Comprehensive Biomarker Testing and Lung Cancer Patient Panel

[Lorren] Thank you so much for joining us for the Caring Ambassadors Program video series, Learn from the Experts. Our main goal is to empower and educate patients and communities to be advocates for their health and to improve their lives.

Today's video is dedicated to living with lung cancer and it highlights one chapter from our book, Lung Cancer Choices. The video series is broken down into short segments, so it's easy to watch and navigate. You can watch the videos in any order, so feel free to choose what interests you the most.

I'm Lorren Sandt, the Executive Director at Caring Ambassadors Program, and I'm joined today a panel of people living with lung cancer and caregiver(s). We're very excited to welcome nurse practitioner, Elizabeth Krueger. Liz will be discussing the chapter, Comprehensive Biomarker Testing, written by her colleague, Kelly Goodwin.

Elizabeth Krueger is a family nurse practitioner who specializes in the care of thoracic oncology patients at Massachusetts General Hospital. She completed her Bachelor of Science degree in Heathcare Policy and Management at Providence College and then went on to receive a Bachelor of Science in Nursing and Master of Science in Nursing from Regis College.

More than a dozen new drugs for the treatment of NCSLC have been approved since 2013, marking an exciting and hopeful time in lung cancer research and care. With improved biomarker testing techniques, an expanding list of molecular targets, and more and more approved and emerging therapies, comprehensive biomarker testing is an essential part of the evaluation and management of all patients diagnosed with non-small cell lung cancer. In this video, Liz will answer

patients' questions about Biomarkers and the importance of advocating for comprehensive testing.
We hope that this video will provide helpful insights and information for patients and caregivers dealing with lung cancer. If you're interested in learning more about the Caring Ambassadors Program and our mission to help patients with lung cancer, please watch the video series.
And please share this information with anyone who might find it useful. Together, we can make a difference in the lives of those affected by lung cancer. Welcome Liz.

[Chris] Hi Liz, good morning how do I know what I was tested for, and also who do I contact if I have questions on the lab or test report?

[Liz] Great question Chris, the first question, the first part, how do you know what you were tested for? I think the discussion should begin with your medical oncologist to review whatever molecular testing was done. If I were a patient I would ask, did I have comprehensive testing that was done or were single gene probes tested? As a patient you would hope that you had comprehensive testing that would explore a variety of genetic alterations, potential alterations in the tumors that could open doors to therapies. Single gene testing when they specifically look for say an EGFR mutation or ALK that can exhaust a lot of tissue after one has had a biopsy so in order to preserve specimens and to get the most I guess bang for your buck a comprehensive test would be the best option, and then discussing that test with your medical oncologist. If he or she is unable to answer questions that you have then they often collaborate with molecular pathology. Some of the reports can be really difficult to interpret and depending on what tests were run, and how they're reported, whether they spell out that it's an EGFR, ALK, or KRAS, or do they just give the specific gene changes, or the address on the genome, that can be really overwhelming and complex to look at. So yes, I would start with your medical oncologist and then you should also feel empowered to ask for that information. The 21st Century Cures Act ensures that patients should have seamless access to their medical information and an exchange of health information so, you should feel comfortable asking to have that in hand. And if you don't feel that your questions have been answered fully, if you have the means, we'd always recommend getting a second opinion at an academic Medical Center that specializes in lung cancer to answer any outstanding questions that you might have.

[Chris] Okay, thank you.

[Sherry] I have a question Liz, oncology practices seem to vary when it comes to additional biomarker testing, is biomarker testing recommended with tissue biopsy after progression or reoccurrence, and is there right time to administer subsequential testing?

