

CURRENT AND FUTURE THERAPEUTIC APPROACHES

Ezetimibe and combination therapy

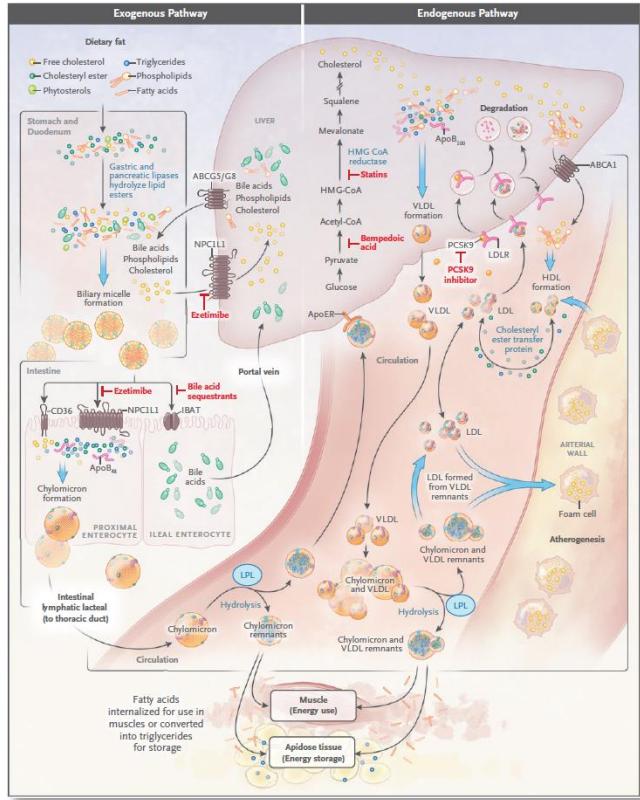
Lluís Masana
Vascular Medicine and Metabolism Unit
"Sant Joan" University Hospital. IISPV. CIBERDEM
Universitat Rovira i Virgili.
Reus (Spain)

CONFLICT OF INTEREST DISCLOSURES

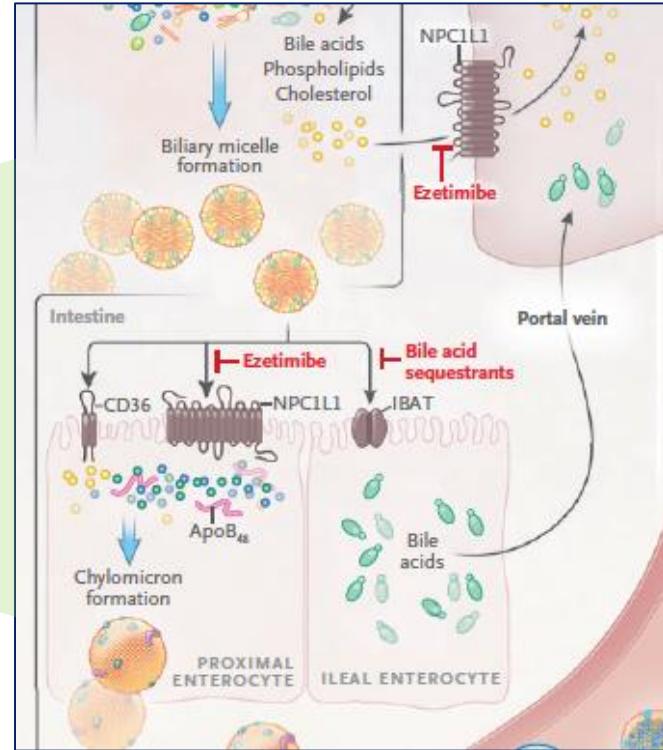
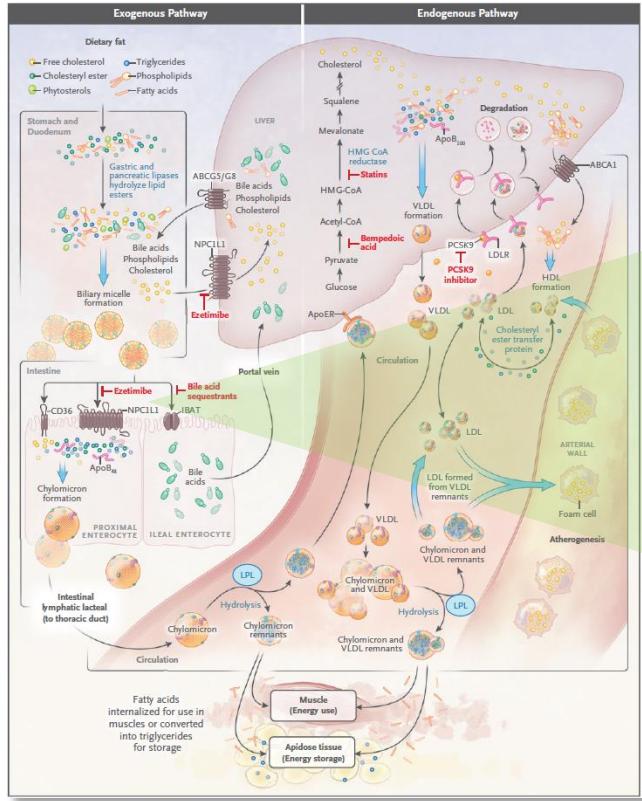
Fees for Lectures or Advisory work from:

Amgen; Sanofi-Regeneron; Mylan; Servier;
Daichii/Sankyo; Amryt.

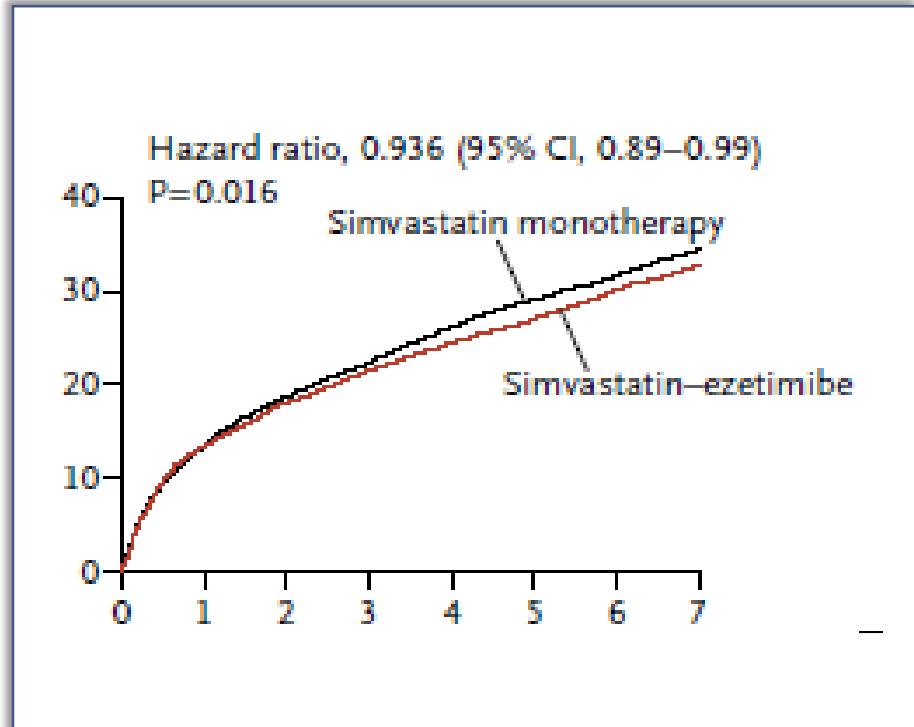
Ezetimibe: Selective Inhibitor of cholesterol transporter NPC1L1



