National Government Services, Inc.

Moderator: Craig Haug, M.D.

10/20/2021

2:35 p.m. CT

Coordinator: Welcome, and thank you for standing by. At this time, all participants are in a listen-only mode until the comment session of today's conference. At that time, you may press star 1 on your phone to make a comment. Today's conference is being recorded. If you have any objections, you may disconnect at this time. I will now turn the conference over to Craig Haug. Thank you. You may begin.

Craig Haug: Thank you, Operator, and good afternoon, and welcome to the NGS J6/JK open meeting. Next slide, please. Just as a reminder, this call is being recorded and transcribed, and we usually post it to our website in a week or two. Next slide. Let me also welcome you on behalf of all the NGS entities listed on the slide. Next slide. Thanks.
The two proposed LCDs up for discussion today, both revisions to existing LCDs include genomic sequence analysis panels in the treatment of solid organ neoplasms, and colon capsule endoscopy. Next slide. So, first up is the LCD genomic sequence analysis panels in the treatment of solid organ neoplasms.

This revised LCD was prompted by several reconsideration requests. The pre-existing LCD covered targeted or small genomic analysis panels for advanced colorectal cancer and non-small cell lung cancer, and was not specific to next-generation sequencing. The newer draft policy section covers a large number of panel, so-called comprehensive genomic profile CGP testing in advanced solid tumor cancer.

CGP is a next-generation sequencing approach that uses a single assay to assess hundreds of genes for a host of relevant cancer biomarkers. It is especially necessary for so-called pan-cancer biomarkers that identify patterns of mutations such as DNA mismatch repair deficiency, microsatellite instability and total mutational burden, or TMB. Next slide.

The LCD coverage criteria on this slide largely tracks the tumor type agnostic criteria allowed under NCD 90.2 for

next-generation sequencing. Specifically, when the patient has either recurrent, relapsed, refractory, metastatic, or advanced stage three or four cancer, and has not been previously tested for the same cancer genetic content, and has decided to seek further cancer treatment, for example, therapeutic chemotherapy. Next slide, please.

We received four requests to reconsider this policy. First up is Dr. Calvin Chao, Tempus Labs' Senior VP of Medical Affairs. Operator, can you see if Dr. Chao's line - or Dr. Chao is now online and available?

Coordinator: Yes. And Dr. Chao, if you are online, if you could please press star 0. Unfortunately, I do not see that he is online yet.

Craig Haug: Okay. Well, let's go to the next speaker then. Let's see. That's Dr. Roger Klein, Chief Medical Officer at OmniSeq. I believe, Operator, Dr. Klein is available. So, if you could open his line. Dr. Klein, are you there?

Dr. Roger Klein: Yes. Hi. Thank you.

Craig Haug: Great. Please proceed.

Dr. Roger Klein: Thank you. So, as one of the submitters of a reconsideration request that helped prompt proposed LCD DL-37810, we agree that the medical evidence, technology requirements, and practical exigencies of oncology practice, support the use of comprehensive genomic profiling in patients with advanced cancers.

Although we will be sending written comments to you, we wanted to take this opportunity to thank National Government Services for this important step in support of oncology practitioners and. most important, in helping to improve care for Medicare beneficiaries with cancer.

Craig Haug: Thank you, Dr. Klein. Okay. The next - I assume, Dr. Chao still isn't here, right?

Coordinator: He actually has joined now.

Craig Haug: Okay? So, he's available?

Coordinator: Yes, I can go ahead and open this line, if you would like.

Craig Haug: Great. Dr. Chao?

Dr. Calvin Chao: Hello, can you hear me okay?

Craig Haug: Yes, we can hear you.

Dr. Calvin Chao: Oh, thank you very much. Sorry for the technical difficulties.

Craig Haug: No problem.

Dr. Calvin Chao: I see my first slide. May I begin?

Craig Haug: Sure. Please proceed.

Dr. Calvin Chao: Thank you very much. Good afternoon, everyone. My name is Calvin Chao. I'm the Senior Vice President of Medical Affairs at Tempus Labs. I'd like to take this time to thank National Government Services for drafting a very thoughtful LCD on the coverage of genomic sequence analysis panels in solid tumor oncology. Next slide, please.

I am a salaried employee of Tempus. I serve as the Senior Vice President of Medical Affairs at the company. Next slide, please. Tempus is a leader in genomic sequencing, providing over 50% of academic medical centers, and well over 40% of all oncologists in the United States, with next-generation sequencing services.

We also work with industry associations such as ASCO to distribute and structure the clinical oncology data collected as a part of the CancerLinQ project. There's a few points I'd like to make about the core product that we'll discuss today, the xT assay. It is a hybrid capture next-generation sequencing, high complexity laboratory-developed test performed in our laboratories in Chicago.

And there's a few points I'd like to make about this test. Firstly, that this is a test that is able to detect actionable oncologic targets in solid tumors and hematologic malignancies by sequencing tumor sample DNA. We perform this in a tumor normal matched approach, meaning that we collect both the tumor sample, as well as a tube of blood or saliva sample, and the latter sample allows us to be able to differentiate genetic findings that may be a part of the germline, and not necessarily representing the tumor somatic gene alterations. And therefore, we really get a better, more accurate read on the somatic tumor alterations that are present.

Secondly, we perform both DNA and RNA sequencing on each sample. The RNA is actually very important to be able to identify gene fusions or translocations. These are less frequent alterations that are found that need to be found in an unbiased and comprehensive manner. And by doing so, we are able to provide a more complete

assessment of whether or not these gene fusions are present, and when found, often these point to approved therapies that are now indicated for patients who have these rare gene alterations. And so, this becomes really quite important for those patients.

And then lastly, the tumor mutational burden and microsatellite instability measures, are important key parts of the xT tumor panel. These assessments can only be conducted using large broad panel sequencing tests, such as the xT. Next slide, please. There's really four key points I'd like to make regarding the medical necessity of the broad panel sequencing approach.

The first is that the biomarkers that require comprehensive genomic profiling, include measures that include TMB, the tumor mutational burden, as well as microsatellite instability. And I'll have a separate slide about this shortly. But these measures, again, are important in a number of different tumor types and have pan-cancer treatment implications and approvals for use of immunotherapies. And again, this requires a broad panel approach and sequencing.

Secondly, the detection of gene fusions is important. These are rarer findings, but when found, have actionable implications. And by conducting RNA, in addition to the DNA, we are able to assess more accurately and completely the presence of these findings that could point to on-label indications for specific therapies.

There are ample data referenced below that show that when conducting RNA sequencing in addition to DNA, such as with the xT assay, we are able to identify on the order of 15%, additional patients who have these gene fusions. Thirdly, this is a very practical point. Many patients in oncology present with only a very small amount of tumor tissue.

These are gathered through needle biopsies, or oftentimes very small snippets of tissue from a bronchoscopy or an endoscopy. And as such, patients have a medical need to preserve their scarce tissue samples, and to be able to maximize the test results from such samples, to be able to guide their treatments.

This is actually an approach recommended by the NCCN guidelines. At one time in the past, patients had to have sequential testing or tests done with smaller panels that are incomplete. And today, we - the guidelines do recognize the importance of being able to conduct a much broader panel that maximizes the information from these single specimens.

And the last point is a need in some very special populations. We know that in 25% of patients, patients present with rarer cancer types. As well, there are patients who are represented by underserved minorities and even pediatric populations.

And for many of these patients, they're really often confronting situations where there are no effective alternative treatment options, unless one is able to conduct comprehensive genomic profiling. And by doing so, physicians can then best guide that appropriate treatment for these patients using what therapies may be available. Thank you. Next slide.

So, I'd like to dwell a considerable amount of time on this tumor mutational burden, which is really an important measure that has really gained a lot of attention in the last 16 months or so since Pembrolizumab received an approval from the FDA for TMB high solid tumors. This occurred in June 2020.

