Beneficios de Regímenes de una sola tableta (STR)
STR vs MTR

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Presenter Disclosure Information

- Research Support: ViiV, BMS, MSD, Jansen
- Speaker's Bureau: Abbvie, Bristol-Myers Squibb, Merck,Jansen, ViiV Healthcare, Stendhal
- Advisory Panel: Gilead, Stendhal, Gador,Jansens, ViiV

Agenda

- Reasons for choosing STR
- STRs positioning in Guidelines (US/EU vs LATAM)
- STRs in Simplification Strategies
- ART: efficiency
- STRs in Hospital Clinic BCN
- ATR: future positioning
- Conclusions

Better Adherence with Once-Daily Antiretroviral Regimens: A Meta-Analysis

Jean-Jacques Parienti,[1,2,3,4] David R. Bangsberg,[5] Renaud Verdon,[2] and Edward M. Gardner[6]

Departments of [1]Biostatistics and Clinical Research and [2]Infectious Diseases, Côte de Nacre University Hospital, Caen, and [3]Pierre et Marie Curie University, and [4]INSERM U707, Paris, France; [5]Partners AIDS Research Center, Massachusetts General Hospital, Harvard Medical School, Boston; and [6]Public Health Department, Denver Health and Hospital Authority, Denver, Colorado

Table 1. Characteristics of studies included in a meta-analysis of once-daily vs. twice-daily antiretroviral therapy regimens.

Study	Year	Treatment regimen		Population or study type	All components given once per day[a]	Duration of follow-up, weeks	Means of assessing adherence
		Once-daily regimen	Twice-daily regimen				
Benson et al. [7]	2004	**FTC,** D4T or AZT, and an NNRTI or a PI	**3TC,** D4T or AZT, and an NNRTI or PI	Switch	No	48	Pill count
Boyle et al. [8]	2008	**D4T XR,** 3TC, and EFV	**NRTIs** and a PI or NNRTI	Switch	Yes	48	MEMS
Eron et al. [9]	2004	**LPV-RTV** and NRTIs	**LPV-RTV** and NRTIs	Treatment-naive subjects	No	48	MEMS
Gallant et al. [10]	2006	**TDF, FTC,** and EFV	**AZT, 3TC,** and EFV	Treatment-naive subjects	Yes	48	Pill count
Kubota et al. [11]	2006	**ABC, 3TC,** and a third agent	**ABC, 3TC,** and a third agent	Treatment-naive subjects	No	12	Pill count
Molina et al. [12]	2007	**LPV-RTV,** TDF, and FTC	**LPV-RTV,** TDF, and FTC	Treatment-naive subjects	Yes	96	MEMS
Parienti et al. [13]	2007	**NVP** and NRTIs	**NVP** and NRTIs	Switch	No	16	MEMS
Porthsmouth et al. [14]	2005	**D4T XR,** 3TC, and EFV	**D4T** or **AZT,** 3TC, and EFV	Switch	Yes	24	MEMS
Rode et al. [15, 18]	2008	**LPV-RTV,** TDF, and FTC	**LPV-RTV,** TDF, and FTC	Initiation	Yes	12	MEMS
Ruane et al. [16]	2006	**AZT, 3TC, ABC,** and EFV	**AZT, 3TC, ABC,** and EFV	Switch	Yes	24	MEMS
Sosa et al. [17]	2005	**ABC, 3TC,** and a PI or NNRTI	**ABC, 3TC,** and a PI or NNRTI	Switch	No	48	Pill count

NOTE. Drugs that were monitored for adherence are shown in boldface font. ABC, abacavir; AZT, zidovudine; D4T, stavudine; EFV, efavirenz; FTC, emtricitabine; LPV, lopinavir; MEMS, Medication Event Monitoring System; NNRTI, nonnucleoside reverse-transcriptase inhibitor; NRTI, nucleoside reverse-transcriptase inhibitor; NVP, nevirapine; PI, protease inhibitors; RTV, ritonavir; TDF, tenofovir; 3TC, lamivudine; XR, extended release.

[a] In the once-daily regimen group.

CID, 2009

STRs

	EFV	RPV	EVG/COBI	EVG/COBI	DTG
	TDF/FTC	TDF/FTC	TDF/FTC	TAF/FTC	ABC/3TC
Brand name	ATRIPLA	EVIPLERA/ COMPLERA	STRIBILD	GENVOYA	TRIUMEQ
N pills/day		 TAF/FTC/RPV ODFESEY		 TAF/FTC DESCOVY 	
Take with food	±	yes	yes	yes	±

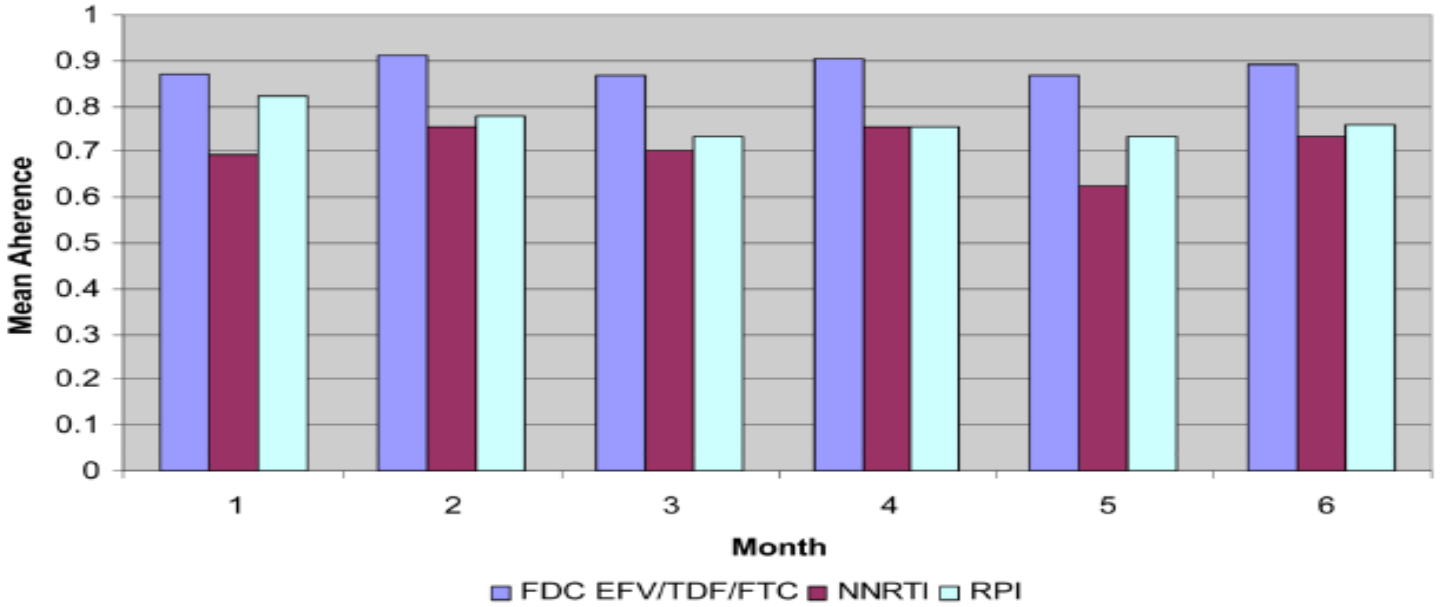
Package insert: Atripla, Eviplera/Complera, Isentress, Stribild, Tivicay, Genvoya

Reasons for choosing STRs

1. General WHO recommendation
2. Common sense!
3. Preference of patients

World Health Organization

A single tablet regimen is associated with higher adherence and viral suppression than multiple tablet regimens in HIV+ homeless and marginally housed people



AIDS 2010, **24**:2835–2840

BMJ open

Association between daily antiretroviral pill burden and treatment adherence, hospitalisation risk, and other healthcare utilisation and costs in a US medicaid population with HIV

Calvin J Cohen,[1] Juliana L Meyers,[2] Keith L Davis[2]

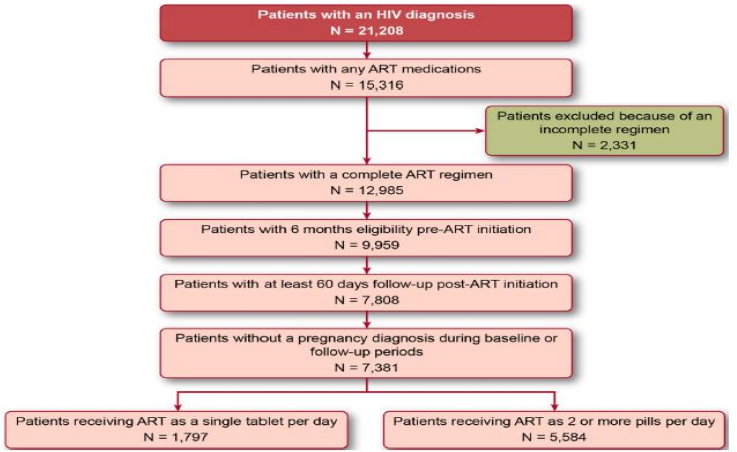


Table 2 Adherence to antiretroviral therapy, by cohort

Cohort	Number of patients	Mean (SD) MPR	MPR/persistency ratio (N, %) <0.8		0.8–<0.85		0.85–<0.9		0.9–<0.95		0.95–1	
STR	1797	0.84 (0.14)	537	29.88%	178	9.91	243	13.52	385	21.42	454	25.26
2+PPD	5584	0.80 (0.15)	2255	40.38	621	11.12	779	13.95	957	17.14	972	17.41
Overall	7381	0.81 (0.15)	2792	37.83	799	10.83	1022	13.85	1342	18.18	1426	19.32
p Value (1 vs 2)		<0.0001	<0.0001		0.1491		0.6477		<0.0001		<0.0001	

2+PPD, two or more pills per day; MPR, medication possession ratio; STR, once-daily single-tablet regimen.

Table 3 Summary of incomplete adherence, by cohort

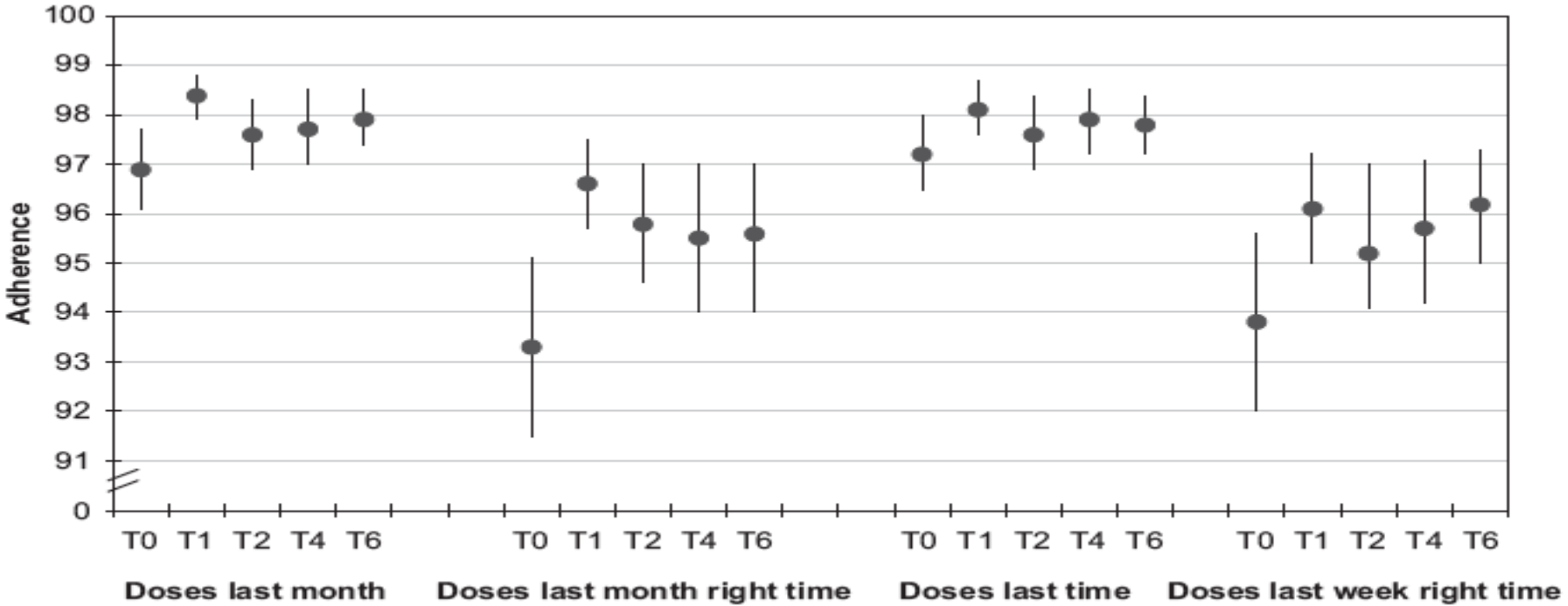
Adherence characteristic	STR (n=1797)		2+PPD (n=5584)		p Value
Percentage of days with complete adherence	84.42%		80.37%		<0.0001
Percentage of days with partial adherence	–		5.56%		–
Percentage of days with no ART medications	15.58%		14.07%		0.0356
Complete adherence days, mean (SD)	299.36	(234.56)	361.87	(315.03)	<0.0001
Partial adherence days, mean (SD)	–		22.24	(45.58)	–
Days with no medication available, mean (SD)	48.81	(54.24)	49.35	(57.11)	0.0356
Total follow-up duration, mean (SD)	348.17	(259.31)	433.46	(351.50)	<0.0001
Maximum consecutive gap in therapy mean (SD)*	19.48	(15.89)	23.92	(16.67)	<0.0001

*Represents either days with a partial regimen or days with no medications.
2+PPD, two or more pills per day; ART, antiretroviral therapy; STR, once-daily single-tablet regimen.

