Prostate Cancer Awareness

Guest Expert: Joseph Kim, MD
GU Oncologist at Yale treating patients with prostate cancer

Yale Cancer Center Answers is a weekly broadcast on
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Welcome to Yale Cancer Center Answers with doctors Francine Foss and Anees Chagpar. Dr. Foss is a Professor of Medical Oncology and Dermatology, specializing in the treatment of lymphomas. Dr. Chagpar is Associate Professor of Surgical Oncology and Director of the Breast Center at Smilow Cancer Hospital at Yale-New Haven. If you would like to join the conversation, you can contact the doctors directly. The address is canceranswers@yale.edu and the phone number is 1-888-234-4YCC. This week, Anees Chagpar is joined by Dr. Joseph Kim. Dr. Kim works in GU Oncology at Yale treating patients with prostate cancer. Here is Dr. Chagpar.

Chagpar Let us start off by having you tell us a little bit about yourself and what you do?

Kim I joined Yale Cancer Center last August as a GU medical oncologist. I just finished my fellowship program at the National Cancer Institute where I finished my medical oncology fellowship program and I completed medical school at Wake Forest in North Carolina, and an internal medicine residency program at Emory in Atlanta Georgia.

Chagpar Perfect, tell us a little bit more about what you do on a daily basis at Yale?

Kim I just began my clinic about a month ago. I specialize in prostate cancer, bladder cancer and testicular cancer. I also joined the Early Drug Development Program lead by Dr. Paul Eder with phase I clinical trials.

Chagpar Tell us a little bit more about what phase I clinical trials are, it sounds high-tech.

Kim For a new drug to be available for patients it takes several steps of a clinical trial, so a phase I trial is the very first clinical trial where we are trying to test the safety and tolerability of a new experimental drug, and then once we see some activity, it will be tested in a phase II trial where we measure activity of the drug as measured by a response phase, that doctors often talk about, and once we see promising activity we can go on to a later phase clinical trial called a phase III trial, where the new therapies are compared with standard therapies.

Chagpar This is kind of that stage where there are new and exciting therapies that have not been tried before but that have showed promise?

Kim Exactly.

Chagpar Tell us a little bit more about those new and exciting therapies, are there things like that for prostate cancer or bladder cancer, or other cancers that you deal with?

Kim Absolutely, here at Yale we have several clinical trials for prostate cancer and bladder cancer, for instance, for prostate we have trials ranging from newly diagnosed metastatic prostate cancer...
patients all the way to those who have had multiple prior therapies such as hormonal therapy, immunotherapy, or chemotherapy. So we have a lot of options available here at Yale Cancer Center.

Chagpar So for people who may have failed previous therapies, or their cancer may have spread, there are new therapies out there for them? I understand that you also study different kinds of therapies, tell us a little bit more about your research.

Kim My past research has been on immunotherapy, and I work with my mentors at NCI where we are involved in clinical development of what we call therapeutic cancer vaccines. A therapeutic cancer vaccine is an immune-based therapy that is designed to stimulate a person's immune system so that the activated immune system can help the patient fight the cancer and this vaccine has undergone several clinical trials. Currently, this is in a phase III clinical trial and has been tested in patients with advanced prostate cancer.

Chagpar So, normally when we think about a vaccine, like the flu vaccine, you often get it before you get the disease to prevent you from getting the disease, but it sounds like this is something that you get after you have the disease, is that right?

Kim Exactly, you make a very good point, this is called a therapeutic cancer vaccine, not a preventive or prophylactic vaccine. When a person hears the word vaccine they think about the pneumonia vaccine or the flu vaccine, and the concept, the underlying principle, is the same. The flu vaccine is designed to stimulate the immune system so that when the person is re-exposed to a virus or bacteria the active immune system can fight the infection, and the same principle applies for a therapeutic cancer vaccine. So this vaccine is designed to stimulate immune response against certain tumor types.

Chagpar Does it work against all kinds of prostate cancers or just with a certain strain?

