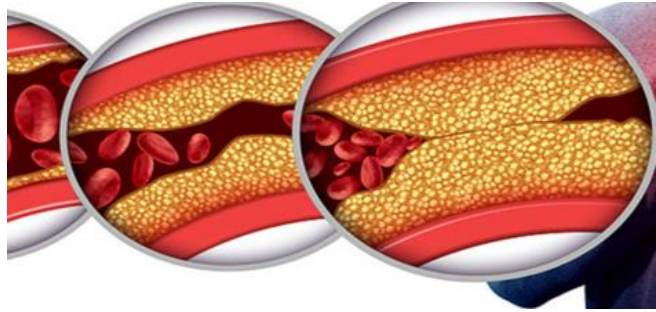


Sesión biobliográfica MI-CAULE

.. Antiagregación en diferentes situaciones.

.. Inhibidores de la proteína de transferencia de ésteres de colesterol (CETP)

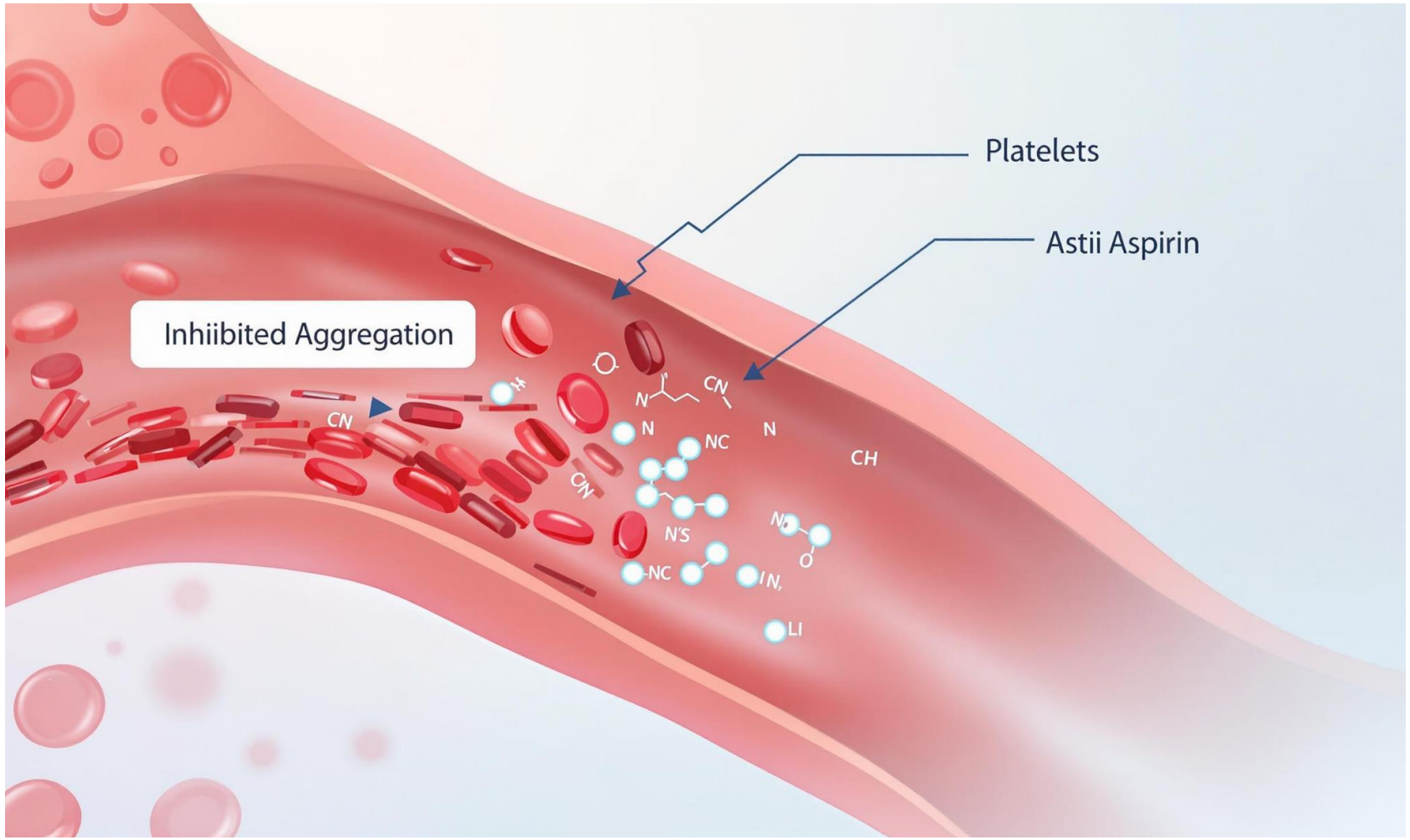
¿ Dónde estamos ?

Christian Teijo Núñez
Unidad HTA y Riesgo Vascular
M. Interna (CAULE)

Junta de Castilla y León · Sacyl · Complejo Asistencial Universitario de León

07/03/2025

Antiagregación en prevención primaria



2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

Recommendations for Aspirin Use

Referenced studies that support recommendations are summarized in Online Data Supplements 17 and 18.

COR	LOE	Recommendations
IIb	A	1. Low-dose aspirin (75-100 mg orally daily) might be considered for the primary prevention of ASCVD among select adults 40 to 70 years of age who are at higher ASCVD risk but not at increased bleeding risk.[S4.6-1–S4.6-8]
III: Harm	B-R	2. Low-dose aspirin (75-100 mg orally daily) should not be administered on a routine basis for the primary prevention of ASCVD among adults >70 years of age.[S4.6-9]
III: Harm	C-LD	3. Low-dose aspirin (75-100 mg orally daily) should not be administered for the primary prevention of ASCVD among adults of any age who are at increased risk of bleeding.[S4.6-10]

40 -70 años

> 70 años

JACC VOL. 74, NO. 10, 2019
SEPTEMBER 10, 2019:e177–232

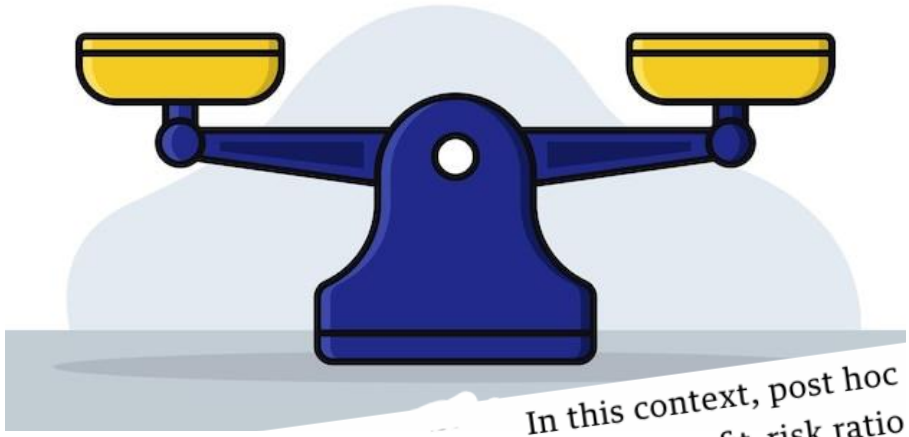
Aspirina en prevención primaria. IIb.

Hombres y mujeres de 40 - 70 años y al menos uno de:

- Antecedentes familiares de ASCVD prematura
- Hipertensión
- Dislipidemia
- Diabetes

CI:

- Hemorragia gastrointestinal o de otros sitios.
- **Edad >70 años.**
- Trombocitopenia, coagulopatía.
- ERC.
- Uso concomitante AINE´s, Cc´s, ACOD.



In this context, post hoc study of older trials suggests that the benefit-risk ratio for prophylactic aspirin generally becomes more favorable at >10% estimated 10-year ASCVD risk (S4.6-15,

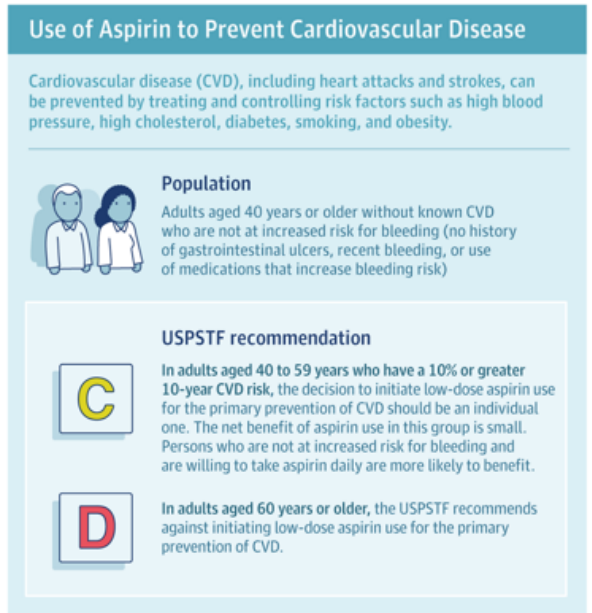
JACC VOL. 74, NO. 10, 2019
SEPTEMBER 10, 2019:e177-232

U.S. Preventive Services TASK FORCE

JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

Aspirin Use to Prevent Cardiovascular Disease
US Preventive Services Task Force Recommendation Statement

JAMA. 2022;327(16):1577-1584. doi:10.1001/jama.2022.4983



C: … AAS en 40 -60 a. **y RCV alto:**
y esperanza de vida ≥ 10 años
y dispuestos a tomar AAS 10 años

ARTÍCULO ESPECIAL

Estándares de la Sociedad Española de Arteriosclerosis 2024 para el control global del riesgo vascular

1º → Controlar FRCV.

2º → se "sugiere " AAS en 40 -70 a. **y RCV alto:**

Antiagregación en prevención primaria + HTA

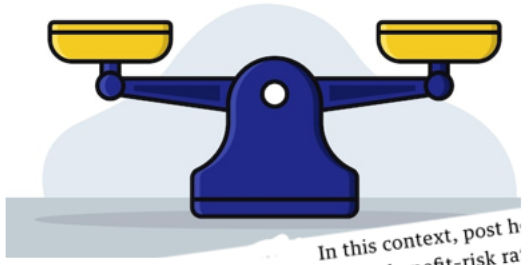
American Heart Association.

2023 ESH Guidelines for the management of arterial hypertension

Aspirina en prevención primaria. IIb.

Hombres y mujeres de 40 - 70 años y al menos uno de

- Antecedentes familiares de ASCVD prematura
- Hipertensión
- Dislipidemia
- Diabetes



In this context, post h
study of older trials suggests that the benefit-risk ra
for prophylactic aspirin generally becomes m
favorable at >10% estimated 10-year ASCVD risk (S4.6

Recommendations of antiplatelet therapy in hypertension

Recommendations and statements	CoR	LoE
Low-dose aspirin is not recommended for primary prevention in patients with hypertension.	III	A
Antiplatelet therapy is recommended for secondary prevention in hypertensive patients.	I	A
Use of a polypill containing low-dose aspirin can be considered in hypertensive patients for secondary prevention.	II	A

Antiagregación en prevención primaria + DM2

2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes

Recommendation Table 12 — Recommendations for patients with diabetes without a history of symptomatic atherosclerotic cardiovascular disease or revascularization

Recommendation	Class[a]	Level[b]
En adultos con DM2 sin antecedentes de ASCVD sintomática o revascularización, se puede considerar el AAS (75-100 mg/24h) para prevenir el primer evento vascular grave, en ausencia de contraindicaciones claras.	IIb	A

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ESC European Society of Cardiology
European Heart Journal (2023) **00**, 1–98
https://doi.org/10.1093/eurheartj/ehad192

DM2 – Antiagregación:

Standards of Care in Diabetes 2025

American Diabetes Association.

