Like norm, showing up at cheers. I think so, but everybody knows Scott and we’re really fortunate that he’s going to ease the research team leader for the thrust conchology program and I think he’s going to tell us what’s new and exciting it’s gone.

Hello.

So before I start a couple of things first of all Don I didn’t realize it was such a powerful public speaker so.

So I thought today, I talked to you about um clinical trials. Just go through you know what a clinical trial. As many of you know what a trial is how we develop them and some of the trials that we have at Yale and then talk about some of the research that we’re doing, and really what we call translation research, which means we take findings from the laboratory and we apply them to the clinic to patients in the clinic and then we take things from the clinic. We bring it back to the laboratory and then we bring it back to clinic back and forth to improve.
The care for our patients.

I'm sorry I took this from the NCI the National Cancer Institute site, which I'd recommend to anyone. There are a lot of resources there a lot of frequently asked questions that you could look at just a couple of quotes from them about what a clinical trial is in clinical trials or research studies that involve people through clinical trials. We find new ways to improve treatments in the quality of life for patients with disease and they go on to remind us that clinical trials are the final step in a long process that begins with research in the lab it's not as though.

You know, we make these drugs are made and then boom. We researched these agents in animal models and other types of models and in particular in cancer models. And if we see promising results, then we would bring it in to the clinic.

So there are 3 types of clinical trials that you may know of. There's phase one that’s the first Phase 1 clinical trials and a Phase 1 clinical trials is asking the question is the treatment safe. The purpose of the trials is to find a safe dose. So you start with a very low dose. The first three patients who are accrued to the trial will get that dose if there are no significant toxicities. Another 3 patients will be treated with a slightly higher dose and so forth until you reach the maximum tolerated dose.

Traditionally, these trials have accrued 15 to 30 patients, but there’s been a change in that these days. We don’t want to wait for the next trial. The Phase 2 trials, so rather than doing a whole another trial. We do these expansion cohorts where we might treat 100 patients with lung cancer in the context of the Phase 1 trial. So most of the trials. The Phase 1 trials that we put our patients on they aren’t 1st in man. You’re one of the first patients getting this treatment there might have been 5060 patients who got the treatment.

Prior to you and that’s the majority of cases.

So a Phase 2 trial, traditionally was a trial that asks a question does the treatment works so you have a Phase 1 trial, you find the safe dose and then you go into a Phase 2 trial, you treat maybe 50 patients
with lung cancer and if you see a good response rate that warrants further
evaluation. The purpose is to. I spent spelling error. But purpose is really to
see if there is a treatment effect. But of course in any phase trial. We’re always
looking for safety signals is there a toxicity that we didn’t realize.
NOTE Confidence: 0.908072769641876

00:04:22.090 --> 00:04:27.260 Early development of this drug this is something
that’s put into all of our trials.
NOTE Confidence: 0.899461448192596

00:04:28.710 --> 00:04:59.000 So then we get the phase 3 trial. These are ran-
donized trials, so question here is this treatment better than what’s already
available. So a generic clinical trial will be say chemo immunotherapy is the stan-
dard first line therapy well, we might do a trial where we do standard chemo im-
umnotherapy compared to standard chemotherapy. Plus, another agent, maybe
a targeted agent or something else. Sometimes that target agents will be.
NOTE Confidence: 0.90602469442749

00:04:59.000 --> 00:05:30.970 A placebo right so you won’t know if you’re getting
the targeted age. Another placebo, but everyone’s getting at least standard of
care people always concerned. They’re going to see. Bo we wouldn’t do that
to a patient ’cause. It would be unethical unless unless there is no standard
therapy and rarely they’ll be tries like that. We don’t have any trials like that,
but that would be the other situation and these trials can have thousands of
patients because you want to establish a new standard of care and the FDA
requires a certain threshold to get to.
NOTE Confidence: 0.932268619537354

00:05:30.970 --> 00:05:32.920 If this is going to be approved.
NOTE Confidence: 0.906234443187714

