"Accessing the Latest Developments in Liquid Biopsies" (Lauren Leiman and Jenn Dickey) [#148]

Brad Power
June 18, 2025

“The reason this is a powerful tool, and one that we advocate strongly for in the oncology community, and one that we actively try to develop and promote the development of new assays for, is because it is less invasive than a standard biopsy and has a lot of functionality that can help improve patients’ lives.” – Jenn Dickey, PhD

“As Allen said, ‘You're just getting lead time. It doesn't change the outcome.’Well, I'm Exhibit A for the fact that that's wrong, and I not only got a liquid biopsy, it wasn't without the advice of a physician, it was against the advice of my physician. He said, ‘Don't do it. They don't work. You're just going to get a false positive, and it's going to scare you.’ One of the very few things that my doctors agree on now is I probably wouldn't be here if I hadn't done that. So you can make all the statistical arguments you want on patient advocacy. I'm not a statistic. I'm a person. And I wouldn't be here without it.” – Roger Royse
[Allen reply: Roger, I was specifically talking about the minimal residual disease space in regard to the concept of lead time promise of benefit and the consensus view of it in my medical community - so we are talking past each other].

“We take the information to our physicians, and we ask for things. We promote the use of technologies of benefit for us, directly to our physicians, as I did recently, because I'm interested in detection in my own body, from my treated and apparently now indolent prostate cancer. Using circulating tumor DNA detection to see if there's something growing that is not being picked up by my PSA. My oncologist said he didn't know anything about this. I said, ‘Well, I want this. Could you please research it and find out how to get it for me? Should I get circulating tumor cell counts or should I get a CtDNA screen, quantitative to what percentage of my circulating DNA is tumor DNA, and then if it's detected, can it be genomically profiled?’” – Paul Van Camp, MD

“In the base case of tissue assessment for comprehensive genomic profiling, there have been several recent publications that indicated that approaching 75% of advanced, non-small-cell lung cancer patients are getting comprehensive genomic profiling, and then the numbers fall precipitously by tumor type after that. In an advanced cancer space, to not have comprehensive genomic profiling of some sort in the era of precision medicine with so many targeted therapies is a real and present danger to our advancement in this space.” – Jenn Dickey, PhD

Meeting Summary

Cancer patients and caregivers need to understand liquid biopsies because these non-invasive tests can provide valuable information about your cancer, guiding treatment decisions, monitoring treatment effectiveness, and detecting early signs of recurrence or progression. Liquid biopsies offer a more convenient and less risky alternative to traditional tissue biopsies, particularly if you have advanced or recurrent cancer. This allows for more frequent and less risky monitoring of cancer progression and response to treatment. Experts believe liquid

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biopsies can potentially revolutionize cancer care by making it more accurate, accessible, and personalized.

Lauren Leiman, Executive Director, BLOODPAC, (Blood Profiling Atlas in Cancer), and Jennifer Dickey, PhD, of Labcorp, are uniquely qualified to lead a discussion on the cutting edge of liquid biopsies. The BLOODPAC Consortium was launched in 2016 to accelerate the development and validation of liquid biopsy tests to improve the outcomes of patients with cancer. It includes representatives from academia, private foundations, industry and government.

Why might liquid biopsies be useful for you in your cancer journey?

- **Less invasive** than traditional tissue biopsies, especially if you are medically fragile or cannot undergo surgical procedures, minimal discomfort; less expensive than a tissue biopsy; can increase testing frequency; especially helpful when tissue biopsy is difficult or impossible
- **Monitor** your cancer progression and treatment response by tracking circulating tumor DNA in your blood; **early detection** of potential cancer recurrence or resistance mutations before they become clinically apparent; determine when to change therapeutic approaches
- **Comprehensive genomic profiling** that can help guide precision medicine treatment decisions; particularly useful if you have non-small cell lung cancer
- **Multi-cancer early detection**, allowing for screening and intervention at earlier stages when treatment is most effective

How can liquid biopsies complement other tests?

- Liquid biopsies can offer a more comprehensive tumor profile by detecting genetic variations across multiple tumor sites, which a single tissue biopsy might miss.
- For monitoring treatment response, liquid biopsies allow frequent, non-invasive tracking of tumor mutations and minimal residual disease.
- In cases of metastatic cancer with unknown primary origin, liquid biopsies can help identify potential tumor origins and guide treatment decisions.
- Liquid biopsies can be used alongside traditional imaging and tissue tests to provide a more complete picture of your cancer status, potentially detecting changes earlier than other methods.

What are the challenges of false positives and false negatives and other potential biases in liquid biopsies, especially for multi-cancer early cancer detection?

- **False positives** can cause psychological distress for patients, may lead to unnecessary additional medical procedures, and raise public health and reimbursement concerns.
- **False negatives** can provide a false sense of security, might delay critical cancer interventions, and reduce patient trust in the technology.

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- **Key challenges** include minimizing false positives (maximizing “sensitivity”) and minimizing false negatives (maximizing “specificity”), determining appropriate patient populations for testing, and developing tests that provide actionable clinical information.
- **Current multi-cancer early detection tests** are still evolving. They're not yet ready to replace existing screening methods like mammograms. Research is refining biomarker identification and establishing clinical standards. Early detection may provide lead time, but not improve your outcome.

How should you decide which service provider you should select for your liquid biopsy?

- **Clinical evidence**: Look for providers with robust published research and clinical validation studies for your specific cancer type, consult with your medical team
- **Test specificity**: Evaluate the test's performance in terms of sensitivity and specificity for your particular diagnostic or monitoring needs
- **Comprehensiveness**: Check the breadth of genomic profiling and the number of cancer types the test can detect
- **Regulatory approvals**: Prefer providers with FDA clearance or CE marking
- **Insurance coverage**: Verify if the test is reimbursed by your insurance
- **Turnaround time**: Consider the speed of test results
- **Cost**: Compare pricing across different providers
- **Reputation**: Research the provider's track record and reviews from medical professionals

How can you access liquid biopsies, e.g., tips for persuading your doctor that you should get a liquid biopsy, navigating reimbursement?

- Research specific liquid biopsy tests relevant to your cancer type or situation, including talking with peers
- Bring scientific literature and recent studies to your doctor demonstrating the test's potential value
- Ask specifically about molecular profiling and whether a liquid biopsy could provide additional insights into your treatment
- If your doctor is hesitant, request a referral to an oncologist more familiar with liquid biopsy technologies
- Check with your insurance provider about coverage - some tests are now being reimbursed, especially for certain cancer types like non-small cell lung cancer
- Consider clinical trials that might provide access to liquid biopsy testing

How can you learn more about liquid biopsies in cancer care?

- Visit the BLOODPAC website for resources and educational materials; offer to provide the patient perspective on the development and implementation of liquid biopsy technologies

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- Contact Lauren Leiman at lauren@bloodpac.org or Jenn Dickey at jennifer.dickey@labcorp.com
- Review educational resources from cancer research organizations that explain the current uses and potential of liquid biopsies; read scientific publications from diagnostic companies; follow ongoing clinical trials and research; attend medical conferences that feature liquid biopsy research
- Consult with oncologists who are familiar with the latest liquid biopsy technologies
- Join patient advocacy groups focused on cancer research
- See previous webinars we have had on liquid biopsies, such as
    - "Liquid Biopsies" (Peter Kuhn and Stephanie Shishido) [#23]
    - "Testing Your RNA with Liquid Biopsies" (Alex Rolland) [#116]
    - "Using Predictive Biomarkers and Liquid Biopsies to Personalize Treatment for Prostate Cancer" (Andy Armstrong) [#64]
    - "The Latest Tests for Personalized Cancer Care" (Tony Magliocco) [#89]
    - "Using RNA Sequencing to Guide Treatment Decisions for Advanced Cancer Patients" (Gitte Pederson) [#42]

For the video recording of this conversation, please see here.

For a transcript of the conversation, please see here.

For the slides, please see here.

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Meeting Notes

KEYWORDS

Liquid biopsy, cancer patient, blood profiling, White House Cancer Moonshot, frameworks, standards, data aggregation, regulatory issues, reimbursement, accessibility, early detection, multi-cancer, clinical trials, patient advocacy.

SPEAKERS

Jenn Dickey (29%), Lauren Leiman (26%), Peter Kuhn (10%), Rick Davis (8%), Allen Morris (8%), Roger Royse (5%), Richard Anders (4%), Paul Van Camp (4%), Dinesh Kumar (2%), Sandra Balladares (1%), Ari Akerstein (1%), Jeff Waldron (1%)

CHAT CONTRIBUTORS

Saed Sayad, Russ Hollyer, Alexander Lalov, Len Sierra, Ari Akerstein, Helen, Rick Davis, Paul Van Camp, Jenn Dickey, Dinesh Kumar, Kamran, Jeff Waldron, Lauren Leiman, Peter Kuhn, Richard Anders, Allen Morris

SUMMARY

Lauren Leiman and Jennifer Dickey discussed the advancements and challenges in liquid biopsy technology for cancer patients. BLOODPAC, led by Leiman, aims to accelerate the development, approval, and accessibility of liquid biopsy technology. They highlighted the importance of creating frameworks and standards, aggregating data, and addressing regulatory and reimbursement issues. Dickey explained the three primary uses of liquid biopsy: diagnostic biopsies, monitoring therapeutic progress, and early cancer detection. They emphasized the need for clinical evidence and the role of patient advocacy in promoting these tests. The discussion also touched on the challenges of false positives and false negatives in early detection tests.

