

Transcription of DTRF Patient Meeting Webinar #1: Desmoid Tumors 101

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: Hello everyone. We welcome you to this first patient meeting webinar. We have many physicians and we have about 300 patients and caregivers and supporters

Jeanne Whiting: Who are registered for this event. Participants from over 18 countries. So this is a wonderful aspect of the virtual format that we're really

Jeanne Whiting: Happy to take advantage of this year.

Jeanne Whiting: I just want to report that yesterday we had a four hour research workshop with our researchers and physicians from around the world.

Jeanne Whiting: Attended by 120 roughly from 20 countries. So this weekend is big and it's worldwide, and we're really happy to have our presenters today, helping us

Jeanne Whiting: Address particular questions of patients. I want to also introduce behind the scenes. We have the other two people who mainly run the foundation with me, my co founder Marlene Portnoy

Jeanne Whiting: And Lynne Hernandez, our director of outreach and operations and you'll be seeing our names on a lot of correspondence. So just wanted to introduce us

Jeanne Whiting: I want to note that on our homepage dtrf.org the "about us" tab I have made a 10 minute presentation and summary of the foundation

Jeanne Whiting: I know a lot of you are probably new to the foundation and I'm not going to take the time today to present information, but you'll see everything that

Jeanne Whiting: We do are our most recent important projects, how we support patients and how patients can support research. So I do encourage you to watch that

Jeanne Whiting: 10 minute video on the "about us" tab on our homepage. Now for the order we're going to follow today. Our first speaker will be Dr. Mrinal Gounder from Memorial Sloan Kettering Cancer Center.

Jeanne Whiting: He's going to talk about how we all interact as a medical professional group with the patient advocacy groups and where that takes us

Jeanne Whiting: Just for the format. The presentation is a live presentation for seven minutes, and then we open it to questions the chat is closed for this with 300 people we

Jeanne Whiting: Are just closing the chat. However, you can address the speaker with your questions via the Q&A.

Jeanne Whiting: For most of you, if you're on a computer computer will be at the bottom of your screen. Just click on Q&A and you can write your question at any time once the speaker finishes his or her presentation.

Jeanne Whiting: They will go through your questions. If your question is not answered, it's still valuable to put it in the Q&A because at the end we will take all questions that were not answered.

Jeanne Whiting: And submit them to the panelists and they have graciously agreed to answer questions in writing these will not be answered to you individually, but will be sent as a group to

Jeanne Whiting: To the everyone who was registered or attended today. So again, questions, we can't. We don't have time to answer all of them, of course, but we'll try to get answers for you.

Jeanne Whiting: I do want to thank the sponsors that have helped this weekend take place, sponsors SpringWorks Therapeutics, Iterion Therapeutics and Ayala Pharmaceuticals. Their support is greatly appreciated and makes these meetings possible. So thank you. And we'll go ahead with Dr. Gounder

Mrinal Gounder: Okay, I'm just going to

share my screen.

Mrinal Gounder: I hope everyone can hear me. Okay. All right. Good morning, everyone. I hope all of you are doing well, staying safe and your families are also doing well.

Mrinal Gounder: It is a little different, very different for all of us on to be interacting and in this way. But I think we're all getting used to this. And the important thing is that

Mrinal Gounder: You know, we're all together and this year's event still goes on 15 years later. So congratulations to Marlene and Jeanne for organizing this and continuing this on.

Mrinal Gounder: So today I'm going to be talking to you about the power of patient advocacy.

Mrinal Gounder: All right. Okay.

Mrinal Gounder: So today I'm going to be talking to you about the power of patient advocacy to advance research and new treatments, particularly in rare diseases such as desmoid tumors.

Mrinal Gounder: These are my

Mrinal Gounder: Disclosures

Mrinal Gounder: These are my disclosures, with Bayer, SpringWorks and Iterion and what I will be discussing today is really just my personal views.

Mrinal Gounder: So I want to begin by saying that, you know,

Mrinal Gounder: For thousands of years,

Mrinal Gounder: Human beings, when we decided to stop being hunter gatherers, and we decided that we're going to live in cities and come together.

Mrinal Gounder: One of the first things that it required for all of us as a society to do was division of labor. So very early on, there were people who are in agriculture others who are

Mrinal Gounder: Educators some were builders soldiers and these were sort of trades and specializations that people have been doing over thousands of years, and this is how our modern society today has also evolved to become.

Mrinal Gounder: In fact, these degrees of specializations have become more and more intricate so today. If you say had a car problem.

Mrinal Gounder: And your car broke down, you know, you have. We all have a certain confidence that all we need to do is to call the mechanic and they will

Mrinal Gounder: Figure it out. You know, and if they don't have a part or something like that, that they are going to call

Mrinal Gounder: Someone else and and and get the parts and fix it. Similarly, whether it's anything else the plumbing is broken. We call the plumber and there is a certain degree of confidence

Mrinal Gounder: That these things have been done before seen before and will get fixed and and this is and there are so many degrees of specializations. If, for example,

Mrinal Gounder: We had some issues with the law, we'd go to the lawyer and in today's world, we just would not pick any lawyer. Right. I mean, the first thing they would ask is, what kind of problems do you have

Mrinal Gounder: And you say that you have some issues with taxes. So you'd get referred, we get we all get referred to a tax lawyer.

Mrinal Gounder: And and and and a lawyer with some other specialization would not be handling that case. And similarly with education as well.

Mrinal Gounder: So I think what has we've all come to accept at a very deep level as a society for thousands of years is that there are certain tasks and certain trades and certain specializations that we've all sort of carved out

Mrinal Gounder: To do and that's what you know worldwide globally our human current society has come to exist and thrive.

Mrinal Gounder: And the same thing is also with healthcare. I mean, when when say like I wake up in the morning and my son has a fever I call the pediatrician.

Mrinal Gounder: I don't really take care of my own son. I, I realized that the pediatricians know what you know will be able to properly diagnose examine and give the right

Mrinal Gounder: Medication or just say, you know, this is really just a fever. You just need to observe and leave him alone. So there is a certain inherent sense of

Mrinal Gounder: Confidence that we have that many of these issues facing all all sorts of things in our, in our lives in our daily lives

Mrinal Gounder: Will get sorted through through people who have spent a lot of time working on it, studying it and getting better at it.

Mrinal Gounder: So even today say that someone is sick or has a fever and the doctor gives you and or gives us an antibiotics, you know,

Mrinal Gounder: It's so simple as getting a prescription, going to the local CVS and picking up the prescription taking the medication and hopefully feeling better in a couple of days later.

Mrinal Gounder: But the story of is really a far more complicated story and I want to briefly tell you about this simple process of just taking a pill how difficult it is in the actual sense of coming to this coming to this point.

Mrinal Gounder: So how do you take an idea and take a drug, all the way into the market. So, and this is pretty much true not just for drugs that are in oncology

Mrinal Gounder: And in cancers, but really for a lot of things, whether it's a vaccine or or whether it is for antibiotics or or an acid suppressor.

Mrinal Gounder: To go from an idea to a market actually takes decades of work. So on the far left hand side. What you're seeing is basic science research. So these are

Mrinal Gounder: People who spent decades to, you know, years and years and years just studying how something works in our bodies and once they figure that out, then, is the process of trying to see, can we come up with a drug, can we come up with a vaccine, can we come up with something to go after

Mrinal Gounder: This process when it is broken.

Mrinal Gounder: So once you figure out that there is a drug that looks promising it takes about a year or two after that to just to make sure that it's actually safe in human beings.

Mrinal Gounder: And it's not a guarantee that all drugs will pass. There is a good number of drugs that even though they may be promising in animals or cell lines

Mrinal Gounder: That when you actually when you when you test it in other animals it turns out to be quite unsafe so many don't make it beyond that.

Mrinal Gounder: And after that, there are a series of clinical trials phase one, phase two, phase three, and these can take anywhere for up to a decade or so.