ISSN 0149-5992

Prevención secundaria:

Aspirina (75-162 mg/día) como estrategia de prevención secundaria en aquellos con diabetes y antecedentes de enfermedad cardiovascular aterosclerótica (ASCVD). A.

La terapia combinada con aspirina más rivaroxabán en dosis baja debe considerarse para individuos con enfermedad coronaria y/o arterial periférica (EAP) estable y bajo riesgo de sangrado, para prevenir eventos adversos mayores de extremidades y cardiovasculares. A.

Prevención primaria:

Aspirina (75-162 mg/día) puede considerarse como una estrategia de prevención primaria en aquellos con diabetes que tienen un riesgo cardiovascular aumentado, después de una discusión exhaustiva con el individuo sobre los beneficios / riesgo. A.

Prevención primaria + DM2:

Aspirina (75-162 mg/día) puede considerarse como una estrategia de prevención primaria en aquellos con diabetes que tienen un riesgo cardiovascular aumentado, después de una discusión exhaustiva con el individuo sobre los beneficios / riesgo. A.

- **Aspirina en prevención primaria. A. :**
- Hombres y mujeres de ≥ 50 años con diabetes y al menos un factor de riesgo importante adicional:

- Antecedentes familiares de ASCVD prematura

- Hipertensión

- Dislipidemia

- Tabaquismo

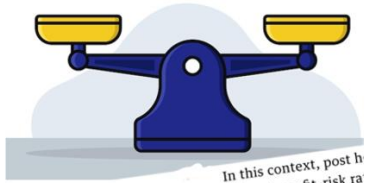
- ERC / albuminuria

American Heart Association.

Aspirina en prevención primaria. IIb.

Hombres y mujeres de 40 - 70 años y al menos uno de

- Antecedentes familiares de ASCVD prematura
- Hipertensión
- Dislipidemia
- Diabetes



In this context, post h
study of older trials suggests that the benefit-risk ra
for prophylactic aspirin generally becomes m
favorable at >10% estimated 10-year ASCVD risk (S4.6

Effects of Aspirin for Primary Prevention in Persons with Diabetes Mellitus

The ASCEND Study Collaborative Group*

ASCEND, 2018[47]	15 480 Patients aged ≥40 years with diabetes, no evident CVD, and substantial uncertainty about whether antiplatelet therapy would confer worthwhile benefit. Low-dose ASA vs. placebo	Non-fatal MI, non-fatal stroke (excluding confirmed ICH), TIA, or death from any vascular cause (excluding confirmed ICH)	Predicted incidence: 1.2–1.3%/year Observed incidence: 1.3%/year Predicted relative reduction: 15% Observed relative reduction: 12%	No difference in fatal bleeding and ICH

Tabla 1: Características Basales de los Participantes en ASCEND

Característica	Aspirina (N=7740)	Placebo (N=7740)
Edad (media)	63.2 ± 9.2	63.3 ± 9.2
Sexo masculino (%)	62.6	62.5
Duración de diabetes (años)	7 (3-13)	7 (3-13)
Uso de estatinas (%)	75.6	74.9

Tabla 2: Eventos Vasculares y Hemorrágicos en ASCEND

Tipo de Evento	Aspirina (%)	Placebo (%)	Razón de tasas (95% CI)
Eventos vasculares serios	8.5	9.6	0.88 (0.79-0.97)
Hemorragias mayores	4.1	3.2	1.29 (1.09-1.52)

Tabla 1: Eventos de Sangrado en el Estudio ASCEND

Tipo de Sangrado	Aspirina (N=7740)	Placebo (N=7740)	Razón de tasas (95% CI)	P-valor
Total de eventos de sangrado	314 (4.1%)	245 (3.2%)	1.29 (1.09-1.52)	0.003
Sangrado fatal	19 (0.2%)	16 (0.2%)	1.19 (0.63-2.25)	0.6
Sangrado gastrointestinal	137 (1.8%)	101 (1.3%)	1.36 (1.05-1.75)	0.02
Sangrado intracraneal	55 (0.7%)	45 (0.6%)	0.98 (0.80-1.19)	0.5
Sangrado ocular (amenazante)	57 (0.7%)	64 (0.8%)	0.88 (0.62-1.27)	0.7
Otros sangrados mayores	74 (1.0%)	43 (0.6%)	1.70 (1.18-2.44)	0.003

Hemorragia grave : Evento hemorrágico que resultó en hospitalización o transfusión o que fue mortal)

tratamiento a largo plazo, de 7.4 años, con aspirina.

N Engl J Med 2018;379:1529-39.
DOI: 10.1056/NEJMoa1804988

Parámetro	Aspirina (100 mg)	Placebo	Diferencia absoluta (%)
Eventos cardiovasculares	8.5%	9.6%	-1.1%
Hemorragias mayores	4.1%	3.2%	+0.9%
NNT (eventos prevenidos)	91	-	-
NNH (hemorragias causadas)	112	-	-

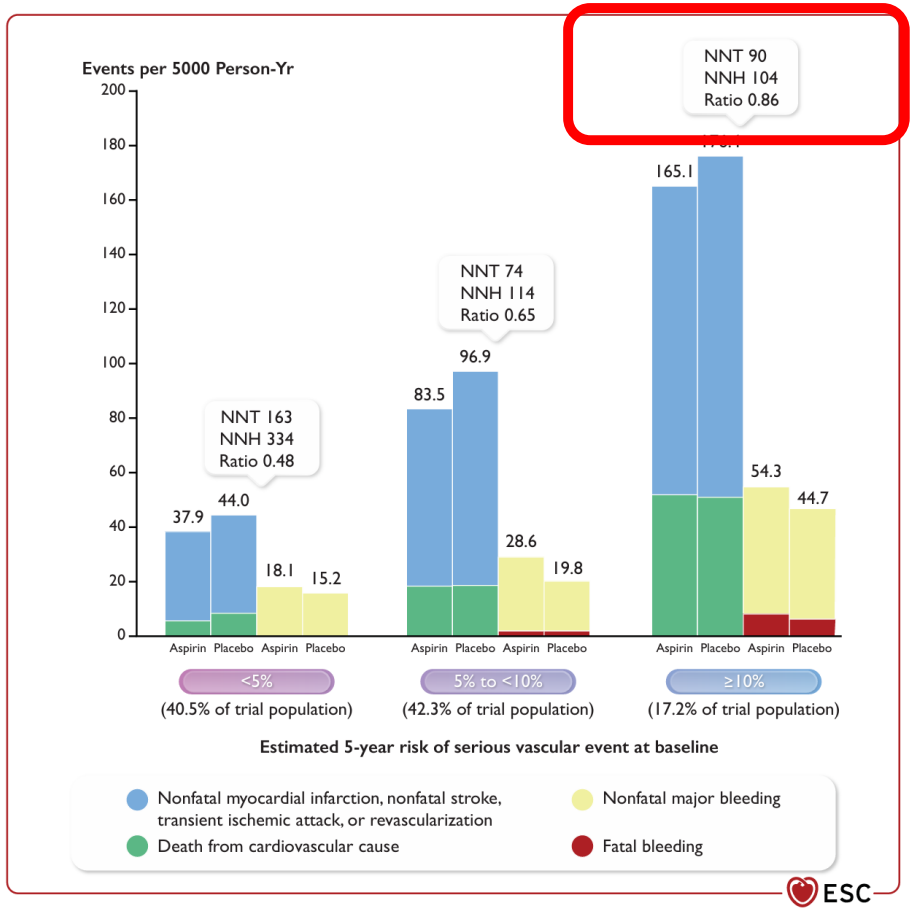


Figure S7 Observed absolute effect in aspirin and placebo groups for serious vascular events, including major bleeding or revascularization. ASCEND, A Study of Cardiovascular Events iN Diabetes; NNH, number needed to harm; NNT, number needed to treat; yr, year. The figure shows the efficacy and safety outcomes in three sub-groups of patients stratified according to the estimated risk of serious vascular events at baseline. The number needed to treat (NNT) and number needed to harm (NNH) are shown in each group, showing no clear difference in the benefit-risk balance according to the baseline risk stratification. The net benefit in each group favours NNT over NNH (ratio NNT:NNH <1). Figure modified from The ASCEND Study Collaborative Group.[47]

Hemorragia grave : Evento hemorrágico que resultó en hospitalización o transfusión o que fue mortal)

Effects of Aspirin for Primary Prevention in Persons with Diabetes Mellitus

The ASCEND Study Collaborative Group*

N Engl J Med 2018;379:1529-39.
DOI: 10.1056/NEJMoa1804988

Standards of Care in Diabetes 2025

American Diabetes Association.

ISSN 0149-5992

- **Aspirina en prevención primaria + DM2. A.**
- Hombres y mujeres de ≥ 50 años con diabetes y al menos un factor de riesgo importante adicional:

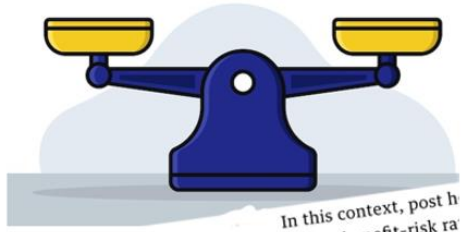
- Antecedentes familiares de ASCVD prematura
- Hipertensión
- Dislipidemia
- Tabaquismo
- ERC / albuminuria

American Heart Association.

Aspirina en prevención primaria. IIb.

Hombres y mujeres de 40 - 70 años y al menos uno de

- Antecedentes familiares de ASCVD prematura
- Hipertensión
- Dislipidemia
- Diabetes



In this context, post h
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for prophylactic aspirin generally becomes m
favorable at ~10% estimated 10-year ASCVD risk (S4.6

Effects of Aspirin for Primary Prevention in Persons with Diabetes Mellitus

The ASCEND Study Collaborative Group*

Total Sangrado: 1.29
Sangrado GI: 1.36

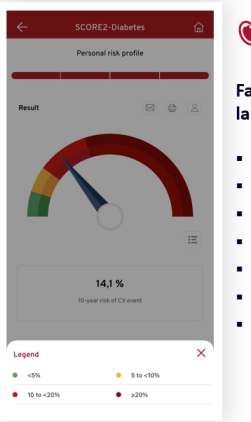
Empleo IBP: 24%

No difference in fatal bleeding and ICH

MACE: 0.88

Duración: 7.4 años con aspirina.