OUTLINE

Introductions and Overview of BLOODPAC

- Lauren Leiman provided an overview of BLOODPAC, and introduced her colleagues Cheyenne Jankowicz, Donna Albers, and Doris Lopez.
- BLOODPAC started with the White House Cancer Moonshot and its mission to accelerate the development and accessibility of liquid biopsy technology for cancer patients.
- BLOODPAC's workflow includes regulatory, reimbursement, and education issues, with Peter Kuhn and Jennifer Dickey playing key roles.
- BLOODPAC's mission is to create frameworks and standards for the community and aggregate data to support these standards.
- BLOODPAC has grown from an initial group of 20 organizations to over 74, including private payers, showing progress in the field.

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- The organization focuses on three main areas: evidence generation, stakeholder engagement, and working groups.
- Jennifer Dickey leads several working groups, including the regulatory Working Group and the blood collection kit project.

Defining Liquid Biopsy and Its Uses

- Jennifer Dickey defined liquid biopsy as using biofluids, primarily blood, to examine circulating tumor DNA or cells for clinical examinations.
- Liquid biopsy is less invasive than traditional biopsies and can help guide therapeutic decisions, especially for medically fragile patients.
- The primary uses of liquid biopsy include diagnostic biopsies, monitoring therapeutic progress, and molecular residual disease detection.
- Future uses include multi-cancer early detection, assessing apparently healthy individuals for early cancer detection.

Challenges in Developing Liquid Biopsy Technologies

- The challenges in developing liquid biopsy technologies include the time, expense, and clinical trials required.
- The field evolves slowly, and it takes time to align analytical and clinical standards.
- BLOODPAC aims to align on lexicon, analytical performance studies, and clinical endpoints to support small companies and new technologies.
- The organization's value lies in creating a pre-competitive space for collaboration and framework development.

Patient Voice and Advocacy

- Rick Davis raised concerns about the lack of patient voice in BLOODPAC, emphasizing the importance of patient advocacy.
- Lauren Leima acknowledged the challenge and explained BLOODPAC's focus on developing standards and frameworks for the industry.
- BLOODPAC partners with patient advocacy groups like Lungevity and the Prostate Cancer Foundation to ensure patient input.
- They aim to educate clinicians on the use of liquid biopsy tests, with a focus on accessibility and education.

Recommendations for Liquid Biopsy Tests

- Allen Morris asks for recommendations on liquid biopsy tests in general, and specifically for each of the spaces - early detection, minimal residual disease monitoring, etc?
- Jennifer Dickey and Lauren Leiman discussed the challenges in recommending specific companies, emphasizing the importance of clinical evidence and collaboration.
- Comprehensive genomic profiling is needed and BLOODPAC is supporting the development of these tests.
- Patient advocacy is important in promoting the use of liquid biopsy tests.

Minimal Residual Disease and Clinical Evidence

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- Allen Morris discussed the use of minimal residual disease tests, particularly for colorectal cancer, and the need for clinical evidence - [and unfortunately the specificity of my comment was lost on my critics.]
- Clinical evidence is important and BLOODPAC plays a role in supporting the development of these tests.
- False positives and false negatives in liquid biopsy tests present challenges.

Future of Minimal Residual Disease

- Sandra Balladares asked about the future of minimal residual disease as standard of care.
- Minimal residual disease will likely be adopted on a tumor-specific and stage-specific basis.

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TRANSCRIPT

Roger Royse
Welcome to this Cancer Patient Lab meeting on “Accessing the Latest Developments in Liquid Biopsies.” We have Lauren Leiman and Jennifer Dickey here today. Lauren is the executive director of BLOODPAC, that's the Blood Profiling Atlas in Cancer. Jennifer Dickey is from a subsidiary of LabCorp. They're going to lead a discussion on the cutting edge of liquid biopsies.

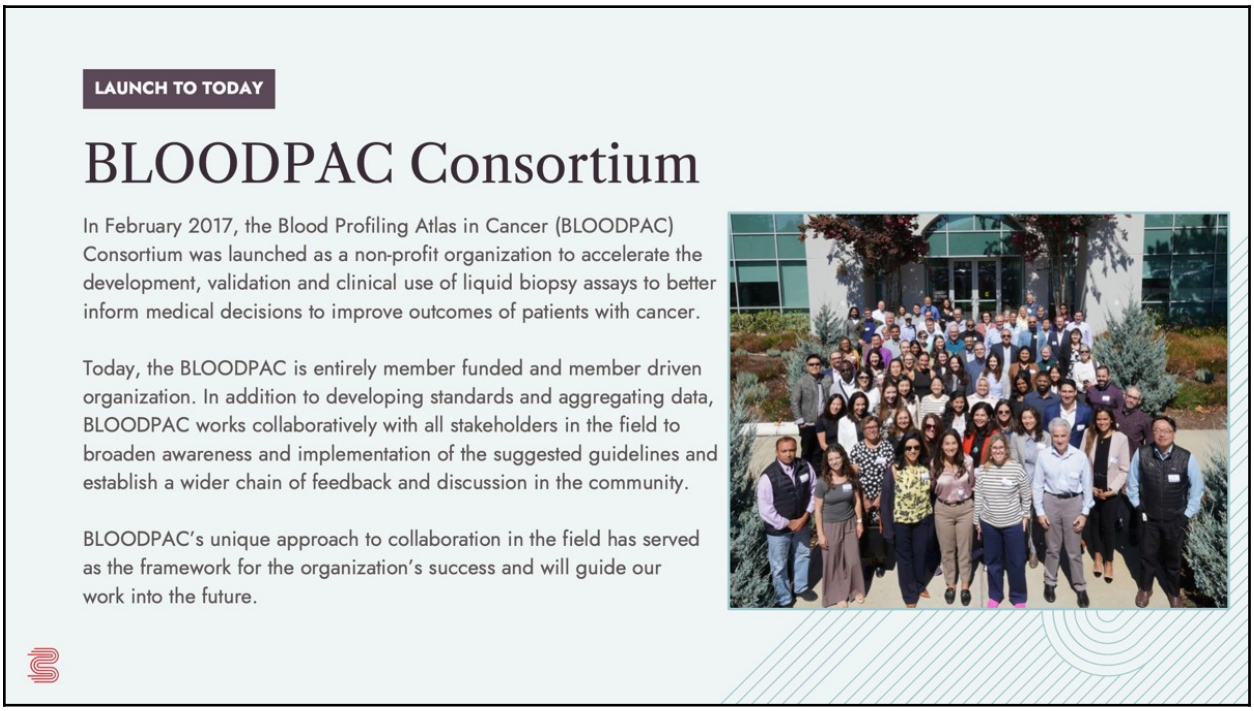
Lauren Leiman 0:32
BLOODPAC is a relatively informal organization, so we encourage you to ask us any questions.

In addition to me, we also have my colleagues, Cheyenne Jankowicz, Donna Albers, and Doris Lopez here. I'm looking for everyone on the screen from BLOODPAC. Cheyenne manages all of our programs. Doris is our Head of Communications, and Donna is our head of data. So if there are any specific questions that you have around any of those topics, you can feel free to ask them as well.

A brief introduction: I'm Lauren Leiman. I'm the executive director of BLOODPAC. About eight years ago, I was at the White House as the head of external partnerships for the initial White House Cancer Moonshot, and Peter Kuhn, who is with us here today, came into our office to talk about liquid biopsy and why it was really something we should be tackling, and how we could tackle it through a commitment to the White House Cancer Moonshot. About 10 months later, we had established a mission statement, which was to accelerate the developments, the approval, and ultimately, we've added the accessibility of liquid biopsy technology for cancer patient benefit. We had decided we were going to do that by creating frameworks and standards for the community at large to use to also aggregate data to support those standards and

frameworks. We also have felt over the past few years that we can be successful in those first two areas, but if we can't get this technology into patients' hands, what is the purpose of all of our hard work? So we have created an accessibility stakeholder engagement workflow as well that focuses on everything from regulatory issues, reimbursement issues, accessibility and education issues – all of those things involved.

Peter Kuhn, I'm excited to say, since he's here, is a co-founder OG (original) BLOODPAC member, and sits on our executive committee and our scientific co-chair committee, and helps guide the organization. Jenn Dickey also sits on our scientific co-chair committee and is an original member of BLOODPAC as well.



