Precision Medicine: Identifying Targeted Cancer Treatments with Genomic Testing

Precision, or personalized, medicine has made a sea-change in cancer treatment. A pipe dream for most patients 10 years ago, it is a reality today. Precision Medicine's keystone is the ability to identify personal gene characteristics and match them to specific treatment options. This discussion will consider many questions surrounding precision medicine and targeted treatment, helping to answer:

- Genetic (germline) versus genomic (somatic) testing
- Who should get tested and for what?
- Getting tested and educating your doctor
- The pros and cons of testing
- Is gene testing affordable?
- What is an actionable mutation?
- How do actionable mutations impact treatment?
- Immunotherapy and personalized medicine

We have a knowledgeable panel of physicians, patients and patient advocates to help patients, caregivers and advocates understand precision medicine and targeted treatment, including David Marshak, Manager Patient Advocacy at Foundation Medicine, based in Cambridge, Massachusetts. Foundation Medicine performs comprehensive genomic sequencing to identify the molecular alterations in each patient's unique cancer and match them with relevant targeted therapies, immunotherapies, and clinical trials.

Rick Davis will be moderating the panel. Rick is a nationally recognized patient advocate and Founder of Answer Cancer Foundation. Diagnosed with locally advanced prostate cancer in 2007 and treated with radiation and hormone therapy, Rick moderates AnCan's High Risk/Recurrent/Advanced Prostate Cancer virtual support group, a weekly online & telephone group.

Full Transcript:

Priya: Hello and Welcome to Cure talks. India. I am your host Priya Menon joining you from India. This is Cure talks 125th episode. Today we are discussing Precision medicine and identifying targeted cancer treatments with Genomic testing. Precision or personalized medicine has made a sea – change in cancer treatment. A pipe dream for most patients about 10 years ago, it is a reality today. Precision Medicine keystone is the ability to identify personal gene characteristic and match them to specific treatment options. Today's discussion hopes to answer your common questions surrounding Precision medicine. We have knowledgeable panel of physicians, patients and patient advocates here on cure talks. Let us meet the panel first. We have Professor William Burhans who is a senior cancer scientist at Roosevelt Park cancer institute joining him is Dr. Prasanth Reddy who is senior Director in medical affairs at foundation medicine, Dr. Samuel Klempner who is clinical and translational researcher at the Angeles Clinic at Los Angeles. Dr.

Sharon Stanley, a cancer patient also an osteopathic physician. She leads the Birmingham centre along with her husband Keith Van, Mike Scott the co-founder and President of Prostate Cancer of International also a member of board of directors of International organization for rare diseases, David Marshak, Manager Patient Advocacy at Foundation Medicine. Moderating the panel is Rick Davis who is nationally recognized patient advocate and Founder of Answer Cancer Foundation. Welcome to Cure Talks everyone. It's a real pleasure to have you all here today. Just for the listeners, we will be addressing questions towards the end of the discussion. You can press 1 on your keypads to let us know if you have a question to ask and we will bring you on air. You may also mail the questions to Priya@trialx.com or post them on curetalks.com. I will now handover to Rick to begin with the panel discussion.

Rick: Good evening and Good afternoon everybody. We have such an illustrious panel gathered to talk about a very complicated subject, which we are going to try and make very simple for everybody to understand and realize the burgeoning importance of precision medicine. We have a lot to get through and we will ask the panel to be pretty concise so that we can have plenty of time for questions at the end as we already have a significant number of questions. We are going to kick off with Dr. Samuel Klempner and you can just explain what precision or personalized medicine is, maybe there is a difference and maybe there isn't and also clarify the difference between genetic and genomic testing and sequencing.

