“Novel Testing to Guide Personalized Cancer Treatment” (RGCC) [#61]

Chad Magnussen, Dr. Lauren Cohen, Dr. Miven Donato, Panagiotis Apostolou, and Brad Power
June 7, 2023

“The current treatment model, even when "personalized," is personalized to the cancer, not the unique expression of the cancer within each individual patient's physiology.” – Dr. Lauren Cohen

“Cancer patients need clear information about what treatment options will be effective for them.” - Dr. Lauren Cohen

Meeting Summary

Advanced cancer patients want personalized treatment, which depends on testing to gather data about each patient's unique profile.

The current treatment model, even when "personalized," is personalized to the cancer, not the unique expression of the cancer within each individual patient's physiology. The one-size-fits-all model in current cancer care has low success rates, typically less than 30%, leaving patients to guess or gamble with their treatment selection, without knowing if they fall within that 30% success group or the 70% failure group before making that decision. Cancer patients need clear information about what treatment options will be effective for them. RGCC testing provides clear information about the quantity and activity level of the cancer cells, genetic expressions showing what drives and inhibits the cancer cell growth, and chemosensitivity testing on chemotherapeutic agents and natural substances to determine which are effective treatment options.

Dr. Lauren Cohen, DC, Managing Director of RGCC International - North America and members of the RGCC Clinical & Scientific Team, Dr. Miven Donato, and Panagiotis Apostolou described the tests they employ to custom tailor cancer treatment uniquely to each patient. Using more and better tests can save time, money, health, and provide peace of mind.

- Not wasting time or money on treatments that won't be effective, leaving resources available for treatments that are.
- Many chemotherapeutic treatments are very hard on the body. If you are going to pay that high a physical price, you want to know the "price" is worth it.
- Being armed with personalized information about what treatment options are right for you, gives you the peace of mind knowing you are not guessing and hoping for the best, but making sound decisions with actionable information.

With the Onconomics Plus test you get information about your circulating tumor cells, you get genetic and physiological expressions such as growth factors, resistance factors, angiogenesis factors, cell cycle regulation, metastasis, drug metabolism and targets, and even radiotherapy and hyperthermia sensitivity. In addition, you get chemo sensitivity testing on 117 chemotherapeutic agents and targeted therapies, along with more than 53 natural substances,

so that when you are making choices about care options, you know exactly which chemotherapy agents and natural substances are going to work for you.

The Onconomics Plus test results consist of 24 pages, this is the test that provides all the information you need to determine what is effective therapy for whatever cancer that is tested. And so the therapeutic options that one will obtain from this test covers a broad number of different therapeutic approaches.

In order to receive RGCC testing, it is essential that you get connected with an RGCC practitioner. RGCC only works with RGCC registered practitioners. So even if you have a naturopath or primary care physician, they can't just order a test unless they are registered RGCC practitioners.

Chad Magnussen, one of the patients in the Prostate Cancer Lab community, got tests from RGCC. He described his experience with RGCC, and RGCC used his test report to illustrate their services, and answer questions such as:

Q: How do you position RGCC's services?
A: RGCC is more than a lab. RGCC has an entire testing system that provides personalized information that guides you through the entire cancer journey. The system contains tests for baselines, cancer cell activity and prognosis, genetic and physiological expressions creating individualized profiles used to create customized treatment protocols for each patient, chemosensitivity testing of chemotherapeutic agents and natural substances, immune status, and monitoring at the microscopic level during treatment for protocol efficacy and early detection of recurrence when traditional medical monitoring is not sensitive enough to detect. Although there are other labs that do individual pieces of what we do, we are the only lab that provides this testing in a comprehensive and cohesive system.

Q: Do you primarily work with blood as input?
A: RGCC specializes in liquid biopsy using blood samples that can be collected at any time during the cancer journey. We can also use fresh tissue samples, but they must be fresh, collected at the time of the excision or biopsy, not paraffin embedded. And of course, this is often a one-time option since surgery is not routinely done every 3 months or so to gather a new sample, and any material left over is embedded in paraffin which preserves the tissue but not the CTCs. In addition, biopsy/excision samples are like a time capsule. Cancer cells mutate over time, especially after treatment is done. Using a tissue sample collected 6 months or more prior, no longer matches the cancer cells currently being expressed in the patient's body. Using fresh blood samples keeps the information current.

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Meeting Notes

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Discussion Outline

1. Disclaimers. (0:00)
2. Introduction to RGCC. (2:41)
3. Personalization and partnership in cancer care. (8:53)
4. Therapeutic options for prostate cancer. (17:11)
5. Hormone-driven cancer. (24:15)
6. How to order a test. (33:18)
7. The remission and recurrence prevention program. (39:52)
8. Which tests do you use for RGCC testing? (43:12)
9. Access and interpretation of the test. (50:17)
10. The missing information about gene expression. (54:46)

SUMMARY KEYWORDS

test, cancer, gcc, patient, agents, work, resistance, genes, practitioner, lab, ctc, question, natural substances, treatment, chad, information, cells, ngs, cancer cells, determine

SPEAKERS

Dr. Lauren Cohen (40%), Dr. Miven Donato (40%), Brad Power (7%), Chad Magnussen (6%), Jonathan Starr (4%), Panagiotis Apostolou (4%), Robert Gurmankin (<1%)

Meeting Notes

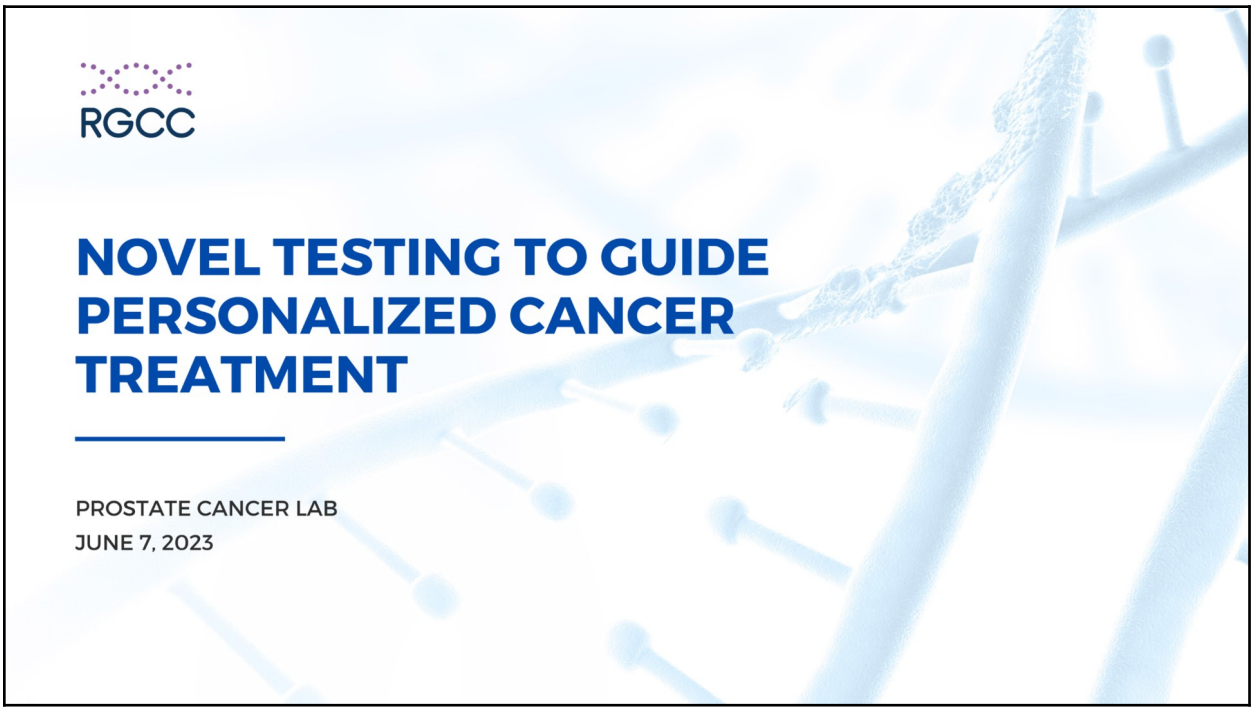
Brad Power 0:03
This is the Prostate Cancer Lab/Cancer Patient Lab. We're pleased to have representatives from RGCC with us who are a testing and diagnostic service, and we'll be learning about the services they can offer to patients.

Chad, can you please do a quick introduction of RGCC and the background for why we're having our session today?

Chad Magnussen 1:18
The reason I started with RGCC is because I’m seeing a naturopath functional doctor, and I was talking to him about the book How to Starve Cancer and how I was interested in blocking certain pathways. And he said to me that the best way to do that would be to get an RGCC report and actually have some actionable ways to block certain pathways. You may be throwing some

supplements out, something that really isn't doing you any benefit. So his suggestion was to get this report. And so we did that, and I have developed a supplement protocol from this report that I have quite a bit of confidence in. The other part is I'd already completed chemotherapy when I got this report, but there's some interesting information that I think they'll touch on that would be very helpful to someone newly diagnosed. So that's how I started. And basically we'll just turn it over to I believe Lauren to present.

Dr. Lauren Cohen 2:41
We just want to say that we are very excited to be here. And Chad, thank you so much for introducing us to this community. This is an amazing patient-oriented community. And what you're going to find is RGCC is very patient focused, and a very different experience with a lab than you may have had before. Something we specialize in is helping patients find personalized information so that they can make informed personalized decisions about their cancer.



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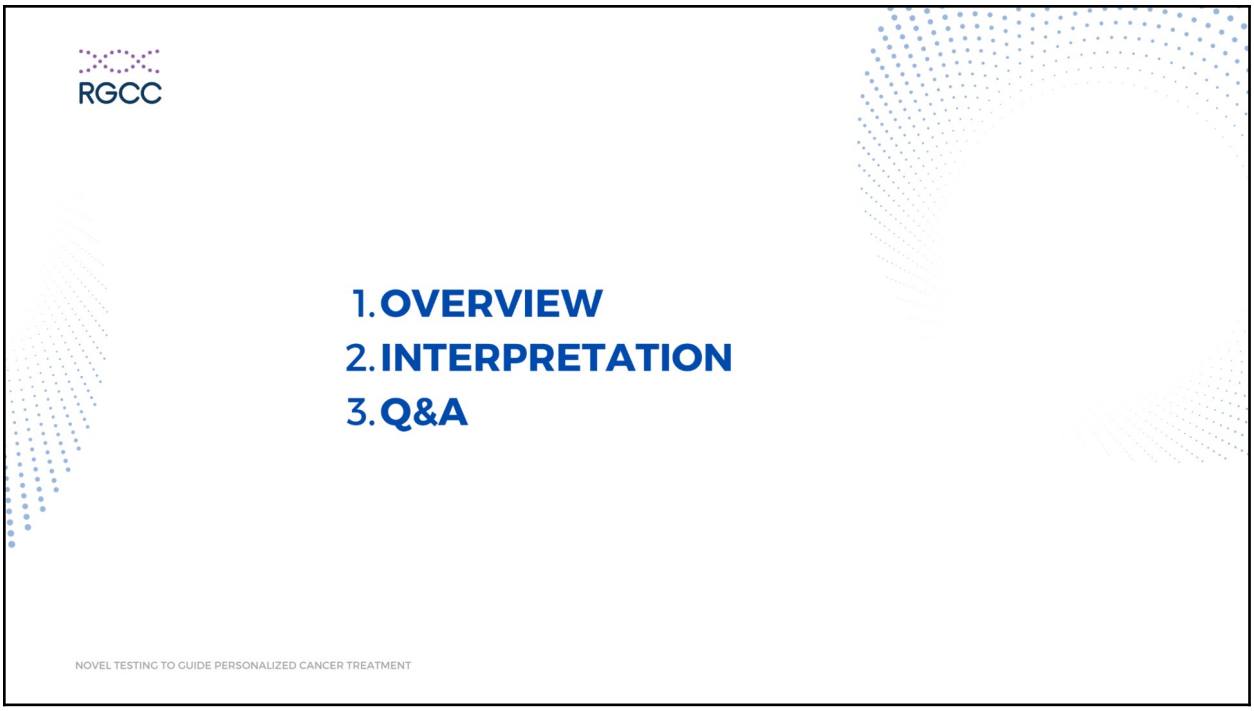

This presentation has a lot of ground to cover. The overview itself could normally take anywhere between, say 30 to 45 minutes, but we're going to do a very brief overview because we're doing something very special today, which is taking one of our tests, our most comprehensive tests, the Onconomics Plus test, and we're going to do an interpretation demonstration. So you can see how the information that you get on your test can be interpreted and utilized to make a very personalized protocol for you as an individual person. And then of course, we're going to leave time for Q & A.

