FAKULTNÍ NEMOCNICE® OLOMOUC

Lékařská fakulta

Univerzita Palackého v Olomouci

Farmakoterapie po AKS

Hypolipidemika

Jan Přeček

I. interní klinika – kardiologická, FN a LF UP Olomouc

23. konference České asociace akutní kardiologie,
1. 12. 2025, Karlovy Vary

Aktualizace doporučení ESC/EAS z roku 2019

ESC European Society of Cardiology
European Heart Journal (2020) **41**, 111–188
doi:10.1093/eurheartj/ehz455

ESC/EAS GUIDELINES

2019 ESC/EAS Guidelines for the management of dyslipidaemias: *lipid modification to reduce cardiovascular risk*

The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS)

Authors/Task Force Members: François Mach* (Chairperson) (Switzerland), Colin Baigent* (Chairperson) (United Kingdom), Alberico L. Catapano[1]* (Chairperson) (Italy), Konstantinos C. Koskinas (Switzerland), Manuela Casula[1] (Italy), Lina Badimon (Spain), M. John Chapman[1] (France), Guy G. De Backer (Belgium), Victoria Delgado (Netherlands), Brian A. Ference (United Kingdom), Ian M. Graham (Ireland), Alison Halliday (United Kingdom), Ulf Landmesser (Germany), Borislava Mihaylova (United Kingdom), Terje R. Pedersen (Norway), Gabriele Riccardi[1] (Italy), Dimitrios J. Richter (Greece), Marc S. Sabatine (United States of America), Marja-Riitta Taskinen[1] (Finland), Lale Tokgozoglu[1] (Turkey), Olov Wiklund[1] (Sweden)

The three chairpersons contributed equally to the document.

*Corresponding authors: François Mach, Cardiology Department, Geneva University Hospital, 4 Gabrielle-Perret-Gentil, 1211 Geneva, Switzerland. Tel: +41 223 727 192, Fax: +41 223 727 229, Email: francois.mach@hcuge.ch. Colin Baigent, Nuffield Department of Population Health, University of Oxford, Richard Doll Building, Roosevelt Drive, Oxford OX3 7LF, United Kingdom. Tel: +44 1865 743 741, Fax: +44 1865 743 985, Email: colin.baigent@ndph.ox.ac.uk. Alberico L. Catapano, Department of Pharmacological and Biomolecular Sciences, University of Milan, Via Balzaretti, 9, 20133 Milan, and Multimedica IRCCS, Milan, Italy. Tel: +39 02 5031 8401, Fax: +39 02 5031 8386, Email: alberico.catapano@unimi.it.

ESC Committee for Practice Guidelines (CPG), National Cardiac Societies document reviewers and Author/Task Force Member affiliations: listed in the Appendix.

†**Representing the EAS.**

ESC entities having participated in the development of this document:

Associations: Acute Cardiovascular Care Association (ACCA), Association of Cardiovascular Nursing & Allied Professions (ACNAP), European Association of Cardiovascular Imaging (EACVI), European Association of Preventive Cardiology (EAPC), European Association of Percutaneous Cardiovascular Interventions (EAPCI).

Councils: Council for Cardiology Practice, Council on Hypertension, Council on Stroke.

Working Groups: Aorta and Peripheral Vascular Diseases, Atherosclerosis and Vascular Biology, Cardiovascular Pharmacotherapy, e-Cardiology, Thrombosis.

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ESC European Society of Cardiology
European Heart Journal (2025) **00**, 1–20
https://doi.org/10.1093/eurheartj/ehaf190

ESC GUIDELINES

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

Developed by the task force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS)

Authors/Task Force Members: François Mach *†, (ESC Chairperson) (Switzerland), Konstantinos C. Koskinas*†, (ESC Chairperson) (Switzerland), Jeanine E. Roeters van Lennep *†, (EAS Chairperson) (Netherlands), Lale Tokgözoğlu, (Task Force Co-ordinator) (Türkiye), Lina Badimon (Spain), Colin Baigent (United Kingdom), Marianne Benn (Denmark), Christoph J. Binder (Austria), Alberico L. Catapano (Italy), Guy G. De Backer (Belgium), Victoria Delgado (Spain), Natalia Fabin (Italy), Brian A. Ference (United Kingdom), Ian M. Graham (Ireland), Ulf Landmesser (Germany), Ulrich Laufs (Germany), Borislava Mihaylova (United Kingdom), Børge Grønne Nordestgaard (Denmark), Dimitrios J. Richter (Greece), Marc S. Sabatine (United States of America), and ESC/EAS Scientific Document Group

Aktualizace doporučení ESC/EAS z roku 2019

1. Odhad kardiovaskulárního rizika s implementací algoritmů predikce rizika SCORE2 a SCORE2-OP
2. Terapie snižující hladinu LDL cholesterolu
3. **Hypolipidemická terapie osob s akutním koronárním syndromem**
4. Lipoprotein (a)
5. Terapie snižující hladinu TAG
6. Statiny v primární prevenci KVO u osob HIV
7. Statiny u osob s vysokým/velmi vysokým rizikem KV toxicity související s protinádorovu léčbou
8. Doplňky stravy

Mach F et al. Eur Heart J 2025 Nov 7;46(42):4359-4378

5. Combination of lipid-lowering therapies during index hospitalization for acute coronary syndromes

U pacientů po ACS (vč. IM) je **velmi vysoké časné riziko rekurentní příhody**:

- cca **10 %** má během prvních ***~100 dní*** po IM druhý IM, CMP nebo KV smrt
- cca **⅓ pacientů** má závažnou KV příhodu během 5 let

- Tento **nejrizikovější časný úsek** (první týdny–měsíce) se v praxi často překrývá s dobou, kdy teprve probíhá „eskalace“ léčby podle staršího stupňovitého schématu (2019)

- V ideálním případě může trvat až ***12 týdnů***, než se pacient dostane na optimální LDL-C léčbu – to je z hlediska rizika příliš dlouho.
- Intenzivní hypolipidemická léčba má lepší klinické výsledky a vliv na prognózu již v časném období
  - princip **„the sooner, the lower, the better“** pro LDL-cholesterol

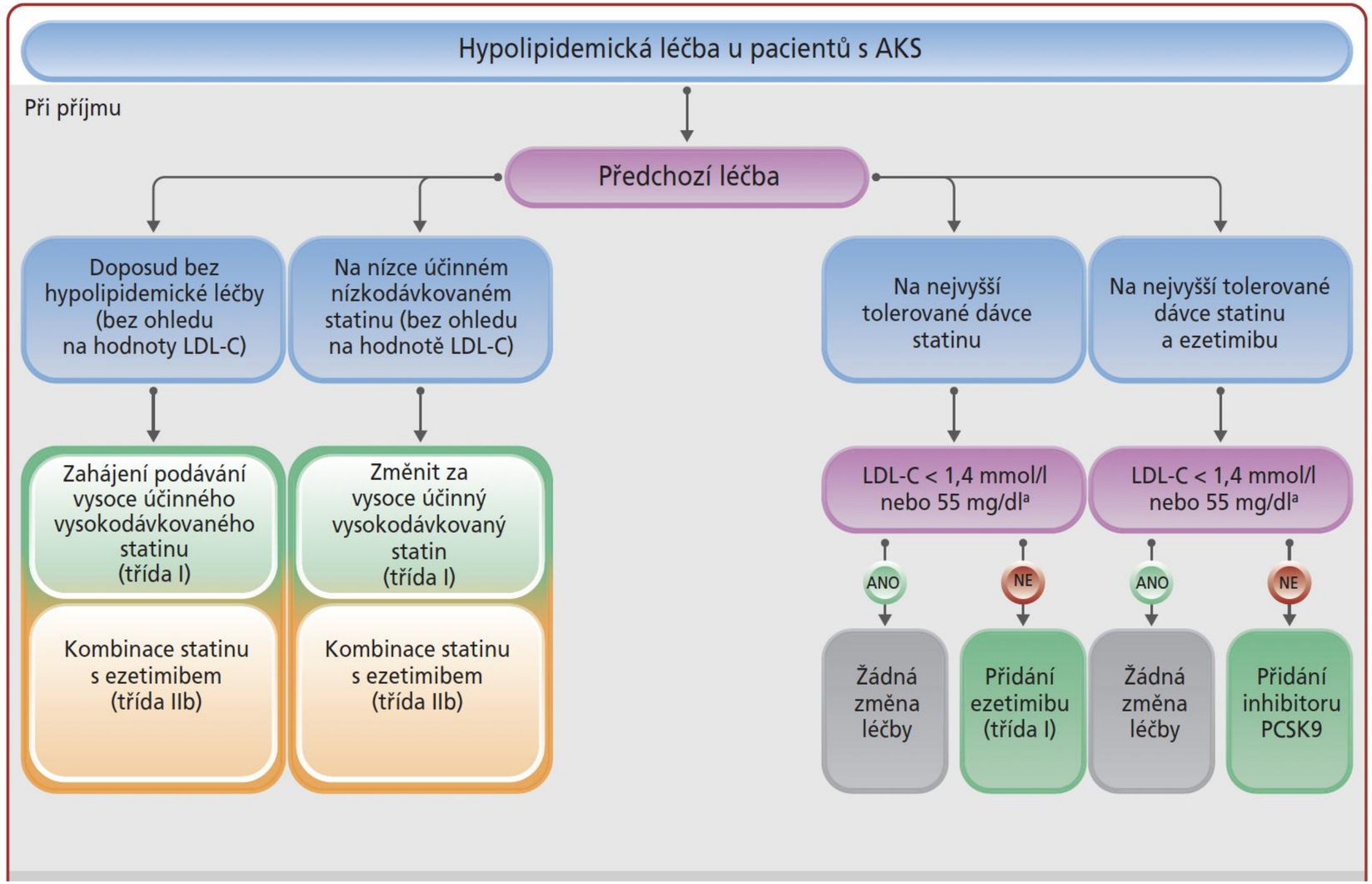
Mach F et al. Eur Heart J 2025 Nov 7;46(42):4359-4378

Běžná realita / observační data

- **intenzivní léčba podle doporučení je často nenasazena** (nižší intenzita statinu, chybí ezetimib/PCSK9i)
- **po propuštění se dávky někdy snižují, nekontroluje se LDL-chol**
- většina pacientů **nedosahuje cílového LDL-chol**
- **preskripční „inertie“**, obavy z nežádoucích účinků, špatná adherence a ztráty z dispenzarizace

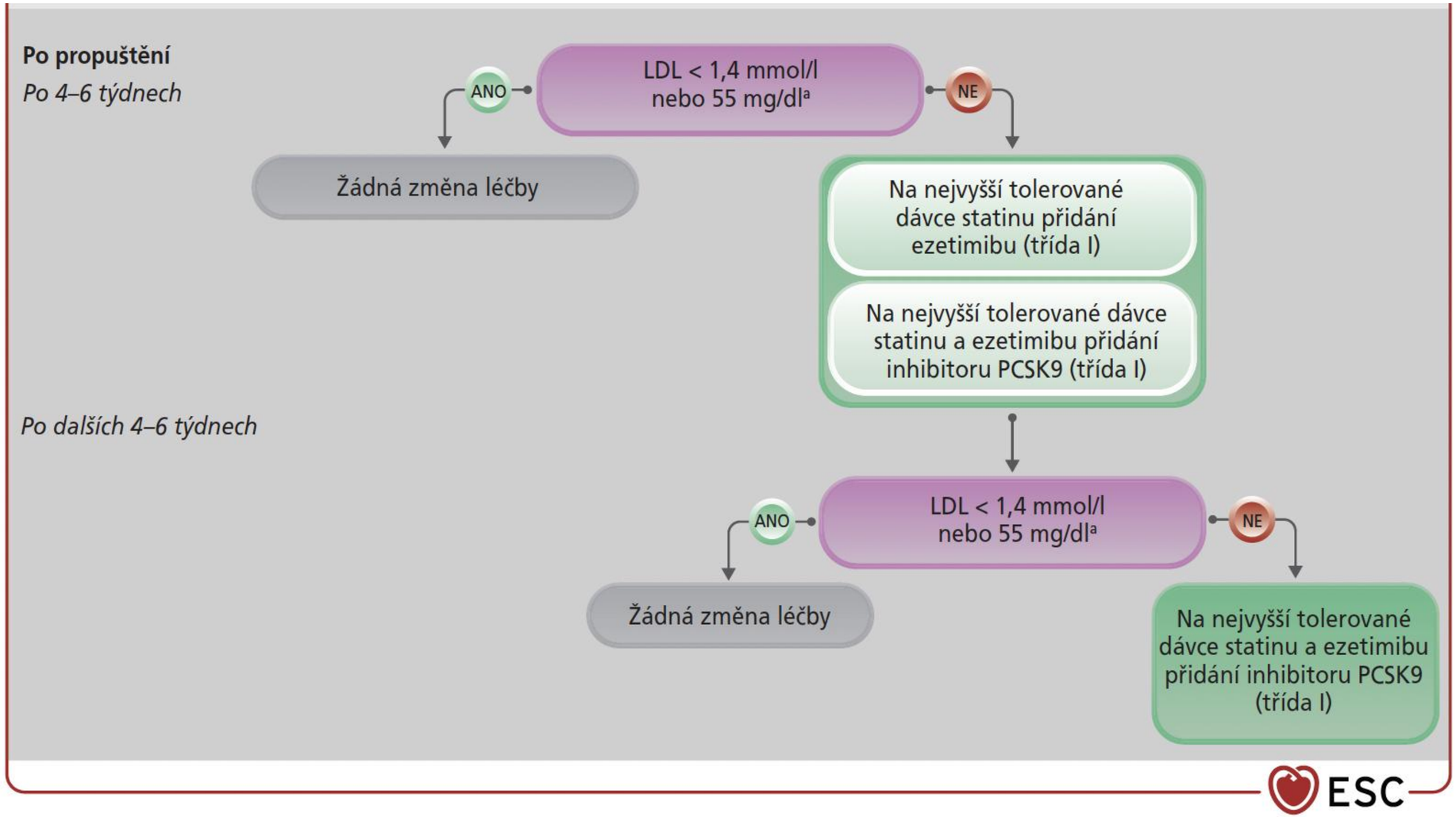
Mach F et al. Eur Heart J 2025 Nov 7;46(42):4359-4378

