ASOCIACIÓN RIS

JORNADAS DOCENTES RIS

"**VIH/Sida en 2022: avances en ciencia básica y clínica**"

Coordinación: Santiago Moreno, Félix Gutiérrez y Pepe Alcamí

4 Octubre

"Avances en tratamiento antirretroviral y PrEP"

Moderador: Santiago Moreno

17:00 horas

"Presente y futuro del TAR: el camino desde el STR a las pautas long-acting"
Dr. Álvaro Mena. C.H.U. A Coruña

"Revisando críticamente la evidencia: beneficios del inicio muy precoz y del tratamiento rápido"
Dr. Carlos Galera. Hospital Virgen de la Arrixaca, Murcia

"PrEP: nuevos datos, guías de práctica clínica e implementación en España"
Dr. Juan Emilio Losa. Hospital de Alcorcón, Madrid

Sesiones virtuales

redris.es/actividades

RIS Red Española de Investigación en Sida

UNIÓN EUROPEA

ELX DEPARTAMENT DE SALUT

UNIVERSITAS Miguel Hernández

MSD

UNITS
UNIDAD DE INFECCIONES
DE TRANSMISIÓN SEXUAL

Revisando críticamente la evidencia: beneficios del inicio muy precoz y del tratamiento rápido

Carlos Galera Peñaranda

Hospital Universitario Virgen de la Arrixaca

Jornadas Docentes RIS 2022

Esquema

- Fundamentos del inicio precoz
- Beneficios esperados
- Evidencias: Ensayos y estudios de cohortes
- Precauciones ante el inicio rápido
- Guías clínicas
- Pautas recomendadas y evidencias
- Conclusiones

Fundamentos

Beneficio clínico del inicio precoz del TAR

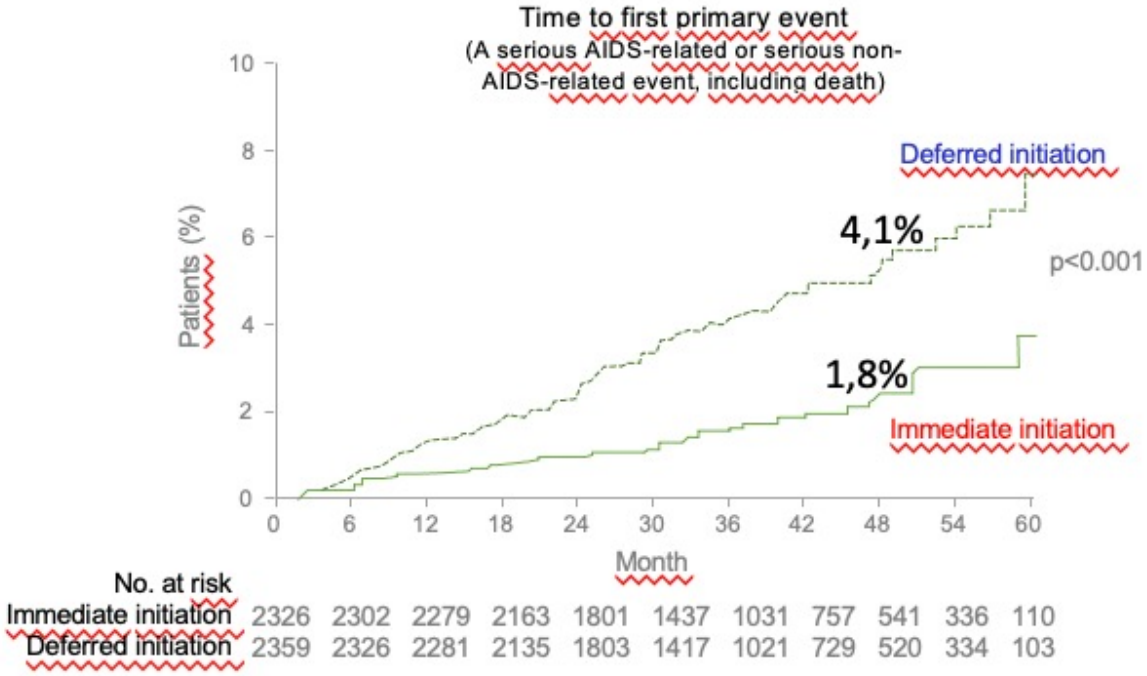
Estudio START[1]
Estudio TEMPRANO[2]

1.INSIGHT START Study Group. Lundgren JD et al. Initiation of anti- retroviral therapy in early asymptomatic HIV infection. N Engl J Med 2015; 373:795–807.
2.TEMPRANO ANRS 12136 Study Group. Danel C et al. A trial of early antiretrovirals and isoniazid preventive therapy in Africa. N Engl J Med 2015; 373:808–822.

Fundamentos

Beneficio clínico del inicio precoz del TAR

Estudio START



1.INSIGHT START Study Group. Lundgren JD et al. Initiation of anti- retroviral therapy in early asymptomatic HIV infection. N Engl J Med 2015; 373:795–807.

Fundamentos

Beneficio comunitario del inicio precoz del TAR: " Treatment as Prevention"

Estudio HTPN 052 [1]
Estudio PARTNER [2]

1.Cohen MS, Chen YQ, McCauley M, et al. Antiretroviral therapy for the prevention of HIV-1 transmission. N Engl J Med 2016; 375:830-9.

2. Rodger AJ, Cambiano V, Bruun T, et al. ; PARTNER Study Group. Sexual activity without condoms and risk of HIV transmission in serodifferent couples when the HIV-positive partner is using suppressive antiretroviral therapy. JAMA. 2016; 316:171–81.

Fundamentos.

U=U

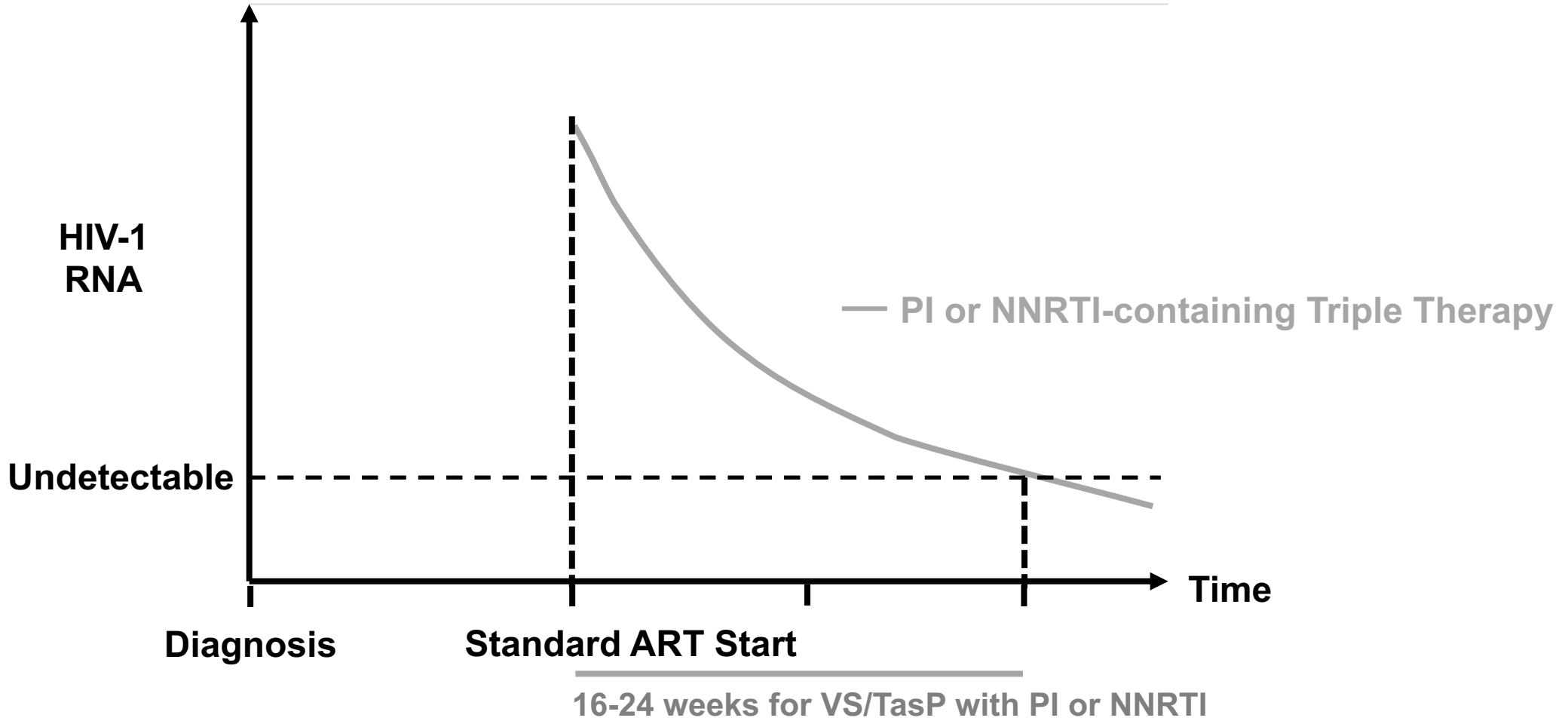
El hecho de alcanzar y mantener una CV < 200 cop/ml con el TAR , previene su trasmisión a través del sexo

Al inicio del TAR se recomienda el uso de preservativos durante 6 meses y hasta comprobar CV < 200 cop/ml

Hay que mantener la adherencia al TAR para mantener la CV indetectable

Prevention Access Campaign. Undetectable = Untransmittable (U = U). http://www.preventionaccess.org.

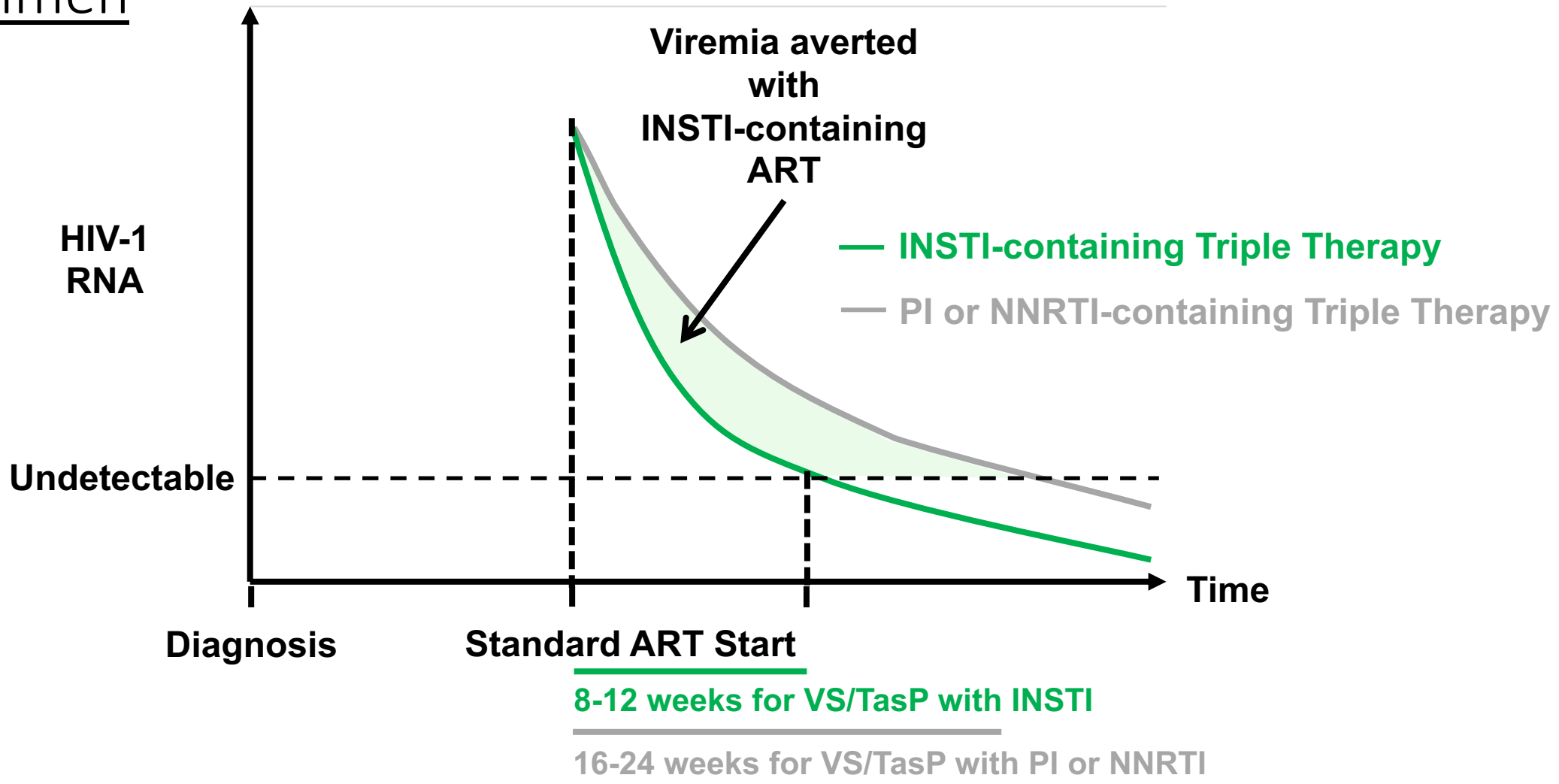
Conceptualized Viral Decay with Standard ART Start



VS, Viral Suppression; TasP, Treatment as Prevention.

