

Literatur herzmedizin 5/2023

Primäre Fettstoffwechselstörungen: Aktuelle Diagnose, Differenzialdiagnose und Behandlung

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Literatur:

1. Mach F et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. *Eur Heart J* 2020; 41: 111–88
2. Ference BA et al. Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel. *Eur Heart J* 2017; 38: 2459–72
3. Katzmüller JL et al. Cutaneous manifestations in familial hypercholesterolemia. *Atherosclerosis* 2021; 333: 116–23
4. Hegele RA et al. Rare dyslipidaemias, from phenotype to genotype to management: a European Atherosclerosis Society task force consensus statement. *The lancet Diabetes & endocrinology* 2020; 8: 50–67
5. Klose G et al. Familial hypercholesterolemia: developments in diagnosis and treatment. *Deutsches Arzteblatt international* 2014; 111: 523–9
6. Marks D et al. A review on the diagnosis, natural history, and treatment of familial hypercholesterolemia. *Atherosclerosis* 2003; 168: 1–14
7. Walma EP & Wiersma TJ. NHG-Standpunt Diagnostiek en behandeling van familiaire hypercholesterolemie. *Huisarts Wet* 2006; 49: 202–4
8. Grenkowitz T et al. Clinical characterization and mutation spectrum of German patients with familial hypercholesterolemia. *Atherosclerosis* 2016; 253: 88–93
9. Khera AV et al. Diagnostic Yield and Clinical Utility of Sequencing Familial Hypercholesterolemia Genes in Patients With Severe Hypercholesterolemia. *J Am Coll Cardiol* 2016; 67: 2578–89
10. Umans-Eckenhausen MA et al. Long-term compliance with lipid-lowering medication after genetic screening for familial hypercholesterolemia. *Arch int med* 2003; 163: 65–8
11. Lee S et al. Genetic testing for familial hypercholesterolemia: Impact on diagnosis, treatment and cardiovascular risk. *Eur J Prev Cardiol* 2019; 26: 1262–70
12. Marz W et al. The German CaRe high registry for familial hypercholesterolemia - Sex differences, treatment strategies, and target value attainment. *Atheroscler Plus* 2023; 53: 6–15
13. Taylor A et al. Mutation detection rate and spectrum in familial hypercholesterolemia patients in the UK pilot cascade project. *Clinical genetics* 2010; 77: 572–80
14. Leren TP et al. Diagnosis of familial hypercholesterolemia in general practice using clinical diagnostic criteria or genetic testing as part of cascade genetic screening. *Community genetics* 2008; 11: 26–35

