

“Brian McCloskey’s Tissue and Testing” (Brian McCloskey) [#22]

Brad Power
August 17, 2022

“I want to use the biopsy of my tumor tissue to do a couple things: (1) to make sure that I get greater depth of understanding regarding my cancer, and (2) to inform my treatment decisions.”
– Brian McCloskey

Meeting Summary

"The Issue is tissue" – getting tumor tissue for potential tests which can guide treatment is a recurring challenge in making personalized cancer treatment decisions. Advanced prostate cancer patient Brian McCloskey is going to get a tissue biopsy which he can use for tests. How should he allocate this scarce resource to increase his understanding of his disease and prioritize the many treatment decisions he is considering?

Brian was diagnosed with prostate cancer in 2016. He has had 9 rounds of treatment, including a prostatectomy, chemotherapy, radiation, and various rounds of androgen deprivation drugs, as his PSA has cycled up and down. In 2020 they found six metastatic lesions in his peritoneum (the lining of his abdomen). He had surgery to remove as much of them as they could, but they knew they didn't get it all. Recent scans found three metastatic lesions. His PSA is rising, so androgen deprivation therapy may be becoming ineffective. He has found 21 options for his next lines of treatment, which he has whittled down to a shortlist of five or so options through conversations with his oncologist.

Through our meetings at Prostate Cancer Lab, Brian has learned about many potential ways to use the tissue from his upcoming biopsy in tests, including whole exome sequencing, IHC (immunohistochemistry), proteomics, spatial phenotyping, and functional testing. He needs a plan to work with his oncologist, addressing the tests that he should consider, the amount of tissue each one needs, the type of tissue in terms of preservation, and anything else that he should consider before the biopsy.

Here are highlights from the discussion of testing options:

- **Whole exome sequencing:** Brian will get this test, which can, among other things, be used to develop a personalized cancer vaccine. Tempus XE is one option, with experts liking BostonGene's new test and Exact Sciences' test.
- **Immunohistochemistry (IHC):** Brian will get this common test that uses antibodies to check for certain antigens (markers) in a tissue sample, usually highlighted by a fluorescent dye. It helps visualize the distribution and localization of specific cellular components within cells and their context.
- **Proteomics:** A proteomics test could allow Brian to analyze the concentrations of 72 different proteins, beyond knowing which proteins are present, which could help predict therapy effectiveness, such as chemotherapy sensitivity, effectiveness of drugs, such as antibody drug conjugates, and immune system dynamics. For example, Brian has

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elevated levels of a biomarker (TDO2) which creates an immune suppressive environment.

- **Functional testing:** While functional tests that try out drugs on fresh tumor tissue “ex vivo” could provide confidence in choosing drugs that perform well, including drug combinations, Brian’s oncologist doesn’t trust these tests.
- **Spatial analysis:** Brian’s oncologist is unenthusiastic.

Brian is looking to align with his oncologist on these tests, or find another physician, to push the envelope in trying innovative tests.

