“Review of Eric Hall's Case” (Eric Hall) [#34]

Eric Hall, Brad Power
November 16, 2022

“The medical oncologist and the radiation oncologist were really against the PSMA. They were transparent, and said they thought he would be high volume based on the Gleason 10 and PSA of 146. If we did the PSMA, it would show high volume, and that would essentially take radiation off the table in their opinion. We disagreed with them that if it was high volume, we wanted to know that it's high volume, and if that did take radiation off the table, then it did, but not to say we didn't lose a lot of sleep about that decision.” – Stephanie Hall

“My big question is: what is the value for me to skip over the standard of care things of surgery and radiation and try to go straight to one of these more targeted drug approaches?” – Eric Hall

Meeting Summary

Eric Hall is a prostate cancer patient, currently on his first line of treatment of androgen (hormone) deprivation therapy and facing a decision on what to do for his next step of treatment. Eric’s situation is unique because from his initial diagnosis he was faced with a very aggressive cancer which didn’t fit well with the standard approaches codified in the “standard of care” (the NCCN guidelines).

The community we have built in the Prostate Cancer Lab has discussed the cases of several advanced prostate patients. The community is a diverse crowd composed mostly of engaged and educated advanced prostate cancer patients, and also including molecular biologists, bioinformaticians, and clinicians. We call this patient case review a “hackathon”. Eric shared his medical history, treatment options, strategic considerations, and leanings, and solicited feedback.

What is Eric Hall’s medical situation?

Eric was diagnosed with “de novo” (at diagnosis) “oligo-metastatic” (cancer cells have traveled from the original or primary prostate tumor site to form a small number of new tumors in one or two other sites) prostate cancer in July 2022 at age 50. Eric's cancer was very unique. The cancer was advanced, as measured by a PSA (prostate specific antigen, the biomarker that measures prostate cancer activity) of 146, and “Gleason” 10. (The lowest Gleason score is 6, which is a low-grade cancer. A Gleason score of 7 is a medium-grade cancer, and a score of 8, 9, or 10 is a high-grade cancer.) His cancer has spread beyond the prostate capsule, but not out of the pelvic area. His tumor measured 4x5 cm, abutted the rectum and pelvic floor, and involved the soft tissues. Eric’s doctors were hesitant about getting a scan to look at the spread of his cancer, assuming that it would show widespread metastasis, given his high PSA and Gleason scores, but relented. They were quite surprised to not see more metastatic sites. His medical diagnosis is “oligo-metastatic; nodally advanced; locally advanced.” It’s metastatic (has spread beyond the prostate), but not too far, which is a rare in-between condition.

In terms of biomarkers, Eric has an “ALK fusion (ALK:DTNB)”. ALK is anaplastic lymphoma kinase, and a fusion is a chromosome mutation. This ALK fusion is extremely rare in prostate cancer, yet is common in other cancers, especially non-small-cell lung cancer. Further testing revealed additional biomarkers: a CHEK2 mutation and high expression for AR and FOLH1 (PSMA) proteins.

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Since his diagnosis four months ago, Eric has started two types of androgen deprivation therapy (Orgovyx - Relugolix and Zytiga - Abiraterone) along with a steroid (Prednisone). In addition to medical treatments, Eric has been very active in researching and implementing many lifestyle changes to heal his cancer, boost his immune system, and detoxify his body, including switching to a vegan diet with fresh-pressed vegetable juices and intermittent fasting, taking several supplements, such as mushroom powders, TUDCA, melatonin, and CBG, and cutting out alcohol and soda. He has increased his exercise.

What treatment options is Eric considering?

Eric is considering two categories of treatment options: standard of care physical treatments (surgery and radiation) and targeted drugs.

Since Eric got the PSMA scan and his recent MRI scan which showed relatively local containment of his cancer, surgery and radiation are treatment options. (Had Stephanie and Eric not pushed to get the PSMA scan, the surgery and radiation options would have been off the table – another example of the importance of active patient and caregiver engagement in testing and treatment decisions.) Under standard of care treatment options, Eric is considering:

- Surgery followed by targeted radiation (IMRT - Intensity-Modulated Radiation Therapy)
- High-Dose-Rate (HDR) brachytherapy (radiated rods placed near the tumors for about ten minutes) followed by targeted radiation (IMRT)
- Open surgery followed by wait and see

As with other patients who are actively engaged with the Prostate Cancer Lab, Eric has received targeted drug recommendations from his medical team (Mayo), Massive Bio, CureMatch, and Cancer Commons. Under targeted drug options, Eric is considering:

- Drugs targeting his ALK fusion (such as ceritinib, alectinib, and brigatinib) – which would need to be delivered off label since Eric is not metastatic, which is a requirement for existing clinical trials
- Functional testing of drugs (which requires live tissue)
- Drug combinations, such as a triplet therapy (e.g., Lupron, chemo, and abiraterone)
- Three clinical trials (from Massive Bio), of which two are for metastatic castrate resistant patients, so not exactly a fit, and the third one is a phase one and two trial, so early in the trial process.

What thoughts did the Prostate Cancer Lab community have for Eric’s treatment decision?

Eric’s main questions were whether he should (1) skip the surgery and radiation options and go straight to one of the targeted drug approaches, and (2) which of the two preferred physical treatment options, surgery plus IMRT or HDR brachy plus IMRT, is better.

The discussion exposed many tradeoffs, which came down to a judgment call depending on Eric’s (and his wife Stephanie’s) intent. He would like to choose a treatment that has a good chance of resulting in a cure now versus a treatment option that is not as effective now but could provide guidance for future treatment options.

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Surgery is attractive. With more treatment, his tumor might shrink even more. Surgery may have fewer consequences than radiation to his prostate. Surgery can remove the tumor tissue and get tissue for functional testing. There was an endorsement of getting functional testing, if adequate fresh tissue is available, and using multiple functional testing sources (e.g., SEngine, Nagourney, Tempus).

But surgery is less effective than high-dose-rate brachytherapy plus IMRT, according to research and anecdotal success stories from patients. Choosing the brachytherapy option now has the best chance at a durable response, and if the cancer recurs and tissue is needed for a targeted therapy, Eric can get tissue from where it recurs.

The targeted drug combinations and clinical trials have access, efficacy, and dosing issues.

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Meeting Notes

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SUMMARY KEYWORDS

surgery, tissue, drugs, cancer, metastatic, tumor, scan, prostate, question, eric, couple, chemo, slide, point, patients, gleason, treatment, medical oncologist, triplet, months

SPEAKERS

Eric Hall (44%), Jonathan Starr (14%), Emma Shtivelman (13%), Stephanie Hall (9%), Brad Power (7%), Anonymous Caregiver (5%), Richard Anders (3%), Jim Ward (3%), Mike Yancey (2%), Rick Stanton (1%).