[Liz] Really good question, I think that throughout either academic medical centers and within the community there are different practices. I can speak to our practice which I feel really confident about, given the team that I work with that we check biomarker testing on all patients in the metastatic setting and individuals with early-stage disease, and we repeat that testing often at progression, and it's a little tricky, sometimes we do blood-based testing so that to look for circulating tumor DNA, other times we do go for tissue biopsy to look at the gene changes in the tissue itself and those decisions are fluid and we often have many people participate in that decision making. So, if for example, a person had scans that demonstrated very significant changes in their disease burden, like there had been very significant growth, we might opt to do tissue based testing in that scenario because with tissue based testing we're also looking at the makeup of the tumor itself and the pathology. On some occasions the pathology of the tumor can change from say a non-small cell lung cancer to a small cell lung cancer. So we always want to make sure we know and what the path is if we see significant changes. And then you mentioned recurrence, in the situation where an individual had been treated for cure, and then on an interval scan there seemed to be evidence of disease we would pursue a tissue biopsy in that situation as well to confirm whether it's related to a prior cancer is it a new cancer and then often the biomarkers can be compared from diagnosis to the one to any recurrent disease. And we do gene blood-based testing too to see if there have been any additional gene changes or resistance mutations that have developed over time so sometimes, or all the time unfortunately, the cancer in the metastatic setting, does figure out a way to outsmart these targeted therapies or pill forms. With gene alterations the cancer is addicted per se to these gene changes and that allows it to just replicate unchecked over time and so over time the cancer will learn to outsmart it unfortunately.

[Sherry] I had a situation where I had a blood biopsy done because my tumor was so tiny it was less than a centimeter so they it wasn't we weren't able to do a tissue biopsy because there wasn't enough tissue so they did the blood biopsy and they just wasn't anything to gain off that because there wasn't enough circulating DNA so it was just a weird position to be in where yeah they really couldn't do anything it was just kind of a watch and wait situation.

[Liz] And, what prompted them to do it? was it just a scheduled I don't know if it was your question or another person's question, that was it like a scheduled annual test or was there a change on the scan that they were reacting to?

[Sherry] Yeah, I had developed multiple tiny nodules and so we knew I was progressing, and it was like do we biopsy? Nothing was really big enough to get enough tissue to risk a tissue biopsy so we did went for the blood biopsy but it just didn't give us any information. So, it's just one of those weird situations.

[Liz] Yeah, that can feel with all of the advances you feel like they sort of failed you or just weren't helpful in that situation and that can be really challenging too.

[Sherry] Yeah, it was tough, but it all worked out I mean I just got lucky and changed my current therapy and it actually worked, it just was just one of those lucky things where sometimes that works sometimes it doesn't. I just got lucky.

[Liz] Yeah, I think that that happens maybe more often than we realize that we have to make a change based on like a clinical suspicion, based on imaging, and try either adding chemotherapy to a targeted therapy or switching targeted therapies if there's an option to do that following the response based on that question.

[Chris] I'd like to follow up I have a question for you, and I know it's real confusing all this talk about tumor and mutations and all that, but can a tumor have multiple mutations and if so, do they have like sub mutations of the mutation, how does that all work?

[Liz] Comprehensive biomarker testing checks for many mutations, and often we find more than one sometimes we find one sometimes we find a couple but the primary focus for clinicians typically when we look at this comprehensive testing

is to see what actionable what drugs do we have that match these gene changes and so we use that that as a tool to help delineate and come up with subsequent lines of therapy there are gene changes that are being explored for clinical trials so those are important too to know that you have if you're if you're thinking about next steps with your with your clinician additionally there are gene changes that can predict the virulence of the cancer and how aggressive it might behave based on some gene changes that we see that are not necessarily targetable but are information for the patient and care team you know that could be used prognostically.

[Lynn] Another kind of follow up to that discussion, we talked about sometimes things change from non-small cell to small cell, you talk about you know biomarker changes they change, or if they change, do they stay with you know their particular biomarker like EGFR 19 to 21, or do we change to a totally different biomarker?

[Liz] Good question. We don't typically see changes within the EGFR mutation itself that you were that you develop a new or different EGFR mutation. We might find that a new mutation has developed over time. Often, we see MET amplification over time and that be that's seen as a resistance mutation something that happens in response to treating the EGFR mutation with something like osimertinib over time. So, we can see a new mutation develop in the setting in that setting like resistance. What we can also see is that on occasion that the original biomarker that you're tested for might not be detectable that doesn't happen all the time, but it can happen, and it can feel funny once you and your provider are sorting out next steps and next lines of therapy. I'd say that just generally we typically continue to treat based on the biomarker that was found at diagnosis but then consider adding in new therapies if it's not detectable again on subsequent lines. I'd say that's not super common but possible.