ESC guidelines 2024 – strategie léčby



Kala P et al. Cor Vasa 2024;66:169–232

ESC guidelines 2024 – strategie léčby



Kala P et al. Cor Vasa 2024;66:169–232

Hypolipidemická terapie po AKS

ESC European Society of Cardiology
European Heart Journal (2025) 00, 1–20
https://doi.org/10.1093/eurheartj/ehaf190

ESC GUIDELINES

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

current Guideline-recommended treatment goals.[72–74] Recent data from the SWEDEHEART (Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies) Registry reported the lowest risk of CV events in those patients who achieved early and sustained LDL-C lowering to recommended goals after MI. A stepwise approach for LDL-C lowering after MI might therefore result in delayed goal attainment as compared with early intensification of treatment.[75,76] These data support 'the sooner, the lower, the better' as a therapeutic strategy for LDL-C lowering in patients with ACS.[58]

Recommendation Table 3 — Recommendations for lipid-lowering therapy in patients with acute coronary syndromes (see also Supplementary data online, Evidence Table 3)

Recommendations	Class[a]	Level[b]
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.[66]	IIa	B

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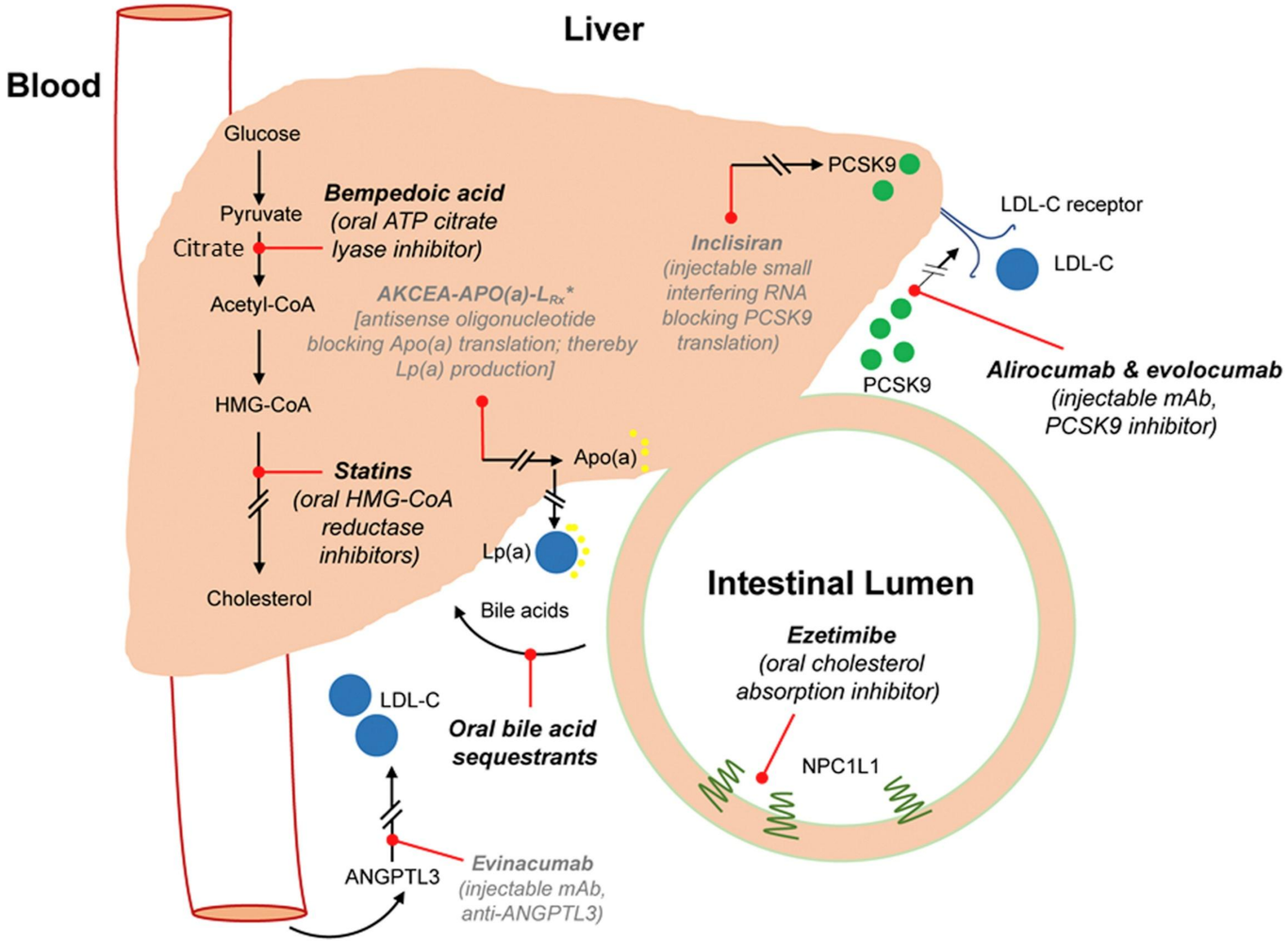
This table complements the ESC 2019 ESC/EAS Guidelines table and does not replace it.
ACS, acute coronary syndromes; LDL-C, low-density lipoprotein cholesterol.
[a]Class of recommendation.
[b]Level of evidence.

Mach F et al. Eur Heart J 2025 Nov 7;46(42):4359-4378

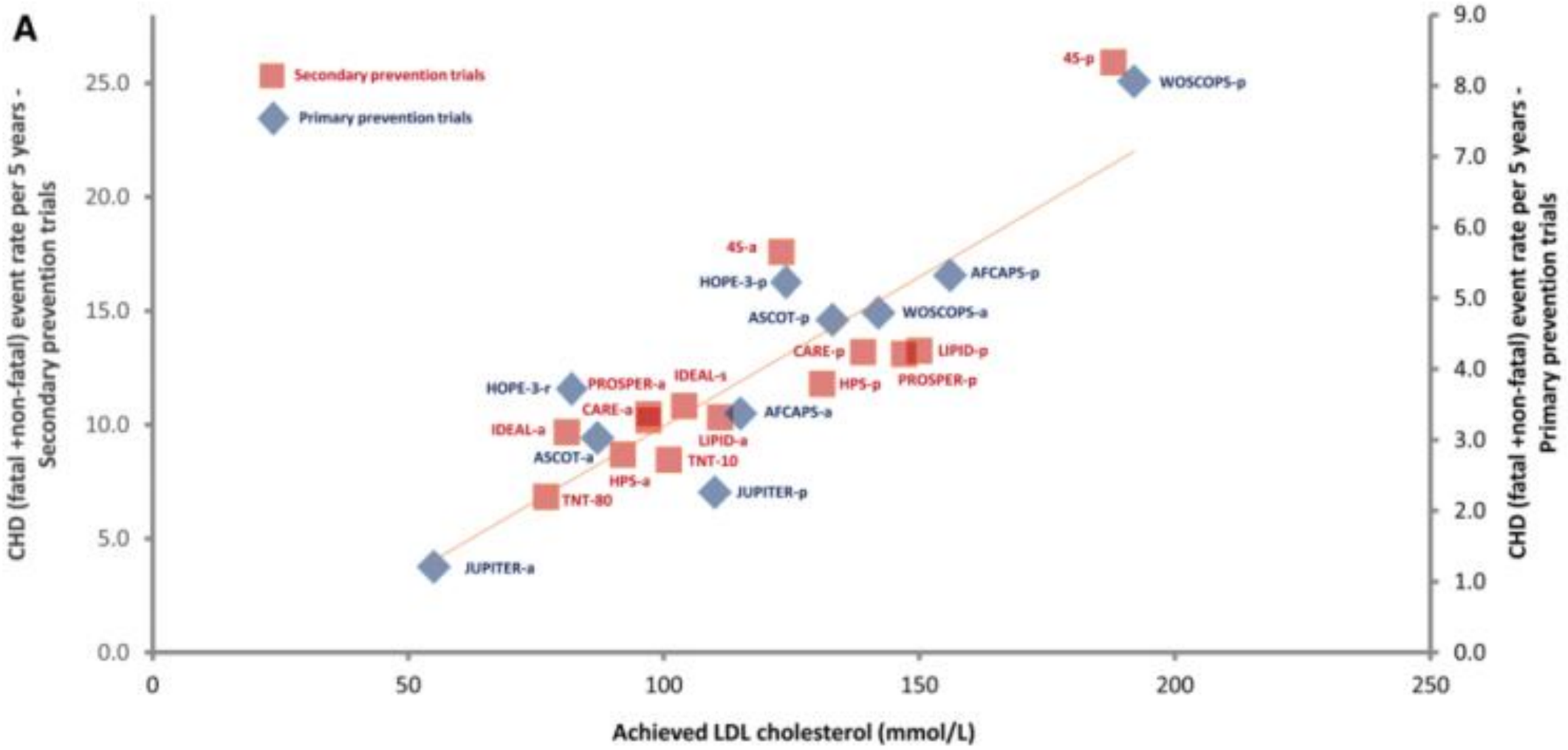
Nástroje ke snížení LDL-cholesterolu



Atar D et al. Atherosclerosis. 2021 Feb;319:51-61.

STATINY

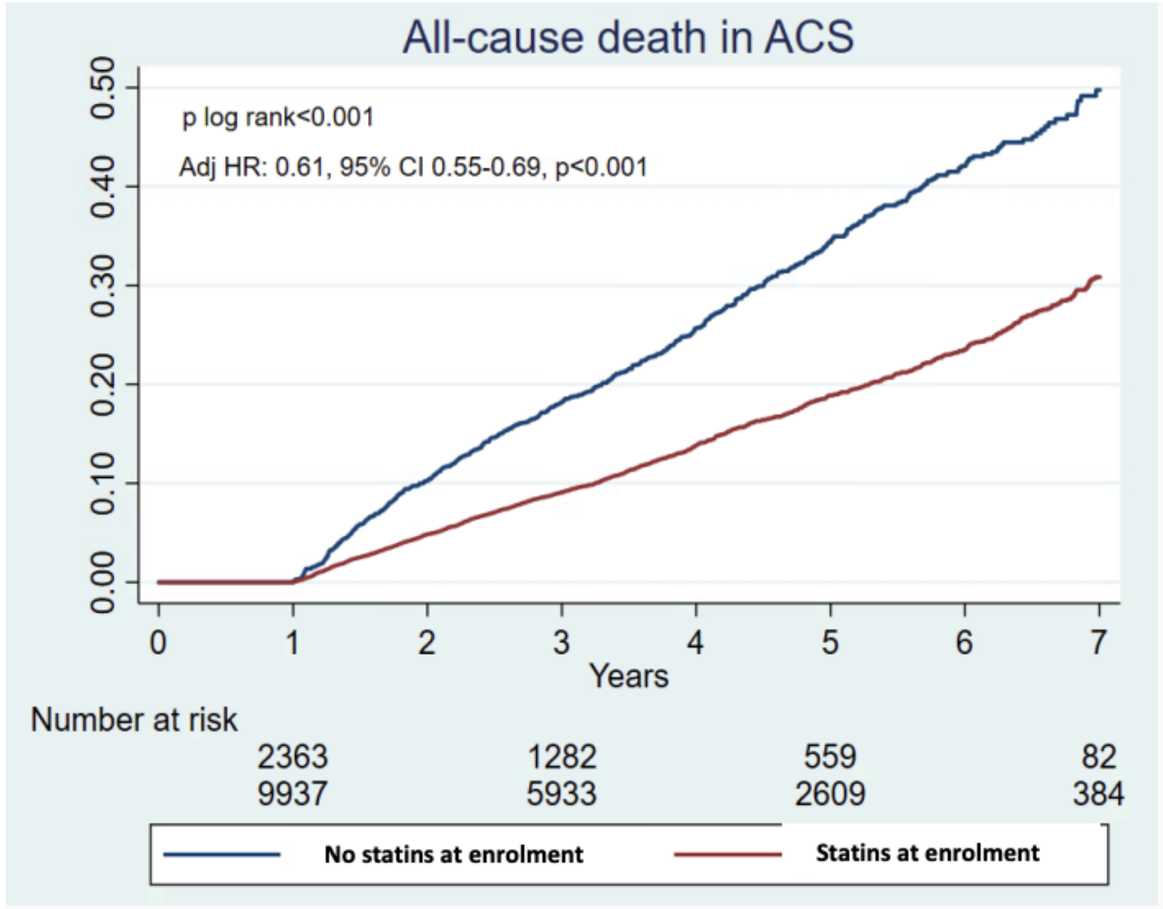
Snížení LDL-cholesterolu a snížení KV příhod

