I ruolo della triplice terapia orale nella gestione del paziente dislipidemico post-SCA

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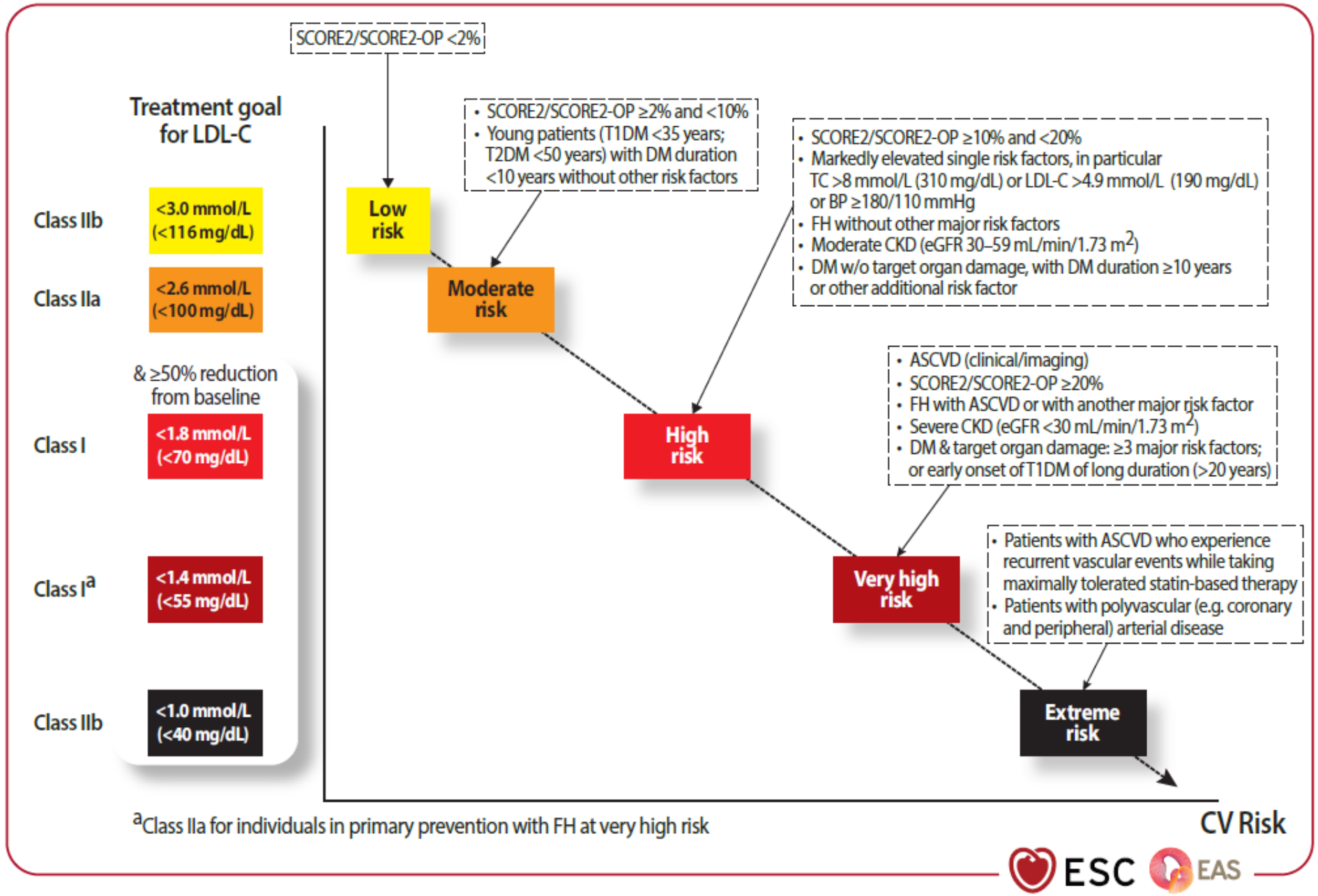
Potential Conflicts of Interest

Advisory Boards and Research Grants:

Eli Lilly, Novo Nordisk, MSD, AstraZeneca, Regeneron

No conflicts of interest relevant to this presentation



F. Mach et al, European Hert Journal. 2025:46,4359–4378

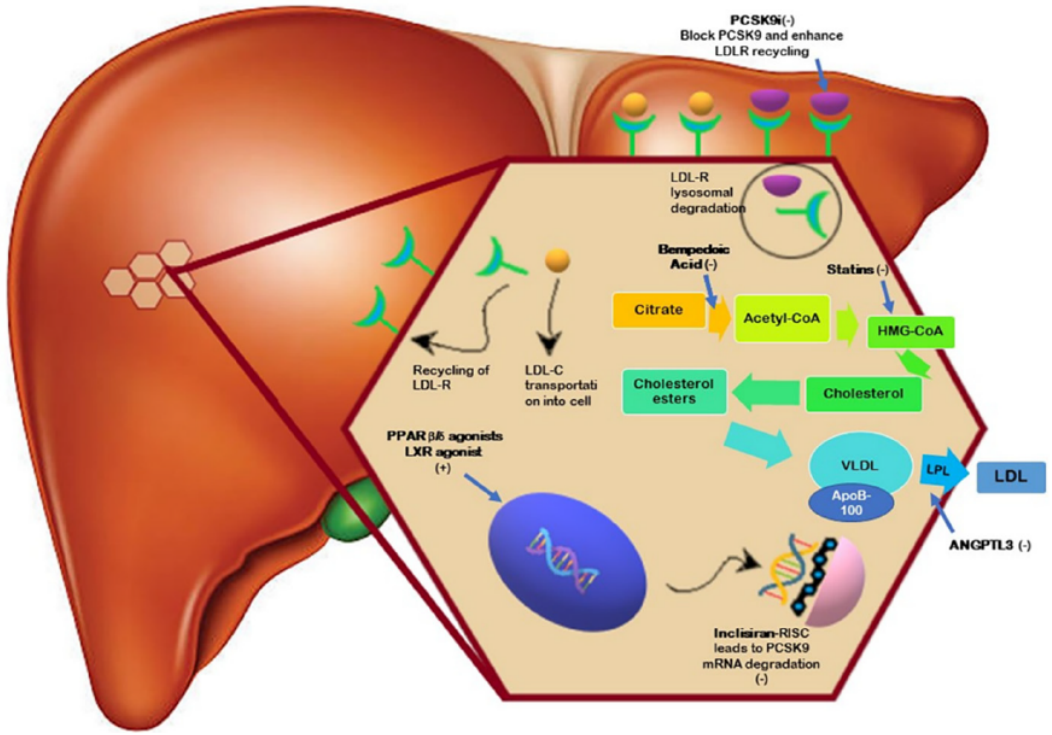
2025 Focused Update of the 2019 ESC/EAS Guidelines: Recommendations for Lipid-lowering Therapy in Patients with Acute Coronary Syndromes

Recommendations	Class	Level
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

ACS, Acute coronary syndrome

Mach F, et al. Eur Heart J. 2025;00:1–20.

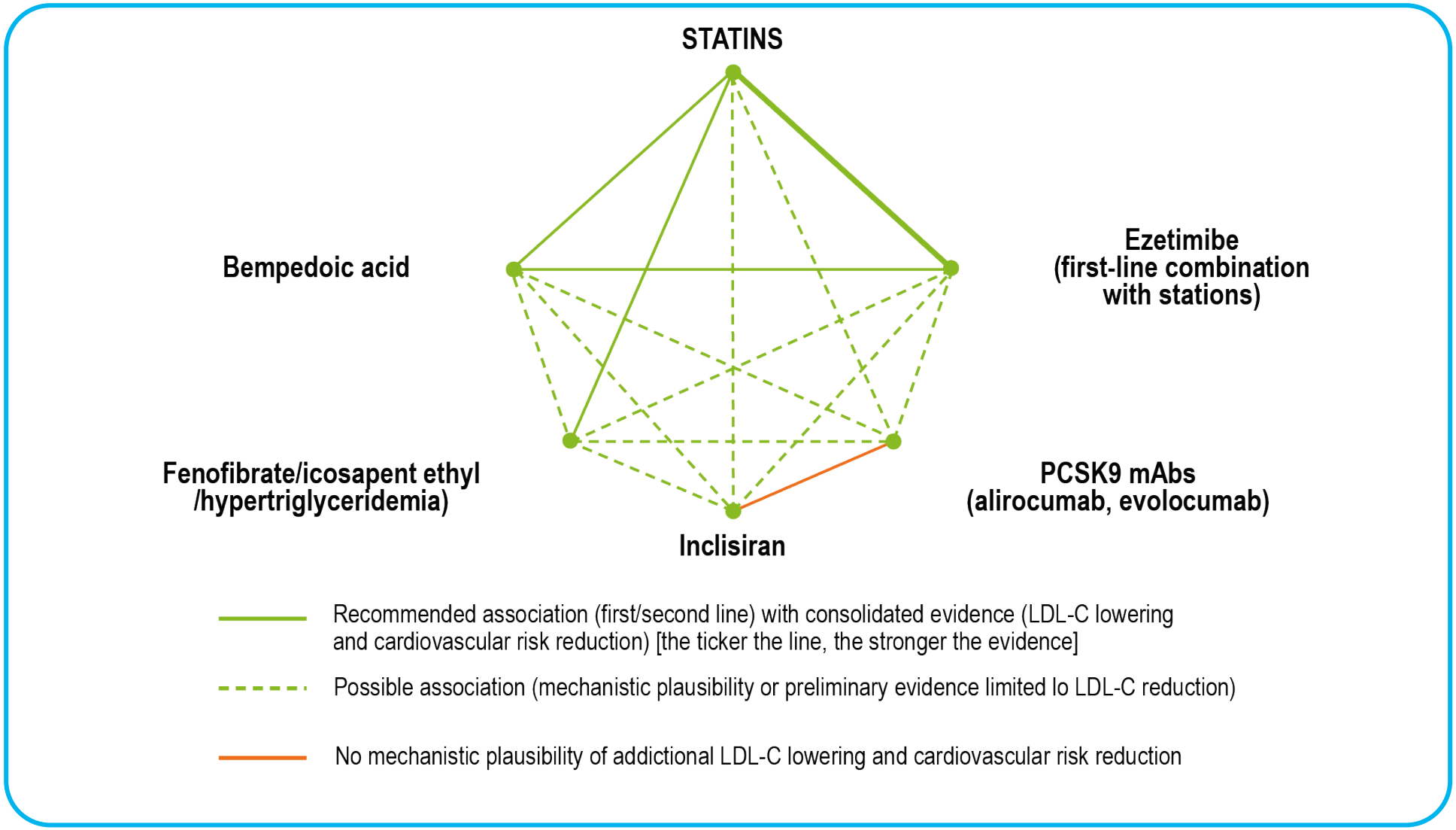
Current Options and Future Perspectives in the Treatment of Dyslipidemia



Muscoli S. et al, JCM, 2022

Drugs	MOA	Efficacy	EMA Approval	FDA Approval
PCSK9-i	Monoclonal antibodies that inhibit PCSK9, diminishing the recycling of LDL-R	Medium decrease of LDL-C: 61.9% [12,13]	✓	✓
Bempedoic Acid	The active metabolite inhibits adenosine triphosphate citrate lyase, leading to reduced acetyl CoA levels in the cholesterol synthesis pathway upstream of HMG-CoA reductase	Medium decrease of LDL-C: 27% [31,32] BA plus ezetimibe decrease LDL-C up to 48% [37]	✓	✓
Inclisiran	siRNA targeting 3′ UTR of the PCSK9 mRNA leading to suppression of hepatic PCSK9 production	Medium decrease of LDL-C: 52.3% [45]	✓	✓
LXR agonists	Activation of LXR in macrophages induces cholesterol efflux. LXR reduce cholesterol absorption and promote intestinal excretion, increasing Apo E expression and downregulating Niemann-Pick C1 like 1	No RCTs available No human	✗	✗
PPARs agonists	Proteins that modulate the transcription of the target genes regulating glucose, TG and lipoprotein metabolism, cell proliferation, inflammation, and vascular tissue function	Seladelpar induce a medium decrease of LDL-C by 18–43% [71–73]	✗	✗
ANGPTL3 inhibitors	ANGPTL3 inhibits LPL from combining with the glycosylphosphatidylinositol-anchored HDL binding protein 1: Inhibition of ANGPTL3 results in lower plasma TG, ApoB, LDL-C and HDL-C	Evinacumab induce a medium decrease of TG levels up to 76% and LDL-C levels up to 23% [78] The addition of i.v. evinacumab to the treatment regimen of HoFH patients resulted in a mean reduction of LDL-C levels by 49% ± 23% after 4 weeks [78]	✓	✓
Mipomersen	Antisense oligonucleotide capable of binding ApoB-100 mRNA leading to decrease production of LDL, VLDL and Lp(a)	Medium decrease of LDL-C up to 71% [91–93]	✗	✓
Lomitapide	MTP inhibitor leading to reduced lipoprotein production (especially of Apo B)	Used for the treatment of FHMedium decrease of LDL-C levels up to 30% [106] In combination with ezetimibe LDL-C was reduced up to 46% [106]	✓	✓
Volanesorsen	Antisense oligo-nucleotide target to reduce hepatic ApoC-III mRNA	Medium decrease of TG levels up to 71.2% [110]	✓	✗

