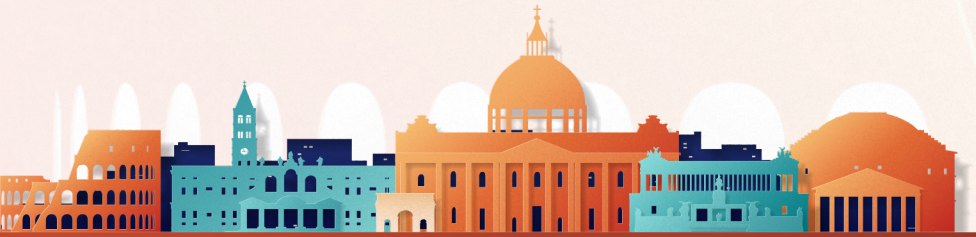
PLACE 2026
PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE

CONGRESSO
ROMA, 25 - 27 Giugno 2026

Dislipidemie 2026: dalle Linee Guida alla pratica clinica

Prof. Stefano Carugo



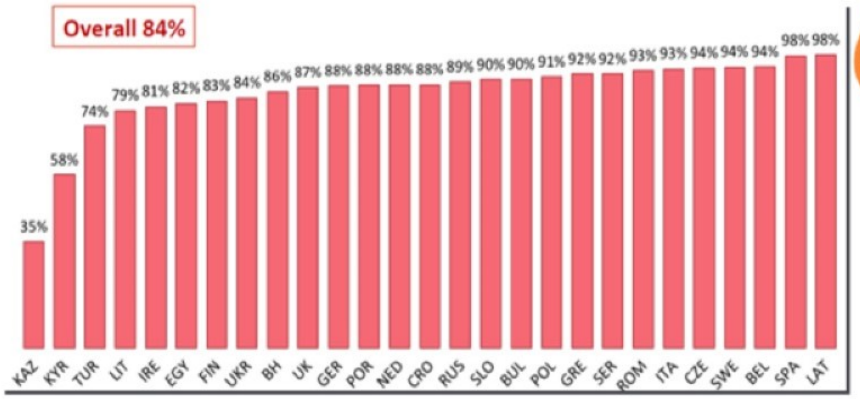
Troppe Linee Guide

Il mondo reale è diverso

Insights From EUROASPIRE V
LDL-C

Patients with CAD at LDL-C goal = 32%, despite most using LLT[a]

Use of LLT*[b]



LDL-C at Goal (< 1.8 mmol/L [< 70 mg/dL]) on LLT*[a,c]

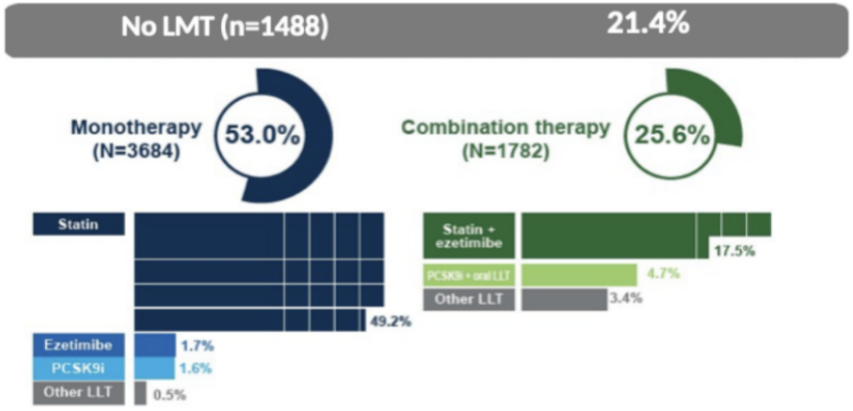
*Standardized for age and sex.

a. Kotseva K, et al. *Eur J Prev Cardiol*. 2019;26:824-835; b. Presented at: EAS Congress 2018; c. Johansson C. EAS2018 Late Breaking Clinical Trial: EUROASPIRE V. May 2018.