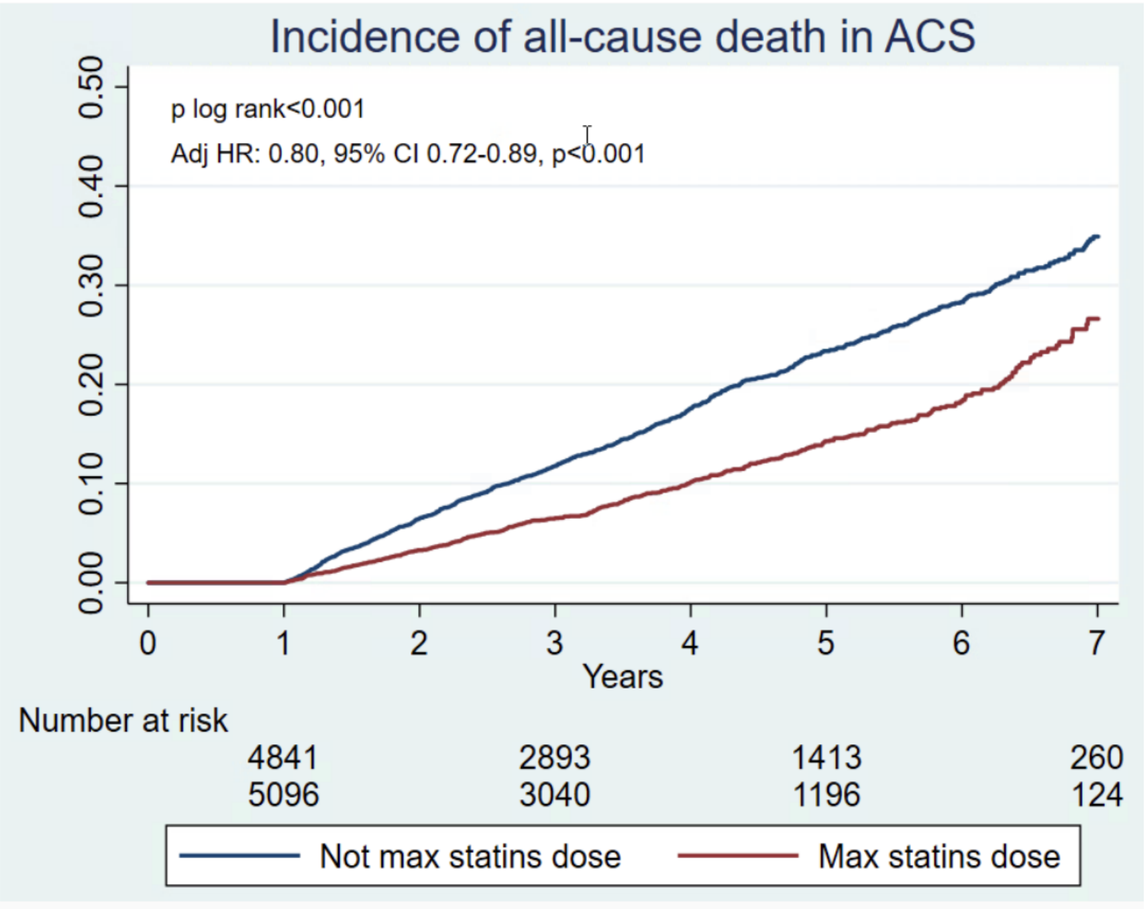


Eur Heart J. 2017;38(32):2459-2472. doi:10.1093/eurheartj/ehx144

Statiny po AKS – registr NW London

- **76 243 pt. (22,4 % ACS, 77,6 % CCS)**

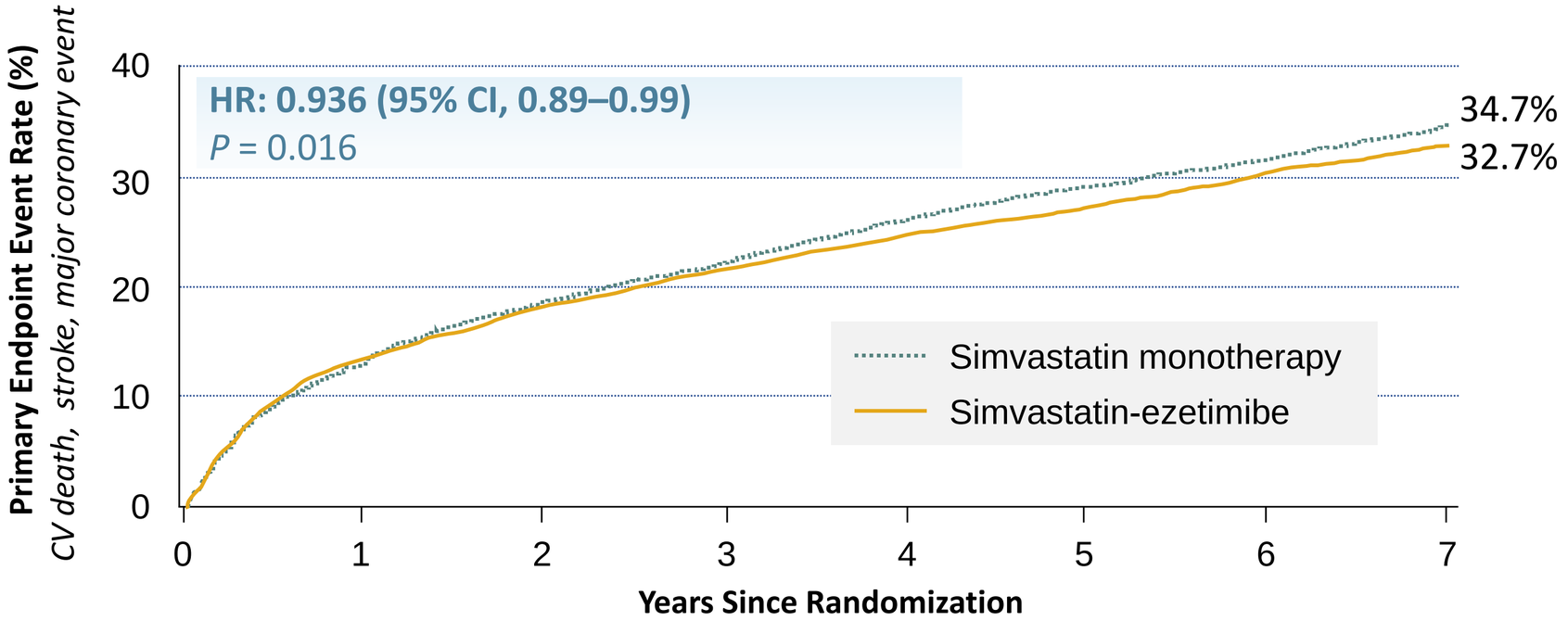




Akhtar M et al. ESC Congress 2024 presentation

EZETIMIB

IMPROVE-IT: ezetimib+statin po AKS



Hospitalization for acute ACS or high-risk UA

N = 18,144 Randomized within 10 days of event

Simvastatin 40 mg + ezetimibe 10 mg + SOC

Mean baseline LDL-C 93.8 mg/dL (2.4 mmol/L)

Simvastatin 40 mg + placebo + SOC

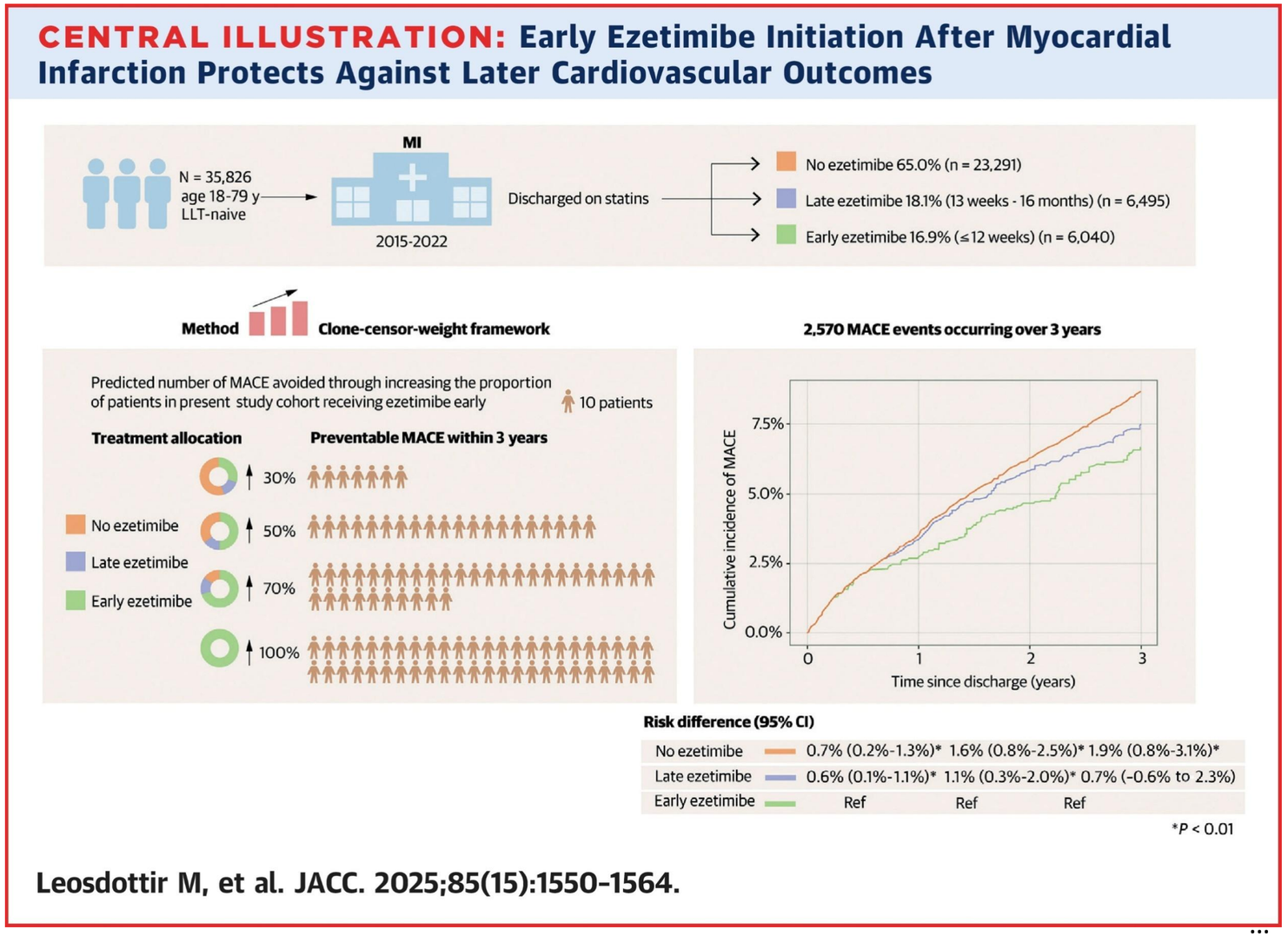
Median follow-up: 6 years

Follow-up assessments conducted at 30 days, at 4 months, and every 4 months thereafter*

Cannon CP. et al. N Engl J Med 2015; 372:2387-2397.

Včasnost zahájení ezetimibu po IM

- Observační kohorta z registru SWEDEHEART, 35 826 pt. po IM (2015–2022)
- Vysoce intenzivní statinová terapie (98 %)
- **Časné zahájení kombinované léčby statinem a ezetimibem po IM výrazně snižuje výskyt MACE a kardiovaskulární mortality**
- Zpožděné přidání ezetimibu nebo jeho nepřidání představuje **zbytečné riziko**
- Důraz na potřebu změnit metody péče a **začít kombinovanou léčbu hned během hospitalizace**

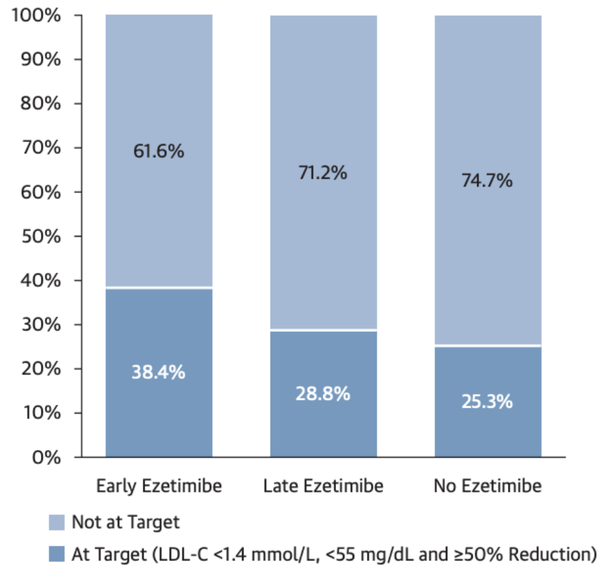


Včasnost zahájení ezetimibu po IM

TABLE 1 Patient Characteristics

	Overall (N = 35,826)	Missing	Treatment Group: Early Ezetimibe (n = 6,040)	Late Ezetimibe (n = 6,495)	No Ezetimibe (n = 23,291)
Admission characteristics					
Age, y	65.1 (57.0-72.1)	0	63.6 (56.0-70.6)	63.4 (55.9-70.5)	66.1 (57.7-72.8)
Female	9,302 (26.0)	0	1,395 (23.1)	1,688 (26.0)	6219 (26.7)
Body mass index, kg/m^2	26.9 (24.5-29.9)	1,471	27.0 (24.6-30.0)	27.1 (24.7-30.1)	26.8 (24.4-29.8)
Current smoker	9,683 (27.7)	895	1,647 (27.9)	1,39 (28.9)	6,197 (27.3)
Hypertension	12,519 (35.1)	179	1,835 (30.6)	2,025 (31.3)	8,659 (37.4)
Diabetes mellitus	3,543 (9.9)	0	451 (7.5)	476 (7.3)	2,616 (11.2)
Charlson comorbidity index	1.0 (1.0-2.0)	0	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)
Medical history					
Previous MI	946 (2.6)	0	125 (2.1)	152 (2.3)	669 (2.9)
Heart failure	549 (1.5)	0	58 (1.0)	64 (1.0)	427 (1.8)
Laboratory and physiological variables					
LDL-C, mmol/L	3.3 (2.7-4.0)	2,327	3.8 (3.2-4.4)	3.6 (3.0-4.2)	3.1 (2.6-3.7)
eGFR, mL/min/1.73 m^2	75.8 (66.5-85.1)	0	77.4 (68.2-86.4)	77.2 (68.1-86.2)	75.1 (65.7-84.5)
Fasting glucose, mmol/L	6.7 (5.8-8.0)	5,239	6.6 (5.8-7.8)	6.6 (5.8-7.9)	6.7 (5.8-8.1)
Systolic blood pressure, mm Hg	150 (133-170)	235	150 (132-170)	150 (133-170)	150 (133-170)

FIGURE 1 Proportion of Patients at LDL-C Target (LDL-C <1.4 mmol/L, <55 mg/dL and ≥50% Reduction) at 1-Year Follow-Up



Only patients attending cardiac rehabilitation with lipid levels measured are included. LDL-C = low-density lipoprotein cholesterol.

Leosdottir M, et al. JACC. 2025;85(15):1550-1564.