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I'm Dr. Lauren Cohen. I am the managing director of RGCC International which is the US-based branch of RGCC International. We have Dr. Miven Donato, who is an active practicing clinician, he's also an RGCC-accredited clinician, and he is also one of the members of our clinical support and training team. And he is going to be doing our interpretation portion of the presentation today. And lastly, we have Panagiotis Apostolou. He's our lab manager in Greece, and he is also a molecular biologist. He won't be presenting today, but he is here so that he can answer as many questions as can be answered, because we do know that you are a community of citizen scientists, and we want to make sure that we have enough staff here to be able to answer any questions that may arise.

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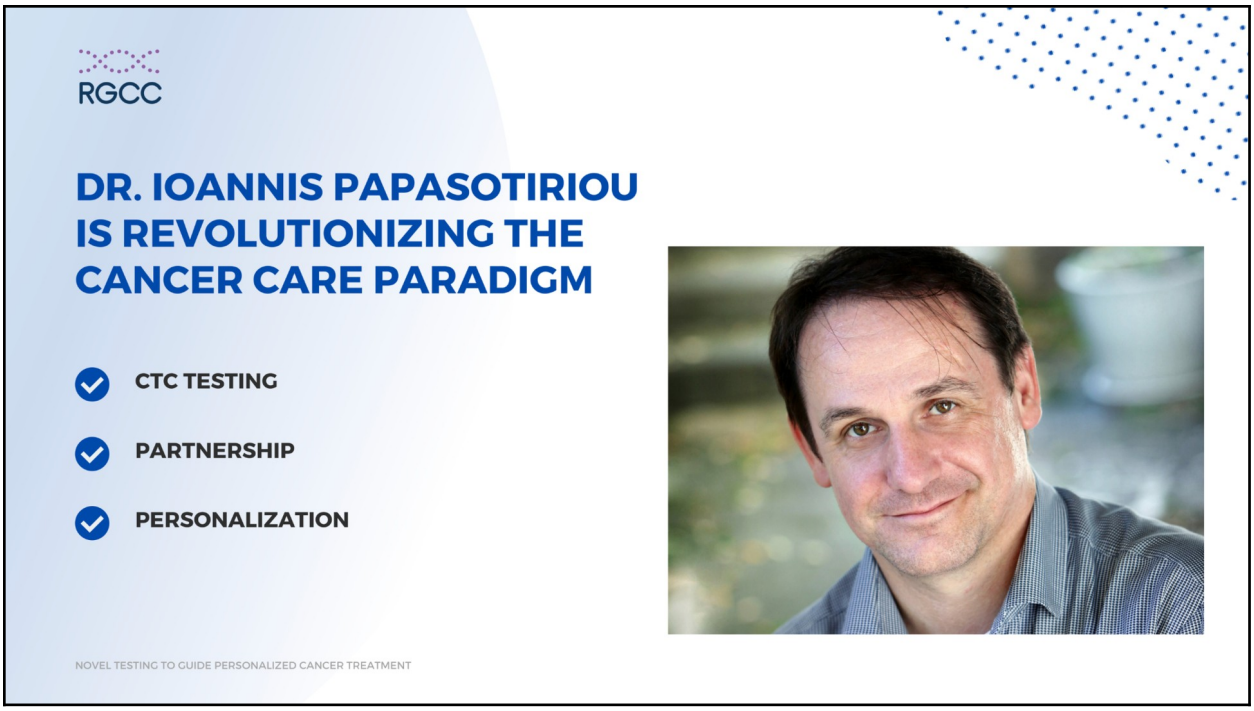
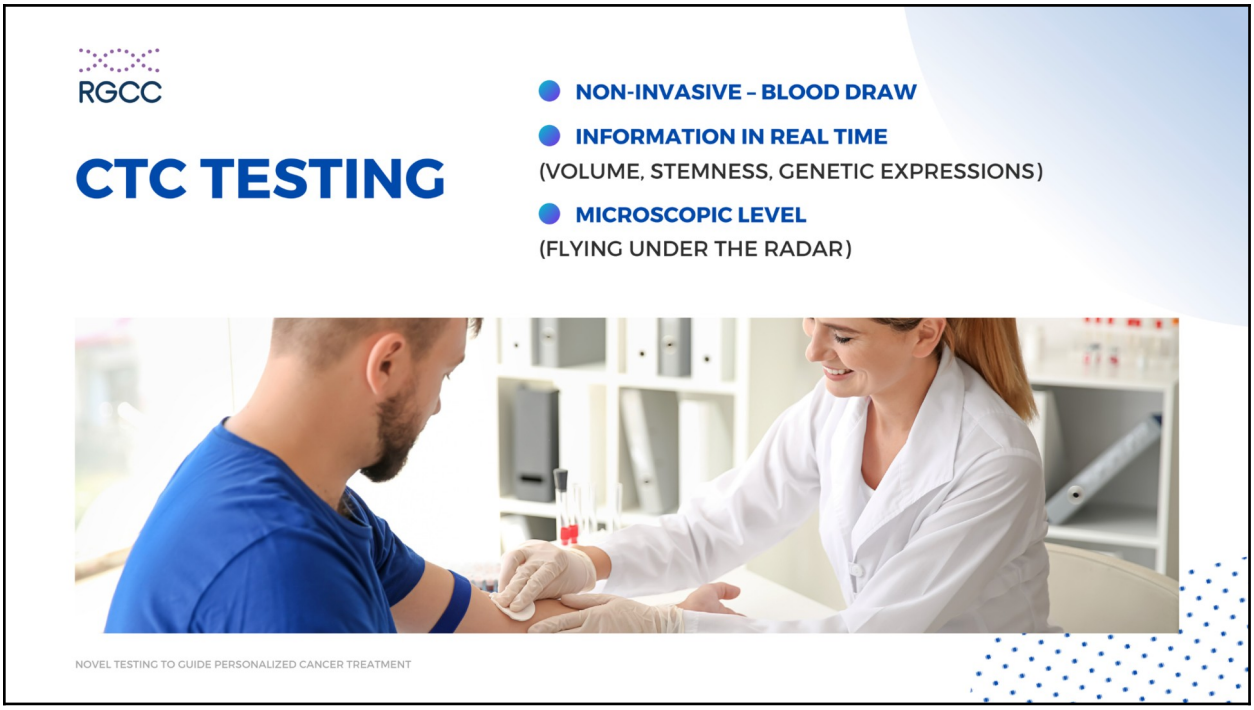


Our founder Dr. Ioannis Papasotiriou has truly revolutionized the cancer care paradigm. That is his vision. And he is putting something very unique and very special together. He's using CTC testing with a culture of partnership and personalization, which is taking the cancer care paradigm, which is very impersonal, and turning it into something very personalized for each individual patient.



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CTC testing for circulating tumor cells, are whole cancer cells that are floating in your system. And utilizing the CTC testing, as opposed to biopsy is very impactful. It's a non-invasive procedure.

You are able to get the information that you need with a simple blood draw. With a biopsy, it's of course, a surgical procedure, it's much more involved. But it also does not provide information in real time, where CTC testing allows you to have information in real time, at all times. When you do a biopsy, and they preserve the tissue, if they utilize that same tissue at a later point in time during your care, you're using old information. Cancer cells mutate, your physiology is changing, and the expression of the cancer within your body is changing. So utilizing blood draw with CTC testing allows you to stay current with the information of how the cancer is expressed in your body at any given point in time. And also, it's done on a microscopic level, so we are not working with medical monitoring that isn't sensitive enough to pick up small quantities of cancer. I call that flying under the radar. So with this testing, when your cancer gets small enough, medical monitoring can't see it. And unfortunately, if the medical profession can't see it, they can't treat it. So when your cancer recedes to a certain degree, they often will say your cancer is gone. But it's not necessarily gone. It's still there on a microscopic level, it just can't be seen. But with RGCC testing, once you get below that radar limit, and it can no longer be seen on medical monitoring, you can continue to monitor. So this is a very powerful tool for you to be able to know exactly where you are at any given point in time. So this also answers that question that you often hear in the cancer world for those that were successful with their original treatment: My cancer was gone, but it came back. How did that happen? It happened because cancer cells were still in circulation at a microscopic level, but no one was monitoring them. And unfortunately, it takes for the cancer to grow large enough to be seen again before they're able to intervene. So CTC testing is a very powerful tool and a very convenient tool.

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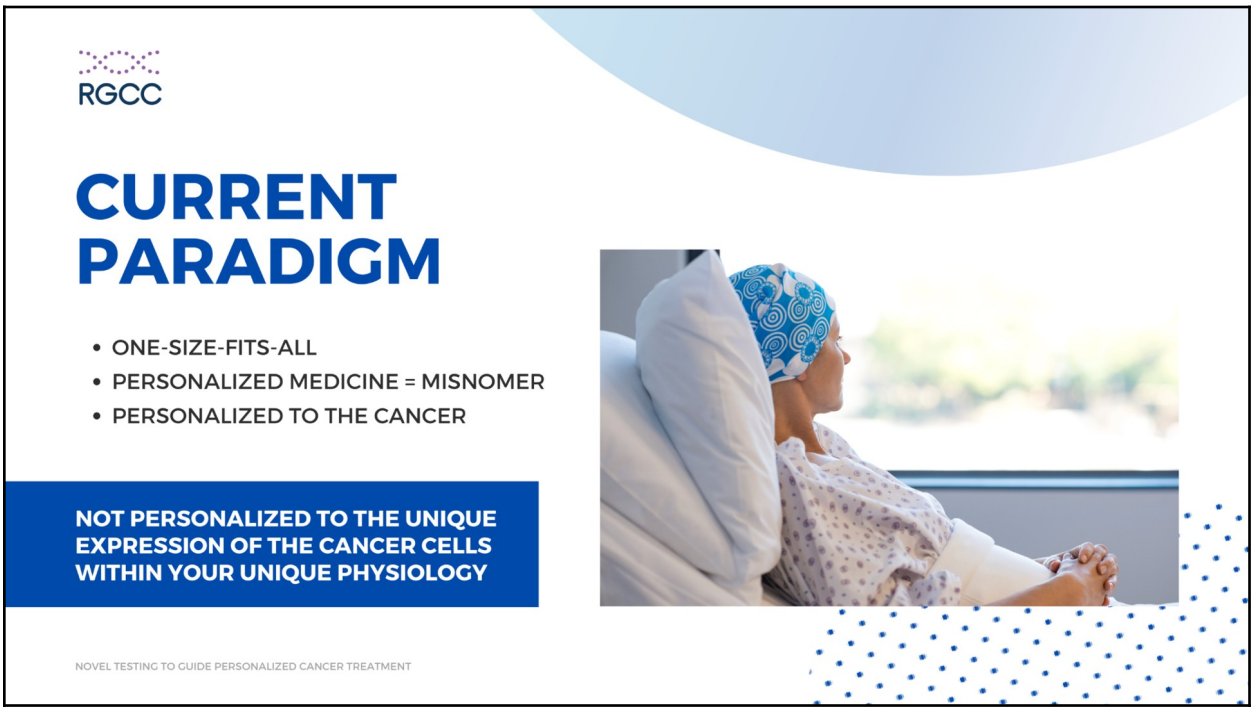

The current paradigm in the cancer care world is a one-size-fits-all model. You have a specific cancer type and everybody gets the same treatment. And of late, you're hearing a lot about personalized medicine. But if you look at the testing that's being done, it's a bit of a misnomer because the personalization is happening to the cancer. It is not not happening in a way that is personalized to the unique expression of the cancer cells within your unique physiology.

