CV suprimida

- Toxicitat
- Prevenció de toxicitat
- Interaccions
- Simplificació (objectiu: millorar adherència, qualitat de vida..)
  - Menys pastilles
  - Menys fàrmacs
- Reducció del cost econòmic
- TAR "*Long-Acting*"

Canvis de TAR en PVIH amb CV suprimida

2 NRTI + ITINN

2 NRTI + IP/p

2 NRTI + INI

RPV/FTC/TAF
DOR/3TC/TDF* (DOR+FTC/TAF)

DTG+FTC/TAF
BIC/FTC/TAF
RAL + FTC/TAF

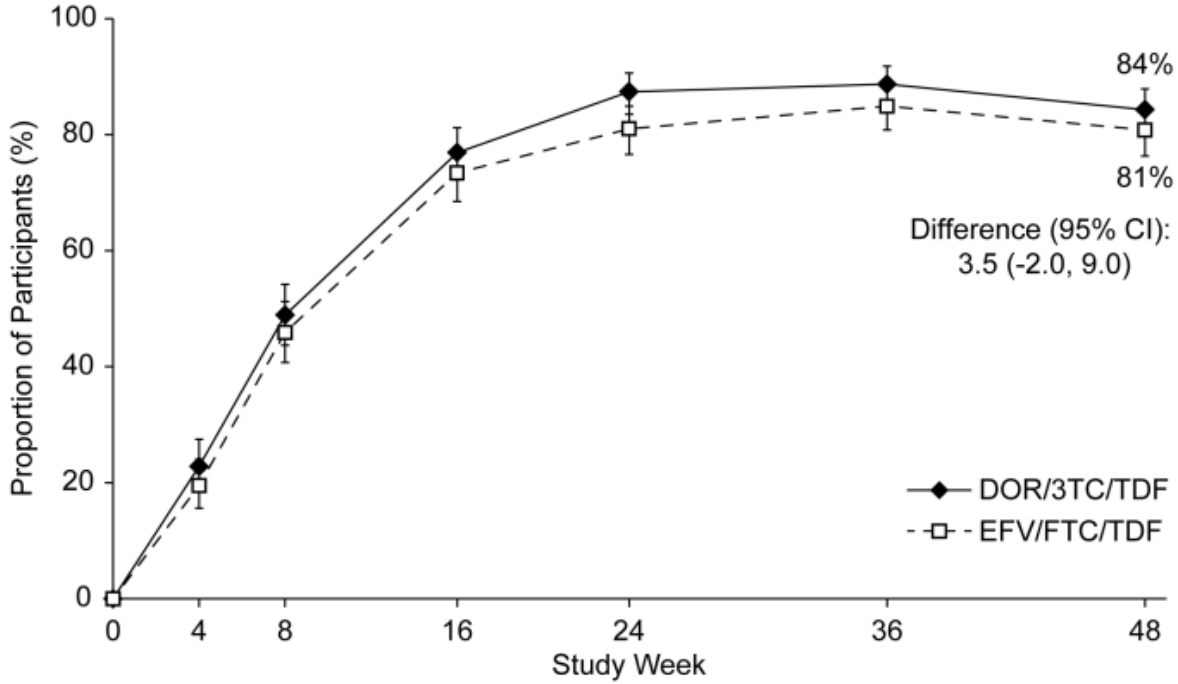
DTG/3TC
DTG/RPV

DRV/cobi/FTC/TAF
DRV/c+3TC

CAB + RPV LA im

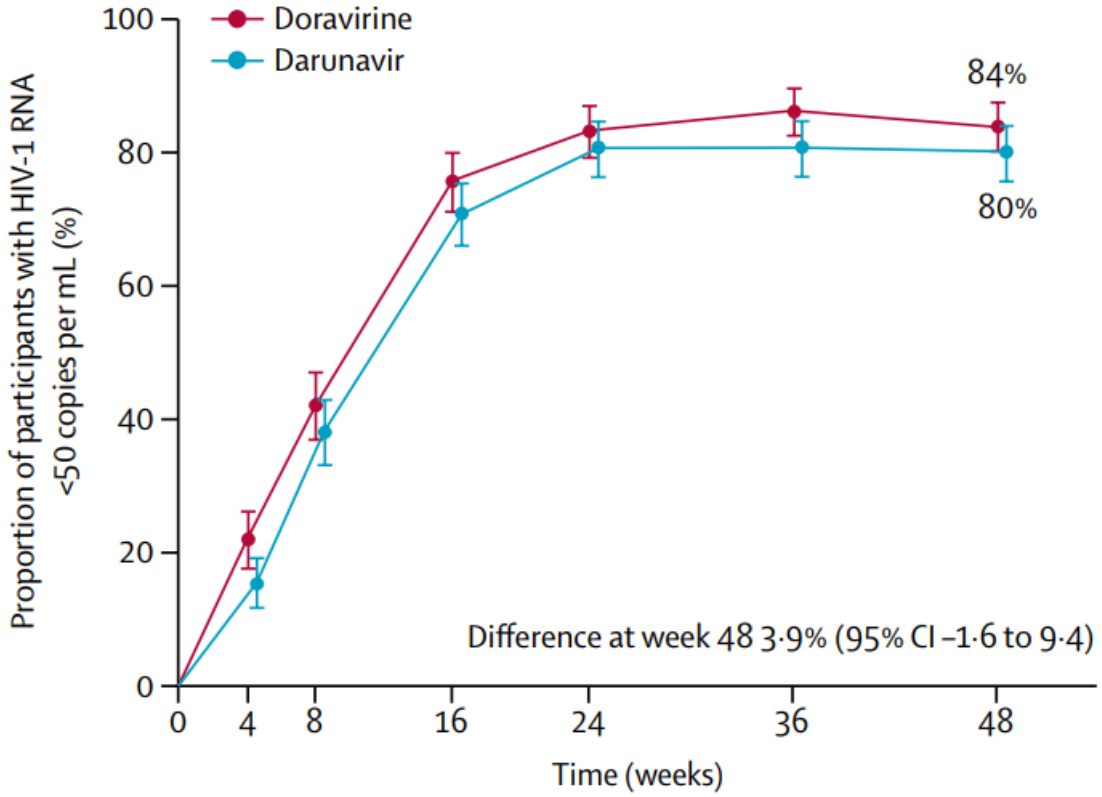
Fernández A, Imaz A. Clinical considerations when switching antiretroviral therapy. Expert Rev Clin Pharmacol. 2024 Jul;17(7):565-577.

