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BREAST CANCER PUBLIC MEETING ON PATIENT-FOCUSED DRUG DEVELOPMENT

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P R O C E E D I N G S

MS. GIAMBONE: All right. So we'll go ahead and get started. So good afternoon, everyone. My name is Soujanya Giambone. I am with the FDA Center for Drug Evaluation and Research Office of Strategic Programs and on behalf of all of my FDA colleagues, I'd like to thank you and welcome you all to the Patient-Focused Drug Development Meeting on Breast Cancer.

So it's really nice to meet so many of you and especially for all of you that I've been speaking to on the phone, it's nice to finally get to meet you all in person and we really appreciate that you're all here because we have so much to learn from you today.

So I'm the facilitator for today's meeting and I'm going to spend just a few minutes going over the agenda. You all should have a copy of that. If not, we have some copies out on the registration desk. And then I'll go over a few housekeeping items and we'll get started.

Okay. So we'll start off today with

some presentations from my FDA colleagues. They are going to provide some opening remarks, an overview of the patient-focused drug development initiative, and a background on breast cancer and current treatment options.

And then I'll come back and I'll go over the discussion format for the day. So we have two discussion topics. Topic 1 is on the disease symptoms that matter most to you as the patient, and topic two is on your perspectives on current approaches to treating breast cancer. And we'll have a panel discussion followed by a group discussion for each of those topics and that'll take us to pretty much the last half an hour of the day which we reserve for open public comment. And open public comment is -- it's basically a time that anybody in the audience, not just patients or patient representatives, but if anybody wants to share additional thoughts or perspectives that are outside of the scope of Topic 1 or Topic 2, we encourage you to sign up for open public comment, and you can sign up out

on the registration desk. There's a signup sheet there and we'll take signup until break time, and then we'll take a look at how many people signed up and how much time each speaker will have. And then we'll wrap up the day with some closing remarks.

So, as you can see, it's a pretty full day of discussion but we're really, really thankful that you're here and we're looking forward to a great day of discussion.

Just a few housekeeping items. The bathrooms are back out into the lobby area and if you make a right and go all the way down the hallway, you'll see the bathrooms there. And you will also see that we have a kiosk that sells basic snacks, drinks, sandwiches for you to purchase if you would like, so please feel comfortable to get up and stretch, take a break, get a snack if you need to. We want you to feel as comfortable as you can and, you know, do what you need to do to just be comfortable.

And also, I just want to mention this

meeting is being recorded and transcribed and within a few days after the meeting, the recording and the transcript will be available on the meeting website.

So with that, can I just have my FDA colleagues please introduce yourselves.

DR. KIM: Hello and thank you, everyone, for coming. My name is Geoff Kim. I'm the Division Director for the Division of Oncology Products 1, where many or most of the drugs related to the treatment of breast cancers are regulated.

DR. IBRAHIM: Hi. I'm Amna Ibrahim. I'm the Deputy Division Director for DOP1.

DR. WEDHAM: My name is Suparna Wedam. I am a medical reviewer in the Division of Oncology Products in the breast cancer group.

DR. McKEE: My name is Amy McKee. I'm the Clinical Team Leader in DOP1 of one of two teams that handles breast cancer products.

DR. MULLIN: Hello, I'm Theresa Mullin. I direct the Office of Strategic Programs in the

Center for Drugs and I am the lead for this patient-focused drug development effort for the Center. Thanks.

MS. SLAGLE: Hello, I'm Ashley Slagle with the Study Endpoint staff in the Office of New Drugs.

DR. BULL: Good afternoon. Jonca Bull. I direct the Office of Minority Health in the Office of the Commissioner.

MS. GIAMBONE: And could I have colleagues over here introduce yourselves?

MR. THOMPSON: Graham Thompson, Office of Strategic Programs.

MS. VAIDYA: Pujita Vaidya, Office of Strategic Programs.

MS. GIAMBONE: Great. Thank you so much. And with that, I'm going to turn it over to Amna for her presentation.

DR. IBRAHIM: Good afternoon again and welcome to today's meeting on breast cancer patient- focused drug development. AS I introduce myself, I'm Amna Ibrahim. I am the Deputy

Division Director of DOP1. Our division houses the breast cancer group where the drugs which are aimed at the treatment of breast cancer reside.

This is a very important meeting and we are looking forward to hearing from participants about their experiences and what they look for in treatments for this condition. We are happy to see so many patients and advocates in the audience and I understand that there are many others joining remotely from the web. Thank you for being here and being part of this meeting.

Today's meeting is one in a series of what is called FDA's Patient-Focused Drug Development Meetings. Theresa Mullin will be talking about this initiative in more detail in a few minutes.

Breast cancer has a significant public health impact on the country. It is the most common cancer among women in the U.S. We are really looking forward to hearing directly from patients about the symptoms they experience and how they view existing and potential therapies for

treating breast cancer and the challenges they face in prolonging life while also maintaining quality of life.

When we discuss drug development, we are referring to the process of identifying and evaluating potential therapies that can help patients treat their cancer. FDA's mission is to protect and promote public heath by evaluating the safety and effectiveness of new drugs. While we play a critical role in drug development, we are just one part in the process. We do not develop drugs or conduct clinical trials. Drug companies, often working with researchers or patient communities, are the ones who conduct the trials and submit applications for new drugs to FDA. We work closely with these drug companies throughout their drug development process. We are, therefore, glad to see such representation and interest in today's meeting from industry, academia, and other government partners in the room and on the web.

I want to spend a few minutes providing a bit of background on FDA's important role in

drug evaluation. For a drug to be approved for marketing, FDA must determine that it is safe and effective for its intended use. Our regulating decisions are based on science, medicine, as well as legal and regulatory standards. First and foremost, the drug must demonstrate a minimum standard of efficacy for its intended use. The safety of a drug should be such that the benefits of the drug should outweigh the risks. The FDA makes determination for the risk- benefit assessment for the new drug based on the totality of information provided by a sponsor in the new drug or biologic application which is a request for marketing authorization in the U.S. FDA benefit- risk assessment takes into account many factors such as the disease setting, the population of patients treated, presence of alternative therapies for the indication and the improvement provided by them, the magnitude of the demonstrated benefit, and the nature of the risks associated with the product.

What we hear today can help us

understand how patients view benefits and risks and will strengthen our understanding of what patients want to see in their treatment options. Sometimes we struggle with how to evaluate treatments that might have a small benefit to patients and a very large risk, so hearing what patients think about these issues can really help strengthen our benefit-risk thinking in those situations.

Thank you again for your participation and for being here today. We do appreciate it. I now turn it over to Theresa Mullin who will provide some background on FDA's overall patient-focused drug development efforts. Thank you.

DR. MULLIN: Thank you, Amna, and good afternoon again and thank you for joining us at this meeting today. This meeting on breast cancer is one of, for us, a series of meetings where we're launching this new effort under this reauthorization of the User Fee program, and I wanted to just spend a minute to put it in that context for you before we get into the specifics

of the questions and the content of the focus of our meeting today.

As Amna -- as Dr. Ibrahim mentioned, she referred to the risk-benefit or the benefit-risk assessment framework that's used by -- in our review of new drugs and even continuing to look at drugs on the market over time, two of the factors in that framework are the severity of the condition, sort of the experience of the patient and the severity of the impact of the disease on their life and, in fact, including the treatment on their life and what treatments are available today, and how well do those treatments work, and what is it like to have to use those treatment for the patient. And those two components really set the stage -- and this is w hat reviewers have told us over -- as we've developed this framework -- that sets the stage for their evaluation of the other evidence that they have, the benefit information, what they hear about the safety issues, how you might manage those risks. So those two components are really where we wanted to

focus and get more information.

And at the start of this effort in 2012, we realized that we had very limited means for getting that kind of information from patients. We have a patient representative program and that's very valuable except that the limitation there is that we have to put the patient representative who may or may not have the disease that is of interest and to -- they have to go through conflict of interest screening. We don't -- because we're talking about a particular drug, we have to make sure there's no conflict there, and so that really limits the input we can get and we know that you can't -- one person really would have an impossible job to represent the views of all the diversity of patients who may be experiencing a condition. And so we wanted to have a meeting structured not around a product but around the disease area so we could not have to deal with that screening and really get a much broader and more diverse range of input from people who are suffering from the disease or in

some cases, people or families who are living with persons and caring for people with a particular disease. So that was the motivation for this.

And we realize we -- you know, patients are the most critical informant, really, for these benefit-risk assessments because the patient is the one who will be using the drug and getting any benefit there is to gain and be suffering any harm there is, that they may be exposed to from the drug. And so how could we get a better richer and broader input from the patient community. And so this is a sort of experiment, if you will. We're doing these 20 meetings. Breast cancer is one of the 20 diseases that we chose and the Review Division identified breast cancer as one of the priorities for them and, you know, you'll hear more from their questions today about what they're hoping to gain and the opportunity there. And so these 20 are really giving us a test bed to figure out where do we go from here in this kind of engaging the patient more and getting more systematic input from patients to inform drug

development. And so this is part of the effort.

We began it in 2012. We put out an announcement with a set of diseases that we got public comment. We got over 4,000 comments from the public about the list that we published, with other ideas as well. We took that list and the input that we got and identified 16 diseases for the first three years of the program. And in a few months, we'll be able to publish the set of diseases that have identified for the final two years of this five-year program. I say "final years" of this program but this is water heaters at we view as the first phase of this effort. We very much plan to continue and evolve it and actually expand it beyond this five-year period.

Here is the list of the diseases that we've included in the first three years and as you can see, today's meeting is focused on breast cancer. We have four more coming up later in this fiscal year so between now and the end of September, we'll have some others. And so -- and as I said, we'll be covering more later.

There are some standard questions related to those two considerations that I mentioned. Severity of the condition and the impact and benefits of the treatments currently available are the focus of every one of these meetings, so there are some standard questions that we will cover related to those in the disease area. And then we'll also be asking other questions. I say "we" but I particularly mean the Review leadership is probably going to be asking other questions as well of things that they may want to probe further taking advantage of the opportunity of having you here in the room land having our participants on the webcast to get firsthand input from you about other things that they may be concerned about or aspects of treatment or development that they think you would be particularly able to help them understand better or inform.

We produce a report after these meetings. It's called "The Voice of the Patient Report" and those are available on our website.

If you "Google" "voice of the patient" -- I mean I'm lazy, that's what I would do but I find -- that's how I find stuff on our website. I go to Google.

(Laughter.)

DR. MULLIN: And don't share that with our IT people please. But it's a report that tries to capture very faithfully not just what people tell us but really what and how they tell it to us because how they describe what they're going through is just very much part of the what and so we recognize that. We try to capture that. We both get the information from the room, from the input from our webcast, and we keep an electronic docket open for any additional information that you may think of or have you want us to include in what we capture as part of this report effort, and other comments that we get are submitted to the Docket. We give a few more weeks for that to come in and then we take all that to produce these reports. And they provide a very useful way to capture that information for

subsequent reference by the Review Divisions. When they maybe get another application for that disease area, they'll go back and that -- and we actually shape up those first two sections. We provided some examples of how -- what they might be thinking about and encapsulate some of it. The reports are short enough that they're readable and reviewers and others, we hope -- I've heard from friends who are patients with some of the diseases that we've had that the reports have resonated with them, too, which is very gratifying for us to hear. That's what we hope to do. But it's a first step. It does provide that context and it's also prompting a certain amount of further thinking on our part about what we want to do to sort of more systematically capture this information longer term, maybe find ways to capture it and measure it so that it can become evidence of benefit in addition to providing very critical context.

And so that's what we're doing with this effort and with t hat, I'll turn it over to Suparna Wedam who is going to give us more

information about the topic of disease and current treatment. Thank you.

DR. WEDHAM: Great. Thank you, Theresa. Good afternoon. So as mentioned earlier, my name is Suparna Wedam and I'm a Medical Officer in the Division of Oncology Products here in the breast cancer group. I also continue to see patients regularly, breast cancer patients in the clinic each week, actually on Thursday so today is my clinic day but I thought it was very important to come to this meeting here. So I am well-aware of the direct impact of our treatment decisions as far as the benefit that they provide, which is obviously the intended goal of our therapy, but also the unfortunate side effects and toxicity that we have to deal with, and this can be wide-ranging from very mild such as some dry skin or mild constipation to much more serious or severe such as blood clots or debilitating neuropathy. And as patients are living longer and the treatments are becoming more chronic, this is more important than ever that we really take these all

into consideration in our treatment decisions.

So again, I'm going to echo the sentiments of my previous speakers that I'm very happy you're here. I think this is a very important forum and it's fantastic that we have this opportunity to hear from you today.

So my task today is to give a brief background on breast cancer and the therapeutic options. So as mentioned earlier, breast cancer remains a major public health concern. We've made major strides over the last few decades but we still have a lot of work to do. It is the second leading cause of cancer-related death among women in the United States, second only to lung cancer. And this year, it's estimated that a little over 230,000 will be diagnosed with breast cancer and a little over 40,000 will die of the disease in this country.

So as with all cancers, breast cancer is very complicated and we don't really know what exactly causes it, but there are many risk factors that have been associated with breast cancer and

implicated in its etiology and these are often divided into unmodifiable and modifiable risks which I have listed in two columns here.

So on the left-hand column are some of the unmodifiable risks which, as the word implies, are things that we cannot change, we do not have control over yet, they put us at a higher risk such as being of female gender, increasing age, certain genetic risk factors. This actually only makes up about 5 to 10 percent of breast cancers and what we most commonly hear about out in the public and the media is BRCA1 and BRCA2, but there are many other genes that increase a patient's increased risk of breast cancer such as ATM, p53, PALB2. They're just much rarer and we don't understand them that well. These are important not only for screening and for monitoring but they may have therapeutic implications as we understand them better. Also important are personal and family history, dense breast tissue, certain breast conditions such as atypia or hyperplasia and the age of menarche and menopause.

In the right-hand column are some modifiable risk factors. So these are things that we have control over and could potentially change:

nulliparity which is not having children, certain hormonal birth control methods, hormone replacement in menopause, breast feeding, alcohol use, obesity, and physical activity. There are many other factors that have been mentioned and discussed and it's not really clear, again, what their association is.

So when patients present to us with a suspected breast cancer, they're actually often asymptomatic. A patient may have a palpable breast mass that they have felt themselves or that has been palpated by a healthcare provider but in this country, actually, most people present after an abnormality has been seen on a screening mammogram or MRI. In the late stage, patients may have some generalized constitutional symptoms such as fatigue, weight loss or decreased appetite, or localized symptoms such as bone pain or abdominal discomfort depending on where the tumor is. But

even then, a portion remain asymptomatic and I think this is important to keep in mind that actually most breast cancer patients, when they're diagnosed, are asymptomatic and feel well but we can make them feel unwell with our treatments. So we want to make sure that that toxicity is really balanced with a clear benefit.

So once breast cancer is suspected, we need tissue confirmation as a diagnosis cannot be made on physical exam or imaging alone. The tissue is important not only to confirm breast cancer but to gain other important information in formulating a treatment plan. And then once the diagnosis is confirmed, we stage the patient according to the TNM system. So this looks at the size of the tumor, the extent of nodal status and whether metastases -- distant metastases are present or not, and the patients are given a stage of one, two, three, or four and this is shown in the schematic here.

So stage one breast cancer is where the tumor is confined to the breast. Stage two is

where the tumor might be slightly larger and may have lymph node involvement. Stage three is where the tumor may be yet a little larger, may have more lymph node involvement and may have some chest wall involvement. And stage four is where the tumor has moved out of the breast and local regional area and actually, only a minority of the patients are diagnosed at stage four at the onset. This is really only about 5 to 10 percent of patients.

So stage is not only important for prognosis but, again, to formulate a treatment plan and to really know what our goal of therapy is, whether it's for curative intent or for palliation. Along with that, we need to know if the tumor is invasive or non- invasive and actually, this we usually know before we stage the patient; tumor histology, the estrogen receptor status, progesterone receptor status and HER2 status. And these are important not only for prognostic reasons but have predictive value also because we have treatments targeted toward these

and we want to make sure that we're using it in our treatment plan. We also look at the histologic grade of the tumor and certain genomic testing may be warranted. And finally, we look at the age and associated comorbidities.

So our understanding of breast cancer has greatly evolved over the last couple decades, and this is really with the advent of molecular profiling and more genomic tests. So we're not at the point that we really understand breast cancer is not just one disease. It's quite varied and diverse and actually, it's a compilation of several different subsets that behave very differently.

In clinical practice, we already subset these to some extent and that's by assessing the hormone receptor status, the HER2 status, and we use certain genomic tests such as Oncotype DX to assess if further adjuvant chemotherapy is needed or not. But there are many other tools that are being used for research purposes in clinical trials. These are not quite ready for routine use

yet but, really, it's only a matter of time. As our understanding of the biology in the subsets continue to mature, we are going to use more and more of these tools in the clinic to help identify the right patient for the right treatment.

So the way that we make a treatment plan now is really a combination of several different modalities and this includes surgery, radiation therapy, cytotoxic chemotherapy, targeted therapy, and one other box I'm missing which is actually on the next slide is hormonal therapy. Some patients may receive all of these or only a few of these. And again, it goes back to all of those factors I discussed earlier, the stage of the patient and the goal of therapy. It's great that we have a lot of options that we can kind of put together and that we can treat patients but unfortunately, none of them are benign. They all come with side effects. They can be overlapping side effects. They can be different side effects and only some of them are listed here. Obviously, it's not a complete list. And some of the side effects can

be quite toxic and so it's very important that we're discussing this with patients as we're making the treatment decisions of how we proceed.

So some of the approved therapies that we do have available to us - -again, this is not an exhaustive list and, in fact, I'm missing one of our most recently approved drugs, palbociclib, on this list but we do have several hormonal agents and we choose to use those based on menopausal status and kind of the stage of therapy or whether it's in the adjuvant setting or metastatic setting. We have several cytotoxic chemotherapy agents that we can use in combination or as single agents and then targeted therapies. And the four that I have listed here are used solely in HER2-positive tumors. So again, we do have many therapies that are approved at this time.

But in approving any of these therapies, it comes back to this balancing act again. In oncology, we are always dealing with a serious disease and unfortunately, our treatments can be

toxic and so in approving a drug, we really want to make sure that we are helping make a patient live better or live longer and so in other words, this means that they have some direct clinical benefit, either improving how they feel or function or prolonging their survival. So I think this is my last slide. So one of the ways that we can get direct measurement of this as far as a treatment benefit is, obviously, from the patient. So we can use these patient-reported outcomes or PROs which are direct measures of treatment benefit and allow the patients to be involved because we know that healthcare providers under-report the side effects. So we can get a more accurate assessment.

Here at the FDA, we definitely encourage use of these if they're used properly because then they can be very helpful and properly means that they're well-defined, reliable, validated tools that are measuring what they say that they're measuring. So that's all I have. Thank you.

