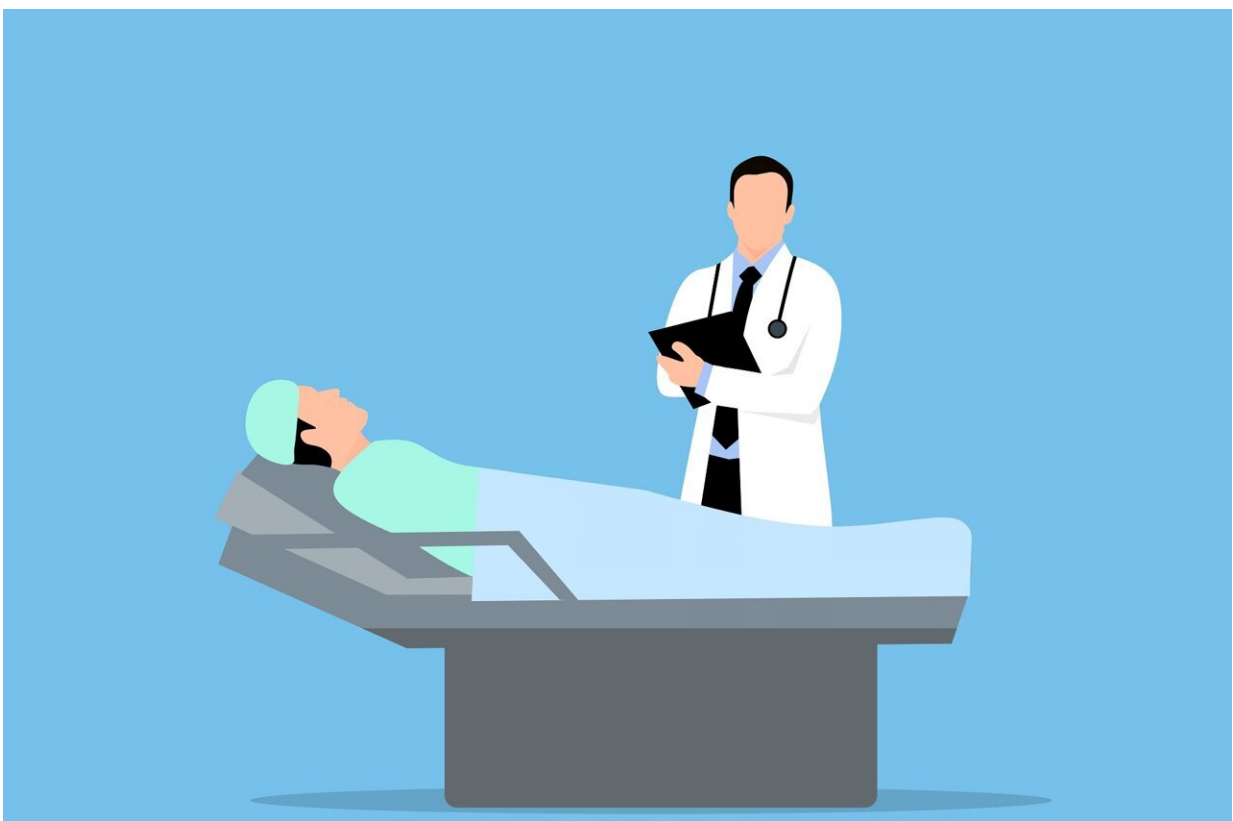


Reversing resistance to PD-1 inhibitors with combination immunotherapy in patients with advanced melanoma

April 8 2022



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Patients with advanced melanoma whose cancer does not respond to treatment with widely used immunotherapy drugs known as PD-1

inhibitors are often switched to treatment with a second type of immunotherapy drug—a CTLA-4 inhibitor such as the drug ipilimumab. New results from a clinical trial by the SWOG Cancer Research Network show that these patients are more likely to benefit from ipilimumab when it is given in combination with the PD-1 inhibitor nivolumab than when given alone.

Patients in the study who got an [ipilimumab](#) and [nivolumab](#) combination had longer progression-free survival (PFS) time than patients who were treated with ipilimumab alone (six-month PFS estimates of 34% vs 13%). The overall rate of response to treatment was also greater on the combination arm (28% vs 9%).

Analysis of patient-derived biopsies also allowed researchers to test the hypothesis that primary anti-PD-1 resistance due to a lack of pre-existing T-cell infiltrate could be overcome by adding treatment with the anti-CTLA4 antibody ipilimumab.

The results are being presented Tuesday, April 12, at the [clinical trials](#) plenary session of the 2022 annual meeting of the American Association for Cancer Research (AACR) in New Orleans.

Ari Vanderwalde, MD, MPH, a SWOG investigator with the West Cancer Center and Research Institute in Germantown, Tennessee, was study chair for the trial and will present the work at the AACR meeting.

"We have known for more than seven years that patients receiving PD-1 inhibitor monotherapy do better than patients receiving ipilimumab alone in the front line setting," Vanderwalde said. "But we still don't know what the appropriate therapy is for patients without BRAF mutations in the second-line setting. This study answers the question of whether patients who progress on PD-1 agents can continue the PD-1 agent in combination with ipilimumab, or if they should be switched to

ipilimumab altogether."

The clinical trial, known as S1616, enrolled 92 patients with advanced melanoma who had been treated with anti-PD-1 or anti-PD-L1 immunotherapy drugs and had not received an anti-CTLA-4 drug. In all cases, the patients' cancer had not responded to this therapy and had become worse or had spread, either while the patient was on this therapy or after the patient had stopped the therapy.

These patients were randomized in a 1:3 ratio to receive either

- ipilimumab alone (3 mg/kg every 3 weeks) for 12 weeks (23 patients) or
- a combination of ipilimumab (3 mg/kg every 3 weeks) and nivolumab (1 mg/kg every 3 weeks) for 12 weeks followed by monthly nivolumab (480 mg) for up to two years (69 patients).

Side effects were consistent with what has been previously described for these agents.

"More than 50% of patients don't achieve a response to PD-1 inhibitors in the front-line setting," Vanderwalde said. "These primary refractory patients have had limited evidence-based options. SWOG S1616 should establish the combination of ipilimumab and nivolumab as the standard in patients who have progressed on first-line therapy that did not contain ipilimumab."

More information: [AACR Annual Meeting 2022](#)

Provided by SWOG Cancer Research Network

Citation: Reversing resistance to PD-1 inhibitors with combination immunotherapy in patients with advanced melanoma (2022, April 8) retrieved 27 April 2024 from <https://medicalxpress.com/news/2022-04-reversing-resistance-pd-inhibitors-combination.html>

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