IX jornadas de sensibilización y formación en VIH y VHC

Actualización en VIH: nuevas estrategias, optimizando el tratamiento antirretroviral

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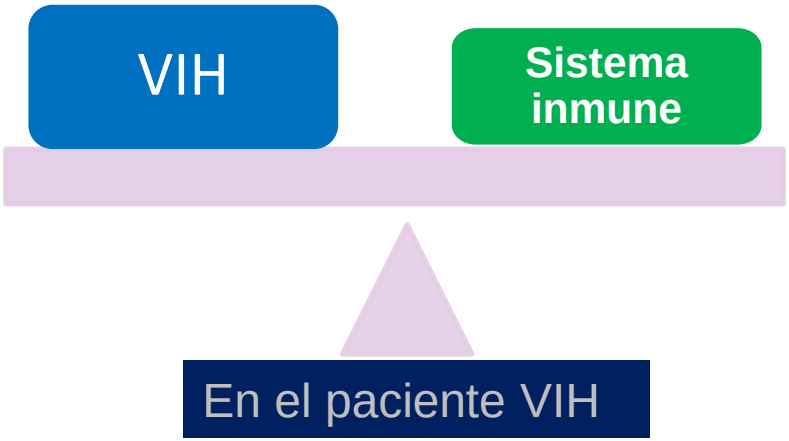
En los últimos años se han producido muchos cambios:

- Perfil de pacientes
- Fármacos antirretrovirales y combinaciones
- Papel del tratamiento antirretroviral

Lo que no ha cambiado

- Número de nuevas infecciones, al menos en nuestro medio
- Diagnóstico tardío

Lo que tenemos claro:



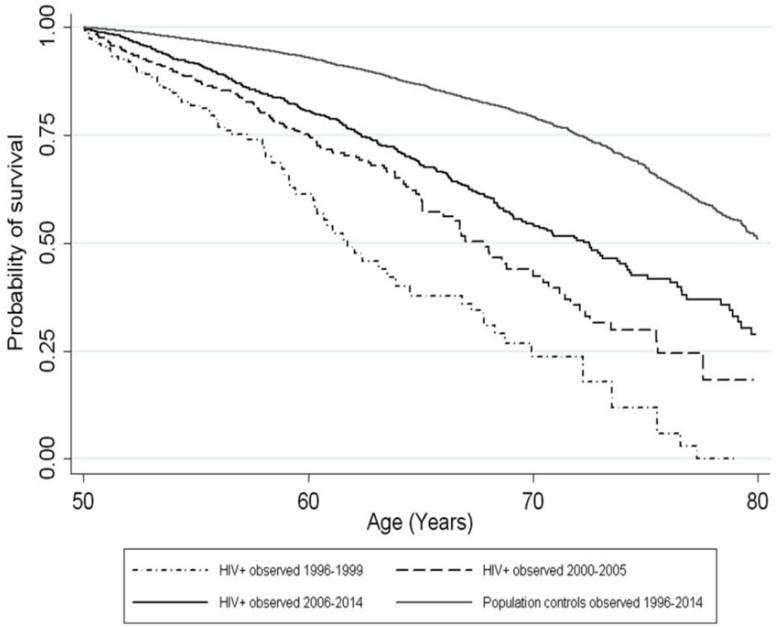


FIGURE 1. Kaplan–Meier curve showing survival from 50 years of age stratified by calendar period among HIV-infected individuals and population controls.

- El tratamiento antirretroviral
  - Bloque la replicación viral
  - Evita la progresión

Legarth RA el al; J Acquir Immune Defic Syndr 2016; 71:213-8

Trends in life expectancy of HIV-positive adults on ART across the globe: comparisons with general population

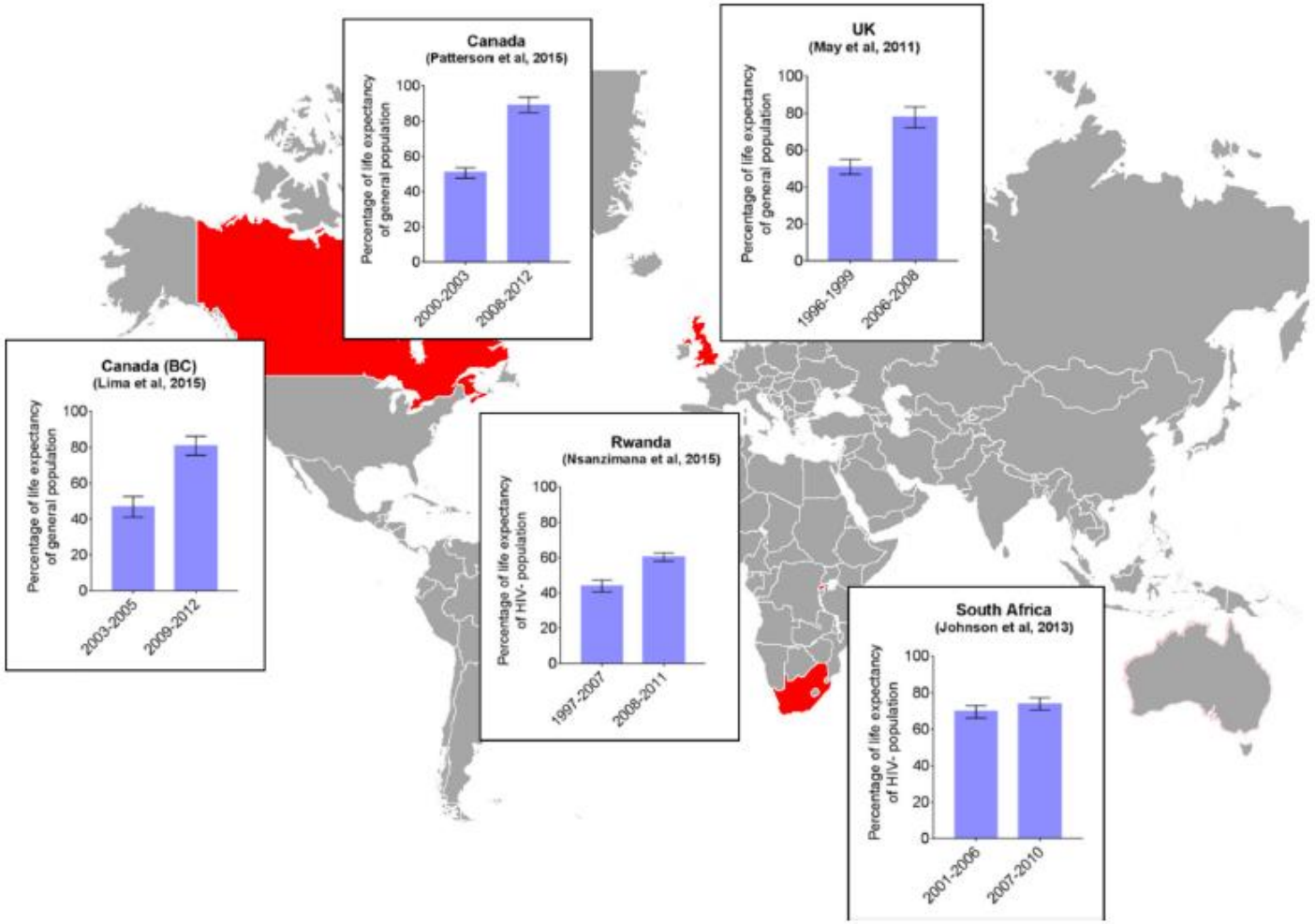


Figure 2.
Life expectancy at age 20 years in HIV-positive individuals initiating ART, by earlier and later calendar period.

Curr Opin HIV AIDS. 2016 September ; 11(5): 492–500. doi:10.1097/COH.0000000000000298.

Trends in life expectancy of HIV-positive adults on ART across the globe: comparisons with general population

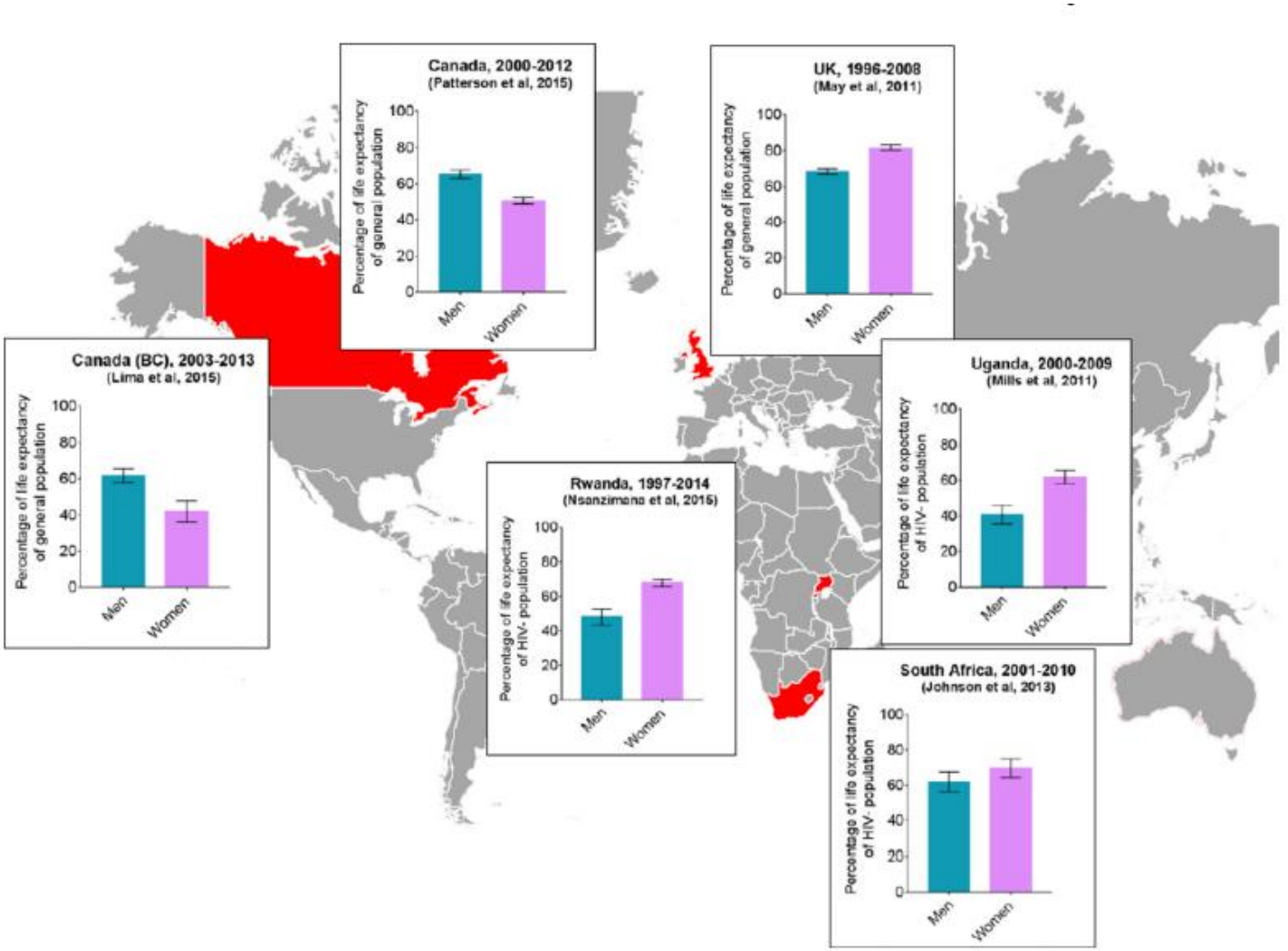


Figure 3.
Life expectancy at age 20 years in HIV-positive men and women initiating ART.

Curr Opin HIV AIDS. 2016 September ; 11(5): 492–500. doi:10.1097/COH.0000000000000298.

La infección por VIH ha cambiado a lo largo de los últimos 30 años, y la mejora en la supervivencia es algo real

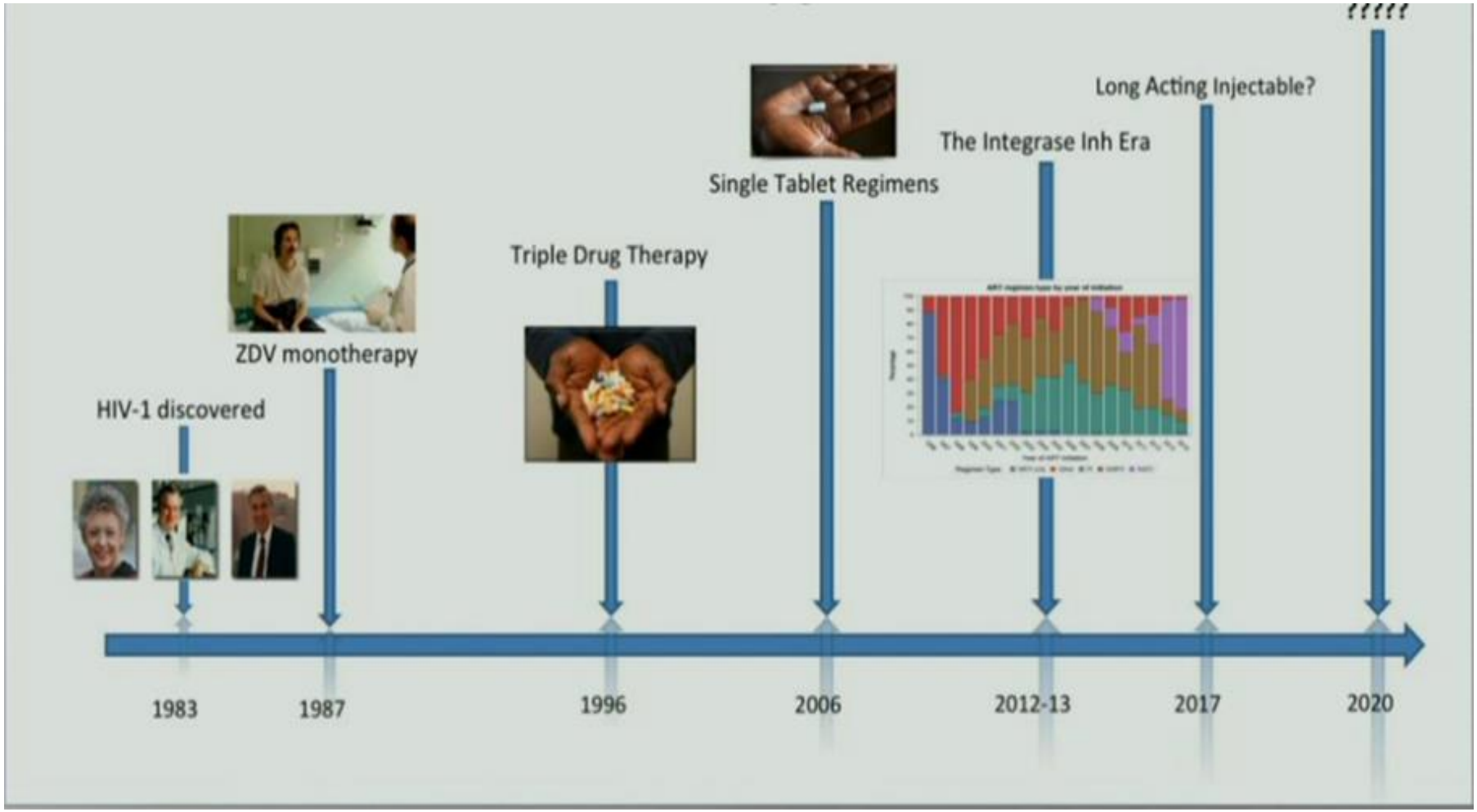
- Tratamiento de las Enfermedades Oportunistas
- Atención hospitalaria (+ cuidados paliativos)

- Tratamiento del VIH
- “Especialistas” en VIH

- Tratamiento de las comorbilidades
- ¿Nuevos modelos asistenciales?

Adaptada y modificada de: Chu C & Selwin P. J Urb Health 2011; 88:556-566.

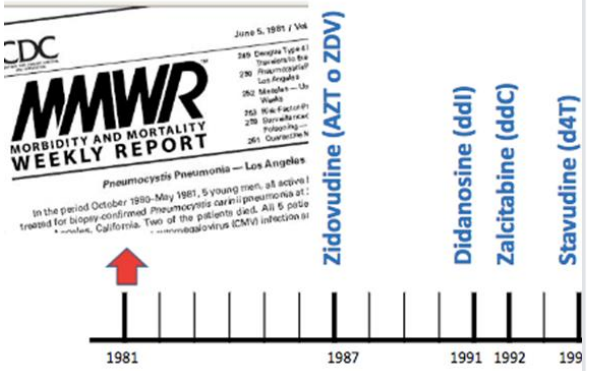
Y es que estamos hablando de la historia del VIH



En la que el tratamiento antirretroviral tiene un papel fundamental

O lo que es lo mismo…

ITIAN: inhibidores de la transcriptasa inversa análogos de nucleós(t)idos
ITINN: inhibidores de la transcriptasa inversa no análogos de nucleósidos
IP: inhibidores de la proteasa
IF: inhibidores de la fusión
ICCR5: Inhibidores CCR5
INI: inhibidores de la integrasa
POT: Potenciador sin actividad antirretroviral



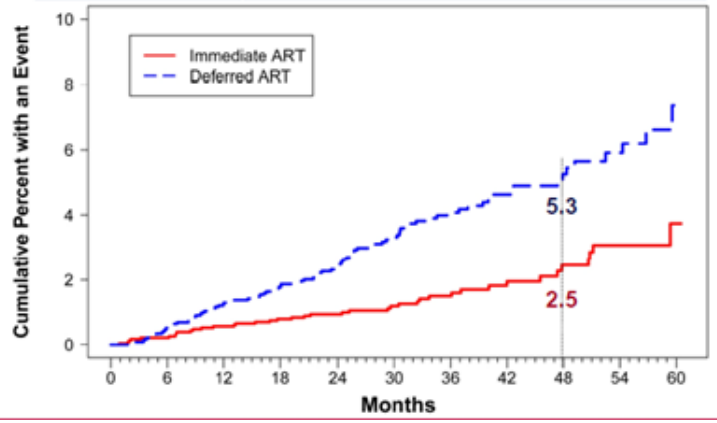
apina (NVP) | r) |), atazanavir (ATV) | r) |), cobicistat (COBI)

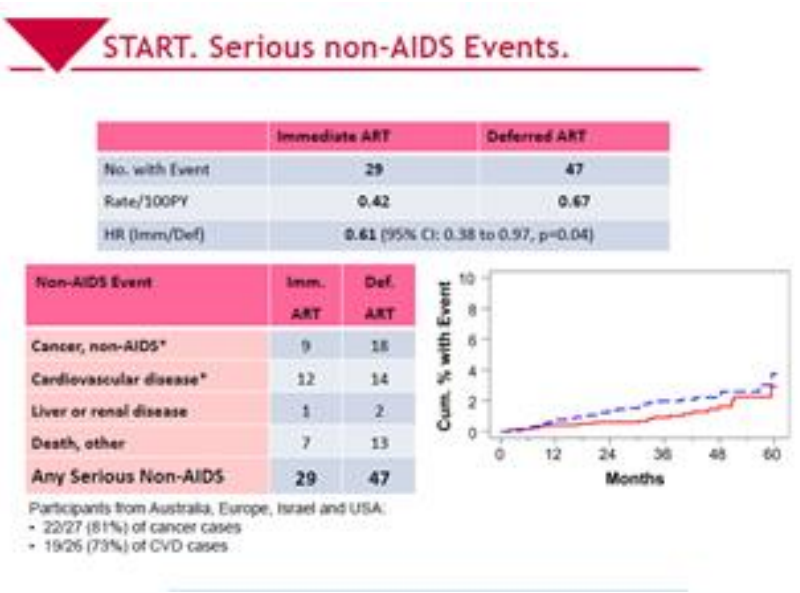
Generic name	Trade name	Formulation	Standard adult dose	Pil
Single-tablet regimens				
Efavirenz/emtricitabine/ tenofovir disoproxil *Generic product, appearance will vary*		Tablet comprising 600mg efavirenz, 200mg emtricitabine, 245mg tenofovir disoproxil	One tablet once a day	
Rilpivirine/emtricitabine/ tenofovir disoproxil	*Eviplera*	Tablet comprising 25mg rilpivirine, 200mg emtricitabine, 245mg tenofovir disoproxil	One tablet once a day	
Rilpivirine/tenofovir alafenamide/emtricitabine	*Odefsey*	Tablet comprising 25mg rilpivirine, 25mg tenofovir alafenamide, 200mg emtricitabine	One tablet once a day	
Elvitegravir/cobicistat/ emtricitabine/tenofovir alafenamide	*Genvoya*	Tablet comprising 150mg elvitegravir, 150mg cobicistat, 200mg emtricitabine, 10mg tenofovir alafenamide	One tablet once a day	
Elvitegravir/cobicistat/ emtricitabine/tenofovir disoproxil	*Stribild*	Tablet comprising 150mg elvitegravir, 150mg cobicistat, 200mg emtricitabine, 245mg tenofovir disoproxil	One tablet once a day	
Dolutegravir/ abacavir/ lamivudine	*Triumeq*	Tablet comprising 50mg dolutegravir, 600mg abacavir, 300mg lamivudine	One tablet once a day	
Darunavir/cobicistat/ emtricitabine/ tenofovir alafenamide	*Symtuza*	Tablet comprising 800mg darunavir, 150mg cobicistat, 200mg emtricitabine, 10mg tenofovir alafenamide	One tablet once a day	

Estudio START: inicio de tratamiento independientemente de la cifra de CD4 en todas las guías

Serious AIDS or nonAIDS events or death

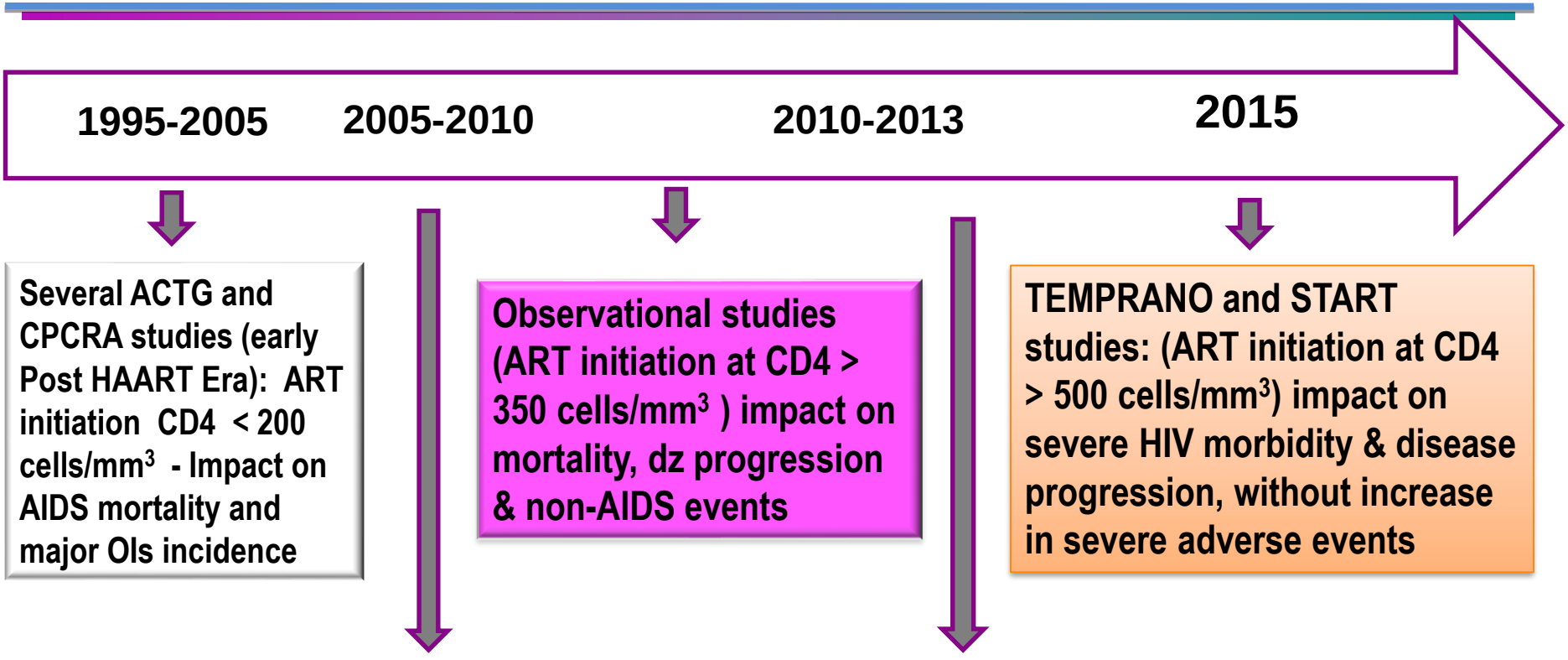
	Immediate ART	Deferred ART
No. with Event (%)	42 (1.8%)	96 (4.1%)
Rate/100PY	0.60	1.38
HR (Imm/Def)	0.43 (95% CI: 0.30 to 0.62, p <0.001)	





Lundgren J. 8th IAS, Vancouver, Canada, July 19-22, 2015. #MOSY0301.
N Engl J Med 2015; 373:795-807.

¿Cuándo empezar el TAR?



Nuevo papel del TAR: Tratamiento como prevención

HPTN 052

	April 2005-May 2011			May 2011-May 2015			Overall		
	PY f/u	All partner infections # (rate)	Linked partner infections# (rate)	PY f/u	All partner infections # (rate)	Linked partner infections # (rate)	PY f/u	All partner infections # (rate)	Linked partner infections # (rate)
Total	3482	46 (1.32)	37 (1.06)	5012	32 (0.64)	9 (0.18)	8494	78 (0.92)	46 (0.54)
Early arm	1751	4 (0.23)	1 (0.06)	2563	15 (0.59)	2 (0.08)	4314	19 (0.44)	3 (0.07)
Delayed arm	1731	42 (2.43)	36 (2.08)	2449	17 (0.69)	7 (0.29)	4180	59 (1.41)	43 (1.03)
Rate ratio		0.09	0.03		0.86	0.28		0.31	0.07
Risk reduction		**91%**	**97%**		**14%**	**72%**		**69%**	**93%**

Rate = # of events/ 100 PY
Risk reduction = 1 – rate ratio

Linked = index to partner transmission

Cohen MS et al. 8th IAS Conference on HIV Pathogenesis, Treatment, and Prevention Vancouver, Canada, July 20, 2015

PARTNER

767 couples contributed 894 eligible couple/y FU, 75 EU sites.
- 445 HSX, 282 MSM.
- Condomless sex, Not using PEP or PrEP.

-Latest HIV VL **<200 copies** (within max past 12 m)
-Diagnosed Iof STIs: 16% of MSM, 5-6% HTSX
-Estimated condomless sex acts: 14.000 – 16.400.
-Phylogenetically linked transmissions

	Number of events	Couple/y FU	Estimated n sex acts	10 year risk
Overall	0 (0-0.00008)	894	44.439	0 (0-4%)
HT m+/f-	0 (0-0.0003)	288	13,728	0 (0-12%)
HT m-/f+	0 (0-0.0003)	298	14,295	0 (0-12%)
* MSM	0 (0-0.0003)	308	16,416	0 (0-11%)

Rodger A, et al. CROI 2014. Abstract 153LB.

PARTNER2: HIV Transmission

- No linked transmissions documented in ~ 77,000 condomless sex acts when HIV-positive MSM partner suppressed to HIV-1 RNA < 200 copies/mL

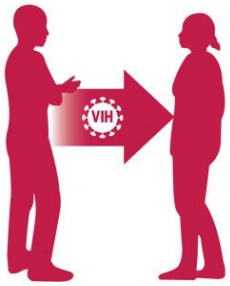
Sexual Behavior Reported by HIV-Negative Partner	Linked Transmissions, n	Upper 95% CI*	Condomless Sex Acts, n	CYFU
Any sex	0	0.23†	76991	1596
Anal sex	0	0.24	70743	1546
Insertive anal sex	0	0.27	52572	1345
Receptive anal sex without ejaculation	0	0.43	23153	867
Receptive anal sex with ejaculation	0	0.57	20770	652
Any sex with an STI	0	2.74	6301	135

*For rate of within-couple HIV transmission per 100 CYFU. †Compared with 0.84 for MSM and 0.46 for heterosexuals in PARTNER1.

- Unlinked transmissions occurred in 15 initially HIV-negative MSM partners

Rodger A, et al. AIDS 2018. Abstract WEAX0104LB.

Slide credit: clinicaloptions.com

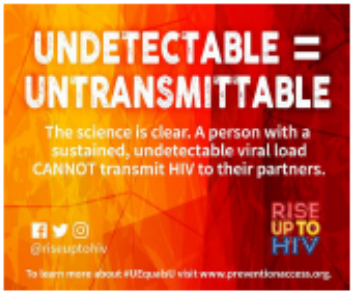


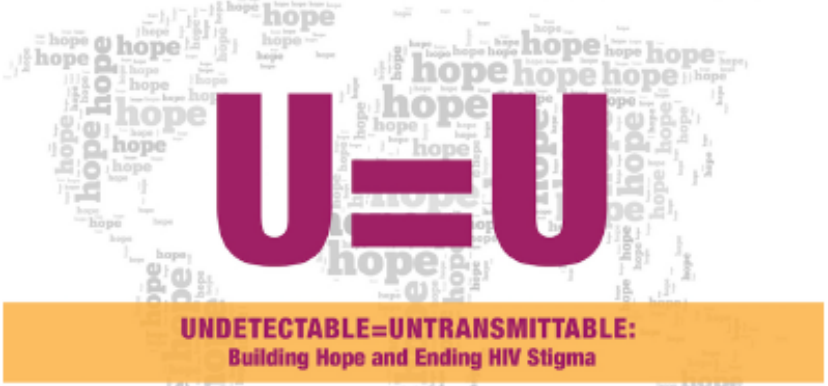
"HIV made me feel unattractive and made me afraid to have sex with my husband, who is HIV negative. Since I learned about U=U, I have lost 20 pounds, I feel sexy, and my husband and I are making up for all the times we missed."

