Discover Fasting Mimicking Diets For Cancer Therapy Transcript

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Origins of Fasting Mimicking Diet Research

Doctor Longo, it's such a pleasure and honor to have you on this segment of Cancer Summit. I mean, you are a leader in this field in regards to the fasting mimicking diet.

I wanted you just to kind of lay the ground first, you know, why did you even get into this direction of fasting, mimicking diet? I mean, why there everything else you could study?

Yeah. So we were many years ago. 20 years ago, we were experts in protecting normal cells against all kinds of toxins. And because we were working on aging and so looking at chemotherapy, it seemed to me that was probably one of the most toxic intervention that a human being will ever get in is or her life.

And so that was the beginning was only fasting. Can we protect the cancer patients first mice and then patients and not the cancer cells against chemotherapy?

There was the idea. Then we started the first trial, a clinical trial in Norris Cancer Center, USC. And it was a disaster because patients did not want to do what fasting.

And the oncologists were very worried about what around the fasting. And yeah, so then we went back to the National Cancer Institute, the National Institute on Aging, and they founded the they co-founded the development of fasting mimicking diet so fast.

Diet actually started with with cancer patients at exciting. And so I we we talked a little bit in the past in regards to, you know, how it protects the healthy cells during chemo and then opens up to the cancer cells for chemo during fast die.

But you've gone so much, so much further beyond that in the research. And there are a lot of clinical trials that are out there right now in regards to how fasting, mimicking diet can then be combined with some of these specific therapies that are out there.

And do you mind sharing a little bit where we're at now with the understanding of fasting, mimicking diet and cancer? Yes. So I think that now we and many, many laboratories have done studies in mice and lots of cancers.

And the first thing that keeps working on almost every cancer that has been tested so far in combination with the standard of care. Right. So so immunotherapy, chemotherapy kinase inhibitor radiotherapy hormone therapy.

And so that's already been very successful in the mice. And then we can talk about clinical trials next. But the I think a lot of the studies or most of the studies show slowing down of the tumor progression.

Major slowdown, much better than chemotherapy, much better in mice, much better than immunotherapy even. Right. So so if you combine fast diet and immunotherapy it works very well.

And in mice the immunotherapy doesn't work well at all. And so but but then what about regressing causing tumor regression. And for that we move to what we call RNA seq.

So that we look at our cancer cell rewires. And then we target this escape pathways. So for example in a paper that we polish a few years ago, Julia in my lab looked at triple negative breast cancer and applied the fasting mimicking directly triple negative breast cancer in mice.

And then the the cancer clearly rewires and turns on pi and ace turns on turns on to turns on CDK for six. So now she targeted with drugs that are already widely used in cancer therapy and the cancer.

Now, instead of growing more slowly reverses course all the way to to zero. So? So now we've done it over and over and over with different models. And so we're very excited about the possibility of in a patient identifying quickly, let's say within a couple of days the escape pathways and target them with FMD which acts as a wild card, plus standard of care drugs that are relatively nontoxic or nontoxic.

So so help me understand. So you have the triple negative. It's hard then to have a target type of chemo or target kind of therapy because you don't have, you know, you don't have the hurt twos, you don't have the recipient, you don't have any ERP are positive.

So so the FMD then kind of re wires has you do the FM d it really wires escape mechanisms. Then all the cancer cells and that it opens up targets that normally was not there prior to FMD.

Yes. Not only opens up but makes it very easy to to know what they are right quickly. So within a few hours we can tell what our cancer as rewired. Right.

And that seems to be very effective in representing all the cancer cells, because we don't see then much of a survival once we target all of them or the major ones.

So the cancer goes down and it stays down, right. So yeah. So now we're still at the beginning of this, but it's working very, very well.

How FMD Rewires Cancer and Improves Standard Therapies

And so now we're hoping that we can isolate cancer cells from the patient's circulating cancer cells. And then we can target quickly learn how they're surviving.