00:05:34.590 --> 00:06:03.570 So there are many potential benefits, an risks of
course, the real benefit is is the is the next home run am I going to get a drug
that looks really good and you know, either laboratory or in Phase 1 trials and
will this really cure my cancer. Well, this really lead to long term. Survival also
your by participating trial. You play an active role in your own health care and
you’re also advancing medical knowledge in some patients and some people feel
very strongly about that.
NOTE Confidence: 0.917646765708923

00:06:04.290 --> 00:06:13.590 There are potential risks well, maybe this treat-
ment is not better than standard of care you know, but again usually if you’re
getting a treatment.
NOTE Confidence: 0.912185549736023
In a randomized way you’re getting standard therapy with or without an. Unfortunately a lot of the standard second or third line therapies for lung cancer. They aren’t very good our main concern is unexpected side effects. So we have a general idea of what to think, but you can see late side effects, which would be concerning.

There’s also the potential for many more visits testing and really cost. I have to get back and forth. You know what? do I do with my kids trials generally if you’re going to have a trial of an experimental agent the agent is provided by the pharmaceutical company or some other source and standard of care costs of the trial. So say you get scans every 2 months when the trial. Insurances are expected to pay that and that’s really set by Medicare and insurance do follow that so it’s very rare that I have a patient wear their insurance wouldn’t.

Cover the standard care of costs and the patient would be required to pay additional costs in the context of trial that said travel copays parking at air rights. All sorts of things and we try to help as best we can with that, but there are limitations of what we can do.

So hopefully myself for doctor here are your doctor in the community will talk to you very early on about clinical trials. Whether you have a stage 123 or 4 lung cancer. And if not feel free to ask them ’cause That’s why they’re there and I think a doctor would be excited. If someone said. Well listen are there any novel clinical trials even if they don’t have trials at their site they know how to find the sites that might have trials that make sense.

And if you’re one of those folks who knows much more than me about a lot of things that I studied years and years about because you spend hours going through Google and stumping me. You know with questions. You can go there different sites. I can go to an 1 great site is this clinicaltrials.gov site, which is a search engin for all the trials that are available for you and they tell you basics of the trial where it’s open how to contact and you can bring that information. You can talk to your doctor you can call this sites directly so I would I would definitely take advantage.
So there’s so many trials that I could talk to you about today. Innovative trials that were doing at Yale and I had to pick one so I picked this one. ’cause I think this is really in the forefront and this is what we call cellular therapy and the idea of cellular therapy is you take an immune cell out of the body and then you make it better you enhance it, you grow it and then you put it back into the body. So now can effectively treat cancer and we know that the immune system has incredible potential ’cause.

Patients who do respond to immunotherapy they can respond with metastatic disease for years and maybe even indefinitely so the first trials of immunotherapy for lung cancer about 910 years ago, where patients these were Phase 1 trials in patients who had multiple prior lines with therapy. They probably prognosis was maybe 3 or 4 months at that point and they got this therapy and here we are 10 years later, with some patients who have no evidence of disease after only receiving a year or 2 of therapy so.

So that potential is tremendous and we’re seeing it’s not just miracle patient. It’s 15%. Ten 15% of patients. We see with metastatic lung cancer who have 5 year survival’s right. We talked to dawn talked about that magic. Mark there, so I mean. This is cellular therapy and basically the way we do it at Yale. Right now is we take out so here you can see a patient with multiple tumors. We take out one tumor and then we remove the immune cells that are in that tumor that specifically recognized that tumor that are supposed to attack that tumor.

But what happens is when they get to the tumor. The tumor poisons them or put them to sleep. So now they can’t really do what they’re supposed to do so. We do is we take those immune cells out outside of the body. You patient goes home and for about 2 or 3 weeks. We take out the cells and then we enhance those cells. We make them better. We rejuvenate them and not only that we multiply them over and over and over, creating a tremendous army of the patients own immune cells that recognize tumor whose only job is to kill.

