OPERATOR: Greetings, ladies and gentlemen, and welcome to the Living Beyond Breast Cancer webinar. At this time, all participants are in listen-only mode. A brief question-and-answer session will follow the formal presentation.

If anyone should require operator or technical assistance during the conference, please press “star, zero” on your telephone keypad. As a reminder, this conference is being recorded.

It is now my pleasure to introduce your host, Ms. Elyse Spatz Caplan. Thank you. You may begin.

ELYSE SPATZ CAPLAN, MA: Thank you so much, operator, and welcome, everyone, to Living Beyond Breast Cancer’s January webinar, “News from the San Antonio Breast Cancer Symposium.” We welcome all of you who’ve taken time out of your busy days to join us and hundreds of others for today’s very important program.

My name is Elyse Spatz Caplan. I’m the director of programs and partnerships at Living Beyond Breast Cancer, and I’m very pleased to serve as the moderator for today’s program.

We know that the annual San Antonio Update is something that is often looked forward to by many of the women and men who are connected to Living Beyond Breast Cancer to learn so much more about the latest medical and quality of life updates that were reported at last month’s annual meeting. There were some exciting developments reported that you will learn more about today.

I’d like to remind all of you that the format to today’s program will be interactive. We will have a speaker presentation, and then we will have the opportunity to answer some of your questions by phone and also take some of the questions that have been submitted via the Web. We may not be able to get to all of your questions, so I’m hoping that when we get to that portion, you’ll keep your questions concise and limited to one, so that we can get to as many people as possible.

We’re really looking forward to hearing updates on chemotherapy, hormonal therapies and targeted therapies for both early-stage and metastatic breast cancer. Living Beyond Breast Cancer is very grateful for the support of AstraZeneca, which has helped to bring today’s webinar to all of us.

Just a couple of program notes: this month, Living Beyond Breast Cancer started a new webinar called Second Tuesdays. It is held the second Tuesday of every month, and it is specifically for women newly diagnosed with breast cancer. If you know of other people who are affected in a more recent diagnosis and you would like to tune in, yesterday’s program was held, and we will have our February program coming up on Feb. 12, so save the date if that is of interest to you. You will also get a lot more information on our website, lbbc.org, for future webinars and conferences that we’ll be conducting.

Our next national conference will be held in Seattle, actually in the town of Bellevue, outside Seattle. It’s our Conference for Young Women Affected by Breast Cancer (C4YW) that we do in partnership with Young Survival Coalition. It’s the weekend of Feb. 22–24, again, in Bellevue, Washington, on Seattle’s Eastside. We do have travel grants and registration fee waivers available for those who want to attend for whom cost may be a
Without further delay, I would like to tell you about today's featured speaker and move forward with our presentation. Today's speaker is Dr. Sara Tolaney, a medical oncologist at Dana-Farber Cancer Institute in Boston, where she focuses on developing new treatments for breast cancer.

Dr. Tolaney is also a medical instructor at Harvard Medical School. She received her undergraduate degree from Princeton University and her medical degree from the University of California, San Francisco, and also completed her residency in internal medicine at Johns Hopkins University and a fellowship in hematology-oncology at the Dana-Farber Cancer Institute.

It is our pleasure to welcome Dr. Sara Tolaney to today's program.

SARA TOLANEY, MD, MPH: Thanks so much, Elyse. Today I’ll be focusing on a lot of the exciting results that came out of San Antonio.

I think probably one of the most exciting topics that came out was focusing on the duration of tamoxifen therapy. I think many of you have probably seen a lot of press about this. This study — it’s called the ATLAS trial — randomized women who had completed five years of tamoxifen to either further treatment with an additional five years of tamoxifen or no additional treatment.

This study looked at rates of recurrence, comparing those who had completed just five years with those who completed 10 years, and it did find a significant reduction in risk of recurrence in patients who completed the 10 years relative to those who received just five years, as well as a significant reduction in mortality from breast cancer. I think, given these results, we feel that extension of treatment with an additional five years of tamoxifen is really warranted, because it is proven to reduce recurrence as well as improve mortality when compared to just five years of treatment.

Some of the caveats we think about are that there was an increased risk of endometrial cancer when patients continued on a total of 10 years of tamoxifen; it almost doubled the risk of endometrial cancer compared with just five years. So, patients who were on tamoxifen for 10 years had a 3.1 percent risk of endometrial cancer over that time period. There was also a significant increase in rates of pulmonary embolism, or blood clot to the lung. We do know that tamoxifen does increase risks of blood clot, and when extending duration of treatment, you do increase the risk of this and of the total incidence of blood clots, which is significant.

We have to keep in mind the risks of toxicity when we weigh it against the benefits, because rates of endometrial cancer really increased predominantly in postmenopausal patients; there really wasn’t a significant increased rate of endometrial cancer in the premenopausal population on this study. I think that makes us feel a lot more comfortable increasing the duration of tamoxifen for the premenopausal patient.

I think right now we are generally recommending premenopausal patients to take a total of 10 years of treatment, particularly those with higher-stage breast cancer and if they’re tolerating treatment well. I think the controversy lies in what to do about postmenopausal patients. Currently the standard has changed since this trial was initiated several years ago. Right now the standard mostly is that postmenopausal patients take five years of an aromatase inhibitor.

The question is what to do when a woman has completed five years of aromatase inhibitor therapy. Do we switch them and put them on tamoxifen for an additional five years so that they’ve had a total of 10 years of treatment? Do we extend the aromatase inhibitor duration? Or do we stop treatment at that five-year mark? Honestly, there isn’t a straightforward answer to this question at this time. There are trials that are looking at extending the duration of aromatase inhibitor therapy. There’s a study, the MA.17R study, that did look at this, but we do not have the data from this to know the safety of a total of 10 years of treatment, so it’s hard to recommend someone to continue on long-term aromatase inhibitor without that safety data.
For patients with higher-risk disease who are postmenopausal when they complete a total of five years of aromatase inhibitor therapy, I don’t think it’s unreasonable to consider switching to tamoxifen and completing 10 years of treatment. This would certainly be without a true trial to demonstrate that this is effective. We do have data in the reverse situation, where patients got five years of tamoxifen and then switched to five years of an aromatase inhibitor who were postmenopausal, and this was beneficial compared with just receiving five years of tamoxifen alone. I think you could use that data to justify extending treatment. This is something you should really talk individually about with your oncologist to make a final decision, because it is still controversial.

Moving on to other topics that were discussed at San Antonio, I think it was interesting to look, again, at the hormonal therapy and looking at whether we can sort of preselect which patients are going to benefit from tamoxifen relative to an aromatase inhibitor. This particular trial looked at the BIG 1-98 study. This was a trial that was done that compared patients getting tamoxifen with those getting an aromatase inhibitor, but they also looked at a few different arms. They also looked at what we call switching arms, where patients got either two years of tamoxifen followed by three years of an aromatase inhibitor, or two years of an aromatase inhibitor followed by three years of tamoxifen. The subgroups that were looked at in this particular study for San Antonio did not look at the switching arms. They were just comparing the arms that looked at tamoxifen versus the aromatase inhibitor alone.

Specifically, they were looking at subtypes of breast cancers. As you probably know, there are two major groups of invasive cancer: lobular and ductal cancers. There are different ways you can classify breast cancers, specifically into luminal A or luminal B subtypes of cancer. There are different ways to do this. The way this particular study did it is by looking at something called the Ki-67, which is sort of a proliferative marker, looking at how fast breast cancer cells are growing. Cells that looked like they were growing more slowly and had lower Ki-67 numbers were classified as luminal A, and those that had higher Ki-67 numbers were classified as luminal B.

When you look at differences in disease-free survival, you can see that there was a significant difference in the lobular cancer arm and when comparing letrozole to tamoxifen, meaning that patients who had lobular cancers and received letrozole tended to do better with the letrozole than they tended to do with tamoxifen. This was also consistent when looking at rates of survival across the subtypes of breast cancer.

What they concluded was that the letrozole, which is an aromatase inhibitor, is associated with a significant reduction in recurrence as well as an improvement in survival, and that the benefit seemed to be higher in patients who had luminal B cancers. They felt that this benefit could justify use of letrozole specifically in the lobular subtype when compared with the ductal subtype. Something to think about, I think, something to discuss with your oncologist, particularly if you had a lobular cancer and you’re postmenopausal, is whether or not it makes sense to use an aromatase inhibitor relative to tamoxifen.

I think a lot of people also have a lot of interest in knowing whether there’s any benefit to taking aspirin therapy. A lot of controversial data have come out over the past year or so, looking at whether taking a baby aspirin a day could help prevent a breast cancer recurrence after a diagnosis. The trial that was presented at San Antonio didn’t honestly present a very conclusive result, given the numbers that were seen in this trial, but I think it’s interesting nonetheless.

This was a trial called MA.27, which compared two different aromatase inhibitors. One of those is anastrozole, the other one being exemestane. Originally the trial was designed looking at celecoxib, which is a COX inhibitor, which decreases inflammation, and compared that to placebo in both arms of the study. This was closed early because of poor accrual early on, but they then looked at patients who also happened to be taking aspirin for other purposes, and also looked at their outcomes relative to whether they were taking that COX inhibitor — so, again, another marker of decreasing inflammation — to see if it had any significant reduction in their risk of recurrence. There was not a significant risk of recurrence when looking
at patients who were taking aspirin or when looking at the group of patients who were taking celecoxib, so they concluded that neither celecoxib or low-dose aspirin seemed to reduce risks of breast cancer recurrence.

It is interesting that patients who were on aspirin tended to not live as long, although I think the reason that is that, generally speaking, patients who are taking aspirin are told to do so by their physicians because of having risks for cardiovascular disease. These patients are at risk for not living as long because of their other health problems, so that’s likely why these patients tended to not live as long.

Given this small amount of data, I think right now there’s no data that suggests that we should tell patients who have a history of breast cancer to take aspirin to prevent a breast cancer recurrence. There isn’t enough data at this time to say that it prevents recurrences, and this trial would certainly support that it doesn’t seem to have an impact on lowering breast cancer recurrence rate.

Another interesting study looked at the use of Avastin. There has certainly been a lot of press about Avastin in the past couple of years. This is an antibody that inhibits VEGF, which is very important for promotion of blood vessel growth to feed tumors. The thought would be that an antibody against this pathway would help prevent blood vessel growth to tumors and allow for tumors to die more quickly. Originally this drug had been FDA-approved for treatment of metastatic breast cancer. However, when it failed to show a survival benefit across multiple studies, the Food and Drug Administration decided to rescind approval for this drug.

There have, however, been a lot of questions about whether Avastin may be useful in other settings, so there have been a lot of trials trying to see if Avastin can prevent breast cancer recurrences. This particular study was looking to see if Avastin could prevent breast cancer recurrences within the triple-negative subgroup of breast cancer. There has been some thought that Avastin may work better in triple-negative cancers relative to other subtypes.

That’s why this particular study was conducted. It’s called the BEATRICE study. It allowed physicians to pick which chemotherapy they wanted to give to patients after a breast cancer diagnosis and combine that chemotherapy with Avastin or not. Again, these women all had triple-negative breast cancer. When you look at rates of recurrence, you can see that there was a trend toward fewer recurrences in women who received Avastin relative to those who did not. However, this was not a significant reduction in terms of risk of recurrence. And, again, when looking at survival, there was no significant difference in the two groups in how long these women lived.

When looking at side effects of Avastin, they again demonstrated that Avastin does have some side effects, particularly increasing rates of having high blood pressure as well as having some protein in the urine. We do know that Avastin has some toxicities, and this trial just supported that.

In general, they concluded that there was no significant benefit from the use of Avastin when combined with chemotherapy for patients after a breast cancer diagnosis who had triple-negative disease, and that the side effects seemed to be consistent with what we’ve seen in the past and other studies looking at Avastin. This sort of supports all the data that’s been done, at least in the metastatic setting, that Avastin really doesn’t seem to pan out in terms of allowing women to live longer after breast cancer.

A question that I thought was interesting that hasn’t really been addressed well in other studies is what to do if a patient comes back with a local recurrence of breast cancer, meaning that a patient had full treatment after a breast cancer diagnosis and within a year or two later came back with another mass in the area where the initial breast cancer had been. Do you give these patients further chemotherapy or not?

This has been an issue of controversy for a long time, and it’s been very hard to do a study to look at this because this isn’t a terribly common occurrence and it’s hard to do a trial to really answer this question. But these investigators were very persistent and were able to finally provide us an answer.

They took patients who had had prior chemotherapy for their original breast cancer and then [had] a local recurrence. These local recurrences were fully surgically
resected. After surgery, they were randomized to get more chemotherapy or not. They found that the women who got chemotherapy did better, so they had fewer recurrences from their breast cancer.

What is interesting, though, is if you look at the benefits by separating them into breast cancer subtypes — looking at the women who had ER positive cancer versus those who had ER negative cancer — you can see that the patients who had estrogen receptor negative seemed to have a bigger benefit from receiving chemotherapy relative to those who had ER positive cancer. They also found that women who got chemotherapy did live longer relative to those who did not after a local recurrence.

This is really the first study to demonstrate this [difference in survival] and is very helpful to both patients and doctors to help make decisions about what to do after a local recurrence. This data does suggest that if a patient has a local recurrence that has been fully surgically resected, that we should consider giving more chemotherapy, particularly in patients who have ER negative breast cancer.

A few other updates that I thought were interesting were looking at the benefits of adjuvant trastuzumab, otherwise known as Herceptin therapy. Initially, one of the studies that was presented at the conference was just an update of data that we’ve already seen before. Many of you probably know there was a very large adjuvant study that looked at adding Herceptin to standard chemotherapy. They updated the results of this study with longer-term follow-up at San Antonio and again showed a very significant and impressive reduction in risk of recurrence when adding Herceptin to standard chemotherapy, with an absolute difference between the two arms of patients being about 11 percent.

They also looked at overall survival and found that there was a significant decrease in survival [among people who received chemotherapy alone], again with an absolute difference between the two arms of almost 8 percent. So, they did conclude … that Herceptin when added to chemotherapy significantly reduces risks of recurrence as well as improves survival and really should be the standard of care, particularly in women who have larger-sized HER2 positive tumors as well as node-positive tumors.

I think the question that has long stood is: How long do you give Herceptin for? All of the trials that were originally done looked at giving a year of Herceptin, but honestly this was a very arbitrary decision to give a year of treatment, and everyone has always wondered whether giving a shorter amount of Herceptin would be just as good. This is really the first study to present results looking at a shorter amount of Herceptin therapy, and everybody had been awaiting these results.

This was a French study called the PHARE trial, which was sponsored by the French government. It took women who had received standard chemotherapy with Herceptin, and after getting Herceptin for six months, they randomized them to either stop Herceptin or continue on an additional six months of Herceptin — so, to complete the standard one-year Herceptin treatment. They were able to randomize more than 3,000 patients to do this, which is very impressive, and they did find that there really wasn’t a significant difference.

This trial is a little complicated in that they did what is called a non-inferiority study, so that they were trying to show if six months was just as good as 12 months of therapy. They were not able to demonstrate that six months was as good, so it’s a little complicated to interpret the statistics. I won’t bore you with all of those details, but the bottom line is that they’re unable to show that six months is as good as 12 months, so at this time, the duration of therapy really still is one year of treatment.

I think many of us wonder if we can give less therapy to patients who have smaller amounts of disease. They’re not able to demonstrate that in this trial, primarily, I think, because the numbers aren’t large enough to really pull out just women, for example, with node-negative disease and demonstrate whether six months of treatment is adequate. I think that question still is not fully answered.

Another trial that was presented, which I didn’t put in this presentation, looked at two years of Herceptin versus
one year, and they did not show that two years was better than one year. Again, the HERA study supported one year of treatment currently as the standard of care, so, I think six months is not good enough and two years isn’t really necessary. One year is still the standard.

Just to conclude what we’ve learned in the adjuvant setting — what to do after an initial diagnosis — the ATLAS study did show that 10 years of tamoxifen is better than five years. An analysis looking at the BIG 1-98 study showed that letrozole may be better than tamoxifen, specifically in lobular cancers. An analysis looking at the MA.17 study showed that low-dose aspirin didn’t seem to reduce risk of recurrence and so shouldn’t be a standard at this point in time. Data looking at Avastin showed that after a breast cancer diagnosis, adding Avastin to chemotherapy in women with triple-negative breast cancer did not reduce risks of recurrence significantly — so this, again, should not be a standard, to add Avastin to chemotherapy.

The CALOR study showed that treating patients with chemotherapy after a local recurrence did seem to be beneficial, particularly after a diagnosis in women with an ER negative cancer. Then, looking at the PHARE study and the HERA study, we can demonstrate again that the duration of Herceptin should really be for one year of treatment, not shorter and not longer.

Turning to studies that were done for metastatic breast cancer, one study that was done compared receiving eribulin, which is a newer chemotherapy, to capecitabine, otherwise known as Xeloda. This study took women who had received three or fewer lines of chemotherapy for their metastatic disease and randomized them to receive Xeloda or eribulin and looked at outcomes. The reason this was done was because eribulin was an agent that was approved for women who had been treated with more than three lines of chemotherapy, so they’re trying to show us [whether] giving eribulin earlier on can be just as effective as Xeloda, which is a very commonly used drug earlier on for metastatic disease.

When you look at the results in these slides, you can see that there wasn’t a significant improvement when giving eribulin relative to Xeloda treatment. There also was not a significant improvement in overall survival when comparing eribulin with Xeloda therapy, so this study did not show a significant superiority of eribulin relative to Xeloda. At this point in time, for the most part, they look fairly equivalent.

Another, I thought, very interesting study was looking at a novel drug. This is a drug made by the Pfizer drug company that inhibits the cyclin-dependent kinase pathway, otherwise known as the CDK 4/6 pathway. There’s a lot of interest in trying to add drugs to an aromatase inhibitor to see if they will improve outcomes. This trial did a study where they randomized women who had been diagnosed with metastatic disease to get either an aromatase inhibitor, so, letrozole, by itself or letrozole with this CDK 4/6 inhibitor.

The results are actually very impressive. They showed that adding the CDK 4/6 inhibitor to the aromatase inhibitor very significantly improved outcomes. They showed that progression-free survival was substantially longer in patients who received the combination relative to just the letrozole by itself. Interestingly, looking at side effects, there really weren’t a lot of additional side effects by adding this new drug to the letrozole. They did show that there was a higher rate of neutropenia, or lowering of white blood cell counts, when getting the combination therapy relative to just getting letrozole by itself. But overall, patients actually did very well with it.

I think it’s very exciting, and it’s nice that there are some newer drugs on the horizon. The combination of the CDK 4/6 inhibitor with letrozole did seem to improve outcomes for patients who have metastatic ER positive cancer, and it was very well-tolerated. There are plans for a study that is a phase III trial, looking at the same combination — the CDK 4/6 inhibitor with letrozole compared with letrozole alone — and this is planned to start very shortly and will certainly, hopefully, lead to a new drug being around in this setting.

So, what have we learned from the conference? I think we learned: that eribulin is not superior to Xeloda for metastatic treatment but did look fairly equivalent when
looking at the studies, so [it’s] a reasonable chemotherapy drug to use for metastatic disease; and that, I think, excitingly, there are some new drugs on the horizon. Specifically, this CDK 4/6 inhibitor seems to reduce recurrences when added to an aromatase inhibitor for patients with ER positive disease.

Overall it was a very exciting conference. I think probably the one trial that really led to a change in standard of care is the ATLAS trial, showing that taking longer-duration tamoxifen is better than shorter. That certainly will, I think, impact a lot of patients’ care.

So, thank you.

ELYSE SPATZ CAPLAN, MA: Dr. Tolaney, thank you so much for, in less than half an hour, covering so many important discoveries, some [of which] may impact changing practice right now and some may not, but they’re good information for people to have as they take questions back to their oncology team. I’m pleased that we were able to cover a number of studies that were presented in the early-stage setting as well as the metastatic.

With that, I would like our operator to come back on and let people know how they can get into the question queue. I will remind folks, if you’re on by phone, please limit your question and keep it concise. We do have a lot of questions already submitted via the website.

OPERATOR: Thank you. We’ll now conduct a question-and-answer session. If you would like to ask a question by phone, please press “star, one” on your telephone keypad. A confirmation tone will indicate your line is in the question queue. You may press “star, two” if you would like to remove your question from the queue. For participants using speaker equipment, it may be necessary to pick up your handset before pressing the star keys.

