Latest guidelines, novel therapies and emerging options for managing dyslipidemias and ASCVD risk in daily practice

Disclaimer

- *Unapproved products or unapproved uses of approved products may be discussed by the faculty; these situations may reflect the approval status in one or more jurisdictions*
- *The presenting faculty have been advised by touchIME to ensure that they disclose any such references made to unlabelled or unapproved use*
- *No endorsement by touchIME of any unapproved products or unapproved uses is either made or implied by mention of these products or uses in touchIME activities*
- *touchIME accepts no responsibility for errors or omissions*

A conversation between:

Dr. med. Mahir Karakas
University Medical Center,
Hamburg, Germany

Prof. Kausik Ray
Imperial College London,
London, UK

touch™ CARDIO

Lipid-lowering goals in patients with dyslipidemias: What do the guidelines say?

Dr. med. Mahir Karakas

University Medical Center,
Hamburg, Germany

touch™ CARDIO

Lipids/lipoproteins are associated with elevated ASCVD risk

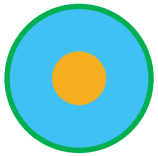
LDL-C[1,2]

- Most abundant ApoB-containing lipoprotein
- Well-established causal relationship between LDL-C and ASCVD risk – determined by magnitude and duration of exposure to LDL-C
- In a meta-analysis (N=170,000), absolute reduction in LDL-C was proportional to relative reduction in CVD risk

Lp(a)[1]

- ~90% of an individual's Lp(a) level is inherited
- Mendelian randomization studies show lifelong elevated Lp(a) is strongly and causally associated with increased ASCVD risk

TGRLs[1,3]



- TG-rich, ApoB-containing lipoproteins (VLDLs and IDLs) account for most circulating TGs
- High circulating TGs are associated with increased ASCVD risk, including in statin-treated patients

ApoB, apolipoprotein B; ASCVD, atherosclerotic CVD; CVD, cardiovascular disease; IDL, intermediate-density lipoprotein; LDL-C, low-density lipoprotein cholesterol; Lp(a), lipoprotein(a); TG, triglyceride; TGRL, TG-rich lipoprotein; VLDL, very-low-density lipoprotein.

1. Mach F, et al. *Eur Heart J*. 2020;41:111–88; 2. Cholesterol Treatment Trialists' (CTT) Collaboration, et al. *Lancet*. 2010;376:1670–81;
3. Farnier M, et al. *Arch Cardiovasc Dis*. 2021;114:132–9.

Guideline recommendations for lipid/lipoprotein targets[1,2]

- **ESC 2021** and **ESC/EAS 2019 guidelines** have adopted much lower LDL-C targets than previously used

	LDL-C	Non-HDL-C	ApoB
ASCVD + second event within 2 y*	Consider **<1.0 mmol/L**		
Very-high CV risk	Reduction **≥50% from BL** and **<1.4 mmol/L**	<2.2 mmol/L	<65 mg/dL
High CV risk	Reduction **≥50% from BL** and **<1.8 mmol/L**	<2.6 mmol/L	<80 mg/dL
Moderate CV risk	**<2.6 mmol/L**	<3.4 mmol/L	<100 mg/dL
Low CV risk	**<3.0 mmol/L**		

- In **apparently healthy** people, 10-year fatal and non-fatal **CV risk** is estimated using the **SCORE2** system
- Pts with documented **ASCVD** are at very-high CV risk
- Pts with **diabetes** are at moderate or higher CV risk, depending on target organ damage, no. of risk factors and diabetes duration
- Pts with moderate/severe **CKD** are at high/very-high CV risk, respectively

- There are no recommended targets for TGs or HDL-C in the ESC/EAS guidelines
- Lp(a) should be measured at least once in an individual's lifetime to identify very high inherited levels

*While on maximum tolerated statin dose.

ApoB, apolipoprotein B; ASCVD, atherosclerotic cardiovascular disease; BL, baseline; CKD, chronic kidney disease; CV, cardiovascular; EAS, European Atherosclerosis Society; ESC, European Society of Cardiology; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; Lp(a), lipoprotein(a); pts, patients; TG, triglyceride; y, years.

1. Mach F, et al. *Eur Heart J*. 2020;41:111–88; 2. Visseren FLJ, et al. *Eur Heart J*. 2021;42:3227–337.

Strategies to reduce ASCVD risk: Understanding the latest guidelines and clinical data on lipid-lowering therapies

Dr. med. Mahir Karakas

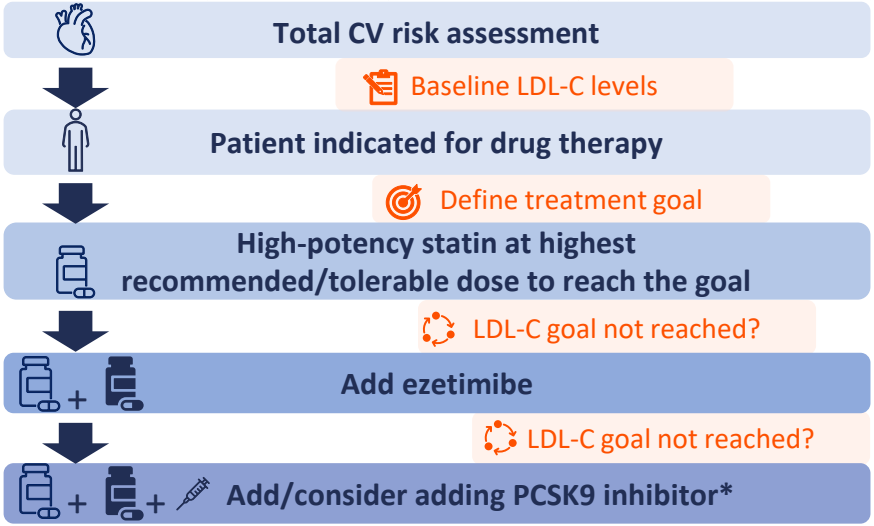
University Medical Center,
Hamburg, Germany

touch™ CARDIO

Pharmacological management of dyslipidemias[1,2]

