WPS Government Health Administrators Open Meeting

Moderator: Dr. Robert Kettler
June 16, 2021
1:00 p.m. CT

OPERATOR: This is Conference # 1838099

Operator: Ladies and gentlemen, thank you for standing by. And welcome to The Draft LCD Open Meeting.

At this time, all participants are in a listen-only mode. After the speaker presentation, there will be a question-and-answer session. To ask a question or make a comment, you will need to press "star" "1" on your telephone. Please be advised that today's conference is being recorded. If you require any further assistance, please press "star" "0."

I would now like to hand the conference over to Dr. Robert Kettler. Thank you. Please go ahead, sir.

Robert Kettler: Thank you, (Shelby). And I want to welcome everybody to the WPS GHA Draft Local Coverage Determination Open Meeting. As (Shelby) mentioned, this meeting is being recorded. Today's date is June 16th of 2021, and the time is a few minutes after 1:00 p.m. Central Daylight Time.

The purpose of this meeting is to take public comment on a number of draft LCDs and that is the only business that is in order during today's meeting. Before we proceed further, what I would like to do is have my colleagues from WPS who are on the line introduce themselves.

And I'll start with the CMDs, and I'll maybe just mention that Dr. Ella Noel is on the line but because of a bad cold is having some difficulty talking. Dr. Noel is one of the J8 contractor medical directors. And then my other CMD colleagues, please?

Denise Nachodsky: Good afternoon. I'm Denise Nachodsky. I am a CMD at WPS for J5 and J8 jurisdictions. My specialty is cardiology. Thank you and welcome, everyone.

Barry Whites: This is Barry Whites, another CMD, J5 and J8, pulmonary critical care specialty. Again, thanks for coming to this open meeting, and look forward to your comments.

Robert Kettler: Thank you. And then if the policy coordinators who are on the call could introduce themselves.

Beth Scanlon: Beth Scanlon.

Michelle McCary: Hi, I'm Michelle McCary.

Melissa Lietz: And I'm Melissa Lietz, one of the policy coordinators.

Robert Kettler: And then any other WPS personnel on the call.

Linda Oliver: Hi, Dr. Kettler, this is Linda Oliver from medical review.

Robert Kettler: And anybody else? OK.

Then I'm going to just give a few of the ground rules so that we can have an efficiently run meeting. And then after, that we will actually proceed to the – to the LCDs. As I mentioned a few minutes ago this is for public comment on seven draft LCDs as posted on the agenda. And this is the only business that is up for discussion today. We do have some formal presentations associated with the – some of the LCDs.

There are a total of five relative to three LCDs. I'm going to take the agenda somewhat out of order to accommodate some scheduling conflicts that we had and I will announce each LCD before we proceed to the presentation. For the presenters when you're called upon please follow the operator's instructions in order to speak.

And please introduce yourself, your affiliation, and briefly disclose any conflict of interest that you may have. We do have a 10 minute limit for the presentations, this is out of fairness to everyone involved so that no one individual or stakeholder takes more time than anyone else.

During your presentation, I will be giving you a warning when you have two minutes left. So, that will be your signal that it is getting to be time to wrap

things up. When you want the slides of your PowerPoint presentation advanced please notify Richard Staley that it is time to advance your slides.

I would ask that all the presenters avoid repetitious presentations if someone else has already made a point it's not necessary to make it again. You should provide us with information that we haven't received to this point and if you do want to say something that's only necessary to say that you agree with the previous speaker's points.

On completion of the presentation, I will allow my colleagues from WPS to ask any questions that they may have. And after the last formal presentation for an LCD we will then go to the phone lines to take public comment. In terms of public comment, again, please follow the operator's instructions for speaking.

Introduce yourself, your affiliation, and disclose any conflict of interest that you may have. We also do have a 10 minute limit on public comment and I will give a two-minute warning if necessary. I would also ask those who are making public comments to avoid repetition, again, if someone else has made the point it's not necessary that you make it again.

We also do ask that anyone making a public comment in addition to providing the public testimony submit the comments in writing. This is both a CMS requirement and also it's just a good way to make sure that your comments get in and we can respond to them in case there is any sort of audio issue during the session this afternoon.

If you do have any issues with WebEx only, you can send a notification of that to Richard at LCDCAC@wpsic.com. And as I say, this is just for issues related to the visual or WebEx portions. With that, excuse me, I'm going to proceed to the LCDs and the public presentation.

The first LCD that we are going to be covering is DL39054. This is Epidural Procedures for Pain Management. This LCD is the result of a collaborative effort among the various MACs. And if adopted will replace the current LCD related to epidural steroids of WPS. This LCD does establish coverage criteria for epidural steroid injections.

And we do have a presentation associated with this LCD so, Dr. Smuck, you may proceed.

Operator: And, Doctor, if you would please press "star" "1." Again, if you would press "star" "1" to have an open line.

Robert Kettler: (Shelby) ...

Operator: We don't have Dr. Smuck dialed in.

Robert Kettler: OK. What we will do then is proceed to any public comments there may be on draft LCD 39054. So, you can open up the phone lines now.

Operator: Open all lines?

Robert Kettler: Just allow people to make a comment if they want.

Operator: If you would like to make a comment please press "star" "1." Again, to make a comment, please press "star" "1." We have no one in the queue.

Robert Kettler: OK, thank you.

The next LCD then is DL38018 MolDX – Decision Diagnosis-Melanoma. We have three presentations on this LCD, which is in response to a reconsideration request of L38018 MolDX – Melanoma Risk Stratification Molecular Testing.

That LCD underwent a number of revisions since it became effective in November 1, 2019. And the recon request was to expand the indications for this particular test. Our first presentation then is going to be from Dr. Vetto.

Dr. Vetto, please proceed.

Operator: Dr. Vetto, please press "star" "1" for an open line. Your line is open.

John Vetto: Great, thank you. Dr. Staley, how long do I have to present? Ten minutes?

Richard Staley: Ten minutes, yes.

John Vetto: All right, OK, here we go. So, I'm John Vetto, thank you very much for having me present today. I want to talk about the clinical use of the 31-GEP assay in melanoma. Next. Can you advance the slide?

Richard Staley: I'm sorry, I'm trying. I've got an issue with ...

John Vetto: Oh, OK. No problem. So, I'll just say that ...

Richard Staley: (There we go).

John Vetto: ... I am a – there we go. So, basically, I'm at the Oregon Health and Science University in Portland, Oregon where we have a fair amount of experience with this GEP test. We have – research that shows it informs important decisions both before and after sentinel node biopsy for melanoma.

And today I'm going to be talking about two of the major indications. First, is to identify a subset of T1, T2 melanomas that are very low risk of a positive sentinel node focusing on the Medicare population. And secondly, to show how the test can inform surveillance opportunities in patients who either didn't have a sentinel node or had a negative sentinel node.

I will not have time today to talk about another indication, which is for stage III disease. I will say that I recently published a paper that I'll be referring today, it was in the American Journal of Surgery, the first author was Sam Arnot, who is a fellow in our lab. And that – to quote that paper, "To the 31-GEP that's prognostic information and the evaluation of primary cutaneous melanoma.

And should be considered in patients who were referred for sentinel node biopsy, which is a population of patients (5C)." Next. So, on the Knight Cancer Center here at OHSU is an NCI-designated cancer center, we have a multi-disciplinary melanoma program, which is large and serves a very large group of – very large demographic and geography.

We found that the GEP improves our risk assessment in the patients who come to our high-risk program. And I do feel that the Grossman and Marchetti articles, which have raised some questions about the test, do not address the data as it relates to sentinel node.

And actually in – someway, and I'll touch on this later, support some of the data we found. But I want to emphasize throughout the talk that number one I'm a surgical oncologist and I see all stages of the tumor and all – and many indications of the test. And secondly, they were using the test in concert with conventional staging and prognostic tools. I think it's important for WPS to hear from clinicians like myself who actually use the test. Next.

So, again, I'll be talking about two major utilities. Let's focus first on sentinel node optimization. Next. The – for the non-surgeons in the crowd, the NCCN tells us to do or not do a sentinel node biopsy based on the probability that the sentinel node is going to be positive. Do it if it's over 10 percent, don't do it if it's less than 10 percent. The trouble is the NCCN doesn't tell surgeons how to know that.

So if you look at the left side of the table, the SSO has provided these numbers, but everybody knows that – or all the surgeons know that if you include T1 patients routinely, your positivity for the sentinel node in your population will actually go to 11 percent. It was 19 percent in the MSLP-1 trial that did not include T1s.

There's lots and lots of literature to show that including T1s dilutes the data and the utility of sentinel node biopsy. Next. So what we did here in Oregon was we looked at – to see if the test could predict sentinel node positivity better than just guessing, and basically these are the results from the paper that I published in Future Oncology.

I – this is focusing on just Medicare-age populations, and you can see that if the test was low score, or low risk, that's the class 1-A patients, that's the blue triangle, you're well below the 5 percent cutoff, whereas conversely if the test is class 2-B, which is high risk, you're well above the 10 percent cut off. So this is very useful in Medicare patients because you can then sit down and inform them on the utility of sentinel node biopsy in their particular case where there's often a lot of comorbidities. Next.

So this is the protocol that we've adopted in Oregon, and patients come in who are Medicare age and eligible for sentinel node biopsy. We'll run the test if the tumor is class 1-A, that's low risk. We can say that their risk of a positive

sentinel node is below the 5 percent threshold. We have a prospective study to have the patients consent in not having the sentinel node in those cases, and this makes certain – management just much easier and avoids a trip to the operating room often in patients with a lot of comorbidities.

Conversely, if the test was intermediate or high risk, then we do offer sentinel node. Now I'll say that if the patients have comorbidities and can't go to the OR, this targets those patients who should get what's called watchful waiting, which is follow-up with exams and ultrasounds for a two year period. Next.

So the other utility of the sentinel node – excuse me, the 31-GEP, is to inform follow-up decisions. Next. This is a – this is the multi-variable analysis from my paper in the American Journal of Surgery, and what we found basically is if for all patients of all ages, class 1 and class 2 (views) are associated with significantly different range of sentinel node positivity, that confirms the data you just saw.

And patients, who are low risk or class 1, had a three full lower risk of recurrence than patients even with a negative sentinel node. So again, a negative sentinel node and a low risk class 1 – or low risk or class 1 score are both indicators of lower risk, but I think this is not – this is more non-(holster) thinking where you're saying the negative sentinel node predicts that the patient doesn't have a nodal (inaudible) type.

The class 1-A predicts the more the patient have a distant – it doesn't have a distant (inaudible) type. And you'll put those two together, it's very powerful as a negative predictor. Within patients who have a negative sentinel node and are considered low risk but then they have a higher risk-GEP, those patients had an eight time more likely to occur – chance to occur.

Let me show you this graphically on the next slide please. On the far left are those double negative patients, what I call double negatives where the low risk for nodal metastatic phenotype, no low risk for distant metastatic failure, and those are patients that in a large university of – like ours, it serves a very large part of the country where patients are coming hundreds of miles to see us, and often traveling with some difficulty, especially if they're Medicare age, we can safely discharge those patients to derm follow-up only because their

risk is as low as we can get it. On the other hand, on the far right of the double-positive patients where those patients need to stay in the high-risk clinic, we need to put them on clinical trials and follow them very closely. What's interesting are the middle two bars where if you're either set on the negative or class – or – excuse me, if they're either sentinel node positive or class 2-B on the GEP score, you have an intermediate risk and you need to be followed as well.

And that's what a lot of the other meta-analyses don't show is that we're using the test in concert. Next – next slide, please. These are standard graphs – oops, can you back one up, these are standard graphs of patients who have a negative sentinel node, and we all know that, yes, these patients do better than if they have a positive sentinel node, but either for relapse resurvival or (inaudible) resurvival, there is a decay (of occurs) where the patients relapse.

What are they doing, they're relapsing (at distant) because, again, sentinel node is mostly a marker for nodal metastatic phenotype and only a surrogate for distant payer. So we run the test, and now we can see among nodal metastatic patient, next slide, who are the double negatives, the patients in the blue line, next slide please, who will do well, and the patients who are at higher risk of failure.

Now it's been pointed out in some of the other studies that having a positive test is not a death sentence, but it clearly marks patients who need closer follow-up, and this is a great tool for knowing who those patients are, and shifting resources from the blue line to the red line. Next.

Robert Kettler: Dr. Vetto, two minutes.

John Vetto: Yes, OK. This is a meta-analysis from my paper again, and basically what you've saw is that GEP independently predicts relapse in the low risk patients, that GEP-2-B is a significant independent – independent predictor that supports all the points I've already made. And we believe the 31-GEP should be used in conjunction with staging. Next.

This is a paper that we wrote early on where we looked at just low risk patients, and we are – we're identified – even among low risk patients, we

can identify that red line where those are the higher risk, low risk patients. These are the patients that we think, even though they're low risk by AJCC, these are the patients that we know make up the majority of melanoma deaths and we can follow them more closely.

Again, not a death sentence but these are patients who need closer follow-up. Next. We are designing it by a way of (ACER) trial for that. So this is what we're doing in Oregon, the double negatives are on the blue line, negative low risk GEP, negative sentinel node, discharge-to-derm, this – the discordant patients are in the second red line. High risk GEP despite a low risk follow those patients with increased intensity, and we are designing a (SWAD) trial for that.

The double positive is the bottom, next slide, and I would say that using this algorithm has saved me 330 visits in the first six months, and it's been three years now and the numbers have only gone up with very, very low risk to patients. So, to summarize, four uses of the test, identify risk of sentinel node metastases, identify the double negative patients who can be safely discharged, identify AJCC low risk patients who are actually at higher risk, and shipping the resources from that second bullet to this third bullet.

And I did not have time to talk about it, but to – we also are using it to look at 3A patients, which as we know there's no data to know whether they get immunotherapy or not. We can run the test and separate out very nice subsets of high risk and low risk 3A patients. Again, I'm a surgical oncologist, I see all stages of melanoma, I see the value of the test in multiple areas of melanoma care.

I recommend to WPS that you include in the LCD my paper, first author Sam Arnot, and the recent paper from (Eddie Shay) at Wash U. and I'll stop there. Thank you.

Robert Kettler: Dr. Vetto. Do any of my colleagues at WPS have any questions for Dr. Vetto?

Barry Whites: Yes, this is Barry Whites. Just been hearing a mention of your potential conflict of interest. I think you did, I missed it, I'm sorry.

John Vetto: Yes, I am on the speaker's bureau but I'm not being compensated for today.

Barry Whites: Thank you, sir.

John Vetto: Yes, and I don't receive any money for any of this research. The Arnot paper was independent and had no commercial branding and no support.

Barry Whites: Great, thank you so much.

John Vetto: You're welcome.

Robert Kettler: Any other questions? OK, thank you Dr. Vetto.

John Vetto: Thank you, my pleasure.

Robert Kettler: Our next presentation, and I'll give Rich a minute or two here to get it loaded up, will be from Dr. Laura Korb Ferris. And again, this is related to DL38018 MolDX – Melanoma Risk Stratification Molecular Testing. Dr. Ferris, please go ahead.

Operator: Dr. Ferris, please press "star", "1." Your line is open.

Laura Korb Ferris: Can you hear me?

Robert Kettler: Yes, we can.

Laura Korb Ferris: OK, sorry. OK, so I'm Laura Ferris, I'm a dermatologist at the University of Pittsburgh but presenting just as myself, not representing my institution. My conflicts of interest, I have, in the past, been an investigator for clinical trials on Castle Biosciences. I am not a personal consultant or a speaker and have received no personal compensation from Castle.

So next slide, so the points that I – there we go, thank you. The points that I really would like to make today are that the existing LCD is appropriate and supported by evidence, and I want to focus on two areas. As a dermatologist, I am often the one who's making the decision of does a patient with invasive melanoma need to go see surgical oncology, do they need somebody like Dr. Vetto who can do a sentinel lymph node biopsy, or should they be followed by me?

And also, even when we have patients who do in fact need surgical oncology, once their work-up is done, I need to work with my colleagues to decide who is going to primarily follow the patient, how intensive surveillance do they need, and I have found this test to be very useful in both areas, and there are – there's good data to support it.

And, again, as Dr. Vetto said, this is something that is not used to replace, but is in conjunction with the existing AJCC staging. And I particularly find this helpful for patients who have earlier stage melanoma, which is most of what we diagnose and treat in dermatology. Next slide.

So the existing LCD is really – is reviewed and was decided to be appropriate and supported by evidence, but I'd like to point out that there are actually multiple new studies that have been published, some of which you just heard about, since the first review. These are all studies that have looked at new data and further supported this test. The – there are also a couple critical articles that have been published. There's really two, I think, that have been most prominent and most discussed, and I'd like to point out that these are actually opinion pieces. These are not pieces that are – with – that are data, these aren't new studies presenting new data, they are the sort of opinions and musings of some dermatologists and oncologists.

So I think that the new evidence that's out there is actually overwhelmingly in favor of, one, providing more data, and two, supportive of the test. And most of them don't actually come – the ones that are new are not by people who have experience with using the test. Next slide. I'd like to address some of those.

The Grossman paper, this was actually a – it was – it's called a consensus, but it was really the report of two surveys that were given. These had a low participation rate in these surveys, about 40 percent, and only 14 percent actually of the invited participants participated in both surveys. They also are – the majority opinion in this case was as low as about 59 percent of people agreeing that a test was or was not useful on this. So this was a rigorous, what we'd call a Delphi process where you work together to reach consensus. This was just a smaller survey.

And this was also a group of – it's not well described who participated, but they're dermatologists, medical oncologists and surgical oncologists. It was also mostly people or almost all people who are in academic large referral practices, so it's a little bit different then first line dermatologists or providers. And a lot of them came from one institution. And so there's – I just would like to say that this was not new research, this was a survey.

Some of the points that were made in here, one of – if you really look at the summary it was, they actually said that they're – the data do support that this was a test that could help to predict which patients are going to metastasize and what their summary was was not that it shouldn't be used, but that it should be used in context of discussion with the patient or in a multi-disciplinary group and not just “don't use this.”

So I think that that's important. I think that any treatment or test should occur with discussion of the patient. And they also had – it suggested areas for further research. Also, as somebody who practices medicine, it's very rare that I'd say we don't need to know any more about this drug, this test or this condition. So I think that those are all not suggestive that we shouldn't be using this test. Next slide.

So in comparison to that survey, I just want to point out that this was another survey, this (Marson) survey that 589 respondents, most of whom had actually used the test. So there are other surveys out there that are larger and there were clearly identified places where this was found to be helpful in clinical management, including in identifying those patients who could maybe have less – scaled back care, the true negatives in the high risk population and also finding those rare patients who by conventional staging may seem to be low risk but are actually high risk. Next slide.

So this is looking at – this is another – this is an expert opinion piece. And this is stating – you can't read it in here, but how this test is used. And this is similar to what we do at the University of Pittsburgh in our multi-disciplinary clinic. It is a way that we can one, find those patients who can potentially avoid sentinel lymph node biopsy. So a lot of times our melanoma patients are older, they have a lot of comorbidities, they're poor surgical candidates.

And so if I can save them the potential of a surgery that involves general anesthesia and has a risk of lymphedema, that's oftentimes a very good thing.

Two, we can use this to either increase or decrease the frequency of radiologic imaging, and it also helps to set up a follow up schedule. Like Dr. Vetto said, some patients can just follow with me in dermatology, some patients need to be seen and scanned every three months, and this let's us take a more personalized approach and not just give everybody the overkill response.

Next slide. Another argument that sometimes has been made is, well, we can get all this information from AJCC staging, and so you don't really need this, it doesn't add anything. But I think importantly this is showing that there are multiple studies actually that have done multi-variable analysis and shown that GEP is actually an independent predictor. So it doesn't just correlate with having a thicker melanoma or an ulcerated melanoma, it is an independent predictor of who is likely to metastasize.

So it does add something on its own, it doesn't just confirm what we already have. The other thing that I want to say is it can – it gives us data without having to put a patient through a surgery that is expensive and carries risk. Next slide. Yes?

Robert Kettler: Dr. Ferris, two minutes.

Laura Korb Ferris: OK. Thank you. This is really just going over again multiple studies that have shown a multi-variable analysis the added benefit. Next slide. This is the Marchetti paper, and this is the – a analysis that was done. I just would like to point out, one, this analysis did not take into account the ability to reduce sentinel lymph node biopsy and it also doesn't use odds ratios, which are sort of a standard way at looking at efficacy of a test like this.

Next. This is a published analysis that actually does use odds ratio and again, shows the value of the test as an independent predictor of sentinel node positivity as well as occurrence. Next. So this is also – looking at – I just want to make the point in this slide that using – if you just use conventional staging, again, this paper can make the point that there are false positives or

false negatives. If we use AJCC staging, every patient with stage one disease who recurs is actually a miss or a false negative.

So, again, we have to remember that AJCC staging has false positives and negatives. Sentinel lymph node biopsy as surgery also has false negatives, people die of metastatic melanoma with a negative sentinel node. Next. So, this is multiple studies that have confirmed the clinical utility in different providers. And again, this is a lot more than a consensus of 16 to 18 patients – physicians.

And next, just want to conclude with – so there – the results of these two opinion pieces I think have flaws and they should be considered in the context that they are not new research. Next, you can just click through these bullet points. So, we talked about the (inaudible)

Robert Kettler: Doctor Ferris.

Laura Korb Ferris: Go ahead, you can click towards the end. I've really made my point. So I – in conclusion, we really need a strategy to decrease surgery as a staging and to be able to more appropriately give personalized recommendations for melanoma patients. Thank you.

Robert Kettler: Thank you, Doctor Ferris. Do any of my colleagues at WPS have questions? OK. Well, again, thank you Dr. Ferris.

Laura Korb Ferris: Thank you for having me.

Robert Kettler: The next presentation is going to be from Dr. Matthew Goldberg. And again, this is relevant to DL38018 MolDX – Melanoma Risk Stratification Molecular Testing. Dr. Goldberg, please proceed.

Operator: Dr. Goldberg, your line is open.

Robert Kettler: (Shelby), do we have Dr. Goldberg on the line?

Operator: Yes. Dr. Goldberg, your line is now open.

Robert Kettler: I think what we'll do is move in, I'm not sure what has happened here.

Matthew Goldberg: Can you hear me? I'm on the line here, this is Matthew Goldberg. Can you hear me?