You may submit your questions online by using the “ask a question” feature on the left side of your screen. Thank you.

ELYSE SPATZ CAPLAN, MA: Let’s start with some of the phone questions.

OPERATOR: Our first question comes from Casselberry, Florida.

WOMAN: Hello. … I have been on Herceptin for three years, three months. I’m hearing you say two years is — well, I’m like, “Golly.” I was wondering, too, that inflammatory breast cancer has come back three times. It’s kind of back in the spine but it’s not really growing, so we’re just watching it. It came back after three years before, and I went on the chemo a second time. For the three years, I call it crap because it makes me feel like crap every Thursday for three years, because it really does a job on me. I was wondering, too, just what you said: How do you feel, you know, if the Herceptin was worth it but yet it’s holding it off or not? That’s really confusing to me.

SARA TOLANEY, MD, MPH: Just to clarify, the studies that were done looking at duration of Herceptin were really done in patients who had surgery and had no evidence of any recurrence of their HER2 positive cancer, so those studies really only answered the question of duration in that particular setting.

Sounds like your particular question is a little bit different in the sense that you’ve, unfortunately, had to deal with some recurrence of the disease. That is a different situation for which we usually do recommend extended treatment with an anti-HER2 drug, meaning we do like patients to be on Herceptin long-term, because our concern is that if we discontinue it, it will allow for the cancer to regrow again.

It’s a tough question in the sense that if you’re feeling fine with it and you weren’t having side effects, you know, it’s much easier to ask you to continue taking it for a long time. It’s obviously more difficult if you are having side effects from it. I don’t know all the details of your cancer, but I think newer and newer anti-HER2 drugs are continuing to come out, and it’s certainly something to talk about with your oncologist, depending on where your cancer is along the way.

ELYSE SPATZ CAPLAN, MA: Thank you, and take good care.
OPERATOR: Thank you. Our next question comes from Vacaville, California.

WOMAN: Hi. Yeah, I have a question on the trial. You were talking about tamoxifen trials, five years versus 10 years. They also have a trial for aromatase inhibitors, five years versus 10 years, as far as I know. Is that right? If so, how long before the completion of that trial, and is that comparing recurrence, improved mortality and safety issues?

SARA TOLANEY, MD, MPH: You’re exactly right. Just as you said, the tamoxifen study that we talked about today and looked at five versus 10 years, is the ATLAS trial. There’s a trial that also looked at an aromatase inhibitor comparing five versus 10 years. This was the MA.17R study. This study we do not yet have the results of, though. Now, this study will look at all of the things you mentioned — the rates of recurrence and survival, as well as side effects — so really will be very helpful to us in helping determine whether we can safely extend duration of aromatase inhibitor treatment.

Unfortunately, we don’t have the results of that yet. This leads to the question of what to do now in patients when they complete five years of an aromatase inhibitor therapy. Unfortunately, there isn’t really a right or a wrong answer. Certainly the standard of care for an aromatase inhibitor now is five years. However, if patients have more rather than less breast cancer, we do sometimes consider trying to give them more [than five years of treatment with hormonal therapy]. With the data from the ATLAS study, one could argue, in someone who had a more high-risk cancer, whether or not we should consider giving them five additional years of tamoxifen, and I think that certainly could be considered.

OPERATOR: Thank you. Our next question comes from Washington, D.C.

WOMAN: Hi. I have a question about triple-negative breast cancer. I apologize — I’m not sure if you covered this in your talk because I had to step out for a few minutes, but I understand from the San Antonio meeting that there was some early research presented on triple-negative and some apparent similarities to ovarian cancer. I’m wondering if you could expand on that.

SARA TOLANEY, MD, MPH: Sure. There [was] a lot of science presented on the biology of triple-negative breast cancer, and some very interesting studies were discussed. There are a couple of trials, actually, from our institution, one of which looked at the biology of triple-negative breast cancer, specifically looking at whether PARP inhibitors could be beneficial for this subtype of breast cancer.

There’s some laboratory work that was done looking at whether giving a PI3 kinase inhibitor — a drug that inhibits a particular pathway that sometimes goes awry in breast cancers — could make triple-negative cancers more susceptible to a PARP inhibitor, which did look very encouraging in the laboratory. There’s now a trial that’s combining both of those agents — a PARP with a PI3 kinase inhibitor — for triple-negative breast cancer that is ongoing.

There’s also data from José Baselga’s lab that looked at the biology of triple-negative breast cancer, specifically looking at inhibiting the PI3 kinase pathway, which then seems to cause an upregulation of an additional pathway, the HER3 pathway. Maybe hitting both the HER3 and the PI3 kinase pathway together for triple-negative breast cancer may be promising. There are several trials that are ongoing looking at that as well – so, a lot of very interesting biology has been looked at for triple-negative cancers that is leading to a lot of studies being done to try to attack what was found in the lab and see if it pans out to be real in people.

ELYSE SPATZ CAPLAN, MA: Thank you.

OPERATOR: Our next question comes from Ithaca, New York.

WOMAN: Thank you very much. I wondered if any comment was made on the metformin studies that are ongoing at San Antonio. Thank you.

