Efficacy and Safety of Sonic Hedgehog and PD-1 Inhibitors in Locally Advanced Basal Cell Carcinoma: A Systematic Review and Meta-analysis (2013-2023)

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Abstract

Managing advanced basal cell carcinoma (aBCC) is more challenging for both patients and physicians than for non-advanced cases. However, the introduction of sonic Hedgehog inhibitors, and more recently, immune checkpoint inhibitors, has offered new hope for improved clinical outcomes. At the same time, it is important to assess the potential adverse effects associated with these systemic medications. This review aims to provide a comprehensive analysis of the clinical effectiveness and safety profiles of various sonic Hedgehog pathway and immune checkpoint inhibitors used in locally advanced basal cell carcinoma (laBCC) over the past decade. The study followed the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). We systematically analyzed data from laBCC patients treated with Hedgehog pathway and immune checkpoint inhibitors between 2013 and 2023 and presented the findings accordingly. Eleven articles were included in the systematic review, with ten included in the meta-analysis of the overall response rate (ORR) and complete response rate (CRR). The ORRs for vismodegib, sonidegib, cemiplimab, and nivolumab were 74%, 50%, 31%, and 17%, respectively. Vismodegib also had the highest CRR at 40%, whereas sonidegib and cemiplimab had much lower CRRs of 2% and 6%, respectively. The most frequently reported side effects of Hedgehog pathway inhibitors included muscle spasms, altered taste perception, and hair loss, while cemiplimab was commonly associated with fatigue, diarrhea, and itching. In conclusion, systemic therapies mark a significant advancement in laBCC treatment, offering notable clinical benefits; however, their use is often constrained by adverse effects. Among the available treatments, vismodegib stands out with the highest overall and complete response rates, suggesting its potential as a preferred option.

Keywords: *basal cell carcinoma, systematic review, meta-analysis, sonic hedgehog inhibitors, PD-1 inhibitors*