FDA is investigating whether CAR-T, a cancer therapy pioneered at Penn, can cause lymphoma

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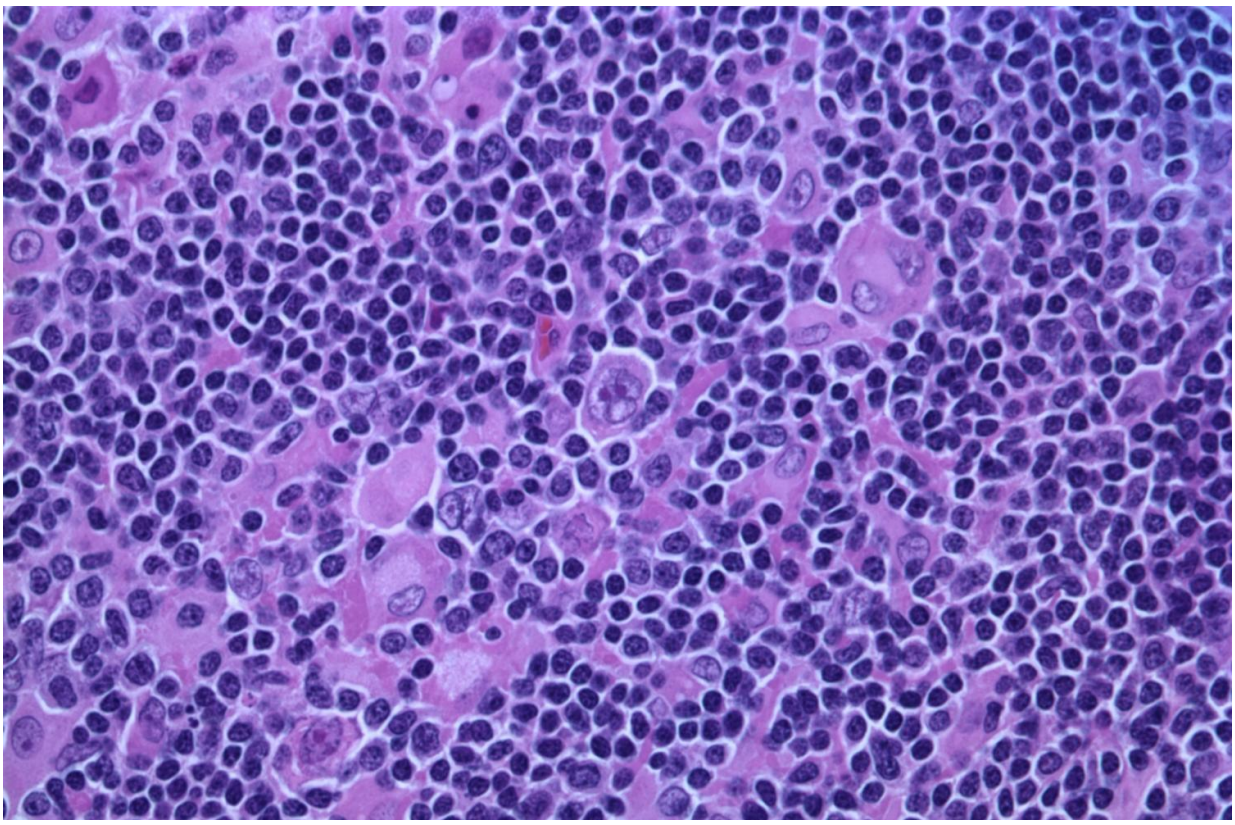

Hodgkin lymphoma, nodular lymphocyte predominant (high-power view) Credit: Gabriel Caponetti, MD./Wikipedia/CC BY-SA 3.0

The University of Pennsylvania plans to continue offering CAR-T

therapy, a cancer treatment pioneered at Penn, after the Food and Drug Administration announced an investigation into whether the treatment may cause cancer in rare cases.

Chimeric antigen receptor T cell, CAR-T, therapy has been hailed as a breakthrough treatment, and possibly a cure, for some types of blood cancer. It involves removing the body's T cells—the white blood cells with a leading role in the body's immune response—and genetically modifying them to target the cancer cells. More than 20,000 patients worldwide, including several hundred in Philadelphia, have been treated with versions of the genetic engineering technique.

The FDA said it would investigate six commercial CAR-T therapies for lymphoma and leukemia after receiving reports of patients who developed T-cell cancers after treatment. The therapies under review are made by Bristol-Myers Squibb, Johnson & Johnson, Novartis, and Gilead.

"Although the overall benefits of these products continue to outweigh their potential risks for their approved uses, FDA is investigating the identified risk of T cell malignancy with serious outcomes, including hospitalization and death, and is evaluating the need for regulatory action," the agency said Tuesday.

David Porter, the director of cell therapy and transplantation at Penn's Abramson Cancer Center, praised the FDA investigation as part of the agency's ongoing efforts to evaluate and improve on a new, lifesaving treatment. He said Penn would be following the review closely.

In the meantime, Penn will continue offering CAR-T therapy, he said.

"For the vast majority of patients, the benefits outweigh what appears to be a very small risk," Porter said.

Penn has not seen any instances of patients developing cancer after treatment, he said.

What is CAR-T?

Penn cancer scientist Carl June was among the first researchers to discover a way to arm the body's own immune system against cancer. His team treated their first adult leukemia patients with CAR-T in 2010. Their first pediatric patient, Emily Whitehead, was cured of a deadly form of leukemia at the Children's Hospital of Philadelphia and is now a freshman at University of Pennsylvania.

In September, June and Michel Sadelain, who developed a similar approach at Memorial Sloan Kettering Cancer Center in New York, were awarded a $3 million Breakthrough Prize for their discovery.

CHOP has treated more than 500 pediatric patients with CAR-T, and Penn has treated hundreds more adults, Porter said.

Penn manufactures hundreds of its own CAR-T therapies for clinical trials, while other patients may receive commercially available infusions.

Why is the FDA investigating CAR-T?

The FDA said it had received reports of patients treated with CAR-T developing T cell malignancies—cancer in the type of white blood cells that are genetically modified during CAR-T treatment. But with few details about the cases, experts were unsure what to make of the FDA's announcement.

"We've been talking about it all day," Porter said.

The concern, Porter said, is whether the genetic material used to turn T cells into cancer-fighting CAR-T cells could inadvertently turn those genetically modified cells into cancer.

It's unclear whether CAR-T caused the T-cell cancers in the handful of cases the FDA is investigating, or whether other risk factors may have contributed. For instance, patients are typically treated with CAR-T after receiving several other treatments, including chemotherapy and radiation, that could make them more vulnerable.

"It's very important that this information is out there and it's very important that these cases be investigated," Porter said.

The agency's investigation includes:

- Abecma, a multiple myeloma treatment by Bristol-Myers Squibb
- Breyanzi, a lymphoma treatment by Bristol-Myers Squibb
- Carvykti, a multiple myeloma treatment by Johnson & Johnson's Janssen and Legend Biotech
- Kymriah, a lymphoma treatment by Novartis
- Tecartus, a lymphoma and leukemia treatment by Gilead's Kite Pharma
- Yescarta, a lymphoma treatment by Gilead's Kite Pharma

Treatment protocol requires patients be monitored for 15 years. The FDA said that patients should be monitored for lifelong risks.