“Comparing Test Results and Treatment Strategies across 10 Advanced Prostate Cancer Patients” (Brian McCloskey) [#45]

February 22, 2023
Brian McCloskey and Brad Power

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“One of the things that we're trying to do is to move patients into more sophisticated testing.” – Brian McCloskey

Meeting Summary

As we approach the one year anniversary of the Prostate Cancer Lab, we have ten very active advanced prostate cancer patients pursuing tests, building a list of treatment options, and developing a strategy for what's next. We wanted to take a step back and reflect on what we are seeing and learning from their experiences.

Brian McCloskey, co-founder of the Prostate Cancer Lab, shared patient stories, aggregated patient data, and drew out patterns and insights from the experiences of the ten active patients in our community. The process for each patient is to share their genomic information from DNA sequencing, RNA sequencing, and other tests, as well as their electronic medical records. Treatment options are then developed for each patient, including inputs from service providers such as CureMatch, Massive Bio, xCures, Cancer Commons, SHEPHERD Therapeutics, Genomic Expression, and mProbe. This information is then used to facilitate conversations between the patients and their care providers.

Mike Yancey and Rick Stanton shared their medical and disease journeys, using their PSA as a timeline, overlaid with different treatments.

What patterns can we see across advanced prostate cancer patients? Are there commonalities in their genomic mutations?

TP53 is far and away the most prevalent gene alteration across the ten patients, followed by TMPRSS2/ERG, PTEN, and then a lot of single gene alterations. There is no commonality in the combinations. Some of the patients share one or two gene alterations, but there are no two patients that look the same. On average, the patients have three alterations or biomarkers. The minimum is one, and the maximum is six.

How do you measure patient experiences?

Prostate cancer patients have many treatment options (including surgery, radiation, chemotherapies, androgen deprivation therapies, and immunotherapies). Each systemic treatment works for a while, and then it fails, and the patient moves on to another therapy. Brian looked at the years that each patient is getting for each systemic therapy before failure. For example, Brian has had five systemic therapies over six-and-a-half years. On average, he’s getting just over a year and a quarter from each therapy. Two patients are outliers. On the high end is Ken Anderson, who has gotten just over two years per systemic treatment. Ken has been

living with aggressive cancer and bone mets, and he had over 25 rounds of chemotherapy (docetaxel). On the low end, unfortunately, is Mike Yancey, who is getting less than six months per systemic therapy. Any therapy that he takes has no durability. Once he completes his treatment, he gets two to three months after that, at best, and then the cancer is on the run again, and he needs to find another treatment.

What are the major findings about the Prostate Cancer Lab community?

We have a really engaged patient group. They are educating themselves and leaning in to try new tests and treatments. Patients are learning from each other.

What have we learned you should do if you are an advanced cancer patient?

1. Use your existing genomic and other data to get a full portfolio of treatment options. There's an opportunity to leverage our treatment matching service partners to get more treatment options.
2. Get deeper diagnostics if you can. If you can get the raw data from your diagnostics vendor, then you can take it to another vendor for additional insights. For example, Mike Yancey took his raw RNA data from Tempus to SHEPHERD Therapeutics for them to run their RNA seq analysis.
3. Talk to your physician about how to maximize the useful life of your systemic therapies.
4. Refresh your diagnostic data as you see more lines of therapy. Monitor your disease progression, such as getting weekly PSA tests.
5. Gather your story into a one-page summary, including your PSA over time, overlaid with treatments, and the treatment options you are considering next, so that you can get advice on priorities and strategy.

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Meeting Notes

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SUMMARY KEYWORDS

patients, data, treatment, psa, cancer, brian, biomarker, rick, mike, mets, systemic therapy, google drive, alterations, oncologist, lab, insights, database, therapy, tumor, working

SPEAKERS

Kevin Fordney, Mike Yancey, Saed Sayad, Rebecca Driscoll, Brad Power, Brian McCloskey, Rick Stanton

Brad Power

We're approaching the one-year anniversary of the Prostate Cancer Lab, which we started in March of last year. It's very appropriate to take stock and see what we've learned and the community that we have built. Brian will share some analysis he's been doing.

I want to qualify this. This is the first time that we've shared this. It's a very rough draft. Please think of it not as a finished product. It's just a working document. Our request is that you help us make it better. If there are questions and things that you think we should be doing, that's the spirit with which we will be sharing.

“Comparing Test Results and Treatment Strategies across 10 Advanced Prostate Cancer Patients” (Brian McCloskey) [#45]

Brian McCloskey 01:35

Thanks everybody for joining. I'm going to have a riveting presentation today. Honestly, it's going to be a little bit more of a weather report than anything. The reason I say that is that as I was exploring and aggregating this data, I remembered my days when I was working in business intelligence and realized that there was a paradigm, which was 80% of the work is in data aggregation and maybe the other 20% is in analytics, or 10% in analytics and then 10% in decision making. Over the course of the past several few days, I realized that that 80% rule is 100% accurate. It goes to the point that everything that we're doing right now is manual. As we have the president of AWS with us here wearing his shirt, hopefully we'll be able to get to a much more automated process to look at our data. This is very much a crawl, walk, run approach and we're in a crawl stage.

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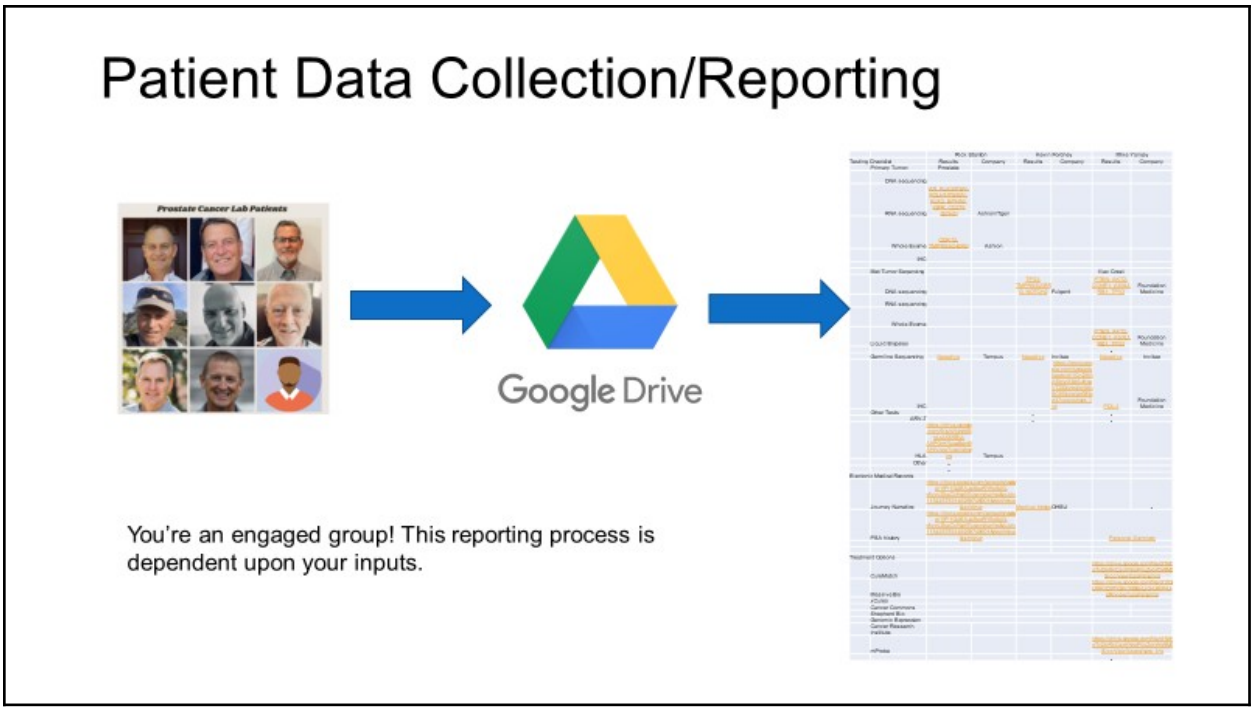

So let me share with you what I have. First off, we have 10 patients. One of them wasn't pictured here, but we have 10 patients that are part of the Prostate Cancer Lab. The way that we set this up is that each of the patients is sharing their electronic medical record information and their genomic reports, or "omics" reports, to a Google Drive. I've taken that Google Drive and looked across each of the various patients, and I use a checklist to make sure their documents are complete. This could become the basis for an analytic tool, but I'm exploring their genomics, primary tumor RNAseq, data from their met tumor, insights from liquid biopsies, germline tests, and other tests such as ARV-7, HLA, IHC, etc. I'm also looking at their electronic medical records. Everyone has some report, whether it's from MD Anderson, UCSF, or wherever, and all of that information is in the Google Drive. I have a section around treatment options. As you know, we have a marketplace of very generous service providers such as CureMatch, Massive Bio, xCures, Cancer Commons, SHEPHERD Therapeutics, Genomic Expression, CRI, mProbe, and hopefully some others. You're going to see how each patient is tracking through the funnel. Each one of these cells is hyperlinked to the document in the Google Drive. This is the process in terms of how I was looking across our datasets. This is as basic as you can possibly get, as we're using Excel, Google Drive, and we're not using any kind of analytic tool to connect the data. This is just a starting point. But sometimes when you get your hands dirty, you begin to understand how this information can come together with more sophisticated tools. This is very much a "crawl, walk, run" process.