Robert Kettler: Oh, I can hear you now.

Matthew Goldberg: That's so strange.

Robert Kettler: Well that's I guess the wonders of modern technology. Please proceed. Dr. Goldberg?

Matthew Goldberg: Yes. Can you hear me?

Robert Kettler: I can hear you now.

Matthew Goldberg: OK.

Robert Kettler: But are you ready to do your presentation?

Matthew Goldberg: I am.

Robert Kettler: OK.

Matthew Goldberg: I am. Yes.

Robert Kettler: Please proceed.

Matthew Goldberg: Thank you. Apologies for the technical difficulties there. My name's Matthew Goldberg, I'm a board-certified dermatologist and dermatopathologist and medical director at Castle Biosciences. For conflict of interest, I'm an employee and stockholder at Castle Biosciences.

In my comments today, next slide please, I'll review the evidence that supports the existing LCD and highlight some new publications that have been published since the LCD went into effect, in close with suggestions for changes to the direct LCD that's currently open for comment. The existing LCD L38018 is based on a strong body of evidence that's only been strengthened since the last reconsideration and therefore the coverage criteria should equally remain unchanged.

Next slide. The existing LCD was approved by all four MACs based on 22 peer reviewed studies which demonstrate the consistent ability for DecisionDX melanoma gene expression profile, or GEP testing, to improve the accuracy of defining risks for health outcomes of interest for patients who receive this test result. There's also a clear clinical utility to identify patients who can safely forgo (inaudible) biopsy procedures and define risk appropriate patient management plan independent from decisions to consider sentinel node biopsy procedure itself.

Next slide. Now these next five slides were previously presented at an open meeting in October of 2019 and for background, the DecisionDX melanoma was developed and validated to access risk of recurrence and metastasis independent from traditional clinical pathologic factors for patients with stage one through three melanoma. And the tests risks stratifies patients with a class one or class two result with the lowest risk in the class 1-A group and the highest risk in the class 2-B group.

Next slide. And DecisionDX melanoma helps physicians answer two questions that inform important clinical decisions that influence patient treatment plans, specifically what is the risk of a positive sentinel lymph node to inform sentinel lymph node biopsy recommendations. And secondly, what are patients' risk of recurrent metastasis after melanoma diagnosis to inform decisions such at an appropriate level of follow-up imaging and multi-disciplinary referral. Next slide. (HACC) version 8 provides risk stratification for patients diagnosed with melanoma and DecisionDX melanoma improves this prognostic accuracy for risk stratification across stage one through three melanoma.

But this table demonstrates how (HACC) provides a population-based risk for each stage which can be further stratified by combining the independent prognostic information, from the GEP result. For example, (HACC) version 8 predicts that a patient with stage 2 disease has a 90 percent five-year melanoma specific survival, or MSS, seen here with a black dot in the second column. However, as the arrows indicate that same patient would be predicted to have a five-year MSS of over 99 percent with a class 1-A GEP result which compares to an almost 84 percent five MSS with a class 2-B result.

Next slide. Dr. Vetto's presentation covered sentinel biopsy guidance substantially and how the DecisionDX melanoma identifies patients who are at low risk of sentinel lymph node biopsy positivity can safely avoid the procedure based on currently accepted risk thresholds. Next slide. And in summary, the information presented previously and reinforced by Dr. Vetto's presentation, DecisionDX melanoma influences sentinel lymph node biopsies discussion and decisions for patients with melanomas 2 mm in thickness or less. And further, DecisionDX melanoma influences decisions for follow up imaging and multi-disciplinary referrals for patients with melanomas greater than or equal 0.3 mm of (inaudible) If you could move forward two slides please. The next slides focus substantially on how the DecisionDX melanoma test impact the performance of sentinel lymph node biopsy decisions in the Medicare population on melanomas 2 mm in thickness or less.

And this was covered, again, by Dr. Vetto's presentation and the figures on the right side of the slide take the findings from the Vetto, et al. paper from 2019 further and highlight at the class 1-A patients in this study are managed according to their less than 5 percent predicted risk of sentinel lymph node positivity, then 65 percent of the patients in this cohort could safely forgo the sentinel node biopsy to procedure.

And this ability to reduce unnecessary sentinel lymph node biopsy procedures would also hold for T1 and T2 melanomas and that's seen separately here at the bottom right of this figure. And it's important that risk stratify patients with (inaudible) invasive melanoma is because Medicare eligible patients with T1 and T2 tumors currently undergo the sentinel node biopsy procedure.

And while guidelines may not endorse the sentinel lymph node biopsy procedure in patients with T1-A melanoma, it remains important to triage these patients as significant numbers of T1-A patients currently do undergo a sentinel lymph node biopsy and what's more, approximately a third of patients with T1-A melanomas without high-risk features obtained the procedure.

Next slide. So for illustration purposes we've modeled what this looks like in current practice based on our data from large surgical centers. In patients with T1-A melanoma, 65 years and older, that have the sentinel lymph node biopsy procedure performed, 94 percent will have negative results and receive no benefit from the procedure.

Next slide. In these patients who underwent a sentinel lymph node biopsy procedure as part of their clinical care, DecisionDX melanoma identifies 82 percent of patients with a Class 1-A result who can there for safely forgo a sentinel lymph node biopsy procedure.

And GEP testing in this group would reduce a large proportion of unnecessary surgical procedures while also improving the yield of sentinel lymph node biopsy positive results in the surgical procedures still performed for those with non-Class 1-A GEP results.

At the interest of time, please skip ahead two slides. Since the reconsideration request in 2019, evidence supporting the utility of DecisionDX Melanoma has increased. And reconsideration of evidence included in the draft LCD should include the whole body of recent evidence, echoing some of the other presenters here.