*"When I learned I was HIV+, I became **isolated and depressed**. I went on medication, but knowing I had the virus made me feel dirty and ashamed. I stayed that way for seven years, stigmatizing myself. **U=U has given me my life back.** Knowing that I can't infect anyone else has allowed me to forgive myself."*

*"It was only when I learned about U=U that I realized that I have been living for all these years carrying this heavy weight. Because I took my meds, I kept on living. **But inside I felt like I was dying.** And that made me afraid to get close to anyone else. **The night I heard about U=U**, I couldn't stop crying. **It was like that burden I didn't even realize I was carrying just fell away.**"*

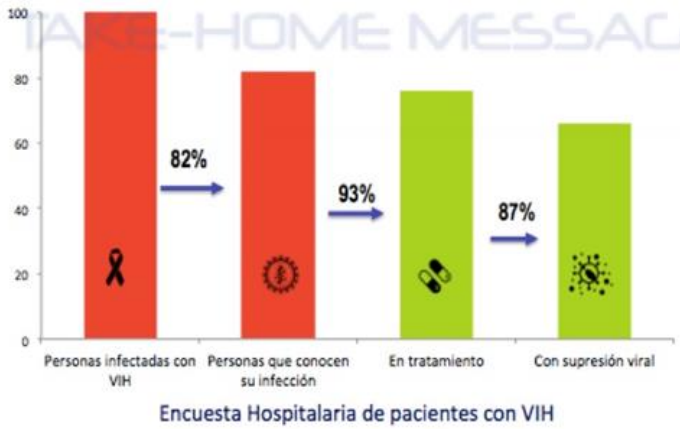
thewellproject



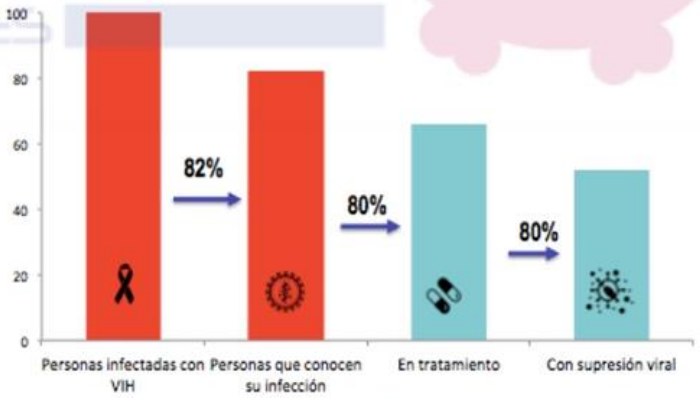


Papel del TAR aún más importante: prevención

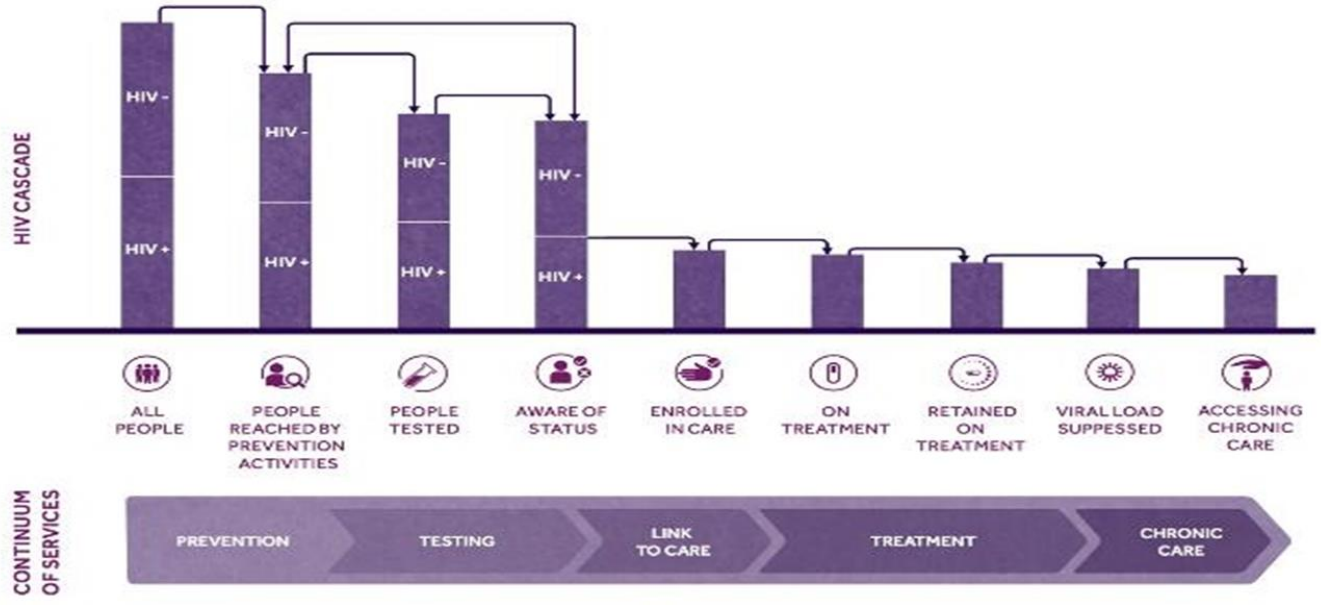
- Situación de la cascada de tratamiento



Encuesta Hospitalaria de pacientes con VIH



CoRIS
Cohorte de la Red de Investigación en Sida



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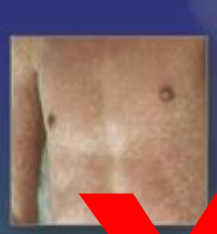
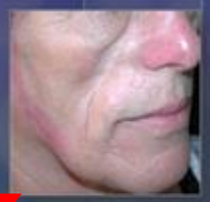
¿ qué entendemos por estrategias y optimización?: conceptos

- Estrategia: serie de acciones muy meditadas encaminadas hacia un fin determinado

- Optimizacíón-optimizar: conseguir que alago llegue a la situación óptima y dé los mejores resultados posibles

En un escenario actual



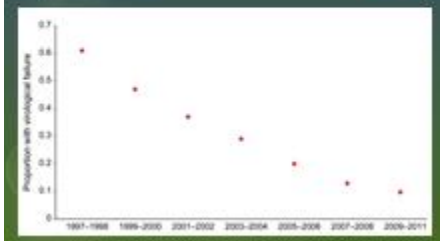


¿Ex va?

Un tratamiento eficaz pero con menos efectos secundarios y más cómodo

Chen RY, et al. *Clin Infect Dis* 2003; 37:714-22.

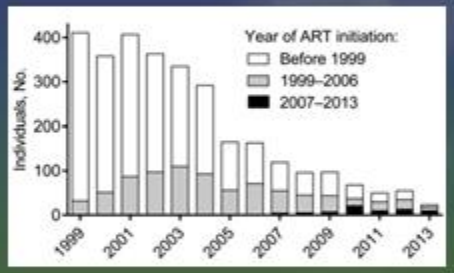
Eficacia virológica a 48 semanas en los últimos ensayos clínicos aleatorizados con regímenes de TAR de 1ª línea



Fracaso virológico

¿Expectativa?

Más comodidad
Menos efectos adversos
Curación



Resistencia

Delaugerre C, et al. *Clin Infect Dis* 2015; 60:463-472.

Scherrer AU. *Clin Infect Dis* 2016, 62, 1310-1317.

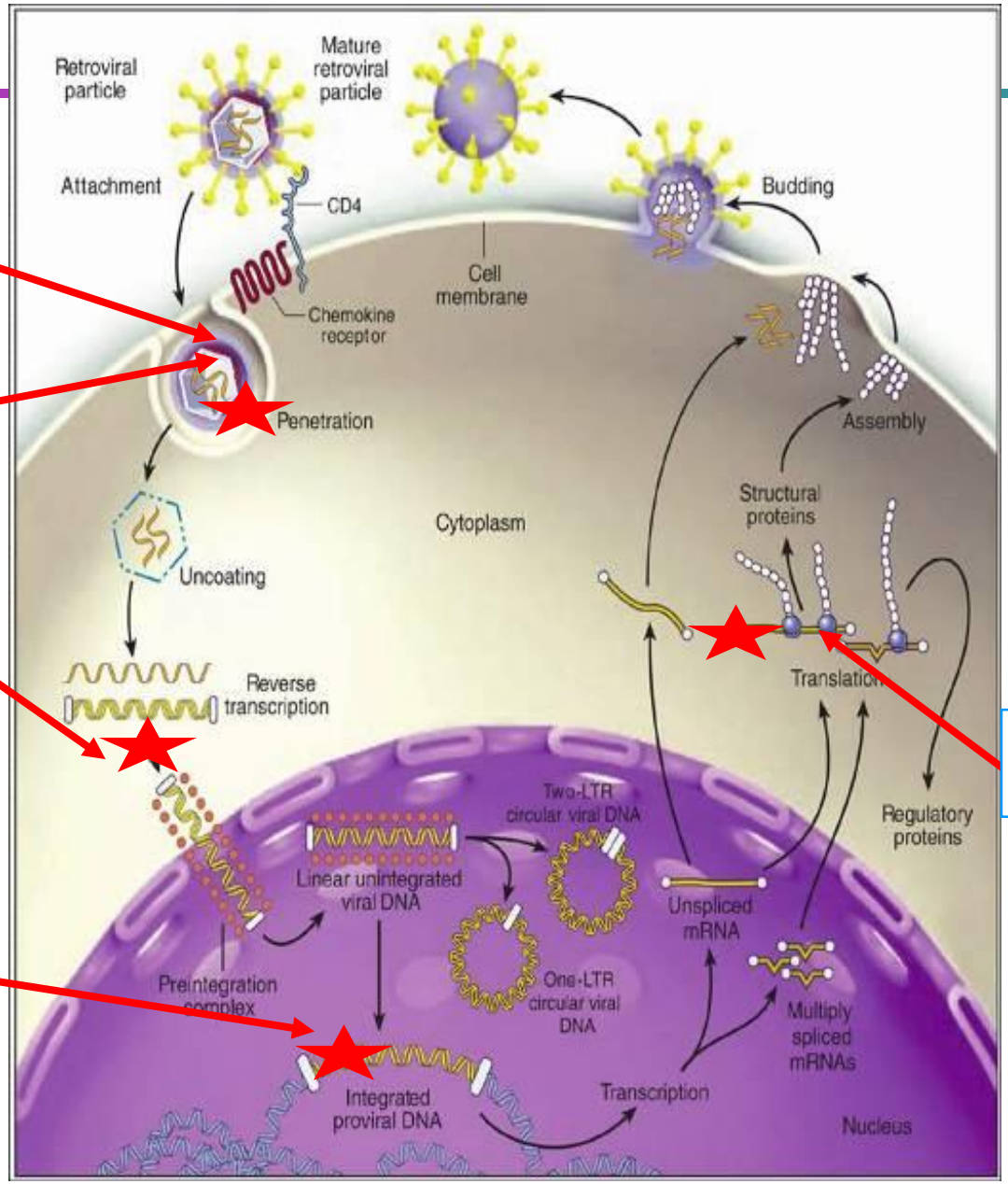
www.youtube.com/watch?v=v2deRuzX52k

Fusion inhibitors

Co-receptor inhibitors

Reverse transcriptase inhibitors

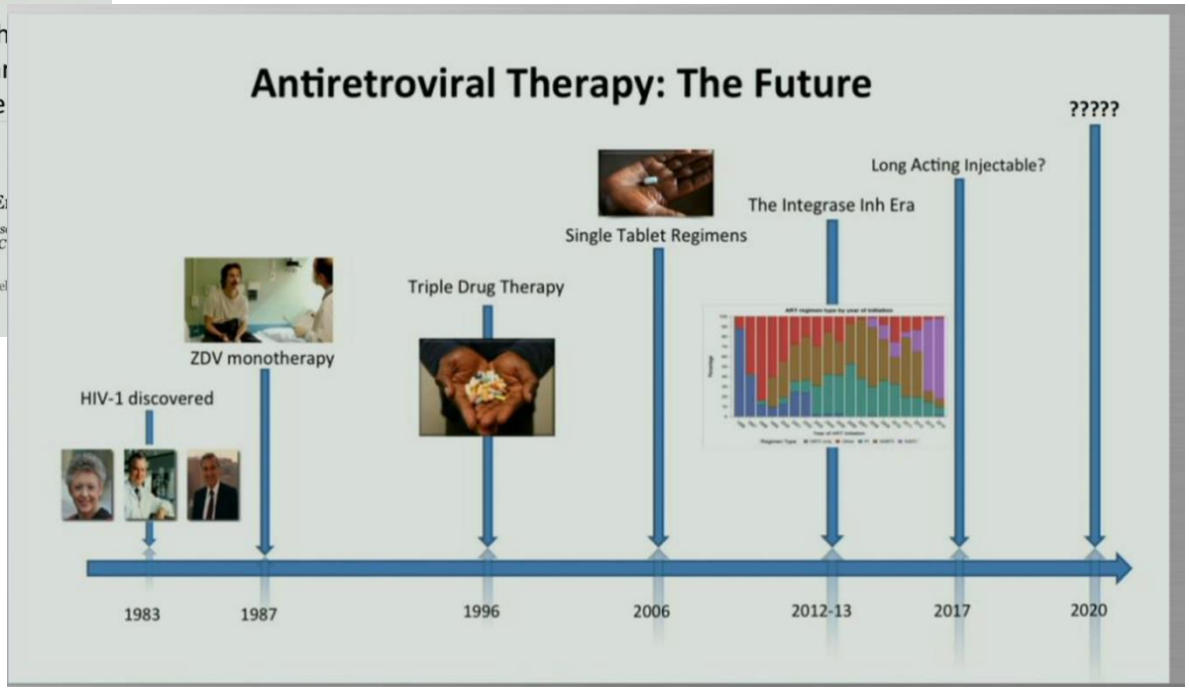
Integrase inhibitors



Protease inhibitors

La realidad en los últimos dos años…

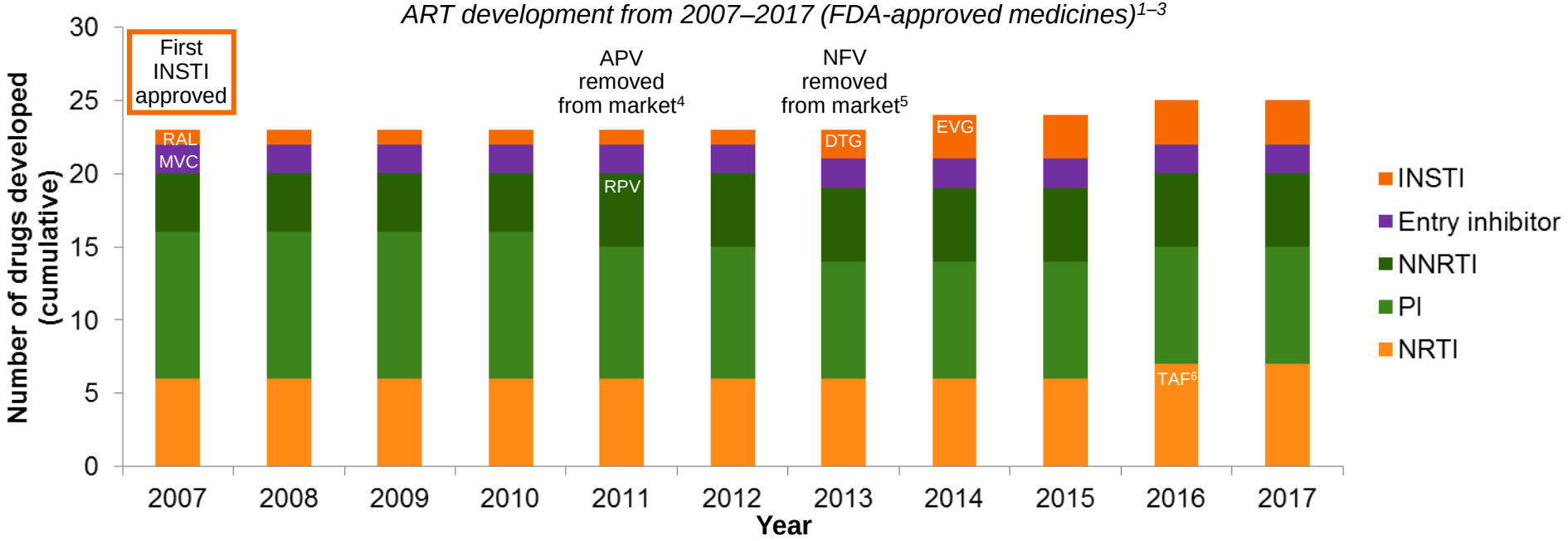
- El tratamiento antirretroviral ha cambiado por completo y va a seguir haciéndolo
  - Momento de inicio
  - Fármacos disponibles
  - Combinaciones de elección



Desarrollo de TAR 2007–2017

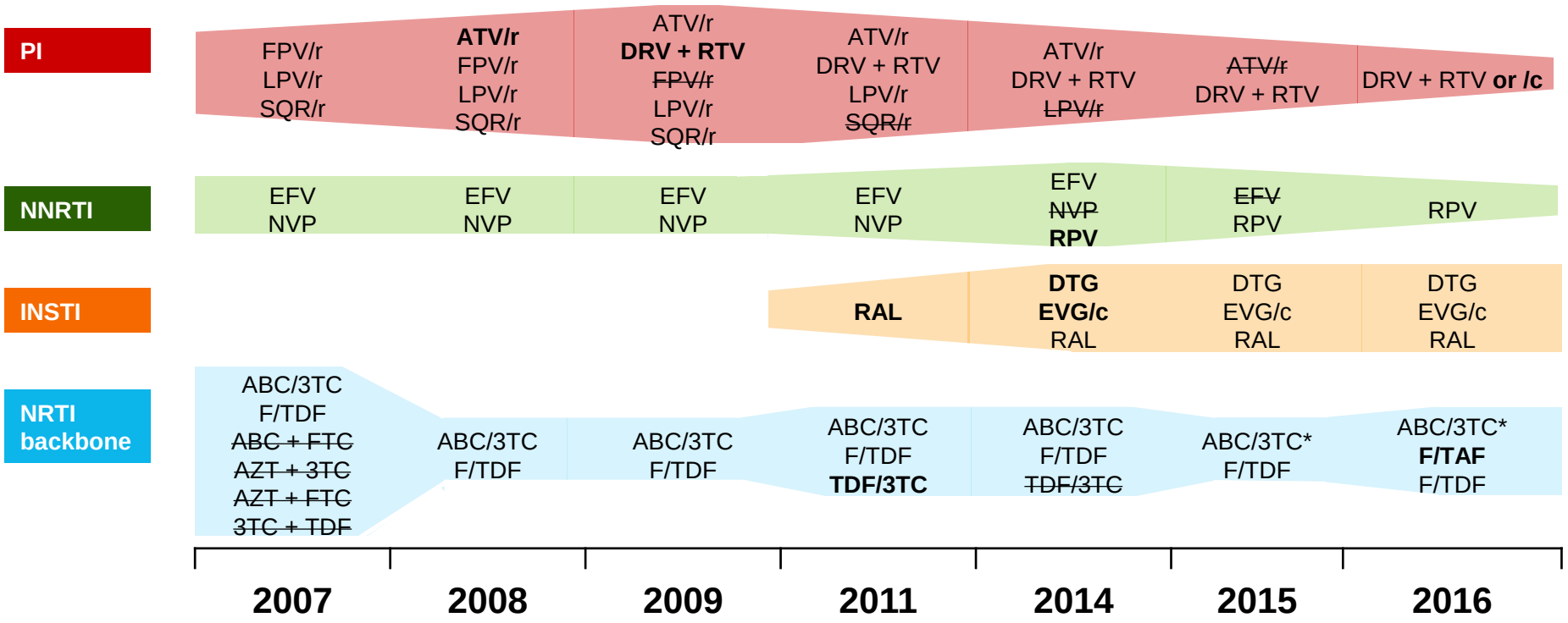
- Desde 2007:[1]
  - No se han comercializado nuevos IPs
  - La eficacia del tratamiento ha mejorado, debido en parte a los NNRTIs de segunda generación y a los nuevos inhibidores de integrasa

ART development from 2007–2017 (FDA-approved medicines)[1–3]



- APV, amprenavir; ART, antiretroviral therapy; ARV, antiretroviral; AZT, zidovudine; DTG, dolutegravir; ETV, etravirine; EVG, elvitegravir; FDA, US Food and Drug Association; INSTI, integrase inhibitor; NFV, nelfinavir; MVC, maraviroc; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; RAL, raltegravir; RPV, rilpivirine; 1. Tseng A et al. Br J Clin Pharmacol 2014;79:182–194; 2. Cohen CJ. J Manag Care Pharm 2006;12(7)(suppl S-b):S6–S11; 3. AIDSinfo. FDA-Approved HIV Medicines (last reviewed 21 August 2017): https://aidsinfo.nih.gov/understanding-hiv-aids/fact-sheets/21/58/fda-approved-hiv-medicines (accessed September 2017); 4. EMA. June 2011:http://www.ema.europa.eu/docs/en_GB/document_library/Public_statement/2011/06/WC500107823.pdf (accessed September 2017); 5. nam aidsmap: Nelfinavir (Viracept): http://www.aidsmap.com/Nelfinavir-iViracepti/page/1731121/ (accessed September 2017); 6. Gilead Sciences, Inc: http://www.gilead.com/news/press-releases/2015/11/us-food-and-drug-administration-approves-gileads-single-tablet-regimen-genvoya-elvitegravir-cobicistat-emtricitabine-and-tenofovir-alafenamide-for-treatment-of-hiv1-infection (accessed October 2017)

Position of preferred antiretroviral agents in EACS guidelines for treatment-naïve individuals[1]



- **EACS guidelines recommend initiation of ART, regardless of CD4 count, in part due to the evolution of drug development[1]**
- **Guidelines emphasise the importance of earlier ART to reduce mother-to-child and sexual transmission[1,2]**

* Only in combination with DTG (ABC/3TC/DTG)[1]

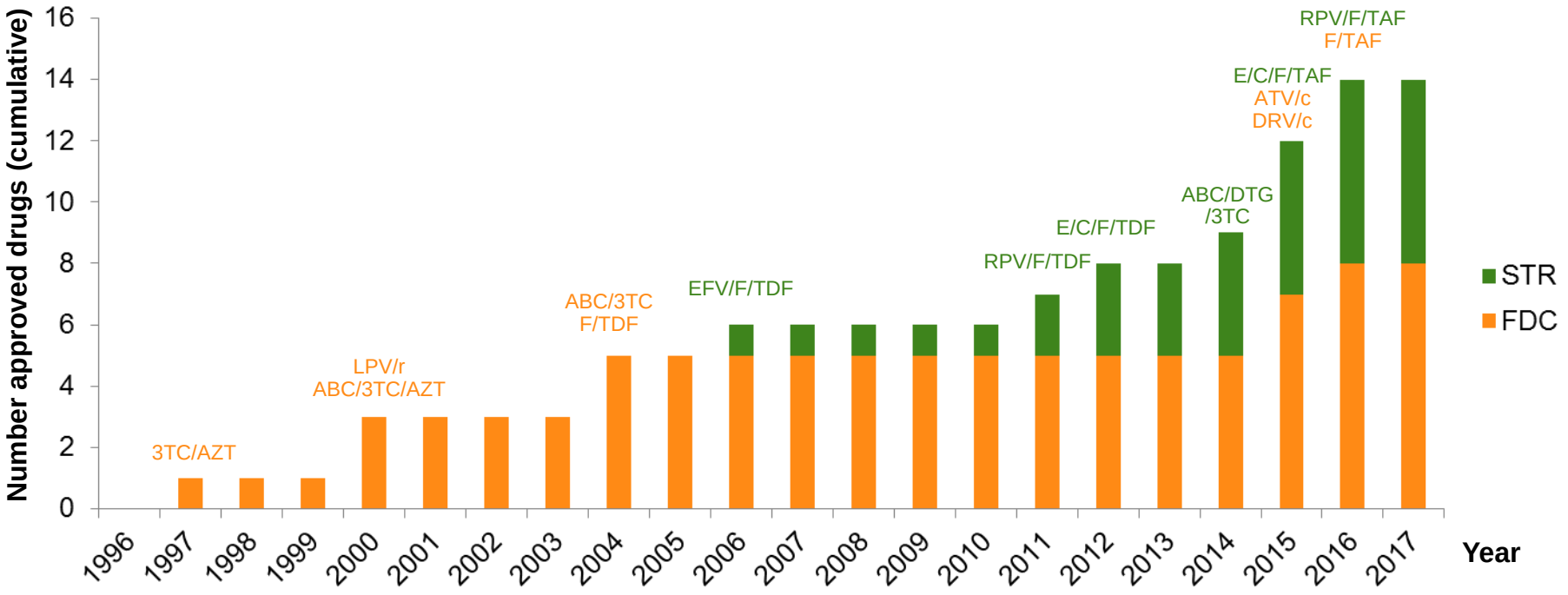
3TC, lami e; ABC, abacavir; ART, antiretroviral therapy; ATV, atazanavir; AZT, zidovudine; /c, cobicistat-boosted; DRV, darunavir; DTG, dolutegravir; EACS, European AIDS Clinical S ; EFV, efavirenz; EVG, elvitegravir; F or FTC, emtricitabine; FPV, fosamprenavir; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; NVP, nevirapine; LPV, lopinavir; PI, protease inhibitor; /r, ritonavir-boosted; RAL, raltegravir; RPV, rilpivirine; SQV, saquinavir; TAF, tenofovir alafenamide; TasP, treatment as prevention; TDF, tenofovir disoproxil fumarate

1. EACS. Guidelines Archive: http://www.eacsociety.org/guidelines/guidelines-archive/archive.html (accessed June 2017);
2. DHHS Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents. January 2016: https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/0 (accessed August 2017)

Desarrollo de combinaciones a dosis fijas y STR

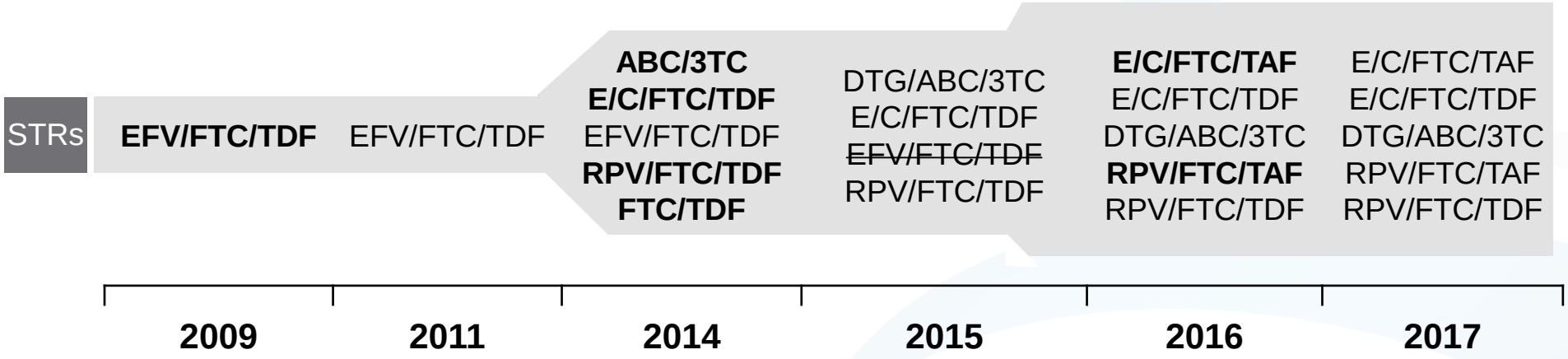
- More FDCs and STRs have been developed over time[2]
  - Initial FDCs included NRTIs 3TC/AZT, ABC/3TC/AZT and F/TDF, and boosted PI eg LPV/r
  - In 2006 the first STR (EFV/F/TDF) was approved

Development of FDCs and STRs from 196–2017 (FDA-approved medicines)[1]



- 3TC, lamivudine; ABC, abacavir; ATV, atazanavir; AZT, zidovudine; /c, cobicistat-boosted; DRV, darunavir; DTG, dolutegravir; E/C/F/TDF, elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate; EFV, efavirenz; FDA, US Food and Drug Association; FDC, fixed-dose combination; F/TDF, emtricitabine/tenofovir disoproxil fumarate; LPV/r, ritonavir-boosted lopinavir; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; /r, ritonavir-boosted; RPV, rilpivirine; STR, single-tablet regimen; TAF, tenofovir alafenamide;
1. AIDSinfo. FDA-Approved HIV Medicines (last reviewed 21 August 2017): https://aidsinfo.nih.gov/understanding-hiv-aids/fact-sheets/21/58/fda-approved-hiv-medicines (accessed September 2017); 2. Astuti N & Maggiolo F. Infect Dis Ther 2014;3:1–17

Position of preferred antiretroviral agents in EACS guidelines for treatment-naïve individuals[1]



- **STRs made their first appearance in EACS guidelines in 2009[1]**
- **Once-daily, single-tablet ARTs have become an important tool in HIV management[2]**

3TC, lamivudine; ABC, abacavir; ART, antiretroviral therapy; C, cobicistat; DTG, dolutegravir; EACS, European AIDS Clinical Society; E, elvitegravir; EFV, efavirenz; F, emtricitabine; RPV, rilpivirine; STR, single-tablet regimen; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate

1. EACS. Guidelines Archive: http://www.eacsociety.org/guidelines/guidelines-archive/archive.html (accessed June 2017);
2. Truong WR et al. P&T 2015;40:44–55

En qué momento nos encontramos?

