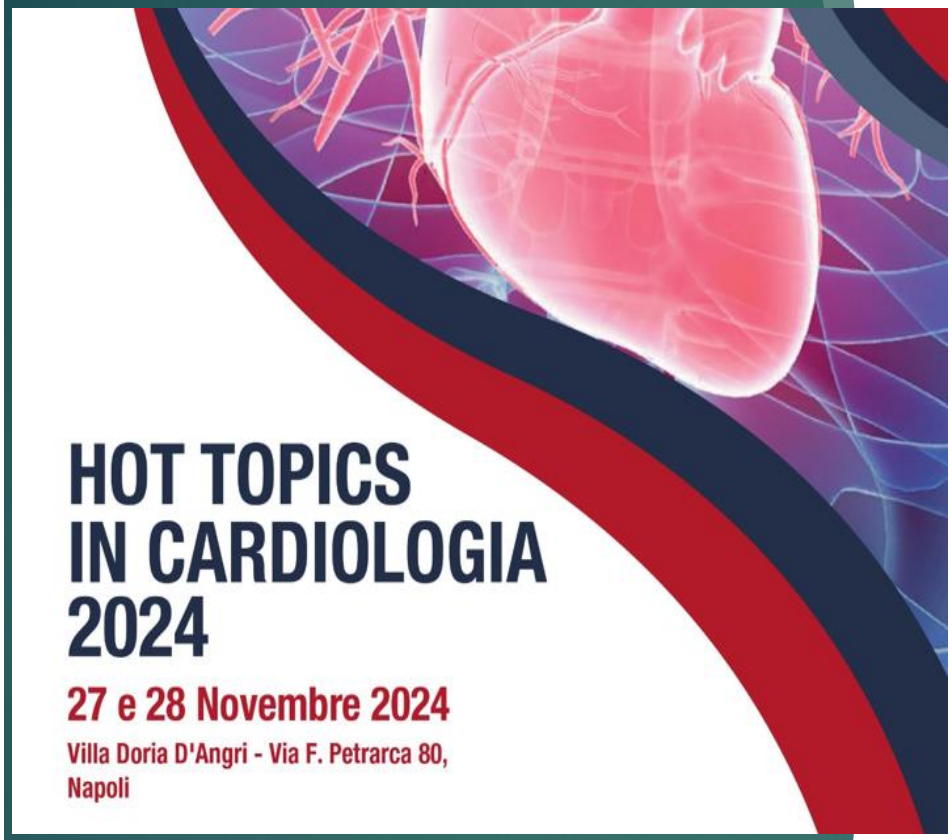



TITOLO: Razionale della triplice terapia anti-dislipidemica nel paziente acuto

RELATORE: A. Tuccillo

Link
profitable solutions

# LDL-cholesterol **is a causal factor** for atherosclerotic cardiovascular disease

ESC European Society of Cardiology
European Heart Journal (2022) **43**, 3198–3208
https://doi.org/10.1093/eurheartj/ehab841

STATE OF THE ART REVIEW
*Dyslipidaemias*

## The dawn of a new era of targeted lipid-lowering therapies

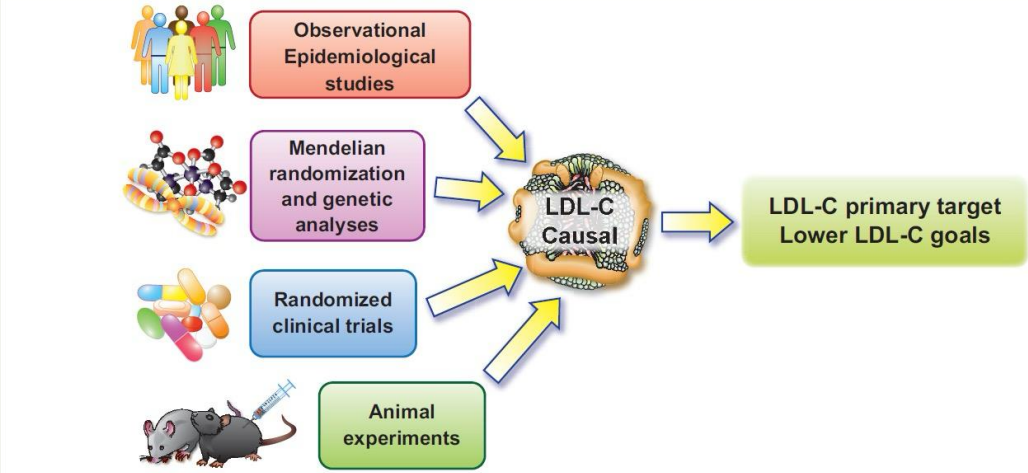


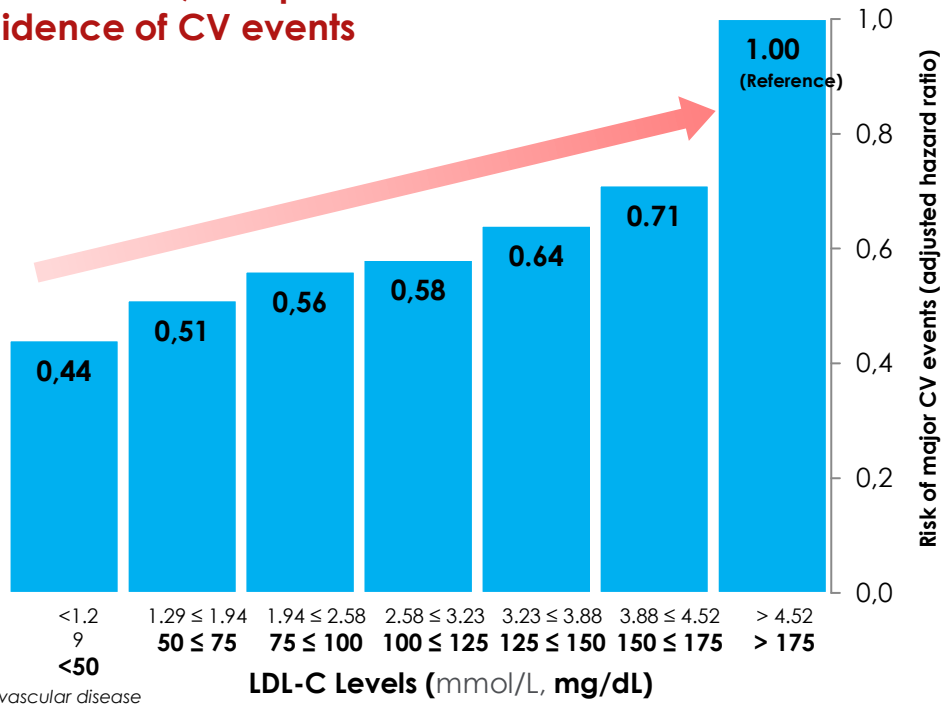

**Figure 2** Multiple lines of evidence showing low-density lipoprotein cholesterol is causal for cardiovascular disease. Data that have accrued from observational data, human genetic analyses, randomized clinical trial results, and animal experimentation in multiple species, all concordantly support a causal contribution of low-density lipoprotein to atherosclerosis.

Lale Tokgozoglu Eurepean Heart Journal 2022

# Increased LDL-C Levels are a Proven and Direct Cause of CV Events

**A high concentration of lipoproteins, in particular LDL-C, is implicated in the etiology of atherosclerosis and increased incidence of CV events**

- Prospective studies, randomized trials, and Mendelian randomization studies have all shown that raised LDL-C is a cause of ASCVD[1–3]
- The cumulative arterial burden of LDL-C drives the development and progression of ASCVD[2]
- Patients who achieve very low LDL-C levels have a lower risk of major CV events than those who achieve moderately low levels[4]



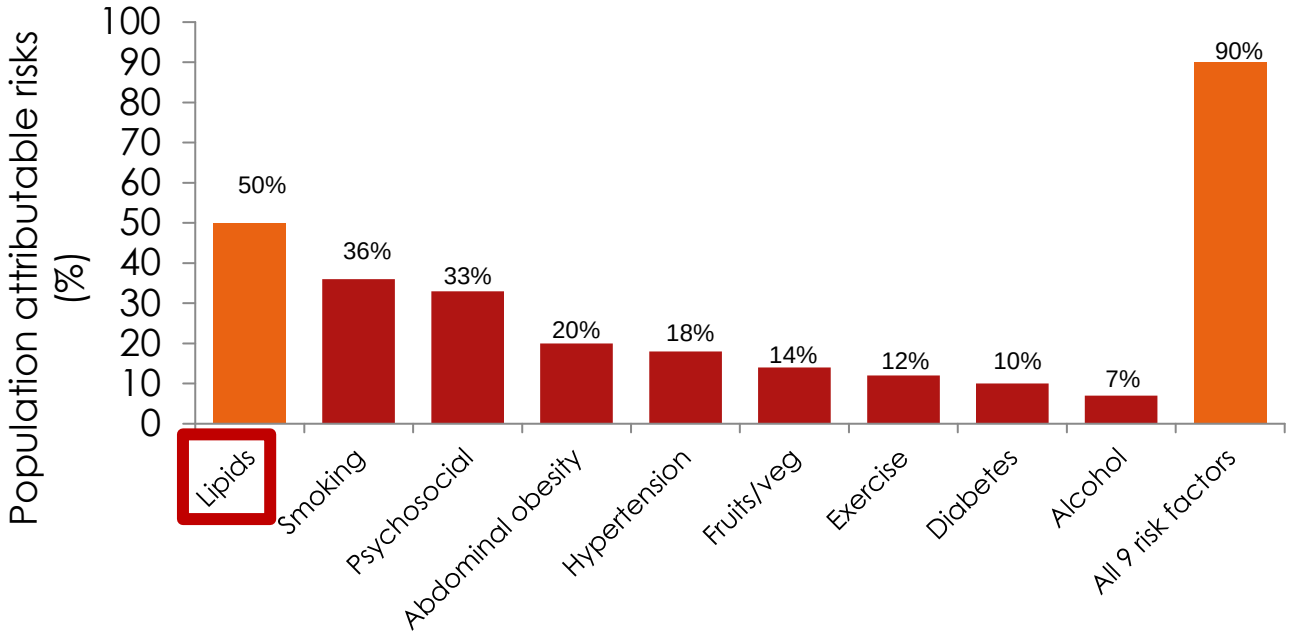

*ASCVD, atherosclerotic cardiovascular disease; CHD, coronary heart disease; CVD, cardiovascular disease*


*1. ESC/EAS Guidelines for the management of dyslipidaemias. Eur Heart J. 2020; 41(1): 111-188;*
*2. Borén J et al. Eur Heart J. 2020; 0: 1-28; 3. Ference BA et al. Eur Heart J. 2017; 38(32): 2459–2472;*
*4. Boekholdt et al. JACC 2014;64: 485–494.*


*Adapted from Boekholdt et al. JACC 2014;64: 485–494*

# Elevated LDL-C is a major modifiable risk factor for ASCVD

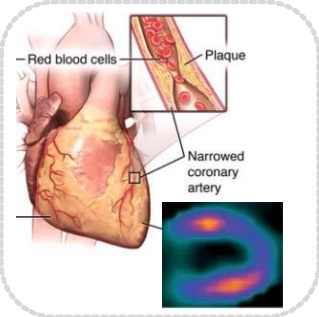
Nine modifiable risk factors account for ≥ 90% of first-MI risk



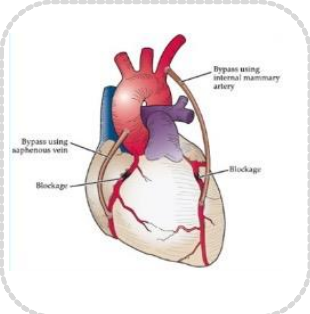

- PAR, population attributable risks.
- Adapted from Yusuf S et al. *Lancet*. 2004; 364:937-52.

# The identikit of the patient at *very high cardiovascular risk* on whom it is crucial to act before they develop an acute event

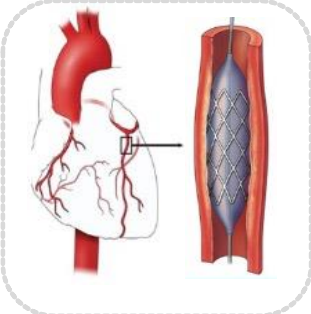
Patients at very high risk of having their first acute cardiovascular event



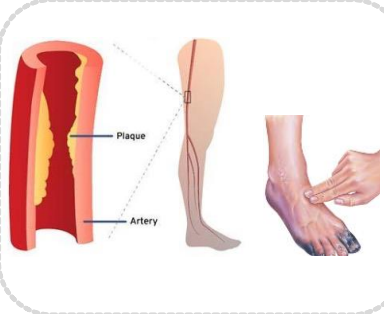

*Coronary Plaque Detection*



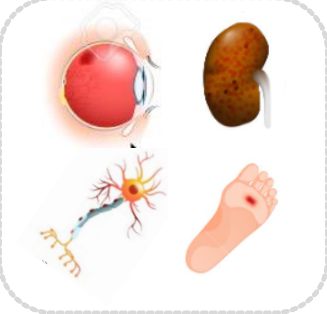

*CABG*



*PCI*



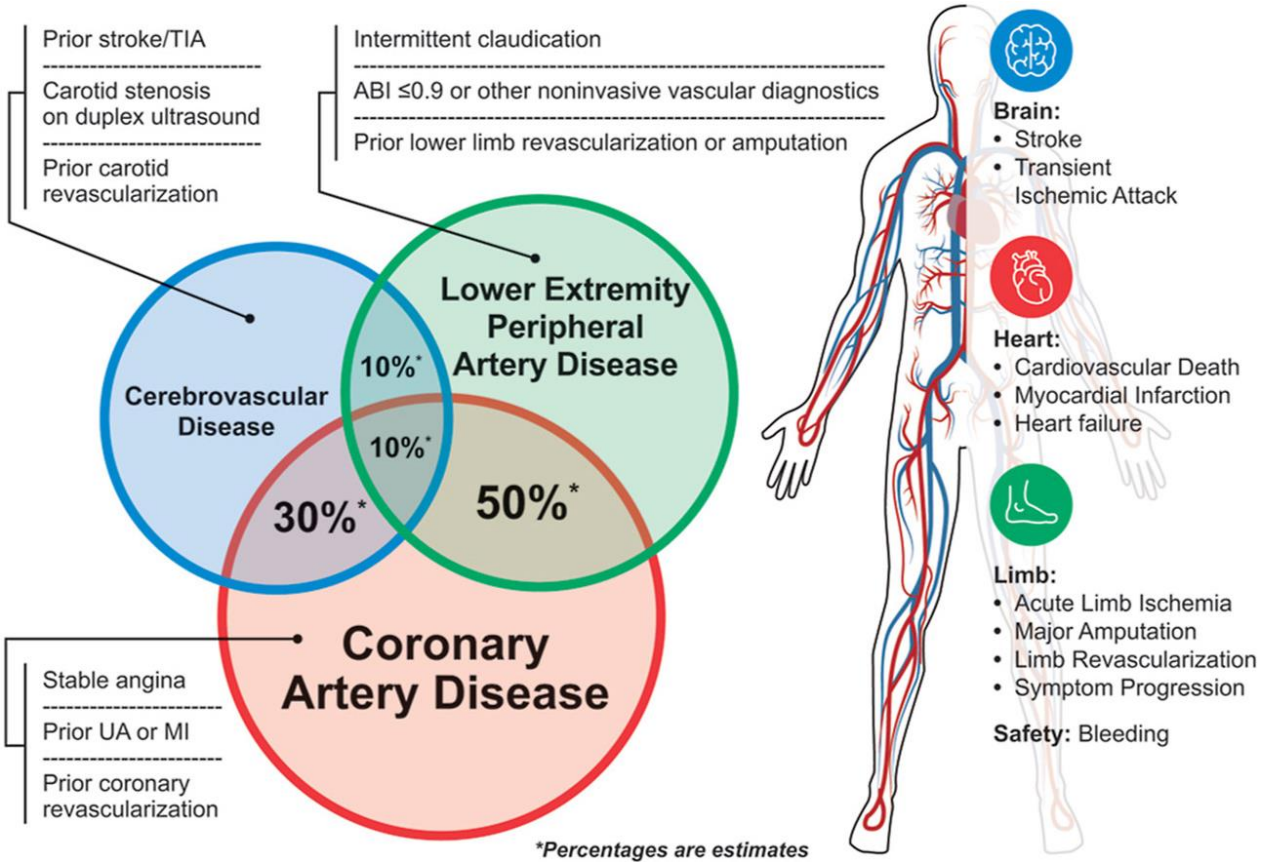

*PAD*



*Diabetes Mellitus with Complications*

Mach F et al. Eur Heart J. 2020; 41(1): 111-88
Fleg JL, Forman DE, Berra K, et al. Secondary prevention of atherosclerotic cardiovascular disease in older adults: a scientific statement from the American Heart Association. Circulation 2013;128(22):2422-46.