Ezetimibe: Selective Inhibitor of cholesterol transporter NPC1L1

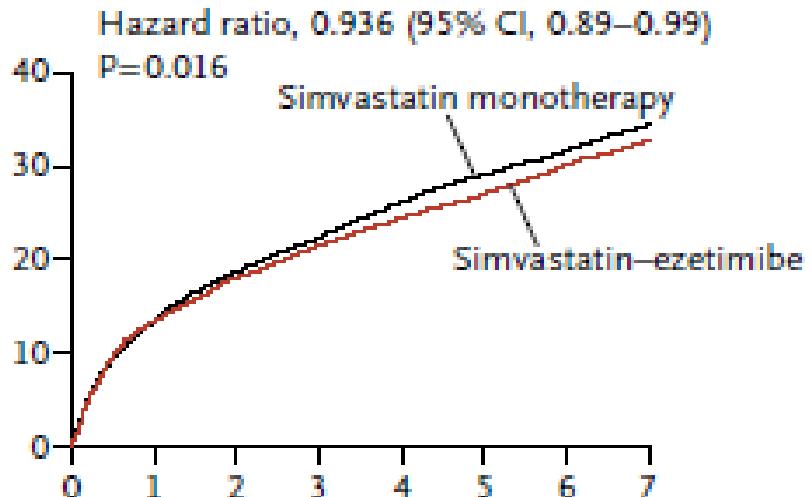


IMPROVE-IT TRIAL

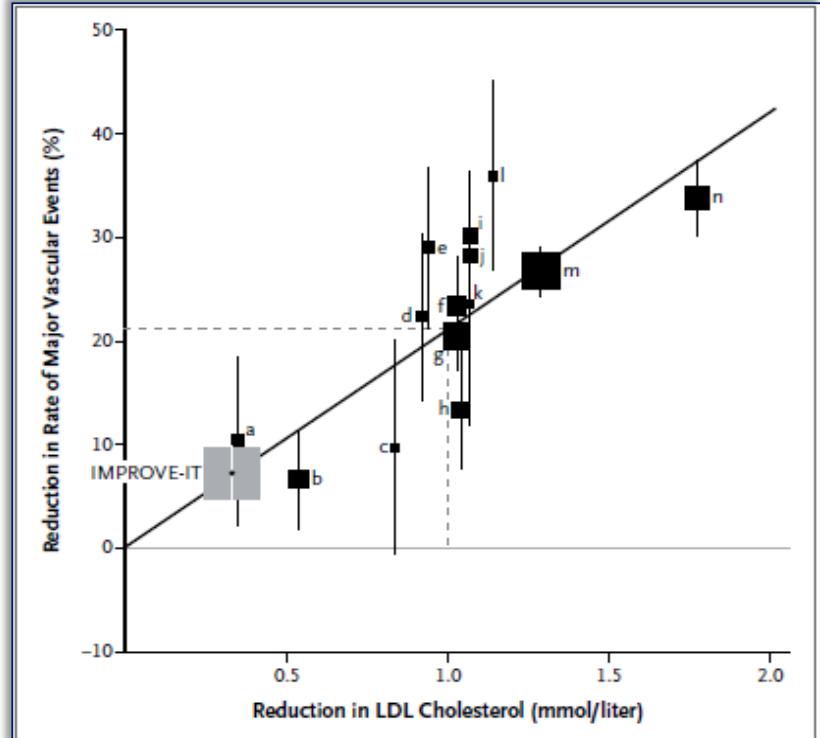


First non statin LLD to show CV benefit

IMPROVE-IT TRIAL

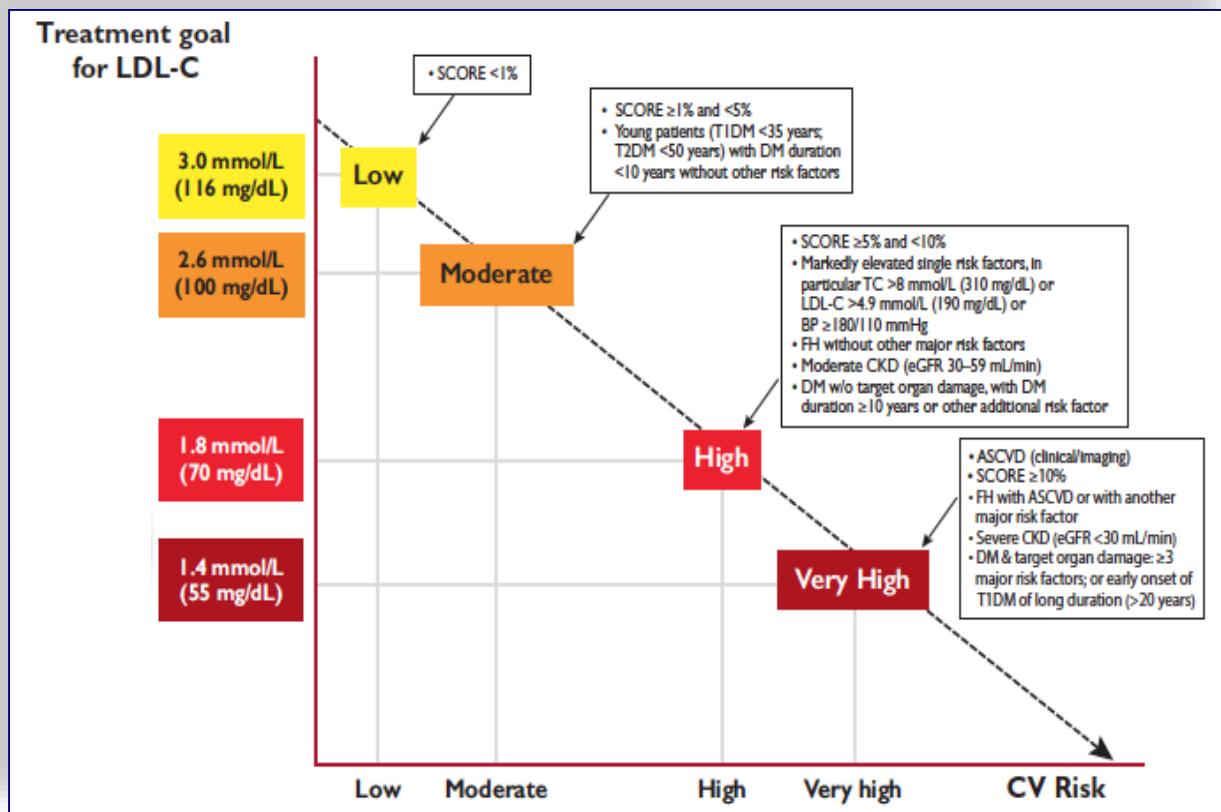


First non statin LLD to show CV benefit

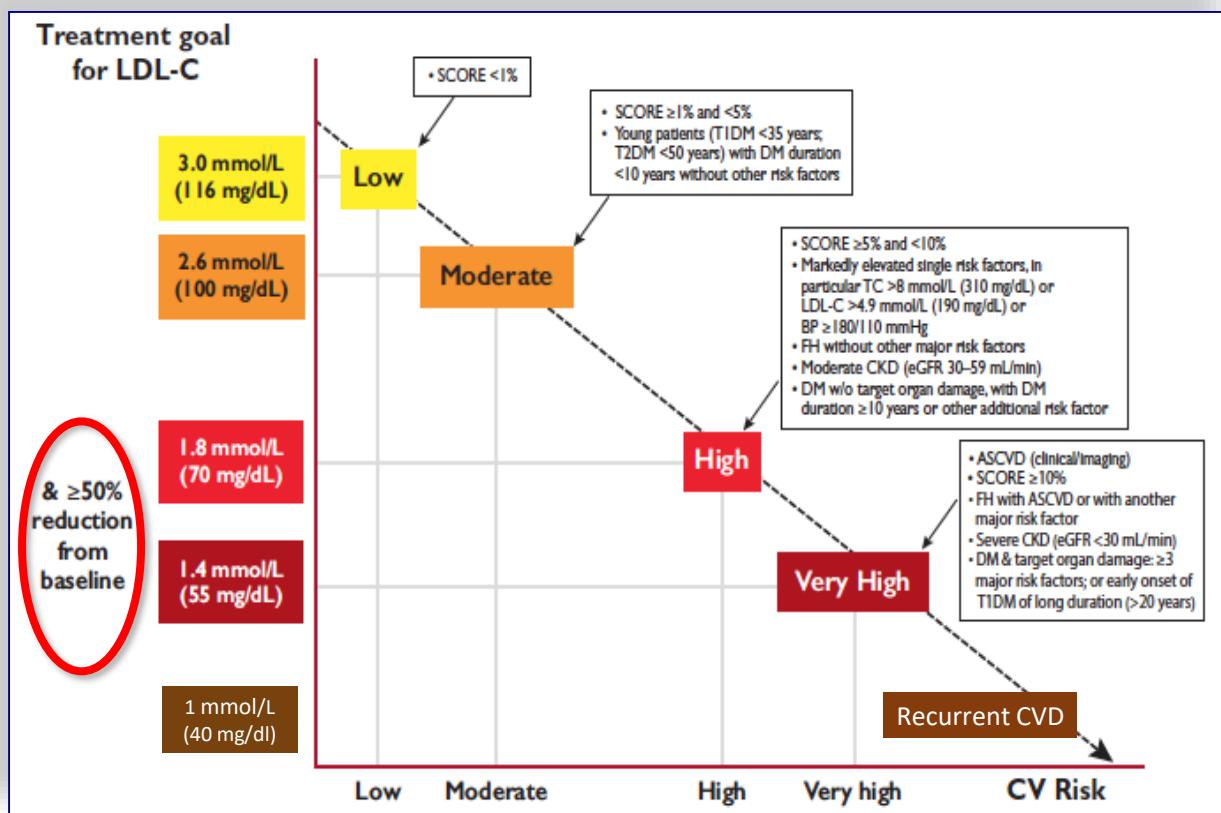


Risk reduction according LDL decrease

ESC/EAS 2019 guidelines: Treatment goals for LDL-C across cardiovascular risk categories



ESC/EAS 2019 guidelines: Treatment goals for LDL-C across cardiovascular risk categories



Very low LDL-C targets (< 55 mg)