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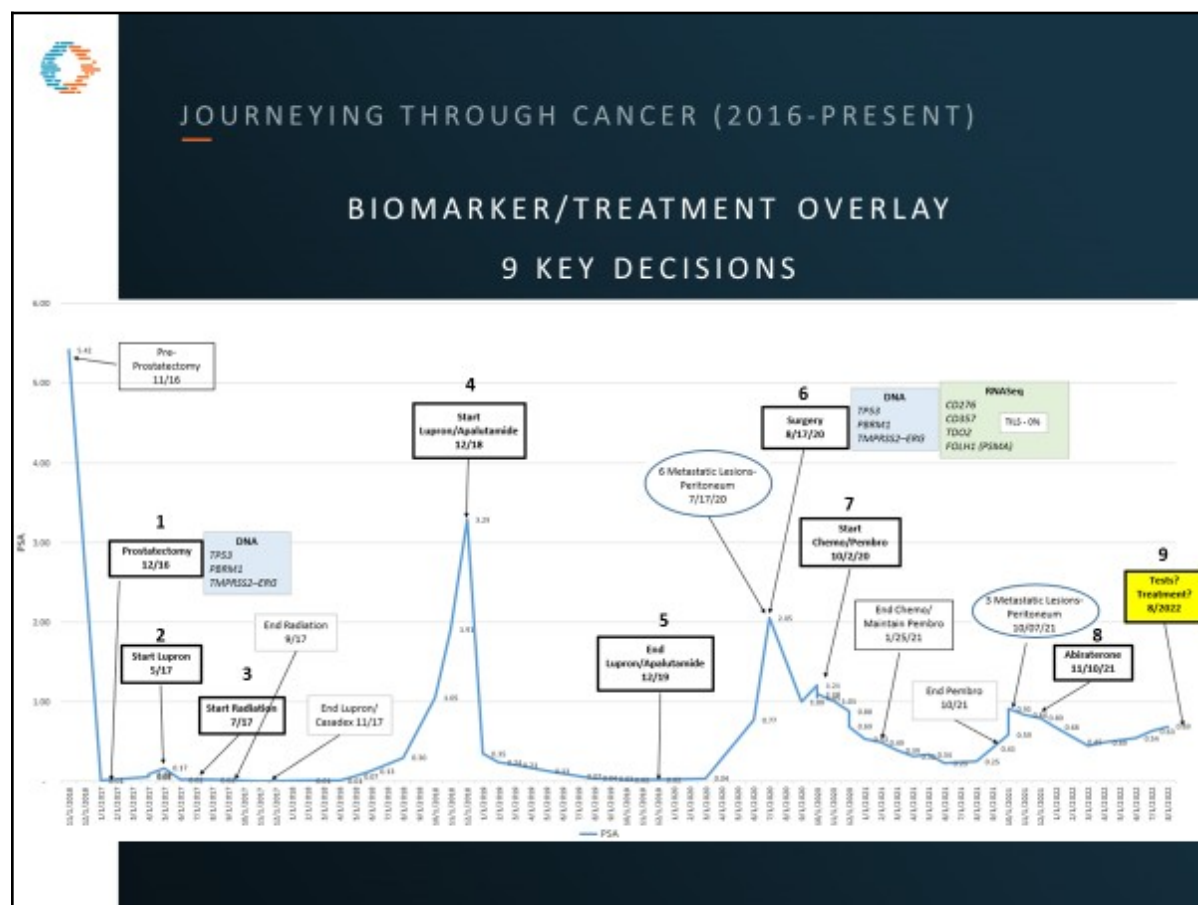
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Meeting Notes

Brian McCloskey: I'm reaching out to you because I need your collective wisdom to help me navigate a really important part of my journey. My cancer is growing in the soft tissue of my peritoneum. That's the bad news, just the way it works. The good news is that it's going to present an opportunity for me to collect tissue. And so the reason why I want your help is that I need to figure out: what am I going to do with this tissue? There are lots of different ways that tissue can be used, and it's a precious resource.

I want to make sure that I am using it to do a couple things: one to make sure that I get greater depth of understanding regarding my cancer, and the second is to inform my treatment decisions.

Some of you may be more familiar with my journey than others. I want to make sure that everyone's on the same page.



My journey started in 2016. I had a prostatectomy. We thought we got it all. We didn't. I had a biochemical recurrence and started first line androgen deprivation with Lupron. I got radiation. That took me all the way through to 2018, when I went on a holiday. You can see that I had a pretty significant spike. I had a Gleason nine. That might explain the rapid rise in my PSA.

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I started apalutamide and saw an immediate response from that.

I then took another holiday in December of 2019, ending everything. Shortly thereafter, I had a repeat performance of what I got in 2018, where I saw a rapid rise in my PSA. We did some imaging. We discovered that I had six metastatic lesions in my peritoneum. That was July of 2020. I had surgery to remove them. They couldn't get everything. There were complications, and this will play into where we're going to go with this discussion. Due to the salvage radiation that I had back in 2017, the tissue gets sticky. It was hard to get margins around the lesions. There are a lot of nerves in that area of the pelvis. You have to be super careful. My doctor at UC San Diego, Dr. Kane, resected six lesions.

I had DNA sequencing. I have three different mutations, TP53, PBRM1, and Tmprss-ERG. Fast forward to my second surgery on these metastatic lesions, and the DNA alterations remained the same. We also did some RNA seq analysis, where we looked at my RNA gene expression relative to a pan cancer cohort of 12,000 patients and a prostate cancer cohort of about 350. This was done with Rick Stanton, myself, and folks at Tempus. We noticed that there are four major genes that I am at least in the 90th percentile ranking relative to those two cohorts.