MS. GIAMBONE: Thank you to my FDA

colleagues for your remarks. So I am going to now go over the discussion format again and as I mentioned, we have two discussion topics for today. The first is on the symptoms that matter most to you. So in this topic, what we're listening for is how do you live with your breast cancer. How do you experience your breast cancer? What are the symptoms that are most important to you, and how do they impact your day-to- day life? So here you can tell us are there activities that you can't do at all or as fully as you would like because of your symptoms.

Also, if I can share with us how your symptoms have evolved over time and how they've changed for you since diagnosis; that would also be very helpful.

In Topic 2, we're going to discuss current approaches to treating breast cancer. So here what we're listening for is, what is your current treatment regimen? What are the benefits that you see of your current treatment regimen? Is it working for you? And vice versa, what are

the downsides? What are the biggest side effects that you experience? Also, what do you look for in an ideal treatment?

We're also going to spend a portion of Topic 2 talking about the factors that go into the decisions you make regarding treatment options.

So first we're going to hear from a panel of patients and on that note, could I have my Topic 1 panelists come on up and have a seat?

So the purpose of the panel discussion is to really set the stage for the greater group discussion. Our panelists reflect a range of experiences with breast cancer, and I have had the privilege of working with them over the last two weeks and I know they've spent a lot of time and put in a lot of effort to put their thoughts down, so we really appreciate that you're here doing this.

Our panelists will have five minutes to present their remarks and after they finish their remarks, we will open the dialogue, broaden the dialogue to invite more patients and patient

representatives in the audience.

So the purpose of the group discussion is to really build on what you've heard from the panel, so share with us not only what is similar for you but also how you experience differently the breast cancer. Periodically, I'll look to my FDA panel for some follow-up questions and we invite you to continue participating in the conversation. You can raise your hand and we'll have microphone runners around the room and they'll come to you. And if you're comfortable to do so, just raise your hand, they'll come to you, and just tell us your first name and you can present your comments.

So there are a few other ways that we're going to be learning from you today and one of those is that we're going to be doing thee polling questions and on that note, could I have the clickers passed out. Thank you. So the polling questions, they're not a scientific survey. It's entirely voluntary but what it allows us to do is to get more understanding of the perspectives in

the room. And we're going to be trying those out in just a bit. So for those of you in the room, you'll use the clickers to answer the polling questions; and for those of you on the web, you can also participate via the webcast. And we do ask that only patients and patient representatives respond to the polling questions, please.

So as I just mentioned, we also have a very active webcast. Today we have nearly 100 people joining us on the web so for all of you on the web, you're a very important part of today's meeting. You're a very critical part of today's meeting and although we can't see you, you're voice is being heard. We will periodically check in with you and we'll have you -- you'll also have the opportunity to call in by telephone and share your comments throughout the meeting. And we will make sure that we capture all of the comments that you're providing us via the webcast and they'll be incorporated into our summary report.

So another last way that we will be getting more information from you, more of your

experiences and perspectives is this very important public docket that we'll keep open for two months after the meeting. So it will be open until June 2nd and you see the website up here. We encourage you to continue to keep visiting this website and continue to share your thoughts, share your comments as they come to mind and they're a very important part of the meeting, so it's an extension of today's meeting to continue to hear from you. All of these comments in the public docket will be -- we will read through those. We will summarize those and incorporate them into our summary report and anyone is welcome to comment.

We also have a few resources here at the FDA that we want to share with you. The first is the FDA's Office of Health and Constituent Affairs, OHCA, and the second is the Professional Affairs and Stakeholder Engagement Group, PASE, and both of these organizations within FDA are -- they're a liaison. They're your link between the FDA and the public and patient groups so we encourage you to reach out to them if you have any

questions at all.

So I'm going to go over, last but not least, a few discussion ground rules for the day. First, we encourage patients to contribute to the dialogue and patients and patient representatives also. So we know that there are academia, government agencies, industry -- we really appreciate that all of you are here today to join us at the meeting. This meeting will be very important to you, too. We just ask that you stay in listening mode. Today is really about listening and learning from the patients and patient representatives.

And on that note, the FDA also, we are in listening mode for the day. Periodically, we will have some follow-up questions from the FDA panel so I'll turn to them. And the third is that the discussion will focus on symptoms and treatments. So as I mentioned, we have two topic questions today and we will -- we're going to -- you know, these are the topic questions that are most beneficial for us at the FDA to learn from

you on. So we will do our best to stay on topic and if there is anything else, as I mentioned, that you'd like to share outside of the scope of Topic 1 or Topic 2, again, we encourage you to sign up for open public comment.

The views expressed today are personal opinions and so on that note, respect for one another is paramount.

And last but not least, let us know how the meeting went today. So we will have evaluation forms out on the registration desk and we'll also pass them out closer to the end of the meeting. It's really important for us that you fill these out and let us know what worked and didn't work so that we continue to improve these meetings for you.

And as I mentioned, I just want to reiterate again that we're just really thankful and grateful that you're here. Again, this is -- we want you to feel comfortable. We want you to go ahead and get up and stretch if you need to. I'm personally very happy that there's nice

weather outside so for those of you that traveled from afar, hopefully, you're experiencing DC beautiful spring weather.

Okay. So, first, what we will do is we're going to start with some polling questions. So everybody get your clickers out. Okay. Oh, they don't have clickers. Okay. Sorry.

(Laughter.)

MS. GIAMBONE: Okay. Everyone have your clicker ready? Great. Okay. So the first one is an easy one. Where do you live? Press "A" or within the DC Metro area, or "B" for outside of the DC Metro area. Press A -- yep. That's okay. Okay and -- oh, it looks like we might be having some difficulties with the Let's try it one more time. Can you click again either "A" or "B"? Not working?

UNIDENTIFIED SPEAKER: No.

MS. GIAMBONE: That's okay. Let's raise hands instead. Okay. So can I just by a show of hands how many of you are from the DC Metro area? Great. So we have a lot of neighbors visiting.

And so I imagine the rest of you are from outside of the DC Metro area, right? So thank you for coming. I know there's been a lot of travel, California, Texas, Massachusetts. I've met so many of you from different parts of the country so thank you for being here. It means a lot to us.

Let's go to the next question. Have you ever been diagnosed as having breast cancer? Shall we give it a try? Okay, let's try this one. Press "A" for "yes" or "B" for "no." No, we're doing hands. We'll do hands again. Thank you all for being such a good sport about this. So can you raise your hand for "A, yes." Okay. And "B, no." Okay. Well, thank you very much for all of you that are here to share your perspectives and experiences with us. You will have -- we have so much to learn from you so we appreciate that you're here.

Okay. So this one, there's going to be a lot of hand raising I guess. Okay. What is your age or your loved one's age: A, younger than 30; B, 31 to 40. Okay, we have a few of you. C,

41 to 50. Okay. D, 51 to 60. Okay. E, 61 to 70. Great. And F, 71 or greater. Great. Thank you. And I'm not sure if they webcast polling is working. Are we seeing similar results?

MR. THOMPSON: Yeah. We had, for the previous question, about 64 percent diagnosed with breast cancer; for this one, 30 percent of people between 41 and 50; 41 percent between 51 and 60; and 10 percent for the other categories.

MS. GIAMBONE: Okay, great. Let's go on to the next one. Are you A, male or B, female? I imagine most of us here are female.

(Laughter.)

MS. GIAMBONE: Okay. And I think this is our last -- or actually, we may have one more. Okay. So what is the length of time since your diagnosis? A, less than one year ago. Okay, so no responses there. B, one year ago to two years ago. Okay. So it looks like we have one newly diagnosed. C, two years ago to five years ago. Okay. So we have about four hands. D, more than five y ears ago. Okay. So it looks like the

majority f people responding are in this category, more than five years ago. And E, I'm not sure. Okay. How about on the webcast?

MR. THOMPSON: On the web, we have 18 percent for less than one year ago; 18 percent again for one to two years ago; 18 percent to two to five years ago, 43 percent for more than five years ago.

MS. GIAMBONE: Okay. So similar to what we're seeing in the room. Great. Okay. Which of the following best describes your current condition? A, my cancer is localized and has not spread outside my breast and/or local lymph nodes. Okay. So we have one. Okay. B, my cancer has spread, metastasized to the rest of my body? Okay. So I'm counting about eight or so, eight or nine. Okay. C, I have been treated for my cancer and currently have no evidence of disease. Okay. So I see about six or seven hands raised. And D, I'm not sure. Okay. How about on the web?

MR. THOMPSON: Thirteen percent say they're cancer is localized; six percent say it is

metastasized; and 80 percent said they have been treated and currently have no evidence of disease.

MS. GIAMBONE: Okay. Thank you. So that will take us to our discussion topic. Thank you all again for bearing with us as our technology did not work. So let's have our Topic 1 panelists please introduce yourselves.

MS. DURHAM: I'm Karen Durham.

MS. GIAMBONE: Okay. Go ahead if you want to just -- yeah, go ahead and introduce yourselves.

MS. McRAE: I'm Katy McRae.

MS. DUNNE: Hi. I'm Debbie Drake Dunne.

MS. FINESTONE: Sandy Finestone.

MS. GIAMBONE: Okay, great. So as I mentioned, our Topic 1 panelists will read off their remarks and I am going to -- I just want to say thank you so much for preparing all of your summary statements and for sharing these stories with us today. So can we start with Karen, if you don't mind?

MS. DURHAM: Good afternoon. As I

introduced myself, I'm Karen Durham and I'm from Lindale, Texas. I was originally diagnosed with an aggressive invasive stage two breast cancer 25 years ago, and you didn't have hardly any treatment options 25 years ago but I went through all of my surgeries. I completed all of my chemotherapy treatments and I did great for 19 years. Then in January of 2009, I was diagnosed with stage four metastatic disease. Surgery was not an option. I went on a clinical trial. I took two drugs -- different drugs a day on the clinical trial. They were pill form. I thought I was doing really well until two months ago, in January 2015, I had disease progression with four new tumors. This was really emotionally challenging because of the length of time between each of the diagnoses was so long. I was lulled into a sense of kind of maybe a security, that that was it, it was not going to go any further. There is no sense of security when you have breast cancer.

Right now I'm doing fine for somebody

that's being treated for metastatic disease, but I do not make any long-term plans. It's 6 to 12 months or less because I never know what the future is going to bring.

To put this a little bit in perspective, in the six years and two months since I was diagnosed metastatic, I have had 193 visits with my oncologist. That's not scan time, treatment time, any other doctor time. That's just with my oncologist. That averages out to about 2.6 visits a month. I have a wonderful caregiver in my husband. He has made all but one of these appointments with me.

I have many side effects from the 25 years, both from the surgery and from the different treatments that I've been on. I have cognitive impairment, hot flashes, dry skin, weight gain, headaches, joint and muscle pain, diarrhea and mouth sores just to mention a few. The list goes on. I have chronic severe lymphedema in my left arm from my surgery which was different 25 years ago. I was prone to

current infections which can be life-threatening if they're not treated properly immediately. Now I'm on a daily antibiotic as a preventative for these infections.

It's very depressing when I go shopping for clothes. I have to try on clothes that fit my left arm, not the rest of my body. To fit my left arm, it's a woman's size 22 to 24. The rest of my body is a size 12. It's depressing.

Fatigue has become a part of my daily life. It's just something I have learned to live with. Some days it's better than other days.

For the six years I was on the two different chemotherapy treatments a day in pill form. Now I have five pills that I take. It's two drugs -- different drugs and I am on a different clinical trial. But, you know, I think back -- I cannot remember when I did not have a queasy stomach and smells made me very nauseous. It's been that long ago in six years and two months. I have peripheral neuropathy in my feet and legs. Sometimes the bottoms of my feet burn

so badly that I cannot stand to have even socks on them. My legs do not feel like they have the strength to hold me up going up or down stairs. Walking on flat surfaces is just fine. So when I go up or down the stairs, it's one stair at a time and I hold onto the handrail with a death grip so I won't fall and risk breaking any bones.

The cognitive impairment I have is not forgetting things. It's the word is there but I can't get the word from my brain to come out my mouth. I can look out my window at home and see a red cardinal and I want to say red cardinal but the words won't come. It just -- there -- something is blocking that from coming out. It's really embarrassing, especially in an environment like this.

The daily activities besides what I Have already mentioned, walking or any type physical exercise, because of the fatigue, working in the garden and doing things like that because of the chance of an infection in my arms is just about impossible.

And then there is one other side effect that no one wants to talk about and that's sexual dysfunction or sexual activity. I, like nearly every woman that has taken an aromatase inhibitor, finds that the traditional position of sexual intercourse is extremely painful and uncomfortable.

And with that, I would just like to thank the FDA for the opportunity to appear here today and present my comments.

MS. GIAMBONE: Thank you, Karen. Katy?

MS. McRAE: My story really begins in 2003. I'm going to read it so I don't diverge or whatever. Two years before my breast cancer diagnosis, I was living in Germany at the time. I had been having issues with my eyes and had laser and cryotherapy treatment of both retinas. A few months later, on my way to see my mom in Ireland, the retina in my left detached. I went straight from the airport with my sister and had an emergency surgery the following morning. Eight weeks, multiple setbacks and three additional

surgeries later, I returned to my husband and four children in Germany. The entire situation was a nightmare. The pain, the fear of recurring blindness -- I had actually gone blind in my left eye at the third detachment -- the discomfort of lying in a certain position called "posturing" for an entire week, getting up only to use the bathroom and eat, I missed my husband's birthday, my birthday, our 20th wedding anniversary, my daughter's graduation -- she was salutatory out of 300 kids -- and my son's Eagle Scout ceremony in the time I was in Ireland in the hospital. On my daughter's 18th birthday, July 3rd, the professor released me and I flew back to Germany.

While in the hospital, I had annoyingly developed depression. So once back in Germany, I had to see a new team of eye specialists for post op oil removal from my eyes, routine follow-ups, cataract surgery, etcetera. We moved house 50 miles away and I got my children started in their new schools. On the day we drove my daughter to the airport to go to university in Ireland, we

went directly after dropping her off to the psychiatric clinic where I was admitted and spent the following three months as an inpatient. There aren't words to describe the horror of depression. Suffice it to say, had it not been for my seven-year-old post vasectomy child at home who I believe still needed me, I would not be here today.

Happily, though, I was one of the lucky ones and eventually got back to living a normal unmedicated life. So I had a nice uneventful year in 2004 but in January of 2005, my mom died and three months later, I was diagnosed with breast cancer. So I tell these stories not because I want a pity party but they give me perspective when I'm dealing with the -- when I dealt with my breast cancer diagnosis. For me, breast cancer was bad, retinal problems were worse, and depression was the absolute pit of despair so in a way, I was luckier than most when I got my breast cancer diagnosis. I'd handled worse. I could do this.

Two of my three sisters had already had breast cancer. One a late stage over 50-year-old and my younger sister who was diagnosed in her early 40's. My other sister developed breast cancer subsequent to my diagnosis. We're four sisters in my family and between us, we have a grand total of two breasts. I have been tested and I'm not positive for the BRCA1 or 2 genes, which is nice. So I was the only one of my sisters to take what I call the scenic route to recovery. I chose elective bilateral mastectomy, chemo, radiation, etcetera. I had breast reconstruction some months later and during that surgery, I had my ovaries removed.

So we relocated to the United States and all went well for about five years until September of 2009. My oncologist was alerted to my changing status after a routine blood test showed an increase in my cancer marker 2729. So metastatic breast cancer was confirmed after a PET scan and once again, the roller coaster was in motion. My son said that living with metastatic breast cancer

was the ultimate chaos and I think he truly, truly nailed it.

For me, personally, the diagnosis of metastatic disease in my bones was very difficult to get my head around. I'm proactive. I face every challenge head on and I'm willing to move heaven and earth to fix my problems but this time, the dreaded word "incurable" was part of the equation. For me, personally, it was a lonely time because metastatic breast cancer is not well understood in the general community and as a non-survivor, I felt somewhat a failure in the primary breast cancer community.

So for months, cancer was the first thought in my head when I woke and the last before I finally slept. I had mixed results in the beginning of my treatment for what should have been a best case scenario, ER-positive metastatic breast cancer to the bone, the best of the metastatics to have, but I wasn't responding well to the usual anti-estrogen regimen.

So my oncologist and I decided that I

should have a bone biopsy taken from a lesion in my left iliac crest and that proved to be HER2-positive which my primary cancer had not indicated and, of course, explained the lack of response to my initial treatments. So when I began to take Herceptin, I had immediate and positive results but then I developed LVEF problems in my heart as a side effect of Herceptin. It was horribly discouraging and I had to suspend my treatment on a number of occasions until my heart recovered.

But at this time, there was great excitement in the HER2 community about the pending improvement of TDM1. I was worried though that because of my LVEF status that I would not be a candidate for the drug when it became approved, so I called Genentech one day. They did the drug and I spoke to a specialist who reassured me, however, that I might be a candidate for the expanded access trial. So I had been on a weekly regimen of Herceptin but the trial dosage was given at three-week intervals and actually, I had no subsequent heart effects because of that regimen.

So I have been on TDM1, which is now known as KADCYLA, for over two years, 2-1/4 years, an amazing virtually totally symptom 2-1/4 years. It's been phenomenal. However, since registering a few weeks ago for today's forum, I've been having some new symptoms and am now resistant to KADCYLA. I will begin radiation treatment on my sacrum tomorrow. I hope to begin a new protocol possibly taking PERJETA within a few weeks.

Metastatic breast cancer is a very different animal than primary cancer. My life is hugely dictated by my three-week chemo cycles. The most I could ever be away for was three weeks which, of course, for most U.S. citizens would be very acceptable but I'm an ex-pat and I have siblings all over, you know, Ireland and Europe and time is always a factor in keeping close family ties and it's something that's hugely important to me and to them.

MS. GIAMBONE: Katy, any closing remarks?

MS. McRAE: Pardon?

MS. GIAMBONE: Any final remarks?

MS. McRAE: No, that's it.

MS. GIAMBONE: Thank you, Katy. Debbie?

MS. DUNNE: Hi. I'm Debbie Dunne and I'm from San Francisco, California, and I want to thank the FDA for convening this meeting and also for giving me the opportunity to share my story.

After finding a lump in my left breast in August 2009, I was diagnosed with breast cancer. While I had two tumors, the cancer had not spread to the lymph nodes or outside my breast. I have been cancer free for the last six years. As the majority of my symptoms and impacts were psychological, I would like to briefly describe my treatment approach as the process of decision-making sent me into a serious state of despair.

Despite doctors telling me that my cancer was caught early and that I had a high likelihood of survival, I was convinced that my diagnosis meant certain death. No one or no data could convince me otherwise. Most family and friends I knew who had cancer had succumbed to the

disease. My stepfather passed away from cancer three months before my own diagnosis. When I heard the words "you have cancer," my body immediately went into flight or fight mode in an extended period of extreme fear and high stress. Normally a very thoughtful and analytical person, I became focused on short-term survival and was unable to think clearly or understand the long-term consequences of my choices. Even my doctor noted that I went from a calm and thoughtful person in my initial visit to a, quote, complete emotional wreck.