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One of the tools that I found yesterday was this cool mapping software, and I wanted to take a look at where all of our patients are. We're all connected, and we are coast to coast, from sea to shining sea. I have pictures for all our patients except for Phil Resch.

There are going to be some data gaps in the data here. We have good coverage of the United States, but hopefully, we're going to be able to fill in all the states and get greater representation across the country. We also want to get more ethnic diversity in our group. If you know people that want to join us, please refer them to us. We've already had a little bit of word-of-mouth marketing, but continue to do that, particularly if you know African Americans. As many of you may know, African Americans have much higher rates of prostate cancer relative to their population than other racial groups. This is a big focus of the Prostate Cancer Foundation and the American Cancer Society. We need to reflect that in our community as well.

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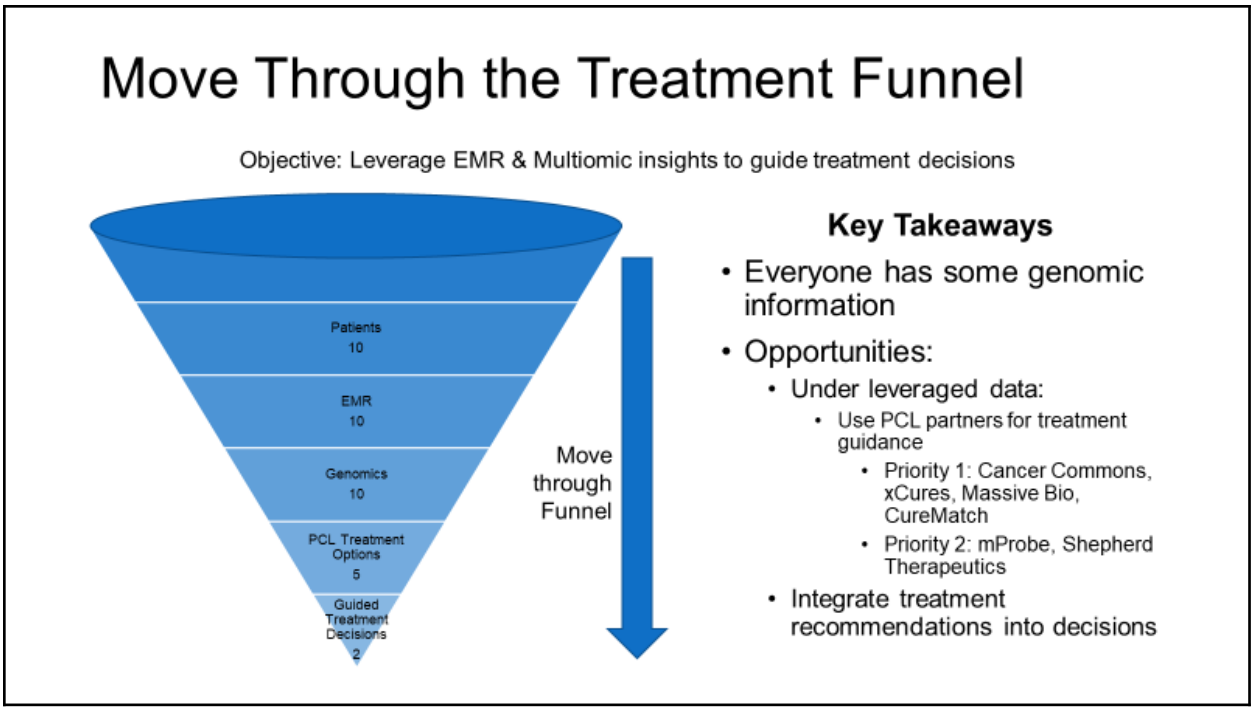
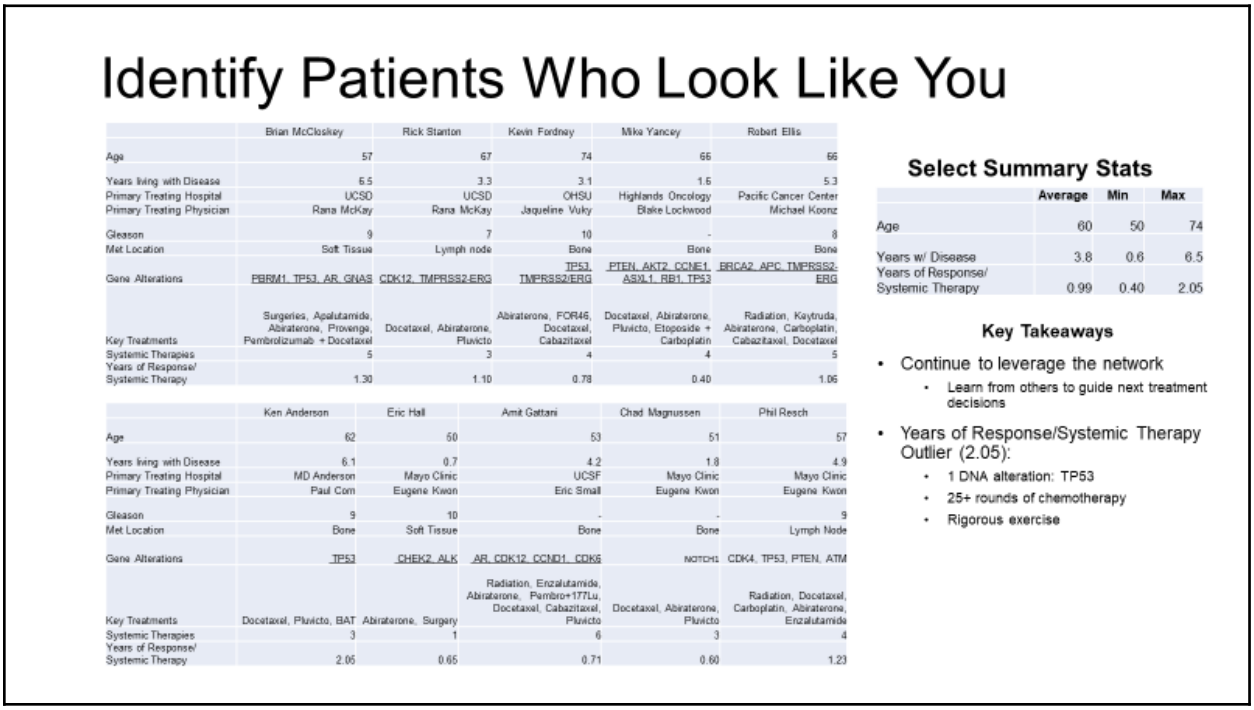


One of the things I wanted to look at was how our patients are moving through what I would call our treatment funnel. As I mentioned, our objective is to integrate electronic medical record information and multiomic insights to guide treatment decisions. If we look at how our patients are moving through that process, we have 10 patients, and the good news is all of them have some electronic medical record information. All of that is integrated into our Google Drive. All of them have some genomic information. We're doing well in terms of collecting the datasets that are required to get treatment decisions.

If you look at the Prostate Cancer Lab treatment options, this is the aggregation of all our service providers (e.g., xCures, Cancer Commons, CureMatch, etc.) and the patients that have taken advantage of those services. About half of them have varying degrees. Of those five, two have had guided treatment decisions from that insight. If we pull back a little bit, I think that there's some low hanging fruit. Because we have this data, it's easy to leverage it. Low hanging fruit would be going after Cancer Commons, xCures, Massive Bio and CureMatch. The reason I say that is that their processes to ingest information are very simple. All our patients have the data that's required to feed them.

There's really no reason why that number of five shouldn't be ten. I know that it can be sometimes daunting to pull all this information together and have conversations and start these processes. I would offer that if you need my help to do that, I've done it for other folks, I'd be happy to do it for you. But it is important because what we're trying to do is elevate the conversation between the patient and the care provider. There are two ways that we do that. One is through these Wednesday sessions, where we offer essentially master classes on cutting-edge science. The second way that we facilitate that conversation, or raise the water level of intelligence, is to offer these treatment opportunities. I can tell you, as I've gone through this process, that it really is very, very helpful. I think you guys have heard that I went into my oncologist and presented 21 different treatment options aggregated across our service providers. My med oncologist went through 21 of them, whittled them down to eight, and then finally to three, and now we're about ready to pull the trigger on one of those. It's an easy

process, but I understand that there's a lot going on just to manage your disease. I'm happy to help you with this process.