Graphics conceptualized based on virologic suppression rates from the following clinical trials: Gallant J, et al. Lancet 2017;390:2063-72; Sax P, et al. Lancet 2017;390:2073-82; Pilcher CD, et al. JAIDS 2017;74(1):44-51; Sax PE. et al. Lancet 2012; 379: 2439–48; DeJesus E. et al. Lancet 2012; 379:2429–38; BoydMA, et al. HIVMed 2019;20(1):3-11.

Conceptualized Epidemiological Consequences of ART Initiation in Standard Time with or without an INSTI-Containing Regimen



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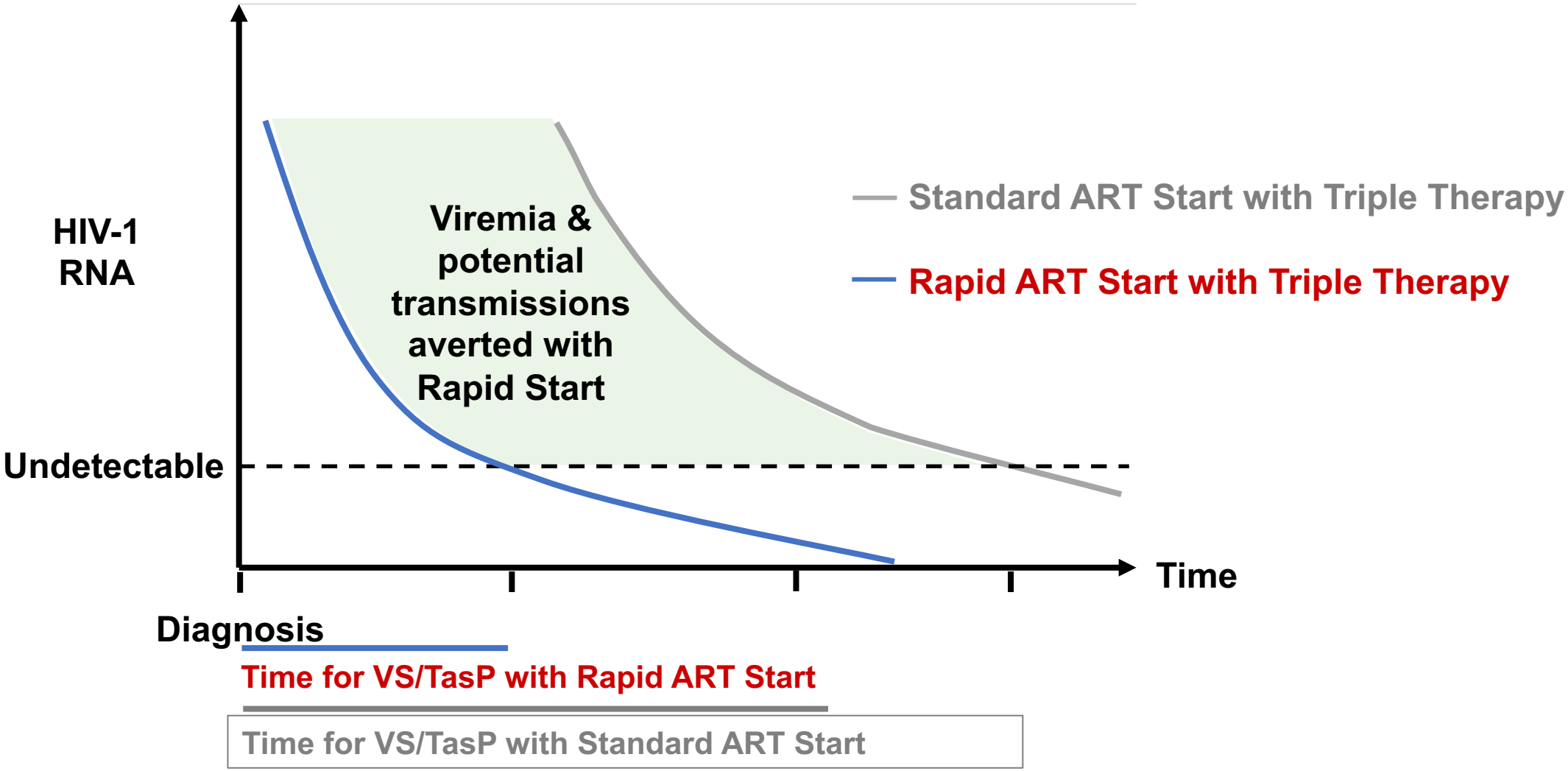
Conceptualized Epidemiological Consequences of ART Initiation in Rapid Start Time



VS, Viral Suppression; TasP, Treatment as Prevention.

Graphics conceptualized based on virologic suppression rates from the following clinical trials: Gallant J, et al. Lancet 2017;390:2063-72; Sax P, et al. Lancet 2017;390:2073-82; Pilcher CD, et al. JAIDS 2017;74(1):44-51; Sax PE. et al. Lancet 2012; 379: 2439–48; DeJesus E. et al. Lancet 2012; 379:2429–38; BoydMA, et al. HIVMed 2019;20(1):3-11.; Veil R, et al. AIDS 2019. epub; Girometti, N et al. EACS 2019. Basel, Switzerland. PE33/4

Beneficios

Para el paciente:

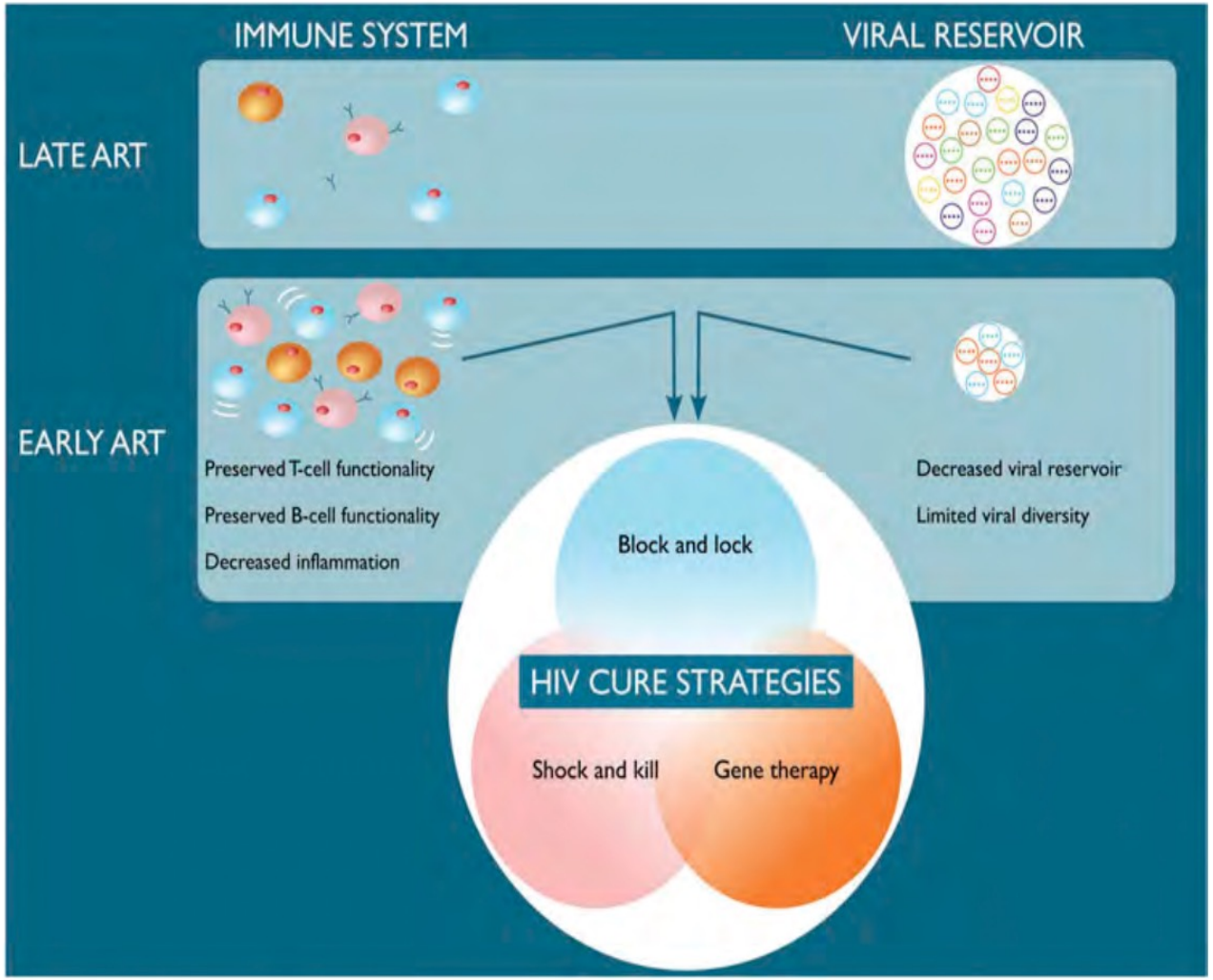
- Reducción del tiempo hasta la supresión viral
- Mayor opción de recuperación inmune
- Reducción del riesgo de Infecciones oportunistas/mortalidad
- Mejora la retención en cuidados
- Reducción de la ansiedad, mejora de la confianza

Para la sociedad:

- Disminuye la trasmisión del VIH
- Disminuye el coste asociado a la morbimortalidad

Beneficios adicionales

- **<u>En el contexto de la Infección aguda</u>** por el VIH, disminuye la diseminación viral→ disminuye el tamaño del reservorio del VIH y preserva un reservorio viral homogéneo con pocas mutaciones de escape[1,2]
- El tratamiento durante la infección aguda , permite un escenario mas favorable para intentar las estrategias de curación de la enfermedad [3]



1.Strain MC, et al. *J Infect Dis*. 2005;191(9):1410–1418.
2. Lee GQ, et al.. *Nat Commun*. 2019;10(1):2737.
3. De Clerq Jet al. Acta Clinica Belgica

Beneficios adicionales

- Revierte parcialmente los biomarcadores epigenéticos de envejecimiento acelerado, y por tanto el riesgo de comorbilidades [4]
- Mejora de los procesos inflamatorios cerebrales asociados a la infección por el VIH [5]