BMJ, 2013

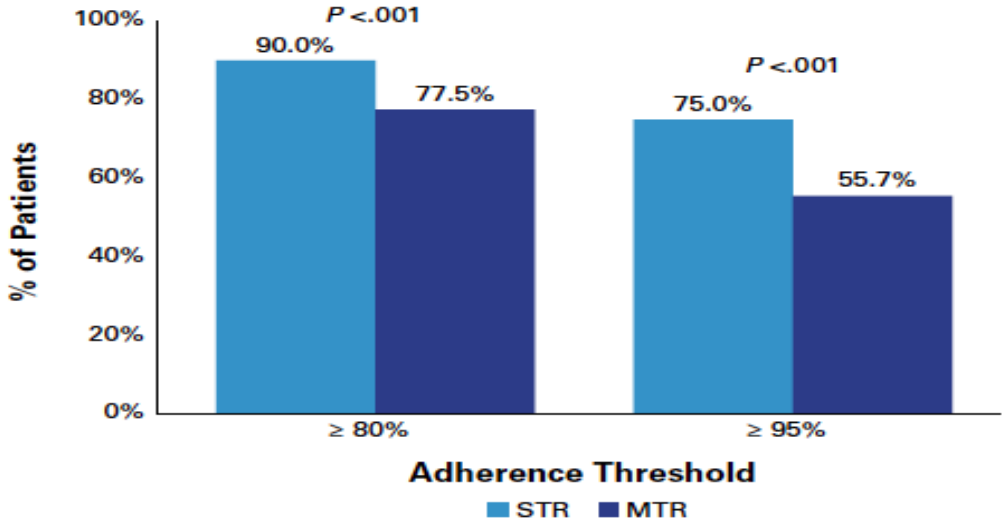
Open Access Full Text Article

One-pill once-a-day HAART: a simplification strategy that improves adherence and quality of life of HIV-infected subjects



Single- Versus Multiple-Tablet HIV Regimens: Adherence and Hospitalization Risk

Figure 1. Unadjusted Adherence Based on MPR Threshold Values[a]

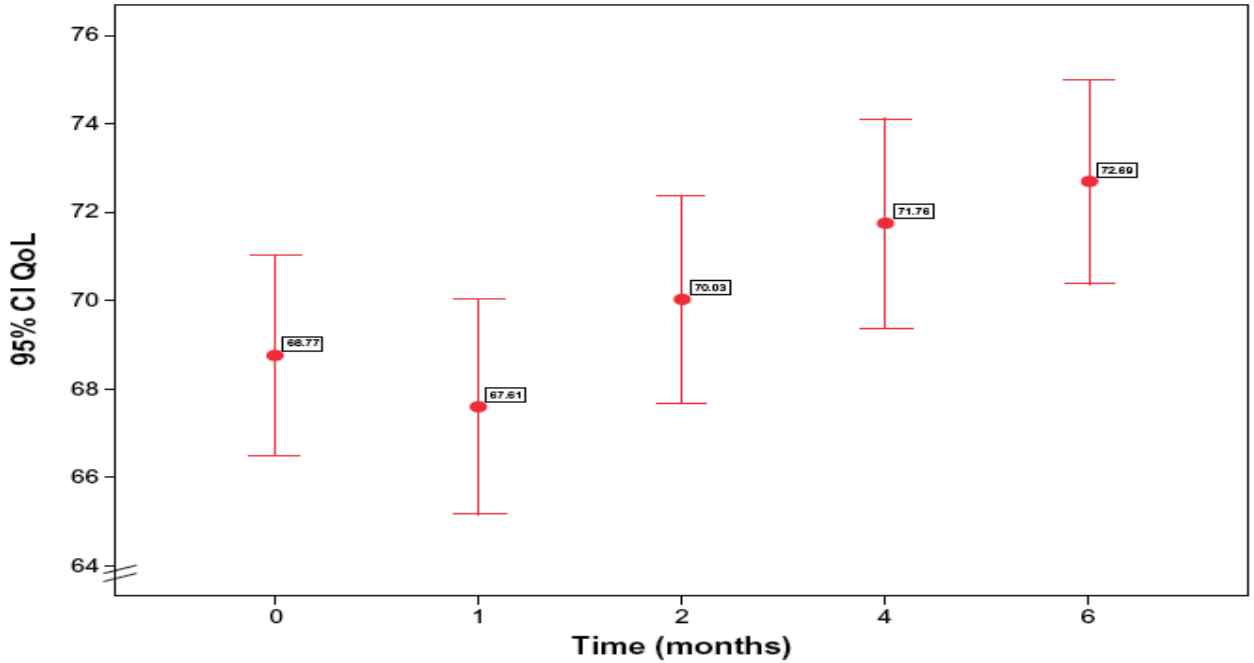


MPR indicates medication possession ratio; MTR, multiple-tablet regimen; STR, single-tablet regimen.
[a]Odds ratio adjusted for covariates at study entry: age, race, geographic region, Charlson comorbidity index score, mental health disorders, drug/alcohol abuse disorders, index year, treatment-naïve status, and undetectable viral load.

Sutton S et al. Am J Manag Care 2016

Open Access Full Text Article ORIGINAL RESEARCH

One-pill once-a-day HAART: a simplification strategy that improves adherence and quality of life of HIV-infected subjects



Is this QOL improvement only associated with the change to a ATR ?

Efficacy, safety, and patient acceptability of elvitegravir/cobicistat/emtricitabine/tenofovir in the treatment of HIV/AIDS

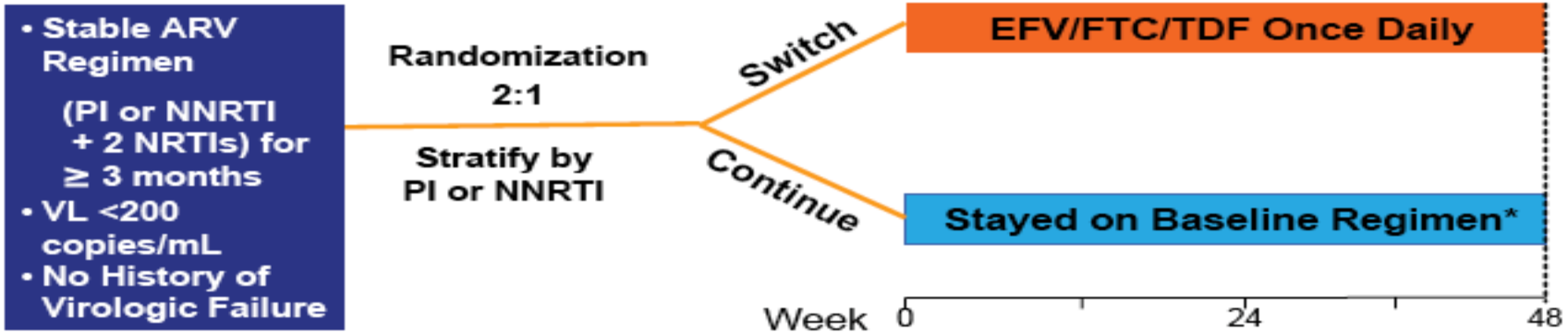
Treatment ease questions (HIV treatment satisfaction questionnaire)
Score per question −3 (much less satisfied) to 3 (much more satisfied)
Treatment ease score range −15 to 15
1. How convenient have you been finding your treatment to be recently?
2. How satisfied are you with the demands made by your current treatment?
3. How satisfied are you with the extent to which the treatment fits in with your lifestyle?
4. How flexible have you been finding your treatment to be recently?
5. How satisfied are you with your understanding of your HIV?

In two subgroup analysis of STRATEGY studies,[35,36] the patient's satisfaction was investigated using an Ease Score. Questions included in the questionnaire are listed in Table 3. In the NNRTI-STRATEGY subgroup analysis, 59 patients switched to EVG/c/FTC/TDF, and 37 continued a non-EFV NNRTI (27 nevirapine, ten rilpilvirine) with FTC/TDF. Switch to EVG/c/FTC/TDF was associated with a higher treatment ease (convenience, flexibility, demand, lifestyle, understanding) score (range: −15 to 15) at week 4 (median: 14 vs 11; P=0.047) and week 24 (median: 14 vs 12.5; P=0.038) than patients who continued their nevirapine- or rilpilvirine-based cART. In the PI STRATEGY subgroup analysis, 113 subjects switched to EVG/c/FTC/TDF; 60 continued a ritonavir-boosted DRV with FTC/TDF. An increased satisfaction with the ease of therapy for subjects who simplified their multitablet DRV-based regimen to the STR EVG/c/FTC/TDF was observed at week 4 (median: 12 vs 9; P=0.006) and week 24 (median: 13 vs 8; P<0.001).

Prinapori et al. Patient Preference nd Adherence 2015

AI266073 Study

- Phase IV, multicenter (55 US sites), open-label study (N= 300)



Primary Endpoint: to assess non-inferiority of EFV/FTC/TDF vs. SBR in terms of maintenance of HIV-1 RNA <200 copies/mL through Week 48 by TLOVR** analysis

*SBR: stayed on baseline regimen

**Time to loss of Virologic Response Algorithm

JAIDS, 2009;51:163-174.

Simplification of Antiretroviral Therapy to a Single-Tablet Regimen Consisting of Efavirenz, Emtricitabine, and Tenofovir Disoproxil Fumarate Versus Unmodified Antiretroviral Therapy in Virologically Suppressed HIV-1–Infected Patients

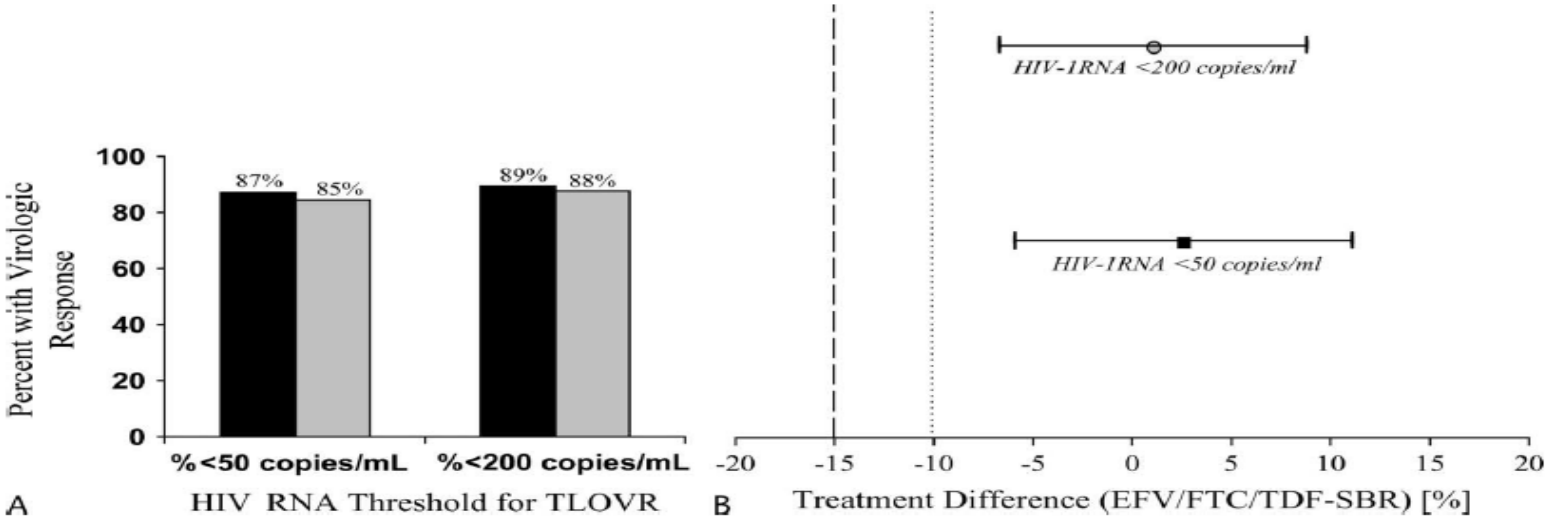
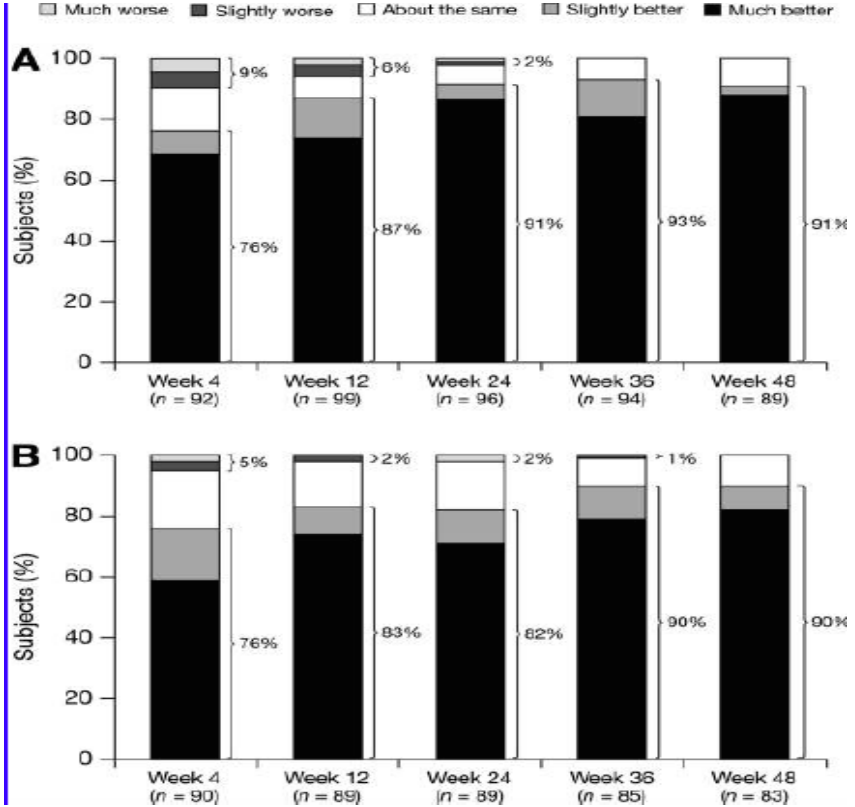