I wanted to do whatever I could to reduce my risk. As I began to contemplate my treatment plan, I quickly became confused and overloaded with information. Where I hoped to find black or white answers, there was only gray. I spent hours on the internet searching for the right answer. As I insisted in getting the cancer out of my body as soon as possible, I had a lumpectomy three weeks after my diagnosis.

Because there was a history of early

onset prostate cancer on my dad's side, I met with a genetic counselor who recommended that I take the genetic test. I tested positive for a mutation of the BRCA2 gene but it was a variant of unknown significance.

What was I to do? They then asked that my father be tested and he also had the same variant so the doctors were pretty sure that, in fact, I had the mutation. I had two options: MRIs, constant surveillance, or remove my breasts and my ovaries. This would not necessarily prevent the cancer from returning but it was the choice that I took, to remove my breasts and my ovaries.

By this time, the doctors realized that psychologically, I needed to feel confident that I had everything -- I had done everything I could to reduce all of my risk or as much risk as possible. My other treatment options were to consider chemotherapy and an aromatase inhibitor. One doctor said chemotherapy was unnecessary as I was low risk while another doctor told me I have a

young son so I might want to do everything I could to be around for him, so I decided to take the oncotype test. Once again, it was not definitive. Eighteen was low risk. I got a 20. So I took chemotherapy.

While I read and was told about all the possible side effects, nothing could prepare me for the emotional and mental upheaval I would experience. I literally felt like I was dying and I questioned my decision to do the chemotherapy. Every day I contemplated quitting.

As I have just described, the symptoms that had the most significance in my daily life were primarily psychological. Fearing for my life, I was paralyzed and immediately became depressed. I was convinced that I would never see my seven-year-old son grow up. I remember sitting in church on Christmas Eve in 2009 thinking this is my last Christmas. I lost interest in being with friends who were living normal happy lives compared to the nightmare I was now experiencing. The thought of work was overwhelming and despite

coworkers being supportive, I couldn't bring myself to go to work so I went out on disability for nearly a year. Many days I didn't get out of bed, instead watching hours of TV to distract myself.

I also spent hours and hours on the internet reviewing the same statistics over and over hoping that it was possible I could survive.

I took anti-anxiety medication to try and stop the feeling that I was jumping out of my skin and to numb the pain that I constantly felt. My world was completely out of control and I really struggled to maintain a sense of calmness. As my mind continually raced night and day, I was unable to sleep for any length of time. I searched for answers wondering why me, how did I get cancer, I'm young, I'm healthy, I was supposed to have a full life ahead.

In addition to the psychological symptoms, I did experience physical symptoms as well. All the treatments and the lack of sleep contributed to an extremely high level of fatigue

I had never before experienced and to this day, some of that fatigue still exists.

Given that my cancer was ERPR-positive, I was prescribed an aromatase inhibitor. The initial bone pain was excruciating so the doctors had me try three different aromatase inhibitors. While some of that bone pain has subsided, I still feel it in my lower back on a regular basis. I have also lost bone density and I now have osteoporosis.

As for specific activities that are important to me that I can no longer do as fully as I would like as a result of breast cancer, this is the biggest area of lasting impact for me. The loss of interest and difficulty with sexual activity and intimacy with my husband has been significant. When discussing the decision about a mastectomy with my doctors, I was told I would lose feeling in my breasts. At that time, I felt like I was fighting for my life and I wanted to do everything I could to reduce my risk of recurrence so I was very aggressive; as I mentioned, multiple

surgeries, actually partial radiation, chemotherapy and an aromatase inhibitor. I had convinced myself I might not even be alive for that long so I wasn't really thinking about longer term impacts of my treatment decisions. Never did I realize that my decision for a double mastectomy and oophorectomy would have much deeper psychological implications than just the loss of physical feeling.

Six years later, I am grateful to be alive. I do not regret any of my treatment decisions but my relationship with my husband has been significantly altered as a result of my decisions.

In closing, given that many breast cancer patients are now going on to live long, productive lives, I think it is critical to discuss and consider treatment options in a different manner. I have had the opportunity to talked with a number of breast cancer patients over the years. Many of us are frightened and in a weakened emotional state when first receiving

our diagnosis. As I mentioned, it was extremely difficult to understand clearly the implications of my decisions should I be one of the fortunate cancer survivors who could potentially be alive for a long time.

As someone who did a lot of research around my various treatment options, I had no way to gauge the validity of the various studies I read. As a result of my experience, I am now focused on helping to improve decision support to cancer patients. I firmly believe we need to strengthen the evidence base for decision making including participation in clinical trials, and better reporting and access to patient-reported outcomes would also provide a huge benefit.

Thank you again for allowing me to share my story.

MS. GIAMBONE: Thank you, Debbie. Sandy?

MS. FINESTONE: My name is Sandy Finestone. I'm from Southern California. I've been fortunate enough not to have to personally

face the challenge of metastatic cancer.

I was diagnosed over 30 years ago when you were offered no options and only one treatment. When I went for my surgery, I signed an authorization allowing the surgeon to do whatever was necessary without any idea what that decision would be. Today women are given many options and these women are expected to make decisions without very much information, decisions that will impact the rest of their lives. This is particularly difficult for the patient who is metastatic at the time of diagnosis.

I woke from my surgery to find that both breasts had been removed and began my journey as an advocate to education women about their disease so when they make a decision, it will be an educated one. I currently facilitate support groups for newly diagnosed patients, those in the middle of treatment, those whose treatment has ended, and those whose treatment will never end. Many concerns are the same for each of these groups but some are very different, very different

when facing the challenge that never to be able to put cancer behind you.

As a therapist, patients share many of their concerns with me during individual therapy sessions dealing with the stress and anxiety of the diagnosis. The symptoms that women mention most are pain, fatigue, hot flashes, neuropathy, lymphedema, memory loss, weight gain, vaginal dryness, loss of libido, and bone loss. Patients are frustrated because many of these symptoms are brought on by the medications that they are taking to treat their cancers or to attempt to prevent them from coming back.

Pain comes in many levels. Some pain is minor and annoying while other is severe and debilitating. Some pain can be managed with over-the- counter medications; some pain requires very heavy medications that can cause other symptoms such as constipation, sleeplessness or confusion. Bone pain can limit movement which leads to many other issues such as increased fatigue or depression.

Fatigue prevents patients from doing many things, both big and small, from going shopping with friends to limiting the type of vacation they can plan due to the inability to be as active as they would like. Sometimes even going to a support group or a doctor's appointment take every ounce of energy they have. One metastatic patient told me that she had to be honest with her family and tell them that she had a limited amount of energy and had to choose, often painfully, which things she had the energy to do and which things she could not do. It's difficult when you've been a member of the family who always plans and prepares the holiday dinners and you can no longer fulfill that role and you begin to see yourself as someone less important in the family.

Hot flashes are the butt of many jokes but when you're life is impacted by them, it's no longer a laughing matter. I had a patient who was an attorney. Her hot flashes were so severe that she had to change her clothing several times a

day. It was so bad that she seriously considered no longer doing court work because her concern was that the juror would see her begin to perspire and think she was lying and that her client was actually guilty. Some women have fleshing with their hot flashes which also embarrassing and as is the constant taking off and putting on of clothing or the issue it presents in an office when other coworkers are not experiencing the same weather that you are.

Neuropathy can be both painful and dangerous. When you cannot feel where you're stepping when you're going down stairs, there's a possibility of a fall. When you cannot feel what you're stepping on, the chances of your injuring yourself become higher. When you are unable to button your blouse or undo a zipper, you become dependent on others. This becomes a bigger issue when you live alone.

Many think that the issue of sexuality and intimacy are issues of only for the young but that's not the case. Many couples continue to be

sexual into their 70's and 80's and treatment often interferes due to fatigue, pain, or vaginal dryness. Many medications effects one libido which can create relationship problems. It's difficult to want to be intimate when you have pain, fatigue, or nausea.

Lymphedema, as we've heard, can both be painful and bothersome. For some women, the pain is constant. Lymphedema intrudes into your life as you must massage your hand and arm several times a day in order to keep the swelling down. It also restricts the type of clothing you can wear as the sleeve opening must be large enough to facilitate the bandaged arm, as we heard from Karen. One of my patients was very distressed as she was unable to wear many of her favorite items of clothing due to the size of her arm. She felt she could no longer wear anything sleeveless so as not to draw attention to the bandaging.

The list I gave you was long and I hope you can appreciate what many women suffer when dealing with this disease. Thank you.

MS. GIAMBONE: Thank you very much, Sandy. So I'd like to ask everyone to give a panelists a round of applause.

(Applause.)

MS. GIAMBONE: What you shared with us, the very personal stories -- and I think I can speak on behalf of all of my colleagues when I say that you are very brave and very courageous to come here and share those personal stories with us, so thank you very much.

So I just want to recap some of the points that we heard from our panelists and then I'd like to see from those of you in the audience how it resonates with you. So Karen mentioned that her life is impacted by just so many doctor appointments. She mentioned that she has cognitive impairment. She said that she can't do some of the things that she enjoyed doing such as gardening or walking and she also mentioned that she has sexual intimacy -- you know, she has experienced the impact on sexual intimacy. So how many people did that resonate with? Okay. So we

have about nine people in the audience that said that.

Katy, you talked about -- I think you described depression. You described that it's a roller coaster rise. How many of you did that resonate with? Okay.

And Debbie, you talked about -- also, you talked about the psychological issues, the fear and the anxiety and the depression. Again, how many of you in the audience did that resonate with? Okay. So five or six people.

And then finally, Sandy, you talked a lot about, again, the stress, the anxiety, pain, fatigue, from all the different patients that you've talked with. Okay, great. Okay. So it sounds like a lot of you in the audience, that you share similar perspectives or experiences from what our panelists shared.

So in just a moment, we're going to hear more from you on how you experience it but first, I'd like to do a polling question. So do we know -- we're going to do hands? Okay. So I'm going

to read this out loud and then we'll just do -- I'm sorry that we're having these technical problems with the clickers but we'll do another hand raising exercise.

So of all the symptoms you have experienced because of breast cancer, which do you consider to have the most significant impact on your daily life? So we'll just go down the list and then you can just raise your hand and then we'll talk more about these in just a moment. So a), pain such as breast pain or bone pain I see about seven hands raised for pain; b) swelling, four hands raised; c) fatigue or lack of energy, I see about 11 to 12 hands raised there; d) depression or anxiety, I see about eight hands raised for that one; e) cognitive dysfunction such as memory loss, about four or so; f) numbness, tingling in the hands or feet, about four hands -- four or five hands; G, fertility issues, I see about two hands for that one; H, menopausal symptoms, about five-six hands raised for that; and I, other symptoms or side effects of cancer

treatments not mentioned, I see about 10 to 11 hands raised for that one.

And can we see on the web; did we hear something similar?

DR. THOMPSON: Actually, pretty much evenly mentioned, every single thing listed on here.

MS. GIAMBONE: Okay. So I believe the one that received the most responses was fatigue; is that correct? Okay. And then followed by, I think we saw, pain? Graham or Pujita, did we see --

(No audible response.)

MS. GIAMBONE: Okay. And then can you remind me of what the third -- was it --

MR. THOMPSON: Depression or anxiety.

MS. GIAMBONE: Okay, depression or anxiety. Okay, thank you. And I'm sorry I'm having to check back. Normally, we see polling results so I see exactly what came up, what the top three answers were.

Okay. So let's talk about -- let's

spend some time talking about some of these symptoms and we'll definitely also spend some time talking about option I, which was other symptoms not mentioned.

So I know this might be a difficult question to ask but, you know, we're going to be spending Topic 2, you know, talking about the treatment but if there is a way you can tease out whether the symptom is due to the underlying disease or if it's a side effect of treatment, that would also be really helpful for us to hear when you're describing. So let's talk about -- can we go back to the previous slide -- so let's start with the fatigue or lack of energy. Would somebody share with us how they experience the fatigue? Would anybody like to start us off? Yes.

MS. O'BRIEN: Hi. So to clarify, I was diagnosed with metastatic breast cancer. I was a de novo presentation at age 43 so I was thrown -- I was -- as a course of my treatments, I was thrown into premature menopause and the first

treatment that I had was tamoxifen and then after that failed, two years later, Femara and now FASLODEX. And I think it would be hard -- I would say that my fatigue has grown progressive as I have been on these drugs. It is true -- one of our panelists mentioned almost a compromise. You decide -- there might be three things I want to do but I know I can only do one of them so this is what I'll do.

The other week, I was babysitting. I have triplet -- two nephews and a niece and I was watching these three children and I felt frustrated because I enjoy being with the kids but even only after spending like four-five hours with them, you know, I was just exhausted. And in terms of my professional life, one of my responsibilities was attending trade shows and it was so frustrating. I would be at Chicago's McCormack Place and wanting to make my rounds and having to sit down and, you know, just -- you know, the spirit is willing but the flesh is not and it's just -- the lack of control and the, you

know, feeling much older than your years is quite frustrating.

MS. GIAMBONE: Thank you, Katherine. And I think, Katherine, you bring up a point that we also heard from the panelists which was the impact of these symptoms on your ability to work. I remember -- I think it was Karen, you mentioned that -- or Debbie, you mentioned that you had to make the decision to stop working because of living with the disease, so thank you for sharing that.

Anybody else, would you like to comment? Yes. And if you could state your name?

MS. KNACKMUHS: Hi. My name is Ginny Knackmuhs and I've had metastatic breast cancer for six years. I thought I'd make my comment now because we're coming up on my nap time.

(Laughter.)

MS. KNACKMUHS: I've had a particular problem with fatigue in the last couple of months. I'm a bit of an outlier and I've been somewhat fortunate in that I was on the same treatment for

5- 1/2 years. I was on Xeloda and I have triple negative breast cancer, androgen receptor, bone only mets. But 5-1/2 years on one treatment, anybody that's got metastatic disease knows that's a pretty good record.

But I had progression in November and one of my problems -- sometimes people get fatigue and it's not really related necessarily to blood counts but in my case, I am chronically anemic now. Once I went off of the chemo, they thought, well, maybe your red blood cells will come back. I'm actually on a hormonal drug now that's used in prostate cancer but it's been four months and it hasn't really -- my numbers haven't come back.

And the thing that's so frustrating to me, not only that it effects how much I'm able to do, I kind of go back to when my mother was in her 80's, her rule was one thing a day and that's what I kind of feel like. You can only plan on one big thing a day, you know. But what's particularly frustrating for me is there doesn't seem to be any treatment. I've been on PROCRIT injections to try

to bring up the red blood cells and, you know, that, I don't think really does work. It seems to have had mixed results and now I'm -- the insurance doesn't cover it anyways. And so, you know, I'm left with doing blood transfusions which, you know, my oncologist is really not happy about because I guess they view it more now as almost a transplant so problems with that.

So it's very frustrating to me because, you know, you don't seem to have an option and this is just something that you're going to have to live with and, you know, it is difficult because I'm -- you know, I'm not young, I'm 65 but I don't think I should go by the "one thing a day" rule that the 89-year-olds used.

MS. GIAMBONE: Thank you, Ginny. So can I ask a follow-up question? Does it -- it sounds like the fatigue is coming as a side effect of the treatment that you're taking? Is that accurate?

MS. KNACKMUHS: Well, in my case, initially they thought it might be the treatment but now it's been too long, so now it's a question

of well, is the cancer actually attacking the bone marrow --

MS. GIAMBONE: Okay.

MS. KNACKMUHS: -- you know, so they don't really know. But a lot of times, fatigue, you just get fatigued for no -- that's why I say mine's a little different. I mean I do actually have low blood counts. A lot of times people have fatigue with breast cancer and you really can't point to anything so it's sort of the same situation. There's -- you know, that's why fatigue is so difficult because there really is nothing to treat it.

MS. GIAMBONE: Okay. How many of you -- yes, Sandy.

MS. FINESTONE: I'd just like to make a comment. Words are very powerful to me and I think fatigue is not the right word. When we as a general audience think about fatigue, it means we stayed out too late or we gardened too much and we're tired and we rest and the fatigue resolves. I think it's important to note that the type of

fatigue that patients experience is not like that at all. They can rest and rest and rest and the fatigue doesn't go away. So when I talk to my patients, I use the word "weakness" and that resonates with them a lot more and they seem to say yes, that's what it is. It's not that I'm tired. It's that I'm weak. I just can't do these kinds of things. So I sort of make it my challenge not to use the fatigue word and I'd like to hear comments from some of the other patients, because I think it's misunderstood.

MS. GIAMBONE: Thank you very much for presenting that perspective. I actually saw several heads nodding as you were speaking so maybe we can do a show of hands here. Does that sound -- does that resonate with you that it's the weakness, this persistent weakness versus a more, I guess, temporary type fatigue? So could you raise your hands and does that resonate with you? Okay, great. Thank you, Sandy. Thank you for clarifying that.

Okay. Any other -- yes. Oh, no, she'll

bring over the microphone to you.

MS. CAPPEL: My voice can be big. Hi. My name is Elizabeth Cappel. I also have metastatic disease. I think the weakness is more when you're going through treatment and when you're not in treatment, the leftover side effects can be fatigue, to clarify that. I think it's two different situations. If you're not in treatment, sometimes the treatment, the long-lasting effects can be fatigue. For me, taking iron supplements helps with that. I have iron deficient blood so my hemoglobin can be fine yet I can still have some types of fatigue left over but the iron does take care of that.

MS. GIAMBONE: Okay, very good to know. Thank you very much. Okay. So let's try to move on to another symptom unless -- does anybody have anything else? Yes, Jonca.

DR. BULL: Another -- a clarifying question on the fatigue and weakness. Are people able to sleep? Where does insomnia fit into this or lack of being able to get good quality rest?

MS. GIAMBONE: Okay. So I'm seeing a lot of nos here. Would anybody like to share their perspective? How about right here, Sarah. Thank you, Jonca, for your question.

MS. WRIGHT: First, I don't have metastatic breast cancer so I'm fortunate but I was diagnosed with breast cancer back in '95, so whatever treatment I had worked. But I would like to say with regard to this fatigue issue, the type of fatigue we're talking about -- I heard some people say they do have trouble sleeping, sometimes you're so fatigued that you can't sleep but even when you do get a good sleep, you are still fatigued. So it's not a tiredness or a fatigue that goes away with rest and that's the difference between someone who has not had cancer and has not had treatment, that when they've overdone it or they've stayed out late and you're healthy and you have always been healthy, you get a good rest and you're rearing to go again.

This is not a type of tiredness that will go away after a few nights of good sleep and

good eating. This is something that is always present and you might have a good day or two but it's always there. It's here right now. I mean you just can't get rid of that. It's hard to explain if you haven't experienced it and I don't know if there is a word to describe it. It just doesn't go away with a good sleep and if you haven't experienced it, you just -- it's hard to understand.

