Immunotherapy Shows Promise for HIV-Related Kaposi Sarcoma

Six out of nine patients experienced cancer remission with Opdivo or Keytruda.

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Treatment with immune checkpoint inhibitors led to complete or partial tumor shrinkage in two thirds of HIV-positive people with Kaposi sarcoma, and none of the treated patients experienced disease progression, according to a recent report in Cancer Immunology Research, a journal published by the American Association for Cancer Research (AACR).

“Based on these results, we think that PD-1 checkpoint blockade may present a promising, novel therapeutic option for HIV-associated Kaposi sarcoma with high efficacy and low toxicity,” Natalie Galanina, MD, of Moores Cancer Center at the University of California San Diego said in an AACR press release.

Once frequently seen among people with AIDS, Kaposi sarcoma (KS) decreased dramatically after the advent of effective antiretroviral treatment as fewer HIV-positive people developed advanced immune suppression with very low CD4 T-cell counts. Nonetheless, KS remains the most common AIDS-defining cancer, even as rates of some non-AIDS-related cancers are rising as people with HIV live longer.

As reported at the International AIDS Conference this summer in Amsterdam, KS remains a concern, especially for African American men in the southern United States who have less access to HIV testing and care. Another study from France found that some people develop new KS or experience KS recurrence even after they start antiretroviral therapy and see a rise in their CD4 counts.

Galanina and colleagues did a retrospective review of patient records from 320 people with HIV who received immunotherapy for cancer between August 2013 and December 2017. Of these, 17 had AIDS-associated cancers, including nine men with KS.

Eight of the patients received Opdivo (nivolumab) and one received Keytruda (pembrolizumab), checkpoint inhibitors that help the immune system fight cancer. The function of cancer-killing CD8 T cells is often impaired in people with chronic HIV infection, making them potentially good candidates for immunotherapy. These drugs are currently approved for several types of cancer and are also being studied in HIV cure research.

Opdivo and Keytruda are monoclonal antibodies that block the PD-1 receptor, an immune checkpoint on T cells. PD-1 plays a role in regulating immune function, and some tumors can hijack PD-1 to turn off immune responses against them. 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 and a greater number of mutations in their tumors tend to do better on this type of treatment, but these are not reliable predictors of individual response.

At the time of treatment, all the men were on antiretroviral therapy. Most had a low or undetectable HIV viral load but a couple still had high HIV levels. CD4 counts ranged from 10 to about 600. PD-L1 levels were available for only four people and were all negative. Among the three people tested, tumor mutation burden was low.

Four of the men had only skin KS, while five had KS involving lymph nodes or internal organs including the intestines and lungs. Six had previously tried chemotherapy or other treatments. Advanced KS is usually treated with cytotoxic (cell-killing) chemotherapy such as doxorubicin, paclitaxel or bleomycin, but this usually does not lead to long-term remission and can cause side effects that people with immune suppression find difficult to tolerate.

The researchers found that five patients achieved partial remission and one had complete remission, yielding an overall response rate of 67 percent. The remaining three had ongoing stable disease. Good responses were seen in people with high HIV viral loads, low CD4 counts and KS involving internal organs. Seven of the men saw their CD4 cell counts rise during treatment and seven had increased CD8 cell counts.

All the men were still on treatment and none had experienced disease progression at the time of the data analysis. After six months of follow-up, the median progression-free survival could not be determined because all were still alive.

Treatment was generally safe and well tolerated, with no severe side effects reported. The most common adverse events were fatigue, itching and muscle or joint aches. Unlike chemotherapy, the checkpoint inhibitors did not cause bone marrow suppression and low blood cell counts. A concern with this type of treatment is immune-mediated side effects. In addition to restoring immune responses against cancer, these drugs can also take the brakes off the immune system more broadly, leading to excessive inflammation of healthy tissue. However, no immune-related adverse events were reported.

In summary, the study authors wrote, “checkpoint blockade demonstrated significant antitumor activity and low toxicity in patients with HIV-associated KS.”

“Typically, checkpoint blockade immunotherapy is more effective in patients with high tumor mutation burden or high expression of PD-L1, yet we saw many patients who responded to treatment without these characteristics,” Galanina explained. “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.”

The researchers noted that the National Cancer's Institute's AIDS Malignancy Consortium is currently evaluating Keytruda alone and a combination of Opdivo plus the CTLA-4 checkpoint inhibitor Yervoy (ipilimumab) for HIV-positive people with cancer.

Click here to read the study abstract.

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