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CRITICAL CARE COMMUNITY

Come minimizzare il rischio in prevenzione secondaria con PCSK9i

Giovanna Geraci

Erice

Fonti di finanziamento

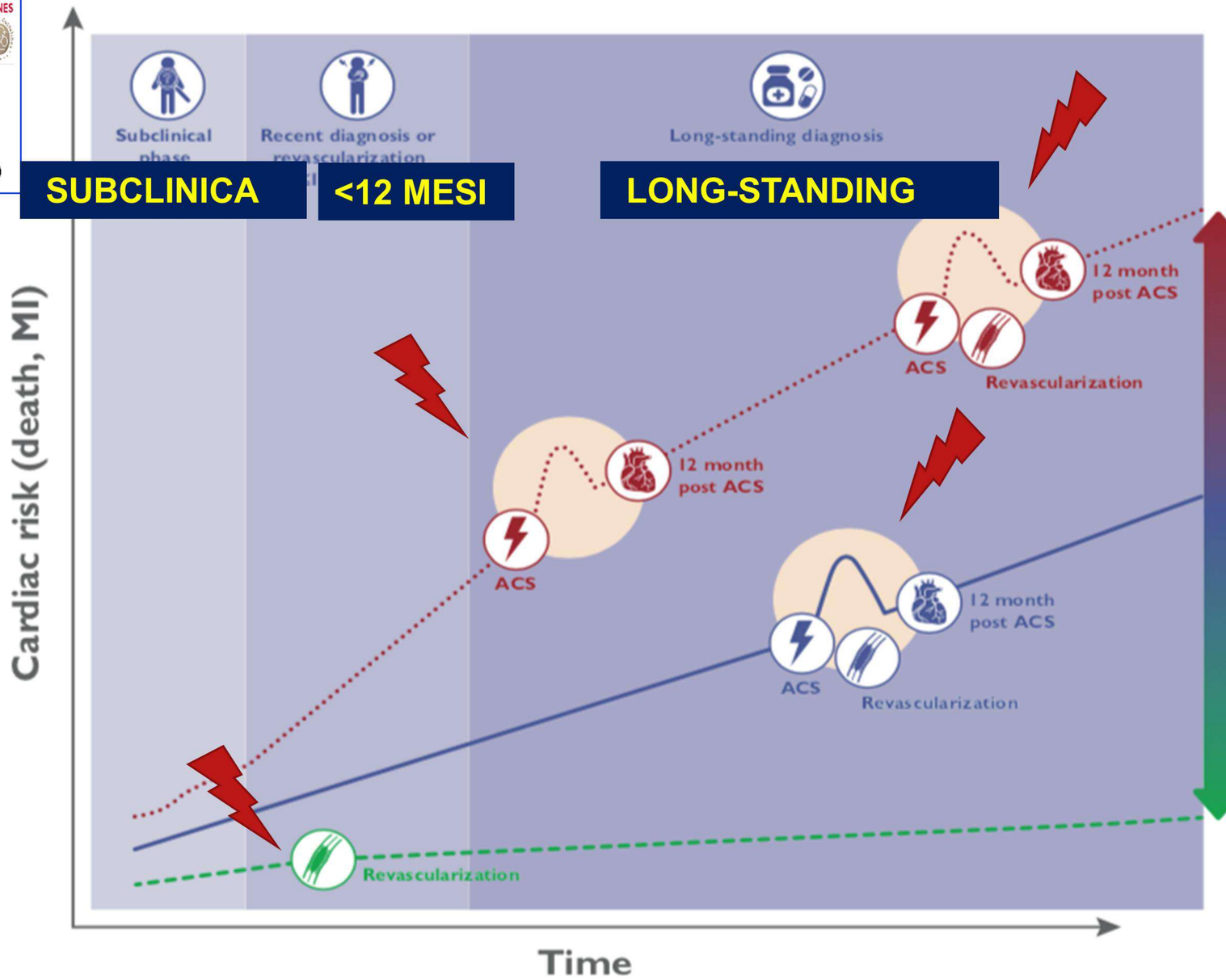
- Servier
- Dompè
- Sanofi

Storia naturale delle SCC

ESC GUIDELINES

2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes

The Task Force for the diagnosis and management of chronic coronary syndromes of the European Society of Cardiology (ESC)



Gradazione del rischio di eventi secondo

- **corretto controllo FR**
- **rivascolarizzazione appropriata**
- **OMT in prevenzione secondaria**

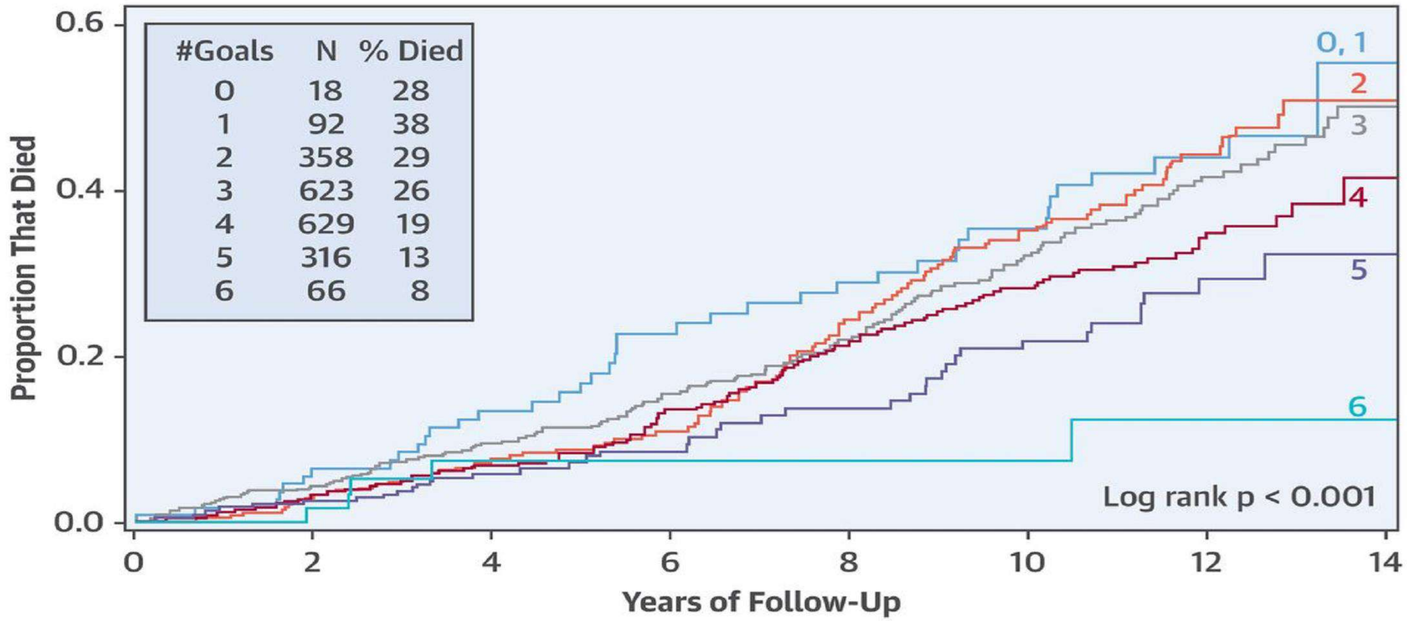
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JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
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PUBLISHED BY ELSEVIER
VOL. 72, NO. 19, 2018

COURAGE...dati osservazionali a distanza

Healthy Behavior, Risk Factor Control, and Survival in the COURAGE Trial

CENTRAL ILLUSTRATION: Multiple Risk Factor Control Predicts Improved Survival: Time to Death by Count of Goals Achieved



Maron, D.J. et al. J Am Coll Cardiol. 2018;72(19):2297–305.

Mortalità ridotta in base a n° FR a target ad 1 anno dall'arruolamento

David J. Maron et al. JACC 2018;72:2297-2305

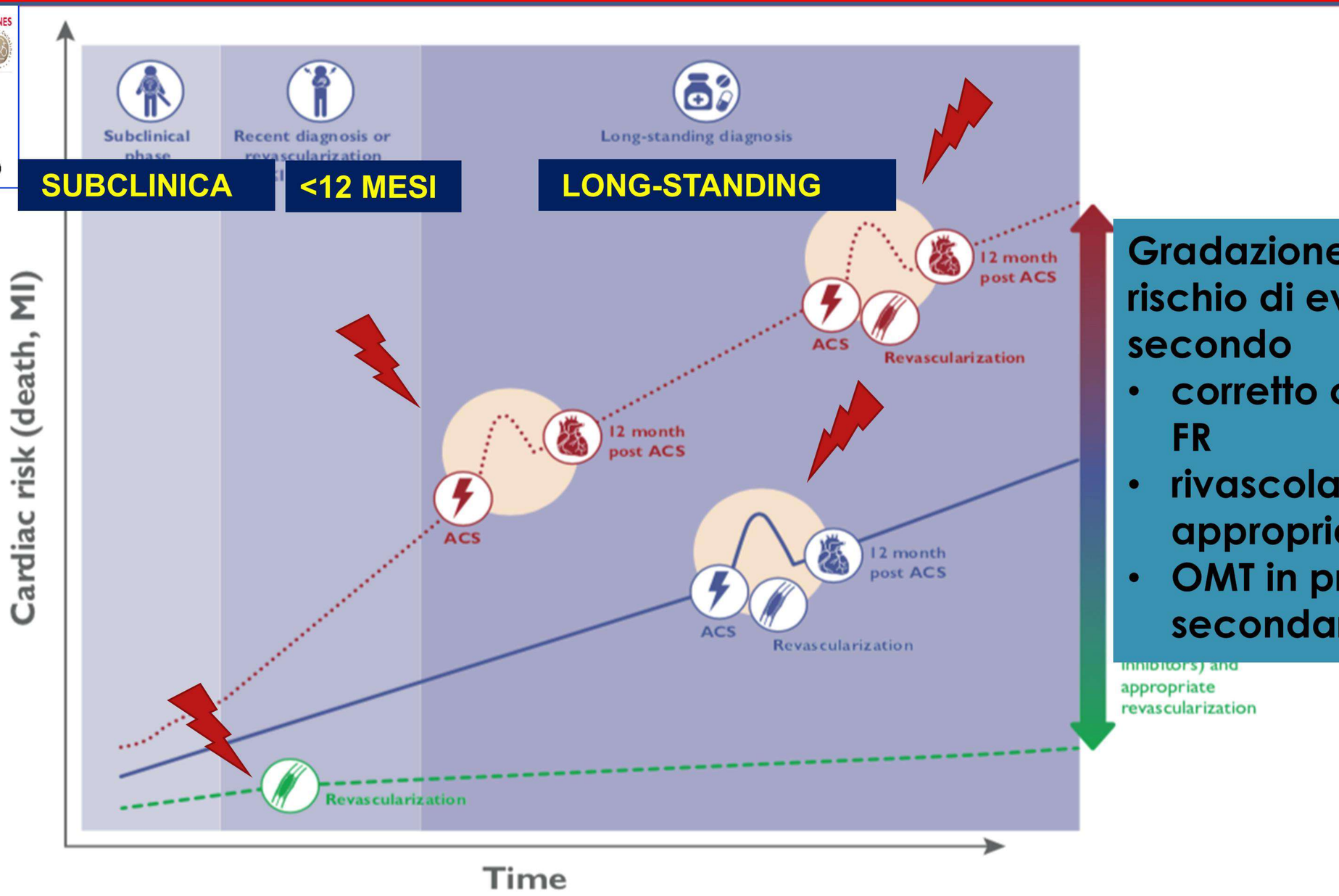
2018 American College of Cardiology Foundation

Storia naturale delle SCC

ESC GUIDELINES

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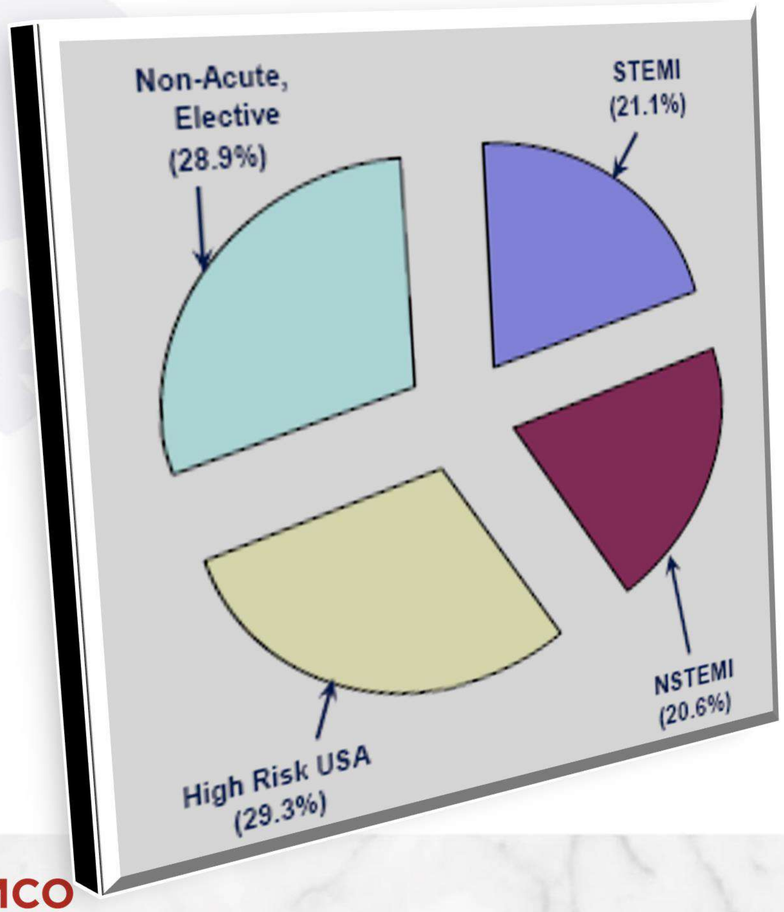
Gradazione del rischio di eventi secondo

- **corretto controllo FR**
- **rivascolarizzazione appropriata**
- **OMT in prevenzione secondaria**

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APPROPRIATEZZA DELLA PCI NEI PAZIENTI CON SCC

Patients within the National Cardiovascular Data Registry undergoing PCI between July 1, 2009, and September 30, 2010, at 1091 US hospitals.



- ✓ Acute PCI
- ✓ 355.417 (71.1%)
  - ✓ 98.6% appropriate
  - ✓ 0.3 % uncertain
  - ✓ 1.1 % inappropriate

- ✓ Non-acute PCI
- ✓ 144.737 (28.9%)
  - ✓ 50.4% appropriate
  - ✓ 38.0% uncertain
  - ✓ 11.6% inappropriate

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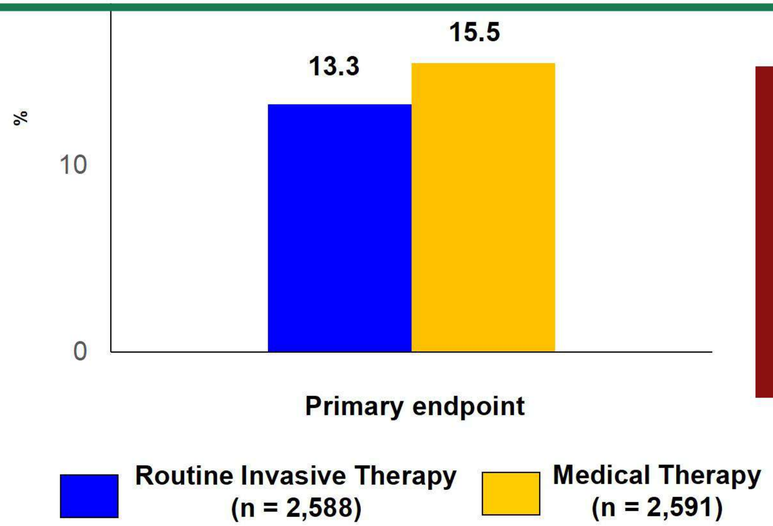
JAMA, July 6, 2011—Vol 306, No. 1

ISCHEMIA

AMERICAN COLLEGE of

CONCLUSIONS

- Among patients with stable ischemic heart disease and moderate to severe ischemia on stress testing, invasive therapy failed to reduce major adverse cardiac events vs. medical therapy. Invasive therapy was associated with increase in periprocedural MI at 6 months and a reduction in spontaneous MI at 4 years.



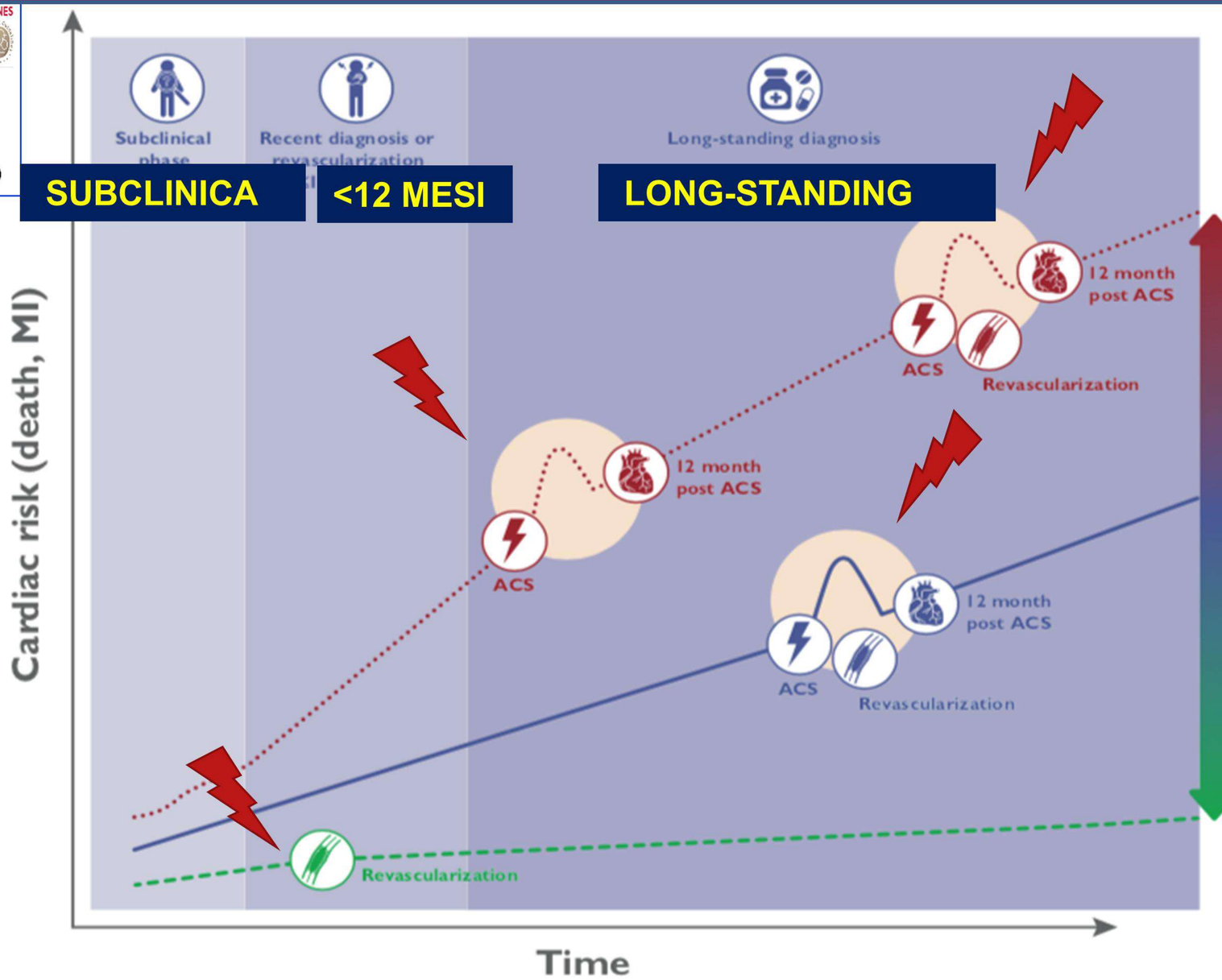
Non è stato dimostrato un vantaggio tra una strategia inizialmente invasiva vs una terapia medica ottimale

Storia naturale delle SCC

ESC GUIDELINES

2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes

The Task Force for the diagnosis and management of chronic coronary syndromes of the European Society of Cardiology (ESC)



Gradazione del rischio di eventi secondo

- **corretto controllo FR**
- **rivascolarizzazione appropriata**
- **OMT in prevenzione secondaria**

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ESC European Heart Journal (2019) 00, 1–71 doi:10.1093/eurheartj/ehz425
ESC GUIDELINES
2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes
The Task Force for the diagnosis and management of chronic coronary syndromes of the European Society of Cardiology (ESC)