After surgery we knew that we didn't get it all. So I needed to start chemo, or at least that was the course of action that we took. We decided to combine that with pembrolizumab. I started that in October of 2020. There were six rounds of chemo. I ended chemo on January 25th, and I maintained pembro all the way through to October of 2021. I saw that I was becoming resistant. We knew that we needed to do something else. I had more imaging done in October of last year. We discovered that I had three metastatic lesions. I should also note that during that year I had imaging done, and there was actually no evidence of disease. So we did a pretty good job, but we knew it was there. It just didn't show up in significant lesions.

I had three metastatic lesions by October of 2021. We started a second line hormone therapy, abiraterone, in November of last year. That's what I'm on today. I've had a pretty good response. My nadir is a little hard to read, but it was at 0.45 in March of this year. It has grown slowly to 0.49, 0.54, and then 0.69 last week. We're recognizing that I'm moving into, or I have moved into a castration resistance setting. I'm going to need to do something.

I've had a number of different imaging techniques. I've had a PSMA PET and a CT scan. I just had a three Tesla MRI done. It's much more powerful than a standard 1.5. The fidelity of the imaging is really important because the lesion in the peritoneum is very close to the bladder, and we needed to understand whether or not the cancer has infiltrated the bladder, or intermeshed with it. If there's enough margin between the bladder and the lesion, I would look at radiation and maybe even surgery. The path that we're currently on with my oncologist, Rana McKay at UC San Diego, is that I'm going to get a biopsy. For me, it's really important to understand what is the nature of my disease and how can it inform my treatments? I'm scheduled for a biopsy a week from today.

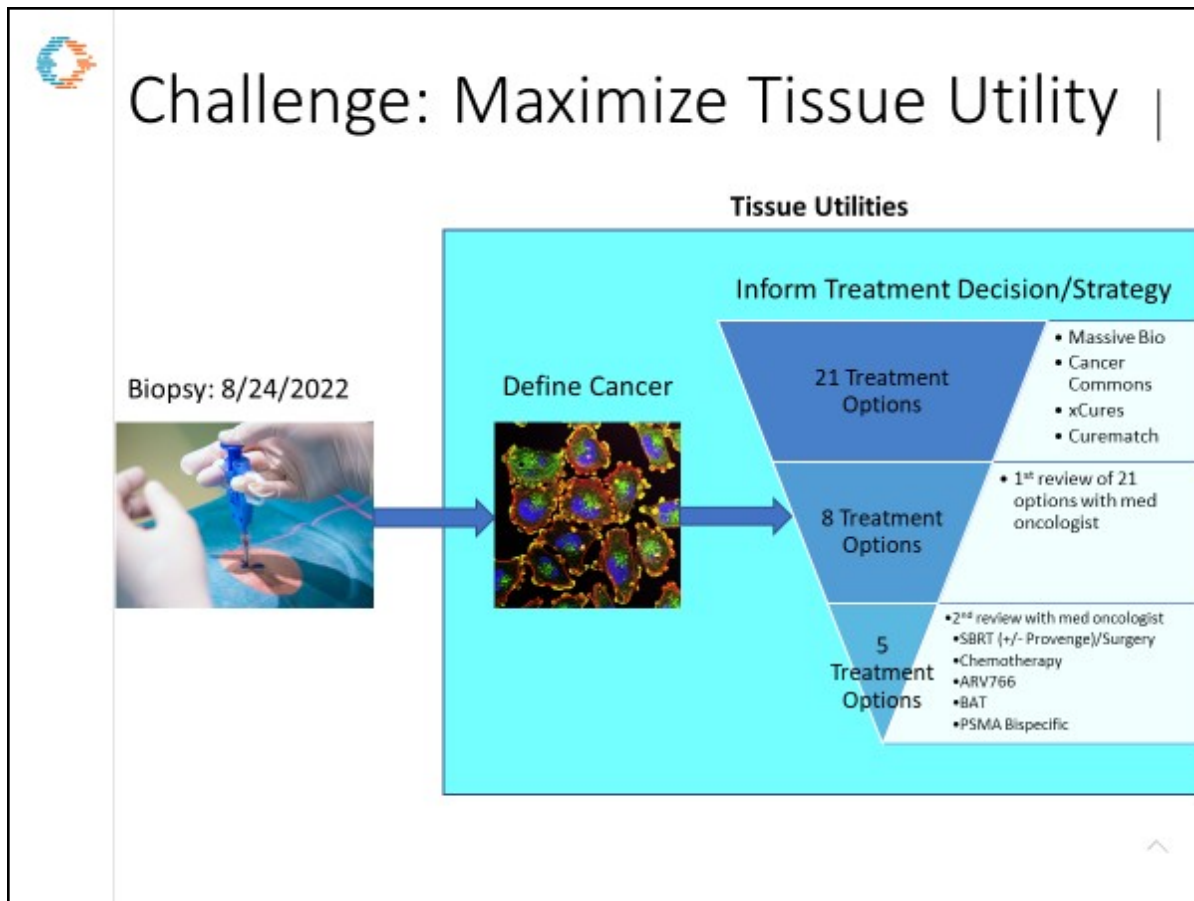
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At the Prostate Cancer Lab we've developed an amazing consortium of providers that take all of our EMR information and genomic information and come up with various treatment options. We've worked with Massive Bio, Cancer Commons, xCures, and CureMatch. Interestingly, across those vendors there was no overlap on the recommended treatment options. I then had a conversation with my oncologist last month where we reviewed those 21 options. All of them. She was amazing. We netted them down to about 8. I won't go into all the reasons right now. Then I had another conversation with her just a couple weeks ago, and we netted them down to five. The five that we're currently looking at are SBRT (radiation), surgery, chemotherapy, ARV766, and a PSMA bispecific. She ruled out BAT (bipolar androgen therapy). I'm putting BAT back on the map because I want to explore that option with her again. While I am newly castration resistant, my AR expression is also very, very high. I don't know if I have AR copy number gain, but I know that I have a high expression of AR, so I don't want to quite dismiss that.