Mrinal Gounder: And after that is all done, and again, provided that many of these drugs actually go through phase one, phase two, phase three

Mrinal Gounder: It can many drugs basically die along the process close to about one in 50 will only make it starting from the very early on.

Mrinal Gounder: And even after a drug has been shown to be promising in the phase three setting it still takes anywhere from six months to two years for a drug to get approved.

Mrinal Gounder: So this simple pill that you know our doctors give to us, whether it's a chemotherapy drug or an antibiotic or something else

Mrinal Gounder: Involves an enormous amount of research that's behind the scenes and this usually involves thousands and thousands of scientists, doctors

Mrinal Gounder: People in the pharmaceutical industry, investors and of course regulatory agencies such as the FDA and the European Medicines Agency so tens of thousands of people come together to make one drug

Mrinal Gounder: Enter into the market. So when you think about this, you may say, well, all of these people must be working together with a single aim and that's far from the truth. Even in major diseases like oncology and cancer

Mrinal Gounder: The basic scientists are spread across the world. And they're all, to some extent, working in silos. Similarly, pharmaceutical companies may be going after the same exact type of

Mrinal Gounder: Molecule that they all want to go after. The doctors may have expertise in one country

Mrinal Gounder: Or in one region and may never even like talk to someone else about how they treat. So a lot of these things, even in the large diseases. There's a lot of silos.

Mrinal Gounder: But especially for big cancer, say you take colon cancer or lung cancer. Some of the most common cancers.

Mrinal Gounder: There are these opportunities such as conferences and things where people come together to present their ideas and and things sort of happen in an organic way but there's really not like a organizing committee that starts putting people together to start working on on new things.

Mrinal Gounder: So here is a chart of the disease burden by cancer types

Mrinal Gounder: In 2017 and what you see at the very top is our diseases such as lung cancer, which is leading globally. And after that is liver cancer. Then stomach.

Mrinal Gounder: And then it's colon cancer, breast cancer. And what you'll notice is that as you go down here. You will not find sarcomas and you will most certainly will not find desmoid tumor here at all. So in terms of

Mrinal Gounder: In terms of the number of people who are working towards these rare diseases. This does not even register in terms of a, a need from a global

Mrinal Gounder: Standpoint so frequently you know when when people with the rare diseases and hear a desmoid tumor, you know, very often we hear from patients that it took five doctors or more before this diagnosis even became clear

Mrinal Gounder: To one. So initially, what happens is when this diagnosis does come it is really you're met with experts, you know, you meet doctors you meet surgeons you meet oncologists. And frequently people will say, you know, I've never seen this before. I don't know how to treat this

Mrinal Gounder: Maybe I'll look it up. But this is not this is really a place which is extremely isolating and and frightening for patients when when patients deal with rare diseases and and especially

Mrinal Gounder: rare cancers, where one, we all go to our doctors, hoping that they would have answers, but when they don't have any answers, it becomes an extremely frustrating, depressing process and anxiety-provoking in so many different ways and and

Mrinal Gounder: It this in this context it is in this context of dealing with a rare disease that a patient advocacy group is so essential and

Mrinal Gounder: When patients who I meet who say, you know, they there they were. They had a desmoid tumor and they really didn't know what it was their doctors

Mrinal Gounder: Had never seen it before, never heard of it before and then they searched on the internet and they came across, and they found this DTRF and they joined DTRF and it was such a people tell me that it's such a relief.

Mrinal Gounder: To be part of this organization.

Mrinal Gounder: And it is and and and people like Marlene

Mrinal Gounder: And Jeanne you know as founders have come together to put this 15 years ago but have really brought together hundreds and hundreds of people scientists in advancing the

Mrinal Gounder: cure for a desmoid tumor. So the what I'm going to talk to you today is really sort of the work that the DTRF has done

Mrinal Gounder: In bringing together new drugs and new therapies and new people into this field. 15 years ago there was really not much happening in fact even 10 years ago, I can say

Mrinal Gounder: There's really not much happening at all. So how does the patient advocacy groups such as DTRF really function in such a successful manner.

Mrinal Gounder: So the first thing is this the patient advocacy group itself

Mrinal Gounder: Plays multiple different roles. So previously, I showed you that you know there's thousands and thousands of scientists and patients and people all come together to try to come up with a new drug saying colon cancer or say a vaccine for COVID

Mrinal Gounder: But for rare diseases which are neglected, there's really only the patient advocacy group such as DTRF becomes sort of the keystone that brings all these different stakeholders together.

Mrinal Gounder: So first and foremost, and the most important function of the Desmoid Tumor Research Foundation really any patient advocacy group is to provide support for patients, you know, this is a isolating diagnosis, family members, you really don't know other people who have desmoid tumors, so

Mrinal Gounder: So coming into DTRF, whether it's this meeting or the Facebook or any of the other virtual or non virtual things

Mrinal Gounder: Really immediately provides people a sense of relief, a sense of connection, a sense of togetherness and that sense of isolation evaporates.

Mrinal Gounder: So the number one function DTRF really does is, or really any patient advocacy does is help support patients.

Mrinal Gounder: And whether this is through just bringing people together or organizing events for fundraising, whatever it is, ultimately, this is your organization where you can lean on to other people for support, no matter where you live, whether it is just in the United States or Canada, Europe globally.

Mrinal Gounder: This is ultimately an umbrella a safe place for people to come to get answers and to search for answers as well.

Mrinal Gounder: So that's the fundamentally most important thing. The second thing is, as I mentioned before,

Mrinal Gounder: One of the most essential aspects of bringing new drugs or to bring a cure or better treatments for disease is to start with basic research. So we want to understand what is a desmoid tumor. How does it grow.

Mrinal Gounder: What makes it grow. What triggers it what I had a great surgery. But why did it come back. These are fundamental basic questions that we need to understand

Mrinal Gounder: In in in this space itself. You know, before DTRF there were certain people certainly working on desmoid tumors there were certainly scientists working on desmoid tumors tumors.

Mrinal Gounder: But they were very few and they were definitely in silos, you know, people would come out and present their work in small meetings.

Mrinal Gounder: Very high likelihood that the other person working desmoid tumors may not even be aware that somebody else is working on it. So what DTRF has really done over the last

Mrinal Gounder: At least for the last 10 years or so is start bringing researchers together. So those people who had some interest all the funds that you raised

Mrinal Gounder: The funds were provided to further accelerate their research to say here's a \$50,000 here's \$100,000, you know, hire people to start working on these basic questions.

Mrinal Gounder: And when they started putting the seed grants together

Mrinal Gounder: More and more people started coalescing around studying desmoid tumors and researchers need money

Mrinal Gounder: To do this research to buy equipment to do to answer their questions. And that's what the Desmoid Tumor Research Foundation did and all with your money that you raised

Mrinal Gounder: And through philanthropy and through other granting mechanisms that money came together to support these researchers

Mrinal Gounder: And these researchers then invited other researchers to come in and start studying about desmoid tumors. And this is just in 2018 the number of different researchers from across the globe

Mrinal Gounder: Studying desmoid tumors. There are people who are studying at the very basic level of just the cells of desmoid tumors and others are working on a mouse model. Others are working on

Mrinal Gounder: frogs that grow desmoid tumors all of this to understand how does this start. Why does this start. How can we stop it. and so on and so forth.

Mrinal Gounder: And right now, you know, there are many, many there are dozens of laboratories around the world where people are growing desmoid tumor cell lines from patients who give it to pattern.org

Mrinal Gounder: Or any other mechanism through their hospitals, there are people in Belgium, who have now grown a frog that grows a desmoid tumor and now they can put

Mrinal Gounder: Specific drugs to it try to understand why does this frog develop desmoid tumors. There are mouse models for desmoid tumors. All of this is to add towards the greater knowledge base of desmoid tumors itself.