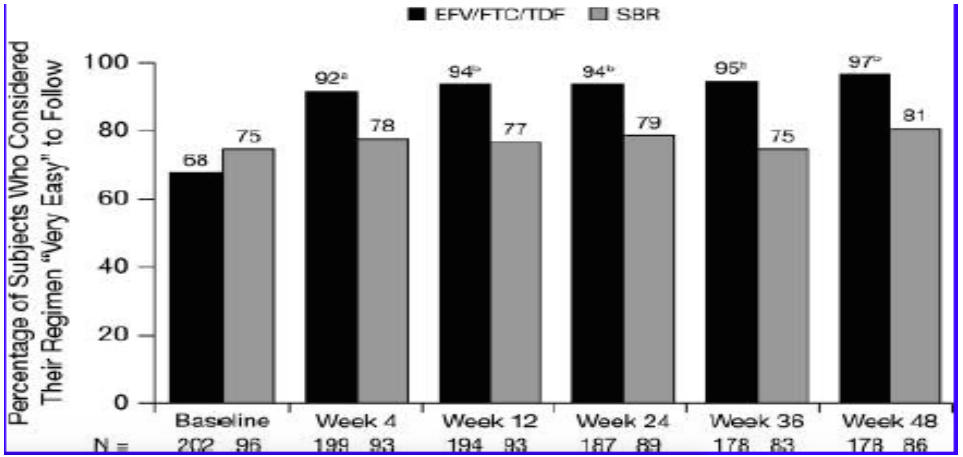
TABLE 3. Analysis of Response by Prior Treatment Stratum for HIV-1 RNA <200 Copies Per Milliliter and HIV-1 RNA <50 Copies Per Milliliter at 48 Weeks (ITT Population, NC = F)

	Treatment Response (TLOVR), %*			Treatment Response (TLOVR), %		
	Prior NNRTI			Prior PI		
HIV-1 RNA threshold	EFV/FTC/TDF (n = 95)†	SBR (n = 45)‡	Difference (95% CI§) [*P*¶]	EFV/FTC/TDF (n = 108)	SBR (n = 52)	Difference (95% CI) [*P*]
<200 copies/mL	92	84	7.1 (−4.8 to 19.1) [0.245]	87	90	−3.3 (−13.6 to 6.9) [0.612]
<50 copies/mL	92	82	9.4 (−3.1 to 21.8) [0.153]	83	87	−3.2 (−14.8 to 8.4) [0.651]

JAIDS, 2009;51:163-174.

Patient-Reported Outcomes in Virologically Suppressed, HIV-1–Infected Subjects After Switching to a Simplified, Single-Tablet Regimen of Efavirenz, Emtricitabine, and Tenofovir DF





AIDS PATIENT CARE and STDs
Volume 24, Number 2, 2010

BMJ open

Association between daily antiretroviral pill burden and treatment adherence, hospitalisation risk, and other healthcare utilisation and costs in a US medicaid population with HIV

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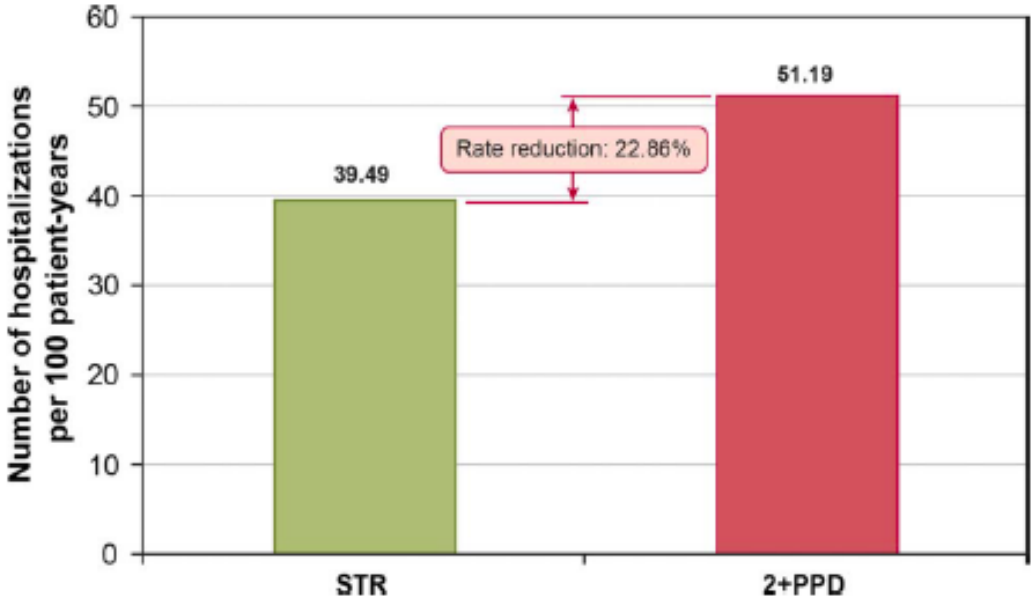
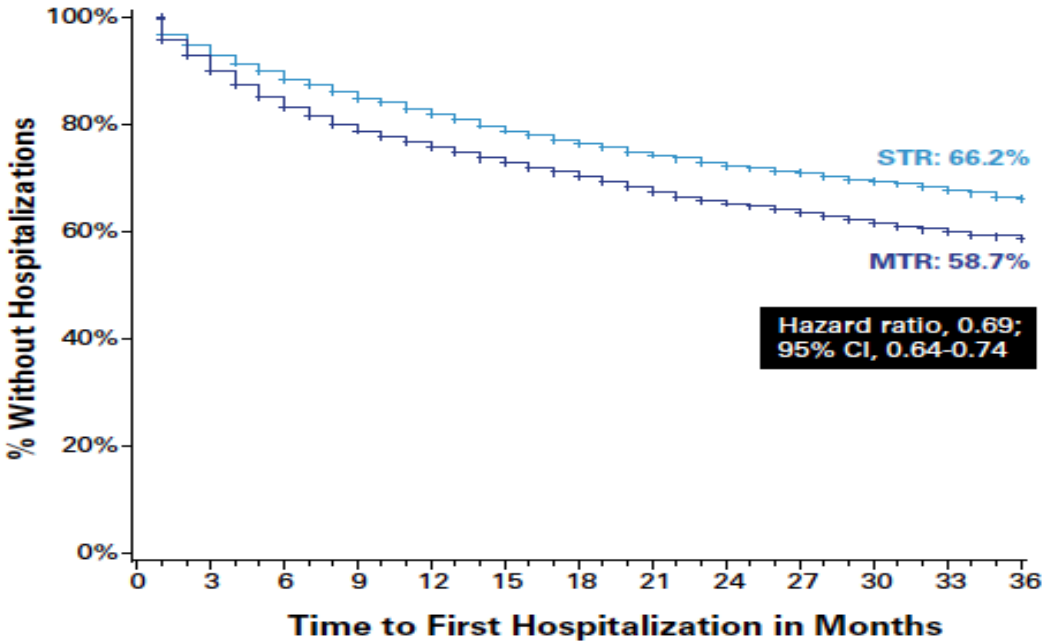


Figure 2 Adjusted rate of hospitalisations per 100 patient-years, by cohort.

BMJ, 2013

Single- Versus Multiple-Tablet HIV Regimens: Adherence and Hospitalization Risk

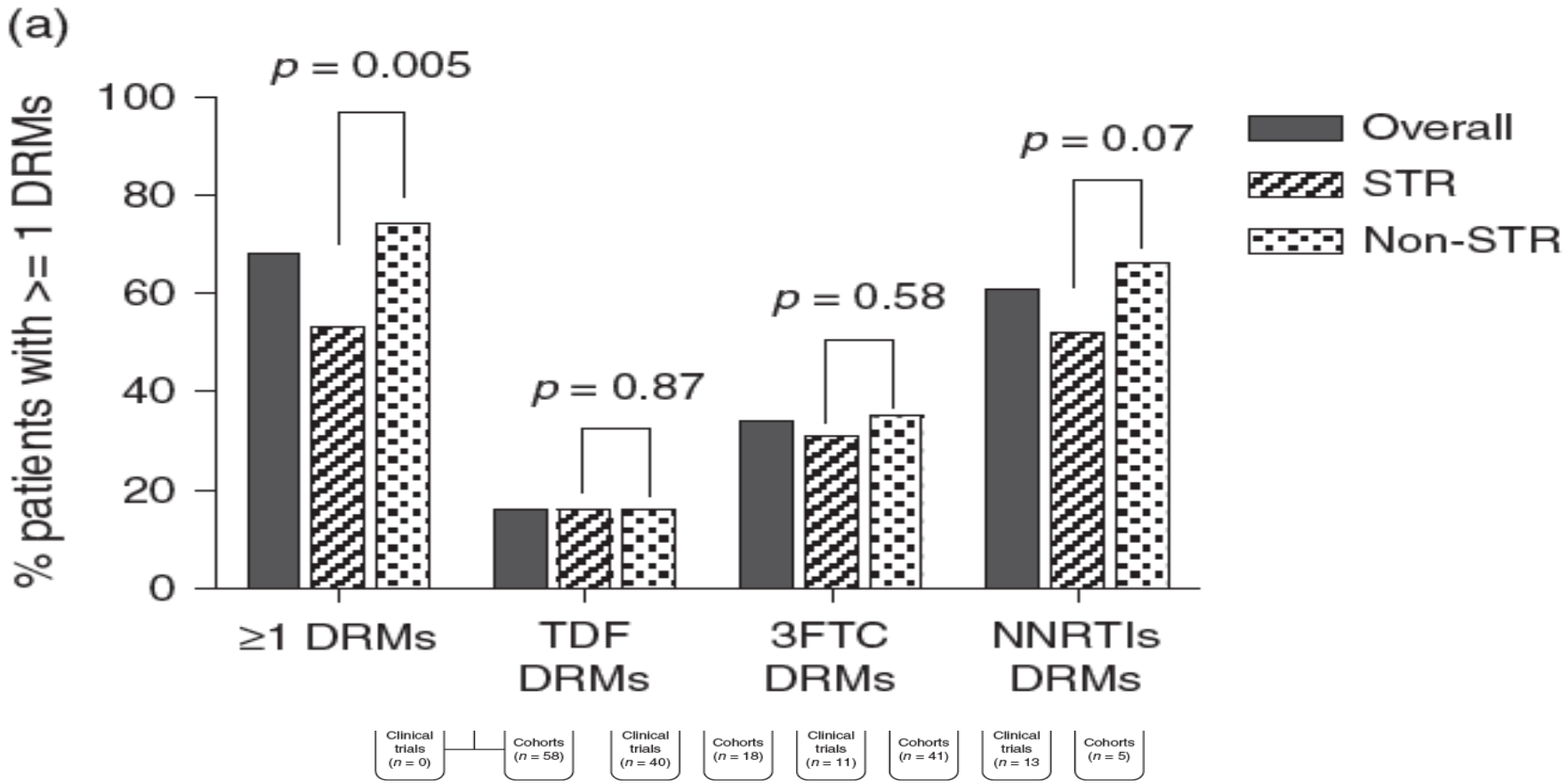
Figure 2. Adjusted Risk of Hospitalization for STR Compared With MTR Cohort



MTR indicates multiple-tablet regimen; STR, single-tablet regimen.

Sutton S et al. Am J Manag Care 2016

Lower prevalence of drug resistance mutations at first-line virological failure to first-line therapy



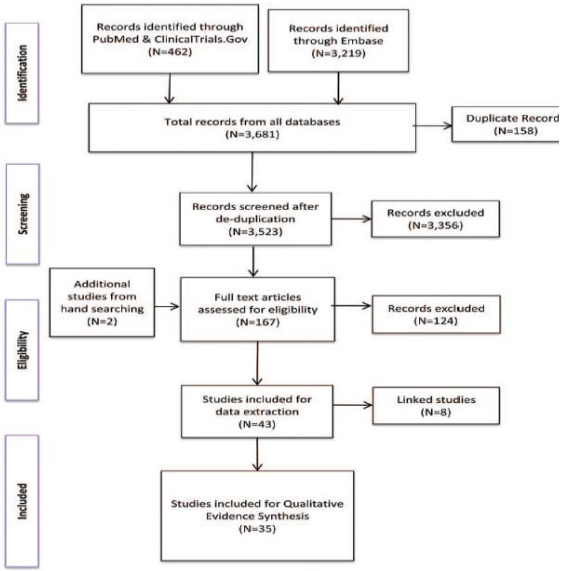
AIDS. 2014 Nov 13;28(17):2531-9

SYSTEMATIC REVIEW AND META-ANALYSIS (PRISMA COMPLIANT)

OPEN

Meta-Analysis of Studies Comparing Single and Multi-Tablet Fixed Dose Combination HIV Treatment Regimens

P.G. Clay, PharmD, S. Nag, PhD, C.M. Graham, PhD, and S. Narayanan, MS, MHS

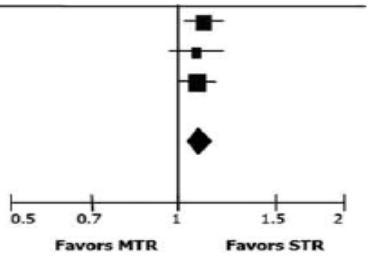


Viral load suppression (<50 copies/ml) at 48 weeks (STR vs. MTR)

Study	STR Events	STR Total	MTR Events	MTR Total	Weight	Risk Ratio IV, Random, 95% CI
Arribas 2014	272	293	121	145	37.2%	1.11 [1.03, 1.20]
Dejesus 2009	177	204	82	102	19.4%	1.08 [0.97, 1.20]
Pozniak 2014	271	292	126	147	43.4%	1.08 [1.01, 1.17]
Total (95% CI)		**789**		**394**	**100.0%**	**1.09 [1.04, 1.15]**
Total events	720		329			

Heterogeneity: Tau² = 0.00; Chi² = 0.31, df = 2 (P = 0.86); I² = 0%

Test for overall effect: Z = 3.61 (P = 0.0003)



