

Proprotein Convertase Subtilisin/Kexin Type 9 Inhibitors and Cancer Therapy: A Review

Adriana Hamiera Zainol Anuar^a, *Rahayu Zulkapli^{b,c*} & Iman Nabilah Abdul Rahim^c

Structure Abstract

Background: Despite progress in cancer treatment, resistance to therapy and poor immune response remain critical challenges. Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9), a protein classically associated with cholesterol regulation, has emerged as a potential immunological modulator in cancer. PCSK9 inhibitors (PCSK9i) such as Evolocumab and Alirocumab may not only lower lipid levels but also enhance immune responses and improve the efficacy of immunotherapy. This review aims to narratively explore the role of PCSK9i in cancer treatment.

Objective: This review aims to provide an overview of the potential role of PCSK9 inhibitors in cancer treatment, focusing on their biological effects, therapeutic applications, and relevance in current cancer research.

Methods: This narrative review is based on the literature, including research articles, reviews, and reference materials published in recent years. Studies were selected through manual searches and reading of relevant sources, with the goal of summarizing key findings related to the use of PCSK9i in cancer.

Results: PCSK9i were found to improve antigen presentation, increase CD8⁺ T-cell infiltration, and reduce tumour progression in animal models. Early human studies and trials (e.g., BOOST-RCC) suggest a synergistic benefit when combined with PD-1 inhibitors. Retrospective studies have reported improved survival outcomes among patients with lower PCSK9 expression. Additionally, PCSK9 inhibition has been associated with reduced cancer stemness and better response to immune checkpoint therapies. Adverse effects remain minimal across reviewed studies.

Conclusion: This review highlights the potential dual role of PCSK9i in cardiovascular and cancer management. Although clinical evidence remains limited, findings support further exploration of PCSK9i as adjuncts to immunotherapy. Well-designed human trials are necessary to validate their therapeutic relevance and expand their role in oncology.

Keywords: PCSK9 Inhibitors, Cancer Therapy, Immune Checkpoint Inhibitors, Evolocumab, Alirocumab

*Correspondence: rahayu88@uitm.edu.my

^a School of Biology, Faculty of Applied Sciences, Universiti Teknologi MARA, Shah Alam, Malaysia

^b Faculty of Dentistry, UiTM Sungai Buloh Campus, Selangor, Malaysia.

^c Cardiovascular Advancement and Research Excellence Institute (CARE Institute), Universiti Teknologi MARA, Selangor, Malaysia.