SARA TOLANEY, MD, MPH: Sure. There’s no current data from those trials, but I think it is a very exciting area of
research in breast cancer. Currently there’s the MA.32 study, which is open, which looks at women who have a history of breast cancer. They’re randomized to metformin or to a placebo for a total of five years to see if taking metformin can help prevent breast cancer recurrences. This study is very interesting, and it’s based on a lot of work that has been done, particularly in the laboratory. There is data to suggest that metformin, which as you all know is a standard drug used to treat diabetes, happens to also inhibit several pathways within cancer cells, that seems to turn off something called the mTOR pathway. It also is important in regulation of things like the insulin receptor and insulin growth factor receptor.

I think a lot of the rationale [for] these studies came out of trials that looked at patients with diabetes. When we compared patients with diabetes who have breast cancer who are taking metformin with those who were not taking metformin, the patients with diabetes and breast cancer taking metformin did better. I think it’s been very interesting. There’s also data recently looking at metformin and ovarian cancer, suggesting that it may be beneficial.

I think it’s an exciting topic, and certainly we need a little more data at this point. Accrual to the MA.32 study is supposed to end at the end of this month, so it will take a few years before we will get the answer to this question, but I think it’s a very important question.

ELYSE SPATZ CAPLAN, MA: Thank you for that. I think we’re going to switch to some of the Web-based questions that have come in. Let’s start, Dr. Tolaney, with any updates presented last month at San Antonio on Perjeta, or pertuzumab, and T-DM1 that you think are worth highlighting.

SARA TOLANEY, MD, MPH: Well, not so much practice-changing [updates] from the current San Antonio [but] I think just some updates. Many patients know about T-DM1 now – [ado-trastuzumab emtansine, or Kadcyla]. Really, that’s a drug that takes Herceptin and conjugates it to a chemotherapeutic agent. A lot of people call it the “smart bomb” because it’s selectively delivering the chemotherapy into a HER2 positive cancer cell, a very exciting concept.

There was a large study presented at ASCO last year that compared T-DM1 with Xeloda [plus] lapatinib, the EMILIA study, and showed that T-DM1 did better. We are anticipating FDA approval of T-DM1 in February, which would allow patients with metastatic HER2 positive breast cancer to get access to T-DM1, which I think would be fabulous. We’ve certainly been giving T-DM1 on clinical trials for a few years now and have seen exciting responses with it. [Editor’s Note: ado-trastuzumab emtansine was FDA approved on February 22, 2013.]

There are trials now that do allow for compassionate use and expanded access to T-DM1 in the interim, until FDA approval is received. If patients need access to the drug now, certainly here at Dana-Farber we do have a trial that allows expanded access in this interval period while we’re awaiting FDA approval.

In terms of Perjeta, or pertuzumab, data that had been presented by José Baselga had looked — this was last year at San Antonio — at combining pertuzumab with trastuzumab, or Herceptin, in combination with a taxane for women with newly diagnosed, metastatic HER2 positive breast cancer. It did show very impressive improvement — so, allowing patients to have longer time to progression when giving the combination of all three drugs compared with just giving chemotherapy with Herceptin.

This did lead to FDA approval of pertuzumab, but right now pertuzumab is only approved in that particular setting, meaning it’s approved only [for] the first time a woman is getting chemotherapy for metastatic, HER2 positive disease. I think many of us would love to be able to give pertuzumab to women in another setting, meaning once they’ve had a couple of lines of chemotherapy. Right now there isn’t enough data to do that. We don’t have insurance coverage to do that. We do have several clinical trials that are looking at pertuzumab in that setting, though. Hopefully, we’ll be able to get patients access to the drug that way.

ELYSE SPATZ CAPLAN, MA: Thanks for giving some of those updates. I know a number of questions have come in, knowing that it’s still in the clinical trial process, and more
analysis needs to be done. I’m sure some folks will be appreciative of that.

There are some questions related to younger or premenopausal women I’d like to ask you to comment on. One is: What, in your opinion, is the benefit of performing an oophorectomy, or removing ovaries, in order to use an aromatase inhibitor rather than tamoxifen?

Separately, but again under the theme of young women, can you please comment on women who are ER positive who want to take a break, perhaps, to achieve a pregnancy? Can you give some of your perspective on the duration of tamoxifen for young women who are thinking about building their family?

SARA TOLANEY, MD, MPH: Sure, two very good questions, not with really easy answers.

The first question, looking at removal of ovaries — having an oophorectomy — in order to be able to take an aromatase inhibitor: Right now there really is no data to suggest that in a premenopausal patient taking an aromatase inhibitor would be better than taking tamoxifen. There was a trial that was done, the ABCSG-12 study, which compared women getting ovarian suppression — in that trial they were taking an injection to shut off their ovaries, or they were allowed to have surgery to do so — in combination with tamoxifen or with an aromatase inhibitor. There was really no difference in outcomes, meaning that getting tamoxifen with your ovaries shut out versus getting an aromatase inhibitor with your ovary function off is no different.

So, if someone has completed five years of tamoxifen and they’re still premenopausal, the standard now after the ATLAS data would be to just do another five years of tamoxifen. I wouldn’t push a woman to get their ovaries out and to do an aromatase inhibitor because now we have good data suggesting 10 years of tamoxifen is a good treatment, so I don’t think there is any additional, at least right now, benefit to doing that.

