"A Patient Uses Novel Testing Services to Guide His Treatment" (Brad Power) [#83]

Brad Power
January 24, 2024

“Emma has been there every step of the way, within a 24 hour response, telling me what this means. If I didn't have her, I don't think I would be useful. Because the intention we have is for you to be a copilot, a partner, with your medical team, to be bringing ideas and to be able to participate, put your finger on the scale for the things that are important to you, whether it's quality of life, whether it's you want to try to hit a home run versus hitting singles, whatever it might be. The patient has a point of view and has something to say in this, but you can't do it if you don't know what the options are, and what the tests are saying. Emma is that translator that allows me to be an active participant.” - Brad Power

“The standard of care is only going to get you so far. It's really incumbent upon the patient to push their care team. You have to work with your care team, or a care team that doesn't have to be the one that you're currently with, to leverage all of the diagnostics that are available. One of the challenges is that many medical oncologists don't know about the tests, or they don't know how to interpret them. And it's really important that the patients get involved to create that bridge. Translational medicine is how you take amazing science, that is, in many ways it's been proven that it works, take it from the lab and get it to the patient's bedside. But there are a lot of barriers that prevent that process from happening. But the role the patient has is really, really important because we do have a powerful voice. At the end of the day, we're responsible for our own decisions.” – Brian McCloskey

Meeting Summary

Advanced cancer patients want to identify more and better treatment options and choose among them to find the best treatment options for their care. Testing can help with both objectives.

But which tests are best, and how can patients access them?

The Cancer Patient Lab has hosted over two dozen discussions with experts about novel testing options, including RNA sequencing, liquid biopsies, proteomics, multiplex immunofluorescence, and functional testing.

Brad Power, Co-founder and CEO of the Cancer Patient Lab, is uniquely qualified to talk about testing options and how to access them. On the one hand, he has been the host of most of these discussions with testing experts. On the other hand, he was recently diagnosed with a recurrence of his cancer and needs to work with his medical team to make decisions on the tests he will get and interpreting the test results to make treatment decisions. Similarly, Brian McCloskey, Co-founder and COO of the Cancer Patient Lab, has developed relationships with testing and treatment matching companies, and used their services to guide his treatment decisions.

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Why should you invest in understanding testing options and advocate to get non-standard tests?

Tests can identify new treatment options and help in selecting the best ones for you. For example, Rick Stanton pushed to get an RNA sequencing test that identified that he had more of a protein, B7-H3, expressed in his cancer cells than normal, and there was a drug to inhibit it. He is currently on this drug and getting good results.

What are the principles that should guide your approach to tests?

- *"Mo' data is mo' bettah."* - Bryce Olson
    - Tests identify treatment options.
    - Tests guide treatment selection. You want to use data to make your treatment plan.
    - Multiple (different) tests give more perspectives.
- I'll be here again. Tests are not just for this treatment but future treatments and treatment strategy. Build your longitudinal story.
- Tissue is the issue.

How can you use the test results to identify treatment options and guide your treatment decisions?

1. Use evolutionary biology and game theory to guide your treatment strategy - beyond next best. Minimize cancer heterogeneity.
2. Combine treatments, including immune system boosting therapies, e.g., exercise.
3. Invest in expert ("second") opinions.
4. Favor immunotherapies. Avoid chemotherapy.
5. Strengthen your immune system and favor treatments that don't hurt your immune system.
6. Pursue personalized dosing at minimum effective level. Consider toxicity.
7. Access new treatments as quickly as possible.
8. Choose the best doctors and clinics.
9. Get as much treatment as your body can take.
10. Dose as low as you can.

What are the challenges in accessing and interpreting tests?

- **Handoffs**: There can be communication issues between departments that affect testing timelines. For example, the pathology department may be very busy sending out samples to testing companies.
- **Financial**: Financial challenges exist in accessing advanced testing technologies. Some startups provide services for free so they can get data. Most testing companies have financial support programs. The Cancer Patient Lab has special deals with its preferred providers. Most are free.

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- **Integrating data between tests:** There's more value from getting different tests than getting more of the same test. Putting energy into getting multiple tests is a principle to give a more complete story of what's going on.
- **Too much data**: Most doctors don't have time to pay attention to the flood of data that we can actually bring to them.

What should you do?

- **Help yourself**: Look beyond the standard of care and advocate to get tests and treatments that aren't standard yet. Engaged patients get better outcomes.
    - Tests that would not have happened without advocacy: Whole exome sequencing, RNA sequencing and interpretation, proteomics, functional testing, immunoprofiling
    - Treatments that became options when considering clinical trials and travel: immunotherapies
    - Treatment strategy: prioritize immunotherapies, consider clinical trials
- **Help others**: Share what you learn – patients as "hacktivists" - warriors and role models. Share your data. Post on social media. Contribute to a learning community.
- **Help the system**: Accelerate "translational medicine" – advocate to get research tests and treatments accessible to patients for clinical use. Compress the "S curves" from innovation to widespread use. Run experiments and scale what works.

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Meeting Notes

SUMMARY KEYWORDS

tissue, tests, patients, testing, gene, work, treatment, boston, brian, treatment options, results, lab, data, lymphoma, brad, follicular lymphoma, cancer, emma, sequenced, talk

SPEAKERS

Brad Power (37%), Brian McCloskey (32%), Michael Hensley (10%), Rick Stanton (8%), Frank Nothaft (6%), Emma Shtivelman (3%), Saed Sayad (2%), Amit Gattani (2%)

OUTLINE

1. Cancer patient Brad Power's journey and lessons learned. (0:03)
2. Lymphoma treatment options with patient history and current symptoms. (1:18)
3. Cancer treatment options and diagnostics. (4:57)
4. Cancer treatment options and testing services. (12:24)
5. Cancer testing and treatment options. (16:51)
6. Cancer treatment options and clinical trials. (23:00)
7. Lymphoma treatment options and side effects. (29:04)
8. Cancer treatment options and diagnostics. (32:53)
9. Medical testing and insurance coverage. (39:04)
10. Personalized cancer treatment and diagnostics. (42:37)
11. Testing accuracy in cancer diagnosis. (48:24)
12. Personalized medicine and cancer diagnosis. (50:07)

SUMMARY

- **Cancer patient Brad Power's journey and lessons learned.** 0:03
    - Brad Power shares his cancer journey with lymphoma and how he applied lessons learned from the Cancer Patient Lab.
- **Lymphoma treatment options with patient history and current symptoms.** 1:18
    - Brad Power shares his experience with follicular lymphoma, discussing his treatment history, including his recent cancer recurrence and upcoming treatment plan with Dr. Merryman at Dana Farber.
- **Cancer treatment options and diagnostics.** 4:57
    - Cancer Patient Lab offers a pipeline of services, including diagnostic testing and treatment guidance, for patients.
    - The services can help identify new treatment options. For example, Rick Stanton, an advanced prostate cancer patient, discovered a new treatment option through RNA sequencing.
    - Brian McCloskey emphasizes the importance of continuous learning and adaptation in cancer treatment, highlighting the need for ongoing testing and diagnostics to stay ahead of the disease.
    - He advocates for a personalized approach to cancer treatment, encouraging patients to identify their own principles and priorities to guide their journey.
- **Cancer treatment options and testing services.** 12:24

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    - Brian McCloskey and Brad Power discuss preferred testing and treatment guidance from the medical teams where they are being treated, and service providers, including BostonGene, Massive Bio, SHEPHERD Therapeutics and Cancer Commons.
    - Brad Power emphasizes the importance of Emma Shtivelman of Cancer Commons in helping him navigate medical tests and treatments by providing quick and accurate interpretations of pathology reports and clinical trials.
    - Massive Bio, provides free recommendations of clinical trials based on an individual's medical history and genomic information.
- **Cancer testing and treatment options.** 16:51
    - Dana-Farber provides basic testing services, including CT and PET scans, while SHEPHERD Therapeutics analyzes RNA data for treatment options.
    - Brad Power's pathology report revealed follicular lymphoma, not diffuse large B-cell lymphoma, guiding treatment options.
    - He is eagerly awaiting his BostonGene test results, which will take four weeks to arrive after his biopsy.
    - He had to follow up with the pathology department after a week of silence to get his tissue tested, highlighting communication issues between departments.
- **Cancer treatment options and clinical trials.** 23:00
    - Brad Power and Rick Stanton discuss the timeline for tissue processing and its impact on cancer treatment.
    - Brian McCloskey suggests process innovation and improvement for managing tissue.
    - Brad Power expresses willingness to travel for the right deal.
    - He will discuss treatment options with his doctor, including rituximab and lenalidomide, and new suggestions from Massive Bio.
    - Immunotherapy is good for blood cancers. Bispecifics have good indications. CAR-T has some issues with efficacy and safety.
- **Lymphoma treatment options and side effects.** 29:04
    - Emma Shtivelman suggests avoiding chemotherapy for follicular lymphoma recurrence, preferring immunotherapies with fewer side effects.
    - Brad Power and Frank Nothaft discuss the most effective treatment options for lymphoma, including combinatorial therapies and targeted drugs.
- **Cancer treatment options and diagnostics.** 32:53
    - Brian McCloskey emphasizes the importance of patients taking an active role in their care, including advocating for themselves and pushing their care teams to leverage diagnostic advancements.
    - McCloskey and other patients on the call share their experiences with using diagnostics to identify new treatment options and help others in similar situations.
    - Brian McCloskey mentions that some tests are free for patients through the Cancer Patient Lab, including functional testing with Travera.
    - Brad Power and Rick Stanton discuss the cost of advanced testing options, with some companies offering free or discounted services to patients.
- **Medical testing and insurance coverage.** 39:04
    - Frank Nothaft and Brad Power discuss challenges in finding and affording cutting-edge medical tests, particularly for translational medicine.
    - Brian McCloskey shares his experience with multiple sequencing tests, revealing concordance and differences between Tempus and BostonGene.
- **Personalized cancer treatment and diagnostics.** 42:37

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    - Michael Hensley discusses challenges in tissue analysis, including exhaustion and quality metrics, and the importance of financial assistance programs for patients.
    - He highlights the difficulty of finding payers to support new testing technologies, which are expensive and often face denials from insurance companies.
    - Michael Hensley and Brian McCloskey discuss the challenges of accessing advanced diagnostics for cancer patients, including financial barriers and limited communication between healthcare providers.
    - BostonGene and other labs sometimes have communication difficulties with healthcare providers, leading to delays in tissue analysis and treatment planning.
- **Testing accuracy in cancer diagnosis.** 48:24
    - Frank Nothaft discusses challenges in comparing results from different cancer testing modalities.
- **Personalized medicine and cancer diagnosis.** 50:07
    - Experts discuss the value of multiple tests in cancer diagnosis and treatment, including the use of liquid biopsies and cytogenetics.
- **Reproducibility of genetic data analysis.** 52:36
    - Rick Stanton describes a test he ran demonstrating reproducible results in whole genome sequencing validated through 78 individual sequencing runs.
- **Using data-driven approaches in cancer treatment.** 55:12
    - Brian McCloskey emphasizes the importance of data-driven decisions in cancer treatment, despite potential discrepancies in test results.
    - Saed Sayad suggests comparing single cell data from the same patient for better understanding of disease nature.