Identify Patients Who Look Like You

	Brian McCloskey	Rick Stanton	Kevin Fordney	Mike Yancey	Robert Ellis
Age	57	67	74	66	66
Years living with Disease	6.5	3.3	3.1	1.6	5.3
Primary Treating Hospital	UCSD	UCSD	OHSU	Highlands Oncology	Pacific Cancer Center
Primary Treating Physician	Rana McKay	Rana McKay	Jaqueline Vuky	Blake Lockwood	Michael Koonz
Gleason	9	7	10	-	8
Met Location	Soft Tissue	Lymph node	Bone	Bone	Bone
Gene Alterations	PBRM1, TP53, AR, GNAS	CDK12, TMPRSS2-ERG	TP53, TMPRSS2/ERG	PTEN, AKT2, CCNE1, ASXL1, RB1, TP53	BRCA2, APC, TMPRSS2-ERG
Key Treatments	Surgeries, Apalutamide, Abiraterone, Provenge, Pembrolizumab + Docetaxel	Docetaxel, Abiraterone, Pluvicto	Abiraterone, FOR46, Docetaxel, Cabazitaxel	Docetaxel, Abiraterone, Pluvicto, Etoposide + Carboplatin	Radiation, Keytruda, Abiraterone, Carboplatin, Cabazitaxel, Docetaxel
Systemic Therapies	5	3	4	4	5
Years of Response/ Systemic Therapy	1.30	1.10	0.78	0.40	1.06

	Ken Anderson	Eric Hall	Amit Gattani	Chad Magnussen	Phil Resch
Age	62	50	53	51	57
Years living with Disease	6.1	0.7	4.2	1.8	4.9
Primary Treating Hospital	MD Anderson	Mayo Clinic	UCSF	Mayo Clinic	Mayo Clinic
Primary Treating Physician	Paul Corn	Eugene Kwon	Eric Small	Eugene Kwon	Eugene Kwon
Gleason	9	10	-	-	9
Met Location	Bone	Soft Tissue	Bone	Bone	Lymph Node
Gene Alterations	TP53	CHEK2, ALK	AR, CDK12, CCND1, CDK6	NOTCH1	CDK4, TP53, PTEN, ATM
Key Treatments	Docetaxel, Pluvicto, BAT	Abiraterone, Surgery	Radiation, Enzalutamide, Abiraterone, Pembro+177Lu, Docetaxel, Cabazitaxel, Pluvicto	Docetaxel, Abiraterone, Pluvicto	Radiation, Docetaxel, Carboplatin, Abiraterone, Enzalutamide
Systemic Therapies	3	1	6	3	4
Years of Response/ Systemic Therapy	2.05	0.65	0.71	0.60	1.23

Select Summary Stats

	Average	Min	Max
Age	60	50	74
Years w/ Disease	3.8	0.6	6.5
Years of Response/ Systemic Therapy	0.99	0.40	2.05

Key Takeaways

- Continue to leverage the network
  - Learn from others to guide next treatment decisions
- Years of Response/Systemic Therapy Outlier (2.05):
  - 1 DNA alteration: TP53
  - 25+ rounds of chemotherapy
  - Rigorous exercise

There's a lot of data here, and I'm going to try to simplify this. We have ten patients here and there are a few core different components that I've considered: age, the years living with this disease from the date of diagnosis, treatment location, treating physician, and Gleason score.

Because we're all advanced, I would expect nothing below a Gleason score of eight, and Rick is an outlier here at seven. There are a few folks here that don't have Gleason scores. That's just something that requires pathology and some follow-up. Sometimes it may be hard to do.

I've looked at the met location. As we've heard, 85% of prostate cancer patients have bone mets, and you can see, we track a little bit below that. We've got 6 patients, and about 60% of us have bone mets, and the others have either a combination of soft tissue or lymph node mets, which is interesting.

I've also looked at gene alterations. I've taken just a very brief snapshot of the treatments that all of you have gotten. I have included surgeries and radiation. I didn't get into the number of each of these different elements. I also did not include any first line hormone therapies such as Lupron (a hormone deprivation therapy), Firmagon (Degarelix, brand name Firmagon, a hormone-based chemotherapy), Rubraca (Rucaparib, brand name Rubraca, a PARP inhibitor used as an anti-cancer agent), or Dutasteride (used to treat symptoms of benign enlargement of the prostate and may reduce the chance of developing an inability to urinate.) I've left them off because all of us are getting those. These are looking at second line hormone therapies, chemotherapy, immunotherapy, et cetera. You can see what we have relative to key treatments.

I did a quick scan of the systemic therapies that each has received and pulled an interesting metric which is to look at simply the years that each patient is getting for each systemic therapy. For example, if you look at me, I've had five systemic therapies over six-and-a-half years. On

average, I'm getting a year and a quarter, or a year and a third, from each therapy. That's interesting. There are a couple of outliers here. On the high end, you see down at the bottom, is Ken Anderson. Ken has been living with the disease for six years. He's at MD Anderson, and he's got a high Gleason. He's got aggressive cancer, bone mets, but he only has one alteration, TP53. It's possible that's changed, but I don't think so. He's only been on three treatments. What's really fascinating about Ken is that he had, I believe, over 25 infusions of docetaxel, I want to say 28. He's been on Pluvicto, and he's currently on B.A.T. He's getting just over two years per systemic therapy. On the low end, unfortunately, Mike is at 0.4. He's getting less than six months per systemic therapy. We're hopeful that he'll get a more durable response with the findings that he has from mProbe, which recommended he take etoposide (a chemotherapy typically used to treat small cell lung cancer) and carboplatin (a chemotherapy). These drugs were completely off the radar before he had his analysis from mProbe.

As you can see on the right hand side, the average years that our patients are living with the disease is about 3.8, and that's growing. The minimum is 0.6 years. That doesn't mean that the patient died, it just means that they were just recently diagnosed. In this case, it's Eric Hall, who's doing quite well, and it's just that he's very early in his disease. The max is six and a half years.

I wanted to create a fancy graph that would have connectors from one patient to another, but I'm going to let you look at this table for connections between this network of patients that we have. As you're thinking about your next therapy, your gene alterations, and your condition, you should reach out to patients who look like you and that's already happened. Each of you has been amazing in terms of offering insights to other patients. As this network grows, hopefully, we're going to have an even stronger network effect.

I also want to note that I have not included Chad's gene alterations because I need to go through with him a huge report that he has. It was a little confusing. We'll need to take that offline. I know that he has gene alterations, I think he has P53.

Rebecca Driscoll 19:23 (from the chat)

Is there a plan in place, via consent, to ask for your XML file of the report from the labs? This allows for structured data to be captured and analyzed. Companies, such as xCures, have a hard time getting these files from labs. But patients can get them, and the most useful version

Brian McCloskey 19:25

We don't have a plan to do that right now, Rebecca, but this is clearly something that we need to do. We would need to potentially even partner with you all because I'm pretty sure that xCures has this.

Rebecca Driscoll 20:03

They don't. That's why I brought it up. The laboratories, because of their statements and monetizing data, will not give it to them. They feel like they’re in direct competition. But I think that people need to get a little bit more familiar with what they're asking for, especially you as the patient can ask for that, and the laboratories will give it. You just must have a place to put it. I think there's opportunities, and as you're analyzing similarities. You started this off by talking about automation, so that's why I'm bringing that up because it makes some of these analyses between all your patients a lot easier.

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Brian McCloskey 20:45

I agree these are just raw ingredients right now.

Rebecca Driscoll 20:54

Yes, this is food for thought. I think people aren't asking for this and they will give it to you.

Brian McCloskey 21:08

It's a great opportunity, so thank you for that, it’s something that we will definitely pursue.

Brad Power 21:20

I want to compliment you, Brian. This is a big step forward. I think the metric you added about years per systemic therapy is something that we've been sensing, but it's nice to see it all laid out in numbers because people like Amit and Mike are really fighting a more difficult battle. Thanks for all your work on this.

Brian McCloskey 21:41

This is still scratching the surface of understanding the relationships between each of these different patients. Of course, as you get more data, then you're going to get more robust relationships. I'm looking forward to fleshing this out and building upon it.

Brad Power 22:05

I don't know that I've ever seen “years per systemic therapy" as a metric, but it shows that when you're patient-led, that's exactly what you'd want to know.

Brian McCloskey 22:19

I think that this is pretty accurate too. I went through a fair bit of work just to make sure that I captured all of the treatments going through the EMR records to make sure that I was accurate. I'm sure I've missed something here. But we need to change this metric, to extend years per systemic therapy.

