XIII Curso Internacional de Enfermedades Infecciosas,
XIV Seminario Integral del Sida
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SIMPLIFICACIÓN DEL TRATAMIENTO ARV

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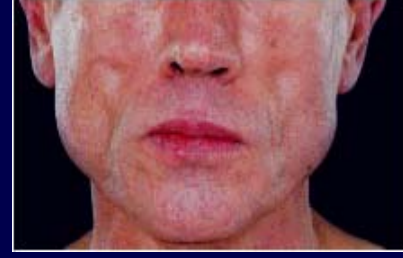
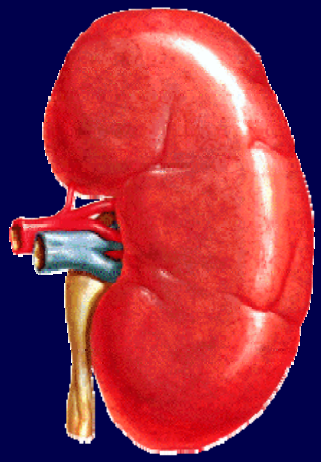
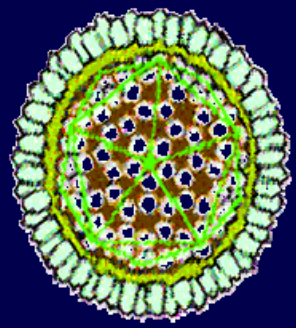
Identificar la opción correcta:

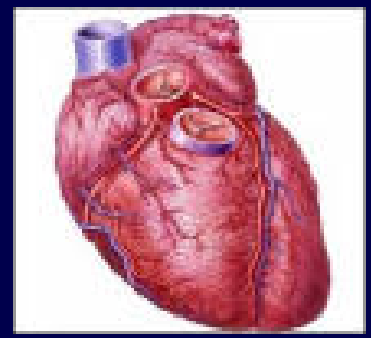
a) **Simplificación de la terapia ARV implica reducción de la potencia.**
b) **Simplificación suele favorecer la adherencia.**
c) **Simplificación resulta siempre en mejor perfil metabólico.**
d) **Simplificación puede aplicarse siempre que la carga viral sea < a 10.000 copias/mL**
e) **No sé, vine a aprender.**

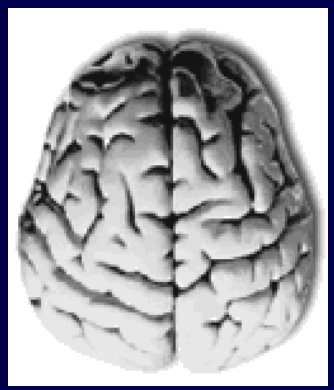
VIH es una enfermemedad crónica

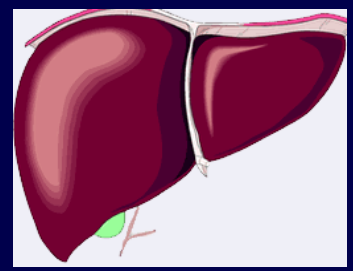






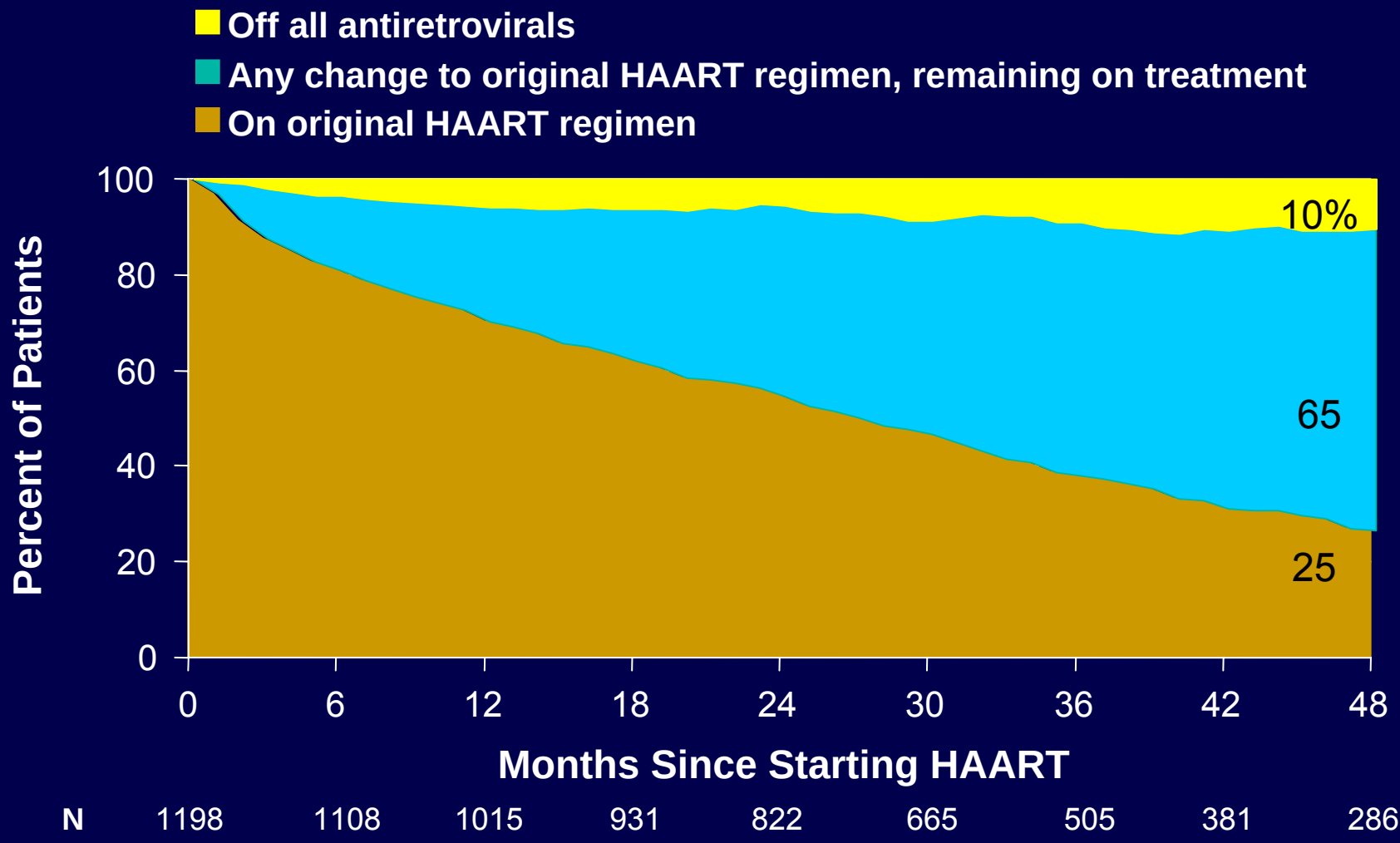






Médicos Tratantes

Changes to a First HAART Regimen Eurosida (n: 1198)



Adapted from Mocroft A, et al.
AIDS Res Hum Retroviruses 2005;21:527-536

¿POR QUE FRACASAN LOS TRATAMIENTOS ARV?

- Potencia
- Farmacocinética
- Interacción de drogas
- Adherencia
- Toxicidad
- Resistencia viral

¿Por qué cambiar un régimen exitoso?

Simplificación

- Mejorar la adherencia a largo plazo

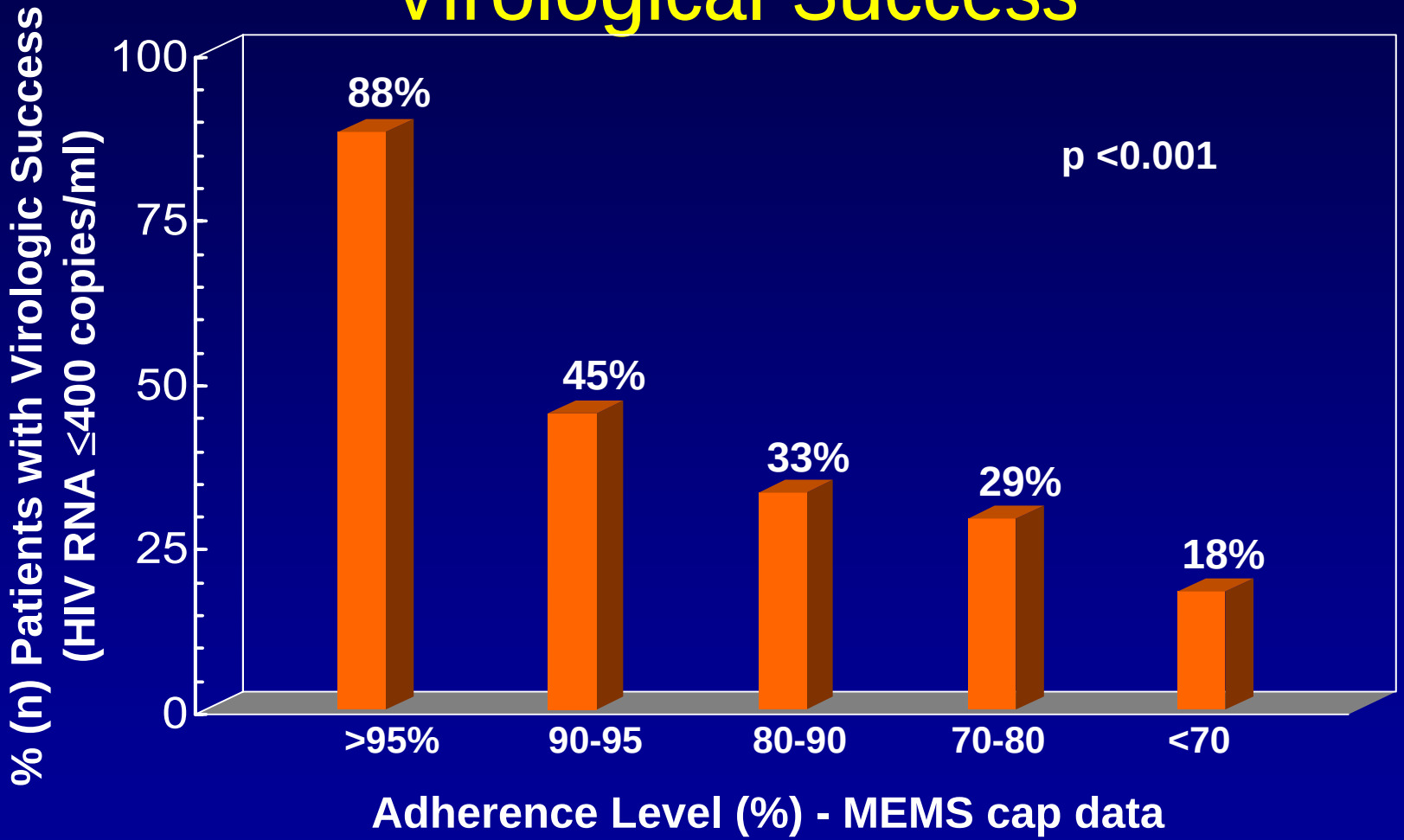
Toxicidad

- Reducir el riesgo de eventos adversos a largo plazo

Farmacocinética

- Maximizar el beneficio farmacológico con drogas de vida media mas larga

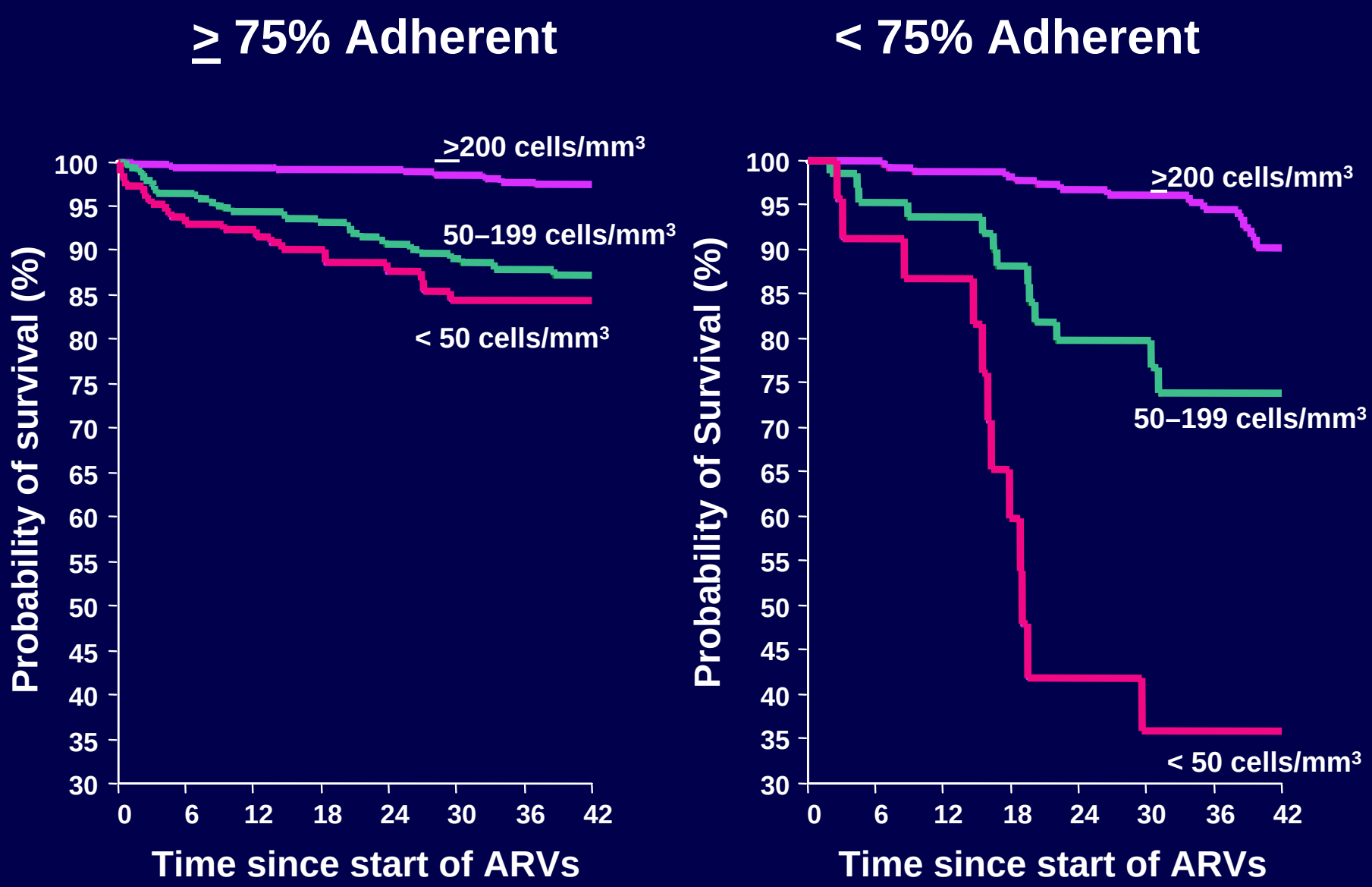
Correlation Between Adherence and Virological Success



→ >95% adherence is required to achieve undetectable viral loads in 80% of patients

