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DISCUSSION FORUM

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.[1] Beyond licenced indications, PCSK9 inhibitors may have application in other high-risk conditions, such as severe hyperlipidaemia with liver failure,[2] supported by pharmacodynamic data,[3] 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.[4] 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[5] and may imply further stabilization of atherosclerotic plaque from LDL-C lowering with PCSK9 inhibition.

Conflict of interest: Potential conflicts of interest of the authors are denoted in reference 1.

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