Advanced lung cancer knocked out in clinical trial

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Lung cancer patient Michel Gueret, left, with his oncologist at UConn Health, Dr. Jeffrey Wasser. Credit: Janine Gelineau/UConn Health Photo

A leading-edge immunotherapy clinical trial at UConn Health's Carole and Ray Neag Comprehensive Cancer Center has packed a one-two

punch, successfully controlling a patient's advanced lung cancer using the combined power of two immunotherapy drugs.

For 50 years Michel Gueret, 67, of Canton was a heavy smoker. That is until May 2012, when he received the devastating news that he had advanced lung cancer while hospitalized for a collapsed lung at UConn John Dempsey Hospital.

"I remember Michel in his hospital bed following discovery of his large lung cancer tumor," recalls his oncologist, Dr. Jeffrey Wasser. "He was very thin, barely able to walk, and was having trouble breathing. I was afraid that his lifespan would be severely reduced, as his large tumor consumed a large portion of his lung, which impaired his ability to walk and made surgery to remove it impossible."

Gueret underwent several aggressive rounds of chemotherapy and radiation to control his cancer's growth. But it was only temporary. His cancer metastasized to stage IV, spreading throughout his body. Doctors warned him that his time might be limited.

"My severe lung cancer probably would have given me a life expectancy of less than a year," says Gueret, adding, "But it is now four and a half years later!"

Gueret's survival is due to his participation in a national 20-site clinical trial called ECHO-202. UConn Health is the only site in Connecticut testing the safety and combined power of the two immunotherapies Epacadostat (INCB024360), an experimental drug, and Keytruda (pembrolizumab or MK-3475), which is FDA-approved for advanced melanoma, non-small cell lung cancer, and selected head and neck cancers.

These drugs are believed to work together to jumpstart the immune

system. They are thought to allow cancer cells that are hidden from the immune system to become more easily recognized and subsequently destroyed by the patient's immune system.

According to Wasser, the clinical trial's principal investigator at UConn Health, Gueret's tumors started to shrink just nine weeks after he began the immunotherapies, with each follow-up imaging scan showing a better and better response.

"Now, a little over a year after the start of his treatment, it is amazing how he is doing," says Wasser. "We can hardly find his cancer. His tumor seems to have regressed significantly over time."

Gueret is overjoyed with his body's response.

"The clinical trial has worked extremely well for me and I am doing great, thanks to Dr. Jeffrey Wasser and the oncology team at UConn Health," he says. "The Cancer Center at UConn Health has put me in a position four years after a deadly diagnosis to have no more signs or symptoms of my advanced lung cancer. I am extremely fortunate, and it is just extraordinary."

Wasser says it feels "pretty good" to have such a positive clinical trial patient result. "This is the part of medicine I enjoy," he adds. "It truly restores hope to cancer patients, and also their medical providers."

Wasser notes that special thanks are due to patients who participate in such early phase clinical trials. Phase 1 trials are done to find a safe dose of a new medication, and there is often little opportunity for the patients to benefit clinically. Exceptions such as Gueret's case are a pleasant surprise when they do occur. Wasser also credits the success of the trial to the team effort and dedication of Cancer Center staff, including APRN Beata Mcauliffe, Chris Sampson, and the regulatory team of the

Clinical Trials Office.

Gueret is sharing his success story to help give hope to other advanced cancer patients.

"Never underestimate what is possible," says Gueret. "Don't lose hope. Yes, we can do something about our advanced cancer diagnoses – whether immunotherapy offers the prospect of long-term management of the disease, or even the possibility of complete remission, instead of just trying to buy one or two more years. …

"My survival story shows the true weight of what the cancer doctors are doing here at UConn Health," he adds.

Tumor cancer cells spread throughout a person's body because the immune system's key defenders, T-lymphocyte cells, get exhausted. One mechanism by which the tumor cells exhaust the immune system is by expressing a protein called PD-L1 and PD-L2 (program death ligand 1 and 2). This leads to the expression of PD-1 receptors on the surface of once healthy T-cells, luring them to bind to cancer cells and destroying their efficiency to fight cancer's spread.

Gueret received Keytruda intravenously, and Epacadostat by mouth. Keytruda is the first FDA-approved PD-1 inhibitor immunotherapy drug of its kind that is allowing shrinkage of tumors by blocking PD-1 receptors or their ligands to extend the life of T-cells to effectively destroy the tumors. Epacadostat is an experimental drug that can help stop a protein in the body known as IDO1, which often plays a role in blocking the immune system's ability to reject a foreign invader such as cancer cells.

"Working together by blocking both IDO1 and PD-1, the drugs may be helping the body's own immune system to better fight cancer and shrink

the tumors in some patients," Wasser says.

The ECHO-202 clinical trial at UConn Health is currently testing the combination of medications in advanced or metastatic lung cancer, as well as other advanced solid-tumor cancers including melanoma, bladder, renal cell cancer, colon cancer, a type of non-Hodgkin lymphoma known as diffuse large B cell lymphoma (DLBCL), and other cancers.

Keytruda alone is already credited for boosting the immune system and the disappearance of advanced melanoma in former President Jimmy Carter, along with up to 35 percent of advanced melanoma patients treated with the drug at UConn Health, who have seen similar results.

Phase 1 of this clinical trial has been completed and patients are currently being considered for the phase 2 portion of the study. In this phase, patients with different tumor types are assigned standardized doses of the drugs in order to test their efficacy in combination.

The study, along with Wasser's research investigations, is funded by the INCYTE Corp. and Merck Sharp & Dohme Corp., the drug makers of Keytruda and Epacadostat.

More information: A Phase 1/2 Study Exploring the Safety, Tolerability, and Efficacy of Pembrolizumab (MK-3475) in Combination With Epacadostat (INCB024360) in Subjects With Selected Cancers (INCB 24360-202 / MK-3475-037 / KEYNOTE-037/ ECHO-202): clinicaltrials.gov/ct2/show/NC … term=echo+202&rank=1

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