INHIBITORY PCSK9

evolocumab

Randomized 27,564 patients

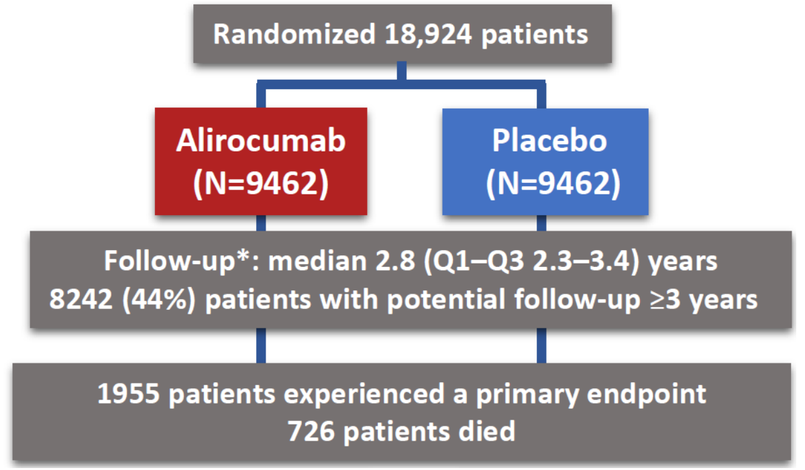
- Evolocumab (N=13,784)
- Placebo (N=13,780)

Follow-up median 26M (IQR 22-30)

2907 patients experienced primary EP

Characteristic	Value
Age, years, mean (SD)	63 (9)
Male sex (%)	75
Type of CV disease (%)	**Median time from recent event <3 yrs**
Myocardial infarction	81
Stroke (non-hemorrhagic)	19
Symptomatic PAD	13
CV risk factor (%)	
Hypertension	80
Diabetes mellitus	37
Current cigarette use	28

alirocumab



Characteristic	Alirocumab (N=9462)	Placebo (N=9462)
Age, years, median (Q1–Q3)	58 (52–65)	58 (52–65)
Female, n (%)	2390 (25.3)	2372 (25.1)
Medical history, n (%)		
Hypertension	6205 (65.6)	6044 (63.9)
Diabetes mellitus	2693 (28.5)	2751 (29.1)
Current tobacco smoker	2282 (24.1)	2278 (24.1)
Prior MI	1790 (18.9)	1843 (19.5)

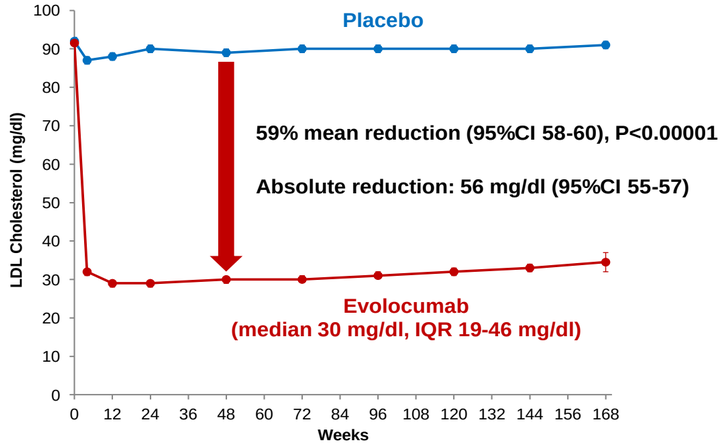
Characteristic	Alirocumab (N=9462)	Placebo (N=9462)
Time from index ACS to randomization, months, median (Q1–Q3)	2.6 (1.7–4.4)	2.6 (1.7–4.3)
ACS type, n (%)		
NSTEMI	4574 (48.4)	4601 (48.7)
STEMI	3301 (35.0)	3235 (34.2)
Unstable angina	1568 (16.6)	1614 (17.1)
Revascularization for index ACS, n (%)	6798 (71.8)	6878 (72.7)

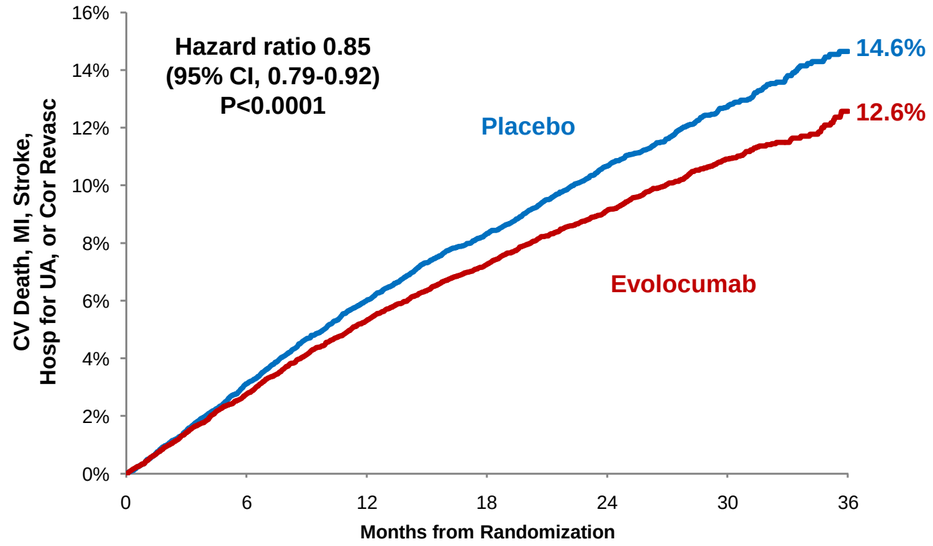
Sabatine MS, et al. N Engl J Med. 2017;376:1713-1722; Schwartz G.G., N Engl J Med 2018; 379:2097-2107

fourier

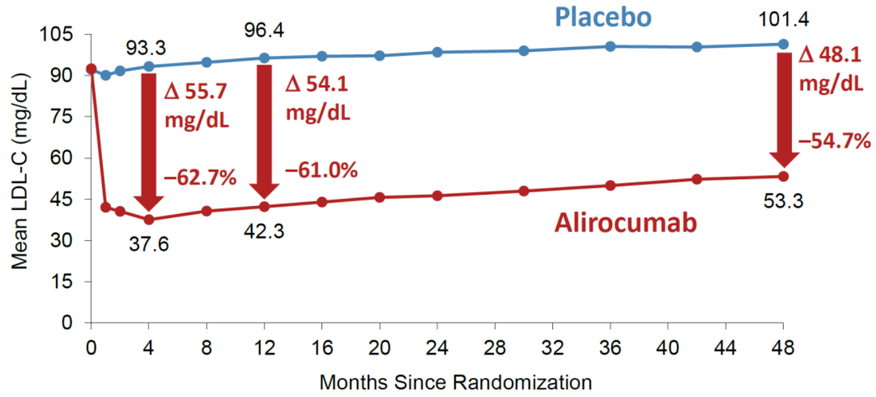
ODYSSEY OUTCOMES

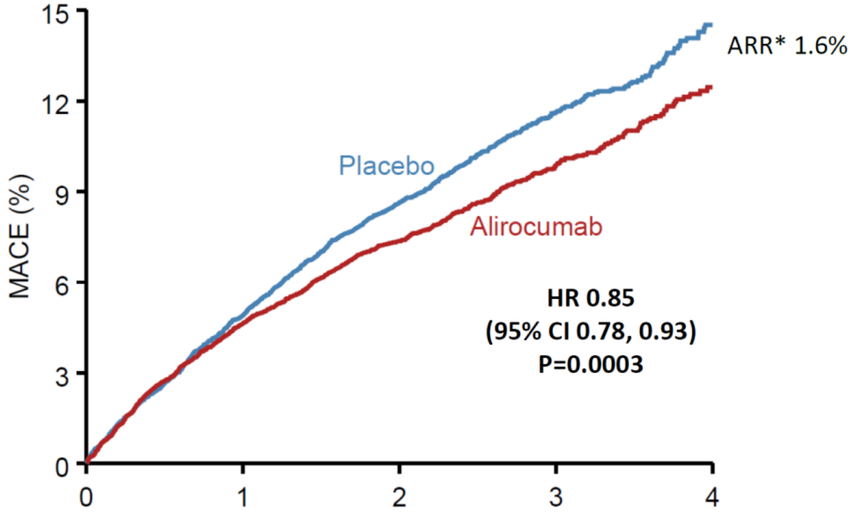
evolocumab





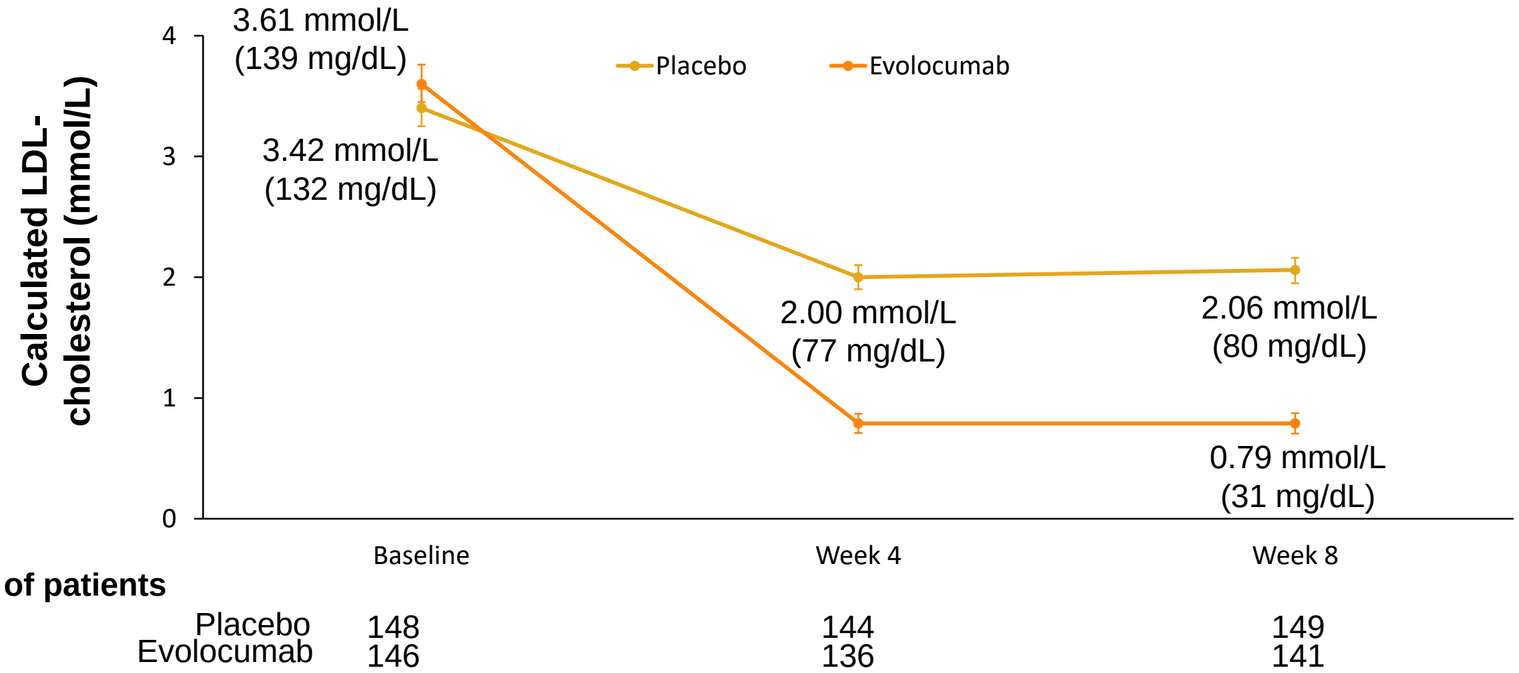
alirocumab



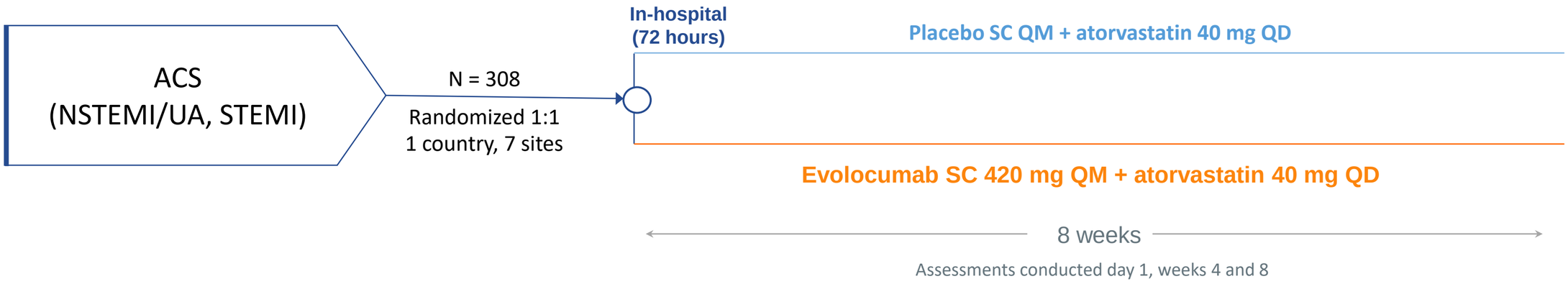


Sabatine MS, et al. N Engl J Med. 2017;376:1713-1722
Schwartz G.G., N Engl J Med 2018; 379:2097-2107