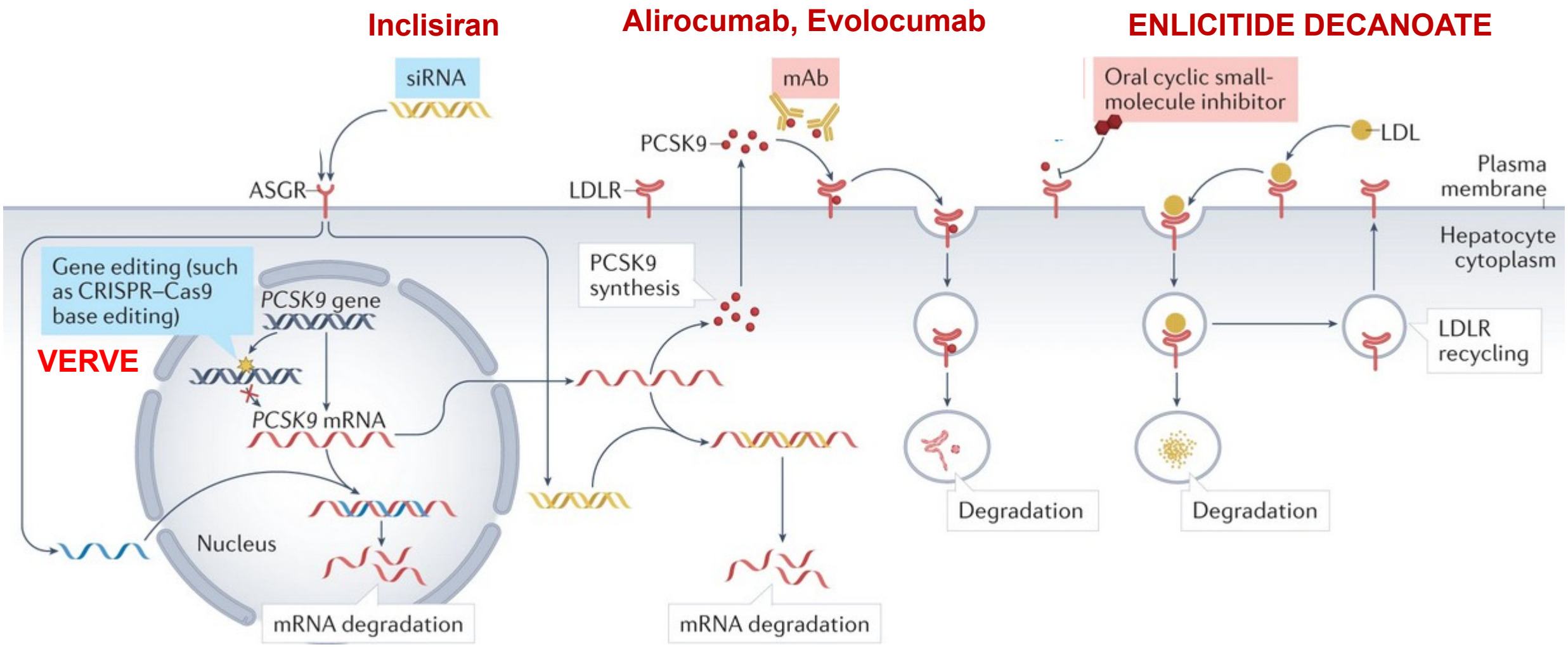
Lipid Lowering combination therapy



C-LDL, low-density lipoprotein cholesterol. **PCSK9i**, proprotein convertase subtilisin/kexin type 9 inhibitor. **mAbs,** monoclonal antibodies.

Raschi et al, Pharmacol Ther. 2023 Oct:250:108507. doi: 10.1016/j.pharmthera.2023.108507.
Beyond statins: New pharmacological targets to decrease LDL-cholesterol and cardiovascular events – ScienceDirect

PCSK9i



Al Rifai M et al. Nature Reviews 2021; 18: 805-806.

Eleggibilità del paziente

Paziente non eleggibile

La risposta alla domanda: "Sono state escluse cause secondarie di ipercolesterolemia (es. patologie come ipotiroidismo, sindrome nefrosica o da farmaci come immunosoppressori, antiretrovirali e inibitori delle aromatasi)?" rende il paziente non eleggibile

Codice Paziente	Centro	Iniz. Paz.	Data Registrazione	Data di Nascita
202606150852430001995 8	AZ. OSP. UNIV. POLICLINICO TOR	GI.CA.	15/06/2026	28/08/1949

INDICAZIONI TERAPEUTICHE

- PRALUENT -

<u>Ipercolesterolemia primaria e dislipidemia mista</u>

Praluent è indicato in adulti con ipercolesterolemia primaria (familiare eterozigote o non familiare) o da dislipidemia mista, in aggiunta alla dieta:

· in associazione ad una statina o ad una statina con altre terapie ipolipemizzanti in pazienti non in grado di raggiungere gli obiettivi per il colesterolo LDL (C-LDL) con la dose massima tollerata di statine, oppure

· in monoterapia o in associazione ad altre terapie ipolipemizzanti in pazienti intolleranti alle statine o per i quali una statina è controindicata.

<u>Malattia cardiovascolare aterosclerotica accertata</u>

Praluent è indicato negli adulti con malattia cardiovascolare aterosclerotica accertata per ridurre il rischio cardiovascolare riducendo i livelli di C-LDL, in aggiunta alla correzione di altri fattori di rischio:

- in associazione alla dose massima tollerata di statina con o senza altre terapie ipolipemizzanti oppure,

- in monoterapia o in associazione ad altre terapie ipolipemizzanti in pazienti intolleranti alle statine o per i quali l'uso delle statine è controindicato.

Per i risultati dello studio relativi agli effetti su C-LDL, eventi cardiovascolari e popolazioni studiate, vedere il paragrafo 5.1 RCP.

(E) Terapie ipolipemizzanti *:

- [ ] Fibrati
- [ ] Resine sequestranti acidi biliari
- [ ] Lomitapide
- [ ] Aferesi lipoproteine
- [ ] Acido bempedoico
- [ ] Evolocumab (E)
- [ ] Inclisiran (I)

MENU

AIFA AGENZIA ITALIANA DEL FARMACO | Italian Medicines Agency

PCSK9-inibitori

NON SONO RIMBORSATI NEI PAZIENTI SOPRA GLI > 80 anni

Limitazione di rimborsabilità AIFA
indipendente dal livello di LDL-C
o dal rischio cardiovascolare.

RIMBORSABILITÀ AIFA
PCSK9-inibitori non rimborsabili nei pazienti con età **> 80 anni**.

L'età anagrafica **> 80 anni** esclude la rimborsabilità, indipendentemente dal livello di LDL-C o dal rischio CV.

LINEE GUIDA ESC/EAS vs RIMBORSABILITÀ AIFA

PCSK9-inibitori: un divario che lascia pazienti non a target senza accesso alla terapia

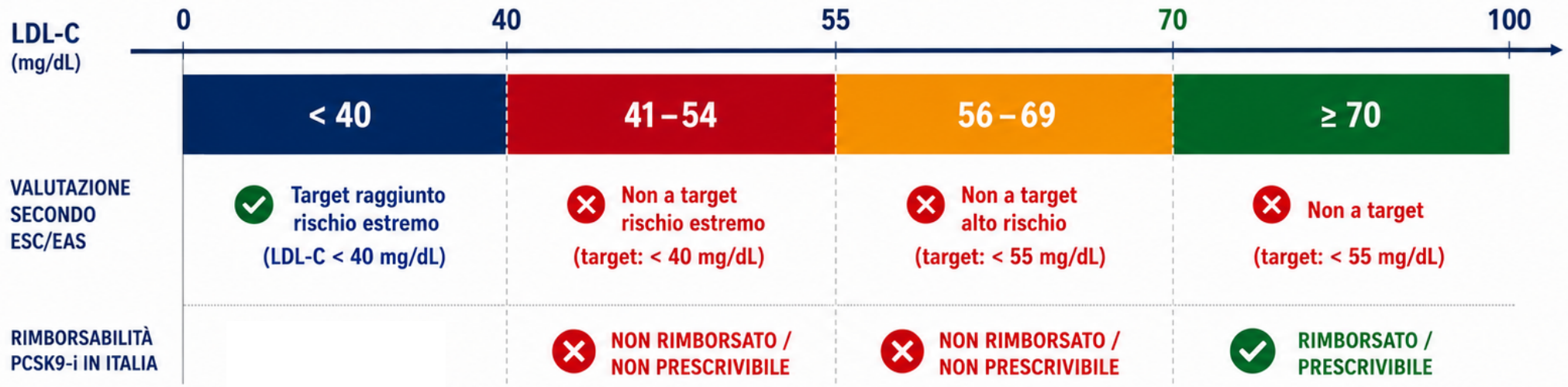
AIFA AGENZIA ITALIANA DEL FARMACO — Italian Medicines Agency

TARGET SECONDO LINEE GUIDA ESC/EAS

- Alto rischio: LDL-C < 55 mg/dL
- Rischio estremo: LDL-C < 40 mg/dL

RIMBORSABILITÀ AIFA PCSK9-inibitori in Italia

- Rimborsato / Prescrivibile solo se LDL-C ≥ 70 mg/dL



TREATMENT GAP

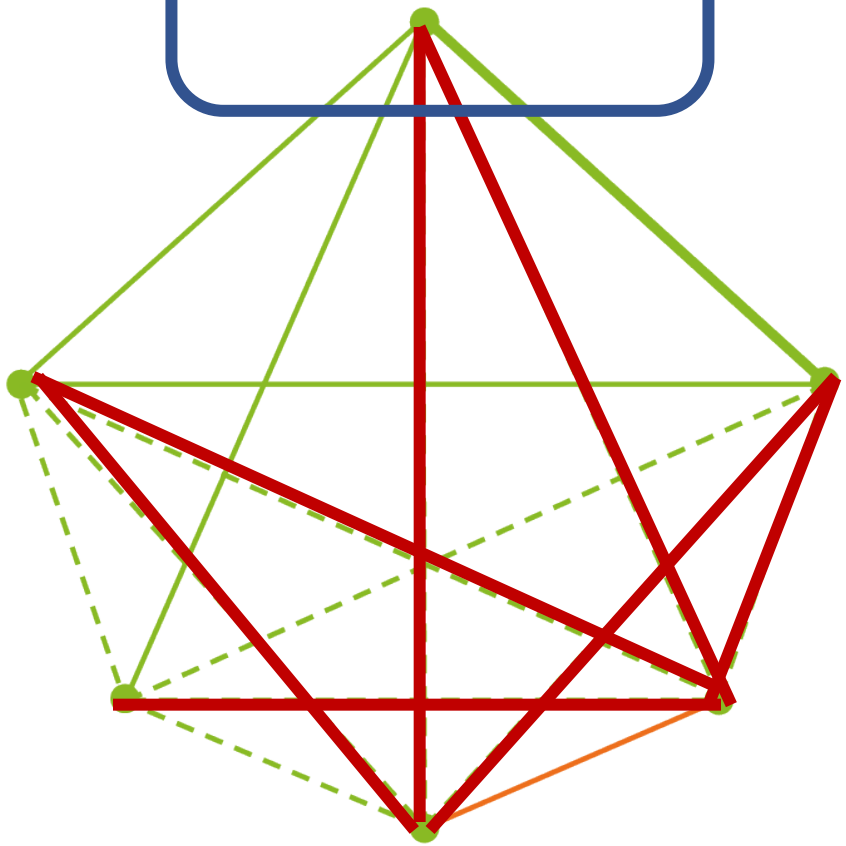
- **LDL-C 56–69 mg/dL:** pazienti ad **ALTO RISCHIO** rimangono sopra il target ESC/EAS (<55 mg/dL) ma non sono eleggibili al rimborso dei PCSK9-i.
- **LDL-C 41–54 mg/dL:** pazienti a **RISCHIO ESTREMO** rimangono sopra il target ESC/EAS (<40 mg/dL) ma non sono eleggibili al rimborso dei PCSK9-i.

