

Transcript Details

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ReachMD

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

New Frontiers in the Imaging and Treatment of Advanced Prostate Cancer

Announcer:

You're listening to *On the Frontlines of Prostate Cancer* on ReachMD. And now, here's your host, Dr. Wayne Kuang.

Dr. Kuang:

This is *On the Frontlines of Prostate Cancer* on ReachMD. I'm Dr. Wayne Kuang, and joining me to discuss the most exciting developments in the treatment and imaging of advanced prostate cancer is Dr. William Oh. He's the Director of Precision Medicine at the Yale Cancer Center and Smilow Cancer Hospital, as well as the Service Line Medical Director at the Smilow Cancer Hospital at Greenwich Hospital. Dr. Oh, welcome to the program.

Dr. Oh:

Thank you, Dr. Kuang. Really my pleasure to be here.

Dr. Kuang:

So let's just dive right in, Dr. Oh. What are the new treatment options in the pipeline, and how are they changing our approach to advanced prostate cancer?

Dr. Oh:

I've been in this field for 25 years now. It's scary how fast time goes by. But when I first started, there were no treatments that improved survival for advanced prostate cancer. Our imaging and diagnostic abilities were really quite crude, but most importantly, patients with, for example, advanced or metastatic prostate cancer typically lived a year or a year and a half. I had some patients living longer, but it was a pretty disappointing disease. We had very few options for patients.

Now, fast-forward and there's so many more treatments that have been approved based on large clinical trials, and in particular, for advanced patients—patients who present with metastatic disease or who become hormone resistant—what we have learned is that some of these new treatments that target androgen receptor but also target PSMA in particular are keeping these men alive longer and actually improving their quality of life as well. So, for example, one of the most exciting recent treatments is Lu177 PSMA. Lu177 is a radioactive particle that actually attaches to any cancer cell that makes PSMA. PSMA is not PSA. It's prostate-specific membrane antigen. But it, like PSA, is expressed primarily by prostate cancer cells. And so whenever you have something that's differentially made or expressed on a cancer cell, it becomes a really good target for therapy. And this is a new class of treatments called theranostics where we can actually target these cancer cells much more accurately with, in this case, a radioactive payload, so instead of just seeing where the cancer is with imaging, you can actually deliver this treatment.

There are other new advances; for example, the concept of precision medicine, which is one of the things I'm really interested in continuing to develop, has really moved forward a lot. So we've seen it in diseases like lung cancer and breast cancer, of course. We start to define these very broad cancers. Rather than just breast cancer or prostate cancer or colon cancer, we start to divide them by their molecular drivers, and we know that prostate cancer is similar so that, for example, there are so-called HRR or DDR mutations—these mutations like BRCA2 is the most famous for prostate cancer—and patients are sometimes confused. They think, "Well, this is a breast cancer gene." But as you and I both know, in men, it expresses as a higher risk of prostate cancer, and we can translate that higher risk into therapies like PARP inhibitors that work specifically in the roughly 20 percent of men who actually have a mutation in one of these HRR mutations.

Dr. Kuang:

Now you've highlighted LU177 as a great way for us to bridge both imaging and treatment—talking to the oncologists out there and the urologists—how are you integrating that into day-to-day management as you're talking to them for imaging and treatment using the PSMA-targeted strategies?

Dr. Oh:

Well, it's really an excellent question because PSMA imaging is the first step to delivering PSMA-targeted treatment, and the imaging has been developed for decades, but it didn't become commercially available in the US until two or three years ago, but it has completely transformed the way we image patients with prostate cancer. And what PSMA does is, of course for advanced patients with metastatic disease, it

helps us define who might be a good candidate for this type of Lu177 treatment, but it also is used from the very earliest diagnosis in high-risk individuals. So if a man walks in with a high PSA and gets a biopsy and has a high Gleason score, let's say 7, 8, 9, or 10, he will get a PSMA PET scan to assess where the cancer is. I used to do a bone scan. I used to do a regular CAT scan, but now we primarily do PSMA PET/CTs. And what that has done from the beginning all the way through advanced diseases is more accurately and more sensitively tell us exactly where the cancer is, and it's transformed the way we decide what kind of treatments people receive, whether they're receiving radiation or surgery, for example, if the cancer has escaped the prostate. If their PSA is rising after local treatment, that's a common type of failure of primary treatment. We can now see much better than we used to where the cancer is, and we can sometimes target it with focused radiation. And in the patients with advanced metastatic disease, we are using treatments like Lu177 when they become hormone resistant.