Paterson D *et al.* Ann Intern Med 2000; 133:21-30

Impact of Adherence

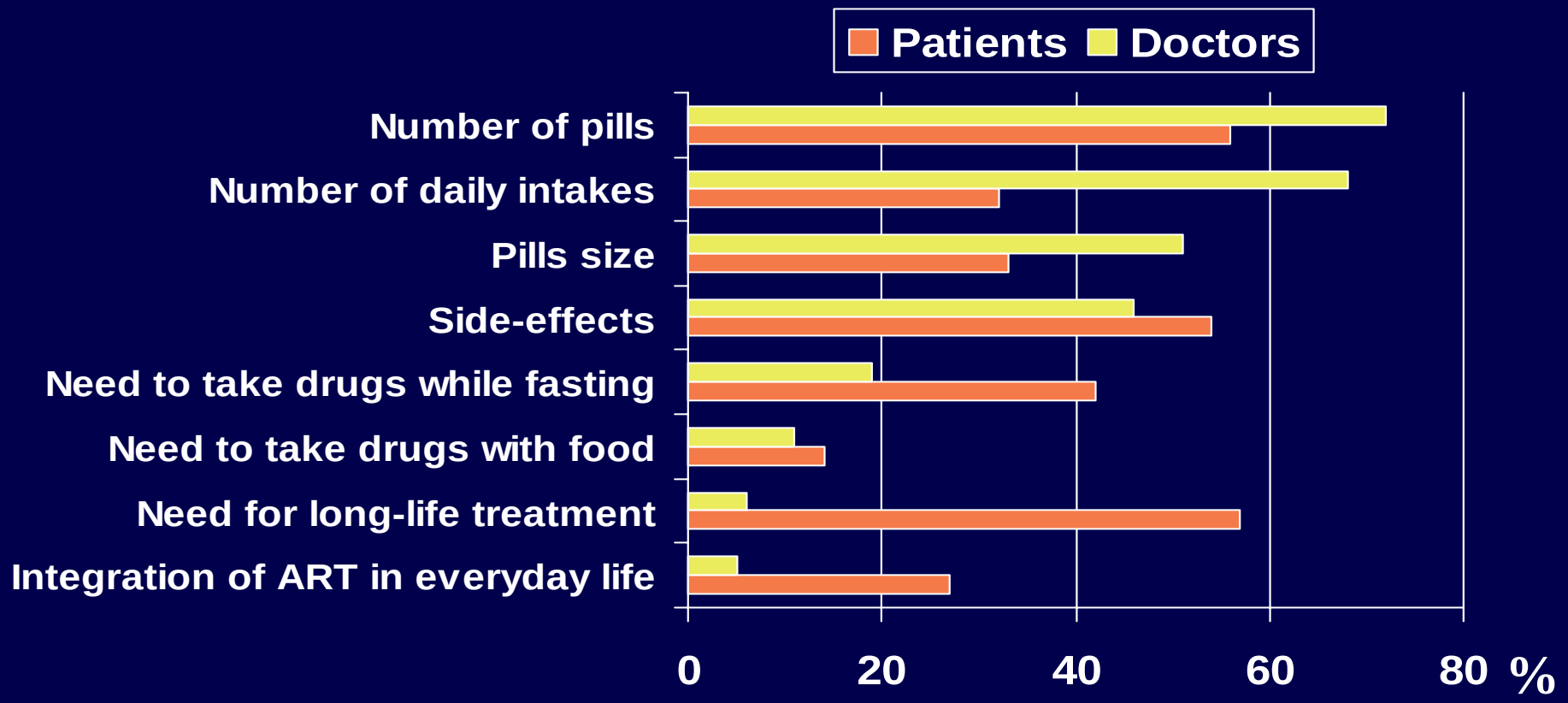


Wood et al. *AIDS*. 2003;17(5):711-20

¿Qué es la adherencia?

Patients and Doctors Perspective on Adherence difficulties

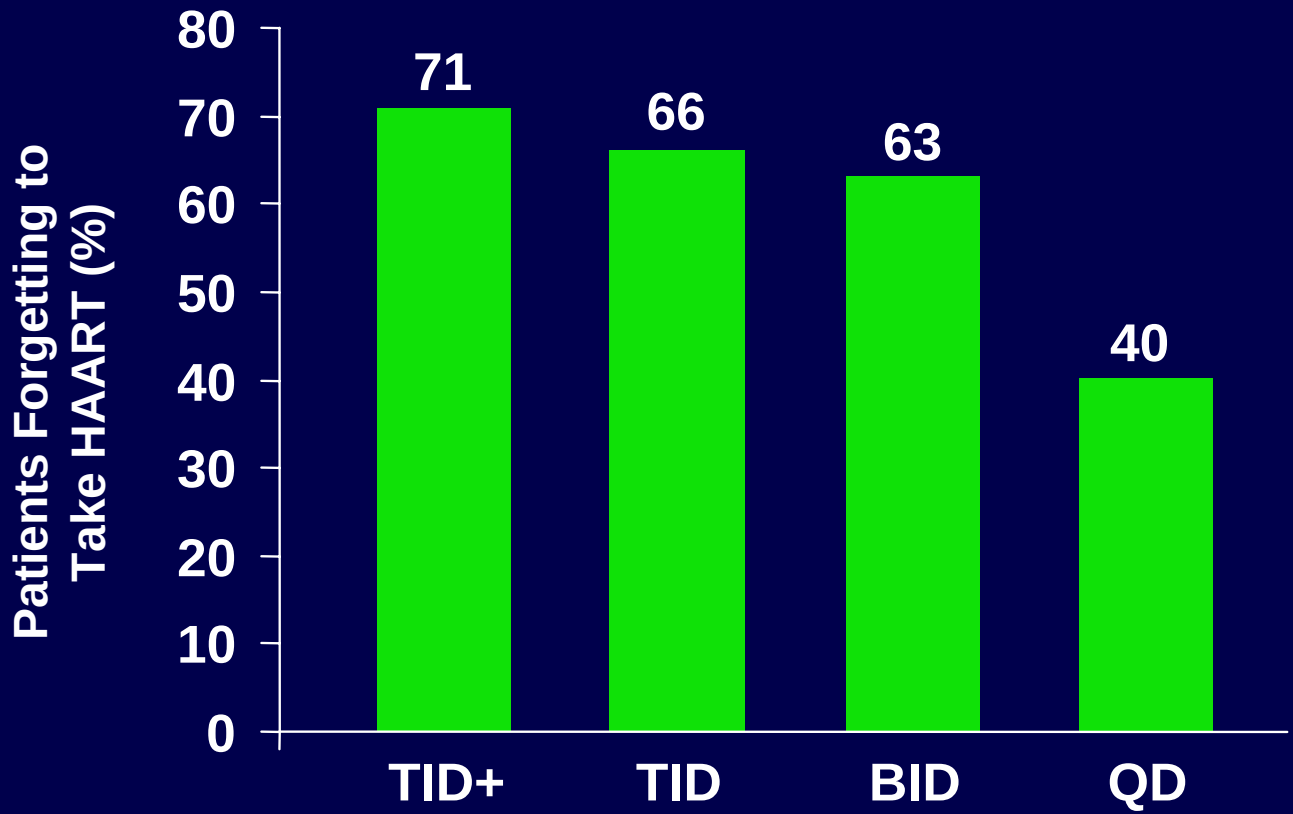
National survey (1999) : 1599 patients, 138 AIDS physicians



AIDES, Fédération Nationale, Nov 1999

F. Raffi, 4/2000

Fewer Patients Forget to Take QD Regimens

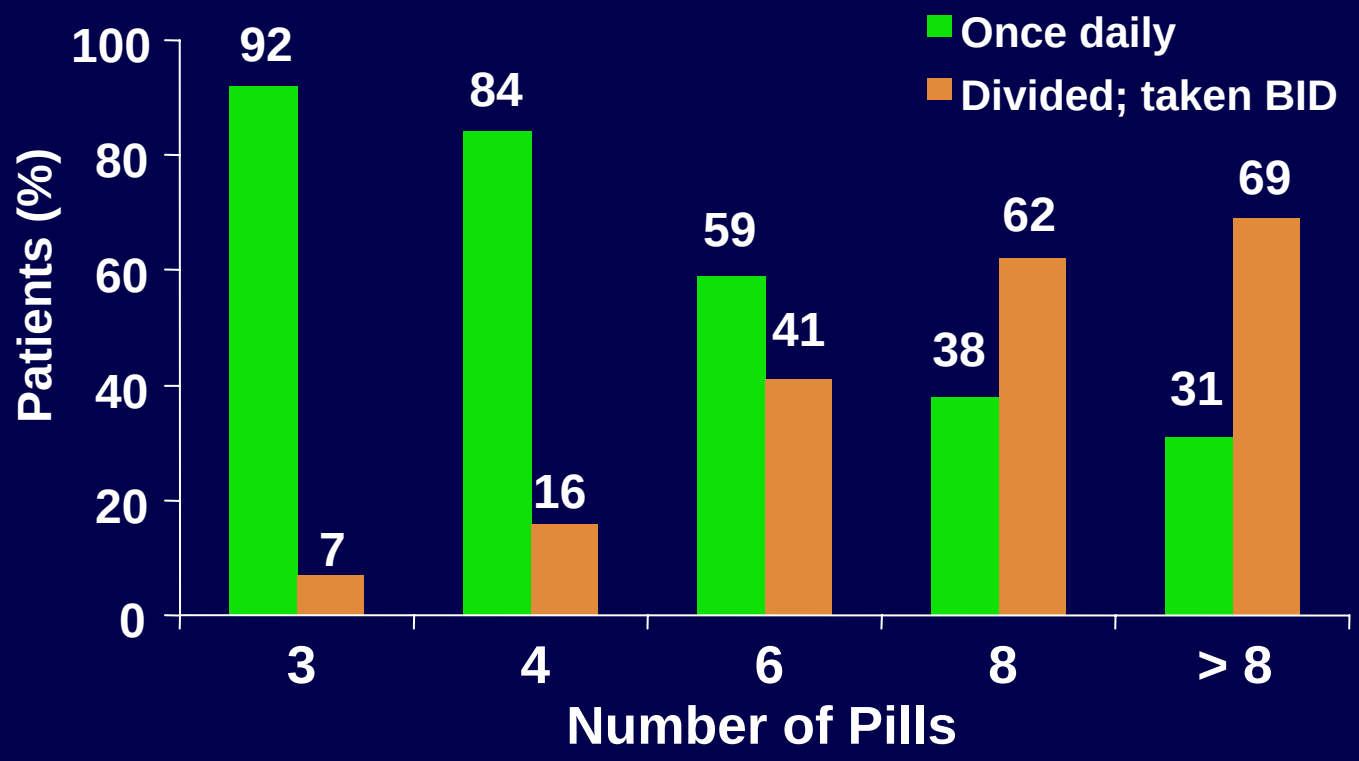


- Forgetting rates reported by 438 of 504 patients in standardized interviews
- Patients answered the APPT-1 pan-European survey

Moyle et al. 6th ICDTHI. Abstract 99.

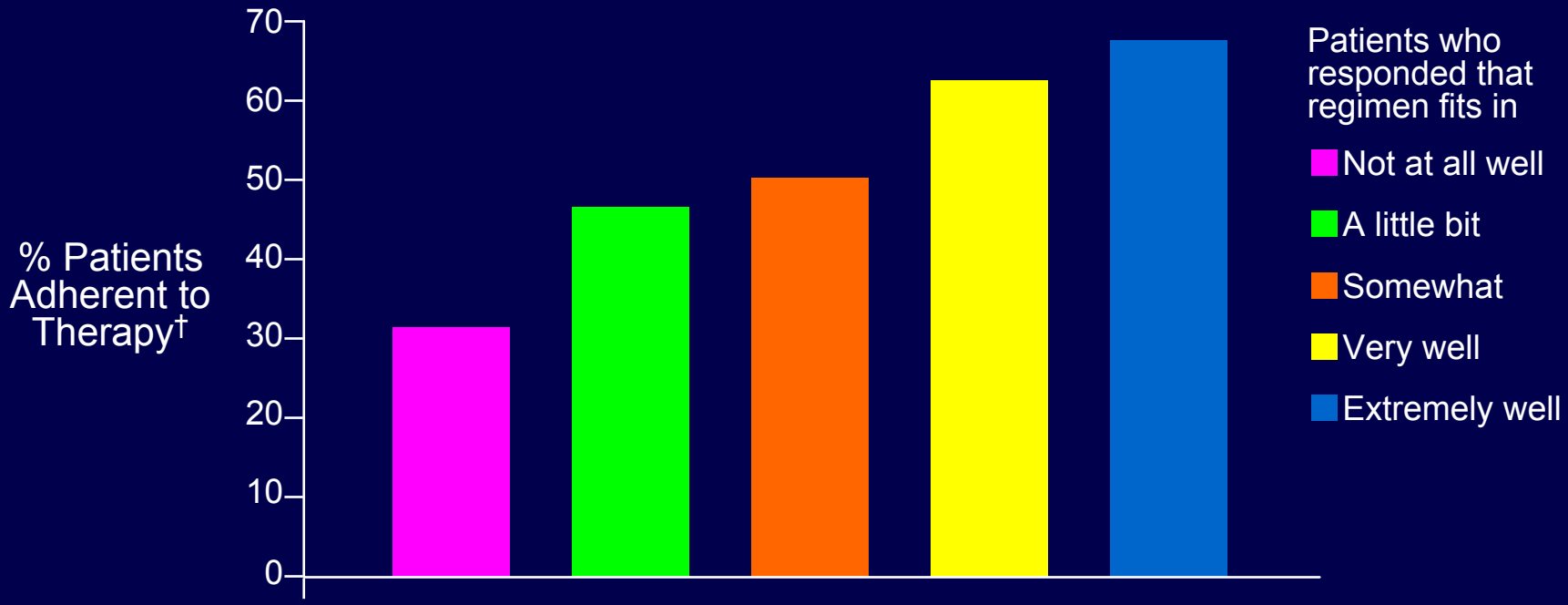
Patients Prefer QD Regimens *If* Low Pill Burden

"If you were to take a certain number of pills each day, how would you prefer them to be administered?"



Moyle et al. 6th ICDTHI. Abstract 99.

Correlation With How Well Regimen Fits Patients' Daily Life* (N = 1910)



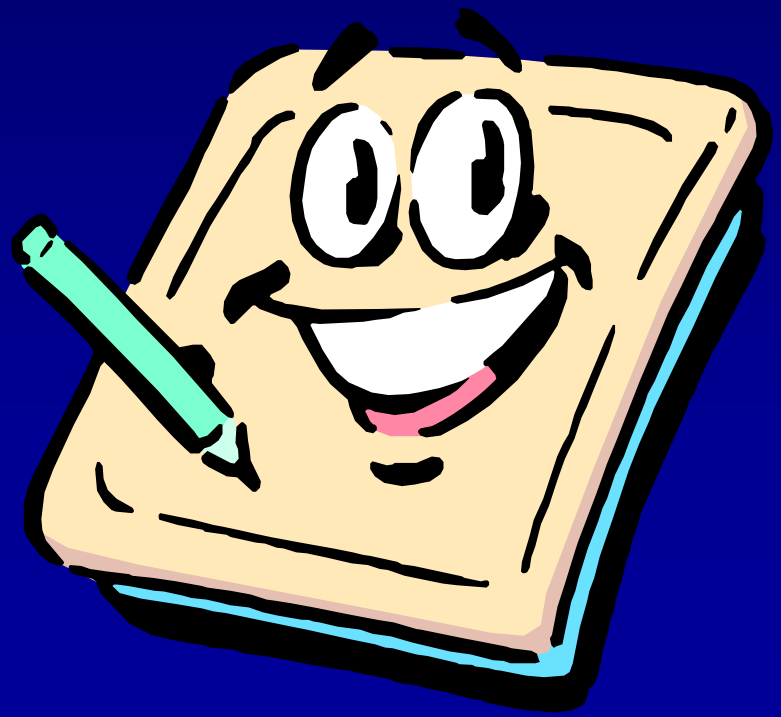
*$P < .001$.