Mrinal Gounder: And this one, as I mentioned before, this is part of pattern.org where you can sign up and tissue that if it is normally collected can go to Broad

Mrinal Gounder: The Institute, which is part of Harvard and MIT where they are now growing the cells for basic science researchers, such as Dr. Jesse Boehm and Mush to work

Mrinal Gounder: On figuring out the fundamentals of desmoid tumors itself. The next aspect of this is, yes, it's great to do all this basic research.

Mrinal Gounder: But how do you take it to the next step and frequently, you know, scientists, they're very good at doing something at the very basic level of molecular biology.

Mrinal Gounder: But they may not have the skill set to take it to the next level to patients. So this is where the Desmoid Tumor Research Foundation

Mrinal Gounder: And the patient advocacy group has started engaging with people who are researchers and conditions to treat patients

Mrinal Gounder: To see how can we bring people who are in basic research and clinical research together so that what we learn in the in the lab can now be translated

Mrinal Gounder: Into the clinic where things that appear promising can now be brought together. And more importantly,

Mrinal Gounder: Also for doctors who are treating patients with desmoid tumors and these remember are very few patients to begin with. So one doctor may see three or four desmoid tumor patients in a year.

Mrinal Gounder: But now when you bring 10 20 30 doctors together it really starts multiplying the knowledge starts starts really magnifying and it's an exponential growth of what happens

Mrinal Gounder: And here's an example of how DTRF really collaborated with the European desmoid tumor and rare disease groups

Mrinal Gounder: And many different foundations to bring together desmoid tumor surgeons, pathologists, radiation oncologists, medical oncologists together to say, Can we all agree on how we should be managing desmoid tumors?

Mrinal Gounder: When is it safe to observe? When is it okay to do surgery? When is it not okay to do surgery? When should you start a drug?

Mrinal Gounder: Should you do radiation or not? So all of these people came together to agree in writing together this what's known as a global consensus paper and these are people from Japan and

Mrinal Gounder: And Europe and the United States and Canada coming together to say let's agree on how to treat this not that you know these are, this is not a mandate, but a general guidance in terms of how we should be thinking about these diseases.

Mrinal Gounder: And the Desmoid Tumor Research Foundation itself also partnered with another organization known as the National Organization for Rare Diseases.

Mrinal Gounder: To say, can you study, can you include desmoid tumors as part of your registry to see how does a patient do from the time that they were diagnosed to

Mrinal Gounder: The time that they have to start surgery or chemotherapy or or or maybe nothing or just observation. So this is a natural history study where now there are 1500 people

Mrinal Gounder: And Dr. Kelly Mercier, who is part of DTRF has spearheaded this effort. And I know many, many of you are already participating in this study.

Mrinal Gounder: So here's an example of how the Desmoid Tumor Research Foundation engaged me. So almost 10 years ago you know I had found in my clinic that this drug, Sorafenib

Mrinal Gounder: Seems to work. And here is a young man who was 35 years old with a desmoid tumor. He had failed all chemotherapies he's had multiple other things radiation

Mrinal Gounder: And the surgeon said the only way we can really deal with your pain and and all this issues is with an amputation of the arm and the young man was frightened and did not want to take that option at all.

Mrinal Gounder: He, he saw me in my clinic and, you know, we said, well, why don't we try this drug Sorafenib. We really didn't know much about it at all. And we did

Mrinal Gounder: And he had a really nice response. And you can see this on one side, it's bright white and the other side it's completely burnt out.

Mrinal Gounder: And at that time, we published this paper about 20-25 patients. It looked promising, we published it in a nice journal

Mrinal Gounder: And as a researcher, I was ready to move on to other diseases or other things or or whatever was on my plate at that time.

Mrinal Gounder: It was at that moment that Jeanne and and Marlene came to me and they said, you know, we read your paper. It looks really

Mrinal Gounder: Promising. Can we get an FDA approval for this drug. And in many ways, it was a very naive question for them to ask

Mrinal Gounder: Because the short answer is absolutely not. You cannot take a study like this that was done in a small clinic by you know a few people with a few patients and take it into the market.

Mrinal Gounder: But it was out of their naive question that made me think, well, you know what, maybe we should work on taking this to the next step.

Mrinal Gounder: And I can honestly tell you that if it were not for the Desmoid Tumor Research Foundation advocacy

Mrinal Gounder: I don't think this paper would have really gone on to the next steps. And it's really with their funding to fund some of the corollary to work and a lot of the pushing and the urging and the

Mrinal Gounder: And really saying, look, we really need something for our patients that led us to, you know, to two years of planning led to a Phase three study. And this was an international study in US and Canada.

Mrinal Gounder: With hundreds of sites that were open. And we said, well, let's study this drug Sorafenib and we did

Mrinal Gounder: And one of the first thing that the people who thought it was impossible to do a research in rare cancer, such as desmoid tumors they said, you know, it's too rare. You're not going to find the patients, you're not going to be able to enroll all patients in time.

Mrinal Gounder: And the Desmoid Tumor Research Foundation really came through. And they said, no, we know we will

Mrinal Gounder: We will inform our patients about this study and and people became aware of it by word of mouth through internet through the DTRF website

Mrinal Gounder: And we set an incredible record in accruing patients to this huge Phase three clinical trial, people thought it's going to take five years to do it. The study was completed in just about 17 months or so.

Mrinal Gounder: And it was really the power of patient advocacy that helped even envision and complete this phase three clinical trial.

Mrinal Gounder: And we of course published this in a nice journal and now we're thinking about how to take it to the next steps.

Mrinal Gounder: And there are other drugs. For example, you know, you'll hear from Dr. Cunningham later on. This is the beta catenin inhibitor, which is a phase one, phase two clinical trial that is going on.

Mrinal Gounder: When this drug first came about they did not, the company, I can tell you did not come to any of the clinicians they did not come to the scientists

Mrinal Gounder: To say, you know, we're interested in this drug, how can we do it. They actually went straight to to Marlene and Jeanne. It was really Marlene and Jeanne's introduction

Mrinal Gounder: And putting them in link with this bigger infrastructure community that that this patient advocacy has built that gave companies like Iterion or SpringWorks

Mrinal Gounder: The confidence that they can, they have the knowledge base. They have the experts, they have the patience to bring together new drugs into the market.

Mrinal Gounder: And this drug, you know, from SpringWorks. You'll hear

Mrinal Gounder: Mary Smith talk about this shortly. You know, this was a Phase three clinical trial that was complete. But most of you will not know that this was originally a drug made by Pfizer

Mrinal Gounder: And Pfizer had tried this on many patients in big larger clinical trials with cancer patients.

Mrinal Gounder: And found that, you know, it was not helpful in say breast cancer, lung cancer, pancreatic cancer and they actually stop this drug. They had no intent on developing this drug at all. It was basically put away.

Mrinal Gounder: It was a lot of urging by the Desmoid Tumor Research Foundation by Dr. Bob Maki who's now at Penn was really an advocate to take this drug from Pfizer and bring it out.

Mrinal Gounder: And and and bring it into desmoid tumors. Were it not for the patient advocacy groups urging

Mrinal Gounder: This study, would this whole thing would not happen at all. So it was a lot of behind the scenes, pushing, pushing, pushing to come to this to come to this place.

Mrinal Gounder: And just earlier this week, the same drug nirogacestat or the gamma secretase inhibitor from SpringWorks is also available for children

Mrinal Gounder: Through the Children's Oncology Group across the United States. So a lot of this again by Dr. Aaron Weiss and others here who have pushed for push for this.

