Total Body Irradiation Did Not Improve Response of Adoptive Cell Transfer

Adding total body irradiation to chemotherapy prior to the adoptive cell transfer of TILs had no effect on tumor regression in patients with metastatic melanoma.

Adding total body irradiation to preparative lymphodepletion chemotherapy prior to the adoptive cell transfer of tumor-infiltrating lymphocytes (TILs) had no effect on tumor regression in patients with metastatic melanoma, according to the results of a study published in the Journal of Clinical Oncology.

However, adoptive cell transfer of TILs did mediate the objective complete response of 24% of patients.

“The nonmyeloablative chemotherapy regimen thus seemed to provide sufficient lymphodepletion for successful adoptive transfer without the need to add total body irradiation,” wrote researchers led by Stephanie L. Goff, MD, of the National Cancer Institute.

According to the study, previous research had shown that adoptive cell transfer was capable of mediating a durable tumor regression in patients with metastatic melanoma. Additional data suggested that the addition of total body irradiation to the nonmyeloablating chemotherapy preparative regimen could increase complete response rate. Therefore, in this study, Goff and colleagues enrolled 101 patients with metastatic melanoma and randomly assigned them to receive nonmyeloablative chemotherapy either with or without 1,200 cGy of total body irradiation before transfer of TILs.

The complete response rate was 24% in both groups of patients. The study revealed no clinical or laboratory parameters that predicted response.

“Recently, analyses of patients who received checkpoint blockade identified neutrophil-to-lymphocyte ratio < 3 and normal lactate dehydrogenase as positive predictors of response; however, in our lymphodepleted patient population, neither separated patients who achieved responses from those who did not clearly enough to warrant use as an inclusion criterion,” the researchers wrote.

The treatment resulted in a median overall survival (OS) of longer than 3 years in both arms of the trial (median OS, 38.2 months for irradiation vs 36.6 months for nonmyeloablating chemotherapy alone; hazard ratio, 1.11 [95% CI, 0.65–1.91]). No significant difference in median progression-free survival occurred between the two treatment arms.

The researchers noted that the addition of total body irradiation did result in a new adverse event. Late-onset thrombotic microangiopathy occurred in 13 of 48 patients (27%) assigned to the irradiation arm. The median time to diagnosis was 6.4 months.

“Although seen more frequently in patients who achieved responses (12 of 31) than in those who did not achieve responses (1 of 19), the diagnosis could be biased toward patients without rapid progression of disease,” the researchers wrote. “Management consisted of antihypertensive agents and transfusion support for associated anemia.”

The researchers also acknowledged that advances in immunotherapy have provided metastatic melanoma patients with new treatment options.

“When evaluating the efficacy of either checkpoint blockade or adoptive cell transfer, one must consider the durability of clinical benefit,” they wrote. “At the time of this writing, median potential follow-up for patients treated with combination checkpoint blockade is < 2 years. Of 24 patients who achieve complete response in this study, plus the 20 patients reported previously by our group, only two have developed recurrent melanoma at 19 and 27 months with a median potential follow-up of 53.4 months.”
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