October 2022 MoIDX Open Meeting Transcript

Dr. Angella Charnot-Katsikas
Yes, we announced that it would record the open meeting.

Dr. Angella Charnot-Katsikas
I'm going say this again. I'm going to re-announce that Palmetto GBA has previously announced that it would record the open meeting and that Palmetto GBA consents to the recording. All right, so I have just started the recording of this open meeting and compliance with CMS for the record, prior to doing so, I announced that Palmetto GBA would make an audio recording of the open meeting and consent it on behalf of Palmetto GBA.

Dr. Angella Charnot-Katsikas
Alright. With that, we now have a number of speakers we'd like to introduce. We have presentations. The very first one is by Dr. Gary Crump from Rheumatology Associates and I want to say that we have to be very careful with our time. Each speaker has been allotted 15 minutes and we have a few remarks at the end and each person at the end gets about 5 minutes. So, with that Dr. Crump, if you're able to show your slides, we can get started.

Dr. Gary Crump
Well, I'm in private practice…rheumatologist running a very busy, a group of five rheumatologists and three nurse practitioners. And very involved with the advocacy for optimal care for patients with rheumatoid arthritis and hip published. Multiple Articles and papers on measuring rheumatoid arthritis and treating to target appropriately, which is the right way to get this disease that has a very high inflammatory burden and a high morbidity and mortality as well as a very high societal cost, uh, to treat these patients optimally.

Dr. Gary Crump
To that end, we employ precision medicine and always as best as the new technology emerges and allows us.

Dr. Gary Crump
I'm also a member of United rheumatology Medical Policy Committee, which is a United Rheumatology is a volunteer Organization of about 625 private practicing rheumatologists and comprises about one-fourth of the private practicing rheumatologist in the US.

Dr. Gary Crump
And a member of the state Rheumatology board here in Kentucky.

Dr. Gary Crump
Let me start by saying that there's been a misconception based on chronology that [inaudible] are always the right way to start treating a rheumatoid arthritis patient when their disease is no longer controlled adequately by the oral medications, and in fact, that happens in the majority of cases

that…the small molecules that are inexpensive, like methotrexate and leflunomide, are not adequate to control.

Dr. Gary Crump
Uh. Rheumatoid arthritis and uncontrolled Rheumatoid arthritis cost the patient in terms of pain, suffering, loss of joint function and increase mortality, including cardiovascular mortality.

Dr. Gary Crump
[Inaudible] your driven models. Basically, the PBM model artificially mandates that we use TNF inhibitors first because they were the first class of drugs that came out and historically and, more importantly, because though those are the drugs that are given the biggest discounts by the [inaudible]. I've had the companies to the PBM and the rebate system is a whole another discussion. But we know oftentimes that a patient will spend three months trying to get benefit from a drug that they will not benefit from.

Dr. Gary Crump
And there are multiple, approximately five other mechanisms of action targeted treatments after oral [inaudible] and not all patients respond to TNF inhibitors.

Dr. Gary Crump
And so when we need to go to second line treatments.

Dr. Gary Crump
Having a tool like the Prism-RA test allows us to precisely and accurately get to the right choice, it might be a TNF inhibitor, if that's what the test dictates, it might not be a TNF inhibitor. There is this disconnect between …what? Payers say we should use next and what we actually should use next and thankfully, Medicare does not require TNF is the first line.

Dr. Gary Crump
You can use whatever drug you think is right, but this test allows us to cut our population according to [inaudible].

Dr. Gary Crump
Do they like the benefit from the TNF inhibitor? Or do they likely need an alternative mechanism of action drug? And so, it gets us to the right treatment for the patient sooner and allows us to not expose that patient to an agent to which they will not respond and will potentially suffer side effects or adverse effects from and certainly will not benefit from disease control for a period of time while they're unsuccessfully trying that new medication.

Dr. Gary Crump
Really, to summarize, and I think there's one more slide that just sort shows schematically, shows how we use the Prism test in practice.

Dr. Gary Crump
It gives us a decision point, too. so with a drug that's the right drug or an alternative drug, and it often can be used even after someone's failed a TNF inhibitor. We can then look and see instead of repeating the [inaudible].

Dr. Gary Crump
Instead of repeating another TNF blocker as sometimes as mandated by certain carriers, we can go right

to an alternative MOA to its the patient would have a much higher chance of responding and benefiting. So, I think I did it well under my 15 minutes. I'm happy to take any questions. Thank you.

Dr. Angella Charnot-Katsikas
So most folks are muted and except for the speakers and the moderators, we have a very large crowd. If there are questions you can please put them in the chat for this meeting. But typically, we don't have a Q&A allowance for this. So, thank you so much Dr. Crump for your presentation. And again, if folks want to put anything in the chat, that's OK. But at the end of the day, you can take these back, perhaps with you and…I'll respond, you know accordingly. Thank you so much for that brief presentation.

Dr. Angella Charnot-Katsikas
And yes, again please submit written comments in the chat. Alright, we are going to move on to Dr. James Mossell, the of the medical director of Rheumatology at the Arthritis and Osteoporosis Center of South Georgia and Internal Medicine Associates of St. John's County.

Dr. Angella Charnot-Katsikas
Dr. Mossell. OK, while we're waiting for Dr. Mossel to get started, any comments or questions, please do submit those in writing to Palmetto GBA as part of the comment period.

Dr. Angella Charnot-Katsikas
You can submit those comments and questions now.

Dr. Angella Charnot-Katsikas
OK, so what we'll do for the sake of time is move on to the next speaker and if Dr. Mossell available in a bit, we'll make sure we circle back to him. So, at this point, I would like to go to our next speaker, Dr. Madeline Feldman, of advocacy and government affairs.

Dr. Angella Charnot-Katsikas
Dr. Feldman?

Dr. Angella Charnot-Katsikas
Dr. Feldman, if you're on the line and … if you're having any technical or audio issues, please put that in the chat so we at least know your present.

Dr. Angella Charnot-Katsikas
We want to make sure that we have unmuted the speakers, you know, so you know, we can't have everybody speaking, but we want to make sure that our speakers are able to speak. So, if you are here and present, please put that in the chat or somehow let us know.

Emily Graham
Hello.

Dr. Angella Charnot-Katsikas
There we go. Who's speaking, please?

Emily Graham
I'm sorry. This is Emily Graham on behalf of the Coalition of State Rheumatology Organizations, Dr. Madeleine Feldman is on the call, but she's unable to get off mute. And I think there's also some

confusion on the part of some presenters because we don't have any link to join a virtual sort of meeting. We just have a dial in number.

Emily Graham
She joined the link right now.

Dr. Madelaine Feldman
Hello, can you hear me?

Dr. Madelaine Feldman
Hello.

Dr. Angella Charnot-Katsikas
We can hear you. Who's speaking please? Is this Dr. Feldman?

Dr. Madelaine Feldman
Yes, let me see if I can turn this up. Can you hear me now?

Dr. Angella Charnot-Katsikas
Yes, we can hear you.

Dr. Angella Charnot-Katsikas
Umm. And you'll be able to click the links through there as well. But anyway, without further ado, please let's begin your presentation.

Dr. Madelaine Feldman
OK. Thank you. Well, as you know, my name is Madeline Feldman and I'm a practicing rheumatologist in New Orleans, La. I'm also the immediate past president and current Vice President of Advocacy and Government Relations for the Coalition of State Rheumatology Organizations, or CSIRO. Now, CSIRO is comprised of over 40 state and regional professional rheumatology societies whose mission is to advocate for excellence in the field of rheumatology, ensuring access to the highest quality of care for the management of our diseases, which are rheumatologic and musculoskeletal diseases, and our coalition serves primarily the practicing rheumatologist. I'd like to share this perspective of our state and regional societies that are members of CSR as it relates to Palmetto GBA's proposed local coverage determination under the molecular Diagnostic services program, titled Molecular Biomarker Testing to Guide Targeted therapy and in rheumatoid arthritis. The MOLDX program covers several Medicare administrative contractor jurisdictions. Therefore, this proposed LCD is of interest to most of the States and regions that are under our umbrella. The CSIRO umbrella and your proposed LCD Palmetto GBA has concluded that quote clinical validity has not yet been established for molecular biomarker tests that guide.

Dr. Madelaine Feldman
Targeted therapy and RA on that basis, Palmetto GBA proposes non-coverage for the emerging technologies in this space. Now this is disappointing considering.

Dr. Madelaine Feldman
That Palmetto GBA's contractor Advisory Committee, subject matter expert, their SME panelists noted that physicians would welcome predictive tests to guide targeted therapy and RA patients and find them useful if they could help minimize the trial-and-error approach of current therapy. So even with

adherence to the ACR, the American College of Rheumatology guideline for treatment of RA, identifying the most effective therapy always seems to involve a try and fail approach after a patient fails conventional DMARDS or disease modifying antirheumatic drugs. The current clinical evidence doesn't really support initiating a treatment with one biologic or a targeted synthetic DMARDS over another.