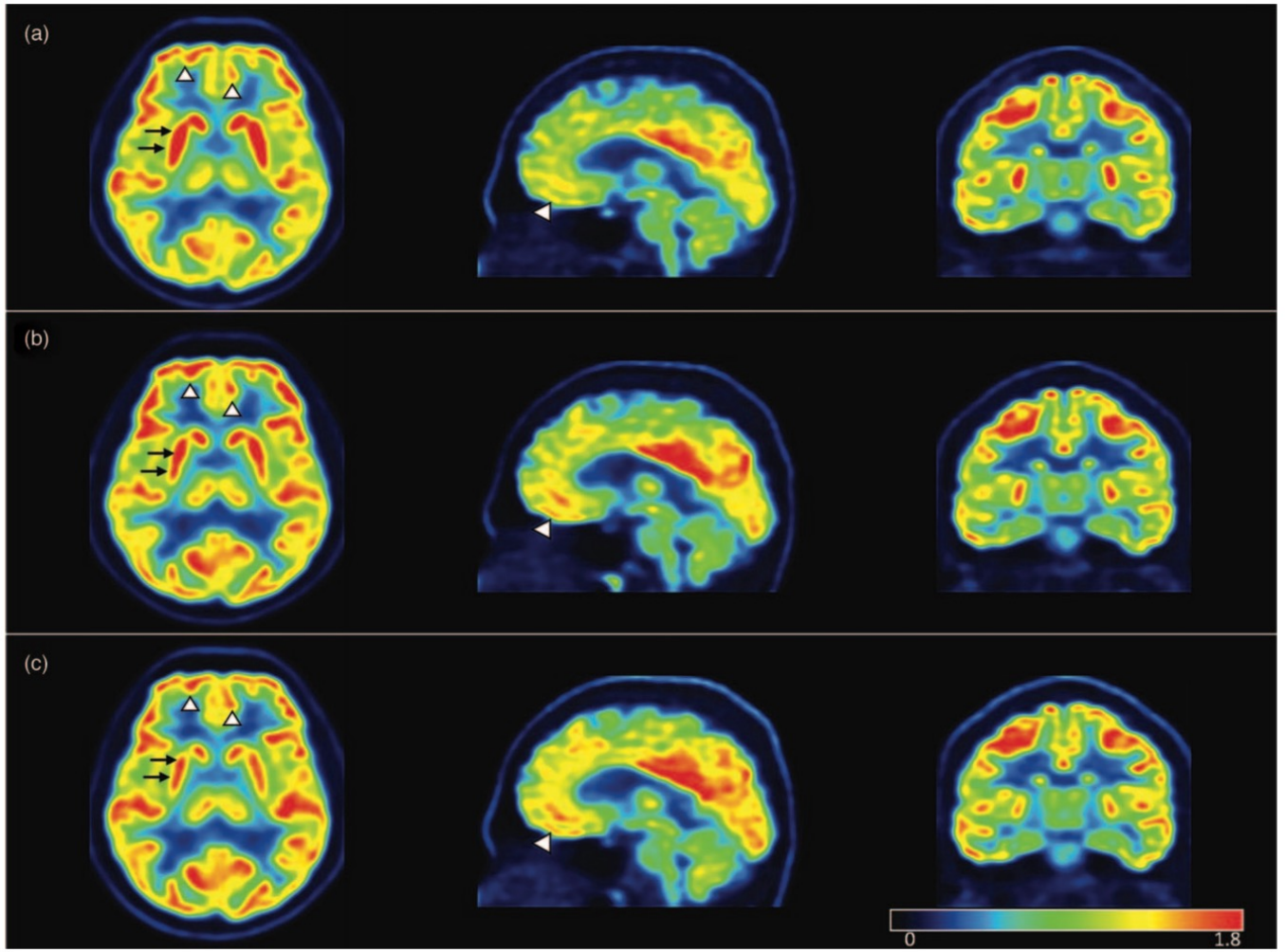


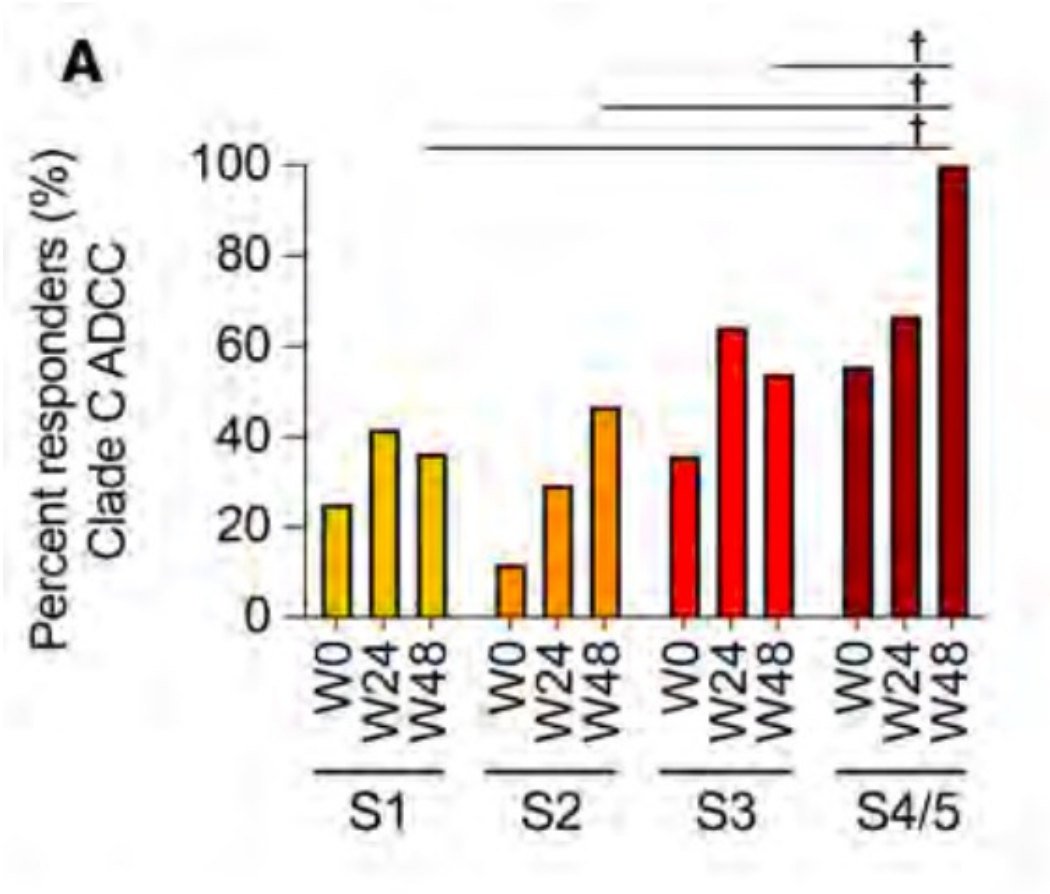
Fig. 5. Relative standardized uptake value parametric maps in one participant at (a) baseline, (b) short-term follow-up and (c) long-term follow-up. Axial, sagittal and coronal maps showing visually detectable decreasing putaminal (black arrows) and increasing cortical uptake (arrowheads) after initiation of ART.

4. Esteban Cantos A. *Lancet HIV* 2021; 8: e197–205
5. Wang Z et al. AIDS 2021; 35: 1209-1219

Anti-HIV antibody development up to 1 year after antiretroviral therapy initiation in acute HIV infection

Table 1. Fiebig stages of acute HIV-1 infection[8]

Fiebig stage	HIV RNA	P24 antigen	Antibody	Western blot
I	+	-	-	-
II	+	+	-	-
III	+	+	+	-
IV	+	±	+	indeterminate
V	+	±	+	+, without p31 band
VI	+	±	+	+



Ac mediados por la citotoxicidad celular(ADCC)

FiebigEW. AIDS.2003;17(13):1871–1879.

Mitchell JL et al. *J Clin Invest*. 2022;132(1):e150937. https://doi.org/10.1172/JCI150937.

Situaciones con claro beneficio del inicio rápido del TAR

- Infección aguda por el VIH
- Pacientes con mayor deterioro inmunológico y/o con enfermedades oportunistas y/o cáncer
- Mujeres embarazadas¿?

¿Como de rápido debe iniciarse el TAR?

- Same Day ART(SDA) o Immediate ART: El tratamiento se inicia el mismo día del diagnóstico o de la primera visita.
- RAPID ART: EL tratamiento se comienza en los 7 primeros días desde el diagnóstico o de la primera visita.

Fundamentos/ Beneficios/Evidencias/Guías/Pautas Conclusiones

Evidencias del Inicio rápido: SDT , Rapid Tr vs Standard

A favor

- Pilcher C, et al. JAIDS 2017;74:44-51
- Coffey S, Bacchetti P, Sachdev D, et al. RAPID antiretroviral therapy: high virologic suppression rates with immediate antiretroviral therapy initiation in a vulnerable urban clinic population. *AIDS*. 2019;33(5):825-832. doi:10.1097/QAD.0000000000002124
- Labhardt ND, Ringera I, Lejone TI et al Effect of offering same-day ART vs usual health facility referral during home-based HIV testing on linkage to care and viral suppression among adults with HIV in Lesotho: the CASCADE Randomized Clinical Trial. JAMA 2018; 319:1103–1112
- Seybolt L, Conner K, Butler I, VanSickels N, Halperin J. Rapid start lead to sustained viral suppression in young people in the South [Abstract 1073] in special issue: Abstracts From the 2020 Conference on Retroviruses and Opportunistic Infections. *Top Antivir Med*. 2020;28(1):407.
- Colasanti J, Sumitani J, Mehta CC, et al. Implementation of a rapid entry program decreases time to viral suppression among vulnerable persons living with HIV in the Southern United States. *Open Forum Infect Dis*. 2018;5(6):ofy104. doi:10.1093/ ofid/ofy104

En contra

- Cuzin L, Cotte L, Delpierre C, et al; Dat'AIDS study group. Too fast to stay on track? shorter time to first anti-retroviral regimen is not associated with better retention in care in the French Dat'AIDS cohort. *PLoS One*. 2019;14(9):e0222067. doi:10.1371/journal.pone.0222067

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- AmstutzA,BrownJA,RingeraI,etal. Engagement in care, viral suppression, drug resistance and reasons for non-engagement after home-based same-day ART initiation in Lesotho: a two-year follow-up of the CASCADE trial. *Clin Infec Dis*. doi:10.1093/cid/ciz1126 Published online November 29, 2019.
- Ross J,Brazier E,Fatti G et al. Same day ART initiation as a predictor of loss to follow up and viral suppression among people living with HIV in sub-Saharan Africa. Clin Inf Dis 2022.ciac 759

C Galera

Evidencias

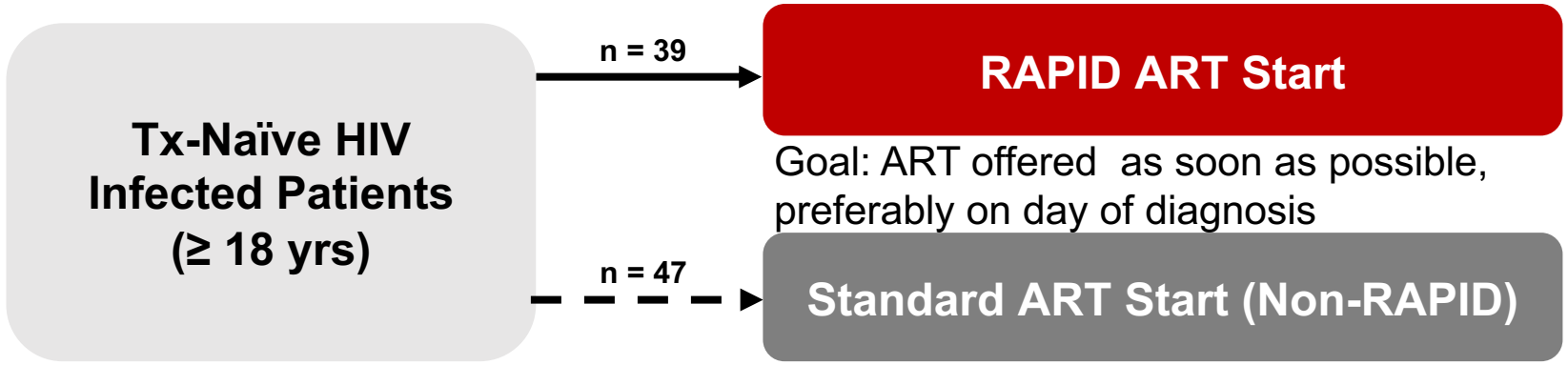
Study	Location	Increased % Starting ART	Shorter Time to VS	Increased Rate of VS	Increased Linkage to/ Retention in Care	Decreased Mortality
RAPID[1-3]	San Francisco		X		X	
Test and Treat[4]	Miami		X		X	
REACH[5]	Atlanta		X			
CrescentCare[6]	New Orleans		X			
JumpstART[7]	New York City	X				
Project RHAE[8]	Baltimore		X	X		
PHARM-D RAPID[9]	Rhode Island		X			