And it's very clear now that based on these findings, a number of guideline and consensus panels have incorporated tumor mutational burden as an essential measure in guiding multiple cancer treatments for use of immunotherapies. The Keynote 158 study was the key study that led to the FDA approval for Pembrolizumab for TMB high tumors.

And since that time, you can see that the ESMO Group actually recommended their guidelines and published them in November 2020 for a number of different cancers, lung cancer, cervical, endometrial, squamous cell, thyroid, neuroendocrine, vulvar and cancer of unknown primary.

And then, in January 2021, TMB was recommended by the NCCN Group for quite a number of their different guidelines, head and neck cancer, testicular, breast, bone, gastric, esophageal, uterine, hepatobiliary, cervical, ovarian, cancer of unknown primary, and thyroid.

These guidelines are being updated almost every month. There are 34 guidelines in total by the NCCN, and we continue to see movement in this area. Furthermore, there have been two recent studies published in April 2021 that add further evidence to the importance of TMB.

The Taper study, the breast subgroup of that Taper study, actually also supports TMB testing in metastatic breast cancer patients. And then lastly, there has been a meta-analysis published in April, with five randomized controlled trials representing over 3800 patients in the first-line non-small cell lung cancer setting, showing overall survival benefit for patients receiving immunotherapy agents versus chemotherapy in TMB-high patients.

Notably, TMB is an important measure that is distinct and independent from other measures such as MSI and PD-L1. And again, one needs to have at least 300 genes assessed in order to be able to measure - to conduct this measurement. Next slide. In conclusion, Tempus supports NGS’s expansion of coverage for comprehensive genomic panels.

We agree that Medicare beneficiaries deserve access to broad panel sequencing to enable treatments that really improve their outcomes with metastatic disease, and we certainly think this should include the use of Pembrolizumab when appropriate, when TMB measures are high, and again, measures that can only be conducted when broad panels sequencing is done.

Furthermore, Medicare beneficiaries also deserve access to comprehensive gene panels, not only by tissue testing, but also by plasma ctDNA testing. And we think that the latter is important when patients are not able to have a successful tissue biopsy assayed, either because of insufficient quantity of tumor, or because simply the patient is unable to safely undergo appropriate biopsies or to be able to have enough tissue sent to be able to complete these analyzes.

And this approach is again recommended by the NCCN Guidelines. And so, the emergence of liquid biopsy as an option, is an important one for many patients. In conclusion, we do encourage the National Government Services to finalize the proposal, expanding access to medically necessary testing through comprehensive genomic profiling. Thank you very much.

Craig Haug: Thank you, Chao. Thank you for these comments. If we could move down three slides, I guess, to Dr. Loo's slides. And we have the next - so, our next speaker is Dr. Eric Loo, a New Hampshire CAC-Representative, speaking for the New Hampshire Society of Pathologists. Operator, if you could open his line.

Dr. Eric Loo: Hello.

Craig Haug: Dr. Loo, we can hear you.

Dr. Eric Loo: Can you hear me okay?

Craig Haug: We can hear you. Please proceed.

Dr. Eric Loo: Oh, thank you. So, if you could just go ahead to the next slide, I guess. My name is Eric Loo. I'm a pathologist at Dartmouth Hitchcock Medical Center, but I'm, I guess, wearing my hat as the society representative from New Hampshire to the NGS CAC. I don't have any conflicts of interest to disclose.

And I just wanted to, I guess, start off by saying that the New Hampshire Society of Pathologists, and probably Dartmouth-Hitchcock, will also be sending letters for commentary as well. But I just wanted to thank you all for being so responsive to our concerns in the past, and in this particular case, taking steps to ensure that appropriate care is always extended to Medicare beneficiaries in our region.

If you could go to the next slide, please. We do have some commentary and questions. I know that this particular portion of the LCD isn't specifically open for commentary, but just wanted to point out that, you know, the wording is still the same and, you know, includes stipulations referring to sequential analysis instead of CGP, and some other things that probably should get looked at.