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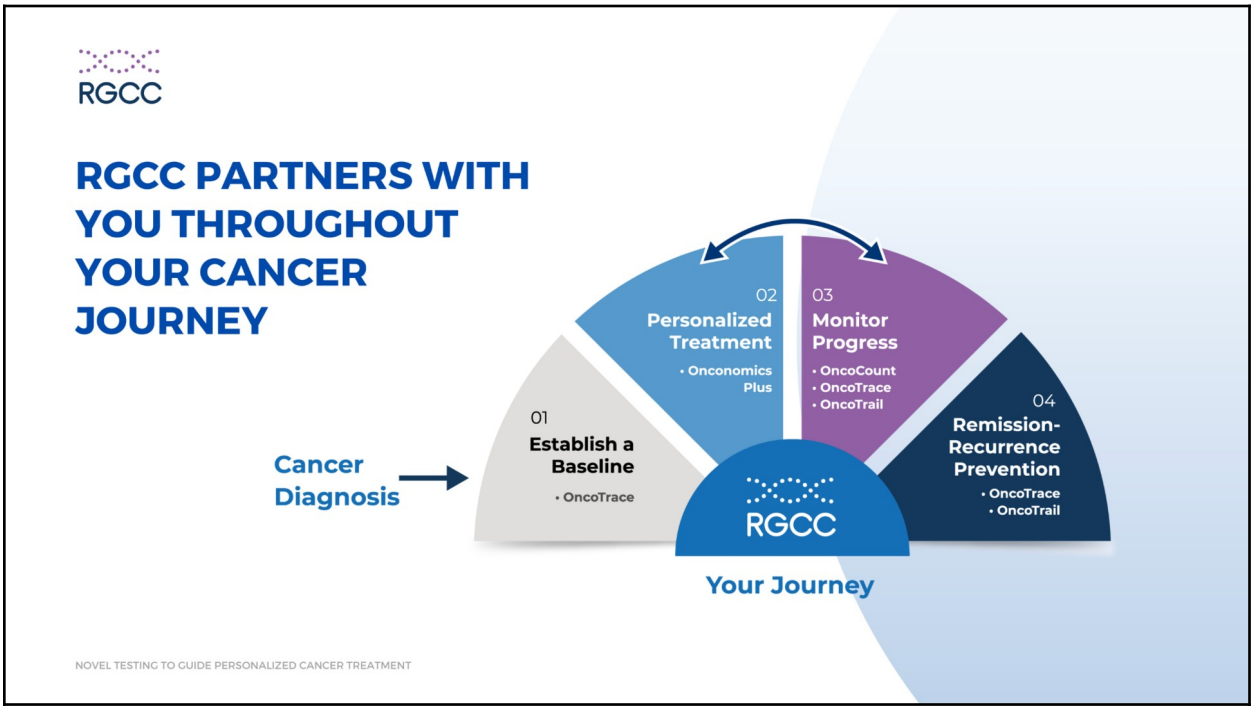
RGCC shines in the personalization. So the information you get is very detailed and very specific to you. What makes RGCC so unique as a lab is the personalization and partnership.



Let's start with partnership. RGCC is able to partner with you throughout your cancer journey. With most testing, each lab does an individual test or individual piece, but there is no consistency or cohesiveness through the program. So you go to different labs, with different science, with different measures and protocols. But with RGCC, once you're diagnosed and you enter into the RGCC universe, we stay with you all the way through the cancer journey. We help you establish a baseline. We have testing for personalized treatment options. We're able to monitor your progress. And we're also able to monitor once you go into remission in what we call a recurrence prevention program. So that you can be proactive. As soon as that cancer is active again, you will know, and you'll be able to intervene at a much earlier stage.

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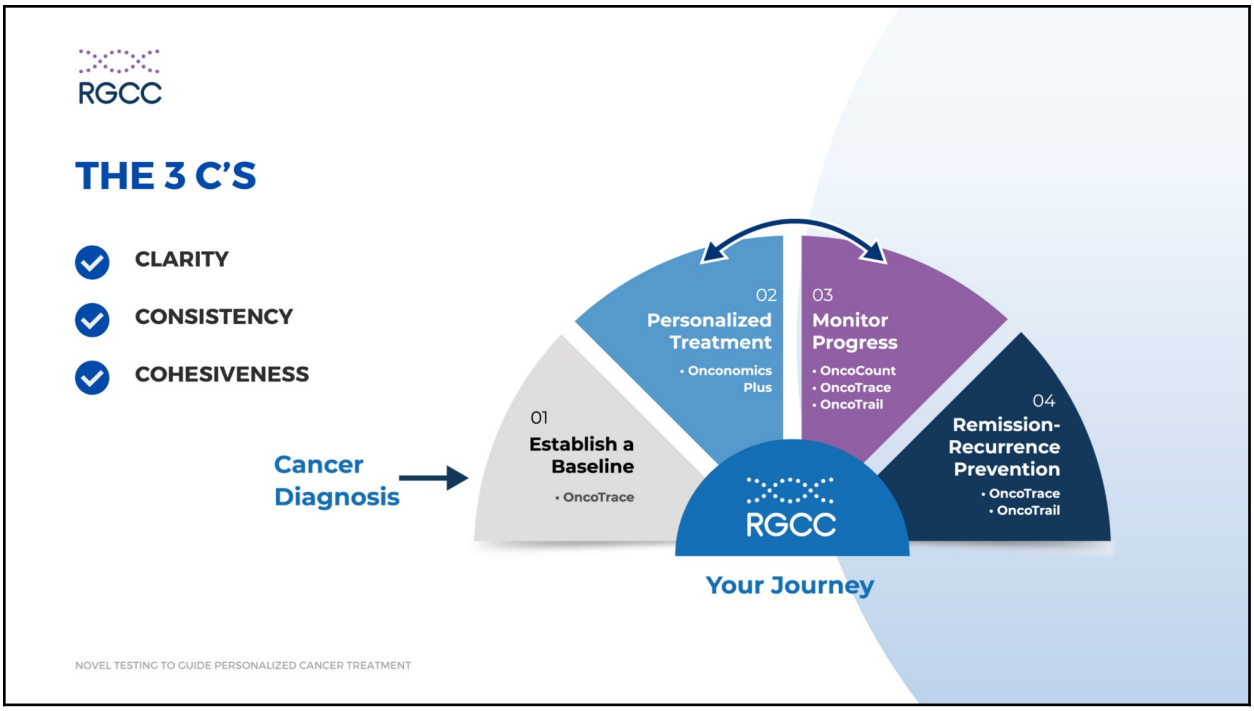

I call this the three C's. The partnership aspect of it provides clarity, consistency and cohesiveness. So with clarity, you get very detailed, personalized information that you can take action on, so if the information is very clear. Consistency. By staying with the same lab doing the testing, you have a consistency across the science. Now one of the things that you may or may not know is that different labs use different science even for the same test. So if you do a CTC test with another lab, they may be using different science. So you're not comparing apples to apples. So you want to make sure that you have that consistency across each test to make sure that the information is consistent for you. And also having a cohesive program by staying with a lab that is able to support you all the way through your journey, you and your practitioner can put together a clear path for your care.

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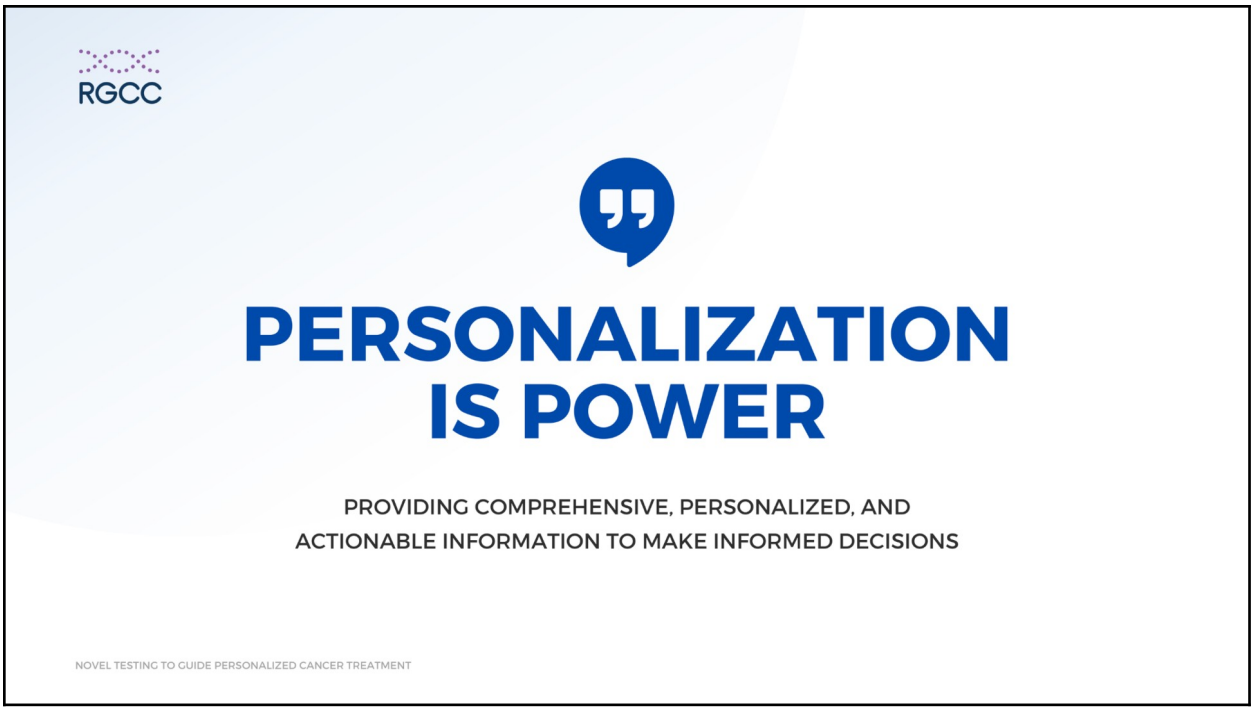
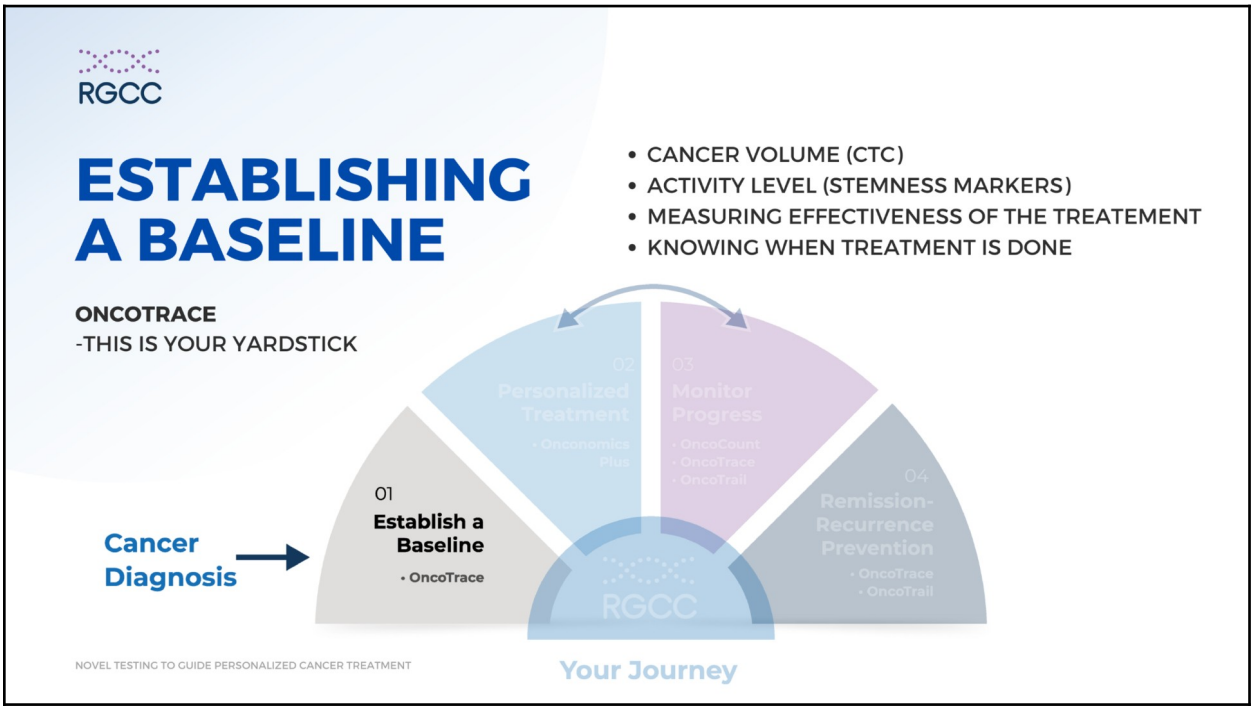
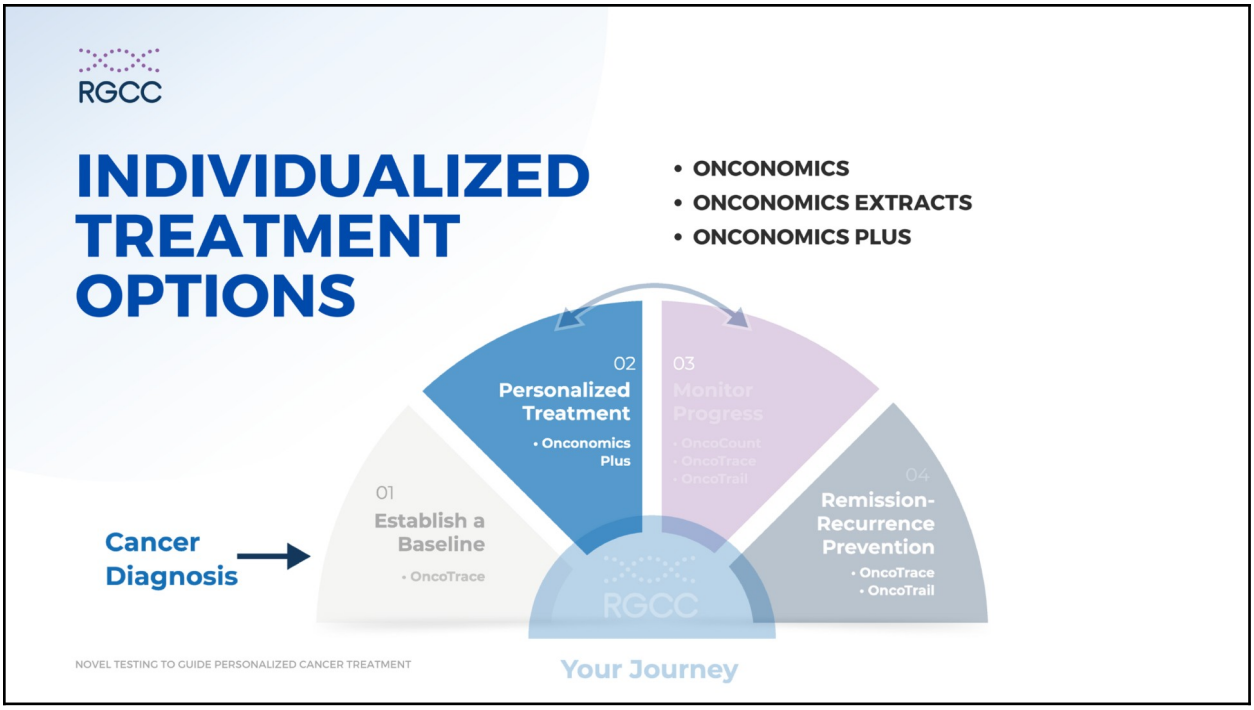