Doravirine/Lamivudine/Tenofovir Disoproxil Fumarate is Non-inferior to Efavirenz/Emtricitabine/Tenofovir Disoproxil Fumarate in Treatment-naive Adults With Human Immunodeficiency Virus–1 Infection: Week 48 Results of the DRIVE-AHEAD Trial



Orkin C, et al. Clin Infect Dis. 2019;68(4):535-544.

Doravirine versus ritonavir-boosted darunavir in antiretroviral-naive adults with HIV-1 (DRIVE-FORWARD): 48-week results of a randomised, double-blind, phase 3, non-inferiority trial



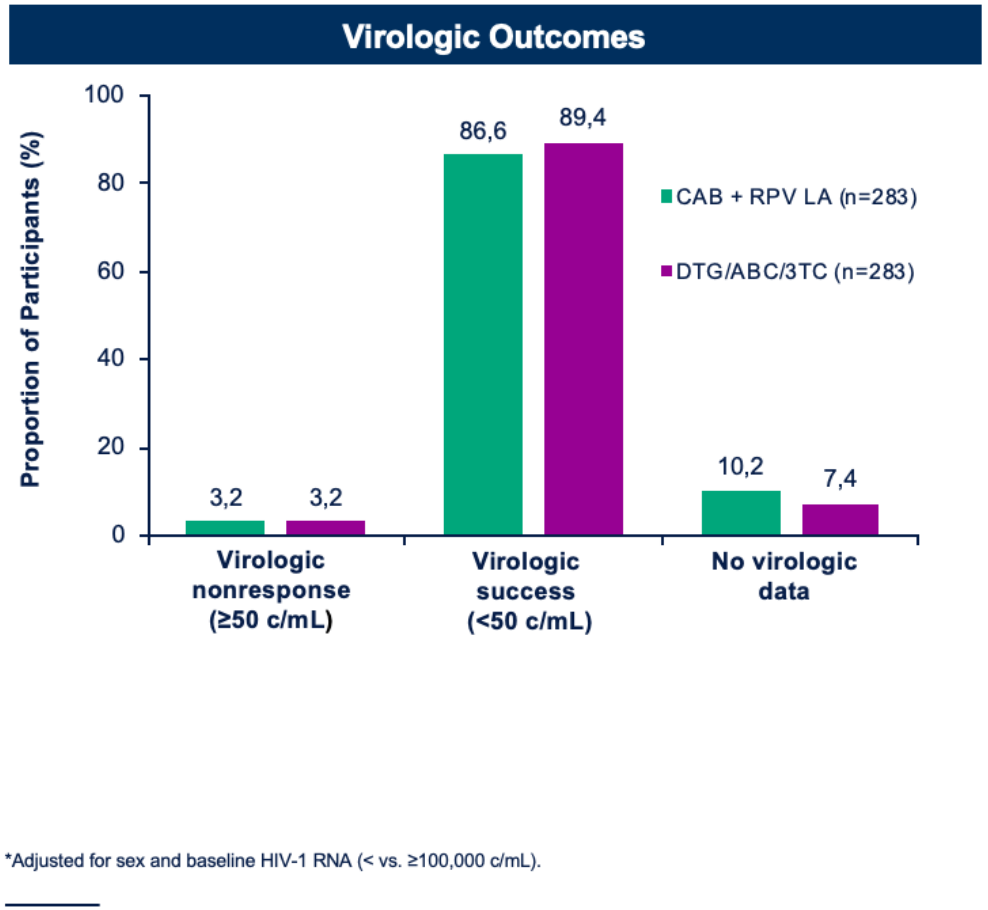
Molina JM, et al. Lancet HIV. 2018;5(5):e211-e220.

