Nuevas estrategias terapéuticas para el VIH y la hepatitis C

II Jornada de Actualización en Infección por VIH para Atención Primaria

aula Clínic

Barcelona, 17-10-2014

Arkaitz Imaz

Unitat de VIH
Servei de M. Infeccioses

Bellvitge Hospital Universitari

IDIBELL Institut d'Investigació Biomèdica de Bellvitge

Estrategias de Tratamiento de la infección por VIH

- Con que tratar
- Cuando tratar

Estrategias de Tratamiento de la infección por VIH

- Con que tratar
  - Qué fármacos
  - Qué combinaciones

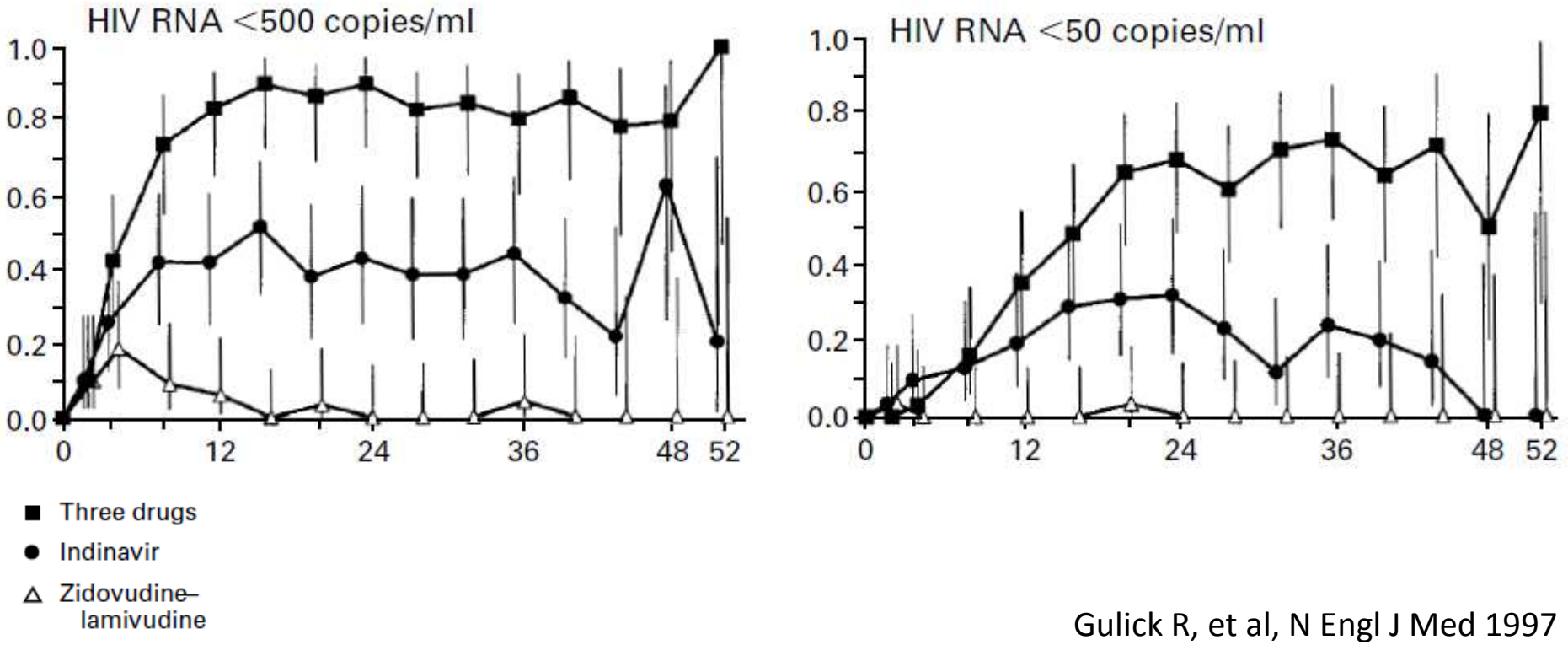
Escenarios

Tratamiento inicial Simplificación Rescate

TAR combinado

The NEW ENGLAND JOURNAL of MEDICINE

TREATMENT WITH INDINAVIR, ZIDOVUDINE, AND LAMIVUDINE IN ADULTS WITH HUMAN IMMUNODEFICIENCY VIRUS INFECTION AND PRIOR ANTIRETROVIRAL THERAPY



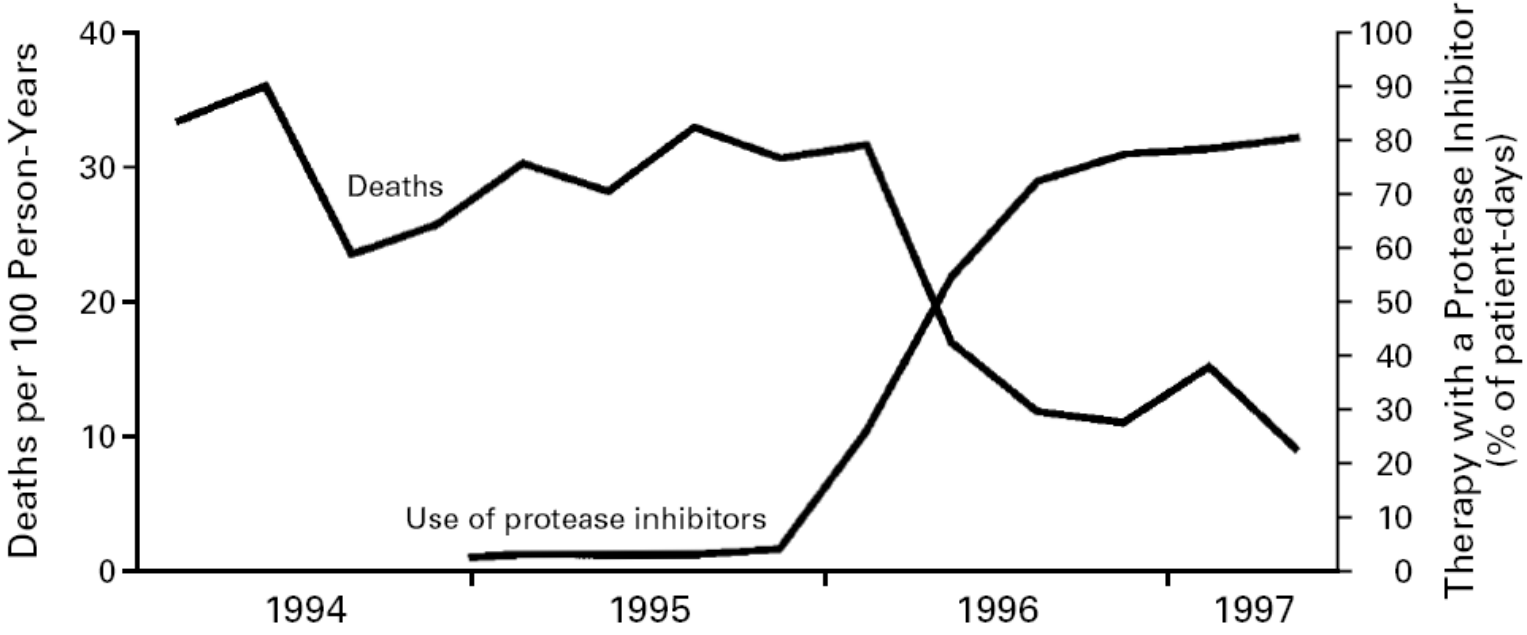
Gulick R, et al, N Engl J Med 1997

The New England
Journal of Medicine

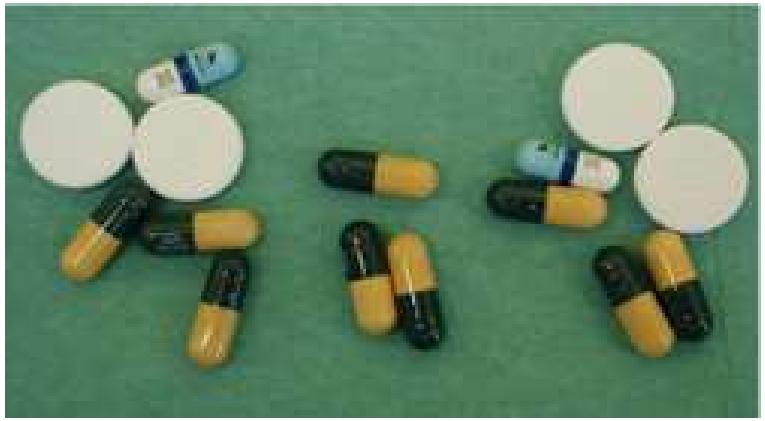
VOLUME 338 MARCH 26, 1998 NUMBER 13

DECLINING MORBIDITY AND MORTALITY AMONG PATIENTS WITH ADVANCED HUMAN IMMUNODEFICIENCY VIRUS INFECTION

FRANK J. PALELLA, JR., M.D., KATHLEEN M. DELANEY, M.S., ANNE C. MOORMAN, B.S.N., M.P.H., MARK O. LOVELESS, M.D., JACK FUHRER, M.D., GLEN A. SATTEN, PH.D., DIANE J. ASCHMAN, R.PH., M.S., SCOTT D. HOLMBERG, M.D., M.P.H., AND THE HIV OUTPATIENT STUDY INVESTIGATORS*



Inicios del TAR combinado (TARGA)

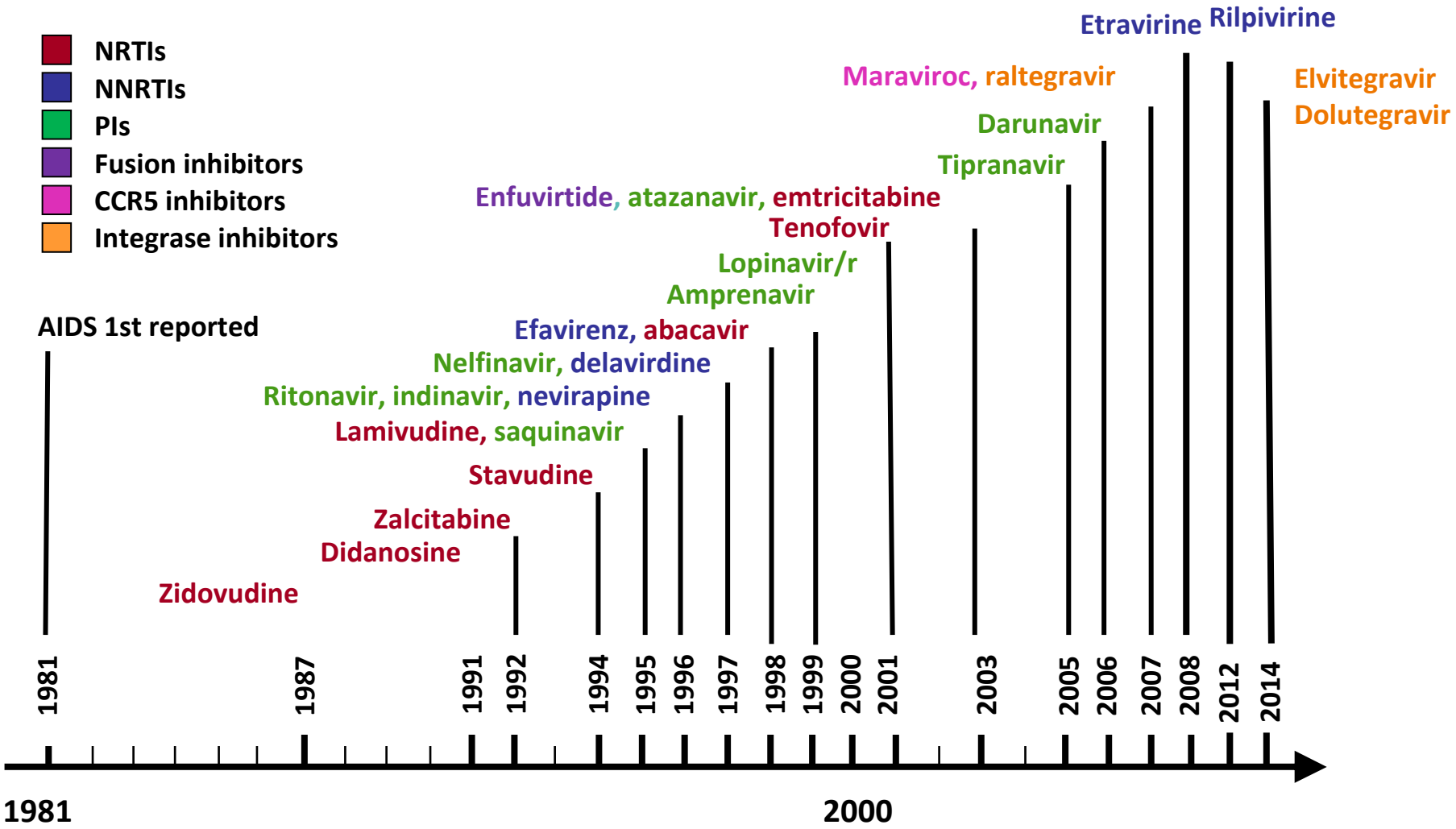


- Problemas de Adherencia
- Problemas de Toxicidad

Resistencia

Opciones limitadas:
ITIAN, ITINN e IP

Evolució del TAR



Fármacos antirretrovirales 2014

Inhibidores de la entrada

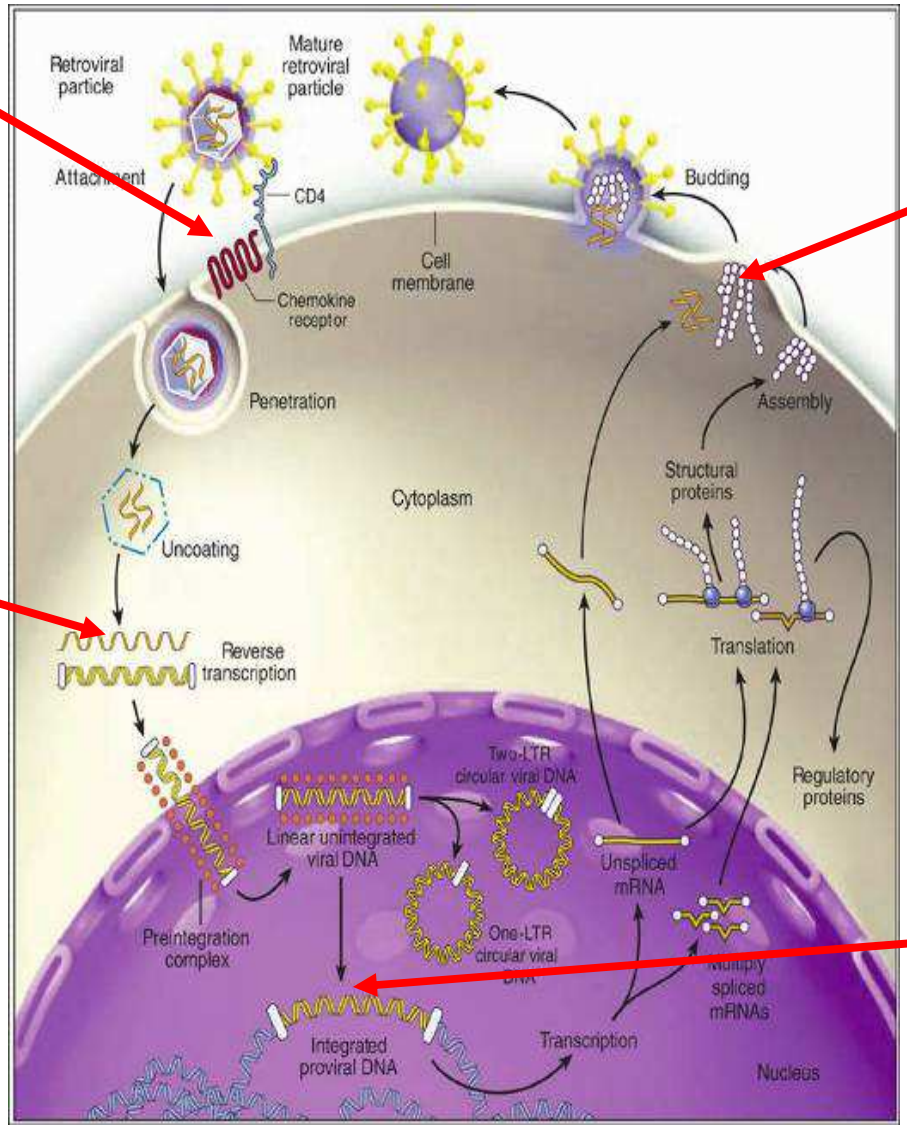
ENF **MRV**

ITI**AN**

AZT ddI
d4T **3TC**
ABC **TDF**
FTC

ITI**NAN**

EFV **ETR**
NVP **RPV**



Inhibidores de proteasa

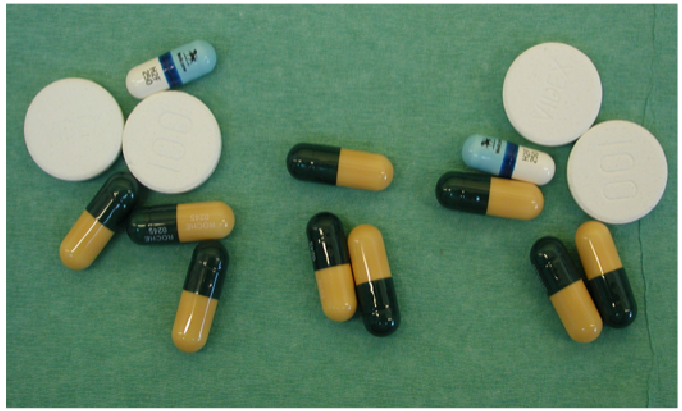
SQV IDV
RTV NFV
FPV **LPV**
ATV **TPV**
DRV

Inhibidores integrasa

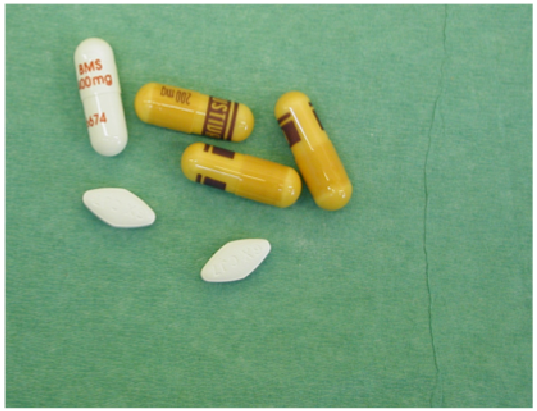
RAL **EVT**
DTG

Evolució del TAR

1996-97



2001-02



2003-04

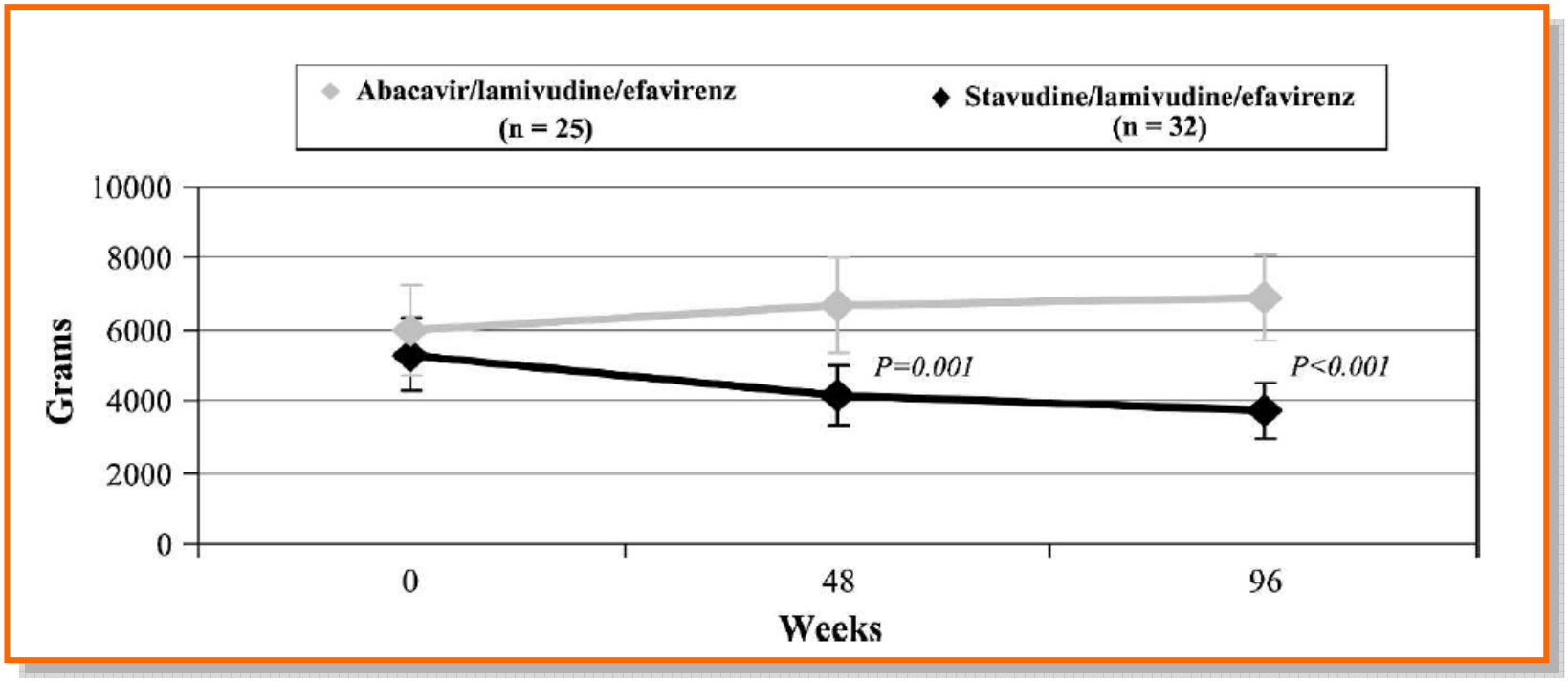
2005-2006

2008

Evolució del TAR

Estudio ABCDE:

Grasa en miembros por DEXA (N=57)



Podzamczer D, et al. JAIDS 2007

The NEW ENGLAND JOURNAL of MEDICINE

Long-Term Control of HIV by *CCR5* Delta32/Delta32 Stem-Cell Transplantation

Hütter G, et al. NEJM 2009

THE LANCET

Barriers to a cure for HIV: new ways to target and eradicate HIV-1 reservoirs

Katlama C, et al. Lancet 2013

TAR: objetivos

- Eficacia
- Simplicidad
- Tolerabilidad
- Baja/nula toxicidad a largo plazo
- Coste

TAR de inicio

1 ITINN

2 ITIAN

Truvada® (TDF+FTC) + **1 IP/r**

Kivexa® (ABC+3TC)

1 INI

TAR de inicio

Per qué 2 ITIAN + 3er fármaco

- Pautas más sencillas
- No interacciones entre ITIAN y otras familias
- Eficacia demostrada en EC
- Gran experiencia

Tratamiento triple sin ITIAN

- Pautas mas complejas
- Posibles interacciones

} Menos opciones
Segunda línea

TRATAMIENTO ANTIRRETROVIRAL INICIAL

3er Fármaco	Pauta‡	Ensayos clínicos aleatorizados
Preferentes		
ITINN	TDF/FTC/EFV[1,2,3]	STARTMRK, ACTG 5202, GS-US-236-0102, GILEAD 934, SINGLE
	TDF/FTC/RPV[2,3,4,5]	ECHO, THRIVE, STAR
IP/r	TDF/FTC+ATV/r [3,4]	CASTLE, ACTG 5202, ARTEN, GS-US-236-0103,
	ABC/3TC+ATV/r[4,6,7]	ACTG 5202
	TDF/FTC+DRV/r[3]	ARTEMIS, FLAMINGO
InInt	ABC/3TC+DTG[6]*	SINGLE, FLAMINGO, SPRING-2
	TDF/FTC+DTG[3]*	FLAMINGO, SPRING-2
	TDF/FTC/EVG/COBI[8]	GS-US-236-0102, GS-US-236-0103
	TDF/FTC+RAL[3]	STARMRK, QDMRK, SPRING-2
	ABC/3TC+RAL[6]	SPRING-2

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 2014)