[Chris] Let me ask you uh there's a I think there's a lot of confusion out there between what is Next Generation Sequencing and is that the same as a biomarker? You hear these terms Next Generation NGS and biomarkers, can you help us understand a little bit better what the differences are, are they the same thing?

[Liz] Sure that's a good question. The terminology really is overwhelming, and a lot of the terminology is swapped back and forth. So Next Generation Sequencing is the same as comprehensive biomarker testing, that's the same idea. So, it's the same broad-based gene testing and when we get the results of those tests we look for, or we hope to find, biomarkers or genes that have changed that can be targeted. So, a biomarker is a gene alteration that is identified on Next Generation Sequencing or comprehensive biomarker testing.

[Chris] I hear a lot when we talk to a lot of the folks a lot of confusion they think I've already done biomarker testing because I did this ancestry testing a long time ago, can you kind of help explain the difference also between those two a little bit?

[Liz] That's a very common question because automatically when we think about genes we think about inheritable genes and things that are passed down from generation to generation like what's done on 23 and me and those tests. But this is much different. So, the comprehensive biomarker testing or the Next Generation Sequencing that we do looks specifically at gene changes within the tumor material and not gene changes that are passed on from generation to generation through egg and sperm. These are also called somatic genetic changes. Changes within the tumor material. They can just be random events that happen when DNA is transcribed into RNA. They can be impacted from one's environment. So, smoking for example, you may develop gene changes from smoking within your tumor, but aren't inheritable. On occasion we do find inheritable gene changes in these sequences, we're not looking for them, but we occasionally do find something that is inheritable on Next Generation Sequencing. In our process if we were to find something like that is that, we you know inform the patient and then refer to genetics so that they can have the appropriate testing done to explore whatever potentially inheritable changes there may be for them and their family.

[Sherry] So I have the ALK positive gene mutation, and I hear people talking about you know different variants of that what type of testing would you have done to find out what variant you are?

[Liz] So Next Generation Sequencing should give you that information, comprehensive biomarker testing should give that information. There are even

broader based panels that you could discuss with your medical oncologist, but typically the standard comprehensive test should show those things. The single tests that are sometimes run I don't think would give you all that detailed information. They test specifically for ALK, they test specifically for EGFR, or other you know PDL-1, things like that. But more of the broad-based testing should.

[Marla] Is PDL-1 a mutation of proteins? And are there and are there any commonalities in people with just a PDL-1 expression and not anything else?

[Liz] Sure great question. PDL-1 is a protein that's on the surface of some cancer cells and it works to trick the body's immune system. So, the immune system is what fights viruses, fights infections, and basically is what the body uses to remove anything that's foreign and doesn't belong. PDL-1 evades the body's immune system and so that it's able to replicate unchecked by the immune system. We use immune checkpoint inhibitors, or immunotherapy, to essentially take the brakes off of the body's immune system, to heighten it so that it's able to recognize the changes in PDL-1 and remove them. As you know based on what you described in your introduction, it's a delicate balance and we have to be careful not to cause too much inflammation in the body. So PDL-1, you know these immunotherapies, are wonderful but occasionally there are a wide variety of potential side effects, and we never really know exactly when we might overstimulate the body's immune system causing autoimmune conditions or inflammation within the body.

[Marla] Can PDL-1 mutate into like one of the ALK positives or EGFRs or anything like that, or does it stay PDL-1?

[Liz] So, it's different, it's on the surface of the cancer cell. It's a protein on the surface of the cancer cell, and we don't typically see other targeted mutations develop over time, but it would still be worth repeating. And I know within the clinical trial space they're doing a lot of research on novel immunotherapies that can be used in that setting too.

