COM ACONSEGUIR ELS OBJECTIUS DE COLESTEROL-LDL?

Xavier Pintó
Unitat de Lípids i Risc Vascular. Medicina Interna.
Hospital de Bellvitge. CiberObn. Idibell. Fipec. UB.

Conflictes d'interès

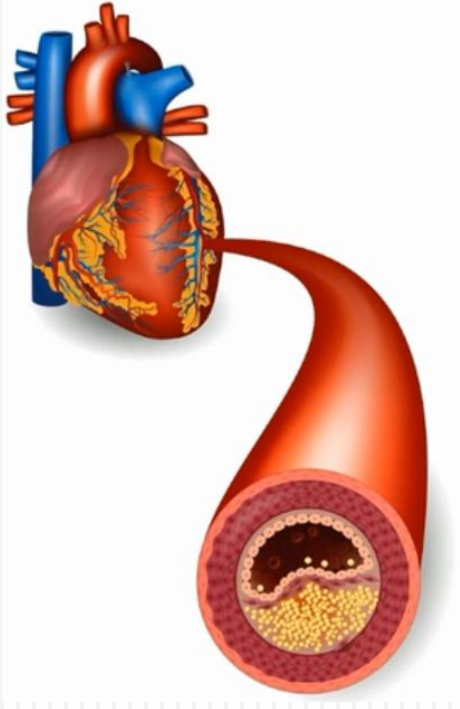
Assessoria/docència:
Amarin Pharma, Amgen, Daiichi-Sankyo, Esteve, Ferrer, Novartis, Viatris, Sanofi, Servier.

Assaigs Clínics:
Amgen, Novartis, Novo, Silence therapeutics, Lib Therapeutics,

No hi ha conflictes d’interès per aquesta ponència

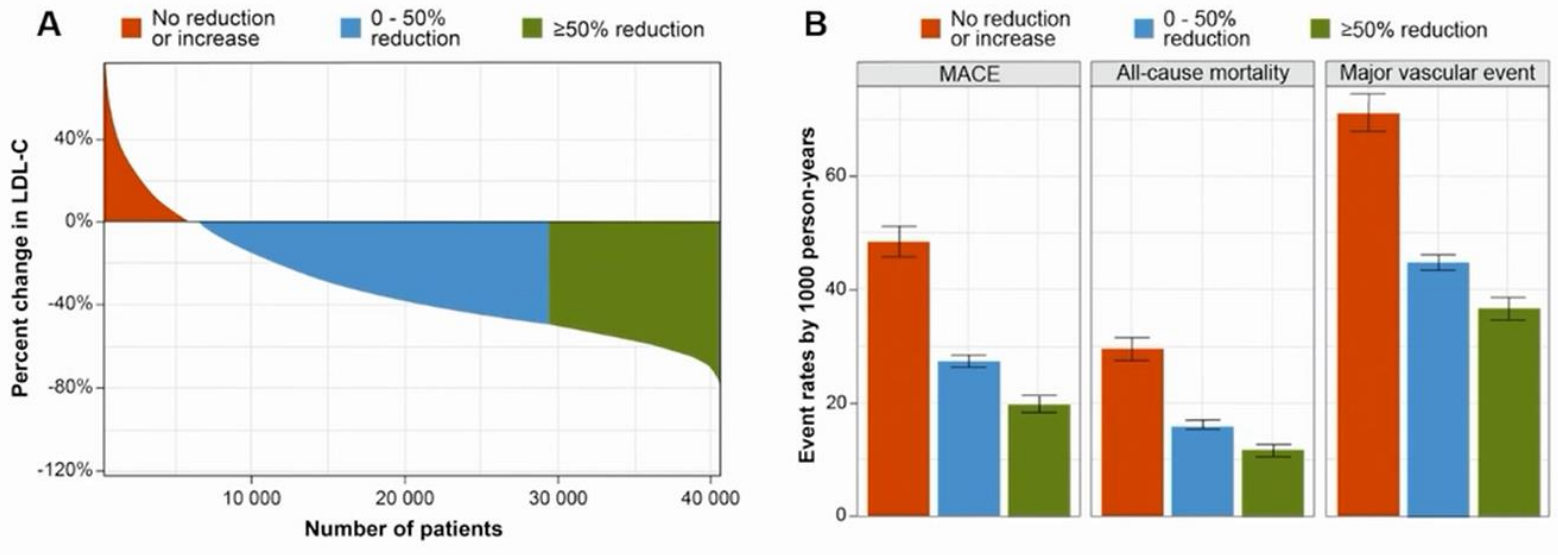
L'excés de c-LDL és la causa principal de la malaltia cardiovascular ateromatosa

LA DISMINUCIÓ ABSOLUTA DEL C-LDL Y LA DURACIÓ D'AQUESTA DISMINUCIÓ SÓN FACTORS PRINCIPALS EN LA PREVENCIÓ DE LES MALALTIES CARDIOVASCULARS



Sources: American Heart Association, CDC, Mayo clinic, Global Health estimates 2016: Deaths by Cause, Age, Sex, by Country and by Regio, 2000-2016, Geneva, WHO; 2018.

EL GRAU DE DISMINUCIÓ DEL C-LDL DETERMINA L'EFICÀCIA EN LA PREVENCIÓ SECUNDÀRIA DE LA MALALTIA CV



Used with permission.

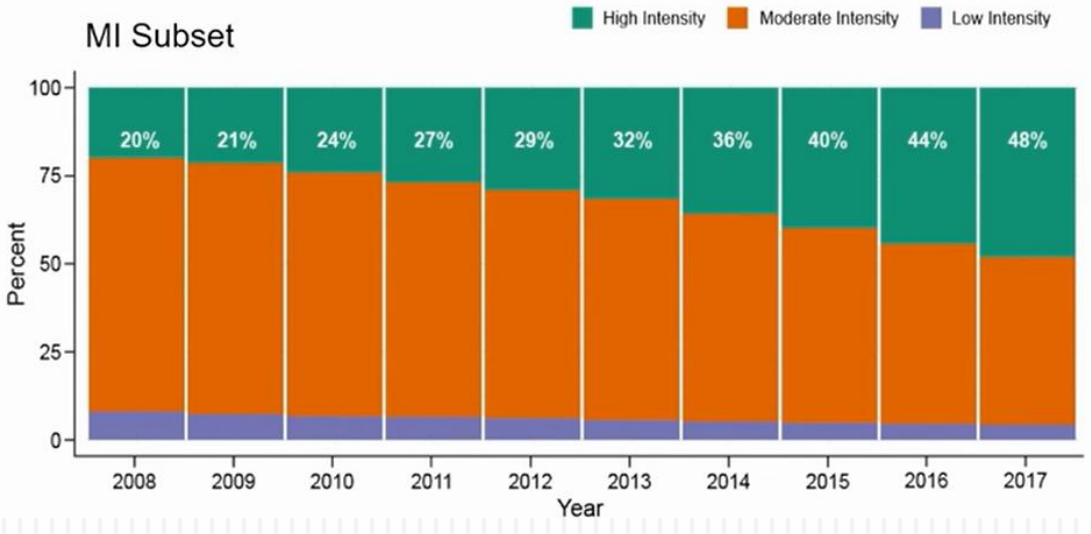
MACE=major adverse cardiovascular events.

Schubert J, et al. Eur Heart J 2021;42:243-252

QUEDA MOLT PER MILLORAR EN EL TRACTAMENT DE LA HIPERCOLESTEROLÈMIA DEL PACIENT ISQUÈMIC

- Retrospective cohort study over 10 years
- Electronic medical records data from primary care practices in the UK

In the real world, a mean LDL-C reduction of only ~8 mg/dL has been observed over 10 years...
...despite increased use of higher intensity statins



The mean LDL-C level declined very slightly over time in both populations, from 2.2 to 2.1 mmol/L in the documented CVD cohort and from 2.2 to 2.0 mmol/L in the MI subset

Danese M, et al. BMJ Open 2022:12:e055015

LA PERCEPCIÓ DISTORSIONADA DEL RISC VASCULAR ÉS FREQÜENT A LA PRÀCTICA CLÍNICA

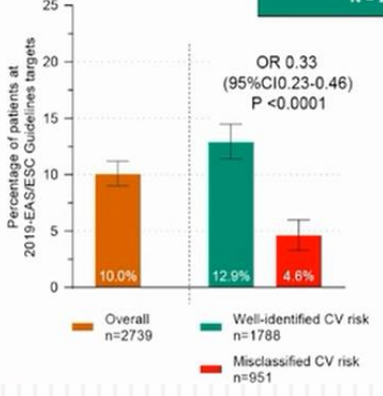
PROVOCA UN INFRATRACTAMENT I UNA MENOR CONSECUCIÓ DELS OBJECTIUS

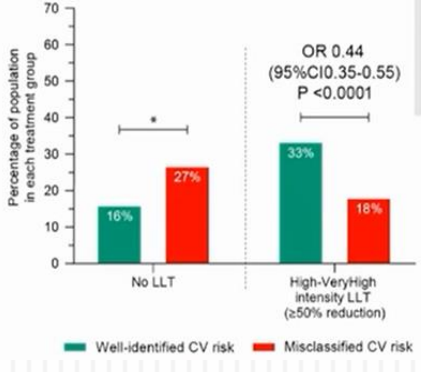
Guidelines-recommended CVD risk stratification and LDL-c recommended targets	Physician-based CVD risk assessment and LDL-c suggested targets: Very-High <55 mg/dl	High <70 mg/dl	Moderate <100 mg/dl	Low <130 mg/dl
Very-high <55 mg/dl	1337	496	127	1
High <70 mg/dl	29	391	328	2
Moderate <100 mg/dl	0	5	26	0

Subjects with physician-based misclassified CV risk N= 951 (34.7%)

Subjects with well-identified CV risk N = 1788 (63.3%)

Relationship between risk classification and achievement of guideline LDL targets





Relationship between risk classification and treatment (LLT vs high-intensity LLT)

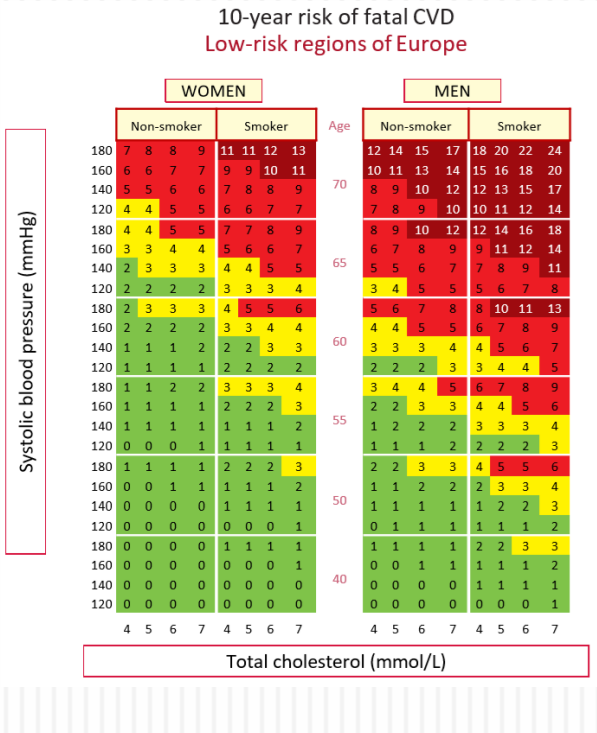
CV=cardiovascular; EAS=European Atherosclerosis Society; LLT=lipid-lowering therapy.