Obviously there will be further information looking at ovarian suppression. There are trials that are pending. There’s the SOFT study and the TEXT trials, which are really trying to answer whether taking out your ovaries adds to taking tamoxifen, which I think is a big question we don’t have the answer to, meaning if you’re premenopausal and you’re still having periods and you’re taking tamoxifen, would taking out your ovaries reduce your risk of recurrence more on top of taking the tamoxifen? Honestly, we don’t really have the answer to that in a straightforward way. The SOFT study will provide that answer to us.

The other question is if you’re premenopausal and you need to take tamoxifen for a long time, how do you manage to have a family? I think that’s a very tough question and without a very straightforward answer. Unfortunately, you can’t get pregnant – physically you can get pregnant on tamoxifen, but it would not be a good thing. It can cause birth defects, so we’re very cautious about women who are premenopausal on tamoxifen, making sure we tell them not to get pregnant.

It’s, however, just not practical. Many women want to have children, and many women get diagnosed with breast cancer and haven’t yet had their children. How do we manage to put that into the plan?

I think most of us like women, if it’s possible, depending on their age, to get through five years of tamoxifen and then try to have a pregnancy. However, for some women, that just isn’t practical. If you’re 38 or 39 and you’re getting diagnosed with breast cancer and you haven’t had a child and you want to have a kid and you need to take five years of tamoxifen, obviously it’s harder to conceive as you get older and it’s just not practical to bank on being able to get pregnant in your 40s, so it is a complicated question.

In those situations, I think it takes more of a discussion about whether or not doing a short time of tamoxifen is OK. That does, I think, take an involved conversation with your oncologist, depending on the risks of recurrence of your cancer, and that’s not a straightforward question.

ELYSE SPATZ CAPLAN, MA: Right.

SARA TOLANEY, MD, MPH: I think the other question is: The people who need 10 years of tamoxifen, how do you then have a kid? Even if you’re 30, if you need 10 years
and you get to be 40, it’s hard to wait to be 40 to have a kid and not, again, practical to bank on that happening. I think many of us are very practical. Again, if you’ve gotten through five years and you [want] to have a kid, you go ahead and take a break and have a child. Then, when you’re done with your childbearing, go back to considering longer-duration tamoxifen.

ELYSE SPATZ CAPLAN, MA: Thanks so much for tackling those complex questions. I think the takeaway is that it is an individual conversation with your oncologist who has the whole profile of a woman’s cancer and can help her get the information she needs to make the best decisions.

SARA TOLANEY, MD, MPH: I think that’s exactly right.

ELYSE SPATZ CAPLAN, MA: Now we’ll take some phone questions.

OPERATOR: Our next question comes from Franklin, Massachusetts.

WOMAN: Hi. I was wondering if there’s any information on taking Herceptin for longer than five years if you have metastatic breast cancer. Do you take it indefinitely?

SARA TOLANEY, MD, MPH: That’s always a tough question. I think the answer to your question does depend a little bit specifically on the circumstances. It’s a little hard to answer without having all the information.

Generally, we know that adding Herceptin to chemotherapy, even after one line of chemotherapy and Herceptin have failed, is successful – meaning if you got, for example, Taxol and Herceptin and it stopped working, going to Navelbine and Herceptin works often, meaning using Herceptin again continues to add benefit. Some patients who’ve had metastatic disease happen to have it, thankfully, all regress and stay under control, and sometimes we’ll pull away the chemotherapy and just leave patients on Herceptin.

Then the question is: Well, how long do you really need to be on Herceptin? Honestly, we don’t really know. Most of us are, frankly, too scared to stop it, because there is some risk that the Herceptin is keeping things controlled and that pulling it away could allow the cancer to kind of rear its head again.

So, I don’t really have an answer in the sense that most of us just do continue it indefinitely with chemotherapy. Now we do integrate a lot of the newer anti-HER2 drugs along the way, including [ado-trastuzumab emtansine], lapatinib and Xeloda. There are a lot of other combinations that can be explored, and if you’re doing well on Herceptin by itself, most of us just continue it.

WOMAN: Thank you.

ELYSE SPATZ CAPLAN, MA: I’ll just add, Dr. Tolaney that, related to the concerns about long-term use, most women are having periodic monitoring of their heart function and other testing that might help you as an oncologist sort of make determinations about duration of use.

SARA TOLANEY, MD, MPH: Oh, exactly, very important point that we do worry about some side effects to the heart with Herceptin therapy, and that does need to be monitored. Obviously, if people are having side effects, it is something we do need to consider. It sometimes does lead to us needing to hold the Herceptin.

ELYSE SPATZ CAPLAN, MA: Thank you.

OPERATOR: Our next question comes from Atlanta, Georgia.

WOMAN: I may just be not informed on this, but when you keep talking about an aromatase inhibitor, is that Arimidex?

SARA TOLANEY, MD, MPH: There are three different aromatase inhibitors. Arimidex is anastrozole, which is one of them. There’s letrozole, or Femara, and there’s exemestane, which is also known as Aromasin. Those three drugs are what we call aromatase inhibitors, because they all function in the same way.
WOMAN: Then they would be under the same 10-year extension as tamoxifen?