Cancer OK so then what we do is we admit the patient and the patient gets some chemotherapy to create the perfect situation environment for these cells to get where they need to go and to do what they’re supposed to do and after we could chemotherapy. We take the army of immune cells and we infuse it back into the patient and then we give an immune stimulant to try to get those cells going even more so I think this represents a very novel approach and this is only available at a handful of sites.
Around the country really even around the world, so we do this with a company called I have ants. But Yale now has the ability to do this and our trial was recently started in Melanoma, where we create all these cells for the trial that we have, we send the resection specimen to a special lab in. They put out the cells for us.

Alright so before moving on to research. I just want to emphasize that you know part of what we do. The main one of the main parts is protecting our patients and this happens, even before a trial is started really initially with scientific review by whoever is sponsoring the trial. So it’s farm, Pharma or if it’s at the NCI. They go through the the protocol that specifies what we’re going to do and then make sure it’s safe for the patient that makes sense for the patient every hospital has an Institutional Review Board where they have to.

Pass the trial that you want to do, and if they feel that it’s not in the patient’s best interest, they will not allow it to be run.

And, of course, there’s informed consent of those folks out there who have gone on trials. They know that it’s a painstaking process, but there’s a 2030 page document that you read through we go through it with you to explain every single risk and potential benefit and then we have have you sign that during the trial. We continue to monitor how the drugs are doing? How the patients are doing to our Institutional Review Board and there’s additional data and safety monitoring board that reviews data as the trial goes and.

The purpose here is to minimize risk to ensure integrity of data and the data monitoring board will sometimes closer trial. ’cause they’ll say this does not make sense it’s not in the patient’s best interest.

Turning to research an A lot of us stand talked about this. A little bit. Rick also we do what’s called translation, Medison as I said before.

Starts either in the lab or the clinic, but then whatever we learn say in the lab will go to the clinic and then will say. Let’s take for example, there’s a drug that is developed in the laboratory based upon
some animal studies and some cell line studies and it looks really good so we bring it to the patient and let’s say 1 out of 10 patients responds so we want to know why that patient responded So what will do is will take go back will take some that patients tissue and then we’ll look at that issue from that patient as well as a tissue from patients we didn’t respond.

NOTE Confidence: 0.914393126964569

00:13:34.650 --> 00:14:04.950 Will bring it back to the laboratory will look at that issue will? Do studies on that issue to try to understand who is the person? Why is the person responding so we can improve the outcome in other patients or for example, say a patient response to therapy and then say you’re too. Later develops resistance will do a biopsy and then we’ll compare that tissue to that issue that we have from before the patient started treatment and will say what happened here and if we can figure out what happened. Maybe we can give another therapy that will overcome.

NOTE Confidence: 0.739024519920349

00:14:04.950 --> 00:14:05.670 That hurdle.

NOTE Confidence: 0.871290922164917

00:14:06.180 --> 00:14:36.400 So to do this you can’t just take tissue and run studies. You need to have a protocol and you need to have consent from the patient so we created an biopsy protocol at Yale, a tissue shall. I say protocol. Yeah, that allows us to go down to say say doctor DB aussi has to do a bronchoscopy on a patient ‘cause of patients coughing up some blood and Unfortunately. Sometimes that happens with lung cancer, so she’ll take her scopes will go into the airway and it you’ll see a tumor.

NOTE Confidence: 0.886935710906982

00:14:36.400 --> 00:15:07.390 And she will debug the tumor, she will cut out pieces of the tumor. She might corduroys areas that are bleeding and what normally happens to that tissue. It goes into a bucket an it’s processed in a certain way that kills a lot of things that we want to look at an it’s processed with put into a wax block and then it sits on the shelf in surgical path for 1015 years until they stored or throw it away. So what this allows us to do is to go down to the bronchoscopy and take a piece of that tissue that Doctor D base, he took out.