Used with permission.

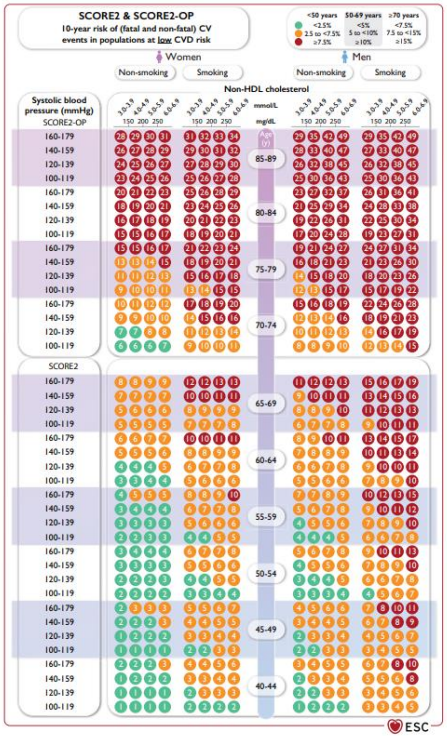
Morieri ML, et al.Cardiovasc Diabetol 2022;21(1):57

Avaluació del RCV

SCORE



SCORE2

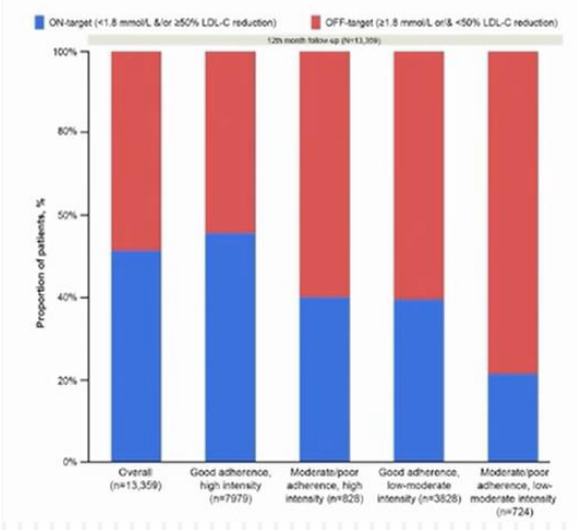


CV RISK	
Low	•SCORE <1%
Moderate	•SCORE ≥1% and <5% •Young patients (T1DM<35 years; T2DM<50 years) with DM duration <10 years without other risk factors
High	•SCORE ≥5% and <10% •Markedly elevated single risk factors, in particular TC >8 mmol/L (310 mg/dL) or LDL-C >4.9 mmol/L (190 mg/dL) or BP ≥180/110 mmHg •FH without other major risk factors •Moderate CKD (eGFR 30–59 mL/min) •DM w/o target organ damage, with DM duration ≥10 years or other additional risk factor
Very-High	•ASCVD (clinical/imaging) •SCORE ≥10% •FH with ASCVD or with another major risk factor •Severe CKD (eGFR <30 mL/min) •DM & target organ damage: ≥3 major risk factors; or early onset of T1DM of long duration (>20 years)

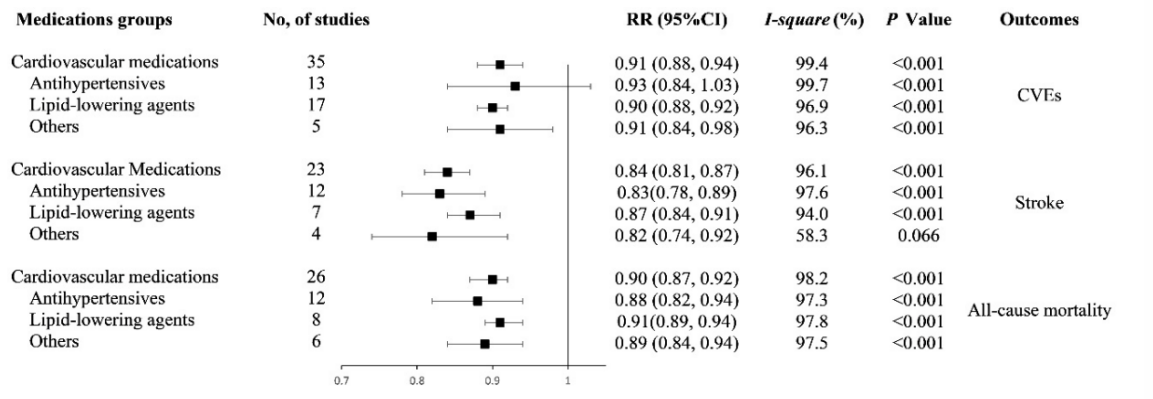
Visseren FLJ et al. European Heart J 2021;42, 3227-337

Mach F et al. Atherosclerosis 2019; 290:140-205

ADHERÈNCIA AL TRACTAMENT I CONSECUCIÓ DELS OBJECTIUS DE C-LDL



LA FALTA D'ADHERÈNCIA PROVOCA UNA MENOR CONSECUCIÓ DELS OBJECTIUS DE C-LDL

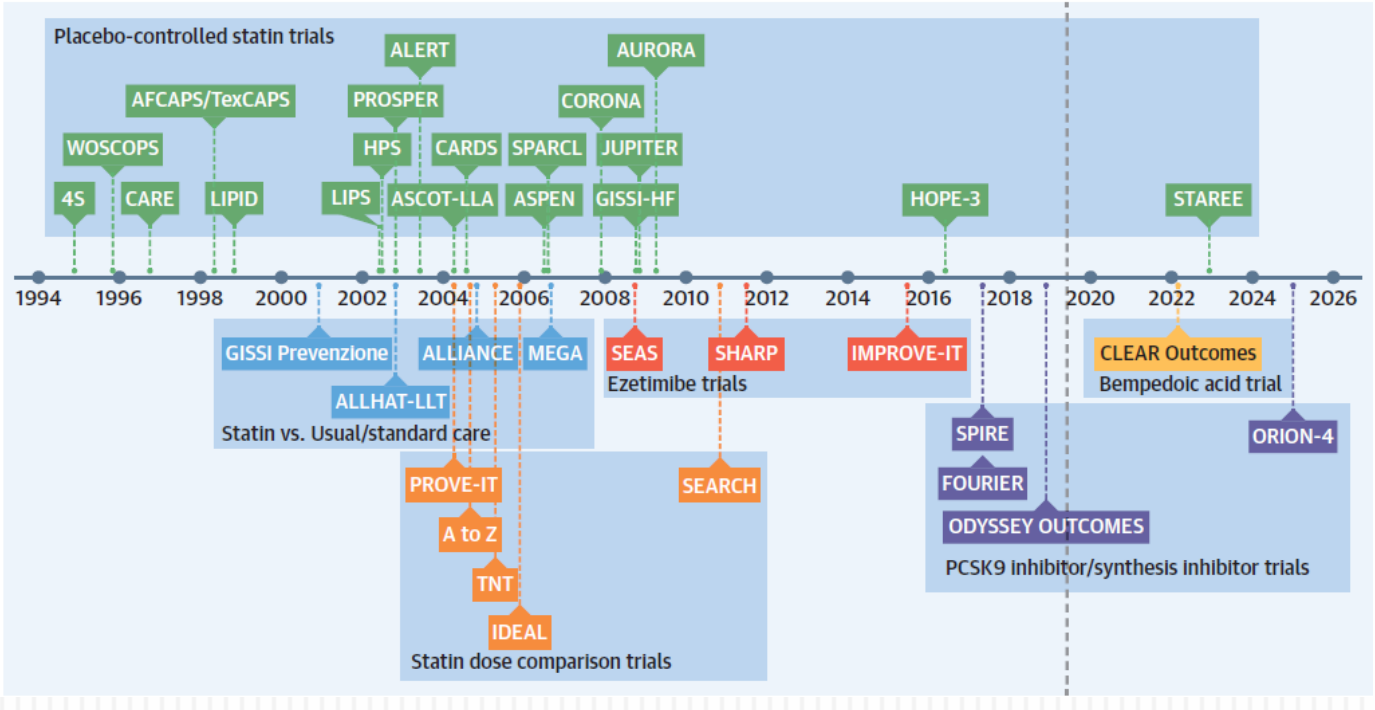


LA BONA ADHERÈNCIA DISMINUEIX EL RISC DE MALALTIA CV, ICTUS I LA MORTALITAT GLOBAL

Mazhar F, et al. Am Heart J 2022;251:78-90

Liu M et al. J. Cardiovasc. Dev. Dis. 2021, 8, 146. https://doi.org/10.3390/jcdd8110146