GeSIDA
Grupo de Estudio del SIDA-SEIMC

Recommended Initial ART Regimen Options for All Patients, Regardless of Pre-ART Viral Load or CD4 Cell Count

NNRTI-Based Regimen:
- EFV/TDF/FTC[a] **(AI)**

PI-Based Regimens:
- ATV/r plus TDF/FTC[a] **(AI)**
- DRV/r plus TDF/FTC[a] **(AI)**

INSTI-Based Regimens:
- DTG plus ABC/3TC[a] **(AI)**—**only** for patients who are HLA-B*5701 negative
- DTG plus TDF/FTC[a] **(AI)**
- EVG/cobi/TDF/FTC— **only** for patients with pre-treatment estimated CrCl ≥70 mL/min **(AI)**
- RAL plus TDF/FTC[a] **(AI)**

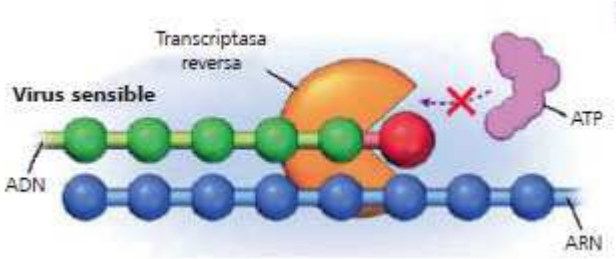
In addition to the regimens listed above, the following regimens are also recommended, but only for patients with pre-ART plasma HIV RNA <100,000 copies/mL

NNRTI-Based Regimens:
- EFV plus ABC/3TC[a] **(AI)**—**only** for patients who are HLA-B*5701 negative
- RPV/TDF/FTC[a] **(AI)**—**only** for patients with CD4 cell count >200 cells/mm^3

PI-Based Regimen:
- ATV/r plus ABC/3TC[a] **(AI)**—**only** for patients who are HLA-B*5701 negative

TAR de inicio

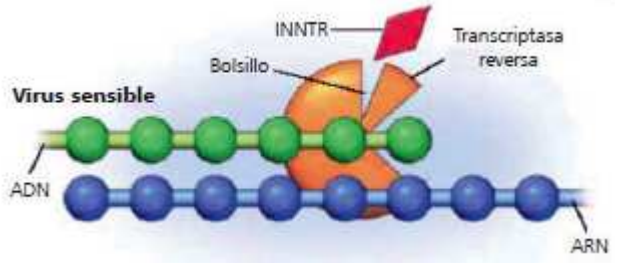
ITIAN



	TDF+FTC (Truvada®)	**ABC+3TC (Kivexa®)**
Ef. Adversos	Renal, oseo (TDF)	HS/HLA B5701 (ABC)
CV >100.000 c/mL	+	-

TAR de inicio

ITINAN



VENTAJAS

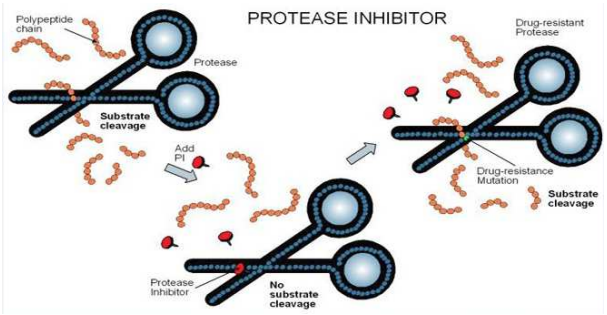
- ✓ Experiencia
- ✓ Tolerabilidad a largo plazo
- ✓ Posología (QD, STR)
- ✓ Coste (G)

INCONVENIENTES

- ✗ Interacciones: P450 (EFV, NVP); omeprazol (RPV)
- ✗ Efectos adversos (EFV, NVP)
- ✗ Barrera genética baja para Resistencia (excepto ETR)
- ✗ RPV: alimentos
- ✗ RPV: No si CV >100.000

TAR de inicio

Inhib Proteasa



VENTAJAS

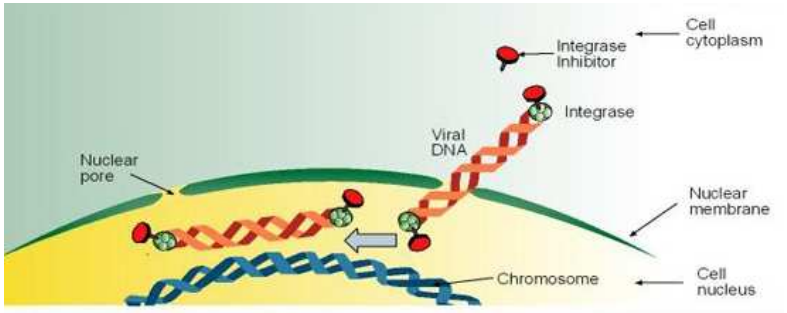
- ✓ Experiencia
- ✓ Potencia
- ✓ Barrera genética alta para resistencia

INCONVENIENTES

- ✗ Interacciones: P450
- ✗ Efectos adversos
- ✗ Posología
- ✗ Coste

TAR de inicio

Inhib Integrasa



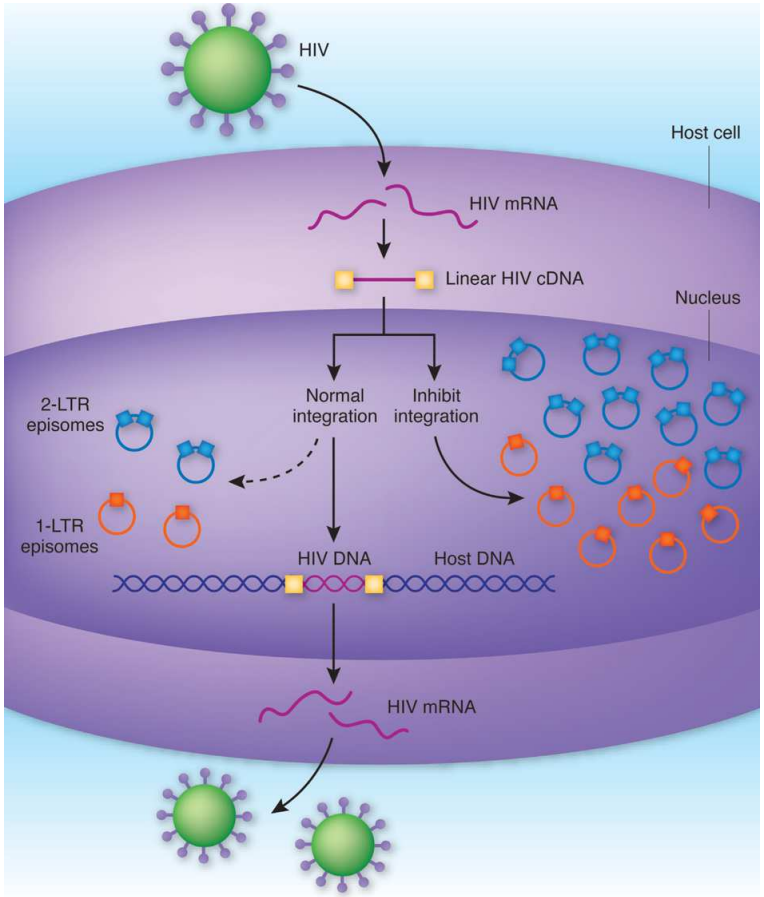
VENTAJAS

- ✓ Potencia
  - Descenso rápido de CV
  - CV alta: igual con cualquier comb de ITIAN
- ✓ Toxicidad/Tolerabilidad
- ✓ Ausencia de interacciones
- ✓ Posología
- ✓ Barrera genética (DTG)

INCONVENIENTES

- ✗ Coste (DTG >RAL>EVG)
- ✗ Barrera genética-Resistencia (RAL, EVG)
- ✗ RAL: Posología BID
- ✗ EVG: potenciación (interacc)

Inhibidores de la INTEGRASA



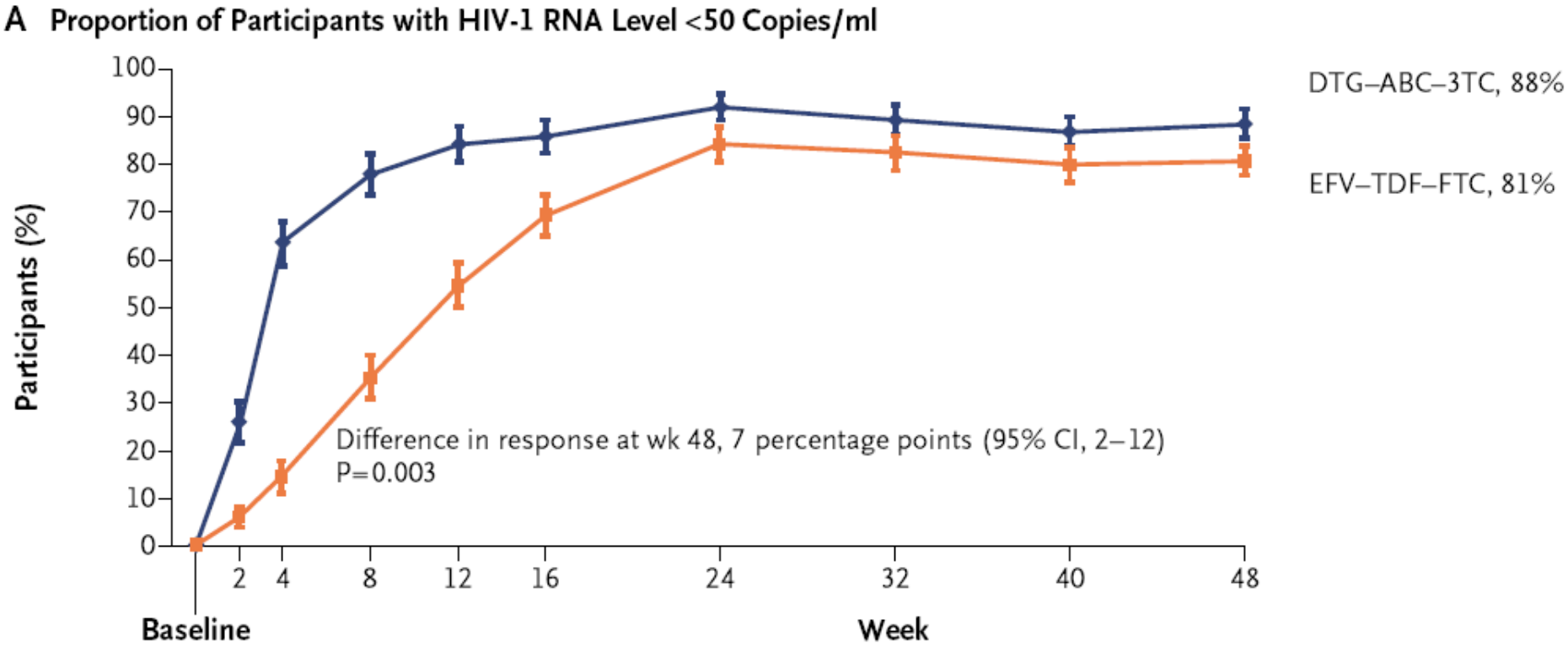
RALTEGRAVIR

ELVITEGRAVIR

DOLUTEGRAVIR

TAR de inicio: INI

Dolutegravir+ ABC/3TC vs **Efavirenz** (EFV/FTC/TDF)

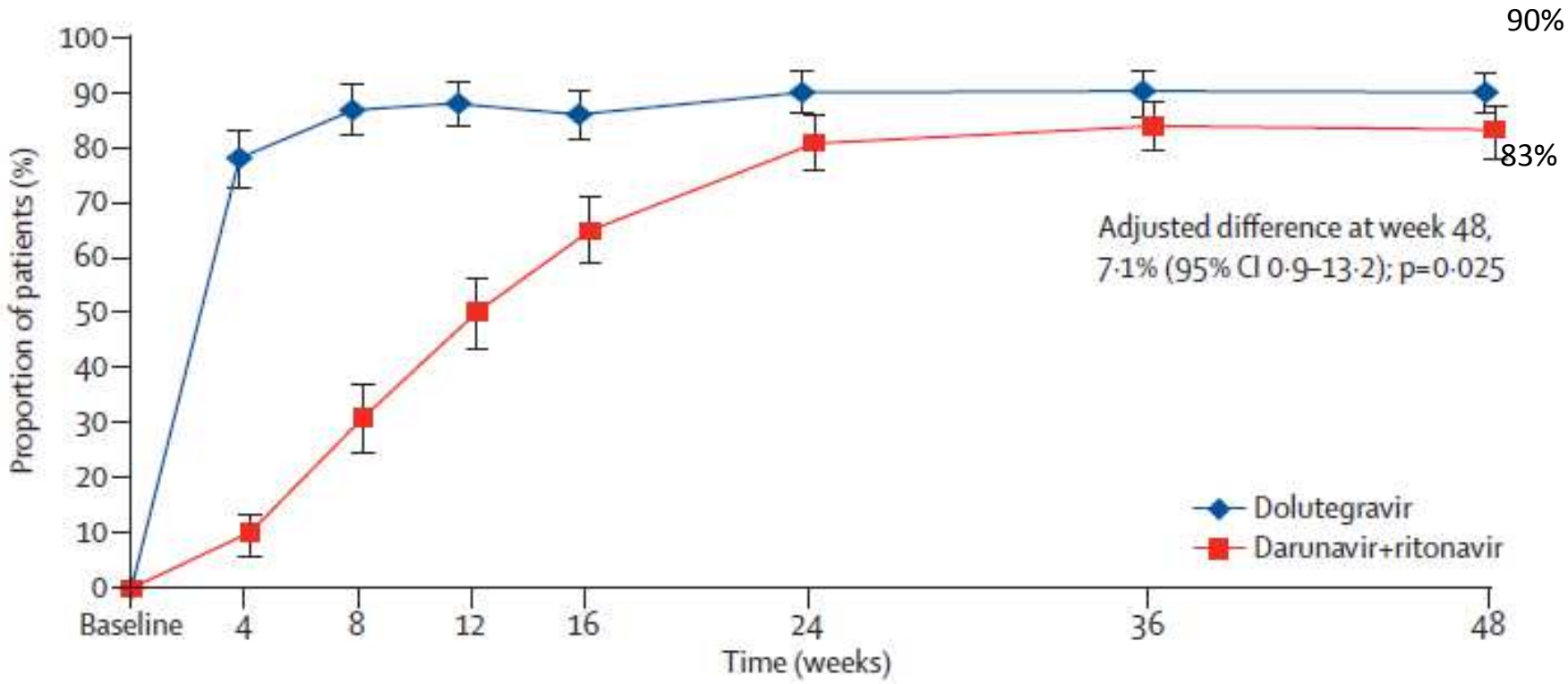


The NEW ENGLAND JOURNAL of MEDICINE

Walmsley SL, et al. NEJM 2013

TAR de inicio: INI

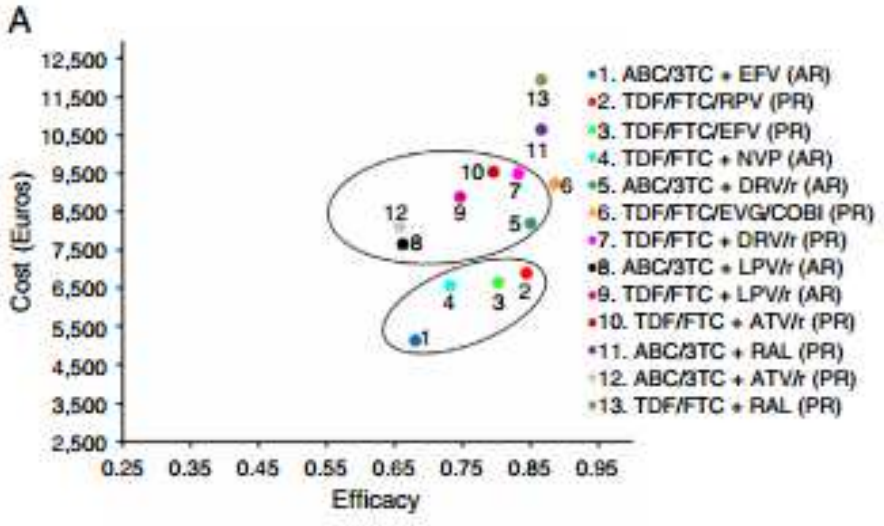
Dolutegravir vs **Darunavir**

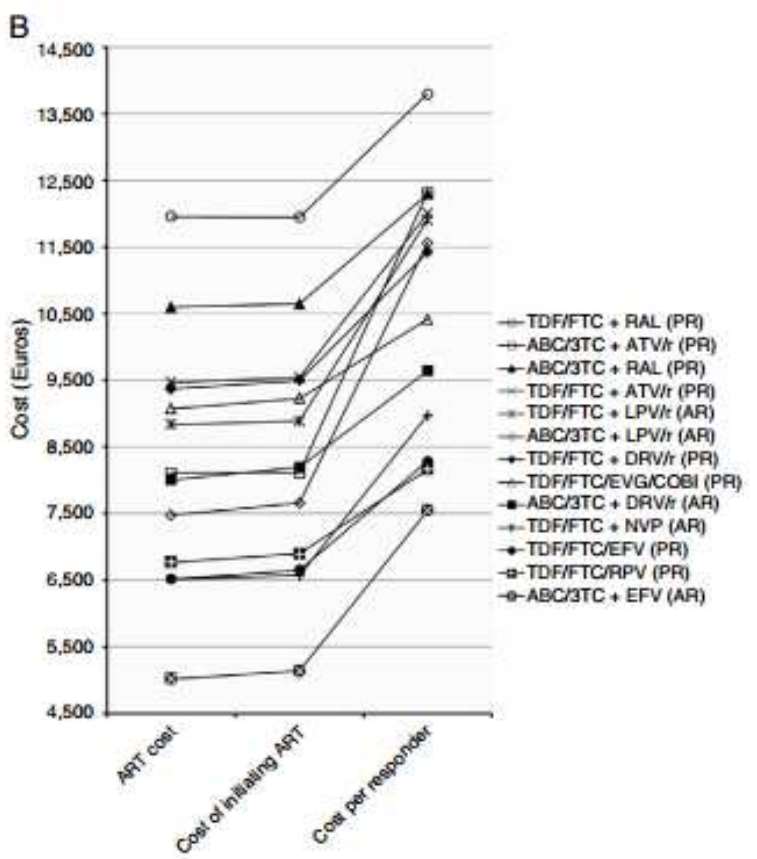


THE LANCET

Clotet B, et al. Lancet 2014

Costs and cost-efficacy analysis of the 2014 GESIDA/Spanish National AIDS Plan recommended guidelines for initial antiretroviral therapy in HIV-infected adults





Blasco AJ, et al. EIMC 2014

Simplificación del TAR: Objetivos

- ❑ Reducir la complejidad del TAR
- ❑ Adaptar el TAR a la situación personal, social i familiar de cada paciente
- ❑ Prevenir, reducir o revertir la toxicidad del TAR

Mejorar o mantener la adherencia

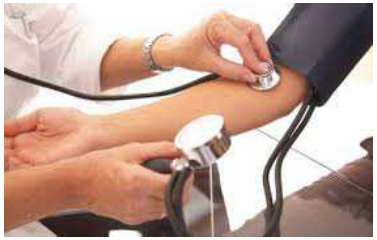
Mejorar la Calidad de vida

Manteniendo la misma Eficacia

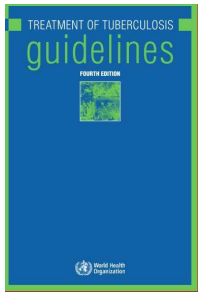
Documento de consenso de Gesida/PNS respecto al tratamiento antirretroviral en adultos infectados por el VIH, 2014

Simplificación del TAR:
1- Combinaciones a dosis fija

✔ Experiencia en otras enfermedades (HTA, DM)



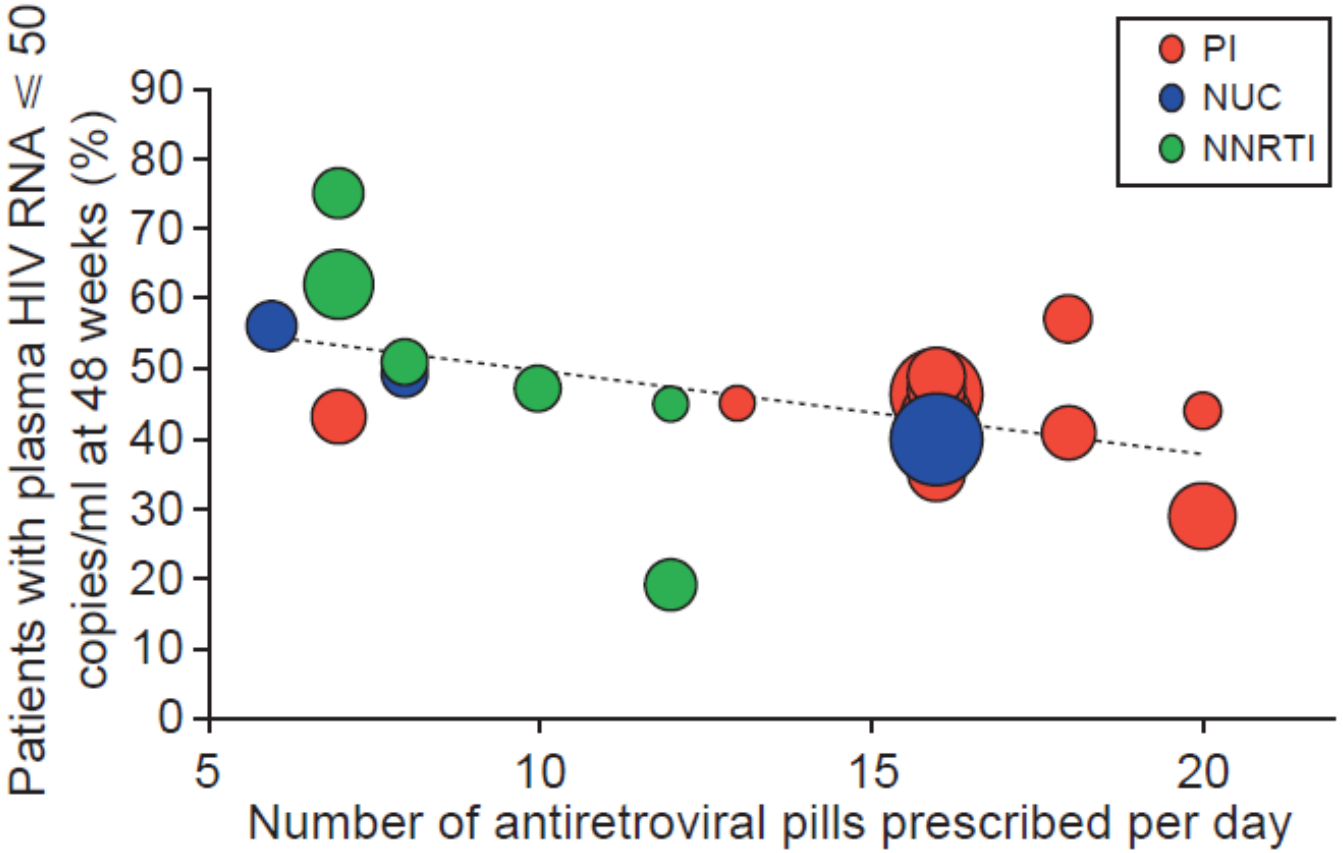
✔ Recomendado por la OMS para el tratamiento de la TB



Belsey JD. J Med Econ 2012

Bendford *et al* . Adv Ther 2012

TB WHO Guidelines 2010



Metanálisis de 23 RCT. 3257 pacientes

1994-2000

Barlett JA *et al*. AIDS 2001

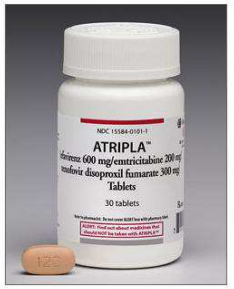
Combinacions a dosi Fixa

- Combivir® (AZT+3TC)
- Trizivir® (AZT+ABC+3TC)

- Truvada® (TDF+FTC)
- Kivexa® (ABC+3TC)

Combinacions a dosi Fixa

- Atripla® (TDF+FTC+EFV)
- Eviplera® (TDF+FTC+RPV)
- Stribild® (TDF+FTC+COBI+EVG)



CLINICAL THERAPEUTICS

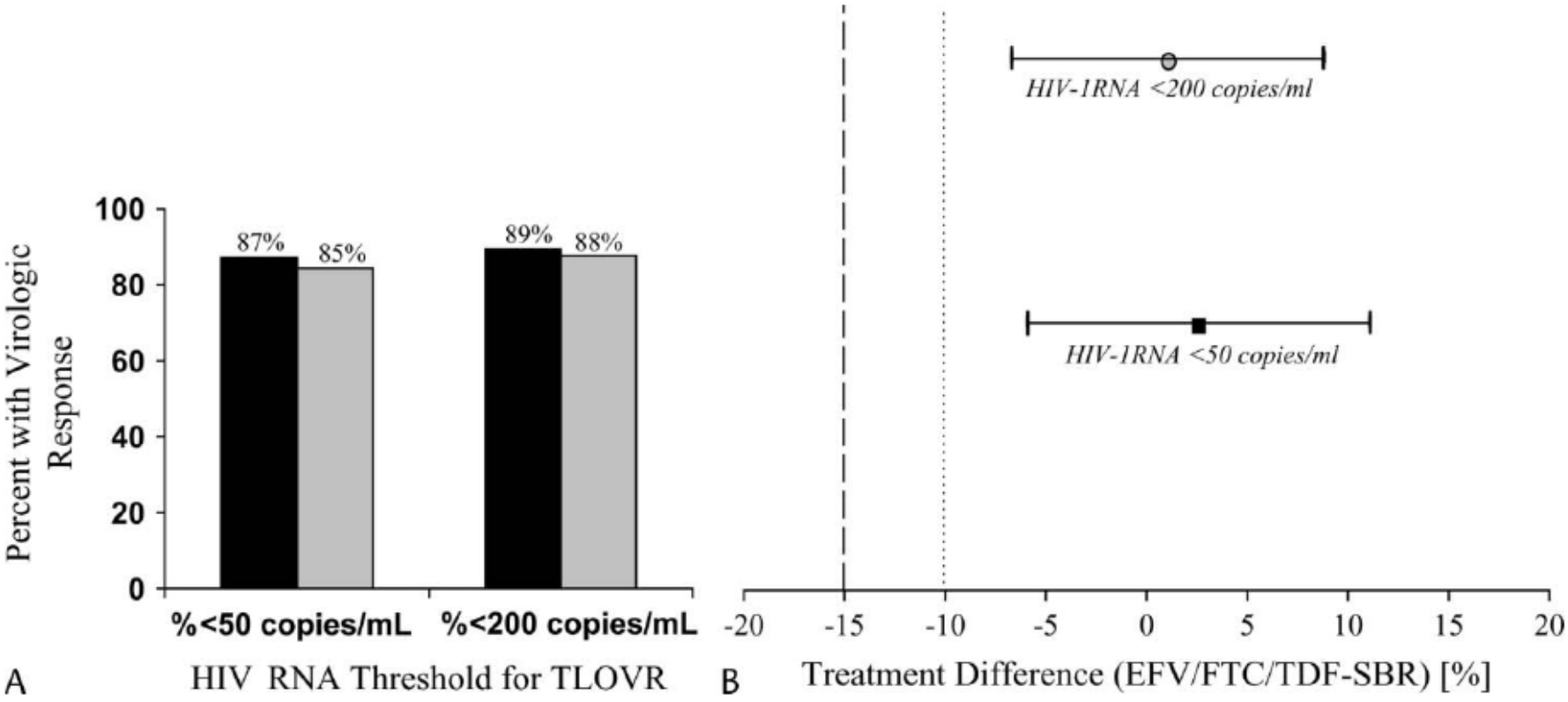
John A. Jarcho, M.D., *Editor*

Single-Pill Combination Regimens for Treatment of HIV-1 Infection

Monica Gandhi, M.D., M.P.H., and Rajesh T. Gandhi, M.D.

Julio 2014

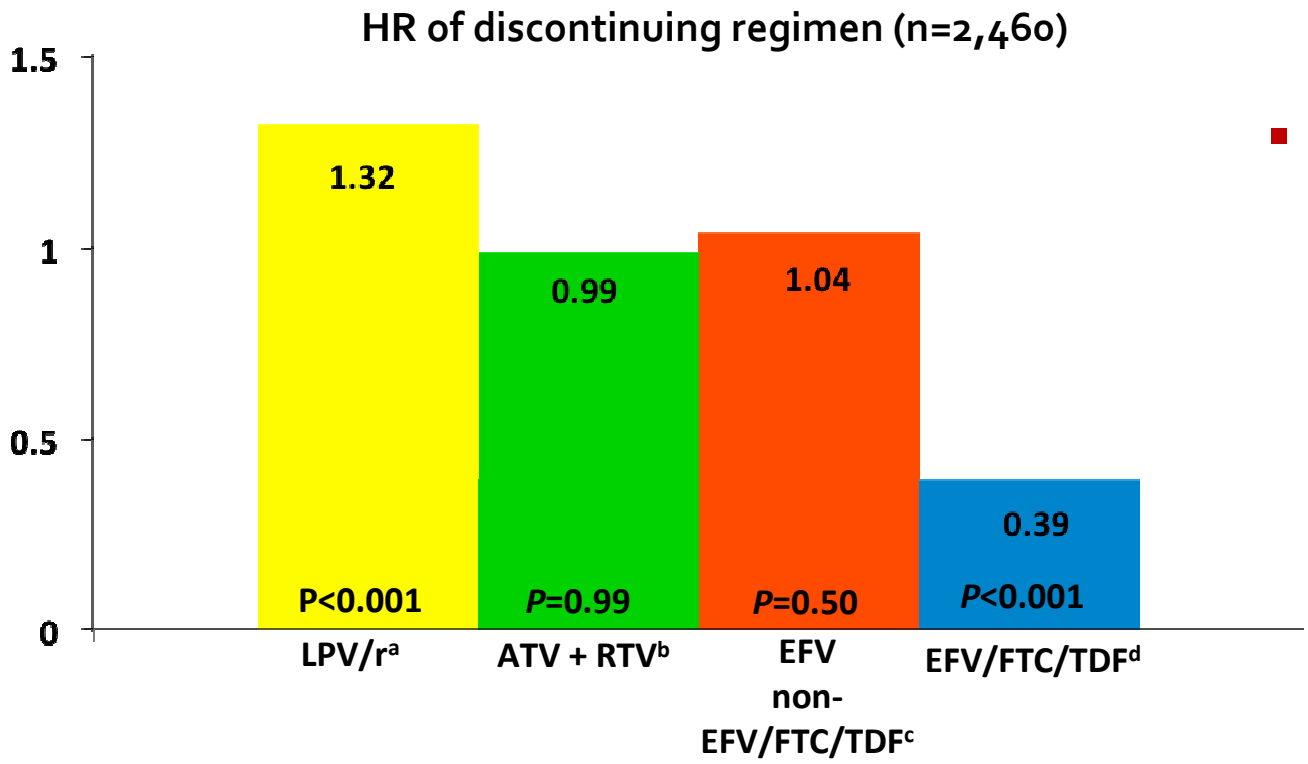
STR



De Jesus E, et al. JAIDS 2009

STR: menor riesgo de abandono

Retrospective cohort using US claims data from the PharMetrics Integrated Outcomes Database; N=37,244 HIV patients (1/03–6/08)



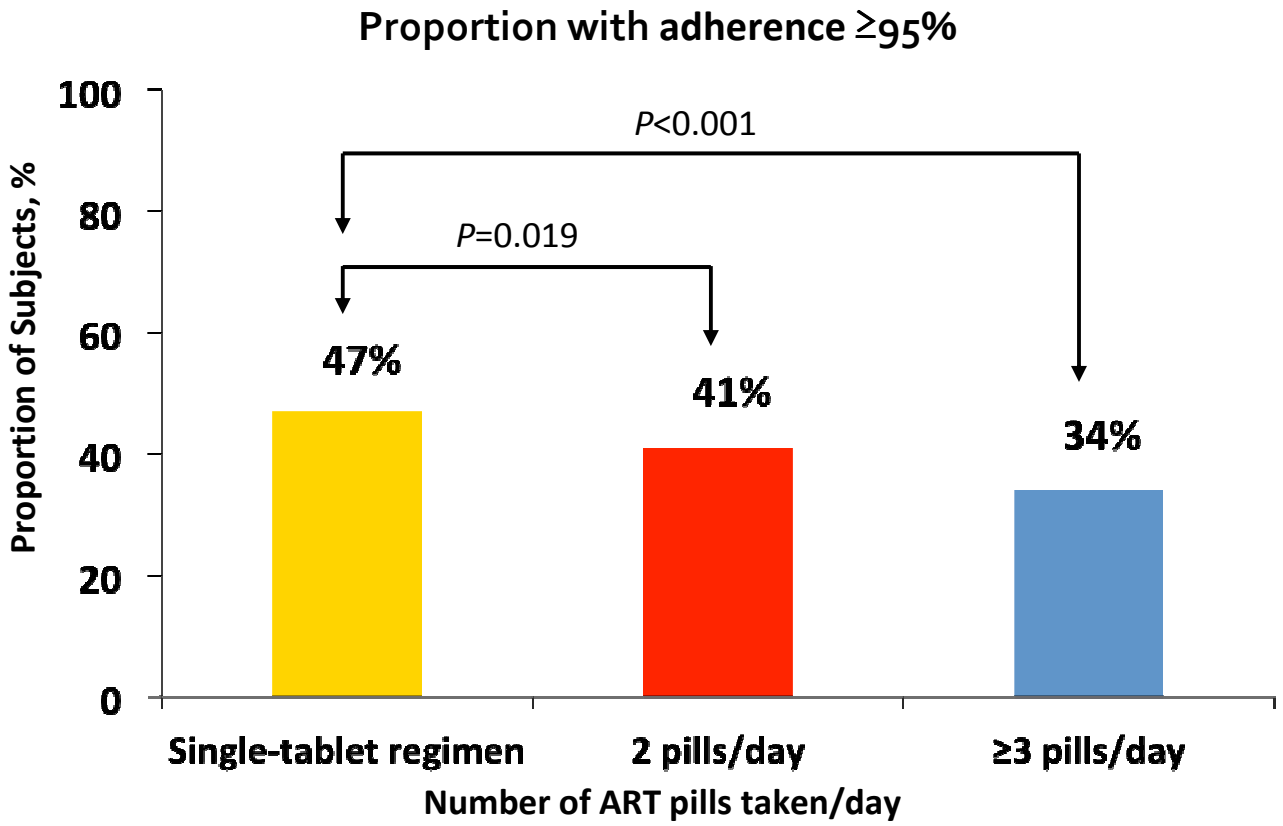
- **EFV/FTC/TDF had 61% lower discontinuation rate vs all other regimens**

Reference regimen for HR is: a) regimens without LPV/r; b) regimens without ATV* ± RTV*; c) regimens without EFV; d) all regimens other than Atripla

Juday T et al. *AIDS Care* 2011

STR: mejora adherencia

Retrospective chart analysis of HIV+ patients in US LifeLink database (N=7,073)

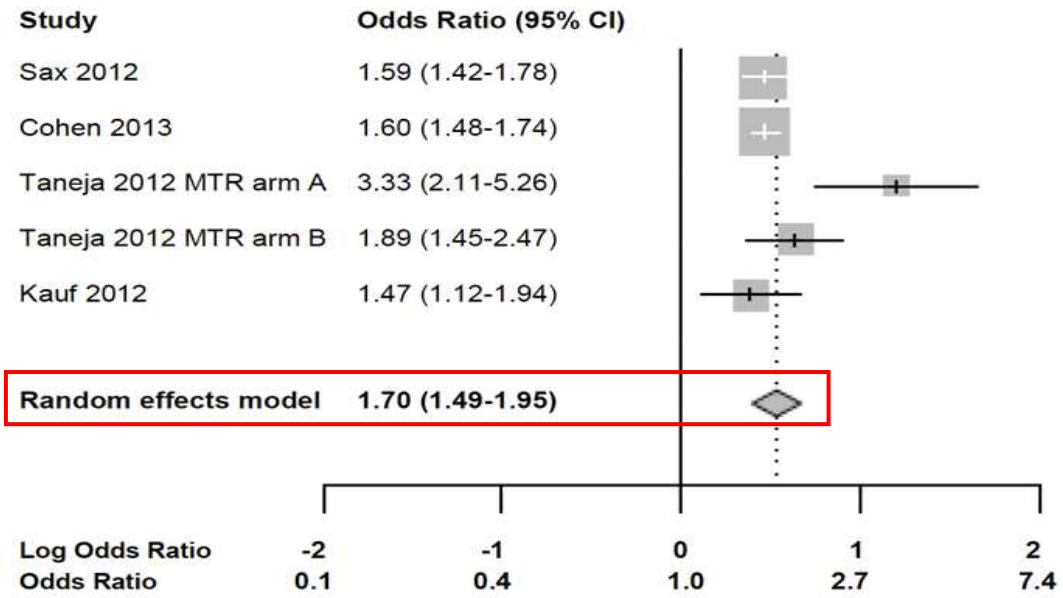


- STR had greater likelihood of achieving ≥95% adherence vs either 2 or ≥3 pills/day (*P*<0.05) and was associated with 59% greater likelihood vs ≥3 pills/day (*P*<0.001)

Sax P et al. *PLoS ONE* 2012

STR vs MTR: a systematic review and meta-analysis of real world adherence

Meta-analysis: odds of achieving ≥95% real-world adherence with STR vs MTR

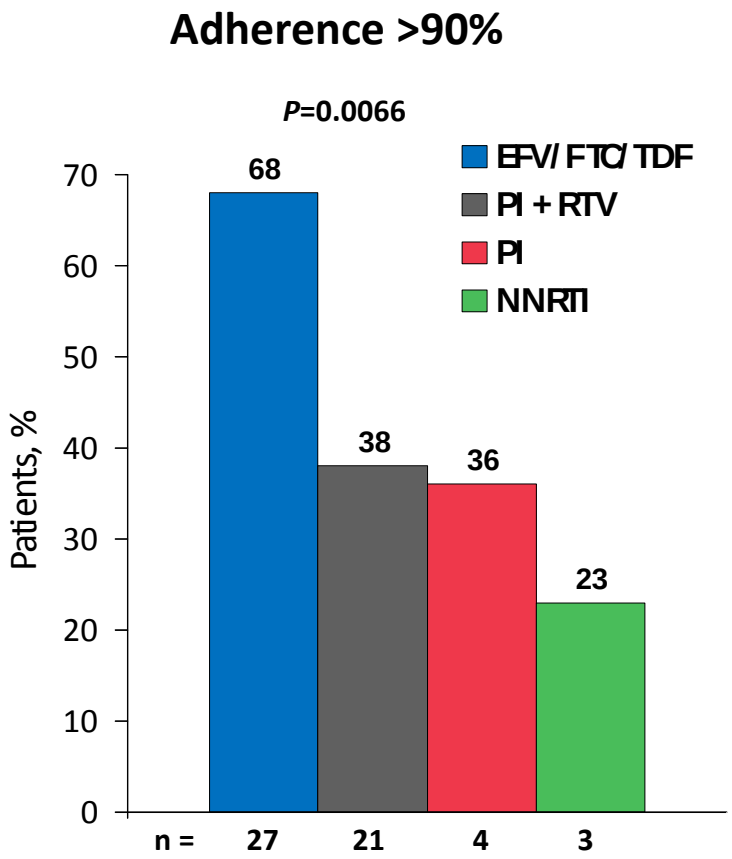


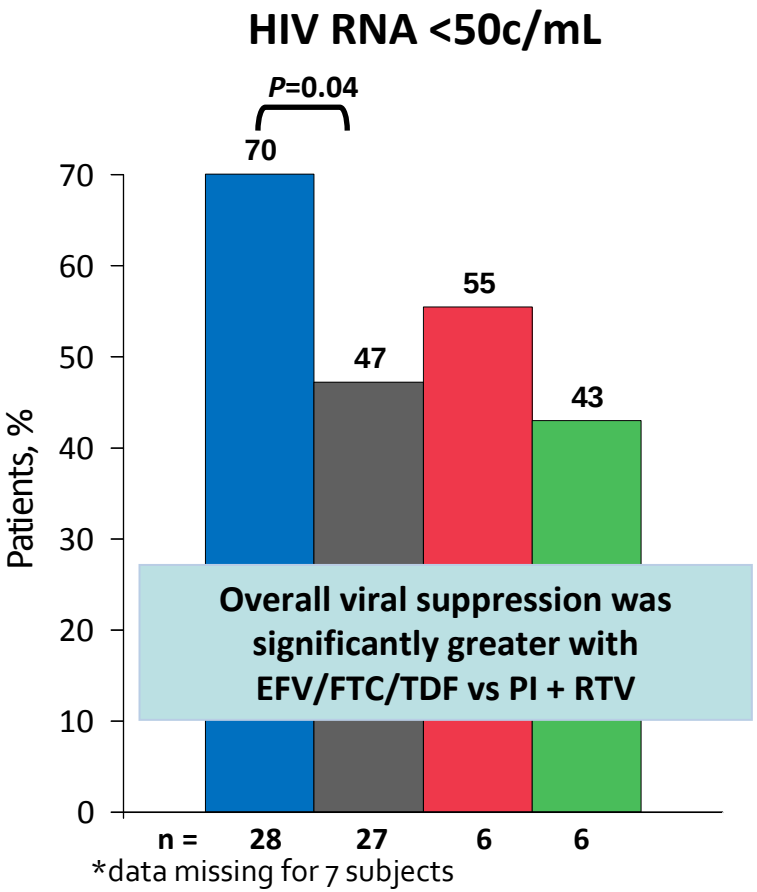
- **In comparative real-world studies, patients receiving STRs vs MTRs had a 70% greater odds of achieving ≥95% adherence**

Sweet D et al. IAC 2014. Melbourne, Australia. #THPE421

STR: mejor adherencia = mayor eficacia

Patients recruited from a cohort of HIV+ homeless and **marginally housed individuals** and from public health clinics in San Francisco[1]

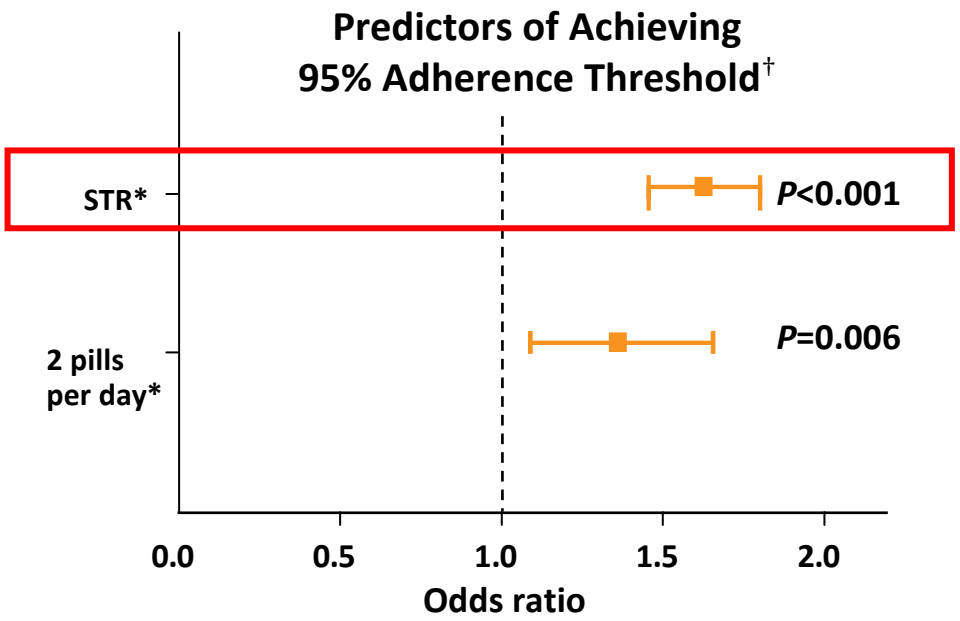


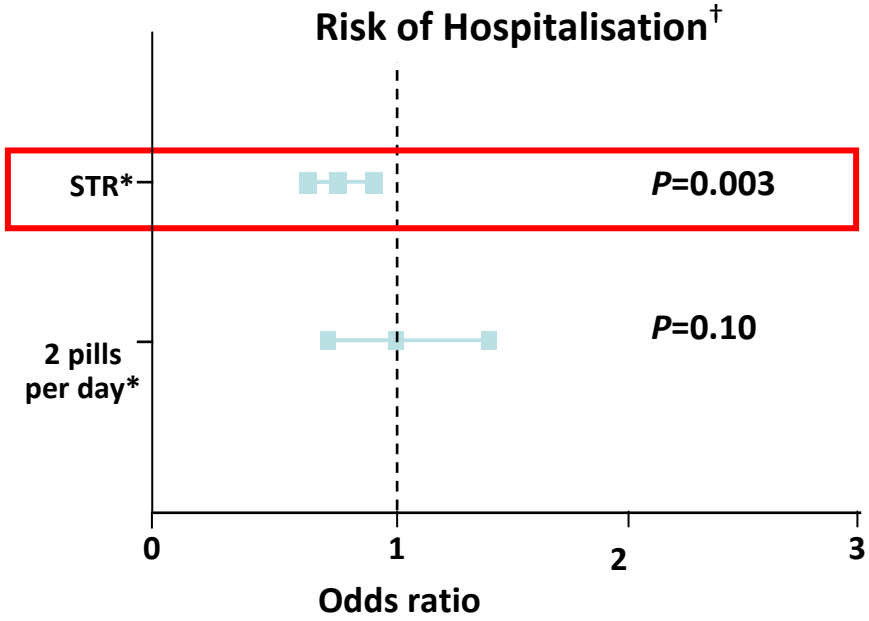


Bangsberg D, et al. CROI 2010; *AIDS* 2010

STR: mejor adherencia = mayor eficacia

Retrospective chart analysis of 7,073 HIV+ patients in the US LifeLink database evaluating the impact of an STR on adherence & hospitalisation risk (6/06–12/08)





- STR had greater likelihood of >95% adherence vs either 2 pills/day (*P*=0.019) or ≥3 pills/day (*P*<0.001)

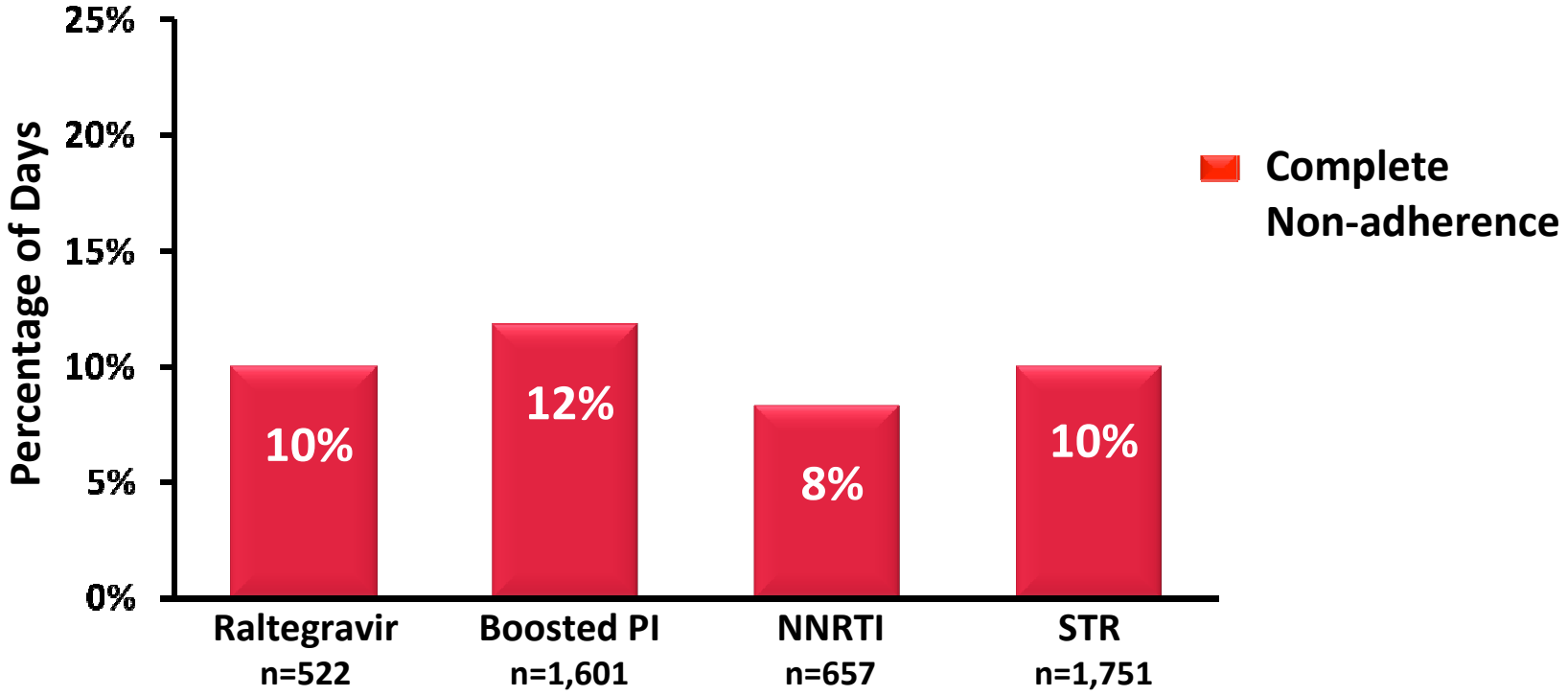
*vs 3 or more pills per day regimen
†Multivariate Logistic Regression

