Jornada 2014 de Actualización en Atención Farmacéutica al Paciente con Patologías Víricas
Madrid, 24-25 de Abril de 2014

Lo mejor en Infección por VIH 2013

Santiago Moreno

Hospital Ramón y Cajal. IRYCIS. Madrid

Lo mejor de 2013

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Lo mejor de 2013

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10. Nuevos fármacos

Available Antiretroviral Agents

Nucleoside RTIs
- Zidovudine (ZDV)
- Didanosine (ddI)
- Zalcitabine (ddC)
- Stavudine (d4T)
- Lamivudine (3TC)
- Abacavir (ABC)
- Emtricitabine (FTC)
- Tenofovir DF (TDF)

Boosters
- Ritonavir (RTV)
- *Cobicistat* (cobi)*

Nonnucleos(t)ide RTIs
- Nevirapine (NVP)
- Delavirdine (DLV)
- Efavirenz (EFV)
- Etravirine (ETR)

Integrase Inhibitors
- Raltegravir (RAL)
- *Dolutegravir**
- *Elvitegravir**

Protease Inhibitors
- Saquinavir (SQV)
- Ritonavir (RTV)
- Indinavir (IDV)
- Nelfinavir (NFV)
- Amprenavir (APV)
- Lopinavir/r (LPV/r)
- Atazanavir (ATV)
- Fosamprenavir (Fos-APV)
- Tipranavir (TPV)
- Darunavir (DRV)

Fusion Inhibitor
- Enfuvirtide (T-20)

CCR5 Antagonist
- Maraviroc (MVC)

* In expanded access or submitted for regulatory approval

July 20, 2012

Available and Future Antiretroviral Agents

Nucleoside RTIs
- Zidovudine (ZDV)
- Didanosine (ddI)
- Zalcitabine (ddC)
- Stavudine (d4T)
- Lamivudine (3TC)
- Abacavir (ABC)
- Emtricitabine (FTC)
- Tenofovir DF (TDF)
- Tenofovir AF (TAF)

Boosters
- Ritonavir (RTV)
- *Cobicistat* (cobi)*

Nonnucleos(t)ide RTIs
- Nevirapine (NVP)
- Delavirdine (DLV)
- Efavirenz (EFV)
- Etravirine (ETR)
- Doravirine (DRV)

Integrase Inhibitors
- Raltegravir (RAL)
- *Dolutegravir**
- *Elvitegravir**

Attachment inhibitor

Protease Inhibitors
- Saquinavir (SQV)
- Ritonavir (RTV)
- Indinavir (IDV)
- Nelfinavir (NFV)
- Amprenavir (APV)
- Lopinavir/r (LPV/r)
- Atazanavir (ATV)
- Fosamprenavir (Fos-APV)
- Tipranavir (TPV)
- Darunavir (DRV)

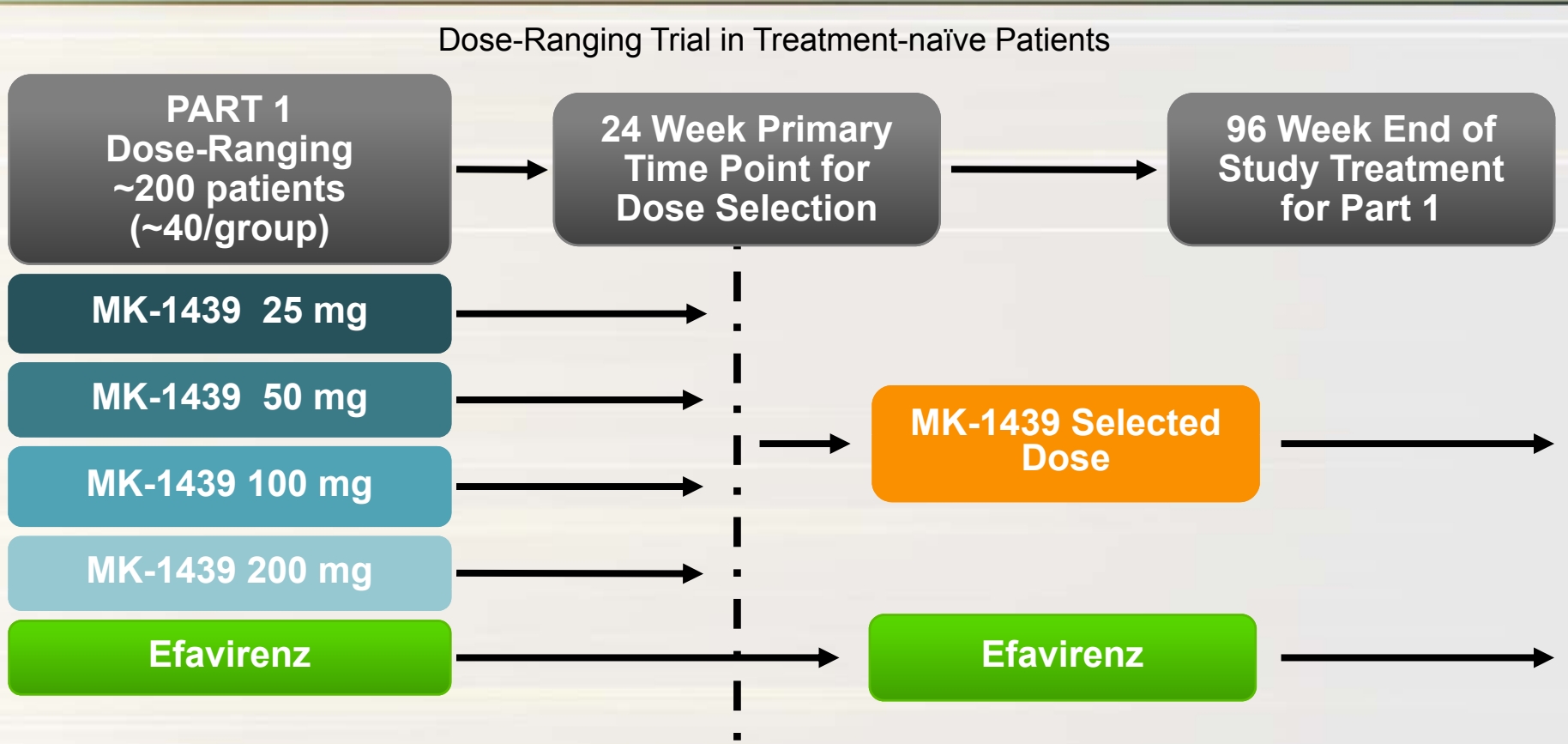
Fusion Inhibitor
- Enfuvirtide (T-20)

CCR5 Antagonist
- Maraviroc (MVC)

* In expanded access or submitted for regulatory approval

July 20, 2012

MK-1439 (Doravirine): A New NNRTI



- **<3-fold potency shift vs. common NNRTI-resistance mutants K103N, Y181C, G190A, E138K(4)**
- **Low potential for CNS effects, drug-drug interactions; lower protein-binding vs. other NNRTIs**

Morales-Ramirez J, et al. 21st CROI; Boston, MA; March 3-6, 2014. Abst. 92LB.

MK-1439: Summary at Week 24

Response Differences in Percent HIV RNA <40 copies/mL at Week 24 (NC=F)

Dose MK-1439	Response Difference vs. EFV	95% CI
25 mg	+15.7%	-4.1, 34.4
50 mg	+11.6%	-8.1, 30.6
100 mg	+6.6%	-13.2, 26
200 mg	+13.4%	-6, 32

- **Adverse Events**
  - Fewer CNS AEs (All MK-1439 arms 20.5% vs. EFV 33.3%)
  - Fewer drug-related AEs compared with EFV
  - Favorable CNS, lipid and AST/ALT profile
- **No dose-response trend was observed**
  - All MK-1439 dose groups had numerically higher response rates than EFV
  - All groups (MK-1439 and EFV) showed increased CD4 counts
- **MK-1439 (Doravirine) 100 mg QD selected for further study**

Morales-Ramirez J, et al. 21st CROI; Boston, MA; March 3-6, 2014. Abst. 92LB.

Lo mejor de 2013

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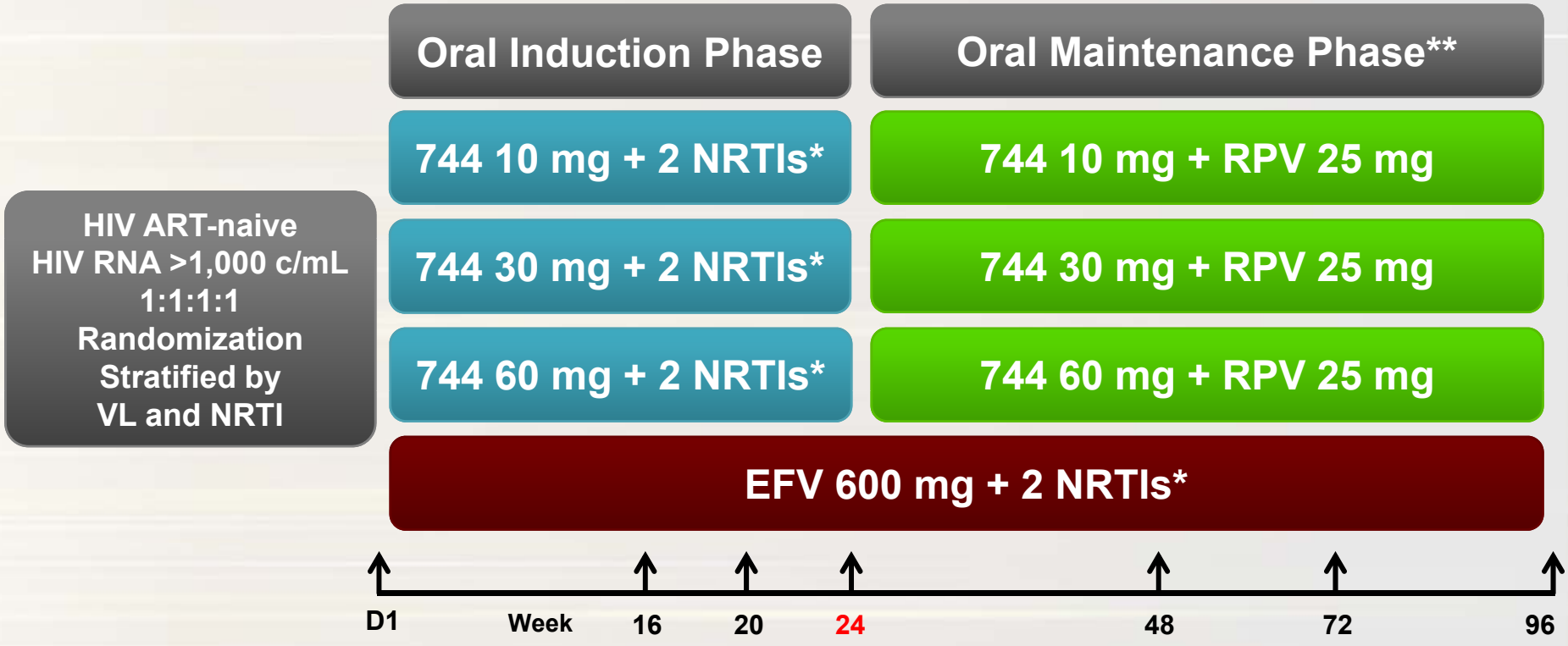
9. Fármacos de acción prolongada
10. Nuevos fármacos: Doravirina (NNRTI)

LATTE: Study Design

- **Phase IIb, randomized, multicenter, partially blind, dose-ranging study comparing S/GSK744 (integrase inhibitor) to EFV**



*ABC/3TC or TDF/FTC
**Patients on 744 + NRTI: If week 20 VL <50 c/mL - simplify to 744/RPV at week 24

Margolis D, et al. 14th EACS; Brussels, Belgium; October 16-19, 2013. Abst. PS7/1.

LATTE Study: Treatment Outcomes – Maintenance Population

- **HIV-1 RNA <50 c/mL by Snapshot (ITT-ME)**

Outcome at Week 48	744 10 mg n=52	744 30 mg n=53	744 60 mg n=55	744 total n=160	EFV 600 mg n=47
Virologic success	**48 (92%)**	**48 (91%)**	**53 (96%)**	**149 (93%)**	**44 (94%)**
Virologic failure	**3 (6%)**	**5 (9%)**	**1 (2%)**	**9 (6%)**	**2 (4%)**
Data in window not <50 c/mL	3 (6%)	3 (6%)	1 (2%)	7 (4%)	1 (2%)
Discontinued for lack of efficacy	0	0	0	0	1 (2%)
Change in ART	0	2 (4%)	0	2 (1%)	0
No virologic data at Week 48	**1 (2%)**	**0**	**1 (2%)**	**2 (1%)**	**1 (2%)**
Discontinued due to AE	1 (2%)	0	1 (2%)	2 (1%)	1 (2%)

- **Similar response rate for 744 + RPV vs. continuing EFV + NRTIs**
- **Similar response across 744 doses**

Margolis D, et al. 21st CROI; Boston, MA; March 3-6, 2014. Abst. 91LB.