PRINCIPALS ASSAJOS CLÍNICS DE PREVENCIÓ CARDIOVASCULAR AMB FÀRMACS HIPOLIPEMIANTS



Preiss D et al. J Am Coll Cardiol 2020;75:1945–55

DISMINUIR EL C-LDL A 1,4 mmol/L ÉS MÉS BENEFICIÓS QUE ASSOLIR VALORS MÉS ELEVATS

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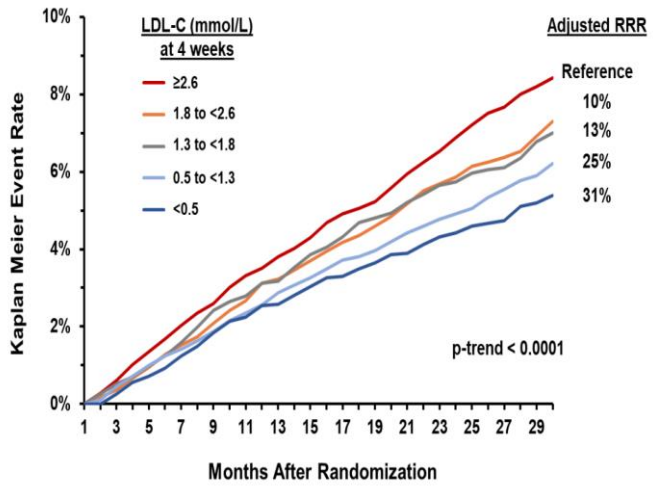
Source of evidence	Mean LDL-C (mmol/L)	Outcome	RR (95% CI)
CTT meta-analysis High-intensity vs. strandard statin; subgroup <2.0 mmol/L	**1.71 vs. 1.32**	CHD death, MI, stroke, coronary revasc.	0.71 (0.56-0.91) per ↓LDL-C by 1mmol/L
IMPROVE-IT Ezetimibe + statin vs. statin	**1.8 vs. 1.40**	CV death, MI, stroke, UA, coronary revasc.	0.94 (0.89-0.99)
FOURIER Evolocumab + statin vs. statin	**2.37 vs. 0.78**	CV death, MI, stroke, UA, coronary revasc.	0.85 (0.79-0.92)
ODYSSEY OUTCOMES Alirocumab + statin vs. statin	**2.37 vs. 1.37**	CHD dearh, MI, stroke, UA	0.85 (0.78-0.93)

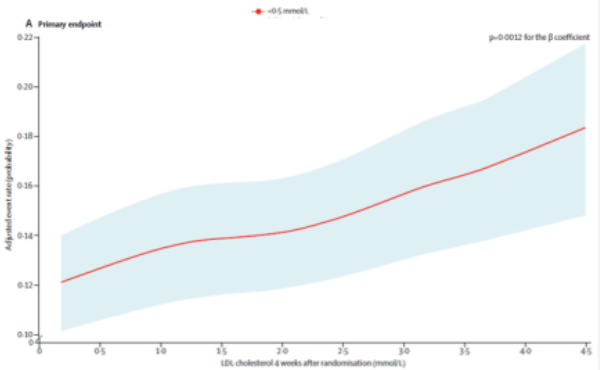
Lancet 2010;376:1670-81; NEJM 2015;372:2387-97; NEJM 2018;379:2097-107

INCIDENCIA DE EPISODIOS DE MUERTE DE CAUSA CV, IAM O ICTUS SEGÚN EL C-LDL ALCANZADO A LAS 4 SEMANAS – ESTUDIO FOURIER



Time-weighted median LDL-c concentrations from week 4 onwards for the five groups categorised by LDL-c at 4 weeks from lowest to highest

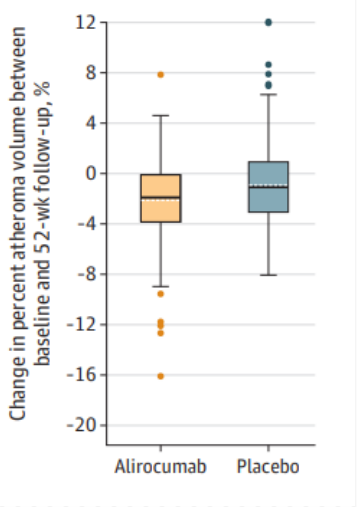
Patel & Giugliano. Global Cardiol Science Pract 2020:39 1

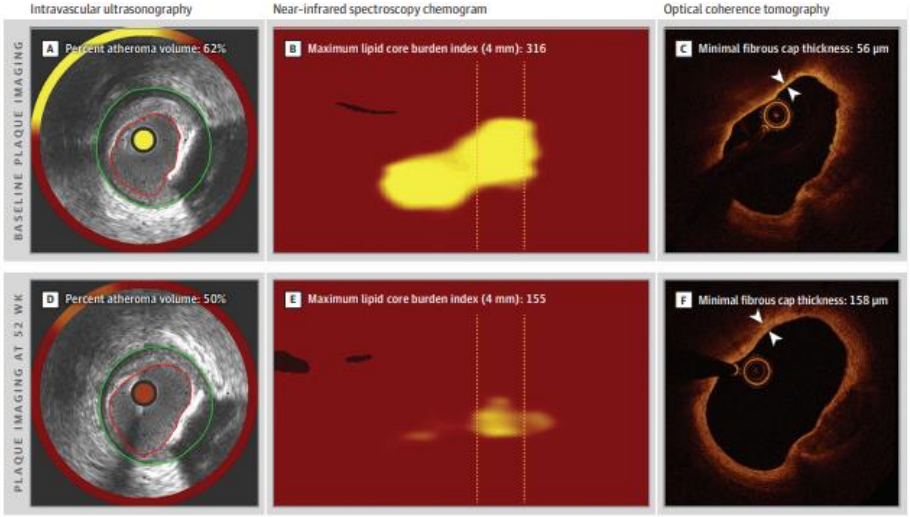


LDL-C 4w after randomization (mmol/L)

Giugliano P et al. Published Online August 28, 2017
http://dx.doi.org/10.1016/S0140-6736(17)32290-0

REGRESSIÓ DE LA PLACA I DEL NUCLI LIPÍDIC, I ENGRUIXIMENT DE LA CÀPSULA FIBROSA AL CAP DE 52 SETMANES DE SEGUIMENT





Canvi en el volum d'ateroma percentual (%)

Alirocumab: – 2.53 %

Placebo: – 2.13 %

Between-group difference, −1.21% [95% CI, −1.78% to −0.65%]; P < .001)

Canvi promig en la càrrega del nucli lipidic maxim en 4 mm

Alirocumab: −79.42

Placebo: −37.60

Between group difference -41.24 (95 % CI −70.71 to −11.77; P = .006)

Canvi promig en en el gruix minim de la càpsula fibrosa

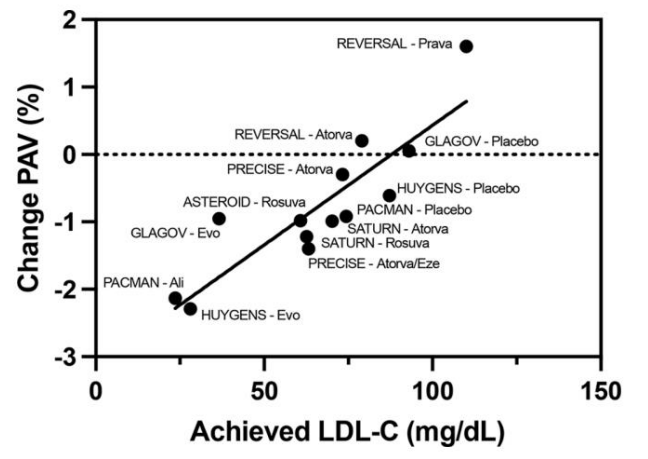
Alirocumab: + 62.67µm

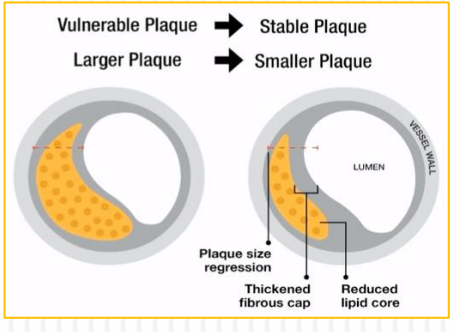
Placebo: + 33.19µm

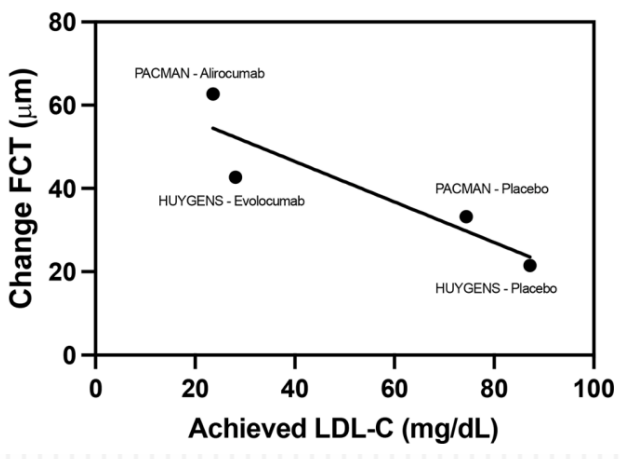
Between group difference 29.65 (95% CI, 11.75-47.55; P = .001)

Räber L et al. JAMA. doi:10.1001/jama.2022.5218 Published online April 3, 2022

TRACTAMENT INTENSIU PER DISMINUIR EL C-LDL i EVOLUCIÓ DE LA PLACA D'ATEROMA







Di Giovani G et al. American Journal of Preventive Cardiology 11 (2022) 100366

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Sociedad Española de Arteriosclerosis