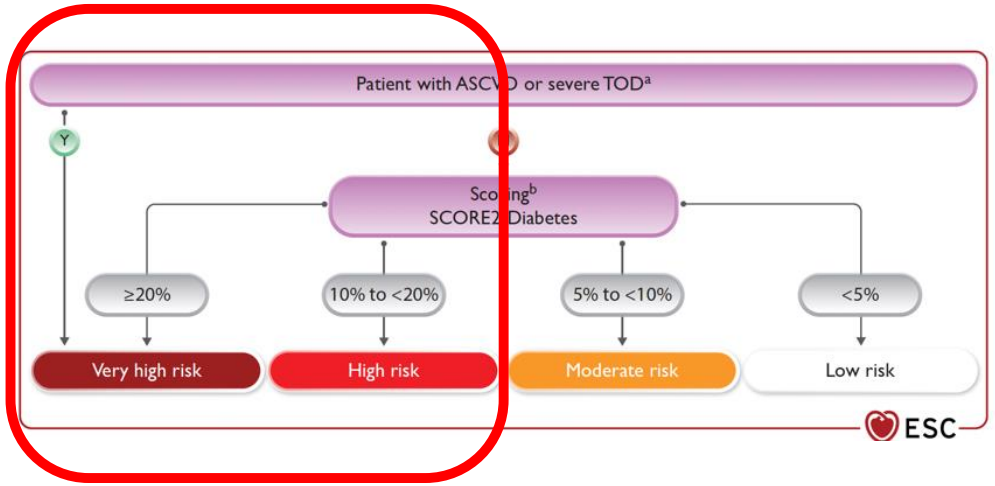
Calculadora de riesgo CV



ESC European Society of Cardiology

Factores a tener en cuenta en la SCORE2-Diabetes:[2]

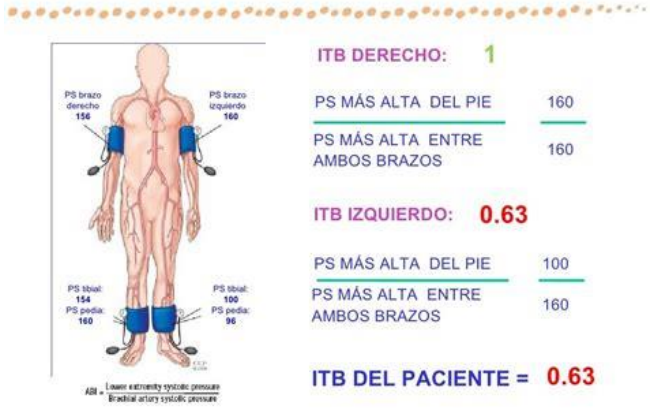
- Edad al diagnóstico de diabetes
- Hábito tabáquico
- Presión arterial sistólica (mmHg)
- Colesterol total (mmol/L)
- c-HDL (mmol/L)
- HbA_{1c} (mmol/mol)
- TFGe (mL/min/1,73 m^2)



EAEI – AAS:

Recommendation Table 9 — Recommendations for lipid-lowering therapy in patients with peripheral arterial and aortic diseases

Recommendations	Class[a]	Level[b]
In patients with atherosclerotic PAAD, lipid-lowering therapy is recommended.[242,334–336]	I	A
An ultimate LDL-C goal of <1.4 mmol/L (55 mg/dL) and a >50% reduction in LDL-C vs. baseline are recommended in patients with atherosclerotic PAAD.[19,242,246,300,335]	I	A
Statins are recommended in all patients with PAD.[328,329,337,371]	I	A
If the target LDL-C level is not achieved on maximally tolerated statins and ezetimibe, treatment with a PCSK9 inhibitor is recommended in patients with atherosclerotic PAAD, to achieve target values.[372,373]	I	A
If the target LDL-C level is not achieved, a combination of statins and ezetimibe is indicated in patients with atherosclerotic PAAD, to achieve the given target values.[247]	I	B
For statin-intolerant patients with atherosclerotic PAAD, at high CV risk, who do not achieve their LDL-C goal on ezetimibe, it is recommended to add bempedoic acid either alone or in combination with a PCSK9 inhibitor.[361]	I	B
Statins for the reduction of growth and rupture of AAA should be considered.[347–349,352,354]	IIa	B



< 0.9	Enfermedad arterial periférica (EAP). Diagnóstico confirmado.
0.6 - 0.89	EAP leve a moderada. Puede haber claudicación intermitente.
< 0.6	EAP severa. Riesgo de dolor en reposo, úlceras o gangrena.
< 0.4	Isquemia crítica. Urgencia médica.
> 1.4	Arterias no compresibles (calcificación severa). Requiere pruebas adicionales, como ecodoppler.

Recommendation Table 14 — Recommendations for antithrombotic therapy in patients with peripheral arterial disease (see also Evidence Table 6)

Recommendations	Class[a]	Level[b]
Use of antiplatelet therapy with aspirin alone (range 75–160 mg o.d.) or clopidogrel alone (75 mg o.d.) is recommended for the reduction of MACE in patients with symptomatic PAD.[488–490]	I	A
Treatment with combination rivaroxaban (2.5 mg b.i.d.) and aspirin (100 mg o.d.) should be considered for patients with PAD, high ischaemic risk,[c] and non-high bleeding risk.[d,429,498,499]	IIa	A
Aspirin (75–100 mg) for primary prevention may be considered in patients with asymptomatic PAD and DM, in the absence of contraindications.[419,487]	IIb	A
It is not recommended to systematically treat patients with asymptomatic PAD without any sign of clinically relevant ASCVD with antiplatelet drugs.[485]	III	B

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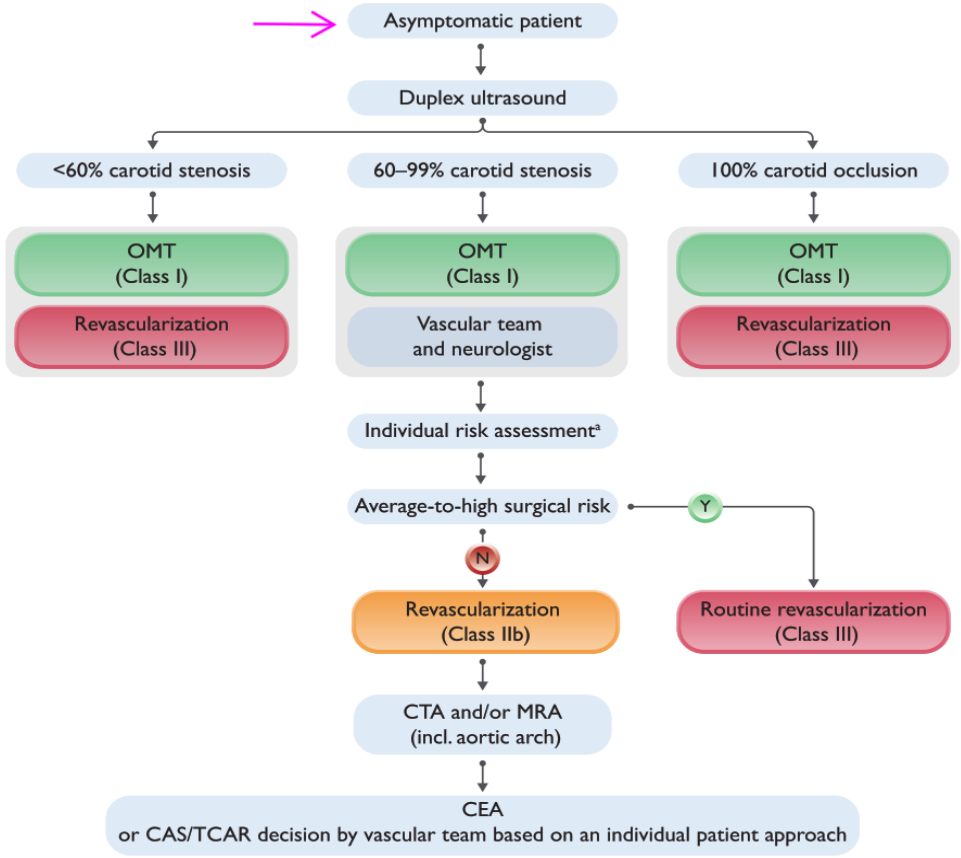
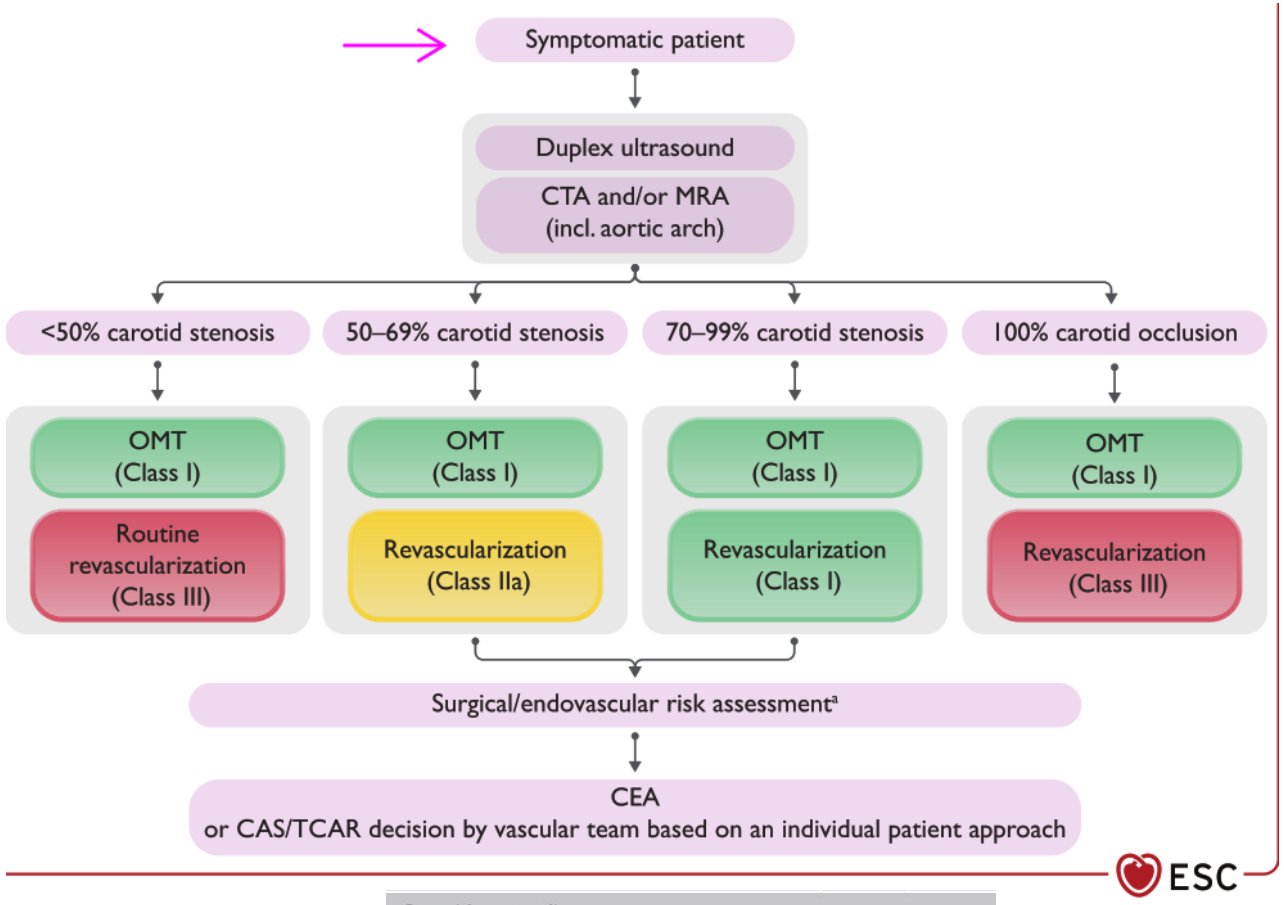
2024 ESC Guidelines for the management of peripheral arterial and aortic diseases

EA Carotidea – AAS:





Carotid artery disease		
In patients with asymptomatic >50% CS, long-term antiplatelet therapy (commonly low-dose aspirin) should be considered if bleeding risk is low.[488,497,670,671]	IIa	C

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Carotid artery disease		
In patients with symptomatic CS, not undergoing carotid endarterectomy or stenting, DAPT with low-dose aspirin and clopidogrel (75 mg) is recommended for the first 21 days or longer, followed by clopidogrel 75 mg or long-term aspirin to reduce the risk of stroke.[667–669]	I	A

Figure 18 Algorithm of carotid artery stenosis management. CAS, carotid artery stenting; CEA, carotid endarterectomy; CTA, computed tomography angiography; MRA, magnetic resonance angiography; OMT, optimal medical treatment; TCAR, transcarotid artery revascularization; TIA, transient ischaemic attack. [a]Assess presence of high-risk features according to *Table 11*. If surgery/revascularization is considered, assess the overall risk related to surgery according to *Table 12*.

