



- **Actualizacion :**
- **Estrategias en el Tratamiento de VIH/SIDA,**
- **« Estamos Envejeciendo »**

VIH: Epidemiología



33.4 Millones de Personas Viven con VIH

40% Saben su Status

5 millones en Terapia

10 millones esperan por Terapias

2 Millones de Muertes este año

VIH: Epidemiologia



33.4 MILLION PEOPLE LIVING WITH HIV

N Africa, Middle East,
Caribbean, Oceania 700,000

E Europe
1.5 million

Latin America
2 million

North America, W & C Europe
2.3 million

US 1.2 million

Asia 4.7 million

India
2.4 million

SUB-SAHARAN AFRICA: 22.4 MILLION

Tanzania
1.4 million

Zimbabwe
1.3 million (15.3%)

Zambia
1.3 million (15.2%)

Mozambique
2.4 million

Nigeria
2.6 million

South Africa
5.7 million
(18.1%)



Avances en el Manejo del HIV

1985 FDA approves first HIV antibody test (ELISA)¹

1987 FDA approves first HIV treatment (NRTI)²

1995 FDA approves first PI²

1996 FDA approves first NNRTI²

2001 AIDS-related deaths/year in US dropped approximately 70% since 1995³

2003 FDA approves first fusion inhibitor²

2007 FDA approves first entry inhibitor and first integrase inhibitor²

HAART becomes standard of care¹

1981 1985 1990 1995 2000 2005 2007

Acquired Immune Deficiency Syndrome (AIDS) defined¹

Kaposi's sarcoma in US termed Gay-related Immune Deficiency (GRID)¹

HIV isolated by Dr. L. Montagnier of France's Pasteur Institute¹

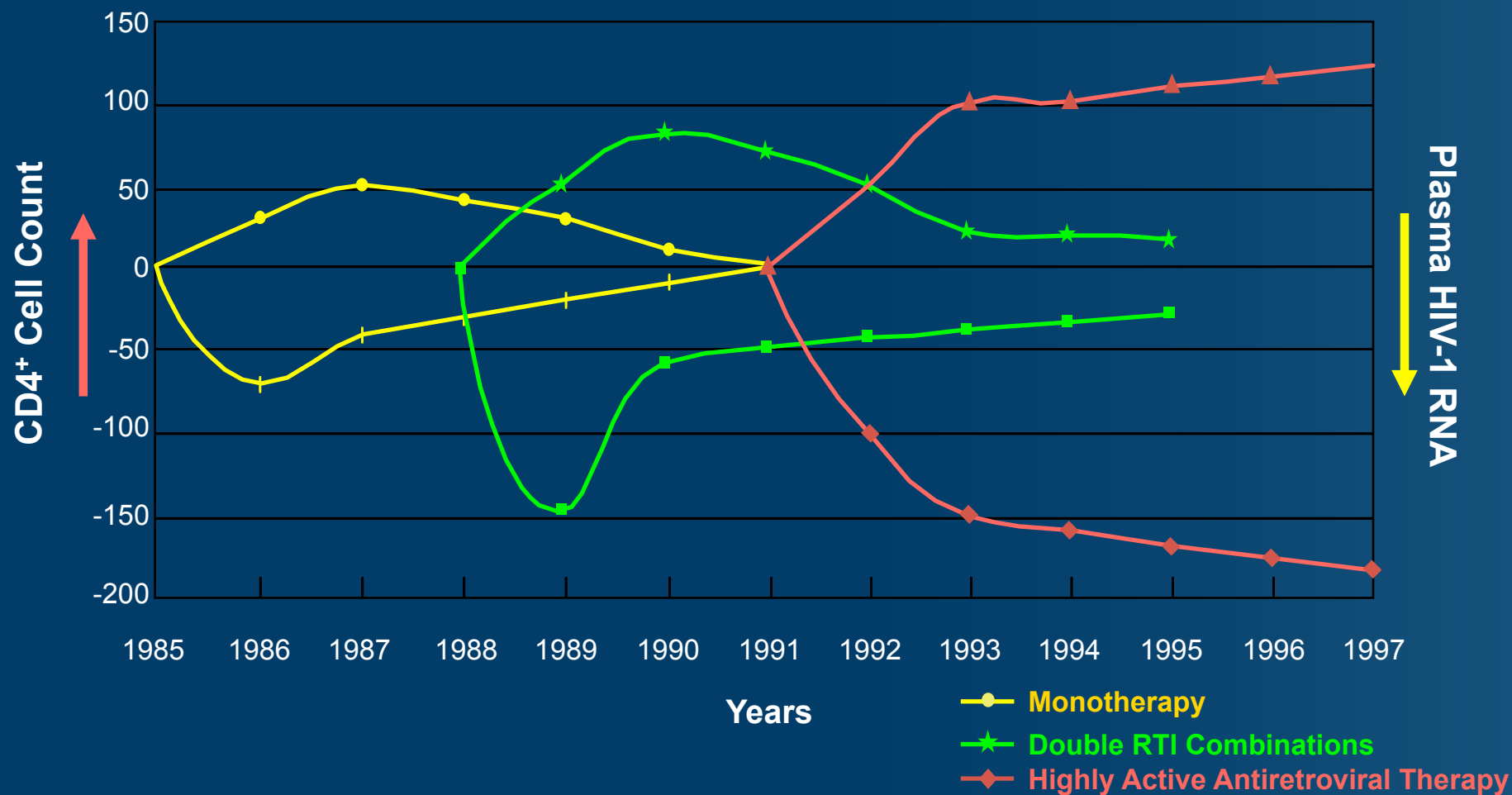
Five million new cases of HIV infection reported worldwide⁴

FDA approves rapid (20 min.) HIV detection test: OraQuick^{®5}

CDC recommends layperson antiretroviral post-exposure prophylaxis⁶

Linea del Tiempo VIH

Impacto (tt) :CD4 / VL



Ciclo de Vida Viral



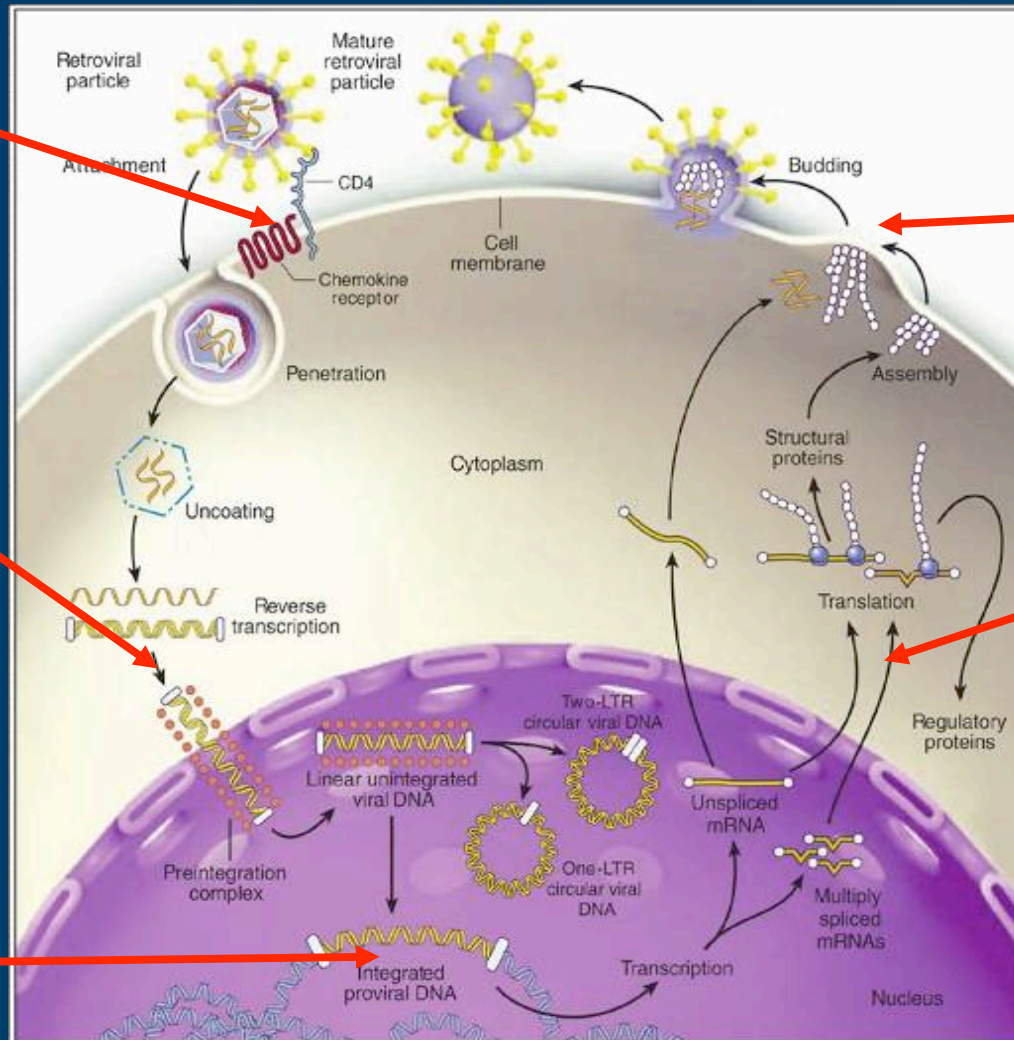
Entry inhibitors

ENF MRV
VCV TNX355
AMD11070

Reverse transcriptase inhibitors:

ZDV NVP
ddI DLV
TDF EFV
d4T
ABC
3TC
FTC

Integrase inhibitors:
Raltegravir
others



Maturation inhibitor
bevrimat

Protease inhibitors
SQV IDV
RTV NFV
FPV LPV
ATV TPV
DRV

Antiretrovirales 2008



NRTIs

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

NNRTIs

- Delavirdine
- Efavirenz
- Nevirapine
- Etravirine

Protease Inhibitors

- Atazanavir
- Darunavir
- Fos-Amprenavir
- Indinavir
- Lopinavir
- Nelfinavir
- Ritonavir
- Saquinavir
- Tipranavir

Entry Inhibitor

- Enfuvirtide

CCR5 Inhibitors

- Maraviroc

Integrase Inhibitor

- Raltegravir

(Actualizadas) Guías de VIH/2009



- **Noviembre**
 - World Health Organization (WHO)
 - Directed at developing countries
 - <http://www.who.int/hiv/pub/arv/advice/en/index.html>
 - European AIDS Clinical Society (EACS)
 - <http://www.europeanaidscinicalsociety.org/guidelines.asp>
- **Diciembre**
 - United States Department of Health and Human Services (DHHS)
 - <http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf>

Guías / VIH 2009: Recomendaciones comunes



- Importante identificación temprana de personas VIH+
- Énfasis en iniciación más temprana en Terapia ARV

Clinical Category	CD4 Cell Count (cells/mm ³)	DHHS	EACS	WHO
AIDS-defining illness or severe symptoms	Any value	Treat	Treat	Treat
Asymptomatic	≤350	Treat	Treat	Treat

DHHS. Available at: <http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf>.

Revision December 1, 2009.

WHO. Available at: <http://www.who.int/hiv/pub/arv/advice/en/index.html>. Revision November 2009.

EACS. Available at: <http://www.europeanaidscinicalsociety.org/guidelines.asp>.

Revision November 2009.

VIH/ Guías 2009: Diversidad de opiniones –Cuando comenzar



Clinical Category	CD4 Cell Count (cells/mm ³)	DHHS	EACS	WHO
Asymptomatic	350-500	Treat	Treat* Consider Treatment [†]	--
	>500	Treat/ optional	Consider treatment [†]	--
Pregnant	Any value	Treat	Defer [‡]	--

*Treatment recommended if hepatitis C coinfection, hepatitis B coinfection requiring therapy, HIV-associated nephropathy or specific organ damage.

[†]Consider treatment if high cardiovascular risk, age >50 years, malignancy, or rapid CD4 decline.

[‡]In general, treat if CD4 <350 cells/mm³. Refer to each guideline for specifics.

DHHS. Available at: <http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf>.

Revision December 1, 2009.

WHO. Available at: <http://www.who.int/hiv/pub/arv/advice/en/index.html>. Revision November 2009.

EACS. Available at: <http://www.europeanaidscinicalsociety.org/guidelines.asp>.

Revision November 2009.

DHHS/ Guías: Cuando comenzar Terapia ARV



Estudios Notables

**History of AIDS-defining illness or
CD4 <350 cells/mm³**

**CIPRA HT-001
SMART**

CD4 between 350 and 500 cells/mm³
Strongly recommended (55% of DHHS Panel)
Moderately recommended (45% of DHHS Panel)

**NA-ACCORD
ART Cohort
Collaboration**

CD4 >500 cells/mm³
Recommended (50% of DHHS Panel)
Viewed as optional (50% of DHHS Panel)

**NA-ACCORD
ART Cohort
Collaboration**

Regimenes Preferidos: Tratamiento en Pcts Nuevos



- NNRTI
 - Efavirenz*/emtricitabine†/tenofovir DF
- Boosted PI
 - Atazanavir‡ + ritonavir + emtricitabine†/tenofovir DF
 - Darunavir + ritonavir (qd) + emtricitabine†/tenofovir DF
- INSTI
 - Raltegravir + emtricitabine†/tenofovir DF
- Pregnant women
 - Lopinavir/r bid + zidovudine/lamivudine†

*Efavirenz should not be used during the first trimester of pregnancy or in women trying to conceive or not using effective and consistent contraception.

†Lamivudine may substitute for emtricitabine or visa versa.

‡Atazanavir + RTV should not be used in patients who require >20 mg omeprazole equivalent/day.

DHHS. Available at: <http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf>.

Revision December 1, 2009.

GUIAS IAS-USA 2010: Cuando Comenzar Terapia ARV



Medidas	Recomendacion
Condiciones Especificas	
Enfermedad VIH Sintomatica	ART recomendado independiente de los CD4
Embarazo	
High HIV-1 RNA >100,000 copies/mL	
Rapido descenso de CD4(>100 cells/mm ³ per year)	
hepatitis B or C* virus co-infection	
ALTO RIESGO Enf Cardiovascular*	
VIH-asociada nephropatia	
VIH-Infeccion Primaria Sintomatica*	
Rieego aumentado HIV transmision *	
CD4 cell count ≤500 cells/mm ³	ART recomendado
CD4 cell count >500 cells/mm ³	ART debe ser considerado [§]

*Differs from 2009 DHHS guidelines

§Unless patient is an elite controller (HIV-1 RNA <50 copies/mL) or has stable CD4 cell count and low-level viremia in the absence of ART

Thompson MA, et al. JAMA 2010;304(3):321-333; US Department of Health and Human Services Guidelines; Revised December 1, 2009.
Available at: <http://aidsinfo.nih.gov/contentfiles/AdultandAdolescentGL.pdf>.

IAS-USA 2010: Guías para Iniciar un Regimen ARV



	Dual NRTI		Key 3 rd Drug
Recommended	TDF/FTC	+	EFV ATV/r DRV/r RAL
Alternative	ABC/3TC		LPV/r FPV/r MVC

Comparison to 2009 DHHS Guidelines:

- “Recommended” therapies are the same as “Preferred” regimens
- In addition to “Alternative” therapies listed, 2009 DHHS Guidelines “Alternative” and “Acceptable” regimens include ZDV/3TC, ddl + 3TC, NVP, unboosted ATV, and SQV/r

Factores a Considerar en el Tratamiento para Pcts con VIH



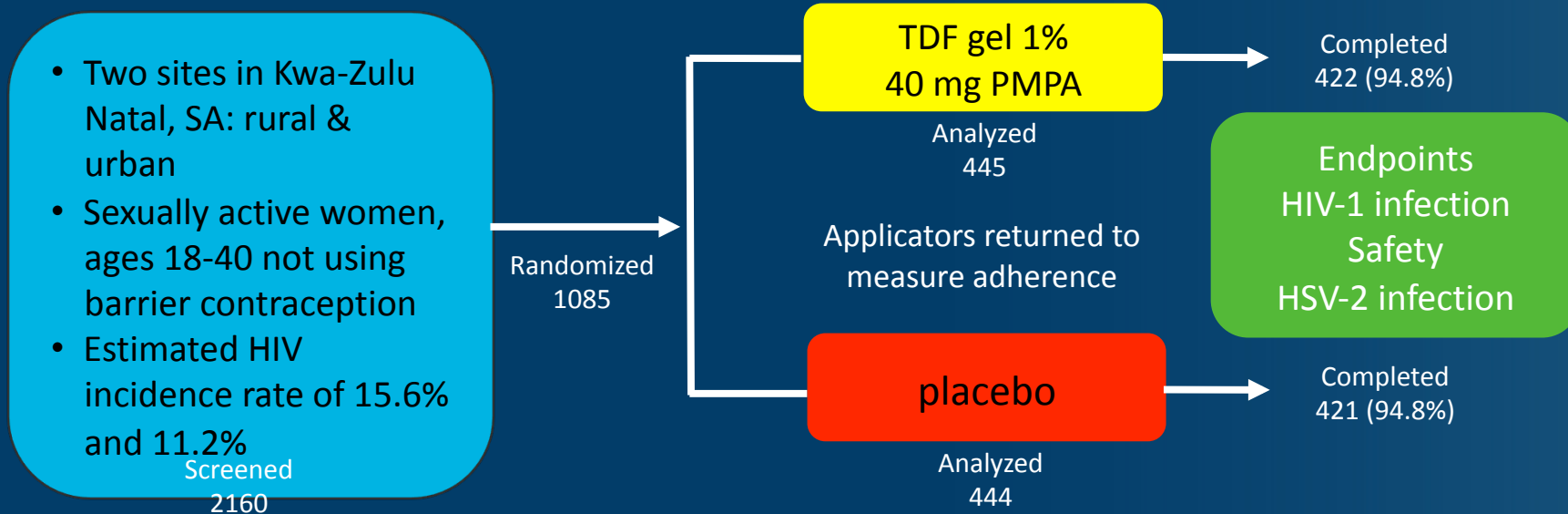
- Suceptibilidad de la Droga
- Cantidad de Pastillas, frecuencia de dosis,
- Tolerabilidad Anticipada ,
- Presencia de otras Enfermedades,
- Perfil de Efectos Adversos,
- El Potencial de crear Mutaciones Resistentes