15. Sharma P et al. Elucigene FH20 and LIPOchip for the diagnosis of familial hypercholesterolaemia: a systematic review and economic evaluation. *Health Technol Assess* 2012; 16: 1–266
16. Vallejo-Vaz AJ et al. LDL-cholesterol lowering and clinical outcomes in hypercholesterolemic subjects with and without a familial hypercholesterolemia phenotype: Analysis from the secondary prevention 4S trial. *Atherosclerosis* 2021; 320: 1–9
17. Klose G et al. [Primary disorders of lipid metabolism: their place in current dyslipidemia guidelines and treatment innovations]. *Inn Med (Heidelb)* 2023; 64: 895–906
18. Cuchel M et al. 2023 Update on European Atherosclerosis Society Consensus Statement on Homozygous Familial Hypercholesterolaemia: new treatments and clinical guidance. *Eur Heart J* 2023; 44: 2277–91
19. D'Erasmo L et al. Autosomal recessive hypercholesterolemia: update for 2020. *Curr Opin Lipidol* 2020; 31: 56–61
20. Damgaard D et al. The relationship of molecular genetic to clinical diagnosis of familial hypercholesterolemia in a Danish population. *Atherosclerosis* 2005; 180: 155–60
21. Civeira F et al. Comparison of genetic versus clinical diagnosis in familial hypercholesterolemia. *Am J Cardiol* 2008; 102: 1187–93, 93 e122.
22. Futema M et al. Analysis of the frequency and spectrum of mutations recognised to cause familial hypercholesterolaemia in routine clinical practice in a UK specialist hospital lipid clinic. *Atherosclerosis* 2013; 229: 161–8
23. Talmud PJ et al. Use of low-density lipoprotein cholesterol gene score to distinguish patients with polygenic and monogenic familial hypercholesterolaemia: a case-control study. *The Lancet* 2013; 381: 1293–301
24. Talmud PJ et al. The genetic architecture of the familial hyperlipidaemia syndromes: rare mutations and common variants in multiple genes. *Curr Opin Lipidol* 2014; 25: 274–81
25. Trinder M et al. Association of Monogenic vs Polygenic Hypercholesterolemia With Risk of Atherosclerotic Cardiovascular Disease. *JAMA cardiology* 2020; 5: 390–9
26. Mikhailidis DP et al. "European panel on low density lipoprotein (LDL) subclasses": a statement on the pathophysiology, atherogenicity and clinical significance of LDL subclasses. *Current vascular pharmacology* 2011; 9: 533–71
27. Hegele RA et al. A polygenic basis for four classical Fredrickson hyperlipoproteinemia phenotypes that are characterized by hypertriglyceridemia. *Hum Mol Genet* 2009; 18: 4189–94
28. Johansen CT & Hegele RA. Genetic bases of hypertriglyceridemic phenotypes. *Curr Opin Lipidol* 2011; 22: 247–53
29. Lewis GF et al. Hypertriglyceridemia in the genomic era: a new paradigm. *Endocr Rev* 2015; 36: 131–47
30. Brahm AJ & Hegele RA. Combined hyperlipidemia: familial but not (usually) monogenic. *Curr Opin Lipidol* 2016; 27: 131–40
31. Koopal C et al. Familial dysbetalipoproteinemia: an underdiagnosed lipid disorder. *Current opinion in endocrinology, diabetes, and obesity* 2017; 24: 133–9

32. Paquette M et al. Dysbetalipoproteinemia Is Associated With Increased Risk of Coronary and Peripheral Vascular Disease. *J Clin Endocrinol Metab* 2022; 108: 184–90
33. Feussner G et al. Molecular basis of type III hyperlipoproteinemia in Germany. *Hum Mutat* 1998; 11: 417–23
34. Baass A et al. Familial chylomicronemia syndrome: an under-recognized cause of severe hypertriglyceridaemia. *J int med* 2020; 287: 340–8
35. https://sobi-deutschland.de/sites/default/files/Fachinformation_Waylivra_Mai_2021.pdf
36. Ginsberg HN et al. Triglyceride-rich lipoproteins and their remnants: metabolic insights, role in atherosclerotic cardiovascular disease, and emerging therapeutic strategies-a consensus statement from the European Atherosclerosis Society. *Eur Heart J* 2021; 42: 4791–806
37. Brown RJ et al. The Diagnosis and Management of Lipodystrophy Syndromes: A Multi-Society Practice Guideline. *J Clin Endocrinol Metab* 2016; 101: 4500–11
38. Kronenberg F et al. Lipoprotein(a) in atherosclerotic cardiovascular disease and aortic stenosis: a European Atherosclerosis Society consensus statement. *Eur Heart J* 2022; 43: 3925–46
39. Moulin P et al. Identification and diagnosis of patients with familial chylomicronaemia syndrome (FCS): Expert panel recommendations and proposal of an "FCS score". *Atherosclerosis* 2018; 275: 265–72
40. Barkas F et al. Diet and Cardiovascular Disease Risk Among Individuals with Familial Hypercholesterolemia: Systematic Review and Meta-Analysis. *Nutrients* 2020; 12
41. Raal FJ et al. PCSK9 inhibition with evolocumab (AMG 145) in heterozygous familial hypercholesterolemia (RUTHERFORD-2): a randomised, double-blind, placebo-controlled trial. *Lancet* 2015; 385: 331–40
42. Farnier M et al. Long-term safety and efficacy of alirocumab in patients with heterozygous familial hypercholesterolemia: An open-label extension of the ODYSSEY program. *Atherosclerosis* 2018; 278: 307–14
43. Raal FJ et al. Inclisiran for the Treatment of Heterozygous Familial Hypercholesterolemia. *N Engl J Med* 2020; 382: 1520–30
44. Aljenedil S et al. Lomitapide for treatment of homozygous familial hypercholesterolemia: The Quebec experience. *Atherosclerosis* 2020; 310: 54–63
45. Parhofer KG, Laufs U. The Diagnosis and Treatment of Hypertriglyceridemia. *Deutsches Arzteblatt international* 2019; 116: 825–32
46. Bhatt DL et al. Cardiovascular Risk Reduction with Icosapent Ethyl. Reply. *N Engl J Med* 2019; 380: 1678
47. Mach F et al. Adverse effects of statin therapy: perception vs. the evidence - focus on glucose homeostasis, cognitive, renal and hepatic function, haemorrhagic stroke and cataract. *Eur Heart J* 2018; 39: 2526–39
48. Waldmann E et al. Effect of PCSK9 inhibition with evolocumab on lipoprotein subfractions in familial dysbetalipoproteinemia (type III hyperlipidemia). *PLoS One* 2022; 17: e0265838
49. Witztum JL et al. Volanesorsen and Triglyceride Levels in Familial Chylomicronemia Syndrome. *N Engl J Med* 2019; 381: 531–42

50. Gouni-Berthold I et al. Efficacy and safety of volanesorsen in patients with multifactorial chylomicronaemia (COMPASS): a multicentre, double-blind, randomised, placebo-controlled, phase 3 trial. *The lancet Diabetes & endocrinology* 2021; 9: 264–75
51. Averna M et al. Practical guidance for combination lipid-modifying therapy in high- and very-high-risk patients: A statement from a European Atherosclerosis Society Task Force. *Atherosclerosis* 2021; 325: 99–109
52. Agha AM et al. Greater than expected reduction in low-density lipoprotein-cholesterol (LDL-C) with bempedoic acid in a patient with heterozygous familial hypercholesterolemia (HeFH). *J Clin Lipidol* 2021; 15: 649–52
53. Stroes ES et al. Statin-associated muscle symptoms: impact on statin therapy—European Atherosclerosis Society Consensus Panel Statement on Assessment, Aetiology and Management. *Eur Heart J* 2015; 36: 1012–22
54. Laufs U et al. Statin intolerance. *Curr Opin Lipidol* 2015; 26: 492–501
55. März W et al. Statin-assoziierte Muskelbeschwerden: Mythos oder Wirklichkeit? *herzmedizin* 2016; 2016: 13–9
56. O'Donoghue ML et al. Long-Term Evolocumab in Patients With Established Atherosclerotic Cardiovascular Disease. *Circulation* 2022; 146: 1109–19
57. Pinkosky SL et al. Liver-specific ATP-citrate lyase inhibition by bempedoic acid decreases LDL-C and attenuates atherosclerosis. *Nat Commun* 2016; 7: 13457
58. Niman S et al. A Review of the Efficacy and Tolerability of Bempedoic Acid in the Treatment of Hypercholesterolemia. *Am J Cardiovas Drugs* 2020; 20: 535–48
59. Nissen SE et al. Bempedoic Acid and Cardiovascular Outcomes in Statin-Intolerant Patients. *N Engl J Med* 2023; 388: 1353–64
60. Baigent C et al. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials. *Lancet* 2010; 376: 1670–81
61. Ray KK et al. Inclisiran in Patients at High Cardiovascular Risk with Elevated LDL Cholesterol. *N Engl J Med* 2017; 376: 1430–40
62. Sinning D, Landmesser U. Low-density Lipoprotein-Cholesterol Lowering Strategies for Prevention of Atherosclerotic Cardiovascular Disease: Focus on siRNA Treatment Targeting PCSK9 (Inclisiran). *Curr Cardiol Rep* 2020; 22: 176
63. Ray KK et al. Two Phase 3 Trials of Inclisiran in Patients with Elevated LDL Cholesterol. *N Engl J Med* 2020; 382: 1507–19
64. Musunuru K et al. Exome sequencing, ANGPTL3 mutations, and familial combined hypolipidemia. *N Engl J Med* 2010; 363: 2220–7
65. Rosenson RS et al. Evinacumab in Patients with Refractory Hypercholesterolemia. *N Engl J Med* 2020; 383: 2307–19
66. Raal FJ et al. Evinacumab for Homozygous Familial Hypercholesterolemia. *N Engl J Med* 2020; 383: 711–20
67. Gusarova V et al. ANGPTL3 blockade with a human monoclonal antibody reduces plasma lipids in dyslipidemic mice and monkeys. *J Lipid Res* 2015; 56: 1308–17
68. Wang Y et al. Inactivation of ANGPTL3 reduces hepatic VLDL-triglyceride secretion. *J Lipid Res* 2015; 56: 1296–307