2024 ESC Guidelines for the management of peripheral arterial and aortic diseases

2024 ESC Guidelines for the management of chronic coronary syndromes

Tabla 1: Indicaciones para el Uso de IBP en Pacientes Antiagregados

Indicaciones para IBP	Descripción	I	A
Historia de úlceras pépticas	Pacientes con antecedentes de úlceras o hemorragias gastrointestinales.		
Dosis altas de aspirina	Pacientes con enfermedad cardiovascular que requieren dosis altas de aspirina.		
Factores de riesgo	Pacientes **> 65 años** o con comorbilidades (ERC, Hepatopatía, OH, CCs, AINE´s, uso de anticoagulantes).		

Use of proton pump inhibitors		
A proton pump inhibitor is recommended in patients at increased risk of gastrointestinal bleeding for the duration of combined antithrombotic therapy (antiplatelet therapy and/or OAC).[646–648,664]	I	A
A proton pump inhibitor should be considered when a single antithrombotic (antiplatelet or anticoagulant) drug is used, considering the gastrointestinal bleeding risk of the individual patient.[646,665–668]	IIa	A

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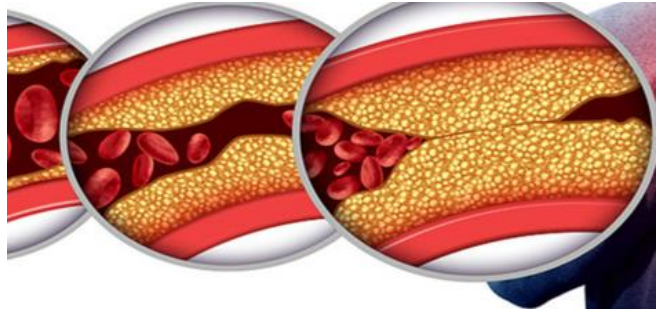
European Heart Journal (2024) **45**, 3415–3537
https://doi.org/10.1093/eurheartj/ehae177



Sesión biobliográfica MI-CAULE

.. Antiagregación en diferentes situaciones.

.. … ???

Torcetrapib, ILLUMINATE:
NEJM 2007; 357:2109-22

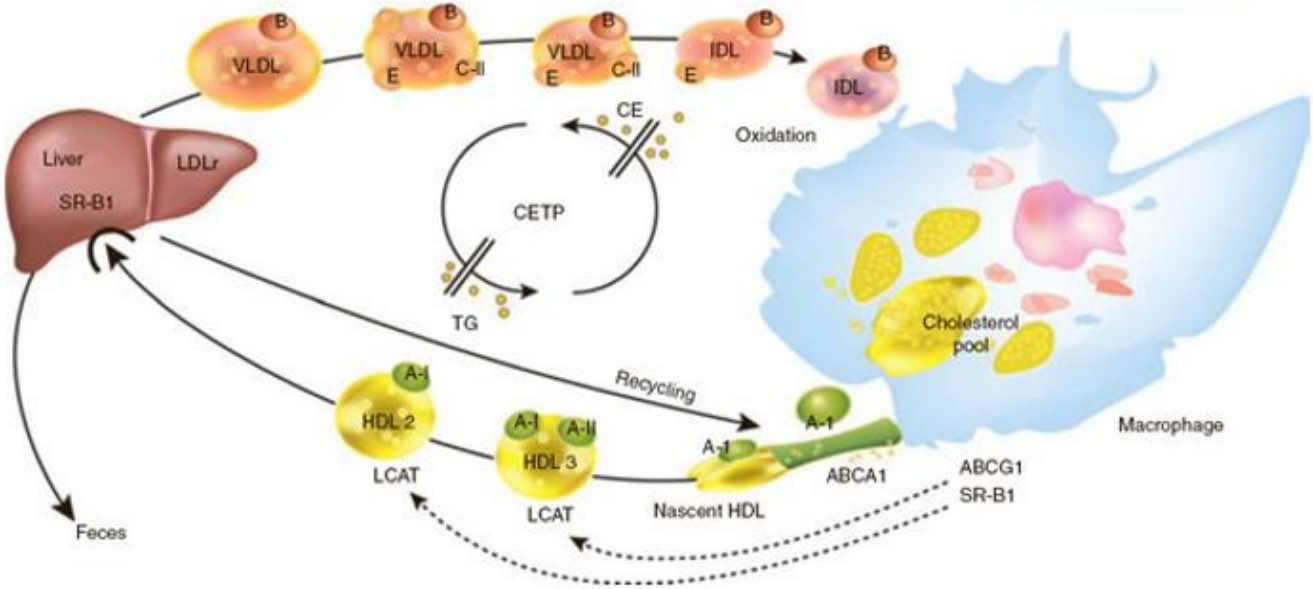
Dalcetrapib, dal-OUTCOMES:
NEJM 2012; 367:2089-99

Evacetrapib, ACCELERATE:
NEJM 2017; 376:1933-42

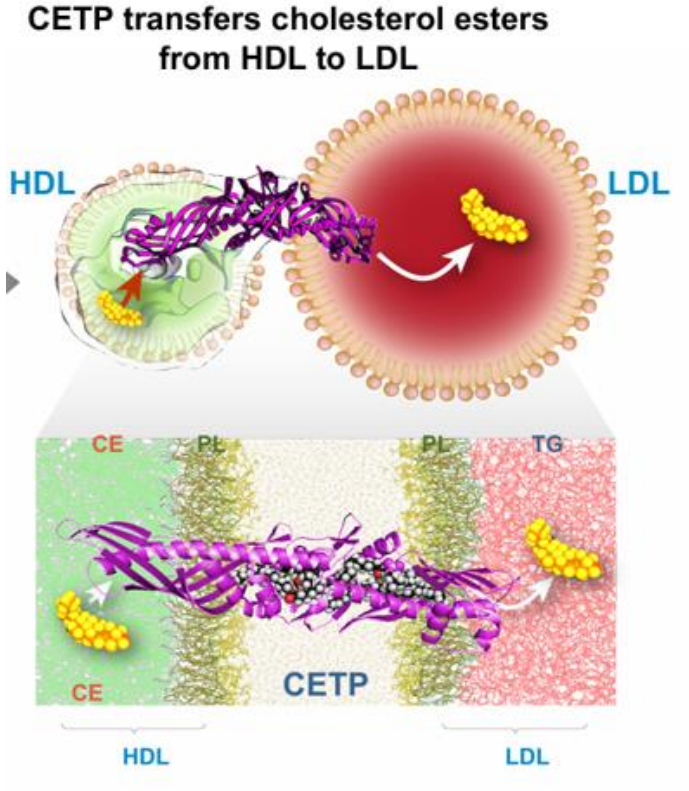
Anacetrapib: REVEAL
NEJM 2017; 377:1217-27

HDL

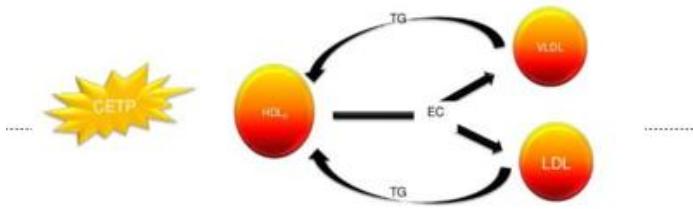
Free cholesterol (FC) in extrahepatic tissues



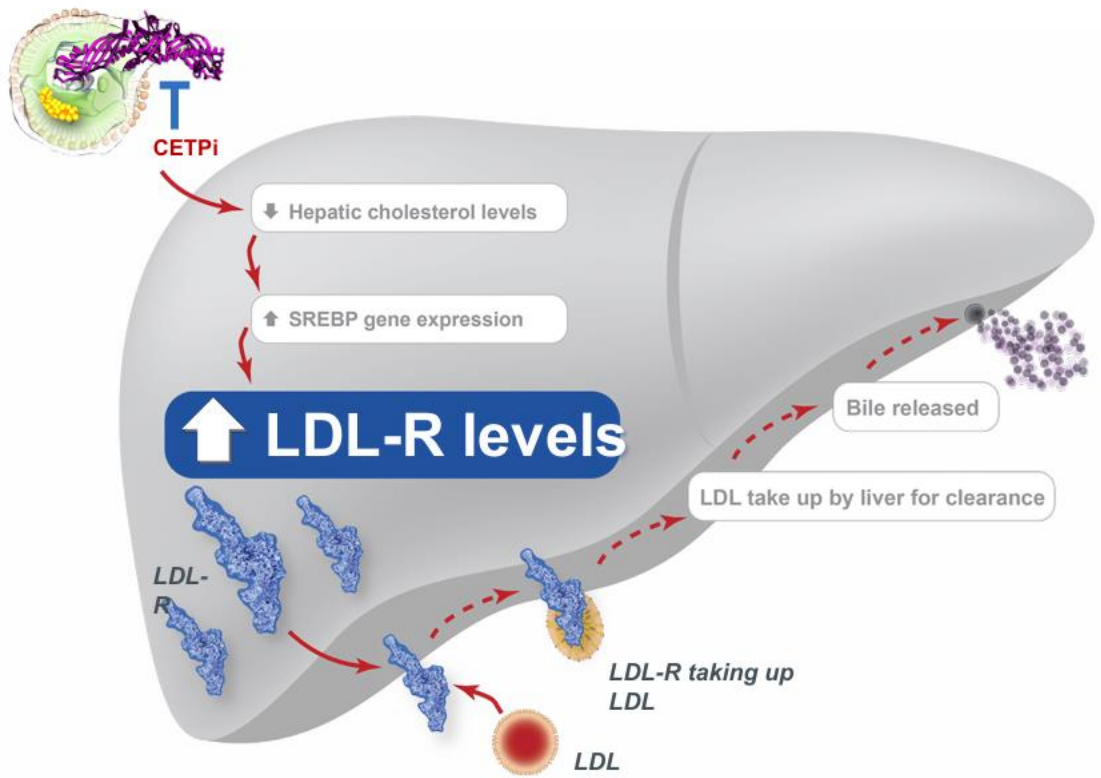
Reverse Cholesterol Transport



Proteína de Transferencia de Ésteres de Colesterol (CETP)