- The ESC 2021 and ESC/EAS 2019 guidelines recommend that, alongside dietary and lifestyle modifications, a stepwise treatment-intensification approach is used to control LDL-C

Treatment algorithm for pharmacological LDL-C lowering



Intensity of lipid-lowering treatment	
Treatment	**Average LDL-C reduction**
High-intensity statin	~50%
High-intensity statin + ezetimibe	~65%
PCSK9 inhibitor	~60%
PCSK9 inhibitor + high-intensity statin	~75%
PCSK9 inhibitor + high-intensity statin + ezetimibe	~85%

* Add PCSK9 inhibitor for: secondary prevention (very-high risk); primary prevention: patients with FH and another major risk factor (very-high risk). Consider adding PCSK9 inhibitor for primary prevention: patients at very-high risk, but without FH. CV, cardiovascular; EAS, European Atherosclerosis Society; ESC, European Society of Cardiology; FH, familial hypercholesterolaemia; LDL-C, low-density lipoprotein cholesterol; PCSK9, proprotein convertase subtilisin/kexin type 9.

1. Mach F, et al. *Eur Heart J*. 2020;41:111–88; 2. Visseren FLJ, et al. *Eur Heart J*. 2021;42:3227–337.

touch™ CARDIO

Update on the treatment landscape

Approved

Agent	Indication	EMA approval
Bempedoic acid[1]	Primary hypercholesterolaemia or mixed dyslipidemia in combination with a statin or alone/in a combination for patients who cannot have a statin	2020
Inclisiran[2]		2020
Icosapent ethyl[3]	Reduction of CV events in adult, statin-treated patients with TGs ≥1.7 mmol/L and established CVD or diabetes and ≥1 CV risk factor	2021

Investigational[4]

Agent	Mode of action	Clinical trials
Pelacarsen	Antisense oligonucleotide targeting Lp(a)	• Lp(a)HORIZON (NCT04023552); phase III • Adults with established ASCVD and elevated Lp(a)
Pemafibrate	PPARα agonist	• PROMINENT (NCT03071692); phase III • Adults with type 2 diabetes
Obicetrapib	CETP inhibitor	• ROSE (NCT04753606); phase II • Adults with elevated LDL-C treated with high-intensity statin
VERVE-101	CRISPR/Cas9 targeting *PCSK9*	• NCT05398029; phase I • Adults with HeFH due to *LDLR* mutations

ASCVD, atherosclerotic cardiovascular disease; CRISPR, clustered regularly interspaced short palindromic repeats; EMA, European Medicines Agency; CETP, cholesteryl ester transfer protein; CV(D), cardiovascular (disease); HeFH, heterozygous familial hypercholesterolemia; LDL-C, low-density lipoprotein cholesterol; LDLR, LDL receptor; Lp(a), lipoprotein(a); PCSK9, proprotein convertase subtilisin/kexin type 9; PPARα, peroxisome proliferator-activated receptor alpha; TG, triglyceride.

1. Bempedoic acid SmPC. Available at: www.ema.europa.eu/en/documents/product-information/nilemdo-epar-product-information_en.pdf (accessed 15 August 2022);
2. Inclisiran SmPC. Available at: www.ema.europa.eu/en/documents/product-information/leqvio-epar-product-information_en.pdf (accessed 15 August 2022); 3. Icosapent ethyl SmPC. Available at: www.ema.europa.eu/en/documents/product-information/vazkepa-epar-product-information_en.pdf (accessed 15 August 2022). 4. All clinical trial information can be accessed at ClinicalTrials.gov.

Managing dyslipidemias in special patient populations: What are the important considerations?

Dr. med. Mahir Karakas

University Medical Center,
Hamburg, Germany

touch™ CARDIO

Managing dyslipidemias in special patient populations[1,2]

≥70 Older patients	• 2021 ESC guidelines revised 'older age' as ≥70 years from 2019 ESC/EAS guidelines • Statin therapy for primary prevention may be considered in high-risk patients • CV risk assessed using SCORE2-OP
Diabetes	• **Very-high risk**: **target organ damage; ≥3 risk factors; or early onset of T1DM of duration >20 years**
Chronic kidney disease	• **Very-high risk**: **severe CKD, eGFR <30 mL/min/1.73 m²** • Statins or statin/ezetimibe combinations are recommended for non-dialysis-dependent, stage 3–5 CKD • Initiation of statin therapy is not recommended in patients with dialysis-dependent CKD who do not have ASCVD
Familial hypercholesterolemia	• **Very-high risk**: **FH with ASCVD or with another major risk factor** • Clinical criteria such as Dutch Lipid Clinic Network, WHO or Simon Broome are recommended for diagnosis of FH

Very-high-risk LDL-C target: ≥50% from baseline and <1.4 mmol/L

ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; CV, cardiovascular; EAS, European Atherosclerosis Society; eGFR, estimated glomerular filtration rate; ESC, European Society of Cardiology; FH, familial hypercholesterolaemia; LDL-C, low-density lipoprotein cholesterol; SCORE-OP, Systematic COronary Risk Evaluation - Older Persons; T1DM, type 1 diabetes mellitus; WHO, World Health Organization.

1. Mach F, et al. *Eur Heart J*. 2020;41:111–88; 2. Visseren FLJ, et al. *Eur Heart J*. 2021;42:3227–337.

touch™ CARDIO