

Novel Approach Prevents Cancer Progression, Spares Surgery for Patients With Precancerous Oral Lesions

Direct injection of Opdivo immunotherapy into precancerous lesions reduced their size and decreased the risk of progression.

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- Precancerous oral lesions can progress to oral cancer and are typically ablated or surgically removed as a preventive measure.
- Direct injection of nivolumab [Opdivo] immunotherapy into lesions reduced toxicities and reduced lesion size by an average of 60%, decreasing the risk of cancer progression.
- More than 80% of treated lesions were cancer-free after one year, and patients reported improved quality of life and tolerable side effects;
- Direct injection approach offers benefits over systemic nivolumab, which could bring excessive toxicities for patients without cancer.

Direct injection of a low dose of the [immune checkpoint inhibitor](#) nivolumab into precancerous oral lesions significantly reduced lesion size and risk of cancer progression, sparing most patients from surgery. This new research from The University of Texas MD Anderson Cancer Center suggests a novel approach to [oral cancer](#) prevention through immune interception.

Results from the first-in-human Phase I trial were presented today at the [American Association for Cancer Research \(AACR\) Annual Meeting 2026](#) by principal investigator [Moran Amit, MD, PhD](#), assistant professor of [Head & Neck Surgery](#). The study explored the feasibility and efficacy of up to four doses of intralesional [immunotherapy](#) with nivolumab for patients with mild to severe oral [dysplasia](#).

“The fact that we were able to prevent surgery in the vast majority of patients is a strong

indication that those lesions changed from bad players to something patients can live with and that we can simply monitor closely,” Amit said. “We are encouraged by these results showing that locally administered immunotherapy is effective in not only preventing these lesions from progressing but also in reducing their risk of progression, opening an avenue for cancer prevention that we didn’t know existed before.”

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What is the current standard of care for precancerous oral lesions?

Precancerous oral lesions are asymptomatic, abnormal cell changes in the mouth. Depending on the level of cell abnormality, or dysplasia, precancerous lesions run the risk of progressing to oral cancer, but there is no known biomarker for determining which lesions will become cancer. Standard of care for these patients is to surgically remove or ablate the lesions as a means of prevention.

While clinicians try to minimize how much of the oral cavity is removed, there are no established approaches for preserving tissue. Two out of every three patients have multiple lesions that can also recur after removal, often resulting in multiple surgeries that remove much of the mouth and tongue. This leaves many patients with difficulty swallowing, speaking and eating, and facing other debilitating symptoms that reduce their quality of life.

How does the current study build upon previous research?

Previous studies have shown that using systemic intravenous (IV) nivolumab, an anti-PD-1 monoclonal antibody, can reduce the size of these lesions and their risk of progression. However, this approach involves a fairly high dose of nivolumab that also comes with toxicities that are considered excessive for patients without cancer.

These studies led Amit and colleagues to design a Phase I clinical trial using a much lower dose of nivolumab – 2% to 4% of the systemic dose – injected directly into the lesion. The trial enrolled 29 patients with at least one oral lesion determined to have a high risk of progression. Of these, 15 patients had high-grade, or severe, dysplasia, and 14 patients had low-grade, or mild, dysplasia. Patients received either 10 or 20 mg of nivolumab injected directly into their lesions every week for four cycles.

What were the key results of this clinical trial?

On the study, 85% of patients experienced a decrease in lesion size after a median follow-up of 14.5 months, with an overall average of 60% reduction in size, while 19 patients (65%) experienced reductions greater than 50%.

Twelve patients (41%) had their lesions downgraded in severity grade, and six patients had no signs of dysplasia after follow-up, meaning they achieved a complete pathologic response. All

except four patients completed the entire trial.

Only six of the treated lesions progressed to cancer and, because these were detected early, were surgically removed. No other patients required further surgical resection. There were no dose-limiting side effects, and most adverse events were grade 1 or 2, with one case each of diarrhea, hyperglycemia and acidosis.

Importantly, patient-reported outcomes showed a much higher quality of life based on head and neck-related symptoms, such as swallowing, mouth soreness, communication and taste.

How does this treatment change the antitumor immune response?

Tissue samples from treated lesions had a greater infiltration of CD4 and CD8 T cells, as well as other indicators of immune activation, whereas untreated lesions from the same patients did not. Pharmacokinetic analyses demonstrated less than 10 micrograms per milliliter of nivolumab in blood samples, which is substantially lower than with systemic administration.

“When given systemically, only a fraction of the drug ends up in the target lesion,” Amit explained. “By injecting straight into the lesion, we can give a fraction of the full dose because the bioavailability is 100% delivered entirely into where it’s needed, potentially bypassing systemic exposure and sparing toxicities.”

What implications does this have for precancer treatment and prevention?

The results show that nivolumab injected directly into precancerous oral lesions is safe and well-tolerated and could be an effective means of preventing progression through immune intervention.

Interestingly, precancerous lesions arise in many other types of cancers – including skin, cervical and colon – suggesting that local immunotherapy administration could potentially serve as a prevention method for those cancers, as well.

While this Phase I trial focused on only treating one lesion, a placebo-controlled Phase II trial is currently being planned to allow the targeting of multiple lesions at once.

“Ultimately, the goal is to help patients avoid repeated surgeries or excessive treatment and preserve their quality of life, especially when they don’t yet have cancer,” Amit said.

“Continuously removing parts from the oral cavity can lead to significant issues that affect quality of life, so this approach would be a substantial advancement over the current standard of care.”

The trial was supported by the Cancer Prevention and Research Institute of Texas (CPRIT). A full list of collaborating authors and their disclosures can be found with the [abstract](#).

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