69. Brandts J & Ray KK. Novel and future lipid-modulating therapies for the prevention of cardiovascular disease. *Nat Rev Cardiol* 2023; 20: 600–16
 70. Musunuru K et al. In vivo CRISPR base editing of PCSK9 durably lowers cholesterol in primates. *Nature* 2021; 593: 429–34
 71. Sahebkar A et al. PCSK9 vaccine: so near, yet so far! *Eur Heart J* 2021; 42: 4007–10
 72. Xu M et al. PCSK9 inhibitor recaticimab for hypercholesterolemia on stable statin dose: a randomized, double-blind, placebo-controlled phase 1b/2 study. *BMC medicine* 2022; 20: 13
 73. Mitchell T et al. Pharmacologic profile of the Adnectin BMS-962476, a small protein biologic alternative to PCSK9 antibodies for low-density lipoprotein lowering. *J Pharmacol Exp Ther* 2014; 350: 412–24
 74. Raal F et al. Long-term efficacy and safety of lerodalcibep in heterozygous familial hypercholesterolemia: the LIBerate-HeFH trial. *Eur Heart J* 2023; 44: 4272–80
 75. Ballantyne CM et al. Phase 2b Randomized Trial of the Oral PCSK9 Inhibitor MK-0616. *J Am Coll Cardiol* 2023; 81: 1553–64
 76. Tardif JC et al. Apolipoprotein C-III reduction in subjects with moderate hypertriglyceridaemia and at high cardiovascular risk. *Eur Heart J* 2022; 43: 1401–12
 77. Estruch R et al. Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. *N Engl J Med* 2018; 378: e34
 78. Cannon CP et al. Ezetimibe Added to Statin Therapy after Acute Coronary Syndromes. *N Engl J Med* 2015; 372: 2387–97
 79. Schwartz GG et al. Alirocumab and Cardiovascular Outcomes after Acute Coronary Syndrome. *N Engl J Med* 2018; 29; 379(22): 2097–107
 80. Sabatine MS et al. Evolocumab and Clinical Outcomes in Patients with Cardiovascular Disease. *N Engl J Med* 2017; 376: 1713–22
 81. Leebmann J et al. Lipoprotein apheresis in patients with maximally tolerated lipid-lowering therapy, lipoprotein(a)-hyperlipoproteinemia, and progressive cardiovascular disease: prospective observational multicenter study. *Circulation* 2013; 128: 2567–76
-

Wie kläre ich meinen Patienten mit Lipoprotein(a)-Erhöhung auf?