My oncology team has been focusing more on radiation, but I'm not going to give up surgery, because after speaking to the radiation oncologist, I'm definitely concerned about the side effects of radiation given the tumor's proximity to my bladder.

The surgeon was not really stoked to do surgery, given the stickiness of the tissue and a few other things. The MRI revealed that my index lesion has actually grown fairly significantly in the past year. It's gone from three centimeters to five centimeters, which is odd because my PSA hasn't increased that significantly and is still lower than where it was when my lesion was 3cm. Now it's beginning to rise a bit more rapidly, but the correlation between my PSA and my tumor volume doesn't seem to correlate. In any event, I do want to put surgery back on the table as an option. Essentially we're down to maybe five or six treatment options. There could be others. We don't have vaccines on here, which is certainly something that I would consider. I guess Provenge to a certain extent.

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The opportunity that's coming up on the 24th with the biopsy, or potentially surgery at a later time, is that I'm going to get some tissue. And the question is, what am I going to do with that tissue?

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Diagnostics Short List

- Whole Exome Sequencing
- IHC
- Proteomics (mProbe)
- Spatial Phenotyping
- Functional Testing

What tests should I request?

Through all of these conversations that we've had as a group, there's a short list of ways to use this tissue: whole exome sequencing, IHC, proteomics, spatial phenotyping, functional testing, or others. I need to have a plan, and I need to take that plan back to my doctor. I need to work with her to make sure that I'm going to get more than just standard sequencing to get data that is going to inform my next treatment decision.

I would love to get feedback in terms of the tests that I should consider. I also need to understand the requirements for those tests such as the amount of tissue I need, the type of tissue that I need in terms of preservation, and anything else that I should consider before I extract the tissue

Jim Ward: It sounds like you and Rana have decided that you are castrate resistant, but it seems like that's a slippery definition. How do you get to that conclusion? If I took my notes down correctly, you started abiraterone in November of last year, and you've been on it for less than a year, and you're keeping your PSA at less than 1.0. To me, that doesn't suggest castrate resistance.

Brian McCloskey: I think the way that she sees it is that I've been on first and second line hormone therapy, apalutamide being the first line hormone therapy, and abiraterone being another second line hormone therapy. What she's seeing is that I hit this nadir at 0.45. And while it's not spiking, like we saw previously, it's moving up. She's seeing that my cancer is

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becoming resistant to second line hormone therapy. I'm sure that there is a medical definition, but I don't know what the definition is, other than you're not responding to first and second line hormone therapy. I sort of am responding. If I took abiraterone away, then I can imagine that my PSA would be going through the roof. That's why I'm still kind of early in this castration resistant setting. It's probably not as black and white as you and I would like it to be.

Jim Ward: I look superficially at the trend line for your PSA, and the kinetics of it don't seem it's accelerating very quickly.

Brian McCloskey: It should be noted that my disease is different. I fit into the 15% of metastatic prostate cancer patients who don't have bone metastases. That's the good news. I don't have any distant mets either. That's also good news. But I have it in this peritoneum area, which creates complications in terms of how you treat it.