And then so within a day we can adjust the aim and use FMD. Plus keep changing the drugs until the cancer disappears. That's a little bit of science fiction right now and I understand that.

But yeah, it's working well, so I don't want to make it sound like it's conclusive for humans. It's very, very promising. And now we need to do the trials. Right.

But for example, the needy group at the National Cancer Institute in Italy combined FMD with chemotherapy for triple negative breast cancer. And after four years, the overall survival was about two and a half times higher in the FMD.

Plus chemo versus chemo alone. Right. So I think now this is four year. Overall survival. We're starting to see. And I think they're going to publish additional papers supporting with more patients supporting the initial results.

So so it's good news already for the last sophisticated intervention chemo plus. And so now where this is why we're optimistic about the more sophisticated intervention.

What if you get rid of the chemo. What if we now use this multiple relatively low toxicity drugs and with the FMD. Yeah. So we're optimistic. But we got to do the trial.

So when we say less toxic because you have the field of repurposed drugs, you have the field of of natural interventions like vitamin C, curcumin, artisanal, you know, repurposed drugs, you know, talk about metformin and all these kind of things.

So is that what you're talking about in regards to less toxic drugs and learning which escape mechanism to target? You know, once the cancer cell rewire and you kind of measure with the circulating tumor cells and see where the genetic instabilities are, sort of say, yeah.

So I think there are two levels. One is the relatively low toxicity, let's say compared to radiotherapy or chemotherapy. Meaning now if we target we have some of these new generation Pi three kinase inhibitors right

there relatively.

I mean whereas the is maybe more toxic. But some of these new generation kinase inhibitor may be less toxic. Right. So that's number one because now we have a lot of options right?

A lot of options. And so we can target almost any escape pathways that we see. And that's what we're doing. It's working very well in the mouse studies.

Then we publish a few years ago FMD plus vitamin C, and now we publish FMD plus vitamin C plus chemo. And that stopped even very aggressive cancers. But now we're saying okay, can we do FMD plus vitamin C.

And as you pointed out we remove the chemo and now we introduce other completely nontoxic drugs. Let's say as you pointed out with forming rapamycin we have to see.

Right. But but some of these of course are now forming a promising are both they're both in trials or about to get into clinical testing to slow down aging.

Right. So that's how our nontoxic they're viewed. Now, I don't know if my colleagues near Barzilai and others are correct about that, but certainly the view is that you could get lifelong treatment with some of these drugs, in fact, to slow down aging.

Right. So this will makes it very exciting, I think, for the cancer field, could we actually use 3 or 4 in the aging drugs to then target cancer cells specifically while helping the normal cells?

You know, yeah, because you had the issue of dealing with excessive senescent cells, excessive immuno senescence and all all these type of things where you're bringing in mice and bringing in metformin and then also with with FMD.

So it almost seems like by addressing the aging process in the body, you're also done addressing cancer at the same time. Yeah, I think there's much more at the cancer prevention lab.

Yeah. So what you said is absolutely true for cancer prevention in this case, I think this is much more powerful because these basically you could probably in some point we may do that like a mathematical model that shows that it's just a matter of time right before we can differentially target normal cells and cancer cells, just because we already know that often with specially during fasting conditions, they go in the exact opposite direction.

Right? So so we push them to make a decision. What are you are you are normal cells. Are you going to go and standby mode or are you a cancer cell just going to ignore by definition.

Right. So the cancer cell you're just going to ignore anti-growth signals. And that's what makes it very easy then to target the escape batteries. So yeah.

So I think this is it's a truly a technology that just quickly identified the shapes and targets them and, and try and progressively with less and less toxic intervention.

And you mentioned that as quickly to find these escape mechanisms. But it sounded almost like when you bring these safe drugs on board that sometimes escape mechanisms and can can change and you have to shift again, is that what I'm hearing?

Or you have to kind of adjust a little bit through that process, or is it just kind of a one way track and we're going to hit the target? Well, it looks like allow the cancers.