NOTE Confidence: 0.88666844367981

00:15:07.390 --> 00:15:40.000 And she will debug the tumor, she will cut out pieces of the tumor. She might corduroys areas that are bleeding and what normally happens to that tissue. It goes into a bucket an it’s processed in a certain way that kills a lot of things that we want to look at an it’s processed with put into a wax block and then it sits on the shelf in surgical path for 1015 years until they stored or throw it away. So what this allows us to do is to go down to the bronchoscopy and take a piece of that tissue that Doctor D base, he took out.
biopsy of a rash to understand what it is, but also we can do additional studies so we can.

NOTE Confidence: 0.905936598777771

00:15:40.000 --> 00:15:59.710 Maybe prevent that rash or treat that rash more effectively in the future but we need to have a protocol to do this we need to have a patient, saying I can send to allow you to learn more about my tumor to help science you know it could help you but that’s not why. We do it. We do it to help science and if we learn something of course, we would use it.

NOTE Confidence: 0.89388906955719

00:16:00.650 --> 00:16:33.740 So through this protocol and the protocol prior to it over the last several years. We have enrolled 550 patients 409 patients have been rolled. We subsequently had an amendment that allowed us to look at patients who had died, but of the 409 patients enrolled 210 patients. We have fresh tissue mean that we went down in 210 patients down to the procedure. We collected tissue and we did. Special studies on them. So I could spend weeks going through what we’ve done and the discoveries that we’ve made.

NOTE Confidence: 0.906581163406372

00:16:33.740 --> 00:16:37.890 And maybe at another talk talk. I’ll do that. But I just want to give you a sense of what we do here.

NOTE Confidence: 0.912541687488556

00:16:38.730 --> 00:17:10.300 We work with many different labs at Yale, Yale’s a great place. It’s got incredible depth when it comes to bench research and when I first started here 15 or so years ago. There wasn’t much of this an I think one of the great things about yells over the last 1015 years. Smile grew an the engagement from the scientist the basic scientists at Yale grew and now everyone wants to do work with us right because we can give their clinical perspective, the scenarios, and we can also.

NOTE Confidence: 0.923748373985291

00:17:10.320 --> 00:17:29.090 Help to get tissue and to understand and do some of the studies with these different labs. So we work with many different labs and any of these guys would love to talk to you about what they do with the tumor specimens or blood specimens or other specimens that you give us so we can learn about cancer so we can improve the care of our patients.

NOTE Confidence: 0.887350142002106

00:17:30.400 --> 00:18:01.610 I I said it was only tell you about 1 trial, but I’m going to tell you about one more and then I’m going to end just to give you a sense of how we can do this in the context of a trial. A clinical trial. So this is a clinical trial for patients newly diagnosed advanced non small cell lung cancer and these patients get a combination of two immunotherapy is one is called nivolumab. You might have heard of Opdivo. Some of you may have had
up devo and the other one is ibor year boy and in this trial. We do a biopsy before the patient.

NOTE Confidence: 0.908014535903931

00:18:01.610 --> 00:18:36.620 Receives therapy and then we do a biopsy on therapy. We also collect blood sputum believer, not stool as well because we’re learning, a lot about what we call the microbiome and the organisms that live in the stool and how that might actually affect your immune system ability to fight cancer. So this trial is technically an industry trial. But we really wrote it with Bristol Myers Squibb, an Kurt Shopper, who is assigned to set yell is really leads the translation will aspect so all the different sites around the country that are participating they send their tissue to us so we can understand.

NOTE Confidence: 0.874783873558044

00:18:36.620 --> 00:18:39.620 And who responds in who doesn’t respond.

NOTE Confidence: 0.900884926319122

00:18:40.490 --> 00:18:55.510 An and I will say one other thing that someone asked. I think you ask the question about smoking, and I want to just say that if we abolish smoking, which would be great, but let’s say smoking was abolished and we go 100 years into the future.