Eric Hall:



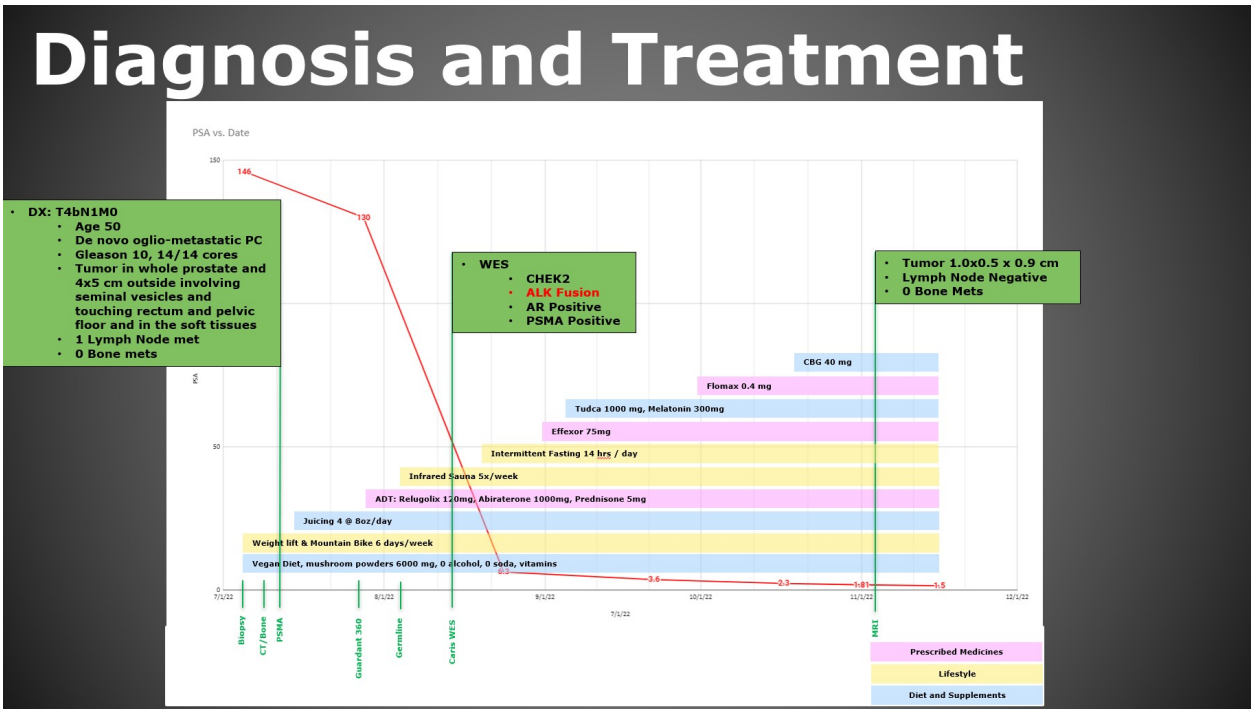
I put together a slide deck to walk through all the data that I have received from various sources to guide our discussion.

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I’m new to the Prostate Cancer Lab and wanted to share a brief intro into my life and family. My wife Stephanie is on this call today and has been the most amazing partner I could ask for in this journey as she has been by my side every step of the way in this journey and is often 2 steps ahead of me. We have been together for 25 years and live in Chapel Hill, North Carolina. We have two boys, Owen, and Andrew. Owen is 13 and Andrew is 25, and he lives in Brooklyn, New York. I am 50 years old with an advanced diagnosis of prostate cancer. I am a very active person whose top three hobbies are family, fitness, and photography, and you can see many photos representing those areas on the slide. Additionally, I love to make things in many media, such as photography, woodworking, 3D printing, home projects, etc. Professionally, I am a Digital Product Manager for John Deere and have been with the company for 22 years with a background in Mechanical Engineering.

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I have compiled the important parts of my diagnosis and treatments into this one slide. The timeline is not very long as I was just diagnosed 4 months ago in July 2022. In the background, the red line, is my PSA over the months. The green tick-marks and lines along the timeline are medical tests I have had and their results. The bars represent treatments I am doing for the period of time indicated by the length of the bar, pink bars are prescription medicines, blue is diet and supplements, yellow is other lifestyle treatments.

At diagnosis my PSA was 146. I did not have any noticeable symptoms, and my PSA was checked at my 50-year-old physical. Within the next 3 weeks I had a blind 14 core biopsy, chest CT scan, nuclear bone scan, and PSMA scan. The results of all of these defined my diagnosis as T4bN1M0, meaning de-novo advanced stage 4 prostate cancer with 1 pelvic lymph node involved and 0 bone metastasis. Additionally, the biopsy showed that my prostate was completely filled with cancer, as all 14 cores contained 60-100% cancer cells, all rated Gleason 9 or 10. Also, the scans showed a tumor extended beyond the prostate capsule measuring 4x5cm and abutting the rectum and pelvic floor and involving the soft tissues. Doctors were quite surprised to not see more metastatic sites given the high PSA and Gleason scores and thus have diagnosed me with several terms; olgio-metastatic; nodally advanced; locally advanced.

Since diagnosis, I have had three genetic/genomic tests.

1. A saliva germline test from Color.com (through the PROMISE study), which showed that I have a heterozygous CHEK2 germline mutation. CHEK2 is a gene responsible for copy repair of bad genetic copies, thus with this mutation my body is not as effective at repairing or eliminating bad copies of genes. The Guardant360 liquid biopsy did not show any actionable mutations.
2. I also had Whole Exome Sequencing done on my tumor biopsy cores thru Caris Life Sciences. WES showed the CHEK2 mutation again along with high expression for Androgen Receptors (AR) proteins as well as FOLH1 (PSMA) proteins. The most surprising result of the WES is that his tumor has an ALK fusion (ALK:DTNB). ALK is

anaplastic lymphoma kinase, and a fusion is a chromosome mutation. This ALK fusion is extremely rare in prostate cancer, yet is common in other cancers, especially non-small-cell lung cancer.

3. Finally I had an MRI taken 2 weeks ago that showed significant volume reduction of the tumor outside the prostate capsule, and this has opened up some more treatment options.

This slide also shows the various treatments I have done in these short four months. Medically on July 28, I started two types of androgen deprivation therapy (ADT), taking Orgovyx (Relugolix) and Zytiga (Abiraterone) along with Prednisone (a steroid) daily. I also started taking Effexor for anxiety and hot flashes, as well as FlowMax for nighttime urination.

In addition to medical treatments, we have been very active in researching and implementing many lifestyle changes to heal my cancer and boost my immune system and detoxify my body. Almost immediately after diagnosis, I switched from a fairly heavy animal protein diet to a vegan diet, which is mostly whole foods, plant-based, and I love the diet and have no plans to ever switch back. In addition to the vegan diet, I have also begun taking several supplements at this time including high doses of mushroom powders (turkey tail, reishi, lion's mane) and cut out alcohol and soda. I was an avid exerciser prior to diagnosis, and I have maintained this activity of mountain biking and even increased my weight lifting to counteract the muscle loss which is normal on ADT. I have also been drinking 32 oz. of fresh-pressed vegetable juices each day. I have had some issues with liver enzymes skyrocketing. I have begun doing infrared sauna five times a week and taking TUDCA (Tauroursodeoxycholic Acid) supplements daily. (TUDCA, is a soluble bile salt that can counteract the toxicity of regular bile acids when the latter are backed up in the liver.) I have worked up to doing 14 hours of intermittent fasting each night. I am now taking high doses of melatonin as a highly potent antioxidant, as it prevents the cancer from spreading. Most recently I started taking 40 mg of CBG oil daily. CBG is an individual isolate of the full spectrum CBD and is known as the anti-tumor isolate. (CBD, or cannabidiol, is the second most prevalent active ingredient in cannabis (marijuana). While CBD is an essential component of medical marijuana, it is derived directly from the hemp plant, a cousin of marijuana, or manufactured in a laboratory. One of hundreds of components in marijuana, CBD does not cause a "high" by itself.)

My lifestyle changes are a large part of his treatment plan and I believe are a major contributor to his significant PSA and tumor size reductions along with feeling minimal side effects from the ADT and I plan on continuing the majority of these lifestyle changes going forward forever at least at a maintenance dose or frequency.