- Hemos pasado de combinaciones complejas, con muchos efectos secundarios y eficacia limitada con supresión viral incompleta a combinaciones bien toleradas, eficaces y seguras a largo plazo[1]

Menos toxicidad: integrasas, cobicistat

favorecer adherencia: STR

Eficacia a largo plazo y reducción de resistencias

EFV, efavirenz; F, emtricitabine; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; STR, single tablet regimen; TDF, tenofovir disoproxil fumarate

1. Tseng A et al. Br J Clin Pharmacol 2014;79:182–194; 2. Astuti N & Maggiolo F. Infect Dis Ther 2014;3:1–17; 3. EACS Guidelines (5). November 2009: Archive: http://www.eacsociety.org/guidelines/guidelines-archive/archive.html (accessed June 2017); 4. Sax P et al. PLoS ONE 2012;7:e31591; 5. Cassetti I et al. J Int AIDS Soc 2010;13:P86

30 años de desarrollo de fármacos frente a VIH (datos de aprobación de la FDA)

1983

1987

- AZT

1990 - 2002

- Didanosine
- Zalcitabine
- Stavudine
- Lamivudine
- Saquinavir HG
- Saquinavir SGC
- Indinavir
- Nevirapine
- Ritonavir
- Combivir
- Delavirdine
- Nelfinavir
- Abacavir
- Efavirenz
- Amprenavir
- Didanosine EC
- Lopinavir/r
- Trizivir (FDC)
- Tenofovir DF

2003 - 2008

- Atazanavir
- Emtricitabine
- Enfuvirtide
- Fos-APV
- Truvada (FDC)
- Tipranavir
- Atripla (FDC)
- Darunavir
- Maraviroc
- Raltegravir
- Etravirine

2011- 2016

- Rilpivirine/TDF/FTC
- Nevirapine XR
- Rilpivirine
- Elvitegravir/C/F/TDF
- Dolutegravir
- Cobicistat
- Dolutegravir/ABC/3TC
- Elvitegravir/C/F/TAF
- Darunavir/COBI
- Atazanavir/COBI
- FTC/TAF (10, 25 mg)
- *Dolutegravir*

2017-2018

- Raltegravir HD
- *FTC/TDF*
- DRV/COBI-TAF/FTC
- (D/C/F/TAF)*
- (Bictegravir/TAF/FTC)*
- (Dolutegravir/RIL)*
- *(Dolutegravir/3TC/TDF)**

Entry inhibitors | Integrase inhibitors (InSTI) | Protease inhibitors (PI)

Fusion inhibitors | RT (non) nucleosidic inhibitors (N-NRTI)

- *(submitted)
- *Generic versions*

Tabla 3. Combinaciones de TAR de inicio recomendadas†

3er Fármaco	Pauta†	Comentarios‡
Preferentes. Pautas aplicables a la mayoría de los pacientes y que en ensayos clínicos aleatorizados han mostrado una eficacia superior frente a otras o mostrando no-inferioridad presentan ventajas adicionales en tolerancia, toxicidad o un bajo riesgo de interacciones farmacológicas.		
INI	DTG/ABC/3TC	ABC está contraindicado en pacientes con HLA-B*5701 positivo
	DTG+FTC/TAF	
	RAL+FTC/TAF	RAL puede administrarse indistintamente como 1 comprimido de 400 mg cada 12 horas, o 2 comprimidos de 600 mg (nueva formulación) cada 24 horas*.
Alternativas. Pautas eficaces, pero que no se consideran preferentes bien porque su eficacia ha resultado inferior a las pautas preferentes en ensayos clínicos o porque tienen desventajas potenciales o restricciones en su indicación. Pueden ser, sin embargo, de elección en subgrupos de pacientes o en casos especiales		
INI	EVG/c/FTC/TAF	Mayor potencial de interacciones que otras pautas basadas en INI
IP potenciado	DRV/c/FTC/TAF* o	Puede considerarse de elección cuando se requiera de una pauta con elevada barrera genética (pacientes con problemas de adherencia)
	DRV/p+FTC/TAF**	Es imprescindible evaluar posibles interacciones
ITINN	RPV/FTC/TAF*	No indicado en pacientes con CVP >100.000 copias/mL
		Puede considerarse de elección en pacientes con CVP <100.000 copias/mL
		Realizar previamente un estudio genotípico que descarte mutaciones de resistencia a ITINN
		Contraindicado si se utilizan inhibidores de la bomba de protones
		Se debe tomar siempre con una comida
Otras pautas posibles. Estas pautas también han demostrado eficacia, pero o bien la evidencia se considera insuficiente, o tienen des-ventajas respecto a las pautas consideradas preferentes o alternativas		
INI	RAL+ABC/3TC	ABC está contraindicado en pacientes con HLA-B*5701 positivo;
		RAL puede administrarse indistintamente como 1 comprimido de 400 mg cada 12 horas, o 2 comprimidos de 600 mg (nueva formulación) cada 24 horas*.
IP potenciado	ATV/p+FTC/TAF**	Evitar si se utilizan inhibidores de la bomba de protones
		Puede considerarse de elección cuando se requiera de una pauta con elevada barrera genética (pacientes con problemas de adherencia)
		Es imprescindible evaluar posibles interacciones
	DRV/p+ABC/3TC**	ABC está contraindicado en pacientes con HLA-B*5701 positivo;
		Es imprescindible evaluar posibles interacciones
ITINN	EFV+FTC/TAF***	Evitar en pacientes con alteraciones neuropsiquiátricas o ideación suicida. Usar con precaución en pacientes que realicen tareas peligrosas.
		Realizar previamente un estudio genotípico que descarte mutaciones de resistencia a ITINN

GeSIDA
GRUPO DE ESTUDIO DEL SIDA-SEIMC

GOBIERNO DE ESPAÑA · MINISTERIO DE SANIDAD SERVICIOS SOCIALES E IGUALDAD

DOCUMENTO DE CONSENSO GeSIDA/PLAN NACIONAL SOBRE SIDA RESPECTO AL TRATAMIENTO ANTIRRETROVIRAL EN ADULTOS NFECTADOS POR EL VIRUS DE LA INMUNODEFICIENCIA HUMANA

(ACTUALIZACIÓN ENERO 2018)

NRTI fixed-dose combinations					
Abacavir/lamivudine *Generic product, appearance will vary*			Tablet comprising 600mg abacavir and 300mg lamivudine	One tablet once a day	1
Emtricitabine/tenofovir disoproxil	*Truvada*		Tablet comprising 200mg emtricitabine and 245mg tenofovir disoproxil	One tablet once a day	1
Emtricitabine/tenofovir alafenamide	*Descovy*		Tablet comprising 200mg emtricitabine and 10mg or 25mg* tenofovir alafenamide	One tablet once a day. The 10mg version is recommended for use in combination with some boosted protease inhibitors	1
Integrase inhibitors					
Dolutegravir	*Tivicay*		50mg tablet	50mg once a day **or** 50mg twice a day if taken with efavirenz, nevirapine or tipranavir, or for HIV known to be resistant to integrase inhibitors	**1 or 2**
Raltegravir	*Isentress*		400mg tablet	400mg twice a day	**2**
Protease inhibitors					
Atazanavir *Generic product, appearance will vary*			150, 200 and 300mg capsules	300mg with 100mg ritonavir once a day	**2 or 3 §**
Atazanavir/ cobicistat	*Evotaz*		Tablet comprising 300mg atazanavir and 150mg cobicistat	One tablet once a day	**1**
Darunavir *Generic product, appearance will vary*			600 and 800mg tablets	800mg with 100mg ritonavir once a day **or** 600mg with 100mg ritonavir twice a day	**2 to 4 §**
Darunavir/ cobicistat	*Rezolsta*		Tablet comprising 800mg darunavir and 150mg cobicistat	One tablet once a day	**1**

DHHS, IAS-USA Guidelines: Recommended Regimens for First-line ART

Class	DHHS[1]	IAS-USA[2]
INSTI	▪ **BIC/TAF/FTC** ▪ **DTG/ABC/3TC** ▪ DTG + (TAF or TDF)/FTC ▪ **EVG/COBI/(TAF or TDF)/FTC** ▪ RAL + (TAF or TDF)/FTC	▪ **BIC/TAF/FTC** ▪ **DTG/ABC/3TC** ▪ DTG + TAF/FTC

Bold text identifies single-tablet regimens.

- Recommendations may differ based on baseline HIV-1 RNA, CD4+ cell count, CrCl, eGFR, HLA-B*5701 status, HBsAg status, osteoporosis status, and pregnancy status
- Data are lacking for women of child-bearing age not using contraception
- IAS-USA now lists EVG/COBI/TAF/FTC and RAL + TAF/FTC as alternative regimens owing to their lower resistance barriers and, respectively, more drug interactions and higher pill burden[2]

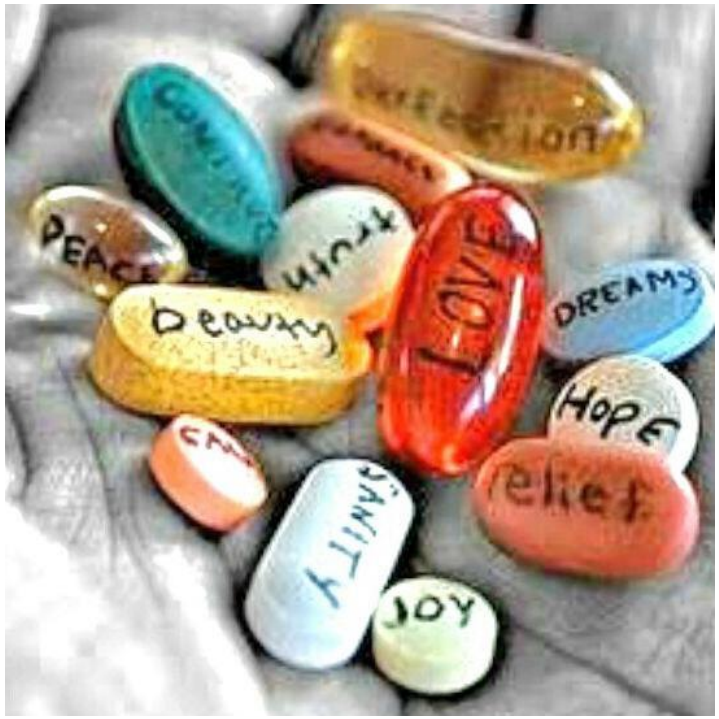
1. DHHS Guidelines. May 2018. 2. Saag MS, et al. JAMA. 2018;320:379-396.

Titulares

- Nos encontramos en la “ERA DE LAS INTEGRASAS”
- TAF o la nueva era de los NRTIs
- Más STR, por favor.
- ¿Necesitamos otras estrategias de tratamiento?
- En busca del fármaco perfecto

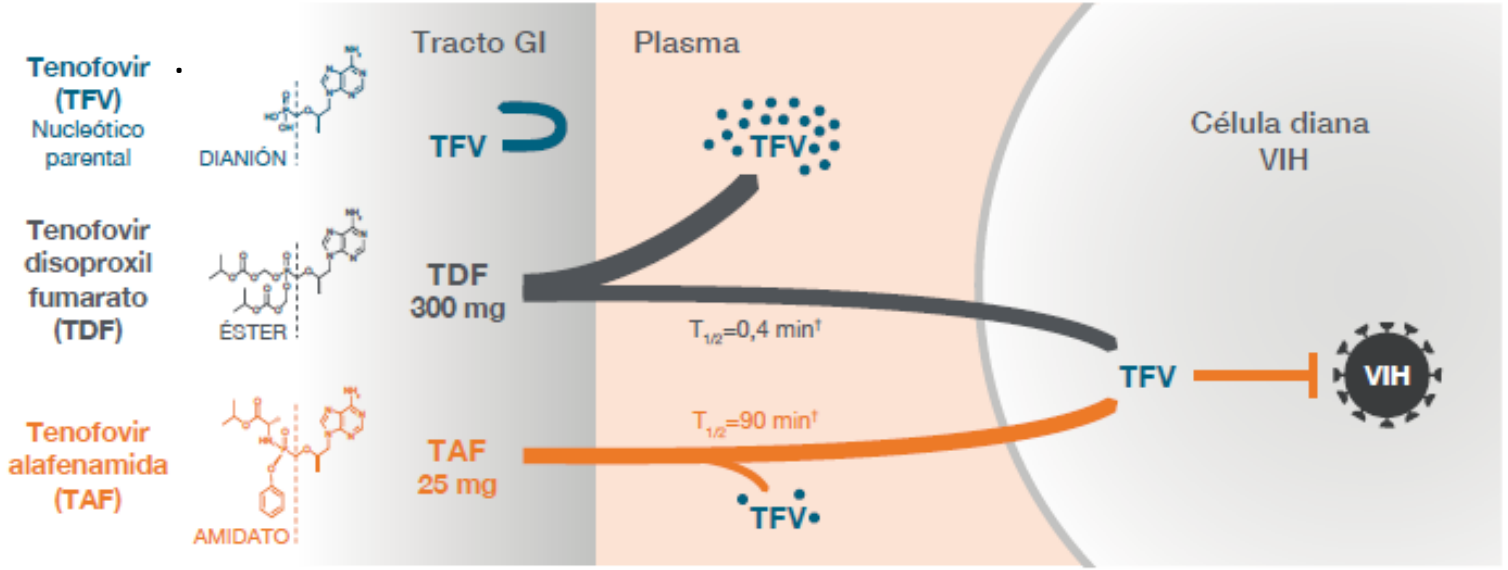
Aspectos que vamos a revisar

- Nuevos fármacos:
  - TAF
    - TAF/FTC (DESCOVY®)
    - TAF/FTC/RPV (ODEFSEY®)
    - TAF/FTC/DRV/C (SYMTUZA®)
  - RAL qd
  - BICTEGRAVIR
    - TAF/FTC/BIC
  - DORAVIRINA
- Nuevas estrategias
  - Biterapias:
    - 3TC+DGT
    - 3TC+IP
    - DGT+RIL
- Nuevas formas de administración
  - Liberación retardada
- Nuevas dianas terapéuticas



TAF O LA REVOLUCIÓN DE LOS NRTIS

Una gran novedad: el Mecanismo de acción



La conversión de TAF en tenofovir tiene lugar principalmente en el interior de las células diana del VIH, reduciendo la exposición sistémica [1,2,3]

† T1/2 basado en los datos plasmáticos *in vitro*.

1. Ficha Técnica Genvoya®, febrero 2016.
2. Ray AS, et al.Review. Tenofovir alafenamide: A novel prodrug of tenofovir for the treatment of Human Immunodeficiency Virus. Antiviral Res. 2016; 125: 63-70.
3. Gupta SK, et al. Subjects with renal impairment switching from tenofovir disoproxil fumarate to tenofovir alafenamide have improved renal and bone safety through 48 weeks. IAS 2015; Vancouver, Canada. Oral Presentation TUAB10. Disponible en: http://www.natap.org/2015/IAS/IAS_23.htm Acceso: 04/16.

¿qué se ha conseguido con el TAF?

- Misma eficacia que con tenofovir
- Posibilidad de más coformulaciones
- Apenas efectos secundarios renales
- No alteraciones óseas
- Mejoría de la osteopenia-osteoporosis, sobre todo en los pacientes que tomaban el tenofovir clásico

Desarrollo clínico completo

Genvoya®

- Naïve:
  - GS-US-292-0104/0111
- Pretratados:
  - GS-US-292-0109 (subestudios)
- Insuficiencia renal
  - GS-US-292-0112
    - Edad
    - Diabetes Mellitus
- Mujer
  - GS-US-236-0128 (OLE)
- Adolescentes
  - GS-US-292-0106

Descovy®

- Pacientes pretratados:
  - GS-US-311-1089

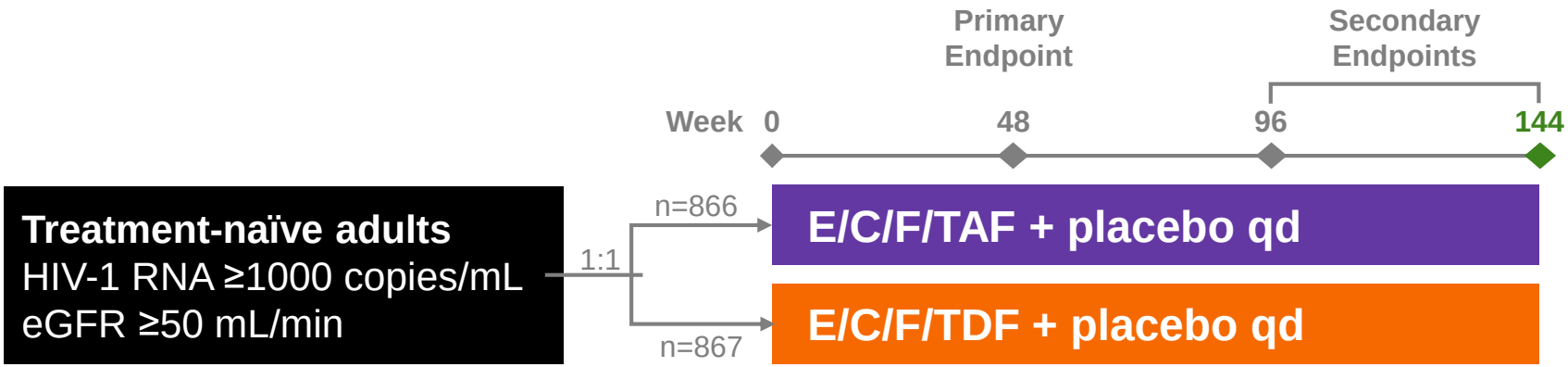
Odefsey®

Pacientes pretratados

-GS-US-Studies 1216 & 1160

Significant Efficacy and Long-term Safety Difference With TAF-Based STR in Naïve Adults

INICIO

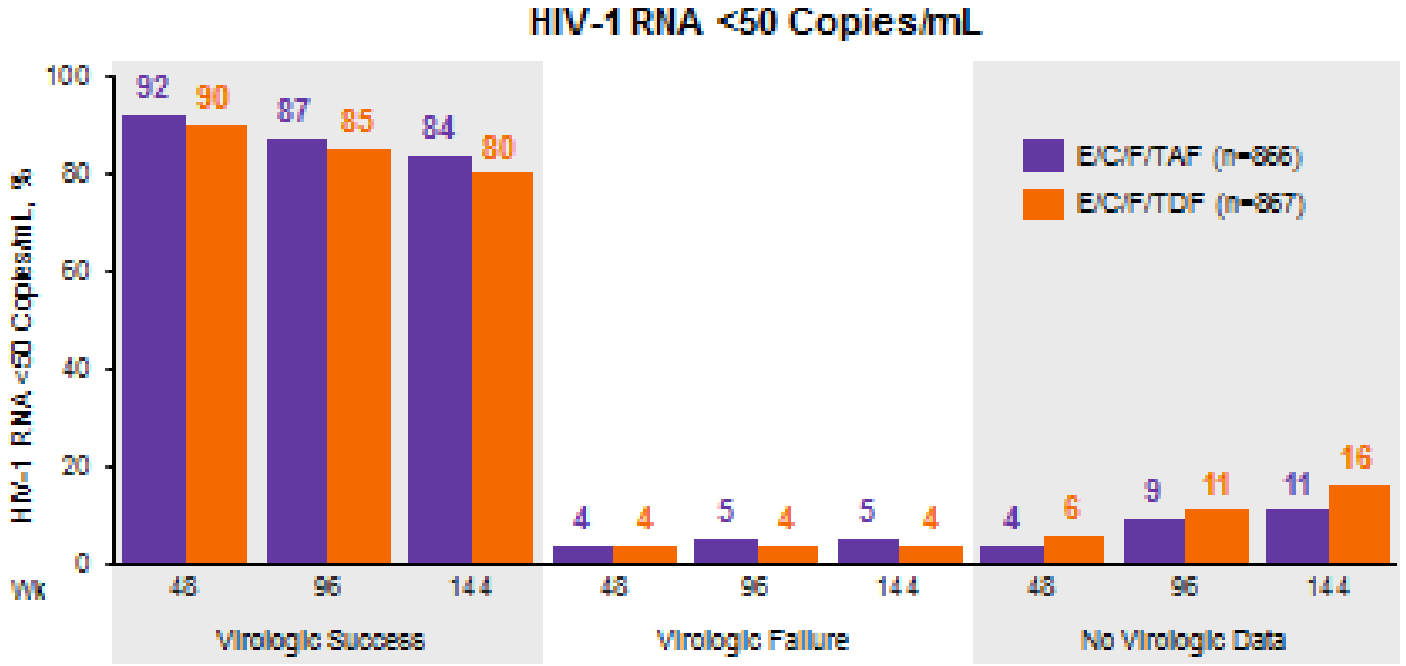


eGFR, estimated glomerular filtration rate.

- Two Phase 3, randomized, double-blind, double-dummy, active-controlled studies[2]
  - Study 104 (North America, EU, Asia); Study 111 (North America, EU, Latin America)
  - Stratified by HIV-1 RNA, CD4 cell count, geographic region
- Primary endpoint met: proportion of participants with HIV-1 RNA <50 copies/mL (COBAS® AmpliPrep/COBAS® TaqMan® HIV-1 Test v2.0, Roche Molecular Diagnostics, Pleasanton, CA)
  - Noninferiority (12% margin) based on Week 48 FDA snapshot analysis
  - Combined efficacy analysis prespecified
- Secondary endpoints: efficacy, safety, and tolerability at Weeks 96 and 144
  - Prespecified safety: serum creatinine, proteinuria, hip and spine bone mineral density (BMD)

Arribas JR et al. CROI 2017, Seattle WA poster 453

Virologic Outcome at Weeks 48, 96, and 144[1,2]



- At Week 144, E/C/F/TAF was superior to E/C/F/TDF in efficacy difference at both <50 copies/mL: 4.2% (95% CI 0.6%, 7.8%; p=0.02) and <20 copies/mL: 5.4% (95% CI 1.5%, 9.2%; p=0.01)

*By FDA snapshot analysis (12% noninferiority margin of TAF to TDF). CI, confidence interval.
1. Sax P, et al. J Acquir Immune Defic Syndr 2014;67:52–8; 2. Sax P, et al. Lancet 2015;385:2606–15.

CROI 2017, Seattle WA poster 453

Efectos adversos renales que conducen a la suspensión de tratamiento

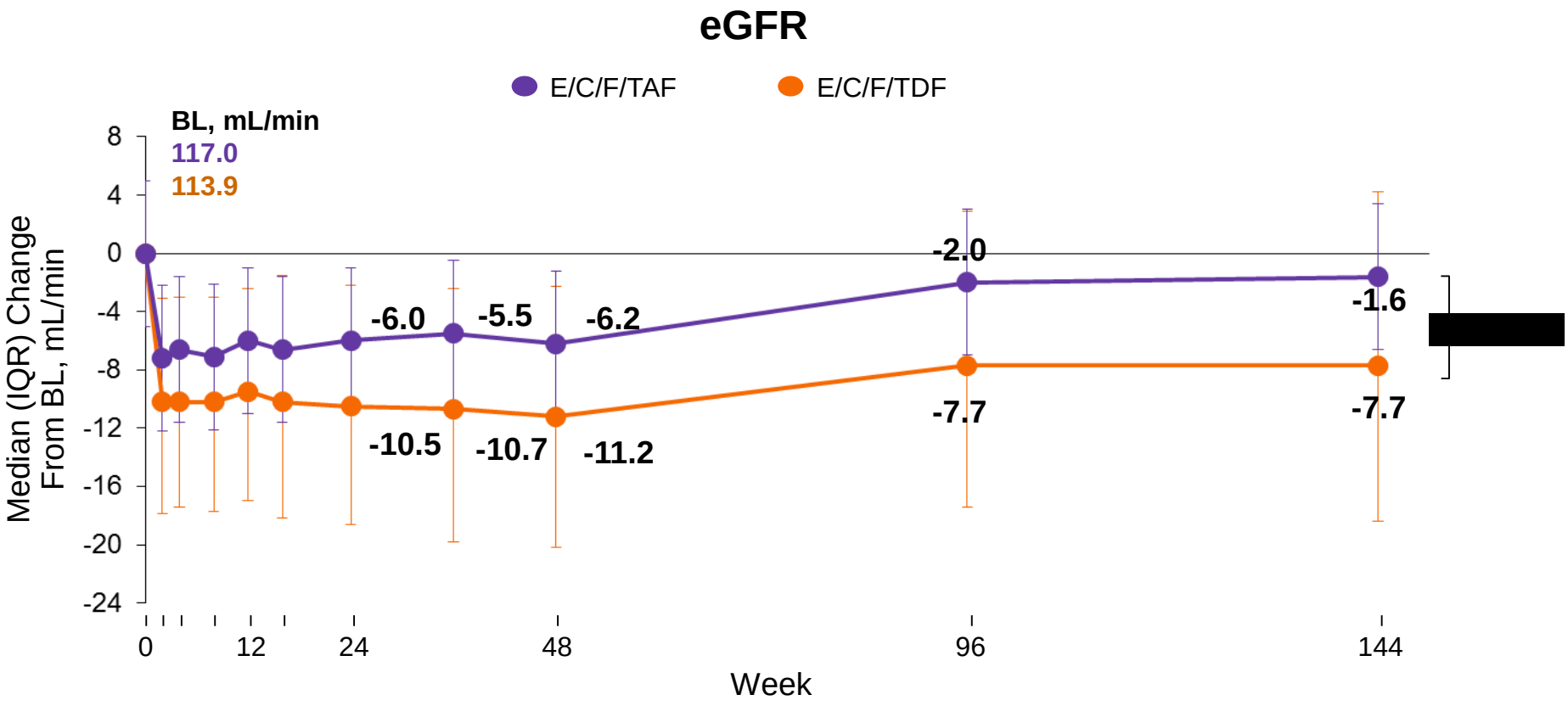
Renal AE D/C, n*	E/C/F/TAF n=866	E/C/F/TDF n=867	p-Value†
Total	**0**	**12**	**<0.001**
Tubulopatia proximal‡	0	4	
Descenso del filtrado glomerular	0	3	
Insuficiencia renal	0	2	
nefropatía	0	1	
Proteinuria	0	1	
Espasmos vesicales	0	1	

*AEs coded as renal and urinary disorders (MedDRA 19.0); †Calculated using Fisher's exact test; ‡Renal tubular disorder, Fanconi syndrome/glycosuria.

- 0 casos de tubulopatía proximal en el brazo E/C/F/TAF vs 4 en el brazo E/C/F/TDF
  - 2 casos adicionales en la rama E/C/F/TDF desde la semana 96

Arribas. CROI 2017, Seattle WA poster 453

Resultados: parámetros renales semana 144*

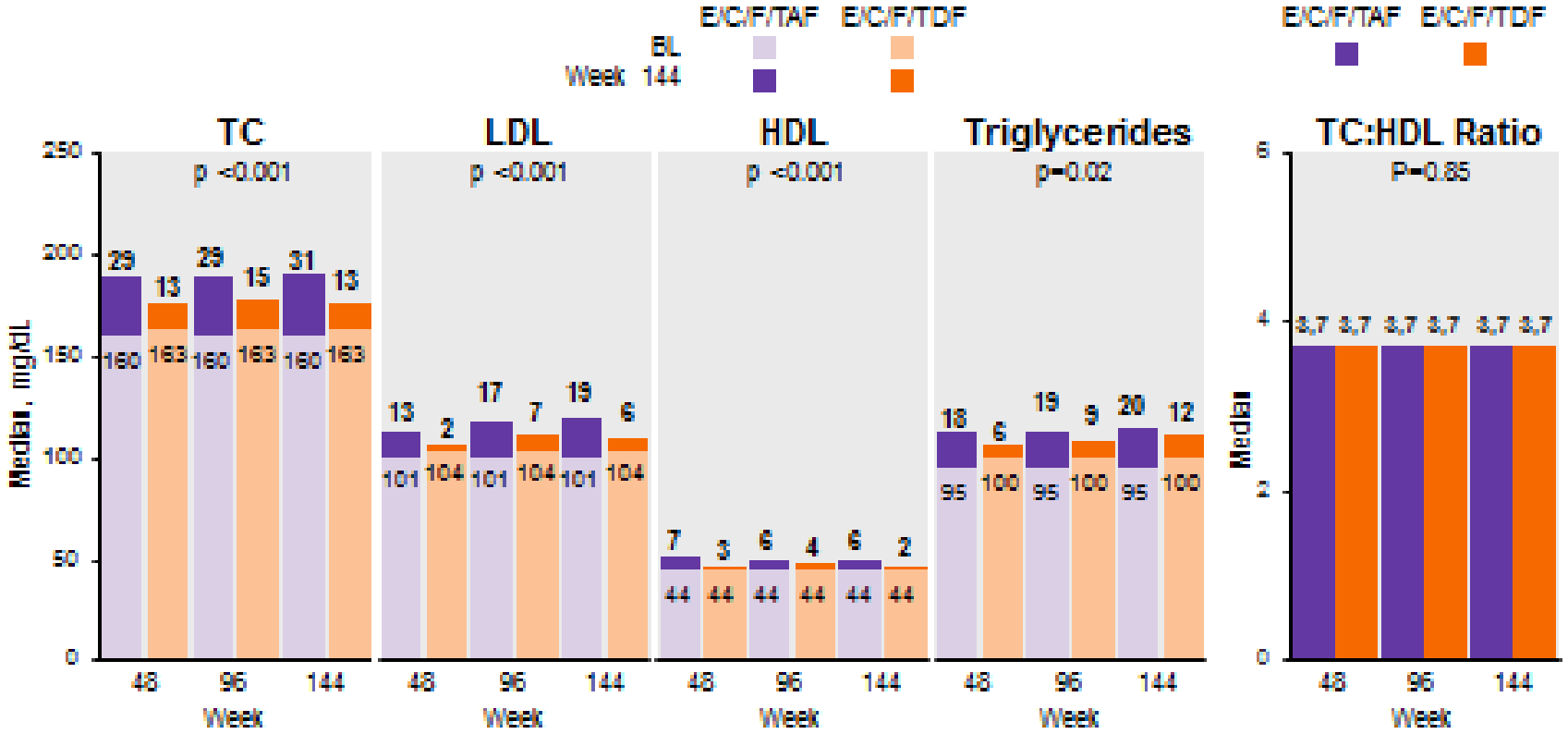


n=	866	842	836	821	771	740
n=	867	841	833	806	756	707

*p-values calculated using 2-sided Wilcoxon rank-sum test to compare treatment groups.

