9-2022

Roundtable discussion: 68-year-old man with mHSPC

Jason M. Hafron

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MODERATOR
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Hafron is chief medical officer and director of clinical research at the Michigan Institute of Urology in Troy and West Bloomfield, and a professor of urology at Oakland University William Beaumont School of Medicine in Royal Oak, Michigan.

PARTICIPANT LIST
(in speaking order)
Mark G. Delworth, MD
Michael A. Gorin, MD
Walter Z. Falconer, MD, FACS
Daniel Voglewede, MD, FACS
Elizabeth K. Chadwell, MD
Pratik S. Desai, MD

Urology Times®' Case-Based Roundtable program encompasses peer-to-peer discussion of clinical cases. This case involves a 68-year-old man with metastatic hormone-sensitive prostate cancer (mHSPC) with vertebral metastases. His pretreatment prostate-specific antigen (PSA) level is 32.6 ng/mL, his hemoglobin level is 9.7 g/dL, and he has elevated liver function test (LFT) results. Comorbidities include congestive heart failure, diabetes, and hypercholesterolemia, all controlled with medication. The patient is started on androgen deprivation therapy (ADT). Six months after initiation of therapy, his PSA is undetectable. Eighteen months later, he reports persistent and worsening back pain. Imaging, CT, and bone scan show progression of existing vertebral lesions and 3 new bone lesions. His PSA level has risen to 29.4 ng/mL.

The following discussion has been edited for brevity and clarity.

HAFRON: Any comments regarding the [treatment] of this patient?

DELWORTH: I wouldn't have used hormone therapy alone initially as monotherapy, I would've put him on combination therapy initially. He's got a PSA [level] of 32 ng/mL with vertebral metastases, so I would've put him on some sort of hormone agent. I would probably go with Orgovyx [relugolix] in this situation to avoid cardiac toxicity. Then I probably would've gone with Xtandi [enzalutamide]. For whatever reason, I try to avoid prednisone with folks with diabetes. I would've managed this patient differently from the get-go; I would've put him on dual agents.

HAFRON: I totally agree. Current NCCN [National Comprehensive Cancer Network] guidelines, since 2015, recommend combination therapy—ADT plus novel hormone therapy or ADT plus docetaxel. We just published a paper and studied the rates of combination therapy with urologists in the United States, and they used combination therapy only 12% of the time. There's a big gap in knowledge in this space among urologists. It shows up in this case. ADT monotherapy is no longer acceptable. These patients have to be treated with combination therapy.

GORIN: I agree, but this patient is challenging because of his medical comorbidities, which include heart failure and diabetes. Additionally, he has anemia and elevated LFTs. As a urologist, I start to become uncomfortable [treating] these more medically complex patients on combination therapy. These patients are likely better served with treatment by a medical oncologist.

HAFRON: That's a reasonable point. I think in our clinic we would manage this patient. I don't think this would be an immediate referral. We'd be comfortable, but we treat a large amount of these patients.

I think the other point that should be brought up is we need to determine the volume of metastatic disease. Unfortunately in this case, we don't know the volume of vertebral metastasis. If it is low-volume metastasis, he could be considered for local therapy with primary radiation therapy. Either way, this man was mismanaged initially. It's commonly done in this country.

He then receives abiraterone and prednisone, has stable disease, then he recurs. His PSA [level] is 65 ng/mL. He has radiographic progression in his bone, so he is up to maybe 5 lesions. He basically has metastatic castration-resistant prostate cancer. He has failed his first line of therapy. Molecular testing is performed on an archival tumor sample from his initial biopsy, using FoundationOne CDx. From the archival primary tumor, they found a *BRCA2* mutation in the original tumor biopsy. They later confirmed it to be a germline mutation. Do you order germline testing when a somatic *BRCA1* or *BRCA2* is discovered?

FALCONER: To me, has the question been answered and does it change what I would do? To answer your question, sometimes maybe and sometimes not. I think having the mutation that's there, even though it's in the somatic form, is it going to change my treatment? I don't know the answer to that. I presume that it would not. I think I'm still going down the path of a PARP inhibitor with this patient. I don't know. I do know we've had some issues with insurance paying for this additional kind of testing when we have this.

VOGLEWEDE: I truly do not know if the incidence of *BRCA2* mutations in the primary tumor [is] not inheritable. If you turn it around and you have somebody that has a negative germline but has a positive somatic, well, I don't have to worry about the family, but if it's the other way around, I am concerned about whether this is inheritable disease or not, because it can affect men and women if it's a *BRCA1/2*, for instance.

HAFRON: Dr Voglewede, you hit the nail on the head. Basically, if you find a somatic *BRCA2*, I agree with Dr Falconer, it's not going to change your management. But we are obligated to look [to see] if this is inherited, because this finding could affect his son, daughter, or any of his other family members. If it is inherited, obviously we want to get him to genetic counseling. The genetic counselors will have to perform cascade testing on his family. It won't change what we do, but it could affect his family members. For those who would consider a PARP inhibitor, if the mutation was a non-*BRCA* like an *ATM* or a *CHEK*, would that change your recommendation for this patient?

VOGLEWEDE: Olaparib [Lynparza] is approved for *ATM* if I remember correctly, so that's what I would consider.

HAFRON: You're totally correct. Olaparib is approved for *ATM* mutations and 13 other homologous recombination repair mutations. It's on their label.

DELWORTH: We [use that] as well. It may not respond as well, but I [also use that].

CHADWELL: How do you decide which one to use if you have a [patient with] *BRCA1* or *BRCA2*?

HAFRON: I mostly would use olaparib, to be honest with you, because rucaparib [Rubraca] is approved in the [patient] post chemotherapy and I have very little experience with this drug. Most of my experience is with olaparib and [patients with] *BRCA1* and *BRCA2*. We know based on the PROfound trial [(NCT02987543) data that] patients with homologous recombination repair mutations will respond very well to olaparib. I'm very comfortable using PARPs in this space. Based on the results of the PROfound trial, *BRCA2*-positive patients respond really well to olaparib. Dr Desai, what are you or your partners doing?

DESAI: We have had a few patients on olaparib, but to be honest with you, [even with] as much testing as we've done, I still have a hard time reconciling that up to 30% because that's not what we're seeing. I don't know how to reconcile that difference. Maybe we're doing it earlier. Maybe we're doing it on patients who do not need the testing. That's been the biggest disconnect for me.

HAFRON: That's a good point. I've heard that multiple times. That 28% they found in PROfound, most people aren't finding in their practice.

DESAI: We're at about 10% whenever I look at our numbers. ●