Transcript Details
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Exploring Sub-Ablative Radiation to Modulate Immunity in Mesothelioma

Announcer:
This is *Project Oncology* on ReachMD. On this episode, Dr. John Cho will discuss the investigational use of sub-ablative radiation to modulate immune response in mesothelioma. He's a radiation oncologist at the Princess Margaret Cancer Centre and an Associate Professor in the Department of Radiation Oncology at the University of Toronto. Let's hear from him now.

Dr. Cho:
I think a lot of interest now is looking at radiation as not so much as an ablative therapy to try to destroy or kill all the tumor clonogens; what we're very interested is whether we can use radiation almost like a systemic therapy because we're trying to tweak the immune system.

The idea now is that instead of cranking up the dose to have really high ablative doses, which obviously can kill cancer cells, it's really high radiation doses, because in your immune system, your white blood cells are very sensitive to the radiation. So when we crank up the dose, it's a bit of a double-edged effect in the sense that yes, we are killing more cancer cells, but perhaps we're giving more radiation than we need, and we're actually hampering your immune system, for example.

So now we're investigating something called sub-ablative radiation or non-ablative radiation. So if you're a radiation oncologist and you looked at these doses, you would kind of laugh because they're not really doses that we would recognize as curative doses in the classical conventional sense. But the point of this radiation is not necessarily to ablate and cure in that sense; it's more as an adjuvant therapy in terms of the immune system.

This is still an active area of research, so we are trying to tease out these effects. But we do believe that there is a link between the dose of radiation and what sort of immune response we're able to generate. And the way I explain to patients is that your immune system is quite complex, and it's almost like we have two subsystems going at the same time. So if you really want to have the maximum immune response, both things need to be working. And so the way I phrase this is you have the inflammatory subsystem, and then you have kind of an immunogenic subsystem, and if one is out of balance with the other, you don't get the most optimal immune response.

So for example, what I mean by that is if we have certain meso tumors where the immunogenic aspect is kind of cranked up; if that happens, then the tendency is that the inflammation will kind of settle down. And what we tend to see is very quiescent, very quiet tumors. And that normally is not a bad thing. But because they're so quiescent, the immune system can't really attack it, or it's not attacking because it's very quiet. So over time, they can become problematic down the road.

So the idea in those types of patients is that we want to crank up the dose and give a, for lack of a better term, inflammatory dose. I'm tuning the radiation dose to try to cause an inflammatory reaction to try to balance out what was lacking before. And by doing that, it appears that the immune response appears to be more optimal.

And then we have the opposite case where they have very strong inflammatory responses. So typically they have sarcomatoid features or epithelial mesenchymal transition. They tend to look a bit more angry. And the problem there seems to be that they're so inflammatory that it kind of suppresses a bit of the immune response, because you would think inflammation is actually good for your immune response. It is part of your immune response, but at least in the cases that we're looking at, the inflammation dominates and it causes fibrosis and all these other fibrocytes and all these other things. And these don't tend to respond. If we were to give them ablative dose, it would just cause more scar tissue and a lot more side effects.

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So what we've noticed that for these patients, if we give a sub-ablative dose of radiation and perhaps some other things, as well to try to increase the immunogenic part of the immune system response, these patients actually do better, because then we're able to establish a proper immunogenic response. So that's kind of the direction we're going now.

Announcer:
That was Dr. John Cho discussing how sub-ablative radiation could modulate immune response in patients with mesothelioma. To access this and other episodes in this series, visit *Project Oncology* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!

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