

LOS TOP EN LAS PUBLICACIONES RECIENTES EN VIH/SIDA

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Oaxaca , Méjico

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Publicaciones que han impactado el manejo del paciente infectado con VIH recientemente

◆ Publicaciones 2008-2009:

- Epidemiología del VIH en los Estados Unidos**
- Transmisión**
- Diagnostico**
- Vacunas**
- Tratamiento**

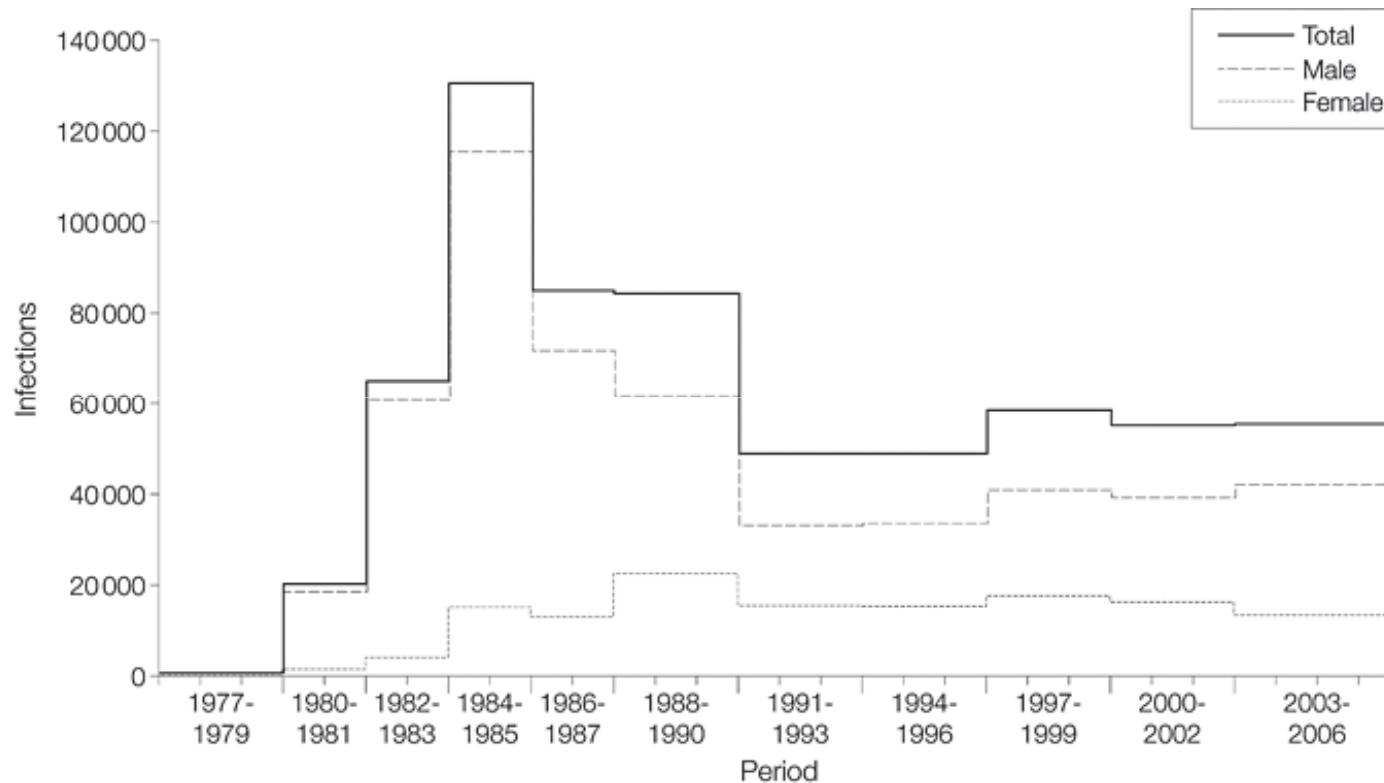
Epidemiologia

- ◆ **Estimation of HIV Incidence in the United States.**
H. Irene Hall et al; JAMA, August 6, 2008—Vol 300,
No. 5

Estimation of HIV Incidence in the United States: JAMA

- ◆ Remanentes de muestras de nuevos casos diagnosticados en 22 estados en 2006 fueron examinadas utilizando “BED HIV-1 capture enzyme immunoassay” para clasificarlas como recientes o a largo plazo, Utilizando esta información mas la información reportada al CDC junto con un acercamiento estadístico novedoso se calcula la incidencia de nuevos casos en los Estados Unidos.
- ◆ 31 % fueron infecciones recientes y la nueva estimación cambio de 39, 400 casos a 55,400 nuevos casos anuales.

Estimated New Human Immunodeficiency Virus (HIV) Infections, Extended Back-Calculation Model, 50 US States and the District of Columbia, 1977-2006



Hall, H. I. et al. *JAMA* 2008;300:520-529.

Incidence decreased after 1985 and reached a low point in the early 1990s, with approximately 49 000 infections per year. Incidence again peaked in the late 1990s at approximately 58 000 incident infections and decreased to 55 000 per year in the most recent intervals (ie, 2000-2002 and 2003-2006).

Estimated Rates of New Human Immunodeficiency Virus Infections, 50 US States and the District of Columbia, 2006a

Table 2. Estimated Rates of New Human Immunodeficiency Virus Infections, 50 US States and the District of Columbia, 2006^a

Characteristic	Rate (95% CI) ^b
Total	22.8 (19.5-26.1)
Sex	
Male	34.3 (29.1-39.5)
Female	11.9 (10.0-13.7)
Race/ethnicity	
White	11.5 (9.6-13.4)
Black	83.7 (70.9-96.5)
Hispanic	29.3 (23.8-35.0)
Asian/Pacific Islander	10.3 (4.2-16.3)
American Indian/ Alaska Native	14.6 (3.0-25.2)
Age, y	
13-29	26.8 (22.8-31.0)
30-39	42.6 (35.7-49.4)
40-49	30.7 (25.8-35.6)
50-99	6.5 (5.1-7.9)

Abbreviation: CI, confidence interval.

