Transcription of DTRF Patient Meeting Webinar #2: Therapies & Clinical Trials for Desmoid Tumors

Please remember that desmoid tumors are very complex and the below information is not intended as medical advice for any individual problem, or as a diagnosis, treatment plan, or recommendation for a particular course of action, and should not be used as a substitute for professional medical advice and services. Please do not delay in seeking professional medical advice regarding your individual circumstances.

Jeanne Whiting: Hi everyone. Welcome. I'm Jeanne Whiting, president and co founder of the Desmoid Tumor Research Foundation.

Jeanne Whiting: Just a couple of announcements on this second webinar if you weren't in our first webinar. I'll repeat that the video presentations the recording of this meeting will be available after.

Jeanne Whiting: You will have access to them and can watch them over and over, if you desire and wait for us we will email you with the link to that.

Jeanne Whiting: And also, any questions that you might have our panelists have graciously agreed to answer during and after the meeting, we will have very limited time in this meeting to answer questions.

Jeanne Whiting: But you're welcome to put them in writing on the Q&A. You'll see for most of you, if you're on a computer it will be at the bottom of your screen it says Q&A

Jeanne Whiting: And you just type your question in. And if we don't have time to get to it during the period of time we have today, we will be sending

Jeanne Whiting: An email to everyone who has attended not specific answers to your specific but a general answer from our panelists in a bulk. Also the chat is closed for this meeting. We had over 300 people registered patients and caregivers registered from 20 different countries attending

Jeanne Whiting: And we also have invited all of our doctors and researchers from our workshop and others from around the world. So, our group is very large

Jeanne Whiting: But we welcome you all. We love this virtual format format this year that allows us all to tune in.

Jeanne Whiting: So I'll ask the the presenters to please keep your presentations to the seven minute requested limit. It is a live presentation and then we'll have seven minutes to answer questions.

Jeanne Whiting: Please keep your questions to the presenter that is presenting that will help him or her scroll through the questions at the time during the time of their presentation or just after and answer what they have time to answer.

Jeanne Whiting: Thank you very much for attending and let's turn the time over to our first speaker, Dr. Eldad Elnekave. No, I'm sorry, it's Dr Bucknor. Thank you.

Matt Bucknor (he/him/his): Okay, thanks. Thanks very much. I'm going to go ahead and share my screen

Matt Bucknor (he/him/his): To get to my talk.

Matt Bucknor (he/him/his): And

Matt Bucknor (he/him/his): Please, of course, let me know if anyone has any trouble viewing anything. It's a real real honor to be here to present today and to talk to you.

Matt Bucknor (he/him/his): All of you about this exciting relatively new approach to treating patients with desmoid tumors.

Matt Bucknor (he/him/his): Known as HiFU, high intensity focused ultrasound or magnetic resonance guided focused ultrasound. Can I try to get through my opening remarks, fairly quickly so I can address as many of your questions as I can.

Matt Bucknor (he/him/his): Nothing to disclose. So I'll just talk a little bit of brief background about the technology.

Matt Bucknor (he/him/his): And talk a little bit about the desmoid tumor treatments and how focused ultrasound offers benefit to patients with desmoid tumors.

Matt Bucknor (he/him/his): And then talk about some new frontiers thinking about, in particular the immune response effects that we think might be associated with focused ultrasound and how that might be something we're thinking about going forward.

Matt Bucknor (he/him/his): So this technology goes by many names. If you've ever tried to Google it, or search it on the web focused ultrasound, focused ultrasound surgery, high intensity focused ultrasound all those

Matt Bucknor (he/him/his): Describe the same fundamental technology of a high energy ultrasonic transducers same basic technology as we use for

Matt Bucknor (he/him/his): diagnostic imaging, but just increasing the energy coming out of it and focusing that energy at a single point. You could add a single point really hot.

Matt Bucknor (he/him/his): And now that technology can be guided by either MRI ultrasound depending on the specific indication or institutional practice, although

Matt Bucknor (he/him/his): For most of the the desmoid tumor treatments in the United States, at least we do MRI guided focused ultrasound.

Matt Bucknor (he/him/his): The best analogy is that it's a lot like a magnifying glass focusing sunlight to generate heat and burn a leaf. You can do the same thing with sound waves coming out of a transducer

Matt Bucknor (he/him/his): A phased array transducer embedded inside of an MRI table producing these focused sound waves and generating heat up to 75 to 85 degrees Celsius in 20 seconds so it gets really hot in a relatively small point very quickly.

Matt Bucknor (he/him/his): This is the device that we use for our treatments at UCSF and is used at several other centers as well. You can see in many ways it looks like a standard MRI table, except it's got this very large power cord that's going essentially to supply

Matt Bucknor (he/him/his): The ultrasound transducer that lives underneath this translucent window. So this device was originally designed to treat women with uterine fibroids.

Matt Bucknor (he/him/his): So you can see that we essentially need to bring whatever we're treating wherever the tumor is in the patient. So it's sitting on top of that area of the table.

Matt Bucknor (he/him/his): This is just a quick snapshot of one of the workstations screens. I get as we're doing the treatment. So we get nice real time feedback that we're

Matt Bucknor (he/him/his): Of exactly where we're targeting and we can see where the heat is collecting with some MRI thermometry sequences is what we call them.

Matt Bucknor (he/him/his): The benefits of the technology that's completely non invasive. There's no ionizing radiation. You could target things pretty precisely and potentially repeat it. There's no inherent dose toxicity.

Matt Bucknor (he/him/his): The key risks are, that there's a risk of the skin burn and that's probably the thing that we worry about the most with soft tissue tumor treatments.

Matt Bucknor (he/him/his): Both concerned about protecting the near field skin where the sound energy is going into the patient and then the far field skin where a little bit of sound energy that is not absorbed may

Matt Bucknor (he/him/his): Reflect back and potentially injure the skin beyond the region of the tumor. So we have to take steps to protect that skin as well.

Matt Bucknor (he/him/his): Thermal damage to adjacent structure. So really, the degree of risk for the treatment is going to be

Matt Bucknor (he/him/his): Driven by exactly how big the tumor is and what is near the tumor. So if it's near something that's really critical that might be a contraindication prevent us from doing the treatment

Matt Bucknor (he/him/his): Or allowing us to only partially treat the tumor. I'll show an example of that. And then pain, pain, it's not really so much of a risk, but usually patients have a few days of moderate pain following the treatment that's easily controlled with medication.

Matt Bucknor (he/him/his): So just an overview of the clinical applications. I mentioned that the device that we use was initially developed to treat women with uterine fibroids and is FDA approved in 2004.