Mike Yancey 22:41

Brian, I'm just going to comment. You did pretty good here with respect to me because that's been the issue with my cancer. Any therapy I take has no durability. Once you complete your treatment, you get two to three months after that, at best, and then the cancer is on the run again. I think this is a great metric that you put together here. And it's close enough to be accurate. That looks pretty good to me.

Brian McCloskey 23:06

I appreciate that.

Saed Sayad 23:19

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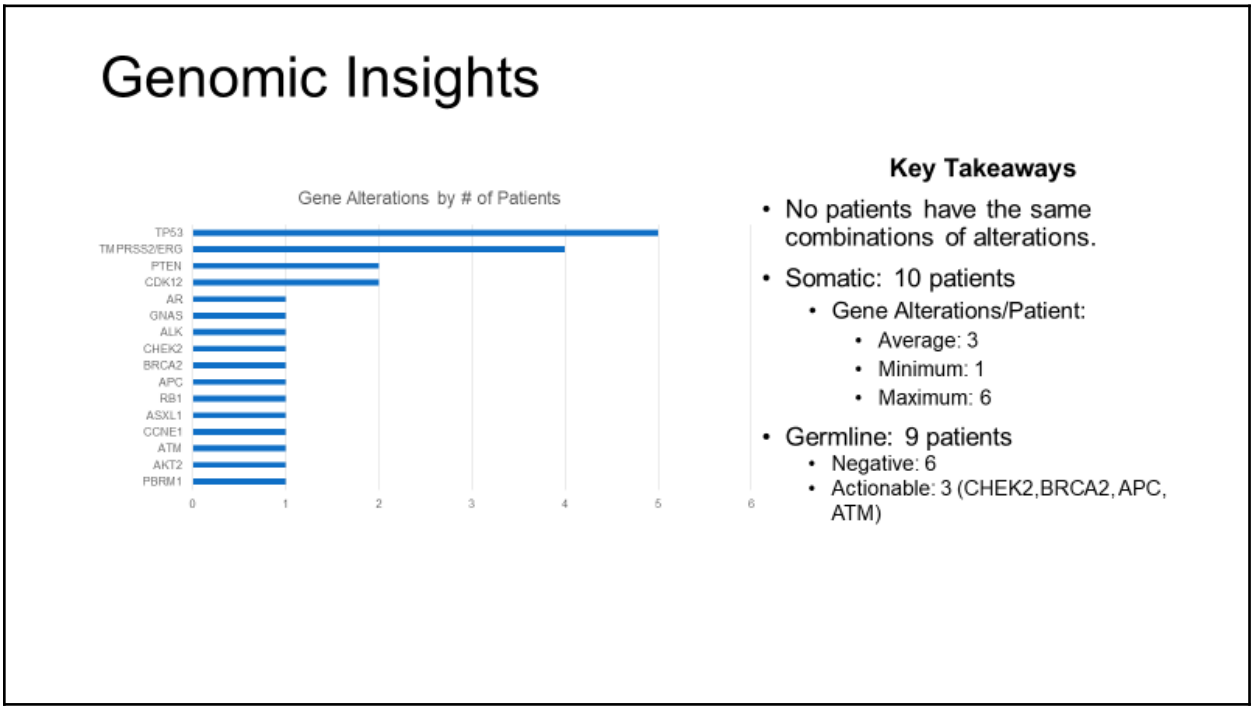
Thank you. I have two comments. First, about your idea of 80% of the work being about data aggregation, and a little bit about the analytics. I agree. But I would change it a little bit to 60% being data aggregation, and 30% to feature extraction and 10% in modeling. If you look at even deep learning, the modeling component is just the old neural network model. The feature extraction is the most important. And the second point here is, still in many of the presentations I see exploration. Exploration doesn't give us the answer to our question. We should start with the question. What questions do patients want answered? They want to know if this drug is better than the other drug for them. If I get this surgery, what's the probability of recurrence? We need to change this approach. Can we find an answer to those questions based on the data we have in our electronic record? As I mentioned, we have more than 5 million omics in the public domain field, but we are not using it. We are just trying to explore the data. What's the end of this exploration? We need to find those gold nuggets. That needs to change - the way we are working it out.

Brian McCloskey 25:18

I agree 100%, Saed. Rick is going to share with you some work that he's been doing right after I present this that will illustrate the community that we're building, and the different recommendations that are coming from different providers. First, you must have the data inputs, and then you have to have enough data to model. Rick's going to show the next iteration of what we're thinking about in terms of having a more holistic view of patient data that captures this community, and the recommendations that the community is providing treatment options. He'll share that soon.



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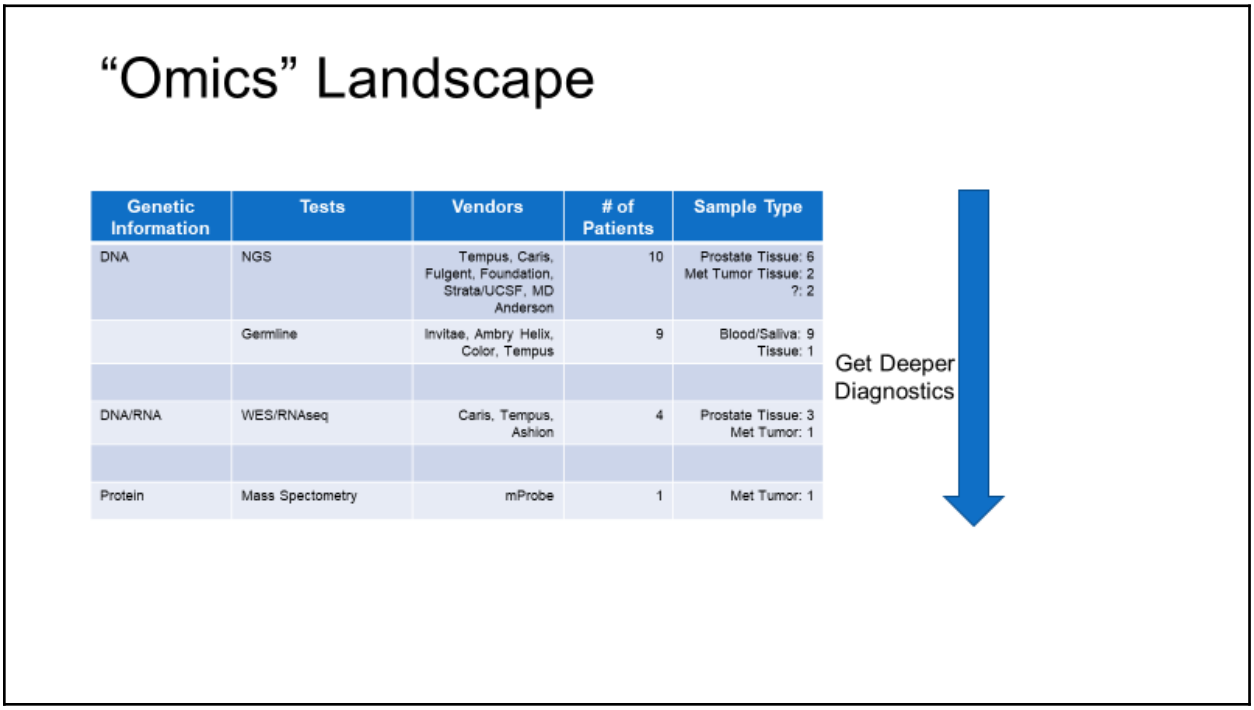
We did look at the germline of nine patients. Six have negative and three have actionable genes.



One of the things that we're trying to do is to move patients into more sophisticated testing. If you look at DNA, we've got plenty of vendors that do NGS for us. All 10 of our patients have it. Several are using the prostate tissue for that, and some are using met tumor. We also have very good representation for germline. Nine of us have germline testing as I mentioned, and these are some of the vendors that they're using. Testing usually comes from either blood or saliva. In one case, we also had a second test that was from tissue. Then as it flows down into DNA and RNA, when we look at whole exome sequencing and RNA sequencing, we've got a few vendors that play in that arena. There are four of us that have whole exome sequencing, three of those that come from prostate tissue, one from a met tumor. Now we're getting into proteomics and mass spectrometry.

We're very fortunate that mProbe has offered to provide our patients free of charge proteomic tests. Mike Yancey is blazing the trail on that. About a month ago, he received his report and has already changed his treatments based upon that insight. I'm having a conversation today with my medical oncologist, and I'm going to be going after proteomics and spatial phenotyping. The point is that we need to keep moving into deeper diagnostics. I recognize that there are some challenges for those of us who have bone mets. It's harder to get some of these tests. Sometimes it requires a bone aspirate, etc. But for those that don't have bone mets, some of these tests could be available to you. As you talk to your doctors about this, you should be going after proteomic testing which is free for you. We really should continue to push the envelope to get more data and deeper insights.