- Regardless of the number of pills received per day, patients were over 40% less likely to have a hospitalisation if they were adherent to therapy (OR = 0.57; *P*=0.001)
- Once-daily STR was associated with 24% lower risk of hospitalisation (*P*=0.003)*

Sax P et al. *PLoS ONE* 2012;7:e31591

STR: mejor adherencia

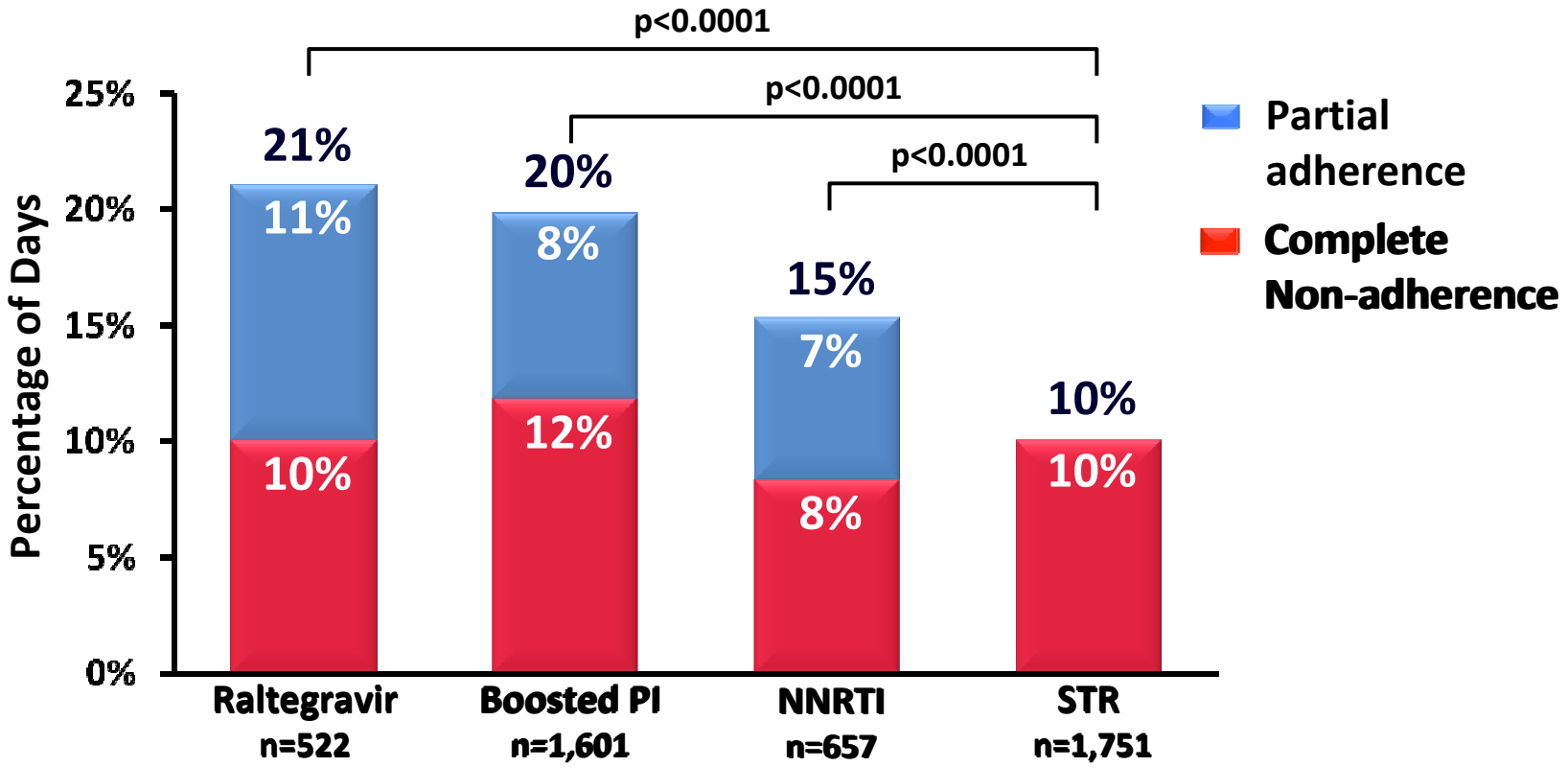
Retrospective analysis of US healthcare claims for commercially insured population (n=4,588) receiving 2 NRTIs plus NNRTI or PI or INSTI based ART (2009 – 2011)



Cohen C, *et al.* ICAAC 2012; San Francisco, CA. #H-211

STR: adherencia

Retrospective analysis of US healthcare claims for commercially insured population (n=4,588) receiving 2 NRTIs plus NNRTI or PI or INSTI based ART (2009 – 2011)

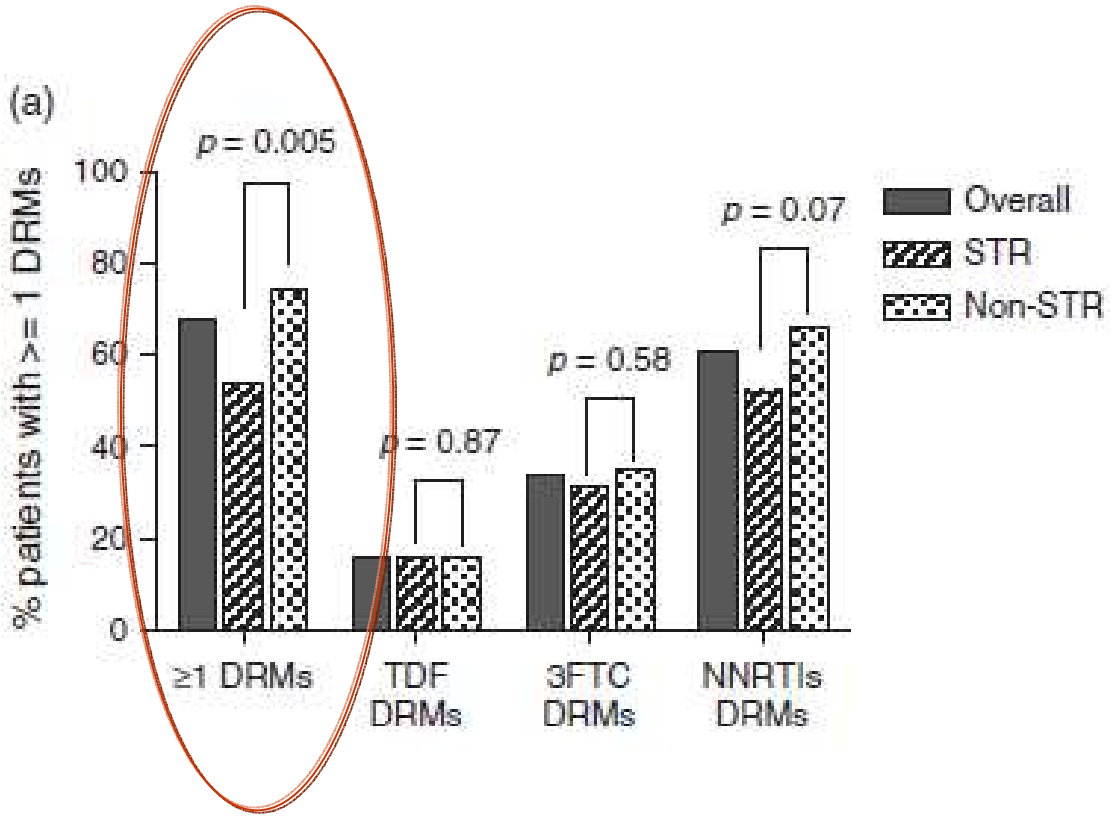


Cohen C, *et al.* ICAAC 2012; San Francisco, CA. #H-211

Lower prevalence of drug resistance mutations at first-line virological failure to first-line therapy with atripla vs. tenofovir + emtricitabine/ lamivudine + efavirenz administered on a multiple tablet therapy

8 prospective clinical cohorts in Europe and North America and 4 RCTs

Significant difference in time to virological failure (p=0.03): 350 days in STR vs 211 days in non-STR participants



Blanco JL et al, AIDS 2014 (epub)

STR

VENTAJAS

- ✓ Facilitan adherencia
- ✓ Mejoran la calidad de vida
- ✓ Menor riesgo de adherencia selectiva
- ✓ Menor riesgo de resistencia

INCONVENIENTES

- × Dosis no modificables (IR, interacciones...)
- × Opciones limitadas:
  - × Barrera genética
  - × Toxicidad
- × Coste

Recomendados en todas las Guías Clínicas

August 25, 2014

FDA Approves New Single-Tablet HIV Regimen, Triumeq

The U.S. Food and Drug Administration (FDA) has approved Triumeq, ViiV Healthcare's single-tablet, triple-combination antiretroviral (ARV) regimen, as a first-line therapy to treat HIV. The tablet is comprised of the integrase inhibitor Tivicay (dolutegravir) plus Epzicom (abacavir and lamivudine) and is the first single-tablet regimen to receive approval that does not contain Truvada (tenofovir/emtricitabine). Consequently, Triumeq is an option for those who have impaired kidney function.

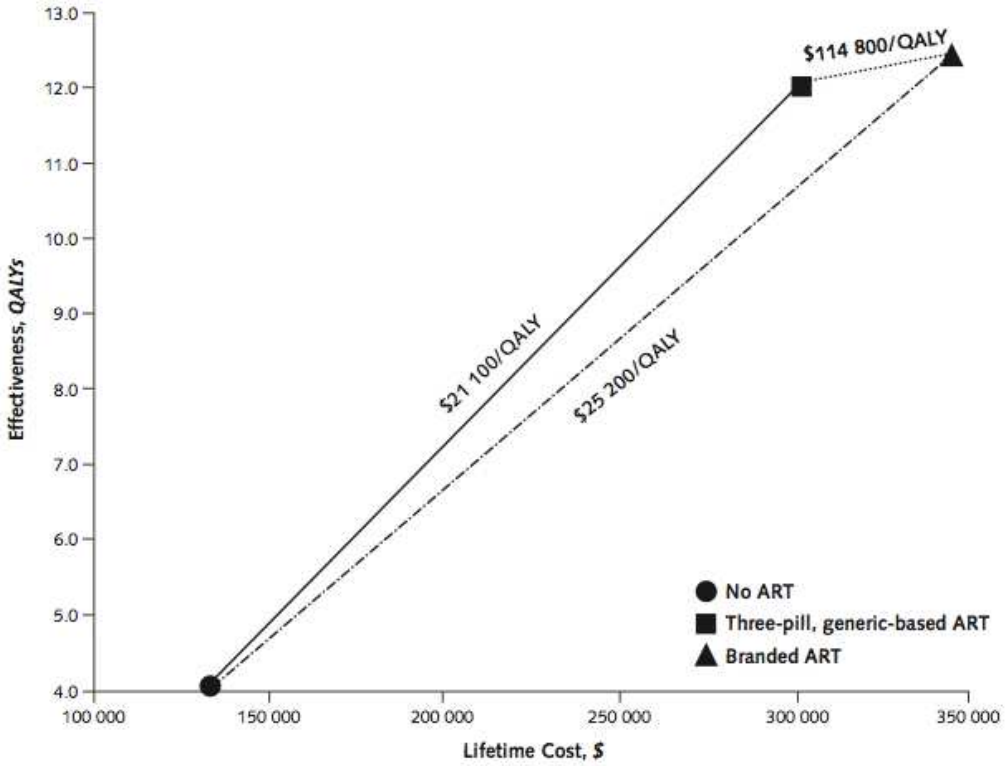
Futuro:

TAF/FTC/COBI/DRV

Crisis económica y simplificación

ORIGINAL RESEARCH | Annals of Internal Medicine

Economic Savings Versus Health Losses: The Cost-Effectiveness of Generic Antiretroviral Therapy in the United States



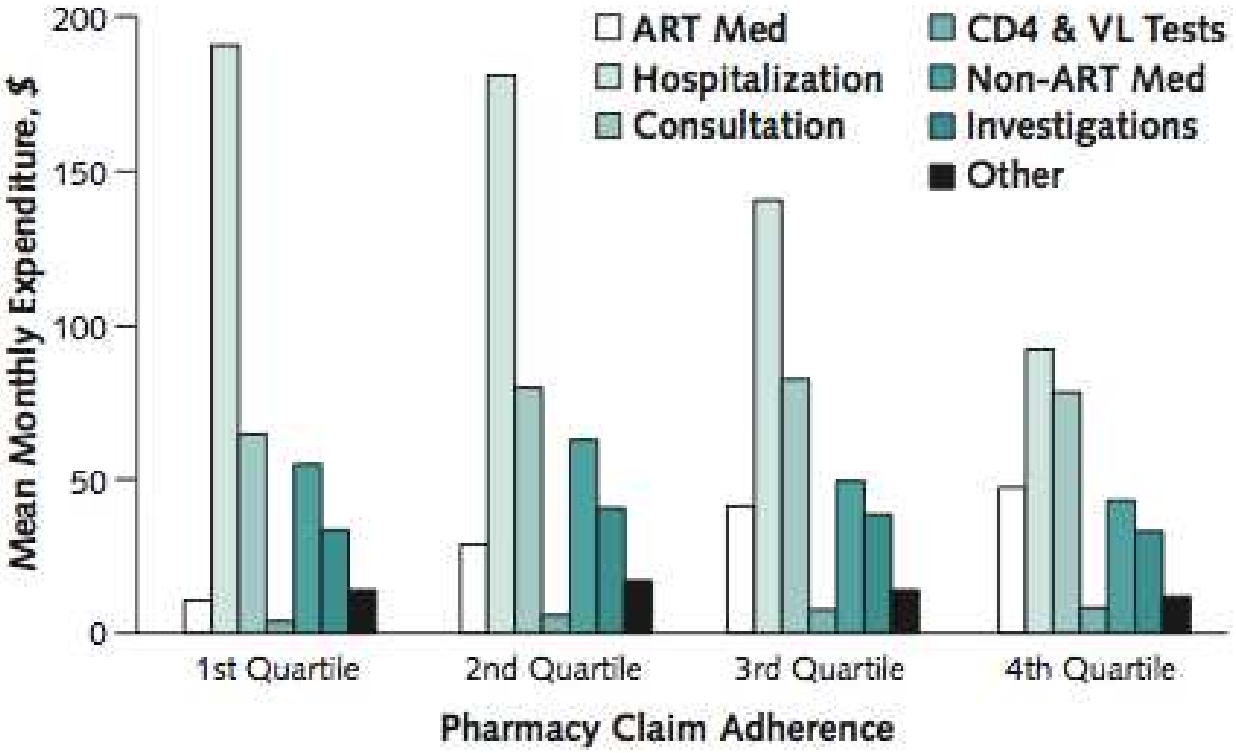
920 milions $
primer any

Walensky RP et al. Ann Intern Med 2013

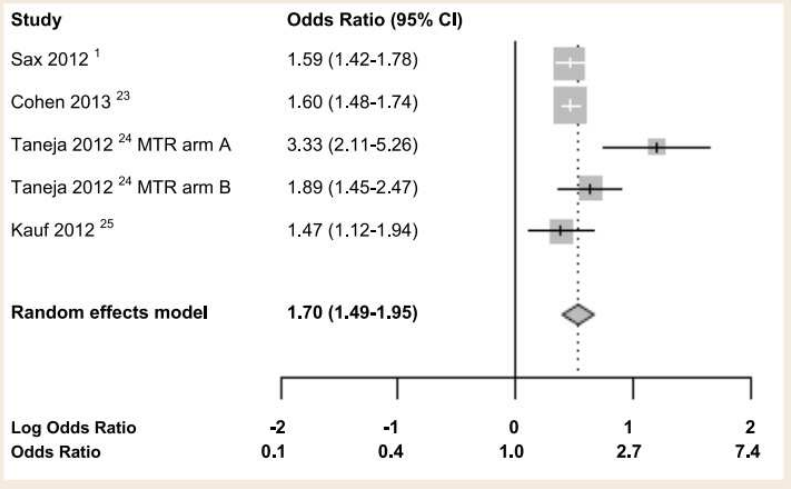
Crisis económica y simplificación

ARTICLE | Annals of Internal Medicine

Association of Antiretroviral Therapy Adherence and Health Care Costs



Nachega JB et al. Ann Intern Med 2010



"Hypothetical population of 9,860 patients initiating an STR and 131,637 patients already receiving an STR"

STR→MTR

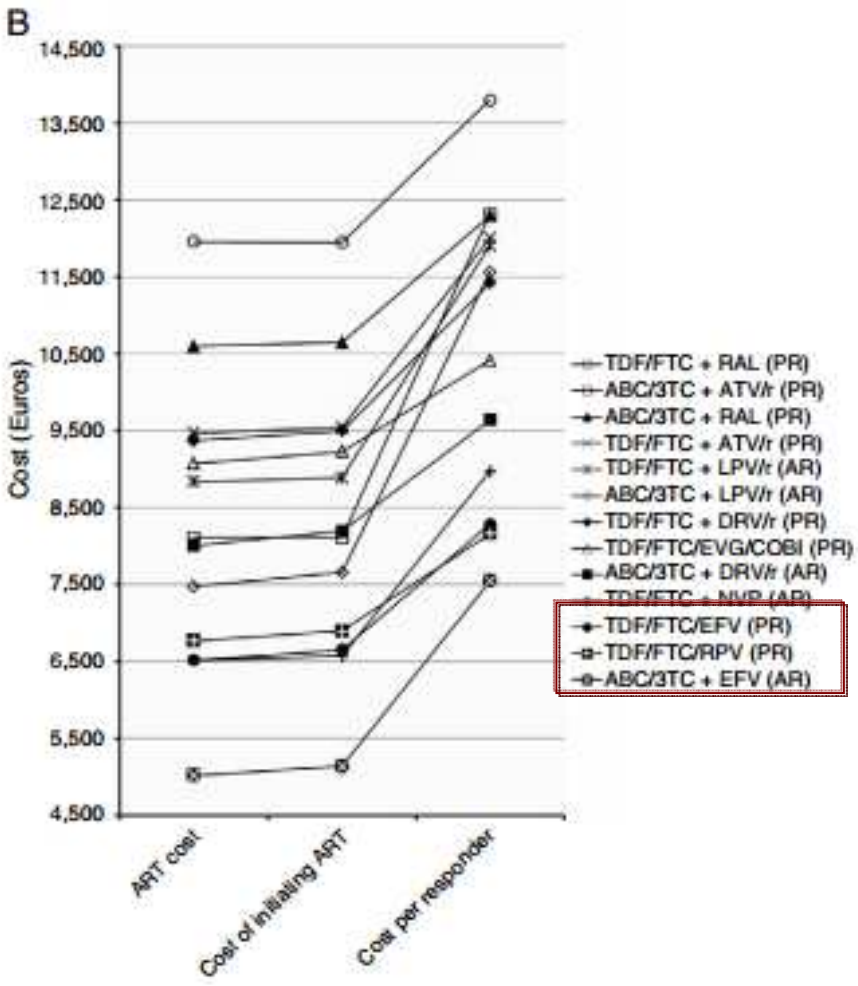
Table 7. Budget impact analysis in the US HIV population

	Scenario 1* - Scenario 2¶		
	Year 1	Year 3	Year 5
Inpatient medical costs	-$483,803,395	-$991,284,720	-$1,289,168,605
Other medical costs	-$3,946,464	-$31,597,306	-$33,452,614
Drug costs	$496,191,821	$880,890,269	$863,778,471
Total costs	$8,441,962	-$141,991,757	-$458,842,748

* Scenario 1: continuing current STR and MTR utilization patterns
¶ Scenario 2: requiring all STR users to switch to MTR, and requiring all new ART initiators to receive MTR

Sweet D et al. IAC 2014. Melbourne, Australia. #THPE421

Costs and cost-efficacy analysis of the 2014 GESIDA/Spanish National AIDS Plan recommended guidelines for initial antiretroviral therapy in HIV-infected adults



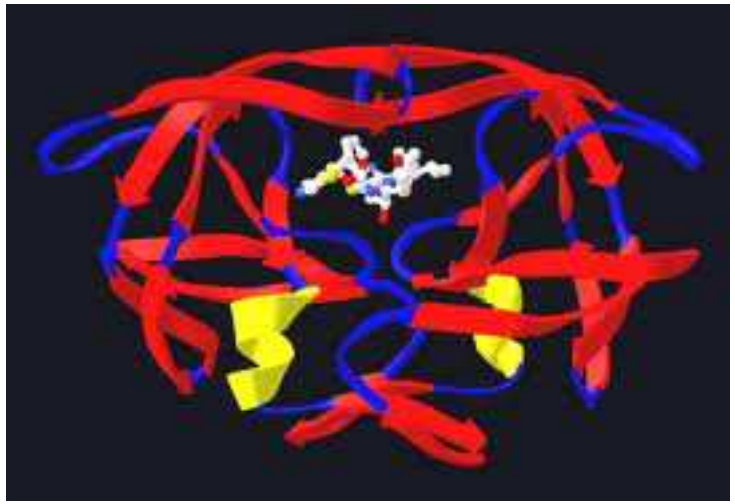
Blasco AJ, et al. EIMC 2014

Simplificación del TAR:
2- Reducción de fármacos

- Reducir o Prevenir toxicidad
- Reservar opciones terapéuticas
- Reducir Coste

Inhibidores de proteasa

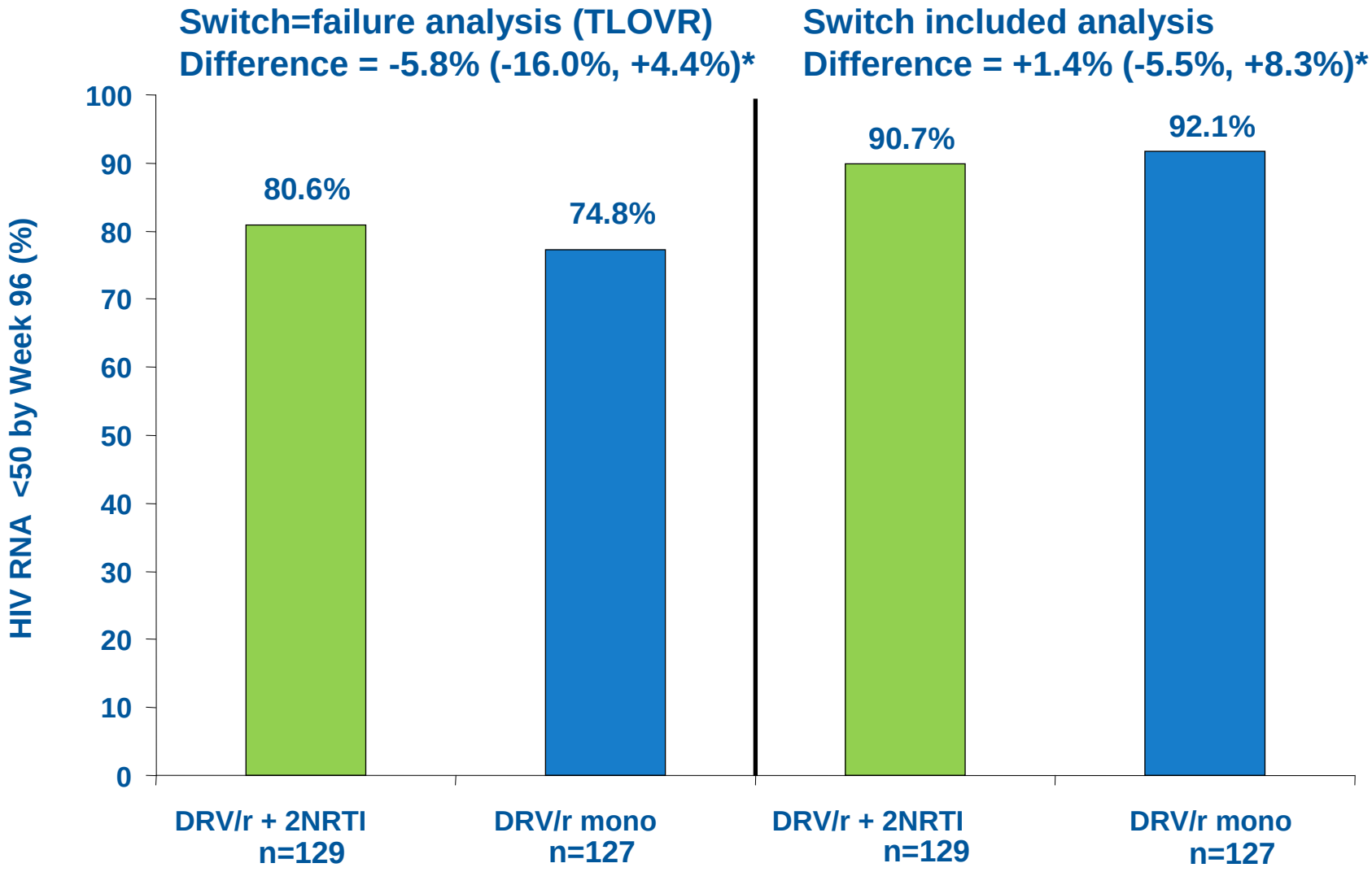
- Gran potencia antiviral
- Niveles plasmáticos altos
- Alta barrera genética:
  - menor riesgo de resistencia