SARA TOLANEY, MD, MPH: No, unfortunately. There are different drugs that compare to tamoxifen, meaning they do have different side effect profiles and different mechanisms of action, so we really do need data looking at 10 years versus five years of an aromatase inhibitor, which we don’t yet have. We only really have this extended-duration tamoxifen data that was presented at San Antonio. We’re waiting on the results of a trial that looked at 10 years versus five years of an aromatase inhibitor, but we don’t have that data yet.

WOMAN: Don’t have that yet. All right, and I’ll discuss it with my oncologist. Thank you so much.

ELYSE SPATZ CAPLAN, MA: Thank you.

OPERATOR: Thank you. Our next question comes from North Prairie, Wisconsin.

WOMAN: What is the best practice to decrease the risk of recurrence for inflammatory breast cancer?

SARA TOLANEY, MD, MPH: That’s a good question, a tough one. Honestly, it depends on a lot of information. I don’t think I can quite generalize it. It would depend on the subtype of inflammatory breast cancer that you have to know what kind of therapy would be most effective, meaning is it ER positive, HER2 positive, triple-negative, because our treatments for inflammatory cancer, just like in non-inflammatory cancer, are really guided by that. There isn’t a different answer at this time, rather than treating it similarly to the way we treat standard breast cancer, with the exception being that we do give the chemotherapy always prior to surgery in that situation.

ELYSE SPATZ CAPLAN, MA: Thank you. Keep asking your questions, and hopefully one day we’ll have more discoveries to report on for inflammatory breast cancer.

OPERATOR: Our next question comes from Houston, Texas.

WOMAN: Hi. Thank you very much. I wonder if there’s been noted an increased correlation between our longer use of tamoxifen and an increased risk of endometrial or uterine cancer.

SARA TOLANEY, MD, MPH: Yes, there has been. The ATLAS study that was reported did show a 3.1 percent risk of endometrial cancer in women who had taken tamoxifen for 10 years. That’s almost double the rate compared with women who took it for just five years. Definitely the risks of endometrial cancer do rise with longer duration of tamoxifen.

One important takeaway point, though, is that this really is predominantly an issue in postmenopausal women, that this increase really isn’t seen in premenopausal patients. That’s why we feel comfortable recommending longer-duration tamoxifen, particularly in premenopausal women, where this increased rate isn’t as much of an issue. Again, [it’s] more complicated in the postmenopausal setting, where there are other drugs available, such as aromatase inhibitors, and knowing how to sequence that isn’t quite clear yet.

But you’re right. There is a higher rate of endometrial cancer with longer-duration tamoxifen.

WOMAN: Thank you.

OPERATOR: Thank you. Our next question comes from San Diego, California.

WOMAN: Yes. I thought it was great to hear that there’s some information on lobular cancer. Rarely do I hear or read anything. Do you mind repeating the finding that you quoted?

SARA TOLANEY, MD, MPH: It is interesting. You’re right. There’s rarely a lot of specific data that shows a difference in the way we treat lobular cancers relative to ductal cancers, so it was interesting. This was comparing the use of letrozole to tamoxifen, looking at rates of recurrence in ductal cancers compared with lobular cancers, based on which drug you took. They did find that there was more of a benefit to taking an aromatase inhibitor, specifically letrozole, in lobular cancers relative to tamoxifen; it does
suggest that taking an aromatase inhibitor for a lobular cancer after diagnosis may be better than taking tamoxifen. The reason for this, I have to be honest, isn’t entirely clear. Why would that be from a biological standpoint? We don’t really have that answer.

ELYSE SPATZ CAPLAN, MA: Thank you for asking that great question. With that, I would like to thank Dr. Tolaney for covering so many topics today and all the folks that either submitted a Web question or had the chance to ask a question by phone. Your questions help to enrich the quality of our programs, and we also know what’s on your mind.

Many questions that were submitted to us that we could not directly answer specifically relate to the ATLAS trial, tamoxifen for 10 years, and what I’d like everyone to take note of is that Living Beyond Breast Cancer’s spring Insight newsletter will feature a cover story on the ATLAS trial. So, moving forward into the early spring, we will be reporting more fully on the study. We also have stories on our website, lbbc.org. Our hope is that some of the questions that you’re bringing that weren’t specifically answered today may be accessible to you through our website.

Dr. Tolaney, do you have any closing remarks before we wrap up today?

SARA TOLANEY, MD, MPH: I think the big thing is that there continues to be more and more exciting results and we continue to learn a lot about breast cancer. There are newer drugs that are coming out, newer drugs that are going to be FDA-approved soon, so I think it’s just a very exciting time. If there are any specific questions, particularly on things that we discussed, it’s always important to relay specific things with your oncologist to take into account the whole picture when figuring out what to do next.

ELYSE SPATZ CAPLAN, MA: Absolutely. With that, a reminder that LBBC’s toll-free Survivors’ Helpline is available for peer emotional support. You can call (888) 753-LBBC (5222) and speak live to a volunteer who has had breast cancer, Monday through Friday from 9 a.m. to 5 p.m. Eastern time. Messages will be returned very promptly.

Again, our thanks to AstraZeneca for the generous support that made today’s webinar possible.

Take care, everyone.

[END OF TRANSCRIPT]