LA RIMBORSABILITÀ PARTE DA 70 mg/dL, MENTRE LE LINEE GUIDA CHIEDONO < 55 mg/dL (ALTO RISCHIO) O < 40 mg/dL (RISCHIO ESTREMO).

STATINS

Bempedoic acid

Ezetimibe
(first-line combination
with stations)



Fenofibrate/icosapent ethyl
/hypertriglyceridemia)

PCSK9 mAbs
(alirocumab, evolocumab)

Inclisiran

FROM THE EDITOR

The Underused Miracle Drugs: The Statin Drugs Are to Atherosclerosis What Penicillin Was to Infectious Disease*

drug within 2 years.

All of this, of course, is good news for coronary angioplasty, coronary bypass, carotid endarterectomy, abdominal aortic resection, and peripheral vascular operative procedures, but it is bad news for patients and an embarrassment for physicians. It took 80 years after it was demonstrated that high cholesterol diets caused atherosclerosis in rabbits before a safe, efficacious, once-a-day drug became available which could actually prevent and/or arrest atherosclerosis. The challenge now is to use these miracle antiatherosclerotic drugs more frequently, to use them in sufficient doses to do their job, and to convince patients that these miracle drugs taken every day are the best antiatherosclerotic insurance they can purchase. The cost of 5 cigarettes readily pays for the drug each day. If the quantity of meat consumed was reduced in half, there would be plenty of money left over to purchase the miracle statin drugs.

William C. Roberts

W.C.Roberts, 1996, THE AMERICAN JOURNAL OF CARDIOLOGY

Secondary Prevention Trials Involving Statin Therapy

Trial name	Duration (years)	Treatment	Patients	LDL-C baseline	LDL-C at end of treatment, or on treatment	Primary result
4S[1]	5.4	Simvastatin 20 mg vs placebo	Stable CHD and dyslipidemia (N=4,444)	Both groups: 260.2 mg/dL (6.7 mmol/L)	Simvastatin: 35% reduction Placebo: 1% increase	30% reduction in primary endpoint: total mortality (P=0.0003)
CARE[2]	5.0	Pravastatin 40 mg/d vs placebo	Unstable CHD and average cholesterol levels (N=4,159)	Both groups: 139 mg/dL (3.6 mmol/L)	Pravastatin: 97 mg/dL (2.5 mmol/L), 32% reduction vs baseline, 28% reduction vs placebo	24% reduction in primary endpoint: death from CHD (fatal MI, sudden death, death during a coronary intervention, death from other coronary causes, p=0.003) or nonfatal MI
LIPID[3]	5	Pravastatin 40 mg/d vs placebo	Unstable CHD and elevated LDL-C (N=9,014)	Both groups: 150 mg/dL (3.9 mmol/L)	Pravastatin: 25% reduction vs placebo (P<0.001)	24% reduction in primary endpoint: death due to CHD (fatal MI, sudden death, hospital death after MI, or death due to heart failure or other coronary cause, p<0.001)
HPS[4]	5	Simvastatin 40 mg vs placebo	High-risk stable CHD with a range of cholesterol levels (N=20,536)	Both groups: 131 mg/dL (3.4 mmol/L)	Simvastatin: –1.0 mmol/L reduction vs placebo	13% reduction in primary endpoint: all-cause mortality (p=0.0003)
TNT[5]	4.9	Atorvastatin 10 mg vs 80 mg	Stable CHD slightly elevated LDL-C (N=10,003)	Atorvastatin 10 mg: 98 mg/dL (2.5 mmol/L) Atorvastatin 80 mg: 97 mg/dL (2.5 mmol/L)	Atorvastatin 10 mg: 101 mg/dL (2.6 mmol/L) Atorvastatin 80 mg: 77 mg/dL (2.0 mmol/L), 21% reduction vs baseline	22% reduction in primary endpoint: death from CHD, non-fatal MI, resuscitation after cardiac arrest, or fatal or nonfatal stroke (P<0.001) for atorvastatin 80 mg vs 10 mg
IDEAL[6]	5	Atorvastatin 80 mg vs simvastatin 20 mg	Stable CHD with dyslipidemia (N=8,888)	Simvastatin 20 mg: 121.4 mg/dL (3.1 mmol/L) Atorvastatin 80 mg : 121.6 mg/dL (3.1 mmol/L)	Simvastatin 20 mg/dL: 104 mg/dL (2.7 mmol/L) Atorvastatin 80 mg/dL: 81.0 mg/dL (2.1 mmol/L) –2.9 mg/dL reduction vs simvastatin	11% reduction in primary endpoint: major coronary events (coronary death, hospitalization for nonfatal acute MI, or cardiac arrest with resuscitation, P=0.07)
SEARCH[7]	6.7 years	Simvastatin 20 mg vs simvastatin 80 mg	Stable CHD at high CV risk (N=12,604)	Both groups: 2.5 mmol/L (38.7 mg/dL)	Simvastatin 80 mg: 2.2 mmol/L -14% reduction (-0.35 mmol/L) vs 20 mg group	6% reduction in the primary endpoint: major vascular events (coronary death, myocardial infarction, stroke, or arterial revascularisation, P=0.10)

MIRACL: Early Intensive Statin treatment

- 3086 pts with UA or non–Q-wave MI randomized to atorvastatin (80 mg/d) or placebo between 24 and 96 hours after hospital admission
- Primary End-point: death, nonfatal MI, cardiac arrest with resuscitation, recurrent symptomatic myocardial ischemia requiring hospitalization

Figure 3. Kaplan-Meier Estimates of Primary Outcomes

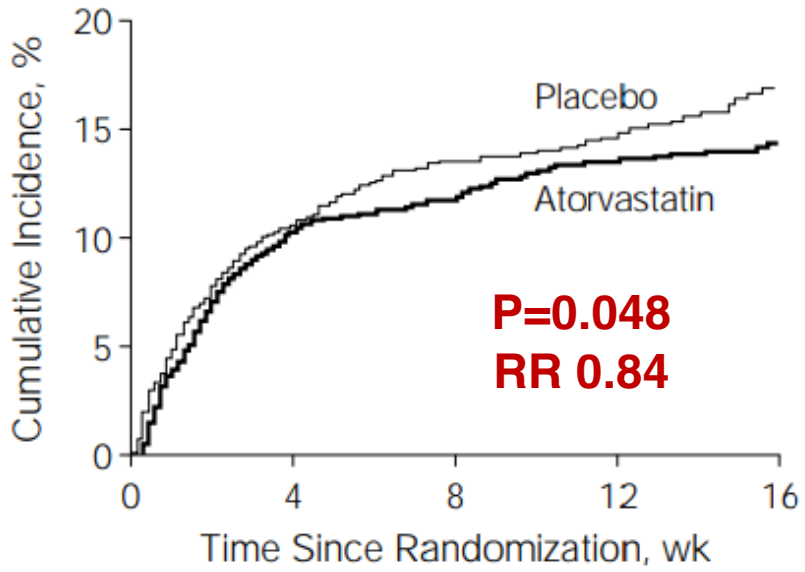
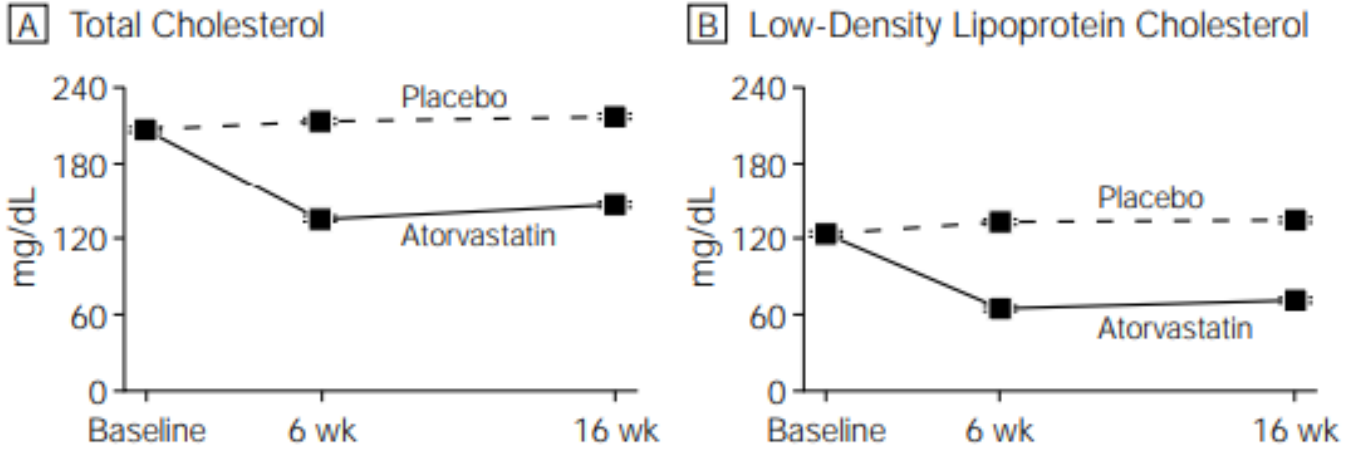


Figure 2. Serum Lipid Levels in Atorvastatin vs Placebo Groups



G.G. Schwartz et al. JAMA 2001;285:1711-1718

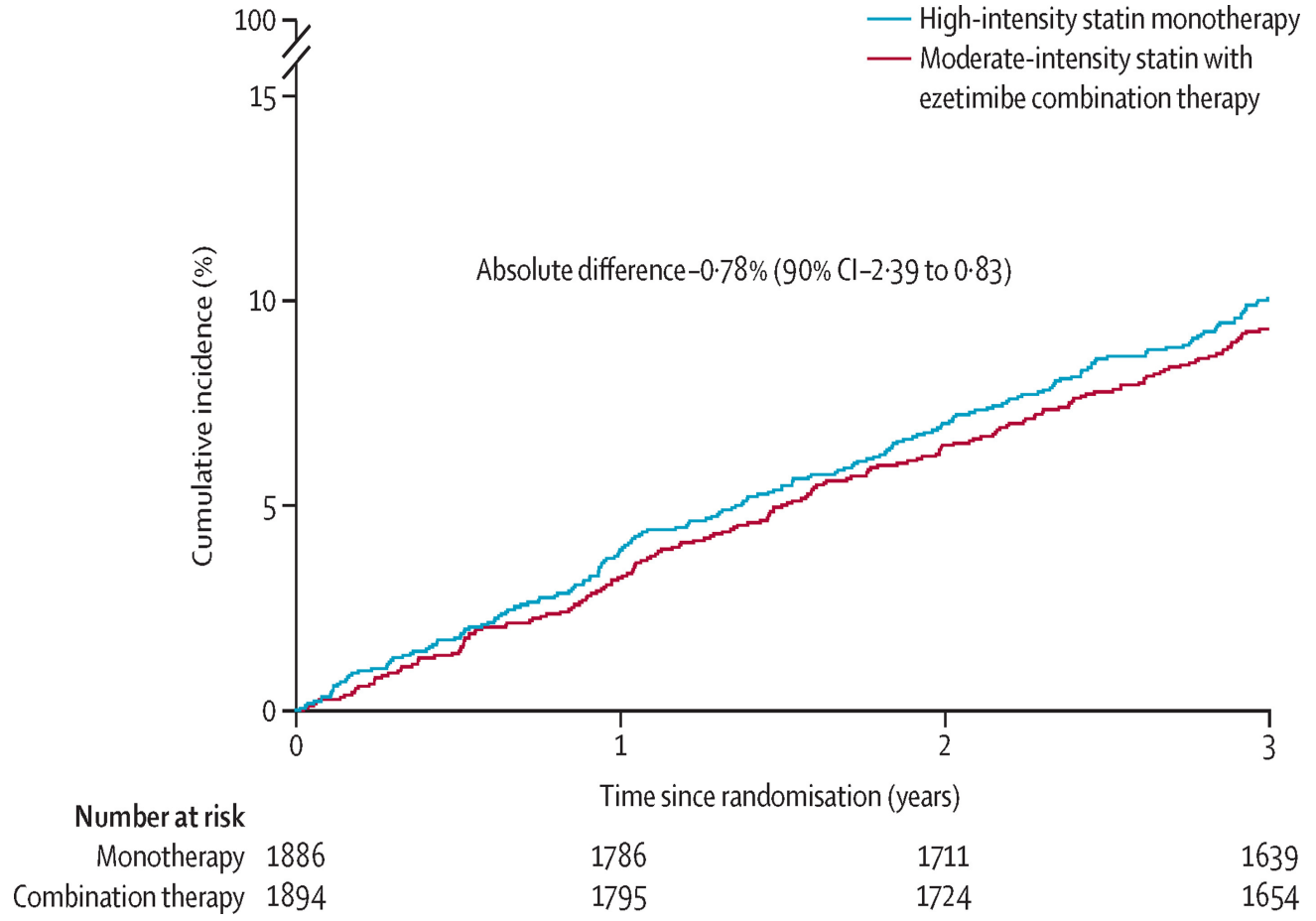
RACING Trial: Rethinking Statin Strategy in ASCVD

Moderate-Intensity Statin Plus Ezetimibe Proven Noninferior to High-Intensity Statin Monotherapy With Better LDL-C Control and Tolerability

Combination therapy was non-inferior for the 3-year composite of CV death, major CV events, or non-fatal stroke

Fewer patients discontinued combination therapy than monotherapy due to side effects (4.8% vs 8.2%; p<0.0001)

More patients achieved an LDL-C <1.8 mmol/L (<70 mg/dL) with combination therapy than with monotherapy after 3 years (72% vs 58%; p<0.0001)



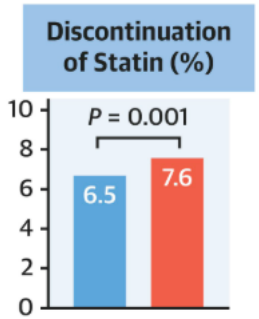
CV, cardiovascular; **LDL-C**, low-density lipoprotein cholesterol.