Rick Stanton:

Where is the lymph node metastasis?

Eric Hall:

It's in the pelvic area. I don't know off the top of my head exactly which one. In part of my treatment, some doctors have called me metastatic and some have not. They've called me locally advanced or notably advanced because it's just one lymph node in the pelvic area. And of course, there's some soft tissue in the pelvic area also, because that tumor is also outside of the prostate capsule.

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Rick Stanton:

I'm not a doctor or a medical professional, but in my experience, from what I've seen, your case is called locally advanced, rather than metastatic. It's a label. At least you don't have a bunch of bone mets in your clavicle or something like that. Hopefully your treatment can be confined to a smaller area.

Eric Hall:

That's it. I'm hoping. I do feel lucky about that. Honestly, we had the PSMA scan done within the first three weeks of diagnosis, and that's pretty unheard of, from what I've learned now. The doctors didn't want to give me that test. I learned that they were thinking that it was just going to light up everywhere. They were afraid of what it was going to show. It was a big surprise with a PSA of 146 and Gleason 10, that I didn't have more metastasis show up. Don't get me wrong, I'm not complaining about that. That's part of what makes my case a little bit unique. One of the challenges I faced is that I'm in an in-between area with this oligo-metastatic diagnosis. I'm not fully metastatic, I'm not fully just contained in the prostate, and a lot of the studies and data and trials go to one of those two things. I kind of sit in between the two of them.

Rick Stanton:

As I'm sure everyone else is thinking, I'm extremely impressed with what you have accomplished and what you did in this short period of time. I've been dealing with this for eight years, I've been in various support groups, and I've never seen anyone else who has done as much research and imaging and everything else in such a short time. It is pretty astonishing.

Jim Ward:

Eric, who is your primary treater?

Eric Hall:

This is a good question. In addition to this, I have been to the University of North Carolina, Duke, John Hopkins, Mayo, and Atrium Health. I’m with Mayo and a local medical oncologist at Atrium Health. Dr. Kwon is a medical oncologist and Dr. Phillips is a radiation oncologist at Mayo.

Richard Anders:

How did you get them to do the scan?

Eric Hall:

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A minute ago I was going to give a huge shoutout to my wife, Stephanie, when you said about getting all this stuff done. A lot of this has been on her shoulders, and she was super convincing and persistent to get this scan done. She said, “This is what we really want.”

Richard Anders:

What did the scan show you that was helpful, as opposed to if you had waited for it? What was your positive deliverable from getting the scan sooner?

Stephanie Hall:

It was at Duke that the medical oncologist and the radiation oncologist were really against the PSMA. They were transparent, and said they thought he would be high volume based on the Gleason 10 and PSA of 146. If we did the PSMA, it would show high volume, and that would essentially take radiation off the table in their opinion. We disagreed with them that if it was high volume, we wanted to know that it's high volume, and if that did take radiation off the table, then it did, but not to say we didn't lose a lot of sleep about that decision.

Rick Stanton:

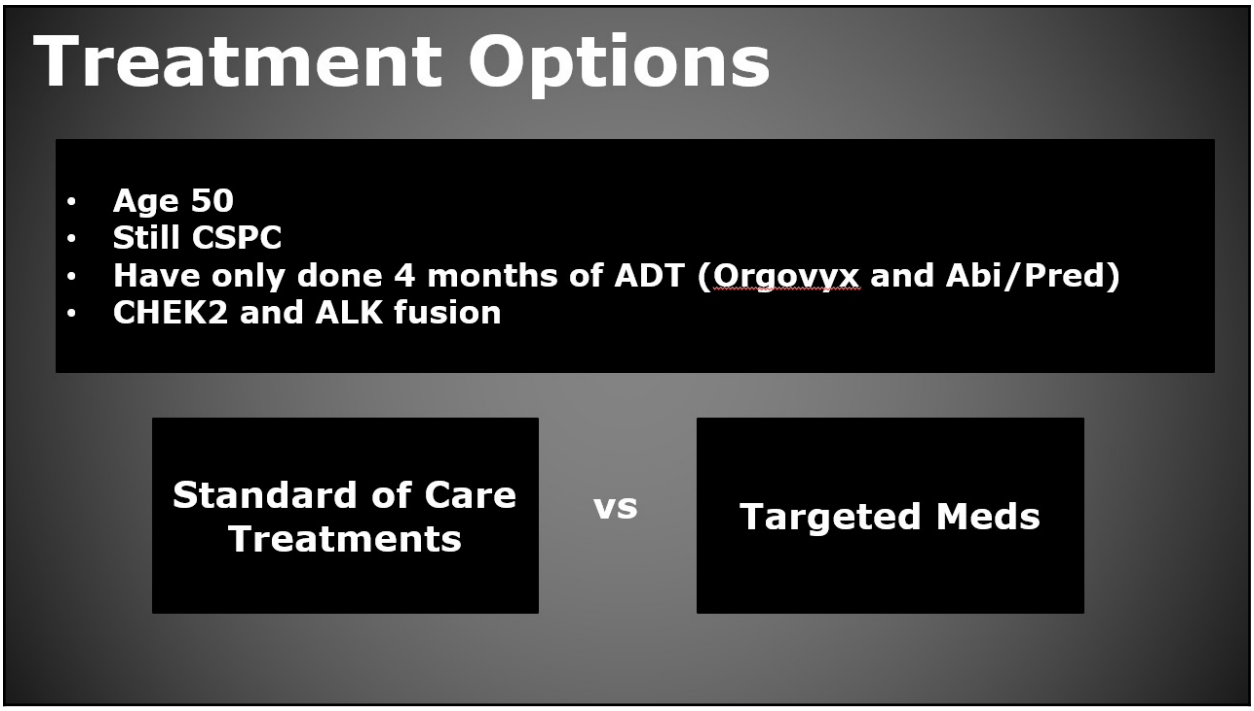
The slide showing all of your medical journey is fantastic. I've been thinking about how to incorporate things besides the prescribed medicines, your lifestyle and diets, date and supplements. I'll probably try to take this concept and evolve it a little bit because I've been seeing Dr. Dawn Lemanne, who's an integrative oncologist, and hopefully I'm about to learn from a battery of blood tests and other assessments of my state what she would suggest. So far the testing and the blood work she's had me do at Quest is well beyond anything a medical oncologist is looking for. I'll be very interested and happy to share.

How did you come about these diets and supplements? And the lifestyle question would be about the infrared sauna. I have no idea what that's about.

