Jak mohou ovlivnit cesta pacientů nová hypolipidemika?

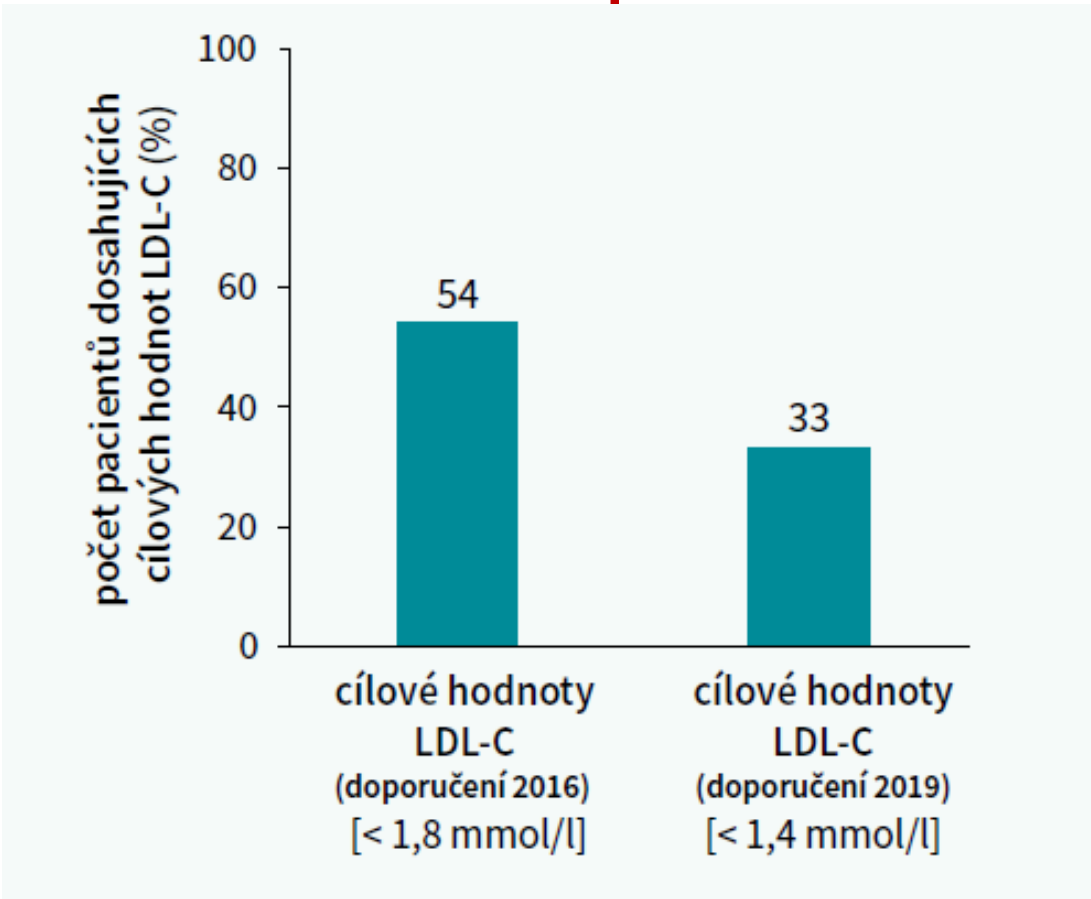
Pavel Kraml

Centrum pro diagnostiku a léčbu dyslipidémií

Interní klinika 3.LF UK a FNKV Praha

XXXIV. výroční sjezd ČKS 9.-12.5.2026 Brno

Srovnání dosahování cílových hodnot dle doporučení ESC/EAS 2016 a 2019 ve studii Da Vinci sekundární prevence



Vrablík M., Athero Review 2021

Low LDL-C goal attainment in patients at very high cardiovascular risk due to lacking observance of the guidelines on dyslipidaemias

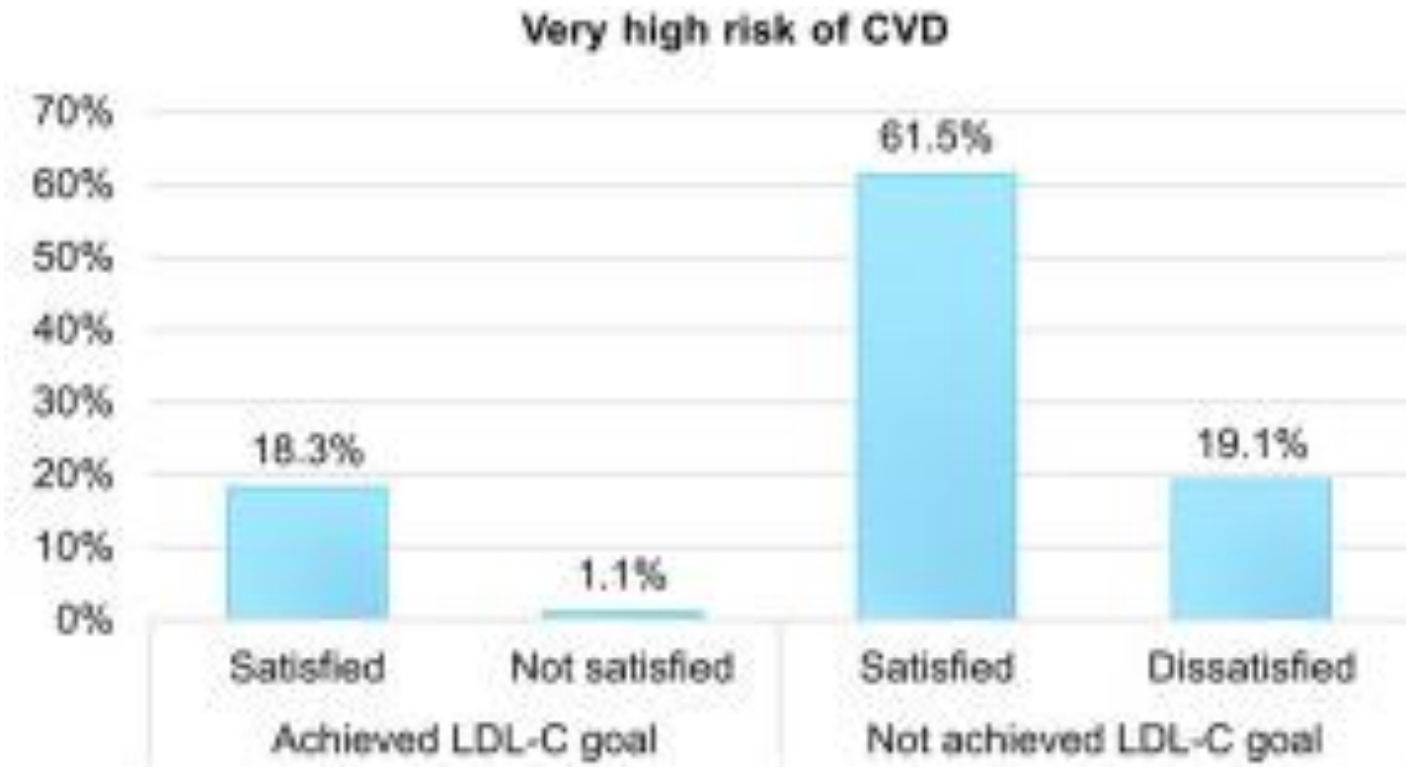
Michal Vrablík, Ivana Šarkanová, Katarína Breciková, Petra Šedová , Martin Šatný , Aleš Tichopád

PLoS One 2023 May 22;18(5):e0272883. doi: 10.1371/journal.pone.0272883

- 450 pacientů velmi vysokého rizika pro ASKVO
- 46 specialistů (kardiologie, interna)
- Náběr 6/2021 - 1/2022

