A tale of two doctors and one groundbreaking cancer treatment

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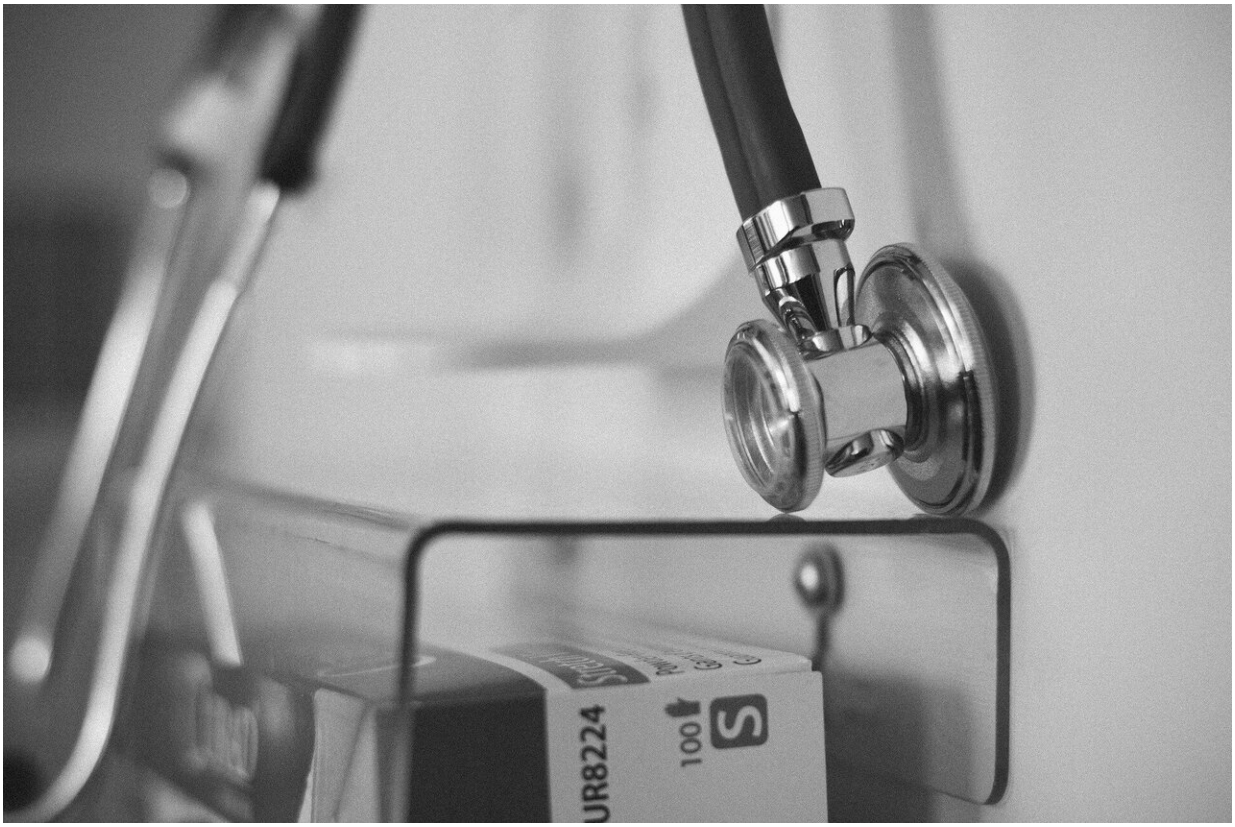

Pay transparency and diverse representation on hiring committees are first steps to leveling the financial playing field in medicine. Credit: CC0 Public Domain

Two University of Rochester physicians—one as an investigator and one as a patient—had major roles in a cutting-edge clinical trial using the

body's own immune cells to fight late-stage cancer. The striking results, showing that 93 percent of the study patients responded to the treatment, were reported in the April 2, 2020, issue of *New England Journal of Medicine*.

