Atherosclerosis: Targeting LDL Cholesterol with Statins and PCSK9 Inhibitors for Cardiovascular Disease Management

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collectively known as cardiovascular disease (CVD). This review article provides an overview of atherosclerosis, its pathophysiology, and the role of elevated LDL (low-density lipoprotein) cholesterol in its development. Furthermore, it examines the therapeutic options of statins and PCSK9 inhibitors, which have shown significant promise in managing LDL [illegible]

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Atherosclerosis stands as the primary culprit behind the development of cardiovascular disease (CVD), a leading global cause of morbidity and mortality. CVD encompasses a range of conditions affecting the heart and blood vessels, including coronary artery disease, stroke, and peripheral arterial disease [1,2]. Among these conditions, ischemic heart disease (IHD), commonly known as coronary artery disease, remains a significant contributor to cardiovascular-related morbidity and mortality. Atherosclerosis is a complex and insidious disease process characterized by the gradual accumulation of lipids, inflammatory cells, and fibrous tissue within the walls of large and medium-sized arteries. The process typically begins in childhood and slowly progresses throughout life, eventually leading to the formation of atherosclerotic plaques [3]. These plaques are the hallmark feature of atherosclerosis and represent localized areas of thickening and hardening of arterial walls. The key players in atherosclerosis development are lipids, particularly low-density lipoprotein (LDL) cholesterol, and inflammatory cells, such as macrophages and T lymphocytes. The arterial endothelium, which lines the inner surface of blood vessels, plays a pivotal role in regulating lipid transport and inflammatory processes within the arterial wall. The development of atherosclerotic plaques starts with endothelial dysfunction, triggered by various risk factors like hypertension, smoking, hypercholesterolemia, and diabetes [4-7]. In this dysfunctional state, the endothelium loses its ability to maintain a healthy vascular environment, allowing LDL cholesterol particles to penetrate the arterial intima, the innermost layer of the arterial wall. Once inside the arterial intima, LDL cholesterol undergoes oxidative modifications, rendering it highly reactive and pro-inflammatory. These oxidized LDL particles attract circulating monocytes, which migrate into the arterial wall and differentiate into macrophages. Within the intima, macrophages internalize the oxidized LDL cholesterol and become engorged, transforming into lipid-laden foam cells. The accumulation of foam cells within the arterial wall leads to the formation of fatty streaks, the earliest visible manifestations of atherosclerosis [8]. Over time, the fatty streaks evolve into more complex atherosclerotic plaques, characterized by the deposition of fibrous tissue, smooth muscle cells, and additional inflammatory cells. The interplay between inflammation and lipid metabolism plays a central role in the pathogenesis of atherosclerosis. Inflammatory mediators released by macrophages and other immune cells further propagate the inflammatory response, leading to increased oxidative stress and promoting further plaque progression. As the atherosclerotic plaques grow, they can eventually obstruct blood flow through the affected arteries. In some cases, these plaques can rupture, leading to the exposure of prothrombotic substances within the plaque's core. This exposure triggers the formation of blood clots, or thrombi, which can partially or completely block blood flow downstream, resulting in ischemic events. If a thrombus forms within a coronary artery, it can cause a myocardial infarction (heart attack). When a thrombus develops within an artery supplying the brain, it can lead to an ischemic stroke. Peripheral vascular disease occurs when atherosclerosis affects arteries in the limbs, causing reduced blood flow and potentially leading to pain, tissue damage, and even limb loss. In conclusion, atherosclerosis is a multifaceted and chronic disease process that plays a central role in the development of cardiovascular disease. The progressive accumulation of lipids and inflammatory cells within arterial walls leads to the formation of atherosclerotic plaques, which can ultimately obstruct blood flow or rupture, causing severe cardiovascular complications. Understanding the complex interplay between inflammation and lipid metabolism in atherosclerosis is critical for developing effective prevention and treatment strategies to mitigate the burden of cardiovascular disease worldwide. Continued research and advancements in medical therapies hold the promise of improving patient outcomes and reducing the global impact of atherosclerosis and its associated cardiovascular events.