DORAVIRINA

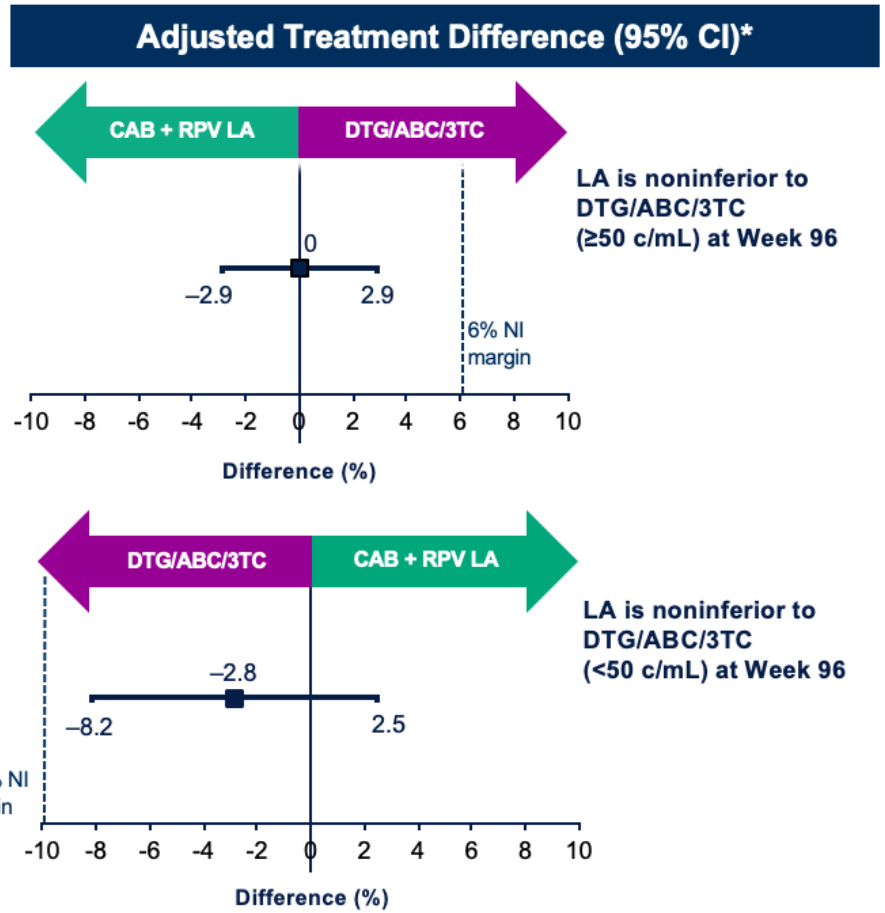
- Eficàcia (naïve i canvis amb CV suprimida)
- Simplicitat
- Bon perfil de seguretat
- Bon perfil d'interaccions
- Perfil de resistències different a altres ITINN

