COMMISSION OF INQUIRY
ON HORMONE RECEPTOR TESTING

BEFORE THE HONOURABLE JUSTICE CAMERON - COMMISSIONER

October 6, 2008

Appearances:

Bernard Coffey, Q.C. . . . . Commission Co-counsel
Sandra Chaytor, Q.C. . . . . Commission Co-counsel

Jackie Brazil, Q.C. . . . . Her Majesty in Right of NL

Peter Browne, Q.C./Jane Hennebury . . . Doctors Kara Laing et al

Daniel Simmons . . . . . Eastern Regional Integrated
. . . . . Health Authority

Laura Brocklehurst. . . . . Members of the Breast Cancer
. . . . . Testing Class Action

Mark Pike, Q.C. . . . . NL Medical Association
Jennifer Newbury . . . . . Canadian Cancer Society (NL Division)
Blair Pritchett. . . . . Central, Western and Labrador-Grenfell
Regional Integrated Health Authorities

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DR. ADAM BRUFSKY - SWORN

THE COMMISSIONER:
Q. Please be seated. Ms. Chaytor?
CHAYTOR, Q.C.:
Q. Good morning, Commissioner. The next witness is Dr. Adam Brufsky.
DR. ADAM BRUFSKY, SWORN, EXAMINATION BY SANDRA CHAYTOR, Q.C.
REGISTRAR:
Q. Would you please state and spell your complete name for the Commission?
DR. BRUFSKY:
A. Sure. Adam Matthew Brufsky, B-R-U-F-S-K-Y.
REGISTRAR:
Q. Thank you.
DR. BRUFSKY:
A. You're welcome.
CHAYTOR, Q.C.:
Q. Good morning, Dr. Brufsky.
DR. BRUFSKY:
A. Good morning.
CHAYTOR, Q.C.:
Q. Commissioner, we have a few new exhibits this morning, which I would ask please to have entered. They are P-3348, P-3349, P-3353 and P-3354.

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THE COMMISSIONER:

Q. Entered.

EXHIBITS ENTERED AND MARKED EXHIBITS P-3348 AND P- 3349

EXHIBITS ENTERED AND MARKED EXHIBITS P-3353 AND P- 3354

CHAYTOR, Q.C.:

Q. Thank you. If we could have, please, Registrar, P-3348? Doctor, this is your curriculum vitae. Perhaps if you could just take us through the highlights of your educational and professional background?

DR. BRUFSKY:

A. Sure.

CHAYTOR, Q.C.:

Q. And with emphasis, of course, on your experience related to breast cancer and breast cancer treatment.

DR. BRUFSKY:

A. Sure. I graduated from Dartmouth College, now this is 23 years ago, no, 25 years ago, was a MD PhD student at the University of Connecticut. I received a PhD simultaneously with my MD. My PhD was in developmental biology and molecular genetics. I then was an intern in internal medicine at Harvard Medical School, Brigham Women's Hospital. That was

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followed by a residency in internal medicine at Brigham Women's Hospital, and at Harvard Medical School, they had a program for people who have an MD and a PhD and it was called short tracking, and what happens is that if you know you're going to be doing research, you skip your final year of medical residency and you become a clinical fellow, which I did in medical oncology at the Dana-Farber Cancer Institute. I was a clinical fellow for one year and then I was a fellow in Bone Marrow Transplantation for about three months. I followed that with three years of research, both clinical and basic science research at Harvard Medical School.

In 1996, I was recruited to the University of Pittsburgh, initially to do prostate cancer actually, but within six months of my arrival there, most of the people who did breast cancer actually left, and so since I was a junior faculty, they asked me to become one of the breast cancer specialists and so I turned my practice and my research to breast cancer.

CHAYTOR, Q.C.:

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Q. And what year would that have been?

DR. BRUFSKY:

A. About 1997, late '96 actually, within six months of getting there, so that was '96. I was successful in starting a clinical trials program in breast cancer there, as well as a clinical research program and a clinical program in medical oncology in breast cancer. When I started, we were seeing 50 new patients a year with breast cancer. Currently -

CHAYTOR, Q.C.:

Q. I'm sorry, how many?

DR. BRUFSKY:

A. 50.

CHAYTOR, Q.C.:

Q. 50.

DR. BRUFSKY:

A. When I started. Currently, we see over 1, 000 new patients, just with breast cancer in medical oncology, just for medical oncology purposes. It's about 2,000 if you include the surgical cancers as well. We have approximately 10 to 20 clinical trials of novel therapies in breast cancer that occur at any one time and we put approximately 300

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women on cancer clinical trials yearly. My own particular practice there, well, because I founded this program, within a couple of years, they made me associate director and now I am currently director of the comprehensive breast cancer program for the University of Pittsburgh, which basically administratively manages the operations of our breast cancer program, as well as the scientific direction of the program. I personally see about 300 to 400 new breast cancer cases a year and my practice is almost entirely breast cancer.

CHAYTOR, Q.C.:

Q. Okay, thank you. Is your mouse working, Doctor?

DR. BRUFSKY:

A. No, my mouse is not working.

CHAYTOR, Q.C.:

Q. Mine is seized up as well. That's what I was just noticing here.

DR. BRUFSKY:

A. Oh, there we go, you can control it.

CHAYTOR, Q.C.:

Q. Every now and then we have a little technical issue.

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DR. BRUFSKY:
A. That's okay. You can control the mouse, if you want to just flip through it.
CHAYTOR, Q.C.:
Q. No, I can't either.
DR. BRUFSKY:
A. You can't either.
CHAYTOR, Q.C.:
Q. Our Registrar will help us.
THE COMMISSIONER:
Q. (Inaudible) slightly earlier version, allow you to do it.
CHAYTOR, Q.C.:
Q. So Doctor, in your studies though, in terms of your residency, you didn't have any particular sub-specialty or concentration in breast cancer?
DR. BRUFSKY:
A. No, I actually concentrated, in fellowship, in prostate cancer, and actually, I did work though in a laboratory on the estrogen receptor, believe it or not.
CHAYTOR, Q.C.:
Q. You worked in a laboratory?
DR. BRUFSKY:

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A. I was in--yes, so what happened when I was a clinical fellow, I took, after my one year of clinical fellowship in 19--this is 1995, no, actually earlier, I think it was '93/94 or '92/93, I then took three years to do research in a laboratory and that laboratory actually was a laboratory that studied various aspects of the estrogen receptor. I personally started the androgen receptor, trying to do a lot of the same research that was analogous to the estrogen receptor on the androgen receptor itself, trying to figure out various things. We were trying to figure out why estrogen binding to its receptor had different effects on different tissues and so my job was to try to do the same thing for the receptor for androgen. I had done some work on the cortisol receptor when I was a medical student, so it kind of fit with my interest.
CHAYTOR, Q.C.:
Q. So you would have spent, obviously then, a proportionate amount of time in the lab which other medical oncologists would not normally get in their residency?
DR. BRUFSKY:

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A. Correct. This is not a clinical lab. This is a research laboratory. Although in the U.S. most--to get Board certification by the American Board of Internal Medicine, you have to do at least 12 to 18 months of some form of research. So most medical oncologists, at least in the United States, have to have some experience with research techniques. It could be basic, it could be clinical. It really depends on the fellow.
CHAYTOR, Q.C.:
Q. And that would put them in a laboratory setting or have some knowledge -
DR. BRUFSKY:
A. Potentially. Probably, I would say currently in our program, we have 21 fellows at any one time in any of the three years total. I would say of the 21, about seven to eight actually are doing basic science research of some kind.
CHAYTOR, Q.C.:
Q. Okay, and I think our technical problem is solved, if you would like to take us through -
DR. BRUFSKY:
A. You can keep going, okay.
CHAYTOR, Q.C.:

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Q. I'll take you through and you can stop me at any point.
DR. BRUFSKY:
A. Sure.
CHAYTOR, Q.C.:
Q. So this indicated that you are, as you say, now the director of academic medical oncology.
DR. BRUFSKY:
A. Yeah, so what happened also is that I was--we integrated a large private practice into our academic practice about five years ago and I was very involved in that, and after that, I became associate chief of the division of hematology oncology at the University of Pittsburgh and so that's a position where I'm responsible for the clinical and financial direction of 26 medical oncologists.
CHAYTOR, Q.C.:
Q. Okay, and then is there anything in terms of your--you have a number of publications.
DR. BRUFSKY:
A. Yeah, most of the--I have--well, this is actually an order version of my CV. I have right now about 54 to--about 55 to 60 publications and the vast majority of them are

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in breast cancer related topics.
CHAYTOR, Q.C.:
Q. Okay.
DR. BRUFSKY:
A. Although some of my earlier work was in glucocorticoid receptors and prostate cancer. After about, I would say 1998, 1999, the vast majority of my publications are on breast cancer.
CHAYTOR, Q.C.:
Q. Okay. If we look at page 34 of the exhibit, flip you through here.
DR. BRUFSKY:
A. You're just going through a number of clinical trials.
CHAYTOR, Q.C.:
Q. Yes, okay, these are clinical trials that you've been involved in, okay, and at page 34, we see a number of invited lectures and I think this goes on for -
DR. BRUFSKY:
A. Currently, I think there's about 180. I don't know how much are on there.
CHAYTOR, Q.C.:
Q. 180 or so there.

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DR. BRUFSKY:
A. Yeah.
CHAYTOR, Q.C.:
Q. And a number of those appear to be tumour board and oncology grand rounds. Perhaps you could just explain to the Commissioner what this section of your resume is all about?
DR. BRUFSKY:
A. So generally, there are several things that happen. I can be giving an invited lecture on a topic in breast cancer or I could actually be invited to a tumour conference, a multi-disciplinary conference where there are medical oncologists, pathologists, surgeons, radiation therapists, radiologists, some of the support staff, where cases are presented and I discuss them and discuss the current treatment of those particular cases. There's a number of those tumour boards in there.
CHAYTOR, Q.C.:
Q. Okay, and so for example, the first one is a tumour board in -
DR. BRUFSKY:
A. Right, that was when I was first recruited. That was prostate cancer.

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CHAYTOR, Q.C.:
Q. Back in 1996.
DR. BRUFSKY:
A. Correct, but there are other tumour boards that are later on that are breast cancer.
CHAYTOR, Q.C.:
Q. Okay.
DR. BRUFSKY:
A. Like number 19, for example.
CHAYTOR, Q.C.:
Q. And then you have, for example, at 19, yes, you have metastatic breast cancer therapy.
DR. BRUFSKY:
A. Correct.
CHAYTOR, Q.C.:
Q. Number 22, we have Grand Rounds at St. Joseph's Hospital, Burbank, California, Beyond Tamoxifen. Perhaps you could just tell us what this was about. This is October 1998.
DR. BRUFSKY:
A. That was a long time ago. It's ten years ago. But at that time, there was a lot of interest in the new class of drugs aromatase inhibitors and I had done some work on that. I know that you have had prior witnesses that have talked

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a little bit about aromatase inhibitors, but literally, that was right about the time where aromatase inhibitors were starting to enter clinical practice. As an expert in aromatase inhibitor therapy, the vast majority of my talk involved aromatase inhibitors and their use, both in prevention of breast cancer, which is a hot topic currently, as well treatment of metastatic breast cancer.
CHAYTOR, Q.C.:
Q. Okay, and then it continues on. You have, for example, number 33. You have Grand Rounds Highland Hospital, Rochester, New York, Advances in the Treatment of Metastatic Breast Cancer and that's about a year later.
DR. BRUFSKY:
A. Yeah, and again, a lot of that has not only to do with the hormonal therapy of metastatic breast cancer, but various novel therapies. Over the years, one of the things that I have sub-sub-specialized in is the treatment of metastatic breast cancer. I've been involved in most of the major clinical trials in North America in metastatic breast cancer, a variety of different therapies, and clinically, my

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experience, I have probably one of the largest practices in metastatic breast cancer in North America, and as a result, you know, people ask me to talk about my experience and my involvement in a lot of clinical trials.

CHAYTOR, Q.C.:

Q. Okay, and number 54, it's Grand Rounds and this one is in Allentown, Pennsylvannia.

DR. BRUFSKY:

A. Yeah.

CHAYTOR, Q.C.:

Q. Adjuvant Therapy for Breast Cancer in the year 2001.

DR. BRUFSKY:

A. Correct.

CHAYTOR, Q.C.:

Q. And what do you mean by Grand Rounds? What's that, in your world?

DR. BRUFSKY:

A. So Grand Rounds is the entire hospital. So there are oncology grand rounds. There are medical grand rounds. So it's usually a conference at eight a.m. or lunch time, depending on when people can get their food tends to be a good inducement, and we tend to-

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-it tends to be, in the case of medical grand rounds, the entire medical staff of internists generally, surgeons occasionally. Oncology grand rounds are more the multi-disciplinary staff involved in the treatment of cancer.

CHAYTOR, Q.C.:

Q. Okay, and you would be invited to speak or present at grand rounds throughout--we're seeing different places here certainly within the United States.

DR. BRUFSKY:

A. Correct.

CHAYTOR, Q.C.:

Q. And number 61, Grand Rounds, the Medical Centre at Beaver, Pennsylvannia, Hormonal Therapy of Breast Cancer, and then we're up to the year 2002.

DR. BRUFSKY:

A. Correct. Around that time, we were talking about the trials comparing Tamoxifen to aromatase inhibitors and how long to use both therapies. Into the early part of the decade, it was a very contentious topic.

CHAYTOR, Q.C.:

Q. Okay, and again, then we see in number 77,

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Tumour Board, Jefferson Regional Medical Centre, Pittsburgh, Breast Cancer Adjuvant Treatment, and this is then a year later, October 16th, 2003.

DR. BRUFSKY:

A. Yes.

CHAYTOR, Q.C.:

Q. And in January then of 2004, you're at Tumour Board in State University New York, Stonybrook New York, and this refers to the San Antonio Breast Cancer Symposium updated January 22nd, 2004.

DR. BRUFSKY:

A. So what that is, is again, what a lot of hospitals and medical programs around the United States like is the perspective of an expert on the major medical meetings, and the San Antonio Breast Symposium is one of the two major medical meetings involved with breast cancer yearly. There's American Society of Clinical Oncology, which is usually in late May or early June, and then the San Antonio Breast Symposium which is usually in mid December, and what a lot of people do is they have an expert come and comment on the

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research that they felt was important, and that's what that was involved with.

CHAYTOR, Q.C.:

Q. Okay. So you would be invited then after the San Antonio Symposium?

DR. BRUFSKY:

A. Correct, to summarize various abstracts and presentations at the Symposium, yes.

CHAYTOR, Q.C.:

Q. And if we look at around 155, we see San Antonio Breast Cancer Conference. So is this your attendance at the conference?

DR. BRUFSKY:

A. No, I attend the conference also, and that's more in the abstract section of my CV. I usually present or my group presents at least four to five abstracts every year at San Antonio and about four to five at ASCO on various topics.

CHAYTOR, Q.C.:

Q. Okay, yes, and this is, you're right, this is the abstract section. So you would actually be presenting annually at that Symposium?

DR. BRUFSKY:

A. Yes, at both ASCO and San Antonio, as well as

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other meetings around the world.
CHAYTOR, Q.C.:
Q. And in terms of the use of tumour boards, tumour board rounds and oncology rounds within your institution, are you able to say what importance or significance that has in terms of a teaching tool and a tool for communication within your discipline?
DR. BRUFSKY:
A. Oncology grand rounds we have, I mean, I'll just describe how they work. We have oncology grand rounds for all of the oncologists, which are held weekly on a Wednesday morning at eight a.m., and those are usually outside speakers that come in, just like I have come in to there. In fact, we often do a trade. You know, I'll give a talk at one institution and they'll come and give a talk at my institution, but we--it's generally an educational session on some important topic, a review of some aspect of oncology. We have a weekly specific breast cancer tumour board and cancer conference, and at that, we not only--that generally is to review perspectively our own cases, which is a little bit different,

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and we educate ourselves around those particular cases.
CHAYTOR, Q.C.:
Q. And is that multi-disciplinary?
DR. BRUFSKY:
A. It is. So it involves all the members of the breast cancer team.
CHAYTOR, Q.C.:
Q. Which would include pathologists as well?
DR. BRUFSKY:
A. Pathologists, medical oncologists, radiation therapists, surgeons, genetics, genetic counsellors, pathology techs. I'm trying to think of--just about anybody you would expect that would be involved in a cancer activity. Social workers, that sort of thing.
CHAYTOR, Q.C.:
Q. And would that--would every new patient go through then your tumour board rounds?
DR. BRUFSKY:
A. It used to be that way, and in fact, the reason we have these and we have it for a number of different reasons, but in the United States, most or most big cancer programs are accredited by the American College of Surgeons

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Commission on Cancer or the Council on Cancer, and there are specific requirements that you have to have that are reviewed by the Commission every three years. So you're reviewed every three years by the Commission. One of those requirements is to have a multi-disciplinary panel review at least ten percent of all of your analytic cases for that year. It used to be that we tried to review every case, but -
CHAYTOR, Q.C.:
Q. And why has that changed?
DR. BRUFSKY:
A. Because we've become very busy.
CHAYTOR, Q.C.:
Q. You've gone from 50 to 1,000.
DR. BRUFSKY:
A. 50 to 1,000, so because of that, we obviously can't review every case or we'd there for days at a time. The conference is one hour a week or one and a half hours every week, on a Thursday afternoon, and so we've actually changed it to review cases that make important points about various aspects of our practice.
CHAYTOR, Q.C.:

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Q. So in a centre such as we have here where there'd be approximately 350 new cases a year, the multi-disciplinary approach to care and treatment, that could probably happen if you had those kinds of numbers?
DR. BRUFSKY:
A. Absolutely. I mean, I think that at a minimum, you could review--to meet the Commission on Cancer's recommendations, you could review 30 or 35. That would actually meet that recommendation, as long as you review ten percent of the cases.
CHAYTOR, Q.C.:
Q. And is this, is part of the purpose of your review of the case to determine treatment options as well?
DR. BRUFSKY:
A. Yes, absolutely. In fact, the purpose of the review is to determine treatment options on each patient, to review any discrepancies that may have come up, any questions any member of the treatment team may have, yes.
CHAYTOR, Q.C.:
Q. And if we could go, please, Registrar, to page 17? And I was noticing here in your CV, and

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again, this talks about abstracts. Number 66 and 67 are abstracts which have been presented at St. Gallen's?

DR. BRUFSKY:

A. Correct.

CHAYTOR, Q.C.:

Q. Okay, and perhaps you could just tell us about that, your involvement with St. Gallen's?

DR. BRUFSKY:

A. So my involvement, St. Gallen's, so what the St. Gallen's conference does is that every other year, they meet, they review the current treatment of breast cancer, review all the state-of-the-art treatment and there are abstracts that discuss this treatment, both in oral presentations and poster presentations. These are actually two poster presentations at St. Gallen's. And then at the end, there's a group of investigators that meet. It's an international panel of experts that meets, reviews the literature and then comes up with recommendations that last two years.

CHAYTOR, Q.C.:

Q. Okay.

DR. BRUFSKY:

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A. And so this research was actually on side effects of aromatase inhibitors. I've been involved--I'm the principal investigator of a national trial or an international trial looking at drugs called bisphosphonates that prevent bone loss from aromatase inhibitors, which is the major side effect of aromatase inhibitors, and so it's just presenting this data. And this was actually presented at the St. Gallen's Conference, for the reason of trying to figure out whether we should be recommending bisphosphonates as therapy to prevent bone lost from aromatase inhibitors, whether that should have been part of the recommendation of the St. Gallen's conference in 2007. It probably--it was not, in 2009 it probably will be, but in 2007, the evidence wasn't quite there yet.

CHAYTOR, Q.C.:

Q. Okay, and in terms of the Commissioner has heard of consensus statements that come out of St. Gallen's.

DR. BRUFSKY:

A. Correct.

CHAYTOR, Q.C.:

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Q. And how would you and your colleagues then stay apprised or become aware of those consensus statements?

DR. BRUFSKY:

A. They're published and they're disseminated through the medical literature. So the St. Gallen's Conference, I believe I have the meeting highlights here. This is one particular journal, which I think is Annals of Oncology, which is a European journal, and they are disseminated through that and generally, we would talk about them in our--in our particular breast cancer conference, we would talk about them. We'd actually have a session where we would go over the St. Gallen's recommendations. We would present at patient or two and say "well, how do the new St. Gallen's recommendations apply to this particular patient." So we would actually go through this in our breast cancer conference.

CHAYTOR, Q.C.:

Q. And would you automatically adopt that then as your practice or would it be done through -

DR. BRUFSKY:

A. Not necessarily. I mean, I think we

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critically evaluate them. I think we, at least, believe, in our institution, that we have enough independent experience that we can kind of evaluate these consensus statements, which really are no more than an expert panel, based on their own clinical experience and their own evaluation of the literature. We can base their recommendations against ours. Generally we adopt them, generally we do. I mean, they're very general. The St. Gallen's criteria are generally fairly general. They leave a lot of leeway for adoption.

CHAYTOR, Q.C.:

Q. Okay, and other than--other than your weekly tumour board rounds, what other interaction would you have in the normal course with pathologists?

DR. BRUFSKY:

A. The general interaction I have with pathologists, we don't have a formal mortality, morbidity conference. We tend to use our breast conference for this sort of thing, if there is some sort of complication of a procedure. Thankfully, in the breast cancer business there are very few major

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surgical complications that need M and M review. It's more discrepancies in pathology, that sort of thing, discrepancies in radiology, system issues that we have to deal with in these conferences. But in terms of my interaction with pathologists, I'm very fortunate in that the pathologists are right around the corner, they're on the same floor as my clinic. So I'm on the fourth floor, the pathologist lab is literally on the fourth floor, as well. When I see a new patient, for example, I will obviously as a medical oncologist look at the pathology report and if there is something on the report that doesn't make sense to me or just doesn't seem to--I have questions about, I will call the pathologist on the phone. And generally there will be a pathologist on call at all times. So if the original pathologist who hasn't signed out that case is not there, someone else will be there to discuss it with.

CHAYTOR, Q.C.:

Q. Okay, and would you also then if there is an unexpected finding on the pathology report, something that appears to be inconsistent with

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either the diagnosis or your understanding of the case, is that something then you would bring up at your weekly tumour board rounds?