Mrinal Gounder: And on one end, you know, engagement. So we've talked about basic research, clinical research doing new clinical trials engaging, but the other key component is also

Mrinal Gounder: Engaging with the regulatory agencies such as the FDA. So here when I did that study with Sorafenib in the phase three, one of the questions that came up in our conversation with the FDA is

Mrinal Gounder: You know we are measuring how tumors shrink, but can we measure how patients feel? How can we take that into account? Does Sorafenib

Mrinal Gounder: Make your pain improve? Does it make your mobility improve? And at that point, we did not have the right tools or the right questionnaires to answer that question in for desmoid tumor patients to use as part of a clinical trial. So Marlene and Jeanne

Mrinal Gounder: Really organized a conversation with the FDA and brought people who are experts in this field

Mrinal Gounder: And successfully came up with a questionnaire. There were a lot of people even experts in the field said that this could not be done. That such a questionnaire and cannot be developed and we and we went ahead and did it and this is Dr. Jean Paty

Mrinal Gounder: Who is an expert in patient advisory group and is also a part of the medical advisory board who heard the story of desmoid tumors who heard the story of the patient advocacy group who was so

Mrinal Gounder: You know he he he he was so impressed with the passion that that the patient advocacy group board and he really did a lot of his work at half the price of what they normally charged so

Mrinal Gounder: It's really sort of the power of patient advocacy group to bring all these people together.

Mrinal Gounder: And what's nice is that with this new questionnaire, we've now put it back into some of these major clinical trials, such as the SpringWorks trial, the Iterion trial.

Mrinal Gounder: The pediatrics trial to ask the question, yes, your tumor shrink, but do you also feel better? And this is one of the questionnaires that will help answer that essential element of the of the research as well.

Mrinal Gounder: And the last part is all of this is happening, but how do you also keep this momentum going forward? How do you keep this knowledge dissemination happening?

Mrinal Gounder: And again, the patient advocacy group DTRF has brought together like all these experts together. So this is a meeting of patients in 2007 in a small room in a small hotel, and this is in 2018, hundreds of people are now participating and similarly, this is

Mrinal Gounder: The late Dr. Dina Lev, who was one of the earliest and most serious researcher in desmoid tumors in 2007 speaking, the only sole single speaker in 2007 from the scientific community. And this is in 2018

Mrinal Gounder: All the new researchers, clinicians, everybody have come together and this was from this was from yesterday and this is only one of three pages screenshot that Lynne captured yesterday. So you can see sort of how this is all building towards a critical mass.

Mrinal Gounder: And again,

Mrinal Gounder: Marlene and Lynne and Jeanne have really, you know, every time there is a paper that is published on desmoid tumors

Mrinal Gounder: They scour the internet. They bring the best high quality paper together so that all of you can read it and all of us can also refer to this one single central bank of knowledge base.

Mrinal Gounder: So 10 years ago or even five or six years ago when if someone had asked me that, if you have a rare cancer or a rare disease, what do you need

Mrinal Gounder: I think most people including myself would have said money we said you need money you need a lot of money to move the field forward.

Mrinal Gounder: But now I don't believe it's money and I think there is a tendency in society to say if there's a problem. We just need to put a lot of money in it.

Mrinal Gounder: But I think what I've learned in my involvement with DTRF as well as other patient advocacy groups that are highly, highly successful

Mrinal Gounder: Is that you want to build a critical mass critical mass building together critical mass is far is really the first, second, and the third most important thing that

Mrinal Gounder: A patient advocacy group can do to to advance that field. And this involves bringing patients to bring researchers, scientists, pharma, industry,

Mrinal Gounder: Knowledge base, everything together in one place so that we can learn from each other and we can take this to the next step. And it's out of this synergy

Mrinal Gounder: That we can do high risk projects out of box thinking to really drive that innovation. And funding, generally, in my opinion, follows when people see that there is a critical mass.

Mrinal Gounder: Somehow they have confidence that this organization will get the job done and then industry comes together and becomes sort of this great cycle that just keeps going on and on.

Mrinal Gounder: And I yesterday, looking at the research meeting, I really felt that we've come a long, long way and we really come together to form this critical mass of all the people necessary to move, move the field forward.

Mrinal Gounder: So in conclusion, the power of patient advocacy in rare diseases is to organize. So it's to build critical mass, spread the word and go global.

Mrinal Gounder: And then to have a common goal and the most, the most important goal, I think, is to refuse to accept the status quo and to keep pushing forward for better things to go for a cure.

Mrinal Gounder: Or two or to go for something that is really transformational and paradigm shifting

Mrinal Gounder: And then to unite all of us need to come together. Scientists, social workers, industry, developers, nurses, all of us patients have to come together in this common goal and mission.

Mrinal Gounder: And, of course, to improve the knowledge, diagnosis, treatments, and quality of life. And lastly, to support each other patients, doctors, caregivers worldwide to to to do that.

Mrinal Gounder: So I will end by saying this. And I was really moved by something in the in the in one of the political conventions. Julian Castro said

Mrinal Gounder: He said, in the end, the American Dream is not a sprint, or even a marathon, but a relay. And it's a relay where everything that we learn we

Mrinal Gounder: pass it on to the next generation understanding that the work that one generation does will remain unfinished, but will pass on to the next generation.

Mrinal Gounder: Of patients, doctors, scientists and that's how we really move the field forward and this is

Mrinal Gounder: That one day, especially in desmoid tumors we wake up when a patient in the future has has a diagnosis of desmoid tumor, they're not looking at despair, but looking at a new morning with hope. Thank you.

Jeanne Whiting: Thank you, Dr. Gounder. Thank you so much for that wonderful presentation. I think because we're over time here we're going to

Jeanne Whiting: Ask attendees if they want to submit any questions for Dr. Gounder to do it in writing, many of the questions that have been posted

Jeanne Whiting: Probably also apply to our next speaker, Dr Breelyn Wilky from University of Colorado, Denver. So we'll turn the time over to Dr. Wilky for an overview of desmoid tumors.

Breelyn Wilky: Sorry about that. Technical difficulties, can everybody see my screen. Let me move everything

Breelyn Wilky: Everybody can see

Breelyn Wilky: Okay.

Breelyn Wilky: Great. So I'm Bree Wilky and from University Colorado and this is going to be a little bit of a whirlwind tour to give you an overview of desmoid tumor 101.

Breelyn Wilky: Many of you are already experts, but it's always nice to take a few minutes and just get everybody on the same page. And so that's what we're going to do.

Breelyn Wilky: So first and foremost, to understand a desmoid tumor, we have to talk about one of the most mighty cells. And that's a fibroblast.

Breelyn Wilky: So a fibroblast is a connective tissue cell. And what that means is, these are cells that hold the structures of our body together.

Breelyn Wilky: And I describe this often as the gristle on the chicken breast. So when you peel the skin off. There's that white material that sort of holding everything together.

Breelyn Wilky: And so what can happen is fibroblasts are normally only growing when there's an injury or repair that needs to be made, or to replace worn out cells otherwise they should just be hanging out

Breelyn Wilky: Sitting there holding things steady and not actively growing unless there's an injury. And so all of that process if they do need to repair, something is tightly regulated

Breelyn Wilky: By a series of genes, including beta catenin, APC and some other genes. So if, if there's an injury or if those cells get activated and don't turn off

Breelyn Wilky: This is what happens in a desmoid tumor. So there's a mistake that causes these pathways to always be active.

Breelyn Wilky: And ultimately, those fibroblasts overgrow and form a mass or tumor. And that is a desmoid. So if you look under the microscope at desmoids,

Breelyn Wilky: They look pretty normal. The cells don't look that bizarre but there definitely are too many of them.

Breelyn Wilky: It's also important to know that these desmoids cannot metastasize or spread to other places. And so this is technically a benign tumor.

Breelyn Wilky: So it's super important to distinguish a desmoid from a sarcoma. So a sarcoma is can also come from a fibroblast but tends to have multiple more complex genetic mistakes or mutations.

Breelyn Wilky: Under the microscope, a sarcoma looks much more ugly. It looks more bizarre and importantly, these tumors can actually metastasize and spread and these are a cancer.

Breelyn Wilky: So, first thing you want to have a biopsy. Make sure you can tell the difference between the two. And also common question I get is that it's essentially unheard of for a desmoid to transform into a sarcoma. So that's reassuring.