†Patients who reported no missed doses in the past week.

Data from Wenger et al. Poster presented at: 6th Conference on Retroviruses and Opportunistic Infections; January 31–February 4, 1999; Chicago, Ill. Poster 98.

SIMPLIFICACIÓN:

¿Se puede simplificar sin perder potencia?



ESTRATEGIAS DE SIMPLIFICACIÓN

- DESINTENSIFICACION
- **MANIPULACION DE INTERACCIONES**
- **EXTENSIÓN DEL INTERVALO DE TOMA**
- **CAMBIO AHORRADOR DE UNA CLASE**
- **FORMULACIONES COMBINADAS / NUEVAS**
- **STI**

ESTRATEGIAS DE SIMPLIFICACIÓN:

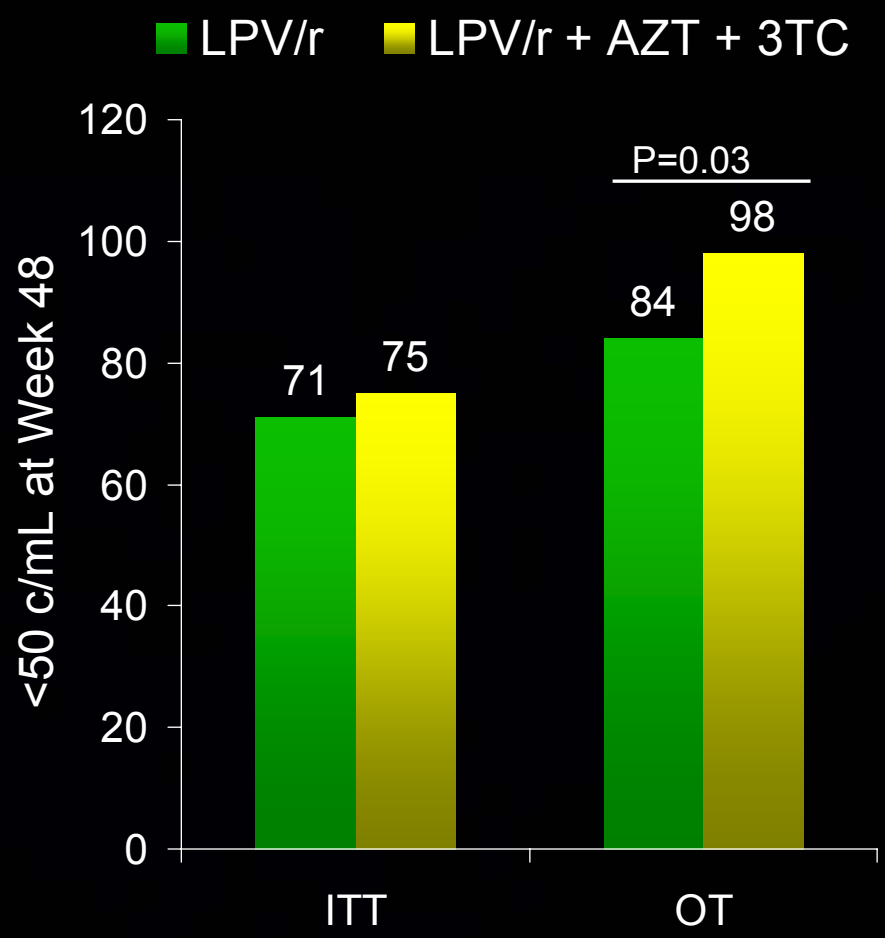
DESINTENSIFICACIÓN

- ADAM: 62 pts, 26 semanas de 4 drogas, CVND, randomizan a 2 ó 4 drogas. A 36 semanas: 64 vs. 9% CV > 50
- TRILEGE: 277 pts, 12 semanas, CVND, randomizan a 2 ó 3 drogas. Fallo: 22 y 31% vs 9%
- ACTG-343: 316 pts, 24 semanas, CVND, randomizan a 1,2 ó 3 drogas. Fallo: 22% vs 3%

Monoterapia con IP/r?

MONARK: LPV/r Monotherapy

- Prospective trial of LPV/r monotherapy in ARV-naïve pts (n=136)
  - LPV/r vs. LPV/r + AZT/3TC
  - HIV RNA ≤100,000 c/ml and CD4+ ≥100 c/mm^3
- Predictive factors for efficacy for monotherapy
  - Viral subtype B vs non B
  - Baseline Viral load
  - Early virologic response
  - LPV trough levels and compliance evaluation were not associated with Virologic response



Studies of Lopinavir/Ritonavir Monotherapy

IMANI study: initial therapy[1]

- Pilot study, 30 treatment-naive pts treated with LPV/r monotherapy
  - 18/30 VL < 50 copies/mL at Week 48
  - 3/30 virologic failure; others stopped or lost to follow-up

Only *Kaletra* (OK) study: maintenance therapy[2]

- 42 pts with VL < 50 copies/mL for > 6 months
  - On LPV/r + 2 NRTIs for > 1 month
  - No history of PI failure
  - Randomized to continue 3-drug HAART or switch to LPV/r monotherapy
- Week 24: 3/21 viral rebound in OK arm, 0/21 in HAART arm
  - No detectable primary PI mutations
  - Pts with rebound had shorter time with VL < 50 than pts without failure
    - 218 vs 1095 days; $P = .002$

1. Gathe et al. Abstract MoOrB1057. **2.** Arribas et al. Abstract TuPeB4486 Bangkok 2004.

CAMBIO DE IP A REGIMENES SIN IP

⇩ Menor nº de comprimidos

⇩ No requerimientos de ayuno/dieta/hidratación

⇩ Menor nº de dosis diarias

⇩ Menor incidencia de efectos GI

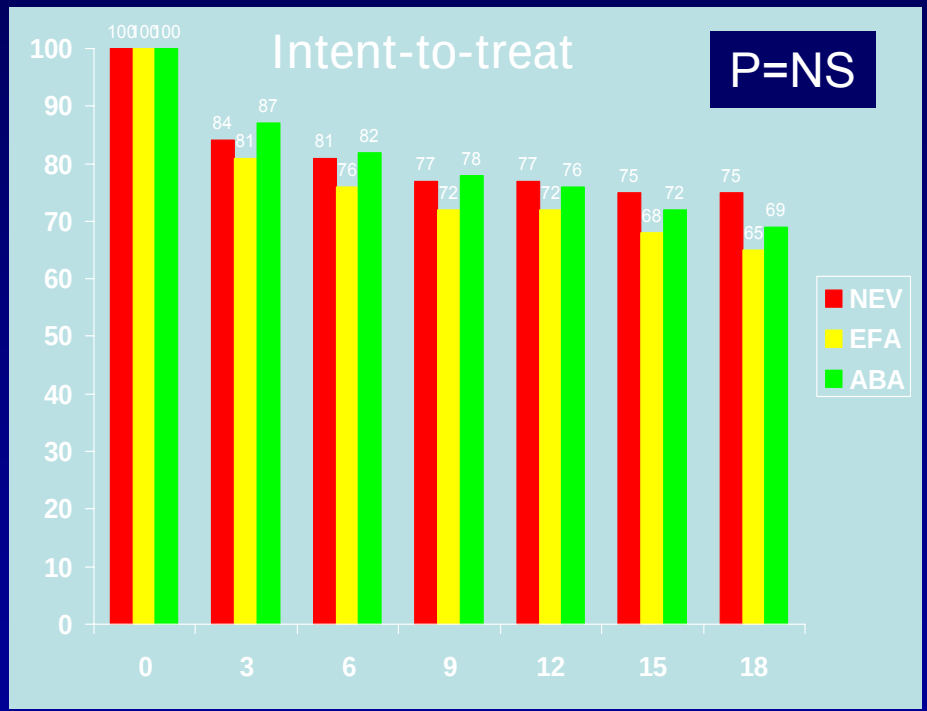
⇩ Menor incidencia de lipodistrofia

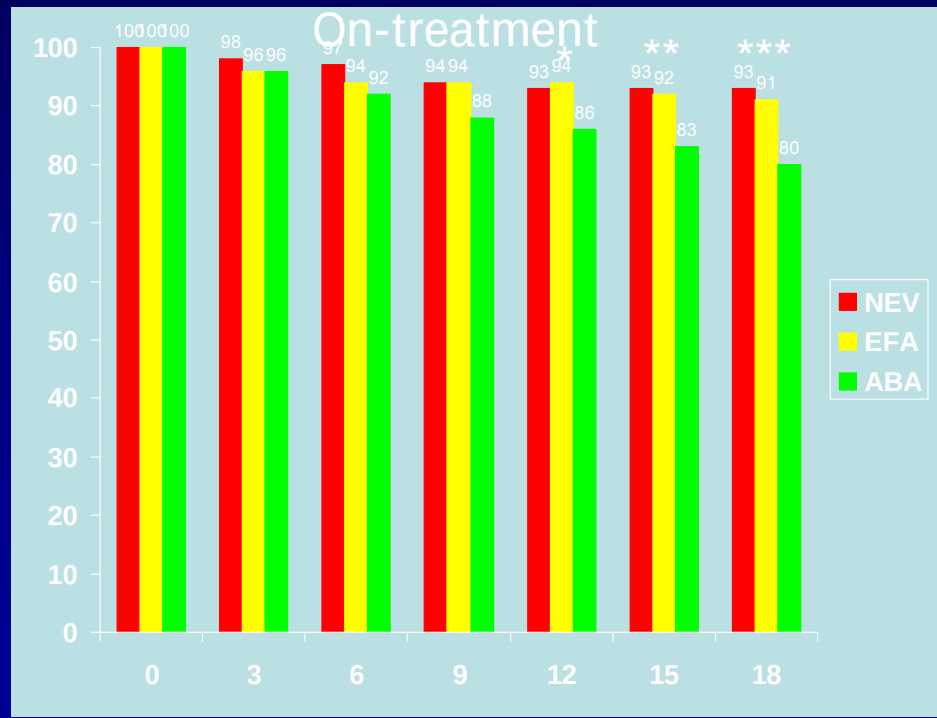
SWITCHING PROTEASE INHIBITORS TO NEVIRAPINE, EFAVIRENZ OR ABACAVIR: A RANDOMIZED, MULTICENTER, OPEN-LABEL, SIMPLIFICATION TRIAL

(**N**EV/**EFA**/**A**BA Trial)

Percentage remaining <200 copies/mL

*P=0.038
**P=0.019
***P=0.002





Virological efficacy vs. treatment-limiting toxicity

The NEW ENGLAND JOURNAL of MEDICINE 2003 349:1036-1046

Frequency of Dosing is Critical to Maintain Adherence in Other Chronic Disease Areas

Regimen	Adherence
Once a day	73%
Twice a day	70%
Three times daily	52%
Four times daily	42%

- Once a day and twice a day regimens are associated with significantly better adherence

Greenberg RN. Clinical Therapeutics 1984; **6**(5): 590-599.

EXTENSIÓN DEL INTERVALO DE TOMA

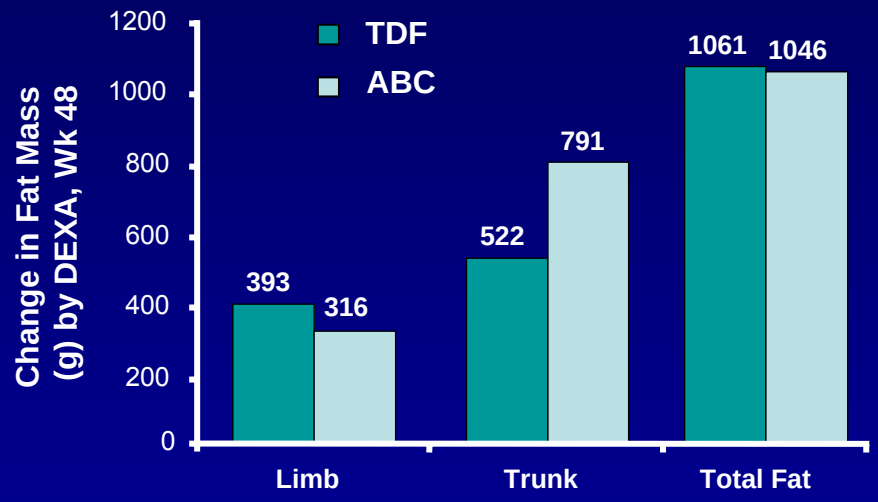
- ddI-EC
- d4T XR
- 3TC
- FTC
- TDF
- NNRTI's:DLV (200 mg) y EFV (600 mg)
- HGC-SQV 800 mg para coadministración con RTV
- HCG-SQV cápsulas 500 mg
- Nelfinavir 625-mg para uso BID
- FOS-APV + RTV OAD

ARVs aprobados para uso UAD:

- Didanosina
- Efavirenz
- Emtricitabina
- Lamivudina
- Tenofovir DF
- Abacavir
- Saquinavir/r
- Atazanavir
- Fosamprenavir
- Tenofovir /emtricitabina
- Tenofovir /emtricitabina/Efavirenz
- Abacavir/lamivudina
- Lopinavir/r

RAVE Study: Switch Thymidine Analogue to ABC or TDF

- Suppressed patients with self-defined lipoatrophy on thymidine analogue NRTI
- 105 pts randomized to replace TA with:
  - tenofovir, or
  - abacavir
- Total limb fat increased to similar extent in both arms over 48 weeks

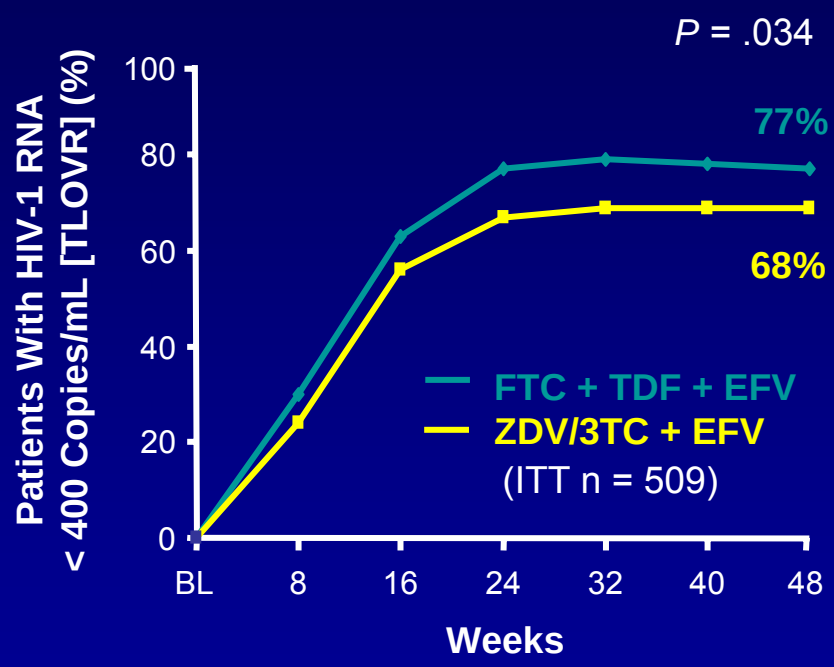


Within-group change in limb fat from baseline: TDF *P* = .01, ABC *P* = .001

Moyle G, et al. CROI 2005. Abstract 44LB.