But since this isn't, you know, theoretically open for commentary, I guess we should just keep going on to the next slide. The first thing that we wanted to ask about was in regards to the test performed must be able to detect the minimum number of genes and genomics positions required, you know, and as per requirement, as stated here, it's referencing the NCCN biomarkers compendium.

And we were hoping to have NGS clarify that - if this requirement will be tied to a particular date or to a particular version of the NCCN biomarkers compendium. The reason for this is because, you know, the addition of a new category 1 or 2a entry could potentially invalidate a clinical laboratory's assay.

And as you probably know, it takes us a significant amount of time and effort, you know, even up to a year sometimes, to get a particular assay of this nature validated for clinical use. So, the time and resources put into, you know, the assay, if you had, you know, a new thing updated to the compendium, you know, a month after the assay goes live, for example, it could really be pretty harmful to a laboratory.

And then the other thing, there was another stipulation further down in this comment saying that testing assays must be FDA approved or if a laboratory-developed test have been published, then peer-reviewed studies supporting the analytic validity of the test needs to be present.

The New Hampshire Society of Pathologists, the College of American Pathologists, the Association for Molecular Pathology, don't all support requiring peer-reviewed studies and the coverage policies for lab-developed tests. This has never been a requirement, you know, under CLIAR.

The CLIAR - the Clinical Laboratory Improvement Act that went into effect in the early '90s, you know, stipulate a large number of, you know, validation steps that need to go into validation of a clinical assay prior to implementation for patient care. And, you know, this additional requirement would really put a damper on things.

It's - this has not been the case before. And yes, we feel that this is an unnecessary and rather onerous burdensome requirement, especially if it's a laboratory-developed test that is only used in like one or other two institutions at first. You know, it's just been approved - if it's been clinically validated, it may be tough for, you know, that laboratory to, you know, produce the study or find other studies, you know, in the literature at that time.

So, I guess that's that comment.

And then next slide. In terms of the utilization guidelines, the particular thing that we had wanted to bring to your attention is that 81455, you know, is being cited as comprehensive genomic profile testing. And that at present is assays that are larger than 50 genes. But there's a significant heterogeneity in the, you know, assays that are present that fall under this CPT code.

For example, the Tempus assay that Dr. Chao had just referenced is - you know, covers about 650 genes. There's a Foundation one assay that covers like - I think it's 300 to 400 genes. The assay that we currently use in-house at Dartmouth-Hitchcock for our solid tumor testing only covers 170 genes.

And so, you know, the descriptor that NGS is using to describe comprehensive genomic profiling assays as being able to detect MSI, tumor mutational burden, and, you know, any number of other items, doesn't actually apply to a number of the tests that would fall under this particular CPT code, TST 170 assay that we're using at Dartmouth, for example, doesn't include microsatellite instability testing.

It doesn't have enough genes to actually do tumor mutational burden analysis. And there are a number of other tests that we wouldn't be able to do with the TST 170 assay, including methylation testing. You know, there's some assessment of various genes that are pertinent to gliomas that we wouldn't be able to, you know, do this testing.

So, we would - we at DH, for example, would need to actually order separate molecular tests on any given particular specimen that we're running this CGP assay. So, we feel that this particular requirement that, you know, any specimen that has 81455 ordered, you know, any additional molecular testing ordered on that particular specimen encounter, would be automatically denied. That doesn't seem quite fair, you know, given the heterogeneity of testing that would fall under this particular CPT code.

And I guess there was - another question that we had was that there are certain cases where we might have to order 81455 on two separate specimens on the same encounter, you know. just as a true-to-life example, a couple of months ago, there was a person that had two separate but synchronous lung cancers that had separate, you know, mutational profiles, and actually had different treatment - implications for treatment because of that.

