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# Challenges to Using of PCSK9i Agents in Routine Clinical Practice

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Atherosclerotic cardiovascular disease (ASCVD) is the number one cause of death globally. Elevated cholesterol plays a key role the development of atherosclerosis[1]. Furthermore agents that lower cholesterol have been demonstrated in trials to prevent ASCVD events. The first inhibitor of 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase (HMG-CoA reductase) was first approved in 1987. Since that time, multiple randomized trials have shown the efficacy of statins lowering the risk of recurrent events in those with or without established ASCVD[2]. Nevertheless, not all patients can have their cholesterol controlled on statin therapy alone and many patients are unable to take statins due to perceived side effects. Therefore, additional LDL-reducing therapies are needed to optimally treat high risk patients with residual ASCVD risk despite statin therapy.

Studying paitents with very low LDL-C, researchers in the Dallas Heart Study idenfiified two loss of function deficits of the proprotein convertase subtilisin/kexin type 9 (PCSK9) gene [3]. In 2015, less than a decade after this discovery, the FDA approved two PCSK9 inhibitors alirocumab and evolocumab for the treatment of adults with heterozygous familial hypercholesterolemia or clinical ASCVD who require additional LDL lowering. Multiple clinical trials have demonstrated that these drugs are highly effectives in reducing LDL-C levels by as much as 70%. Recently both agents have conducted and completed their pivotal large cardiovascular outcome trial (CVOT), each demonstrating that the drug reduced ASCVD events by approximately 15% when used on top of maximally tolerated statins[4-5].

While both PCSK9 agents are effective and safe, the drugs are quite costly which has resulted in significant challenges to their wide-spread use [6-7]. This talk will review the clinical benefits of PCSK9 inhibition from the major RCTS; discuss who are candidates for PCSK9 therapy. I will also cover the current day challenges to their routine use including costs, co-pay and pre-authorization hurdles. Finally I will covers strategies on how to select patients who stand to maximially benefit from these agents.

**References:**

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