

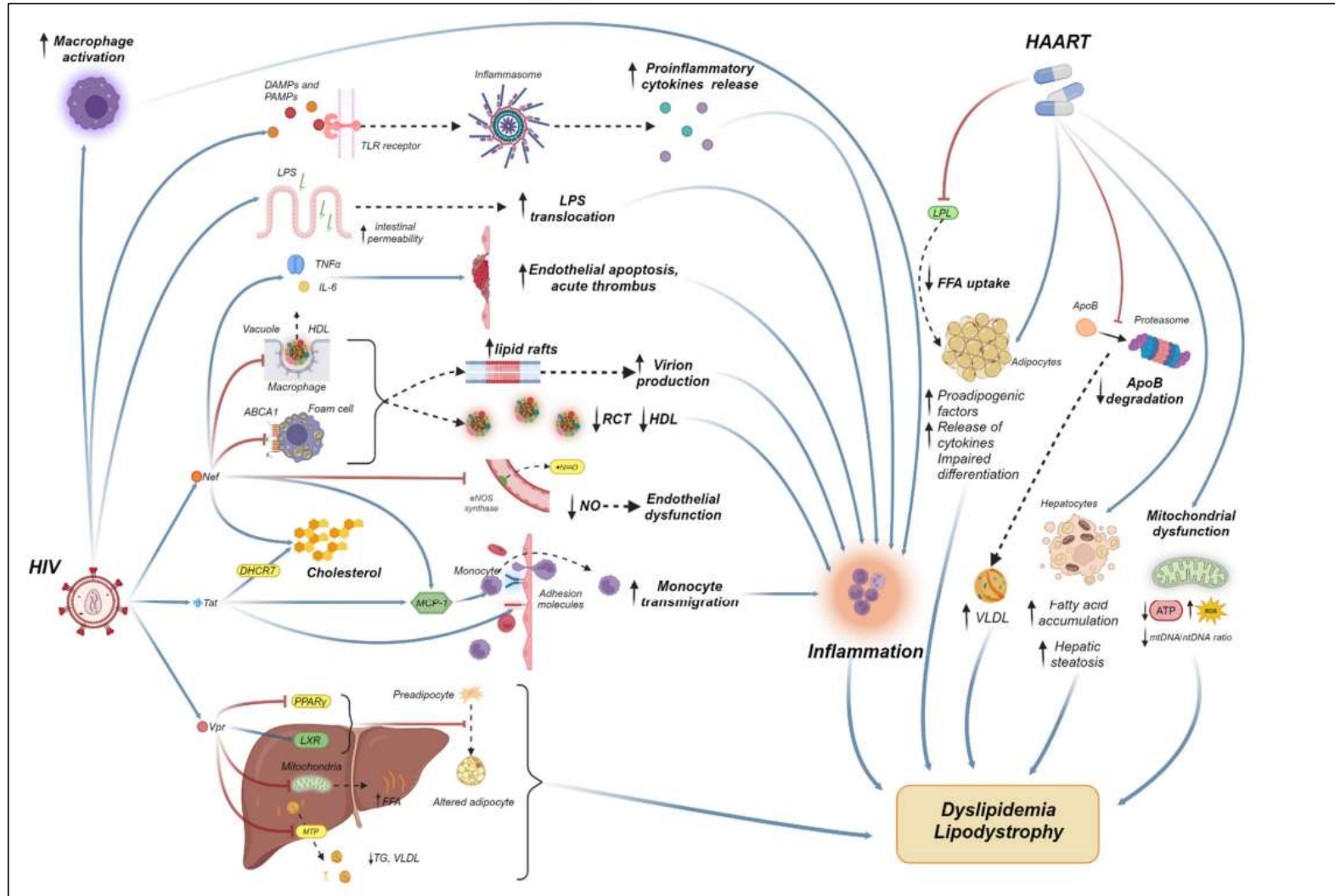


Manejo de los trastornos lipídicos en las PVVIH

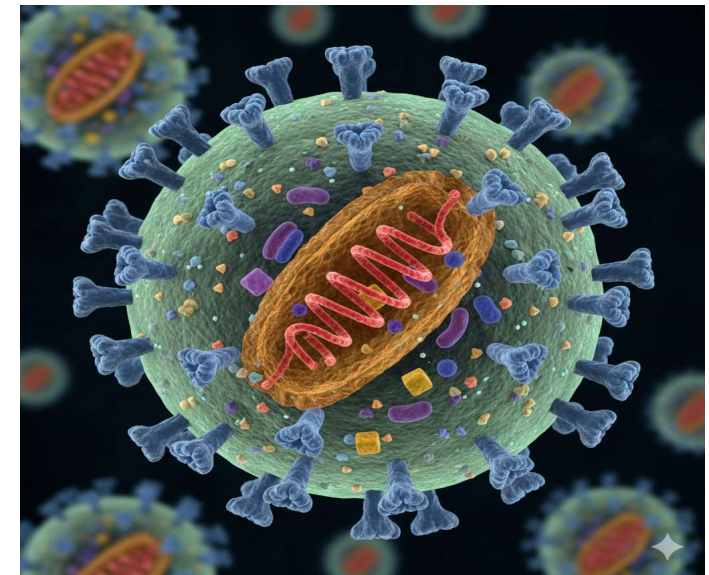
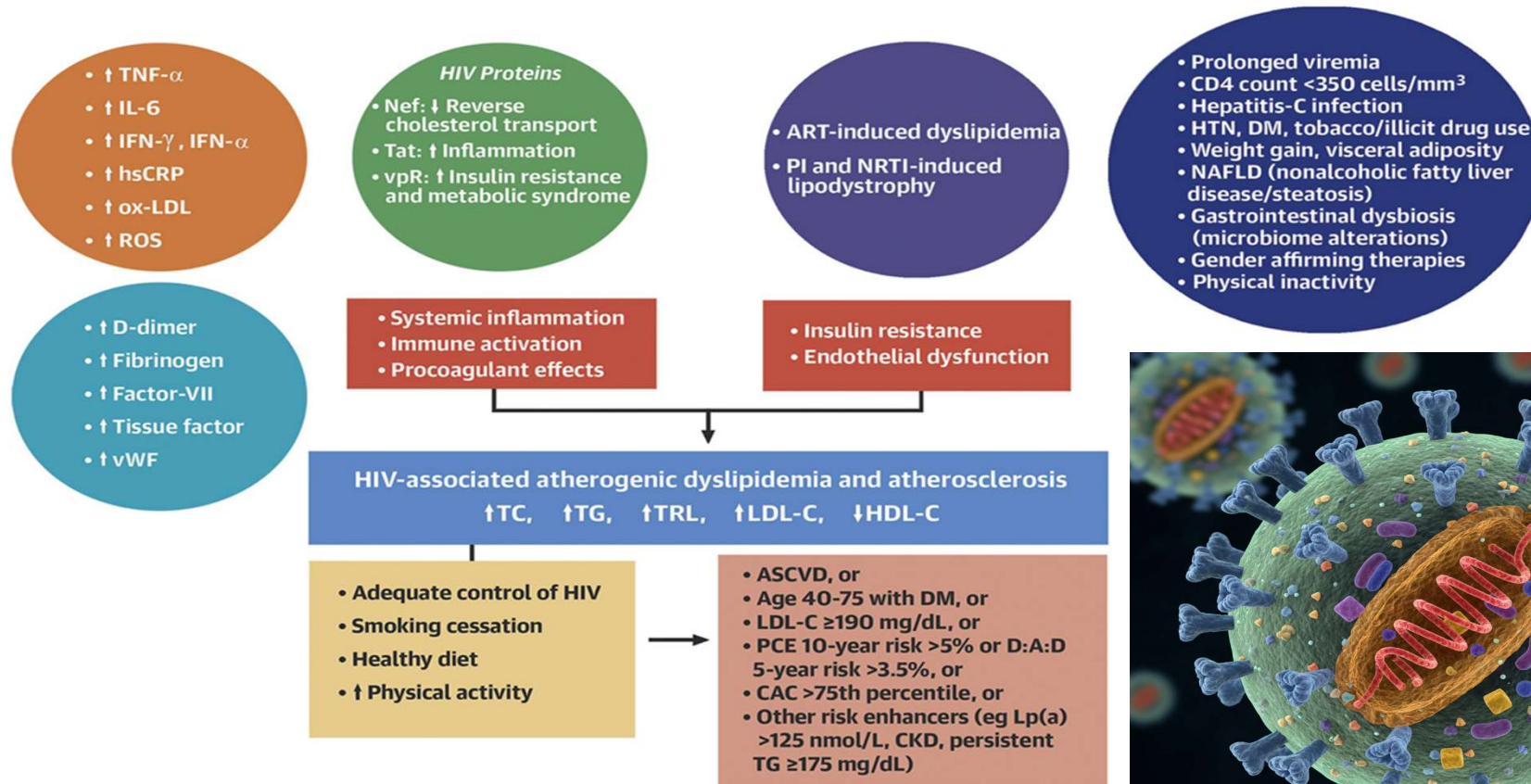
José Luis Hernández Hernández
Servicio de Medicina Interna
Unidad de Lípidos y Riesgo vascular
Hospital Marqués de Valdecilla-IDIVAL
Universidad de Cantabria