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8. Comparación de tercer fármaco
9. Fármacos de acción prolongada: 744/RPV
10. Nuevos fármacos: Doravirina (NNRTI)

Choice of Initial Regimen

Tenofovir/emtricitabine (TDF/FTC) *OR*
Abacavir/lamivudine (ABC/3TC)

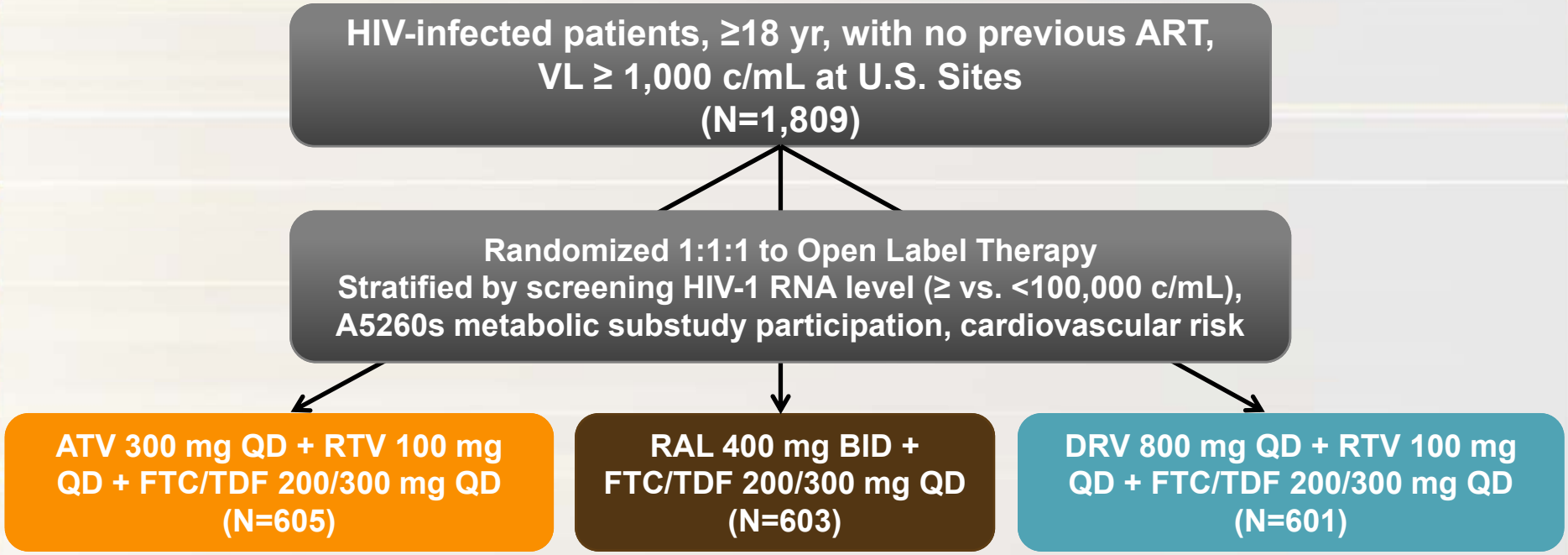
WITH

Third agent (NNRTI, boosted PI, or InSTI):

- Efavirenz *OR*
- Atazanavir/r *OR*
- Darunavir/r *OR*
- Raltegravir

Thompson et al, *JAMA*, 2012.

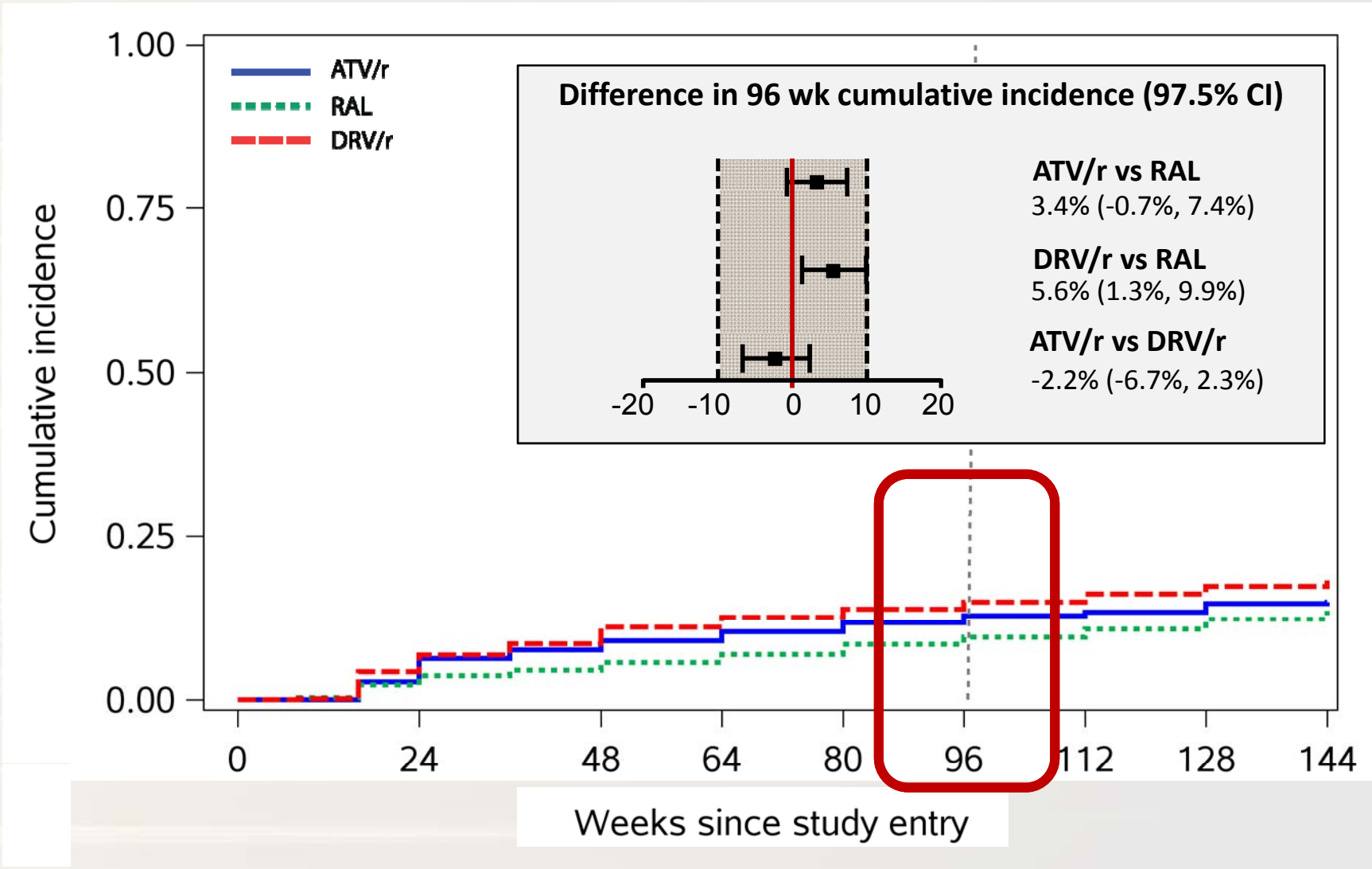
ACTG 5257: Study Design



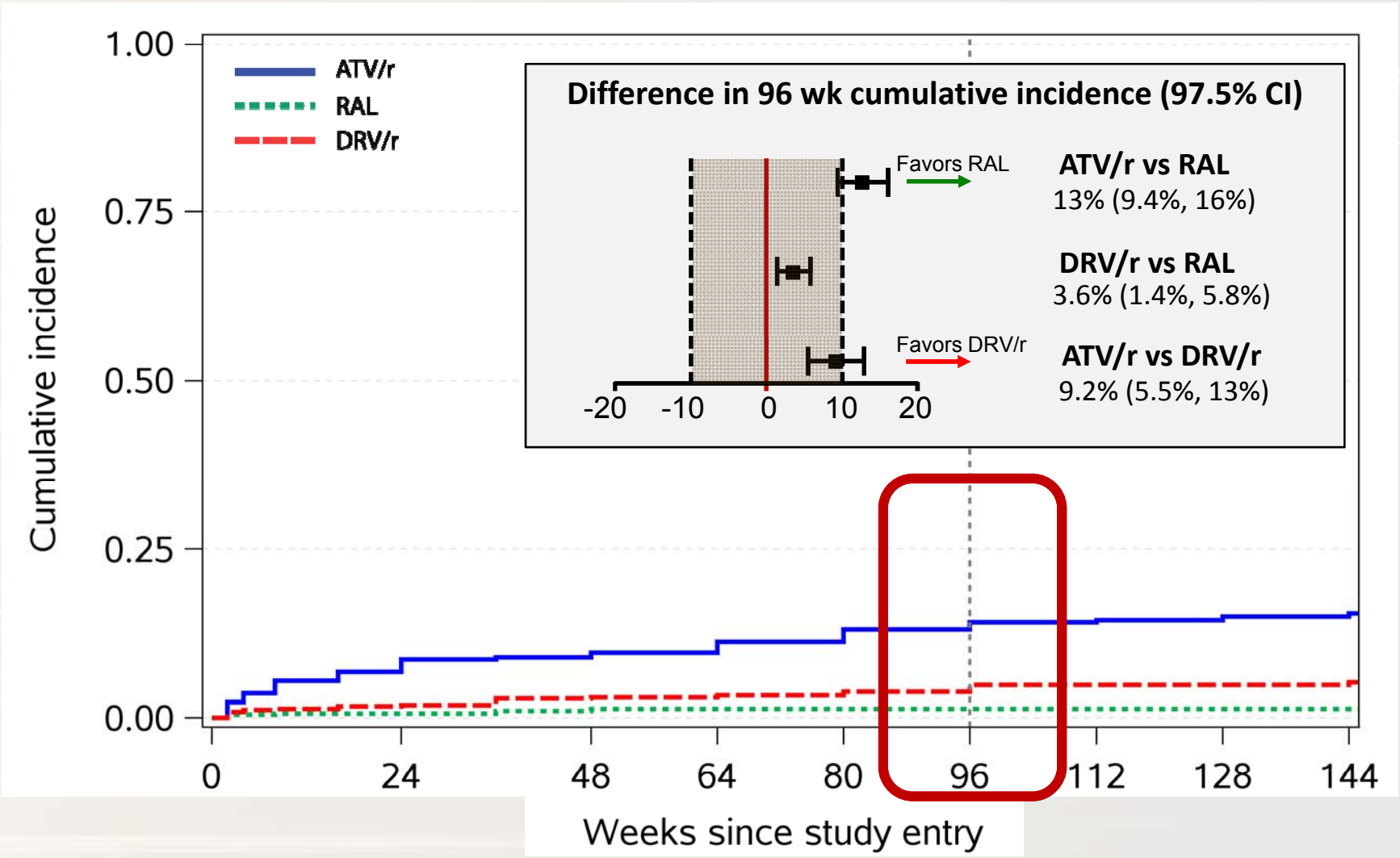
- **Primary Endpoints***
  - Time to HIV-1 RNA >1000 c/mL wk 16 to before wk 24, or >200 c/mL at or after wk 24 (VF)
  - Time to discontinuation of randomized component for toxicity (TF)
- **Pre-planned Composite Endpoint**
  - The earlier occurrence of either VF or TF in a given participant

Landovitz L, et al. 21st CROI; Boston, MA; March 3-6, 2014. Abst. 85.

ACTG 5257: Cumulative Incidence of Virologic Failure



ACTG 5257: Cumulative Incidence of Tolerability Failure



ACTG 5257: Toxicity Associated Discontinuation

	ATV/r (N=605)	RAL (N=603)	DRV/r (N=601)
Any Toxicity Discontinuation	95 (16%)	8 (1%)	32 (5%)
Gastrointestinal Toxicity	25	2	14
Jaundice/Hyperbilirubinemia	47	0	0
Other Hepatic Toxicity	4	1	5
Skin Toxicity	7	2	5
Metabolic Toxicity	6	0	2
Renal Toxicity (All Nephrolithiasis)	4	0	0
Abnormal Chem/Heme (Excl. LFTs)	0	0	2
Other Toxicity	2	3	4

Landovitz L, et al. 21st CROI; Boston, MA; March 3-6, 2014. Abst. 85.