Kim Prostate cancer, in general, is what we call very mixed; each prostate cancer differs from your neighbor's prostate cancer. So, in general, this particular cancer vaccine is designed to stimulate the response against prostate specific antigen which is very common in prostate cancer patients.

Chagpar Prostate specific antigen, that sounds like that test.

Kim This antigen is very common in patients with prostate cancer, it circulates in the patient's blood and we use this antigen to screen for prostate cancer, but also use this to monitor a patient’s certain therapy as well.

Chagpar So this vaccine, should all men with prostate cancer be getting it, because it seems to me that a lot
of men have prostate cancer and are told by their doctor that they can just watch and wait, that their prostate cancer is not going to hurt them. Is this something that they should be getting a vaccine for?

Kim  This is in a phase III trial, we’d like to use this vaccine for patients who have known prostate cancer, but this will be tested in the phase III trial, so it is coming along.

Chagpar  In the phase III trial, which patients are eligible?

Kim  This trial will enroll patients with metastasis on the scan and for those who have very minimal symptoms from their prostate cancer.

Chagpar  Are these patients who have already had surgery or radiation for their prostate cancer or should they still have their prostate, how does that work?

Kim  It does not matter actually because many of our patients have prior radiotherapy or surgery and over time some of these patients eventually develop metastasis, so these patients can certainly go on this trial and if they have a new metastatic prostate cancer progressing on hormonal therapy, they can certainly go into this trial as well.

Chagpar  That sounds really exciting, that one day there might be a vaccine that revs up your immune system and helps you fight prostate cancer which is a really ubiquitous disease. When do you think that trial is going to wrap up and you are going to have the data so that the rest of the men who are listening to our show may be able to avail themselves of that therapy?

Kim  I would like to see data sooner rather than later, currently this is a phase III trial, so I think they are planning to finish accrual by 2014, so it will be another three to four years I would say.

Chagpar  I also understand that you won a Young Investigator Award. Tell us a little bit more about that.

Kim  Yes, I was very honored to receive the award with the help of my mentors at the NCI and this award was given so that I can study the impact of a new prostate cancer therapy called enzalutamide on the immune system. One of the trials that I developed at the NCI was a phase II trial involving this particular drug enzalutamide with a prostate cancer vaccine. This trial was developed on this basis of very good scientific data to suggest that there is potentially a synergistic effect on the immune system particularly in the making of new early T cells, called naive T cells. So my question was, whether this drug would have a favorable effect on the immune system and whether this better immune response may correlate with the better clinical outcome?

Chagpar  What exactly is enzalutamide?

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Enzalutamide is a new hormonal therapy that blocks the activity of androgen at the receptor level.

So you have a drug that blocks androgens, androgens are male hormones, right?

Exactly.

And male hormones drive prostate cancer, is that how it works?

Exactly, yes.

So that combination, plus revving up the immune system, might make your prostate cancer disappear even faster than it would with either one of the two individually.

Yes, we hope to see that.

Tell us a little bit about how exactly you are studying that?

We are randomizing that particular trial, randomizing patients to receive either enzalutamide alone or the combination of the enzalutamide and the vaccine, and the patient will be treated with the assigned treatment and then will be followed for their time to progression, or their survival.

And are those patients who are eligible for that trial need to have distant metastases?

Yes.

When do you think that trial might finish, because that is another one that seems really exciting?

That trial was opened at the NCI last July, so we are accruing about 70+ patients on the trial, so we hope to finish accrual by the end of next year or two and then we will be able to analyze the data thereafter.

And is enzalutamide a commonly given therapy, is that standard of care?

Yes, enzalutamide was approved by the FDA in August of 2012 in patients with metastatic prostate cancer who failed hormonal therapies, and also have failed chemotherapy, so yes it is commercially available.

Do patients on the trial have to have failed chemotherapy and hormonal therapy? Is this like a last ditch effort?