[Marla] Oh that's good, because my doctor said the next time they start to grow, because I've sat there for like two and a half years not doing anything, that I would have to look at a breast cancer trial because I also have the breast cancer gene which they found out when they found the lung cancer problem. So, he was

saying you'd have to go on a breast cancer trial and I'm like oh, but if they have new approaches, thank you, that's given me a lot of possibilities.

[Liz] Yeah, I think that you know there's definitely lots of other options. There are trials and all with varying criteria but I think it's great news that you have other options that can be considered down the line and you know we're always cautiously hopeful when people have a significant response to immunotherapy and have a side effect because often that that activates the immune system for sometimes we don't know how long but for many years even though you're not receiving the treatment actively.

[Marla] He's instead of looking at five years now, he's looking at 10 years, he said the worst side-effects you have the longer you tend to live.

[Liz] Sometimes that sometimes that's true I know.

[Marla] I had rashes all over, my mouth was covered. Oh, I'm not ever gonna die then.

[Liz] If there's an upside to all of that, those side effects you've endured then I think that's a positive you should hold on to.

[Marla] Well they're gone now so I'm good. So, are there any commonalities in people with just a PDL-1, like weight, or age, or work environment, something?

[Liz] There's never a hard fast rule. We can see it in individuals that have tobacco exposure but not always, that I would say is the one of the biggest things. But it's also seen with other gene changes in the tumor, other genetic alterations. So, it could be seen with ALK, could be seen with EGFR, it is often seen with KRAS too.

[Marla] Yeah, I got nothing, all right.

[Liz] But, all that to say is that's why we need to do comprehensive biomarker testing is because there's no one size fits all for each person. We are often surprised by things that we find in patients. So, we would never want to just test for certain biomarkers based upon an individual's race or their smoking exposure. etc

[Marla] I never smoked but my mom did, when she passed, she was up to three packs a day, taking care of her that's the closest I came to smoking.

[Liz] And, sometimes you know unfortunately we just don't know.

[Marla] That's right never do.

[Liz]Which is not satisfying.

[Marla] Got me out of work. (laughter)

[Sherry] Yes so speaking of PDL-1, this might be a difficult question to answer because I know there's a lot of variables that come into play, if you run out of options with targeted therapies but your PDL-1 is high, is immunotherapy ever an option, or is it too dangerous?

[Liz] I think that's a good question. So I can tell you anecdotally and through some of our research is unfortunately when we see PDL-1 coupled with ALK or EGFR, it doesn't typically confer a good response to PDL-1 Inhibitors, regardless of like PDL-1 level. That being said I think it would be a discussion with your provider if they would you know try it, to see to if there were, if there were not other options. In the lung cancer space from my experience, we do not. Looking at NCCN guidelines we do not combine immunotherapy with targeted therapy because it really increases the risks of adverse events, so it would need to be like a TKI would be stopped or targeted therapy would stopped and then immunotherapy could be considered.

[Sherry] How long do they stop it because I heard that the target therapy can remain in your system for a while?

[Liz] I'm not sure I think that would have to be a discussion. I'm sure as Chris knows, in KRAS setting we do use imuno, so it's sort of reverse to first line for metastatic KRAS positive non-small cell lung cancer is chemoimmunotherapy, and then in the second line setting we can consider adding a targeted therapy. Something called Sotorasib or adagrasib and so occasionally we see some toxicity

given the prior immunotherapy, but I'd say overall it's pretty well tolerated in that sort of reversed picture.

[Sherry] Thank you

[Chris] Hi Liz, I hear a lot when I'm in a different settings talking to different doctors and all that and I kind of wanted to help everyone understand what is the difference between a small molecule drugs and monoclonal antibodies?

[Liz] So, small molecule drugs are just as they said, they're small they're tiny. They are typically come in pill form because they're so small they can be digested and cross cell membranes easily and get into cancer cells. Because of their small size they can also in many instances permeate the cerebral spinal fluid so, into the blood, past the blood brain barrier. Which is sort of atypical for other drugs. We only have a couple of drugs that we know that certainly past the blood brain barrier in terms of like chemotherapy but many of these small molecules treatments can get into the cerebral spinal fluid and treat CNS disease. So, they're small because they're small and they can get through membranes. Monoclonal antibodies are different, those are typically in an IV form. They are engineered antibodies that flag the attached typically to the cancer cells and the immune system removes them so they're different and then and have different effects. And monoclonal antibodies are typically combined with chemotherapy they're not typically given on their own.