^aStratified extrapolation approach. See Table 1 for numerator information.

^bPer 100 000 population; postcensus estimates from the US Bureau of the Census.

Hall, H. I. et al. JAMA 2008;300:520-529.

Prevención/Transmisión

- ◆ **Sexual transmission of HIV according to viral load and antiretroviral therapy: systematic review and meta-analysis.** Attia S, Egger M, Müller M, Zwahlen M, Low N. AIDS. 2009;23:1397-1404

Sexual transmission of HIV according to viral load and antiretroviral therapy: systematic review and meta-analysis ; AIDS

- ◆ Repaso sistemático y meta- análisis de artículos y abstractos que reportan el riesgo de transmisión de VIH por sexo sin protección de acuerdo a cargas virales y el uso de TARV.
- ◆ Se identificaron 11 cohortes reportando en 5021 parejas heterosexuales y 461 eventos de transmisión de VIH. La transmisión de pacientes tratados fue de 0.46 (95% CI 0.19–1.09) por 100 personas-años, basado en 5 eventos. La transmisión de persona seropositiva con una carga viral de menos de 400 copias/ml en TAR, basado en dos estudios fue de cero

Resumen del impacto de TARV en la transmisión sexual de VIH

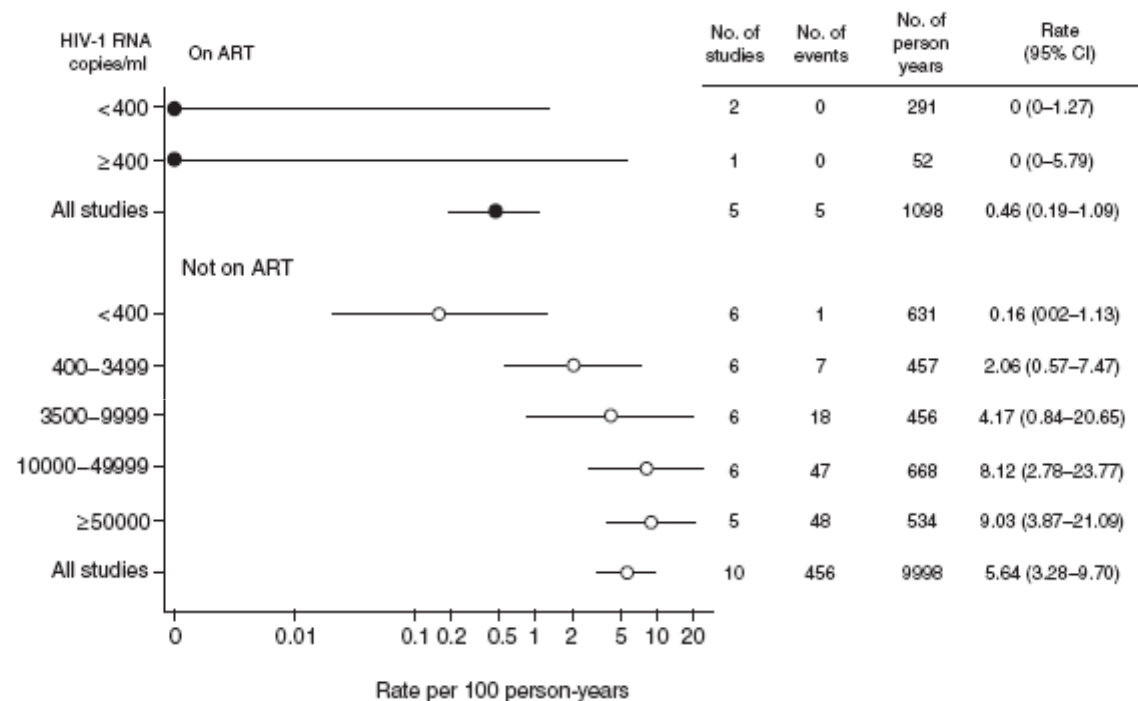


Fig. 2. Forest plot of summary HIV transmission rates, per 100 person-years, according to use of antiretroviral therapy and plasma viral load. ART, antiretroviral therapy; CI, confidence interval; the meta-analysis of couples where the HIV-infected partner received ART included two studies with viral load data [10,11] and three studies without viral load data [18,23,24]; the meta-analysis of couples with the HIV-infected partner not receiving ART included seven studies with viral load data in at least one category [9,10,11–14,17] and three studies without viral load data [21,23,24]. Note that not all studies with viral load data

Diagnostico y acceso a terapia

- ◆ Granich RM, Gilks CF, Dye C, De Cock KM, Williams BG. Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model. Lancet. 2009;373:48-57.

Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission; Lancet

- ◆ Estrategia teórica que explora la idea de pruebas voluntarias universales con acceso inmediato a TARV. Se asume: que se hace prueba a todos los adultos mas de 15 anos anualmente, tratamiento inmediato luego del diagnostico y que todas las transmisiones son heterosexuales.
- ◆ Estrategia podría convertir la presente endemia de VIH a una fase de eliminación. Reduciendo la transmisión y mortalidad a menos de un caso por 1000 personas/ anos en 10 anos. Disminuiría la prevalencia a menos de 1% en 50 anos.