RAGGIUNGIMENTO DEI TARGET DI C-LDL NEL MONDO REALE

SANTORINI

Characteristic	Overall (N=9044)	No ASCVD (N=2089)	ASCVD (N=6954)
Male, n (%)	6563 (72.6)	1218 (58.3)	5345 (76.9)
Age, years, mean (SD)	65.3 (10.9)	62.5 (12.1)	66.1 (10.4)
LDL-C, mean (SD), mmol/L	2.4 (1.21)	2.8 (1.37)	2.3 (1.13)
LDL-C, mg/dL	**93**	**108**	**89**
LDL-C at goal, n (%)	1821 (20.1)	1438 (20.7)	383 (18.3)



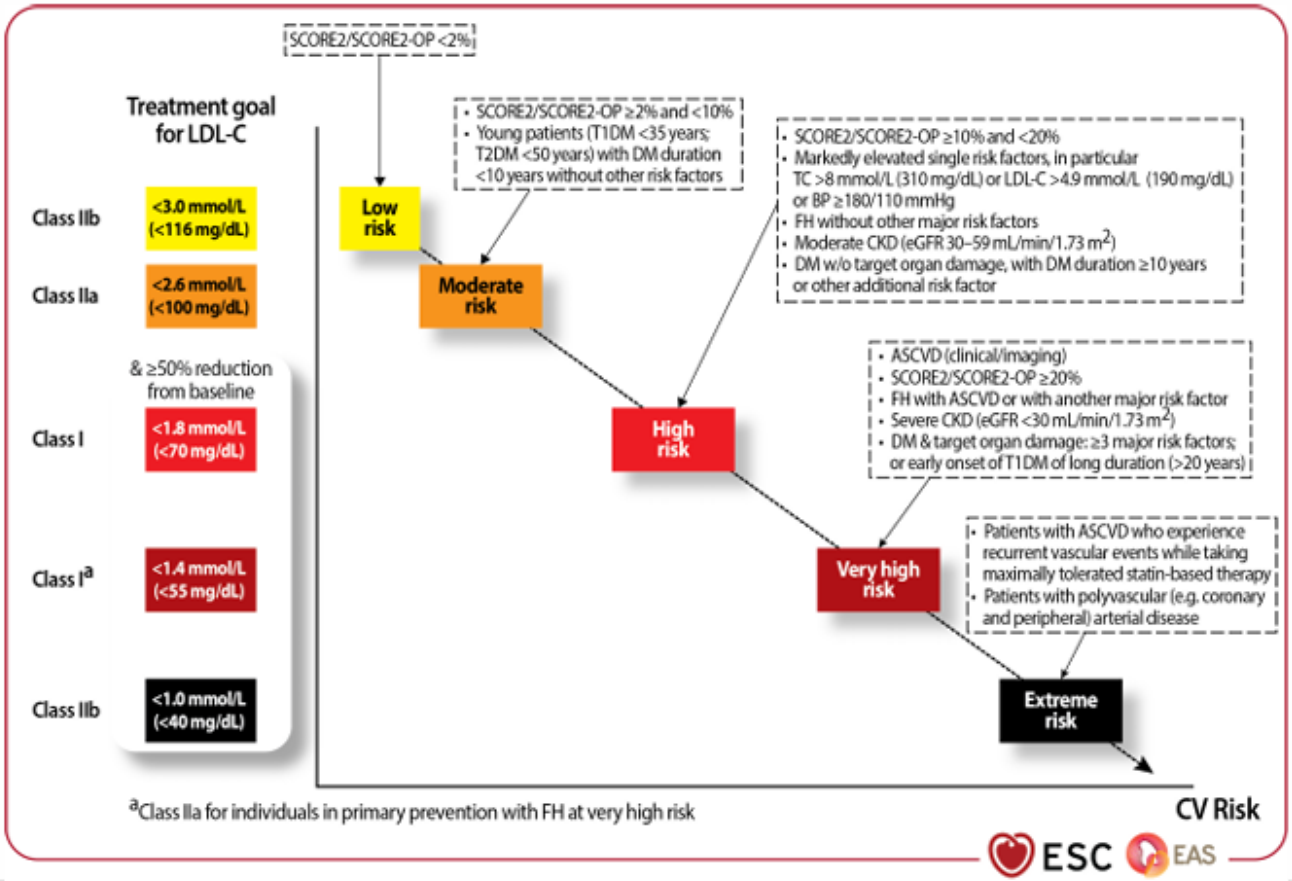
Ray, KK et al. ESC 2022

50% ASSUME MONOTERAPIA!!

