First-in-class histone deacetylase inhibitor gel shows promise for the treatment of patients with basal cell carcinoma

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Remetinostat, a topical cream and first-in-class inhibitor of histone deacetylation, showed signs of clinical efficacy in patients with basal cell carcinoma, according to results from a phase II clinical trial published in *Clinical Cancer Research*.

Basal cell carcinoma (BCC) is the most common form of skin cancer and is typically treated with surgical excision, explained Kavita Sarin, MD, Ph.D., senior author of the study and an associate professor of dermatology at Stanford University.

"While BCC is not associated with high mortality, surgical excision can be a costly and burdensome treatment, particularly for patients who develop multiple BCC lesions," she noted.

A potential alternative strategy is to treat BCC with a topical cream; however, existing topical treatments for BCC are only effective for the superficial subtype of BCC, highlighting the need for more widely applicable topical treatments, Sarin explained.

Sarin and colleagues previously identified histone deacetylase (HDAC) inhibition as a promising therapeutic approach for BCC. In their latest study, a phase II clinical trial, Sarin and colleagues evaluated the safety and efficacy of the HDAC inhibitor remetinostat in adult patients with BCC. Unlike systemic HDAC inhibitors, which can be associated with

various toxicities, remetinostat is designed to lose potency once it is absorbed beyond the skin, allowing its activity to be localized to the skin lesion.

The study enrolled 30 patients, each of whom had at least one BCC measuring 5 mm or greater in diameter at diagnosis. Ninety percent of patients identified as non-Hispanic white, and almost half had a prior history of skin cancer. Eight patients had multiple eligible tumors, resulting in a total of 49 tumors in the study. The tumors were found in both sun-exposed and non-exposed parts of the body, and the majority had either nodular or superficial histology.

Participants applied remetinostat gel to their tumors three times per day for six weeks. After eight weeks, any remaining tumor was surgically removed and examined histologically.

Of the 33 tumors included in the final analysis, 69.7 percent responded to the topical treatment, with 17 complete responses and six partial responses. On average, tumor diameter decreased by 62.3 percent, and tumor area decreased by 71.5 percent.

Responses were observed across multiple BCC subtypes: there was a 100 percent response rate among the six superficial BCC tumors in the analysis (five complete responses, one partial response), 68.2 percent response rate among 22 nodular BCCs (10 complete responses, five partial responses), and 66.7 percent among three infiltrative BCCs (two complete responses). No responses were observed in the two tumors of micronodular subtype.

There were no systemic or serious adverse events reported. The most reported adverse event was an eczema-like skin reaction at the site of remetinostat application.

"While further research is needed, our results suggest that remetinostat could be a safe and promising alternative to surgical treatment of BCC due to the high rate of complete responses we observed," said Sarin. "However, if a therapy is to replace surgical treatment, it needs to not only induce a complete response, but also a durable one." Future trials will examine the longevity of the response to remetinostat, Sarin noted.

"Our study also showed remetinostat's clinical efficacy against nodular BCC, one of the more common BCC subtypes," Sarin added. "An ideal therapeutic for BCC should treat both nodular and superficial BCCs, and ideally the other subtypes as well."

Limitations of the study include the small sample size, its single-arm design, and the lack of durability data. The study was supported by Medivir AB, the Damon Runyon Foundation, the National Cancer Institute, the American Skin Association Medical Student Grant, and Stanford Medical Scholars. Sarin declares no conflicts of interest.

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