Personalization is power, providing comprehensive, personalized and actionable information to make informed decisions. One of the things that you don't have is time to waste on treatment options that don't work for you. So we want to make sure that you have the information that you need, so that you can make very strategic decisions with specific information that will be appropriate for you. So again, moving away from the one size fits all model into a very personalized approach.



Establishing a baseline. One of our premier tests is an Oncotrace test. This is going to give you the cancer volume, the activity level of those cancer cells, and it's going to help you measure the effectiveness of your treatment. And it's also going to help you know when your treatment is done. Now, from a patient advocacy standpoint, this test is your most important test. Why? Because this is your yardstick as a patient. You want to know where you are in your treatment at any given point in time. Is it working? Is it not? So that you can make good decisions and make changes in your protocols as soon as you can if you need to.



Dr. Lauren Cohen 13:19
This is what you may have called the Greek test. It is our most comprehensive panel. It gives you amazing personalized information on exactly what is happening within your cancer, and the expression of that cancer within your body. We have three different panels. But our most comprehensive is our Onconomics Plus and that is the test that Chad did and it's the test that we're going to be doing some interpretation with today.

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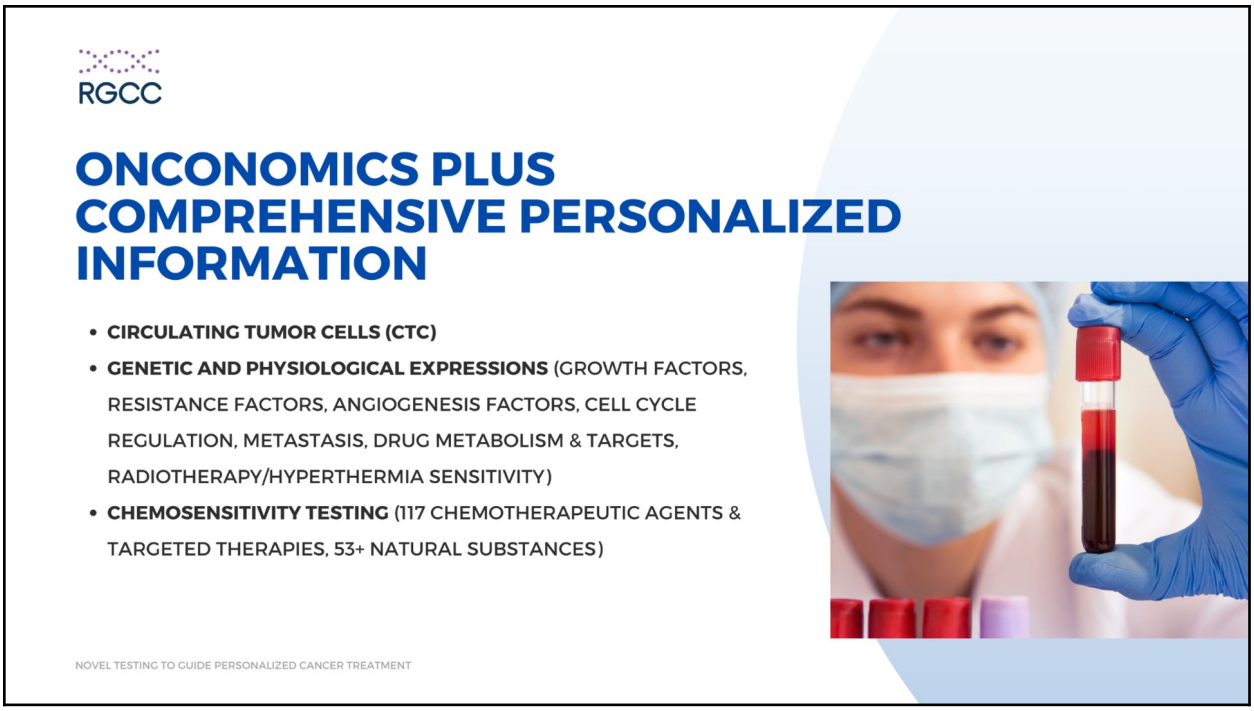

With our comprehensive personalized information from our Onconomics Plus test, you get information about your circulating tumor cells, you get genetic and physiological expressions such as growth factors, resistance factors, angiogenesis factors, cell cycle regulation, metastasis, drug metabolism and targets, and even radiotherapy and hyperthermia sensitivity, so you know if heat therapeutic options are right for you. In addition, we do chemo sensitivity testing on 117 chemotherapeutic agents and targeted therapies, along with more than 53 natural substances, so that when you are making choices about care options, you know exactly which chemotherapy agents and natural substances are going to work for you.

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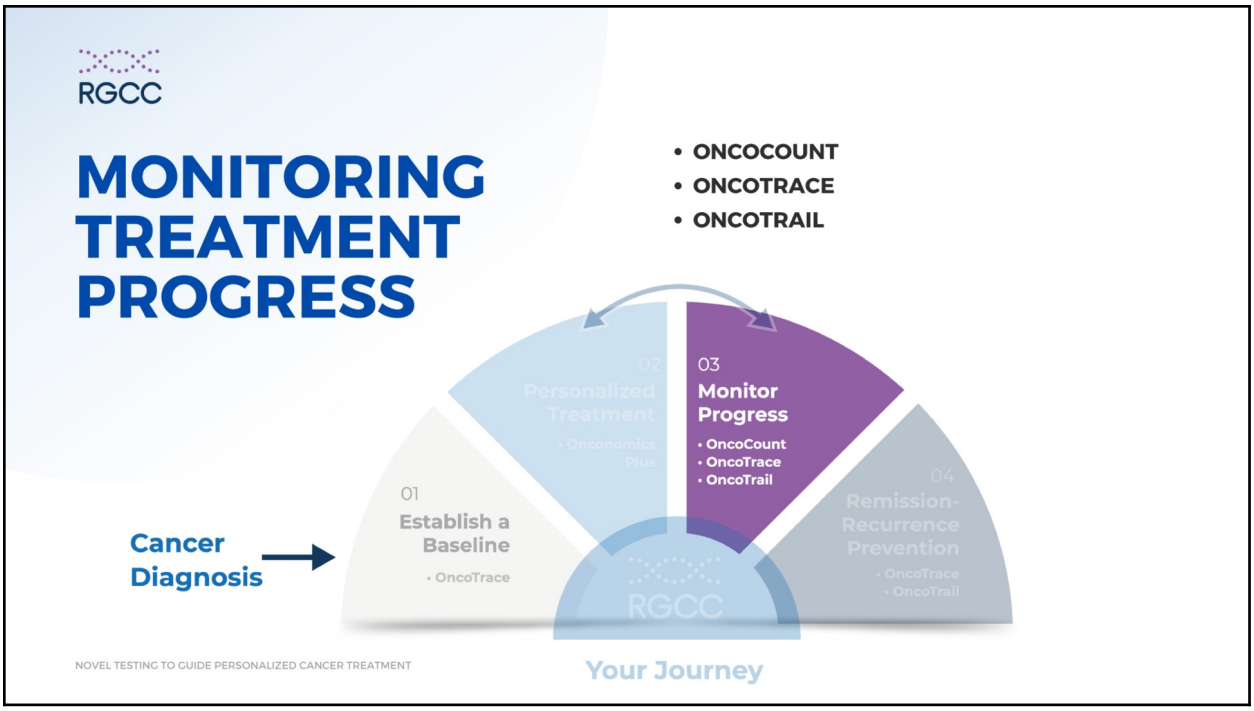
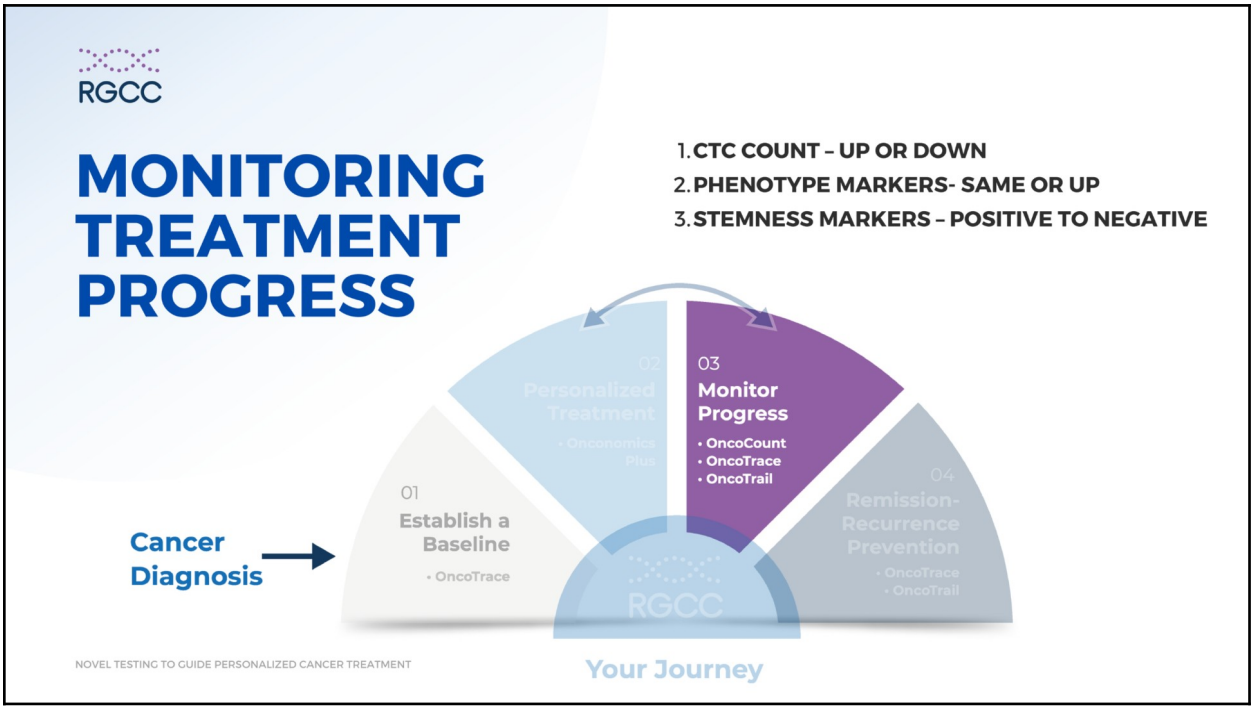