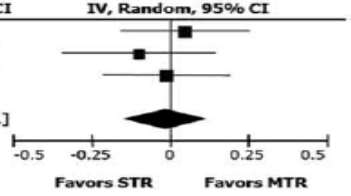
A

Change in CD4 Cell Count at 48 Weeks (STR vs. MTR)

Study	STR Mean	STR SD	STR Total	MTR Mean	MTR SD	MTR Total	Weight	Std. Mean Difference IV, Random, 95% CI
Arribas 2014	40	170	290	32	166	139	36.8%	0.05 [-0.15, 0.25]
Dejesus 2009	6	49.11	203	10.75	43.02	97	25.7%	-0.10 [-0.34, 0.14]
Pozniak 2014	56	147	290	58	179	143	37.5%	-0.01 [-0.21, 0.19]
Total (95% CI)			**783**			**379**	**100.0%**	**-0.01 [-0.14, 0.11]**

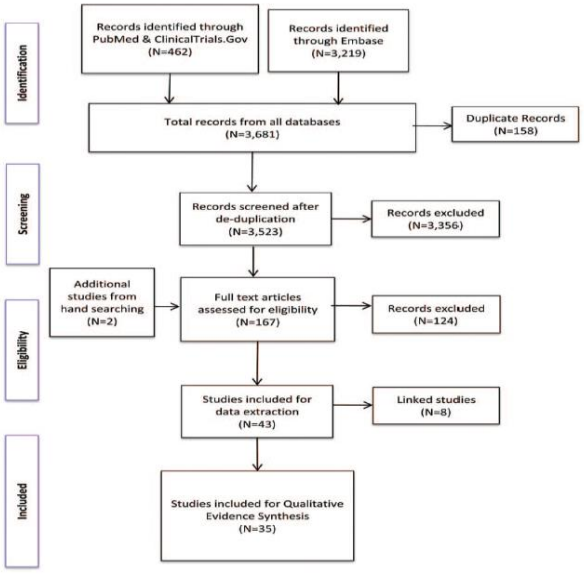
Heterogeneity: Tau² = 0.00; Chi² = 0.84, df = 2 (P = 0.66); I² = 0%

Test for overall effect: Z = 0.21 (P = 0.83)

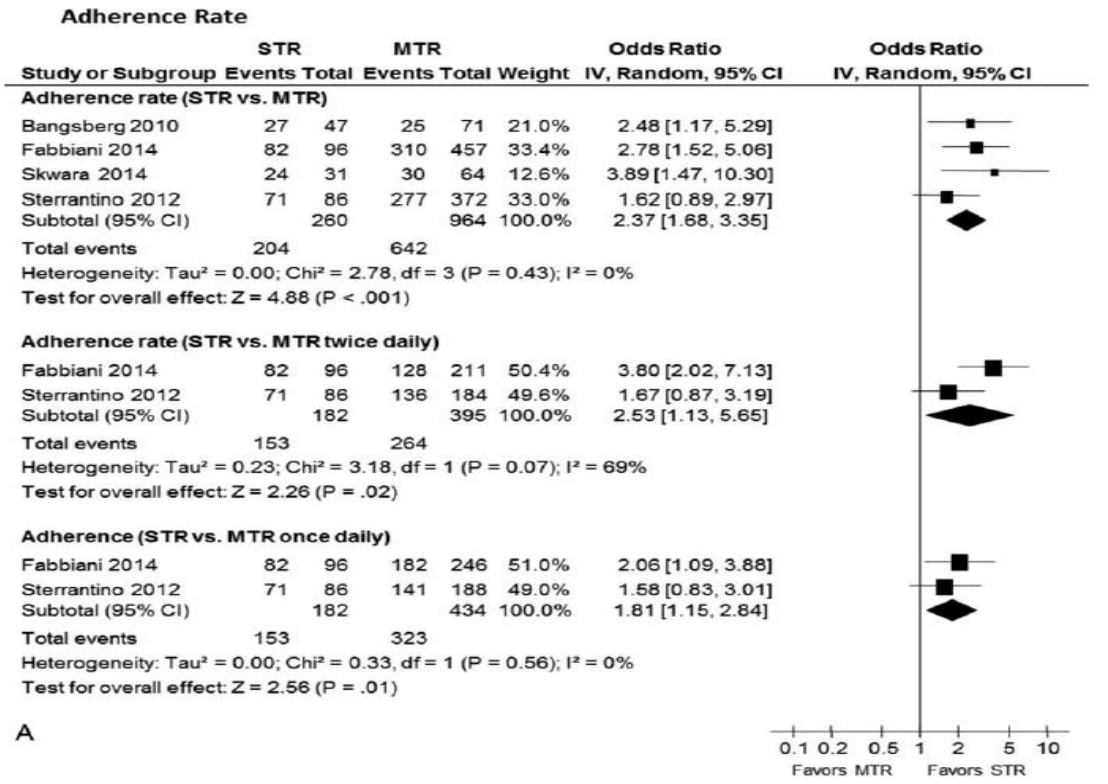


B

BMJ, 2013


Identification
Records identified through PubMed & ClinicalTrials.Gov (N=462)
Records identified through Embase (N=3,219)
Total records from all databases (N=3,681)
Duplicate Records (N=158)
Screening
Records screened after de-duplication (N=3,523)
Records excluded (N=3,356)
Eligibility
Additional studies from hand searching (N=2)
Full text articles assessed for eligibility (N=167)
Records excluded (N=124)
Studies included for data extraction (N=43)
Linked studies (N=8)
Included
Studies included for Qualitative Evidence Synthesis (N=35)

BMJ, 2013


Adherence Rate
STR MTR Odds Ratio Odds Ratio
Study or Subgroup Events Total Events Total Weight IV, Random, 95% CI IV, Random, 95% CI
Adherence rate (STR vs. MTR)
Bangsberg 2010 27 47 25 71 21.0% 2.48 [1.17, 5.29]
Fabbiani 2014 82 96 310 457 33.4% 2.78 [1.52, 5.06]
Skwara 2014 24 31 30 64 12.6% 3.89 [1.47, 10.30]
Sterrantino 2012 71 86 277 372 33.0% 1.62 [0.89, 2.97]
Subtotal (95% CI) 260 964 100.0% 2.37 [1.68, 3.35]
Total events 204 642
Heterogeneity: Tau² = 0.00; Chi² = 2.78, df = 3 (P = 0.43); I² = 0%
Test for overall effect: Z = 4.88 (P < .001)
Adherence rate (STR vs. MTR twice daily)
Fabbiani 2014 82 96 128 211 50.4% 3.80 [2.02, 7.13]
Sterrantino 2012 71 86 136 184 49.6% 1.67 [0.87, 3.19]
Subtotal (95% CI) 182 395 100.0% 2.53 [1.13, 5.65]
Total events 153 264
Heterogeneity: Tau² = 0.23; Chi² = 3.18, df = 1 (P = 0.07); I² = 69%
Test for overall effect: Z = 2.26 (P = .02)
Adherence (STR vs. MTR once daily)
Fabbiani 2014 82 96 182 246 51.0% 2.06 [1.09, 3.88]
Sterrantino 2012 71 86 141 188 49.0% 1.58 [0.83, 3.01]
Subtotal (95% CI) 182 434 100.0% 1.81 [1.15, 2.84]
Total events 153 323
Heterogeneity: Tau² = 0.00; Chi² = 0.33, df = 1 (P = 0.56); I² = 0%
Test for overall effect: Z = 2.56 (P = .01)
0.1 0.2 0.5 1 2 5 10
Favors MTR Favors STR
A
Adherence per Pill Count (STR vs. MTR)
STR MTR Std. Mean Difference Std. Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI IV, Random, 95% CI
Bangsberg 2010 86 18 47 73.62 22.05 71 56.6% 0.60 [0.22, 0.98]
Buscher 2012 98.25 2.26 34 95.89 3.25 65 43.4% 0.79 [0.36, 1.22]
Total (95% CI) 81 136 100.0% 0.68 [0.40, 0.97]
Heterogeneity: Tau² = 0.00; Chi² = 0.45, df = 1 (P = .50); I² = 0%
Test for overall effect: Z = 4.73 (P < .001)
-2 -1 0 1 2
Favors MTR Favors STR
B
Note: IV – Inverse Variance; Random – Random Effects model; CI – Confidence Interval

Agenda

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- STRs in Hospital Clinic BCN
- ATR: future positioning
- Conclusions

Preferred Regimens in ART Guidelines (May 2017)

	EACS Oct' 16 [1]	DHHS July' 16 [2]	IAS-USA July' 16 [3]	GESIDA/PNS ' 17 [4]
DTG + ABC/3TC	Preferred	Preferred	Preferred	Preferred
DTG + TDF/FTC	Preferred (or TAF)	Preferred (TDF or TAF)	Preferred (only TAF)	Preferred (TDF or TAF)
RAL + TDF/FTC	Preferred (or TAF)	Preferred	Preferred (only TAF)	Preferred (TDF or TAF)
RAL + ABC/3TC	Alternative	Other	Alternative	Other
EVG/$_{COBI}$/FTC/TDF	Preferred	Preferred		Alternative
EVG/$_{COBI}$/FTC/TAF	Preferred	Preferred	Preferred	Preferred
EFV/TDF/FTC	Alternative	Alternative	Alternative	Other (TDF or TAF)
RPV/TDF/FTC	Preferred (or TAF)	Alternative (VL<10^5 & CD4>200)	Alternative (VL<10^5 & CD4>200)	Alternative (TDF or TAF)
DRV/r + TDF/FTC	Preferred (or DRV/c, or TAF)	Preferred (or TAF or /c)	Alternative (or /c)	Alternative (or DRV/c, or TAF)
DRV/r + ABC/3TC	Alternative (or DRV/c)	Alternative	Alternative	Other
ATV/r + TDF/FTC	Alternative (or ATV/c, or TAF)	Alternative (or ATV/c)		Other (or ATV/c , or TAF)
ATV/r + ABC/3TC	Alternative (or ATV/c)	Other (or ATV/c)		

1. EACS Guidelines, version 8.1, Oct 2016. Available at: http://www.eacsociety.org/. 2. DHHS Panel. Available at: https://aidsinfo.nih.gov/guidelines . 3. JAMA 2016;316(2):191-210. 4. GESIDA/PNS. Disponible en: http://www.gesida-seimc.org/.

Selección del primer tratamiento en las guías Latinoamericanas

País, año	AZT/3TC	ABC/3TC	TDF/FTC	EFV	NVP	RPVc	LPV/r	ATV/r	FPV/r	DRV/r	RAL	DTG	EVGc
Ecuador, 2012													
Chile, 2013													
Venez, 2014													
Colombia, 2014				o STR									
Argent, 2016				STR		STR		o ATV/c			+TDF/F		+/- TAF
Brasil, 2017		+ DTG		+TDF/3							+TDF/3	+TDF/3	
México, 2017		+ DTG	TAF !	o STR		STR		o ATV/c				o STR	TAF !

→ Retraso hasta de 3 años en la adopción de nuevas terapias (INIs, STR, TAF)

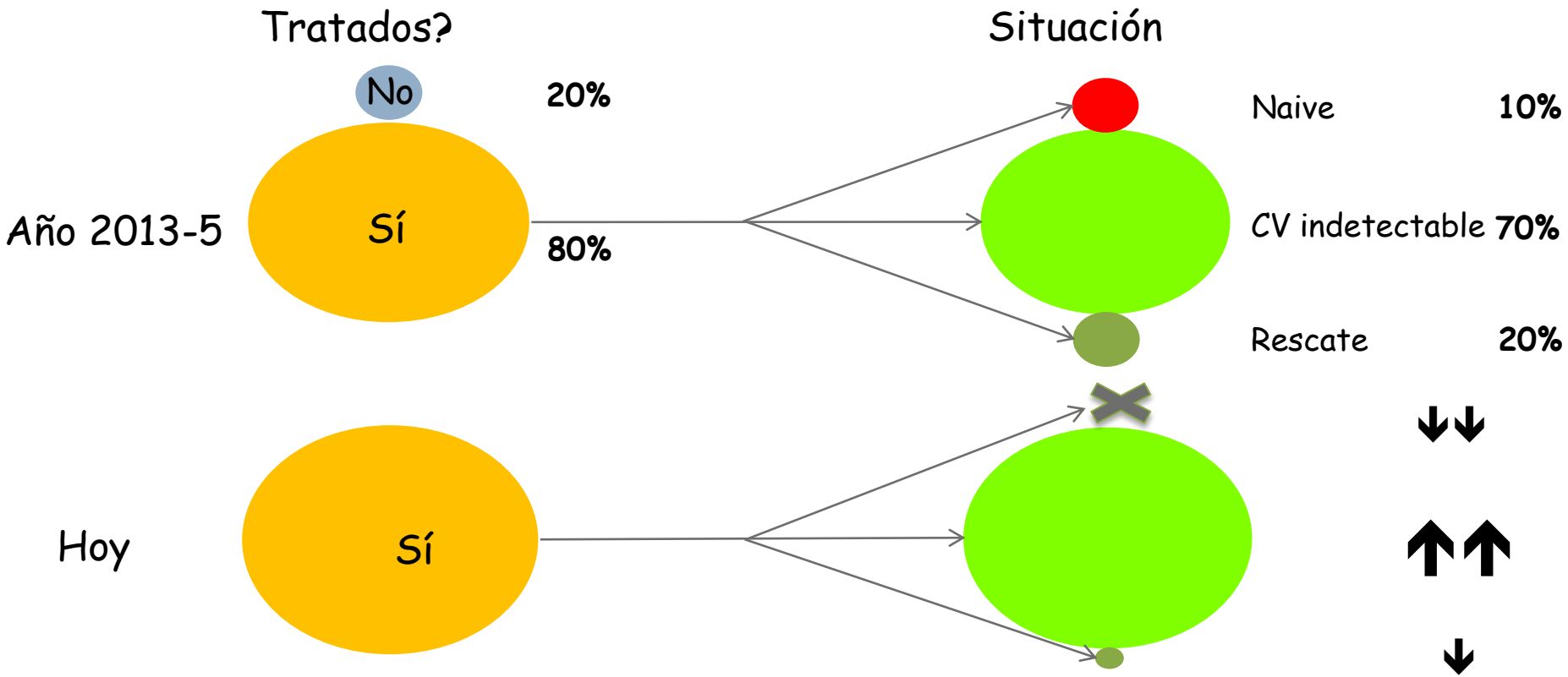
→ Limitante en la individualización de la terapia antirretroviral

Courtesy E. Martinez

Agenda

- Reasons for choosing STR
- STRs positioning in Guidelines (US/EU vs LATAM)
- STRs in Simplification Strategies
- ART: efficiency
- STRs in Hospital Clinic BCN
- ATR: future positioning
- Conclusions

¿Cuál era la situación de nuestras consultas y hacia dónde vamos?