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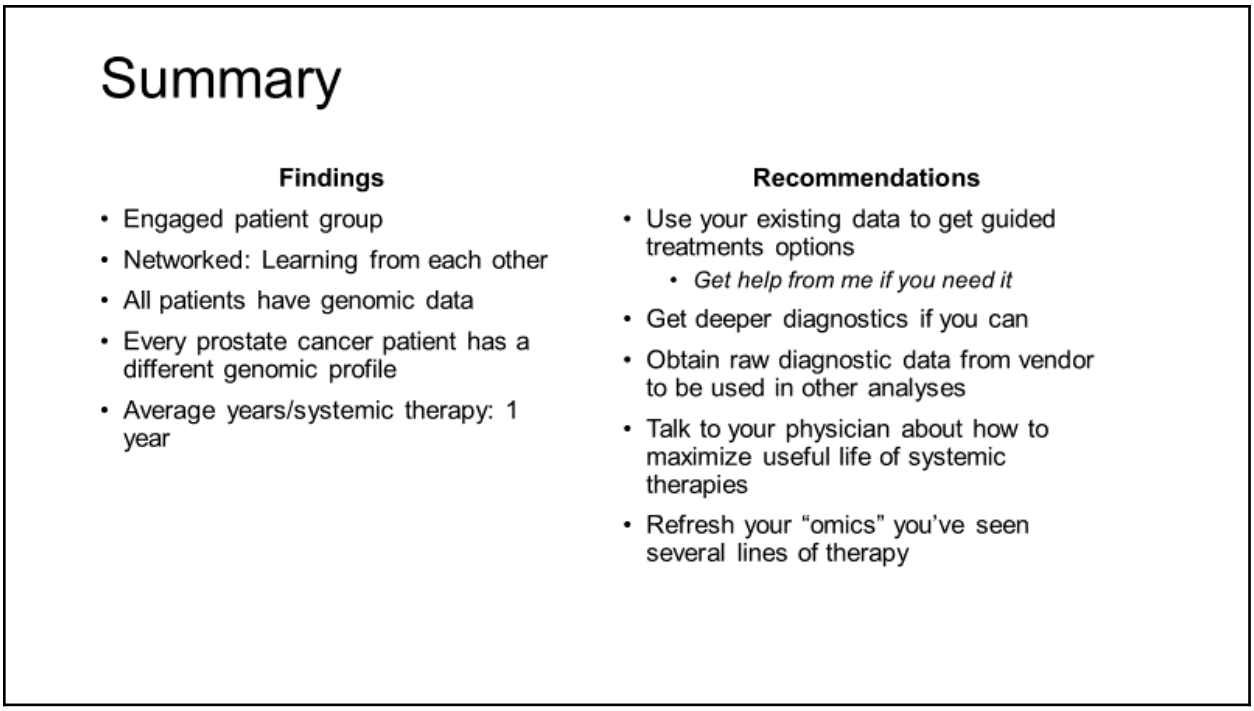

In summary, we have a really engaged patient group. I know it's a hassle to upload your docs into the Google Drive, but I've noticed that many of you continue, or, most of you continue to use the Google Drive to update your information, which is great.

We've seen examples of how patients are learning from each other and that's always super inspiring.

In terms of recommendations, use your existing data to get guided treatment options and get help from me if you need it. This goes back to the point that you all have genomic information. But there's an opportunity to leverage our partners to get those guided treatment decisions.

Second, as I just talked about, let's get deeper diagnostics if you can. If you can get the right raw diagnostics from your vendor, then that's helpful because you can just pick that up and then take it to another vendor for additional insights. An example of that is that I'm currently working with Mike to send over his raw data from Tempus to SHEPHERD Therapeutics for them to run their RNA seq analysis.

Talk to your physician about how to maximize the useful life of systemic therapies. Now you have some data that gives you insight on how long these are lasting. Perhaps there's a plan that you can build with your physician to extend the useful life of those therapies. Now you're armed with some data to make that point even stronger. You also know where you fit on the bell curve.

There are two more things that I wanted to chat about. Mike, you have prepared a presentation that encapsulates your journey. I think you did an amazing job. Mike, if you can kind of take us through this. This could be useful for other patients. And then Rick, I'm going to have you chat about how you've mapped your journey.

Mike Yancey 34:06

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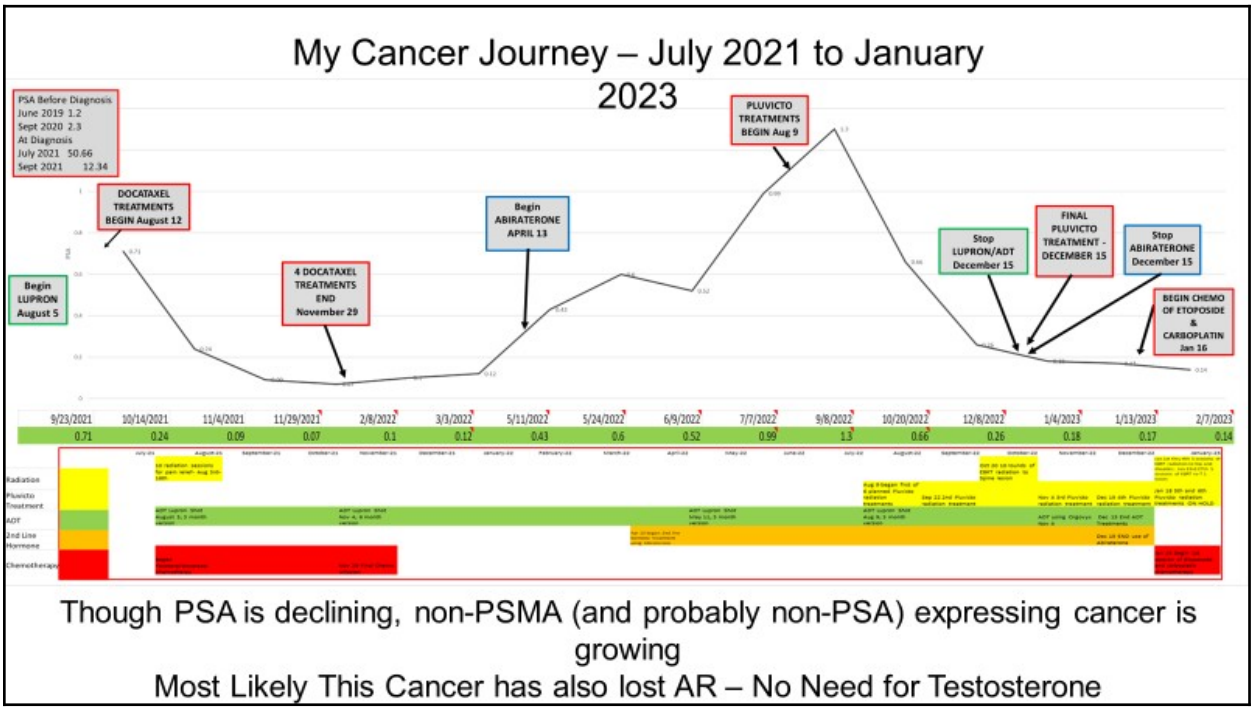


Basically, one interesting thing about me is that I always had annual physicals, and in June 2019 my PSA was 1.2. A little over a year later, September 2020, it was 2.3. I ended up in the hospital in July of 2021. That's when I was diagnosed. At that point in time, my PSA had jumped up to 50.66. Then as we got going with some drugs, it had dropped to 12.34 in September of 2021.

The takeaway that everybody needs to know with me is that even though my cancer is very aggressive, it does not put out a lot of PSA with respect to how much cancer I have. We use the PSA as this kind of reference point. In some cases where people would have their PSA changed by let's just say 100 points, in my case, a change of 0.1 or 0.2 may be about the equivalent.

As you can see here, I began Lupron right after I got diagnosed, and my PSA dropped down pretty good. I also started docetaxel a few days thereafter on August 12, and that worked. I finished up my docetaxel November 29. At that point in time, my PSA started to rise once again. And they gave me abiraterone around April 13. Abiraterone did absolutely nothing. Effectively, everything kept climbing. I finally got Pluvicto treatments on August 9th. I peaked out shortly thereafter, and then with Pluvicto my PSA dropped significantly.

One thing that's not explicitly stated here is that we discovered in October of 2022 that I had lesions that were now attacking my spine, causing a couple of spinal cord compressions that did not put out PSMA, which is what Pluvicto targets Therefore, that cancer also does not put out much in the way of PSA. You don't see any jump at that point in time. I had some radiation to take care of all that, and we were rocking along pretty good.