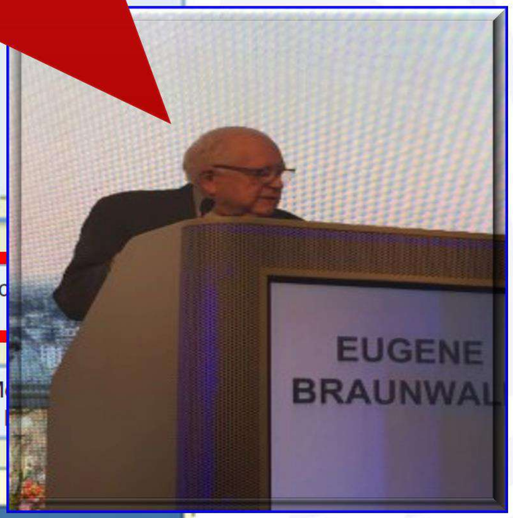
Terapia medica ottimale

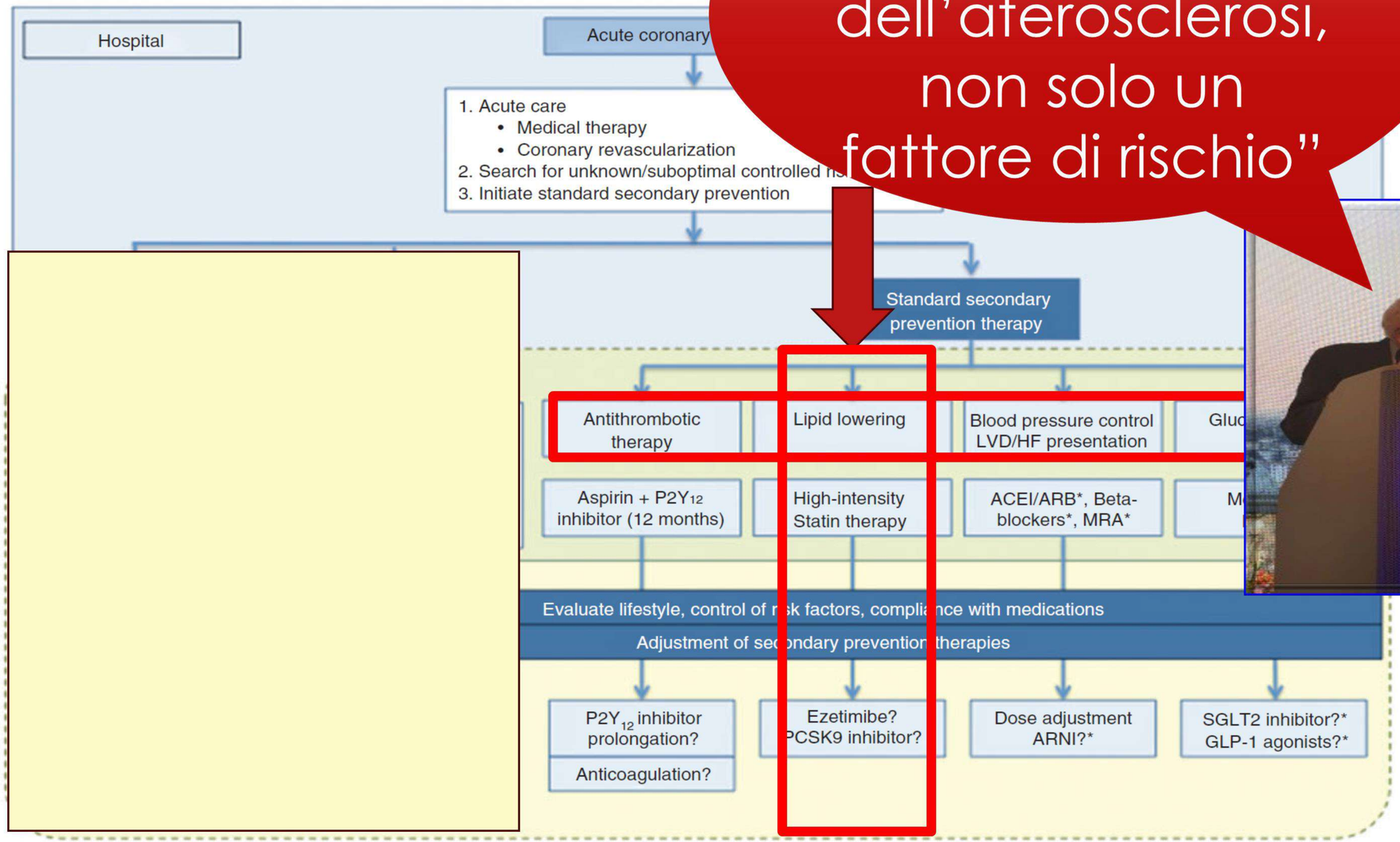
3.3.1.1 General strategy

Optimal treatment can be defined as the treatment that satisfactorily controls symptoms and prevents cardiac events associated with CCS, with maximal patient adherence and minimal adverse events.[188–191] However, there is no universal definition of an optimal treatment in patients with CCS, and drug therapies must be adapted to each patient's characteristics and preferences.[192] Initial drug therapy usually consists of one or two antianginal drugs, as necessary, plus drugs for secondary prevention of CVD.[193] The initial choice of antianginal

Secondary Prevention for Re duction

"Il colesterolo **è la causa** dell'aterosclerosi, non solo un fattore di rischio"



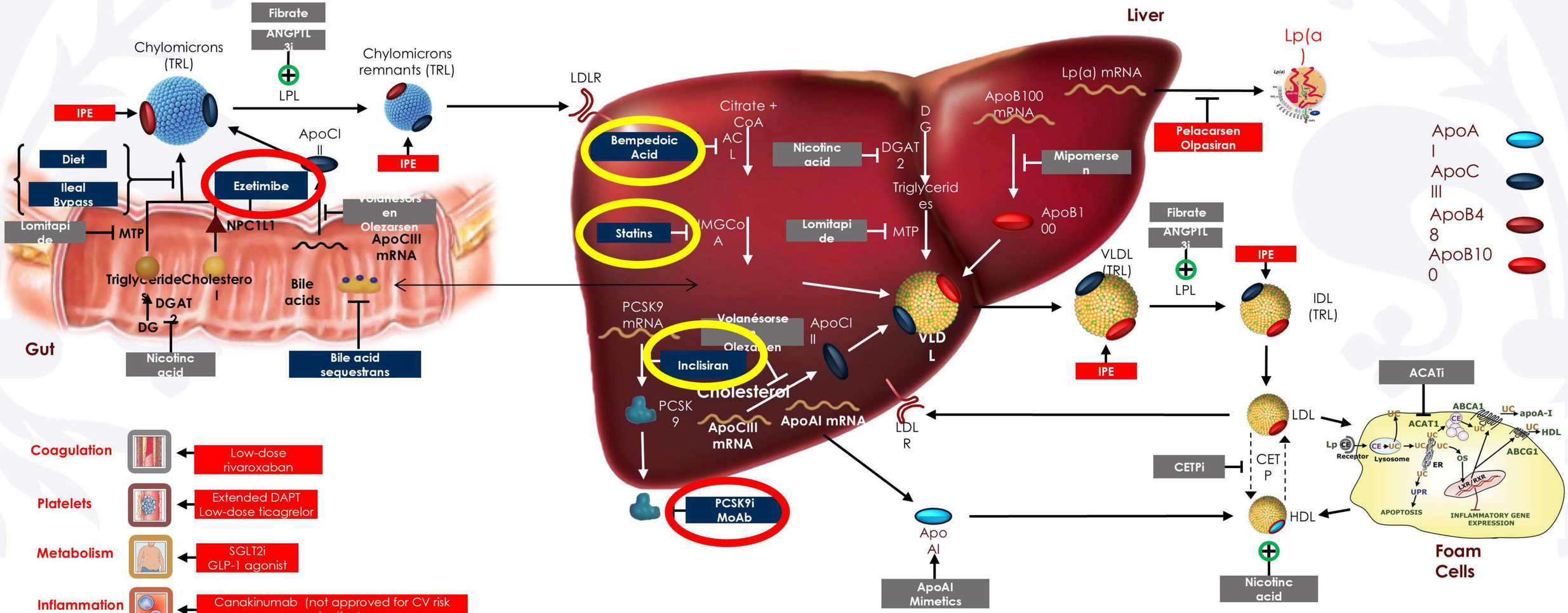


* When specifically indicated

European Journal of Preventive Cardiology 2017, Vol. 24(3S) 22–28

Target ambiziosi ma tante strategie per raggiungerli

LIFESTYLE | APHERESIS



Elements depicted in red are strategies directed against what is considered responsible for residual cardiovascular risk

Elements depicted in blue reduce blood LDL-C levels incresing LDLR number on hepatic cell surface

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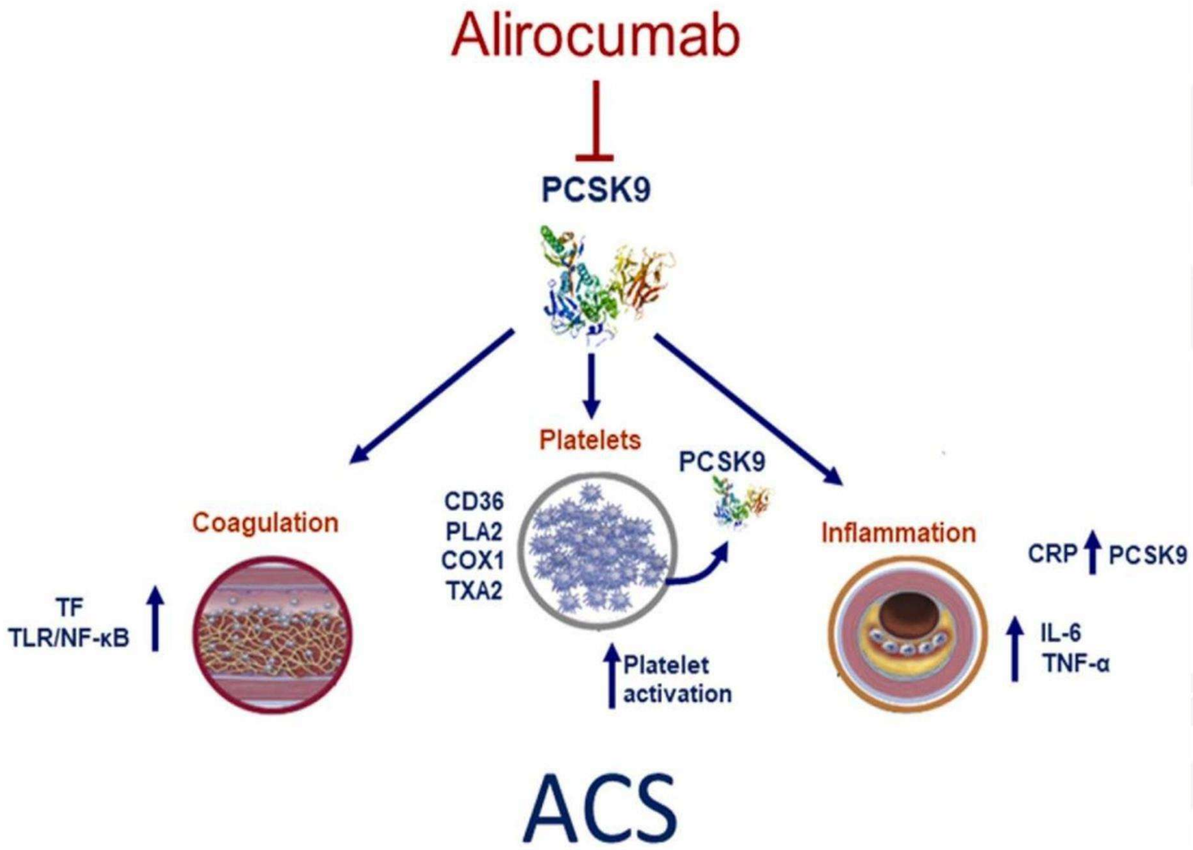
J Am Coll Cardiol. 2021 Mar, 77 (12) 1564–1575; modificata
Circulation. 2018;137(24):2551–2553; modificata

Cells . 2023 Jun 16;12(12):1648.

Pharmacological rationale for the very early treatment of ACS with *PCSK9i mAbs*

Rationale for the rapid and aggressive pharmacological intervention with PCSK9 mAbs in ACS**:**

1) Circulating PCSK9 levels are raised during ACS;
2) PCSK9 may stimulate platelet reactivity;
3) PCSK9 is associated with intraplaque inflammation, macrophage activation and endothelial dysfunction;
4) PCSK9 concentrations are associated with inflammation in the acute phase of ACS
5) Statins raise PCSK9 levels



Very rapid (within 4 h) and effective suppression of circulating unbound PCSK9 (>95%)

Significant reduction of LDL-c after 48h (35%) with a full effect after 7–10 days (55–75%)

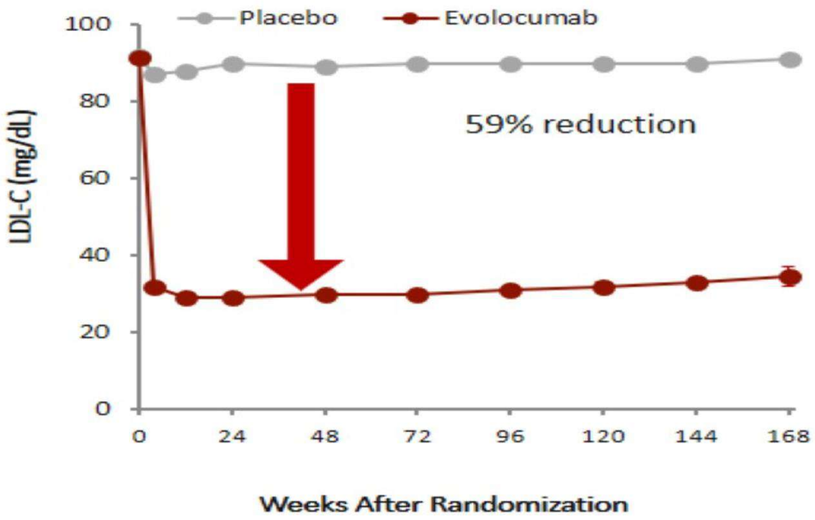
Ferri N. Pharmacological Research 184 (2022) 106439

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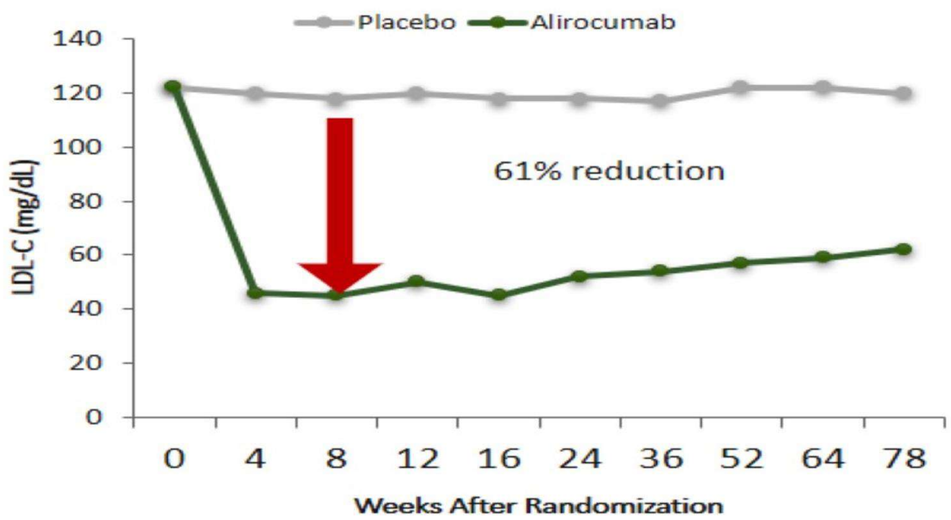
Results of PCSK9 Inhibitors on LDL-C Levels
FOURIER and ODYSSEY OUTCOMES

- PCSK9 inhibitor use in high-risk patients reduced LDL-C levels from baseline by 50% to 60%[a,b]

FOURIER [a]
Change in LDL-C Over Time

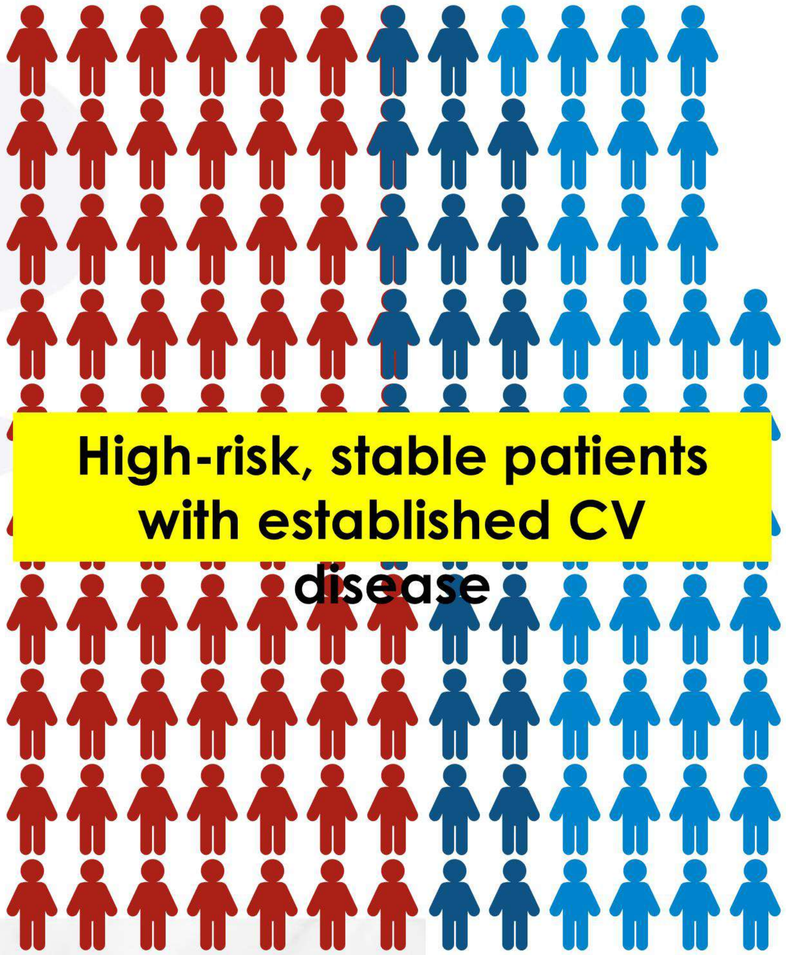


ODYSSEY OUTCOMES[c]
Change in LDL-C Over Time



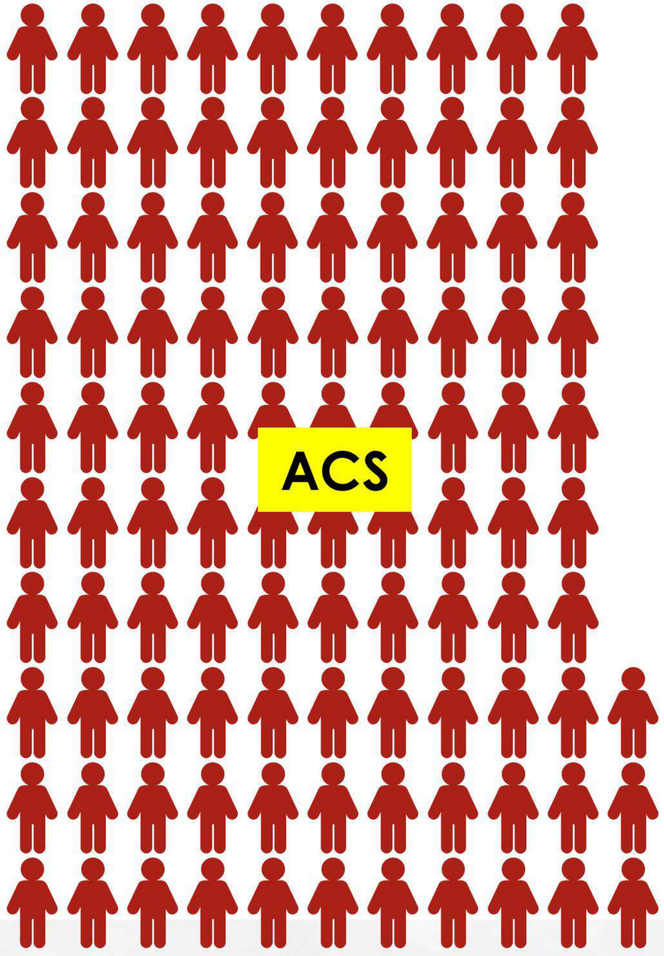
a. Sabatine M, et al. *N Engl J Med.* 2017;376:1713-1722; b. Steg PG, et al. *N Engl J Med.* 2018;379:2097-2107;
c. Robinson JG, et al. *N Engl J Med.* 2015;372:1489-1499.

fourier



Sabatine MS, et al. N Engl J Med 2017;376:1713

ODYSSEY OUTCOMES



Schwartz GG et al. N Engl J Med 2018;379:2097

FOURIER

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 4, 2017 VOL. 376 NO. 18

Evolocumab and Clinical Outcomes in Patients with Cardiovascular Disease

Marc S. Sabatine, M.D., M.P.H., Robert P. Giugliano, M.D., Anthony C. Keech, M.D., Narimon Honarpour, M.D., Ph.D., Stephen D. Wiviott, M.D., Sabina A. Murphy, M.P.H., Julia F. Kuder, M.A., Huei Wang, Ph.D., Thomas Liu, Ph.D., Scott M. Wasserman, M.D., Peter S. Sever, Ph.D., F.R.C.P., and Terje R. Pedersen, M.D., for the FOURIER Steering Committee and Investigators*

ABSTRACT

BACKGROUND

Evolocumab is a monoclonal antibody that inhibits proprotein convertase subtilisin–kexin type 9 (PCSK9) and lowers low-density lipoprotein (LDL) cholesterol levels by approximately 60%. Whether it prevents cardiovascular events is uncertain.

METHODS

We conducted a randomized, double-blind, placebo-controlled trial involving 27,564 patients with atherosclerotic cardiovascular disease and LDL cholesterol levels of 70 mg per deciliter (1.8 mmol per liter) or higher who were receiving statin therapy. Patients were randomly assigned to receive evolocumab (either 140 mg every 2 weeks or 420 mg monthly) or matching placebo as subcutaneous injections. The primary efficacy end point was the composite of cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina, or coronary revascularization. The key secondary efficacy end point was the composite of cardiovascular death, myocardial infarction, or stroke. The median duration of follow-up was 2.2 years.

RESULTS

At 48 weeks, the least-squares mean percentage reduction in LDL cholesterol levels with evolocumab, as compared with placebo, was 59%, from a median baseline value of 92 mg per deciliter (2.4 mmol per liter) to 30 mg per deciliter (0.78 mmol per liter) (P<0.001). Relative to placebo, evolocumab treatment significantly reduced the risk of the primary end point (1344 patients [9.8%] vs. 1563 patients [11.3%]; hazard ratio, 0.85; 95% confidence interval [CI], 0.79 to 0.92; P<0.001) and the key secondary end point (816 [5.9%] vs. 1013 [7.4%]; hazard ratio, 0.80; 95% CI, 0.73 to 0.88; P<0.001). The results were consistent across key subgroups, including the subgroup of patients in the lowest quartile for baseline LDL cholesterol levels (median, 74 mg per deciliter [1.9 mmol per liter]). There was no significant difference between the study groups with regard to adverse events (including new-onset diabetes and neurocognitive events), with the exception of injection-site reactions, which were more common with evolocumab (2.1% vs. 1.6%).

CONCLUSIONS

In our trial, inhibition of PCSK9 with evolocumab on a background of statin therapy lowered LDL cholesterol levels to a median of 30 mg per deciliter (0.78 mmol per liter) and reduced the risk of cardiovascular events. These findings show that patients with atherosclerotic cardiovascular disease benefit from lowering of LDL cholesterol levels below current targets. (Funded by Amgen; FOURIER ClinicalTrials.gov number, NCT01764633.)

From the Thrombolysis in Myocardial Infarction (TIMI) Study Group, Division of Cardiovascular Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston (M.S.S., R.P.G., S.D.W., S.A.M., J.F.K.); Sydney Medical School, National Health and Medical Research Council Clinical Trials Centre, University of Sydney, Sydney (A.C.K.); Amgen, Thousand Oaks, CA (N.H., H.W., T.L., S.M.W.); International Centre for Circulatory Health, National Heart and Lung Institute, Imperial College London, London (P.S.S.); and Oslo University Hospital, Ullevål and Medical Faculty, University of Oslo, Oslo (T.R.P.). Address reprint requests to Dr. Sabatine at the TIMI Study Group, Division of Cardiovascular Medicine, Brigham and Women's Hospital, 60 Fenwood Rd., Boston, MA 02115, or at msabatine@partners.org.

*A complete list of the Further Cardiovascular Outcomes Research with PCSK9 Inhibition in Subjects with Elevated Risk (FOURIER) steering committee and investigators is provided in the Supplementary Appendix, available at NEJM.org.