E i target sono sempre più ambiziosi

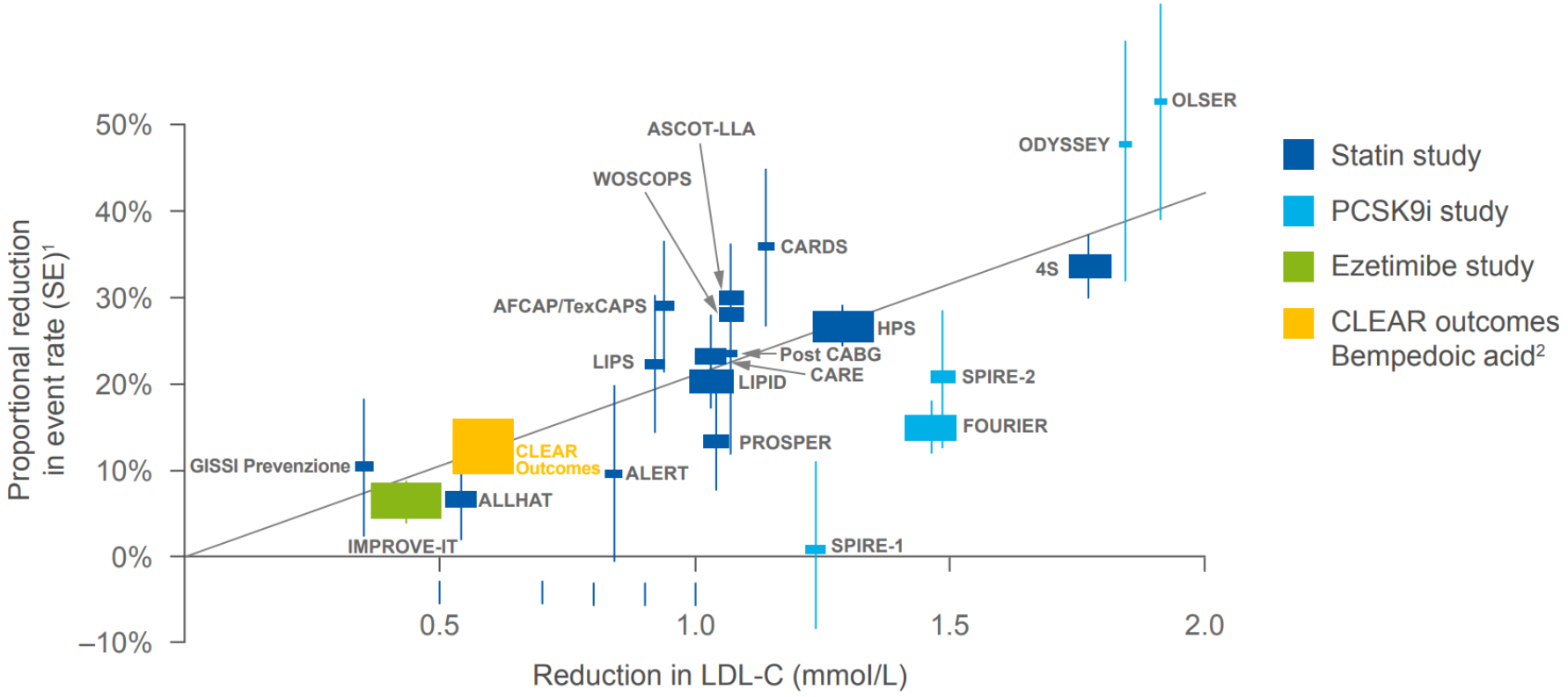
Figure 1

Treatment goals for low-density lipoprotein cholesterol across categories of total cardiovascular risk.



