Insight Molecular Diagnostics Inc – KOL event ***(Fast-Follow Transcript)***

Call Participants

Moderator

Josh Riggs
CEO, Insight Molecular Diagnostics

Nick Loannou
VP of Medical Affairs, Insight Molecular Diagnostics

Max Liebo
Transplant Cardiologist, Loyola University

Thomas Flaten
Analyst, Lake Street

Mark Massaro
Analyst, BTIG

Alex Nowak
Analyst, Lucid Capital Markets

Mike Matson
Analyst, Needham

Ben Mee
Analyst, Stephens

Presentation

Moderator

Good morning, and welcome to the Insight Molecular Diagnostics virtual session. We will follow the formal presentation and fireside chat. If you would like to submit a question, you may do so by using the Q&A text box at the bottom of the webcast player. To our analysts joining us live, please use the raise hand feature to indicate you have a question. As a reminder, this call is being recorded, and a replay will be made available on the website following the conclusion of the event. I would now like to turn the call over to Josh Riggs, Chief Executive Officer at Insight Molecular Diagnostics. Please go ahead, Josh.

Josh Riggs
CEO

Thanks, Sarah, and welcome everybody. We are going to just do one quick slide on forward-looking statements. All right, there they are. Thank you. We can move forward. Last year, we did our first KOL call, with Dr. Anthony Langone of Vanderbilt University, about how blood-based DNA tests have made it easier to manage kidney transplant patients. Now, our test, GraftAssureDx, is working its way through the FDA for exactly that indication. After we finish with kidney, our team is preparing to start work on a claims expansion into heart. Today, we are grateful to have transplant cardiologist, Dr. Max Liebo of Loyola University, on to talk about how these types of tests are used to manage heart transplant patients here in the U.S. Thank you, Dr. Liebo, for joining and offering to share some of your time and expertise.

Guiding us through the conversation will be our very own Dr. Nick Loannou, our Vice President of Medical Affairs, to whom I will now turn the call over. Thank you.

Nick Loannou
VP of Medical Affairs

Thank you, Josh. Josh started by telling us what was happening a year ago with Dr. Kenneth, who came and talked about kidney transplants. I want to start by telling you what was happening about 10 years ago when I started talking to my fellow colleagues, transplant nephrologists, transplant cardiologists, about these donor-derived cell-free DNA tests. Ultimately, most of them, when I was in there talking to them about these tests, they were saying, "These are great tests. Will we be able to do these here in our labs?" The answer back then was no. But you know what? Now that answer is yes. I want to walk you through, I want to take about 5 minutes, maybe even less, then walk you through some milestones, probably like seven dates, how heart transplant has evolved.

It starts off back in 1967 when the first heart transplant was performed by a fellow South African colleague, Dr. Christiaan Barnard. After that, heart transplant became pretty common. Many hearts were transplanted, but the problem is there was a lot of rejection due to the body's immune system protecting itself. It would see a foreign heart, and it would say, "This is not part of me. I have to reject it." In 1983, things changed because in 1983, the FDA approved cyclosporine, and that drug works by suppressing the body's immune system. This led to an increase in heart transplantation rates. The health of the newly transplanted hearts is monitored by performing biopsies. These biopsies, also known as endomyocardial biopsies, where a catheter is inserted from one of the veins and it removes pieces of heart for microscopic examination.

There's 3 to 5 samples that are removed, and the pathologists look at those, and they can tell if there's biopsy or not. Now, that first year after a heart transplant, on average, it's between 14 to 18 biopsies. Only in that first year. There's a lot of biopsies that are happening in that first year. Between 2019 and 2023, there were prospective multi-center trials that validated donor-derived cell-free DNA as a biomarker for acute rejection. In 2022, expert review by the American College of Cardiology highlighted donor-derived cell-free DNA as a promising non-invasive alternative to endomyocardial biopsies. In 2024, as per the SRTR, the Scientific Registry of Transplant Recipients, there were 4,636 heart transplants performed in the U.S.A. Max and I have known each other for a while now. Max, I'm going to ask you a few questions.

Question And Answer

You're here because you're the expert, so please tell us how you guys are doing these things. My first question is, at your center, prior to donor-derived cell-free DNA testing, how many protocol biopsies were performed that first year on your patients?

Max Liebo
Transplant Cardiologist

Thank you. A great question, Nick, and thanks for giving me a heads up on it. I actually was able to pull out our old protocols because it's been a while since we've only performed biopsies where we haven't used some non-invasive form of doing rejection surveillance. As of about a decade ago, our protocol would entail, I think it was 17 biopsies, heart biopsies, within the first year alone. The protocol continues on through 5 years post-transplant. Ultimately, these would just be surveillance biopsies. Each patient would be subjected to 26 invasive procedures during the first 5 years, just by protocol for surveillance. That doesn't include for-cause biopsies that are indicated by a clinical change in the patient that is concerning for rejection, as opposed to just doing surveillance.

Nick Loannou
VP of Medical Affairs

Great. Max, thanks, and especially thank you for telling us about the for-cause and the surveillance biopsies and differentiating there. Most of us, I think you are the only cardiologist on this call, so most of us are not cardiologists. Please help us understand, after you get that positive biopsy, what is the process? What is your treatment regimen?

Max Liebo
Transplant Cardiologist

So depending on a number of different things, the short of it is we will almost always going to treat for rejection. If a biopsy shows that somebody is having rejection, there are two main forms of acute rejection. You could either have purely cellular rejection, which is the white blood cells themselves are mounting in a direct attack on the heart muscle. Or you could have antibody-mediated rejection, which is another acute form of rejection where it is really the antibodies that are not white blood cells but are created by white blood cells. It is the antibodies themselves that go and basically plant a flag on the heart and notify the body that this is a foreigner. Either one of those forms of rejection can either occur by themself or can be mixed picture.

Depending on which kind of rejection somebody is having, they are going to be getting treated for at least, at a minimum, three days in the hospital. But usually it would be closer to a week, especially if it were treated for antibody rejection. And they get treated with IV steroids, or for antibody rejection, we would be treating with even more invasive things like plasmapheresis, which is essentially like a large dialysis machine that is used to strain all the antibodies out of the patient. That, along with forms of chemotherapy that are used to prevent antibodies from occurring. So the treatments are pretty aggressive, and they are warranted if somebody is having rejection. But I guess what I would say is the actual number of biopsies that come back positive for rejection is not very high compared to the number of biopsies we do.