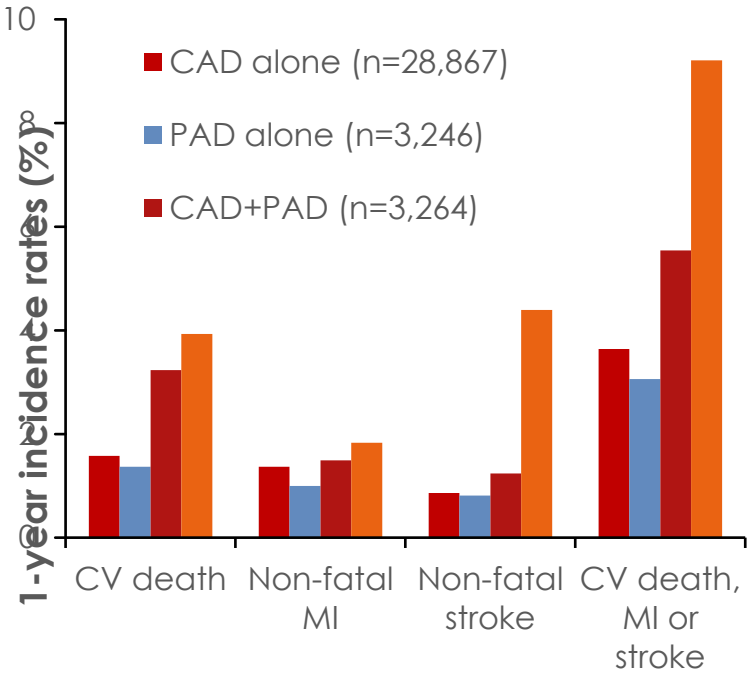
# Atherosclerosis is a systemic disease



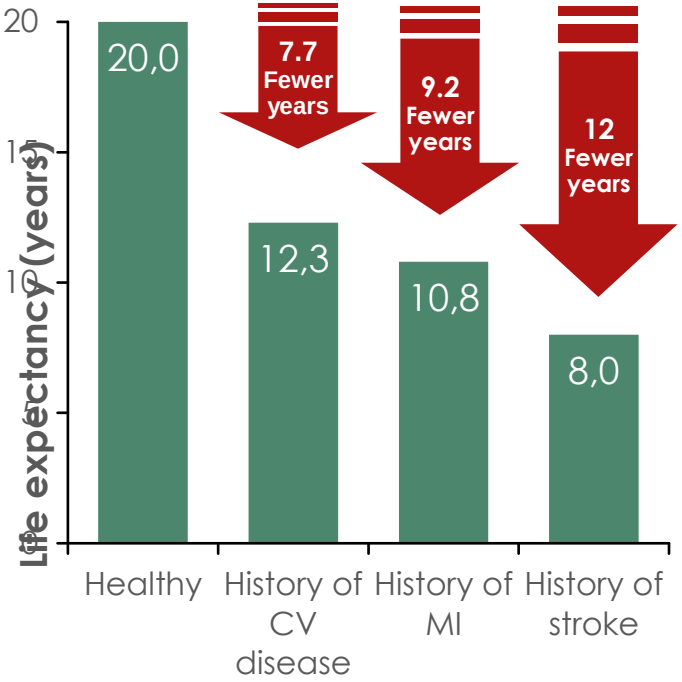

E.H. Weissler et al. Atherosclerosis 315 (2020) 10–17

# Atherothrombosis is an Unpredictable and Life-Threatening Consequence of Chronic, Progressive Atherosclerosis

- 1-year outcomes in patients with atherosclerotic disease[1]




- Life expectancy in patients aged 60 years ± atherosclerosis[2]



# Variations in lipoprotein levels after myocardial infarction and unstable angina: the LATIN trial

Claudio Fresco [1], Aldo P Maggioni, Stefano Signorini, Piera A Merlini, Paolo Mocarelli, Gianna Fabbri, Donata Lucci, Marco Tubaro, Marinella Gattone, Carlo Schweiger; LATIN Investigators

**Results:** We enrolled 1864 patients (1275 with MI and 589 with UA). Serum levels of total and LDL-cholesterol decreased significantly after admission, both in MI and UA patients. After 3 months, serum levels of total cholesterol returned to baseline, while those of LDL-cholesterol were still significantly lower. Between admission and the following morning, total and LDL-cholesterol decreased significantly by 7 and 10% respectively for MI and by 5 and 6% for UA. Lipid measurements not performed at admission accounted for a significant decrease in the number of patients identifiable as hyperlipidemic and suitable for lipid-lowering treatment (18% of MI patients and 11% of UA patients).

# Lipid levels after acute coronary syndromes

Bertram Pitt [1], Joseph Loscalzo, Joseph Ycas, Joel S Raichlen

Affiliations + expand

PMID: 18402897 DOI: 10.1016/j.jacc.2007.11.075

**Results:** Of 507 patients available for analysis, 212 were admitted for STEMI, 176 for non-STEMI, and 119 for UA. The LDL-C levels decreased in the 24 h after admission (from 136.2 to 133.5 mg/dl), followed by an increase over the subsequent 2 days (to 141.8 mg/dl). These changes did not seem to be clinically meaningful. Similar changes were observed for total cholesterol and smaller changes for high-density lipoprotein cholesterol; fasting triglyceride levels did not change.

**Conclusions:** Mean lipid levels vary relatively little in the 4 days after an ACS and can be used to guide selection of lipid-lowering medication.

The NEW ENGLAND JOURNAL of MEDICINE



ORIGINAL ARTICLE

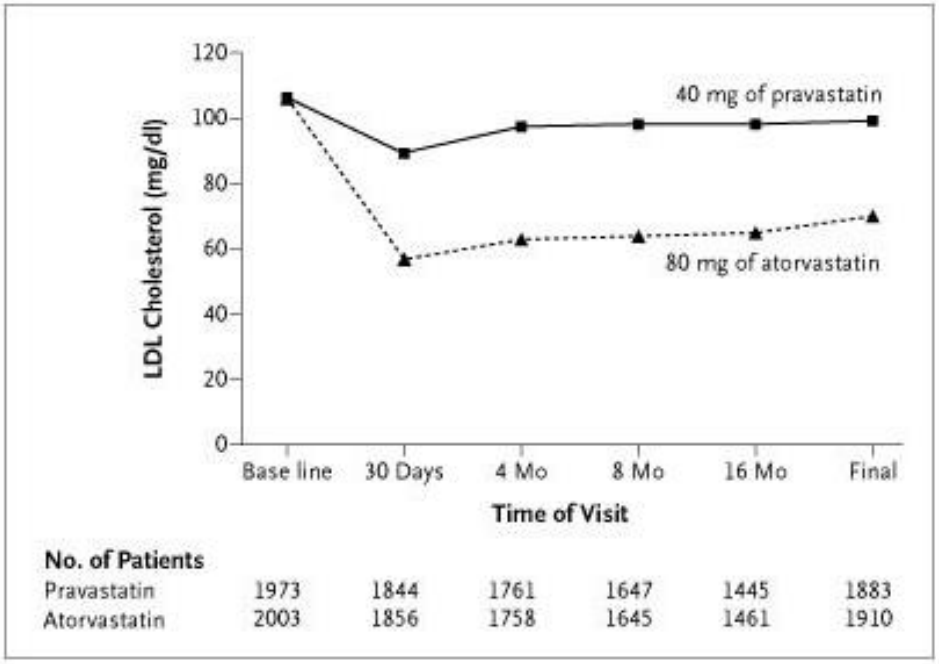
# Intensive versus Moderate Lipid Lowering with Statins after Acute Coronary Syndromes

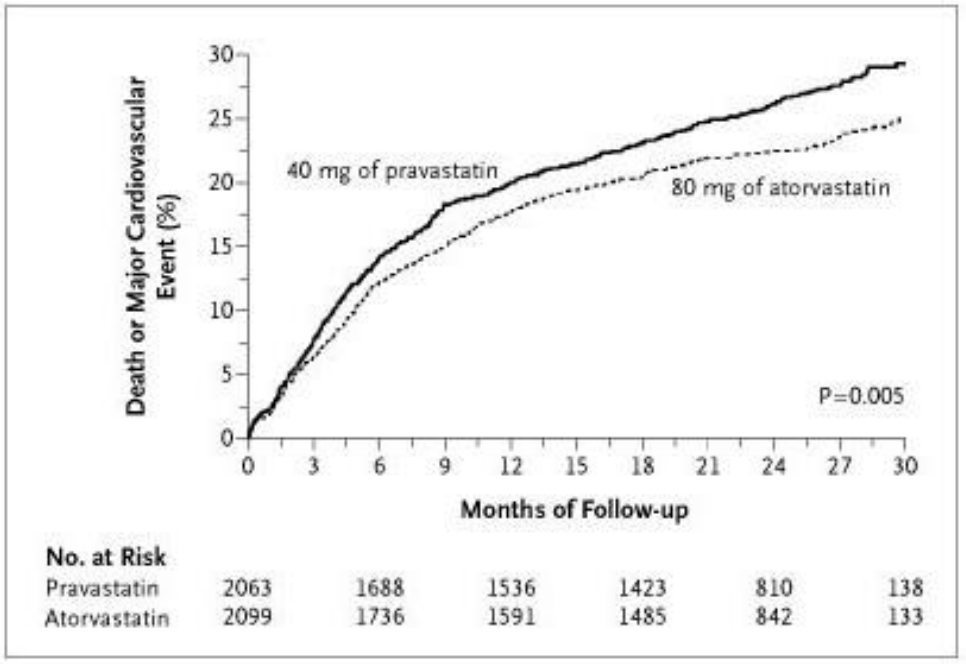
This article has been corrected. VIEW THE CORRECTION

**Authors**: Christopher P. Cannon, M.D., Eugene Braunwald, M.D., Carolyn H. McCabe, B.S., Daniel J. Rader, M.D., Jean L. Rouleau, M.D., Rene Belder, M.D., Steven V. Joyal, M.D., Karen A. Hill, B.A., Marc A. Pfeffer, M.D., Ph.D., and Allan M. Skene, Ph.D., for the Pravastatin or Atorvastatin Evaluation and Infection Therapy–Thrombolysis in Myocardial Infarction 22 Investigators* Author Info & Affiliations

Published April 8, 2004 | N Engl J Med 2004;350:1495-1504 | DOI: 10.1056/NEJMoa040583 | VOL. 350 NO. 15





# Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials

Cholesterol Treatment Trialists' (CTT) Collaboration*

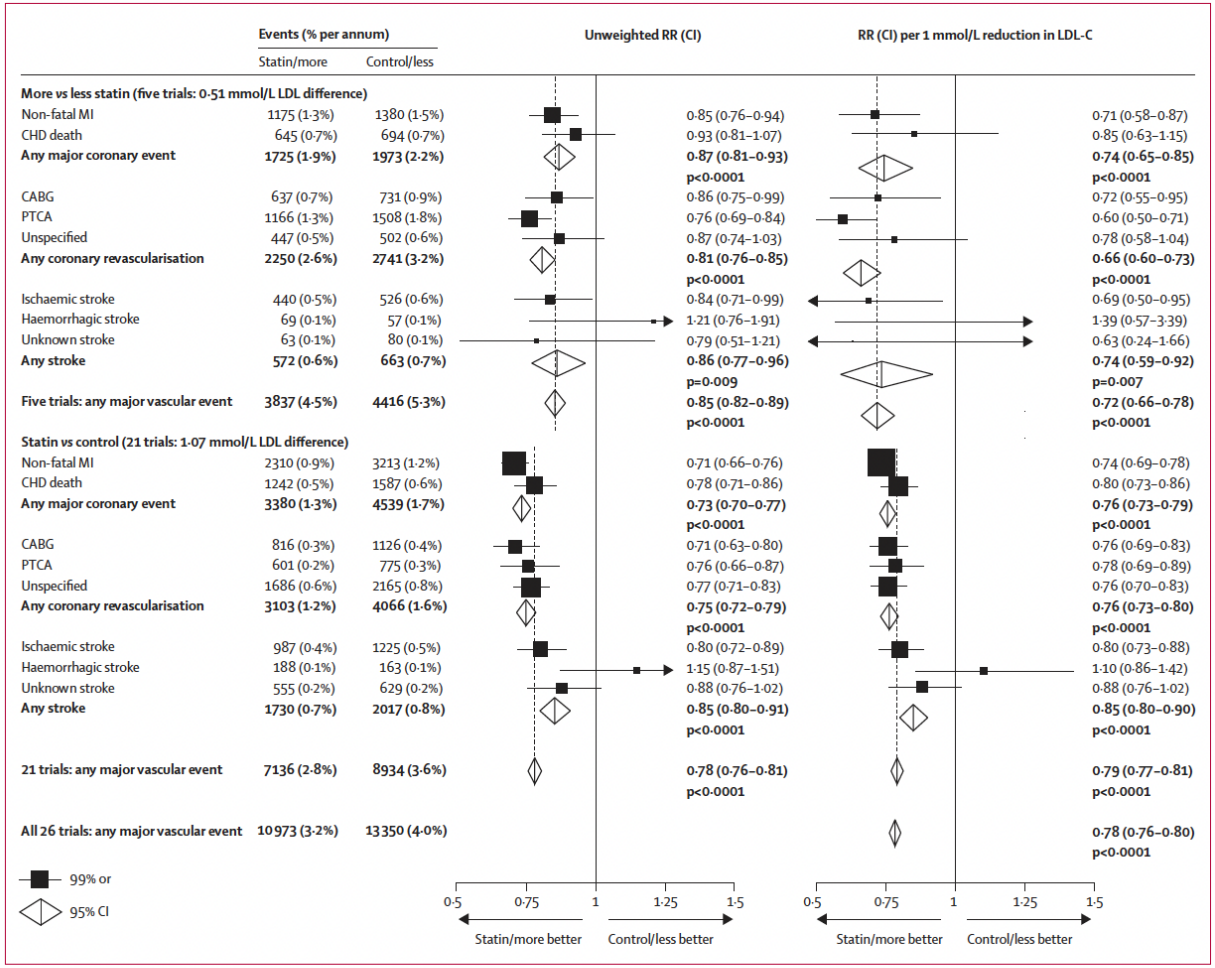



***Figure 2*: Effects on each type of major vascular event**

In the left panel, unweighted rate ratios (RRs) are plotted for each comparison of first event rates between randomly allocated treatment groups. In the right panel, RRs are weighted per 1·0 mmol/L LDL cholesterol (LDL-C) difference at 1 year. RRs are shown with horizontal lines denoting 99% CIs or with open diamonds denoting 95% CIs. MI=myocardial infarction. CHD=coronary heart disease. CABG=coronary artery bypass graft. PTCA=percutaneous transluminal coronary angioplasty.

# Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials

Cholesterol Treatment Trialists' (CTT) Collaboration*

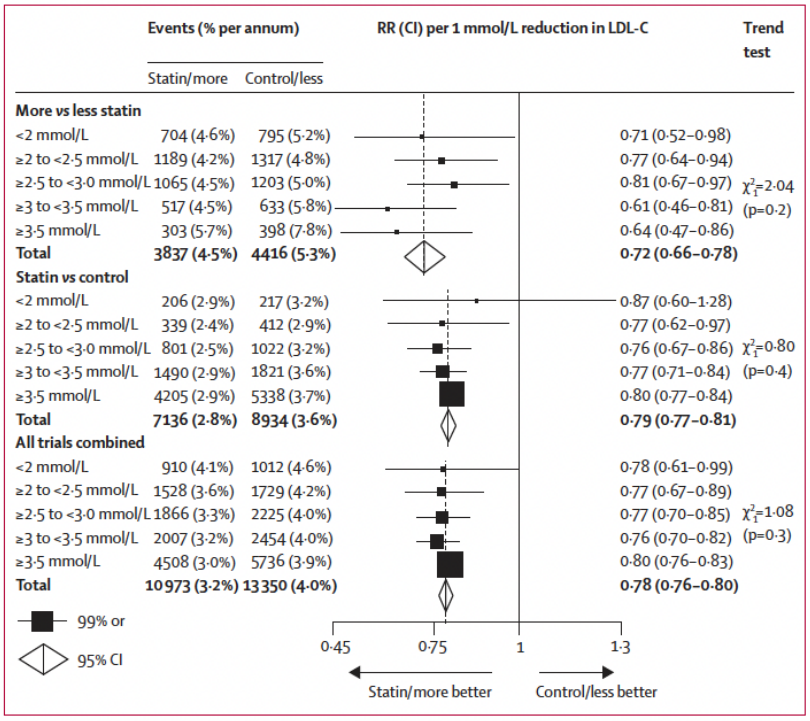



*Figure 4*: **Effects on major vascular events per 1·0 mmol/L reduction in LDL cholesterol, by baseline LDL cholesterol concentration on the less intensive or control regimen**
Rate ratios (RRs) are plotted for each comparison of first event rates between treatment groups, and are weighted per 1·0 mmol/L LDL cholesterol (LDL-C) difference at 1 year. Analyses were done with trial-specific and subgroup-specific LDL weights for each baseline LDL cholesterol category. Missing data are not plotted. RRs are shown with horizontal lines denoting 99% CIs or with open diamonds showing 95% CIs.

