

**SPEAKER:** One of the things that was initially quite astounding about the CTCL responses is the recognition that we can make these broad statements of therapeutic recommendations at all because each of these patients is distinct in a number of ways. Each of the patients have a different number of malignant cells in the blood. And when we look at them, each of them, by molecular markers and genetic analysis of the blood cells are their own story.

So it's quite remarkable that the dose response curves that allow us to make the generalizations of the recommendations that we do make is even possible. It shows that it is quite a favorable dose response curve. Again, suggesting a relationship to normal physiology.

The next question that comes up is, are there patients who have been actually cured of the disease? Well, we have seen them and others have seen them and reported them. But they clearly are a minority of the patients.

Again, one has to not be depressed by that, and this is less than 10% of the total population being treated, because you have to remember that what we're trying to do is use an anti-cancer vaccination or immunotherapy to treat an already existing disease. None of us typically think of a post-exposure vaccination. You don't get vaccinated to polio after we have polio. We do it before we have polio. Same with other vaccinations.

So it's quite a large hurdle to use this kind of cellular immunotherapy as effectively as it has been. And now, of course, we believe that we know how to do it potentially more effectively. One of the things that we used as an initial proof of principle that this is a dendritic cell therapy was a published report in a clinical trial that's quite instructive.

It was published by our group with Mike [INAUDIBLE] as the lead author some 10 years ago. And that is that if we take patients who are not responding to ECP, CTCL patients, of course, and we now modify the therapy slightly. And this was in an experimental study, which is not yet approved by the FDA to do it this way.

What we did is, instead of returning the blood directly to the patient right after the therapy, we held the blood overnight in an incubation chamber, giving the dying cancer cells-- dying because of their exposure to 8-MOP-- and the new dendritic cells a chance to caucus, so to speak, meet overnight in an incubation chamber rather than have to reconnoiter inside the body after having been sent back immediately. The concept was that if ECP was really an immunotherapy involving new dendritic cells that have been induced by the therapy, internalizing, processing, and presenting the 8-MOP killed cancer cells, then making it easier for these two cell populations to come together by holding them overnight would lead to enhanced responses.

In fact, with all of the patients entering that study having already failed ECP, conventional ECP, 50% of them responded to that small change of simply delaying the return of the cells overnight. So what we now know is that we're dealing with a situation that can be improved.

I can't give specific recommendations as to how to do that. I can't tell you at this point whether a larger number of patients would be able to go off of therapy altogether and even be considered potential complete cures. But these are the kinds of things that we need to investigate.