Dr. Klempner: Precision medicine is an approach to the care of cancer and in which we are trying to match the best therapy with the optimal patient, In order to do that we look for as much information about, both the patient and their disease, as possible. In cancer, that has gone a lot into genomic testing, it is safe and we are looking at the changes in the tumor cells which are different from the changes in the normal cells. When we speak about genetic v/s genomic it is more of a semantics discussion but in general genetics refers to germ line changes which are changes that are present in all of the cells in our body both the normal and any tumor cells. Genomic generally in the cancer stage refers to changes that happen in the tumor cells normally. If you analyze a tumor cell by DNA sequencing you will find changes in the tumor cells that are different from the normal cells. If there is a gene that is present in the normal cells it will also be present in the tumor cell. If you truly need to analyze both the tumor and the normal DNA then you need what's called a Matched normal control where you get a piece of the tumor and then generally you get a piece of normal tissue or blood then you can truly distinguish genomic changes in the tumor than the genetic changes that can be passed on. Tumor changes cannot be passed on from one individual to another that's an important distinction and sometimes an area of confusion.

Rick: In other words when we talk about genetic testing most of the time we are talking about genes that have been inherited from family members. When we are talking about genomic testing we are talking about your own tumor and somatic changes from your own tumor.

Dr. Klempner: Yes, I think that's an accurate summary and genetic testing looks at genes which may increase your risk of developing a cancer and genomic changes are changes that are acquired in the tumor and are considered more likely to be target for precision medicine therapy or targeted therapy.

Rick: Thank You! Dr. Reddy would you like to add anything to that or maybe you could just talk a little bit about who is a good candidate to get tested and what exactly are they getting tested for?

Dr. Reddy: Sure Rick, My feeling is really all patients with the diagnosis of cancer should at some point in their clinical journey to go for testing to identify for some of these genomic molecular changes that are contributing to their disease. Deep understandings of these molecular changes have already lead to a transformation in cancer care and diseases like chronic myelogenous leukemia, breast cancer, non small cell lung cancer ; the list goes on and on, where individual treatment decisions can be made at each individual patient level. When we continue to study appropriately in a clinical setting it is all available, how genomic information can be best used in for these individual patient decisions. I do believe that taking an order of the panel, kind of approach of molecular testing like the comprehensive genomic profile approach is more likely to capture any given molecular alteration and can be a valuable first half identifying mutations that could underwire predisposition to cancer. Certainly, patients those are most likely to benefit from obtaining

comprehensive genomic profile early in their clinical journey maybe those patients with known aggressive cancers such as sarcomas, cancers with well documented and targetable alterations like non small cell 1 cancer, patients with hard to define cancer such as carcinomas 1 primary and certainly patients are likely to benefit who avail multiple standard therapies like chemotherapy as well. The testing can be done on tissue after a biopsy of the patient's tumor or other samples that may have tumor DNA as well such as in the blood, or sometimes in the urine and detecting these changes are likely to play critical role in helping your physician or doctor to choose between several treatment options whether it is standard chemotherapy or targeted therapy or maybe even harnessing a patient's own immune system to fight cancer the so called immunotherapy. Whether a patient has just a simple or doesn't have a specific mutation can help prioritize between these therapies as well.

Rick: Dr. Reddy how exactly does a patient get tested?

Dr. Reddy: The actual process is relatively straightforward for the patient. Like I said in most instances we do the testing on the tumor itself. At the time of diagnosis and again the diagnosis is gonna be obtained through a tissue biopsy in most cases. In this particular situation what we would do is obtain a tissue from the biopsy sample and then that tissue would be processed undergoing a number of steps, without getting into the weeds where we basically extract the DNA and then analyze the DNA after these molecular changes. Sometimes we also analyze a cousin of DNA which is called RNA to detect some of these changes. We are then able to decide which one of these alterations are likely driving the patient's cancer and then hopefully based on that information then make a decision on how best to treat that individual patient.

Rick: By and large, your observation has been that most of this genomic testing for treatments that are indicative by the changes in the actual tumor itself, are later in the disease stage rather than the time of diagnosis.

Dr. Reddy: This is an area that is actively being studied. I would tell you that in most of the instances the clinical utility of this kind of testing tends to be in the patients that tend to have more advanced disease. If it is a metastatic disease or stage 4 diseases a number of trials or underway to see whether patients may benefit from this kind of approach perhaps earlier in the disease, earlier stage patients, stage 2 or stage 3 patients or other kinds of cancers.