CETPi decreases hepatic cholesterol -> upregulation of LDL-R -> improved LDL and ApoB clearance through the liver



Decrease in hepatic cholesterol

Increase in hepatic LDL receptors

Decrease in plasma LDL levels

Genetically lower CETP associated with lower cardiovascular risks

The Ashkenazi Jewish Longevity Gene Project

Individuals with exceptional longevity had significantly higher (up to 3.6-fold) homozygosity for the 405 valine (I405V) allele of CETP (VV genotype) vs controls

Barzilai et al. JAMA 2003;290(15):2030-40

The Copenhagen City Heart Study

Prospective study, n= 10,261; ~34 years follow-up

Carriers of CETP (inactivating) genotpes had decreased LDL cholesterol levels

and lower cardiovascular risk:

ischemic cardiovascular event: HR 0.7

ischemic heart disease: HR 0.65

ischemic cerebrovascular disease: HR 0.71

Johannsen et al. JACC 2012,60(20):2041–8

Inhibidores de la proteína de transferencia de ésteres de colesterol (CETP)

Ultra-short summary of the complex history of pharmacologic CETP inhibition

Torcetrapib, ILLUMINATE: negative study, off-target effects (e.g. increased BP)
NEJM 2007; 357:2109-22

Dalcetrapib, dal-OUTCOMES: neutral study, no LDL-C lowering
NEJM 2012; 367:2089-99

Evacetrapib, ACCELERATE: non-significant trends, study underpowered / too short
NEJM 2017; 376:1933-42

Anacetrapib: REVEAL: modest effect, insufficient LDL-C lowering (~-11mg/dl)
NEJM 2017; 377:1217-27

Reducción MACE (HR 0.91; 95% IC, 0.85-0.97; P=0.004)

Effects of Anacetrapib in Patients with Atherosclerotic Vascular Disease

The HPS3/TIMI55–REVEAL Collaborative Group*

ABSTRACT

- 30,449 adultos
- Anacetrapib 100 mg diarios o placebo
- (+) Atorvastatina.
- Seguimiento mediano de 4.1 años

- **Descenso LDL: 11 mg/dL , - 17% respecto basal**

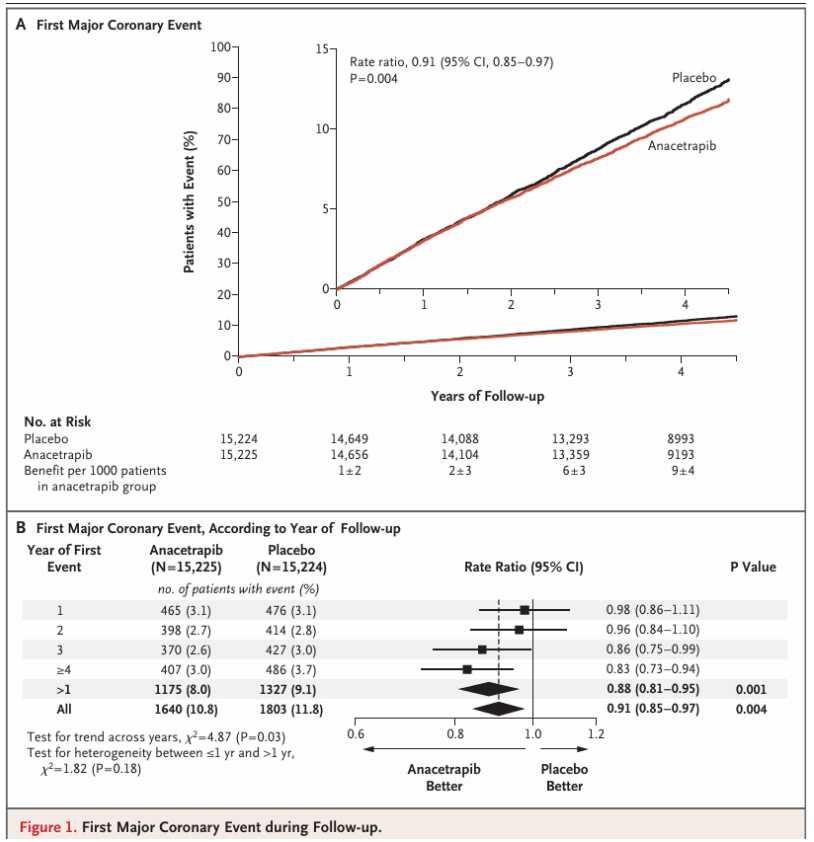


Figure 1. First Major Coronary Event during Follow-up.

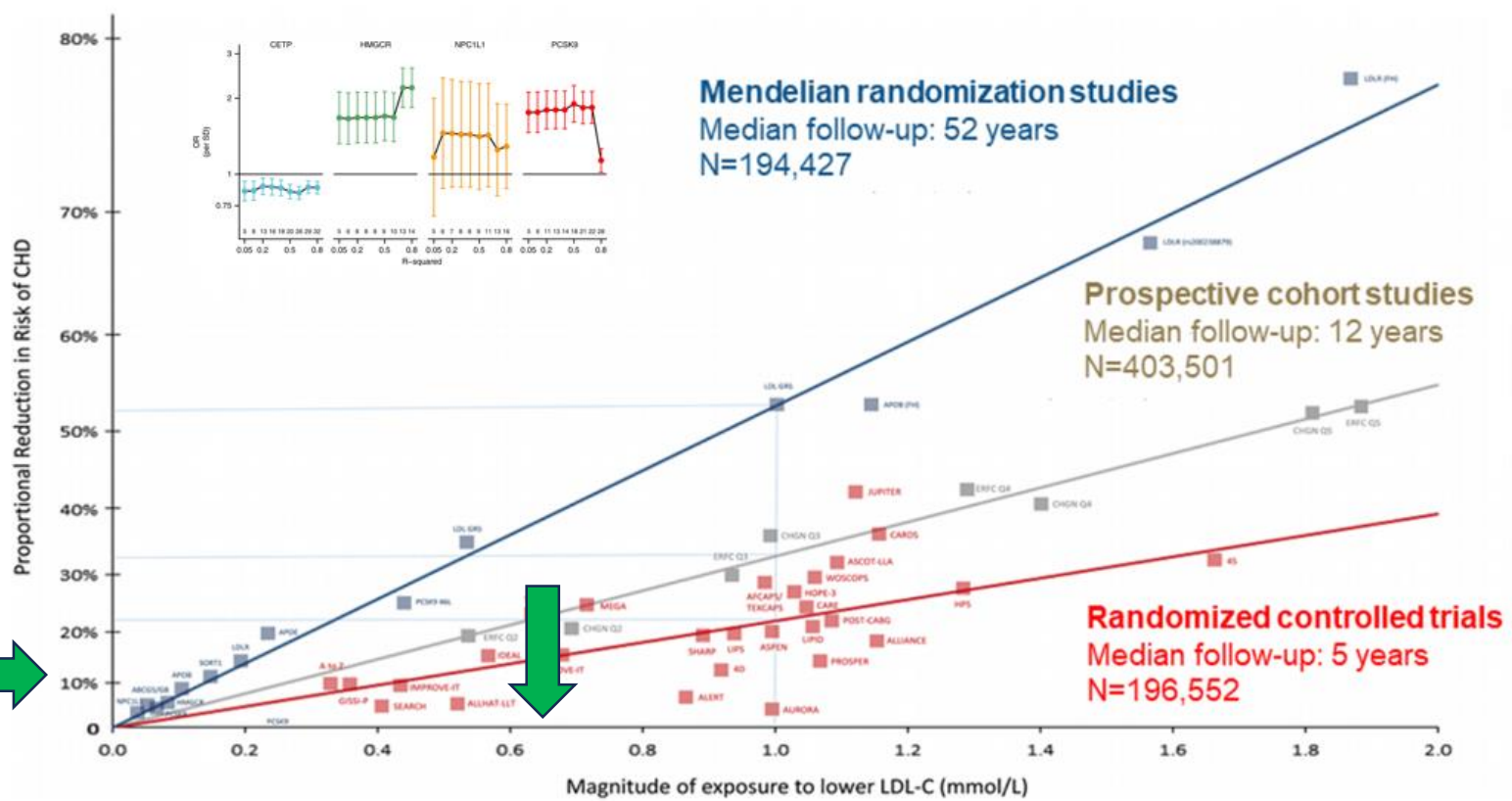
Reducción MACE (HR 0.91; 95% IC, 0.85-0.97; P=0.004)

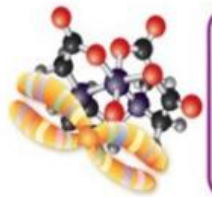
ESC European Society of Cardiology
European Heart Journal (2022) **43**, 1416–1424
https://doi.org/10.1093/eurheartj/ehab863

European Heart Journal (2017) 0, 1–14
doi:10.1093/eurheartj/ehx144

CURRENT OPINION

Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel





Mendelian randomization and genetic analyses

Observational Epidemiological studies

Randomized clinical trials

Animal experiments

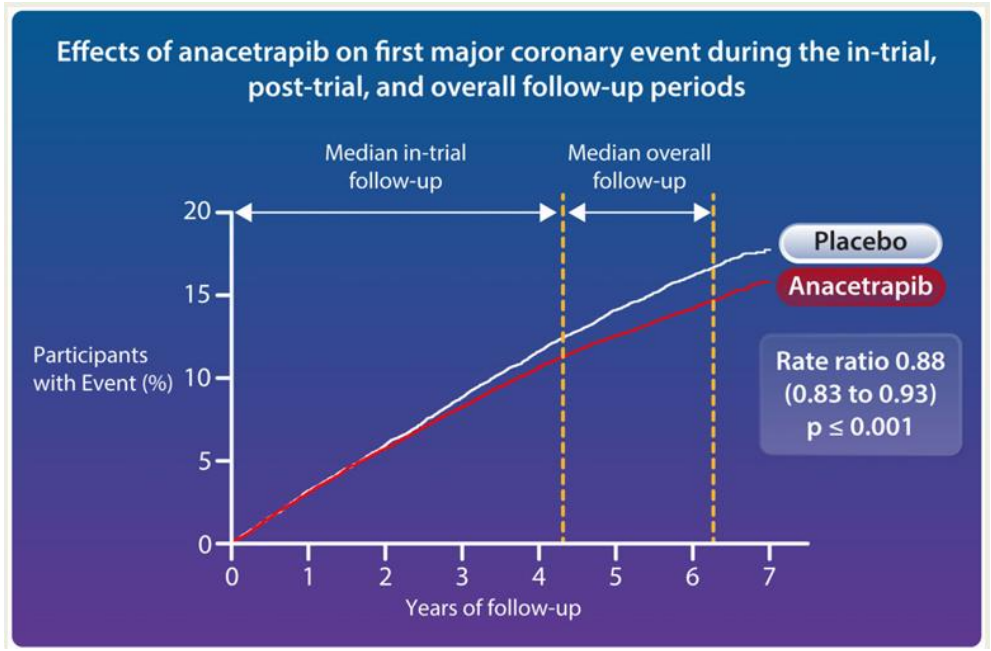
Conclusion Consistent evidence from numerous and multiple different types of clinical and genetic studies unequivocally establishes that LDL causes ASCVD.