Next slide. The inclusion of supportive articles and the revision to the LCD is important because it would provide an improved context of evidence available for those (DecisionDX Melanoma) test.

Specifically, the additional articles below address points raised in the recently added text to the draft LCD. For example, all Stage I and II patients included in the (Green-Hall) meta-analysis from 2020 has been staged using AJCC version 8 and the paper includes multivariable analysis that demonstrates the statistical independents for the DecisionDX Melanoma test from clinical pathologic factors incorporated in staging. And the same can be said for Arnot, et al., and Shay, et al., listed below.

For the next several slides I'll walk through highlights from the (Green, Hall, and Shay) manuscript side. Next slide. DecisionDX Melanoma was consistently a significant productive of risk independent of relative prognostic clinical and pathologic factors across multiple studies.

It's important to highlight that outside of AJCC staging there is no other nationally accepted tool available that integrates all clinical and pathologic features to provide prognostic information.

Therefore, evaluation of the ability of DecisionDX Melanoma to improve the accuracy of defining risk for tested patients has focused on comparisons to multiple clinical pathologic factors and AJCC version 8 stage itself.

Next slide. The table here on this slide is adapted from the Green-Hall meta-analysis and demonstrates the next cohort of 1,479 patients. DecisionDX Melanoma significantly stratifies risk within AJCC stages and this study highlights how DecisionDX Melanoma can serve as adjunct to staging, not a replacement for staging.

The survival rates from AJCC only demonstrate stratification of melanoma specific survival but don't give information on recurrence free survival, RFS, and distant metastasis free survival, DMFS.

And this information is used by clinicians to guide important management decisions such as the frequency of follow up imaging referral in multidisciplinary clinics. Next slide. So DecisionDX Melanoma significantly stratifies risk within AJCC stages and provides added prognostic information to an approach that relies on staging alone.

Based on this recent prospective study from Dr. Shay et al., patients with early-stage disease and high risk class 2-B results had a recurrence risk similar to patients with later stage disease who are currently recommended to receive more intensive follow-up surveillance imaging and referrals to multidisciplinary care.

So and this way DecisionDX Melanoma testing identifies the level of risk in early stage patients that's determined to be clinical actionable by national guidelines, next slide. And further Dr. Shay study, et al., shows that overall sensitive of risk prediction is enhanced when DecisionDX Melanoma and AJCC version 8 staging are combined as DecisionDX Melanoma is more sensitive than AJCC version 8 staging alone for predictions of the endpoints of RFS, DMFS, and death.

Again, this recently published perspective multicenter study should be considered by the draft LCD as it demonstrates that DecisionDX Melanoma improves the accuracy of defining risk for health outcomes of interest for testing patients, especially when combining DecisionDX Melanoma with AJCC staging to identify recurrences in metastases. Next slide.

From the study from (Green-Hall) et al., the meta-analysis, 867 patients had both GEP testing and sentinel lymph node biopsy performed and it shows that the DecisionDX Melanoma outperforms the prognostic accuracy of sentinel lymph node biopsy ...

Robert Kettler: Dr. Goldberg, (two) minutes.

Matthew Goldberg: Yes. OK. Thank you. Just a few more slides here. The – this again highlights that DecisionDX Melanoma augments current risk ratification approaches when GEP results are considered in the context of AJCC staging.

So on this slide here, since 2018, the original LCD effective date, DecisionDX Melanoma's been ordered by – on Medicare age patients by 4,700 clinicians and over 2,700 institutions including 40 leading academic centers.

DecisionDX Melanoma's been included in the multidisciplinary workforce at many academic hospitals to integrate AJCC staging and decision DecisionDX Melanoma across the spectrum of patients with Stage I through III melanoma. And the schematics of those clinical (workflows) are seen here at the bottom of the slide, next slide.

So in conclusion, the data published today continued to support the validity and utility decision DecisionDX Melanoma to identify patients with tumors two millimeters in thickness or less who have a low risk of metastasis to the sentinel lymph node who can safety forgo the sentinel lymph node biopsy surgical procedure.

And we request consideration of research that evaluates DecisionDX Melanoma test results on conjunction of AJCC staging and other clinical

pathologic features to improve the accuracy of risk prediction for patients with Stage I through III melanoma.

The Grossman and Marchetti articles recently added the draft LCD did not contribute additional tested patients to the published literature and have limitations that are not currently outlined in the draft LCD as others have mentioned.

The Grossman article is an opinion statement informed by survey data with low response rate of 14 percent to both surveys. And Marchetti at all does not make comparison to the accuracy of GEP testing to accuracy of AJCC staging alone or consider the improvement in prognostic accuracy provided by combining GEP with AJCC staging approaches as has been performed in multiple studies such as (Green-Hall, Shay, Arnot) and others.

And what's more, both articles do not address the clinical utility of DecisionDX Melanoma to inform sentinel lymph node biopsy decision making. Finally, around 8,000 clinicians and thousands of institutions have adopted the DecisionDX Melanoma test to improve patient care and the many physicians with clinical experience for how GEP test results can be incorporated into clinical workflows to inform their management decisions.

And last slide here, we will submit specific language for draft LCD modification during this open comment period but broadly speaking we recommend removing the two paragraphs recently added to the draft LCD that cite the Grossman and Marchetti articles. And in that event that their paragraphs remain ...

Robert Kettler: Please finish up.

Matthew Goldberg: Yes. We recommend including – thank you. I recommend including a discussion of limitations of both articles as well as thorough discussion of the numerous studies published since the LCD went into effect to further support the prognostic accuracy to the DecisionDX Melanoma to guide sentinel lymph node biopsy decision making and augment risk prediction for recurrence in metastasis, many of which were touched on today in this presentation. Thank you for your time and attention. And sorry for the technical difficulties at the beginning of the presentation.