GeSIDA: Circunstancias que obligan a cambiar el TAR eficaz

- El cambio proactivo es obligado cuando evidencias sólidas avalan que el paciente tiene más riesgo de presentar un efecto adverso grave o irrecuperable si se mantiene el TAR actual que si se cambia. Un ejemplo paradigmático es la lipoatrofia causada por los análogos de nucleósidos timidínicos.
- El cambio reactivo es obligado si el efecto adverso va a desaparecer tras el cambio de TAR, como por ejemplo los efectos adversos del SNC causados por EFV.
- Los efectos adversos que ocasionan el cambio precoz del TAR inicial en un paciente naive son de tal intensidad que el cambio se realiza frecuentemente antes de haberse alcanzado la supresión de la replicación viral. Es obvio que si un paciente tiene la carga viral suprimida es porque es capaz de continuar tomando la pauta prescrita. El clínico no debe olvidar que en ocasiones ese nivel de adherencia se consigue gracias a un sobresfuerzo del paciente, que es capaz de sobrellevar efectos adversos que pueden ser erróneamente entendidos como inevitables. El médico no debe asumir que un TAR es óptimo para su paciente sólo porque la carga viral está suprimida. Este comité recomienda que en todas las revisiones el clínico pregunte con detalle sobre el esfuerzo que necesita el paciente para adherirse al TAR pautado.

Documento de consenso de GeSIDA/Plan Nacional sobre el Sida respecto al tratamiento antirretroviral en adultos infectados por el virus de la inmunodeficiencia humana (Actualización enero 2016). Disponible en: http://www.gesida-seimc.org/guias_clinicas.php?mn_MP=406&mn_MS=407. Acceso: 08/16

GeSIDA: Motivos para cambiar un TAR eficaz

- Existen muchos motivos para cambiar un TAR eficaz: intolerancia, toxicidad, nuevas comorbilidades, interacciones farmacológicas, disminución del número de pastillas o dosis diarias, requerimientos dietéticos, embarazo y coste del propio TAR. El cambio puede ser proactivo cuando se realiza preventivamente o reactivo cuando el régimen actual ha dejado de ser el ideal para el paciente debido a alguno de los motivos reseñados.

- **Recomendaciones**

El cambio desde un pauta con dos ITIAN más un IP/r a dos ITIAN más un ITINN, INI o ATV no potenciado con ritonavir solo debe hacerse si se puede garantizar la actividad antiviral de los dos ITIAN y la del tercer fármaco acompañante (A-I). Sin olvidar que el objetivo prioritario es mantener la supresión virológica, el clínico debe realizar una evaluación minuciosa del perfil de toxicidades, interacciones, restricciones dietéticas y actividad sobre el VHB (si fuera necesario) del nuevo régimen.

El objetivo del cambio del TAR es mantener la supresión virológica y optimizar el TAR de acuerdo a las características y la preferencia del paciente.

Documento de consenso de GeSIDA/Plan Nacional sobre el Sida respecto al tratamiento antirretroviral en adultos infectados por el virus de la inmunodeficiencia humana (Actualización enero 2016). Disponible en: http://www.gesida-seimc.org/guias_clinicas.php?mn_MP=406&mn_MS=407. Acceso: 08/16

Aspectos a considerar en el switch del TARV

Regimens "accepted" in switch in ART Guidelines (May 2017)

Courtesy J.M Llibre

	EACS Oct' 16 [1]	DHHS July' 16 [2]	IAS-USA July'16 [3]	GESIDA/PNS ' 17 [4]
DTG + ABC/3TC	A PI/r may be switched to ATV_{400}, an NNRTI, or an INI if full activity of the 2 NRTIs can be guaranteed	Some examples of between-class switch strategies are replacing a boosted PI or an NNRTI with an INSTI		AI
DTG + TDF/FTC				
RAL + TDF/FTC				AI
RAL + ABC/3TC				AI
EVG/$_C$/FTC/TDF(TAF)				AI
DTG/RPV *	?	?	?	?
CAB LA + RPV LA *#	?	?	?	?
EFV/TDF/FTC				BI
RPV/TDF/FTC				AI (or TAF)
ATV_{400} + ABC/3TC				AI
LPV/r + 3TC				AI
ATV/r + 3TC				AI
DRV/r + 3TC				AI

1. EACS Guidelines, version 8.1, Oct 2016. Available at: http://www.eacsociety.org/. 2. DHHS Panel. Available at: https://aidsinfo.nih.gov/guidelines .
3. JAMA 2016;316(2):191-210. 4. GESIDA/PNS. Available in: http://www.gesida-seimc.org

* RPV only approved in naives. # CAB not licensed yet.

Switch options. The science (randomized studies).

Courtesy J.M Llibre

	NVP	EFV	ATV_{400} + ABC/3TC	DRV/r QD Mono	RPV/TDF/ FTC	RAL BID	EVG/c/F/T	ATV/r + 3TC
Acronym	NEFA	NEFA	ARIES, ASSURE	MONET PROTEA	SPIRIT	Switchmrk I/II, SPIRAL	STRATEGY PI / NNRTI 109	SALT
Applies to…								
Ctrol arm OK?								
Non-inf ?								
Superior ?								
Pot new tox?								
Additional benefit demonstrated?								
Resistance at VF?								
STR?								

Switch options. The science (randomized studies).

Courtesy J.M Llibre

	NVP	EFV	ATV_{400} + ABC/3TC	DRV/r QD Mono	RPV/TDF/ FTC	RAL BID	EVG/c/F/T	ATV/r + 3TC
Acronym	NEFA	NEFA	ARIES, ASSURE	MONET PROTEA	SPIRIT	Switchmrk I/II, SPIRAL	STRATEGY PI / NNRTI (109)	SALT
Applies to…	Old PIs	Old PIs	ATV/r	PI no DRV, NNRTI	Current PI/r	LPV/r (ATV/r)	Current PI/r /NNRTI (+ INsTI)	PI/r /NNRTI ATV, LPV, EFV
Ctrol arm OK?	No	No	Yes	No	Yes	Yes	Yes	No
Non-inf ?	No	No	Yes	Yes/No	Yes	No/Yes	Yes	Yes
Superior ?	No	No	No	No	No	No	**Yes** / No	No
Pot new tox?	Yes	Yes	No	Not sure	No	No	No	No
Additional benefit demonstrated?	Yes, lipids	No	Yes: lipids, Bi, kidney tub & bone markers	No	Yes: lipids	Yes: lipids	Yes, GI and lipids (PI), and CNS (EFV)	Not yet
Resistance at VF?	Yes	Yes	No	No	Low	Yes/Low	No	?
STR?								

Switch options. The science (randomized studies).

Courtesy J.M Llibre

	NVP	EFV	ATV_{400} + ABC/3TC	DRV/r QD Mono	RPV/TDF/ FTC	RAL BID	EVG/c/F/T	ATV/r + 3TC
Acronym	NEFA	NEFA	ARIES, ASSURE	MONET PROTEA	SPIRIT	Switchmrk I/II, SPIRAL	STRATEGY PI / NNRTI (109)	SALT
Applies to…	Old PIs	Old PIs	ATV/r	PI no DRV, NNRTI	Current PI/r	LPV/r (ATV/r)	Current PI/r /NNRTI (+ INsTI	PI/r /NNRTI ATV, LPV, EFV
Ctrol arm OK?	No	No	Yes	No	Yes	Yes	Yes	No
Non-inf ?	No	No	Yes	Yes/No	Yes	No/Yes	Yes	Yes
Superior ?	No	No	No	No	No	No	**Yes** / No	No
Pot new tox?	Yes	Yes	No	Not sure	No	No	No	No
Additional benefit demonstrated?	Yes, lipids	No	Yes: lipids, Bi, kidney tub & bone markers	No	Yes: lipids	Yes: lipids	Yes, GI and lipids (PI) and CNS (EFV)	Not yet
Resistance at VF?	Yes	Yes	No	No	Low	Yes/Low	No	?
STR?	No	Yes	No	Not yet	Yes	No	Yes	No

Reason for switching

The Ethics of Switch/Simplify in Antiretroviral Trials: Non-Inferior or Just Inferior?

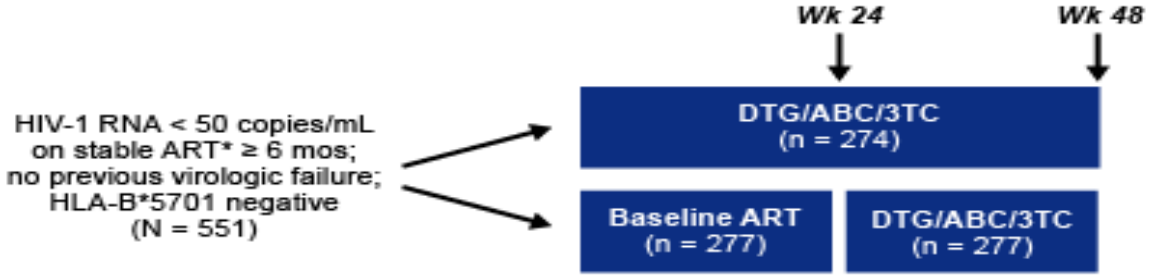
Andrew Carr[1,2]*, Jennifer Hoy[3,4], Anton Pozniak[5]

Summary Points

- The high efficacy of antiretroviral therapy has resulted in more trials that switch or simplify existing therapy in patients whose HIV is fully controlled.
- The primary outcome of about half of these trials is virological non-inferiority. As participants already have fully controlled HIV on existing therapy, these trials offer no virological benefit.
- Many trials (i) enrol patients who cannot benefit with the switch, (ii) do not capture (or report) all potential risks, and (iii) are designed with a view to a pharmaceutical company's profits rather than participant benefit.
- A switch/simplification trial is only ethical if participants can meaningfully benefit from the treatment change and are more likely to benefit than suffer harm, and if the study is powered to assess the key expected benefit and reports all end points.

Switching to TRIUMEQ® (STRIVING)

Schematic of Study Design

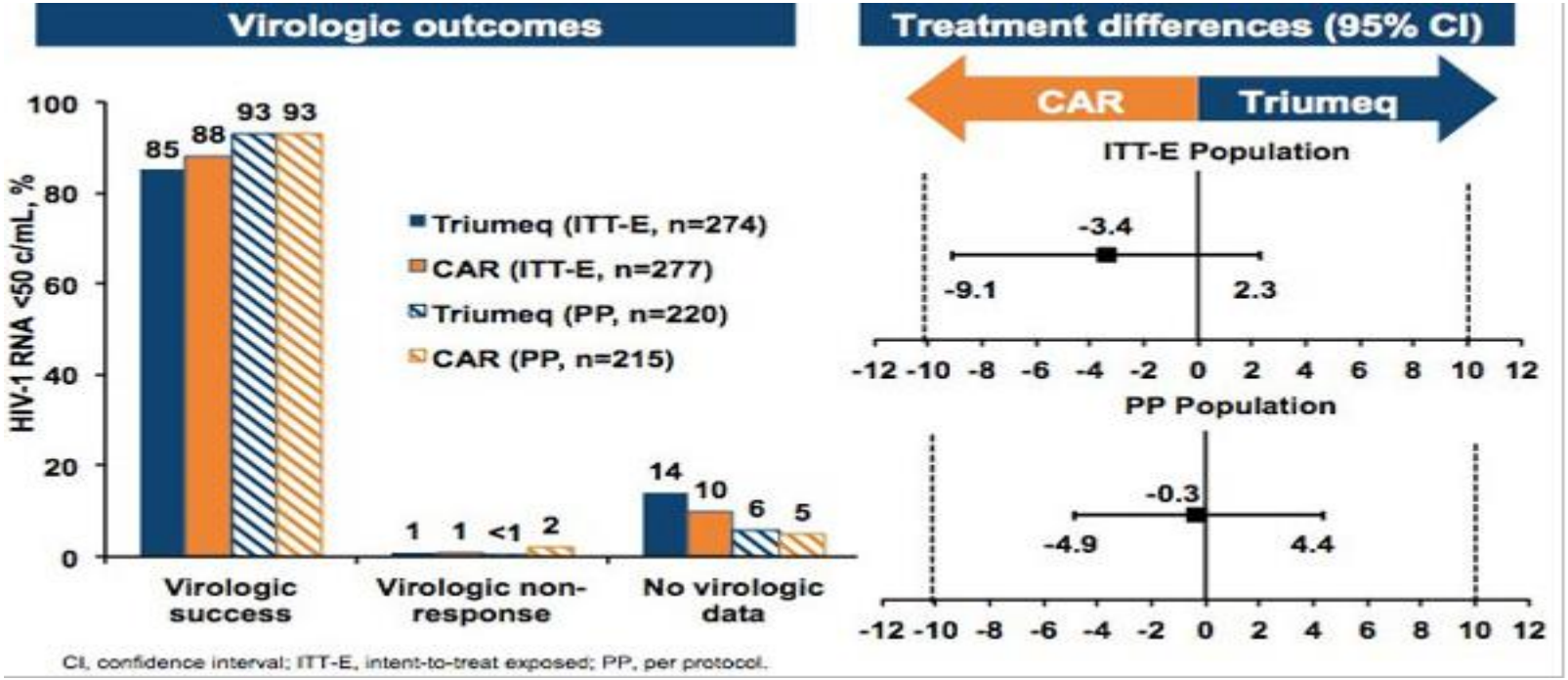


*Containing 2 NRTIs plus NNRTI, PI, or INSTI.