U. Schatz

Literatur:

1. Schatz U et al. Cardiovascular risk factors in patients with premature cardiovascular events attending the University of Dresden Lipid Clinic. *Atheroscler Suppl* 2019; 40: 94–9
2. Tsimikas S. A Test in Context: Lipoprotein(a): Diagnosis, Prognosis, Controversies, and Emerging Therapies. *J Am Coll Cardiol* 2017; 69(6): 692–711
3. Kronenberg F et al. Lipoprotein(a) in atherosclerotic cardiovascular disease and aortic stenosis: a European Atherosclerosis Society consensus statement. *Eur Heart J* 2022; 43(39): 3925–46

4. Kronenberg F et al. Consensus and guidelines on lipoprotein(a) - seeing the forest through the trees. *Curr Opin Lipidol* 2022; 33(6): 342–52
 5. Nestel PJ et al. Plasma lipoprotein(a) concentration predicts future coronary and cardiovascular events in patients with stable coronary heart disease. *Arterioscler Thromb Vasc Biol* 2013; 33(12): 2902–8
 6. Emerging Risk Factors Collaboration et al. Lipoprotein(a) concentration and the risk of coronary heart disease, stroke, and nonvascular mortality. *JAMA* 2009; 302(4): 412–23
 7. Arsenault BJ et al. Lipoprotein(a) levels, genotype, and incident aortic valve stenosis: a prospective Mendelian randomization study and replication in a case-control cohort. *Circ Cardiovasc Genet* 2014; 7(3): 304–10
 8. Laschko lnig A et al. Lipoprotein (a) concentrations, apolipoprotein (a) phenotypes, and peripheral arterial disease in three independent cohorts. *Cardiovasc Res* 2014; 103(1): 28–36
 9. Mach F et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. *Eur Heart J* 2020; 41(1): 111–88
 10. Anderson TJ et al. 2016 Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult. *Can J Cardiol* 2016; 32(11): 1263–82
 11. Wilson DP et al. Use of Lipoprotein(a) in clinical practice: A biomarker whose time has come. A scientific statement from the National Lipid Association. *J Clin Lipidol* 2019; 13(3): 374–92
 12. van Buuren F et al. Incidence of elevated lipoprotein (a) levels in a large cohort of patients with cardiovascular disease. *Clin Res Cardiol Suppl* 2017; 12(1): 55–9
 13. Nordestgaard BG et al. Lipoprotein(a) as a cardiovascular risk factor: current status. *Eur Heart J* 2010; 31(23): 2844–53
 14. Albers JJ et al. Relationship of apolipoproteins A-1 and B, and lipoprotein(a) to cardiovascular outcomes: the AIM-HIGH trial (Atherothrombosis Intervention in Metabolic Syndrome with Low HDL/High Triglyceride and Impact on Global Health Outcomes). *J Am Coll Cardiol* 2013; 62(17): 1575–9
 15. Khera AV et al. Lipoprotein(a) concentrations, rosuvastatin therapy, and residual vascular risk: an analysis from the JUPITER Trial (Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin). *Circulation* 2014; 129(6): 635–42
 16. Kamstrup PR et al. Genetically elevated lipoprotein(a) and increased risk of myocardial infarction. *JAMA* 2009; 301(22): 2331–9
 17. Enkhmaa B & Berglund L. Non-genetic influences on lipoprotein(a) concentrations. *Atherosclerosis* 2022; 349: 53–62
 18. Nordestgaard BG & Langsted A. Lipoprotein (a) as a cause of cardiovascular disease: insights from epidemiology, genetics, and biology. *J Lipid Res* 2016; 57(11): 1953–75
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Was kann ich meinen Patienten mit hohen Triglycerid-Werten raten?

A. Vogt

Literatur:

1. Mach F et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. *Eur Heart J* 2019
2. Kristensen FPB et al. Triglycerides and risk of cardiovascular events in statin-treated patients with newly diagnosed type 2 diabetes: a Danish cohort study. *Cardiovascular Diabetology* 2023; 22(1): 187
3. Balling M et al. Elevated LDL Triglycerides and Atherosclerotic Risk. *J Am Coll Cardiol* 2023; 81(2): 136–52
4. Kaltoft M et al. Triglycerides and remnant cholesterol associated with risk of aortic valve stenosis: Mendelian randomization in the Copenhagen General Population Study. *Eur Heart J* 2020; 41(24): 2288–99
5. Thomsen M et al. Low nonfasting triglycerides and reduced all-cause mortality: a mendelian randomization study. *Clin Chem* 2014; 60(5): 737–46
6. Nordestgaard BG & Varbo A. Triglycerides and cardiovascular disease. *Lancet* 2014; 384(9943): 626–35
7. Ginsberg HN et al. Triglyceride-rich lipoproteins and their remnants: metabolic insights, role in atherosclerotic cardiovascular disease, and emerging therapeutic strategies-a consensus statement from the European Atherosclerosis Society. *Eur Heart J* 2021; 42(47): 4791–806
8. Schwartz GG et al. Fasting triglycerides predict recurrent ischemic events in patients with acute coronary syndrome treated with statins. *J Am Coll Cardiol* 2015; 65(21): 2267–75
9. Sanchez RJ et al. The association of triglyceride levels with the incidence of initial and recurrent acute pancreatitis. *Lipids Health Dis* 2021; 20(1): 72
10. Castera L et al. High Prevalence of NASH and Advanced Fibrosis in Type 2 Diabetes: A Prospective Study of 330 Outpatients Undergoing Liver Biopsies for Elevated ALT, Using a Low Threshold. *Diabetes Care* 2023; 46(7): 1354–62
11. Papus M et al. Motivational interviewing to support medication adherence in adults with chronic conditions: Systematic review of randomized controlled trials. *Patient Educ Couns* 2022; 105(11): 3186–203
12. Khera AV et al. Genetic Risk, Adherence to a Healthy Lifestyle, and Coronary Disease. *N Engl J Med* 2016; 375(24): 2349–58
13. Guo J et al. Meta-analysis of safety of the coadministration of statin with fenofibrate in patients with combined hyperlipidemia. *Am J Cardiol* 2012; 110(9): 1296–301
14. Skulas-Ray AC et al. Dose-response effects of omega-3 fatty acids on triglycerides, inflammation, and endothelial function in healthy persons with moderate hypertriglyceridemia. *Am J Clin Nutr* 2011; 93(2): 243–52
15. Jun M et al. Effects of fibrates on cardiovascular outcomes: a systematic review and meta-analysis. *Lancet* 2010; 375(9729): 1875–84
16. Wierzbicki AS. Fibrates: no ACCORD on their use in the treatment of dyslipidaemia. *Curr Opin Lipidol* 2010; 21(4): 352–8

17. Maki KC et al. Triglyceride-lowering therapies reduce cardiovascular disease event risk in subjects with hypertriglyceridemia. *J Clin Lipidol* 2016; 10(4): 905–14
 18. Jo SH et al. Fenofibrate Use Is Associated With Lower Mortality and Fewer Cardiovascular Events in Patients With Diabetes: Results of 10,114 Patients From the Korean National Health Insurance Service Cohort. *Diabetes Care* 2021; 44(8): 1868–76
-

Eskalationsstrategie der LDL-C-senkenden Therapie und Wirtschaftlichkeit

H. Hahmann

Literatur:

1. Statistisches Bundesamt (2022) Anzahl der Todesfälle nach den häufigsten Todesursachen in Deutschland in den Jahren 2019 bis 2021.
<https://de.statista.com/statistik/daten/studie/158441/umfrage/anzahl-der-todesfaelle-nachtodesursachen/>, Zugegriffen: 01.07.2023
2. Ference BA et al. Lowdensity lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel. *Eur Heart J* 2017; 38: 2459–72
3. Baigent C et al. Cholesterol Treatment Trialists' (CTT) Collaborators. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. *Lancet* 2005; 366: 1267–78
4. Mach F et al. The 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. *EurHeart J* 2019; 37(3): 2999
5. Arzneimittelkommission der deutschen Ärzteschaft (AkdÄ) (2023) Medikamentöse Cholesterinsenkung zur Vorbeugung kardiovaskulärer Ereignisse. Leitfaden der Arzneimittelkommission der deutschen Ärzteschaft (AkdÄ).
https://www.akdae.de/fileadmin/user_upload/akdae/Arzneimitteltherapie/LF/PDF/Cholesterinsenkung.pdf, Zugegriffen: 01.07.2023
6. Lincoff AM et al. ACCELERATE Investigators. Evacetrapib and cardiovascular outcomes in high-risk vascular disease. *N Engl J Med* 2017; 376: 1933–42
7. HPS/TIMI/REVEAL Collaborative Group et al. Effects of anacetrapib in patients with atherosclerotic vascular disease. *N Engl J Med* 2017; 377: 1217–27
8. Grundy SM et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2019; 73(24): e285–e350
9. Sozialgesetzbuch (SGB V) Fünftes Buch - Gesetzliche Krankenversicherung - Zuletzt geändert durch Art. 9 G v. 16.8.2023 I Nr. 217 § 12 SGB V Wirtschaftlichkeitsgebot)
10. Stellungnahme des AOK-Bundesverbands.
<https://www.aok.de/pp/lexikon/wirtschaftlichkeitsgebot>, Zugegriffen: 16.10.2023

11. Katzmann JL et al. Non-statin lipid-lowering therapy over time in very-high-risk patients: effectiveness of fixed-dose statin/ezetimibe compared to separate pill combination on LDL-C. *Clin Res Cardiol* 2022; 111: 243–52
12. Ray KK et al. Treatment gaps in the implementation of LDL cholesterol control among high- and very high-risk patients in Europe between 2020 and 2021: the multinational observational SANTORINI study. *Lancet Reg Health Eur* 2023; 29: 100624
13. Ray KK et al. Treatment gaps in the implementation of LDL cholesterol control among high- and very high-risk patients in Europe between 2020 and 2021: the multinational observational SANTORINI study. *Eur J Prev Cardiol* 2020; 29: 100624
14. Wright RS et. al. Pooled Patient-Level Analysis of Inclisiran Trials in Patients With Familial Hypercholesterolemia or Atherosclerosis *J Am Coll Cardiol* 2021; 77(9): 1179–81
15. Katzmann JL et al. Europäische Leitlinien zu Lipiden 2019. *Herz* 2019; 44: 688–95
16. Lee YL et al. Rosuvastatin versus atorvastatin treatment in adults with coronary artery disease: secondary analysis of the randomised LODESTAR trial. *BMJ* 2023; 383: e075837
17. LIT Cholesterol Treatment Trialists' Collaboration. Effect of statin therapy on muscle symptoms: an individual participant data meta-analysis of large-scale, randomised, double-blind trials. *Lancet* 2022; 400: 823–45
18. Parhofer KG & Nitschmann S. Muskuläre Symptome unter Statintherapie. *Innere Medizin* 2023; 64: 295–97
19. Cannon CP; IMPROVE-IT Investigators. Ezetimibe added to statin therapy after acute coronary syndromes. *N Engl J Med* 2015; 372: 2387–97
20. Lee SJ et al. Moderate-Intensity Statin With Ezetimibe Combination Therapy vs High-Intensity Statin Monotherapy in Patients at Very High Risk of Atherosclerotic Cardiovascular Disease. *JAMA Cardiol* 2023
21. Nissen SE et al. Bempedoic acid and cardiovascular outcomes in statin-intolerant patients. *N Engl J Med* 2023; 388: 1353–64
22. Sabatine MS; FOURIER Steering Committee and Investigators. Evolocumab and clinical outcomes in patients with cardiovascular disease. *N Engl J Med* 2017; 376: 1713–22
23. Schwartz GG; ODYSSEY OUTCOMES Committees and Investigators. Alirocumab and cardiovascular outcomes after acute coronary syndrome. *N Engl J Med* 2018; 379: 2097–107
24. Kausik K et al. Inclisiran and cardiovascular events: a patient-level analysis of phase III trials. *Eur Heart J* 2023; 44: 129–38
25. PCSK9 als last line bei Hypercholesterinämie und Dyslipidämie (Information nach § 73.8 SGB V), BARMER Rundschreiben März 2023