

FDA Media Call
Potential Risk of Anaplastic Large Cell Lymphoma (ALCL) in Women with Breast Implants
Moderator: Erica Jefferson
January 26, 2011

Coordinator: At this time, all participants are in a listen-only mode. After the presentation, we will conduct a question and answer session. If you would like to ask a question, please unmute your phone, press star 1 and record your name when prompted.

Today's conference is being recorded. If you have any objections, you may disconnect at this time.

Now I would like to turn the call over to Miss Erica Jefferson. Ma'am, you may begin.

Erica Jefferson: Thank you Rosie. Good afternoon and thank you for participating in today's call. My name is Erica Jefferson and I'm from the FDA's office of Public Affairs.

This is a media briefing to announce a possible association between both saline and silicone gel-filled breast implants and a very rare form of lymphoma or cancer called anaplastic large cell lymphoma or ALCL.

An FDA news release on this announcement has been posted on our Web site and distributed via PR newswire.

Today I'm joined by Dr. William Maisel, Deputy Director for Science and Chief Scientist in the Center for Devices who will begin the call with brief remarks. After Dr. Maisel's remarks, we will move to the question and answer portion of the call.

In addition to Dr. Maisel, we also have several technical experts to help answer your questions. They will identify themselves.

Reporters will be in listen-only mode until we open up the call for your questions. When asking a question, please remember to state your name and affiliation. Also, please limit yourself to one question and one follow-up question so we can get to as many questions as possible.

Before we begin the briefing, I want to bring your attention to several important materials that are now posted to FDA's Web site and can be accessed from a link in the news release.

A resource page has been created that contains links to a white paper and a device safety communication that Dr. Maisel will highlight in just a moment.

With that I will now turn it over to Dr. Maisel for his opening remarks. Dr. Maisel?

William Maisel: Thank you Erica and good afternoon.

Today we're here to inform healthcare professionals and the public about a possible association between both saline and silicone gel-filled breast implants and a very rare form of lymphoma called anaplastic large cell lymphoma or ALCL.

Before I briefly summarize what our analysis found, I want to spend a couple of minutes explaining what lymphoma and ALCL are.

Lymphoma is a cancer involving the cells of the immune system. ALCL is a very rare type of lymphoma occurring in approximately 1 of every 500,000 women in the United States. ALCL located in the breast is even more rare occurring in 3 out of every 100 million women in the United States.

Importantly, ALCL located in the breast is not the same as breast cancer that you may be familiar with. Although very rare, the FDA believes that women with breast implants may have a small but increased risk of developing ALCL.

Well how did we get here today? As part of the Agency's post-market surveillance of medical devices, we became aware of rare reports of ALCL. We conducted an extensive review of the scientific literature published from January, 1997 through May, 2010 and identified 34 unique cases of ALCL in women with breast implants worldwide.

Additional information was collected through FDA's contact with other international regulators, scientists and breast implant manufacturers and through a review of adverse event reports submitted to FDA.

In total, the FDA is aware of approximately 60 case reports of ALCL in women with breast implants worldwide.

The exact number of cases is difficult to verify because reports from regulatory agencies and scientific experts may duplicate those found those found in the scientific literature.

Most cases reviewed by the FDA were diagnosed when patients sought medical treatment for implant related symptoms such as pain, lumps, swelling

or asymmetry. These symptoms developed long after the initial surgery had been performed and after the surgical sites had fully healed.

These symptoms can be caused by several factors including collections of fluid around the implant called peri-implant seroma, hardening of the breast area around the implant called capsular contracture or lumps or masses discovered around the implants.

In most cases, examination of the fluid in capsules surrounding the breast implant led to the ALCL diagnosis.

Women with breast implants who are not showing any symptoms or problems such as pain, lumps, swelling or asymmetry require only routine follow-up. And I'm going to say that again because it's one of our most important messages today that women with breast implants who are not showing any symptoms or problems require only routine follow-up.

Today the Agency is recommending the following: Healthcare professionals should consider the possibility of ALCL if a patient has late onset and persistent fluid around the implant. By sending a sample of this fluid to a pathology lab, a healthcare professional can test for ALCL.

