New therapeutic options for reducing atherosclerotic cardiovascular disease residual risk

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Adults with atherosclerotic cardiovascular disease (ASCVD) bear a significant risk of recurrent ASCVD events, particularly those classified as very high risk, despite current standard-of-care therapies. While addressing lifestyle modification efforts to reduce this “residual risk” must remain the foundation of ASCVD risk reduction efforts, there is significant interest in the development of newer therapies that may provide further benefit. Important domains for targeting therapies include those directed at lipid, inflammatory, metabolic, and thrombotic residual risk. With respect to therapies addressing lipid targets, ezetimibe and PCSK9 monoclonal antibody therapies have been shown to reduce ASCVD risk beyond statin therapy. Inclisiran, currently approved in the European Union, also lowers LDL-C, with cardiovascular outcome data pending as to whether it will provide further ASCVD risk reduction. Further, therapies to lower lipoprotein(a) are in development that hold promise for reducing lipoprotein(a)-associated residual risk. Also, of interest has been whether targeting inflammation will reduce ASCVD risk. While canakinumab did demonstrate proof of concept in being the first such therapy to selectively reduce inflammation resulting in ASCVD event reduction, cost and fatal infections precluded its further development. Moreover, clinical trials of colchicine have also shown benefit, but recommendations are yet to adopt this as a therapeutic option to reduce ASCVD risk. Metabolic agents include icosapent ethyl, SGLT2 inhibitors, and GLP1 receptor agonists that now have evidence for reducing cardiovascular outcomes. Finally, in high risk individuals, antithrombotic therapy with rivaroxiban or dual antiplatelet agents have shown benefit. The potential remains great for the development and use of newer therapies to address residual ASCVD risk.

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