Promising Early Phase Clinical Trial for Advanced Head and Neck Cancer
Nine out of 10 patients treated with the experimental therapy saw their tumors shrink

April 17, 2018 By Rachel Tompa

For many survivors of head and neck cancer, the disease — and its treatment — leave a lifelong, unmistakable mark. Surgeries to remove tumors in the mouth, neck or throat often leave patients with disfiguring scars and difficulty speaking or swallowing. Some may not even be able to perform these tasks at all.

When you look at Carla Stone, you might not guess that she was diagnosed with stage 4 head and neck cancer just two years ago. The only visible sign of her disease and treatment — and you have to know what you are looking for — is the tiny dot tattooed on her chest, the marker for the radiation she received to her throat.

Stone, a 66-year-old bookkeeper from Monroe, Washington, had ongoing symptoms for nearly two years before her doctors finally detected the tumor that had been growing on the base of her tongue. Her primary care physician dismissed the lump in her neck she found in 2014, Stone said, and a series of doctors kept giving her different antibiotics for the chronic sore throat she developed in early 2016.

Eventually, when the antibiotics didn’t work, Stone sought out an ear, nose and throat specialist, or ENT. This doctor didn’t dismiss the lump.

When Stone’s CT scan results came back, the ENT said, “I went to a lecture last week by a doctor at Fred Hutch about this new treatment he has,” Stone recounted. “I want you to call him as soon as you get out of here.”

That doctor was the late physician-scientist Eduardo Méndez, MD, an expert on head and neck cancer at Fred Hutchinson Cancer Research Center. And that “new treatment” was a recently launched early-phase clinical trial testing a new cancer drug that Méndez hoped could shrink advanced head and neck tumors to the point where surgeries for his patients wouldn’t be nearly so disfiguring.

Reducing surgery’s side effects
“Part of Eddie’s desire in designing this study was to take patients who would otherwise require a very large, very deforming surgery that could leave them with minimal function at the end of their treatment and see what we could do, not only to boost their chances of being cured, but to leave them with the best functional outcome at the end,” said Cristina Rodriguez, MD, a clinical research colleague of Méndez and fellow oncologist at Seattle Cancer Care Alliance, the Hutch’s clinical care partner.

Méndez became Stone’s oncologist and she became the seventh participant enrolled in his clinical trial.

“I said, ‘OK, I want to try it,’ because I’m a gambler,” she said. “So let’s have at it.”

For Stone, the gamble paid off. The drug, AZD1775, in combination with two chemotherapies, shrunk her tumor to the point that it was undetectable, she said. She had a minimally invasive surgery to remove some of her lymph nodes and a course of radiation to her throat after that, but there was no sign of the original tumor.

The 30 days she spent taking the experimental drug and undergoing chemotherapy were no picnic, Stone said. She had pretty severe gastrointestinal side effects. But she could also tell that the treatment was doing something.

“My sore throat was gone in about two weeks, which was amazing to me,” she said.

A promising first step

Méndez’s research team published the results of that clinical trial last month in the journal Clinical Cancer Research. Including Stone, 10 people with advanced head and neck cancer were treated with the experimental drug combination. All the participants were either ineligible for surgery or, like Stone, their tumors were such that surgery would have been significantly disfiguring.

Nine of the 10 participants had a partial or complete response to the drug, seven of whom were able to go on to a successful surgery. The 10th patient’s cancer progressed in the middle of the experimental treatment and died soon after.

Méndez himself passed away from another cancer in January, but he was able to see the results of the trial through, said Fred Hutch head and neck cancer researcher and SCCA oncologist Laura Chow, MD, senior author on the study.

The Phase 1 study was small and designed to figure out the drug’s safety as well as its most tolerable dose, Chow said. The next step would be a much larger, Phase 2 trial with more patients to nail down whether the experimental combination therapy — AZD1775, made by the pharmaceutical company AstraZeneca, plus two chemotherapies, cisplatin and docetaxel — really works for many patients with this cancer.

But of the nine patients who did respond, the responses were much more dramatic than she and
her colleagues had anticipated. Of the nine, several were able to have much less invasive surgeries than usually warranted.

“The interesting thing is it had more of an effect than we expected. People actually had dramatic shrinkage of their cancers to the point that they didn’t have cancer left at time of surgery,” Chow said. “It changed the outcomes more than we thought it would.”

“When basic science and clinical research come together”

The study was born on Méndez’s own laboratory bench, through a series of preclinical studies spearheaded by Méndez and Fred Hutch colleague Christopher Kemp, PhD.

The research team used a technique termed “functional genomics,” which sifts through hundreds or thousands of genes to find cancer cells’ weak spots. The genes the researchers are looking for are those which, when shut off, kill cancer cells but not healthy cells. Those are promising new targets for drugs that could selectively kill cancer without harming the rest of the patient.

When Méndez and Kemp applied the functional genomics technique to head and neck cancer cells with mutations in a gene known as p53, which is mutated in approximately two-thirds of head and neck cancers, their screen identified a gene known as Wee1 as a potential Achilles heel for these tumor cells. Luckily for the researchers, there was already a drug — AZD1775 — that targets Wee1.

When Méndez and Chow designed the clinical trial, they allowed patients with or without mutations in p53 to join — additional preclinical data from Méndez’s team had found that the drug also seemed to work on cancerous cells without a p53 mutation but where the cancer was triggered by HPV infection, a cancer-linked virus that inactivates p53 in a different way.

Indeed, three of the trial participants who had a good response to the drug did not carry p53 mutations in their tumors but were HPV-positive.

“I think the trial is really a great example for what can happen when basic science research and clinical research come together,” said Rodriguez, who is also one of the study authors. “This turned out to be a successful approach both in the petri dish and in human beings.”

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