Ultimately, we do a lot of these invasive procedures to identify on surveillance testing rejection that would warrant treatment. It has really been over the last decade or more now, about 13, 15 years now, we have had these different forms of molecular testing that we can use for non-invasive surveillance to really limit the number of biopsies we have to do in order to identify that patient who does warrant treatment.

Nick Loannou
VP of Medical Affairs

Wonderful. Hey, thanks for walking us through that. Thanks for touching on the second question I was thinking of asking. How long have you been using donor-derived cell-free DNA? That's good, about 15 years, 12-15 years you said.

Max Liebo
Transplant Cardiologist

Yeah. Well, sorry, Nick. I would say initially the molecular testing we were doing was the gene expression profiling. When I first graduated from fellowship and took a job here, that was one of the first things I did, was actually not replace our biopsy protocol, but added essentially an AlloMap protocol that allowed us to substitute these non-invasive molecular serum-based tests for what otherwise would just be a mandatory biopsy. If the serum-based test looked normal, that was usually enough to forego doing a biopsy at that time point. Initially, we didn't have cell-free DNA to guide us in this. We were using what I consider at the time was the best we had, but what I would consider a less sensitive and less specific assay to try to reduce the number of biopsies we were doing on patients.

But for maybe it's been about a decade now, I think it was around 2017, 2018 is when we really started using the AlloSure, which was the first available cell-free DNA for doing surveillance. We've been doing that for maybe about a decade, if that.

Nick Loannou
VP of Medical Affairs

Wonderful. From what you're saying, sounds like you're using the cell-free DNA technology for surveillance, right?

Max Liebo
Transplant Cardiologist

Absolutely. That is really where it is, in my mind, the main power is. Although, a lot of that is based on the fact that we do not get the results back super quick with our current cell-free DNA assays we have. From that standpoint, if you are looking to use a test to make an immediate diagnosis, something you would want to do in the hospital with somebody presenting with a complaint and deciding whether or not we need to do a biopsy. If we had an assay where I could get a cell-free DNA back, let us say, within 24 hours, then that would be a test I would want to potentially do when the patient presents. I would use that as a screening for rejection for somebody when there is this question about whether or not they need to move on for a biopsy.

That said, right now, our current assays, they are not available in-house, and they take usually at least probably 3 to 5 days to get the result back. By then, if somebody is presenting with clinical concern for rejection, you have either already empirically treated them and they finished the treatment before you even get the answer, or you are basically waiting on treatment that. Ultimately, we could get a biopsy done and get the result back with that quicker. That said, just much the way we use a troponin or a BNP as a marker for an MI or for heart failure and somebody who is presenting to the ER with complaints that are concerning, I could absolutely foresee using cell-free DNA technology, since we have seen that it does start to become abnormal sooner than when the biopsy even becomes abnormal.

It has a lot of characteristics that would make it a better rule-out test for rejection, even at the point of care, if we could get a rapid result.

Nick Loannou
VP of Medical Affairs

You touched base on how waiting those 3 to 5 days affects you. As you said, most of the time, these patients are going to be treated empirically, right? Let us talk about the patient now. How does that waiting time, the 3 to 5 days, affect them?

Max Liebo
Transplant Cardiologist

When we're using it for surveillance, I don't think it's much of an issue. The patient knows even if they were coming in for a surveillance biopsy, it's usually for 24 to 40 hours before we have the results of a biopsy to tell them whether or not this shows any concern for rejection. The patients are more than happy to just do a blood test, even if it means waiting an extra day to find out whether or not there's any concern for rejection.

If there is concern for rejection, if the assay comes back 3 to 5 days after we sent it and it looks abnormal, then we have to put it together in the clinical context of that patient about whether or not we are concerned enough that this is rejection that's causing the abnormality with the cell-free DNA that we would then warrant getting a biopsy. I want to be clear, the cell-free DNA technology, as good as it is, it is not specific for acute rejection. I don't necessarily treat patients with steroids or plasmapheresis. I don't treat them for acute rejection based off of an abnormal cell-free DNA.

Rather, that test lets me know which patient I need to be doing more testing in as opposed to if it's a normal test, then I don't need to go down the path of biopsies or any other kind of invasive testing. From a surveillance standpoint, Nick, getting an assay that's drawn in the clinic, whether or not we necessarily get it back 12 hours later or 3 to 5 days later, I'll be very honest with you, it probably doesn't change anything. It is the testing that we. How do I put it? It would be very nice for our patients to be able to get the blood draw with the rest of their labs when they're drawn in clinic.

I could absolutely foresee us using that kind of an assay if we had a way to draw it in our hospital, regardless of how quickly the turnaround is, even in those surveillance patients, because frankly, it's a lot nicer than having to then go to a separate lab to get a blood draw.

Nick Loannou
VP of Medical Affairs

Well, good. Max, you did start off by saying that a lot of the biopsies that were done in the past, the majority of them were coming back as normal. Talk about doing a procedure that really wasn't needed. With this cell-free DNA technology, what I'm hearing is, if it highlights, if it shows that there's possible rejection or some kind of injury, those are the candidate patients that you would move forward to do a biopsy. Am I hearing that right?

Max Liebo
Transplant Cardiologist

That's correct. The power of this is it's a great rule-out test for rejection. If we do a cell-free DNA assay and it comes back negative, there's really no reason for us to subject the patient to that biopsy. Those 17 protocolized biopsies in the first year really get cut down to probably less than 10 anyway. We generally are still using biopsies for the first month or 2 after the transplant, since none of the cell-free DNA technology's really been thoroughly evaluated in the early post-transplant period to know whether or not we can safely use that during the first month or so.

But after 2 months, we pretty much exclusively just use, for surveillance purposes, we just use a cell-free DNA technology now, and if it's only for the minority of patients where it comes back abnormal, will they then have to go and do biopsies. The rest of the patients are much happier, much better off not dealing with the pain or the discomfort or the risk of the procedures, of those unnecessary biopsies.

Nick Loannou
VP of Medical Affairs

Wonderful. Good. Max, you and I have talked, and you know that here at IMDX, we do have a donor-derived cell-free DNA assay that's based on droplet digital PCR technology that does not need to be sent out to the company's laboratory. It can actually be done in-house, and you guys can have the results back within 12 hours. How do you think this shortened time to results will impact your patients and their quality of life?