Eric Hall:

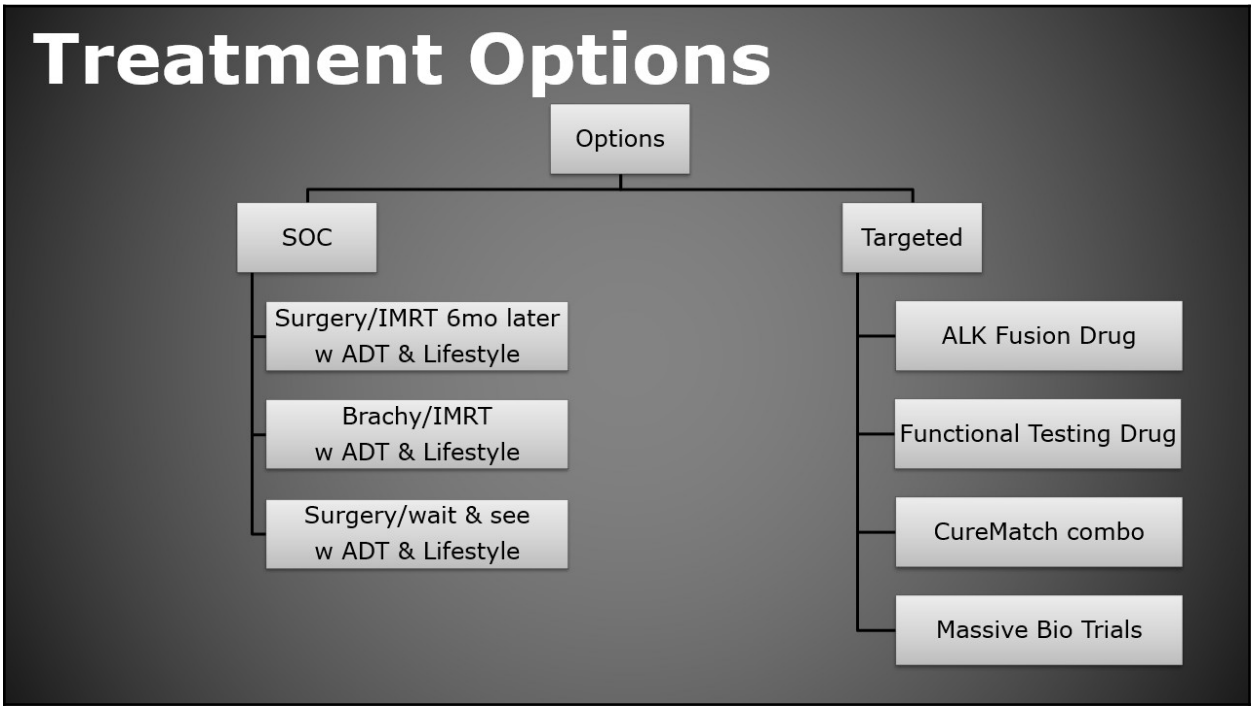
I anticipated I might get some questions about this. I will come back to that after I get through the rest of my story.

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I'm 50. I'm still pretty young. I still have castrate-sensitive prostate cancer. I've only done the four months of hormone meds plus all the lifestyle things. And of course, I found the CHEK2 and the ALK fusion.

This leaves me with two treatment options: standard of care treatments and targeted medicines.

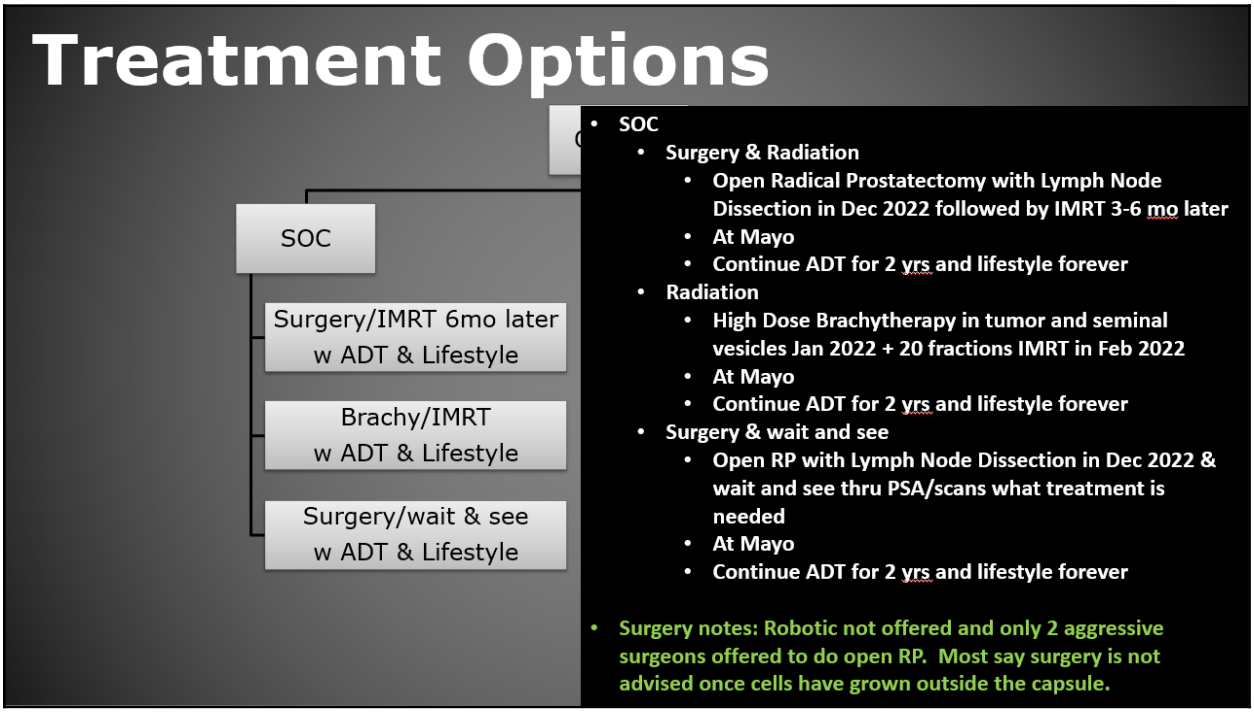


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I see two buckets of options, as you can see in this flowchart. I'll dive into each of these boxes in more detail in the next slide.

Under the standard of care options I am considering:

1. **Surgery followed by IMRT**. Because the MRI showed that my tumor has shrunk, I'm now a candidate with a couple of surgeons. Most of the surgeons I have spoken to have said I'm not a candidate for surgery. The surgery would be followed by IMRT (Intensity-Modulated Radiation Therapy manipulates photon and proton beams of radiation to conform to the shape of a tumor) about six months later. This would be an open surgery. Of course, I would continue the hormones and the lifestyle.
2. **High dose brachytherapy plus IMRT**. (Brachytherapy is a form of radiation therapy where a sealed radiation source is placed inside or next to the area requiring treatment. Brachy is Greek for short.) A lot of people are familiar with low dose brachytherapy, which is also known as the brachy seeds, where they implant low-dose radioactive seeds in you that remain radioactive for many months. What I'm talking about here is high-dose brachy, which is where they insert hollow needles into the tumor, and then they insert radioactive rods into those hollow needles. They leave them in place for 10 or 15 minutes and take them out. It's an outpatient procedure, and then you come back a couple of weeks later to do the IMRT.
3. **Surgery and wait and see** what happens and determine next steps from there.