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

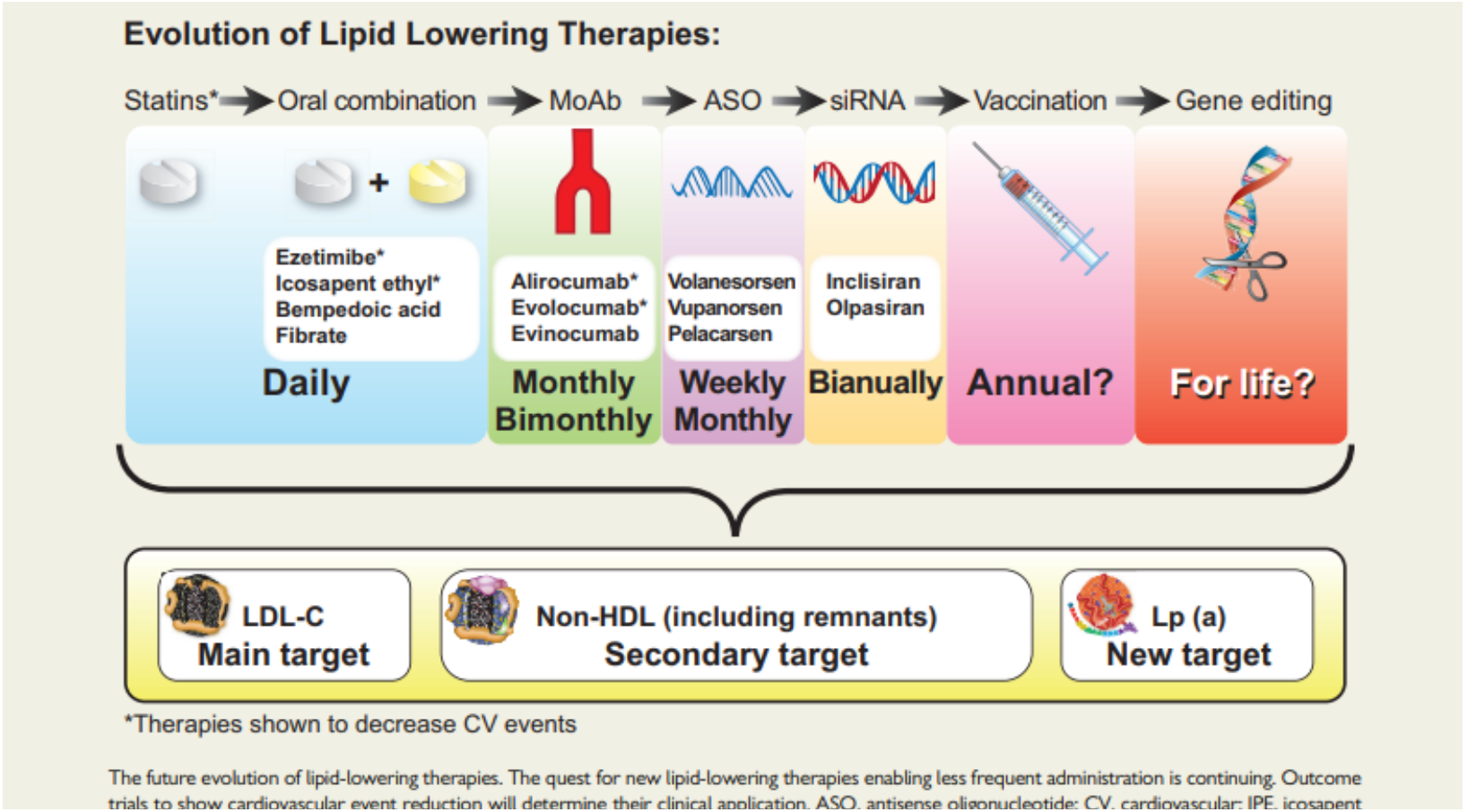
The Lower the Better



CV, cardiovascular; **LDL-C**, low-density lipoprotein cholesterol; **MACE**, major adverse cardiovascular event; **PCSK9i**, proprotein convertase subtilisin/kexin type 9 inhibitor; **SE**, standard error