EVOPACS – časné nasazení evolocumabu u AKS

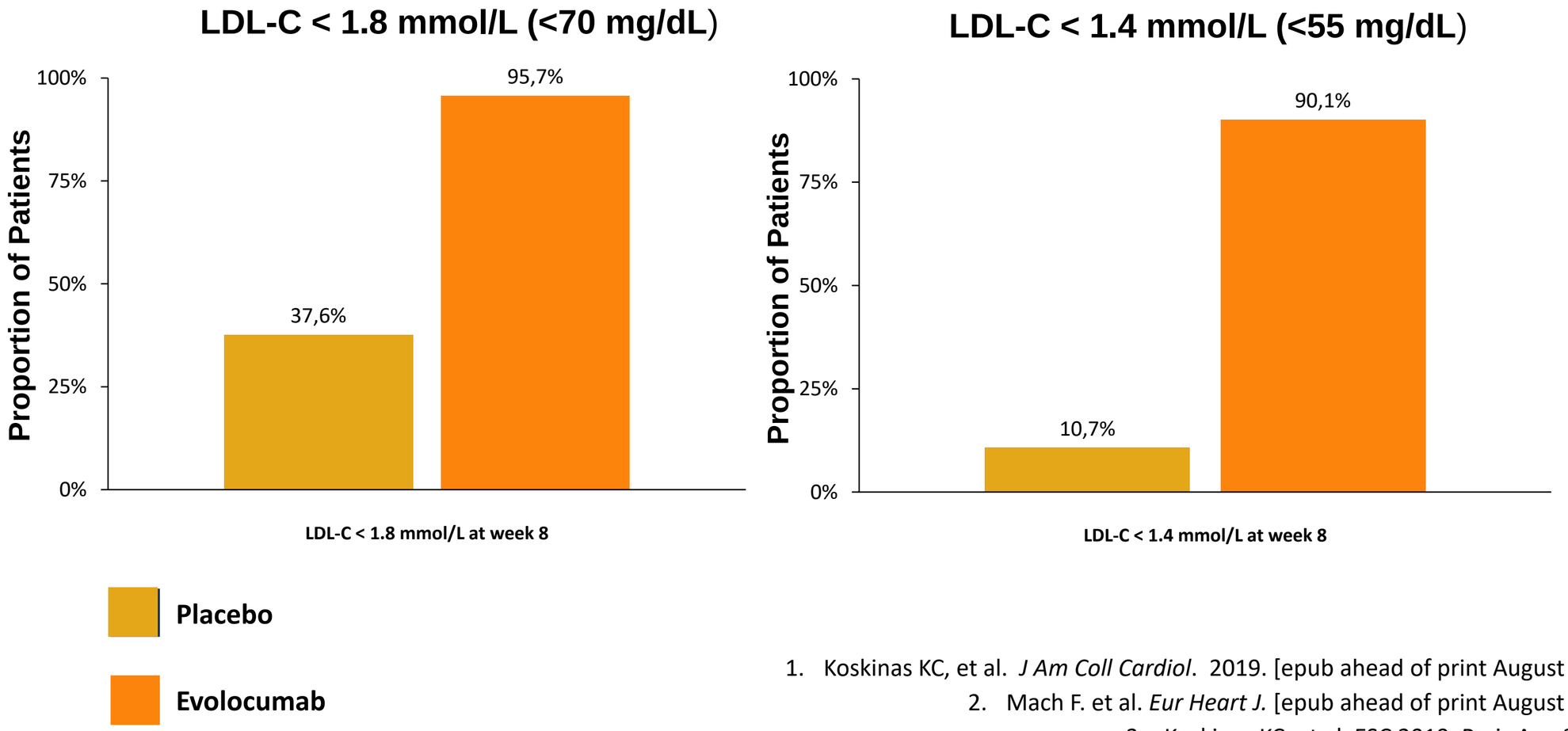


No. of patients			
Placebo	148	144	149
Evolocumab	146	136	141



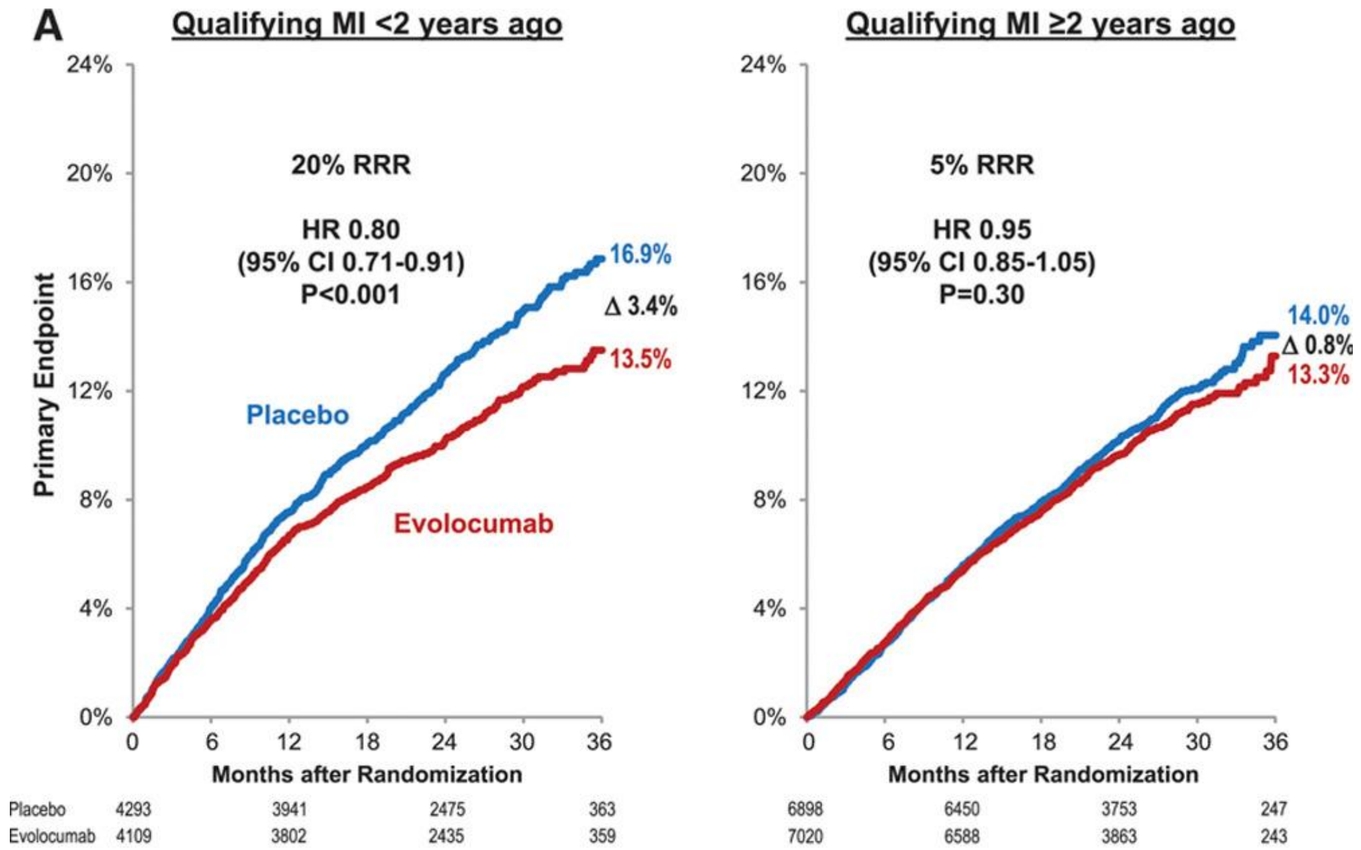
Koskinas KC, et al. *J Am Coll Cardiol*. 2019.

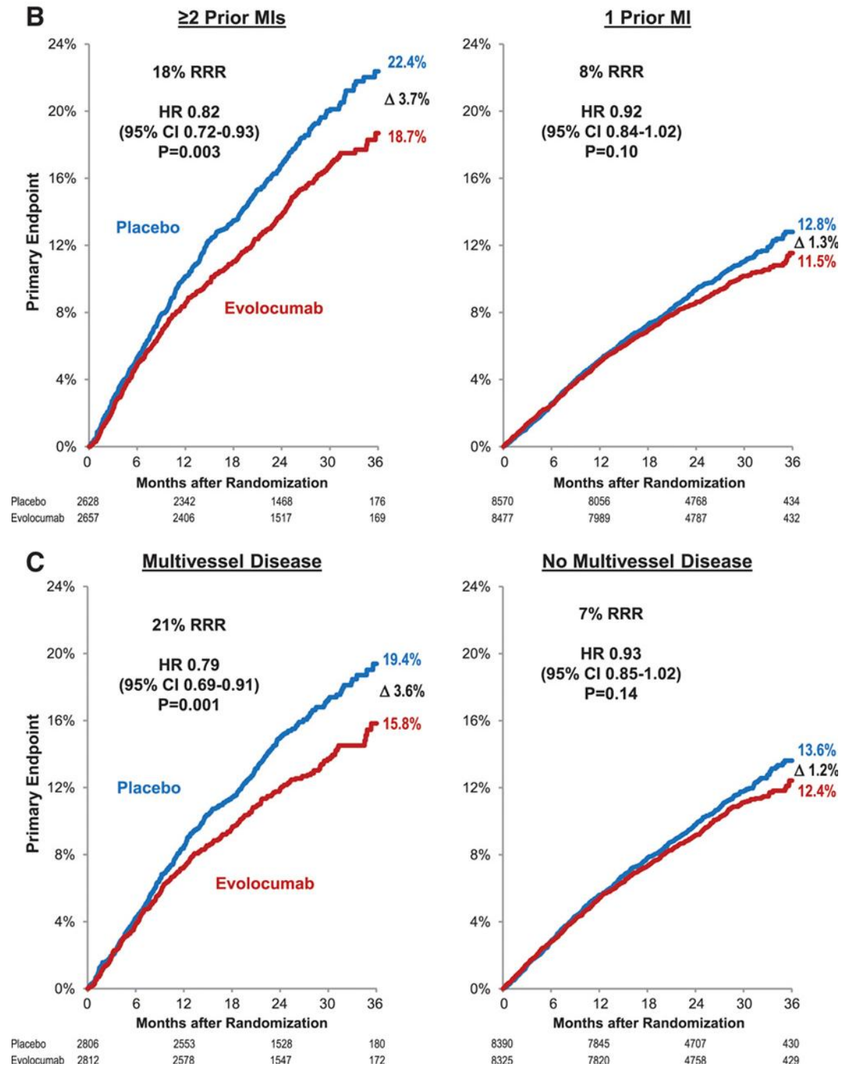
EVOPACS – dosažení cíle LDL-cholesterolu



1. Koskinas KC, et al. *J Am Coll Cardiol*. 2019. [epub ahead of print August 31, 2019]
2. Mach F. et al. *Eur Heart J.* [epub ahead of print August 31, 2019]
3. Koskinas KC, et al. ESC 2019, Paris Aug 31-Sept 4.

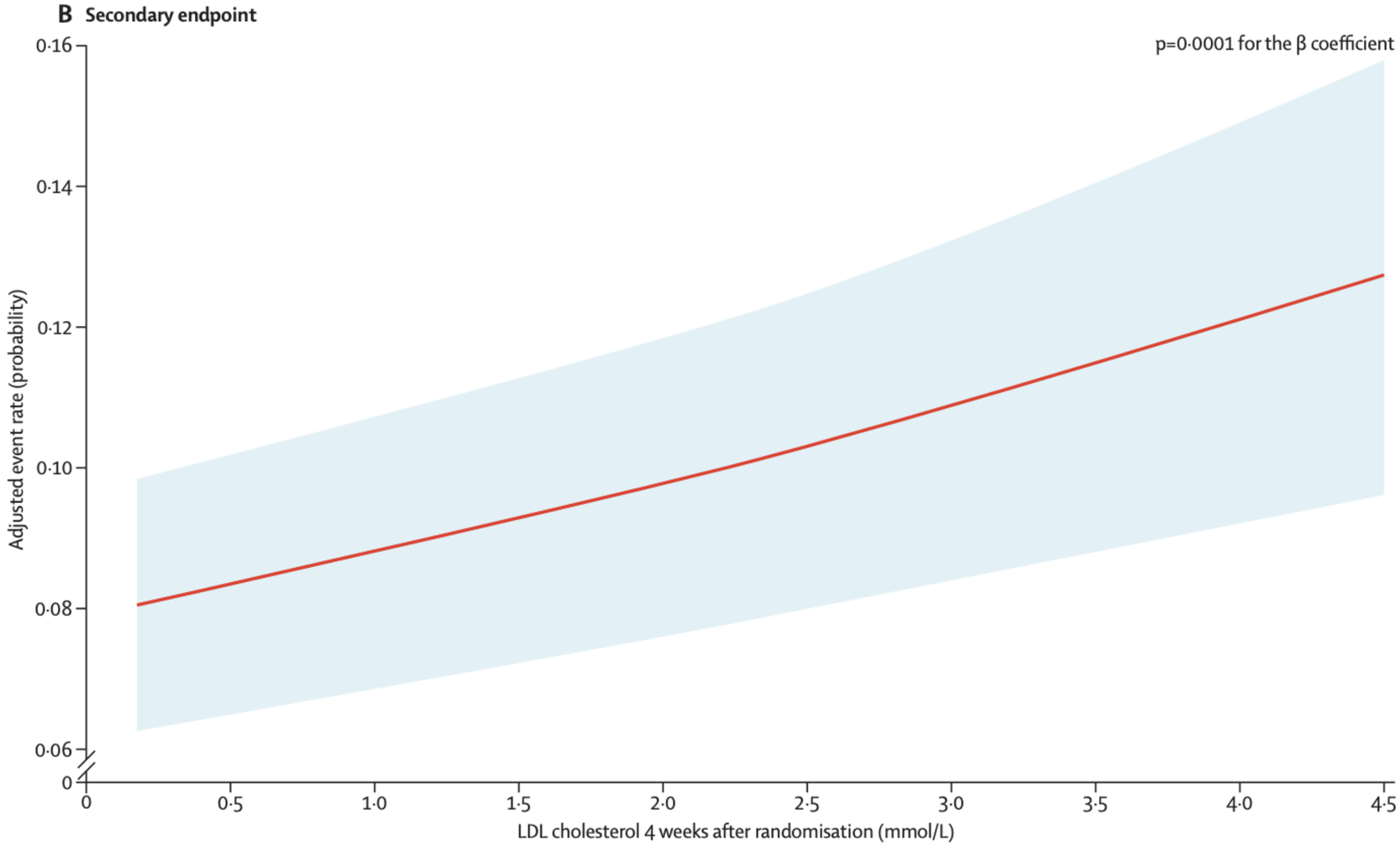
PCSK9i – benefit stoupá se včasností zahájení a závažností ICHS





Sabatine MS et al. Circulation 2018 Aug 21;138(8):756-766.