CLÍNICA E INVESTIGACIÓN EN ARTERIOSCLEROSIS

www.elsevier.es/arterio

ARTÍCULO ESPECIAL

Estándares SEA 2022 para el control global del riesgo cardiovascular

Jose Maria Mostaza[a,*], Xavier Pintó[b], Pedro Armario[c], Luis Masana[d], José T. Real[e], Pedro Valdivielso[f], Teresa Arrobas-Velilla[g], Ramón Baeza-Trinidad[h], Pilar Calmarza[i], Jesús Cebollada[j], M. Civera-Andrés[k], J.I. Cuende Melero[l], J.L. Díaz-Díaz[m], J. Fernández Pardo[n], C. Guijarro[o], C. Jericó[c], M. Laclaustra[p], C. Lahoz[a], J. López-Miranda[q], S. Martínez-Hervás[e], O. Muñiz-Grijalvo[r], J.A. Páramo[s], V. Pascual[t], J. Pedro-Botet[u], P. Pérez-Martínez[q], N. Plana[d], J. Puzo[v], M.Á. Sánchez Chaparro[w] y L. Vila[x]

ESC European Society of Cardiology

European Heart Journal (2021) 42, 3227–3337 doi:10.1093/eurheartj/ehab484

ESC GUIDELINES

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

Developed by the Task Force for cardiovascular disease prevention in clinical practice with representatives of the European Society of Cardiology and 12 medical societies

With the special contribution of the European Association of Preventive Cardiology (EAPC)

Authors/Task Force Members: Frank L.J. Visseren* (Chairperson) (Netherlands), François Mach* (Chairperson) (Switzerland), Yvo M. Smulders[2] (Task Force Coordinator) (Netherlands), David Carballo[2] (Task Force Coordinator) (Switzerland), Konstantinos C. Koskinas (Switzerland), Maria Bäck (Sweden), Athanase Benetos[3] (France), Alessandro Biffi[3,10] (Italy), José-Manuel Boavida[3] (Portugal), Davide Capodanno (Italy), Bernard Cosyns (Belgium), Carolyn Crawford (Northern Ireland), Constantinos H. Davos (Greece), Ileana Desormais (France), Emanuele Di Angelantonio (United Kingdom), Oscar H. Franco (Switzerland), Sigrun Halvorsen (Norway), F. D. Richard Hobbs[13] (United Kingdom), Monika Hollander (Netherlands), Ewa A. Jankowska (Poland), Matthias Michal[14] (Germany), Simona Sacco[4] (Italy), Naveed Sattar (United Kingdom), Lale Tokgozoglu[5] (Turkey), Serena Tonstad (Norway), Konstantinos P. Tsioufis[6] (Greece), Ineke van Dis[3] (Netherlands), Isabelle C. van Gelder (Netherlands), Christoph Wanner[4] (Germany), Bryan Williams (United Kingdom), ESC Scientific Document Group

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

European Heart Journal 2019; 00, 1-78

ESC European Society of Cardiology

EAS

Task Force Members:

François Mach (ESC Chairperson) (Switzerland), Colin Baigent (ESC Chaiperson) (United Kingdom), Alberico L. Catapano (EAS Chairperson) (Italy), Konstantinos C. Koskinas (Switzerland), Manuela Casula[1] (Italy), Lina Badimon (Spain), M. John Chapman[1] (France), Guy G. De Backer (Belgium), Victoria Delgado (Netherlands), Brian A. Ference (United Kingdom), Ian M. Graham (Ireland), Alison Halliday (United Kingdom), Ulf Landmesser (Germany), Borislava Mihaylova (United Kingdom), Terje R. Pedersen (Norway), Gabriele Riccardi[1] (Italy), Dimitrios J. Richter (Greece), Marc S. Sabatine (United States of America), Marja-Riitta Taskinen[1] (Finland), Lale Tokgozoglu[1] (Turkey), Olov Wiklund[1] (Sweden).

Published in final edited form as:

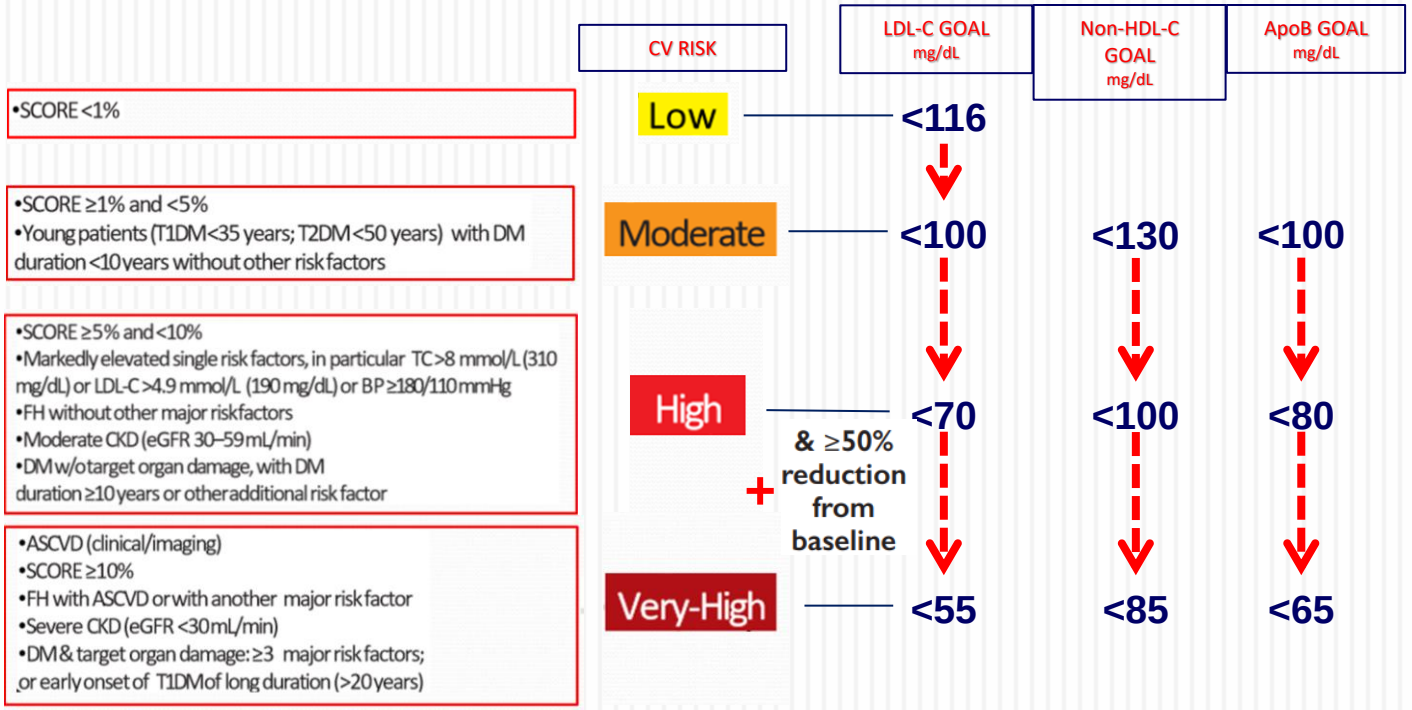
Circulation. 2019 June 18; 139(25): e1082–e1143. doi:10.1161/CIR.0000000000000625.

2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/ APhA/ ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: Executive Summary:

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

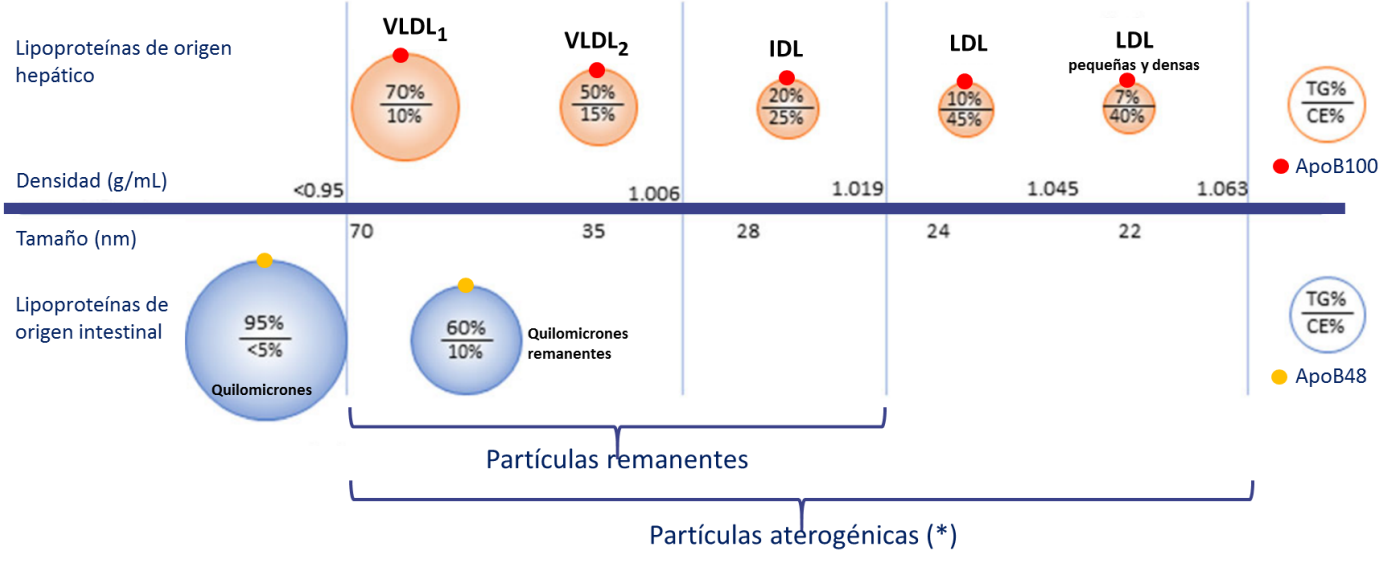
Scott M. Grundy, MD, PhD, FAHA, Chair[*], Neil J. Stone, MD, FACC, FAHA, Vice Chair[*], Alison L. Bailey, MD, FACC, FAACVPR[†], Craig Beam, CRE[*], Kim K. Birtcher, MS, PharmD,

OBJECTIUS LIPÍDICS SEGONS EL GRAU DE RISC CARDIOVASCULAR



PACIENTS AMB MALALTIA CV TRACTATS AMB DOSI MÀXIMA TOLERADA D'ESTATINA I UN SEGON EPISODI VASCULAR EN ELS 2 ANYS SEGÜENTS: **C-LDL < 40 mg/dL** (Class **IIb**, Level **B**)