Matt Bucknor (he/him/his): There's an FDA approval for palliation of bone metastases in 2012. There's a different device, it looks a little bit like a hairdryer that was FDA approved to treat essential tremor

Matt Bucknor (he/him/his): Targeting spots in the brain in 2016 and then you know that's those are the major Mr guided focused ultrasound FDA approved indications. So we do other other treatments

Matt Bucknor (he/him/his): off label indications of benign bone tumor soft tissue tumors, but these are not FDA approved, we were simply able to

Matt Bucknor (he/him/his): To treat patients within the scope of our practice, when we think that it's a good option for patients.

Matt Bucknor (he/him/his): So on to desmoid tumors. I want to. I'm not going to talk too much about the background of desmoid tumors because I know all of your familiar but

Matt Bucknor (he/him/his): I do want to speak a little bit about why does surgery fail. And why might focus ultrasound offer some benefit. So one of the challenges I think with surgery is that

Matt Bucknor (he/him/his): When we have a desmoid tumor like this. So this is a cross sectional image at the level of the hip. Here's the ball and

Matt Bucknor (he/him/his): socket joint of the hip. So the femur and the acetabulum this is the intra pelvic area and we're we're sort of slicing through the body. And this way, transverse or axial slice.

Matt Bucknor (he/him/his): This patient as a desmoid tumor just just beneath the skin at the lateral aspect of the hip sort of superficial to the gluteal musculature.

Matt Bucknor (he/him/his): And you can see that a surgeon might not have much time identifying this mass dominant mass if they

Matt Bucknor (he/him/his): Were to operate. But I think what's hard so hard with these tumors, is that there's often almost always this very infiltrative component that extends

Matt Bucknor (he/him/his): And can be very, very difficult to identify. I think microscopically. So that's the part that can be hard to see surgically and which MR guided interventions can

Matt Bucknor (he/him/his): Really excel it a targeting and treating. So here's an example of a large desmoid tumor that we we've previously treated in this young, young pediatric patient, you can see it's a large tumor in the interior compartment of a thigh.

Matt Bucknor (he/him/his): We've given contrast in this image. So the contrast tells us where the tumor is viewable essentially homogeneously throughout the tumor.

Matt Bucknor (he/him/his): And we can see that immediately following the, the focus ultrasound treatment that that area, all these areas that were bright indicating that they were viewable and alive.

Matt Bucknor (he/him/his): Or now dark. So we have extensive non enhancement throughout the tumor.

Matt Bucknor (he/him/his): This is just another cross sectional image you can see this is the actual transducer inside of MRI table.

Matt Bucknor (he/him/his): We have a gel pad that helps to make sure that sound energy goes into the patient smoothly and then there's the tumor that we saw again used to be totally bright meaning was all live

Matt Bucknor (he/him/his): And now it's very essentially dark over a series of images. So, this can be a really effective treatment in

Matt Bucknor (he/him/his): several cases. Another great thing with this technology is can be fairly precise. So here we have a tumor that is encasing the sciatic nerves largest nerve in the body. It's not a nerve you want to damage and

Matt Bucknor (he/him/his): Surgeons obviously are reluctant to operate in this situation, but we can do here is not necessarily totally ablate the tumor but we can offer partial ablation

Matt Bucknor (he/him/his): sparing as much as we can, while providing a pretty good ablation of the posterior aspect of the the tumor. In this case, allowing for some symptomatic improvement and reduction in tumor burden, we can bring back the patient periodically and treat treat them over time in that way.

Matt Bucknor (he/him/his): This is one of the larger studies for that we have retrospective studies for desmoid tumors, not, not a huge number of patients enrolled, but

Matt Bucknor (he/him/his): What we did see is that there was significant tumor volume decrease 63% and improvement in pain scores with focused ultrasound treatments.

Matt Bucknor (he/him/his): Now, it's important to talk about the limitations of the technology for one of the cases can be quite long 4-8 hours and that's it has challenges.

Matt Bucknor (he/him/his): In terms of the anesthesia often complete ablation is not entirely possible depending on exactly where it is. And if there's a key structure next to it that that's going to limit our ability to really

Matt Bucknor (he/him/his): Go aggressively at every aspect of the tumor. I think focused ultrasound works best when paired with concurrent medical therapy. I almost think the medical therapy can do a great job

Matt Bucknor (he/him/his): At just slowly bringing down the size or at the very least stabilizing the mass and focused ultrasound kind of whack out big parts of it over time, allowing us to help to bring the, the overall tumor volume burden

Matt Bucknor (he/him/his): Or burden of tumor volume under control. And while it's difficult to completely eradicate these tumors

Matt Bucknor (he/him/his): focused ultrasound offers the possibility of sort of managing them as a chronic disease with with steady improvement over time.

Matt Bucknor (he/him/his): Now, another important limitation that there's limited access. There aren't that many centers that are able to offer this and that's really important.

Matt Bucknor (he/him/his): UCSF where I work, is one of the centers, Stanford Children's National but not not many others in the United States.

Matt Bucknor (he/him/his): Here's a list of I found on this great website The Focus Ultrasound Foundation has that sort of lists comprehensively internationally, where these

Matt Bucknor (he/him/his): These tumors are treated with focused ultrasound you can see the list. This is not that long. So that's, that's definitely a place where we need to

Matt Bucknor (he/him/his): To try to expand. I just want to spend just a few last slides talking about immunotherapy because I think it is very exciting in the field of focus ultrasound.

Matt Bucknor (he/him/his): When I say immunotherapy or when I'm talking about immune response effects, it's the fact that, in addition to this ablative property of the focus ultrasound where we can

Matt Bucknor (he/him/his): can burn tissue and destroy it that way. There are other mechanical properties of this

Matt Bucknor (he/him/his): Technology as well. So you can have mild hyperthermia or mechanical obstruction sort of ripping apart cells as opposed to thermally fixing them.

Matt Bucknor (he/him/his): And each of these different properties can be selected for based on the parameters of the focus ultrasound.

Matt Bucknor (he/him/his): And each of them can have different effects that can potentiate the immune response system. And that's been seen

Matt Bucknor (he/him/his): over a course of number of preclinical studies. So there's a lot of excitement in the focused ultrasound community about how we can use this in combination with immunotherapies or other medical

Matt Bucknor (he/him/his): Therapies and antineoplastic agents to try to promote synergy in the response to to the tumor treatments. I just want to leave you with one last

Matt Bucknor (he/him/his): Personal example one anecdote of why I have hope for that approach. And that's that this is 25 year old woman with a history of a left leg desmoid tumor.

Matt Bucknor (he/him/his): That you can see there, and we treated it. There's the pretreatment appearance. You can see immediately after the treatment. We didn't have that quite that solid area of darkness within the tumor. So it didn't seem like it was a total success.

Matt Bucknor (he/him/his): But over time, we see that the margin of the tumor becomes fuzzier and fuzzier

Matt Bucknor (he/him/his): And by a year or two years out, we consider tumor is just sort of slowly fading away. And that's a really unique response. I've actually never seen this response ever again.

