Immunotherapy Benefits Patients With Advanced Merkel Cell Carcinoma

‘Incredibly big change’ in treatment of deadly skin cancer, new data show

June 21, 2018 By Susan Keown

Before 2016, patients with advanced Merkel cell carcinoma — a rare and extremely deadly skin cancer — had no good treatment options to extend their lives more than a few months. Then, with two pivotal trials, everything changed.

On June 4, investigators presented new, long-term data from these trials that show immunotherapy drugs help a significant subset of patients with this cancer survive much longer than would otherwise be possible. These results crystalize preliminary results from 2016 and 2017 that were promising enough to change the standard of care for MCC and gain a drug approval from the U.S. Food and Drug Administration, the cancer’s first.

Compared with chemotherapy, the only previously available treatment, the benefit of immunotherapy drugs for these patients now “is so blatantly, strikingly obvious,” said Paul Nghiem, MD, PhD, of the University of Washington and Fred Hutchinson Cancer Research Center, pointing to the growing gap between patient outcomes on his teams’ nonrandomized trials compared to the historical results from three recent chemotherapy trials in MCC.

“This is so different from chemotherapy, and for the people who benefit, it’s an incredibly big change,” said Nghiem, who presented the updated data from the trials of pembrolizumab (Keytruda) and avelumab (Bavencio) in back-to-back talks on June 4 at the annual meeting of the American Society of Clinical Oncology, which ran from June 1 to 5 in Chicago.

MCC kills as many as half of those who develop it. Chemo works on MCC about half the time, but typically for no more than a few months. The contrast with the data Nghiem presented is striking:

In 50 patients with advanced MCC who received pembrolizumab as their first systemic therapy on one trial, 28 patients saw their tumors shrink or disappear after at least one dose of the drug, similar to the proportion of patients in historical data whose cancers respond to chemo. But patients on the immunotherapy had an 80 percent chance their MCC would not have come back at 18 months, compared to only 6 percent for patients who had initially responded to chemotherapy, Nghiem reported.

Nghiem and colleagues showed that nearly two-thirds of patients treated with pembrolizumab on the trial survived to three years. In contrast, historical data show that only about 10 percent of patients with advanced MCC who received first-line chemotherapy would survive that long.

The other trial, of avelumab, involved a group of patients with even fewer options: 88 people with metastatic MCC whose cancer started growing back after chemotherapy. More than two years after each participant's first dose of the drug, Nghiem reported, 29 patients' cancers had shrunk or disappeared, and 19 of those responses have continued. The average survival for these patients on avelumab was about a year, the team estimated.

In comparison, not a single chemotherapy-treated patient from any of three recent retrospective studies survived past one year by using additional rounds of chemo after a first round failed, and most died within just a few months.

"These findings show that what we were hoping was real two years ago has indeed come true — for the people who initially responded to immune therapy, it persisted to a far greater extent than for chemotherapy," Nghiem said about the follow-up data from both trials.

The emerging data are also showing more clearly how the effectiveness of immunotherapy drugs drops after patients receive chemotherapy, he explained: Immunotherapy benefits about 60 percent of patients who have never gotten chemo, 40 percent who received one round of chemo and just 20 percent after two or more rounds.

Immunotherapy for MCC: Major questions remain

Even though the benefit of immunotherapy drugs for patients like those on the trials is now clear, Nghiem said, significant questions remain.

The most important is how to help those whose cancers seem immune to the drugs or bounce back after an initial response. And, similarly, how to help the many patients who cannot receive the drugs at all because they have a compromised immune system or another condition that would make immunotherapies too dangerous.

"Half of people don't persistently respond — that's a huge number still. We're trying hard to address that need," Nghiem said about his and his collaborators' current research. "We do have some examples of people who turned around by using other treatments that made their cancers responsive [to immunotherapies], but for the most part, we're operating in the dark there."

Clinical trials have sprung up to test whether immunotherapies might be more effective in combination with other drugs, or at different points in the progression of the disease. For example, in the same ASCO session as Nghiem's two talks, his collaborator Suzanne Topalian, MD, of Johns Hopkins University presented the results of a trial testing whether there might be benefit to using an immunotherapy drug even earlier in the course of disease — in patients who will soon have surgery to remove a localized MCC tumor.

Nghiem and collaborators are also trying to develop methods to guide therapy by predicting, upfront, whether a patient's cancer is likely to respond long-term to an immunotherapy. Currently, they have no reliable way of knowing which patients will benefit and which won't.

Which leads to the hairy, but hopeful, question: Are any of Nghiem's patients cured?

"I would not be able to identify specific patients now who I would look in the eye and say, 'You are cured.' However, there's a population of about a quarter of our patients who've done fantastically, and I think a lot of them will not have their cancer come back and are not going to need more therapy," Nghiem said.

"To me, that sounds like a cure."

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