1. Waters and Hsue. *Circ Res*. 2017;120(10):1537–1539; 2. Nissen SE, et al. *N Engl J Med*. 2023; 388:1353–1364.

DISLIPIDEMIA: QUALI TERAPIE?
L'evoluzione delle terapie ipolipemizzanti



The future evolution of lipid-lowering therapies. The quest for new lipid-lowering therapies enabling less frequent administration is continuing. Outcome trials to show cardiovascular event reduction will determine their clinical application. ASO, antisense oligonucleotide; CV, cardiovascular; IPE, icosapent

13) Tokgözoğlu, L., & Libby, P. (2022). The dawn of a new era of targeted lipid-lowering therapies. European Heart Journal, AdvanceArticle, 1-1.

FARMACI E COMBINAZIONI PER CONSENTIRE UN APPROCCIO “STRIKE EARLY AND STRONG”[37]*

Riduzione media dei livelli di C-LDL con diverse terapie farmacologiche con comprovati benefici cardiovascolari[37]

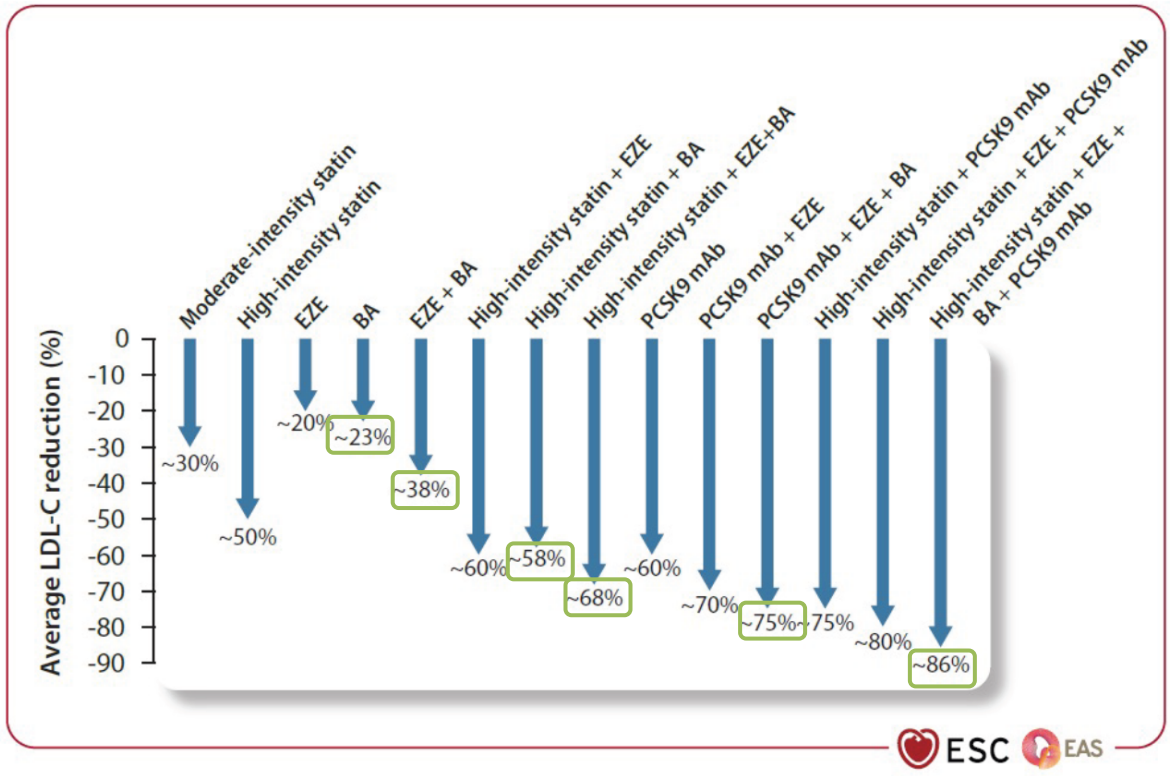


Figure 2 Average reduction in low-density lipoprotein cholesterol levels with different pharmacological therapies with proven cardiovascular benefits. BA, bempedoic acid; EZE, ezetimibe; LDL-C, low-density lipoprotein cholesterol; PCSK9 mAb, proprotein convertase subtilisin/kexin type 9 monoclonal antibody.