NOTE Confidence: 0.917767524719238

00:18:56.060 --> 00:19:23.720 Lung cancer will still be a relatively common disease. It is not just a disease of smokers. OK, an 1520% of patients never smoked. So considering lung cancer is such a common cancer. If you took away smoking. It still would be a tremendous problem for us, so as you as you may know November is lung cancer Awareness Month. And I’m here to answer any questions and thank you all for coming.

NOTE Confidence: 0.437599033117294

00:19:30.890 --> 00:19:32.300 One file.

NOTE Confidence: 0.866718530654907

00:19:33.590 --> 00:20:08.600 So when I look at it is in a patient’s going to go in and I personally think I think all patients being a trial considering the types of trials that we have is what I would do because it’s the only way you’re going to improve things in considering your most these trials. You’re going to get standard plus but the way I look at it is, we have 2 or 3 potential trials for you and if the first one doesn’t hit. You do the second one third one. There are different trials. And when we look at patients have advanced lung cancer and their trials for Stage 1 Stage 2, but when you look at patients who have?

NOTE Confidence: 0.889665007591248

00:20:09.090 --> 00:20:36.420 Advanced lung cancers two general paths that we take one is we evaluate what we call targeted therapy. So some patients.
The minority but some patients. Maybe 15-20% of patients. We will find a molecular alteration that drives the tumor that fuels the tumor and that’s the most important thing in the tumor and some of you. I know EGFR is one. Ross is one. Met is one.

And so we have these targeted agents that really block that pathway and so we that’s one and there are approved therapies for some patients. But if they failed those or there are no approved therapies are trials. We could focus on that targeted pathway. That’s one path. The other patients that don’t have a specific molecular alteration that we can go after and that’s really where we concentrate on immunotherapy. We see responses to immunotherapy across the board.

So what will do is maybe will try immunotherapy or maybe will try you know the cellular therapy and again patient goes on. One therapy on a trial if it works, great if it doesn’t. If a patient is healthy. There’s always going to be another trial. As long as a patient is fit enough to do on a trial and a patient wants to some patients don’t you know they really want to concentrate on quality of life and then we do that.

So there are eligibility and in that particular trial, which I hope to amend with the company. It’s pretty lax in that you can only have no more than 3 prior lines of therapy.

OK and you certainly you can have major autoimmune conditions. You have to have a certain breathing ability, which you would have and so most patients would be eligible, but that is a tough trial because you get tough chemotherapy. You get tough immunotherapy and you’re in the hospital for 2 weeks for that trial so you would probably reserve that for someone who you think can withstand that treatment whereas most other trials aren’t that’s probably one of the most potentially toxic.
00:22:32.430 --> 00:22:33.670 Any other questions.

NOTE Confidence: 0.800233423709869

00:22:36.160 --> 00:22:58.690 Can doctor Grainger can clinical trials be taken at other satellites. Milo clinics for instance. I live in Westerly and these Milo clinic. Satellite just opened there so there. We are trying their currently trials open at many of the care centers a smile cancer care centers.

NOTE Confidence: 0.892095983028412

00:22:59.230 --> 00:23:25.480 And we’re trying to open more. Some of the more intensive Phase 1. Ish type trials. They’re tough to do there ’cause. There’s many ancillary services that you need and and so we have patients who may go on a trial and out in Westerly and then maybe the next trial might be at Yale. This Milo at the New Haven campus. This one because it’s a Phase 1 trial, but we’re trying to get more and more trials open out in the community.

NOTE Confidence: 0.845398545265198

00:23:26.000 --> 00:23:28.440 And just another question.

NOTE Confidence: 0.858199179172516

00:23:29.130 --> 00:23:51.770 Um having been a patient fairly recently since I was diagnosed in July, spoken to a lot of health care professionals and there seems to be quite a bit of disagreement about sugar and it’s a causation is it worsens your disease. I’ve been told by people up at Dana Farber that.