DR. BRUFSKY:

A. Yes, yes, we would.

CHAYTOR, Q.C.:

Q. And discuss as a group?

DR. BRUFSKY:

A. Yes, yes.

CHAYTOR, Q.C.:

Q. And other than the--obviously you attend symposiums and conferences. How else do you and your colleagues keep apprised and current in your field and the changes that happen at a fairly rapid pace?

DR. BRUFSKY:

A. So with the internet it's--I mean, everybody has their own way of doing it. Generally a lot of us do it through the internet, so, you know, we'll review abstracts that come out of the major meetings, we'll review the abstracts or scan--most of the major journals are delivered to us via e-mail, so the vast majority of us will get our information that way.

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CHAYTOR, Q.C.:

Q. Okay. And, Doctor, I don't know if there is anything else I've--that's about what I was going to cover in your CV, unless there's anything else that you wanted to point out or speak to?

DR. BRUFSKY:

A. No.

CHAYTOR, Q.C.:

Q. Okay. At the time then in the 1992, I guess it was, to '95 when you did your medical oncology residency, your fellow in medical oncology then in Boston, what method was used for carrying out ER/PR testing at that point in time?

DR. BRUFSKY:

A. At the time it was the Ligand binding assay. And I know that because I had to do it myself on samples in the laboratory, so -

CHAYTOR, Q.C.:

Q. And when was your first experience then with the IHC method?

DR. BRUFSKY:

A. IHC method really was not--I mean, it was beginning to be developed toward the late

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'90s. So really kind of when I was already an attending, I would have to say. I mean, the Ligand binding assays were used maybe for two years, again, '96, '97, '98, probably '98, '99, that area, we first started doing immunohistochemistry.

CHAYTOR, Q.C.:

Q. Okay, and at that point in time, in 1998, 1999 when your first introduction to the IHC method, what was being utilized then as the cutoff for positivity?

DR. BRUFSKY:

A. We generally used ten percent. I don't recall ever using 30 percent or any other number.

CHAYTOR, Q.C.:

Q. Okay. And we've heard, of course, the 30 percent number here.

DR. BRUFSKY:

A. Correct.

CHAYTOR, Q.C.:

Q. Are you aware of any literature in terms of where that 30 percent -

DR. BRUFSKY:

A. Actually, no. As a medical oncologist, I'm not.

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CHAYTOR, Q.C.:
Q. Okay. What--perhaps you could just tell us briefly, and the Commissioner has heard some evidence on this, but it might be helpful to hear from you about the significance of ER/PR testing in your practice?
DR. BRUFSKY:
A. Well, it's an incredibly important test because it really speaks to one of the most effective therapies we have for breast cancer. Anti-hormonal therapy is probably the most effective therapy we have for breast cancer. And knowing whether a woman has estrogen and progesterone responsive breast cancer is extremely important in knowing what therapy to design for her one way or the other.
CHAYTOR, Q.C.:
Q. Okay, and so what criteria would you use to determine if a patient is a candidate for anti-hormonal therapy?
DR. BRUFSKY:
A. Well, presently in 2008 I would use ten percent of the cells being positive. Now, there's been a lot of debate over the last several years of several consensus panels and

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I know, I think you've heard evidence prior to me about the use of one to ten percent. I think that's somewhat controversial. And I think amongst my colleagues some use it as low as one percent. I personally do not. I do not believe that there is a enough responsiveness in someone who has estrogen receptor levels less than ten percent to make hormone therapy worthwhile.
CHAYTOR, Q.C.:
Q. Okay, and in terms of other criteria that you would look at or other things peculiar to your patient, obviously you put a lot of reliance on the outcome in the hormone receptor test, but what other criteria do you -
DR. BRUFSKY:
A. So in other words, though--I kind of understand where this question is going. So what factors do I used to determine -
CHAYTOR, Q.C.:
Q. Yeah.
DR. BRUFSKY:
A. - what therapy a woman has?
CHAYTOR, Q.C.:
Q. Yes.

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DR. BRUFSKY:
A. So -
CHAYTOR, Q.C.:
Q. In terms of hormone therapy.
DR. BRUFSKY:
A. Versus a hormone therapy?
CHAYTOR, Q.C.:
Q. Yes.
DR. BRUFSKY:
A. The biggest--I mean, I think that there are a lot of factors that go into what therapy a woman has. And I'll tell you kind of the pre 2006 way of doing it and then the post 2006 way of doing it. Before, in 2006, 2007 there was a test called oncotype DX that I'll talk about a little bit in a minute that I think has changed things a little bit. But generally what we do when a woman comes to us, we look at the size of the cancer, which is basically it's T stage, the number of lymph nodes, which is the N stage, and then whether it's metastatic or not outside of the breast in regional lymph nodes. Those are very important. We look at the age of the patient and whether she's pre and whether she's pre or

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post menopausal, whether there are any co-morbidities, that is, whether the woman is fairly sick looking or fairly healthy looking and then put it all together to come up with a treatment plan. Generally the big question that we have in a woman who is estrogen receptor positive that is sensitive to hormonal therapy is whether she should get chemotherapy in addition to hormonal therapy. I think most people will treat women now, no matter what the tumour size is, as long as the estrogen receptors are greater than ten percent. I think the vast majority of oncologists in the United States and in my practice would give somebody either Tamoxifen in the case of an estrogen receptor positive in a woman who's pre-menopausal or an Aromatase inhibitor such as Arimidex in the case of someone who's postmenopausal. However, the art of oncology, to some degree, until very recently, was trying to figure out who needs chemotherapy in addition to that. Now, to help us out there has been a new test that's been developed called oncotype DX that's widely available in the United States,

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I'm not sure how available it is in Canada right now. But what that is is that we take three paraffin slices, ten micro slices of the tumour and send it to a company in California, Genomic Health, and we look at the expression. There is a way of actually looking at RNA in paraffin embedded tissues that they've developed and actually optimized it and developed it. And they look at the expression of 16 genes. And statistically they have come up with a model where they can total that up into one number called a recurrence score. If that recurrence score is greater than 30 based on some retrospective studies that they've done, generally women will benefit from chemotherapy. If it's less than 30, she may not benefit as much. And so there's actually a debate about what cutoff to use and whatnot. But oncotype DX, at least for lymph node negative breast cancer, is rapidly becoming a very common, commonly used assay to try to figure out whether we should be using chemotherapy in addition to hormonal therapy.

CHAYTOR, Q.C.:

Q. Okay.

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DR. BRUFSKY:

A. So these are the sort of things, at least the more recent things that are being done now.

CHAYTOR, Q.C.:

Q. Okay, and how important is the degree of positivity or the percent of positivity -

DR. BRUFSKY:

A. Extremely. I mean, I think that generally it used to be that our pathologists did not report degree of positivity. We've gone through cycles of this.

CHAYTOR, Q.C.:

Q. Okay. And when did that change, when -

DR. BRUFSKY:

A. It kind of, there was a period where they reported it, then--they've always reported percentages, but now they've gotten a little bit more detailed than that and I'm sure Dr. Dabbs may have talked about this, but they report something called and H score.