We look at affair. We get to escape number 2 or 3. They're done. Right. So over and over and over in many kinds of types. So but even if they escape the blocking of the escape path ways, we could go back and say, okay, how did you do that?

Right. So it's and then it becomes progressively more obvious because there's probably only one left. So now there's one way that you might be able to get away from three drugs plus the FMD plus the wild card.

Right. And then so the expectation and what we're seeing now is something really lights up. And and now we can go after that. So so explain to me a little bit.

And for the audience what does an escape mechanism look like. And what would be an example of an escape mechanism. An example of and how to dress that mechanism.

Yeah. So an example maybe for example poor signaling. Right. So tall normally during fasting goes down, but in lots of cancer cells it goes up. So the cancer is trying to do protein synthesis is using the thought pathway to make more proteins more amino acids.

But it can't do that right. So well I can up to a certain point. And that's how it survives. Right. But if you target that now it's in trouble. Right. But that's usually not enough. Right.

So if you do fasting plus store. So for example to reverse triple negative breast cancer Julia had to do three drugs Act inhibitor PI3 and Ace inhibitor and two and CDK four six or Tora inhibitor plus the FMD.

And now I started to work in another case with e. R positive breast cancer. So the hormone therapy now the fasting mimicking diet reduce insulin IGF one and Latin rite plus CDK four six inhibitor plus e r signaling estrogen receptor signaling and is a quintuple.

So five different blockades right. And then and only then you see the two more coming down. And the mice are fine for a long time. Right. So no toxicity to the mice.

And slowly they regress. And until you see a cancer free survival. So now we've done it in people both triple negative and also we are positive and are positive.

We'll be able to do it for years.

Targeting Escape Pathways and Personalized Combinations

And we're starting to see women do very well and survive in a lot longer than expected. But you know, there are no formal clinical trial. I need positive.

And so so now we're encouraging, of course, lots of cancer centers to take it up and test it out. And these kind of checkpoint inhibitors, you know, that you're bringing in.

Is that like Keytruda of Devo, you know, that that's very safe or what kind of what do you use? What are some of the common ones that that you look at?

Yeah. Now, so far we haven't talked about immunity immunotherapy, but we've also combined the FMD with immunotherapy. And so yes PD one Pd-l1 inhibitors.

And those are in those are fairly effective in slowing down the cancer. We're not really seeing with that combination cancer free survival. That's why I, I like more because I think in a sense I mean people.

And of course immunotherapy is great, but you're still sort of hoping that the immune system does does it all for you. Right. There's just a hope. Right.

Whereas with the escape path with target and it's not a hope it's truly learning. Are you survive and targeted and yeah. So I'm more optimistic, believe it or not about the this combination therapy with the non immunotherapy intervention.

Although we'll see we're also doing the combination with immunotherapy. And that's working very well. But that's far we struggle to see any cancer free survival in any mouse model with immunotherapy plus plus.

So I don't think it's going to be that easy to get a lot of cancers in check with that combination. But maybe if we do more so for example, a USC, we're starting now a fast imaging diet plus vitamin C plus Ctla four plus PD one or Pd-l1 inhibitor.

Yeah. So then now with the quadruple intervention this is impatience, right. Will we see remission. And now the lab showed a couple of years ago they did 100 patient trial.

And the under patient trial. They show if the patients they got fasting mimicking diet it was clearly a much more immune infiltration into the tumors, all kinds of tumors, all kinds of combination.

And but then they had five cases which they felt it was very it was so unusual that they had five stage four, it was breast, colorectal and pancreatic and yeah.

So breast colorectal and pancreatic cancer and lung and one lung cancer. So stage four and all of them by combining immunotherapy plus FMD or chemotherapy.

And all of them went into remission right. Long term remission. And they felt they were so unusual that to see that they published the paper describing these five cases. So okay.

Of course it's just an anecdote. It's five cases, but enough for a group of oncologists to say, that's really strange, right? We can see 1 or 2 cases, maybe by chance, stage four ending up in remission, but long term remission for five cases within the same trial.