Eligibility

- Main inclusion criteria
  - HIV-1 RNA < 50 copies/mL on ART containing 2 NRTIs plus either PI, NNRTI, or INSTI
  - Stable on current ART ≥ 6 months
  - No previous virologic failure
  - HLA-B*5701 negative

Switching to TRIUMEQ® (STRIVING)

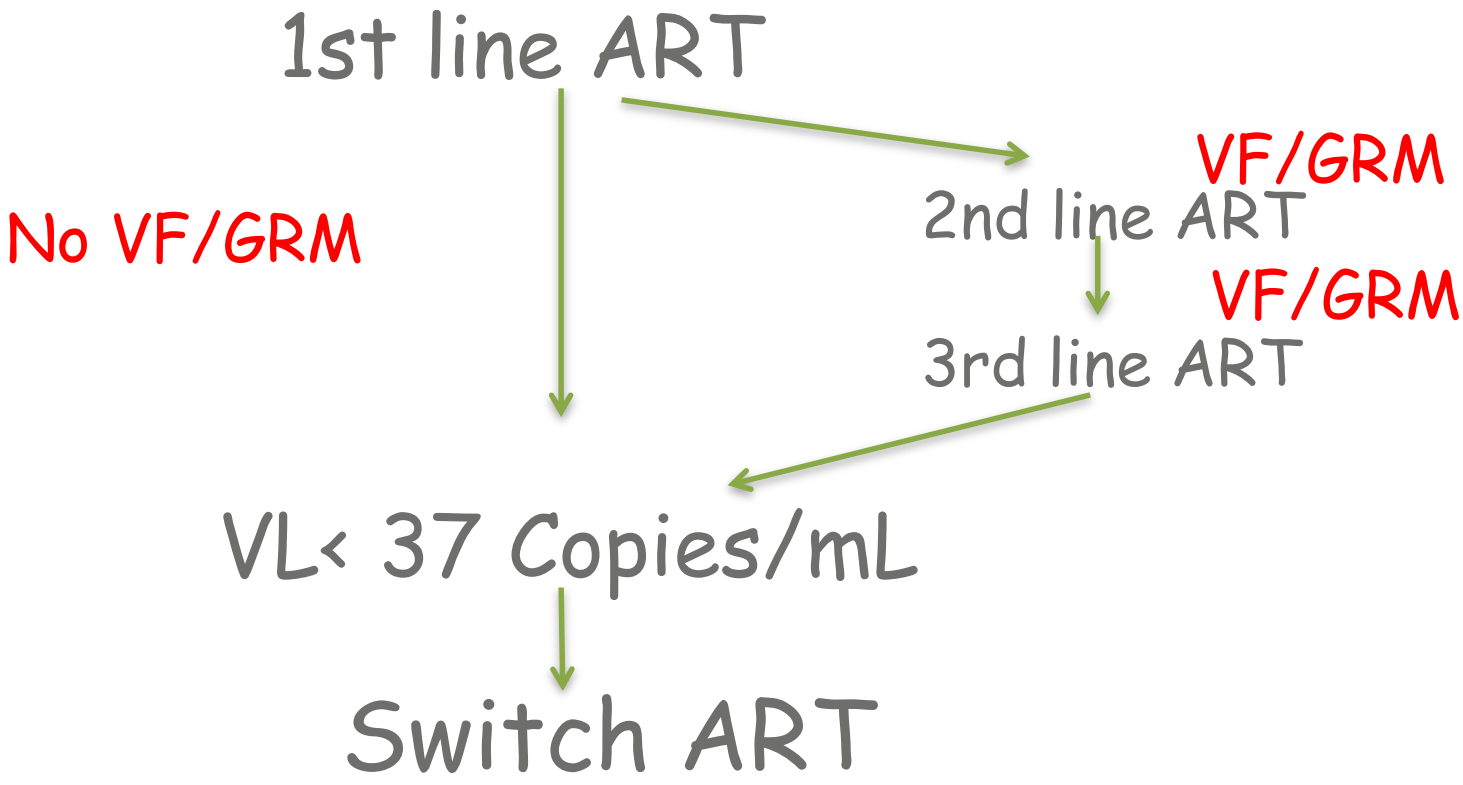


CI, confidence interval; ITT-E, intent-to-treat exposed; PP, per protocol.

Switching to TRIUMEQ® (STRIVING)

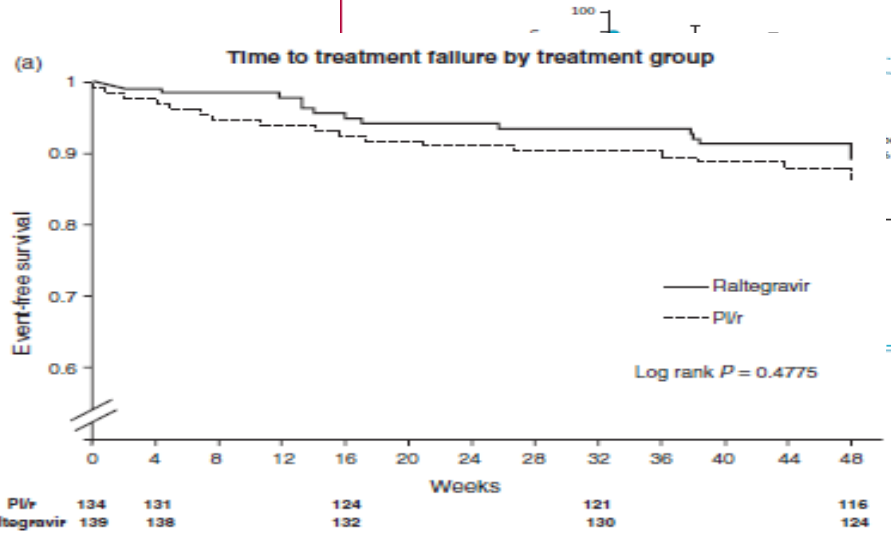
But there were 10 patients in the switch arm vs zero patients in the continuation arm who actually discontinued treatment owing to adverse events. Most of these adverse events were mild, but they still led to discontinuations.

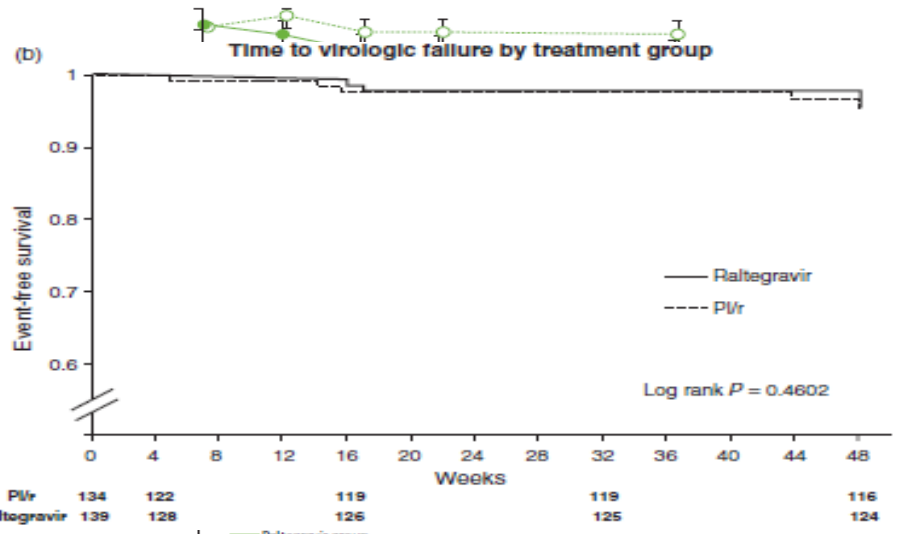
Switch Studies

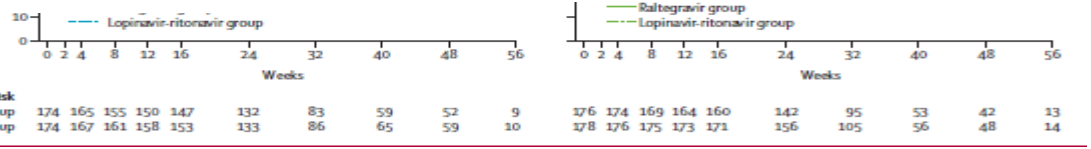


Substitution of raltegravir for ritonavir-boosted protease inhibitors in HIV-infected patients: the SPIRAL study

Esteban Martinez[a,*], María Larrousse[a,*], Josep M. Llibre[b], Felix Gutierrez[c], Maria Saumoy[d], Antonio Antela[e], Hernando Knobel[f], Javier Murillas[g], Juan Berenguer[h], Judit Pich[a], Ignacio Pérez[a], José M. Gatell[a], for the SPIRAL Study Group







Switch Studies

ClinicalTrials.gov

Search for studies: Search

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IMPORTANT: Listing of a study on this site does not reflect endorsement by the National Institutes of Health. Talk with a trusted healthcare professional before volunteering for a study. Read more...

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Home > Find Studies > Search Results > Study Record Detail Text Size

Trial record **1 of 6** for: genvoya and switching

Previous Study | Return to List | Next Study ▸

Switching to Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (E/C/F/TAF) Fixed Dose Combination (FDC) in Virologically-Suppressed HIV-1 Infected Adults Harboring the Archived Isolated NRTI Resistance Mutation M184V/M184I

This study is currently recruiting participants. (see Contacts and Locations)

Verified May 2017 by Gilead Sciences

Sponsor:
Gilead Sciences

Information provided by (Responsible Party):
Gilead Sciences

ClinicalTrials.gov Identifier:
NCT02616029

First received: November 24, 2015
Last updated: May 9, 2017
Last verified: May 2017
History of Changes

Full Text View | Tabular View | No Study Results Posted | Disclaimer | How to Read a Study Record

Purpose

This study will evaluate the efficacy of elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) fixed dose combination (FDC) after **switching** from a stable regimen consisting of emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) or abacavir/lamivudine (ABC/3TC) plus a third antiretroviral agent in participants harboring the archived nucleoside/nucleotide reverse transcriptase inhibitor (NRTI) resistance mutation M184V and/or M184I in HIV-1 reverse transcriptase.

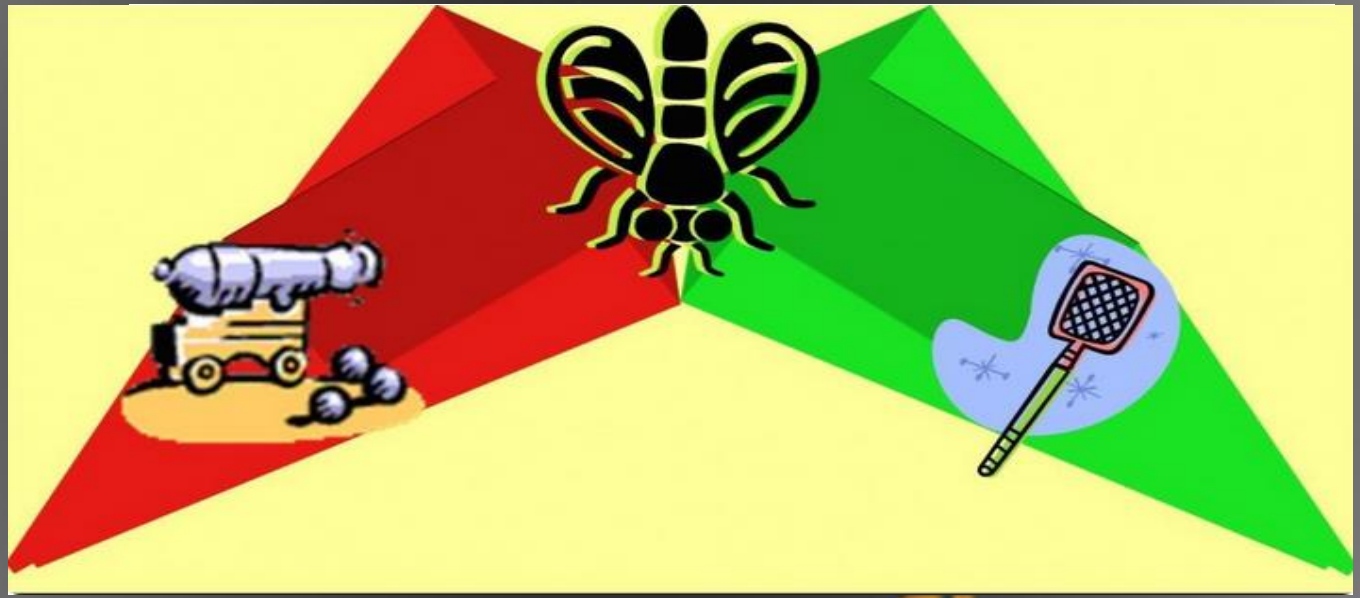
Agenda

- Reasons for choosing STR
- STRs positioning in Guidelines (US/EU vs LATAM)
- STRs in Simplification Strategies
- ART: efficiency
- STRs in Hospital Clinic BCN
- ATR: future positioning
- Conclusions

Efficiency

$$\frac{\text{COST}}{\text{EFFICACY}}$$

eficiencia



eficacia

Messi es el mas eficaz (marca mas goles). Pero,
¿quien es el más eficiente ?