Dr. Kuang:

And to drill a little deeper there, with all these advances in imaging, if we can recap, how is it refining your patient selection and the response assessment across these different lines of therapy for advanced prostate cancer?

Dr. Oh:

Well, ironically, there's still a very cheap, quick test we can do to assess response to any treatment, and that's PSA. PSA is a very controversial test, as you know, for screening; although, I think it should be less controversial now. It's a good test to pick up cancer. It doesn't tell you what you should do about it, but it's a very good test to pick up cancer. But the dirty secret of our field is that once you have a diagnosis of prostate cancer, PSA becomes a really critical assessment over that man's lifetime. And what I mean by that is PSA going to undetectable after treatment for local therapy, for example, is a prerequisite to knowing that the cancer has been eradicated after surgery or stays low after radiation. If it starts to go up, then that is when we will actually use this imaging. So instead of imaging triggering something right away, PSA triggers imaging, which then helps us to decide what type of treatment these patients should receive.

So the reminder here is sometimes good old tests, if you use them correctly, can be very insightful and helpful to know what's happening to your patient, so PSA remains a mainstay of monitoring. But then it usually triggers this type of PSMA PET imaging, which has become, again, the standard of care of knowing where the cancer is with the greatest degree of sensitivity.

Dr. Kuang:

For those just tuning in, you're listening to *On the Frontlines of Prostate Cancer* on ReachMD. I'm Dr. Wayne Kuang, and I'm speaking with Dr. William Oh about new technologies, new therapies, and imaging tools for advanced prostate cancer.

Now, Dr. Oh, new therapies often come with new challenges to consider, so how can we navigate treatment sequencing and combination strategies in the metastatic setting?

Dr. Oh:

Really good question, Wayne, because what's really happening is all these treatments that we have are shifting earlier, and what that means is these men are living longer, but they're also exposed to these drugs for longer periods of time. That has an effect on their quality of life. But even more important is down the road, we're running out of treatments, so we have to continue to find things that actually work. If you move everything to the early stage, then what are you going to do when those patients become resistant? And unfortunately, all of these new advances are not curative at this point if you have metastatic disease. We can control the disease, but we can't cure it, so in truth, we still have a lot of work to do about optimizing combination treatments and also the sequencing of treatments.

Dr. Kuang:

And as you said, despite all these advances, there are unmet needs and research gaps. So at your Center for Precision Medicine, how are you trying to address those unmet needs and research gaps?

Dr. Oh:

Yeah. I think the fact is that prostate cancer is still the second leading cause of cancer death in the United States, so if we use that one fact as a metric, then we have to do better. And one of the things we know is that these cancers eventually become very resistant to hormonal therapy. They go through sometimes a process called neuroendocrine differentiation, and neuroendocrine prostate cancer no longer responds to hormonal therapies. And there's a lot of active research going on as to how to target those resistant cells, but that's a clear unmet need. As long as men still die of prostate cancer, we have work to do.

Dr. Kuang:

And thinking for all those oncologists that look to you and your visionary leadership, what are the words of wisdom? How do we stay ahead of the curve when treating these patients with advanced prostate cancer, especially in this overwhelmingly rapidly evolving landscape? Any tips, tricks, strategies? How do we stay ahead?

Dr. Oh:

Yeah. It's so challenging, and I have such respect for generalists who treat many different kinds of cancers. It's so hard to keep up with everything, but I speak around the country at CME talks and, of course, people are listening to podcasts like this and they're reading all the time to learn, and I think the key issue is, whenever you come up across a challenge that you haven't seen before, if you want to get an update, use some of these tools. There are some excellent, reliable evidence-based tools that are out there that can help you to learn. Something called OpenEvidence that's led by *The New England Journal* can help you really do a quick literature search. This is where maybe AI can be really helpful for the average doctor as we're seeing these challenging cases and we're trying to make sure we give the right treatment to each patient.

Dr. Kuang:

Well, thank you for your vision and your leadership, and these are all great comments for us to think on as we come to the end of today's program. And I want to thank my guest, Dr. William Oh, for joining me to discuss how new therapies and imaging tools are reshaping how we treat advanced prostate cancer. Dr. Oh, it was great having you on the program.

Dr. Oh:

Thank you, Dr. Kuang. I really appreciate it.

Announcer:

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