Dr. Madelaine Feldman
Nevertheless, tumor necrosis factor inhibitors are what we call TNF's are the most frequent first line biologic DMARDS prescribed. This is despite the fact that approximately 30 to 40 percent of patients don't always achieve a meaningful clinical improvement with this particular mechanism of action. Unfortunately, because of insurer requirements such as in-class cycling, moving to another mechanism of action is often challenging, meaning patients may spend an extended period of time on a therapy that won't work for them.

Dr. Madelaine Feldman
The consequence to the patient is increased disease severity, disability and pain, and not to mention diminished quality of life and difficulties with their ADL activity of daily living. It should be noted also that sustained high level of disease activity is associated with increased costs not only now but in the future.

Dr. Madelaine Feldman
Those patients with uncontrolled disease are often required increasing doses of steroids leading to diabetes, infections and osteoporosis, as well as a myriad of other well-known side effects.

Dr. Madelaine Feldman
So looking to the future are a patient with active disease can incur more joint replacements. We know it's a very strong risk for heart attacks and even some malignancies which will lead to long term increases in costs.

Dr. Madelaine Feldman
Rheumatologists and our patients are desperate for solutions to this sort of fail first, umm, you know, try and fail paradigm that we've been living under. Molecular biomarker tests are the first tool offering an objective science-based approach to identifying appropriate medication therapies for RA treatment.

Dr. Madelaine Feldman
Recent studies support the clinical validity and utility and most rheumatologists and their patients.

Dr. Madelaine Feldman
Well, we're all eager to gain access to this position met medicine tools and clinical practice to improve our outcomes.

Dr. Madelaine Feldman
The proposed LCD seems to suggest that such precision tools may never be available for RA patients, but that in any event, the current, you know, approach is good enough.

Dr. Madelaine Feldman
On behalf of our patients, we reject that assertion. Our colleagues and oncology have experienced remarkable growth in the field of genetically-driven precision diagnostics and therapies, which is greatly improved not only the survival rates, but also the management of certain cancers. Our patients deserve

no less in terms of proactive data-driven disease management, but we are concerned that the proposed LCD sends the message that investment in this field is simply not worth it.

Dr. Madelaine Feldman
Given the aforementioned, our coalition urges you to establish a local coverage policy and associated payment for the use of molecular biomarker testing to guide targeted therapy and RA with the following caveats.

Dr. Madelaine Feldman
The ordering and interpretation of molecular biomarker testing…should be at the sole discretion of the treating rheumatologist. And as we've always said, patients who are stable on their medicine should not be switched to a different drug or denied coverage of their current medication by the Medicare program, including Medicare Advantage. Based on the results of molecular biomarker testing or any other type of utilization management tool.

Dr. Madelaine Feldman
Thank you for considering the feedback of practicing rheumatologists and if you have any questions. I can be contacted at the email address provided in our formal written response.

Dr. Angella Charnot-Katsikas
Great. Thank you very much for your presentation. And also, we want to be clear that anyone who is speaking may be able to share, but we want to make sure that everyone who's not speaking is both muted and not sharing their screen please.

Dr. Angella Charnot-Katsikas
Alright, let's see if Dr. Mossell is available to provide his presentation.

Dr. Angella Charnot-Katsikas
OK, there is an echo with some beeping, so please again mute yourself if you are not speaking. All right, we'll go on and we'll try again to circle back…. So, the next speaker on our list is Dr. Max Hamburger from United Rheumatology.

Dr. Angella Charnot-Katsikas
Dr. hamburger.

Dr. Max Hamburger
This is Dr. Hamburger. But you're a little early for me.

Dr. Max Hamburger
So I can be ready to go in about 10 minutes, but I'm not ready to go right now.

Dr. Angella Charnot-Katsikas
OK. We will, we will circle back. Thank you for letting us know that, we will circle back to you, all right? The next presentation then is Dr. Soloman of the Arizona Arthritis and Rheumatology Research Center. Dr. Solomon, are you available?

Dr. Nehad Soloman
I am available. Can you see me and hear me?

Dr. Angella Charnot-Katsikas
We can, yes. Thank you.

Dr. Nehad Soloman
OK, perfect. So let me start by introducing myself. My name is Dr. Nehad Soloman. I'm a medical director at Arizona Arthritis Rheumatology Research Center. I've served in the Phoenix metro area for the past 17 years, actively engaged in clinical trials, research for many rheumatic diseases currently serve on the Phoenix Rheumatology Association, which is our citywide board. I've been past present current the vice president also served on the state coalition here in Arizona. I certainly would like to say I echo what Dr. Crump and Dr. Feldman have already said for sure. I'd like to kind of give you a lens from a slightly different perspective in as much as our group was actively involved in the clinical trials for the precision medicine studies here with these Prism-RA testing.

Dr. Nehad Soloman
And we know that rheumatoid arthritis is a heterogeneous disease, and we know that patients may respond to some medications and not others. And unfortunately, we don't have the Holy Grail, but the Prism-RA test is one step closer to that precision type medicine where rather than playing the guessing game, we can use a bit more insight from the distinct biology of the individual patients to assess whether or not they would respond to a TNF drug, once there is a failure, inadequate response to.

Dr. Nehad Soloman
As the traditional disease modifying agents and unfortunately over the last 17 years, we've had nothing but a constant restrictions constant jumping through hoops to get the drugs that we believe are appropriate for our patients. As …both Dr. Crump and Dr. Feldman have already stated, oftentimes we have to follow formularies that are based on revenue and discounts and not really in the best interest of our patients. We need both patients and rheumatologists need precision medicine tools to help tailor therapy based on patients. Disease biology. Specifically, each patient, not just a generalized understanding. And this definitely requires biomarker analysis to predict types of response. There is no perfect biomarker at this point, but we are getting one step closer.

Dr. Nehad Soloman
Is my firm belief. After doing the clinical trials research that Prism-RA is a validated test that helps us get closer to this type of precision medicine. If we wait for the ACR guidelines, which can take anywhere from 5 to 8 years to update, we will be doing a disservice to our patients. Many of us attend the large meetings, we listen to our colleagues thought leaders out there.

Dr. Nehad Soloman
And we do know that there's an ever-changing science when it comes to rheumatology selection of even a first line biologic that's not suitable for a patient's biology will dramatically impact their outcomes and disease progression.

Dr. Nehad Soloman
We know that we can oftentimes give a drug three to six months to work, and if we know off the bat they're not going to respond, or the likelihood of response is less than 10 percent, then there is no sense in trying a therapy like that. And so, and this is the type of insight that the Prism-RA tool provides for us and for our patients with RA.

Dr. Nehad Soloman
Just going to share with you a case study: 67-year-old female with seropositive RA Shogun syndrome and osteoporosis has had already since 2003 had been treated with a variety of different therapies including sulfasalazine, methotrexate, Enbrel, Humira and Remicade. In the early part of this century in 2020 was treated with Symponi…for four months. As you can see, this sort of repeated treatment for very partially because these were the treatments available, partially because of [inaudible].

Dr. Nehad Soloman
But it's within our various insurances. Initial response…lasted for a few months, and then response was lost. Insurance started to dictate repeated TNF trials. When we looked at the Prism-guided therapy, we found that the patient had a high likelihood of non-response. Now, had we had this type of test at the early part of the…

Dr. Nehad Soloman
Yeah, the treatment course, we could have avoided the needless use of 1 TNF after the next after the next. As a result of having this insight, we switched the patient to Orencia, which is a totally different mechanism of action, and now doing much better. Her CDAI, which is a disease activity index of rheumatoid arthritis was 22 initially, and then after six months of Orencia was down to five, which is low disease activity.

Dr. Nehad Soloman
And so, uh, what we see here is that we need to have more information. We need to have more precise information so that after the patient has experienced a failure or an inadequate response, whether it be to methotrexate or conventional DMARD or even a targeted synthetic DMARD, or even after the first biologic considering a second TNF.

Dr. Nehad Soloman
In the presence of a test that shows likelihood of non-response, is wasting time, it's wasting precious time for the patient and potentially worsening their disease state. These are all the references of many of the things that I've spoken about today, and again I'd like to thank everybody for this time as well as stress the importance of precision medicine.

Dr. Nehad Soloman
The fact that in clinical trials so far, we've had dramatic responses and improvement in our ability to manage patients, been using this test now in our clinical practice and have been thrilled with the information that I've gotten and the patients' improvement over time without the guessing game. And with that, I'd like to thank everyone for their time.

Dr. Angella Charnot-Katsikas
Great. Thank you very much, Dr. Solomon. The next speaker on our list is Dr. Priya Reddy of the Florida Society of Rheumatology. Dr. Reddy, are you on the line? Again, Dr. Reddy, if you're on the line and having issues, please either send us your email with your phone number or raise your hand in the chat so we know your presence. OK. Well, we have a few folks to circle back to. Let's see if Dr. Mossell is now available. Dr. James Mossell. All right. Dr. Max hamburger.