Monitoring your treatment. Again, you always want to know exactly what is happening with your care. We have three different monitoring panels. Oncocount is used for interim only. It just simply provides the CTC testing. With the OncoTrace and the OncoTrail, it also includes your phenotype and your stemness markers so that you can monitor the activity level of the cancer as it's progressing.



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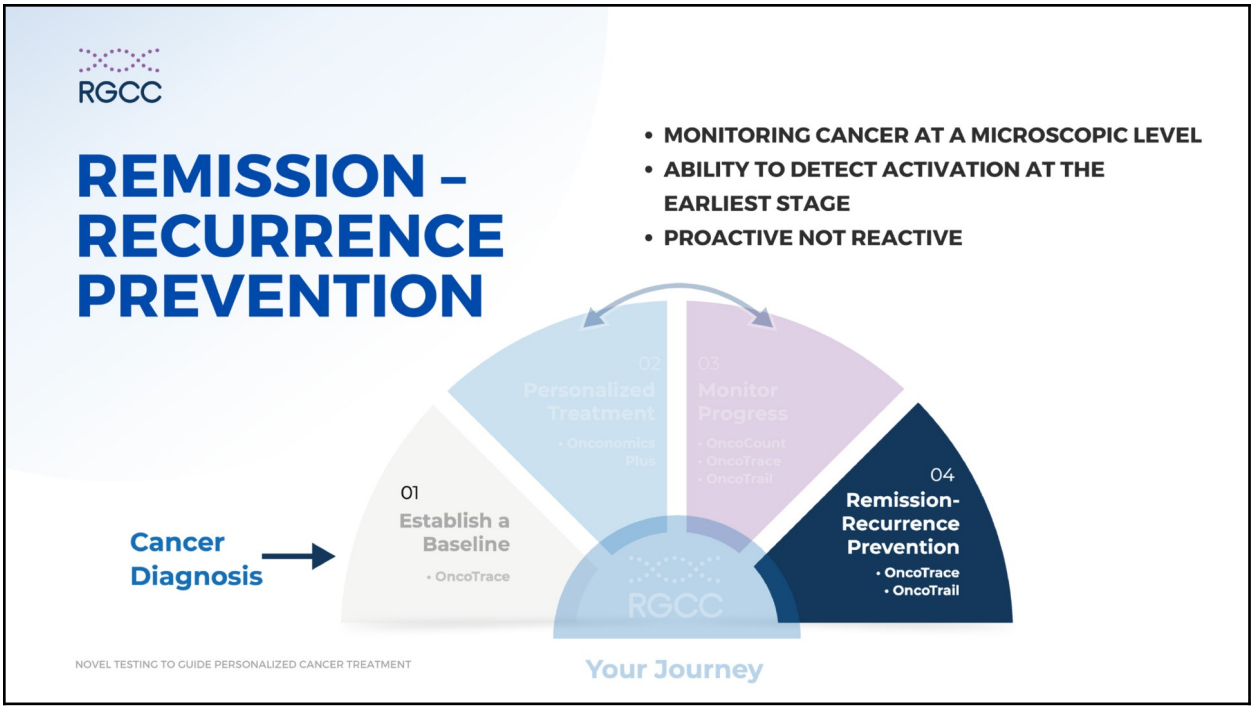
This is again, your most important test, because you're going to start with your baseline and then you're going to know where you are. If your CTC is going up, then you know that the treatment options are not working, you need to change course. If it's staying the same, it's working somewhat. You might need to change your options or add something to add a little oomph to your protocol. If the numbers are going down, you know that the care is effective. And with your stemness markers, it's showing the activity level. It presents the cancer's propensity to proliferate, to recur, or to metastasize. We want to watch these markers, because we want to see them go from positive to negative.



And you're going to continue on an every three month rotation monitoring so that you make sure you're staying on top of the progress, and you can make changes in your care at the earliest possible times when necessary. And then when you do move into remission, again, we're able to monitor on a microscopic level. We have the ability to detect activation of those cells at the earliest possible stages, which puts the power back in your hands so that you can be proactive with your care instead of reactively waiting for the cancer to get big enough to be seen on imaging and other medical monitoring.

Okay, so that was a very brief overview. Now we're going to shift into doing some interpretation. And again, Chad, thank you for allowing us to utilize your test. This is going to be a really interesting opportunity, not only for us to present, but for you as patients to be able to see how this information is utilized. So I'm going to turn the presentation over to Dr. Miven Donato. And he is going to continue on with the interpretation.

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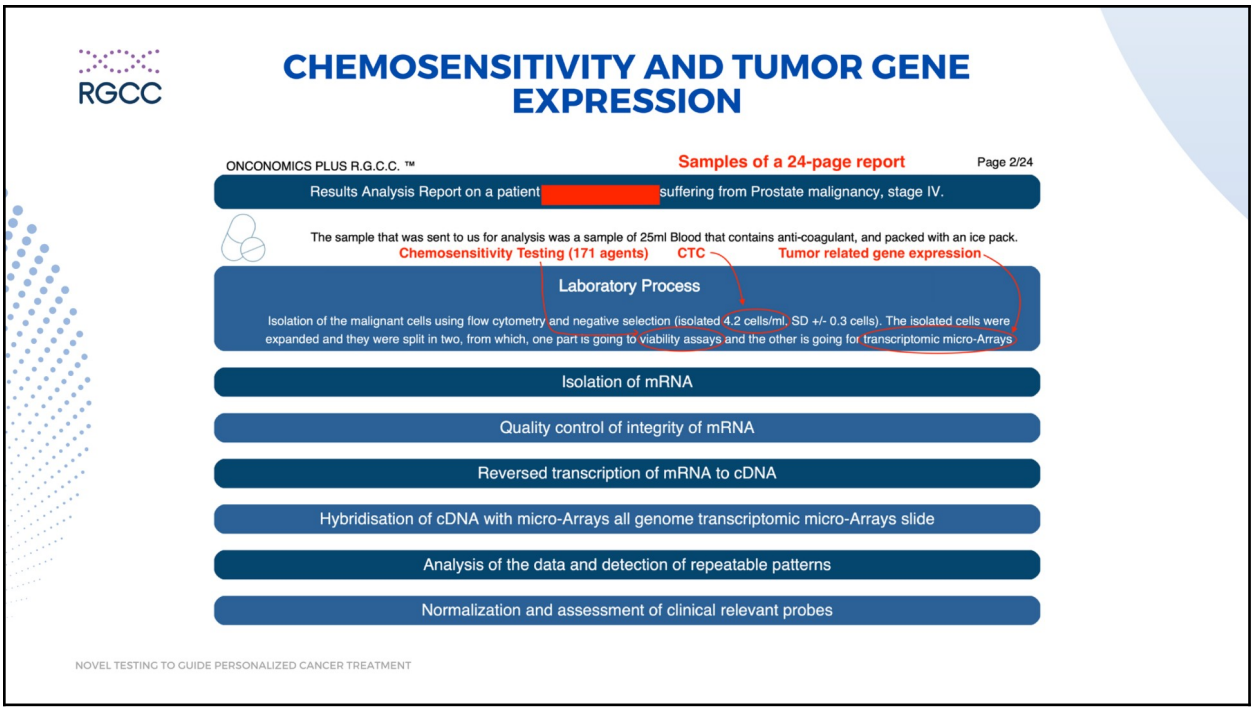
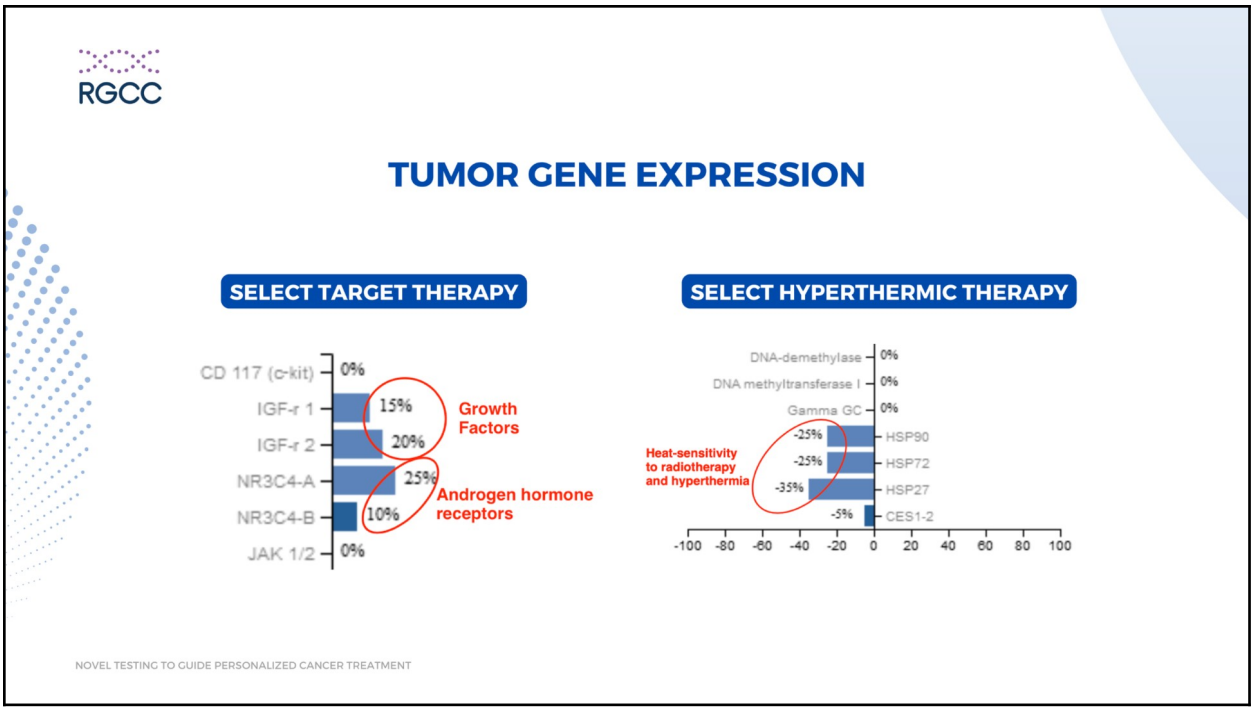


