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/project-oncology/prostate-cancer-care-improving-hormonal-therapy-sequencing-post-treatment-intensification/17903/

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

Prostate Cancer Care: Improving Hormonal Therapy Sequencing Post-Treatment Intensification

Announcer:
You're listening to *Project Oncology* on ReachMD. On this episode, we'll discuss sequencing hormonal therapies after treatment intensification in patients with prostate cancer with Dr. Zachery Reichert. Dr. Reichert is a Clinical Associate Professor and medical oncologist at University of Michigan Health. He also presented a session on this exact topic at the 2024 ASCO Genitourinary Cancers Symposium. Let's hear from him now.

Dr. Reichert:
So our session really focused on how do we approach a patient who has disease that's showing biological patterns of being very challenging. So we used a case-based discussion focusing on a patient who had widespread metastatic disease at diagnosis of their prostate cancer and then was treated with what we would call triplet therapy of hormonal therapy with ADT, chemotherapy for six cycles with docetaxel, and then also an oral agent like darolutamide until progression. And this patient then progressed though within 18 months with both a slight PSA rise and also pain. So the question then to all of the colleagues and I was how would we approach this patient with early failure of hormonal and systemic therapies?

Because we discussed treatments such as chemotherapy, hormonal therapies, external beam radiation, radiopharmaceuticals like radium or lutetium PSMA, and even potentially PARP combinations, my focus was on the use of alternate hormonal therapies or chemotherapy. The major issue we have with alternating hormonal therapies is the resistance patterns to one hormonal therapy often can be carried to the next hormonal therapy, thereby decreasing the likelihood of response. Using data from prior studies, most patients do not respond to switching of oral hormonal agents: for example, from abiraterone to enzalutamide or enzalutamide to abiraterone or even some ARSIs like enzalutamide to apalutamide or darolutamide. Looking backwards, the response rate for those patients is typically under 20 percent if you take them all together or 4 percent for switching to abiraterone or maybe 30 percent for switching to an enzalutamide after abiraterone. For this patient that we were discussing who was having pain as a symptom of their progression, these likelihood of responses are too low to really be a good use for the patients.

So if we're not looking at hormonal therapies as being good options, chemotherapies would be another thing that we would consider. There is a study that looked at comparing using another hormonal agent or using chemotherapy, and that was called the CARD trial. Now all patients in that study had received docetaxel typically in the resistant setting and also an oral ARSI in the resistant setting, so it's unclear if that actually translates to patients who develop resistance in the hormone-sensitive phase, as our patient is in this case.

Regarding that though, I do think it's reasonable because 70 percent of patients in that study actually had pain when they entered the study, and when we look at the patients that received hormonal therapy, only 19 percent of them had any improvement in pain while 45 percent had improvement in pain with using a chemotherapy. So for patients with pain who are progressing on an oral agent, you need to switch to a different agent, like chemotherapy. Now which chemotherapy is a good question because you could reuse docetaxel again because you stopped it—not because of resistance, but because of a planned duration. We, unfortunately, don't have a lot of prospective data looking at it, but it does seem in retrospective studies that only about 20 percent of patients respond to docetaxel when it's used again in the resistant setting. Looking then at cabazitaxel as an alternate chemotherapy, that response rate does seem to be closer to 40 percent to 45 percent, such that, again, looking at a patient who is having symptoms and has had a fairly short duration of control with using hormonal therapy and chemotherapy up front, moving to a different chemotherapy like cabazitaxel seems the most reasonable.

But one important thing to consider also when looking at chemotherapies would be what side effects are expected from those

chemotherapies. So docetaxel and cabazitaxel actually compared head-to-head in the first-line setting in CRPC in the FIRSTANA trial that was published. Now that study showed that they both were equally effective in patients who had never received chemotherapy before, but the side effect profile was very different. And especially thinking of a patient who received docetaxel in the hormone-sensitive phase, their likelihood of having neuropathy with rechallenge with docetaxel is probably higher than naïve, and 25 percent of patients had Grade 1 or 2 CTCAE neuropathy with docetaxel in the upfront setting while only about 12 percent did with cabazitaxel. And as that's a permanent side effect, I think that's an important thing to consider as we think about the chemotherapy choice also at this stage.

One last thing to also consider is ultimately what other adjunct therapies are critically important for this patient. Two big things to highlight would be external beam radiation can very safely be done with these chemotherapies and has a very good chance of symptomatic control, and also, bone-supporting agents like bisphosphates or rank ligand inhibitors have been shown to decrease both pain and risk of fracture in the future and often, fortunately, been underutilized in practice. So using those supportive care therapies also are highly important to consider for this patient.

So it's critically important to remember that this is a patient who's progressing with pain and with a very early progression of their disease such that we need to make rapid decisions fast and also not use therapies that have a low chance of success. So chemotherapy is clearly superior in this kind of scenario versus an alternate oral agent. And then also it's very important to use all of the tools available to us to improve pain and the quality of life of our patients such that external beam radiation should also be considered concurrently and also bone-supportive agents to prevent these issues happening for this patient in the future.

Announcer:
That was Dr. Zachery Reichert talking about his presentation at the 2024 ASCO Genitourinary Cancers Symposium that focused on sequencing hormonal therapies after treatment intensification in patients with prostate cancer. To access this and other episodes in our series, visit *Project Oncology* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!