Nuevas Estrategias, Metodos,
Agentes Terapeuticos

INVESTIGACION

Estudio:CAPRISA 004:



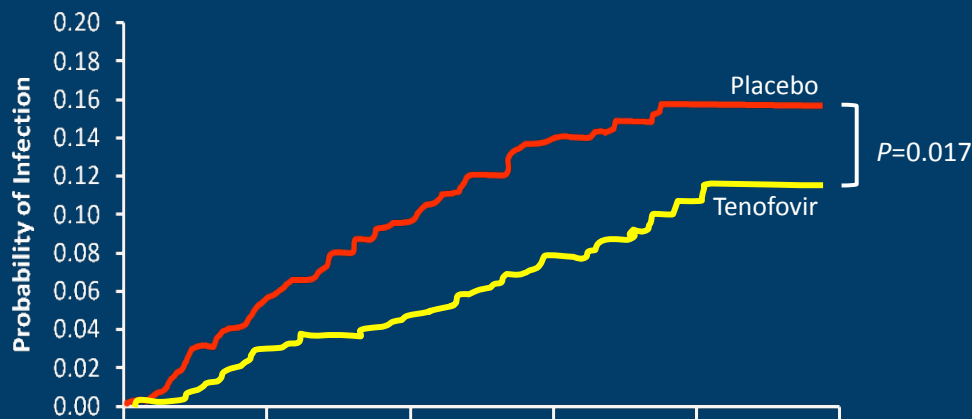
Administracion de TDF gel:

- Insert 1 dose within 12 hours Before sex
- Insert 1 dose ASAP, within 12 hours After sex
- No more than 2 doses within 24 hours

CAPRISA 004: Resultados

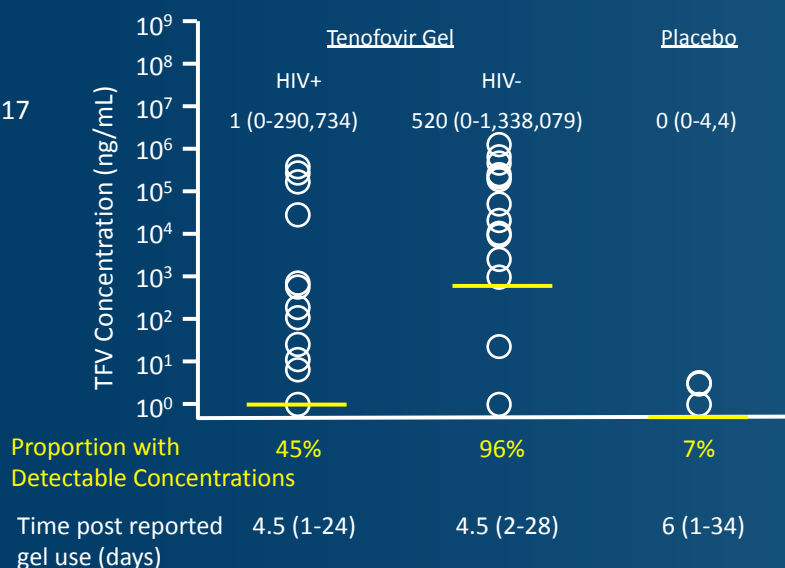


HIV Infections Over Time



Months of Follow-up	6	12	18	24	30
Effectiveness (P-value)	47% (0.069)	50% (0.007)	43% (0.004)	40% (0.013)	39% (0.017)

CVF Concentrations were Lower, and Detected Less Frequently in HIV+ Women



- Among high adherers, >80%, the rate of protection was 54% (11 vs. 25 infections)
- HSV infection rate: 29/202 vs. 48/224 (IRR 0.49 $P=0.003$)

- Safety
 - No TDF resistance
 - No evidence for renal or bone toxicity
 - Increased rate of mild diarrhea in TDF group (17% vs. 11%)
 - No adverse outcomes with pregnancies

(Test and Treat): Modelo de Costo



- Modelo de costo- efectividad para Pruebas expandidas y tratamiento ARV en algunos escenarios en Africa del Sur¹

40 Year Projections

	Current	<350	<500	Universal
Person yrs ART (millions)	79	109	131	134
New HIV infections (millions)	8.7	7.3	5.7	4.0
Deaths (millions)	12.5	10.6	8.7	7.1
HIV costs (billions)	75.3	71.5	66.5	61.5

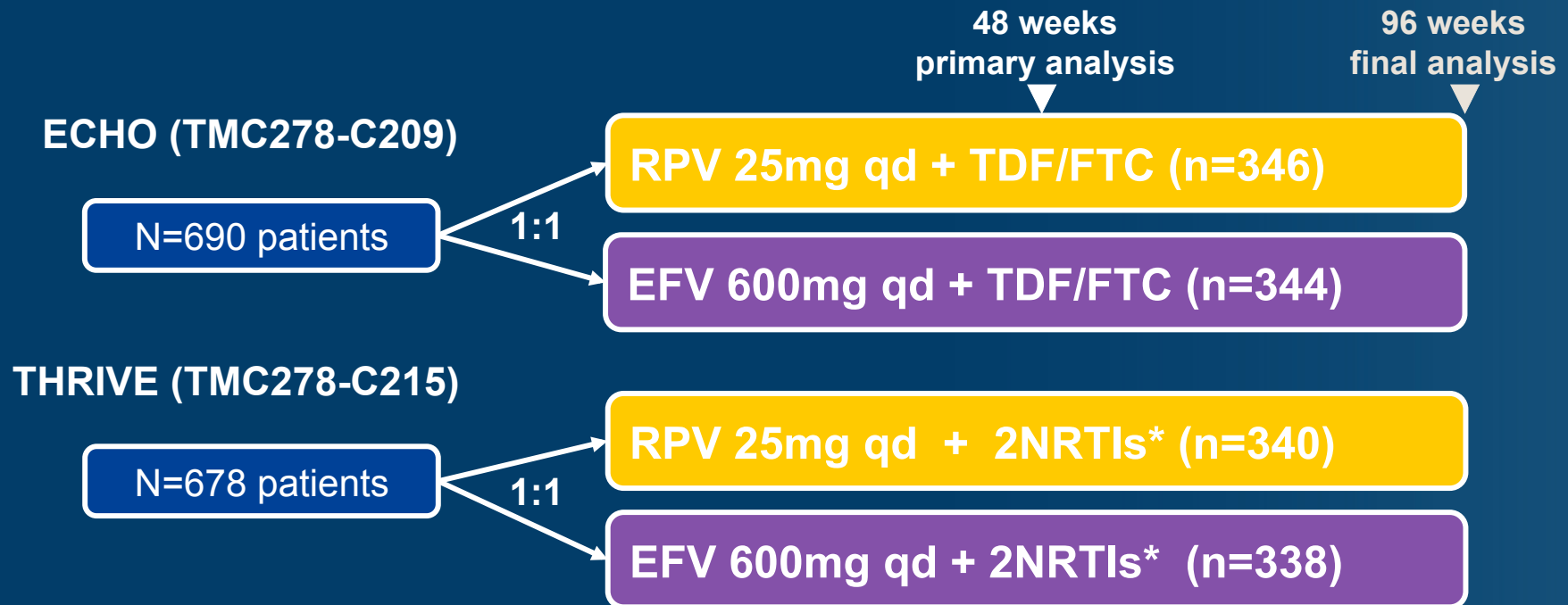
Tratamiento como PrevencionT: El moviminto de hacer pruebas y Tratar²

- NIH funded, Botswana Cohort Pilot (*Essex*)
- HPTN 065 in US: NYC and Washington, DC (*El-Sadr, Mayer*)
- Population ART in Tanzania (*Fiddler, Hayes, Watson-Jones*)
- HPTN concept in development for Africa (*Mastro, Hodder*)
- Kenya (*Little*)
- ANRS (*Hirschel and Dabis*)



Estrategias de Tratamiento ARV en Pacientes “treatment-Naïve”