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7. Inhibidores de la integrasa
8. Comparación de tercer fármaco: ACTG 5257
9. Fármacos de acción prolongada: 744/RPV
10. Nuevos fármacos: Doravirina (NNRTI)

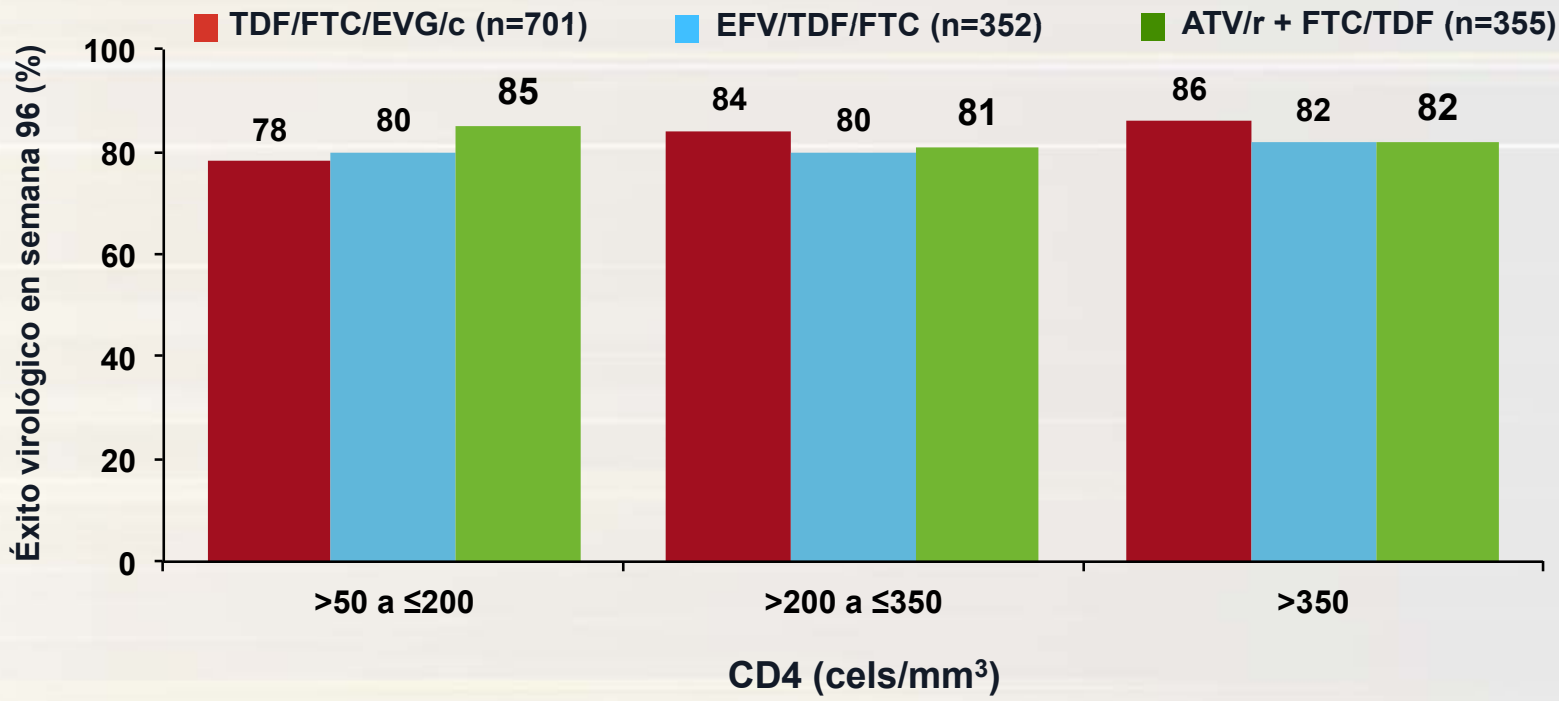
ACTG 5257: Failure Comparisons at 96 Weeks

Virologic Failure			
Arms	**Difference**	**97.5% CI**	**Favors**
ATV/r vs. RAL	3.4%	-0.7%, 7.4%	Equivalent
DRV/r vs. RAL	5.6%	1.3%, 9.9%	Equivalent
ATV/r vs. DRV/r	-2.2%	-6.7%, 2.3%	Equivalent

Tolerability Failure			
Arms	**Difference**	**97.5% CI**	**Favors**
ATV/r vs. RAL	13%	9.4%, 16%	RAL Superior
DRV/r vs. RAL	3.6%	1.4%, 5.8%	RAL Superior
ATV/r vs. DRV/r	9.2%	5.5%, 13%	DRV/r Superior

Cumulative Failure			
Arms	**Difference**	**97.5% CI**	**Favors**
ATV/r vs. RAL	15%	10%, 20%	RAL Superior
DRV/r vs. RAL	7.5%	3.2%, 12%	RAL Superior
ATV/r vs. DRV/r	7.5%	2.3%, 13%	DRV/r Superior

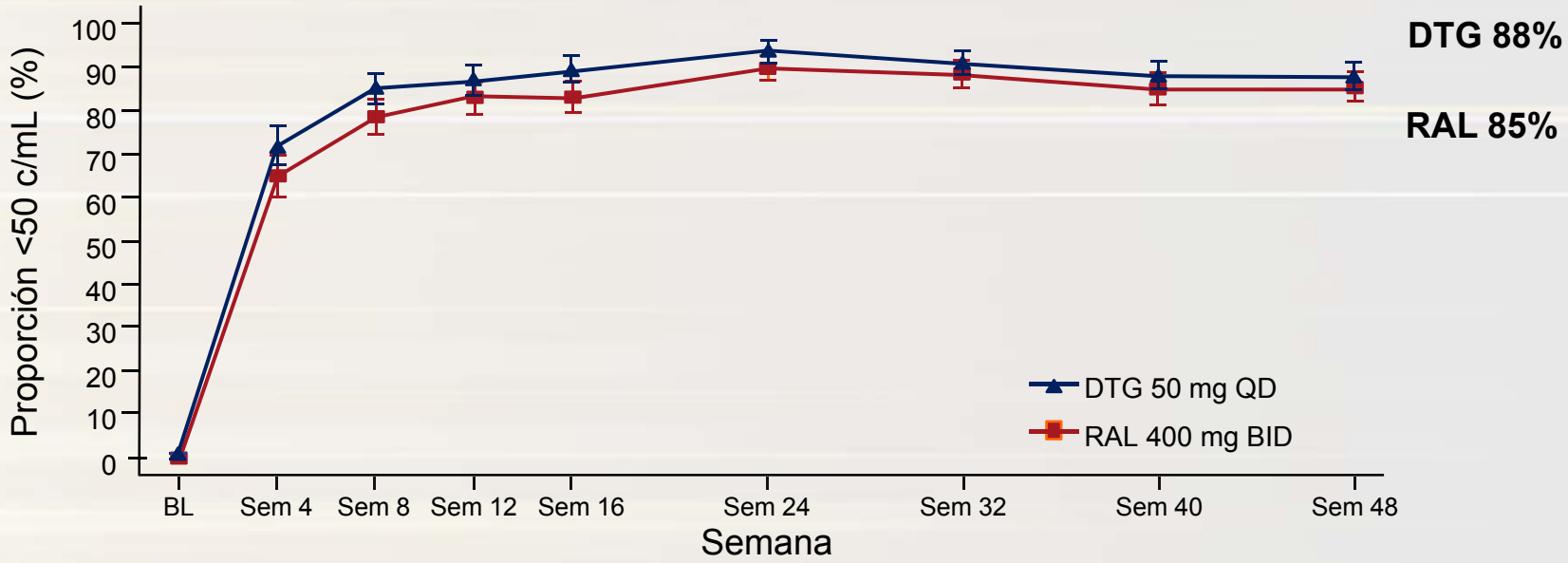
Elvitegravir/c: Eficacia y seguridad en los estudios 102 y 103 en semana 96



- Subgrupo de CD4 < 50 (n=30).
- 11/19 EVGc con éxito virológico. 8 fueron fracasos (todos con CV > 100 K c/mL, 4 con adherencia subóptima.
- 5/6 EFV con éxito virológico; 1 fracaso (CV > 100 K c/mL, con adherencia subóptima).
- 5/5 ATV/r + TDF/FTC con éxito virológico.

Zolopa A. et al. 20th CROI. Atlanta. 3 – 6 Marzo 2013. #553

Dolutegravir (estudio SPRING-2). Análisis de eficacia a 48 semanas

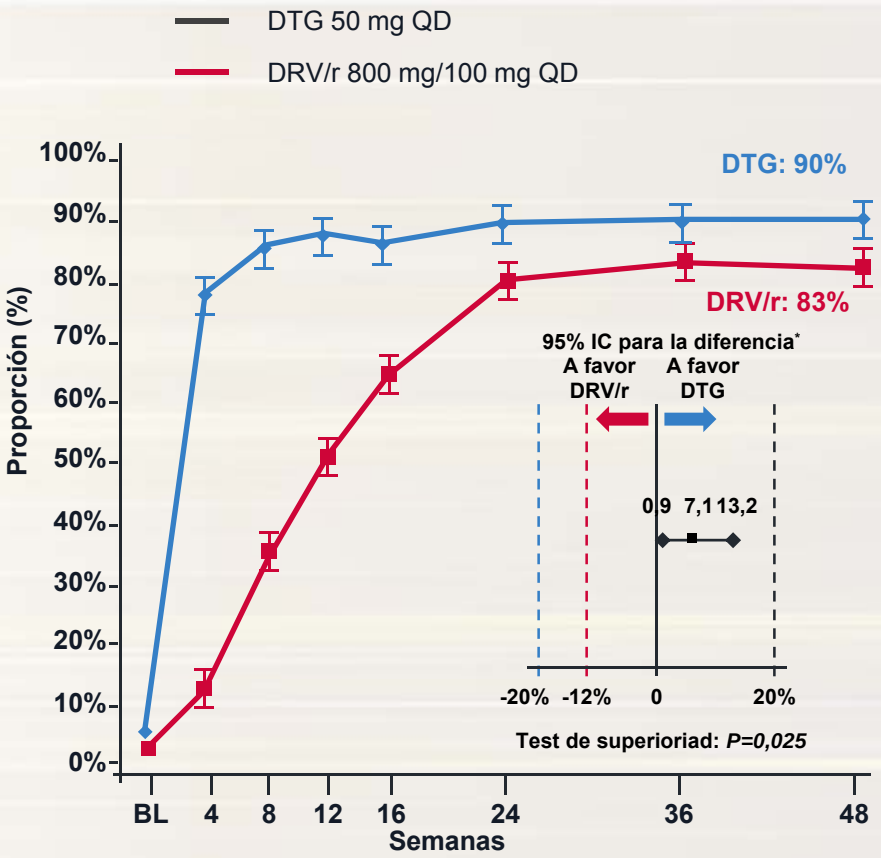


- **DTG es no-inferior a RAL con un margen del 10%: Diferencia: 2,5%; IC95% (-2,2% a 7,1%).**
- **No-inferioridad demostrada con > 100.000 c/mL 7,5 (-3,1 a 18).**
- **No-inferioridad demostrada con TDF/FTC: 4,6 (-1,3 a 10,6) y con ABC/3TC -0,8 (-8,2 a 6,6).**
- **Similar recuperación de CD4 entre DTG y RAL (+230 CD4 a las 48 semanas).**
- **Fallo virológico a 48 semanas: DTG 20 (5%; 1 con CV>400); RAL: 28 (7%; 5 con CV>400).**
- **Resistencias: con DTG: 0 a integrasa, 0 a nucleósidos; RAL: 1 a integrasa, 4 a nucleósidos.**
- **Efectos adversos grado 2-4: 6% DTG vs 7% RAL. Abandonos por EA: 2% DTG, vs 2% RAL.**
- **Incremento de creatinina (grado 1/2): 2%/0,6% para DTG vs 2%/0% para RAL.**

Raffi F, et al. IAS 2012. Washington DC. 19 - 27 Julio. #THLBB04

Estudio FLAMINGO: DTG es superior a DRV/r en pacientes naïve

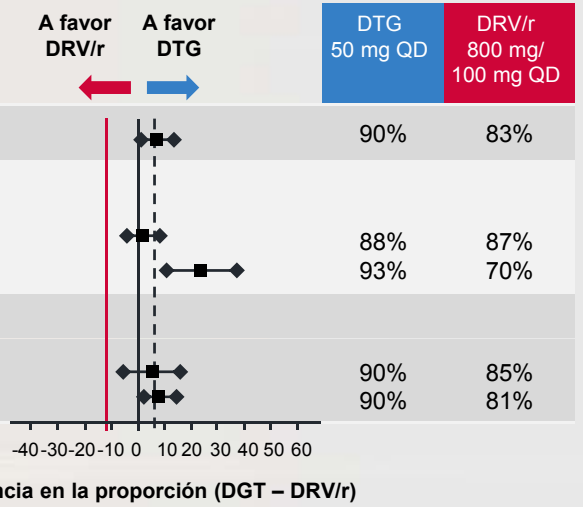
Proporción (IC 95%) de individuos con RNA VIH-1 <50 c/mL en el tiempo-snapshot



*Diferencia ajustada (DTG-DRV/r) basada en un análisis estratificado CMH ajustando por HIV RNA basal y los nucleósidos acompañantes.
Resultados confirmados en el análisis por protocolo: 91% DTG vs. 84% DRV/r, Δ (IC): 7,4 (1,4 – 13,3).