; accepted 8 March 2017

Un descenso de 1 mmol/L (38.7 mg/dl) de C-LDL se asocia a una reducción aproximada del 20% del riesgo CV

Long-term safety and efficacy of anacetrapib in patients with atherosclerotic vascular disease

The HPS3/TIMI55-REVEAL Collaborative Group



B

Year of First Event	Anacetrapib (N=15225) No. of participants with events (%)	Placebo (N=15224) No. of participants with events (%)	Rate Ratio (95% CI)	P Value
Year 1	465 (3.1)	476 (3.1)		
Year 2	398 (2.7)	414 (2.8)		
Year 3	370 (2.6)	428 (3.0)		
Year 4	349 (2.6)	402 (3.0)		
Year 5	255 (2.0)	335 (2.7)		
Year 6+	309 (2.7)	364 (3.3)		
All	**2146 (14.1)**	**2419 (15.9)**	**0.88 (0.83–0.93)**	**<0.001**

Eur Heart J. 2022 Apr 6;43(14):1416-1424.

ROSE study: Obicetrapib in combination with high-intensity statins

Inclusion criteria

- stable dose of HIS (A 40/80 mg; R 20/40 mg)
  8 weeks prior to screening
- LDL-C levels >1.8 mmol/L

Exclusion criteria

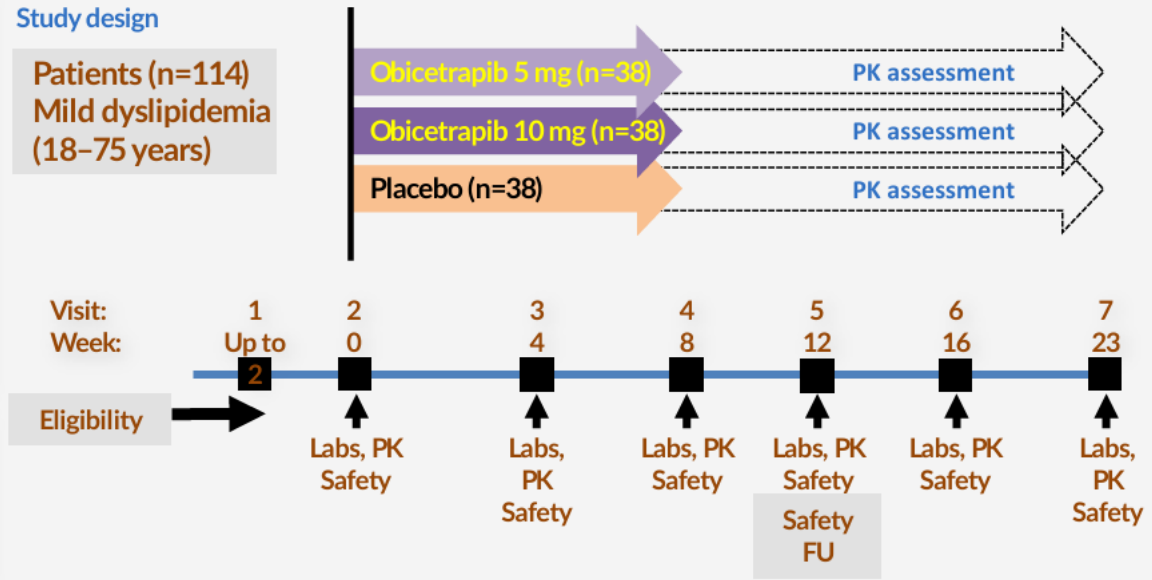
- significant CV disease
- diabetes mellitus
- uncontrolled hypertension

Primary efficacy endpoint

- Percent change from baseline in LDL-C compared to the placebo group

Study design

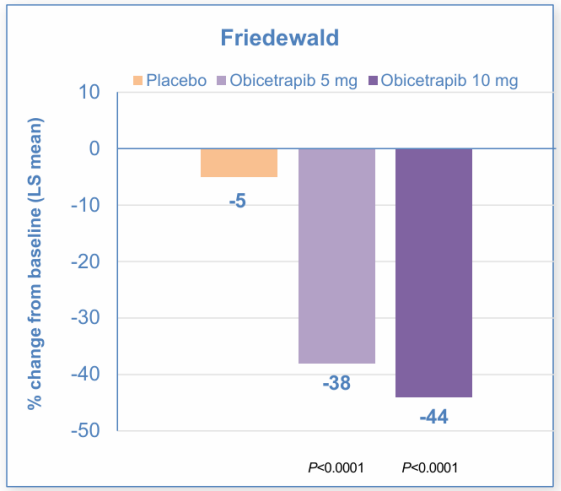
Patients (n=114)
Mild dyslipidemia
(18–75 years)

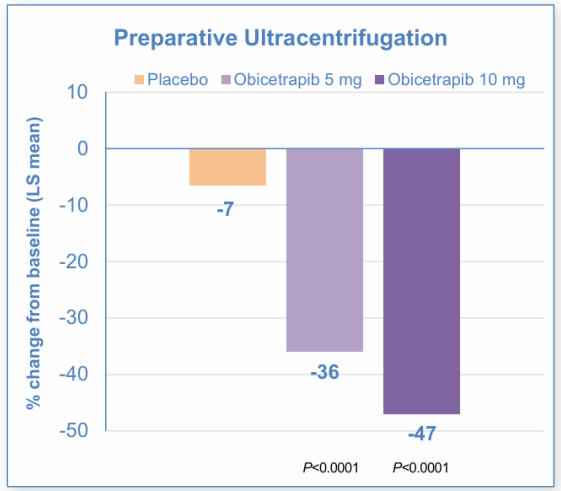


Pre-specified assessment of LDL-C levels by preparative ultra-centrifugation and Friedewald

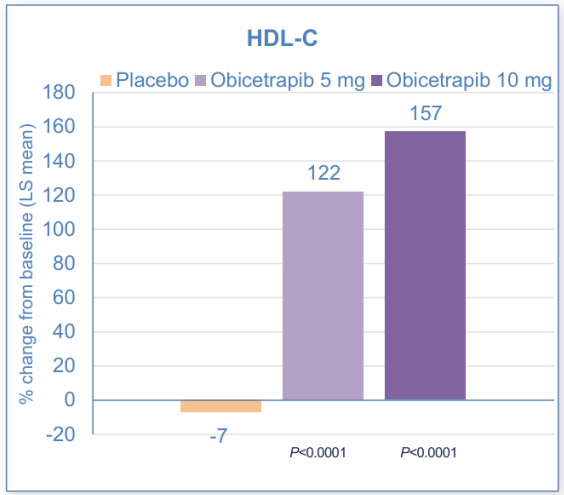
Rose study. Nicholls SJ et al. Nat Med 2022;28(8):1672-8

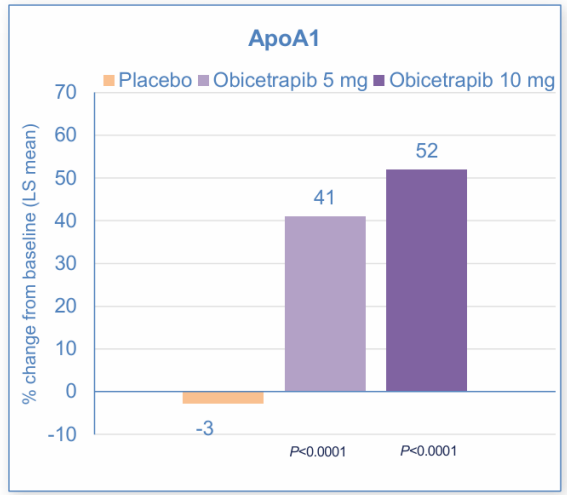
ROSE study: LDL-Cholesterol Lowering



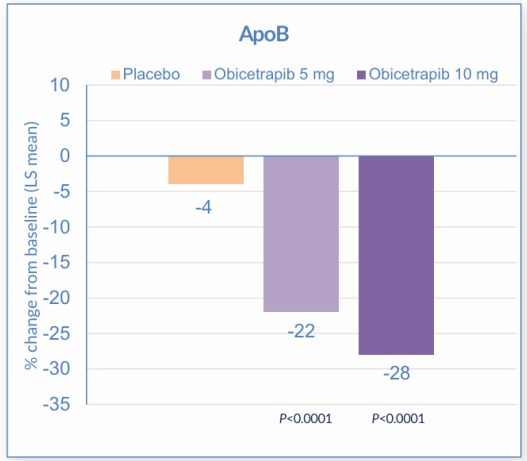


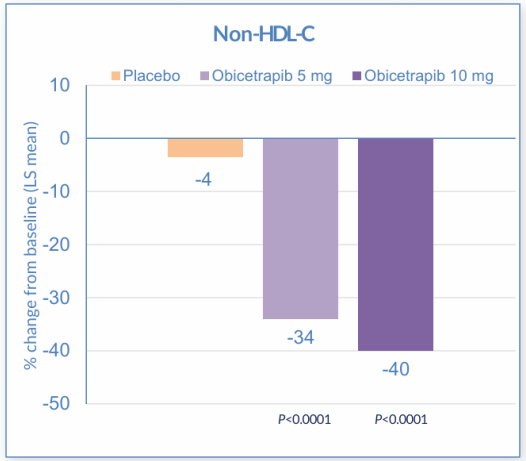
ROSE study: HDL-Cholesterol and ApoA1 increase