1. Pilcher C, et al. JAIDS 2017;74:44-51
2. Bacon O, et al. CROI 2018. Boston, MA. Oral 93
3. Christopoulos KA, et al . AIDS 2020. PEB0267
4. Poschman K, et al . CROI 2019. Seattle, WA. 903
5. Colasanti J, et al. Open Forum Infectious Diseases. 28JUN2018
6. Halperin J, et al. AIDS Pt Care STDs 2018;32:39-41
7. Blank S, et al. CROI 2018. Boston, MA. 1108
8. Jones et al. CROI 2019. Seattle, WA. P514
9. Brotherton A, et al. CROI 2020. Boston, MA. 498

San Francisco General Hospital RAPID Program – Rapid ART Program for Individuals with an HIV Diagnosis

Study Design and Baseline Characteristics

Single-center cohort study between 2013 – 2014 combined with retrospective historical control



Exclusion:
- Diagnosis > 6 months prior

- **Primary Analysis (intervention vs. no intervention)**
  - Time to viral suppression (<200 copies/mL)
  - Time to first clinic visit, first PCP visit, and ART initiation
- **Secondary Analysis (pre-intervention/post-intervention)**
  - Time to viral suppression (<200 copies/mL)

Characteristics	RAPID N=39	Non-RAPID N=47	P-value
Age, mean (range)	31.6 (21-47)	34.8 (19-68)	0.14
Race/ethnicity, n (%)			0.034
Black	2 (5.1)	12 (25.5)	
Latino	18 (46.2)	15 (31.9)	
Male, n (%)	39 (100)	44 (93.6)	0.11
Major mental health disorder, n (%)	21 (53.9)	15 (31.9)	0.04
Homeless/unknown, n (%)	14 (35.9)	16 (34.1)	0.97
Illicit substance use, n (%)	18 (46.2)	18 (38.3)	0.75

92% reported not having a primary care provider at the time of referral

Pilcher C, et al. JAIDS 2017;74:44-51

San Francisco General Hospital RAPID Program – Rapid ART Program for Individuals with an HIV Diagnosis

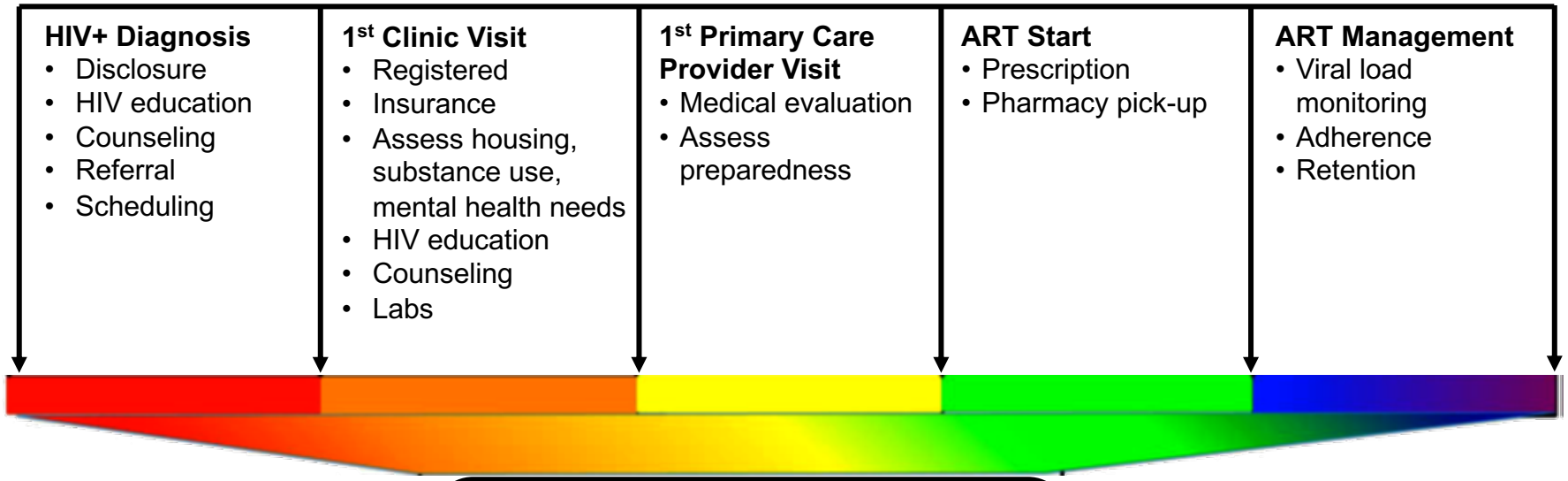
RAPID Program Interventions

- Same day access to an HIV provider
- Same day medical visit including:
  - HIV education, risk reduction, sexual health and benefits of ART
  - Possible contraindications of ART discussed
  - Baseline laboratory tests drawn but not typically available prior to ART start
    - Included: CD4 cell count, HIV viral load, renal and liver function tests, hepatitis serologies, HLA B*5701 testing, HIV resistance genotyping
- Accelerated insurance approval process
- Preapproved ART regimens
- Five day starter packs were available if needed
- Directly observed administration of first dose
- Telephone follow-up by RAPID nurses within the first 7 days

Pilcher C, et al. JAIDS 2017;74:44-51

San Francisco General Hospital RAPID Program – Rapid ART Program for Individuals with an HIV Diagnosis

Standard vs. RAPID Models



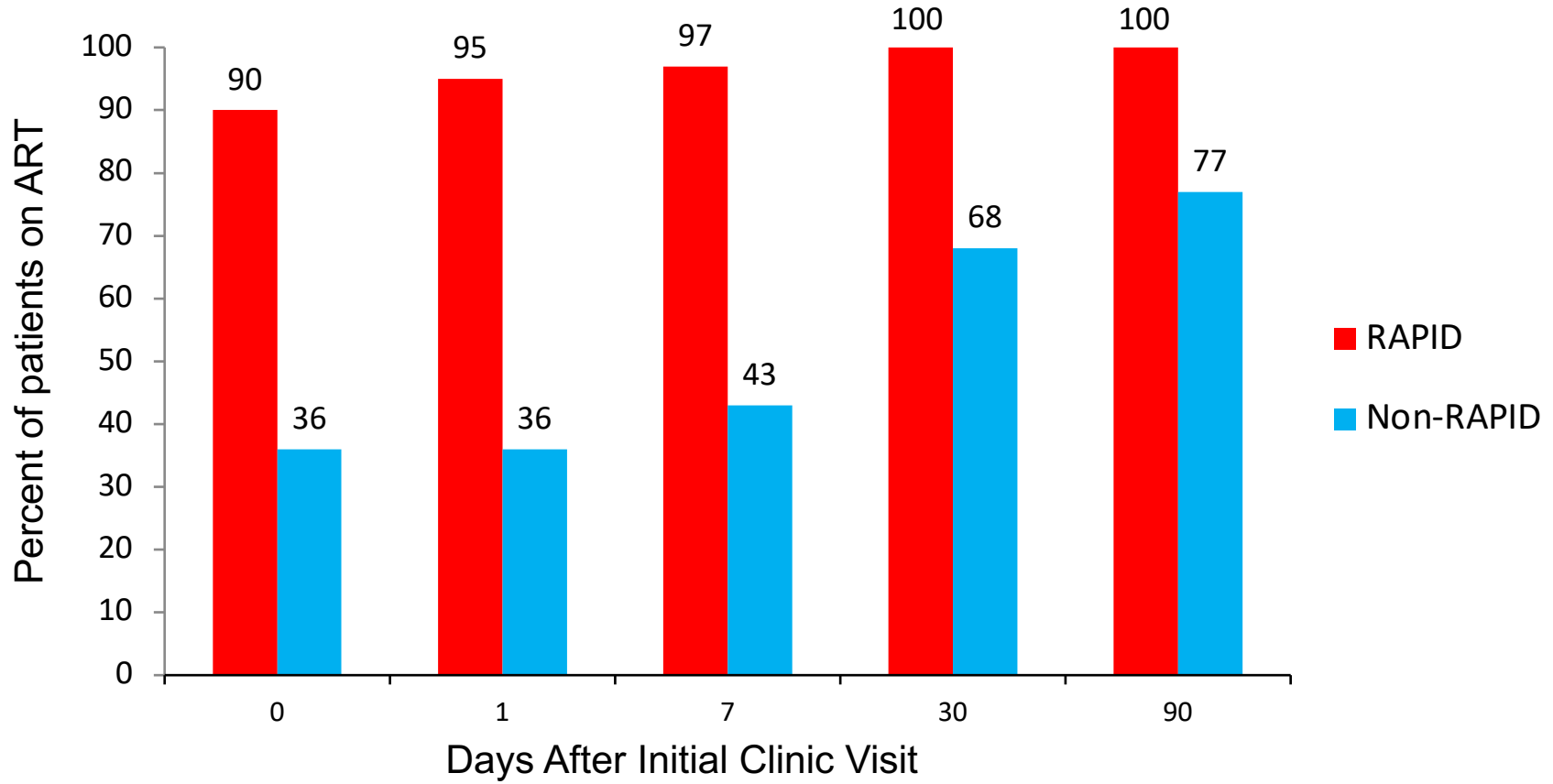
RAPID Visit: ART Start
- Disclosure, counseling
- Registration
- Insurance
- Assess housing, substance use, mental health needs
- Labs
- HIV education
- Counseling
- Medical evaluation
- Assess preparedness
- ART dispensed
- Telephone follow-up

Primary Care Provider Visits: ART Management
- Viral load monitoring
- ART management
- Adherence
- Retention

Pilcher C, et al. JAIDS 2017;74:44-51

San Francisco General Hospital RAPID Program – Rapid ART Program for Individuals with an HIV Diagnosis

