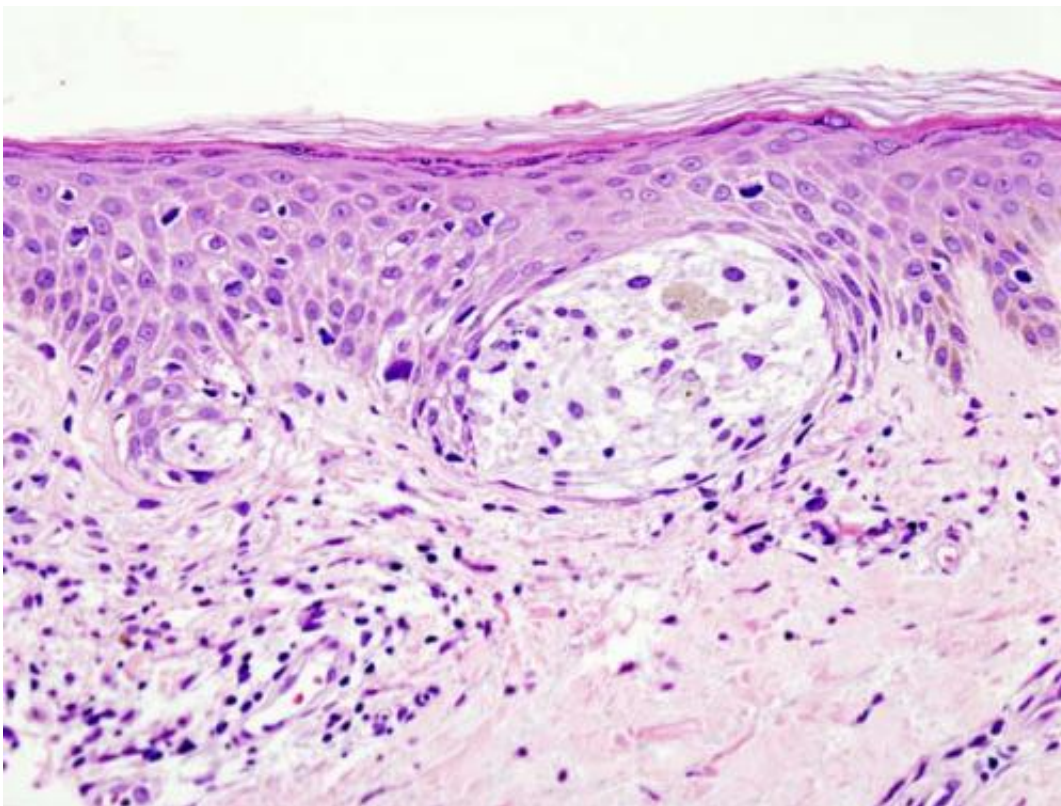


Adoptive transfer of tumor-infiltrating lymphocytes may be less effective in patients with metastatic melanoma

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Melanoma in skin biopsy with H&E stain—this case may represent superficial spreading melanoma. Credit: Wikipedia/CC BY-SA 3.0

Patients with metastatic melanoma that had relapsed on anti-PD-1 therapies or BRAF/MEK inhibitors did not respond as well to an

investigational therapy that involves the adoptive cell transfer of tumor-infiltrating lymphocytes (ACT-TIL) as patients naïve to these treatments, according to results of a study published in *Clinical Cancer Research*.

Recent treatment options for patients with [metastatic melanoma](#) include immunotherapies such as anti-PD-1/PD-L1 antibodies or molecularly targeted therapies such as inhibitors of BRAF and/or MEK, components of the MAPK pathway. Many patients eventually develop resistance to these therapies, however, and seek other options, such as ACT-TIL.

"We noticed, over the last few years, we were seeing fewer responses to ACT-TIL in metastatic melanoma patients, which coincided with these newer therapies coming on board," said Stephanie Goff, MD, an associate research physician in the Surgery Branch of the National Cancer Institute of the National Institutes of Health. "We wanted to see if there were differences in responses between those who had received prior immunotherapy or targeted therapies and those who did not."

"The data in this manuscript demonstrate that if you wait to use ACT-TIL as a later-line therapy, you may not get the same durable responses as when you use it up front," Goff said. "We should think about utilizing TILs earlier in the disease course."

Goff and colleagues studied the outcomes of 226 patients from four completed ACT-TIL [clinical trials](#), 83 percent of whom had disease that relapsed on a prior therapy. They examined differences in response based on characteristics such as age, sex, tumor size and location, and prior treatments.

While age and sex had no effect on outcome, elevated lactate dehydrogenase, a prognostic indicator for melanoma, or a larger baseline tumor were associated with poorer prognosis.

The objective response rate was 56 percent among patients who had never received anti-PD-1 therapy (but may have received other therapies), which fell to 24 percent among patients who had received prior anti-PD-1 therapy. In patients who received prior MAPK inhibitors, objective response rate was 21 percent, compared to 60 percent in MAPK inhibitor-naïve patients.

Similarly, the median progression-free survival was 6.5 months among patients who had never received anti-PD-1 therapy, which fell to 3.2 months among patients who had received prior anti-PD-1 therapy. In patients who received prior MAPK inhibitors, [median progression-free survival](#) was 2.5 months, compared to 6.6 months in MAPK inhibitor-naïve patients.

In order to perform ACT-TIL, investigators harvest lymphocytes from a tumor sample, induce them to proliferate outside of the body, and return them to the patient to help eliminate the tumor. Tumors exposed to prior treatments may pose some hurdles, including yielding fewer or less robust lymphocytes for the ACT-TIL to be effective, Goff explained.

According to Goff, these data present an argument for harvesting treatment-naïve lymphocytes before a patient tries other therapies, so that ACT-TIL is available if the patient relapses. "If we harvest the lymphocytes before they've seen any medications, we could potentially develop it into an effective later-line [therapy](#) with better response rates," she said.

Limitations of this study include the large window of time (2000-2020) in which these trials were performed, which creates a discrepancy in screening and care systems between patients treated earlier vs. later in that window. Additionally, overall and melanoma-specific survival statistics may be skewed by the treatments patients received following ACT-TIL, which the authors were unable to track in [patients](#) who

developed progressive disease.

More information: Impact of Prior Treatment on the Efficacy of Adoptive Transfer of Tumor-Infiltrating Lymphocytes in Patients with Metastatic Melanoma, *Clinical Cancer Research* (2021). [DOI: 10.1158/1078-0432.CCR-21-1171](https://doi.org/10.1158/1078-0432.CCR-21-1171)

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