All stage four. All in trouble. Yeah. So so I think that has to shows that the potential now is just a question of how do we get a lot more patients and how do we prove it.

Randomized clinical trials. Well I mean all those those four cases are abnormalities. I mean all those four because I mean regular standard of care is very is not very successful in regards to addressing these type of cancer.

So so I mean, obviously that's a huge observation. And you're absolutely right. I mean, small small caseload doesn't really prove anything, but it really gives, you know, pause to kind of see the potential of what can be.

Yes, yes. What if right what if a stage for a lung cancer patient now can be can go into remission by combining immunotherapy with FMD as they did in this one case.

And so what what doesn't these clinical trials. What does FMD look like. Because I know you have the five day prolonged pack that I use for patients and other people use for patients.

What in a in a trial. What does that look like. And the trial looks a lot. It has a lot less calories, about 600 calories per day last five days. And it's got a lot of options.

Why is that? Meaning that you have a soup, but then you have two backup soups and then abroad. And so we we did it because often a cancer patient developed food aversion.

And they started disliking any one or several of the ingredients that they, that they have to consume together with whatever therapy they're receiving.

So yeah. So now we've learned and and we, we're, we're making it easier or much easier for patients because there's a lot of flexibility in the things they can do during those five days.

And so now we're getting a pretty high compliance in the clinical trials. We just finished another trial, 120 patients at USC for analyzing the data now. But in most of the trials, with one exception, they compliance was high.

That's incredible. So the and and it's five days a month or how what do we what are we looking at in regards to you know to to keep that state to really, you know, to open up these escape mechanisms that you can then address.

I think it depends on the therapy. Right. So if it was chemotherapy, let's say v three weeks, that was the trial USC with breast cancer and prostate that was done together with the bolus chemotherapy three days before one after.

And a big warning here with chemotherapy because as we had suspected for a long, long time, never combining chemo with feeding or radiation refilling, what does it mean? There's a paper.

It was a mouse paper, but a scary one, I think, looking at intermittent fasting. So one day and one day off and in mice and then give them doxorubicin.

I think it was in showing increased cardio cardio toxicity. Right. Which is exactly what we expect because now you have a high doses of chemotherapy in the moment where the mouse feeds.

And we suspect the same problem you will see in patients. So I'm that's a warning to people that think fasting doesn't matter how you do it, it's all going to be working and it's called is going to be effective.

It makes a big difference how you do it. And I think in this case it should be very respectful of the FDA type trials. Right. So many trials in a standardized way.

And the oncologists and the physicians out there to sort of say, okay, this was done in the trial. It worked. It was safe. I'm just going to follow exactly that.

Rather than fasting. Let me just figure out the way that I want to do it. Yeah, because that's an important point, because a lot of a lot of patients out there, they do the intermittent fasting and, you know, they do ketogenic intermittent fasting with it.

And so you're saying that around the chemo that it can actually be more detrimental than for the heart muscle, you know, to do that if you don't follow kind of the strict guidelines in regards to how to do it with, with the fasting mimicking diets.

So it's a big difference between the two. Yeah. Big difference. The opposite. Right. So if you do three days of fasting or fasting mimicking diet, then you give the chemo, then you wait 24 to 48 hours and then you feed high protection against observation.

Really remarkable to the point where sometimes we see all alive mice, all that so all alive with the fasting, making diet, all that with the regular diet.

Now, if you do intermittent fasting, one day you, the mice eat, one day they don't. Or 16 hours or whatever. Now you see the opposite, because now you have high levels of chemotherapy when mice are referred.

So now I have one insulin glucose. They are going up very rapidly. They're promoting cellular proliferation and cellular activation, including probably the cardiomyocytes.

And now that combination is toxic or highly toxic. So so you have people then obviously that they're concerned about. And so if they do kind of a shorter version where 72 hours, is that not advisable during the process.

It's a five day set. That's really what you got to do. Well there are exclusion criteria right. So it also depends on the stage. Right. So if somebody's stage one and they've lost a lot of weight, probably not a good idea to do the fasting making diet. Right.