Rick: Dr. Reddy some of our listeners may have heard about liquid biopsies, who might would be eligible for liquid biopsy and why would get a liquid biopsy and is it inferior to a tissue biopsy?

Dr. Reddy: It's an excellent question and It's a difficult question to 100% know down, everybody is eligible for a liquid biopsy. However not all tumors shed DNA into the blood and separate from that fact there is some potential that the findings that we have in the tissue don't always line up with the findings that we have in the blood. That is what is discordant between the findings of the tumor tissues versus the blood. The bottom line is that at this point in time what I would say is sampling the tissue and the blood are complementary to each other and I would encourage the patients to discuss this further with their individual physician as to why my tissue or blood based testing upfront. There could be handful of reasons why we might prefer blood based testing and those include patients that may have contra indications of reasons why they are high risks of getting tissue based testing either because of conditions that they have such as being on anti-coagulation, the location of the tumor, patient preference, etc.

Rick: I want to come back to Dr. Klempner. Dr. Klempner, Dr. Reddy mentioned briefly that we do some testing and maybe from that testing we find another treatment. Why exactly would you encourage your patient to get tested and what might you hope would come out of that test and how exactly would it indicate different types of treatment?

Dr. Klempner: Yes this is a great question, an area of my own research. I think I would call an analogy like a pie. We are continuously trying to divide cancer up into smaller and smaller pieces of pie and these are slices of the pie they tend to be molecularly defined sub-groups. The classical teaching that a breast cancer,

lung cancer and colon cancer are very different and has been called into question by some of these large scale genomic analogies where you see the mutation may be common in lung but may rarely exist in a colon cancer or a breast cancer may respond to the same therapy targeted at that specific change. The paradigm of looking and examining everyone's tumor to determine whether or not it falls into any of these molecular subgroups, the approach is becoming more appropriate in cancer as a whole and continues to be tested in a lot of these trials. The national institute has a trial of – The match. The American society of clinical oncology has a trial of the taper study, which are prospectively testing with the question whether or not we should base the therapy independent of the anatomic location but more based on the genomic changes. Dr. Reddy also touched on another important area which is immunotherapy , maybe there are some early bio-markers trying to decide who is the most likely to benefit from a given therapy as a very important area of cancer and something like a very high number of mutations in the cancer, something called microsatellite instability or other mutations which can produce a very high mutational burden such as POL E mutation. We may identify patients with regardless to where the tumor started and they may respond to a given immunotherapy. It really is about trying to identify patients where you can match the patient against the optimal therapy based on some biological information whether it is for Funneling the patient for immunotherapy, molecular specific point mutation or an early arrangement. Really it is trying to divide it up into groups to identify people and I think the fact that those exists rarely across tumor types, really underscore the importance of sort of broad profiling approach which is now endorsed by the guideline for a couple of tumor types.

Rick: This really brings to a couple of treatments that were identified for two of our panelists, both of whom have a fairly unique background. I believe that the drug you took was a drug that was approved for lung cancer?

Dr. Klempner: Yes.

Rick: What kind of cancer did you have? And how did genomic sequencing help in your treatment?

Dr. Klempner: Well! You know fundamentally I am alive because of it. I went through uterine cancer, advanced stage and very aggressive type of sarcoma. I went through a chemotherapeutic regimen which I also had the license of protocol done on, which was individual, but I did not go through a full remission and because I think I was elder in the clinic and had PD1A and a POLE mutation certainly I had uterine cancer, and there was an opportunity because of the number of mutations as well, to get onto which I responded very well in the past year. If this hadn't happened statistically the likelihood of me being alive the point was under 10% and now I'm headed into previously what appears to be a full remission and even better news is that it is an opportunity for individual treatment based on these markers that are supposed to be the classic treatment based on tumors based on tissue type and I was given the immunotherapy that unlike chemotherapy with the great number of mutations I had would go with that and make it obsolete and not doable any further. This continued to help me if I needed over a long period of time. I really would love patients everywhere to have this sort of possibility.