TAR long-acting per via intramuscular

FLAIR Week 96 Virologic Response

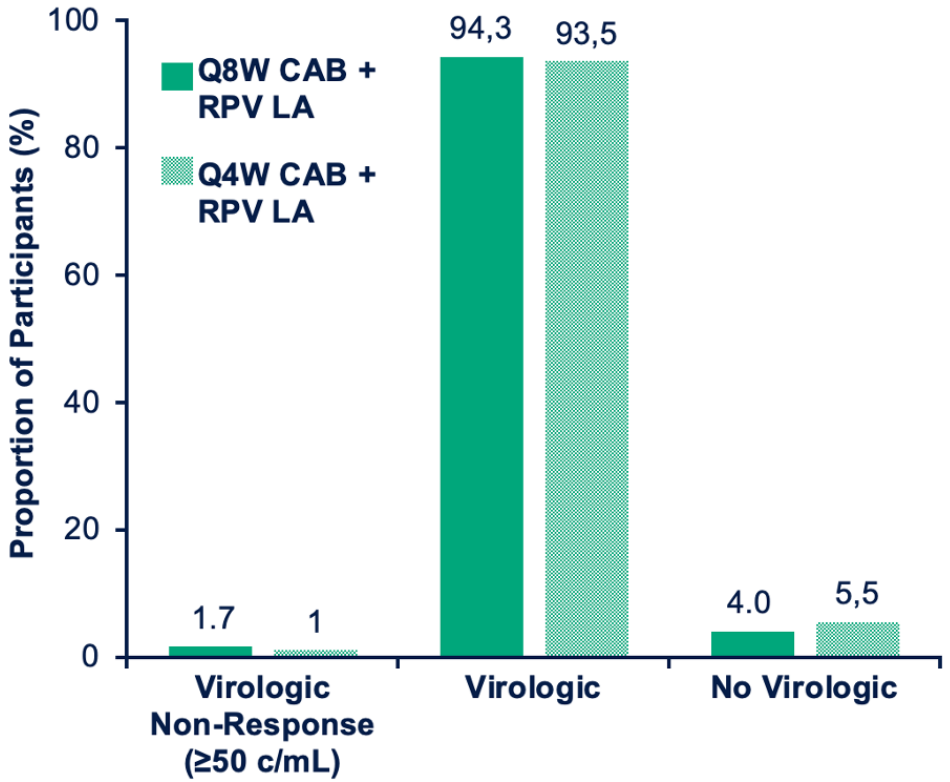


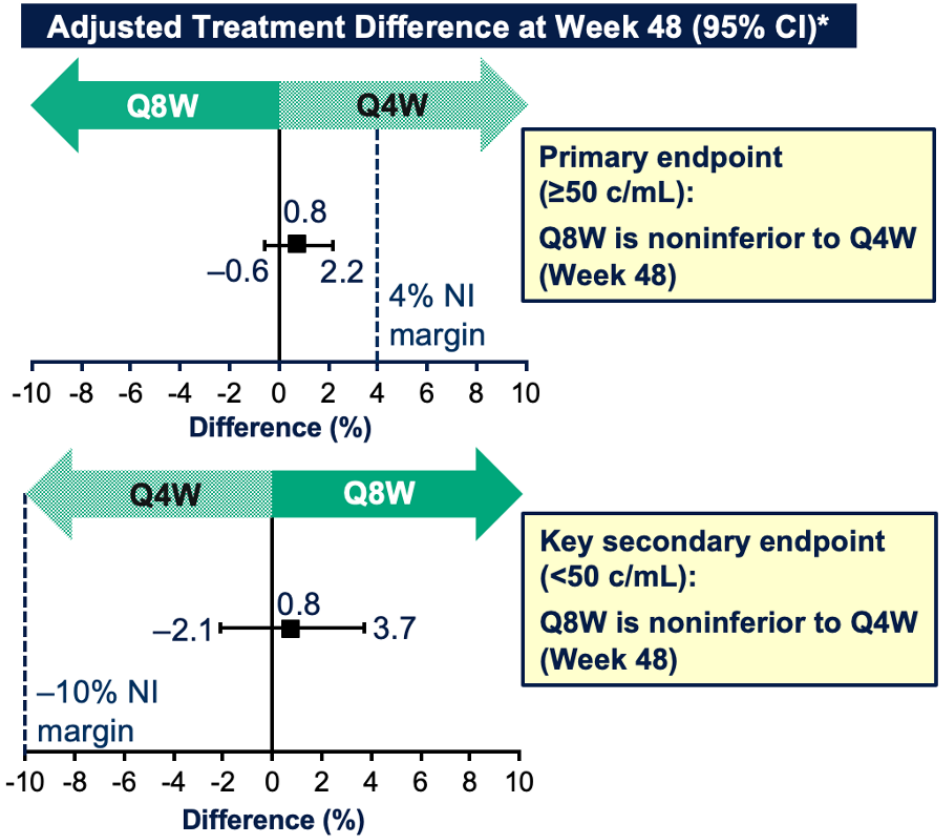
*Adjusted for sex and baseline HIV-1 RNA (< vs. ≥100,000 c/mL).



Orkin C, et al. Lancet HIV. 2021 Apr;8(4):e185-e196; Orkin et al. CROI 2020; Boston, MA. Poster 482LB.

TAR long-acting per via intramuscular





Overton ET, et al. Lancet. 2021 Dec 19;396(10267):1994-2005; Overton et al. CROI 2020; Boston, MA. Presentation 334.

CAB/RPV LA intramuscular. Limitacions

Outcome, n (%), ITT-E	Q8W (n=522)	Q4W (n=523)
Number of injections	8470	15,711
Number of ISR events (events/injections)*	2507 (30)	3152 (20)
Grade ≥3 – severe†	43 (<1)	48 (<1)
Injection site reactions‡		
Pain	2014 (24)	2567 (16)
Nodule	113 (1)	204 (1)
Discomfort	92 (1)	110 (1)
Withdrawals due to injection-related reasons, participant n (%)§	6 (1)	11 (2)

Factors associated with risk of virologic failure

Overall, **1.25%** (n=13/1039) of participants in RCT experienced CVF

Significantly associated ($p<0.05$) with increased odds of CVF:
- Proviral RPV resistance-associated mutations (RAMs)
- HIV-1 subtype A6
- Higher body mass index
- Lower Week 8 RPV trough concentrations

Few participants (0.4%) with zero or 1 baseline factor had CVF. Only a combination of ≥2 baseline factors (observed in 3.4%; n=35/1039) was associated with increased CVF risk (25.7%, n=9/35).

Orkin C, et al. Clin Infect Dis. 2023;77(10):1423-1431

Long-Acting Injectable CAB/RPV is Superior to Oral ART in PWH With Adherence Challenges: ACTG A5359

Aadia I. Rana
University of Alabama at Birmingham, Birmingham, AL, USA

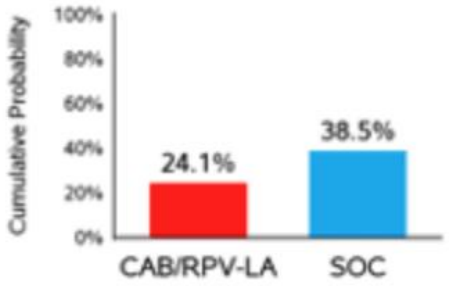
Phase III, prospective, randomized, open-label trial

CAB+RPV LA monthly (n=145)
SOC (n=148)

Primary Outcome

Regimen Failure

Difference	Nominal 98.75% CI
-14.5%	(-29.8%, 0.8%)



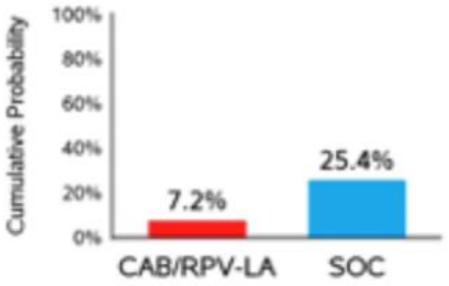
Number of participants

Regimen Failure	28	47
VF	5	28
TRT-DISC	23	19

Secondary Outcomes

Virologic Failure

Difference	Nominal 98.75% CI
-18.2%	(-31.1%, -5.4%)