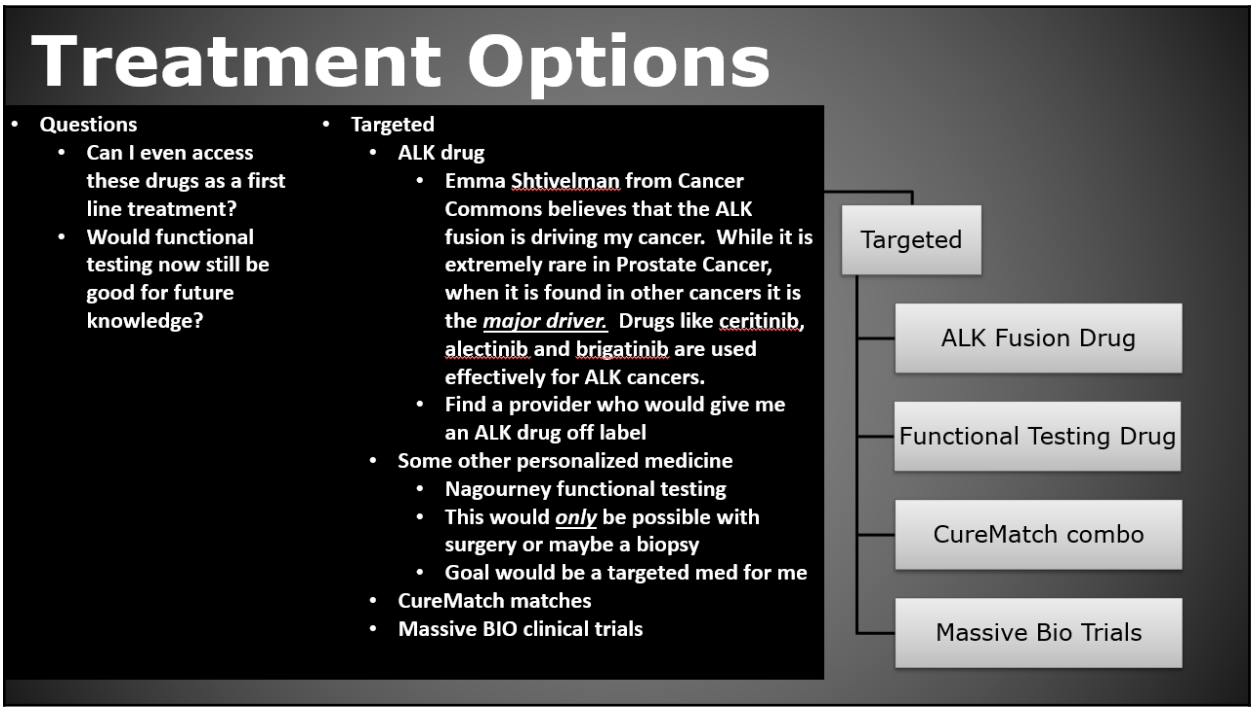
The surgery would be an open radical prostatectomy with a lymph node dissection. I would do that in December of 2022, followed by the IMRT, three to six months later at Mayo in Minnesota.

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The radiation would be high-dose brachytherapy in the tumor and seminal vesicles. I would do that in late January 2023 and then follow that up again with 20 fractions of IMRT in February 2023, again at Mayo in Minnesota.

The third option is just to do the same surgery, but not do anything else, and wait and see through the PSA and scans what treatment is needed.

On surgery, I've not been offered robotic surgery. When I was initially diagnosed, surgery was not on the table. It's only been on the table in the last couple of weeks since I had that latest MRI that showed the tumor shrinking, and it's only available by two aggressive open surgeons who are willing to do that. Most people I've talked to have said surgery is not advised once the cells have grown outside of the capsule.



On the targeted treatment options, I mentioned the ALK fusion. Some drugs that have been identified for other cancers can target the ALK fusion. Functional testing, like Dr. Nagourney presented here a couple weeks ago to this group, is an option. I've met with him and could do something like that. The CureMatch and the Massive Bio analyses have come through the Prostate Cancer Lab.

The targeted drug options I am considering are:

1. **An ALK drug**. This was discovered by Emma Shtivelman. She's on the phone here from Cancer Commons. I've had a lot of emails back and forth with her and really appreciate her insight. Thank you, Emma! I quote you: “While it (the ALK fusion) is extremely rare in

prostate cancer, when it is found in other cancers, it is the major driver of those cancers. Drugs like ceritinib, alectinib and brigatinib are effective for the ALK cancers.” The plan if I did this route would be to find a provider who would give me an ALK drug off label at this early stage. Unfortunately, there are no trials that we've identified to do that, for my case.

2. **Functional drug testing**. This would be what Dr. Nagourney presented here a couple of weeks ago. I would send Dr. Nagourney live tissue from the surgery with the goal of finding a targeted medicine that he could prescribe. Obviously, that requires live tissue. I don't know if that's possible or not. I have a meeting with him later today asking if he can do a biopsy and get enough tissue without having to do the surgery.
3. **CureMatch drug combinations**.
4. **Massive Bio clinical trials**. I have more detail about both of these on the next slides.

Emma Shtivelman:
On ALK, there is one published case report of ALK translocation in prostate cancer, so it's extremely rare. Second point, the particular translocation found in your cancer is reported probably in a couple of patients. There are many types of file translocation with the ALK gene that's the driver, but it gets translated to probably 12 other genes, maybe more. It's a type of transportation found in 15% of lung cancer, adenocarcinoma in particular. It's not like ALK translocation is not a new entity. It happens in other kinds of cancers, just not in prostate. In rare events, not in prostate cancer, and this particular translocation was reported like once or twice. It doesn't even matter that it's rare. The consequences should be pretty much the same activation by default. There are at least half a dozen trials that will give ALK inhibitors to patients with metastatic cancers. You cannot get it through a trial since you are not metastatic. There are those trials and a tumor-blind trial that says, any type of cancer, it doesn't matter where it is. That's the comment about ALK: it’s very rare, and your case is amazing.

I would be all for functional testing. I would however, prefer not to use Dr Nagourney’s testing, which is fine, but SEngine, which does functional testing with organoids. You need either biopsy or surgery tissue to provide tissue. SEngine is very good because they have a long list of drugs that I have somewhere in my files. They will also choose the drugs to test based on your mutational context, which is great. I would consider SEngine. If you want you can do both. The difference is that SEngine uses organoids. It's not cells that are isolated and dispersed and put on plastic. It's kind of little chunks of tissue, which is more faithful than monolayer cultures. And also it's very fast. It's based on a very rational choice of drugs, and they have a lot of drugs.

Stephanie Hall:

Emma, can the functional testing that you mentioned be done on the 14 core biopsies that he had initially like the whole exome testing, or does it have to be fresh tissue?

Emma Shtivelman:

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The functional testing only works on fresh tissue because you need live cells to see what kills them.

Brad Power:

I’d like to introduce Brian's experience and the lessons from that just quickly, because he was trying to get surgery to free up tissue. He had SEngine, Tempus, and Dr. Nagourney as possibilities. He chose to focus on Tempus because he could get both genome sequencing and RNA sequencing, and they would create an organoid for him for testing. It's a short story: UCSD completely messed up and lost all of the tissue. In retrospect, I'd like to get Emma's comment on this. If you give tissue to SEngine, what percentage of the time are they actually able to create solutions? It would seem to me that as in your situation, Eric, from a portfolio diversification perspective, you would want to take the tissue and send it out to two or three places on the possibility that some will break down and have nothing. Setting up some of these models have success ratios that I think are well less than 100%. To give yourself a chance to at least one of them will do something that you can use, it would be useful to send your tissue to multiple places. What do you think of that argument?

Emma Shtivelman:

If it's possible, I would do functional testing. it's Nagourney and SEngine. Tempus doesn't do functional testing, they do DNA sequencing and RNA sequencing.

Brad Power:

They haven't done so in the past. This is something that Brian tapped into at Tempus, which is always pushing forward, unlike some of the other testing companies. This is something new that they're getting into, that they have not done in the past, but will be in the future. They were willing to do it for free.

Rick Stanton:

That was another factor. In addition, they were going to do spatial analysis.

Emma Shtivelman:

That's good. I would have respect for them. Usually they're very good. If they start a new venture, I would trust them. SEngine is also very solid. I had probably 10 patients doing SEngine, and it worked in all cases.

For Eric, the concern is, and it's a good concern to have, as he had a great response to treatment so far, since the tumors shrunk, it won't be a big chunk. He will have to consider the tissue availability.

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Eric Hall:

My big question is: what is the value for me to skip over the standard of care things of surgery and radiation and try to go straight to one of these more targeted drug approaches?