CHAYTOR, Q.C.:

Q. Yes, he told us that.

DR. BRUFSKY:

A. Which is kind of how many cells stain, for example, like there's one plus, two plus and three plus and a H score is generally a single number that tells us how many score--how many cells have stained with each intensity. And generally the H score is fairly important to us. I think that Dr. Dabbs, who is a world class immunohistochemist is trying to get us to move away from the oncotype DX test, which he thinks is redundant, and so he reports to us in great detail the degree of estrogen receptor positivity. And we believe that if a patient has a very estrogen receptor positive tumour, her response to chemotherapy will likely be less and her response to hormonal therapy will likely be more. But in terms of a cutoff for the use of the therapy, I'd still say we us H scores, but still, if I don't have an H score, ten percent ER positivity is generally what I use.

CHAYTOR, Q.C.:

Q. Okay, and but you would expect a patient who is 80 percent ER positive to respond better to anti-hormonal therapy than a patient who is 20 percent?

DR. BRUFSKY:

A. Potentially. I think the better way to say it is I would expect a woman who has an estrogen receptor positive score, say, a H score of 300, which is as high as it can go, and maybe have other characteristics of her cancer maybe a lower tumour grade, a smaller size to not respond as well to chemo. I think it's--I would say it's the opposite of that. As opposed to the absolute response of hormonal therapy, it's hard to know whether a woman who is 20 percent ER responds better than a woman who is 80 percent ER. I think there is some literature that could go back that way. I look at it as women who are very high, who have tumours that are very high ER generally will not have as good a response to chemotherapy.

CHAYTOR, Q.C.:

Q. Is there also a difference in how a patient will respond to hormonal therapy depending if they're ER and PR positive versus one or the other?

DR. BRUFSKY:

A. That's a good question. And I think that it used to be that we thought, and there is some literature I think has been presented here

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already, looking back to the website that you have, where that appear to be the case. However, I have in one of my exhibits here recent data from the San Antonio Breast Symposium that was presented by Sir. Richard Peto a year ago, almost a year ago at the San Antonio 2000 Breast Symposium. And I don't know what exhibit you called that.

CHAYTOR, Q.C.:

Q. We have the--3349, I believe.

DR. BRUFSKY:

A. Yeah, and so just going through this really briefly, and really the important part of this, I think, is -

CHAYTOR, Q.C.:

Q. And you can just take us through if you wish in the--on the exhibit with your mouse, Doctor.

DR. BRUFSKY:

A. Sure, I can do that. That would be easier to do. Let's make sure my mouse is working.

CHAYTOR, Q.C.:

Q. Is your mouse working?

DR. BRUFSKY:

A. Hold on, I think so.

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CHAYTOR, Q.C.:

Q. Okay, that's fine.

DR. BRUFSKY:

A. Either--there we go.

CHAYTOR, Q.C.:

Q. I'll take you through then.

DR. BRUFSKY:

A. This just shows that mortality is decreased. You can go--you can pass through this slide.

CHAYTOR, Q.C.:

Q. Okay.

DR. BRUFSKY:

A. And you don't need that part either. So these are trials, actually, of five years of Tamoxifen. So what the meta-analysis is, you may--I think Dr. Laing discussed this a little bit in her presentation, looking through her transcript, but there is what's called the meta-analysis that Dr. Peto and his colleagues around the world have come up with, and what they do is every five years or so they look at the results of all the clinical trials that have been done, roughly, in breast cancer of a certain type. And so this is the important thing on page 5, these are trials of estrogen-

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-of Tamoxifen versus no Tamoxifen. And these are on women who are estrogen receptor negative and progesterone receptor negative. And what you can see here is that there's no benefit to Tamoxifen. The ten-year recurrence rate is about 28 to 29 percent, as you can see on the left-hand side of the panel. And then the patients that are ER poor, PR positive, you can see here there's no difference either. So progesterone receptor by itself does not appear to be a predictive factor for benefit to Tamoxifen. Let me go back one here. Oh, actually, let me go up one. Now, looking at it a different way, women--if you look at the right-hand side of these, in the ten year, this is now the ten year recurrence re survival, what you can see here that if you're estrogen receptor positive, progesterone receptor positive, your recurrence rate is 38 percent, but it's 25 percent with Tamoxifen. But if you now look at the left-hand panel, the estrogen receptor positive, progesterone receptor negative patient population, the benefit is about the same. The control group has a 44 percent recurrence rate versus 29

Page 44

percent when given Tamoxifen. So if you're ER positive, PR positive, your overall--your survival rates are a little bit better, but the absolute benefit you get from Tamoxifen is the same. So most of the predictive effects of ER and PR come from ER, not PR. At least that's my interpretation of this. Now, again -

CHAYTOR, Q.C.:

Q. And that would have been patients with primary disease?

DR. BRUFSKY:

A. This is all patients with primary breast cancer.

CHAYTOR, Q.C.:

Q. Yes.

DR. BRUFSKY:

A. We have very little date from meta-analysis. We have one meta-analysis, actually, from 1998 that was done with metastatic breast cancer, but that's all with chemotherapy. There's very little hormonal therapy meta-analysis. There's one, but it's not divided based on ER/PR status and content. So the bottom line is that PR at least for the adjuvant setting,

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for prevention of breast cancer recurrence does not appear to be a predictive factor and it's a minor prognostic factor, at least in my opinion. This is still fairly new data. In fact, it's not been published yet, but it will probably be published. The meta-analysis this is based on will likely be published in the next year.

CHAYTOR, Q.C.:

Q. Okay. And well then perhaps you can discuss for us the use of hormonal therapy in the adjuvant setting versus in the metastatic setting?

DR. BRUFSKY:

A. Sure, okay.

CHAYTOR, Q.C.:

Q. I'm sorry, is there anything else, though, on this?

DR. BRUFSKY:

A. No, no, no, no, no, this doesn't have that on it. I was just going through to see what -

CHAYTOR, Q.C.:

Q. Is there anything else, though, in this before we leave it?

DR. BRUFSKY:

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A. No, no, no. This is fine. I mean, basically I could just show you just a few more things.

CHAYTOR, Q.C.:

Q. Yeah, sure, take us through it, yeah.

DR. BRUFSKY:

A. Again, just ER positive patients are the ones that, it just shows you breast cancer mortality on page 8. Just go back to page 7. Now, this is recurrence. Just showing you that most of the benefit really ER is a good predictor. And that's pretty much it from this, these slides. The difference between metastatic treatment and adjuvant treatment. Adjuvant treatment, what you're trying to do is you're making an assumption that there's micro metastatic disease throughout someone's body, based on the characteristics of her primary tumour that you can't see by any imagining technology. And the idea behind adjuvant hormonal therapy is to suppress those micro metastatic deposits so they can either be eliminated by immune system or just never grow to a case where they will cause the patient problems. In metastatic breast cancer generally clinically detectable metastatic

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breast cancer has tumour deposits in the order of a billion cells or more and it is next--at least with the current thinking, it's thought that it's not possible to eliminate every single one of those cells that have escaped beyond the lymph nodes, the regional lymph nodes. In that case the goals of metastatic hormonal therapy are mostly to delay progression of the disease, not so much as be palliative, that is, it is to relieve symptoms, but it's also to delay progression of symptoms. It turns out that there is a little bit of data that suggests there's probably a small survival benefit to women in the metastatic setting getting inter-hormonal therapy, but it's small. The goals generally are to delay progression of the disease and prevent symptoms in someone who has metastatic breast cancer.

