Unleashing the Immune System to Fight Lung Cancer

Scientists are trained to be skeptical, especially when research results seem too good to be true. Even if the results are confirmed, and confirmed again, scientists often call them preliminary and keep a lid on their enthusiasm.

But cautious dispassion is hard to maintain when it comes to the findings on nivolumab, a new immunotherapy drug against lung cancer that has been in clinical trials for several years at Yale and elsewhere.

“There are two great things about this therapy,” said Scott Gettinger, MD, Associate Professor of Medicine (Medical Oncology), and the principal investigator for many clinical trials of nivolumab at Yale/Smilow. “First, unlike with chemotherapy, most patients have little or no side effects.”

“Second,” he continued, “responses tend to be durable, and unlike chemotherapy, do not appear to be less frequent in patients who have received a number of prior chemotherapies. Truly remarkable are the ongoing responses in some of our chemotherapy refractory patients started four to five years ago, patients who had a diagnosis at that time of only a few months.”

The results of the trials were so impressive that in March nivolumab became the first immunotherapy drug approved by the FDA for lung cancer. (The drug’s maker, Bristol-Myers Squibb, markets it under the trade name Opdivo.) At the moment, nivolumab is approved only for patients who have metastatic squamous non-small cell lung cancer that progressed after chemotherapy. That sounds narrow, but according to Dr. Gettinger, much wider applications are sure to follow.

Unlike chemotherapy and other targeted treatments, nivolumab fights cancer by harnessing the body’s immune system. Normally, the immune system detects invaders such as viruses or cancer, and attacks them. But lung cancer, like other cancers, has evolved ways to disguise itself and trick the immune system into passivity as cells mutate. Immuno-drugs strip off cancer’s disguise, revealing it to the immune system, which then attacks.

In lung cancer and several others, the disease blocks attack by the immune system with the use of a brake called Programmed Death Ligand 1 (PD-L1), which is generated by the tumor and effectively immobilizes the immune cells that recognize the tumor and are primed to attack. Nivolumab releases this brake, awakening these stunned immune cells that can now do what they are meant to: attack cancer.

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