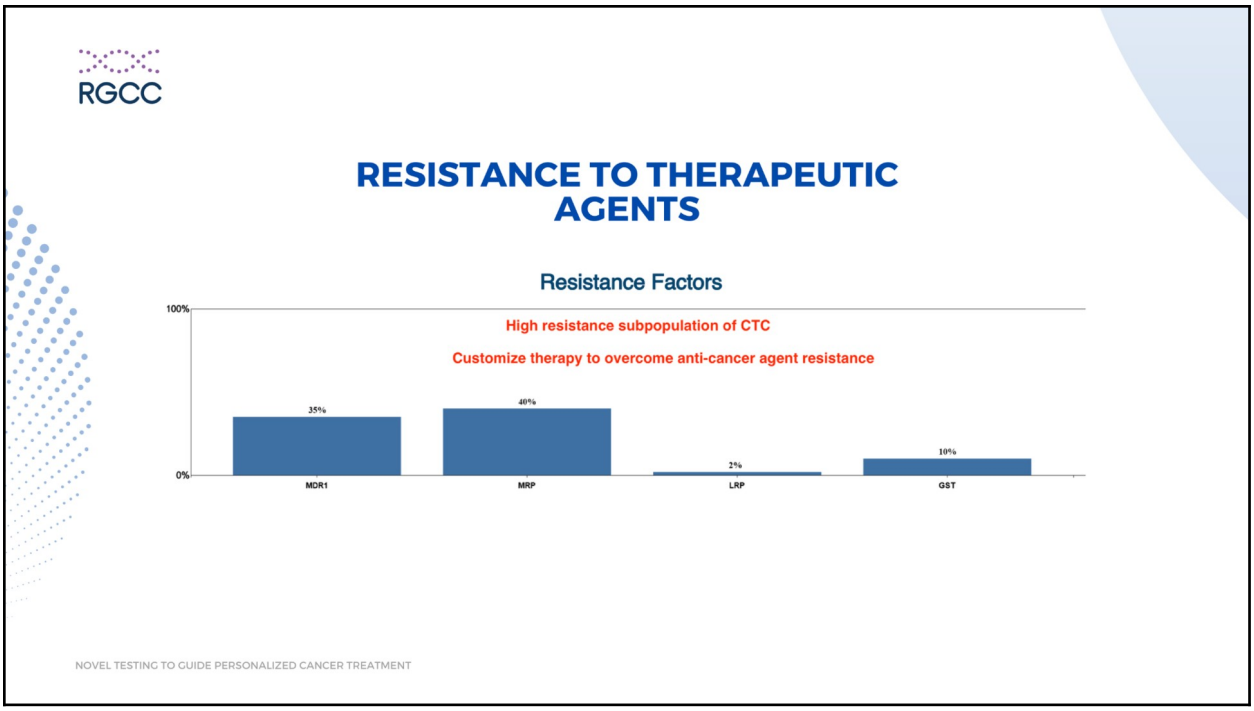
Miven Donato 17:11
Let's go ahead and look at that slide. So the Onconomics Plus test results consist of 24 pages. The most important thing to remember is this: this is the test that provides all the information you need to determine what is effective therapy for the cancer, for whatever cancer that is tested. And so the therapeutic options that one will obtain from this test pretty much covers a broad number of different therapeutic approaches. There's chemotherapy, and selecting the high sensitivity chemotherapy agent is, of course, going to provide the most effective therapy for this particular CTC. And then, of course, there's the targeted therapies. That's the monoclonal antibodies, and the small molecular weight agents. And then there's the radiotherapy and hyperthermia treatments. So those are selection, depending on what's considered high sensitivity, and you want to utilize only the ones that work. This basically removes the guesswork of what is effective. And then there's the off label drugs or repurposed drugs. And then there's the natural substances. And there's 53 natural substances that are routinely tested. And so those are what the practitioner can select as the strategy in creating a therapy.



Miven Donato 19:14
Okay, so you're looking at several pages, this is page two. And so what you're seeing here is that when the specimen arrives at the lab, and once they have isolated the circulating tumor cells, or CTCs, and you can see here the CTC count is 4.2 cells per mil with a standard deviation of plus or minus 0.3 cells. So if this is the first test, then this would constitute the baseline which is 4.2. And, for prostate cancer, there's a statistical cut off of less than 20 cells per mil and so if this was the first time this person has had testing and there's no treatment yet, then this would constitute a relatively low load of cancer, or it would be a considered early disease. And so there's no staging like conventional stage one, stage two, stage three, stage four, it's basically a cut off, where is it less than 20? Or is it greater than 20. So it would constitute an advanced disease, if it's greater than 20. And in this case, it is an early disease. And as far as the isolated cells, once they're isolated, they're expanded or grown in the lab. So that one part can be tested for chemo sensitivity test, which is the viability assay. And the other group goes for transcriptome microarray, which is the RNA transcripts and determines the expression rates of these genes. And so by doing that, it provides the practitioner the ability to create a very specific target, so that it is very personalized for this particular case. And so, not only we will just select the correct agent, that will either destroy or that will inhibit the growth and at the same time, modulate the immune system. It will also provide a specific way to determine how you can target specific genes that's overexpressed. This is the validated cancer genes that are expressed, and they can be either inhibited if its receptor can be blocked, or it could be interfered in the metabolic pathways. And so this is where the practitioner will be able to narrow down into the very specific treatment

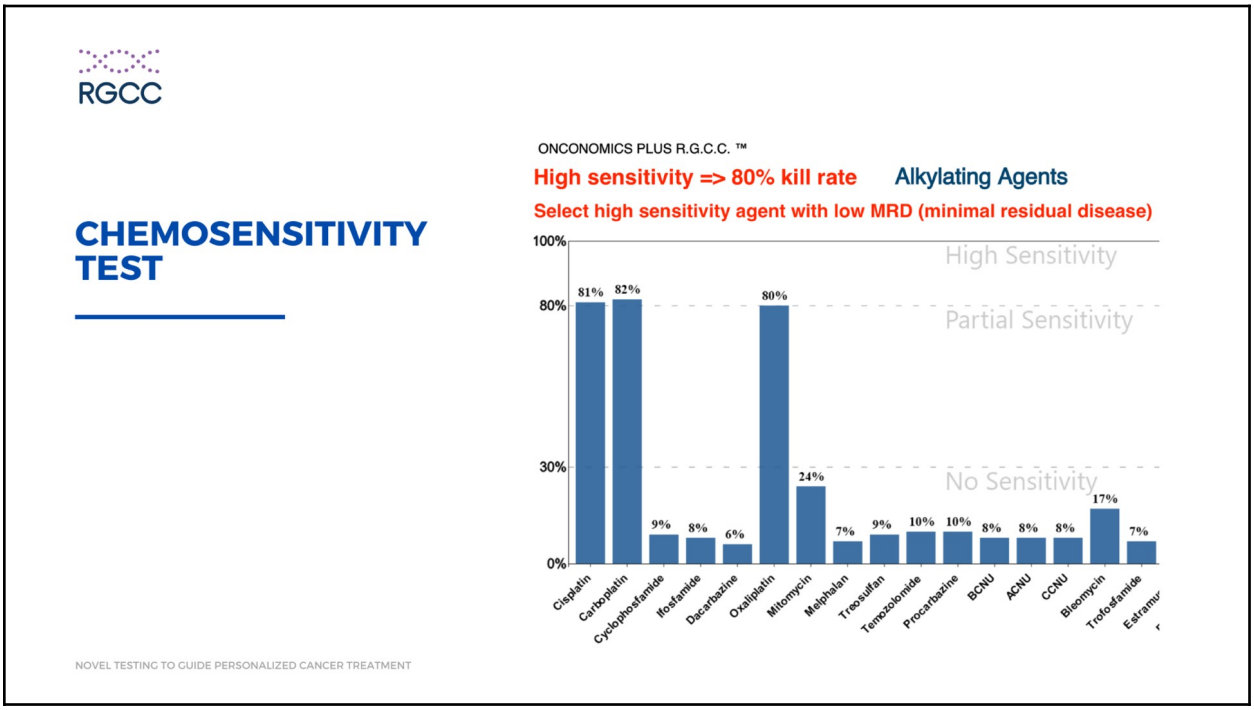
Miven Donato 22:18

that will be effective without having to guess what will work as in a group setting, which is difficult in a conventional system system. It's not personalized. And so go ahead into the next slide. This is an example of defining specific targets. So with a gene expression, these are the validated tumor related genes. In this particular case, you're looking at these blue bars that are going to the right, that's an overexpression of the genes, and if it is going to the left of the line that's down regulating. In this particular case, the IGF receptors, one and two are overexpressed. These are insulin growth factor receptors that are overexpressed for the CTC or circulating tumor cells, it would mean that any insulin surge due to consuming carbohydrates, or anything that causes an insulin surge, particularly high glycemic carbs, will will cause these receptors to grab the insulin, due to its increased affinity for insulin. And then of course, that brings the sugar nutrients into this cancer cell. And so that's one way to help proliferate or grow the cancer. The other thing here is the NR3C4-A and NR3C4-B are the androgen receptors, the hormone receptors. When they're overexpressed like this, there's no question that this is a hormone driven cancer. And so one of the things that is conventionally done is if you want to get a hormone blocker or hormone blockade, this is where drugs like Lupron which is an injection is given to the patient because it's going to block the hormone but you have to realize that there are 75 validated tumor related genes so it can't block everything. You're going to block only some of them or one or two, which is common in conventional practice. But yet all the other genes are still overexpressed and it's causing the cancer to proliferate. That's why we cannot just destroy cancer completely. The more genes that can be blocked or interfered in terms of the growth, that's when the therapy becomes more effective. So this is where the clinician can really make a difference when they are specific, and able to block as many genes as possible. On the right side of the slide is the down regulation of the heat shock protein (HSP). And these are the ones that when it's down regulated, very high, it means that the cells do not have tolerance for heat or hyperthermia treatments. And so they get destroyed easily compared to the healthy cell, which is going to be 0%. So when it's downregulated, this far, you can be assured that radiotherapy or hyperthermia treatments will work really well.