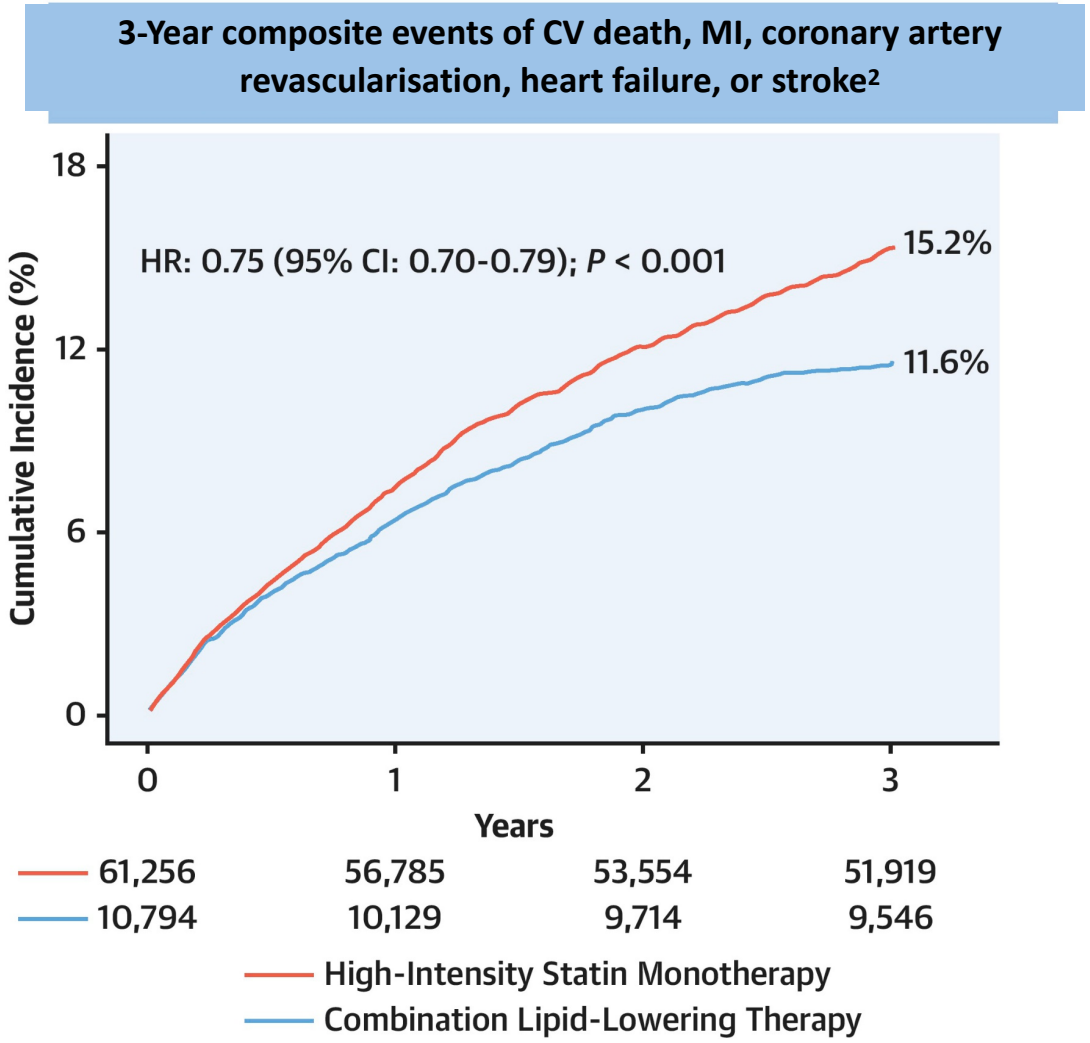
Kim BK, et al. Lancet. 2022;400:380–390.

Combination Lipid-Lowering Therapy in Patients Undergoing Percutaneous Coronary Intervention: RWE

10,794 patients with rosuvastatin 10 mg plus ezetimibe 10 mg (combination lipid-lowering therapy) and 61,256 patients with rosuvastatin 20 mg monotherapy

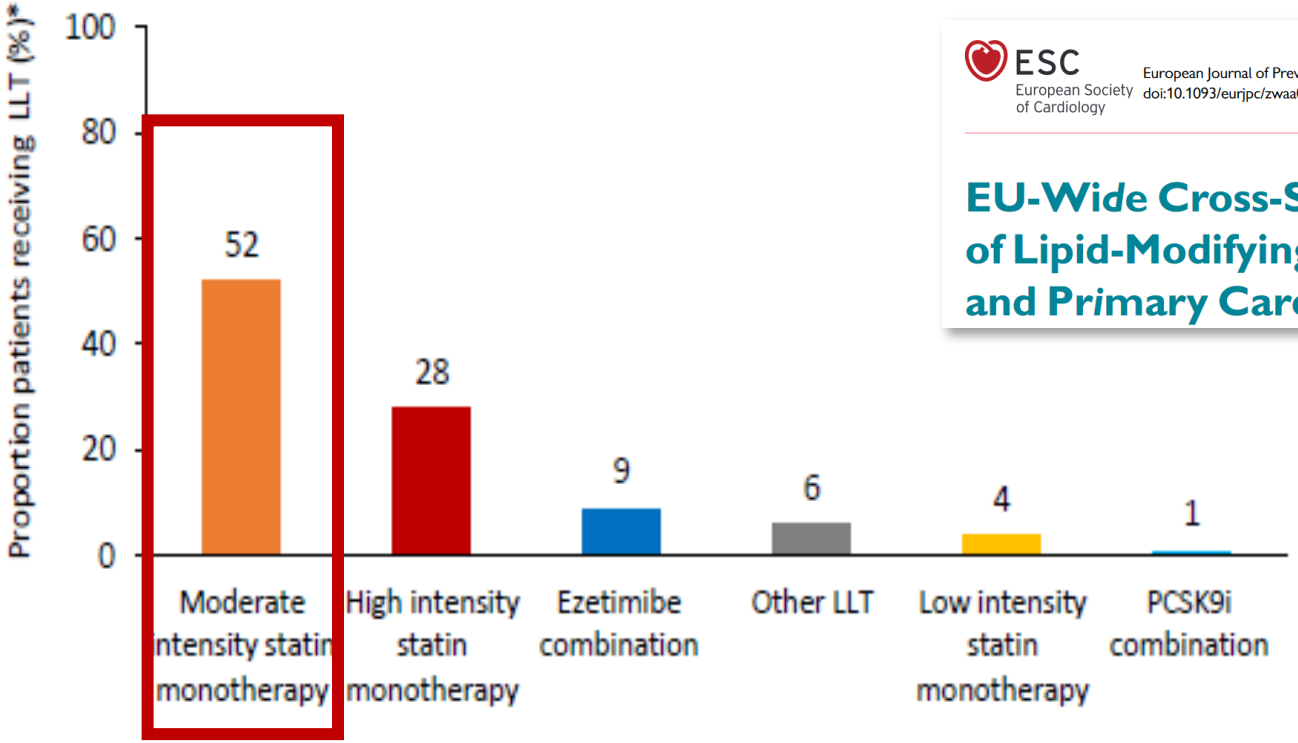
Combination lipid-lowering therapy was associated with a lower occurrence of the primary endpoint (11.6% vs 15.2% for those with high-intensity statin monotherapy; HR: 0.75; 95% CI: 0.70-0.79; P < 0.001)





Seung-Jun Lee et al. *JACC* 2023; 82:401-410.

LO STUDIO DA VINCI (2021) HA MESSO IN LUCE CHE ANCORA POCHI PAZIENTI (~40%) RICEVONO TERAPIE IPOCOL. AD ALTA EFFICACIA



ESC European Society of Cardiology
European Journal of Preventive Cardiology (2021) **28**, 1279–1289
doi:10.1093/eurjpc/zwaa047
FULL RESEARCH PAPER

EU-Wide Cross-Sectional Observational Study of Lipid-Modifying Therapy Use in Secondary and Primary Care: the DA VINCI study

La maggior parte dei pazienti riceve LLT con statine a moderata intensità

- SOLO IL 28% riceve una statina AD ALTA INTENSITÀ
- SOLO IL 9% riceve una COMBINAZIONE CON EZETIMIBE

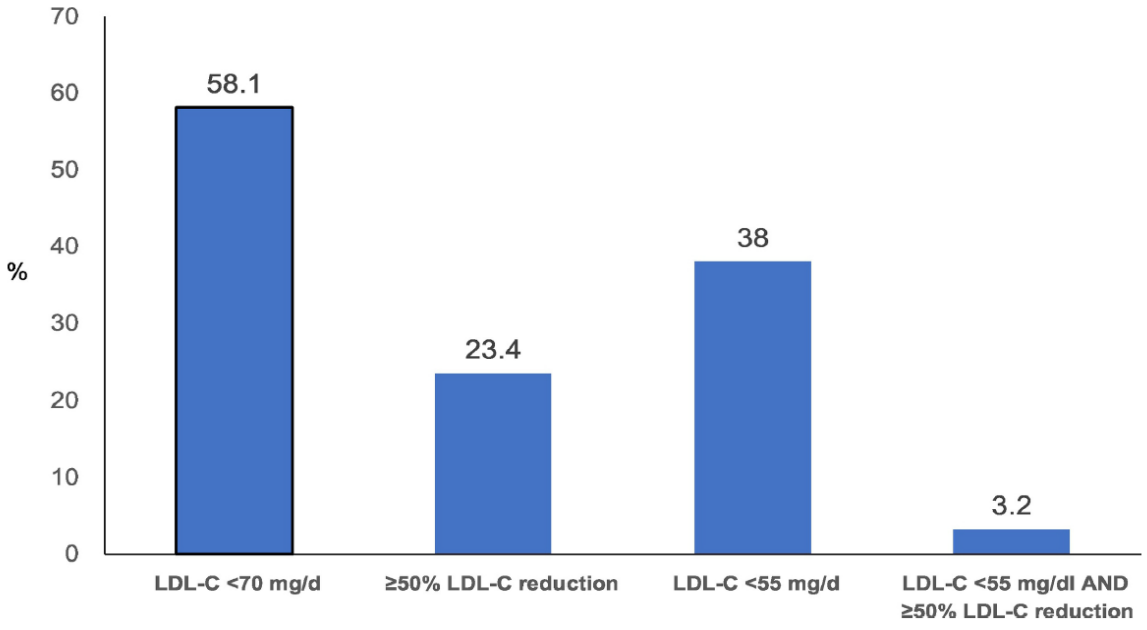
Ray et al. (2021); European Journal of Preventive Cardiology; 28, 1279–1289.

IL REGISTO START CONFERMA QUESTO SCENARIO

Registro Start

Studio osservazionale, prospettico, su 5053 pazienti con malattia cardiovascolare aterosclerotica.

4751 pazienti (94%) a rischio molto alto



Guideline ESC/EAS 2016

Guideline ESC/EAS 2019

SOLO NEL 4,8% dei casi è stata prescritta l'**associazione statina ad alta intensità/ezetimibe**

SOLO IL 3,2% dei pazienti **ha raggiunto il target terapeutico** definito dalle linee guida ESC/EAS 2019 (C-LDL <55 mg/dl e riduzione C-LDL ≥50%)

De Luca et al. (2020); Int J Cardiol; 316: 229-235.