Rick: Professor Burhans, I have to admit to the audience that I have a patch history to a situation where you were researching a drug for several years has been approved for ovarian cancer. I'm confident in saying you did not have ovarian cancer but you did have very advanced prostate cancer and maybe you'd like to talk a little bit about how the genomic sequencing helped you and the drug that you are taking and how is it used?

Professor Burhans: Sure. I do have to tell you that I was asked the question once by a clinician on the telephone whether or not I have ovarian cancer or hysterectomy. Sometimes those mistakes are made. I was diagnosed in 2013 with an aggressive prostate sarcoma and I went through the huge treatments that are applied in that case and because of the aggressive nature of my tumor, the benefits of the treatments lasted for only a short time before the progression of the tumor. I was tested for germline mutation so this is the genetic testing that Dr. Klempner was speaking about at the beginning of this discussion. My entire germ line was sequenced and it was determined that I had mutation POCH2G which is associated more frequently with ovarian and breast cancer. It is found in prostate cancer in some cases as well. I should also point out

that I had a very strong history of cancer in my family which made it certainly worthwhile to be tested for germline mutations. After it was determined that I had a pathogenic mutation the BRCA2 gene, I began keratinine with a drug called Olavarin which was approved last year for treating patients who had ovarian cancer who also had mutations. This gene is a related gene and I had it for a little more than two years. I was told at the beginning of my treatment, right before it started that I probably had no more than few months of survival left and at this point I am almost completely regions, I have one metastatic region that is detectable in bone scans and I am healthier than otherwise. I think this is similar to Dr. Stanley's success of her treatment. This is a tremendous example in the utility of application of genetic cancer treatment.

Rick: We heard definitely about the pros of testing. Other than the testing, Mike Scott, what should people watch out for if there are considering genomic sequencing or genetic sequencing for that matter? Do we have Mike Scott with us? Priya we do not have Mike scott with us?

Priya: Mike is here with us!

Rick: Why don't you see if you can find Mike, and in the meantime I think that Sharon you wanted to respond to something that Phil said, is that right Sharon?

Mike: Can you hear me now?

Rick: We can hear you now. Let me just hold you up for a second, I just wanted to go back to Sharon. I think Sharon wanted to respond to something that Phil said, is that right Sharon?

Dr. Stanley : Congratulations to you too, it's really wonderful to still be here and I am in a fully healthy just doing practices and spinning up significant amount of time informing patients about this is a possibility and I know this works with the pitfalls and insurance coverage and educating other physicians and that sort of things.

Rick: We will come to that later. Mike heard me but I'm concerned that somebody is going to accuse me of stacking the deck here and we heard about the pros but what are the disadvantages or why might somebody be vary of getting either a genetic or a genomic test?

Mike: I think we need to be very careful of the language here. The risk is not the test itself. Tests provide information and it is the interpretation of that data under potential consequences of interpretation of that data that can provide difficulties for different people and I don't want to state anything where what which has been said about the two successes. We know a number of diseases now that will when you have regret with genetic mutations within the tumors respond extremely well to various different types of therapy. This goes back years to things like Philadelphia chromosome patients with chronic leukemia so we understand this that the potential well. The problem is, if you look at the disease eg: I use prostate cancer because several others know about it where progressive disease is often a matter of multiple mutations, it's not just one particular mutation that is the problem. Interpreting exactly what the genomics may imply in a particular patient is complicated. We don't necessarily have data what says for many patients that any particular drug will work that much better in them. The way I like to think about all of this is that it is best considered unless we have very well defined situations which we do for the Braco 1,2 patients which we do for patients with Philadelphia chromosomes Mothers that outside that scope we are basically practicing translational medicine into clinical time and that is best done within the clinical trial where we have very highly defined situations. It is incumbent upon the researches to explain carefully to patients exactly what the risks and benefits of any particular form of treatments are based on any particular form of genetic or genomic information. The test itself is not a risk, it's the potential consequences.