Snapshot por estrato de randomización en la semana 48

Se demostró superioridad global



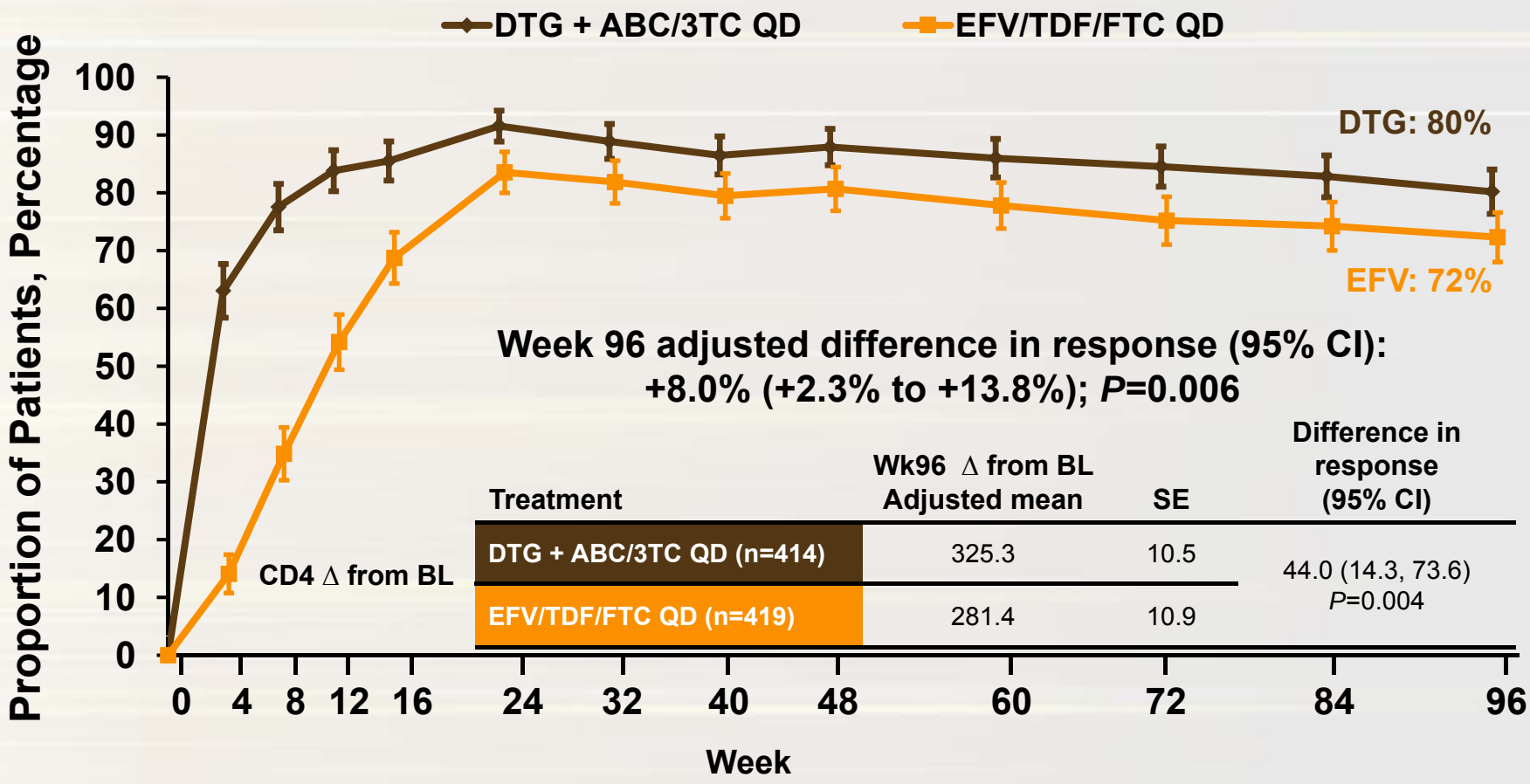
		DTG 50 mg QD	DRV/r 800 mg/ 100 mg QD
Global[a]	n=484	90%	83%
HIV-1 RNA basal[b]			
≤100.000 c/mL	n=362	88%	87%
>100.000 c/mL	n=122	93%	70%
Nucleósidos[b]			
ABC/3TC	n=159	90%	85%
TDF/FTC	n=325	90%	81%

[a]Diferencia ajustada (DTG-DRV/r) basada en un análisis estratificado Cochran-Mantel-Haenszel ajustando por HIV RNA basal y los nucleósidos acompañantes. .
[b]Las diferencias no ajustadas apoyan la no-inferioridad de DTG vs DRV/r en los estratos de HIV-1 RNA basal y de nucleósidos acompañantes.

Feinberg J. et al. ICAAC. Denver, 10-13 Septiembre 2013. #1464a

SINGLE: Virologic Suppression

(HIV-1 RNA <50 c/mL; FDA Snapshot)



Week 96 adjusted difference in response (95% CI): +8.0% (+2.3% to +13.8%); *P*=0.006

Treatment	Wk96 Δ from BL Adjusted mean	SE	Difference in response (95% CI)
DTG + ABC/3TC QD (n=414)	325.3	10.5	44.0 (14.3, 73.6) *P*=0.004
EFV/TDF/FTC QD (n=419)	281.4	10.9	

Walmsley S, et al. 21st CROI; Boston, MA; March 3-6, 2014. Abst. 543.

SINGLE: Resistance Mutations

Individuals Who Met PDVF Criteria

Mutation	DTG + ABC/3TC QD (n=414)	EFV/TDF/FTC QD (n=419)
NRTI TE Major Mutations	0	1 (K65R)
NNRTI TE Major Mutations	0	6 (K101E, K103N, G190A)
INI-r TE Major Substitution	0	0

Walmsley S, et al. 21st CROI; Boston, MA; March 3-6, 2014. Abst. 543.

Lo mejor de 2013

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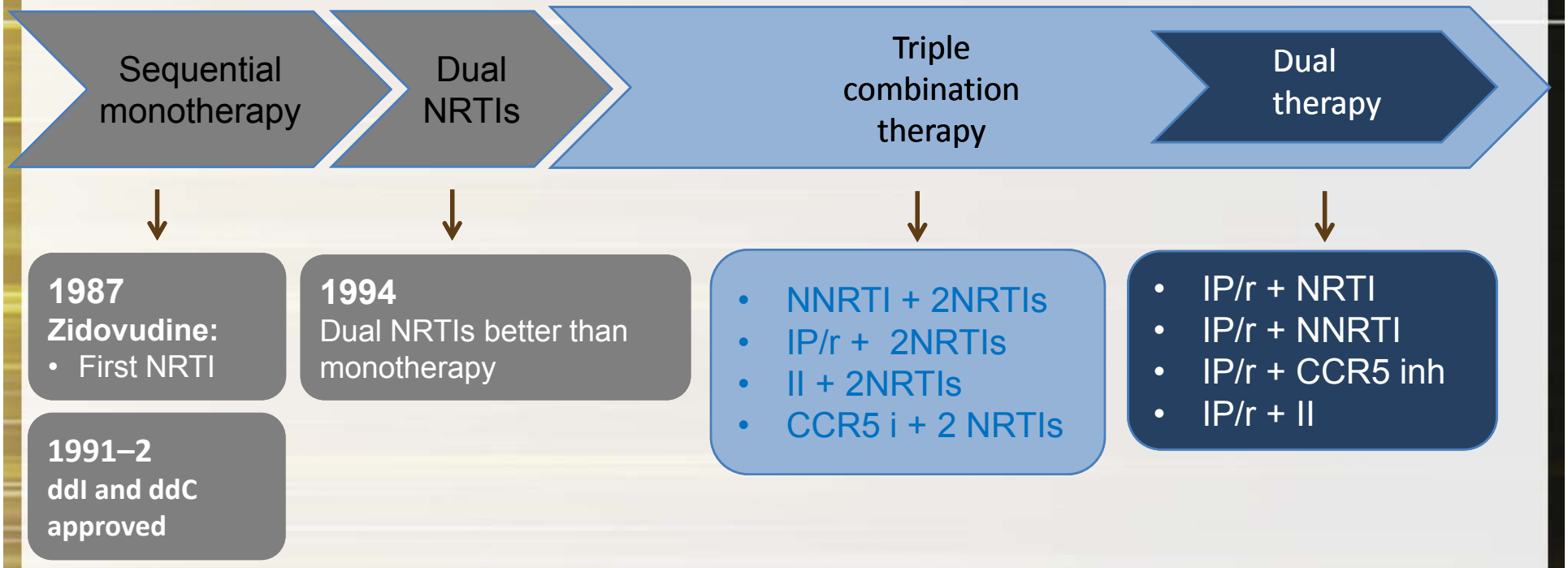
6. Pautas de 2 fármacos en tratamiento de inicio
7. Inhibidores de la integrasa: Una invasión.
8. Comparación de tercer fármaco: ACTG 5257
9. Fármacos de acción prolongada: 744/RPV
10. Nuevos fármacos: Doravirina (NNRTI)

Evolución del tratamiento antirretroviral de inicio



IP/r + MVC en TARV de inicio

	Study	PI/r + MVC arm PI component	Comparator arm
First line	A4001078	ATV/RTV	ATV+RTV + TDF/FTC
	VEMAN	LPV/r	LPV/r + TDF/FTC
	MIDAS	DRV/RTV	-
	MODERN	DRV/RTV	DRV+RTV + TDF/FTC

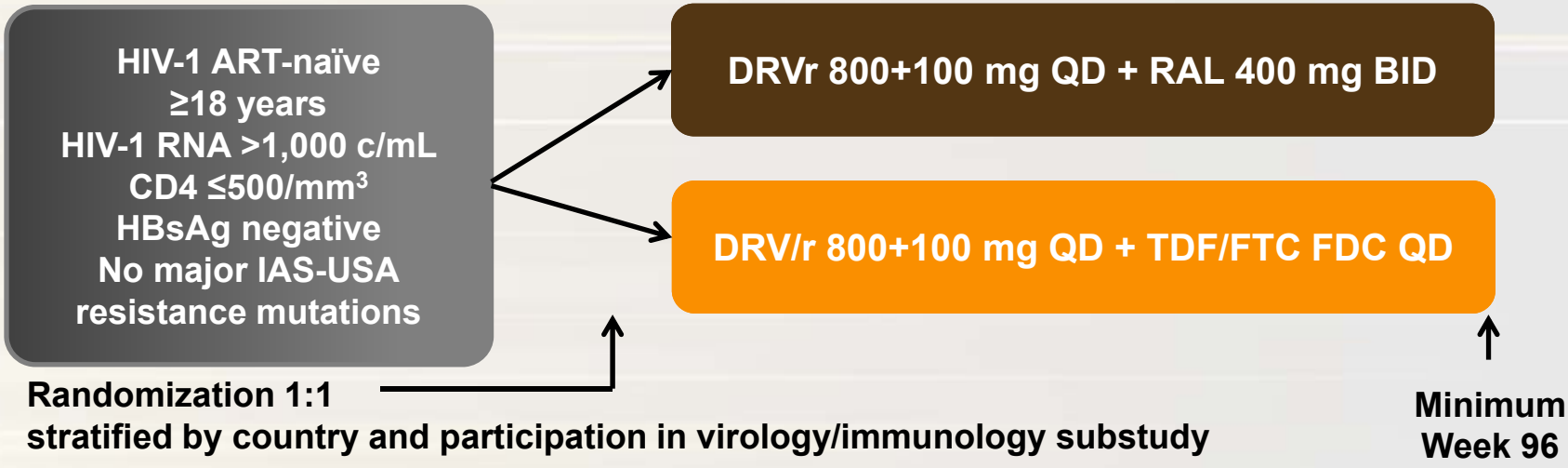
Mills A, et al. IAC 2012, Abs. TUAB0102.
Taiwo B, et al. XIX IAC, Washington 2012, #TUPE099.

IP/r + RAL en TARV de inicio

	Study	PI/r + BID RAL arm PI component	Comparator arm
First line	SPARTAN	ATV	ATV+RTV + TDF/FTC
	PROGRESS	LPV/r	LPV/r + TDF/FTC
	RADAR	DRV+RTV	DRV+RTV + TDF/FTC
	A5262	DRV+RTV	-
	NEAT 001	DRV+RTV	DRV+RTV + TDF/FTC

Kozal MJ, et al. HIV Clin Trial 2012;13:119–30.

NEAT 001: DRV/r + RAL vs. DRV/r + TDF/FTC



- 78 sites, 15 European countries
- Composite virological and clinical primary endpoint (6 components)

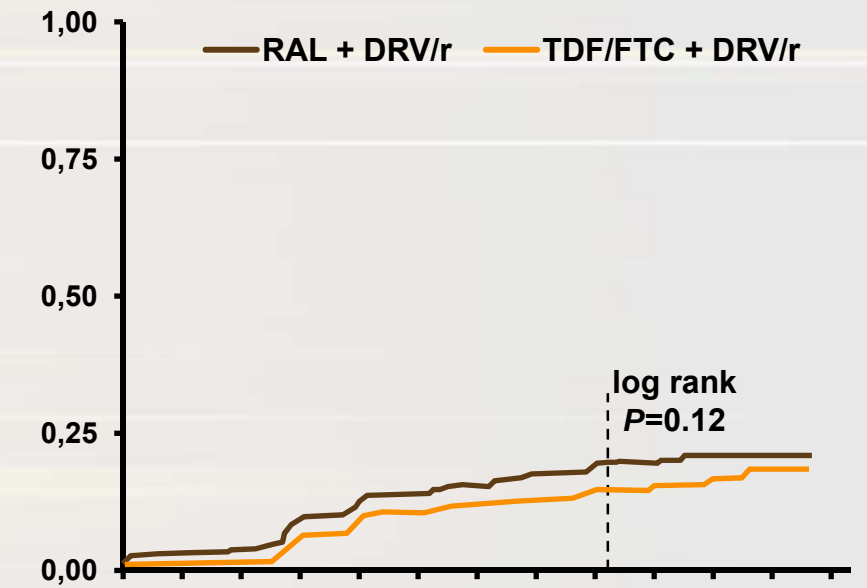
Raffi F, et al. 21st CROI; Boston, MA; March 3-6, 2014. Abst. 84LB.