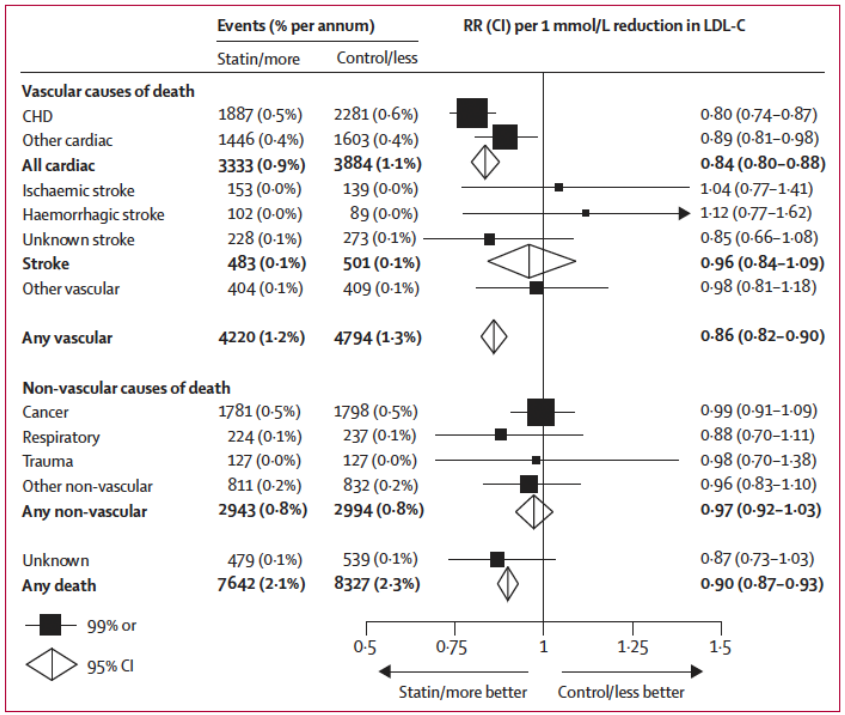



*Figure 5*: **Effects on cause-specific mortality per 1·0 mmol/L reduction in LDL cholesterol**
Rate ratios (RRs) are plotted for each comparison of first event rates between treatment groups and are weighted per 1·0 mmol/L LDL cholesterol (LDL-C) difference at 1 year. RRs are shown with horizontal lines denoting 99% CIs or with open diamonds showing 95% CIs. CHD=coronary heart disease.

European Heart Journal (2006) 27, 1799–1804
doi:10.1093/eurheartj/ehl125



# Patients using statin treatment within 24 h after admission for ST-elevation acute coronary syndromes had lower mortality than non-users: a report from the first Euro Heart Survey on acute coronary syndromes

Timo Lenderink[1], Eric Boersma[2], Anselm K. Gitt[3], Uwe Zeymer[3], Lars Wallentin[4], Frans Van de Werf[5], David Hasdai[6], Shlomo Behar[7], and Maarten L. Simoons[2*]

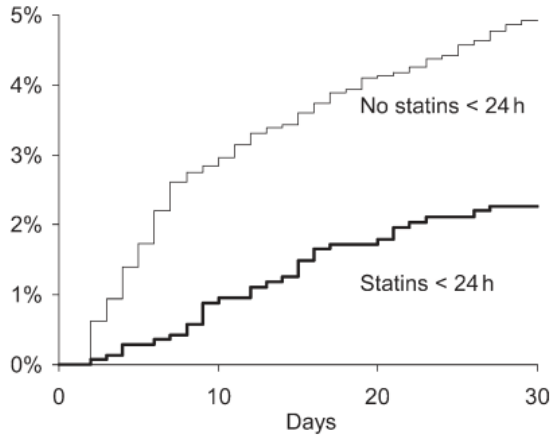



**Figure 2** The Kaplan–Meier curves for mortality in all patients surviving the first 24 h and stratified according to statin treatment within 24 h after hospitalization or not.

**Methods and results** Data from a large cohort of 10 484 consecutive patients with an ACS were analysed. Of this cohort, 1426 first-time statin receivers and survivors of the first 24 h were compared with 6771 first-day survivors not receiving statin therapy. A propensity score for the likelihood of receiving statin therapy within 24 h was developed and used with other established risk factors in a multivariable analysis. There was a significantly reduced all-cause 7-day mortality in patients receiving early statin therapy [0.4 vs. 2.6%, unadjusted hazard ratio (HR) 0.16, 95% confidence interval (CI) 0.08–0.37, adjusted HR 0.34, 95% CI 0.15–0.79]. Statistical significance was observed in patients presenting with STE-ACS (adjusted HR 0.17, 95% CI 0.04–0.70) and not in NSTE-ACS patients. However, no statistical evidence of heterogeneity in treatment effect was observed between these groups.

**Conclusion** These data suggest that very early statin therapy is associated with reduced mortality in patients presenting with STE-ACS; however, these findings have to be confirmed by prospective, randomized controlled trials before firm treatment recommendations can be given.

ESC European Society of Cardiology
European Heart Journal (2021) **42**, 243–252
doi:10.1093/eurheartj/ehaa1011

**CLINICAL RESEARCH**
*Ischaemic heart disease*

# Low-density lipoprotein cholesterol reduction and statin intensity in myocardial infarction patients and major adverse outcomes: a Swedish nationwide cohort study

**Jessica Schubert [1]*, Bertil Lindahl [1,2], Håkan Melhus [1], Henrik Renlund [2], Margrét Leosdottir [3,4], Ali Yari [5], Peter Ueda [6], Stefan James [1,2], Stephanie R. Reading [7], Paul J. Dluzniewski[7], Andrew W. Hamer[7], Tomas Jernberg [5], and Emil Hagström[1,2]**

[1]Department of Medical Sciences, Uppsala University, Uppsala, Sweden; [2]Uppsala Clinical Research Center, Uppsala, Sweden; [3]Department of Cardiology, Skåne University

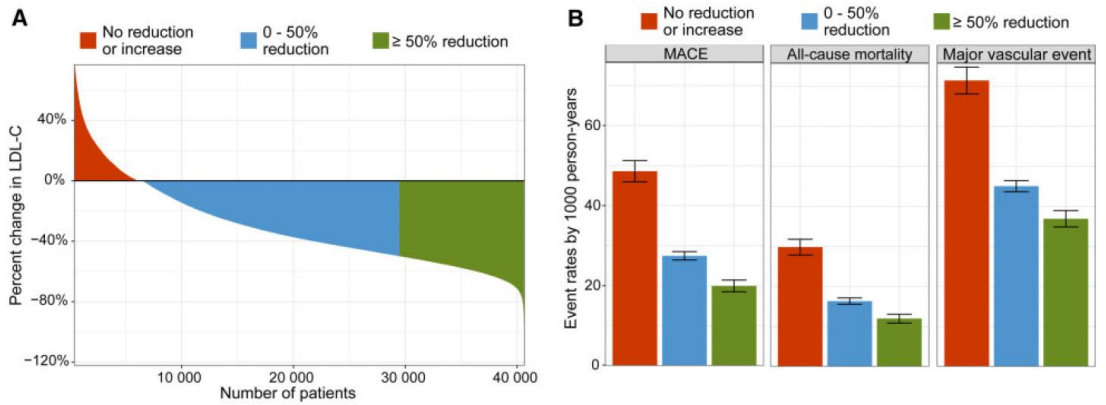
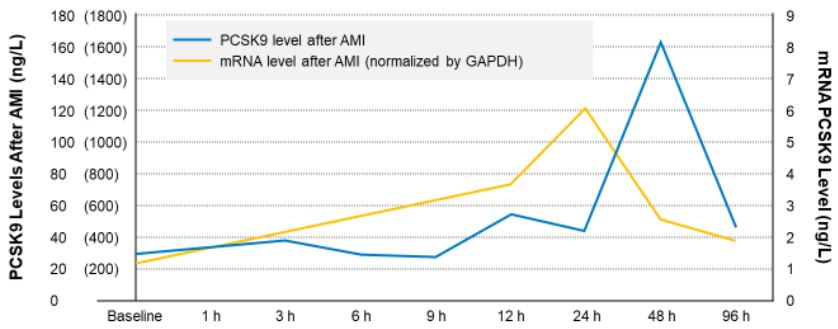



**Figure 4** Change in low-density lipoprotein cholesterol (LDL-C) and incidence rates. Data are shown for no reduction or an increase in low-density lipoprotein cholesterol (red), >0 but <50% reduction (blue), and ≥50% reduction (green) between index event and cardiac rehabilitation visit. Waterfall plot for change in low-density lipoprotein cholesterol (*A*) and concordant incidence rates per 1000 person-years with confidence intervals (*B*). MACE, major adverse cardiovascular event is the composite outcome of cardiovascular mortality, myocardial infarction, and ischaemic stroke. Major vascular event is the composite outcome of cardiovascular mortality, myocardial infarction, ischaemic stroke, and coronary revascularization (coronary artery bypass grafting or percutaneous coronary artery intervention).

# Livelli di PCK9 e SCA

## PCSK9 PEAK LEVELS RISE UP TO 48 HOURS IN ACS




Elaborato da Gencer

## PCSK9 LEVELS PREDICT MACE FOLLOWING ACS

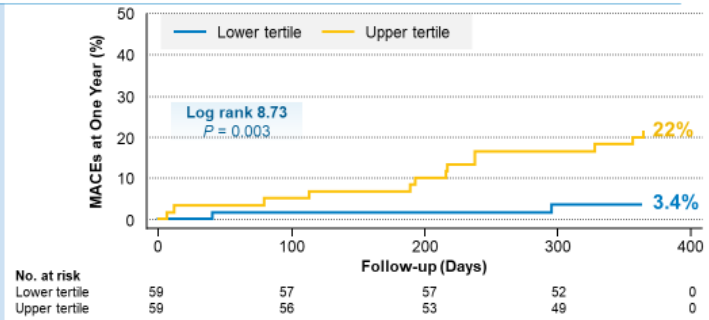
**PCSK9-REACT**
**Prospective, Single-Center, Observational Study in Austria**

**Patients:**
N = 333
hospitalized for ACS

Median age: 57

Follow-up: 1 year

MACE = CV death, MI, UA, stent thrombosis, repeat revascularization and ischemic stroke

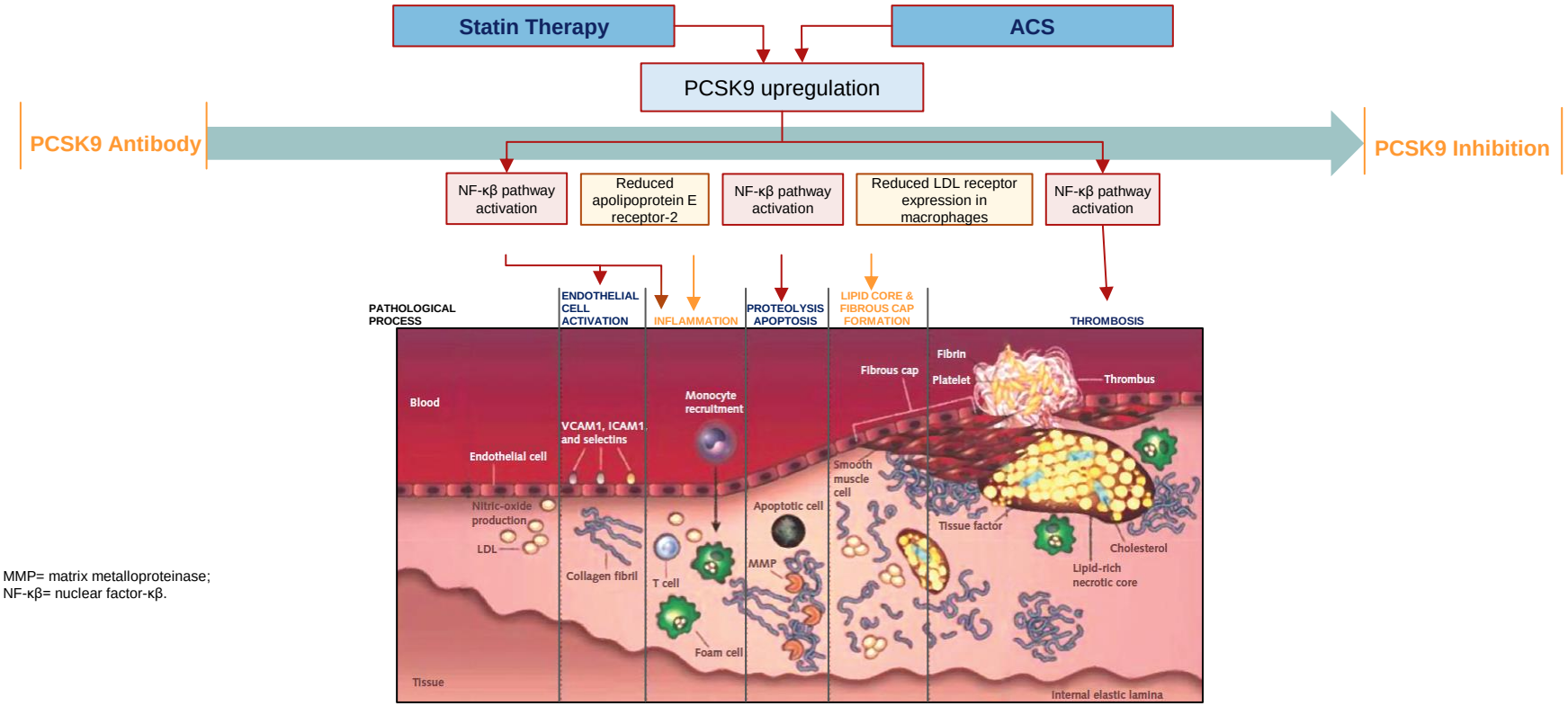



Upper tertile = higher PCSK9 concentration
Lower tertile = lower PCSK9 concentration

Elaborato da Navarese

# L'upregulation di PCSK9 a seguito di SCA determina uno stimolo dannoso sull'omeostasi lipidica ed infiammatoria

VULNERABLE PLAQUE WITH INCREASED NECROTIC CORE IN ACS



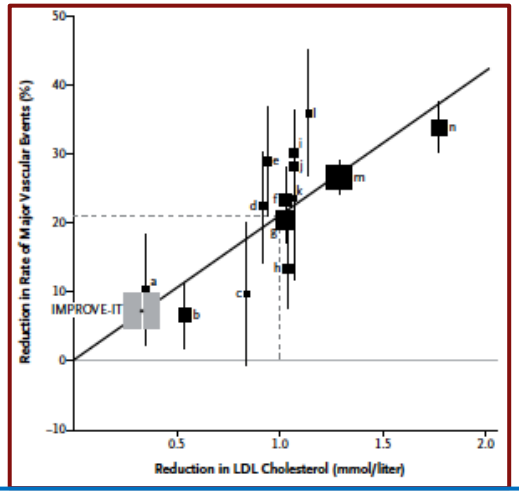

MMP= matrix metalloproteinase;
NF-κβ= nuclear factor-κβ.