Evolokumab – redukce KV úmrtí, IM a CMP



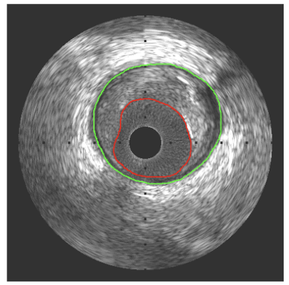
Giugliano RP et al. Lancet 2017 Oct 28;390(10106):1962-1971

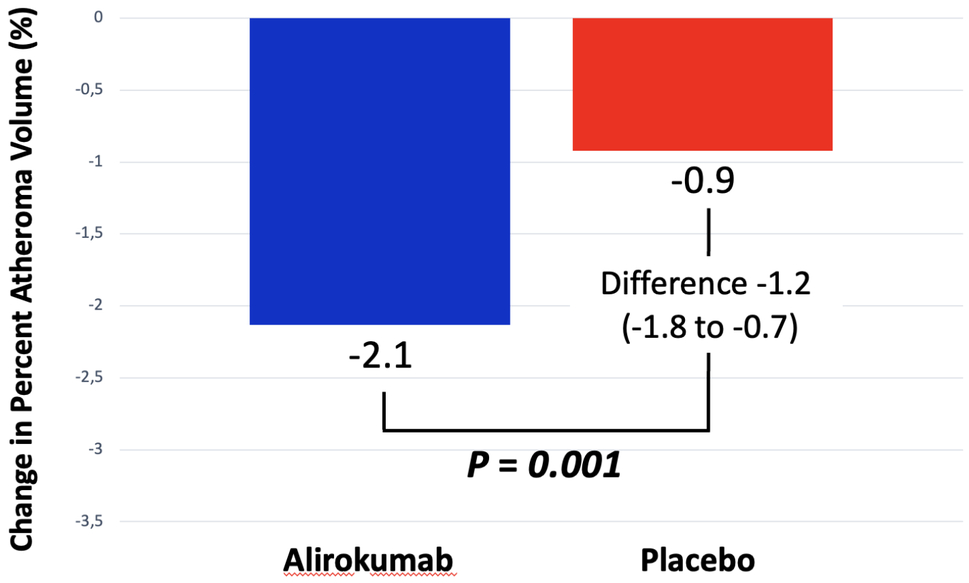
PACMAN AMI – časné nasazení alirocumabu po AKS

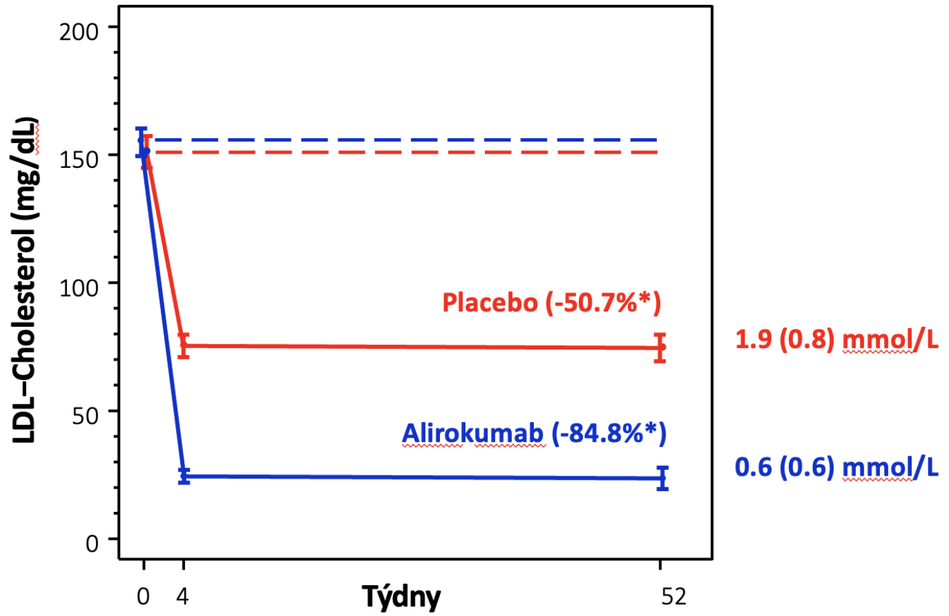
- Léčba alirokumabem zahájená v akutní fázi AIM, přidaná k intenzivní statinové léčbě, vedla **ke zmenšení aterosklerotického plátu, snížení obsahu lipidů a zesílení fibrozní čepičky po 52 týdnech sledování**
- Tyto výsledky ukazují **regresi a stabilizaci koronárního plátu** s pomocí alirokumabu a podporují časné zahájení intenzivní hypolipidemické léčby u AIM

Primární EP:

Změna v Percent Atheroma Volume (IVUS)

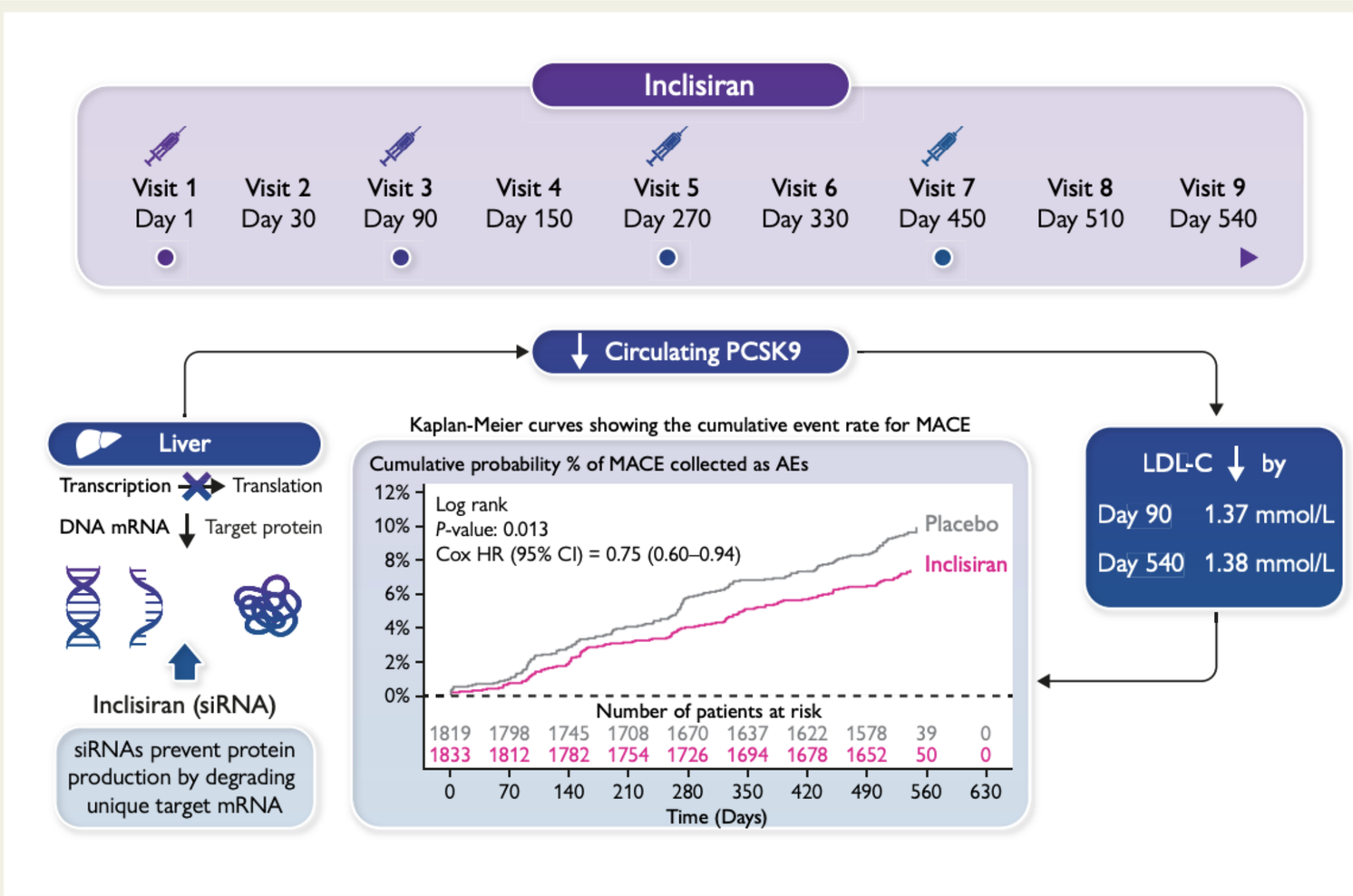






Räber, L et al. *JAMA* 2022. doi:10.1001/jama.2022.5218

Inklisiran



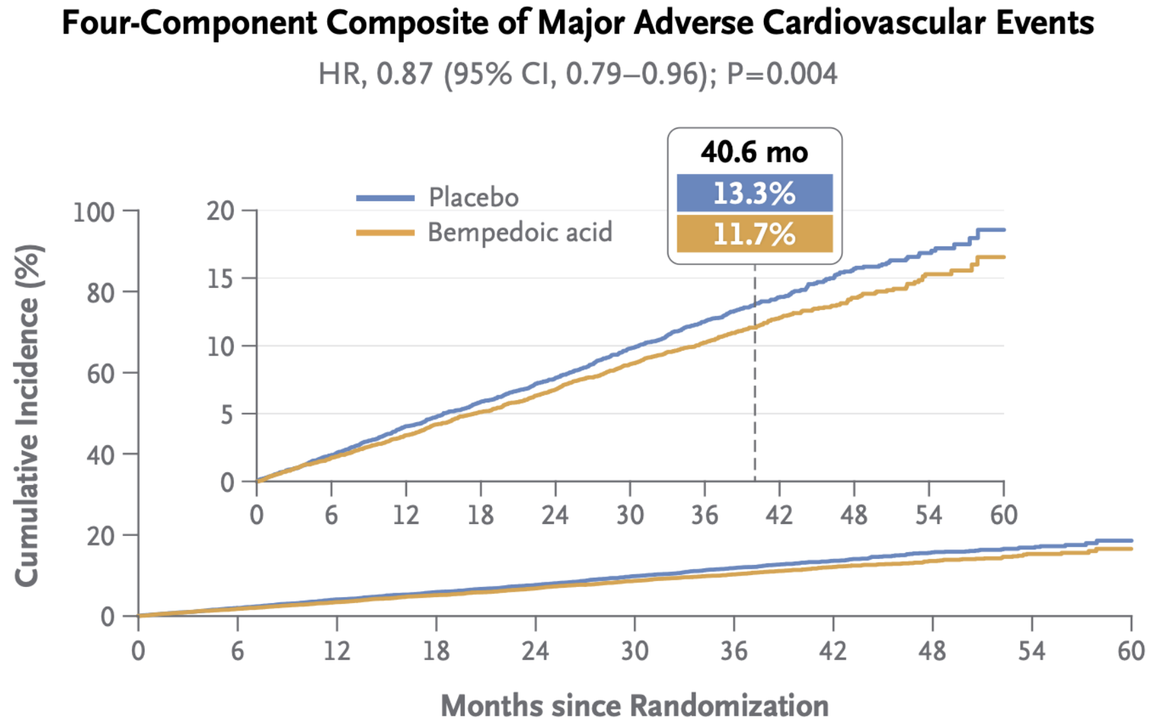
Inclisiran and risk of reported MACE from the patient-level pooled ORION-9, ORION-10 and ORION-11 trials.

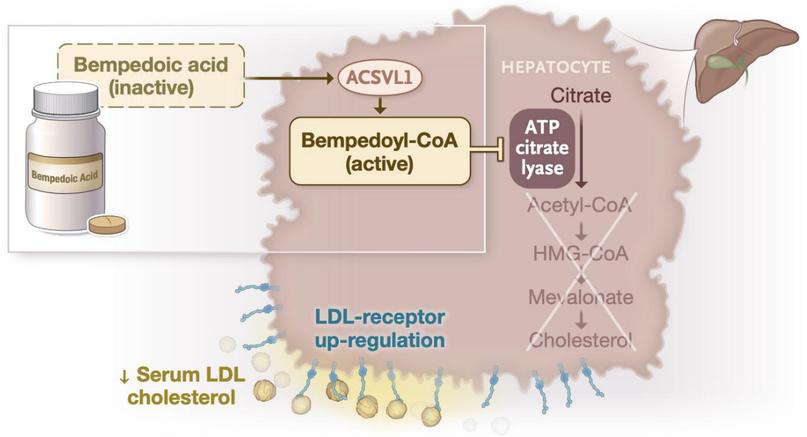
Ray KK et al. Eur Heart J . 2023 Jan 7;44(2):129-138.

Bempedoová kyselina

Bempedoic Acid and Cardiovascular Outcomes in Statin-Intolerant Patients

Nissen SE et al. DOI: 10.1056/NEJMoa2215024





Adverse Events

	Bempedoic acid (N=7001)	Placebo (N=6964)
	no. of patients (%)	
Any adverse event	6040 (86.3)	5919 (85.0)
Elevated hepatic enzymes	317 (4.5)	209 (3.0)
Renal impairment	802 (11.5)	599 (8.6)
Hyperuricemia	763 (10.9)	393 (5.6)
Gout	215 (3.1)	143 (2.1)
Cholelithiasis	152 (2.2)	81 (1.2)

*Nissen SE et al. **N Engl J Med 2023;388:1353-1364***

Aktualizace doporučení ESC/EAS z roku 2019

1. Odhad kardiovaskulárního rizika s implementací algoritmů predikce rizika SCORE2 a SCORE2-OP
2. **Terapie snižující hladinu LDL cholesterolu**
3. Hypolipidemická terapie osob s akutním koronárním syndromem
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8. Doplňky stravy

Mach F et al. Eur Heart J 2025 Nov 7;46(42):4359-4378

Kyselina bempedoová, evinacumab

Recommendation Table 2 — Recommendations for pharmacological low-density lipoprotein cholesterol lowering (see also Supplementary data online, Evidence Table 2)

Recommendations	Class[a]	Level[b]
Non-statin therapies with proven cardiovascular benefit,[c] 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.[4,53,54]	I	A
Bempedoic acid is recommended in patients who are unable to take statin therapy to achieve the LDL-C goal.[4]	I	B
The addition 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.[42,55]	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.[5,50,51]	IIa	B

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CV, cardiovascular; LDL-C, low-density lipoprotein cholesterol; PCSK9, proprotein convertase subtilisin/kexin type 9.
This table complements the table of recommendations for pharmacological low-density lipoprotein cholesterol lowering in the 2019 ESC/EAS Guidelines and does not replace it.
[a]Class of recommendation.
[b]Level of evidence.
[c]Ezetimibe, PCSK9 monoclonal antibodies, bempedoic acid.

Mach F et al. Eur Heart J 2025 Nov 7;46(42):4359-4378

Terapie snižující hladinu LDL-cholesterolu

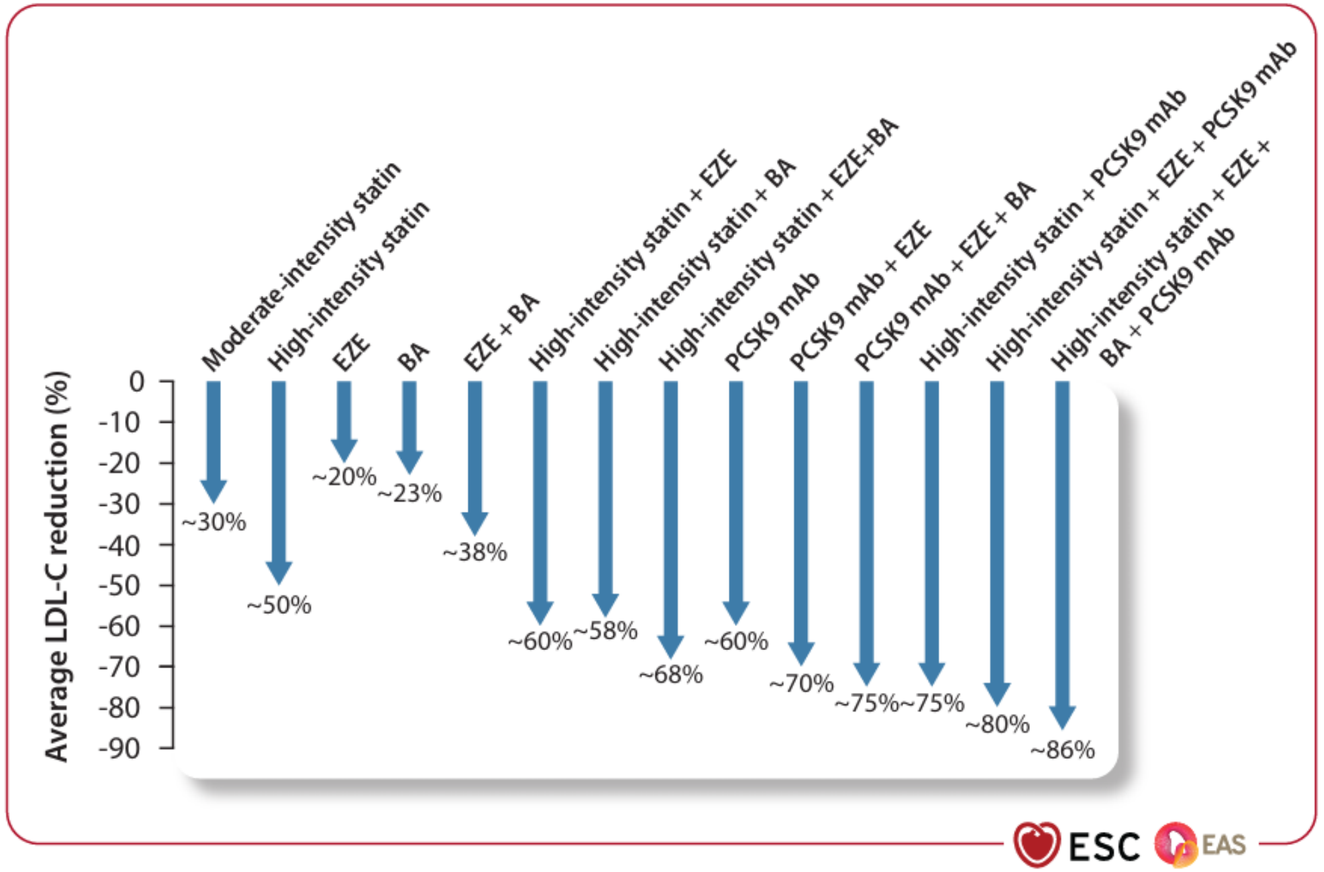


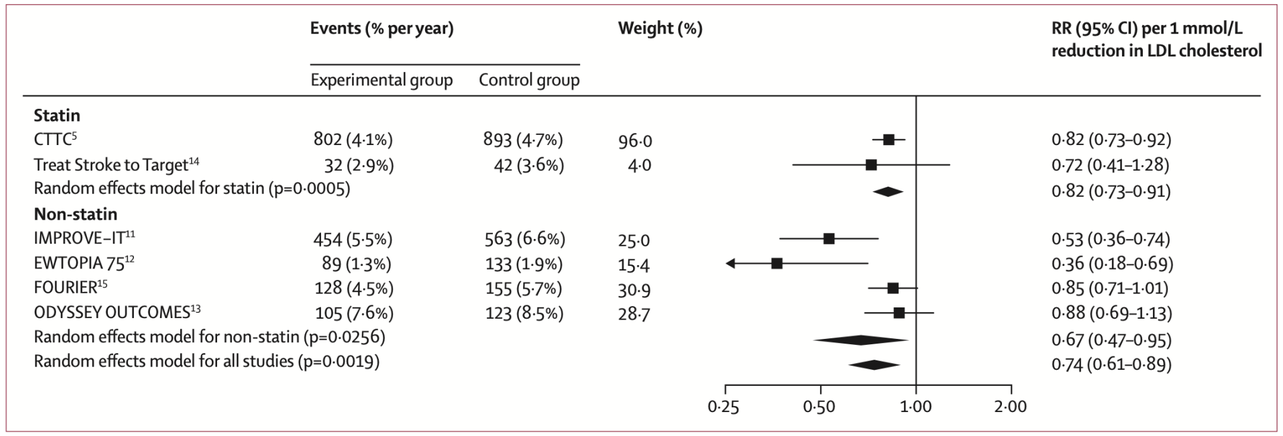
Figure 2 Average reduction in low-density lipoprotein cholesterol levels with different pharmacological therapies with proven cardiovascular benefits. BA, bempedoic acid; EZE, ezetimibe; LDL-C, low-density lipoprotein cholesterol; PCSK9 mAb, proprotein convertase subtilisin/kexin type 9 monoclonal antibody.

Mach F et al. Eur Heart J 2025 Nov 7;46(42):4359-4378

Terapie u pacientů ve věku ≥ 75 let

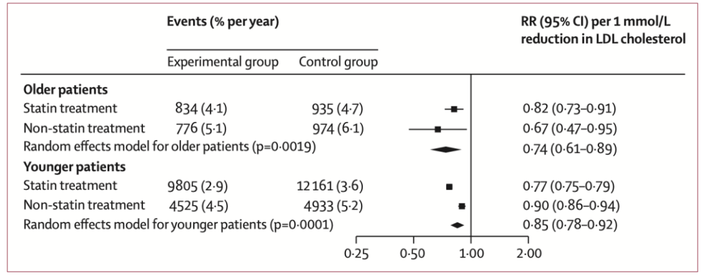
Efficacy and safety of lowering LDL cholesterol in older patients: a systematic review and meta-analysis of randomised controlled trials

Baris Gencer, Nicholas A Marston, KyungAh Im, Christopher P Cannon, Peter Sever, Anthony Keech, Eugene Braunwald, Robert P Giugliano, Marc S Sabatine



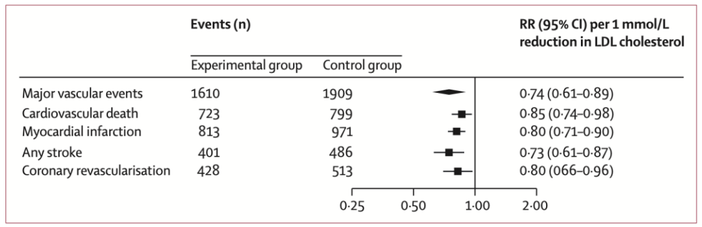
	Events (% per year)		Weight (%)	RR (95% CI) per 1 mmol/L reduction in LDL cholesterol
	Experimental group	Control group		
Statin				
CTTC[5]	802 (4·1%)	893 (4·7%)	96·0	0·82 (0·73–0·92)
Treat Stroke to Target[14]	32 (2·9%)	42 (3·6%)	4·0	0·72 (0·41–1·28)
Random effects model for statin (p=0·0005)				0·82 (0·73–0·91)
Non-statin				
IMPROVE–IT[11]	454 (5·5%)	563 (6·6%)	25·0	0·53 (0·36–0·74)
EWTOPIA 75[12]	89 (1·3%)	133 (1·9%)	15·4	0·36 (0·18–0·69)
FOURIER[15]	128 (4·5%)	155 (5·7%)	30·9	0·85 (0·71–1·01)
ODYSSEY OUTCOMES[13]	105 (7·6%)	123 (8·5%)	28·7	0·88 (0·69–1·13)
Random effects model for non-statin (p=0·0256)				0·67 (0·47–0·95)
Random effects model for all studies (p=0·0019)				0·74 (0·61–0·89)

Figure 1: **Effect of LDL cholesterol lowering on the risk of major vascular events with statin and non-statin treatment in older patients**
Older patients were aged 75 years or older. RRs per 1 mmol/L reduction in LDL cholesterol were generated from a random effects model. In the ODYSSEY OUTCOMES trial, the event numbers were provided at 4 years, whereas the RR is for the entire duration of trial. CTTC=Cholesterol Treatment Trialists' Collaboration. EWTOPIA 75=Ezetimibe Lipid-Lowering Trial on Prevention of Atherosclerosclerotic Disease in 75 or Older. FOURIER=Further Cardiovascular Outcomes Research with PCSK9 Inhibition in Patients with Elevated Risk. IMPROVE-IT=Improved Reduction of Outcomes: Vytorin Efficacy International Trial. ODYSSEY OUTCOMES=Evaluation of Cardiovascular Outcomes After an Acute Coronary Syndrome During Treatment with Alirocumab. RR=risk ratio.



	Events (% per year)		RR (95% CI) per 1 mmol/L reduction in LDL cholesterol
	Experimental group	Control group	
Older patients			
Statin treatment	834 (4·1)	935 (4·7)	0·82 (0·73–0·91)
Non-statin treatment	776 (5·1)	974 (6·1)	0·67 (0·47–0·95)
Random effects model for older patients (p=0·0019)			0·74 (0·61–0·89)
Younger patients			
Statin treatment	9805 (2·9)	12 161 (3·6)	0·77 (0·75–0·79)
Non-statin treatment	4525 (4·5)	4933 (5·2)	0·90 (0·86–0·94)
Random effects model for younger patients (p=0·0001)			0·85 (0·78–0·92)

Figure 2: **Effect of LDL cholesterol lowering on the risk of major vascular events in older versus younger patients**
Older patients were aged 75 years or older and younger patients were younger than 75 years. RRs per 1 mmol/L reduction in LDL cholesterol were generated from a random effects model. RR=risk ratio.



	Events (n)		RR (95% CI) per 1 mmol/L reduction in LDL cholesterol
	Experimental group	Control group	
Major vascular events	1610	1909	0·74 (0·61–0·89)
Cardiovascular death	723	799	0·85 (0·74–0·98)
Myocardial infarction	813	971	0·80 (0·71–0·90)
Any stroke	401	486	0·73 (0·61–0·87)
Coronary revascularisation	428	513	0·80 (066–0·96)

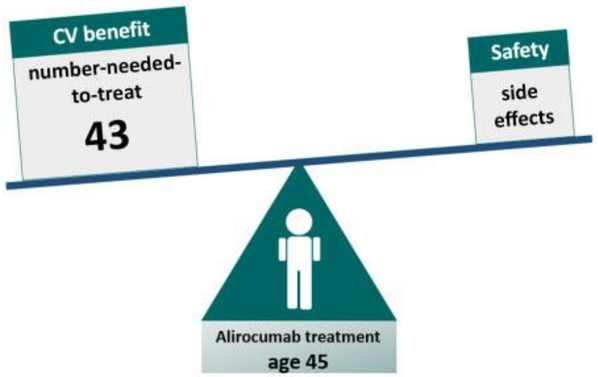
Figure 3: **Effect of LDL cholesterol lowering on the risk of individual efficacy endpoints in older patients**
Older patients were aged 75 years or older. RRs per 1 mmol/L reduction in LDL cholesterol were generated from a random effects model. RR=risk ratio.