[Marla] What's the difference between precision and targeted medicine?

[Liz] That's a good question there's a lot of semantics that can be difficult to sort of tease out. So, Precision medicine is the practice of doing gene testing and finding the right medicine or the precise drug that is right for the patient and their genetic alteration. Targeted therapy is the practice of finding the right drug to target the genetic change. Does that answer your question?

[Marla] I think so.

[Liz] It's sort of the same. Precision medicine is the practice of checking biomarker testing and finding the right drug to target for whatever gene change we might find.

[Marla] Are pills part of the targeted therapy or is it IV drugs?

[Liz] Great question. So, targeted therapy is typically I'd say for the most part an oral therapy of small molecule drugs that are absorbed through the GI tract and able to pass into the cancer and get the cancer cells in that way. There are a couple of IV targeted therapies that can be used in certain situations. There's one approved for a specific EGFR mutation, , so they're a little bit different. So just sort of to touch on that, you know just because it's a pill doesn't mean that it's less toxic than an IV Therapy. These are still really potent drugs that work really well but they do have side effects that that need to be monitored really closely. And typically, when we start them, we check labs every two weeks for the first six to eight weeks, and see patients frequently, because there are certainly many side effects that that can pop up in the short term, or over time, that can be just as significant as those medications that are delivered through an IV.

[Marla] and I was just wondering is it more like a chemo pill or what?

[Liz] Good question, it's not chemotherapy, it's sort of its own bucket of treatment. So, you sort of think of chemo as one group, and chemo goes after cells that divide rapidly. There's immunotherapy in another group that uses the body's immune system, and then there's targeted therapies that focus on gene changes and either blocking or inhibiting cell growth by connecting to certain proteins. So it's different.

[Chris] We talked a lot about the biomarkers, I guess one of the things that we run into a lot is with the co-mutations and I think there's a lot of questions around how does that impact my treatment, if you have multiple mutations going, on how do you typically look at determining what to treat if you have two different things?

[Liz} I think that it depends if they're targetable too. Are they targetable gene changes, right, do we have a drug that we know is effective in treating whatever gene change you have. I can say that we really do not see so like ALK with EGFR like that we would have to make a decision between those two. So, it's very uncommon to have two targetable gene changes that could be targeted with a

small molecule drug, unless over time another develops and that the most common one that can be develop over time is MET, that we can see.

[Chris] Yeah, what I was asking because like I know in the g12c drugs we're seeing those mutate to other types of variants and my question was, some people are saying should I still take the g12c drug along while attacking a different variant ?

[Liz] With what, with chemotherapy? Knowing these gene changes is important for you and for your clinician. You can go on to clinical trials.gov to explore what potential clinical trials are available to you based on whatever gene changes you might have, or reaching out to academic Medical Center for a second opinion, with any significant turning points in your care, so that you know you'll know what may be available locally. But then you can also know like what other options there may be for you now or in the future based on what was seen. But to touch upon some of those co-mutations, I think that's mostly being explored in the clinical trial space right now.

[Chris] To follow up in your experience, what are the most common side effects of a targeted therapy? Because it sounds scary, in some cases a targeted therapy they're giving me this powerful pill. What do you see in most cases that people should be on lookout for?

[Liz] That's a that's a good question. So, there are class effects typically that we see with each different grouping of targeted therapy. We'll start with EGFR, if you have an EGFR mutation, I'd say typically we see diarrhea, we can see rash, oral irritation, irritation to the fingernail beds, so that's EGFR. That's sort of a class effect of EGFR Inhibitors. With ALK we can see edema or swelling, we can sometimes see muscle markers increase, and then depending on the drug, we have to follow cholesterol levels. And then if we think about KRAS, we think about myalgias, which are like muscle aches or pains, and diarrhea can often happen. So those are class effects. Across the board we're always cognizant of something called pneumonitis or if there were patients can develop inflammation in the lungs. So if you had new shortness of breath, new cough, that's something that we're really in tune to and that can occur across the board with tyrosine kinase inhibitors or drugs used for lung cancer but to varying degrees, depending on the drug and the disease. So, I'd say that you can identify side effects by class or mutational markers. And then the other thing is we’re on third generation of

some of these medications within each mutation, and the drugs are getting better over time, and they're getting easier to tolerate, and the side effect profiles are improving, so the tolerability's improved over time, and I just hope that that that continues as they become more efficacious.