GS934: Week-48 Virologic Response

- N = 517 antiretroviral-naive patients randomized to:
  - TDF + FTC + EFV
  - ZDV/3TC FDC + EFV
- Superior efficacy with TDF + FTC
- More discontinuations for AEs with ZDV/3TC
- Less dyslipidemia with TDF + FTC
- Greater increase in limb fat with TDF + FTC



Excluding pts with baseline NNRTI resistance
FTC + TDF 80% vs ZDV/3TC 70% (*P* = .021)

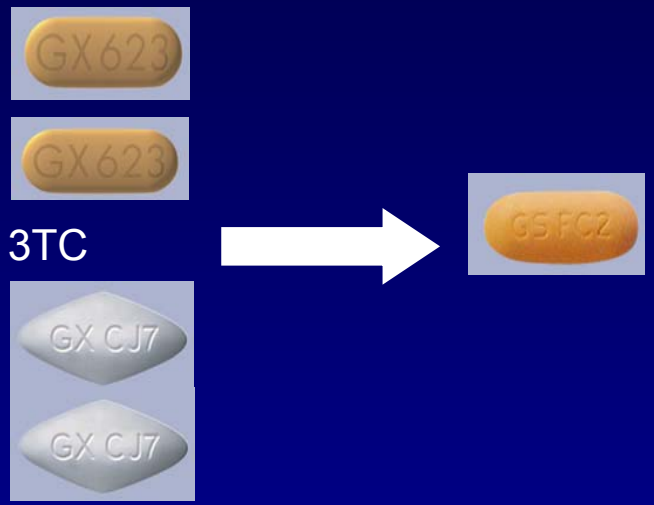
1. Pozniak AL, et al. IAS 2005. Abstract WeOa0202.
2. McColl D, et al. IAS 2005. Abstract TuPp0305.

GS934: Week-48 Treatment Outcomes

Outcome (ITT Analysis)	TDF + FTC + EFV (n = 255)	ZDV/3TC FDC + EFV (n = 254)	*P* Value
HIV-1 RNA < 400 copies/mL, %	81	70	.005
Virologic failure,* %	2	4	NS
Discontinuation due to adverse event, %	4	9	.016
Fasting triglycerides, mean change, mg/dL	+3	+31	.384
Total cholesterol, mean change, mg/dL	+21	+35	< .001
Total limb fat, mean change, kg	8.9 ± 5.4 (n= 50)	6.8 ± 3.8 (n = 46)	.031

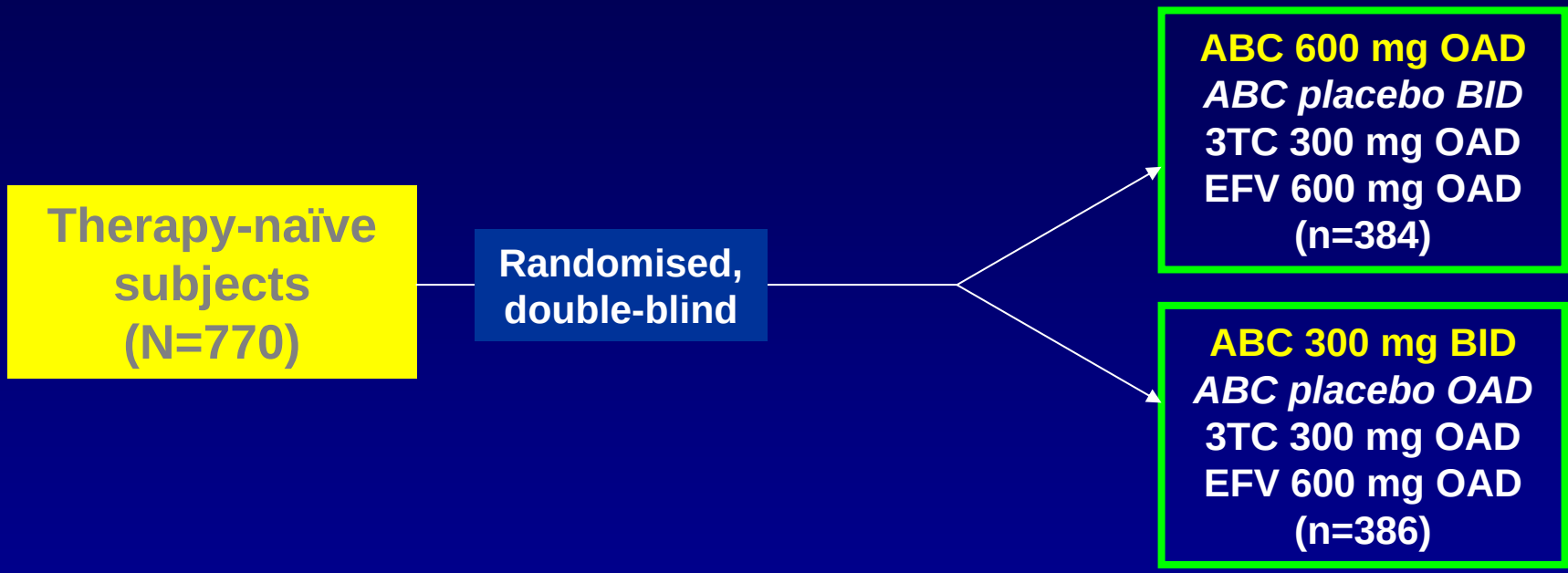
1. Pozniak AL, et al. IAS 2005. Abstract WeOa0202.
2. McColl D, et al. IAS 2005. Abstract TuPp0305.

Abacavir/Lamivudine (ABC/3TC)



- Approved August 2004
- Formulation
  - Orange tablet containing 600 mg ABC and 300 mg 3TC
- Recommended dose
  - 1 tablet daily, with or without food
- Adverse effects
  - Hypersensitivity reaction
- Impaired renal/hepatic function
  - Do not use if creatinine clearance < 50 mL/min
  - Not recommended in patients with hepatic impairment
- Comments
  - Severity of ABC hypersensitivity may be higher when ABC dosed once daily

CNA30021: Abacavir OAD Versus BID in Combination With Lamivudine and Efavirenz in ART-naïve Adults



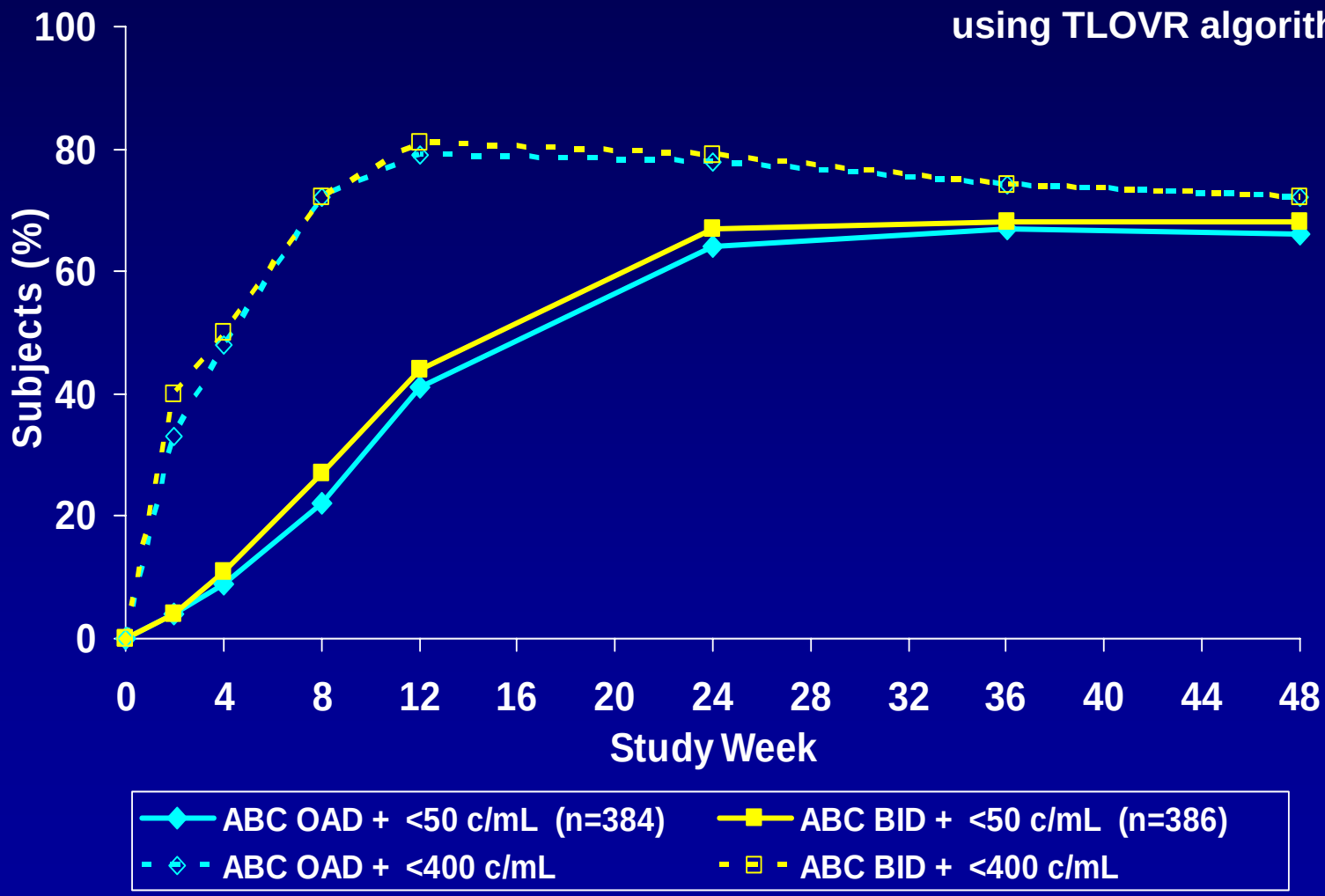
- **To assess non-inferiority of ABC OAD vs. ABC BID**
- **Endpoint: virological response (HIV-1 RNA <50 copies/mL) at 48 weeks, using TLOVR algorithm**

Moyle et al. JAIDS, in press

OAD – once-daily
BID – twice-daily

CNA30021

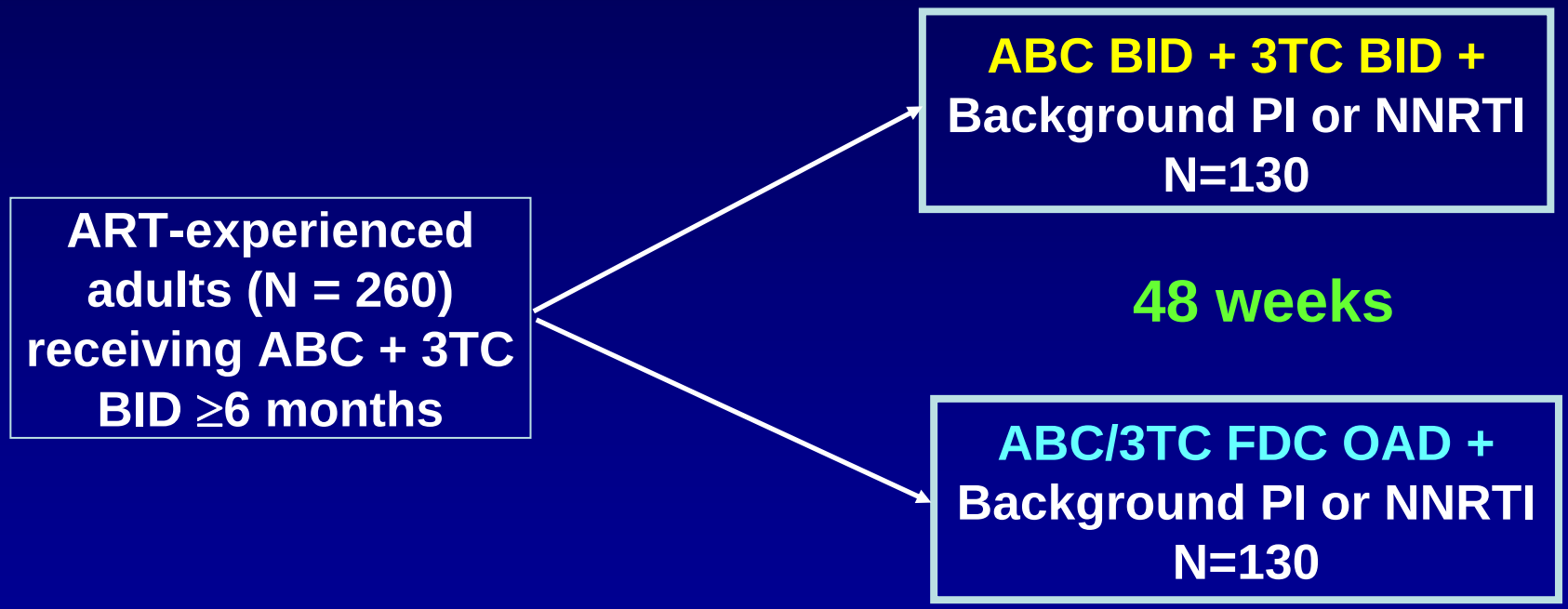
Virological Response Over 48 Weeks - ITT



Moyle et al. JAIDS, in press

ESS30008 Study Design

Phase III, randomised, open-label, multicentre study

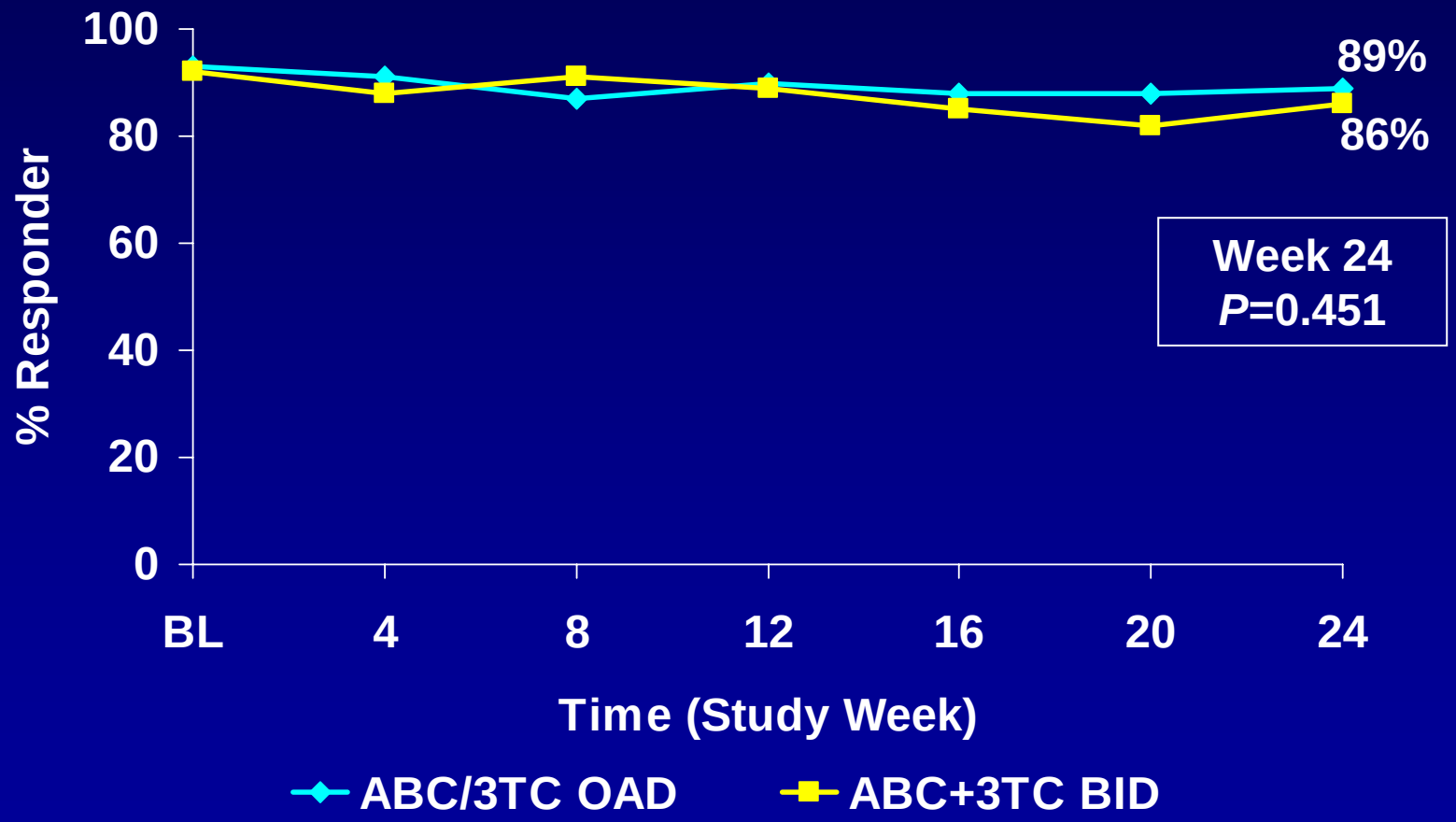


- ≥6 months ABC + 3TC BID + PI or NNRTI (initial regimen)
- HIV-1 RNA <400 copies/mL for ≥3 months
- CD4+ ≥50 cells/mm^3
- Enrollment stratified by background ART (PI or NNRTI)