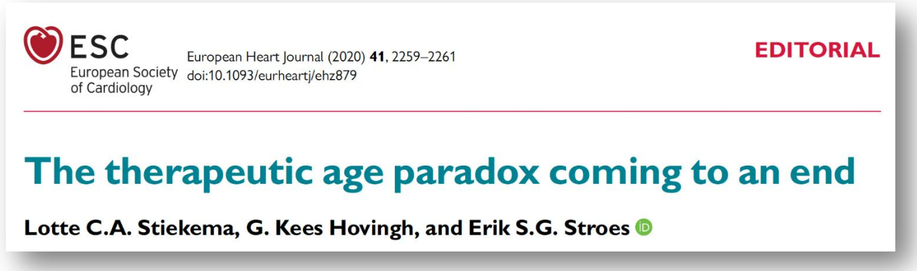
- Meta-analýza - 29 studií (244 090 pacientů), z toho **21 492 pacientů ≥75 let**
- **Statiny** (11 750 pt.), **Ezetimib** (6209 pt), **PCSK9 inhibitory (evolocumab, alirocumab)** (3533 pacientů)
- **Snížení MACE: 26 % na každé 1 mmol/l snížení LDL-c** (RR 0,74; 95% CI 0,61–0,89; p=0,0019)
  - účinek byl podobný jako u pacientů <75 let (p = 0,37)
  - žádný rozdíl mezi statiny a nestatinovou léčbou (p = 0,64)

Gencer B et al. Lancet 2020 Nov 21;396(10263):1637-1643

Benefit PCSK9i u pacientů vyššího věku

- **Alirocumab (PCSK9 inhibitor) - ODYSSEY OUTCOMES - významný přínos u starších pacientů**:
  - pt. <65 let HR 0,89, pt. ≥65 let HR 0,78
  - konzistentní přínos až do 85 let věku (HR 0,68 ve věku 85 let)
- **Absolutní benefit roste s věkem** díky vyšší incidenci KV příhod - NNT (počet léčených pro zabránění 1 příhodě):
  - 45 let: 43
  - 75 let: 26
  - 85 let: 12
- **Bezpečnostní profil zůstává příznivý** i ve vyšším věku
- Starší pacienti profitují **nejvíce v absolutních číslech** z intenzivní hypolipidemické terapie (zejména v sekundární prevenci)
- **Paradox "čím starší, tím méně léčit" by měl skončit - v**ýběr pacientů by měl zohledňovat biologický spíše než kalendářní věk a kvalitu života.




ESC European Society of Cardiology

European Heart Journal (2020) **41**, 2259–2261
doi:10.1093/eurheartj/ehz879

EDITORIAL

The therapeutic age paradox coming to an end

Lotte C.A. Stiekema, G. Kees Hovingh, and Erik S.G. Stroes

Eur Heart J 2020 Jun 21;41(24):2259-2261

Aktualizace doporučení ESC/EAS z roku 2019

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8. **Doplňky stravy**

Mach F et al. Eur Heart J 2025 Nov 7;46(42):4359-4378

Doplňky stravy

Recommendation Table 8 — Recommendations for dietary supplements (see also Supplementary data online, Evidence Table 8)

Recommendation	Class[a]	Level[b]
Dietary supplements or vitamins without documented safety and significant LDL-C-lowering efficacy are not recommended to lower the risk of ASCVD.[10,11]	III	B

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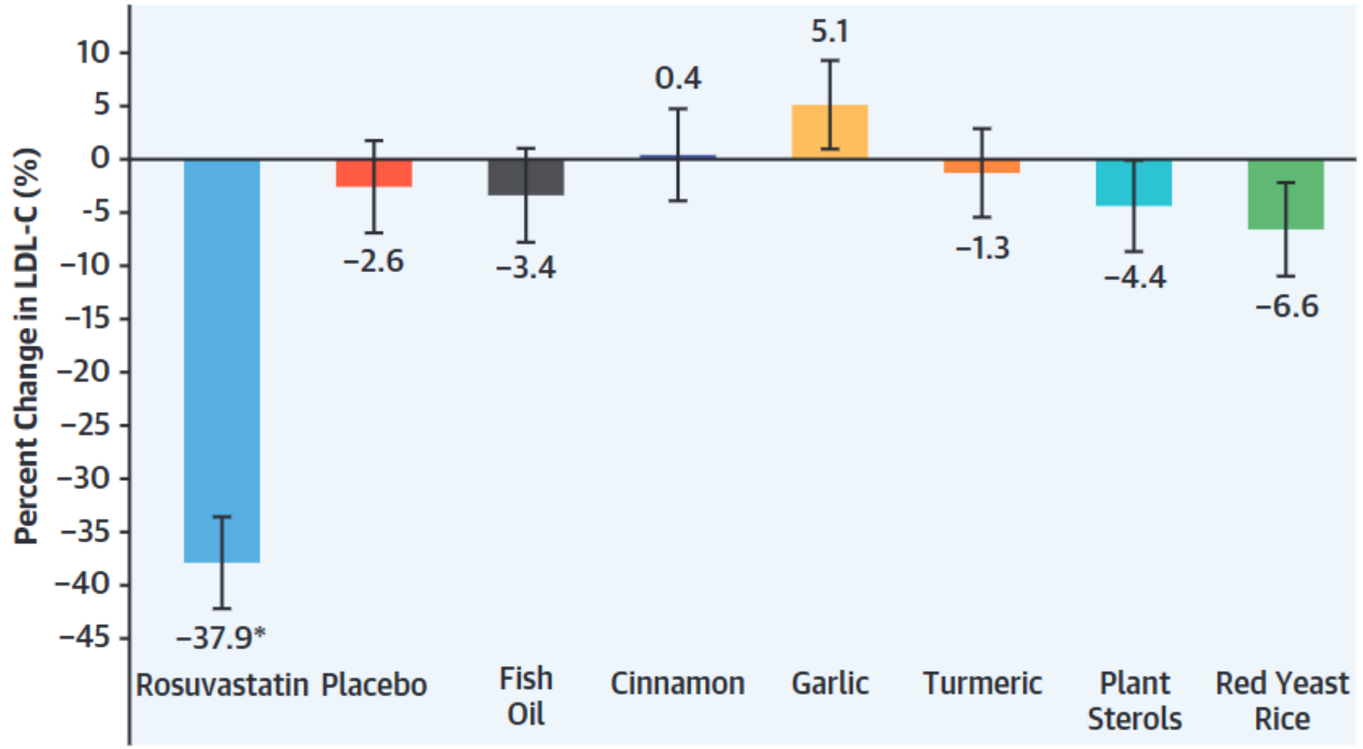
ASCVD, atherosclerotic cardiovascular disease; LDL-C, low-density lipoprotein cholesterol.
[a]Class of recommendation.
[b]Level of evidence.

- Omega-3 mastné kyseliny (derivat eikosapentaenové kyseliny) v dávce 4 g denně u osob s hypertriglyceridémií

Potravinové doplňky?

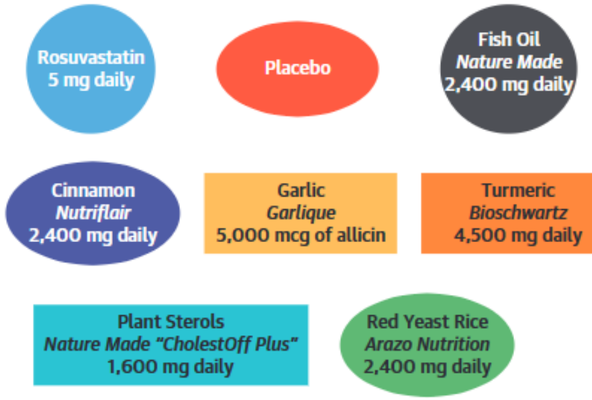
FIGURE 2 Mean Percent LDL-C Change

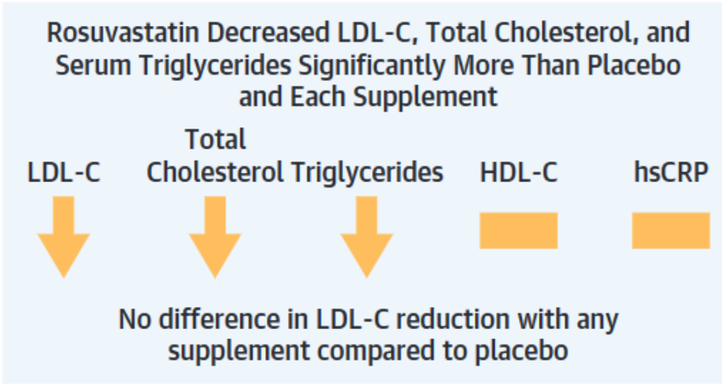


Least-square means (adjusting for baseline laboratory values, age, and sex) and 95% CIs are displayed. *$P < 0.001$ all other group comparisons to rosuvastatin. LDL-C = low-density lipoprotein cholesterol.

Comparative Effects of Low-Dose Rosuvastatin, Placebo, and Dietary Supplements on Lipids and Inflammatory Biomarkers

Luke J. Laffin, MD,[a] Dennis Bruemmer, MD,[a] Michelle Garcia, RN,[b] Danielle M. Brennan, MS,[b] Ellen McErlean, MSN,[b] Douglas S. Jacoby, MD,[c] Erin D. Michos, MD,[d] Paul M Ridker, MD,[e] Tracy Y. Wang, MD,[f] Karol E. Watson, MD,[g] Howard G. Hutchinson, MD,[h] Steven E. Nissen, MD[a,b]





Laffin LJ, et al. J Am Coll Cardiol. 2023;81(1):1–12

Potravinové doplňky?

TABLE 4 Adverse Effects

	Rosuvastatin (n = 25)	Placebo (n = 25)	Fish Oil (n = 24)	Cinnamon (n = 25)	Garlic (n = 25)	Turmeric (n = 25)	Plant Sterols (n = 25)	Red Yeast Rice (n = 25)
Serious adverse events	0 (0.0)	1 (4.0)[a]	1 (4.2)[b]	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Adverse events	4 (16.0)	4 (16.0)	3 (12.5)	3 (12.0)	5 (20.0)	4 (16.0)	7 (28.0)	7 (28.0)
Gastrointestinal	3 (12.0)	1 (4.0)	2 (8.3)	1 (4.0)	2 (8.0)	2 (8.0)	3 (12.0)	2 (8.0)
Musculoskeletal	0 (0.0)	2 (8.0)	0 (0.0)	0 (0.0)	1 (4.0)	1 (4.0)	1 (4.0)	2 (8.0)
Neurological	0 (0.0)	1 (4.0)	1 (4.2)	0 (0.0)	1 (4.0)	0 (0.0)	1 (4.0)	3 (12.0)
Increase in ALT to >3× ULN	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Change in ALT from baseline, U/L	1.9 ± 7.6	−1.0 ± 4.6	−0.6 ± 4.3	0.5 ± 4.1	1.2 ± 7.2	0.3 ± 2.0	1.3 ± 6.8	−0.8 ± 4.7
Increase in AST to >3× ULN	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Change in AST from baseline, U/L	1.3 ± 3.7	−0.1 ± 3.6	1.1 ± 4.0	0.5 ± 3.7	1.2 ± 5.0	−0.8 ± 2.0	−0.5 ± 5.4	−0.4 ± 5.8
Change in alkaline phosphatase from baseline, U/L	−2.5 ± 7.6	1.0 ± 8.0	−3.0 ± 6.3	−1.6± 6.3	0.4 ± 6.31	−0.3 ± 6.60	4.0 ± 23.54	0.9 ± 8.86
Change in total bilirubin from baseline, U/L	0.0 ± 0.16	0.0 ± 0.22	0.1 ± 0.13	0.0 ± 0.15	0.1 ± 0.21	0.0 ± 0.20	0.0 ± 0.08	0.0 ± 0.16
Change in eGFR, mL/min/1.73 m^2	1.8 ± 9.03	1.3 ± 3.53	2.6 ± 8.86	1.4 ± 8.18	−0.4 ± 4.43	2.9 ± 10.00	1.6 ± 6.28	−0.3 ± 4.22
Change in blood glucose, mg/dL	0.5 (−4.0 to 5.5)	−1.0 (−7.0 to 4.0)	3.5 (−3.0 to 7.0)	−1.0 (−3.0 to 5.0)	2.0 (−2.0 to 8.0)	−1.0 (−8.0 to 3.0)	−0.5 (−5.5 to 2.5)	1.0 (−6.0 to 3.0)

Values are n (%), mean ± SD, or median (IQR). [a]Deep venous thrombosis. [b]Diagnosis of liver adenocarcinoma before any investigational product was taken.
ALT = alanine transaminase; AST = aspartate transaminase; eGFR = estimated glomerular filtration rate; ULN = upper limit of normal.

Laffin LJ, et al. J Am Coll Cardiol. 2023;81(1):1–12

Optimální strategie po IM –“ strike early and strong“

- **U všech pacientů s AKS dbát na časnou, intenzivní (kombinovanou) léčbu hypolipidemiky během indexové hospitalizace**

- **Okamžitě zahájit vysokodávkový statin** (např. atorvastatin 40–80 mg nebo rosuvastatin 20–40 mg)

- **Kombinační léčbu** (1 nebo více nestatinových léků s prokázaným KV benefitem) přidat **hned podle potřeby**, nikoli až po (4-6) týdnech:
  - pokud pacient už před IM/ACS **užíval statin** a stále má vysoké LDL-C
  - pokud je výchozí LDL-C tak vysoké, že jen statin s velkou pravděpodobností cíle nedosáhne
- Volba přidaného léku se má řídit **potřebným dodatečným poklesem LDL-C**:
  - *Menší dodatečný efekt*: ezetimib
  - *Střední až velký dodatečný efekt*: PCSK9 mAb (alirocumab, evolocumab) nebo bempedová kyselina, případně kombinace

X realita úhradových omezení ZP

Závěr

- **Intenzivní snížení LDL-cholesterolu je zásadní pro sekundární prevenci.**
  → Cílová hladina **< 1,4 mmol/l** a snížení alespoň o **50 % oproti výchozí hodnotě**.
- **Čím dříve zahájíme intenzivní hypolipidemickou léčbu, tím lépe.**
  → Včasné nasazení kombinační terapie (statin + ezetimib, případně + PCSK9i) již během hospitalizace zlepšuje prognózu.
- **Hypolipidemická léčba, vč. PCSK9 inhibitorů přinášejí významný benefit i u starších pacientů.**
  → Absolutní redukce KV příhod narůstá s věkem, léčba je dobře tolerována i ve vyšším věku.
- **Kombinační léčba je často nutná k dosažení cílových hodnot.**
- **Velmi nízké hladiny LDL-C (< 1,0 mmol/l) jsou bezpečné.**
- **Potravinové doplňky nenahrazují farmakologickou léčbu.**

DĚKUJEME ZA POZORNOST

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