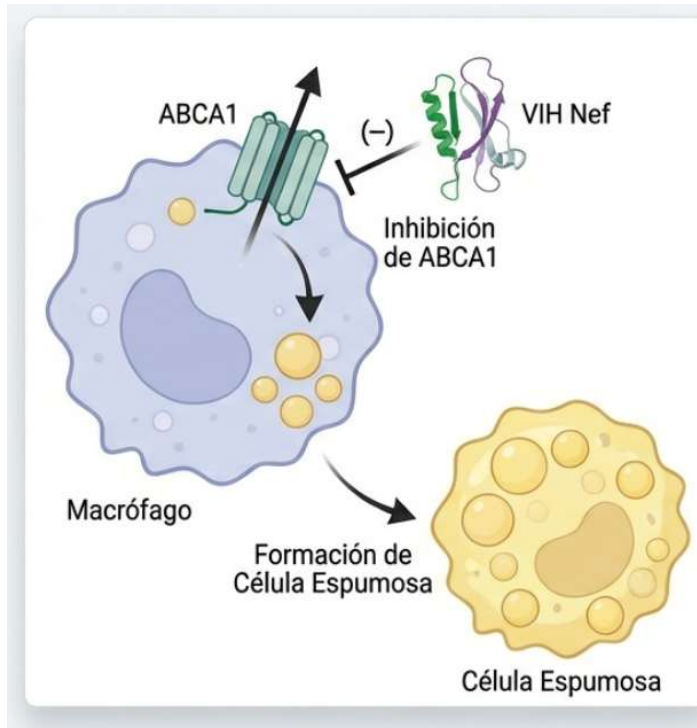
Patogenésis de la dislipemia en PVVIH



Mecanismos de la dislipemia en PVVIH



Mecanismos de la dislipemia en PVVIH



Mecanismo 1: Alteración Lipídica Directa

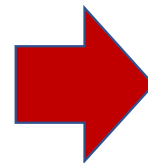
La proteína viral Nef interfiere con el transporte inverso de colesterol (ABCA1), reduciendo la funcionalidad del HDL.

Mecanismo 2: Activación Inmune Crónica

- Aumento de citoquinas (IL-6, TNF- α).
- Activación de monocitos/macrófagos asociada a placa no calcificada.
- Oxidación del LDL facilitada por el entorno inflamatorio.

Nef

↓ Eflujo de colesterol hacia ApoA-I
↓ Formación de HDL
↑ Acumulación de colesterol intracelular

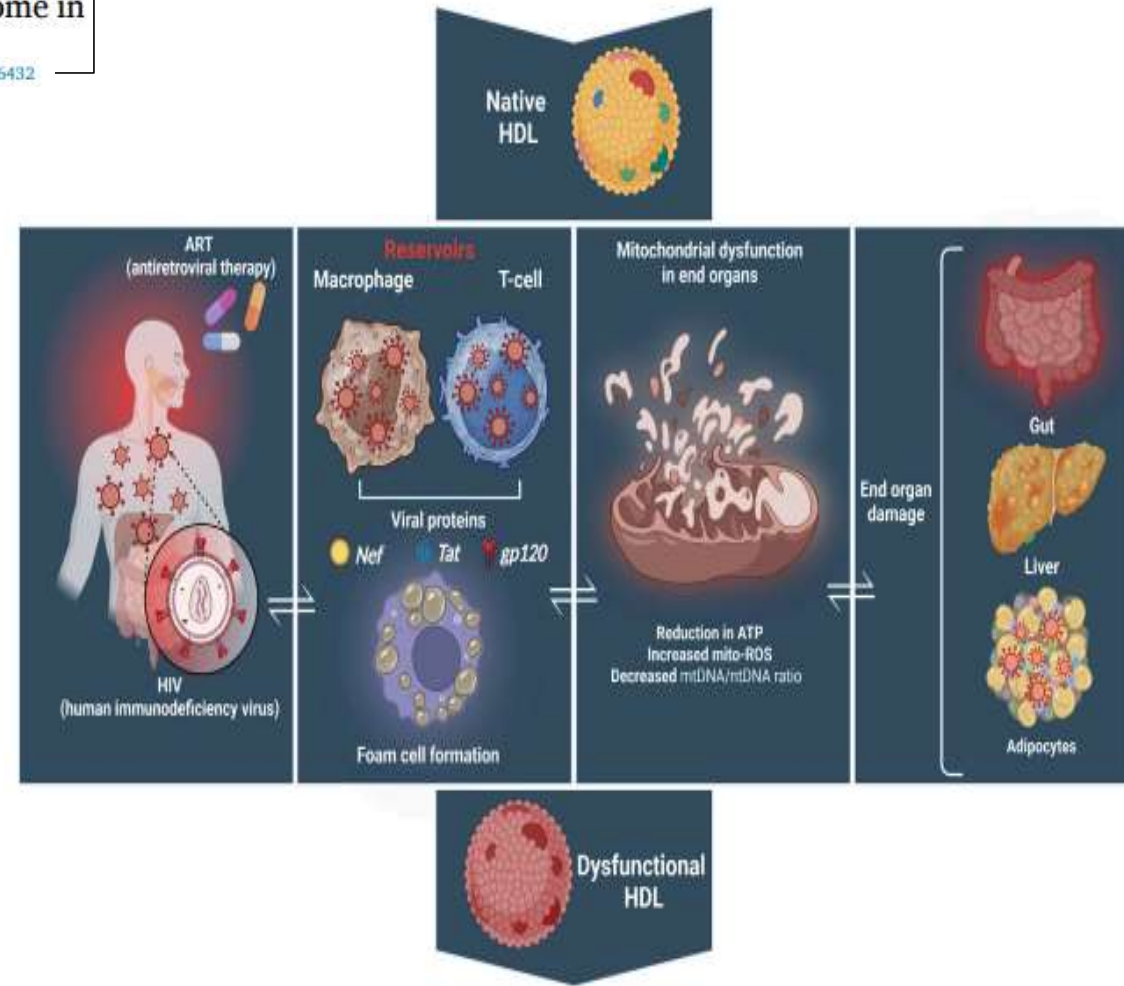
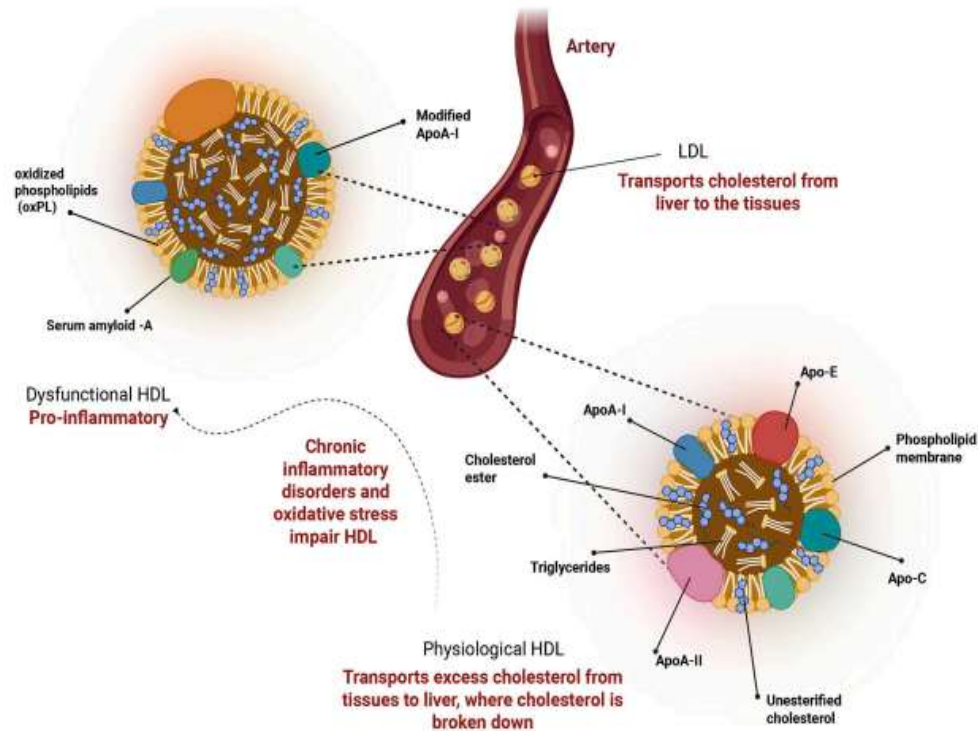


Mejora su ensamblaje
 Produce viriones más infecciosos
 Favorece la disfunción de macrófagos

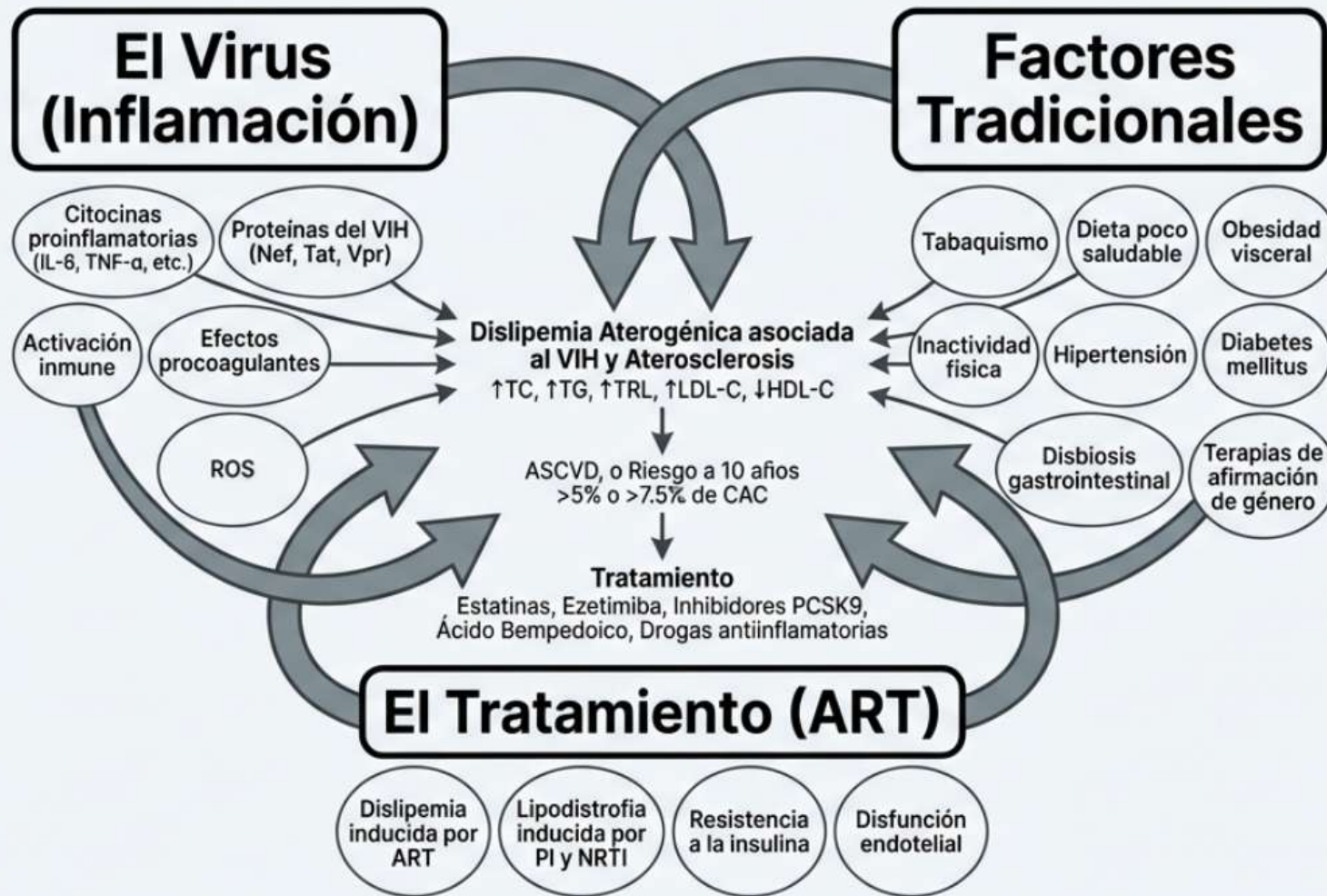
Papel del HDL en la dislipemia en PVVIH

HDL dysfunction: a role in the pathogenesis of cardiometabolic syndrome in chronic HIV infection?

Metabolism 175 (2026) 156432



La tormenta perfecta



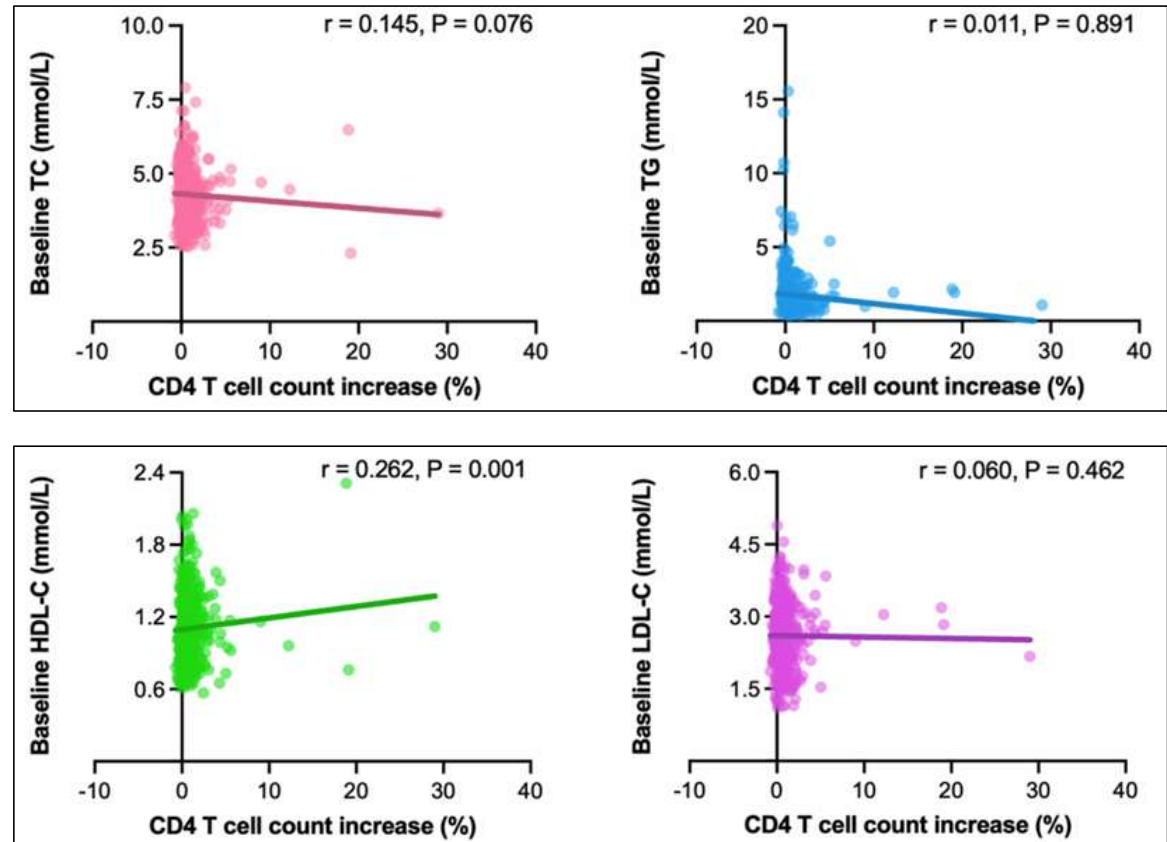
Dislipemia y reconstitución inmune

The predictive value of dyslipidemia for immune reconstitution outcome among HIV/AIDS patients after 24 months of viral suppression: a retrospective cohort study

N=429

TAR

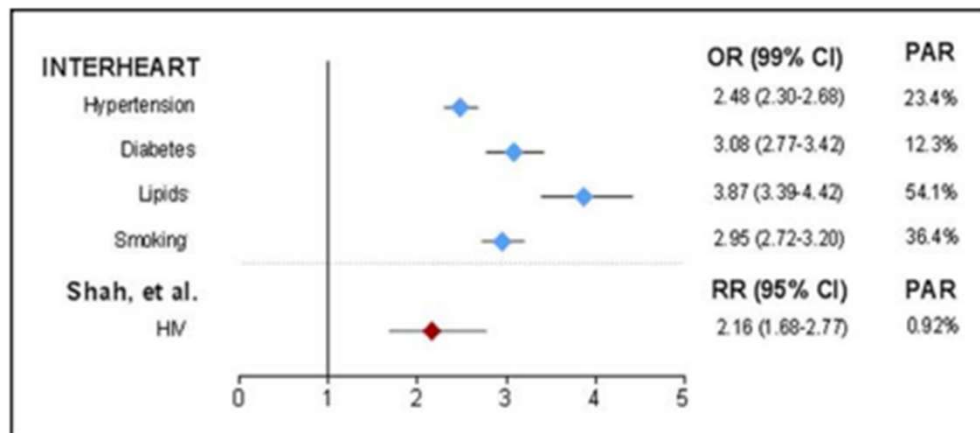
El nivel basal de HDL-C puede servir como marcador pronóstico para una mala reconstitución inmunitaria en PVVIH



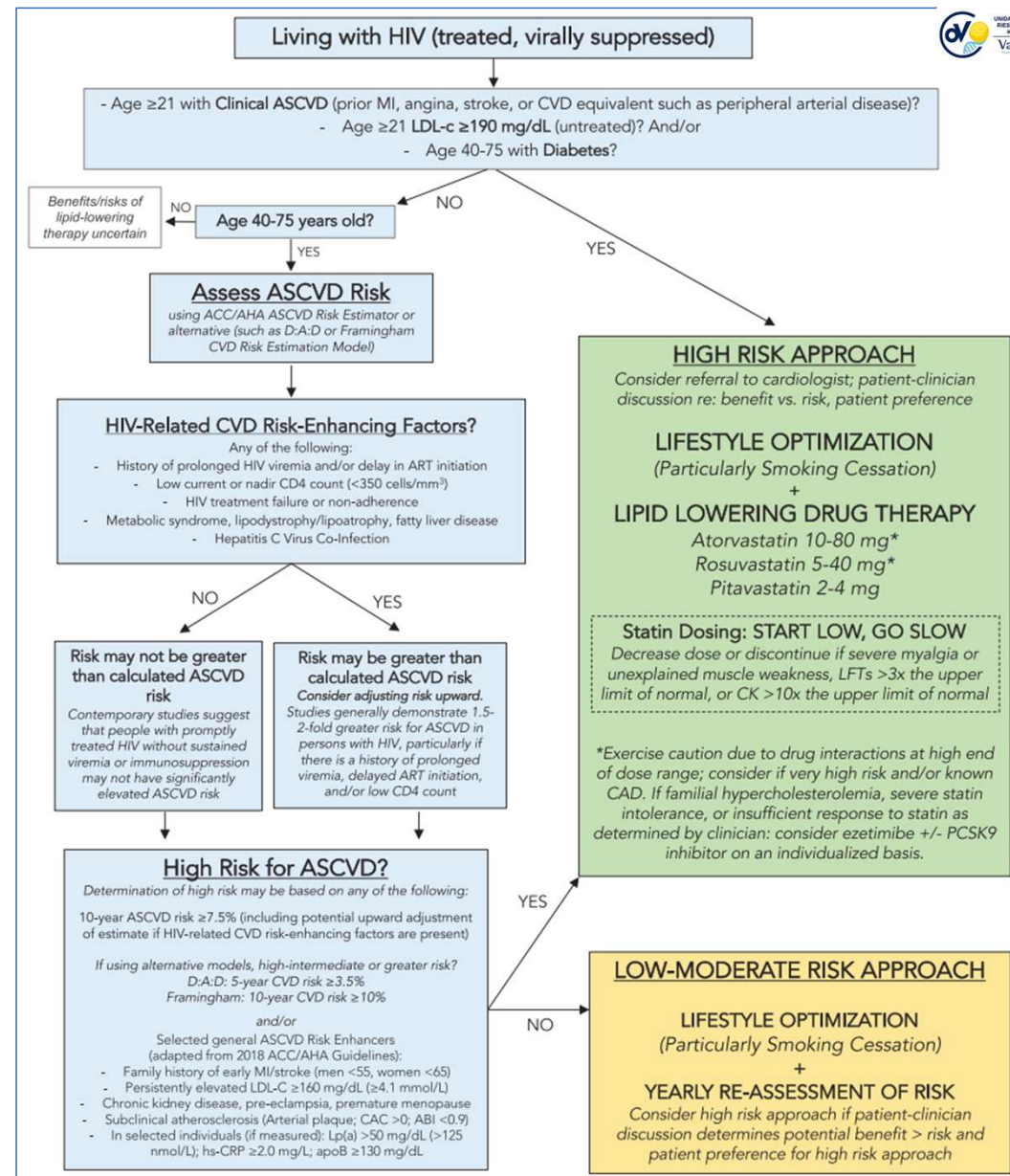
Characteristics, Prevention, and Management of Cardiovascular Disease in People Living With HIV

A Scientific Statement From the American Heart Association

Circulation. 2019;140:e98–e124.1



PAR: population-attributable risk



Guías clínicas: Manejo de la dislipemia en el PVVIH

2019 ESC/EAS Guidelines for the management of dyslipidaemias: *lipid modification to reduce cardiovascular risk*

Recommendations	Class ^a	Level ^b
Lipid-lowering therapy (mostly statins) should be considered in HIV patients with dyslipidaemia to achieve the LDL-C goal as defined for high-risk patients. The choice of statin should be based on their respective potential drug–drug interactions.	IIa	C

2023 AHA/ACC/ACCP/ASPC/NLA/PCNA Guideline for the Management of Patients With Chronic Coronary Disease: A Report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines

Circulation

Volume 148, Issue 9, 29 August 2023; Pages e9-e119



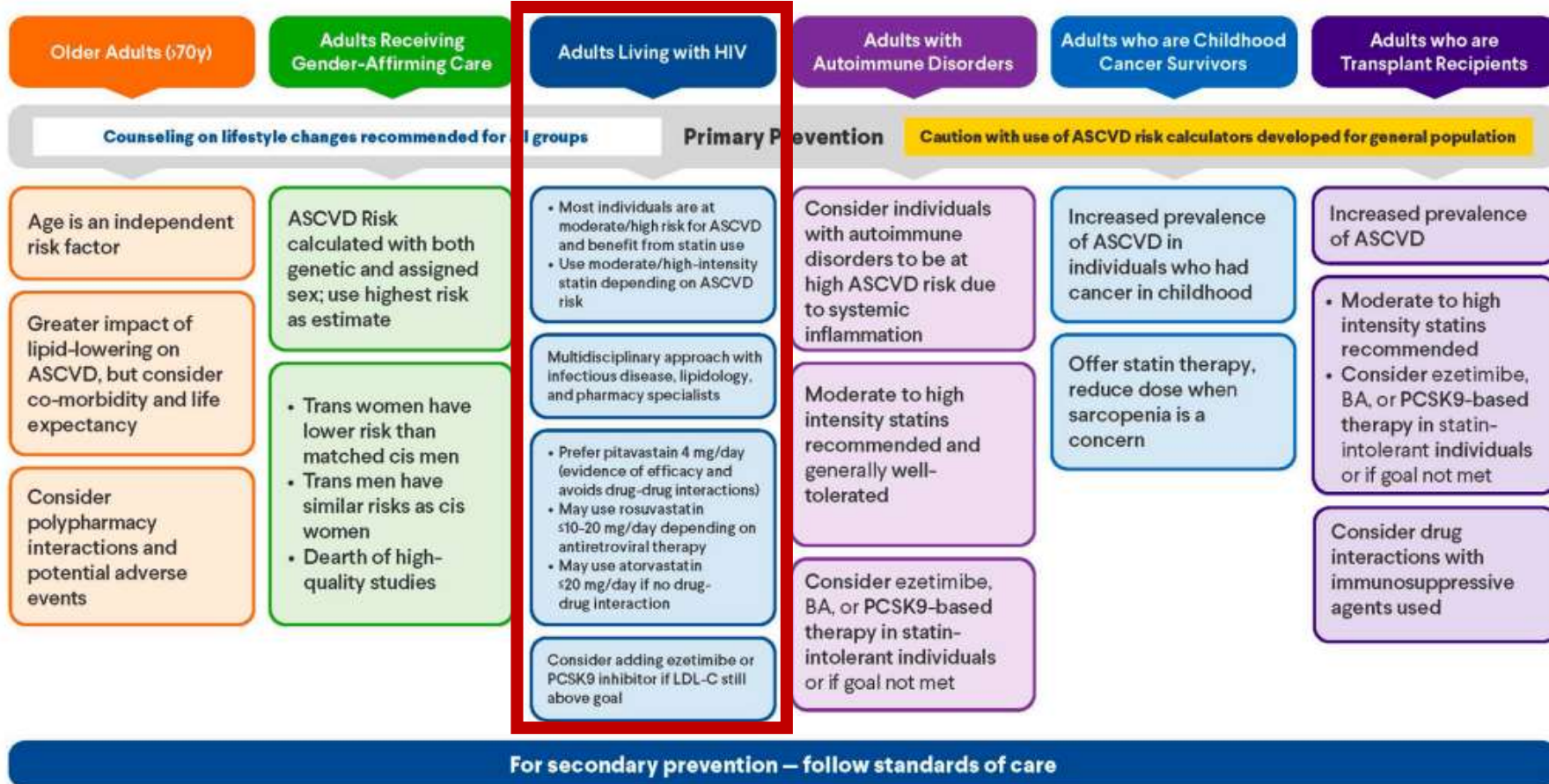
Class	Drug	Effect on Blood Lipids
Protease inhibitors	Atazanavir	Increases HDL-C and decreases LDL-C levels
	Darunavir	Increases HDL-C levels
	Fosamprenavir	Hypertriglyceridemia
	Ritonavir*	Increases HDL-C levels
	Saquinavir	Neutral
	Tipranavir	Dyslipidemia
NRTIs	Abacavir	Increases total cholesterol, LDL-C, and HDL-C levels ★
	Lamivudine	Increases total cholesterol, LDL-C, and HDL-C levels ★
	Tenofovir fumarate disoproxil	Lowers LDL levels
	Zidovudine	Hypertriglyceridemia
NNRTIs	Efavirenz	Increases total cholesterol, LDL-C, HDL-C, and triglyceride levels ★
	Nevirapine	Neutral or decreases lipid levels
	Rilpivirine	Neutral
Integrase inhibitors	Dolutegravir	Neutral
	Raltegravir	Increases HDL levels

Recommendations for HIV		
COR	LOE	Recommendations
HIV		
1	B-R	1. In adults with CCD and HIV, antiretroviral therapy is beneficial to decrease the risk of cardiovascular events. ^{1,2}
2a	B-R	2. In adults with CCD and HIV, it is reasonable to choose antiretroviral therapy regimens associated with more favorable lipid and cardiovascular risk profiles with consideration of drug-drug interactions. ³⁻⁵
3: Harm	C-LD	3. In adults with CCD and HIV, lovastatin or simvastatin should not be administered with protease inhibitors as this may cause harm. ^{6,7}

American Association of Clinical Endocrinology Consensus Statement: Algorithm for Management of Adults with Dyslipidemia – 2025 Update

Endocrine Practice 31 (2025) 1207–1238

Management of Special Populations with Dyslipidemia



Statin use in HIV: European AIDS Clinical Society guidance for the primary prevention of cardiovascular disease