They were two separate lung cancers that were both excised on the same date of service, and, you know, the current LCD would have been pretty restrictive to that person. And I think that's it. Maybe the next slide? Yes. So, just wanted to say that we'll also be sending commentary in letter form after this, and wanted to, again, say thank

you for helping to clarify things and letting us participate in the draft LCD process. Thank you.

Craig Haug: Thank you, Dr. Loo, for your comments, and also for being a New Hampshire CAC-Representative. Thanks a lot for that. Next slide, please. The last registered speaker is Dr. Joe Lennerz, Medical Director, Center for Integrated Diagnostics at MGH. Operator, can you see if he's online and his line is open?

Joe Lennerz: Hello. Can you hear me?

Craig Haug: Yes, we can, Dr. Lennerz. Am I pronouncing that correctly?

Joe Lennerz: Yes, that's correct. Lennerz. That's fine. Thank you very much. First off, I have no conflicts of interest, and I'm speaking on behalf of the Mass. General Brigham healthcare system, nonprofit healthcare system representing the Harvard-affiliated teaching hospitals, Mass. General Brigham and Women's Hospital, Mass. Eye And Ear, Spaulding Rehab Center, and a few other community healthcare centers.

As one of the employers in Massachusetts with about 80,000 employees, we strongly support the coverage of comprehensive genomic sequencing for patients with all types of malignancies in advanced stage after recurrence, relapse, or treatment resistance. As the policy is written, it is very meaningful.

The tests that are supported by this LCD policy, enable treatment with potentially life-extending therapies across a broad spectrum of mutations and cancers, and applying the panels in this setting is extremely meaningful. So, instead of running separate individual tests and individual cancers one at a time, this comprehensive genotyping is the most efficient and scalable solution that will keep pace with these new advancements in oncology and cancer therapeutics to improve patient outcomes.

So, again, we strongly support the coverage of comprehensive genomic sequencing panels performed in certified CLIAR laboratories. So, with tests that are either FDA-authorized or demonstrated analytical validity and published peer-reviewed medical literature. We find that this is absolutely meaningful, and both approaches and the FDA authorization, or demonstration of validity in the published peer-reviewed literature, are both strong indicators of test quality.

And combined with CLIA regulations governing that quality, will ensure the quality and safety for our patients. So, again, from our side representing Mass. General Brigham, we support this LCD policy as written, and we thank National Government Services for proposing this LCD, and for the opportunity to share our comments at this forum. Thank you very much.

Craig Haug: Thank you, Dr. Lennerz, for your comments. Okay. Operator, at this time, I'd like to ask if there are any other commenters online that would like to make a comment.

Coordinator: Thank you. And if you would like to make a comment, please press star 1 and record your name. If you need to withdraw your comment, press star 2. Again, to make a comment, please press star 1, and it will take a few moments for the comments to come through, so please stand by.

Craig Haug: Again, if we do have somebody who wants to comment, if they could identify themselves, as well as state if they have any conflict.

Coordinator: And currently, we have no one in queue. Oh, my apologies, it looks like one just came in. So, Mahesh Mansukhani. Your line is open.

Mahesh Mansukhani: Hello. Hi. I'm Mahesh Mansukhani. I'm from Columbia University Medical Center. And I'd like to thank NGS too for coming up with this LCD. And I'd like to make one comment about the requirement for publishing validation.

Craig Haug: And speakers, before you start - just before - sorry to interrupt, do you have any conflict that we should know about before you make a comment?

Mahesh Mansukhani: I have no conflicts of interest. Sorry.

Craig Haug: Thank you.

Mahesh Mansukhani: I work for Columbia University, a nonprofit.

Craig Haug: Thank you. Go ahead.

Mahesh Mansukhani: Thank you. And the one comment I want to make is that here in New York State, all our assays are reviewed - our validations are reviewed by the Clinical Laboratory Evaluation Program of the New York State Department of Health, and that should be considered as equivalent to a peer-reviewed publication. Thank you. That is all I wanted to comment.

Craig Haug: Thank you. Operator. …

Coordinator: Thanks. And our next …

Craig Haug: So, we have others. Okay, go ahead. Sorry.