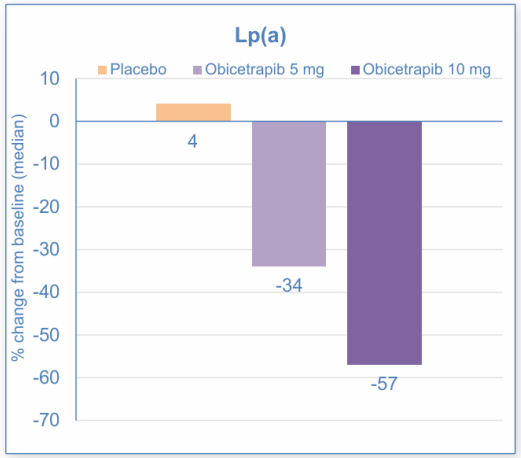


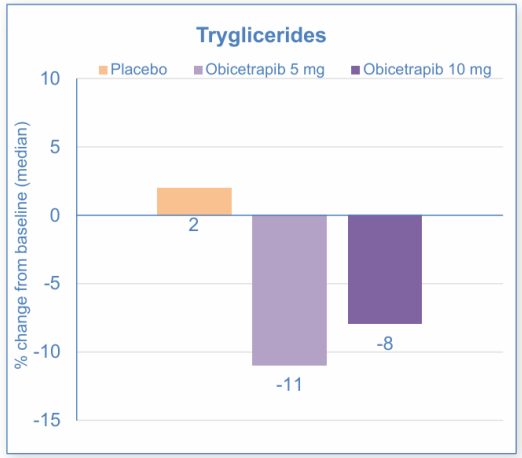
ROSE study: ApoB and Non-HDL-C Lowering





ROSE study: Lipoprotein(a) and Triglyceride Lowering





Nicholls SJ et al. Nat Med 2022;28(8):1672-8

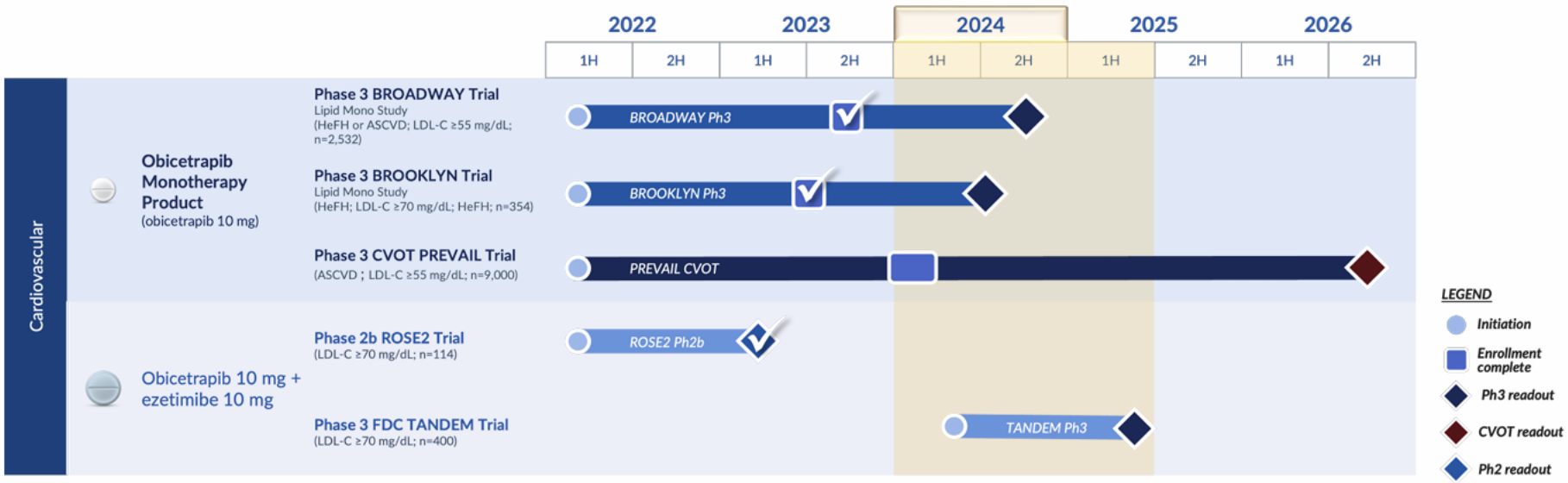
ROSE: Adverse Events

Adverse events occurring in ≥2 subjects in any treatment arm in the safety population

MedDRA System Organ Class/Preferred Term	Placebo N=40 n (%)	Obicetrapib 5 mg N=40 n (%)	Obicetrapib 10 mg N=40 n (%)
Musculoskeletal and connective tissue disorders	4 (10.0)	4 (10.0)	4 (10.0)
Muscle spasms	2 (5.0)	0	0
General disorders and administration site conditions	4 (10.0)	3 (7.5)	2 (5.0)
Fatigue	2 (5.0)	2 (5.0)	1 (2.5)
Gastrointestinal disorders	4 (10.0)	3 (7.5)	0
Nausea	2 (5.0)	1 (2.5)	0
Nervous system disorders	3 (7.5)	2 (5.0)	2 (5.0)
Investigations	3 (7.5)	2 (5.0)	0
Respiratory, thoracic and mediastinal disorders	3 (7.5)	2 (5.0)	0
Infections and infestations	3 (7.5)	1 (2.5)	0
Injury, poisoning and procedural complications	1 (2.5)	3 (7.5)	1 (2.5)
Metabolism and nutrition disorders	0	2 (5.0)	0
Type 2 diabetes mellitus	0	2 (5.0)	0
Neoplasms benign, malignant and unspecified[a]	2 (5.0)	0	0
Basal-cell carcinoma	2 (5.0)	0	0
Vascular disorders	0	2 (5.0)	0
Hypertension	0	2 (5.0)	0

Nicholls SJ et al. Nat Med 2022;28(8):1672-8

Obicetrapib projected clinical studies



Study Design and Baseline Characteristics of Phase 3 Trials

BROOKLYN

1º endpoint – week 12

N = 354

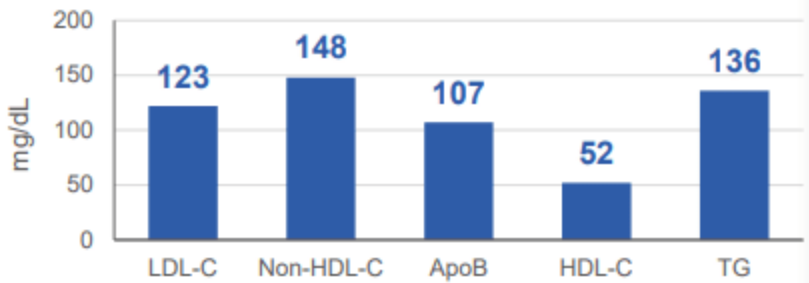
- Obicetrapib 10 mg (2:1 randomization)
- Placebo

13-months

Key Inclusion Criteria

- HeFH
- LDL-C ≥70 mg/dL
- Maximally tolerated lipid lowering therapy

Baseline Lipids (obicetrapib 10mg mean)



Baseline Lipid Modifying Therapy

- Any statin 89%
- High intensity statin: 79%
- Ezetimibe: 54%
- PCSK9i 14%
- Other 8%

BROADWAY

1º endpoint – week 12

N = 2530

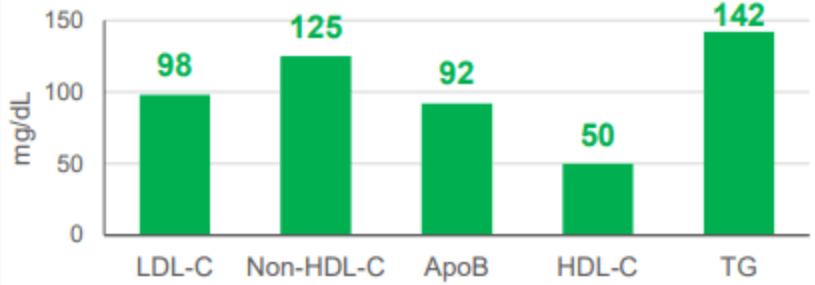
- Obicetrapib 10 mg (2:1 randomization)
- Placebo

13-months

Key Inclusion Criteria

- ASCVD or HeFH
- LDL-C ≥55 mg/dL w/risk factors, or
- LDL-C≥ 100 mg/dL
- Maximally tolerated lipid lowering therapy

Baseline Lipids (blinded mean)



Baseline Lipid Modifying Therapy

- Any statin 91%
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- Ezetimibe: 26%
- PCSK9i 4%
- Other 11%

PREVAIL

LDL-C endpoint

N = 9541

- Obicetrapib 10 mg (1:1 randomization)
- Placebo

54-months

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- LDL-C ≥55 mg/dL w/risk factors, or
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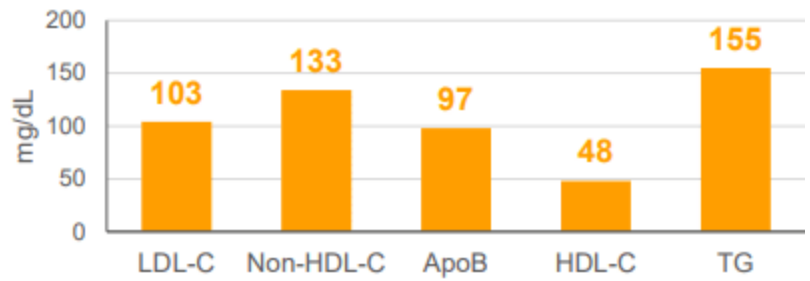
- Maximally tolerated lipid lowering therapy

Baseline Lipids (blinded mean)