Breelyn Wilky: What causes desmoids? There are two main groups of desmoid tumors called sporadic tumors. And then those that come from a disease called FAP or Gardner's syndrome.

Breelyn Wilky: And it's about 90% sporadic and about 10 to 15% FAP. So we, the way we can tell about these is basically again these mutations.

Breelyn Wilky: So most sporadic tumors come from beta catenin that gets flipped on and some of the causes of these tumors can be an injury. So surgery or trauma. Again, leading to something not getting turned off in the fibroblast when it's supposed to.

Breelyn Wilky: Hormone exposure, which you'll hear about from Dr. Raut here in a few minutes, including pregnancy. But I've also seen desmoid tumors in patients who've been treated

Breelyn Wilky: With hormones mainly estrogen for fertility or replacement therapy.

Breelyn Wilky: Any kind of foreign body like a breast implant or a bullet fragment or some sort of other foreign body that causes inflammation can be associated with desmoids.

Breelyn Wilky: Often patients asked me about diet. The answer is probably not. There's a case report of soy, which is an estrogen like material or food.

Breelyn Wilky: Potentially influencing a desmoid, but this is extremely rare and not well documented. Overall many times these are unknown so we don't have a great explanation as to why the desmoid occurred.

Breelyn Wilky: FAP, so again, this is an inherited gene. So all cells in a patient with FAP have a mutated or broken APC.

Breelyn Wilky: This is why patients can also get colon cancer in this disease and why patients can get multiple desmoids, because unlike sporadic where there's just one mistake in one potential spot

Breelyn Wilky: That leads to the desmoid formation these patients have an underlying tendency to develop desmoids so very different.

Breelyn Wilky: Treatment options. What do we do, there are many treatment options. And so, in the interest of time, I'm going to go through these pretty quickly.

Breelyn Wilky: First and foremost, we want to think about watching and waiting. Why? Because Dr. Gounder's studies showed that even patients who are on placebo

Breelyn Wilky: Could have up to a 20% shrinkage rate. We don't understand exactly why this is, but somehow, many people can have their desmoid ultimately, calm down and begin to regress without doing anything.

Breelyn Wilky: Additionally, up to 50% of patients will be stable at five years without therapy. And so this is always a great option.

Breelyn Wilky: Surgery can be the right answer for some patients, but again we have to weigh the risks of the surgery and the high chance of recurrence, which is usually could be up to 40 to 50% and some series.

Breelyn Wilky: Radiation treatments, very effective. However, carries other risks like damage to the surrounding tissue as well as the risk of secondary cancers.

Breelyn Wilky: There's some really new technologies we're very excited about that are called ablations.

Breelyn Wilky: These basically involves putting a needle into the desmoid tumor and either freezing, burning, microwaving, electrocuting there's a variety of different strategies.

Breelyn Wilky: And then this technique called HiFU or high frequency ultrasound, which is being explored probably most rigorously at Stanford really exciting technology to allow for a less invasive management of a desmoid tumor.

Breelyn Wilky: From a systemic treatment approach, there's a lot of different drugs that can be used, ranging from full intensity chemotherapies

Breelyn Wilky: To targeted chemo pills like Sorafenib, Imatinib and others, including nirogacestat, the new gamma secretase drug

Breelyn Wilky: And then we've also used estrogen blocking therapies. So really, how do we pick the treatment that's right for you or what do we mean by the treatment actually being effective?

Breelyn Wilky: Keep in mind to disappear your desmoid is actually very rare. We are aiming for shrinkage. If we can stabilization can often be very beneficial.

Breelyn Wilky: And ideally you want death of the tumor where it goes from being an active breathing desmoid back to a scar tissue collagenized area. And hopefully along the way the goal always has to be improvement and symptom and quality of life with any or all of these factors.

Breelyn Wilky: So picking the right treatment we talked about your symptoms. We talked about the location. How badly do we need a shrinkage or response.

Breelyn Wilky: We look at the growth pattern over time. I saw a question about the rate of growth of desmoids. This can vary. There are people that may grow a few millimeters per year and people that may grow a few centimeters per year.

Breelyn Wilky: We look at whether there's obvious estrogen exposures, patient preferences between oral or IV drugs and other medical conditions that may complicate therapy.

Breelyn Wilky: Common issues when you're picking a treatment approach. There's a lot of anxiety over watching and waiting and doing nothing.

Breelyn Wilky: How long are we willing to wait for a response, just again going with that anxiety piece. Some of these treatments can take six to 12 months to see maximal shrinkage, or even beginning to see shrinkage.

Breelyn Wilky: Can we get to better options? If we can shrink or kill the tumor and are always are there clinical trials or other options that might be available.

Breelyn Wilky: So I'm going to go through these quickly. These are my top 10 tidbits that I think every desmoid patient should think about when you especially when you're first diagnosed

Breelyn Wilky: Find a team you trust. Consider a second opinion at a sarcoma center or have your case presented at the DTRF virtual tumor board that Dr. Weiss will probably mention

Breelyn Wilky: Screen for FAP, if young, family history, colon cancer or multiple desmoids.

Breelyn Wilky: If you're thinking about surgery, we have to look at how invasive or how big the healing is going to be from the surgery with the high risks of potential recurrence

Breelyn Wilky: If you're doing medical treatment, balance the need for desmoid shrinkage with the risks and side effects of the treatment, the more aggressive the therapy, the higher the chance of a shrinkage, but more side effects and even long term risks.

Breelyn Wilky: They don't have to disappear. We want to get it back to a scar and trying to take it out, can actually cause more harm than good.

Breelyn Wilky: With good monitoring pregnancy is not prohibited with a previous or current desmoid tumor. Everyone's story is different.

Breelyn Wilky: Desmoids may not be cancer, but they can have the same impact on patients lives. So, ask your doctor demand that your doctor advocate and educate for you, particularly for insurance, disability and work restrictions.

Breelyn Wilky: And then finally, as we've already heard DTRF is a tremendous resource for support, research and connections. So again, sorry for flying through that but I'll take time for questions now. Thank you.

Jeanne Whiting: Uh Breelyn, we have a very short time period for questions, could you pick out a couple of essential ones you'd like to answer for the group.

Jeanne Whiting: And I suggest that we extend this to perhaps another discussion. Another time for even more detailed questions, you can also put your questions in the Q&A

Jeanne Whiting: I will also say that these video presentations will be accessible after this meeting after this live session. So you'll have time to go back through it at detail probably want to watch it many times.

Breelyn Wilky: These are some great questions. I agree. Let's just go ahead and and and keep submitting your questions on the Q&A. A we will answer these after the meeting and potentially

Breelyn Wilky: You know, we can set up a time to chat. But otherwise, I think our other speakers aren't going to have time to have to get their talks. Thanks.

Jeanne Whiting: Okay, let's go on to the next speaker of Dr. Aaron Weiss is going to talk about pediatric and desmoid tumors.

Jeanne Whiting: Okay.

Aaron Weiss: All right. You can see this. Okay.

Aaron Weiss: Okay, so I'm just going to give a brief overview of desmoid tumors and children. Breelyn touched upon a number of things.

Aaron Weiss: That I'll you know, talk about as well. There is a lot of overlap between pediatric and adult desmoid. And to be honest

Aaron Weiss: We still don't really understand the differences. Very well. But I thought I would just highlight some some differences in pediatric desmoids that are a little bit nuanced compared to the adult

Patients

Aaron Weiss: So this is my disclosure

Aaron Weiss: So in terms of incidence and causes in children.

Aaron Weiss: We really don't know the true incidence in children, honestly. We're not even sure of the true incidence in adults because it's very hard

Aaron Weiss: To capture that information. But we do know there's about 15,000 children diagnosed with cancer per year and as Breelyn said, even though it's not maybe technically a cancer, many of us think of it as a cancer and certainly it tends to fall within the oncology

Aaron Weiss: Realm, and therefore we treat these patients typically in pediatric cancer centers. But generally, we think of these as about less than point 0.1% of all pediatric cancer.