MS. GIAMBONE: Pervasive exhaustion?

MS. WRIGHT: Oh, I'm sorry. I'm told I didn't say my name. My name is Kim Wright (ph).

MS. GIAMBONE: Kimberly. Thank you so much, Kim. I appreciate it. So I'm going to -- oh, yes. Let's take one more comment.

MS. HOLLOWAY: Hi. My name is Jamie Holloway. I was diagnosed in 2012 with triple-negative breast cancer and had a complete response to neoadjuvant chemotherapy. And I will say the fatigue is definitely a lot stronger when you are undergoing treatment and we've heard from a lot of women who have metastatic disease so they're still

undergoing treatment.

I was not thrilled to find that I still have fatigue now two years later and it's not nearly as bad and it's not the one a day thing like when I was in treatment. I have young children so I likened it to when you have a newborn baby. You can do what you want in the morning but you must be home at noon because you have to sleep or you can't function. And it's not as bad as that but it's -- there are a lot of times in the evening where I feel like it's just too much energy to open up my computer and like get something off of Amazon. That's just too much energy and I don't want to do it.

And so -- and there are definitely afternoons where I'm just so sleepy and it feels like sleepy but it doesn't go away just because I sleep and I think that's something that we've kind of talked about. And I'm guessing it's still lasting effects from treatment. You know, I'm not on any hormonal therapy now or anything but, you know, it's been a good two years and it still

lingers.

MS. GIAMBONE: Okay. Thank you very much, Jamie. Okay. So to recap, we're hearing you summarize that it's a pervasive exhaustion. We heard that it can be worse during treatments but that it's still lingering post treatments. In some cases, it sounds like it's sort of worsened over time, as you mentioned earlier, that, you know, you had treatment several years ago but you've kind of -- you feel as though it's getting worse now. And you mentioned that it is something that with the tiredness and sleepiness, that it's not something that's -- it's not just you sleep it off or anything, it kind of lingers and continues to be there. So thank you for sharing those thoughts with us.

Any follow-up questions regarding the fatigue? Yes, Geoff.

DR. KIM: I'm just curious. Actually, for Katy, while you were on KADCYLA and you had -- you said that it seemed to be a very positive experience, did you have that lingering fatigue

during the treatment, too, or was it put away for a little bit?

MS. McRAE: No, not on KADCYLA. It was an absolutely amazing drug for me and -- but I also feel I'm sorry of very positive and I walk. I love to walk and so sometimes I would choose to just push myself a little bit --

DR. KIM: Yeah.

MS. McRAE: -- and go out and do that walk. I think a lot of this has sort of a psychological component as well and that was my way of dealing with it. Right now I'm --

MR. THOMPSON: Right.

MS. McRAE: -- fatigued since I've been off KADCYLA and going through some more stuff but -- so no, KADCYLA was an amazing drug.

DR. KIM: Right. And I wonder if you have a shared experience with the Xeloda, too, for 5-1/2 years. Did you have the same type of fatigue, too, as well or did that somehow abate a little bit during the treatment while you're having a prolonged response and then it came back

after the treatment didn't work as well or upon progression?

MS. GIAMBONE: Ginny.

MS. KNACKMUHS: Yeah. I didn't experience a lot of fatigue when I was on Xeloda. It's really only been in the last year-and-a-half when my blood counts really took a hit and, you know, that is a side effect of being on chemo for a long time.

DR. KIM: Right, right.

MS. KNACKMUHS: And now I just can't seem to get beyond it even though I'm off the drug and it, you know, points to maybe, you know, something a little more serious than just the effect of the -- of being on the drug so

DR. KIM: Thank you for sharing that.

MS. GIAMBONE: Thank you, Ginny. Thank you, Geoff. Are we hearing anything on the web specifically regarding the fatigue?

MR. THOMPSON: Yes. We heard very similar perspectives. One person saying that in her experience, the most common thing she's heard

patients talk about is fatigue, second being sleep. One person saying that fatigue can vary very much among patients depending on what treatment they are on, and another person echoing something we heard about sleeping saying that she feels sleepy all the time and it doesn't go away when she does sleep.

MS. GIAMBONE: Thank you. Okay. Let's move on to some of the other symptoms that you've all identified. So I believe pain was also identified by several of you. So would anybody like to talk about how their pain manifests and how do you experience it? Yes.

MS. JONES: Hi. I'm Thelma and I was diagnosed in July of 2007. The pain that I experience can be sometimes almost from head to toe. In the beginning, I had very mild arthritis or either carpal tunnel syndrome and then over time, it's gotten worse so there -- my fingers are sort of now lumping up and on some days, it's excruciating with the pain or there are days that my hand is in so much pain that I literally have

to pry my fingers open. And so that affects my daily activity because I'm a very active person. And there are times that I get the pain in my breasts and when it happens often, I mean, naturally, I think, oh, has the cancer returned, so I return to my doctor and they may say that it could be, it's probably the side effects of the radiation.

And then on a daily basis -- I think one of the panelists mentioned about the lower back pain -- and you have these pains so much that it's either you do some type of medication or drug, which I'm trying to stay away from except the ones that I'm on, exemestane, the hormonal therapy. But I'm really trying to focus more on complementary therapies because I keep thinking about the toxicity of the drugs. I'm HER2-positive with an unknown primary so I underwent a lot of drugs in the beginning and I'm just always concerned about the long range implications of those drugs.

MS. GIAMBONE: Okay. Thank you very

much for sharing that. So head to toe pain, pain in the hands. You mentioned pain in your breasts. Okay. Anybody else? Yes, Karen, let's hear from you.

MS. DURHAM: Well, mine is bone, particularly joints and also muscles and it's not just one place. It moves around. One day my left knee may just hurt really, really bad for two-three days and then all of a sudden it's gone and then it's something in my right arm. It's -- it just moves all over.

MS. GIAMBONE: Okay. Thank you for sharing that. Anybody experience that sort of pain that moves throughout the body? Katy, yes.

MS. McRAE: I -- it's kind of interesting because for the first -- I've only had pain for two weeks. It started two weeks ago it was and after six years of metastatic and it was just excruciating. I couldn't believe it but the types -- like even in the one episode, it's -- there's a sharp skewer type pain. There's a dull ache. There's a throbbing pain and it comes out

of -- I mean the intensity and the sudden onset has just shocked me, you know, in the last two weeks. And I thought -- when you said, Karen, about the muscle pain, I thought I'd pulled a muscle or whatever because, you know, I walk four miles a day and I thought, okay, I've pulled a muscle or whatever. Well, now it turns out that it's all because of, you know, the nerve damage across my -- the sacral ileac and into the sacrum, but it's just the intensity. I look at my body. I'm saying, who are you, where's this stuff coming from in two weeks?

MS. GIAMBONE: Right.

MS. McRAE: I can actually almost physically feel the cancer just -- you know, just pinging me. It's going to do with it wants to do and you're just along for the ride.

MS. GIAMBONE: Okay. Thank you for sharing that perspective. Is there anything that leads to the worsening of the pain, any -- is there an activity or is there something about a particular day, is there an average day of pain

versus a more severe day of pain, or is it sort of always there? Would anybody like to -- yes, Debbie.

MS. DUNNE: I was just going to say it's always there, it just kind of moves around. But again, to your point about not really wanting to take the drugs, I've done a lot of holistic things myself and doing exercise and hands-on healing, acupuncture and all of those really do help.

MS. GIAMBONE: Okay, great. Yeah. So let's take one more comment.

MS. JONES: And I also detect when I'm extremely tired, the pain is greater as well so the two sort of are intertwined.

MS. GIAMBONE: Okay. So you see a correlation between the pain and the tiredness or the fatigue or weakness?

MS. JONES: Exactly.

MS. GIAMBONE: Okay, very good to know. Yes, we'll take -- Sandy.

MS. FINESTONE: I think it's very confusing to women is the pain they're

experiencing due to treatment, due to aging, due to hormonal manipulation, so it's very confusing. Should they act on this pain and go to see their physician because possibly it's a recurrence of their cancer or progression of their cancer, or is it just a natural sort of aging kind of thing because the lack of estrogen and the manipulations? It's very confusing and as well as hurting.

MS. GIAMBONE: Okay. So I think that's a good place to do a show of hands. So it sounds like it is difficult then to tease apart whether it's due to the disease or whether it's due to the treatments? I see a lot of heads nodding. Can you -- could you all raise your hand and say -- is that a fair statement, that it's difficult to tease that apart? Okay, great. Okay. Thank you for sharing that with us.

Okay. And then what we'll do is -- I know you've all mentioned -- you identified several of these symptoms. I do want to ask is there a particular symptom that you didn't know to

expect or something that has really sort of surprised you that, you know, it sounds like you've all done lots of research and you've talked to all your doctors, but did something come up that you just didn't know to expect? Yes.

MS. JONES: One of the challenges I had very early was dental. I've had -- I mean bought everybody's dental four or five times over and in the beginning, in 2007 when I presented this to my doctor, my dentist, he wasn't very receptive to the idea that that's what was causing it. And that was very important for me to -- for him to understand that because the copayment on my insurance would have been less and so was the out-of-pocket expense. But when I asked him to document that, he couldn't seem to agree with me. So as a result, I ended up paying thousands of dollars out-of-pocket and now because I'm a patient navigator and talk to a lot of people, one of the things that I strongly encourage is that if you have dental challenges now, you want to make sure that you've corrected that before you go into

serious treatment because it does have an implication.

MS. GIAMBONE: Okay. Thank you. Dental effects. Yes.

MS. CAPPEL: Living with metastatic disease and doing it for a while now -- I'm going on 9 years, 12 years all together and 9 years metastatic -- they're finding that there are more side effects that they were not aware of because people weren't living as long as this. So what's recently happened in the last year was that I have a hole in my septum in my nose, and they said that that is from prolonged use of chemotherapy and the blood vessels aren't receiving enough blood in my septum and it actually caused it to erode. So there's nothing they can do for it. It doesn't really bother me. It feels a little weird but it doesn't bother me. But that's one thing that I definitely did not anticipate was that my nose was going to fall apart but the rest of it's still okay, so it's hanging in there.

MS. GIAMBONE: Okay.

MS. CAPPEL: So just finding more and more things since you're living long-term with breast disease.

MS. GIAMBONE: Right, okay. So nasal issues.

DR. IBRAHIM: Can I ask a follow-up question?

DR. IBRAHIM: Oh, sorry, go ahead.

MS. DURHAM: I was just going to say that I think anybody that goes through treatment understands that they're going to have some degree of nausea, diarrhea, constipation, and a few of those things. And if you read what side effects are, even on over- the-counter medications, there are so many of them there, and I don't think any of us that have been treated or are being treated for breast cancer know the magnitude that we're going to have the majority of those side effects and how much we're going to have them.

MS. GIAMBONE: Okay. I saw a lot of heads nodding to what you just said, Karen, so that sounds like it's a shared perspective. Yes.

MS. FARIS: Hi. My name is Susan Faris and I just want to echo. You know, I recently read a study that talked about how the doctors will underestimate what kind of -- how severe the side effects are going to be for a medication, and I hear that repeated by nurses and oncology units all the time, that the doctors do underreport them. They -- for me, it was the severity of -- I mean I looked at the list and I did not realize how bad it was going to be so that's really what the surprise to me was, like, you know, it was sort of like I thought I was going to go on a roller coaster ride but instead I did the straight drop down and it was not fun so, you know, that kind of thing.

MS. GIAMBONE: Okay, thank you. So the severity or the intensity of what you are experiencing, there's nothing to prepare you for that. Yes, Amna.

DR. IBRAHIM: So I'd like to tag a question onto that. Some patients say that if they knew that they are going to have hair loss,

they would have wanted a different kind of treatment whereas others are willing to take much more toxicity. So I'm wondering are there any -- is there any toxicity that you can identify which you think would have changed the treatment that you were seeking, that if you knew that that toxicity was going to occur, you would have actually gone for another treatment?

MS. GIAMBONE: Yes, let's go ahead and hear from Katherine.

MS. O'BRIEN: My answer will be slightly maybe outside of what you asked but when I was given the anti-estrogen treatment, tamoxifen, I was told, you know, I would be in -- and also had ovarian suppression -- so early -- premature menopause. And my doctor said almost certainly I would have hot flashes and so on. And so I did have some symptoms but I waited -- you know, I waited in dread for these hot flashes and I am on the minority in that but thankfully, it didn't happen. But overall, it shows you how difficult it is to evaluate treatment because you can now

that these are side effects. What you don't know is how is it going to happen to you specifically and what is your tolerance for what the treatment may be.

So I think it is extremely difficult to quantify because even -- I have not had a treatment that causes hair loss but I know it's a very important issue for, I would say, all patients but even -- some patients have found -- they were told they were going to lose their hair, maybe they had thinning and if they had -- and they had good results with the drug, so if they went strictly by "I will lose my hair," they would not -- they would have missed out on a drug that proved to be well for them.

So I think what I am saying is the other side effects is the -- this ties into the anxiety. You don't know what is going -- you don't -- there is -- you don't know what the treatment will mean for you specifically.

MS. GIAMBONE: Thank you, Katherine. And I'd like to just make a call-out. For those

of you who are on the web, if you'd like to dial in to share any phone comments, please go ahead and do so now. And we'll take just another comment and then we'll check in with the web. Yes, Debbie.

MS. DUNNE: So despite all the research I was doing, I really wasn't considering toxicity because again, my mindset was I'm fighting for my life so if I lose my hair and I feel pain and I don't even know if I'm going to be alive in a year, so I'm not going to worry about toxicity. So that's where I was coming from.

MS. GIAMBONE: Thank you, Debbie.

MS. FINESTONE: I would just like to add as well. Women -- when you're diagnosed, you think you're going to die. Now is there concern about losing your hair? Absolutely. And will some women make the decision not to treat? They will but those women are few and far between. Most women will actually do more -- at least that's been my experience -- the maximum in order to save their lives. But everyone starts from a

very naive position. When you say "nausea," well there's nausea and there's nausea and each of us are our own little, you know, clinical trials, how we respond and how we don't. I don't think that -- we're not informed enough. You know, it's like being dropped into a foreign country and I'm not pointing a finger at anyone, but physicians, clinicians use language we as patients don't understand, and you're asked to make decisions without the information you need to make that decision, and you don't have time, you don't have time to educate yourself about the language of cancer, the effects of cancer or how, as someone mentioned, how am I going to respond.

Now I didn't have chemotherapy or radiation therapy or any therapy but I have hot sweats -- hot sweats -- what are they -- hot flashes that are --

UNIDENTIFIED SPEAKER: And sweats.

MS. FINESTONE: -- they are sweats -- that are horrible. I have joint pain and that all comes with aging but I would have done whatever it

took to save my life. I was diagnosed young and had two small children. That's what was foremost in my mind. Losing my hair, no one wants that to happen but I don't think -- a very, very, very small majority of women will opt not for treatment for something like that. That's my experience.

MS. GIAMBONE: Thank you, Sandy. Thank you. So Sandy -- yes, it looks -- let's hear from -- I don't think we've heard from you.

JOANNE: Yes. I'm listening to everybody and I'm relating to what everyone's saying and I'm a survivor of two years now. And the thing that I would -- you know, if I -- my wish -- my wish is that we could know what to expect, you know, onset, duration and intensity of any of these side effects, whether they happen. You know, you hear oh, it's going to -- you know, you're fatigue's going to get worse with each cycle, right? Well, I wasn't quite prepared for how fatigued I would be by my sixth cycle, just wasn't. I fell flat on my face. I literally did and have recovered well. I'm doing well, wasn't

quite prepared for, hmm, I still am very active with lots of energy and yet I have less energy than I had before I was treated. So no one would really notice that I may be more fatigued than I was before.

And so, you know, I'm thinking about, boy, I would love some research out there that looks at for whom, under what circumstances, under what conditions can we expect, you know, that someone would be feeling, you know, tired, exhausted, or fatigue, pain, because I think more than anything, I want to be able to plan. If I know when I'm going to be experiencing that, then I can work around that, I'll feel less out of control. And that's one of the other themes I'm hearing, too, just feeling -- that's part of the anxiety, what -- you know, when I'm going to feel what.

MS. GIAMBONE: Okay. Thank you. And you're name?

JOANNE: I'm Joanne.

MS. GIAMBONE: Joanne. Thank you,

Joanne. So correlating the lack of -- or the -- or not understanding right away what to expect or the intensity or severity of what to expect, correlating that to the anxiety that you feel. Okay.

MS. JONES: And can I just share because I think that's an interesting question but a paradigm shift on the way we are addressing it, because the women here, I get the impression we're all fairly well read but then there is that segment of the population that a, you have challenges in just getting them to a mammogram because of fear. So then if you start telling them after they've gotten a diagnosis from that fearful mammogram that has taken them years to get, if you start telling them about the challenges that they are going to experience, then I can assure that that's going to delay their treatment even greater.

MS. GIAMBONE: Okay.

MS. JONES: So we have to find a way to not only mitigate their fears but to help them to

understand their treatment choices in a way that they will reach out to -- and that's very difficult when the fear factor is very pervasive, because they've heard everybody in their neighborhood say all of the horrible things about it. They rarely hear the benefits of undergoing any type of cancer treatment.

MS. GIAMBONE: Thank you very much. And we'll take another comment.

MR. THOMPSON: Just want to point out we're going to be going to a break pretty soon but we will talk much more about treatments and treatment considerations in the afternoon, so

MS. GIAMBONE: So we'll take one more comment and then we'll check in with the phone and we'll go to break. Yes.

MS. KNACKMUHS: Ginny Knackmuhs again. I was just thinking when Sandy made her comment, and I thought it was a very good one, that in early stage cancer, you know, you're trying to save your life so losing your hair in the, you know, long-term is not that big a deal. And I

think that's a great point to illustrate the difference between early stage and metastatic. I mean, you know, early stage, yes, you're trying to save your life and, you know, you'll put up with just about anything, you know, because what is it going to be, six months a year, you can get through it.

When it comes to considering symptoms and side effects for metastatic, it's quite a different decision. You know, you're going to go on this drug. You're going to lose your hair. Well, for how long? Will I ever get it back? So, you know, it's a different -- obviously, it's a different perspective but I'm a patient but I'm also a patient advocate for a metastatic breast cancer network. We're a patient group and what I've noticed is that -- and I just want to say this for all the young women out there, particularly those that are raising families that are metastatic -- they are willing to put up with so much more toxicity just for the sake of being there as long as they possibly can for their

children.

MS. GIAMBONE: Thank you, Ginny. So let's go to the phones and do we have any callers on the line? Operator, do we have anyone lined up for a phone?

THE OPERATOR: Jennifer, your line is open.

JENNIFER: Hi. This is Jennifer. Can you hear me?