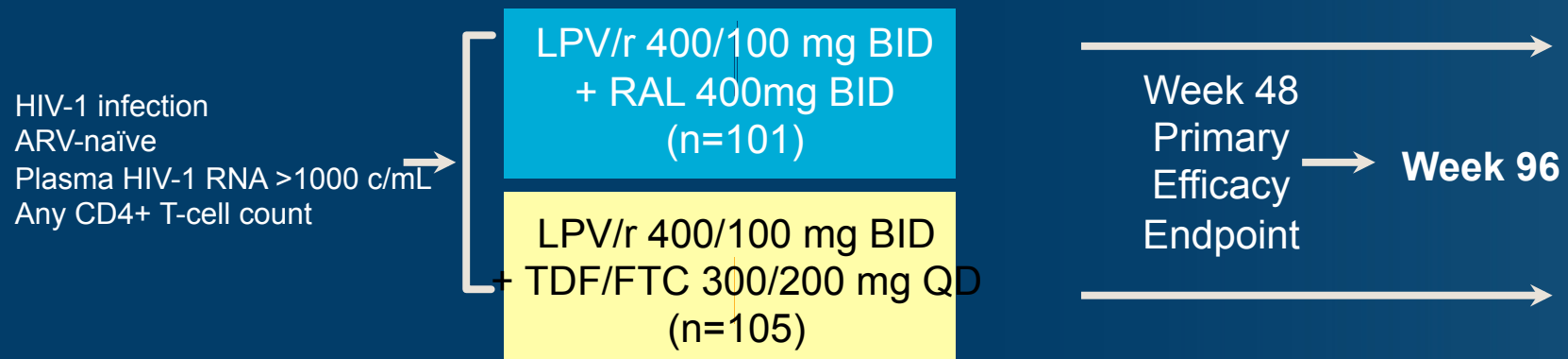
ECHO and THRIVE: Rilpivirine (TMC278) vs. EFV



- Inclusion criteria: viral load (VL) $\geq 5K$; no NNRTI RAMs; sensitivity to the NRTIs
- Primary objective: demonstrate non-inferiority (12% margin) vs. EFV in confirmed virologic response (VL < 50 copies/mL, ITT-TLOVR) at Week 48
- Stratification factors by screening VL (both) and NRTI background (THRIVE only)

* Investigator's choice: TDF/FTC; AZT/3TC; ABC/3TC

PROGRESS: Lopinavir/r with Raltegravir or TDF/FTC



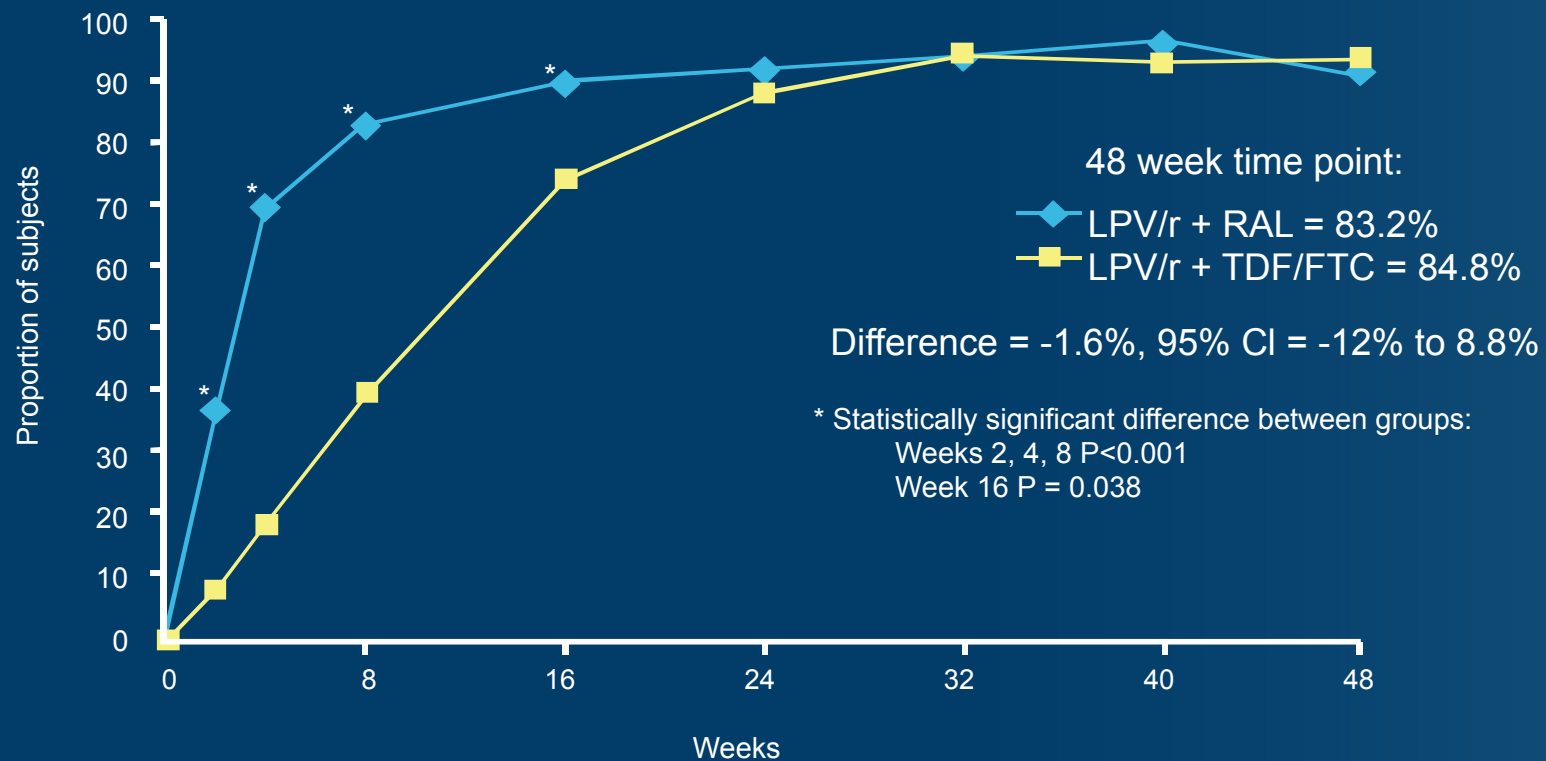
Baseline characteristics

Variable	LPV/r +RAL (n=101)	LPV/ + TDF/FTC (n=105)	Total (N=206)
Males, n (%)	88 (87.1)	86 (81.9)	174 (84.5)
White, n (%)	74 (73.3)	81 (77.1)	155 (75.2)
Black, n (%)	22 (21.8)	22 (21.0)	44 (21.4)
Other, n (%)	5 (4.9)	2 (1.9)	7 (3.4)
Mean age ± SD, years	39.8 ± 9.9	39.4 ± 11.2	39.6 ± 10.6
Mean BL HIV-1 RNA, log ₁₀ copies/mL (range) [†]	4.24 (2.0 - 6.0)	4.25 (2.7 - 6.0)	4.25 (2.0 - 6.0)
Mean BL CD4, cells/μL (range)	289.3 (5 - 668)	297.6 (5 - 743)	293.5 (5 - 743)

PROGRESS: Resultados a la semana 48



HV RNA <40 copies/mL (ITT-TOLVR)

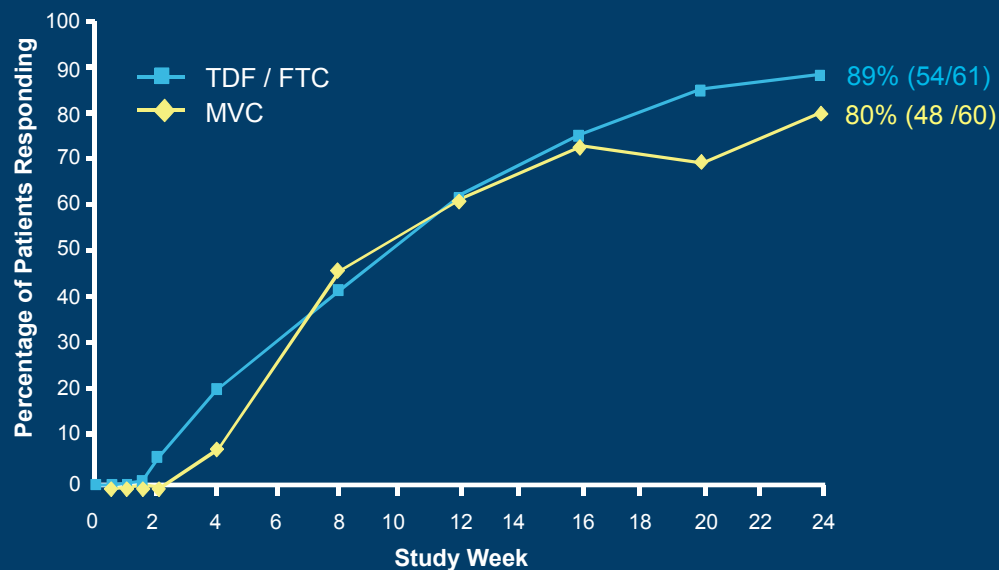


- Adverse event rate similar
- Additional analyses planned: Adherence, DEXA scans (fat/bone), anthropometric measurements, patient reported outcomes