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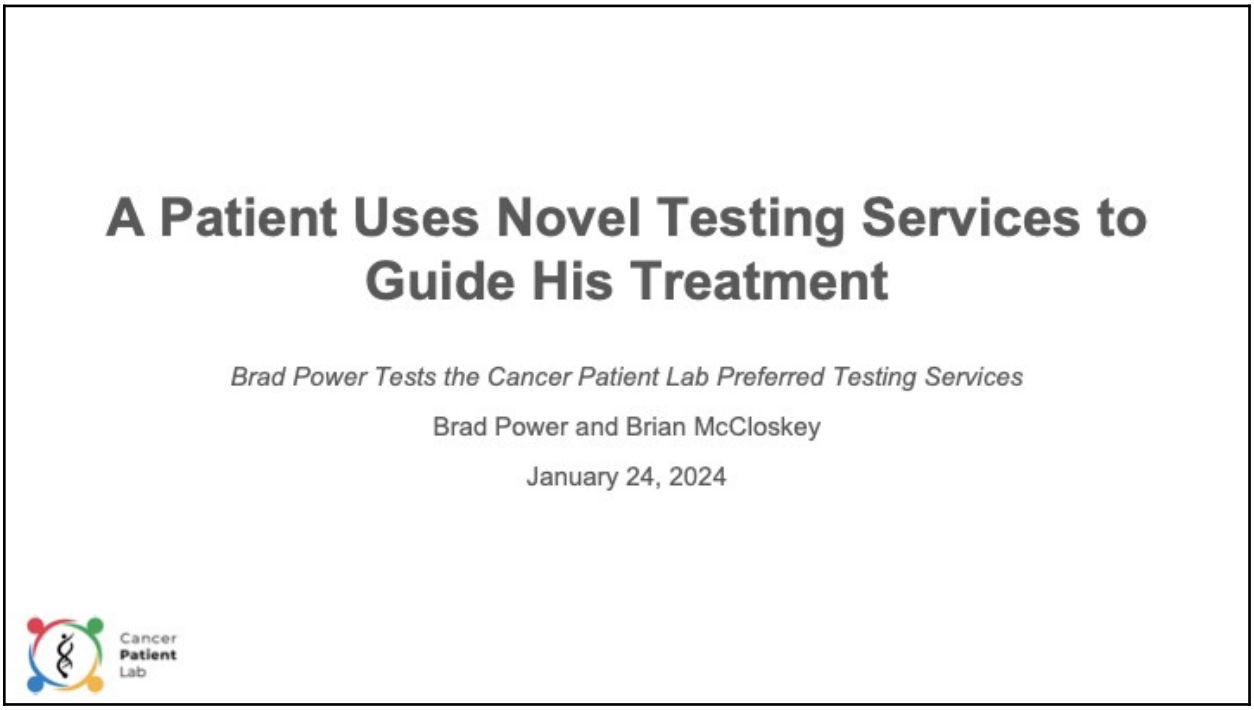
TRANSCRIPT

Brian McCloskey
Welcome to the Cancer Patient Lab.

Today we have a special guest, none other than our co-founder and CEO, Brad Power.

The reason that we are gathered here is to learn about Brad's cancer journey with lymphoma, and to understand how he has applied lessons learned from the Cancer Patient Lab, as well as services that we provide through the Cancer Patient Lab to address this part of his journey.



Brad Power 1:51
Our intention is 80% to share the pipeline that we've developed for testing options for people and a little bit into the treatment options, and then 20% to talk about my case as a test of that pipeline, and then also get any advice that anyone might have for me.

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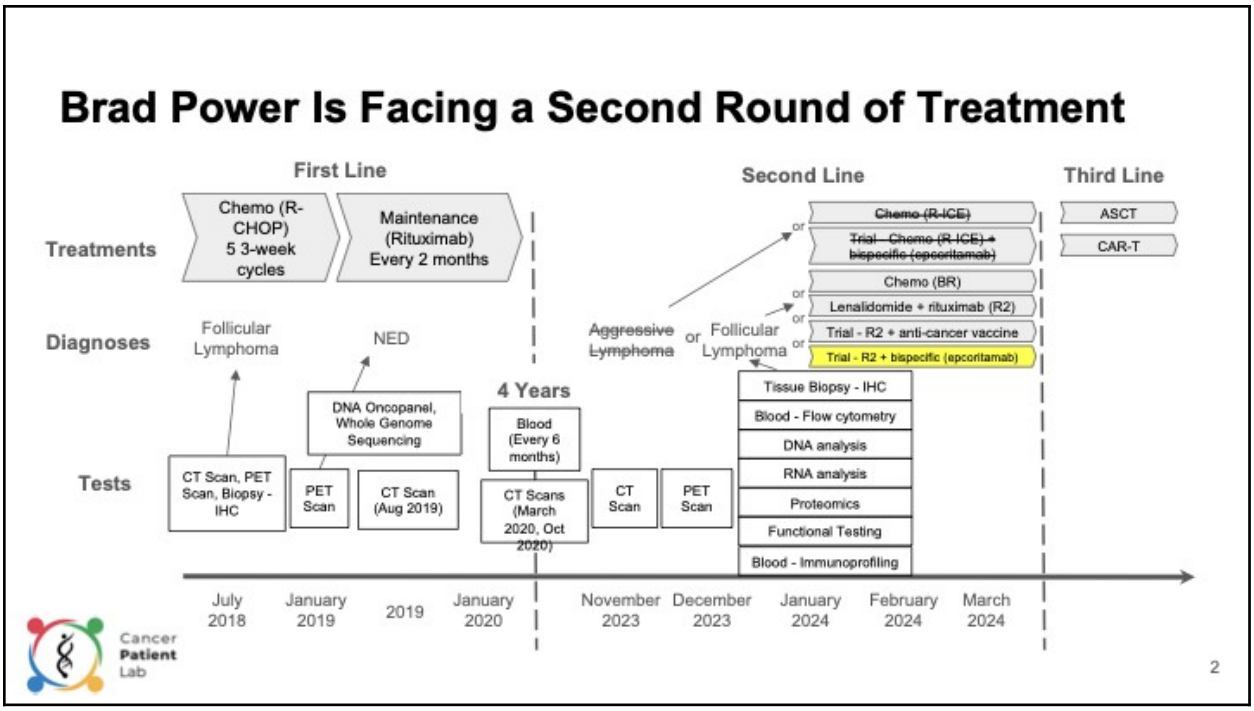


Brad Power 2:17
My medical history is that I've had no evidence of disease for four years. I was originally diagnosed in 2018 with follicular lymphoma. I went through the standard of care, which is a chemo cocktail called R-CHOP, and then went on maintenance. When we ran into the pandemic, we stopped the rituximab. Because it's lymphoma (a disease of the immune system), it's depressing your B cells (white blood cells), which means you don't respond well to a COVID vaccine. So we stopped it a little bit early so that I could get the COVID vaccine and be protected from COVID.

About two months ago, I was having some pain in my abdomen and it seemed like the symptoms I had had five years before. We did a CT scan, and it confirmed that I had had a recurrence. It basically shows up as the lymph nodes look bigger. Then they did a PET scan. Many of you probably know PET scans. It's where you get an injection of some radioactive stuff, and it lights up. It shows where the cancer is, and how bright it is determines how aggressive it is.

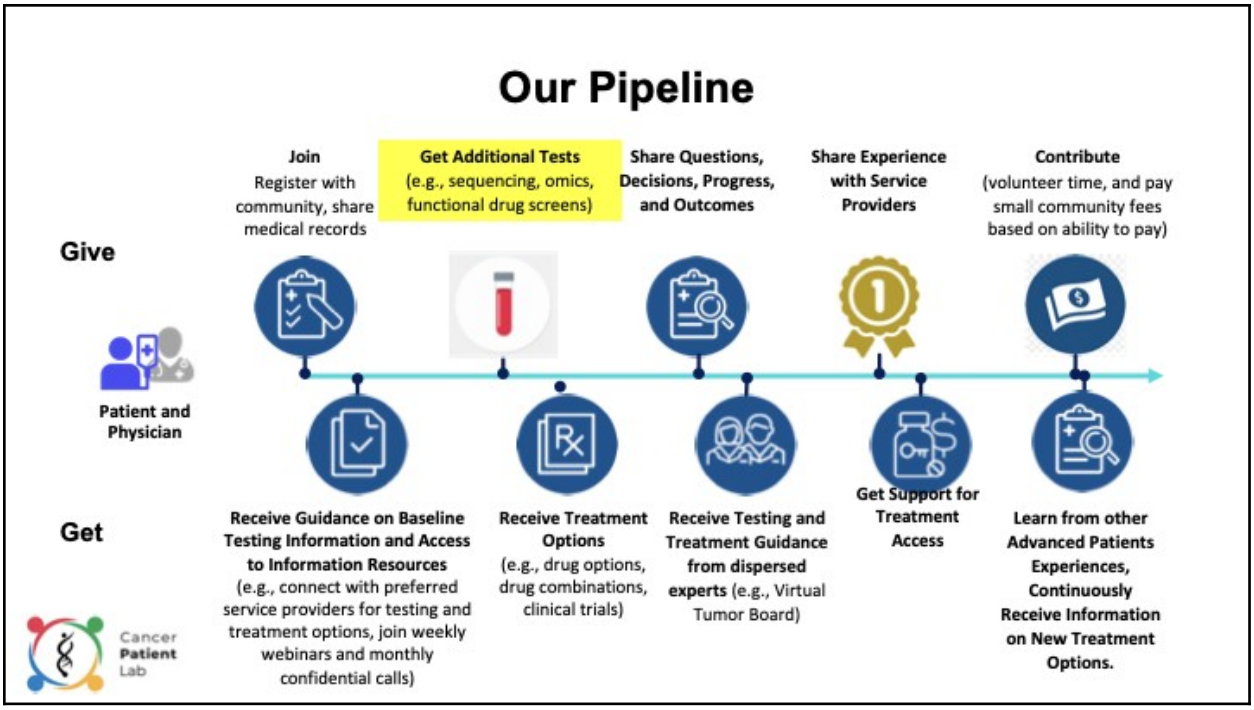
The column there indicates the tests that I initiated based on what I've learned from Cancer Patient Lab. Most of these are non-standard. We'll go into what the standard tests are. Typically, they take a biopsy to get tissue. I had a biopsy of a lymph node on my neck. Then you get what's called “IHC”, where they stain a tissue sample, and then they can tell what cancer it is and whether it's aggressive or not.

You can see on the chart where the diagnosis is aggressive lymphoma or follicular lymphoma. Follicular lymphoma is a less aggressive lymphoma. That's a determination which can only

really be made from the tissue. I was lucky that there was a lymph node that was close to the surface, and they could get a lot of tissue.

Brian can speak to this eloquently. Tissue is the issue. You want to manage your tissue and tissue can become scarce, but in my case, they got a lot of tissue from my lymph node.

On the right you see the layout of the treatment options. They were ones that were presented to me by my oncologist with my first first consultation when we were going over the fact that it had recurred. The testing we're doing is going to help us determine which of these we pursue. I'm meeting with my oncologist Dr. Merryman at Dana Farber tomorrow, and that's where we'll be laying out the treatment plan.



Brian McCloskey 5:01
One of the things that we offer patients that come to the Cancer Patient Lab is a pipeline of access to various services. This is like a process flow, which describes what the patient gets and how Cancer Patient Lab supports them through the process. This is important to talk about because some of you may only know us through the weekly webinars that we do. But in fact, we've had many patients who have gone through and used, particularly diagnostic services from our partners. This is just a quick overview of what we offer. This is really meant to describe the relationship that the patient has with the physician. When you come to the Cancer Patient Lab and you join with us, you get access to the community. You can share your medical records, if you want, and then you're going to receive guidance on basic testing. We'll talk a little bit more about who the test providers are. Then you take those test results back, along with treatments, to your physician. You get additional tests, or you get treatment, and you get additional tests as

appropriate. The journey continues. I'm not going to go through each element of this, but you get the idea.

I've used this pipeline for myself several times. As some of you may know, I did this two years ago, where I had 21 different treatment options from – at the time – three different service providers. They were primarily looking at my DNA and RNA. I can tell you that it's really, really important to particularly go through the diagnostics, because what I learned is that we uncovered treatment options that really weren't part of the discussion. When you start looking at targets that arise from the results of your sequencing, it opens up doors. For example, for me, I have advanced prostate cancer. I learned that I had a moderate expression of HER2. HER2, as we all know, is associated with breast cancer, and not commonly associated with prostate cancer, but that opened up discussion about HER2 being a target that we could go after with a known drug.

This is just a reminder for all patients and caregivers that are part of the Cancer Patient Lab, to what we have a pipeline, and that you should really take advantage of it when you need it.

Brad Power 7:51
Rick identified that he overexpressed B7-H3 from RNA sequencing, which is not a standard test, as another example.

Rick Stanton 8:05
I'm on a B7-H3 clinical trial right now, and so far responding.

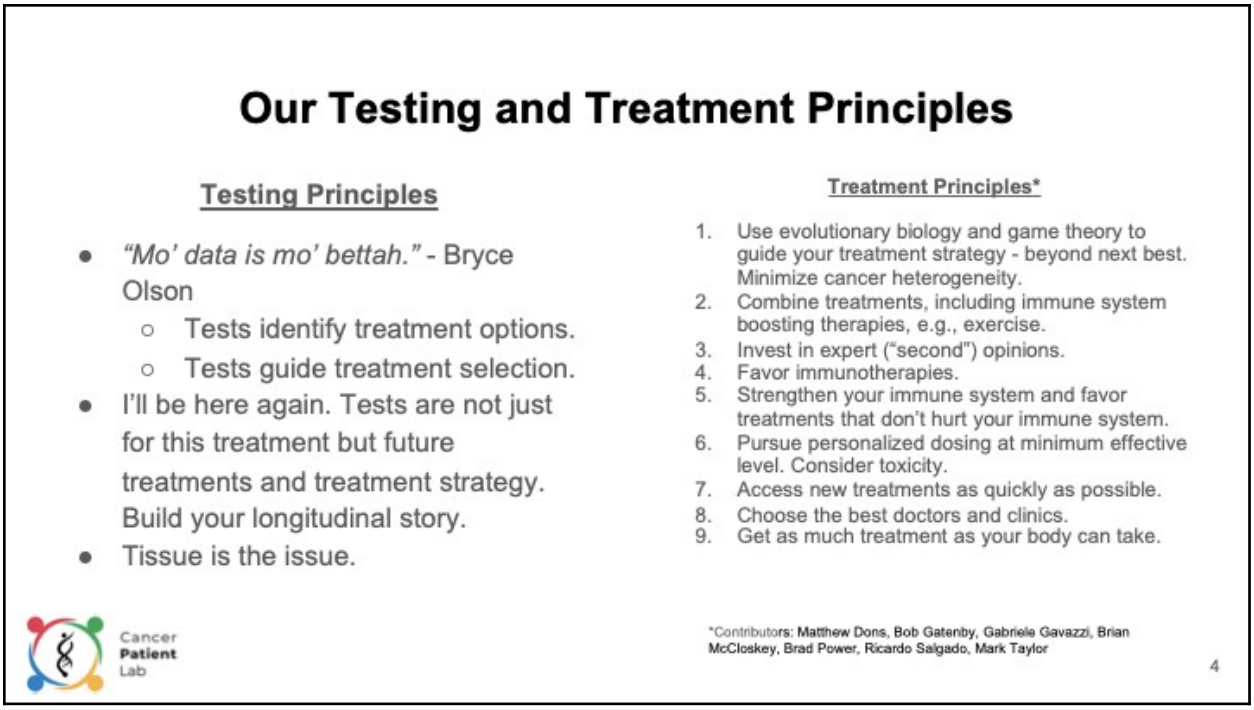
Brian McCloskey 8:14
You would not have known had you not gone through these tests.

Rick Stanton 8:20
Right. I would have known to a generalized degree. But we analyzed the RNA seq data, and it was wonderful that I was expressing 98% – super high expression – of B7-H3. It was a good match, not just a shot in the dark. It was wonderful to have that confidence. Because, like you, I had all these choices. To have one that was actually molecularly-guided was important. So far, I'm responding. We'll see.

Brian McCloskey 9:07
There's this iterative process. You need to get additional tests. It depends upon your cancer type. But when you're subjected to various treatments, your cancer changes. That's why it's important, if you can, to get additional diagnostics.

I just went through a process with BostonGene, and we reviewed the results yesterday. It's just absolutely amazing. We're going to do a separate session on that. But my cancer has changed over the course of the past seven-and-a-half years. That means that what was working previously is not going to work going forward. However, there are other targets that we can go

after. For certain cancers, it's an iterative process, where you're constantly getting more data, and you're making decisions as you go.



Brad and I talked several years ago about writing down what are the things that are really important to you as a cancer patient as you go through your journey. He wrote down some of these, and some of these we share.

The first is, as Bryce Olson said, “Mo data is mo betta”, which we just talked about. It does identify treatment options, and often ones that may not even be known.

I'll be here again. Tests are not just for this treatment, but for future treatments and treatment strategy. You're laying out a menu of different options. Then you're hopefully working with your medical oncologists to figure out a sequence. That sequence is going to change, again, depending upon what additional tests you get.

As we all know, tissue is critical. For many of us, it's hard to get tissue. So it's really important that you maximize the utility of that tissue.

From a treatment principles perspective, I'm not going to go through all of them.

We like this idea of evolutionary biology, which really comes from Bob Gatenby. We are big proponents of that.

Combined treatments include immune system boosting therapies.

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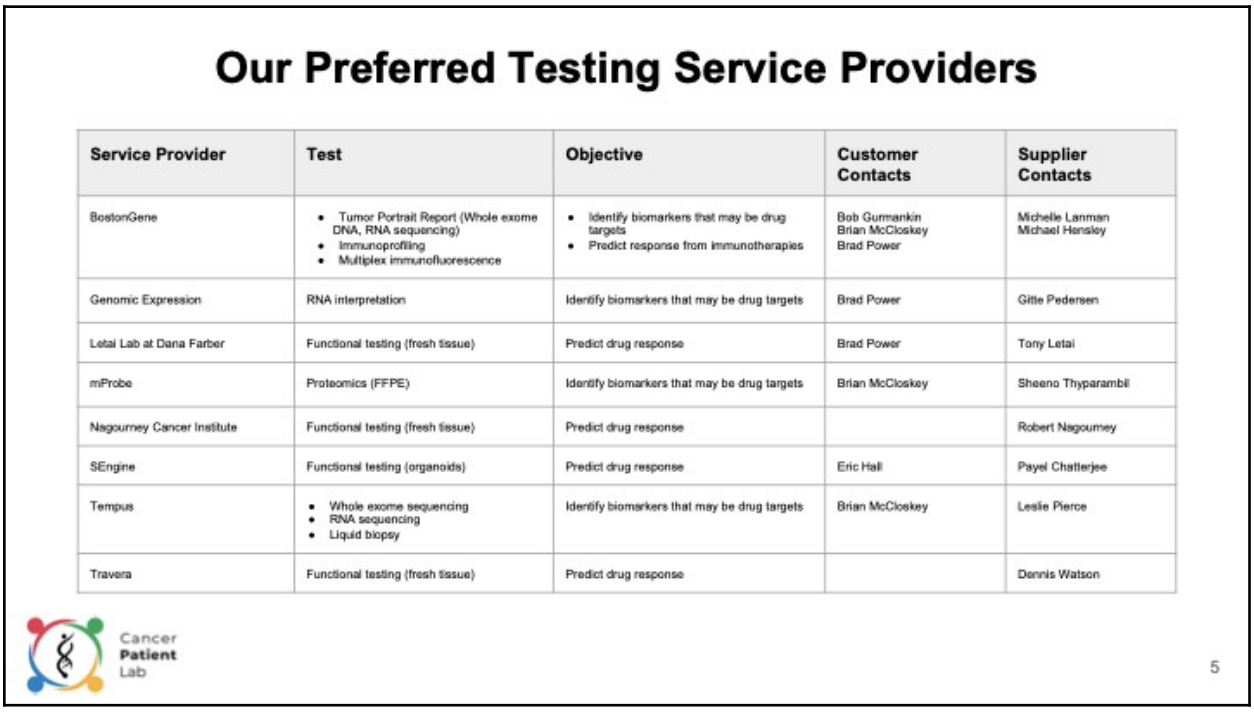
Invest in second opinions, favor immunotherapies, you get it.

The point is, is that for you, as a cancer patient, or caregiver, it's important to have this bedrock of principles that are going to guide your journey. If you write them down, you come back to them. They will evolve as you go through your journey, but it's nice to have it, and this document will be made available to everyone. So this could be your starter document, then you come up and customize it for yourself.



Our Preferred Testing Service Providers

Service Provider	Test	Objective	Customer Contacts	Supplier Contacts
BostonGene	• Tumor Portrait Report (Whole exome DNA, RNA sequencing) • Immunoprofiling • Multiplex immunofluorescence	• Identify biomarkers that may be drug targets • Predict response from immunotherapies	Bob Gurmankin Brian McCloskey Brad Power	Michelle Lanman Michael Hensley
Genomic Expression	RNA interpretation	Identify biomarkers that may be drug targets	Brad Power	Gitte Pedersen
Letai Lab at Dana Farber	Functional testing (fresh tissue)	Predict drug response	Brad Power	Tony Letai
mProbe	Proteomics (FFPE)	Identify biomarkers that may be drug targets	Brian McCloskey	Sheeno Thyparambil
Nagourney Cancer Institute	Functional testing (fresh tissue)	Predict drug response		Robert Nagourney
SEngine	Functional testing (organoids)	Predict drug response	Eric Hall	Payel Chatterjee
Tempus	• Whole exome sequencing • RNA sequencing • Liquid biopsy	Identify biomarkers that may be drug targets	Brian McCloskey	Leslie Pierce
Travera	Functional testing (fresh tissue)	Predict drug response		Dennis Watson

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I'll wrap up my section here by just talking a little bit about who our preferred testing service providers are.

- **BostonGene**: We just had an amazing session with BostonGene yesterday with Michael Hensley. They do a variety of different reports from one of the most in-depth tumor portrait reports that I've seen, and I've seen many of them. They've done profiling and spatial phenotyping.
- **Genomic Expression**: Another company that we work with is Genomic Expression and Gitte Pederson. They do RNA interpretation.
- **Letai Lab at Dana Farber**: Brad is going to talk a little bit about Tony Letai and his team at Dana Farber.
- **mProbe**: mProbe has been an amazing partner with the Cancer Patient Lab. They do proteomics, and I can tell you that proteomics is really what highlighted HER2 for me. That was really an important test for my treatment options.
- **Nagourney Cancer Institute**: The Nagourney Cancer Institute does functional testing. They require fresh tissue. They're based in Orange County, California.
- **SEngine**: SEngine does functional testing using organoids.

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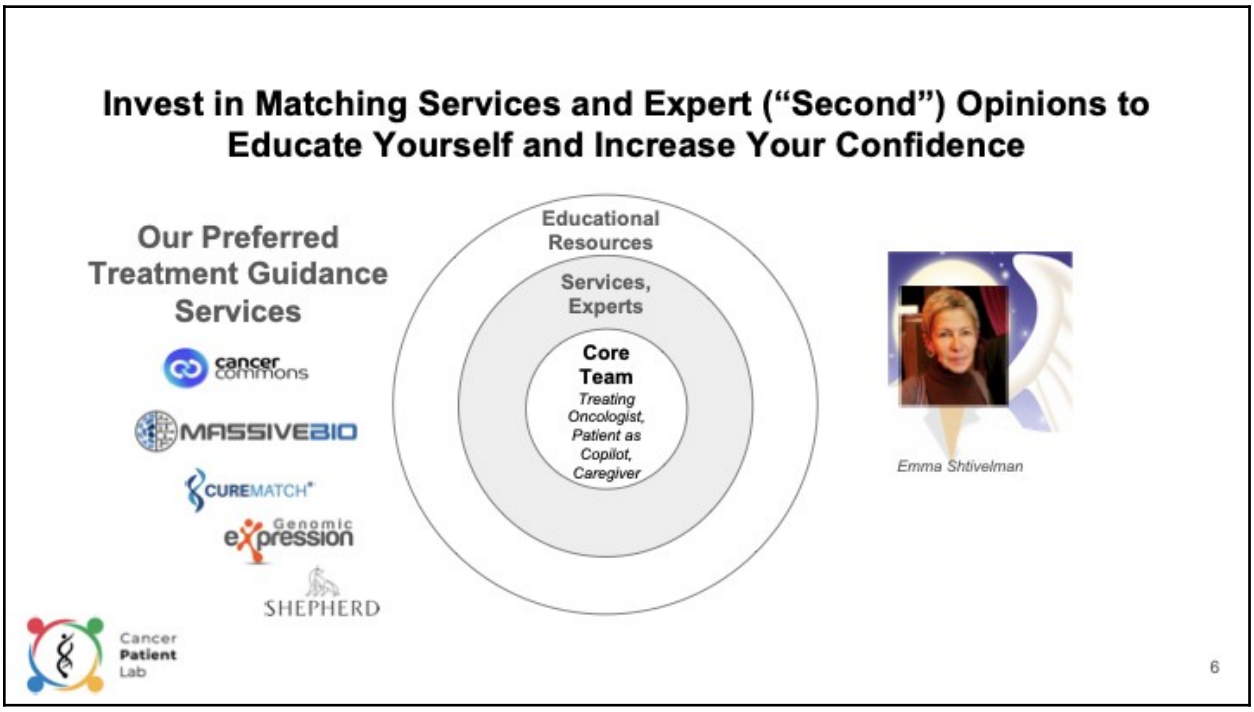
- **Tempus**: Rick referred to Tempus earlier. We did a whole bunch of transcriptomic analysis with them for both himself as well as me.
- **Travera**: Travera spoke here maybe two months ago, discussing their very unique approach to functional testing.

These are all service providers that you have at your fingertips, that we have worked with, and that we endorse and that we think are best in class.



Brad Power 14:20
Once you get all the data, then you need to make sense of it and prioritize it. We have a number of service providers here as well that we work with.

- **Cancer Commons**: Cancer Commons is our close partner. They have PhD microbiologists, such as Adrienne Nugent and Emma Shtivelman. They look at the medical records and the history and the genomic information, and then identify treatments or clinical trials. It's all handcrafted at this point. Their intention is to have more AI, but it's just amazing detailed information. They do it for free. It's a nonprofit. We should be donating to them, but they do it for free. It's like having a doctor in your corner. I tried to use DALL-E to come up with making Emma a guardian angel. That's what that image is. Emma's been with me every step of the way, every time I get a test, every time I get a pathology report. When you get a pathology report, it's impossible for a human to read. Doctors can read it. Pathologists can read it. But your average layperson can't read it. But Emma can translate it to say, these are the key points. Then as the cytogenetics report comes out, she tells me what the key points are out of that. Every one of these tests requires an interpretation. I'll show you the functional testing as well.

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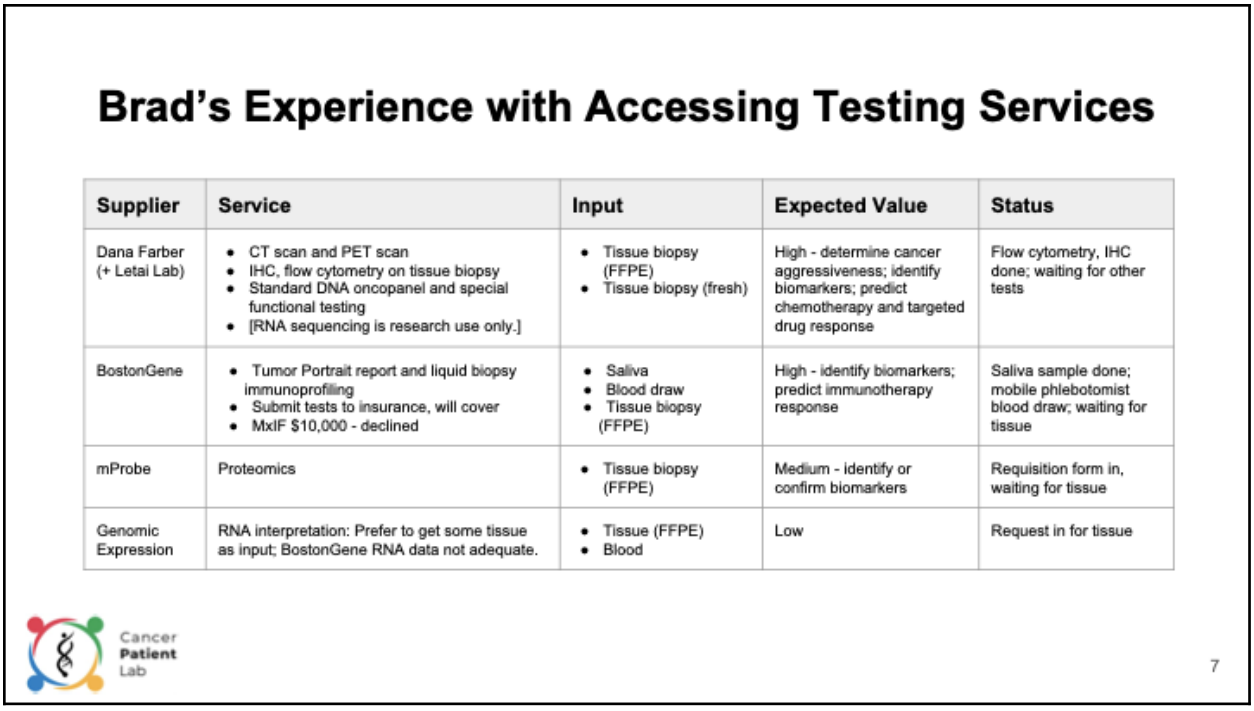
Emma has been there every step of the way, within a 24 hour response, telling me what this means. If I didn't have her, I don't think I would be useful. Because the intention we have is to be a copilot, a partner, with your medical team to be bringing ideas and to be able to participate, put your finger on the scale for the things that are important to you, whether it's quality of life, whether it's you want to try to hit a home run versus hitting singles, whatever it might be. The patient has a point of view and has something to say in this, but you can't do it if you don't know what the options are, and what the tests are saying. Emma is that translator that allows me to be an active participant.

- **Massive Bio**: Massive Bio provides clinical trials guidance. Also free. You give them your medical records access, and they're very service-oriented. They gave me a list of clinical trials. I'll share that with you.
- **CureMatch**: CureMatch takes your biomarkers and gives you drug combinations. I haven't taken advantage of that, because I'm still waiting to get my oncopanel results, or the BostonGene results from my latest biopsy.
- **Genomic Expression**: Genomic Expression, as Brian mentioned, Gitte Pederson, does an analysis mostly focused on RNA.
- **SHEPHERD Therapeutics**: SHEPHERD takes RNA data and then does interpretation on it. Again, because I don't have that data yet, I haven't used them yet, but expect to. They will work with whoever does your RNA sequencing to import the raw files, FASTQ files, to then put into their algorithms to identify treatment options.



Brad's Experience with Accessing Testing Services

Supplier	Service	Input	Expected Value	Status
Dana Farber (+ Letai Lab)	• CT scan and PET scan • IHC, flow cytometry on tissue biopsy • Standard DNA oncopanel and special functional testing • [RNA sequencing is research use only.]	• Tissue biopsy (FFPE) • Tissue biopsy (fresh)	High - determine cancer aggressiveness; identify biomarkers; predict chemotherapy and targeted drug response	Flow cytometry, IHC done; waiting for other tests
BostonGene	• Tumor Portrait report and liquid biopsy immunoprofiling • Submit tests to insurance, will cover • MxIF $10,000 - declined	• Saliva • Blood draw • Tissue biopsy (FFPE)	High - identify biomarkers; predict immunotherapy response	Saliva sample done; mobile phlebotomist blood draw; waiting for tissue
mProbe	Proteomics	• Tissue biopsy (FFPE)	Medium - identify or confirm biomarkers	Requisition form in, waiting for tissue
Genomic Expression	RNA interpretation: Prefer to get some tissue as input; BostonGene RNA data not adequate.	• Tissue (FFPE) • Blood	Low	Request in for tissue

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Brad Power 17:50
These are the main testing services that I've taken advantage of.

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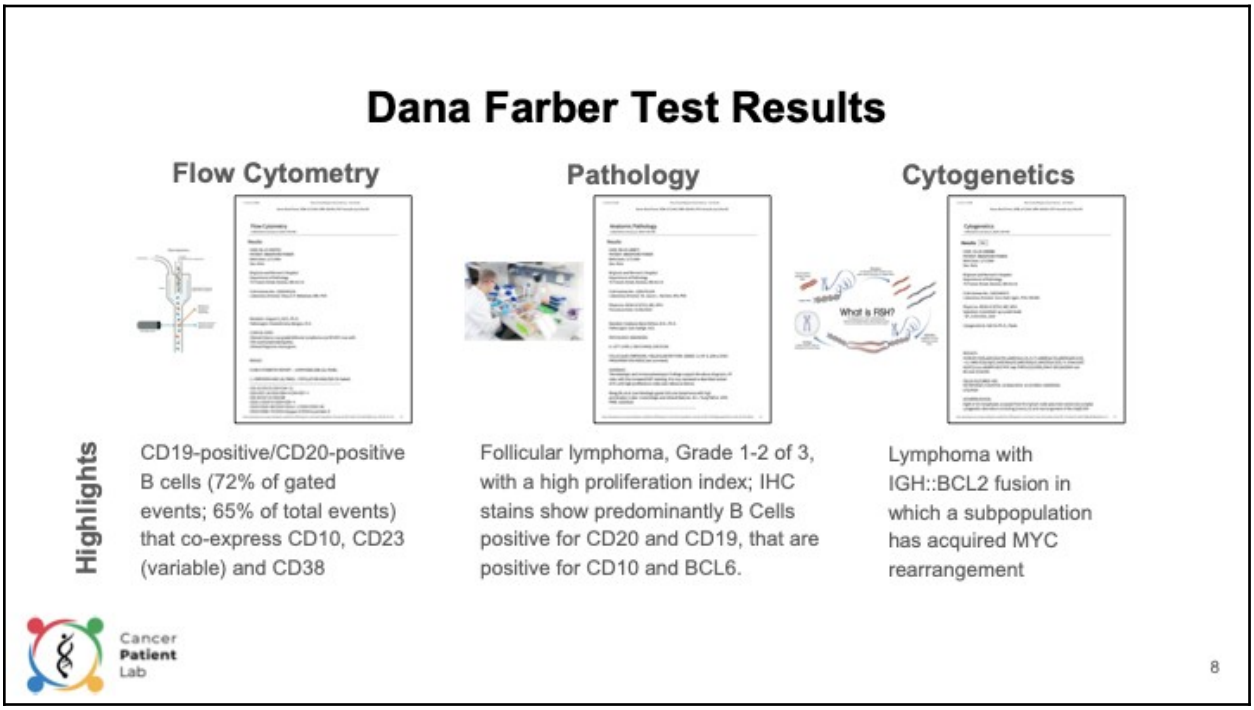
Dana Farber provides basic services that are standard: the CT scan and the PET scan, IHC. They are going to do an oncopanel, looking at the major genes and how they show up. You already see some of that from the IHC. So classically with lymphoma it's CD19 and CD20. But there's more detail behind that. They couldn't do RNA sequencing for me, but BostonGene will be doing RNA sequencing. mProbe is in process. They're getting tissue and also waiting to involve others behind that.



I'll just quickly flash some of the test results because there is a lot of detail.

- **Flow Cytometry**: There's flow cytometry, which, as you can see in the little picture, they run the cells by a counter in a flow. I have, as I mentioned, CD19 and CD20, which is typical for lymphoma.
- **Pathology**: From the pathology report, the key finding is that it's follicular lymphoma, not a diffuse large B-cell lymphoma, which is a more aggressive cancer. So there was that fork in the road, are you on the less aggressive cancer or the more aggressive cancer? I'm on the less aggressive side which then points to a particular set of treatment options.
- **Cytogenetics**: The cytogenetics get into some detailed genomic analysis, which again, is beyond me, but these are other indicators that can guide treatment options they made. Again, they made sense to Emma. For example, it says BCL-2, that's B-cell lymphoma two, and for that particular gene, there are some BCL-2 inhibitors, which we will point out next without going into the details.

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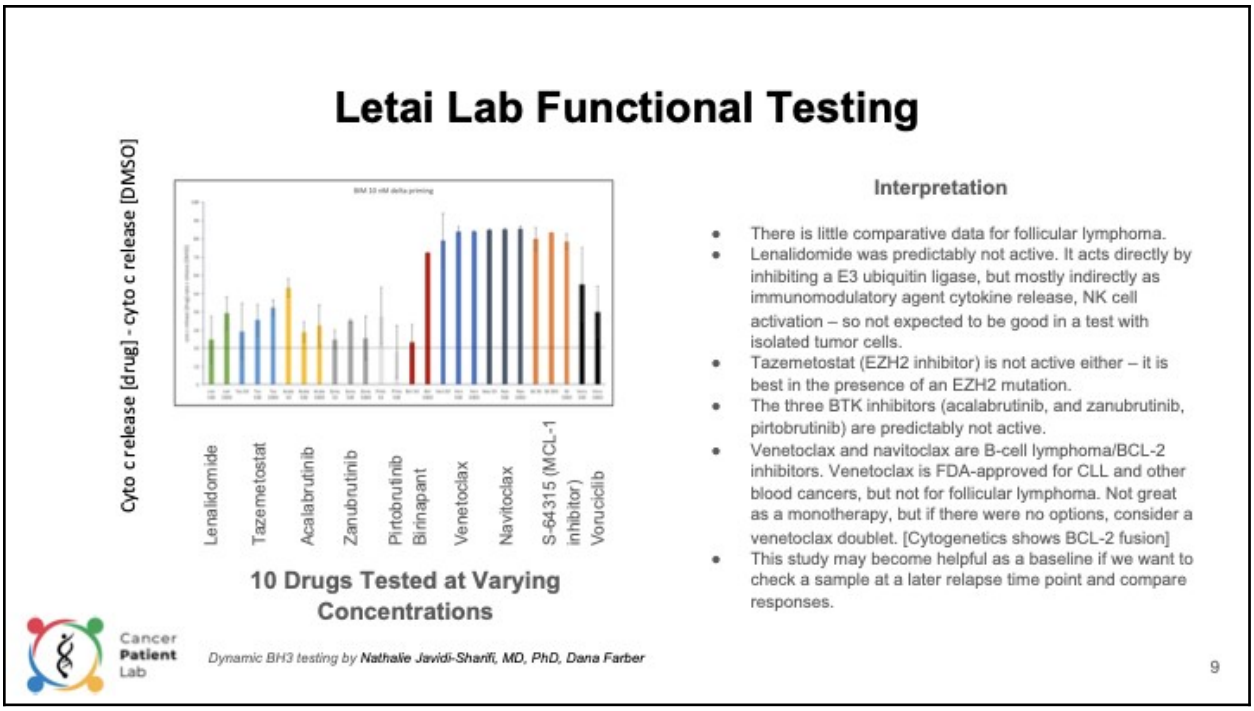

These are the functional testing results. This is a test that most patients don't get. This is typically a test for research use only. You have to ask for this. They tested 10 drugs at different concentrations, which you can see from left to right. The ones that are on the right are having a bigger response. All other things being equal, this tells you which drugs you might want to choose because they're more effective.

We've had five sessions on functional testing, including one with Tony Letai, that explains the technology, this dynamic BH3 testing. He explains how that all works. But from a patient's point of view, it's more information that would tell you that maybe one of these ones on the right is a better candidate than some of the ones on the left. The analysis and interpretation here goes into that analysis.

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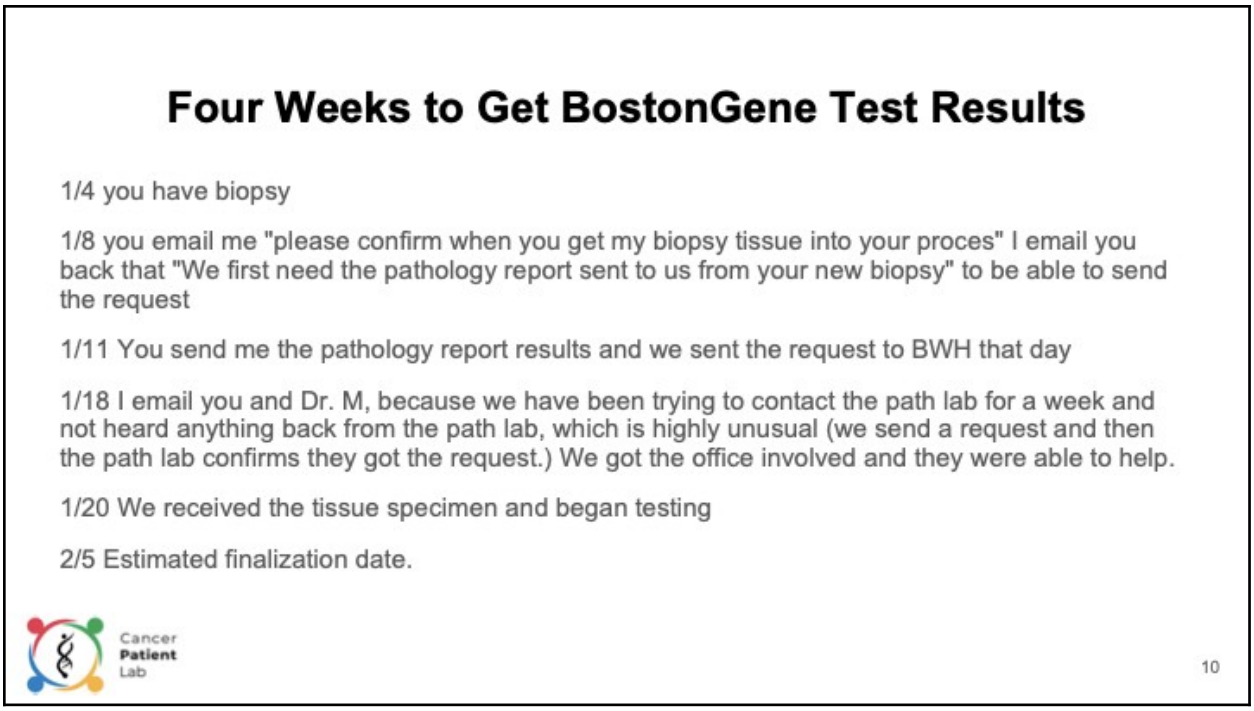


Brian talked about BostonGene a lot. I'm very much looking forward to getting those test results. But it takes four weeks. Unfortunately, the test results will be coming in after I have my consultation with my doctor tomorrow. We'll be talking about whether we want to wait to get those test results and actually use them to influence treatment decisions, or whether we know enough to go ahead and decide on what my treatment will be, then maybe use these for confirmation when they come in.

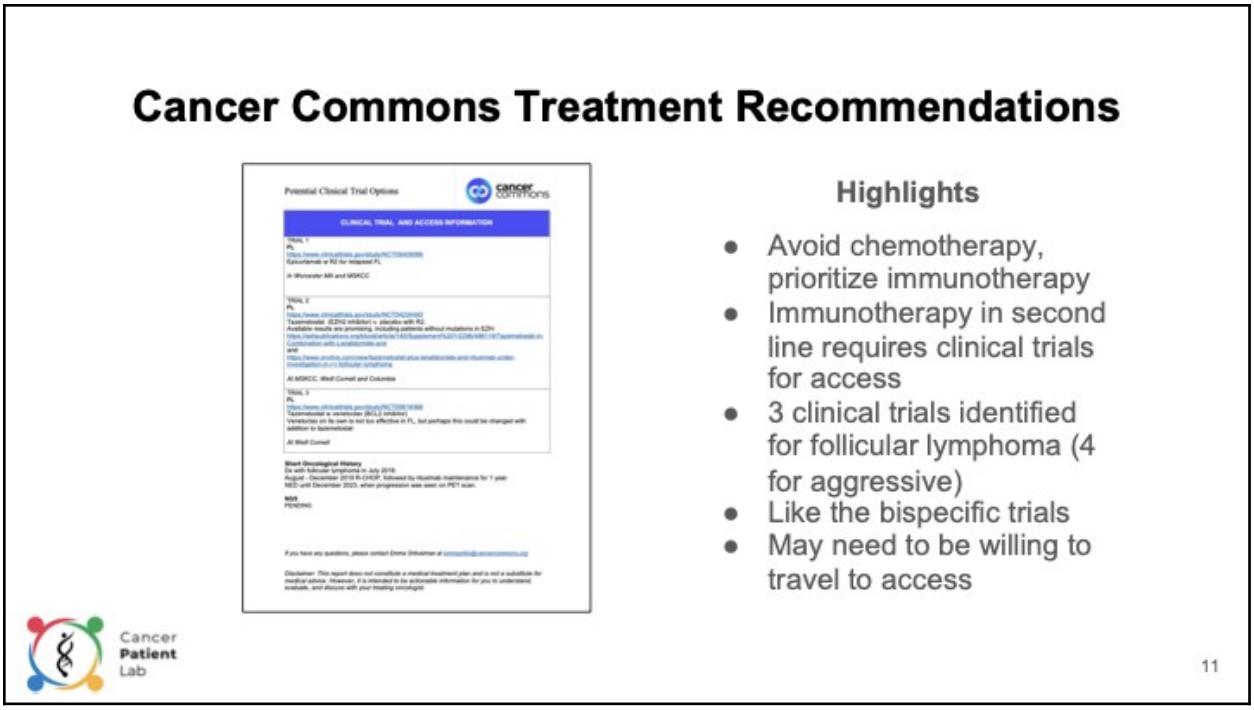
Rick Stanton 21:28
Could you go over that timeline a little bit?

Brad Power 21:37
I had my biopsy on January 4. And in my simple mind, from the time I got my biopsy, and the tissue, it would go out the next day in overnight mail to BostonGene. But no, they were waiting to get the confirmation, and they wanted to see the pathology report. I don't know why that's so, but they do. Maybe it's because they want to be sure that the tissue is there and useful. Then once the pathology report was in, which I saw because it showed up in the patient portal, I sent them a message saying, “Here's the pathology report.” By the way, I don't get an email when the pathology report hits my portal; I have to be checking it every day. But that's another story. I only found out about it a couple days after. But as soon as BostonGene knew that the pathology report was in, they then contacted Dana Farber pathology department, but then nothing happened. Brian can tell his story if he wants to about how the pathology department doesn't always communicate well with the outside. Then it was only when I followed up with them and said, “Hey, have you gotten the tissue yet?” And they said, “No, we haven't. Let us follow up with Dr. Merryman's office” And once they got Dr. Merryman's office talking to the pathology lab, then that sprung into action, but there was a week lost there, as you can see. There was like

two or three weeks there that if I was a process innovation consultant, which I am, then I would look at that and say, “Why couldn't we do that in a day instead of three weeks?” Then once the tissue hits BostonGene, I have every confidence that they'll turn it around in their normal time, which is like 10 to 12 days, or whatever it is. So it works. That's how it ends up being four weeks, instead of what I would have thought should be like a week or two, which would have put it inside the window, being able to be used with my doctor for treatment planning.

Rick Stanton 23:37
I want to emphasize that for Brian, the tissue just never got lost or never got sent. It was ridiculous. Brian was queuing it up as best he could. He's going under anesthesia. That just didn't get sent. We were emphasizing that “tissue is the issue”. It just seems I've never had this on metastases. Hopefully I'll be able to follow up with a similar path that you guys are going down, but it seems very disorganized.

Brian McCloskey 24:26
There's a lot of room for process innovation and process improvement when it comes to managing tissue. We've had at least one session on it. The Cliff Notes are available.



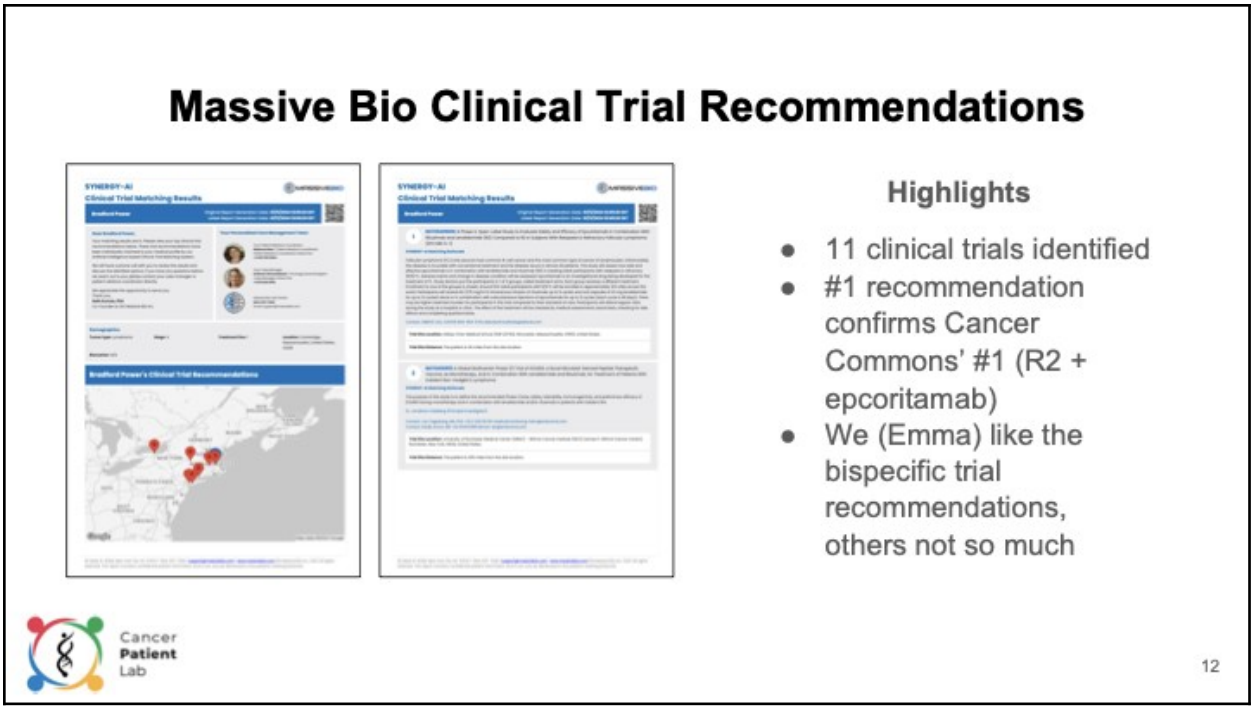
Brad Power 24:41
Emma put together a report which had two versions. One was if I had the more aggressive cancer, and one was if I had the less aggressive cancer. This is the list for the less aggressive cancer.

One of the questions she asked, which I hadn't even thought about, since I just assumed Dana Farber would have everything that I would need, but she asked, “Are you willing to travel?” I

said, “Oh, yeah, I suppose so, for the right deal. I could go to New York. I have family in New York. I could stay there.” So we expanded the lens, and that opened up more possibilities.

This first one, that is the preferred one, is a couple of drugs: rituximab is a common one for all lymphomas. It's a monoclonal antibody. Lenalidomide is a common second line treatment. It's an immune system enhancer. And the third one is a bispecific. A bispecific is an immunotherapy. It grabs on the CD20 on one side, which is the cancer, and then it grabs on a CD3, which is a T-cell and says, “Hey, you guys, let's get together, and then T-cell kill the cancer cell.” Adding that bispecific increases the duration of the response. Then Emma looked at some of my genomics, like the MYC rearrangement, and said, probably this extra thing, this boost, would be good for you.

I'm now armed with these suggestions or these ideas to bring to my doctor. He's asked me what I've heard from Cancer Commons and from Massive Bio.



Massive Bio had the same number one treatment recommendation that Emma had, and a bunch of other ones, some of which, at least Emma looked at, and said she was not so keen on the BTK ones that are on the list, but the other ones with the bispecific are interesting. I had a subsequent conversation about one of the other drugs, which is typically used in CLL. And now it looks like I would get a good response to Venetoclax.

Frank Nothaft 27:21
When you talk about liking the bispecific versus not liking some of the other recommendations, was that just based on like, early readouts from the studies that were going on? What were you thinking about efficacy from the disease biology side?

Brad Power 27:43
There are probably two or three answers to that.

The first is, blood cancers have been the best responders to things like CAR-T. These immunotherapies are moving from like third and fourth line therapies to then third line therapies, then second line therapies, then first line therapies, and the way you access them is through clinical trials. So in general, immunotherapy is good, because they work well in blood cancers, because they're systemic, and there's a lot of stuff floating around in the blood. That's principle one: immunotherapy is good.

I'm not, but Emma is, diving into the details. I don't know if you all saw, but there are some issues with CAR-T, which was just in the press in the last week. Some people got cancer from the CAR-T. Emma is also looking at the efficacy of CAR-T, and saying it's not as good as the bispecific. The trial results on the bispecifics look more effective than the trial results on the CAR-T. Let's prioritize that.

Emma Shtivelman 29:03
CAR-T is way down the road for you but may be needed. Even for the high grade follicular lymphoma, that is like in safe, first line of treatment, there is no debate. What's better, there is still no answer if CAR-T is better than bispecific, but there are two types of options which are not available for the first recurrence, except bispecifics are now because they're obviously easier to use, because the they work really well in DLBCL, and the results in follicular lymphoma and so on. So it's a good option. If you think about CAR-T down the road sometime, I think it's better to avoid chemotherapy for now.

Brad Power 30:00
The third thing is chemo. We know what the side effects of that are. I think the side effects would be less desirable. They carpet bomb your immune system, you lose your hair, all the things that go with chemo. I think the side effects are different side effects for immunotherapies, like inflammation and cytokine storms, and what have you. The general impression I have is that the side effects from immunotherapies are less. Regarding lenalidomide, a friend who's a doctor told me that it's very well tolerated. I had the rituximab before. That was well tolerated, at least by me. Now I'm looking at those, as opposed to chemo.

Emma Shtivelman 30:48
I think I told you that I think that your doctor may just want to go ahead with R2, which is rituximab and lenalidomide, because your lymphoma is luckily not high grade. That's the standard treatment, and it works really, really well. It works much better than reintroducing rituximab with chemotherapy as the second line of treatment. But I would be a little more aggressive. And with the available bispecific in a trial, it's a no brainer if you can join the trial. I'm concerned about the subpopulation of your lymphoma cells that have a MYC rearrangement, which is not a good prognostic marker. So it's better to hit it early.

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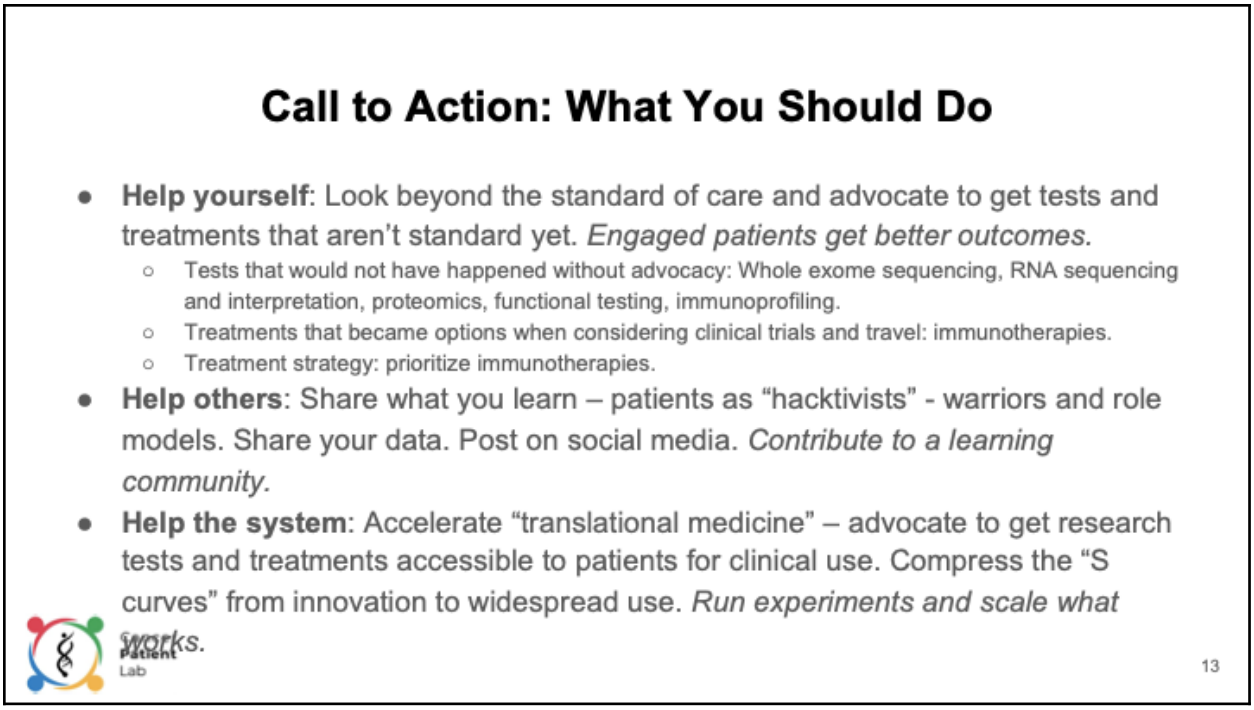
Brad Power 31:49
Hit it early, and hit it harder. That's another principle we have, which is that combinations are better, and are more effective. They have more durable responses. As Emma is saying, rather than using R2, which is lenalidomide plus rituximab, use R2 plus this bispecific. Now you're getting three drugs. That gives you “hit it high, hit it medium, hit it low” is the way I look at it.

Frank Nothaft 32:20
That makes a ton of sense. Thanks for the explanation.



Brad Power 32:27
What's the call to action? What should you as patients learn? What might you want to learn or adopt from what Brian and I have been talking about? In terms of what you can do for yourself, what can you do for others and for the system?

Brian McCloskey 32:53
This is something that I feel really strongly about, which is that the standard of care is only going to get you so far. It's really incumbent upon the patient to push their care team. You have to work with your care team, or a care team that doesn't have to be the one that you're currently with, to leverage all of the diagnostics that are available. One of the challenges is that many medical oncologists don't know about the tests, or they don't know how to interpret them. And it's really important that the patients get involved to create that bridge. Translational medicine is how you take amazing science, that is, in many ways it's been proven that it works, take it from the lab and get it to the patient's bedside. But there are a lot of barriers that prevent that process from happening. But the role the patient has is really, really important because we do have a powerful voice. At the end of the day, we're responsible for our own decisions.

We can get second opinions. It's critical to have data-driven decisions. When you have advanced diagnostics, like the ones that we're talking about, where we're getting transcriptomics and proteomics, or just even interpretation of your DNA, it can illuminate treatment options that were not formerly part of the discussion. I know that there are several patients who have gone through this process, and it's worked for them. It's worked to identify new treatment options.

The other point here is helping others. Not only do I feel like I have an obligation to help myself, but also to push the boundary for other patients. But we hope that all the members here, whether you're a patient or you are a caregiver, are also interested in doing that.

The notion about helping the system and this translational medicine, which is what I just talked about, it's all hands on deck. If we don't make our voices heard, then it's just going to make the adoption of these diagnostics that much slower, and we just don't have time.

That's really what we wanted to share with you today, as Brad was going through his new diagnosis. Unfortunately, he's no longer NED. Now he has to put all this knowledge that he's acquired to his own case. As he reflected on his case, and he and I talked about it, there's a lot of components of Cancer Patient Lab that are helping to guide him in his treatment. We hope that that's true for the other patients and caregivers.

Rick Stanton 36:55
On one of your slides, you had a $10,000 charge for a test and declined. Then I saw in the chat, “Are any of these covered by insurance in these advanced testing options?” That's a barrier. Any comments there?

Brad Power 37:25
Brian should talk about how we've cut special deals with like mProbe, who will do proteomics for free. For example, I think Genomic Expression – Gitte can comment on this – is free. When we're working with startups, they are very willing to do things for free because it gives them data that allows them to then publish results and make their test commercially available, if they're at that stage. BostonGene was kind enough to say, “Submit it to your insurance, and if they deny it, we will make you whole.” But that was a special deal. We have some special deals that are unique to Cancer Patient Lab, and we have them individually. Brian can can refer to those, but most of the tests that we have are free to the patient.

Brian McCloskey 38:23
You got it. Like Travera, as another company that will do functional testing. They are free for our patients. As you explained with BostonGene, some companies like Tempus have come to me and said, “Hey, run this through your insurance.” I've never had to pay anything to Tempus for any of the sequencing that they do. Frank Nothaft can probably speak to that a little bit better than I can, but I've never had to pay anything. They're being paid by big pharma. They have other sources of income, than from patients directly.

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Frank Nothaft 39:04
I'm not affiliated with Tempus anymore, but actually, just this morning, they announced that the tests are now generally covered under all Humana plans. The startup versus established testing provider dichotomy is pretty spot on. In the startups, it's a big thing for them to get tests so that they can demonstrate efficacy and accuracy of the readouts. Whereas for like, a lot of the more established testing labs, if they aren't well covered by insurance, they are pushing very heavily, whether it's the major payers, whether it's going Medicare, that is probably a good place to shop around a little bit. “Shop around” colloquially because there are differences In what tests are covered by what disease, what testing providers, and what tests are covered for which diseases in which payers. In some cases, like if you have comparable testing providers that could give you the same readout, that's a good place to just do a little bit of comparative research.

Brad Power 40:31
In translational medicine, a lot of the tests we'd like to get, like for the multiplex immunofluorescence, which is very cutting edge, the first challenge is finding a CLIA-certified lab that a patient can get to to get that test, which we've been discussing with BostonGene, for example. Then on the backside, what does it cost, because it is new, and it's typically only used in a research environment.

Brian McCloskey 41:02
There's a question that came in from Bapcha, “Has anyone tried using the same test twice to ensure that data was nearly identical in both cases?” Bopcha: I have been sequenced several times. I've had three surgeries that yielded the tissue for sequencing, all three of those were sequenced by Tempus. And they've identified certain alterations. Just within the past two months, I've been working very closely with Michael Hensley from BostonGene, to do some extensive testing. They pulled new tissue from my first first surgery, and from my last surgery, so both of these were already sequenced by Tempus. Now keep in mind, these are fresh cuts of tissue that we just did on these samples. What is interesting is there was concordance between Tempus and BostonGene on my 2016 resection, but there was some overlap, but there were some differences as well between Tempus and BostonGene on my surgery from last year, which is interesting.

Michael Hensley 42:36
Tissue is probably the bane of my existence because it's so tough. We always want the most recent tissue, but there are many times when tissue will be having 80% purity on the first cuts. And by the time we're getting it in our lab, we're down to like our threshold of like 30%. So what really happens is a lot of IHC stains, slides or cuts or various markers. And so this can really affect the quality. There are many times when tissue is on the verge of exhaustion, so we may be only successful with a DNA extraction versus DNA and RNA extraction. There's a lot of different things that come into play here. But obviously, all of us have very important quality metrics in place to ensure the accuracy of our calls that we deliver into the report. If the most current tissue is exhausted, we will go back in time a little bit, but obviously various treatments, immunotherapy or chemotherapy, whatnot, can certainly change certain markers, and in expression levels as well as in the microenvironment.

As Frank said, all of us have robust financial assistance programs for patients. We built a special one at MD Anderson, because everybody wasn't interested and usually comes with previous testing. So we will attempt to bill an insurance company, but some insurance companies may not pay for additional testing, because they've just paid for something. We have to show that patients have progression or a new anatomic site or whatnot. That's for us to worry about, but we ensure that the patients aren't going to be financially liable because insurance denies it. Most of the strong companies have these programs.

On the other question about doing multiple tests: when the patient's qualified for financial assistance, we will do testing at whatever specimen they have, but if they do have progression or a future biopsy, we will do additional testing on that free of charge to the patient as well. I couldn't agree with you guys more. One of the most frustrating parts about being an innovative company is that these technologies are incredibly expensive. It makes finding payers to support these new testing very difficult. So it does limit the ability for patients to get this unless it's out of pocket or under a research trial. Everyone is trying to move that needle to show the utility. But like in Brian's case, maybe one of these wasn't the greatest clinical utility. It's combining this multi omics approach to really personalize his care where you find the greatest utility, and that's very hard to share with providers and get them on board. But it's moving at a snail's pace, but it's definitely moving forward.

Brian McCloskey 46:02
We're going to change that trajectory, Michael, here real, real quick. BostonGene, if I can just plug them and the work that Michael did, because Michael really spearheaded it, they just did an amazing job grabbing my original prostatectomy, 2016 tissue, and then a met resection from 2022. Then they did a tumor evolution report, which shows all the various treatments that I've been under, and then how my cancer has changed over that seven year period of time. And how treatments also have changed, too. So there's other stuff that they did, which was absolutely amazing. We're going to have a whole session or two around BostonGene here coming up very soon. But I will just say that these guys are really on the cutting edge of advanced diagnostics,

Michael Hensley 47:05
Everything on that front part, we do all the time for patients. We lock them in with financial assistance, which the vast majority of patients are covered at 100%. Because it's not only income based, but it's situational based, like travel expenses, debt, retired, and so forth. We can do all that what Brian just mentioned in testing.

Many pathology labs severely limit our communication because of just the volume of reference labs send outs, not just BostonGene, but everybody. When the data collection of a biopsy, a lot of times, we won't start following up on that until about three or four days after that, because the pathologist has to get the tissue sample signed out, do all the write-up. Then we work on that. Usually the first tissue we get pretty quickly. But we've had turnaround times in 15 days, we have turnaround times in three months, when we're requesting multiple tissues, just because of

low tumor content. It's all about tissue and it's all about just getting it at the right time. So it's tough, it's a lot of moving parts. Regarding our tests, they are very dependent on receiving tumor and normal DNA samples with sufficient tumor content of at least 30% tumor purity…once both samples are received in BostonGene lab and pass Pathology Quality Control review, we usually deliver the report to the physician in 10-14 calendar days.

Frank Nothaft 48:24
I was just going to piggyback on some of the comments Michael was making around testing accuracy. It does get somewhat hard to look at results between two tests taken at different time points, because it's hard to say what is concordance versus changes in the tumor itself. Generally speaking two tests that come from the same timeline will have fairly high concordance. You run into issues around the tissue, as Michael was pointing out, especially like when you get tumor tissue that is more or less contaminated, that can cause definite changes. You will fairly consistently run into some comparison issues, if you go from one testing modality to another testing modality, for instance, if you look at a liquid biopsy versus solid tumor testing. That's not necessarily a bug. In some cases, that can actually be a pretty good feature of using those two orthogonal testing modalities. But it's definitely very situational. There are some cases where people are using two testing modalities, like solid tumor and liquid biopsy, and scoring all the results, essentially combining all the results together and that's giving them a much, much wider range of therapies that they have access to. It's somewhat somewhat situational. But overall, the test generally have had very good concordance.

Brad Power 50:07
I was at a conference, and I asked someone from Foundation Medicine, “The cost curve is going down on DNA sequencing. So now you can get more. Would you also expand the number of genes that you look at? Because typically an oncopanel has 300 or 400 genes? Would you go to 500, 600, or 700 in the future? Or would you go to whole exome?” He said, “There's more value from getting different tests than getting more of the same test.” So just as Frank was saying, maybe a liquid biopsy looks at what's floating around in the blood, gives you a different lens on the same information. If you saw my reports, you've got the cytogenetics, the flow cytometry and IHC, looking at something under a slide. Putting energy into multiple tests would be a principle to give a more complete story of what's going on. Emma was pointing out that for me, there's a MYC rearrangement. You only see that on the cytogenetics report, so rather than worrying about the same test with multiple vendors, maybe we should be worrying about multiple tests, and seeing how we can get new information from different kinds of tests.

Michael Hensley 51:38
So I can help a little bit about that. Bapcha, we will report findings that are focused on that primary diagnosis that have targeted therapies. But we also will report findings in the BostonGene Tumor Portrait that are of known significance for a positive prognosis or an inferior prognosis, as well as something that would demonstrate a lack of efficacy with a certain therapy. So we do both targeted biomarkers for targeted therapies as well as prognostic capabilities.

Rick Stanton 52:36
On reproducible results: I was at Human Longevity. We sequenced a particular individual 78 times, whole genome sequencing, not only the whole exome, to validate migration of chemistry from Version Two to Version Three chemistry. We were moving our whole platform chemistry, and we wanted to validate it. So we sequenced an individual 78 times. And the concordance was spectacular. Reproducible results aren't because you're feeding the same data into the same platform. It's like Michael said, if the data quality is different, when the lab received it, or the chemistry is different. But if you have a good lab that has high quality input, those results should be pretty damn good. I'm just being someone who's been under the hood. My observation is that this is not shaky stuff. This is pretty repeatable. It was amazing. Most of the variance that we saw. 78 times. 78 out of 78. Okay, some 76 but it wasn't a shaky deal.

Saed Sayad 54:32
This is true, actually. Yeah, your point is on target. It means if we can control all the variables. The problem here is we need to generalize our findings for other patients. It means I've been saying we want to get the biomarker from 1000 patients, then use it for other patients, then that's the major reach.

Brian McCloskey 55:11
We're trying to make data-driven decisions and sequencing, and these advanced diagnostics that we're talking about are at the heart of these data-driven decisions. I agree with what Brad said earlier, which is, if you can get different tests, to provide a complementary view of what your existing tests are, I think generally, that's a good thing. But where things start to get interesting is when you may not have concordance, or you may have different data, or different results coming from tests. You have to draw conclusions across different types of tests, then you get into this equation of art and science. I'm about ready to go through that process again. But at the end of the day, I'd rather have as much data to make my decision as possible. And having multiple different views of my cancer, I think at the end is only going to result in better decisions for me, but also learning. So even if it doesn't work for me, hopefully somebody else is going to be able to benefit from whatever we learned going through a rigorous data-driven process, or as rigorous as we can possibly make it.

Saed Sayad 56:37
It's true that having some data and some knowledge is better than having nothing. Just adding one point, just as based on my personal experience, the best method I found on all those data sets I saw is those coming from single cell, which you have the from the same patient, you have the cell, the normal cell, if possible, and the cancer cell, comparing these two groups, you should get the best result of understanding the nature of your disease. That's just based on my analysis.

Amit Gattani 57:26
One of the choke points in the process that we haven't discussed, and that the industry needs to address, is that most of the onco teams just don't have time to pay attention to the flood of data that we can actually bring to them. It's like a 20/80 rule or 10/90, that 10% of the researchers will

be all over it. But 90% of the oncologists look at this as a lot of data. I really don't know what to do with that and how to make it actionable. And that's a choke point in the industry that needs to get resolved and understood. And we need to figure out how to make that more effective, as well, because that's even working with the National Cancer Institute, so I've seen that, that issue. Okay, great. You got all the data. Not sure where we go with that. So there's a lot to be translated in that space.

Rick Stanton 58:39
Yay, Emma.