- 361 (80,2%) pacientů VERY HIGH RISK
- 57 (12,7%) pacientů HIGH RISK

Vrablík M. et al PLoS One 2023



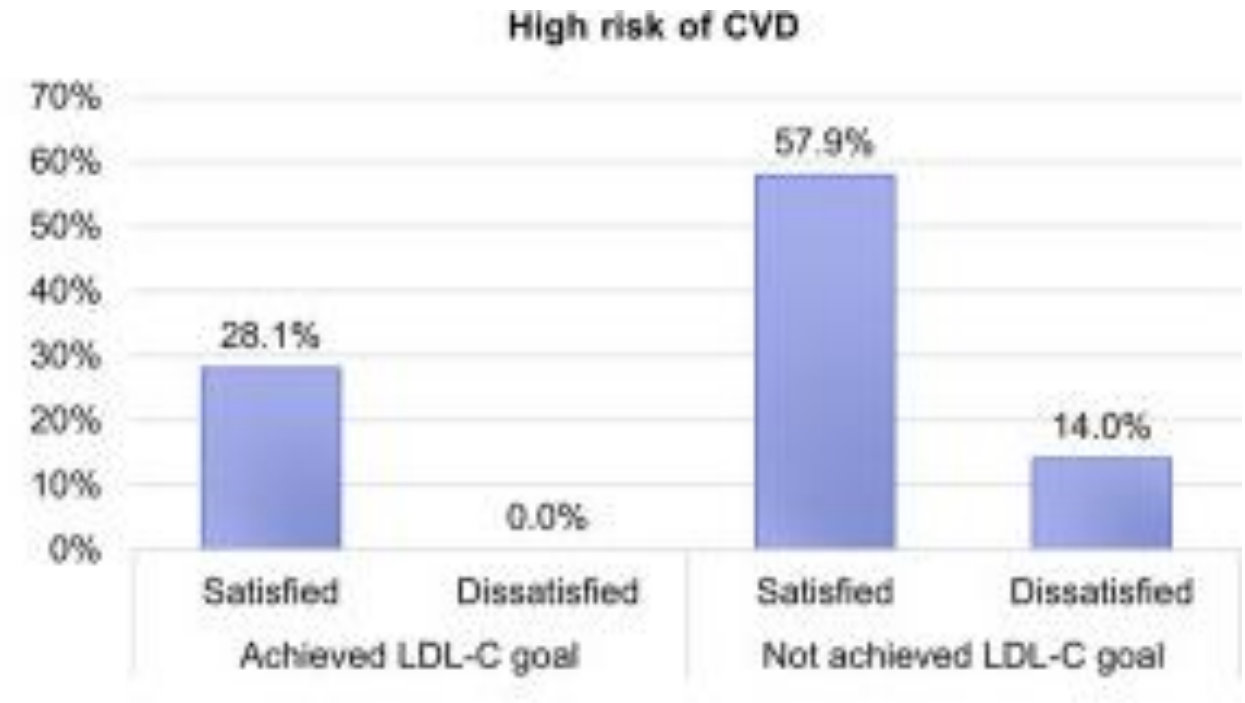
19,4 %

80,6 %

Vrablík M. et al PLoS One 202

Very high risk of CVD

Vrablík M. et al PLoS One 2023



28,1 %

71,9 %

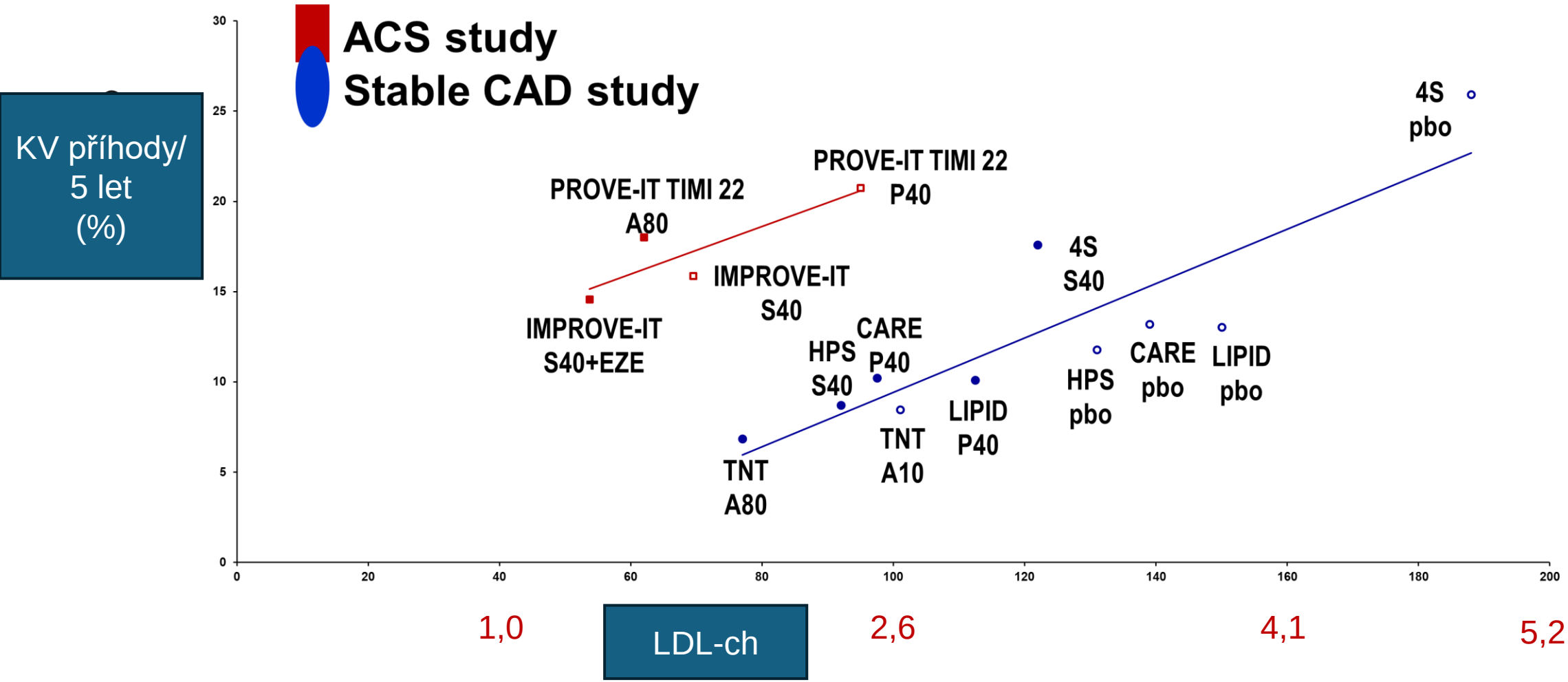
Vrablík M. et al PLoS One 2023

High risk of CVD

	Achieved LDL-C goal	Not achieved LDL-C goal
no change is neede	15.8%	17.5%
prefer no change	10.5%	29.8%
thinking about change	1.8%	8.8%
change is neccesary	0.0%	15.8%

Vrablík M. et al PLoS One 2023

Pokles LDL-ch a KV příhody za 5 let



Cannon CP, JACC 2020; 75(17)

EFEKT SNÍŽENÍ LDL-CH NA MACE:

⬇ LDL-ch o 1 mmol/l → ⬇ 19-23% MACE

Andersson NW et al. JACC 2023, Burger PM et al. Atherosclerosis 20

Proč PCSK9 inhibitory mění prognózu

EVOLOCUMAB: FOURIER: stabilní ASCVD

Evolokumab ke statinu

Populace	27 564 pacientů se stabilní ASCVD
Vstup	IM / CMP / PAD; LDL-C ≥1,8 mmol/l nebo non-HDL-C ≥2,6 mmol/l
Intervence	evolocumab 140 mg q2w nebo 420 mg q4w
Kontrola	placebo + optimální statinová léčba
Medián sledování	2,2 roku

LDL-C −59 %

Primární cíl:
CV smrt/IM/CMP/ NAP hospit./ Koron.revask.

HR 0,85
ARR 1,5%

Sekund. cíl:
CV smrt/IM/CMP/

HR 0,80
ARR 1.5 %

Sabatine MS et al., NEJM 2017, 376(18): 1713-1722

ALIROCUMAB: ODYSSEY OUTCOMES: pacient po recentním ACS

Alirokumab ke statinu po 1–12 měsících od akutního koronárního syndromu

Populace	18 924 pacientů po recentním ACS
Vstup	na vysokointenzivním / maximálně tolerovaném statinu; elevace aterogenních lipidů
Intervence	alirokumab 75/150 mg q2w titrovaný k LDL-C 0,6-1,3 mmol/l
Kontrola	placebo + standardní léčba
Medián sledování	2,8 roku

LDL-C −54,7 %

Primární cíl:
KV smrt/
Fatal-Nonfatal MI
CMP/
NAP hospit.