Matt Bucknor (he/him/his): I think it really suggests the need for more research to understand how focused ultrasound might help the body to activates immune response in

Matt Bucknor (he/him/his): In the presence of these types of tumors. So in summary, this is a very effective new treatment for desmoid tumors. It works best I think as part of a combination approach for controlling chronic disease burden.

Matt Bucknor (he/him/his): And research into the immune response effects is an exciting new frontier. I think for the field. So with that, I'm happy to answer any questions that anyone has. I'm going to

Jeanne Whiting: Jump out of my PowerPoint. Yes.

Jeanne Whiting: Can you hear me, something's happened with my video. If you could just please describe again the availability of this worldwide. We have a worldwide audience here.

Matt Bucknor (he/him/his): Yeah.

Jeanne Whiting: How they could get more information on availability also covered by insurance.

I said, Yeah.

Matt Bucknor (he/him/his): Sure, yeah. So worldwide availability. So this is the list of sites that I

Matt Bucknor (he/him/his): That I'm aware of that offer this technology. So feel free to go ahead and screenshot that or you can go to this website at the Focused Ultrasound Foundation and

Matt Bucknor (he/him/his): Click through to the technology and treatment sites, you can see just three sites listed in the United States. I think there is a site in the Midwest and maybe in Kansas City that's going to come online soon but

Matt Bucknor (he/him/his): Not quite available there yet. So really, not many places where it's available. In terms of insurance coverage, it's pretty hit or miss.

Matt Bucknor (he/him/his): I'd say we were successful at getting insurance coverage around and 70% of cases, but it's not something that, for example, Medicaid covers very consistently. So, that that is a challenge, but better better than

Matt Bucknor (he/him/his): Better than for some other focused ultrasound indications for sure. So let me

Jeanne Whiting: About the safety of HiFU compared to cryoablation

Matt Bucknor (he/him/his): Um, I think that they're the the safety profiles of the treatments are fairly similar.

Matt Bucknor (he/him/his): The biggest difference is that focused ultrasound is totally non invasive, right. So, any, any of the risks that are related to puncture with

Matt Bucknor (he/him/his): The needle device and the probes. So the risk of bleeding, the risk of infection won't be present for for focused ultrasound ablations so that I think that really comes

Matt Bucknor (he/him/his): Into play in terms of the size and what the tumor is near whether or not accessing the tumor with a percutaneous needle device is that much riskier than treating it with focused ultrasound. But I think focused ultrasound does have the advantage of being totally non invasive.

Jeanne Whiting: Dr. Kasper says we need a study on this.

Matt Bucknor (he/him/his): Yeah. Yeah, no, I think that would be great. We would love to be able to support more research into this technology.

Matt Bucknor (he/him/his): And I know that there are some sites that are enrolling desmoid tumors as part of larger studies with regard to sarcoma, but I would love to see it desmoid tumor specific study because I think it is a little bit different.

Jeanne Whiting: Okay, and

Jeanne Whiting: One final question is the treatment applicable for intra abdominal desmoids, mesenteric?

Matt Bucknor (he/him/his): Yeah, I would say, right now, in my opinion, it's not. I don't think it's ready to go there. There are some

Matt Bucknor (he/him/his): Researchers there's a investigator in Europe, who's developing this focus ultrasound to treat pancreatic lesions. And I think if

Matt Bucknor (he/him/his): If we're able to overcome some of the limitations in terms of the motion of

Matt Bucknor (he/him/his): The abdomen during treatments as well as the rest of the bowel, there's a significant risk that you could burn the bowel during the course of these treatments and those can be overcome, it might be possible, but I think it's, it's not quite there yet for intra abdominal desmoid tumors.

Jeanne Whiting: Okay, thank you. If you haven't any other questions, please put them in the Q&A and what to keep on time here we'll move on to Dr. Eldad Elnekave, who's going to talk about inter arterial doxorubicin treatments.

Jeanne Whiting: Eldad, Are you there?

Eldad Elnekave: I'm here now can you

Jeanne Whiting: Make I

Jeanne Whiting: Can you see my screen? We can see your screen, but not your slides yet.

Okay.

Jeanne Whiting: Now, we can hear you. So you're good to go.

Eldad Elnekave: Okay, excellent.

Jeanne Whiting: Alright.

Eldad Elnekave: So there we go. I'm

Eldad Elnekave: Going to be speaking about targeted inter arterial doxorubicin for desmoid tumors and briefly, I have no financial disclosures.

Eldad Elnekave: OK, so the overview the goals for my presentation. I want to make sure that we describe what doxorubicin alluding treatment is as a therapeutic option.

Eldad Elnekave: share our experience over the last six years in using this approach for desmoid patients and then practically talk about how you or your patient can get assessed for this option.

Eldad Elnekave: So we we published about two years ago with our initial results. This was for four patients all pediatric patients and all extra abdominal tumors and so then we created we consider this

Eldad Elnekave: As a, as a promising approach for a perplexing disease and it's perplexing because as we know

Eldad Elnekave: Desmoids are local diseases but but they don't really respond well to the classic response to therapy for locals. It's just surgery.

Eldad Elnekave: And then systemic options are varied, but generally suboptimal as of yet. Now one promising therapeutic option systemically has been doxorubicin a potent drug which is used commonly for other soft tissue diseases, sarcomas, fibrosarcoma.

Eldad Elnekave: And had some promise has some promise for for desmoids it's but it's very toxic and so the systemic administration, meaning you give it anywhere in the body has real limitations in terms of dose

Eldad Elnekave: Which means limitations in terms of the efficacy for the target tissue.

Eldad Elnekave: And one way to overcome that is by taking advantage of the, the actual composition of the drug. So doxorubicin itself is composed of a positive and an ionic portion which is red. That's the active part and then a both a buffering are stabilizing negative portion

Eldad Elnekave: When you look at the solution that's red if you introduce small particles. These are about 100 microns. So about 10 times the size of a red blood cell.

Eldad Elnekave: And they can vary in size but ultimately these particles can be coated in very negatively charged substance.

Eldad Elnekave: And so as as they shrink as they sink into the solution. They actually attract the drug, and then you're left with a lot of particles that can deliver the drug.

Eldad Elnekave: Now you can leverage that ability. So, you know, you've, you've got a systemic therapy which can be delivered locally, if you can get it into the tumor through the blood supply. So you navigate through the arteries to find the

Eldad Elnekave: The actual vessels which supply the tumor and here you're also leveraging the inherent hyper vascularity of desmoids, often they create their own blood supply, as is the case with many tumors.

Eldad Elnekave: And many have a couple of examples and share our experience. So this was one of our first presentation to see. Oh, one of our first patients and

Eldad Elnekave: And this was a six year old girl with a as you can see a very large axillary tumor.