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Kim Actually it is not, that is the really good thing about this trial because enzalutamide and this vaccine are very well tolerated. So we would like to move these agents earlier in the disease setting.

Chagpar Can you tell us a little bit more about clinical trials and how patients respond when you offer them a clinical trial? I think that there is a lot of misperceptions on the part of many people as to what clinical trials are. Oftentimes people think that a clinical trial is what you take when there is no other option. Tell us a little bit more about that.

Kim Actually a clinical trial is the only way that we can discover new therapies and more effective therapies, and potentially offer better options for our patients. But again, we cannot be 100% certain about these new therapies and that is why they are being tested, and that is one of the goals of the clinical trial, even though there is really good science behind a clinical trial, and I certainly think that participation in clinical trials will certainly advance the field in general and also potentially offering benefits for our patients as well.

Chagpar As I often say on the show, one of the things that a lot of people do not recognize is that people who participate in clinical trials often do better than people who do not participate in clinical trials, very much for that same reason.

Kim Yes.

Chagpar They are offered therapies that are newer and better. It seems to me that a lot of your work really focuses on the immune system and cancer and a lot of people I think are really interested in how that interplay occurs. Can you give a sense of how the immune system interplays with cancer?

Kim As a cancer develops, the cancer cells learn how to evade recognition by the immune cells and that is the part of the carcinogenesis.

Chagpar We want to learn more about how cancer cells get away from the immune system and what we can do to rev up the immune system so that the immune system can recognize these cancer cells and get rid of them, but we are going to have to take a short break for a medical minute. We will pick up this conversation as soon as we get back so please stay tuned to learn more information about the immune system, prostate cancer, and what we are doing about it with my guest Dr. Joseph Kim.

Medical Minute The American Cancer Society estimates that the lifetime risk of developing colorectal cancer is about one in twenty and that risk is slightly lower in women than in men. When detected early, colorectal cancer is easily treated and highly curable. Men and women over the age of 50 should have regular colonoscopies to screen for the disease. Each day more patients are surviving.
colorectal cancer due to increased access to advanced therapies and specialized care, which is giving colorectal cancer survivors more hope than they ever had before. Clinical trials are currently underway at federally designated comprehensive cancer centers like the one at Yale to test innovative new treatment for colorectal cancer. New options included Chinese herbal medicine being used in combination with chemotherapy to reduce side effects of treatment and help cancer drugs work more effectively. This has been a medical minute and more information is available at yalecancercenter.org. You are listening to the WNPR Health Forum on the Connecticut Public Broadcasting Network.

Chagpar Welcome back to Yale Cancer Center Answers. This is Dr. Anees Chagpar and I am joined today by my guest Dr. Kim. We are discussing prostate cancer and specifically, right before the break, we were talking about your research which really focuses on the immune system and cancer and you were beginning to tell us how in cancer, the cancer cells learn how to sneak around the immune system and hide away from them. Tell us a little bit more about how the immune system and cancers interplay.

Kim As I mentioned, as cancer develops, the cancer cells learn their way to evade recognition by the immune cells and they do so by producing a protein called immune checkpoints and these are the signals that are produced by the tumor cells to the immune system that do not kill me. It is a self-survival signal to say, do not kill me, kind of thing.

Chagpar Okay, and so keep going with that, so cancer it is interesting that they have this camouflage that says, I am okay, do not kill me. How do they get that and what do we do about it?

Kim This is, as I mentioned, a self survival signal and actually this protein was discovered by one of our immunologists here at Yale, Dr. Lieping Chen and there are several classes of immune checkpoint inhibitors and we are learning more about that, and his discover will lead to the development of promising immunotherapeutic agents, and this is called an anti-programmed death 1 ligand antibody.

Chagpar So this anti-PDL-1, is kind of an immune checkpoint marker that had been in the news a while ago with melanoma. Tell us a little bit more about how exactly that therapy works? Does it get the immune system to recognize this immune checkpoint and say, wait a minute, I see that that is camouflage, or does it somehow give your immune system more muscle to fight these cancers? How does that work?