HR 0,85

Sekundární cíl:
Kompozit. primární cíl
+ celková mortalita:

HR 0,86

Sekundární cíl:
Celková mortalita

HR 0,85

Největší absolutní přínos byl u pacientů s vyšším vstupním LDL-C ≥2,6 mmol/l

Schwartz GG et al.,NEJM 2018; 379: 2097-2107

INCLISIRAN: ORION 9, 10, 11 (POOLED DATA)

Inclisiran ke statinu

18.MĚSÍC

ORION 9 He FH	241 inclisiran vs. 241 placebo LDL-ch ≥ 2,6 mmol/l
ORION 10 ASCVD (ICHS,CMP, PAD)	781 inclisiran vs. 780 placebo LDL-ch ≥ 1,8 mmol/l
ORION 10 ASCVD (ICHS,CMP, PAD) + ASCVDrisk ekvivalent: -DM 2T -10 leté KV riziko ≥ 20% -He FH	810 inclisiran vs. 810 placebo LDL-ch ≥ 1,8 mmol/l

LDL-C
−55%

Primární cíl:
CV smrt/
Nonfatal MI/
Fatal-Nonfatal CMP

HR 0,85

MI
(fatal/nonfatal)

HR 0,81

CMP
(fatal/nonfatal)

HR 0,80

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

KYSELINA BEMPEDOOVÁ: CLEARE OUTCOMES

60.MĚSÍC

CLEARE OUTCOMES
Intolerance statinů

Prim.prev. 30%
Sek.prev. 70%

DM 45%
Statin 23%
Ezetimib 12%

6992 KB vs. 6978 placebo
Prům. LDL-ch 3,6 mmol/l

LDL-C
−26%

Primární cíl:
KV smrt/
Nonfatal MI/
Nonfatal CMP/
Koronár.revask

HR 0,87

Nissen SE et al., NEJM 2023; 388: 1353-1364

PACIENT MÁ VYŠŠÍ TRIACYLGLYCEROLY

ICOSAPENT ETHYL (čistý EPA): REDUCE-IT

60.MĚSÍC

4089 EPA 2x2 g vs. 4090 placebo

LDL-ch 1,06 - 2,59 mmol/l
TAG 1,5 – 5,6 mmol/l

Primární cíl:
KV smrt/
Nonfatal MI/
Nonfatal CMP/
Koronár. revask./
NAP

HR 0,75

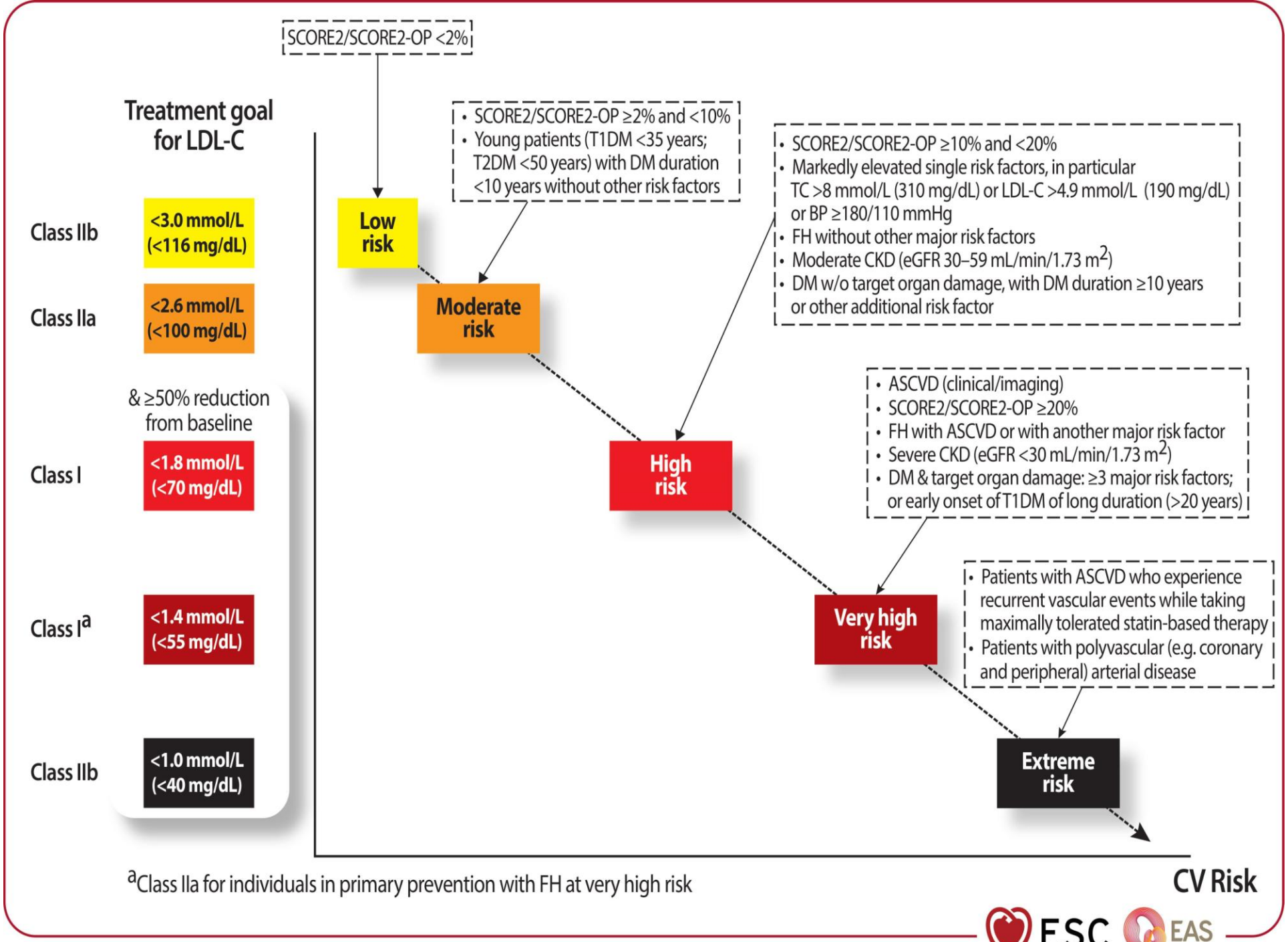
Bhat DL et al., N Engl J Med 2019;380:11-22

EPA* A DOPORUČENÍ ESC/EAS 2025

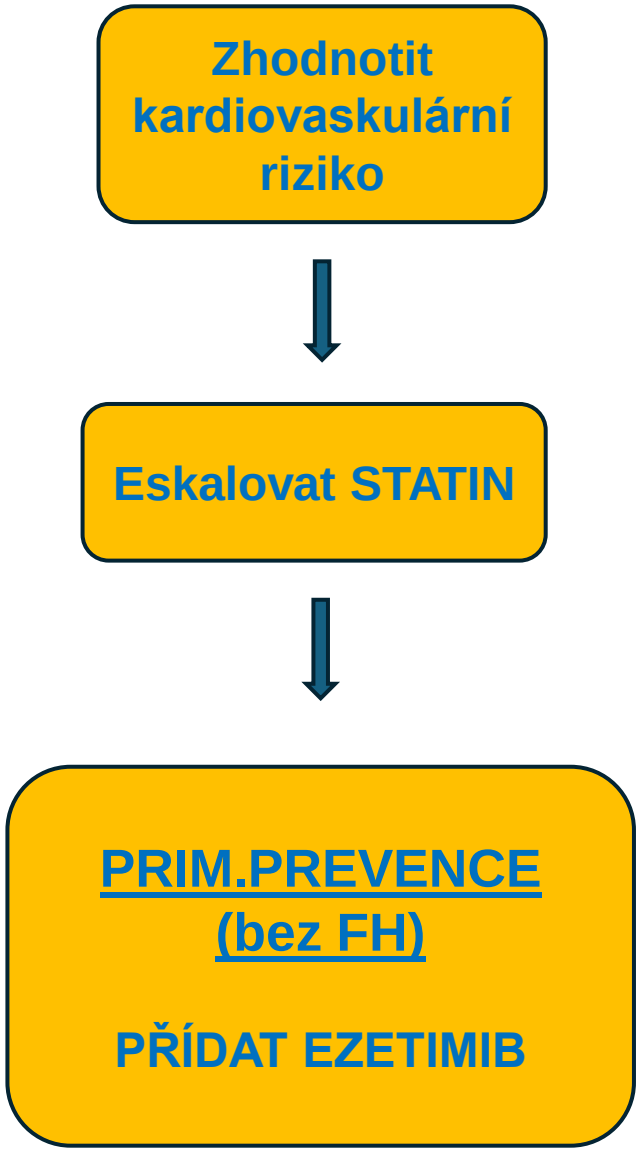
PACIENTI:	ZÁKLADNÍ LÉČBA:	TAG (mmol/l)	Class	Level
HIGH RISK/ VERY HIGH RISK	STATIN	1,52-5,63	IIa	B

* TÝKÁ SE POUZE PURIFIKOVANÉ EPA (VASCEPA) NIKOLI DHA ČI SMĚSI EPA/DHA !