Aaron Weiss: Most of them, as you heard occur spontaneously and children without any known predisposing factors which can be very frustrating. That's the number one question people ask is where this came from. And we often aren't able to provide a very good answer.

Aaron Weiss: Typically, we see a peak incidence between the ages of six to 15 and then another one from puberty to 40 years of age in women.

Aaron Weiss: So, so this is something that we will, and do see in children is not an exclusively adult adult process. There tends to be a slight male predominance, but that there is for obvious reasons, a female predominance during, during adolescence.

Aaron Weiss: So trauma, you had heard that we have a really good understanding at least now. And even though we don't exactly know the specific cause that there is

Aaron Weiss: Typically, some local trauma that may precede the development of desmoid in a number of cases and in children. We think this happens about 20% of the cases.

Aaron Weiss: Abdominal desmoid tumors followed surgical trauma in that same region in this, we believe happens typically within five years of that surgical surgical trauma.

Aaron Weiss: So it suggests that there's an underlying defect in connective tissue repair during wound healing.

Aaron Weiss: You heard a little bit about FAP just specifically in regards to children.

Aaron Weiss: The peak, the children that tend to get FAP tend to be younger, they tend to be male and they typically have abdominal wall or mesenteric locations for their desmoid tumor.

Aaron Weiss: So when we see patients of these young ages as Breelyn mentioned, it'll often behoove us to do this testing because it has significant implications for this patient, as well as multiple family members.

Aaron Weiss: Tumor location age. We also have some pretty good evidence that children in terms of where these things may appear tend to be a little bit different than adults, those that get in the head and neck area tend to be younger than those that get it in the torso, or in the extremity.

Aaron Weiss: And so head and neck region is an area that we think about often in those young presenting patients.

Aaron Weiss: So how about management because that's certainly I think one of the trickiest things

Aaron Weiss: Well surgery was mentioned. And I'd say, historically, that was the primary treatment for desmoid tumors in children and most the time

Aaron Weiss: As oncologists, we would find out about these patients after the fact.

Aaron Weiss: Even though ideally for any type of cancer, it would be nice for us to see these patients first so that we could help direct care and allow some of the surgeons who may not know some of the more current guidelines of what the, what the practice is.

Aaron Weiss: But even with surgery and even with complete removal, as mentioned, there is a fairly high recurrence rate.

Aaron Weiss: And often patients undergo multiple resections in just in pursuit of a cure or removal of the disease.

Aaron Weiss: And there are a lot of post surgical complications, particularly in children. As you can imagine, this is lifelong

Aaron Weiss: For these young children to have to endure and there and the other obviously concern with surgeries that just the surgery itself might stimulate more desmoid tumor growth.

Aaron Weiss: So radiation, I have to say, in children. This is quite controversial and most of us do not use this front line or even in subsequent

Aaron Weiss: You know refractory type tumors, we rarely use this intervention, unless it's

Aaron Weiss: Really an emergency, because of the long term effects and treatment related problems. This can have in terms of function of the of the

Aaron Weiss: Location and stiffening and limited in motion, and a lot of nerve and muscle complications.

Aaron Weiss: So when it comes to medical therapy in children, vinblastine and methotrexate, which is a type of chemotherapy given in low dose

Aaron Weiss: Over kind of like a weekly every other week period of time is probably are considered our frontline. It was the first clinical trial actually in children

Aaron Weiss: With desmoid, where they tested this and was shown to be to have benefits.

Aaron Weiss: There have been other studies, there was a clinical trial, looking at hormonal therapy. However, this didn't really have great outcomes compared to the

Aaron Weiss: Previous trial and there were a lot of females who developed ovarian cysts. So, at least in children. This isn't really one of our frontline modalities.

Aaron Weiss: So what about alternative therapy approaches in children? Hydroxyurea is

Aaron Weiss: Commonly used, but it's important to realize that, although it's world well tolerated, because we have a lot of experience with other diseases, such a sickle cell disease and using this

Aaron Weiss: We really don't know the benefit and there has been no clinical trial data to date. It's all retrospective, looking back. So this isn't usually our frontline therapy, but at least we sometimes consider it.

Aaron Weiss: Tyrosine kinase inhibitor well studied and as Dr. Gounder mentioned, these are all available to us, however, and we know there's generally safe

Aaron Weiss: But, and there you can take them orally and there's beneficial

Aaron Weiss: Results in adults. But really, the long term safety in children is unknown, and we don't have any clinical trial data in children. So even though we do use these, you do have to keep that

Aaron Weiss: In mind. I will mention, and this was just mentioned on the earlier talk that just this week,

Aaron Weiss: A gamma secretase study for studying nirogacestat just opened through the Children's Oncology Group and

Aaron Weiss: Anyone who has a child with this tumor or any type of cancer can be treated in any medical center essentially in this country in North America as well as Australia, New Zealand for desmoid tumors.

Aaron Weiss: I'm just going to quickly mention here. These are some of the alternative local control options that Breelyn mentioned, we also use these in children at times, but generally

Aaron Weiss: They're at some of the larger centers that would have more experience. But these are safe. Most often, especially in children.

Aaron Weiss: With minimal complications. And so it's a really important thing to think about when other options are not available.

Aaron Weiss: And I don't want to forget this watch and wait approach. Not only is it used in adults. But in Europe, where a lot of this started

Aaron Weiss: There was a study where they actually observed children with desmoid tumors. And if they once they exhibited progression or symptoms,

Aaron Weiss: They would get treatment, but there was a good quarter of the patients who never required any type of therapy, you either had stable disease or regression of their tumor. So oftentimes we would take this approach in patients that were relatively low risk.

Aaron Weiss: So ultimately, how does one make individual decisions for their child with a rare disease and a relatively limited data?

Aaron Weiss: Well, I think, as Breelyn mentioned seeking opinion from someone with pediatric desmoid expertise is always beneficial.

Aaron Weiss: There is a desmoid tumor virtual tumor board that the DTRF sponsors that's been very successful in the last three years, and you're if you have a case

Aaron Weiss: And you're interested in having your case presented, please just reach out to your provider.

Aaron Weiss: Or to Lynne and we can work to get that case presented. There's also a registry, but I will point out that only 16 pediatric patients had been included in this registry out of

Aaron Weiss: A large number. So we would you know if you are a parent of a child or someone here who's listening who had pediatric desmoid tumor, it's important to get that data so that we can learn more about the disease.

Aaron Weiss: And finally, as Dr. Gounder mentioned coming together to build evidence based approaches for these types of diseases is very important. And we're starting to do this in pediatrics as well.

Aaron Weiss: So future directions, is to gain a better understanding of the causes and biology of desmoid tumors and children understand the differences between children and adults.

Aaron Weiss: We're working on clinical trial development for children as you seen, we've had a few and we have one currently happening.

Aaron Weiss: And then ultimately better measures of treatment outcome and success than just a traditional shrinking of tumor and survival.

Aaron Weiss: How about, you know, using MRI to characterize these early markers in the blood that could help indicate whether something is helpful, and most importantly, quality of life, particularly in children, where we lack a lot of those measures, particularly in validations

Aaron Weiss: And that's the end of my presentation, I think, you know, based on time, we might save some of these questions till the end. And I can answer in written form.

Jeanne Whiting: Okay, thank you so much, Dr. Weiss, we will again have these presentations available after this meeting.

Jeanne Whiting: We do have a hard stop at 1220 we're going to go over time, a little but we have a hard stop to set up for the next webinar which starts at 1230 so we'll save any questions for extra time, we might have after Dr. Raut's presentation will turn the time over to you.

All right.

Chandrajit Raut: Okay, thank you, everyone. I can let me know. I think you can see my slides here.

Chandrajit Raut: So I'm going to talk on a very specific topic which is although it's a smaller topic than the sort of cross cutting talks, you've heard earlier today, it's critical. It's a critical topic for so many people in the desmoid community. And that's the issue of pregnancy and desmoid tumors.