Rick: It's the same old story definitely just not about information it's what you do with that information. Dr. Klempner do you have to address this situation on a day to day basis on my talks about of appropriateness of selecting treatments where we are not exactly sure if that gene mutation will respond or will not respond, how do you address that with your patients?

Dr. Klempner: Yes I think it is definitely based on practice setting. I am lucky enough to practice in a place where we have molecular tumor boards and expert consents and are able to participate in a lot of prospective mechanism such as to ask for taper trial and NCI match trial, which I agree with our generally prefered mechanism to examine this question but in many situations clinical trials may not be available to just availability of the trial on a distance to a trial or a location for patients. We are forced to make judgements based on the cumulative date itself out there and varying levels of evidence so you have prospective large based trials which provide very good support for decision down to anecdotal evidence from case reports and pre-clinical work which may provide a good signal but certainly not the same level of data. They have to examine each case individually and whether or not the patient has experienced all of the standard options which have been proven to be a benefit on the average in clinical trial. If they have exhausted standard options or they are not a candidate for standard options or if they have a tumor type that has documented responses to particular mutations those are pieces of information that we factor into the decision but ultimately it comes down to a discussion with the patient about the risks and benefits of the therapies and I think I agree with my critical to understand that the treatment decision may be based on a large amount of information or maybe based on limited amount of information and in those situations seeking the opinion of people that have experience with this type of testing or this type of approach, I think it's beneficial seeking consultation with academic institutions with molecular tumor boards where you can feel supported by the consensus of people who deal with this on a day to day basis. All these things are important but the general approach has been to trying to incorporate clinical trials as much as possible so that we can now learn more about this approach more. The discussion really comes down to the cumulative analysis of the data for a given operation in a given patient and then the discussion of factual side effects of the therapy and whether that risk balance is comfortable with both patient and the physician and if not then probably some additional opinion according to the forum working on a course that is perhaps based on less evidence.

Rick: So this is all good when a patient is living in a big city, maybe a center of excellence or a sophisticated practitioner like this, who works with centres of excellence and is well aware with what's going on. But, I am sure there a bunch of people listening who are living in smaller towns and cities around this country and where they are treated by oncologists who practice community medicine and may not be aware of some of these recent advances that are remarkable advances in cancer treatment. But, they are listening to us and then go and talk to their doctor who knows their eyes and says I don't know what the application is for this for you. Dr. Reddy, how do you suggest that patients educate their doctors which Sharon mentioned earlier on, Dr. Stanley mentioned earlier, how do they go about educating their doctors and bringing these advances to their knowledge so these patients in lesser senses can get treated?

Dr. Reddy: Yeah this is the critical challenge I think where Mike said that the information necessarily is not the bad thing but it's the interpretation but the first step is to get the information in the first place. If we don't empower our patients to at least get information so that we can then decide whether the next best step is a clinical trial or potentially treatment which is not found or accessible that's the critical question. I think part of this is educating the patients as well to bring up the topic with their physician themselves. That's the first step, secondary today is obviously the field itself needs to continue to educate patients through their professional society such as ASCO which is the American Society of Clinical Oncology and we have to do a better job as physicians to have some expertise in this area in sharing that information to go through conferences, seminars, other educational venues. But I do think that patients should be empowered. Our job is to ensure that patients have access to all of the potential tools that they can use in their fight against cancer and part of that stands from at least knowing the critical pieces of information about their cancer.

David: Rick could I just comment on that?

Rick: Yes please do.

David: I live in a large city just outside the city on the East coast and something is going on here that I actually find rather worrisome which is that a number of major cancer centers in the region are actually indulging in, what I would describe as competitive advertising and how wonderfully they can now treat nearly everything even cancers. I am a great believer in the value of hope in the management of cancer but I also

find that the nature of that advertising very distasteful because the details are not available to the patients in that advertising and everything is presented in an extraordinarily positive light. When the reality is just isn't that at all. Yes, we get these phenomenal responses but we don't hear about the patients who don't get the good responses. I have to say I find that concerning.