And but if somebody's stage four, even though they lost a lot of weight, the oncologist and the doctors have to make a decision, right. You know, what are the options?

Are there viable option. And then, yeah, there's going to be a compassionate use type of situation.

Clinical Trial Results and Dosing Protocols

Right. So it could still work very well. Even somebody lost a lot of weight and make a big difference. And then they have all the time in the world to regain the weight.

But yeah, in general, I think that if somebody has lost a lot of weight and they have something else that we know about 98% chance of overall survival, I wouldn't think even consider the fasting making diet, but somebody has 25% chance of surviving five years.

Then I think that the risk could be higher, even considering the weight. And now a lot of patients, of course, don't lose weight. Or on therapy they gain weight, but in hormone in prostate and breast cancer.

But for those gastrointestinal etc. type of cancers for which there is a lot of weight loss, then I think it's a matter of identity personalized. Right? So some patients can do it and should do it in.

Some patients probably are better off not doing it. Now keep in mind that we don't see any lean body mass loss even after many cycles. So in the trial, for example, we with breast cancer women in Italy, we did not see any lean body mass loss, only fat loss even after 7 or 8 cycles of the fasting diet.

So I think for the majority of people, great majority of people is not a shoe, because once they feed, they will regain back whatever muscle mass they've lost.

But in some cases there might not be the case here. And so it doesn't need to be that the five day or the 72 hour still have a benefit. No, not only has to be five days, it has to be five days following the what is being clinically tested.

And so say four days before the chemo, then 24 hours after the chemo treatment or same thing. Now for the for the immunotherapy trials. Right. So 3 to 4 days before immunotherapy and then immunotherapy and then continuous.

But again each protocol a lot of this has been published already either by us or by venir or by other other groups clinically. So I think the oncologists should just look at the papers and see for that particular treatment what was used.

So for example, for the hormone therapy which is a continuous therapy, this the FMD was done for five days once a month. And just pick in no particular time if patients will say I'm fulvestrant and or other CDK four six inhibitors.

I mean it's huge what you guys are presenting to be able to turn these kind of cancers around, the triple negative and potentially pancreatic sage for lung, etc.

that's just tremendous to show what you can do and how you can manipulate the immune system and cancer wiring just using diet. Yes, yes. And I think the diet is just making the standard of care work a lot better.

Right? So I always say I'm never I'm almost never cured anything with fasting. Right. And so cancer once right now for all diseases at work but for cancer just slow it down.

But when you combine it with the right standard of care. So I think that's also nice because I think it's also respectful. And all the, all the decades of work that a lot of people have done with immunotherapy, chemotherapy and extra etc..

Right. So, so those that's the combination that works very well. And so that combination of course, takes the 30 years of work in immunotherapy and now makes it better and maybe may turn something that's slow down into something that now regresses and talk to me a little bit.

I mean, we talked to, you know, briefly about, you know, because some people don't want to do chemo, they don't want to do, you know, and here you're talking about like something simple as vitamin C.

So what have you seen? You have this kind of ptosis type of protocols where you, you know, you do vitamin C in artisan, you know, to trigger oxidation of the iron that's within the cancer cells.

And so how does that combine then with the FMD and what happens. Yeah. So so if you give to the entry lab and others as shown. And Linus Pauling had been talking about this for, you know, since 50 years ago.

And but what happens is and we tested this in lots of different cancer, lung cancer, colorectal cancer, pancreatic cancer. What happens if you give a lot of vitamin C the there is increased toxicity and there is oxidative stress within the cancer cell.

And there is that right. But then when we look at it molecularly, it turns out that the cancer cell is marked and it turns on the ferreting pathway. Right.

So it produces a lot of scavengers of iron. Right. And so now you get some toxicity, but you get little toxicity because there is a ton of this ferritin.

He is one and ferritin. But when you pass them when you do the fasting making diet this as a differential effect on ferritin meaning in the normal cells it increases parity.