Eldad Elnekave: And what you can identify on this slide is catheter is is the main kind of the subclavian artery, the axillary artery and then selecting vessels.

Eldad Elnekave: I mean me to make sure everyone sees the large tumor in the actual. This is the two to one way to MRI and coronal view.

Eldad Elnekave: You can see collapse of the right hemithorax with pressing of the of the lung, and then the what you see in black here, our vessels contrast material from the angiography

Eldad Elnekave: You can select the vessels which go into the tumor and then deposit these beads achieving a very high dose

Eldad Elnekave: Of the drug locally with a very low exposure of the drugs systemically. And so after four treatments of one year, what we see here is a remarkable shrinkage of the tumor in this case of the 97% reduction in volume and a lot of redish discoloration of the skin which and

Eldad Elnekave: Which we often see in these cases are first

Eldad Elnekave: Anyway, after those first four cases, we saw a reduction of volume between 52% and 97% in those in that pediatric population. We expanded the trial to include adults and to include tumors, which were both

Eldad Elnekave: Extra abdominal and also intra abdominal and, for that matter, anywhere. So, and patients with with with desmoids to the mediastinum were treated as well. I'll show a couple of examples.

Eldad Elnekave: This is the 17 year old who has treated over the course of one year he was given four treatments. And so you can see this large forearm desmoid

Eldad Elnekave: And then what we have in the middle is the angiographic image selection of the intraosseous

Eldad Elnekave: Branch of the of the arteries supplying forearm, where we could deposit the the beads with doxorubicin. And our last follow up here, we have really kind of reduction of the of the of the tumor. Some reddish discoloration, as we see, often with doxorubicin. But, but a good response.

Eldad Elnekave: Another patient. This is a 27 year old with a neck based desmoid and we can see just a photograph on the left. On the right you have catheterization of the ascending cervical artery.

Eldad Elnekave: And we can see that those vessels which are supplying the mass and that kind of classic appearance for an interventionalist of a blush supplying a tumor so treatment from that one position. There were several others.

Eldad Elnekave: But a follow up view here, nine months later we we have almost symmetry of the right and left side of the neck and the appearance on MRI on a T2-weighted MRI

Eldad Elnekave: Is similar. So the T2-weighted MRI is is really critical, from our perspective in terms of identifying both the size the volume but also the cellularity of the tumor and how well it's responded to your treatment.

Eldad Elnekave: Another example here of an intramesenteric mass. The 51 year old woman. So what we have here is the pubic synthesis

Eldad Elnekave: And above that a little bit of bladder. This is bowel and then really almost most of the abdominal cavity is occupied by this desmoid

Eldad Elnekave: And the growth here was remarkable. So over the course of four months it grew from a relatively small mass to just this enormous mass and she was at this point really having difficulty just eating.

Eldad Elnekave: What it looks like when you target these vessels in the mesentary something like this. So you've got catheterization of the superior mesenteric artery right here. A lot of these vessels are supplying small bowel, and then the ileocecal. So the ilium and then colon

Eldad Elnekave: Over here. What I've demonstrated in red here is the the actual catheter. So the catheter curves up

Eldad Elnekave: And then it enters and this blue part is really where we want to go because this is what the suspected tumor supply was

Eldad Elnekave: And we can see what that looks like here. So now you selected just that branch that seems to be supplying the tumor, we can confirm that on the angiography table using a CT

Eldad Elnekave: To make sure that we're not targeting bowel or anything else that can be injured and that's an important the key consideration in these in these procedures.

Eldad Elnekave: This is the follow up 10 months later, so really am a reduction of almost 90% of the volume of the tumor. We treated her twice, and she was hospitalized for one day each

Eldad Elnekave: Each treatment with a total dose of about 150 milligrams total into the beats. So that's the view on coronal on the I mean axial view.

Eldad Elnekave: What you see here is the kidneys and the backs of the spine in the back, belly button on the front.

Eldad Elnekave: This is the tumor and then 10 months later, almost a flat belly and really you can also see kind of the increase in fat that's that's that's the positive over that interval.

Eldad Elnekave: And she looks much healthier. So our preliminary results with 18 patients treated with a median followup of 27 months, six kids, 12 adults, median age 37. Limb, chest wall, abdominal wall, those were 10 patients. Mediastinal, pelvic and intra abdominal or mesenteric desmoids those were eight

Eldad Elnekave: More in our preliminary results 94% have a two year progression free survival. One patient progressed. 89% decreased volume at first follow up.

Eldad Elnekave: And the medium volume decrease at the first follow up, which is around three months is 52%. Medium volume decreased by the last follow up with median follow up of two 2.3 years 74%.

Eldad Elnekave: Median treatments per patient is three and they usually spend, but one day admission follow up after treatment.

Eldad Elnekave: 17-18 patients completed therapy without a significant adverse event. So without a grade three or grade four adverse event. One patient had a

Eldad Elnekave: Vascular dissection, which required rehabilitation and and those are those are our preliminary results. And importantly, if you know how can you find

Eldad Elnekave: Treatment here. Well, these. So, this requires consultation with an interventional radiologist someone who is minded to interventional oncology and delivering therapies to tumors.

Eldad Elnekave: doxorubicin eluding particles are widely available. There are several different types of them we in this in this study used really all three.

Eldad Elnekave: And we've just we've discussed and advised doxorubicin eluding embolization for desmoid patients across the globe. So we know it's going on.

Eldad Elnekave: Again consultation with an interventional radiologist and oncologist to team up if there are questions, they can contact me us for a little bit of guidance or questions. And that's the end of my presentation. Thank you.

Jeanne Whiting: We'll let you scroll through the questions, could you just please go over the availability worldwide of this?

Eldad Elnekave: So, you know, this is there's nothing proprietary about the the the drug or the part of the particles. The challenge is, is just finding a team that's minded to interventional oncology as a procedure.

Eldad Elnekave: interventional radiologists who who do a significant amount of work, treating, treating tumors and and that that really is available it worldwide. I would say most academic centers will have you know someone who who's dedicated to this.

Eldad Elnekave: Let me look at the Q&A

Eldad Elnekave: Is this the same thing as Doxil? Doxil so Doxil is a little bit different. Doxil takes advantage of doxorubicin and it coats doxorubicin in a liposome

Eldad Elnekave: Doxil is still administered systemically throughout the body, but it is more heavily targeted towards tumors because of something called because of basically inflammation within the tumor and it has a lower toxicity profile, but that it's it's it's different from Doxil.

Eldad Elnekave: Risks associated with this method. The main risks here are procedural

Eldad Elnekave: So it is this isn't surgery but it is more or more and more interventional

Eldad Elnekave: Meaning the risks are very dependent on anatomically what you're treating if you're treating something in the arm there could be a risk that particles will go into the hand if you are

Eldad Elnekave: Treating

Eldad Elnekave: Something in the abdomen or the neck. The risks are quite different.

Eldad Elnekave: So the risks are very dependent

Eldad Elnekave: Really

Jeanne Whiting: Could you just repeat that last part? You blipped out there. We lost your stream for a

Jeanne Whiting: couple seconds. Okay.

Eldad Elnekave: Yes, and I can't see you guys but the risks are very dependent on the on the case. They're procedural. This is not a pill that you take

Eldad Elnekave: But, but if it's a. So, again, there are there are situations where it's lower risk. And I would say extremity lesions tend to be lower risk. Mesenteric and mediastinal masses higher risk. It just requires more diligent planning preparation and precautions during the procedure.

Jeanne Whiting: Okay, maybe one more, one more question, please.

Eldad Elnekave: Marlene, I can't actually see it see the screen for some reason. So, is there another question that can be posed me verbally.

Marlene Portnoy: Jeanne, Ok. Jeanne, Do you want to answer? Ok I'll ask a question.

Jeanne Whiting: .

Eldad Elnekave: See here ok now we're back.

Eldad Elnekave: Okay, what are the side effects, I think. So this is

Eldad Elnekave: How can I just say, and

Eldad Elnekave: It. Okay. So the question is, can this be performed during pregnancy. If the tumor is growing and

Eldad Elnekave: So I don't think pregnancy is a contradiction. The we haven't, I haven't shared all of our pharmacokinetic data because it's too early, but from all the evidence we have so far the systemic exposure of doxorubicin is minimal.

Eldad Elnekave: I would still it I would, I'd be cautious.

Eldad Elnekave: Because there can be transmission of doxorubicin through the placenta and I would say depends on the size of the tumor and how much doxorubicin we would need to give

Eldad Elnekave: judgment call. And it's not a it's not an absolute contradiction for us.

Jeanne Whiting: Okay, thank you so much. We'll you can keep posting questions in the chat again as I said at the beginning.

Jeanne Whiting: We our presenters are willing to answer questions and writing and those will be sent in bulk to those who are registered here. We'll turn next to our next speaker, Dr. Mary Smith with SpringWorks Therapeutics, who's going to discuss the Phase 3 nirogacestat trial.

Mary Smith: Hi. Can everybody hear me okay

Lynne H: You're fine.

Jeanne Whiting: That's good to be here.

Mary Smith: Alright, so I have to first apologize. I'm not able to share my slides, we had a little bit of a technical issue so

Mary Smith: I'm going to actually be giving my talk without slides so apologies ahead of time, we'll make sure that these get posted and I can address any questions.

Mary Smith: So first off, I'd like to thank the DTRF for inviting me to participate in the panel discussion today.

Mary Smith: I wish we could all be together in person, but I'm very grateful that this meeting is able to occur virtually and even more thankful that I'm actually able to give this talk, even though I'm on my phone right now.

Mary Smith: So a little bit about SpringWorks we're a biotech company that's advancing a diversified pipeline of targeted oncology programs. Both both as mono therapies or in combination with

Mary Smith: Other agents in some cases. Importantly for today's discussion, I'll give you an update on our ongoing DeFi three trial which is investigating nirogacestat

Mary Smith: In adults with progressing desmoid tumors. And as you heard earlier from Drs. Weiss and Gounder, we just announced a collaboration with the Children's Oncology Group

Mary Smith: To study nirogacestat in pediatric and adult patients and that trial is activated so

Mary Smith: What am I going to talk about today. So we'll discuss a little bit about nirogacestat and how it works and what it is and discuss a little bit about the results from our early phase one and two studies that led to

Mary Smith: Our phase three study. And then, of course, talk a little bit about the DeFi trial and where we are in that. So nirogacestat is an investigational oral selective

Mary Smith: Reversible small molecule. It's an inhibitor of gamma secretase. So what is gamma secretase and apologies. Again, I don't have my nice pictures but

Mary Smith: Gamma secretase is an integral membrane protein that cleaves multiple other trans membrane proteins, one of which is notch.

Mary Smith: And specifically gamma secretase is able to cleave notch once once the notch receptor has been

Mary Smith: Engaged by its ligands and the gamma secretase will cleave notch and it releases what's called the notch intracellular domain.

Mary Smith: And that's a transcription factor. And once it gets to the nucleus. It actually leads to modulation of gene expression for certain target genes, one of which is

Mary Smith: Has one, for example. This can in the case of tumors, for example, that have these activating mutations, it can actually lead to proliferation uncontrolled proliferation.

Mary Smith: Of tumors, for example. So blocking the Notch signaling pathway using a gamma secretase inhibitor like nirogacestat actually will inhibit that

Mary Smith: That whole mechanism from occurring and subsequently the downstream overexpression of some of these genes and will hopefully arrest the tumor.

Mary Smith: As you're aware, and you've heard in other presentations, the majority of desmoid tumors arise spontaneously and are associated with mutations in beta carotene or in the case of FAP, they can result from mutations in the APC gene.

Mary Smith: Both of these both beta catenin and APC are part of the Wnt signaling pathway and mutations in either one lead to stabilization of the beta catenin protein, which leads to accumulation of beta catenin and activation of target genes which may underlie the

Mary Smith: The desmoid biology.

Mary Smith: Inhibition again of the notch pathway is thought to have an effect on the Wnt pathway, because there is a

Mary Smith: Hypothesis that there's crosstalk between these two pathways. In other words, that at that has one gene that inhibiting notch one may actually play a role in the effects of beta catenin and and and driving the desmoid tumor.

Mary Smith: So because apparent notch signaling has been implicated in a number of different tumor types, the very first study that was conducted with nirogacestat

Mary Smith: Was conducted in a solid tumor all commerce study, and this was really a study. It was a phase one study

Mary Smith: To evaluate the dose to find out what was the best goes to use and also to determine the safety of nirogacestat again in this all solid tumor all commerce study.

Mary Smith: There was a number of different tumor types that were studied in that in that study colon breast thyroid lung, etc.

Mary Smith: But importantly, there was a subset of patients that had desmoid tumors that were included in this study.

Mary Smith: And what I would show you if I could, is that all of these desmoid patients. There were seven patients that had valuable tumors and all of those tumors actually shrunk on nirogacestat. Importantly the tumor shrinkage was actually maintained for an extended period of time.

Mary Smith: In fact years in some cases we look, there was a variety of different doses that were explored in that study, the maximum tolerated dose and all of the the tumor types that were tested was 220 milligrams and the, the phase two dose that we carry forward was 150 milligrams dose twice a day.

Mary Smith: Again, there was about 70% of patients that responded in that study. That led to a specific study that was conducted by the National Cancer Institute. It was a phase two study that

Mary Smith: Actually evaluated both the safety and efficacy of nirogacestat. There were 17 patients that were enrolled. And again, this was a patient population

Mary Smith: That had progressing desmoid tumors. And it was a very heavily pretreated patient population. So these patients had had were considered refractory. They had failed anywhere between one

Mary Smith: And nine lines of therapy and again these patients were able to respond to nirogacestat. Their tumor shrunk and in 30% of the cases that had a partial response.

