

Immunotherapy Study Offers Hope for Pancreatic Cancer Patients

In a research letter to the journal *JAMA Oncology*, clinical researchers at Sylvester Comprehensive Cancer Center in the University of Miami Miller School of Medicine showed that immunotherapy can be an option for at least one subgroup of pancreatic cancer patients. The study found that patients with inherited BRCA and other similar mutations can achieve complete responses – in some cases going from near death to durable recoveries.



Peter Hosein, M.D.

“This is a highly selected subpopulation of patients with pancreatic cancer who carry specific mutations, most commonly in their BRCA gene,” said Peter Hosein, M.D., co-leader of Sylvester’s Gastrointestinal Cancers Site Disease Group, associate professor of clinical medicine in the Division of Hematology/Oncology and senior author of the study. “Their

cancers respond to immunotherapy when most pancreatic tumors do not.”

Tumors often evade immune system surveillance by sending false signals, essentially telling immune cells they are normal tissue and not cancer. Some immunotherapies thwart this mechanism by blocking these signals and unleashing the immune response. While this approach has been effective in several cancers, it has failed often in pancreatic cancer.

However, in 2017, a single patient with relapsed pancreatic cancer was successfully treated in a large clinical trial called ASCO TAPUR. The patient was selected because of their inherited BRCA mutation, which led to a relatively high tumor mutational burden and other changes that made immunotherapies effective.

“BRCA and RAD51C mutations make tumors genetically unstable, creating abnormal proteins called neoantigens that sensitize the immune system,” said Dr. Hosein. “Pancreas cancer is usually immunologically cold – it doesn’t generate an immune response. But these mutations, which appear in about 5% of pancreatic cancers, make the tumors immunologically lukewarm and more likely to respond to immunotherapies.”

Seeing this success, Dr. Hosein and colleagues embarked on their own small study of 12 patients with BRCA, RAD51C and similar mutations. The drugs were on the market but had not been approved to treat pancreatic cancer, so the researchers had to use them off-label.

All the patients in the study had been treated with chemotherapy and other drugs but had developed resistance.

After receiving two different immunotherapies (ipilimumab and nivolumab), four patients had complete responses, one had a partial response, and two had stable disease – an incredible success rate for patients with advanced, treatment-resistant pancreatic cancer.



From left, Peter Hosein, M.D., and Luis Rios

Luis Rios is one of the patients with a complete response. He was diagnosed with pancreatic cancer in July 2017. For two years, his disease was controlled through chemotherapy and other drugs. But by summer 2019, his cancer had become resistant to all treatments, a common occurrence in pancreatic and other tumors.

“We put him back on chemotherapy and he didn't respond at all,” said Dr. Hosein. “We tried three different types of very intensive chemotherapies, but his cancer was completely resistant.”

Rios was lethargic, losing weight and was taking two powerful opioids to control his pain. But because his tumor had a rare

RAD51C mutation, Dr. Hosein thought he might benefit from immunotherapy.



Luis Rios and his wife, Maria Brolley

This good news came with a caveat: Because the treatments were being delivered off-label, insurance would not cover them. Rios paid for his first infusion out of pocket, but it was a good investment. Within two weeks, he was completely off his pain medications and his tumor marker levels had plummeted.

“It was dramatic,” said Rios. “Dr. Hosein’s colleagues came from all over to look at the blood tests and scans because the improvement after just one session was incredible. I started to feel great again.”

After two years of treatment, Rios had no detectable disease. He has now been off treatment for 10 months, with no evidence of cancer recurrence.

“This is a real breakthrough,” said Dr. Hosein. “Quite honestly, once the cancer develops resistance, these patients die quickly. Pancreatic is one of the deadliest cancers – the five-year survival rate is only around 10%. This encouraging research means we can continue to improve those results for our patients.”

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