MS. GIAMBONE: Yes, we can hear you. Hello.

JENNIFER: Hi. So, yes, I was diagnosed about two years ago at the age of 34, very active person. I am triple-positive. I had double mastectomy, 13 lymph nodes removed and there was cancer found in the lymph nodes. Had no problems with chemotherapy, didn't need any kind of radiation or anything like that -- I was actually a stage three -- but have severe problems with tamoxifen including very bad hot flashes, depression for the first time in my life, bloating, abdominal pain that just -- that would

have me sometimes double over, so I have chosen to stop taking tamoxifen. And I have also chosen to not go in an AI because my quality of life is more important to me than living with something that makes me feel less like a woman. And being young, the other thing, too, is I lost the ability to want to be intimate or sexual with anyone, and that's something that's very important to me and if I can't have that, I would rather go through chemotherapy and other treatments again if the cancer comes back versus go through something that's going to take away my quality of life.

MS. GIAMBONE: Thank you so much for sharing that. Thank you.

JENNIFER: Thank you.

MS. GIAMBONE: And no more -- okay, so there's no more -- okay. And can we just get a summary of anything else we've heard on the web for Topic 1?

MR. THOMPSON: Just two small points from an earlier conversation, so one person was talking about pain and tingling where their lymph

nodes were removed and also just getting pain over random body parts after the surgery. And somebody else was talking about suffering from cataracts and thrombophlebitis after tamoxifen treatment and wasn't sure if it was a side effect or something related to the cancer.

MS. GIAMBONE: Okay. Thank you. I know there is so much more that we could discuss for Topic 1, but we'll take a short break now, let's say 10 minutes. We'll take a 10-minute break and then we'll come back and talk about Topic 2. Thank you, again.

(Whereupon, off the record at 2:45 p.m., and back on the record at 2:55 p.m.)

MS. GIAMBONE: So we're going to get started and how about I just have our Topic 2 panelists come on up and have a seat. Okay. So we will go ahead and get started again.

We had such a great discussion for Topic 1, for the first half of the meeting, and I think that the one theme that just kept coming up --

again, I think my FDA colleagues would agree is that biggest part of your life or the biggest impact of living with breast cancer is the treatments and the management of your breast cancer, the doctors' appointments, the decision-making as it has to do with treatments, so thank you for bringing up this very, very important part of your life and sharing that with us. And we're going to go into much further detail with this topic which focuses on treatment and I know we already -- we started bringing that up. You know, you shared so much of that in Topic 1 and it's very understandable. So we're looking forward to exploring that even more in this discussion.

And certainly, if there are other aspects, you know, or downsides or side effects that you are experiencing with your treatment that you mentioned in Topic 1 that we didn't get to explore too much, I encourage you to continue to bring those up now and share those with us.

Okay. So just to reiterate again how our topic will look -- so for Topic 2, we're going

to be discussing treatments: So, what are you doing to manage your breast cancer, to treat your breast cancer and how do you experience the treatments; what are the benefits that you see; what are the downsides that you're experiencing? And we're also -- as I mentioned, we're going to spend a portion of this discussion talking about -- - and we already brought this up a bit -- is the decision-making, the factors that you consider in deciding what treatments you will be taking.

So with that, let me turn it over to our panelists and, Colleen, if you could just get started. And we'll have each one of you introduce yourselves and then you can start your presentation.

MS. DUFFEY: So Good afternoon. I'm Colleen Duffy. I'm a 34-year-old wife, mother, and engineer. I was diagnosed with stage four breast cancer which is HER2-positive in December of 2012. It was just four months after my second baby was born. It has since spread to my bones, skin, lymph nodes, lung and my brain. I have

completed a variety of treatments and am very grateful for the opportunity to share my perspective on the current approaches with you all.

My cancer has recently progressed and I started a new drug, KADCYLA, on Monday. I will continue infusions of that drug every three weeks until the cancer progresses again. It's just been a few days since I started this new drug so I'm going to focus on the treatments that I have had up to this point. So my first treatment after diagnosis was a traditional chemo and a targeted therapy. So I started on Taxotere, Herceptin, and PERJETA. I completed six cycles with the Taxotere and stopped it but continued the Herceptin and PERJETA until about two weeks ago. I have an infusion of ZOMETA every six weeks and I've also taken an oral chemo pill, Xeloda, had a mastectomy, undergone whole brain radiation and heat therapy, and a targeted radiation.

The most significant downsides of all of these treatments are that they stop working. The

tumors outsmart them and grow. Then there becomes the need to switch. I would be happy to tolerate the side effects and inconveniences caused by any of the treatments if they worked forever. This issue affects my life by not allowing me to make long-term plans, interrupting my routine, my work schedule, and my family's routine.

I do many supportive care treatments to manage my side effects. I currently attend a support group, participate in therapy, take a prescribed antidepressant, Lexapro, to manage my mental health. I have also attended many seminars, end-of-life preparation, healthy eating, coping strategies, future research and therapies.

As far as my physical side effects, I take Imodium A-D and/or Lomotil to control my diarrhea. For pain management, I have taken OxyContin, Percocet, and Fentanyl patches but I try to stick to the ibuprofen and getting massages. I had to take steroids for the swelling in my brain. I had hyperbaric oxygen treatments for the wounds I had following the heat and

radiation therapies. I have also done acupuncture but following the mastectomy, my oncologist does not recommend it due to the risk of lymphedema.

So my mental health has been very well managed thanks to the support networks in my community. The diarrhea is mostly manageable by the medication but depending on my chemotherapy, it has become extreme. At that point, I go to the oncologist's office and get fluids. Pain management is a challenge because there is a fear of becoming addicted to the pain pills. I am also adversely impacted by impairment when I take Percocet, OxyContin, and Fentanyl patches. The steroids greatly negatively impacted my emotions and my self-control. The hyperbaric oxygen treatment worked very well but it was a daily therapy that required driving.

The only side effect that hasn't been addressed through drugs or alternative therapy is fatigue. I am always so tired.

I weigh the importance of prolonging my life much higher than improving the symptoms I

experience due to breast cancer. Staying alive is my main goal in treatment. I have found that most of the side effects I have experienced will pass in time. Since my diagnosis, the good days, days when the side effects don't consume me, have outnumbered my bad days, and there are many reasons why staying alive is so important to me. One is that I'm a mother to young children. My will to live for my children is worth suffering to me. I will take on many more side effects if I get to stay on a particular drug longer. This is one more month I get to participate in the raising of my children, one more day I get to see their smiles, hear their laugh, and show them my love. I am also young and I still have a good immune system. I try to prolong each drug I am on for as long as possible. I have yet to encounter a side effect that would be bad enough for me to ask to stop taking the drug or to end a treatment earlier than recommended.

There are many factors I use when making treatment decisions. My overall strategy is to

stay on each chemo drug for as long as I can. I try to stretch the use by including other treatments. When I was diagnosed with a brain metastases, it was determined that my current systemic treatment was still controlling the cancer in the rest of my body. Instead of abandoning Herceptin and PERJETA, I underwent whole brain radiation, added Xeloda to the drug regimen. Instead of switching targeted therapy drugs for the skin metastases, I added heat therapy and targeted radiation. Instead of switching targeted therapy for the lymph node progression, I added a local radiation. So far this has given me an additional year on the same targeted therapy drugs.

My overall goal is to prolong my life and I am doing this by carefully considering other approaches with my oncologist before abandoning systemic treatments I take that may still be somewhat effective. Common and uncommon side effects from these drugs do not play a major role in my treatment decisions. Their effectiveness in

prolonging my life is the most important criteria that I consider when choosing a treatment plan. As long as I stay on my targeted therapy, I can endure the side effects of the other treatments.

As a stage four breast cancer patient with major progression, I am much more likely to die from the breast cancer than a side effect of the treatment. I'll take my chances in regards to the serious risks. I would much rather try a treatment in the hopes of prolonging my life long enough to see a cure.

Thank you so much for allowing me the opportunity to share my experience.

MS. GIAMBONE: Thank you, Colleen. Susan?

MS. FARIS: My name is Susan Faris and good afternoon, ladies and gentlemen, and thank you so much for letting me speak today. I really appreciate it.

I -- 30 percent of women who are diagnosed with early breast cancer will move on to metastatic status. I am the six percent who was

diagnosed right out the door as metastatic. I am HER2-positive and I was diagnosed on January 2012 at age 47. The cancer had not only formed in my breast but it had encumbered my entire liver. I was immediately put onto weekly Taxol and Herceptin treatments that lasted for 24 weeks. The side effects of this were severe and got worse over time. I experienced extreme neuropathy of my hands and feet so bad that I would often fall over and I could not button my own shirt or pick up small items or put on jewelry. I had extreme pervasive fatigue. I had steroid-induced bouts of mania and acne covered my body due to steroids. I had acid reflux, constipation, edema in my legs, muscle aches, renewed sciatica, insomnia, loss of taste, hair loss, and nails that lifted, infected, and fell off. These are typical side effects of systemic chemos.

The result was that I was disabled. I was barely able to leave my house or care for myself and I was increasingly isolated. I became hopelessly depressed in spite of counseling and

antidepressants. The chemo that I was on was extended several times from 15 weeks to 20 to 24 weeks and finally, I demanded that it be stopped because it was killing me.

After this, I was considered stable. I had scar tissue on my liver and I was maintained on Herceptin, and I could go back to working full-time and the neuropathy went away. The side effects of Herceptin are minor. I had some sinus issues. I had some fatigue. That was about it.

But then in November 2013, I had what I call a "flare-up." I refuse to use the word "progression." Anyway, when I was told that I had a five-centimeter mass on the dome of my liver at the appointment with my oncologist, I began to ask questions. I had a list of questions but instead, I broke down into sobs and I told her repeatedly I did not want to go onto a systemic chemo again. The treatment that she put me onto was KADCYLA, which is a targeted chemo. The negative impacts of this chemo are mostly limited to the cancer itself although it does have some systemic

effects. There is no such thing as no side effects. It is a question of severity. So I experienced minor fatigue, mild neuropathy, acid reflux, minor constipation, elevated liver enzymes, and lowered platelets. My oncologist has reduced the dosage a few times to minimize the neuropathy and the elevated liver enzymes and the lowered platelets but the treatment, knock on wood, is continuing to work.

These side effects are easily treated with Prilosac for the acid reflux, constipation is treated with a stool soften, and I use supplements such as alpha lipoic acid and vitamin B6 for the neuropathy.

As long as I can live my life and continue to work full-time, that is my goal. My focus is on quality of life when I am choosing a new treatment. The average survival time for a metastatic breast cancer patient is 2.5 years. I've exceeded that. So, I, in the time that I have left, would like to live a quality life, not one where I'm suffering.

I judge potential treatments based on high potential benefit but also significant immediate negative side effects. If a treatment has higher immediate negative impacts that would severely limit my life, I will not choose that treatment, even if the treatment would prolong my life. Neuropathy is one of my greatest fears. Medicines or supplements can do little to treat neuropathy at this point and since I am very prone to this side effect, if the treatment has that as a side effect, I will experience it. I would rather my oncologist reduce the dosage on a treatment and risk the cancer growing than to continue on a higher dosage and risk permanent neuropathy.

The factors I consider when choosing a treatment are the possible long-term impact against the severity of immediate side effects, the likely length of my life, and the percentage of patients who may suffer that long-term side effect. Acceptable risk for me, for instance, is the heart toxicity of Herceptin. Thirty-four

percent of patients treated with Herceptin, you know, have that experience but it has a significant progression free survival time, plus the heart toxicity fits into my goal of dying of a heart attack instead of cancer.

I've announced this goal to my oncologist and when I first met my cardiologist, I told him this was my plan. His response was to ask to -- was for him to ask me to let him know when I would like to schedule that.

(Laughter.)

MS. FARIS: I knew I'd met my man. And if a side effect is manageable with medicines that do not themselves have significant side effects, then that is acceptable as well. I balance between staying alive and living with quality of life. I focus on targeted treatments because of the minimal side effects and high benefit of targeted therapies such as Herceptin, pertuzumab, TYKERB, and KADCYLA, these are my focus. My hope is that they are -- these type of treatments are moved quickly into market so that I can continue

to live. I regularly search clinicaltrials.gov, PubMed and scan Twitter looking for the current research on these therapies, things that have not even made it to PubMed yet.

My goal is to stay away from systemic chemos. That's just my preference due to their extreme side effects for me and their disabling qualities. When I've exhausted targeted treatments and only have systemic chemotherapy as a choice, I will try one or two of these treatment types. But if my quality of life is greatly minimized by these treatments, I will turn these systemic chemos down and I will choose the right to die.

MS. GIAMBONE: Thank you, Susan. Any final remarks?

MS. FARIS: Nope.

MS. GIAMBONE: Thank you very much. Elizabeth?

MS. CAPPEL: Good afternoon. My name is Elizabeth Cappel. I was diagnosed with early stage two invasive ductal carcinoma. I have no

family history of breast cancer or of any type of cancer whatsoever. Like Susan, I was supposed to die of heart disease but instead I have breast cancer. I was checked for the BRCA1 and 2 gene and I am negative for that. I was diagnosed in March of 2003. I have four children. I had four young children at that point and my youngest was three months old. She's now 12. And I am triple-positive for HER2.

I had a lumpectomy and radiation in the beginning with the stage two invasive ductal carcinoma. I had no lymph node involvement and I had clean borders so I was looking pretty good.

I was fine for about 3-1/2 years. When I first was diagnosed, I had Adriamycin and Cytoxan AC which is the normal thing, four rounds. The reactions were hair loss -- I have actually lost my hair three times from chemo -- mouth sores, nausea, vomiting, fatigue, low blood counts, the usual, radiation fatigue and skin blistering.

I was on Tamoxifen for 3-1/2 years and

then I had a recurrence. When I had a routine mammogram, they found DCIS of my right breast. It was in my right breast to begin with and I asked for a PET scan, which they didn't think was important but I demanded a PET scan and it showed a benign hemangioma on my liver. So we went ahead with a bilateral mastectomy with reconstruction. A week later, I had a deep vein thrombosis of my right leg. Three days later, I passed out in the doctor's office with a bilateral pulmonary embolism. I needed a Greenfield filter which I was very young for since I was early 40's.

A few months later, my blood work showed that I had increased liver enzymes and, in fact, I did have liver metastasis, so the mastectomies were not actually need. I had an MRI of the liver. It showed that about three-quarters of my liver was involved with only a few liver cells that were actually viable. I was told at that point that I would have, at best, two years to live -- that was from Fox Chase and my primary doctors -- oncologists -- two years, at best, to

live; during that time, I would be on chemo continuously and quality of living would be really bad and that I would no longer ever have hair again. As you can see, I have a really nice head of hair right now.

So that was almost nine years ago which is pretty incredible. What I had for treatment would be Nevelbine and Herceptin right after that. I had extreme reactions to that, loss of finger and toenails also, which my toenails are still not normal, very bad reaction, shaking on infusion -- they all it shake and bake -- increased blood pressure, red face and neck -- they slowed the infusion, added Benadryl and Decadron -- mouth sores, vomiting, fatigue, body pain, neuropathy.

I went onto TYKERB, Xeloda, also loss of nails, bad, bad joint pain, and then we just went on Doxal and Herceptin. Doxal actually was one of the more gentle drugs for me. I had hair loss, nausea, fatigue, infusion reactions; we used Zofran a lot. But then we continued on with Herceptin.

With Doxal, we got to a point about 2-1/2-3 -- well, no, three years ago where the -- everything was progressing and the liver mets were still growing and we couldn't get them under control, so we used Doxal and we threw in something unusual. We threw in CyberKnife. Now with metastatic breast disease, you don't typically do CyberKnife or radiation to the site of the problem with the liver, but we decided that why not try it. So we did the CyberKnife.

Problem with the CyberKnife was I was coming off of Doxal so there was a lot of fatigue but also that I had three to four ribs that were broken. Now that plays into would you have chosen a different alternative to treatment. They weren't aware that this could happen so I now have three -- definitely three ribs that are broken permanently, which means that they disintegrated. So I need to have things for pain management. So I have nerve ablations done every three to four months to manage that pain because my ribs flail.

I stayed on Herceptin after that but I

became very toxic to Herceptin which is unusual and I couldn't stay on it any longer. And that is the plan, that you stay on the Herceptin but I had one of the worst reactions they've ever seen and I went to Sloan and saw Larry Norton, who is one of the people who did, you know, work on Herceptin from the beginning and he said it's one of the worst reactions he's ever seen. I completely dump all of my histamine and get terrible body pain where I can't move. So we decided to stop it and that was over two years ago.

So I am on no treatment whatsoever right now. I get checked every four weeks for my cancer markers, my 2729s. I get scans every three months. Right now I have zero to one circulating tumor markers which means there's no sign of cancer in my body. My liver mets are completely gone. It comes back no sign of metastatic disease, and my bone scans have been clean for years. So, right now I just stay on this course of treatment or non-treatment I should say. And I think it's really important to get that

information out there, because it's scary as anything to have metastatic disease and to have four young children and to just want to live. So there's absolutely a chance for everyone to have survival and you just have to keep plugging away, and research and development is key to this and I thank you for that.

MS. GIAMBONE: Thank you very much, Elizabeth. Shirley?

MS. MERTZ: Hello, everyone. My name is Shirley Mertz. Before I begin, I want to pay tribute to the 108 women and men who will die today of metastatic breast cancer.

My journey with breast cancer began 24 years ago when I was diagnosed with early stage in 1991. Because I wanted to survive, I decided to have a bilateral mastectomy and 12 years later, my metastatic disease appeared in 2003 and I received treatment then consisting of capecitabine as the chemotherapy, targeted therapy, Herceptin and palliative radiation. My metastatic disease presented in my spine and quickly spread

throughout my skeleton and into my liver. After about a year of treatment, I went into complete remission and remained so for 7-1/2 years.

Approximately a year ago, I had a progression of my disease into a lymph node and after biopsy, it was discovered that my cancer had mutated and I started -- I added a different treatment. Because of having only one lesion in my body, I decided to undergo stereotactic radiation therapy which removed the lymph node, and so I now have a treatment regimen that includes the Herceptin or I should say trastuzumab, bisphosphonate for bones that I've been on for quite some time, and a anti-estrogen agent called Exemestane.

To me, the most significant downsides of an anti-hormonal agent are what we've heard so far, bone and joint pain, difficulty sleeping, and as I've learned recently, a negative impact on one's immune system. Trastuzumab has had some issues on my heart but I am able to continue receiving that treatment. Of course, my kidneys

have to be watched because of the zoledronic acid and for radiation, stereotactic radiation, I did experience three weeks of intense fatigue which we've all tried to explore today of what that means. For me, it was difficulty doing household chores, taking care of my elderly mother whom I'm responsible for, and going anywhere outside the house.