NOTE Confidence: 0.90466183423996

00:23:52.280 --> 00:24:23.730 That’s a myth other health care professionals feel that that is not the case that sure can be provided negative impact cancer. I don’t think there’s any consistent decent evidence that suggests that sugar is harmful or helpful for your cancerer certainly something I hear a lot and I would eat what you want to eat and you know, obviously be either healthy meal and exercise and do all that, but

NOTE Confidence: 0.818710446357727

00:24:23.730 --> 00:24:27.960 I would alter your sugar dot personally, I wouldn’t alter your sugar diet for that now.

NOTE Confidence: 0.877771973609924

00:24:28.760 --> 00:24:40.830 You know there’s evidence an were blinded as clinicians clinicians scientists. We need to see a trial 500 patients get a lot of sugar 500 patients don’t go out of sugar who does better.

NOTE Confidence: 0.909201323986053

00:24:41.510 --> 00:24:53.600 You know there’s evidence an were blinded as clinicians clinicians scientists. We need to see a trial 500 patients get a lot of sugar 500 patients don’t go out of sugar who does better.

NOTE Confidence: 0.909201323986053

00:24:55.120 --> 00:24:58.120 I mean you might have a special diet for you and they might be on to something right and they have anecdote an maybe if they’ve treated thousands of patients. Maybe
anecdote makes sense, but but for us. We need more evidence an over the years. You've seen dietze that are good for cancer that are bad for cancer and right now. I would eat what you want to eat and just follow just general guidelines about eating nutritious you know.

NOTE Confidence: 0.722998201847076

00:25:13.860 --> 00:25:16.050 And almost wanted too much sugar right so.

NOTE Confidence: 0.896336674690247

00:25:16.840 --> 00:25:23.950 My son doesn't let me know if I have a beer or my son, says that was 6. Slices of bread dad. I don’t know where he got that from.

NOTE Confidence: 0.918696939945221

00:25:27.720 --> 00:25:29.550 Thank you very much.

NOTE Confidence: 0.876764953136444

00:25:30.130 --> 00:25:50.180 In the evidence of using viruses to attack cancer and kill it outright 0 that we’ve been looking at that for decades, and as we get more sophisticated what we can do to a virus. Yes, virus what we call uncle lytic viruses that you can inject into a tumor or?

NOTE Confidence: 0.902277648448944

00:25:51.110 --> 00:26:21.980 Right now, you’re limited because if you can get in. We do this we inject into a tumor and it can kill parts of the tumor. If you inject it here and it goes throughout the body. You might have some side effects from issues but we are creating virus viruses that will hone into cancer cells and then they will do their damage in those cancer cells. So yes, there is a lot of interest in all sorts of different virus vectors to introduce things or to kill things. But you can also give a tumor something that doesn’t have through a virus.

NOTE Confidence: 0.830782115459442

00:26:21.980 --> 00:26:24.280 That would be helpful in ISM.

NOTE Confidence: 0.69159722328186

00:26:25.690 --> 00:26:29.480 Recipes for another clinical trial that.

NOTE Confidence: 0.377301037311554

00:26:30.120 --> 00:26:31.820 Filiated with

NOTE Confidence: 0.842018127441406

00:26:34.750 --> 00:26:37.960 So if it’s at one of the care centers, it would.

NOTE Confidence: 0.870166063308716
Either if it wasn’t a care center or it was another hospital. It’s the doctor at that place.

Although you know if I knew that there was a great trial in Boston or New York for a patient. I would get on the Phone. I called my colleague and button. I’ve done this so many times and they’ve called us for especially for immunotherapy trials were very strong with that. But for example, EGFR mutant trials. You know, I would say I get in the Phone. I’d say Doctor Elena. You know what do you got and then I would set it up so we’re all in it together whether you’re in Boston, NY or kinetic. I don’t know about.

Out West but certainly on the East Coast, where one big family and we’re here to find the best trial for patients.

Alright well, thanks thanks everyone for coming. I’ll see many of you and then your future.