Brad Power:

That was the point I was raising there because surgery is a “two-fer”, you get debulking of the tumor, and you get material that can be used for testing that targets future work. It's a double win. The problem is that in the system, and Brian can give you chapter and verse on this, is that the medical establishment doesn't value the tissue for these testing purposes. As much as you and I might.

Mike Yancey:
I'm very sensitive at this point to the potential side effects of surgery or radiation. If you were to pursue surgery on the margins for tissue, you would want to make sure your side effects are as minimal as possible. If you decide to do surgery to get tissue, I would want them not to cut the part that's really close to the nerves and other organs. You need to stay far enough away to avoid major side effects.

Eric Hall:

I see you're saying just do surgery enough to get tissue but maybe not cause some of the extra side effects by cutting away too much tissue.

Brad Power:

Or going into a zone or you could get into danger of hitting other things that could cause trouble.

Emma Shtivelman:

What would be the other things that cause trouble if surgery is good? You'll do a radical prostatectomy and lymph node dissection. The tumor will no longer be present, but the rectum is a concern. It sounds like it shouldn't be a very complicated surgery. By December with one more month of treatment, it might shrink even more. It will no longer be a large lobulated, connected, and entangled tumor. According to the results of the scan and the general rule for any oligo-metastatic cancer, cut out whatever is primary and the one or two metastatic lesions. Just get rid of them because it has benefits. Then adjuvant treatment, of course, should be continued. Surgery will have maybe fewer consequences than radiation to the whole prostate.

Stephanie Hall:

A concern that we were told about surgery was that the tumor was abutting the soft tissues of the rectum, pelvic floor, and the seminal vesicles. Radiation would be necessary anyway after

surgery, in their opinion. We would need to wait about six months after surgery to do that. So we're looking at getting into about the twelfth month of being on hormone therapy, and no one knows for sure, but there is a slight concern that the hormone therapies would stop working before the radiation could be completed. Dr. Nagourney suggested that maybe a new biopsy could be done to give him enough tissue if surgery didn't become an option. One concern we have is whether the surgery gives him a lot of advantages if he's not considered metastatic yet, and he's not castrate resistant yet. All those drugs that might be used to treat the ALK fusion, can they even be obtained if we were to get this tissue now? Or if they can't, wouldn’t we need different tissue later on if he had a recurrence?

Emma Shtivelman:

It will be difficult to find an oncologist to prescribe a targeted drug for the ALK fusion mutation that has never been used in prostate cancer, and that is approved for lung cancer only when it's metastatic. It's not even approved yet for first line treatment for lung cancer. You can have lung cancer in stage two, three and get treated by surgery, and then you get adjuvant treatment and maybe if there’s a EGFR mutation, you can take advantage of a drug. It's not yet approved for ALK. I don't know why.

Stephanie Hall:

If it is so difficult to get it now, yet if the functional testing showed a targeted drug that would work now, would that same drug work later if we had a recurrence?

Emma Shtivelman:

Most likely. The metastasis can have different mutations, but usually new mutations develop within when there is resistance to treatment. Metastases are by and large very similar to the primary tumor, according to Bert Vogelstein, who did an extensive study of sequencing metastases versus primary tumor in thousands of patients in different cancers. In general, it's still valid, especially when there is one strong driver gene. It doesn't go away.

Brad Power:

Functional testing provides direction towards drugs. It could be chemo. In fact, a lot of the work that Dr. Nagourney has done is in chemo-sensitivity. It's identifying the drugs that would be the most effective treatment options. In the SEngine webinar that we hosted, they said that some of the drugs they identify can be very far afield and complete, exceptional surprises. It could be an asthma drug, it could be anything that's an FDA-approved drug that they're reusing, and it can be way off on the side of not ever having been used for cancer. Functional testing can find more options to add to the list that might be in any sphere. Targeted drugs typically are things that have a diagnostic front end that is genomic and then points to, let's say, an immunotherapy.

Jonathan Starr:

What is Dr. Kwon recommending?

Eric Hall:

Dr. Kwon wanted me to do chemo from the start as triple therapy. Two things about this: (1) I didn't really want to do that, and (2) I couldn't find a local place to give it to me because I was oligo-metastatic.

Richard Anders:

Is that the standard standard of care, or is that his standard of care?

Eric Hall:
The standard of care is to not give chemo unless you're metastatic with five sites or more. Dr. Kwon wanted to give me the chemo given that I had the high PSA and the Gleason 10, as he thought that I might have micro metastatic sites, and if we waited a couple of months, I probably would be metastatic. The second issue is Dr. Kwon doesn't actually infuse the chemo himself; he sends people to other places to get that. In Minnesota he has a few places he works with, but otherwise he leaves it up to the patient to find a local provider to give a chemo infusion. We looked around, and I struck out five times trying to get chemo locally. So I eventually moved on.

Richard Anders:

If you were given a drug recommendation that you had to go through great lengths to get, in hearing you talk, you seem like the kind of person who would go wherever you needed to go and do whatever you needed to do to get that drug. So the fact that they don't deliver it locally is not the issue, or is it that you have reservations about it, or is it both?

Eric Hall:

Honestly, I never really wanted to do the chemo from the start. The numbers we researched were showing it was a 5-10% better outcome in high volume cases. There is no data for chemo in oligo-metastatic cases like mine. There are no studies for my case. I never had a good logical decision that said, “Yes, this is worth going through this effort to go get it.” However, you are right, Richard, that I am the kind of person that if this is going to work for me, then I'm going to go there and get it. But I wasn't convinced that that was going to work for me.

Stephanie Hall:

A lot of the oncologists said it's only meant for high volume metastatic, not low volume. Some of them would say he is also not even low volume metastatic or locally advanced, and then it would change depending on whoever we talked to. Some would say, “No, you probably are low volume metastatic.” What it comes down to now is we've looked at that for so long that if we

were to start the chemo now it's five more months after starting the chemo before he could do the surgery or the radiation, and we're concerned that Dr. Kwon had said, “You don't know how long these ADT drugs are going to work for you.”

Richard Anders:

It sounds like you don't have a standard of care, unlike some patients who come in and they fit into a place, and they fit in pretty quickly. They can decide if they want to accept where they are in that place or not. For them, it's kind of obvious, and it sounds like for you, it's not that clear.

Stephanie Hall:

The very high risk Gleason and the stage T4B with no mets, we have been told, do not fall on the standard of care, but then they sometimes make some of the oncologists question if that is the correct point of direction for him.

Anonymous Caregiver:

I've seen surgery happen with a crack team for someone with Gleason 10 and extensive locally advanced. They needed surgery and radiation and a plan to do both of those back to back. It is an unusual situation.

Jim Ward:

I can't really speak with much of a foundation, but even if it's not standard of care, I came across an article recently, which unfortunately I don't have at my fingertips, that suggests that this triplet therapy is coming on in terms of evidence within the medical community. Now, granted that may be in higher volume cases, but that's just my impression in my recollection from an article that I just stumbled across.

Brad Power:

What are the three drugs in the triplet therapy?

Jim Ward:

Triplet therapy is ADT with chemo and a second generation ADT like Zytiga (abiraterone). I’m far from an expert on this, but it may be that you can have different triplet triplet combinations, if you googled triplet therapy. Although, Eric, you strike me as a guy who's probably already done that.

Eric Hall:

Maybe a couple of times.