And in the cancer cells it decreases parity. So now you see just a major major increase, sometimes tenfold in the toxicity specific to cancer cells. When you put the first meeting die together with vitamin C.

So now the excitement doesn't even come from this because we're so far we haven't cured very much with C plus FMD, but the excitement comes from escape bad ways now also targeted.

And that's the next generation. I think we're one year away from describing this. And so. So how do they escape from vitamin C and FMD and how can you can you get it with other nontoxic drugs.

Right. Yeah. So that I think we're very close to that showing that. And yeah. So that I think that's going to be very exciting because this introduces this possibility of like an antibiotic for cancer.

Right. So can you imagine going to the doctor and the doctor say, yeah, take this cocktail for a month. Let's see if this goes away. Right. Yeah. So now at least theoretically understood it's a reality.

But theoretically, I think it's important to start seeing this possibility that you have the cocktail is completely and toxic. Take it for a month. Let's see if it goes away.

If not, let's see what how the cancer survives and then change around and give you something. Answer. That is incredible, because these are the kind of things that we've been barking down the same or barking up the same tree for.

Yeah, yeah, since the 1970s, almost in a way, you know, in the medical field. And there's been some kind of in addition there. But this just seems like all the research that that has been done, like you're saying, people have been researching 30 plus years is now really then we're able to use that and just take that to the next level where we're really seeing the effect.

Yeah. And I think the technology, right. We just did not have like these RNA seq, single cell RNA seq. It was science fiction, you know, even ten years ago.

Right. So now to be very rapidly being able to take a single singular insight and tell us, educate us on what's the escape hours, this cancer and this patient surviving this combination therapy.

Yeah. So this technology is making a big, big difference. So this is the 30 years of research, but also the new technology that allows us to. And this is without even bringing in I right then I can I think make it even easier I think eventually to to get to it.

But even without the AI just a computational straightforward computational strategy, as we've shown a couple of years ago in, in, in our paper, that's enough to to be very effective now.

Yeah. Of course, understanding that it could take very little it could take a long time to get there for lots of cancers. So we'll see. We'll see what we try to go as fast as possible and see what happens here.

And you mentioned earlier also you talked about that. There's more with the fasting mimicking diet and some of these therapies that there are more kind of an immune cells that were found within the tumor environment, the tumor microenvironment.

So you almost it's like a moon system activation that you bring in by bringing in the FMD along with some of these therapies. Yeah. So what we think is that, for example, with most therapies, chemotherapy, radiation, even vitamin C, you now have the cancer cell, as you pointed out, making a lot of free radicals like I run you know, I drop so radical superoxide hydrogen peroxide is.

Safety, Immunotherapy, and Future Directions

So we think that that's making the cancer cell much more visible to the immune system. Right. So by creating all these antigens that were maybe not as visible or not as a variety of antigens, right.

So we haven't demonstrated this, but all the data that we have is consistent with that. And so now you have a lot of DNA damage, a lot of new possibility opportunities for the immune system to make a decision.

That's not a normal cell, I will attack it and I will attack all of the ones that have the same mutations as presented by antigen presenting cells as this one that I just attacked.

So it's almost like it's creating a vaccine effect in a way, you know, where you have more antigens that are being expressed, and then the immune system can then trigger creation of antibodies or whatever immune system component that's needed to, to address that.

Yeah. So now, for example, Moderna is generating vaccines, RNA based vaccines to expand the level of these antigens within the cancer cells. And so make it much more visible to the immune system.

And and so maybe the fasting making diet is is doing some of that on its own by just, you know, within sell or sell a generation of a lot of mutations and a lot of, potential antigens.

So with this, then, I mean, so since we're able then to kind of capture some of these mRNA and really kind of analyze what that is, and, you know, they really kind of fast tracked then how to create vaccines based upon our mRNA, you know, so it almost seems like, you know, then we can create a more targeted vaccine quickly for that specific individual.