Women with breast implants who are not showing any symptoms or problems do not need to change their healthcare routine. ALCL is rare and has occurred in a very small number of women when compared to the millions who have breast implants.

FDA is not recommending the routine removal of breast implants in patients without symptoms or other abnormality. Women should monitor their breast

implants and discuss any noticeable changes with their doctors, in particular those that occur after the breast implants are fully healed.

Patients considering breast implants surgery should discuss the risks and benefits with a healthcare professional.

Given the rarity of ALCL and the small number of detailed reports available for review, FDA would like to collect more information to help us fully understand any possible link between breast implants and ALCL.

And to do that, we are asking healthcare professionals to report all confirmed cases of ALCL in women with breast implants in MedWatch, FDA's safety information and adverse event reporting program. Contact information can be found in today's news release.

In addition, the FDA is working with the American Society of Plastic Surgeons and other experts to establish an ALCL breast implant patient registry so that we can better understand the nature of this disease among breast implant patients.

Although the registry is not operating yet, we will announce more details when they are available.

In an effort to ensure that patients receiving breast implants are informed of the possible risk of ALCL, the Agency will be working with breast implant manufacturers in the coming months to update their product labeling materials for patients and healthcare professionals.

Later this year, FDA plans to provide a comprehensive update on the interim findings from several ongoing FDA required post-approval studies of silicone

breast implants that are currently sold in the United States, as well as updating adverse event reports submitted to FDA and providing a review of the scientific literature on these products.

With that, I'll turn it back over to Erica and we can take your questions.

Erica Jefferson: Thank you Dr. Maisel. At this time we will begin the question and answer portion of the briefing. Rosie, we'll take the first question.

Coordinator: One moment please.

Our first question comes from Jennifer Corbett of Wall Street Journal.

Jennifer Corbett: Yes, hi, thanks for taking my question. One question I have is you mentioned that you're seeing these cases with both the silicone and the saline but do you have an actual breakdown of the cases for silicone and saline implants?

William Maisel: Yes, in the white paper that has been posted on our Web site, we have a table summarizing the 34 published cases of ALCL that are in the literature. And in that is a table that describes the features of the implants. Of the 34 cases, 24 were silicone, 7 were saline.

Jennifer Corbett: Oh, I see it.

William Maisel: And the rest were not specified.

Jennifer Corbett: Okay. Thank you.

Coordinator: Our next question comes from Lisa Richwine of Reuters.

Lisa Richwine: Hi. Thanks for taking my question. I have a few things I want to ask about but I guess I'll start with some consumer advocates are saying the companies are far behind on their post-approval studies. Can you provide an update on that on where they are?

William Maisel: As part of their approval, medical device companies that manufacture breast implants had several post-approval requirements. We've been carefully monitoring the performance of those studies. The companies are required to submit annual reports to us which we have been receiving on time and we will be providing a complete summary of updated information later this spring on the status of the post-approval studies.

Lisa Richwine: And does that mean that they're on time if you're saying they've been submitting their annual reports on time, does that mean the studies are on time?

William Maisel: It means that we have been monitoring the performance of the post-approval studies. There have been certain studies that have had trouble enrolling patients, for example, and FDA has worked with manufacturers to increase enrollment and make sure that the studies provide the information as they were designed to provide.

Lisa Richwine: Okay, thanks.

Coordinator: Our next question comes from Denise Grady of the New York Times. One moment.

Denise Grady: Thank you.

Coordinator: Your line is open, ma'am.

Denise Grady: Okay, thank you. How bad is this disease? Is it fatal or can be it? What happens to people who get it and what - is it treatable and if it is treatable, what has to be done?

William Maisel: As we've discussed, ALCL is a type of lymphoma which is a form of cancer. There are several treatment options available for ALCL in general which include chemotherapy, radiation, therapy and surgery.

There's some suggestion from the literature and some of the scientific community believes that ALCL associated with breast implants may be a less aggressive form of the disease.

And in some cases, there's a suggestion that removing the breast implants, removing the fluid around the breast implant and removing the capsule may be sufficient treatment in some patients.

The data is limited. Some of the follow-up of those patients is limited so FDA does not feel comfortable recommending a specific treatment for all patients but we do recommend that patients seek medical attention with their healthcare provider, as well as with a team of experts including oncologists and breast surgeons.