Vacunas

◆ Vaccination with ALVAC and AIDSVAX to Prevent HIV-1 Infection in

Thailand Supachai *Rerks-Ngarm, M.D., Punnee Pitisuttithum, M.D., D.T.M.H., Sorachai Nitayaphan, M.D., Ph.D., Jaranit Kaewkungwal, Ph.D., Joseph Chiu, M.D., Robert Paris, M.D., Nakorn Prem Sri, M.D., Chawetsan Namwat, M.D., Mark de Souza, Ph.D., Elizabeth Adams, M.D., Michael Benenson, M.D., Sanjay Gurunathan, M.D., Jim Tartaglia, Ph.D., John G. McNeil, M.D., Donald P. Francis, M.D., D.Sc., Donald Stablein, Ph.D., Deborah L. Birx, M.D., Supamit Chunsuttiwat, M.D., Chirasak Khamboonruang, M.D., Prasert Thongcharoen, M.D., Ph.D., Merlin L. Robb, M.D., Nelson L. Michael, M.D., Ph.D., Prayura Kunasol, M.D., Jerome H. Kim, M.D., for the MOPH-TAVEG Investigators* **N Engl J Med 2009**. Volume 361:2209-2220, December 3, 2009

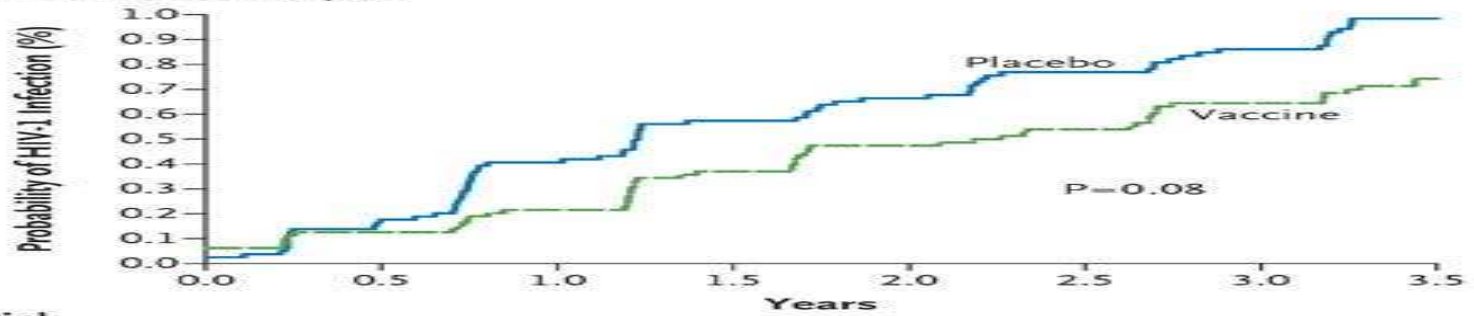
Vaccination with ALVAC and AIDSVAX to Prevent HIV-1 Infection in Thailand; N Engl J Med

- ◆ Estudio en Tailandia, randomizado, doble ciego/placebo. Se evaluó la *recombinant canarypox vector vaccine (ALVAC-HIV [vCP1521])* con dos revacuaciones de *recombinant glycoprotein 120 subunit vaccine (AIDSVAX B/E)*. Se administró a 16,402 hombres y mujeres saludables entre 18 y 30 años. Los voluntarios a riesgo de transmisión heterosexual se monitorearon : infección por VIH y para viremia temprana. Luego de vacunación por 6 meses y seguidos por tres años.

Vaccination with ALVAC and AIDSVAX to Prevent HIV-1 Infection in Thailand; N Engl J Med

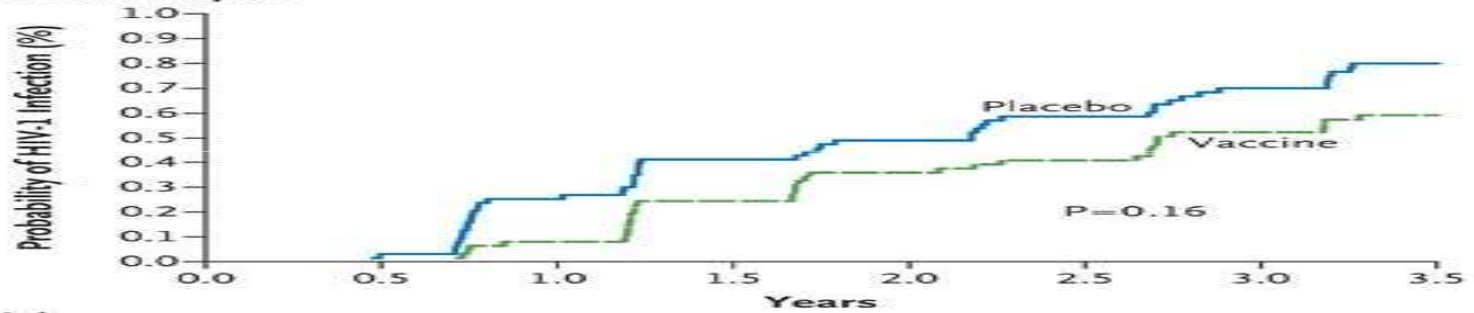
- ◆ En el análisis *Intention to Treat* :16,402 sujetos, la eficacia fue de **26.4%** (95% confidence interval [CI], –4.0 to 47.9; P=0.08) . En el análisis **per-protocol**: 12,542 sujetos, la eficacia fue de **26.2%** (95% CI, –13.3 to 51.9; P=0.16) (Panel B). En el análisis **modified intention-to-treat** analysis:16,395 sujetos (Excluyendo 7 sujetos que ya estaban infectados),la eficacia fue de **31.2%** (95% CI, 1.1 to 51.2; P=0.04)
- ◆ No hubo efecto en las cargas virales o CD4
- ◆ Resultados modesto que sugieren mas investigación.