Sosa et al. 7th ICDTH, Glasgow, 2004

ESS30008

HIV-1 RNA <50 Copies/mL Through Week 24 (ITT Missing = Failure)



Sosa et al. 7th ICDTH, Glasgow, 2004

ESS30008

Treatment-related Adverse Events (>1%)

	ABC/3TC OAD (n=130)	ABC+3TC BID (n=130)
Subjects with ANY treatment-related AE	15 (12%)	6 (5%)
Nausea	4 (3%)	0
Diarrhea	2 (2%)	1 (<1%)
Asthenia	2 (2%)	0
Dizziness	2 (2%)	0
Hypercholesterolemia	0	2 (2%)

Sosa et al. 7th ICDTH, Glasgow, 2004

ABC/3TC

- Bien tolerado
- 1 píldora diaria, sin restricciones dietarias
- Sin evidencia de toxicidad mitocondrial
- L74V>K65R: no cruza con TDF
- Mejor respuesta de CD4+ que AZT/3TC
- ABC HSR, factor de confusión con NNRTIs
- Requiere instrucciones especiales al paciente
- El fallo con M184V → ↓ susceptibilidad a ABC & 3TC

AZT/3TC

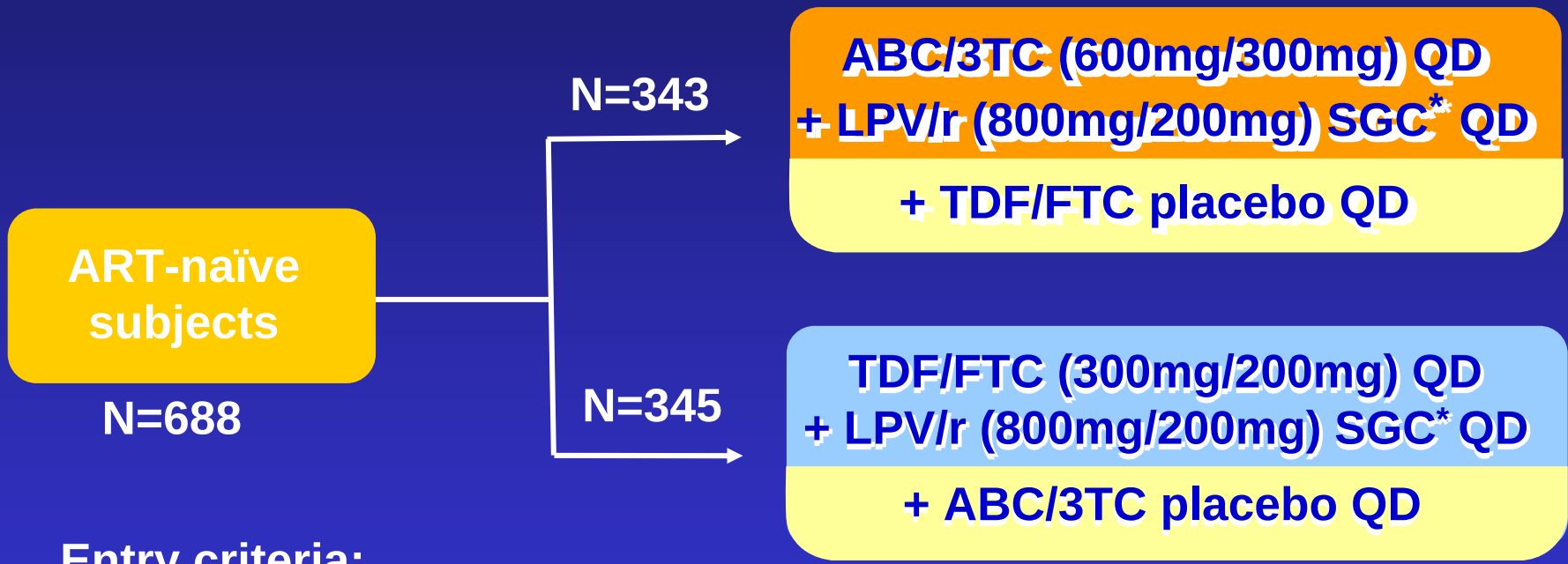
- Años de experiencia clínica
- Prevención de K65R o L74V
- Emergencia gradual y secuencial de TAMs
- BID , 2 píldoras/día
- TAMs :Resistencia cruzada
- Efectos adversos GI
- Toxicidad hematológica
- Toxicidad mitocondrial

TDF/FTC

- La > vida media intracelular
- Bien tolerada
- 1 píldora QD, no restricciones dietarias
- No evidencias de toxicidad mitocondrial
- M184V →↑ susceptibilidad a TDF
- TDF: Nefrotoxicidad?
- FTC: hiperpigmentación
- K65R: Resistencia cruzada con ABC, ddI

The HEAT Study

Randomized (1:1), double-blind, placebo-controlled, multicenter study conducted at 78 sites in the US and Puerto Rico over 96 weeks



Entry criteria:

- **HIV-1 RNA ≥1000 c/mL**
- **No CD4 cell count restrictions**

Stratified by entry HIV-1 RNA <100,000 or ≥100,000 c/mL

***All subjects switched to LPV/r tablets at Week 48**

Smith *et al.* 15th CROI 2008 Abstract no. 774.

Primary Endpoints

Week 48

- Proportion of subjects with plasma HIV-1 RNA <50 c/mL
  - **Non-inferiority of ABC/3TC QD to TDF/FTC QD can be concluded if the 95% confidence interval (CI) for the difference in response rates is > –12%.**

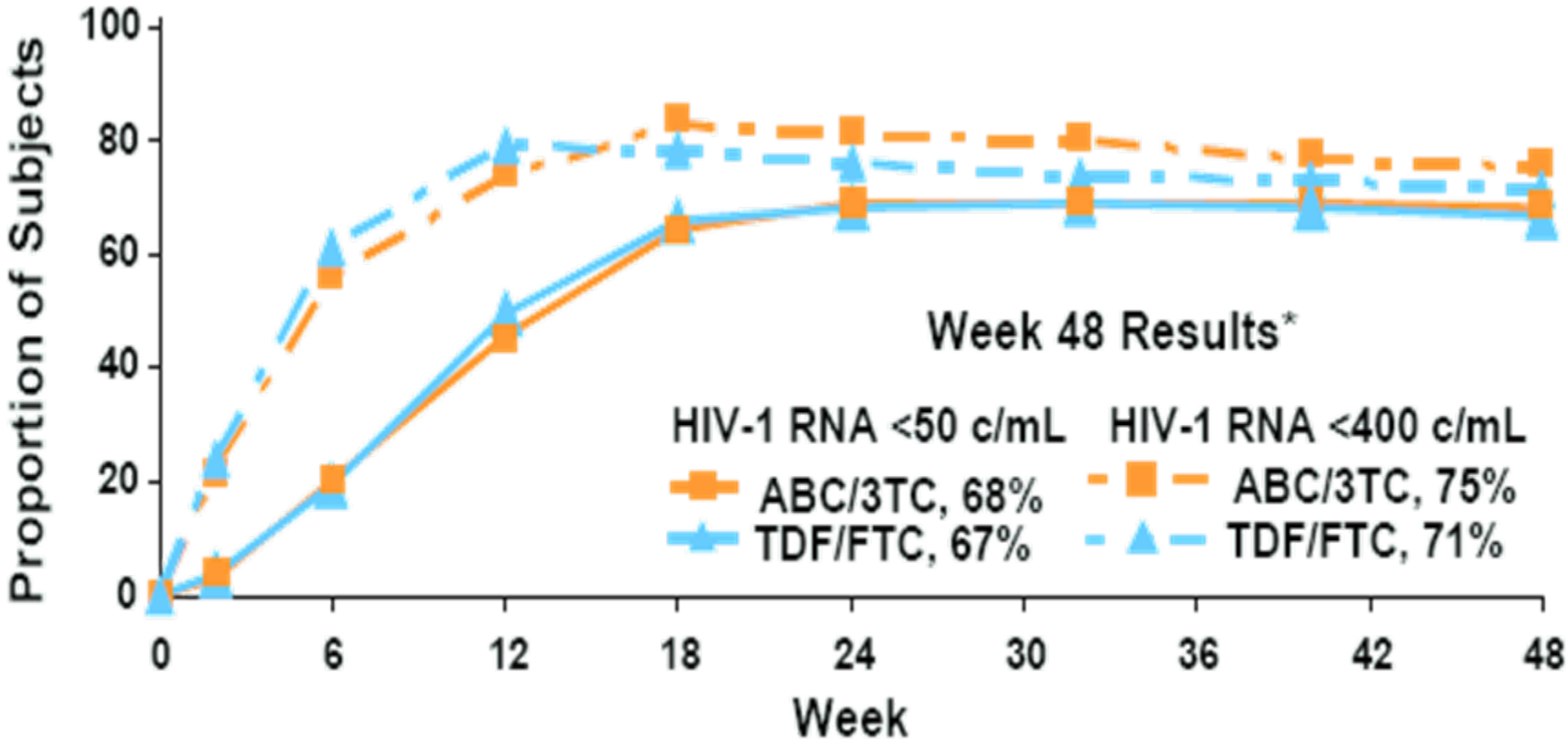
Week 96

- Treatment-limiting adverse events (AEs), Grade 2-4 AEs, events moderate to severe in intensity, and Serious Adverse Events

No *HLA-B*5701* screening was performed

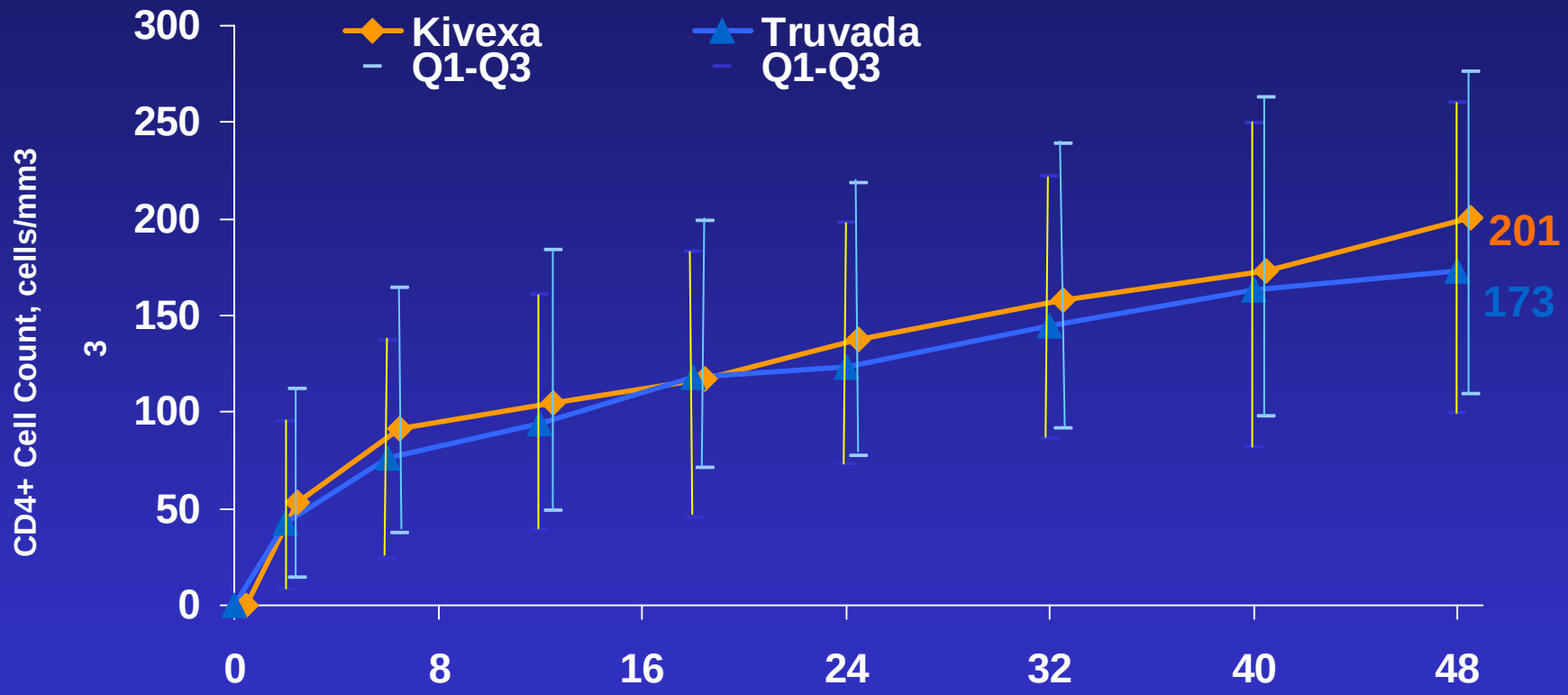
Smith *et al.* 15th CROI 2008 Abstract no. 774.

HIV-1 RNA <50 and <400 c/mL through Wk 48, ITT-E (M=F)



*95% CI of treatment difference (ABC/3TC – TDF/FTC):
HIV-1 RNA <50 c/ml: [-6.63, 7.40] ; HIV-1 RNA <400 c/ml: [-2.71,10.56]

Change from Baseline in CD4+ Cell Count (ITT-E, Obs)



Median CD4+, 214 cells/mm^3 429

n (obs) Kivexa	= 343	317	310	294	294	285	275	272
Truvada	= 345	318	306	297	287	277	270	267

Resistance Through 48 Weeks

	ABC/3TC (Kivexa) (N=343)	TDF/FTC (Truvada) (N=345)
Confirmed virologic failure (CVF) per protocol	40 (12%)	39 (11%)
Matched GT data at both BL and VF	35	32
Subjects with treatment-emergent mutations	12 (34%)	17 (53%)
NRTI-associated mutations	7 (20%)	14 (44%)
M184V or mixtures	7	14
K70K/R	1	0
NNRTI-associated mutations	1 (3%)	0
PI associated mutations*	6 (17%)	6 (19%)

*No primary PI associated mutations detected. Secondary PI associated mutations seen were as follows: M36M/I, V77V/I, A71A/T, I62I/V, L10L/V, V11V/I, G16E, I13I/V, L10L/F.

Treatment-Related Adverse Events (AEs)

	ABC/3TC (Kivexa) (N=343)	TDF/FTC (Truvada) (N=345)
Treatment-Related Grade 2-4 AEs (>3%)		
Any Event (all subjects)	154 (45%)	152 (44%)
Diarrhea	**61 (18%)**	**64 (19%)**
Nausea	**25 (7%)**	**20 (6%)**
Hypertriglyceridemia	**20 (6%)**	**17 (5%)**
Hypercholesterolemia	**22 (6%)**	**12 (3%)**
Glomerular filtration rate decreased	**17 (5%)**	**16 (5%)**
Vomiting	**11 (3%)**	**11 (3%)**
Suspected ABC HSR	**14 (4%)**	**3 (1%)**
Treatment-Related Serious AEs (≥2 subjects)		
Any Event (all subjects)	18 (5%)	10 (3%)
Suspected ABC HSR	**14 (4%)**	**3 (1%)**
Immune reconstitution syndrome	**2 (<1%)**	**0**
Anaemia	**1 (<1%)**	**1 (<1%)**
Renal failure	**0**	**2 (<1%)**

Conclusions

- ABC/3TC was virologically non-inferior to TDF/FTC through 48 weeks when each was combined with LPV/r.
- Efficacy results were consistent and robust to multiple analyses including when switches were counted as failures.
- Median CD4+ cell responses differed between arms at Week 48 (429 cells/mm^3 for ABC/3TC and 370 cells/mm^3 for TDF/FTC).
- A conservative definition of virologic failure resulted in a somewhat elevated failure rate in both arms. Twice as many subjects receiving TDF/FTC failed therapy with an M184V or mixture which was a finding not previously reported.
- No new safety findings were observed for either NRTI backbone.

D:A:D Study: NRTI Use and Risk of MI

- D:A:D study
  - 33,347 HIV patients on HAART
- 517 patients developed MI over 157,912 person-years of follow-up
  - Recent didanosine use (n=124)
  - Recent abacavir use (n=192)
  - Recent other NRTI use (n=237)
- Recent use of abacavir and didanosine (but not cumulative or past use) associated with increased risk of MI
  - Risk persists regardless of length of use
  - Risk was reversible with discontinuation of drugs
  - Most MIs occurred in patients with existing cardiovascular risk factors

Recent use	Relative Risk (95% CI)	*P* Value
Zidovudine	0.97 (0.76- 1.25)	0.82
Stavudine	1.00 (0.76-1.32)	0.93
Lamivudine	1.25 (0.96-1.62)	0.10
Abacavir	1.90 (1.47-2.45)	0.001
Didanosine	1.49 (1.14-1.95)	0.003

Implications:

Use caution in the interpretation of these preliminary findings and await further studies

Sabin C, et al. 15th CROI. Boston, 2008. Abstract 957C.

Abacavir and risk of MI:
evaluation of potential biologic mechanisms

Clinical Information

- **Metabolic syndrome** (dyslipidemia, insulin/glucose effects, fat accumulation)
  - ABC metabolic impact well characterized and generally agreed as favorable among NRTI class
- **Hypertension**
  - No evidence of hypertensive effects in clinical trials
- **Mitochondrial toxicity & lipoatrophy**
  - ABC demonstrated to improve mitotox and inc. adipose tissue following thymidine analogue therapy

Abacavir and the risk of myocardial infarction: A summary and evaluation of more than 14600 subjects in 54 GSK-sponsored clinical trials.

J Hernandez, A Cutrell, Jane Yeo,
W Burkle, C Brothers, W Spreen.

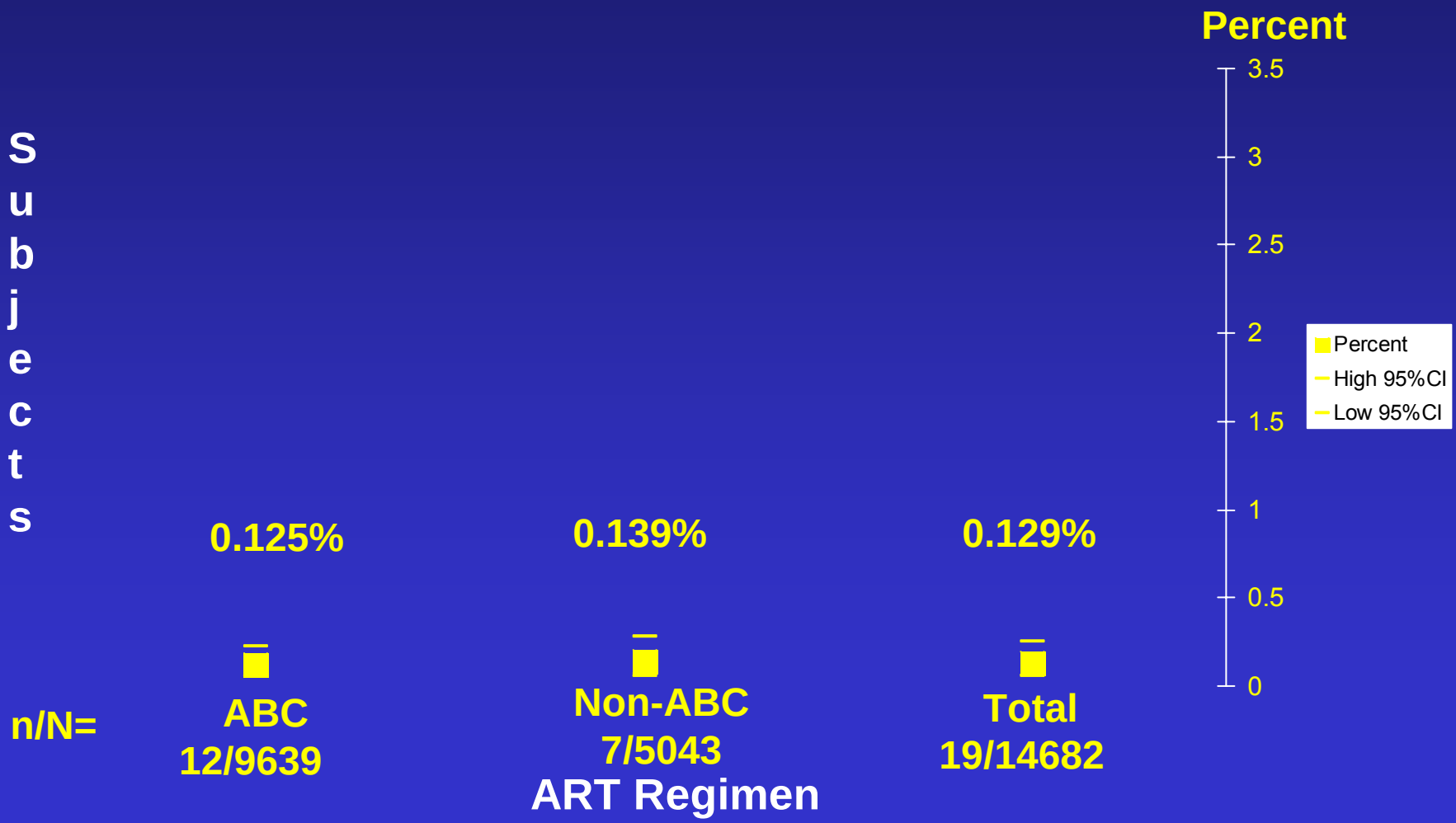
Not Presented

Methods

- All GSK-sponsored clinical trials with ≥ 24 weeks of ART finished from January 1995 to September 2007 and with applicable data were analyzed.
- Descriptive statistics were summarized for naïve and experienced subjects treated with and without ABC.
- Adverse events reported in the coronary artery disorders and ischemic coronary artery disorders HLTs were used to select the events of interest, myocardial ischemia or infarction.
- Rates per 1000 person/years were calculated, and Poisson regression models were used to calculate relative rates and p values using SAS.

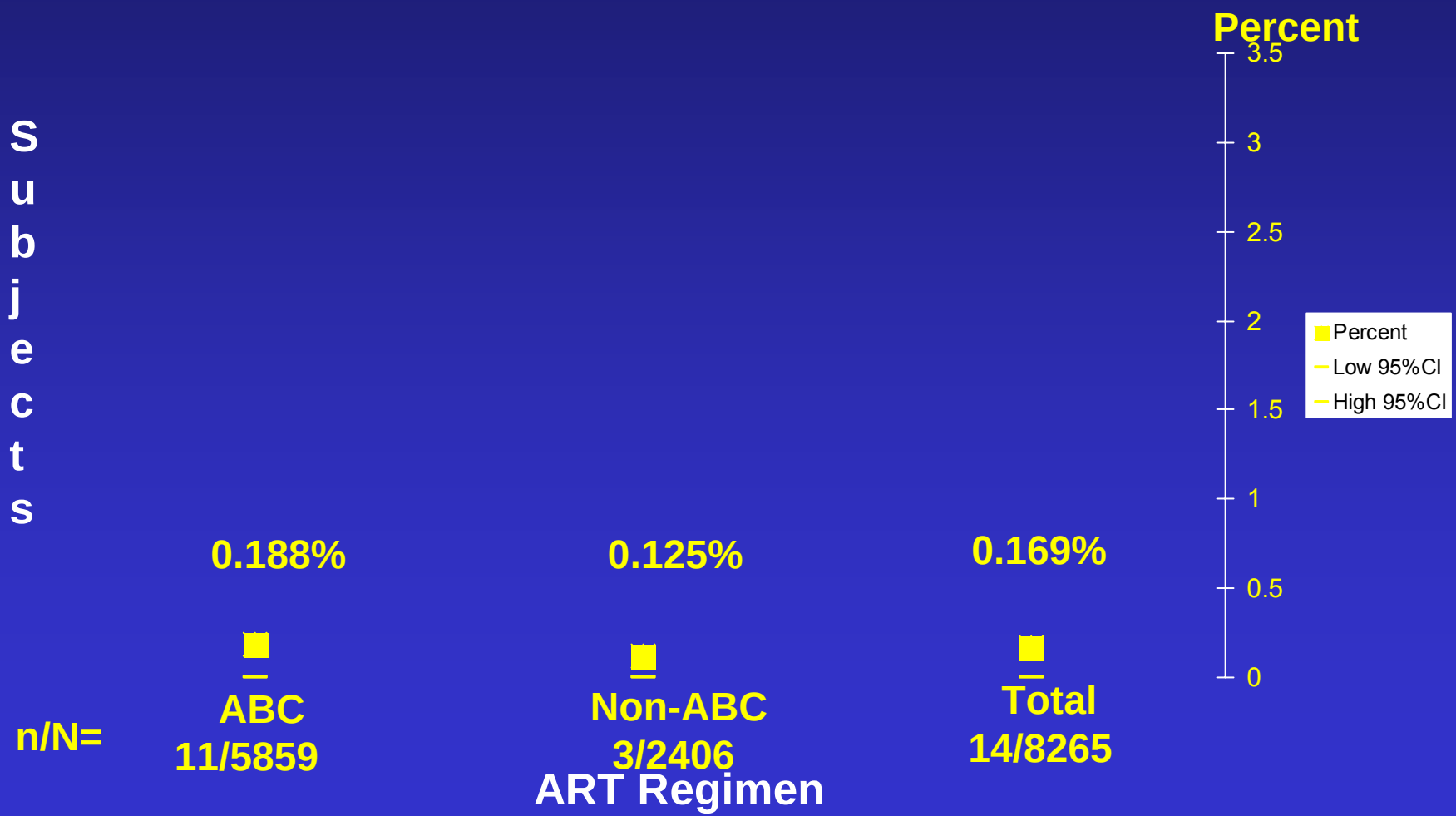
Hernandez J, Cutrell A, Yeo J et al. 2008

Proportion of Subjects on ART +/- ABC Reporting MI or Acute MI among 14682 Subjects



Hernandez J, Cutrell A, Yeo J et al. 2008

Proportion of ART-naïve Subjects on ART +/- ABC Reporting MI or Acute MI among 8265 Subjects



Hernández J, Cutrell A, Yeo J et al. 2008

Relative Rate of Events Per 1000 Person Years of Exposure to ABC Compared with No Exposure to ABC

Exposure to ABC	Person Years	Number of events	Rate /1000 PersonYears	Relative rate (95% CI)	p-value
Any ischemic coronary artery disease or disorder:					
None	4641.873	27	5.817		
ABC CART	7831.88	27	3.447	0.593 (0.348 1.010)	0.055
Any Myocardial Infarction or Acute Myocardial Infarction					
None	4652.945	11	2.363		
ABC CART	7845.185	13	1.657	0.701 (0.314 1.565)	0.386

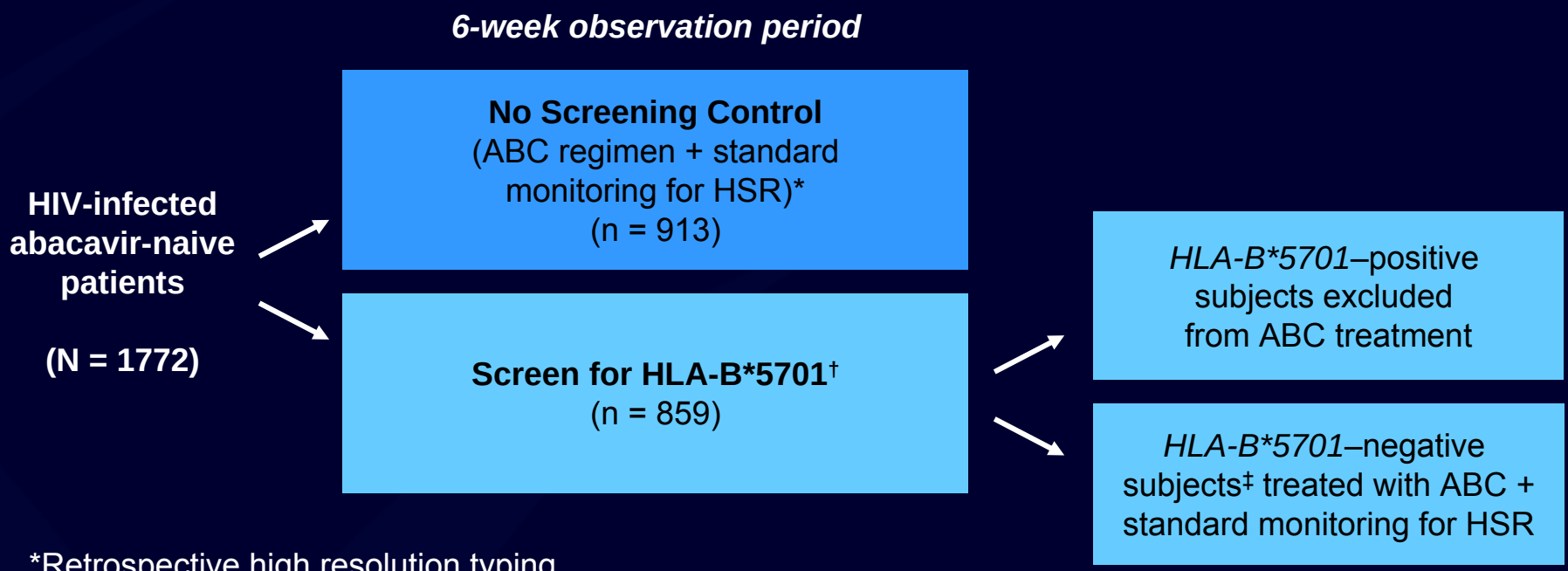
Conclusion

- This review did not show an increased incidence of ischemic coronary artery events, coronary artery disorders, myocardial ischemia or infarction in subjects who received abacavir-containing combination antiretroviral therapy (CART) compared to subjects that received non-ABC containing CART.

Issue 2: HLA Testing for Abacavir Hypersensitivity

"It's in your genes."