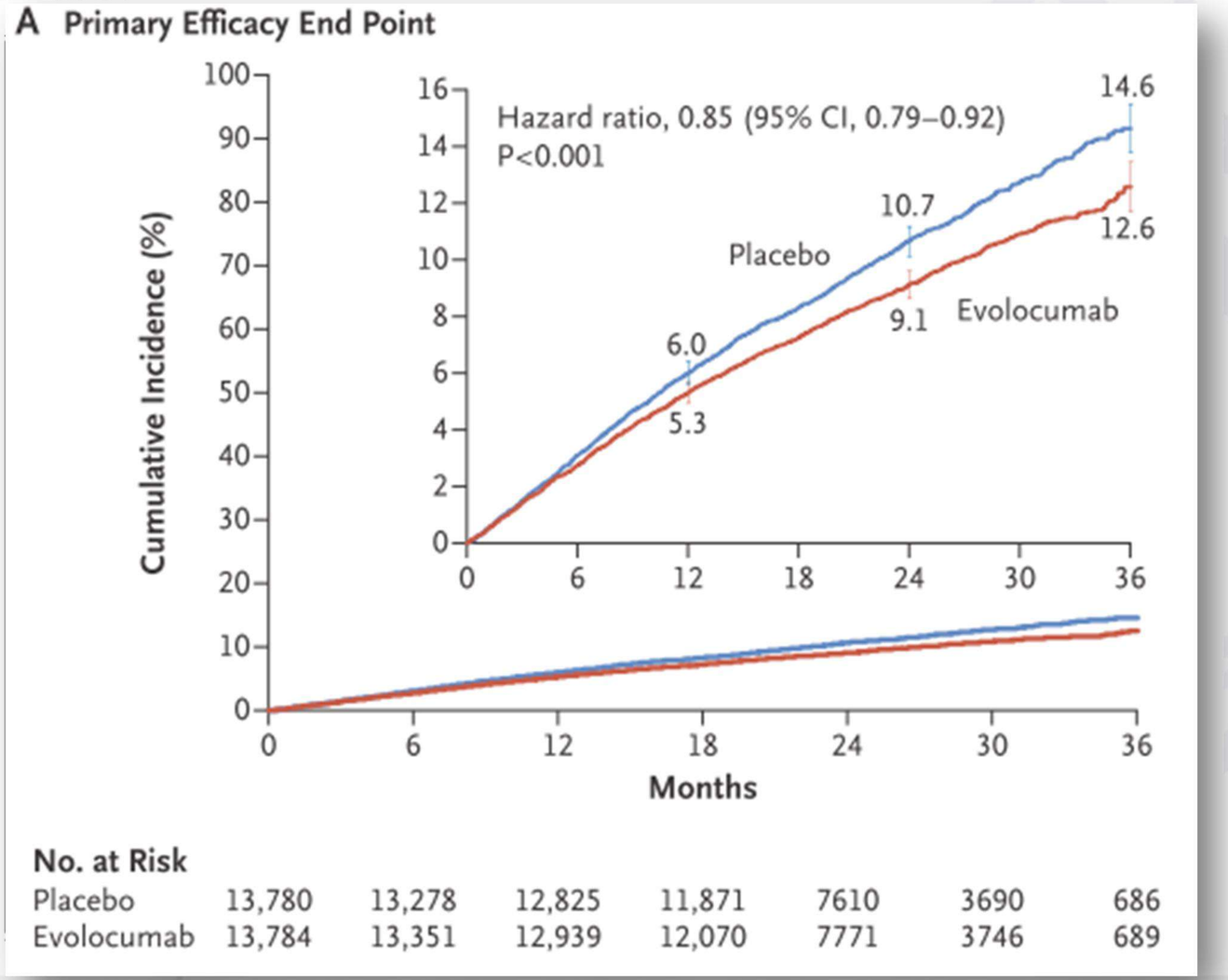
This article was published on March 17, 2017, at NEJM.org.

N Engl J Med 2017;376:1713-22.
DOI: 10.1056/NEJMoa1615664

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Primary end point: CV death, myocardial infarction, stroke, hospitalization for unstable angina, or coronary revasc.



Sabatine MS et al. N Engl J Med 2017;376:1713-1722.

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ODISSEY OUTCOMES

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 29, 2018 VOL. 379 NO. 22

Alirocumab and Cardiovascular Outcomes after Acute Coronary Syndrome

G.G. Schwartz, P.G. Steg, M. Szarek, D.L. Bhatt, V.A. Bittner, R. Diaz, J.M. Edelberg, S.G. Goodman, C. Hanotin, R.A. Harrington, J.W. Jukema, G. Lecorps, K.W. Mahaffey, A. Moryusef, R. Pordy, K. Quintero, M.T. Roe, W.J. Sasiela, J.-F. Tamby, P. Tricoci, H.D. White, and A.M. Zeiher, for the ODYSSEY OUTCOMES Committees and Investigators*

ABSTRACT

BACKGROUND

Patients who have had an acute coronary syndrome are at high risk for recurrent ischemic cardiovascular events. We sought to determine whether alirocumab, a human monoclonal antibody to proprotein convertase subtilisin–kexin type 9 (PCSK9), would improve cardiovascular outcomes after an acute coronary syndrome in patients receiving high-intensity statin therapy.

METHODS

We conducted a multicenter, randomized, double-blind, placebo-controlled trial involving 18,924 patients who had an acute coronary syndrome 1 to 12 months earlier, had a low-density lipoprotein (LDL) cholesterol level of at least 70 mg per deciliter (1.8 mmol per liter), a non–high-density lipoprotein cholesterol level of at least 100 mg per deciliter (2.6 mmol per liter), or an apolipoprotein B level of at least 80 mg per deciliter, and were receiving statin therapy at a high-intensity dose or at the maximum tolerated dose. Patients were randomly assigned to receive alirocumab subcutaneously at a dose of 75 mg (9462 patients) or matching placebo (9462 patients) every 2 weeks. The dose of alirocumab was adjusted under blinded conditions to target an LDL cholesterol level of 25 to 50 mg per deciliter (0.6 to 1.3 mmol per liter). The primary end point was a composite of death from coronary heart disease, nonfatal myocardial infarction, fatal or nonfatal ischemic stroke, or unstable angina requiring hospitalization.

RESULTS

The median duration of follow-up was 2.8 years. A composite primary end-point event occurred in 903 patients (9.5%) in the alirocumab group and in 1052 patients (11.1%) in the placebo group (hazard ratio, 0.85; 95% confidence interval [CI], 0.78 to 0.93; P<0.001). A total of 334 patients (3.5%) in the alirocumab group and 392 patients (4.1%) in the placebo group died (hazard ratio, 0.85; 95% CI, 0.73 to 0.98). The absolute benefit of alirocumab with respect to the composite primary end point was greater among patients who had a baseline LDL cholesterol level of 100 mg or more per deciliter than among patients who had a lower baseline level. The incidence of adverse events was similar in the two groups, with the exception of local injection-site reactions (3.8% in the alirocumab group vs. 2.1% in the placebo group).

CONCLUSIONS

Among patients who had a previous acute coronary syndrome and who were receiving high-intensity statin therapy, the risk of recurrent ischemic cardiovascular events was lower among those who received alirocumab than among those who received placebo. (Funded by Sanofi and Regeneron Pharmaceuticals; ODYSSEY OUTCOMES ClinicalTrials.gov number, NCT01663402.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Schwartz at the Division of Cardiology, University of Colorado School of Medicine, Box B130, Aurora, CO 80045, or at gregory.schwartz@ucdenver.edu.

*A complete list of the ODYSSEY OUTCOMES committee members, investigators, and contributors and their institutional affiliations is provided in the Supplementary Appendix, available with the full text of this article at NEJM.org.

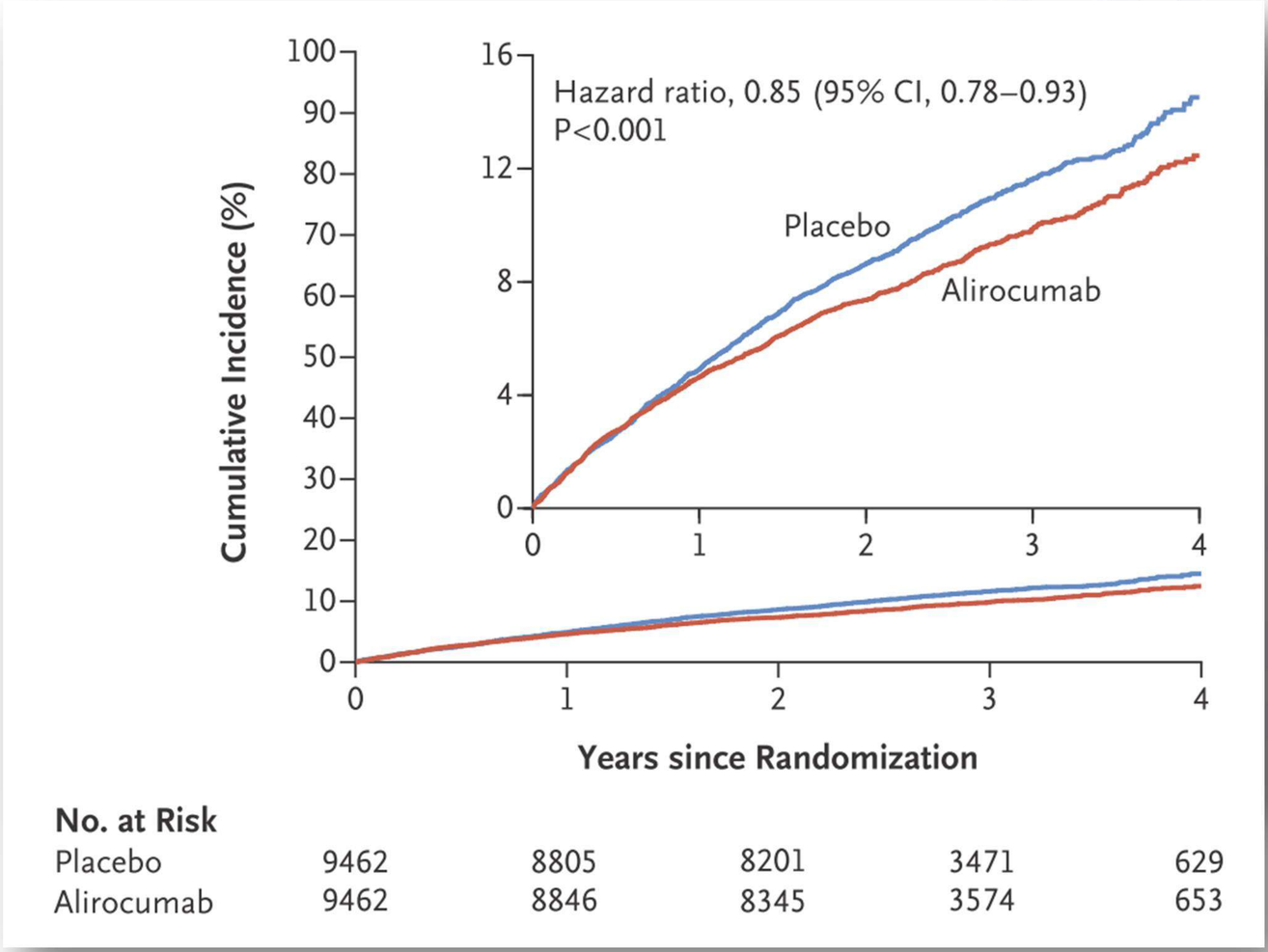
Drs. Schwartz and Steg contributed equally to this article.

This article was published on November 7, 2018, and updated on February 15, 2019, at NEJM.org.

N Engl J Med 2018;379:2097-107.
DOI: 10.1056/NEJMoa1801174
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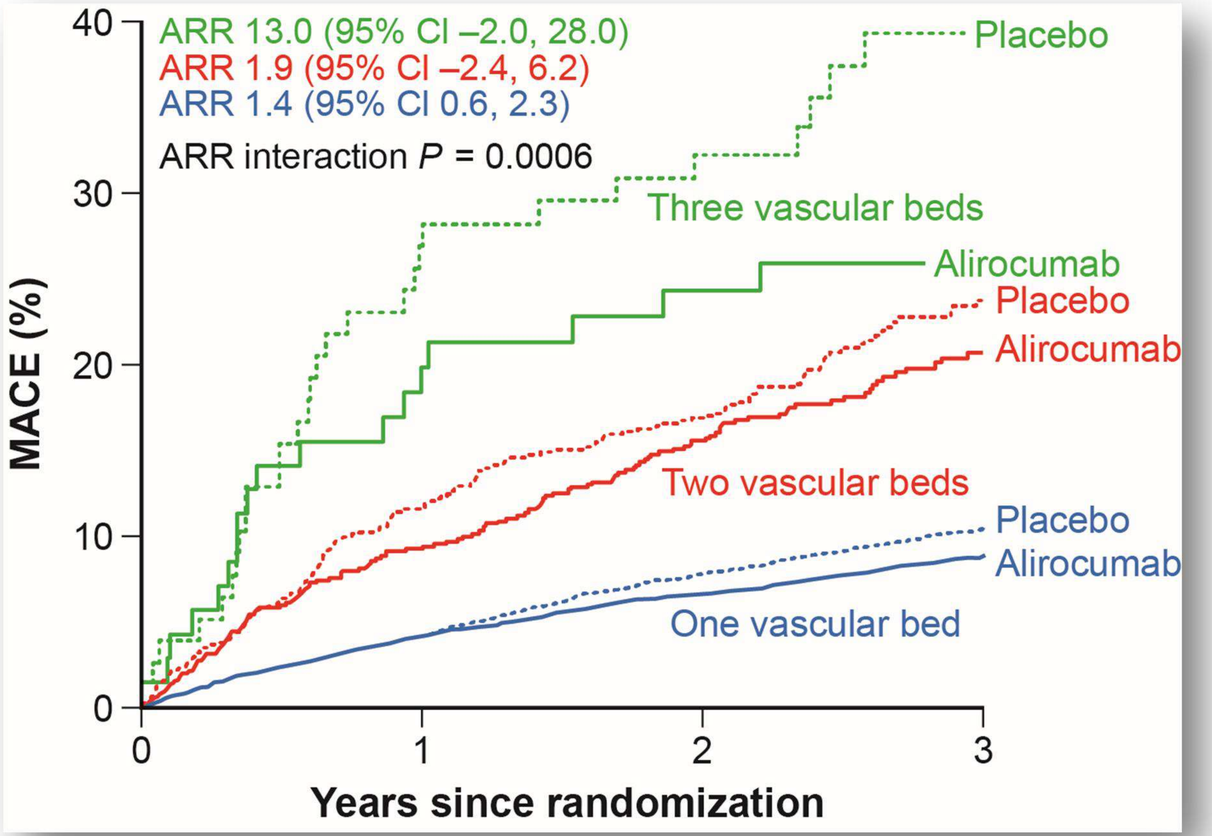
Primary end point: composite of death from coronary heart disease, nonfatal myocardial infarction, fatal or non-fatal ischemic stroke, or unstable angina requiring hospitalization



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Schwartz GG et al. N Engl J Med 2018;379:2097-2107.

Polyvascular disease is associated with high risks of MACE and death. The large absolute reduction of these risks with alirocumab represents a potential benefit for these patients



3 Vascular Beds : ARR 13.0

2 Vascular Beds : ARR 1.9

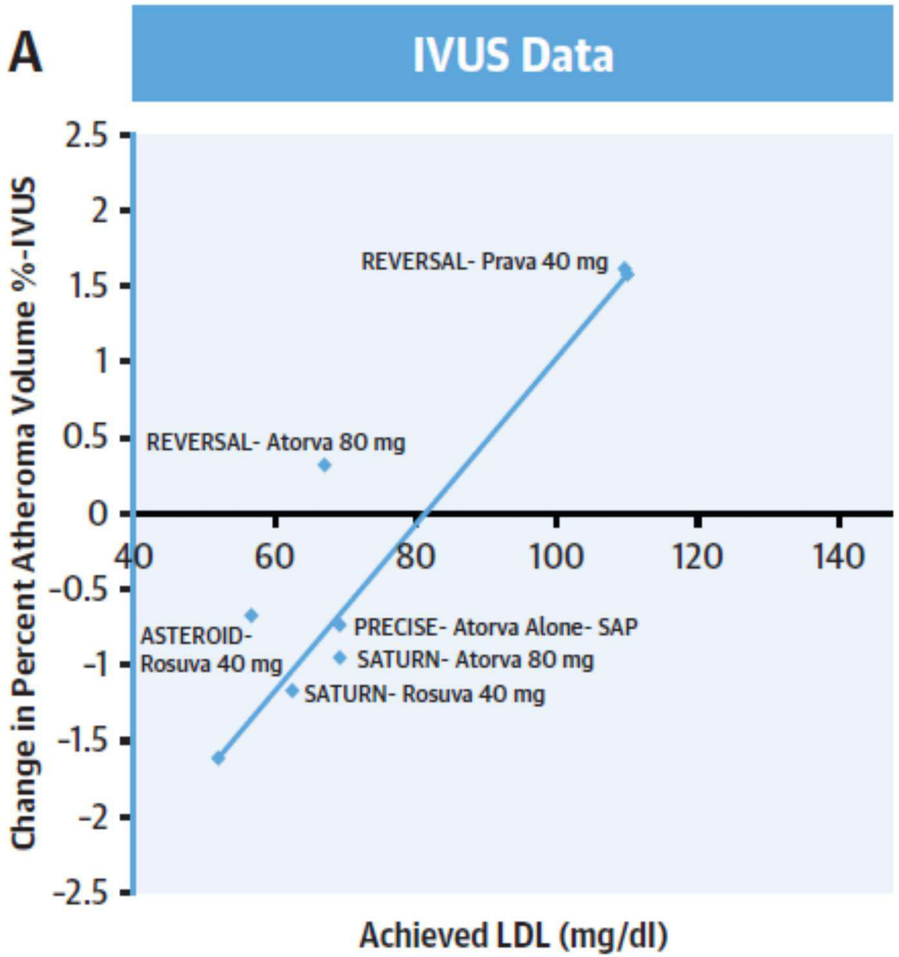
1 Vascular Bed: ARR 1.4

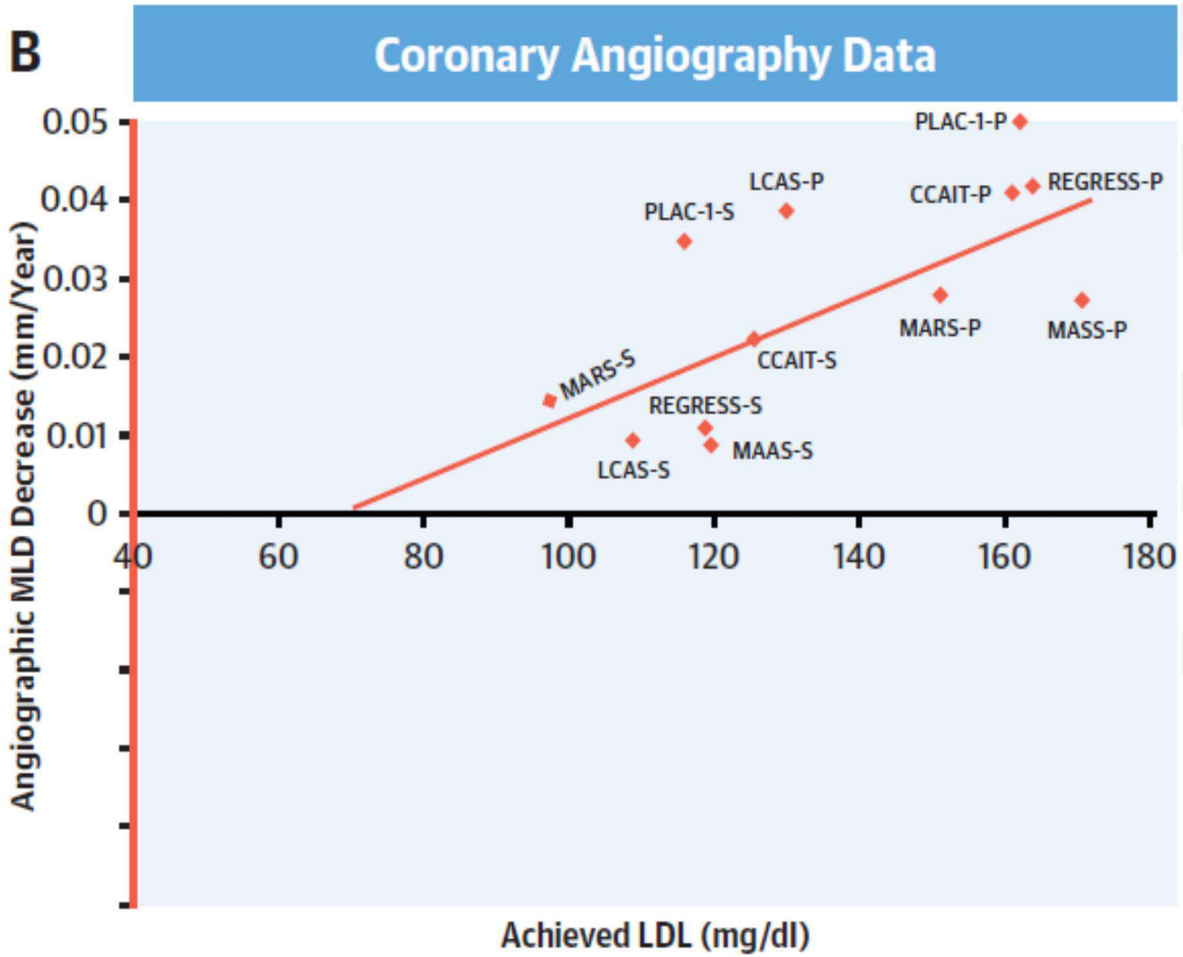
Jukema JW, *et al. J Am Coll Cardiol*. 2019;74(9):1167–76.

Most coronary events occur as a result of plaque rupture.