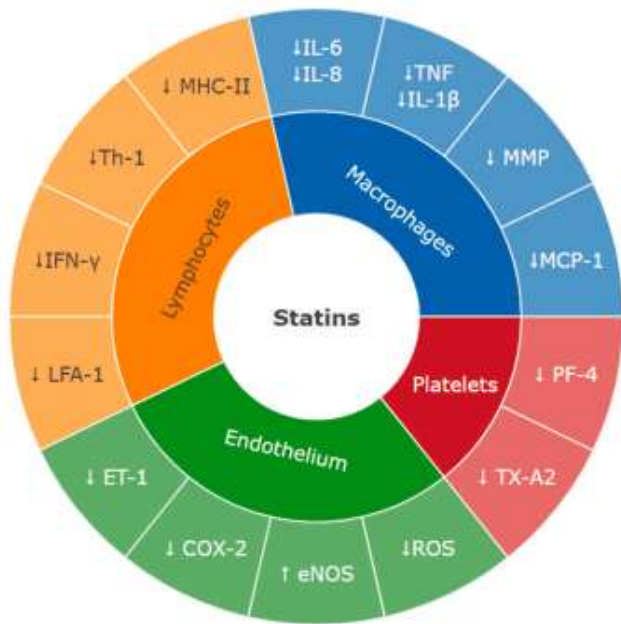
Lancet HIV 2025; 12: e382-92

	Individuals at very high risk of ASCVD	Individuals at high risk of ASCVD	Individuals at low-to-moderate risk of ASCVD
Level of ASCVD risk	Individuals with established ASCVD or diabetes with target organ damage or severe CKD (eGFR <30 mL/min/1.73 m ²) or SCORE2 ≥ 10% or >7.5% if younger than 50 years	Individuals with SCORE2 ≥5% to <10% or ≥2.5% if younger than 50 years	Individuals with SCORE2 <5%
Statin therapy recommendations	High-intensity statin therapy consisting of atorvastatin (40 mg or 80 mg) once daily, or rosuvastatin (20 mg or 40 mg) once daily	Moderate or high-intensity statin therapy are recommended depending on ASCVD risk category. High-intensity statin therapy* consisting of atorvastatin (40 mg or 80 mg) once daily, rosuvastatin (20 mg or 40 mg) once daily; or moderate-intensity statin therapy† consisting of pitavastatin (4 mg) once daily, atorvastatin (20 mg) once daily, or rosuvastatin (10 mg) once daily	Moderate-intensity statin therapy might be considered, consisting of pitavastatin (4 mg), atorvastatin (20 mg) once daily, or rosuvastatin (10 mg) once daily; shared medical decision between health-care professional and patient
Additional notes	LDL cholesterol target values <55 mg/dL (1.4 mmol/L) and 50% decrease from baseline LDL cholesterol values	LDL cholesterol target goal <70 mg/dL (1.8 mmol/L) and 50% decrease from baseline LDL cholesterol values	N/A

These recommendations are for people aged ≥40 years with HIV, stratified according to ASCVD risk. EACS=European AIDS Clinical Society. ASCVD=atherosclerotic cardiovascular disease. CKD = chronic kidney disease. LDL=low-density lipoprotein. N/A=not applicable. *High-intensity statin is recommended in individuals with at least one markedly elevated risk factors, in particular: total cholesterol >8 mmol/L (>310 mg/dL), LDL cholesterol >4.9 mmol/L (>190 mg/dL), or blood pressure ≥ 180/110 mmHg; individuals with familial hypercholesterolemia without other major risk factors; people who have had diabetes for at least 10 years or another additional risk factor without target organ damage; moderate chronic kidney disease (estimated glomerular filtration rate 30–59 mL/min/1.73m²); and SCORE2 ≥ 7.5% in people younger than 50 years, ≥10% in people aged 50–69 years, and ≥15% in people aged 70 years or older. †For individuals not considered as per the criteria listed, moderate-intensity statin is recommended.

Dyslipidemia and statin use in people with HIV-1 infection: beyond the lipid-lowering effect

Nutrition, Metabolism and Cardiovascular Diseases 35 (2025) 104110

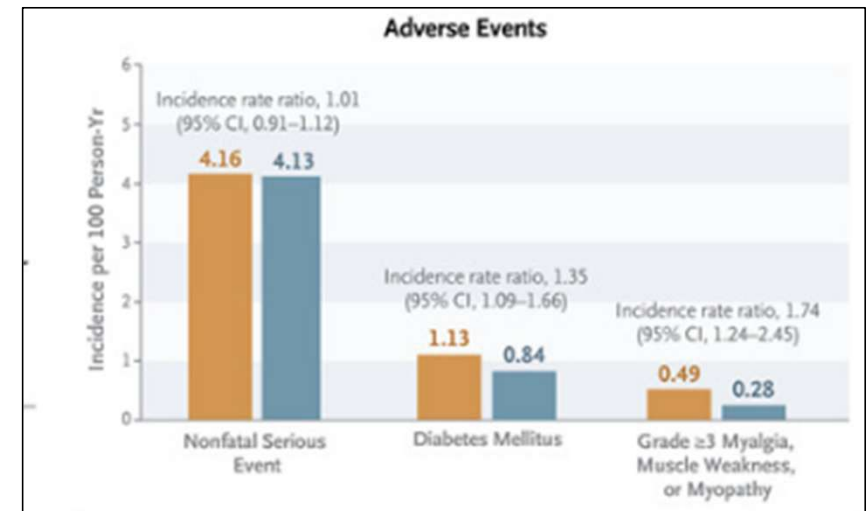
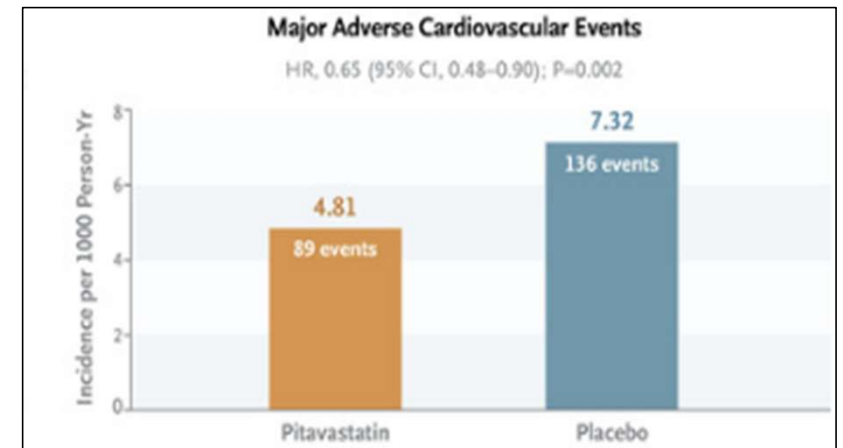


ART Class	Drug	Statin							
		Atorvastatin	Ezetimibe	Fluvastatin	Lovastatin	Pitavastatin	Pravastatin	Rosuvastatin	Simvastatin
Entry, Attachment and Capsid Inhibitors	Albuvirtide (ABT)	✓	✓	✓	✓	✓	✓	✓	✓
	Enfuvirtide (ENF)	✓	✓	✓	✓	✓	✓	✓	✓
	Fostemsavir (FTR)	I	✓	I	I	I	✓	I	I
	Ibalizumab-uiyk (IBA)	✓	✓	✓	✓	✓	✓	✓	✓
	Lenacapavir	W	✓	✓	I	✓	✓	W	I
	Maraviroc (MVC)	✓	✓	✓	✓	✓	✓	✓	✓
	Bictegravir/Emtricitabine/Tenofovir alafenamide (BIC/FTC/TAF)	✓	✓	✓	✓	✓	✓	✓	✓
Integrase Inhibitors	Cabotegravir [oral] (CAB oral)	✓	✓	✓	✓	✓	✓	✓	✓
	Cabotegravir PrEP [long acting] (CAB LA, PrEP)	✓	✓	✓	✓	✓	✓	✓	✓
	Cabotegravir/rilpivirine [long acting] (CAB/RPV LA)	✓	✓	✓	✓	✓	✓	✓	✓
	Dolutegravir (DTG)	✓	✓	✓	✓	✓	✓	✓	✓
	Dolutegravir/ Lamivudine/ Tenofovir-DF (DTG/3TC/TDF)	✓	✓	✓	✓	✓	✓	✓	✓
	Dolutegravir/Abacavir/ Lamivudine (DTG/ABC/3TC)	✓	✓	✓	✓	✓	✓	✓	✓
	Dolutegravir/Lamivudine (DTG/3TC)	✓	✓	✓	✓	✓	✓	✓	✓
	Dolutegravir/Rilpivirine (DTG/RPV)	✓	✓	✓	✓	✓	✓	✓	✓
	Elvitegravir/Cobicistat/ Emtricitabine/Tenofovir alafenamide (EVG/e/FTC/TAF)	I	✓	I	⊗	W	I	✓	⊗