So while treatments have certainly lengthened my life -- I have lived now 11-1/2 years with metastatic breast cancer and I truly feel blessed -- at the same time, I know that they can have a significant impact on my internal organs, my vital organs and my daily system. Of course, I still feel that I am glad to be here as opposed to not and as a side effect, of course, I guess an inconvenient side effect, one's life, as we've heard today for metastatic patients, has to be arranged around weekly visits to the hospital for infusions, medical tests and visits with doctors. I chose to be treated at a comprehensive cancer center which is an hour from my home and

I've visited that place every three weeks for the last -- since 2004.

Because treatment as well as the mental challenges of metastatic disease have had an impact on my ability to fall asleep, I take prescription medication each night to fall asleep. I do take a daily vitamin D to strengthen my bones. I can -- I try to walk each day to support my bone care as well as to help with fatigue, though that was counterintuitive to me when someone told me that.

I also participate in cognitive therapy with a social worker to try to cope with the fact that I worry about progression and I also have to deal with the fact that I -- my life will be shortened by this disease. I practice daily meditation and visualization and prayer. Those I consider all a part of my supportive integrative medicine to my clinical treatments.

While I consider -- I consider my goals in treatment to live as long as possible with the best quality of life. However, I must say that my

-- in making treatment decisions, when I reflected on preparing for today, when I first heard I had metastatic disease, I was so angry, so shocked because I thought what more could I have done with -- my initial diagnosis in '91 was ductal carcinoma in situ. And I thought, okay, how could this be that it came back. So when I met with my first oncologist and he suggested a treatment, I was ready to go; sure, whatever you say; you know, I want to take action and now.

I've since discovered -- well, I had really no information about metastatic breast cancer at the time. I relied on my doctor to make the first decision and then I started going on the internet, finding sources of information which are not always available back then for metastatic patients. Things are somewhat better today but still most oncologists do not hand anything to a patient about their disease. And so now I approach decision-making a little different. For example, with my lymph node, even though it was biopsied and I could have entered a clinical trial, because

of the mutation, I decided not to because of the severe toxicity that I read about. So I chose to go in another direction with the radiation, CyberKnife, or whatever you would like to call it.

I think it's important for patients to consider what the doctor is suggesting, why is he or she suggesting a treatment, is there an option, what toxicities can I expect, can those toxicities be addressed by over-the-counter medication or in many cases, the dosage can be reduced or a treatment stopped for a while. If there are really serious -- in the questions, it was asked what would you do about very serious potential toxicities like liver or kidney failure, blood clots or heart attacks, those would be deal-breakers for me because I, for example, have heart disease in my family and you can't live without a working liver or kidney.

MS. GIAMBONE: Thank you, Shirley.

MS. MERTZ: I just have one more comment.

MS. GIAMBONE: Okay, sure.

MS. MERTZ: And I understand the time. I think for each of us, metastatic disease is unique. I just want to say to the panel metastatic patients are used as the participants in clinical trials to find out if the drugs that pharmaceuticals are exploring will reduce the size of a tumor. For us, you asked what would be your ideal treatment in the future. We would like to see treatments that prevent the outgrowth of our metastatic spread and that is different than the reduction of a tumor, because we feel that if -- until a treatment can be found -- a cure can be found, we are willing to live with this disease if it doesn't spread any further than where it is when we find it, when it's found. And so long as we can keep it from attacking organs, that's the type of drug that metastatic patients would like. And we would like the FDA to support clinical trials for that.

And final point, when I've asked pharmaceuticals why don't you develop drugs like this, we have -- I have been told that clinical

trials do not permit that type of endpoint. So I want to use this platform to please ask you to reconsider endpoints that prevent metastatic outgrowth. And I thank you the opportunity today to comment.

MS. GIAMBONE: Thank you, Shirley.

(Applause.)

MS. GIAMBONE: Thank you again to all of our Topic 2 panelists for sharing these stories again and as I said with the Topic 1 panelists, you are all just very, very strong and brave people for coming here and sharing such personal stories with us so thank you. So could we give everyone -- could we give our panelists a round of applause?

(Applause.)

MS. GIAMBONE: And similar to what we did in the first half of the day, can we see by a show of hands how many of you felt as if your experiences are -- that you shared similar experiences to those shared by the panelists? Okay. So we see a few hands raised here. Thank

you.

Okay. So what we'll do now is we'll do another polling question. Are the clickers working?

(No audible response.)

MS. GIAMBONE: Okay. So we're going to give the clickers a try. Okay. Have you ever used any of the following cancer treatments to help reduce or control the spread of your breast cancer -- and we definitely have touched upon many of these so let's just get a count for what we're seeing -- a) chemotherapy; b) radiation therapy; c) surgery to remove the tumor or tumors or any part of the breast; d) targeted drug therapy; e) hormone therapy; f) other; g) I have not undergone any cancer treatments; or h) I'm not sure.

So I think they can choose multiple -- okay, so you can choose multiple responses here. Thanks, Theresa.

Okay. So here's what we're seeing for the perspectives in the room. Looks like the majority of you, over 90 percent of you have

undergone chemotherapy and surgery followed by radiation therapy. And then we're seeing about over half of the people in the room that responded also used targeted drug therapy or hormone therapy. And then we also have some "other treatments" listed here.

Is that similar to what we're seeing on the web?

MR. THOMPSON: About 66 percent, chemotherapy; 90 percent surgery; 45 percent radiation therapy; 22 percent targeted drug therapy; and 55 percent hormone therapy.

MS. GIAMBONE: Okay, great. Thank you. So as I mentioned, you all have brought up many of your experiences using these range of therapies. So what I'd like to ask is instead of focusing on -- instead of me asking a question focusing on just one of these particular treatments, could one of you begin to share with us how you have -- how this particular treatment, whatever treatment it is that you have used that you'd like to comment on, how is that managing your breast cancer? Yes,

Katherine.

MS. O'BRIEN: I was diagnosed with metastatic breast cancer. I was a de novo presentation. As we learned, that's unusual. Only about 10 percent of patients have this. Surgery is not standard of care for metastatic breast cancer. At the time that I was diagnosed in 2009, it was thought that there was some benefit, so after I had been stable on my treatments for, I think it was like, six months, I was given the option of having a unilateral mastectomy. It was stressed this would not -- was not curative, it was not known if it would be beneficial for me. So I did research. Another patient with a similar diagnosis really did the research. She had collected all of the scholarly papers. I read the papers. I felt confident in my decision.

One thing that was hard to quantify was psychologically, I wanted the surgery. I think that's hard to understand even though logically no benefit potentially, no promises, I wanted this

cancer out of me. So I did have the surgery; close margins so I also had radiation. Reconstruction was not an option. The reason -- and as far as I know, I don't -- you know, I don't think it particularly harmed me. I don't know if it helped me.

Meanwhile, last year, I believe, at the San Antonio Breast Cancer Symposium -- at the time of my surgery, there was no prospective data on mastectomy in the metastatic setting. At the San Antonio conference, they presented the results of the first prospective study and basically, they found there really wasn't much benefit or it wasn't sufficient benefit. So I look back on that and I try to think, well, you know, first of all, it shows you how things change, even in such a short time period. But also, I look back on that and I think it illustrates the difficulty of making a decision but also, I think -- I have no regrets about the decision. I believe it was the correct one for me.

I think one of the hardest things to

quantify is patient preference and I was grateful that that was given to me. But, you know, I do -- I can't prove that it helped me. I hope that it did but again, when we are talking about the decision-making process, I think my experience illustrates some of the challenges.

MS. GIAMBONE: Thank you, Katherine. Would anybody else like to share their experiences on the treatment that they've undergone?

CINDY: Hi. I'm Cindy and I'm very fortunate to be a 20-year breast cancer survivor. I was diagnosed with an early but very aggressive cancer 20 years ago that was treated very aggressively. Respectfully, I really think we need to look at the differences between metastatic patients and early breast cancer patients because it's one disease but there are many forms of it. I likely had triple- negative disease which still has not targeted therapy but it wasn't consistently tested for back then.

Twenty years later, I have all of the symptoms that were listed on the chart before.

Would I have made decisions differently? I don't know because nobody told me what those outcomes might be and I don't know that it would have mattered when I had two young children. But now that I am who I am, I might make a different decision.

So I just want to say we need to think about all the different types of breast cancer. We need to think about the context, so metastatic patients make different decisions than early stage patients. And we also need to think about the diversity and age, ethnicity. So these questions are important and I really appreciate the opportunity to talk about them, but we -- I mean these were the most amazing stories I've heard and I've been doing this for a long time. I think we need to keep that in context.

MS. GIAMBONE: Thank you so much, Cindy. And in fact, to your point, in just a short while, we'll do exactly that, we'll explore more of the decision-making and we'll ask -- we have some questions for you on how you make those decisions

based on, you know, various aspects of your life, your age, your family, whatever it may be.

Okay. So let me ask you this question. I know that in Topic 1 or in the first part of the day, you brought up a range of, you know, side effects or downsides that you experienced because of the treatment that you're on or that you have taken. And I want to see if you'd like to elaborate on those further and can you tie them to specifically one of these treatments? For example, you mentioned the loss of sexual interest. You talked about acne. I mean there is a full range. You talked about pain. I know that one of our panelists mentioned blisters on the feet. So can you explore these further and maybe tell us after you tried one of the -- or, you know, you underwent one of these treatments, what was that experience like and explore those symptoms or explore that downside a little bit further? Would anyone like to comment or comment on any one of these treatments and how you experienced it?

MS. HOLLOWAY: I'm Jamie. I had stage two breast cancer and currently no evidence of disease. You know, I had chemo and it ended a couple of -- two years ago, a little more than that, and I still have some fatigue that I think has to be related. All of my symptoms are so minor that in the -- one of them is I can't always think of the word that I'm trying to think of and this is one of those times -- in light of what everyone else is saying here, it's a lot more minor, but I think it is important to see that there's a whole range and it's not all terrible all the time. I do have some cognitive problems where I can think of the letter that the word starts with but I can't think of the word, like it's just so close but it's not there.

And I still sometimes have neuropathy in my feet. It's not like I'm going to trip and fall neuropathy but it's just like my toes reminding me that I had breast cancer. It's just one more thing. It doesn't happen all the time but it's that same like weird feeling that I had when I was

on Taxol.

And surgery, I opted to have a bilateral mastectomy. I would echo what Katherine said so much. There's so much personal choice and just how you feel about it. It has -- I was very aware there was a lot of talk -- I think it was maybe at San Antonio last year -- that women were not informed enough and that's why they were choosing bilateral mastectomy even though there's no survival benefit, and that kind of hurt my feelings because I didn't make that decision because I was not smart enough to know what effect my decision was going to have on me. It's because I knew that I would be worried about that mammogram every six months, and I have little kids, and I didn't want it to be one more thing that I worried about. And I knew cosmetically, it would look better if I had the reconstructive done bilaterally at the same time. You know, I've got some aging left to do and it wouldn't turn out the same if one breast was aging and one was not. And I was really thankful that my doctor could realize

that even though I knew it wasn't a survival thing, it was a quality of life thing that was important to me.

That being said, the side effects that I noticed the most are because of the surgery. I wouldn't change anything. I think maybe Debbie made the comment that she went through a lot and she wouldn't change it but she didn't love it. You know, I still have nerve sensation issues. I don't like the seatbelt to touch me so I have actually worn a grove in the car where I pull it out and the seatbelt has like cut through the plastic of the seatbelt thing because I just always pull it out because it just bugs me. And so there are a lot of things like that. None of them are deal-breakers by any means but there are a lot of long-term things that you don't think about when you're first diagnosed because you just want it to be gone. And it wouldn't have changed my mind at all but it's definitely things to consider.

MS. GIAMBONE: Thank you, Jamie. Thank

you. Yes. Let's see, why don't we go to Sandy.

MS. FINESTONE: I just want to make a comment about decision-making in that my experience has been for most women, they think this is a one-time issue. They're diagnosed and they're willing to do almost anything for -- to get through it. But the majority of women don't -- they think it's going to be over, that once the surgery is done, the treatment is done, then my life is going to go back the way it was. They're not prepared for the long-time -- long-term inconveniences or after effects. They're just not prepared for that and I think that we need to educate women more about it that, yes, for many women it is, it's over, their life just goes back but for many, many other women, it does not.

Reconstruction is an issue that's really not talked about a lot. I'm 30 years and I'm still dealing with issues of reconstruction. I have pain from that surgery from 30 years ago. That shouldn't be and no one ever told me that was going to happen.

MS. GIAMBONE: Thank you, Sandy. FDA panel, any follow-up questions? Jonca, go ahead.

DR. BULL: Okay. It might be a quick one.

MS. GIAMBONE: Okay.

DR. BULL: I was just wondering if we could get some elaboration on the supportive care treatments. I was particularly intrigued, Ms. Cappel, as -- if you're not on anything, are there other supportive things that you're doing even though you're not on chemotherapy now?

MS. GIAMBONE: So let me actually interject here and say we're going to go onto that. We're going to actually do a polling question so I'll make sure I get to Elizabeth to answer that question for you and also others in the audience.

DR. BULL: Okay.

MS. GIAMBONE: -- but let's -- great question. We'll definitely address that one. Suparna, did you have one that you wanted to ask?

DR. WEDHAM: No. I mean one of the

questions was supportive meds. It was regarding -- I think I talked to one of the panelists during the break -- that I was very interested in the patients' decisions regarding holistic and complementary meds and how many have chosen that and if that's something that you actually discuss with your oncologist or things that people are doing independently just out of curiosity.

The other question that I just did want to ask is, you know, we hear about the side effects a lot which we know that all of these treatments have and we're kind of hearing both camps of people willing to take anything, quality of life versus the side effects. Bt I was just curious by maybe even a show of hands how many people have actually changed therapy -- I know there are a couple of patients up here at the panel -- but how many have actually changed therapy because of the side effects or is it something that you kind of just push yourself through knowing that it kind of sucks, you don't like it, it's there and you -- but, you know, how

many actually changed the therapy because of the side effects?

MS. GIAMBONE: Let's do a show of hands. How many have changed therapies because of the side effects?

UNIDENTIFIED SPEAKER: Sometimes you can change therapies because you're forced (inaudible) choosing (inaudible).

DR. WEDHAM: Exactly, not because of, you know, progression of disease or, you know, something but, you know, simply because of the side effects. I'm just, you know, curious.

UNIDENTIFIED SPEAKER: (Inaudible) --

MS. GIAMBONE: Okay.

DR. WEDHAM: Right. No -- right.

UNIDENTIFIED SPEAKER: -- (inaudible) because of toxicity.

DR. WEDHAM: Yes, because of toxicity.

MS. GIAMBONE: Okay, great. And we saw about five hands raised there. So I think with the questions that have been raised, it's actually a good segue to our next polling question. So

let's get our clickers out again.

Besides your cancer treatments, what therapies have you taken to help manage your symptoms you have experienced because of your breast cancer or your breast cancer medication? And here again, you can select multiple responses: a) pain medications; b) dietary supplements or diet changes; c) complementary or alternative therapies such as massage or acupuncture; d) herbal remedies such as soy supplements; e) other therapies; or f) I am not doing or taking any therapies to treat symptoms. Okay.

Okay. So it looks like c, complementary alternative therapies such as massage or acupuncture is what we see the most of in this room followed by pain medications and dietary supplements or diet changes. And then there's also some "other therapies," so let's make sure we definitely touch on some of those also, followed by herbal remedies. What are we seeing on the web?

MR. THOMPSON: One hundred percent say

they take pain medications and then about two-thirds, dietary supplements or complementary alternative therapies, and about one-third say herbal remedies or other therapies.

MS. GIAMBONE: Okay. Thank you very much. So let's come back to Jonca's question and Suparna's question and Elizabeth, why don't we start with you and can you talk to us a little bit more about some of these supportive care therapies?

MS. CAPPEL: Okay. The pain medications I take for the ribs but I'm not on any of them now that we found that we can do the nerve ablation so then I don't need the pain medication so I'm not on that anymore. There are no dietary supplements other than iron because my iron stores are low. I've done massage but because of the broken ribs, I can't do massage anymore. They have me on Lupron to keep me in medically induced menopause since I'm triple-positive. We're going to do that for at least another year or two and that's about it.

MS. GIAMBONE: Would anybody else -- thank you, Elizabeth. Would anybody else like to share? Yes.

MS. DUNNE: So actually, as a result of my breast cancer, one of the positive impacts was all the changes that I made to my lifestyle. So I significantly changed my diet, stopped drinking alcohol, and did a lot of complementary therapies: acupuncture, hands-on healing. The pain medication or anti -- I don't remember exactly which pill it was but I want to touch on this because I was very concerned about becoming addicted and so I just stopped taking it and after two or three days, I thought I was hallucinating and I actually happened to go to my acupuncturist who said, "Well, the drug you're taking is actually withdrawals are as bad as heroin." And so I think in taking some of these medications, it would be helpful to have a better understanding of the full life cycle of those drugs and once you take them what you need to do to come off of them and some of the other effects. So I am big

proponent of these complementary and alternative therapies.

MS. GIAMBONE: Thank you very much.

MS. FARIS: I can talk if you want to --

MS. GIAMBONE: Yes, Susan.

MS. FARIS: Susan Faris. I don't know if you can hear me. So during my chemotherapy, I mainly sought out complementary therapies by myself. I had acupuncture to deal with the sciatica. I would say, "stab me in the ass," and I would feel better. It worked. Anyway, so I also took up yoga which makes a huge difference and I use -- and I now work with a supportive care-palliative care doctor -- I prefer supportive care and when she brought the priest in the room, that freaked me out. But anyway -- but -- so she knows that I really don't want the side effects of further medication so for my neuropathy, she told me to put capsaicin on the bottoms of my feet for two weeks and that really helped a lot. And we use, you know, the combo of the vitamin B6 and the alpha lipoic acid to deal with, you know, that

sort of thing. So I try to sue as many complementary therapies as I can just because they have a lower side effect. And if I do ever get to the point of needing pain meds, God help me, because of all the side effects of the opioids, the constipation, the fact that it just knocks you out -- I luckily live in DC which has now legal marijuana and I hope it stays that way, but we also have medicinal marijuana and I would want to try that first before anything else.

MS. GIAMBONE: Thank you, Susan. So I think we had one other comment here.

MS. JONES: Thank you. So I've tried a number of complementary therapies having gone through chemotherapy, radiation and now on hormonal therapy. So I've done yoga quite a bit. As a matter of fact, I was just with a group at Smith Center and we were doing a whole yoga filming. And so not only have I tried through a support group, which is in many ways a type of therapy for some people, that I host a support group monthly and I share these things to try and

encourage others to try them because when you look at it from an ethnicity standpoint, African Americans still are reticent about many complementary therapies and it's, in part, the way it's presented. If you think of yoga, 9 times out of 10, when you see a display or advertisement on yoga, it's not a person who looks like me.

