Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/clinicians-roundtable/an-emerging-vaccine-helps-prevent-prostate-cancer/3628/

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

An Emerging Vaccine Helps Prevent Prostate Cancer

IS THE VACCINE TO BECOME PART OF THE TREATMENT FOR CANCER OF THE PROSTATE

Is the vaccine to become part of the treatment for cancer of the prostate? You are listening to ReachMD XM 157, The Channel for Medical Professionals. Welcome to The Clinicians Roundtable, I am your host Dr. Maurice Pickard and joining me today is Dr. James Gully. Dr. Gully is the Director of the Clinic Trial Group of the Laboratory of Tumor Immunology and Biology at the National Institute of Health and also a senior staff clinician within the medical oncology branch at the National Cancer Institute.

DR. MAURICE PICKARD:

Thank you very much for joining us today.

DR. JAMES GULLY:

Oh, it's my pleasure to be here, Dr. Pickard.

DR. MAURICE PICKARD:

We have always looked at vaccine as being preventative, but now we have began to see that vaccine have a possible use in the treatment of cancer of the prostate and may be other cancers as well. Can you tell me, to begin me, how immunotherapy may play a role in this disease?

DR. JAMES GULLY:

Yes, I think, it's a very interesting in view area for immunotherapy. I think that what we have been able to see is that early indication suggests that we can mount immune responses against tumor-associated antigens or tumor-specific antigens in prostate cancer. There are several things about prostate cancer that make it amenable to treatment with immunotherapies including generally it is an indolent-growing disease and that allows time for an immune response to be mounted. In addition, the number of targets that we have available to us in prostate cancer is quite a few and these have been well-described, well-developed, and so based on this, there are at least three vaccine platforms that are in advanced clinical trial testing.

DR. MAURICE PICKARD:

Could you tell me something about those platforms?

DR. JAMES GULLY:

Yes, so we have the three platforms including the antigen-presenting cell based platform, perhaps the furthest one. This is a platform that takes the antigen-presenting cell, which is part of the immune system. Basically, these are the cells that can teach the T cells and B cells how to behave, what targets to look for, and these antigen-presenting cells, can be taken from the patient grown up in the laboratory and then given back to the patient along with the target of interest for this Sipuleucel-T vaccine or the provenge vaccine, this target of interest is prostatic acid phosphatase. It is linked to an immune stimulator molecule, GM CSF.

DR. MAURICE PICKARD:

And there are other platforms as well?

DR. JAMES GULLY:

Yes, there are 2 other platforms that are being used relatively widely; one is the whole tumor cell platform GVAX. This is the platform that is comprised of 2 different prostate cell lines that are grown in the laboratory, both of these have been modified slightly genetically to make GM CSF. Again, the same protein that can help stimulate the immune system, these cells are grown up, then irradiated, killed, and given as a vaccine to the patient. And the final vaccine platform is the vector viral platform. This platform is interesting because you can put in a variety of different genes with the viral vector such as target genes for PSA or other tumor-associated antigens, as well as genes for stimulatory molecules and once such platform is the PSA-TRICOM vaccine. This vaccine has been in a variety of different phase 2 clinical studies.

DR. MAURICE PICKARD:

You mentioned that there are good markers for this process. I am intrigued by the fact that possibly even without metastatic disease, there are good markers, different in, say, other cancers and this might also make it a good example to try?

DR. JAMES GULLY:

That's absolutely right. So, what we have found is obviously in patients with prostate cancer, that have undergone radiation or surgery, approximately one-third of the patients will developed biochemical recurrence, that is their PSA will start to rise following local treatment. It is these patients have very low volumes of disease and usually slow-growing disease indicated by slowly-rising PSA that may be the ones that are more likely to benefit from vaccines and PSA does serve as a very good marker for these patients.

DR. MAURICE PICKARD:

We don't need the gland, prostate to live a normal health life and so the destruction of normal cells may also be an advantage using a

vaccine as opposed to the liver, for example where when you try different modalities, you are trying not to injure the healthy cell?

DR. JAMES GULLY:

That is a good point. So, as we know, if you have prostate cancer that is localized and you remove it surgically, the patients do find, they don't need the prostate to live. The fact that we can use any target that is tissue specific, allows us to use many more different types of targets, so we can use PSA, which is not expressed not only on the normal cells, but also on the tumor cells as a target and we can get the immune system to go in and eradicate the tumor cells as well as perhaps some residual normal cells.

DR. MAURICE PICKARD:

You bring up an interesting point in that there are different targets. Are we combining vaccines with other modalities, in other words, are we exploiting the use of vaccines with other modalities and try to compare this to conventional combination chemotherapy?

DR. JAMES GULLY:

Yes, that's a very good question. We have looked at a variety of different combination here at the National Cancer Institute. We have been able to show that we can combine vaccine therapy with hormonal therapy or androgen-depravation therapy. We have been able to combine vaccine with radiation therapy and been able to combine vaccine with chemotherapy and in all of those cases, we have been able to show that we can generate good immune responses despite the combinations of vaccine with the standard therapies and there are very interesting rationales behind each of these.

DR. MAURICE PICKARD:

Could you tell me some of them?