Results – Uptake of ART after Diagnosis

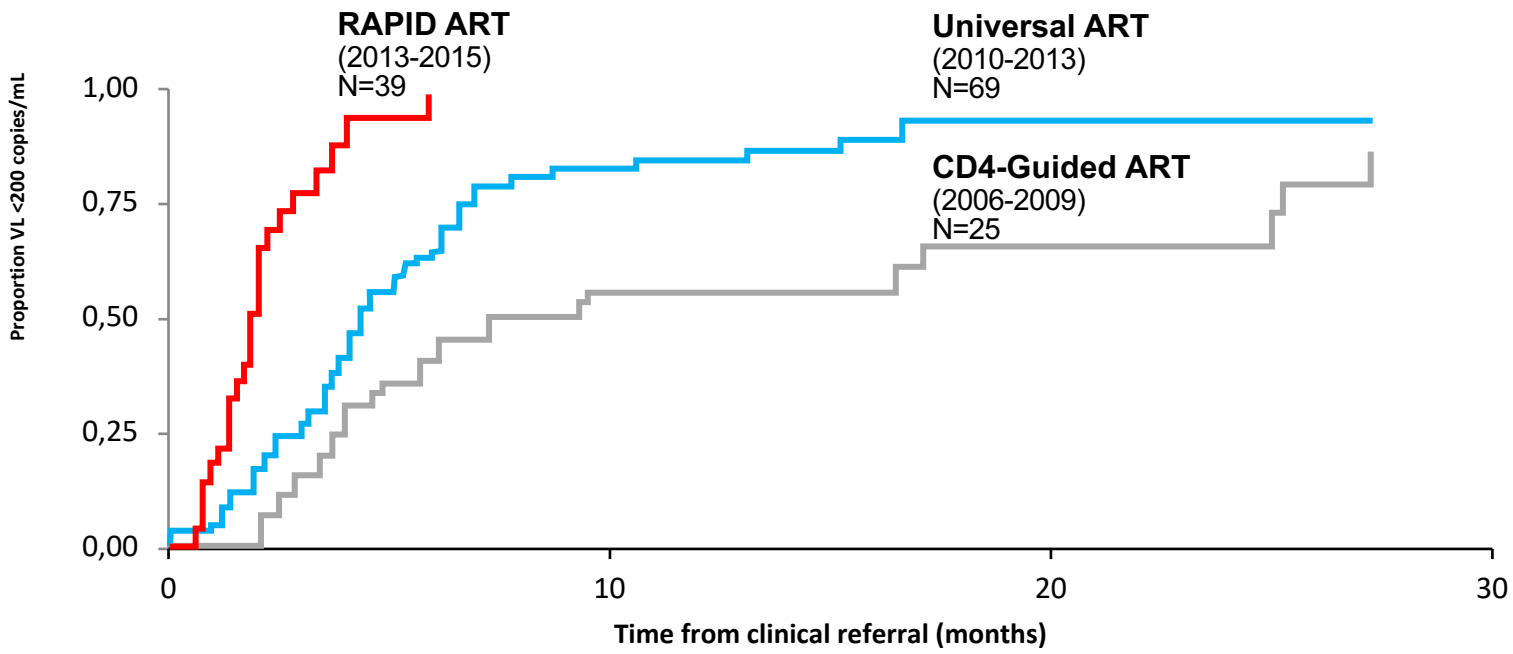


Day 0 = took their first dose in the clinic on their first visit
Day 1 = took their first dose within 24 hours of their first visit

Pilcher C, et al. JAIDS 2017;74:44-51

San Francisco General Hospital RAPID Program – Rapid ART Program for Individuals with an HIV Diagnosis

Results – Time to Viral Suppression



Treatment Strategy (Years Utilized)	Patients (n)	Months to VL suppression (<200 c/mL)	P value vs RAPID
RAPID (2013-2015)	39	1.8	
Universal ART (2010-2013)	69	4.3	<0.0001
CD4-Guided (2006-2009)	25	7.2	<0.0001

Pilcher C, et al. JAIDS 2017;74:44-51

San Francisco General Hospital RAPID Program – Rapid ART Program for Individuals with an HIV Diagnosis

Regimens, Resistance and Conclusions

Regimen	Patients % (n)
DTG + FTC/TDF	73.5% (26)
EVG/COBI/FTC/TDF	16.5% (7)
DRV/r + FTC/TDF	10% (4)
RAL + FTC/TDF	2.5% (1)
DTG/ABC/3TC	2.5% (1)

- No resistance-driven ART changes were necessary after genotype results became available
- No ART modifications for virologic failure throughout the study period

- Prioritizing immediate ART initiation can reduce the time to achieving virologic suppression in newly diagnosed patients without negative consequences to the patient
- A shorter time to viral suppression offers both clinical benefits to patients and prevention benefits to the community

Pilcher C, et al. JAIDS 2017;74:44-51

San Francisco General Hospital RAPID Program (2013-2017)

225 pacientes, 216(96%) immediate ART;
edad media 30 años, 7,9% mujeres, 11,6% afroamericanos, 26,9 % hispanos,
51% con Hº de abuso de sustancias, 48% con dx de enfermedad mental

Seguimiento medio 1.09 años; (0-3.92 años):
14% rebote viral, de ellos el 78% resuprimidos

Supresion viral del 92,1% en la ultima CV recogida

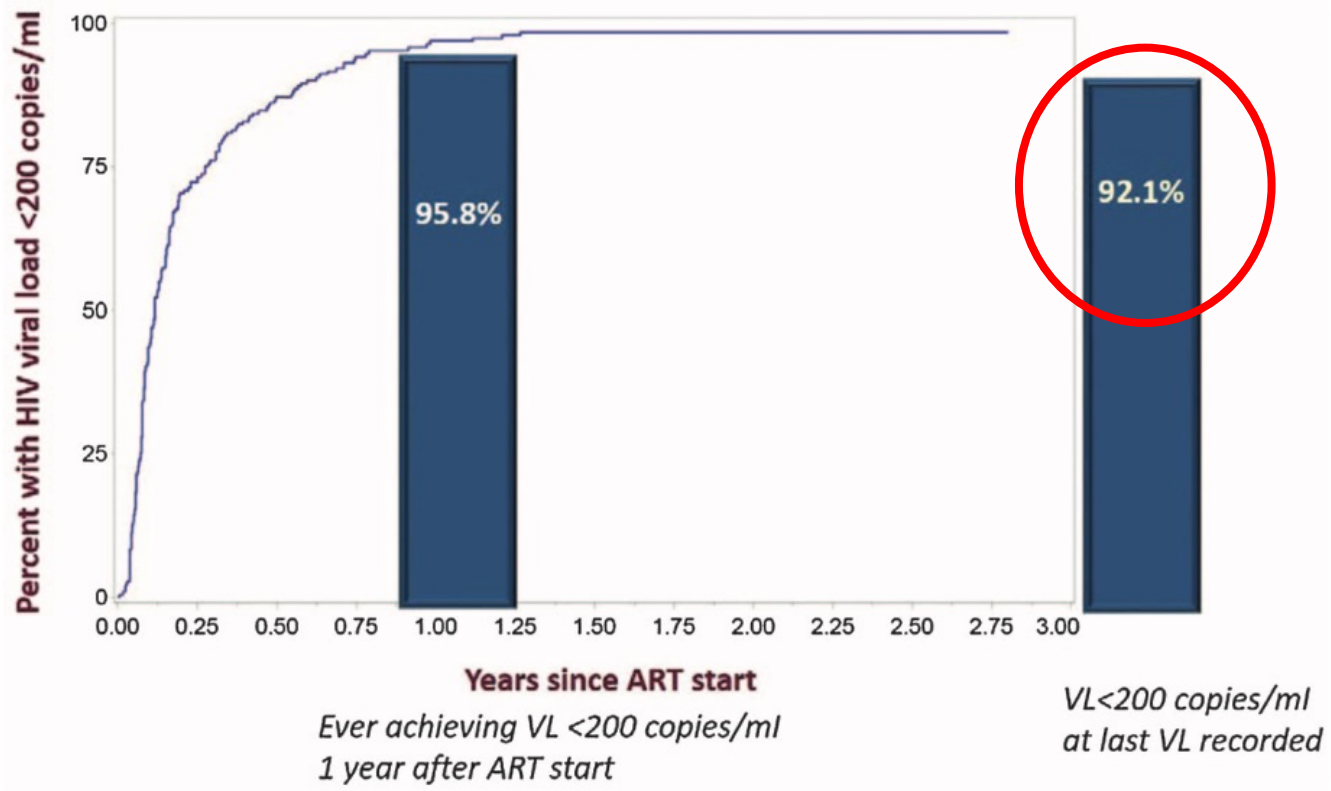


Fig. 1. Time from antiretroviral therapy start to first viral load less than 200 copies/ml in Ward 86 RAPID ART Program 2013–2017 (and % with viral load <200 copies/ml at last viral load recorded).

Coffey et al. AIDS 2019, 33:825–832

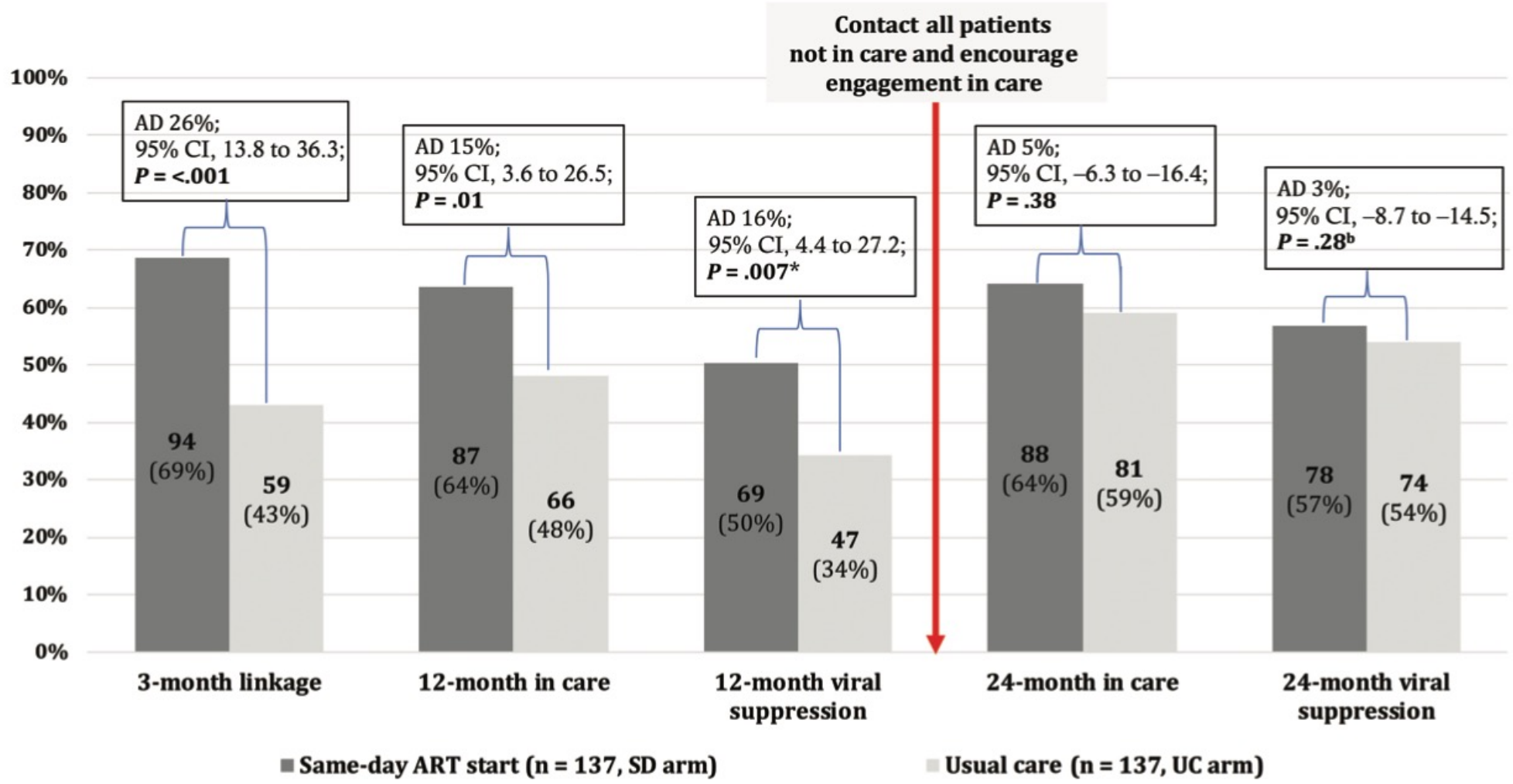
CASCADE Trial (Lesotho): estudio inicial [1] y a los dos años [2]

- Estudio abierto, aleatorizado, de dos grupos, realizado en Lesotho, tras campaña de dx VIH en domicilios en >6.600 personas, 60 aldeas rurales y 17 áreas urbanas, entre 2/2016- 9/2017
- 278 VIH + de nuevo dx >18 años, 268 asignados a: SDT 134 pac (tto el 1er día) vs tto usual 137pac (derivados al centro de salud, al menos 2 visitas pre-ART y seguimiento habitual)
- 1er estudio resultados a 12 meses, 2º estudio resultados a 24 meses tras contacto y recuperación de los pacientes perdidos a los 12 meses

1.-Effect of Offering Same-Day ART vs Usual Health Facility Referral During Home-Based HIV Testing on Linkage to Care and Viral Suppression Among Adults With HIV in Lesotho: The CASCADE Randomized Clinical Trial. JAMA 2018; 319:1103–1112

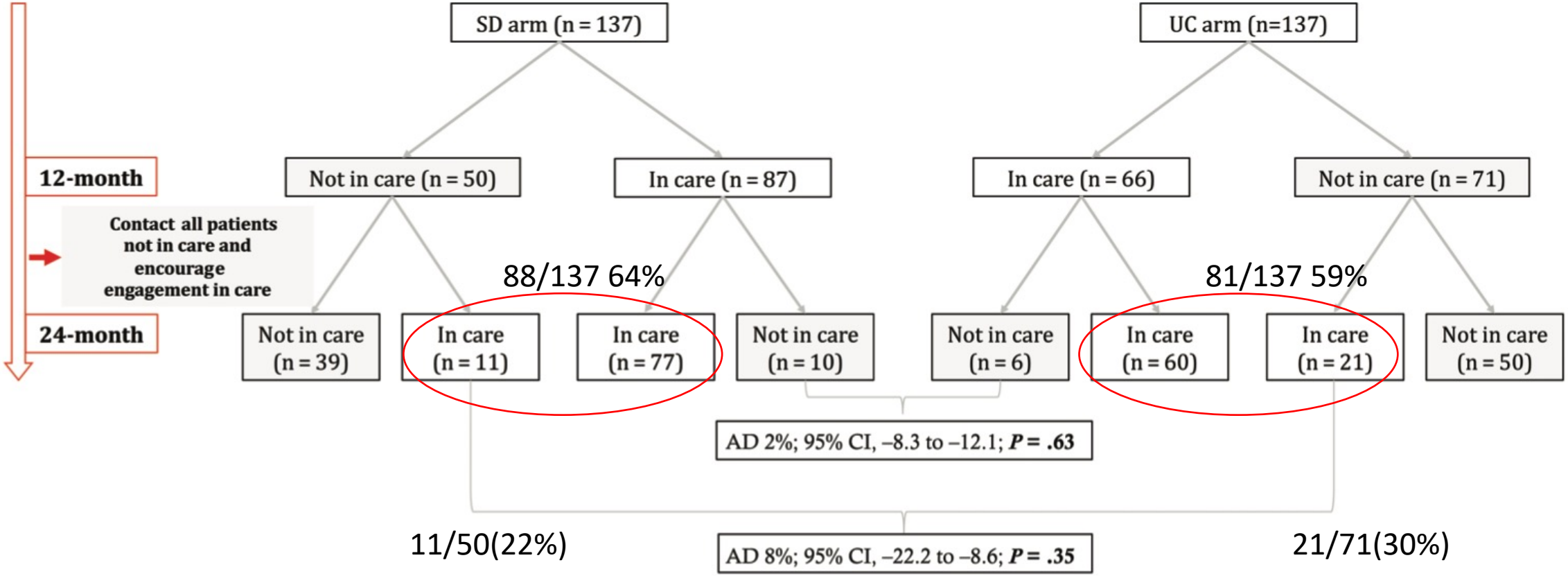
2. Amstutz A,etal. Engagement in care, viral suppression, drug resistance and reasons for non-engagement after home-based same-day ART initiation in Lesotho: a two-year follow-up of the CASCADE trial. *Clin Infec Dis*. doi:10.1093/cid/ciz1126 Published online November 29, 2019

Cascade Trial (Lesotho): estudio inicial y a los dos años



24 Months Outcomes After Same-day ART • **cid 2020:71 (15 November)**

Cascade Trial (Lesotho): estudio inicial y a los dos años



Las diferencias existentes al año entre SD vs Usual Tr, seguimiento de los cuidados y SV, no se mantienen a los dos años

24 Months Outcomes After Same-day ART • **cid 2020:71 (15 November)**

Too fast to stay on track? Shorter time to first anti-retroviral regimen is not associated with better retention in care in the French Dat'AIDS cohort

23 centros en Francia. Nuevos dx entre 2010-2015

Time from first medical visit to first ART (days)		< 9 N = 1881	9–27 N = 1784	28–90 N = 1800	> 90 N = 1780	P
Alive and in care at month 12 after ART prescription (%)		79.9	84.5	85.9	85.2	<0.0001
Time from diagnosis to undetectable VL (days; median, IQR)		194 (108–351)	210 (130–361)	232 (152–357)	527 (311–924)	<0.0001
Length of first ART (months; median, IQR)		14 (5–32)	17 (7–35)	21.5 (7–39)	22 (7–42)	<0.0001
End of study situation	Dead (%)	2.2	3.1	1.9	0.9	0.002
	LTFU (%)	14.3	12.4	13.4	12.5	0.002
VL < 50 copies/mL after 6 months of ART (%)		72.1	69.8	78.9	79.6	<0.0001
VL < 50 copies/mL after 12 months of ART (%)		78.0	81.5	84.1	81.4	0.12
VL < 50 copies/mL after 18 months of ART (%)		83.7	85.5	86.9	87.9	0.15

https://doi.org/10.1371/journal.pone.0222067.t004

Cuzin L. Cotte. on behalf of the Dat'AIDS Study Group. *PLoS One*. 2019;14(9):e0222067. doi:10. 1371/journal.pone.0222067

Too fast to stay on track? Shorter time to first anti-retroviral regimen is not associated with better retention in care in the French Dat'AIDS cohort

		HR	CI95%	P	aHR	CI95%	P
Age at HIV diagnosis*	< 28 y	Reference			Reference		
	28–36 y	1.39	1.18–1.65	0.0001	1.44	1.21–1.71	<0.0001
	37–46 y	1.56	1.32–1.86	<0.0001	1.67	1.40–2.00	<0.0001
	> 46 y	1.59	1.33–1.89	<0.0001	1.78	1.48–2.14	<0.0001
Sex/route of acquisition	Women	Reference			Reference		
	MSW[a]	0.79	0.67–0.93	0.007	0.72	0.61–0.86	0.0001
	MSM[b]	1.09	0.93–1.28	0.3	1.10	0.94–1.28	0.94
	Trans M>W[c]	0.60	0.33–1.15	0.10	0.62	0.34–1.19	0.32
CD4 cell count at diagnosis*	<200	Reference					
	200–350	1.22	1.00–1.50	0.04			
	351–500	1.13	0.92–1.38	0.22			
	>500	0.98	0.80–1.19	0.85			
Year of HIV Diagnosis	2010	Reference					
	2011	0.98	0.79–1.22	0.9			
	2012	1.03	0.83–1.29	0.7			
	2013	1.02	0.82–1.27	0.8			
	2014	1.03	0.83–1.27	0.8			
	2015	1.14	0.91–1.42	0.2			
Time from first visit to ART (days)*	< 9 days	Reference			Reference		
	9–27	1.37	1.16–1.63	<0.0001	1.36	1.14–1.61	<0.0001
	28–90	1.53	1.29–1.82	<0.0001	1.52	1.28–1.82	<0.0001
	> 90	1.45	1.22–1.72	<0.0001	1.48	1.24–1.76	<0.0001

*: classes following quartiles

[a]: Men having sex with women

[b]: men having sex with men

[c]: transgender men to women

Cuzin L. Cotte. on behalf of the Dat'AIDS Study Group. *PLoS One*. 2019;14(9):e0222067. doi:10.1371/journal.pone.0222067

Benefits and risks of rapid initiation of antiretroviral therapy (WHO Meta-Analysis)

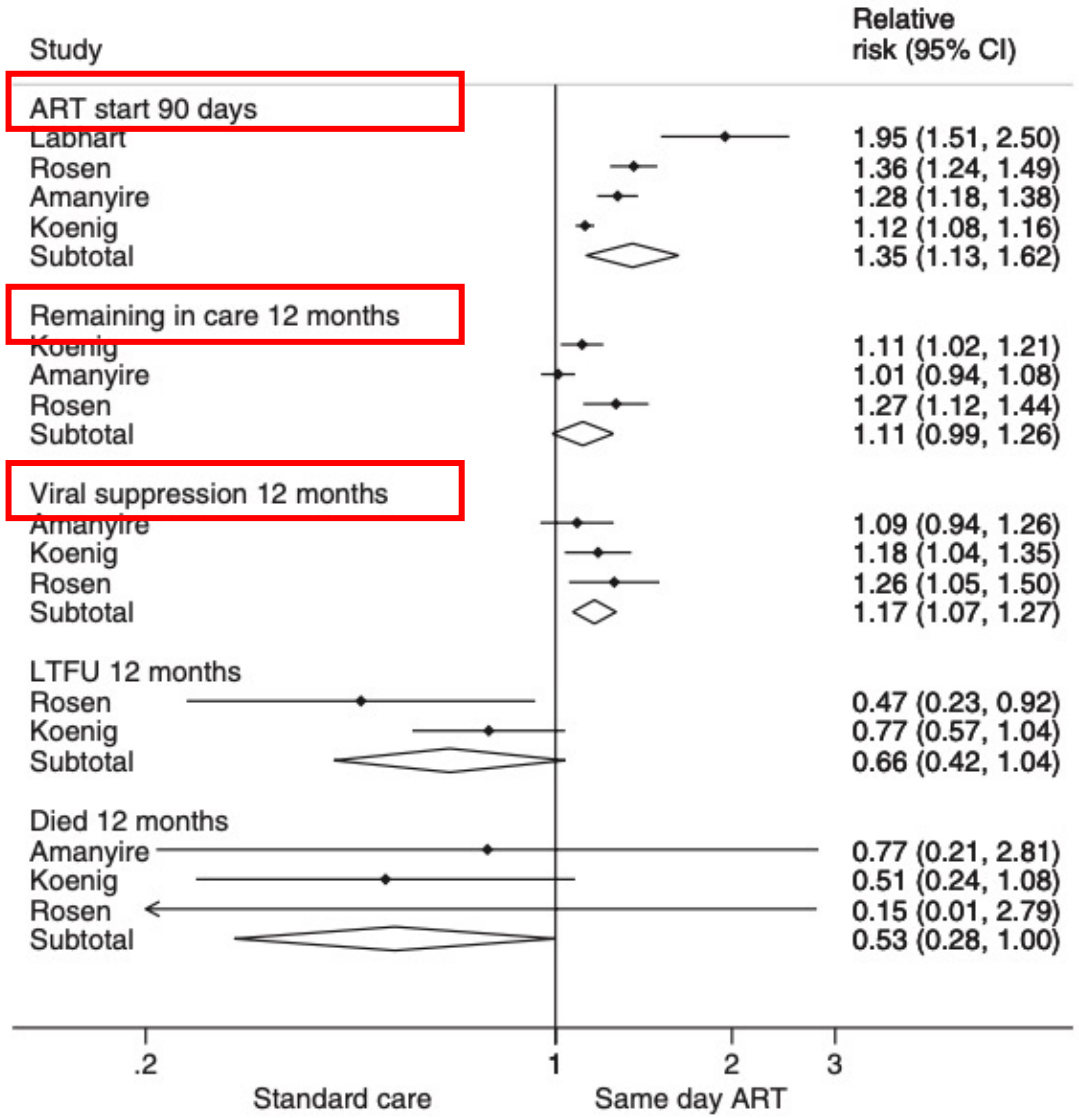
Rapid Initiation of ARV – Study Design

- Systemic literature review of randomized and quasi-randomized controlled trials, observational studies and qualitative studies reporting outcomes of accelerated ART initiation
  - Defined as starting within 14 days of diagnosis of HIV
- From a screen of 3886 titles, 22 studies were included

	#	Countries
RCTs	2	Haiti & S Africa
Cluster RTs	2	Uganda & Lesotho
Observational Studies	11	China, Ethiopia, Malawi, S Africa, Swaziland, Thailand, UK & US
Qualitative Studies	5	
Totals	22	12

Ford N, et al. AIDS 2018;32:17-23

Benefits and risks of rapid initiation of antiretroviral therapy (WHO Meta-Analysis)



Ford N, et al. AIDS 2018;32:17-23

Same-day ART initiation as a predictor of loss to follow-up and viral suppression among people living with HIV in sub-Saharan Africa

Impact of ART Initiation Timing on Loss to follow up and viral supression

Observational cohort from 11 subsaharian countries

ART naïve adult PLHIV participating in the International Epidemiology Databases to Evaluate AIDS consortium (IeDEA)

Who enrolled in care after Treat –All implementation and prior to January2019

	Same day ART	ART>1 day	Adjusted Hazard Ratio
	18584(64%)	10433(36%)	
Lost to follow up	27.7%	20.6%	0,66 (95CI 0.57-0.76)
Viral supression*	88,1%	88,1%	1 (95CI 0.98-1.02)

Same day ART led to higher proportion of LTFU vs ART >1 day, with no difference in time to viral suppression. LTFU higher among men vs women, younger(15-34) vs older(>34), and district hospital vs health centers

* %VS in patients with viral load measured

Ross J, CID 2022, ciac 759

Fundamentos/ Beneficios/Evidencias/Guías/Pautas Conclusiones

Guias clínicas

GeSIDA
GRUPO DE ESTUDIO DEL SIDA-SEIMC

2022

•*Se recomienda la administración de TAR a todos los pacientes con infección por el VIH-1 para evitar la progresión de la enfermedad, limitar el efecto nocivo sobre posibles comorbilidades y disminuir la transmisión del virus* ***(A-I)***.