Brad Power: Our friend Willie Hoos pointed out that you could prioritize the testing if you knew the treatment that you are considering, and it would give you more confidence to point to that treatment. Am I correct that there is no immunotherapy on your treatment list?

Brian McCloskey: There's Provenge and the idea that we would do SBRT (radiation) with Provenge – the radiation could maybe make the cold tumor hot and more susceptible to Provenge. But that's the only immunotherapy.

Brad Power: There are certain tests, like IHC, that you could use for immunotherapy. If you're not going to pursue immunotherapy as one of your treatment options, that would lower IHC on the list. That's one filter.

Related to your strategy, since we're fresh off of listening to Bob Gatenby, would you be considering drug combinations or drugs in rapid succession? If so, you might want to do functional testing on that combination. For example, you could take the five on your short list and then maybe combinations of those five and do functional testing on those and their combinations to help you figure out which is the best. Functional testing seems like it should be very high on the list, doing this handshake between the treatments, the treatment strategy, and the testing.

Brian McCloskey: I've had this conversation with Rana regarding functional testing, and she doesn't really trust ex vivo functional testing. She's not going to treat based upon functional testing. I wish I had a different answer, but that's what I've got.

Brad Power: I would be assertive and say, “while I wouldn't treat based on it, it might help.” The way Rick phrased it with Tanya Dorff was, “if you were equal between these five, or two of the five or something, would that put the finger on the scale to tip it in the direction of one?” It's not that I'm going to base a decision on it, but I'm going to be influenced by the information. It could be presented in that softer way. I would certainly think that way.

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Brian McCloskey: It's on my list. I don't want to abandon it. I see the value in it, for sure. I just have to figure out how to get her to see that. I'll be speaking to another prostate cancer oncologist, William Oh, later today, and can see what he thinks.

Mike Yancey: I'm familiar with PSMA, but what's a PSMA bispecific? I'm not familiar with that terminology.

Brian McCloskey: it is an engineered T cell to target the expression of PSMA (prostate specific membrane antigen).

Mike Yancey: I know you've had the scans, et cetera. Do you know what kind of uptake values you were seeing? Mine were in the 30 to 40 range on the PSMA when they did the radioisotope, et cetera, on the imaging, which is pretty high.

Brian McCloskey: I don't know. I will go back and I will check that out. That could help determine whether or not a PSMA bispecific might be helpful. I know from my RNA data that I have a pretty high expression of PSMA, in the top 90% of prostate cancer patients.

Mike Yancey: I'm on Pluvicto, and it seems to be able to do radiation with limitations to affecting other tissues.

Brian McCloskey: We talked about Pluvicto. It's on the list of the top eight. It didn't make the final cut. She thinks that there should be some other therapies that I pursue before I do Pluvicto. So that's why we're down to the five that we have.

Brad Power: On the bispecific, the “bi” means two. It's grabbing prostate specific membrane antigen and CD3, which means that the T-cell has more to grab onto.

Anonymous Caregiver: I want to go back to the idea of an FDG (fluorodeoxyglucose) (PET) scan, and that's because of heterogeneity in the localized setting. I have seen examples of a clinical progression, the size of a tumor growing while the PSA drops, and that can be due to what's called “PSA leak”. Steven Strom had written about that, which is that the higher grade will throw off lower PSA. So I don't know if that's at all applicable in the metastatic setting, but it makes me want to bring back into this conversation that there's another imaging scan that you can do to complement the PSMA, rather whole body imaging that you've done, which is sensitive and can detect the areas where your cancer actually got resistance. Then you'd want to compare that to where your PSMA avid and see if they are in sync or do you actually have areas that are showing up in FDG that are not in the PSMA or vice versa? Because you may need a combination treatment therapy for your different types of tumor cells. Before you do any treatment, can you gauge more that would determine the range of differences that you have? The FDG results can then be used to correlate with all the other work that you've done around your sequencing and your unique characteristics.

I just saw that the Mount Sinai Health System has announced an ambitious new partnership with Regeneron. There's a lot of genetic sequencing, but is there anybody who's putting their

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reputation out there now in precision medicine who might be interested in taking your information, sucking it up into what they can offer? Especially since you've done a lot of advanced work. Are you interested in partnering with a range of places in this telemedicine era? It might be easier to do this without having to travel and widening the filter on what range of sample types you could be collecting. You can send them to different places which are willing to do that work on your behalf.