Denise Grady: Thank you.

Coordinator: Our next question comes from Miss Lisa Stark of ABC News.

Lisa Stark: Sorry, it's kind of a two-part question, also. Just for clarification, you say some of this has shown up years after the implant, can you be more specific so to help women out like how many years out might they have to be worried.

And finally, do you have any idea on the mechanism like why this might be causing this cancer problem? Thank you.

William Maisel: So again, in our white paper that's on the Web site, there's a table that describes the range of implant time. The range that we've seen in the cases reported in the literature is from approximately one year post-implant to as many as 23 years post-implant. The average time is around 8 years post-implant that it's been identified. But again, we need to recognize this is based on relatively limited data.

Regarding the mechanism, there's some suggestion that the cell - certain types of cells around breast implants may contain silicone, particularly in implants that rupture, but even implants that don't rupture because they're surrounded by silicone may have some of the silicone taken up by the cells.

That type of chronic stimulation of these cells may be capable of inducing lymphoma in these rare cases, although please understand that that is speculative and a hypothesis.

Coordinator: Our next question comes from Deborah Kotz of The Boston Globe.

Deborah Kotz: Hi there. Thank you very much for taking my question. Looking at the white paper, I'm just trying to figure out; you have a breakdown of women who had this - the implants for reconstruction purposes versus augmentation. And it looks like there are fewer women who had reconstruction who developed these cancers at least that were reported.

And what I'm trying to figure out if, you know, in terms of the numbers, if it's still more common given that probably fewer women are having

reconstruction versus augmentation, if it's still a higher risk in patients who had previous breast cancer and then reconstruction versus those who are getting breast implants purely for cosmetic purposes.

William Maisel: That's a good question and we're very interested in trying to understand more specifically which types of patients may be at more risk, which types of breast implants may provide a higher or lower risk.

The data, we need to recognize the number of cases is very small. It's hard to know precise numbers of women who have received breast implants for a given reason for reconstruction or for augmentation.

After our review of the data, we do not believe that there is a distinction to be made between the reason for implants.

Deborah Kotz: Thank you very much.

Coordinator: Our next question comes from Heather Tesoriero of CBS News.

Heather Tesoriero: Quick clarification on the numbers, the 34 versus the 60, so are the 34 cases were those U.S. and the 60 was worldwide?

William Maisel: No, the 34 cases were the cases that we identified from our review of the scientific literature. In our methods for how we went about reviewing the scientific literature are described in the white paper. But that is the scientific literature throughout the world English language scientific literature.

Actually there were 37 cases in the literature but three of them were duplicates so that left us with 34 unique cases. The additional cases we identified through our interactions with international regulators, scientists or adverse event

recording system and through our interactions with manufacturers, that's how we came up with this 60 - approximately 60 cases worldwide.

Heather Tesoriero: So for accuracy in reporting, it's appropriate to say that thus far the FDA has identified a total of 60 cases worldwide?

William Maisel: We've identified approximately 60 cases. The reason we're not saying precisely 60 cases is because we can't absolutely verify that each of those cases is unique and it's possible that there may be some reporting in the literature of some of those other cases we identified.

Heather Tesoriero: Okay. Thank you for that.

Erica Jefferson: Thanks Heather. Can take the next question?

Coordinator: Our next question comes from Daniel DeNoon of Web MD.

Daniel DeNoon: Thank you for taking my question. Going back to the mechanisms, so we talked about silicone implants and silicone might have something to do with this, but we're also talking about saline. Is there a mechanism proposed for that?

And I also noticed from the white paper that the texture of the implant surface that when that was - when that information was available all of these cases were in textured implants. What mechanism might that be associated with?

Erica Jefferson: Just a moment, Dan.

William Maisel: So again, the mechanism is unknown. We do not know why there appears to be this possible association between breast implants and ALCL. What we do

know are that both silicone and saline implants are surrounded by silicone and the implants themselves also contain other products and substances.

So some of the silicone has been found in the cells around breast implants and it's theorized that this may be capable of stimulating the T-cells and inducing lymphoma.

Daniel DeNoon: And the textured surfaces?