# The lower is better

- La riduzione del C-LDL diminuisce la morbilità e mortalità cardiovascolare con un beneficio clinico che è proporzionale alla riduzione dei livelli di C-LDL

**1 mmol/L (39 mg/dl) di riduzione del colesterolo LDL si associa alla riduzione del rischio cardiovascolare del 21%**

IMPROVE-IT



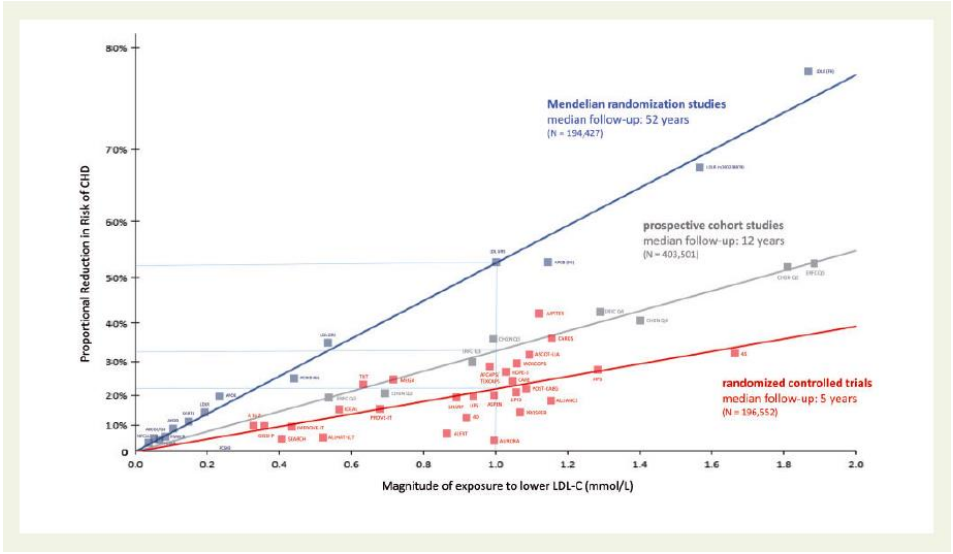

N Engl J Med 2015;372:2387-2397

- ✓ **Riduzione del 22% degli eventi vascolari maggiori**
- ✓ **Riduzione del 23% degli eventi coronarici maggiori**[1,2]

ESC European Society of Cardiology
European Heart Journal (2017) **38**, 2459–2472
doi:10.1093/eurheartj/ehx144

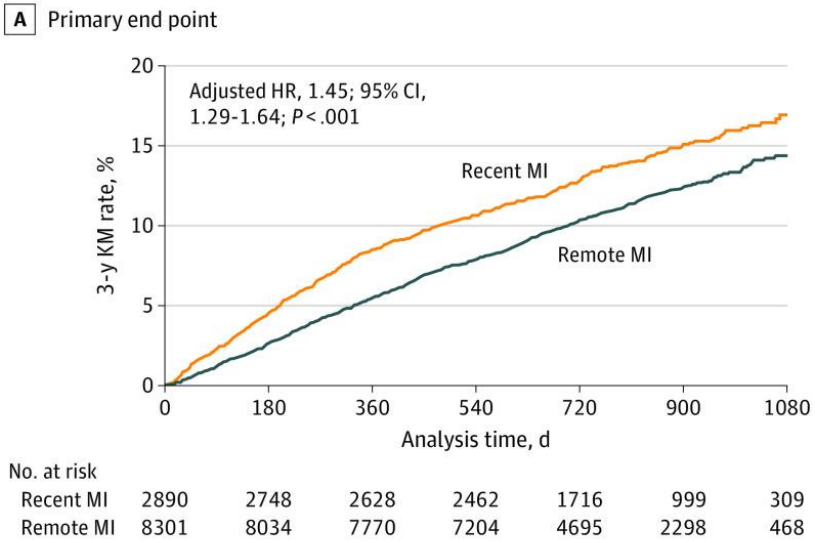
CURRENT OPINION

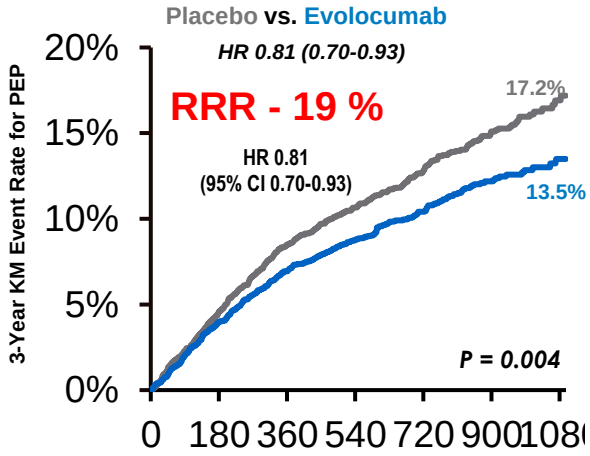
# Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel



# Efficacy of Evolocumab on Cardiovascular Outcomes in Patients With Recent Myocardial Infarction
## Analysis From FOURIER

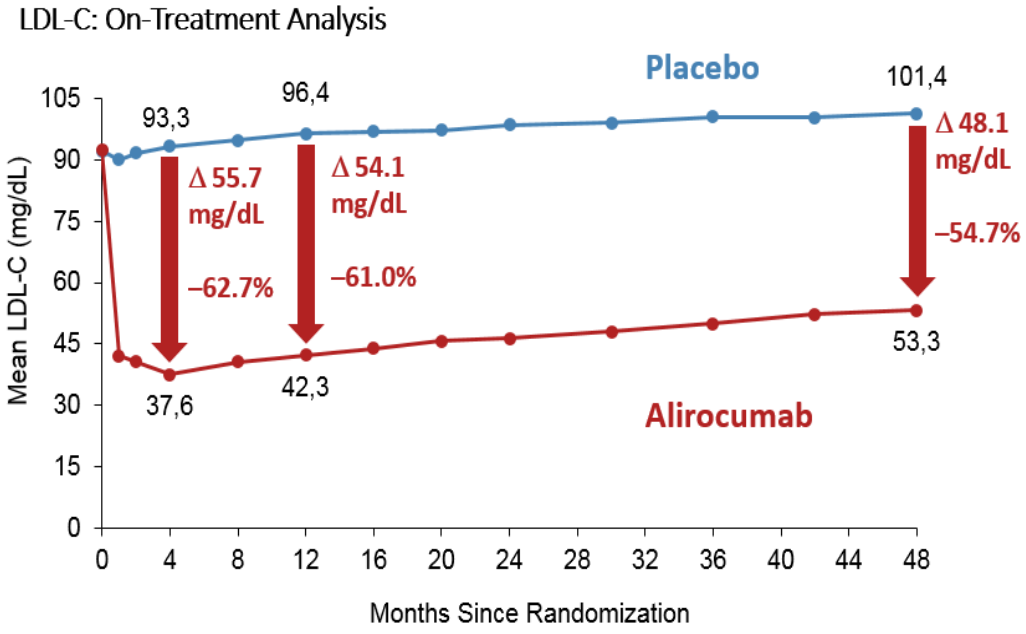
Primary EP: CVD, MI, stroke, Hospitalizaton for unstable angina or coronary revascularization

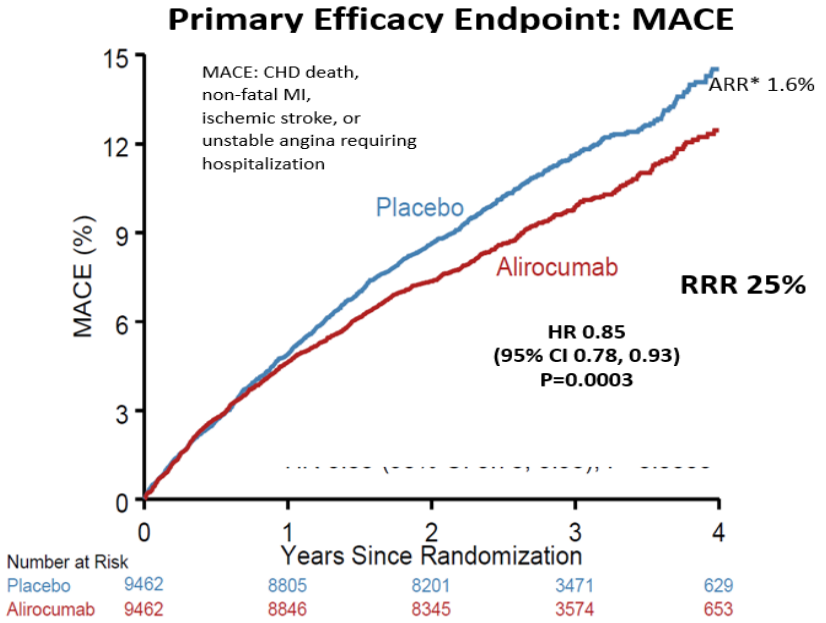



**I pazienti con un MI recente, mostrano il maggior beneficio da una terapia ipolipemizzante aggressiva**

# The ODYSSEY OUTCOMES Trial: Topline Results Alirocumab in Patients After Acute Coronary Syndrome



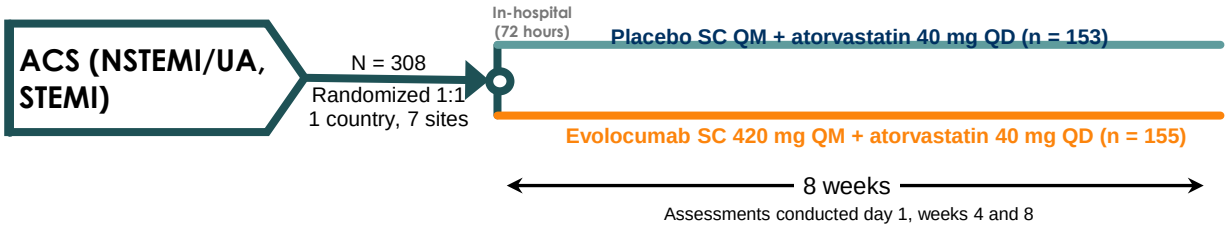




18 924 pazienti con recente sindrome coronarica acuta
C-LDL ≥70 mg/dl o non HDL C ≥100 mg/dl o apo B ≥80 mg/dl in trattamento con statine ad alte dosi

Schwartz GG, et al. Am Heart J 2014;168:682-689.e1.

# Evolocumab for Early Reduction of LDL Cholesterol Levels in Patients With Acute Coronary Syndromes (EVOPACS)

Konstantinos C. Koskinas, MD, MSc,[a] Stephan Windecker, MD,[a] Giovanni Pedrazzini, MD,[b] Christian Mueller, MD,[c] Stéphane Cook, MD,[d] Christian M. Matter, MD,[e] Olivier Muller, MD,[f] Jonas Häner, MD,[a] Baris Gencer, MD,[g] Carmela Crljenica, MD,[b] Poorya Amini, PhD,[h] Olga Deckarm, MD,[a] Juan F. Iglesias, MD,[g] Lorenz Räber, MD, PhD,[a] Dik Heg, PhD,[h] François Mach, MD[g]




**PRIMARY ENDPOINT**

- LDL-C change from baseline at week 8

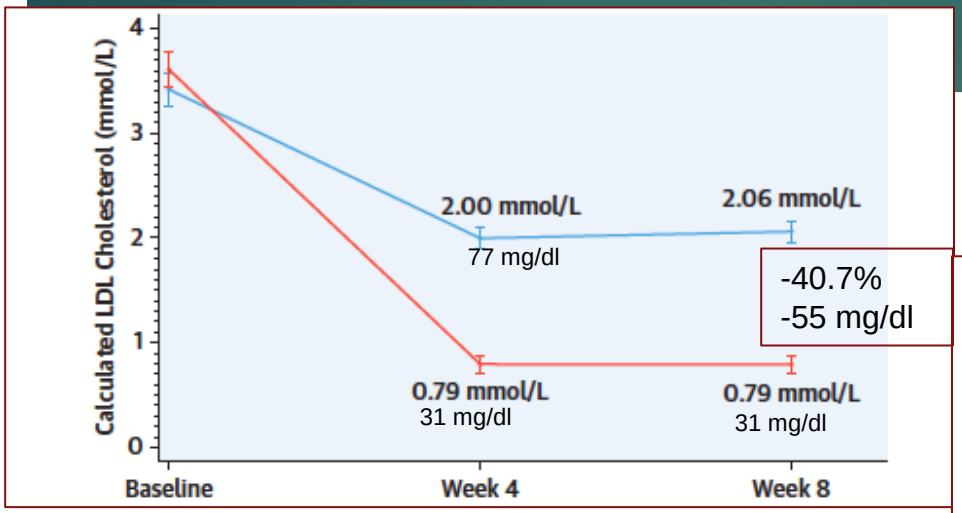
**SECONDARY ENDPOINT**

- Safety and tolerability

**INCLUSION CRITERIA**

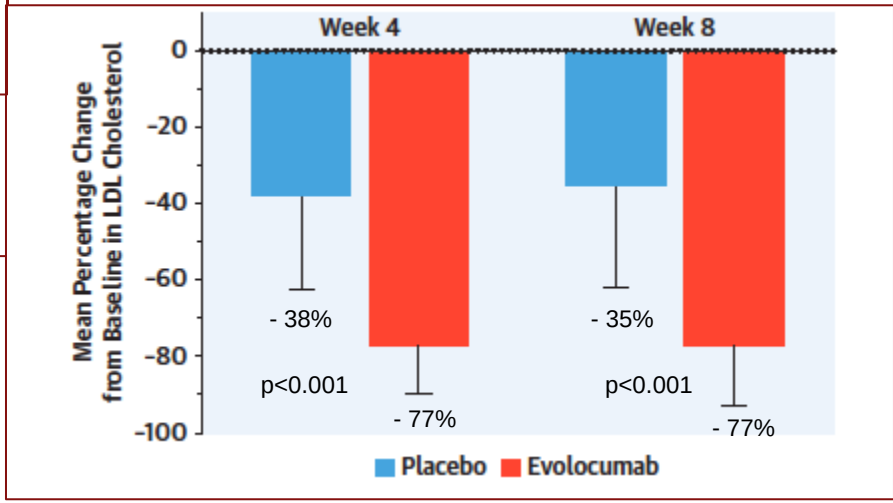
- ACS (NSTEMI/UA < 72H, STEMI < 24H)
- LDL-C levels
  - ≥ 1.8 mmol/L (70 mg/dl) in patient previously on stable treatment with high-intensity statin OR
  - ≥ 2.3 mmol/L (90 mg/dl) in patients previously on stable treatment with low- or moderate intensity statin OR
  - ≥ 3.2 mmol/L (125 mg/dL) in statin naive patients or patients not on stable statin treatment

# Lo studio EVOPACS ha mostrato una riduzione significativa dei livelli di C-LDL dopo 8 settimane




-40.7%
-55 mg/dl

**La riduzione del C-LDL era evidente già a 4 settimane e mantenuto fino a 8 settimale**

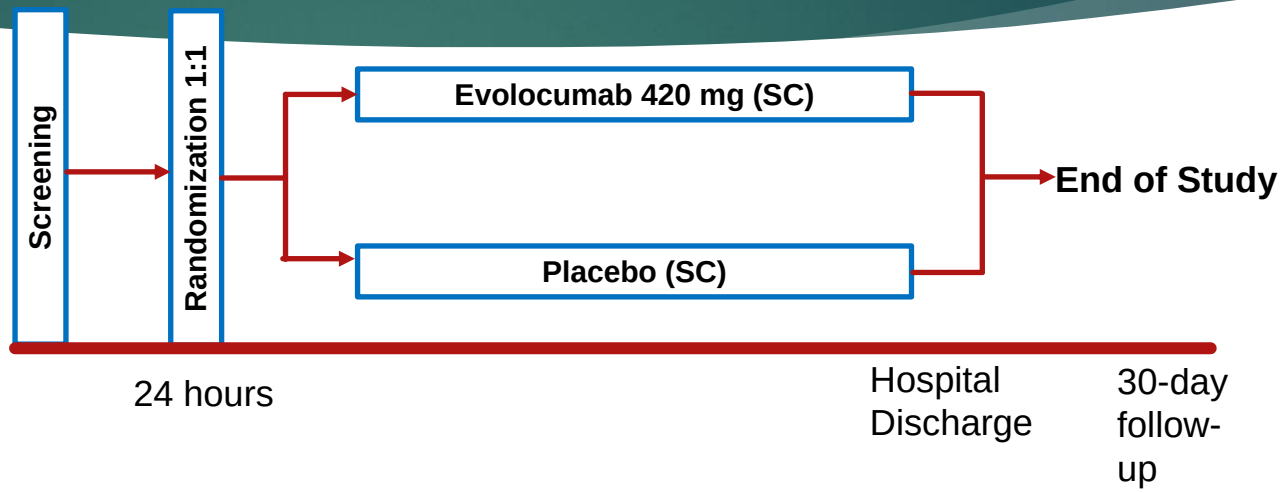



**La riduzione del C-LDL a 8 settimane rispetto alle baseline era del 77% nel gruppo Evolocumab e del 35% nel gruppo placebo**