Miven Donato 26:02
The test results also show the resistance to therapeutic agents. And so these CTCs have characteristics that make them resistant. And one of the things that's not featured here, which is the OncoTrace test, which is always done with a baseline Onconomics Plus test, is that it tells you already from the phenotype that these are resistant type cancers. And everyone's going to have different resistance phenotypes. And so in this case, this MDR1 is a multidrug resistance factor. And then there's the MRP, which is the multidrug resistance protein associated. And then the LRP is the lung resistance protein associated. And the GST is the glutathione-s-transferase. So these are different factors of resistance to therapeutic treatments that the cancer cell exhibits. And so one of the things that we do is we determine if it's a high resistance, as in this case, then we would customize the therapy to get around this resistance barrier. And one of the things we do is to determine the frequency of exposure of the therapeutic agent to the CTCs because the higher the resistance, the more likely the CTCs will develop secondary resistance in a very short time. And usually between four to six months you already see resistance developing and the CTC numbers are no longer decreasing and the steep dive is starting to plateau. So that's when you know the therapeutic agent is no longer effective, or there's resistant clones forming. And this is basically the feature of the high resistance sub-population of CTCs, and there are many different populations, just bear in mind, this is not a homogeneous population but rather heterogeneous. And it's this small segment of CTC subpopulation, that the chemotherapies cannot destroy, and they end up being the MRD or minimal residual disease, which is basically represented well in this sub-population. So we would rotate the agents more frequently, that's one of the things that will help. And at the same time, we use certain agents to help reduce the resistance barrier and increase sensitivity to cytotoxic agents. And when we add these agents in, it overcomes that barrier of resistance. And the GST, again that's has to do with glutathione or elimination as far as detoxification goes and that is what some people have,

a very high GST that’s able to eliminate the cytotoxic agents faster, which means that the person will not get the therapeutic benefit because the CTCs are able to basically detox themselves. Next



Miven Donato 29:31
Here's an example of chemosensitivity results. RGCC recommends using or selecting the high kill rate. So this is expressed in percentage, which is sensitivity, or kill rate and this alkylating agent group is a section taken from the report and it shows here that we've got three alkylating agents that show 80% or higher. And so that would mean that those are the three agents that would be recommended to be selected as a high sensitivity. And that would mean the residual disease is a lot less, you're talking 18 to 20% MRD or minimal residual disease, and you don't want that residual to be high, because it would cause a problem down the road as they start to increase in their numbers and be much more difficult to destroy. So you want to have a high kill rate, and a low MRD. And so there's different categories or classes of chemo drugs, this is just the alkylating agents

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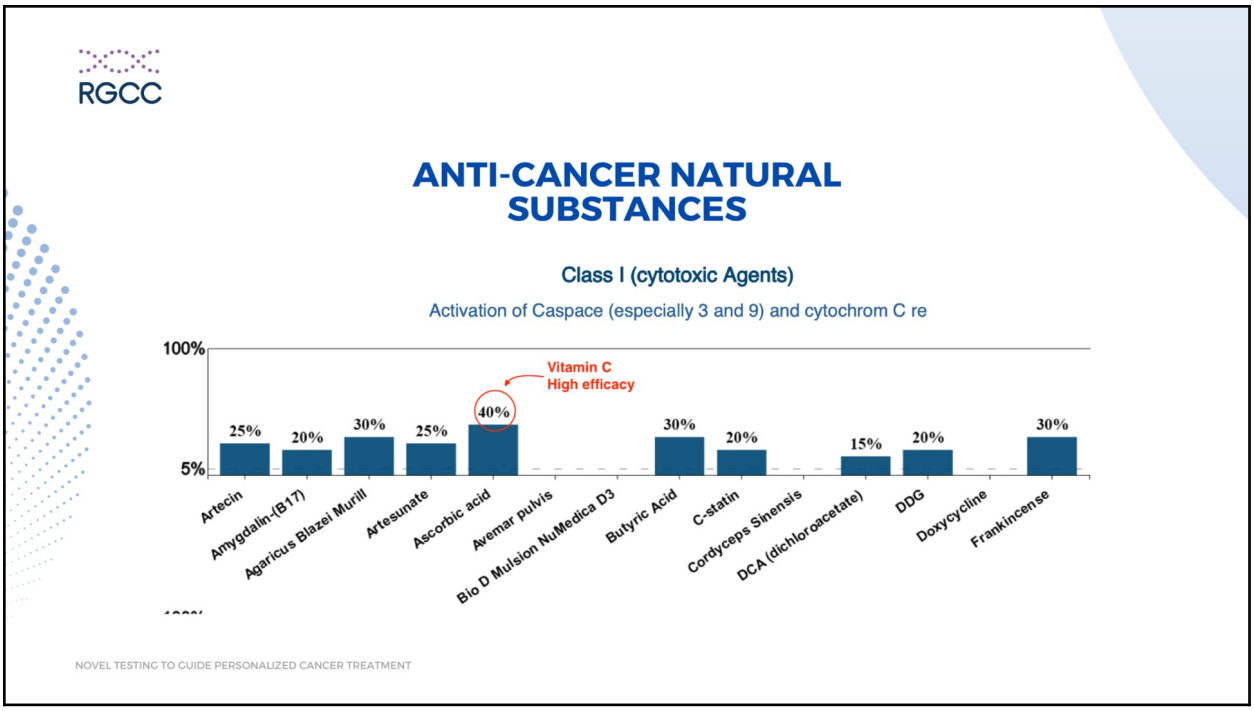
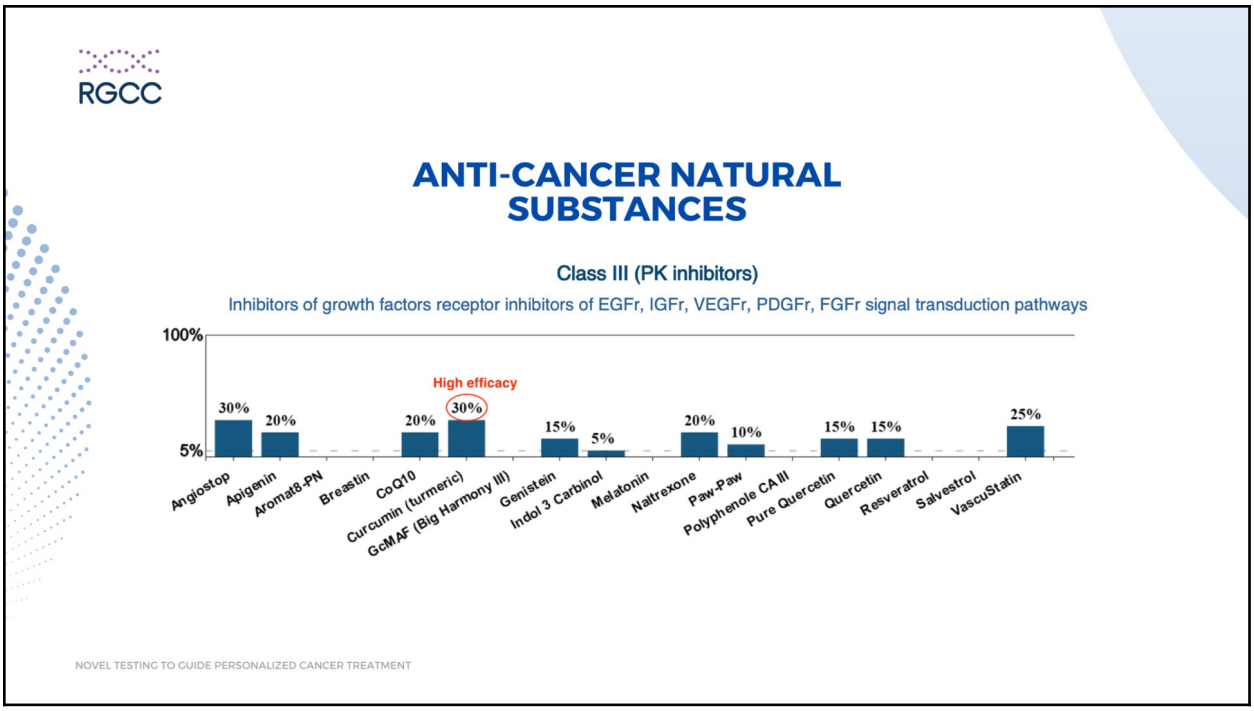


Miven Donato 30:50
in this particular one, we're now looking at the sensitivities for the natural substances, and Class I, which is cytotoxic agents, we're looking here at a percentage that's based on the one dose whereas in the previous slide, it was based on six doses in six days, this is one dose, and then they determine the efficacy. And you can see here that ascorbic acid, which is vitamin C, has a very high efficacy at 40%, the sensitivity threshold is 5%. Anything above that would be considered sensitive, but we tend to recommend more of the 15% or higher to start and then we rotate the agents, we start the most sensitive agents over the lesser ones because we want to target the cancer with the most effective agents, because that first six months is crucial since secondary resistance starts to develop. So we only utilize the most effective agents first.



Miven Donato 32:00
So these are the Class III protein kinase inhibitors. And so with this group, it has a very broad effect, you can see it inhibits EGFr, which is the epidermal growth factor receptor, the IGFr, the insulin growth factor receptor, and the VEGFr, PDGFr, and FGFr receptors (these receptors are involved with angiogenesis). So you know, one of the things that are commonly done in conventional oncology is to select an anti-angiogenesis drug, because cancers are mostly overexpressed in angiogenesis, due to the need for increased blood supply and nutrients. The signal transduction pathways can also be blocked. And so this group of Class III agents have a broad effect. And so we look at the gene expression rates, and we find the areas here that we want to use to block certain genes. And so curcumin (turmeric) shows high efficacy. And so we would definitely select that, again note the 5% threshold, anything 15% or higher, is what we'll select for the patient to use, and then we rotate them through the year. Next slide. Okay, back to you, Lauren.

Dr. Lauren Cohen 33:18
Thank you. What we want to do is leave a lot of time open for questions and answers. I just want to let you know, this is an international lab. We do have branch offices and independent distributors around the world. In order to get RGCC testing, you do need to be connected with an RGCC practitioner. And since this is a worldwide audience, we are going to direct you to the contact pages because not all of the people in your audience will be connected with our branch. What I suggest you do is go to RGCC-international.com. In the lower right hand corner, you're going to see a purple button that says “Order a test.” Just click on that button. It will take you to a page where, if you are a registered clinician and interested in registering as an RGCC clinician, but also right here is “I am a patient.” When you click on that link, it will take you to a contact form. Your information will be sent to our main office in Switzerland and then it will be

redirected to the appropriate branch office in your region of the world. And now we're just going to open it up to questions and answers. I'm going to stop sharing my screen for the moment. There we go. We can always bring that slide presentation back up if there's something specific. So Brad, I'm going to allow you to manage the various questions and our team is here to address them.

Brad Power 34:54
That was a great overview. It inspired me to want to click on that purple button.

I'd like to give Chad a first a chance to just share a little bit on the value he's received. One of the ways that we work, just for the folks at RGCC, is we have a pioneering patient, like Chad, who runs into a service provider, tries it, has an experience. They're like a secret shopper, and then they recommend it to others, and then more of us take it up. For some of the service providers that we have found, we say we recommend all of the patients get this test. We have that kind of relationship with a handful of companies. Somebody like mProbe, that does proteomics, for example. You're on that pathway to a recommendation, but it really starts with Chad, and the peer-to-peer review that he would give of your services and how he's found value with it.

So I'd like to start with Chad and say, you were introduced to this through your integrative oncologist, you got the test, what's your candid review of the value you've received?

Chad Magnussen 36:26
I have some confidence in my supplementation program. Now that I am blocking pathways, like angiogenesis that was identified as being highly upregulated for me. So, for me to try to regulate that now is very important. So I think I found some benefit in that. Like I said before, I had already received chemotherapy and was already deep into my treatment plan.

One of the things I find very interesting is they have a conclusion at the end of the report. And one of the conclusions I found is that I have a very upregulated, overexpression of MDR1, which is the resistance protein or the resistance. And it says here, this specific tumor appears to have resisting populations because of MDR, one overexpression that can be reversed by the use of inhibitors of ABCG2 pumps. So if someone could address what that means? I think that would be important for any of us deciding to do another round of chemotherapy. So that one is interesting.

And then I also have a question about the recurrence resistance program. That seems interesting. What does that look like? I mean, what are you doing? What is RGCC doing for that program? So a couple of questions to start with.

Miven Donato 38:33
Well, I can first answer that portion, inhibitors that we use are flavonoids. And what happens is when you're using flavonoids, with cytotoxic agents, the presence of flavonoids will help to increase the cancer sensitivity to the cytotoxic agent. And so that's a sense of overcoming that

barrier of resistance. And so that would be an ABCG2 pump inhibitor. There are drugs that are used, like certain antifungal drugs, like ketoconazole, is one but that's not what we emphasize other than the natural options, to help improve that sensitivity. So it does reduce that resistance. And then, of course, the rotation of the time of the agents is important, because we want to make sure that the agents remain effective, because over time the cancer cells are mutating and they become less and less sensitive to the agents. So those are the combinations that we work to help address that barrier. And what was the second question?

Lauren Cohen 39:52
The second question was about the remission and recurrence prevention program.

