Advanced Prostate Cancer: Immunotherapy Research Update

Emmanuel Antonarakis, MD
Assistant Professor, Oncology
Johns Hopkins School of Medicine

Russell Szmulewitz, MD
Associate Director, Genitourinary Oncology Program; Assistant Professor of Medicine
University of Chicago Medical Center

Joel Nowak, MA, MSW
Patient Advocate and Director, Advanced Prostate Cancer Program
Malecare

Tomasz Beer, MD, FACP
Deputy Director, OHSU Knight Cancer Institute
Oregon Health & Science University

Dr. Beer:
Welcome, everyone, and thank you for joining us. Today we're going to discuss the latest findings from the annual meeting at ASCO.

By way of introduction, I might offer a comment. I think we've had a rich meeting with a lot of new data about biomarkers, predictors of outcome, new information about chemotherapy and some additional information about local treatments and hormonal therapies in prostate cancer. I think we might describe this meeting as one that builds foundations for the future. I'm not seeing major presentation that will dramatically change how we care for men with prostate cancer today.

But a lot of the research that we're seeing at this meeting I think will serve as a basis for future changes in therapy that we expect to see n years to come. One of the major areas of interest at this meeting has been the affirmation and additional data about the new biomarkers that we're seeing that help us better understand the disease and potentially better select patients' treatments on an individual basis.

No area is more compelling, I think, than the ARV7 story that Dr. Antonarakis has played a key role. There were a couple of important presentations on circulating tumor cells ARV7, circulating tumor cell heterogeneity at this meeting. Emmanuel, would you like to comment on those?

Dr. Antonarakis:
Sure. The ARV7 story I think is expanding more and more each year. I think the story broke about two years ago. So the ARV7, an abnormal version of the antigen receptor that we think predicts resistance to the new hormone therapies like enzalutamide abiraterone. The interesting thing is that the data seems to hold up across a variety of platforms for measuring circulating tumor cells. So the Hopkins group used one particular CTC assay, and another group led by Dr. Howard Scher at the Memorial Sloane Kettering used a different assay. The interesting and important thing is different assays measuring the same ARV7 showing the same results.

And that really speaks to the credibility and the importance of the biomarker. The main findings, I would say to summarize them, are that patients that have ARV7 in their circulating tumor cells appear to respond less well to drugs like enzalutamide and abiraterone. But they may still have some sensitivity to chemotherapy agents such as taxanes, docetaxel and cabazitaxel. And I think that data is beginning to accumulate and emerge. Within the next six months, I think that there will be some commercially available biomarkers to test for this abnormality so that patients can be tested.

Dr. Beer:
Joel, can I turn to you? Why is this important for patients?

Joel Nowak:
A lot of us are feeling frustrated, because we go into a treatment, and we're not aware if it's going to help us or not, have any effect. We're pretty much sure that we're going to have some sort of side effect, and it's hard to pay the price of side effects without knowing there's going to be a positive flip on the other side.

So having biomarkers that we're able to use to predict whether perhaps a treatment is going to be effective, and also to know how long it's going to be effective because right now, we give somebody a treatment and it's not always so clear as to when that treatment may have stopped working. And getting a better handle on when it's appropriate to move onto another treatment is really going to be important. So this, for me, is one of the more exciting things that I've heard at the meeting.

Dr. Beer:
Another area that the field is very interested in is DNA repair defects. Would you like to introduce the audience to the concept? Why are we interested in this, and what's happened at this meeting?

Dr. Szmulewitz:
Let me start off by giving a very top-line explanation of what it is, DNA repair, and how it gets altered and what the implications of that are. So as part of the cells' process to make more cells, it's got to make more DNA. And in that process, there are occasional errors that come up or breaks in the DNA that come up.

And there are certain processes within all cells whose job it is to repair that damage. And there are a host of enzymes, a host of proteins or mechanisms that work together to make that possible within a cell; not just a cancer cell, any regular cell. What we know is that cancer in general sometimes is predisposed to have mutations or changes in these DNA repair genes, and that allows them to then accumulate other mutations that makes them more aggressive or grow and live despite other cues that tell them not to.

However, what we are now learning is that in prostate cancer, these mutations, these DNA repair mutations, may also make them more sensitive to a specific type of therapy called PARP inhibitors. It's an exciting time in that field.

We've been talking about how do we make cancer care more precise for our men with prostate cancer, how do we refine and give the right therapy to the right patient? And I think that this development might be one of the first times in which we have, I think, more clear evidence of who might benefit from a very specific therapy.

So to be more specific, a new drug called olaparib, which is a PARP inhibitor, was recently shown and published in a large Phase II trial that in patients who have mutations in very specific DNA repair genes, some of those like BRCA-1 and 2, we knew about and are very commonly known in the lay community; some of them such as ATM or other enzymes in that pathway, regardless, patients who had a mutation in that had a very, very high—nearly 90 percent—response rate.

Whereas if you didn't, it was much lower. So it offers the potential hope that if we detect these mutations, we might be able to target that biology and create lethality with this medication.