# EVACS: A Double-Blind, 1:1 Randomized, Placebo-controlled Trial

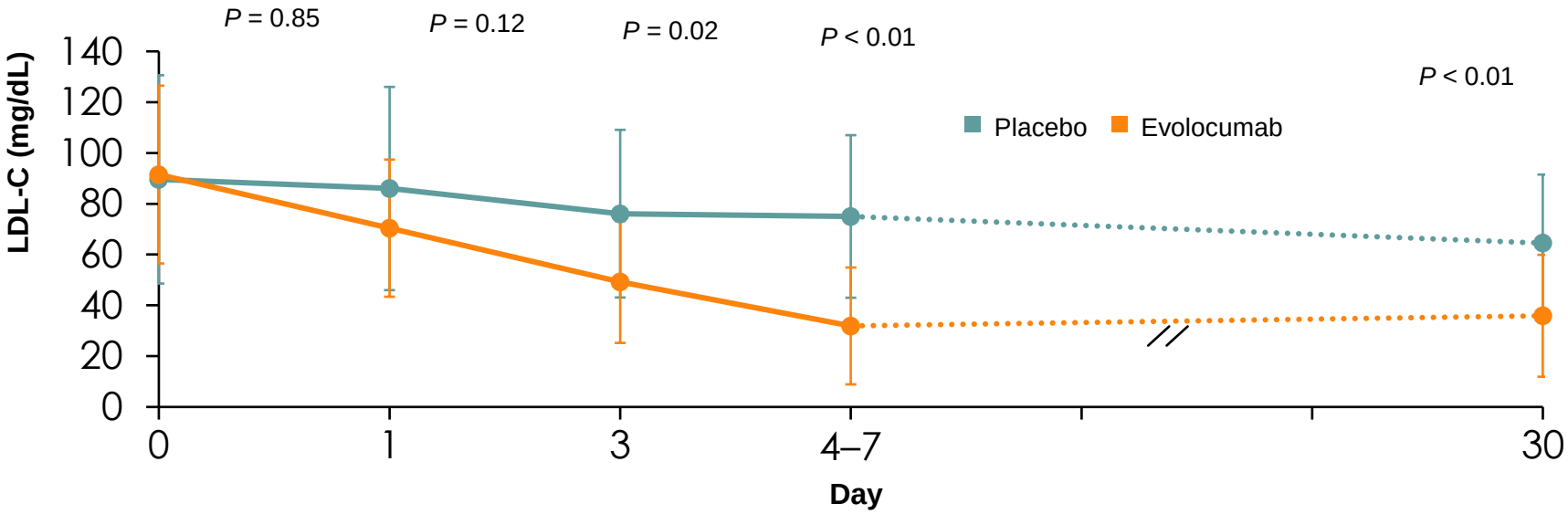
**Eligibility Criteria**:
- Type 1 Non-STEMI
- Troponin I ≥ 5 ng/mL

**Study Endpoints:**
Primary: Change in LDL-C at Day 30
Secondary: Change in other atherogenic lipoproteins




- 57 patients met eligibility criteria and were included in the study
- **Patients were randomized (1:1 ratio) to receive a single dose of either evolocumab SC 420 mg or matching placebo within 24 hours of presentation**
- **All participants received high-intensity statins unless contraindicated and were treated per current ACS guidelines**

# EVACS: LDL-C Levels Declined as Early as Day 1 After Administration Of Evolocumab and Were Significantly Reduced Compared to Placebo By Day 3

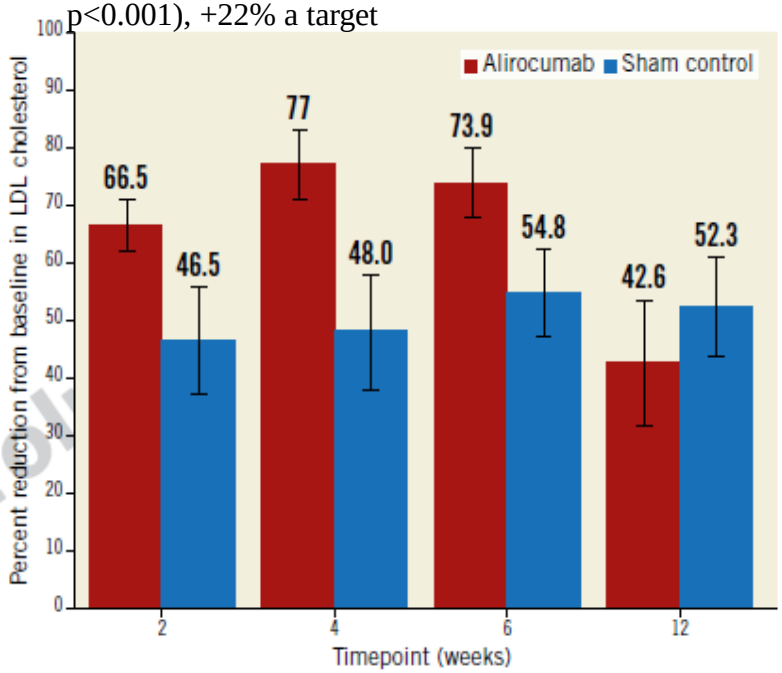


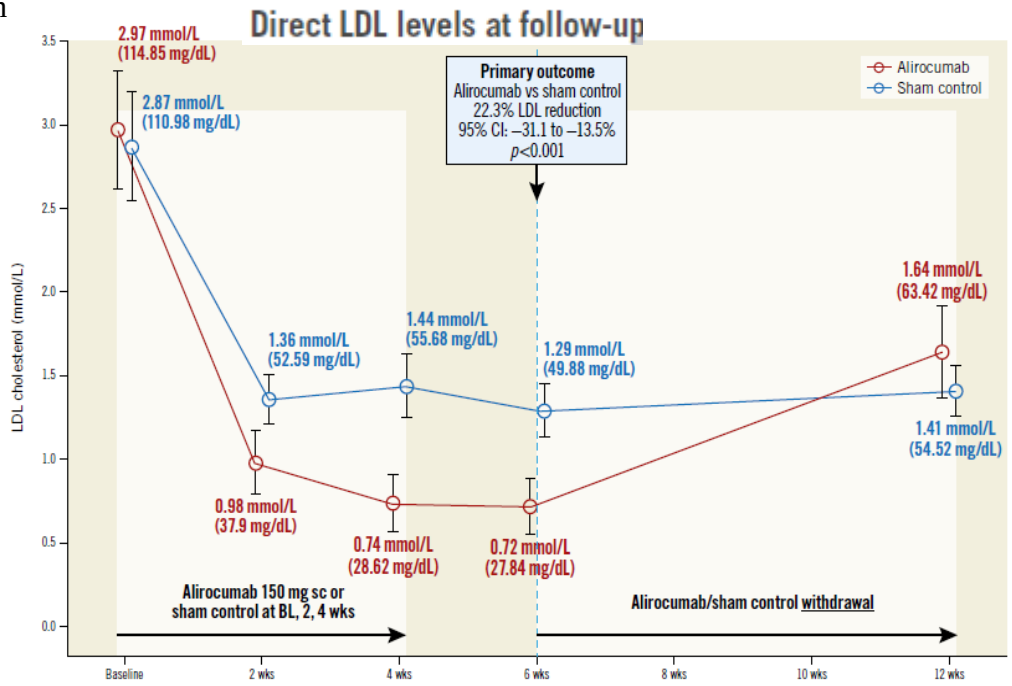

| | | | | | |
|---|---|---|---|---|---|
| **Placebo** mg/dL | 89.6 ± 41 | 86.0 ± 40 | 76.1 ± 33 | 75.0 ± 32 | 64.5 ± 27 |
| **Evolucumab** mg/dL | 91.5 ± 35 | 70.4 ± 27 | 49.2 ± 24 | 31.9 ± 23 | 35.9 ± 24 |

**Evolocumab, added to statin therapy, significantly reduced LDL-C levels throughout hospitalization and the 30-day follow-up in comparison with the placebo group (statin alone) (35.9±24mg/dL evolocumab vs. 64.5±27 mg/dL; *P* < 0.01).**

# Effects of routine early treatment with PCSK9 inhibitors in patients undergoing primary percutaneous coronary intervention for ST-segment elevation myocardial infarction: a randomised, double-blind, sham-controlled trial

(target of LDL ≤55 mg/dl in 92.1% alirocumab vs sharm 56.7%;
p<0.001), +22% a target

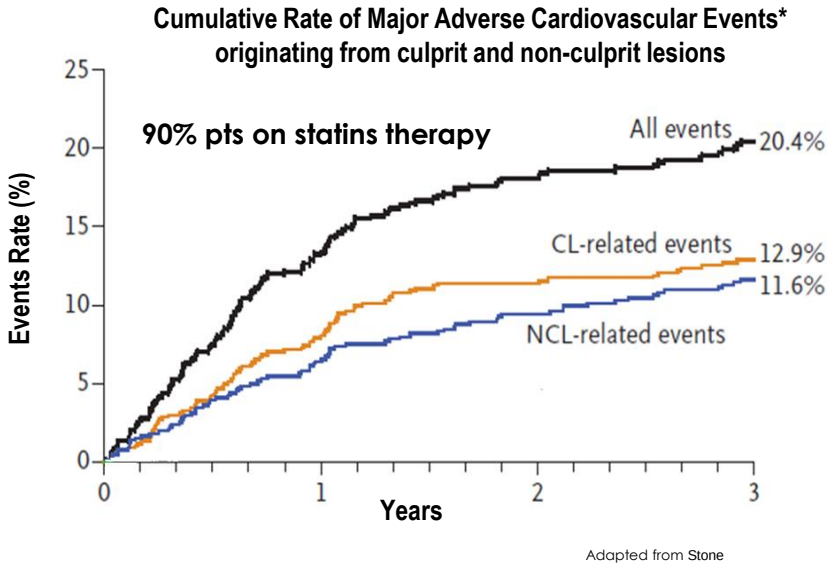


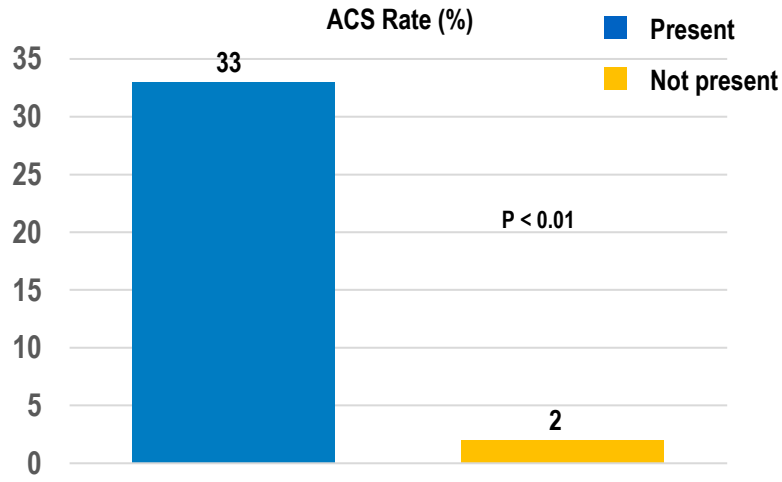

EuroIntervention 2022;18:e888-e896

# ACS patients are at significant risk for future CV events, specifically in the first year, originating from culprit as well as non-culprit lesions

## PROSPECT STUDY




Adapted from Stone

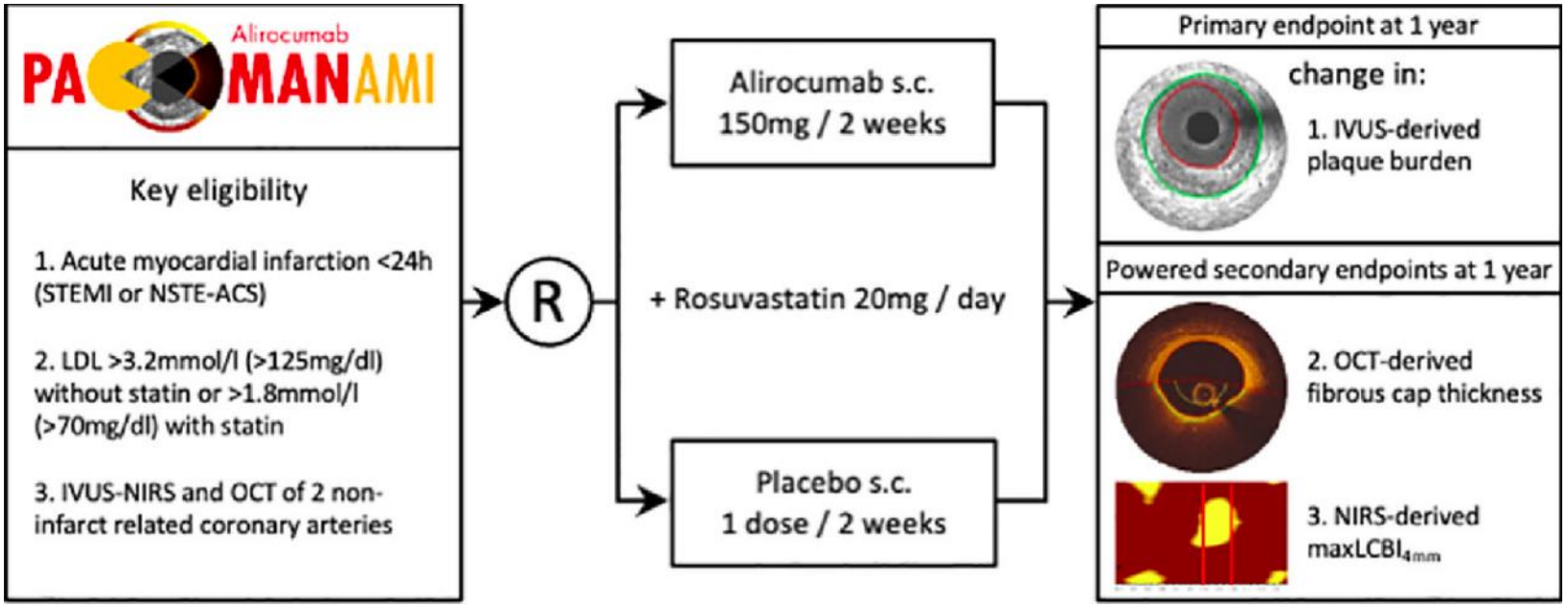



LRP: lipid-rich plaque
TCFA: thin-cap fibroatheroma

Adapted from Kubo

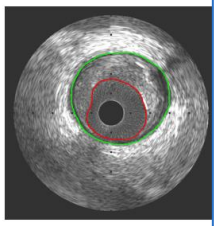
**A recent study identified non-culprit lipidic plaques to be associated with ~17-fold increase in subsequent ACS during a median 6-year follow-up period**

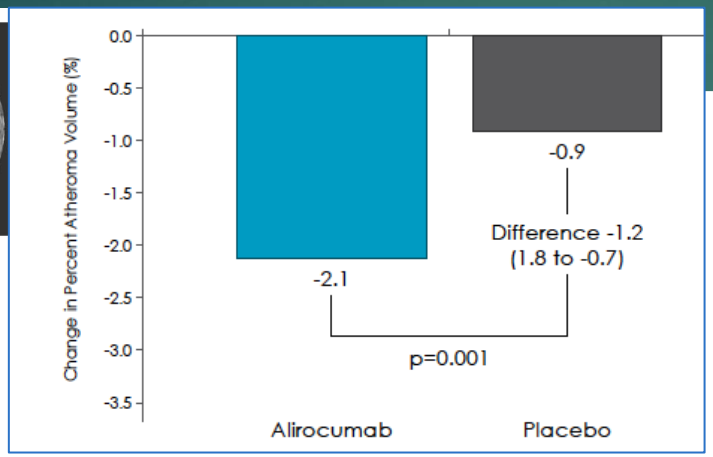
# Effects Of Alirocumab On Coronary Atherosclerosis Assessed By Serial Multimodality Intracoronary Imaging In Patients With Acute Myocardial Infarction: A Double-blind, Placebo-controlled, Randomized Trial (PACMAN-AMI)



# Primary End Point

**Change in Percent Atheroma Volume (IVUS)**

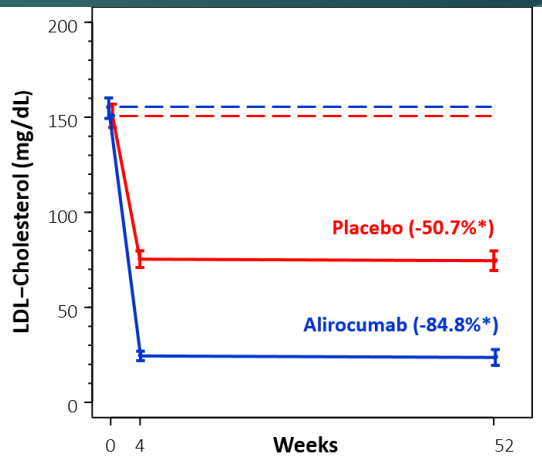





## Change in LDL-C, mean (SD)

**154.8 (31) mg/dL**
4.00 (0.8) mmol/L

**150.9 (36) mg/dL**
3.9 (0.9) mmol/L



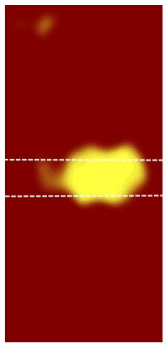

**74.4 (31) mg/dL**
1.9 (0.8) mmol/L

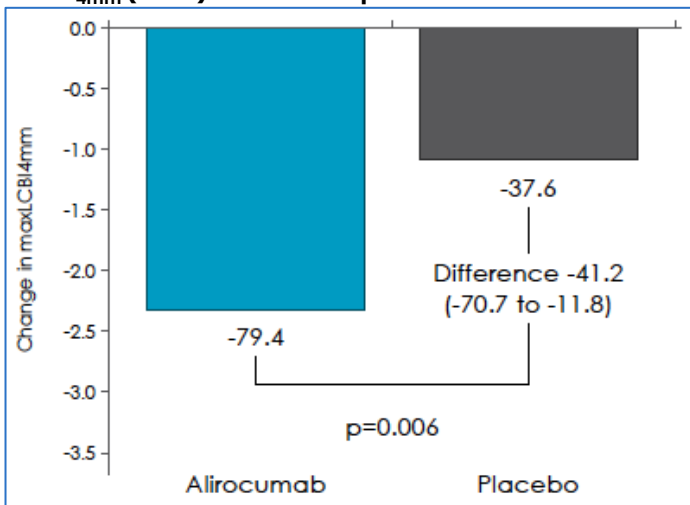
**23.6 (24) mg/dL**
0.6 (0.6) mmol/L

* Week 52 vs. Baseline

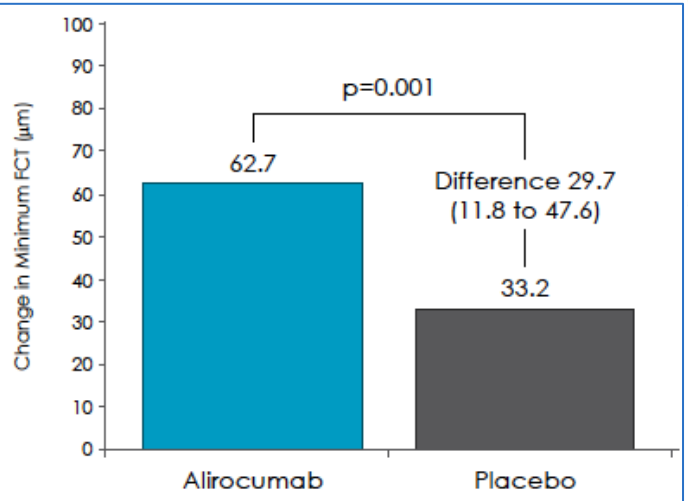
# Powered Secondary End Point

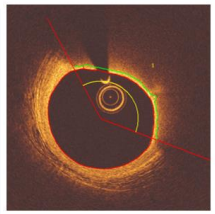
**Change in maxLCBI$_{4mm}$ (NIRS) maximal lipid-core burden index**






## Change in Minimum FCT (OCT)



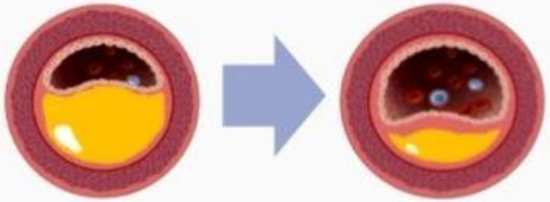
JAMA Cardiology

Biccirè FG, Kakizaki R, Koskinas KC, et al.