Mary Smith: In other words, they are and the rest of the patients had disease stabilization. And again, this was really independent and both studies of whether or not patients had an APC mutation or they had a beta catenin mutation.

Mary Smith: So if we look at the totality of that data and all the patients in the phase one and phase two study, we look at what the tolerability of nirogacestat was in those patients. And again, this was probably about 70 patients.

Mary Smith: The most commonly reported adverse events are similar to those seen with other gamma secretase inhibitors and include gastrointestinal issues such as diarrhea, nausea, vomiting,

Mary Smith: hyperphosphatemia which is a decrease of phosphate and in the blood, which actually can be supplemented with oral phosphate replacement and then patients also developed rash.

Mary Smith: So where are we right now with our DeFi study. Most importantly, I think you heard from some of the previous talks that the DeFi trial has completely enrolled. So I'm really happy to say that, where we are right now is that

Mary Smith: You know we had a target enrollment of about 115 patients and we met that target enrollment this summer. We had about 50 sites

Mary Smith: That were that conducted this study, and this was across the US, Canada and the EU. So again, a shout out to everybody there. The study was designed as follows. It's

Mary Smith: An excuse me, it's a double blind placebo controlled study. The patient population that was included for participation had progressing desmoid tumors. Patients were randomized one to one.

Mary Smith: And there was an open label or is an open label extension for patients who

Mary Smith: Progress on study. The primary endpoint for this study is progression free survival, very similar to the sorafenib study that has been reported out previously.

Mary Smith: And we have a number of key secondary endpoints that we're looking at, of course, safety and tolerability but also what is the objective response in these patients. What's the duration of response.

Mary Smith: And as Dr. Gounder has also mentioned in his talk previously through the development and the collaboration of the DTRF and and

Mary Smith: Memorial Sloan Kettering, they developed a desmoid-specific tool that we are able to use in our study to help validate that tool so we can see how well we are able to or nirogacestat is able to affect the quality of life in patients.

Mary Smith: Again, we started this study in the first half of 2019 and I'm happy to say we are fully enrolled today. So what does that mean right now so

Mary Smith: What, what happens in this type of study is that we're in what's called the maintenance phase. So we patients will continue to be evaluated for tumor responses and will be assessed and once we reach a targeted

Mary Smith: Number of events, then we would be able to analyze this study. So we're basically in that maintenance mode right now.

Mary Smith: So, and that sort of concludes my discussion, but I just want to actually say a very heartfelt thank you to all of the patients

Mary Smith: And the investigators who are involved in the DeFi study and are still involved today. And a special thank you to the DTRF for

Mary Smith: Not only their tireless advocacy here but again, also for all of the work that they do for the desmoid community. So thank you very much again. I'm very sorry that you just had to look at me during this talk and I didn't have my slides. But, you know,

Mary Smith: I'll make sure those get posted

Jeanne Whiting: Thank you. That was a great presentation. Am I correct that you cannot see the chat the Q&A?

Mary Smith: Hold on one second. I am able to

Mary Smith: I see a list.

Jeanne Whiting: Can I

Jeanne Whiting: Just pass on one question I'd like you to start with and you can scroll through. The

Jeanne Whiting: Availability to patients now that the that the study is full

Jeanne Whiting: To this drug. Whether compassionate use or otherwise.

Mary Smith: .

Mary Smith: That is correct. So we do have a compassionate use program you can go to our website, which actually. Well, let me just back up for one second, if

Mary Smith: There is a patient who is interested in nirogacestat they would have to discuss this with their treating physician. The treating physician would then

Mary Smith: Make a query to SpringWorks through the website, there is a link there requesting access to to nirogacestat and again. It really just depends on the situation. Each case is evaluated on a case by case basis. So that's how

Mary Smith: You would be able to access it, but it's through your treating physician, they would have to request it.

Mary Smith: Let's see, what are the locations of the majority of tumors, you are speaking to. So in our study we did not

Mary Smith: Limit the location of the tumor. So again, this is a this is a blinded study just as a reminder. We enrolled patients that have extremity tumors, intra abdominal tumors, but we did not have any restriction on mutational status so patients that had

Mary Smith: You know FAP were able to be included in the study.

Mary Smith: Okay, let's see. Um so compassionate access. We talked about. So again, I encourage everybody to go and talk to their investigator.

Mary Smith: Let's see.

Mary Smith: Let's see, could you please comment on this.

Mary Smith: Let's see. So in so side effects are in. So somebody had said that the side effects are intolerable, but the tumor has shrunk. So again, what I would suggest that you know, again, it's a blinded study if there is a patient who is out there that is on this study that needs to discuss

Mary Smith: Their adverse event profile with their investigator, I would suggest that they do that specifically with their treating physician, because there are some things that can be done. For example

Mary Smith: A dose reduction, depending on the adverse event, etc. Um, let's see several patients that had stress fractures due to bone density loss.

Mary Smith: I will have to get back to you on this talking about stress fractures in the phase 2. I'm not familiar with that specifically, so I'll have to go back and look at that. As a reminder

Mary Smith: That was a study that was conducted by the, the National Cancer Institute. That's actually an on. I don't want to say it's ongoing there are patients that are actually still continuing in that study.

Mary Smith: So in terms of the information that we have, we are in discussions with the National Cancer Institute to obviously get the full breadth of the data from that study. So again, they are there are still patients that are ongoing on that study. I believe it's five still six years later.

Mary Smith: Can we take one

Jeanne Whiting: More question, Mary.

Mary Smith: Yes, let me just sorry in order to look I have to go back and forth.

Mary Smith: So, excuse me here. The side effects. I think I talked a little bit about those

Mary Smith: Again, we've seen a number of side effects in the phase one and phase two study. Let me pull them up. Again the most common events that we do see are those gastrointestinal. This is actually a very common side effects with other gamma secretase inhibitors. So the nausea

Mary Smith: Vomiting and diarrhea is diarrhea is actually one of the most common adverse events. And again, if, if this is something that is being observed, you should talk to your investigator about that

Mary Smith: To seek some treatment for that. In addition to that, rash was observed. I mentioned the hyperphosphatemia and you know sometimes you can also get other side effects with some of your blood levels and things like that so

Jeanne Whiting: And there's questions about early menopause or fertility, future fertility concerns.

Mary Smith: Yes. So obviously the study is is ongoing. So any kind of long term effects on those types of outcomes are still being evaluated as part of the study. Again, it's a blinded study

Mary Smith: And we continue to evaluate all adverse events so that we can fully characterize them and understand. For example, when they occur

Mary Smith: And if they are any of these events are reversible upon stopping treatment. So all of that information is being gathered as part of this study so that we can more accurately be able to assess each, each of the adverse events.