However, I did stop ADT. That was my choice. My oncologist works with me well. I'm always willing to try something out of the box. Most oncologists would never stop your ADT, Lupron. I

just want to see what happens. I started December 15 and because of the growing lesions on my spine, we also could no longer go forward with Pluvicto. We stopped that also on December 15. I stopped taking abiraterone because it was doing absolutely nothing. As Brian has already referenced, I began the chemo, Etoposide and carboplatin, January 16th. Even though after I started that my PSA continued to drop. The actual PSA numbers are the green stripe. I've tried to color code to some degree in between radiation and Pluvicto, which is a form of radiation. I know the writing is very small here, that's all in the yellow, and then I tried to color code that ADT in the green. So that's kind of a combination of abiraterone and Lupron. The Abiraterone is orange. I've had two types of chemo at this point in the red.

The issue I've got is that this cancer in my spine is mutated even though we did a biopsy. What was very interesting about it is it still retains most of the mutations that we'd had done with the bone from the original biopsy in July of 2021 as well as some liquid biopsies. It's remained relatively consistent. But I expect that this cancer on my spine has also most likely lost all AR. In other words, it didn't need testosterone. I'm hoping to try that out as soon as I finish chemo. We're going to finish chemo by June 1. I'm going to be traveling a little bit in July, but I'm hoping that when I get back that we're probably going to see things start to grow once again. We're going to try B.A.T., bi-bipolar androgen therapy, but because this new cancer probably is not sensitive to testosterone, we're probably going to see no change like other people have had with that.

Brian McCloskey 39:13

This is great. I love how you laid this out. It tells a story or a journey that you've been on. It would be great if we could understand all of these treatments and start looking at them across patients, relative to their biomarkers and other variables. Maybe Rick can help us understand how he's thinking about it.

Brad Power 39:47

Qne quick question on Mike's story: This is the first I've ever heard of someone where the PSA is not really being a good biomarker, and we're lucky in prostate cancer to have PSA as a marker of disease progression. In his case, maybe PSMA is also not indicating what's going on because it's mutated around that. Are there any other biomarkers for disease progression for prostate cancer if those two are not working so well?

Mike Yancey 40:19

Basically, it is all scans, a combination of PSMA PET scans as well as CT scans, etc. That's the only way we can keep up with what's happening. Something very interesting in my case that we have discovered is that when my cancer really takes off and begins to grow, I start spiking fever. We're talking 103 degrees and up. Anytime that I get a fever that spikes, I better get into the oncologist quickly because we have a problem.

Brad Power 40:51

I recall you've also had bone pain that's another indicator for you?

Mike Yancey 40:55

Yes, absolutely. The spiking fever and then shortly thereafter spiking bone pain is basically what happened to me at the end of December. I had the spiking fever every evening for several days and then by the latter part of December, after Christmas, the pain was so bad I could not walk. And that's when I ended up in the hospital.

Brian McCloskey 41:15

I have one comment on that too, Brad. I have a low PSA relative to my tumor volume. It's a real issue. There is a friend of our community, I won't name him, but he is working right now on identifying another biomarker for prostate cancer. He seems pretty optimistic about it, but it hasn't been published.

Rick, I want to cue you up to share what you're working on in terms of capturing your state and how you're aggregating what we're doing.

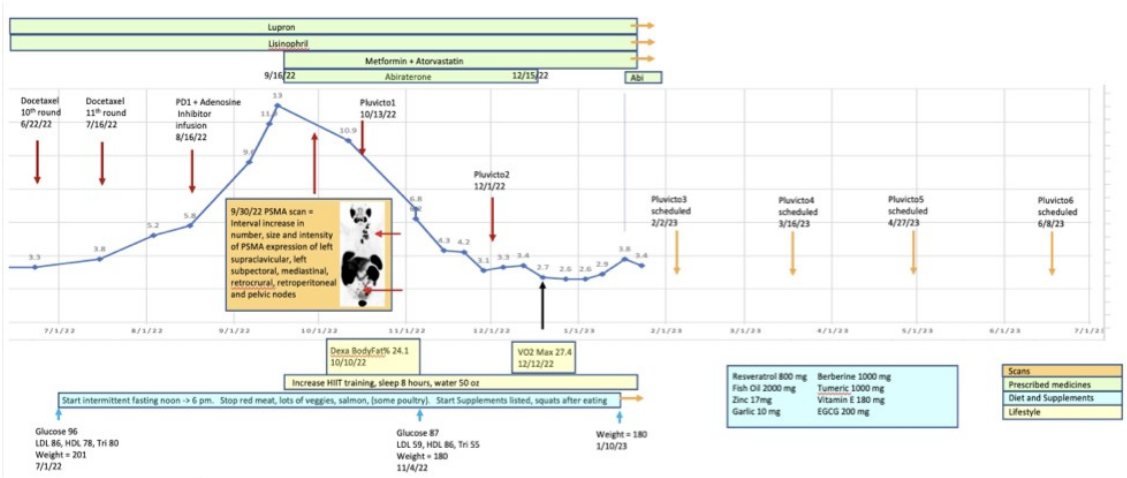
Rick Stanton 42:27

I look at things through a database view and automation view, AI view. I thought about what is the value of our Cancer Patient Lab or Prostate Cancer Lab? Why do we take the time to get together? It's to give. I could be playing guitar, playing golf, or whatever. I could still be spending time with my wife. But it's a balance, and I want to give, but there's also a need to get some value out. We need some value to keep coming. I tried to think of what to get out of here? To me, before I delve into the slide, it's a decision. When things are working, I don't really need this group that bad, and I shift more towards giving. But when things are not working well, and the therapy parachute that I'm on starts to fail, I need help. I thought about how we can create a report or a summary of a patient that captures the value that our lab gives through this collective knowledge.

“Comparing Test Results and Treatment Strategies across 10 Advanced Prostate Cancer Patients” (Brian McCloskey) [#45]

Cancer Patient Lab header, logo, address, etc

Patient Summary	
Patient Name	Rick Stanton
age	67
dateDiagnosis	2/2/20
prostatectomy	5/6/2020: pT3b, pN0, cM0, 4+3, seminal vesical and perineural invasion
treatments	lupron, casodex, darolutimide, docetaxel, abiraterone, pluvicto
primary tumor DNA	Exact/TGen: CDK12 LOF, TMPRSS2-ERG fusion, MSI stable, TMB low, HRD proficient, ch8q copy gain
primary tumor DNA	Tempus: CDK12 LOF, TMPRSS2-ERG fusion, MSI stable, TMB low
primary tumor RNA	Tempus/Stanton: Over expression: AR, PSA (KLK3), PSMA (FOLH1), KLK2, EPHA3, IGFR, B7H3, BRAF, PVRIG
primary tumor IHC	0-5% TILS
last CTDNA	8/5/2022 - Tempus XF: PBRM1 missense
last PSMA Scan	9/30/22 - Interval increase in number, size and intensity of PSMA expression of left supraclavicular, left subpectoral, mediastinal, retrocrural, retroperitoneal and pelvic nodes



Guidance Summary	
Dr. Rana McKay	Pluvicto
Dr. Tanya Dorff	Pluvicto
Dr. Treverdosky	Pluvicto
Dr. Lemanne	Pluvicto + Olaparib [PSA weekly for Gatenby modeling - goal pulsing to delay developed resistance]
Dr. Shen	Pluvicto as first option, other clinical trials noted
Cancer Commons	Pluvicto (Emma S.)
Curematch	Pluvicto + Pembrolizumab + Ponatnib
MassiveBio	TBD
Shepard	TBD
Xcures	TBD
Block Center	Liz Gold nutrition: pescatarian, juicing, exercise, no alcohol, eat 6 small meals a day
Block Center	Keith Block, Penny Block - currently being scheduled - goal: help my my body inhospitable to cancer
Plan	
next action	Continue [Pluvicto + Abiraterone] rounds 4,5,6 - round 6 ends 6/8/2023. Continue/tune diet, exercise
investigate	personalized vaccine
investigate	complementary approaches such as high dose intervenous vitamin C
investigate	[biopsy + tissue query + functional testing] + EBRT to debulk
investigate	tune diet and exercise per Block Center guidance

Signed: xxxxxx, manager, technical computing
Legal disclaimer…..

“Comparing Test Results and Treatment Strategies across 10 Advanced Prostate Cancer Patients” (Brian McCloskey) [#45]

Here's my cut at the report for me.

I start off with just the basics. Who I am. My treatments. I thought Brian's summary was excellent. This could all be put in a database easily. Here's my RNA. Here's what's going on with me from a 20,000-foot view. Here's a graphic. You can see my mets here with the red lines going here. They're nodal. My metastases are in my lymph nodes. One I feel the most is in the center of my chest. I know Pluvicto is working when I'm not driving along, minding my own business and there's a discomfort that is starting to be a pain in my chest. That's when things are not working. When that disappears, I know Pluvicto is working independent of any biomarker.