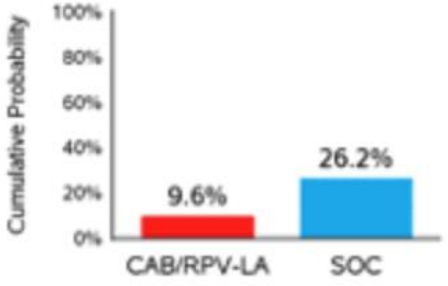


Number of participants

Virologic Failure	6	28

Treatment-related Failure

Difference	Nominal 98.75% CI
-16.6%	(-29.9%, -3.3%)

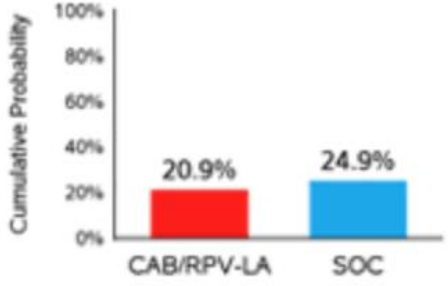


Number of participants

Treatment-related Failure	9	29
VF	6	28
TRT-DISC (AE)	3	1

Permanent Treatment Discontinuation

Difference	Nominal 98.75% CI
-4.1%	(-18.0%, 9.8%)



Number of participants

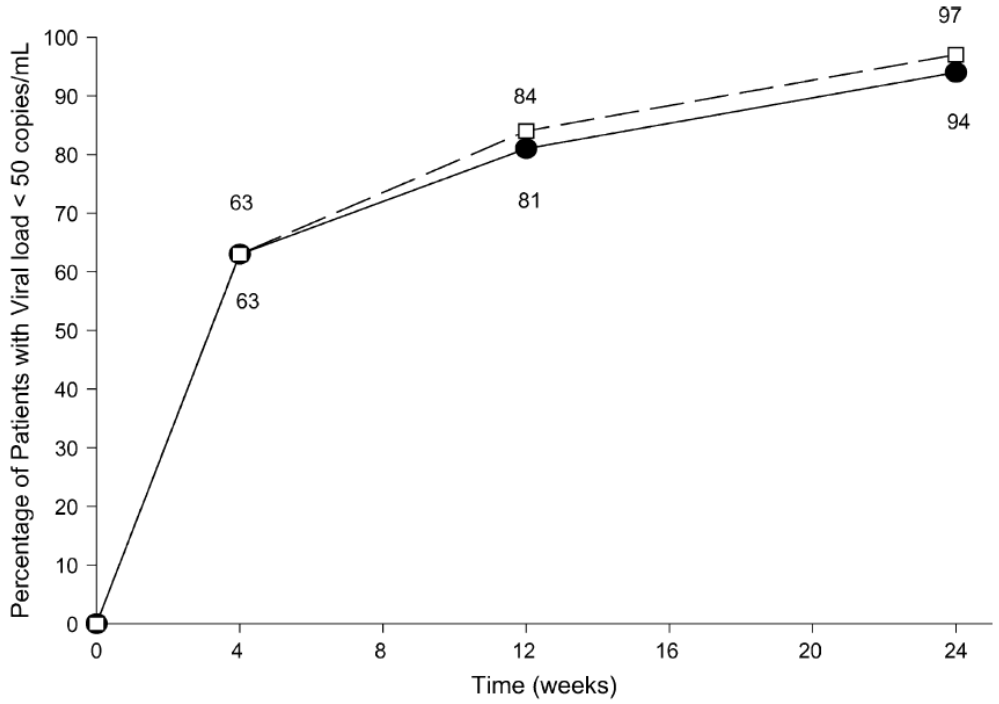
Permanent TRT-DISC	25	30

Rana AI, et al. CROI 2024; Denver, CO. Presentation 212.

VF with selection of resistance: 2/6 vs 2/28

Simplificació del TAR en situació de multi-resistència

Raltegravir, Etravirine, and Ritonavir-Boosted Darunavir: A Safe and Successful Rescue Regimen for Multidrug-Resistant HIV-1 Infection



Imaz A, et al. JAIDS 2009;52(3):382-6

Switching to bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) plus darunavir/cobicistat in heavily antiretroviral-experienced, virologically suppressed HIV-infected adults receiving complex regimens

Daniel Podzamczer[1]*, Arkaitz Imaz[2], Ana Lopez-Lirola[3], Hernando Knobel[4], Mar Masiá[5], Chiara Fanciulli[6], Cristina Hernández[7], María Lagarde[8], Angela Gutierrez[9], Adrià Curran[10], Luis Morano[11], Marta Montero-Alonso[12], Jesús Troya[13], Raúl Rigo[2], María Casadellà[14], Antonio Navarro-Alcaraz[14], Fernando Ardila[2], Mariona Parera[14], Enrique Bernal[15], Patricia Echeverria[16], Vicente Estrada[17], Carmen Hidalgo-Tenorio[18], Juan Macias[19], Paula Prieto[20], Joaquín Portilla[21], Eulalia Valencia[22], María Jesús Vivancos[23] and Antonio Rivero[24,25]