• *Se recomienda iniciar el TAR tan pronto como sea posible, idealmente en los primeros 14 días tras el diagnóstico* ***(A-II)***.

EACS
European
AIDS
Clinical
Society

2021

Starting ART is recommended for all PLWH regardless of CD4 count to reduce the morbidity and mortality associated with HIV infection, and to prevent HIV transmission (START and TEMPRANO trials, HPTN 052, PARTNER Study). Evidence is accumulating that starting ART on the same day after establishing a diagnosis of HIV infection is feasible and acceptable to PLWH. Nevertheless, assessment of the readiness to start ART is essential to enable PLWH to express their preference and not feel pressured to start ART immediately, unless clinically indicated

Guias clínicas

DHHS 2022

Panel's Recommendations
• Antiretroviral therapy (ART) is recommended for all persons with HIV to reduce morbidity and mortality **(AI)** and to prevent the transmission of HIV to others **(AI)**.
• The Panel on Antiretroviral Guidelines for Adults and Adolescents recommends initiating ART immediately (or as soon as possible) after HIV diagnosis in order to increase the uptake of ART and linkage to care, decrease the time to viral suppression for individual patients, and improve the rate of virologic suppression among persons with HIV **(AII)**.
• When initiating ART, it is important to educate patients regarding the benefits of ART and to deploy strategies to optimize care engagement and treatment adherence **(AIII)**.

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. Available at https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv. Accessed (30/09/2022)

Guias clínicas

IAS -USA 2020

Box 1. Key Recommendations for When to Start Antiretroviral Therapy (ART)

- Initiation of ART is recommended as soon as possible after HIV diagnosis, including immediately after diagnosis if the patient is ready to commit to treatment (evidence rating: AIa)
- Structural barriers that delay receipt of ART should be removed to allow newly diagnosed persons to receive ART at the first clinic visit after diagnosis if they and their clinicians determine that this approach is appropriate (evidence rating: AIa)
- Initiation of ART is recommended within 2 weeks of initiation of treatment for most opportunistic infections (evidence rating: AIa), except:
  - For individuals with tuberculosis and CD4 cell counts of 50/μL or above, ART should be initiated within 2 to 8 weeks of initiation of tuberculosis treatment (evidence rating: AIa)
  - For individuals with cryptococcal meningitis, ART should be initiated within 4 to 6 weeks after starting antifungal therapy (evidence rating: BIa)
- Initiation of ART is recommended immediately in the setting of a new diagnosis of cancer with attention to drug-drug interactions (evidence rating: BIIa)

JAMA. doi:10.1001/jama.2020.17025 Published online October 14, 2020.

Precauciones para el inicio rápido

- Preparación del paciente para iniciar TAR
- Uso de pautas con determinadas características
- Descartar la presencia de meningitis criptococica o tuberculosis al iniciar el TAR
- Revisar las analíticas basales y el estudio de resistencia tan pronto este disponible

Causas para diferir el inicio TAR: Perspectiva del paciente

- Dificultades en la aceptación del dx de infección por VIH
- Incertidumbre sobre el test dx y deseo de repetir y confirmar la prueba
- En mujeres embarazadas , el deseo de consensuar la decisión con su pareja
- Necesidad para mentalizarse del inicio de un tto de por vida
- Interpretación errónea de los mensajes para reforzar la adherencia
- Miedo a ser identificados como pacientes VIH al recoger la medicación
- Sentirse bien y tener miedo a tener efectos secundarios al iniciar TAR

Mwamba C et al. Annals of Medicine 2022: 54(1): 830-836

Fundamentos/ Beneficios/Evidencias/Guías/Pautas Conclusiones

Guias clinicas: Fármacos recomendados para inicio muy rápido

GeSIDA
GRUPO DE ESTUDIO DEL SIDA-SEIMC

"En caso de plantearse el inicio del TAR de forma inmediata, ... Debe cumplir:

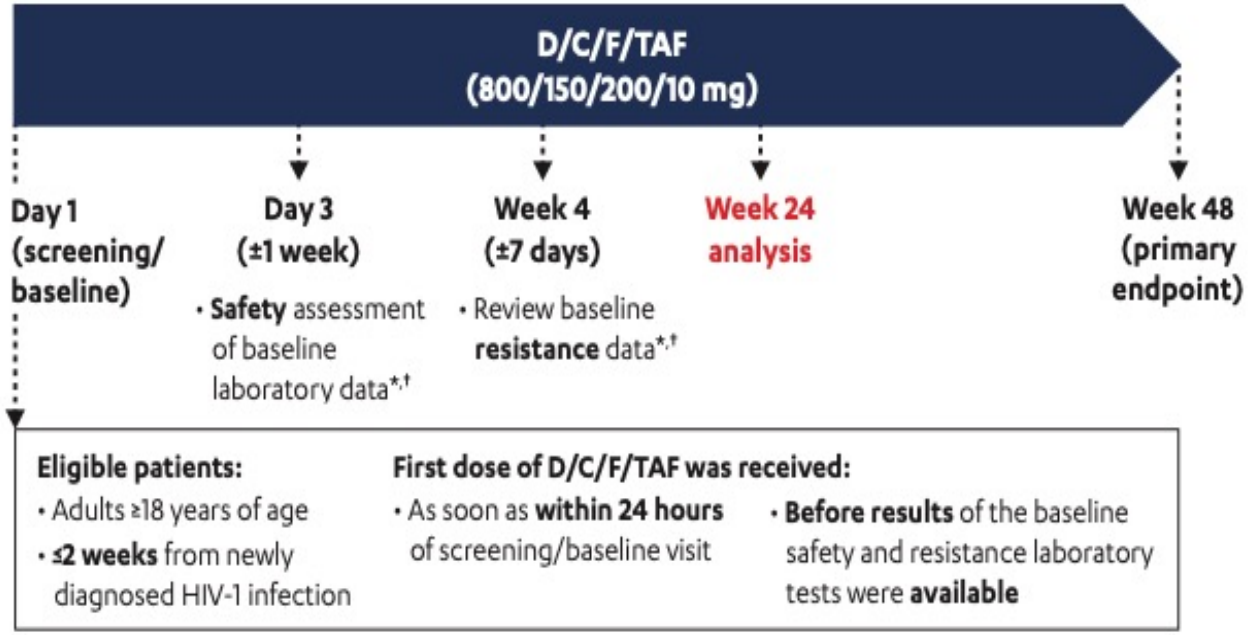
-facilidad de toma
- buena tolerabilidad
- No requerir estudio previo de HLA-B*5701
- mínimo riesgo de interacciones farmacológicas
- alta probabilidad de mantener actividad antiviral en presencia de CVP elevadas, cifras bajas de linfocitos CD4+ o de virus con mutaciones de resistencia basales
- idealmente capacidad de suprimir la replicación del VHB en caso de coinfección por el mismo "

TAF/FTC+DTG
TAF/FTC/DRV/cobi
TAF/FTC/Bictegravir

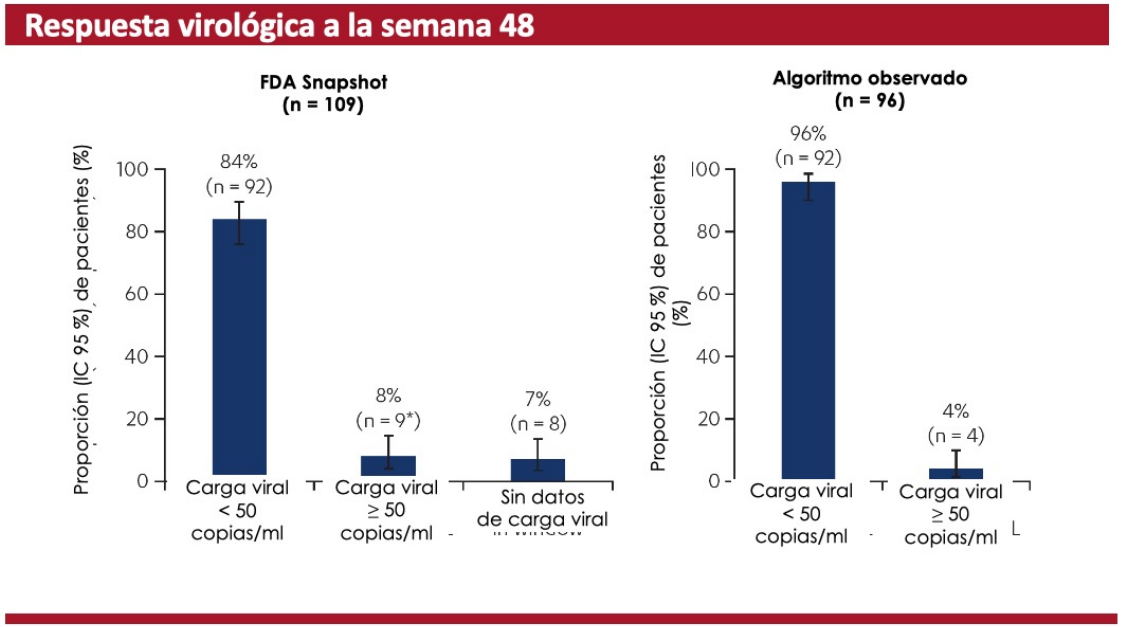
TAF/FTC/DRV/cob en un modelo de inicio rápido (Diamond Study)

OBJETIVOS

- To assess the efficacy and safety of D/C/F/TAF in a rapid initiation model of care in newly diagnosed, HIV-1–infected, treatment-naïve patients
- To assess baseline viral resistance in the study population
- To assess HIV Treatment Satisfaction Questionnaire status version (HIVTSQs) results at Weeks 4 and 24