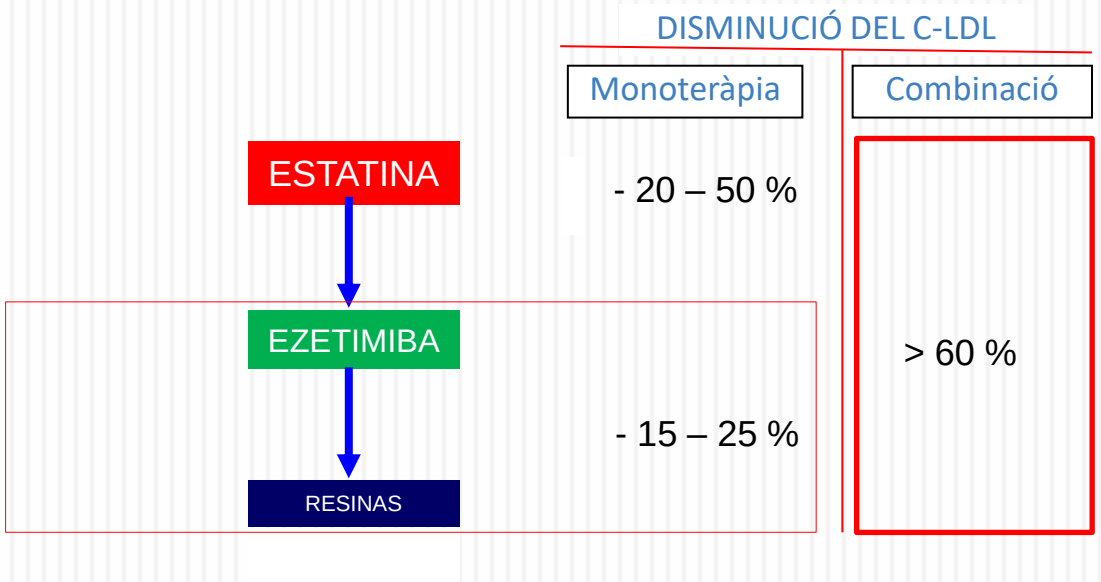
TAMAÑO Y DENSIDAD DE LAS PRINCIPALES LIPOPROTEÍNAS QUE CONTIENEN APOB



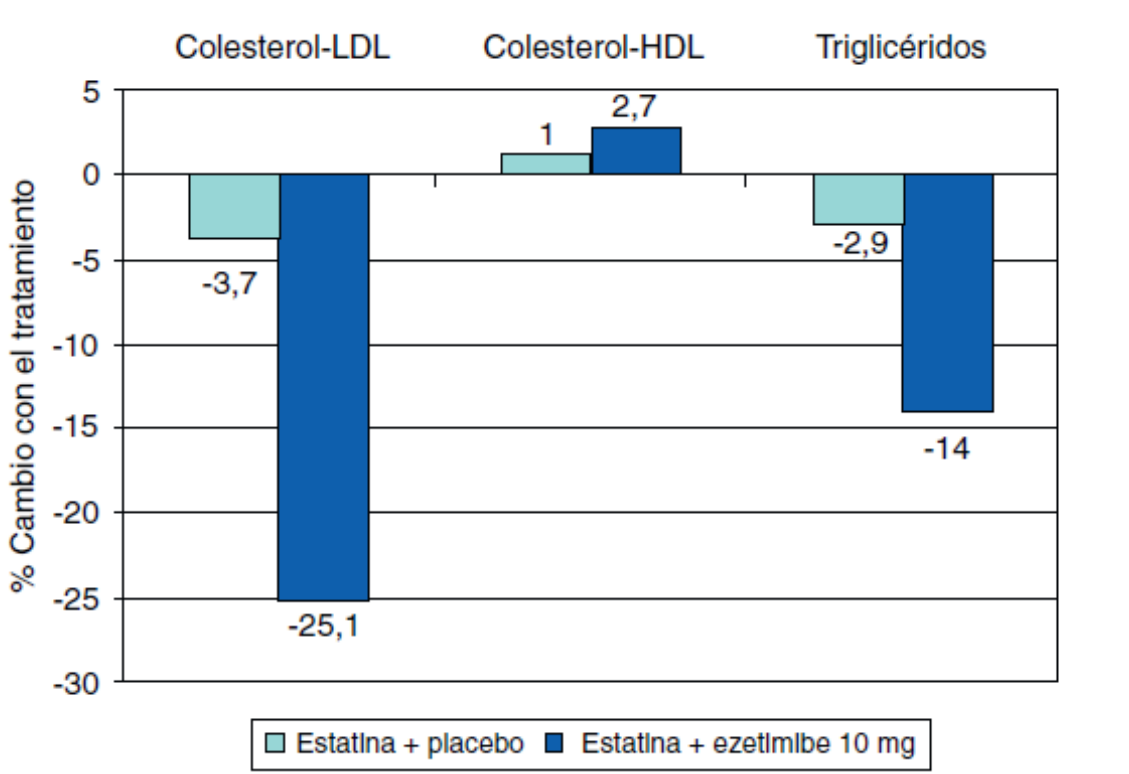
TG: Triglicéridos
CE: Colesterol esterificado
* Su contenido en colesterol se denomina *colesterol-No HDL*

Ginsberg HN et al. European Heart Journal (2021) 42, 4791–4806

FÀRMACS PER TRACTAR LA HIPERCOLESTEROLÈMIA



EFECTES LIPÍDICS DE L'ASSOCIACIÓ ESTATINA - EZETIMIBA



CLASSIFICACIÓ DE LA INTENSITAT DEL TRACTAMENT AMB ESTATINES I EZETIMIBA SEGONS EL GRAU DE DISMINUCIÓ DEL COLESTEROL-LDL

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BAIXA: < 30%

Simvastatin 10 mg
Pravastatin 10–20 mg
Lovastatin 10–20 mg
Fluvastatin 40 mg
Pitavastatin 1 mg
Ezetimibe 10 mg

ALTA: 50-60%

Atorvastatin 40–80 mg
Rosuvastatin 20–40 mg
Simvastatin 20–40 mg + Ezetimibe 10 mg
Pravastatin 40 mg + Ezetimibe 10 mg
Lovastatin 40 mg + Ezetimibe 10 mg
Fluvastatin 80 mg + Ezetimibe 10 mg
Pitavastatin 2–4 mg + Ezetimibe 10 mg
Atorvastatin 10–20 mg + Ezetimibe 10 mg
Rosuvastatin 5–10 mg + Ezetimibe 10 mg

MODERADA: 30-49%

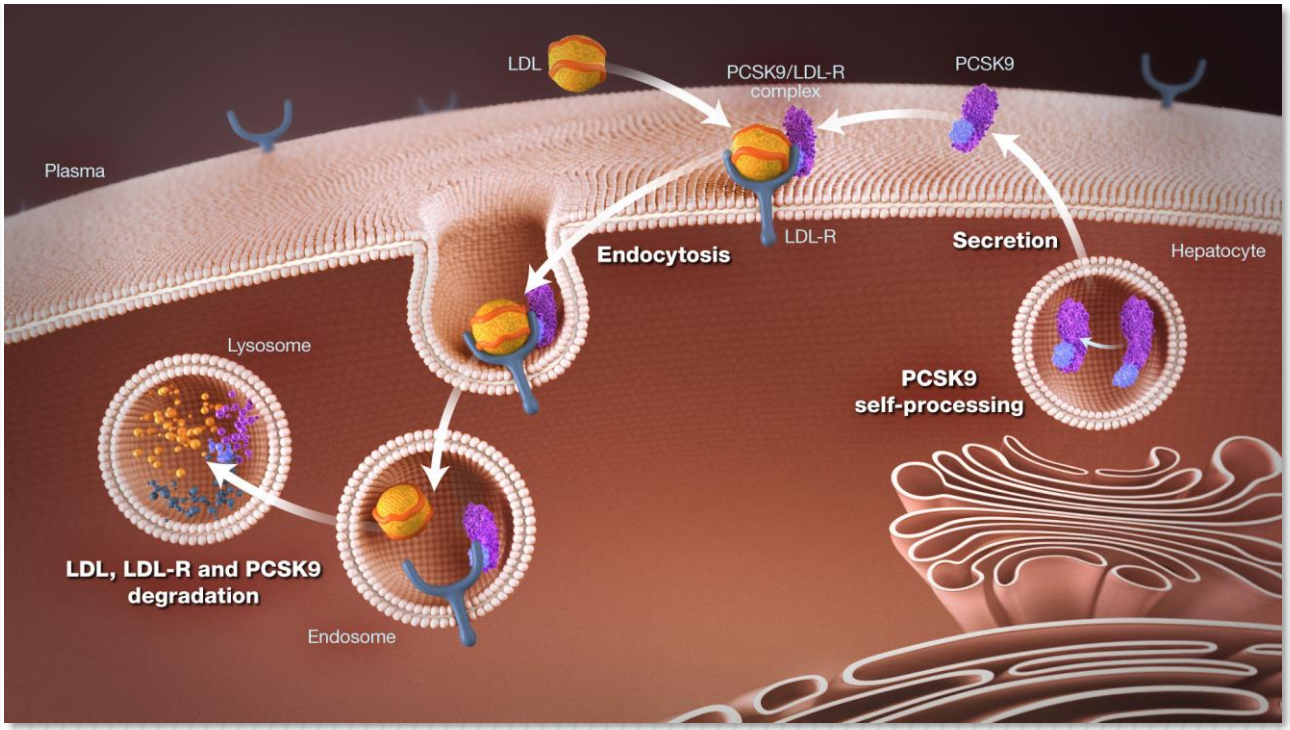
Atorvastatin 10–20 mg
Rosuvastatin 5–10 mg
Simvastatin 20–40 mg
Pravastatin 40 mg
Lovastatin 40 mg
Fluvastatin XL 80 mg
Pitavastatin 2–4 mg
Simvastatin 10 mg + Ezetimibe 10 mg
Pravastatin 20 mg + Ezetimibe 10 mg
Lovastatin 20 mg + Ezetimibe 10 mg
Fluvastatin 40 mg + Ezetimibe 10 mg
Pitavastatin 1 mg + Ezetimibe 10 mg