ATV/r + MVC vs. ATV/r + TDF/FTC: Resultados a la semana 24



HIV-1 RNA < 50 copies / mL at Week 24



N = 60
N = 61

56
58

	MVC + ATV/r n=60	TDF/FTC + ATV/r n=61
Any AEs, n (%)	56 (93.3)	57 (93.4)
Serious AEs, n (%)	5 (8.3)*	10 (16.4)**
Grade 3 or 4 AEs, n (%)	20 (33.3)	13 (21.3)
Grade 3 or 4 AEs related to hyperbilirubinemia, n (%)	16 (26)	8 (13)
Grade 3 or 4 laboratory hyperbilirubinemia, n (%)	35 (59.3)	30 (49.2)
Discontinued due to AE, n (%)	2 (3.3)*	0 (0)

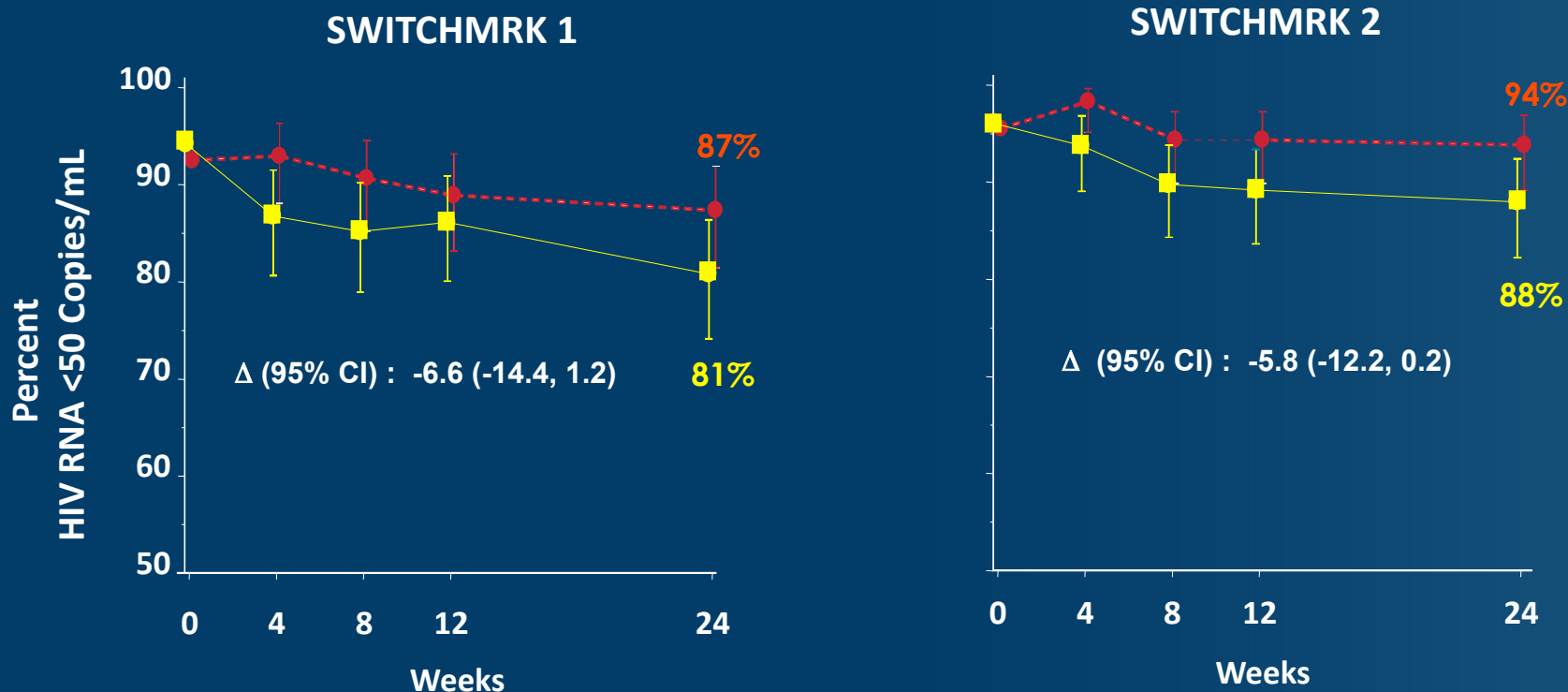
5 MVC, 1 TDF/FTC switched to darunavir per protocol for jaundice and/or scleral icterus
No resistance seen in either arm, and no change in phenotypic tropism result



“ Switch ”

SIMPLIFICACION DE REGIMEN

SWITCHMRK 1 and 2: Virologic Outcomes (NC=F)



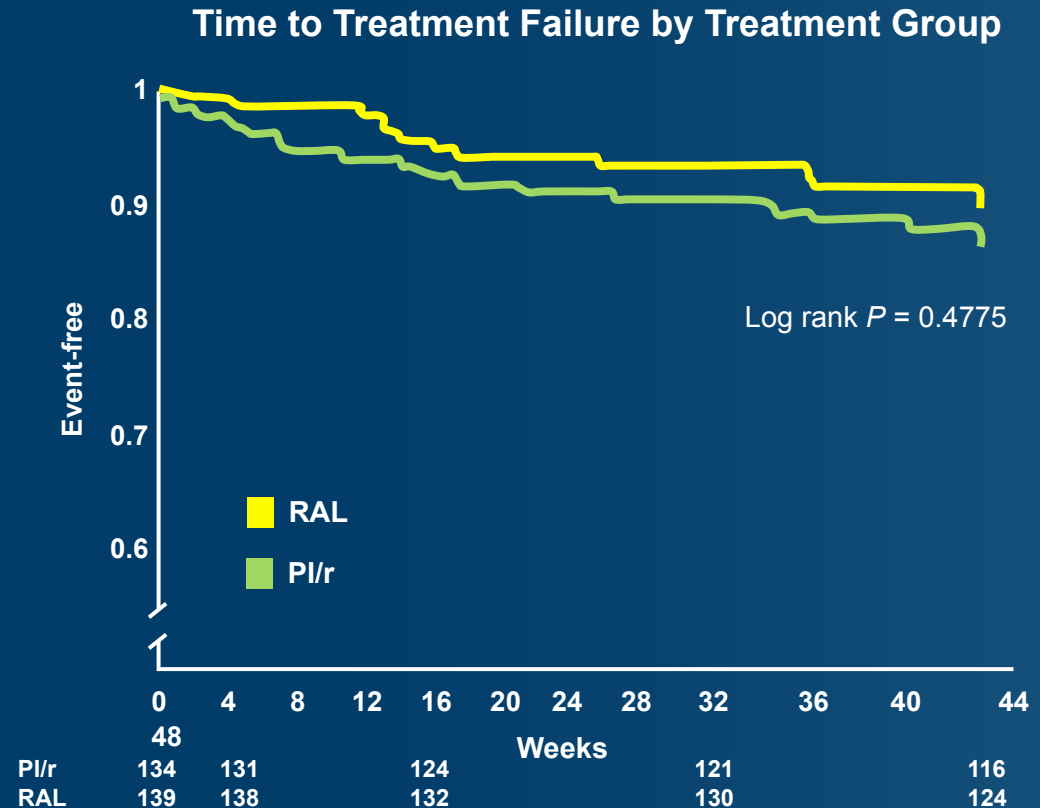
Number of Contributing Patients

■ RAL + ARTs	174	166	169	173	172	176	176	176	176	175
● LPV/r + ARTs	174	171	171	171	174	178	178	177	177	178