Dr. Max Hamburger
I am ready to go. I [am] Max hamburger, I am 75 years old, which means that I've been practice for a

long, long time. Med school at Albert Einstein, internship, and residency here NYU Bellevue was remarkably fortunate to be able to train at the National Institutes of Health, where I work both under Mike Frank and Shelly Wolf, and Tony Fauci and Allergy and Infectious Disease Lab of Clinical Investigation, where I got a remarkable background. Then in the knology and infectious disease. And then also their bridge program with John Decker and Paul plots and Jack Klippel and others.

Dr. Max Hamburger
On the arthritis branch, which certified me to sit for the rheumatology boards and I've been in practice since leaving the NIH in 1979.

Dr. Max Hamburger
So I've gotten to see rheumatoid arthritis management evolve remarkably. When I first started in practice, we had Prednisone, we had two drugs that barely worked deep penicillamine and gold salts. Then we jumped over to ACE the Fire print, which didn't work very well. And then in the early 80s, we saw the advent of methotrexate. And then in the late 90s, we moved to targeted therapies that were developed based on a.

Dr. Max Hamburger
Understanding of the pathobiology of rheumatoid arthritis with the advent of the biologics, the outcomes for this disease changed incredibly and it now becomes very hard to show trainees what bad women told arthritis can look like because eventually we can get many patients under good control.

Dr. Max Hamburger
But we can't get them all under adequate control to the extent that there are issues that occur to rheumatoid [inaudible], which are quite serious, and rheumatoid arthritis itself, rarely is a fatal disease. There are a few things that can happen to rheumatoid [inaudible] which can be fatal, cervical spine disease. But the death of death rates in rheumatoid arthritis patients are way above their colleagues of similar age because of comorbidities. And one of the consequences of inadequately suppressed chronic inflammation is cardiovascular disease, and that an infection remains very high on the list of causes of death of our patients so.

Dr. Max Hamburger
We still are in a situation where a large percentage of patients end up disabled because of the effects of their disease and the comorbidities, and so we have the conflict of far greater efficacy and safety in many of the drugs we use. But as yet many patients not yet getting on to the right drug at the right time because we have not had markers. That said, this is the drug to use for this particular patient.

Dr. Max Hamburger
We currently go more or less in one of two directions. We go historically, and that is that the TNF inhibitors came out first. So, we tend to use those first. We became familiar with them, they had efficacy. So, we were impressed and many managed care companies and this is critical have adapted an approach where the first drug has to be a TNF, sometimes the second drug has to be a TNF. The so-called JAK class cannot prescribe for patients who have not failed at least two TNF.

Dr. Max Hamburger
Yeah, [inaudible], even if those aren't the best drug for the patient.

Dr. Max Hamburger
And so we need now to look for approaches to the management of related arthritis that bring precision medicine capabilities to our toolbox.

Dr. Max Hamburger
Dealing with the biology of rheumatoid arthritis, trying to assess disease activity on a molecular basis and trying to tease about the different phenotypes of rheumatoid arthritis because what looks like rheumatoid is not always the same thing, particularly when one looks at where the disease actually is. And that is in the synovium the lining of the joint where we can find multiple different phenotypes of rheumatoid arthritis that to the outside look very, very similar.

Dr. Max Hamburger
One might say, well, you know what? What's wrong with you? [Inaudible]. And what's wrong with your science? You've had these biologics for 25 years, and you still don't know what to do, and it is not at all for lack of trying. We have remarkable scientists, Peter Gregersen, at the Feinstein at Northwell on Long Island, who's done probably Nobel Prize winning work on the genetics of rheumatoid arthritis. We have Costantino Pitzalis and others.

Dr. Max Hamburger
In Europe, looking now at synovial biopsies to see how that plays out, and there have been hundreds and hundreds of papers looking at different biomarkers to see if what's in the blood tells us anything. So at this point, I think my colleagues and I would probably agree that what's in the blood is by no means sufficient.

Dr. Max Hamburger
And maybe we're going to get on to looking at synovial biopsies over in the future as a way of guiding, but I think all of us would agree that subjecting every patient with rheumatoid arthritis to a synovial biopsy every time treatment choice was going to be made would be an invasive procedure that we would prefer not to have to compel our patients to do. None of us are really trained to do that. So, there's been an enormous amount of work.

Dr. Max Hamburger
That has culminated as a first measure in the Prism-RA test. I think that I first learned about this test…four or five years ago at the Congress of Clinical Rheumatology. So, I've watched the company and the science of this mature in a dramatic fashion to the point that now, as others have pointed out and as the references can speak to the Prism-RA test can tell us with a great deal of reliability who will not respond to the TNF inhibitors. And so, if we have a 90 percent likelihood that the result of the Prism-RA test is correct and that the patient so pointed out will not respond to a TNF inhibitor, we skip that class of drugs and we go on to the other drugs that are there. Now some people have said, well, maybe the Prism-RA test just points at patients who don't respond to drugs. But the studies are very clearly shown that is not correct.

Dr. Max Hamburger
Because these patients do respond in an enhanced way to abatacept, which is a T-cell modulator, or Tocilizumab and sarilumab, which are inhibitors of IL-6, or to rituximab, which is a B-cell inhibitor, or to the JAKs, which work on intracellular mechanisms. So, the response to those drugs is all enriched if one

looks at the TNF in the non-responder because now we have not wasted six months to a year trying to get patients to respond to drugs that they are biologically not programmed to do.

Dr. Max Hamburger
Why is it so important to get patients on to the right drug first? Because damage occurs quickly in the first several years. Disability accrues when patients are not on the most effective drug, and the seeds are sown for cardiovascular comorbidities, which again are the comorbidities that eventually lead to the enhanced mortality in a patient with rheumatoid and as well the worst 10th deciles of patients with rheumatoid arthritis we know has a marked increase at 25-fold increase in the risk of lymphoma, so we need to move our patients from the worst deciles and the worst quartiles into the lowest quartiles and deciles because those are the patients where the disease will not get them, and the comorbidities will not get them.

Dr. Max Hamburger
There aren't enough rheumatologists. This is another critical point in looking at wasted time. So in most communities, the wait to see a rheumatologist as a new patient may be two to three to four to six months, and in the parts of the country which are more rural, a patient may have a 150 mile drive to get to see a board-certified rheumatologist. And so, if you're talking about the Western states in particular, like Idaho and Montana and the Dakotas, etc., there may be eight or 10 rheumatologists across the state. That's 500 miles wide and 300 or miles or 400 miles north to South. So, the physicians are overworked. The patients face enormous obstacles in getting care, and the last thing that we want is for a patient to have to travel 150 miles repeatedly because the physician has to examine that patient.

Dr. Max Hamburger
And the right drug cannot be chosen at the right time. I think the statistics are there, that the inadequate supply of rheumatologists probably is at about the 40 percent or so mark we have 40 percent fewer than we need. And so, we need to optimize our time. We need to accelerate the patients getting on to the correct drug at the right time. We need to be able to push back at a PBM and specialty pharmacy-contracted guidelines which necessitated TNF inhibitor perhaps first and second before we go to another drug merely because managed care contracting on behalf of a company manufacturer has struck a deal with a PBM or a specialty pharmacy where no pathway and no science has anything to do with it.

Dr. Max Hamburger
Is the Prism-RA test perfect? No, we need to do better. We need to extend its observations to see what are the predictors of response or non-response to other drugs. The algorithm needs to be trained further and, I'm sure with more work and expanded studies and knowing the scientists who are involved in developing this, the algorithms will be trained further so that the sharpening of the pencil will become more and more fine, and we will know.

Dr. Max Hamburger
Which patient is most likely to respond or not respond to drug ABC&D? And so, we can take these biological marvels we have and treat these patients in the most effective way. So, I am entirely puzzled when I see how the Prism-RA test was lumped together with data from, for example, cost that SALAIS [inaudible] doing groundbreaking work looking at synovial biopsies.

Dr. Max Hamburger
But [inaudible] is years away from being ready. He has thousands of samples, or hundreds of samples, at least sitting in tissue banks that he has to continue to analyze. Having spent a year and a half working with costs, trying to see if we could help him advance his data, it became very clear that the fruits of his remarkable work and his colleagues in Europe will take another three to five years to come to the point where they are useful, will they very likely be enormously useful.

Dr. Max Hamburger
Yes. Are they ready for use in the clinic tomorrow? No. Is the Prism-RA test ready for use in the clinic tomorrow? Yes. And so, of the three markers that were considered and blocked, I think a that that was a strategic mistake. I'm sorry if that offends anybody, but sure, nobody made this mistake on purpose. But we lumped together multiple different modalities which are very, very different and in completely different stages of evolution.