And it brings up the point, not criticizing, but I am a little curious as to how the panel on this side as well as the women who spoke were chosen because, again, when I look around -- and if I don't see many people that look like me, it makes me wonder then are my concerns, issues really being addressed, because we all know that breast cancer or cancer in general is not monolithic. If affects everyone differently and so when we have these type of forums, I really feel it's important that it's representative of the population that we're serving and particularly since we're here in the Nation's Capitol where the numbers and the statistics on breast cancer are off the chart.

And then the other kinds of cams (ph) or complementary therapies I've tried, of course, is exercising, massaging, acupuncture. Because I have lymphedema -- decided not to wear my sleeve today -- I have to do a lot of lymphedema therapy. As a matter of fact, when I was undergoing radiation treatment daily, I had to do lymphedema therapy weekly. And I've done water aerobics and the other ones, some -- so this is chemo brain now that I can't think of the other ones but I am really interested and big on pushing complementary therapies because of the amount of toxicity that's not involved with them.

MS. GIAMBONE: Thank you so much for sharing those comments. Thank you. So let's take a few more comments and I'll also check in with the web before we move on to our next discussion. I know several of you chose "other therapies." You chose "other" not only for these, you know, supportive care therapies but you also chose "other" for the first polling question that we had on treatments that you're undergoing. Would

anybody like to share some of these "other" therapies that you are tying or that you're using that are or are not working for you?"

MS. McRAE: Was that included in the "other," the bisphosphonates, because they're quite commonly used now but I didn't see it here? Is that -- would that be in this polling question or would that be in the one previous to this one like with the bone strengthening and stuff because I mean that's -- I mean I've been taking that and I think it's probably --

MS. GIAMBONE: It can actually go under probably both, you know.

MS. McRAE: Okay.

MS. GIAMBONE: Yeah, it's going to be both because it's helping strengthen the bones and treating the disease, you know, from the metastatic disease but it's also helping with the symptoms --

MS. McRAE: Exactly.

MS. GIAMBONE: -- so the pain and everything so I think you're absolutely right, it

could be in both. Yeah.

MS. McRAE: So I take that. I would consider it, you know, one of the other therapies and it has been, I think, quite -- you know, I feel it's helped me.

MS. GIAMBONE: Okay. Thank for bringing that up and I'm sorry, I didn't catch the name of what you just said. What was the name of the --

MS. McRAE: Bisphosphonates.

MS. GIAMBONE: Oh, okay. Does anybody else in the audience -- by a show of hands, is anybody else taking that therapy? Three. Okay. So we have about three people in the audience doing that. Okay. Anything else before we move on to any other therapies? Yes, Jamie.

MS. HOLLOWAY: When I was undergoing chemotherapy treatment, I did go into early menopause because of the chemotherapy and had hot flashes. And, you know, since I didn't have a lot of the other symptoms really bad, I just kind of thought it was not a big deal and am thankful that

my oncologist really prodded me and instead of trying to sort of underreport the side effects wanted to be sure that I mentioned anything that was manageable, and so I did take gabapentin at night for the hot flashes and then eventually took an antidepressant in the morning because apparently, the antidepressant wouldn't let me sleep well so I take that in the morning and then take gabapentin that would knock you out at night, and that made it a lot more manageable. And so, you know, it was not a complementary therapy but it really made some of the side effects so much more manageable for me that I think that was important.

And in the support group that I attend, there are a lot of -- it's for women who have young children and there are several women there who take antidepressants just to manage the anxiety of the diagnosis with -- especially the women who have very, very little children. That's a lot of energy expended and it's very tough for them. And I think being very proactive about the

use of antidepressants and, you know, keeping in mind that a lot of times, it's a short-term thing but it's an important thing for quality of life. For one of my friends, it made a huge difference so

MS. GIAMBONE: Thank you, Jamie. So let's actually move on to our next -- what we're going to do here because many of you have brought up this -- we've talked about decision-making and the factors that you consider and what's important to you in choosing a particular treatment. So what we would like to do is pose a scenario question for you, and we've already sort of touched on -- you've already sort of touched on some of these aspects but let's spend some time exploring it further.

So let's go to this one. And I'm going to read this to you and let you know beforehand that we're not providing you with a whole lot of information here, but we want to hear the first things that come to mind after we finish reading this.

So drug x is a chemotherapy drug being developed for patients with breast cancer and it was studied in a clinical trial comparing standard of care chemotherapy plus drug x versus standard of care alone. The clinical trial's result showed that the addition of this drug x prolonged survival on average two months longer. In addition to toxicities related to standard of care chemotherapy, patients treated with drug x had more diarrhea and rash and had more rare but serious toxicity such as liver injury and lung inflammation. So again, we know there's not a lot of information here but can you tell us what are the first things that come to mind, even if that first that comes to mind is a question?

UNIDENTIFIED SPEAKER: (Inaudible).

MS. GIAMBONE: Okay, sure. So let's go through this again. Drug x is a chemotherapy drug being developed for patients with breast cancer. It was studied in a clinical trial comparing standard of care chemotherapy plus drug x versus standard of care alone. In the clinical trials,

it showed that the addition of drug x prolonged survival on average two months longer, so the median survival was 12 months on drug x plus standard of care versus 10 months for standard of care alone. However, in addition to toxicities related to standard of care chemotherapy, patients treated with drug x had more diarrhea and rash and had more rare but serious toxicity such as liver injury and lung inflammation. Okay., so --

UNIDENTIFIED SPEAKER: Okay. I was thinking we were talking about metastatic. I'm curious if --

MR. THOMPSON: Please use the microphone so that people on the webcast can hear you.

MS. GIAMBONE: Let's use the microphone.

UNIDENTIFIED SPEAKER: I'd like to know how this is being used. Is it a first line treatment or is it something for metastatic patients who've undergone prior treatments? I think that makes a difference.

MS. GIAMBONE: Okay. So, okay. Let's see, Shirley?

MS. MERTZ: Well, you're not going to do it first? You don't mind if we have comments?

MS. GIAMBONE: Oh, go ahead. Absolutely, please share your comments.

MS. MERTZ: Okay. Well, I mean I think it shouldn't matter whether it's early stage or advanced stage. Only two months more, that's, to me, not enough to warrant the added cost. And I have yet to meet a cancer drug that doesn't cost much, so

MS. GIAMBONE: Okay.

MS. MERTZ: And secondly, I think a significant point here is the added toxicity, more diarrhea. How much, it doesn't tell us. Rash and serious toxicities are possible so I mean if I was presented with this option even though I want to live a longer time, I would say this is not an option for me, what else do you have.

MS. GIAMBONE: Okay. Thank you, Shirley. Yes, Elizabeth.

MS. CAPPEL: Well, I'd like to know -- it's saying two months longer. However, I think

that that could very much be wrong because in my situation, they said in certain drugs, I would get six months longer and I'm 8-1/2 years out. So if you're saying the average person; what if you're not the average person? What if you're the outlying person? Then you're not going to take that chance of two months where maybe you would end up being me and not being two months. So I think that it's skewed, the numbers are skewed. You're saying that there's maybe an 80 percent chance that you won't go longer but what if you're in that 20 percent chance that you can live longer? Then it's worth that. So the two months may necessarily not be you. You may be the 20 months and in that case, it is worth it. So I think that's very skewed.

MS. GIAMBONE: Okay, very good to know. Yes, Shirley.

MS. MERTZ: Can I just -- I have to add this --

MS. GIAMBONE: Yes.

MS. MERTZ: -- because this is what I

dream about, sitting in front of the FDA panel and being able to say this. I kid you not, okay; I kid you not.

(Laughter.)

MS. MERTZ: What I want you to think about -- we have genomic sequencing now. Why can't clinical trials, within the context of a clinical trial, a pharmaceutical be required to follow its patients who do well and know something about their genetic makeup that distinguishes between good responders -- I know I shouldn't say good -- efficacious responders and those that are not so that in the case of like an Elizabeth, maybe there are 10 more Elizabeths out there who would respond and when my doctor and I looked at this -- the results of this clinical trial that ultimately the drug was approved by the FDA but now as a patient, knowing my genetic sequence or my makeup of my tumor, I then can make a more intelligent decision of whether would I be benefitted, would I be an outlier, or would I really not gain much other than two months? And I

mean that's the promise of the future. It will require more but the cost of genetic sequencing has come down so it is doable. It would mean that clinical trials would be more -- I think could have fewer people in them, less costly, and be more informative to both the doctor, the physician, and the patient. So thank you, one of my bucket list has been fulfilled.

(Laughter.)

MS. GIAMBONE: Oh, thank you, Shirley.

MS. CAPPEL: I need to respond to Shirley also.

MS. GIAMBONE: Yes.

MS. CAPPEL: She's absolutely right because I've just had genetic testing and they said that they would like to do some studies on me to find out if there is something different in me that is actually working, and so that's what we're looking into. And I said I would more than be happy to be a test subject, you know, because if I can help with that, that's extremely important. So I am willing to take all my blood and figure it

out.

MS. GIAMBONE: Okay. Thank you, Elizabeth. We have several more hands here so, let's just go in order.

MS. DUNNE: I just want to reinforce what both Shirley and Elizabeth said because my first question would be who's in the clinical trial and how do they compare to me. And to some of the earlier points, for folks of different ethnicities and races, they are so underrepresented in clinical trials, so I just want to highlight that. I mean I've actually been doing some research on that for a class I'm taking and I was actually shocked to see the numbers, and I actually got my data by going on clincialtrials.gov. So again, who is in the clinical trial and how do I know if I'm the high or low end of the average or not affected at all?

MS. GIAMBONE: Okay. We'll have Katy and then we'll come this way. Okay.

MS. McRAE: Ladies, I have been in contact actually with a woman who is in Harvard, I

think associated with Harvard. They are doing -- they're trying to do a huge database at the moment. I'll give you some information here where you can contact her. And they're actually using the breast cancer cohort of patients because I guess, you know, we're easy to contact and whatever. And they will take your information from you and use it for that very purpose, and this thing is being sort of spearheaded as we speak, so it is out there. It's being done.

MS. GIAMBONE: Thank you, Katy. Yes, Ginny.

MS. KNACKMUHS: Hi. I absolutely agree with what Shirley and Elizabeth said but I just have like a general statement I wanted to make that, you know, I think for too long we're accepting these drugs that, you know, show two or three months of progression-free survival, maybe not even overall survival and, you know, they're more expensive. You know, they're not -- you know, I don't care if you happen to be an outlier, you know, it's just not acceptable. You know,

there really -- for the cost of drugs and for what patients have to go through, we can't be happy with a couple of months and think that this is really progress. You know --

MS. GIAMBONE: Thank you, Ginny.

MS. KNACKMUHS: -- I mean I think that's got to end.

MS. GIAMBONE: So I'm seeing a lot of heads nodding to that. Okay. And we'll take another comment here. Yep.

MS. JONES: Hi. Thanks. And when we're talking about a dream of getting before FDA, not just before FDA but NCI, CDC and all of them, I'd really to see more people of color in clinical trials. The data is significantly skewed and when we think about how long we've been dealing with breast cancer or cancer in general, and in 2015, the percentage of African American or people of color is less than two percent, there's something wrong with that and we are all intelligent people so we don't have to wonder why but we need to look at the methodology, the way we are approaching

people, and really think about how serious are we in eradicating the disease period. And if we have to do that, we have to look across the board. We have to look at more evidence-based information as to why people of color are not involved and then we have to actually take those steps based on what has been said to ensure that they're involved.

I have never -- I'm a community navigator -- I have never been asked by any of my doctors "would you like to be in a clinical trial," so I've had to explore that on my own. So no one has asked me and I'm articulate and educated. What about little Miss Mary in public housing or Rosetta who has a language challenge or a Japanese or other nationality who have all of their cultural barriers? There's something wrong with that and the FDA want to spend more time and money looking at that so that we can have better representation in this if we want to really get rid of the disease. Thank you.

MS. GIAMBONE: Thank you very much. So we've heard some really, really great comments

about diversity in clinical trials, perhaps genomic testing to understand how people that are in the clinical trials relate to you as a patient and how it would impact you specifically if you took this particular drug. Any other comments before -- yes, let's do Karen and then we'll move on to a polling question.

MS. DUNNE: Mine goes back to the genetic testing, the genomic testing on that. When I was in my first clinical trial, the average time to disease progression was about eight months. They had one person go 24 months. I went six years on it and the drug manufacturer was not interested in genomic testing to see why I was the one that responded for six years out of 240 people.

MS. GIAMBONE: Thank you, Karen.

MS. DUNNE: Probably because of the expense of the drug.

MS. GIAMBONE: So Geoff, I believe you had a question?

DR. KIM: Right. I think it ties into

this perfectly because I think we are at the genomic age certainly, but it's also interfacing with the immunology age and along with the proteomic age along with every other "omic" and we're finally getting the sense of check the tumor out. And I think we kind of take it for granted but breast cancer actually is leading personalized medicine, all -- HER2 is one of the key innovative discoveries in cancer development in over -- in the last decade and really has changed the poorest prognosis subgroup to one of the better prognosis because of accurate drug development and accurate selection of the patients.

But it also comes at a cost, too, because a lot of the genomic material that we want is from the tumor and so in order to do that, you know, across the standard of care in clinical practice, when someone is diagnosed with metastatic disease in the setting of previously diagnosed, clinical practice says go get a biopsy to make sure that the markers are the same as it was in the (inaudible). And then each subsequent

progression or flare, as you eloquently put it --

UNIDENTIFIED SPEAKER: (Inaudible).

DR. KIM: -- yes, exactly -- you want to check to see whether resistance mutations are some type of character mutations but I was wondering if we could get like the patient experience with all these biopsies and undergoing multiple biopsies and the uncertainty and the risk and anxiety that comes along with that, especially has there been any negative aspects to undergoing biopsies just for the sake of determining mutation status or biomarker status?

MS. GIAMBONE: Thank you, Geoff, for your question. Shirley.

MS. MERTZ: I do considerable advocacy work with the Translational Breast Cancer Researchers Consortium and it has like 19 comprehensive centers, etcetera, and the patient advocates -- and I happen to be metastatic but most of them are not metastatic -- there's one per center -- we have all said to oncologists, If you explain to your patients the value of a biopsy and

the fact that treatment is impacted by the information you get with a biopsy, that patients will willingly undergo it assuming it's not, the biopsy itself is not a dangerous place where you can't get to it or it could have some really bad affect.

I mean you've heard in the room here today how strong women are to survive not only for themselves but for their families, their partners, their spouses, and I mean we're strong enough that once we hear that there is a possibility that your progression could be different than your previous cancer or even in early stage without an accurate diagnosis, you don't get the personalized or precision type of treatment. So I don't think biopsy -- requiring biopsies in clinical trials, that is a must, too.

And so you can tell I'm very passionate about it. I happen to be one person who's mutated twice now, different in my -- presented differently in my metastatic setting and the last progression I've talked about, I'm different

again. So -- and I know I'm in the minority but it does happen. Thank you.

DR. KIM: And your experiences with the biopsies, were things carefully explained to you; were they carefully laid out for you; were there any areas of confusion that should have been better delineated in your experience?

MS. MERTZ: Well, I happen to be treated in a comprehensive cancer center where the oncologist did explain the value of a biopsy. In fact, the -- she said to me initially, I will not -- I came to her as a second opinion -- she said, "I will not recommend any treatment until I know more about your tumor." And so I think that is helpful and it doesn't always happen in community settings and so there's really a need for educating the oncologists about what they can do better so they just don't throw a treatment at the patient but rather really select carefully. Thank you.

MS. GIAMBONE: Thank you, Shirley. Yes, Jonca.

DR. BULL: Hi. Just wanted to share with our audience that FDA does take the issue of diversifying clinical trials very seriously. We have an action plan that was announced last August that has three priority areas, the first being to improve data quality, get people in the trials; second, to look at what the barriers to participation are and work with regulated industry to advance this; and the third is greater transparency of data. And I just want to highlight an initiative that CDER has in place, the drug snapshots site that does bring greater transparency to inclusion. We're not going to fix the is problem overnight. The Agency will not fix this alone but working with stakeholders, with regulated industry, with advocates, I think we can really, looking ahead, make a big difference. So I just want to make sure that everyone's aware that the Agency is actively engaged in this and looking for solutions.

MS. GIAMBONE: Thank you, Jonca. Okay. We'll take one more comment and then we'll move on

to our next question.

MS. McRAE: For me, having the bon biopsy was transformational. I mean I had been on the anti- hormone treatments because of my previous ER-positive -- PR-positive cancer as a primary. But, you know, I think about that year's time, you know, where I was on those treatments and it was kind of -- you know, I was never really satisfied that treatments were going well, but I was the one who had to talk to my oncologist. She was fantastic. She listened to me. You know, we made an informed decision. I actually went to Dr. Lisa Carey in North Carolina who did the research. The biopsy itself, I had absolutely no problems with it but I think it's so important and I think it's still being left too much to the oncologist. I think patients are not informed enough and I don't know what the insurance status is for people. I was able to get it paid by my insurance but, you know, it's this constant battle between what we can do, what we can afford to do and patients are kind of, a lot of the time, left in

the dark. I think we need to be more informed.

MS. GIAMBONE: Thank you, Katy. So I've been the okay that we have 10 more minutes so within those 10 minutes, what I'd like to do is we have two more questions for you, polling questions for you and then we'll check in with the web and see if anybody would like to dial in. So on that note, for those of you on the web, if you'd like to call in, please go ahead and do so.

So again, we've touched on some of these already but we'll explore this just a little bit more.

So here's the question for you and please have your clickers out. Of the following factors, which two would you rank as most important to your decision about using treatments to help reduce or control the spread of your breast cancer; please select up to two options -- responses: a) whether the treatment is expected to help relieve the symptoms I experience because of my cancer; b) the small but significant risk of serious side effects associated with treatment

such as blood clots or kidney failure; c) how long the treatment would probably prolong my life; d) how long the treatment could possibly prolong my life for longer than expected; e) the expected side effects of the treatment such as nausea, loss of appetite or other; or f) how the treatment is administered such as how long the treatment takes, whether it requires hospitalization, requires doctor visits and so on?

Okay. Did everyone have a chance to enter their responses? Okay. So it looks two-thirds of those of you responding selected c) how long the treatment would probably prolong my life followed by d) how long the treatment could possibly prolong my life, and e) the expected side effects of treatment such as nausea or loss of appetite. How about on the web? What do we see there?

MR. THOMPSON: Three-quarters of participants chose how long the treatment would probably prolong my life and the expected side effects of the treatment such as nausea, and then

one-quarter chose how long it could possibly prolong my life and how the treatment is administered.

MS. GIAMBONE: Okay. Thank you very much. So let's just spend -- let's have a few comments on why you made -- why you selected what you did. So what is it based on? What does this weighing depend on, for example, your age or your prognosis? Would anybody like to share a comment? Yes.

UNIDENTIFIED SPEAKER: Every patient wants to survive and I kind of had struggled with the difference between c and d, like what's the different data between those two.