Rick: David, before you were Director of patient advocacy for Foundation medicine, you spent two or three years in facing directly with patients themselves when they had issues about getting tests. Do you have anything to add on how patients can bring attention to the doctor in their community setting, do you have anything to add to what Mike said about overuse or creating an over optimistic view of testing.

David: I think that having the most comprehensive texture is helpful and so for all the patients listening in to this call, whether you know a lot about this kind of testing already and you are looking to compliment to your knowledge or you may be learning about a lot this for the first time and you are doing the right thing. There are a lot of patient advocacy groups out there that are really striving to give patients the information they need as well and that's another opportunity to get involved with an advocacy group potentially for that specific type of cancer and just continue to find opportunities to learn about your specific cancer and how testing could potentially provide options at the same time keeping in mind that testing is not gonna provide an answer for everybody it's about providing the opportunity for an answer and if there is a treatment out there on targeted therapy, immuno-therapy or something from the clinical trials that can be beneficial and you know about that by getting testing. I think like what Dr. Reddy said there is work to be done on both sides which community oncologist of the country have conferences are other opportunities and I know from actually having attended a recent Community Oncology Association Conference that these conversations are happening but certainly there are going to be patients who encounter physicians who are less open to this and so just taking advantages of many opportunities to learn about how this could impact them taking some of their general information provided here and how might have their specific cancer and continuing to ask questions and hopefully be on the progress.

Rick: Before we go to our questions, I have one last area that I wanted to touch on you David, How affordable is genetic and genomic sequencing and what is the attitude of the insurance companies to covering these costs?

David: That's something that's very purposeful for patients and it's not one of the first questions but maybe the second question they ask because cancer treatment is expensive and the therapies various aspects, care, hospitalisation and something like this which could provide helpful information that has a financial cost is a factor and you know the answers vary and I can give a little bit of context but want to stress that each patient based on their insurance and how that may vary but to give kind of some general framework at Foundation Medicine, where we teach normal testing, we do accept all insurances which often covers testing and patient may have out of pocket expenses like co pair deductible. Insurance does not always cover this and those situations we would pursue a cure for patients those out of pocket expenses can be quite a bit and based on insurance as performed and this is a base line the list price for the Foundation 1 test is 58,000 dollars and that's not what a patient would pay as it is the list price and for someone considering a test where there is another company or another facility that performs testing, at our company we have a program where a patient can fill a financial assistance application so we can give an idea upfront for the maximum out of pocket expense would be. Insurance gets billed after testing and so you don't always know upfront what the insurance will or not cover but filling out the financial assistance application can give you that idea upfront of what maximum amount would be and they also have client services group available to talk to the particulars of any one situation so that they can get better sense upfront of what cost might be and at that point I'd add in terms of thinking about costs it is just considering in the larger context is just the cost of the testing which is the fact that potentially finding a therapy as a result of test providing opportunity for patient to get on a therapy which is more individualized to them versus being on potentially less effective therapy which they are paying for. That is something to consider but as mentioned early keeping in mind that not every patient is going to get that answer.

Mike: Could I ask another question about that Rick?

Rick: I will come right back to you but let me just ask one question if I may with David because I'm sure a lot of people are thinking about what exactly is gonna cost me out of pocket. Obviously it depends on each person's financial situation but by and large across the board over the last two or three years what range do you see for a patient having to pick up? Is 100 dollars, 500 dollars or is it usually a little more than a 100 but not less than a 1000 dollars. Can you give us some figure?

David: I can give a very broad range but I think it's not more than what you are saying as I do not have access to that data in terms of seeing patient by patient and what their out of pocket expenses would be but I think we consider their co-pays or deductible or can be arranged on 100s or sometimes more for patients who pay out of pocket and that is significantly reduced to lowest price but there are patients who could have a 3000 dollars charge to them but it does range quite a bit.