Chandrajit Raut: And

Chandrajit Raut: Okay. So just to give you a little bit of background about this. I'm not going to reiterate what Dr. Wilky is already stated, but the term desmoid was first coined in 1838 by Johannes Muller

Chandrajit Raut: And John MacFarlane and 1832 previously before the term desmoid was used

Chandrajit Raut: Had described in an organized sarcomatous tumor between the layers of the abdominal muscles and women who had children. So this is probably a first real description of what we now know as it desmoid arising in or after pregnancy.

Chandrajit Raut: Desmoids are often diagnosed in young women during or after pregnancy. This raises concern about potential progression during the

Chandrajit Raut: Current pregnancy if it's diagnosed during the course of pregnancy or recurrence with the subsequent one. And this raises a lot of question is that it's also led to a lot of misinformation based on lack of data about

Chandrajit Raut: Family planning and there are limited existing data to guide women about desmoids and they're treating clinicians regarding future pregnancies. So we put together this study which we published in 2014 it was led by Marco Fiore in Milan and it combined data from

Chandrajit Raut: Milan from

Chandrajit Raut: Institute sorry Villejuif in France, Toronto and our institution here in Boston. And basically we combined our experience of women who had

Chandrajit Raut: Desmoids identified during pregnancy or had desmoids and then got pregnant or had desmoids that are in place or removed and tried to understand some natural history.

Chandrajit Raut: So the effect is of the study was some focus on three specific groups, those who had desmoids identified during or right after being pregnant,

Chandrajit Raut: Those that had desmoids in place that were had risen either sporadically or in this context initially of FAP, who later got pregnant and those who had desmoids removed in the past and who later got pregnant.

Chandrajit Raut: We wanted to identify risk of progression with watchful waiting, a risk of recurrence after resection and risk of recurrence during a subsequent pregnancy.

Chandrajit Raut: So these are the four institutions which combined data and we included women as described there we ultimately decided to exclude the FAP subset of patients just because we did not have enough individuals to really make much of

Chandrajit Raut: An analysis. We also excluded those with infantile fibromatosis and plantar and palmar fibromatosis.

Chandrajit Raut: And so, and we had a total of 92 patients that you see here on the one the first subset, those that that included women with pregnancy associated desmoids included 44 women.

Chandrajit Raut: Initially, those. And now one thing to keep in mind is that a lot of these patients that were treated

Chandrajit Raut: Were treated at a time when most of our management was focused on where there's a lot more surgery involved in initial management. And I think that

Chandrajit Raut: We're actually planning on updating our series on Dr. Fiore is going to lead that effort. Again, and we've discussed this in the last few weeks.

Chandrajit Raut: And I suspect that in that group will see a lot more individuals who are managed without surgery compared to our initial study

Chandrajit Raut: But in this first group of 44 women, we had 15 that were treated with surgery, 2 that were treated with various medical therapies that Dr. Wilky described and 27 that were treated

Chandrajit Raut: Without any surgery or any intervention, two of those women that underwent surgery had surgery during pregnancy and 13 had it postpartum

Chandrajit Raut: During during the course of pregnancy or immediately afterwards in their postpartum period, those that were treated initially with watchful waiting progressed.

Chandrajit Raut: Sorry 17 progressed, 10 did not progress and of those that progressed, those that did not progress, 10 were still managed with watchful waiting approach

Chandrajit Raut: Never required any intervention. Of those that did progress six went onto surgery, six went onto medical management and five were still managed with watchful waiting. So when we look at our entire group

Chandrajit Raut: Of 44 women 21 ended up having surgery. That number would probably be less now. Eight were treated with medical management and I'm curious to see what's going to happen in our updated series with that with this subset

Chandrajit Raut: And 15 were able to avoid any sort of intervention whatsoever. So a third did not require any intervention.

Chandrajit Raut: And this is just the percentages, which I'll just sort of skip through in the interest of time.

Chandrajit Raut: Now this is a case example that from the Milan cohort, which still sticks with me and

Chandrajit Raut: This was a young woman who was diagnosed with a three centimeter abdominal desmoid during her first pregnancy. Afterwards she was treated with watchful waiting had no growth postpartum

Chandrajit Raut: Then got pregnant again the tumor grew after a postpartum the tumor stop growing. And so she was again watched with just managed non operatively

Chandrajit Raut: Without any medical management. She had a third child. And again, the tumor grew and then she'll ultimately underwent surgery postpartum because the tumor had gotten to the point where it was causing discomfort.

Chandrajit Raut: So then what about people who have had it women who've had a desmoid that's been removed and then get pregnant. We had 28, 29 women who fit that description. 19 primary desmoid

Chandrajit Raut: Presentations, 10 recurrent.

Chandrajit Raut: So these are unresected desmoids. 16 progressed during pregnancy, 13 did not progress. Of those that progressed, six underwent surgery, two were treated medically, and eight were watched

Chandrajit Raut: And thus, 55 women, 55 percent of women with unresective desmoids progressed during pregnancy. And that's something to keep in mind and and this number source, again, is one that sticks with me when when I advise women with the desmoid who are considering getting pregnant.

Chandrajit Raut: What's interesting is that those that were watched were managed with watchful waiting, did not

Chandrajit Raut: Progress further to a point that they required intervention, again, that was a selection bias there likely in terms of who we pick for watchful waiting.

Chandrajit Raut: And then the final cohort is the group that had previously resected desmoids, who then got pregnant. 19 women, 4 progressed during pregnancy and 15 did not

Chandrajit Raut: And so two of those required surgery, one was treated medically and one was treated with watchful waiting so about 21% of 19 against is a percentage of a small number of women

Chandrajit Raut: That had prior previously resected desmoids developed recurrence or progression of potentially microscopic disease during pregnancy. So to conclude, um, I think that what this tells us and and Dr. Wilky I think this was her take home point number seven.

Chandrajit Raut: Mentioned that having a desmoid does not preclude getting pregnant or getting pregnant again. In the past, I think, or something I learned from when I first gave this talk at

Chandrajit Raut: At the same Symposium, six years ago, was that many women had been told that should never get they should avoid getting pregnant and we currently have no evidence to support that recommendation.

Chandrajit Raut: Women should also not be advised to routinely have an abortion, if they're pregnant. There are individual circumstances that may impact the health of the mother or the child that may supersede these recommendations, but desmoids are not a contraindication to having children.

Chandrajit Raut: Desmoids arising during pregnancy or already present before pregnancy may grow

Chandrajit Raut: But over half of patients can avoid an operation. Some may need medical management, but many do not need any intervention whatsoever.

Chandrajit Raut: And those undergoing surgery can still recur although the recurrence rate seems to be lower than for other sporadic desmoid tumors and desmoids resected during pregnancy recur infrequently. So the majority women still do not required but 21% do.

Chandrajit Raut: Thank you.

Jeanne Whiting: Could I ask one question that is has been appearing?

Jeanne Whiting: What is the impact, if any, of the location of the desmoid tumor on all of this, all of these women? Were they intra-abdominal? If they have a tumor in the arm, rather than in the intra-abdominal area, how, how does all of this get impacted?

Chandrajit Raut: And this is an excellent question. In fact, I think one of the questions that was submitted.

Chandrajit Raut: Before the meeting addresses this as well. So most of the women that have pregnancy that arises have desmoids that arise during pregnancy seem to have abdominal wall desmoids often wreck the sheath unclear why potentially some stretching of the muscles that leads to

Chandrajit Raut: Essentially, some kind of scarring reaction, we don't really have the details. Those appear to have beta catenin mutations. But we are now that we're sequencing those particular tumors, we're finding some other mutations, which I hope will have more data on soon. The

Chandrajit Raut: Concern, of course, is for women who have a mesentary desmoid because if that grows that's going to potentially impinge on the growing gravid uterus.