J Antimicrob Chemother 2023; 78: 2696–2701

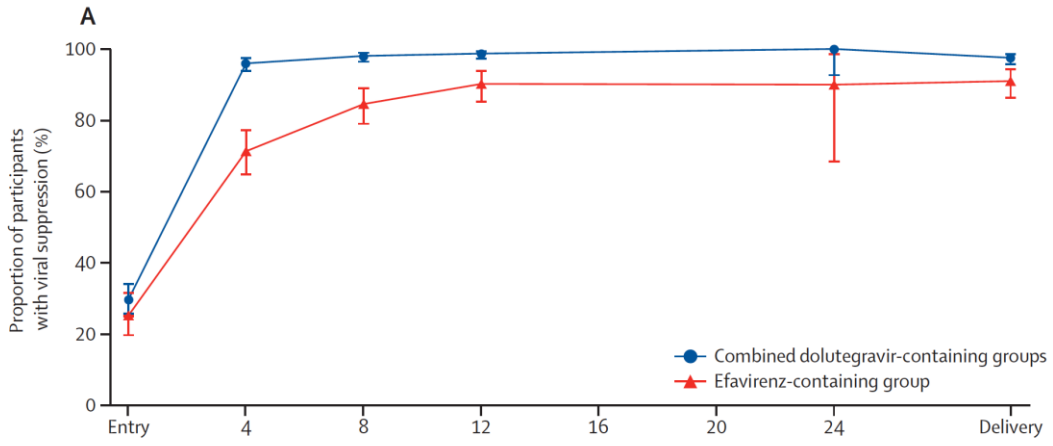
A Randomized Trial of Dolutegravir Plus Darunavir/Cobicistat as a Switch Strategy in HIV-1-Infected Patients With Resistance to at Least 2 Antiretroviral Classes

José R. Santos,[1] Pere Domingo,[2] Joaquín Portilla,[3] Félix Gutiérrez,[4,5,6] Arkaitz Imaz,[7] Helem Vilchez,[8] Adrià Curran,[9] Nieves Valcarce-Pardeiro,[10] Antoni Payeras,[11] Enrique Bernal,[12,13] Marta Montero-Alonso,[14] Miguel Yzusqui,[15] Bonaventura Clotet,[1,16] Sebastià Videla,[17,18] José Moltó,[1,6] and Roger Paredes[1,16,19]; on behalf of the 2D Study Group

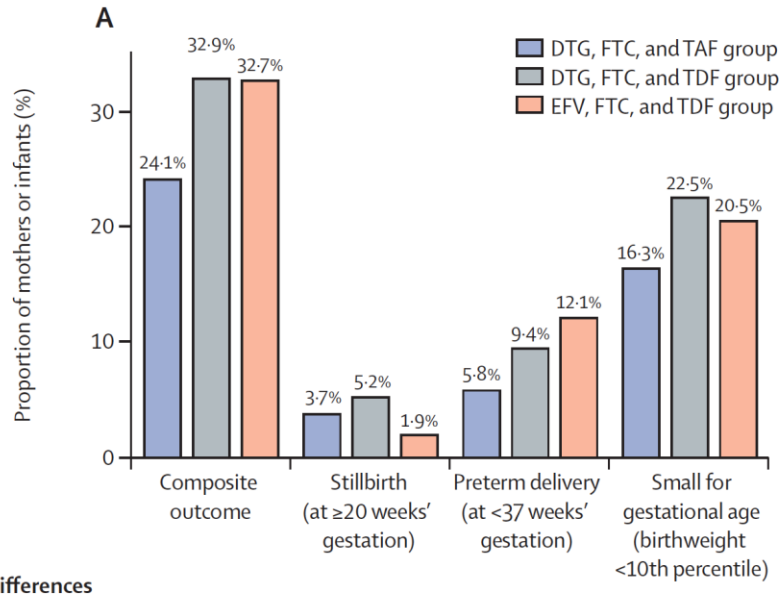
Open Forum Infect Dis. 2023 Oct 31;10(11):ofad542

TAR durant l'embaràs

Multicentre, open-label, randomised controlled, phase 3 trial done at 22 clinical research sites in 9 countries (Botswana, Brazil, India, South Africa, Tanzania, Thailand, Uganda, the USA, and Zimbabwe).
Pregnant women (aged ≥18 years) with confirmed HIV-1 infection and at 14–28 weeks' gestation were eligible.