Rick: Thanks a lot and Mike, the floor is yours.

Mike: I was just curious whether the insurance is more likely to pay when the tests used to find specific genes where we know there are effective therapies supposed to the situation where we are hoping to obviously in lung cancer and CML and some other conditions we have very good information about where specific genetic change has therapy to benefit associated with it from a particular drugs.

David: The answer is yes and you provided the example of Lung cancer and in fact for lung cancer we have been deciding to campaign and do Medicare area and I can peep and see that in certain types of cancer where there are those larger lists of approved therapies that are associated with that specific cancer where that can affect reimbursement.

Mike: Thank You

Rick: Priya, I am sure we have some people queued up for questions. I would just like to ask all the questioners that please focus on the question rather than your own medical history because the doctors can't really answer anything about your own medical history but then keep the questions general as short as you can. Priya …

Priya: Yes, Rick I have the questions here

Rick: Do we have anyone on the phone who would want to ask a question?

Priya: No, they have sent the questions just now as the talk was going on so I just quickly go over them.

Rick: Let me just go to David and may be you could communicate them to David.

David: Sure

Rick: We don't have really have anyone queued up on waiting to ask a question on the telephone. Let us know if someone comes in on the telephone and we'll try to get in David, since you have answered so many of the questions over the last several years and so perhaps you could pick out some of the questions whether they have been asked and we haven't covered yet.

David: There have been some questions that have come through which I can see, which I think have been answered nicely on the discussion we've been having. One of them which we've briefly touched on but could go a little more in detail is the timing of utilizing the results of genomic testing. Sometimes patients may be looking to get treatments soon after diagnosis and sometimes they've entered multiple rounds more stage able recurrence so I think potentially for either Dr. Klempner or Dr. Reddy considering the stage of cancer that this information may be useful.

Dr. Klempner: I'll just say a little bit on this topic; I think there is argument to be made for testing and

numerous chemical scenarios or layout to more common arguments. Probably perhaps the most well supported is with people who have received a targeted therapy and are no longer responding to it so the best data here comes from lung cancer where we have more targets and other tumor types. Understanding why a patient's tumor is no longer responding is now capable of guiding what you would do next for example the classical T79GN mutation in lung cancer, we now have one drug approved specifically for that indication in out clearing lung cancer. The resistant landscape actually is a very hard area and depending on specific resistance mutation whether it's a secondary augmentation or a bypass tracked in another part of the cell connects can actually quite well inform the next line of therapy. Resistance or progression after targeted therapy is a very well supported indication perhaps the others are when you are exhausted standard of care so patients with CI cancers who receive two lines, three, or four lines of therapy where there is no further therapies that have been shown. The associated with the survival benefit, that's the time in clinical care when you should look for new approaches whether that be clinical trials or genomically directed therapy of label access to trail. Personally my bias is the test basically a diagnosis of metastatic disease to use that information and sometimes we keep it in our back pockets if it's not going to change our initial management. We have that as a base point to compare over time and there is perhaps less data to support that approach but I think all of our ongoing trials are believers in that approach and so we are collecting this data but it will take large data sets and prospective collection that bares out but most commonly is exhaustion of standard of care or progression on targeted therapies, evaluation for immunotherapy and testing as first diagnosis. I would say the first thing that I am adopting but maybe that's universally adopted at this time.

Rick: I'd like to add one thing to that and this is certainly not true for all cancers but in the cancer that I know the most about which is Prostate cancer. We do know that the cancer mutates over time so what you might see from a biopsy of tissue diagnosis of what Dr. Klempner referred to as a baseline is quite likely to change over time particularly if a patient has been through many different treatments. Even if there is no actionable gene which means gene might respond to treatment if you are first sequenced on diagnosis that does not mean to say that later in the disease progress you would not have an actionable gene. Any Dr. on the panel would you like to comment on that? Any of the Doctors?

