“A Hackathon (Molecular Tumor Board) for Advanced Prostate Cancer Patient and Cancer Researcher Dr. Elliot Davis” [#114]

Brad Power and Gabrielle Ruvinsky
September 25, 2024

“I'm at the point where chemotherapy is losing effectiveness, although it still works somewhat. The PSA goes down when I get the treatment, then it goes up again.” – Elliot Davis

“You're in a position now that I think you need to go to a cancer center that has a lot of trials, like ours, Sloan Kettering, Mount Sinai, Johns Hopkins, Fred Hutchinson, UCSF, something like that, where you're going to have access, and not only access, you're going to have doctors that are going to think outside. Because I know what trials we have here, but I have access to those other doctors, so that when I see them next week at one of the conferences, I'm going to be like, ‘Hey, I got this patient. Do you have a trial for him? Here's his lines of treatment.’ That's what you need.” – Sumit Subudhi, MD, PhD, MD Anderson

Meeting Summary

Advanced cancer patients often have relatively easy decisions at diagnosis. There is a standard treatment -- maybe surgery, chemotherapy, or radiation, or some combination -- with a high success in getting a complete response. Increasingly the treatment landscape may also include drugs that are targeted to your unique genetic mutations. If you're lucky, there is an immunotherapy with a high response rate and durable response. But as the options increase, your treatment selection decision gets more difficult. Newer treatments have less of a long-term track record. And the more rounds of treatment you receive, the more complicated the decisions about your next treatment become.

Dr. Elliot Davis is in a predicament. He is a stage 4 (metastatic) prostate cancer patient, who has been battling the disease for over eleven years. He is 79, and was diagnosed when he was 69. He is on his seventh line of treatment in eleven years. His PSA has been in the 0 to 400 range, but is now in the 5 - 15 range. His metastatic lesions are probably mostly in his bones, which are painful and hard to biopsy. After getting Pluvicto (a new drug that grabs onto prostate cancer cells and delivers a radioactive payload), the cancer spread to his liver. However, the liver tumor was resolved after switching to cabazitaxel (a chemotherapy treatment used to treat advanced prostate cancer that has spread to other parts of the body), and it seems it may be losing effectiveness. It is awful stuff, with terrible side effects. He also is getting Orgovyx (Relugolix) which lowers testosterone. He probably will soon have to try some less standard therapy. The treatments have sequentially provided relief for less and less time.

Why is Elliot’s treatment decision difficult?

Prostate cancer has benefited from a continuous stream of available treatment options. For example, “radioligands” which bind to unique receptors on prostate cancer cells have become available in the last two years. But these new therapies add to the complexity of choosing those treatments. Some advanced cancer patients find that they don't get durable responses from any treatments, and their condition continues to deteriorate. They need to identify new treatment options while also dealing with side effects, weakening health, and blows to their resiliency.

How have others made these complex treatment decisions?

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Our spiritual founder of the Cancer Patient Lab, Bryce Olson, faced a similarly difficult decision in December 2020. Bryce told his friend Brad Power that after seven years and eight rounds of therapy for his metastatic prostate cancer, he had hit a wall and feared that he had run out of treatments that had a chance of knocking down his cancer. As cancer patients like Bryce try more and more lines of therapy, they look less and less like other patients, and they get farther away from treatments that have solid evidence to support them. In January 2021, the urgency for finding a solution increased as Bryce’s prostate-specific antigen (PSA) test (a measure of the activity of the prostate cancer) spiked up. By mid-January he also presented with radiographic progression as measured by novel (“PSMA-PET”) scans at UCLA along with conventional imaging at UCSD – all indicating that his cancer was being more aggressive.

Brad suggested that they could organize a hackathon – a collective effort to find out what was driving Bryce’s cancer and stop it. By engaging a broad community of experts with diverse experience, they hoped to identify new molecular drivers and biomarkers along with treatment options that could complement ideas from Bryce’s extremely talented oncologist. Their goal: Get Bryce his next treatment in a couple months. Bryce put his extensive medical data and reports in a cloud repository and permissioned access to anyone who wanted to review it. The collaborative effort achieved its goal to help Bryce and his medical team decide on his best next treatment. The PSMA-targeted radionuclide therapy which was chosen was not on Bryce’s list of treatment options going into the hackathon. The main benefit of the hackathon to Bryce and his medical team was greater confidence in that selection, and the consideration and upgrading or downgrading of other options, which may be useful if a next round of treatment is needed.

What was the advice that Elliot received regarding his decision on his next treatment?

- Get advice from a specialist on his specific cancer at an academic research medical center
- Try a medical grade probiotic to help with the weight loss caused by chemotherapy (cabazitaxel)
- Find a clinical trial under a solid, knowledgeable genitourinary medical oncologist
- Identify the type of cancer in the body to get the best treatment possible for that type
- Introduce platinum therapies with the cabazitaxel

How can you learn more?

- You can reach Elliot Davis at elliot@cancerantibodies.com.
- To learn more about prostate cancer treatment options, please see our discussions with Dr. Oliver Sartor here and Dr. Sumit Subudhi here.
- Elliot also runs a non-profit cancer research institution Cancer Antibodies Inc. (CAI). Recently they made breakthroughs in breast cancer and prostate cancer targeted immunotherapy which were presented at ASCO and AACR. For prostate cancer, they isolated a variety of antibodies that bound to prostate cancer cells while not binding to normal cells. For breast cancer, they identified a novel biomarker that exists only on the surface of breast cancer cells. Antibodies against this target were complexed with toxic drugs (ADCs) which then selectively killed the cancer cells. An overview of their research is available here: https://docsend.com/view/n7ev4fv4gbc8dprv

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Meeting Notes

KEYWORDS

trial, treatment, dr, atm, cancer, prostate cancer, neuroendocrine, patients, psa, mets, scan, dr davis, parp inhibitors, liver, foundation, mutations, chemotherapy, call, doctor, respond

SPEAKERS

Elliot Davis (32%), Sumit Subudhi (29%), Rick Davis (17%), Brian McCloskey (12%), Joe Davis (6%), Frank Nothaft (2%), Brad Power (2%)

CHAT CONTRIBUTORS

Sumit Subudhi, Rick Davis, Brad Power, Robb Owen, Brian McCloskey, Frank Nothaft, David Plunkett, Chad Magnussen

SUMMARY

Elliot Davis, a stage four metastatic prostate cancer patient, discussed his treatment journey, including seven lines of therapy and the current ineffectiveness of cabazitaxel. His PSA levels have risen despite treatment, and he seeks alternative treatments or clinical trials. The community suggested maintaining health through probiotics and calorie counting. Genetic testing revealed low-frequency ATM and BRCA1 mutations, which are not actionable. Dr. Subudhi recommended a clinical trial or platinum-based chemotherapy. Elliot's liver biopsy results showed metastatic prostate adenocarcinoma. The discussion emphasized the need for a knowledgeable oncologist and explored potential treatments like PARP inhibitors and bispecifics.

OUTLINE

Elliot Davis' Cancer Journey

- Elliot Davis describes his cancer journey, starting with his initial diagnosis 11 years ago and the various treatments he has undergone.
- He mentions the effectiveness of cabazitaxel initially but notes its declining efficacy and the severe side effects.
- He shares a graph showing his PSA levels over time, indicating the rising PSA despite treatment.
- He expresses a desire to find alternative treatments or participate in a clinical trial.

Community Insights and Suggestions

- Brian McCloskey opens the floor for questions and suggestions from the community.
- Dr. Subudhi asks for a list of Elliot's prior therapies, which Elliot provides.
- Dr. Subudhi and other participants discuss the importance of maintaining health during treatment and the potential benefits of medical-grade probiotics.
- Dr. Subudhi suggests that Elliot consider a clinical trial or alternative treatments, emphasizing the need for a solid genitourinary medical oncologist.

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Genetic Testing and Mutations

- Elliot shares his genetic test results from Foundation One, showing ATM and BRCA1 mutations.
- Dr. Subudhi and other participants discuss the significance of these mutations and the potential for PARP inhibitors.
- Frank Nothaft suggests retesting the genetic sample to see if the allelic fractions have changed.
- Dr. Subudhi and Rick Davis discuss the importance of having a knowledgeable oncologist and the potential benefits of PARP inhibitors for certain mutations.

Treatment Options and Clinical Trials

- Dr. Subudhi emphasizes the need for Elliot to see a clinical trialist and discusses the potential benefits of clinical trials.
- Elliot expresses concerns about the effectiveness of cabazotaxel and the need for a break from treatment.
- Dr. Subudhi suggests adding carboplatin to cabazotaxel or considering a clinical trial as a backup plan.
- Rick Davis and Dr. Subudhi discuss the importance of having a solid genitourinary medical oncologist and the potential benefits of platinum-based chemotherapy.

Final Thoughts and Next Steps

- Elliot shares his research on finding unique biomarkers for cancer treatment and the potential for using these antibodies therapeutically.
- Dr. Subudhi and other participants discuss the importance of identifying the type of cancer and exploring all treatment options.
- Elliot expresses interest in discussing further with Dr. Subudhi and other participants.
- The meeting concludes with a plan to continue the discussion offline and explore potential treatment options.

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TRANSCRIPT

Brad Power
This is the Cancer Patient Lab.

I'll do the housekeeping chores before we get started with our honored guest, Elliot Davis.

This is not medical advice. This is information which we hope will be useful for you to bring to your medical team.

We are a nonprofit patient-led community, so we welcome any donations you might be inspired to give, which you can do at our website, at Cancer Patient Lab.

Brian McCloskey 1:00
Elliot, it's nice to meet you. Today's session is a little bit different than most of the ones that we have – a mini hackathon where you're going to present your case as a stage four metastatic prostate cancer patient who's gone through seven lines of treatment – or is on your seventh line of treatment right now.

Our intent is to be able to get insights from the community, specifically those on the call today in terms of their experiences that may have a bearing on your treatment plans. When I read your bio, I could certainly relate – I am also an advanced metastatic, castrate-resistant prostate cancer patient. I've gone through many of the lines of treatment that I think that you've gone through.

Elliot Davis 2:24
Thank you very much.

I'm at the point where chemotherapy (cabazitaxel) is losing effectiveness, although it still works somewhat. The PSA goes down when I get the treatment, then it goes up again.

Eleven years ago, I was first diagnosed with prostate cancer. It was all over my body. I had tumors all over, including the neck and back, and they recommended a large amount of radiation to get rid of the tumors. Just androgen deprivation therapy - it worked marvelously. But it wore off after a while, and they tried subsequent treatments that still were aimed at the testosterone antigen at ADR (androgen receptor), at the antigen deprivation axis. Eventually all of them lost effectiveness. About a year ago or so, they recommended cabazitaxel, and it worked very well initially, but it's starting to lose effectiveness. The side effects are horrible. I've lost probably 60 pounds, and there’s nausea and an inability to eat.

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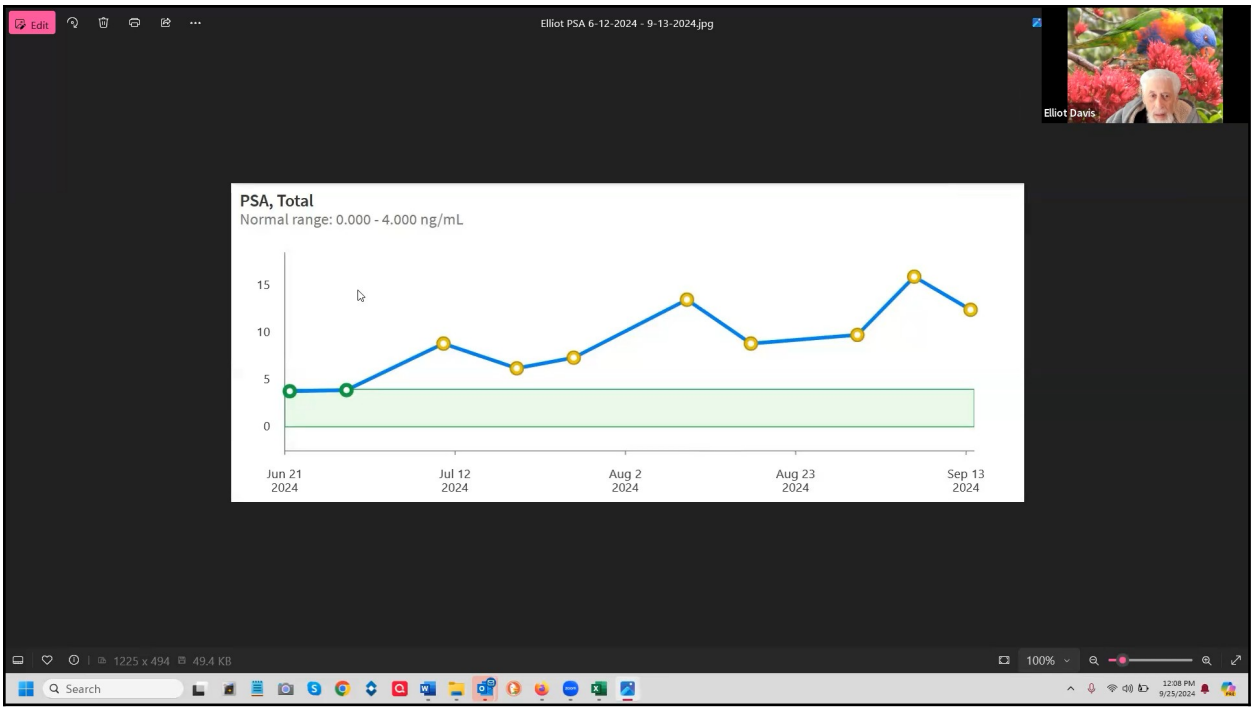

Here's the graph showing my PSA while I've been getting cabazitaxel from June 21 to now. The PSA is rising, although it still has some effectiveness. It would be wonderful to get into some sort of a trial, or find some sort of an alternative treatment.

I haven't found anything that looks overly promising. One month ago I got a blood sample from Advent Health, on September 4, a Foundation One test. I didn't hear anything. I called around, including Foundation One, and they knew nothing about this. Finally, this morning I got a call saying that they sent the sample to the wrong people. They didn't send it to Foundation One. Also they sent the wrong people the wrong instructions. So being obviously a very responsible group, they canceled everything, and now I am here without any genetic results at all.

I have genetic results about a year ago, which Dr. Subudhi has seen, which shows some efficacy with PARP inhibitors (PARP inhibitors block PARP, which helps repair damaged DNA in cells. This prevents cancer cells from repairing their DNA, causing them to die. PARP inhibitors are especially effective against cancers with gene mutations that affect DNA repair, such as BRCA gene mutations.), but that's about it. So the way I see it, my only decent option now is to get on some trial, and if you people know of any, or can suggest some sort of alternative treatment that's realistic I would love to hear about it. I do cancer research myself, and we do have some promising results with prostate cancer, but we can discuss that later.

Do you have any suggestions?

Brian McCloskey 7:48
I see that Dr. Subudhi is on so he may have some thoughts.

I'm going to give you a suggestion that isn't related so much to treatment right now, but is really related to your current condition with cabazitaxel. I started cabazitaxel two and a half months ago. I just finished my fourth round of it. I'm combining it with carboplatin, but I've lost about 13% of my body weight. So that's not as much as you, about 25 pounds.

In the last three weeks or so, I started a medical grade probiotic. I don't know right now whether or not it's completely working, but it seems to be. I'm five or six days out from my last treatment, and my stomach is fine. I don't really have diarrhea or anything like that, which is just really poor for keeping your weight on. Since I started this, I've gained about eight pounds back. I'll put in the notes here the link to the medical grade probiotic that I am using.

I'm also doing something that I've never done, which is counting my calories. So I have an app that is, counting my calories, making sure that I get at least 2400 calories a day. So far, those things are really helping., I'm really touching on something that is important for you to get to your next treatment, which is to maintain or to improve your existing health.

You can't take on some of these drugs unless you're physically fit and healthy to be able to take it on. I don't know the research behind the probiotics. I know there has been some research recently about the effect that chemo has on the gut microbiome, but this probiotic does seem to be working. I'll put it in the notes for you.

There have been a number of questions that have come into the chat. The first is from Dr. Subudhi, and it requests a list of prior therapies. Do you have those?

Joe Davis 10:38
This is Joe, Elliot’s son. I'm going to share my screen:

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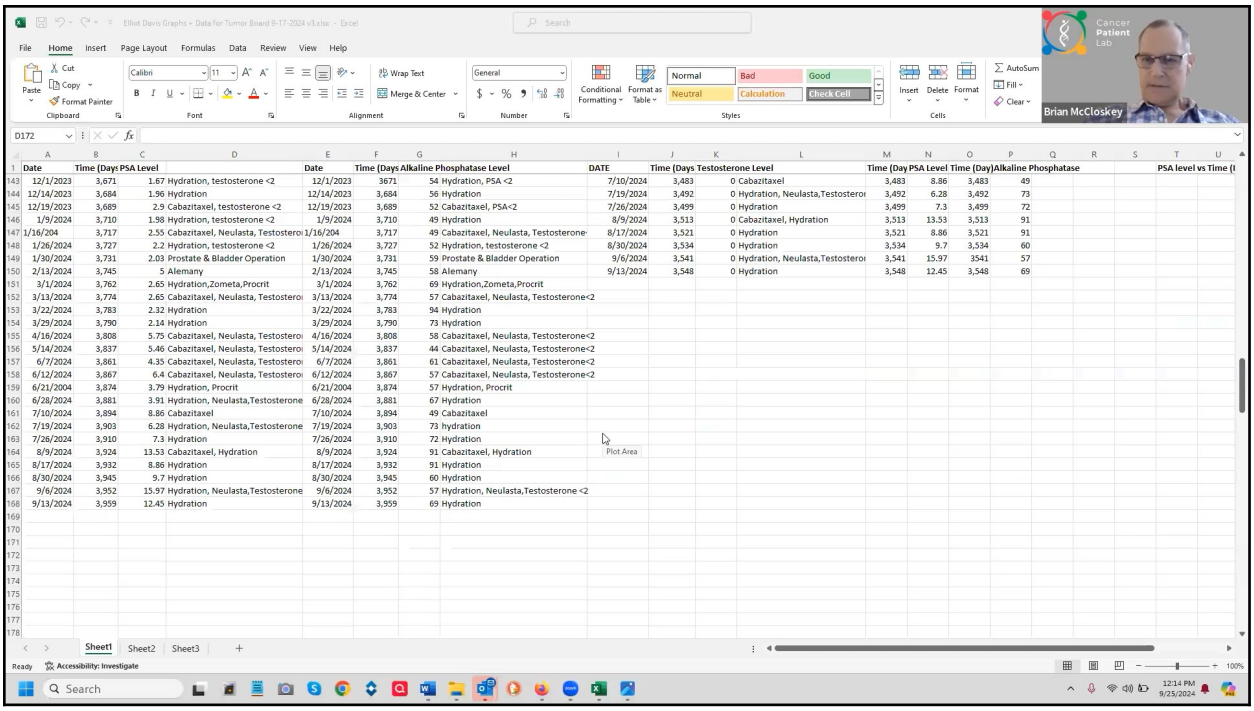

Joe Davis 10:48
He started out with intermittent Degarelix (a drug that decreases the amount of the male hormone testosterone produced by the body). This may slow or stop the spread of prostate cancer cells that need testosterone to grow back in 2013 and was on that until 2018. In 2018 I switched to Zytiga (abiraterone, a drug which blocks the body's production of testosterone), intermittently until 2020 and then Nubega (darolutamide, a second-generation hormone therapy that blocks the activity of testosterone inside cancer cells). There was some radiation. We opted for a stereotactic, curative dose as opposed to palliative. Originally, the physicians wanted to do palliative treatment, and Elliot requested curative treatment instead. Of course, it doesn't wipe out the cancer everywhere, but where it's hitting, it does, and that actually worked extremely well for a while. So we were playing whack-a-mole with the radiation. Then in 2022 he got one round of docetaxel (a chemotherapy), and then switched to cabazitaxel (another chemotherapy) immediately afterwards. In 2023 he did two rounds of Pluvicto (a radiopharmaceutical that binds to a protein called prostate-specific membrane antigen on the surface of some prostate cancer cells and emits radiation that can kill the cancer cells), which did not work at all – his PSA shot up to something like 600 and then switched to cabazitaxel in combination with Orgovyx (a type of hormone therapy which blocks certain hormones, which in turn reduces the level of the hormone testosterone in the body) in 2023, and that's been the course until now.

Brian McCloskey 12:35
Then there's also a question that has come in regarding any mutations from last year. I know that the most recent tissue exchange didn't work. What can you tell us about any mutations that have been discovered?

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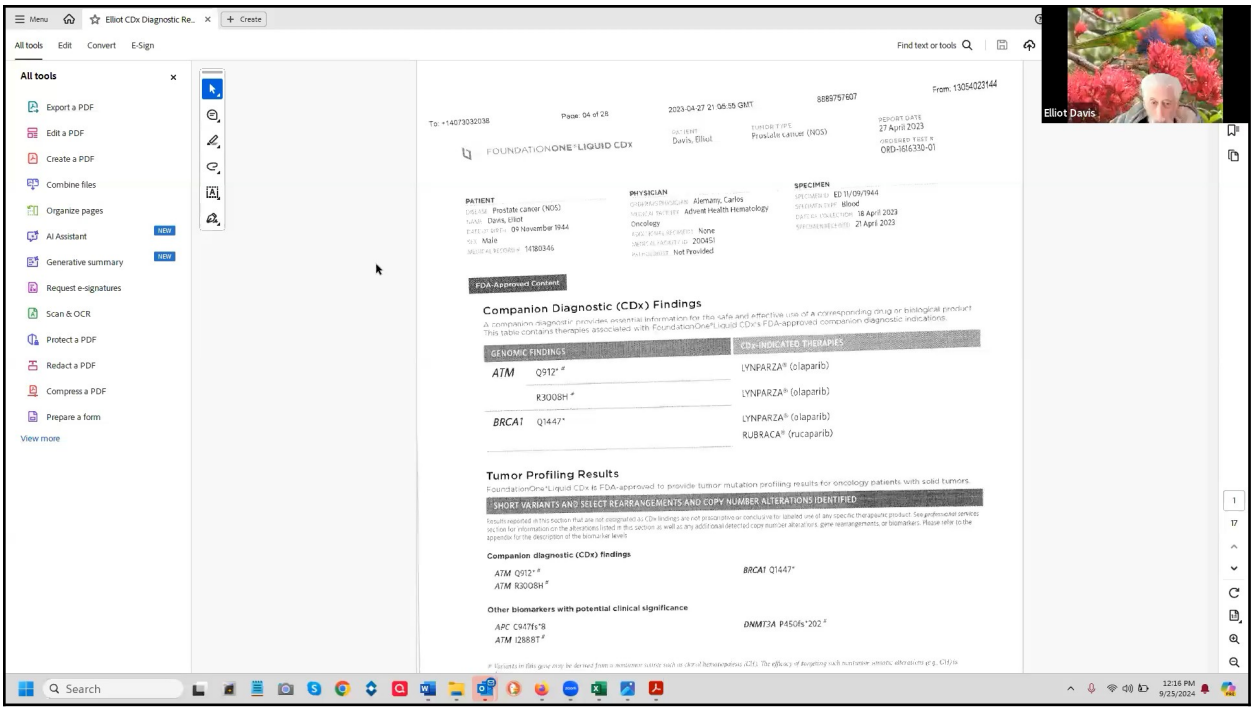

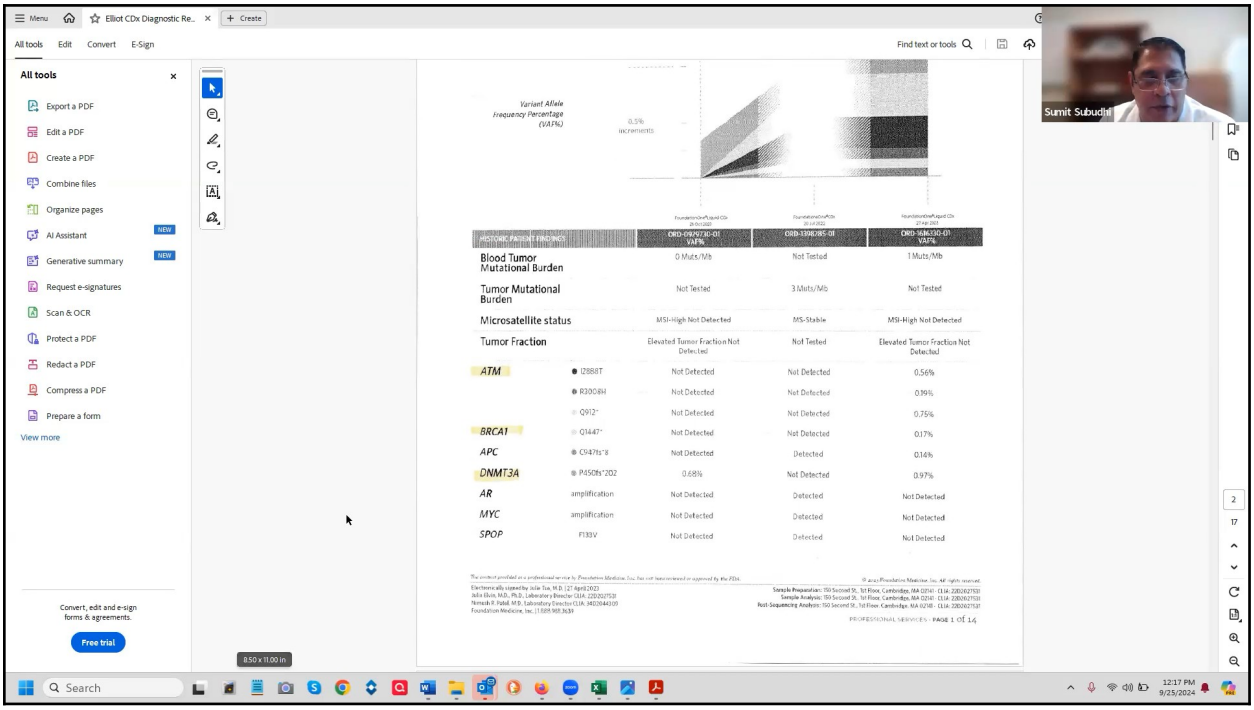

Joe Davis 12:52
This is the Foundation One report from a little over a year ago. There's an ATM mutation (The ATM gene is a "cancer protection" gene that helps prevent prostate cancer.) and a BRCA1 mutation. (BRCA1 is a genetic error that increases the risk of developing certain cancers, such as breast, ovarian, prostate, and pancreatic cancer. BRCA1 is a tumor suppressor gene that helps repair DNA damage in cells. When a person has a BRCA1 mutation, their cells are unable

to repair DNA breaks as quickly, which can lead to the accumulation of damaging mutations. This can cause cells to grow and divide out of control, which can lead to tumors.)

Sumit Subudhi 13:23
We got excited when we saw this, and then our group looked at it. The frequency is so low that they're not considered actionable at all.

Elliot Davis 13:35
So what is an actionable percentage?

Sumit Subudhi 13:38
Something like 25% or higher.

Frank Nothaft 13:50
If you're able to get the most recent sample retested to see if the allelic fractions (the proportion of a specific variant allele or mutation, providing insight into the abundance of a mutation within a population of cells) have changed, that would probably be worthwhile, because the PARP inhibitors (PARP inhibitors target the enzyme poly ADP ribose polymerase, which is involved in repairing single-strand DNA breaks. PARP inhibitors trap PARP at DNA damage sites, causing an accumulation of unrepaired breaks that lead to double-strand breaks. These double-strand breaks can't be repaired in cancer cells that lack homologous recombination proteins, leading to cell death.) show very strong efficacy for patients with BRCA1, 2 and ATM mutations. So if the frequency has gone up over time, that would be somewhat promising from an effectiveness side. But I do agree the fractions there are very small.

Sumit Subudhi 14:28
These are promising drugs. I don't believe in PARP inhibitors for the ATM. There are ATR inhibitors that target ATM better, and I would consider that. But again, the fractions have to be reasonable.

Frank Nothaft 14:45
ATM is pretty interesting because I guess there are three PARP inhibitors now in the mCRPC (metastatic castrate-resistant prostate cancer) setting, and they show variable efficacy with ATM, and I think CDK1 and 2. (Cyclin-dependent kinases (CDKs) are a family of proteins that regulate cell division.) So it's very variable, even by just the individual PARP inhibitor. I would agree that the effect size is much stronger in BRCA1 and 2.

Rick Davis 15:12
I have to contradict you. Frank – ATM is not actionable. As Dr. Subudhi correctly says, it's all a myth. It goes back to Dr. Hussein's original trial, and the way it was set up. And we have been campaigning for years to get ATM removed from actionability. There is very thin evidence for any PARP inhibitor, and ATM, as Dr. Subudhi correctly says, BRCA1, yes. BRCA2, yes. But the rest of them – almost nothing. ATM possibly, but it's really thin, and the rest of them not at all. And please check the evidence.

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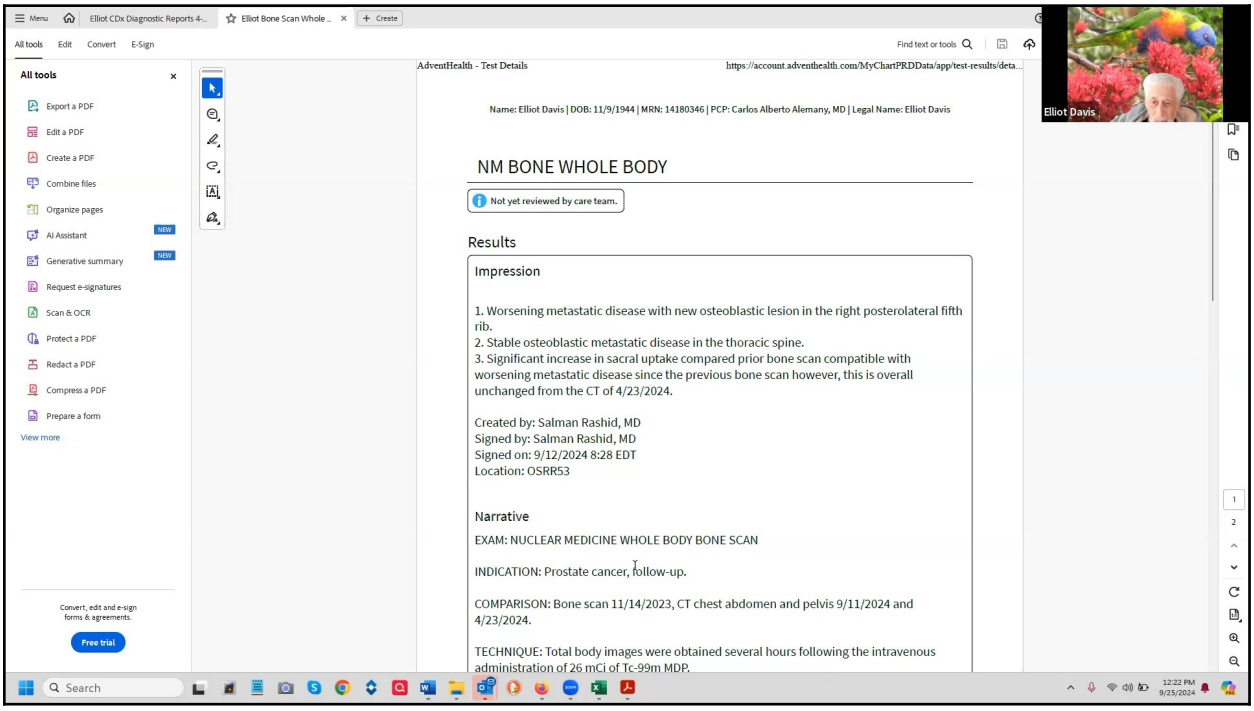
Elliot Davis 18:00
Then I got Pluvicto, which almost killed me.



I have some questions.

Here's the bone scan. Obviously, there's still significant disease in the sacrum. There's some in the thoracic spine, and I think one spot on a rib. I was thinking maybe doses of X-rays might be a short-term way to knock it down?

Sumit Subudhi 18:50
What did the CAT scan show?

Joe Davis 18:53
Let me pull up the CAT scan.

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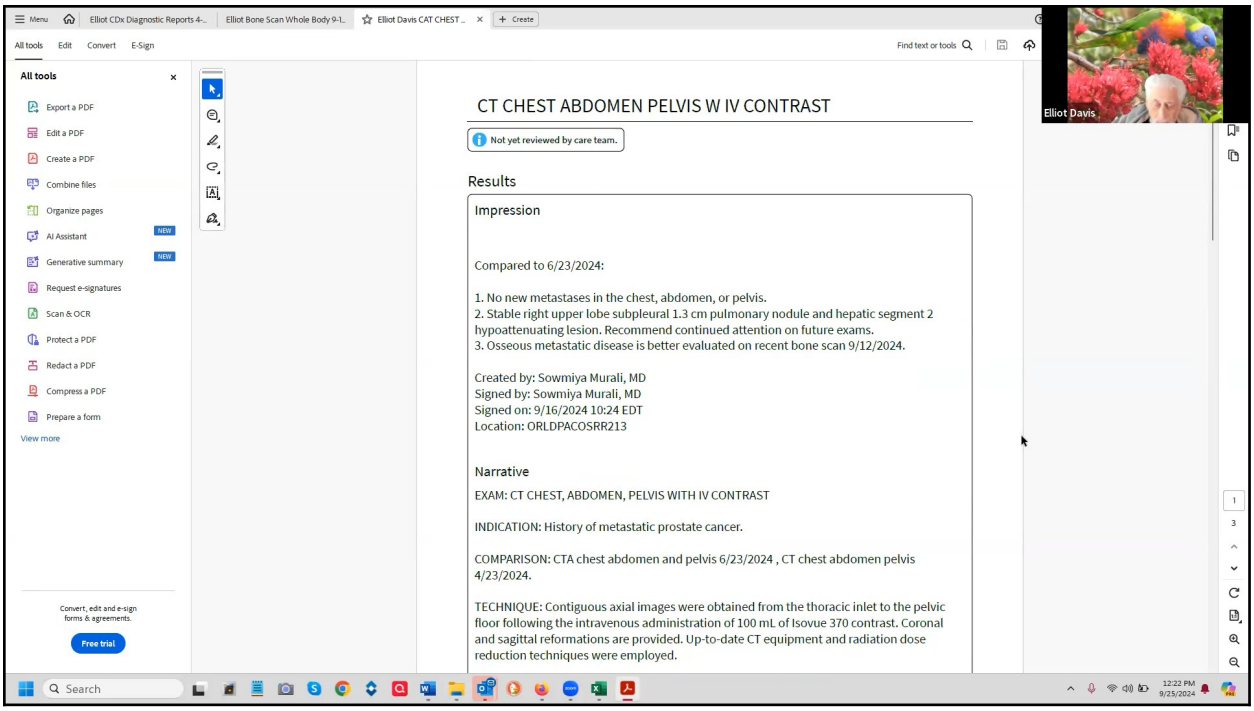


Sumit Subudhi 19:08
Have you had an MRI to the liver yet?

Elliot Davis 19:17
I believe I did.

Joe Davis 19:22
Not recently.

Sumit Subudhi 19:25
Since the CAT scan?

Joe Davis 19:26
No.

Sumit Subudhi 19:29
The reason why I say that is that 10% of the time prostate cancer will go to the liver. It's rare, but it does happen up to 10% of time, and especially someone that's been in six lines – I count six lines of treatment.

Joe Davis 19:47
Elliot had metastases to the liver over a year ago, and they completely resolved.

Elliot Davis 19:52
That was when I got Pluvicto.

Joe Davis 19:56
When he was getting Pluvicot, he got metastases to the liver. Then with subsequent cabazitaxel, they were completely resolved. He got multiple MRIs after that.

Rick Davis 20:07
I was going to ask Dr. Subudhi, and then maybe you can come in with your thoughts and include this. I find it really interesting regarding Dr. Davis's response to the Pluvicto, to the radionuclide, for a couple of reasons: One is that we seem to think in recent research that ATM might actually help the effectiveness of Pluvicto. There have been some reports that ATM is positive for Pluvicto. Secondly, we've often seen a flare. Now this is a huge flare, although I don't know what Dr. Davis's PSA was when he started the Pluvicto, but he'll tell us. And I'm wondering whether this was just an enormous flare, especially in light of the fact that it may have resolved some of the metastases in soft tissue.

Please go ahead with what you were going to say, and maybe you can respond to what you think about the Pluvicto issue? Maybe lighter doses of Pluvicto? What's your thought?

Sumit Subudhi 21:29
So I don't know what his symptoms were, but biologically, it's not surprising that someone with the ATM mutation, which leads to more DNA damage breaks, would respond well to Pluvicto, which is a lutetium Beta emitter. So it's radiation that's causing more DNA damage breaks. So biologically, that is not surprising. Yes, we have seen flares with many drugs, including cytotoxic drugs. I've seen giving chemotherapy where someone's PSA will go up dramatically. But what that really tells us is that the cancer is dying, and that's why there is a huge release of PSA. So we have seen flares, especially in light of what we were just shared by Joe, that the liver metastases disappeared.

Joe Davis 22:24
The metastases actually didn't resolve after the Pluvicto – they got much worse. It was after the cabazitaxel that they resolved. So the liver metastases seemed to form while he was on Pluvicto.

Elliot Davis 22:34
This flare thing raises my hackles because the physician I was seeing at that time, which was another one, where another group cancer specialist or something, so I got the first dose of Pluvicto, and the PSA went from 22 to 115 and I said, this is not good. And he said, Well, it's probably just a flare so let's continue. Before this, I had no metastases in the liver at all. So we continued, and then the PSA went to the 306. That's when the liver test, and they found out that I had two huge tumors in the liver, so Pluvicto did not work spectacularly.

Sumit Subudhi 23:37
That's fine. I'm not a big fan of “spot welding” a patient, meaning going after the all the bone metastases, especially in someone that has already received two taxing based therapies and a

radio ligand, because the bone marrow has only so much reserve, and that's one of the things that we have to think long term.

And if a PARP inhibitor, or anything in that class, and I include ATR inhibitors, they can also, they can be very effective in the right patient population, but they can also cause pancytopenia (low levels of red blood cells, white blood cells, an platelets). And what I'm afraid of is that if you go for the “spot welding”, which is, going for these few metastases, in the long run, there are circulating tumor cells that are going to nest somewhere else. So it buys you a little bit of time, but I'm worried that your bone marrow reserve is going to diminish with every bit of additional radiation you get, and then may take you away from the ability to handle, potentially a PARP inhibitor or anything in that class.

Elliot Davis 24:49
I agree with you, and along those lines, I'm right now in Augusta, Georgia, for a while. I have a doctor here who's a very good doctor and he scheduled me tomorrow to do a Foundation One. So hopefully within a week or so, we will have the new genetic results. So the indication, and he also thinks it is probably a good idea at this point, which I concur, to give myself a break from the cabazitaxel. I'm afraid that I'm going to get liver metastases again. Given the amount of time and frequency I've taken this stuff, it's killing me. I'd love to know some thoughts about that.

Joe Davis 25:54
He's been getting cabazitaxel since June of 2023 with no stop.

Sumit Subudhi 25:59
But the last scan you had was in June. Which scan?

Joe Davis 26:08
The bone scans and the CAT scans were both done a couple of weeks ago, in September.

Sumit Subudhi 26:14
I think I saw June, or maybe the ones that you pulled up, I thought was June.

Joe Davis 26:19
This CAT scan was done September 12, 2024.

Sumit Subudhi 26:29
Sorry, I was reading “compared to”, my bad.

Joe Davis 26:33
The bone scan was done at the same time.

Rick Davis 26:43

Was this an FDG bone scan? (FDG, fluorodeoxyglucose, refers to a type of PET scan called FDG-PET. FDG acts as a radioactive tracer for where the body is using glucose. Cancer cells use glucose more actively and will be brighter.)

Joe Davis 26:52
Technetium-99m (a radioactive tracer that gets injected before a bone scan).

Rick Davis 26:55
Have you had an FDG scan compared to a PSMA scan? (PSMA, prostate-specific membrane antigen, refers to a PSMA-PET scan. PSMA is a radioactive tracer that binds to prostate cancer cells to help localize prostate cancer cells.) Have they done that simultaneously and compared the two scans?

Elliot Davis 27:09
I'm not sure what an FDG scan is.

Rick Davis 27:12
An FDG scan is going to pick up any significant activity in your body that is stimulated by glucose. And the reason why it's important, and please correct me technically if I'm wrong – before we start doing PSMA treatments, we want to make sure that all of your lesions respond to PSMA, and if there are some that don't, it may indicate a different type of cancer.

The reason I'm asking is because we would be suspicious that maybe there is a different type of cancer going on in your body, and it's hard to identify whether that's the case. There are scans like dotatate (an imaging procedure that uses a radioactive tracer to help diagnose and treat neuroendocrine tumors) that might pick it up, but one easy way to pick it up is to take a look at a PSMA scan that at the very same time that an FDG scan and see if there are areas where the FDG does not light up on the PSMA. And that's why we're asking.

The second thing I really want to encourage you to do is to get yourself to a really solid genitourinary medical oncologist like Dr. Subudhi – that you don't have one as a member of your team. There are some in Florida, we would direct you to Elizabeth Guancial, who was a protege of Dr. O. She is fabulous. She has a wonderful manner with her patients, and she's super smart. There are others, but in Orlando, it's a bit thin. There's no one we personally like Moffitt and our go-to person down there, if you can get in to see her is Dr. Guanciale, but you've got to get yourself to somebody really solid. You don't have a solid genitourinary medical oncologist running your care. As a patient advocate we've counseled so many people on this.. It's our first advice.

Sumit Subudhi 29:46
I don't disagree with that because my father, as you know, has metastatic prostate cancer, and my father-in-law was just diagnosed with localized prostate cancer, and they're both being seen by doctors at Memorial Sloan Kettering Cancer since they both live in that area, and so I'm doing that for my own family members, and I don't disagree with that recommendation. If I can

comment, unless there's a question about that, if there is, let's take that and then I would want to comment on the FDG PET and stuff.

Elliot Davis 30:23
I understand that, but the elephant in the room is the fact that the cabazitaxel is losing effectiveness, and there doesn't seem to be any easy or obvious .. there is one thing that seems promising.

Brian McCloskey 30:53
Synchromune?

Elliot Davis 30:53
There’s a company called Synchromune. I think there's a guy named Williams who did some research with Williamson?

Brian McCloskey 31:03
Yes, he spoke here just about a month ago.

Elliot Davis 31:07
Supposedly, their treatment went through Phase 1. It looked extremely promising, and we've been trying to get in contact with them, but there's been no response. It is based on the following principle: They find the tumor, it does work, supposedly with prostate cancer, they do some cryoablation (a minimally invasive procedure that uses extreme cold to destroy abnormal tissue, such as cancerous tumors or precancerous skin moles) of the tumor, thereby releasing tumor specific antigens.

Then they try to stimulate the T cells using various techniques, which they say are proprietary, and this induces the body to make an immune reaction against the cancer cells and not the normal cells. Their initial results were sort of spectacular. I've heard of other such things where they try to stimulate the body's own immune system by disrupting the tumor. So does anybody have any knowledge or thoughts about that as a potential option?

Rick Davis 32:27
The elephant in the room is not that the cabazitaxel is working. The elephant in the room is that there's nobody who's super knowledgeable guiding you to the right treatments. You're flapping around looking for marginal solutions when there may be some more obvious solutions, and those obvious solutions are going to be found by super knowledgeable doctors in the genitourinary field. For example, if it were me, and other people can comment, I wouldn't be sending your test tomorrow to Foundation Medicine. I'd be sending it to Tempus. Why? Because Tempus is a better test today, and your doctor doesn't seem to know that. So ask him to send it to Tempus. There's a whole bunch of issues here Dr. Davis. I want to pass this off to Dr. Subudhi to talk about the FDG scan.

Elliot Davis 33:30

I have some information about that. What's your name again?

Sumit Subudhi 33:39
Mr. Rick Davis, is that what you're asking?

Elliot Davis 33:42
Rick Davis. Oh, that means you must be knowledgeable.

Sumit Subudhi 33:49
Got it.

Elliot Davis 33:51
The saga that I described to you in the beginning, where my blood sample was sent to the wrong people, I believe was sent to that group you mentioned. What was it called?

Brian McCloskey 34:06
Tempus.

Elliot Davis 34:08
She said that was who it was sent to, and they should have sent it to Foundation One, and Tempus got the wrong instructions anyway. So they canceled everything and destroyed the blood sample. So all I can say is so much for the efficiency of the medical system.

Brian McCloskey 34:51
That's another red flag in terms of, who knows where it got lost? Did it get lost on Tempus’ side? Did it get lost on the Advent side, or wherever you are now? There's a lot of areas where it can go wrong, but that's a pretty simple test to actually have done.

Sumit Subudhi 35:13
I've offered to see Mr. Davis.

Elliot Davis 35:20
I have been waiting to follow through with you. I'm very grateful for that. I've been waiting to follow through to get the results of the genetic test.

Sumit Subudhi 35:31
I want to address everything that's been said. So I'm going to go back first to the FTG, and then I'll talk to you why I think it's more urgent to see each other or someone – it doesn't have to be me. I can send you to someone else that I think is equally qualified somewhere else.

I agree with Rick that sometimes adenocarcinoma, which is a classic prostate cancer that responds classically to all the treatments that you've gotten in the past, can de-differentiate into a neuroendocrine. It can be a pure neuroendocrine, like a small cell, which is the extreme, or it can be something in between. Sometimes it stays as an adenocarcinoma, but clinically acts like

a neuroendocrine. Our group calls it “aggressive variant prostate cancer”, because it doesn't have to be histologically a neuroendocrine – it can still act like a neuroendocrine.

I only do the FDG when I'm thinking about giving Pluvicto, because I agree the data supports that even if you're PSMA positive, but if you also have high FDG positivity, then your likelihood of responding to Pluvicto is significantly less. I think that there are other markers in the blood, just like PSA, that you could use to get at what Rick is suggesting. I use CEA, which is a blood marker commonly seen in colorectal cancers, but also neuroendocrine type cancers can express CEA. And the other one is prostatic acid phosphatase, or PAP, which is the target for Provenge (an immunotherapy drug that stimulates the immune system against prostate cancer), but it's also, again, in these neuroendocrine cancers, CEA and PAP can be highly elevated, and it's a lot easier to get than getting an FDG PET scan. (A fluorodeoxyglucose-positron emission tomography scan is a noninvasive imaging test that uses a radioactive substance to detect cancer and other conditions. The scan uses a radiotracer called FDG, which is similar to glucose, to highlight areas of the body that are active. Cancer cells use more glucose than normal cells, so the FDG will accumulate in those areas.)

Elliot Davis 37:36
What I'm hearing is a lot of wonderful talk about the possibilities of what this may be and the various tests to verify it. However, I'm not hearing anything about a potentially effective treatment.

Sumit Subudhi 37:58
So the problem is that you've basically used up every effective treatment we have that's FDA approved, with the exception of Provenge and Xofigo (a radiopharmaceutical used to treat prostate cancer that has spread to the bones), those are the only two, and you will never get either one of them because they're not indicated for anyone with visceral metastases, that includes liver metastases.

So you've gotten every FDA approved drug, and now you're here saying, now I want a trial because that's all you have left. And that's to me, a problem with your oncologist, because I don't wait for my patients to exhaust everything and then be like, “Now I'm desperate, and I need something.” I put trials in between. The analogy I use, because I'm in Texas, I'm not a gun person, but, a lot of my patients are – is that you have seven bullets, and every time you use one, you really can't go back to them.

So I like to keep some bullets in my back pocket. I would have kept Nubeqa as the last treatment. When you are tired of flying out or going anywhere, it's an oral pill, you take it and you'll have a great quality life without seeing an oncologist. I always save that second oral pill, whether it's Zytiga or Nubeqa or Xtandi (an oral hormone drug that blocks androgens from binding to its receptor). I always save that for last. I don't think you're in a position now to be like, “I'm looking for the best trial”. I think you need to see what trials are out there. Because with all these treatments, you're excluded from a lot of trials. Some of the hottest drugs we have with

the bispecifics, they're excluding people who've had two taxane (a class of chemotherapy) therapies, or they're excluding people with Pluvicto.

You're in a position now that I think you need to go to a cancer center that has a lot of trials, like ours, Sloan Kettering, Mount Sinai, Johns Hopkins, Fred Hutchinson, UCSF, something like that, where you're going to have access, and not only access, you're going to have doctors that are going to think outside. Because I know what trials we have here, but I have access to those other doctors, so that when I see them next week at one of the conferences, I'm going to be like, “Hey, I got this patient. Do you have a trial for him? Here's his lines of treatment.” That's what you need.

Elliot Davis 40:23
Okay, so the practical logistics of going to a place like that- what are they? What are the costs? How long am I expected to stay? Am I expected to travel back and forth? Is there any help financially?

Sumit Subudhi 40:41
When you visit the place, you already have recent scans, so I don't think they're going to rescan. You'll just do blood work. It'll be a meet and greet, and I'd say a one or two day visit at most at these places. If you came here, not only would you meet with me, but I’d also want you to meet with our phase one group. It's a separate department outside of genitourinary. They do first in human trials (a clinical trial in which a new treatment would be tested in humans for the first time) with drugs or combinations. So it could be a novel combination or a monotherapy, so that you have access to both of us, or trials in both groups.

That would again be a one- to two-day visit. With regards to trials, every trial has different rules. So what do I mean by different rules? Some have travel paid for, and some don't, depending on how big the company is. So if it's a company like BMS (Bristol Myers Squibb), they'll probably have travel paid for. If it's a small company, they're not going to be able to afford to cover travel. Most trials need everything to be done here. We had the NCI MATCH trial for one of my patients who also has liver metastases, and he lives in North Carolina. We offered the trial where he’d have to come here to MD Anderson, but Duke had the same trial, and so we just sent him to Duke. We just transferred, we made a phone call, and within two weeks, he was seen by them, and he's responding well because he has an AKT mutation (an oncogene) that's responding to one of the PI3 kinase inhibitors (a class of drugs that blocks a cell growth pathway associated with the AKT mutation). So again, the trials don't always have to be at the mother institution. If there's a local institution that has the same trial, then you can do everything locally. But wherever you start, that's where you have to continue all the trial stuff. So if you started a trial with me, you're not going to be able to get the treatment somewhere else.

Elliot Davis 42:48
You have to live there for an extended time? Or can you go back and forth?

Sumit Subudhi 42:53

I have a patient that flew to see me weekly for a bispecific trial. His PSA was 600 and now his PSA is zero. He flew back and forth weekly to get the drug. And the only reason why he stopped doing it was because he had an immune toxicity that prevented him from getting more doses of it, and so he was taken off the trial, but he was going to come weekly.

Elliot Davis 43:18
Okay, thank you. That's been very helpful.

Rick Davis 43:22
There are many doctors like Dr. Subudhi who have connections and affiliations locally, particularly between Texas and Florida. So it may be that Dr. Subudhi may know somebody locally who could administer treatments for you. If it's not a trial, and they have an idea, if it might be an off label drug that they are able to access. They act as your quarterback, but they work with somebody locally. It sounds like you live in the Orlando area. Is that correct?

Elliot Davis 44:06
Correct.

Rick Davis 44:09
With virtual appointments today, a lot of doctors, especially the Texas doctors, can see people in Florida. So there's a lot of ways that we can work with you, but I come back to two things.

The first is, you've got to have a really good quarterback, a genitourinary medical oncologist, who is guiding this.

And secondly, we've really got to identify the type of prostate cancer that you have, and as Dr. Subudhi correctly points out, we're not really sure, because it's just not responding. I couldn't take in your chart as well as Dr. Subudhi. I don't know if you've done platinum-based chemotherapy (chemotherapy drugs that use platinum compounds, which interfere with the DNA of cancer cells, leading to cell death). It's not an easy treatment, but that might be something that, based on the results of this next sequencing, that might be something. And again, all of these chemotherapies can be adjusted. You don't have to be taking full doses. You don't have to be taking full doses of cabazitaxel all the time. And these are adjustments that a really good quarterback doctor is going to see and going to make.

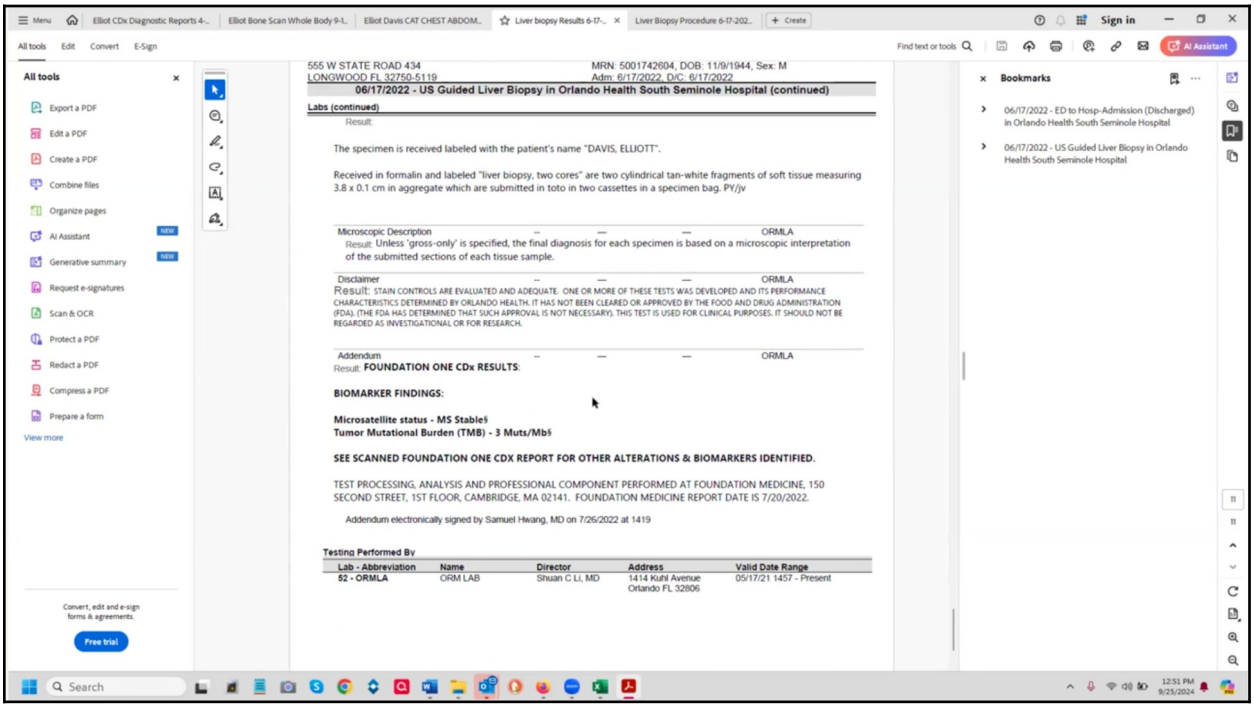
Joe Davis 45:27
We have liver biopsy results from 2022.

Sumit Subudhi 45:42
I think Brian's doctor is actually adding the platinum to the cabazitaxel, which we would normally do with our patients with liver metastases, because we believe your cancer is part of that spectrum of aggressive variants.

Brian McCloskey 45:55

Yeah, and my RNA supported that for sure.

Joe Davis 46:00
Just to clarify, I think I said this before, but maybe not, the liver metastases, according to the scans, were completely resolved after cabazitaxel as of a year ago. Okay, so here's the liver biopsy.



Sumit Subudhi 47:02
Yep, metastatic prostatic adenocarcinoma. So was this sent out for a Foundation One or some other testing? Because that's what I would have sent.

Brian McCloskey 47:29
What were the results of that testing, of that sequencing?

Frank Nothaft 47:35
Was this the Foundation One CDX, with the BRCA1 and ATM mutations that we were looking at earlier?

Joe Davis 47:39
No, that was a blood test, circulating T cells. Sorry that was a liquid biopsy. This is from the liver biopsy. This one says Foundation One CDX results. I guess they did do a Foundation One on the liver as well.

Elliot Davis 48:02
I have all of that information.

Joe Davis 48:05
All this is on our Google Drive.

Elliot Davis 48:16
Right now, I'm visiting Augusta, Georgia, and the doctor here. As Dr. Subudhi also felt that I was getting an excessive amount of cabazitaxel, and it might be a good idea just to take a break. I would love to take a break. Do you think there's a terrible risk if I do that?

Sumit Subudhi 48:43
I just think you need a good backup plan for when you do take that break. That backup plan can be going back to cabazitaxel but adding carboplatin (a platinum based chemotherapy drug) to it at a lower dose of both drugs, so you're not suffering from more toxicities. Or the backup plan would be a clinical trial. I actually prefer clinical trial, because if you progress on the next line of treatment, I am concerned that there's always a reflection point where the cancer is just going to take off, and I think you're going to come close to that, where it takes off so fast that we can't even get you onto a trial. Because most trials take about three to five weeks to set up, meaning all the screening procedures and everything else. So that's why I’d like you to be seen – I think Rick and I are saying the same things – by someone, a clinical trialist, that can at least have many of the things teed up for you and ready to go.

Elliot Davis 49:53
Okay, I get the message loud and clear. I would like to talk to you after this is over.

Brian McCloskey 50:01
One other point that I saw Chad mentioned, which is regarding CancerX.
Dr. Subudhi, I’d like your thoughts on them as well. We had a patient who was referred to CancerX in Omaha, Nebraska for an Actinium trial. I believe all of the costs of the trial, including travel, were covered. I believe that's Dr. Nordquist’s MO. I don't know what his business model is exactly, but Dr. Subudhi, do you think that that would be another option for him to consider?

Sumit Subudhi 50:39
I think at this point he has to really be open to all options. Because, like I said, there's only two plays left in the playbook, as far as I'm concerned. I think he needs a break because there's only so much a body can take. I usually give at most 10 cycles of chemotherapy at a time. And then we're talking about holidays. Or sometimes I do the holiday sooner, depending on how the body is doing. And so the two plays are adding platinum treatment at the time of progression. Or we take a regimen that was taken from lung cancer called CAV, or cyclophosphamide adriamycin vincristine (a chemotherapy regimen). It has a low response rate but again, something that we have enough data to support in prostate cancer, we’ll give it. But those are only two lines that I see left, besides going back to maybe Xtandi and stuff which most likely won't work in someone's cancer that’s progressed on two lines of second generation hormones.

Rick Davis 51:49

Do you think Dr. Davis might be a candidate for some of the DLL (delta-like ligand. A molecule that is involved in a cell signaling pathway that regulates cell growth) stuff that's going on, especially the radionuclide DLL stuff?

Sumit Subudhi 52:07
So we did that trial in prostate cancer and we did not see any response. So I think the DLL3 works really great in the small cell lung cancers, but in prostate cancer, (we weren't putting patients with small cell prostate cancer, we were putting patients with neuroendocrine prostate cancer) I think the data just doesn't seem strong enough. Now at the same time, if he has nothing else, it'd be worth a shot. Because if it works, great, because it's dramatic when it works.

Getting the tumor tested for DLL3 expression would be excellent. But I have to take a step back. With bispecifics, it's very different from radioligands. What we're finding, I can't speak for DLL3, but with PSMA bispecifics, you can have low SUV expression. SUV is a measure of how intense the PSMA is taken up on the scans. And you can have low expression of PSMA and still respond to the PSMA T cell bispecifics. That's different from radioligand therapy. Rick, that's what you were referring to, where you need at least a greater than 10 to be a responder.

Rick Davis 53:26
I may be wrong, but I thought that MSKCC (Memorial Sloan Kettering Cancer Center) actually had a bispecific with DLL3 as opposed to radioligand. I know [unintelligible] stuff is with radioligand, but I thought…

Sumit Subudhi 53:39
Amgen has it and we're using it off label, because you're allowed now as standard of care, that if you have neuroendocrine prostate cancer, you can actually use that, but you need to show that…[overlapping speech]

Rick Davis 53:55
I absolutely agree with you that we've got to try and find some testing to see if there's a sign of a neuroendocrine or small cell disease in there, which is not easy. In your view do the dotatate scans work for prostate cancer, or not?

Sumit Subudhi 54:15
It has to be a really aggressive neuroendocrine for it to work.

Elliot Davis 54:43
I do research in cancer, and we've had spectacular results with breast cancer. The object of our research is to find biomarkers on the cancer cells that are not on the normal cells. I really mean that – just about everybody else says they find unique biomarkers, but they're simply overexpressed.

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Recently, we found a biomarker on breast cancer that is definitely unique. We did some testing of my method on prostate cancer. The method entails injecting cancer cells into a rabbit, getting the result, collecting the resulting antibodies, filtering out those that bind to normal cells, and then seeing what the remaining antibodies bind to. When we did that with prostate cancer cells, we found antibodies that bound to the prostate cancer cells but did not bind to the normal cells for a whole bunch of different varieties of prostate cancer cells, including neuroendocrine.

So we've been trying to continue that testing, and we are now waiting for an influx of matched pairs of prostate normal cells, which we ideally will have within the week, and then we can do a definitive test to see whether we indeed can use these antibodies as a therapeutic. So I think this should be of interest to everyone. If the results are as good as they seem once you have the antibodies, it should not be a difficult task to utilize them. The problem is that they are antibodies created by a different species, which will induce an immune response, which can be quite harmful. But these antibodies can be humanized, and there are various ways to do that. But in any case, if you want to know more about that I can direct you to our website if you have any questions: https://www.cancerantibodies.com/

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CHAT DISCUSSION

00:21:37 Sumit Subudhi: Can we see his list of prior therapies?
00:21:44 Rick Davis, AnCan Foundation: What are his mutations from last year?
00:22:50 Brad Power: Elliot is a stage 4 (metastatic) prostate cancer patient, who has been battling the disease for over eleven years. He is 79, and was diagnosed when he was 69. He is on his seventh line of treatment in eleven years. His PSA has been in the 0 to 400 range, but is now is in the 5 - 15 range. His metastatic lesions are probably mostly in his bones, which are painful and hard to biopsy. After getting Pluvicto, the cancer spread to his liver. However, the liver tumor was resolved after switching to Cabazitaxel. The treatments have sequentially provided relief for less and less time.
00:22:59 Robb Owen: You should also look into prebiotics as well. Both are critical in muicronutrient absorption.
00:23:06 Sumit Subudhi: I cannot recall what his mutations were, but our group did not find it actionable in regards to PARP inhibitor trials
00:23:31 Rick Davis, AnCan Foundation: Sounds like he does not have a lead GU med onc? Where does he live? Who/where is Advent? Florida???
00:23:45 Brad Power: Yes: Florida
00:23:48 Sumit Subudhi: What were his lines of treatment besides cabazitaxel?
00:27:51 Rick Davis, AnCan Foundation: NOT ATM
00:36:19 Brian McCloskey: https://www.amazon.com/dp/B07WX1LVHL?ref=ppx_yo2ov_dt_b_fed_asin_title
00:37:25 Rick Davis, AnCan Foundation: Elizabeth Guancial, Florida Oncology Sarasota.
00:37:52 Rick Davis, AnCan Foundation: platin based chemo;
00:38:12 Rick Davis, AnCan Foundation: was a PSMA compared to a FDG scan?
00:39:17 Rick Davis, AnCan Foundation: has any testing been done for neuroendocrine/small cell signatures?
00:47:40 Frank Nothaft: Tempus
00:47:46 Sumit Subudhi: Tempus
00:47:55 Frank Nothaft: (In disclosure: I am former Tempus)
00:48:02 Brian McCloskey: Reacted to "(In disclosure: I am..." with 👍
00:48:05 Sumit Subudhi: Reacted to "(In disclosure: I am..." with 👍
00:48:32 David Plunkett: I didn't catch a mention of a PSMA PET scan. Does the failure of Pluvicto indicated that Dr. Davis is not PSMA-avid?
00:50:03 chad magnussen: I have interest in Copper 64, but this is another Radioactive Isotope so may not apply in your case. Dr. Luke Nordquist at XCancer is running clinical trials and has stated he is excited for the potential.
00:55:53 Rick Davis, AnCan Foundation: Pfizer Inc.’s experimental drug for cancer weight loss was shown to help patients regain weight in a mid-stage study, offering fresh promise for treating the dangerous muscle-wasting condition." https://ancan.us14.list-manage.com/track/click?u=ece3f3da90f82cb974b407396&id=db4e3f4b6e&e=838454d636
00:56:08 Brian McCloskey: Reacted to "Pfizer Inc.’s experi..." with 👍

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01:01:12 Robb Owen: Rick is correct, I adapted my dosage of Cisplatin for stage 4 HNSCC to 41% of total recommended dosage with 60% of EBRT with complete resolution. You really need an oncologist willing to make adaptive adjustments based upon real time data of tumor response.
01:02:36 David Plunkett: Reacted to "Rick is correct, I a..." with 👍
01:06:00 Robb Owen: I need to hop off for another meeting. Elliot and Joe, please reach out to me when you have time. If Elliot takes a break from treatment, there are many things I can help with on the front end of nutrition that may help your body regain strength.
01:07:39 Frank Nothaft: I need to drop for another meeting. Best of luck, Elliot.
01:07:51 chad magnussen: I’ve heard of some good results of taking Xtandi + Zytiga together for a late stage treatment after failing both.
01:11:02 Elliot Davis: https://www.cancerantibodies.com/