Proportion of participants (%)						
Combined dolutegravir-containing groups	129/432 (30%)	404/421 (96%)	404/412 (98%)	382/387 (99%)	47/47 (100%)	395/405 (98%)
Efavirenz-containing group	53/209 (25%)	147/206 (71%)	170/201 (85%)	166/184 (90%)	18/20 (90%)	182/200 (91%)



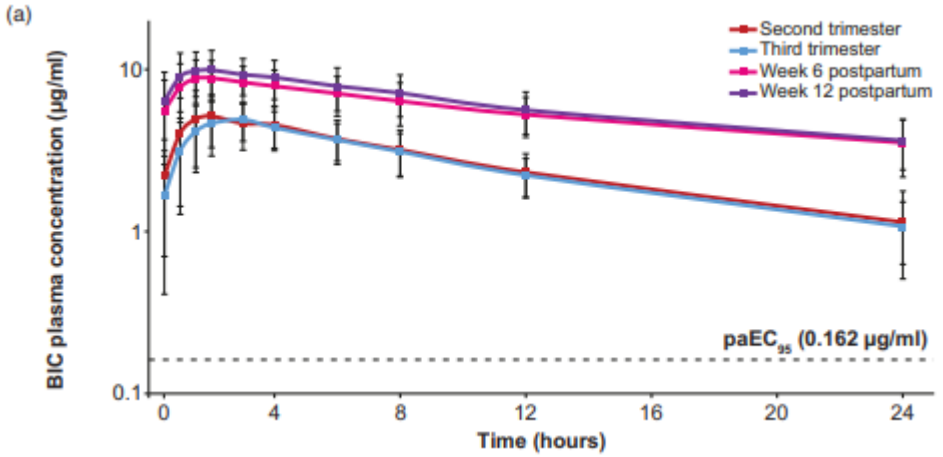
Group differences (95% CI)				
DTG, FTC, and TAF group *vs* DTG, FTC, and TDF group	−8·8% (−17·3% to −0·3%)	−1·5% (−5·4% to 2·4%)	−3·6% (−8·8% to 1·5%)	−6·2% (−13·9% to 1·5%)
DTG, FTC, and TDF group *vs* EFV, FTC, and TDF group	0·2% (−8·8% to 9·1%)	3·3% (−0·2% to 6·8%)	−2·7% (−8·7% to 3·3%)	2·0% (−6·0% to 10·0%)
DTG, FTC, and TAF group *vs* EFV, FTC, and TDF group	−8·6% (−17·1% to −0·1%)	1·8% (−1·3% to 4·9%)	−6·3% (−11·8% to −0·9%)	−4·2% (−11·7% to 3·4%)

Lockman S, Brummel SS, et al. Lancet 2021; 397: 1276–92

TAR durant l'embaràs

A study of the pharmacokinetics, safety, and efficacy of bictegravir/emtricitabine/tenofovir alafenamide in virologically suppressed pregnant women with HIV

Zhang H, et al. AIDS. 2024 Jan 1;38(1):F1-F9.11



Clinical Infectious Diseases

BRIEF REPORT

IDSA Infectious Diseases Society of America

hivma hiv medicine association

Bictegravir Use During Pregnancy: A Multicenter Retrospective Analysis Evaluating Human Immunodeficiency Virus Viral Suppression and Perinatal Outcomes

Holt LM, et al. Clin Infect Dis. 2024 Apr 26:ciae218. Epub ahead of print.