We were formed during the White House Cancer Moonshot, the first one back in 2016 and 2017. You should know we are a nonprofit. We started with an original group of about 20 organizations, pharmaceutical companies, diagnostic partners, academics, foundations, funding in the space and in several government agencies to help, again, achieve our goal of accelerating the development, the approval and the accessibility of liquid biopsy for cancer patient benefit.

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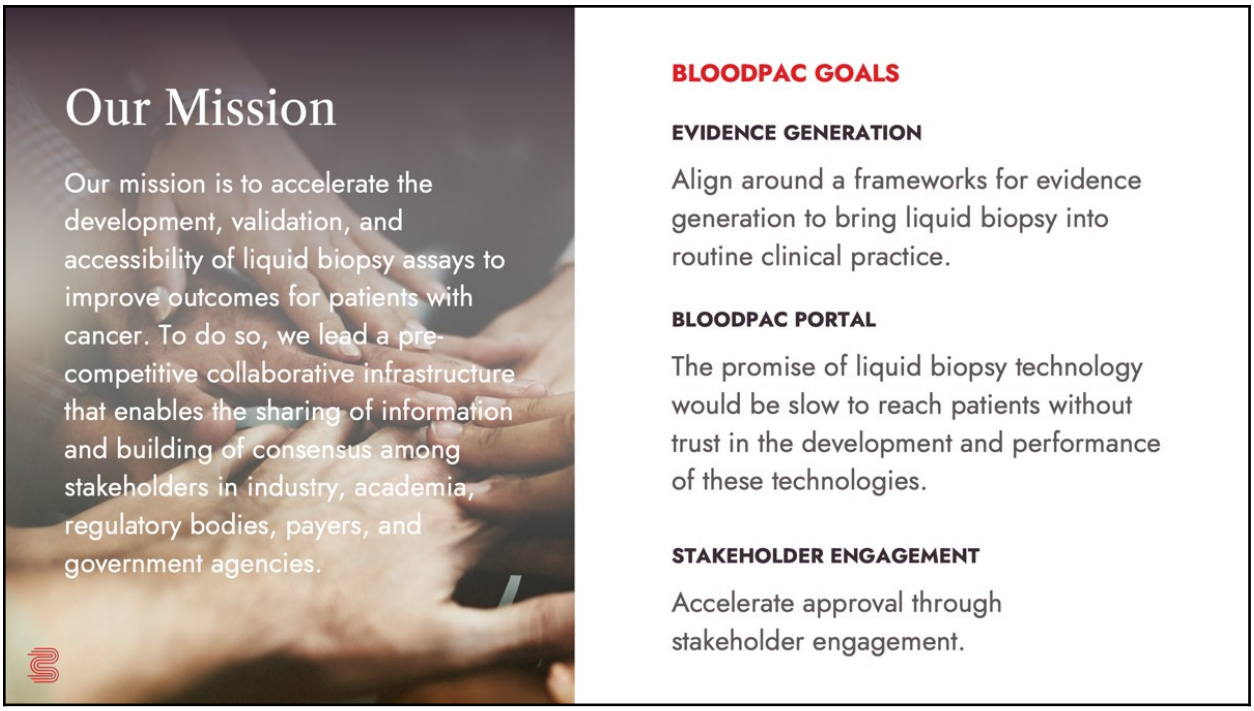

We do that in three different areas, three large buckets:

- Evidence generation: I'm not sure if I love that title anymore, but it's really aligning around frameworks, creating standards for the community to utilize, creating, aggregating the data to support those, or running, in some cases, we do run a few different prospective studies to create, generate that evidence as well,
- BLOODPAC portal,
- and then we have this larger stakeholder engagement bucket.

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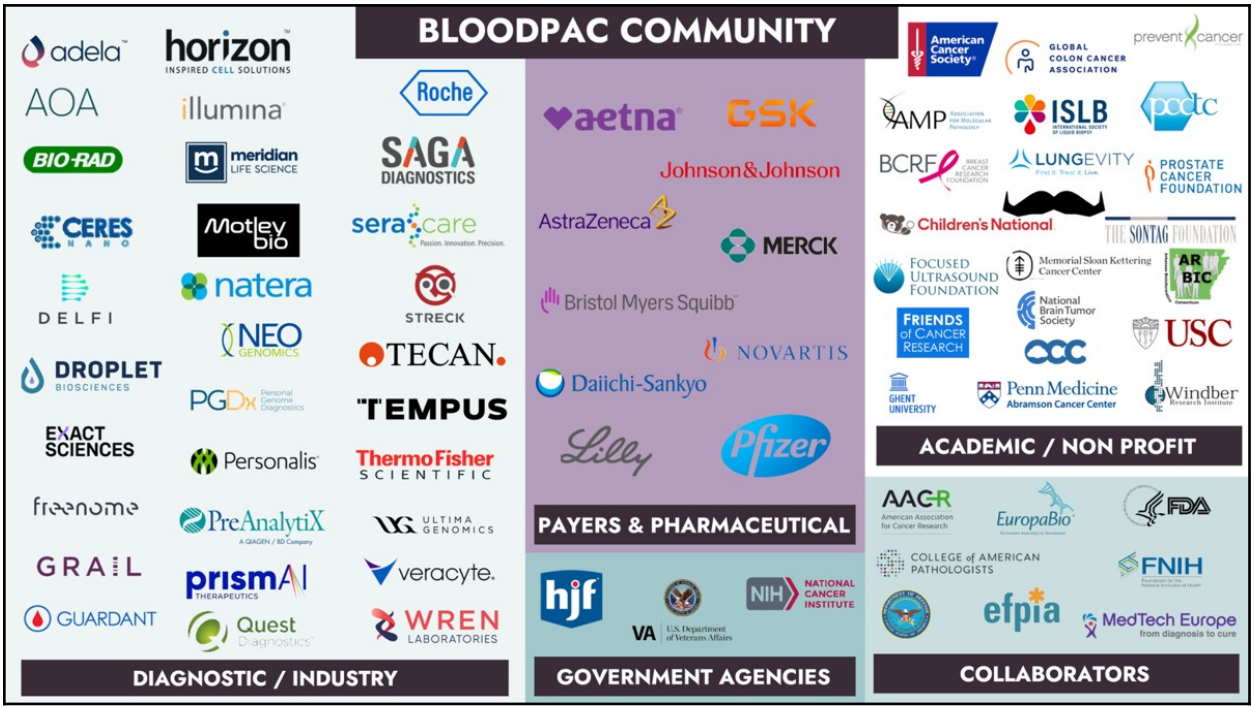
Today, we have over 74 different organizations that collaborate and are members of BLOODPAC. The only addition to the original that I mentioned from the original 20, the diversity from the first 20 was we have started to add private payers to the conversation recently, which is an added benefit to what we're capable of doing, and also shows the progress of the field generally.



