

PLENARY 4 (PL4): Advances in lipid-modification for the prevention of vascular disease

Professor Jane Armitage



Jane Armitage is Professor of Clinical Trials and Epidemiology and Honorary Consultant in Public Health Medicine in the Nuffield Department of Population Health (NDPH) at the University of Oxford. She joined the Clinical Trial Service Unit, now part of NDPH, in 1990 from a background in clinical medicine, with particular experience in respiratory medicine, geriatrics and diabetes. She coordinates a series of large-scale clinical trials including the MRC/BHF Heart Protection Study, SEARCH and HPS2-THRIVE, which are trials of lipid modification in people with or at risk of vascular disease, as well as the ASCEND trial of aspirin and fish oils in diabetes. Her main research interests are in lipids and the epidemiology of cardiovascular and other chronic disease including osteoporosis.

SUMMARY

Objectives :

1. To understand the importance of different lipids to vascular disease risk and how genetics have helped
2. To reiterate the value and safety of statins as a first line therapy for lipid modification
3. To explain the potential role of newer lipid-lowering agents: PCSK9 inhibitors, cholesterol ester transfer protein inhibitors and small interfering RNAs to block lipid-related protein synthesis

Observational studies indicate a clear, positive and continuous relationship between coronary heart disease risk and blood LDL-cholesterol levels and inverse associations with HDL-cholesterol. Recent genetic evidence also supports a causal role for CETP, lipoprotein (a) [Lp(a)], apoC3, ANGPT3 and PCSK9 in vascular risk.

Large, well-designed randomized trials of statins and meta-analyses of trials show that reductions of 20-25% in the risk of vascular events are seen per 1 mmol/L reduction in LDL-cholesterol, with larger reductions producing greater benefits. Statins are safe and well tolerated although the risk factors for the rare side-effect of myopathy need to be understood to allow their use most safely and effectively. The results of trials of HDL-raising have so far been disappointing, both because older drugs were toxic (niacin) and other studies may have been underpowered to detect plausible effects. An alternative explanation is that HDL-cholesterol is not causally related to vascular disease but only associated and there is supportive genetic data for this view.

Newer agents such as monoclonal antibodies against PCSK9 and CETP inhibitors are currently in Phase 3 trials and clearly reduce LDL levels substantially with CETP inhibitors also increasing HDL-cholesterol and show promise for vascular risk reduction but are likely to be very expensive and are not yet proven. Results will emerge in the next couple of years.

Session chair: Dr Channa Ranasinha