MOLT ALTA: > 60%

Atorvastatin 40–80 mg + Ezetimibe 10 mg
Rosuvastatin 20–40 mg + Ezetimibe 10 mg

Masana L et al. Atherosclerosis 2015

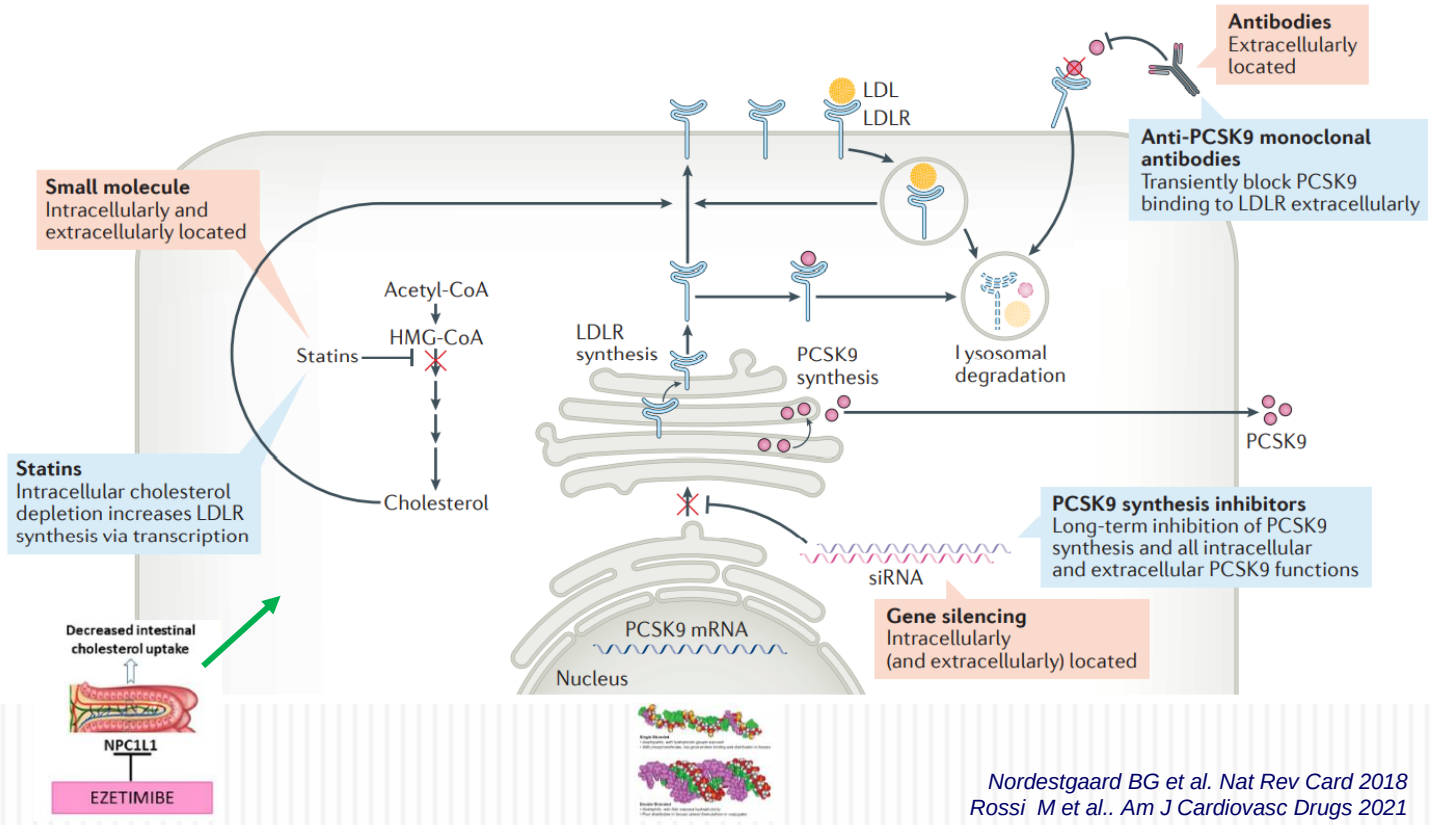
LA PROTEÏNA PCSK9



Qian YW, Schmidt RJ, Zhang Y, et al. J Lipid Res. 2007;48:1488-1498.
Horton JD, Cohen JC, Hobbs HH. J Lipid Res. 2009;50(suppl):S172-S177

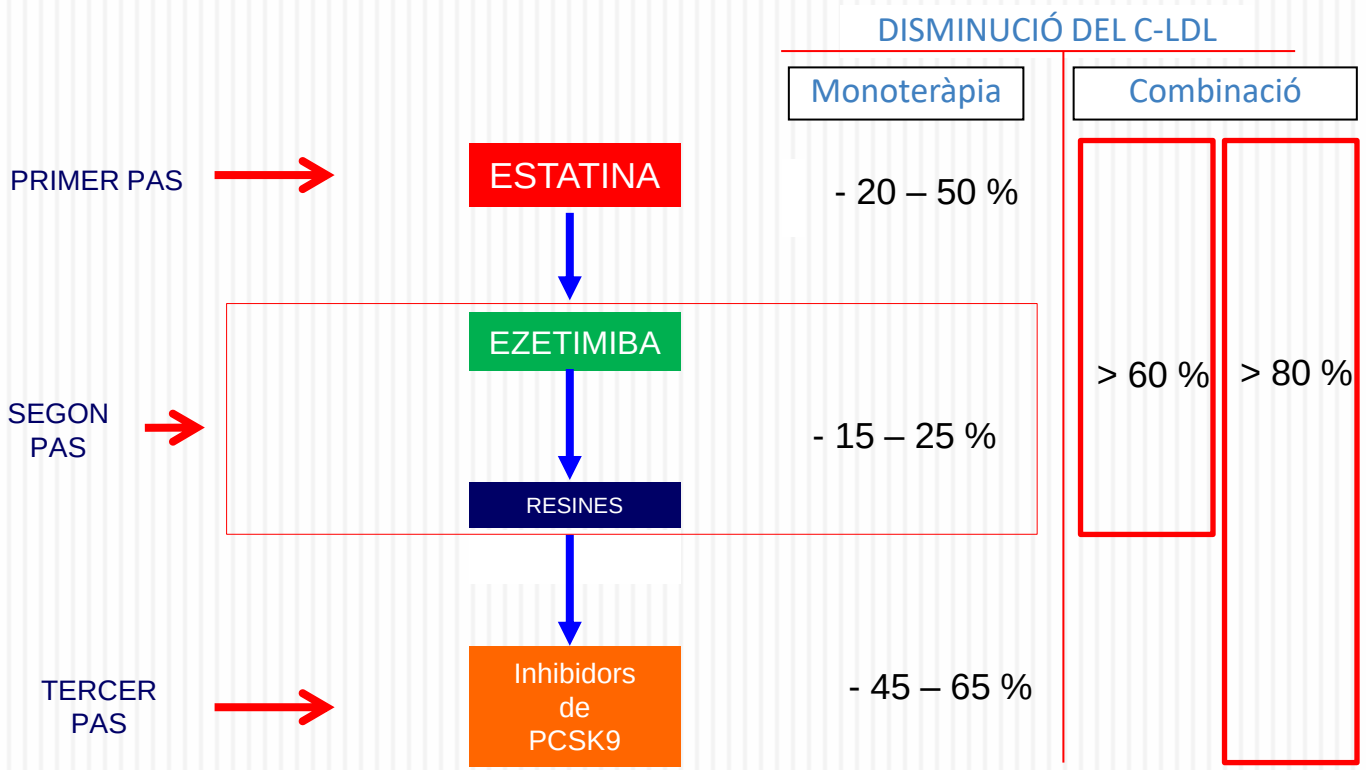
FÀRMACS PER DISMINUIR EL COLESTEROL-LDL

Basats en molècules petites, en anticossos i en silenciament genètic a nivell cel·lular

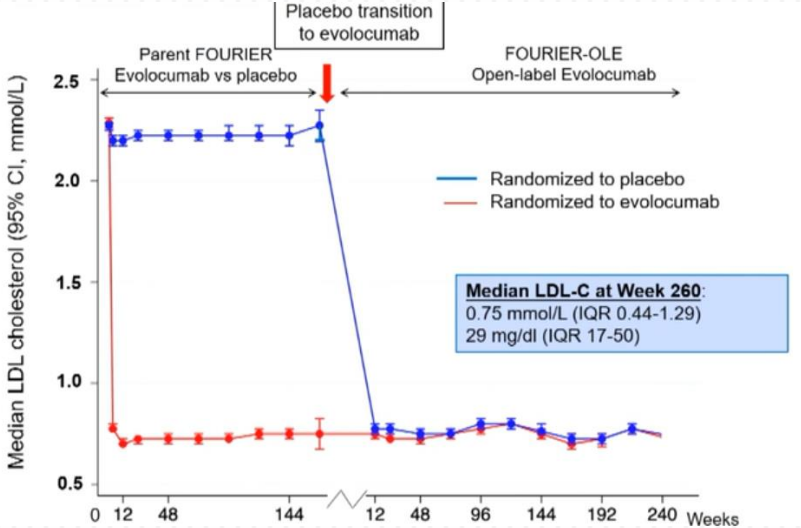


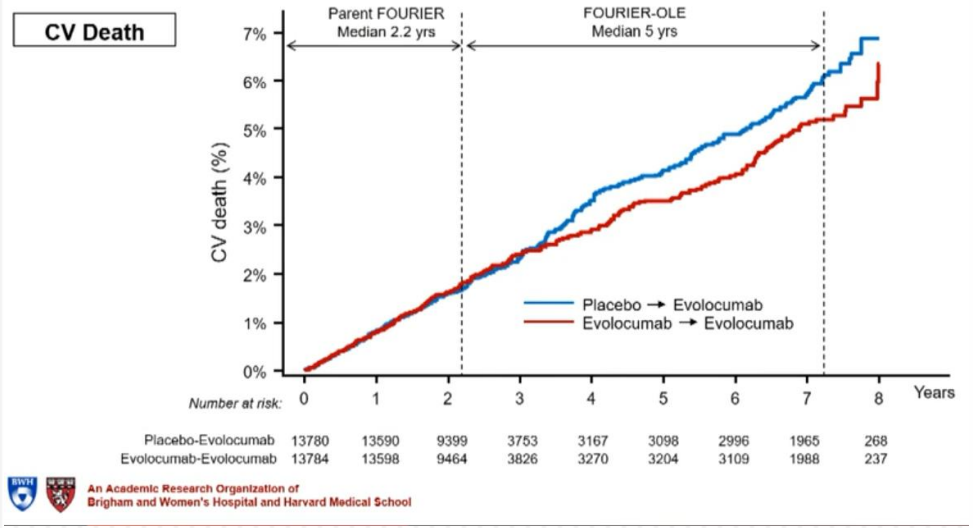
Nordestgaard BG et al. Nat Rev Card 2018
Rossi M et al.. Am J Cardiovasc Drugs 2021