Dr. Max Hamburger
There are multiple publications on the Prism-RA test in peer reviewed journals that include as authors some of the most prolific and well-known investigators in molecular biology and rheumatology that the strand, Jeff Curtis, Stan Cohen list, goes on and on and on. These are some of our, you know, decades in clinical trial researchers who have looked at the data here and the data has spoken so.

Dr. Max Hamburger
As somebody who goes back to the office on Monday, well, I won't be going back to the office this Monday, just as a side note, I always like to find out what my patients are going through. So, this Monday I've chosen to have my right knee replaced. So, if my patient gets a knee replaced, I'll be able to say, hey, you know, I did that. So, I'm glad to have been able to squeeze this in before I go under the knife on Monday. But when I come back two or three weeks later, I face 25 to 30 patients every day, four to five new patients every day. My practice sees 5,000 new patients a year of whom probably 2,500 have RA. We can do a great job. Now we can do a vastly better job with the precision medicine tool. And so, I strongly second and stand with my colleagues. I know Dr. Feldman for decades and her dedication to advocacy.

Dr. Max Hamburger
The tireless energy that she has put in, with no compensation going to Washington, testifying. All of us are very robust patient advocates because we've watched the damage that can occur. And then we've seen now, what the good is that we can do as a closing remark. Why did I go into rheumatology when I was 13? My father spent a year with a mysterious illness that nobody could decipher. He underwent muscle biopsies he underwent hundreds and hundreds of different kinds of tests, and after several years he finally was diagnosed as having A and A-positive rheumatoid factor, negative rheumatoid arthritis. He was a smoker. We now know that was a risk factor. He didn't have the best dental hygiene. We know that was a risk factor. He died at the age of 70. In that 10th decile of lymphoma, before we had started to use methotrexate. So, I went from having a dad that could toss the ball around to me to a dad who was disabled from a very, very early age. Now I have the opportunity to never have my patients have that happen if I have precision medicine available to me. So, in my dad's name and in the name of all of the patients that we all treat, I would strongly urge your organization, which I'm sure is trying to do the right thing, to reconsider and extend authorization to payment for the Prisma-RA test.

Dr. Max Hamburger
But I went a little fast. I'm sorry. Just wanted to make room for my colleagues.

Dr. Angella Charnot-Katsikas
Alright, thank you very much, Dr. Hamburger. We're going to circle back again. Let's see. Is Dr. James Mossell on the line? Dr. James Mossell. Dr. Priya Reddy? We'll try again at the very end. So, our next speaker is Dr. Robert Levin of Bay Area rheumatology, Dr. Levin. Dr. Levin, are you on the line? We'll circle back to you as well.

Dr. Angella Charnot-Katsikas
And our last presentation, our last scheduled presentation is by Dr. Sam Asgarian of Scipher Medicine Dr. Asgarian.

Dr. Sam Asgarian
Perfect. So, we at Scipher, our very appreciative of the opportunity to present at the public meeting today.

Dr. Sam Asgarian
We are, however, understandably disappointed that Palmetto GBA has decided not to cover our test as part of the draft LCD and look forward to continuing to work with you to further support our coverage application and thereby provide this vital test to Medicare beneficiaries. Very briefly, I want to introduce myself a little further as it relates to both precision diagnostics and clinical coverage. I'm an internist by training and background and spent the greater part of a decade at Aetna and then subsequently CPS Health helping run both utilization management and care management as well as our clinical policy operations that covered both the commercial lives as well as the Medicare Advantage lines of business.

Dr. Sam Asgarian
And then I moved to the world of precision diagnostics and screening solutions as Chief Medical officer of Thrive Earlier Detection, helping that company achieve a formal protocol agreement letter with the FDA as well as launch an LDT pathway for its machine learning classifier-based blood test detecting cancer that was incorporated and integrated into the exact sciences pipeline where I helped build out a further flesh dot product roadmap for earlier detection and screening solutions.

Dr. Sam Asgarian
I'm now leading similar efforts here at Scipher Medicine and my goal is a practicing and then as a non-practicing physician has always been to bring more preventive and curative care delivery solutions to healthcare so that physicians can spend time detecting and mitigating the risks and adverse events that come from diseases and disorders such as rheumatoid arthritis.

Dr. Sam Asgarian
Towards that end, today I'll be providing a brief introduction and background to our company and our blood test Prism-RA, which is continued to gain adoption by the rheumatology community. As noted today in parallel with the progression and continuation of the studies that use our precision medicine test to first previously establish and now further confirm the validity and utility of the test.

Dr. Sam Asgarian
I will conclude with similar sentiments as those shared by his team. Specialists at this meeting regarding the need for this test within the rheumatology specialty.

Dr. Sam Asgarian
So our company side for medicine is focused on providing physicians like those today with the right tools and solutions to deliver precision-based care to their patients. Doing so helps achieve the critical aims of improved outcomes, lower costs and more efficient healthcare delivery, similar to what we've seen occur in the diagnosis and treatment of cancer patients. Today we combine the capabilities and machine learning with the advancements and next generation sequencing to help physicians learn more about the underlying Physiology of their patient's immune autoimmune diseases.

Dr. Sam Asgarian
The test you're discussing today is already experiencing large, [inaudible] option across the country throughout the United States, physicians and their practices as a whole have been ordering our test given its utility and necessity in the care of patients. Many of those patients are, and have been, covered by Medicare and, as such, our goal is to continue to work collaboratively to improve access and coverage of the test as we are doing today by providing an objective data point to rheumatologists. Our test captures and conveys information about the DZ pathology.

Dr. Sam Asgarian
Not capable of being measured by current metrics or exam techniques, patients can then receive an appropriate treatment sooner and with more robust outcome results.

Dr. Sam Asgarian
This is the most important area that I want to cover today, right? So, what we really have been aspiring to do is build this body of evidence. This clinical world of studies that have shown validity and utility our tested, the intended use is for both naive and previously exposed to tumor necrosis factor inhibitor therapy patients. We've been seeing the study findings capture and proved outcomes across the patient populations and increasingly greater numbers. We have developed an extensive body of evidence that depicts the value of the test and the objectives we achieve when it comes to predicting response to TNF.

Dr. Sam Asgarian
Size and the overall improvements outcomes that come with it are test has been validated both retrospectively across approximately 600 patient samples and prospectively across another approximately 1,500 patient samples.

Dr. Sam Asgarian
As you can see on this slide, we have three groups of clinical utility papers moving and increasing number of N from 85 to 478. What's important for me to note is we really rarely ever drop out patients after they've been rolled due to the low invasiveness of our test, as well as just the simple need to have them follow up with their rheumatologists, who continues to manage their care predominantly as the primary quarterback. But they should stay enrolled. What you see here is the typical maturation of outcomes.

Dr. Sam Asgarian
Data at the very beginning of clinical utility paper number one in December, we had fewer patients achieve six-month outcomes [inaudible] than they did in April, when clinical utility paper number two was published. Then, they do now, and clinical utility number three has been pending publication. Knowing this, we've always worked closely to further validate the end points that these end numbers

show. So, when we originally published paper number one, we used ACR 50 as our endpoint and we showed considerable improvement in the [inaudible] that received our test.

Dr. Sam Asgarian
And care was followed based on the results of the test when it came to achieving ACR 50 in a six-month period. We heard loud and clear from this same position community, who has spoken today that ACR 50 isn't always the best metric used in clinical practice. They advocated that we look at SDAI scores and measure a primary endpoint using SDAI. The second paper did that and concluded at 1.8 times greater reduction in overall SDAI high score as noted by Dr. Solomon. Guideline-based care focuses on truth to target, not simply a reduction in the metric but moving those patients from a category of high and moderate disease.

Dr. Sam Asgarian
To a category of low disease activity in remission, as noted by Dr. Hamburger, our goal is to really allow for the rheumatologist to focus on the sickest patients and to triage them appropriately as they come to the clinic. The third paper, which will be published very shortly, looks at that as compared to standard of care and showed that using precision-based medicine and our test Prism-RA resulted in up to 2.6 times greater odds of receiving or reaching that low disease activity and remission state.

Dr. Sam Asgarian
As a quick side note, I want to also note that it's important for us to make sure that this focus is on the patients who are eligible and receive Medicare, looking only at the 65 and up eligibility criteria, and not the disability eligibility criteria. In our first paper, I'm happy to report that of that 8,519 of them were 65 and older and therefore eligible for Medicare of the 274 and the second paper 71. We're 65 and older and therefore eligible for Medicare and in the third paper of that four 78,178 reliable.

Dr. Sam Asgarian
Now those are simply demographics. That's just based on age of eligibility. As we delve deeper into it, we know that this disease predominantly impacts women more than it does men. The majority of these Medicare-eligible patients were women. In fact, of the 19 in the first paper, 16 were women. Of the 71 in the second paper, 59 were female. And of the third 478 in the third paper, 143 were female. And I'm also happy to report that [inaudible] the total Medicare eligible by age [inaudible] only population within our studies.