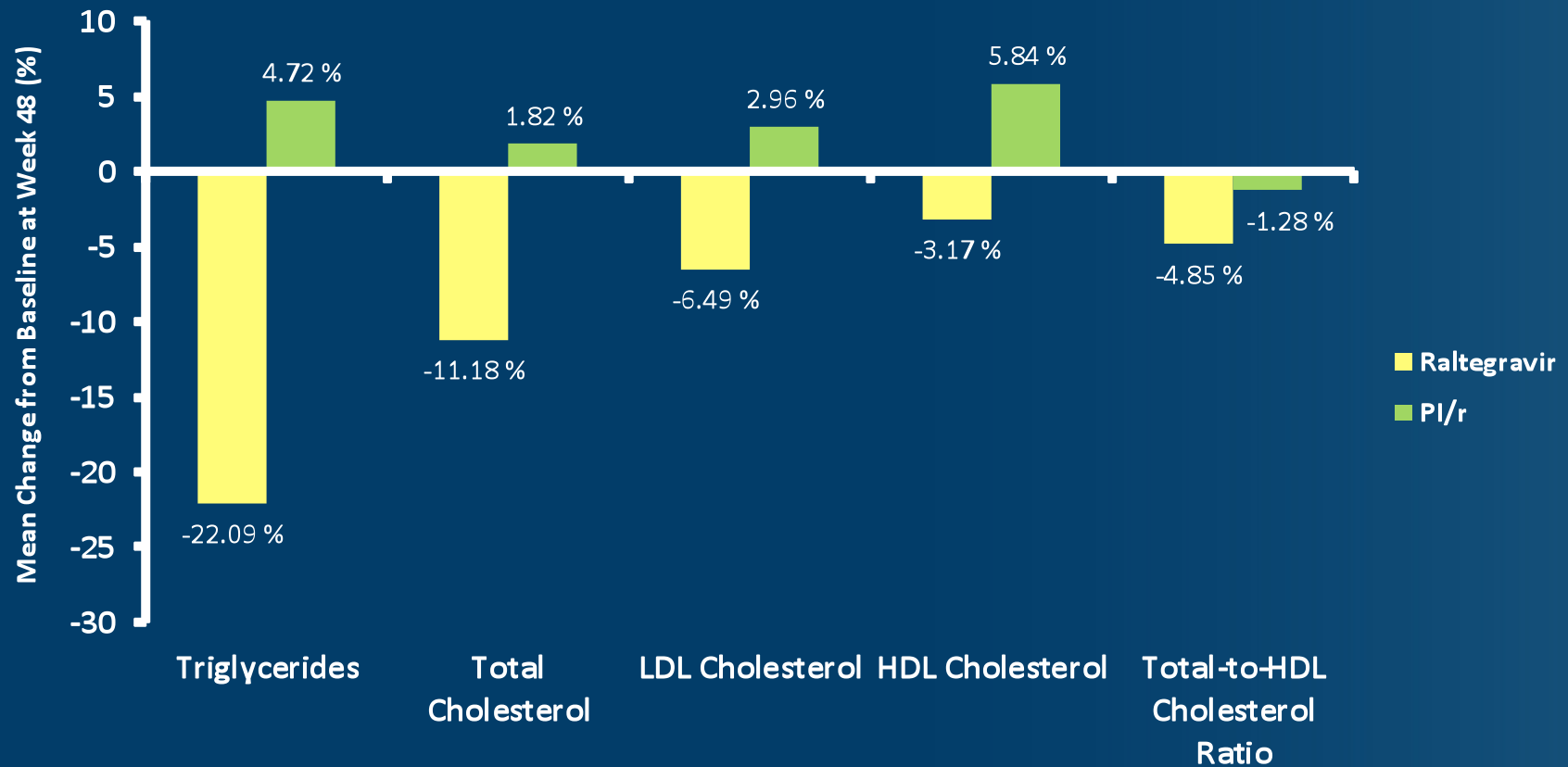
SPIRAL: PI/r to RAL en Pacientes con Supresion Viral



- Pts on stable PI/r ART
 - VL <50 copies > 6 mos
- Randomized (1:1)
 - Continue PI/r
 - Switch RAL
- Primary endpoint
 - % <50 at 48 wks
- Virologic failures
 - 4 RAL arm
 - 6 in PI/r
- Well tolerated w/ few D/C for AE in both arms



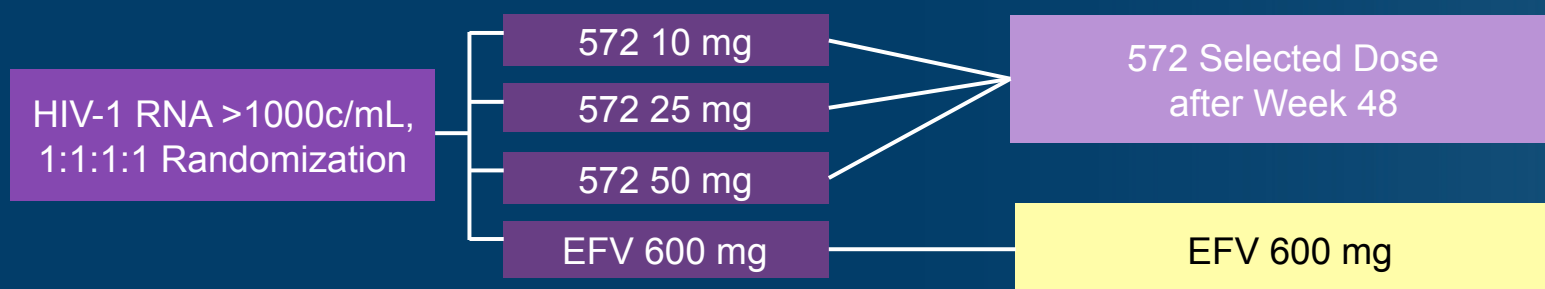
Spiral: Cambio(%) en Lipidos a 48 Semanas



SPRING: GSK 572 vs. EFV (Paciente-Nuevos)



- Phase IIb dose-ranging, partially-blinded trial
- N=205 therapy-naïve patients
- Primary endpoint: % <50 copies/mL at 16 weeks (TLOVR)



Age (Median and range in years)	37 (20 – 79)
Male gender	177 (86%)
Race	
White	164 (80%)
Baseline HIV-1 RNA	
Mean (log ₁₀ copies/mL)	4.46
>100000 copies/mL	44 (21%)
Mean Baseline CD4+ (cells/mm ³)	324.3
Investigator-selected NRTIs	
TDF/FTC	138 (67%)
ABC/3TC	67 (33%)

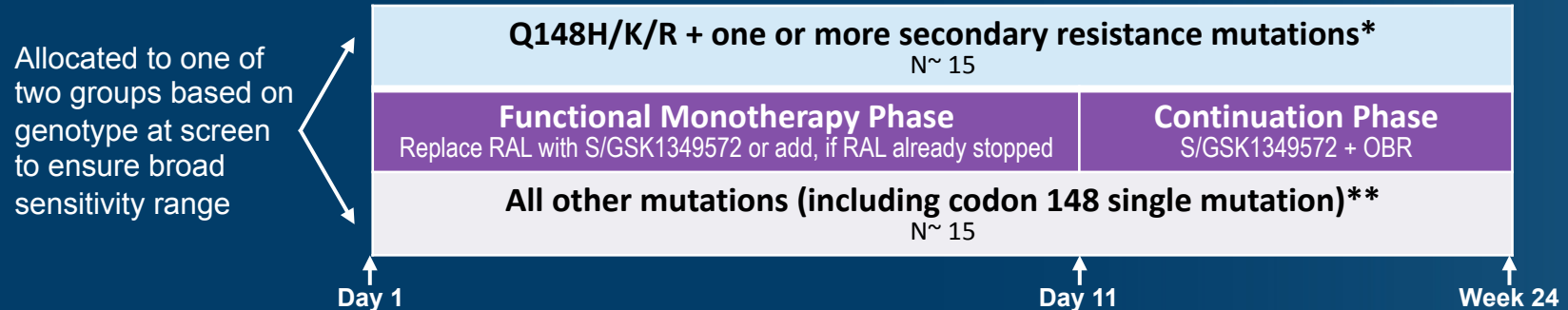
VIKING: GSK 572 Pacientes Experimentados



- Virologic failure may occur with raltegravir use
 - 23% in BenchMRK 1 and 2
- 3 RAL resistant pathways identified
 - Y143, N155, Q148
- GSK 572 *in vitro* appears active against some pathways
 - Minimal cross resistance from N155 and Y143

VIKING Study Design Cohort I

- Current or historic RAL-failures with evidence of RAL-resistance
- At least 3 ART-class resistant (includes INI)
- All subjects receive S/GSK1349572 50mg QD



*Q148H/K/R plus changes in L74 and/or E138 and/or G140

**N155H and Y143H pathways or Q148H/K/R single mutants

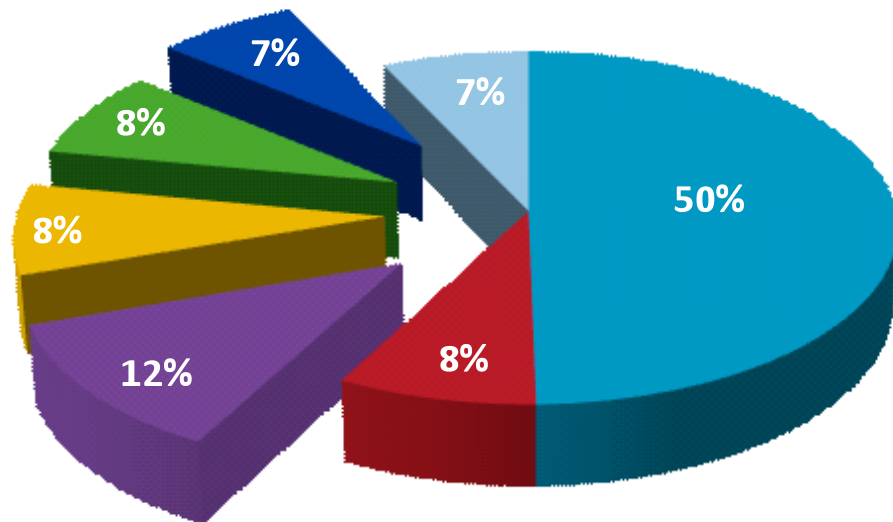


NUEVOS ISSUES

Mitad de la Muertes en Pcts. con VIH NO estan asociadas a SIDA



Cause of Death in HIV+ Individuals Initiating ART
(Europe and North America, 1996-2006, n=1597*)