Patrick Reagan, M.D., assistant professor of Hematology/Oncology at UR Medicine's Wilmot Cancer Institute and senior author, helped to run the national clinical investigation of the immunotherapy, known as CAR T-cell therapy.

The treatment involves injecting billions of immune cells, which have been supercharged outside of the body in a bio-manufacturing facility, back into the patient to seek and destroy tumors.

Patrick Brophy, M.D., physician-in-chief at UR Medicine's Golisano Children's Hospital, was a patient in the study. He suffered from a rare, aggressive subtype of lymphoma (mantle cell) and was one of the 74 individuals who took part in the trial between 2016 and 2019.

The promise of CAR T-cell therapy is based on decades of research into how the immune system interacts with cancer and how it can be manipulated to fight the disease. So far, CAR T-cell therapy is being offered for lymphoma and leukemia to eligible patients. Research is continuing into other types of cancer.

Brophy and the other 73 individuals in the mantle cell lymphoma study had undergone standard therapy and yet their cancer returned. The median survival is less than 10 months for patients in that predicament; mantle cell lymphoma also carries certain high-risk gene signatures and afflicts mostly adults 60 or older—although Brophy was younger, in his 50s.

"Being able to participate in this study helped to advance science, and

for me, it also saved my life," Brophy said. "Had I not been in Rochester, I wouldn't have had the opportunity for CAR T-cell therapy through this clinical trial."

Results, as reported in *NEJM*, showed that after a primary analysis with the majority of the patients treated, 93 percent responded and 67 percent experienced complete remission—meaning their cancer was gone—in the weeks following treatment. The overall survival rate was 83 percent, which is much higher than what doctors expect from other cancer treatments in this scenario.

"This is an important new therapy that has the potential to offer patients hope," Reagan said. "Patients with mantle cell lymphoma who have relapsed after chemotherapy and targeted treatments have a poor prognosis and limited options. The response rates seen on this study are truly unprecedented and have been durable in a substantial number of patients."

More than 12 months after receiving CAR T-cell therapy, 57 percent of the patients in the clinical trial were still in remission, the study also showed.

Before a patient can receive the reprogrammed CAR T cells, the person must be stable enough despite having end-stage disease to withstand the life-threatening side effects and toxicities that often accompany treatment.

In Brophy's case, the side effects were severe: He slipped into a coma and ended up in the hospital for 56 days—needing dialysis to support his kidneys. Since then, he has completely recovered and returned to his leadership position at work and to favorite activities, such as skiing, skating, hiking, and golf.

"The side effects of CAR T cells make it difficult for some patients who have other medical problems to receive these treatments," Reagan said. "Research is progressing, though, and we are trying to develop ways to deliver these types of therapies more safely and with improved effectiveness."

Brophy received the treatment in October of 2018 and is doing well.

"Keeping hope is important," Brophy said. "It's an old adage but it's really about family and friends, being there and being present. Those are things I've focused on a lot more."

Wilmot has been at the forefront of this type of immunotherapy since 2016, when it was selected as a national site to carry out an early clinical trial evaluating CAR T-cell therapy in diffuse large B-cell lymphoma patients. A year later, the U.S. Food and Drug Administration approved the CAR T-cell treatment, called Yescarta, for that disease. Yescarta was developed by Kite Pharma, a Gilead company. After the FDA approval, Wilmot again was among the first sites in the world to offer the treatment to qualifying lymphoma patients outside of the clinical trial setting. Kite funded the *NEJM* study.

Recently, Wilmot expanded its studies of CAR T-cells for patients with acute lymphoblastic leukemia (ALL), indolent lymphoma, and is planning a trial for chronic lymphocytic leukemia.

More information: Michael Wang et al. KTE-X19 CAR T-Cell Therapy in Relapsed or Refractory Mantle-Cell Lymphoma, *New England Journal of Medicine* (2020). DOI: 10.1056/NEJMoa1914347

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