It looks like Mike's. I think we should standardize whatever makes sense. It includes what I'm doing for supplements and exercise, but here it comes down to what's the value to me when I'm in trouble? Right now, I failed docetaxel. I was on a clinical trial that had failed. My guidance at that time was from Dr. McKay. She was an angel to make Pluvicto available to me because it's not available to everyone. You can just see the complete consensus on Pluvicto. Some doctors said a combination, and Dr. Shen at UCLA mentioned there's other clinical trials that I could consider if I couldn't get Pluvicto. But I should get Pluvicto. I didn't do Massive Bio, and I should. I didn't do a few of these other vendors because it was clear. At Cancer Commons, I'd like to thank Emma Shtivelman. It was obvious which treatment I should pursue. When I asked Dr. McKay if I could do something else with Pluvicto, she did not – just do Pluvicto; it was clear what I should do next. That's the value of looking at this data in this way. I was deemed to be castrate resistant by Dr. McKay and Dr. Shen since I had failed darolutamide. I was in bad shape, and I couldn't get Pluvicto for six weeks.

Why did I go from being in trouble with a PSA of 13 and doubling pretty fast to a sudden drop? That was because of this Prostate Cancer Lab. I talked with Brian, Brad, and Bryce Olson. Bryce came up with the idea of trying abiraterone, but I had been deemed to be castrate resistant. Dr. McKay said, “Don't do it, it's not going to work.” Dr. Shen said, “Don't do it.” But "Dr. Bryce Olson said, "You've got nothing to lose. Try it.” Talk about the value I get from Prostate Cancer Lab. I went from a very scary slope to actual reduction prior to my first Pluvicto. So clear value.

Here's what everyone said. I can look at all the ideas. I still want to get xCures and SHEPHERD and anything I can because I'm coming to the end of Pluvicto. I'm going to have to have a plan. My plan right now is to continue Pluvicto and abiraterone, tuning my diet and exercise with the Block Center. More on that later. I think we should all investigate a personalized vaccine if that's an option for us and then look into other options. Everyone hopes that we can push this down and get some altitude, so to speak. This value will go into the collective, but it's also benefiting me by being associated with this Cancer Patient Lab. Not only knowledge and how I interact with my oncologist, but a place for me to go determine what I do next. What are all my inputs? Is there a consensus? Okay, so that's me.

“Comparing Test Results and Treatment Strategies across 10 Advanced Prostate Cancer Patients” (Brian McCloskey) [#45]

Cancer Patient Lab header, logo, address, etc

Patient Summary	
Patient Name	Kevin Fordney
age	
dateDiagnosis	
diagnosis	full blown bone mets: neck, spine, ribs, pelvis
treatments	Abiraterone, FOR46 trial, Cabazitaxel
tissue? tumor DNA	TP53, TMPRSS2/ERG
tissue? tumor RNA	?
primary tumor IHC	?
last CTDNA	?
last PSMA Scan	2//6/20 - Full blown bone mets
PSA annotated	

Guidance Summary	
Plan	

Signed: xxxxxx, manager, technical computing
Legal disclaimer…..

“Comparing Test Results and Treatment Strategies across 10 Advanced Prostate Cancer Patients” (Brian McCloskey) [#45]

I did a similar one for Kevin Fordney. I don't have as much information, but I did a little graph. You can see how he did on Abiraterone and the 446 trial. I don't know what that is. But it started to fail, and now he's doing cabazitaxel. It's easy to see what's going on. I can see what he's been on and how he's responding.

“Comparing Test Results and Treatment Strategies across 10 Advanced Prostate Cancer Patients” (Brian McCloskey) [#45]

Backup Slide1 – automated PDF generation code snippet

Handy pdf rendering library!

CSS

Start of PDF layout

….

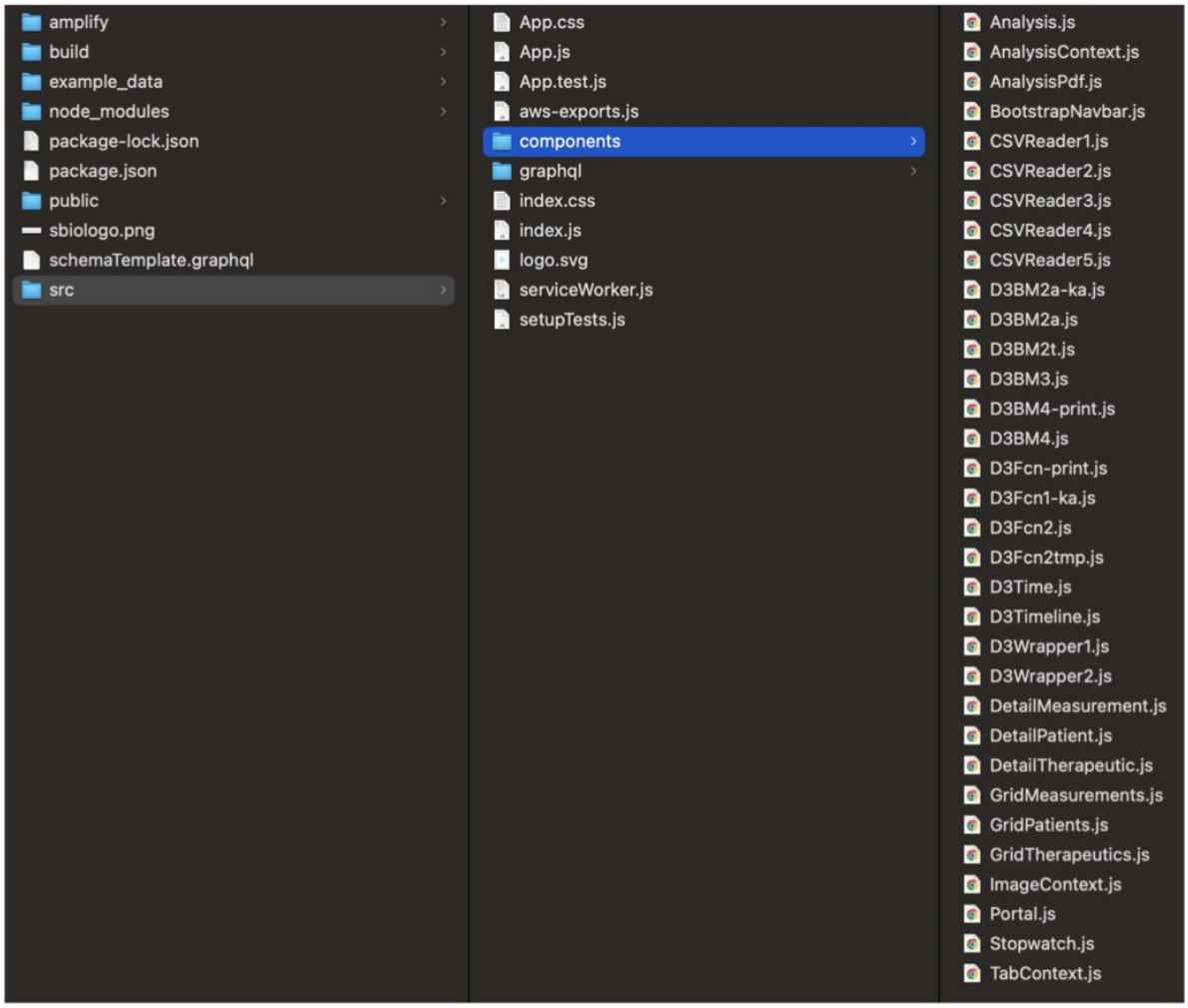
```
import React from 'react';
import { Page, Text, View, Document, StyleSheet, Image } from '@react-pdf/renderer';

// Create Document Component
const AnalysisPdf = (props) => {


  // Create styles
  const styles = StyleSheet.create({
    page: {
      flexDirection: 'row',
      backgroundColor: 'white'
    },
    section: {
      margin: 10,
      padding: 10,
      flexGrow: 1
    },
    fullWidth: {width: "100%", marginTop: 30},
    headerRow: {width: "100%", height: 60, display: "flex", flexDirection: "row", marginTop: 15},
    headerColLarge: {width: "40%"},
    headerColMed: {width: "35%"},
    headerColSmall: {width: "25%"},
    bottomRow: {width: "100%", height: 80, display: "flex", flexDirection: "row", marginTop: 60},
    bottomColLeft: {width: "48%", borderStyle: "solid", borderWidth: 1, marginRight: 15},
    bottomColLeftBorderless: {width: "48%", marginRight: 15},
    bottomColRight: {width: "47%", borderStyle: "solid", borderWidth: 0, borderBottomWidth: 1},
    bottomColRightBorderless: {width: "47%"},
    bottomRow2: {width: "100%", height: 230, display: "flex", flexDirection: "row", marginTop: 20},
    img: {width: 200, display: "block"},
    imgFull: {width: "100%", marginBottom: 10},
    smallText: {fontSize: 10},
    tinyText: {fontSize: 8, margin: "auto"},
    tinyTextBottom: {fontSize: 8, margin: "auto", marginTop: -5},
    bottomTextLarge: {fontSize: 12, fontWeight: "bold"},
    bottomTextBigger: {fontSize: 16, fontWeight: "bold"},
    tinyTextLeft: {fontSize: 8, marginTop: 5},
    titleText: {fontSize: 20, color: "#106ba3", display: "block", paddingTop: 10, paddingBottom: 10},
    table: { display: "table", width: "auto", borderStyle: "solid", borderWidth: 1, borderBottomWidth: 0
    tableRow: { margin: "auto", flexDirection: "row", borderStyle: "solid", borderWidth: 1, borderTopWid
    tableRowEven: { margin: "auto", flexDirection: "row", borderStyle: "solid", backgroundColor: "lightg
    tableRowTop: { margin: "auto", flexDirection: "row", borderStyle: "solid", borderWidth: 1, borderLef
    tableHeader: { margin: "auto", flexDirection: "row", backgroundColor: "#106ba3", color: "white", wid
    tableColLeft: { width: "25%", borderStyle: "solid" },
    tableCol:     { width: "75%", borderStyle: "solid" },
    tableColFull: { width: "100%", borderStyle: "solid" },
    tableCell: { marginLeft: 5, marginTop: 5,  marginBottom: 2, fontSize: 10 },
    tableCellTitle: { marginLeft: 5, marginTop: 5, marginBottom: 2, fontSize: 16 }
  });

  return (
    <Document>
      <Page size="A4" style={styles.page}>
        <View style={styles.section}>

          <View style={styles.headerRow}>
            <View style={styles.headerColLarge}>
              <Image src="./ashionlogo.PNG" style={styles.img}/>
            </View>
            <View style={styles.headerColMed}>
              <Text style={styles.smallText}>xxx Co</Text>
```

