What Are Targeted Cancer Therapies?

Urs Weber, MD, walks us through a family of focused treatments that can block or slow cancer's growth.

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Over the last few decades, targeted therapies have grown in importance as powerful weapons in the cancer-fighting arsenal.

Targeted therapies are more precise than many other cancer treatments, focusing on proteins that control how cancer cells grow and spread. Unlike traditional chemotherapy, which can damage healthy cells as it attacks cancer cells, targeted therapies go after cancer cells and mostly leaves normal cells alone.

To learn more about targeted therapies and how they're used against cancer, we turned to Urs Weber, MD, a University of Colorado Anschutz Cancer Center member who specializes in treating lung cancerand finding new therapies. Weber is an assistant professor of medicine in the CU Anschutz Division of Medical Oncology.

What is targeted therapy?

It exploits specific vulnerabilities in a cancer. For example, in lung cancer, we see a lot of what we call driver mutations at the DNA level – the on-switch that can make a cell behave like a cancer cell, growing, dividing uncontrollably, and spreading. The most common driver mutations in lung cancer are in the EGFR and ALK genes, but there are many others. Targeted therapies are designed to go after these driver mutations and turn them back off.

What cancers are targeted therapies used for?

At this point, they have a role in managing most if not all types of cancer. In lung cancer, we probably used them more than in any other type of cancer. And there's a lot of targeted therapy use in the blood cancers – leukemia and lymphoma – as well as breast

cancer, colorectal, melanoma, prostate, and many others.

How are targeted therapies different from other treatments?

Generally speaking, targeted therapies tend to be better tolerated than other types of cancer treatment because they are designed to go after something that only exists in the cancer itself, not other parts of your body.

Chemotherapies will do the exact same thing in every single cell in your body, which is why you have a lot of side effects. Immune therapy activates the immune system, making it more active everywhere, which is why you see autoimmune-type toxicities, where the immune system is damaging healthy parts of your body.

As with any medication, there will still be some side effects. But most patients on targeted therapies will not experience the sort of side effects that impact their day-to-day life. And they may not even look like they have cancer, which for many people is important.

Are there different kinds of targeted therapy?

There are lots of different kinds. There are small-molecule inhibitors, which tend to be pills a patient can take orally and block a specific protein in a cancer cell. For example, in EGFR-mutated lung cancer, we have pills that contain a compound that's specifically designed to block that mutated EGFR protein. This is probably the most common type of targeted therapy.

We also have antibody drug conjugates (ADCs), which are administered intravenously. These are treatments with an antibody that is designed to stick to a particular target in the body, and the antibody is connected to a chemotherapy payload. There's still chemotherapy involved, but the chemotherapy is not floating around freely in your body, going everywhere. It's attached to this antibody that delivers that chemotherapy to a specific target. A good example of a target is HER2, for which we have an ADC approved in breast and lung cancer.

We also have other antibody-based treatments that don't involve chemotherapy at all. These antibodies bind to one or more receptors on the surface of cancer cells and thereby inhibit signals that would otherwise be pushing the cancer cell to grow and make more cancer cells.

Given that there are many kinds of cancer that respond differently to treatment, what are the

likely outcomes of treating cancer with targeted therapies?

Generally speaking, targeted therapies – especially small-molecule inhibitors that tend to taken orally – are best thought of as good, long-term disease-control drugs. We're not curing a lot of people with these drugs, but we are effectively blocking their cancer from growing over long periods of time.

To use another example from lung cancer, for ALK-positive non-small cell lung cancer, our preferred first-line treatment is called lorlatinib, which is a small-molecule inhibitor of ALK. In a pivotal clinical trial for this treatment called the CROWN study, they put patients with ALK-positive stage 4 incurable lung cancer on lorlatinib, and it's been seven years of follow-up on this study and the median progression-free survival has not been reached. That means more than half of the patients on this drug in the study are still taking the drug after seven years and their cancer has not grown.

When the CROWN study team presented their five-year update, they got a standing ovation, because the results were so remarkable for a disease that used to have a life expectancy of maybe a year or a year and a half, and they had people going five-plus years on their first treatment with no disease progression. They were able to take a pill every day and have a fairly normal life.

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