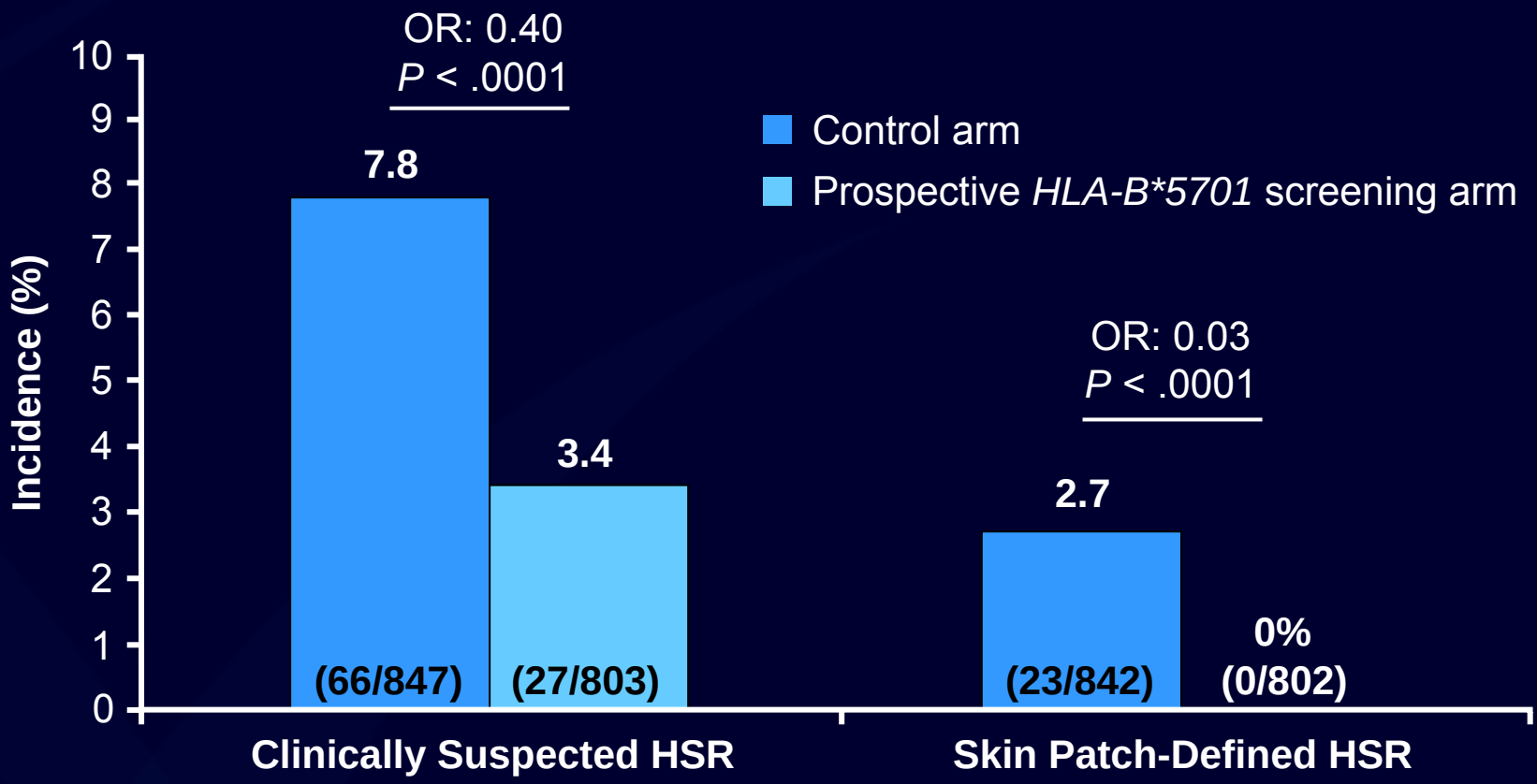
PREDICT-1: *HLA-B*5701* Allele Screening to Reduce ABC-HSR



*Retrospective high resolution typing.
†Prospective high resolution typing.
‡Physicians not informed of screening status.

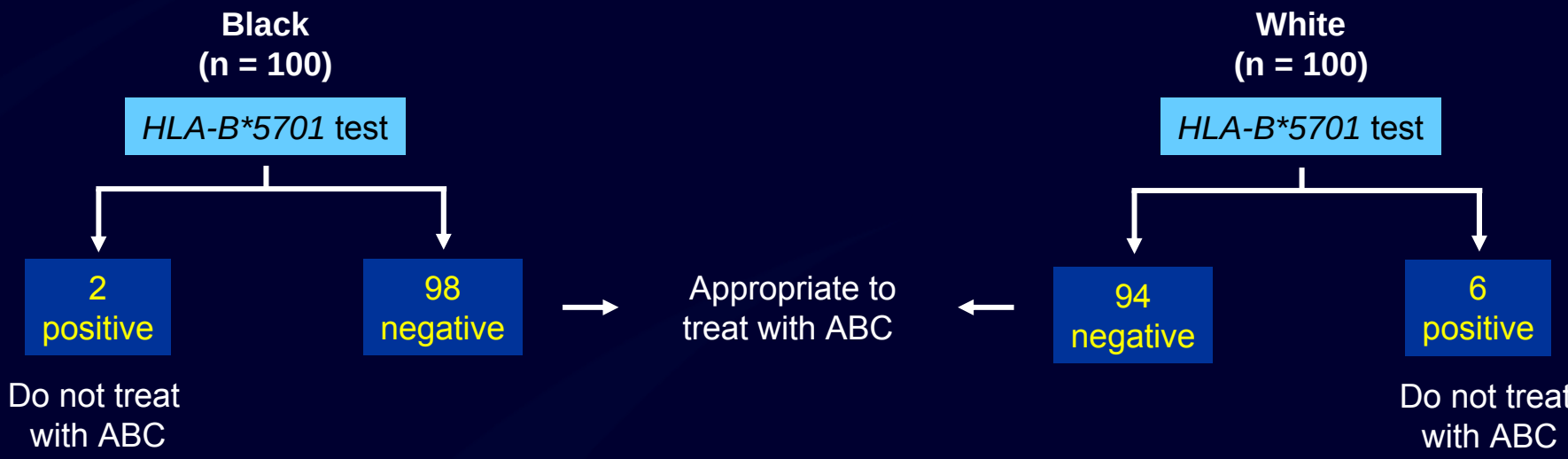
Mallal S, et al. IAS 2007. Abstract WESS101.

PREDICT-1: Clinically Suspected or Skin Patch–Defined HSR



Mallal S, et al. IAS 2007. Abstract WESS101.

Potential *HLA-B*5701* Screening Implications



Test 100 black patients

- Treat 98 patients at low risk for ABC HSR
- Prevent 1 ABC HSR event
- Exclude ABC unnecessarily in 1 patient

Test 100 white patients

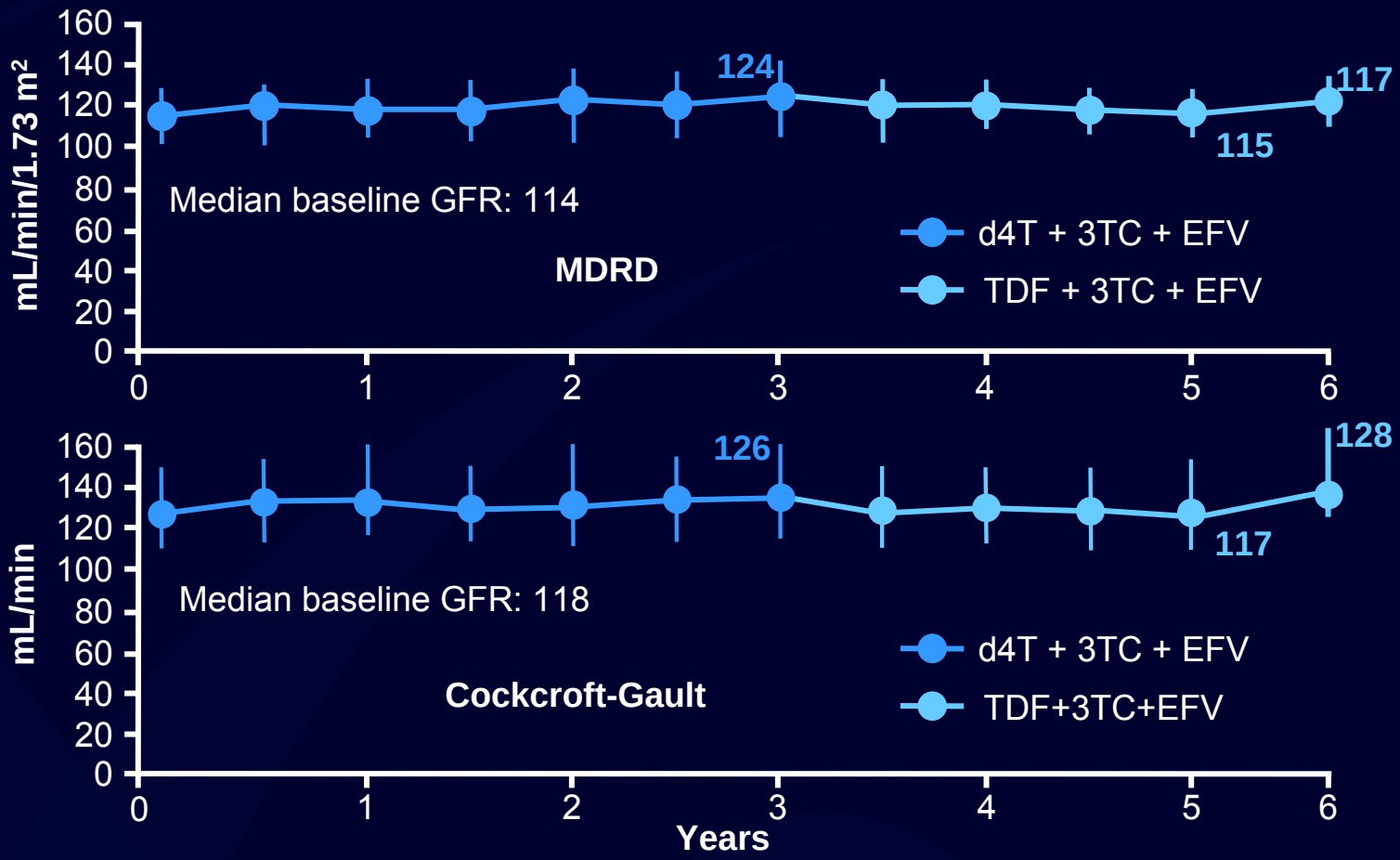
- Treat 94 patients at low risk for ABC HSR
- Prevent 4 ABC HSR events
- Exclude ABC unnecessarily in 2 patients

Example shown is based on PPV derived from PREDICT-1 and SHAPE data.

Saag M, et al. IAS 2007. Abstract WEAB305.

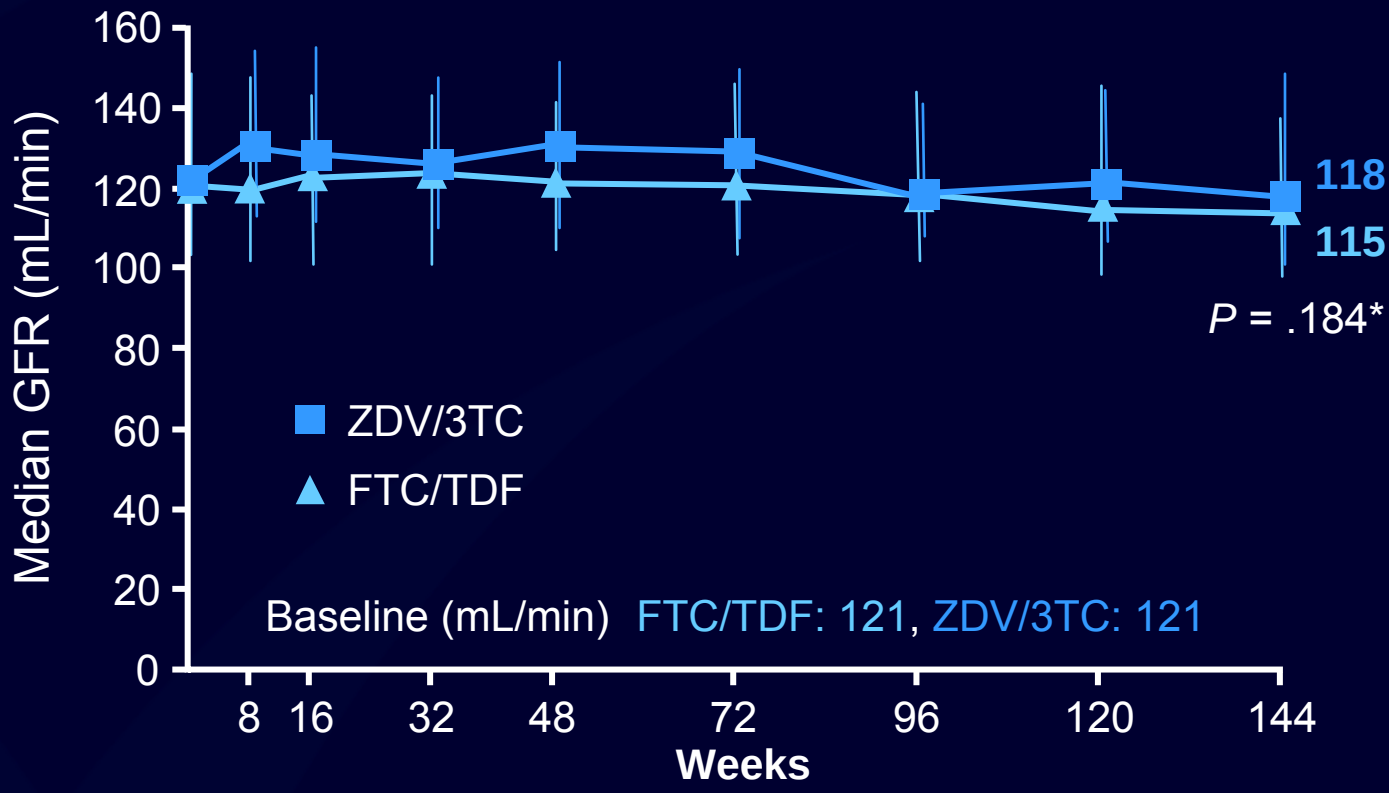
How Clinically Relevant Are TDF-Associated Renal Issues?

GS 903E: Estimated Median GFR After d4T to TDF Switch



Madruga J, et al. IAS 2007. Abstract WEPEB030.

GS 934: Steady Renal Function Over 144 Weeks Using Cockcroft-Gault



FTC/TDF + EFV n =	247	240	222	210	188	173	166	162
ZDV/3TC + EFV n =	238	225	198	182	162	145	137	131

*Wilcoxon rank-sum test.

Arribas JR, et al. IAS 2007. Abstract WEPEB029.

TDF-Related Renal Issues

- What we know
  - TDF has relatively little clinically relevant renal toxicity (in contrast to adefovir, cidofovir)
  - Rates of drug discontinuation for TDF-related renal events are extremely low in both clinical trials and cohort studies
  - A small (but often statistically significant) reduction in GFR occurs with TDF vs comparator regimens—but GFR still well within the normal range, and stabilizes
- What we do not know
  - Does this matter now? Will it matter later?

Arribas JR, et al. IAS 2007. Abstract WEPEB029.

¿Qué factores influyen en las recomendaciones para la elección de un régimen antirretroviral?