# Lesion-Level Effects of LDL-C–Lowering Therapy in Patients With Acute Myocardial Infarction

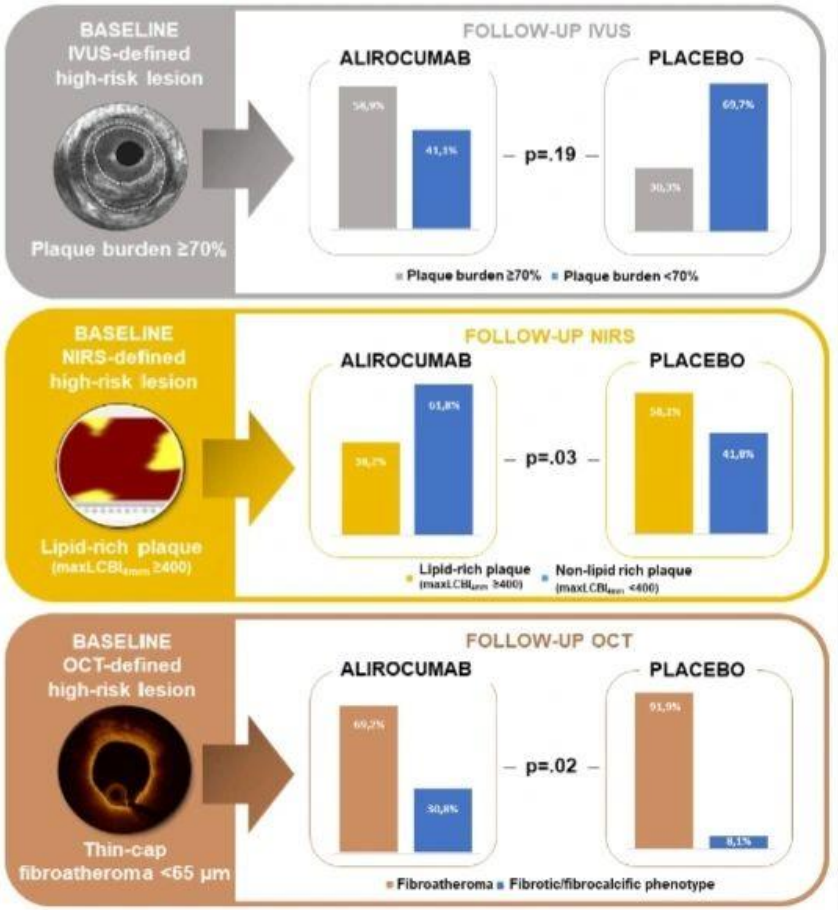
A Post Hoc Analysis of the PACMAN-AMI Trial

## Results



**61.8% of LRPs in alirocumab arm *vs.* 41.8% of those in placebo arm were non-LRP at follow-up (p=.03).**

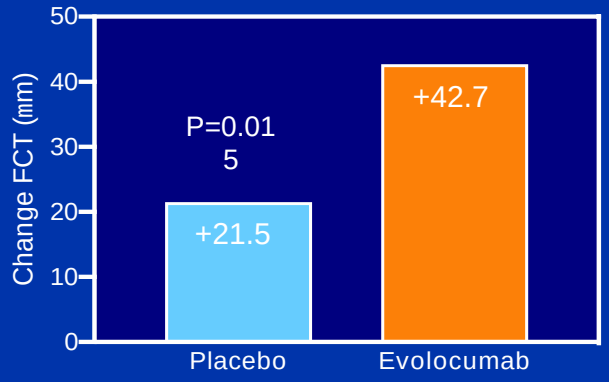
**30.8% of TCFAs in alirocumab arm *vs.* 8.1% of those in placebo arm showed a fibrous/fibrocalcific plaque phenotype at follow-up (p=.02).**



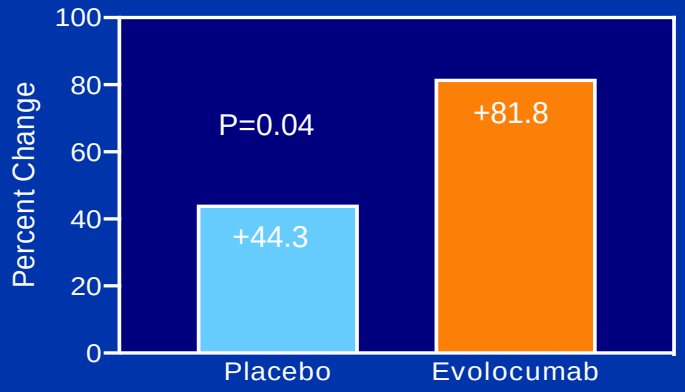
# HUYGENS Primary Endpoint:

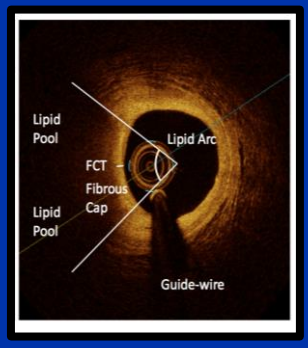
**Assessing the Impact of EVOLOCUMAB Inhibition on Coronary Plaque Phenotype with Optical Coherence Tomography**

## Minimum Fibrous Cap Thickness

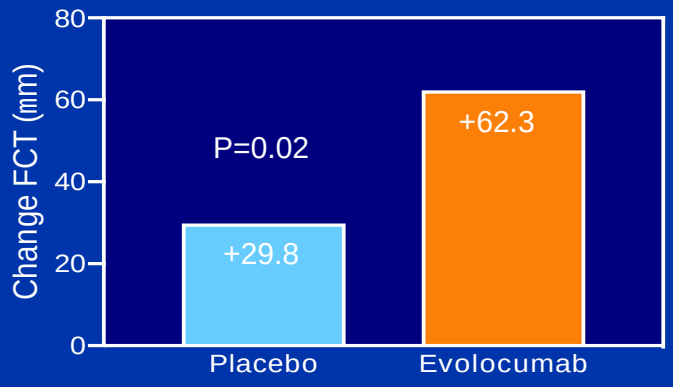



## Percent Change Minimum Fibrous Cap Thickness

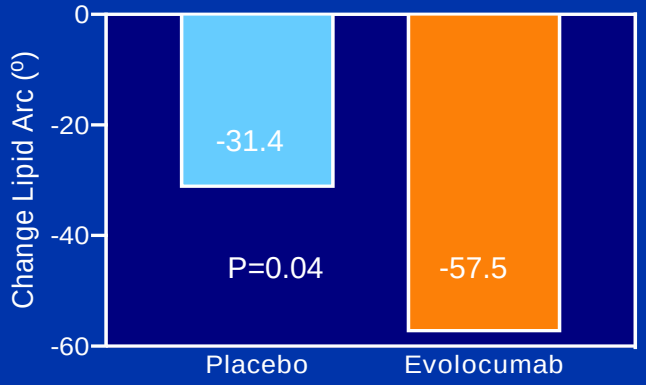



## Mean Minimum Fibrous Cap Thickness

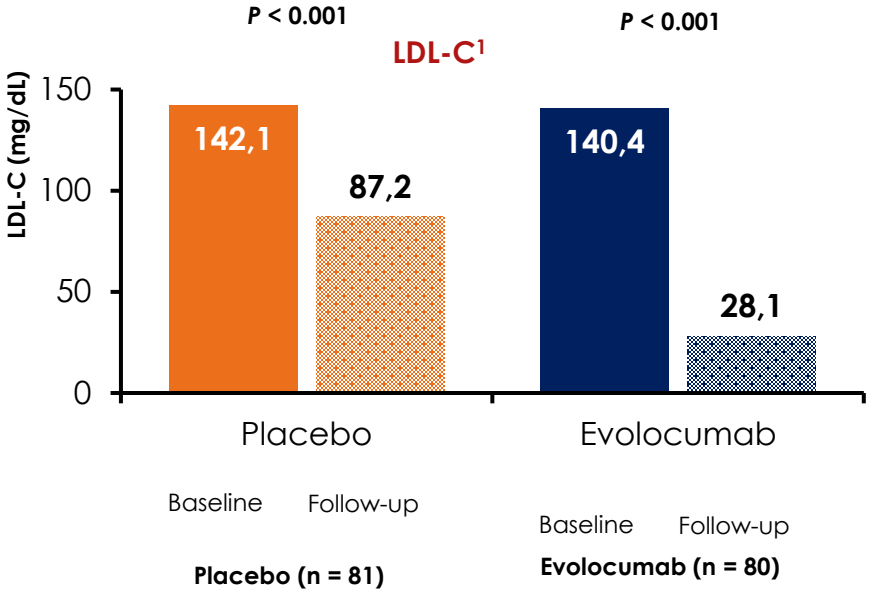


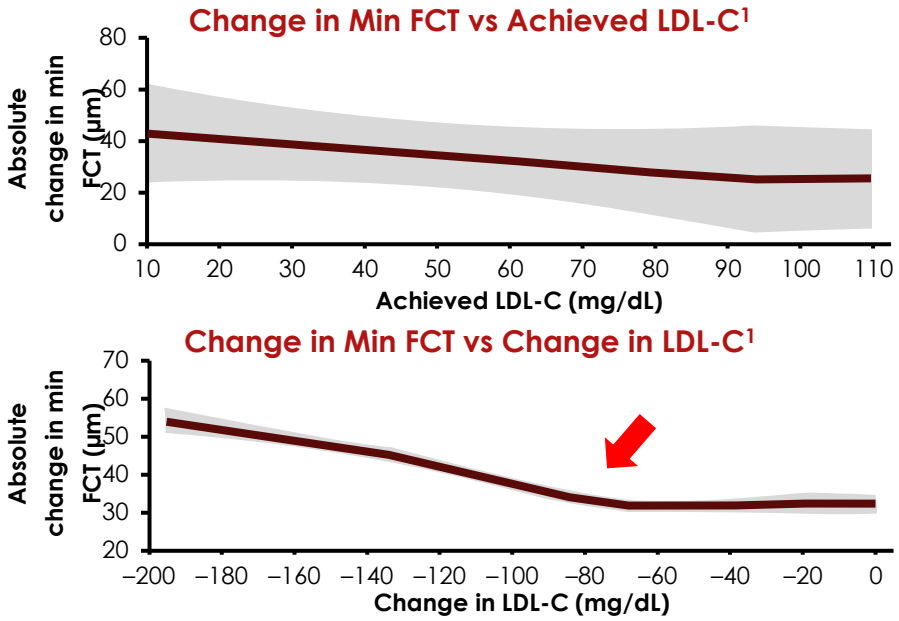

## Maximum Lipid Arc




161 patients with (i) NSTEMI, (ii) angiographic CAD, (iii) LDL-C ≥60 mg/dL on high-intensity, ≥80 mg/dL on low/moderate-intensity or ≥130 mg/dL on no statin at screening, (iv) subsequently treated with maximally tolerated statin and (v) target segment on OCT containing at least one image with a FCT <120 µm and one image with lipid arc >90°

# The Degree of FCT Increase Was Related to the Intensity of Lipid Lowering Observed




**LDL-C was reduced by 80% in the evolocumab group, compared with 39% in patients on maximally tolerated statins alone. A correlation between achieved LDL-C and change in minimum FCT was shown.[1]**

The primary and secondary endpoints were analyzed using ANCOVA.[2]

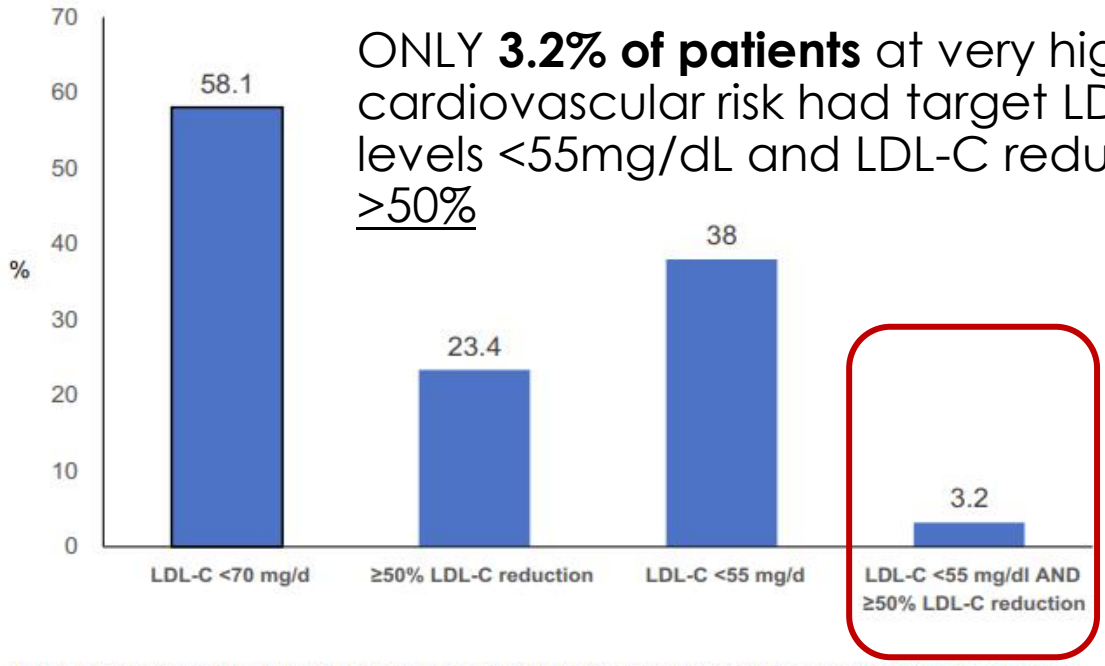
*This trial was not designed to assess a correlation between changes in FCT and cardiovascular events.*

ANCOVA, analysis of covariance; FCT, fibrous cap thickness; LDL-C, low-density lipoprotein cholesterol.

1. Nicholls SJ, et al. [published online ahead of print March 16, 2022]. *JACC Cardiovasc Imaging*. doi:10.1016/j.jcmg.2022.03.002.
2. Nicholls SJ, et al. *Cardiovasc Diagn Ther*. 2021;11:120-129.

