An FDA-backed metric used to determine effectiveness of rectal cancer drugs may be unreliable, says new study

July 18, 2025 9:36 AM Andrew Yawn
ayawn@tulane.edu
(504) 247-1443

The absence of detectable tumors after treatment — a key metric in clinical cancer drug trials known as pathologic complete response or pCR — does not reliably predict an improvement in long-term survival for patients diagnosed with rectal cancer, a new study found. (Photo by iStock)

A new study by a Tulane University researcher casts doubt on a widely used shortcut in rectal cancer drug trials, raising concerns that some treatments may be fast-tracked for approval without evidence they help patients live longer.

The study, published in JAMA Network Open in collaboration with researchers at Mayo Clinic in Arizona, found that the absence of detectable tumors after treatment — a key metric in clinical cancer drug trials known as pathologic complete response or pCR — does not reliably predict an improvement in long-term survival for patients diagnosed with rectal cancer.

Traditionally, the success of treatments for these patients was determined by measuring “overall survival,” or the years between a person’s diagnosis and death. Since 2012, the U.S. Food and Drug Administration has allowed pharmaceutical companies to use tumor-free status post-therapy as a surrogate for overall survival to cut down on time and expenses needed to approve new cancer treatments.

The researchers conducted a meta-analysis of 25 clinical trials involving nearly 12,000 rectal cancer patients. They found no statistical relationship between pCR and overall survival, meaning cancer drugs may be moving toward development without showing meaningful long-term improvements over existing treatments, said first author Kavin Sugumar, chief resident of general surgery at Tulane University School of Medicine.

“This is about patient outcomes, but it’s also about how we evaluate whether a new drug works,” Sugumar said. “The FDA has approved pCR as a substitute for a result that would normally take years to determine, but we found that pCR should not be used as a sole endpoint to determine if a cancer treatment has been effective.”

PCR remains vital for effectively determining if cancer has been cleared locally from tissue, and patients whose tumors disappear often fare better than those who don’t.

Still, the metric may fail to capture the full picture, such as whether the patient has lingering toxicity from chemotherapy or undetected cancer cells elsewhere in the body.

The use of pCR as a gold standard for drug approval may also increase costs for drug companies, which may invest in approved therapies that cannot guarantee improved survival rates.

“Overall survival is a costly and time-consuming endpoint to determine, and I don’t think we’ve found the ideal surrogate yet,” Sugumar said. “Instead of relying solely on pCR, we should maybe include a combination of surrogate endpoints that also includes pCR.”

“The FDA has approved pCR as a substitute for a result that would normally take years to determine, but we found that pCR should not be used as a sole endpoint to determine if a cancer treatment has been effective.”
Kavin Sugumar