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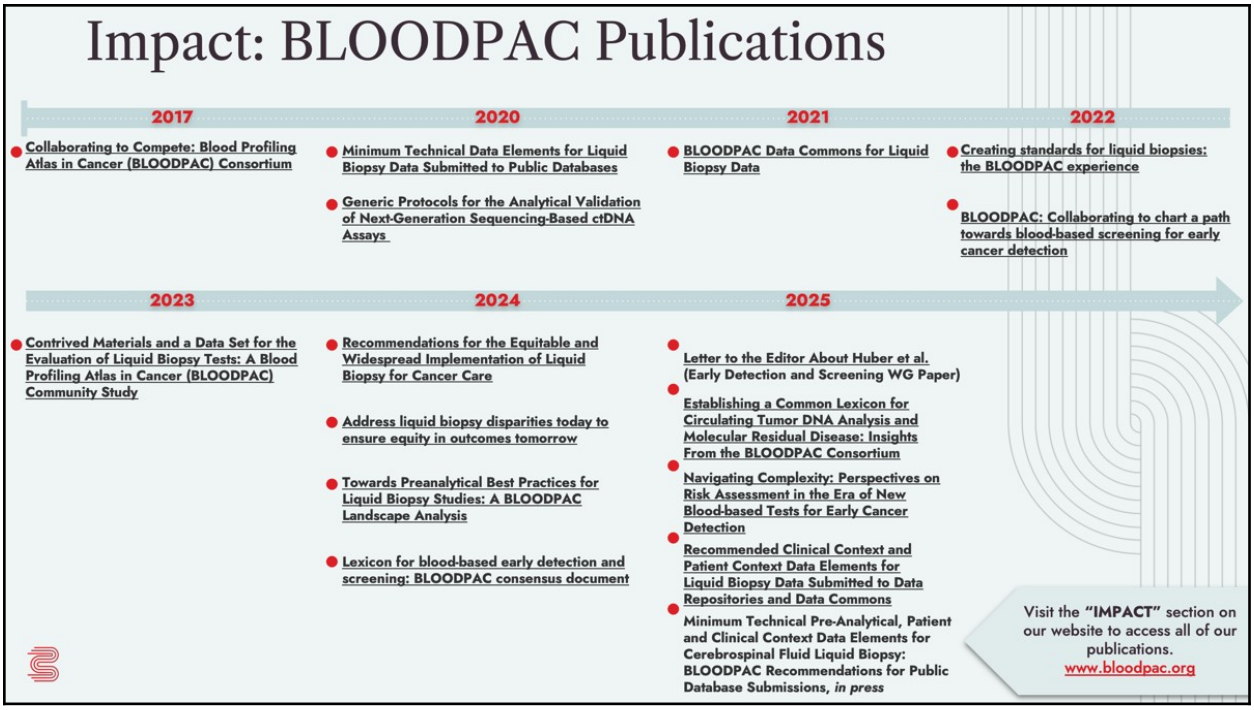
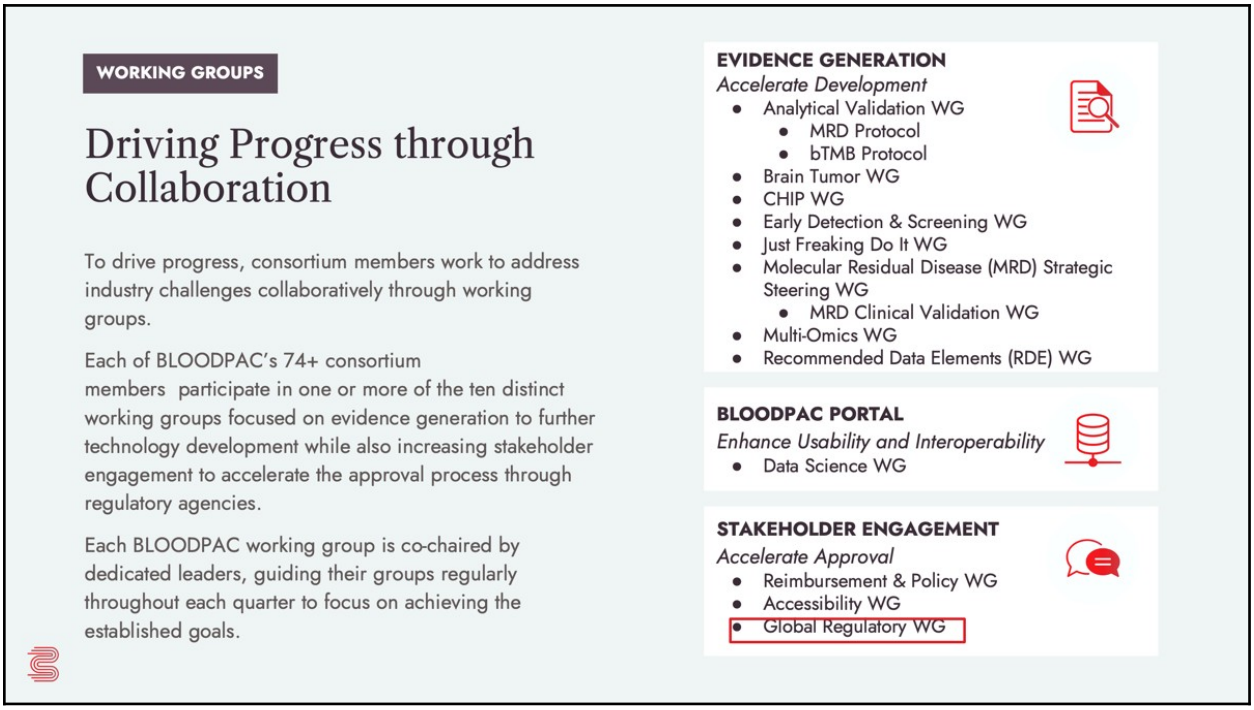
This gives you a good visualization of who's involved in BLOODPAC. You can see the depth and breadth of who we work with. I will stress that we are pretty heavy on the diagnostic and pharmaceutical side, so the corporate side, and have very few academics who work with us, primarily those who have been leaders in the field for decades, who have been pioneering this space, and have the capacity to help guide us as a whole.





We work in those three buckets. We work in working groups. Jenn also leads several of our working groups. As Peter said earlier, she's the head of our regulatory Working Group. She also partners with us on our blood collection kit project that falls underneath accessibility.

Jenn, I'm going to ask you to define liquid biopsy. What is it? What are we? And then also maybe talk about, what are the three primary uses today and the future for liquid biopsy. I know for many of you, this may sound extremely kind of beginners – liquid biopsy 101 – however, we have discussed, we have submitted, actually, articles to stat, and we've had them accepted, and it seems that there's confusion today, still around what we can do today: what the uses are, the potential, what we can do today, what we can do tomorrow, and what we can potentially do tomorrow, where we're aiming to take the industry as a whole. That might be a nice general background to give everyone, if you're able to do that.

Jenn Dickey 6:58
Thanks for passing it off to me, Lauren, and giving me the hard task of defining a very broad field of study. In essence, if you think of liquid biopsy, it's the notion that a biopsy traditionally would be where one takes tissue from the body to examine it clinically to understand its characteristics. Many, many decades ago, it was discovered that tumor cells and tumor DNA float in the circulation of the body when they're present, and so a liquid biopsy is basically using biofluids, generally blood, but taking that circulating tumor DNA or cells out of the body and doing clinical examinations on that tumor DNA that's available in your blood. The reason this is a powerful tool, and one that we advocate strongly for in the oncology community, and one that we actively try to develop and promote the development of new assays for, is because it is less invasive than a standard biopsy and has a lot of functionality that can help improve patient lives.

Breaking it down into the three buckets of things you could think about immediately using liquid biopsy for: one is similar to a biopsy. Take blood from a patient and examine those tumor cells or tumor DNA for the characteristics that would help a clinician determine a therapeutic odyssey for that patient. Help them find the variants and genes that are mutated that would guide them towards a precision medicine solution. This is great for liquid biopsy, because there are frequently patients with cancer who are too medically fragile to undergo a full biopsy. This gives a quicker and easier, less invasive way to obtain that information, particularly for patients who aren't able to provide a biopsy. The second obvious use, and one that gets used already today, is for monitoring, so as a patient's therapeutic journey progresses, they may develop resistance mutations or DNA signatures that would indicate when it's time to change a drug or reconsider a therapeutic option, and that monitoring, while you can re-biopsy a solid tumor, monitoring in a low invasive way with blood. It's actually an extremely powerful way to make sure that the therapy is there and it's working.

Moving into the tomorrow, moving into the next step, we can take that monitoring and then use that to gain sensitivity of our assay, gain a sense for understanding when we have what we call molecular residual disease detection. This would be like prognostically saying whether a therapy is working and therefore they don't need any additional therapeutic interventions, or maybe that there may be an early sign of a relapse or recurrence of the disease, and so maybe we could

get to treatment earlier, get ahead of progression, and move it towards a happy therapeutic outcome quicker.

The other bucket is then moving earlier in the cancer continuum. This would be what's called “a multicancer early detection”. This would be the notion in the future, where we're going, is the ability to assess apparently healthy individuals, people who don't have a diagnosis of cancer, and then determine early or in in time for meaningful clinical interventions that they would that they have cancer, and in this way prevent the growth and development of advanced cancer, if at all possible.

Those are the buckets, as Lauren likes to call them, of analytical studies we look at. We look at things for comprehensive genomic profiling, for treatment, we look at things for molecular residual disease, for prognosis or monitoring, and then we look at multi-cancer early detection or detection to help as a screening tool to detect cancer better and earlier. All of these with a number of different technologies, though many of them involve next generation sequencing technologies and other kinds of more advanced diagnostic techniques, which makes it an exciting, exciting adventure. Where I come in is then an exciting discussion with the FDA about how those products and services should be regulated and make sure we're all on the same page.

Lauren Leiman 12:29
Jenn, can I ask you to tag on one thing? As someone working for a company, PGDx originally, that was developing these tools, why is it so hard, and why do so many of them not succeed? As a level groundsetting, we should establish a ground floor basis so people understand how hard this is and why we've been working for eight years now, and I don't have a new job.

Jenn Dickey 13:08
Lauren is not in danger of losing her job anytime soon. It does take a lot of time, energy and investment to bring new, cutting edge technologies to the clinic. Part of that is because of the time and expense of clinical trials, and another part of that is as the clinical field evolves, it takes time to align to analytical standards, clinical standards, and acceptable even the lexicon of how we are going to describe these clinical scenarios, how we're going to define what is good enough. How do we define what's a clinical response? Getting to these things is very difficult. I was previously at the FDA, but I left the agency, went to industry, originally with a small startup company, Personal Genome Diagnostics. We have since been acquired by LabCorp Oncology. But one of the reasons small companies struggle is the technology does not start off being cheap. It needs to be developed, which takes an extensive R&D development operation, and then getting it through a regulated body, getting it through the FDA, getting it through reimbursement, getting it through all of these things, requires the generation of evidence. The generation of evidence is generally clinical trials, prospective, retrospective, analytical studies, comparative studies, etc. And these studies are expensive, difficult to design and statistically hard to execute in particularly rare cancer populations.