Valoraciones económicas en Futbol

Costes / Resultados = Eficiencia

1.Salario

2.Ficha

3.Incentivos/Primas

4. Vivienda y coche

5.rGH

6. Parte del salario de INIESTA

7.Total

1.Goles

2.Publicidad

3.Imagen

4.Contratos adicionales

5.Total

Courtesy J.M Gatell

Valoraciones económicas en Sanidad/Salud

Costes	/	Resultados	=	Eficiencia
1.Fármacos (PVL+IVA)		1.Eficacia (Ensayos)		
2.Directos: SNS (farmacos, ES, ingresos)		2.Efectividad: (Cohortes)		
3.Indirectos: País (Productividad)		3.Utilidad: (QALY´s)*		
4.Totales		4.Beneficio (Dinero)		
		5.Totales		

Courtesy J.M Gatell

Valoraciones económicas en Sanidad/Salud

Costes	/	Resultados	=	Eficiencia
1.Fármacos (PVL+IVA)		1.Eficacia (Ensayos)		
2.Directos: SNS (farmacos, ES, ingresos)		2.Efectividad: (Cohortes)		
3.Indirectos: País (Productividad)		3.Utilidad: (QALY´s)*		
4.Totales		4.Beneficio (Dinero)		
		5. Totales		

Courtesy J.M Gatell

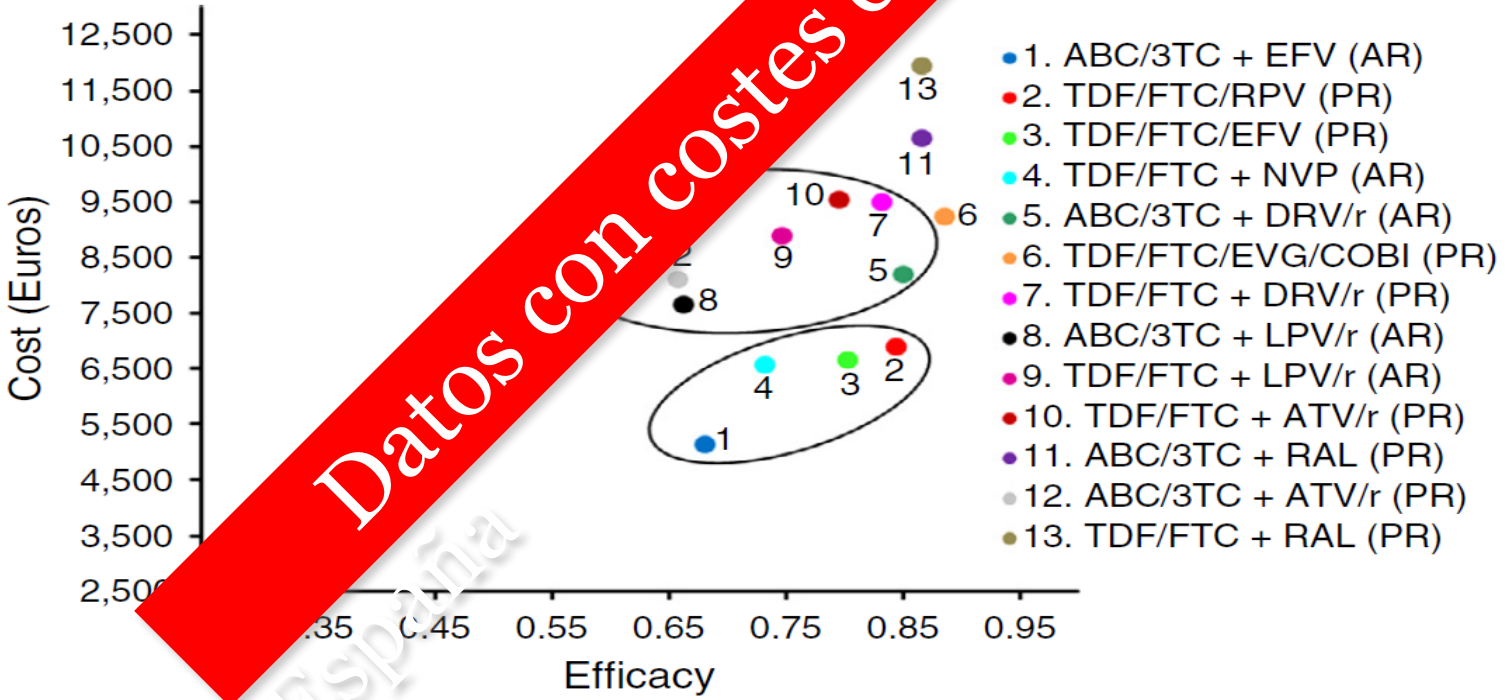
Enfermedades Infecciosas y Microbiología Clínica
www.elsevier.es/eimc

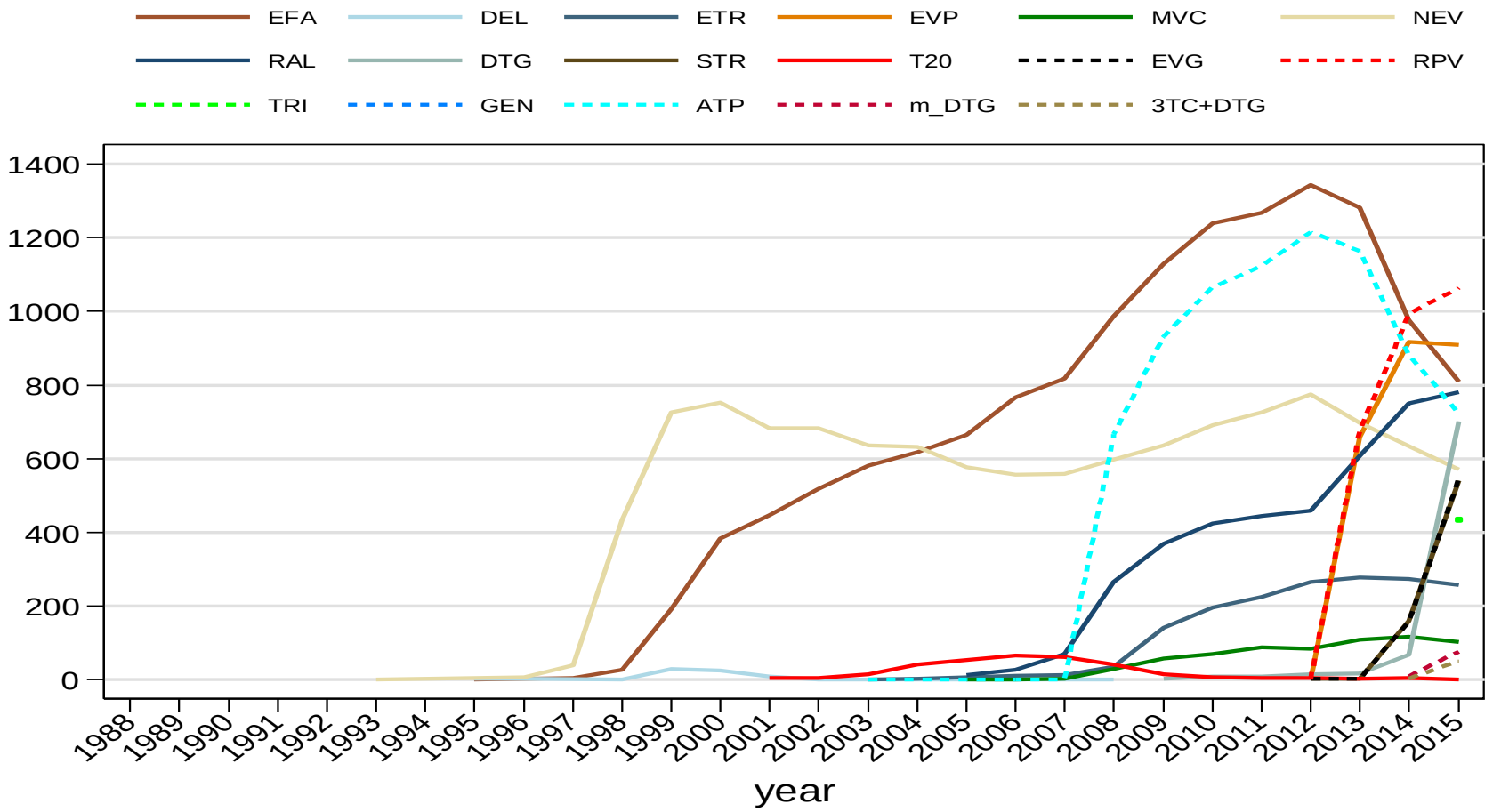
Original article

Costs and cost-efficacy analysis of the 2014 GESIDA/Spar
AIDS Plan recommended guidelines for initial antiretro
in HIV-infected adults

Antonio Javier Blasco[a], Josep M. Llibre[b], Juan Berenguer[c], Juan
, Hernando Knobel[e], Fernando Lozano[f], Daniel Podzamczer[g], Federico Pulido[h], A
ontserrat Tuset[j], Pablo Lázaro[a], Josep M. Gatell[k,*], on behalf of the GESIDA A
udy Group[l]

A




EFA
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NEV
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TRI
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J Antimicrob Chemother 2014; **69**: 1742–1747
doi:10.1093/jac/dku058 Advance Access publication 5 March 2014

Journal of Antimicrobial Chemotherapy

Has the time come to abandon efavirenz for first-line antiretroviral therapy?

Francois Raffi[1]*, Anton L. Pozniak[2] and Mark A. Wainberg[3]

[1]Division of Infectious Diseases, Nantes University Hospital, Nantes, France; [2]HIV Department, Chelsea and Westminster Hospital NHS Foundation Trust, London, UK; [3]Departments of Medicine and of Microbiology, Jewish General Hospital, McGill University, Montreal, Canada

*Corresponding author. Tel: +33-240-083-372; E-mail: francois.raffi@wanadoo.fr

Efavirenz has been recommended as a preferred third agent together with two nucleos(t)ides for first-line combination antiretroviral therapy (ART) for >15 years. The availability of efavirenz in a fixed-dose combination makes it very attractive. However, because of (i) adverse events associated with efavirenz, (ii) a poorer overall efficacy of efavirenz compared with newer antiretrovirals, (iii) the ranking of efavirenz as FDA Pregnancy Category D and (iv) the relatively high prevalence of transmitted drug-resistance mutations, there is a need to reconsider the role of efavirenz in first-line ART. We review the available evidence that challenges efavirenz's current position in first-line HIV treatment guidelines. Apart from its animal teratogenic potential, and moderate neuropsychiatric adverse events associated with its use, efavirenz has recently been associated with an increased risk of suicidality when compared with other antiretroviral drugs. Most importantly, efavirenz has demonstrated overall inferior efficacy to various comparator drugs, which include rilpivirine, raltegravir and dolutegravir, in antiretroviral-naive patients. Furthermore, epidemiological data indicate that the prevalence of non-nucleoside reverse transcriptase inhibitor resistance has reached 5%–8% in various parts of the world, and minority transmitted non-nucleoside reverse transcriptase inhibitor resistance-associated mutations can have a negative impact on the outcome of first-line efavirenz-based ART. Based on considerations of efficacy, toxicity and resistance, it is time to reconsider the routine use of efavirenz in ART. This, of course, presupposes that other antiretrovirals will be available in place of efavirenz, and may not be applicable in certain developing country settings where this is not the case.

Published in final edited form as:
Ann Intern Med. 2014 July 1; 161(1): 1–10. doi:10.7326/M14-0293.

Association between Efavirenz as Initial Therapy for HIV-1 Infection and Increased Risk of Suicidal Ideation, Attempted, or Completed Suicide

Katie R. Mollan, M.S.[1,2], **Marlene Smurzynski, Ph.D.**[1,3], **Joseph J. Eron, M.D.**[2], **Eric S. Daar, M.D.**[4], **Thomas B. Campbell, M.D.**[5], **Paul E. Sax, M.D.**[6], **Roy M. Gulick, M.D.**[7], **Lumine Na, M.S.**[1], **Lauren O'Keefe, B.S.**[1], **Kevin R. Robertson, Ph.D.**[2], and **Camlin Tierney, Ph.D.**[1]

Abstracts of the HIV Drug Therapy Glasgow Congress 2014
Smith C et al. *Journal of the International AIDS Society* 2014, **17(Suppl 3)**:19512
http://www.jiasociety.org/index.php/jias/article/view/19512 | http://dx.doi.org/10.7448/IAS.17.4.19512

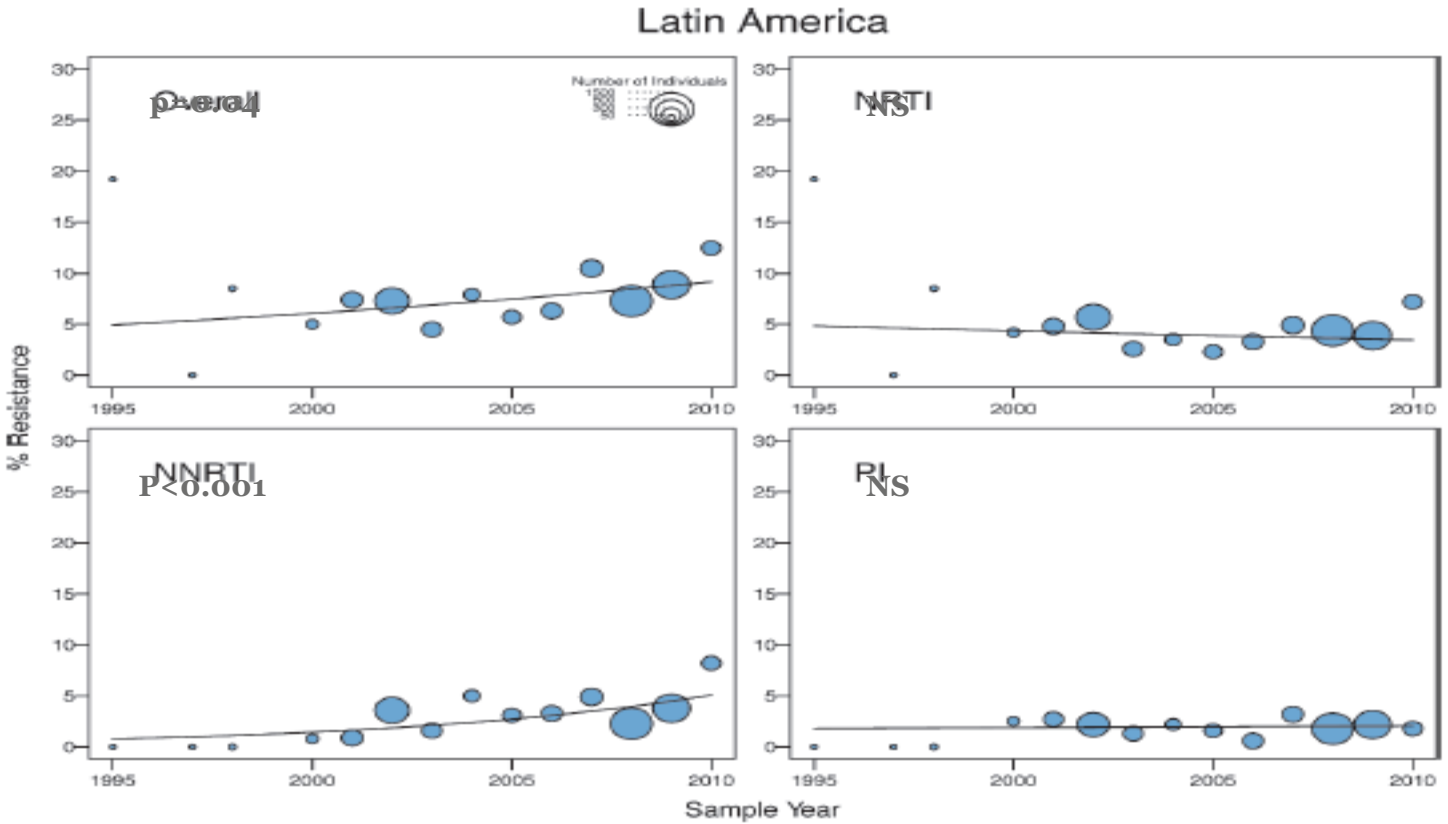
JIAS Journal of the International AIDS Society