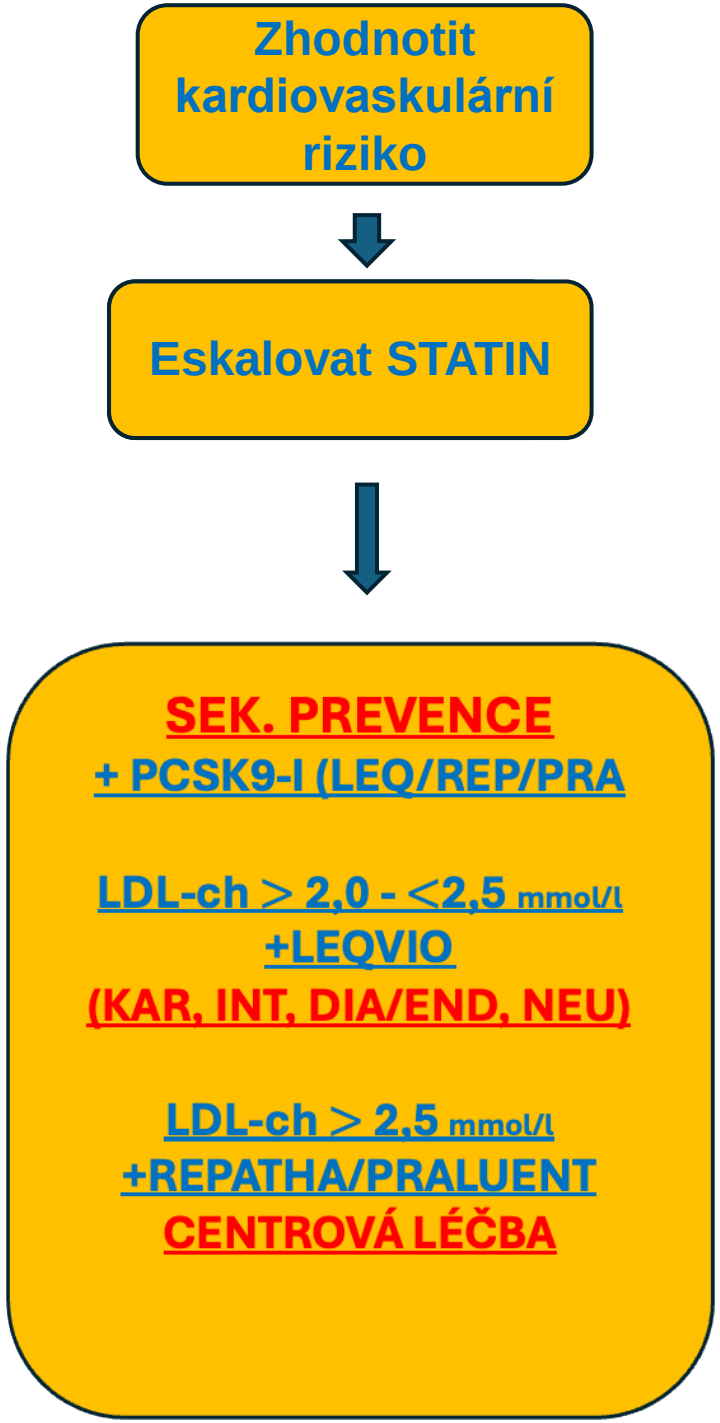
Focused Update of the 2019 ESC/EAS Guidelines, Eur Heart J 2025


SCORE2/SCORE2-OP <2%
Treatment goal for LDL-C
Class IIb
<3.0 mmol/L (<116 mg/dL)
Class IIa
<2.6 mmol/L (<100 mg/dL)
& ≥50% reduction from baseline
Class I
<1.8 mmol/L (<70 mg/dL)
Class I[a]
<1.4 mmol/L (<55 mg/dL)
Class IIb
<1.0 mmol/L (<40 mg/dL)
Low risk
• SCORE2/SCORE2-OP ≥2% and <10%
• Young patients (T1DM <35 years; T2DM <50 years) with DM duration <10 years without other risk factors
Moderate risk
• SCORE2/SCORE2-OP ≥10% and <20%
• Markedly elevated single risk factors, in particular TC >8 mmol/L (310 mg/dL) or LDL-C >4.9 mmol/L (190 mg/dL) or BP ≥180/110 mmHg
• FH without other major risk factors
• Moderate CKD (eGFR 30–59 mL/min/1.73 m2)
• DM w/o target organ damage, with DM duration ≥10 years or other additional risk factor
High risk
• ASCVD (clinical/imaging)
• SCORE2/SCORE2-OP ≥20%
• FH with ASCVD or with another major risk factor
• Severe CKD (eGFR <30 mL/min/1.73 m2)
• DM & target organ damage: ≥3 major risk factors; or early onset of T1DM of long duration (>20 years)
Very high 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
Extreme risk
CV Risk
[a]Class IIa for individuals in primary prevention with FH at very high risk
ESC
EAS

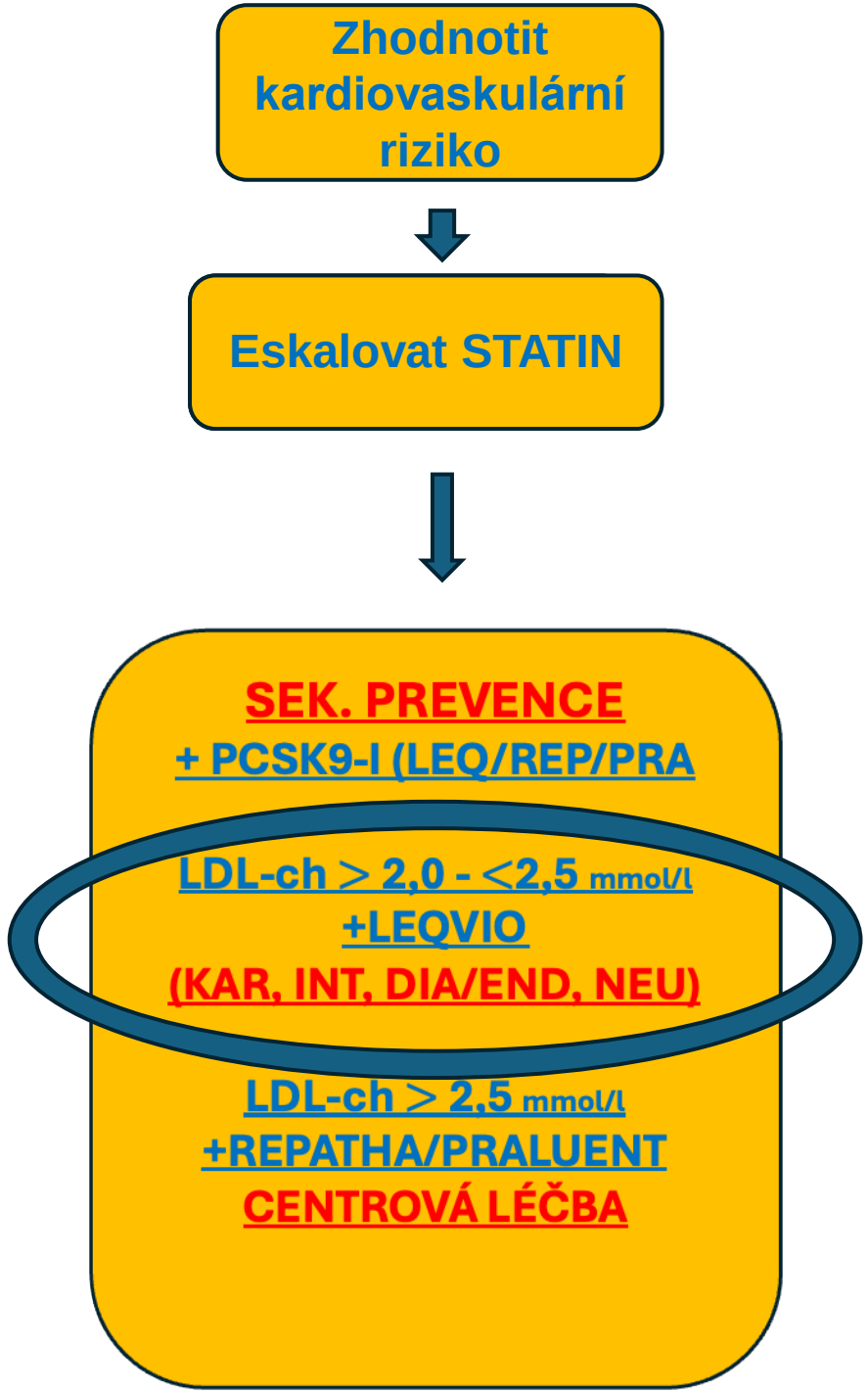
PACIENT TOLERUJE STATIN:



PACIENT TOLERUJE STATIN:



PACIENT TOLERUJE STATIN:



PACIENT TOLERUJE STATIN

FH

Zhodnotit kardiovaskulární riziko

Eskalovat STATIN

FH - SP
+ PCSK9-I (LEQ/REP/PRA)