“Comparing Test Results and Treatment Strategies across 10 Advanced Prostate Cancer Patients” (Brian McCloskey) [#45]

This is not that hard to do from an automation sense. This is how to program creation of a PDF from the database. This is code in React. This is hosted on AWS. This is the CSS, or the PDF layout. Basically, you have an HTML driving a PDF, and it's pulling data such as, “This is Kevin. This is Rick. This is Mike.” This is just a glimpse of what that code looks like.

“Comparing Test Results and Treatment Strategies across 10 Advanced Prostate Cancer Patients” (Brian McCloskey) [#45]

Backup Slide2
Code base for web/mobile application serverless hosting on AWS
AWS Amplify deployment
AWS security,
AWS DynamoDB and GraphQL database queries
Automated graphics using D3.js
Codebase: React.js



“Comparing Test Results and Treatment Strategies across 10 Advanced Prostate Cancer Patients” (Brian McCloskey) [#45]

This is the full code base that I've worked out for hosting web and mobile applications in AWS. It uses this fantastic tool called Amplify Deployment. It has world class security. It uses AWS databases and a brand new noSQL called Graph QL. It's an amazing database structure and query engine. The graphics are in a JavaScript library D3, which stands for data driven documents and the code base React. Here's all the upper level, the source code goes down into here. The components are where the rubber meets the road. Here's the JavaScript file that I just showed you to generate the PDF, how to upload data, how to do stopwatches and tabs. That's one way that we can address automation. I think it's important that we consider the value that we give to patients rather than just collect and suck like other entities.

Brian McCloskey 52:28

Rick, what I love about this is the guidance summary component. All the PSA charts are awesome, but they're the baseline for what we're doing. You've done a really good job of showing it. How difficult would it be to take this and then create it for the other patients?

Rick Stanton 52:51

Super simple. If we give every patient a little Excel file, a template and say who's your doctor or whatever you want to put in it, we create a template. It's standardized, and it goes up. I've created the portal. As Rebecca knows, once you standardize your input, that's the hardest thing. We could create an Excel file template and tell all patients just put this in so that you don't have to go combing through different disparate records.

Brian McCloskey 53:40

I think that the power of this is to have almost a molecular tumor board that's weighing in and have all the insights centralized. All of us received, as you have just shown here, different inputs and different recommendations. If there's a way to present that to the community of doctors through a molecular tumor board, that can be very, very powerful.

Rick Stanton 54:19

If we look at Kevin or any of us, we all need to know what we're going to do next. It'd be good to have a plan. If you look pessimistically, we're all going to fail at something sometime. Although I don't really believe that's true, I still have hope. We're all going to have challenges on our journey. Just knowing what's ahead, or having a contingent plan is just a great idea. I know for me, there's a lot of worry. The most worried I've ever been is when I'm failing a therapy I'm on, and then it's not really clear what I should do because I'm already at the end of the NCCN Guidelines, and it's a very unnerving time, which doesn't help. Getting proactive - I think that's part of what our lab offers. It's that kind of awareness. "Okay, what's coming up next?"

Kevin Fordney 55:31

Thank you and Brian for all the efforts you put in. I don't have the ability to create all the Excel stuff. I've had one result since I sent you my stuff. I'm going to have a scan and look at Pluvicto. Is it the type of thing that if I had an Excel file, that I could continue to just add things in, as opposed to keep sending things to you to have you do it?

Rick Stanton 56:16

The way I designed the system that I made is that anyone that we wish to grant security authority can upload directly without a steward. AWS provides the ability to have full security, and how I've uploaded data into the cloud is via a little portal, and that will suck in that Excel file. If you change it, it'll suck in the changes. If we, as a group, say, "Hey, we want everyone to be able to do their own thing.” Then it's open. It's super simple. It's kind of fun because my son, Eric, put a little timer on it. However, if the group wants to do it, it's wide open. It's easy to set the security.

Kevin Fordney 57:40

I would only want to alter my records, and if I goofed something up or had a question even for people like me to be able to share some of the burden to become a little more independent on some of this. As it grows, to have some of you guys that are doing so much on our behalf, not have to do everything.

Rick Stanton 58:23

That's a great thought. Thanks for that sentiment. I think the most important thing is, what do we capture? I glossed over, and so did Brian, the details. These were our initial thoughts, and they need to be evolved. It's easy to add with this DynamoDB, noSQL database. It's non structured so you can put in images or scans or data.

Brad Power 59:11

How can we make this better? Particularly for the patients, is there anything that you would want to see added? For example, you'd want to know about the other patients or anything that comes to mind for you?

Saed Sayad 59:33

It depends on the question. Based on the question we have, we need to organize our data. I believe the number one source of data is the electronic record. For the prostate cancer group, we need to do our best to have access to the data, somehow anonymize it. Because at the end, if you don't have that data, we are just repeating the same thing again and again. We need data to answer a question properly. With 10 patients, it's just a guessing game. Then, as a group, we should work together to get that data out of it. I said there's some public data. We need that data.

Brian McCloskey 1:01:07

That's an interesting thought. This is data exploration that we were doing today. It's a small data set, as you noted, and maybe there are opportunities for us to partner with folks who have larger datasets and use our perspective in terms of what we want as patients to guide data acquisition for our treatment decisions. Start with the end in mind. The end is, "I want to get the best treatment that I possibly can or a series of treatments that I possibly can extend my life." We clearly don't have enough data right now to be able to do that.

Saed Sayad 1:01:54

The point here is we have a huge amount of data in our hands right now. Millions of data points, omics data. Let's focus on a couple of questions and see how we can find the best answer

based on the existing data. If you don't have access to it, let's see how we can access that data. I see a great team here. Everybody can take part in this task. We can reach our goal, and it's going to be one good exercise. It can be a use case for many other groups. This is not just a problem of this group. This is the problem for every aspect of medical data problems.

Rebecca Driscoll 1:03:37

Awesome presentation. This just makes me think about a lot of things that I've been working on around data. What I did not share with you at the beginning is I've been working on real world data initiatives since 2011, of various types. I completely agree about small cohorts, but there are other cohorts to match up to that can be significant. One of the things I've witnessed quickly as you guys have all experienced in community, urology and uro-oncology, is that, no surprise, a lot of these tumors are not being profiled. I have a relationship with a very, very large urology group that has a database of real-world data patient outcomes. They haven't been profiling their patients. This is more recent for them because they're looking at targeted therapy options. It's just newer to them. I'm wondering if there's an opportunity to sync up with groups like this, who are very large urology practices. Janssen has a huge interest in some of the work that they're doing, and maybe we can integrate these interesting things based on the way we were treated. Maybe these are the kinds of patients you should be profiling. Help them identify the best patients to profile just as a starting point. It's just food for thought. Although this is a small cohort now where you could start looking at comparative analysis with things that have not been done to help other patients. I love where you guys are going with that. I think there's opportunities for you guys to automate some of this. I can see that there's a lot of manual work, as you stated Brian upfront, but I think that there's some opportunities with some existing databases to make your guy's life a lot easier as well as control your data as a community of people that can compare and use that data with other datasets without losing the integrity of your own community of data.