Plaque progression is a modifiable phase

Atherosclerotic ***plaque progression*** or regression is directly related to ***LDL-C levels***



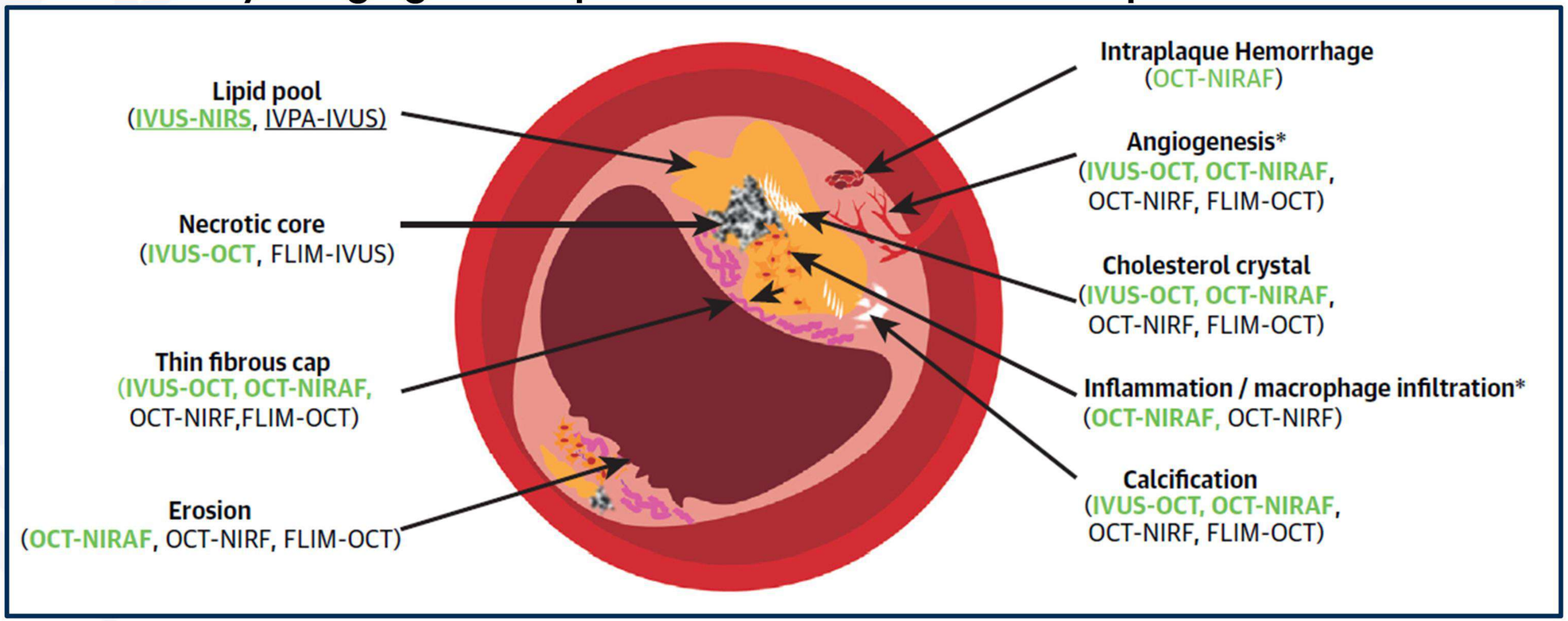


Proprietary Information – Do not photograph or otherwise copy or distribute

J Am Coll Cardiol 2019;74:1608–17

The future is now: identifying vulnerable plaque to predict CV events

Multimodality Imaging Techniques to Detect Vulnerable Plaque Characteristics



Schematic showing a coronary artery plaque and different features associated with increased risk of plaque rupture and atherothrombotic complications. According to Prati et al., including what had been published until December 2020, the types of multimodality imaging technology best suited to detect each high-risk feature are presented in parentheses. Techniques labeled in green have been successfully used in humans. Techniques labeled with underlines can get clear images in vivo without the need for blood clearance. *The ability of clinically available OCT to detect angiogenesis and macrophage infiltration is limited, due to its shallow penetration depth and resolution.

Li J et all. JACC Cardiovasc Imaging. 2022 Jan;15(1):145-159

ORIGINAL RESEARCH

Effect of Evolocumab on Coronary Plaque Phenotype and Burden in Statin-Treated Patients Following Myocardial Infarction

HUYGENS Study

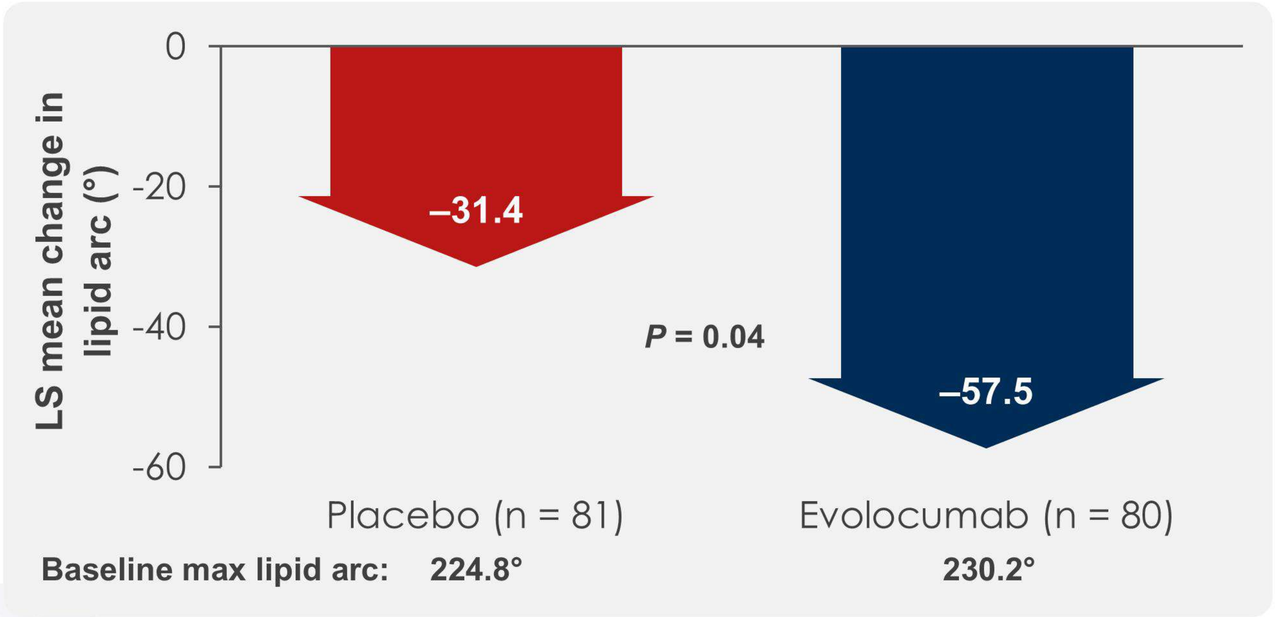
- NSTEMI Patients were treated with or placebo for 52 weeks.
- Serial OCT and IVUS within a matched arterial segment of a nonculprit vessel.
- Primary analysis: change in the minimum fibrous cap thickness

and maximum lipid arc throughout the imaged arterial segment.

Nicholls SJ, et al. JACC: CARDIOVASCULAR IMAGING, Volume 15, Issue 7, July 2022, Pages 1308-1321

Evolocumab improved Features of Plaque Stability Compared With Placebo after an ACS

HUYGENS Secondary Endpoint: Maximum Lipid Arc[1]



Adapted from Nicholls

Lipid Arc Reduction in a patient treated with Evolocumab

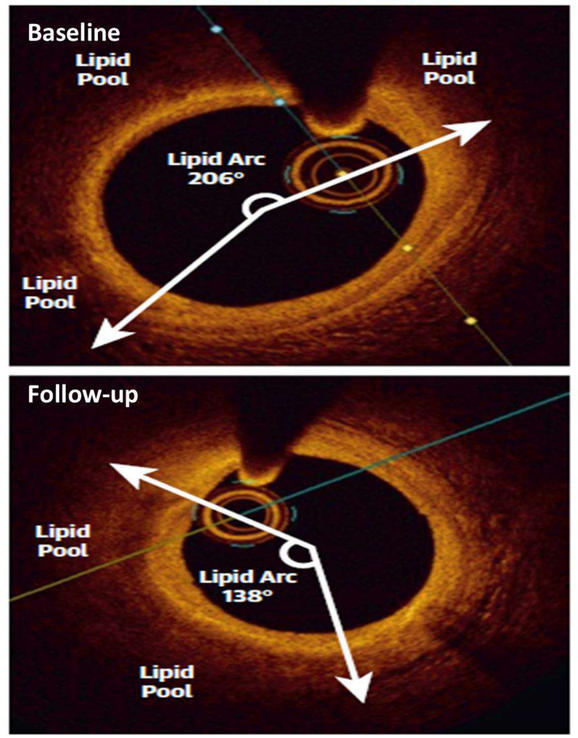


Image courtesy of Nicholls SJ, et al. JACC 2022

Addition of evolocumab to intensive statin therapy greatly reduced maximum lipid arc compared with maximally tolerated statin therapy alone.

LS, least squares.

1. Nicholls SJ, et al. JACC: CARDIOVASCULAR IMAGING, Volume 15, Issue 7, July 2022, Pages 1308-1321

Patients with AMI (N-STEMI/STEMI) undergoing coronary angiography & successful PCI of the infarct vessel & 2 non-infarct related arteries with non-obstructive lesions

Alirocumab PACMANAMI



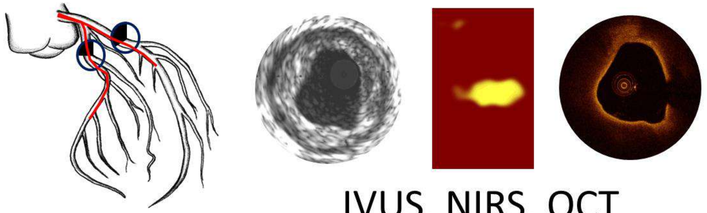
POC

No statin, LDL >125 mg/dL (>3.2 mmol/L)

On Statin, LDL >70 mg/dL (>1.8 mmol/L)

Enrollment of 300 Patients

Baseline



IVUS, NIRS, OCT

Baseline blood sampling

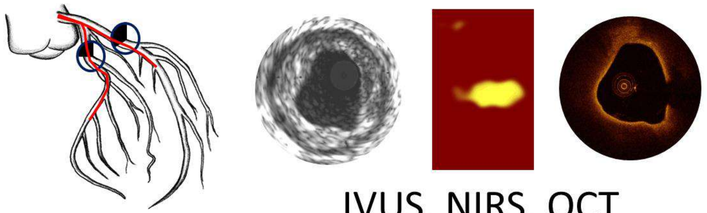
Alirocumab s.c. 150 mg / 2 weeks + Rosuvastatin 20 mg

R 1:1

Placebo s.c. / 2 weeks + Rosuvastatin 20 mg

Initiated <24 hrs after PCI

52 weeks



IVUS, NIRS, OCT

Blood sampling 4 weeks
3 visits, 4 phone calls
Blood sampling 52 weeks

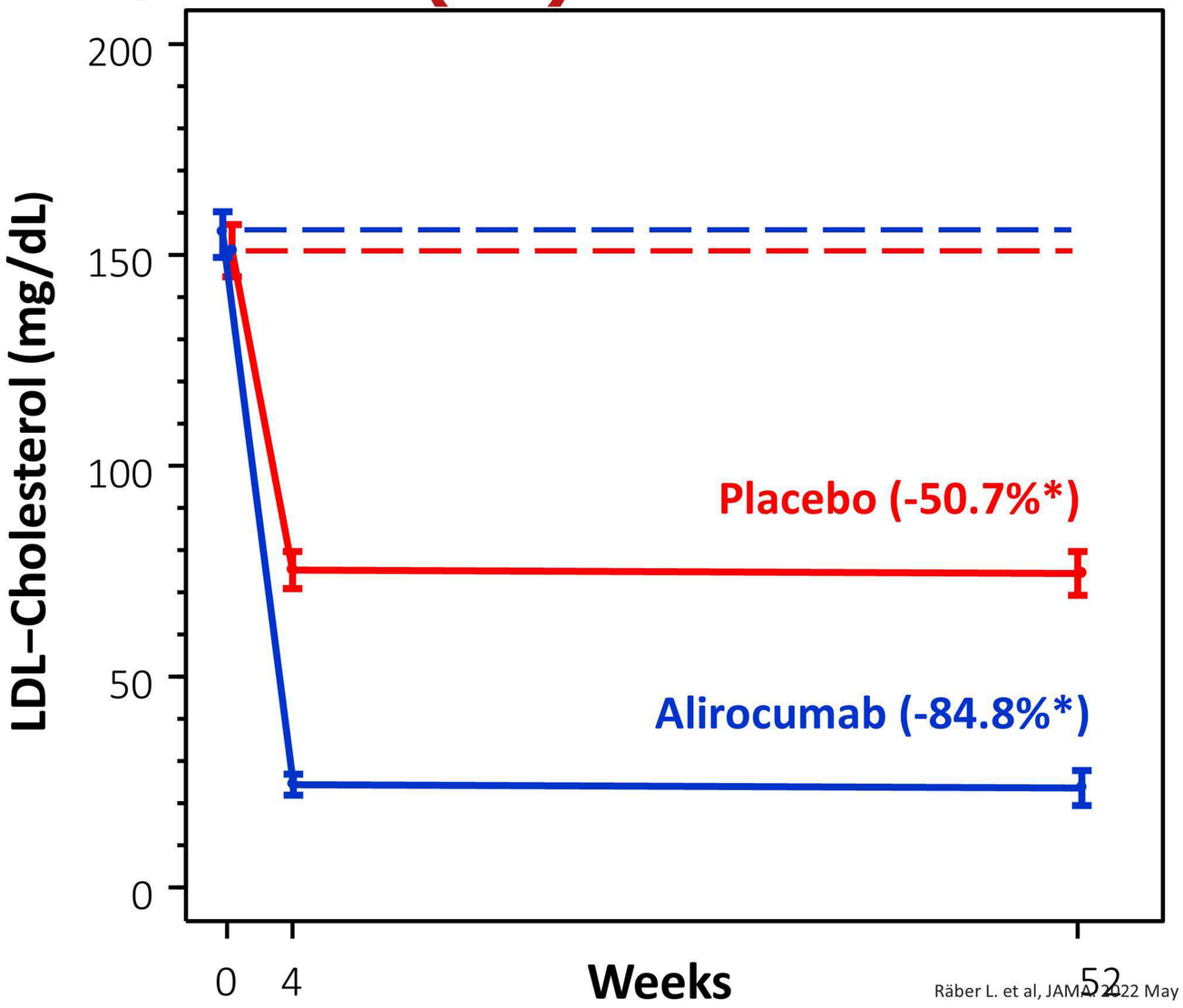
UTIC CLUB | ANMCO CRITICAL CARE COMMUNITY

Am Heart J 2021;238:33-44

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

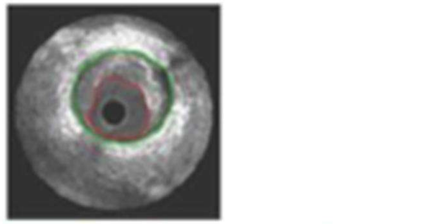
23.6 (24) mg/dL
0.6 (0.6) mmol/L

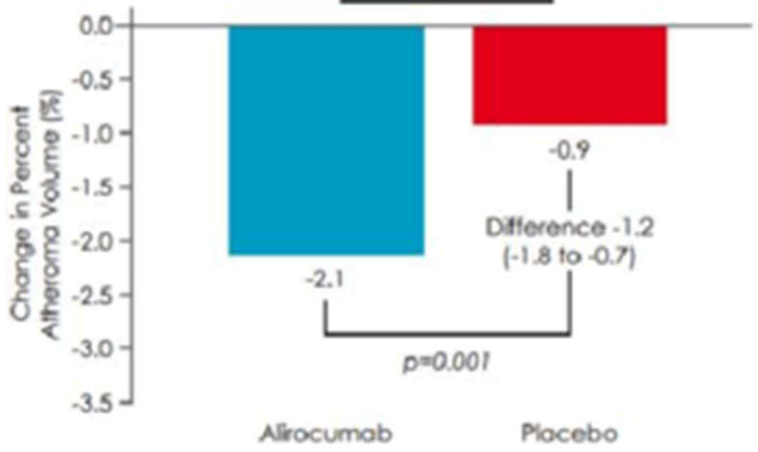
* Week 52 vs. Baseline

Räber L. et al, JAMA. 2022 May 10;327(18):1771-1781. doi: 10.1001/jama.2022.5218.

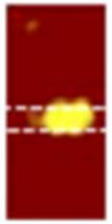
Alirocumab **reduces plaque burden** in **non-culprit** plaques

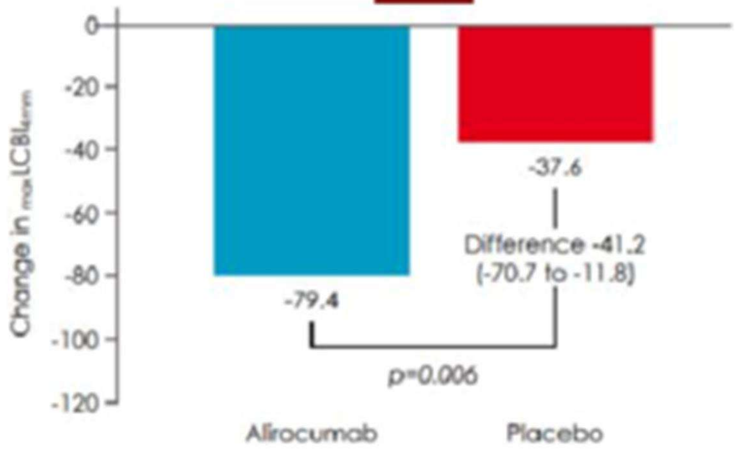
Primary EP:
Change in Percent Atheroma Volume (IVUS)



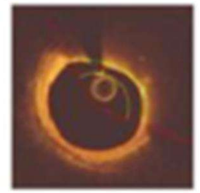


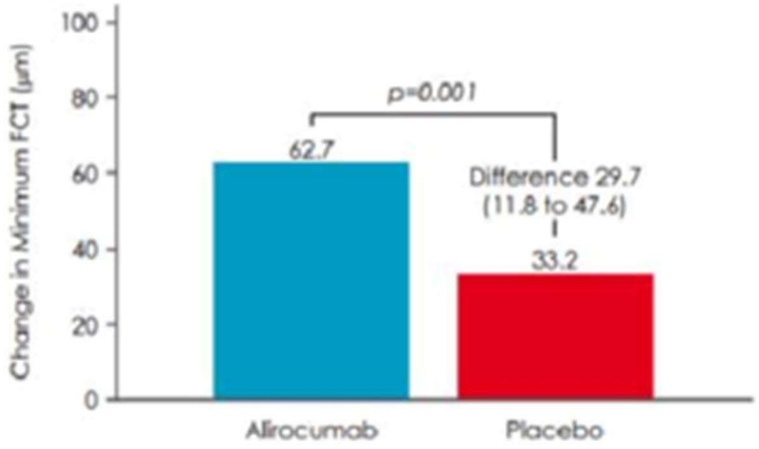
Powered Secondary EP:
Change in maxLCBI$_{4mm}$ (NIRS)





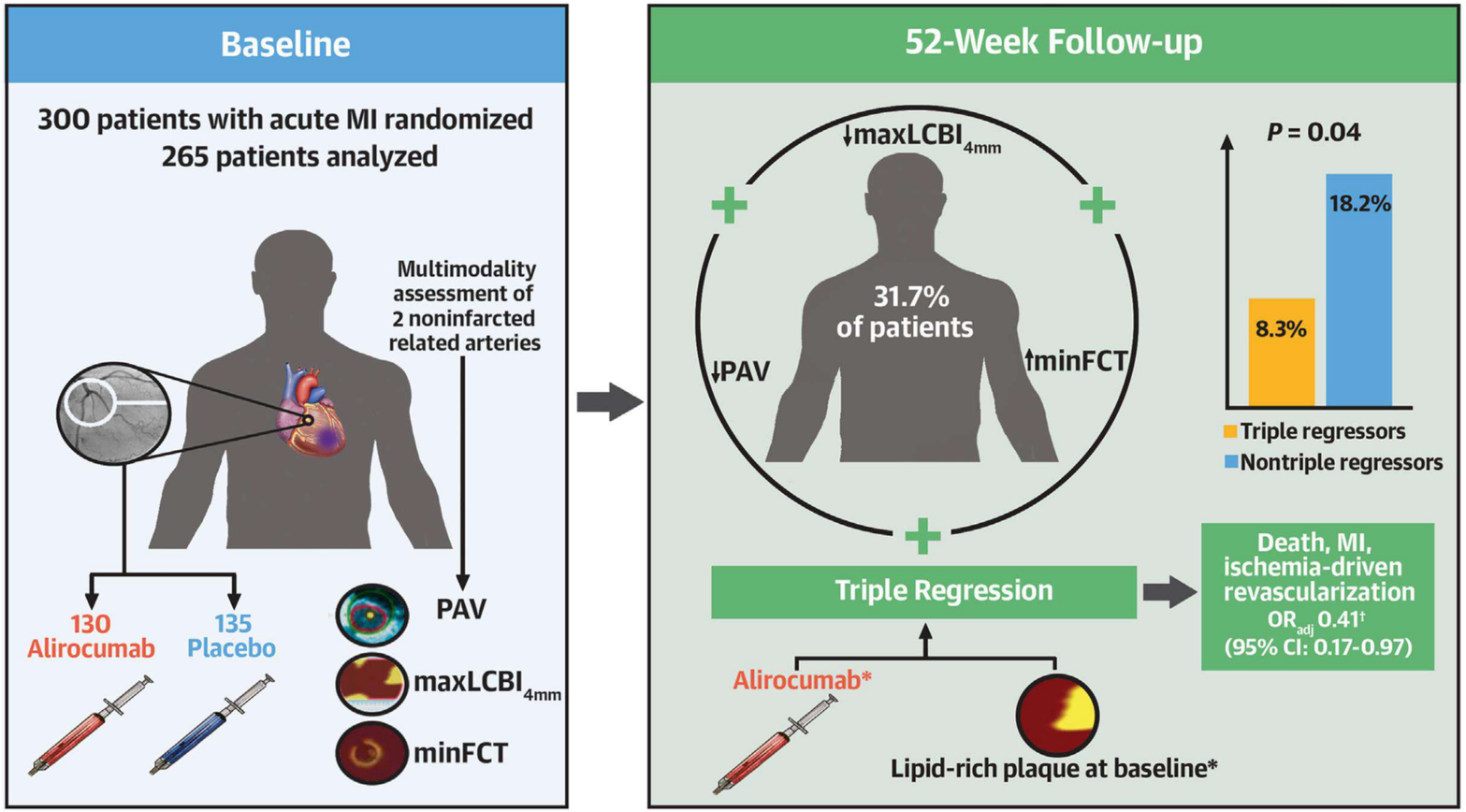
Powered Secondary EP:
Change in Minimum FCT (OCT)





Räber L. et al, JAMA. 2022 May 10;327(18):1771-1781. doi: 10.1001/jama.2022.5218.

PACMAN-AMI: The triple regression was associated with a reduced risk of cardiovascular events.