LDL-ch > 2,5 mmol/l
+REPATHA/PRALUENT
CENTROVÁ LÉČBA

FH - PP
+ PCSK9-I (LEQ/REP/PRA)

LDL-ch > 3,1 mmol/l
+REPATHA/PRALUENT
CENTROVÁ LÉČBA

PACIENT TOLERUJE STATIN

FH

Zhodnotit kardiovaskulární riziko

Eskalovat STATIN

FH - SP
+ PCSK9-I (LEQ/REP/PRA)

LDL-ch > 2,5 mmol/l
+REPATHA/PRALUENT
CENTROVÁ LÉČBA

LDL-ch >2,5 - <3,1 mmol/l
+LEQVIO
(KAR, INT, DIA/END, NEU)

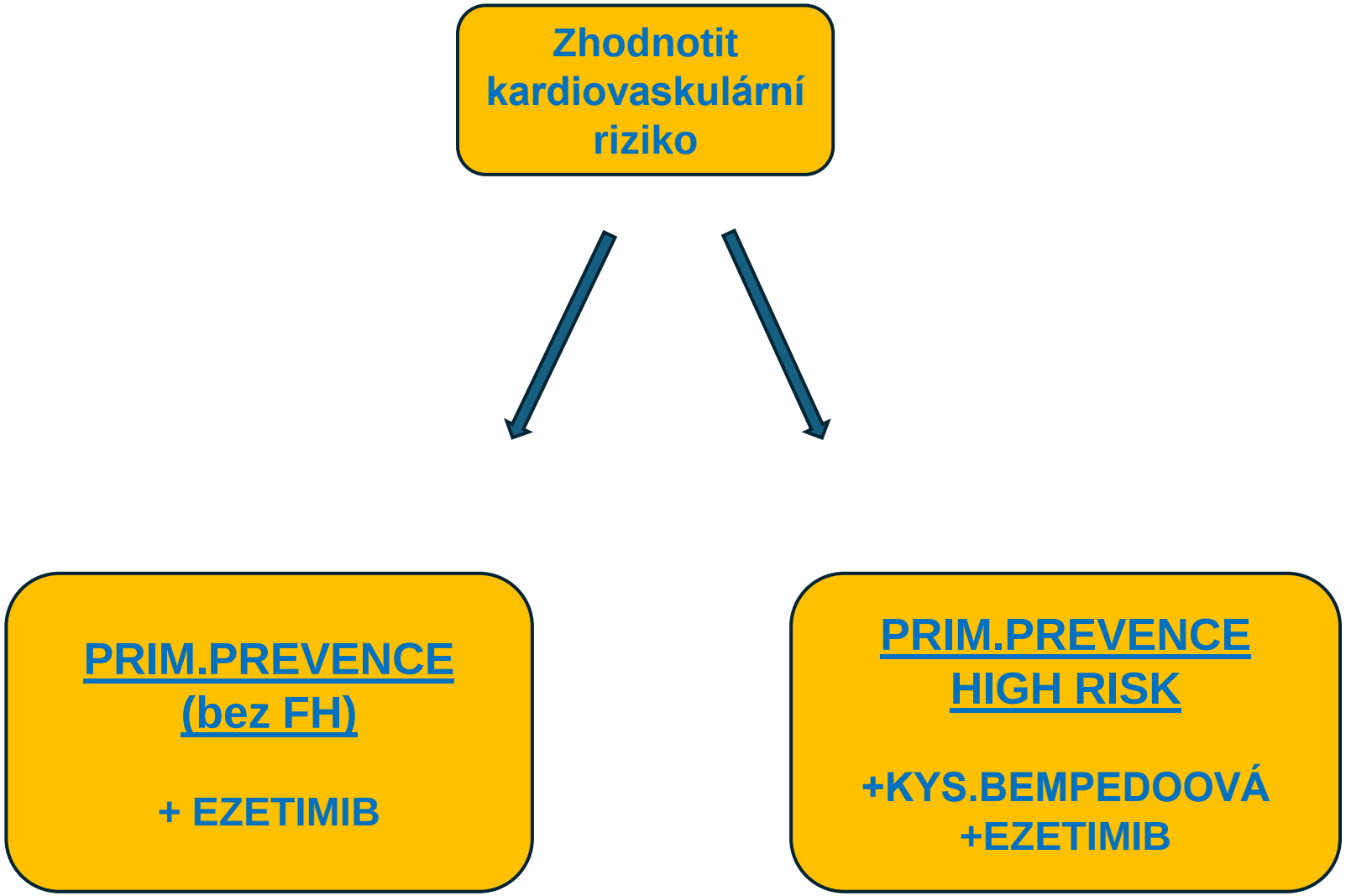
MOŽNO ZKUSIT

FH - PP
+ PCSK9-I (LEQ/REP/PRA)

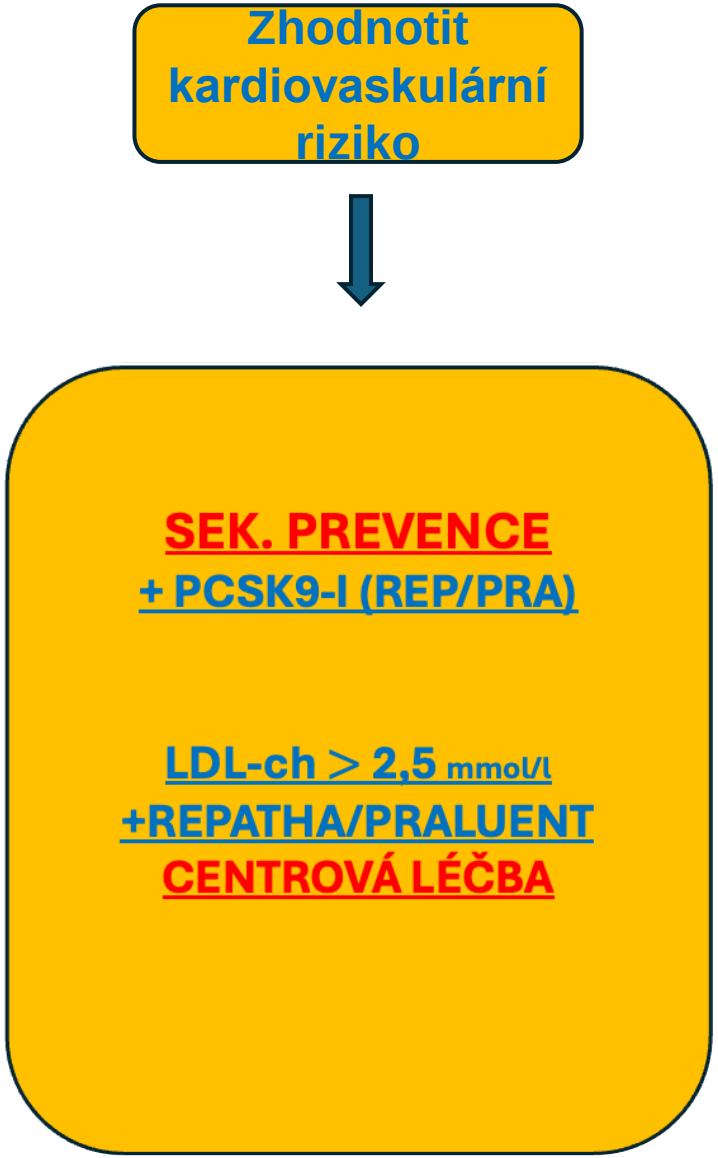
LDL-ch > 3,1 mmol/l
+REPATHA/PRALUENT
CENTROVÁ LÉČBA

LDL-ch > 3,1 mmol/l
+LEQVIO
(KAR, INT, DIA/END, NEU)

PACIENT NETOLERUJE STATIN:



PACIENT NETOLERUJE STATIN:



PACIENT NETOLERUJE STATIN:

FH

Zhodnotit kardiovaskulární riziko

FH - SP
+ PCSK9-I (REP/PRA)

LDL-ch > 2,5 mmol/l
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CENTROVÁ LÉČBA

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+ PCSK9-I (REP/PRA)

LDL-ch > 3,1 mmol/l
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CENTROVÁ LÉČBA

PACIENT NETOLERUJE STATIN:

FH

Zhodnotit kardiovaskulární riziko

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LDL-ch > 2,5 mmol/l
+REPATHA/PRALUENT
CENTROVÁ LÉČBA

MOŽNO ZKUSIT

FH - PP
+ PCSK9-I (LEQ/REP/PRA)

LDL-ch > 3,1 mmol/l
+REPATHA/PRALUENT
CENTROVÁ LÉČBA

LDL-ch > 3,1 mmol/l
+LEQVIO
(KAR, INT, DIA/END, NEU)