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Rick Stanton:

I sent a link to this group, where there was a Grand Rounds urology presentation, which covered this topic, triplet therapy. It was a review of major recent clinical trials, and there are a couple of clinical trials about triplet therapy versus doublet. The doublet is Lupron plus chemo. They found that if you add an androgen receptor blocker, that performed substantially better than just Lupron plus chemo. Okay, but they did not do it the other way around, which is that they didn't start with Lupron plus a second generation ADT like darolutamide and then add chemo. There's still a very strong possibility that most of the benefit came from the two hormone drugs, rather than the chemo. But that hasn't been shown, and as he talked about in the presentation, it never will be shown because no one has a financial interest in doing that test. So it'll probably never be done. When you hear this triplet versus doublet, just be aware what that means when they say triplets have been shown to be better than doublets. So far, it's not that the triplet has been better than the doublet of what you're already doing. The triplet is better than the doublet of Lupron plus chemo.

Emma Shtivelman:

I think the name of the trial was Harrison's. The first one that you mentioned combined darolutamide with docetaxel and the second one on the right combined Lupron with docetaxel and was for high volume castrate-sensitive prostate cancer. The results were good, but right now it’s probably a little too late to discuss chemotherapy because Eric had an excellent response to just Abiraterone and prednisone.

Rick Stanton:

Eric, you mentioned that you're considering HDR (high dose radiation) brachytherapy plus IMRT to the lymph node and any other identified things in the vicinity and presumably to the prostate. I'm not a doctor. But I have been to many support groups. First of all, I've seen that recommended many times. If you look in many of these guidelines, that's often a recommended treatment. What I've seen among my peers in support groups was that that treatment has worked extremely well, many times. Not always, of course, but for the ones who've done very well.

Eric Hall:

This is interesting that you say that, because that matches the research that we've done. If you think about those two options, I'm talking about surgery plus IMRT, or HDR Brachy plus IMRT. I'm trying to compare the effectiveness difference between the surgery and the HDR Brachy, because both of them are followed by the same IMRT to the whole prostate bed. The research has shown, though there's not a ton of research, that the high dose Brachy generally comes out with better numbers than the surgery in terms of effectiveness.

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One of my questions when I talk about doing surgery is to maybe get tissue for doing functional medicine and other stuff. Those are great options I see for the future. But at the same point, looking at my current treatment options, it's not the most effective in the research that I've done for my current presentation. So should I look at a more effective route that's staring right in front of me versus an option for later that is not as effective now but gives more future options possibly?

Rick Stanton:

What you've just said matches what I've seen too.

Eric Hall:

Okay. And you can corroborate that.

Rick Stanton:

There was a clinic in Seattle. I have forgotten their name.

Stephanie Hall:

Seattle Cancer Care, maybe?

Rick Stanton:

It was a group that was headed by a guy named Dr. Bob Grimm. Unfortunately, he died recently. But you still may be able to identify the group through his name. But he did these comparative analyses between tests and different clinical trials of these different approaches. In one way or another, they came up with actual comparisons. When I looked at it, the HDR Brachy plus IMRT seemed to be the one with the most favorable outcomes, and I think there are other things that corroborate them. But let me tell you this, I did not do that myself. I didn't even know about HDR Brachytherapy. Nobody told me about it when I had my initial treatment. I'm not saying that's what I did, so you should do it. I didn't do it. Maybe I would have if I had known about it.

Stephanie Hall:

I guess maybe that's one of the pros. But the real con is how do you get the tissue to test for this ALK fusion gene? Our local medical oncologist has said, “Don't make your decision now based on assuming you're going to have a recurrence, and you're going to need tissue to treat it with a targeted therapy later. We can get the tissue later if it recurs from where it recurs.” We want to hear your all's experience because it doesn't seem like it's as easy as he paints that picture to be.

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Eric Hall:

The flip side of that is that I'm still trying for a cure here. I'm still on my first line of treatment, and the doctors have said that with the radiation plan there's a chance of having it as a cure. I'm trying to estimate what's my highest percent chance of actually curing this now.

Rick Stanton:

You haven't gone to UCSF? It's probably not a major trip for you. The guys that I know, who did what you are thinking of doing, mainly went to UCSF, and that's what they got there.

Anonymous Caregiver:

I can validate that, and that goes back as far as 2012 when HDR Brachy was the best way to treat aggressive high grade cancer that's localized and locally advanced. At the time, there wasn't enough data yet on CyberKnife, so Dr. Roach advised a patient, who was also, by the way, newly diagnosed at age 50. We had to do a lot of other staging for this person to make sure that we could find the extent of the cancer, similar to what you did with a whole bunch of scans. At the time the best that was available to somebody who was newly diagnosed was C11 choline, which you need to be recurrent for. It doesn't help the newly diagnosed guy.

At this point, CyberKnife will be on the table for you too, Eric.

In terms of EBRT (external beam radiotherapy) you can also get hypofractionated (shorter) and dose-escalated. For instance, this person got high dose Brachy. But the EBRT ended up being 2.5 Gray fractions that were delivered, versus the standard 2.0 gray. That was from a protocol that was literally 10 years ago. I don't know how much it's improved since. Maybe that's still optimal. There's plenty of data on the efficacy of that method in patients that it doesn't work well for, but it definitely includes high grade, high Gleason grade cancer.

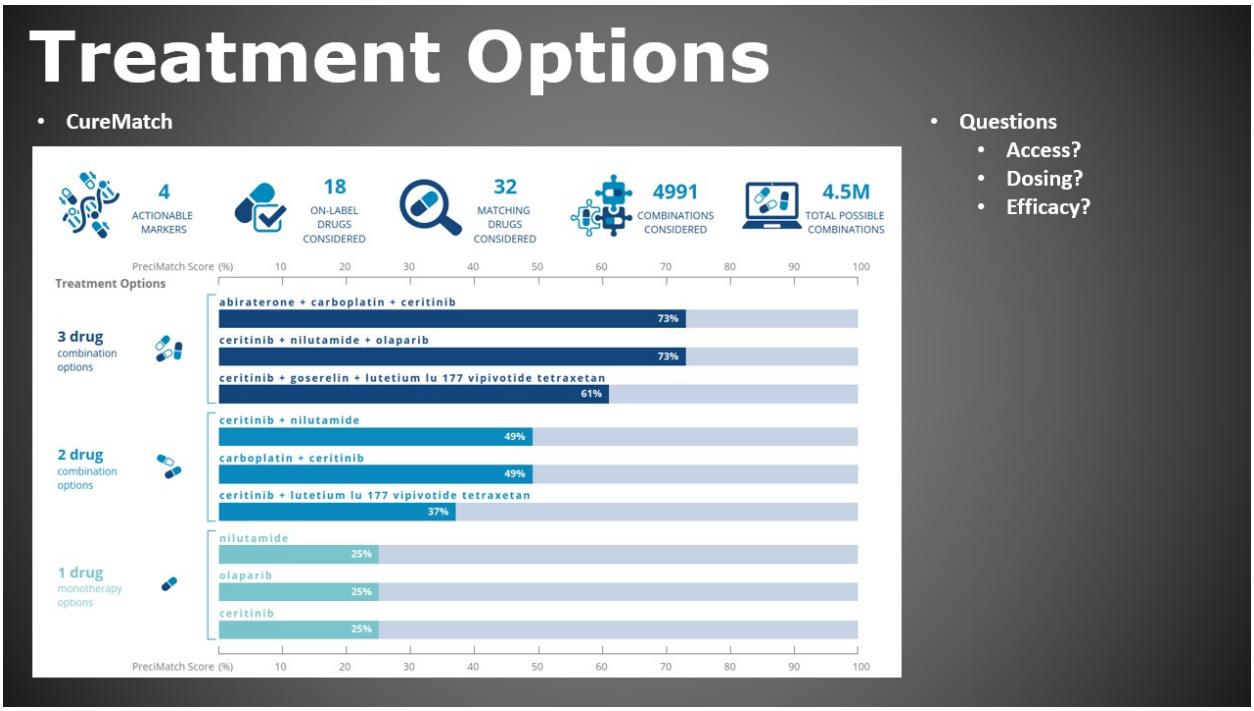
Eric Hall:

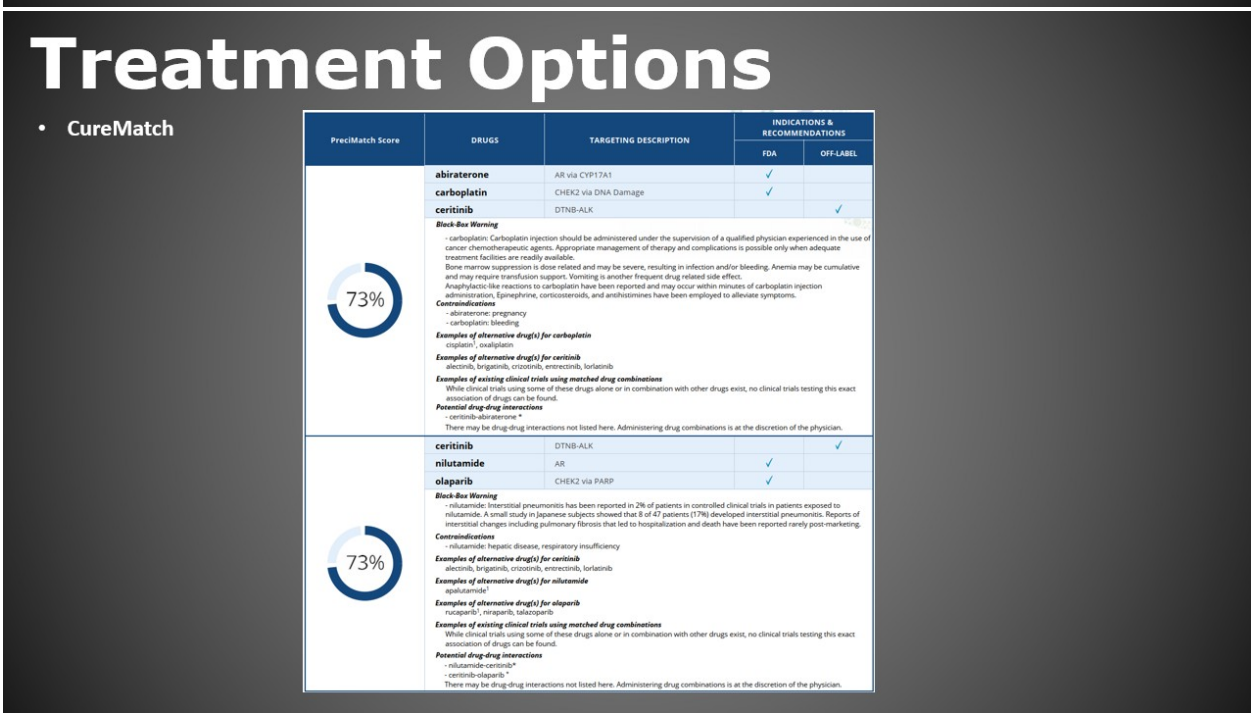
Here are a couple slides for CureMatch and Massive Bio, just to round out the options that I have. CureMatch identified four actionable markers: CHEK2, ALK, AR positive, and the PSMA positive. I'm looking at the three-drug combinations. There are a couple options here:

1. Abiraterone for the AR, carboplatin for the CHEK2, and the Ceritinib for the ALK. I'm doing the Abiraterone already, but I'm not doing the other ones.
2. Ceritinib again for the ALK, Nilutamide for AR, and Olaparib for the CHEK2.

The big question about all this is access: can I even get these things given my stage? Of course there are the efficacy and dosing questions.

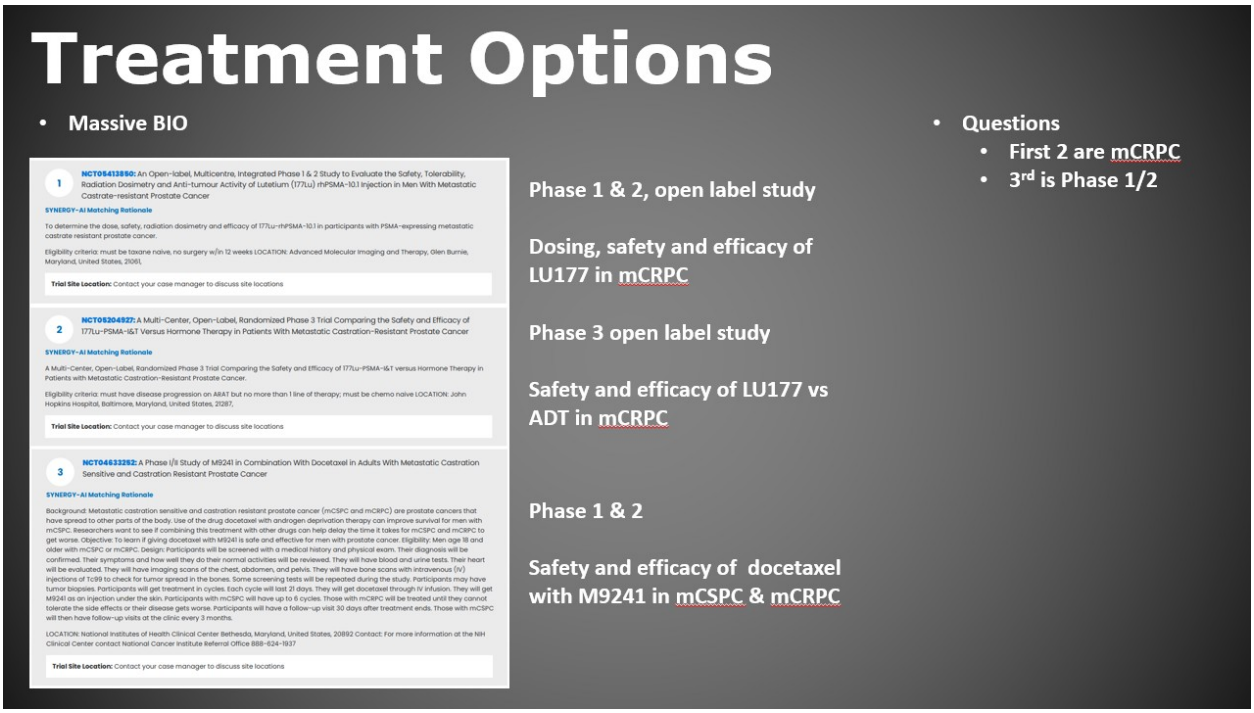
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I'll move to Massive Bio now. They recommended three trials. The first two are for metastatic castrate resistant patients, so not exactly me. The third one is a phase one and two trial. It's looking at the safety and efficacy of docetaxel with M9241. I'll be honest, I just got this a couple days ago. I haven't done a lot of research. I'm not even sure what M9241 is. But it is for castrate sensitive patients. It does say metastatic, so not sure if I qualify or not. The other thing is, it's phase one or phase two. Not sure I want to toss my hat in that bucket at this point in time.

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This brings me back to this slide: do I go with one of these standard of care options, or do I try to do a targeted option?