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What BLOODPAC does, or the value that BLOODPAC brings to the community, is, if we can align in a pre-competitive space on, for example, the lexicon, what are the words we're going to use to describe our technology? What are the analytical performance studies and expectations, sensitivity, specificity, accuracy, and what are the clinical endpoints that we're going to seek and define? What are we going to do to frame these big questions into definable, tackleable, achievable chunks, and then work together to lay out that framework. That framework is extremely valuable for small companies entering the space and also for advancing new technologies that we see great promise in, but are very difficult to design studies around when you're working in a vacuum. That's the value of our community.

Peter Kuhn 16:10
What Jenn just described is really, really important for everybody to wrap their head around. It helps us explain this better and quicker and in just a single sentence, because when I listen to Jenn, and Jenn goes like, “and then we get so excited because we get to talk to the FDA”, which Jenn truly enjoys. When Jenn comes to my lab, Jenn looks at me like, “Oh, my God. This is awful what you are doing, Peter?” I'm like, “Dude, I have no idea how this thing works, but I think I can make it work, maybe once, maybe twice. That should be good enough.” That is where I get excited. And then when Jenn goes like,”Let's go to the FDA.” I'm like, “Oh, god, no. Do we really have to? I showed that it worked right once. That should be good enough. Let's get it out to patient benefit.” Because I'm a physicist, I know exactly what patient benefit is. That is the complexity of the space. That's why so often when we put a scientific manuscript out there, it's like, “Oh, my God, we can detect cancer early.” At this point, detecting cancer early was resolved, like, I don't know, five, eight years ago, roughly. The science of it, exactly. Look at Jenn being like, “Dude, seriously, no. We haven't.” That's the importance here. There's a huge difference between, “Hey, we can find cancer early,” and making it meaningful. The purpose of BLOODPAC is to make it meaningful, because only then will the patient community benefit. And that transition is incredibly hard. I wish that Lauren, Jenn, I, all of us, we could say, and another eight months from now, we will have all lost our jobs. That would be the ultimate dream, honestly, but that's just the science perspective on the other side of it.

Jeff Waldron 18:28
I'm assuming you know Mera Aspinal. She's written a great paper on the limitations of liquid biopsy. She published about a week ago. She writes a weekly newsletter on the limitations of multicancer early detection.

The other you probably know her equally well. She's in France. Alex Panafier Kathy.

Peter Kuhn 18:55
I know them.

Jeff Waldron 18:58
A lot of people are promoting multicancer early detection, but the false positives are pretty limiting, as you probably know,

Jenn Dickey 19:06
That's why I darted between terms, because I believe the field, and speaking to Peter is like the research field, gets very excited. “Oh, we solved it. It's there. There's DNA. It's going to work.” But then, when the rubber meets the road in a defined and controlled clinical study, what you realize is that multicancer early detection is actually quite a bit harder in large patient cohorts than you would think. I don't want to dismiss where the field has gotten, because where the field has gotten is incredibly impressive. What the field has been able to do is be able to define biomarkers that help you say in what organ or organ system a tumor may be appearing, and define some of the signatures of cancer in the blood where the field is currently struggling.

You're absolutely right, first of all defining and then achieving a level of clinical sensitivity and specificity that is meaningful for a large public health output so at so when you look at the risk of a false positive right or a risk of a false negative, you have to look at the risk of both of those things, not just to the patient, because there could be psychological concern from a false positive and a false sense of security from a false negative, but also from a public health standpoint, reimbursement standpoint, what level of clinical sensitivity does an assay need to achieve to be able to be used broadly in the public, to be able to be embraced by the clinical community? And then what subsequent clinical procedures or screenings, would you do? I don't think anyone in the multicancer early detection field would say, “Stop getting a mammogram.” Nobody would say that ever. But crafting that understanding of where in the clinical space these tests are most appropriate is in the high risk population, the low risk population, and what kind of degree of clinical performance it needs to achieve to be kind of in the spotlight and ready for real time are active conversations in the field. You're absolutely right.

Peter Kuhn 21:36
What you mentioned there as well is and again, as Jenn just pointed out, it's really important that we separate out the individual terms. When we talk about liquid biopsy, we talk about a much larger space. Oftentimes we talk about the CtDNA tests. Guardant Health and others have delivered on actual specific tests for specific clinical utilities in managing patients with cancers. We have to say that's amazing, the fact, and I somewhat flippantly said that, like 6, 7, 8 years ago, we solved a problem of early detection with a blood sample. Now, remember 10 and 12 years ago, if we would have the conversation, “Oh, I think we can detect cancer early in the blood.” It would have been a ridiculous statement. It took years of just really careful, very high end research to get us to a place where, “Hey, wait a minute. There is a signal of early cancer that we might actually be able to find in the blood.” So the scientific breakthroughs have been absolutely outstanding.

Coming to Mara Aspinall commentary 10 days ago, whenever, that was really, really important. In many ways, it summarized the BLOODPAC session that Lauren and team just organized at the AACR meeting, and that had to do with what Jenn just pointed to: what should performance criteria look like? That is a really, really tricky one.

And with that, we get to some of the other comments that you made around false positives, for example. Whether we talk about positive predictive value, negative predictive value, or false

positives, false negatives of the multicancer early detection tests. Remember, they're called “cancer detection tests”, not “screening tests”. They're not called “diagnostic tests”, because those are specific utilities in the clinic. We don't know yet. We know that these tests can detect cancer. We do not know yet how to best use them. That is the work that's currently at hand, and that has to be an equally thoughtful and careful process.

Dinesh Kumar 24:28
This is Dinesh from Roche. I just wanted to add to that. In terms of the liquid biopsy, or CtDNA, it's not only about the MRD or early cancer detection. It could play a very important role in the the comprehensive tumor profiling also. A lot of new papers are showing that when you use plasma as a complementary way, or the CtDNA approach as a complementary to the tumor, then you add a lot more variants than what you learn from tissue alone or tumor alone. In some cases, you learn way more from CtDNA from plasma than the tissue itself, because tissue you might be taking from a particular site, in terms of the metastatic setting, or other settings, but in the plasma, you may get a more comprehensive picture. So if you combine both the tissue tumor plus plasma or the CtDNA, then you can get a much more comprehensive picture. In many cases, you could avoid doing further surgeries, or you can decide on what treatment type you could select and all that. I just wanted to add another application area which is very interesting.

Richard Anders 26:01
This is a complicated space because it is so easy to develop multiomic tests with a lot of parameters and then convince yourself that you know the data is absolutely air clad, and you've and you've got great p values. Maybe even on the second study, since there are so many people trying, you get a great p value the next time. When you do a drug, you know what the mechanism is. You have a pretty strong Bayesian inference that it's likely these days to work. And then, of course, it doesn't work most of the time, but at least you have that kind of correlation. In this you have a lot of different variables, and you're mixing them and matching them.

I thought that it would be really useful to develop some kind of consumer guide to the studies, which would still make the problem really difficult, but at least have something like a consumer guide that helps patients evaluate this. I know you're partly an industry association, so you can't get into this. Do certain tests re-evaluate their clinical trial results in a phase four where they take a bank of what the patients are finding, 2, 3, 4 years into this study? Are there any other things that people could use to make a determination of whether this is a great retrospective signal on retrospective data and maybe one lucky trial, but it actually is proving itself time and time again in the field?

Jenn Dickey 27:42
There's a fair bit of pressure in the field to keep going. You develop your assay. To your point, I don't know how many times I go to scientific conferences and don't train to your test set. Make sure you have independent assessment of your variables, make sure you have statistically sound methods going on. The BLOODPAC has analytical validation protocols that we suggest

people use, and we try to publish standards by which people should use to establish the analytical and clinical validity of their test. But to the point, I would say right now, what's kind of putting the pressure on the field to keep going and give real world evidence, or continuing evidence of success are reimbursement pressures in the United States. To define clinical utility and identify patient populations that have benefited from these technologies, but also, then in Europe, regulatory pressures to do post-market performance followup and other sorts of studies in the clinical population to make sure you're maintaining state of the art and in the scientific state of the art. There is pressure on the field to move there, and a lot of very good providers are publishing a lot of very interesting papers as we start to get more clinical experience with some of these tools. But you're right, it's an ongoing saga.

Richard Anders 29:18
The regulatory pressure isn't coming on LDTs – laboratory developed tests – for people's benefit. Those are tests where you can almost put the test out into the marketplace with low levels of evidence. Those aren't getting a lot of regulatory pressure to do post-market studies. But are there any databases you could find of which tests, if you had a list of 10 tests you were considering? Is there a database you could find that says, easily, “Here's the tests that have been through post-market surveillance. Here's what the testing looks like.” Because that would really be helpful to people, if they know how to use them.

Jenn Dickey 30:25
That's why I highlighted reimbursement pressures in the United States and then regulatory pressures in Europe, the regulatory status of diagnostic testing in Europe under the new regulatory paradigms of the IVDR, don't have the same laboratory developed test structure that the United States currently has. It does get confusing, maybe for patients, about where you can get information about tests, though a lot of the major providers of liquid biopsy are prolific in their publications. Guardant Health, Foundation Medicine, these sorts of companies do prolifically publish, and are under pressure to publish, mainly because of reimbursement, to make sure they've defined the clinical utility of their test. They are continuing to expand that clinical utility. But a consumer guide for liquid biopsy, I don't know.

Lauren, we could put that into our “to do list”, but I don't know how we would make it.

Richard Anders 31:41
I would love to talk to you about how that might be done. It would be really important to be independent of industry, even though it would have to work with industry for obvious reasons. If that were something that you think would be of interest, I'd love to talk to you about it. It could be really helpful to consumers, and might sell a lot more product because consumers would be involved in making sure this was useful to them.

Rick Davis 32:25
We at AnCan have a long history in liquid biopsy and advocating going back to probably the mid teens, which is relatively a long, long time ago, remembering papers from the late Felix Peng and others on the equivalence of liquid biopsy to tissue biopsies and all of that. I've worked with

Foundation Medicine since about 2015 2016. My question really comes back to Lauren. This often happens with PACs (political action committee). When I look at your PAC, I don't see the patient voice. And that really bothers us. The list of organizations that you have include ACS and PCF, the closest you've got to the patient voice is Lungevity, because there are patients that Lungevity does listen to. At AnCan, it's all about the patients. That's what we're doing every day. We feel that for advocacy efforts like yours, the patient voice has to be loud. There has to be somebody saying, “Well, this is how this type of test affects me and why I need it.” Advanced cancer patients who don't know whether their disease has come back, talking about the importance of a CtDNA test, for example, in prostate cancer, where it's very hard for us to get CtDNA tests right now, we would say that your efforts are great. We endorse what you do, but where's the patient voice?

Lauren Leiman 34:28
I appreciate that. It's an interesting topic. This goes back, and I'm looking at Peter, to the failure of our name. We are not a political action committee. We are not at all. It just happens to be our name. The Blood Profiling Atlas in Cancer happens to be our name. Many people do think it is a common problem. People think that we are a PAC, which we are not. We do partner with several patient advocacy groups. Lungevity happens to be one of them, a few in the early detection space, Prostate Cancer Foundation, Breast Cancer Research Foundation, less patient advocacy groups and research groups, but they do have the patient voice. Our mission in the development and the approval of these tests has been very laser-focused. It's not that we don't seek out the patient voice and do engagements like this, where we are trying to receive more feedback and content from patients and be able to reflect back. But the majority of our work, almost all of it, in fact, even our education project that will focus on accessibility, essentially for patients, is actually focusing on the education of clinicians themselves.

What role do we as primarily diagnostic developers and pharmaceutical companies, based on our expertise in the field, what can we contribute to helping educate physicians specifically? We do not attempt to say we should be educating patients or patient advocates at all. We are laser-focused. We appreciate that that is a role that needs to be filled. But there are really spectacular organizations that are doing that and doing it very well right now, and we have taken the approach that we would like to maintain our focus on the very relatively narrow space that we fill, creating these standards, creating these frameworks for the industry, and collecting the data to support them, and then provide that content to other organizations who are able to translate that content and have the expertise to translate that content to patients.

That said, again, we greatly appreciate the patient voice, and have a few of those select organizations like Lungevity or Prevent Cancer who sit on our accessibility overarching working group who review the content that we put out there. If we create a lexicon of terms – we have a dictionary online that I encourage everyone to go to. It hopefully will be helpful to patients around MRD, around early detection, it'll eventually be around chip that that content has been reviewed by few patient advocacy groups in an effort to say, “Is this going to be helpful or meaningful to patients? Are they going to be able to understand it?” However, we have found that the majority of our lexicon and definitions will never reach the patient. They are very,

extremely scientifically-based. It's required for them to be stringently scientific, and most patients will never hear those terms. We are a layer above where patients actually hear us. Does that make sense?

Rick Davis 38:20
Not really. To be honest, the reason it doesn't make sense is that it's a very patronizing approach to the patients that you're taking. Yes, you need to address the physicians, but half the time, people that we navigate finish up addressing the physicians and teaching them what they need to know, because they're hearing it from us. It has to be a collaborative effort that includes both patients and physicians in developing your message.

I also feel that when you talk about PCF or some of these other organizations, they're not the patient voice. They have people in there who speak for the patient. But do they send out your terms to the patients and ask the patients, “Can you understand them?” They don't. And if you drill down on them, why don't they? Because they don't have contact with the patients. They may represent the patients, but they don't have the contact. What I'm saying is, if you have somebody like a Len Sierra on on that, on your board, you're hearing it from the patient, from a person who has a deep scientific understanding, who is a peer, who is a patient, and these are the sorts of people you need. Their input is part of what you're developing, and it isn't represented. I would ask you, and happy to help you, happy to work with you, happy to point.

You were just at AACR. Ben Nathanson, one of our guys had a poster in there on AnCan, on about what we're doing, and he's deeply scientific. We have these people who see it from both sides. In developing your message, you need to hear it directly from from the patients who may be educated, but they're going to help you in how to explain your message to the patients who are not educated, because they see both sides.

Peter Kuhn 40:41
The nuances of the words that we are using are really important here. I want to make sure that as Lauren pointed out, we are not an industry organization. When Lauren just used the word “in the industry”, she meant the entire space of liquid biopsy, which is participated in by academic groups, just as it is by industry groups. In fact, within BLOODPAC, while the majority of members are industry folks, it's their scientists that are part of the group. In fact, we are more scientific-driven, or more academically-driven, than most academic organizations are. So it's really important that, because somebody else asked about market validation studies, etc., and whether or not we can talk about it again, it's really important. BLOODPAC is not an industry organization. It doesn't represent industry. It's really meant to support the process of development, validation, accessibility of liquid biopsy, very much in this context of and the reason why I played this bit back and forth between Jenn and myself, is so that Jenn and myself, so the people who actually are part of this process, from the very beginning all the way through regulatory approval, are aligned on what's required, because typically, people in my spot don't actually understand what it takes to get to that finish line. Doing this in a public, private or in this public setting of BLOODPAC as a nonprofit, really educates everybody across

the board, and that is really the purpose of this entire organization, and I just want to make sure that that's clarified.

Allen Morris 42:46
I'm going to go through the individual spaces and ask if you have any recommendations. Richard already asked you, and I thought the hint was that, since you have Natera, Guardant, Tempus, and Foundation, and all these other biotech companies in your consortium that you probably can't recommend. Let's take multi-cancer early detection. Do you have a company you recommend?

Lauren Leiman 43:28
I don't recommend any companies over one or another. I would strongly suggest that you take time to look at the companies that participate in BLOODPAC who are willing to share their information, their pre-competitive content and data to improve tests for the community as a whole. I tend to be relatively skeptical of the companies who at this point are too small to join BLOODPAC. That's another issue. But there's some that are, “Oh. I don't want to work in BLOODPAC because I don't want to share my learnings and to help benefit the industry as a whole. And to that, I say,”If you come across companies that are larger, who aren't on our list of companies, I'd probably ask, “Have you participated?” We have early detection and screening working groups, so those who are working in single cancer screening as well as multicancer early detection, I don't recommend anyone over another. I actually know Grail just came out with some positive data today. I can put the link into the chat if you'd like me to, but they all work very well together. That didn't used to be the case several years ago. They're extremely collaborative now and host a lot of discussions. I'm not qualified. Everyone should know I'm neither an MD nor a PhD. I'm a lowly MBA. So I am not qualified to make that assessment, even if I loved one over another.

Allen Morris 45:12
In the diagnosis space, it's not just early detection. There is another diagnostic space and it is in regard to what used to be a very common entity, called metastatic cancer of unknown primary. I ask you for a recommendation for that part of the diagnosis space. So, when oncologists have a case of metastatic carcinoma of unknown primary where they're trying to decide what's the primary site so they can go into, for example, NCCN guidelines, and decide what the best treatment is for a patient. The cell of origin tests can be and not uncommonly are wrong. That just speaks to the thing that lay people frequently overlook which is false positives and false negatives.

You mentioned Grail. Roger is our case in point. Roger would testify for Grail because he, unbelievably, has a miraculous story where he had a Grail positive signal which led to an MRI which detected his early pancreatic cancer. And now he is “no evidence of disease”, seemingly cured. So he's a miracle of Grail, and he could get up and be a Grail salesman. But Grail, I'm sure, suffers even more than cell of origin testing companies regarding false negatives and false positives, and that is why, in part, it is still not FDA-approved or better stated - does not have a

positive consensus statement. — Of course, in the future, with more data Grail may very well get a consensus positive pronouncement from experts. I hope so.

Now on to minimal residual disease. It turns out the most penetrated company in our community - part of it is commercialization and marketing - is Natera, followed by Guardant. And Natera has the most advanced studies and their studies are most advanced in colorectal cancer. Our clinicians are ordering the Signatera for minimal residual disease monitoring in people that have colorectal cancer, less so but a little in breast cancer and urothelial cancer. But, there's a debate in our community, and most of our oncologists will say that there is no evidence yet for any of the liquid biopsies (for minimal residual disease) showing improvement in overall survival. What the liquid biopsies are literally doing, that people would agree, is getting lead time. You're getting a lead time, maybe it's six months earlier or maybe even 1 year whatever for detecting a recurrence. But for example, colorectal patients are faced with things like FOLFIRINOX, a pretty strong chemotherapy regimen. [If the recurrence is in select sites and oligometastatic- there may be better options such as Metastasis Directed Therapy (whether surgery or radiation) as opposed to systemic chemotherapy - liquid biopsies do not have the divining rod capability of localization - and therefore may actually be harmful in the above decision making context].

The push here is patient advocacy. We've got to educate our clinicians - as if our clinicians are not educated. They're not dummies. They're hearing about the promise of liquid biopsies [in the minimal residual disease space] as much as all of you people that are patient advocates. They just are waiting for efficacy signals because, unfortunately, it's a bad phrase here, it's called “standard of care”, and what's approved, but better stated what is proven. Oncologists are weighing proven efficacy versus the risk of all these treatments. — [Yes, practicing oncologists know very little of the avalanche of promising hypotheses and pre-clinical and phase 1 and 2 studies; but they live and breath the phase 3 positive practice changing studies that are incorporated in consensus compendiums - that is what they do - day in and day out-]

Do you recommend a minimal residual disease company, and for what cancers and what stage do you recommend them?

Jenn Dickey 49:21
With respect to comprehensive genomic profiling and real world evidence, your experience echoes our own: we put out comprehensive genomic profiling assuming our majority patient population would be non-small-cell lung cancer, because that's the cancer population that has the most precision-targeted therapies. We found more than a third of our volumes were actually, if not properly, “unknown primary”. It was where the pathologist was between two. It's like, “It could be either this, or this. Or it could be maybe this. Or it's either this primary or a reoccurrence of this previous malignancy.” These sorts of things. That echoes our own experience, which is comprehensive profiling. We thought it would be very straightforward, like it's going to be lung cancer patients looking for their precision therapy. In the end, most of the utility comes from that refinement of diagnosis that has been valuable in the field.

Allen Morris 50:35

"Accessing the Latest Developments in Liquid Biopsies" (Lauren Leiman and Jenn Dickey) [#148]

Do you recommend a company for a metastatic carcinoma of unknown primary?

Jenn Dickey 50:42
There is no company that I know that makes an explicit claim about metastasis of unknown primary – even Foundation, I don't believe.

Allen Morris 50:53
They have a test called Foundation One. — [Jenn, you are correct, my mistake: I recalled FoundationOne incorrectly - the company/product includes CancerTypeID (for identifying cell/tissue of origin) among a few others and they are not liquid biopsies]

Lauren Leiman 51:01
Rick, I agree with you: we have found some people who are an extraordinary group of individuals and patients who are intentionally driven and knowledgeable about many cases, your own disease, or others' diseases, as well as clinicians who work perhaps at Memorial Sloan Kettering or MD Anderson, who are extremely knowledgeable about these tests. The reality is, I think someone just told me, and Sandra, you probably know this number better, like there's like the 80/20 rule: 20% of patients or clinicians know about these tests, and 80% don't know. And that may be generous. I have to, unfortunately, disagree with Allen. I don't think most people are aware of these tests and are knowledgeable in any real meaningful capacity.
[Allen reply: Rick and Lauren - Yes, practicing oncologists know very little of the avalanche of promising hypotheses and pre-clinical and phase 1 and 2 studies; but they live and breath the phase 3 positive practice changing studies that are incorporated in consensus compendiums - that is what they do - day in and day out- Liquid biopsies are largely still a work in progress, except for genomic profiling, especially in the minimal residual disease space - the space, the context, I was commenting about]

Roger Royse 52:18
Not only primary care physicians. Allen mentioned my name, so I'll tell you, I'm exhibit A, and I've correspondent with the US Preventive Task Force Service, which recommends against pancreatic cancer screening. As Allen said, "You're just getting lead time. It doesn't change the outcome." Well, I'm Exhibit A for the fact that that's wrong, and I not only got a liquid biopsy, it wasn't without the advice of a physician, it was against the advice of my physician. He said, "Don't do it. They don't work. You're just going to get a false positive, and it's going to scare you." One of the very few things that my doctors agree on now is I probably wouldn't be here if I hadn't done that. So you can make all the statistical arguments you want on patient advocacy. I'm not a statistic. I'm a person. And I wouldn't be here without it.
[Allen comment: My lead time comment was in reference to the minimal residual disease space, not the MCED space].

Rick Davis 53:13
I'd like to point Allen to the research that's been done by Money Tieno at Illumina and Neil Shore on testing frequency. What we're seeing is exactly what Lauren is saying, that the take up by community oncologists of genomic profile testing is just atrocious. If you look at their actual

research and show how many people tested for the existence of a PARP-sensitive mutation is really low. They had a poster this year at GU ASCO. They had a poster last year at ASCO. We know it's really poor.
[AM comment: Rick - We are talking about 2 different things: I was talking about liquid biopsies, the topic of this learning session, which largely, despite their promise and sexiness (no need for a biopsy procedure), have in the MRD and MCED space not reached prime time and you are talking about genomic profiling largely done on tissue or cell (not liquid) biopsies.].

Paul Van Camp 54:17
Because it's pertinent to previous discussions about activist patients, patients who are very involved in their care and research their options, like the people who are here on this forum and other forums, and myself included in the advanced prostate cancer space. We take the information to our physicians, and we ask for things. We promote the use of technologies of benefit for us, directly to our physicians, as I did recently, because I'm interested in detection in my own body, from my treated and apparently now indolent prostate cancer. Using circulating tumor DNA detection to see if there's something growing that is not being picked up by my PSA. My oncologist said he didn't know anything about this. I said, "Well, I want this. Could you please research it and find out how to get it for me? Should I get circulating tumor cell counts or should I get a CtDNA screen, quantitative to what percentage of my circulating DNA is tumor DNA, and then if it's detected, can it be genomically profiled?" I said, "I want you to do this."

The precedent for this is in the pharmaceutical industry. Turn on your television and see how many very expensive new drugs are being promoted directly to patients to go ask your physician about them, because that's found to be a channel that works. I disagree with ignoring the patient orientation towards promoting wider appropriate use of liquid biopsies, not just in my cancer, but in many cancers.

Ari Akerstein 56:30
Who isn't getting liquid biopsies, given the state of play today? Are there one or two, not multiomics, but single? I heard that maybe non-small-cell lung cancer was a good use case. But who isn't getting this that should be getting it today? However specific, however pointed the test actually is?

Jenn Dickey 57:09
In the base case of tissue assessment for comprehensive genomic profiling, there have been several recent publications that indicated that approaching 75% of advanced, non-small-cell lung cancer patients are getting comprehensive genomic profiling, and then the numbers fall precipitously by tumor type after that. In an advanced cancer space, to not have comprehensive genomic profiling of some sort in the era of precision medicine with so many targeted therapies is a real and present danger to our advancement in this space.

The hope of BLOODPAC is that for patients who can't get a tissue-based biopsy or a tissue-based comprehensive profile, a liquid biopsy would minimally be executed upon. But I would say, recent data says most patients are not getting a liquid biopsy, and even those that that

maybe would most benefit from it, particularly in non-small-cell lung cancer and other tumor types that have a lot of precision targeted drugs. That's why Lauren and our group has added an accessibility arm to our organization, to address that kind of problem in our field.

Sandra Balladares 58:49
Since you are in the front line working with all the organizations, when do you think that minimal residual disease, or molecular residual disease, is going to be the standard of care timewise?

Jenn Dickey 59:16
It's been discussed maybe already, but it's going to depend on tumor modality. Minimal residual disease is assessed in hematological malignancies today, as standard of care very normally. Probably the case of colon cancer is the solid tumor modality that probably has the most clinical evidence to-date, following behind that, probably lung cancer, bladder cancer, et cetera. This is going to be indication-specific, tumor modality-specific, and a stage-specific rollout of the use of molecular residual disease. It's like trying to identify high risk patients with maybe stage 2 colon cancer who you're trying to decide between a surgical intervention that could be curative versus needing a round of FOLFIRINOX (chemotherapy). It has already been discussed, and so that seems like maybe the first, most obvious, hard clinical utility evidence that's moving into the field. I'd welcome anyone else's thoughts, but I'd say it's going to come slowly, similar to how minimal residual disease has integrated itself into the hematologic malignancy space. It'll come into solid tumors, and it'll come indication by indication.

Sandra Balladares 1:00:43
Is there anything that an organization, a patient organization, such as the Cancer Patient Lab, could do in order to help to accelerate the approvals or implementation of any sort?

Lauren Leiman 1:01:22
I would like Rick to answer this question as a better person to answer.