CROI 2017, Seattle WA poster 453

Fasting Lipids through Week 144*



- Participants on E/C/F/TAF had greater increases in TC, LDL, and HDL than those on E/C/F/TDF, with no difference in rate of initiation of lipid-modifying agents (E/C/F/TAF: 5.5% [n=48]; E/C/F/TDF: 5.8% [n=50])

*p-values calculated using 2-sided Wilcoxon rank-sum test to compare treatment groups. HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol.

CROI 2017, Seattle WA poster 453

Resultados: resumen seguridad semana 144 *

Participants, n (%)	E/C/F/TAF n=866	E/C/F/TDF n=867	p-Value†
Any AE	**817 (94.3)**	**833 (96.1)**	**—**
Grade 3 or 4 AE	140 (16.2)	137 (15.8)	—
Serious AE	121 (14.0)	124 (14.3)	—
Death	4 (0.5)†	5 (0.6)‡	—
AE-related D/C			
Week 48	8 (0.9)	13 (1.5)	0.38
Week 96	10 (1.2)	20 (2.3)	0.10
Week 144	11 (1.3)	29 (3.3)	0.01

*Safety analysis set included all participants who received ≥1 dose; †Calculated using Fisher's exact test to compare treatment groups; ‡Stroke (n=2), alcohol intoxication (n=1), suicide (n=1); ‡Alcohol and drug intoxication (n=1), myocardial infarction (n=2), cardiac arrest (n=1), unknown (n=1). D/C, discontinuation.

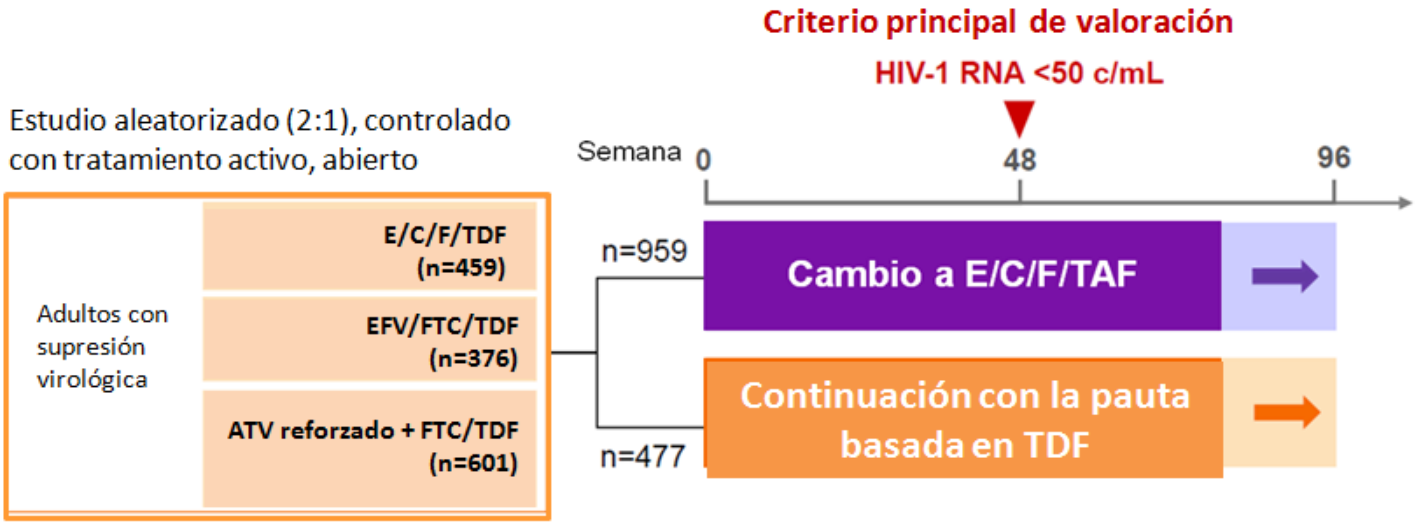
- AEs leading to D/C in the E/C/F/TAF group primarily happened early, whereas in the E/C/F/TDF group, AEs leading to D/C continued to accumulate, with a significant difference in total number of events at Week 144

CROI 2017, Seattle WA poster 453

CAMBIO

Diseño del Estudio GS-US-292-0109

Cambiar a E/C/F/TAF en adultos con supresión virológica*



- Todos los pacientes:
  - VIH-1 RNA <50 copias/mL por ≥96 semanas en pauta estable basada en TDF
  - FG estimada >50 mL/min
- E/C/F/TAF = EVG 150 mg, COBI 150 mg, FTC 200 mg, TAF 10 mg
- E/C/F/TDF = EVG 150 mg, COBI 150 mg, FTC 200 mg, TDF 300 mg

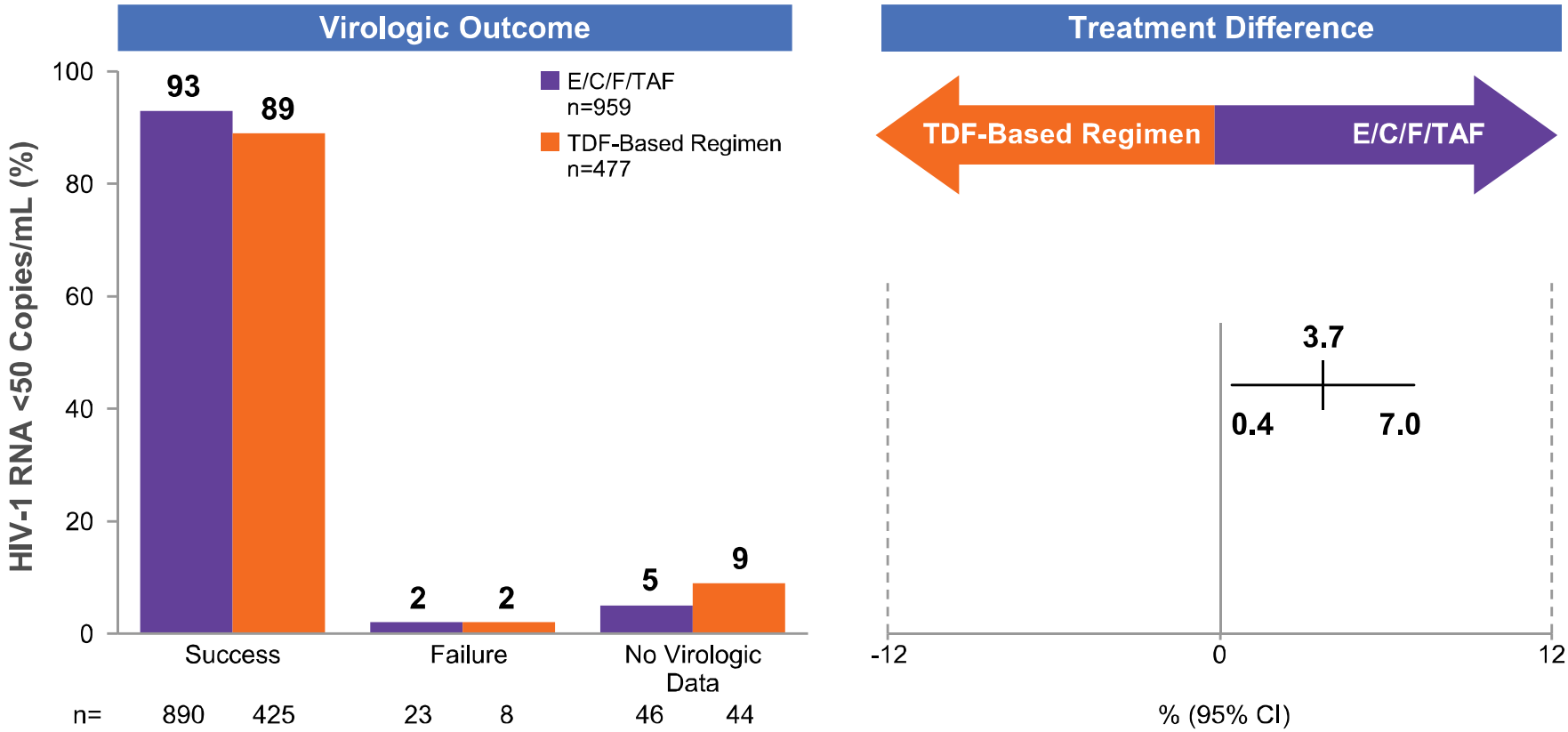
*Supresión virológica: VIH-1 RNA < 50 copias/ml

No inferioridad

1. Mills, A et al. Switching from tenofovir disoproxil fumarate to tenofovir alafenamide in antiretroviral regimens for virologically suppressed adults with HIV-1 infection: a randomised, active-controlled, multicentre, open-label, phase 3, non-inferiority study. The Lancet Infectious Diseases. Volume 16, No. 1, p. 43–52, January 2016.
2. Mills, A et al. Switching from a Tenofovir Disoproxil Fumarate (TDF)-based regimen to a Tenofovir Alafenamide (TAF)-Based regimen: data in virologically suppressed adults through 48 weeks of treatment. 8th International AIDS Society Conference on HIV Pathogenesis, Treatment and Prevention (IAS) 2015, Vancouver, Canada. Oral presentation.
3. Supplement to: Mills A, Arribas JR, Andrade-Villanueva J, et al. Switching from tenofovir disoproxil fumarate to tenofovir alafenamide in antiretroviral regimens for virologically suppressed adults with HIV-1 infection: a randomised, active-controlled, multicentre, open-label, phase 3, non-inferiority study. Lancet Infect Dis 2015; published online Nov 2.

RESULTADOS

HIV-1 RNA <50 Copias/mL a la semana 96



CI, confidence interval.

DeJesus E, AMS Microbe, 2016, #LB-087

Desarrollo clínico

6 Label-Enabling Studies (N = 3,562)

- **Study 112:** Adults with Renal Impairment (N = 248 Treatment-Naïve or -Experienced)
- **Study 104:** Treatment-Naive Adults (N = 867)
- **Study 111:** Treatment-Naive Adults (N = 866)
- **Study 109:** HIV Suppressed Adults (Switch) (N = 1436)
- **Study 106:** Treatment-Naïve Adolescents (n = 50) HIV suppressed Children (n=23)
- **Study 1249:** HIV/HBV Co-infected Adults (N = 72)

2 studies to investigate a poorly studied population

- **WAVES OLE:** HIV suppressed Female Adults (Switch from a TDF based regimen)
- **CoSTaR:** HIV/HCV Co-infected Adults treated with SOF/LDV (N=148)

3 additional studies to support unmet medical needs

- **Study 119:** Simplification to E/C/F/TAF + DRV (N = 135)
- **Study 1823:** HIV Suppressed Adults Switched from a ABC/3TC regimen (N = 274)
- **Study 1824:** HIV Suppressed Adults with M184V/I Switched to E/C/F/TAF (N = 100)

MOPEB0292

Efficacy and Safety of Tenofovir Alafenamide vs Tenofovir DF in HIV-Infected, Virologically Suppressed, Older Adults at Week 96: Subgroup Analysis of a Randomized Switch Study (Study 311-1089)

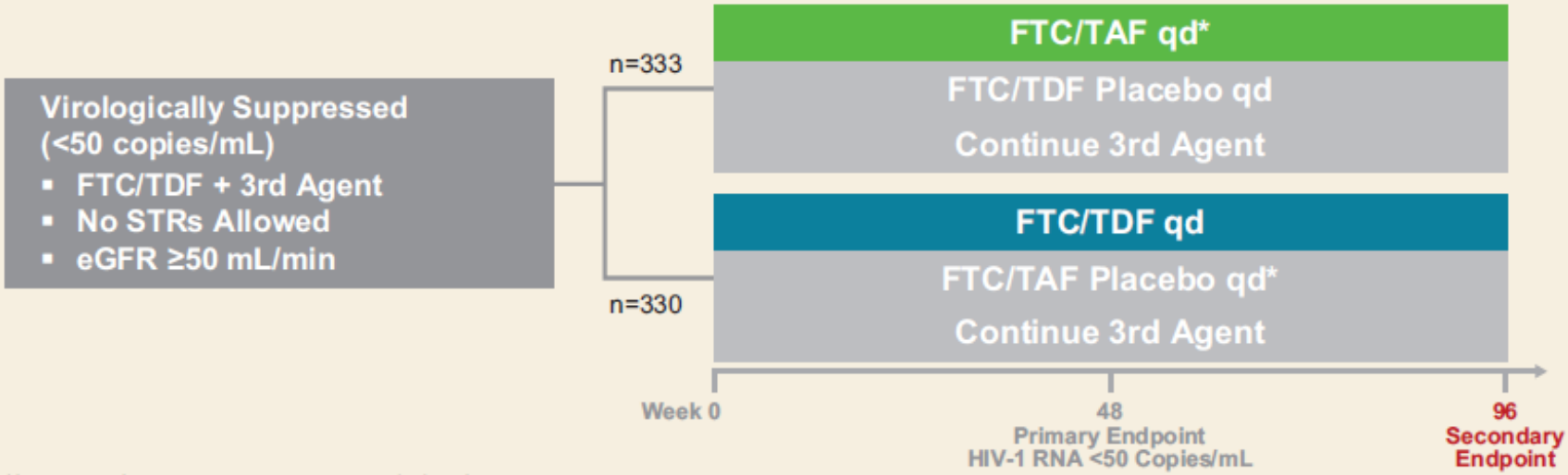
Yazdan Yazdanpanah,[1] Francois Raffi,[2] Jacques Reynes,[3] Margaret Johnson,[4] Chloe Orkin,[5] Nathan Clumeck,[6] Brian Conway,[7] Adriano Lazzarin,[8] Franco Maggiolo,[9] Martin Rhee[10]

[1]Hôpital Bichat-Claude Bernard, Paris, France; [2]Hôtel-Dieu, Nantes, France; [3]Hôpital Gui de Chauliac, Montpellier, France; [4]Royal Free London NHS Foundation Trust, London, UK; [5]Barts Health NHS Trust, Ambrose King Centre, Royal London Hospital, London, UK; [6]CHU St-Pierre, Bruxelles, Belgium; [7]Vancouver Infectious Diseases Research & Care Centre Society, Vancouver, British Columbia, Canada; [8]Ospedale San Raffaele, Milano, Italy; [9]Azienda Ospedaliera Papa Giovanni XXIII, Bergamo, Italy; [10]Gilead Sciences, Inc., Foster City, CA, USA

GILEAD
Gilead Sciences, Inc.
333 Lakeside Drive
Foster City, CA 94404
800-445-3235

Study Design

Switch From FTC/TDF to FTC/TAF



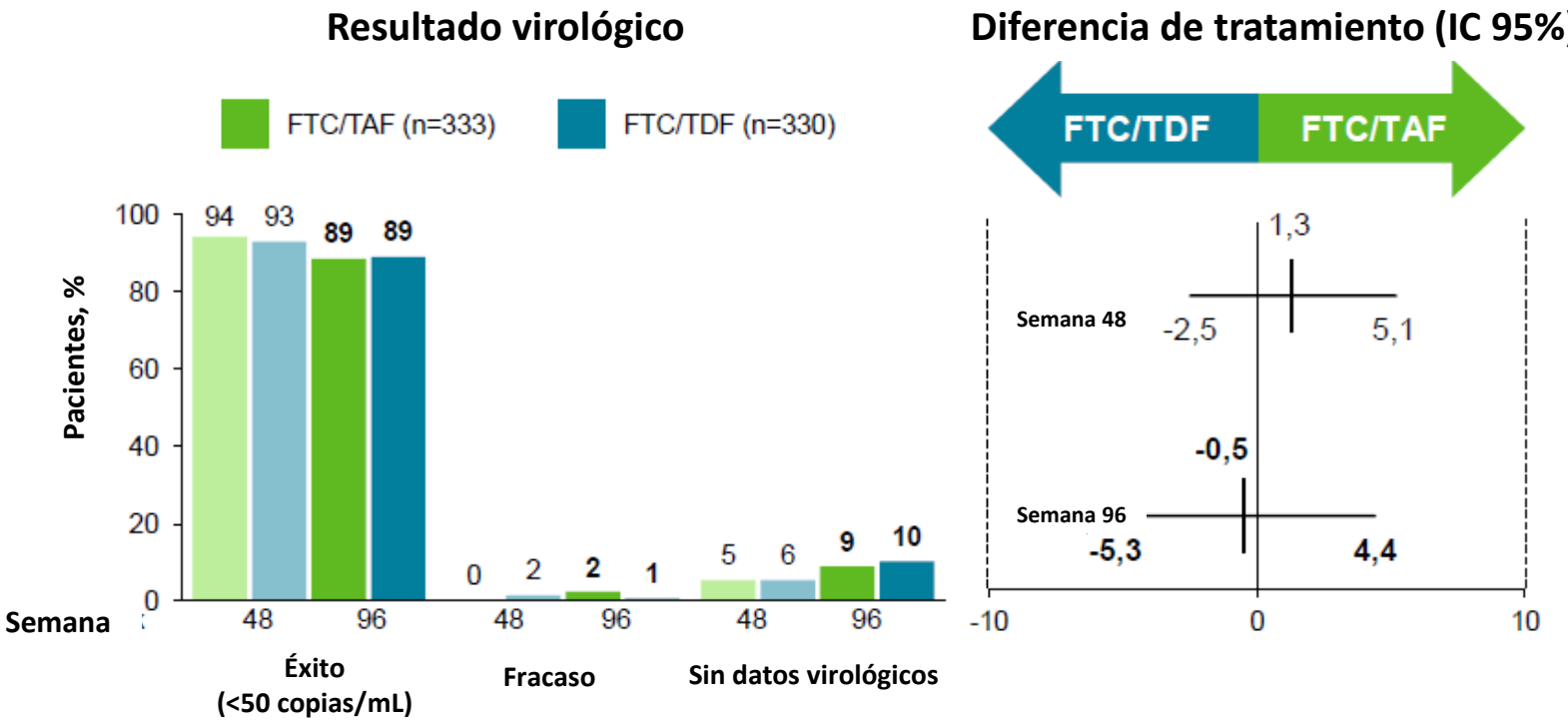
*FTC/TAF dose: 200/10 mg with boosted protease inhibitors (PIs); 200/25 mg with unboosted 3rd agents.

- Randomized, double-blind, double-dummy, active-controlled study (ClinicalTrials.gov NCT02121795)

Yazdanpanah Y. MOPEB0292 IAS 2017

ESTUDIO GS-US-311-1089
Eficacia virológica

ESTUDIO GS-US-311/1089: Eficacia virológica



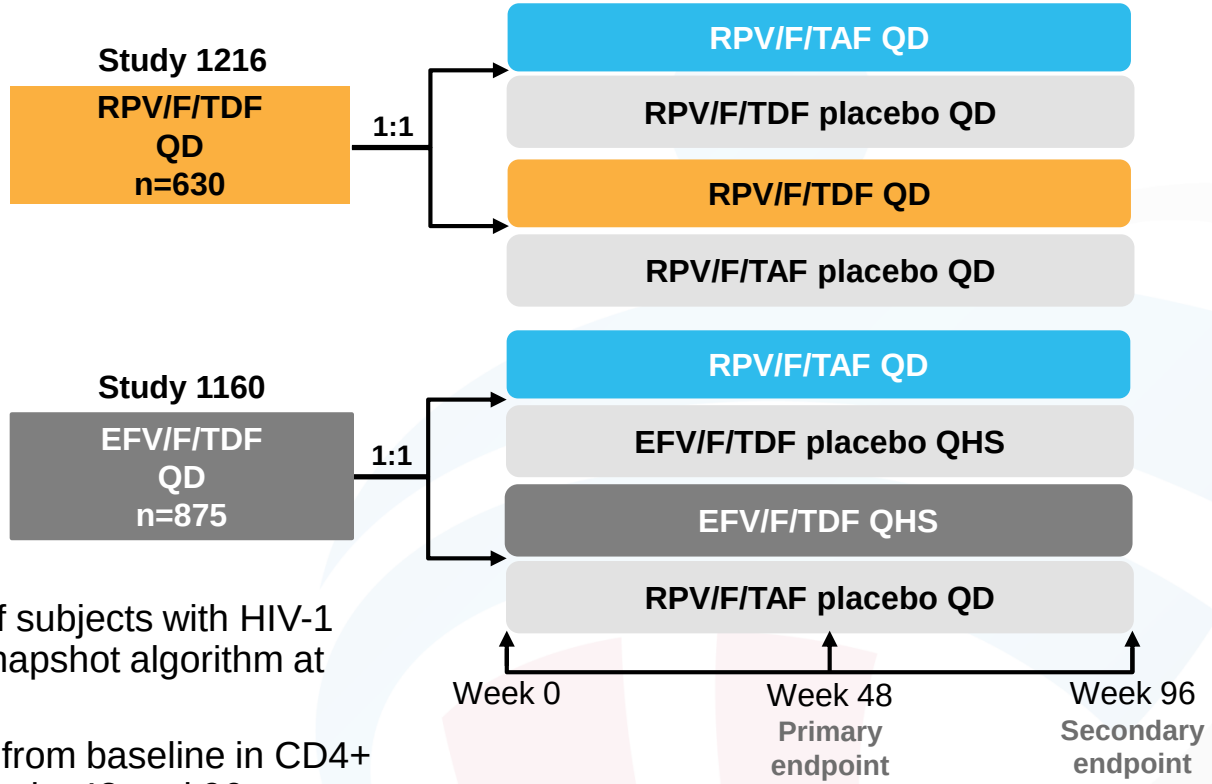
Descovy® combinado con un tercer agente **ha demostrado no inferioridad a FTC/TDF en las semanas 48 y 96**

Raffi F, et al. 96-week Results from Study 1089: Switching to Tenofovir Alafenamide From Tenofovir Disoproxil Fumarate-Based Regimens. Póster presentado en el Congreso HIV Glasgow 2016. 23-26 octubre 2016, Glasgow, UK. Presentación 0125

Study design*

Two separate phase 3b, 96-week, randomised, double-blind, active-controlled studies evaluating switch from RPV/F/TDF or EFV/F/TDF to RPV/F/TAF in virologically suppressed adults

Virologically suppressed adults
HIV-1 RNA <50 copies/mL (for 6 months)
Previously treated with NNRTI STRs for ≥6 months
No history of resistance
eGFR ≥50mL/min
N=1,505

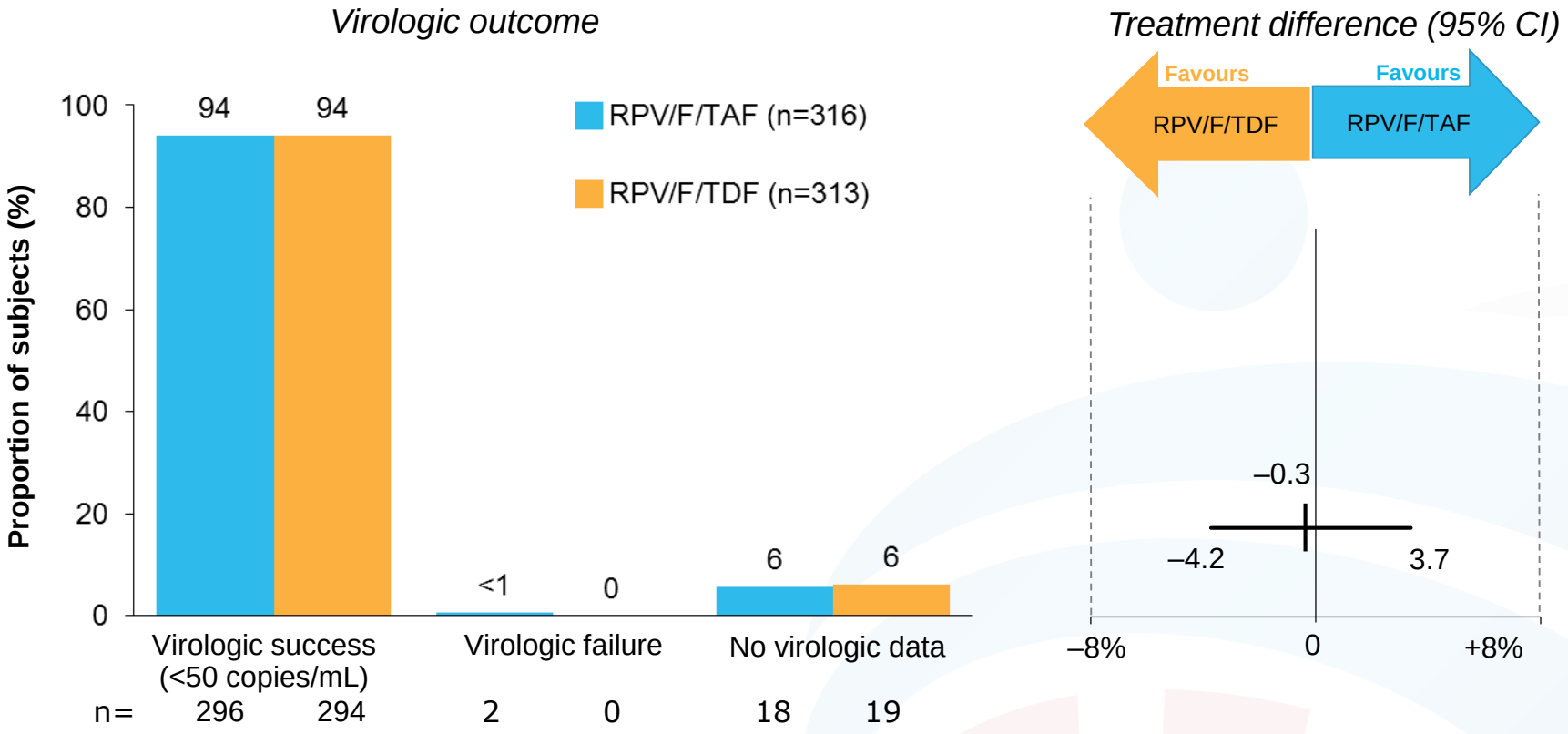


- Primary endpoint: Proportion of subjects with HIV-1 RNA <50 copies/mL by FDA Snapshot algorithm at Week 48
- Secondary endpoints: Change from baseline in CD4+ and BMD (hip and spine) at Weeks 48 and 96

ClinicalTrials.gov Identifiers: NCT02345252 NCT02345226

This slide may contain information relating to a product that is not currently reimbursed in your country
Studies 1216 and 1160 (North America, EU)
* Dietary counselling: RPV STRs/placebo with food (no restrictions specified); EFV STRs/placebo without food
ART, antiretroviral therapy; BMD, bone mineral density; EFV, efavirenz; eGFR, estimated glomerular filtration rate; F, emtricitabine; NNRTI, non-nucleoside reverse transcriptase inhibitor; QD, once daily; QHS, every bedtime; RPV, rilpivirine; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; STR, single-tablet regimen
Orkin C et al. HIV Drug Therapy 2016. Glasgow, UK. #O124

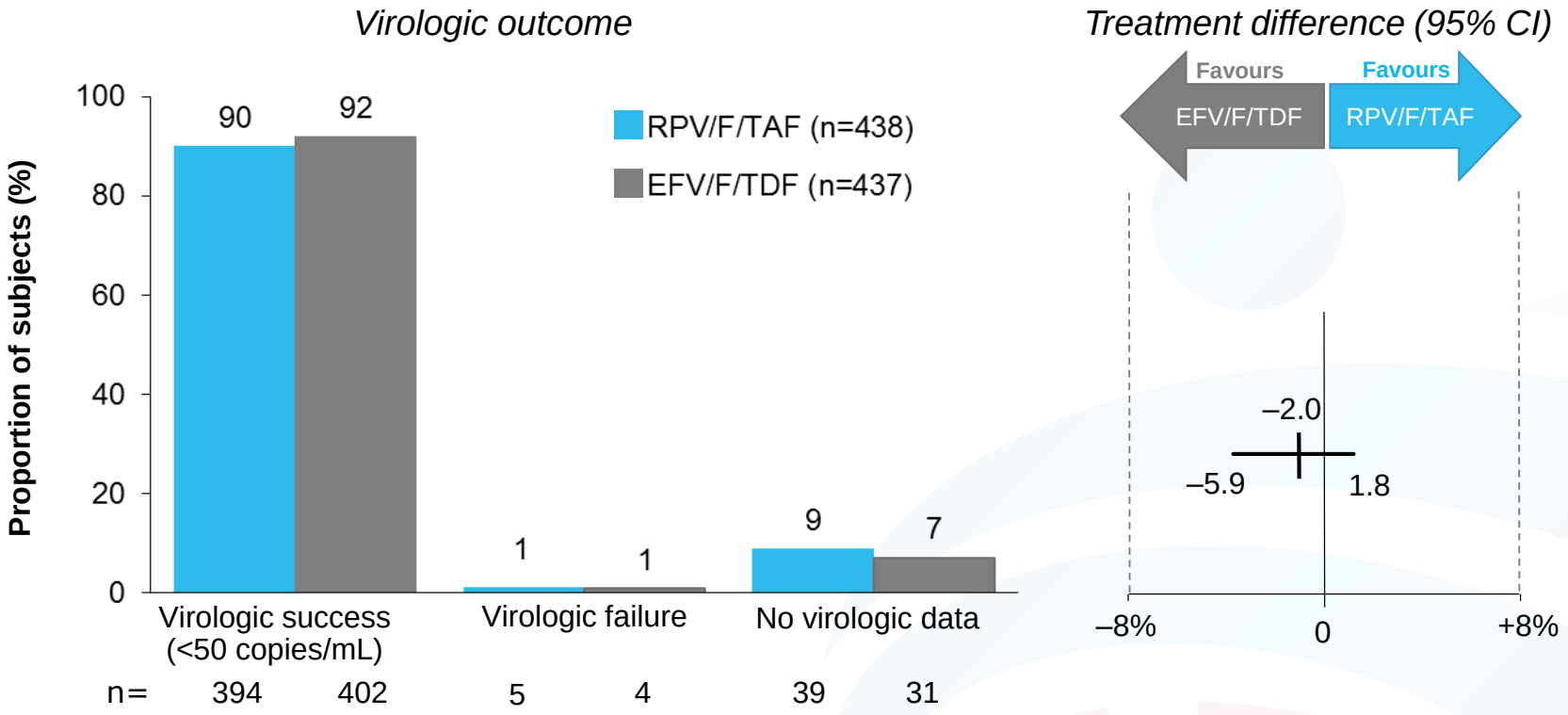
Virologic outcomes at Week 48 (FDA Snapshot)