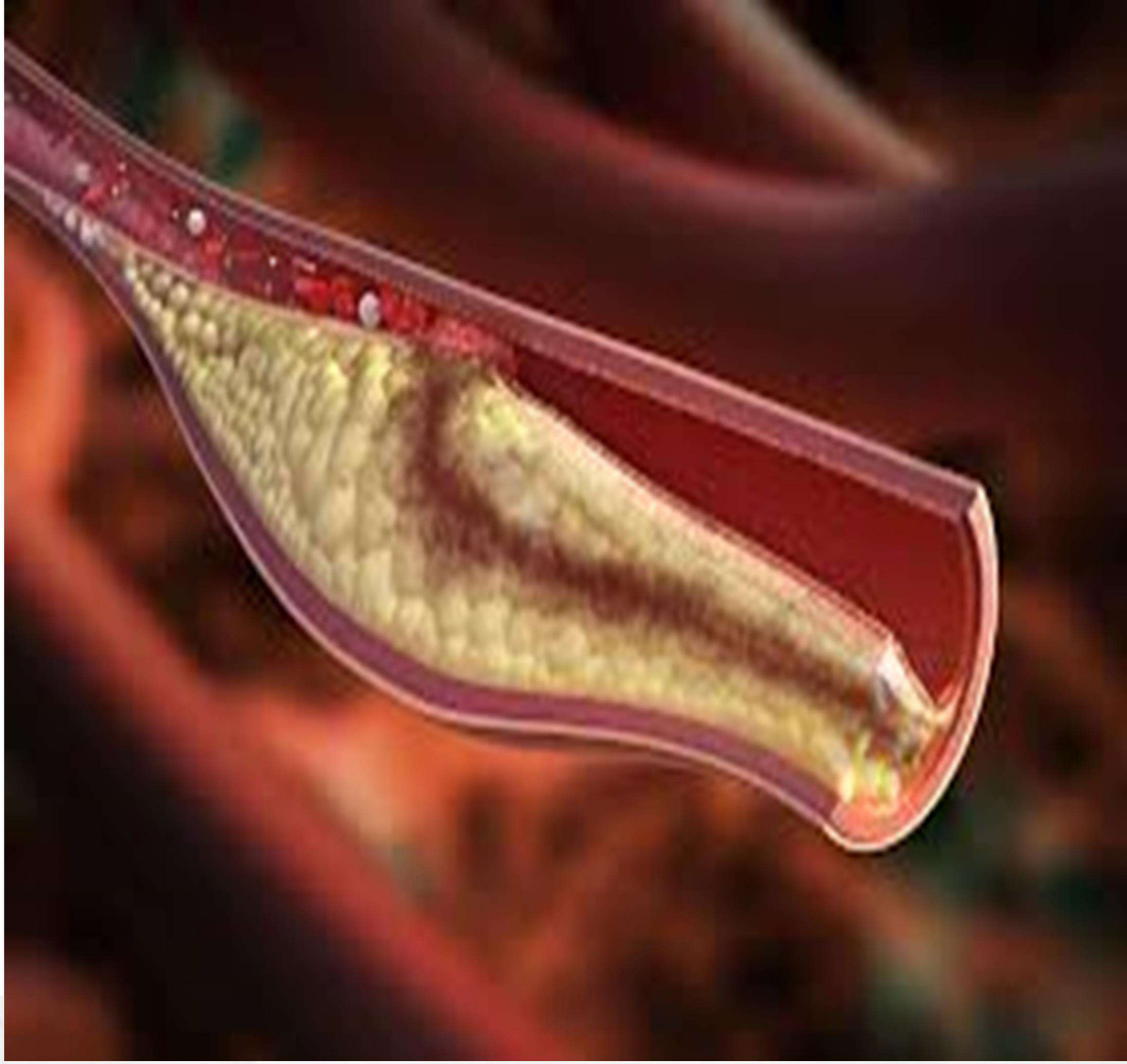


31.7%

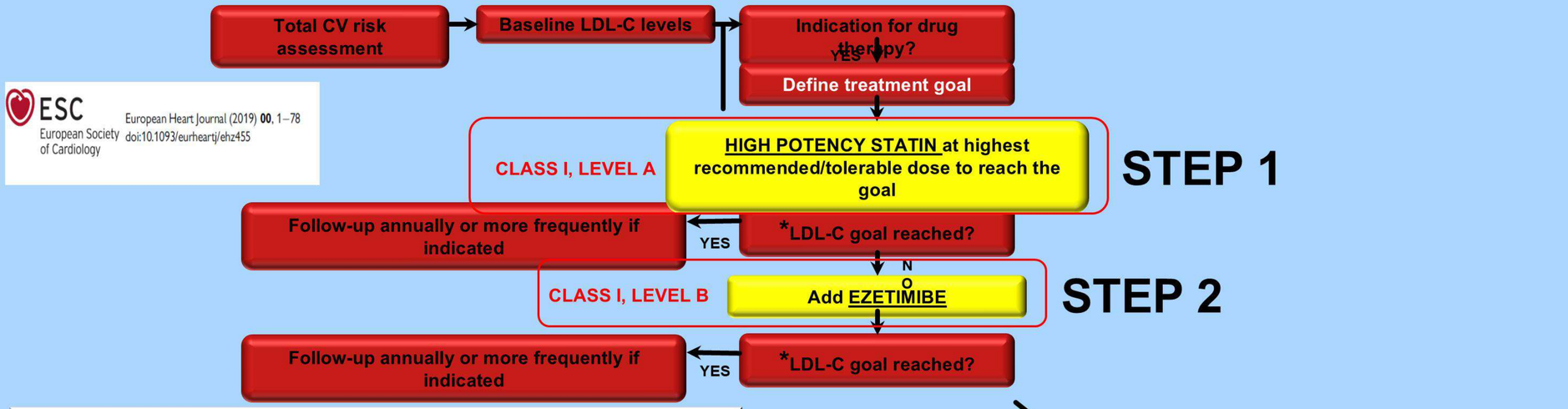
The composite endpoint of death, myocardial infarction, and revascularization occurred less frequently in patients with triple regression compared to those without it (8,3% vs. 18,2%, p=0,04).

- Biccirè FG, et al. J Am Coll Cardiol. 2023;82(18):1737–1747.

La Terapia ipocolestrolemizzante : quando le linee guida sono pigre ad aggiornarsi



2019 ESC/EAS Guidelines: Treatment algorithm for pharmacological ldl-c lowering



ESC European Society of Cardiology

European Heart Journal (2019) **00**, 1–78
doi:10.1093/eurheartj/ehz455

/kexin type 9.

Stepwise Treatment Approach:

Titration LDL-C lowering treatment!

4-6 Months to complete!

Multiple visits!

The STEPWISE STRATEGY does not work in EUROPE

No LLT optimization during FU

A cross-sectional ESC-EORP survey (EUROASPIRE V) at 131 centers in 81 regions in 27 countries including patients with coronary artery events or interventions

***Low rate of patients at (2016) target* (<70 mg/dL): 32% men, 23% women**

Change in the LDL-C-lowering therapies from discharge to interview.

Prescribed at hospital discharge	Used at the time of interview	% (n)
No LLT	No LLT	5.0 (374/7528)
Low/Moderate intensity LLT	Low/Moderate intensity LLT	20.2 (1521/7528)
High intensity LLT	High intensity LLT	42.3 (3181/7528)
High intensity LLT	Low/Moderate intensity LLT	10.0 (755/7528)
High intensity LLT	No LLT	6.2 (463/7528)
Low/moderate intensity LLT	No LLT	4.6 (350/7528)
No LLT	Low/moderate intensity LLT	3.9 (297/7528)
No LLT	High intensity LLT	3.2 (241/7528)
Low/moderate intensity LLT	High intensity LLT	4.6 (346/7528)

At first prescription (discharge): 58,5*% are treated with ***high intensity statins.

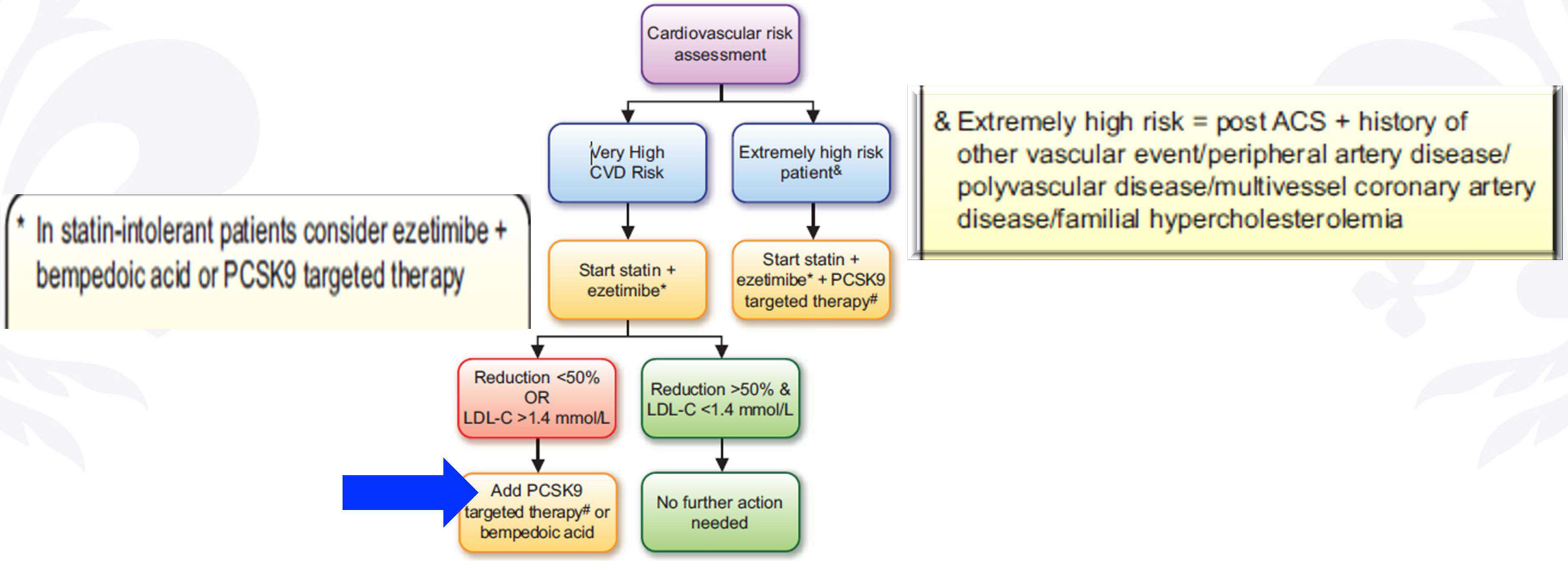
- During FU, there is a **decrease** to low/moderate intensity (or no LLT) **in 20,8%**
- During FU: there is an **increase in LLT** in **11.7%** during FU

=> Instead of an increase, there is mostly a decrease in LLT intensity during FU

ESC European Society of Cardiology
European Heart Journal (2021) 00, 1–4
doi:10.1093/eurheartj/ehab718

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

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]

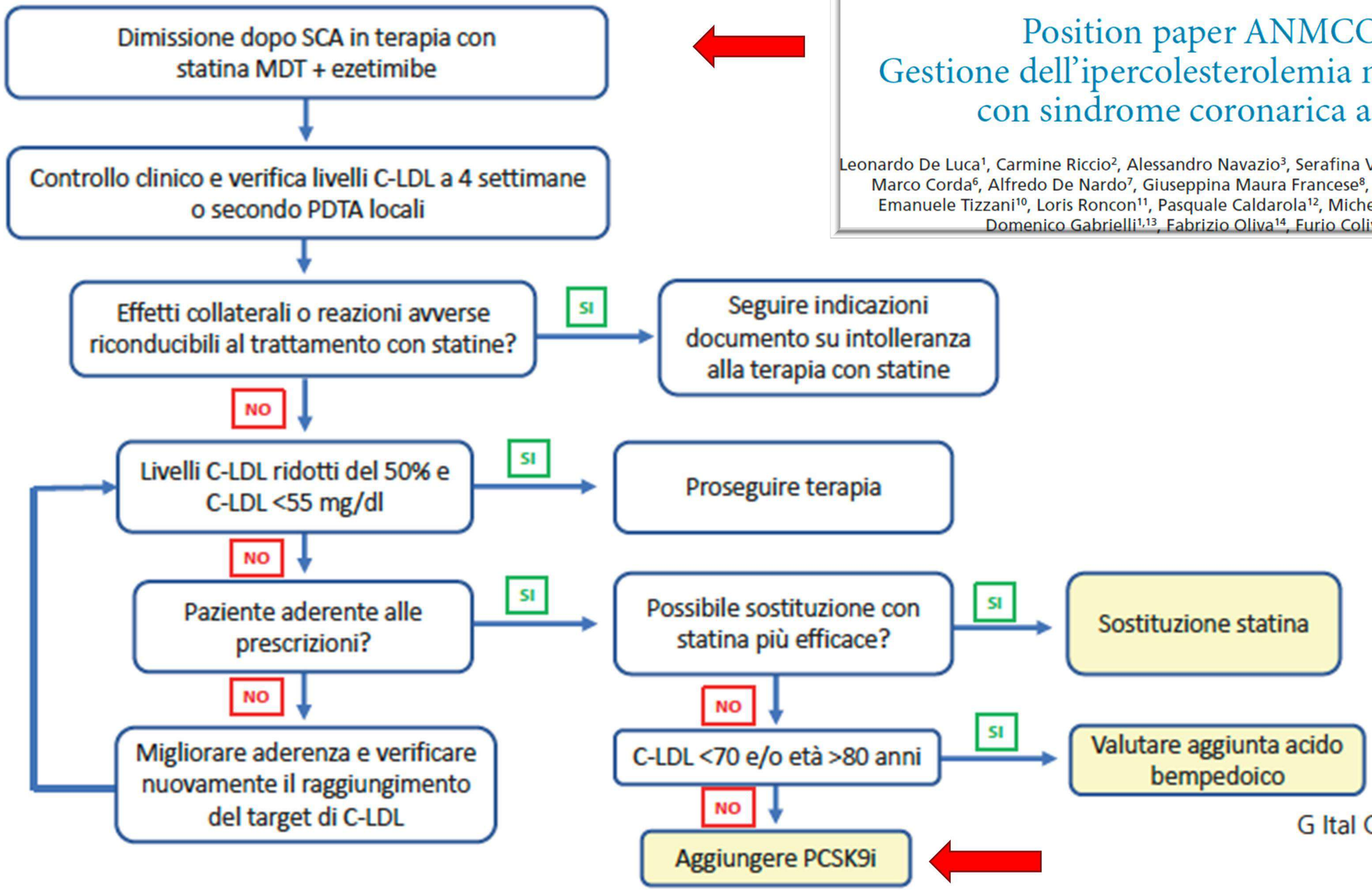


*Corresponding author. Tel: +44 20 7594 0716, Email: kray@imperial.ac.uk
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POSITION PAPER

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]



G Ital Cardiol 2023;24

2025 Focused Update of the 2019 ESC/EAS Guidelines for the management of dyslipidaemias

ESC European Society of Cardiology

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New Recommendations (3)

Recommendations	Class	Level
Recommendations for pharmacological low-density lipoprotein cholesterol lowering		
Non-statin therapies with proven cardiovascular benefit, taken alone or in combination, are recommended for **patients who are unable to take statin therapy** to lower LDL-C levels and reduce the risk of CV events. The choice should be based on the magnitude of additional LDL-C lowering needed.	I	A
Bempedoic acid is recommended in patients who are unable to take statin therapy to achieve the LDL-C goal.	I	B
The addoctin of bempedoic acid to the maximally tolerated dose of statin with or without ezetimibe should be considered in patients at high or very high risk in order to achieve the LDL-C goal.	IIa	C
Evinacumab should be considered in patients with homozygous familial hypercholesterolaemia aged 5 years or older who are not at LDL-C goal despite receiving maximum doses of lipid-lowering therapy to lower LDL-C levels.	IIa	B

LDL-C, low-density lipoprotein cholesterol; **CV**, Cardiovascular

2025 Focused Update of the 2019 ESC/EAS Guidelines for the management of dyslipidaemias (European Heart Journal; doi: 10.1093/eurheartj/ehaf190)

Reactive medical use only

New Recommendations (4)

Recommendations	Class	Level
Recommendations for lipid-lowering therapy in patients with acute coronary syndromes		
Intensification of lipid-lowering therapy during the index ACS hospitalization is recommended for patients who were on any lipid-lowering therapy before admission in order to further lower LDL-C levels.	I	C
Initiating combination therapy with **high-intensity statin plus ezetimibe** during index hospitalization for ACS should be considered in patients who were treatment-naïve and are not expected to achieve the LDL-C goal with statin therapy alone.	IIa	B

Therefore, and in line with the current 2023 ESC Guidelines ,for the management of patients with ACS this Task Force proposes a strategy of early, intensive LDL-C lowering to be considered in all patients with ACS, with immediate initiation of statin therapy and combination treatment with one or more classes of non-statin therapy with proven CV benefit as needed, depending on each patient's lipid-lowering therapy prior to the ACS event. The choice of drug for combination therapy should be based on the magnitude of additional LDL-C lowering required.

LDL-C, low-density lipoprotein cholesterol; **ACS**, Acute Cardiovascular Syndrome
ESC, European Society of Cardiology; **CV**, Cardiovascular

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Reactive medical use only

2025 Focused Update of the 2019 ESC/EAS Guidelines for the management of dyslipidaemias (European Heart Journal; doi: 10.1093/eurheartj/ehaf190)

2019 ESC/EAS Guidelines: Treatment algorithm for pharmacological ldl-c lowering

NON INDICAZIONI PRECISE CHE TENGANO CONTO DEL :

1. **RISCHIO DEL PAZIENTE**
2. **TERAPIA PRECEDENTE**
3. **DISTANZA DAL TARGET**
4. **TEMPO NECESSARIO PER RAGGIUNGERE IL TARGET**

STEP 2

LDL-C goal reached?

- **L… …CA after 4-6 weeks**
- **C… …wise after 8(±4) weeks**

NO

ADD PCSK9 INHIBITOR

STEP 3

- **Secondary prevention (also FH) (very high-risk) (CLASS IA)**
- **Primary prevention: patients with FH and another major risk factor (very high-risk) (CLASS IC)**

CV = cardiovascular; FH = familial hypercholesterolaemia; LDL-C =l ow density lipoprotein-C; PCSK9 = proprotein convertase subtilisin/kexin type 9.
Adapted from: Mach F, et al. Eur Heart J 2019. doi:10.1093/eurheartj/ehz455. Epub ahead of print.

Proviamo a disegnare la road map del trattamento ipocolesterolemizzante dopo SCA



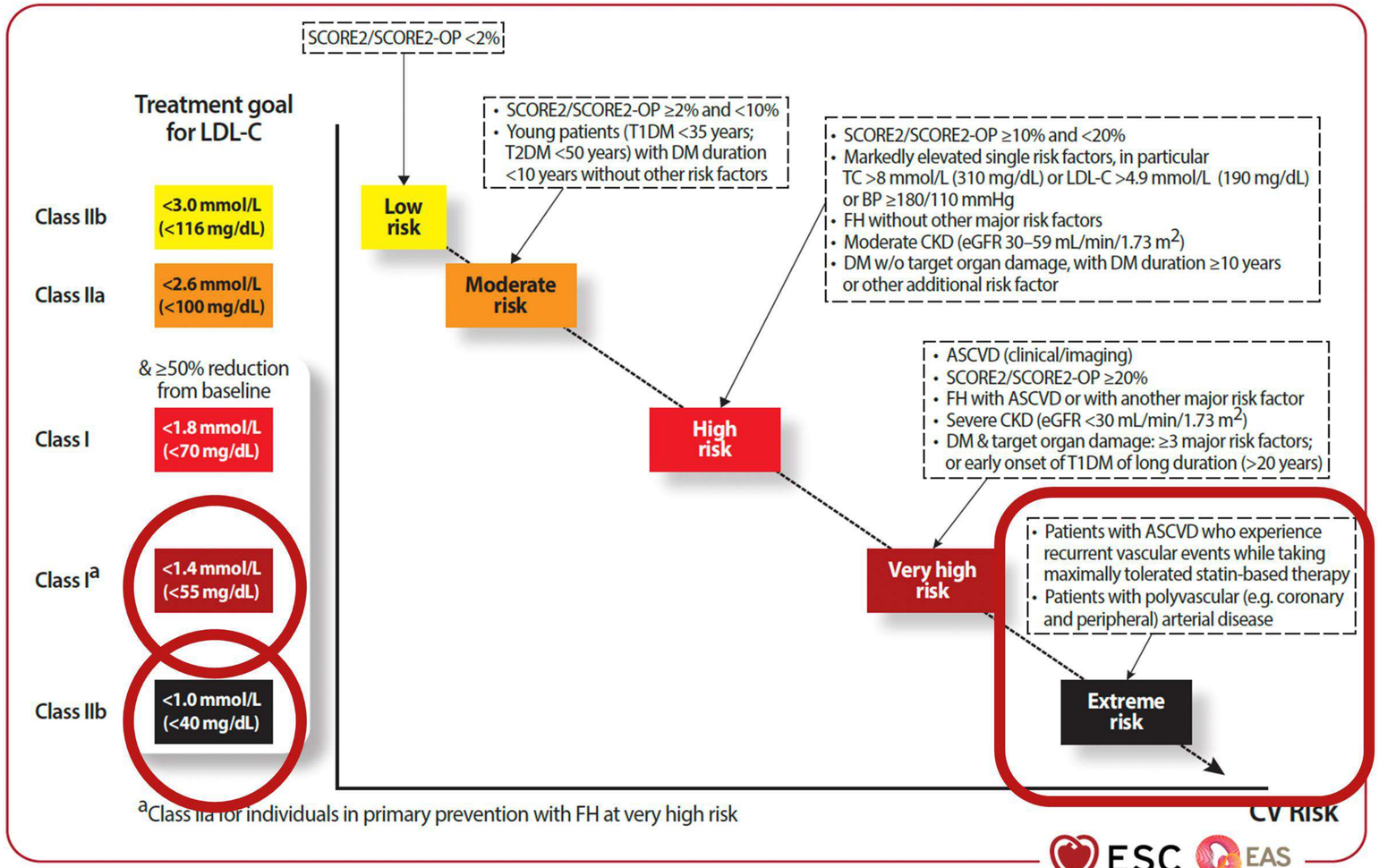
Il profilo di rischio

1°: il profilo di rischio del paziente

SAME LDL-C GOLAS AS THE 2019 ESC/EAS GUIDELINES

EXTREME RISK:

- Patients with ASCVD who experience **recurrent vascular events** while taking maximally tolerated statin-based therapy
- **Patients with polyvascular** (e.g. coronary and peripheral) arterial disease



Miteva K et al, J Cardiovasc Med, 2025

Proviamo a disegnare la road map del trattamento ipocolesterolemizzante dopo SCA



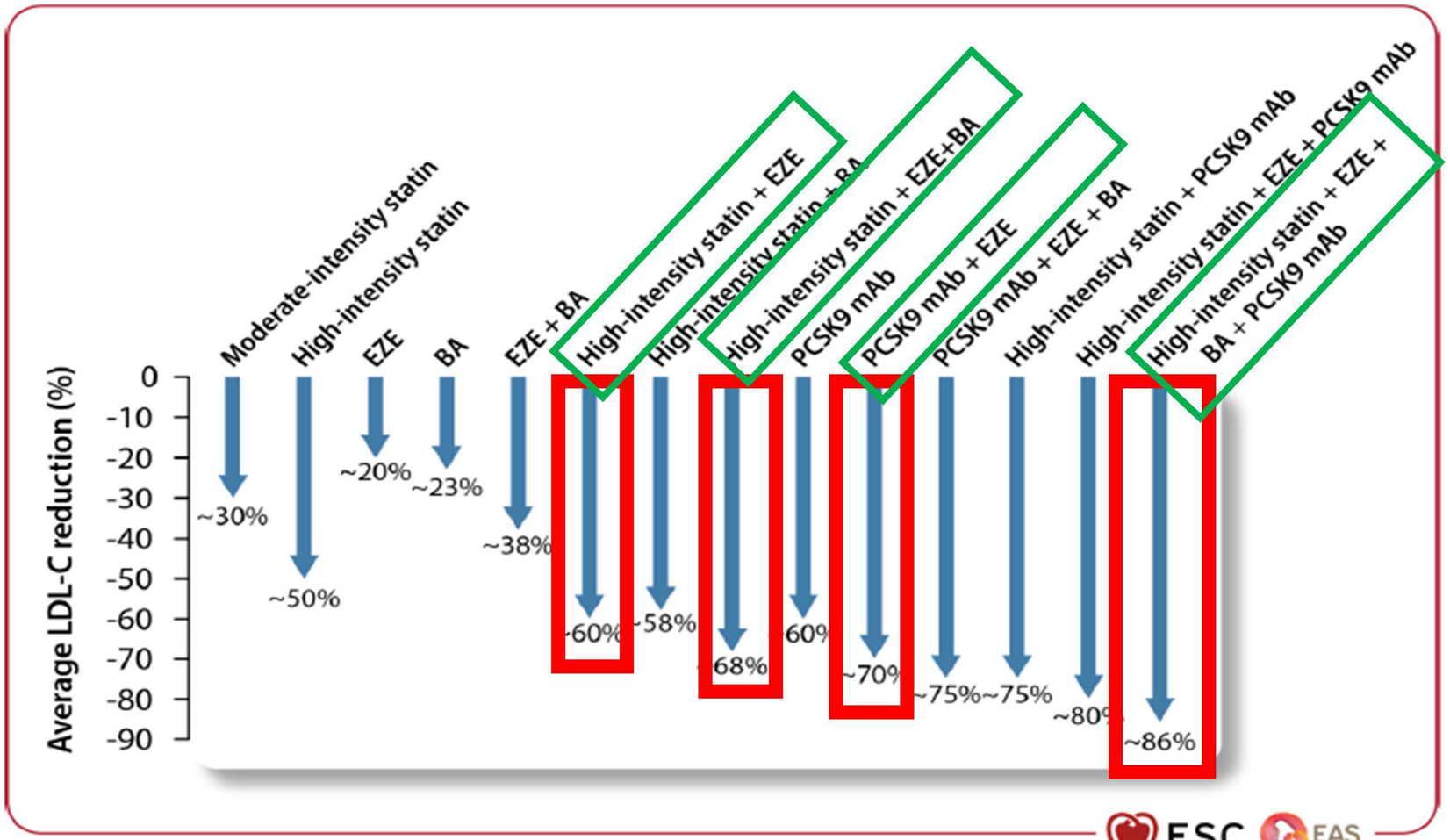
Il profilo di rischio

La distanza dal target

2°: in funzione della distanza dal target valutare i risultati attesi dai diversi trattamenti

Figure 2

Average reduction in low-density lipoprotein cholesterol levels with different pharmacological therapies with proven cardiovascular benefit.



