FDA Approves First Immunotherapy for Anal Cancer

Zynyz, a PD-1 checkpoint inhibitor, extended progression-free survival and may improve overall survival.

June 12, 2025 By Liz Highleyman

On May 15, the Food and Drug Administration (FDA) approved Zynyz (retifanlimab) immunotherapy for people with advanced anal cancer based on promising results from a late-stage clinical trial. This makes it the first-ever approved first-line treatment for this population, including people living with HIV.

“Patients with inoperable locally recurrent or metastatic anal cancer have historically faced poor five-year survival rates and limited treatment options,” Marwan Fakih, MD, of City of Hope cancer center, said in a news release. “This approval marks an important advancement as it makes a new treatment approach available for this challenging cancer.”

Specifically, the FDA approved Zynyz in combination with platinum-based chemotherapy (carboplatin and paclitaxel) for initial treatment of adults with inoperable locally recurrent or metastatic squamous cell carcinoma of the anal canal and as a single agent for those who experience disease progression or cannot tolerate the chemo regimen.

Anal cancer, like cervical cancer, is usually caused by human papillomavirus (HPV), a common sexually transmitted infection. The virus triggers abnormal cell growth that can progress to precancerous lesions and invasive cancer. (It is distinct from rectal cancer, which is related to colon cancer.) Anal cancer is rare overall. Gay and bisexual men and people living with HIV are at greater risk, but a recent study found that this malignancy is rising most among older women. The HPV vaccine lowers the risk of acquiring the cancer-causing virus. Anal cancer screening is not recommended for the general population and is underutilized among groups at higher risk.

Zynyz, from Incyte, is a monoclonal antibody that targets PD-1, an immune checkpoint protein on T cells. Some tumors can hijack PD-1 to turn off immune responses, and checkpoint inhibitors can release the brakes and restore T-cell activity. The FDA granted accelerated approval of Zynyz for advanced Merkel cell carcinoma in 2023. None of the previously approved checkpoint inhibitors—such as Keytruda (pembrolizumab) and Opdivo (nivolumab)—are specifically indicated for anal cancer, though some can be used to treat solid tumors with specific genetic characteristics regardless of location.

The new approval is supported by results from the Phase III POD1UM-303 trial (NCT04472429), which enrolled previously untreated people with inoperable or metastatic anal cancer, and the Phase II POD1UM-202 study (NCT03597295), which enrolled patients who experienced disease progression after platinum-based chemotherapy. The FDA previously declined approval of Zynyz based on POD1UM-202 data in 2021, saying it wanted to see the results from POD1UM-303.

[Update June 12, 2025: The POD1UM-303 findings were published in the June 14, 2025 issue of The Lancet.]

POD1UM-303 enrolled 308 participants. About 70% were women, most were white and the median age was 62 years. Unlike many cancer trials, people with well-controlled HIV were eligible (4% of the study population). They were randomly assigned to receive IV infusions of Zynyz or a placebo, both in combination with carboplatin and paclitaxel, every four weeks for six cycles, followed by Zynyz or the placebo alone for up to a year. Those who experienced disease progression in the placebo group could cross over to Zynyz, and 45% did so.

Results presented at the 2024 European Society for Medical Oncology Congress last fall showed that progression-free survival time was 9.3 months for people in the Zynyz group versus 7.4 months for those in the placebo group, reflecting a 37% reduction in the risk of disease progression or death. The overall response rates (tumor regression) were 56% and 44%, respectively, and the median duration of response was about twice as long with Zynyz (14.0 versus 7.2 months). Overall survival data are not yet mature but so far appear to favor Zynyz by about six months (29.2 versus 23.0 months). HIV-positive participants maintained viral suppression and did not experience additional or worse side effects.

POD1UM-202 enrolled 94 people. They received Zynyz infusions every four weeks for up to two years or until they experienced disease progression or unacceptable toxicity. Results showed that the overall response rate was 14% and the median duration of response was 9.5 months. Median progression-free survival and overall survival times were 2.3 months and 10.1 months, respectively.

The most common adverse reactions for people treated with Zynyz plus chemotherapy include fatigue, peripheral neuropathy, nausea, diarrhea, decreased appetite, hair loss, muscle and joint pain, bleeding, rash and itching. Adverse reactions are generally similar but less common when Zynyz is used alone. Checkpoint inhibitors that restore immune responses against cancer can also cause immune-mediated inflammation affecting any organ.

“Patients with anal cancer often face a troubling lack of public awareness and understanding when it comes to risk factors, symptoms and their overall cancer journey,” said David Winterflood, CEO of the Anal Cancer Foundation. “The approval of Zynyz marks a step forward for advanced [anal cancer] treatment, brings attention to a long-overlooked condition with limited treatment options and offers patients whose anal cancer has returned or spread an option to treat their disease.”

Click here for full prescribing information for Zynyz.

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