Dr. Sam Asgarian
Approximately 20 percent were of a minority status. That further shows to us that this test is being adopted and continues to see great integration not just in clinical practice but across the wide spectrum of individuals who are afflicted by rheumatoid arthritis, especially across our heterogeneous country. In the demographics that we see within the United States.

Dr. Sam Asgarian
Now I'd like to spend a little bit of time, but not too much on each one of those papers. Primary endpoints on the first scenario, I'd like to specifically start with what we believe to be a key misinterpretation of a result related to the utility of the test on the first paper, what we noted and what you see at the bottom of the slide is that Palmetto GBA is rationale for non-coverage in the determination of this test.

Dr. Sam Asgarian
Said that, for example, in the molecular signature response classifier studies, the response to [inaudible] in the predicted non-response group should have exceeded that observed with tumor and across this factor inhibitors at baseline. But it did not. We were surprised at this, and we considered a misinterpretation because this is truly one of the primary and secondary endpoints of the paper as we've brought here the predicted non-responder group that still received tumor across this factor inhibitor because his Dr. Feldman pointed out the rheumatologist is still the quarterback and the care of these patients and makes the final call as to what therapy they receive.

Dr. Sam Asgarian
Our job is to report the outcomes and show that the outcomes are improved when they receive the therapy that our test made better indicate the absolute baseline CDI score for this population was 30.8 over the average of the group for the Alt Moa receiving group that again received a predicted nonresponse signal. It was very close which we expected it to be at 32.4. But when we look at the results between the two, the primary endpoint again was ACR. Only 10 percent of those that were predicted non-responders that received 200 process factor inhibitor therapy.

Dr. Sam Asgarian
Achieved an ACR at six months, more than threefold. That patient population at 34.8 percent achieve the ACR at 50 at six months on an alt mechanism of action drug. If we simply look at CDI as well, which we did in this paper and maybe reported it out as a supplemental or additional endpoint, the group that received the Alt MOA, it's experienced a 1.8-fold, greater improvement in CDI scores than patients with a molecular signature treated with that tumor and Persis factoring Peter.

Dr. Sam Asgarian
We believe this is critically important because the potential misinterpretation of these data points led to a train of art of logic used to argue against the value of the Prism-RA test in comparison with current standards of care, which we found surprising because the evidence we have been generating has established the exact opposite conclusion in further support of that, as you see, our second papers primary endpoint, when we look now at C dive, we saw that regardless of whether it was 200 costs factor inhibitor therapy.

Dr. Sam Asgarian
For an old mechanism of action, when the test results were followed in clinical practice, the patients achieved better outcomes and they're achieving them faster than they would through the traditional and empirical and sequential or trial and error approach to the limited arthritis treatment and therapy.

Dr. Sam Asgarian
Then we also have covered this with Palmetto GBA, and I believe secondary just to the fact that we know there's a need to stop reviewing at some point in time. This paper was not a part of the overall decision we will resubmit this through the formal comment period and we look forward to it being incorporated as part of the review into the final draft coverage decision.

Dr. Sam Asgarian
Which you see here ultimately is in this group where you got a predicted non-responder that again receives a tumor necrosis factor inhibitor therapy. There's SDAI reduction over the course of 6 months was lower than the group that did not have that signal that still received 200 crisis factor inhibitors so

again when the physician has a more confident ability to prescribe that same drug their patients do better knowing that the test result was an objective data point that allowed them to prescribe that trip when they receive a different drug.

Dr. Sam Asgarian
When there's significant.

Dr. Sam Asgarian
Signal with nonresponse. Again, those patients do significantly better, statistically significant, and a paper that was published in peer reviewed standpoint, again with a higher end number where we did see a fair number of Medicare eligible patients.

Dr. Sam Asgarian
In addition to this, paper will also be submitting for consideration in this formal comment period. Our next paper, which now stops looking at simply a comparison or a comparator of our test when it's followed and when it's not in clinical practice, but actually compares our test to a standard of care control arm in a very large or higher number of an end value. When we looked at this and we looked specifically at this row again from a treat to target standpoint, it's statistically significant group of patients were reaching low disease activity or remission.

Dr. Sam Asgarian
When the molecular signature response classifier test was used as part of their therapy and treatment, then when the traditional trial and error approach to treatment was used, this again occurs in a very short period of time in 180 days of a readout. These patients are getting to low disease in remission, so again to Dr. hamburgers point that allows the specialist to spend far more time seeing new patients or seeing their patients faster because now you have more security knowing that your patients are well managed and on a maintenance mode.

Dr. Sam Asgarian
That's our ultimate goal. So, while we will be submitting more comments and more papers throughout in the formal comment submission period, I just want to spend a little bit more time in the interest of time today on the validity and utility of the test as well as its medical necessity.

Dr. Sam Asgarian
After listening to and rereading the transcript from the contractor Advisory Committee meeting on December 7th of last year, we had said from medicine were surprised to hear that the contractor believes that tools and metrics are already available to practicing physicians and that the utilization of hypothetical combinations of these metrics and values would provide predictive power and improved outcomes comparable to that of our test.

Dr. Sam Asgarian
The physicians and advocacy groups that are previously supported archaeology coverage application have continued to provide their expert viewpoint refuting this belief. We additionally have published studies and conducted analysis as our evidence generation has matured, which shows that clinical features alone do not provide the same capabilities, efficiencies and improved outcomes as genomic features that capture the underlying pathology of this complicated disease. The combination, of course, is what works best.

Dr. Sam Asgarian
As it allows the physician to incorporate all available information based on the patient's presentation to prescribe the most effective treatment targeting the underlying disease pathology. These studies and subsequent analysis will be submitted to Palmetto GBA during this open comment period, and we are looking forward to discussing them after this blackout period concludes.

Dr. Sam Asgarian
Lastly, as a physician myself, I fully understand the value of these tests in the need to provide coverage for them so that they can be made available to patients. As Dr. Feldman noted, as previous primary care provider and someone that advocates for preventive medicine, knowing that you have proactive data-based disease management as one of the highest forms of practice that a physician has at his or her available disposal, especially for a disease where we know that today our eight patients suffer from debilitation due to irreversible joint damage.

Dr. Sam Asgarian
Sometimes it's treated with the most invasive surgeries and procedures ultimately still leading to permanent handicaps and a decreased quality of life. Even when these patients adhere to and stay compliant with their prescribed treatment measures with Prism-RA patients can avoid treatment. They are unlikely to respond from and get on the right treatment sooner. I believe that members from that same contractor Advisory Committee from December 7 along with these additional providers. Experts, caretakers, and specialists have provided facts data and evidence in support of coverage for Prism.

Dr. Sam Asgarian
Right, as well as other molecular signature response classifier tests as they have been throughout this review period.

Dr. Sam Asgarian
As such, I will now conclude our presentation and defer to the rest of the presenters for their perspectives, experiences, and conclusions. Thank you again to Palmetto GBA on behalf of Scipher medicine for the opportunity to present today.

Dr. Angella Charnot-Katsikas
Great. Thank you, Dr. Asgarian, for your presentation. We do have still a few of our speakers or are planned speakers that were not able to present. We want to see if you are now on the line Dr. James Mossell. Have you now joined this conference? Dr. James Mossell. All right, Dr. Priya Reddy. Dr. Priya Reddy. OK. Dr. Robert Levin.

Dr. Robert Levin
Yes, I'm here.

Dr. Angella Charnot-Katsikas
Ah, I see you there. Perfect. OK, wonderful. Dr. Robert Levin of Bay Area Rheumatology, please go ahead with your presentation.

Dr. Robert Levin
Thank you very much and I really appreciate the opportunity to speak for speak with you today on something that I really feel is an advance in rheumatology and would really be a shame if it was not

something that was available to Medicare beneficiaries. Let me pull up my slides and I'll be right with you.

Dr. Robert Levin
Alright, well, let me start. So, first slide is just about me. I am a practicing rheumatologist in the Clearwater, Fla. area and I've been here in practice for over 30 years.

Dr. Robert Levin
I've been I'm a board-certified rheumatologist and I've got several faculty appointments, including an assistant affiliate professor of medicine for the family practice, as well as room, residency, and rheumatology fellowship as well at the University of South Florida.

Dr. Robert Levin
I am a medical director doing clinical research and I've been involved in doing clinical trials with Prism-RA. I'm a fellow member of the American College of Rheumatology and American College of Physicians. I am on the Board of directors of the Coalition of State rheumatology organization, Florida Society of Rheumatology.

Dr. Robert Levin
And I'm on the Board of directors of our medical Super group, the American arthritis, and Rheumatology Associates.

Dr. Robert Levin
So I have a wealth of experience utilizing this test, it has been something that I've tried to incorporate into my practice. And I found I have found that it's been incredibly useful.