ART Class	Drug	Statin							
		Atorvastatin	Ezetimibe	Fluvastatin	Lovastatin	Pitavastatin	Pravastatin	Rosuvastatin	Simvastatin
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)	Elvitegravir/Cobicistat/ Emtricitabine/Tenofovir-DF (EVG/e/FTC/TDF)	I	✓	I	⊗	W	I	✓	⊗
	Raltegravir (RAL)	✓	✓	✓	✓	✓	✓	✓	✓
	Dapivirine (DPV, PrEP)	✓	✓	✓	✓	✓	✓	✓	✓
	Dolutegravir/Rilpivirine (DTG/RPV)	✓	✓	✓	✓	✓	✓	✓	✓
	Doravirine (DOR)	✓	✓	✓	✓	✓	✓	✓	✓
	Doravirine/Lamivudine/ Tenofovir-DF (DOR/3TC/TDF)	✓	✓	✓	✓	✓	✓	✓	✓
	Efavirenz (EFV)	I	✓	W	I	✓	W	✓	I
	Etravirine (ETR)	W	✓	W	I	✓	W	✓	I
	Nevirapine (NVP)	W	✓	✓	I	✓	✓	✓	I
	Rilpivirine (RPV)	✓	✓	✓	✓	✓	✓	✓	✓
Nucleoside or Nucleotide Analogues (NRTIs)	Rilpivirine/ Emtricitabine/ Tenofovir alafenamide (RPV/FTC/TAF)	✓	✓	✓	✓	✓	✓	✓	✓
	Rilpivirine/ Emtricitabine/ Tenofovir-DF (RPV/FTC/TDF)	✓	✓	✓	✓	✓	✓	✓	✓
	Abacavir (ABC)	✓	✓	✓	✓	✓	✓	✓	✓
	Emtricitabine (FTC)	✓	✓	✓	✓	✓	✓	✓	✓
	Emtricitabine/Tenofovir alafenamide (FTC/TAF)	✓	✓	✓	✓	✓	✓	✓	✓
	Emtricitabine/Tenofovir alafenamide for PrEP (FTC/TAF, PrEP)	✓	✓	✓	✓	✓	✓	✓	✓
	Emtricitabine/Tenofovir-DF (FTC/TDF, PrEP)	✓	✓	✓	✓	✓	✓	✓	✓
	Lamivudine (3TC)	✓	✓	✓	✓	✓	✓	✓	✓
Protease Inhibitors (PIs)	Tenofovir-DF (TDF)	✓	✓	✓	✓	✓	✓	✓	✓
	Zidovudine (AZT, ZDV)	✓	✓	✓	✓	✓	✓	✓	✓
Protease Inhibitors (PIs)	Atazanavir + ritonavir (ATV/r)	I	I	W	⊗	W	I	I	⊗
	Atazanavir alone (ATV)	I	I	W	⊗	W	I	I	⊗
	Atazanavir/cobicistat (ATV/c)	I	I	W	⊗	W	I	I	⊗
	Darunavir + ritonavir (DRV/r)	I	W	W	⊗	✓	I	I	⊗
	Darunavir/cobicistat (DRV/c)	I	W	W	⊗	W	I	I	⊗
	Darunavir/Cobicistat/ Emtricitabine/Tenofovir alafenamide (DRV/c/FTC/TAF)	I	W	W	⊗	W	I	I	⊗
	Lopinavir/ritonavir (LPV/r)	I	✓	✓	⊗	✓	✓	I	⊗
	Ritonavir (RTV)	I	✓	✓	⊗	✓	✓	I	⊗

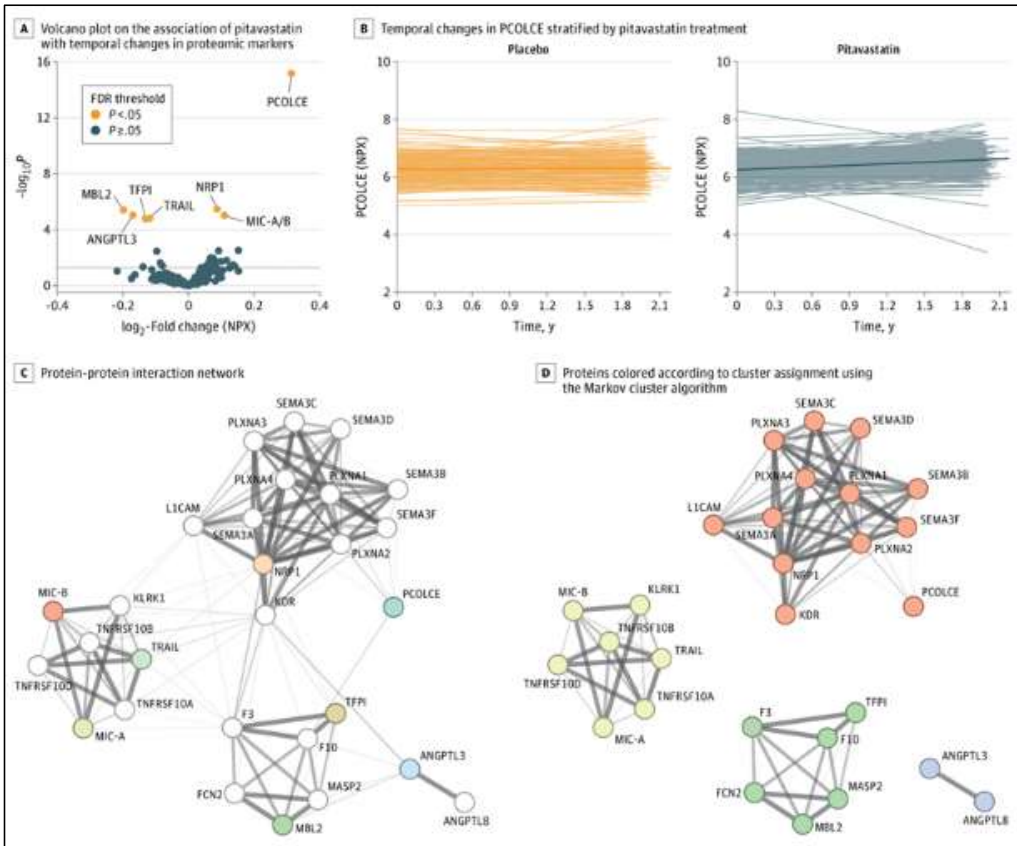
Pitavastatina y MACE en PVVIH (estudio REPRIEVE)

- ❑ Fase 3. Multinacional. ECA controlado con placebo
- ❑ VIH con tratamiento antiretroviral estable
- ❑ Bajo y moderado RCV
- ❑ Pitavastatina 4 mg
- ❑ N=7769 (40-75 años)
- ❑ Mediana LDL: 108 mg/dl
- ❑ MACE (*muerte CV, IAM, ingreso por angor inestable, ACV, AIT, EAP, revascularización o muerte de causa indeterminada*)
- ❑ Seguimiento: 5,1 años

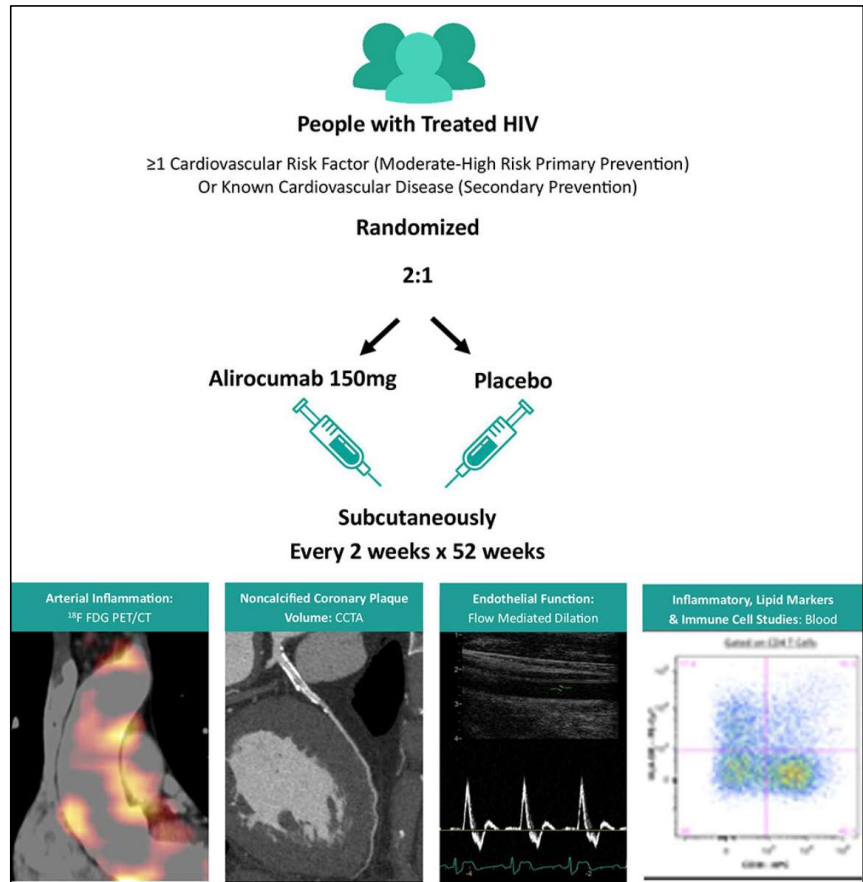


Pitavastatin, Procollagen Pathways, and Plaque Stabilization in Patients With HIV

A Secondary Analysis of the REPRIEVE Randomized Clinical Trial



Rationale, design, and baseline characteristics of the Effect of PCSK9 Inhibition on Cardiovascular Risk in Treated HIV Infection: EPIC-HIV Randomized Clinical Trial



Más allá de las Estatinas: Terapia Combinada

Ezetimibe

Seguro y eficaz.

Reduce LDL (~24 mg/dL) sin interacciones con el TAR.

Ideal cuando no se alcanzan objetivos con dosis máximas de estatinas.