[Chris] Thank you very much. I think that's real helpful to make people so they're not afraid to try.

[Liz] Yeah and I think the biggest thing that I would say to my patients is if something's bothering you, you report it to us, and it's our job as the your care team to to figure out if whether or not it's pertinent whether or not it needs to be explored we always want to know what's going on at home with you and how you're feeling, you're never bothering us, and we are here for you to make this as easy as possible.

[Lynn] And I'm one of the lucky ones, I mean I've been on Tagrisso for four years and I've never.

[Liz] Really it's amazing.

[Lynn] So I mean I think it's important to tell people that too.

[Liz] That's very true, it can be very tolerable.

[Lynn] And of course, you know given lung cancer, we never lose our hair. But I had another question too. From two perspectives like how can we ensure that every patient, that would be with a need, gets access to biomarker testing, and how can we make sure that insurance companies cover biomarker testing or do you know or is it now become routine?

[Liz] So, it is recommended, so it's part of NCCN guidelines that all patients especially within the metastatic setting have comprehensive biomarker testing. So, that is a like a class one recommendation. In terms of coverage, it is typically covered at diagnosis, and with any significant changes, but we never know what the out-of-pocket cost will be for a patient unfortunately. As a clinician it's important for us to make a recommendation in what we think is the best for the patient and their outcomes and then we can explore how to support them

financially sort of in parallel. But we never want to make a decision about a patient's care without being clouded by insurance. We just want to make sure that this is our standard recommendation, this is what we think is best for you, and then we can help to work through some of that. I can say that our molecular pathology team is very helpful in working with insurance often when there are Representatives that work with some of the circulating tumor DNA companies that help to work with insurance and often, they'll say they can ensure that the out-of-pocket max is like x amount if it weren't covered by insurance. So, I think there are ways to bring costs down too if that's a consideration. And then how do we ensure that it is available to everybody I think that's a really good question, particularly if you're being seen in the community, and a community physician may be treating multiple different types of cancer and how do they possibly keep up with recommendations. I know that there are companies that are working on this. One called Precision Medicine where they're working on an algorithm that can be used for Physicians to help sort out when and what to order. But how do we mandate that? I think that's a really good question that probably needs to continue to be explored.

[Sherry] So follow up to that how often will insurance pay for biomarker testing I mean some people only last like four months, seven months maybe, on their target there before they have progression, and then say if they're on Medicare or Medicaid, how are they with paying for biomarker testing, like if you have to have, or if you're progressing often?

[Liz] It unfortunately varies, insurance to insurance, but typically that it is covered at baseline and then with any progression, or significant progression, typically. so but I think that could also be explored with the institution's patient Financial Services Department too before making any decisions about how and what to pursue.

[Sherry] okay I didn't realize that they would that you could get biomarker testing at each significant…

[Liz] maybe, yeah, like not every time I mean it it's also up to the discretion of the physician too and you know what doors do they potentially see opening in terms of therapy to with that testing.
[Sherry] Right

[Liz] So we wouldn't want to do testing if we didn't think that there would be not a reason to do it.

[Sherry] Great, thank you.

[Lynn] As a follow-up to that too, you know acquiring resistance to a particular therapy you're on is really scary yeah how is a person to know you know what the next line of therapy is or if they're getting the best next line of therapy particular you mentioned particularly if they're in a rural or you know a community hospital it is not academic.