A Intention-to-Treat Analysis



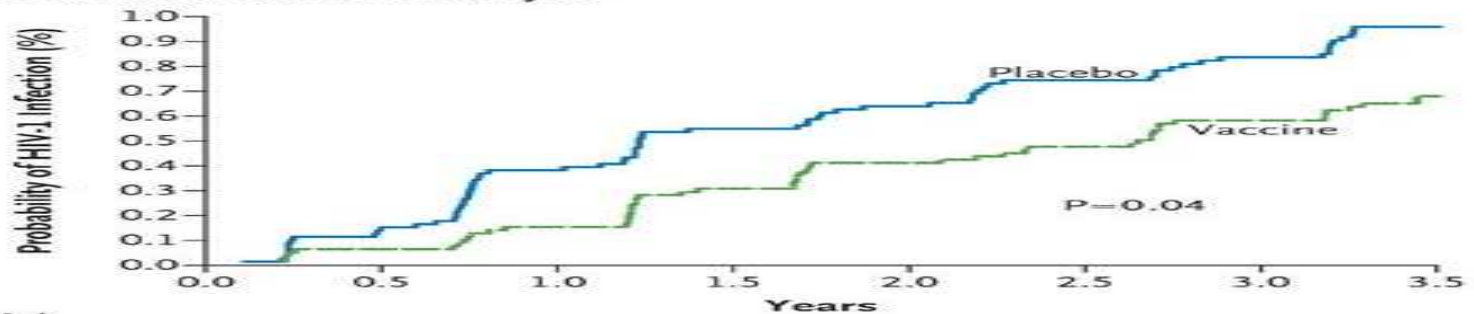
No. at Risk					
Placebo	8200	7775	7643	7441	7325
Vaccine	8202	7797	7665	7471	7347
Cumulative No. of Infections					
Placebo		32	52	67	76
Vaccine		17	37	50	56

B Per-Protocol Analysis



No. at Risk					
Placebo	6366	6283	6220	6089	6002
Vaccine	6176	6140	6068	5958	5874
Cumulative No. of Infections					
Placebo		16	31	44	50
Vaccine		5	22	32	36

C Modified Intention-to-Treat Analysis

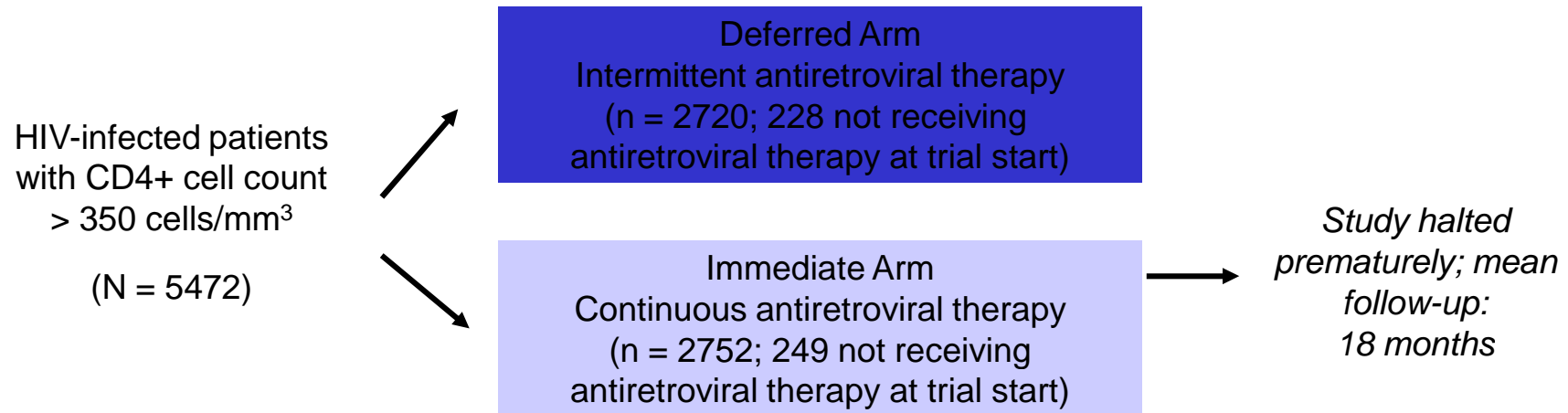


No. at Risk					
Placebo	8198	7775	7643	7441	7325
Vaccine	8197	7797	7665	7471	7347
Cumulative No. of Infections					
Placebo		30	50	65	74
Vaccine		12	32	45	51

Tratamiento: Cuando comenzar

- ◆ The Strategies for Management of Antiretroviral Therapy (SMART) Study Group. **Major clinical outcomes in antiretroviral therapy (ART)-naive participants and in those not receiving ART at baseline in the SMART study.** J Infect Dis. 2008;197:1133-1144.
- ◆ Kitahata MM, Gange SJ, Abraham AG, et al; for the NA-ACCORD Investigators. **Effect of early versus deferred antiretroviral therapy for HIV on survival.** N Engl J Med. 2009;360:1815-1826.