Coordinator: That's Okay. We just have one more. And it comes from Michael Kluk with Cornell. And your line is now open.

Michael Kluk: Hi. Can you hear me?

Craig Haug: Yes.

Michael Kluk: Okay, great. Yes. Michael Kluk here from Weill Cornell. I thank everyone for this effort. This is a very significant development in NGS testing, and it has been an obstacle for several centers to expand their NGS testing. So, we're very happy to see progress being made and opportunity to provide feedback.

I would echo the sentiments of Mahesh and also Dr. Loo, who spoke with regards to their two comments. I would agree that ancillary tests are an important component of the comprehensive genomic profiling that's done, specifically with respect to turnaround times and sensitivities.

Certain standalone tests can provide quick answers when needed clinically on the order of days rather than weeks, which it may take to turn around a larger panel by NGS. So that ancillary testing, we do feel is important. And prohibiting reimbursement for a larger panel that would complement that, we feel could be prohibitive or detrimental.

And the second point that Dr. Loo made that I'd like to echo is also the requirement for publication. Although it does seem reasonable, relevant as a sort of a first-half test - objective test of acceptability of an assay, these types of papers are particularly challenging to publish in the literature as pure like technical validation studies.

So, although that is one measure to assess the assay, we feel - require that it would need to be published is an onerous step. As Mahesh mentioned along these lines, we're also in New York State, and the New York State validation process is a very rigorous review process for any clinical test that we use in the US State, must be reviewed by New York State Department of Health and be implemented themselves. They've approved it.

So, this is - review process in New York State is just as onerous, if not more rigorous than a publication. So, we would request that the NGS consider that as an additional means test of adequacy of the assays to be used under this indication. Thank you.

Craig Haug: Thank you, Dr. Kluk. Is that the correct pronunciation, Kluk?

Michael Kluk: It's K-L-U-K, Kluk. Yes. Thank you.

Craig Haug: Okay. Kluk. Thank you again. Operator, do we have any other commenters?

Coordinator: No, there are no other commenters in queue.

Craig Haug: Okay. Then comments on this policy for this open meeting are now closed. Can we have the next slide? The next policy up for comment is colon capsule endoscopy. This LCD revision was prompted by an update to the NCD. This is an internal generated change, not a reconsideration request, prompted by an update to the NCD 210.3, which added blood-based biomarkers to the list of approved colorectal cancer screening tests.

The existing policy had included the prior approved screening test, if positive, as a potential indication for colon capsule endoscopy. So, it seems appropriate to include the latest one. Next slide. This slide outlines the indications for CCE or colon capsule endoscopy, either as a secondary procedure where an optical colonoscopy is incomplete, or as a primary procedure when optical colonoscopy is medically contraindicated.

Both of those situations include provision for CCE as a diagnostic procedure when one of the NCD approved colorectal cancer screening tests are positive. And as I mentioned before, this revision simply added the latest approved screening test, which is highlighted in yellow to the other two. Operator, can you see - there were no registered commenters on this policy. Can you see if there are any online?

Coordinator: And I do not have any in queue, but I apologize, I cannot see your online information.

Craig Haug: Well, yes. No, I'm just referring to anyone on the phone.

Coordinator: Okay, thank you. Currently, there are still no comments in queue.

Craig Haug: I'll just give it another second or two to receive any.

Coordinator: And again, please press star 1 if you'd like to make a comment.

Craig Haug: Still none?

Coordinator: Yes, we still have none in queue.

Craig Haug: Okay. So, this is a relatively straightforward change. So, then comments on this policy for this open meeting are now closed. We can go to the next slide. This slide simply shows that the official comment period ends on November 13. Next slide. And this slide shows where to send either via email or snail mail. I think we prefer email. And this concludes our NGS J6/JK open meeting. Thank you for attending.

Coordinator: Thank you. And that concludes today's conference. Thank you for participating. You may disconnect at this time.

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