[Liz] It is scary because those drugs are your lifeline, and to think having to think forward and about them potentially not working as well as they did initially can be really frightening. I think that knowing that there are more options, and that you could, if you know I it's easy to say go to an academic Medical Center for a second opinion, that's not possible for everybody. But if it is going at a time when you've had significant progression, or just an informational visit to know. Could you hypothetically lay out next lines of therapy for me so I know what my options might be moving forward. Knowing that genetic testing might change some of those options or new clinical trials would be opened. There are certainly new therapies, and then we combine therapies. If there's progression you know, say for example there's just a spot of one single spot that is progressed maybe say in the liver or lung there's one isolated spot of progression, but the rest of the disease is in check, sometimes we use radiation to those spots to those isolated spots of progression and then continue to use the targeted therapy. We really like to exhaust our lines of therapy and use them for as long as possible before making changes. And then other times we add chemotherapy to the targeted therapy depending on the gene change. And then there are subsequent lines of chemotherapy, we often keep the targeted therapy on if we can, if it's tolerated, particularly in situations where patients have CNS disease, or disease in the brain, because we know that those drugs can typically really protect those areas.

[Sherry] If a person is diagnosed early stage with lung cancer, like say stage one or stage two, and they have a genetic mutation, do you think the standard of care will be to go on a targeted therapy for a couple years after they have curative therapy?

[Liz] I think that's a really good question and that a lot of that is being explored now in the clinical trial space. So for EGFR, for example, there's a study called the ORCHARD that has shown to improve progression free survival post surgically patients went on Osimertinib versus a placebo for three years after curative therapy, which was the surgery. So they said do we tack this on at the end because we know there's a gene change and the outcomes are positive. I know that they're continuing to explore this in other gene changes. Many of these drugs these oral cancer therapies the TKIs were developed for use in the metastatic setting, right, so they're you that was their primary, that's when they were developed they were for metastatic disease, and now we're managing that really well with these drugs. But knowing these gene changes how do we incorporate that into patients that we know we can cure too and so that's they're starting to incorporate some of the other TKIs into the curative setting.

[Sherry] It'll be so exciting to see down the road what happens. I know someone with stage two who's doing a TKI for a couple years, so it'll be so exciting to see if you know 10 years from now.

[Liz] I agree, a lot of exciting work is being done in lung cancer right now and a lot of reason to have hope.

[Marla] I hope this isn't too convoluted. Given there are generalities associated with different mutations are they looking for something very specific, for example Ross-1 is more common in Asian women, is there something like could they test early or is there something are they looking at things they can do to counteract that mutation from actually happening in these Asian women for instance or MET with older female non-smokers yeah is there something specific found that turns their the mutation on or do you think they'll ever get that specific?

[Liz] I don't think that we would get that specific because, although we can see you know that MET is comprised of older non-smoking women, we see it across histologies, we see it across genders, we see it across smoking history. So, it would do a disservice I think to pigeonhole people into certain groups and focus on that. So, I think we need to follow more broadly.

[Marla] I guess the thing I'm getting at is that because of my age I was 51 or 52, or something like that, and I never smoked, had clean X-rays, I could never get a cat scan. My lungs were perfectly clear because my cancer was under my sternum, it was around my aorta and pulmonary artery veins. so that's part of the reason they went so along two years before they even looked for it. By then it was on my vocal cord and stopped me from talking. You think they'll ever get to the point where they'll say okay, you know let's look at it you, you fit some criteria, maybe?

[Liz] I see, for example would they broaden the criteria they use currently for screening chest CAT scans or something like that? Right now you need to have x amount of smoking history in order to qualify for it. So I think the answer is maybe and I don't know but I hope that we're able to catch this disease earlier.

[Marla] I had two years of coughing, 24/7 coughing, and a runny nose the whole time. I worked as a travel nurse, so I was in many different ERS, went to many different allergists for you know, each area I went to I'd have to get a new one, and even my own ER I went to in in November. And I was coughing, I couldn't talk, short of breath, because I was getting really worse by then. And in December the ENT finally went down, and said, oh your vocal cord is paralyzed you, need a chest CT. I just basically cried all the way to the back to the hospital, to say I want a CT and I want it now. I had a little bit of leeway because I work there but you know they have to do more to say you know you're older, you're heavy ,you're gonna fit something, as you're female you're gonna fit something, you're male, you're whatever, you're gonna something, and at least that will help screen some people.