LPV/r

DRV/r

Estudio MONET:
Eficacia (HIV RNA <50 copies/mL) 96 semanas



*** 95% confidence intervals from univariate analysis**

Rieger et al. WAC July 2010. Clumeck N, et al JAC 2011

Monoterapia con IP/r

Marcadores de eficacia en ensayos clínicos y estudios

- ✓ Tiempo con CV <50 copies/ml antes del cambio a MT
- ✓ DNA viral en células mononucleares (reservorio)
- ✓ CD4 nadir
- ✓ Adherencia

Pulido et al. AIDS Rev 2010; Arribas et al. AIDS Research and Therapy 2013

Monoterapia con IP/r en las Guías

Gesida 2014, EACS 2014

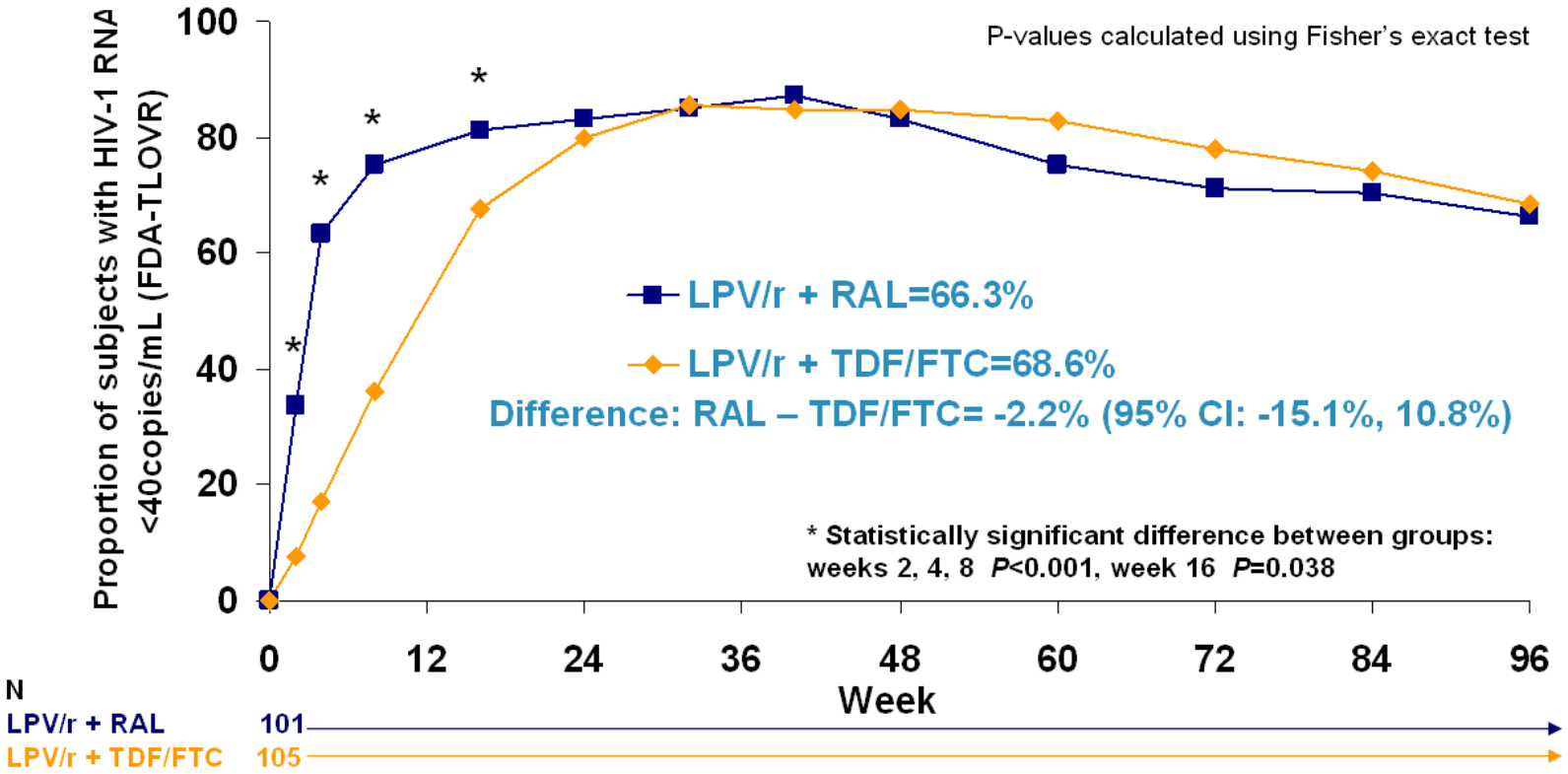
- Opción de TAR para pacientes con intolerancia ITIAN o simplificación
- No resistencia o fracasos con IP
- CV indetectable en últimos 6 meses
- No Hepatitis crónica VHB
- Buena adherencia

DHHS 2014

- No recomendado

Biterapia

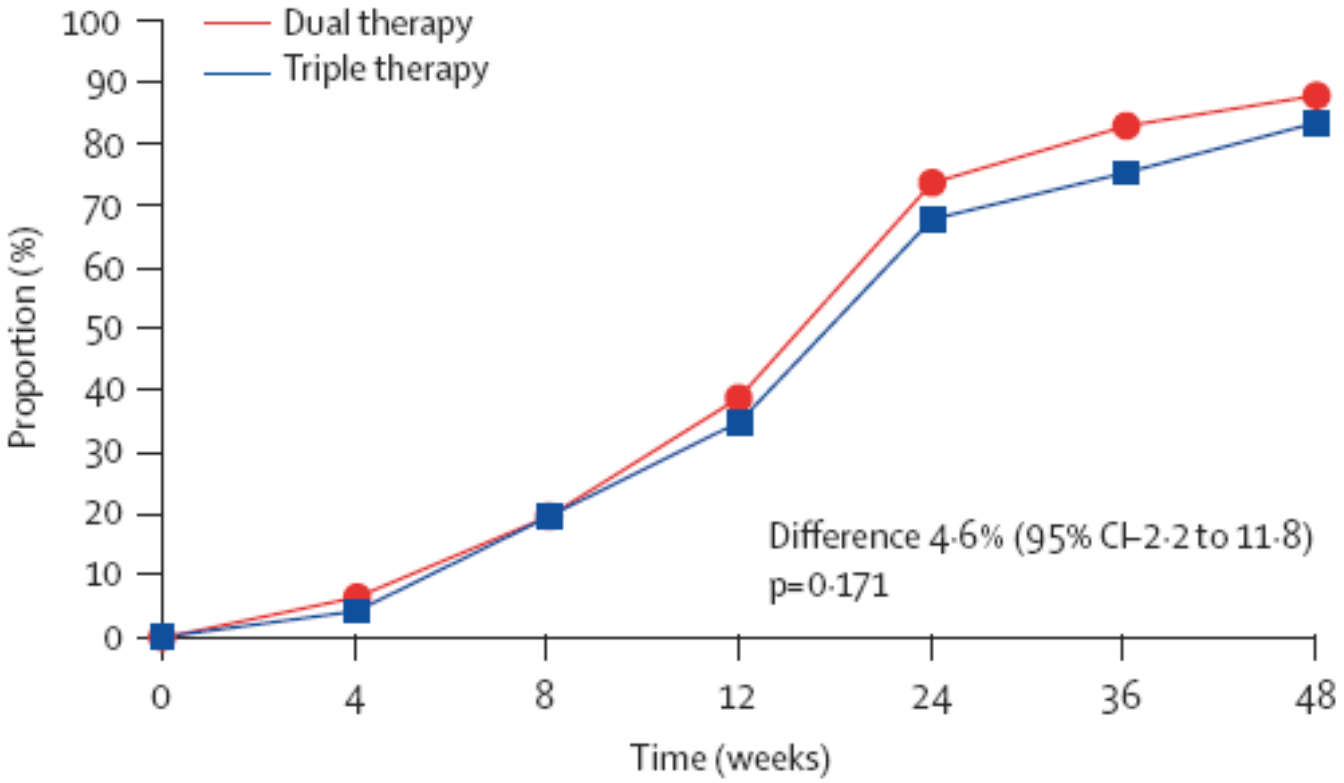
RAL + LPV/r (PROGRESS)



Week 96 FDA-TLOVR response for subjects with BL plasma HIV-1 RNA ≥100,000 copies/mL:
LPV/r + RAL= 6/15, LPV/r + TDF/FTC= 10/19

Reynes JA et al. AIDS Research and Human Retroviruses 2013

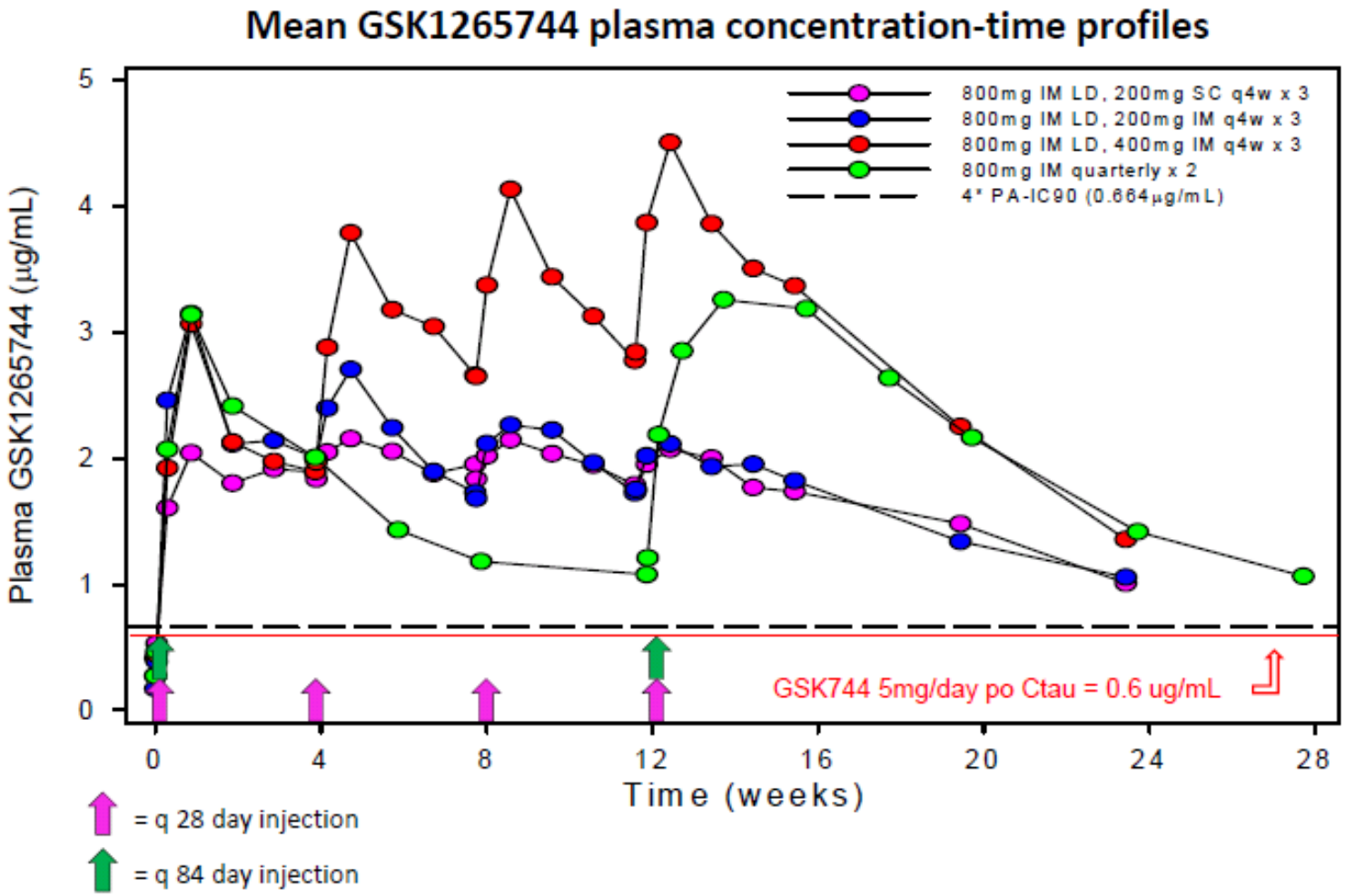
Biterapia



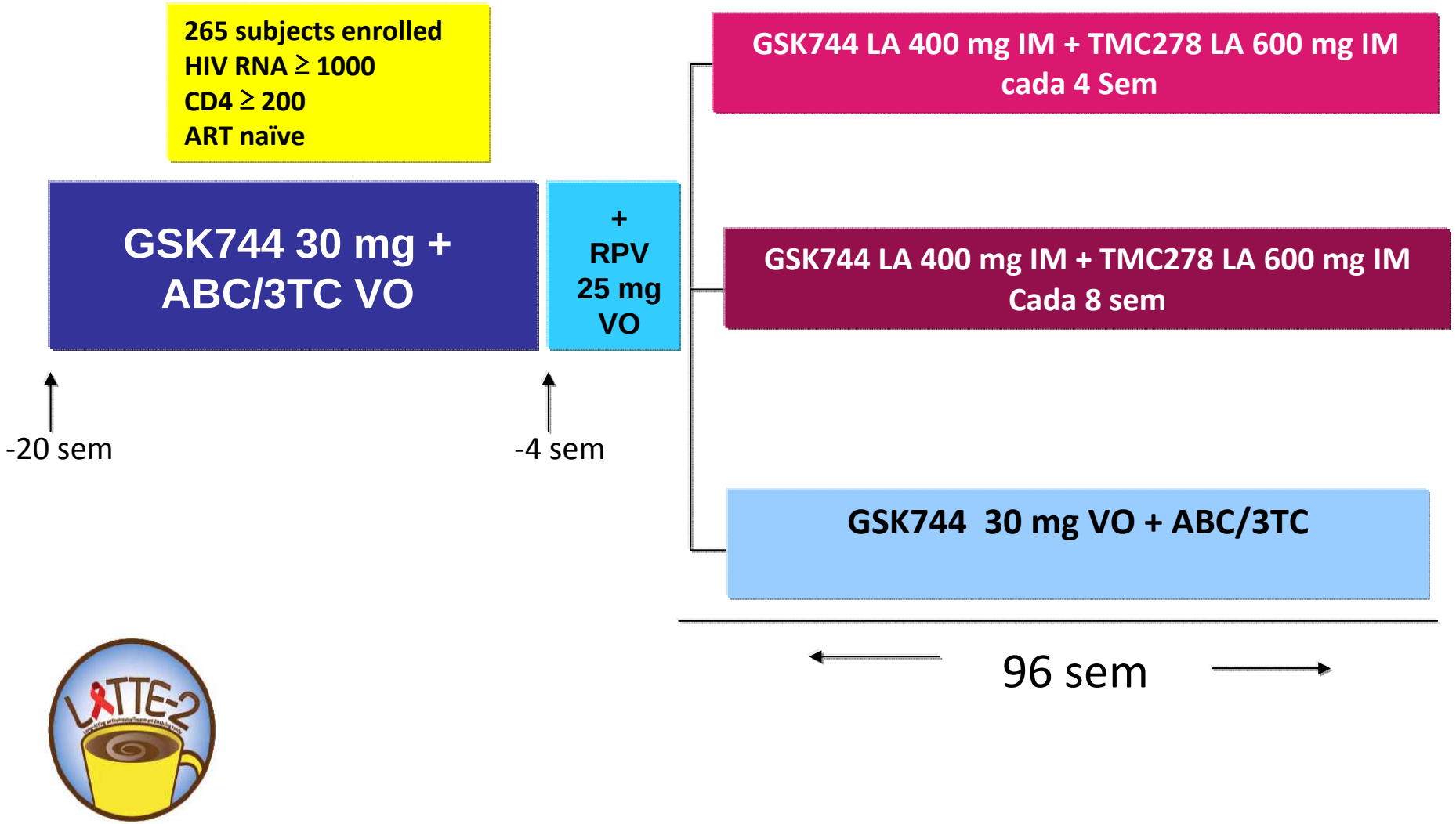
GARDEL
GLOBAL ARV DESIGN ENCOMPASSING LOPINAVIR/RITONAVIR AND LAMIVUDINE VS LOPINAVIR/RITONAVIR BASED STANDARD THERAPY

Cahn P, et al. Lancet Infect Dis 2014

Simplificación del TAR:
"Long acting drugs"



Simplificación del TAR:
"Long acting drugs"



Simplificación del TAR:
"Long acting drugs"

Long-acting HIV drugs advanced to overcome adherence challenge

BOSTON — The results from a particular drug trial presented here last month at the annual Conference on Retroviruses and Opportunistic Infections (CROI) may not have seemed particularly noteworthy. It simply showed that two pills performed as well as another combination of medicines. But the antiretroviral agents tested in the trial were not your ordinary drugs.

The regimen consisted of two drugs: an HIV integrase inhibitor called GSK744 and a non-nucleoside reverse transcriptase inhibitor called rilpivirine. Although there are already many similar agents on the market from both HIV-fighting drug classes, only these two compounds are proven to have one important property: both can be formulated as long-acting injectables.

Long-acting drug formulations could solve one of the thorniest problems in HIV management: people do not stick with the daily pill regimens that their doctors recommend. And poor adherence is no trivial matter—beyond placing patients at risk of getting sick, it can also contribute to the rise of drug-resistant forms of HIV. A treatment that someone could receive once a month, or even less frequently, could translate into better outcomes and improved drug compliance. First, however, the specific agents included in such a regimen would need to demonstrate efficacy as daily oral doses, the current gold standard for HIV treatment.

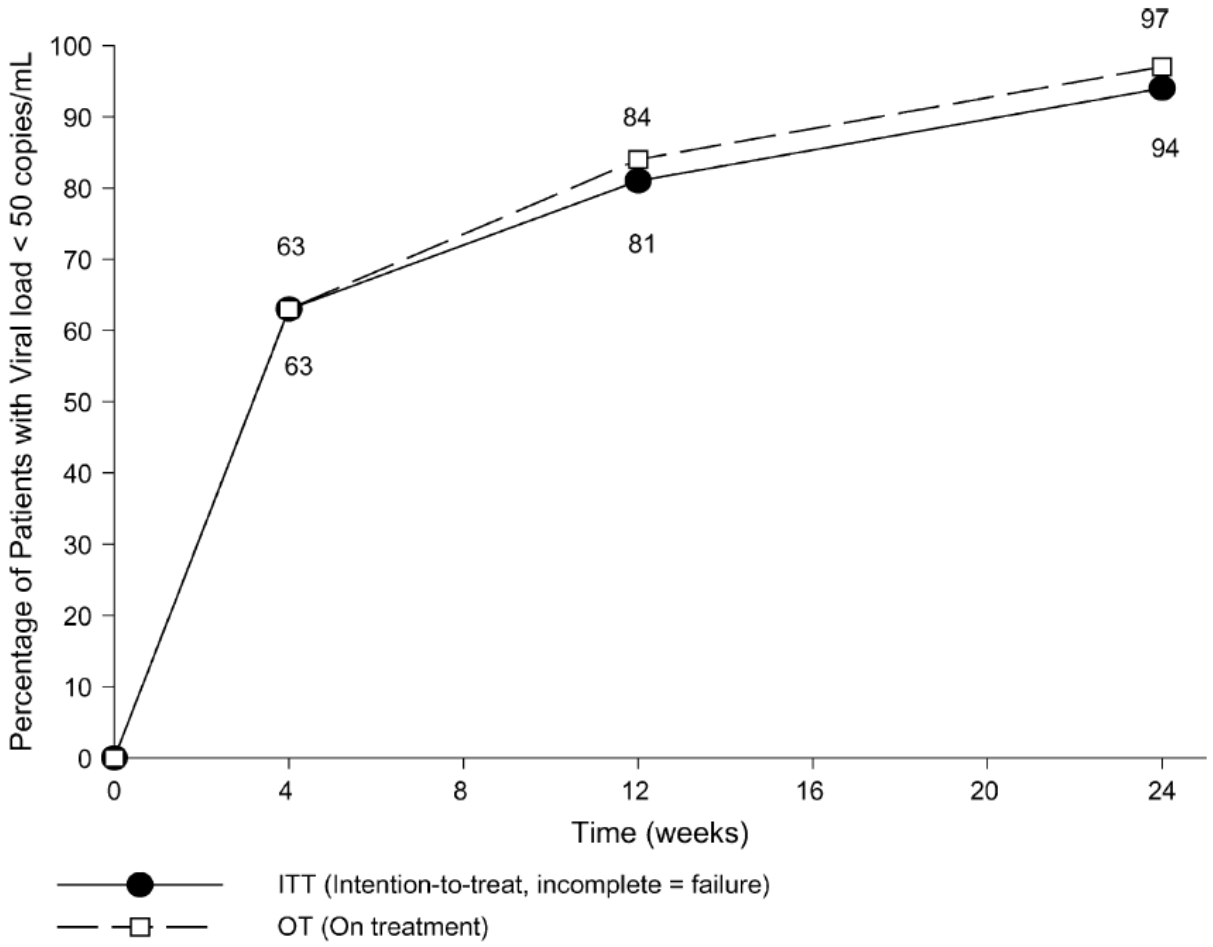
In the 243-person Long-Acting Antiretroviral Treatment Enabling (LATTE) study presented at CROI, daily oral doses of GSK744 and rilpivirine taken together provided similar antiretroviral activity to a standard two-pill cocktail, with a comparable safety profile. A trial reported at last year's International AIDS Society meeting in Malaysia showed that long-acting versions of GSK744 (an experimental analog of dolutegravir, which is marketed by GlaxoSmithKline as Tivicay) and rilpivirine (which was approved for use in 2011 and is marketed by Janssen Therapeutics as Edurant) were well tolerated and widely distributed in the bodies of healthy volunteers when administered together as injections once monthly or every three months.