Max Liebo
Transplant Cardiologist

Well, again, from a surveillance standpoint, I am not sure it will change a whole lot other than them being able to get their lab draw at the facility where they get the rest of their labs drawn, which I think that actually shouldn't be understated. That is, making patients make a separate trip just to get this one blood test is, one, it is a nuisance to the patient. But two, sometimes it means we do not actually get the test done, whereas when I have them in my office, I can get the lab draw. If I have the ability to run the lab, I can do it all on-site. So that is a big bonus.

But as far as where I do see this in-house and sort of rapid availability of the results changing is, like I was saying before, in patients that actually get admitted to the hospital, which is not a trivial number of patients per month that are coming in, whether their transplant was within the last year or if it was 20 years ago. But when they show up with shortness of breath and you have got some very other non-specific things in the ER, like an X-ray or an EKG, and not quite sure if this is. None of them are really validated to determine whether or not somebody is having rejection.

And whether or not you need to keep that person in the hospital for three days to treat them empirically, or you find out within 24 hours that their cell-free DNA is normal and that their symptoms are very unlikely to be related to rejection, I could see that very much helping the patients, and that they wouldn't have to sit around the hospital getting unnecessary treatments, but rather be able to get maybe more appropriate treatment and get out of the hospital quicker. So I do think that there is a lot of benefit if we could get the test back quicker. And I am not sure, I was really pleased to hear when you were telling me about this new product that you guys have that it sounds like we should have the ability to do this.

But I don't know that we have necessarily sorted that out totally with our lab yet. But that would be the dream, would be able to get cell-free DNA technology both for our inpatients and outpatients and be able to get it all done here at Loyola.

Nick Loannou
VP of Medical Affairs

You see, obviously, there's going to be logistics, getting things into the lab and training the lab personnel. But ultimately, do you see that the contributions of such a test and of having that availability to do this in-house would benefit your practice or your transplant center?

Max Liebo
Transplant Cardiologist

Absolutely. Yeah. And like I said, we're already largely adopted it as our primary surveillance for these patients. And I could see it becoming a primary way of making a diagnosis in a sort of for-cause patient as well.

Nick Loannou
VP of Medical Affairs

Max, as MDs, we care about our patients. They're our family. I was presenting at SIOT in Scottsdale, and a chap raised his hand and asked a question, and he was from the Transplant Families. It's a volunteer organization, but he's the chair there. And he actually has a son, a 14-year-old son, who has received a kidney transplant. And he heard about the turnaround time and all that, and he goes, "I have to tell you, Dr. Nick, waiting those three days, those five days, whatever they may be, it's heartbreaking for a parent because here's your baby, and we don't know what's going on. Will they have to go through another kidney transplant now?" From that perspective, it resonated. And then I spoke to more people from his organization, but he says when he's speaking, he's not just speaking for himself, he's representing this Transplant Families.

That's where we want to go. We know we can make a change in the industry, but when you make that change one patient at a time, that's what gives me satisfaction as a medical doctor. And I know you care about your patients, and I know you see that, too. Well, Max, I think-

Max Liebo
Transplant Cardiologist

Yeah, we do.

Nick Loannou
VP of Medical Affairs

Sorry, go ahead.

Max Liebo
Transplant Cardiologist

I should say, we do get a phone call from patients 24 hours, 48 hours after tests, inquiring about the results. I echo what you are saying. Absolutely.

Nick Loannou
VP of Medical Affairs

Well, Max, that is all the questions I have for you. Do you have any closing statement or anything like that? Because after that, we can turn it over for questions from our audience.

Max Liebo
Transplant Cardiologist

Yeah. I am happy to just jump right into other questions if you guys have them. I think that it is a pretty straightforward technology, at least in terms of from the clinical aspect, is what it sounds like to me. If we can get this technology we have already learned to sort of be comfortable with and how to use it, but be able to use it more readily and in more patients, I think, to me, this is very exciting.

Nick Loannou
VP of Medical Affairs

Yeah. And see, it is this excitement that Max has about the industry and where we are going that he is here today. He is not getting paid. He is doing it because of the love of the industry, the love for his patients, and to help advance the science. With that said, thanks, Max, and I will open it up for some questions.

Moderator

Awesome. Thanks, Dr. Nick and Dr. Liebo. Yeah, so at this time, we will be doing a Q&A session with all three of our speakers. To our analysts who have joined us live to ask a question, I will just give you guys a quick reminder to please raise your hand to indicate you have a question. So please hold for a brief moment.

Nick Loannou
VP of Medical Affairs

We are still holding or is it frozen?

Moderator

Yes.

Max Liebo
Transplant Cardiologist

Holding.

Moderator

We will be taking the first question from Thomas Flaten at Lake Street. Please go ahead, Thomas. Thomas, you could go ahead with your question.

Thomas Flaten
Analyst

Thanks so much for that. Dr. Liebo, thanks for your time. I just want to clarify. Is your primary interest here in ruling out or ruling in a rejection, depending on specifically in the case of a for-cause patient?

Max Liebo
Transplant Cardiologist

Somebody who is coming in for cause. By that, I mean they're coming in with symptoms.

Thomas Flaten
Analyst

Yep

Max Liebo
Transplant Cardiologist

Or maybe their echocardiogram suggests that there may be a drop in their ejection fraction. Something to make us concerned they may be having rejection. The purpose of it is really to look for both. We would do the cell-free DNA assay to look to see if there's any evidence that the heart is leaking more DNA than the rest of the body is. That's essentially what this technology is. It basically looks at the amount of DNA that's coming from non-self, and it compares it to how much DNA is floating around the bloodstream that's from your own person. If that percent of the DNA in your bloodstream that's non-self starts to go up relative to the rest of the DNA that your body's leaking, we become concerned there's some active process attacking the heart, whether it's rejection or vasculopathy or myocarditis or a heart attack.

That we don't necessarily know from the results of this test. What we do know is either that there's a problem at the level of the heart or not. If that test in the for-cause patient comes back saying there's not a problem at the level of the heart, I'm not going to say I'm going to be completely done testing their heart. We've generally sent off what we call donor-specific antibodies to see if there's any evidence to help sort of make us determine just how concerned we are about possible antibody-mediated rejection. Ultimately, that cell-free DNA level really does impact our immediate concern about just how severe or whether or not something really is going on at the level of the heart. If it comes back negative, I'm generally fairly reassured that their symptoms may be more pulmonary in nature.