FÀRMACS PER TRACTAR LA HIPERCOLESTEROLÈMIA



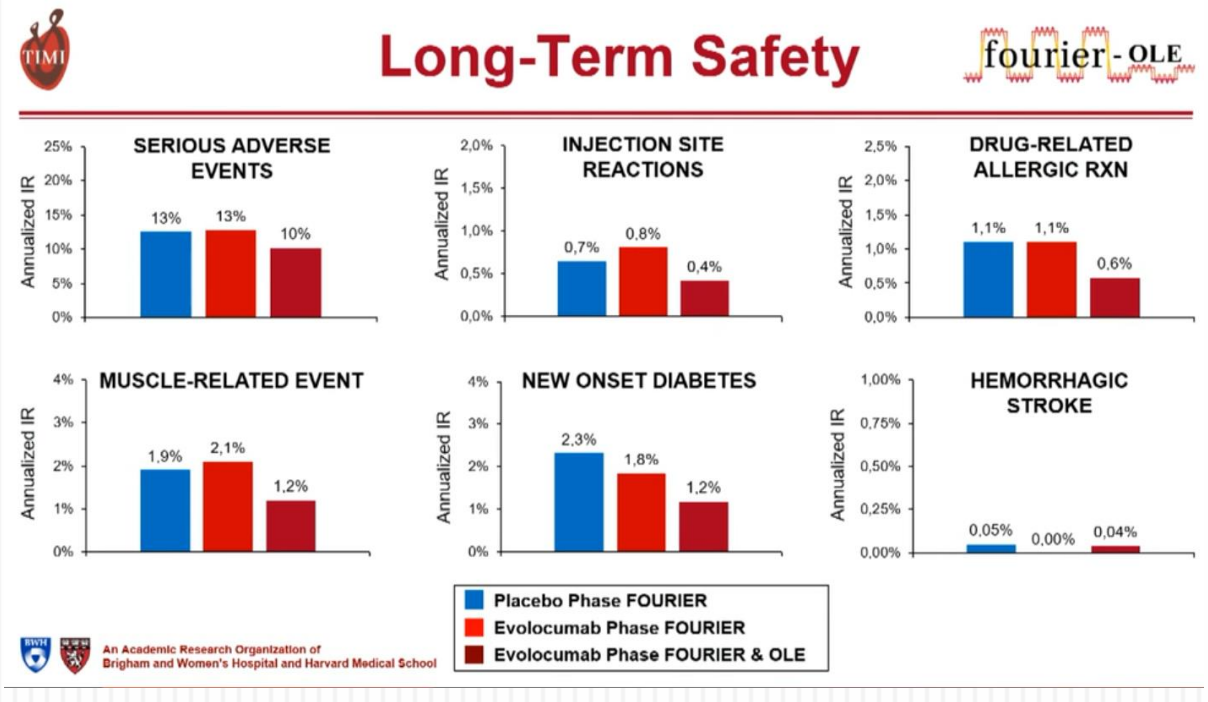
Efficacy during FOURIER & FOURIER-OLE





O'Donoghue ML et al. Circulation. 2022 Aug 29. doi: 10.1161/CIRCULATIONAHA.122.061620

SEGURETAT DEL TRACTAMENT AM EVOLOCUMAB A LLARG TERMINI EN ELS PACIENTS AMB MALALTIA CV ATEROESCLERÒTICA (FOURIER-OLE)



O'Donoghue ML et al. Circulation. 2022 Aug 29. doi: 10.1161/CIRCULATIONAHA.122.061620

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

The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS)

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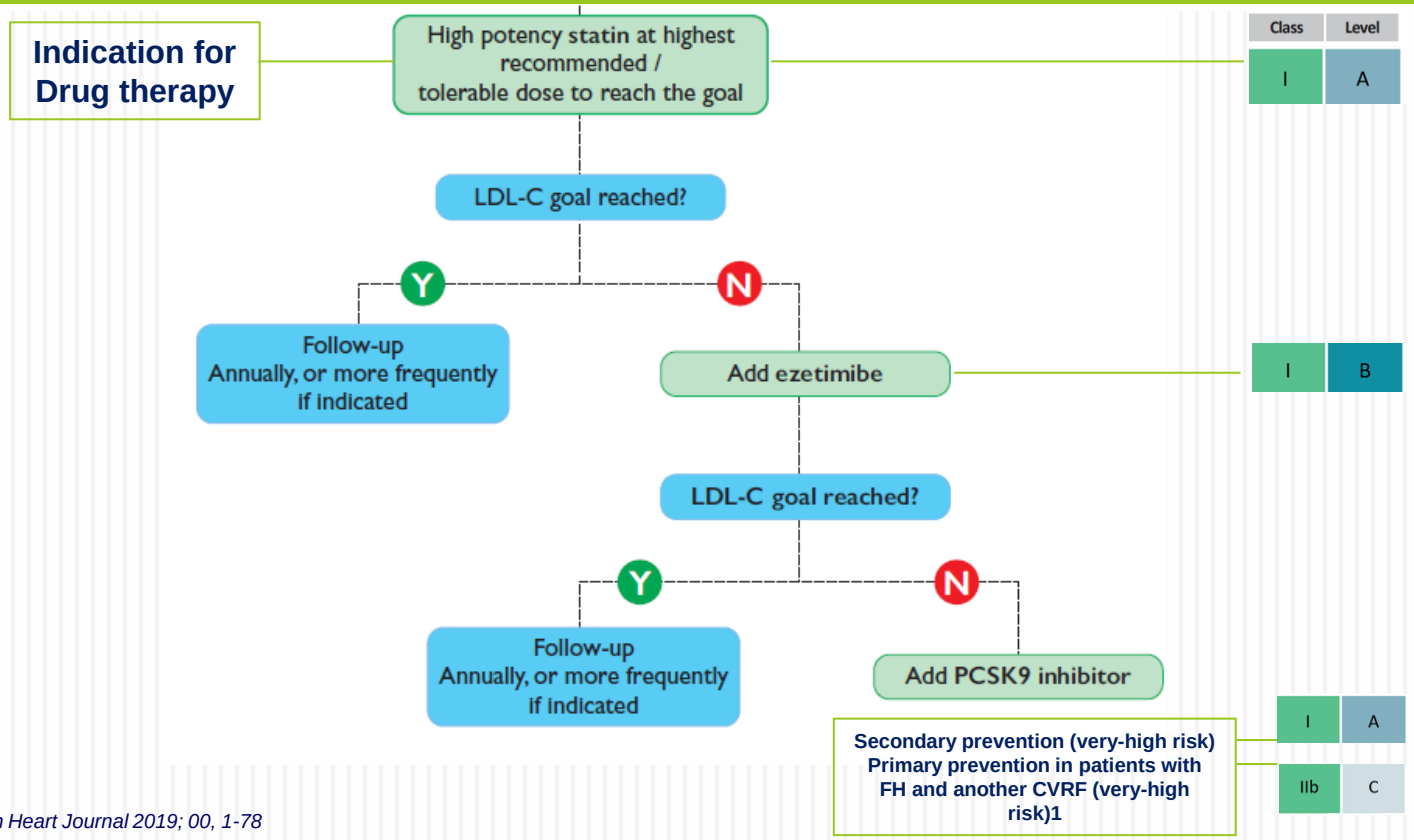
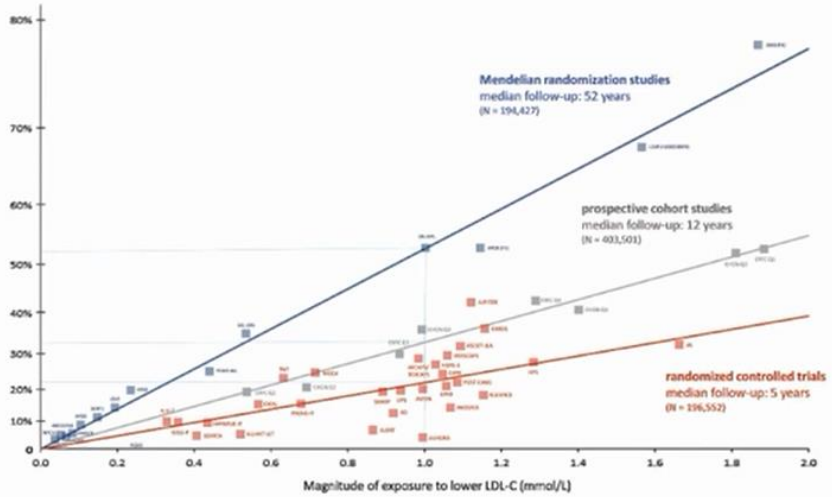


Mach F et al. European Heart Journal 2019; 00, 1-78

EL C-LDL TÉ UN EFECTE CAUSAL I ACUMULATIU SOBRE EL RISC CV

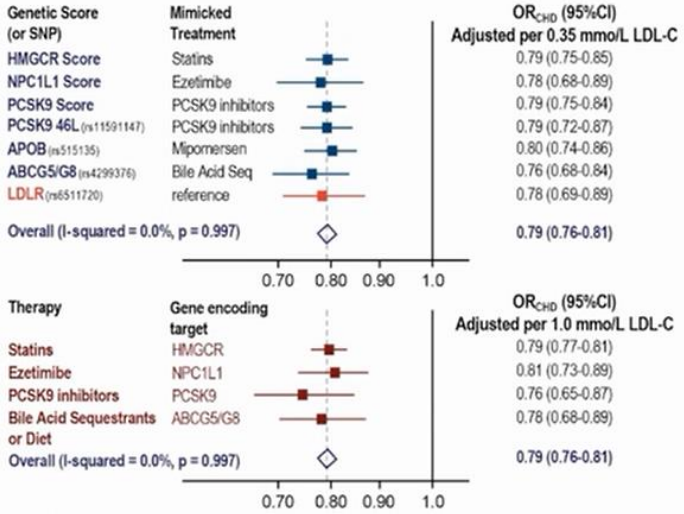
EL BENEFICI DE LA DISMINUCIÓ DEL C-LDL ÉS INDEPENDENT DEL MECANISME

Relationship between LDL-C exposure and risk of CVD from 3 types of evidence across multiple studies



Used with permission.