Jeanne Whiting: Okay, thank you very much. And again, your questions, or your free to put them in the Q&A, thank you. We'll move on to our final speaker, Dr. Cunningham

Jeanne Whiting: from Iterion Therapeutics.

Casey Cunningham: Okay, thanks.

Casey Cunningham: So welcome everybody. And of course, I want to add my thanks to the DTRF

Casey Cunningham: And actually, I'd like to start by congratulating Mary and the SpringWorks team, those of us who are in the business of bringing drugs to patients know how rare and special it is

Casey Cunningham: To get all the way to a phase three trial and get that completed and I offer complete congratulations to to her and her team.

Casey Cunningham: So I'm gonna go to share my screen now. And yeah, so I want to talk about

Casey Cunningham: A phase one to trial of a drug called Tegavivint. Those of you that have been the previous DTRF meetings have heard me speak before about this trial. But for those of you that

Casey Cunningham: Are new to this, I'm going to spend just a second, sort of giving you the mechanism of action of the drug.

Casey Cunningham: So common question from people with desmoid tumors, is if beta catenin is the problem, why aren't we just drugging beta catenin?

Casey Cunningham: And the answer is that over the years we've tried. The difficulty is that beta catenin has other roles in cells, besides just

Casey Cunningham: Its actions in the nucleus. And if you globally inhibited beta catenin function, you would also inhibit those other roles, some of which have to do with how

Casey Cunningham: Cells stick to each other. And so you get a lot of side effects, particularly gastrointestinal

Casey Cunningham: Side effects. So that's why most drugs that you've heard talked about have other mechanisms of action that then trying to indirectly impact

Casey Cunningham: the nuclear beta catenin and Tegavivint takes that approach too although it's a little closer to the to the target. So, it binds to a protein called TBL1

Casey Cunningham: That binds to beta catenin in the nucleus. And so the hope was and what the early research at the bench and and pre clinically showed was that

Casey Cunningham: Binding to TBL1 inhibited the nuclear activity of beta catenin but not the other roles that are contained in place in the cell. So we had some idea and some hope that this will escape the toxicities that some of the other drugs in that pathway have seen

Casey Cunningham: And how we decided to conduct a first in human trial, and I have to emphasize this. I have at previous meetings that this is the first time that people had been given this drug.

Casey Cunningham: So there's going to be a lot that we don't know, and we have to proceed very carefully in these early trials. So this was an open label trial.

Casey Cunningham: It was held at several centers. It was not randomized because this is again, what we're trying to show in this trial is whether or not the drug is safe as the primary goal and then we'll also look for evidence of activity.

Casey Cunningham: So it was a two part study in the first phase, we took small groups of patients and gave them a dose of the certain dose level of the drug. And then we watch them.

Casey Cunningham: And the schedule was that they get this is an intravenous drug. It's not oral they got an infusion.

Casey Cunningham: For three weeks in a row. It takes about four hours to get the infusion followed by a week off and after the first month

Casey Cunningham: If they looked okay we would take the next group of patients and give them a slightly higher does the drug and keep marching up like that until we saw

Casey Cunningham: Some signals that said we didn't need to go any higher. In most phase one trials those signals are side effects.

Casey Cunningham: You begin to see side effects that you know are going to just increase if you get more of the drug. And so you stop.

Casey Cunningham: And I'll also say, and I'll repeat this later if you want more information about this trial clinicaltrials.gov is of course a great resource. So, so far what have we seen well we've gotten

Jeanne Whiting: Some patients are saying we can't see slides. Did you have slides or not?

Casey Cunningham: Yes, I'm showing slides.

Jeanne Whiting: Oh we're not seeing them.

Casey Cunningham: Okay, let me see.

Jeanne Whiting: You share your screen, please.

Casey Cunningham: Yeah, I was. Let's try it again.

Jeanne Whiting: There you go. Now we've got it.

Okay.

Casey Cunningham: Can you still see it?

Jeanne Whiting: We can, yeah.

Casey Cunningham: That was where the glitch occurred before

Casey Cunningham: So this is the slide I was talking about the mechanism of action.

Casey Cunningham: And it's just the usual cartoon.

Casey Cunningham: And then this is the the some of the description that I was giving you about the trial.

Casey Cunningham: I was so awe-struck by Mary's presentation without slides, I guess.

Casey Cunningham: Do that.

Casey Cunningham: So here's the summary of the results to date

Jeanne Whiting: .

Casey Cunningham: And as I said, this is a Phase one trial so

Casey Cunningham: Our primary concern is what, what is the drug safe and what are the side effects. So we enrolled 19 of the planned 25 patients so far.

Casey Cunningham: It's actually been very well tolerated. That's what we expected, but we're still relieved to report that. We've not had any toxicities that required lowering the dose or stopping

Casey Cunningham: The drug. What we ended up doing was saying that the the sort of recommended go forward dose was based on blood levels. We saw that as we're getting to increase the dose at some point the blood levels just leveled off and so giving more would not have been any more good

Casey Cunningham: The other point to note is that because patients have tolerated the drug well, they've been able to stay on quite a long time.

Casey Cunningham: And so, and even though it's only a few patients in total numbers since so many of them had been on the drug for for months and months, we've got more than 160 cumulative follow up months.

Casey Cunningham: And so we think that leverages the the signal that we're seeing, even though the numbers are small. So what have we seen in terms of efficacy

Casey Cunningham: Well, here's the swimmers plot. Remember that and you know this better than anybody that desmoid tumors are pretty slow to respond, even when they do respond

Casey Cunningham: So it takes a while. So, so far we've seen, and it's also important to note that all the patients that were enrolled had actively growing tumor symptoms related to the desmoid when they came on. So, so far we've seen where

Casey Cunningham: Hope this thing's not doing this automatically. So, so far that we've seen, we've seen

Casey Cunningham: Two partial responses and a partial response under our criteria is defined as tumor shrinkage 50% we've got a third, a patient has closing in on that and we'll see what the next scan shows

Casey Cunningham: Most people have have had some tumor shrinkage, but it just qualifies as a stable disease right now. We've got nine patients remaining on treatment

Casey Cunningham: With stable tumor, several for greater than one year and anecdotally several patients reporting less pain.

Casey Cunningham: Now we're also going to use that patient reported outcome tool that Mary alluded to in their trial. We'll do that as patients get on the

Casey Cunningham: Go forward dose and we did I'll also mention that the patients in the lower dose cohorts. We did offer the option if they were still on the trial to increase their dose up to the one that we were going to carry forward.

Casey Cunningham: So here are the clinical centers that are currently enrolling patients in this trial. There's one in Toronto. The rest are in the United States, Seattle and Boston, MD Anderson in Houston, Memorial and Ohio State.