Major clinical outcomes in antiretroviral therapy (ART)-naive participants and in those not receiving ART at baseline in the SMART study_J Infect Dis



◆ Definiciones para sub-analisis

- Deferido: esperar a CD4+ < 250 cells/mm³, CD4+ < 15%, o sintomas
- Inmediato: TAR comenzada inmediatamente al ser randomizado

◆ Análisis Primarios

- Enfermedad Oportunista o muerte por cualquier causa (OD/death)
- Enfermedad oportunista fatal o no fatal
- Evento serio no relacionado con SIDA
- OD mas Evento serio

Resultados

- ◆ El grupo inmediato experimento menos eventos que el diferido
 - Riesgo excesivo : 5.4 eventos per 100 personas-anos

Event, n (Rate per 100 Person-Yrs)	Deferred Arm (n = 228)	Immediate Arm (n = 249)	HR (DC/VS)	95% CI	P Value
OD/death	15 (4.8)	5 (1.3)	3.5	1.3-9.6	.02
OD only	11 (3.5)	4 (1.1)	3.3	1.0-10.3	.04
Serious non- AIDS events	12 (3.9)	2 (0.5)	7.0	1.6-31.4	.01
Composite	21 (7.0)	6 (1.6)	4.2	1.7-10.4	.002

Otros resultados

- ◆ Una proporción mas alta de efectos adversos en el grupo deferido
 - Deferido : 25 pacientes
 - Inmediato: 18 pacientes
 - HR (deferido/inmediato): 1.6; 95% CI: 0.9-3.0

- Eventos Oportunistas
 - Herpes zoster
 - Esophageal candidiasis
 - Tuberculosis
 - Mycobacterium avium complex
 - Herpes simplex
 - Death due to OD
 - Kaposi sarcoma
 - Non-Hodgkin's lymphoma
 - Death due to non-Hodgkin's lymphoma
 - Bacterial pneumonia

- Eventos Serios no SIDA
 - Hepatic cirrhosis
 - End-stage renal disease
 - Death due to cardiovascular disease
 - Myocardial infarction
 - Coronary artery disease surgery
 - Silent myocardial infarction
 - Death from digestive system disease
 - Accidental death
 - Death due to renal disease
 - Death due to non-AIDS cancer

Effect of early versus deferred antiretroviral therapy for HIV on survival_N Engl J Med

- ◆ Dos análisis paralelos envolviendo 17,517 pacientes asintomáticos con VIH en EU y Canadá. 1996-2005
- ◆ Se estratifican de acuerdo a cuando comienzan terapia
 - Grupo de 350-500: 8362 pacientes de los cuales 2084 (25%) iniciaron terapia con el CD4 de 351-500
 - Grupo de > 500: 9155 pacientes de los cuales 2220 (24% comenzaron terapia con TARV)

NA-ACCORD

Table 3. Risk of Death Associated with Deferral of Antiretroviral Therapy, According to CD4+ Count at Baseline, with Adjustment for HIV RNA Level, Age, and Sex.*

Variable	351-to-500 CD4+ Count		More-Than-500 CD4+ Count	
	Relative Risk (95% CI)	P Value	Relative Risk (95% CI)	P Value
Without inclusion of HIV RNA data				
Deferral of antiretroviral therapy	1.69 (1.26–2.26)	<0.001	1.94 (1.37–2.79)	<0.001
Female sex	1.21 (0.89–1.64)	0.24	1.85 (1.33–2.59)	<0.001
Older age (per 10-yr increment)	1.68 (1.48–1.91)	<0.001	1.83 (1.62–2.06)	<0.001
Baseline CD4+ count (per 100 cells/mm ³)	1.13 (0.72–1.78)	0.59	0.93 (0.87–0.99)	0.03
With inclusion of HIV RNA data				
Deferral of antiretroviral therapy	1.63 (1.21–2.19)	0.002	1.85 (1.20–2.86)	0.006
Female sex	1.47 (1.02–2.12)	0.04	1.35 (0.85–2.15)	0.20
Older age (per 10-year increment)	1.89 (1.69–2.11)	<0.001	1.81 (1.58–2.07)	<0.001
Baseline CD4+ count (per 100 cells/mm ³)	0.74 (0.55–1.00)	0.06	0.97 (0.89–1.05)	0.45
Baseline HIV RNA level (per log ₁₀ copies/ml)	1.11 (0.96–1.28)	0.15	1.13 (0.96–1.33)	0.14

