

# FDA-approved drug daclizumab makes established cancer vaccine work better

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A team from the Perelman School of Medicine and the Abramson Family Cancer Research Institute at the University of Pennsylvania found that the FDA-approved drug daclizumab improved the survival of breast cancer patients taking a cancer vaccine by 30 percent, compared to those patients not taking daclizumab. This proof-of-concept study is published this week in *Science Translational Medicine*. Senior authors of the study are Robert H. Vonderheide, MD, DPhil, associate professor of Medicine, and James Riley, PhD, associate professor of Microbiology.

The team proposed that daclizumab, already used for [kidney transplantation](#), would be effective in depleting [regulatory T cells](#) (Tregs) and restoring the immune system's ability to fight tumors. Tregs are an important population of [white blood cells](#) that help turn off the immune system when the system's job is done. [Cancer immunotherapy](#) has been used for the last decade, but researchers have been trying to tweak the system to get immune cells to react more robustly to destroy tumors. In time, though, the body slams on the breaks, rendering vaccines less effective.

[Tumor cells](#) exploit Tregs, drawing them to the tumor area. Tregs are essentially hijacked by the tumor, surrounding even the smallest tumors in a protective shell, preventing other tumor-fighting white blood cells from getting to tumor cells at the core.

Tregs rely on a particular protein, called IL-2, for most of their functions. Daclizumab is an antibody that binds to the CD25 receptor on

the surface of Tregs to which IL-2 binds. Tregs are deprived of IL-2 in the presence of daclizumab since it binds to the CD25 receptor instead of IL-2. But rather than causing Tregs to die, using normal lymphocytes from a [biobank](#) at Penn run by Riley, the team found the lack of IL-2 forces Tregs to convert into normal T cells that no longer surround the tumor. Once this happens, the tumor-fighting [immune cells](#) might be able to make their way into the tumor.

To bring this idea to patients, the team then designed a clinical trial, which was directed by co-author Kevin Fox, MD, professor of Medicine, and administered daclizumab to 10 patients with metastatic breast cancer prior to giving them an experimental breast cancer vaccine developed and manufactured at Penn.

"Daclizumab worked incredibly well," says Vonderheide. There were no detectible side effects, and the T-cell conversion in the patients on daclizumab lasted two months. Their tumors didn't shrink, but in six out of the 10 patients the tumors did stop growing. And, the daclizumab patients had an increased survival of about seven months compared to patients on the cancer vaccine alone.

To date, says Vonderheide, all previous attempts to eliminate Tregs have been toxic and short-lived, but the effects of daclizumab were observed to be rapid, prolonged, and consistent.

"Although we tested our approach in patients with breast cancer, we know that Tregs can block the immune response against most human cancers," says Vonderheide. "Drugs like daclizumab might be useful for most cancer patients, especially those receiving other types of immune therapy. Although Tregs do help prevent autoimmunity, we did not observe an autoimmune response because we did not convert all Tregs in the body, only those cells that seem to protect the tumor. Going after only some, but not all Tregs, we believe, was an important and unique

aspect of our study. Although there is a great deal of work to do to confirm our findings, we believe this will have major implications for [cancer vaccine](#) regimens in other types of cancer."

Although daclizumab is not currently available from its manufacturer, a second trial with a related FDA-approved drug is slated to open for enrollment at Penn this summer for patients with metastatic [breast cancer](#).

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Provided by University of Pennsylvania School of Medicine

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