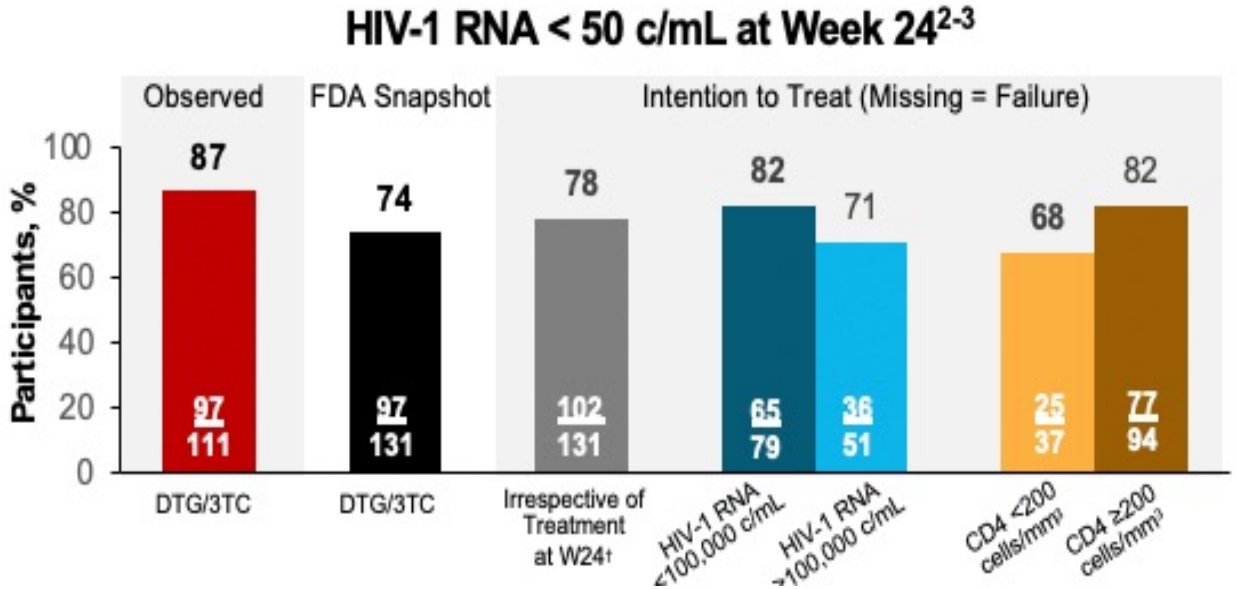
CID 2020:71 (15 December) • Huhn et al



HIVTSQs : 58/60 en la semana 24 y 48

FEASIBILITY, EFFICACY, AND SAFETY OF USING DOLUTEGRAVIR/LAMIVUDINE (DTG/3TC) AS A FIRST-LINE REGIMEN IN A TEST-AND-TREAT SETTING FOR NEWLY DIAGNOSED PEOPLE LIVING WITH HIV (PLWH): **THE STAT STUDY**

Phase IIIb, multicenter, open-label, single arm, pilot study of adult PLWH treated within 14 days of diagnosis* (N=131)
July 2019 to April 2020[1]



Reason for switch[2-3]	Modified ART	HIV-1 RNA at Wk 24
Baseline HBV	DTG/3TC+TAF (Wk 1)	< 40 c/mL
Baseline HBV	DTG/3TC+TAF (Wk 8)	< 40 c/mL
Baseline HBV	DTG+FTC/TDF (Wk 4)	< 40 c/mL
Baseline HBV	B/F/TAF (Wk 1)	NA[a]
Baseline HBV	B/F/TAF or DTG+FTC/TDF[b] (Wk 4)	49 c/mL
Baseline M184V	DTG/RPV (Wk 8)	NA[c]
Decision by participant/proxy	B/F/TAF (Wk 4)	NA[d]
AE (rash)	B/F/TAF[e] (Wk 12)	< 40 c/mL

- Tiempo medio desde el dx al ingreso en el estudio 5 días(5—15 días)
- 7 pacientes (5%), tuvieron HB sAg, 2 permanecieron con DTG/3TC y los otros 5 cambiaron el TAR
- La CV , CD4 y serologías fueron informados en la semana1 , y el estudio de resistencia en la sem 4

Rolle et al. HIV Glasgow 2020; Poster P020.

FAST: National, prospective, single-arm multicenter study (France)

Efficacy and Safety of B/F/TAF in a Rapid Start Model

N = 112 (ITT)

PLWH initiating B/F/TAF before any laboratory results were available (rapid start)

Outcome

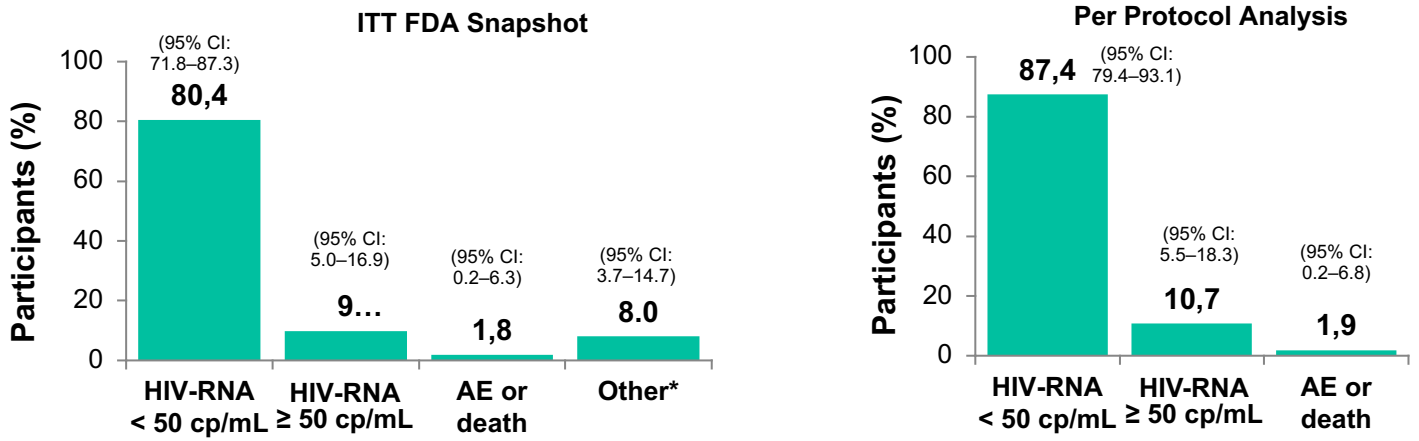
Proportion of PLWH with HIV-1 RNA < 50 cp/mL at Week 24 (FDA Snapshot analysis)

Nov 2019–Sept 2020

Baseline Characteristics

Baseline characteristics, median (IQR) or n (%)	ITT (n = 112)
Age, median (range), years	36 (28–47)
Male	98 (87.5)
HIV RNA, log_{10} cp/mL HIV RNA > 500,000 cp/mL Primary infection	4.8 (4.4–5.5) 21 (18.8) 23 (19.6)
CD4 count, cells/mm^3 CD4 < 200 cells/mm3	369 (240–570) 19 (17.2)
Time to enrolment since first HIV diagnosis, median (range), days	8 (5–17)
Positive HBsAg	2 (1.8)
Time between inclusion and initiation of treatment, days 0 1	 110 (98.2) 2 (1.8)

Virologic Outcomes at Week 24



No emergent RAMs were detected in PLWH who failed to achieve HIV-1 RNA < 50 cp/mL at Week 24

B/F/TAF is safe and effective for same-day ART initiation in a rapid start setting

Other: resistance at baseline (n = 3, 2.7%), lost to follow up (n = 4, 3,6%) missing value (n = 2, 1.8%)

HBsAg, hepatitis B surface antigen; ITT, intent-to-treat; VL, viral load Bachelard A, et al. EACS 2021, Poster PE2/7

BIFAST: Phase 4, open-label, nonrandomized, single-center study (Spain)

Impact of Starting B/F/TAF at the First HIV Specialist Appointment

N = 59

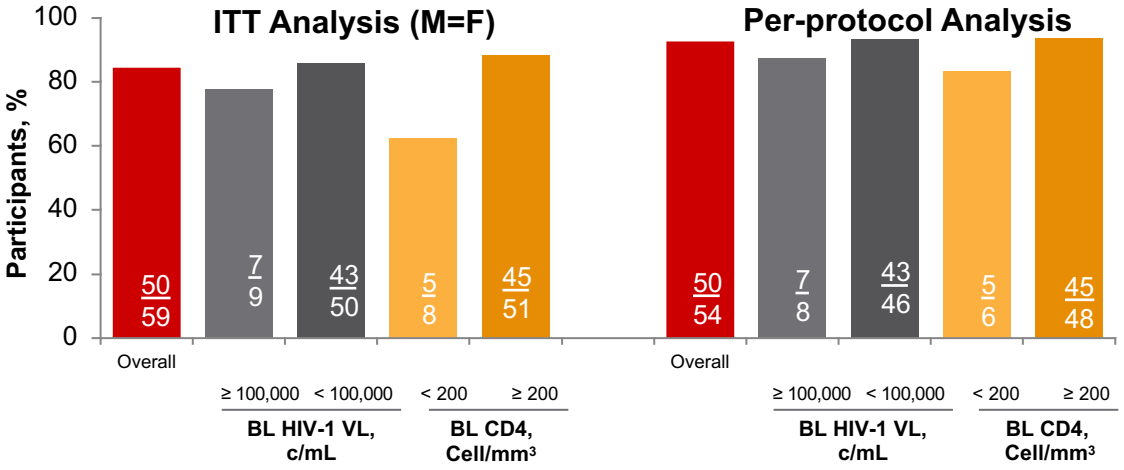
PLWH attending first HIV-specialist appointment

Outcomes

Viral load, CD4 cell count and PROs at 24 weeks*

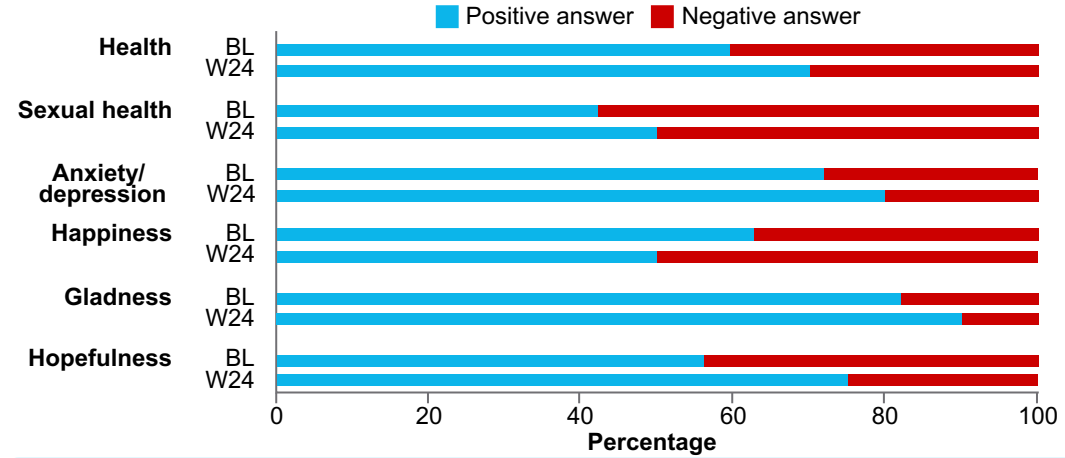
N/A

HIV Viral Load < 50 c/mL at Week 24



Four individuals had viral load > 50 c/mL at Week 24

PROs at Baseline and Week 24



Improved self-perception at Week 24

- Decrease in anxiety/depression symptoms
- Increase in gladness and optimistic perception about the future

Starting ART with B/F/TAF at the first HIV-specialist appointment demonstrated high rates of virologic suppression and trends toward improved PROs

*Data are shown combined for those with (n = 39) and without (n = 20) laboratory data at BL. One patient discontinued due to suspected tuberculosis infection and four patients were lost to follow-up

BL, baseline; ITT, intent-to-treat; M=F, missing = failure; N/A, not applicable; PRO, patient-reported outcome; VL, viral load

Al-Hayani AWM, et al. AIDS 2022, Poster EPB153

Conclusiones

Existen evidencias de alta calidad (ensayos clínicos aleatorizados) a favor del inicio rápido del TAR tras el dx VIH(TAR universal) vs TAR diferido

No existe una ensayo clínico aleatorizado, doble ciego que demuestre beneficio del TAR inmediato/SDT, primeras 24-48h, frente TAR iniciado en los 7-15 primeros dias

Tampoco existen datos a largo plazo >2 años concluyentes en un sentido u otro

Existen numerosos estudios de cohortes y ensayos aleatorizados de menor calidad, que muestran beneficios del TAR inmediato, en las primeras 24-48h,sin esperar resultados vs TAR iniciado >7 días o tras recibir resultados

La pauta de TAR elegida para el tratamiento inmediato debe reunir unas determinadas características: sencilla, bien tolerada, eficaz en escenarios difíciles, barrera alta a las resistencias, pocos efectos secundarios y pocas interacciones

No todos los pacientes están preparados para un inicio inmediato del TAR, en ellos es preciso abordar las barreras sin presionarlos

Gracias por vuestra atención