Robert Kettler: That's quite all right. Thank you, Dr. Goldberg. Do any of my colleagues have questions for Dr. Goldberg?

OK. Thank you, Dr. Goldberg.

Matthew Goldberg: Thank you.

Robert Kettler: This concludes the formal presentations on DL3018. (Shelby), could you please allow any public comment.

Operator: If you would like to a make a comment, please press "star" "1." That is "star" "1" if you would like to make a comment. Again, to make a make a comment, please press "star" "1." We have no one in the queue.

Robert Kettler: Thank you. Our next draft LCD is DL39042. MolDX Biomarkers to Risk Stratified Patients at Increased Risk for Prostate Cancer. And we do have a presentation on this from Dr. Jeff Tosoian. Dr. Tosoian, please proceed.

Operator: Dr. Tosoian, please press "star" "1" to have an open line. Your line is open.

Jeff Tosoian: Are we also able to give Dr. Niknafs an open line as we're planning to present simultaneously.

Operator: His line is open as well.

Robert Kettler: Thank you. Proceed please.

Yashar Niknafs: Hello, can everyone hear me?

Jeff Tosoian: Dr. Niknafs, go ahead. Yes.

Yashar Niknafs: Hi, am I – can people hear me.

Robert Kettler: Yes, we can hear you.

Yashar Niknafs: Awesome. Thank you so much. Thanks for the opportunity to present and I just want to thank WPS for putting the draft LCD together. We're very excited to see support for prostate cancer pre-biopsy markers and I'm excited to tell

you a little bit about us and the test that we have. So if you go to the next slide.

So I am – as you saw the chief executive officer at LynxDX. We're a start-up company that spawned out of the University of Michigan. We're located in Ann Arbor. So we fall under the WPS jurisdiction so we wanted to show you the data for our test and introduce ourselves and hopefully build a relationship between ourselves and WPS as we move forward and expand the clinical use test.

So we're working to get the prostate score test in the hands of clinicians and spread its clinical usage. The test itself was developed at the University of Michigan where I received my PhD. I worked on this test. So we spun the company out to take it from an academic endeavor to translate it into being in the hands of clinicians.

So the byproduct is that MPS – and we refer to it as MPS, M-P-S, has very strong academic support. There's been many publications that have come out supporting its utility and validity over the past – almost a decade. And so – and support from many different institutions around the country and the NIH and so we are very recently LynxDX was formed to go take the next step and actually commercialize the test and make it actually used by patients.

So that's a little of a background. If you go to the next slide this is the – so the test itself just to kind of get your – everyone up to speed on the technology, it's a urine test, post DRE and it measures the expression of multiple prostate cancer markers, PCA3 and then the TMPRSS2 ERG Fusion.

Those are two cancer – prostate cancers to the specific markets measured in the urine. In addition to the serum PSA levels a risk score is calculated and that risk score estimates the risk of detecting high grade prostate cancer on biopsy.

So the goal for the test is a low MPS score will prevent the proceedings of biopsy in patients that have elevated suspicion for prostate cancer. Of note we – the test has a PLA code, 0113U. That is on the fee schedule. And so we just want that on the radar as I'm sure further communications will ensue on billing and coding for the test.

Next slide please. So the LCD – obviously we're discussing this LCD, so WPS and MolDX released the LCD, a broad LCD on biomarkers for – pre-biopsy biomarkers for prostate cancer. And so although MPS was not explicitly mentioned in the LCD or the summary of evidence, it does have extensive evidence, suggesting that it is in line with the goals of the LCD.

So – and we'll show you a little bit of the performance and the data but we believe that MPS provides that desired clinical impact that's outline in the LCD and we also believe that inclusion of the test and the summary of evidence will provide clinicians with a strong and reliable tool to accomplish the goals that WPS and MolDX have outlined and what they desired from the LCD.

At this point I'm going to hand it over to (Jeff) – sorry, Dr. Tosoian, so he can tell you about the test and some of the data.

Jeff Tosoian: Great. Thank you so much. We can go the next slide please. Again, thanks so much for the opportunity to speak today. I'm Jeff Tosoian. I'm finishing a fellowship in neurologic oncology at the University of Michigan and will be joining faculty at Vanderbilt as Director of Translational Cancer Research later this summer.

My research is focused in this exact space, the diagnostic and prognostic views to biomarkers and prostate cancer, and my clinical practice is similarly in neurologic oncology. And so, as a clinician that makes these decisions with patients as to whether to perform a biopsy or not, we have been underpowered and performing unnecessary biopsies for far too long.

And so there's a great need for tools like MPS that can guide those decisions as the LCD speaks to. I was also, personally as a clinician somewhat frustrated by the data that was available on existing tests which often included poorly defined populations and patients that really wouldn't qualify to benefit from biomarker testing such as those with a PSA level greater than 200.

So as a clinician and clinical researcher myself, with the opportunity to lead some of this work, on the MPS test we really (aim) to design these studies as clearly and transparently as possible to the intended purposes.

And so, to that point, in our recent validation paper to (condition four) we clearly provided the test results – the findings of using MPS in a large guideline directed population, and as the name implied, the guideline directed population is based on the criteria set forth by the NCCN for patients who do serve to benefit from use of tests such as MPS, specifically nations with a PSA of three to 10, or suspicious rectal exam. I'll speak to the specific accuracy on a later slide.

Next slide, please. Similarly as the LCD outlined the importance of tests being validated in separate external cohorts, and the literature has gone further as to recommend that validation is performed in multiple external cohorts. We did, again, perform validations in two large external cohorts. One from community clinics and one from an academic – and from academic practices which will better ensure generalized ability outside of the study setting.