- **Switching to RPV/F/TAF was non-inferior in efficacy vs continuing RPV/F/TDF at Week 48**
  - Efficacy was comparable across age, sex, geographic region
- **No emergent resistance mutations were detected in either group**

This slide may contain information relating to a product that is not currently reimbursed in your country
ART, antiretroviral therapy; CI, confidence interval; F, emtricitabine; RPV, rilpivirine; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate
Orkin C et al. HIV Drug Therapy 2016. Glasgow, UK. #O124

Virologic outcomes at Week 48 (FDA Snapshot)



- **Switching to RPV/F/TAF was non-inferior in efficacy vs continuing EFV/F/TDF at Week 48**
  - Efficacy was comparable across age, sex, geographic region
- **No emergent resistance mutations were detected in RPV/F/TAF group**
  - One subject in EFV/F/TDF group developed emergent mutations (M184V, V106I/L, Y188L)

This slide may contain information relating to a product that is not currently reimbursed in your country

ART, antiretroviral therapy; CI, confidence interval; EFV, efavirenz; F, emtricitabine RPV, rilpivirine; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate

Orkin C et al. HIV Drug Therapy 2016. Glasgow, UK. #O124

F/TAF-based regimens and components

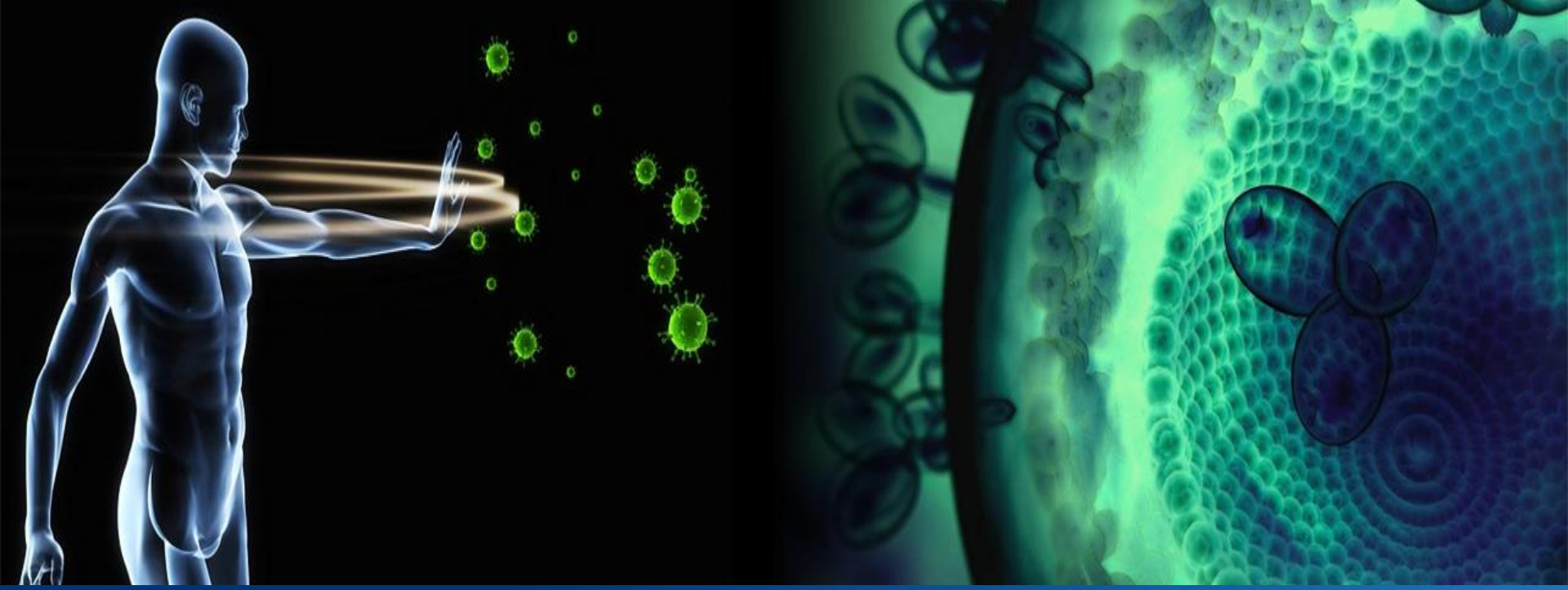
Drug	Abbreviation	Components	
Descovy 200mg/10mg 	F/TAF	Emtricitabine Tenofovir alafenamide	200mg 10mg*
Descovy 200mg/25mg 		Emtricitabine Tenofovir alafenamide	200mg 25mg‡
	Descovy is indicated in combination with other antiretroviral agents for the treatment of adults and adolescents (aged 12 years and older with body weight at least 35kg) infected with human immunodeficiency virus type 1 (HIV-1)[1,2]		
Genvoya (Single-tablet regimen) 	E/C/F/TAF	Elvitegravir Cobicistat Emtricitabine Tenofovir alafenamide	150mg 150mg 200mg 10mg*
	Genvoya is indicated for the treatment of adults and adolescents (aged 12 years and older with body weight at least 35kg) infected with HIV-1 without any known mutations associated with resistance to the integrase inhibitor class, emtricitabine or tenofovir[3]		
Odefsey (Single-tablet regimen) 	R/F/TAF	Rilpivirine Emtricitabine Tenofovir alafenamide	25mg† 200mg 25mg‡
	Odefsey is indicated for the treatment of adults and adolescents (aged 12 years and older with body weight at least 35kg) infected with HIV-1 without known mutations associated with resistance to the non-nucleoside reverse transcriptase inhibitor (NNRTI) class, tenofovir or emtricitabine and with a viral load ≤100,000 HIV-1 RNA copies/mL[4]		

Images shown do not represent actual size

This slide may contain information relating to a product that is not currently reimbursed in your country

* TAF fumarate equivalent to 10mg of TAF; ‡ TAF equivalent to 25mg of TAF; † rilpivirine hydrochloride equivalent to 25mg of rilpivirine; § 300mg of TDF equivalent to 245mg of tenofovir disoproxil or 136mg of tenofovir

1. Descovy (10mg) SmPC, www.ema.europa.eu (accessed August 2017); 2. Descovy (25mg) SmPC, www.ema.europa.eu (accessed August 2017); 3. Genvoya SmPC. Descovy (10mg) SmPC, www.ema.europa.eu (accessed August 2017); 4. Odefsey SmPC, www.ema.europa.eu (accessed August 2017)



Efficacy and safety of switching from boosted-protease inhibitors plus emtricitabine/tenofovir disoproxil fumarate regimens to the single-tablet regimen (STR) of darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) in virologically suppressed, HIV-1-infected adults through 24 weeks: EMERALD Study

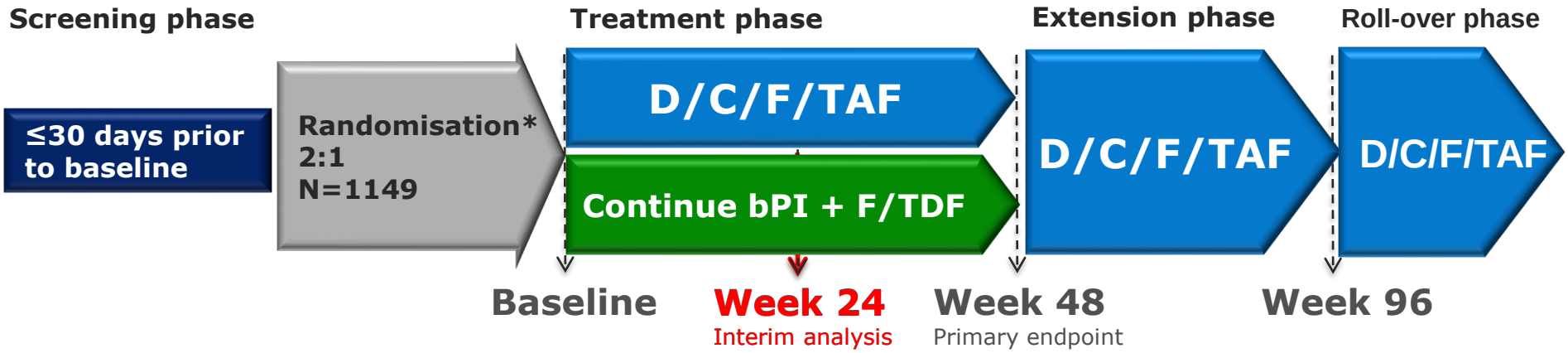
Jean-Michel Molina[1], Joel Gallant[2], Chloe Orkin[3], Eugenia Negredo[4], Laveeza Bhatti[5], Joseph Gathe[6], Erika Van Landuyt[7], Erkki Lathouwers[7], Veerle Hufkens[7], Simon Vanveggel[7], Magda Opsomer[7]

[1]Department of Infectious Diseases, St-Louis Hospital, University of Paris Diderot, Paris, France; [2]Southwest CARE Center, Santa Fe, New Mexico, USA; [3]Barts and Health NHS Trust, London, UK; [4]Germans Trias i Pujol University Hospital, Badalona, Spain; [5]AIDS Healthcare Foundation, Beverly Hills, California, USA; [6]Therapeutic Concepts, Houston, Texas, USA; [7]Janssen Pharmaceutica NV, Beerse, Belgium

Janssen Infectious Diseases & Vaccines
PHARMACEUTICAL COMPANIES OF Johnson & Johnson

Molina J-M, et al. 9th IAS 2017. Abstract TUAB0101

EMERALD: Open-label, Randomised, Multicentre, Parallel-group, Non-inferiority Phase III Trial



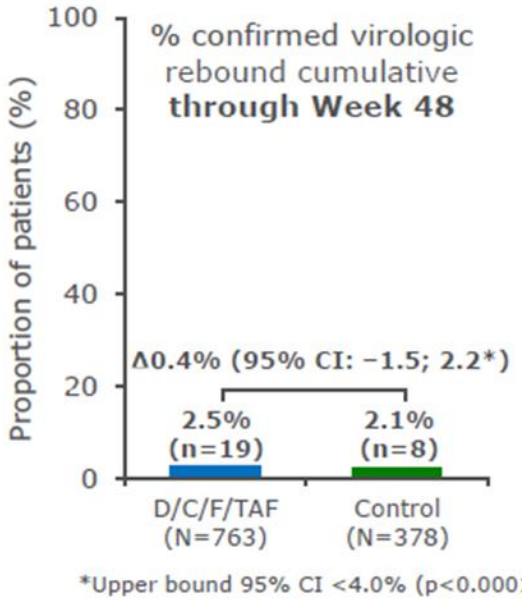
Objective: Non-inferiority and safety of switching to D/C/F/TAF vs continuing bPI + FTC/TDF regimens in virologically suppressed HIV-1-infected adults at Week 48

Key inclusion criteria:

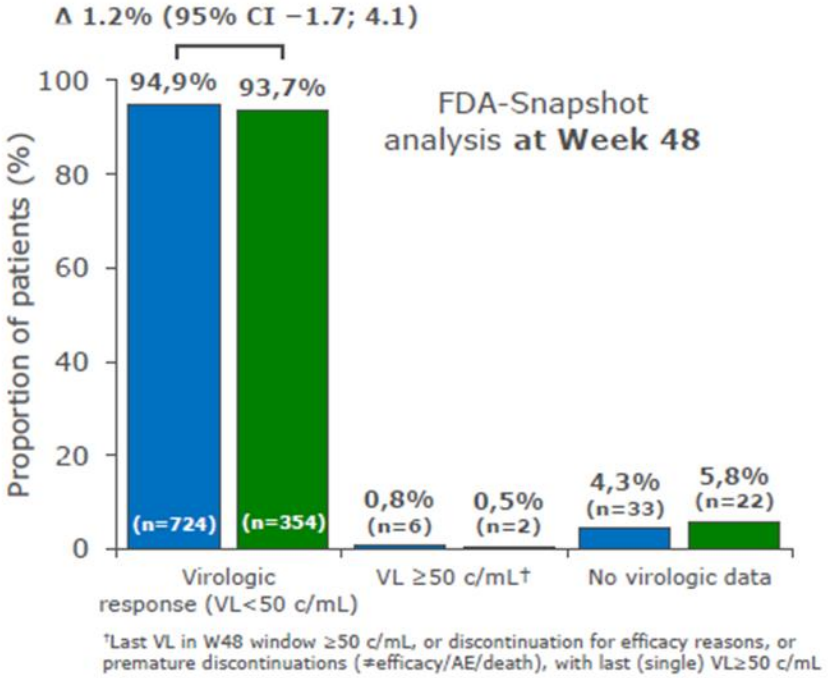
- Previous ART VF allowed
- Absence of history of VF on DRV, and if historical genotype available, absence of DRV RAMs†
- Viral load (VL) <50 c/mL for ≥2 months before screening; one VL≥50 and <200 c/mL within 12 months prior to screening allowed
- Creatinine clearance (by Cockcroft-Gault) ≥50 mL/min

*Stratified by bPI (protease inhibitor boosted with low-dose ritonavir or cobicistat) at screening;
†DRV RAMs: V11I, V32I, L33F, I47V, I50V, I54L or M, T74P, L76V, I84V or L89V (IAS-USA)

Week 48 Efficacy



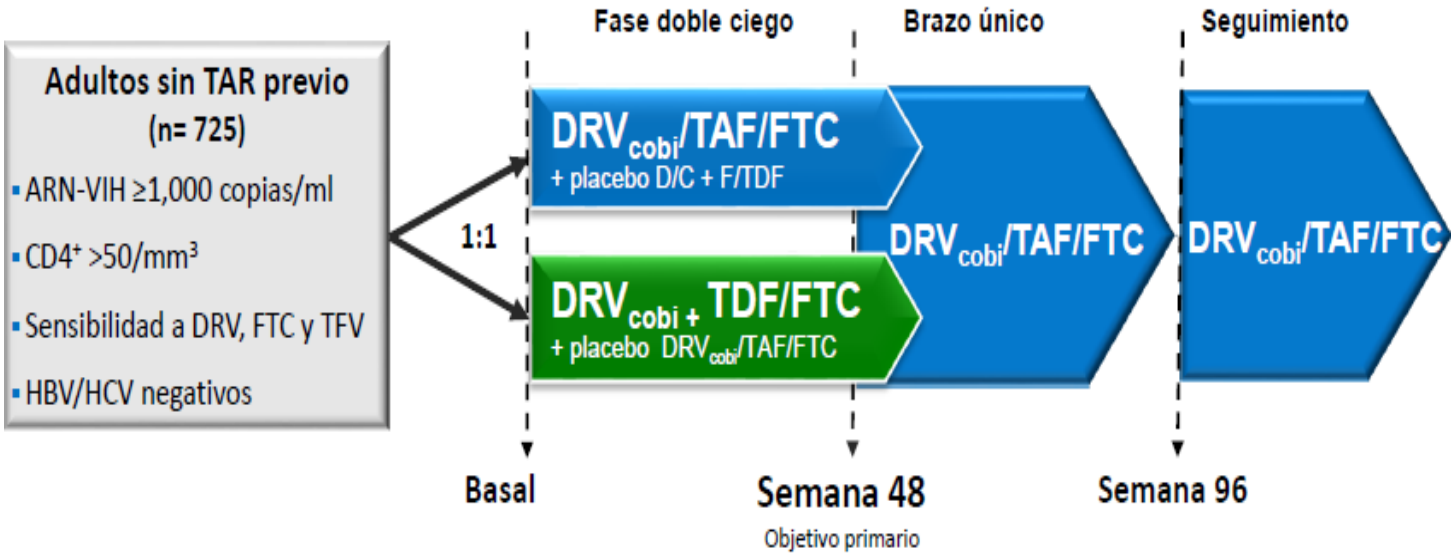
*Upper bound 95% CI <4.0% (p<0.0001)



†Last VL in W48 window ≥50 c/mL, or discontinuation for efficacy reasons, or premature discontinuations (≠efficacy/AE/death), with last (single) VL≥50 c/mL

- No discontinuations for efficacy reasons
- Most rebounders (12/19 D/C/F/TAF and 4/8 control) resuppressed (<50 c/mL) at Week 48

Estudio AMBER D/C/F/TAF vs. DRV/c + FTC/TDF



- **Objetivo primario:** evaluar la no inferioridad de D/C/F/TAF vs. DRV/c + FTC/TDF según la proporción de pacientes con CV <50 copias/ml a las 48 semanas

Phase 3, Randomised, Double-blind, International,* Multicentre Trial *

121 sites in USA, Canada, Belgium, France, Germany, Italy, Poland, Russia, Spain, UK

†Lower limit of 95% CI of stratified Mantel-Haenszel difference between D/C/F/TAF and control >–10%

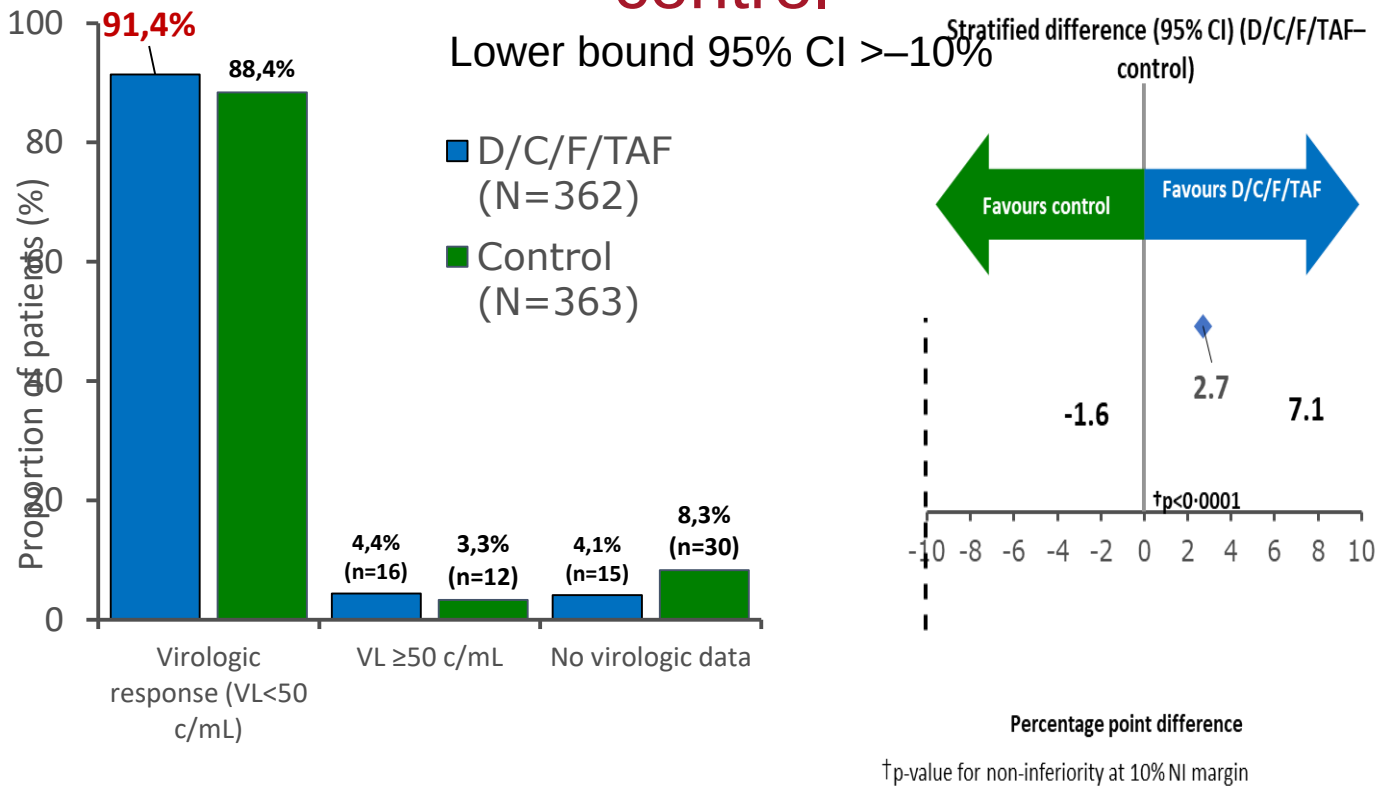
(NI margin 10%; FDA-Snapshot algorithm)

Estudio AMBER

D/C/F/TAF no inferior al control

D/C/F/TAF non-inferior to control

Lower bound 95% CI >–10%



FDA Snapshot; VL<50 c/mL) (ITT)

Estudio AMBER: Análisis de resistencias a semana 48

	DRV_{cobi}/TAF/FTC n= 362	Control n= 363
Fracasos virológicos con genotipos basales y en FV*, n	7	2
Desarrollo de mutaciones (IAS 2015) durante el estudio, n		
Mutaciones a DRV	0	0
Mutaciones primarias a IPs	0	0
Mutaciones a Análogos	1 (M184I/V)†	0

*Post-baseline genotyping/phenotyping performed for patients who met the criteria for protocol-defined virologic failure (virologic non-response, virologic rebound, and/or viraemic at final timepoint) and who had VL ≥400 c/mL at failure (unconfirmed or confirmed failure) or at later time points

†Patient had K103N at screening, indicating transmitted NNRTI (efavirenz/nevirapine) resistance, and developed M184I/V, conferring resistance to FTC and 3TC

Estudio AMBER: Efectos adversos s 48

Incidence, n (%)	D/C/F/TAF N=362	Control N=363
≥1 AE, any grade	312 (86.2)	307 (84.6)
≥1 grade 3–4 AE	19 (5.2)	22 (6.1)
≥1 serious AE	17 (4.7)	21 (5.8)
≥1 AE leading to permanent discontinuation	7 (1.9)	16 (4.4)
Deaths	0	0
AEs at least possibly related to study drug		
Any	126 (34.8)	151 (41.6)
Most common (≥5% either arm)		
Diarrhoea[†]	31 (8.6)	40 (11.0)
Rash	22 (6.1)	14 (3.9)
Nausea	20 (5.5)	36 (9.9)

Ninguna discontinuación por EA óseos, renales o del SNC

Más del 90% de los pacientes toleran el tratamiento - 1,9% de discontinuaciones por EA

[†]Most cases were mild: Grade 1: 24 (6.6%) vs 32 (8.8%); Grade 2: 7 (1.9%) vs 8 (2.2%)

CNS, central nervous system

Raltegravir 1200 mg Once Daily Versus Raltegravir 400 mg Twice Daily, in Combination With Tenofovir Disoproxil Fumarate/Emtricitabine, in Previously Untreated HIV-1 Infection Through Week 96

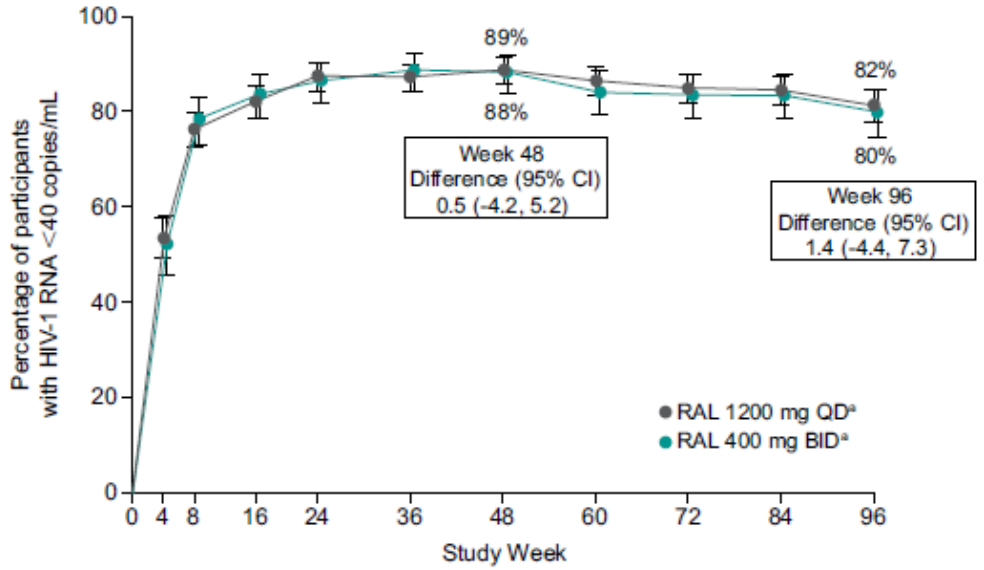
Pedro Cahn[1]; Richard Kaplan[2]; Paul Sax[3]; Kathleen Squires[4]; Jean-Michel Molina[5]; Winai Ratanasuwan[5]; Mohammed Rassool[7]; Xia Xu[8]; Yan Zhou[8]; Brenda Hornony[8]; Deborah Hepler[8]; Hedy Teppler[8]; George Hanna[8]; Bach-Yen Nguyen[8]; Wayne Greaves[8]; for the ONCEMRK Study Group

[1]Fundación Huesped, Buenos Aires, Argentina; [2]Desmond Tutu HIV Foundation, Cape Town, South Africa; [3]Brigham & Women's Hospital, Harvard Medical School, Boston, MA, USA; [4]Thomas Jefferson University, Philadelphia, PA, USA; [5]University of Paris Diderot, Hôpital Saint-Louis, Paris, France; [6]Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand; [7]University of Witwatersrand, Helen Joseph Hospital, Johannesburg, South Africa; [8]Merck & Co., Inc., Kenilworth NJ, USA

Efficacy

- RAL 1200 mg QD was non-inferior to that of RAL 400 mg BID at both Week 48 and 96 (**Figure 3**)

Figure 3. Proportion of Participants with HIV-1 RNA <40 copies/mL Over Time (NC=F, FDA Snapshot Approach).



[a]In combination with TDF/FTC QD.
BID, twice daily; CI, confidence interval; FTC, emtricitabine; NC=F, non-completer=failure; QD, once daily; RAL, raltegravir; TDF, tenofovir disoproxil fumarate.

- Consistent efficacy was observed regardless of baseline HIV-1 RNA and CD4+ T-cell levels

Raltegravir 1200 mg Once Daily Versus Raltegravir 400 mg Twice Daily, in Combination With Tenofovir Disoproxil Fumarate/Emtricitabine, in Previously Untreated HIV-1 Infection Through Week 96

Pedro Cahn[1]; Richard Kaplan[2]; Paul Sax[3]; Kathleen Squires[4]; Jean-Michel Molina[5]; Winai Ratanasuwan[6]; Mohammed Rassool[7]; Xia Xu[8]; Yan Zhou[8]; Brenda Hornony[8]; Deborah Hepler[8]; Hedy Teppler[8]; George Hanna[8]; Bach-Yen Nguyen[8]; Wayne Greaves[8]; for the ONCEMRK Study Group

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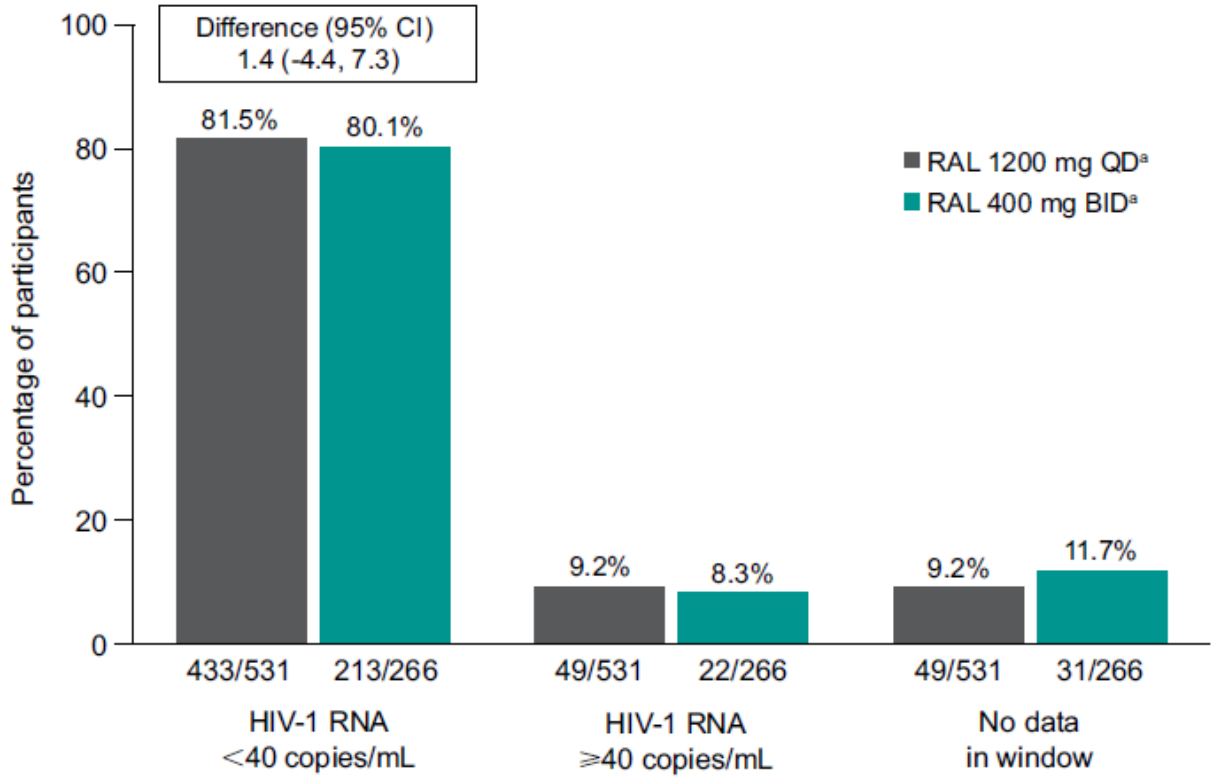
Figure 4. Virologic Outcome at Week 96 (NC=F, FDA Snapshot Approach).