The SANTORINI Study

LDL-C Levels and patients achieving target at baseline and at the 1-year follow-up

SANTORINI ITALIA

	Overall (N=1850)		High risk (N=436)		Very high risk (N=1414)	
	Baseline	1-year follow-up	Baseline	1-year follow-up	Baseline	1-year follow-up
LDL-C, mg/dL, mean (SD)	97.9 (49.3)	73.1 (35.1)	110.1 (54.4)	89.1 (40.1)	94.2 (46.9)	68.2 (31.9)
Patients at LDL-C goal, %	**20.8** →	**34.9**	**22.3**	**33.9**	**20.4**	**36.1**

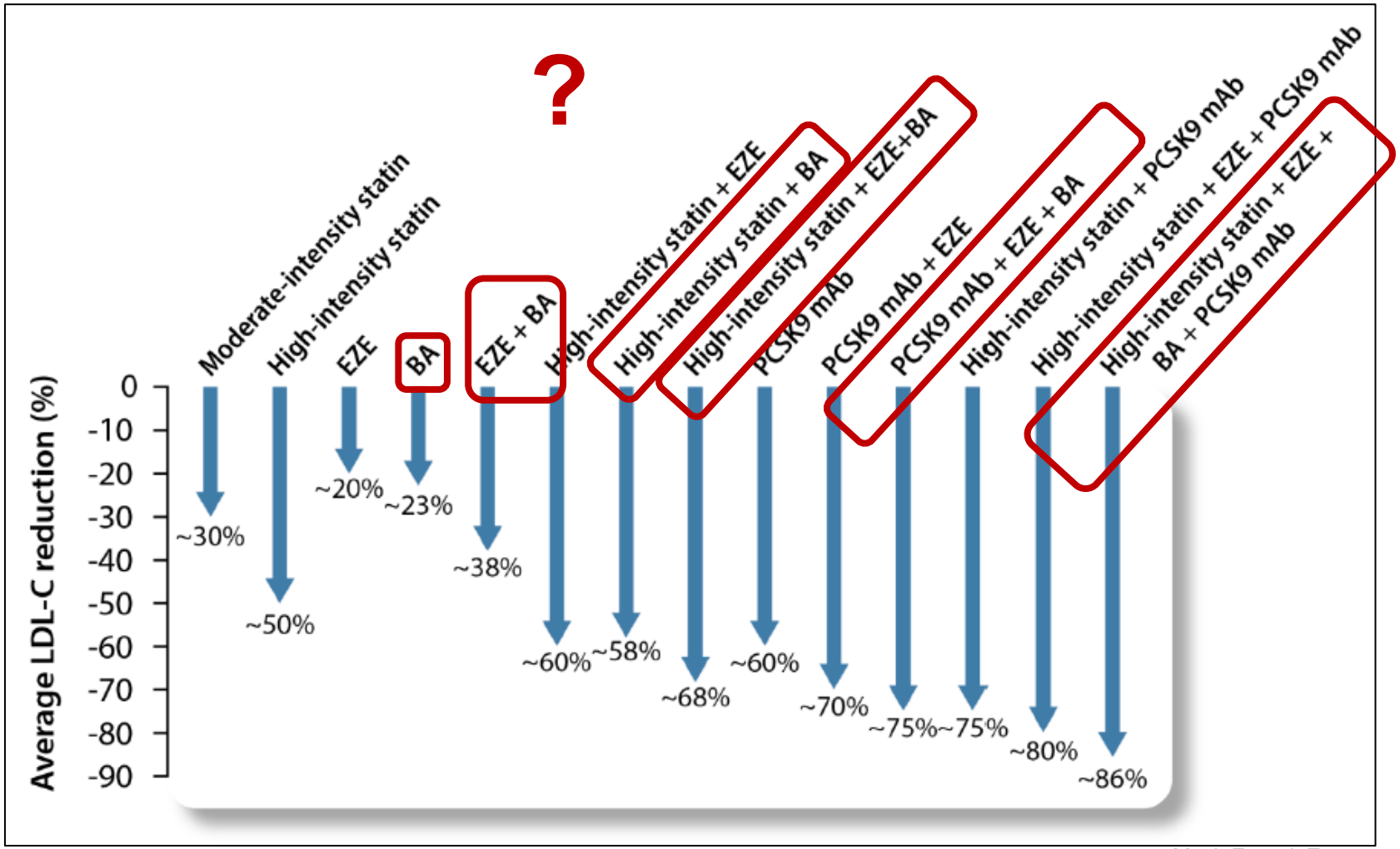
- **Overall, LDL-C was reduced in both risk groups at follow-up versus baseline**
- **Among patients with available LDL-C data, more patients reached their LDL-C goals at follow-up versus baseline**

Combination therapy rather than monotherapy should be considered as standard of care for high- and in particular for very high-risk patients

LDL-C, low-density lipoprotein cholesterol; SD, standard deviation

Presented by Arca M et al. at SIC (Italian Society of Cardiology) Congress, Rome December, 2023

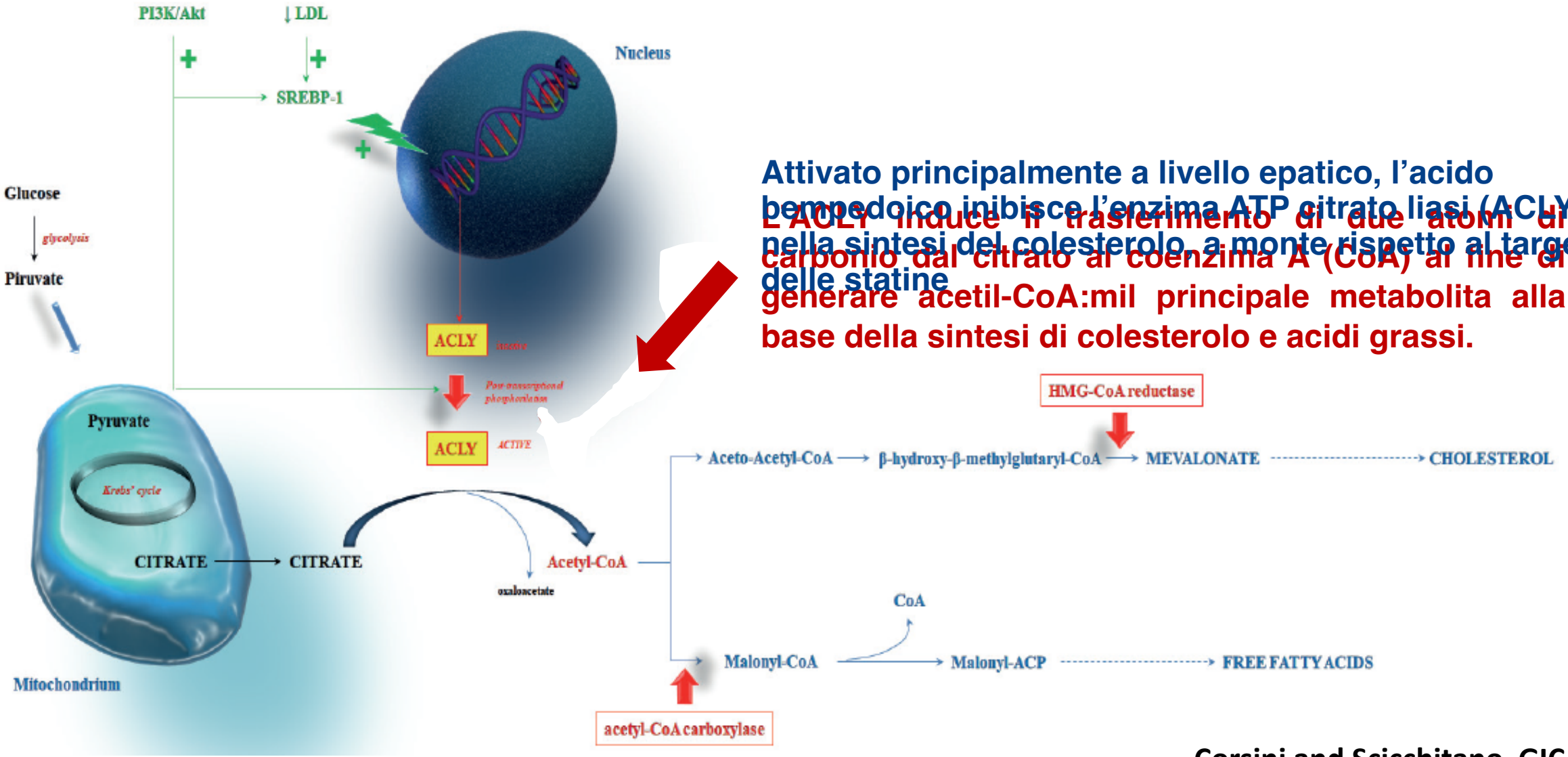
2025 Focused Update of the 2019 ESC/EAS Guidelines:
Riduzione media dei livelli di LDL-C con diverse terapie farmacologiche con comprovati benefici cardiovascolari



Mach F. et al, European Heart Journal (2025) 00, 1–20

EZE, Ezetimibe; **BA**, Bempedoic Acid; **PCSK9 mAB,** Proprotein Convertase Subtilisin/Kexin type 9 Monoclonal Anti Body; **LDL-C,** low-density lipoprotein cholesterol
ESC, European Society of Cardiology; **EAS**, European Society of Lipidology

Adenosin-trifosfato citrate liasi (ACLY) ed effetti dell'acido bempedoico sul metabolismo lipidico:

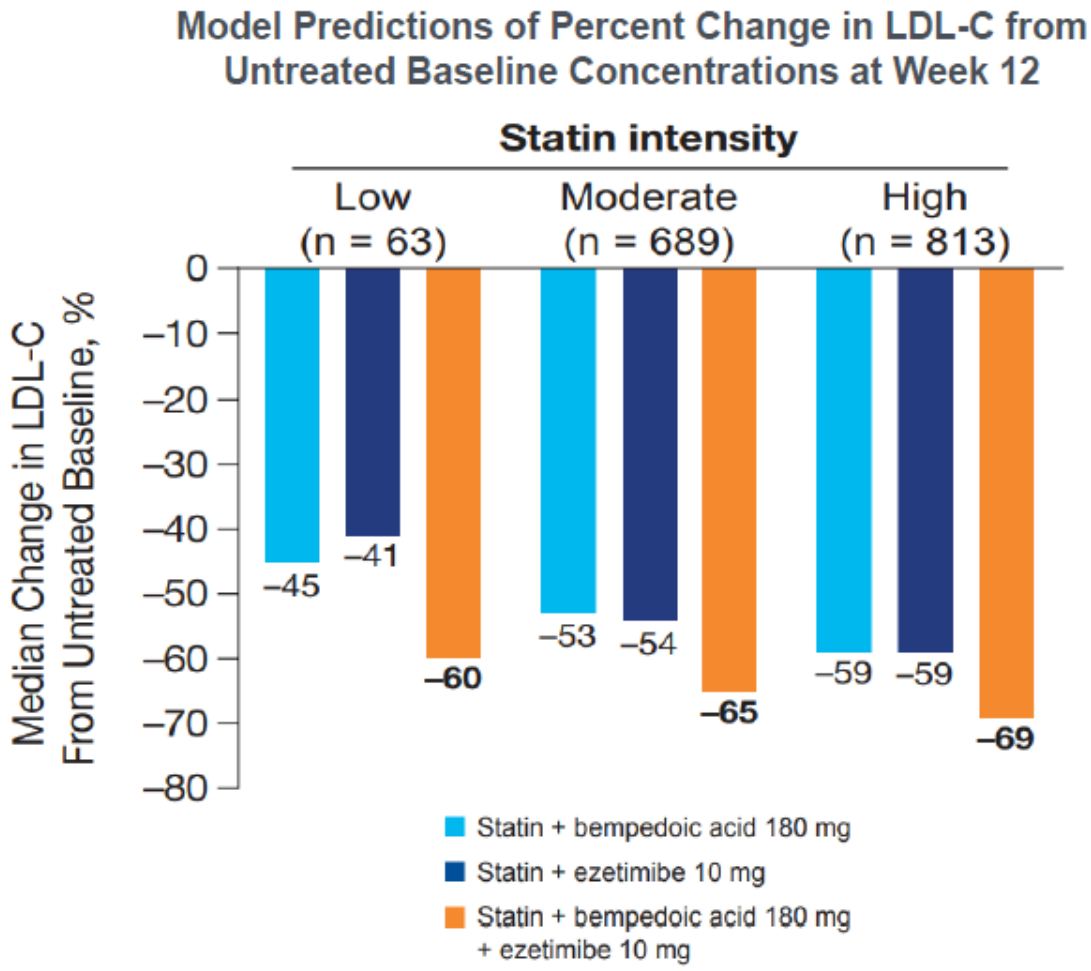


Attivato principalmente a livello epatico, l'acido bempedoico inibisce l'enzima ATP citrato liasi (ACLY) nella sintesi del colesterolo, a monte rispetto al target delle statine