[illegible] Atherosclerosis, once considered solely a lipid storage disorder, is now increasingly recognized as a chronic inflammatory disease. The early stages of atherosclerosis involve endothelial dysfunction, a process initiated by various risk factors, such as hypertension, smoking, hypercholesterolemia, diabetes, and other conditions that promote oxidative stress. The endothelium,

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on the surface of hepatocytes. LDL receptors on hepatocytes are responsible for removing LDL cholesterol from the bloodstream by endocytosis. However, PCSK9 binds to these receptors and induces their degradation, reducing the number of LDL receptors available for LDL clearance. This process leads to elevated LDL cholesterol levels in the bloodstream, contributing to atherosclerosis development. PCSK9 inhibitors work by blocking PCSK9's function and preventing it from interacting with LDL receptors. As a result, more LDL receptors remain available on the hepatocyte surface, leading to increased uptake and clearance of LDL cholesterol from the bloodstream. By enhancing LDL receptor recycling and reducing LDL cholesterol levels, PCSK9 inhibitors offer a potent means of managing hypercholesterolemia. Clinical trials evaluating PCSK9 inhibitors have consistently demonstrated their efficacy in significantly lowering LDL cholesterol levels. When used as an adjunct to statin therapy in individuals with familial hypercholesterolemia or high cardiovascular risk, PCSK9 inhibitors have shown impressive results in achieving LDL cholesterol reductions beyond what statins alone can achieve. Furthermore, the profound reduction in LDL cholesterol levels achieved with PCSK9 inhibitors has translated into notable cardiovascular benefits in clinical studies. These benefits include a substantial reduction in major adverse cardiovascular events (MACE), such as myocardial infarctions (heart attacks), strokes, and cardiovascular mortality.

[illegible] Numerous clinical trials have been conducted to assess the efficacy and safety of both statins and PCSK9 inhibitors in managing LDL cholesterol levels and reducing MACE. Statin trials, such as the landmark HPS (Heart Protection Study) and PROVE-IT TIMI 22 (Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis In Myocardial Infarction 22) trials, have consistently shown that statin therapy significantly lowers LDL cholesterol levels and leads to a reduction in cardiovascular events. These trials have been instrumental in establishing statins as a cornerstone of cardiovascular disease management. Similarly, clinical trials evaluating PCSK9 inhibitors, such as FOURIER (Further Cardiovascular Outcomes Research with PCSK9 Inhibition in Subjects with Elevated Risk), have demonstrated the efficacy of PCSK9 inhibitors in further reducing LDL cholesterol levels and reducing MACE in patients at high cardiovascular risk. The combination of statins and PCSK9 inhibitors has shown even more potent LDL cholesterol-lowering effects and cardiovascular benefits. These therapies have revolutionized the management of hypercholesterolemia and have proven to be valuable additions to the armamentarium of cardiovascular disease management strategies. In conclusion, both statins and PCSK9 inhibitors have emerged as effective and vital therapies for managing LDL cholesterol levels and reducing major adverse cardiovascular events. Statins act by inhibiting HMG-CoA reductase and reducing hepatic cholesterol production, while PCSK9 inhibitors target PCSK9 to enhance LDL receptor recycling and enhance LDL cholesterol clearance. The combination of their LDL cholesterol-lowering effects and pleiotropic benefits makes these therapeutic approaches indispensable in preventing and managing atherosclerosis and its associated cardiovascular complications, ultimately improving patient outcomes.

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Atherosclerosis stands as a complex and chronic inflammatory disease that lies at the heart of cardiovascular disease progression. Elevated LDL cholesterol plays a pivotal role in the pathogenesis of atherosclerosis, emphasizing its significance as a crucial therapeutic target in managing cardiovascular risk. The therapeutic approaches of statins and PCSK9 inhibitors have demonstrated remarkable efficacy in reducing LDL cholesterol levels and mitigating major adverse cardiovascular events, marking significant advancements in atherosclerosis management. Statins' pleiotropic effects, including anti-inflammatory properties and endothelial function improvement, complement their LDL cholesterol-lowering abilities, contributing to their overall cardiovascular benefits. Furthermore, PCSK9 inhibitors offer a promising avenue for achieving profound reductions in LDL cholesterol levels by targeting the PCSK9-LDL receptor axis, providing an innovative approach to combating hypercholesterolemia and its associated complications. However, the journey towards optimal atherosclerosis management does not end here. Continued research and clinical trials are imperative to deepen our understanding of the long-term safety and efficacy of these therapeutic agents. By gaining further insights into potential side effects and identifying patient populations that would benefit most from these treatments, we can refine our therapeutic approaches and maximize patient outcomes.