Brian McCloskey: Coincidentally, I was just setting up a telemedicine appointment with Dr. William Oh from Mount Sinai. I've spoken to him, and the idea is that potentially he would be willing to think a little bit more progressively about how to incorporate testing into my care. I'd love to get Sheeno's (Thyparambil of mProbe) take on this because I am really interested in doing work with you, and we have this golden opportunity to, at a minimum, take advantage of my biopsy. Do you think, given what you know about my case, your testing would be helpful in making treatment decisions for me?

Sheeno Thyparambil: Yes. Since you're obviously doing histochemistry, the ability for you to see like 72 different proteins from our testing to tell you at least the scale of everything where you stand. Especially given the fact that chemotherapy is still an option, to say, what kind of chemo might be beneficial? I also want to see about the newer generations of the antibody drug conjugates. Are there targets in you that have not been examined before that we could figure out if that is a place that you might be able to get into some clinical trials, or not? I also noticed in your RNA sequencing data, that your TDO2 was elevated, right?

Brian McCloskey: Yes.

Sheeno Thyparambil: We don't have a TDO2, but we have an IDO1, which is essentially the same path. The function of this is to create an immune suppressive environment. Even though your T-cells might be coming into that environment, when you have the presence of IDO1 or TDO1, they're putting out molecules that essentially stop the T-cells from attacking a tumor. It might be an opportunity to see if you have high levels of IDO1 in there as well. You could enroll yourself in some clinical trials, if that is the case.

Brian McCloskey: You see there's CD276 from my RNA seq. That's B7H3. There is an ADC that actually targets that gene and was part of my top eight treatment options. Unfortunately, there's no clinical trial that's available in my region. The closest one is up at Fred Hutch. Peter Nelson is running it. I would certainly consider doing it, I could put that back on the table for sure. Are there other tests that when combined with mProbe's tests, for example WES or IHC, that you look at in aggregate to get a more complete picture from the data that you're looking at? You're looking at proteins, but do you look at other information to get a more holistic picture of my cancer?

Sheeno Thyparambil: We are only looking for 72 biomarkers. But if you step back and start looking into the genomics landscape, there are mutations that are definitely actionable. Over time did your cancer pick up additional mutations that you could target now? Maybe it's a PARP

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inhibitor or there's something else in this space that you can play with? Yes, it has to be holistic, both genomics and proteomics.

Brian McCloskey: One of the challenges with prostate cancer is that it's a cold, solid tumor cancer. Even if you identify these biomarkers that could be relevant for me, there could be challenges just in terms of developing a therapy that's actually going to penetrate the tumor cells. I've looked at my TILs, and I have 0 TILs.

Sheeno Thyparambil: That makes sense because if you have high levels of TDO2, your lymphocytes are not going to get into the tumor because the tumor microenvironment is very immunosuppressive.

Brad Power: Are there TDO2-targeted therapies?

Sheeno Thyparambil: The whole IDO1 and the TDO field imploded after a few clinical trials. There was a company that I last knew that had a TDO2 clinical trial called ITEOS, I guess it's called ITS Therapeutics. I'm hoping that they still have that clinical trial ongoing. There are very few companies out there still doing IDO1 clinical trials.

Brian McCloskey: What is the best way to arm me with data that I can take to my medical oncologist to sell mProbe? What's the best way to handle that?

Sheeno Thyparambil: There are definitely papers that we can point to. The antibody drug conjugate space most recently has been a hot topic. We have work that we put out in JCO, which is where the oncologists tend to gravitate, but there's also the basic science work as well. Different oncologists will look for different information. I'll send you the papers.

Ricardo Salgado: Are you getting significant pushback from your medical oncologist on using mProbe or proteomics? Because medical oncologists are super excited about proteomics. Maybe they just don't know mProbe, or am I missing something?

Brian McCloskey: I haven't mentioned mProbe specifically. That was going to be part of my next conversation. I have gotten resistance to spatial phenotyping, which is odd because Akoya Biosciences is instantiating their machines at UC San Diego. Yet my oncologist isn't really excited about using spatial phenotyping to get insight about my cancer. It's a bit of a conundrum to get adoption for some of these tests, which is one of the reasons why we're all having this conversation. I'm looking for proof points that I can use to convey to my oncologists why we need to do this. I want more data about my cancer. I feel like, quite frankly, the road that I'm going down is just perfunctory testing.