Dr. Robert Levin
Therapy selection for patients with RA is often driven by payer criteria and rebates. This is really in terms of Medicare beneficiaries, applies much more to Medicare Part D than to Medicare Part B, where in Medicare Part B beneficiaries we have the option to choose any covered medication as long as it's we following the LCDs for the drugs that are being given, so we have the opportunity to pick what we think is best for the patient using shared decision-making. And I think that that's obviously the ideal for us is that we really like to have the opportunity to figure out what's best for our patients. But honestly, when payer criteria come in, a lot of it is driven by finances and not necessarily what the patient or the patient and the Dr. feel are most important.

Dr. Robert Levin
Clinical guidelines do not recommend one biologic class over another and, simply put, I think in the last presentation we saw that without having a test like Prism-RA, we really can't figure out which drug might be best. Just looking at the clinical trials and trying to line them up side-by-side — obviously, you can't compare.

Dr. Robert Levin
A drug efficacy or drug safety?

Dr. Robert Levin
Formally looking at one at patients that are enrolled in different studies, but we do that, and we try to pick out based on the patient's individual characteristics what might be best and that's. And so, the

guidelines have been unable to come up with a recommendation for one because all of the FCC data and pretty much for the safety information looks fairly similar in the clinical trials of.

Dr. Robert Levin
The drugs. So, there are a number of drug class options with comparable efficacies for rheumatoid arthritis. The most common class being the TNF inhibitors, which we [inaudible] by habit because they've been on the market the longest, and also based on drug formularies. We tend to pick first, but that does not necessarily mean that that's the best drug for that individual patient. And the Prism-RA test, as I think was demonstrated very clearly in the last presentation shows that if we can use a test that actually will help us predict lack of response to a TNF inhibitor, that's something that's incredibly valuable.

Dr. Robert Levin
Because we know that in rheumatoid arthritis, getting a patient to low disease activity and remission earlier using the right treatments will lead to better outcomes, less joint damage, better function, and an overall increase in patient satisfaction.

Dr. Robert Levin
Patients who do not respond to their in initial targeted therapy are less likely to respond to subsequent lines of targeted therapy, and that's especially true if the patient does not change the mechanism of action of the drug that they're using. So, if we've gone to targeted therapy and we start with a TNF inhibitor and we then are obligated to use a second TNF inhibitor, which is commonly seen in drug formularies by insurers and Medicare Part D.

Dr. Robert Levin
Then we are less likely to see a good response than if a patient changes their mechanism of action. Unfortunately, we don't always have that choice because again, its pair driven and it's driven by finances and rebates rather than efficacy, safety, and what might be best for that individual patient.

Dr. Robert Levin
So there is a lack prior to the Prism-RA, there's been a lack of tools to guide effective RA treatments. Rheumatologists don't have tools that are able to tell us which targeted therapy are patients will or not will not respond well to, and you can't. I'm sorry, but you cannot use rheumatoid factor. CCP antibody, SED rate, CRP, joint counts. Any other metric that we have does not indicate which type of therapy, which mechanism of action might be the best for that individual, and, prior to the development and approval of Prism-RA, we have not had such a tool. I think that the data that's been presented that was presented during the last talk clearly showed that using that Prism-RA, we are much more likely to get a favorable response initially which is so important for our patients.

Dr. Robert Levin
Biomarkers are required in-order to predict response in RA and [inaudible] is a heterogeneous disease and some patients respond to certain drugs, and some don't. And I think that Prism-RA really takes that into account. The 23 different pieces of information, whether they're biologic, a genetic information or their clinical information, when that's all combined and we come out with a Prism-RA score that really helps us guide who is like more likely or less likely to respond to a TNF inhibitor therapy which, like I said, is the most commonly used biology class. And oftentimes the drug that is used first. If I know that a patient has a low likelihood of responding to a TNF inhibitor by the Prism-RA test, then I am likely and

almost certainly going to choose a different mechanism of action in that patient because that patient's more likely to respond to something else and the TNF inhibitor is less likely to be effective. And like I said, that's an outcome that we both the physicians, the medical providers and the patients are looking for.

Dr. Robert Levin
We need to get patients on the right drug early at in their diagnosis to reach, treat to target goals of low disease activity and remission and prevent debilitating, often irreversible long-term damage for the patient. We know that long term damage to the joints occurs early in the course of the disease and getting the patient on effective therapy that is effective for that patient is the best way to prevent damage and ultimately lead to the best outcome possible.

Dr. Robert Levin
And Prism-RA is a critical tool that we have that's available right now that should be covered. That's something that can help us achieve that goal.

Dr. Robert Levin
Repeated medication changes also expose our patients to significant adverse events with limited benefit and all I can say about that is that there are studies out there showing that when we have to change drugs, especially switch patients off of medications that are effective, there are increased adverse events. Many more doctor visits, many more hospitalizations, many more complications.

Dr. Robert Levin
And that's based on formulary changes and things that really can negatively impact our patients. And so, we need a tool to tailor therapy based on the patients, individual disease biology for rheumatoid arthritis. And I think that Prism-RA really speaks to that really has achieved the goal and with the increased amount of data that's been published and is to be published in terms of the large-scale clinical trials that have been read out and are in process. I think that the more data that comes out, the stronger and the better this test looks. So, with that I have a list of references on this slide, I'll conclude. Thank you very much for your attention. I'd be happy to answer any questions.

Dr. Angella Charnot-Katsikas
Thank you, Dr. Levin. As we mentioned earlier, we don't have the opportunity for a Q&A, but everyone is welcome to submit their comments to Palmetto GBA as part of the comment period. Let's see. I do see. I believe Dr. Priya Reddy has joined. Wonderful. So, Dr. Priya Reddy of the Florida Society for Rheumatology. Please go ahead with your presentation.

Dr. Shanmugapriya Reddy
OK, wonderful. Thank you all for being here and allowing me the opportunity to speak. I'm just going to…share my slides. Yeah. Let me know if you're able to see my slides.

Dr. Angella Charnot-Katsikas
Yes, we see them.

Dr. Shanmugapriya Reddy
OK, wonderful. So, my name is Priya Reddy. I'm a practicing rheumatologist in Riverview, Fla. For those of you who are not familiar, this is in Hillsborough County and the greater Tampa Bay area. I wear a lot of different hats professionally. I'm an assistant professor in the division of Rheumatology at USF brand

of Regional Hospital. I'm also on the Board of Directors with Dr. Levin for the American Arthritis, Rheumatology Associates and Secretary, treasurer of the Association of Women in Rheumatology.

Dr. Shanmugapriya Reddy
And I want you today really sort of focus on the most important hat that I wear, which is providing patients with diagnosis and treatment and providing the best care that I can for my patients because that really is what drives all of the other professional goals that I have, to provide them with a scientific basis for their diagnosis and their treatment as well as optimized the patient journey of chronic illness, which in rheumatology, encompasses diseases that are really poorly understood on the best of days. They are under-diagnosed as a result of that, and they're under-treated as a result of that. And today I'm going to focus obviously on rheumatoid arthritis and I'm going to talk about how the Prism-RA test effects and improve specifically that under treatment aspect of our diseases.

Dr. Shanmugapriya Reddy
So we really do need precision medicine tools in therapy selection for our patients who have rheumatoid arthritis. This is really important. The time is now to use the tools and the science to move forward in rheumatoid arthritis and to allow us to use these tools to optimize this patient journey. Remember that when a patient is diagnosed with rheumatoid arthritis.

Dr. Shanmugapriya Reddy
This is for the rest of their life, and when I told you earlier about the misdiagnosis, this is someone that we see in our clinic who is a patient who's been struggling with joint pain, disability, a lot of stiffness, possibly already damage to their joints because it's taken a really long time for them to get this diagnosis. So, when they come and see us, it's really important for us to treat them and treat them on target with the right tools quickly and the ACR American College of Rheumatology really doesn't specify that we need to do one targeted therapy over another one. Once a patient has tried our gold standard, which is methotrexate. And typically, patients who we move on past methotrexate therapy are people who are in moderate to severe rheumatoid arthritis disease activity. So, these are people that are quite active with disease and carry a large disease burden.

Dr. Shanmugapriya Reddy
Already we do know that if they fail, that first targeted therapy, they're less likely to respond to the next targeted therapy. This has really been shown quite clearly in the literature, and Dr. Levin alluded to that earlier in his talk and what winds up happening is that we have this trial-and-error approach where we look at specific therapies, we select doses, we change until we find that right fit.

Dr. Shanmugapriya Reddy
And meanwhile, the patient is experiencing a lot of side effects of different medications that probably were not the right choice for that patient. And they have cycled through medications while disease is active and ongoing. So, Prism-RA really fills this gap here. And what we've seen in studies done so far is that patients who were prescribed to treatment that was aligned.

Dr. Shanmugapriya Reddy
With that Prism-RA result had a significant improvement in their clinical response rate, and this was more than three times higher when therapy was not aligned with the test results. And what we know is, as I said earlier is that if patients have an inadequate response to their initial targeted

immunomodulator, they are less likely to respond to the next one. And as I said, this ongoing disease activity, debilitation.

