Can AI Help Predict Which Cancer Patients Should Be Treated with Immunotherapy?

An AI-based tool that uses information from a cancer patient's blood tests and medical records may predict whether immune checkpoint inhibitors will help the patient live longer.

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A class of immunotherapy drugs called immune checkpoint inhibitors have proven transformative for people with some types of cancer. In a small number of patients with advanced forms of melanoma, lung cancer, and other tumor types, deposits of cancer scattered throughout their bodies simply melt away. In notable but rare cases, the cancer never comes back.

However, in most patients immune checkpoint inhibitors don't have any effect on the cancer or, if they do, the cancer returns. So, because these drugs can have serious and sometimes deadly side effects, as well as a high price tag, researchers have been racing to find ways to identify the patients who are most likely to benefit from these treatments.

In a new study, researchers tested an artificial intelligence–based tool that may be able to meet this need. The tool, called SCORPIO, was more accurate than Food and Drug Administration–approved tests in predicting whether patients' tumors would shrink following treatment with immune checkpoint inhibitors and how long they were likely to live after the treatment, according to findings published January 6 in Nature Medicine.

According to the study's lead investigator, Diego Chowell, Ph.D., of the Icahn School of Medicine at Mount Sinai, what's particularly noteworthy about SCORPIO is that it's "constructed using information pulled only from routine blood tests and patients' medical records."

It's becoming increasingly important to develop these sorts of predictive tools, said Eytan Ruppin, M.D., Ph.D., of NCI's Center for Cancer Research.

"In many patients, you can consider a few different types of drugs," explained Dr. Ruppin, who has developed similar models but was not involved with the current study. "So, we'd like to know which one a patient's cancer is most likely to respond to, to help us carefully weigh the benefits versus the risks and side effects."

Dr. Chowell said that his team is conducting additional studies on SCORPIO and moving ahead with

efforts to make the tool available for use beyond research settings.

Improving predictive power

Two tests are currently approved by the Food and Drug Administration for predicting whether a person's cancer is likely to respond to treatment with an immune checkpoint inhibitor.

One test measures the amount of a protein called PD-L1 found in tumor samples. The other uses gene sequencing to tabulate the number of mutations in a tumor to produce a score called tumor mutational burden, or TMB. (Mutated proteins are more likely to be targeted by the immune system.)

People with higher scores on one of these two tests are often more likely than those with lower scores to have their tumors shrink following immune checkpoint inhibitor treatment, Dr. Ruppin said.

But the tests are far from perfect. Some people with low scores can end up having an impressive response to treatment, Dr. Ruppin noted. And some people with high scores may not benefit from immune checkpoint inhibitors. This makes PD-L1 and TMB less-than-ideal biomarkers.

In 2024, Dr. Ruppin's lab at NCI, in collaboration with Dr. Chowell's team and other researchers, reported the results of a study using a prediction model similar to SCORPIO that they had developed, called LORIS. Although LORIS uses information commonly captured from standard blood tests, LORIS also includes several other pieces of information, including TMB and history of previous treatments.

The LORIS model was based on a smaller number of patients than the SCORPIO model, Dr. Ruppin said. It also predicted tumor response to an immune checkpoint inhibitor "and was helpful even in patients with low TMB," he added.

However, TMB tests are expensive and, despite being approved by the FDA as "companion diagnostics" to be used together with immune checkpoint inhibitors, they often aren't covered by insurance, Dr. Chowell explained. In their new study, he and his colleagues took things a step further and removed TMB from the prediction equation entirely.

Building SCORPIO from the basics

To build and test SCORPIO, Dr. Chowell and his colleagues used data from nearly 10,000 people who had been treated with one or a combination of immune checkpoint inhibitors at Mount Sinai and Memorial Sloan Kettering Cancer Center in New York.

A total of 21 cancer types were included in SCORPIO's development. The most common types were melanoma and cancers of the bladder, liver, lung, and kidney.

The researchers initially built SCORPIO using data from about 2,000 patients treated at Memorial Sloan Kettering Cancer Center. They found that simple clinical factors such as age, sex, body mass index, and measurements from standard blood "panels" were key factors that could predict survival and tumor response after immune checkpoint inhibitor treatment.

The team then tested the new model's performance using several validation sets of data collected from patients in two other large real-world cohorts and participants in 10 clinical trials who had been treated with immune checkpoint inhibitors. SCORPIO accurately predicted survival, with performance ranging from 72% to 76% in different patient groups over the next two and a half years.

"That's a remarkable performance, just using routine blood tests and basic [patient] data," said Dr. Chowell. The model could also distinguish between people who were more or less likely to benefit from treatment with an immune checkpoint inhibitor. This included a broad range of responses, from tumors that grew to those that remained stable (i.e., neither shrinking nor growing) and those that were completely eliminated.

SCORPIO was much better than TMB at predicting which patients would live longer after treatment.

"And [SCORPIO] performed better in the real-world cohorts than in the clinical trial cohorts," Dr. Chowell explained. This finding, he said, shows that incorporating data from a wide variety of treatment scenarios and a diverse variety of people with different health profiles made the tool more accurate than if it had been built from clinical trial data alone.

What's next for SCORPIO?

Dr. Chowell's team will next be working with hospitals and clinics to test how well SCORPIO performs in cancer patients who haven't yet received an immune checkpoint inhibitor (although the score will not be used to determine whether they should get one).

The team is also building a cloud-based platform for the tool that will be publicly accessible. LORIS is publicly available on NCI's website.

Researchers working on models to predict the response to various treatments are also looking for other information that can be added to further increase the predictive power of these models, Dr. Ruppin explained.

"It's possible that we're reaching a plateau [of what we can predict using data from routine blood tests], because tumors are complicated. But that merits further exploration and only time will tell."

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