Next slide, please. This slide just notes on two recent publications, which speaking to condition six, one demonstrates clinical validity of the test, and one clinical utility of the test, meaning that it did in fact impact decision making clinically, as I will specify in coming slides.

Next slide, please. And so there are several papers to the – demonstrating the validity and additional emerging papers – the utility of the MPS test specifically.

Next slide, please. So as a clinician, myself, I was also frustrated by how previous tests were validated at levels of negative predictive value sensitivity that really weren't sufficient to change clinical practice. For example, where patients with a negative test would still have a 13 to 15 percent risk of potentially lethal cancer, which, in my opinion for the majority of patients is not low enough to forego biopsy.

Next slide, please.

Robert Kettler: Dr. Tosoian, two minutes.

Jeff Tosoian: Very good. And to that point, MPS, has been validated to very high sensitivity and negative predictive value of 97 percent in that specific population. In terms of clinical utility, (here) from a real time clinical use of MPS in clinical practice.

You can see that (approximately) a little less than half of patients did not go onto biopsy looking at the factors across those who did who did not proceed to biopsy we found that the MPS test was actually the only significant factor in actually guiding clinical decision-making.

Next slide, please. An external group (route) (inaudible) group that is truly world renowned and the economic evaluations of testing has recently spoken to the cost effectiveness of these tests, and as one may suspect urinary tests including MPS provide greater economic value, greater cost effectiveness than the approach of MRI or previous approaches such as biopsy (OMEN) in this grey zone.

Next slide, please.

Yashar Niknafs: I'll just step in here just to ...

Jeff Tosoian: Yes?

Yashar Niknafs: Yes, so just in summary the – (My Process Score) is a post-DRE urine biomarker test, it's an extensively validated, performs extremely well and we think meets all the criteria outlined in the LCD draft. We don't need to go into those details there. And in conclusion we're requesting that this be considered for coverage under the LCD, and be named as one of the tests that is appropriate to apply for the LCD. And we thank you for your time.

Robert Kettler: Thank you. Are there any questions on this presentation?

Barry Whites: Yes, this is Barry. A question on your – where you talk about clinical utility and its utilization in getting a biopsy or not doing a biopsy. Do we have patient outcome data based on those decisions?

Jeff Tosoian: Yes, I'll go ahead and answer that. So yes, the specific population from that clinical utility study, approximately 280 patients as the full manuscript details. The validity of MPS was preserved meaning that inpatients to did undergo biopsy, we saw the same associations that have been demonstrated in the larger validity studies, meaning that lower MPS scores were of course associated with negative or low-grade cancers, whereas higher MPS scores were associated with potentially lethal disease, grey groups two through five cancer. And these relationships persisted after we adjusted for even the use of MRI.

Robert Kettler: Any other questions? OK, well, thank you both.

Jeff Tosoian: Thank you so much.

Robert Kettler: I realized I didn't give the summary of this LCD, so before we take the public comment, I will just do that. This LCD does provide coverage criteria for prostate biomarker diagnostic tests to identify men who may benefit from a biopsy of the prostate gland.

And (Shelby), we can take any public comments if there are any.

Operator: If you would like to make a comment, please press "star" "1." That is "star" "1" to make a comment.

Again, to make a comment, please press "star" "1."

We have no one in the queue.

Robert Kettler: Thank you, (Shelby). The next (draft LCD) – and we are done with the formal presentations now. I'm going to go ahead and finish off the MolDX LCDs before going to the others. This is DL39044 MolDX – Multiplex Nucleic Acid Amplification Test (NAAT), Panels for Infectious Disease Testing. This is a limited coverage LCD for multiplex NAAT panels that defines a panel, clarifies that this LCD applies to outpatient, not inpatient testing, and provides coverage as well as non-coverage criteria.

(Shelby), we can take any public comments on this LCD.

Operator: If you would like to make a comment, please press "star" "1." Again, that is "star" "1" if you would like to make a comment. We have no one in queue.

Robert Kettler: Thank you. The next LCD is DL39040, MolDX – Next Generation Sequencing Lab Developed Tests for Inherited Cancer Syndromes. And this LCD provides clarification of Medicare administrative contractor discretion and how that discretion would be applied in the case of next generation sequencing for hereditary cancer syndromes.

And (Shelby), we can take any comments on this LCD.

Operator: If you would like to make a comment, please press "star" "1."

Again, to make a comment please press "star" "1."

We have no one in queue.

Robert Kettler: Thank you, (Shelby). The next LCD is DL34635, Botulinum Toxin Type A and Type B. WPS does currently have an LCD for Botox. (However), during the process of prior authorization which began about a year ago, we became aware that there were some changes in practice and so we have modified the LCD to make it more in line with current practice.

(Shelby), we can take any comments on this LCD.

Operator: If you would like to make a comment, please press "star" "1." Again, that is "star" "1" if you would like to make a comment. We have no one in queue.

Robert Kettler: Thank you. The last draft LCD is DL39051 Cosmetic and Reconstructive Surgery. Again, this is a revision of a current LCD and this is an attempt to bring it into line with current specialty society guidelines. And we can take any comments on this LCD, (Shelby).

Operator: If you would like to make a comment, please press "star" "1." Again, that is "star" "1" if you would like to make a comment. We have no one in queue.

Robert Kettler: OK. Thank you. That does conclude our agenda for the day. I'd like to thank (Shelby) for her assistance with this call. I'd like to thank my colleagues here at WPS for participating. And most importantly I do want to thank Mr. Richard

Staley for all his efforts before, during, and also what will be after this meeting to make things function so well. With that, everybody have a good day. Bye, now.

Operator: Ladies and gentlemen, this concludes today's conference call. You may now disconnect. Speakers, please remain on the line.

END