Dr. Shanmugapriya Reddy
Is obviously going to increase a healthcare utilization, medical costs and indirect costs due to patient being unable to work and work loss. So just to summarize what I want to highlight again is that these are patients who have already a moderate to severe, they have ongoing disease activity. They've tried methotrexate. What does this mean to the patient? They cannot take care of their families. They cannot take care of themselves.

Dr. Shanmugapriya Reddy
So they Need their family to take care of them? They cannot work and continue to be employed. And if we think about this one person and that burden of disease for however long it takes to reach targeted therapy, we're really seeing a much larger economic burden to the community and not to mention that this ongoing disease activity causes inflammation and active destruction of their joints, which then obviously only leads to more disability. So, if this patient is able to get a Prism-RA test and we're able to align the treatment selection with that result. What happens? We get a much quicker reduction in disease activity, which then is obviously going to improve these symptoms that the patient is having, not only of pain and destruction of the joints and disabling inability to use the joint, but also fatigue and stress, you can imagine that someone going through this is experiencing a considerable amount of fatigue and stress and now this patient has an appropriate targeted therapy based on that Prism-RA result, they can complete adls care for their family, return to work and obviously we're able to really put out this fire, so to speak or at least lessen the flames of the fire of inflammation and reduce their inflammatory burden. So, this is clearly a task that's based in science. And as physicians, we want to utilize science to improve the patient journey and provide better care for our patients. So, thank you very much for your time and I so appreciate you giving me the opportunity to speak. Thank you.

Dr. Angella Charnot-Katsikas
Thank you Dr. Reddy for your presentation. All right, so we are now going to circle back once again and see if Dr. Mossel has joined. Dr. James Mossell. All right, with that, that actually could include the formal presentations that we have received. But we do have a number of physicians who have reached out to provide a few comments. And so, we have five minutes allotted per presenter here. So, we have first on our list, these were late comers and didn't make the, and didn't make the agenda. So, Dr. Gwenesta Melton, are you on the line?

Dr. Gwenesta Melton
I'm on the line. Can you hear me?

Dr. Angella Charnot-Katsikas
Yes, we can hear you.

Dr. Gwenesta Melton
Thank you. My name is…

Dr. Dr. Angella Charnot-Katsikas
Thank you. Please go ahead with your with your discussion.

Dr. Gwenesta Melton
My name is Dr. Gwenesta Melton. I'm the current vice president and co-chair of advocacy for the Association of Women in Rheumatology, also known as aware. I've been a practicing rheumatologist for 34 years in North Carolina, aware is dedicated to promoting the science and practice of rheumatology, fostering the advancement in education of women in rheumatology and advocating access to the highest quality health care and management of patients with rheumatic diseases.

Dr. Gwenesta Melton
Our Rheumatology members across the country, including members across the globe in over 30 countries, are committed in helping find a solution to the continuous rise of out-of-pocket costs and access challenges for our patients. This includes supporting new technologies like precision Medicine Aware was disappointed to learn that Palmetto GBA determined that clinical validity was not yet proven for Rheumatoid Arthritis.

Dr. Gwenesta Melton
These innovative tests have begun to allow members of aware and other rheumatologists to better identify the right medication at the right time. As you know, trying and failing, medications can have a lasting impact on patient's disease, stability, and an association with increased cost to the healthcare system, even in the exciting therapeutic era of biologic disease, modifying antirheumatic drugs, most patients fail to achieve the desired high-level response equivalent to low disease activity or remission and almost 40 percent of all patients treated with biologic Dmards do not even experience minimally acceptable improvement. This means individual patients are treated sequentially with different drugs selected using little mechanistic rationale. As my colleagues have alluded, consequently leading to increased costs, unnecessary toxicity and sub-optimal effectiveness.

Dr. Gwenesta Melton
Knowing the struggle to find the right medication at the right time for RA patients is more important than ever to consider the precision medicine data in support of predictive testing in RA. This would include all supporting clinical evidence that Palmetto GBA may not have taken into consideration before issuing the negative determination, or where is committed and working with Palmetto GBA and helping provide rheumatologists with a new innovative tool that says patient from the trial in failed gauntlet while providing an overall cost savings to the healthcare system. We urge you to implement a policy that provides for access and reimbursement from molecular biomarker testing to guide targeted therapy and RA.

Dr. Gwenesta Melton
We appreciate your consideration of our viewpoints and encourage you to contact us directly should you have any questions and thank you for my ability to share these comments.

Dr. Angella Charnot-Katsikas
Thank you, Dr. Melton, for your comments. Next on our list, we have Dr. Greg Niemer of Low Country Rheumatology, Dr. Niemer.

Dr. Gregory Niemer
Yes, thank you very much for allowing me to be able to speak. I appreciate it.

Dr. Gregory Niemer
I want to thank all of my colleagues who've already spoken and made some very good points. I'll, I'll try to be focused on my rheumatologist. Have been in practice for over 20 years in Charleston, S.C., I've served on our state Rheumatology Society Board, both on the education and the advocacy side and part of a large single specialty Rheumate, logy practice and also a large single specialty group purchasing organization.

Dr. Gregory Niemer
And have been and have the have had the privilege of taking care of, my gosh, 1,000 rheumatology, rheumatoid patients, over the past 20 years. And the importance of looking at this test I think can't be overstated and we've done a fantastic job within rheumatology field over the past 20 years of aggressively treating our RA patients to the point that through getting them on medications such as methotrexate, and then moving to biologics and using treat to target, we're able to achieve remission and low disease activity and a large percentage of our patients are. Our challenge continues to be that that first decision as far as which file logic to use and this is very important because we know from data that that window for achieving [inaudible] disease activity or remission in our patients is not long. If you look at data, if patients have active disease for six to 12 months, then they're their chances of receiving or achieving low disease activity or emission drop considerably. So, this is this is something that we need to understand that our decision from the beginning is not something that can just be [inaudible].

Dr. Gregory Niemer
[Inaudible] made-up for as time goes on, sometimes these levels of disease activity can't be recaptured, and so if we start a patient on a biologic, we give them a trial which usually takes three months and then we go to a second biologic. That trial takes three months. Oftentimes, we have to stay within the TNF blocker class for that second medication. By the time you go through your two trials, you're already halfway through that window of having the best opportunity to achieve low disease activity or remission for your [inaudible] for our patients, and that's why it is so vital that we make the decision from the beginning, the best decision based upon objective measures for which to this date, we have not had. So, this gives us that first opportunity for true precision medicine within our rheumatoid arthritis treatment algorithm.

Dr. Gregory Niemer
Umm so.

Dr. Gregory Niemer
It's been argued that this, that this treatment, or this test, may not be medically necessary, but it is a medical necessity that we prevent unnecessary side effects for our patients on treatments where there is more knowledge that the efficacy of that drug may be suspect so. So, this is something that we need to take into account and do our very best to make sure that we're making the right decision and initially with which medication is chosen and the cost of the test.

Dr. Gregory Niemer
And comparison to long-term, some consequences of active rheumatoid arthritis, as some of my colleagues have already have described, there's no comparison between those two costs and a lot of these long-term complications are unnecessary and preventable if we are able to start the right medication as soon as possible, and thankfully now we have tests such as prison more than allow us the opportunity to be able to get our patients on the right medication and a more-timely fashion. So, thank

you very much for allowing us the opportunity to share our opinions and explanation of why we think that this test is so important that it be available to us.

Dr. Angella Charnot-Katsikas
Thank you Dr. Niemer for your comment. Next, we have Dr. Joseph Huffstutter of Arthritis Associates. Dr. Huffstutter. I do see. That you are sharing. If you on the line there, there we go.

Dr. Joseph Huffstutter
Thank you so much, and I know that people on the panel are just sick of hearing from rheumatologists, and they're just going, “Oh, no, another rheumatologist.” I haven't heard from this many rheumatologists in a long time, but I'm going to give you a little bit about my perspective. I'm a practicing rheumatologist and Hicks and Tennessee, which is a suburb of Chattanooga.

Dr. Joseph Huffstutter
And I'm more of a bottom-line kind of person. I'm. I know you've heard a lot of science about this and to be perfectly honest…I don't think I'm qualified to address some of the scientific issues around the test, but I am kind of a bottom-line person and I treat patients five days a week in our office here so that when I see a patient with rheumatoid arthritis, I try to quickly and as accurately as possible to make the diagnosis and then initiate treatment. And as you've heard before, methotrexate is the standard treatment that we start people on, and we do that in most people without too many difficulties.

Dr. Joseph Huffstutter
And most people tolerate it pretty well, although not everybody responds. And that's where we get into some of the issues because when they don't respond or don't tolerate methotrexate, then we're kind of at a dilemma and or crossroads about which therapy would choose. And we've looked at this for a long time. In fact, there's a test that Medicare approves for doing twice a year, called a Vectra DA, that actually predicts how people may do and tells how active their disease is.

