Medical Xpress

# Study results offer new hope for advanced lung cancer patients being treated with immunotherapy

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Patients with advanced lung cancer had a better chance at survival when their treatment combined chemotherapy with a drug designed to turn the immune system against cancer, according to two studies released Sunday at a conference in Paris, France.

In both trials, 20% of participants who took chemotherapy plus the drug Keytruda, from Merck, survived for at least five years after their diagnosis. That's twice as long as is typical for advanced lung cancer patients.

Seventy percent of patients who were able to complete two years of treatment with the drug and chemo were still alive a year later.

While both Keytruda (pembrolizumab) and a similar drug, Opdivo (nivolumab), from Bristol Myers Squibb, were approved to treat lung cancer in 2015 , the new studies for the first time quantify the duration and magnitude of their benefits when combined with chemotherapy.

Lung cancer doctors are quick to point out that these studies also show the drugs' limitations. For every patient who gets spectacular results, there are four more who die within a few years of their diagnosis.

Still, for a disease that used to be a certain death sentence, the results from immunotherapy drugs are remarkable.

"It's wonderful to see," said Dr. Pasi Jänne, a lung cancer specialist at the Dana-Farber Cancer Institute in Boston, who was not involved in the new research. In lung cancer, "we didn't have the long-term survivors like you see in breast cancer and other cancers. Now we do."

Lung cancer is the leading cause of cancer death, with more than 230,000 Americans diagnosed in 2020 and 130,000 killed by the disease. The five-year survival rate for metastatic lung cancer has been 7%.

Dr. Jacob Sands, a volunteer medical spokesperson for the American Lung Association, compared the standard treatment with chemotherapy to hitting a single or a double in baseball. It gets patients in the right direction. But immunotherapy is a potential home run for some patients, Sands said.

"The fact that there's even a question as to whether or not there are individuals who will never need another treatment again, that's incredible. That had been a dream 10 years, 5 years ago," he said. "The fact that we're seeing that is really extraordinary. Very exciting."

## A second opinion leads to immunotherapy—and another shot at life

Larry Whipple, 77, was shocked five years ago when his biopsy came back with a diagnosis of metastatic lung cancer.

Both his primary care doctor and lung cancer specialist had told him there was no chance the spot they'd noticed on his lung scan was dangerous.

Then his oncologist said he wasn't a good candidate for immunotherapy—treatment that aims to harness the power of the body's

immune system to kill cancer cells.

Whipple, a New Jersey native, was unconvinced and managed to get another opinion at MD Anderson Cancer Center in Houston. It likely saved his life.

For several months Whipple, who now lives in Cary, North Carolina, was treated with chemotherapy along with Keytruda. The chemo was a drag, he said, because he had to sit still for 2 to 5 hours during his infusions. Whipple, a former lawyer who now trades stocks, does not like to sit still.

But he didn't even notice the immunotherapy, which was added to his infusions. Neither gave him any noticeable side effects.

The 40 radiation treatments he was given to make sure the cancer didn't return were far more difficult. His esophagus was scarred, forcing him to eat in small bites.

He lost 60 pounds. "Not a good way to lose weight," Whipple noted, and has put 40 back "to my regret."

But by August 2018, just under a year after he was diagnosed, he was given the all-clear. His semi-annual scans have been cancer-free ever since and he hasn't needed any more therapy.

## More treatment options are helping patients

When Dr. Marina Garassino started her career 25 years ago, she had little to offer except harsh chemotherapy. Some patients chose to die rather than take it and even those who got treated rarely survived much more than a year.

Now, she said, her lung cancer patients don't even lose their hair on chemotherapy. "It's quite well tolerated," she said.

Combining it with Keytruda doesn't compound immune side effects, said Garassino, who led one of the recent trials, though some patients suffer auto-immune reactions that can often be effectively treated.

In her study, 70% of the patients who were able to complete 2 years on the chemo-immunotherapy combination were still alive at five years.

They get infusions every three weeks for those two years, but most can work during treatment.

"The quality of life of these patients is quite high," Garassino said. A shrinking tumor often corresponds with a better quality of life, she said, as breathing eases and weight loss stops.

Unfortunately, immunotherapy success stories like Whipple's remain the minority. Doctors don't yet understand why or what they can do to expand the benefits.

Jänne, who directs Dana-Farber's Lowe Center for Thoracic Oncology, said he'd like to be able to identify ahead of time who will benefit and who won't. "We have some ideas, but they're imperfect," he said.

Better identifying who will benefit could spare patients the false hope that stories like Whipple's can offer. But sometimes, people who don't look like they're responding to immunotherapy on their first scans will have a great response later. "It's hard to predict," Jänne said.

## Immunotherapy can boost success of chemo in some patients

About 80% of patients aren't diagnosed until after their cancer has spread beyond the lung.

Smokers with lung cancer actually fare better on immunotherapy than non-smokers, Jänne said, likely because tobacco causes lots of mutations in the cancer, making the tumors easier for the immune system to recognize.

Sometimes, smokers can just be given immunotherapy without chemotherapy, said Dr. Eric Rubin, senior vice president of clinical oncology for Merck.

But non-smokers and people with low levels of PD-1, the immune marker targeted by Keytruda and Opdivo, are generally treated with both chemo and immunotherapy. (Whipple quit smoking 40 years ago.)

Doctors used to worry that combining the two approaches "would somehow poison the immune system. That's been proven wrong," Rubin said.

Instead, studies have shown that killing cancer cells with chemotherapy can help the immune system recognize tumor cells as "foreign," while the immunotherapy releases a brake that has held back an immune response.

Now, Garassino said, researchers are looking to add to this combination to hopefully help more patients. Unfortunately, targeted therapies, designed to go after mutations in certain tumors, appear to be toxic when combined with immunotherapy "for reasons that are totally unknown or only partially understood," she said.

It remains unclear how long the benefits of immunotherapy will last or whether the word "cure" can ever be used. But "If the disease hasn't

come back in 5 years that's a pretty good sign that it may not," Rubin said.

Whipple credits immunotherapy, his positive attitude and his caregivers for his great results.

"I'm still trying to figure out why I survived cancer," he said, "God bless the professionals. They were right in terms of what they wanted me to do."

Whipple took a 5,000-mile road trip this summer, checking Mount Rushmore off his bucket list. He tries to make the most of the extra time he feels he's been given, spoiling his six "phenomenal" grandchildren, contributing to charities and trying to make a positive difference in the world.

"Spending every day trying to do something decent. That's been one of my themes," he said. "People tell me I've been successful. I'll leave that for others to decide."

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