The lower
the better

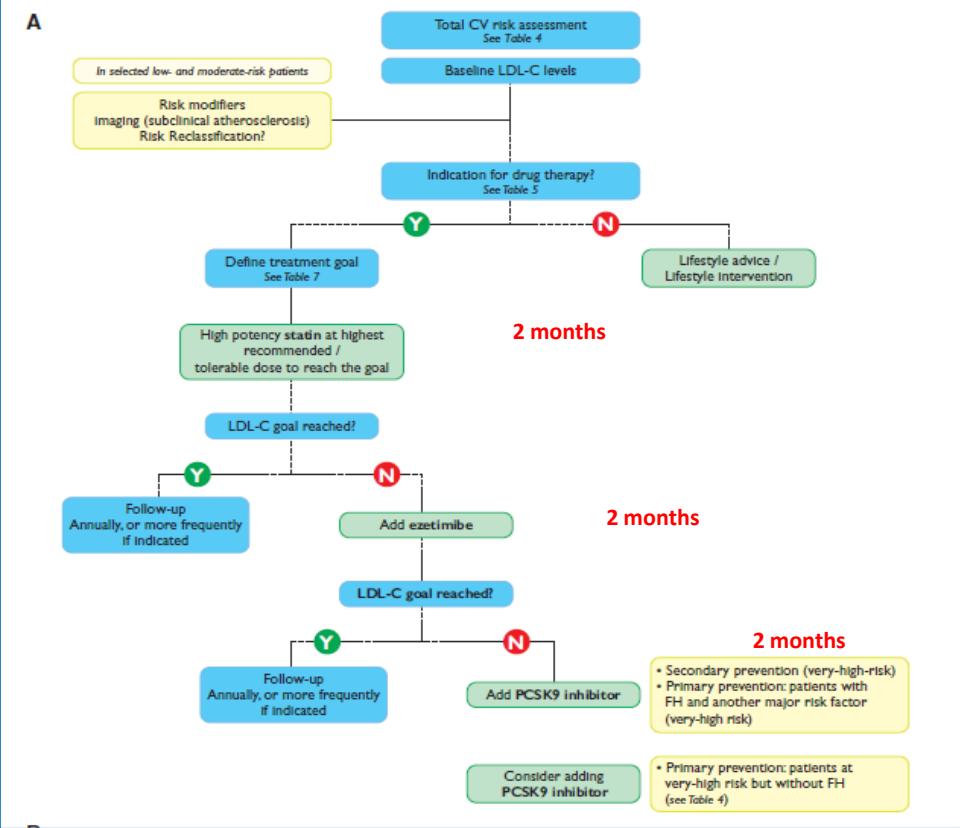


Lipid lowering therapy
addressed to CV risk reduction

Scientific
evidence

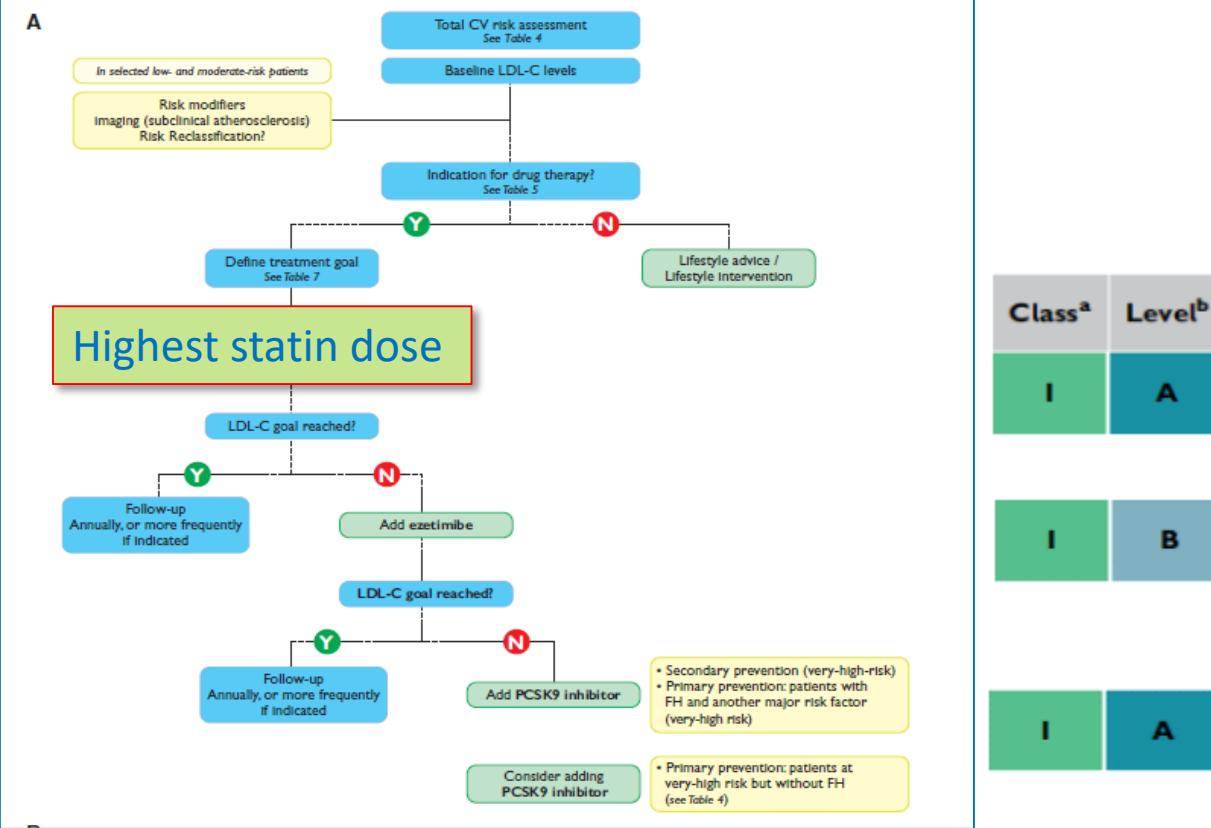
At least 50% LDL reduction

2019 ESC/EAS dyslipidemia guidelines: Therapy strategy

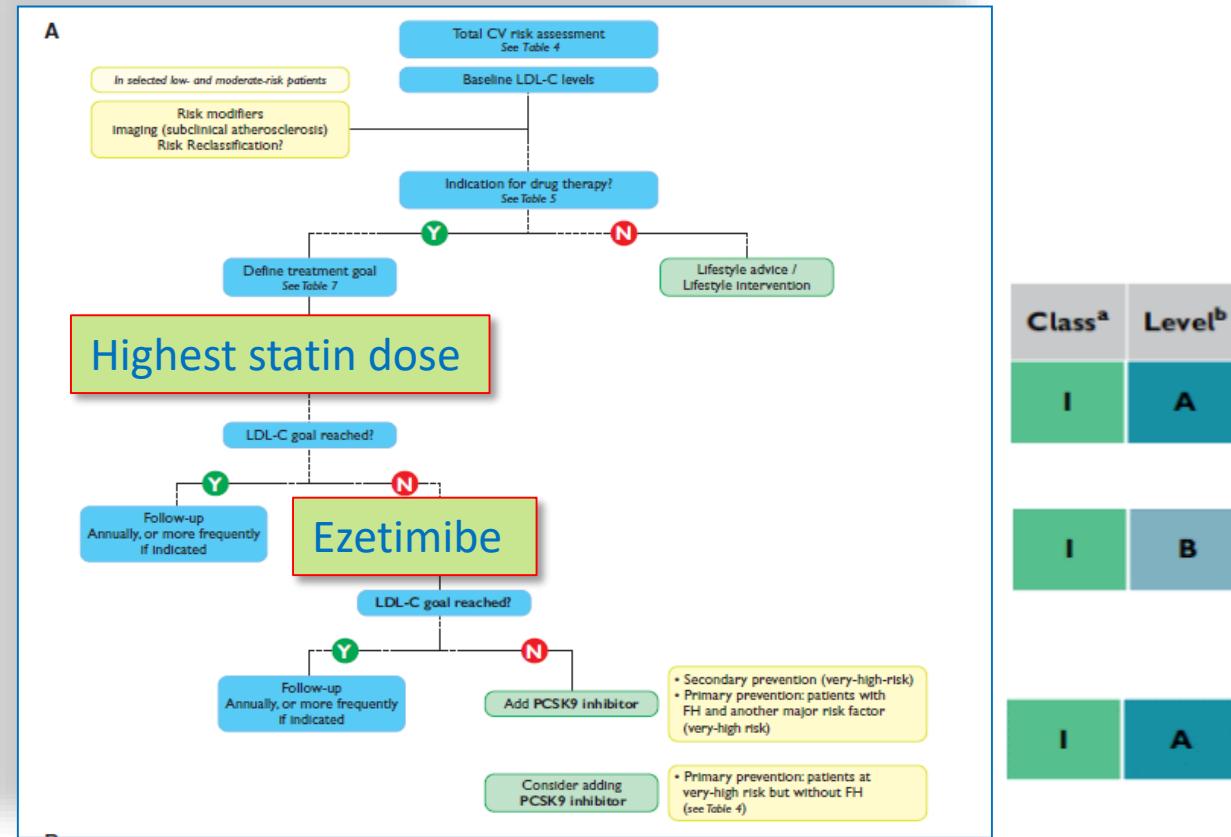