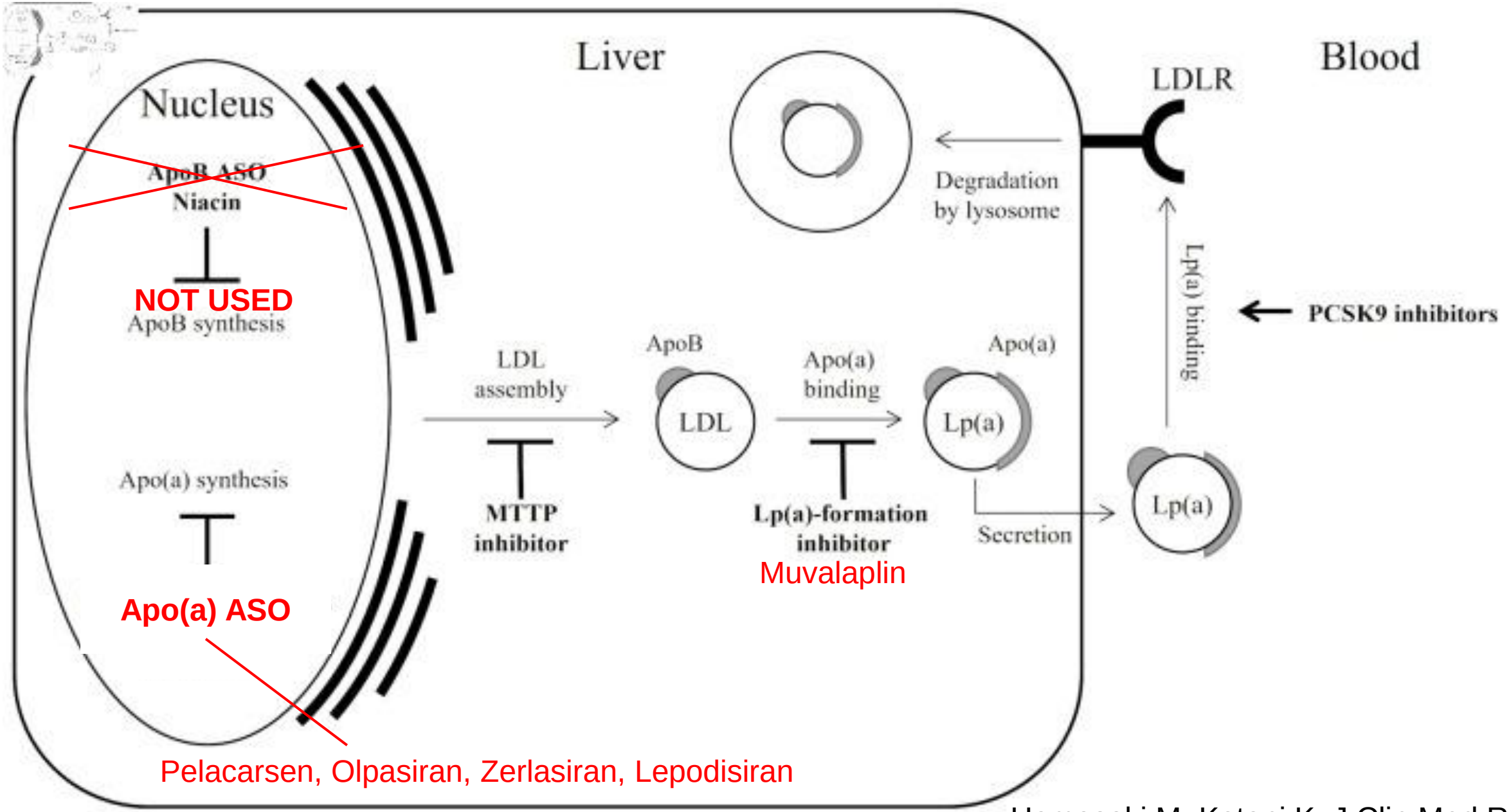
PACIENT MÁ VYŠŠÍ LP(a)

EFFECT ON Lp(a)

Drug and reference	Lp(a) level	Dose, mg	Duration, week	Studied subjects	Comments
Statins	↑ (+10.6%)	2 - 80/day	8 - 24	HC, CVD, T2DM	Dose dependent effect
Fibrates	→ (-1.76 mg/dL)	145 - 1,200/day	8 - 24	HC, HT, T2DM	
~~Niacin~~	~~↓ (-22.9%)~~	~~500 - 3,000/day~~	~~8 - 12~~	~~HC, CVD, T2DM~~	~~Dose independent effect~~
Ezetimibe	↓ (-7.1%)	10/day	12	HC	
PCSK9 Ab inhib. Evolocumab, Alirocumab	↓ (-26.9%)	75 - 150/2weeks, 420/4weeks	24 - 104	HC	
PCSK9 ASO Inclisiran	↓ (-21.9%)	284/12 or 24 weeks	77	Severe HC	
Pelacarsen	↓ (-80.0%)	20/week	24	Severe HC, secondary prevention of CVD	Phase III study **Lp(a)HORIZON(a)**
Olpasiran	↓ (-40.0%)	225/12 weeks	48	CVD	Phase II study (continued)
Zerlasiran	↓ (-80.0%)	300 - 450/24 weeks	60	CVD	Phase II study (continued)
Lp(a)-formation inhibitor Muvalaplin	↓ (-65.0%)	30 - 800/day	2	Healthy adults	Phase I study (continued)

Hamasaki M, Kotani K. J Clin Med Res 2025

MECHANISM OF ACTION

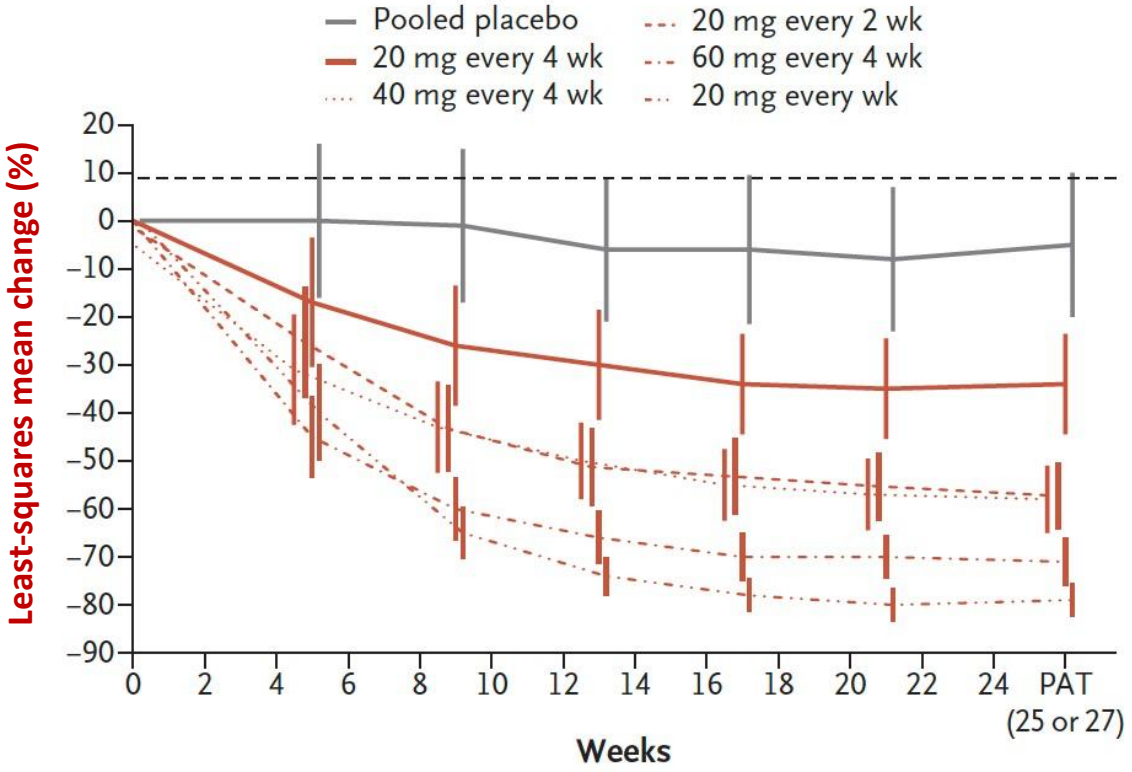


Hamasaki M, Kotani K. J Clin Med Res

PELACARSEN Results: Efficacy

- Median baseline Lp(a) levels in the 6 groups ranged from 204.5 to 246.6 nmol/L. Mean decreases in Lp(a) were:
  - Pelacarsen 20 mg Q4W: -35%
  - Pelacarsen 40 mg Q4W: -56%
  - Pelacarsen 60 mg: -72%
  - Pelacarsen 20 mg Q2W: -58%
  - Pelacarsen 20 mg QW: -80%
  - Placebo: -6% (p=0.003 to <0.001 across the dose range)
- Percentage of participants who achieved plasma Lp(a) ≤125 nmol/L (≤50 mg/dL):
  - Pelacarsen 20 mg Q4W: 23%
  - Pelacarsen 40 mg Q4W: 63%
  - Pelacarsen 60 mg: 81%
  - Pelacarsen 20 mg Q2W: 65%
  - Pelacarsen 20 mg QW: 98%
  - Placebo: 6%