Dr. Joseph Huffstutter
And one of the interesting things about this is it actually checks two separate cytokines. One of them is anti-TNF and the other one is IL-6, and you think, wow, those people that have high TNF levels, they should respond to a TNF medicine.

Dr. Joseph Huffstutter
And it's absolutely not the case and you think, well, gee, these IL-6 levels are great. We've got drugs that really can suppress IL-6 if they're high. That's really what's driving their inflammation. That's what you need to choose.

Dr. Joseph Huffstutter
And it's not the case. Those do not correlate with a person's response to either one of those mechanisms of action. So, with this new test that's available, it improves the likelihood for me being able to pick the right drug for the right patient.

Dr. Joseph Huffstutter
It's not a perfect test, it's not 100 percent, but it does kind of guide our therapy so that as quickly as possible. I can get the right drug to the right patient, and I think that's important in our patients that have really active rheumatoid arthritis because.

Dr. Joseph Huffstutter
For those of you that don't treat this this illness, I would think that I would give you an analogy of, you know, your house gets on fire. It's a kitchen fire and if you can catch it as a kitchen fire and throw a lid on the skillet, you muffle the fire. The fire is out. There's not a lot of damage to the house. Everything's cool, you're happy. But if you don't get that fire, put out and the fire spreads to the to the rest of the kitchen and the living room and the dining room, you have to get the fire trucks in. You get the fire companies, and he takes a lot of water and there's a lot of damage to the house.

Dr. Joseph Huffstutter
But eventually you get the fire put out, and what we're trying to accomplish with this idea of precision medicine is getting the right drug to the right patient as expeditiously as possible, so that there's less damage to the patient.

Dr. Joseph Huffstutter
I really think that there's some data to show that as quickly as you can treat these patients effectively then it actually costs less for the whole system. So, you know it's not a test that I'm going to use on all my rheumatoid, the majority of my rheumatoid might not even need this test because they'll respond to methotrexate, or they will…they don't have TNF as they have problems with taking at and if they have chronic infections. So, you may not be able even able to use biologics in these patients, but I think we really need access to this tool as you don't have to, you can have it actually have an LCD for this to. So, you can look at which patients you may want to use this in and out. I'm OK with that. I'm a member of the CAC for Tennessee and I'll help with crafting an LCD so that the test is not abused, but I really want to have access to this test, so it'll help guide therapy from patients. And I'll shut up. Thank you for listening.

Dr. Angella Charnot- Katsikas
Thank you Dr. Huffstutter for your comment. Next, we have Dr. Ferris Kassab from South Charlotte Rheumatology. I believe I saw you a moment ago. Perfect. Thank you. Welcome.

Dr. Firas Kassab
Hello, thank you for allowing me to speak. I'm sorry, I just finished with a patient. I'm getting my comments here on the screen ready. I'm sorry I missed the rest of the meeting. I had a schedule of a busy schedule this afternoon. So my name is Dr. Firas Kassab, M.D., with South Charlotte Rheumatology. Thank you for providing me the time to speak today.

Dr. Firas Kassab
I'm providing comments today on behalf of the North Carolina Rheumatology Association, or NCRA. I'm an independent community-based rheumatologist in Charlotte, N.C. and currently serve as a board member at NCRA and have served in the past as a President of the organization. I have worked in rheumatology for over 15 years and NCRA's mission is to promote the science and practice of rheumatology and advocate access to the highest quality healthcare and management of patients with rheumatic diseases.

Dr. Firas Kassab
So with regards to predictive biomarker tests, NCRA fully supports the future use of these precision medicine tools as important tools to optimize the care of our patients with rheumatic diseases.

Dr. Firas Kassab
NCRA feels that the clinical data presented to demonstrate the clinical utility of the tests is currently sufficient to allow the use of these tests in clinical practice, and further delay is really not warranted or necessary. Hopefully, those tools will continue to improve with time, but they are desperately needed now to improve the quality of care and the clinical evidence presented to support this is more than sufficient in our opinion.

Dr. Firas Kassab
Each trial of an TNF inhibitor in a patient who is unlikely to respond is going to delay bringing the disease activity down and really increases the risk of negative outcomes, let alone the potential side effects or risks associated with these medications. So, it's really would be beneficial if a test can give a clinically validated prediction of response of this class of drugs even if this test changes the treatment algorithm for some and not all of the patients.

Dr. Firas Kassab
These would be huge advantages, both in terms of clinical outcomes and for cost savings.

Dr. Firas Kassab
The first failed first methodology which is the current imposed method of finding the appropriate treatment for RA, is not really appropriate anymore where time versus cost is a significant issue in controlling disease activity. Predictive tests based on available data provide rheumatologists with an option to bypass these failed first approaches. Furthermore, based on their review described in the proposed LCD of the December 21, 2021, CAC meeting, [inaudible] said that the subject matter expert panelists commented that insurance companies often require — and I'm quoting here — insurance companies often require a trial of one to two TNF inhibitors before covering other targeted therapies, and there was consensus that the requirement that the insurance companies for patients to fail multiple TNFC inhibitors prior to paying for an alternative targeted therapy is unreasonable. This policy really doesn't have anything to do with the efficacy of these medications, and more to do with driving patients to the drugs with higher rebates.

Dr. Firas Kassab
We all know that, although this is not completely related to today's discussion, which we all agree should focus on the value of the tests themselves, it is important to recognize that the positive impact of these tests will have for the patient. Access and outcome will also actually impact cost reduction.

Dr. Firas Kassab
In conclusion, the North Carolina Rheumatology Association fully supports the use of predictive biomarker tests and urges MRI DX to generate an LCD policy and allow coverage for these tests. I'm available to answer any questions or concerns by phone or email or right now at the meeting, and I again thank you so much for giving me the time to speak.

Dr. Angella Charnot-Katsikas
Thank you. Dr. Kassab, we've mentioned earlier that we are not able to do a Q&A at this meeting, but we certainly welcome comments on submitted to Palmetto GBA as part of the comment period. Thank you very much for your comments. Let's see, at this point, we are on our last speaker, Corey Greenblatt, senior manager of Advocacy at Global Health Living Foundation.

Corey Greenblatt
Hello everyone. Thank you so much. Thank you for the opportunity to provide comments today on the draft LCD. My name is Corey Greenblatt and I'm the senior manager of policy and advocacy with the Global Healthy Living Foundation.

Corey Greenblatt
GHLF supports access to biomarker testing for our patient community to facilitate a faster connection between patients and medications that will best help them. By way of background, our organization is a 501 (c) (3) nonprofit group that works to improve the quality of life for people with chronic disease, often focusing on those least able to advocate for themselves through our websites, social media channels and conventional media. GHF reaches more than 10 million chronically ill patients monthly in the United States, in English and Spanish.

Corey Greenblatt
Our patient community is often forced to try multiple different types of medications before finding the one that works best for them. Biomarker testing such as Prism-RA is an important, innovative step that can reduce this time and ensure that most of the effective medications are in the hands of patients as soon as possible.

Corey Greenblatt
Or sickest and most vulnerable members of our society rely on expensive therapies that ensures label is specialty drugs. These patients that use these types of drugs have incredibly complex disease profiles and often several comorbidities together with their physicians. They select very specific treatment options based on disease progression, disease activity, individual immunogenicity to issues, lifestyle preferences and associated out of pocket costs. Without biomarker testing, patients are commonly forced to try multiple different treatments or combinations of medications before finding the treatment plan that works best for them. This trial-and-error period often leads to debilitating symptoms and a reduced quality of life. While patients suffer ineffective medications, precision medicine and biomarker testing offers a chance to minimize or entirely eliminate these steps and more quickly connect patients to their ultimate goal. Finding a successful and sustainable treatment plan.

Corey Greenblatt
Evidence shows that these types of tests have been successful in other fields of health care, such as cancer, and the CDC itself has a page promoting the benefits of precision medicine. We just hope to see these benefits passed on to our patient community as we look to reduce patient burdens and increase the likelihood of successful therapies on behalf of those in our community looking for access to innovative tools that will improve their quality of life. We hope that you will revise your draft determination and allow rheumatoid arthritis patients to realize the benefits of precision medicine by providing coverage for Prism-RA testing. Should you need to hear it from patients directly, we are ready to connect you with those who would benefit from these types of tests. Thank you very much for your time.

Dr. Angella Charnot-Katsikas
Thank you, Mr. Greenblatt. OK, we have now concluded with our speaker presentations and comments. So, we want to thank you all for your attention and to participation. Share that you know, we appreciate these comments on the draft policy and the feedback regarding our evaluative process. We also want to once again apologize for the difficult audio issues we were having initially, but we have managed to

conclude our program on time, our open meeting on time. And so, with that, I want to go ahead and formally conclude the meeting. Thank you all and have a great rest of your afternoon.