# Lipid lowering therapies and the achievement of LDL-C targets in patients at very high cardiovascular risk: **data from the START registry (2020)**

**#4751 VHR patients**

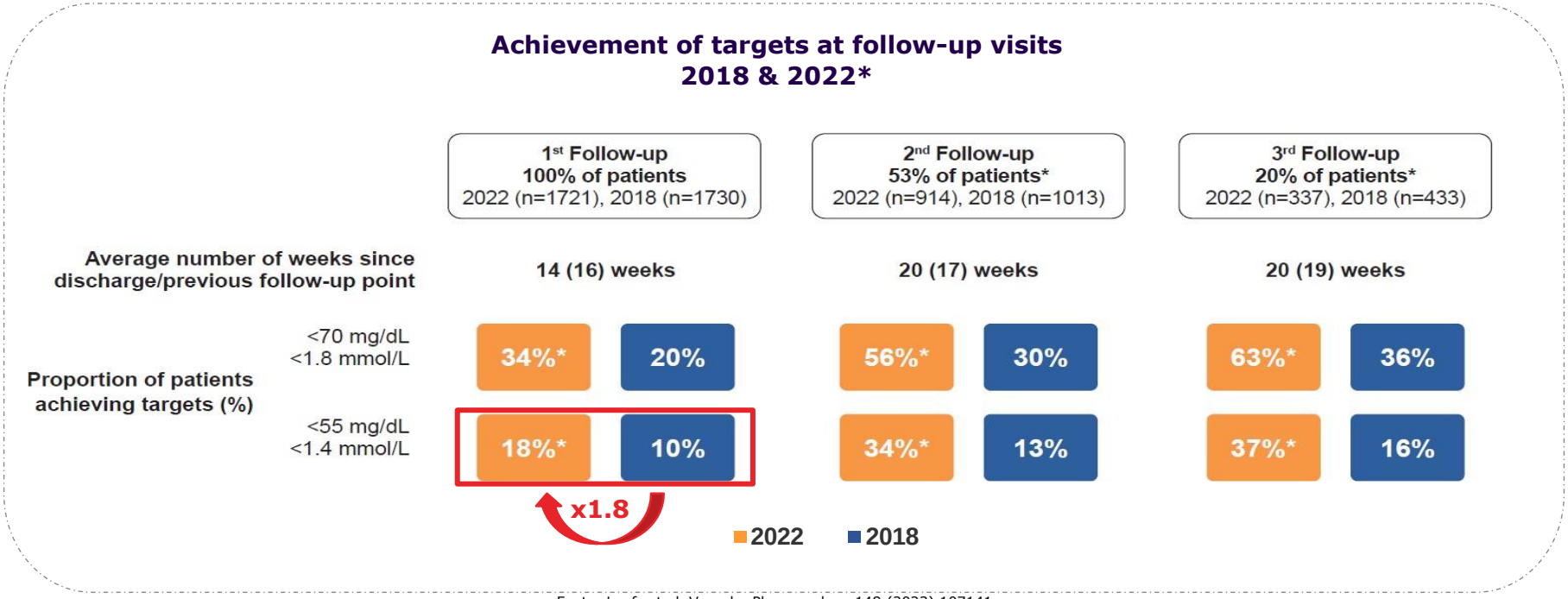



ONLY **3.2% of patients** at very high cardiovascular risk had target LDL-C levels <55mg/dL and LDL-C reduction >50%

**Fig. 4.** Frequency of VHR patients reaching LDL-C goals recommended by 2016 and 2019 ESC/EAS guidelines.

De Luca L, Arca M, Temporelli PL, Meessen J, Riccio C, Bonomo P, Colavita AR, Gabrielli D, Gulizia MM, Colivicchi F; START Investigators. Current lipid lowering treatment and attainment of LDL targets recommended by ESC/EAS guidelines in very high-risk patients with established atherosclerotic cardiovascular disease: Insights from the START registry. Int J Cardiol. 2020.

# Results from an ACS Europath survey of 2650 SCA patients in 6 European countries: management in SCA patients remains sub-optimal (**82% do not reach target at 1st follow-up**)




Fonte: Laufs et al, Vascular Pharmacology 148 (2023) 107141

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



# 2024 ESC Guidelines for the management of chronic coronary syndromes

**Developed by the task force for the management of chronic coronary syndromes of the European Society of Cardiology (ESC)**

***Endorsed by the European Association for Cardio-Thoracic Surgery (EACTS)***

## Recommendation Table 18 — Recommendations for lipid-lowering drugs in patients with chronic coronary syndrome (see also Evidence Table 18)

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Lipid-lowering treatment with an LDL-C goal of <1.4 mmol/L (55 mg/dL) and a ≥50% reduction in LDL-C vs. baseline is recommended.[64,670,671] | I | A |
| A high-intensity statin up to the highest tolerated dose to reach the LDL-C goals is recommended for all patients with CCS.[670,671] | I | A |
| If a patient's goal is not achieved with the maximum tolerated dose of statin, combination with ezetimibe is recommended.[674] | I | B |
| For patients who are statin intolerant and do not achieve their goal on ezetimibe, combination with bempedoic acid is recommended.[680] | I | B |
| For patients who do not achieve their goal on a maximum tolerated dose of statin and ezetimibe, combination with a PCSK9 inhibitor is recommended.[675,676] | I | A |
| For patients who do not achieve their goal on a maximum tolerated dose of statin and ezetimibe, combination with bempedoic acid should be considered. | IIa | C |
| For patients with a recurrent atherothrombotic event (not necessarily of the same type as the first event) while taking maximally tolerated statin therapy, an LDL-C goal of <1.0 mmol/L (<40 mg/dL) may be considered.[675,676] | IIb | B |



CCS, chronic coronary syndrome; LDL-C, low-density lipoprotein cholesterol; PCSK9, proprotein convertase subtilisin/kexin type 9.
[a]Class of recommendation.
[b]Level of evidence.

# Consensus Statement 2023 ESC-ACVC-EAPC: *Strike early, Strike Strong*

The '*strike early and strike strong*' approach **considers the use of** of **PCSK9i in the *acute phase post ACS event*,** especially **if other very high CV risk factors are present** such as patients with recurrent events, multivessel coronary artery disease, polyvascular disease, familial hypercholesterolaemia

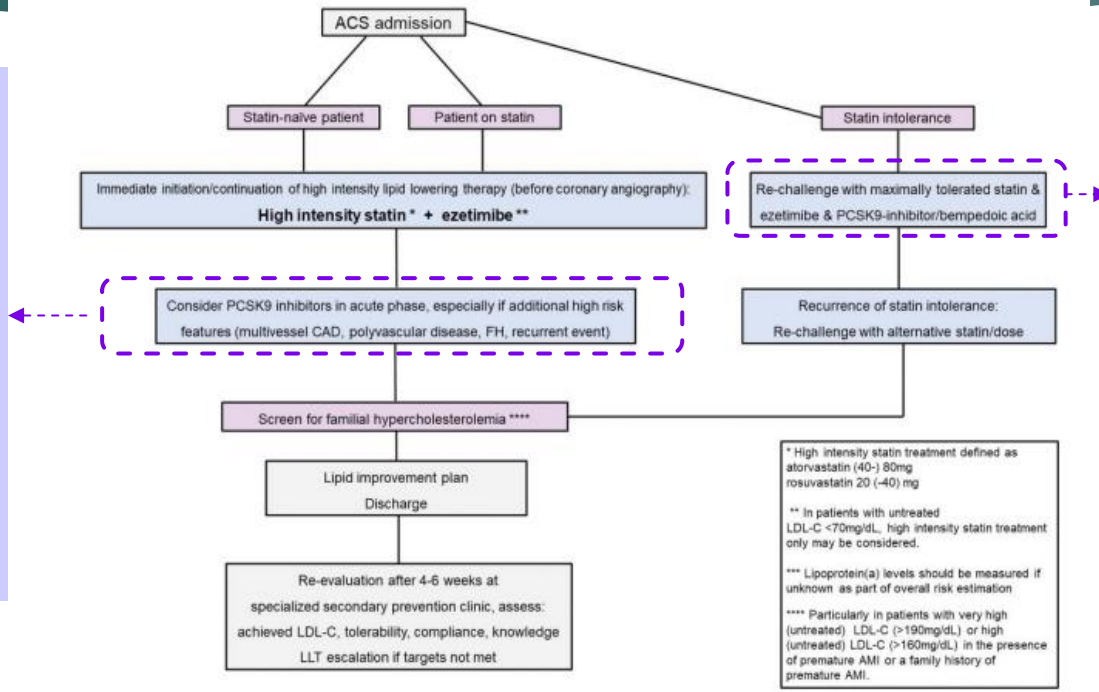



**Figure 2** Proposed lipid-lowering algorithm after ACS. A combination therapy consisting of a high-intensity statin and ezetimibe, preferably as a

In case of statin intolerance: **MTD statin** re-administration **+ ezetimibe + PCSK9i**

Fonte*:* Krychtiuk KA et al. Eur Heart J Acute Cardiovasc Care. 2022; 11(12): 939-49.

REGIONE CAMPANIA

# PERCORSO DIAGNOSTICO TERAPEUTICO ASSISTENZIALE

## Sindromi Coronariche Acute (SCA)

Gennaio
2022

### *3.1.2 Terapia alla dimissione*

La prevenzione secondaria di eventi ischemici e quindi la riduzione del rischio residuo inizia già in fase ospedaliera ed in fase di dimissione. La dimissione rappresenta un momento clinico fondamentale per istruire il paziente ed i caregivers sull'importanza del trattamento farmacologico, dell'aderenza terapeutica e dei target da raggiungere.
Nello specifico:

...

- Il trattamento ipolipemizzante deve mirare ad un target precoce di LDL <55 mg/dL e/o ad una riduzione di LDL >/= 50% rispetto al valore di partenza (o <40 mg/dL se la SCA si verifica entro due anni da un precedente evento cardiovascolare). Pertanto, dovrà già in fase di pre-dimissione essere identificato il target per ogni specifico paziente e di conseguenza, a seconda della distanza dal target stesso, in base alla riduzione attesa con le varie strategie farmacologiche, identificare la terapia ipolipemizzante ottimale. Per la maggior parte di pazienti dovrà essere, già al momento della dimissione, prescritta una terapia di associazione orale (statina ad alta efficacia ed Ezetimibe), preferibilmente in associazioni precostituite per migliorare l'aderenza nel lungo termine. Inoltre, potranno già in fase di pre-dimissione essere identificati alcuni fenotipi di pazienti che possono giovarsi del ***fast-track*** per la prescrizione di inibitori di PCSK9 (prescrizione sulla base di una sola determinazione di LDL), ovvero: pazienti già in trattamento con statina ad alta intensità e valore di LDL al ricovero >70 mg/dl, pazienti con nota intolleranza alla statina, pazienti con valore basale di LDL (>/=140) tale da non poter raggiungere i target raccomandati con la sola statina ad alta intensità o con una combinazione di statina ad alta intensità più ezetimibe (4).

## L' importanza di una terapia ipolipemizzante intensiva dopo SCA: cambiare il paradigma per migliorare il raggiungimento dei target

- *Paziente con SCA in terapia con Statine ed Ezetimibe ed LDL > 70 mg/dl*
  Aggiunge i-PCSK9 alla dimissione

- *Paziente con SCA in terapia con Statine ed LDL > 70 mg/dl*
  Aggiunge eventualmente Ezetimibe ed i-PCSK9 alla dimissione

Nuova rimborsabilità AIFA 100 =>70

- *Paziente con SCA naive da Statine con LDL > 70 mg/dl e < 140 mg/dl*
  Aggiunge combinazione Statina ed Ezetimibe alla dimissione e controllo a 1 mese per valutare i-PCSK9

- *Paziente con SCA naive da Statine con LDL > 140 mg/dl*
  Aggiunge combinazione Statina, Ezetimibe e i-PCSK9 alla dimissione

a terapia prescritta

128

150

a riduzione

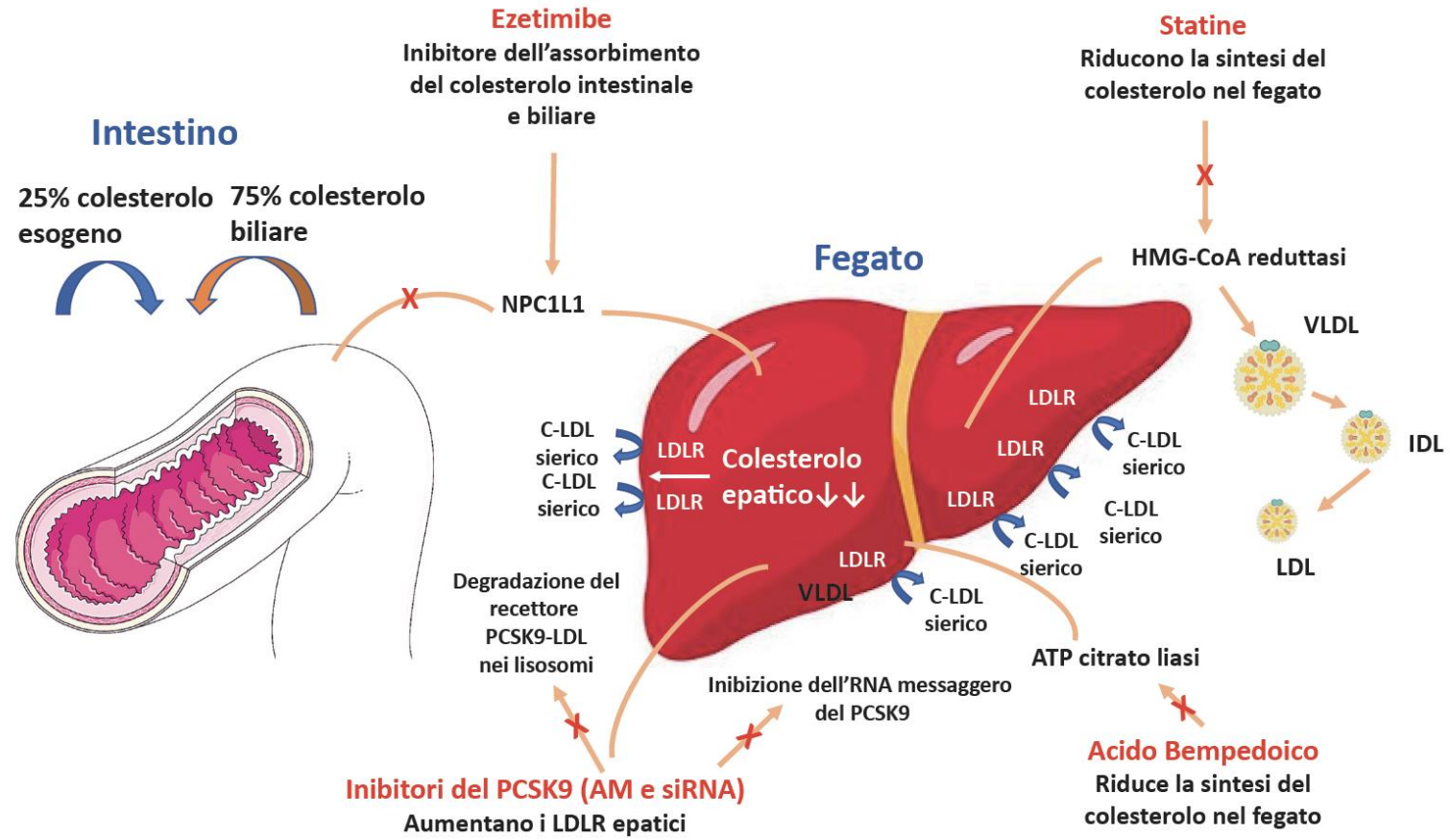
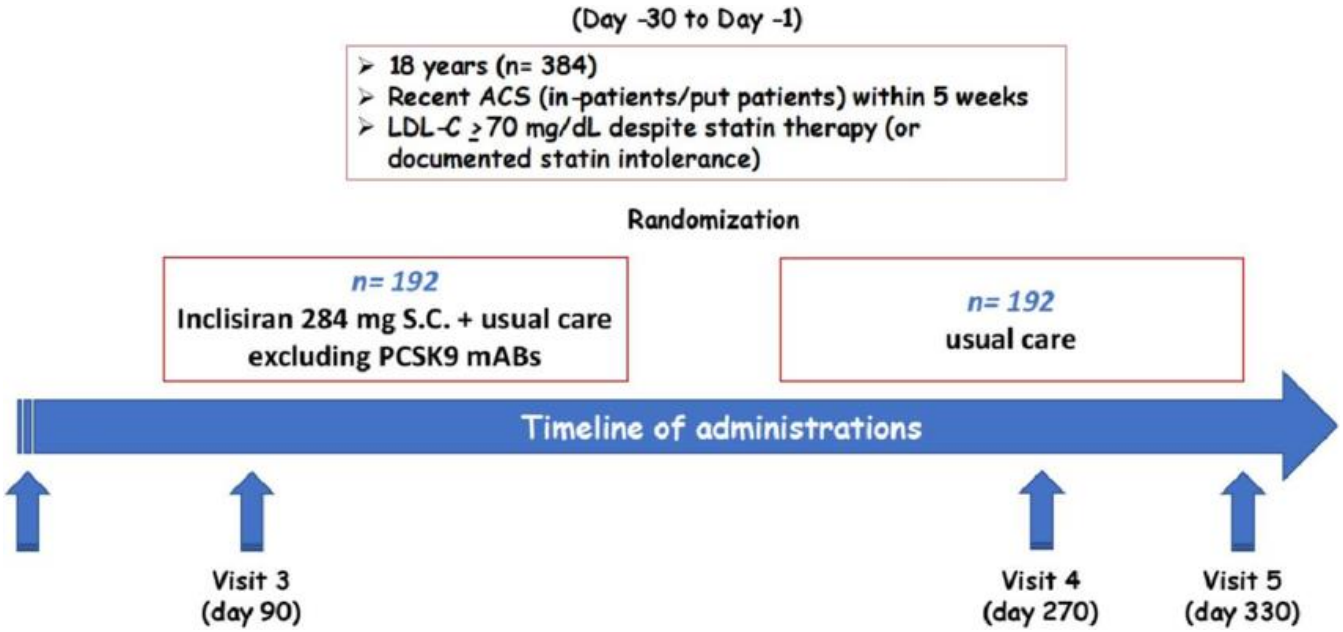



**Figura 1.** Principali molecole disponibili per la riduzione del colesterolo LDL.
AM, anticorpi monoclonali; ATP, adenosina trifosfato; C-LDL, colesterolo LDL; HMG-CoA, idrossimetilglutaril-coenzima A; IDL, lipoproteine a intermedia densità; LDL, lipoproteine a bassa densità; LDLR, recettori delle lipoproteine a bassa densità; NPC1L1, Niemann-Pick C1-Like 1; siRNA, small interfering RNA; VLDL, lipoproteine a densità molto bassa.