Dr. Reddy: Yeah Rick, I'll jump in here, I'm Dr. Reddy, I' 100% agree on what Dr. Klempner said which is exactly the same approach that I use in the clinic and for my perspective sometimes it can also be helpful in sequencing treatments. As we've talked about immunotherapy, there are situations with broader based molecular profiling where certain biomarkers makes you to believe that immunotherapy is more or less is likely to be helpful in that patient. Even when you don't need to do testing to have approval for that immunotherapy and so in a situation like that it may fade a physician's choice on whether to pursue a different kind of therapy. That's another kind of situation where having testing is useful. As far as what you said that is also absolutely true, it is particularly true when patients are on targeted therapies, even more so when they are on chemotherapy that they should get tested for molecular alterations throughout the course of their disease. Another thing I'll throw on here is just briefly is this question of monitoring disease progression and this is a very in its infancy right now short of say a disease like chronic leukemia which is brought up several times tonight. Basically there is this question of potentially using this kind of testing approach to potentially monitor for progression as well but this is again in its infancy.

Rick: Priya, do we have any phone with any questions?

Priya: no Rick, nobody on the line yet.

Rick: Let me go back to David, do we have any more questions that people have sent in for us?

David: Yeah I think there is one question that kind of dealt nicely on what Dr. Reddy was just saying about different uses of testing and precision medicine and we have talked about predictive component on trying to predict which targeted therapy or immunotherapy a patient might respond to, Dr. Reddy also touched on the monitoring aspect. There is also prognostic potentially in terms of what's the patients prognosis gonna be so I think since we did spend so much time on the predictive aspect and this question actually mentions preventive also so what are some of the other uses of this information?

Dr. Klempner: Prognosis information is important and at a lot of times it comes as a bonus when you are looking at more broad based genomic profiling, say for colon cancer for example BRAF mutations and K-ras mutations or absence there are of along with clinical factors are all independent prognostic factors that give us some information about the biology of that patient's disease and it's possible that with time actually more than looking at one mutation we are looking at large panels of mutations and the context that prognostic mutation exists may further refine the prognosis e.g. if you look at KRAS alone where as if you have any other information about KRAS, DRAS, micro satellite status, mutation of Berlin and other mutations you may actually be able to give a roughly more granular estimate as we gather more data. I think prognostic information is important preventative medicine using genomic data is a fascinating area and there are some large scale ongoing efforts mainly based off collecting circulating tumor DNA and Dr. Reddy has suggested such as the project using the diagnostic tests, early detection and potential early intervention. I think these are phenomenal areas of very important work but still agreed and it's incomplete.

Dr. Reddy: Only other thing I would bring there is just certain germline mutations when you are talking about prevention certainly if you have BRCA mutations you may choose to undergo prophylactic or even if you had breast cancer for example so in certain hereditary cancer syndromes that are defined by some of these genetic changes there are some standard of care kinds of recommendations so potential prevention of future cancer but that's a very specific more of a hereditary cancer syndrome preventative measure.

Rick: I don't think we are going to have time for any more questions, am I right Priya?

Priya: Yes, we just have to cover up minutes more

Rick: Let me just, before I hand back to you, I just want to thank this panel for a really excellent presentation. We have covered a huge amount of material in a very short period of time. I hope it's been understandable for the listeners that are out there. If you need to follow up on any of this then you can certainly write in to Cure talks or you can write to Answer Cancer Foundation and we'll try and get on answer for you. We are at info@ancan.org and we'll try and answer any questions that we might not have addressed and with that I'm gonna hand it back to Priya.

Priya: Thank you Rick, thank you everyone, I think that was a very informative session and Rick and David special thanks to you for getting such a great panel together for Cure Talks. This talk would be available on Curetalks website along with its transcript or you can visit Curetalks.com for details on our upcoming talks. Also, do please check out our new no code app development plan for launching your mobile research studies in a matter of 5 minutes at curetalks.com/appbakery . Thankyou everyone and have a great evening.

Rick: Thanks and Good Night everybody.