2025 Focused Update of the 2019 ESC/EAS Guidelines for the management of dyslipidaemias (European Heart Journal; doi: 10.1093/eurheartj/ehaf190)

ESC European Society of Cardiology
European Heart Journal (2020) **41**, 3900–3909
doi:10.1093/eurheartj/ehaa034

CLINICAL RESEARCH
Dyslipidaemias

Application of the 2019 ESC/EAS dyslipidaemia guidelines to nationwide data of patients with a recent myocardial infarction: a simulation study

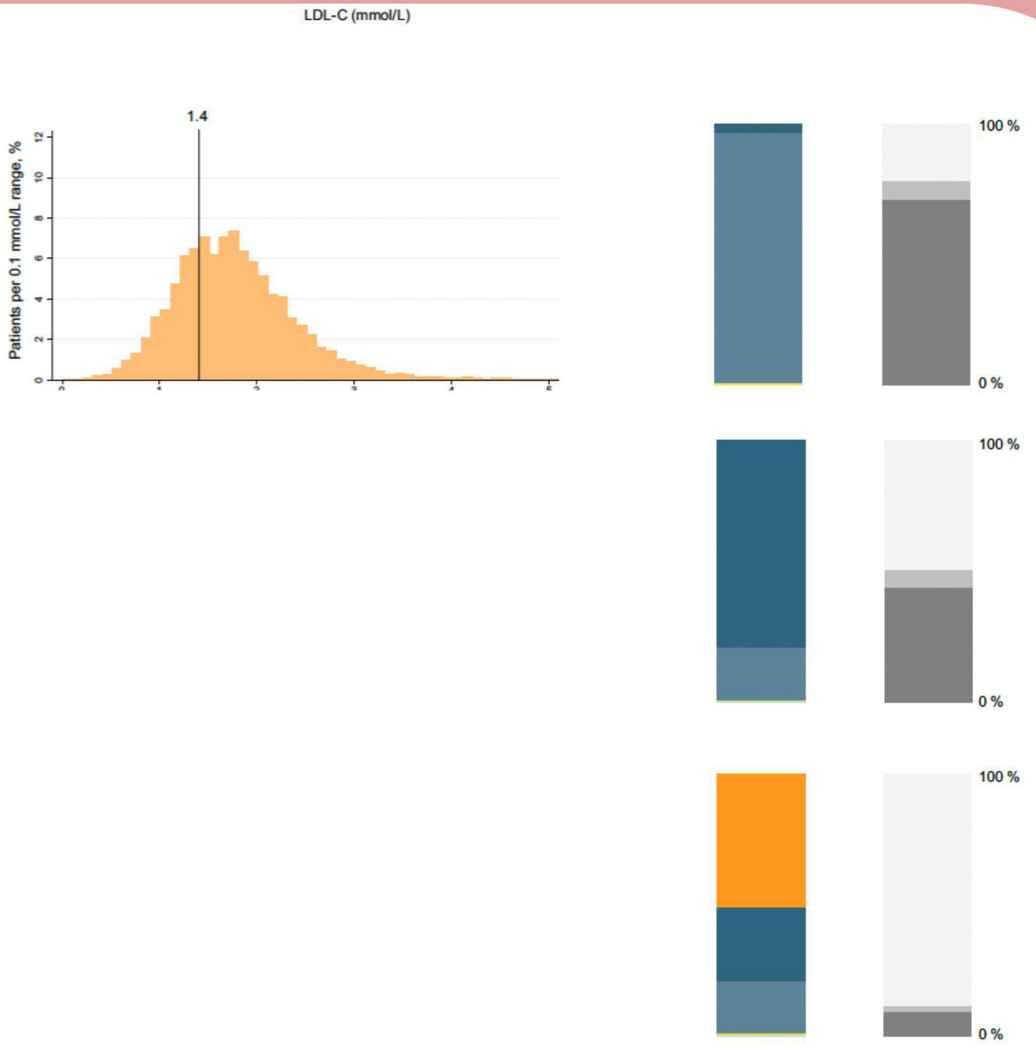
Ali Allahyari [1], Tomas Jernberg [1], Emil Hagström[2,3], Margrét Leosdottir [4,5], Pia Lundman [1], and Peter Ueda [6]*

[1]Department of Clinical Sciences, Danderyd Hospital, Karolinska Institutet, 18288 Stockholm, Sweden; [2]Department of Medical Sciences, Uppsala University, 75185 Uppsala, Sweden; [3]Uppsala Clinical Research Center, 75185 Uppsala, Sweden; [4]Department of Cardiology, Skane University Hospital, 20502 Malmo, Sweden; [5]Department of Clinical Sciences Malmo, Lund University, 20502 Malmo, Sweden; and [6]Clinical Epidemiology Division, Department of Medicine, Solna, Karolinska Institutet, 17176 Stockholm, Sweden

eived 30 September 2019; revised 28 November 2019; editorial decision 16 January 2020; accepted 24 January 2020; online publish-ahead-of-print 18 February 2020

Simulated

Add/uptitrate to high-intensity statin



Lipid-lowering therapy

- HIS + ezetimibe + PCSK9i
- LMIS + ezetimibe + PCSK9i
- ezetimibe + PCSK9i
- HIS + ezetimibe
- HIS only
- LMIS only
- LMIS + ezetimibe
- ezetimibe only
- No lipid-lowering therapy

LDL-C target attainment

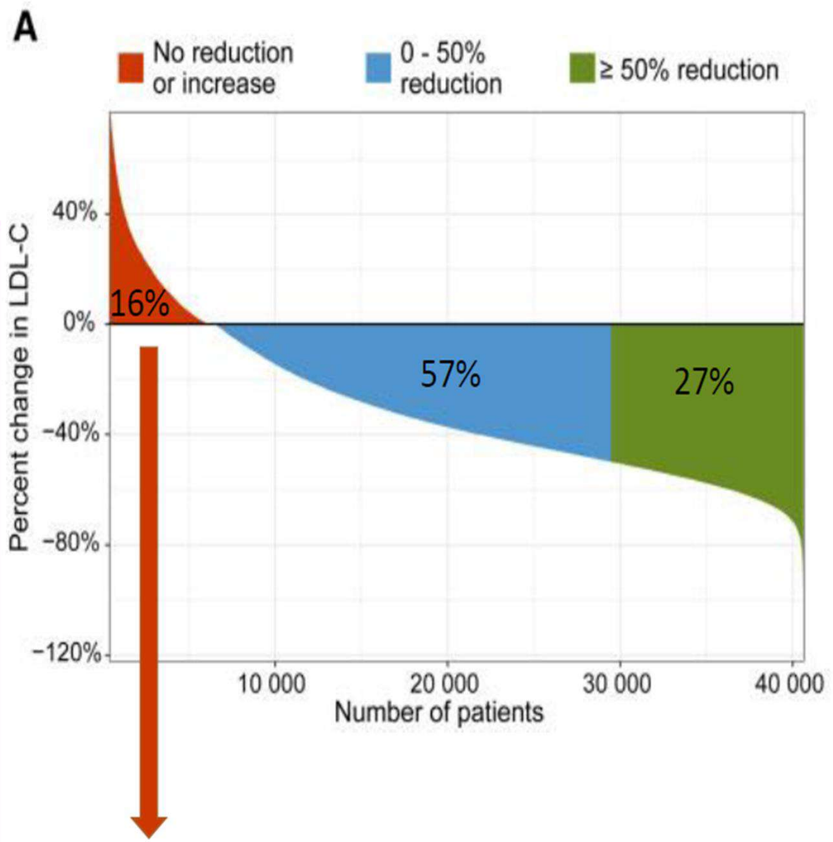
- LDL-C target attained
- LDL-C <1.4 mmol/L but <50% LDL-C reduction
- LDL-C ≥1.4 mmol/L

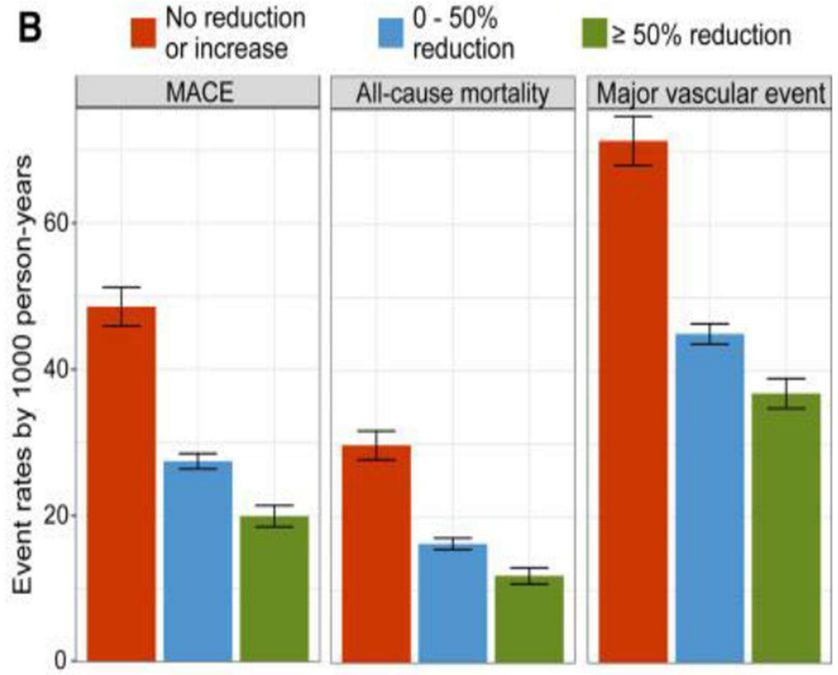
HIS: high-intensity statin
LMIS: low/moderate-intensity statin
PCSK9i: PCSK9 inhibitor

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]

- **40 607 pazienti dopo SCA, f.u.medio 3.78 anni**
- I pazienti con una **maggiore riduzione di C-LDL** già a 6-10 settimane presentavano un **più basso tasso di eventi CV**





at CR visit:
56% low/medium-intensity statin
33% high-intensity statin
10% No statin treatment

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

Proviamo a disegnare la road map del trattamento ipocolesterolemizzante dopo SCA

L'aderenza alla terapia

La distanza dal target

Il profilo di rischio



3°: valutare gli ostacoli all'aderenza

07:45 4G

vita.it

VITA ACCEDI

L'America mette sotto accusa 5 farmaci killer

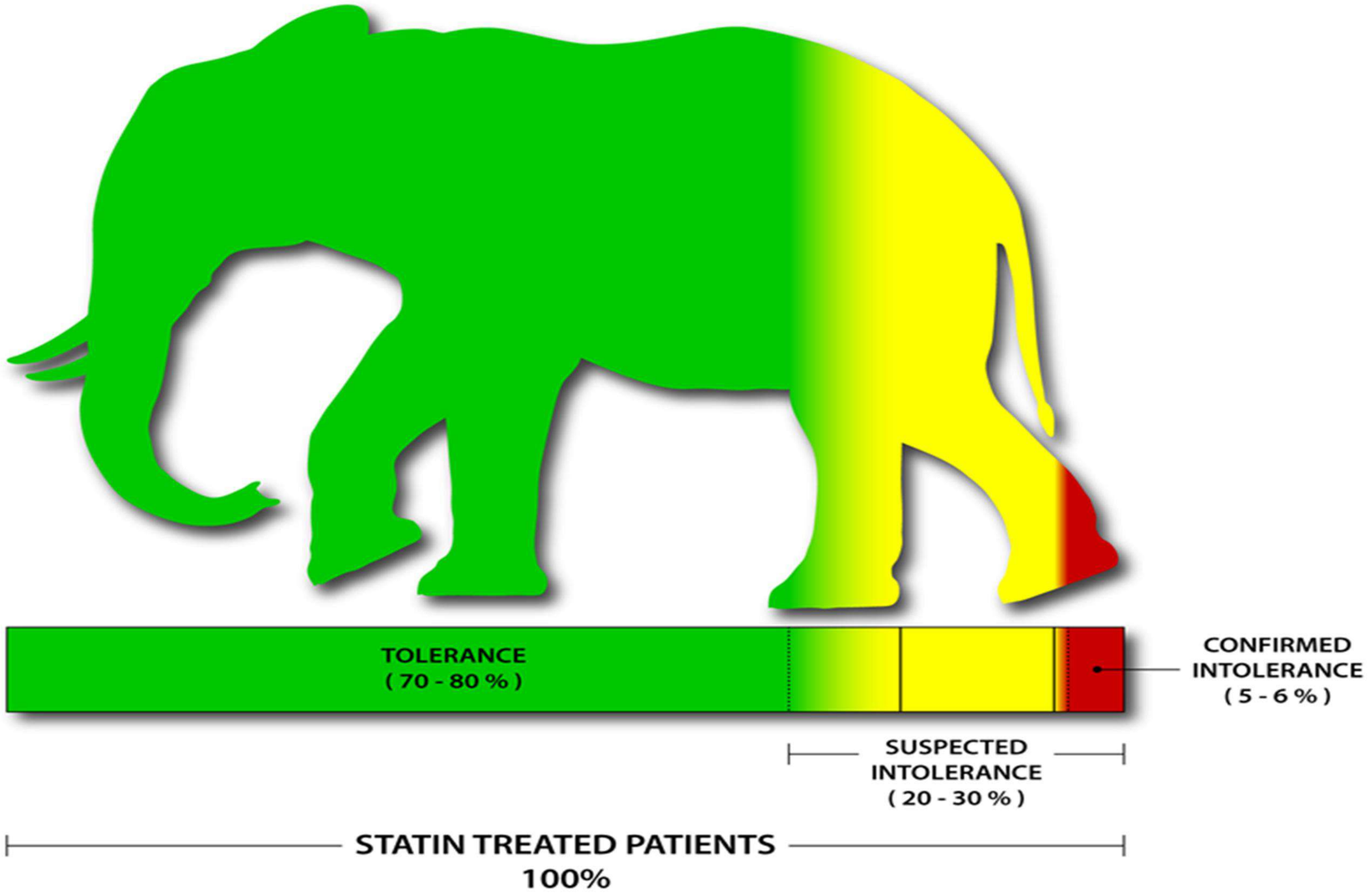
di Gabriella Meroni | 22 agosto 2001

Sono ancora le statine le sostanze ritenute più pericolose

Dagli Stati Uniti arriva un nuovo allarme sui farmaci anticolesterolo arriva. Non è solo la cerivastatina, cioè il Lipobay della Bayer ad avere provocato casi di rabdomiolisi nei pazienti, con molti successivi decessi, ma l? intera classe dei farmaci a base di statine. Secondo le cifre della Food and Drug Administration americana dall'ottobre 1997 al dicembre 2000, cerivastatina a parte, ci sono stati nei soli Stati Uniti almeno altri 385 casi di malattia, con 52 morti riferibili alle altre statine tuttora in circolazione, e quasi tutte in commercio anche in Italia. E cioè: simvastatina (prodotta da Zocor e Merck), atorvastatina (Lipitor, Pfizer), pravastatina (Pravachol, Bristol-Myers Squibb), lovastatina (Mevacor, Merck) e fluvastatina (Lescol, Novartis). E poiché già

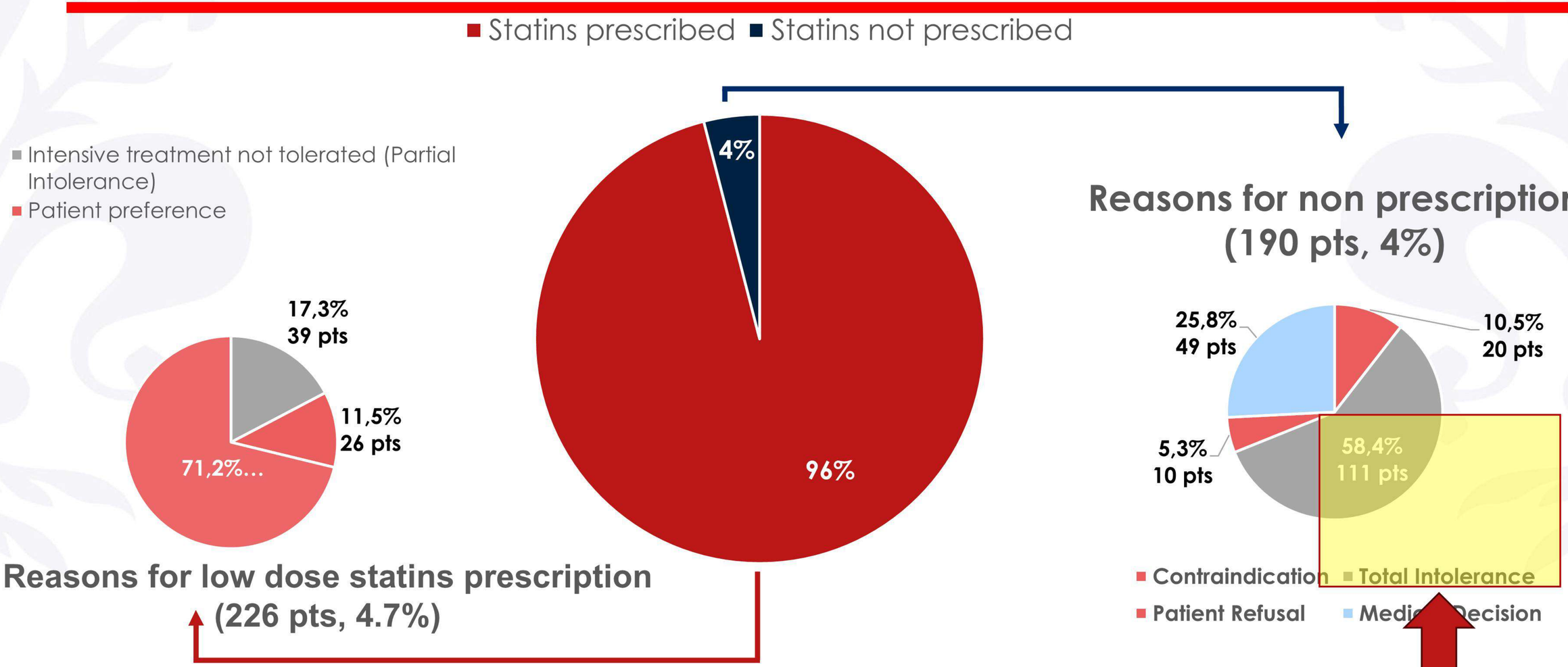


Clinical Experience vs Randomized Clinical Trials: The Elephant in the Room regarding Goal-Inhibiting Statin Intolerance (GISI)



Mancini et al, DOI: http://dx.doi.org/10.1016/j.cjca.2016.01.003

Total and Partial Statins Intolerance
(n.150/4790=3.1%)



ESC European Society of Cardiology
European Heart Journal (2022) **00**, 1–16
https://doi.org/10.1093/eurheartj/ehac015

META-ANALYSIS
Dyslipidaemias

Prevalence of statin intolerance: a meta-analysis

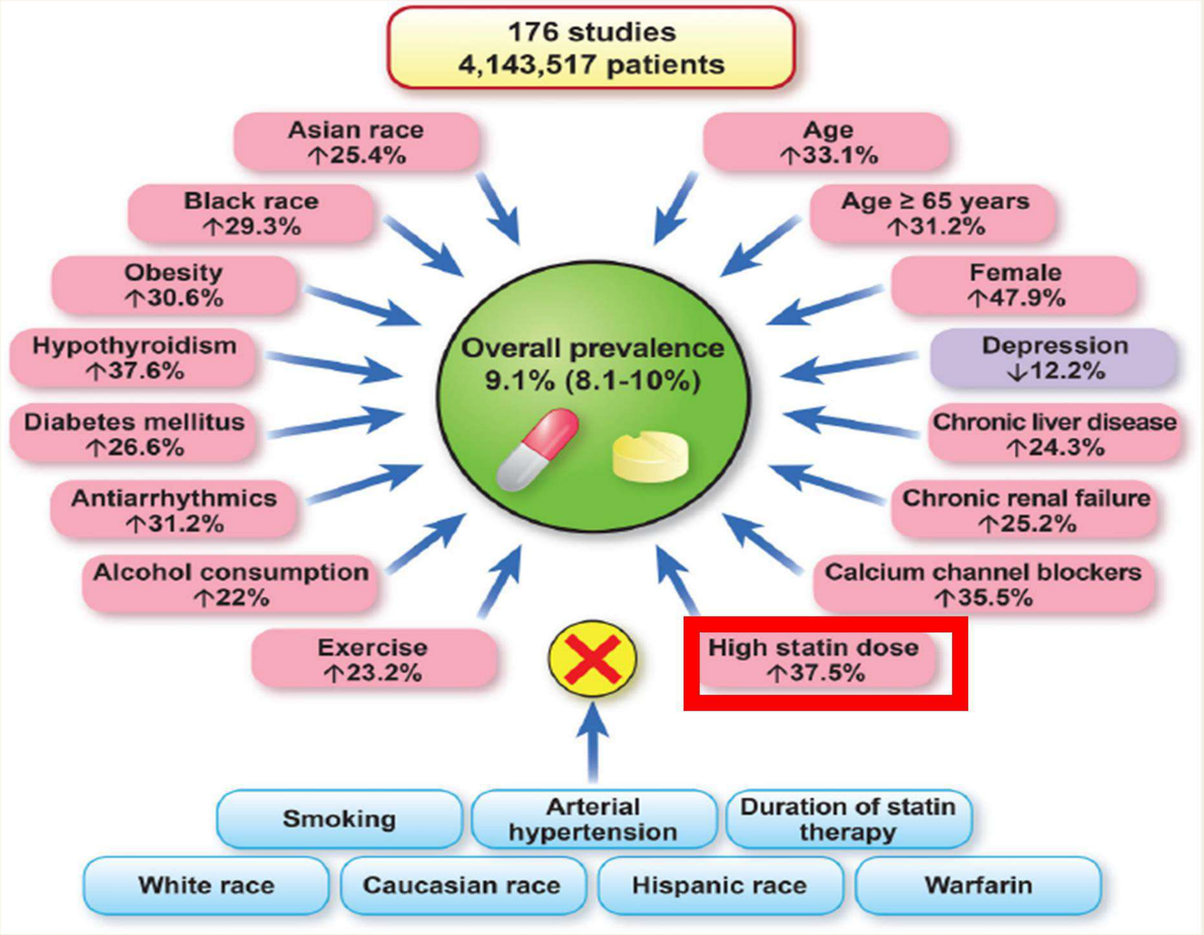
Ibadete Bytyçi[1,2], Peter E. Penson[3,4], Dimitri P. Mikhailidis[5], Nathan D. Wong[6], Adrian V. Hernandez[7,8], Amirhossein Sahebkar[9,10,11], Paul D. Thompson[12,13], Mohsen Mazidi[14,15], Jacek Rysz[16], Daniel Pella[17], Željko Reiner[18], Peter P. Toth[19,20], Maciej Banach[21,22]*, and on behalf of the Lipid and Blood Pressure Meta-Analysis Collaboration (LBPMC) Group and the International Lipid Expert Panel (ILEP)

Conclusion Based on the present analysis of >4 million patients, the prevalence of SI is low when diagnosed according to international definitions. These results support the concept that the prevalence of complete SI might often be overestimated and highlight the need for the careful assessment of patients with potential symptoms related to SI.

