How a patient's role in a clinical trial for acute lymphocytic leukemia brought a cancer-free diagnosis, FDA approval

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The first time Becky Yu saw the Philadelphia skyline lit up at night was the evening she and her husband, Brian Currie, drove from their home in Delaware to Penn Medicine to begin her treatment for acute

lymphocytic leukemia (ALL), a type of blood cancer that affects bone marrow.

She'd had a long time to prepare—it took three months and multiple bone marrow biopsies to determine her exact diagnosis. So when her oncologist Selina Luger, MD, called on Thursday, Aug. 8, 2019 to see when she could come in to begin treatment, Yu didn't waste any time. Her treatment included joining a clinical trial that has now defined the new standard of care for certain adults with newly diagnosed ALL.

The therapy she received was approved by the FDA in June 2024, shortly before the results of the clinical trial Yu participated in were published in the *New England Journal of Medicine*.

Penn Medicine patients, including Yu, and clinicians, including Luger, who was a co-senior author on the study, were major contributors to making this cancer treatment advance possible. It will be the newest FDA-approved therapy on a growing list that can be substantially credited to research contributions at Penn Medicine.

Long road to leukemia diagnosis

Yu's first sign that something was wrong was a bout of lower back pain that was intense enough to send her to the emergency room in April 2019. She was discharged with pain medication, but landed back in the ER a few weeks later when the pain became so intense it was hard for her to speak. This time, the tests hinted at a cancer diagnosis. The doctors suspected leukemia, but told Yu they'd need to do a bone marrow biopsy to be sure.

"There were so many medical terms, and English is not my first language, but I understood leukemia and knew it was serious," recalls Yu, who was born in Taiwan. "At the time I didn't have the energy to

think about myself. The first thing that came to my mind was my kids—I had to be strong for them."

Yu's daughters were age 7 and 5 at the time. Over the next three months, she endured more tests and bone marrow biopsies as doctors attempted to nail down her diagnosis.

There are several different types of leukemia, and it's important to begin with an accurate diagnosis to determine the most effective treatment. After the third bone marrow biopsy failed to yield a diagnosis, Yu's doctor recommended she go to the Abramson Cancer Center at Penn Medicine.

"He said if it was his family, he'd do the same thing. I was so grateful he shared that with us and sent me to Penn," Yu said. "I had a lot of time to prepare my kids and my family for the road ahead. Lots of patients get a diagnosis immediately and don't have that time to prepare, so I was grateful."

Clinical trial for newly diagnosed acute lymphocytic leukemia

By the time Yu began treatment, she was ready. The first phase of treatment for ALL is called induction therapy and involves intense chemotherapy to induce cancer remission. It's followed by four to six months of consolidation therapy, then at least two years of maintenance therapy.

Leukemia specialist Selina Luger, MD, a professor of Hematology-Oncology at the University of Pennsylvania's Perelman School of Medicine, explains the lengthy treatment regimen is designed to protect against the cancer returning, which still happens too often, "Despite the

fact that we get most of these patients into remission, there's a high chance of relapse even in those with the best results after induction therapy."

"If patients relapse, there's a high chance they won't survive, so we want to be able to improve their outcomes."

To combat this challenge, Luger and colleagues in the ECOG-ARIN Cancer Research Group, designed a clinical trial that adds an immunotherapy drug, called blinatumomab, to consolidation chemotherapy for a particular group of patients with ALL.

Specifically, the trial enrolled adults with newly diagnosed Philadelphia chromosome-negative B-ALL who had no remaining signs of cancer after induction therapy, even when using specialized tests to detect cancer cells we cannot see (known as measurable residual disease). Luger was involved in the multi-site Phase III study as the chair of the ECOG-ACRIN Leukemia Committee.

"Cooperative group trials allow us to enroll patients through many different types of hospitals, including large academic centers, like Penn Medicine, and smaller community programs that may only see one or two patients each year with a given diagnosis," Luger explained. "It's much more relevant to real world care than a single-institution study."

After receiving her diagnosis at Penn, Yu learned she was a candidate for the clinical trial, and she chose to enroll. In order to participate, Yu had to receive a continuous IV infusion (24 hours a day) for four 28-day cycles—four months in total in addition to the standard chemotherapy.

Carrying the pump bag around was just like carrying an extra purse, she said. The tradeoff for such a large commitment is that the immunotherapy doesn't have the same side effects as chemotherapy,

such as hair loss or nausea.

"I didn't mind carrying it with me all the time—it was easy," Yu said. "I took the pump on bike rides with my kids, to Girl Scouts, on hay rides at the pumpkin patch. I did all of my normal activities."

Yu completed the clinical trial in spring 2021 and continues to enjoy life cancer-free. In December 2022, Luger's colleagues presented the clinical trial results at a national oncology meeting, showing that adding blinatumomab to consolidation chemotherapy improved overall survival.

As the published study showed, after three years, 85% of patients who received the immunotherapy drug were still alive, compared to 68% who received chemotherapy alone. These study results supported the FDA's decision to approve blinatumomab for patients with CD19-positive, Philadelphia chromosome–negative, B-cell precursor ALL in the consolidation phase.

"Based on what we learned from this study, we've improved the outcomes for patients with ALL and more ALL patients will survive while avoiding additional treatment toxicities," Luger said. "This progress is only possible through clinical trials."

More information: Mark R. Litzow et al, Blinatumomab for MRD-Negative Acute Lymphoblastic Leukemia in Adults, *New England Journal of Medicine* (2024). DOI: 10.1056/NEJMoa2312948

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