[a]In combination with TDF/FTC QD.

BID, twice daily; CI, confidence interval; FTC, emtricitabine; NC=F, non-completer=failure; QD, once daily; RAL, raltegravir; TDF, tenofovir disoproxil fumarate.

The triumph of HIV treatment: another new antiretroviral

Since the approval of the first integrase strand inhibitor (INSTI) raltegravir for the treatment of HIV 10 years ago, INSTIs have become agents of choice in combination with two nucleoside reverse transcriptase inhibitors (NRTIs) in many international guidelines.[1,2] This was

and tenofovir alafenamide with dolutegravir plus coformulated emtricitabine and tenofovir alafenamide, and showed 48-week response rates of 89·4% (286 of 320 participants) in the bictegravir group versus 92·9% (302 of 325 participants) in the dolutegravir group

Published Online
August 31, 2017
http://dx.doi.org/10.1016/S0140-6736(17)32297-3

See Online/Articles
http://dx.doi.org/10.1016/S0140-6736(17)32299-7 and

BICTEGRAVIR

Bictegravir, emtricitabine, and tenofovir alafenamide versus dolutegravir, abacavir, and lamivudine for initial treatment of HIV-1 infection (GS-US-380-1489): a double-blind, multicentre, phase 3, randomised controlled non-inferiority trial

Brar, Eric S Daar,

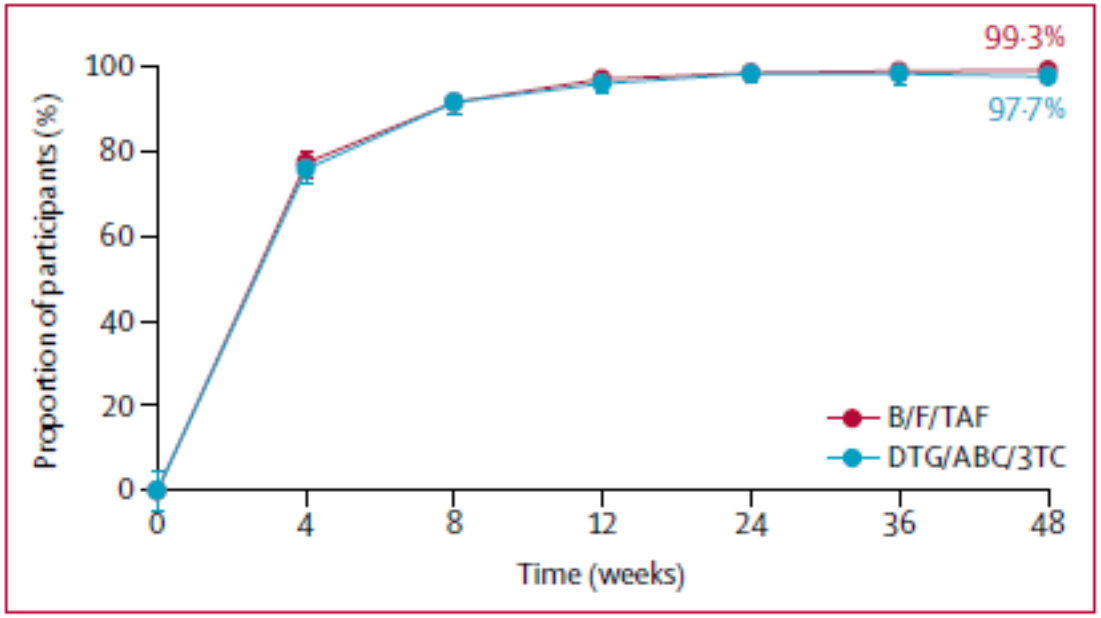


***Figure 2*: Proportion of participants with HIV-1 RNA less than 50 copies per mL**
Missing-as-excluded analysis. Error bars represent 95% CIs. B/F/TAF=bictegravir, emtricitabine, and tenofovir alafenamide. DTG/ABC/3TC=dolutegravir, abacavir, and lamivudine.

Published Online
August 31, 2017

Bictegravir… dolutegrav… HIV-1 infec… phase 3, ra… …nide versus …treatment of …d, multicentre, …ial

Joel Gallant, Adriano Laz… David Wohl, Jürgen Rock… Indira Brar, Eric S Daar, …k

	B/F/TAF group (n=314)	DTG/ABC/3TC group (n=315)
Any adverse event	265 (84%)	283 (90%)
Grade 3 or 4 adverse event	23 (7%)	24 (8%)
Serious adverse event	19 (6%)	25 (8%)
Drug-related adverse event	82 (26%)	127 (40%)
Drug-related serious adverse event	1 (<1%)	1 (<1%)
Any adverse event leading to study drug discontinuation	0	4 (1%)*
Adverse events occurring with ≥5% incidence in either group		
Nausea	32 (10%)	72 (23%)
Diarrhoea	40 (13%)	41 (13%)
Headache	36 (11%)	43 (14%)
Upper respiratory tract infection	20 (6%)	34 (11%)
Nasopharyngitis	23 (7%)	29 (9%)
Fatigue	19 (6%)	27 (9%)
Syphilis	12 (4%)	25 (8%)
Insomnia	14 (4%)	20 (6%)
Arthralgia	11 (4%)	19 (6%)
Vomiting	12 (4%)	17 (5%)
Cough	20 (6%)	8 (3%)
Bronchitis	10 (3%)	16 (5%)
Abdominal pain	9 (3%)	16 (5%)

Data are n (%). B/F/TAF=bictegravir, emtricitabine, and tenofovir alafenamide. DTG/ABC/3TC=dolutegravir, abacavir, and lamivudine. *Chronic pancreatitis and steatorrhoea (n=1), nausea and generalised rash (n=1), depression (n=1), and thrombocytopenia (n=1).

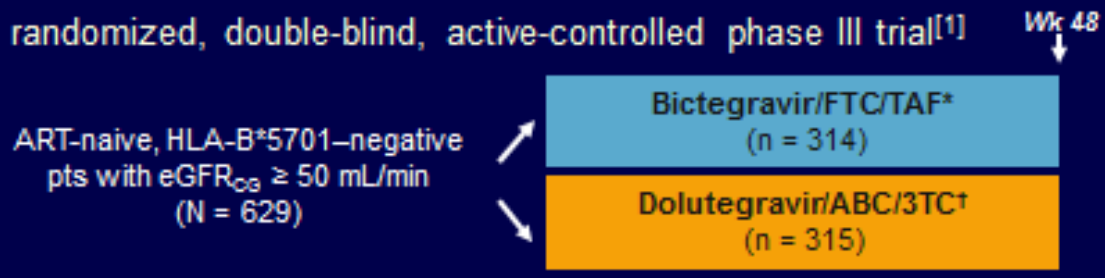
Table 3: Adverse events

Published Online August 31, 2017

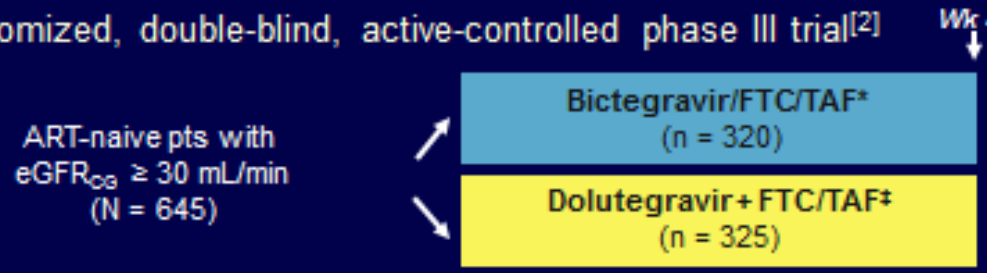
Nueva integrasa en STR

Bictegravir/FTC/TAF vs Dolutegravir-Containing Regimens for Treatment-Naive Pts

- **Bictegravir**: novel QD unboosted INSTI coformulated with FTC/TAF
- GS-1489: randomized, double-blind, active-controlled phase III trial[1]



- GS-1490: randomized, double-blind, active-controlled phase III trial[2]



All pts also received placebo tablets for comparator regimen (eg, pts in GS-1489 who received BIC/FTC/TAF also received DTG/ABC/3TC placebo). *BIC/FTC/TAF, 50/200/25 mg PO QD. †DTG/ABC/3TC, 50/600/300 mg PO QD. ‡DTG + FTC/TAF, 50 + 200/25 mg PO QD

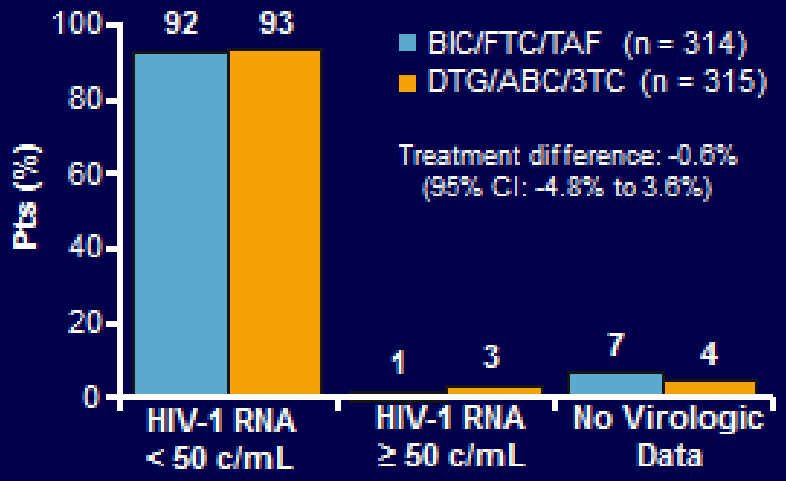
1. Gallant J, et al. IAS 2017. Abstract MOAB0105LB. 2. Sax PE, et al. IAS 2017. Abstract TUPDB0201LB.

Slide credit: clinicaloptions.com

Nueva integrasa en STR

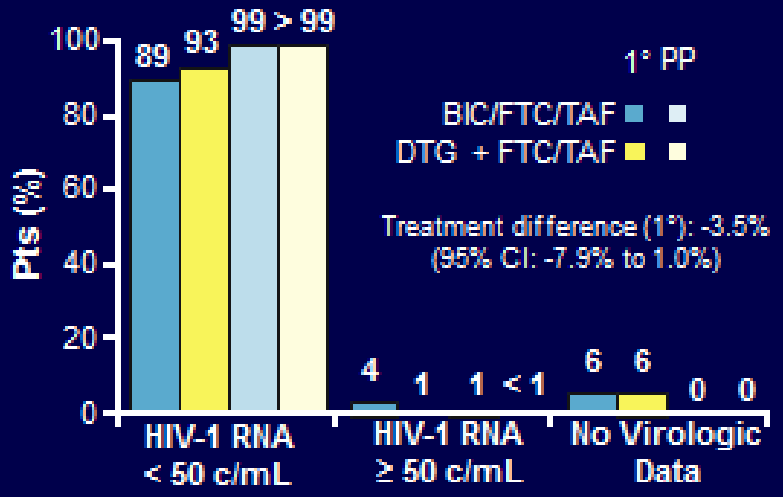
BIC/FTC/TAF vs DTG-Containing Regimens: Key Efficacy Findings

GS-1489: Wk 48 Virologic Efficacy[1]



- No resistance for any regimen components detected for either group

GS-1490: Wk 48 Virologic Efficacy[2]



- No resistance for any regimen components detected for either group

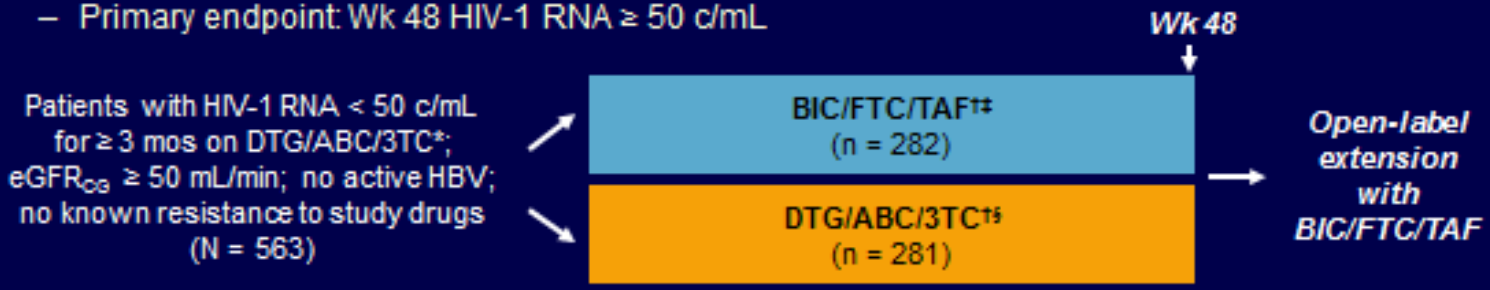
1. Gallant J, et al. IAS 2017. Abstract MOAB0105LB. Reproduced with permission.
2. Sax PE, et al. IAS 2017. Abstract TUPDB0201LB. Reproduced with permission.

Slide credit: clinicaloptions.com

Y en cambio de tratamiento

Study 380-1844: Switch From Suppressive DTG/ABC/3TC to BIC/FTC/TAF

- BIC/FTC/TAF: once-daily STR with novel, unboosted INSTI; now FDA approved for treatment-naive patients and virologically suppressed patients with no history of treatment failure or resistance to regimen components
- 380-1844: randomized, double-blind, international, active-controlled phase III trial
  - Primary endpoint: Wk 48 HIV-1 RNA ≥ 50 c/mL



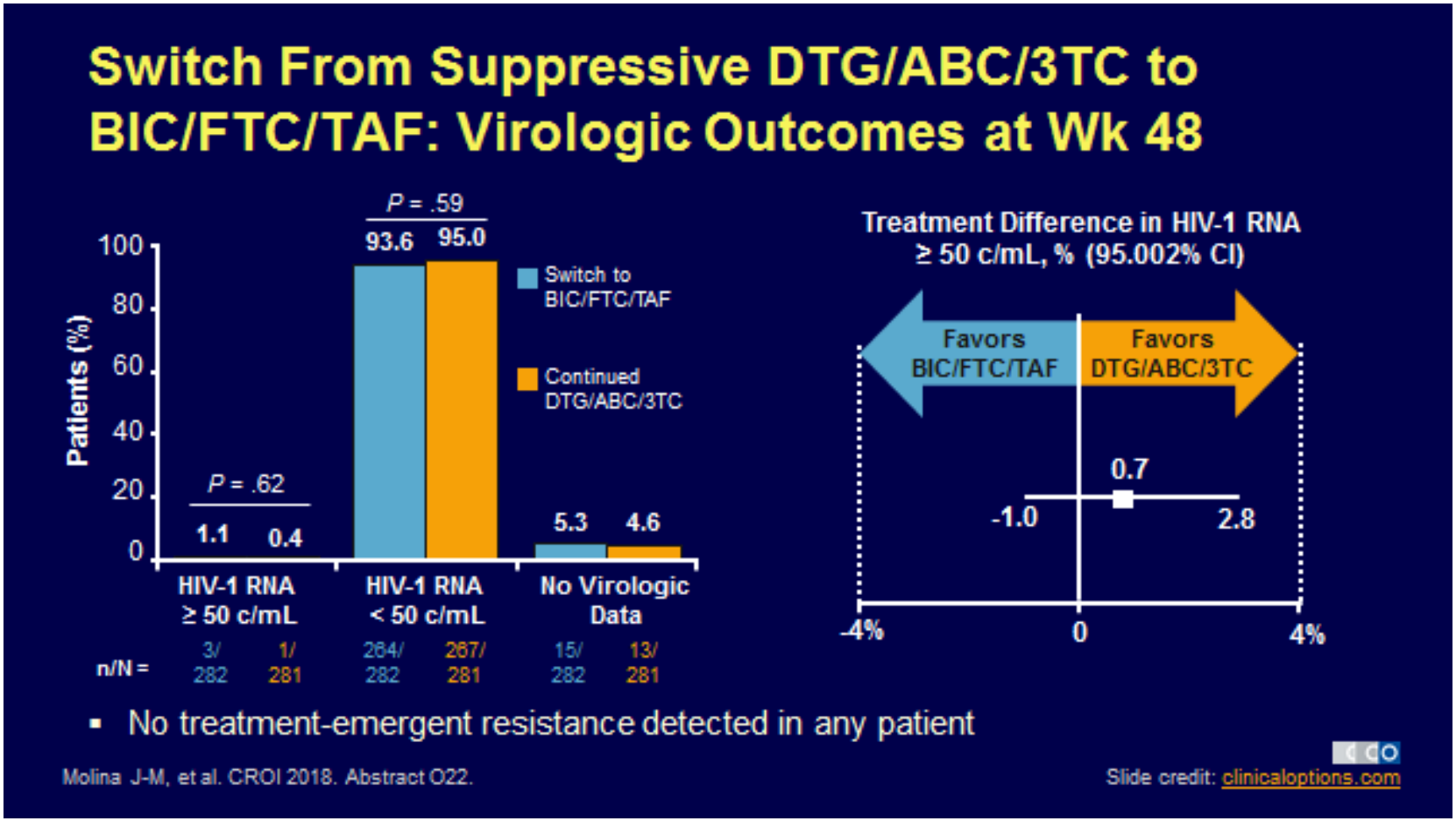
- Baseline: male sex, 88% to 90%; black race, 21% to 22%; median age, 45-47 yrs; median CD4+ cell count, 661-732 cells/mm^3; median eGFR$_{CG}$, 101 mL/min

*Could be STR or as separate components. †All patients also received placebo tablets for comparator regimen. ‡BIC/FTC/TAF 50/200/25 mg PO QD. §DTG/ABC/3TC 50/600/300 mg PO QD.

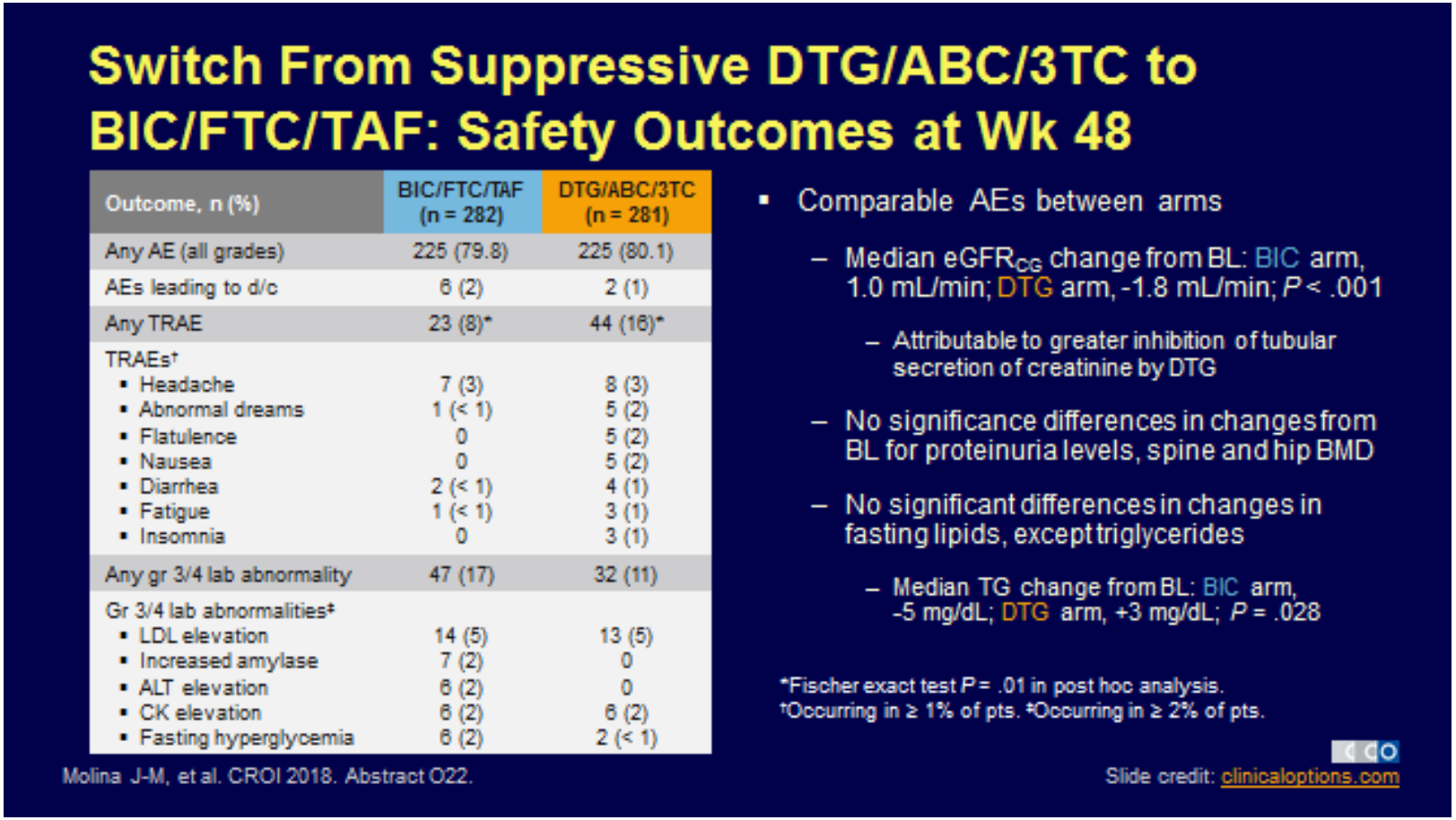
Molina J-M, et al. CROI 2018. Abstract O22.

Slide credit: clinicaloptions.com

Y en cambio de tratamiento



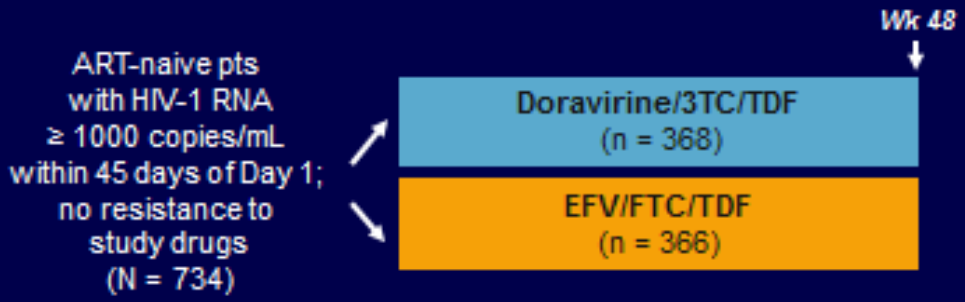
Y en cambio de tratamiento



Un nuevo NNRTI

DRIVE-AHEAD: Doravirine/3TC/TDF vs EFV/FTC/TDF for Treatment-Naive Pts

- **Doravirine:** NNRTI with unique resistance profile, low drug–drug interaction potential; doravirine + 2 NRTIs noninferior to DRV/RTV + 2 NRTIs with improved lipid profile in phase III DRIVE-FORWARD[1]
- DRIVE-AHEAD: randomized, double-blind, active-controlled phase III trial[2]



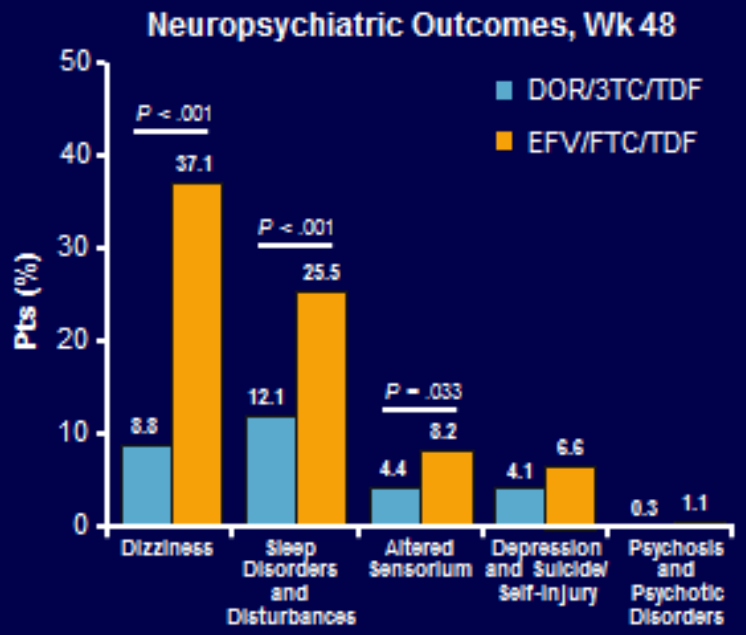
- Baseline: male, 84% to 85%; mean CD4+ cell count, 416-435 cells/mm^3 (12% to 13% ≤ 200 cells/mm^3)

1. Molina JM, et al. CROI 2017. Abstract 45LB. 2. Squires KE, et al. IAS 2017. Abstract TUAB0104LB.

Slide credit: clinicaloptions.com

Un nuevo NNRTI

DRIVE-AHEAD: Key Safety Findings



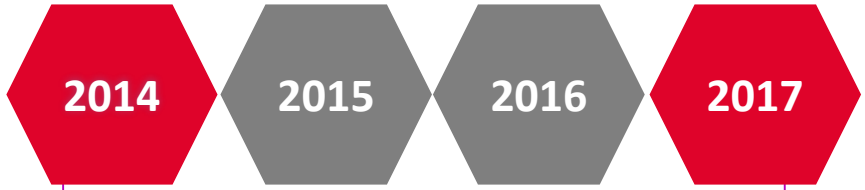
AEs at Wk 48, %	DOR/3TC/TDF (n = 364)	EFV/FTC/TDF (n = 364)	Difference (95% CI)
Drug-related AE, %	31	63	-31.9 (-38.6, -24.8)
D/c for AEs, %	3	7	-3.6 (-6.9, -0.5)
Lipid Δ From BL at Wk 48, mg/dL	**DOR/3TC/TDF (n = 364)**	**EFV/FTC/TDF (n = 364)**	***P* Value**
LDL-C	-1.6	8.7	< .0001
Non–HDL-C	-3.8	13.3	< .0001
Cholesterol	-2.0	21.8	NR
Triglycerides	-12.4	22.0	NR
HDL-C	1.9	8.5	NR

Squires KE, et al. IAS 2017. Abstract TUAB0104LB. Reproduced with permission.

Slide credit: clinicaloptions.com

DOBLES TERAPIAS

Ensayos clínicos con 2DRp: **IP/r + 3TC** en ***naive***



GARDEL[1]

LPV/r + 3TC (n=214)
LPV/r + 2 NRTIs (n=202)

- No inferioridad global: DT-TT dif 4.6% (-2.2 a 11.8)
- No inferioridad para CV>100k: DT-TT dif 9.3% (-2.8 a 21.5)
- No más fallo virológico con 2DR.
- No mutaciones a IP. 2 pacientes 184V en 2DR.