NEAT 001: Primary Analysis

Primary Endpoint

	RAL + DRV/r	TDF/FTC + DRV/r
N	401	404
N with Primary Endpoint	76 (19%)	61 (15%)
V1. Regimen Change for Insufficient Response		
<1 log_{10} c/ml HIV RNA Reduction W18	1	0
HIV RNA ≥400 c/ml W24	1	0
V2. HIV RNA ≥50 c/ml at W32	27	28
V3. HIV RNA ≥50 c/ml after W32	32	22
C1. Death	3	1
C2. AIDS Event	5	3
C3. SNAIDS Event	7	7

Probability of Reaching Primary Endpoint

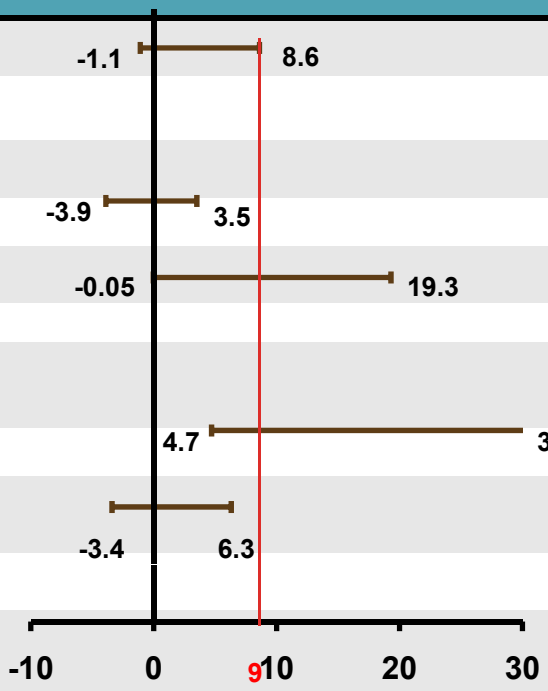


Estimated proportion reaching primary endpoint at W96
RAL: 17.4% vs TDF/FTC: 13.7%
Adjusted Difference: 3.7% (95% CI: -1.1, 8.6%)

Raffi F, et al. 21st CROI; Boston, MA; March 3-6, 2014. Abst. 84LB.

NEAT 001: Primary Endpoint by Baseline Characteristics and Resistance

		RAL + DRV/r	TDF/FTC + DRV/r
Overall	n = 805	17.4%	13.7%
Baseline HIV-1 RNA			
< 100,000 c/ml	n = 530	7%	7%
≥ 100,000 c/ml	n = 275	36%	27%
			P=0.09*
Baseline CD4+			
< 200/mm^3	n = 123	39.0%	21.3%
≥ 200/mm^3	n = 682	13.6%	12.2%
			P=0.02*



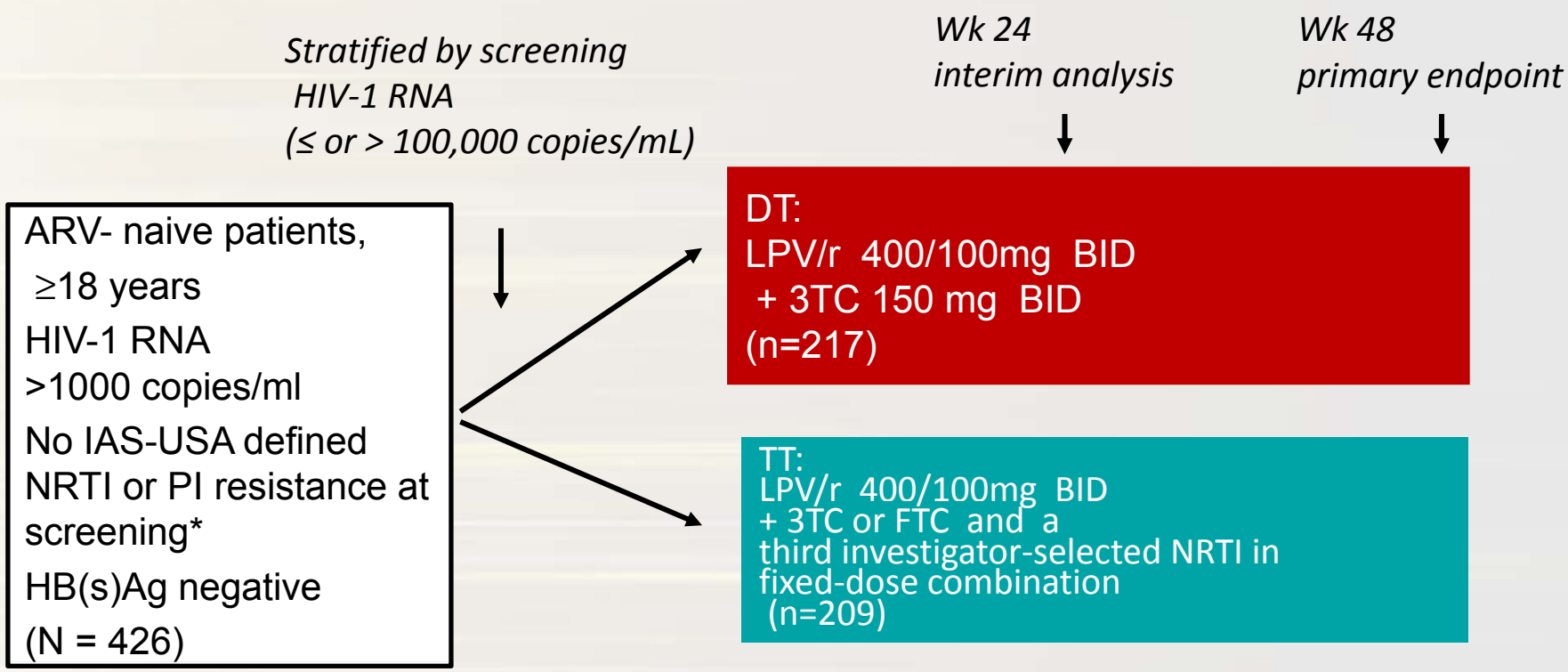
Genotype Done, n	28/36	13/15
Major Resistance Mutations, n	5	0
NRTI	1 (K65R)	0
PI	0	0
INI	5 (N155H)*	-

Raffi F, et al. 21st CROI; Boston, MA; March 3-6, 2014. Abst. 84LB.

Estudio Gardel: LPV/r + 3TC

GARDEL: Design

- Phase III, randomized, international , controlled, open-label study
- Study included adult patients from Argentina, Chile, Mexico, Peru, Spain, US.

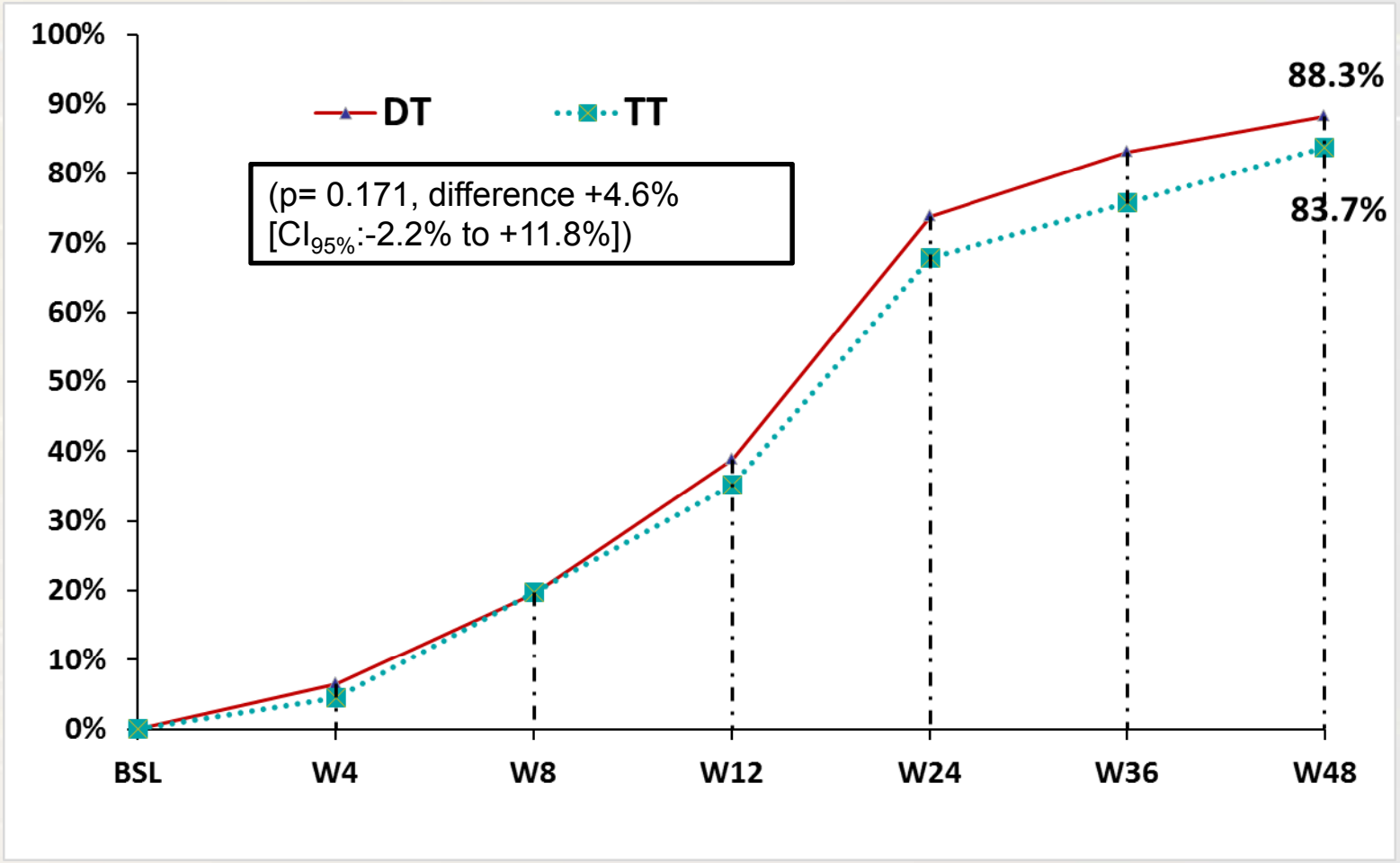


*Defined as ≥ 1 major or ≥ 2 minor LPV/r mutations)
LPV major mutations include the following mutations: V32I; I47V/A; L76V; V82A/F/T/S

Cahn P, et al. EACS, 2013. Brussels, Belgium.

Estudio Gardel: LPV/r + 3TC

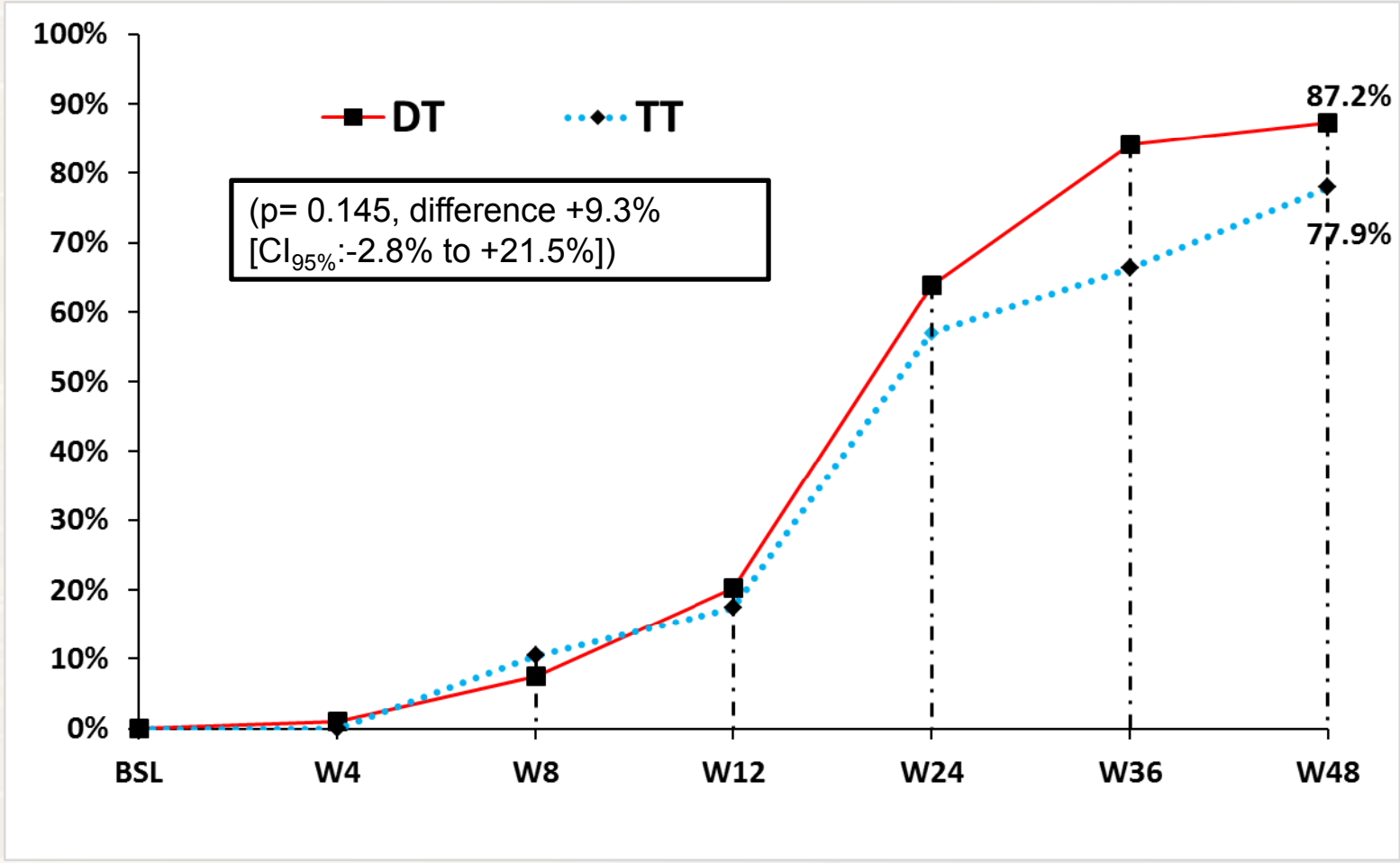
GARDEL: Viral load <50 copies/mL at week 48 (ITTe)



Cahn P, et al. EACS, 2013. Brussels, Belgium.

