

Multiple Myeloma Is Treatable, Not Curable. Is That Set to Change?

Some experts believe a “functional cure” for multiple myeloma—a cancer of the bone marrow—is already within reach.

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At age 89, Cal Crow plays water volleyball three days a week, then chases that with a 1,000-foot swim; on his off days, he logs at least a mile around his neighborhood — and that’s with a cancer diagnosis.

In 2019, Crow was having trouble hearing and went to see a physician who misdiagnosed him. He sought a second opinion at Fred Hutch Cancer Center, where a full body scan revealed that Crow had multiple myeloma.

“I didn’t know what that was,” said Crow. “All I knew was that I had an acquaintance who died of that. When I found out I had the same thing, I took notice.”

[Multiple myeloma](#) is cancer of the bone marrow; the “multiple” part refers to cancer cells that appear in various areas of the body as cancerous plasma cells overtake healthy blood cells.

A common treatment is a [bone marrow transplant](#), but Crow was not eligible due to his age. So he embarked on a year of chemotherapy, which he found difficult to tolerate. He was hospitalized multiple times and developed eye infections and sores on his body. His Fred Hutch hematologist-oncologist Edward Libby, MD, now retired, recommended he pause his treatments because of these side effects.

“I was happy to stop treatment because being in the hospital three times was not fun,” said Crow. However, he continued to wonder whether he would have to start treatment again at some point.

Crow was surprised but relieved when his new hematologist-oncologist, [Rahul Banerjee, MD, FACP](#), suggested that he could stay off treatment indefinitely.

It’s not that Banerjee was giving up on Crow — far from it.

Instead, that recommendation was consistent with the opinion of a growing number of physicians who are starting to shift their thinking about multiple myeloma’s prognosis. For years, patients

have been told that multiple myeloma is treatable but not curable. Yet data continues to accumulate about a subset of patients that remains disease-free for so many years that experts are wondering if a cure may in fact be possible.

Within the world of oncology, “cure” is a tricky term.

“Part of the problem is how one even defines ‘cure,’” said Banerjee, who now oversees Crow’s care. “We sometimes talk about a ‘functional cure’ or ‘operative cure’ whereby most patients live as long as they would otherwise while simultaneously remaining vigilant for the risk of myeloma coming back. You’re still under surveillance, but when you die, you’re not dying with myeloma or from a side effect. I would call that ‘cure.’ But if ‘cure’ means being able to walk away from ever having to see an oncologist or check myeloma labs again, then we’re really not there in myeloma.”

These functionally cured patients may continue on maintenance therapy, but others, like Crow, discontinue treatment.

“A lot of patients are nervous about this,” said Banerjee, who gave the example of a patient in remission for several years who was enrolled in a study where he was taking lenalidomide, an oral drug that modulates the immune system.

“He didn’t need to be in the study any more, but I really had to convince him to come off the study. He said, ‘This drug saved my life,’ but I said, ‘In your case, your disease’s biology is such that it’s not coming back.’”

What constitutes a cure?

One of the biggest problems providers face is predicting which myeloma patients will stay in remission. With current therapies, about 70% of patients enter remission following their first line of treatment and typically stay in remission at least five years, even without a transplant, said Banerjee.

Standard treatment for multiple myeloma involves multi-drug therapy. Most patients receive a combination of four drugs; if they’re below age 75, they’re considered for a stem cell transplant after the drug regimen is complete. Transplants for multiple myeloma are not curative, but they tend to extend the length of remission by several years.

As a rule, [Andrew Cowan, MD](#), clinical director of the myeloma service at Fred Hutch, doesn’t like using the term “functional cure.”

“To me, that’s semantics,” he said. “It plays into oncologists wanting to feel good about what they’re telling patients. The way I usually discuss this is I say some patients can have really long remissions, 10 or 20 years, but I have always seen the disease come back. I’m a very straightforward person and that’s my take.”

In Crow's case, Cowan agreed that intolerable side effects could warrant stopping treatment. But that decision needs to be made on an individual basis. "It's not a one-size-fits-all approach," he said. "It's fair to say to an older patient in their 60s or 70s that our treatments are very good, but the data suggests that ongoing therapy is [standard of care](#)."

That said, Cowan hopes that continued advances in therapies will ultimately lead to more confidence in advising patients that they can stop treatment. He's also optimistic about [research](#) that showed improved survival for patients with smoldering myeloma, a precursor to multiple myeloma, who received a drug under consideration for approval by the U.S. Food and Drug Administration (FDA).

"Smoldering myeloma is fairly common," said Cowan, who served as investigator for the study's trial site at Fred Hutch. "We are treating patients who feel fine and some may never go on to get multiple myeloma, so we have to be careful thinking about potential drug toxicity."

Eradicating disease with immunotherapy

As the incoming head of the Fred Hutch Myeloma Program, [Madhav Dhodapkar, MBBS](#), wants to nudge the conversation from talk of functional cures to actual cures. "My own personal bias is this is an opportunity for us to go even higher and really talk about true cures in myeloma," he said.

"A lot of these so-called functional cure approaches were achieved with therapies that did not necessarily fully eradicate the tumor but turned it into a dormant stage that often requires medication to maintain that dormancy," he said. "But now we have the emergence of new therapies to achieve a much higher tumor cell kill rate and the goal for us has to be to get to a stage where we have disease eradication that does not require ongoing therapy. Time-limited therapy that leads to eradication of disease is a truer cure for patients."

Some of the newer approaches include [T-cell engagers](#), antibodies designed to guide immune system T cells to destroy cancerous cells, and [CAR T-cell therapy](#), which similarly engineers T cells to seek out and kill identified cancer cells.

"This is all evolving at a fairly significant pace, so we have an opportunity to think bigger," said Dhodapkar, who noted that these approaches will need to be tested in clinical trials. "I have done this 30-plus years and one of the most common questions is, can we get rid of it completely?"

To that end, Dhodapkar and immunologist [Phil Greenberg, MD](#), recently received funding for a proposal titled, "Toward curative immunotherapy for myeloma," intended to lead to new clinical trials at Fred Hutch to immunologically eradicate the persister cells — which withstand treatment and underlie recurrence — and explore cures. Greenberg holds The Rona Jaffe Foundation Endowed Chair.

"We are willing to put that in the title," he said. "Do patients want that? Absolutely. That goal is not unrealistic."

A few months before his 90th birthday, Crow feels that he's already achieved a cure, for all intents and purposes.

"The multiple myeloma is there, but it's at such a low level that it's not bothering me," said Crow, who retired as an educational consultant five years ago at the age of 84. "I feel like I have a clean bill of health."

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