Kim That is a very good point, these therapies target these proteins that block the interface between the tumor cells and the immune cells, and this therapy will get rid of the barrier between the tumor cells and the immune cells, and not only that, this will also activate the immune system so that the T cells will be able to fight off the cancer cells.
Chagpar: That is very, very cool. Has that therapy been tried in prostate cancer?

Kim: This therapy has not been tried in prostate cancer yet, but this therapy is available in a trial here at Yale Cancer Center in multiple tumor types including bladder cancer and as you mentioned, melanoma, kidney cancer, and also head and neck cancer, and breast cancer as well.

Chagpar: And so with that, do you have to receive chemotherapy, or does it rely solely on your immune system saying, that is a tumor cell, I know that you are there and I am going to kill you all by myself?

Kim: Although, we would like to combine this class of therapy with another therapy such as chemotherapy or hormonal therapy, and I think that given the trial design as is, this therapy alone will work in patients with any solid tumor types such as bladder cancer, kidney cancer, or any other solid tumor types.

Chagpar: That sounds really cool. It sounds like that is going to revolutionize cancer management if your immune system can actually figure out that a tumor is there and attack it, and you can avoid other kinds of chemotherapy.

Kim: Right.

Chagpar: So tell us more about those clinical trials, are they open to anybody with cancer? Do you have to have metastatic disease, how does that work?

Kim: For these trials that employ this Anti-PDL-1, most of these patients have to have metastatic disease and some of these trials would actually require a tumor biopsy or archived tumor samples from the original surgery or prior biopsies.

Chagpar: And the reason for the biopsy is?

Kim: Is to see whether the tumor, whether the patient’s tumor, expresses the targets on their tumor cells. But we are also working on a trial that may not require tumor biopsies.

Chagpar: So, it would just treat with this agent regardless?

Kim: Yes.

Chagpar: Excellent, so outside of clinical trials and I think that the clinical trials that we have talked about today really focus on getting your immune system to find and target, seek and destroy, cancer, are

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incredibly exciting and novel and innovative, but that seems like it is a little bit away from standard of care at the moment given that it is still in a clinical trial. So how do we treat cancers of the prostate and bladder today?

Kim The treatment of prostrate cancer, I will categorize into three for the audience. The first is a localized prostate cancer. The second is recurrent prostate cancer as evidenced by rising PSAs but no evidence of metastases on the skin. The third category will be the patients with known metastases that you can see on the bone scan or CT scan. So for localized prostate cancer, there are many options available. Again, the treatment decision really depends on the patient’s preference, value and other comorbidities and so on. So, for the localized prostate cancer, patients are usually treated with either surgery or ablation therapy, and actually some of these patients can be on active surveillance and for the patients with biochemical recurrent prostate cancer, we do not have a really good therapy that has been shown to improve survival in these patients.

Chagpar So if there have not been better therapies for recurrent cancers, do we just treat them the same way we treat local cancers?

Kim For some of these patients, if they are deemed curable and they can salvage radiation therapy as an reasonable option for these patients, if they have never received prior radiotherapy, but for the people who have biochemical recurrent cancer as evidenced by PSA values, these patients can be on the active surveillance with repeat PSAs or repeat scans, or these patients can be started on the hormonal therapy. Again, as I mentioned, this hormonal therapy is very effective in lowering the PSA levels and do delay time to metastases, but unfortunately, we do not have high level of evidence to say that hormonal therapy at this point will prolong your survival. Unfortunately, we do not have the data to say that. So when I see a patient with a biochemical recurrent cancer I take time and go over their PSA values and the implications of this and potential side effects of a hormonal therapy and so on.

Chagpar And then for the third group, the metastatic, how do we treat those patients currently?