Change from baseline over time in Lp(a) level



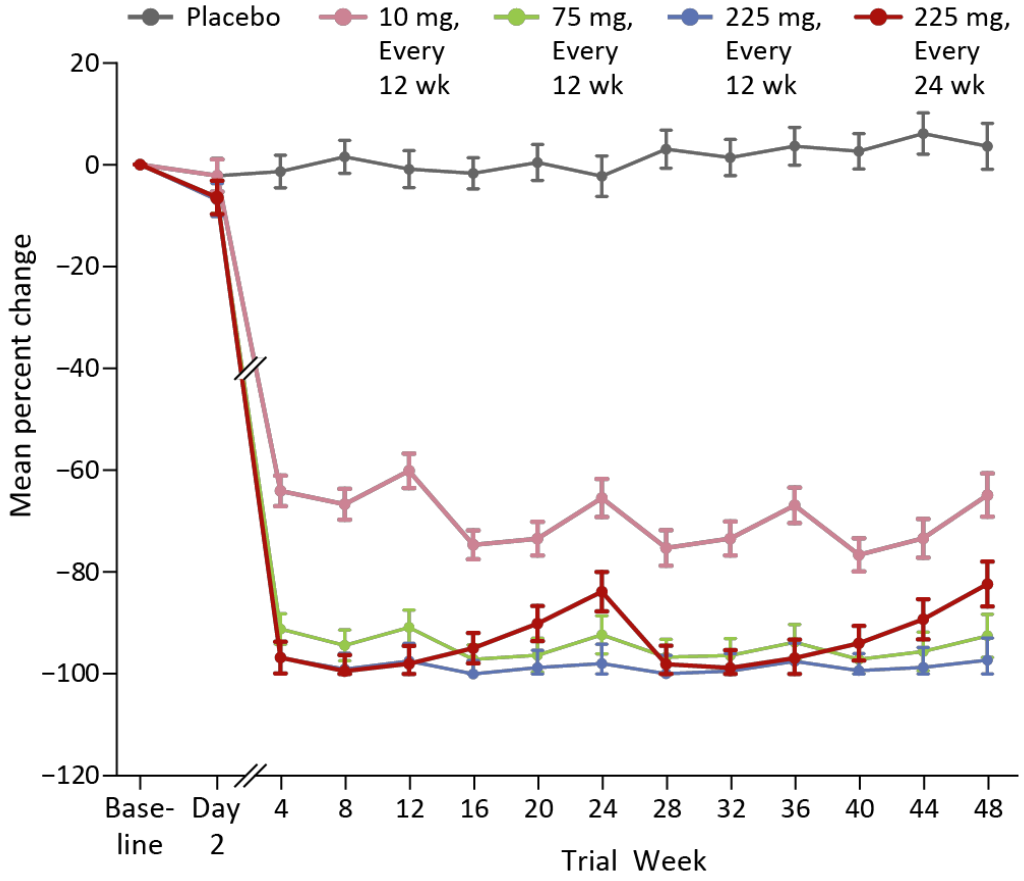
Source: Tsimikas S, Karwatowska-Prokopczuk E, Gouni-Berthold I et al; AKCEA-APO(a)-LRx Study Investigators. Lipoprotein(a) Reduction in Persons with Cardiovascular Disease. N Engl J Med. 2020 Jan 16;382(3):244-255.

Lp(a) FORUM
Lipoprotein(a) EDUCATION & RESEARCH

OLPASIRAN Results: Efficacy

- Across cohorts, median baseline Lp(a) concentration was 260.3 nmol/L
- Placebo-adjusted change from baseline in Lp(a) at week 36 was:[1]
  - Olpasiran 10 mg Q12W: -70.5%
  - Olpasiran 75 mg Q12W: -97.4%
  - Olpasiran 225 mg Q12W: -101.1%
  - Olpasiran 225 mg Q24W: – 100.5%
- There was a dose response effect of olpasiran on placebo-adjusted change in apoB-associated oxidised phospholipids (OxPL-apoB) at week 36 and week 48 (p<0.001 for all):[2]
  - Olpasiran 10 mg Q12W: -51.6%, -50.8%
  - Olpasiran 75 mg Q12W: -89.7%, -100.2%
  - Olpasiran 225 mg Q12W: -92.3%, -104.7%
  - Olpasiran 225 mg Q24W: –93.7%, -85.8%
- No significant effect was seen on the inflammatory markers, hs-CRP, and hs-IL-6
- In an off-treatment extension, patients previously dosed with olpasiran ≥75 mg sustained a ~40-50% placebo-adjusted reduction in Lp(a) nearly a year after the last dose[3]

Percent change in lipoprotein(a) concentration



Source: 1. O'Donoghue ML, Rosenson RS, Gencer B et al; OCEAN(a)-DOSE Trial Investigators. Small Interfering RNA to Reduce Lipoprotein(a) in Cardiovascular Disease. N Engl J Med. 2022 Nov 17;387(20):1855-1864; 2. Rosenson RS, López JAG, Gaudet D et al; OCEAN(a)-DOSE Trial Investigators. Olpasiran, Oxidized Phospholipids, and Systemic Inflammatory Biomarkers: Results From the OCEAN(a)-DOSE Trial. JAMA Cardiol. 2025 Feb 12:e245433; 3. O'Donoghue ML, Rosenson RS, López JAG et al; OCEAN(a)-DOSE Trial Investigators. The Off-Treatment Effects of Olpasiran on Lipoprotein(a) Lowering: OCEAN(a)-DOSE Extension Period Results. J Am Coll Cardiol. 2024 Aug 27;84(9):790-797

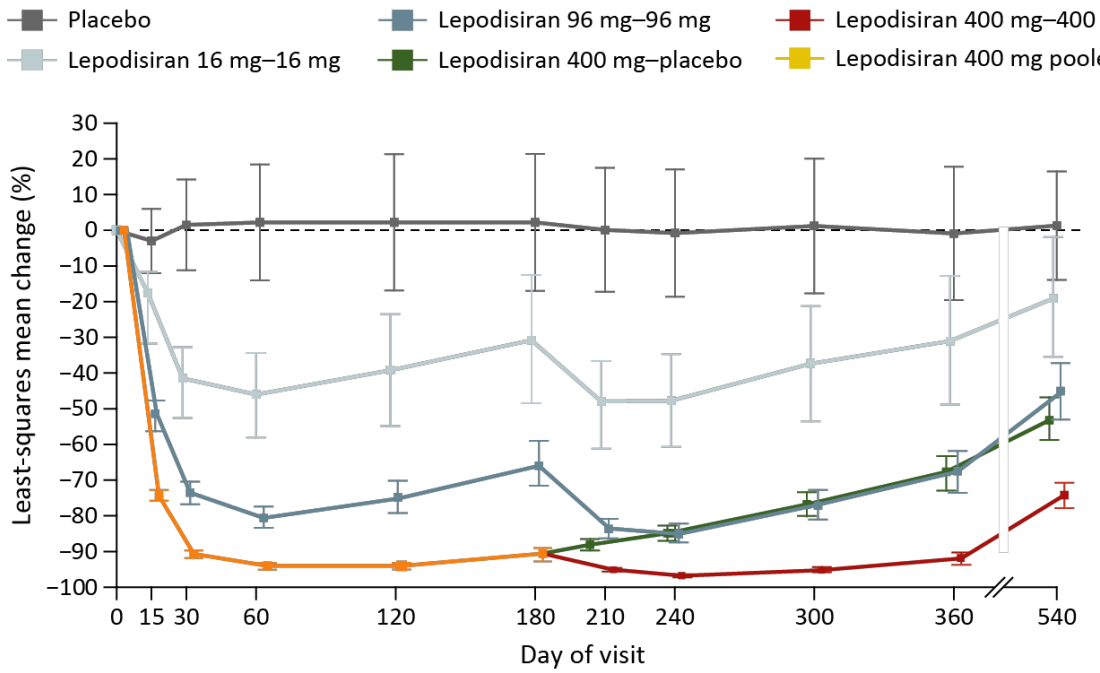
Lp(a) FORUM
Lipoprotein(a) EDUCATION & RESEARCH