LPV/r no recomendado ni alternativa en Guías Terapéuticas

ANDES[2]

DRV/r + 3TC (n=75)
DRV/r + TDF/FTC (n=70) + 190

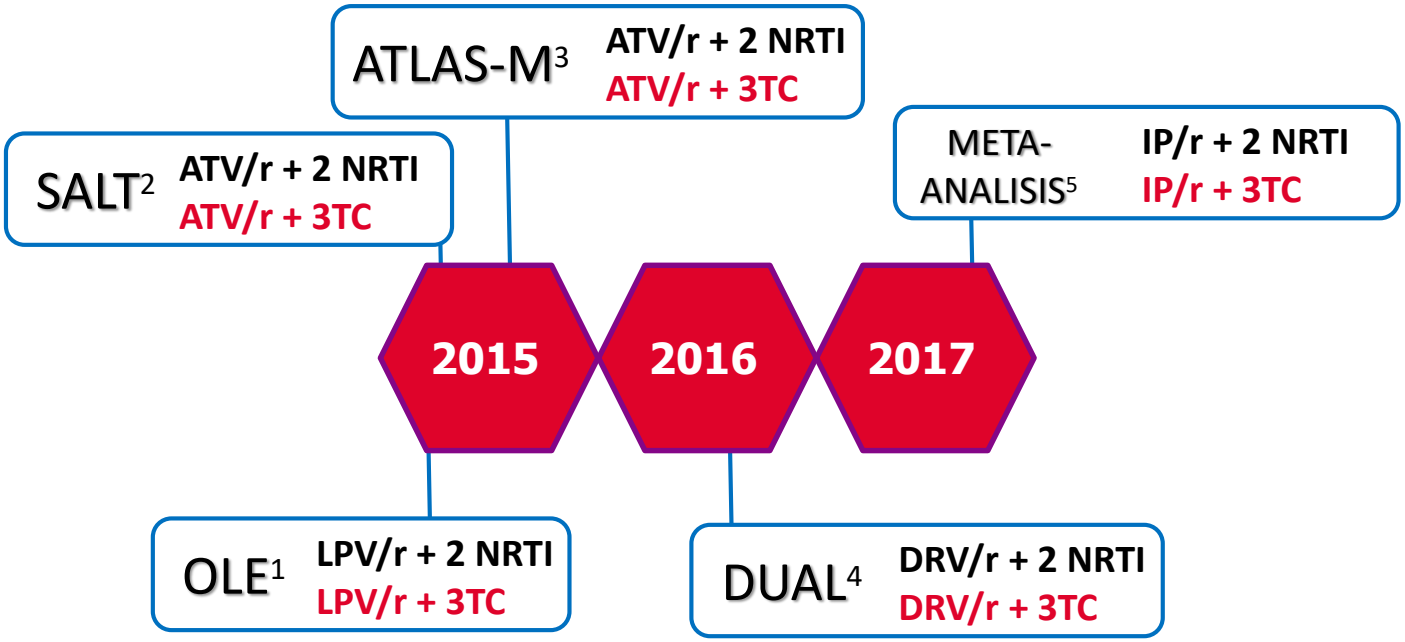
Datos muy preliminares a 24 semanas:

- CV<**400**: TT 97 vs DT 95% (-2.5%, -7.9 a 2.9)
- Virological failure: DT 0 vs TT 1
- Discontinuations: DT 4 (5%) vs TT 1 (1%)

1. Cahn P, et al. Lancet Infect Dis 2014;14:572–80. 2. Sued O, et al. IAS 2017 Paris # MOAB0106LB.

Diapositiva elaborada por Ribera E. GeSIDA 2017 Vigo. Disponible en: http://congresogesida.es/images/site/ponencias/2Miercoles/E_Ribera.pdf (acceso: enero 2018)

Ensayos clínicos con 2DRp: **IP/p + 3TC** en simplificación



1. Arribas JR, et al. Lancet Infect Dis 2015;15:785–92. 2. Pérez-Molina JA, et al. Lancet Infect Dis 2015;15:775–84. 3. Di Giambenedetto S, et al. J Antimicrob Chemother. 2017;72:1163-71. 4. Pulido F et al. Clin Infect Dis 2017; Aug 17. doi: 10.1093/cid/cix734. 5 Pérez-Molina JA, et al. EACS 2017. # PS1/1.

Diapositiva elaborada por Ribera E. GeSIDA 2017 Vigo. Disponible en: http://congresogesida.es/images/site/ponencias/2Miercoles/E_Ribera.pdf (acceso: enero 2018)

Dobles terapias: IP inducción mantenimiento

Study	Treatment Setting	N	Regimen	Results
NEAT001[1]	Initial	805	DRV/RTV + RAL	Similar efficacy as DRV/RTV + FTC/TDF; poor efficacy in pts with high HIV-1 RNA, low CD4+ cell counts
GARDEL[2]	Initial	426	LPV/RTV + 3TC	Similar efficacy as LPV/RTV + 2 NRTIs
MODERN[3]	Initial	813	DRV/RTV + MVC	Inferior efficacy vs DRV/RTV + FTC/TDF
SPARTAN[4]	Initial	94	ATV + RAL	Similar virologic suppression, higher VF and hyperbilirubinemia rates vs ATV/RTV + FTC/TDF
ANDES[5]	Initial	145	DRV/RTV + 3TC	Similar efficacy as DRV/RTV + 3TC/TDF
OLE[6]	Switch	250	LPV/RTV + 3TC	Similar efficacy as continued standard ART
KITE[7]	Switch	60	LPV/RTV + RAL	Small study; encouraging efficacy
SALT[8]	Switch	286	ATV/RTV + 3TC	Similar efficacy as ATV/RTV + 2 NRTIs
ATLAS-M[9]	Switch	266	ATV/RTV + 3TC	Improved efficacy vs ATV/RTV + 2 NRTIs
DUAL-GESIDA[10]	Switch	257	DRV/RTV + 3TC	Similar efficacy as DRV/RTV + 2 NRTIs

1. Raffi F, et al. Lancet. 2014;384:1942-1951. 2.-Cahn P, et al. EACS 2015. Abstract 961. 3.-Stellbrink H-J, et al. AIDS 2014. Abstract TUAB0101. 4.- Kozal MJ, et al. HIV Clin Trials. 2012;13:119-130.5.- Sued O, et al. IAS 2017. Abstract MOAB0106LB. 6. Arribas JR, et al. Lancet Infect Dis. 2015;15:785-792. 7.- Ofotokun I, et al. AIDS Res Hum Retroviruses. 2012;28:1196-1206. 8.-Perez-Molina JA, et al. Lancet Infect Dis. 2015;15:775-784. 9.- Di Giambenedetto S, et al. EACS 2015. Abstract 867. 10. Pulido F, et al. Clin Infect Dis. 2017;65:2112-2118.

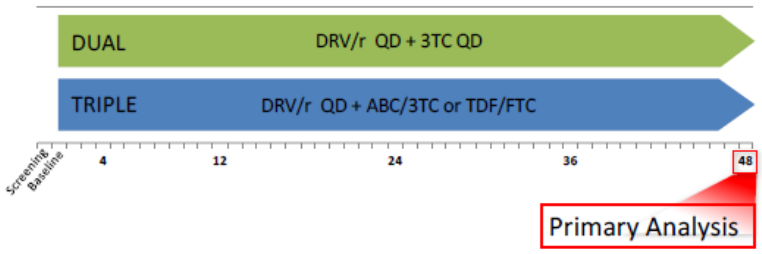
MOPEB0311

Switch to 3TC+Darunavir/ritonavir (DRV/r) dual therapy Subgroup analysis of DUAL clinical trial (GESIDA-8014-RIS-EST45)

Federico Pulido. Esteban Ribera. María Lagarde. Ignacio Pérez-Valero. Jesús Santos. José A. Iribarren. José Sanz. Pere Domingo. Antonio Payeras. María J. Téllez. Francisco J Rodríguez. Otilia Bisbal. Miguel Cervero. Belén Alejos. María Yllescas. José R. Arribas.
DUAL-GESIDA-8014-RIS-EST45 Study Group

DUAL STUDY DESIGN

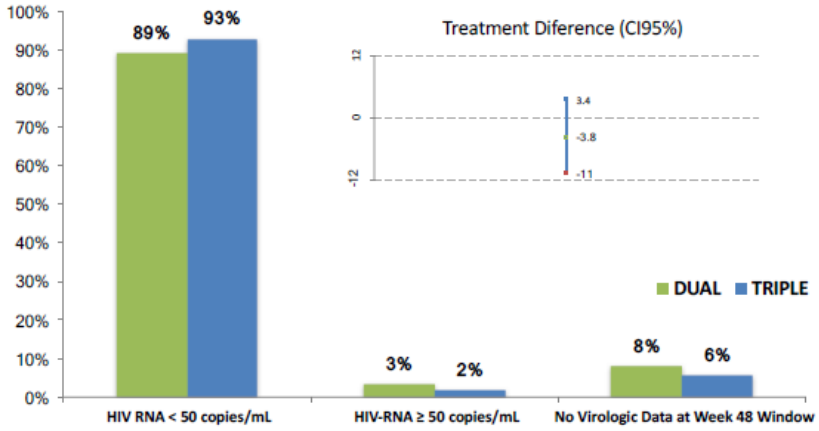
- VL < 50 c/mL > 6 months
- No resistance to DRV/r o 3TC
- On treatment with DRV/r + ABC/3TC or TDF/FTC ≥ 2 months
- HBsAg negative
- Randomized 1:1. Stratified by baseline nucleos(t)ides



PRIMARY ENDPOINT

Proportion of patients with suppressed viral load (HIV-RNA < 50 copies/mL) after 48 weeks of follow-up according to the FDA snapshot algorithm in the ITT exposed population.

PRIMARY ENDPOINT: Snapshot, ITT-e population



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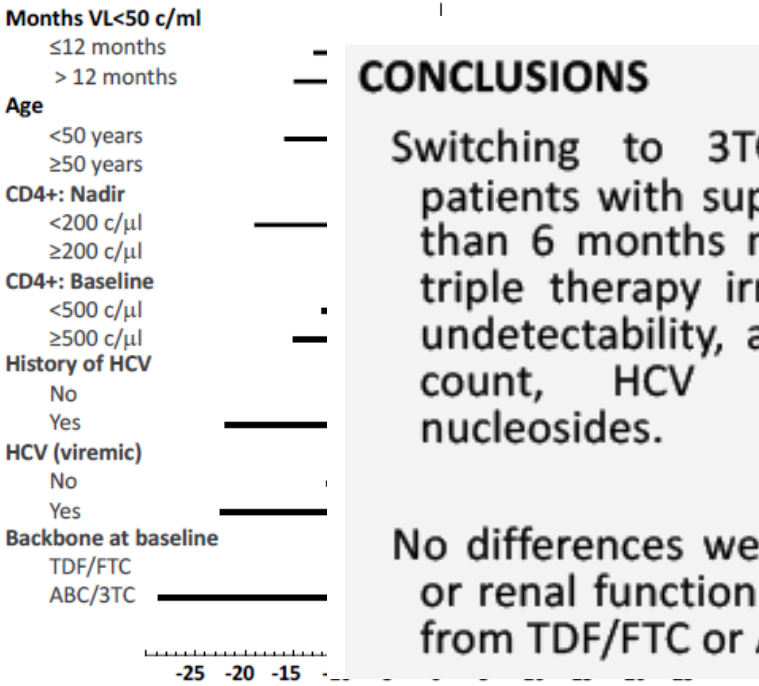
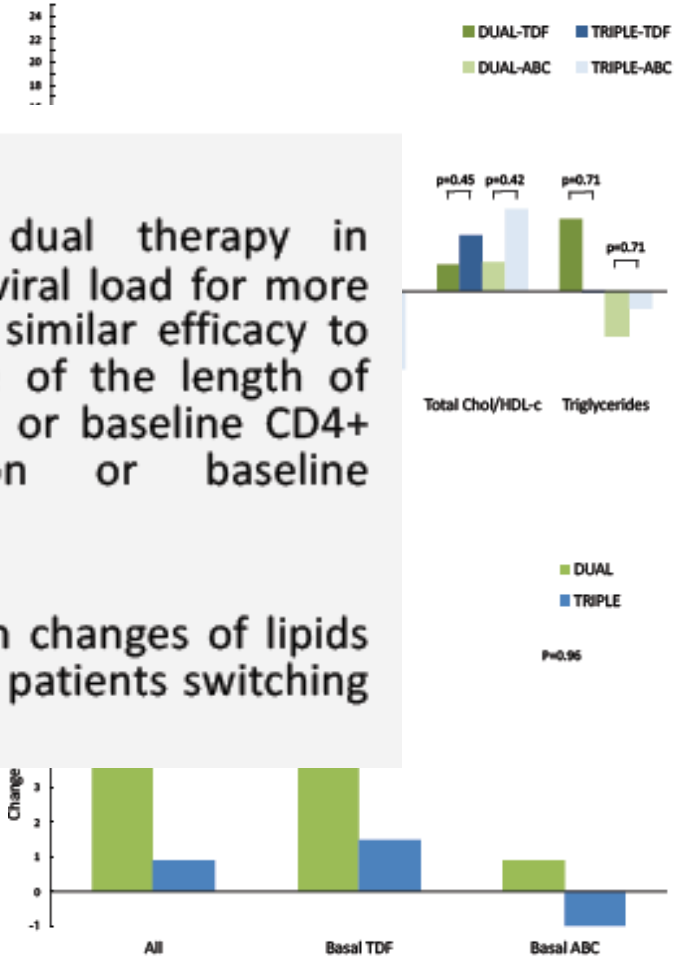


CONCLUSIONS

Switching to 3TC+DRV/r dual therapy in patients with suppressed viral load for more than 6 months maintains similar efficacy to triple therapy irrespective of the length of undetectability, age, nadir or baseline CD4+ count, HCV coinfection or baseline nucleosides.

No differences were seen in changes of lipids or renal function between patients switching from TDF/FTC or ABC/3TC.



DTG *core agent* para 2DRs

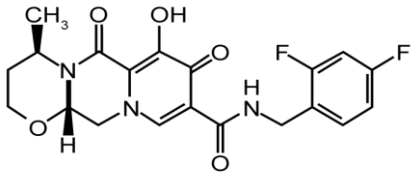
Actividad antiviral rapida y potente[1]

DDIs
- Libre de potenciador
- Pocas DDIs clínicamente significativas

Alta barrera a resistencias[6,7]
- Resultados in vitro apoyados por datos de la Fase III

Alta unión a la integrasa[8]
- La disociación de los complejos integrasa-ADN mutados es más lenta vs RAL o EVG

Dolutegravir



Bien Tolerado
- Pocas interrupciones debidas a los EA en los ensayos clínicos[2–5]

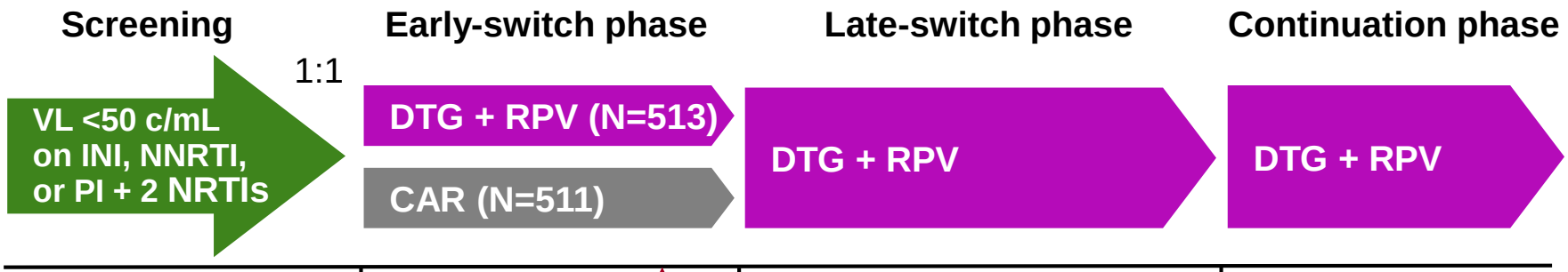
Robustez y gran numero de datos de los ensayos clínicos[2–4]

Larga vida media; Baja variabilidad en la exposición
- DTG (50 mg QD) 19 veces por encima de la IC_{90}[9]
- Concentraciones en plasma hasta 216 hrs post dosis[10]

1. Min S *et al*. *AIDS* 2011;25:1737–1745; 2. Walmsley S *et al*. *N Engl J Med* 2013;369:1807–1818; 3. Clotet B *et al*. *Lancet* 2014;383:2222–2231; 4. Cahn P *et al*. *Lancet* 2013;382:700–708; 5. Raffi F *et al*. *Lancet* 2013;381:735–743; 6. Kobayashi M *et al*. *Antivir Res* 2008;80;213–222; 7. Kobayashi M *et al*. *Antimicrob Agents Chemother* 2011;55:813–821; 8. Hightower KE *et al*. *Antimicrob Agents Chemother* 2011;5:4552–4559; 9. van Lunzen J *et al*. *Lancet Infect Dis* 2012;12:111–118; 10. Elliot E *et al*. IWCPHIV 2015;abst 13

SWORD-1 and -2: Phase III Study Design

Identically designed, randomised, multicentre, open-label, parallel-group, non-inferiority studies



Inclusion criteria

- On stable CAR ≥6 months before screening
- 1st or 2nd ART with no change in prior regimen due to VF
- Confirmed HIV-1 RNA <50 c/mL during the 12 months before screening
- HBV-negative

Primary endpoint at 48 weeks: subjects with VL <50 c/mL (ITT-E snapshot)*

Countries:

Argentina	Australia	Belgium	Canada
France	Germany	Italy	Netherlands
Russia	Spain	Taiwan	United Kingdom
United States			

*8% non-inferiority margin for pooled data. -10% non-inferiority margin for individual studies

HBV, hepatitis B virus; ITT(-E), intent to treat (- exposed); NRTI, nucleoside reverse transcriptase inhibitor

Llibre JM, et al. CROI 2017. Oral Presentation 44LB. Llibre JM, et al. Lancet. 2018;391:839-849.

SWORD-1 and -2: Snapshot Outcomes at Week 48

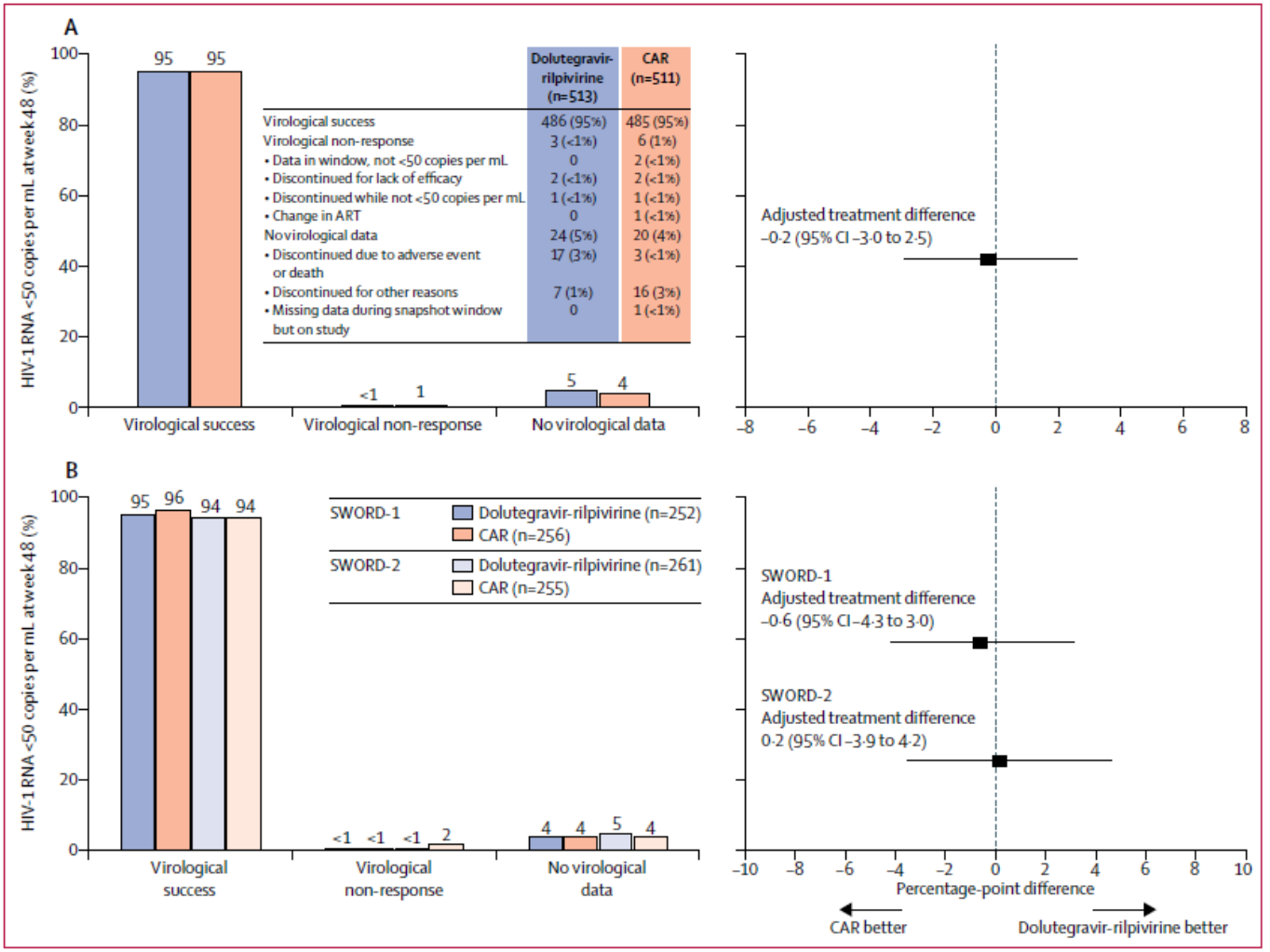


Figure 2: **Virological outcomes at week 48 (US Food and Drug Administration snapshot) in the pooled SWORD-1 and SWORD-2 intention-to-treat study population (A) and separated by study (B)**

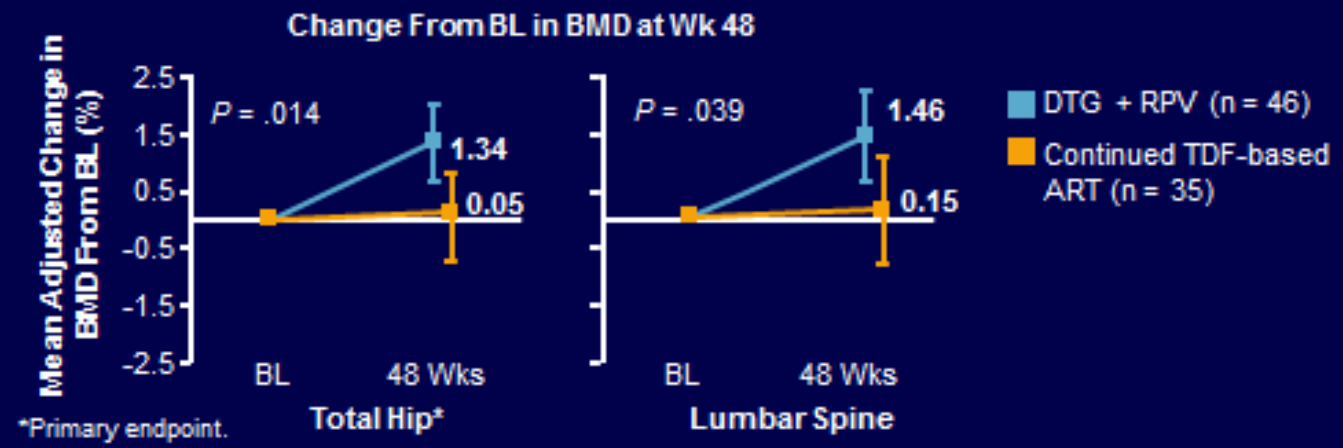
Treatment difference was adjusted for age and baseline third-agent class. CAR=current antiretroviral regimen. ART=antiretroviral therapy.

Llibre JM, et al. Lancet. 2018 Mar 3;391:839-849.

Densidad mineral ósea

SWORD 1 & 2 Substudy: BMD Impact of Switch From TDF-Based ART to DTG + RPV

- Randomized, open-label, multicenter phase III trials demonstrated that switch to DTG + RPV noninferior to remaining on baseline ART at Wk 48 in virologically suppressed pts[1]
- Current analysis assessed BMD in pts who continued on TDF-containing triple ART regimen or switched from TDF-containing triple ART to DTG + RPV (N = 102)[2]



*Primary endpoint.

1. Llibre JM, et al. CROI 2017. Abstract 44LB. 2. McComsey G, et al. IAS 2017. Abstract TUPDB0205LB.

Ensayos clínicos con 2DR: **DTG + 3TC** en ***naive***

2016

PADDLE [1,2]

DTG + 3TC (n=20)

- HIV RNA <100,000 c/mL and
- CD4 count >200 cells/mL

2017

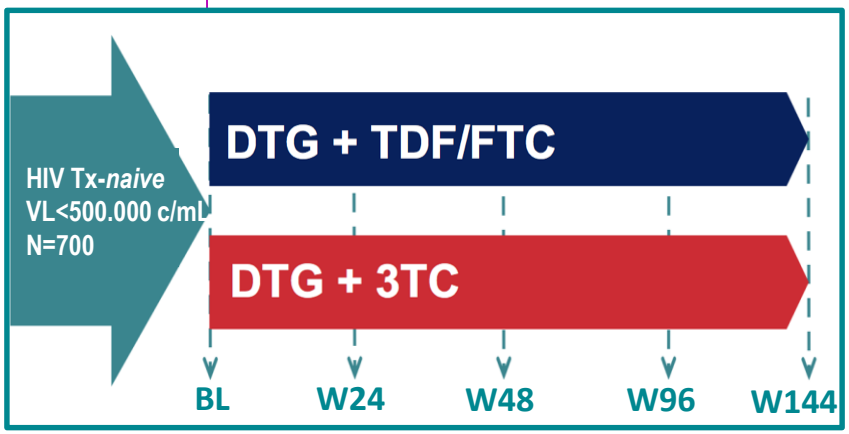
ACTG 5353 [3]

DTG + 3TC (n=120)

- HIV RNA <500,000 c/mL

2018, 2019, …

GEMINI 1&2 [4,5]



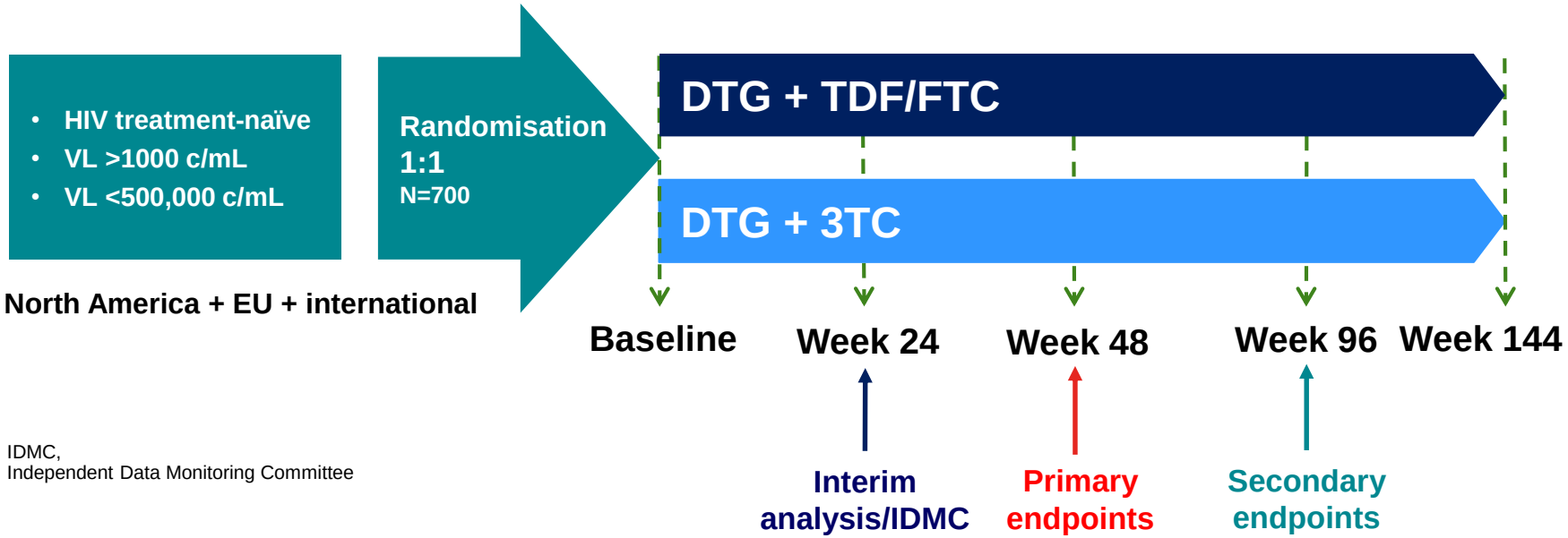
1. Cahn P, et al. J Int AIDS Soc 2017; 20(1):1-7. 2. Figueroa MI, et al. IAS 2017 Paris #MOPEB0287. 3. Taiwo B, et al. IAS 2017 Paris #MOAB0107LB
4. https://clinicaltrials.gov/ct2/show/NCT02831673. 5. https://clinicaltrials.gov/ct2/show/NCT02831764

Diapositiva elaborada por Ribera E. GeSIDA 2017 Vigo. Disponible en: http://congresogesida.es/images/site/ponencias/2Miercoles/E_Ribera.pdf (acceso: enero 2018)

GEMINI-1 and -2: Study Design

Phase III, randomised, double-blind, multicentre, non-inferiority study[1,2]