Key question
What is the overall prevalence of statin intolerance (SI) worldwide? What are the main risk factors of SI?

Key finding
The overall prevalence of SI is 9.1% and even lower using the international definitions: National Lipid Association, International Lipid Expert Panel, European Atherosclerosis Society (7.0, 6.7, 5.9%). Female gender, hypothyroidism, high statin dose, advanced age, antiarrhythmics, and obesity are the main factors that increase the risk of SI.

Take-home message
Clinicians should use these results to encourage adherence to statin therapy in the patients they treat.



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L'uso degli inibitori di PCSK9 potrebbe aumentare l'aderenza alla terapia?

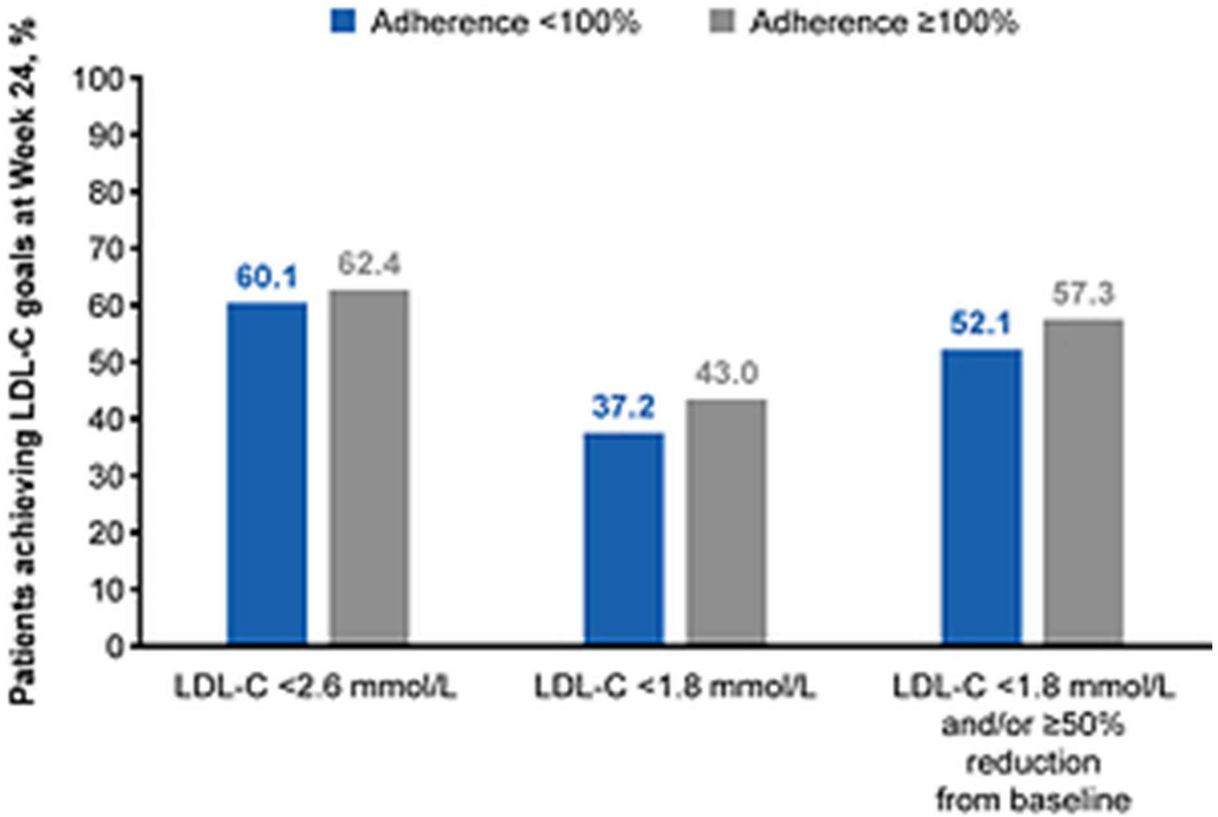
Treatment adherence and effect of concurrent statin intensity on the efficacy and safety of alirocumab in a real-life setting: results from ODYSSEY APPRISE

Maciej Banach[1], José Luis López-Sendon[2], Maurizio Averna[3], Bertrand Cariou[4], Megan Loy[5], Garen Manvelian[6], Isabela Batsu[5], Yann Poulouin[7], Daniel Gaudet[8], on behalf of the ODYSSEY APPRISE study investigators

Arch Med Sci 2022; 18 (2): 285–292

L'analisi post hoc dello studio ODYSSEY APPRISE ha esaminato l'aderenza del paziente al trattamento, nonchĕ l'efficacia e la sicurezza di alirocumab in base alla terapia di base con statine e al precedente trattamento con ezetimibe, in pazienti con grave ipercolesterolemia ad alto o altissimo rischio di futuri eventi CV.

Nello studio ODYSSEY APPRISE, l'aderenza ad alirocumab è stata elevata (**96,6%**) per una durata media del trattamento di 72,4 settimane.



Una percentuale più alta di pazienti con aderenza al trattamento con alirocumab ≥100% ha raggiunto obiettivi di C-LDL di < 2,6 mmol/l (100 mg/ dl), < 1,8 mmol/l (70 mg/dl) e) e/ o riduzione ≥ 50% rispetto al basale , alle settimane 12 e 24 rispetto ai pazienti che erano aderenti ad alirocumab con una percentuale <100%

SERIE GENERALE

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Anno 165° - Numero 61

GAZZETTA UFFICIALE

DELLA REPUBBLICA ITALIANA

PARTE PRIMA — Roma - Mercoledì, 13 marzo 2024 — SI PUBBLICA TUTTI I GIORNI NON FESTIVI

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- **5ª Serie speciale:** *Contratti pubblici (pubblicata il lunedì, il mercoledì e il venerdì)*

La **Gazzetta Ufficiale, Parte Seconda,** "Foglio delle inserzioni", *è pubblicata il martedì, il giovedì e il sabato*

New simplified web plan

Il registro di monitoraggio è aggiornato e convertito in Piano terapeutico *web-based* per l'uso del medicinale «Praluent», a base di alirocumab per le indicazioni ammesse alla rimborsabilità:

Alirocumab Once Montlhy

«300 mg soluzione iniettabile in penna pre-riempita» -1 penna - A.I.C. n. 044500193/E (in base 10);
classe di rimborsabilità: «A»;

Atherosclerosis 366 (2023) 14–21

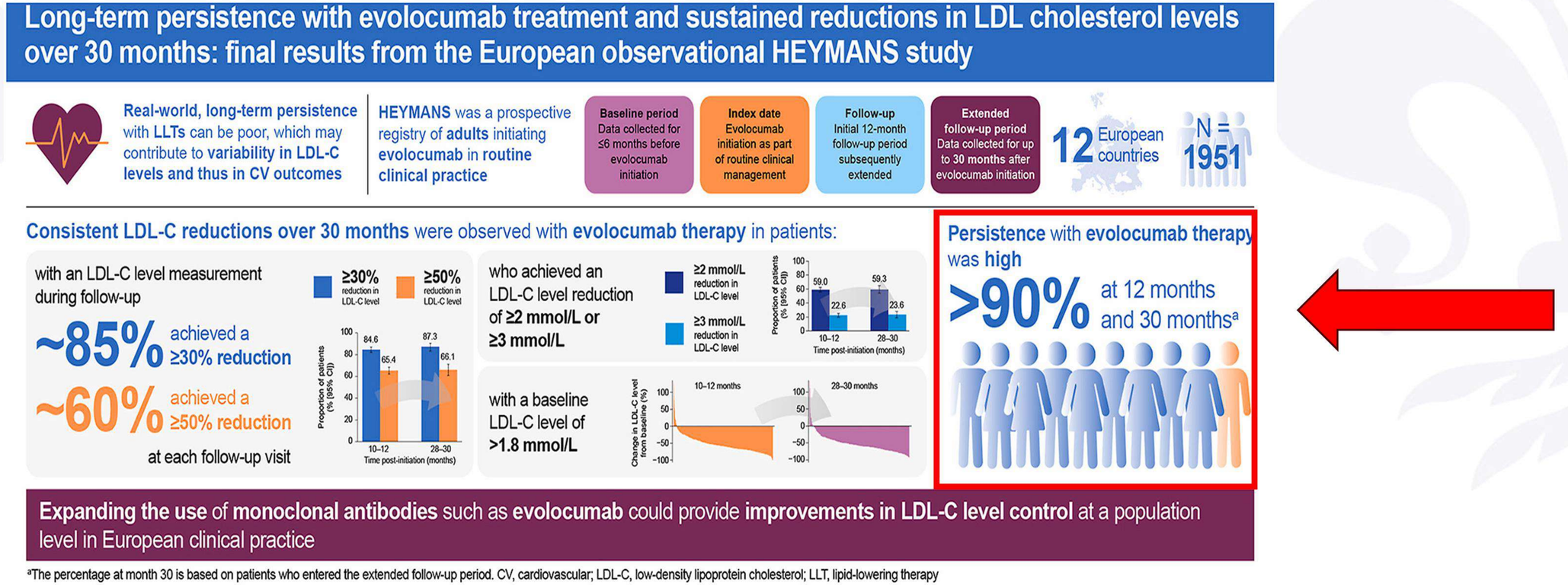
Contents lists available at ScienceDirect

Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis

Long-term persistence with evolocumab treatment and sustained reductions in LDL-cholesterol levels over 30 months: Final results from the European observational HEYMANS study

L'analisi del Registro HEYMANS mirava a valutare la persistenza e l'interruzione di evolocumab per oltre 30 mesi di trattamento e a valutare nella popolazione la variabilità delle riduzioni del livello di LDL-C durante il periodo di studio.



1951 pazienti sono stati inclusi nello studio. La riduzione mediana dei livelli di LDL-C è stata del 58% entro 3 mesi dall'inizio del trattamento con evolocumab; tale riduzione è stata mantenuta nei 30 mesi. Più del 90% dei pazienti ha continuato a ricevere evolocumab a 12 mesi e 30 mesi di follow-up. Dei pazienti con una misurazione del livello di LDL-C durante il follow-up, circa l'85% ha raggiunto una Riduzione ≥30% rispetto al basale ad ogni visita di follow-up e circa il 60% ha raggiunto una Riduzione ≥50%.

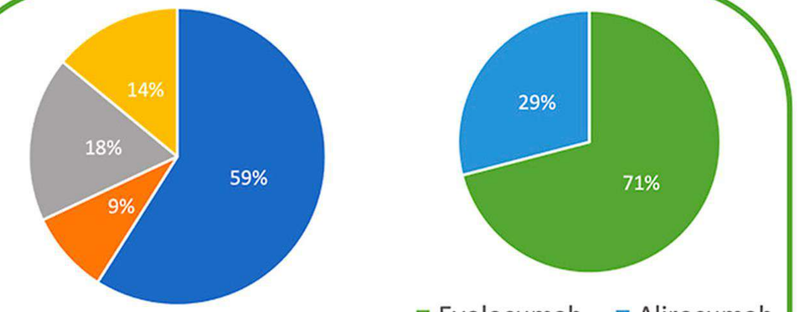
Atherosclerosis
Volume 366, February 2023, Pages 32-39

Efficacy, safety, adherence and persistence of PCSK9 inhibitors in clinical practice: A single country, multicenter, observational study (AT-TARGET-IT)

Paola Gargiulo [a], Christian Basile [a], Arturo Cesaro [b], Federica Marzano [c], Davide Buonocore [a], Gaetano Asile [a], Vincenza Abbate [a], Francesca Vicidomini [a], Stefania Paolillo [a], Carmen Anna Maria Spaccarotella [a], Angelo Catalano [d], Giulio Spirito [d], Piera Angelica Merlini [e], Alessandro Maloberti [e f], Gabriella Iannuzzo [g], Marco Matteo Ciccone [h], Anna Paola Zito [h], Leonardo Paloscia [i], Alberto D'Alleva [i], Ferdinando Varbella [j]…Pasquale Perrone-Filardi [a]

AT-TARGET-IT è un registro unico nazionale, multicentrico, osservazionale, retrospettivo, di fase IV di pazienti italiani che iniziano PCSK9i come parte della loro gestione clinica di routine, sulla base delle indicazioni delle linee guida ESC/EAS
Sono stati arruolati 798 pazienti

Efficacy, Safety, Adherence and Persistence of PCSK9 Inhibitors in Clinical Practice: The AT-TARGET-IT Study



Median LDL-C (IQR):
147.6 mg/dL (120.9, 181.6)

After a median follow-up of 19 months

LDL-C -65%

- 64% of patients achieved LDL-C target for their CV risk class
- 95% Adherence
- 97% Persistence

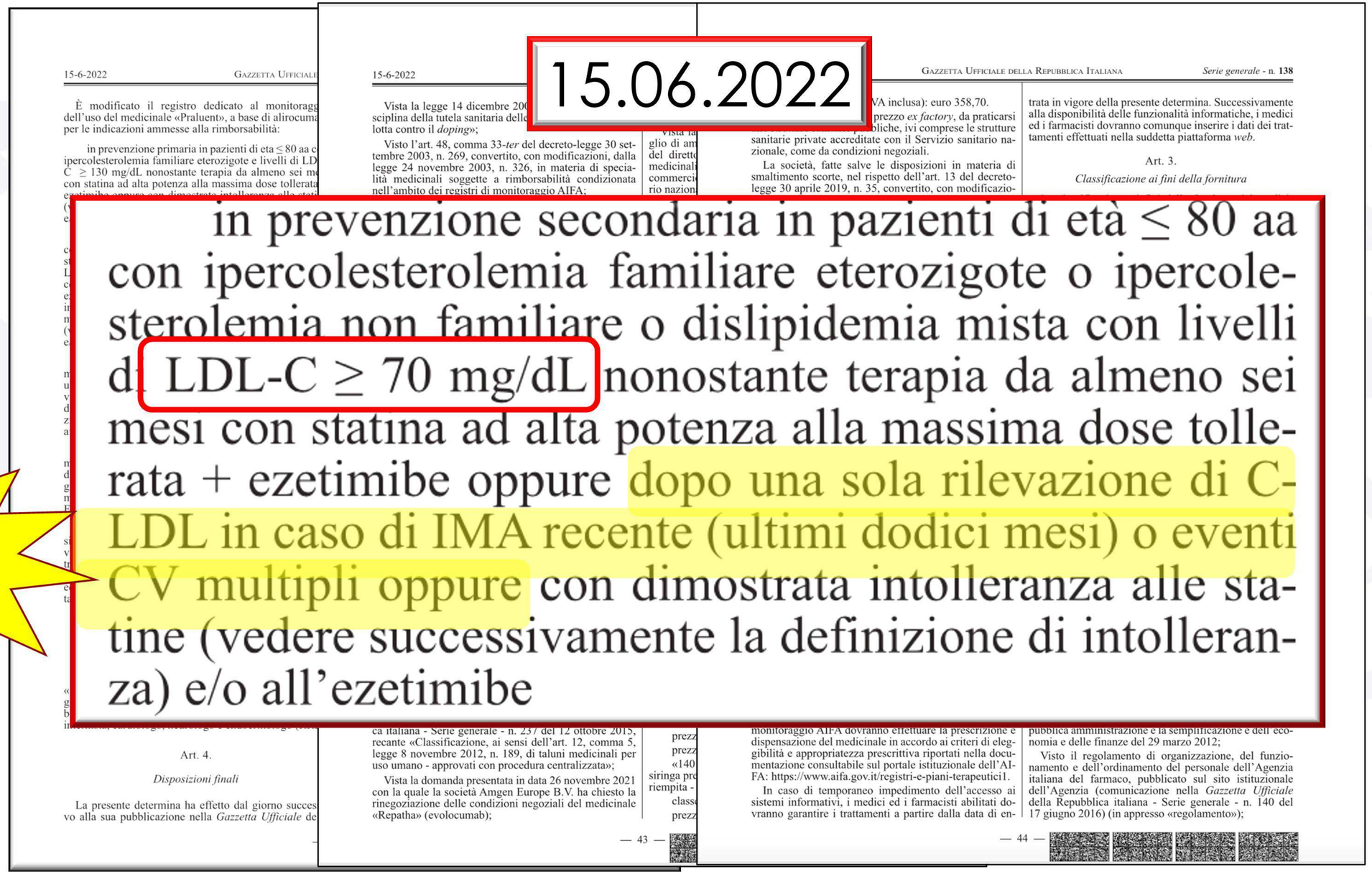
Conclusion

PCSK9i are safe and effective in clinical practice, leading to very high adherence, persistence to therapy and achievement of recommended LDL-C target in most patients, especially when used as combination therapy.

Pooled analysis 14 trials con alirocumab
Non effetti negativi associati a valori anche molto bassi di LDL-C

Primary system organ class, % (n) Preferred term, % (n)	Pooled control (n=1894)	Pooled alirocumab (n=3340)	Pooled alirocumab ≥2 LDL-C <25 mg/dL (n=796)	Pooled alirocumab ≥2 LDL-C <15 mg/dL (n=288)
Patients with any TEAE	**73.7** (1396)	**74.3** (2483)	**68.2** (543)	**67.0** (193)
Patients with any treatment emergent SAE	**13.3** (251)	**13.6** (453)	**13.1** (104)	**9.7** (28)
Patients with any TEAE leading to death	**1.0** (18)	**0.4** (15)	**0.4** (3)	**0** (0)
Patients with any TEAE leading to permanent treatment discontinuation	**6.6** (125)	**6.2** (207)	**3.5** (28)	**4.9** (14)

:1411–6; 2. Hsia J, et al. J Am Coll Cardiol 2011;57:1666–75; 3. Giugliano RP, et al. Presented at European Sociey of Cardiology, London, 2015.



15.06.2022

15-6-2022 GAZZETTA UFFICIALE

È modificato il registro dedicato al monitoragg
dell'uso del medicinale «Praluent», a base di alirocuma
per le indicazioni ammesse alla rimborsabilità:

in prevenzione primaria in pazienti di eta ≤ 80 aa c
ipercolesterolemia familiare eterozigote e livelli di LD
C ≥ 130 mg/dL nonostante terapia da almeno sei m
con statina ad alta potenza alla massima dose tollerata

Art. 4.

Disposizioni finali

La presente determina ha effetto dal giorno succes
vo alla sua pubblicazione nella *Gazzetta Ufficiale* de

15-6-2022

Vista la legge 14 dicembre 200
sciplina della tutela sanitaria dell
lotta contro il *doping*»;

Visto l'art. 48, comma 33-*ter* del decreto-legge 30 set-
tembre 2003, n. 269, convertito, con modificazioni, dalla
legge 24 novembre 2003, n. 326, in materia di specia-
lità medicinali soggette a rimborsabilità condizionata
nell'ambito dei registri di monitoraggio AIFA;

ca italiana - Serie generale - n. 237 del 12 ottobre 2015,
recante «Classificazione, ai sensi dell'art. 12, comma 5,
legge 8 novembre 2012, n. 189, di taluni medicinali per
uso umano - approvati con procedura centralizzata»;

Vista la domanda presentata in data 26 novembre 2021
con la quale la società Amgen Europe B.V. ha chiesto la
rinegoziazione delle condizioni negoziali del medicinale
«Repatha» (evolocumab);

— 43 —

GAZZETTA UFFICIALE DELLA REPUBBLICA ITALIANA *Serie generale* - n. **138**

VA inclusa): euro 358,70.
prezzo *ex factory*, da praticarsi
bliche, ivi comprese le strutture
sanitarie private accreditate con il Servizio sanitario na-
zionale, come da condizioni negoziali.

La società, fatte salve le disposizioni in materia di
smaltimento scorte, nel rispetto dell'art. 13 del decreto-
legge 30 aprile 2019, n. 35, convertito, con modificazio-

monitoraggio AIFA dovranno effettuare la prescrizione e
dispensazione del medicinale in accordo ai criteri di eleg-
gibilità e appropriatezza prescrittiva riportati nella docu-
mentazione consultabile sul portale istituzionale dell'AI-
FA: https://www.aifa.gov.it/registri-e-piani-terapeutici1.

In caso di temporaneo impedimento dell'accesso ai
sistemi informativi, i medici ed i farmacisti abilitati do-
vranno garantire i trattamenti a partire dalla data di en-

trata in vigore della presente determina. Successivamente
alla disponibilità delle funzionalità informatiche, i medici
ed i farmacisti dovranno comunque inserire i dati dei trat-
tamenti effettuati nella suddetta piattaforma *web*.

Art. 3.