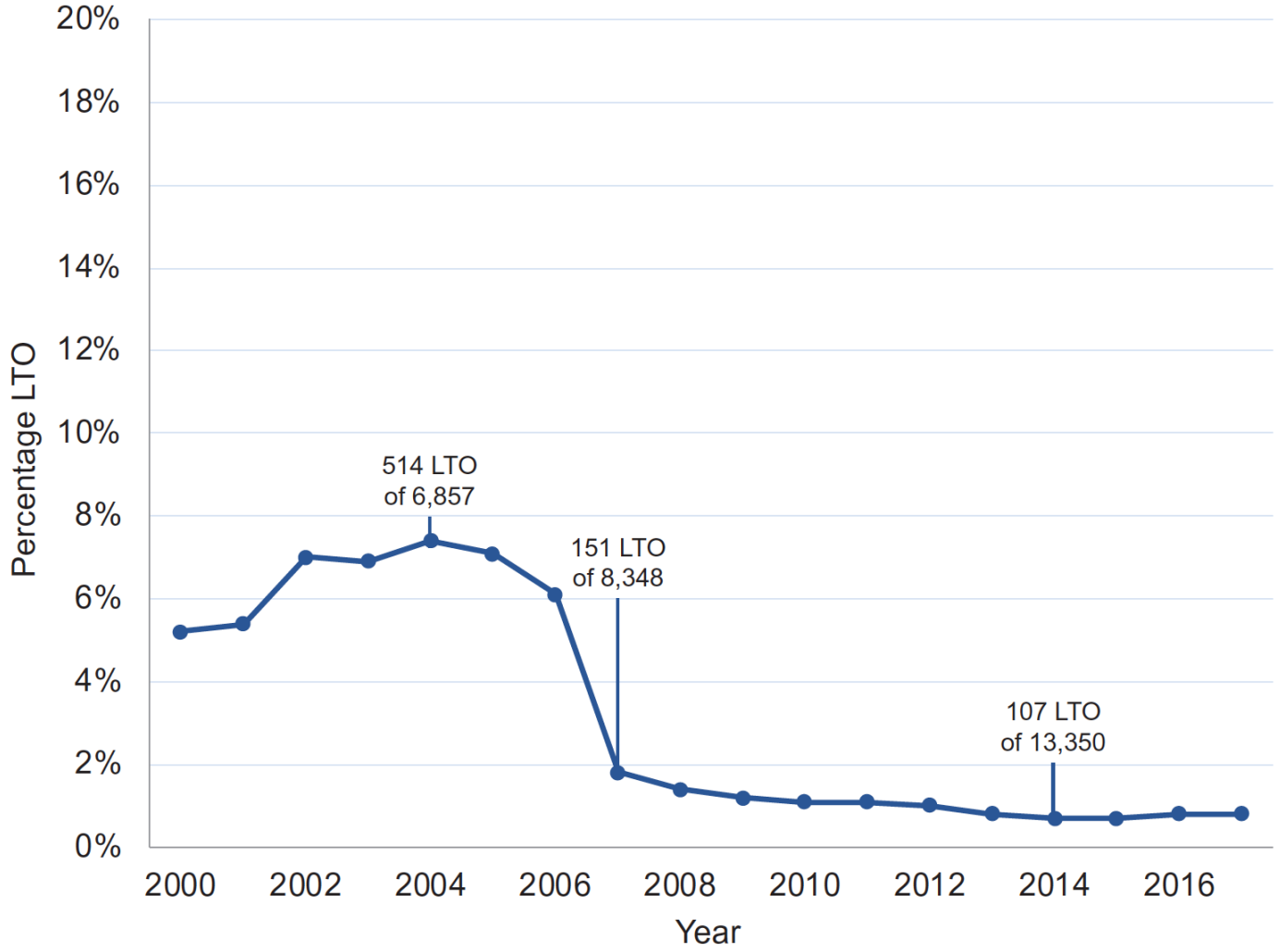
pHACS Pediatric HIV/AIDS Cohort Study

A Study of the National Institutes of Health

Birth outcomes following bictegravir exposure during pregnancy

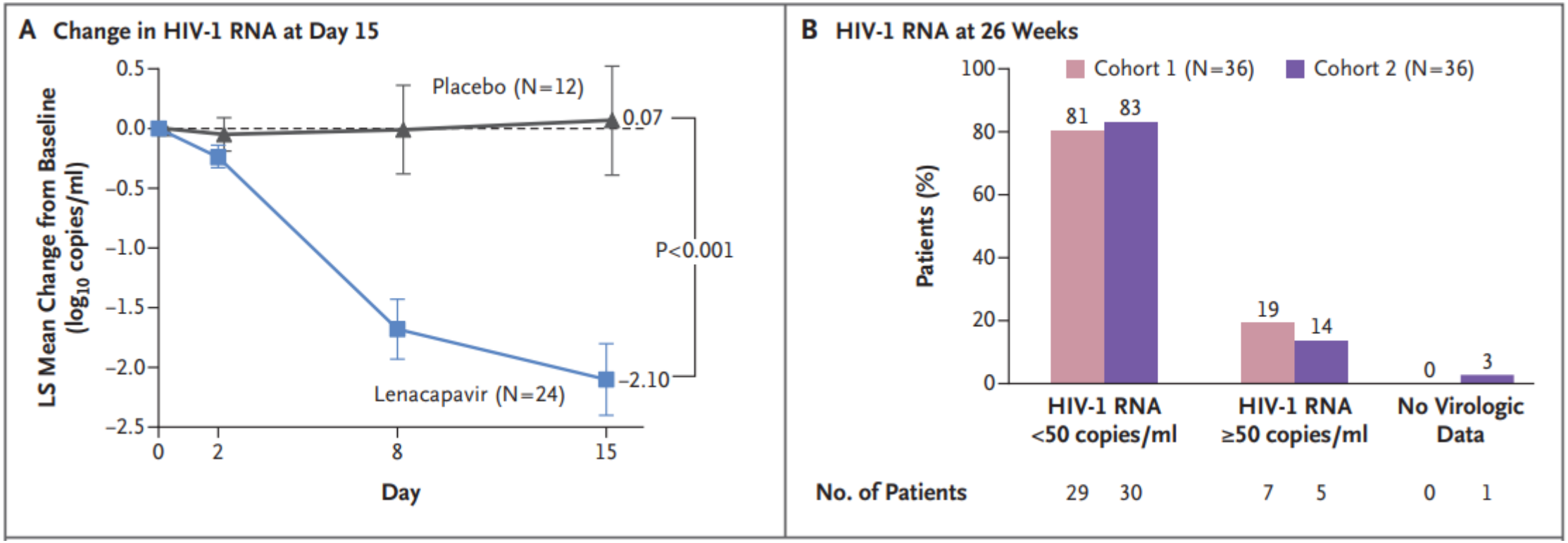
Olivero R, et al. AIDS. 2024 Oct 15. Epub ahead of print

Nous fàrmacs per PVIH amb opcions limitades de TAR



Bajema KL, et al. AIDS 2020, 34:2051–2059

Capsid Inhibition with Lenacapavir in Multidrug-Resistant HIV-1 Infection



Segal-Maurer S, et al. N Engl J Med 2022;386:1793-803.

CONCLUSIONS

TAR actual: elevada eficàcia i simplicitat
... Però no és perfecte (toxicitat, interaccions, pautes orals diàries a molt llarg termini...)

Recerca en TAR cap a:
- Pautes amb menys fàrmacs
- Tractaments "l*ong-acting*"
- Noves vies d'administració

A l'horitzó: Erradicació, cura funcional, vacuna preventiva

Mentrestant:
PrEP: noves opcions long-acting (Cabotegravir, Lenacapavir)

Moltes Gràcies!

CAMFiC
societat catalana de medicina familiar i comunitària