Oral Presentation — Abstract O315

Lack of association between use of efavirenz and death from suicide: evidence from the D:A:D study

Smith, Colette[1]; Ryom, Lene[2]; d'Arminio Monforte, Antonella[3]; Reiss, Peter[4]; Mocroft, Amanda[1]; El-Sadr, Wafaa[5]; Weber, Rainer[6]; Law, Matthew[7]; Sabin, Caroline[1] and Lundgren, Jens[2]

Increasing trend in the yearly proportion of individuals with NNRTI TDR in LA



Rhee SY, Blanco JL et al., PLoS Med 2015

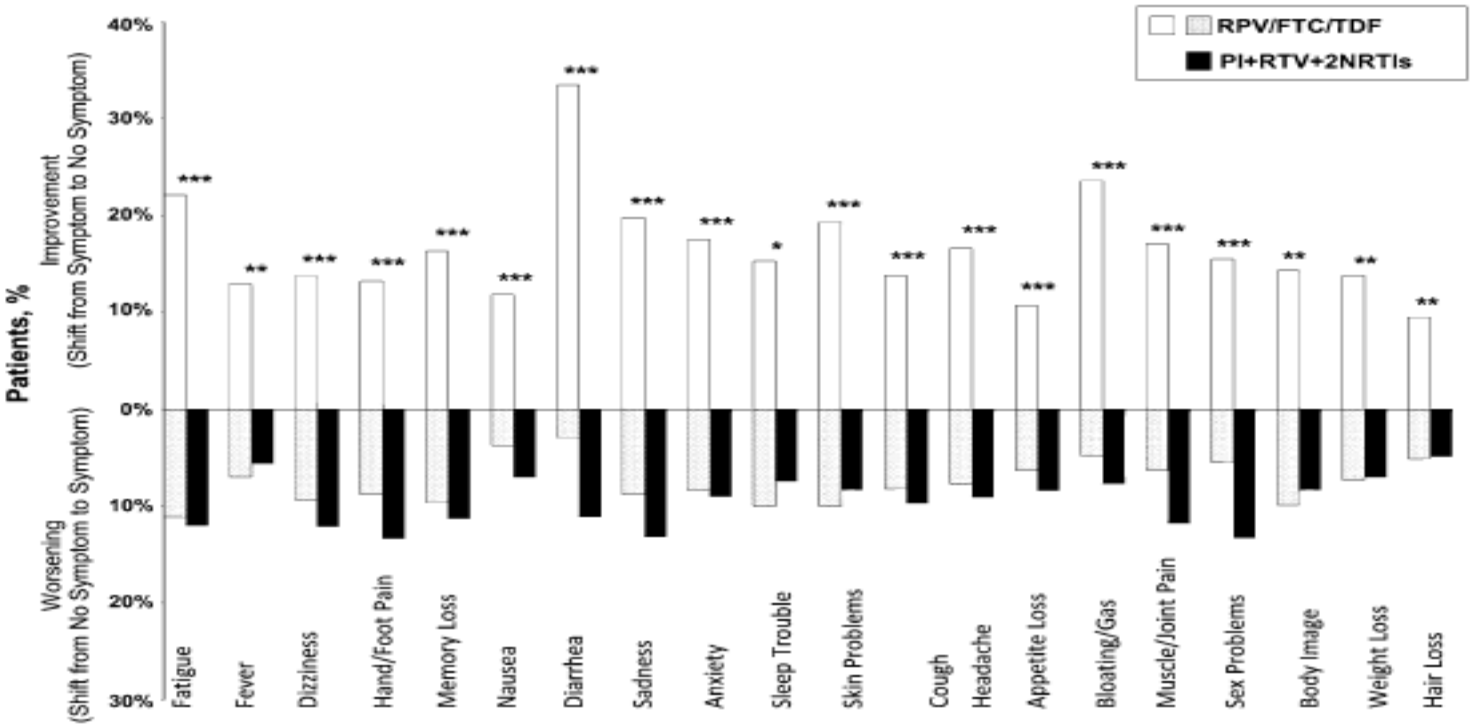
Conclusiones

- Los esquemas en STR, además de recomendados por WHO y soportados por la lógica, han DEMOSTRADO favorecer adherencia, ser preferidos por los pacientes y mejorar su calidad de vida y seleccionar menos resistencias.
- La mayoría de los regimes preferentes en las guías "occidentales" son STR.
- Hasta la fecha la única pauta que ha demostrado SUPERIORIDAD en la estrategia de switch/simplficación es la de STRIBILD®
- La eficiencia mejor que el coste debería ser una variable más a la hora de decidir la pauta de inicio de TARV
- EFV: una decisión personal

Gracias !

Patient-Reported Outcomes After a Switch to a Single-Tablet Regimen of Rilpivirine, Emtricitabine, and Tenofovir DF in HIV-1-Positive, Virologically Suppressed Individuals: Additional Findings From a Randomized, Open-Label, 48-Week Trial

Table 4 HIV Treatment Satisfaction Questionnaire[a] total score

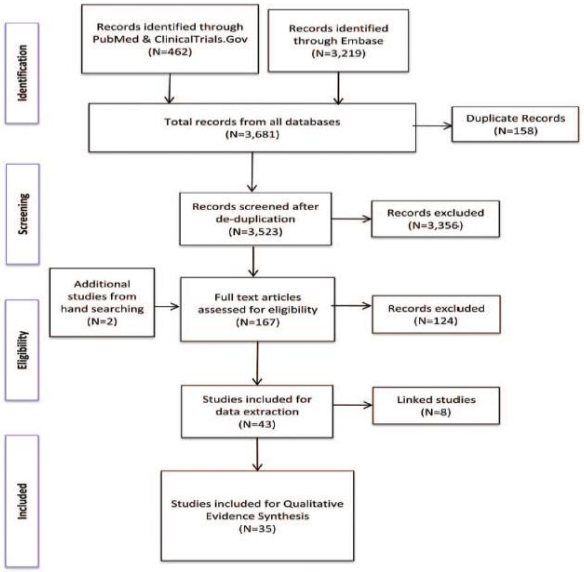


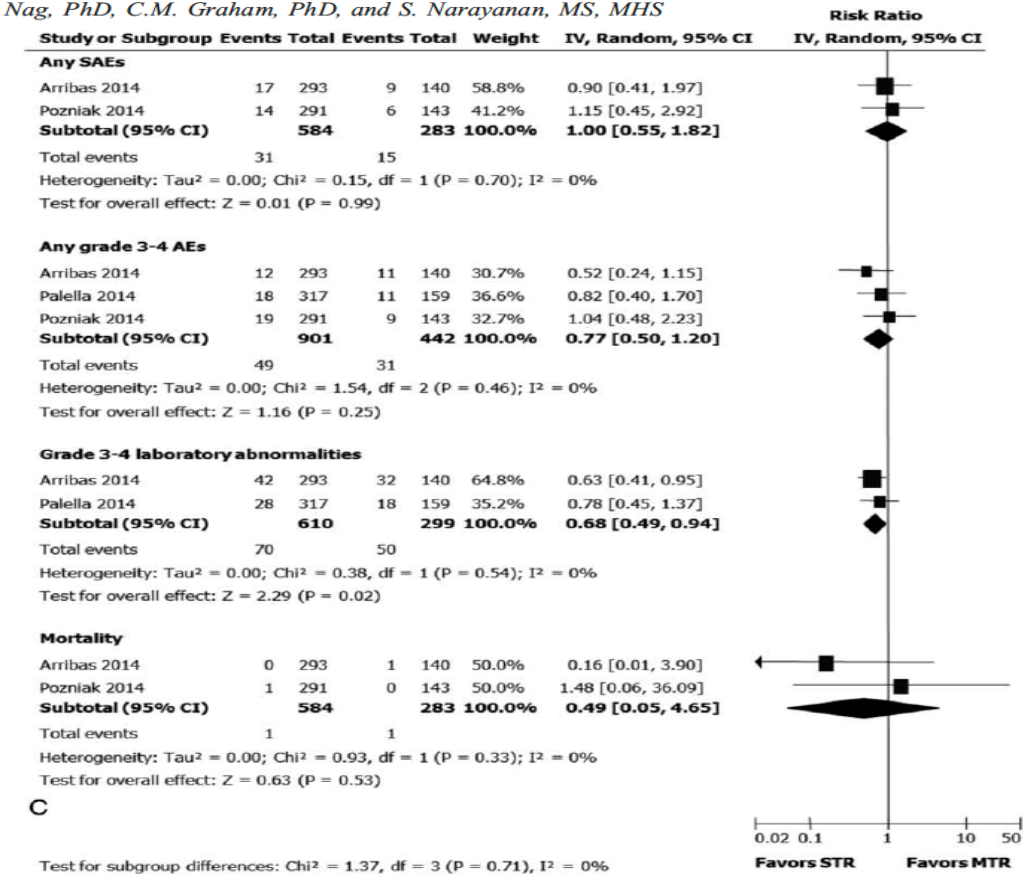
Bruneta et al. Patient 2015

OPEN

Meta-Analysis of Studies Comparing Single and Multi-Tablet Fixed Dose Combination HIV Treatment Regimens

P.G. Clay, PharmD, S. Nag, PhD, C.M. Graham, PhD, and S. Narayanan, MS, MHS





BMJ, 2013

B: Quality of Observational Studies Included in Quantitative Evidence Synthesis (Meta-Analysis)

CASP Section	Question	Fabbiani et al[43]	Skwara et al[59]	Buscher et al[9]	Bangsberg et al[14]	Sterrantino et al[60]
Are the results of the study valid?	Did the study address a clearly focused issue?	Yes	Yes	Yes	Yes	Yes
	Was the cohort recruited in an acceptable way?	Yes	Cannot tell	Yes	Yes	No
	Was the exposure accurately measured to minimize bias?	Yes	Yes	Yes	Cannot tell	Yes
	Was the outcome accurately measured to minimize bias?	Yes	No	Yes	Yes	No
	Have the authors identified all important confounding factors?	Yes	No	Yes	Cannot tell	Yes
	Have they taken account of the confounding factors in the design and/or analysis?	Yes	Cannot tell	Yes	Yes	No
	Was the follow up of subjects complete enough?	Yes	Yes	Yes	Cannot tell	Cannot tell
	Was the follow up of subjects long enough?	Yes	Yes	Yes	Yes	Cannot tell
What are the results?	What are the results of this study?	STR found to be associated with higher adherence, lower virological failure and low CNS toxicity compared to MTR	STR was associated with improved adherence, quality of life and efficacy compared to MTR	STR showed better adherence compared to MTR (twice daily) in both overall and ART naive population. However, the difference was not significant for STR vs MTR (>1 pill regimen) for all population	One-pill per day STR was associated with good adherence and viral suppression in a challenging population	Nonadherence was lower in the STR as compared to multi-tablet regimen
	How precise are the results?	Results appear precise as confidence intervals were not so wide	Results were not presented with the variance	The study findings were precise as inter quartile ranges were found to be narrow	Precision was unclear as study did not report results with the confidence intervals	The study results were precise enough
	Do you believe the results?	Cannot tell; uncontrolled bias can occur in the retrospective studies	Cannot tell	Yes	Yes	Yes
Will the results help locally?	Can the results be applied to the local population?	Yes	Yes	Yes	Yes	No
	Do the results of this study fit with other available evidence?	Yes	Yes	No	Yes	Yes
	What are the implications of this study for practice?	There was difference in baseline characteristics between the treatment groups so the results should be considered cautiously	The results should be considered cautiously as the treatment duration was longer in patients using multi-tablet regimens	The study results could not be generalized as patients, who did not receive HAART during the study, died or was not followed up	Simplification of therapy represents an important step forward in supporting adherence and treatment success	The study overestimates the adherence, as patients were on steady cART; also self reporting may overestimate the level of adherence
	Overall quality	Medium	Satisfactory	Medium	Satisfactory	Satisfactory

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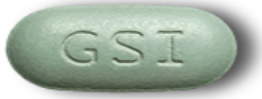
STRs

	EFV TDF/FTC	RPV TDF/FTC	EVG/COBI TDF/FTC	DTG * ABC/3TC
N pills/day				
Posology	QD	QD	QD	QD
Take with food	±	Sí	Sí	±

Package insert: Isentress, Stribild, Tivicay