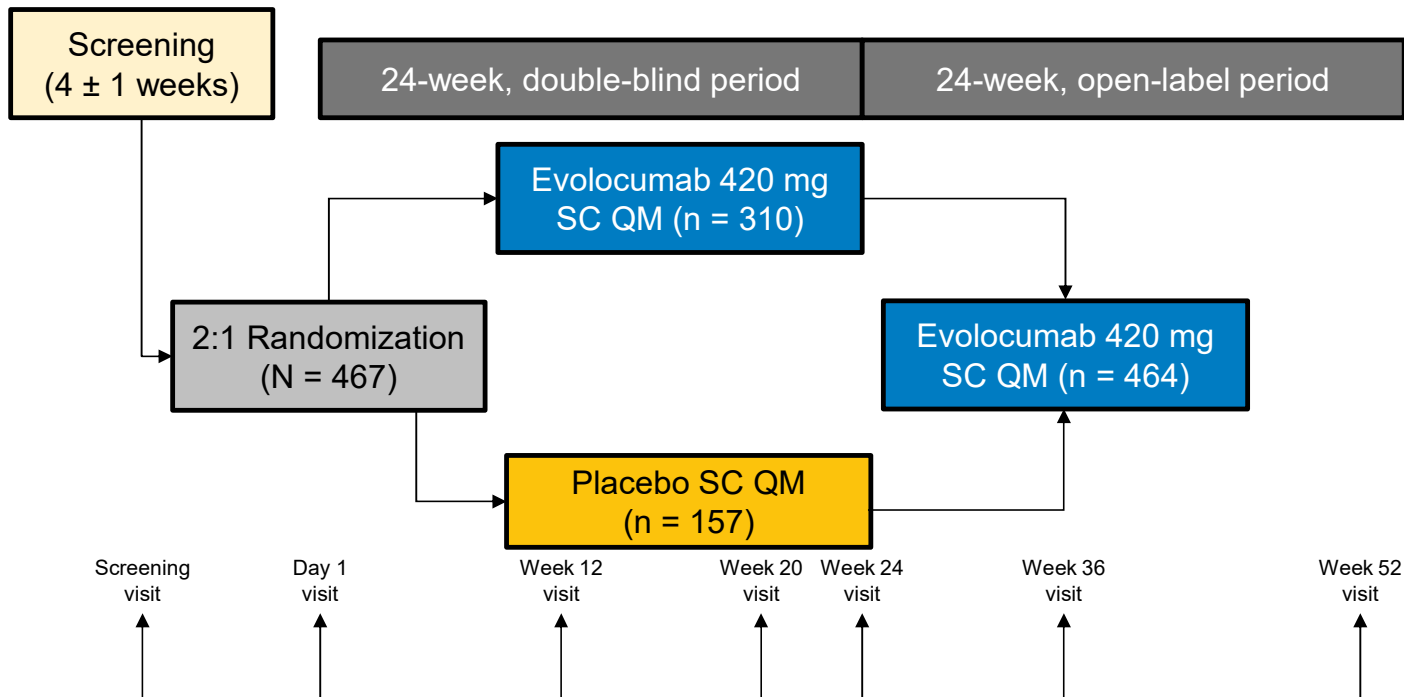
Manejo de Hipertrigliceridemia

Tratar si TG > 500 mg/dL (Riesgo Pancreatitis).



- **Fibratos:** Preferir Fenofibrato (menos riesgo muscular que Gemfibrozilo).
- **Omega-3:** Icosapento de etilo como adyuvante.

Evolocumab Effect on LDL-C Lowering in Subjects with Human Immunodeficiency Virus and Increased Cardiovascular Risk (BEIJERINCK)



Objective

- To assess the lipid-lowering efficacy and safety of evolocumab in patients with HIV and hypercholesterolemia and mixed dyslipidemia

BEIJERINCK Study: Evolocumab

BEIJERINCK study: PVVIH

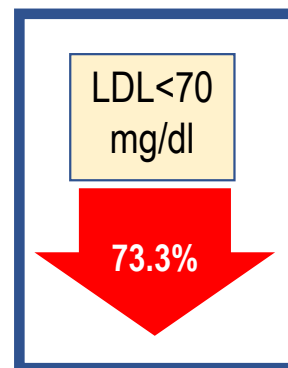
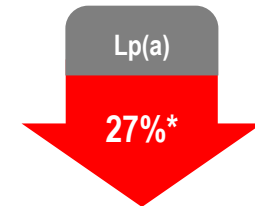
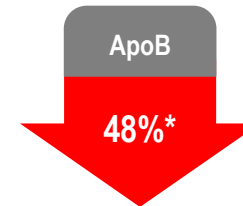


Estatina ▶ 79%

Ezetimibe ▶ 19%

Intolerancia o contraindicación a estatina ▶ 21%

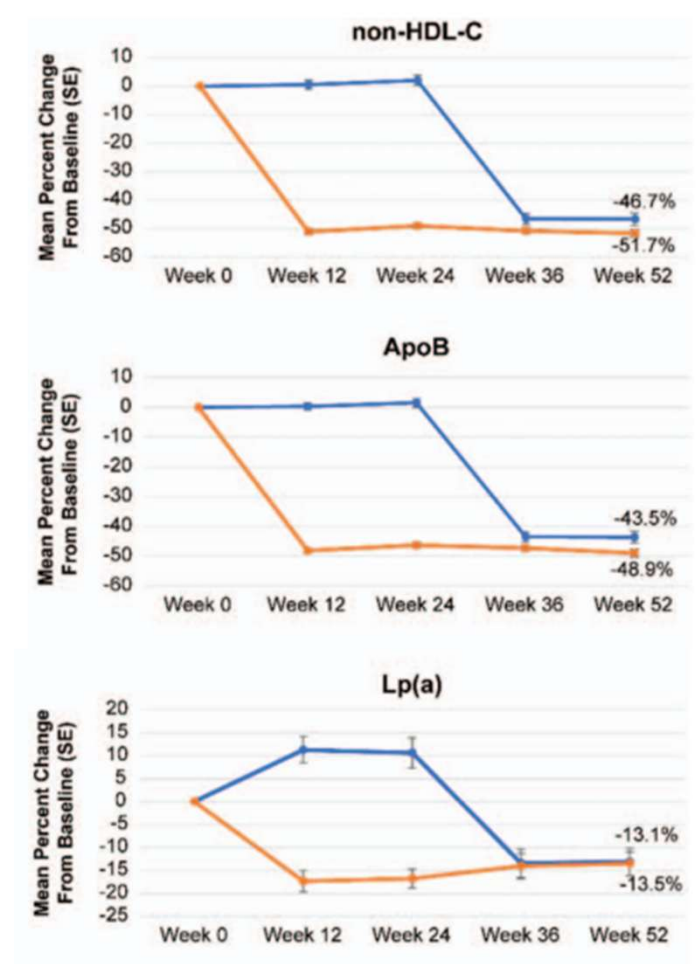
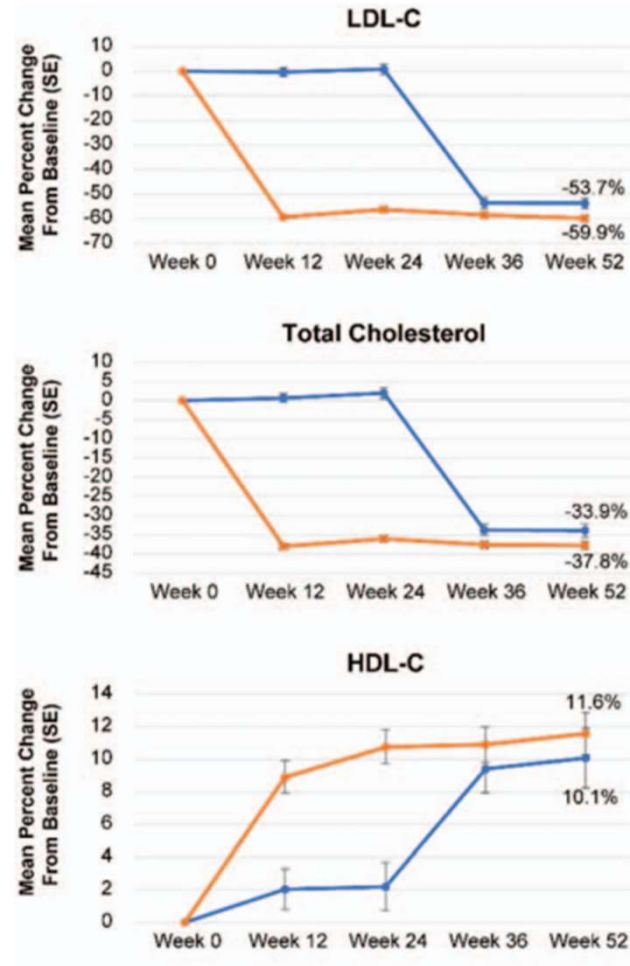
Evolocumab reduce significativamente los parámetros lipídicos respecto a placebo (basal vs. semana 24)



* % medio de cambio tras corregir por placebo

Long-term effects of evolocumab in participants with HIV and dyslipidemia: results from the open-label extension period

N=451 (OLE)
P → E (152)
E → E (299)



Tratamientos emergentes

Ácido Bempedoico

Inhibidor de ATP-citrato liasa. Profármaco activado en el hígado, ideal para pacientes con intolerancia muscular a las estatinas.