I have to look for something else. I'm not really too concerned about rejection if that cell-free DNA is normal. That said, I'm very interested in that patient. There's a reason I'm doing it, is because I'm concerned for cause. So I'm very interested in making the diagnosis of rejection if they have it. If that cell-free DNA level comes back abnormal in that for-cause patient, then that patient absolutely is going to be getting dosed with IV steroids and then is going to undergo a biopsy. If that biopsy doesn't confirm that they have rejection that is going to improve from the steroids I've given them or warrants antibody treatment, then the next test we're probably doing on that patient is an angiogram to see if they've developed any vasculopathy or any coronary lesions that would benefit from a stent.

Ultimately, that cell-free DNA assay whether it's in the surveillance patient or if it's in the patient for cause, it's really helping me determine whether or not I need to continue to look at the heart as a source of the problem, or I can look into other organ systems.

Nick Loannou
VP of Medical Affairs

Max, allow me-

Thomas Flaten
Analyst

Got it. Thank you.

Nick Loannou
VP of Medical Affairs

Sorry, Thomas and Max, allow me to chime in here real quick. Thomas, the way the industry has trained us, many doctors practicing transplant physicians, is to use these tests as rule-outs because they have got high negative predicted values.

With that is what you are doing. You are ruling something out. What we have seen in kidney, we have got a very high positive predicted value, and that is what will give confidence to the physicians to go, "Okay, now I am seeing high positive predicted values, so when I see this above the threshold, now I can start trusting it that I can rule it in that something is going on." That trust will eventually happen, but right now the industry is exactly like how Max explained it. He has to use his judgment as the physician there, but ultimately, they are all rule-outs, high rule-outs.

Thomas Flaten
Analyst

Just one more follow-on if I may. Does it matter to you, Dr. Liebo, if the test has a specific ability to discriminate between cell-mediated versus antibody-mediated rejection, or does it not matter at that kind of initial case? You just want to know if there is rejection, period.

Max Liebo
Transplant Cardiologist

That's correct. The short of it is, it cannot tell me with any kind of certainty whether it's cell-mediated or antibody-mediated. We do have some idea. The literature has suggested that antibody-mediated rejection generally presents with a bit higher of a cell-free DNA elevation than the cell-mediated rejection, but there's a lot of overlap. No, at the end of the day, this test is basically to let us know whether or not, as Nick put it's a rule-out test. If it comes back negative, that's very powerful in my clinical assessment then, about helping me shape my clinical assessment about what is going on and where an invasive test is needed and where it's not.

But if it's abnormal, I should say, if it's elevated, then it's just letting me know that I need to go ahead and do that biopsy to determine which form of rejection this is. If it hasn't been sent already, we need to send off antibodies for this heart to see if there's any suggestion that the patient has now formed antibodies to his own heart. We would then use that information to determine whether or not he needs to be further treated for rejection, or we need to continue to look with angiography or an MRI or look with other things to figure out why the heart is leaking if it doesn't look like it's actually rejection.

Thomas Flaten
Analyst

Appreciate that. I'll jump back in the queue. Thank you.

Nick Loannou
VP of Medical Affairs

Thank you, Thomas.

Moderator

Yes. Thanks for the questions, Thomas. Our next question comes from Mark Massaro at BTIG. Please go ahead, Mark.

Mark Massaro
Analyst

Great. Thank you. Doctor, this is a great presentation. I just wanted to get a sense. My impression is that you might have been using the CareDx products based on your remarks earlier. If you were to make a change, would this be something that you would have a significant influence in making for your entire health system, or would this be something that maybe you might start using, but maybe can you walk me through how a change in your health system would work across multiple clinicians?

Max Liebo
Transplant Cardiologist

Yeah, I do my best with this. I have experience using both the CareDx product as well as the Natera, and in fact, that's really where I've kind of grown to become very comfortable using cell-free DNA technology is because we've participated in both of those registries previously, the AlloSure Registry as well as the ProActive Registry. We've accumulated a lot of our patients, even when they were still getting their biopsy protocols per protocol as part of the registry, they were getting these assays, so I was able to then sort of see how the assays are matching up with biopsies. In those patients who then had graduated out of our biopsy protocol, I was able just to get used to managing these patients based off of whichever product, whichever cell-free DNA product we were using.

As a health system, we are not beholden to either one of the companies. I would say I think we probably do about 50/50 in terms of sending out Prosperas versus AlloSUREs when it comes to our current available cell-free DNA products that we're using. I personally can't say much about how things would go with the whole health system. What I could speak for would be Loyola itself. To be fair, Loyola is, I believe, at least for heart transplant, the only facility in our health system. Trinity Health, I don't believe has another heart transplant center. If they do, there's just one or two on the East Coast. It's not much. I would assume that any transplant center would kind of adopt this the same way that I foresee myself and my other two colleagues here at Loyola using it.

As saying, we don't really have a preference over the cell-free DNA technology in terms of there's not been one study showing that one is superior to the other, but rather what's the most convenient for our patients and what's the most clinically helpful, useful. In this case, that's why I say I would foresee us using this exclusively, ultimately, if we had the ability to draw this and run it in our own hospital and we're getting results back 3 to 5 times faster than we do our current, whatever you want to call it, logistics.

Mark Massaro
Analyst

Okay. That's really helpful. Then, I would love to ask about the economics of testing, and this might not be something that you have to deal with because you're caring for patients, which I really appreciate. But if you could perhaps take a stab at this. So, in the event that your system was able to benefit in the favorable economics of surveillance testing, is that something that you think about, or is that maybe the CFO of your health system or a program director? Because, as an analyst, sometimes we, of course, think about how some clinicians could be financially motivated to make a switch. If you took it in-house, I think you could benefit from the economics yourself rather than sending it to CareDx or Natera.

Maybe just walk me through maybe the economic argument, if that even is something you think about, or maybe it's something that someone else at your system thinks about.

Max Liebo
Transplant Cardiologist

Yeah. Thank you for the question, Mark. I would say, I personally, as you alluded to, I really more in the exam room with the patient, and I'm more focused on the medical decision making and what is best for the patient in terms of their medical care and their comfort and their convenience. The financial side of it doesn't cross my mind all that much. I try not to let that sort of sway me from doing the right tests on patients.

That said, absolutely there's somebody here at Loyola, and at Trinity, who would very much, I'm sure be in favor of, if this was something that was financially better for us than using another product, or if this was financially better for the healthcare system or for our system than doing a biopsy, I'm sure they would only further encourage this to get accepted as a tool here at Loyola.

Mark Massaro
Analyst

Okay.

Max Liebo
Transplant Cardiologist

I'm not sure. Nick, you may actually have a better feel for it. To be honest, there was a point when I first started over a decade ago where I think I did know what the cost of a biopsy was and how much the hospital made from a biopsy, versus what it cost for an AlloMap or an AlloSure back then. But I don't have those numbers off the top of my head right now.

Nick Loannou
VP of Medical Affairs

Max, I'm with you on that. When it comes to economics and numbers, I always punt those questions. If I'm out with sales, they can answer them. Now we've got our CEO, so Josh, I don't know if you want to take that.

Josh Riggs
CEO

No, I think the answer was perfect.

Nick Loannou
VP of Medical Affairs

It was.

Josh Riggs
CEO

Clinicians decide if it's useful for patients, and that's the first question that has to be answered. Once that question has been satisfied, then it becomes a CFO question. Can they afford to bring it in-house? Does it make sense for their system? The first hurdle is always convincing clinicians that this is the right thing for their patients.

Mark Massaro
Analyst

Fantastic.

Josh Riggs
CEO

Thanks, Mark Massaro.

Mark Massaro
Analyst

Maybe last question from me. Dr. Liebo, I know there's been, at least in the last couple of years, there's been uncertainty with respect to surveillance testing in heart and kidney and lung testing. That, I think, is because there's been some discussions with the Medicare group and some other groups in the government. I just wanted to get a sense for, one, were you aware of any of that Medicare limbo? Two, did you make any changes to your surveillance protocol? Then three, now that Medicare is clarified and finalized, maybe can you walk me through how important developing a surveillance protocol is in your practice?

Max Liebo
Transplant Cardiologist

Thank you, Mark. I got to tell you, it sounds like you could maybe educate me some on this, because I'm not real familiar with the issues with Medicare and surveillance right now, other than I can tell you, for as long as I've been doing this, especially when it's covering for one of my colleagues, there are definitely things on our surveillance protocol. Not usually about the heart itself, it's usually more about the surveillance we're doing for cancer or for other infections, things like that, in our patients with transplants. But there are definitely some testing we'd have on our current protocols that routinely lead to us having to do sort of peer-to-peers or appeals to the insurance companies to pay for it, for concern about there's really not data that supports a lot of the stuff that's in the surveillance testing of patients post-transplant.

I guess I would say I wouldn't be totally surprised to hear that this has been coming up about whether or not this is a good use of resources, that patients are getting full body CTs every year and things like that. But as far as when it comes to the surveillance of the allograft, I wasn't aware that there was a whole lot of issues with saying that we're not sure that there's actually value in it.

I think that all the guidelines are pretty clear that at least for the first 5 years after a heart transplant, it's time and again in the guideline documents, it's been recommended that we're monitoring patients weekly for the first couple of months after a heart transplant, and then starting to reduce the frequency after that, but still relatively frequent, like monthly assessments for the bulk of the first year, and then at least quarterly for the next few years. I don't think that we're going to see surveillance testing for rejection going away. I think that what we're seeing is a big change in the modalities we're using instead of being these, frankly, I say this with all respect, I'm the one who does the procedures here, but the biopsies are fairly barbaric, and they do come with the risk of complications.

Not necessarily a high risk of life-threatening things, but you can actually damage the heart you just gave somebody. And you guys are all aware, Nick mentioned how there's only about 4,000 transplants a year, and there's probably a half million people that would potentially be better off with one a year. Ultimately, these aren't things that they're easy to come by, and when you get one, the last thing you want to do is ruin it. I think that for surveillance, at least for the heart rejection, I don't foresee a problem getting. I think these assays, whether it's IMDX or if it's the ones that are already presently in commercial use, I don't see them going anywhere.

I think that they're actually just going to more and more take over the biopsies and reduce the unnecessary biopsies we've been subjecting our patients to over the years.

Mark Massaro
Analyst

Yeah, that makes perfect sense. Thanks so much for the time.

Max Liebo
Transplant Cardiologist

Yeah. Thank you.

Moderator

Yes. Thanks for the questions, Mark. Our next question comes from Alex Nowak at Lucid Capital Markets. Please go ahead, Alex.

Alex Nowak
Analyst

All right, great. Good morning, everyone, and thanks for the call and the discussion. Multimodality testing has been a really big thing in the heart transplant community for a while now, combining donor-derived cell-free DNA and gene expression. Is there potential to do multimodality testing here with droplet digital PCR, or would you say that's largely unnecessary, just given digital PCR sensitivity?

Max Liebo
Transplant Cardiologist

Thank you, Alex. I don't know enough about the technology of IMDX about whether or not there is any discussion about trying to create a gene expression profile product to go along with the cell-free DNA. I leave that to Dr. Nick and Josh to answer that. But I will tell you that while the gene expression profiling was obviously the first of the molecular testing to come in, that was validated as a reasonable substitute for biopsies to at least to screen for cellular rejection, over a decade ago now, and so that's been in use for a while.

I can tell you just clinically from my own experience, it seems like over half the time we get one of those assays, the result comes back elevated, and it's so nonspecific for rejection and pretty much anything that is causing inflammation or causing any kind of infection, any kind of stress on the body seems to perturb that. I've really almost stopped looking at that. When we do order a CareDx study to get an AlloSure, we always end up getting an AlloMap with it, and there's a recent document out done about a year ago now, I think it was Dr. Jeffrey maybe was the one who published on this.

But they did show there was some strength in combining an abnormal AlloMap with an AlloSure in terms of further sort of refining that this is somebody you actually have to be worried about versus somebody who has that high AlloMap like we commonly experience, but their AlloSure is low, that's somebody that we basically can kind of throw away the AlloMap result, the gene expression profile result. Because ultimately, it seems like most of the power of these molecular testing is coming from that cell-free DNA. And we kind of see that with this other company, with Natera, who they are not my understanding, they're not looking at gene expression profiling at all, but rather they're all in on the cell-free DNA.

That does seem to be with their. They published on their using both the percent cell-free DNA and the quantity, the absolute quantity of cell-free DNA, using that as sort of their discriminator to help them further enhance their ability to sort of rule in or rule out rejection. That said, I don't know if there's been any discussion at IMDX about it. My understanding was that the Droplet Digital was purely cell-free DNA right now, and again, that's really the test that we are predominantly using for surveillance at this point. So to me, this is still a potential replacement for what we're currently using.

Nick Loannou
VP of Medical Affairs

Max, very well said. Thank you. Look, folks, we're at the infancy of a heart transplant monitoring program. Right now with digital droplet PCR technology, that's where we are, right? There's no way I can tell you where we'll go with it in the future and what capabilities we'll have. Ultimately, we're learning. I have been part of Natera in the past, and I know with their tests, like Max mentioned too, that's where they are, that's where they're comfortable and that's where we see right now we can make a big impact in the industry and help patients and the physicians who monitor those patients.

Alex Nowak
Analyst

Yep. Super helpful and very clear. Thank you. I agree that the literature on donor-derived cell-free DNA is super strong in both kidney and heart transplant testing. What do you think the unanswered questions that are out there by

your transplant colleagues, though? Like why would they not adopt donor-derived cell-free DNA testing more within their practice, more to reduce the unnecessary biopsies? Does it really come down to the logistics side, or is there more data that can be accumulated here that perhaps, even like GraftAssure or Droplet Digital PCR could help kind of resolve some of those questions?

Nick Loannou
VP of Medical Affairs

Max, do you want to take that or do you want me to take that one?

Max Liebo
Transplant Cardiologist

I'll take a quick stab at it. As far as say it's hard to say exactly what motivates one person, one cardiologist versus another. How much of it is inertia, and some of these protocols have been written years ago, and they're fine. They feel like things aren't broken, so we're not necessarily trying to revamp things. I don't think there's going to be a whole lot of I don't think there should be a whole lot of resistance to these taking over the coming years. Every meeting I go to or that I read through is just more and more abstracts and oral presentations on this.

The most recent transplant guidelines just a couple of years ago dedicate the first few paragraphs of the discussion about rejection, about screening for rejection, to basically saying that these tests are this is going to be the future of it, about rejection screening.

I think as far as how to get other people to start utilizing it more, I think it's going to come down to just a little more experience and getting more. Potentially, I know there are a few studies that are currently being looked at right now or being completed, where we're actually taking patients and showing that you can actually start using the cell-free DNA to treat in patients that show a rise in the cell-free DNA, that you would treat them potentially before you then go ahead and get their biopsy within the next few months, and ultimately determine whether or not those follow-up biopsies look like they're better after the treatment. This is all based off of data that shows that the cell-free DNA often goes up early in somebody having rejection before you'll actually see that on biopsy.

All too often, and this has happened to me at least once, where I've had a patient who had a little jump in their cell-free DNA. Our protocol said let's go ahead and get a biopsy within a week. We did it. The biopsy looked totally normal. Then we waited, I think it was about four weeks before we rechecked the cell-free DNA, and it was going back down. So we thought, "Oh, this all looks great. It was probably nothing." Unfortunately, a few months later, the patient presented with actually having more clinical signs of rejection, and at that point, we did the biopsy. We see that he's got pretty severe both cellular and antibody-mediated rejection. More and more, I think the transplant community is becoming aware of this, although it depends how closely you're following the literature if you're actually seeing this.

Frankly, a lot of this I'm seeing because I've been part of these other registry studies where we then go back and review our own patients and all the data from even just from our own single institution and look and see what these molecular assays showed in our patients, that we also have all the clinical data, and we know what their outcomes are. We know when their biopsies showed rejection. What we've found is that there are these patients who are. The cell-free DNA is frankly better than the biopsy at figuring out when there's diagnosing the rejection early, and it can help us in those situations either decide to treat them a little bit earlier, even before you have a biopsy.

That's what's currently being studied, and I think if that study comes back positive and that will show up in a big journal, I think that potentially does fundamentally change the way that we approach these, and that more cardiologists will have to come in line with it because it's not just a substitute, but it's actually superior as opposed to being non-inferior in that situation. I think some of it's just time. I think there's still a lot of cardiologists in the field that have been practicing for a long time and are not necessarily changing their strategies the moment they see a new technology come out, but they wait a little bit longer.

Nick Loannou
VP of Medical Affairs

Max, very well answered. I just want to add one thing. Back in 2019, when I was talking to cardiologists, quite many of them, the main thing was the older ladies and guys out there who had been practicing for many, many years, those were a little harder to persuade about the technology of DNA, cell-free DNA technology. But with time, even they became adopters, utilizing Natera's and CareDx's products. There are some out there that are still holding on, but ultimately, I foresee them retiring in the next few years because, as Max said, the literature, all these conferences we go to, it's pointing the industry, the cardiology transplant energy to utilize these tests as an extra tool.

Max Liebo
Transplant Cardiologist

My colleague, the one who had the most resistance to using this sort of technology, and although he did come around to start using the protocols once he saw that my patients weren't all dropping dead. Even he came around to it. But he's also, like you say, he actually just retired. So now in my group, it's just me and 2 other guys who are basically the same or earlier career than I am, and so everybody's very much in line. This is the way we're all practicing now. I could see how financially from a physician standpoint, it does take away a procedure from me. The biopsies are procedures. That is money I can make by doing procedures. But again, it's just to me, there's other ways for me to make my money.

I can be using that time to see patients in clinic instead, and I can spare patients this, what is not a necessary procedure for the vast majority.

Alex Nowak
Analyst

Thank you. Very helpful. Appreciate the time.

Max Liebo
Transplant Cardiologist

Thank you, Alex.

Moderator

Yes. Thanks for the questions, Alex. Our next question comes from Mike Matson at Needham. Please go ahead, Mike.

Mike Matson
Analyst

Yes. Thanks. Dr. Liebo, I was wondering, just with your current transplant patients, what portion of them are you currently using the donor-derived cell-free DNA test on? Are you using it on basically 100% of them or does it depend on things like the patient's insurance or other factors?

Max Liebo
Transplant Cardiologist

Yeah. It's 100%. I use it on everybody. We've been fortunate. I should say I've been fortunate. I've got a great office. I've got great support from our assistants and my nurses and everybody, so they make it happen. I think that the companies so far have also been very helpful about trying to figure out how to get the patients these tests, even if their insurance does give us any kind of a pushback. I haven't heard about that being a problem, and I generally use it in all my patients. I think, for those who have never had a history of rejection, they're great.

As long as the test looks negative, as long as that cell-free DNA percent is low and below the thresholds, I feel super comfortable letting those patients go, frankly, biopsy free after a couple of months, and they may never get a biopsy again. For patients who have had a history of rejection, it's the same thing. Once they've been treated for rejection and once the biopsy shows that the rejection's cleared, we go right back to just using the cell-free DNA surveillance before instead of making them continue to do biopsies just because they had an episode of rejection in the past. Frankly, I use it even in my patients who have ongoing rejection. Unfortunately, there are some patients who they do develop this sort of antibody-mediated rejection.

Their body creates antibodies even with the treatment for acute antibody rejection, with steroids and IVIG and plasmapheresis and rituximab. Even with all that, the antibodies don't completely clear, and the patient may still have kind of a low level cell-free DNA leak that's just sort of chronic. I don't necessarily make them continue to go through aggressive treatment for acute rejection if they're essentially clinically stable, even though we can see there's some smoldering rejection going on. But in those patients, we will then use the non-invasive assays both for the cell-free DNA as well as for their donor-specific antibodies to help guide as to when is it time to treat them again.

The short of it is, basically, I've figured out a way to use this with just about every patient. I assume, maybe I shouldn't assume, but I assume that any other kind of forward-thinking cardiologist, or sort of first half of their career anyway, cardiologist is thinking very similar to the way I am and is using these frankly, probably even beyond a little

bit of what they've sort of clinically been validated for, just for the need, because we want to take care of our patients.

Mike Matson
Analyst

Yeah. Okay. That's helpful. It sounds like you'd be a big proponent of GraftAssure when it became available to you, and sounds like you'd probably switch to using it for most patients. But what about the transition timeframe to switch over to GraftAssure, and would you sort of need to do your own kind of mini head-to-head study where you sort of do sendouts and then do GraftAssure at the same time to compare the results to get comfortable with it? Or would you just be comfortable kind of relying on third party data that it's accurate enough?

Max Liebo
Transplant Cardiologist

I think actually, Nick, you correct me if I'm wrong, but I believe we're actually talking about initiating a study here now where we're going to start collecting the data along with our patients with their sort of current standard clinical care. I believe we're basically in the process at this point of confirming that this test could replace the ones that we're currently using, the ones that are logistically less favorable to the patients.

Mike Matson
Analyst

Oh, got it. Got it. Sorry, I missed that your part-

Max Liebo
Transplant Cardiologist

No, you're good.

Mike Matson
Analyst

Okay.

Max Liebo
Transplant Cardiologist

Yeah.

Mike Matson
Analyst

You're going to-

Max Liebo
Transplant Cardiologist

I wouldn't just adopt it without. There needs to be some data that shows that it works. Yeah.

Mike Matson
Analyst

Yeah. Do you think your peers in other transplant centers would be comfortable relying on the study that you're going to run versus just needing to kind of do it and see it for themselves that it compares to the other tests?

Max Liebo
Transplant Cardiologist

I think most would not. But again, everybody is a little bit different. Like I said, my colleague, it took him probably 5 years before he started writing his first prescriptions for ENTRESTO just because he just wanted to make sure that it was going to be okay. So I think there's going to be earlier adopters, and there's going to be later adopters. But I think, honestly, to me, as long as the technology works, as long as it's shown that it gives us a reading similar to what we're getting with our other assays, I don't think that every facility is going to want to do their own single institution trial of it to make sure that it works. Yeah.

Mike Matson
Analyst

Yeah. Okay. Then, finally, it sounds like with the sendout test, the patients have to go elsewhere to have their blood drawn. Did I hear you correctly on that? Why is that?

Max Liebo
Transplant Cardiologist

Yeah.

Mike Matson
Analyst

Yeah.

Max Liebo
Transplant Cardiologist

Yeah. Great question. My understanding is that primarily it has to do with the logistics of the actual preparing the specimen, where a little bit more than our lab was willing to sort of take on clinically. That is, it's not just a simple blood draw and then drop it in an envelope and send it to California or wherever the testing center is. But rather, they have to take time to centrifuge it. It has to be handled in a very particular way to make sure that the assay isn't wasted. In fact, even with that, at times, we do get a non-result. We'll end up getting a result from CareDx or from Natera saying that the sample thawed or there's some issue with it, and so we actually have to then redraw it.

But as far as where the patients go to get it, historically, there were three or four different outpatient labs around Illinois that they could go to, and we knew where they were, and they would go to the closest one. More recently, the companies have been sending, they basically send a mobile draw, a nurse to their house to draw the labs. But it is still a bit clunky because the patients describe it as they get something in the mail from the company, essentially the test tube. Then that can come a week before a nurse is going to show up to their house. But then eventually those two pieces show up to their house, they get the lab draw, it goes off, and then it takes, like I said, it takes probably at least 3 days for us to get the result on it.

So at this point, the patients are not necessarily having to go somewhere else, but they are having to wait around at their house and have to get a separate needle stick, and they have to coordinate all this with a home health company and with the test company to get it all done. So I guess what I am saying, as far as what was the barrier to getting them in, I think some of it was cost, and some of it was also just the technology was not easy enough for our lab to take over. I do not know that IMDX necessarily has a solution to this, but that is sort of what Nick, when he approached me about it not too long ago, had suggested that this was something that we could get done here in our own lab at our own hospital.

Mike Matson
Analyst

Okay, got it. Just as a follow. Yeah, go ahead, Nick.

Nick Loannou
VP of Medical Affairs

Sorry, Mike. Just to tell you, Mike mentioned that there was a procedure that they would have to spin it and then put it on ice, whatever, to send it out. With our assay, no spinning is needed, no ice to ship it out. If they had to send it, as a send out, because we have the portion of our test that can be sent out. So that aspect would not be there, and therefore, centers can actually draw it at the facility. Now, once they get the DX portion of it where they can run the test A through Z and finish and get results within 12 hours, of course, the centrifugation will be required there, but their lab will be set up for it, and the training will be done, too.

Mike Matson
Analyst

Okay, great. Just given this factor, is this something where doing it in-house will have a noticeable impact on compliance? Will it increase patient compliance with the test, you think?

Max Liebo
Transplant Cardiologist

Yeah, I think it will. I think one of the main things about it that actually frustrates our patients in my office is that the test is supposed to be run ideally within a few days of when they get an echocardiogram. The pair of the echo and the blood test together are what really reassure us that there's no rejection, or, on the other hand, make us concerned there may be rejection. The patient generally gets their echocardiogram the same day they come and see me in the clinic, which is also the same day we often draw the rest of their labs.