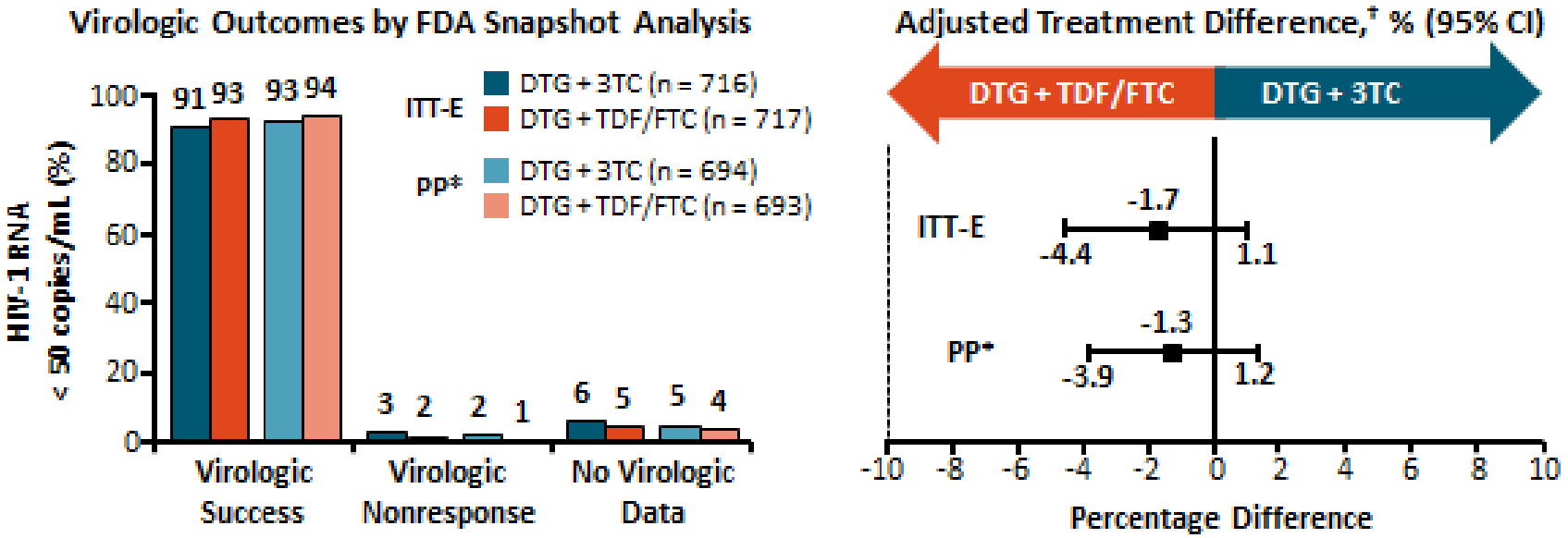
- **Objective:** to demonstrate the non-inferior antiviral activity of DTG + 3TC QD compared with DTG + TDF/FTC QD over 48 weeks in HIV-1-infected ART-naïve subjects[1,2]
- **Primary endpoint:** the proportion of subjects with plasma HIV-1 RNA <50 c/mL at Week 48 using the FDA snapshot algorithm (missing, switch or discontinuation = failure)[1,2]
  - non-inferiority margin: 10%[1,2]



IDMC,
Independent Data Monitoring Committee

1. GEMINI-1. Available from: https://clinicaltrials.gov/ct2/show/NCT02831673. Accessed Aug 2017
2. GEMINI-2. Available from: https://clinicaltrials.gov/ct2/show/NCT02831764. Accessed Aug 2017

GEMINI-1 and -2: Virologic Response at Wk 48



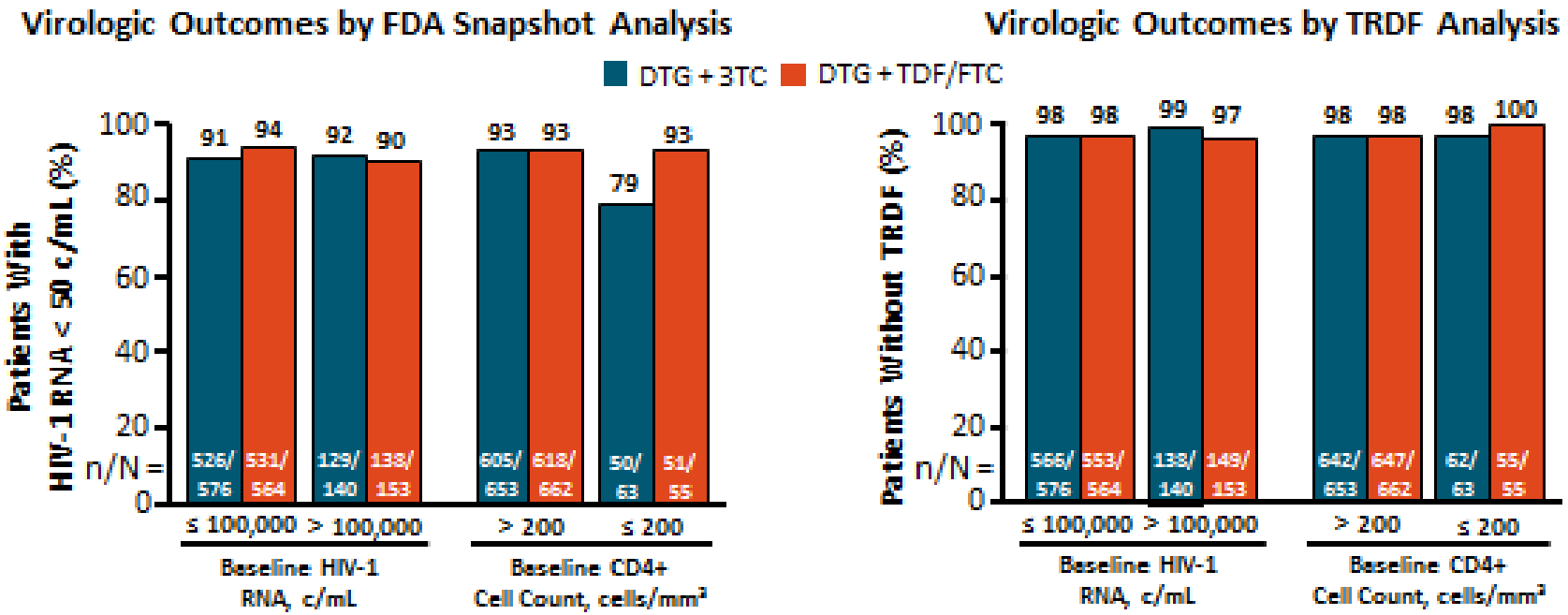
*ITT-E population excluding significant protocol violations.

†Adjusted for HIV-1 RNA (≤ vs > 100,000 copies/mL), CD4+ cell count (≤ vs > 200 cells/mm^3), and study (GEMINI-1 vs GEMINI-2).

Cahn P, et al. AIDS 2018. Abstract TUAB0106LB.

Slide credit: clinicaloptions.com

GEMINI-1 and -2: Virologic Response at Wk 48 by Baseline HIV-1 RNA and CD4+ Cell Count

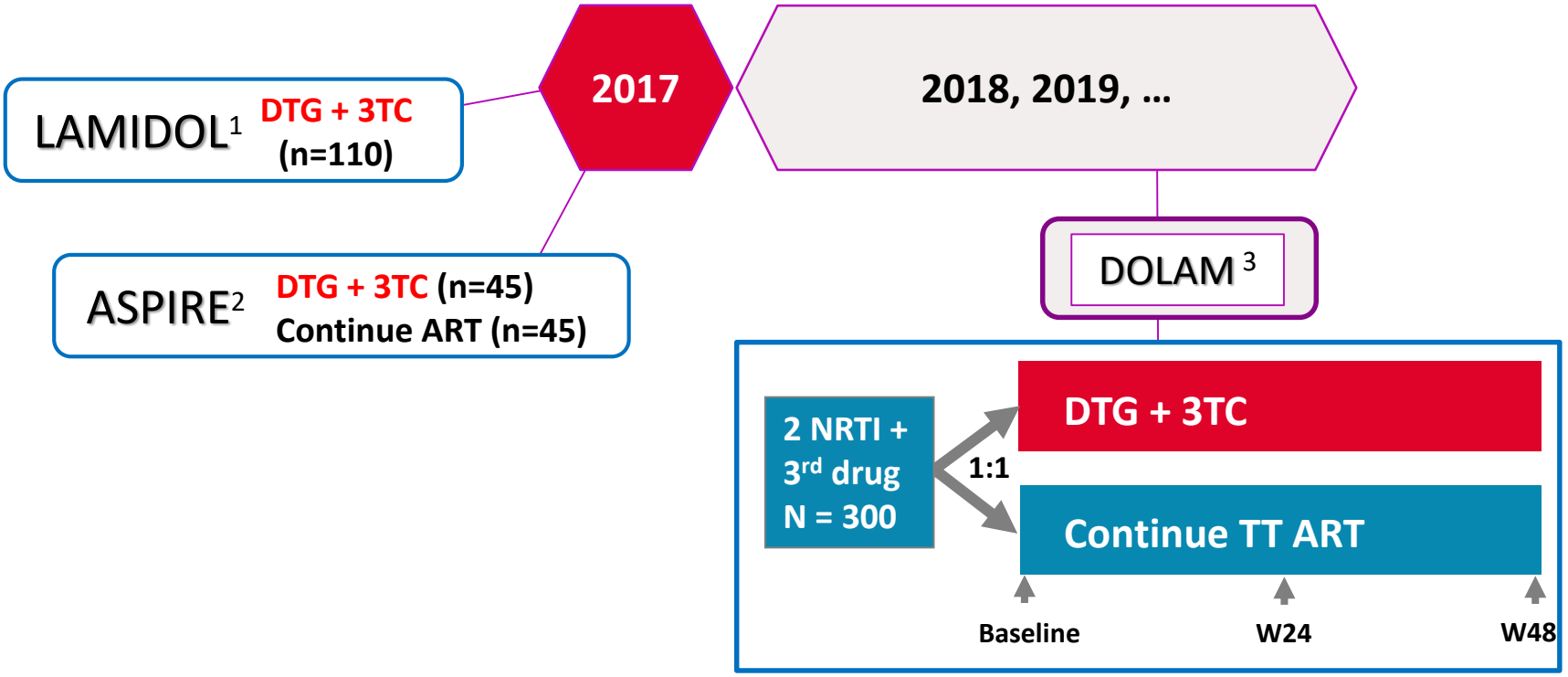


- TRDF includes confirmed virologic withdrawal, withdrawal for lack of efficacy or treatment-related AEs, and participants meeting protocol-defined stopping criteria

Cahn P, et al. AIDS 2018. Abstract TUAB0106LB.

Slide credit: clinicaloptions.com

Ensayos clínicos con 2DR: **DTG + 3TC** en simplificación



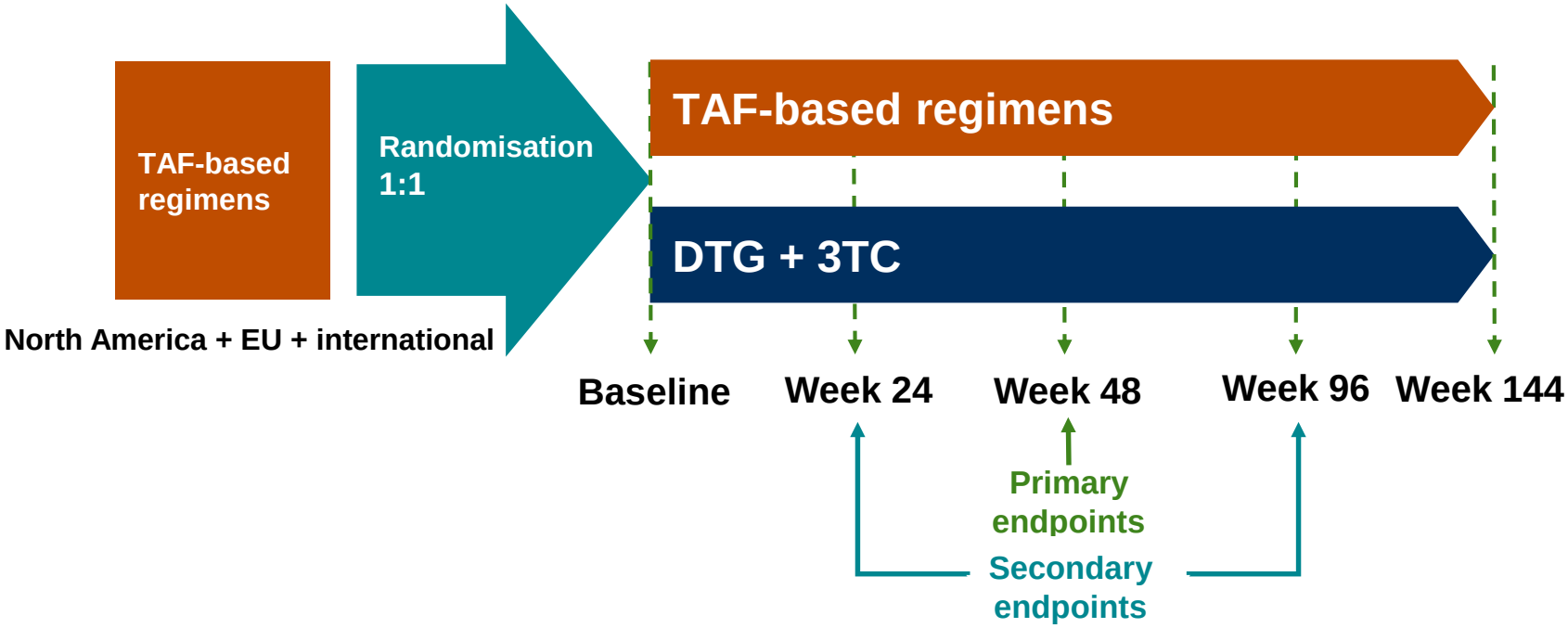
1. Joly V, et al. CROI 2017 Seattle #458. 2. Taiwo BO, et al. EACS 2017 Milan #PE8/5. 3. https://clinicaltrials.gov/ct2/show/NCT02582684

Diapositiva elaborada por Ribera E. GeSIDA 2017 Vigo. Disponible en: http://congresogesida.es/images/site/ponencias/2Miercoles/E_Ribera.pdf (acceso: enero 2018)

TANGO: Switch Study Design

Phase III, randomised, multicentre, parallel-group, non-inferiority study

- **Objective:** to demonstrate non-inferior antiviral activity of switching to DTG + 3TC QD compared with continuation of current ARV regimen over 48 weeks in HIV-1-infected ART-experienced subjects
- **Primary endpoint:** the proportion of participants who meet the Snapshot virologic failure criteria at Week 48 using the ITT-E population
  - non-inferiority margin = 4%; Week 48 primary endpoint



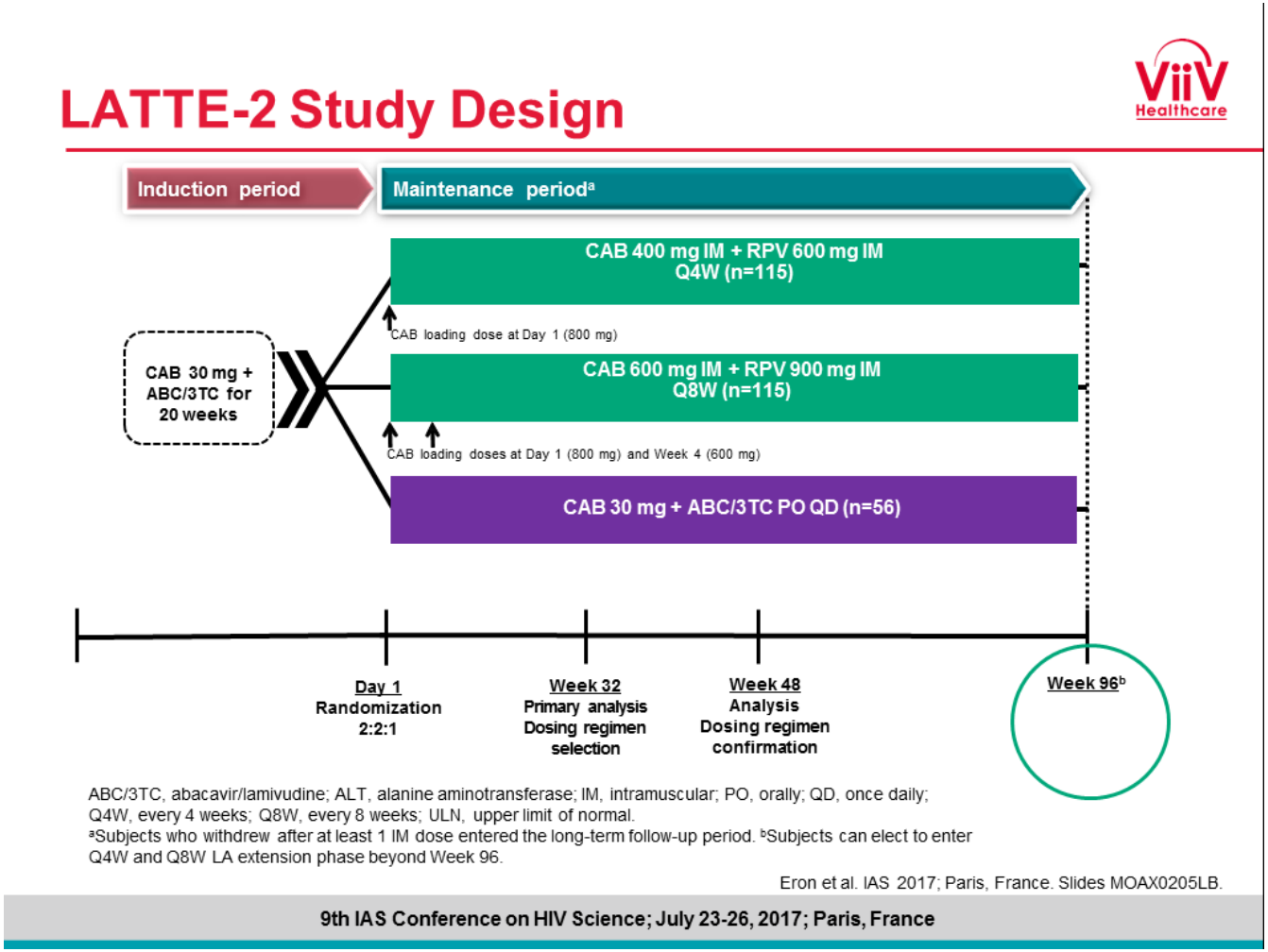
MÁS OPCIONES: NUEVAS FORMAS DE ADMINISTRACIÓN

Cabotegravir Long-Acting (LA) Injectable Nanosuspension

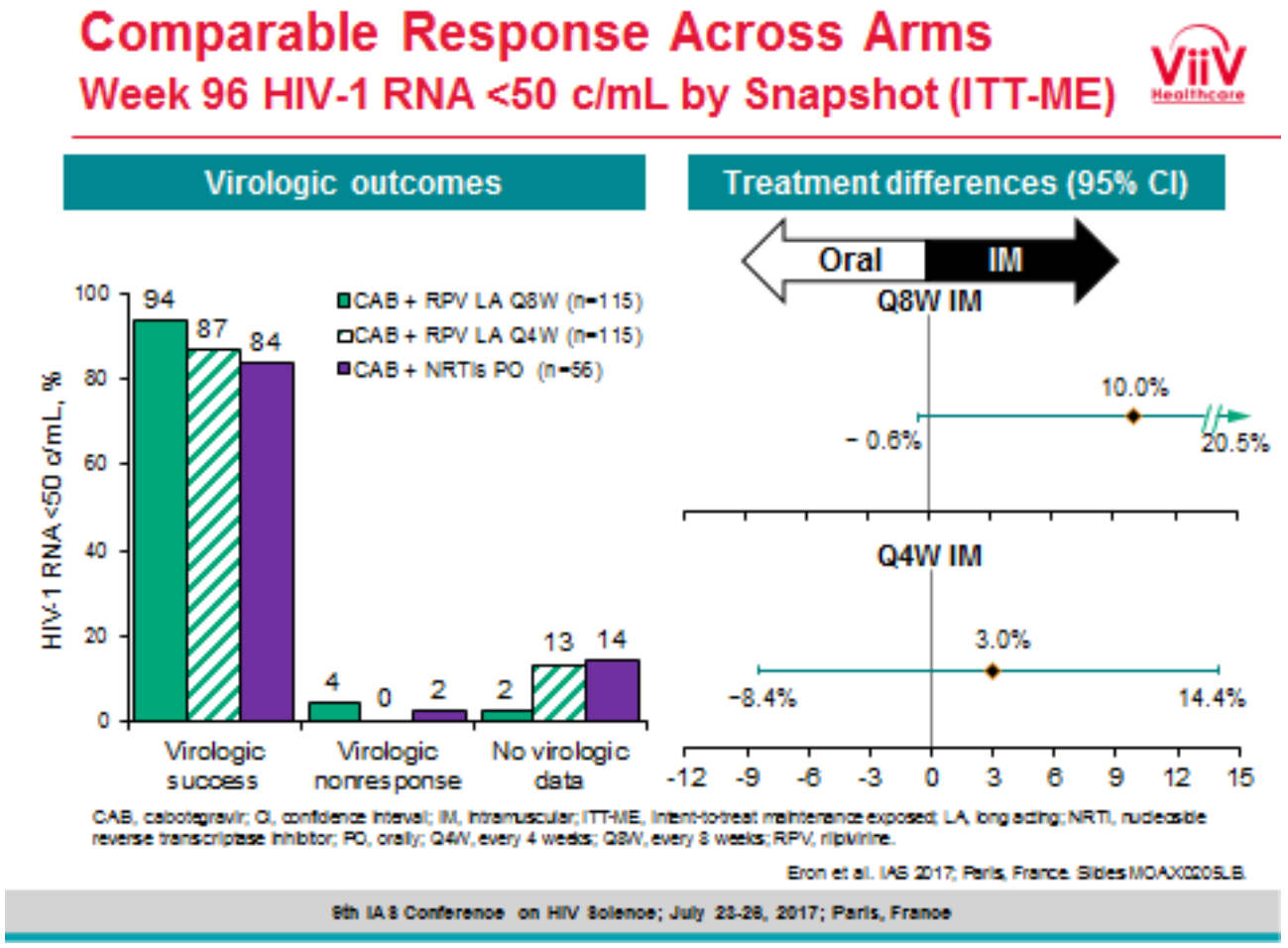
Bill Spreen, for ViiV Healthcare & GSK Development Team

17th HIV-HEPPK – June 2016

Cabotegravir y Rilpivirina: LATTE-2 96 semanas



Cabotegravir y Rilpivirina: LATTE-2 96 semanas



Cabotegravir y Rilpivirina: LATTE-2 96 semanas

Conclusions
LATTE-2 96-Week Results

- IM CAB LA + RPV LA, dosed every 4 or 8 weeks, successfully maintained HIV-1 viral load <50 c/mL
- 2 participants on LA dosing met PDVF criteria, no participants after Week 48
- Injection tolerability
  - Majority of ISRs were grade 1 to 2 pain, with a median duration of 3 days
  - <1% of participants had an ISR that led to discontinuation
  - High overall patient-reported satisfaction
- Dose selection
  - Q4W dosing selected and under evaluation in 2 pivotal phase III studies
  - Week 96 data demonstrate long-term durability of both Q4W and Q8W dosing options
  - Q8W dosing to be evaluated in upcoming phase III study
- Manuscript is being published in *The Lancet* today, July 24, 2017

CAB, cabotegravir; IM, intramuscular; LA, long acting; Q4W, every 4 weeks; Q8W, every 8 weeks; RPV, rilpivirine.

Eron et al. IAS 2017; Paris, France. Slides MOAX0205LB

Otros long acting

Additional Longer-Acting Investigational Agents (Phase II/III)

Agent	MoA	Phase	Implications
3BNC117[1,2]	Anti-CD4 receptor mAb	II	▪ Studies ongoing in treatment-experienced and naive pts
TMC278 LA[3]	LA injectable RPV (IM)	II	▪ Potential as long-acting injectable (Q8W)
UB-421[4]	Anti-CD4 receptor mAb	II	▪ Studied as possible ART alternative for maintenance therapy in suppressed pts
VRC01[5,6]	Anti-CD4 receptor mAb	II	▪ Phase II PrEP and treatment trials ongoing

1. Caskey M, et al. Nature. 2015;522:487-491. 2. ClinicalTrials.gov. NCT03041012. 3. Bekker L-G, et al. CROI 2017. Abstract 421LB. 4. Wang C-Y, et al. CROI 2017. Abstract 450LB. 5. ClinicalTrials.gov. NCT02716675. 6. ClinicalTrials.gov. NCT02568215.

Slide credit: clinicaloptions.com

Y EN CUANTO A ESTRATEGIAS DE INICIO

Immediate Antiretroviral Therapy Initiation on the Day of HIV Diagnosis

Since many individuals may fail to engage in care during the delay between initial HIV diagnosis (or first clinic visit) and the time ART is prescribed, some groups have proposed rapid ART initiation on the same day of HIV diagnosis as a strategy to increase engagement in care and increase the proportion of individuals who achieve and maintain ART-mediated viral suppression. This strategy was recently tested in a randomized controlled tri h Africa who had recently received HIV diagnoses. Those randomized to receive im iagnosis were significantly more likely than those randomized to usual care (thr supp in ca contr health iers to engagement in care, and underlying HIV and TB epidemics in South Africa ralizability of these findings to the United States, these studies suggested that sar be feasible and could potentially improve clinical outcomes. While no randomi trials have been performed in the United States, a recent pilot study of 39 individuals in

What's New in the Guidelines? (Last updated October 17, 2017; last reviewed October 17, 2017)

Hacia el 90/90/90/90
Starting early Francisco

Program Design and Implementation

Citywide RAPID Protocol:

All new confirmed HIV diagnoses linked to care ≤ 5 working days;

At 1st care visit: Baseline labs collected, counseling, medical/psychosocial assessment, **ART started unless risk for fatal IRIS**

[TFV+FTC] + [INSTI *or* DRV/r] with option for 4-drug regimen if HIV infection suspected on PrEP

Dissemination:

HIV clinics identified using HIV surveillance data, trained on RAPID procedures by in-service (2015) and individual provider detailing (2016)

Linkage navigators used **RAPID Provider Directory** to identify optimal HIV clinic for each newly-diagnosed patient, by insurance coverage, psychosocial needs.

Full protocol and RAPID detailing brochure for clinicians disseminated electronically at http://www.gettingtozerosf.org/rapid-committee/ and at open quarterly SFGTZ consortium meetings

Median Time to Care, ART, and Virologic Suppression

Metric	2013	2014	2015	2016	%Δ 2013-16
In Care within 1 year (%)	372 (93)	318 (97)	282 (96)	258 (97)	
Diagnosis to care (days)	8	7	7	5	-38%
1st Care Visit to ART (days)	27	17	6	1	-96%
ART to VL<200c/mL (days)	70	53	50	38	-46%
Diagnosis to VL<200 c/mL (days)	134	92	77	61	-54%

- **Time from diagnosis to VL<200** decreased significantly in all groups
- **Time from diagnosis to first care visit** decreased significantly for males, whites, Latinos, youth (13-29) and the housed
- **Time from first care visit to ART** decreased significantly in all groups
- **Time from ART to VL<200** decreased significantly for males, under 40 y.o., whites, Latinos, Asian/Pacific Islanders, and the housed


blah blah blah
mrwonderful.es


IDEAS
TAKE
AWAY

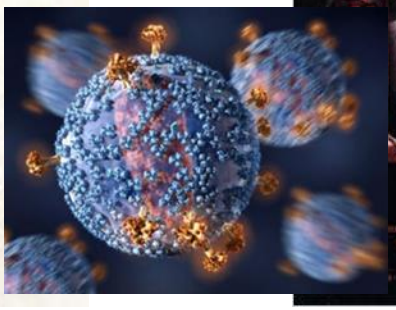
conclusión

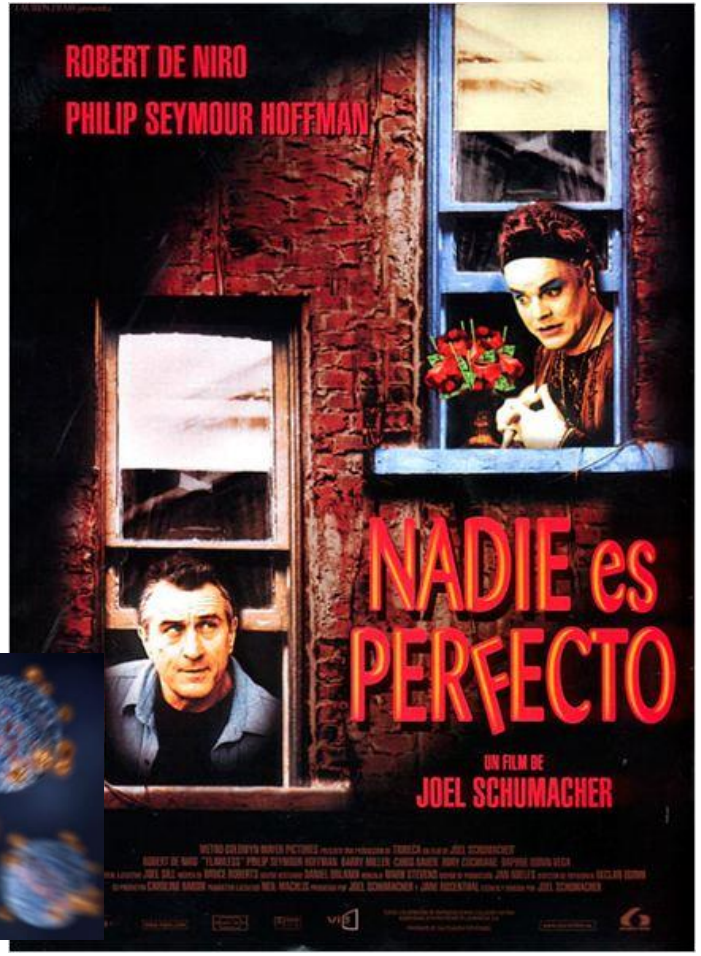

TAKE AWAY


TAKE
AWAY

- El tratamiento antirretroviral sigue evolucionando
- Disponemos de fármacos seguros, eficaces y cómodos de tomar con experiencia a largo plazo
- Mientras se consiga o no la curación, es necesario seguir avanzando para conseguir mejorar la calidad de vida de nuestros pacientes


BASADO EN UNA EXTRAORDINARIA HISTORIA REAL
NAOMI WATTS
EWAN McGREGOR
LO IMPOSIBLE
UNA PELÍCULA DE J.A.BAYONA
11 OCTUBRE 2012




ROBERT DE NIRO
PHILIP SEYMOUR HOFFMAN
NADIE es PERFECTO
UN FILM DE
JOEL SCHUMACHER

MUCHAS GRACIAS