Adoptive T-Cell Therapy Induced Response in Metastatic Uveal Melanoma

By Leah Lawrence [3]

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More than one-third of patients with metastatic uveal melanoma had objective tumor regression when treated with adoptive transfer of autologous tumor-infiltrating lymphocytes (TILs), according to results of an unplanned interim analysis published recently in Lancet Oncology.

“We observed that a single infusion of TILs after a non-myeloablative lymphodepleting conditioning regimen could induce objective tumor regression,” wrote Smita S. Chandran, PhD, of the Center for Cancer Research at the National Cancer Institute in Bethesda, Maryland, and colleagues, “including individuals whose disease was refractory to immune checkpoint blockade.”

Unlike cutaneous melanoma, use of immune-based therapies in the rare uveal melanoma have been disappointing. Recent studies have shown that adoptive T-cell therapy led to salvage responses in a variety of refractory solid tumors. Therefore, with this study, Chandran and colleagues tested whether adoptive transfer of TILs could mediate tumor regression in uveal melanoma.

The phase II study included patients aged 16 or older with metastatic uveal melanoma. Metastasectomies were performed to obtain tumor tissue and generate the autologous TIL cultures. Patients were given lymphodepleting chemotherapy. The primary endpoint was objective tumor response.

The trial included 21 consecutive patients who received TIL therapy, of which 20 were evaluable. Of the 20 patients, seven (35%) had objective tumor regression.

“These results challenge the belief that uveal melanoma is a cancer resistant to immunotherapy,” wrote Chandran and colleagues.

One patient achieved a complete response of hepatic metastases. The additional six patients had partial responses, two of which are ongoing. Three of the responders were refractory to previous immune checkpoint blockade.

“The precise mechanism for the anti-tumor responses observed in this study is still under investigation,” the researchers wrote. “All patients received a single cycle of fludarabine and cyclophosphamide, not intended as a direct cytotoxic therapy, but rather as a lymphocyte-depleting regimen before cell transfer to enhance T-cell engraftment and efficacy. Although neither of these chemotherapies has shown activity in metastatic melanoma, we cannot completely exclude their possible role in the tumor responses.”

The most common grade 3 or worse chemotherapy-related adverse effects were lymphopenia, neutropenia, and thrombocytopenia.

In an editorial that accompanied the study, Kimberly M. Komatsubara, MD, and Richard D. Carvajal, MD, of Columbia University Medical Center in New York, wrote that “the proportion of patients achieving a response as a measure of clinical efficacy is not an established surrogate for progression-free or overall survival in uveal melanoma and must be interpreted with caution.” They added that further data will be important in interpreting the clinical effect of this therapy.

“Although promising, the results reported by Chandran and colleagues are based on 20 assessable patients and thus must be considered preliminary, requiring confirmation in a larger patient population,” they wrote. “Overall, however, these data provide important evidence that the immune system can be harnessed to treat uveal melanoma and serves to identify adoptive transfer of TILs as a high-priority avenue of further research for patients with this disease”
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Links:
[3] http://www.cancernetwork.com/authors/leah-lawrence