Casey Cunningham: So we are pleased that we've we've gotten this far in the trial. It's still early days yet we've just determined the dose. So we're we're pleased at the side effect profile, where we think we're beginning to see some signs of of activity.

Casey Cunningham: But it's, you know, I can't emphasize enough when you do drug development like this. You have to proceed slowly and cautiously. And because of that, there are some restrictions and who can be on the trial and and that would include

Casey Cunningham: Me stop sharing the screen and and that would include currently we're not allowing patients with FAP on. We're not allowing children on

Casey Cunningham: As we get more knowledge and comfort with the drug and its activity and making start to relax some of those parameters, but since this was the first time the drug was going to be given to people

Casey Cunningham: We wanted to be as cautious as we could. And so with that I'll, I'll stop. And I'm going to start scrolling through the questions.

Casey Cunningham: Yeah.

Jeanne Whiting: Could you describe the difference. Now you've moved into phase 2A of the trial

Casey Cunningham: Yeah so phase 2A just means that we we now know the dose that we're going to carry forward.

Casey Cunningham: And so you could call it a phase 2 trial. So the, the, the jargon and clinical trials is Phase 1 is where you're defining the dose and the side effects.

Casey Cunningham: Phase 2 is where you're where you're asking the question, does that the drug work in a particular kind of tumor.

Casey Cunningham: It's kind of, it's sort of been the fashion recently to do your even your phase 1 trial in patients with only one kind of tumor. So you sort of combine those two

Casey Cunningham: But generally, a phase 2 trial, a true phase 2 trial is going to be a bigger crowd. You know, it's going to be north of 40 or 50 patients.

Casey Cunningham: And a phase 1 is is generally 25 or less.

Jeanne Whiting: You have another question. So the side effect profile, you've seen so far.

Casey Cunningham: Yeah. So we haven't, I mean that's there's been a

Casey Cunningham: Sort of a list of because we we quiz people every time they come in. Are you feeling anything what what what what's happening. And so they have a variety of

Casey Cunningham: Symptoms that they see. And then it's up to the investigator to decide whether that could be due to the drug or not.

Casey Cunningham: One way you do that is if the symptom occurs when you give the drug. And then remember I said there's that week off.

Casey Cunningham: We deliberately put that in there so that if we saw certain symptoms that came on and then they got better when you aren't getting the drug than we know it's more likely to be

Casey Cunningham: The drug. So, you know, people have had the, the usual sorts of things that you get going through life.

Casey Cunningham: headaches and stomach upsets and and joint pains and this and that and the other, but we haven't been able to identify anything that consistently shows up when you're getting the drug. So that's that that's one reason why we're still studying and

Jeanne Whiting: There's one question there about neuropathy. Has that become an issue?

Casey Cunningham: Yeah, so

Casey Cunningham: There was a report or 2 of some patients that had some numbness and tingling in there.

Casey Cunningham: I think it was through one patient had it in their leg at one of the centers. The investigator alerted us. And so we immediately went through the database. All this is captured electronically

Casey Cunningham: To see if anybody else had had that. We didn't find anybody, but we're continuing to follow that pretty closely because

Casey Cunningham: It is something that you'd want you know that's the kind of side effect that occurs over time. And then, and then it often doesn't get improve all that much when you stop the drug.

Casey Cunningham: You know, I'd go back to the fact that we've had patients on for more than a year now. So fingers crossed that that's not going to be a problem. But we're watching that pretty closely.

Jeanne Whiting: Okay, I think we covered most of the questions.

Casey Cunningham: Yeah, most

Jeanne Whiting: Summarize again please. How many patients or spots do you still have available?

Casey Cunningham: So right now, they're the there have been 19 enrolled and the study size was to be 25 so there should be six additional slots. It's possible, there could be

Casey Cunningham: A few more if we need if some of the earlier patients was determined that they, you know, they didn't, we didn't get all the information that we needed but but that's it. At some point you have to go on to the next trial. So I would say there's there's probably about six slots left

Jeanne Whiting: Okay, thank you so much. And again, any other questions, please put them in the Q&A in writing.

Jeanne Whiting: It's been an incredible experience to bring people and

Jeanne Whiting: doctors and researchers in from around the world for us as a foundation. It's really been incredible. We thank you all for attending.

Jeanne Whiting: I wanted to close with just a couple of announcements. Again, we thank our sponsors who have helped make the weekend meetings possible SpringWorks Therapeutics, Iterion Therapeutics and Ayala Pharmaceuticals.

Jeanne Whiting: And we thank you all for attending. Again, these webinars will be accessible via our website eventually, and we will send you answers to the questions that were not answered.

Jeanne Whiting: Just give us a little time and will email that out to all of you. So you'll, you'll have that information.

Jeanne Whiting: Do any of my colleagues I just want to close introducing Marlene Portnoy and Lynne Hernandez, the three of us basically run the Foundation together.

Jeanne Whiting: We're used to the virtual format because we're in three different states as it is and we work very efficiently for many years in this format, but do either of you have anything you wanted to close with? Marlene, Lynne? You could unmute.

Marlene Portnoy: Thank you. I just want to thank everybody for coming. This is our first venture as Jeanne said to the virtual world having a virtual meeting and it's been really successful but we look forward to seeing everybody in person next year. So, but thank you for attending.

Jeanne Whiting: And on that score. Please save the dates.

Jeanne Whiting: Saturday and Sunday, September 25 and 26, correct?

Jeanne Whiting: Will send the save the date in the email but we're already prepaid in Philadelphia, because we moved this year's

Jeanne Whiting: Contract into next year. So we're sure hoping we can all be there in person.

Jeanne Whiting: Okay, thank you, everybody. Goodbye.

Lynne H: Hi, sorry, one more thing.

Lynne H: So I just want to to remind you guys that tomorrow we have our RFA Virtual Challenge Ceremony which is taking place from 11 to 11:30am Eastern

Lynne H: This is going to be a great opportunity for you guys to see the faces and hear the stories of other desmoid tumor patients. It's going to be uplifting. It's going to be inspiring. So we joined us. We joined. We invite you to join us to close the weekend with us tomorrow.

Jeanne Whiting: And it has been so successful because of all of you taking the virtual challenge. You'll be so excited to hear how much we raised.

Lynne H: Yes.

Jeanne Whiting: Well, it's just going to be a fun celebration. Whether you participate or not, please sign it, it's just our fun party at the end of the weekend.

Lynne H: Yes. Join us on the detail Facebook page, you'll be able to find us live

Jeanne Whiting: Alright, thank you everybody. Best of luck on your desmoid journeys. Thanks to all our doctors and researchers who take care of our patients and are moving the research forward towards different and new and effective therapies and eventually a cure. Goodbye will see you tomorrow.

Lynne H: Bye everybody.