Class ^a	Level ^b
I	A
I	B
I	A

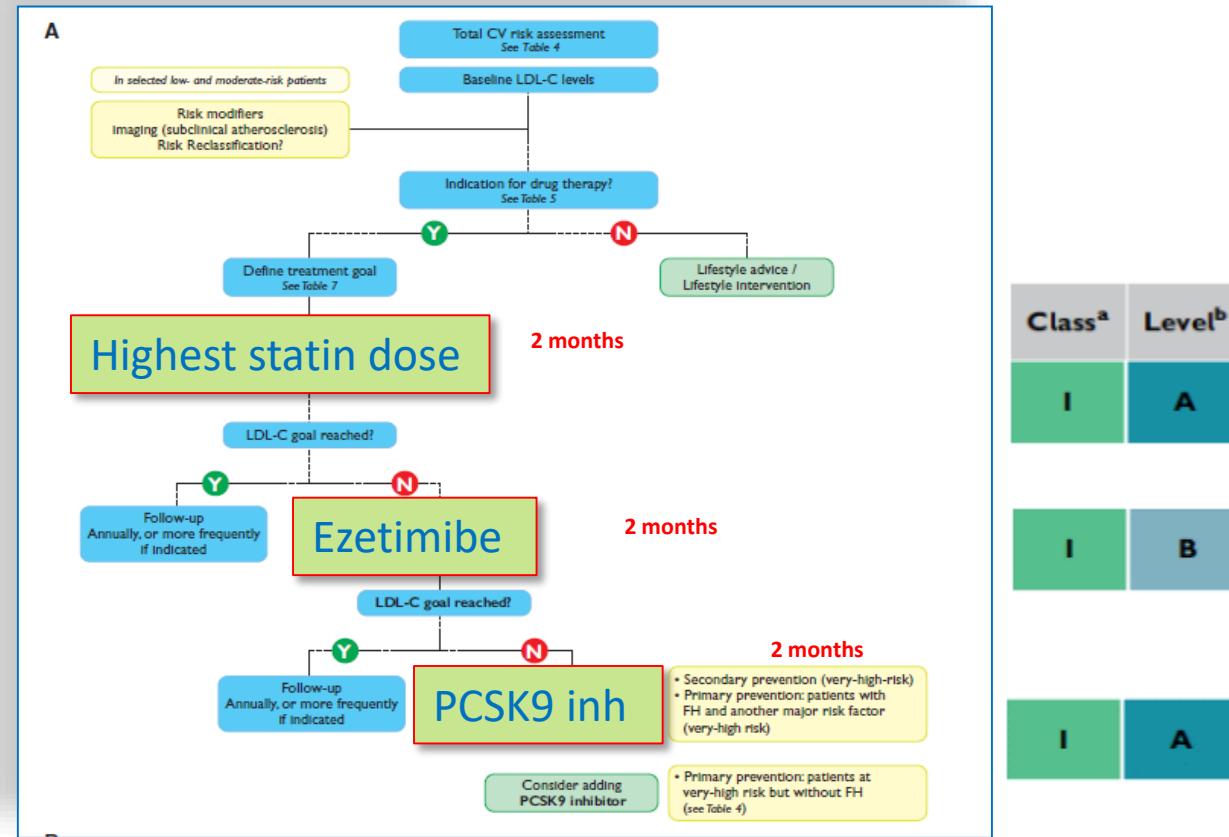
2019 ESC/EAS dyslipidemia guidelines: Therapy strategy



2019 ESC/EAS dyslipidemia guidelines: Therapy strategy



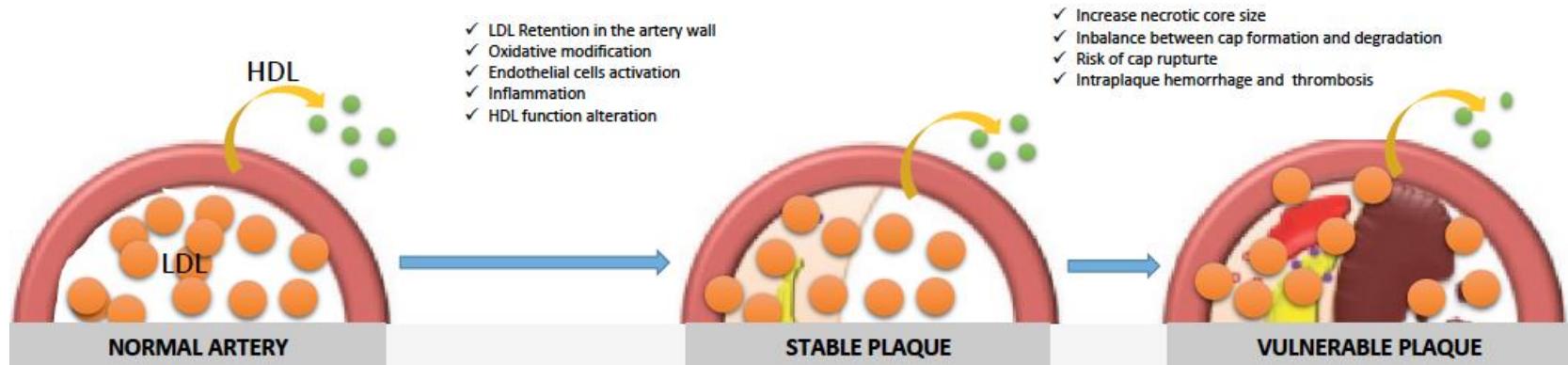
2019 ESC/EAS dyslipidemia guidelines: Therapy strategy