2025 Focused Update of the 2019 ESC/EAS Guidelines for the management of Dyslipidaemias
European Heart Journal (2025) 00, 1–20 https://doi.org/10.1093/eurheartj/ehaf190

Nel mondo reale che domande ci fanno i pazienti?

Prof ho mal di gambe e prendo la statina…..

1. Ho letto che……
2. La mia vicina
3. Non ce la faccio più
4. Sono depressa/o
5. Impotente
6. Capelli blu
7. Etc etc etc

What is Statin Intolerance?

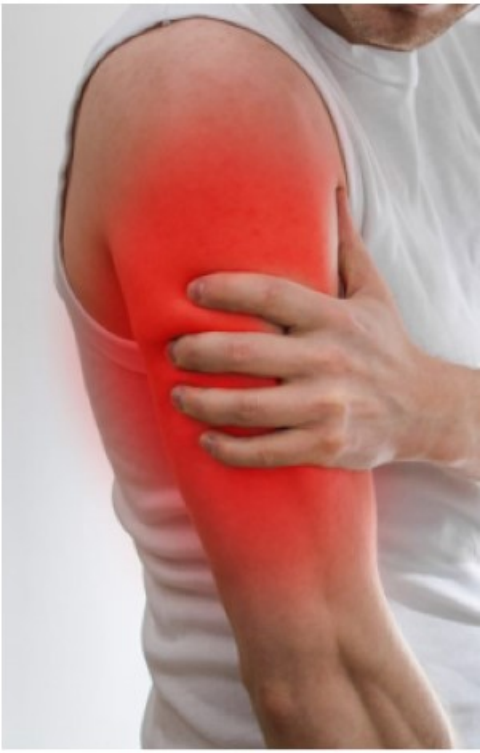
Most patients can tolerate a different statin, dosing, or other non-statin therapy

- Instead of statin intolerance, the 2018 Guideline on the Management of Blood Cholesterol suggested to use the terms:

Statin–associated side effects (SASE)

or

Statin-associated muscle symptoms (SAMS)



Grundy SM, et al. *Circulation*. 2019;139:e1082-e1143.

Statin Intolerance

Prevalence

SAMS are observed in 5% to 20% of patients[a]

- Myalgias reported more frequently in observational studies and clinical setting

Nocebo effect

- May or may not be biologically related to statin, but still, patient cannot tolerate[b]

62% stopped statin because of side effects (former statin user survey)[c]

a. Grundy SM, et al. *Circulation.* 2019;139:e1082-e1143; b. Alonso R, et al. *J Atheroscler Thromb*. 2019;26:207-215; c. Thompson PD, et al. *J Am Coll Cardiol*. 2016;67:2395-2410.

4.2.11. Management of Statin-Attributed Muscle Symptoms

Recommendations for Management of Statin-Attributed Muscle Symptoms
Referenced studies that support recommendations are summarized in the Evidence Table.

COR	LOE	RECOMMENDATIONS
1	C-LD	1. In adults with statin-attributed muscle symptoms, assessment should include evaluation for secondary causes (Table 24), and in those with severe myalgias or weakness, objective clinical measures of muscle strength[1] and measurement of CK are recommended to assess severity of the condition.