Kim It is a very exciting area for metastatic patients. We now have five new therapies that have been approved by the FDA in the last three years. Traditionally, there has been only one chemotherapy that was approved by the FDA and that is called docetaxel, but since 2010, a new chemotherapy called cabazitaxel was approved and also a two-hormonal therapy called enzalutamide or abiraterone has been approved and also the first-in-class of a therapeutic cancer vaccine has been approved by the FDA as well and recently a new drug called radium-223, which is a radiopharmaceutical that targets the bones, the bony metastasis of prostate cancer patients, and all of these agents have shown to improve survival in our patients.

Chagpar That is really exciting and so now some of the clinical trials are looking at agents like enzalutamide plus or minus other therapies that are FDA approved to see which of these is better.
As you were talking about survival in the locally recurrent prostate cancer, in the biochemically recurrent prostate cancer, I wondered about whether one of the reasons why we may not have survival data is because men with prostate cancer may actually do quite well. Can you tell us a little bit about survival rates for men with prostate cancer? It seems to me that there are a lot of guys I know who have had prostate cancer.

Kim Yes, certainly prostate cancer has a very long natural history, but again, because prostate cancer is a very heterogenous tumor, some people would have a very long natural history and would not cause any problem in their lifetime, but some tumors can behave aggressively as well, so in range a patient can live up to more than 10 years since the time of diagnosis but some people would eventually die of their disease in a much shorter time than that.

Chagpar What determines whether somebody is going to live long and prosper with their prostate cancer or is going to have a much more aggressive course?

Kim This is certainly a very active area of research. At this point we do not know how to answer that question, but certainly there is research ongoing to identify the patients who have very aggressive features of their prostate cancer.

Chagpar Getting back to your research, I wonder whether part of it might be not just the cancer itself, but their immune system. Do we know anything about people who have immuno-deficiencies, whose immune systems may be suppressed for whatever reason, are they more likely to get prostate cancers and are they more likely to get aggressive prostate cancers, do we know?

Kim This is a very good question. As far as I know there is not much data to say whether a comprised immune system can lead to development of prostate cancer. Certainly, there is a lot of data about the immune system and development of some lymphomas, for instance.

Chagpar And you think about patients who have HIV and Kaposi sarcoma and other malignancies that can occur, so clearly this whole concept of the immune system interplaying with cancer seems to be an incredibly important area. I saw a patient just today who asked me about the immune system in cancer and wondered about all of the other things that people do to kind of help their immune system and I want to get your thoughts on that. So people say that if you sleep enough, it will help your immune system, if you drink orange juice and vitamin C, it will help your immune system. If you do not stress, if you meditate, that will help your immune system, do these things help with cancer?

Kim I certainly want to know the answers to these questions, and at this point, certainly exercise and certain diet patterns may help in boosting the immune system, but the reality is that there
is no data to say one or the other, but certainly maintaining a healthy lifestyle by exercising, maintaining a good diet and getting good rest, certainly those things not only help cardiovascular health, but also cancer related health as well.

Chagpar I think it would be such a cool area of research to look at all of those things and how that affects cancers. So aside from immunotherapies and the clinical trials that we have talked about, so far with regards to prostate cancer, what else is on the agenda? What else is new and exciting in the wonderful world of GU oncology and prostate cancers? Are there new therapies that you are excited about or new screening modalities that you are excited about or new things that you think are coming down the pike that people should be thinking about?

Kim In the world of prostate cancer therapy, there are certainly many promising agents that are currently in Phase II clinical trials here at Yale Cancer Center and one of them actually is a hormonal therapy called TAK-700 which is similar to another hormonal therapy called abiraterone and this clinical trial is available for patients with metastatic prostate cancer, newly diagnosed prostate cancer, and this therapy, unlike the abiraterone, does not require the prednisone to minimize your side effects. So this is certainly one of the very interesting, very promising drugs that is available in clinical trials.

Dr. Joseph Kim works in GU Oncology at Yale treating patients with prostate cancer. If you have questions or comments, we invite you to visit yalecancercenter.org where you can also get the podcast and find written transcripts of previously broadcast episodes. You are listening to the WNPR Connecticut Public Media Source for news and ideas.