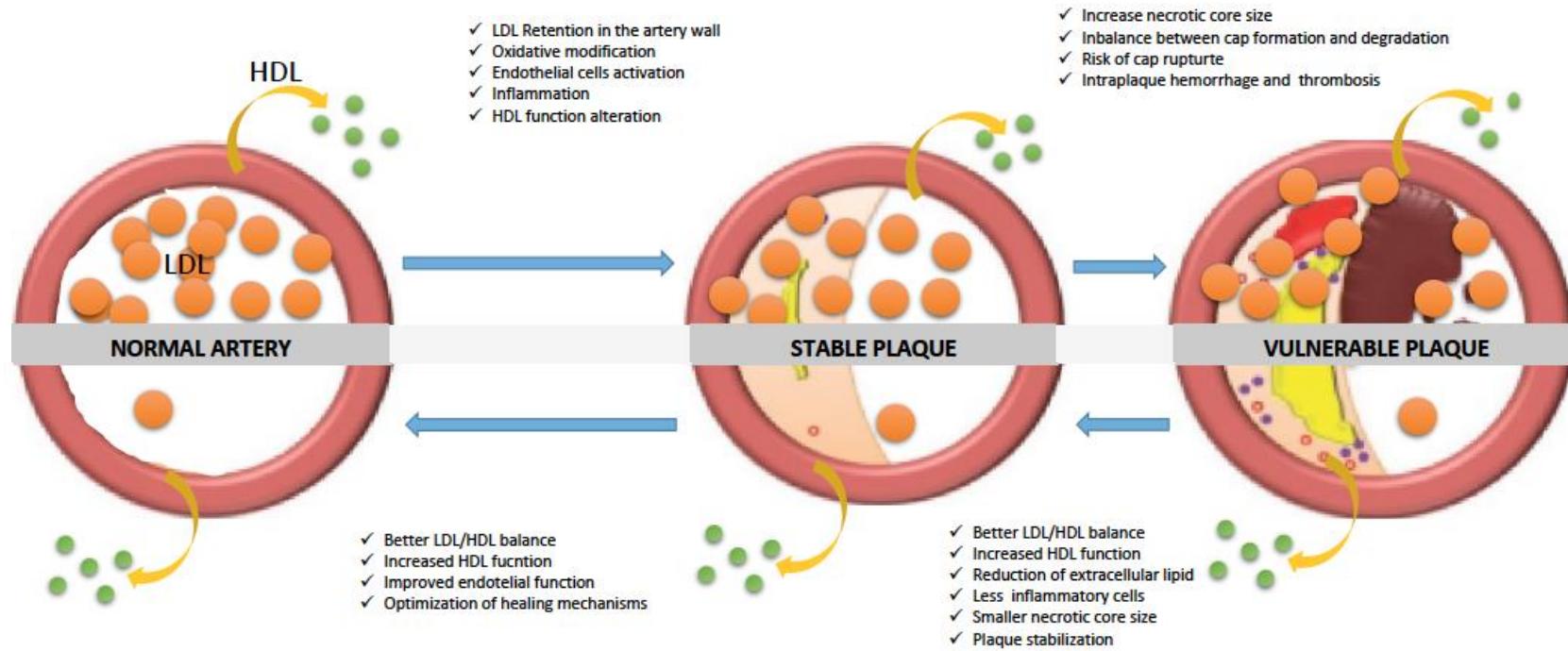


LDL
STATINS

HIGH LDL

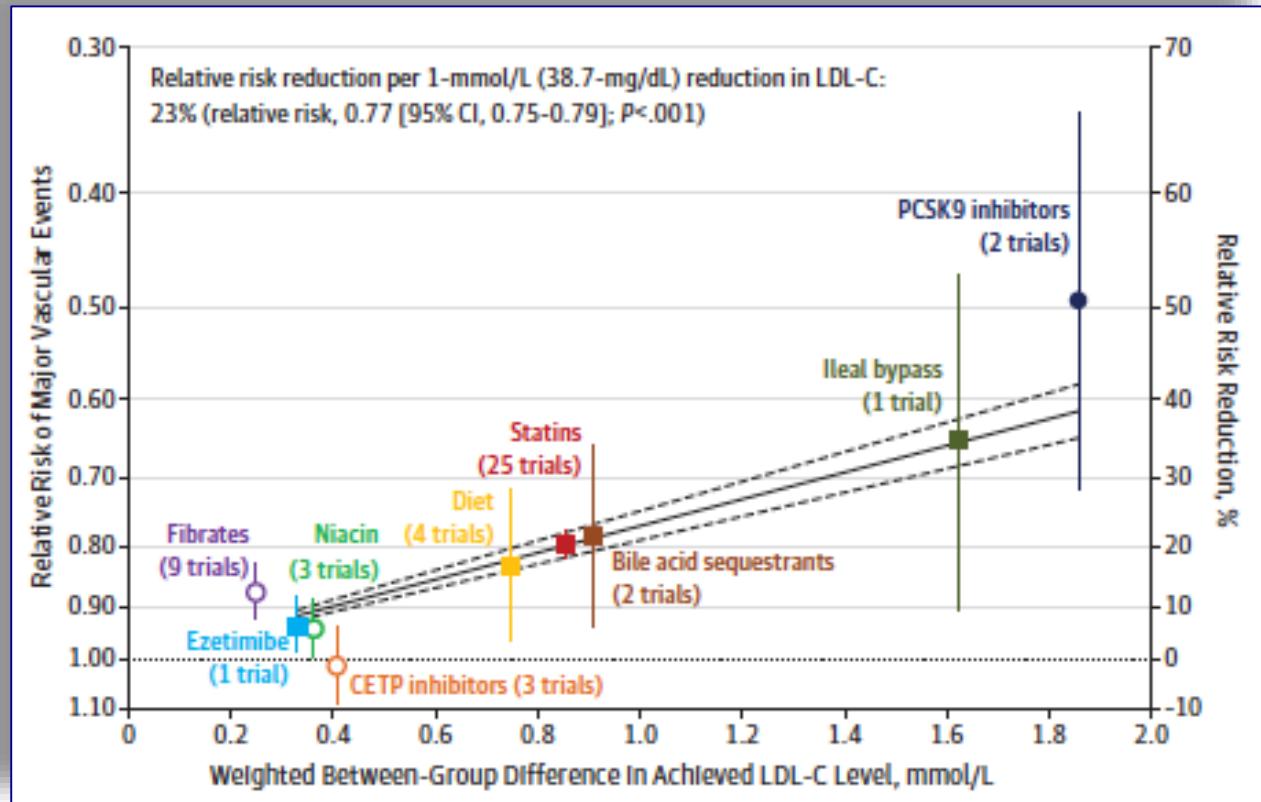


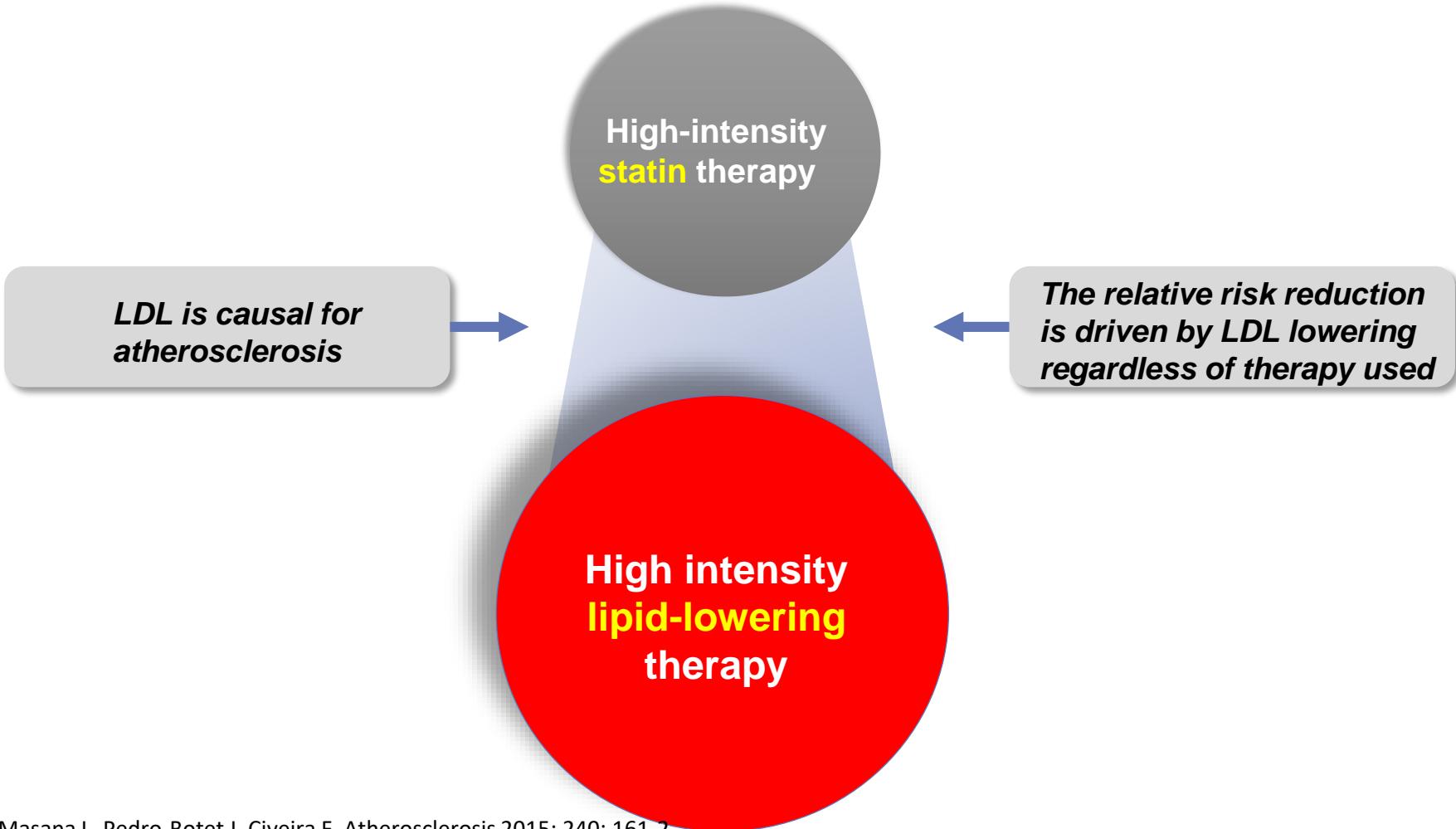
HIGH LDL



LOW LDL

Relative Risk Reduction is driven by LDL-C Lowering regardless of therapy used





High-intensity LDL lowering therapy: Something else than high-intensity statin therapy !!!

Low-intensity cholesterol-lowering therapy (LICLT) ↓ LDLc < 30%	Mild-intensity cholesterol-lowering therapy (MICLT) ↓ LDLc 30–49%
Simvastatin 10 mg	Atorvastatin 10–20 mg
Pravastatin 10–20 mg	Rosuvastatin 5–10 mg
Lovastatin 10–20 mg	Simvastatin 20–40 mg
Fluvastatin 40 mg	Pravastatin 40 mg
Pitavastatin 1 mg	Lovastatin 40 mg
Ezetimibe 10 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

High-intensity LDL lowering therapy: Something else than high-intensity statin therapy !!!

Low-intensity cholesterol-lowering therapy (LICLT) ↓ LDLc < 30%	Mild-intensity cholesterol-lowering therapy (MICLT) ↓ LDLc 30–49%	High-intensity cholesterol-lowering therapy (HICLT) ↓ LDLc 50–60%	Very-high-intensity cholesterol-lowering therapy (VHICLT) ↓ LDLc > 60%
Simvastatin 10 mg Pravastatin 10–20 mg Lovastatin 10–20 mg Fluvastatin 40 mg Pitavastatin 1 mg Ezetimibe 10 mg	Atorvastatin 10–20 mg Rosuvastatin 5–10 mg Simvastatin 20–40 mg Pravastatin 40 mg Lovastatin Fluvastatin Pitavastatin Simvastatin Pravastatin Lovastatin Simvastatin 20–40 mg + Ezetimibe 10 mg Fluvastatin Pitavastatin	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	Atorvastatin 40–80 mg + Ezetimibe 10 mg Rosuvastatin 20–40 mg + Ezetimibe 10 mg

