New prospects for PCSK9 inhibition?


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This commentary refers to '2017 update of ESC/EAS task force on practical clinical guidance for proprotein convertase subtilisin/kexin type 9 inhibition in patients with atherosclerotic cardiovascular disease or in familial hypercholesterolaemia', by U Landmesser et al., 2018;39:1131–1143.

In 2017, this Task Force updated practical guidance for clinical use of proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibition following publication of FOURIER. Beyond licenced indications, PCSK9 inhibitors may have application in other high-risk conditions, such as severe hyperlipidaemia with liver failure, supported by pharmacodynamic data, although the lack of trials to date does not allow recommendations.

Recent insights from FOURIER help to define patients at highest risk with elevated low-density lipoprotein cholesterol (LDL-C) levels who benefit most from PCSK9 inhibition. These include those with symptomatic peripheral artery disease (PAD), a group often underrecognized and undertreated, in whom evolocumab reduced major adverse cardiovascular events (MACE) by 27% and major adverse limb events by 37%, with benefits extending to LDL-C levels <0.26 mmol/L. Patients with recent or recurrent myocardial infarction (MI), or multivessel disease, at 34–90% higher risk of a MACE, also derived greater benefit from evolocumab than those without these characteristics (Sabatine MS, Annual Scientific Sessions, American Heart Association, 13 November 2017). Thus, irrespective of other vascular disease, symptomatic PAD, the timing and frequency of MI, or multivessel disease, associated with residual LDL-C burden, indicate very high-risk patients who merit consideration of PCSK9 inhibition.

Will results from ODYSSEY OUTCOMES extend use of PCSK9 inhibitors to early post-MI patients? Such findings would align with the MIRACL trial and may imply further stabilization of atherosclerotic plaque from LDL-C lowering with PCSK9 inhibition.

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References