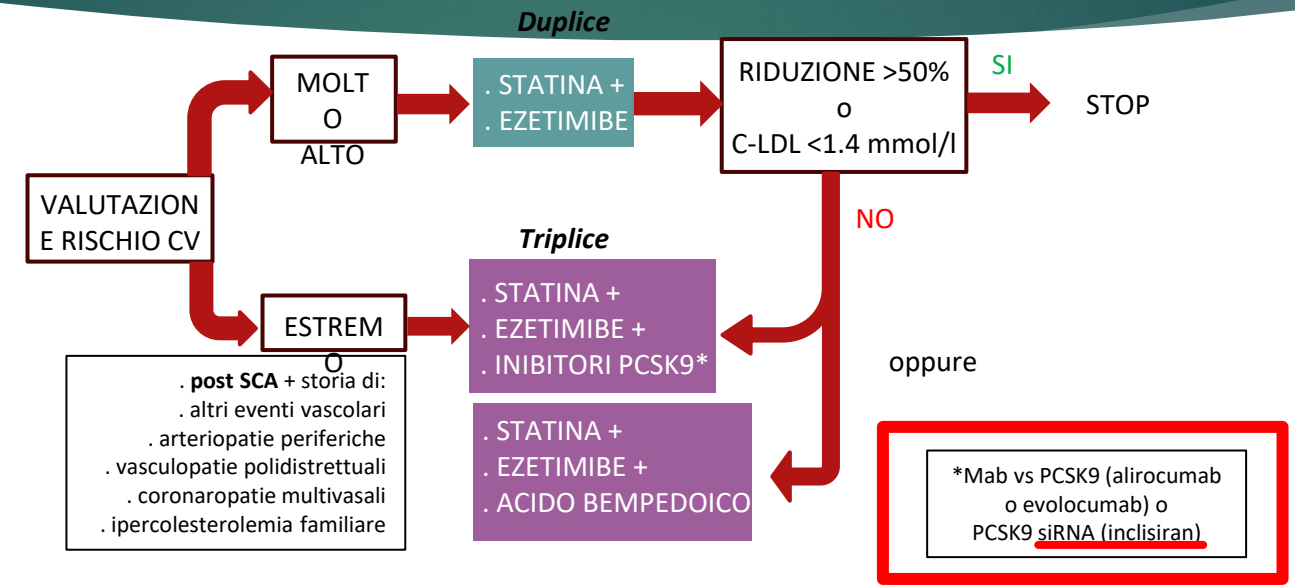
ABSTRACT | Originally Published 30 October 2022 |



# Abstract 10851: A Randomized Study to Compare LDL-C-Lowering Effects of Inclisiran With Usual Care vs Usual Care Alone in Patients With Recent Hospitalization for an Acute Coronary Syndrome: Rationale and Design of the VICTORION-INCEPTION Trial



# Le maggiori società scientifiche Italiane suggeriscono l'utilizzo da subito della triplice associazione nei pazienti a rischio estremo con LDL-C molto lontano dal target




L'aggiunta tempestiva di una terapia mirata alla riduzione della PCSK9 risulta quindi preferibile:

- **nei pazienti a rischio CVS molto alto ed estremo (eventi cv multipli o secondo evento entro 2 anni) che non raggiungono i goal terapeutici con statina/ezetimibe o che sono molto lontani dal target, per cui anche con HIS+EZE non potrebbero raggiungere il target**
- **nei pazienti che sono intolleranti alle statine**

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

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VIEWPOINT
*Epidemiology and prevention*

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

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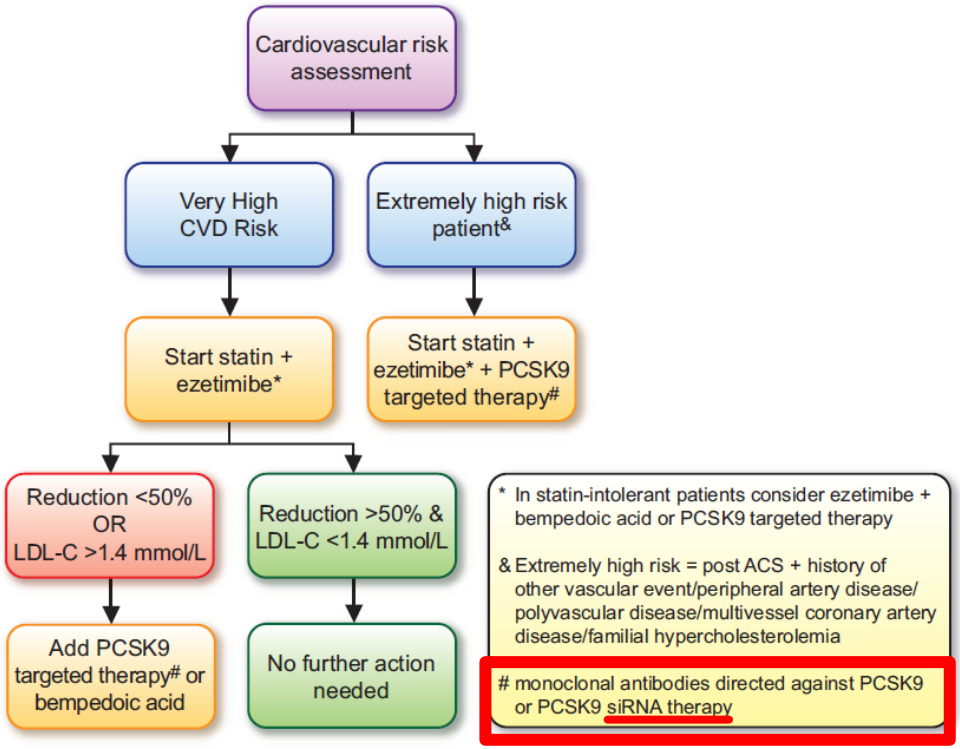


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# Position paper ANMCO: Gestione dell'ipercolesterolemia nei pazienti con sindrome coronarica acuta

Leonardo De Luca[1], Carmine Riccio[2], Alessandro Navazio[3], Serafina Valente[4], Manlio Cipriani[5], Marco Corda[6], Alfredo De Nardo[7], Giuseppina Maura Francese[8], Cosimo Napoletano[9], Emanuele Tizzani[10], Loris Roncon[11], Pasquale Caldarola[12], Michele Massimo Gulizia[8], Domenico Gabrielli[1,13], Fabrizio Oliva[14], Furio Colivicchi[15]

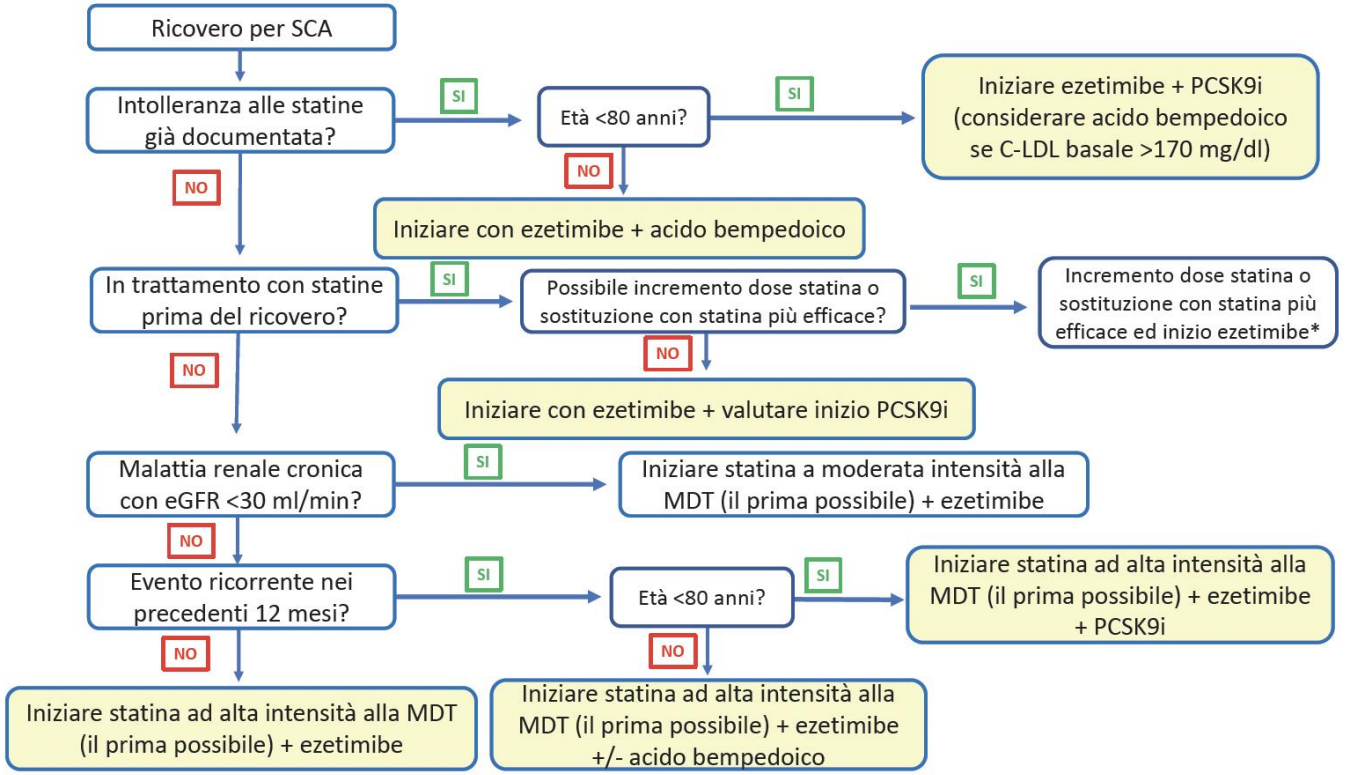


**Figura 3.** Avvio della terapia ipolipemizzante durante il ricovero nel paziente con sindrome coronarica acuta.
C-LDL, colesterolo LDL; eGFR, velocità di filtrazione glomerulare stimata; MDT, massima dose tollerata; PCSK9i, inibitori del PCSK9; SCA, sindrome coronarica acuta.
*Valutare anche l'aggiunta di PCSK9i in caso di evento ricorrente.

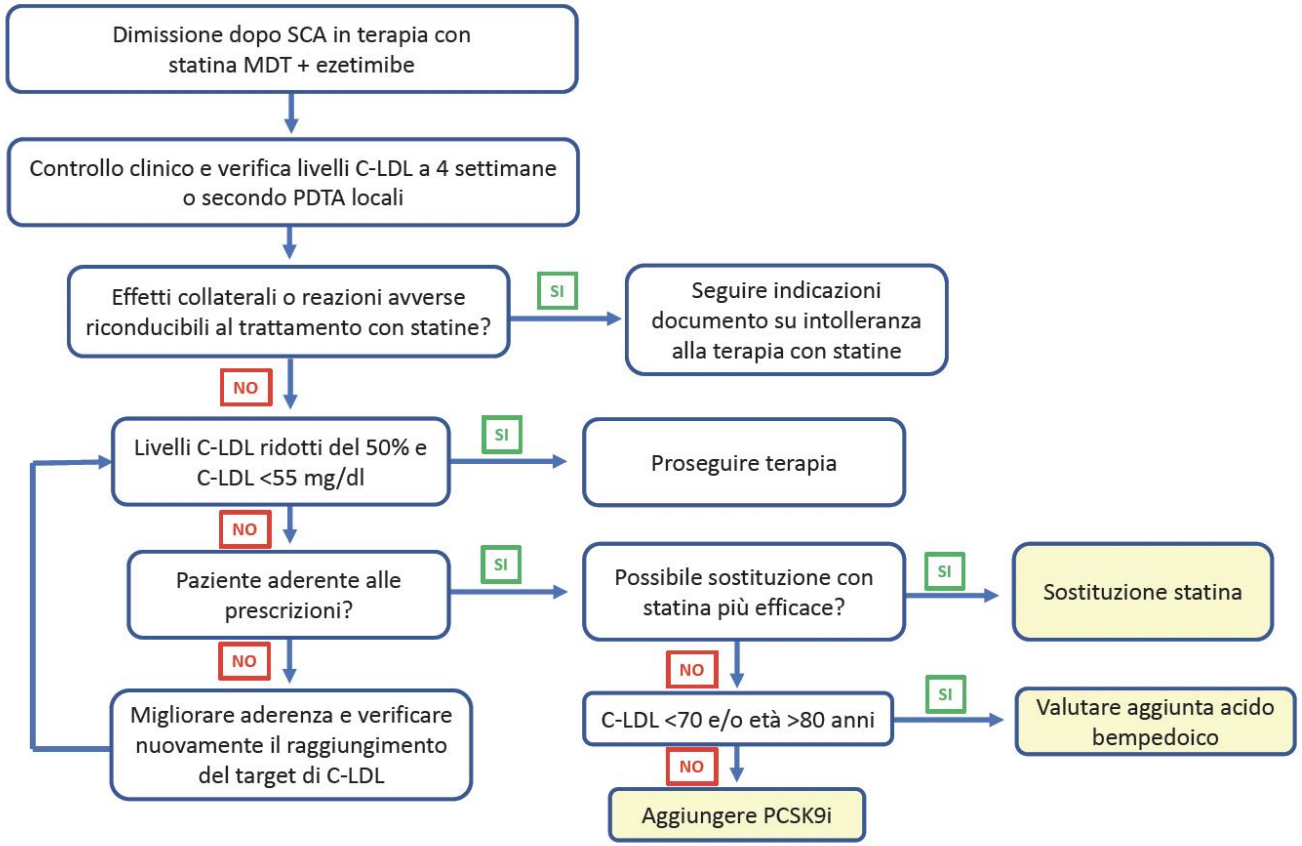


**Figura 4.** Gestione del trattamento ipolipemizzante dopo la dimissione ospedaliera per sindrome coronarica acuta in pazienti già in trattamento con la combinazione statina/ezetimibe.
C-LDL, colesterolo LDL; MDT, massima dose tollerata; PCSK9i, inibitori del PCSK9; PDTA, percorso diagnostico-terapeutico assistenziale; SCA, sindrome coronarica acuta.

# Take Home Message

**Razionale**

- La riduzione precoce del LDL-C (con statine) si è dimostrata efficace nella riduzione della mortalità e morbilità
- Ancora troppo pochi i pazienti con ACS  a target
- Una terapia anche con statine ad alta intensità/efficacia o in associazione con Ezetimibe non potrà mai consentire a pazienti a rischio molto alto il raggiungimento dei target terapeutici

**Fattibilità**

- Sufficienti dati che indicano una correlazione tra riduzione rapida e mantenimento constante di bassi livelli di LDL-c e riduzione degli eventi CV attraverso una precoce stabilizzazione delle placca e delle lesioni non culprit
- L'abbassamento della soglia della prescrivibilità a valori di LDL-c ≥ 70 mg/dl in prevenzione secondaria ed in pazienti ad alto rischio CV con IMA < 12 mesi (con una singola determinazione dell'LDL-c) consente di ampliare e già in fase acuta la popolazione dei pazienti

**Sicurezza**

- Assenza di effetti collaterali, neurocognitivi e immunitari in relazione a valori di LDL-c permanentemente bassi

# GRAZIE PER L'ATTENZIONE