Estudio Gardel: LPV/r + 3TC

GARDEL: Viral load <50 copies/mL at week 48 (ITTe), baseline VL > 100.000 copies/mL)



Cahn P, et al. EACS, 2013. Brussels, Belgium.

Estudio Gardel: LPV/r + 3TC

GARDEL: Virologic Outcome at W48

	DT (n=214)	TT (n=202)	P [IC95%]
HIV – RNA < 50 copies/mL (n; %)	189 (88.3%)	169 (83.7%)	0.171 [-2.2% ; +11.8%]
HIV – RNA >50 copies/mL (n; %)	10 (4.7%)	12 (5.9%)	0.720 [-6.1%; +3.5%]
No Virologic data at week 48 window Reasons: Discontinued study due to adverse event or death	2 (0.9 %)*	10 (4.9 %)**	0.03 [-7.8%; -3.0%]
Discontinued study for other reasons***	13 (6.1%)	11 (5.4%)	0.948 [-4.3; +5.6]

* *1 death: Sepsis, 1 nephrotic syndrome*

** *2 Rash, 3 anemia, 5 GI intolerance*

*** (Non compliance with study procedures, consent withdrawal, adherence, opportunistic infection, lost to follow-up, pregnancy)

Cahn P, et al. EACS, 2013. Brussels, Belgium.

Lo mejor de 2013

1.
2.
3.
4.
5. Donación de órganos
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7. Inhibidores de la integrasa: Una invasión.
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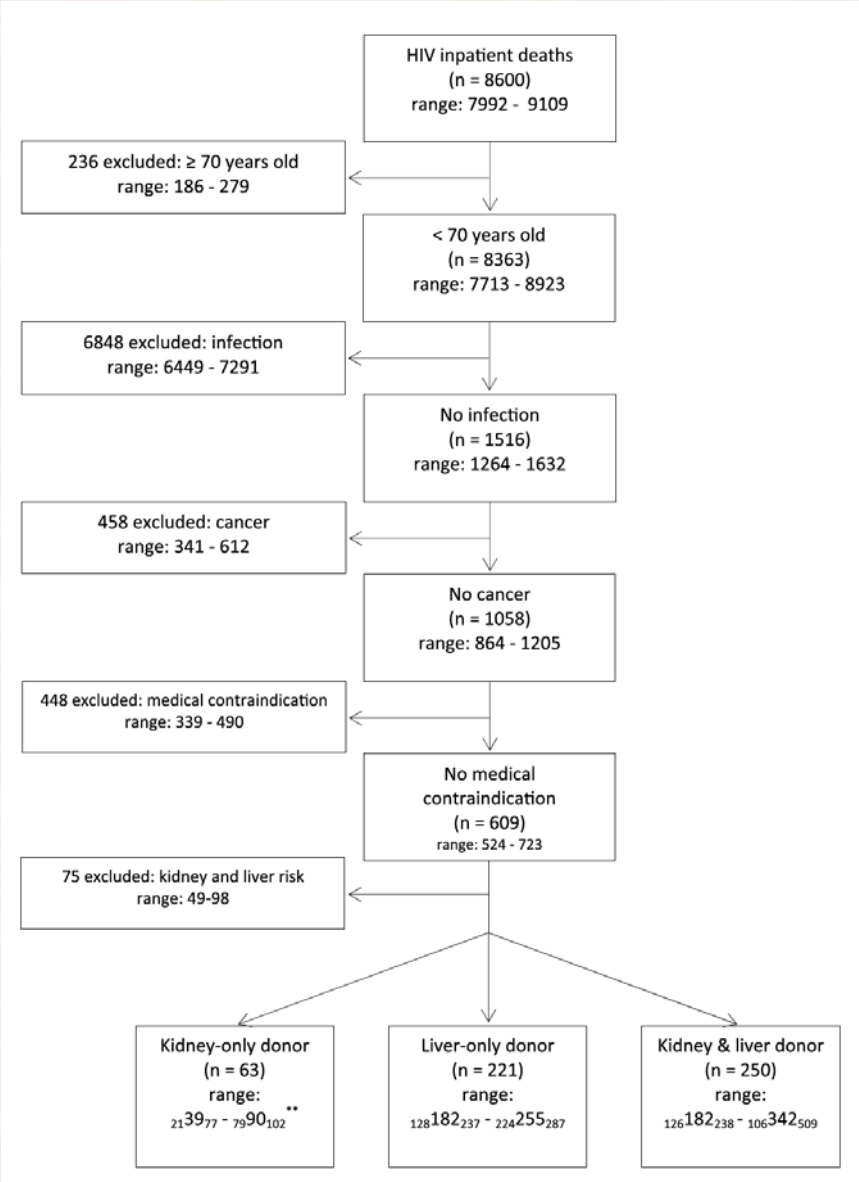
10. Nuevos fármacos: Doravirina (NNRTI)

Eligibility criteria for potential organ donors identified in NIS 2005–2008



Boyarsky BJ. Am J Transplant 2011; 11: 1209–1217

Estimating the Potential Pool of HIV-Infected Deceased Organ Donors in the United States

Human immunodeficiency virus (HIV) is no longer a contraindication to transplantation. For HIV-infected patients, HIV-infected deceased donors (HIVDD) could attenuate the organ shortage and waitlist mortality. However, this practice would violate United States federal law. The goal of this study was to estimate the potential impact of legalizing transplantation of HIV-infected organs by quantifying the potential pool of HIVDD. Using Nationwide Inpatient Sample (NIS) data, HIV-infected deaths compatible with donation were enumerated. Using HIV Research Network (HIVRN) data, CD4 count, plasma HIV-1 RNA level, AIDS-defining illnesses and causes of death were examined in potential HIVDD. Using UNOS data, evaluated donors who later demonstrated unanticipated HIV infections were studied. From NIS, a yearly average of 534 (range: 481–652) potential HIVDDwere identified, with 63 (range: 39–90) kidney-only, 221 (range: 182–255) liver-only and 250 (range: 182–342) multiorgan donors. From HIVRN, a yearly average of 494 (range: 441–533) potential HIVDD were identified. Additionally, a yearly average of 20 (range: 11–34) donors with unanticipated HIV infection were identified from UNOS. **Deceased HIV-infected patients represent a potential of approximately 500–600 donors per year for HIV-infected transplant candidates**. **In the current era of HIV management, a legal ban on the use of these organs seems unwarranted and likely harmful.**

Boyarsky BJ. American Journal of Transplantation 2011; 11: 1209–1217

HIV Organ Policy Equity (HOPE)
21 de Noviembre de 2013

Obama Lifts Ban on Research Into Possibility of Transplanting Organs From HIV-Positive Donors

From CDC National Prevention Information Network

November 22, 2013

An article in *StarTribune* recently reported that on November 21 President Barack Obama signed a bill entitled the HIV Organ Policy Equity (HOPE) Act into law that **lifts a ban on research into the possible transplant of organs from one HIV-positive individual to another and directs the federal health department to develop and institute standards for conducting this research.**

The HOPE Act also allows the health secretary to **permit such transplants if the research demonstrates that the change is warranted**.

According to Obama, the HOPE Act is an important step, since it will improve medical care for HIV-positive individuals.

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2.
3.
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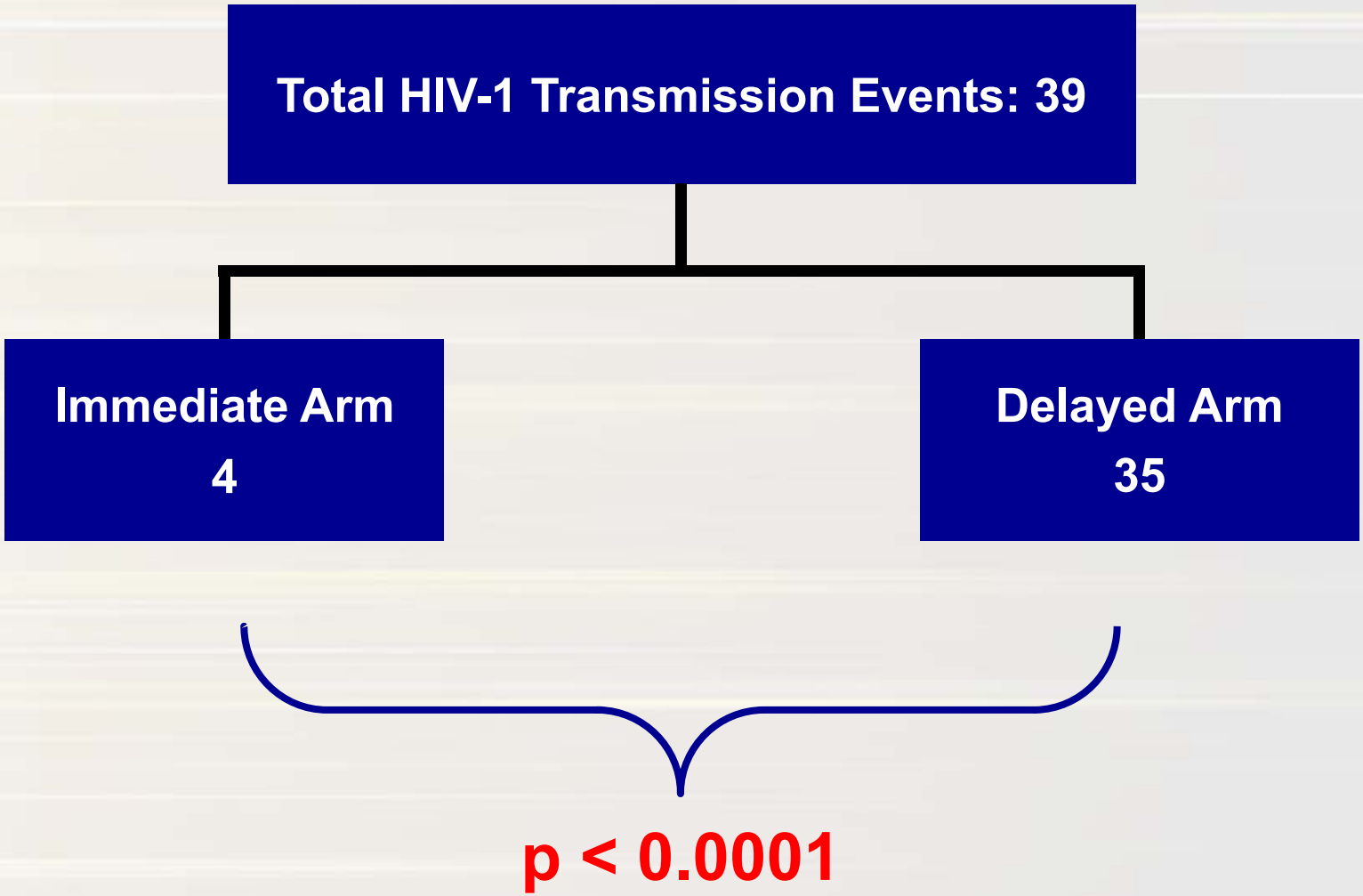
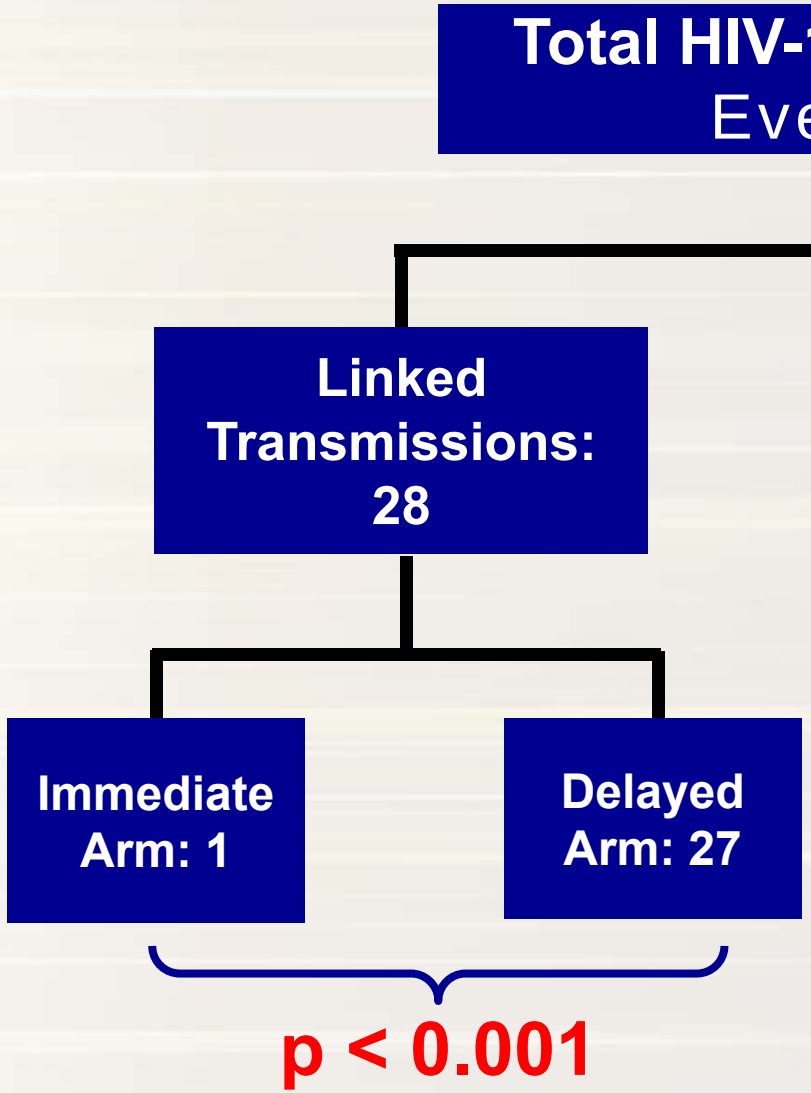
HPTN 052: HIV-1 Transmission