LEPODISIRAN Results: Efficacy

- Placebo-adjusted time-averaged % change from baseline in serum Lp(a) concentration from day 60 to day 180 was:
  - Lepodisiran 16 mg: -40.8% (95% confidence interval [CI], −55.8 to −20.6)
  - Lepodisiran 96 mg: −75.2% (95% CI, −80.4 to −68.5)
  - Pooled lepodisiran 400 mg groups: −93.9% (95% CI, −95.1 to −92.5)
- Corresponding changes from day 30 to day 360 were:
  - Lepodisiran 16 mg: −41.2% (95% CI, −55.4 to −22.4)
  - Lepodisiran 96 mg: −77.2% (95% CI, −81.8 to −71.5
  - Lepodisiran 400 mg-placebo: −88.5% (95% CI, −90.8 to −85.6)
  - Lepodisiran 400 mg-400 mg: −94.8% (95% CI, −95.9 to −93.4)
- Sustained reductions of 53.4% were recorded with lepodisiran 400 mg at 540 days after a single dose and 74.2% at 540 days following a second dose of lepodisiran 400 mg at day 180

Lepodisiran 400 mg Q 6 M

Change in lipoprotein(a) concentration



No. of participants

Placebo	69	69	68	68	67	66	64	64	64	64	60
Lepodisiran 16 mg–16 mg	36	36	36	35	36	35	33	33	33	33	32
Lepodisiran 96 mg–96 mg	74	73	73	73	72	72	67	67	69	68	65
Lepodisiran 400 mg–placebo	72	71	71	69	70	69	65	66	64	64	62
Lepodisiran 400 mg–400 mg	69	69	67	68	68	63	61	63	63	63	61

Source: Nissen SE, Ni W, Shen X et al. Lepodisiran — A Long-Duration Small Interfering RNA Targeting Lipoprotein(a). New England Journal of Medicine 2025; 392:1673-1683

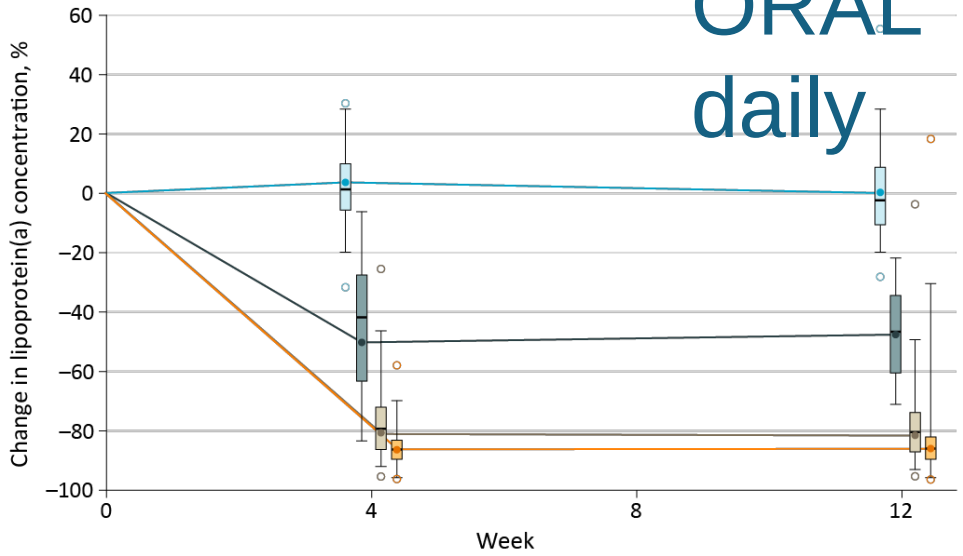
Lp(a) FORUM
Lipoprotein(a) EDUCATION & RESEARCH

MUVALAPLIN Results: Efficacy

- Using an intact Lp(a) assay, placebo-adjusted Lp(a) reductions were:
  - Muvalaplin 10 mg/day: 47.6% (95% CI, 35.1%-57.7%)
  - Muvalaplin 60 mg/day: 81.7% (95% CI, 78.1%-84.6%)
  - Muvalaplin 240 mg/day: 85.8% (95% CI, 83.1%-88.0%)
- Using an apolipoprotein(a)-based assay, placebo-adjusted reductions in Lp(a) were:
  - Muvalaplin 10 mg/day: 40.4% (95% CI, 28.3%-50.5%)
  - Muvalaplin 60 mg/day: 70.0% (95% CI, 65.0%-74.2%)
  - Muvalaplin 240 mg/day: 68.9% (95% CI, 63.8%-73.3%)
- Dose-dependent reductions in apoB were:
  - Muvalaplin 10 mg/day: 8.9% (95% CI, -2.2% to 18.8%
  - Muvalaplin 60 mg/day: 13.1% (95% CI, 4.4%-20.9%)
  - Muvalaplin 240 mg/day: 16.1% (95% CI, 7.8%-23.7%)
- No change in high-sensitivity C-reactive protein was observed

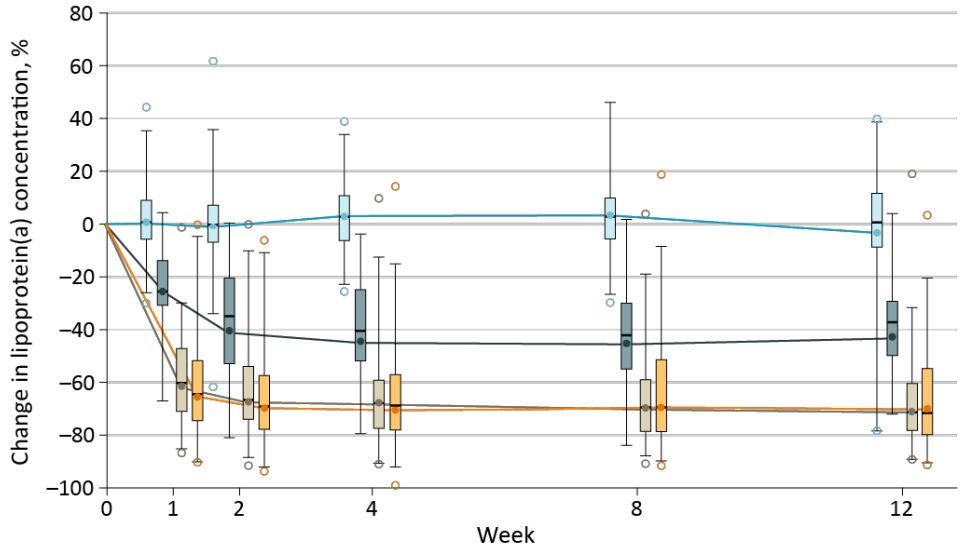
ORAL daily

Intact lipoprotein(a) assay



No. of patients				
Placebo	57	54		49
Muvalaplin, 10 mg/d	27	27		23
Muvalaplin, 60 mg/d	52	51		45
Muvalaplin, 240 mg/d	55	55		47

Apolipoprotein(a)-based assay



No. of patients						
Placebo	67	66	65	64	65	60
Muvalaplin, 10 mg/d	34	34	32	33	32	29
Muvalaplin, 60 mg/d	62	60	60	61	60	56
Muvalaplin, 240 mg/d	68	67	68	64	61	57

Placebo | Muvalaplin 10 mg/d | Muvalaplin 60 mg/d | Muvalaplin 240 mg/d

Data are presented as least-squares means (solid dots), medians (lines), IQRs (boxes), 2.5th and 97.5th percentiles (whiskers), and outliers (open circles)

Source: Nicholls SJ, Ni W, Rhodes GM et al. Oral Muvalaplin for Lowering of Lipoprotein(a): A Randomized Clinical Trial. JAMA. 2025 Jan 21;333(3):222-231

Lp(a) FORUM
Lipoprotein(a) EDUCATION & RESEARCH

DOPORUČENÍ ČSAT 2026 K Lp(a)

- < 105 nmol/l nízké KV riziko
- 105 – 400 nmol/l nutno intenzivně léčit LDL-ch* a všechny RF
- > 400 nmol/l odeslat do lipidové poradny

* on-line kalkulátor pro cíle LDL-ch dle hladiny Lp(a)
www.athero.cz

ZÁVĚR:

1. **VČAS PŘIDÁVAT PCSK9-I KE STATINU**
2. **INCLISIRAN MIMO CENTRA, KDE JE TO MOŽNÉ**
3. **U INTOLERANTŮ STATINŮ V PRIMÁRNÍ PREVENCI KYS. BEMPED.+EZE**
4. **MĚŘENÍ Lp(a) MÁ SVŮJ VÝZNAM**