

Advanced melanoma survival improves significantly when immunotherapy is given before targeted therapy

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A clinical trial led by clinicians at Georgetown Lombardi Comprehensive Cancer Center showed a remarkable 20 percent

advantage in the two-year overall survival rate for people with advanced melanoma who first received immunotherapy (72 percent survival rate) versus those who initially got targeted therapies (52 percent survival rate). Progression-free survival, where the cancer is stable or improving, was also trending in favor of those who started on immunotherapy.

The multicenter, phase III trial, DREAMseq, was led by oncology professor Michael Atkins, MD, deputy director of Georgetown Lombardi Comprehensive Cancer Center, on behalf of the ECOG-ACRIN Cancer Research Group and sponsored by the National Cancer Institute. The findings appeared September 26, 2022, in the *Journal of Clinical Oncology* and were presented preliminarily at the inaugural American Society of Clinical Oncology (ASCO) Virtual Plenary Series in November 2021.

"While still a potentially devastating disease, advances in treatment for patients with [metastatic melanoma](#) have been nothing short of remarkable this past decade," Atkins said. "In addition to DREAMseq, results from a major nationwide clinical trial (1) that enrolled patients at Georgetown Lombardi showed that if an [immunotherapy](#) called pembrolizumab was given both before and after, rather than after just surgery to remove tumor tissue, the two-year tumor-free survival rate increased from 49% to 72%. These two findings, along with other recent advances, point to significant promise for many people with [melanoma](#)."

The DREAMseq trial found that for patients with melanoma that have a mutation in the *BRAF* gene, specifically a *BRAF* V600 mutation, immunotherapy is the better initial approach than giving drugs that specifically target this mutated pathway.

Starting in 2015, 265 trial participants with metastatic melanoma were randomly assigned to two groups: one group received a targeted drug combination (dabrafenib and trametinib) followed by an immunotherapy

combination (ipilimumab and nivolumab) if their [cancer](#) resisted the first combination and the other group received the immunotherapy combination first and the targeted therapy if necessary. The trial was stopped early due to the clear evidence of benefit for giving immunotherapy first.

According to the National Cancer Institute, there will be an estimated 99,780 new cases diagnosed and 7,650 deaths due to melanoma in 2022. A steep drop in melanoma deaths from 2015 to 2019 of about 4% per year is largely attributable to advances in treatment.

"With further analysis of the data since our initial report, we not only know that patients with metastatic *BRAF*-mutant melanoma in general do better when combination immunotherapy is administered prior to combination targeted therapy, but we also have a better idea as to why. Specifically, combination immunotherapy, in contrast to targeted therapy, produces more long-lasting tumor shrinkage, reduces the risk of disease progression in the central nervous system and doesn't interfere with the subsequent effectiveness of the alternative treatment approach," said Atkins.

"NCI-designated cancer centers and consortiums like ours are valuable and essential for practice-changing research," said Andrew Pecora, MD, who led the clinical trial at John Theurer Cancer Center, a part of Georgetown Lombardi. "Our clinical trial collaborations allow more opportunities for patients across a wider geographic area to have access to these important studies and that in turn leads to advances that can make a significant difference in people's lives."

A sub-analysis of the DREAMseq findings to look at the impact of the treatments on quality of life was recently presented and further analysis of the primary finding is ongoing and will be reported in 2023. What this study does not resolve is which immunotherapy regimen is the best

initial treatment, Atkins explains. That question is continuing to be addressed in other [clinical trials](#).

The investigators are conducting cellular therapy trials that are designed to improve the immune system's ability to fight cancer and, so far, the outcomes are encouraging. Also, in a [national trial](#) led by Georgetown Lombardi's Geoffrey T. Gibney, MD, investigators are looking at biomarkers that may help clinicians decide when it is safe to stop an immunotherapy in order to prevent toxicity and lift the burden from patients of the need for frequent visits to the oncology clinic for therapy. Preliminary data look promising, and the approach is currently being validated in a large nationwide trial (2). Those results are still several years away.

More information: Combination dabrafenib and trametinib versus combination nivolumab and ipilimumab for patients with advanced BRAF-mutant melanoma: The DREAMseq Trial—ECOG-ACRIN EA6134, *Journal of Clinical Oncology* (2022).
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