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COR	LOE	RECOMMENDATIONS
1	B-R	2. In adults with statin-attributed muscle symptoms, the clinician-patient discussion should acknowledge patient side effect concerns, inform the patient of the heightened ASCVD risk associated with statin discontinuation, and provide alternative treatment options to reduce ASCVD risk.[2,3]
1	B-R	3. In adults with clinical ASCVD who experience statin-attributed muscle symptoms on the recommended intensity of statin therapy (secondary causes excluded) and are unable to achieve recommended treatment goals, use of a reduced statin dose (if tolerable) and the addition of bempedoic acid,[3] ezetimibe,[4] or a PCSK9 mAb,[5,6] alone or in combination, are recommended to lower LDL-C and reduce ASCVD risk.
1	B-R	4. In adults without a history of clinical ASCVD who experience statin-attributed muscle symptoms on the recommended intensity of statin therapy (secondary causes excluded) and are at high ASCVD risk based on a PREVENT-ASCVD equation of ≥10% or a CAC score ≥300 AU, or women >65 years of age or men >60 years of age with diabetes, the addition of bempedoic acid[7] and/or ezetimibe[4] is/are indicated to lower LDL-C to <70 mg/dL (1.8 mmol/L) and non-HDL-C <100 mg/dL (2.6 mmol/L) and to reduce ASCVD risk.
1	B-R	5. In adults without a history of clinical ASCVD who experience statin-attributed muscle symptoms on the recommended intensity of statin therapy (secondary causes excluded) and are at high ASCVD risk based on a PREVENT-ASCVD equation of ≥10% or a CAC score ≥300 AU or diabetes and are unable to achieve recommended treatment goals, the addition of a PCSK9 mAb[8] is recommended to lower LDL-C.[9]

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COR	LOE	RECOMMENDATIONS
2a	B-NR	6. In adults with clinical ASCVD who experience statin-attributed muscles symptoms (secondary causes excluded) and are unable to achieve recommended treatment goals on bempedoic acid[3] with or without ezetimibe,[4] it is reasonable to add inclisiran in those unable to tolerate or obtain evolocumab or alirocumab or who have a strong preference for less frequent dosing to achieve an LDL-C goal <55 mg/dL (1.4 mmol/L) and non-HDL-C <85 mg/dL (2.2 mmol/L).[10]
2b	B-R	7. In adults without a history of clinical ASCVD who experience statin-attributed muscle symptoms on the recommended intensity of statin therapy (secondary causes excluded) and are at borderline to intermediate ASCVD risk based on a PREVENT-ASCVD equation of 3% to <10%, and in whom the decision to treat with ezetimibe and/or bempedoic acid is uncertain, coronary calcium scoring may be reasonable to aid in ASCVD risk stratification[11,12] to inform decision-making about add-on therapy to reduce ASCVD risk.
2b	B-NR	8. In adults without a history of clinical ASCVD who experience statin-attributed muscle symptoms on the recommended intensity of statin therapy (secondary causes excluded) and are at borderline or intermediate ASCVD risk based on a PREVENT-ASCVD equation of 3% to <10%, the addition of ezetimibe[4] and/or bempedoic acid[7] may be reasonable to lower LDL-C to <100 mg/dL (2.6 mmol/L) and non-HDL-C to <130 mg/dL (3.4 mmol/L) and reduce ASCVD risk.

Synopsis

Complaints of myalgia or muscle weakness, or the fear of developing these symptoms, are the most frequently reported reasons for failure to tolerate or adhere to statin therapy. These symptoms may occur with or without CK elevation. They may be due to the prescribed statin alone, altered statin metabolism due to DDI, excessive muscular activity, primary muscle or metabolic disorders, or patient expectations that statin therapy is responsible. A statin-related etiology is supported by

TABLE 20 Lipid-Lowering Therapies During Pregnancy and Lactation

	Pregnancy	Lactation
Statins	Should be discontinued in most pregnancies Can be considered in high-risk individuals (ASCVD or FH[29])	Avoid use[30]
Ezetimibe	Avoid use due to insufficient data regarding risk to fetus[31]	Avoid use[31]
Bile acid sequestrants	Safe to use. No evidence of risk in humans due to lack of systemic absorption[12] Known to interfere with absorption of fat-soluble vitamins High rate of gastrointestinal side effects	Not excreted in human milk[12] Caution if used—associated with malabsorption of fat-soluble vitamins (A, D, E, and K). Prenatal vitamins may not be sufficient
Niacin	Avoid use due to insufficient data regarding risk to fetus or clinical utility for the mother[12]	Avoid use[12]
Fibric acid derivatives	Can be considered (after the first trimester) for severe hypertriglyceridemia only if the potential benefit justifies the potential risk to the fetus[12]	Avoid use during lactation. If taken during pregnancy, lactation can be resumed 5 days after last dose of fibric acid derivatives[12]
Omega-3 fatty acids	Can be considered for severe hypertriglyceridemia[12]	Known to be excreted in human milk. Effects on infants are unknown Caution if used during lactation[12]
Bempedoic acid	Avoid use due to insufficient data regarding risk to fetus[12]	Avoid use[12]
PCSK9 mAb	Avoid use due to insufficient data regarding risk to fetus[12]	Avoid use[12]
Inclisiran	Avoid use due to insufficient data regarding risk to fetus[29]	Avoid use[29]
Evinacumab	Avoid use due to insufficient data regarding risk to fetus[32]	Avoid use[32]
Lomitapide	Avoid use due to risk of embryo-fetal toxicity[31]	Avoid use[33]