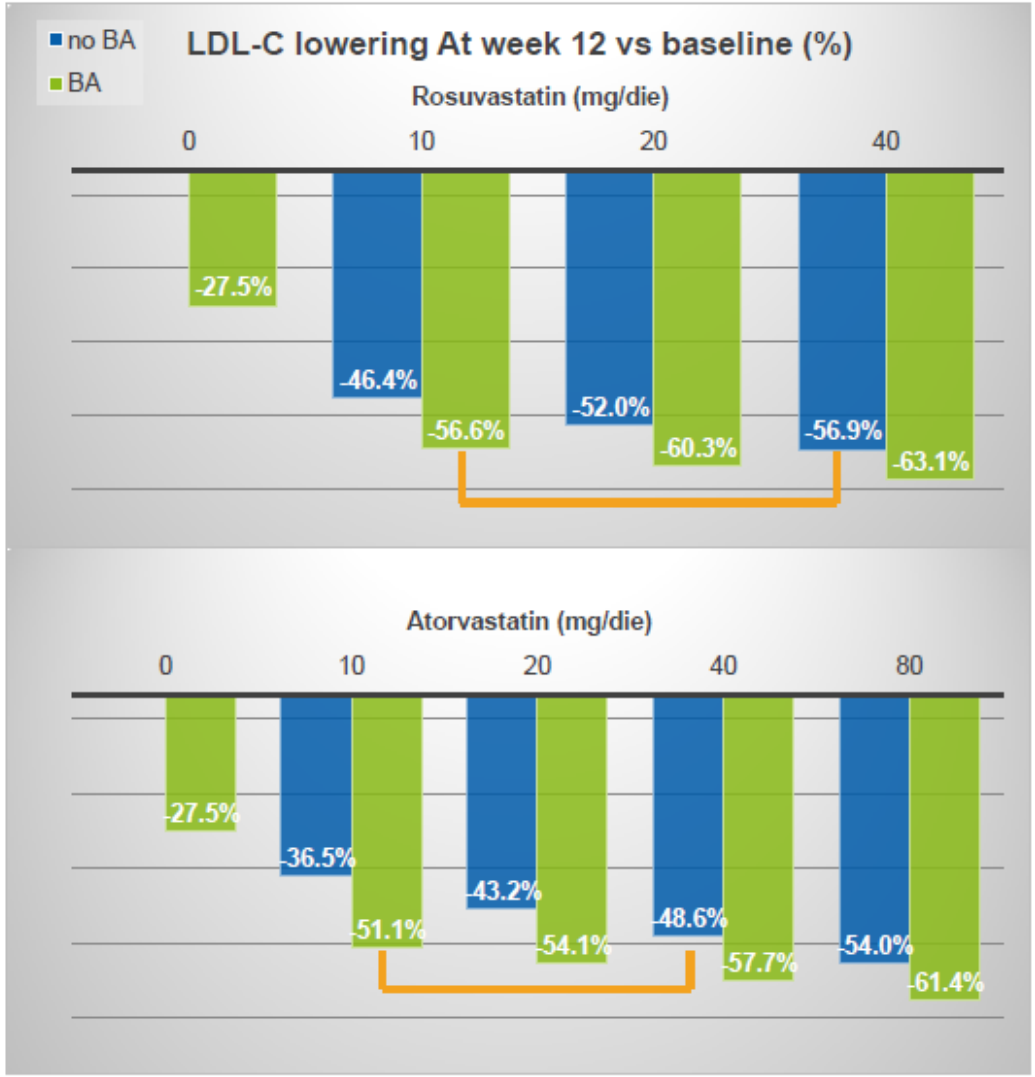
L'ACLY induce il trasferimento di due atomi di carbonio dal citrato al coenzima A (CoA) al fine di generare acetil-CoA:mil principale metabolita alla base della sintesi di colesterolo e acidi grassi.

Corsini and Scicchitano, GIC, 2021

Bempedoic acid impact on lipid control



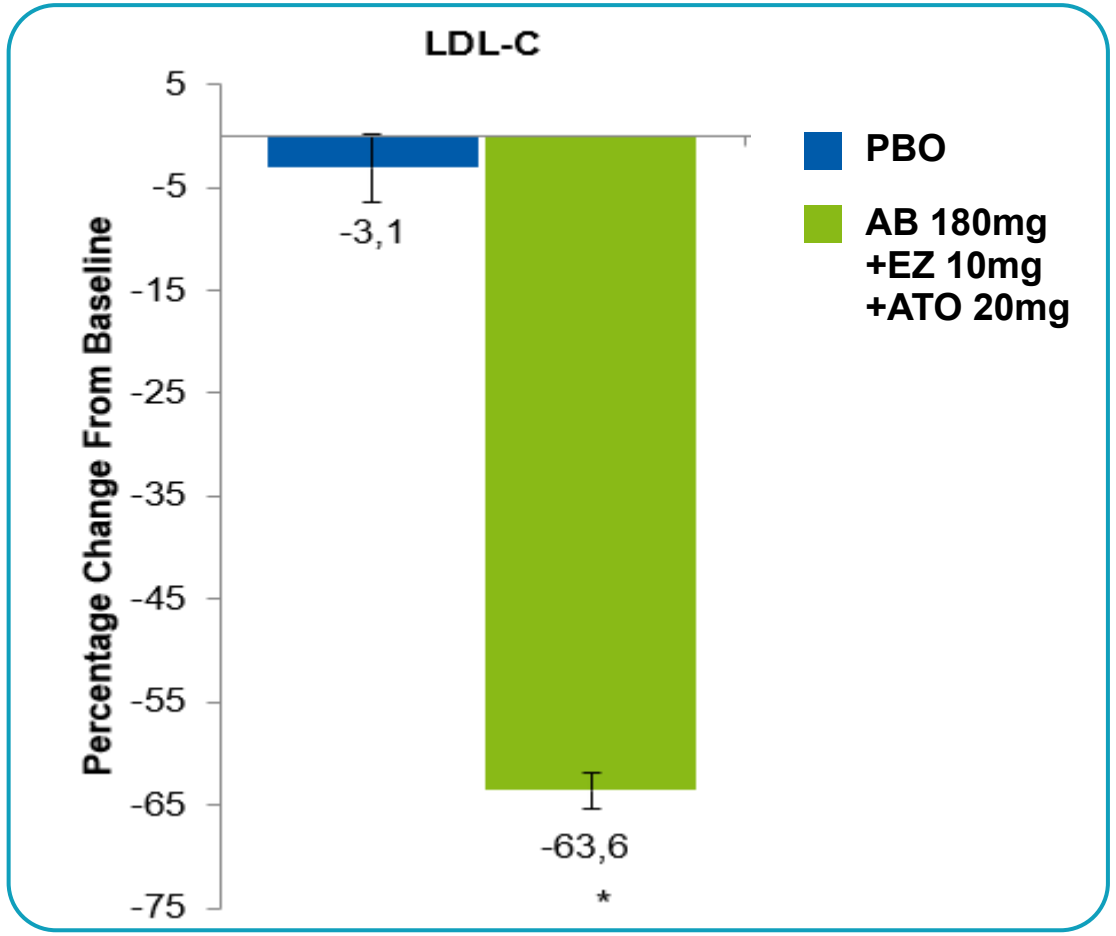
Epling D, et al. Presented at ASCPT Annual Meeting 2023, 22–24 March 2023



Jadhav SB et al,
European Heart Journal - Cardiovascular Pharmacotherapy

Triple Add-on: Bempedoic Acid, Ezetimibe e Atorvastatin 20 mg

A phase 2 study showed that the *add-on* therapy lowers LDL-C levels more than 60% compared to baseline



At week 6:

- **95% of patients reduce their LDL-C ≥50% compared to baseline**
- **90% of patients showed LDL-C below 70 mg/dL**
- **58.5% of patients showed LDL-C below 55 mg/dL**

Triple Oral Combination

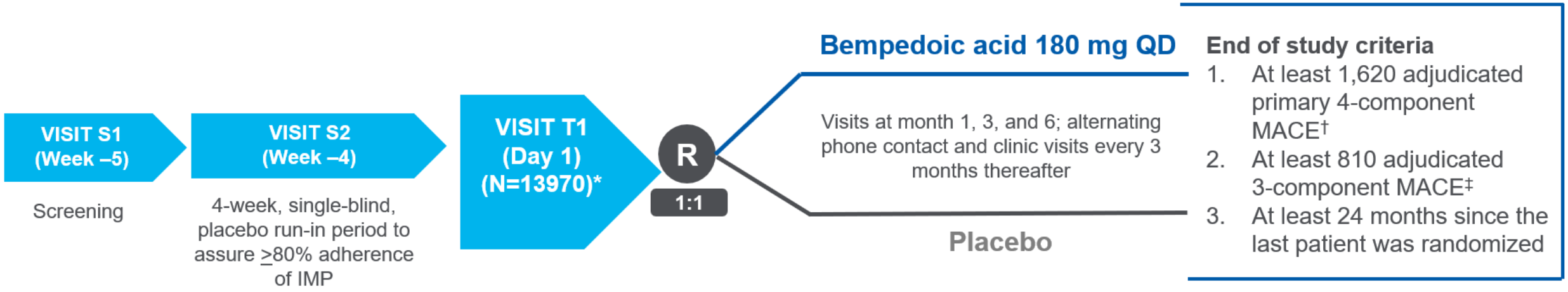
A combination strategy offering an effective reduction in cholesterol levels for high-risk patients who fail to reach their treatment target with conventional therapies.

Least squares mean percentage changes from baseline to Week 6. Values are least-squares mean±SE
*p < .001 for the comparison of triple therapy vs placebo

LDL-C, low-density lipoprotein cholesterol; **TC**, total cholesterol.

Rubino J. et al., Atherosclerosis, 2020, https://doi.org/10.1016/j.atherosclerosis.2020.12.023

Bempedoic Acid: CLEAR OUTCOME



Objective

To evaluate whether long-term treatment with bempedoic acid versus placebo reduces the risk of MACE-4 in patients with, or at high risk for, CVD who are statin intolerant

Composite primary efficacy endpoint:

Time to first occurrence of MACE (composite of CV death, nonfatal MI, nonfatal stroke, or coronary revascularization)

Key secondary endpoints:

Time to first occurrence of:

- The composite of CV death, nonfatal MI, nonfatal stroke (MACE-3)
- Fatal + nonfatal MI
- Coronary revascularization
- Fatal + nonfatal stroke

Time to:

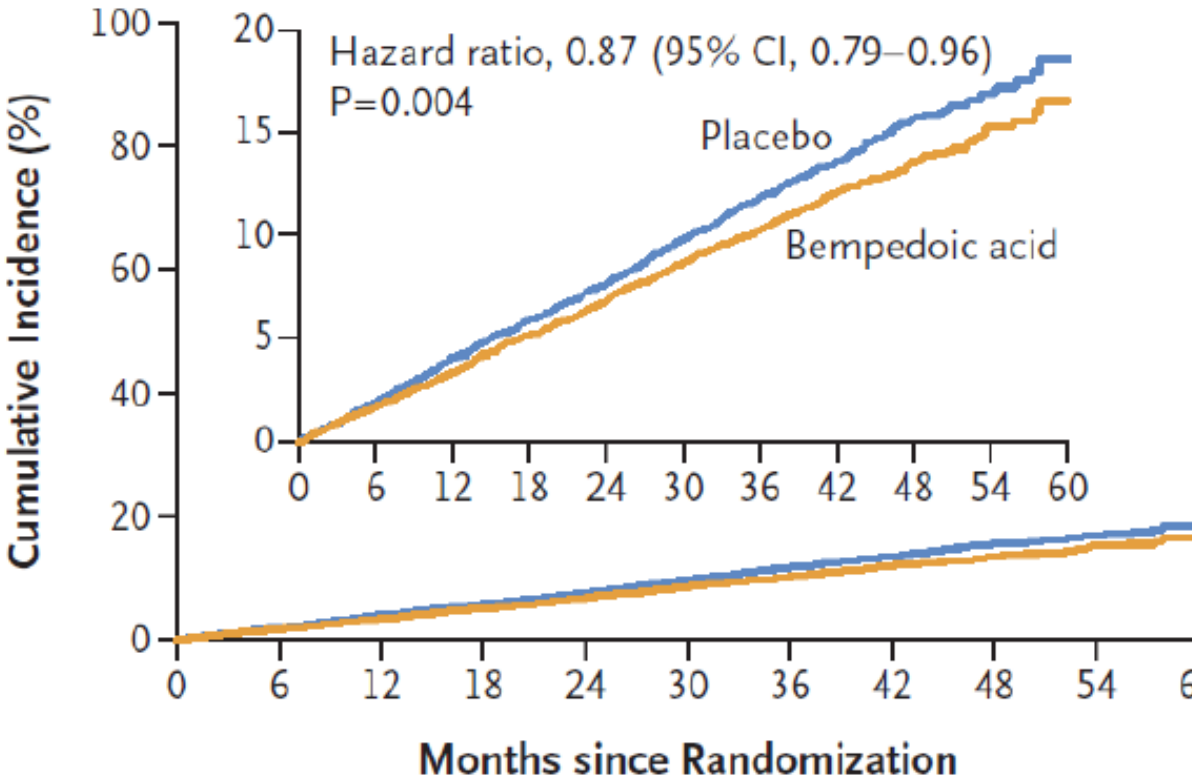
- CV death
- All-cause mortality

Sequential testing

*Enrolment of high-risk patients without a history of atherosclerotic CVD was capped at 30%. †Including CV death, nonfatal MI, nonfatal stroke, or coronary revascularisation. ‡Including CV death, nonfatal MI, or nonfatal stroke. **CVD**, cardiovascular disease; **HbA1c**, haemoglobin A1c; **IMP**, investigational medicinal product; **LDL-C**, low-density lipoprotein cholesterol; **MACE**, major adverse cardiovascular event; **MI**, myocardial infarction, **QD**, once daily

Nissen SE, et al. N Engl J Med. 2023 doi: 10.1056/NEJMoa2215024

CLEAR Outcome: 4-P MACE



Bempedoic acid (11.7%) vs. placebo (13.3%)[1]

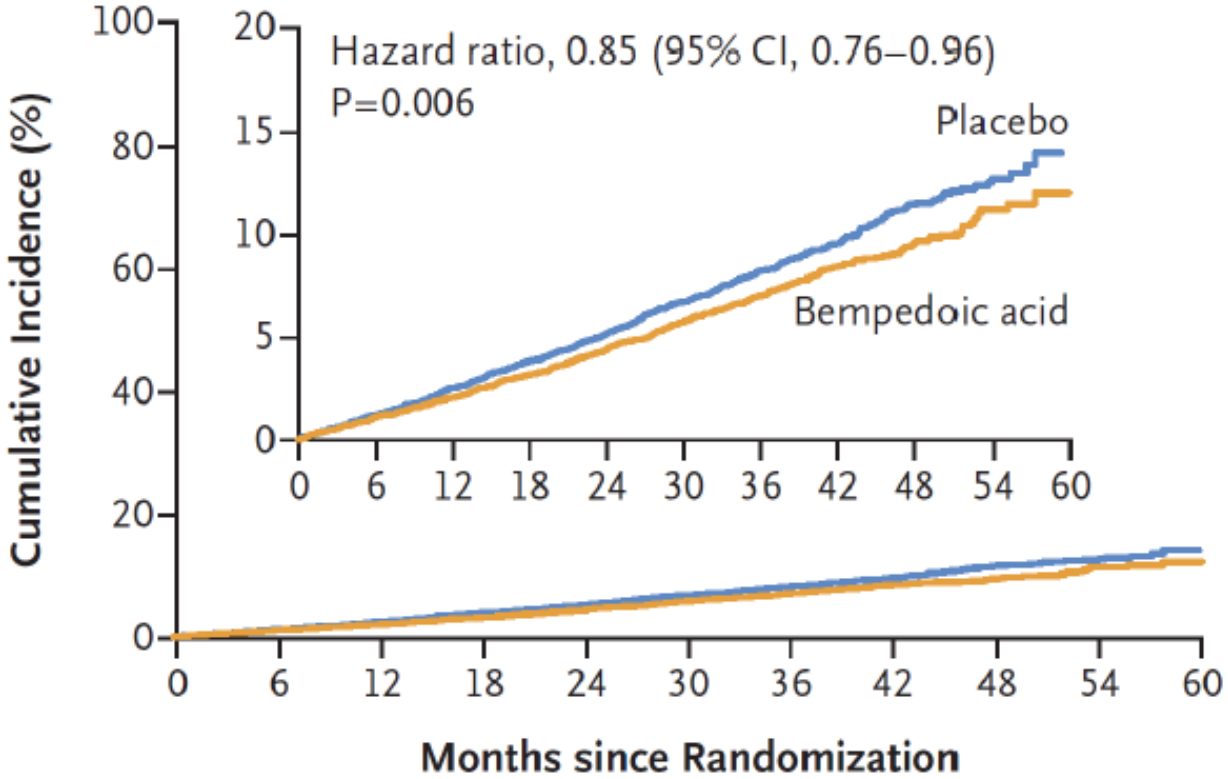
1.6% ARR

HR 0.87, 95% CI: 0.79–0.96, P=0.004[1]

13% RRR[1]

NNT 63[2]

CLEAR Outcome: 3-P MACE



Bempedoic acid (8.2%) vs. placebo (9.5%)[1]

1.3% ARR

HR 0.85, 95% CI: 0.76–0.96, P=0.006[1]

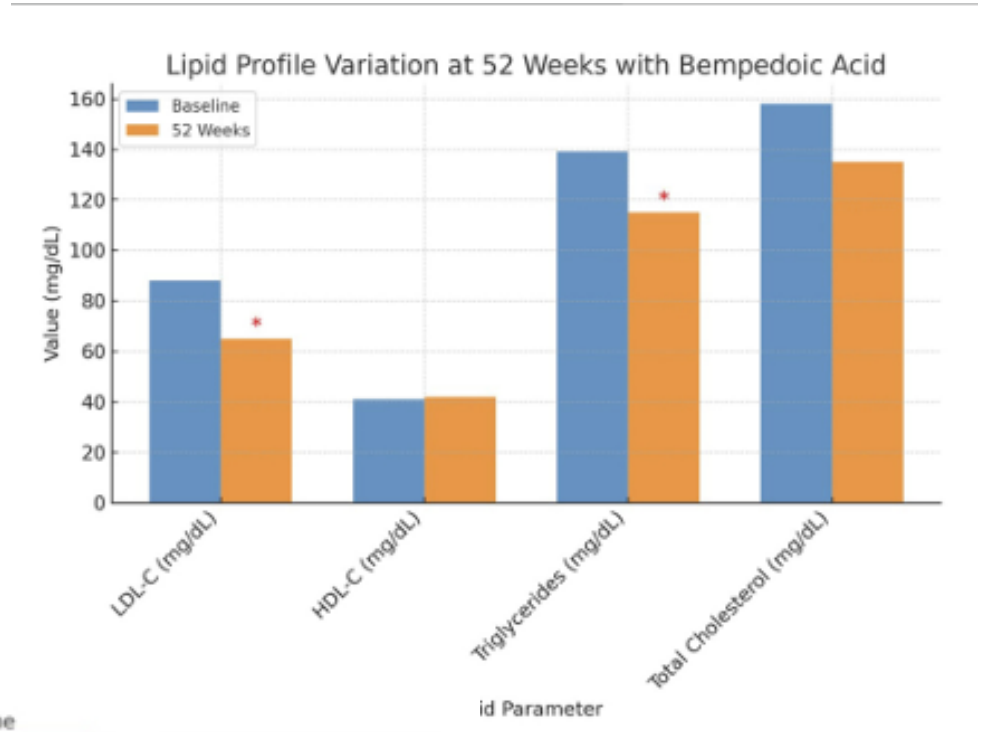
15% RRR[1]

NNT 72[2]

Nissen SE, et al. N Engl J Med. 2023 doi: 10.1056/NEJMoa2215024

Evaluation of bempedoic acid in elderly patients: real-world evidence from the REALIST study

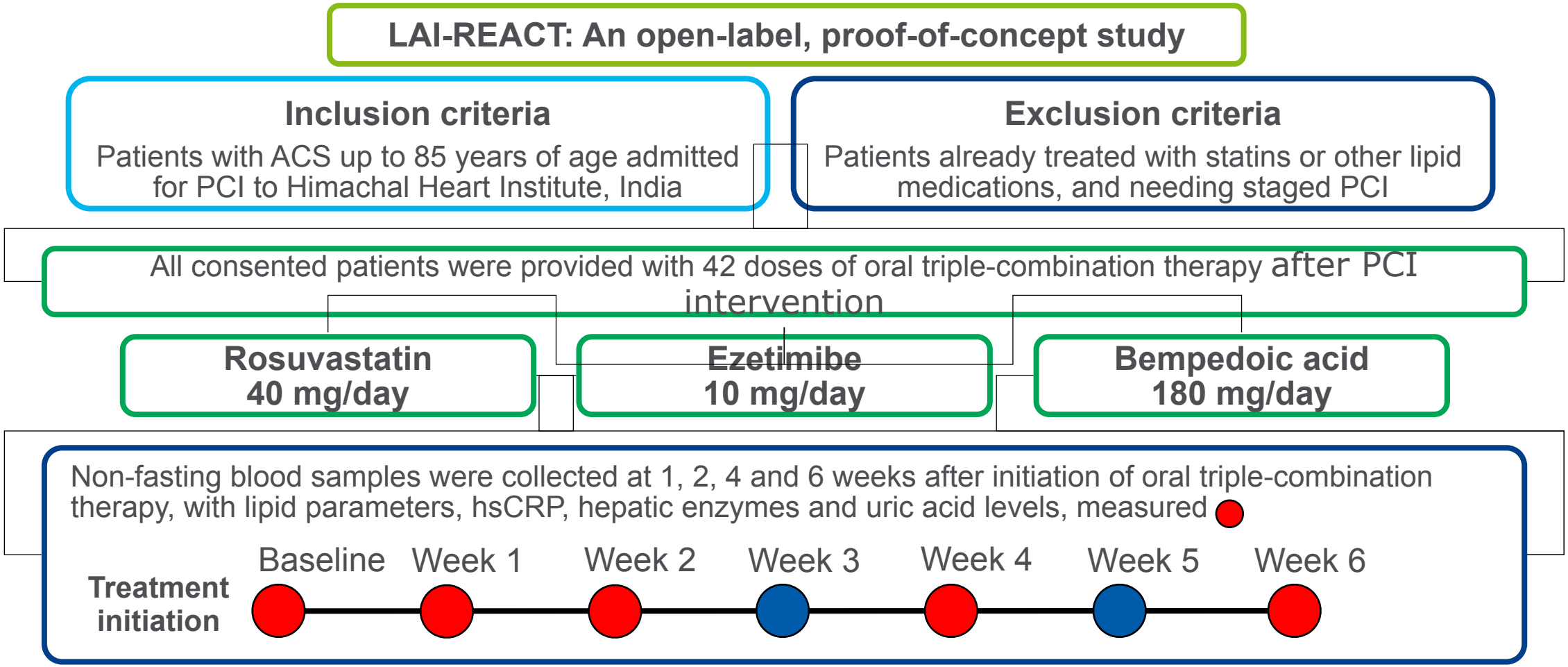
Characteristic	Baseline values
Age (years)	>81 (inclusion criterion)
Female (%)	30%
BMI (kg/m^2)	25 ± 6
Coronary artery disease (%)	94%
Peripheral artery disease (%)	14.8%
Cerebrovascular disease (%)	5.5%
Diabetes (%)	72.2%
Hypertension (%)	90.7%
Statin use (%)	72.2%
Ezetimibe use (%)	27.8%
LDL-C (mg/dL) ±SD	88 ± 8
HDL-C (mg/dL) ±SD	41 ± 5
Triglycerides (mg/dL) ±SD	139 ± 21
Total cholesterol (mg/dL) ±SD	158 ± 17
Creatinine (mg/dL) ±SD	1.2 ± 0.8
GFR (mL/min/1.73m^2) ±SD	58 ± 15
ALT (U/L) ±SD	31 ± 8
AST (U/L) ±SD	33 ± 6
Uric acid (mg/dL) ± SD	5.9 ± 2.7



Muscoli S. et al, Frontiers in Aging, 2026

Immediate Use of Oral Triple-Combination Therapy in Patients with ACS

LAI-REACT Study



ACS, acute coronary syndrome; **hs-CRP**, high-sensitivity C-reactive protein; **LAI-REACT**, Lipid Association of India Recommended Early and aggressive lipid lowering in ACS with triple Combination Therapy; **PCI**, percutaneous coronary intervention

Mahajan K, et al. J Clin Lipidol. 2024; 18,5: e867-e872

Immediate Use of Oral Triple-Combination Therapy in Patients with ACS

LAI-REACT Study

To examine if LDL-C would be rapidly and safely reduced in patients with ACS, oral triple-combination therapy with rosuvastatin 40 mg, ezetimibe 10 mg and bempedoic acid 180 mg was evaluated in 122 Indian patients with ACS (after PCI) over 6 weeks.