Put the two trial results together, and it seems safe and promising now to test whether long-acting GSK744 and rilpivirine can control viral counts as well as daily oral dosing does. In the next few months, GlaxoSmithKline—through its spinoff ViiV Healthcare, an HIV-focused joint venture with Pfizer—hopes to launch such a trial of monthly or bimonthly injections of GSK744 and rilpivirine. It would be the first such efficacy trial involving an entirely long-acting regimen for HIV.

If it proves effective, such a long-acting antiretroviral therapy (LA-ART) would "set up a new paradigm of monthly or quarterly therapy for some patients," says David Ho, scientific director and chief executive of the Aaron Diamond AIDS Research Center at Rockefeller University in New York. "In the coming years, we'll see a fair amount of development in this area," he adds.

Multi-resitencia: TAR de Rescate

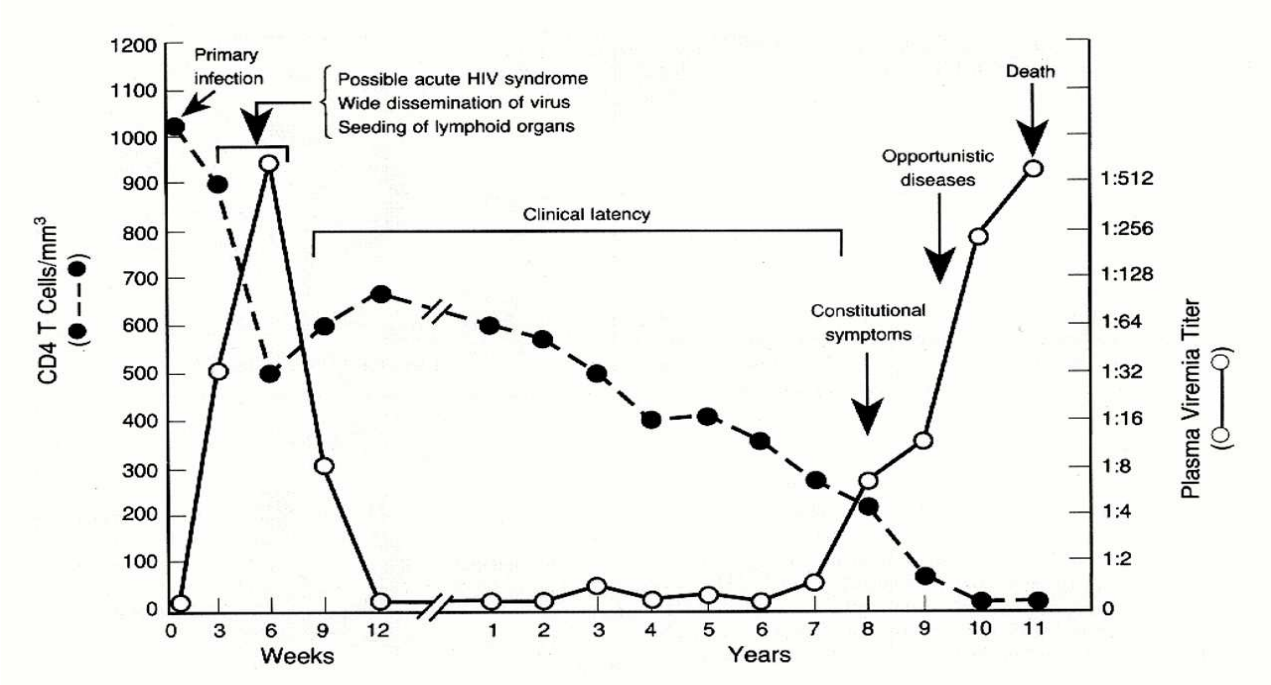
Raltegravir+Etravirina+Darunavir/r



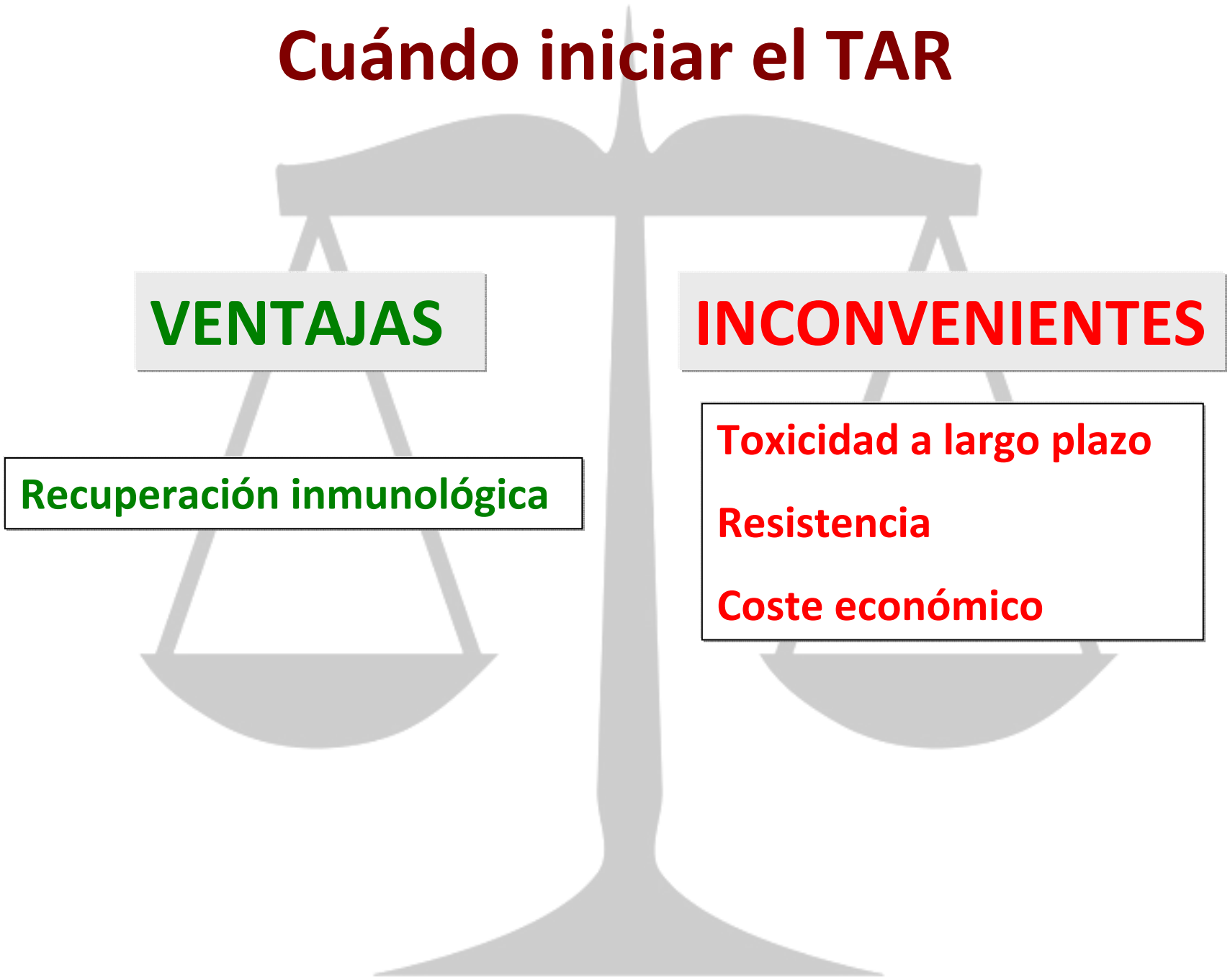
Imaz A, et al. JAIDS 2009

Estrategias de Tratamiento de la infección por VIH

- Cuando tratar



Cuándo iniciar el TAR



VENTAJAS

Recuperación inmunológica

INCONVENIENTES

Toxicidad a largo plazo

Resistencia

Coste económico

Cuándo iniciar el TAR

VENTAJAS

Recuperación inmunológica

INFAMACIÓN

INMUNOACTIVACIÓN

TAR como PREVENCIÓN

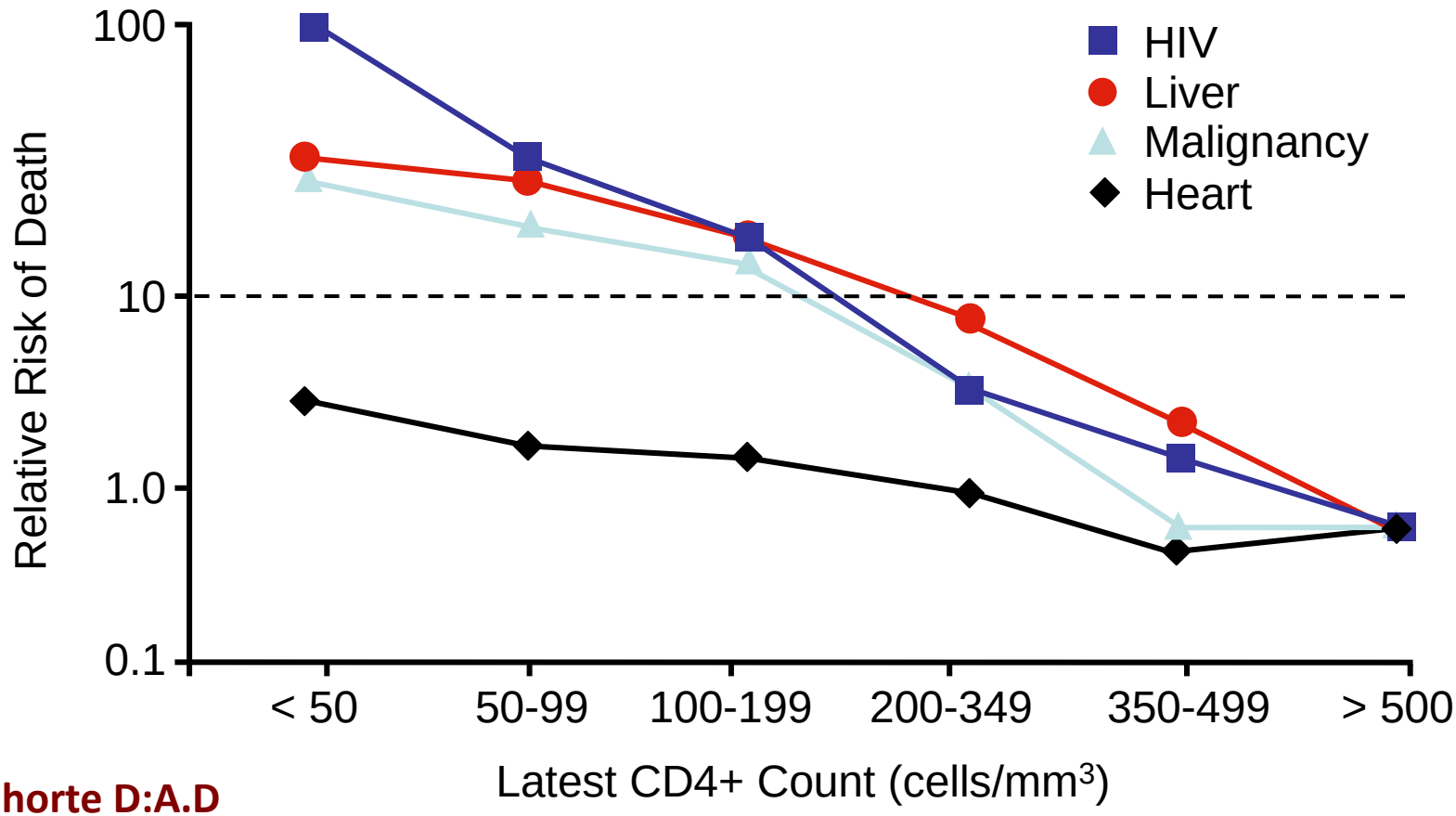
INCONVENIENTES

Toxicidad a largo plazo

Resistencia

Coste económico

El valor de CD4 se asocia con el riesgo de muerte por enfermedad no-SIDA

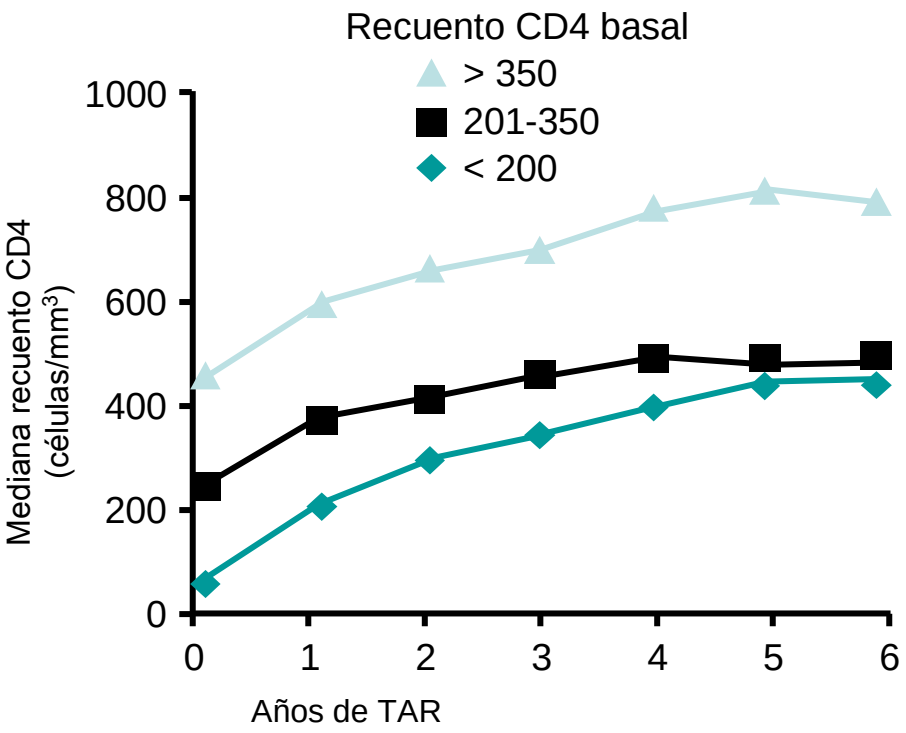


Cohorte D:A.D

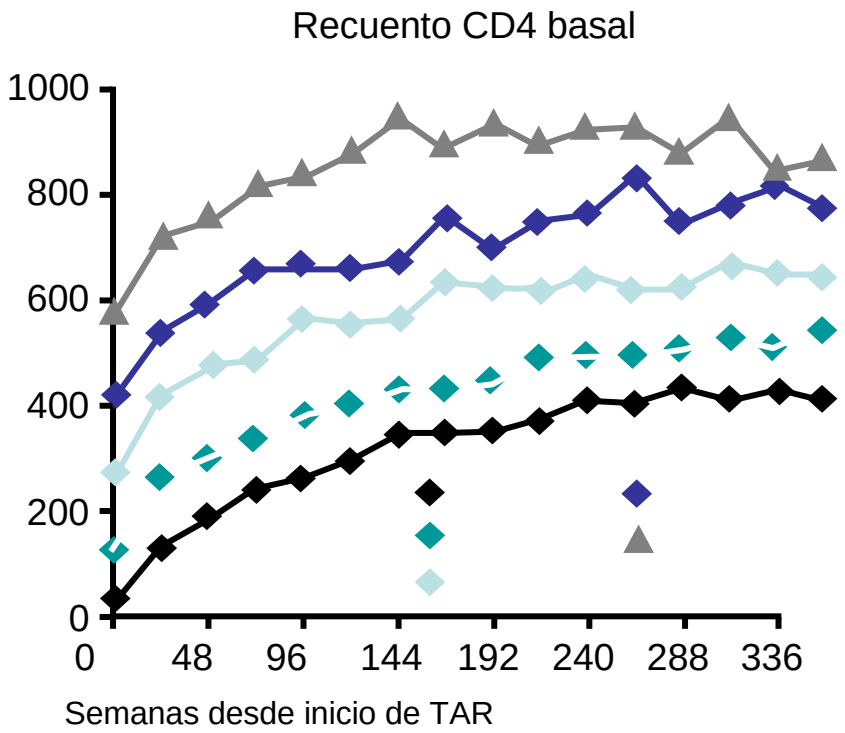
Weber R, et al. CROI 2005. Abstract 595.

La probabildad de conseguir un recuento de CD4 “normal” depende del nivel al inicio del tratamiento

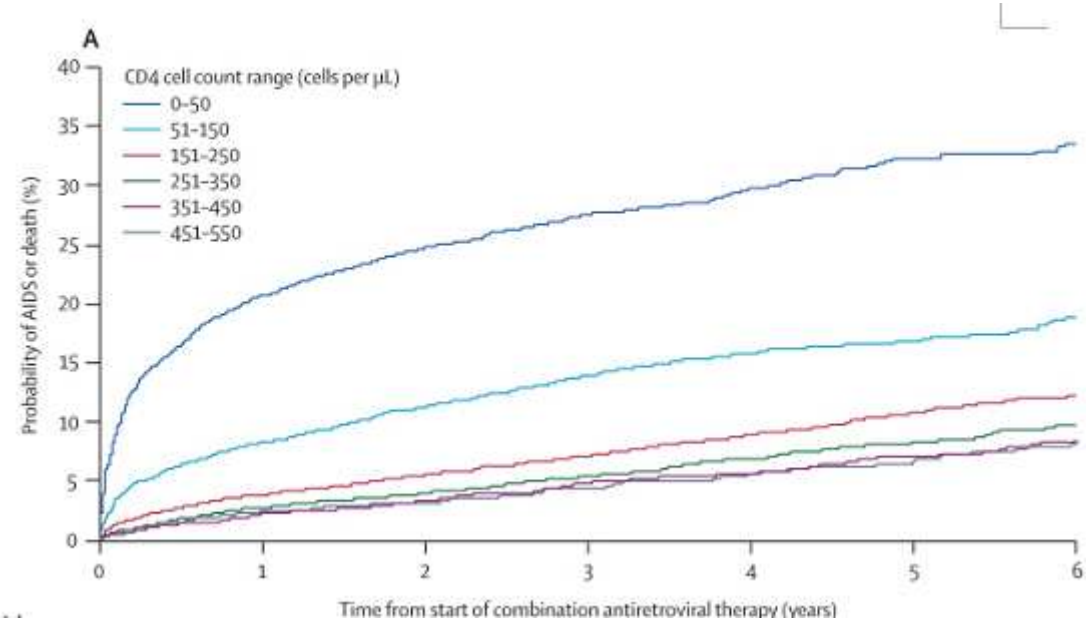
Cohorte Clínica VIH de la *Johns Hopkins* (1)



Cohorte ATHENA (2)



1.Moore RD, et al. Clin Infect Dis. 2007; 2. Gras L, et al. JAIDS 2007



When to Start.

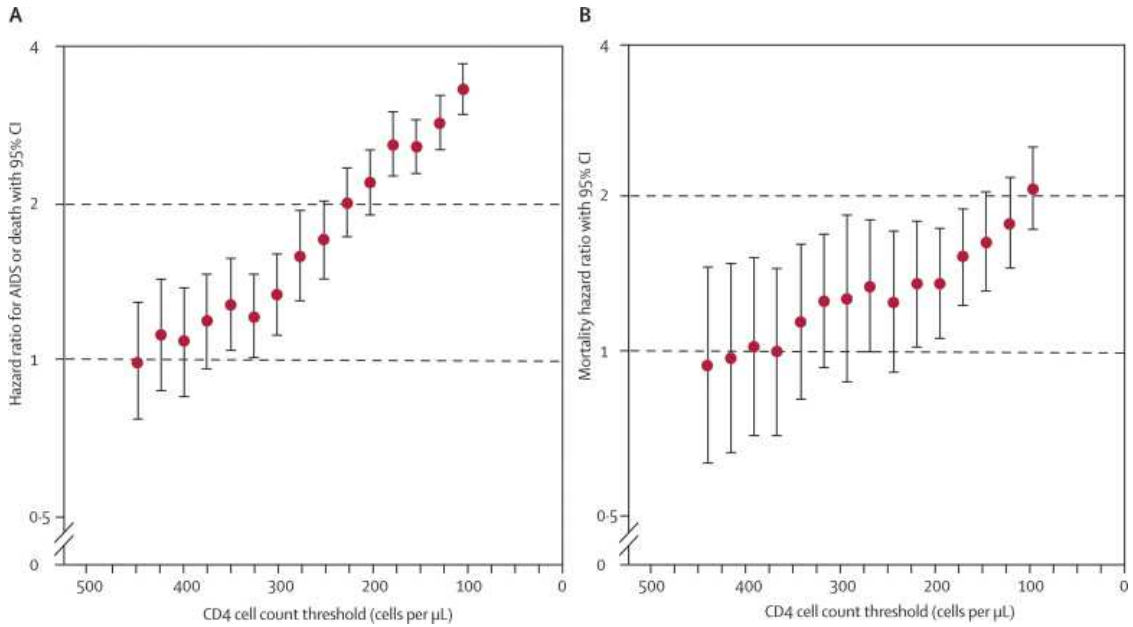
<350 vs 350-450

18 HIV cohorts

21,247patients

Primary outcome:

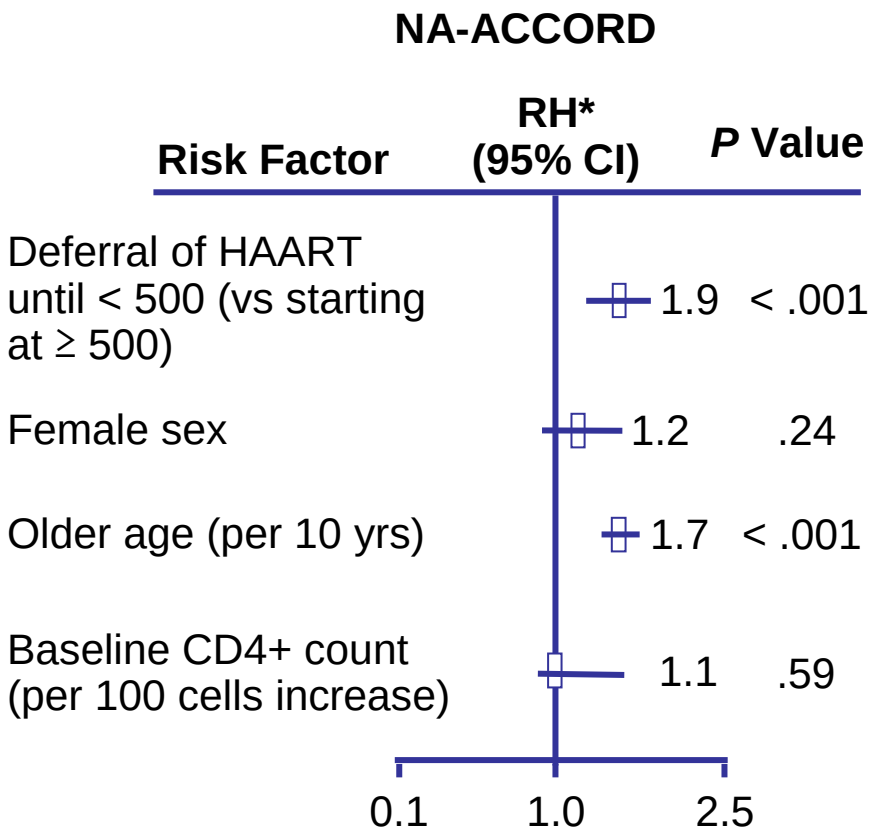
death from any cause



Lancet 2009

The NEW ENGLAND JOURNAL of MEDICINE

Effect of Early versus Deferred Antiretroviral Therapy for HIV on Survival

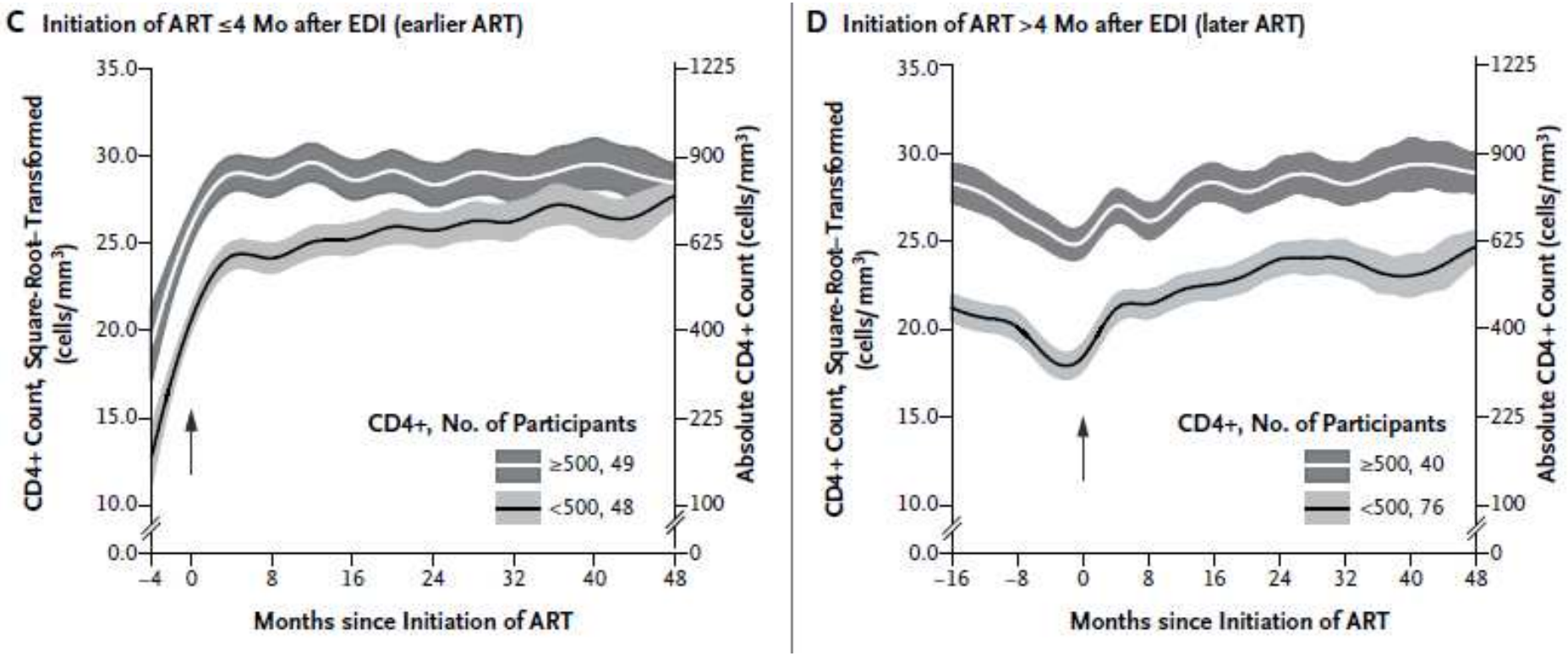


22 HIV research cohorts
17,517 patients

Primary outcome:
death from any cause

Kitahata MM, et al. NEJM 2009

Enhanced CD4+ T-Cell Recovery with Earlier HIV-1 Antiretroviral Therapy



Probabilidad conseguir ≥900 CD4/µL

Inicio TAR ≤ 4 meses vs > 4 meses: 64% vs 34% (p<0.001)