Moreover, the pursuit of novel targets and interventions holds great promise for advancing atherosclerosis management in the future. Precision medicine and personalized therapies may offer tailored approaches to address the diverse manifestations and risk profiles of patients with atherosclerosis.

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In summary, atherosclerosis remains a major global health challenge, necessitating relentless efforts to uncover new insights and therapeutic strategies. By focusing on reducing elevated LDL cholesterol levels through agents like statins and PCSK9 inhibitors, medical practitioners can forge a path towards improved treatment outcomes and enhanced cardiovascular risk reduction. Through continued research, we aspire to make significant strides in combating atherosclerosis, reducing its burden on individuals and societies, and ultimately, promoting heart health and well-being worldwide.

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Not applicable.

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References

1. Ridker PM, Danielson E, Fonseca FA, Genest J, Gotto AM, et al. (2008) Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. N Engl J Med 359:2195-2207.
2. Ridker PM, Everett BM, Thuren T, MacFadyen JG, Chang WH, et al. (2017) Antiinflammatory therapy with canakinumab for atherosclerotic disease. N Engl J Med 377:1119-1131.
3. Kimura T, Tse K, Sette A, Ley K (2015) Vaccination to modulate atherosclerosis. Autoimmunity 48:152-160.
4. Mills CD, Ley K, Buchmann K, Canton J (2015) Sequential immune responses: the weapons of immunity. J Innate Immun 7:443-449.
5. Ley K, Pramod AB, Croft M, Ravichandran KS, Ting JP (2016) How mouse macrophages sense what is going on. Front Immunol 7:204.
6. Lundberg AM, Hansson GK (2010) Innate immune signals in atherosclerosis. Clin Immunol 134:5-24.
7. Wolf D, Zirlik A, Ley K (2015) Beyond vascular inflammation–recent advances in understanding atherosclerosis. Cell Mol Life Sci 72:3853-3869
8. Ait-Oufella H, Salomon BL, Potteaux S, Robertson AK, Gourdy P, et al. (2006) Natural regulatory T cells control the development of atherosclerosis in mice. Nat Med 12:178-180.
9. Kimura T, Kobiyama K, Winkels H, Tse K, Miller J, et al. (2018) Regulatory

CD4+ T cells recognize MHC-II-restricted peptide epitopes of apolipoprotein B. Circulation 138:1130-1143.

10. Ley K (2016) 2015 Russell Ross memorial lecture in vascular biology: protective autoimmunity in atherosclerosis. Arterioscler Thromb Vasc Biol 36:429-438.
11. Chackerian B, Remaley A (2016) Vaccine strategies for lowering LDL by immunization against proprotein convertase subtilisin/kexin type 9. Curr Opin Lipidol 27:345-350.
12. Cohen JC, Boerwinkle E, Mosley TH, Hobbs HH (2006) Sequence variations in PCSK9, low LDL, and protection against coronary heart disease. N Engl J Med 354:1264-1272.
13. Gistera A, Klement ML, Polyzos KA, Mailer RK, Duhlin A (2018) LDL-reactive T cells regulate plasma cholesterol levels and development of atherosclerosis in humanized hypercholesterolemic mice. Circulation 138:2513-2526.
14. Lehrer-Graiwer J, Singh P, Abdelbaky A, Vucic E, Korsgren M, et al. (2015) FDG-PET imaging for oxidized LDL in stable atherosclerotic disease: a phase II study of safety, tolerability, and anti-inflammatory activity. JACC Cardiovasc Imaging 8:493-494.
15. Kobiyama K, Vassallo M, Mitzi J, Winkels H, Pei H, et al. (2018) A clinically applicable adjuvant for an atherosclerosis vaccine in mice. Eur J Immunol 48:1580-1587.