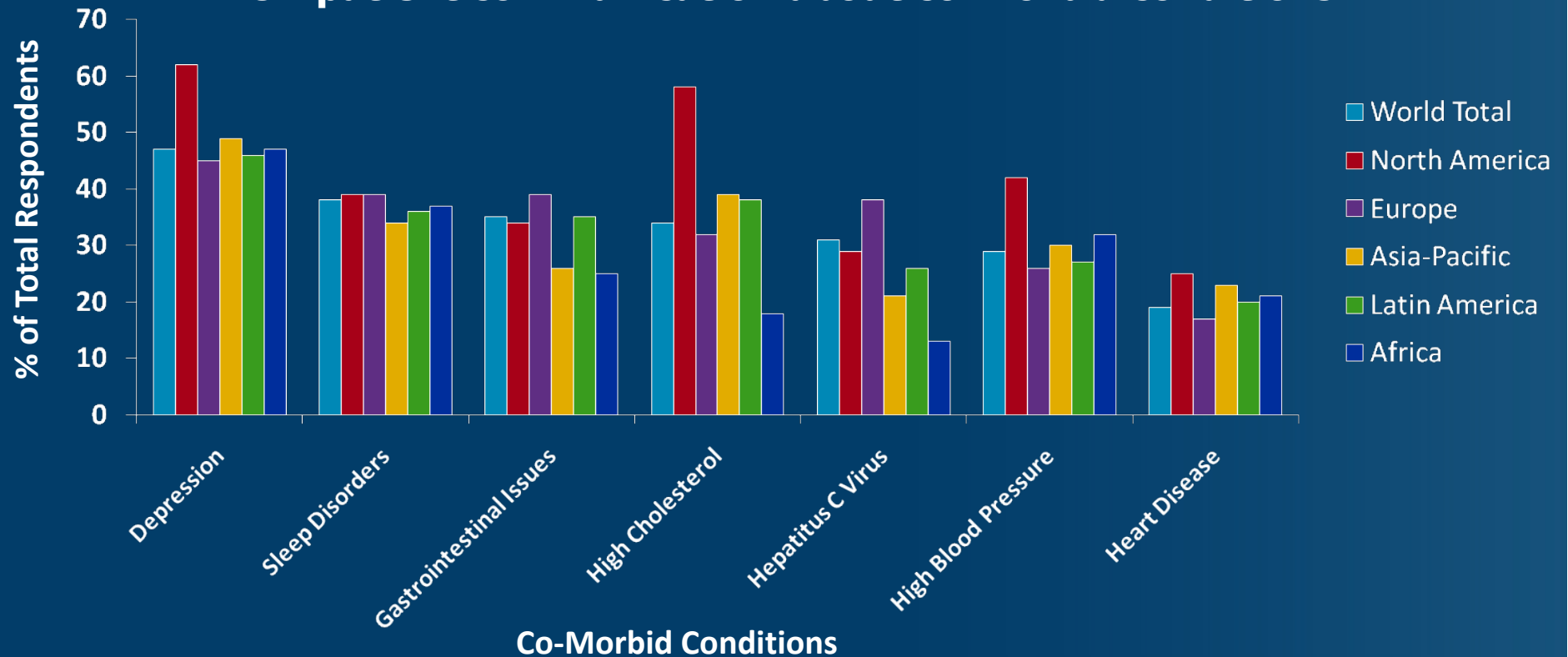
- AIDS-related
- Violence or Drug-related
- Non-AIDS Malignancies
- Non-AIDS Infections
- Cardiovascular Disease
- Liver Disease
- Other

*N=39

ATLIS: Encuesta Global de 2035 Pacientes VIH +

- ATLIS: Multi-country, comparative, treatment awareness survey of 2,035 people living with HIV/AIDS (PLWHA)
- Examines global attitudes and perceptions of HIV

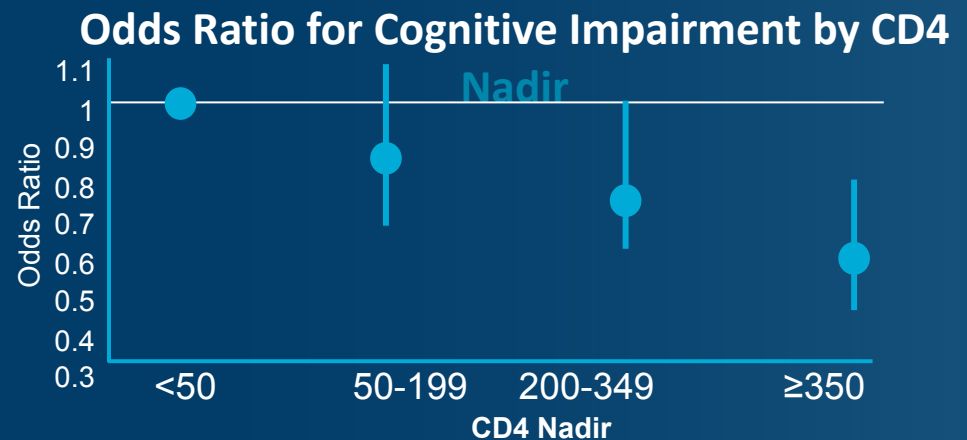
HCP-patient communication about co-morbid conditions



Desordenes Neurocognitivos: Asociados con el conteaje de CD4 Nadir



- Multicenter cohort study of 1526 HIV+ patients
- Complex testing consistent with defined criteria used to determine HAND
 - 603 had HAND (without a substantial confounder); 726 not impaired
 - Most with HAND (n=428) were asymptomatic and only a few (n=27) had frank dementia
- Multivariate analysis: Higher CD4 nadir associated with lower risk of HAND



¿Que esta Asociado con un Alto Riesgo de Fracturas entre Pacientes VIH(+)?



- Data Source: Veterans Affairs' Clinical Case Registry
- Predictors:
 - HCV co-infection: ICD-9 codes for HCV or HCV antibody +
 - Chronic kidney disease: Estimated GFR<60 by MDRD
 - BMI, Age, Race, Antiretroviral exposure, Smoking
- Outcomes:
 - Osteoporotic fractures: Vertebral fractures (ICD-9 codes 805.2 through 805.7), Hip fractures (820.0 through 820.9), and Wrist fractures (814.0, 814.1, 813.4 and 813.5)
 - All-cause mortality
- Patients: 56,660 included in the analysis; 98.1% male; 17,281 (31.2%) HCV+; Mean age at entry: 45.0 (SD:10.4)
- Follow-up: 305,237 patient-years; mean: 5.4 yrs/pat. (range: 0 – 23.8 yrs)

