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Clinical Use of the Mechanism of Locally Advanced Basal Cell Carcinoma

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DESCRIPTION

Non-melanoma skin cancers, also known as keratinocyte tumors, are becoming more common worldwide, with basal cell carcinoma and squamous cell carcinoma being the most common. Surgery is the gold standard of treatment for both tumors, but in some cases the disease is advanced or metastatic and targeted therapy may be required. Hedgehog signaling plays a key role in the development of basal cell carcinoma, and its inhibition holds the key to new therapeutic options in the treatment of locally advanced and metastatic basal cell carcinoma. Cutaneous squamous cell carcinoma is the second most common malignant skin cancer. If the disease is advanced or metastatic, alternative treatments may be needed. Semiplimab, a human monoclonal antibody directed against the programmed cell death-1 receptor that blocks T-cell inactivation, is the first drug approved for the treatment of adult patients with the metastatic studies are ongoing evaluating pembrolizumab, ipilimumab, and nivolumab as the alternative treatments for advanced squamous cell carcinoma.

Advanced basal cell carcinoma represents a small fraction of the basal cell carcinomas unsuitable for standard therapy due to lack of the efficacy, high recurrence risk, and excessive morbidity. Involvement of the sonic hedgehog pathway in the development of basal cell carcinoma has led to the development of the systemic sonic hedgehog pathway inhibitors, providing new therapeutic options and improved survival for the patients with advanced basal cell carcinoma. There are currently two Food and Drug Administration-approved Sonic Hedgehog inhibitors for advanced basal cell carcinoma: Vismodegib and sonidegib. Vismodegib is approved for the locally advanced basal cell carcinoma and metastatic basal cell carcinoma, and sonidegib is approved for locally advanced basal cell carcinoma. These agents have also been used to prevent nevus-like basal cell carcinoma syndrome and as neoadjuvant therapy before surgery, and we believe that sonic hedgehog inhibitors have an increasing role in these settings. There are no direct randomized controlled studies comparing vismodegib with sonidegib. Adverse events cause most patients to the discontinue treatment and may limit the usefulness of these agents. Therefore, it is important that the prescribing physician can anticipate and manage the most common side effects, such as muscle cramps, hair loss, taste disturbances and nausea. Other Sonic hedgehog inhibitors, including the antifungal drug itraconazole, have been investigated in the smaller studies, but more research is needed before the routine clinical use can be recommended. In addition, several new drugs are being investigated that may improve the efficacy against resistant tumors by exploiting mechanisms of the action different from the two currently approved drugs.

In locally advanced basal cell carcinoma and metastatic basal cell carcinoma had sufficient studies on vismodegib, but not sonidegib, to warrant a pooled analysis. Vismodegib was found to have a consistently significant effect on the mean duration of treatment in locally advanced basal cell carcinoma and metastatic basal cell carcinoma. Although the response to metastatic basal cell carcinoma is superior to any conventional approach, the response rate to the locally advanced basal cell carcinoma can be compared with the other standard treatment options such as surgery and radiotherapy.

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CONFLICT OF INTEREST

The author's declared that they have no conflict of interest.

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