- **Eficacia** - básicamente determina qué es lo que *no* debe prescribirse (eg. IP no potenciado, triple NRTI)
- **Toxicidad** – razón principal para determinar regímenes preferidos versus alternativos
  - **NNRTI: EFV (preferido) vs. NVP (alternativo: riesgo de hipersensibilidad a los fármacos)**
  - **NRTI: TDF o ABC+ FTC o 3TC preferido) vs d4T (lipoatrofia, acidosis láctica, neuropatía) ABC (riesgo de hipersensibilidad a los fármacos). TDF(riesgo renal/óseo)**
- **Adherencia** – carga de pastillas, régimen de dosis, disposición a iniciar Rx
- **Interacciones medicamentosas**
  - **Sistema citocromo P_{450}: interacciones complejas**
    - **CYP3A4 (ej.: rifampicina, estatinas, Hierba de San Juan, fármacos cardíacos, SSRIs)**
  - **Inhibidores de la bomba de protones: ↓ los niveles de Atazanavir e Indinavir (no potenciados)**

¿Qué otros factores determinan la elección del tratamiento?

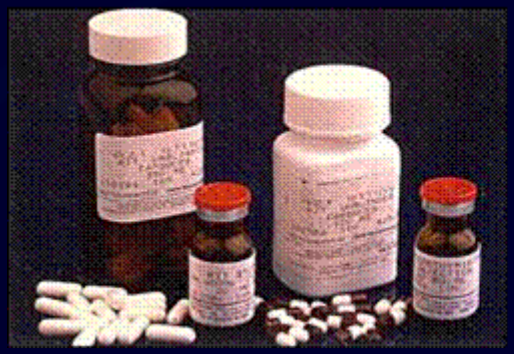
- **Otras enfermedades**
  (ej.: dislipidemia, diabetes, enfermedad cardiovascular / cerebrovascular)
- **Otros medicamentos**
  (ej.: estatinas metabolizadas por el CYP3A4 y terapia con IP potenciado)
- **Cuestiones relativas al estilo de vida / laborales**
  (ej.: historial régimen alimentario, actividad física)
- **Recuento de CD4+ previo al tratamiento**
  (recuento de CD4 más bajo → colesterol HDL y LDL más bajo)
- **Probabilidad de embarazo**
- **Test de resistencia farmacológica en el valor inicial**

Evaluación metabólica inicial

Todavía no se ha incorporado en las recomendaciones del Rx

Aspectos históricos de la terapia antirretroviral : Reducción de la carga de pastillas

Era pre-HAART

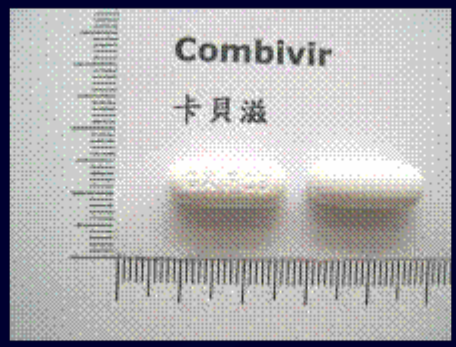


Regímenes de elevada potencia, múltiples dosis por día

AZT

Inicialmente cada 4 horas, día + noche

Era HAART 'Temprana'

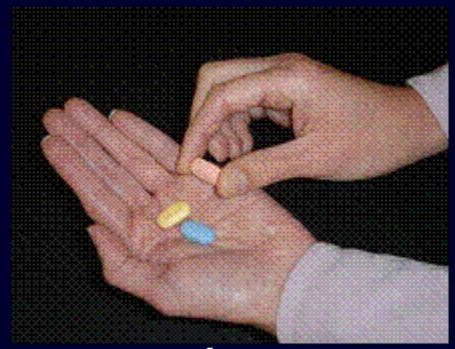


Regímenes coformulados **dos** veces al día

AZT + 3TC

AZT + 3TC + ABC

Era HAART 'Tardía'



Regímenes coformulados **una** vez al día y formulaciones compactas

ABC + 3TC

TDF + FTC

TDF + FTC + EFV

Fos-AMP/r*- LPV/r*- ATV/r

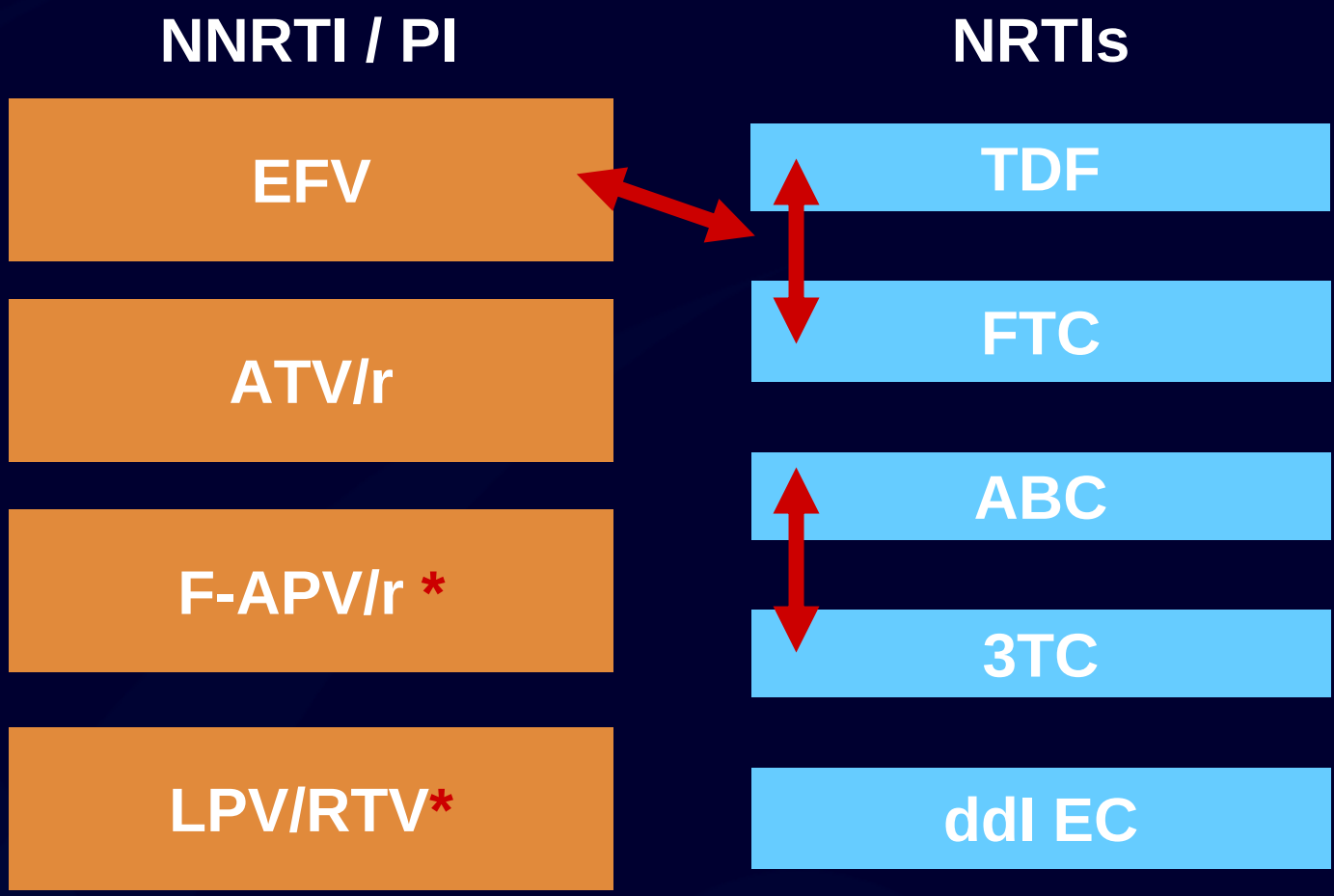
1987

1995 (países desarrollados)

2000-2002 en adelante (países desarrollados)

*** BID en fallo**

Regímenes 1 x D



* Solo en *naive*

Opciones de IP

IP # tabletas	Dosificación	Guías	Lípidos	Efectos Adversos
ATV/r 2	1 x D	DHHS IAS/USA	+	Ictericia
LPV/r 4	1*-2 x D	DHHS IAS/USA	+++	GI
FPV/r 4	1*-2 x D	DHHS IAS/USA	++	GI
SQV/r 5	2 x D	IAS/USA	++	GI

** Solo en naive*

Recommended Initial Regimens for ARV-Naive Patients, 2008

DHHS Guidelines "Preferred," January 2008[1]			
NNRTI-based regimen	EFV*	+	TDF/FTC ABC/3TC§
PI-based regimen	ATV/RTV FPV/RTV BID LPV/RTV BID		
IAS-USA Guidelines "Recommended," August 2006[2]			
NNRTI-based regimen	EFV NVP†	+	TDF/FTC‡ ZDV/3TC§ ABC/3TC§
PI-based regimen	LPV/RTV ATV/RTV FPV/RTV SQV/RTV		

*Except during first trimester of pregnancy or in women with high pregnancy potential. †Avoid in women with CD4+ cell count > 250 cells/mm^3 and men with > 400 cells/mm^3. ‡Or lamivudine. §Or emtricitabine.

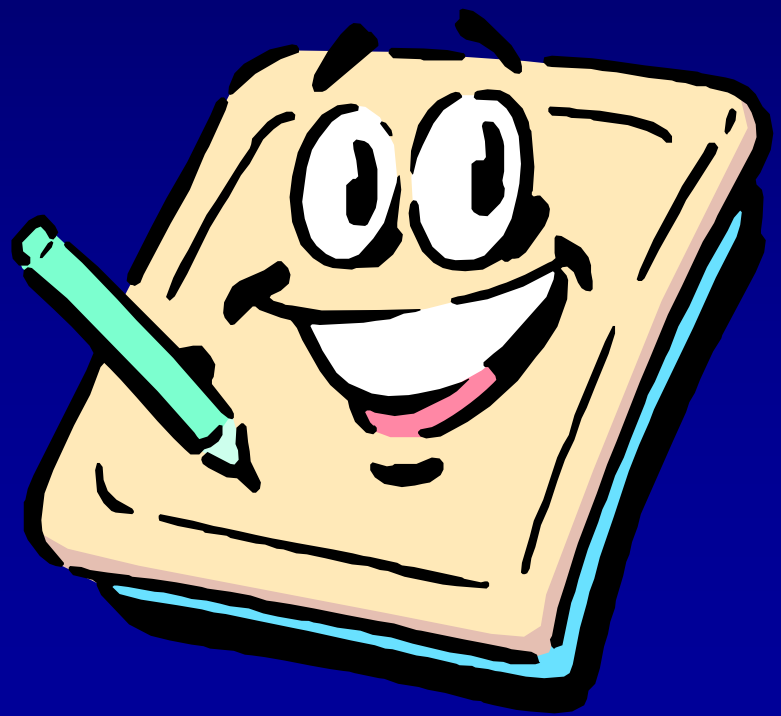
1. DHHS Guidelines. Available at: http://AIDSinfo.nih.gov.
2. 2. Hammer SM, et al. JAMA. 2006;296:827-843.

Simplificación

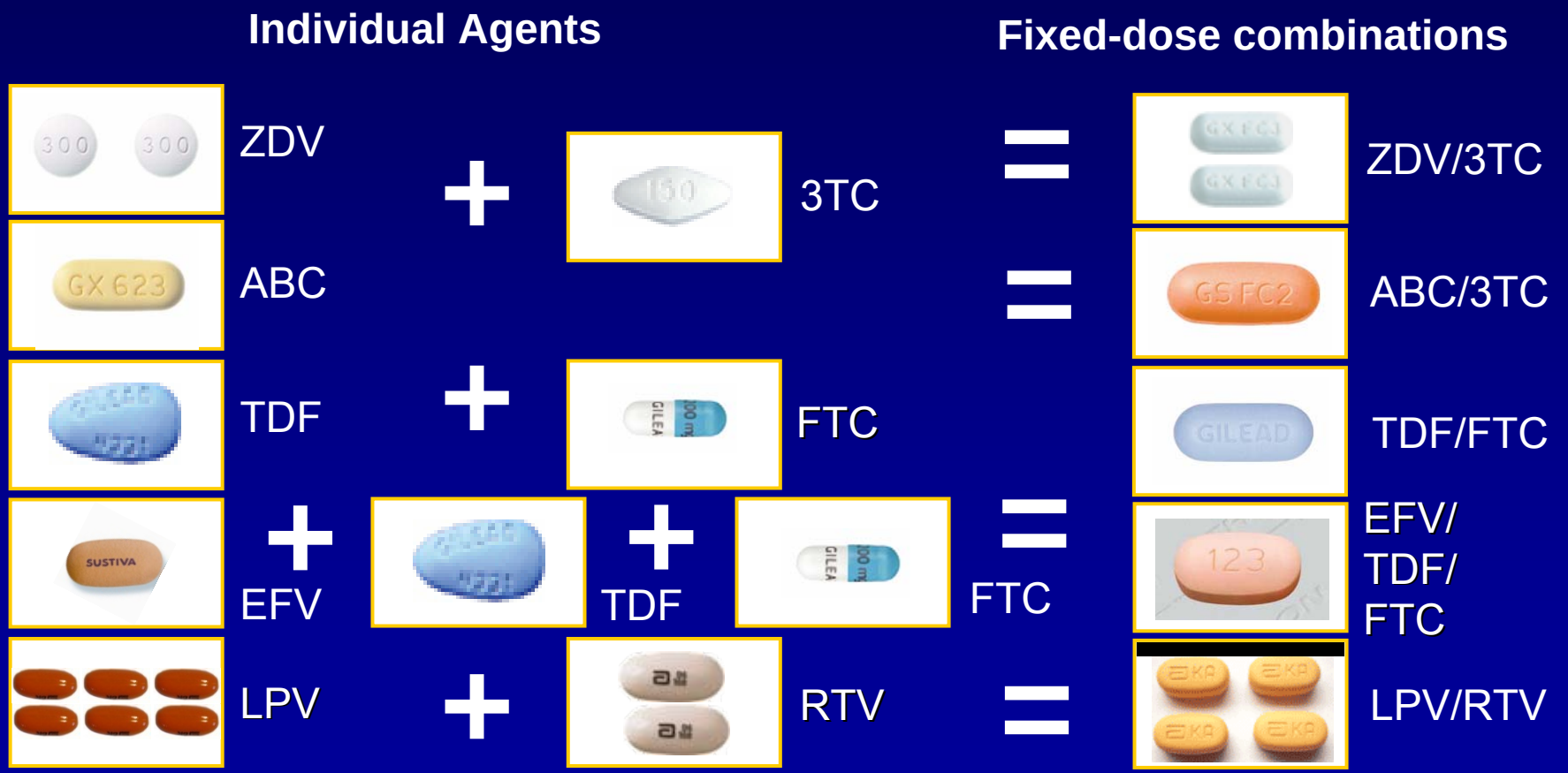
- No hay criterio de “talle único”
- La simplificación es un camino de doble vía
- Lo que no está roto no se arregla
- Nuevas opciones, nuevas expectativas
- Nuevas causas de morbimortalidad
- ***Simplificar sin perder potencia***

SIMPLIFICACIÓN:

Se puede simplificar sin perder potencia!!



Fixed-Dose Combinations



Identificar la opción correcta:

a) **Simplificación de la terapia ARV implica reducción de la potencia.**
b) **Simplificación suele favorecer la adherencia.**
c) **Simplificación resulta siempre en mejor perfil metabólico.**
d) **Simplificación puede aplicarse siempre que la carga viral sea < a 10.000 copias/mL**
e) **Lo siento, NO aprendí.**