William Maisel: So the textured surfaces, the smooth versus textured surfaces for the breast implants is another question that remains unanswered. As you'll see in the table we provided, among the cases in the literature, four were identified as having textured surfaces, but the remaining 30 did not report what type of surface the breast implants had.

There is some - there are some reports in the scientific literature that textured implants may be more associated with ALCL, but after our review of all the data available, we do not feel that there is evidence that that is the case.

Daniel DeNoon: Thank you.

Erica Jefferson: Next question please.

Coordinator: Our next question comes from Bridget Kuehn of JAMA Medical News.

Bridget Kuehn: Hi, thanks for taking my call. I was just wondering Dr. Maisel, could you give us a little bit more detail on the post-marketing trials that have been requested of the companies, like what are the questions you're trying to answer?

William Maisel: There are several different types of post-market studies that were required as part of breast implant approval. One of them, for example, is to follow the initial group of patients who were studied to assess the long-term complication rate associated with breast implants and to understand the health of those patients.

The companies have also been required to perform additional mechanical testing on breast implants to monitor patients very carefully with MRI scans, for example, to detect the rate of rupture including asymptomatic rupture in patients who may not be aware that it happened.

And there are some large studies enrolling more than 40,000 patients so that we can get a better idea of the safety and performance of these devices over time.

Bridget Kuehn: Okay, thank you.

Coordinator: Our next question comes from Matt Perrone of the Associated Press.

Matt Perrone: Hi guys, thanks for taking our questions. Maybe I missed this, could you just - what prompted the FDA's review and when did it begin roughly?

William Maisel: We continually monitor the safety of medical devices including breast implants and there have been reports in the scientific literature of ALCL, rare reports that we became aware of.

And so as part of our due diligence we began investigating further to perform a more formal analysis of the available literature and to contact other regulatory agencies and scientists to try to better understand the issues.

We're coming out with this today and now for a couple of reasons. One is we just recently felt that we developed the evidence that supports the possible association.

Two is we think it's very important that women with breast implants understand the information that we have, that women considering undergoing breast implantation have all the available information available to them so that they can make smart decisions with their family and healthcare providers and because we're asking for more information from the healthcare community.

We want them to be able to report to us detailed information about confirmed ALCL cases. And as you know, we're developing a registry, as well.

Matt Perrone: I see. But this information you didn't have it or you weren't aware of it in 2006 when the silicone devices were put back on the market?

William Maisel: That's correct. This information has developed since that - since the approval of these devices.

Matt Perrone: Okay, thanks.

Erica Jefferson: Thanks Matt.

Coordinator: Our next question comes from Lynne Peterson of Trends-in-Medicine.

Lynne Peterson: Thank you. My question was asked and answered.

Erica Jefferson: Okay. I think we can take the next question. Thanks Lynne.

Coordinator: Our next question comes from Matt Herper of Forbes.

Matthew Herper: Hey, just wondering if you could talk a bit about - I know that the mechanisms you're proposing are merely hypotheses at this point, but can you talk about how secure are you in the existing database in excluding risks of other types of cancer given that you just proposed a mechanism by which this could be causing this type of cancer? I mean, what can we exclude?

William Maisel: Well there's been extensive studies that have been done looking at the association of breast implants with breast cancer, the more typical type of breast cancer that you would think of when you hear that phrase. And there has been no evidence that there is an association between breast implants and...

Matthew Herper: What about other lymphomas?

William Maisel: There's no - we don't have evidence to suggest that breast implants are associated with other types of lymphomas.

Matthew Herper: Okay.

William Maisel: That's part of the reason why we're suggesting that there is a possible association because of the very specific and rare type of lymphoma that's been observed and because of the specific types of proteins that has been seen on the outside of the cells of this lymphoma, in some respect it has a very unique fingerprint that suggests the possible association.

Matthew Herper: Okay.

Coordinator: Our next question comes from Andrew Zajac of the LA Times.

Andrew Zajac: Hi. Could you clarify the frequency with which the increased risk for women with breast implants? You say that ALCL is diagnosed in 1 out of 500,000 women in the U.S., one out of how many women with implants?