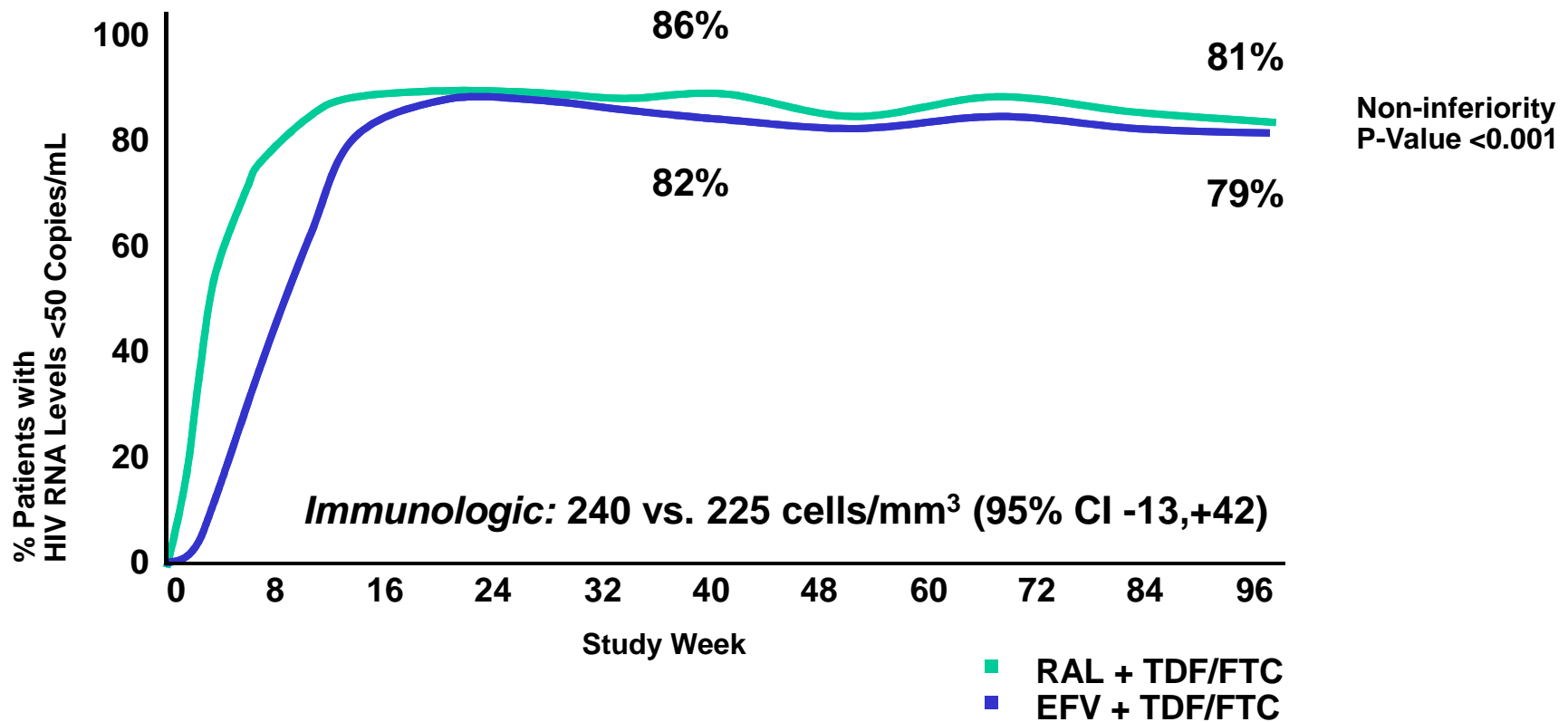
* The CD4+ count was measured in cells per cubic millimeter. Results were calculated with the use of Cox regression analyses with inverse probability-of-censoring weights. HIV denotes human immunodeficiency virus.

Nuevas estrategias de tratamiento

- ◆ Lennox JL, DeJesus E, Lazzarin A, et al. **Safety and efficacy of raltegravir-based versus efavirenz-based combination therapy in treatment-naive patients with HIV-1 infection: a multicentre, double-blind randomised controlled trial.** Lancet. 2009;374:796-806.
- ◆ Mills AM, Nelson M, Jayaweera D, et al. **Once-daily darunavir/ritonavir vs. lopinavir/ritonavir in treatment-naive, HIV-1-infected patients: 96-week analysis.** AIDS. 2009;23:1679-1688
- ◆ Molina JM, Andrade-Villanueva J, Echevarria J, et al. **Once-daily atazanavir/ritonavir versus twice-daily lopinavir/ritonavir, each in combination with tenofovir and emtricitabine, for management of antiretroviral-naive HIV-1-infected patients: 48 week efficacy and safety results of the CASTLE study** Lancet. 2008;372:646-655

Safety and efficacy of raltegravir-based versus efavirenz-based combination therapy in treatment-naive patients with HIV-1 infection: a multicentre, double-blind randomised controlled trial; Lancet

**Patients with HIV RNA <50 c/mL Through 96 Weeks
(Non-Completer = Failure)**



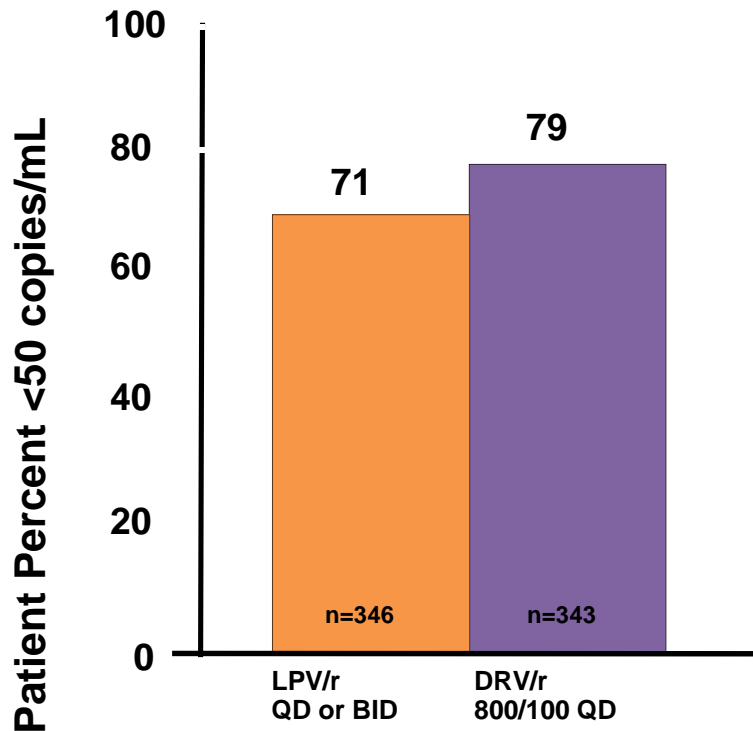
Safety and efficacy of raltegravir-based versus efavirenz-based combination therapy in treatment-naive patients with HIV-1 infection: a multicentre, double-blind randomised controlled trial; Lancet

- ◆ Efectos adversos similares en ambos brazos
- ◆ SNC mas alto en brazo con EFV:
 - pasajeros, leves y ocurrieron en las primeras 48 semanas
 - Pocas discontinuaciones
 - Índice de depresión similar en ambos grupos

