I. Questions --- Shevrin & Stadler

Participant

Is there a difference between Lupron and Zoladex?

Walter Stadler, MD

All of these drugs cause castration, and whether one gives a medication to cut down the testosterone or one removes the testicles, it has the same effect. In fact, I would argue that if we want to save a billion dollars in this country on Medicare, everyone with advanced cancer should have surgical castration because it's a one-time procedure. We would save millions of dollars with LHRH agonists that cost a ton of money.

Daniel Shevrin, MD

Intermittent therapy would also be an alternative in terms of cost.

Participant

You said that radiation reduces pain. Is it also curative?

Daniel Shevrin, MD

It reduces pain when you irradiate a bone lesion, but that is not curative. Once the tumor has spread to bones, it is by definition not a curable situation. It is a situation that we hope to manage for many years and really treat as a chronic disease, but it is not curative. The only place that radiation is curative is for treatment of the primary tumor.

Participant

For a patient who has been on standard hormone therapy in which the PSA has been controlled but now begins to rise, would the next best thing to move to be Abiraterone?

Walter Stadler, MD, FACP

The logic for that would be in some ways correct. There is a large phase III trial looking at that question specifically, and that trial has completed accrual. We are awaiting the results. The short answer is it has the potential, but we are waiting on the data. In essence we are asking a sequencing question because most of these patients are likely going to get both docetaxel and something like Abiraterone. The question really is the sequence, and I don't know the answer to that. I suspect that the trial that has just been completed is going to positive. I suspect we are going to be spending a lot of time debating the appropriate order of these drugs. I just will point out, however, that docetaxel is not as bad as some people might think.

Participant

Regarding the white blood cells that are necessary for Provenge therapy, what about the order of Provenge? Should you use that before giving the patient chemotherapy, or does that compromise the white cells?

Walter Stadler, MD, FACP

In the phase III trial, about two-thirds of the patients had no prior chemotherapy. About one-third had prior chemotherapy. There was no differential benefit in patients who did or did not receive prior chemotherapy so it doesn't seem to make a difference. That being said, our practice has been to typically use this agent prior to chemotherapy because our practice has generally been to use chemotherapy in patients who have had at least some symptoms and to use the Provenge on patients who have metastatic disease but no symptoms.

Daniel Shevrin, MD

I don't think there is any data that it's going to interfere with later treatment at all in terms of white blood cells. It's a treatment that is extremely well tolerated, and therefore it's a very nice option for men who are progressing in whom we really don't want to proceed with chemotherapy. I agree that one thing I sometimes worry a little bit about is that chemotherapy with an extremely effective agent, Taxotere, is kicked further down the road with these agents. My fear is that when a man really needs Taxotere that window is closing.

Participant

If a patient fails Lupron, what are the various sequential steps for treatment?

Walter Stadler, MD, FACP

First of all, we always consider the availability of clinical trials and whether the patient should get treatment or should be observed for a while before going to the next treatment. With those caveats, we tend to add an anti-androgen, withdrawn an anti-androgen, think about Sipuleucel-T, think about Docetaxel, tend to jump toward Abiraterone and then think about something like Cabazitaxel.

Daniel Shevrin, MD

As I listed, we have a number of choices, and some of it really does depend on the particular patient's disease characteristics. You can tell pretty early on how hormonally sensitive the cancer is. If you try Casodex and the PSA drops and you get a good response for six to nine months, then you may use Flutamide or Nilutamide. I use ketoconazole in relatively low doses, sometimes even without cortisol. Then you can use something like Provenge. So, sometimes a man who demonstrate sensitivity to hormones can be treated even with advanced disease for quite a long time.

Now, if the Casodex worked very briefly or not at all, then we realize that we have a different situation and you're not going to use Flutamide or Nilutamide and you'll move a little bit more quickly to other agents, maybe Provenge. The trick with Provenge is that because you lose PSA as a marker, it puts the onus on the oncologist to monitor a man in other ways. Even scans become problematic because many can progress on scans and it's still working.