Immunotherapy may be efficacious in patients with HIV-associated Kaposi's sarcoma

September 7 2018

Among a small cohort of patients with HIV-associated Kaposi's sarcoma treated with immune checkpoint inhibitors, more than 65 percent had partial or complete remission.

The study is published in *Cancer Immunology Research*, a journal of the American Association for Cancer Research, by Natalie Galanina, MD, oncologist at Moores Cancer Center at UC San Diego Health.

"Despite the successful and prevalent use of antiretroviral medications to treat human immunodeficiency virus (HIV)-positive patients, about 15 percent of this population still develops Kaposi's sarcoma, which is an incurable malignancy with significant morbidity," said Galanina. "Due to a paucity of novel therapeutic options for this disease in recent decades, we wanted to investigate if immune checkpoint inhibition was effective in treating this virally mediated cancer."

The standard of care for patients with Kaposi's sarcoma is liposomal doxorubicin, a type of chemotherapy. While roughly half of patients respond to this therapy, most suffer relapses and require repeated treatments, noted Galanina. Because the standard of care is not curative, and Kaposi's sarcoma can persist in patients with an undetectable viral load, new treatments for this disease represent a clinically unmet need, she explained.

Galanina and colleagues analyzed data from nine men with Kaposi's sarcoma treated with anti-PD-1 immune checkpoint inhibitors at Moores Cancer Center between August 2013 and December 2017. All patients had received retroviral therapy and a median of one prior line of treatment for Kaposi's sarcoma. Eight patients were treated with nivolumab (Opdivo), while one patient was treated with pembrolizumab (Keytruda).

In addition to survival data, the researchers utilized next-generation sequencing data from tissue and circulating tumor DNA to analyze tumor mutational burden (TMB) and PD-L1 expression levels, biomarkers for anti-PD-1 treatment.

Following treatment with immune checkpoint inhibition, five patients had a partial response, three patients had stable disease, and one patient had complete remission. All patients remained on treatment, and no patient had shown disease progression at 6.5 months of follow-up.

PD-L1 expression was negative in all four evaluable patients. Furthermore, all three evaluable patients had low TMB (between 1-4 mutations per megabase).

"Typically, checkpoint blockade immunotherapy is more effective in patients with high TMB and/or high expression of PD-L1, yet we saw many patients who responded to treatment without these characteristics," said Galanina. "It is possible that the viral immunogenomic mutanome is sufficient to induce changes to the immune system, enabling a response to treatment with checkpoint inhibition."

While treatment with standard chemotherapy can have significant side effects, patients treated with PD-1 inhibitors experienced limited toxicity in this study, noted Galanina. "Importantly, treatment with PD-1 inhibitors did not cause myelosuppression, which is an important finding

in this patient population," she added.

Furthermore, seven patients treated with PD-1 inhibitors had an increase in both CD4+ and CD8+ T cell levels, although not statistically significant.

"Based on these results, we think that PD-1 checkpoint blockade may present a promising, novel therapeutic option for HIV-associated Kaposi's sarcoma with high efficacy and low toxicity," said Galanina.

Limitations of the study include a small sample size and the paucity of available archival tissue material to corroborate PD-L1 expression findings.

More information: *Cancer Immunology Research*, DOI: 10.1158/2326-6066.CIR-18-0121

Provided by American Association for Cancer Research