Adapted with permission from Agarwala et al.[12] ©2024 Elsevier. Adapted with permission from Jacobson et al.[31] ©2015 Elsevier.

ASCVD indicates atherosclerotic cardiovascular disease; FH, familial hypercholesterolemia; mAb, monoclonal antibodies; and PCSK9, proprotein convertase subtilisin/kexin type 9.

TABLE 4 ASCVD Risk Related to Lp(a) Concentrations*

Lp(a) concentration nmol/L (mg/dL)	ASCVD Relative Risk: Increase Compared With Population Median (20 nmol/L, 7 mg/dL)
430 nmol/L (180 mg/dL)	4-fold
350 nmol/L (150 mg/dL)	3-fold
250 nmol/L (100 mg/dL)	2 -fold
125 nmol/L (50 mg/dL)	1.4-fold
75-124 nmol/L (30-49 mg/dL)	1.2-fold
<75 nmol/L (<30 mg/dL)	Reference

Data in the table are derived from the UK Biobank Study,[14] are intended as a general guide and may differ in other populations. For example, relative risk of 2-fold has been observed for levels of 200 nmol/L in some populations. Equivalence of levels between nmol/L and mg/dL is approximate. An Lp(a) level of 50 mg/dL (125 nmol/L, ~ 80th percentile) is associated with an ~40% relative risk increase in ASCVD compared with 7 mg/dL (20 nmol/L, median in a reference population).[1,2] An Lp(a) level of 100 mg/dL (≥250 nmol/L, ~95th percentile) approximately doubles the ASCVD risk. An Lp(a) level of 180 mg/dL (≥430 nmol/L, ~99th percentile) increases the ASCVD risk by ~4-fold, similar to the risk of heterozygous familial hypercholesterolemia.

*Lp(a) concentrations in this threshold range may be considered for repeat testing.

Recommendation for Reproductive Risk Markers
Referenced studies that support the recommendation are summarized in the Evidence Table.

COR	LOE	RECOMMENDATION
2a	B-NR	1. In adults without ASCVD, consideration of reproductive risk markers, such as early menopause (<45 years) and history of adverse pregnancy outcomes (gestational hypertension, preeclampsia, gestational diabetes, preterm delivery) is reasonable to personalize ASCVD risk assessment when considering the potential benefit of initiating LLT as an adjunct to lifestyle management for primary ASCVD prevention.[1-5]

a.

Continued

COR	LOE	RECOMMENDATIONS
1	B-NR	3. In adults at intermediate risk and select adults at borderline risk, if the CAC score is >0 AU, it is recommended to initiate LLT, particularly if the CAC score is ≥100 AU or ≥75th standardized percentile to reduce ASCVD risk.[5]

Continued

COR	LOE	RECOMMENDATIONS
1	B-NR	2. In adults with active cancer currently on statin therapy, treatment should be continued to reduce ASCVD risk unless there is concern for a specific drug interaction or life expectancy is <1 year.[7-9]
2b	B-R	3. In adults with active cancer, initiation of statin therapy may be considered to prevent anthracycline-induced cardiotoxicity.[10]

Che fare?

1. Parlare con i pazienti
2. Terapia semplice
3. Far capire al paziente i veri benefici
4. Spiegare gli effetti collaterali
5. Non assecondare sempre le volontà del paziente
6. Spiegare la terapia ai MMG
7. Non avere il «braccino corto»

Grazie per l’attenzione