Triglyceride lowering

Statins

Cholesterol lowering

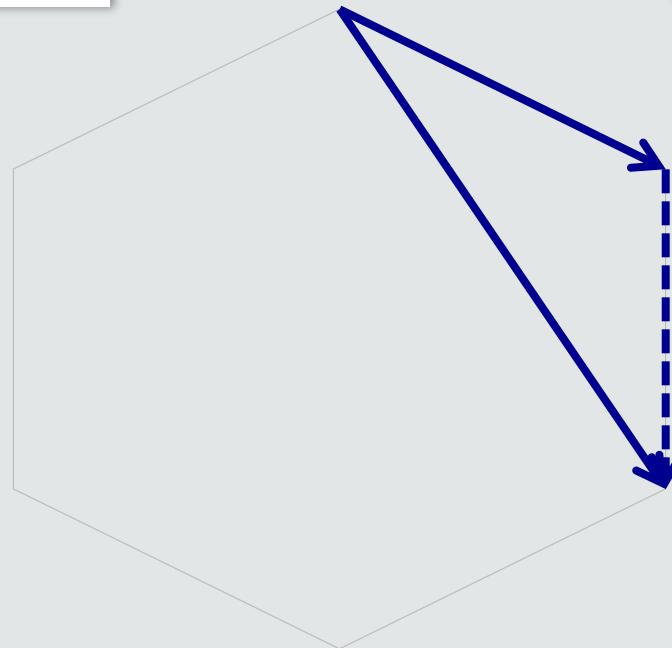
Fibrates

Omega-3
Fatty Acids

Ezetimibe

PCSK9 inhibitors

Resins



Triglyceride lowering

Statins

Cholesterol lowering

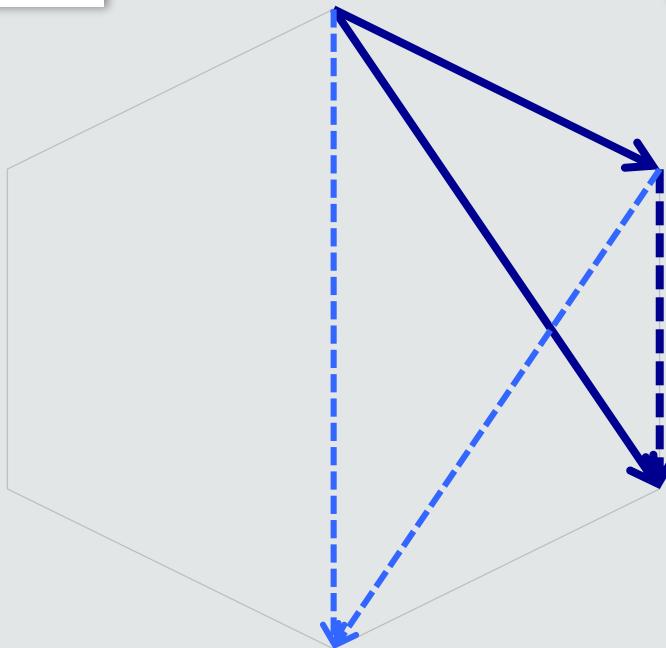
Fibrates

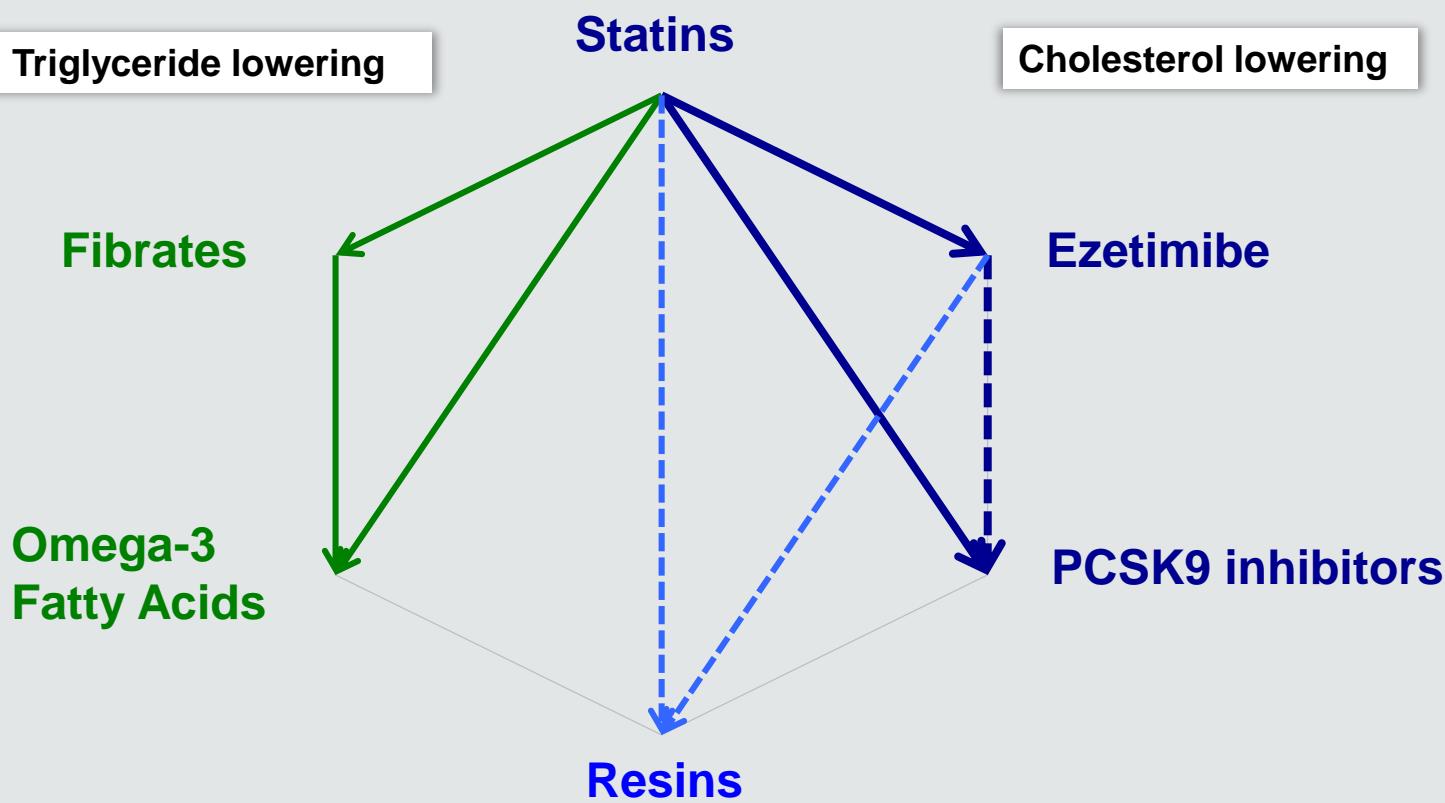
Omega-3
Fatty Acids

Ezetimibe

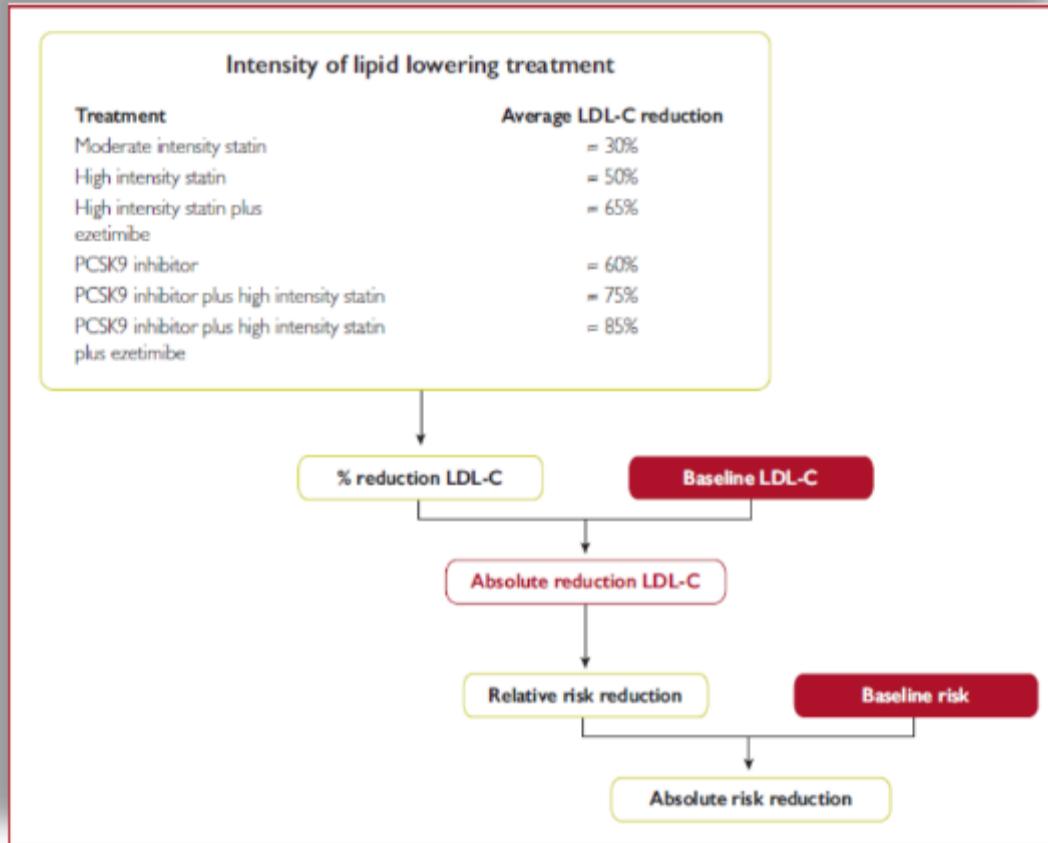
PCSK9 inhibitors

Resins



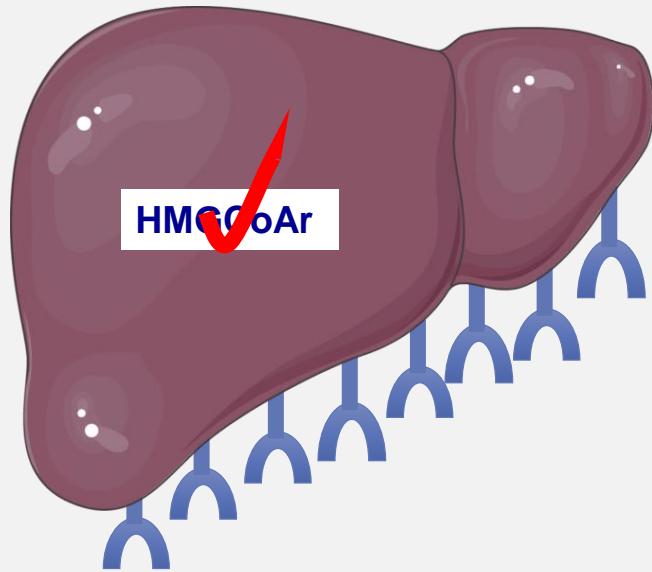


2019 ESC/EAS dyslipidemia guidelines: Therapy strategy



LIPID LOWERING COMBINATION THERAPY = SINERGY

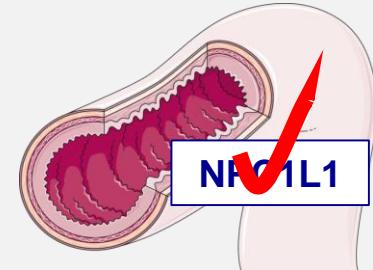
STATINS



PCSK9 INH

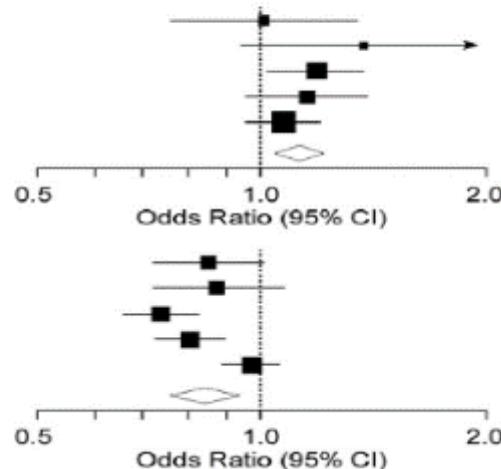


EZETIMIBE



The diabetogenic effects of statins appear to be dose-related.

	Cases/Total, No. (%)		
	Intensive Dose	Moderate Dose	OR (95% CI)
Incident Diabetes			
PROVE IT_TIM 22, 2004	101/1707 (5.9)	99/1688 (5.9)	1.01 (0.76-1.34)
A to Z, 2004	65/1768 (3.7)	47/1736 (2.7)	1.37 (0.94-2.01)
TNT, 2005	418/3798 (3.7)	358/3797 (9.4)	1.19 (1.02-1.38)
IDEAL, 2005	240/3737 (6.4)	209/3724 (5.6)	1.15 (0.95-1.40)
SEARCH, 2010	625/5398 (11.6)	587/5399 (10.9)	1.07 (0.95-1.21)
Pooled odds ratio	1449/16408 (8.8)	1300/16344 (8.0)	1.12 (1.04-1.22)
Heterogeneity; $\tau^2=0\%$; $P=.60$			
Incident CVD			