I think we would do a lot better, even if the patients are getting their studies done, when they're separated by more than a week or 2, either we start to lose a little confidence in the results, or maybe even more importantly, the patients start to lose a little confidence in the results. The idea of being able to get it all done simultaneously, I think will improve. We'll definitely not have issues with us not getting results, or either the draw didn't get done because we couldn't get it set up outside or something got lost in transport to another state. But ultimately, I think there will be probably at least a slight increase in adherence.

Again, I think with all trust in sort of that these assessments are being done appropriately and that we're able to use those results and that the patients can get it all done with the least amount of sort of stress on their part about having to arrange for things. I think that it kind of helps with all those situations.

Mike Matson
Analyst

Okay, great.

Nick Loannou
VP of Medical Affairs

Let me chime in there.

Max Liebo
Transplant Cardiologist

Thank you.

Nick Loannou
VP of Medical Affairs

Guardant Health, with their Shield test, has shown how doing that blood test there at the center instead of sending them the kits, doing them home, how that has improved the compliance or the adherence, it is synonymous, to 96%-98%. Normally when people receive their kits at home, this is for colorectal cancer screening, 60%-65% are adherent to actually finish the test and send it back in or go to the lab, whatever is required. Whereas if the blood test is happening there at the center, 96%, 98%, depends on which study that you look at, but above 96% every single time. Big studies have done that, too. We foresee it, yes, adherence will increase.

Josh Riggs
CEO

I'm sorry to interrupt. Dr. Liebo, you've been so generous with your time. We are at the hour. If you're able to continue on, we'd be happy to ask you more questions. I think we have a few more analysts and some questions in the chat, but I understand you have a very important job to get back to. Let us know what we can do.

Max Liebo
Transplant Cardiologist

Yeah. I've got a few more minutes this morning if you guys have a few more questions.

Nick Loannou
VP of Medical Affairs

Thank you.

Josh Riggs
CEO

Very good. Thank you. Go ahead, Taryn.

Moderator

Great. Yes. Thank you, Dr. Liebo, and thanks Mike for the questions. Our next question comes from Ben Mee at Stephens. Please go ahead, Ben.

Ben Mee
Analyst

Hey, good morning, and thank you for taking the question and taking the time this morning. I'll just keep to one quick here. Could you expand on the logistical barriers that might exist today for bringing a test in-house, at your center, versus continuing to use the mail-out providers?

Max Liebo
Transplant Cardiologist

Yeah. Honestly, Ben, I can't. I don't have a great feel for exactly what's going on in the administrative level with our lab. I'm sure I could get Josh and Nick in touch with somebody from that aspect of Loyola to see if we can get a straightforward answer to your question. But I know the general barriers is usually just money and manpower and the cost. I think that was clearly the issue with the other two vendors that we're currently using their exam or their test, but we're just doing it in the way that our hospital could most afford. I don't know. Nick, I'm happy to try to put you in touch with whoever might be able to help you from that.

Nick Loannou
VP of Medical Affairs

In due time, we'll get to that. Yes. Thanks, Max.

Moderator

Great. Thanks for the questions, Ben. We are now going to turn to the written questions, and we will prioritize medical questions as several of the questions that coming in are concerning the business strategy and were answered substantially on the company's earnings call a week ago. Please visit investors.imdxinc.com to read the shareholder letter and transcript and see a replay of the week ago earnings call. Our first question, how would an in-house test need to perform relative to an established centralized test for clinicians to feel comfortable adopting it? Would comparable analytical and clinical performance be enough, or would it need to demonstrate an additional advantage?

Max Liebo
Transplant Cardiologist

It is a great question. I think just to take the last part of it, I do not think it would have to demonstrate any additional advantage. I think the advantage would be that we could get it done in-house and get the results back quickly. I think that the additional advantage is already kind of baked into it.

As far as do we need to validate that the results we get from an in-house, I guess the way I am reading this is, the results we would be getting from our own machine in our lab here, would they be the same as if we sent that sample to a centralized, to the IMDX centralized lab? That would be important. We would want to make sure that the machine that we are running our tests on was giving us the same kind of results as what we would expect from the central lab.

That would be something we would have to confirm.

Moderator

Great. Thanks, Dr. Liebo. Next question, will the assay be available on NGS?

Josh Riggs
CEO

No.

Max Liebo
Transplant Cardiologist

I apologize. What is NGS? Remind me.

Josh Riggs
CEO

Yeah. It's next-generation.

Nick Loannou
VP of Medical Affairs

Next-generation.

Josh Riggs
CEO

sequencing, and the answer is no.

Nick Loannou
VP of Medical Affairs

Yes, because this technology is based on droplet digital PCR technology.

Moderator

Great, and our final question comes from a doctor. They talked to transplant caregivers and partners that state the dd-cfDNA testing they have had is not always approved for insurance coverage of charges. How do we ensure this test is getting paid for as our patients need it?

Max Liebo
Transplant Cardiologist

That's a really great question, and I'd have to consult my nurses, the ones who actually take care of all these phone calls and usually putting through all the paperwork. The long story short, from the way I understand it, is at least the current vendors we've been working with, they've generally, I think, if for some reason a test we ordered and drew wasn't covered by the insurance, I believe they were either just waiving the cost of the test. I'm not sure if that's just because we were participating in the registry studies or exactly how that was working. But I do know that this was not, if that was an issue, it really wasn't a very frequent issue. I believe these are all being covered fairly well by insurance. But I could definitely query my nurses or the ones who deal with it when there's pushback.

Moderator

Great.

Max Liebo
Transplant Cardiologist

I personally haven't had any patients come to my clinic and bite my head off about some bill they got in the mail for this investigational test I just did that their insurance company is telling them that I'm just a quack of a doc. I haven't had that personal experience.

Moderator

Great. Thanks, Dr. Liebo. That's all the time we have for questions. I'll turn it back to Josh for some quick closing remarks.

Josh Riggs
CEO

Yeah. Thanks again, Dr. Liebo. I think we're very excited to work on this head-to-head study with you and show that you can get equivalent results with GraftAssure technology. Really appreciate the time and the straightforward answers on how you use donor-derived cell-free DNA in your clinic on a daily basis. Thank you again, and appreciate everybody for showing up with very thoughtful questions.