CHAYTOR, Q.C.:

Q. So to try and get more symptom-free time for the patient?

DR. BRUFSKY:

A. Correct. It's we call the symptom-free interval.

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CHAYTOR, Q.C.:

Q. Yes.

DR. BRUFSKY:

A. That's right.

CHAYTOR, Q.C.:

Q. And if we could look, please, at P-3353?

DR. BRUFSKY:

A. Yeah, this is actually relevant. This was actually presented last week in the New England Journal of Medicine, this particular case. And this is actually an example of several things. A multidisciplinary case conference, number one, and number two, the discussion about a particular patient in a multidisciplinary conference. And this particular woman, who was 47, who was peri-menopausal or pre-menopausal had a breast lump with a lesion in her spine that was biopsied and found to be estrogen receptor positive, and that's actually shown on the next page. You can see how the staining of these cells actually works, if you haven't seen it in this-I don't know -

CHAYTOR, Q.C.:

Q. Okay.

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DR. BRUFSKY:
A. - controlling the mouse here. This is on page 4, I believe, of the exhibit.
CHAYTOR, Q.C.:
Q. Okay, just scroll down there.
DR. BRUFSKY:
A. And this is the spinal biopsy just showing the lesion and the fact that it's estrogen receptor positive. I think that's panel D.
CHAYTOR, Q.C.:
Q. Panel D, so this -
DR. BRUFSKY:
A. That just shows how the immunohistochemical stain is done. And this is very positive. And so this is a woman who actually was treated, the bottom line to this case is that this woman had a little bit of back pain and was treated with anti-hormonal therapy. She was treated with LHRH agonist and that's to put her in menopause, that suppresses her estrogen levels, and was given, I believe, Tamoxifen, as well, in combination. So this is how this woman was treated. Now, it's interesting in that in oncology, at least in breast cancer oncology, the thought was that

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we wouldn't treat someone locally, so we would not treat her primary tumour because the cancer had already escaped and spread to the lymph nodes, spread to the bone. But it turns out that hormonal therapy has done such a good job, as we've found we've gotten better and better at figuring out who we treat, that in a woman like this her survival could be five years or longer and that it then becomes important for us to consider treating her local cancer. And, in fact, that's what a lot of the discussion of this case is about, discussing whether they should treat her local cancer or not. In fact, what happened to this woman and the conclusion of this case is that she was treated with hormonal therapy and two years later she presented with a new cancer in her other breast. So new primary cancers do become an issue. In fact, this is really at the cutting edge of breast oncology right now is in women with very little metastatic disease, are they essentially cured of their disease or do they live long enough to get new cancers and should we do screening - should we be screening these women now for new primary

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breast cancers that may affect them in the future. So breast cancer oncology is changing continuously, at least the thinking about how to manage women like this.
CHAYTOR, Q.C.:
Q. And in terms of the treatment of pre-menopausal women, was there some change in the thinking in the late 1990s regarding the hormonal treatment of pre-menopausal women?
DR. BRUFSKY:
A. No, I think - well, in the adjuvant setting, yes. I think in the adjuvant setting, it was felt that at least until 2000 - actually, there was a consensus conference at the National Cancer Institute, but until 2000, it was felt that pre-menopausal women should not be treated in the adjuvant setting with hormonal therapy. It was about 2000 when I think that changed. It was the '98 or the 2000 consensus conference. In the late 1990s, there was a conference that felt there was enough benefit from drugs like Tamoxifen, for example, in these women. After that point, most women began to be treated--pre-menopausal women began to be treated with Tamoxifen.

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CHAYTOR, Q.C.:
Q. Perhaps you can tell us then the benefits of Tamoxifen. For example, in this case, as you're aware, 2005 is when the look back began in terms of looking at patients who had been diagnosed, and the look back went all the way back to 1997 and some of those patients who, in fact, were diagnosed in 1997, then in 2005 and 2006 were actually offered Tamoxifen or some related treatment. Does the benefit of hormonal therapy diminish the further in time you are removed from diagnosis?
DR. BRUFSKY:
A. That's an interesting question, and I think that the initial thinking was, yes, that the longer you were away from diagnosis, specifically in the adjuvant setting, the less benefit you would get, and I think that generally still is true, so - there still is benefit, however, and I know you have an article here that, I think, was Exhibit 2582.
CHAYTOR, Q.C.:
Q. Okay, we can bring that up, please.
DR. BRUFSKY:
A. That you presented previously about that, and

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I think that, in and of itself, is with Tamoxifen. It's an old study, but there is newer data actually from a Canadian trial, MA 17, that was done by the NCI of Canada, and in that trial women were on Tamoxifen for five years and they then were randomized to receive Letrozole, an aromatase inhibitor, or no therapy. These were post-menopausal women, and after two and a half years the benefit was so substantial for the women receiving Letrozole that the trial was discontinued. They had an anonymous committee that looked at the trial, realized there was a huge benefit, it was unethical to continue and they stopped the trial. At that point, there was a cohort of women, about 2500, who had not received any hormonal therapy for two years. They were allowed to receive at their benefit either Letrozole or no Letrozole, and it turns out about two-thirds of those women, so about 1600 women received Letrozole, 600 chose not to, and those women were then compared and it turns out that there still was a substantial benefit, a prevention of new primary breast cancers, a prevention of recurrence that

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occurred in the women who had no therapy for two years and then suddenly went back on -or two to three years, and then suddenly went back on Letrozole. So the bottom line to this is that there is benefit of not only extended hormonal therapy, but of reinstitution of hormonal therapy if you haven't had it for a few years. That's what that trial shows us. The one question we can't answer is whether that benefit is the same as if someone started that therapy from scratch and continued it.

CHAYTOR, Q.C.:

Q. Yes, in that trial -

DR. BRUFSKY:

A. I don't think anybody knows the answer to that yet.

CHAYTOR, Q.C.:

Q. In that trial, they had been on it, and stopped, and then went back to it?

DR. BRUFSKY:

A. Correct, yes. So we don't know whether the benefits are the same, and I think people are trying to figure out ways of potentially analysing that data to get at that answer, but right now we don't have that answer. We know

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there is a benefit, we just don't know whether it's the same degree as if they had continued the therapy from the start.

CHAYTOR, Q.C.:

Q. We certainly have a class of those patients now here in Newfoundland and Labrador.

DR. BRUFSKY:

A. Correct.

CHAYTOR, Q.C.:

Q. Doctor, so in terms of the reduction of the risk of recurrence, are you able to say what percentage of patients tend to benefit from Tamoxifen?

DR. BRUFSKY:

A. Women who have an estrogen receptor - I think if I'm understanding correctly, women who have an estrogen receptor level of 10 percent or greater have at least a reduction in the risk of recurrence in proportional terms of about one-third to one-half. So if a woman walks in and we predict her risk of recurrence as 15 percent with no therapy at all, if she were to go on Tamoxifen, if she had estrogen receptor positive breast cancer, if she were to go on Tamoxifen for five years, her reduction and

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risk of recurrence would be about 5 to 7 percent in absolute terms.

CHAYTOR, Q.C.:

Q. And it depends, I guess, in the absent of benefit, depends on the risk?

DR. BRUFSKY:

A. Absolute benefit is determined by the absolute risk without a therapy, correct.

CHAYTOR, Q.C.:

Q. And this article, we'll just take you to the end here, 2582, page five. The conclusion in this particular - and again, as you say, this is dated, it's 1999, and accepted in March of 2000.

DR. BRUFSKY:

A. Right, this is a very - the conclusions are very similar to the MA-17 conclusions with Letrozole, which says basically that giving Tamoxifen several years after surgery, even if it's delayed by two or more years, is still of benefit.

CHAYTOR, Q.C.:

Q. Okay.

DR. BRUFSKY:

A. And again this is the only trial of its kind.

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There are no other studies like this that are out there. I mean, the only trials really that are out there now with Tamoxifen that are remaining are trials of five years versus ten, and even those trials are not designed very well. It's been very difficult to kind of figure out whether that data is useful or not, I guess, is a good word to use.