PROVE IT_TIM 22, 2004	315/1707 (18.4)	355/1688 (21.0)	0.85 (0.72-1.01)
A to Z, 2004	212/1768 (12.0)	234/1736 (13.5)	0.87 (0.72-1.07)
TNT, 2005	647/3798 (17.0)	830/3797 (21.9)	0.73 (0.65-0.82)
IDEAL, 2005	776/3737 (20.8)	917/3724 (24.6)	0.80 (0.72-0.89)
SEARCH, 2010	1184/5398 (21.9)	1214/5399 (22.5)	0.97 (0.88-1.06)
Pooled odds ratio	3134/16408 (19.1)	1214/16344 (22.5)	0.84 (0.75-0.94)
Heterogeneity; $\tau^2=74\%$; $P=.004$			



Three opportunities to prescribe combination therapy



LI statin plus ezetimibe

Statin intolerant patients

L-MI statin plus ezetimibe

Optimized therapy without maximum statin dose.

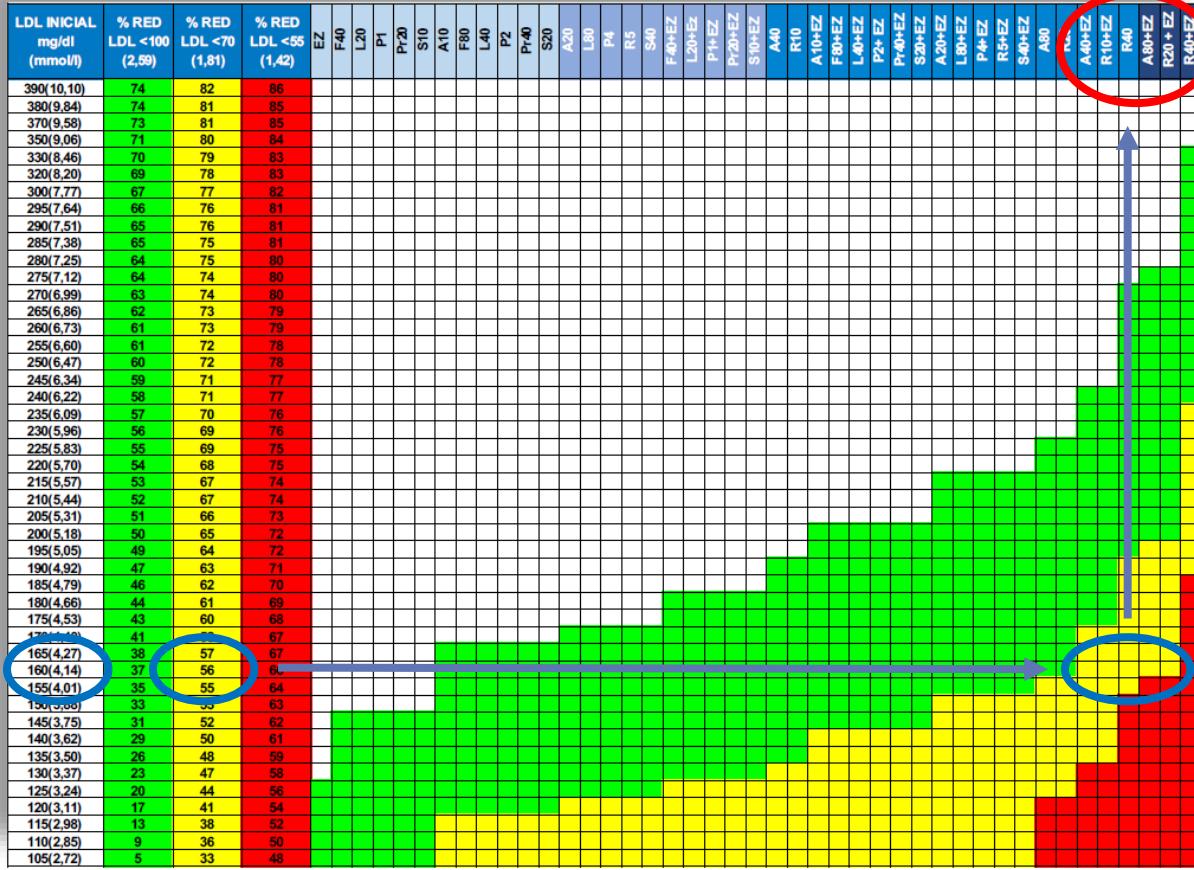
Higher adherence/efficacy

HII statin + ezetimibe

To obtain the maximum LDL reduction

Very high risk patients

TABLE ORIENTED TO OBTAIN THE LDL THERAPEUTIC OBJECTIVES
Masana and Plana Table (4th edition)



To take home:

Over and over again ! The number of patients achieving the LDL targets is unacceptably low

LDL is an etiological factor for atherosclerosis.
LDL lowering therapy drives risk reduction

Therapy should be personalized according our patients needs

Our patients must be on HIGH INTENSITY LDL LOWERING THERAPY

Combination therapy (statin + ezetimibe) provides higher adherence and efficacy