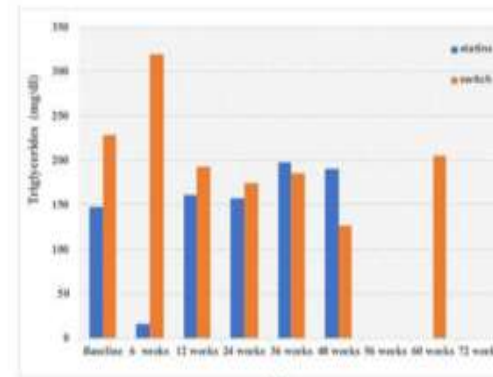
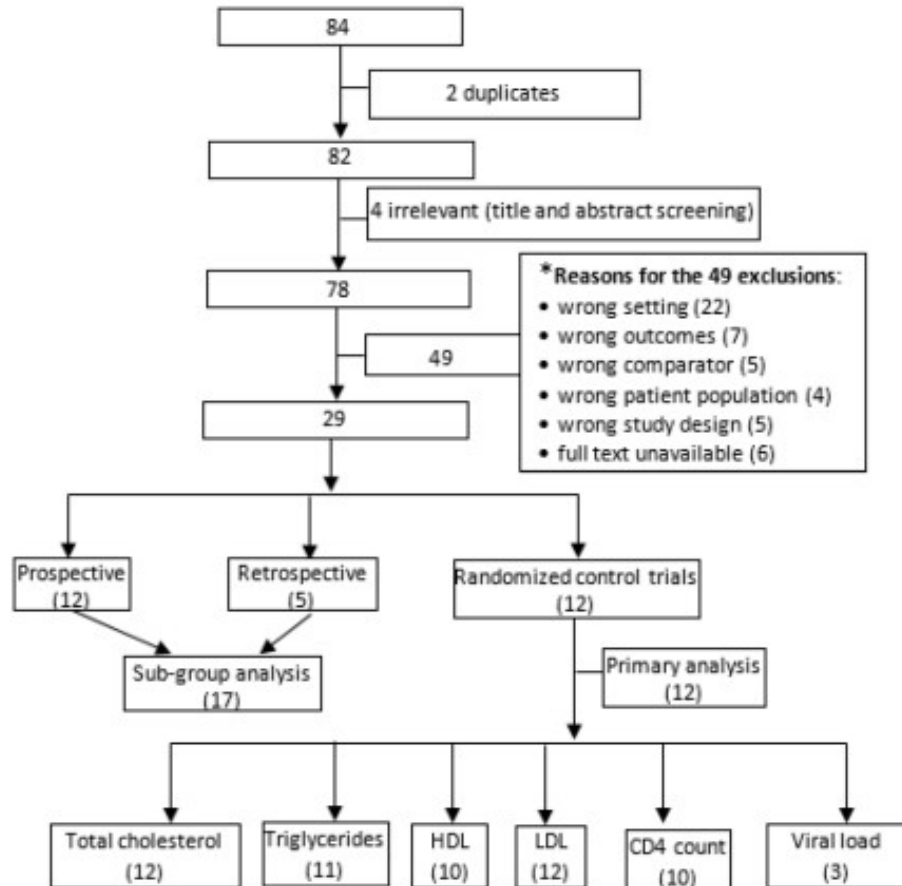
Inclisiran

Terapia de interferencia de ARN (siRNA).
Administración semestral.
Prometedor para mejorar la adherencia a largo plazo.

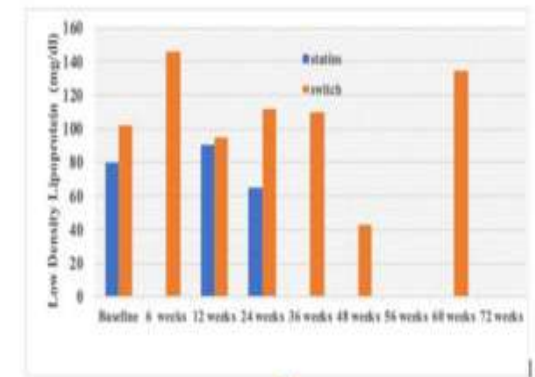


Comparison of Switching Between Antiretroviral Agents Versus Introducing Lipid-lowering Agents for HAART-induced Dyslipidemia

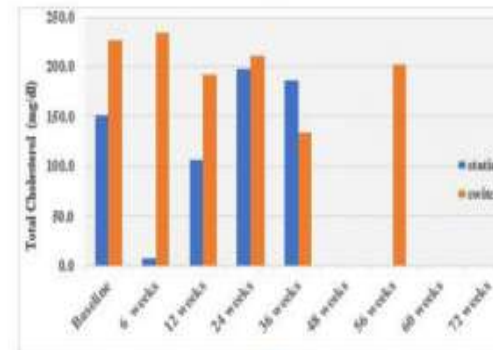
Clinical Therapeutics 46 (2024) e114–e124



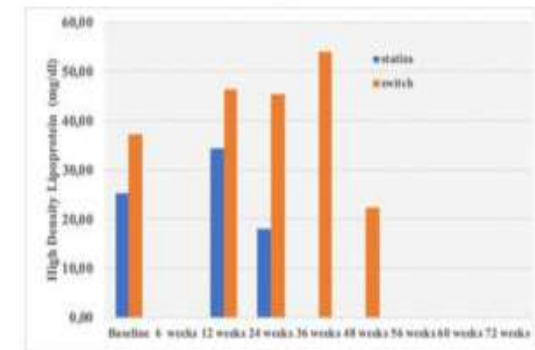
(a)



(b)



(c)



(d)

Las estatinas fueron tan eficaces como el cambio de terapias antirretrovirales en el manejo a corto plazo del CT y los triglicéridos en pacientes con dislipidemia inducida por TAR

Estrategia 1: Optimización del TAR (Switching)

Régimen Tóxico



- Regímenes basados en IPs (Lopinavir/r)
- Efavirenz

Considerar Cambio
(Si es virológicamente seguro)

Régimen Optimizado



- Inhibidores de Integrasa (INSTIs)
- Doravirina

! Precaución:

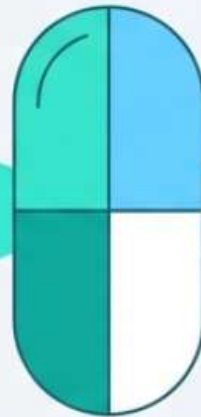
Cambiar de TDF a TAF puede elevar el colesterol al perderse el efecto lipo-reductor del TDF.

A menudo, añadir una estatina es más efectivo y seguro que cambiar un TAR exitoso.

Estrategia 2: Estatinas y el Poder de la Pleiotropía

Reducción de Lípidos

Disminución efectiva del
LDL-C.



Reducción de Inflamación

Disminución de marcadores de
activación inmune (sCD14, LDL
oxidado).

Estudio INTREPID: Pitavastatina redujo marcadores inflamatorios vs. Pravastatina.
Estudio SATURN-HIV: Rosuvastatina frenó la progresión del grosor íntima-media carotídeo.

Conclusiones

Dislipidemia en Personas que Viven con VIH (PVVIH): Riesgo Cardiovascular y Manejo Clínico

Epidemiología y Carga: Un Riesgo Cardiovascular Duplicado

PVVIH (con VIH): RIESGO DE ENFERMEDAD CARDIOVASCULAR CASI EL DOBLE

REFERENCIA

PREVALENCIA DE DISLIPIDEMIA: ~40% de las PVVIH

MUJERES CON VIH: Tasa de Riesgo Relativo de Infarto de Miocardio **2.98** (vs. Control Sin VIH)

HOMBRES CON VIH: Tasa **1.40** (vs. Control Sin VIH)

Fisiopatología: Alteraciones Lipídicas e Inflamación

La infección por VIH reduce HDL, luego reduce LDL. Al iniciar TAR, LDL y Triglicéridos aumentan, HDL suele permanecer bajo.

PRESENCIA DE LDL PEQUEÑO Y DENSO: Proaterogénicas, se oxidan fácilmente, penetran pared arterial, forman placas vulnerables y no calcificadas.

LIPODISTROFIA ASOCIADA AL VIH: Resistencia a la insulina, esteatosis hepática y redistribución de grasa corporal, potenciado por TAR.

LIPODISTROFIA ASOCIADA AL VIFIH: Resistencia a la insulina, esteatosis hepática y redistribución de per TAR.

Potencial de Dislipidemia por Clase de TAR

CLASE DE FÁRMACO	POTENCIAL DE DISLIPIDEMIA	EJEMPLOS
IP (Inhibidores de Proteasa)	**Alto	Lopinavir/r, Tipranavir/r
ITRNN (No nucleósidos)	Bajo/Intermedio	Nevirapine (Rajo), Efavirenz (Intermedio)
ITRN (Nucleósidos)	Intermedio	Tenofovir alafenamide, Zidovudina
Insti (Integrasa)	Bajo	Dolutegravir, Bictegravir
Antagonistas CCRS	Bejo	Maraviroc

Evaluación del Riesgo y Cribado

Calculadoras convencionales (e.g., Framingham) suelen subestimar el riesgo. **VIH = Potenciador de riesgo**

MOMENTO DEL CRIBADO: Al diagnóstico, 1-3 meses tras iniciar TAR, cada 6-12 meses (con factores de riesgo)

PUNTUACIÓN DE CALCIO CORONARIO (CAC): Refina riesgo fronterizo (5%-7.5%) para decidir inicio de estatinas.

Estrategias de Tratamiento y Manejo: Piedra Angular y DDIs

ESTATINAS: Reducen LDL, inflamación arterial y volumen de placa no calcificado.

INTERACCIONES MEDICAMENTOSAS (DDI): IPs y cobicistat inhiben CYP3A4, aumentando niveles de ciertas estatinas.

Guía Rápida de Estatinas en PVVIH

ESTATINA	RECOMENDACIÓN	NOTA DE SEGURIDAD
Pitavastatina	Proferida (Dosis estándar)	Sin interacciones significativas con IP/sobicistat.
Rosuvastatina	Usar dosis bajas (≤ 10 mg)	Iniciar con cautela si se usa con ciertos IP.
Atorvastatina	Usar dosis bajas (≤ 30 mg)	Evitar con Tipranavir; precaución con otros IP.
Simvastatina	CONTRAINDICADA	Alto riesgo de toxicidad muscular con IP.
Ezetimibe	Complemento seguro	Útil si no se alcanza la meta con estatinas.



GRAZAS