And then using fasting, mimicking diet to, to create more of these kind of die off material to, to be able to see more what was seen to be done. Yeah. So Moderna is already doing that, right?

So Moderna is already personalizing it. So finding out what the mutations are in a particular cancer patients and then generating the vaccine specifically for that cancer patient.

And so now the question is what happens if you combine it with with the fasting mimicking diet. And so that's something that I hope we can convince Moderna to test.

That's exciting. So where do you see kind of this this research be you know, that like in a year from now. I mean,

you're seeing the directions. I mean, where do you feel will be in the year, two years from now in regards to cancer therapies?

I hope that within a year or so we can begin the first trial. Proof of principle. Right. So say 100 patient trial. Can we this escape pathway targeting.

Does it work consistently in humans. And so we'll see. Right. So that's the first one. And then who we in the patient for whom it doesn't work. Is it easy enough to undo the escape batteries and target them.

And or at least I mean as you know the trials are not don't go as fast as you like, but at least if we are if isolated cancer cells from patients that don't respond, and then we see a clear signature of escape, even though in the same trial we wouldn't be allowed to target that.

But we will have to wait for another trial. But I think if some patient responded and all this patient escaped, but we clearly see how they're escaping, I think that would be a very exciting success, at least initial success.

And how do you feel the oncology community is responding to, to this type of science that that's coming for you feel that they are open to it, or do you have to push a little bit harder to for them to to see the the possibilities of this?

Yeah, I think that the science has always been the same way. And, and I think the immunotherapy Alison Andre and all, they found out many years ago when everybody said immune immunotherapy, what is that going to do.

Right. So yeah. So you have to go through 20 years of nobody taking it seriously. And then all the way to the clinic, you know, and I was reminded that in a meeting that that the first immunotherapy trial was viewed as a failure.

And it wasn't until they went and looked at a subgroup that they realized it's not a failure. It's working, but it's not working for everybody, right?

And so that's how hard it is to, I think, to convince the community. So all the way to this big trial, everybody had doubts that it would not work. And then of course, started with immunotherapy with a subgroup and, and then slowly move to lots of uses.

I think that we don't know what is. The first thing we can do in the same category is the last is a more right. So in mice certainly works better. That's interesting right.

In mice a lot of the mouse models that we do triple negative breast cancer, lung cancer, melanoma, the FMD works better than the either city of Oxford and Pd-l1 and PD one. Right.

So we try them. All right. So yeah of course it doesn't mean anything in people. It works but in lots of cancers. But so I'm just saying that the fundamental theoretical level, at least in many mouse models that we tried the the FMD, the first thing that works better than the immunotherapy, again, no claims about humans.

But that's an interesting start if you think about that. Yeah, it's a phenomenal observation and it's really intriguing them to see, as you're saying, when we bring it to the clinical trials in humans.

And then obviously we there are other factors we have to dress. And as we then kind of refine, you know, how the therapies are being administered based upon, we're seeing I mean, that's that's exciting times ahead.

Yes. Yes, absolutely. Yeah. So I think also so we follow we have foundation clinics and we follow tons of cancer patients. And I think it's also important.

Certainly if I was a cancer patient I would want to think that there's always an option. Right. There is always a possibility that a and this is why we really love this nontoxic right intervention.

Because we're thinking if we can get within a year or two to the point where where we can say, okay, try right.

Compassionate use to all to the oncologist, if the oncologist goes for a trial.

So that's what I really like it. No, no matter what, you know, as we've seen for this stage for patients, you can say, okay, you know, not easy not not likely maybe but could work.

Right. And so I really like that that part. And I think if I were a cancer patient I would want those options ever you know laid them I come but I would want that.

What if it is stage four if the oncologist says doesn't look good at all, that could be a an option. Yeah, yeah yeah. Love it. Well, Doctor Longo, I so appreciate that you're driving this forward to kind of make safer options available, safer options that are more powerful than the tools that we currently have.

Thank you. Thank you so much for putting this on the map. Thank you, thank you.