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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

The Potential Link Between COVID-19 and Cancer Regression

Dr. McDonough:
Welcome to *Clinician's Roundtable* on ReachMD. I'm Dr. Brian McDonough, and joining me to discuss his findings on a potential relationship between COVID-19 and cancer regression is Dr. Ankit Bharat. Dr. Bharat is a Professor of Surgery at the Northwestern University Feinberg School of Medicine and also serves as the Chief of Thoracic Surgery. Dr. Bharat, welcome to the program.

Dr. Bharat:
Thank you for having me.

Dr. McDonough:
Let's dive right in, Dr. Bharat. What inspired your research on COVID-19 and its possible role in cancer regression?

Dr. Bharat:
At Northwestern, just like many other institutions, we got slammed with really sick COVID patients. And one of the things we had done early on was pioneer this double lung transplant procedure that was ultimately nationally adopted and will be adopted, and many patients end up benefitting from it. But because for the longest time we were the go-to center since no other centers were doing it, we were seeing a lot of patients who wanted to come to us or who came to us and then ultimately didn't end up making it to the transplant. In that process, what ended up happening was many of these patients coming to Northwestern had cancers, and despite all the mortality that we saw in these patients, one intriguing observation that our team had made was, in a handful of patients that got really sick from COVID and had stage IV cancer, their cancers seemingly shrunk. And we were quite puzzled by that observation. We were wondering, is it a red herring? Is it real? And then as we talked with our colleagues across the country, a few of them observed the same thing, so that was the start of the four-year journey that resulted in the discoveries that we published in our paper.

Dr. McDonough:
Now, looking at the results from your study, over those four years, what were the main findings?

Dr. Bharat:
So it's very fascinating. What we discovered was in some patients, the RNA of the COVID virus—which is the genetic program of the virus, and the virus uses it to infect and transmit and perform its function—the RNA of the virus can enter the bloodstream. And when it gets to the bloodstream in sufficient amounts, it can bind to an immune cell called monocyte, which all of us have. And typically, these monocytes are recruited by cancer cells there where the cancer cells are, and they are recruited to the site to transform them into becoming cancer-friendly cells. That's one of the big mechanisms by which cancers evade the body's own immune system.

What we found was that the RNA of the COVID virus, but not influenza and other types of viruses, could transform these monocytes to becoming cancer-fighting cells before they're recruited to the sites of cancer. So what happens is that these cancer cells end up getting transformed into becoming cancer-fighting cells, and cancer cells still recruit them thinking they can transform them into becoming friendlier cells. But when that recruitment happens, these cells that have been transformed by the virus RNA start to bring in the entire army of the immune system to cause cancer regression.

Dr. McDonough:
So could you expand upon these results and look at future implications for treatment in humans?

Dr. Bharat:
What's really exciting about this is that this whole mechanism utilizes the body's own immune cells. We are not really altering in an

abnormal way their capacity to fight cancer cells, because ultimately, what we discovered was the main cancer cells that end up getting to the site of cancer and killing them are called natural killer cells. Think of this as a battle going on between the cancer and the body's own immune system. So the natural killer cells are the super marines—they're the ultimate cancer fighting cells. So once they get there, they can be very effective. They can go to any site that the cancer is present. And more importantly, they don't utilize the T-cells, which are the cells that conventional immunotherapies utilize.

Now, immunotherapies have become a mainstay for pretty much every type of cancer, particularly patients who have stage IV cancers, and they are quite effective. But one of the big problems of immunotherapies is that most patients end up developing resistance over time because the cancer cells develop resistance mechanisms against those T-cells. There is no known resistance mechanism against the natural killer cells. These super marines are able to get to the site of cancer using the mechanisms we have discovered, so that's what's really exciting.

And the final thing I'll add to that is obviously we're not going to inject patients with COVID or the RNA. The most impactful thing about this is we've discovered the same effect can be achieved using a class of drugs or compounds.

Dr. McDonough:
For those just tuning in, you're listening to *Clinician's Roundtable* on ReachMD. I'm Dr. Brian McDonough, and I'm speaking with Dr. Ankit Bharat about COVID-19 and how it may play a role in cancer regression.

So, Dr. Bharat, while this discovery is promising, the research is clearly in its early stages; what are the major steps that need to be taken before this approach can be considered for clinical use?

Dr. Bharat:
I think all of this has been established and proven in preclinical models. We used many different types of cancer metastases in animals, including lung, breast, colon, and melanomas, and in all of these settings, it works really well. We also discovered that we can take those monocytes from the humans and transform them outside the human body using the class of compounds. So from this point, the next step would be to take this into phase I clinical trials and study the effectiveness of this mechanism in patients who have advanced cancers, so that's what we are planning on doing in the next phase.

Dr. McDonough:
And continuing to look ahead, what challenges do you anticipate as you move forward with the clinical trials?

Dr. Bharat:
That's the big mountain ahead because drug discovery or bringing anything to the clinical arena takes so long. It requires us to jump through so many hoops, lots of types of regulations, and then funding. We have to apply for funding. We were so excited about this work. We didn't file for any IP. We think it should be available for anybody who wants to pursue this just in case we are not able to get funding in a short amount of time, but if someone else has, they can absolutely use these findings and conduct this independent of us. But we are hopeful that through the current extramural funding mechanisms or through philanthropy, we'll be able to get the funding to get the phase I clinical trials, and if that shows efficacy, then we'd get to phase II and phase III. So hopefully, within the next five some years, we'll be able to get this to patients if not sooner.

Dr. McDonough:
What do you hope to achieve as you expand upon this research just within the next few years?

Dr. Bharat:
We hope that this will usher a potential new way of using immunotherapies. As I mentioned before, the conventional immunotherapies only utilize T-cells, and this mechanism should be classified as immunotherapy in my opinion because we are using the immune system of the human body to fight cancer cells. We think it will be exciting because it's using a different arm of the immune system against which cancers don't have known resistance mechanisms. The second aspect is in all the preclinical studies, we have not seen any of the conventional side effects that immunotherapies are causing, specifically autoimmune conditions. The conventional immunotherapy super charges the T-cells, and while they become effective in killing cancer cells, they also attack the body's own organs, which is a big problem in patients receiving that. But in our mechanism, we don't see that. So hopefully, with those two and the fact that it's broadly relevant to so many different types of cancers, it's going to benefit a lot of patients.

Dr. McDonough:
With those forward-looking insights in mind, I want to thank my guest, Dr. Ankit Bharat, for joining me to discuss his research on how COVID-19 may help with cancer regression. Dr. Bharat, it was great having you on the program.

Dr. Bharat:

Thank you for having me again. Pleasure talking to you.

Dr. McDonough:
For ReachMD, I'm Dr. Brian McDonough. To access this or other episodes in our series, visit *Clinician's Roundtable* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening.