“How Do You Choose Your Diagnostics? – A Guide” (Richard Anders and Brad Power) [#100]

Richard Anders and Brad Power
June 5, 2024

“The Cancer Patient Lab … is a ‘user group’ of people who are trying to collaborate and figure out how collectively to improve everybody's understanding of what they deal with as patients.” – Richard Anders

“When you have all of that information coming at you, how do you make sense of it? How do you interpret it, especially in the face of tremendous stress, time pressures, and the need to understand and act on it quickly?” – Richard Anders

“If we could create the Services Guide such that it is the gold standard, not just the gold standard for patients, but also for clinicians, insurance companies, pharma, and other life sciences companies, then you can bring these constituents together, such that they're having a conversation around the value of these service providers.” – Brian McCloskey

“I don't see anything that's more compelling in medicine right now than to actually pursue something like this. This is really, really important. We're onto something.” – Brian McCloskey

Meeting Summary

Cancer should not be a spectator sport. Actively engaging in your care can give you and your caregivers more control over your life, a better understanding of what to expect and how to deal with it, and even, perhaps, better outcomes. But to do this, you must take a page from the playbook we’ve all grown up with when buying a car or a house. You need to become an educated consumer and shop around for these services.

To help patients and caregivers (and physicians!), Brad Power, co-founder and CEO of the Cancer Patient Lab, has assembled a robust guide that identifies services providers in over sixty areas of cancer care. These range from mental health and financial experts to care consultants and data management services. One of the most important of these categories is testing and diagnostic services. Testing and diagnostic services provide the data that can uncover new treatment options and help you make decisions between treatment options.

Richard Anders is uniquely qualified to help patients, caregivers, and physicians navigate complex diagnostic decisions. Richard is an active member of the Cancer Patient Lab community, the Founder and Executive Director of Mass Medical Angels, one of the country’s leading life-science focused angel groups, and Managing Director, Rubin/Anders Scientific. For ten years he taught life science entrepreneurship at the Sloan School at MIT and the Harvard/MIT Health Sciences and Technology MD-PhD program.

Why should you get as many diagnostic tests as possible to guide your cancer treatment?

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Diagnostic tests provide the data to help you select your best treatments. Historically, your treatment decisions were guided by a stained image of your tumor tissue and scans. Then “next generation sequencing” became available around 2011 to analyze the DNA of your tumor tissue and identify genetic mutations. In the future, your tissue images will be integrated with many diagnostic tests (next generation sequencing, RNA sequencing, proteomics, spatial transcriptomics, metabolomics, single cell analysis and potentially functional studies on animal or cell-based models) leading to more personalized treatment guidance. Biomarkers will be identified which will select which treatments might work best, and predict your likely outcomes. Multiple fluorescence stains will be applied to tissue and stacked to visualize your tumor and its microenvironment. Artificial intelligence will be applied to your scans and other test data and do a better job than a pathologist at interpreting them and predicting your prognosis and drug response.

What are the challenges that patients, caregivers, and physicians face in navigating possible diagnostic tests?

- **Awareness**: There are many new tests coming to market that few people know exist or how they can help guide treatment decisions. Everyone, including physicians, struggles to keep up with the rapidly evolving landscape of tests and treatments.
- **Understanding**: Navigating testing options is a complex area, to put it mildly. As consumers we know what a house looks like or how a car should handle. But what do we know about the “AUC” (area under the curve, a measure of the usefulness of a model) of a diagnostic test, “RNA-seq” (ribonucleic acid sequencing, a laboratory technique to reveal the presence and quantity of RNA molecules in a biological sample), “tumor heterogeneity” (differences in cancer cells within tumors or between tumors), or “immunocompetent mice” (mice that have the ability to produce a normal immune response)? To be an educated consumer in the diagnostic field requires a whole different order of understanding.
- **Selection**: Every cancer patient should get standard tests for their disease, e.g., an EGFR test for lung cancer, but many do not. Rapid growth of targeted treatments has created an explosion in demand for companion diagnostics. What tests should you get? How can you access all of the tests that are needed to point to your personalized treatments?
- **Interpretation**: Up to 30% of patients have an incorrect or incomplete diagnosis. Over 60% of oncologists say they have difficulty trying to understand what tests to use, and what the results mean. Your doctor won’t order a test unless they know how to interpret it and how it will be used to guide your treatment. It is very confusing for anyone trying to keep up with this. Does your doctor know what to do with all the possible test results, such as RNA sequencing and proteomics? Different test results may conflict. What do you do if the tests seem to contradict each other? How do you bring together all of your test results into a comprehensive view of your disease and which treatments are best for you?
- **Expense and Reimbursement**: New tests are not reimbursed for clinical use. How do you pay for the additional tests and test integration?

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- **Tissue**: Many of the tests require tumor tissue, including some that require fresh tissue.
- **Conservatism**: Under the guidelines physicians use, new technologies are treated very cautiously and adopted slowly. Physicians are trained under these guidelines and do not deviate from them lightly. But some – especially in more difficult situations – are willing to go to the powers that be to push for something outside the guidelines.

What are the potential benefits of a guide to diagnostic tests?

- Give you more data to make better data-driven treatment decisions
- Provide a standard reference so that various stakeholders (patients, caregivers, physicians, diagnosticians, payers) can build on it to collaborate on driving better patient outcomes
- Provide a tool to help you be a more knowledgeable patient, which will give you more power and influence as you seek the best care

What questions should a consumer guide to cancer diagnostics answer?

- Where does this test stand in the FDA regulatory cycle? Is this test for “research use only”, a “Lab Developed Test”, in clinical trials, or FDA-approved for commercial use?
- How long has this test been around?
- Whether or not it’s approved, are there [many] clinicians who are using it?
- Is this a test which changes treatment?
- Is this a test which applies to certain types of cancers? What kind of cancer is this for?
- What stage of cancer is this for?
- Is this test ideally for a particular stage in treatment, e.g., early detection, diagnosis, or monitoring progression?
- Is this standard of care or not standard of care? Is this test in the NCCN guidelines?
- How much does this test cost? Is this test reimbursed by insurance? If so, what do you need to do to get it reimbursed?
- What do you need to provide to obtain the test (tumor samples? Blood? Other?) Is the facility where you're getting your care able/willing to provide this? Is the test otherwise available at your facility?
- Must your clinician prescribe this test or is it available directly to you as a consumer?
- What degree of proof is there for this test? What is the level of evidence or confidence in this test?
- What is the evidence you can bring to justify this test to a treating physician?
- Does the testing company provide patient support (financial or navigation services)?
- Can the test provider interpret across multiple tests to inform treatment recommendations?
- What has been the experience of other patients and caregivers using this test provider?

How can you learn more?

- Read our discussion with Tony Magliocco, founder and CEO of Protean BioDiagnostics on using diagnostic tests to guide personalized treatment here.

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How can you help us develop the cancer diagnostics services guide?

- Volunteer to join our working group to further discuss needs, collect ideas, define work products, develop our methodology, and provide oversight for the Services Guide project – email Brad Power at bradpower@cancerpatientlab.org.
- Review the transcript, slides, or video recording of this discussion, and add questions and comments
- Request a copy of the services guide; provide feedback; help build out the sections
- Provide introductions to diagnostic companies that might be interested in this project and being included in the guide
- Provide introductions to medical oncologists who might like to contribute clinical perspectives

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Meeting Notes

KEYWORDS

patients, oncologist, clinicians, people, brad, cancer, medical oncologist, guide, started, diagnostic, services, service providers, working, nccn guidelines, talked, reimbursed, doctor, questions, care, thought

SPEAKERS

Richard Anders (31%), Glenn Sabin (15%), Brian McCloskey (13%), Brad Power (11%), Jeffrey Dwyer (8%), Allen Morris (7%), Jeff Krolick (6%), Chris Apfel (5%), Jane Wilkinson (3%), Robert Gurmankin (2%)

SUMMARY

Navigating complex cancer diagnosis and treatment information is hard for patients and caregivers. A personalized oncology service providers database and a comprehensive services guide for cancer patients and caregivers could help. New diagnostic technologies need to be adopted and integrated into clinical practice. The adoption of diagnostic technologies depends on collaboration, clinical validation, regulatory approval, and evidence-based medicine.

OUTLINE

Creating a guide for cancer diagnostics, drawing parallels with computer industry history.

- Richard Anders discussed the history of user groups in the computer industry and drew parallels with cancer patient communities, highlighting their importance in self-education and collaboration.
- He noted the challenges of making sense of complex information in the face of uncertainty and time pressure, particularly for cancer.
- The evolution of the personal computer industry could have parallels to the evolution of patient driven care in the health industry. The personal computer magazine industry could have parallels to the development of tools such as a guide to cancer diagnostics.
- Brad Power has developed a comprehensive guide to cancer services, which Richard hopes will supplement and deepen the conversation.

Cancer patient resources and service providers.

- Brad Power shared an evolving list of 60+ services for cancer diagnosis and treatment, including sound therapy.
- Richard Anders mentions a working document detailing service providers for immune system analysis, which they are willing to share with interested parties.

Categorizing medical diagnostic tests based on their stage of development (research vs commercialized).

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- Allen Morris discusses the importance of categorizing established treatments by how long they have been used.
- He highlights Natera's commercialization of minimal residual disease tests in colorectal cancer.

Cancer treatment options and the importance of staying up-to-date with research.

- Jane Wilkinson thinks that a guide can be helpful equally for patients and physicians.
- Patients can educate oncologists, who need continuous learning and must adapt to new information.
- Richard Anders notes that clinicians struggle to keep up with the rapidly evolving landscape of medical research and treatments.

Challenges in getting new cancer diagnostic tests approved and used by clinicians.

- Chris Apfel suggests bringing an oncologist to the meeting to provide valuable insights.
- Oncologists are bound by NCCN guidelines, which can limit their ability to innovate.
- Robert Gurmankin's oncologist is willing to try a standard of care drug despite its age, citing a functional test with promising results.
- Clinicians discuss challenges in prescribing and reimbursing personalized cancer treatment.

Patient-led guide for cancer treatment options.

- Jeff Krolick experienced the slow adoption of new innovations in cancer care.
- Patients learn about cancer treatment options through personal experience and research.

Personalized oncology service providers database and navigating patient workflow for cancer treatment.

- Richard Anders and Brian McCloskey discuss the challenges of navigating the complex landscape of cancer treatment, including the importance of considering patients' perspectives and the need for a comprehensive guide to help patients make informed decisions.
- Glenn Sabin highlights the prevalence of off-label prescribing in cancer treatment, with 40% of FDA-approved anti-cancer drugs currently being prescribed off-label, and emphasizes the importance of understanding the interconnected pieces of prescribing and combinations.
- He discusses compiling a list of oncologists open to prescribing alternative cancer treatments.
- Cancer Commons is developing a precision oncology database with diagnostic workups for GBM and other diseases.
- Glenn Sabin discusses vetting service providers for rare disease patients.

The value of a comprehensive guide for cancer patients to access medical services.

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- Brian McCloskey: We need a Services Guide to make better data-driven treatments and extend lives.
- A future Services Guide could be a gold standard resource, enabling more focused and valuable conversations by constituents.
- Enable a more patient-centered approach to cancer treatment, involving service providers, peer review, and user groups.
- Eric Topol's perspective – “The Patient Will See You Now” – on user groups, critical mass, and scale to affect change in cancer treatment.

Details of Implementation.

- Richard Anders: "We need to discuss legal questions and how to actually do this."
- A working group or committee review board would be useful.
- We can manage this through emails and our online discussion forum.
- Bring together various stakeholders in a working group.

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TRANSCRIPT

Brad Power
This is the Cancer Patient Lab.

I'm broadcasting to you from Dana Farber, where I've got my IV ready and my wristband.

As usual, this is information only. This is not medical advice. You should use the information in this session to get information to take to your medical team.

Cancer Patient Lab is a patient-led volunteer community. We request a donation if you are so inclined.

Today we're going to be talking about a Services Guide. This is something that I've been working on for a couple of years gathering service providers that patients and caregivers can take advantage of, to inform them about various aspects of their care, everything from mental health to financial issues to how do you keep communication with friends and family. But it starts with diagnostics. Then it also goes into treatment matching.

Richard is going to lead us in a discussion about ideas we have for building out this Services Guide, and focusing on diagnostics in particular.

Richard Anders 2:02
I come from the computer business, at least in an earlier life. What I remember about the computer business is it was marked by things called “user groups”. User groups have a venerable tradition. I did a quick Google search, and it led me to believe that the British Royal Society, was actually an early user group, consisting of a bunch of amateurs who banded together to start talking about sciences and developed it into one of the world's most prestigious scientific institutions. In 1975 there was the Homebrew Computer Club, which in a way was where Apple Computer started. Perhaps some of you remember the Boston Computer Society started in 1977 by a 13-year-old kid with thousands or even tens-of-thousands of members.

These groups were characterized by dedicated amateurs dealing with a need to understand extremely complex information, to self educate themselves, with a pressing need and desire to develop the tools and the camaraderie to work together to try to figure all that out.

The Cancer Patient Lab started in 2022 and it, I think, is a similar kind of effort. It's a user group of people who are trying to collaborate and figure out how collectively to improve everybody's understanding of what they deal with as patients. And in thinking about these user groups, there are lots and lots of issues, particularly in a complex area such as cancer care.

I've been a patient, and I have family members who've been patients. I would not say I had a particularly difficult diagnosis, at least so far, but I’ve had family members with more difficult diagnoses. I understand how extraordinarily hard it can be in the face of uncertainty and time pressure, to make sense of really complicated information, which is not only very important, but

also hard to access and understand and evaluate because it's not extremely well curated. Also, the content is not definitive; it's developing in real time. When you have all of that information coming at you, how do you make sense of it? How do you interpret it, especially in the face of tremendous stress, time pressures, and the need to understand and act on it quickly?

What I remember of the computer business in the 1980s was the evolution of the quasi consumer magazines. There were hundreds of them. Maybe some of you remember the ones like PC Magazine, and from the 1970s, perhaps even the granddaddy of them all, Byte magazine. I spent some time in the magazine area, and I remember many of these magazines, which provided people with extremely technical information, but in a consumer way, and how much they helped create the personal computer age. They would deal with questions like “What is the best router?” “What's the best ADSL technology?” “How do you find a good switch?” This is not the kind of stuff that an average person would want, yet the magazines had the production values of a friendlier publication – the graphics and reviews and headlines almost as if it was a Consumer Review Guide to cars.

Looking at that history and thinking about it, I came to the conclusion that for evaluating cancer diagnostics, there are a lot of similarities. The field could perhaps benefit from some kind of similar editorial effort.

The purpose of today's discussion is to start trying to figure out with everybody's help, because this is by no means something that I am equipped to figure out myself, what that might look like. I think with the people in this room, and others, we can perhaps start to make some progress on a number of questions, including whether we want to actually do it, or how we would do it or what it would look like.

Talking about that guide is where we're going to start this effort. I should say that, in some ways, what's going on in the cancer personal cancer diagnostics area right now reminds me a little bit of the computer business. Maybe those of you who were students of industrial organization and many other businesses, there are an enormous number of cancer diagnostics that are just constantly emerging. I can tell you that in five or ten years, there are going to be far fewer of them, and they will be a lot better. But right now, there are lots of them. Trying to curate and make sense of them is what we’d like to do.

Brad has developed and shared with me a fantastic guide to cancer services. It's very robust, and really an impressive effort. This conversation today will by no means replace that guide, but hopefully will supplement and deepen it in the cancer diagnostics area. But I think that maybe the first thing we should do is hear from Brad to talk about the guide that perhaps many of you are familiar with, but maybe not all of you.

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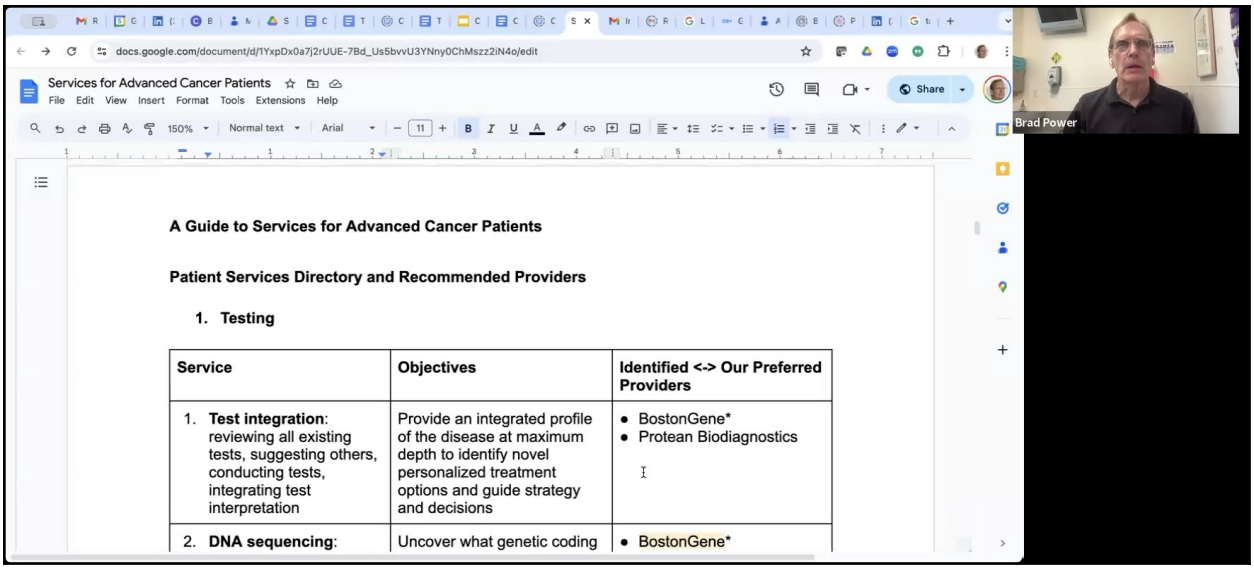

Brad Power 8:17
This has been a working document that we have had. Every time I hear about a new service provider, I add it to the list, and there are over 60 services.

There's a preamble up at the front which says, “Use this at your own risk.” It's broken into, like I said, over 60 services, so test integration, DNA sequencing, RNA sequencing, …

This is the diagnostic section: liquid biopsies, proteomics, functional testing, spatial analysis, animal testing, microbiome testing, metabolomics, pharmacogenomics, scan interpretation, radiology services, and immune system profiling. These are 14 testing services, and then it goes on to others, such as treatment options and matching services. And as I said before, mental health, exercise.

I add to this every day. For example, yesterday I spoke to a company, SonALAsense, which has a sound therapy where they inject a drug that is combined with ultrasound. This is constantly evolving and changing, every day practically, as I learn about new companies.

I'm happy to share this with anyone. This sets up the context. What do they say about eating an elephant? You need to take small bites. If we took this whole thing on and tried to make it all great, it would be a lot. It's already just in the diagnostic space here. As you can see, there are 14 different services. We have a process. It may not be visible to everyone. But at the Cancer Patient Lab, we ask many of these companies to pitch us, to basically tell us about their service. Then patients raise their hand and say, “Let me get that service.”

For example, Brian just had a session last week with BostonGene. Michael Hensley is on today. We like BostonGene. They're one of our more favored service providers. I'm going to get a test from Natera for my immune system analysis. In each of these areas, we've both identified all the service providers that we know about, as well as starting to identify ones that we like, let's say, more than others, or where there is experience among the patients in our community.

That's basically the backdrop to this. As I said, I'm happy to share it with anyone who is interested. It's a working document, and you can see pretty much what it entails.

Richard Anders 11:08
Maybe a week or so ago, I sent Brad a few pages of questions for a guide. That’s a lot for a first pass. But you can just look at all the different categories in Brad’s guide and see that there are an enormous number of questions that you can raise. One idea of what we could do today, but we're not going to, is just start going through a list of really specific questions about what we're going to ask. For example, does your service use mice? Are they immunocompromised mice? Are they white mice? How long are the studies? Proper science is concerned with stuff like that. Should consumers be at what level? We'll need to get to those kinds of questions if we move forward with this, but I thought that perhaps the best way to start was with a working session where we start at a little bit higher level than that. Perhaps we should start with what are the very first questions. Perhaps those are clear, but this is an esteemed group and many have a significant stake in these issues, so perhaps they could weigh in.

Allen Morris 12:46
I didn't catch the recitation of the history of the 1970s groundswell of computer hacking started by a 13-year-old in the Boston area, as I just joined the meeting, but I actually lived in the epicenter of that groundswell, so Richard and I overlap in time and place.

Speaking of history and timetables, I would like to introduce a timetable framework for thinking about treatment and diagnostics.

As far as framing treatment and diagnostics, I think a timetable concept is important, as a superarching or backdrop concept, to try to divide Tx and Dx into a timetable with cutpoints.
For example, if a treatment is established in practice compendiums, then I think it is important to subdivide that established treatment into categories, maybe 3 categories.
I submit that something that has established use experience for 30 years, treatment that has been established for five years, and treatment that has been established for one year should be viewed very differently. Indeed, the "established" is solidified in so-called "phase 4" studies aimed at long term effects, mainly adverse side effects, not efficacy in deference to the "do no harm" mandate.
I believe that is lost on most, who are focused on pushing the frontier.

This is really important because if somebody says it's established, if it has been for 30 years, and we know all the side effects over 30 years and the experiences of clinicians prescribing the given treatment for that very mature time period, that is very different than if some treatment only landed, the new SOC, in the last year, in which case, clinicians themselves don't have

much experience at all, especially at recognizing and mitigating the short term, let alone the long term side effects.
For example Brian with Rana McKay may be exploring frontier treatment. The anti-Her2Neu treatments should be viewed very differently than all the others because they, in a sense, collectively have a track record of decades. Considering it is clear to me, Dr. McKay adheres to the "do no harm" mandate, straying little from the guardrails of evidence-based medicine, mainly only to IRB vetted phase 1/2 trials, the established timetable concept should be in the backdrop of this copilot team.

For example, the diagnostic PSMA PET CT was FDA-approved in late 2021. Ask yourself, “How much experience do all the clinicians have with it?” I can give you the answer, except for the researchers that developed it, they've only had < 3 years of experience. If you view it that way, in the way of time experience, in that sense, there is no expert on PSMA PET/CT scan. And this lack of experience is magnified by all the players. It is not just the medical oncologist's lack of experience, but more importantly begins earlier in the cycle, with the readers of the films, the diagnostic radiologists. I have talked to them. Believe it or not, Diagnostic Radiologists have a significant learning curve to climb to get somewhat proficient. It is not see one, do one, teach one. The reports will usually say consistent with or suggestive of; not a definitive diagnostic of, for even seasoned readers who developed the studies. Or maybe it even begins with the delivery of the isotope and the skill of the Radiation Technologist who injects. Just ask Marty Tenenbaum regarding his nurse who injected the melanoma vaccine which miraculously cured him. This speaks to everyone just thinking about the captains of the ship; whereas, there is a whole beehive of people who deliver care, not just the medical oncologist. And the medical oncologist, is not even physically present for most of this, even the chemotherapy IV room that they specifically “oversee”. Just ask Marty if Dr. Morton actually watched him receive the vaccine injections?

I perform bone marrow aspiration and biopsy. If a patient asks me, "How many years of experience do you have as a doctor doing this procedure?” And they occasionally do. If I say 2 years, I presume the patient will not have much confidence in me. Yet, that is all anyone has in PSMA PET/CT scan. In summary, knowing the maturity of something is important, not just that something is established but how long it has been established.

Then you can move forward to the frontier, which is not yet established but may look promising enough to be supported in phase 1 and 2 studies. Maybe you guys can develop words for it. But words that have come to my mind are: Imminent, Emergent, intermediate, and futuristic. And I don't know what the time cut points should be between all these terms.

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For example, Brad once lamented, “All this molecular, precision oncology looks like it's going to be a breakthrough with combination approaches, but probably in 20 years or 30 years. Then we heard a talk by Michael Castro, who had a proprietary Artificial Intelligence algorithm to get at these complex molecular pathways, that he likened to the Paris Subway System, that targeted therapy is aimed at. You know, all these innumerable cascades of proteins that are being enumerated right now, that make up human being's complex biological systems; these beyond complex pathways, that will make anyone’s head spin, especially with all the cross-over redundancies. So Brad thought, “This is going to be some futuristic thing”. So, I infer his definition of futuristic is 20 to 30 years from now. Then he heard the Dr. Michael Castro talk and revised his thinking, “Maybe this is going to be in 10 years, maybe 5.” So, is 5-10 years an intermediate frontier time range and 10-30 years futuristic?
I remember Brad also saying that if it is not in 6 months, I am not interested in it. I want to know what is within that timetable. I believe the 6 month timetable is especially important for GBM and PDAC patients and patients with otherwise indolent cancers that are nearing the end of the line. So, Brad what would you call the 6 month window of the frontier. May I propose "imminent"?

So for the frontier, maybe I propose
1. Imminent: less than 6 months, likely to happen at any moment, FDA priority review
2. emergent: 6 months to 2 years, near future
3. Intermediate 3-10 years
4. futuristic 10-30 years.

Or is this frontier timetable not a worthwhile exercise.

Let me give you an example: Dr. Rech's lecture concerning the Tumor Microenvironment which I thought was an amazing learning session.
But it taught me that determining what a dominant immunosuppressive element in the TME is, is in its infancy and that low dose cyclophosphamide is a shot in the dark. A good shot, but just that a best guess. So, my guess is the sussing out of the TME into a real science enabling prediction of the dominant element is at least a 3-10 year window to get significant color?
Does that make Rech’s learning session not -worthwhile as it is an intermediate frontier goal?
Probably it is not worthwhile for an advanced cancer patient whose window is less than 6 months, but maybe for others or for those who are just interested in learning.

This timetable concept regarding the frontier should apply to diagnostics as well. For example concerning liquid biopsies for Minimal residual disease monitoring, where is that in the frontier. Is it imminent, emergent, intermediate, or futuristic?

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So, CPL (Cancer Patient Lab) has identified all these companies: Natera, Guardant, Tempus, etc. in the liquid biopsy race including the minimal residual disease, sub-race

Well, let me tell you about Natera. Natera is actually in the NCCN guidelines, as a suggested diagnostic for the specific indication: stage 2 - 3 colorectal cancers. And people on the ground, even in the backwater where I am, are actually using the tool on a real-world basis. Therefore, Natera’s Signatera MRD test actually is not in the futuristic, intermediate, or even emergent part of the frontier, but it is actually, not even imminent, it is for real now.

Other terminology that is recognizable as fitting into a timetable framework for all these new start up tests, include the following 2 categories: “research only” versus “this is already commercialized” e.g. FDA approved as a companion test or some other certification - I am not a lawyer to know how you go from having to put the research disclaimer in your reports vs. omitting that disclaimer.

Things are moving fast. So, I thought Natera was the lone front runner as they're in NCCN guidelines, the gold standard oncology practice compendium. But it turns out, Tempus literally just sent in my inbox on June 3, 2024, that they are commercial now with their minimal residual disease test. So, Tempus has changed their designation from research only, to commercially available. Note: Boston Gene is research only. And I don't know how to divide all these categories up, but certainly making it into the NCCN guidelines should warrant the term established.
Now for liquid biopsies in the screening space, I believe is still a significant work in progress, my guess is 3-7 years, despite Cologuard’s commercial penetrance. I say this because because, not only the American College of Physicians, not only Peter Attia, but my local gastoenterologists, do not recommend Cologuard over either Colonoscopy or cheaper screening tests such as FOBT and FIT tests.

What do you all think of this proposed framework: a timetable framework for thinking about not only what is established, but what is in the frontier; considering CPL has interest at being at the forefront as well as possibly pushing the envelope with N of 1 frontier stuff?
Or is the timetable framework not a worthwhile topic?

Richard Anders 17:05
I think that that's really helpful. I want to stay at a little bit of a high level. Maybe I'm being unduly deliberate. If people want to burrow right into the details at that level or even beyond. Some of the higher level questions I would want to explore include the one of: “Who is the guide for?” It seems like an obvious question. It's for patients and families, I assume. But is it

something that clinicians might find useful? Is it something that an insurance company trying to figure out if something should be reimbursed would find helpful? The NCCN guidelines often determine a good chunk of cancer patient reimbursement as I understand it. If it's in the guidelines, it can be reimbursed even though it's not necessarily FDA-approved for that use. Is it obvious who this guide is for? Or do we want to think about that a little bit more broadly? If it's obvious, just say that, but I think that might be a question.

Jane Wilkinson 19:03
I've been in this space a relatively short time, but one thing I have seen, especially coming from the rare cancer space, which is where I'm living, is I do think this is helpful for patients and physicians equally. There are a lot of patients who are going to oncologists and saying, “Hey. What about this? Have you heard about this?” And in some of these cases, some of the oncologists are actually saying, “I haven't heard about this. Tell me more.” So the patients – and I know you've all been here and experienced this – are actually the educators back to the oncologist. So I do think this does have a value to the oncologist.

One thing I can't speak to is the mess that is the insurance and reimbursement world, but I think this really does have a very strong value to the patients and the oncologist equally.

Brad Power 20:10
To underline what Jane just said, I had a conversation last week with Moyez Jiwa, who is a professor in a medical school in Australia. He said two things: doctors have to realize that they are continuous learners that they're going to have to learn over their whole career because the world's changing every few months. And secondly, doctors can learn from patients. The logic is a patient comes to a fork in the road and has to make a decision. They survey what's out there. Then they bring it to their doctor, and their doctor might know what the answer was three months ago, six months ago, a year ago. But that might be different than the answer today. So patients are continuously surveying the treatment and testing possibilities, and then bringing it to their doctors. So their doctors really should recognize that they're going to be learning from their patients.

Richard Anders 21:06
It reminds me, Jane, of that comment again: you keep going back to the things you know, and one of the things I knew once upon a time was the computer business. I remember these MIS directors and companies were frantic because all of a sudden, non-expert employees were telling them what kind of computer software they wanted to install on these microcomputers that they were bringing into the office. They were subverting the control and power of the established departments. So I could imagine that clinicians have got to be struggling with all of the different tests that are out there.

Jane Wilkinson 21:41
In complete defense of the amazing healthcare providers that we do have, a lot of them don't have the time carved out to be able to stay on top of the research. As I focus on appendiceal cancer right now, it is typically a surgical oncology approach. It rarely moves into medical

oncology, because it takes a primary surgical approach. The surgical oncologists have even less bandwidth to be able to immerse themselves into some of the more research modes as well.

Chris Apfel 22:27
It would be great if perhaps Glenn Sabin can bring some oncologists on board to our meeting. I think they would be very valuable. I'm delighted that Allen is here as a pathologist, and therefore can also provide more of the physician's perspective.

Like Richard, the analogy of how it started back then in the computer world, and now how things are evolving here, there is a little difference. The difference is that the ultimate decision on what will be made is basically a decision of the physician. There the healthcare system is fairly established. If the patient says, “I want a, b and c.”, and the oncologist says, “Nope, I don't think so, because my guidelines say something different.” Then you can come up with all the material that we have, with all the data, with all the evidence, and they will just say, “No, I can't do that. Sorry, I would love to, but my NCCN guidelines won't allow me to do so.” Or, “This is experimental.” Or, “This is preclinical.”

One thing is: how much bandwidth does an oncologist have to educate him or herself? That's one part. There are oncologists out there that really have tried to stay on top of it. Dr. Castro is one of those examples, who actually pushes the guidelines and is constantly seeking what's the best possible way to treat this patient. But for the majority of oncologists, especially those in the NCCN guidelines centers, they are basically bound by the NCCN guideline rules. If they were going out of their way to go beyond that, it's actually not only a question of time, it's also a question of, are they practicing outside of guidelines? Will it be covered by insurance? Will they actually open themselves up for attack from not meeting the standard of care? So there's more to that because in the healthcare system

The customer is not identical with the decision-maker, and just addressed as an example. Therefore, it would be helpful to get an oncologist or cell oncologist on board in our discussions that can actually also provide this guidance and perspective.

Richard Anders 25:26
That's a really good point. There are a number of considerations. They range from topics like “is this a reimbursed test?” “Is this a test which changes treatment?” “Is this a test which applies to certain types of cancers?” These all are sorts of questions that we should examine how or if we want to explore in a guide and that’s something I hope we can get to today.

Robert Gurmankin 26:34
I think it depends on the oncologist. I just started chemo with cabazitaxel and carboplatin. I did functional testing with Dr. Apfel’s company, Sage Medic. What showed up as the most efficacious is mitoxantrone, which was 25 or 30 years ago the standard of care. My oncologist said, “Let's try the standard of care. If we don't get results, we have the drug in our pharmacy. I'm very willing to do it. I haven't used it since fellowship.” But he's willing to go outside the box.

If we can get this under control, he’s also willing to do double immunotherapy, which is basically in phase 2 trials in England. I'm at Fox Chase Cancer Center. He's going to the powers that be to get the preapproval to do this. So I think it's very individualized, and maybe also has to do with the institution.

Richard Anders 27:57
Today is not of course a discussion of the difficulty of getting something prescribed. But I think it does raise the issue as a topic to be discussed. Maybe one of the issues that should be in a guide is a discussion of what is the way in which this thing would be prescribed by a clinician, or what is the way in which this thing would be reimbursed by a clinician. Again, I assume that a well organized diagnostics testing company will have clinicians and methods of getting their product used by clinicians and ways of potentially getting it reimbursed. A product that's great that no one can prescribe or no one can pay for is not as good a product that someone can so that sounds like a topic that should be included.

Jeff Krolick 29:22
My experience prior to my cancer diagnosis was in the behavioral health field. I was a senior manager with responsibilities that included administratively overseeing the medical staff including psychiatrists and across the board.

The psychiatrists, the medical staff, in particular, the MDs were the slowest to respond to any innovation, such as electronic health records. We had people dictating for years and years after electronic health records. My point is that the adoption of something new – this is what I've heard people talking about – is very, very slow. Again, my experience is the standard of care limits, the range that an oncologist can practice in, although I have had the experience of a radiation oncologist being very clear, “Here's the standard of care. What you and your medical oncologist are asking is outside of that. I'm willing to do it. We're covered with the release. But I just want to make you say it like five times: this is outside the standard of care.”

I think there's a great variability in that. My medical oncologist, who has more flexibility, for better or worse, is a private pay. She says she does that because otherwise she feels she's working for the insurance company, in all decision matters. So this lets me and the oncologist step outside of that, and she can reach out to other experts. She's very responsive. If there's something I would like to do, it's so individual, in terms of, each of our experiences with our medical oncologists. My perspective is, it would have some limited appeal to some oncologists who have the latitude and wherewithal, who are not so concerned about the liability to explore some of those other avenues. I think this is more for patient use, for those of us that want to advocate. We're clearly pretty creative and clever, and getting our needs met in that way.

Richard Anders 32:34
So you're seeing this guide as a patient pull, that is something led by patients and not necessarily of strong utility to the practitioner…

Jeff Krolick 32:56

Yeah, that would be my limited perspective, and based on how well we can advocate and marshal our resources, we may be able to interest an oncologist in moving in a particular direction.

Richard Anders 33:14
Chris also sees it as a patient guide. I thought that if it was well done, it might be the sort of thing that a clinician would say, “Well. I've never heard of that test. But let me look in more detail at it.” We’d have to be careful if we aspired to that, because with ratings or reviews we would have obviously to be more scientifically defensible if we were to appeal to clinicians. But that seems to be a good topic for serious discussion as we move forward.

Brad Power 33:48
Another feature that I hear behind this is the patient would need to be armed with the evidence to bring to their doctor.

Richard Anders 33:57
This guide could have that. I mean, among other things, I love evidence.

Jeffrey Dwyer 34:14
I was thinking about what your intended use is for this guide, Brad. I rolled back in my thought pattern to what I did five years ago, when most patients are diagnosed with any cancer, but for my case, it was prostate cancer, you have not focused on this at all. But you know, anecdotally from friends and family, that it's bad. So now you have to learn about it.

How do you learn about it? As a patient, it would be incredibly helpful to know that there's layers, that when you come to the fork in the road that Brad describes, you don't go down that particular fork, because you're going to run up against something that you will later learn is a dead end. For instance, what Jeff just talked about, when he said that his radiation oncologist won't work outside standard of care. When you just start your journey with cancer, you don't understand what the standard of care is. And you don't understand, as was pointed out, that the decision is not yours.

The fallacy is that you can make a decision when you read about something in some article. “I can get that.” Except you probably cannot because one of the gentlemen who presented here was eye opening to me. It was a doctor from Dana Farber, and his program was very interesting. But as he later pointed out, all these things are wonderful. But because they haven't gotten their progress through the randomized clinical trial, he can't take that to the clinic. In fact, anything I've talked about today, I can't take to the clinic because it's not been vetted by my colleagues in the professional community, vetted by insurance companies, and vetted by my hospital. So you realize that he's a wonderful guy to talk to at a cocktail party, but he's not going to help you in the treatment you have to select next week, is it surgery or radiation? Is it whatever for your particular cancer?

So if it's a guide for patients, from patients, it would be really helpful, as Allen talks about.

Is this an emerging thing? Or has it been around for a while? Bob just talked about a cancer ADT (Androgen Deprivation Therapy) drug that has been around for 20 years, and I have no problem getting it, except that the medical oncologists no longer use it. Is it because at the last professional standards group, it was taken off the standard of care list, but it's not what they've all agreed they're going to do next year, they're going to use third generation, or the fourth generation. So as a cancer guide, if this is going to be useful, you've got to try to continually update it for what happened last year, that is now approved for paying, because that's what it comes down to real fast. Is it the facility where you're going to get your care? Will they get reimbursed from the insurance company? Because if they're not going to be, you're not going to get that special thing you just read about in Science Today. It's not going to happen.

Richard Anders 38:57
It's a really interesting topic that we're obviously converging on. We of course need to pay respect to clinicians. I know everybody has tremendous respect for the job they do and also try to understand the issues from the clinician’s point of view, what their issues and concerns must be. I think clinicians view their role as one of guardianship – they are the ones keeping out the white walkers, preventing everything from descending into chaos. And that's a very tough line for them to navigate.

On top of that is the question of whether something is reimbursed or not. If you were a billionaire like Dr. No in James Bond, you could afford to pay for anything. But perhaps this guide should have a meta purpose of helping patients thread the needle of how to actually get it for their use, not just reimbursed, but also prescribed whether on- or off-label.

I saw Allen's really interesting comment about a level of evidence thermometer or scale or whatever. I think that's a really nifty idea.

Glenn Sabin 40:45
Thank you, Brad, for growing this amazing resource that you've been working on over the last couple years. I've been able to contribute a little bit here and there. It's a wonderful foundation that would serve multiple purposes over time.

What we're discussing has a lot of interconnected pieces. In terms of prescribing off label and combinations, etc., right now, about 40% of the FDA approved anticancer drugs are prescribed off label. It's a matter of finding out who some of these prescribers are within the community and even academic settings. I've been consulting with Cancer Commons and helping them with some business development on a couple key projects. I can speak to two of them quickly.

One is an N-of-1 physicians network, which we started collecting names. We have a few dozen that have been contributed from various folks. Jeff Krolik, I would love to learn who your concierge medical oncologist is. This list so far comprises both academics and community oncologists. It will be expanded to include some surgical oncologists, some radiation oncologists, pathologists, even some interventional radiologists, that are doing some really

innovative work. It will be free for those very well vetted practitioners that go through an application process that will live on the back end of Cancer Commons, which should go live but in a very kind of private way in the next several weeks. There's different criteria through which various types of oncologists will prescribe in this way, when you look at neurons as an example that are dealing with with GBM, and some really difficult pediatric malignancies, they're more open to others, because the standard of care, like with GBM, starts with a trial at this point. So it varies under what condition. So not everyone is going to necessarily work with patients this way, in a pan cancer kind of way, at a community level. We're actively putting together this list then the usage guidelines to develop this in a meaningful way that various testing companies can utilize responsibly, and where patients at some level will be able to have access to a few matches based on their particular situation and desired geography, to work with a provider, etc. That's the N-of-1 Physicians Network. In terms of service providers, awesome.

I’m also working on a database that will live on the back end of Cancer Commons. It's essentially a precision slash personalized oncology service providers database where various companies such as Sage Medic will upload their data information into forms, all validation information will be collected, and will be updated regularly. It will go through a vetting process through the Cancer Commons scientific team. There'll be folks such as Chris, hopefully, that will be on an advisory board that will provide input to the processes and the questions that are asked, and how we go about collecting some of this key information. From there, we'll be working with a partner to develop diagnostic workups for specific kinds of buckets of disease. At least at the beginning, we'll be starting with GBM, because that's where the scientific team at Cancer Commons has a lot of experience in that area. Specifically, Adrienne Nugent, and the connections with Al Musella, Vanessa Hugo, and others. It will be working with a major diagnostic lab who will help figure out that diagnostic workup that will then inform the navigation patient workflow that will put together not just their own proprietary tests, but will include third party testing, so essentially covering all the molecular DNA, RNA testing, functional assays, multi-omics, etc, other types of testing.

Richard Anders 46:45
What do you mean by “cover” Glenn?

Glenn Sabin 46:47
So the amount of testing is really vast, and it goes beyond just the molecular testing that's typically done. Hopefully more should be done. But that's kind of the go to where you have targetable mutations and biomarkers through that molecular kind of process of testing that's done through next gen sequencing and whole exome sequencing, etc. Then you have all the functional types of testing: organoids and tissue-based and that's sort of a compendium. It's a whole wide, vast range, within the database that will speak to, “Is this commercially available? Under what situations? Are there CPT codes, or payers covering it? Is it cash pay? Does the company provide patient support?” BostonGene, as an example, is really phenomenal in supporting folks that can't afford these tests, because maybe they're not viewed as clinically indicated, and therefore, covered by CMS, or through commercial payers, just as an example.

The same partner will also be charged with the critical unmet need of interpreting across all multiple data sets, to better inform treatment recommendations. It is very ambitious. Right now we've got some momentum. We're making progress on all fronts, even on drug acquisition, and hopefully beyond just compassionate use.

Richard Anders 48:56
Humanitarian exemption for devices? Right to try?

Glenn Sabin 49:00
These all connect. The idea to have a list of services that are vetted by scientists through a nonprofit to have that imprimatur to be a preferred provider, the idea of connecting it to commerce, where there's actually a marketplace, where folks will be able to purchase very easily, but with guidance, different services, whether it's through CMS or commercial providers or direct pay, or in many cases could be a quid pro quo for tissue.

Richard Anders 49:54
I think that that sounds great. It sounds in a lot of ways like what we want to do, and that's what this discussion is teeing up. Thank you very much for talking about that. It’s a great project.

Brian McCloskey 50:14
Thanks so much for making this a topic of discussion. This is a really good one. I love it in terms of how it shapes what we do today, but also how we think about it in the future.

There are three points that I wanted to bring up.

One is: why do we need this? There is a today version. There is maybe a more lofty reason to have it in the future. For today, we want to use this Services Guide to make better data-driven treatments, which will ultimately extend our lives as patients and improve our quality of life. We already have many examples of how Cancer Patient Lab patients have taken advantage of these service providers, whether it's BostonGene, or it’s SEngine, or it's Sage Medic, or mProbe for proteomics. In many of these cases, these patients are bringing the services to their medical oncologist to make better data-driven decisions. I know, certainly, that's the case for me. Bob just talked about how he used Sage to bring data to his oncologist. They decided to go maybe in a little bit different direction, but they still have the treatment option that Bob mentioned in their back pocket. Why we're doing this is critical. It's really our True North. This is to make better data-driven treatment decisions.

There was a really interesting part in this discussion, as we talked about the constituents. If we think about a second reason for the “why”, the future, perhaps we could create the Services Guide such that it becomes the gold standard. At one juncture in my career, I always considered the gold standard to be like the Lloyds of London of banking. It had this incredible reputation. If we could create the Services Guide such that it is the gold standard, not just the gold standard for patients, but also for clinicians, insurance companies, pharma, other life sciences

companies, then what you do is you actually can bring these constituents together, such that they're having a conversation around the value of these service providers.

There's another layer, we've talked about the various levels of maturity, what I would almost describe sort of the maturity of each of these different service providers. Some of them are “research use only”. Some of them are already in practice. We can filter in that layer in terms of how we think about the service providers. That would be part of the qualifications that we would use. The peer review also came into that as well. That's how I see this from a “why” perspective, extend patient lives, make better data-driven decisions, and then also just another tool for us to bring all of these constituents together, because today, they often don't. They're not on the same page. We need to do that.

The third point I wanted to make is that I would really love to have someone like Eric Topol weigh in on this. One of the very first books that I read, when I started my journey, was “The Patient Will See You Now”. He made a lot of parallels to the computer industry, and just access to information. Richard, you started this conversation around the notion of user groups is really, really important. I'd love to get his perspective on how a user group like Cancer Patient Lab can help to bring this together. How do we get that critical mass? How do we get that scale such that we can really affect change, such that his vision of how “the patient will see you now” actually becomes a reality?

Dr. Apfel, I know that you said that the doctor is the decision-maker. That's generally true. However, we also have to remember that patients can always get second opinions. It's not just a single doctor, but it's multiple doctors. If you think about it from that perspective, who really is the decision-maker? Is it a doctor? Or is it the patient choosing across different doctors, of course, each of those different doctors have various guidelines, they have guardrails, NCCN guidelines, etc. But we all know that you will get different care based upon who your doctor is, and where you are in your journey. There are a whole lot of different layers of complexity. To say that it's just the doctor that is making this decision, there's some gray area and room for debate about that.

Richard Anders 56:08
That is a fabulous set of observations from someone who's thought deeply about this.

I want to throw a lightning round of some things that we might want to think about. I don't think we even have time to react to them. But there are some issues that I think are worth at least putting in the hopper. I'm happy if I get the emails to send the deck, which starts the conversation. There are a lot more questions that I've written down that would follow from this.

Some things that we want to think about:

- What degree of proof is this?
- Is this standard of care or not standard of care?
- Are there trials?

“How Do You Choose Your Diagnostics? – A Guide” (Richard Anders and Brad Power) [#100]

- Is this FDA approved?
- Where does it stand in the FDA cycle?
- Are there many clinicians who are using it, whether or not it's approved?
- Is it an LDT, or if more strongly regulated, with what proof and what claims?
- What kind of cancer is this for?
- What stage of cancer is this for?
- What change in treatment?
- Does it have a stage in treatment?

There are a lot of questions.

One set of questions we haven't talked about at all are the legal questions and another set of questions we haven't talked at all about is how we would do this.

- What should this thing look like?
- Are we going to have a 50-page review of every company?
- Are we going to ask the companies to fill out questionnaires that we provide them? Maybe that's a starting point, and then we collate that information, and then put the questionnaires together with interviews?

There's an awful lot more to say. This is really the very beginning of this effort. Maybe what we should do is have another meeting or working group or something.

Brad Power 58:50
It would be very useful for us to have a working group or a review board. We can call it what we want, but we need to have more minds focusing as we both ask these questions and get responses. Maybe we should make that a request that we can put out. We can manage this through emails. I have email addresses for everyone here, which I can send it out to, as well as we have our discussion forum, which I would encourage us to use as a place where we can be public as we have discussion.

Richard Anders 59:24
On Brian's idea that this could be a standard: from observation I have seen that sometimes the early entrants into a field define the parameters and the rules of play. If this is a good guide, it could probably be very influential and that would be very useful for everybody.

Brian McCloskey 59:47
If I can just put a plug in here for our logo for just a second and explain our logo. If you guys can actually see this. What we're talking about today is really embodied in our logo, which is that in the center, you have sort of this double helix, right? On either side of the helix, there is the doctor that's represented. It's very hard to see. But down at the bottom, there's a little stethoscope. At the top is a little head here, which is the patient. That's the commingling of the patient and the doctor, of course, grounded by science, which is really the whole double helix is

all about. That is surrounded by the community, which are each of the four colors and people that are represented around this.

If I think about our logo, I think about this discussion, this discussion is all about our logo, and our logo is all about or this discussion, which is: How do we take all of this science? How do we bring the community together? Not just this community, but all of the constituents that we talked about: insurance companies that aren't represented here, et cetera? How do you bring them together in this Services Guide? It's a grand vision, and it's a lot of work. We have to think about how we get the energy and the right people in the room to actually make it happen. But I don't see anything that's really more compelling in medicine right now than to actually pursue something like this. This is really, really important. We're onto something. Brad's done an absolutely amazing job putting the services guide together. I know it's going to evolve, but it's going to take a lot of work and a lot of different people to get involved to make it work. I'm totally in favor of a working group and excited about it.