CHAYTOR, Q.C.:

Q. So in terms then of the benefits of the hormonal therapy, what are the potential effects of not having received the appropriate hormonal therapy at the time of diagnosis?

DR. BRUFSKY:

A. I would say a high risk of recurrence, specifically in that time that they were not receiving the hormonal therapy.

CHAYTOR, Q.C.:

Q. And could it be that patients may have received inappropriate therapy, for example, chemotherapy, that they may not have otherwise received?

DR. BRUFSKY:

A. Yes, I think that if someone came to me and had an estrogen receptor negative tumour, say,

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that was two centimetres in diameter and she was, say, 45 or 50 years old, I would give her chemotherapy. If she came to me and that tumour was strongly estrogen receptor positive, I may have had second thoughts on whether to give her chemo, yes.

CHAYTOR, Q.C.:

Q. And is there also - so there's an increased risk of recurrence?

DR. BRUFSKY:

A. Yes.

CHAYTOR, Q.C.:

Q. She may have received inappropriate therapy?

DR. BRUFSKY:

A. Correct.

CHAYTOR, Q.C.:

Q. Is there also an increased risk of death?

DR. BRUFSKY:

A. There is. I think that - again looking at these MED analysis figures, you can see actually if you want to go back to that exhibit, and I don't know what page it is.

CHAYTOR, Q.C.:

Q. Okay, that's P-3349. Thank you.

DR. BRUFSKY:

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A. If we want to go back to that, I can show you. You can actually see this in the MED analysis data.

CHAYTOR, Q.C.:

Q. No, this is not the right one, it's 3349. There we go.

DR. BRUFSKY:

A. Let me go back to page - I believe it's page eight. So five years of - look in the left hand panel, five years versus not, ER positive only breast cancer mortality. So at fifteen years, these are women who did not receive Tamoxifen - these were women who received Tamoxifen for five years versus those who didn't. There is an absolute benefit of a little under - 9.3 percent, you can see right on the slide, 9.3 percent at fifteen years. At five years, it's 12.9 versus 8.9. So it's about 3.3 percent at five years. So there are clear benefits in mortality, the women not getting Tamoxifen versus getting it.

CHAYTOR, Q.C.:

Q. And in a situation such as occurred here where there was quite a number of patients that ultimately ended up on hormonal therapy that

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weren't originally at the time of diagnosis, in that situation, would time be of the essence in introducing their hormonal therapy?

DR. BRUFSKY:

A. I think so. I mean, you know, I think that there would have been some women like who would have received benefit immediately, and there may have - again it depends on the individual cases, it's hard to know without knowing the exact particular instance of each patient because the absolute benefit is going to be different in these patients. It's really going to depend on the various characteristics of that particular patient, but in general there would likely have been some women who did not receive Tamoxifen who likely would have recurred having not received it and potentially have died.

CHAYTOR, Q.C.:

Q. And in terms of - would it be of particular concern for patients with metastatic disease that they have their treatment introduced then as quickly as possible once the error was discovered?

DR. BRUFSKY:

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A. Again that's a matter of debate, and I would have to say that there are oncologists who would say it doesn't matter if they're asymptomatic, that all the Tamoxifen is doing is preventing symptoms. However, there are other oncologists, and I probably fall in that camp, who would say the early introduced of Tamoxifen probably prevented these women from getting symptoms of their cancer for a number of months or years.

CHAYTOR, Q.C.:

Q. Okay. So for patients who have not had recurrence in their disease, those patients, could the effect of a - any of them, I guess, but if it's debatable in terms of metastatic, the effect of a further delay of weeks and perhaps months after the error has been detected in introducing then the appropriate treatment, could that have an effect?

DR. BRUFSKY:

A. I wouldn't say weeks. I would probably say more to months to years. I'd say that. You know, there's been a - again I think clearly getting hormonal therapy at any point, anti-hormonal therapy at any point in someone's

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disease process is a good thing, as we've seen, both for metastatic disease as well as adjuvant therapy. I think the sooner it's done, the closer to surgery, I think the better in the end of the day it will be for the patient, yes.

CHAYTOR, Q.C.:

Q. And so in terms of a delay of weeks, but when you get into months, two, three, four -

DR. BRUFSKY:

A. Weeks are probably not an issue. Months probably become more of an issue. I think our cutoff - generally in most clinical trials is what we've used, and we generally use eight to 12 weeks before initiating therapy. So that probably works out to two to three months.

CHAYTOR, Q.C.:

Q. Okay, and the potential then negative effects of receiving therapy such as chemotherapy that otherwise might not have warranted, what are the potential negative effects of that?

DR. BRUFSKY:

A. Well, obviously there's hair loss, but that is a cosmetic effect that generally is resolved. Obviously, it's not good for the woman having

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it at the time. More importantly, however, there is a tiny risk of Leukemia, probably less than .1 percent. For most of the chemotherapies there is a risk of infection. With anthracycline chemotherapy such as adriamycin or epirubicine, there is a small, but significant, probably less than 1 in 500 risk of heart damage, or in some rare cases heart failure. In the case of taxanes, like Taxol or Taxotere, there is some risk of neuropathy which can last upwards of two to three years, if not longer. Some nail changes, that sort of thing. So there are myriad side effects of chemotherapy that you can have.

CHAYTOR, Q.C.:

Q. Okay, and Doctor, is there any relationship between the aggressiveness of the cancer and one's receptor positivity?

DR. BRUFSKY:

A. Yes, generally, there's a general - there's a general relationship. The more aggressive a cancer or high grade it looks like under the microscope, the less estrogen receptor positives the cancers generally tend to be.

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CHAYTOR, Q.C.:

Q. Okay, and perhaps then you could just say a little more about the prognostic versus the predictive role of hormone receptor testing?

DR. BRUFSKY:

A. So predictive in that it predicts response to Tamoxifen. It's prognostic in that it tends to - it tends to prognosticate for slower growing tumours. In other words, when an oncologist goes in to see a patient, and again the Oncotype DX's that I talked about before is doing this more and more, but before the Oncotype DX is available, generally if someone comes in with a very high estrogen receptor content tumour, it's generally a slower growing lower grade tumour, which allows us to say to a woman you have a slower growing tumour, it is less - there is more things we can do for you, you know, maybe you don't need chemotherapy, we can treat you with Tamoxifen only, etc.

CHAYTOR, Q.C.:

Q. Okay, and can tumours evolve over time so that they use their hormone receptivity?

DR. BRUFSKY:

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A. Yes, and right now the current thinking is about 10 to 15 percent of breast cancers do that. What's really been very difficult, and, in fact, is one of the active areas that a lot of us are trying to push forward as research in breast cancer is that it's very difficult to harvest tissue from women once they've had metastatic disease. It's very difficult for me to ask a woman, gee, let me biopsy your liver, you know, or your lung or whatever, with a needle. We generally have to try to have accessible areas, say, in the skin, but even now we're getting better and better and the technology is getting better where we minimal morbidity we can actually now begin to biopsy some of these previously not as accessible areas like liver, like bone, like lung, and check to see whether the cells are estrogen receptor positive or not. It's interesting, I mean, I think that we don't even know - we don't even know, for example, if a woman has two different bone metastases, is one estrogen receptor positive and the other negative, if she has a liver and a bone metastasis, a liver and a bone metastasis, is

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the liver positive and the bone negative, we don't know the answers right now in oncology to these simple questions because really until very recently the technology to get these biopsies done in a very safe manner repetitively has not been here. So the short answer to your question is that probably 5 to 15 percent of all estrogen receptor positive cancers will likely become negative over time.