[Liz] Yeah, making that a little bit more widely available.

[Marla] They need to say, oh I got this lady, she's coughing, she's of this background, maybe we should check, you know like they do for heart and cholesterol and stuff.

[Liz] Yeah, just broaden those screening requirements. I know that they're working on it and I know that they're working on screenings like blood-based screenings for cancer too, even within the lung cancer space. Some of our team has been doing that, so I think there's a lot of work being done. The hope is that they're actually going to be using AI to help determine how to stratify risk for

individuals too. So, I'm hopeful that that that question will be answered at some point in the future and I know that working on it.

[Marla] Thank you.

[Lynn] Actually I'm working with our local hospital that has an early screening initiative.

[Liz] Oh great.

[Lynn] Includes you know people who don't get the profile for testing they've identified I think it was up to over 500 last year which they could cure. It's pretty cool.

[Liz] It's amazing, They're studies ongoing with for firefighters for example that are exposed to smoking that way and getting screening done for those individuals that are at high risk too.

[Lynn] So you know you mentioned AI, you know as we look to the Future there's talk about vaccinations for these mutations. I mean it would be so cool to get a vaccination.

[Liz] It would be wonderful. I know that they're doing work. The immune system has proven, particularly in lung cancer, to be an incredible tool treating individuals. So, it's definitely on the horizon and in the clinical trial space. and I'm hopeful that those will be effective and safe for patients.

[Marla] Where are they in the clinicals are they coming to people soon?

[Liz] Yup I think they're all variable now. I can't I don't know the ins and outs to be honest, but I know that there are ongoing vaccine trials.

[Chris] I'm kind of curious cuz, I've been to a few of the conferences, and I have a handle with all the different research you're doing. I wanted to kind of get your feel and your take on it. Where do you see this going in the next five to 10 years as far as biomarker testing, make getting it for the masses. I know ctdna has really

progressed a lot. And there are vaccines for other types of cancers. Where do you see this going into the lung space in the next say three to five years?

[Liz] I know that there will continue to be advances. I know that they are working on Next Generation drugs for a lot of these targets and so I hope that we see more tools in our toolbox in the coming year. And more lines of therapy and better lines of therapy to offer to patients. I hope that there is more broadly covered and performed comprehensive biomarker testing. I think it will start to even become broader over time. I know that changed to help inform our scientists so that they can help to develop new drugs. So, I think it's an exciting time. I think it's a time of hope, looking back on the past 10 years or so, things have come such a long way, so I can only hope and envision that that will continue.

[Chris] Let me ask you Liz, with your experience how can patients, and advocates, and so forth like us, help move that along and help get the word out, to the doctors, the oncologists, the scientist, what can we do in your opinion to help that process move even quicker, or if not quicker, at least get the word out to more people?

[Liz] Yeah, I'd say Chris you're doing that right with the Kass kickers and the group that you've brought together is a wonderful resource for patients. I think that you know, there's lots of support groups online groups, even this what we're doing here today is making information available on the internet to patients, to inform them, and hopefully empower them to ask questions, and seek advice, and other opinions. There's no harm in asking questions and you should feel empowered to do so your life is on the line.

[Lorren] Does your practice use tele medicine to treat rural patients that aren't able to get into an oncology setting at a university?

[Liz] Good question, so during covid Obstetricians and nurse practitioners were allowed to practice medicine across borders. Now you're only allowed to practice within your state that you're that you're credentialed in. So, I'm credentialed in Massachusetts, I can only practice within Massachusetts and see patients within Massachusetts. But Massachusetts borders a lot of states that are close by, so I'd say that very often patients will hop in their cars and drive over the mass border

and have their visit that way. But in terms of more remote, you know, I'm sure there are other ways that care teams operate, but from a licensing standpoint that's what we do.

[Lorren] Thank you, this has been great really, really, great thank you.

[Liz]Really great to talk to all of you and hear more about your stories and these are great insightful questions that you're asking.