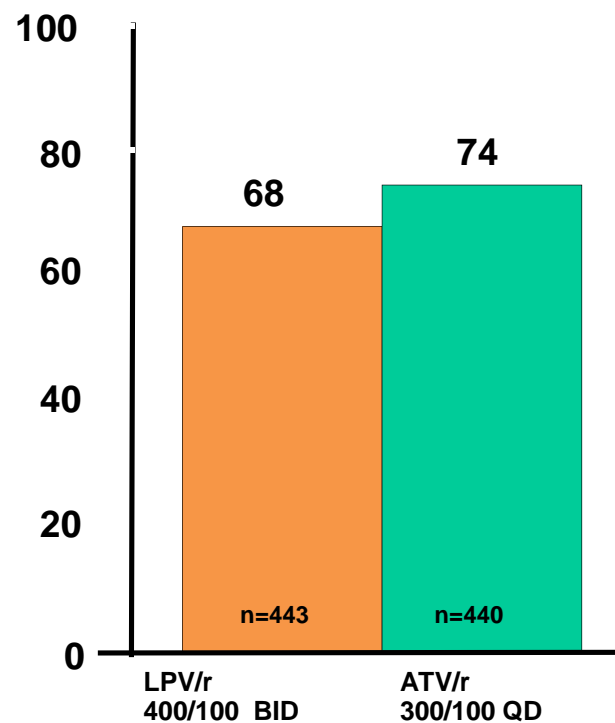
AEs	RAL (%)	EFV (%)	P value
Overall AE	266 (94.7)	275 (97.5)	0.086
Drug Related AE	132 (47)	220 (78)	<0.01
Serious Clinical AE	40 (14)	34 (12)	0.457
Deaths	3 (1)	0	
Malignancies	3 (1)	11 (4)	
CNS	81 (29)	171 (61)	<0.001

DRV/r and ATV/r in ARV-Naïve Patients: Higher Response Rates than LPV/r

ARTEMIS¹
(ITT, TLOVR)*
96 weeks



CASTLE²
(ITT, NC=F)
96 weeks

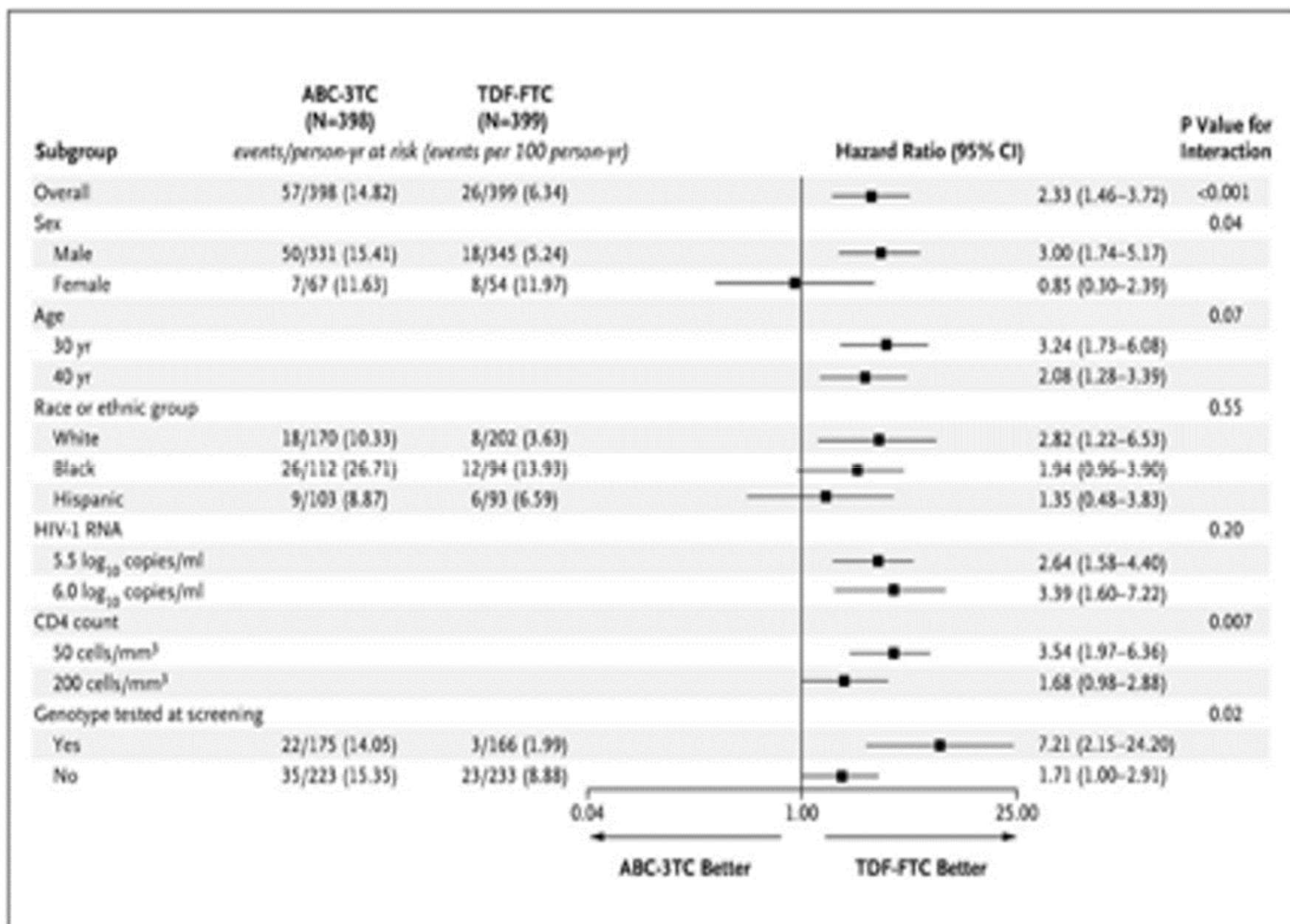


*Estimated difference in response vs LPV/r for superiority: ITT = 8.3% (95% CI 1.8;14.7, P=0.012)

