Cancer researchers ready to aim for cures

New head of oncology research hopes to build on recent advances, explore new therapeutic approaches and beat certain cancers for good.

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As a young doctor working with cancer patients in 2001, Jeff Engelman delivered a lot of bad news. At the time, treatment options were limited. For advanced cancers, oncologists relied on chemotherapy - a blunt and impotent instrument against tumors. Engelman focused on lung cancer, a disease with particularly tough odds. Most of his patients lived a matter of months after receiving a diagnosis.

Jeffrey Engelman, Global Head of Oncology, Novartis Institutes for BioMedical Research

“It was just devastating,” Engelman recalls. “For so many patients, there was truly no hope.”

Fast forward 15 years. Oncologists now have an arsenal of tools, including therapies that target molecular changes in cancer cells and treatments that coax the immune system to fight tumors. They approach each patient’s cancer as a biological problem with a potential solution - an incredible evolution in thinking.

Engelman, who became Global Head of **Oncology** at the Novartis Institutes of BioMedical Research (NIBR) on June 1, is determined to expand on recent advances in cancer research and explore new treatment approaches. The former Director of the Center for Thoracic Oncology and Molecular Therapeutics at Massachusetts General Hospital and Harvard Medical School professor also believes that the field has matured to the point where cures are within reach for certain cancers.

Here is an excerpt from a conversation with him about the evolution of cancer treatment and the future of oncology research.

Looking back at the last 15 years, which discoveries were paradigm-shifting for the oncology field?

There were three major ones. First, the discovery that you could genotype a patient’s cancer, find a mutation that activates a certain gene, develop a drug that targets the gene product, and then see a tumor melt away. Second, understanding how cancers become resistant to such targeted therapies - and how to put resistant cancers back into remission. And third, the finding that immunotherapies could induce dramatic remissions in a

variety of cancers. Whole treatment approaches were born of those discoveries.

Are we at the point where we understand how cancers become resistant to treatment?

Yes, and my group at Mass General contributed to that understanding. We've led efforts to repetitively biopsy patients to figure out mechanisms of resistance. We've done studies on tumor tissue in the lab to understand what type of therapeutics would kill drug-resistant cancer cells, and we've worked with colleagues to bring those ideas back to the clinic. We're also at a point where we think about resistance before it arises. Every time a new therapy works, we're already thinking about how cancer will get around it. We're trying to figure out how to block resistance from developing in the first place.

How have the discoveries that you've highlighted changed the prognosis for lung cancer patients?

We're using all of the new approaches that we discussed, and we've seen patients with certain types of lung cancer now living on average more than four or five years, whereas five years ago they were living for less than a year. That's nothing to sneeze at. If you can live to see a new grandchild born in your family or see a grandchild graduate, it matters. But for the vast majority of patients - even the ones that respond to targeted therapy or immunotherapy - we eventually lose the battle with cancer.

What's next for cancer research?

We need to bring together various targeted therapies and immunotherapies to have a much more dramatic effect on cancers - and to help more patients. We may be able to unleash the full potential of these treatments by combining them in thoughtful and creative ways. We also need to be open to new approaches. For example, there are efforts underway to get rid of the proteins that are driving cancer by degrading them. I think that there's a lot of enthusiasm and excitement for new types of tools.

You mentioned combining targeted therapies and immunotherapies. Have they been used separately?

They've been treated as siloed approaches because they are each toxic to cancer cells in their own right. But we have a wonderful opportunity at Novartis to bring them together. In the lab, we're seeing that targeted therapies can work well with immunotherapies in ways that we hadn't anticipated. We're going to build infrastructures and settings that allow the creative juices of our scientists to flow freely between groups.

What do you hope to achieve for patients?

There's nothing like saying, "You have a chance for a cure." I want to start an initiative aimed at turning remissions into cures. The science has evolved enough to support it. I want to focus on some cancers where we have biological insights, good tools available, and see if we can put these things together to start curing some subsets of cancers. Anyone who is affiliated with Novartis would be proud to be part of an effort that did that for patients, and there's no reason that we shouldn't go for it. I'm hoping that we can change the face of cancer research and care.