William Maisel: That's an excellent question. So I'll walk you through the numbers so that you can understand what we know and what we don't know. We know that about 1 in 500,000 women in the U.S. are diagnosed with ALCL. That's not ALCL of the breast. That's ALCL anywhere in their body and that's in women who do not necessarily have breast implants.

We know that about 3 out of 100 million women are diagnosed with ALCL in the breast. And again, that's in all-comers not just women with breast implants.

We also know that we've identified 60 cases of ALCL in the breast in women with breast implants among an estimated 5 million to 10 million with breast implants worldwide. Now because the numbers of women with breast implants is uncertain, it's hard to put a precise number on it for you.

Andrew Zajac: Can you sort of ballpark it, one out of approximately how many?

William Maisel: I just told you there's approximately 60 cases we've identified worldwide and there's approximately 5 million to 10 million women with breast implants worldwide.

Andrew Zajac: Okay.

Erica Jefferson: All right. Thanks Andy. Can we take the next question?

Coordinator: Robert Lowes from Medscape Medical News, your line is now open.

Robert Lowes: Thanks. Thanks for taking my question. I have a question about nomenclature. In regards to this collection of fluid associated with breast implants, is it called peri-implant seroma or persistent peri-implant seroma?

The - in these various FDA documents I see different ways this is phrased and I wasn't clear how the word persistent fit in. So is it persistent peri-implant seroma which is the technical name for this fluid collection or is it just peri-implant seroma?

William Maisel: So a fluid collection is called a seroma and when it occurs near an implant it is a peri-implant seroma. Now seromas can occur - they can come and go, if you will, for example, after a device is first put in; after a breast implant is first implanted, a woman might have some swelling and some fluid that goes away and that's part of the normal healing process.

But persistent means that long after a woman has healed she develops a seroma near her implant and it persists. It does not go away. That's a persistent peri-implant seroma.

Robert Lowes: Okay. Thank you very much.

Erica Jefferson: We have time for two more questions operator.

Coordinator: Thank you. Our next question comes from Alicia Mundy of Wall Street Journal.

Alicia Mundy: Thank you for taking my call. I think my question was almost completely answered but just to go back to 2006 when silicone implants came - were reapproved and came back on sale, was none of this information available at

the time or available in a way that FDA or reviewers or scientists had noticed since it had been developing and some of the - I think some of the reports on ALCL had been out by then.

William Maisel: So the vast majority of the data that we used in our analysis has developed since the approval of silicone breast implants. We provided a detailed table in the white paper that shows the dates of publication for all of the reports and you'll see that the vast majority of them occurred after 2006.

In addition, the adverse events information we have received is almost exclusively since the approval of the devices. So this information was not available at the time of the breast implant approvals.

Alicia Mundy: Thank you. That's very helpful. Thanks.

Coordinator: Our...

Erica Jefferson: Can we take our final question?

Coordinator: Yes, our last question comes from Virgil Dickson at FDA News.

Virgil Dickson: Hi. Thank you for taking my question. The first one was besides possible labeling changes, is there anything else that device makers may be required to do to address this adverse event?

William Maisel: So we've identified a possible association with ALCL and so we certainly are interested in collecting more information. We believe that this is more general than any one specific manufacturer and any one specific model or product and that's why we're working with the American Society for Plastic Surgeons to

develop a registry so that all patients with ALCL and breast implants can be tracked and we can learn more about the disease.

I also want to underscore that there are a couple of important messages we've talked about today. One is that women who have no symptoms and no abnormalities in their breast implants only require routine follow-up and we are not recommending prophylactic replacement for those patients.

The other is that we will be continuing to collect information and we'll certainly provide updates if we have additional information to provide to the public.

Virgil Dickson: How many device makers make these kind of products and can you say their names?

William Maisel: Sure, the information if you go to our breast implant Web site - if you go to the main FDA Web site and type in breast implants under the Search field you'll get to our main breast implants Web site.

Right now there are two manufacturers that have approved devices and they are Mentor and Allergan.

Virgil Dickson: Thank you.

Erica Jefferson: Thanks Virgil. This concludes today's media briefing. An audio replay will be available in about an hour and will be available for about 30 days. Please be sure to check FDA's online resources for breast implants on today's announcement.

Thank you for your participation and everybody stay dry.