Adapted from: 1. Mills A, et al. AIDS May 29, 2009 [Epub ahead of print]; 2. Molina J-M, et al. 48th ICAAC/46th IDSA , Washington, DC, 2008. Abst. H-1250d

Tratamiento

- ◆ **Abacavir–Lamivudine versus Tenofovir–Emtricitabine for Initial HIV-1 Therapy**
Sax P. E., et al, The AIDS Clinical Trials Group
Study A5202 Team
N Engl J Med 2009; 361:2230-2240, Dec 3, 2009;



Otros estudios que comparan ABC/3TC y TDF/FTC

	A5202	HEAT	ASSERT
Sponsor	NIAID	GSK	GSK
Sample Size	1858 (797 HIV RNA > 100,000 c/mL)	688	385
Blinding	Double-Blind	Double-Blind	None
3rd Drug	EFV or ATV/r	LPV/r QD	EFV
Primary Endpoint	Time to Virologic Failure*	<50 c/mL at 48 wks	Change in GFR at wk 48 by MDRD
HLA-B*5701 Testing	Permitted, not required	No	Required, only negative pts enrolled
Key Results	For those with HIV RNA >100,000 c/mL, study stopped early due to higher rate of virologic failure with ABC/3TC	ABC/3TC non-inferior	No difference in eGFR; proportion <50 c/mL favored TDF/FTC (71% vs. 59%; difference 11.6%, 95% CI 2.2-21.1); Total hip and lumbar spine BMD decline more with TDF/FTC

*Confirmed >1000 c/mL between wks 16-24, >200 c/mL wk 24 on)

Publicaciones: Tratamiento de VIH

- ◆ US Department of Health and Human Services. **Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents.** December 1, 2009; 1-161.
- ◆ World Health Organization. **Rapid Advice. Antiretroviral therapy for HIV Infection in Adults and Adolescents. November 2009.** Available at:
http://www.who.int/hiv/pub/arv/rapid_advice_art.pdf Accessed November 30, 2009.

New DHHS Guidelines



DHHS: Guidelines for Use of ARV in HIV1 Infected Adults and Adolescents

December 2009

DHHS HIV Guidelines December 2009: Cuando comenzar el tratamiento

Clinical Condition and/or CD4 Count	Recommendations
<ul style="list-style-type: none">◆ History of AIDS-defining illness◆ CD4 \leq350◆ Pregnant women◆ HIVAN◆ HBV co-infection when HBV treatment is indicated◆ CD4 350-500	<ul style="list-style-type: none">◆ Start ART◆ Start ART 350-500<ul style="list-style-type: none">– 55% Panel strong– 45% Panel moderate
<ul style="list-style-type: none">◆ CD4 >500	<ul style="list-style-type: none">◆ 50% of Panel in favor◆ 50% of Panel optional

Regímenes preferidos para pacientes -Naïve Patients: DHHS 2009

<p><u>NNRTI based Regimen</u> EFV/TDF/FTC</p> <p><u>PI based Regimen</u> ATV/r + TDF/FTC DRV/r (once daily) + TDF/FTC</p> <p><u>INSTI based Regimen</u> RAL + TDF/FTC</p> <p><u>Preferred Regimen for Pregnant Women</u> LPV/r (twice daily) +ZDV/3TC</p>	<p>Comments:</p> <ul style="list-style-type: none">◆ EFV should not be taken during the first trimester of pregnancy or if the women is trying to conceive◆ ATV/r should not be used in patient who require >20mg of Omeprazole per day
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•LPV/r-based regimens are now listed as “Alternative” instead of “Preferred” regimens, except in pregnant women

•Monotherapy with DRV/r has been added to the list of regimens not recommended

New WHO Guidelines



WHO: ARV Therapy for HIV Infection in Adults and Adolescents

November 2009

WHO: Cuando comenzar Terapia

- ◆ Comenzar TARV en todos los pacientes con **CD4 count ≤ 350 cells/mm³**

2006 Guidelines

Comenzar TARV en todos los pacientes con enfermedad clínica avanzado y/o un CD4 de **200 cells/mm³ or menos**



2009 Recomendaciones

Promover tratamiento a todos los pacientes cuando CD4 baja a **350 cells/mm³**, irrespectivo de síntomas

WHO

- ◆ **Comenzar uno de los siguientes agentes en individuos que no han sido tratados y son elegibles para tratamiento:**
 - **TDF + 3TC or FTC + EFV**

 - **TDF + 3TC or FTC + NVP**

 - **AZT + 3TC + EFV**

 - **AZT + 3TC + NVP**

- ◆ **Disminuir el uso de Stavudina (d4T) como un agente de preferencia**

WHO: Rol de los estudios diagnosticos/laboratorio

- ◆ Expandir el monitoreo de laboratorio , incluyendo ambos CD4 y carga Viral para mejorar la calidad del tratamiento y cuidado del VIH.
- ◆ La introducción de los estudios de la carga viral puede reducir el cambio prematuro a regímenes costosos.
- ◆ Acceso a TAR no debe ser negado si no se tienen estos exámenes disponibles.

Resumen

- ◆ Literatura reciente nos ha informado sobre:
 - Nuevas estimaciones epidemiológicas
 - Nuevas estrategias de tratamiento
 - Consecuencia de no tratar
 - Posibles direcciones en cuanto a la prevención

- ◆ Muchas Gracias!!