DR. JAMES GULLY:

Sure. So, with the combination of vaccine and hormonal therapy, what we know is that hormonal therapy can cause a reemergence or regrowth of the thymus gland. Now, you may remember that the thymus gland is where all the T cells get trained and this reemergence of the thymus can result in the generation of naive or new T cells that could potential recognize and attack the tumor. In addition, clinical studies have shown that use of hormonal therapy in patients with prostate cancer prior to prostatectomy, has resulted in a significant increase in an inflammatory response within the prostate. Similarly, with radiation therapy and with chemotherapy, we have shown that those 2 modalities, can actually alter the way the tumor looks to the immune system, so that there is upregulation of markers on the tumor cell that make it easier for the immune system to recognize or kill the tumor. In addition, chemotherapy can actually rub up a T cell response. The T cells can actually make more interferon for instance, which makes them more active and more readily able to kill the tumor cell.

DR. MAURICE PICKARD:

You mentioned the word response that I would like to just dwell on. Early on, as in most cancer research you chose and the people and other investigator shows the people with the most advanced cancers, to try this modality and they used the distinction tumor response or RECIRS, which is response evaluation criteria in solid tumors and compared it to the patient's response. Could you comment on this word response and how it plays into the use of vaccines?

DR. JAMES GULLY:

Yes. I think this is a very important concept and one that is just evolving as we are learning to use targeted therapy such as vaccines or even drugs like the tyrosine-kinase inhibitors that had been just recently approved for renal cell cancer. The idea of looking at a patient's response versus a tumor response is an important new idea. The idea is that what we are really trying to get at is improving the long-term outcome of patient, improving survival. If we have a modality that shrinks the tumor, that's nice, but if it doesn't ultimately benefit the patient by improving symptoms or improving survival, that is not enough. It turns out that perhaps these vaccines may not be able to do what, in terms of shrinking tumors, but they may actually be able to cause a prolonged stabilization of disease and in fact that may result in improved survival. It would be nice, if we could turn metastatic cancer into something more like diabetes or heart disease, where we can chronically manage them.

DR. MAURICE PICKARD:

For somebody in practice, we have been looking at cancer of the prostate in many different ways and there is a tension that exists that we may be over-treating people. Is it fair to say that with this new idea of vaccine, that in some ways, there should be some kind of selection that if we are going to use this treatment modality, we should be selective. I realized that question has many answers, but again should we be selective in who we use this on and has our research, reached a point where we can make this selection?

DR. JAMES GULLY:

This is very interesting question. So, we recently completed analysis of a small phase 2 study that we did here at the National Cancer Institute and we presented those findings at the 2008 American Society clinical oncology meeting. In that trial, what we found was that the patients were treated with vaccines and these were all patients with metastatic disease that had failed hormonal therapy, but had not gone on to get chemotherapy, but those patients actually did better than predicted in terms of overall survival and that was encouraging to us, but perhaps more telling was a subset analysis of that overall survival, was that the patient with more indolent disease, that were expected to live longer than 18 months versus those who were expected to live shorter than 18 months and this can be done easily using the Halabi nomogram in this patient population. What we found was that those patients that lived shorter than 18 months, they did about as expected compared with the Halabi nomogram when they were treated with the vaccine; however, the patients that were expected to live longer than 18 months, actually had a substantial improvement in their overall survival compared with expected. So, their overall survival was about 2 years longer than expected. Now, this was just a small study and survival was not the primary influent of the study; however, this does raise the question as to whether treating the patients with more indolent disease may be better, in other words those patients may be the ones more likely to benefit and it should be pointed out that this criteria used to determine how long the patient is expected to live, was based on the patients that were getting hormonal therapy or chemotherapy, not the patients that were not getting treated for their cancer.

DR. MAURICE PICKARD:

And that you factor in their Gleason?

DR. JAMES GULLY:

Yes. So, that's important. The criteria for this score include the Gleason score. It includes several laboratory parameters and includes their performance status how much energy they have basically and also it includes whether or not they had disease that was more

aggressive looking in their scans, so as they had liver disease for instance.

DR. MAURICE PICKARD:

Today, we have been discussing how immunotherapy may play a role in developing a vaccine that will have a significant role in the treatment of cancer of the prostate and I think it isn't too difficult to think that if it has a role with cancer of the prostate; it may have a role in other kinds of cancers. I want to thank Dr. James Gully, Director of the Clinic Trial Group of the Laboratory of Tumor Immunology and Biology at NIH for being with us and discussing this very provocative and hopefully new advancement in the treatment of a difficult cancer.

I am your host Dr. Maurice Pickard and you have been listening to The Clinicians Roundtable on ReachMD XM 157, The Channel for Medical Professionals. To listen to our on-demand library, visit us at www.reachmd.com and if you have comments of suggestions, call us at 888-MD XM-157. Thank you for listening.

You are listening to ReachMD XM 157, The Channel for Medical Professionals. Here is a sample of the great shows airing this week.

This is Dr. Mark Nolan Hill. This week we will be speaking with Dr. Mark Busec at Joe DiMaggio Children Hospital in Holly wood, Florida. We will be talking about pediatric heart transplantation after cardiocirculatory death.

This is Susan Dalwin. Join me this week when my guest will be Dr. Athena Tsimikas, Executive Director and Chief Medical Office of the Whittier Institute for Diabetes, discussing type 2 diabetes.

This is Dr. Lee Freedman. Please join me this week on The Clinicians Roundtable when I am joined by Dr. Alice Yellow from the University of Michigan School of Public Health and she will take us through a discussion about household antimicrobial products. Are they more helpful or more harmful?

Thank you for listening to ReachMD XM 157 where we change topics every 15 minutes. For our complete week guests and program guide, visit us at www.reachmd.com