Ricardo Salgado: Along my journey as we talked to all the ALK experts – we talked to 10 of them – we got a different answer from each one of them. You can always find the answer you want. Eventually you find it. You pick your main medical oncologist, who is the quarterback, and you're not switching around all the time, but there could be some contention. Let's say your

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medical oncologist is at MGH, for example, but let's say that MDA is telling you something that you want to hear, and you want to push back, but your MGH person doesn't agree. What I found is that there's a point where you're in control, as long as it's not super risky, and you have a certain amount of discretion to push certain things. Even if they don't like it, for tests like this, you eventually find the person that you want the answer that you're looking for, and then you can push back and get what you want. For you, it's more a question of, “how much tumor do I need to get what's the most relevant? How would I prioritize it? Who's the quarterback doing that?” Maybe that's happening now. Maybe that quarterback is your main medical oncologist where the tissue's going to be, who doesn't like proteomics or mProbe, and then you'll struggle, but you just have to manage through it and make the arguments. Ultimately you're the one. It's your tissue.

Brian McCloskey: I agree. As a patient, you understand the challenges. This is why I'm having a conversation with William Oh from Mount Sinai, and why I am being treated at City of Hope, and I have Dr. Agus at the Larry Ellison Institute for Transformative Medicine. It's also challenging to manage the “round Robin” of oncologists. I am trying to find that quarterback who is willing to do these types of tests.

Anonymous Caregiver: It's too bad Dr. Myers is not still in practice. He was at the NIH for decades and then went off and specialized in prostate.

I agree with Ricardo. It's like the dilemma in health insurance, where you sign up before you know your situation, and then you learn the insurance company is not the best fit for what you actually need. Same thing with the health system. If you get aligned with a health system, then as you notice more about how your cancer changes, you might learn, “Hey, I need a different type of practitioner, a different philosophy.” Are they only private practice oncologists like Mark Scholz's operation in LA, or are there big name health systems that are staking their reputation on precision medicine? Who are the people who are the institutions or the individual practices that are saying, “this is what we do. This is our philosophy. We are not just your quarterback. We partner with you. We get it. We want what you want.”

Brian McCloskey: I'm in search of that. Hopefully I'll have a good conversation with William Oh, or I can bring Rana back to the table to pursue some of these other testing techniques.

Jonathan Starr: Do you meet with Dr. Scholz?

Brian McCloskey: I don't. No.

Jonathan Starr: I do. He would support you whatever you wanted to do. He would learn from it. He likes aggressive patients like you. He's supportive of doing original things. Most of the doctors you're going to are part of institutions, and they're under a lot of institutional pressure to just stick to the NCCN guidelines, or do whatever their internal practice is, and also to just do things that are offered within their institution. That's what I've found. “Oh, we're offering that test. Okay, great. You go get that.” But something outside the institution? “Well, no, we've got this

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test here in our institution. Go do that one.” But Mark Scholz doesn't have those constraints. He fancies himself as being at the cutting edge of everything. You might find him very receptive to doing the things you want to do.

Brian McCloskey: That's a great idea. He's been on my radar for a while. I've heard good things, but also, I've heard he's controversial. However, maybe that's what I need – somebody who is thinking outside the box. I'm going to put him back on the list, and maybe I'll have a conversation with him. He's up in Marina Del Rey.

Brad Power: Picking up on Ricardo's recommendation that you have a quarterback, a subject matter expert who knows how to manage the question which you have of how to allocate the tissue. This is very specific. How much do you get out of a needle biopsy and how much do each one of these tests need? SEngine needs something different for organoids than Robert Nagourney needs for functional testing, than somebody else needs for another test. What is the job description of that person? It's not a general oncologist. I think it's a pathologist, but I just don't know the specialties well enough. Ricardo, maybe if you thought about it, what, what would that quarterback job description be and what would they look like? Where would Brian find that quarterback?

Ricardo Salgado: It's ideally the pathologist, but it's very difficult to have direct access unless you're ingrained with the institution because they protect the pathologists. You usually don't interact directly with the pathologist. That's what I found. It's the medical oncologist who is talking to the pathologist about how much tissue is left, what can we do with it. All of those specifics. Unfortunately I don't have a good answer. I haven't gotten there yet. I'm actually learning here. I'm not leading on this one.

Brian McCloskey: I reached out to Jonathan Epstein from Johns Hopkins, and he would review my pathology slides. He was very short, like a three-word answer to a much longer email. He's a busy guy, but he's also supposedly one of the best, if not the best pathologist in prostate cancer. I heard him speak at an NASPCC event in DC.