Chandrajit Raut: And that could be a reason to either have surgery or, you know, talk to the gynecologist about management of the pregnancy. In our series of 92 women we the only

Chandrajit Raut: And again, this is a small subset of patients. The only patient that had to have a change in the plan, the management of her pregnancy because of the desmoid was one who had a desmoid

Chandrajit Raut: Within the vaginal canal, so she could not have a natural childbirth. She did have to have a cesarean section. But I think that the biggest concern is for women who have mesenteric desmoids that could

Chandrajit Raut: Affect or impact the the course of pregnancy.

Chandrajit Raut: What this one other point and I took out the slide in the interest of time, which is if I do counsel women who had

Chandrajit Raut: If they're going to have surgery for an abdominal wall desmoid and plan on getting pregnant again

Chandrajit Raut: That they need to work, not their surgeon should work very closely with a plastic surgeon. And so whenever I operate on a patient who wants to get pregnant again

Chandrajit Raut: I have the plastic surgeon come and do the reconstruction and the reason is that traditionally for

Chandrajit Raut: The abdominal wall defect that needs to be closed so there's there's a there's basically a gap in the muscle and to bridge that gap so you don't get a hernia, we have to put in, usually a piece of mesh.

Chandrajit Raut: The typical mesh that we use for most hernias is really has no real elastic property. It just doesn't stretch

Chandrajit Raut: There are other types of biologic meshes or flaps that can be brought into that can stretch better, particularly if the desmoid arose on the lower part of the abdominal wall.

Jeanne Whiting: Okay, thank you. As you all four have been reading through the questions we have about seven minutes left. Dr. Wilky, do you have a question that you're just anxious to answer. While we have a minute.

Breelyn Wilky: Yeah, there's, there's a few questions that again are going back to this question of, you know, this

Breelyn Wilky: Calling out to the DTRF and to others to tackle this benign versus malignant issue.

Breelyn Wilky: So benign and malignant are really pathologic determinations I mean it's it's this is not a comment on the impact from the disease or the fact that patients with desmoids can die from desmoid tumors, even though it's not cancer.

Breelyn Wilky: You know so I think I think that was what I was trying to get across in my talk is that although technically by the rules, these are these are locally aggressive tumors these don't spread, they don't

Breelyn Wilky: metastasize all of these things I certainly did not mean to downplay the you know the impact on quality of life and certainly from treatments

Breelyn Wilky: That can range from amputation or full blown chemotherapy, like you would for a cancer. So I completely agree to working with the DTRF and potentially trying to come up with a more accurate

Breelyn Wilky: Classification or, you know, and, and we've had these debates and other research workshops too where are we, is it better to call it benign because of insurance. So if you have a cancer that's a pre existing condition

Breelyn Wilky: Does that cause issues with you being able to keep your insurance or things like that. I mean, so there's both sides to it, but

Breelyn Wilky: I'm happy to talk more with people that that that came up quite a bit in these questions and I'm welcome other panelists please jump in with how you you counsel patients on this issue.

Aaron Weiss: Yeah, I have to say. I mean, that's exactly right. This it is a very, it really depends on the

Aaron Weiss: Specific definition, you're using versus the classification and but we understand that this, even if it's benign. It's not benign in most the time, and because we're oncologists

Aaron Weiss: We tend to think of these as cancers in terms of how we manage it and think about it and so

Aaron Weiss: It's really just in the terminology. But in terms of like being able to advocate and get treatment for patients, I mean, what we usually do kind of talk about them and express them in, in the, in the context of a cancer.

Aaron Weiss: Because it's important to stress to people who don't aren't familiar with this, what desmoid tumors that have how aggressive it can be and that it's it's not something that is typically benign for many people.

Jeanne Whiting: Well, the definition of benign, meaning it doesn't metastasize.

Jeanne Whiting: In the way other cancers do.

Jeanne Whiting: Right. And when you use that term that's what you're saying benign versus malignant right but in the context of the experience of the patient, the way the tumor can invade the local area very aggressively, it's a different description so

Jeanne Whiting: Okay. Thank you, Dr. Gounder did you have a question that you saw somewhere on the Q&A that you wanted to answer?

Jeanne Whiting: Yeah.

Mrinal Gounder: I think one of the questions that has come up quite often is the risk of someone already has a desmoid tumor. And, you know, was dealt with and

Mrinal Gounder: Thinking about a second surgery, whether a second surgery in the same location or different location would increase the risk of a desmoid tumor. And I think, you know, I think the jury's out there.

Mrinal Gounder: In in in and it's really sort of anecdotal evidence

Mrinal Gounder: I, I, the short answer is we don't know, but I've seen a lot of patients with desmoid tumors undergo surgery

Mrinal Gounder: For unrelated things do just fine. And there are some who who have tumors recur right after surgery. So, but I have to say the vast overwhelming number of people

Mrinal Gounder: With desmoid tumors or something, who need some other surgery generally end up doing well but i think i think Dr. Raut is much closer to this than many of us are maybe he can speak to this.

Chandrajit Raut: Sorry. Good. Could you clarify that I was just trying to respond to one of the questions.

Mrinal Gounder: Yeah, the risk of recurrence with surgery.

Chandrajit Raut: Yeah, so you know that the data are conflicting and I think that Bernd Kasper put together a nice chart in one of his papers that looked at various different series that looked at different rate, the rates of recurrence based on the use of negative versus positive margins and

Chandrajit Raut: Use of radiation and the data are all over the place. And so I think now that we rarely do surgery now, and really the only group that I seem to regularly consider for an operation of the women who want to get pregnant again after a

Chandrajit Raut: Desmoid in place, but we tend to be a little bit more

Chandrajit Raut: cautious about our margins and so that subset the recurrence rate seems to be lower. So we're kind of skewing towards a more favorable group, um,

Chandrajit Raut: So it's hard. You know, I think that there's been such a sea change in surgical management that that the data just different now. I'm not sure if that really answers the question, but

Mrinal Gounder: I think the question is if somebody has a desmoid tumor and say they needed some other unrelated surgery

Chandrajit Raut: Oh, yeah, yeah. So this comes up a lot, too. And I think what there was one question that came up, if they're if someone's undergoing IVF therapy, are they at risk for

Chandrajit Raut: a desmoid arising along the track of a needle or if they're going to get their gall bladder taken out, are they at risk. We just don't have data really to be certain about that. So ultimately, I tell individuals

Chandrajit Raut: It's best to have the treatment that you need, whether it's having a bariatric procedure for weight reduction or taking your gall bladder out or having a hernia repair.

Chandrajit Raut: And we'll just follow along. Because even if you get a desmoid, there's a really good chance we can avoid surgery on that anyway.

Chandrajit Raut: Does any other thoughts, Bree or Aaron?

Breelyn Wilky: Yeah, I agree. I mean, we get that question a lot, especially patients with FAP where they're like any any intervention, they're going to get a desmoid there. And at the end of the day if your appendix is blowing up that you need to take care of that. So yeah.

Aaron Weiss: I think it's a risk. It's always a risk benefit and it's important discussion to have, but we really don't know.

Aaron Weiss: I think in certain high risk patients like I do have patients who have like Gardner's syndrome FAP and do

Aaron Weiss: You know, have an increased risk of recurrence at surgeries. But you know, that's a small small number of patients. So I think you just have to weigh the importance of the of the procedure, you're having done

Jeanne Whiting: Thank you everyone for your participation. These are great answers great presentations. Again, they'll all be accessible. Anyone who is attending and wondering, you don't have to write us to ask

Jeanne Whiting: For these answers that we're going to be sending out or to access the video we will be sending you that, please be patient. It could take some time.

Jeanne Whiting: But if you're registered for the webinar or attending the webinar, you're going to get that in your email.

Marlene Portnoy: Thank everybody for coming.

Marlene Portnoy: Thank you.

Jeanne Whiting: Feel free to get up, take a break, get a drink of water and we'll see you again in 10 minutes. Thank you.