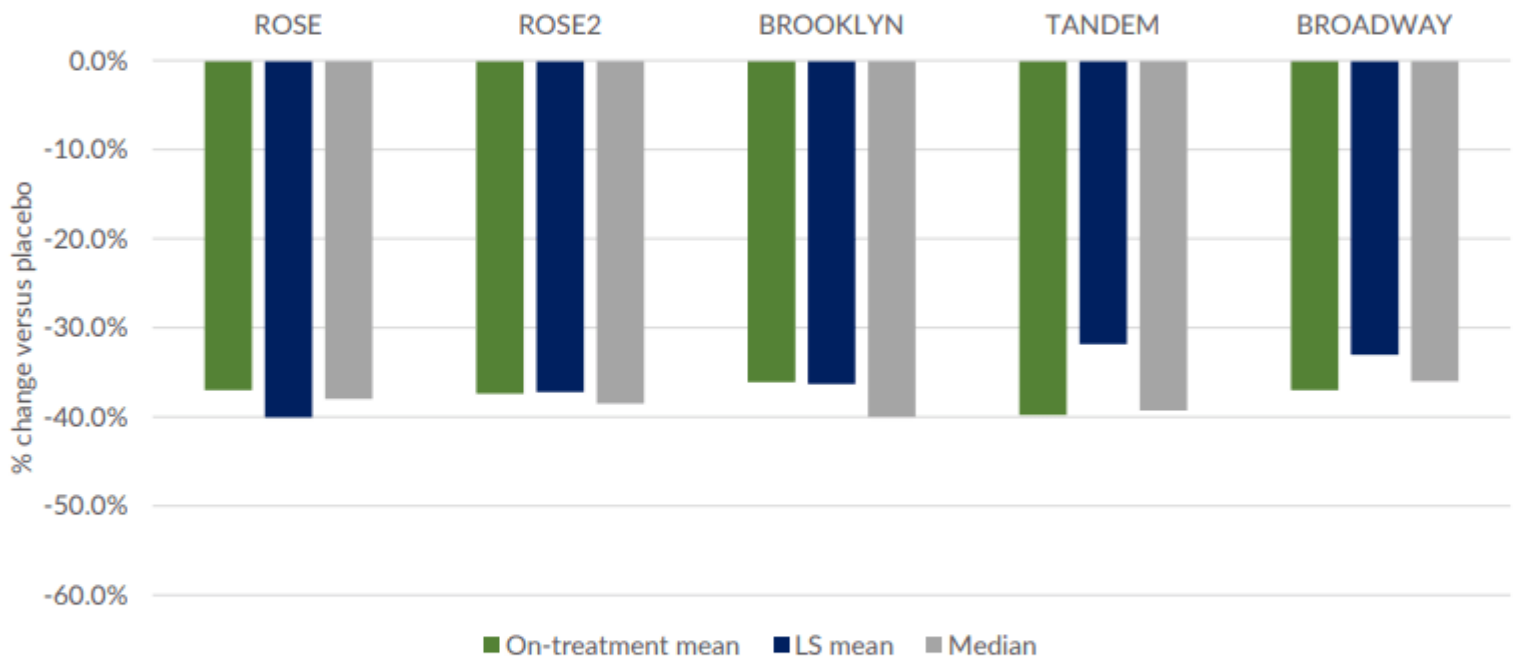


Baseline Lipid Modifying Therapy

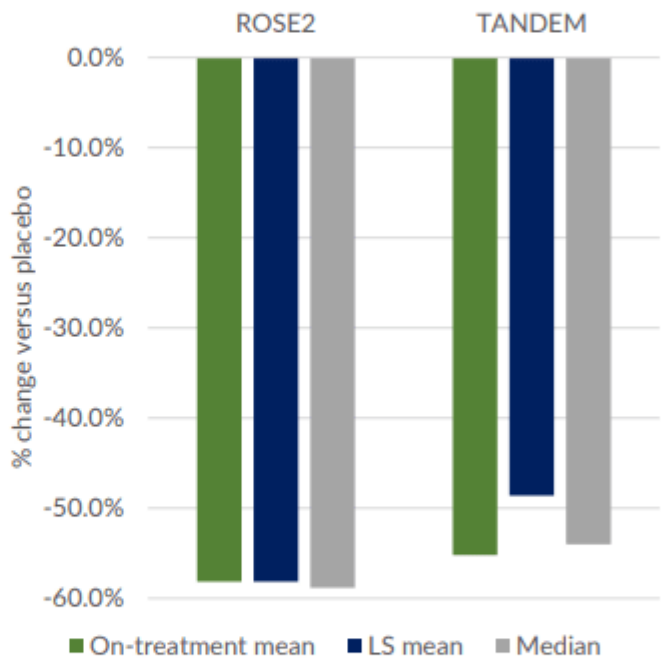
- Any statin >90%
- High intensity statin: 70%
- Ezetimibe: 23%

Consistent LDL-C Reduction Observed Across Our Phase 2 and Phase 3 Trials

Obicetrapib 10 mg monotherapy



Obicetrapib plus ezetimibe



Monotherapy reductions of 35-40%

Combo reductions of 50-60%

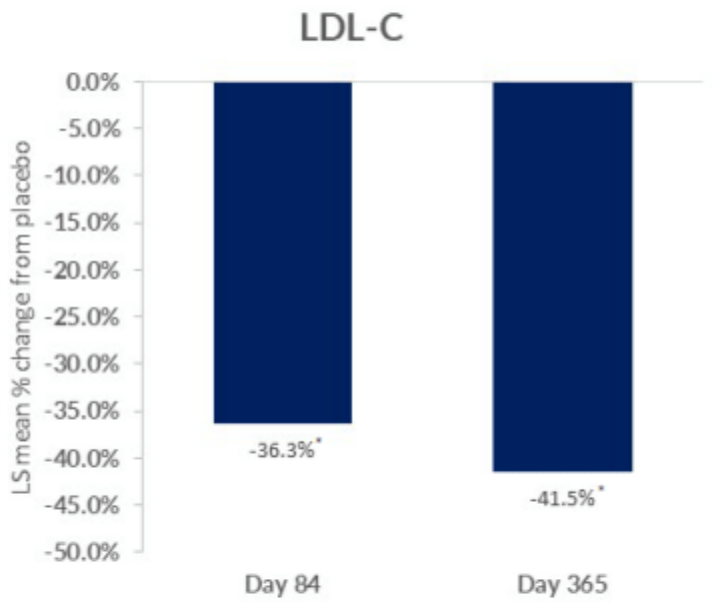
Note: ROSE at week 8, ROSE2, BROOKLYN, BROADWAY, and TANDEM as of week 12.

NewAmsterdam Pharma

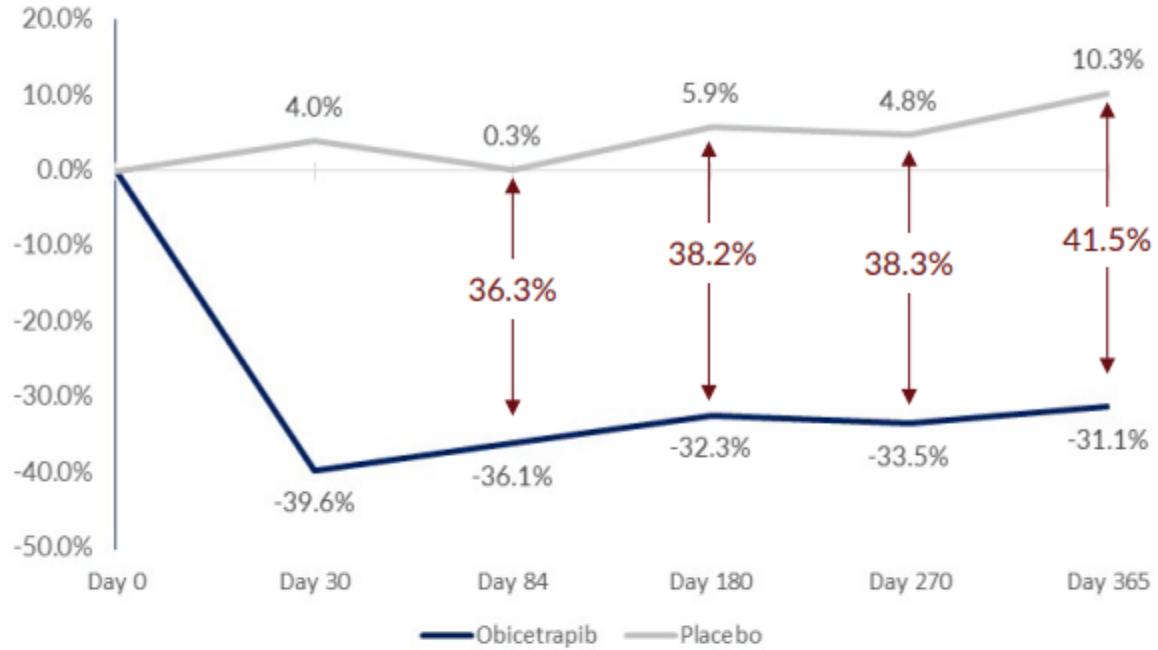
BROOKLYN

Consistent LDL-C Reduction Observed Over One Year Trial Duration

LS Mean % change vs. placebo



LDL-C reduction over time (ITT population)



Note: * = p<0.0001. Martin Hopkins mean changes at baseline, day 30, Day 180, Day 270 and LS mean by PUC at Day 84 and Day 365.

NewAmsterdam Pharma

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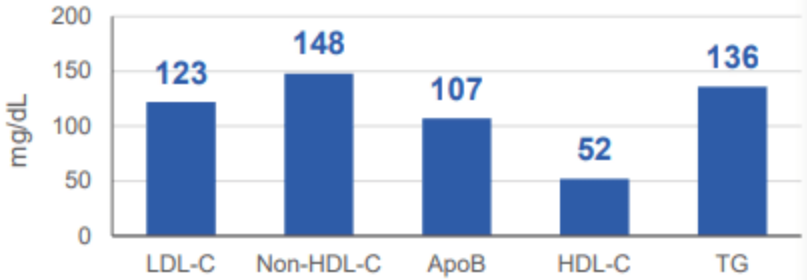

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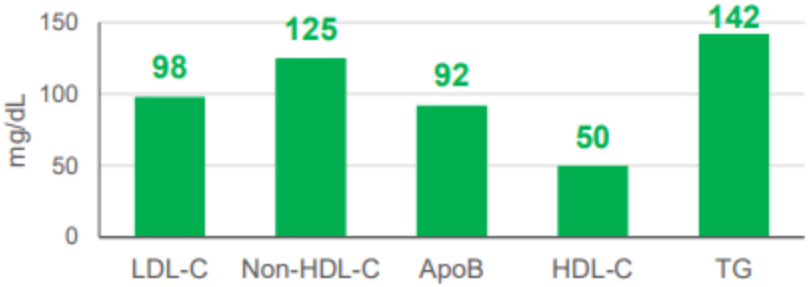

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54-months

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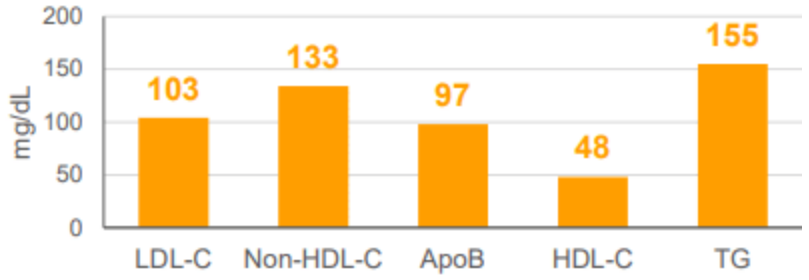

Baseline Lipid Modifying Therapy

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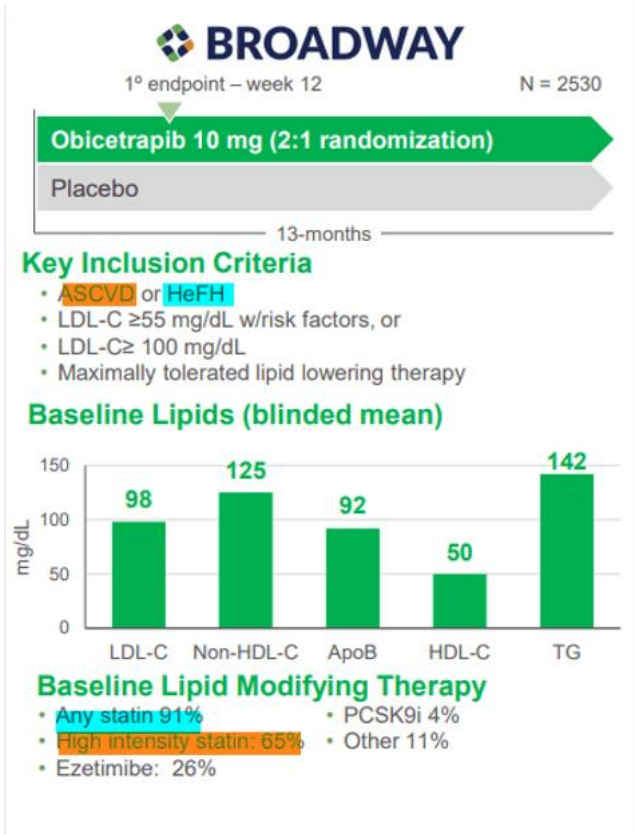
- **Seguridad y tolerabilidad:** Obicetrapib fue bien tolerado con un perfil de seguridad comparable al placebo.



Importantly, here, the drug also **showed a 21% reduction in major adverse cardiovascular events at one year**, although reduction of MACE was not thetrial's primary endpoint.


That's all Folks!