Reduction of risk for CV events based on genetic variation (top) and lipid-lowering therapies (bottom)



Adapted with permission.

ABCG5/G8=ABC-transporter G5 and ABC-transporter G8; APOB=apolipoprotein B; HMGCR=3-methyl-glutaryl-coenzyme A reductase; LDLR=LDL receptor; NPC1L1=Niemann-Pick C1 like1; OR=odds ratio; SNP=single nucleotide polymorphism.

Ference BA, et al. *Eur Heart J* 2017;38:2459-2472.

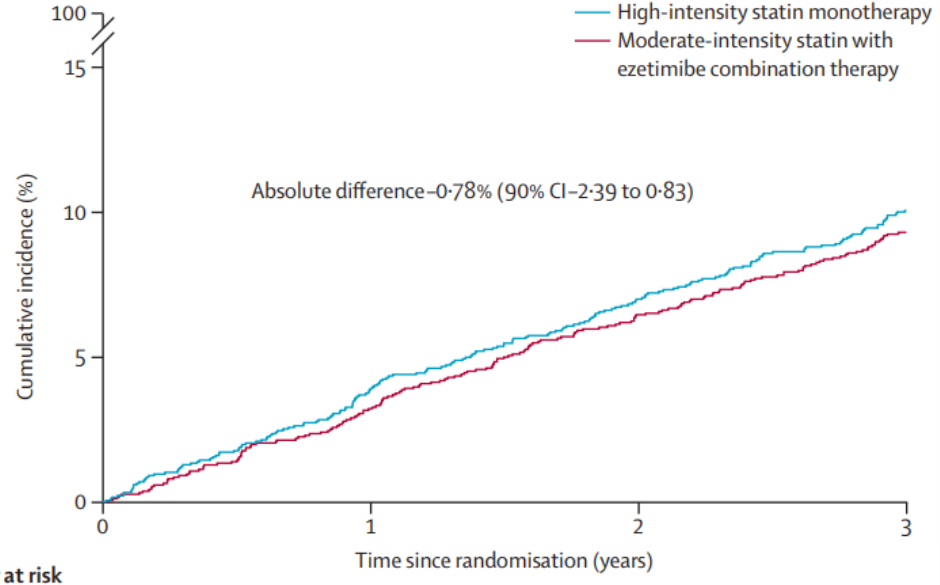
Long-term efficacy and safety of moderate-intensity statin with ezetimibe combination therapy versus high-intensity statin monotherapy in patients with ACVD (RACING): a randomised, open-label, non-inferiority trial

Estudio aleatorizado, multicéntrico, abierto y controlado en 3780 pacientes con ECVA

Estatina de moderada intensidad (Rosuvastatina 10 mg) + Ezetimiba 10 mg

VS

Monoterapia con estatina de alta intensidad (Rosuvastatina 20 mg)



Number at risk				
Monotherapy	1886	1786	1711	1639
Combination therapy	1894	1795	1724	1654

Byeong-Keuk Kim et al. Lancet 2022; 400: 380–90

RACING STUDY

Proportions of the patients with LDL-C < 70mg/dL at 3 years (Intention to treat population)

	Moderate-intensity statin with ezetimibe combination therapy	High-intensity statin monotherapy	Absolute differences in proportions, % (95% CI)
Number of patients	1349	1315	..
Number of patients with LDL cholesterol concentrations <70 mg/dL	978 (72%)	759 (58%)	14·8 (11·1 to 18·4)
LDL cholesterol concentration (mg/dL)	58 (47–71)	66 (54–80)	..

Data are number of patients (%) or median (IQR).

	Moderate-intensity statin with ezetimibe combination therapy (n=1846)	High-intensity statin monotherapy (n=1832)	Absolute difference (95% CI)
Serious adverse events			
Death	26 (1·4%)	22 (1·2%)	0·21 (–5·88 to 1·01)
Adverse events			
Discontinuation or dose reduction of study drug due to intolerance	88 (4·8%)	150 (8·2%)	–3·42 (–5·07 to –1·80)

En els pacients amb MCVA una estatina de moderada intensitat associada a ezetimiba no és inferior a una estatina d'alta intensitat quant a la incidència de MCVA al cap de 3 anys, i és superior en la consecució dels objectius de c-LDL amb una incidència menor d'intoleràncies.

Byeong-Keuk Kim et al. Lancet 2022; 400: 380–90

Current Cardiology Reports (2020) 22: 66
https://doi.org/10.1007/s11886-020-01326-w

LIPID ABNORMALITIES AND CARDIOVASCULAR PREVENTION (SECTION EDITORS)

Reasons Why Combination Therapy Should Be the New Standard of Care to Achieve the LDL-Cholesterol Targets

Lipid-lowering combination therapy

Lluís Masana[1,2] · Daiana Ibarretxe[1,2] · Núria Plana[1,2]

ESC European Society of Cardiology
European Heart Journal (2021) 42, 253–256
doi:10.1093/eurheartj/ehaa1008

EDITORIAL

Changing the paradigm for post-MI cholesterol lowering from intensive statin monotherapy towards intensive lipid-lowering regimens and individualized care

Kausik K. Ray *

Imperial Centre for Cardiovascular Disease Prevention, Department of Primary Care and Public Health, Imperial College, London, UK

Rev Esp Cardiol. 2020;73(2):161–167

Special article

Recommendations to improve lipid control. Consensus document of the Spanish Society of Cardiology

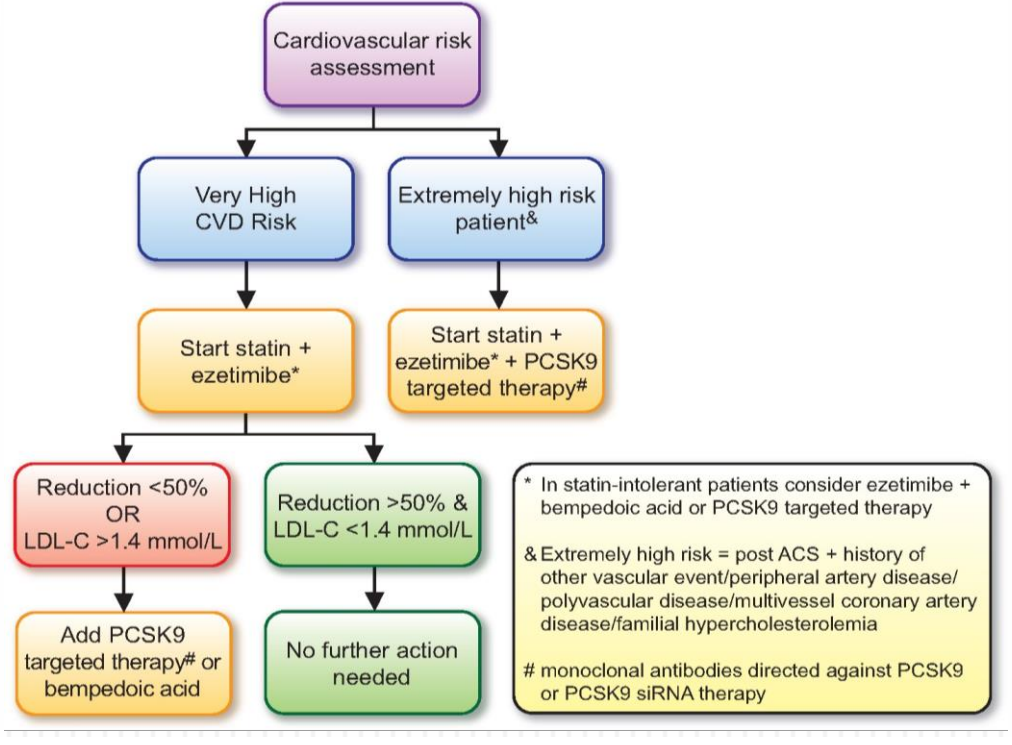
Carlos Escobar,[a,*] Manuel Anguita,[b] Vicente Arrarte,[c] Vivencio Barrios,[d] Ángel Cequier,[e] Juan Cosín-Sales,[f] Isabel Egocheaga,[g] Esteban López de Sa,[a] Luis Masana,[h] Vicente Pallarés,[i] Leopoldo Pérez de Isla,[j] and Xavier Pintó,[k]

Expert reviewers: José Ramón González Juanatey,[l] and José Luis Zamorano[d]

Combination lipid-lowering therapy as first-line strategy in very high-risk patients

VIEWPOINT
Epidemiology and prevention

Kausik K. Ray[1]*, Laurens F. Reeskamp[2], Ulrich Laufs[3], Maciej Banach[4], François Mach[5], Lale S. Tokgözoğlu[6], Derek L. Connolly[7], Anja J. Gerrits[8], Erik S. G. Stroes[2], Luis Masana[9], and John J. P. Kastelein[2]



Ray KK et al. European Heart Journal (2022) 43, 830–833

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Moltes gràcies