Classificazione ai fini della fornitura

pubblica amministrazione e la semplificazione e dell'eco-
nomia e delle finanze del 29 marzo 2012;

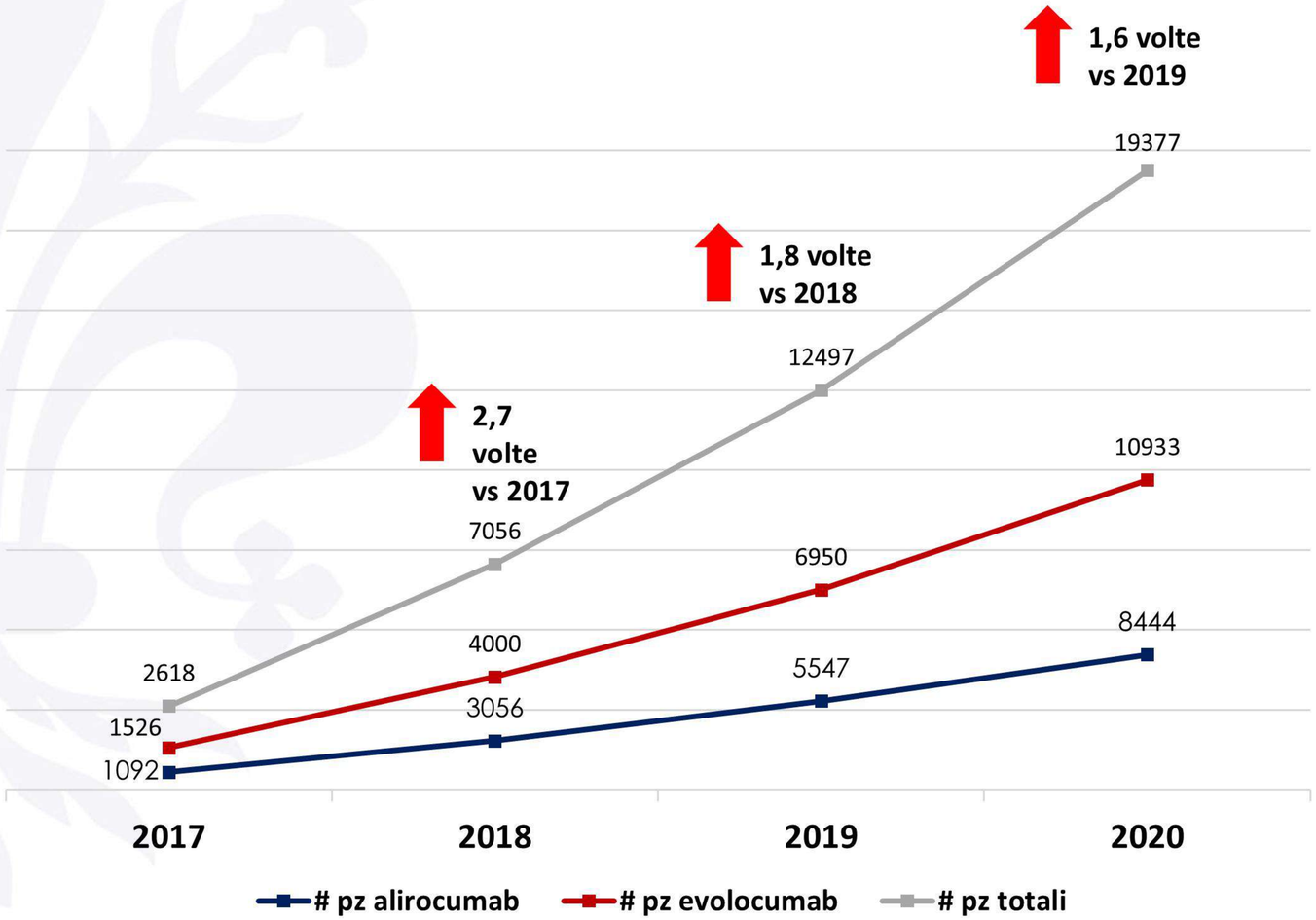
Visto il regolamento di organizzazione, del funzio-
namento e dell'ordinamento del personale dell'Agenzia
italiana del farmaco, pubblicato sul sito istituzionale
dell'Agenzia (comunicazione nella *Gazzetta Ufficiale*
della Repubblica italiana - Serie generale - n. 140 del
17 giugno 2016) (in appresso «regolamento»);

— 44 —

in prevenzione secondaria in pazienti di età ≤ 80 aa con ipercolesterolemia familiare eterozigote o ipercolesterolemia non familiare o dislipidemia mista con livelli di LDL-C ≥ 70 mg/dL nonostante terapia da almeno sei mesi con statina ad alta potenza alla massima dose tollerata + ezetimibe oppure dopo una sola rilevazione di C-LDL in caso di IMA recente (ultimi dodici mesi) o eventi CV multipli oppure con dimostrata intolleranza alle statine (vedere successivamente la definizione di intolleranza) e/o all'ezetimibe

Fast track

NONOSTANTE L'INTRODUZIONE DEL "FAST TRACK" NON C'È STATO UN MAGGIORE UTILIZZO DEI PCSK9i



A fine 2020 si registrano 19.377 pazienti cumulati trattati in Italia con PCSK9i.

AIFA aveva stimato nel 2016 che ci fossero già 60.000 pazienti eleggibili e pronti a ricevere un PCSK9i

% di prevenzione, diagnosi e comorbidità dei pazienti trattati con PCSK9i Ab costanti nel periodo 2017-2020

Caratteristiche pazienti in trattamento – Focus 2020

- 65% uomini, età mediana 62 anni
- prescrizioni per diagnosi: 51,9% ipercolesterolemia non familiare, 26,6% dislipidemia mista
- 87,5% in prevenzione CV secondaria vs 12,5% in prevenzione primaria
- comorbilità: malattia CV (71,1%), ipertensione arteriosa (63,6%) e diabete mellito (20,5%)
- Intolleranze: alle statine 53,7%, all'ezetimibe 5,4%

Osservatorio Nazionale sull'impiego dei Medicinali - Rapporto Nazionale 2020

BRING•UP PREVENZIONE

ENDPOINT PRIMARIO

Percentuale di pazienti a goal per **colesterolo LDL (<55 mg/dL)** a 6 mesi.

L'ipotesi è quella di migliorare il livello di aderenza alle linee guida del 50% (20% assoluto), avendo alla fine dello studio un tasso di pazienti a goal per colesterolo LDL del 60%.
Ipotizzando un reclutamento di 1000 pazienti, la stima del 60% dei pazienti a goal avrà un IC del 95% di 57-63%.



Altri ipolipemizzanti prescritti (4504 pts)

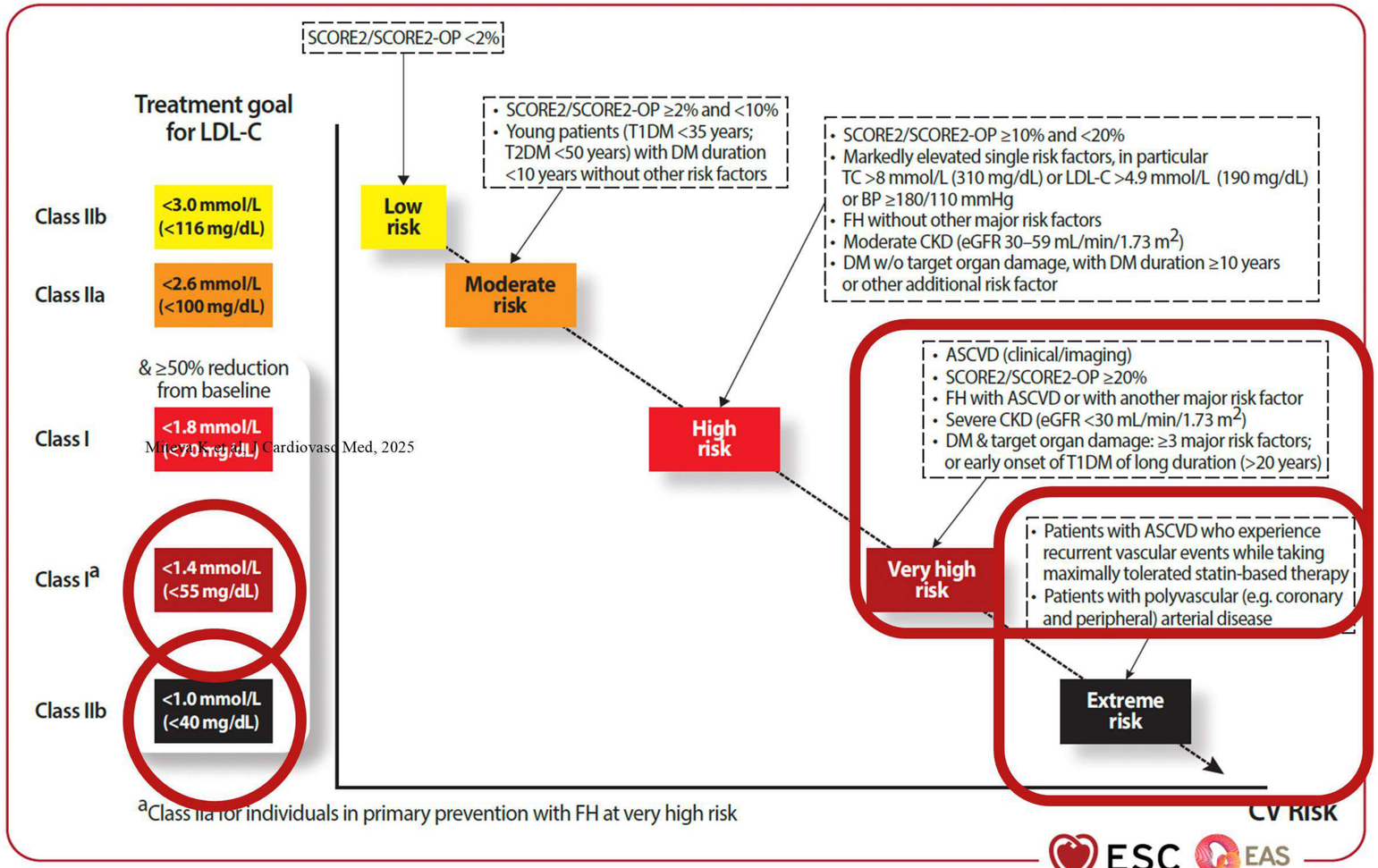
Farmaco	Basale n. (%)	FU a 6 mesi Pre-visita n. (%)	FU a 6 mesi Post-visita n. (%)
Almeno un altro ipolipemizzante	3569 (79.2)	3630 (80.6)	3886 (86.3)
Ezetimibe	3478 (77.2)	3537 (78.5)	3782 (84.0)
Fibrati	33 (0.7)	28 (0.6)	32 (0.7)
Evolocumab	141 (3.1)	129 (2.9)	159 (3.5)
Alirocumab	157 (3.5)	155 (3.4)	187 (4.2)
Inclisiran	68 (1.5)	82 (1.8)	104 (2.3)
Acido Bempedoico	194 (4.3)	231 (5.1)	390 (8.7)
	6.6%		**7.7%**

il profilo di rischio del paziente

SAME LDL-C GOLAS AS THE 2019 ESC/EAS GUIDELINES

EXTREME RISK:

- Patients with ASCVD who experience **recurrent vascular events** while taking maximally tolerated statin-based therapy
- **Patients with polyvascular** (e.g. coronary and peripheral) arterial disease



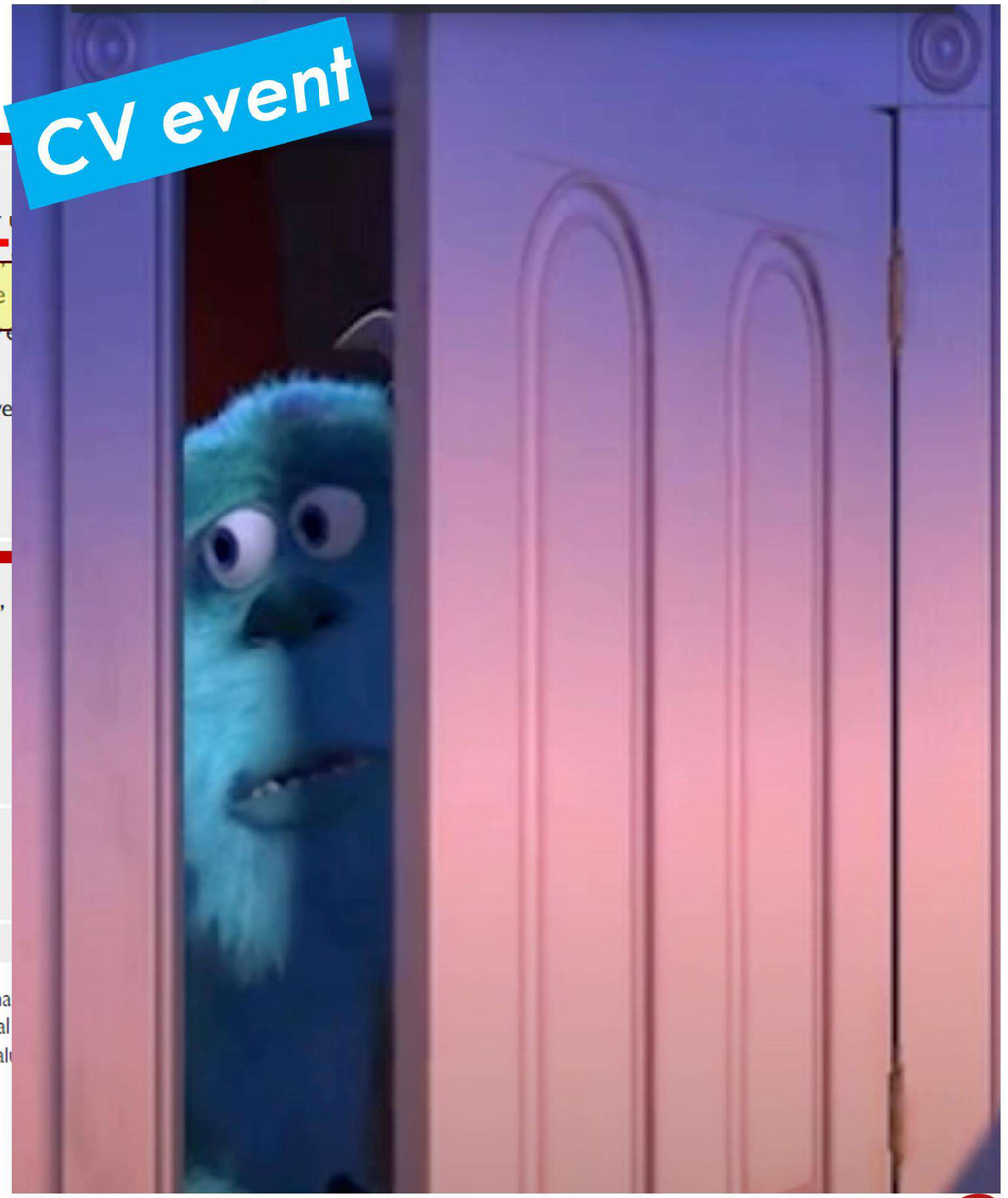
Mach F, et al. J Cardiovasc Med, 2025

2025 Focused Update of the 2019 ESC/EAS Guidelines for Dyslipidaemia: new updates in CV risk stratification

Table 3 Cardiovascular risk categories

Very high risk	People with any of the following: • Documented ASCVD, either clinical or unequivocal on imaging. Documented ASCVD includes previous ACS (MI or u chronic coronary syndromes, coronary revascularization (PCI, CABG, and other arterial revascularization procedures), peripheral arterial disease. Unequivocally documented ASCVD on imaging includes those findings that are known to be events, such as significant plaque[a] on coronary angiography or CT scan or on carotid or femoral ultrasound or markedly e by CT[b] • DM with target organ damage,[c] or at least three major risk factors, or early onset of T1DM of long duration (>20 ye • Severe CKD (eGFR <30 mL/min/1.73 m^2) • A calculated SCORE2 or SCORE2-OP ≥20% for 10 year risk of fatal or non-fatal CVD • FH with ASCVD or with another major risk factor
High risk	People with any of the following: • Markedly elevated single risk factors, in particular TC >8 mmol/L (>310 mg/dL), LDL-C >4.9 mmol/L (>190 mg/dL), BP ≥180/110 mmHg • Patients with FH without other major risk factors • Patients with DM without target organ damage,[c] with DM duration ≥10 years or another additional risk factor • Moderate CKD (eGFR 30–59 mL/min/1.73 m^2) • A calculated SCORE2 or SCORE2-OP ≥10% and <20% for 10 year risk of fatal or non-fatal CVD
Moderate risk	People with any of the following: • Young patients (T1DM <35 years; T2DM <50 years) with DM duration <10 years, without other risk factors • Calculated SCORE2 or SCORE2-OP ≥2% and <10% for 10 year risk of fatal or non-fatal CVD
Low risk	• Calculated SCORE2 or SCORE2-OP <2% for 10 year risk of fatal or non-fatal CVD

ASCVD, atherosclerotic cardiovascular disease; ACS, acute coronary syndromes; BP, blood pressure; CABG, coronary artery bypass graft surgery; CAC, corona chronic kidney disease; CT, computed tomography; CVD, cardiovascular disease; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; FH, familial LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction; PCI, percutaneous coronary intervention; SCORE2, Systematic Coronary Risk Eval Systematic Coronary Risk Evaluation 2-Older Persons; T1DM, type 1 DM; T2DM, type 2 DM; TC, total cholesterol; TIA, transient ischaemic attack.
[a]Typically defined by >50% stenosis.
[b]e.g. CAC score >300.
[c]Target organ damage is defined as microalbuminuria, retinopathy, or neuropathy.

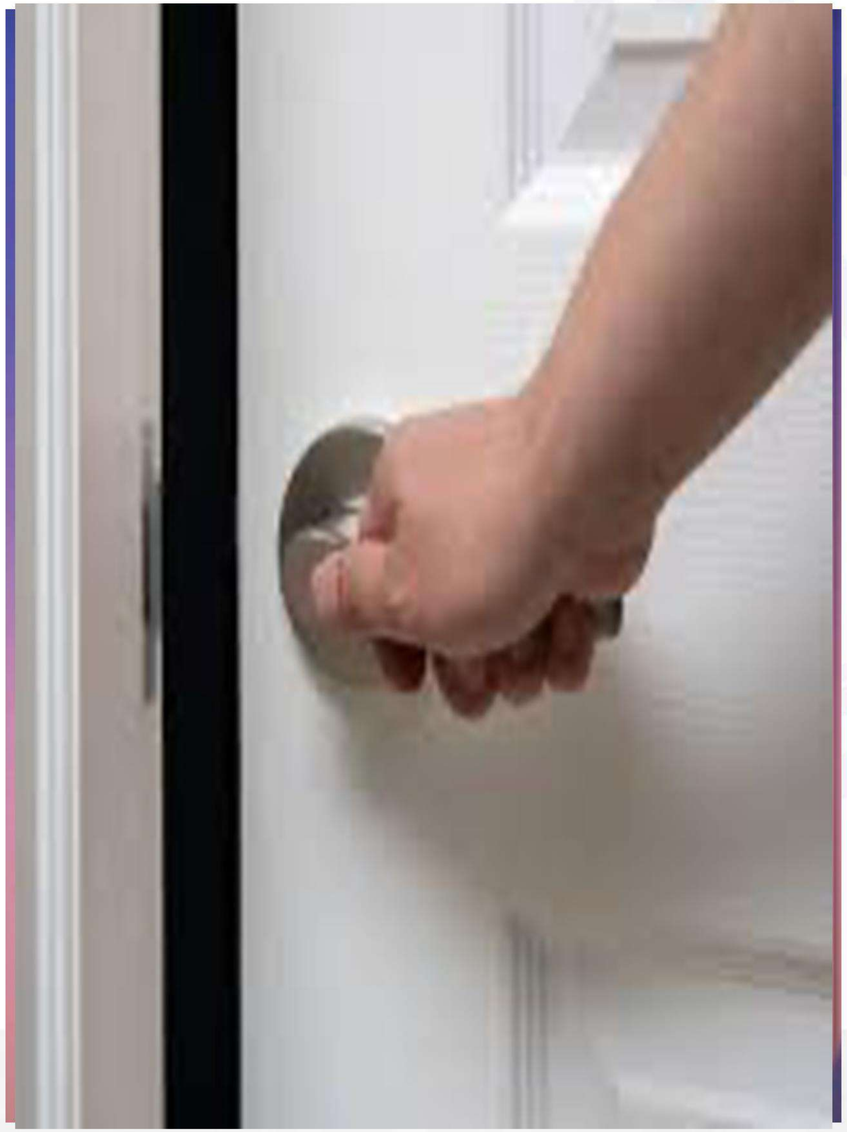


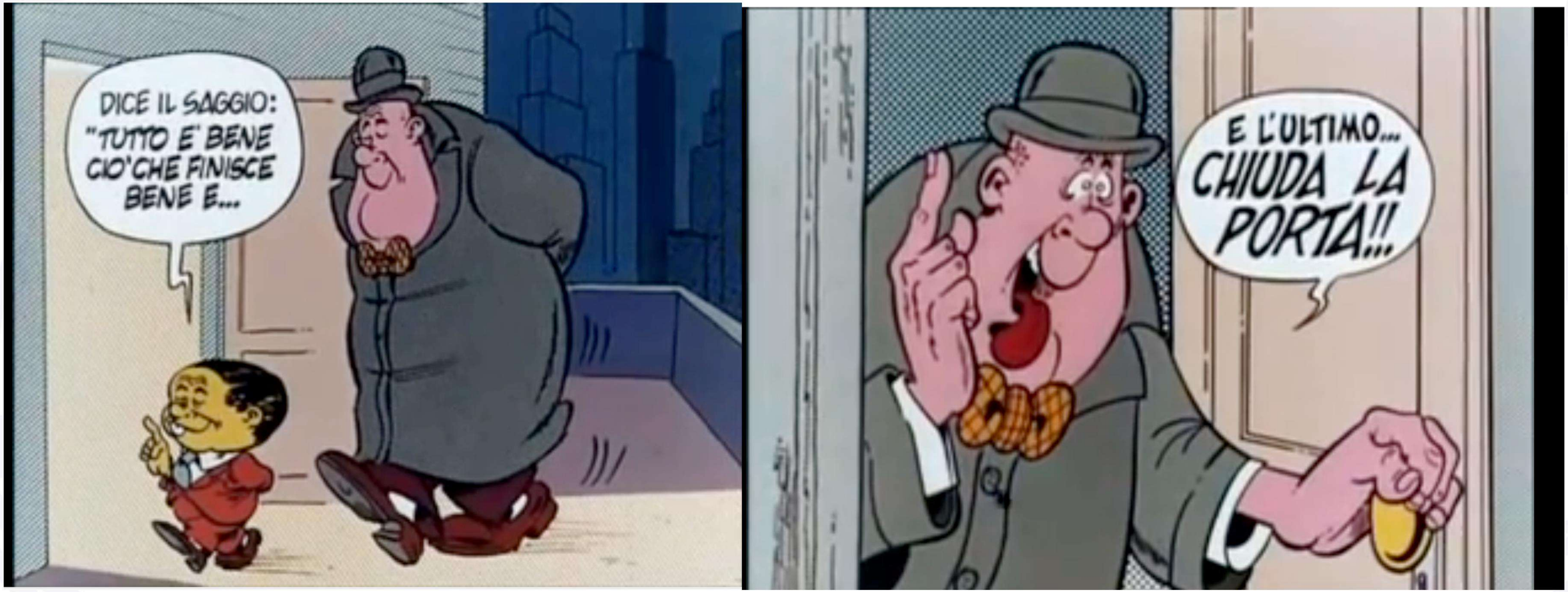
Miteva K et al, J Cardiovasc Med, 2025

Right therapy,
Using soon PCSK9i when needed, means
Get to the target, and…



Close the door to CV events!




DICE IL SAGGIO: "TUTTO E' BENE CIO' CHE FINISCE BENE E...
E L'ULTIMO... CHIUDA LA PORTA!!

Thanks

e