Can Gangrene-Causing Bacteria Help Fight Cancer?

Injecting Clostridium bacteria into tumors slows disease progression.

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Bacteria that cause gas gangrene can destroy cancer cells when injected into tumors and appear to trigger an immune response against cancer elsewhere in the body, according to results from a small early study presented at the International Cancer Immunotherapy Conference, taking place this week in New York City.

“Even after a single injection of this bacterial therapy, we see biological and, in some patients, clinically meaningful activity. This strategy is feasible, has manageable adverse effects and could be clinically meaningful in patients with few therapeutic options,” Filip Janku, MD, PhD, of the University of Texas MD Anderson Cancer, said in a press release issued by the American Association for Cancer Research, one of the groups putting on the conference.

Unlike traditional chemotherapy, which kills fast-growing cells throughout the body, immunotherapy helps the immune system fight cancer. Checkpoint inhibitors disable mechanisms that turn off T cells. Others, including CAR-T therapies, train T cells to recognize and attack specific cancer cells. Still others generate inflammatory responses that recruit immune cells to tumors.

Janku and colleagues tested whether injecting Clostridium novyi-NT spores into tumors could help control cancer growth. These anaerobic bacteria thrive in low oxygen environments with a limited blood supply—characteristic of the interior of tumors but not of normal tissue.

“By exploiting the inherent differences between healthy and cancerous tissue, C. novyi-NT represents a very precise anticancer therapeutic that can specifically attack a patient’s cancer,” Janku said.

Prior attempts to use bacteria as anticancer therapy led to infection and severe side effects, Janku explained. C. novyi wound infection can cause gas gangrene, a type of tissue death with a buildup of gas. It is related to the Clostridium difficile bacteria that often cause hospital-acquired infections. C. novyi-NT is an attenuated, or weakened, form that is missing a lethal toxin.

This first-in-humans Phase I trial enrolled 24 people with advanced solid tumors who did not respond to other treatments. Fifteen had sarcomas, seven had various types of carcinoma and two

had melanoma.

All participants in this open-label study received a single injection of C. novyi-NT into a tumor, at doses ranging from 10,000 to 3 million spores. Two people who received the highest dose developed severe sepsis or gas gangrene, leading the researchers to set 1 million spores as a maximum tolerated dose with manageable side effects. People treated with lower doses did not develop infection elsewhere in the body, although a couple did have detectable bacteria in their blood. Tumors were exposed to C. novyi-NT for a week before patients were given antibiotics to kill off the bacteria.

Looking at the injected tumor, all but one of the 22 evaluable participants (95 percent) had stable disease, meaning no further progression. About a quarter experienced tumor shrinkage greater than 10 percent. When considering both injected and uninjected tumors, 86 percent of patients had stable disease.

About half of the patients showed evidence of the bacterial spores germinating in their tumors, leading to cancer cell death, or necrosis. But some individuals had improved tumor-specific immune responses—including an increase in tumor-infiltrating lymphocytes and cytokine production—even in tumors with no bacterial growth. This suggests that C. novyi-NT can activate immune responses in addition to directly causing tumor destruction, Janku said.

Janku also noted that the usual response criteria of tumor shrinkage may not fully capture the benefit of this treatment. “When we inject the tumor, the cells within it die and become necrotic while the remaining tissue becomes inflamed, making the lesion larger in size than the original tumor,” he said, so in the short term the criteria may not accurately reflect the reduction in tumor burden.

Because C. novyi-NT elicits an innate immune response, Janku thinks this type of treatment might work well in combination with checkpoint inhibitors, which are only effective if T cells can get into a tumor. A Phase I clinical trial is now testing C. novyi-NT together with Keytruda (pembrolizumab).

“We were extremely encouraged by the results of this trial, especially in patients with advanced sarcomas, where immunotherapy hasn’t proven very efficacious,” Janku said. “This bacteriolytic strategy has the potential to be clinically meaningful, especially in combination with checkpoint inhibitors, for patients with advanced solid tumors.”

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