From my perspective, our success has been driven by us staying in our swim lane of helping to develop these tests collectively.

We have invited many patient advocates individually and as parts of other groups. We have several colon cancer groups now as part of BLOODPAC to join our conversations. They find it extremely difficult to keep up with or be able to do exactly what you're saying, keep up, translate the science, the minutiae of the science and the details of what we're trying to create in the development of these tests to something that's valuable for a patient or a clinician, which is why there is a whole separate working group that we have to say, “Now we have a test. How do we get you to actually use it so that it can, ultimately, be approved and used in standard of care?” Although there was an argument yesterday on one of our calls about what is standard of care and how does one define standard of care? We are so far upstream from a lot of these conversations. I wish we were there. There are so many things for groups like this to be doing, I struggle with trying to identify how to best incorporate specifically into BLOODPAC, unless it's indication-by-indication or disease-by-disease.

"Accessing the Latest Developments in Liquid Biopsies" (Lauren Leiman and Jenn Dickey) [#148]

We have a specific brain tumor working group. We don't have any other disease-specific groups. In that group we have brain tumor foundations that are funding in the brain tumor space. We have one patient advocacy group. We have several academics. So the majority of our academics sit in that group. Because the brain tumor industry within industry is so small so far, we have to lean heavily on our academics. There is an interesting space for our advocates in that area, specific to brain tumors. But other than that, I struggle to identify where within BLOODPAC we can best utilize, other than also having on our sessions at like AACR, we have had Prevent Cancer and others as the voice of the patients, sit on our panels and say why the creation and continued investment for the multicancer early detection space is relevant and useful to the community as a whole.

Sandra Balladares 1:04:11
I agree. And thank you, Lauren, perhaps, as you said, down the road, once the evidence is ready for guideline inclusion, perhaps that will be a good point of interaction.

"Accessing the Latest Developments in Liquid Biopsies" (Lauren Leiman and Jenn Dickey) [#148]

CHAT DISCUSSION

00:34:26 saed.sayad: Any success stories so far?
00:35:08 Russ: Success like? Patient success in tracking cancer or?
00:37:06 saed.sayad: Patient success, biomarker success
00:37:56 Russ: Me. MRD 2022 0.0, later 0.16, later 1.16 MTM/mL. Finally PSMA PET picked up 2 mets. SBRT then MRD went to zero.
00:38:27 Alexander Lalov, Indiana, USA: Reacted to "Any success story so..." with 👍
00:39:41 Len Sierra: MRD tracking is not yet FDA approved, is it?
00:41:14 Russ: Some for some types of cancer. Which one?
00:41:18 ari akerstein: Given the state of various tests and the science avail today (via Guardant, natera et al), Which specific patient populations/conditions would most benefit from them, but don't get them (for whatever reason)... .what would these use-cases be?
00:42:19 Len Sierra: Answering Russ: Prostate Cancer?
00:42:32 Russ: No. Clia approved though.
00:43:01 Russ: Natera, Guardant Reveal are the ones I'm familiar with. But I think there might be another.
00:43:22 Len Sierra: Which means the patient pays, right?
00:43:45 Russ: Depends. I never pay. But my MO does things I don't understand.
00:44:07 Len Sierra: Reacted to "Depends. I never pay..." with 🙂
00:45:20 Helen: @Jeff Waldron you mentioned Catherine Alix-Panabières in "France." I'm in France, too. Should I be looking her and her research up in France?
00:45:45 Rick Davis: I think ctDNA may only be FDA approved for lung right now???
00:46:15 Russ: No. Lots of ctDNA tests are FDA approved for PCa.
00:46:51 Russ: MRD requires a high level of resolution. ctDNA is like Guardant360, FoundationOne 360
00:47:41 paul: Hi Russ. I got here late. Did they discuss ctDNA for MRD?
00:47:42 ari akerstein: How reproducible are those tests (is a separate question about this prolific need for the industry to publish)
00:47:56 Russ: Not really. This seems more regulatory stuff.
00:49:12 Russ: Ari, sensitivity and specificity and AUC?
00:50:02 Kamran: What role do you see extraction and analyte input quantity and quality playing in driving assay sensitivity and helping to control testing costs?
00:53:21 Jenn Dickey: Of interest with respect to liquid biopsy FDA authorization: FDA authorized liquid biopsy for CGP by crafting a regulation 21 CFR 866.6085. This regulation includes "Special Controls" which includes a description of the testing a developer must do to obtain FDA authorization for this use. This is available on the FDA website: Correspondence Generator (CorGen)
00:58:27 Jeff Waldron: @Helen sent private msg w/Cathie's
01:00:59 Lauren Leiman - BLOODPAC: https://grail.com/press-releases/grail-announces-positive-top-line-results-from-the-galleri⓻-pathfinder-2-registrational-study/
01:03:37 Rick Davis: @Russ - we need to discuss the difference between ctDNA and CTC technology. We do not consider Guardant nor FMI to be ctDNA technology at the level of Natera. FMI has no test to find MRD through ctDNA. No even sure Guardant does??

"Accessing the Latest Developments in Liquid Biopsies" (Lauren Leiman and Jenn Dickey) [#148]

01:04:40 Richard Anders: In response to Jenn's post, I am not sure whether Jenn is using the term "authorization" in a true regulatory sense, because that has a very special meaning, which is that it may be marketed under an emergency use authorization. In many (most?) cases a liquid biopsy is not truly FDA approved, so does not go through the full complex approval path that people may expect of FDA. Happy to hear more clarification from Jenn.
01:05:08 Russ: Guardant Reveal. MRD. Just a difference in resolution and what they are made to find. CTCs are a different issue. CellSearch is an example for CTCs. Better for CRPC.
01:05:42 Russ: Mine would probably be zero. I haven't had that test (I'm HSPC).
01:06:31 Rick Davis: We disagree strongly with @Allen - too many physicians do NOT understand genomic profiling. That's why testing rates for advanced cancers are so low in many cancers, especially prostate.
01:06:43 Russ: I'll write something up for AnCan. I just haven't gotten around to it and want to see my MO first to ask her for some input.
01:06:54 Russ: Rick, totally agree!
01:07:42 Jenn Dickey: authorization in the case I discussed was a full marketing authorization (not for emergency use)....many liquid biopsy assays are FDA authorized, but not all
01:07:45 ari akerstein: Maybe 95/5
01:07:55 Russ: Ari, 99/1?
01:07:59 ari akerstein: Reacted to "Ari, 99/1?" with ❤️
01:08:51 Richard Anders: So by authorized, you mean "approved" in the full FDA sense? Meaning they went through a PMA?
01:08:53 Peter Kuhn: @brad it would be useful to discuss this group's balance of wanting to get access to tests early vs. waiting for completed outcome studies to understand lead time bias amongst many potential long time problems
01:09:28 Russ: Richard? Me?
01:09:42 Richard Anders: Sorry, I was posting for Jenn.
01:10:15 Jenn Dickey: The regulatory path we went through to have a liquid biopsy CGP regulation published and available to everyone is called a de novo authorization. The data required is similar to a PMA but PMAs dont result in a regulation that other assays can follow
01:10:58 Richard Anders: So De Novo are granted (in contrast to 510K ordinary, which are cleared). The regulatory path is usually far more lax than PMA
01:11:01 Allen Morris: Regarding liquid biopsies, the topic of this learning session, I was talking about diagnosis of metastatic cancer of unknown primary and minimal residual disease testing. -=---- not the whole omic space which is largely done on tissue/cell biopsies not liquid biopsies.
01:11:18 Dinesh Kumar: Thanks all for great discussion. I need to drop now.
01:11:27 Jenn Dickey: I disagree that the regulatory path is more lax....it is frequently more stringent
01:11:35 Richard Anders: I don't mean lax as bad, just easier
01:11:57 Jenn Dickey: LOL! I disagree that it's easier either :)
01:12:40 Richard Anders: I have never heard of a 510(k) path being more complex than a PMA, all things being equal. There are tough 510(k) but I have never heard of a company that would rather get a PMA than 510(k) in a given case

"Accessing the Latest Developments in Liquid Biopsies" (Lauren Leiman and Jenn Dickey) [#148]

01:13:47 Rick Davis: @Lauren - what you're hearing is that the voice of the knowledgeable peer advocate who walks the line between the organizations and the patients. is significant. Please do not hesitate to reach out to us at AnCan .... rd@ancan.org
01:14:16 Lauren Leiman - BLOODPAC: Thank you Rick! 🙂
01:14:25 Helen: Following up on @ari akerstein question - on who isn't getting Biopsy… Are women with extremely rare ovarian cancers getting LBs?
01:14:34 ari akerstein: Reacted to "Following up on @ari..." with 👍
01:15:20 Rick Davis: Have to jump to another presentation.... thanks Bloodpac et al! rick d rd@ancan.org
01:17:57 saed.sayad: Thank you.
01:18:14 Richard Anders: Great presentation, thank you for speaking!
01:20:27 ari akerstein: Great conversation.
01:20:44 Russ: 👍