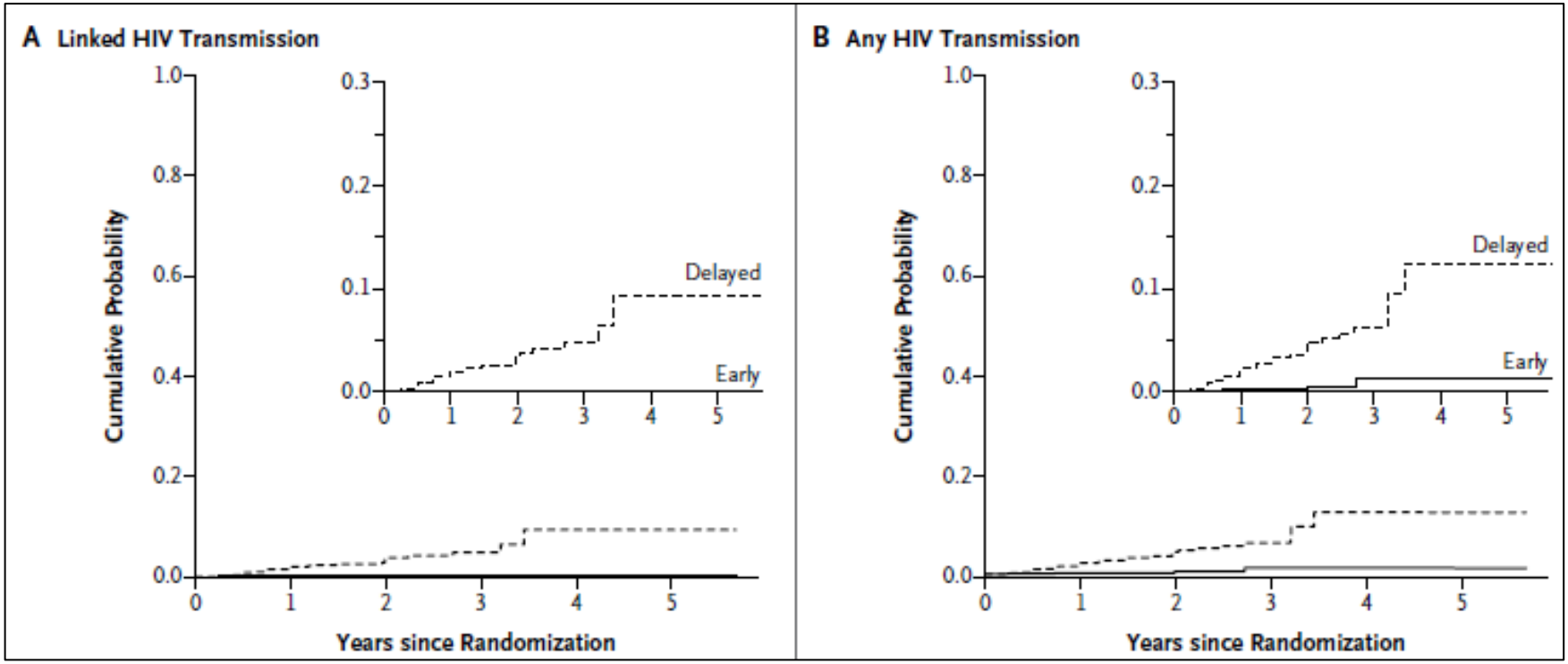
Le T, et al. NEJM 2013

TAR como prevención de nuevas infecciones

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Prevention of HIV-1 Infection with Early Antiretroviral Therapy

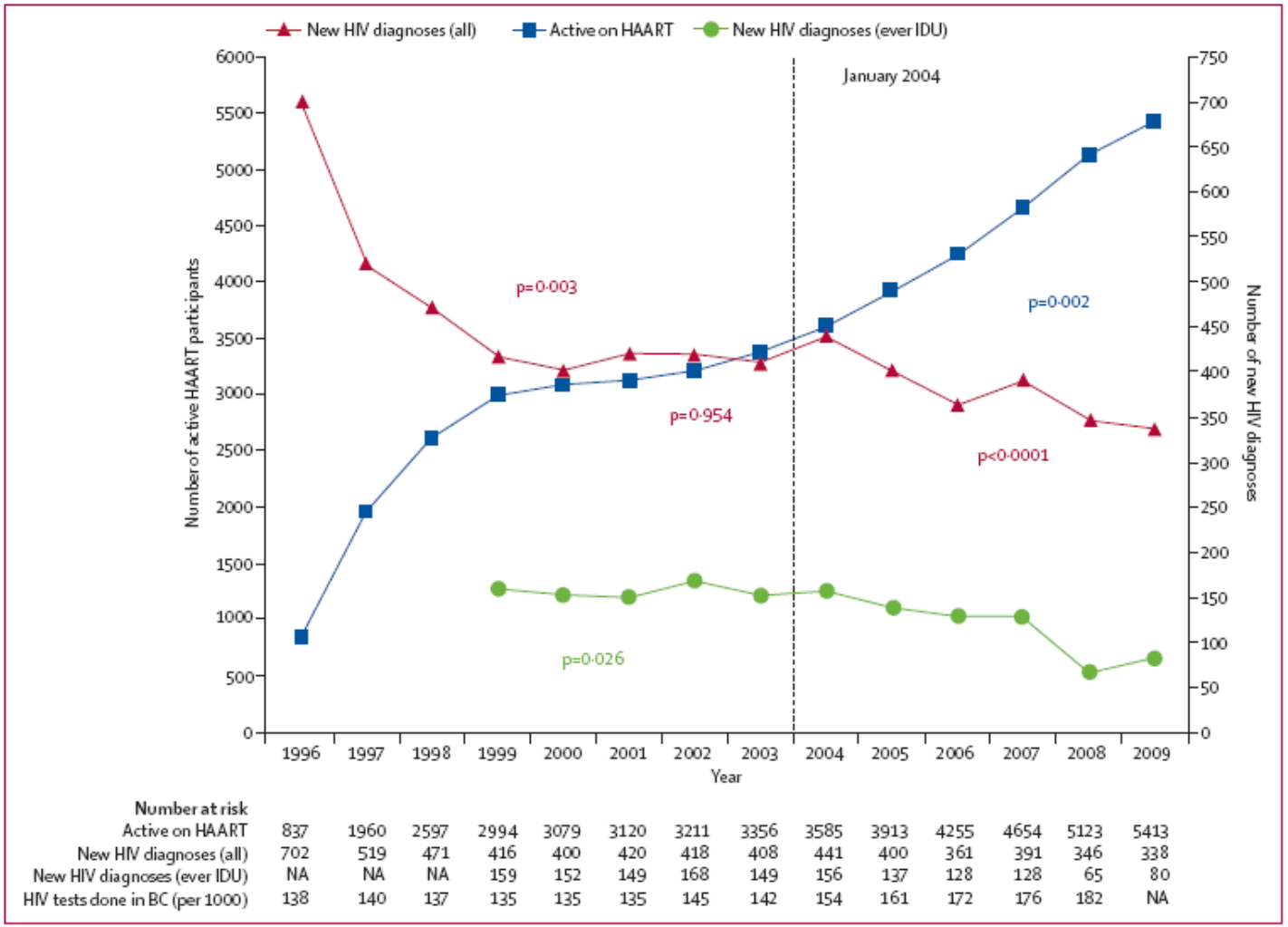


Cohen MS, et al. NEJM 2011

TAR como prevención de nuevas infecciones

Association of highly active antiretroviral therapy coverage, population viral load, and yearly new HIV diagnoses in British Columbia, Canada: a population-based study

Julio S G Montaner, Viviane D Lima, Rolando Barrios, Benita Yip, Evan Wood, Thomas Kerr, Kate Shannon, P Richard Harrigan, Robert S Hogg, Patricia Daly, Perry Kendall

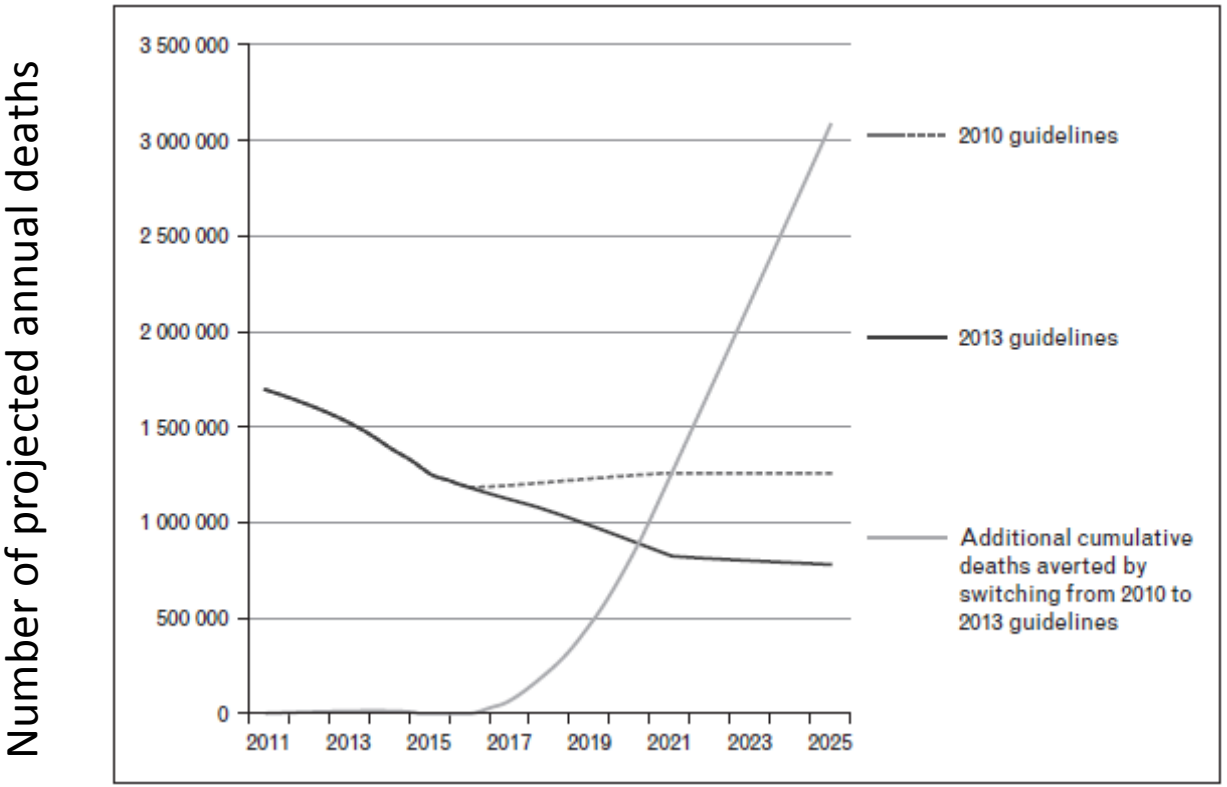


Number at risk	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Active on HAART	837	1960	2597	2994	3079	3120	3211	3356	3585	3913	4255	4654	5123	5413
New HIV diagnoses (all)	702	519	471	416	400	420	418	408	441	400	361	391	346	338
New HIV diagnoses (ever IDU)	NA	NA	NA	159	152	149	168	149	156	137	128	128	65	80
HIV tests done in BC (per 1000)	138	140	137	135	135	135	145	142	154	161	172	176	182	NA

The Lancet, 2010

The 2013 WHO guidelines for antiretroviral therapy: evidence-based recommendations to face new epidemic realities

Meg Doherty, Nathan Ford, Marco Vitoria, Gundo Weiler, and Gottfried Hirnschall



Curr Opin HIV AIDS 2013

RECOMENDACIÓN GENERAL	
Se recomienda la administración de TAR a todos los pacientes con infección por VIH[ǂ]. La fuerza y gradación de la recomendación varía según las siguientes circunstancias:	
CONDICIÓN / CIRCUNSTANCIA	**FUERZA Y GRADACIÓN**
Enfermedades B o C del CDC	A-I
Cifra de linfocitos T CD4+	
<350/µL	A-I
350 a 500/µL	A-II
>500/µL	B-III
Comorbilidades	
Nefropatía por VIH Hepatitis crónica por VHC Hepatitis crónica por VHB Edad ≥55 años Riesgo cardiovascular elevado Trastornos neurocognitivos Neoplasias	A-II
Riesgo de transmisión	
Mujeres gestantes	A-I
Transmisión heterosexual	A-I
Transmisión sexual entre varones	A-III

START

PARTNER

Gesida 2014

Conditions Favoring More Urgent Initiation of Therapy

Several conditions increase the urgency for therapy, including:

- Pregnancy **(AI)**. Clinicians should refer to the Perinatal Guidelines for more detailed recommendations on the management of HIV-infected pregnant women.[139]
- AIDS-defining conditions, including HAD **(AI)**
- Acute OIs (see discussion below)
- Lower CD4 counts (e.g., <200 cells/mm^3) **(AI)**
- HIVAN **(AII)**
- Acute/Early Infection **(BII)**. See more discussion in the Acute/Early Infection section.
- HIV/HBV coinfection **(AII)**
- HIV/HCV coinfection **(BII)**
- Rapidly declining CD4 counts (e.g., >100 cells/mm^3 decrease per year) **(AIII)**
- Higher viral loads (e.g., >100,000 copies/mL) **(BII)**

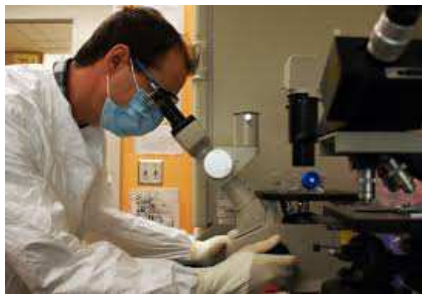
DHHS 2014

Estrategias para el Futuro:

Erradicación del VIH??

Disrupción de latencia

Terapia génica



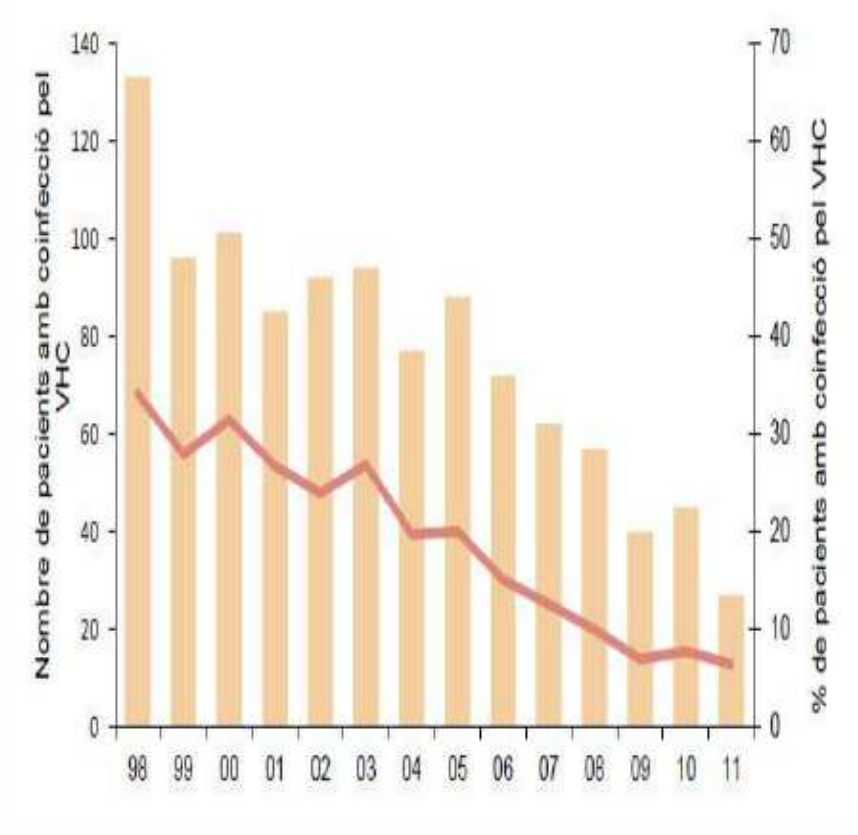
Vacuna terapéutica

Anticuerpos neutralizantes

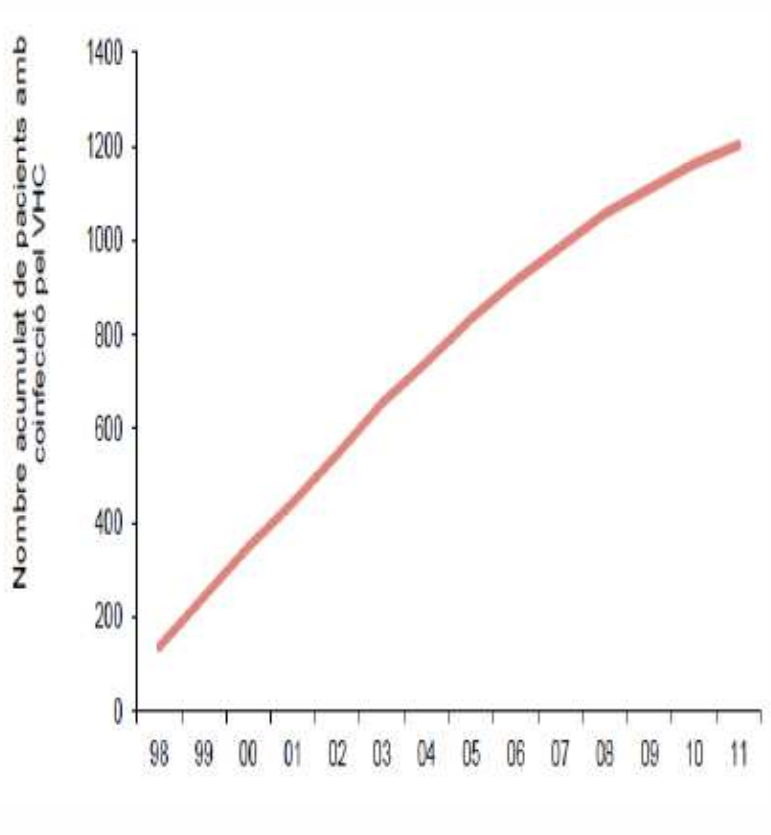
Nuevas estrategias de tratamiento de la hepatitis por VHC

INFECCIÓ PER EL VHC EN PERSONES VIH+

CEEIS Cat
Centre d'Estudis Epidemiològics sobre les Infeccions de Transmissió Sexual i Sida de Catalunya



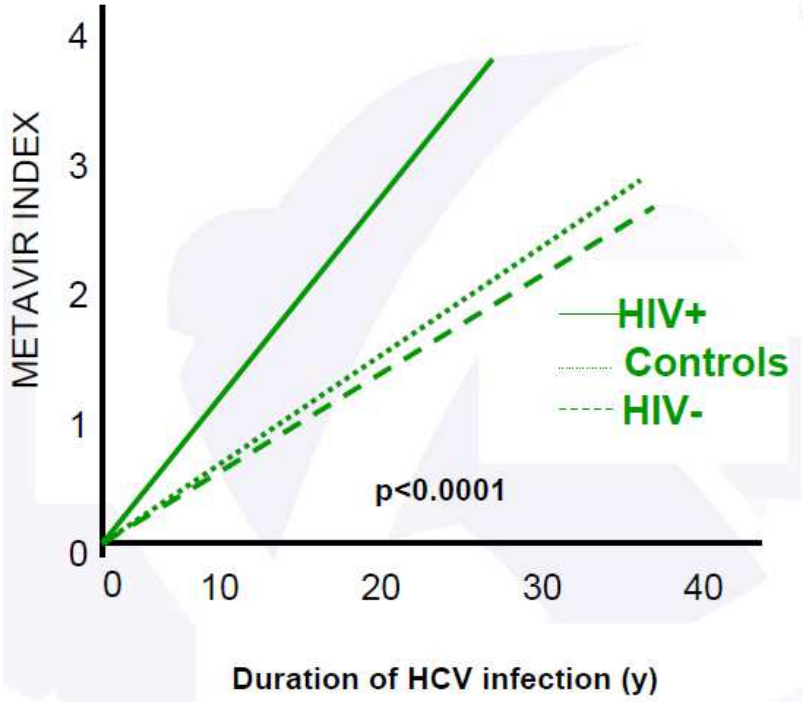
Coinfecció per el VHC en els nous Dx de VIH



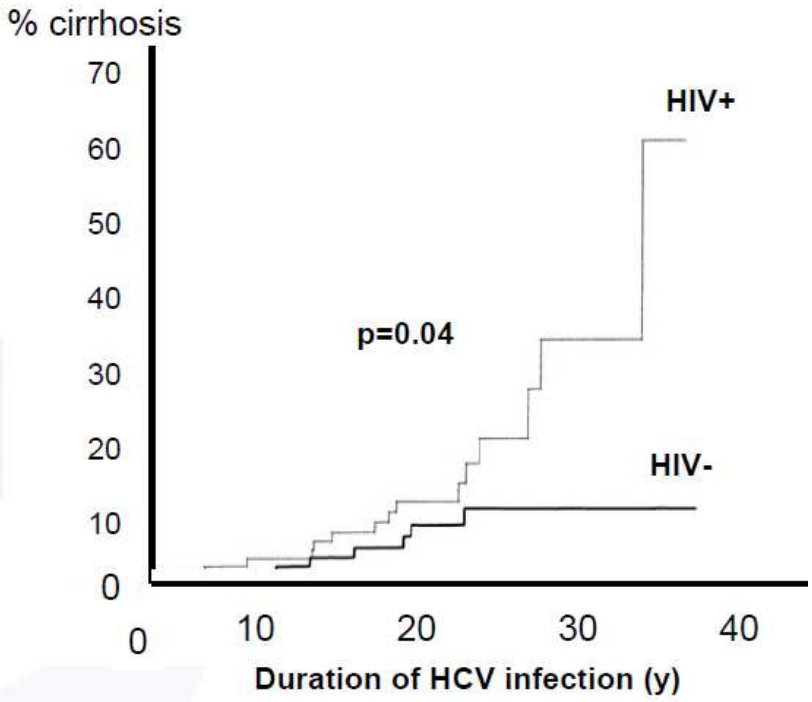
Persones amb coinfecció VIH-VHC a Catalunya

Coinfección VIH-VHC

Impacto en la progresión de fibrosis hepática



Benhamou et al, 1999; 34: 283-287

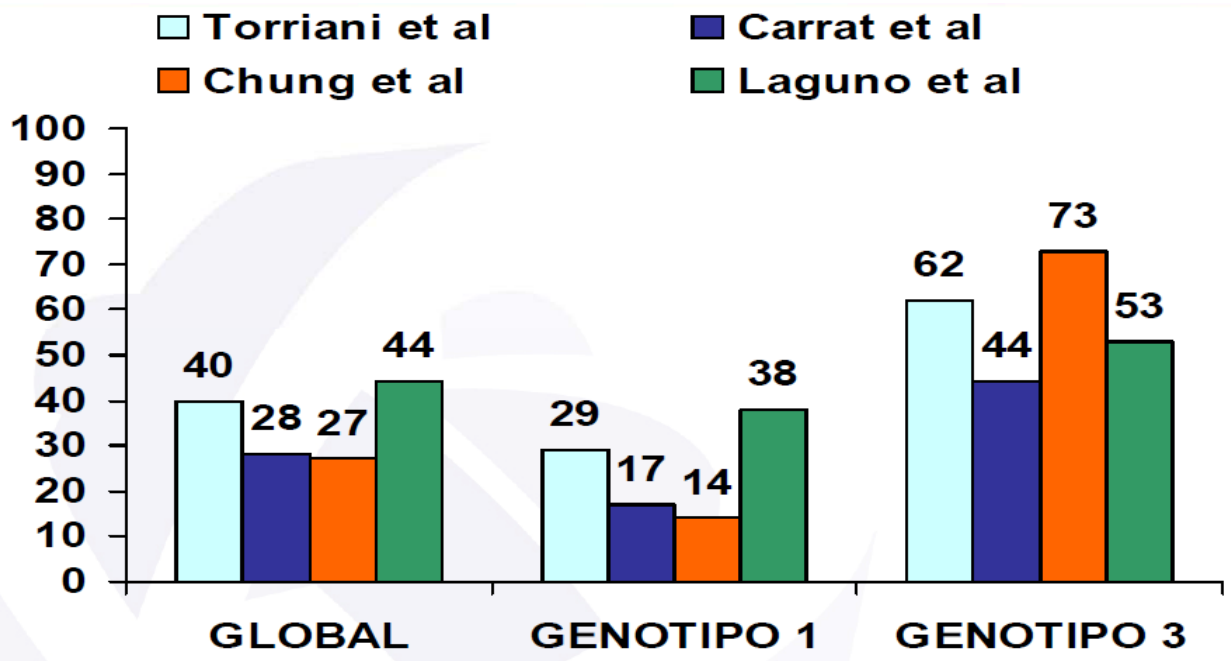


Di Martino, 2001; 34:1193-1199

Arch Intern Med 2006;166:1632-1641.