MS. GIAMBONE: Okay.

UNIDENTIFIED SPEAKER: So I think if you added those, you'd have 100 percent.

MS. GIAMBONE: Okay, okay. And Elizabeth, I think I heard you ask what was the question that I asked which is why did you choose what you did; what factors weigh into that decision. So would you like to respond?

MS. CAPPEL: I think I speak for most of us here is we want to live so we base our treatment on what is the best probability of living and c and d are kind of -- they work together in my mind. So I think that's pretty much, if we put those together, again, 100 percent of us would like to live longer.

MS. GIAMBONE: Okay. Yes, let's -- we have two comments on this side.

MS. O'BRIEN: So I guess I had two things. As one of the -- as part of my treatment, I get a bisphosphonate because I have bone mets and originally, the bisphosphonate that I got was a 20- minute infusion but it requires a blood test and it will be a, you know, hour or two hours at the hospital. And then there was research that came out that found that you could -- it was quarterly rather than the monthly that I had been getting it. So I then switched -- oh, I'm sorry -- - when it was monthly, a new bisphosphonate came out that was a shot, a shot that you got -- after you had your monthly oncologist visit, you get the

shot. It was a considerably more expensive but I felt my time was worth it so I opted for the shot. Then when the dosing guidance changed that you could have this drug quarterly, I think switched to -- I switched back to the more time- consuming yet cheaper infusion because I only had to do that -- quarterly I could deal with. Monthly, it was a pain.

But the other thing I would also say that is not perhaps widely understood is that a patient often perceives a drug's effectiveness on how harsh the side effects are and that is not always true, but patients are not doctors. Patients perceive, you know, I lost my hair, I feel nauseous, I have diarrhea, this is one fantastic drug and that's not the case.

And I know many times I'm asked to speak to newly diagnosed stage four women and with stage four, it's the least toxic option first. And I recall even in my own experience having to tell my insurance company I wasn't going to -- first, I wasn't going to have surgery and the

administrator, you know, no surgery. "You're not going to have chemotherapy? "No, you know, I won't. I'll take t his daily pill." And she just goes, "Well, they don't seem to be doing very much for you, are they?" And it has -- it's not understood that a non-chemotherapy and anti-estrogen can be equally effective as a chemotherapy, but sometimes doesn't have that choice. If they have an aggressive disease, if they have a disease like triple-negative where there is no receptor to act upon, then chemotherapy is essentially their only option. But if it's six of one, half dozen of another, oftentimes, again, the patient goes through a motion of, you know, this drug -- you know, they're not looking at the little printout that came with the drug. They're going, "Well, you know, I look terrible, I feel terrible, this drug is really doing the trick."

MS. GIAMBONE: Thank you.

MS. O'BRIEN: And I think that clinicians struggle perhaps to communicate that.

MS. GIAMBONE: Thank you, Katherine. Let's do -- let's go on to our next polling question and then we'll be sure to hear you comment. Okay. So the purpose of this question, it's to hear the other side now. So we're going to ask the contrary question here.

Of the following factors, which one would you rank as least important to your decisions about using treatments to help reduce or control the spread of your breast cancer: a) whether the treatment is expected to relieve the symptoms I experience because of my cancer; b) the small but significant risk of serious side effects such as blood clots or kidney failure; c) how long the treatment would probably prolong my life; d) how long the treatment could possibly prolong my life; e) the expected side effects of the treatment such as nausea or loss of appetite; or f) how the treatment is administered such as how long the treatment takes, whether it requires hospitalization or required doctor visits? So here you're going to select one that you would

rank as the least important.

Okay. So, the least important to your decision was "f," how the treatment is administered. And again, we acknowledge and appreciate that there are many, many factors into your decision-making so we appreciate that you're, you know, choosing with one of the options here. So, okay, let's make sure we hear your perspective.

MS. JONES: Thank you. I really think that's interesting because on the previous ones, in addition to what others have said about "c" and "d," "f," how the treatment is administered was a great concern of mine because it was so how long is this going to take. If I have long-term, temporary employment, is this going to impact that or maybe my insurance; am I going to lose that or is this going to be a free clinical trial kind of thing; whether it requires hospitalization; where will I be hospitalized, and about the doctors; will I lose the relationship that I have with my current doctors that I'm still kind of struggling

with and developing a trust, so when this comes in, do I have to get used to all new doctors again. So those are -- and just the transportation issue. Let's say, live in Southwest. I may have to go Bethesda or NIH. That's a huge stretch so those are the kind of concerns I have.

MS. GIAMBONE: Thank you very much. So let me turn to the web and if you could -- what polling results do you see there and perhaps you could summarize what you're hearing on the web and then we'll take some phone calls.

MR. THOMPSON: Similar to what we had in person. We had three-quarters saying "f" as the most answered thing. Nobody currently on the phone, so I'm going to summarize some of the comments I'm getting.

Going back to something we've been talking about earlier about what do you keep in mind when you're thinking about treatments, in several comments, we had one person saying it would be nice to be informed ahead of time about

side effects, but you're never going to be able to know how your body is going to respond to them.

Another person said it would be nice to know which side effects would not go away after you're done with the treatment.

There was one person who said her main concern was her fertility because she was diagnosed when she was 31, but there was no information, no studies that were going to talk about how this would impact her fertility.

There was one person who was talking about the difference between metastatic and non-metastatic patients, when they're considering treatment.

In terms of other therapies are taking, people also talked about exercise and yoga and about support and the importance of peer sharing things with other patients to help them overcome isolation and depression.

And in response to the question about biopsies, one person said it's different between diagnostic and investigational purposes. So if

you're getting a biopsy, if it's investigational, he would probably consider where the metastatic lesion was located, for example, skin and bone would be a lot easier than a liver biopsy and then one person talking about genomic medicine said that while they're promising, they're still early so it's -- people need to keep in mind that some of these treatments -- some of these approaches are very limited right now.

MS. GIAMBONE: Okay. Thank you very much. So we're going to wrap up this portion of the meeting today and we're going to be moving on to open public comment. But I would just like to, on behalf of all of my FDA colleagues, just thank you all so much for sharing these stories with us and really teaching us so much today. I think -- yes, Geoff -- yes.

DR. KIM: I had a quick question. Just a really quick show of hands. Has anybody ever ready the little thing that comes with the medicine also called the drug label? If you have, can you -- and any feedback? I know we're

probably going to get a lot but was it helpful in describing the side effects and expectations or -- I think we're going to get a lot of comments but just kind of get a -- it helps us a lot to --

MS. FARIS: Can I address that real quickly?

MS. GIAMBONE: Let's do a show of hands. Can we do a show of -- okay, yes, Susan.

MS. FARIS: Just real quickly. I definitely read the side effects on it and I, you know, try not to freak out but the thing is, for instance, when I started KADCYLA, it is so new, it was so -- I like to pronounce it "KOD-ZILLA," like, you know, Godzilla. Anyway, but I definitely read what the drug company was putting out but the fact is that with any of these drugs, they do not talk about everything that is really going to happen. There is stuff that I think either they don't want to admit, you know, and a prime example would be Paxil which is still not admitting how hard the withdrawal off of Paxil is. And so a lot of times, I have to look not only at what the drug

company provides but then go off into the forums, to trusted forums and hear what other people are talking about to find out the real story. You know, I mean there are books that are written on how to withdraw from Paxil and that's still like not -- that's a secret. Anyway, so

MS. GIAMBONE: Great. And so -- okay, let's -- we'll take one more comment.

MS. JONES: We discussed that just sort of over the break and with my last label, I thought, "oh my God, this looks different than the last one," but I didn't have the last one to compare. I think the information is -- it's quite technical, it is a lot to consume and most people, I don't think -- well, let me retract that -- the population that I serve, I can assure you a lot of them do not read that and if they do, their health literacy is not at a level that they can totally comprehend it so it could be to their advantage.

MS. GIAMBONE: Thank you. Thank you, Geoff, for your question. So thank you all again so much for being part of today's meeting.

(Applause.)

MS. GIAMBONE: Pujita, I'll turn it over to you.

MS. VAIDYA: Hello, everyone. I'd like to thank you all for coming here today. We are now moving into the open public comment session and for those of you who are not aware, the purpose of this session is to allow an opportunity for those who have not had a chance to speak on issues that are not related to the topic discussion questions today. This is an opportunity for folks who are not a patient or a patient representative to comment. Please keep in mind that we will not be responding to your comments but they will be transcribed and be a part of the public record.

Since we would like to -- like this process to be transparent, we encourage you to note any financial interest that you have that are related to your comment. If you do not have any such interest, you may state that for the record. And if you prefer not to provide this information,

you can still provide your comments.

So we have collected signup before the meeting and during break. We have four people signed up and about 15 -- 10 minutes for this session, so please be respectful of your other colleagues here and other patients and stick to the two-minute limit. We won't have a timer but I will be using my phone here to keep track just so that you don't go over. And if you do approach the two-minute mark, I will have to ask you to wrap up.

So I'll run through the order of speakers and I apologize if I mispronounce your name. So the order will be first, Joanne Buzaglo, Katherine Crawford-Gray, Kimberly Beer, and then Katherine O'Brien. So first, may I have Joanne Buzaglo to the mic?

MS. BUZAGLO: Hello. Thank you. I do not have any financial disclosures to present. Okay. I applaud you for hosting this meeting today and I'm very grateful and applaud all the people who spoke up. It is not easy to do so.

I bring the voice of over 3500 patients who have shared their voice in the cancer experience registry. I bring that with me. I would encourage you to strongly consider the comments the cancer support community has submitted to you about integrating distress screening and follow-up into the clinical trial design to ensure that the types of patient-reported outcomes that we've been discussing are collected in real time and over time and over the course of disease and treatment so that it can inform your ultimate decisions about medical solutions.

One question I would like to specifically respond to is the question about toxicity and risk- benefit tradeoff decisions. It is clear from our data that patients, especially with metastatic disease, have unique needs in their cancer journey and each is willing to tolerate a benefit-risk profile based on very personal considerations. We do know from our cancer experience registry that over 50 percent of

women living with metastatic breast cancer are unable to work due to their cancer. Meanwhile, they are balancing other very real life commitments, child care, elder care, etcetera. Additionally, we know that they have different definitions of value depending on their experience.

As you consider your definition of an appropriate risk-benefit scenario, I encourage you to ensure that it is based on the data emerging from the voice of the patient and move further to collect it in real time and allow it to inform your thinking in ways it may not have been done in the past. So we look forward to partnering with you on this. Thank you.

MS. VAIDYA: Thank you, Joanne. Next we have Katherine Crawford-Gray.

MS. CRAWFORD-GRAY: Thank you. Thank you so much. On behalf of the Metastatic Breast Cancer Alliance, I appreciate this opportunity to make a short statement and thank you particularly to all the women who have spoken here today.

The Metastatic Breast Cancer Alliance is comprised of more than 30 member organizations, many who are in this room or are online today, and these include the three largest private funders of breast cancer research in the U.S., 16 leading advocate non- profits providing information and support services for breast cancer patients and caregivers, 6 pharmaceutical corporations invested in treatments for metastatic breast cancer as well as individuals who advocate for and work with patients on a daily basis. And the Alliance applauds the FDA's work today and its commitment to expanding treatment options for people living with metastatic breast cancer, and we also commend the FDA's dedication to continuous education of its reviewers so that they can focus on the different needs of opts that arise from the various types and stages of breast cancer and particularly, the differences between early stage and metastatic breast cancer.

Last year the Alliance undertook research which was published in October in their

report, "changing the landscape for people living with metastatic breast cancer," and based on this research, we are advocating that in order to accelerate research and treatment benefitting metastatic breast cancer patients, the following aspects of clinical trials be a priority for the FDA. The first aspect is updating clinical trials for metastatic breast cancer including new trial designs with meaningful endpoints. For example, tumor shrinkage may be but one endpoint relevant to tumor spread or metastasis. Additional endpoints such as time to next metastasis need to be introduced. Qualify of life measures that are valued by patients living with the disease and inform their treatment decisions need to be additionally standardized and required in all phase three trial designs.

The second aspect is that there is also a need for multi-center collaborative phase two trials. By helping to incentivize multi-institution, multi- investigator trials, metastatic breast cancer research will be

accelerated. Barriers to clinical trial design include there being too many "me too" trials in industry and reward systems for single investigators conducting single institution phase two trials. These, along with other barriers, need to be removed for research benefitting metastatic breast cancer patients and for the research to be conducted at a faster pace.

Accelerating the speed of research and the development of new treatment that extend the lifespan of, while maintaining a high quality of life for people living with metastatic breast cancer, is a primary goal of the Alliance. And we appreciate the opportunity to have had input to this process today as well as the pubic docket coming up and trust our views are helpful for FDA staff and reviewers and the progress of research for patients. Thank you.

MS. VAIDYA: Thank you, Katherine. Next, I have Kimberly Beer.

MS. BEER: Thank you. I'm Kimberly Beer. I'm the Director of Public Policy at Susan

G. Komen, and I want to thank the FDA for giving us this opportunity to invite patients to come and share their stories. And we have had the pleasure of working with the FDA to ensure proper representation; however, I am significantly disappointed that the breadth of the diversity in the breast cancer community is not represented here. And so Komen is committed to ensuring that during the pubic docket period that we really, really emphasize outreach to those folks who are not women, only women -- breast cancer impacts men, diversity in ethnicity, diversity in health literacy, diversity in stage and type of disease.

This meeting is critically important and so we look forward to working with you in ensuring that we have patients comment on the docket as well as we look forward to hearing what those folks on the web also submit. Thank you.

MS. VAIDYA: Thanks, Kimberly. And lastly, we have Katherine O'Brien.

MS. O'BRIEN: Thank you. When Shirley started here remarks, she mentioned that today 108

U.S. people will die from metastatic breast cancer. That is 40,000 per year. One thing that we don't know is how many people are currently living with metastatic breast cancer. We say that there are 150,000 U.S. people living with metastatic breast cancer but that is an estimate only because our U.S.

cancer registry does not count metastatic recurrence. Women are counted when they die or when they are de novo presentation such as myself. But we know that only 10 percent are people like me, people who are metastatic from their first diagnosis. Most people join the metastatic breast cancer ranks having been treated for early stage cancer but we do not track that, and what we do not count, the pole we do not count, we do not provide for.

Finally, I'm reminded of an advocate, a late advocate whom I had much respect and admiration for, Susan Davis. Susan had many, many chemotherapy regimens and she always said she could handle the worse side effects, the harshest

drug, and Susan said, "I live in hopeful dread. I hope that my next set of scans that I have every three months will be good but I dread that they will be not, they won't, that they will not." And that is the reality for the estimated 150,000 U.S. people living with metastatic breast cancer. They live in uncertainty.

Oftentimes in popular parlance, when we talk about breast cancer treatment, we talk about slash, burn, poison. For the metastatic community, another way to put it would be scan, treat, repeat because every three months for most people, you have a set of scans which determines whether your treatment is working. If it is not working, you have to try and find another drug. We've talked today about what the implications of those drugs might be.

So I thank you very much for this opportunity. Thank you.

MS. VAIDYA: Thank you, Katherine. And so before we get started with our last agenda item, I'd like to ask Sarah and Kathy to please

pick up the clickers from the tables. And then I'd also like to remind you that we do have evaluation forms outside and we would really appreciate your feedback. So please leave -- if you could fill it out and please leave them at the table, that would be great.

Now lastly, I'd like to call Dr. Amy McKee to the stand for our closing.

DR. McKEE: So I think I'm going to summarize with there are two things I've heard today consistently. One, every patient is an individual; every patient is going to have their own story about how their disease responds to treatment and how they handle the toxicities of that treatment. And I'll go back into that a little bit more. And the second thing is that we have a lot of work to do. There is a lot of work to be done.

So I want to thank you all for sharing your stories because it's really important for us to hear, as regulators, how these treatment affect you both in terms of how they work and how you

think about it when you choose them and how you have to handle all the toxicities and the doctors' appointments that go along with those treatments.

I think one of the things that we were really interested in hearing from you because it's something that we deal with with every drug that comes before us where we have to make a decision is how do we describe whether or not you should pick this treatment for yourself. And so we use clinical trials to do this and we use statistics to try to summarize it and you sort of saw a little bit of that with that question, "If you had an average two-month improvement in survival but lots of toxicity, would you choose that for yourself?" And this is what we have to do every day. We have to think about for this population, for these specific patients, do we think that there's enough benefit that the risks are worth it, and we use statistics to try to decide that but that could never answer the question for an individual patient, and that's where you all have to come in with your oncologist and your family

and yourselves to make that decision.

And then the second thing is there is a lot of work to be done. We want to continue this dialogue with you. We encourage all of you to engage with the FDA and with clinical trials and with advocacy groups as much as you can. I'm actually a little bit bleary- eyed because I've been trying to stay up for the last three nights to watch PBS's series, "Emperor of All Maladies." And last night I think the most hopeful thing about it was there is a lot of work to be done but we're such an exciting time right now. We know we've talked about genomic sequencing; we're talking about immunotherapies. There are so many more options than some of the women who are in this room who were diagnosed at a time when there were almost no options beyond extremely toxic therapy and surgery and you might not even know what surgery you were going to get when you went under anesthesia. And so it's an exciting time and a hopeful time and I really thank you all for sharing your perspective because it is very

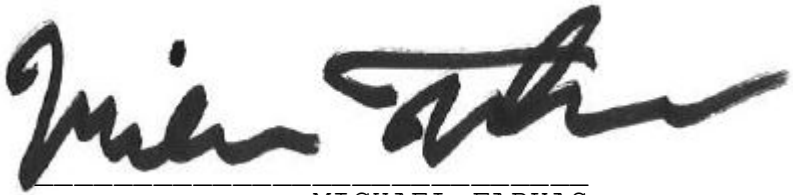
important when we make decisions and we evaluate the data about not how it's going to affect the population but how it's going to affect each individual patient. So I thank you and please fill out your evaluations because it's really important for us to read them because we take it all into account. Thank you very much.

(Applause)

(Whereupon, at 4:40 p.m., the meeting was adjourned.)

CERTIFICATE OF NOTARY PUBLIC

I, MICHAEL FARKAS, the officer before whom the foregoing hearing was taken, do hereby certify that the testimony appearing in the foregoing hearing was taken by me in audio recording and thereafter reduced to typewriting under my supervision; that said transcription is a true record of the proceedings; that I am neither counsel for, related to, nor employed by any of the parties to the action in which this deposition was taken; and, further, that I am not a relative or employee of any counsel or attorney employed by the parties hereto, nor financially or otherwise interested in the outcome of this action.



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I, LUCY T. TURNBULL, hereby certify that I am not the Court Reporter who reported the following proceeding and that I have typed the transcript of this proceeding using the Court Reporter's notes and recordings. The foregoing/attached transcript is a true, correct, and complete transcription of said proceeding.

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