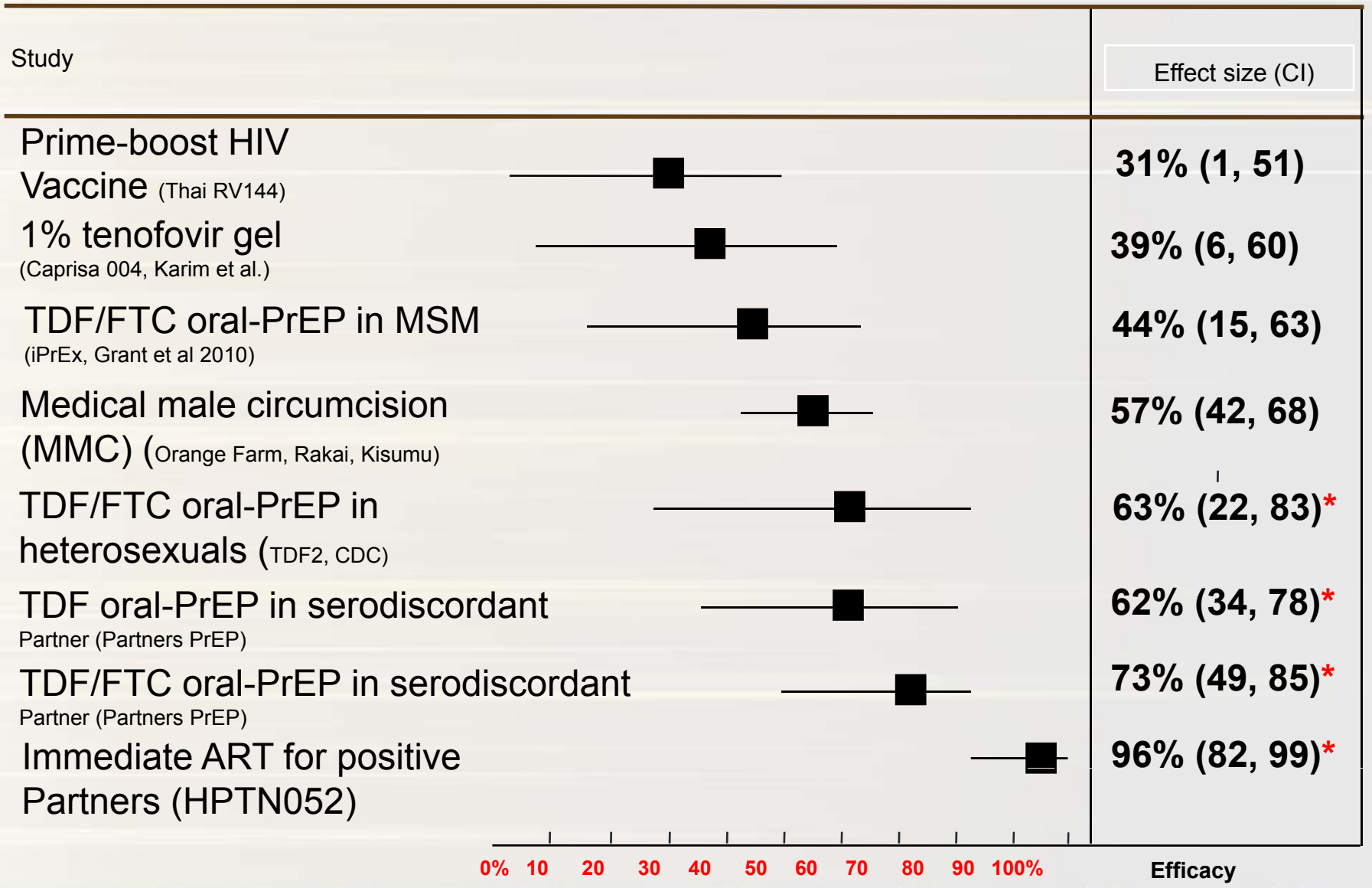


HPTN 052: HIV-1 Transmission



- 18/28 (64%) transmissions from infected participants with CD4 >350 cells/mm^3
- 23/28 (82%) transmissions in sub-Saharan Africa
- 18/28 (64%) transmissions from female to male partners

New biomedical intervention strategies



Partner Cohort Study: HIV Transmission Risk Despite Condomless Sex

- **International Observational Cohort Study of sero-discordant couples**
- **Analyzed transmission risk from HIV+ on ARVs with undetectable viral load from condomless sexual acts – no PEP nor PREP used in HIV-**
- **Analysis of transmissions linked to partner thru phylogenetic analysis**

	Observed Transmissions	95% CI for 100 couple years
Overall	0	0-0.4%
Anal sex	0	0-0.96%
Receptive Anal, with or without ejaculation	0	0-1.97%

- Ten-year risk of HIV Transmission:
  - 0-3.9% overall
  - 0-9.2% for condomless anal sex

Rodger A, et al. 21st CROI; Boston, MA; March 3-6, 2014. Abst. 153LB.

Lo mejor de 2013

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Profilaxis Post-Exposición

INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY SEPTEMBER 2013, VOL. 34, NO. 9

US PUBLIC HEALTH SERVICE GUIDELINE

Updated US Public Health Service Guidelines for the Management of Occupational Exposures to Human Immunodeficiency Virus and Recommendations for Postexposure Prophylaxis

David T. Kuhar, MD;[1] David K. Henderson, MD;[2] Kimberly A. Struble, PharmD;[3]
Walid Heneine, PhD;[4] Vasavi Thomas, RPh, MPH;[4] Laura W. Cheever, MD, ScM;[5]
Ahmed Gomaa, MD, ScD, MSPH;[6] Adelisa L. Panlilio, MD;[1]
for the US Public Health Service Working Group

Profilaxis Post-Exposición

(3) PEP medication regimens should be started as soon as possible after occupational exposure to HIV, and they should be continued for a 4-week duration.

- Although animal studies demonstrate that PEP is likely to be less effective when started more than 72 hours after exposure, the interval after which no benefit is gained from PEP for humans is undefined.

(4) New recommendation—PEP medication regimens should contain 3 (or more) antiretroviral drugs for all occupational exposures to HIV.

Profilaxis Post-Exposición

Preferred HIV PEP Regimen

Raltegravir (Isentress; RAL) 400 mg PO twice daily
Plus
Truvada, 1 PO once daily
(Tenofovir DF 300 mg emtricitabine [FTC] 200 mg)

Lo mejor de 2012

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Consenso sobre el inicio del tratamiento: Recomendaciones de GESIDA 2014

RECOMENDACIÓN GENERAL	
Se recomienda la administración de TAR a todos los pacientes con infección por VIH^{+}. 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

Consenso sobre el inicio del tratamiento: Recomendaciones de la DHHS

Recuento de CD4 (cél/mm$^{3)}$	DHHS 2013
<350	TAR recomendado (AI)
>350 a <500	TAR recomendado (AII)
>500	TAR recomendado (BIII)

Gesida 2014: Combinaciones de TAR de Inicio

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

DHHS Guidelines Update October 2013: Combinaciones de TAR de Inicio

	Preferred Regimens	Alternative Regimens
NNRTI	▪ EFV/TDF/FTC	▪ EFV + ABC/3TC ▪ RPV/TDF/FTC or RPV + ABC/3TC
Boosted PI	▪ ATV/RTV + TDF/FTC ▪ DRV/RTV + TDF/FTC	▪ ATV/RTV + ABC/3TC ▪ DRV/RTV + ABC/3TC ▪ FPV/RTV + (TDF/FTC or ABC/3TC) ▪ LPV/RTV + (TDF/FTC or ABC/3TC)
INSTI	▪ **RAL + TDF/FTC** ▪ **EVG/COBI/TDF/FTC** ▪ **DTG + ABC/3TC** ▪ **DTG + TDF/FTC**	▪ **RAL + ABC/3TC**

Lo mejor de 2013

1. Tratamiento del VHC
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4. Transmisión en serodiscordantes
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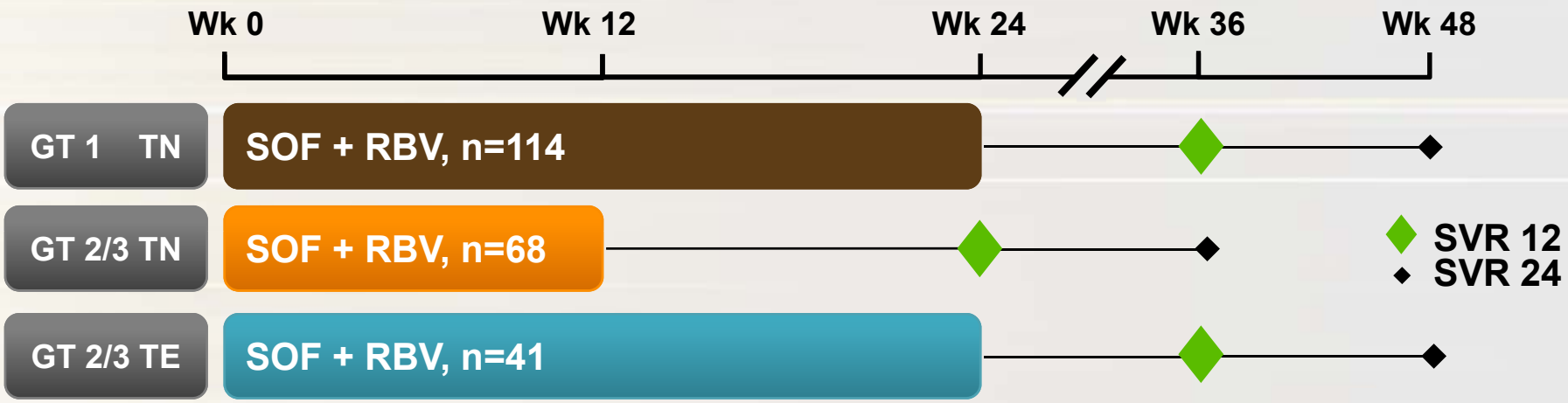
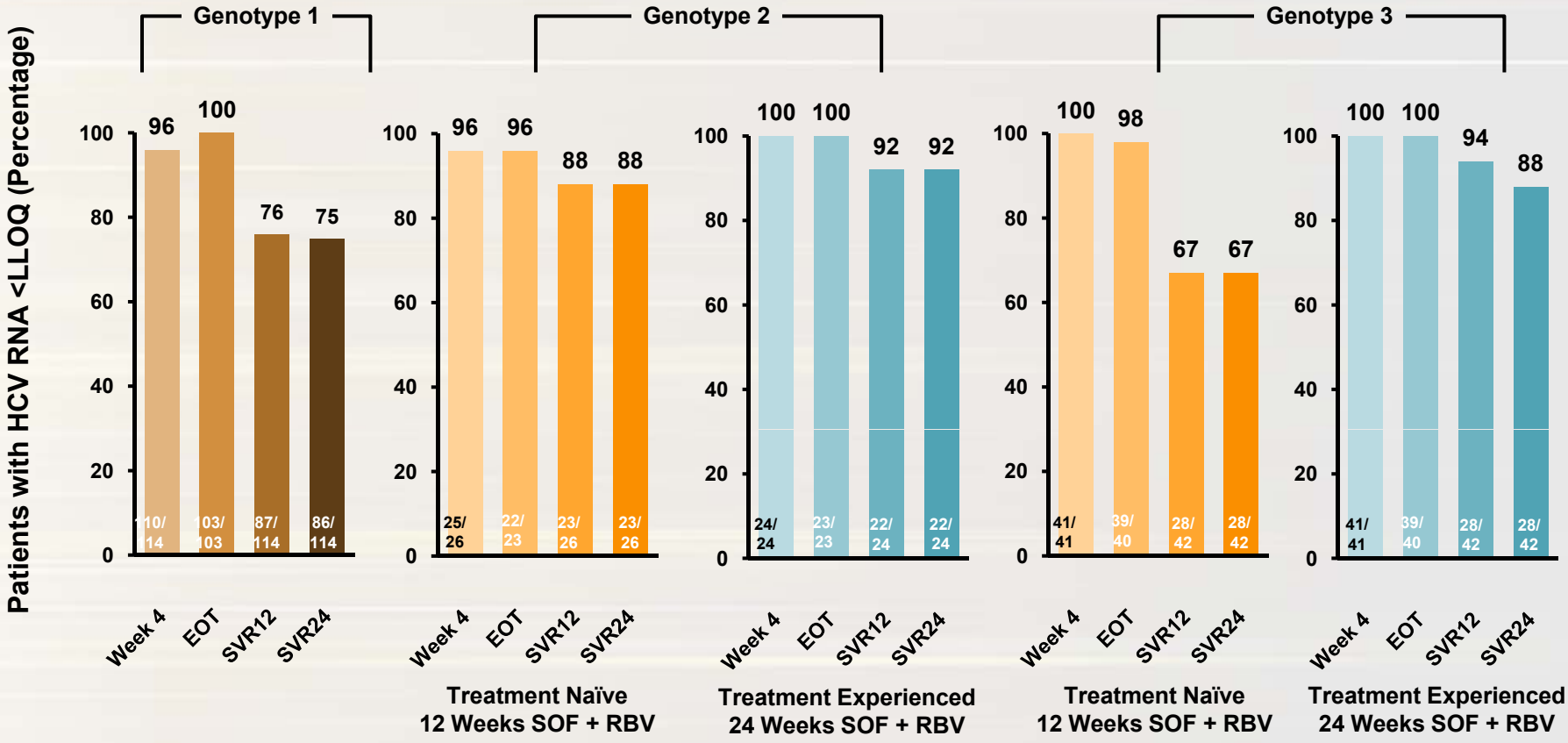
PHOTON-1: Study Design