Ricardo Salgado: Is this where you're getting your tissue biopsy done?

Brian McCloskey: No. It would be done at UC San Diego.

Ricardo Salgado: Theoretically, the quarterback of the tissue is where you get it done. I'm not an expert on it because I haven't gone through it yet. My tissue is at MSK, and I'm in clinical treatment somewhere else. I'm literally in the middle of navigating all of that. But if you have a pathologist in the place you're getting it done, that's amazing. You're thinking, what are the three different scenarios and what would I be doing under those three scenarios ahead of time. Because you know this shit happens really fast. I'm really impressed by your curve. Your curve hasn't really accelerated. And you're already all over it, which is great. Let's say that progression happened, then one of the key things that I'm very excited about is TILs and cell therapy. So you have those conversations with these medical centers and they are very focused. I need live

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tissue, and I need it here because transferring it from somewhere else to here is exceptionally difficult. I don't get a sense that these were the clinical trials that you're looking at, but if that was at some point in time something that you were looking at, then it's really important for you to consider where you get the the tissue, particularly if there's a live component of it on how to handle it, minimizing mistakes, et cetera.

From a few conversations I had on whole exome sequencing and who does that, I hear a lot about the Tempus XE. You know about that? Earlier this week, talking to Mark Laabs, he also recommended BostonGene, which has additional information than the Tempus XE. A super patient that has gone through it before kind of giving you who the vendors are, or there's multiple vendors beyond that.

I was very focused on Tempus, but I have also started looking at BostonGene.

Brian McCloskey: BostonGene came up in a conversation that Brad and I were in a week or so ago, and also Exact Sciences, formerly Ascion. They're the top two. I think there've been some challenges with Tempus and XE. Does it go deep enough? I'm going to try to get a little more data on whether their sequencing methodology has improved. I'm working with those guys on getting access to my data. There are differences in all of these platforms and tests, and that can make a difference in terms of outcomes.

Brad Power: Ricardo highlighted that if your medical oncologist is the quarterback, then you don't have a direct conversation with the pathologist. It seems to open up the potential for communication breakdowns. It's like how you as a patient are not involved in your molecular tumor board, and they're making decisions about you. It feels wrong to me. You're the integrator. You should have a direct pipe, a direct relationship, with your pathologist, and have that quarterbacking with all of your strategic intent. Like all the stuff you've already covered today.

Brian McCloskey: I agree.

Anonymous Caregiver: I'd like to pick up on someone like Dr. Scholz. When you think about the economic interests of who you're approaching, and who they're beholden to, or who they're not, whether it's an institution or a company: there is PCRI. Mark Scholz is co-founder. That's how I have met people that I was able to recommend to patients. It's a network, a group of researchers and practitioners across the nation. If you can get in with somebody who is affiliated with that massive patient education effort that they do twice annually, you'll then be able to get introductions, such as to pathologists. Dr. Epstein has spoken there. It's a way to meet people who are in this system. If you're not an MD, they don't want to talk to you. That problem makes me think about needing relationships with people inside the system. Who can you meet? Who can make those introductions inside the system?

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Brian McCloskey: A lot of my doctors are part of these institutions that have a lot of shackles, which is what I think Jonathan (Starr) you were talking about. Maybe it is time to step outside and look at alternative healthcare models, and PCRI could be one of those.

Anonymous Caregiver: The best is that these are bidirectional relationships. For example, Ricardo is very active, and he is bringing a lot of value to the table to interested physicians, and even to ones who are maybe not interested in the stuff that he stirs up. It's a partnership, and practitioners like Dr. Myers are very friendly to commercially available tests and would recommend doing things that are outside of regular institutional university-type standard of care. It comes down to who is going to be philosophically most patient-centered in their approach, not institution-centered.

Jonathan Starr: I was about to bring up PCRI too. They have a patient conference in early September every year. I assume they're going to do that this year too. It's really good usually. In the past it has been in person at the Marriott by LAX. The last couple years it's been virtual. There are a lot of things that they present that you're way past, but still, it's an incredible opportunity to meet the professionals in the field and to meet other patients and get guidance from them. And you could meet Dr. Scholz. That's just a couple weeks away. You might want to consider participating or attending.

Brian McCloskey: I'll see if I can make that. Those are great opportunities to meet people, and I'll try to get in the queue before then with him.

Jonathan Starr: It's September 10th through 11th, if it's going to happen. They record it. If you want to go back and see previous presentations by Jonathan Epstein among others, it's a great opportunity.