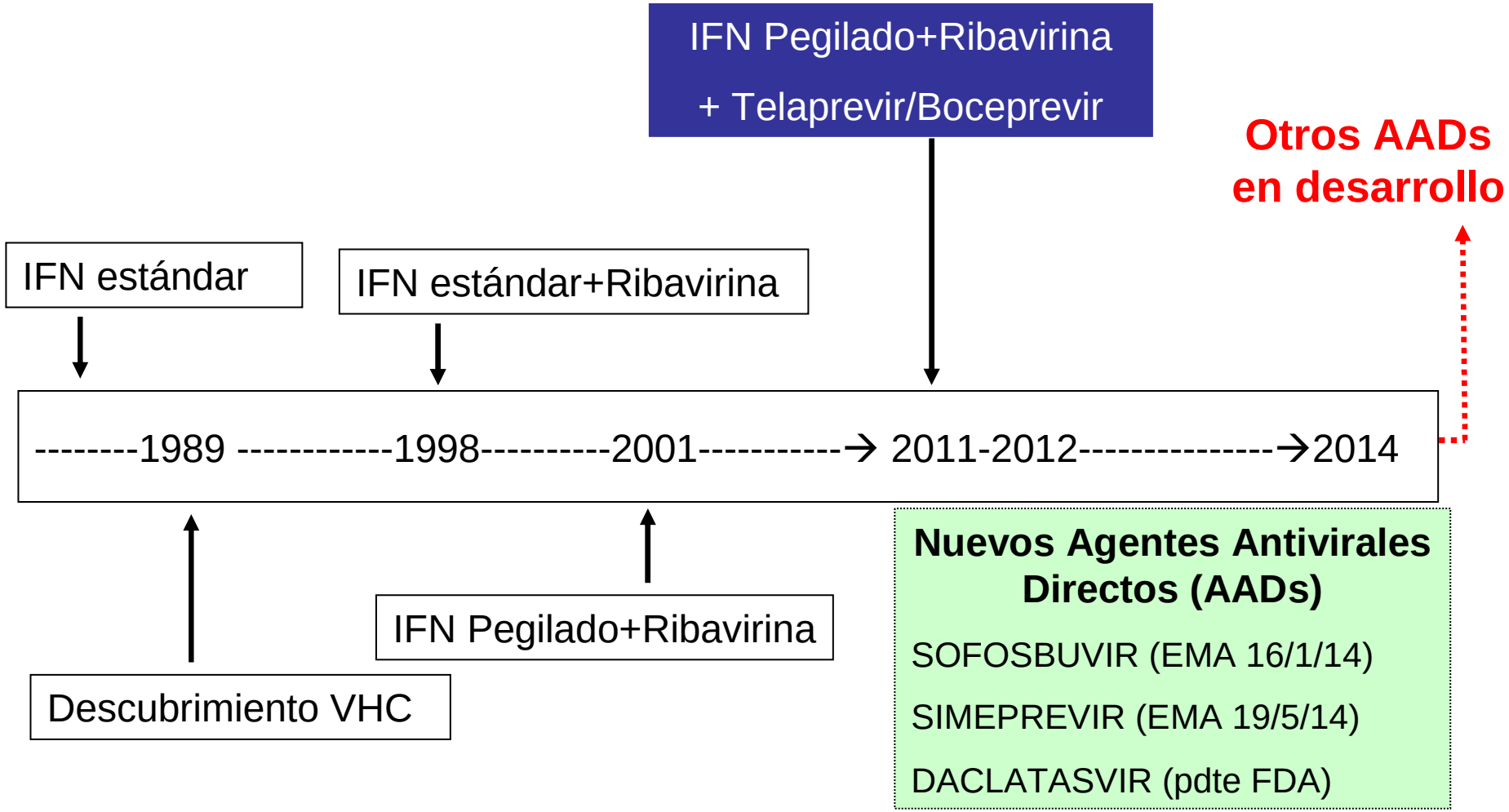
Tratamiento de la hepatitis crónica VHC en el paciente co-infectado VIH-VHC

Peg-Interferón alfa+ Ribavirina



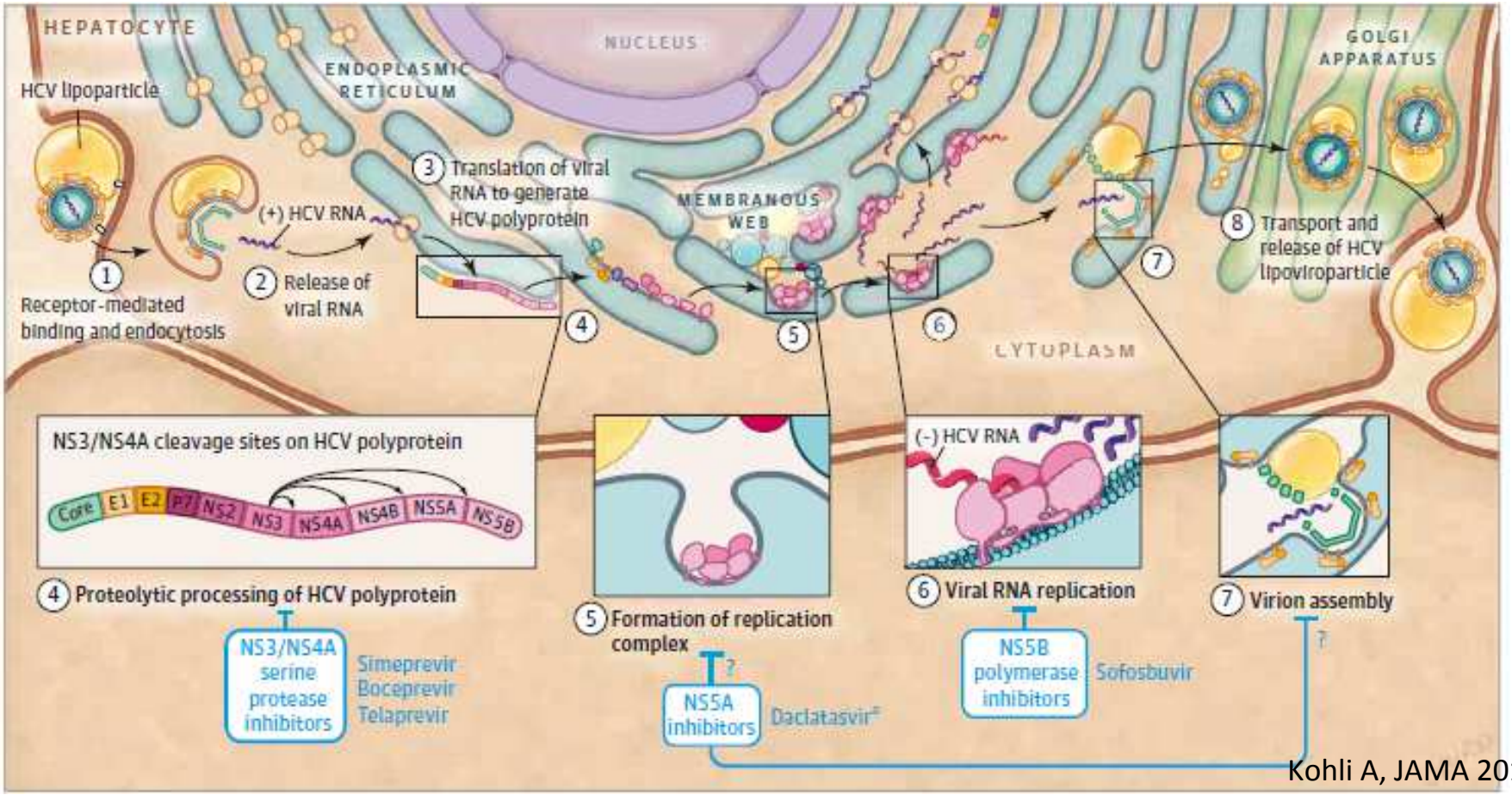
Torriani et al. N Engl J Med 2004; 351: 438-50; Carrat F et al. JAMA 2004; 292: 2839-48; Chung RT. N Engl J Med 2004; 351: 451-59; Laguno M et al. AIDS 2004; 18: F27-36

Evolución del tratamiento de la Hepatitis crónica por VHC



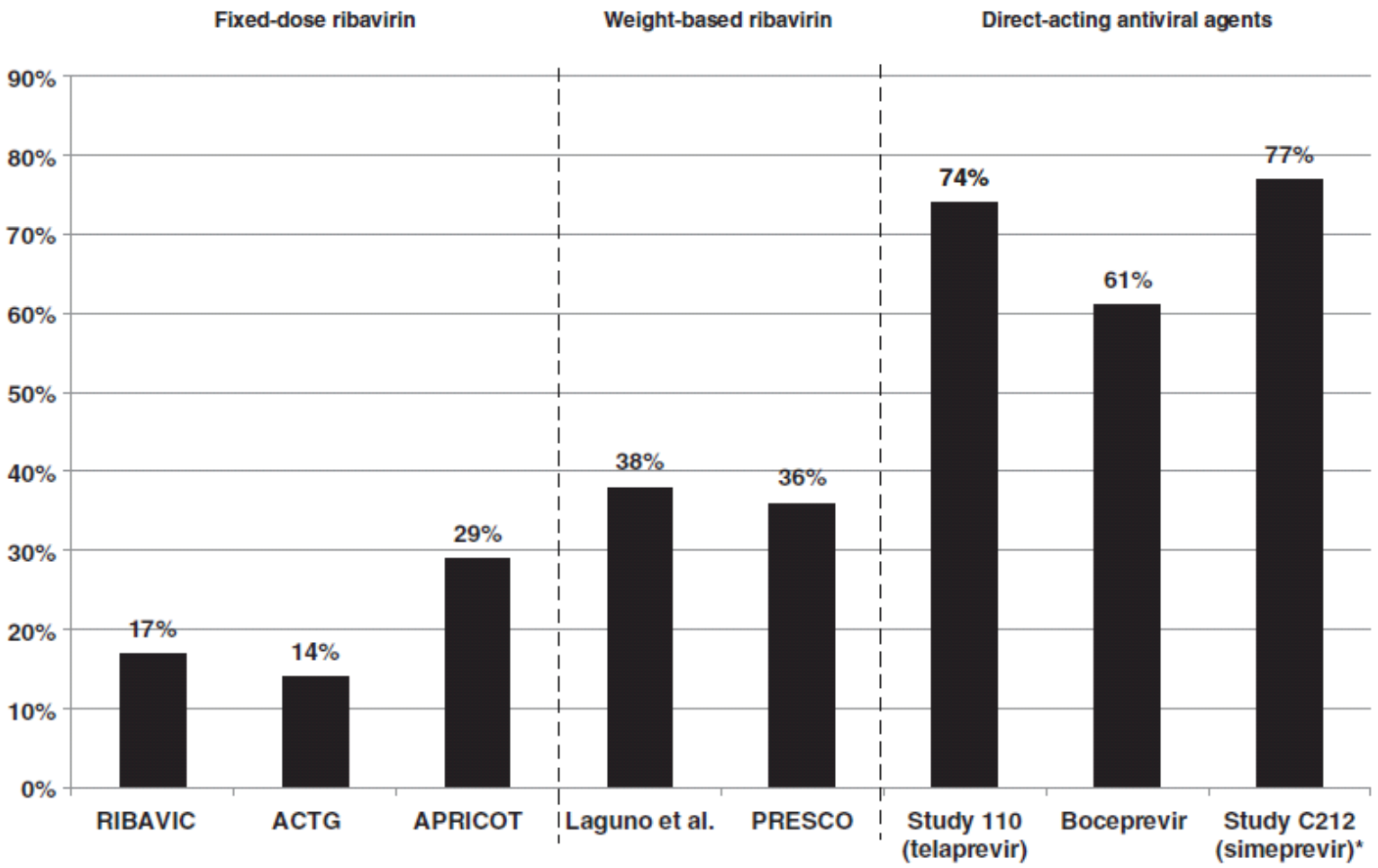
Tratamiento de la hepatitis crónica VHC en el paciente co-infectado VIH-VHC

Nuevos AAD



Kohli A, JAMA 2014

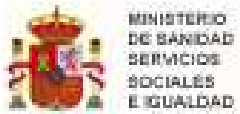
Primeros AAD: Telaprevir y Boceprevir



Martel-Laferrerière V, el al. J Clin Gastroenterol 2014

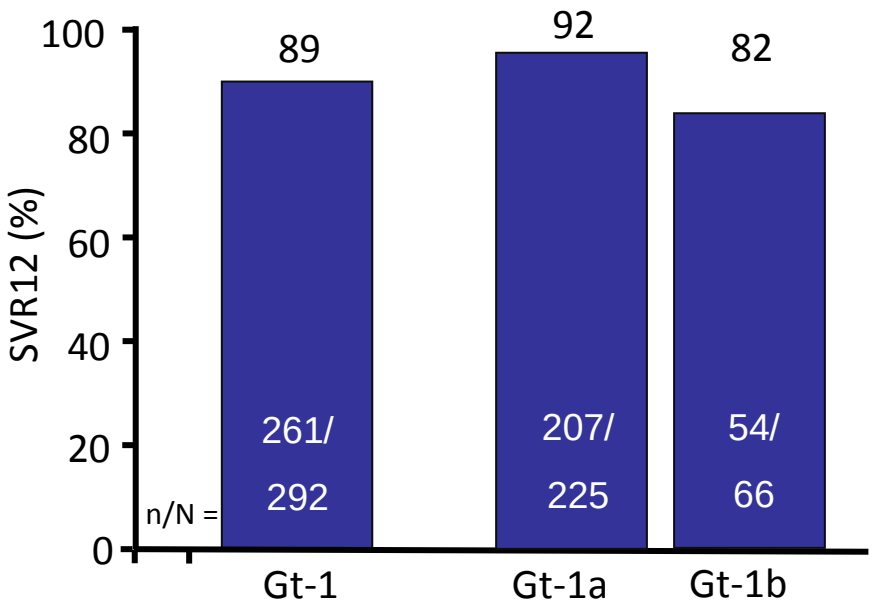
▶ 02/10/2014 | FARMACOLOGÍA

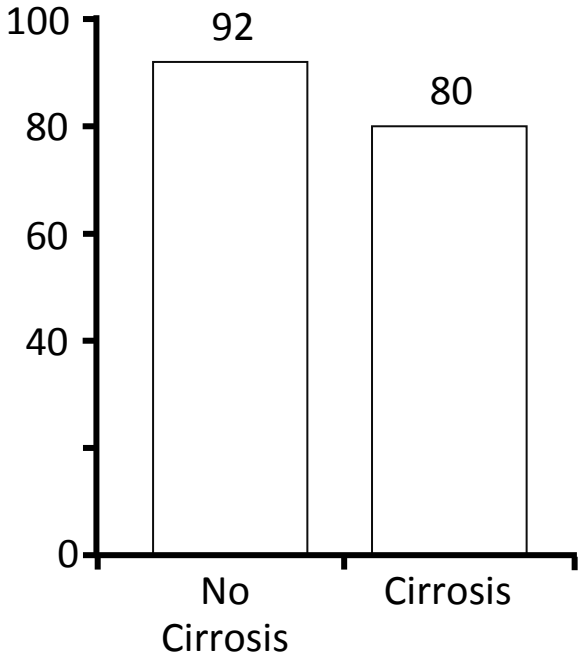
Sanidad financiará Sovaldi® (sofosbuvir) a partir del 1 de noviembre



El techo de gasto en este medicamento se situará en 125 millones de euros durante el primer año de comercialización

Estudio NEUTRINO (F-III)
SOFOSBUVIR + PegIFN+Ribavirina
12 semanas





Lawitz E, et al. N Engl J Med. 2013

Interacciones DAAs/ARV

	TVR	BOC	SIM	SOF	DAC	LED	ABT 3D	MK 2D
ATV/r								
DRV/r								
LPV/r								
EFV								
ETR								
RPV								
DTV								
EVG/c								
RAL								
MVC								

Tratamientos sin Interferon

ORIGINAL ARTICLE

Daclatasvir plus Sofosbuvir for Previously Treated or Untreated Chronic HCV Infection

Sulkowski MS et al.

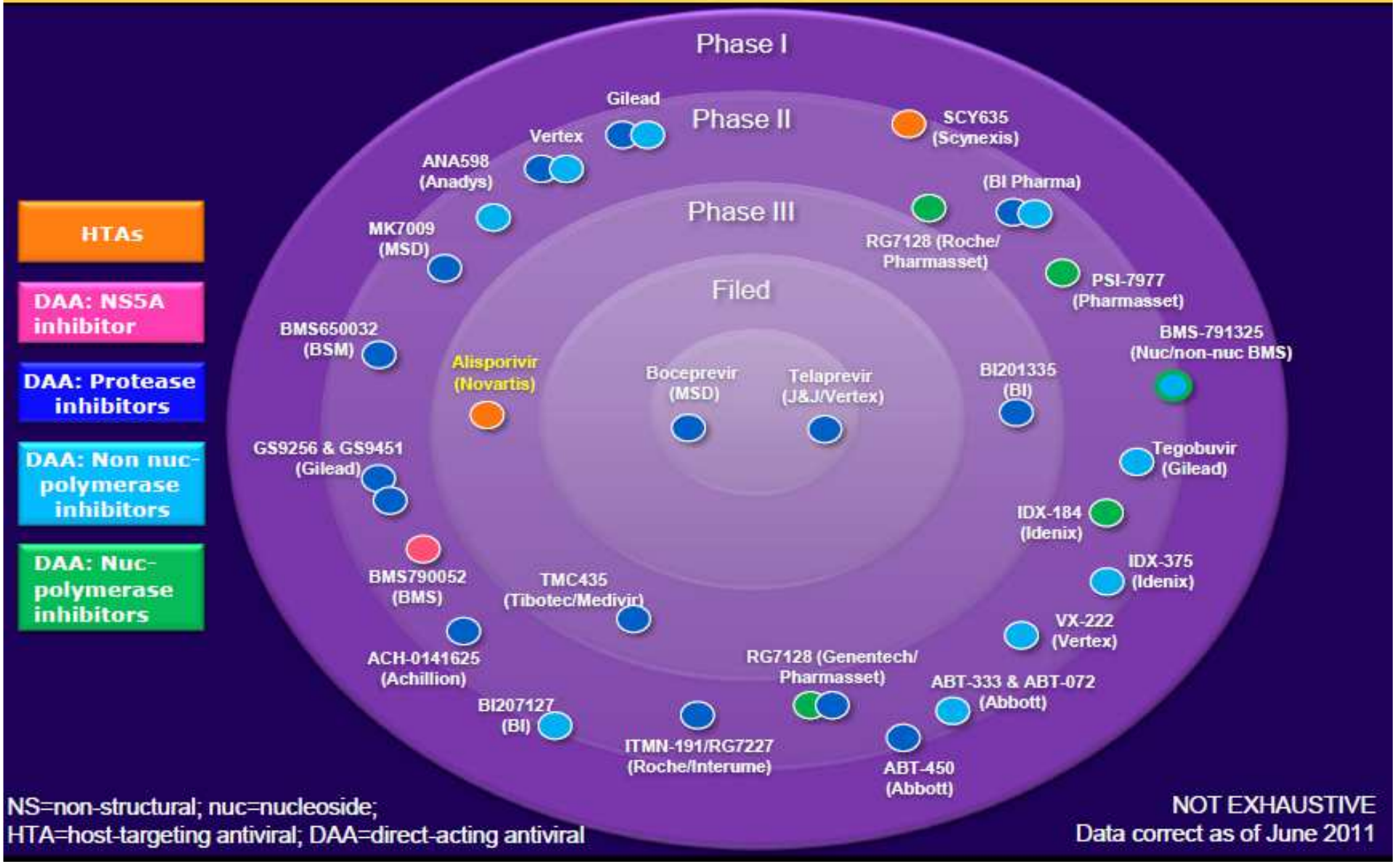
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 15, 2014 VOL. 370 NO. 20

Ledipasvir and Sofosbuvir for 8 or 12 Weeks for Chronic HCV without Cirrhosis

Kowdley KV et al.

Treatment options for HCV will increase dramatically in the coming years



NS=non-structural; nuc=nucleoside;
HTA=host-targeting antiviral; DAA=direct-acting antiviral

NOT EXHAUSTIVE
Data correct as of June 2011

Ideas finales

- VIH: La mejoría de los fármacos ARV (potencia, posología, efectos adversos) ha permitido diseñar y utilizar estrategias de tratamiento que permiten mejorar su eficacia así como facilitar la adherencia y reducir la toxicidad.

- VHC: Los nuevos fármacos antiVHC (AAD) permiten (permitirán) elaborar estrategias terapéuticas mucho mas eficaces, mas sencillas, mejor toleradas y mas cortas.

Gràcies!!!!