- **Broad inclusion criteria**
  - Cirrhosis permitted with no platelet cutoff
  - Hemoglobin: ≥12 mg/dL (males); ≥11 mg/dL (females)
- **Wide range of ART regimens allowed**
  - Undetectable HIV RNA for >8 weeks on stable ART regimen
- **Baseline CD4 count**
  - ART treated: CD4 T-cell count >200 cells/mm^3 and HIV RNA <50 c/mL
  - ART untreated: CD4 T-cell count >500 cells/mm^3

Naggie S, et al. 21st CROI; Boston, MA; March 3-6, 2014. Abst. 26.

PHOTON-1 Study: Virologic Response - Genotype 1, 2, and 3



Naggie S, et al. 21st CROI; Boston, MA; March 3-6, 2014. Abst. 26.

PHOTON-1 Study: Virologic Outcome

Outcome, n (%)	Treatment Naïve			Treatment Experienced	
	GT 1 n=114	GT 2 n=26	GT 3 n=42	GT 2 n=24	GT 3 n=17
SVR12	87 (76)	23 (88)	28 (67)	22 (92)	16 (94)
HCV virologic failure	26 (23)	1 (4)	12 (29)	1 (4)	1 (6)
Relapse	25 (22)	0	12 (29)	1 (4)	1 (6)
Completed study drug	19	0	11	0	1
Did not complete study drug	6	0	1	1	0
HCV viral breakthrough	1 (<1)	1 (4)	0	0	0
Other	1 (<1)	2 (8)	2 (5)	1 (4)	0

Naggie S, et al. 21st CROI; Boston, MA; March 3-6, 2014. Abst. 26.

PHOTON-1 Study: Safety Summary

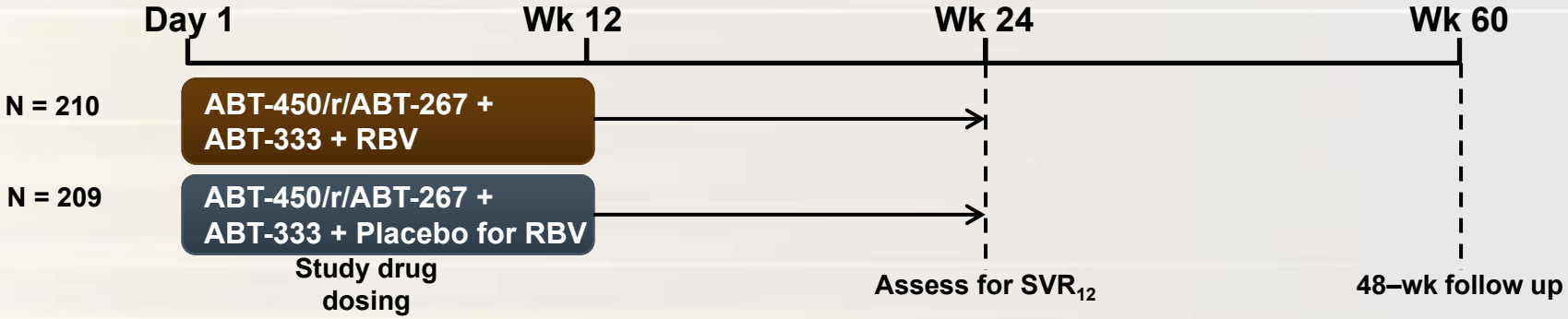
Patients, %	SOF + RBV	
	24 Weeks (n=155)	12 Weeks (n=68)
AEs	92	84
AEs in ≥10% of patients		
Fatigue	39	35
Insomnia	15	21
Headache	14	13
Nausea	15	18
Diarrhea	11	9
Irritability	10	10
URI	12	12
Grade 3-4 AEs	12	10
Serious AEs	6	7
Treatment D/C due to AEs	3	4
Death	0	1

Naggie S, et al. 21st CROI; Boston, MA; March 3-6, 2014. Abst. 26.

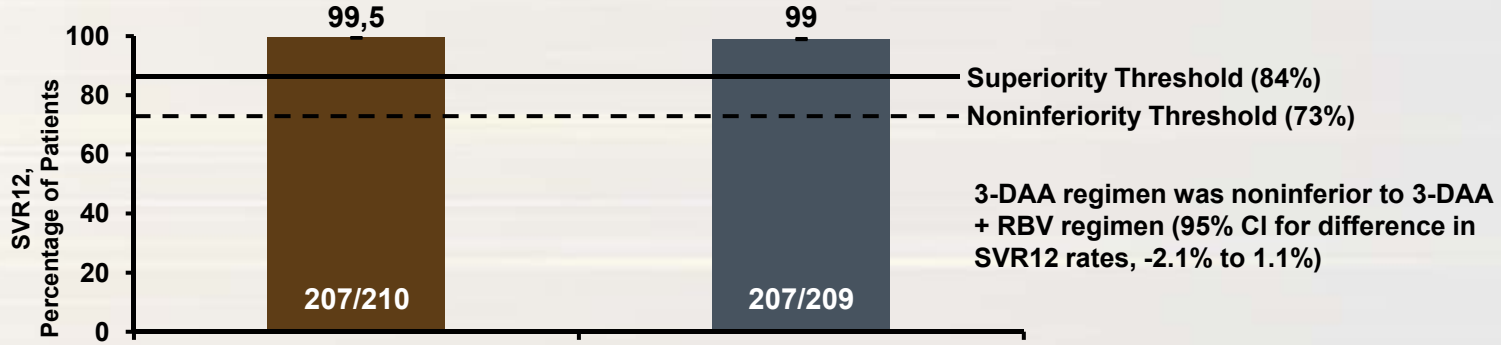
PEARL-III Study: ABT-450/r/ABT-267 + ABT-333 ± RBV in treatment-naive GT1b

Study Design

- ABT-450/r/ABT-267: 150 mg/100 mg/25 mg QD
- ABT-333: 250 mg BID
- RBV: 1,000 mg if body weight was <75 kg, 1,200 mg if body weight ≥75 kg, or matching placebo



SVR_{12} ≥99% Achieved after 12 Weeks with 3-DAA ± RBV



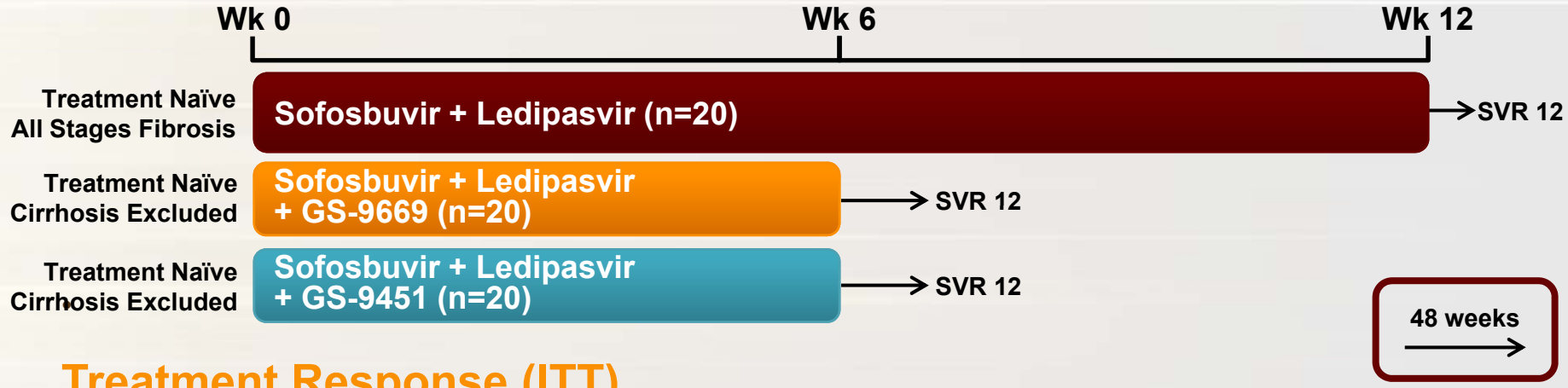
ITT population
Dashed horizontal line depicts noninferiority threshold
Solid horizontal line depicts superiority threshold

Ferenci P, et al. 21st CROI; Boston, MA; March 3-6, 2014. Abst. 29LB.

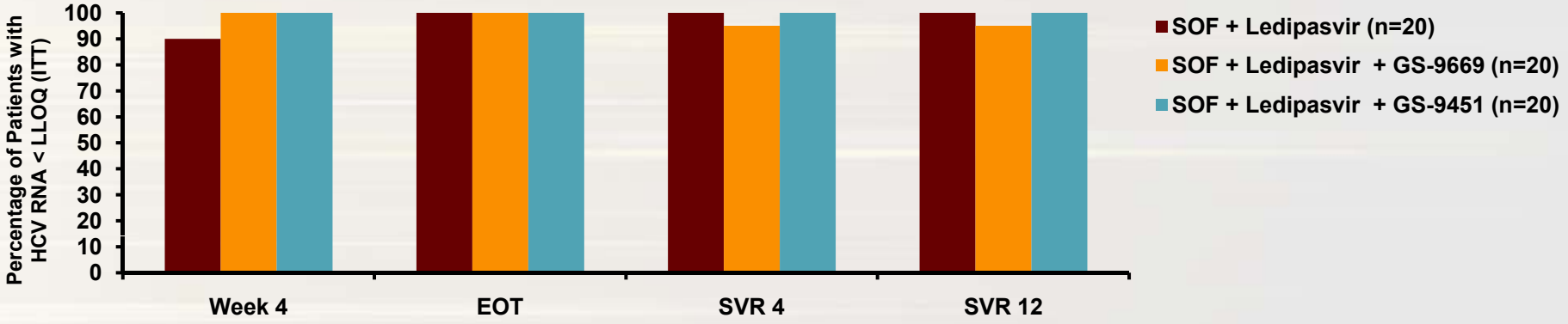
SYNERGY (NIH Trial): Sofosbuvir + Ledipasvir ± GS-9669 or GS-9451 in HCV GT1

Study Design

- Sofosbuvir (nucleotide NS5B inhibitor) 400 mg/ledipasvir (NS5A inhibitor) 90 mg once daily
- GS-9669 (non-nucleoside NS5B inhibitor) 500 mg once daily
- GS-9451 (a protease/NS3/4 inhibitor) 80 mg once daily



Treatment Response (ITT)



Kohli A, et al. 21st CROI; Boston, MA; March 3-6, 2014. Abst. 27LB.

Lo mejor de 2013

1. Tratamiento del VHC: Una revolución
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