Factores Predictivos de Fracturas por Osteoporosis en Pts VIH

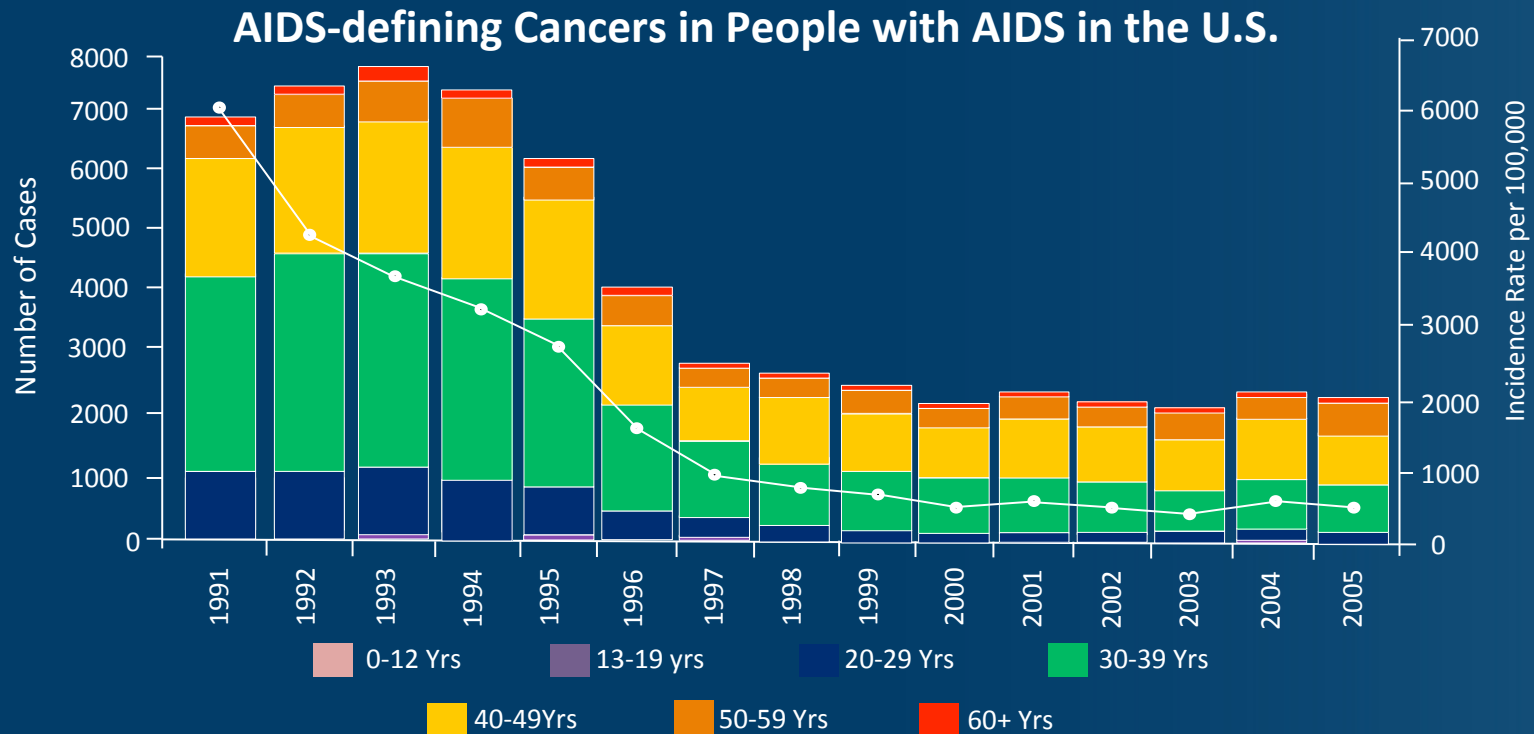


Factors	Hazard Ratio (95% Confidence Interval; p value)	
	Univariate Analysis	Multi-variable Analysis
HCV Co-infection	1.27 (1.11 - 1.44; <i>P</i> =0.0003)	1.43 (1.22 - 1.69; <i>P</i> <0.0001)
CKD (eGFR <60)	1.34 (1.03 - 1.74; <i>P</i> =0.03)	1.10 (0.77 - 1.58; <i>P</i> =0.61)
White Race	1.64 (1.41 - 1.89; <i>P</i> <0.0001)	1.75 (1.49 - 2.04; <i>P</i> <0.0001)
Age (per 10 year increase)	1.49 (1.40 - 1.59; <i>P</i> <0.0001)	1.50 (1.38 - 1.63; <i>P</i> <0.0001)
ART Use	0.57 (0.48 - 0.67; <i>P</i> <0.0001)	0.44 (0.35 - 0.56; <i>P</i> <0.0001)
Tobacco Use	1.30 (1.14 - 1.48; <i>P</i> <0.0001)	1.48 (1.26 - 1.75; <i>P</i> <0.0001)
Diabetes	1.18 (1.02 - 1.37; <i>P</i> =0.02)	1.02 (0.85 - 1.22; <i>P</i> =0.85)
BMI < 20	1.54 (1.29 - 1.82; <i>P</i> <0.0001)	1.40 (1.13 - 1.73; <i>P</i> =0.002)

Numero de Casos Cancer entre Personas VIH+ en Estados Unidos



- Estimate the total number of cancers (cancer burden) in patients with AIDS as well as in HIV-patients without AIDS in the US
- CDC collects HIV data from US states
 - AIDS from entire country from 1991-2005
 - HIV only from 34 states 2004-2007
- NCI HIV/AIDS cancer match study

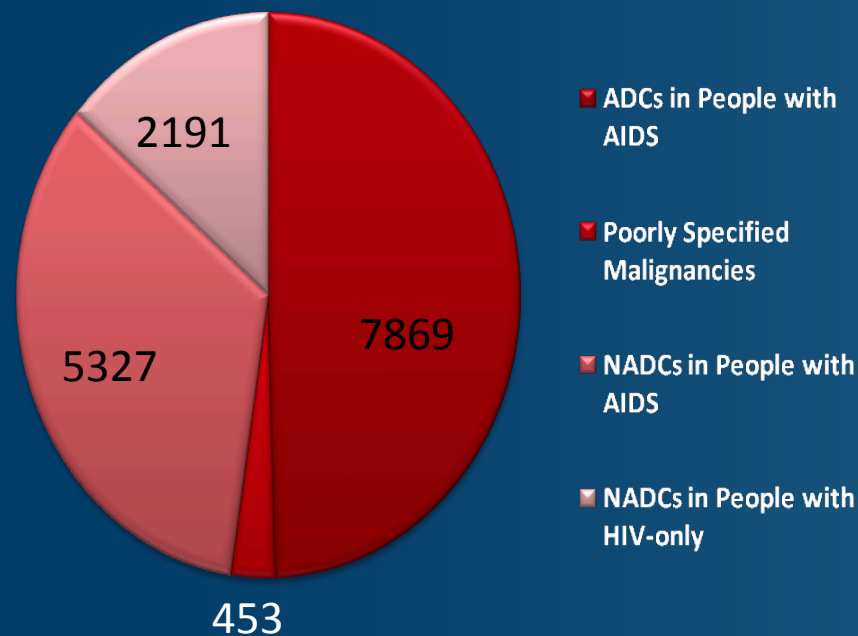
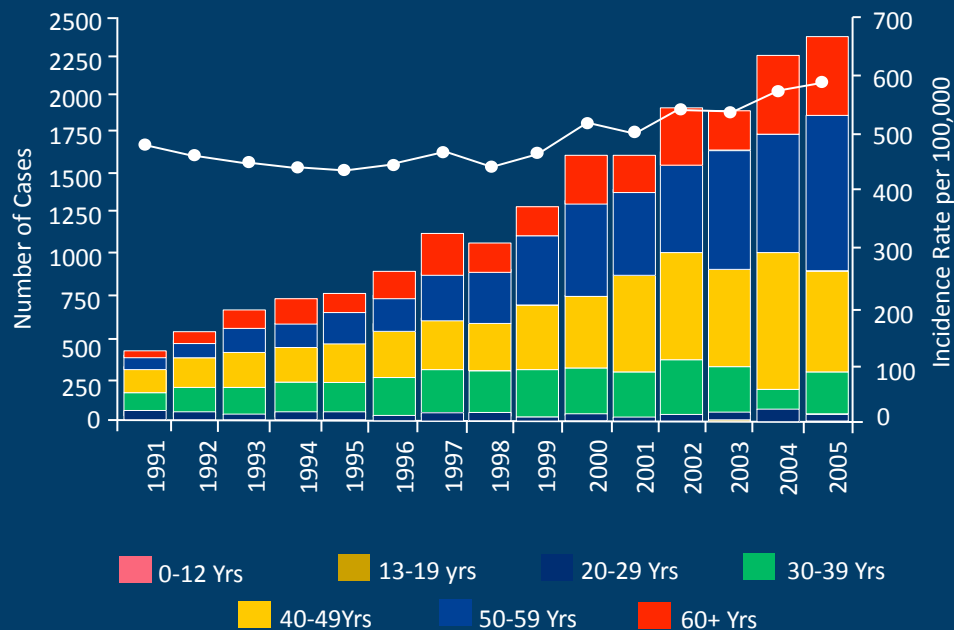


Numero de Casos Cancer entre Personas VIH+ en Estados Unidos



Non-AIDS-defining Cancers in People with AIDS in the U.S.

Overall Cancer Burden in HIV-infected People (Both HIV-only and AIDS)
N=15,885 Total Cancers



Data for 34 U.S. States (2004-2007)

Eficacia de la Vacuna HPV Quadrivalente en Hombres



- Randomized double-blind placebo controlled trial of Quadrivalent HPV vaccine 6/11/16/18; 3 doses: 0, 2, 6 months
- Subjects: 3,463 men ages 16-23; 602 MSM ages 16-26
- Inclusion criteria
 - 1-5 partners in past year
 - No history of genital warts
- Per protocol population – seronegative and PCR negative to vaccine HPV types, received all 3 injections within accepted range, developed infection after month 7

Per protocol analysis

Population	Quad vaccine		Placebo		% Efficacy	95% CI
	Cases	Rate	Cases	Rate		
All subjects	3/1397	0.1	31/1,408	1.1	90.4	69.2 – 98.1
MSM	5/299	1.3	24/299	5.8	77.5	39.6 – 93.3

Ingredientes para el Exito



- Tu
- Tu Prveedor de la Salud
- Tus Medicamentos

Tu



VIH es una de las situaciones mas dificiles que vas a tener que bregar en tu vida

- ¿ Estas preparado emocional y fisicamente?
- ¿ Tienes el apoyo necesario?
Familia, una pareja y/o un ambiente favorable ,
(techo, comida, libre de influencias negativas y de la violencia)
- ¿Tienes la informacion que necesitas?

Tu



Verdad o Mito

- Verdad: Personas que viven con el VIH que abusan del uso de drogas y/o ingieren alcohol excesivamente no hacen también como el que está libre de ellas.
- Antes de poner algo dentro de cuerpo preguntate:

¿Esto me ayudara a mi lucha contra el VIH?

¿NO? “PICHEALO”

TU Derecho



- El Conocimiento es tu mejor arma (poder)
- ¿Sabes lo que significa: CD-4, Carga Viral?
- ¿Conoces los nombres de tus medicamentos?
- ¿Quieres mas informacion? ¿ Entras al internet?
- Chequea: NATAP.ORG, P OZ, Positvely aware...
- Preguntale a tu medico o profesional de la salud