The proportion of patients achieving LDL-C ≤55 mg/dL at 4 weeks after treatment initiation was >75%

LDL-C lowering with oral triple-combination therapy was comparable to the reported efficacy of high-intensity statins in combination with PCSK9i,[1,2] and it was well generally tolerated.

Reduction in LDL-C concentration and LDL-C goal attainment following oral triple-combination therapy[3]

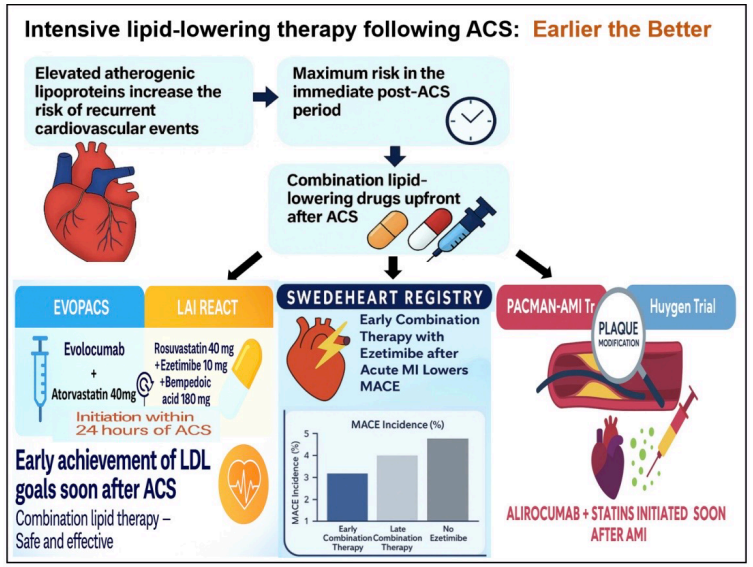
Parameter (N=122)	Baseline	1 week	2 weeks	4 weeks	6 weeks
LDL-C (mg/dL), mean ± SD	115.6 ± 35.5	48.9 ± 18.2*	44.3 ± 17.1*	44.1 ± 16.6*	45.6 ± 16.5*
Percentage (%) reduction in LDL-C	-	57.7	61.7	61.9	60.6
Proportion (%) of patients with LDL-C <55 mg/dL† (ESC goal)[4]	2.4	72.8	79.8	78.5	73.3
Proportion (%) of patients with LDL-C <70 mg/dL (ACC goal)	8.2	90.3	92.2	92.6	86.6
Proportion (%) of patients with ApoB <65 mg/dL	13.1	-	-	73.9‡	-

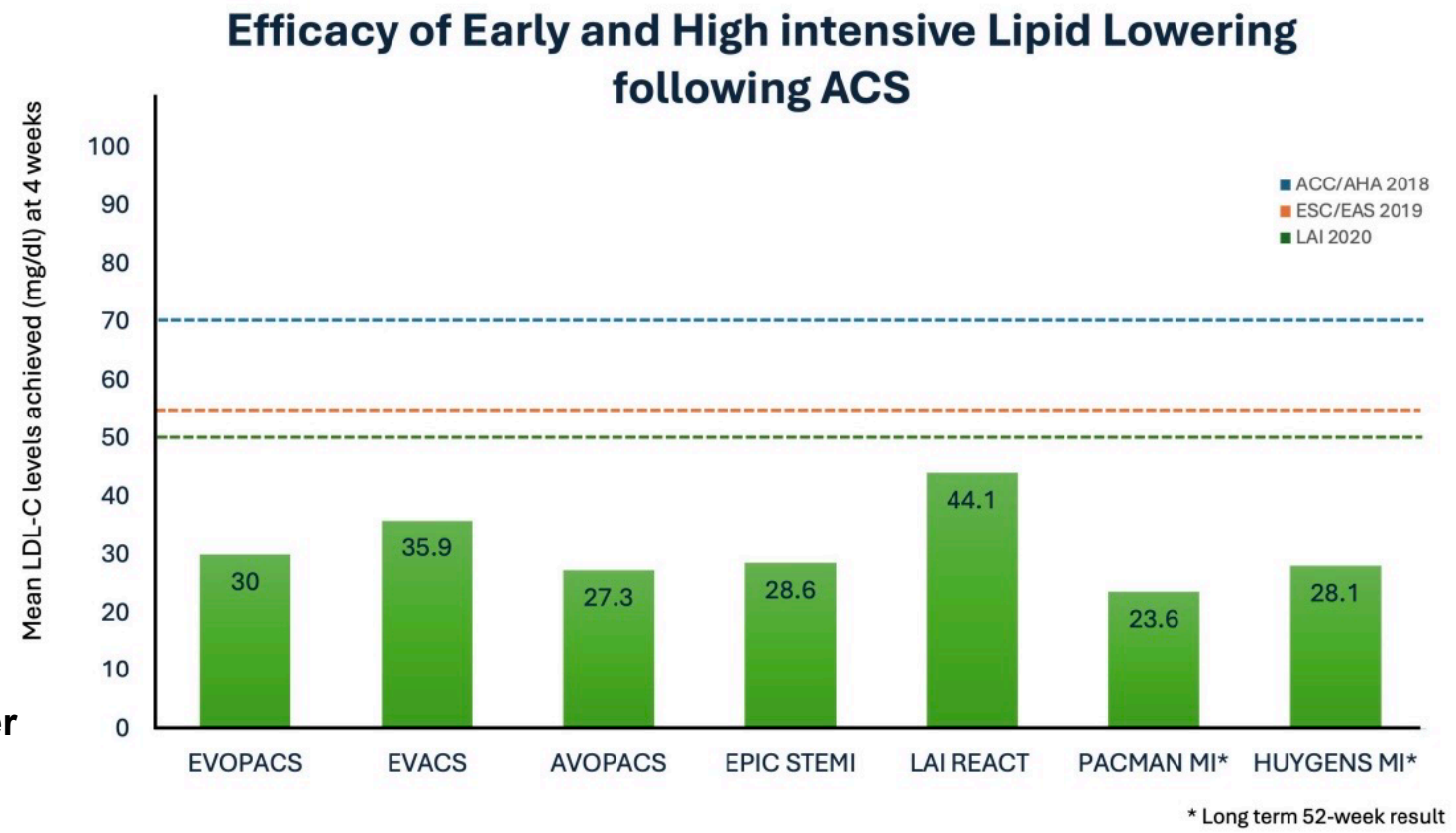
*p<0.001 compared to baseline. †ACC goal as per 2022 expert consensus for very high-risk patients.[5]
‡Apo-B measurement at 4 weeks was repeated in 87 patients only

ACC, American College of Cardiology; **ACS**, acute coronary syndrome; **ApoB**, apolipoprotein B; **ESC**, European Society of Cardiology; **HDL-C**, high-density lipoprotein cholesterol; **LDL-C**, low-density lipoprotein cholesterol; **PCI**, percutaneous coronary intervention; **PCSK9i**, proprotein convertase subtilisin/kexin type-9 inhibitor

1. Koskinas KC, et al. J Am Coll Cardiol. 2019;74(20):2452–62; **2.** Leucker TM, et al. Circulation. 2020;142(4):419-1; **3.** Mahajan K, et al. J Clin Lipidol. 2024;<vol and page no. to be added> **4.** Mach F, et al. Eur Heart J. 2020;41(1):111–88; **5.** Jones JE, et al. J Clin Med. 2023;12(23):7432

Intensive Lipid-Lowering Therapy Following Acute Coronary Syndrome: The Earlier the Better





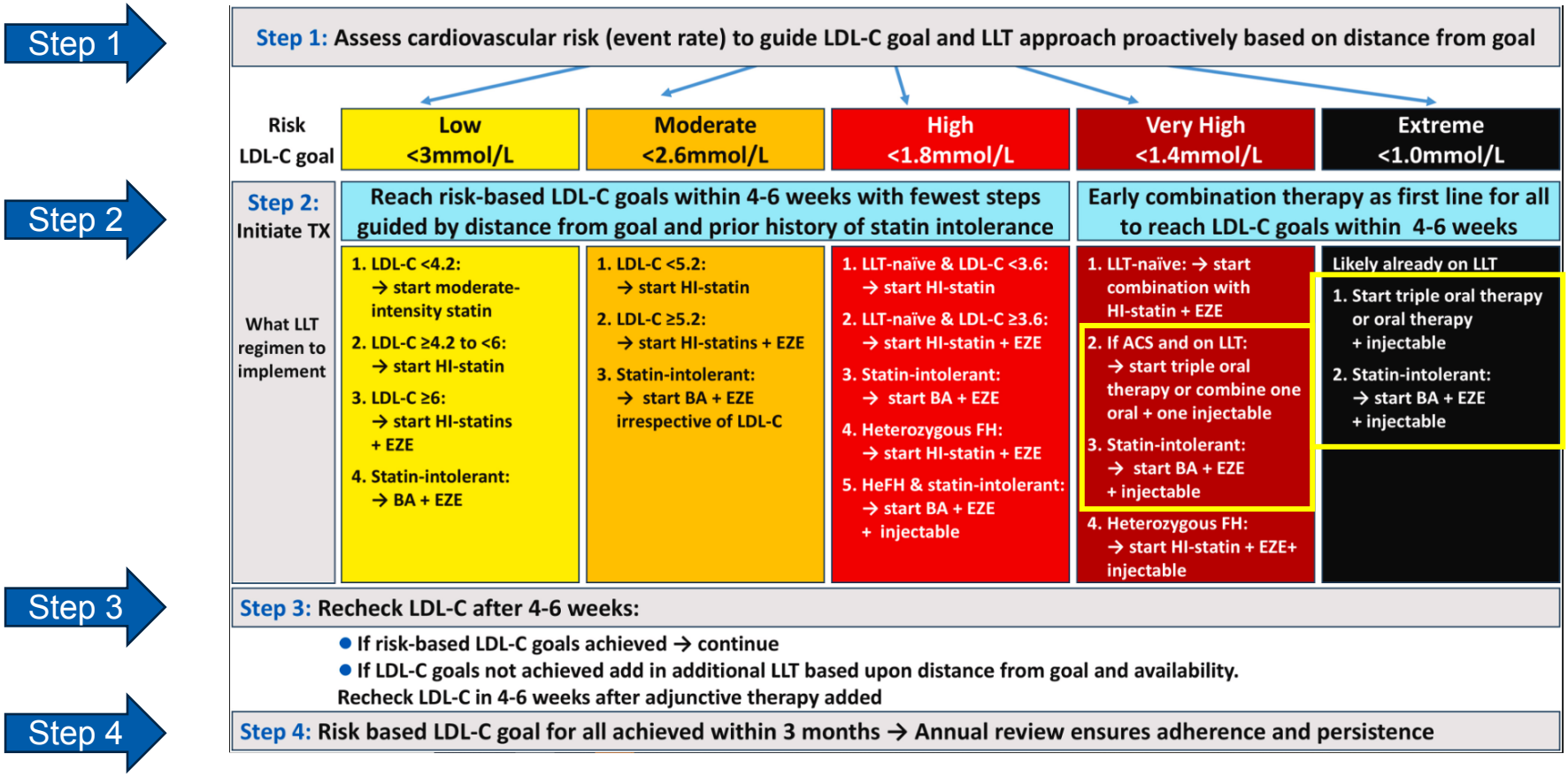
Access limitations to advanced therapies, particularly PCSK9 inhibitors due to cost constraints, further hinder goal attainement.

Triple REB therapy quickly and effectively lowers LDL-C after ACS, with significant reductions seen in one week and maintained for six weeks.

REB, Rosuvastatin 40mg+Ezetimibe+Bempedoic Acid

Pradham et al., J. Cardiovasc. Dev. Dis. 2025, 12, 300

Approach for lipid-lowering treatment to achieve risk-based LDL-C goals.



"In patients with very hight and extreme risk start with a triple oral therapy or oral therapy plus injectable"

Ray et al Atherosclerosis 413 (2026) 120636