Opdivo Is Safe in Kids With Cancer, but Works Only in a Small Minority of Cases

In a small, early-stage study, the PD-1 checkpoint inhibitor was effective against only some cases of pediatric lymphoma.

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The PD-1 checkpoint inhibitor Opdivo (nivolumab) was safe and tolerable in children and adolescents who had previously been treated for cancer in a recent early-stage trial, MedPage Today reports. However, the treatment was effective against only some of the cases of lymphoma.

Opdivo is a monoclonal antibody that blocks PD-1, a checkpoint receptor on T cells that helps regulate immune function. Some tumors can hijack PD-1 to turn off immune responses. Drugs that block the interaction between PD-1 and its binding partner, known as PD-L1, can release the brakes and restore T-cell activity.

People with higher levels of PD-L1 in their tumors tend to do better on Keytruda, another PD-1 checkpoint inhibitor, although this is not a reliable predictor of individual response.

As described in The Lancet Oncology, Crystal Mackall, MD, of Stanford University School of Medicine, and colleagues conducted the Phase I/II Children's Oncology Group ADVL1412 trial of Opdivo among 85 pediatric patients with a median age of 14 years old. The study ran between 2015 and 2018.

The most common types of cancer were osteosarcoma (15%), rhabdomyosarcoma (14%), Hodgkin lymphoma (14%), non–Hodgkin lymphoma (12%), Ewing sarcoma (13%) and neuroblastoma (6%), followed by epithelioid sarcoma, unspecified sarcoma, undifferentiated sarcoma and melanoma (1% to 2% for each).

During the first phase of the study, the children received 3 milligrams of Opdivo per kilogram of body weight every two weeks. Considering that there were no dose-limiting toxicities or dose reductions at that dose, it was selected for the second phase of the study. During that phase, 7% of the participants had dose-limiting toxicities.

The children metabolized the drug at that dose similar to the way adults do when receiving the standard dose of 240 mg of Opdivo every 14 days.

Of the 20 children with lymphoma about whom there were sufficient data, four responded to treatment with Opdivo, including one child who experienced a complete response. Among the 63 children with solid tumors, none responded to the treatment.

The treatment was generally safe, however. Among the 75 children about whom there were sufficient data, the most common treatment-related toxicities were anemia (47%), fatigue (37%), decreased white blood cells (32%), decreased lymphocytes (29%) and decreased platelets (19%). Thirty-six percent of the children experienced severe or life-threatening (Grade 3 or 4) adverse health events.

Unleashing T cells with checkpoint inhibitors like Opdivo can lead to a strong immune response that also harms healthy organs. The most common immune-related adverse events were liver toxicity (AST and ALT liver enzyme increases of 29% and 24% respectively), low-grade hypothyroidism (13%) and rash (12%).

“This study defines the recommended Phase II dose and establishes a favorable safety profile for nivolumab in children and young adults, which can serve as the basis for its potential study in combinatorial regimens for childhood cancer,” the study authors concluded.

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