Miven Donato 39:59
So you will reach the remission level when your numbers are very low like one or zero, basically, that's kind of a remission status. And that's on the CTC. But you also have to make sure that the phenotype markers are also negative or very close to negative, dim or negative. That's actually more important because the subpopulation which the ones with the tumor stem cell markers, they're the ones that drive the disease. So if you don't look at that phenotype markers, and you just rely on the CTC number, sometimes that's misleading, because when the CPC number starts at a certain level, and then it's going down, if it's not yet down to that 1.2 or less CTC, you still have a higher risk of metastasis, because you haven't addressed that small segment of population, they're the last to go. So when the CTC numbers are decreasing, you're actually destroying the weaker cells, the ones that are not as strong as the dominant ones that are only a small segment of that CDC. So you have to pay attention, that sub-population is very important. And you can only see that on the OncoTrace or the OncoTrail tests as you monitor that. And once you reach that 0-1 level, which is a very low risk, or remission level, then you just monitor it once a year to make sure that it's not coming back up because of some changes in the internal environment of the cancer, maybe the gene expressions are starting to be overexpressed again. And so that's when you can detect the change early on, and then address it right away.

Lauren Cohen 41:43
Right, and I want to add a little something to that in terms of the recurrence prevention program, and the panels. I have a question that came up in the chat. So as long as there are CTCs in circulation, we're able to run the Onconomics Plus panel and you're able to see options, but you may not be able to do chemotherapeutics. Again, if they can't see it, they can't treat it, but you now have all of those natural agents that you could utilize to continue to support your system along with monitoring, just to make sure that those stemness markers don't reactivate. Because again, you can have a very low cell count, but if that low cell count is still active, your care is not done. But then, you know care is done, when those markers do go into the negative, so they're no longer active. You want to continue to monitor but you also still have information on what natural substances and therapies you could potentially use to continue to support a non cancer environment? Okay, So Rick, you actually have a question here in the chat, and I'm going to hand this one over to Panos. And the question is, I'm a little surprised that you use microarray technology. Is that because of low volume of sample, why not use NGS?

Panagiotis Apostolou 43:14
As we discussed, we have many different labs. They may use different sites and protocols and different techniques. So in our case, we use microarrays since we started in 2004. And of course, we also use NGS. So we try to make some validation to see what is more effective. All the techniques have pros and cons. So microarray is okay and very well established and well known technique. NGS is the new area that came out last years. So still some issues.We have to face some more things that we need with NGS, but no, it's not the low volume of sample. On the contrary, the NGS needs much lower quantity. The microarray, the platform that we use, first of all, enables us to study the whole gene expression profile. Also, there are platforms in NGS that they can do that. And we have tested them and we have seen that the data are comparable. So we don't have statistical significance. It's really important with microarray and the platform that we use that we can test several samples in parallel. So imagine that we can have a few dozens of samples tested per day. It's also feasible with NGS, but it's really more dedicated and you need more expensive equipment. So it saves the platform. But definitely yes, we have compared the results of microarrays with NGS and it's really important that all the assets that we use are accredited, so we have validated with other labs with other techniques to make sure that the data we provide are accurate, and comparable, if they're using the same technique

Rick Stanton 45:06
Do you use Affymetrix? (Affymetrix is a brand of DNA microarray products. The Affymetrix company is now Applied Biosystems. It was sold by Thermo Fisher Scientific. It originated with an American biotechnology research and development and manufacturing company of the same name.)

Panagiotis Apostolou 45:09
We have also used Affymetrix. But we also have a supplier that provides us customized printed slides. So one slide for all the gene expression profiles, more than 180,000 probes.

Dr. Lauren Cohen 45:28
Thank you. And I do see another good question in the chat from Robert. “None of us, I believe, are newly diagnosed, or heavily GYN and have been heavily treated. How would that affect which tests to use and when to use it?” It actually doesn't affect which tests. In an ideal world, you would know about RGCC as soon as you got diagnosed, and you can step into the system before you start treatment. But the reality is, most people have gotten treatment before they find RGCC. And hopefully, that will start changing as we begin to expand and people become more familiar with RGCC testing. But whether you are newly diagnosed, or you have already been treated, you still step into the RGC universe, right? We call it our family, into our community, and you start with the testing in the same way. So you would start with your OncoTrace to establish your baseline. You would then go into your Onconomics panels, and then you would continue to monitor and then also into remission. So there is no difference, whether you are newly diagnosed, or you have already been treated, you would still follow the same process, the same procedure, the same formula that we have in our system. Our system is open to patients in all

aspects of their care whether newly diagnosed, or you've already been in treatment, and you're looking for new or additional options.

Robert Gurmankin 47:18
What is the cost and insurance coverage? Is there Medicare coverage?

Dr. Lauren Cohen 47:26
At this stage, none of RGCCs tests are covered by insurance. That is something that our team is working on. Again, this is outside of standard of care. And as you know, when you step outside of standard of care, if you move into the integrative and natural care spaces, unfortunately, much of that is not covered. It is either cash or out of pocket, We do have price sheets, as well as the cost of the various tests are listed on the website. When you go into the website, you click on each individual test, scroll down to the bottom of the page, and you'll see the pricing listed in euros. Depending on what region of the world you're in, you may have to do a conversion. If you're in the North America region, we already do that for you. We have a price sheet listed out that has all of the prices in euros and then an estimated conversion rate because it does vary based on every day that conversion rate changes. It gives you an approximation in US dollars, so that you have a sense of what that is. But again, because this is an international audience, US dollars may not make so much sense, so you would do your conversion from Euros into whatever currency you have in your part of the world.

Brad Power 48:59
Chad, could you say how much it cost you – to give people a ballpark sense of what we might be looking at?

Chad Magnussen 49:09
I think the test itself was right around $2,000 And then there was some consulting with the doctors prior and after another $750. So you know it was reasonably expensive. And now I think next month I'm going to do the follow up. So I'll be doing another round to see where I'm at.

Dr. Lauren Cohen 49:30
The different tests all have different price points. The economics plus is one of our more expensive tests where the OncoTrace is at a lower price point. The pricing is on the website or, if you are able to reach out to us, we can provide you with that price on the price sheet. And keep in mind that those are prices for the testing. It does not include in-office fees like consultations and blood draws, and those types of things. There would be additional fees that the practitioners themselves would ask for.

Brad Power 50:14
To what extent do you think that patients would be able to get the test? You have a direct-to-patient option, like, “I'm a patient, I want the test.”? Are they able to make sense of the test themselves? Or do you find that they need an integrative oncologist or some kind of practitioner to partner with them to interpret these 24 pages of results?

Dr. Lauren Cohen 50:39
We do not offer direct-to-patient. In order to receive RGCC testing, it is essential that you get connected with an RGCC practitioner. We only work with RGCC registered practitioners. So even if you have, say, a naturopath or primary care physician, they can't just order a test. And again, this is something a little bit different about our lab. And you can see the complexity of the information on this test. We have something called RGCC college and all practitioners must go through our training so that we can ensure that you, as a patient, are going to be matched with a practitioner who is versed in interpretation and how to take that information and turn it into a personalized protocol for you. You can see the complexity. If you do get the test somehow, someone is willing to just run the test, or you just get that report, it's going to be impossible for you to interpret it. And that's why we have the training that we do, because we know how important this is. And I want to stress that both my mom and sister are active stage four cancer patients. So when I speak this, I'm speaking this from the patient side, that you want to be paired with someone who is fully versed, so that you can use the information in its most powerful way. You don't want to be misinterpreting or delaying time trying to interpret a lot of information. That doesn't make sense. And I don't know if you know, I think Chad may be one of the only people in this community right now that has done our testing. But we have had patients where they take their panels, they even walk into their medical oncologist and they have no idea what they're looking at. Right? It's not a standard test, like a CBC with differential where everybody knows how to interpret that kind of information. It's very complex. Iit has a lot of nuance to it. And we want to make sure that you are paired and partnered with a practitioner who is going to be able to really work with you so that you get the most impact from the testing and the information.

Brad Power 53:08
That's great advice. Thank you, Lauren. That's very clear about access and interpretation. I'll just mention that members of our community are often in that boat, that they've got an RNA seq test, or they've got a proteomics test, and their treating physician has never seen an RNA seq report or a proteomics report. So they're having to educate their clinician in the course of trying to say, “I think this is what this means. And I think this is what I need.” But they're having to bring sometimes treatment options. We're used to being in that boat is my point.

Jonathan Starr 53:50
You said this report was about 20 pages or 24 pages long and we only saw like three or four. What are we missing? Do you determine when you recommend flavonoids, or Metformin or anything else, carboplatin? Are you recommending dosages and treatment protocols? Or is all you're doing is showing the presence of these different things and leaving it to your RGCC physician to interpret it? My guess is you're going to say the latter. But I'm also wondering, what didn't we see in all those other 20 pages?

Miven Donato 54:46
A lot. There's a lot to cover, but basically, you only saw the the insulin growth factor receptors and the the heat shock proteins and some growth factors But the ones that you are missing are angiogenesis, signal transduction pathways, you're missing information about cell cycle rate,

which is how fast the cancers growing. And we check, you know, there's three main genes that control that cell cycle rate, the P 53, P 27 P 16 genes, and then we're, you're also missing the metastasis genes that are overexpressed, or downregulated, depending on the situation. And so that tells us how much risk there is involved in metastasis for this particular cancer, they're also missing information of certain genes that are overexpressed, that may be effective to find a targeted drug for it. And for example, the CDK4/CDK6, as in certain cancers, like breast cancer, then usually you'll locate in the next few pages, a targeted drug to see if there's effective, such as palbociclib, which is CDK4/CDK6 inhibitor. And so you know, you're able to match up the chemosensitivity and the gene expression rates to make sure that it's effective. And then the other thing is the longevity of the cancer, or is it the kind of cancer that's going to be there for a very long time, and that's the H-tert gene. And so when it's highly expressed you're looking at something that is not going to go away easily. It's not unusual to see a high expression H-tert gene for cancer that was diagnosed back in 2004, a prostate cancer which I have cases like that, where it's been around a long time and this person is not in remission, but it's more like living with cancer. Okay, so there's lots of information to cover, and then we create a strategy and how to address all those over expressions. And what can be, how can we down regulate them, and not just depending on the chemo sensitivity, although the chemo sensitivity really takes precedence over the gene expression rates, because you're actually looking at the reaction of the CTCs to these agents. And that's what gives the consistent ability to be selective to the one that works rather than trying to go for the guesswork, which is typically what is seen in conventional oncology, relying on statistics of group diagnostic sampling and determining what fits according to the FDA, from the clinical trials. Well, we don't do that. We determine what will work for you rather than what could work for the group because there's going to be some that are not going to work for them, because their CTCs are not responding to that drug. Well, you're not going to be guessing when you're doing RGCC testing. It removes the guesswork.

Jonathan Starr 58:11
How are you measuring patient success from your treatment recommendations? Or do you have any data on what someone should choose that is something that you guys have recommended, that is not standard of care? Do you have any data on what the outcomes have been?

Miven Donato 58:43
I can tell you one thing, if you're not working in a standardized format, everything is not going to be comparable to another person just like a fingerprint. So we look at the baseline first, which is the OncoTrace test. And then what we do is we determine from a follow-up OncoTrace if the response to treatment is good for that particular person. And then we make adjustments as we check this quarterly. So it's not really easy to just create a group average, because everyone is so different, you know, some people get sick easily, and some people don't. So how in the world can you create a very good measurement for a group of people, when they're all different? That's where the standardized treatment becomes an issue. So really, we look at cases on an individual level, how are you performing in six months? And that's why some people are doing very well, because they respond really well to therapy, and some don't do well. We minimize the non-response case by determining what will work for that particular patient.

Jonathan Starr 59:49
I get your approach, and it's a very innovative and ambitious approach, and I hope it works well. I would just be curious to get some actual documentation of results. Let's say for your flavonoids: How would you determine a dosage for that?

Miven Donato 1:00:15
RGCC testing does not tell us the dose. This is based on what information we have applied from a scientific level to the clinical level. So over time, since 2004, we've created much data for physicians to come up with the typical starting dose. And so there are general guidelines, what's been done before as to how much to start and then they kind of work up from there. It depends on the physician's experience, but no, we're not giving specific doses. There's a recommended dose but that's from the clinical aspect.