Keytruda Shows Promise for People With Advanced Anal Cancer

Immunotherapy may prolong survival compared with standard chemotherapy.

February 6, 2020 By Liz Highleyman

The checkpoint inhibitor Keytruda (pembrolizumab) demonstrated encouraging overall survival and manageable side effects for people with inoperable or metastatic anal cancer, according to a report at the recent American Society of Clinical Oncology Genitourinary Cancers Symposium in San Francisco.

Although just 12 out of 112 participants in this Phase II clinical trial experienced complete or partial tumor shrinkage—largely driven by those who tested positive for a biomarker known to predict response to the drug—those who did had durable responses lasting up to 33 months.

Anal squamous cell carcinoma, usually caused by human papillomavirus (HPV), is uncommon, but new cases and related deaths have risen rapidly in the Unites States in recent years. About 8,600 people will be diagnosed with anal cancer and nearly 1,400 people will die from it this year, according to the American Cancer Society. Standard therapy involves surgery, radiation and chemotherapy, but outcomes are typically poor.

Aurélien Marabelle MD, PhD, of Gustave Roussy cancer center near Paris, presented results from a cohort of patients with anal cancer in KEYNOTE-158, a so-called basket study evaluating the safety and efficacy of Keytruda in people with various types of solid tumors.

Researchers previously reported promising results from a cohort of trial participants with cervical cancer, a similar malignancy also caused by HPV. These findings led to the Food and Drug Administration approval of Keytruda for advanced cervical cancer in 2018.

Keytruda is a monoclonal antibody that helps the immune system fight cancer. It 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, although this is not a reliable predictor of individual response.

The anal cancer cohort included 112 participants. Just over 80% were women, and the median age

was 61. More than 90% had metastatic cancer that had spread elsewhere in the body. About two thirds were classified as having PD-L1 positive tumors. They had previously received at least one prior medication regimen, with about 40% having tried three or more regimens; over 90% had received radiation therapy.

Participants in this nonrandomized, single-arm study received Keytruda administered by IV infusion every three weeks for up to 35 cycles or until they experienced disease progression or intolerable side effects.

Over a median follow-up period of 12 months, the overall response rate was 10.7%. Six patients (5.4%) achieved complete remission, and six (5.4%) had partial tumor shrinkage. An additional 15.2% had stable disease, but two thirds experienced cancer progression.

Results were a bit better among the 75 participants with PD-L1 positive tumors. This subgroup had an overall response rate of 14.7%, a complete response rate of 8.0%, a partial response rate of 6.7% and a stable disease rate of 14.7%. But those with PD-L1 negative cancer did worse, with only one person (3.3%) seeing a partial response.

Although the proportion of patients who responded was low, those who did so saw a durable benefit, with 90.0% still responding at the one-year and two-year marks.

The median time to disease progression was two months. At the six-month mark, 18.9% were still alive without their disease worsening (known as progression-free survival), falling to 15.0% at one year.

The median overall survival duration was 11.9 months, with 49.1% still alive after one year on treatment and 25.0% still alive after two years.

Keytruda was generally safe, although side effects were common, experienced by 60.7% of participants. The most frequent adverse events were fatigue, diarrhea, low thyroid function and nausea. Twenty people (17.9%) experienced severe (Grade 3 or 4) adverse events, and five people (4.5%) stopped treatment due to side effects. Three quarters of participants died during the study, underlining the aggressive nature of this cancer.

Unleashing T cells with checkpoint inhibitors can lead to a strong immune response that also harms healthy organs. In this study, 23.2% of participants experienced immune-mediated adverse events or infusion reactions, including five (4.5%) with severe side effects and three (2.7%) who stopped therapy for this reason. The most common immune-mediated events were underactive thyroid function (hypothyroidism), overactive thyroid function (hyperthyroidism) and lung inflammation.

Based on these findings, the researchers concluded that Keytruda demonstrated antitumor activity, durable response and encouraging overall survival with manageable safety in heavily pretreated patients with advanced anal cancer.

Click here to read the study abstract.
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