CHAYTOR, Q.C.:

Q. Okay, and so, I take it then, you do wherever possible try and repeat the test and have hormone receptor test carried out on the metastatic area?

DR. BRUFSKY:

A. We try, but if you went around, at least in the US and looked in most major centres, I would say less than 5 percent to 10 percent of oncologists currently subscribe to that practice.

CHAYTOR, Q.C.:

Q. Okay, and what about the other way, can a tumour go from being negative to being positive?

DR. BRUFSKY:

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A. Very, very uncommonly, and generally if that happens, we assume that potentially there was something wrong with the original staining on the primary tumour.

CHAYTOR, Q.C.:

Q. So that would cause you to question your original result if that happened?

DR. BRUFSKY:

A. Absolutely, yes, and we would go back to the primary tumour and see. We actually recently in our breast conference, now that you bring it up, actually had a case like that. We had a case where someone supposedly became estrogen receptor positive after having three or four different biopsies that were negative, not just one, but three or four, and that to us - at different institutions the biopsies were done, and we were all very mystified by that. We still are because it's a very rare occurrence if it happens the other way.

CHAYTOR, Q.C.:

Q. And does it matter if it's pre or post - if the person is pre or post-menopausal?

DR. BRUFSKY:

A. Not necessarily, no. I mean, I think that it

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used to be - what used to happen is that in the ligand binding assays that used to be done, say, before 1998, 1997, a pre-menopausal woman would have a lot of estrogen in their body, and so - and that would be - the way they did a ligand binding assay is you would apply radio-labelled estrogen, and you probably have talked about this in the past here, you'd apply a radio-labelled estrogen to a tissue sample. If there was already a lot of estrogen in that tissue sample, that could make it artificially low, would compete for the radio-labelled estrogen. So immunohistochemical tests don't do that. They generally look at the levels of the receptor and generally those sometimes correlate, in my opinion, to the degree of estrogen floating around, but not necessarily. Immunohistochemical assay generally is not as affected by estrogen receptor - peripheral estrogen in the tissues.

CHAYTOR, Q.C.:

Q. Unlike the ligand binding -

DR. BRUFSKY:

A. Unlike the ligand binding assay which was.

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CHAYTOR, Q.C.:
Q. And the case that you spoke about where you were mystified that there were all these biopsies which were negative and then positive, I take it that was something that was so rare that it caught your attention and was the subject of discussion?
DR. BRUFSKY:
A. And we had presented at our breast cancer conference one week and we talked about it for about an hour; it was almost the entire conference. Because, again, we had the pathologist look at the tissue, re-stain it. We actually had a pathologist re-stain the tissue several times because as medical oncologists we couldn't believe it, and the surgeons, we looked at each other and we just said this is so uncommon. But again, like any phenomena in medicine, it happens, I mean, it was just very uncommon.
CHAYTOR, Q.C.:
Q. And, Doctor, there are certain types of cancers that an oncologist would expect to be hormone receptor positive.
DR. BRUFSKY:

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A. Yes.
CHAYTOR, Q.C.:
Q. And perhaps you can tell us what those are?
DR. BRUFSKY:
A. The most important one of those is lobular carcinoma, so invasive lobular carcinoma traditionally are almost a hundred percent positive. Now, that's changed over time as we've gotten a little bit better at defining what a lobular carcinoma is, so it's not quite a hundred percent. It's probably, I would still say in the current thinking it's still 85 to 90 percent positive.
CHAYTOR, Q.C.:
Q. Okay, and when did you learn that?
DR. BRUFSKY:
A. When I was a fellow.
CHAYTOR, Q.C.:
Q. And, Doctor, if you were to have a lobular that, invasive lobular that showed ER negativity, what would you do?
DR. BRUFSKY:
A. I would question it and again I would probably have it retested.
CHAYTOR, Q.C.:

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Q. And is that true of any ER/PR test that doesn't meet your expectations?
DR. BRUFSKY:
A. Pretty much, I mean, I think that again--I'll give you another example, if someone comes in with a very low grade cancer, you know, and we grade cancers in a variety of different ways. There's one that's probably been discussed already, Nottingham Score, if someone came in with a Nottingham four or five, I mean, which is really low, no one is really Nottingham four, but Nottingham five, with say a tubular histology, it looked very benign looking under the microscope and it came out as estrogen receptor negative, I would call the pathologist up and go, "are you sure?" if I saw that on a pathology report, yes. But again, breast cancer is all I do, so I used to this. I think a general oncologist in practice may not be as sensitive to some of this.
CHAYTOR, Q.C.:
Q. And if we could have, please C-0156. This is a pathology report here in St. John's from--it was done in St. Clare's Mercy Hospital and

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it's the report of Peggy Deane and she's referred to her as the index case from time to time. And unfortunately Mrs. Deane is passed away. Her original test was done and I believe this to be July 8th, 2002 and it was found immunohistochemical staining for estrogen and progesterone receptors shows weak staining for progesterone receptors in less than 10 percent of lesion cells, negative staining for estrogen receptors. And the tumour was infiltrating lobular carcinoma. And then on the next page under the microscopy section, overall comment, "For the most part, this tumour is comprised of a mixture of lobular carcinoma in situ with invasive lobular carcinoma. It is noted that both the in situ as well as invasive components in areas attain a somewhat ductal appearance, however, this is not a prominent finding." Doctor, so in July 2002 if you were to receive this outcome in ER/PR, what, if anything, would you have done?
DR. BRUFSKY:
A. Well I would call, I mean now, because I'm sensitized to it in general having seen a lot

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of breast cancer, I would call the pathologist and I would go, "this is a lobular cancer, are you sure?" And even I remember cases of my own from 2002, 2003 where I actually did that, I called and I said, "this is a lobular cancer", I mean, let me give you another example that's maybe a little relevant. So what happens a lot of times given that we're a tertiary care referral centre, we'll get a lot of cases from--consult cases, people coming for second, third opinions, et cetera, and I'll get a report like this occasionally from a lab in a centre that doesn't have as high a volume, and I will actually have our pathologist--this is one of the things that I would then say, I would call--we would have our pathologist call that other pathology lab, have the tumour block sent to us and we would re-stain them if I saw this sort of thing. So this is clearly a red flag for me, I would say, if I did not--lobular cancers are almost, again, almost always estrogen and receptor positive.

CHAYTOR, Q.C.:

Q. And if I could have, please, C-0175? And,

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Doctor, this is another pathology report and in this particular case, I'll just take you to--there's two addendums. The first one is entered on May 6th, 2003 and then the second is May 9th, 2003 and this is entered on the patient's chart. "The stains have been delayed due to unavailability in the lab. When compared to controls, the specimen is negative for HER2/neu ER and PR." And then three days later, "The ER and PR were repeated due to quality assurance issues. The repeated stains show the following: ER positive in 80 percent of the cells; PR positive in 10 percent of the cells. This replaces the previous report phoned to the Cancer Clinic voice mail on May 9th, 2003." Doctor, if this were--if you were to be presented with a report and three days later there were to be a change in the results, what would happen? What would you do?

DR. BRUFSKY:

A. Well, I mean, obviously it depends on when I would see the patient, so if I saw the patient before the addendum--this has happened, this happens quite a bit, actually, either labs

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aren't ready by the time the patient sees us for whatever reason or occasionally do get changed, I mean, if it's three days later, it generally, it would be okay.

CHAYTOR, Q.C.:

Q. If you hadn't already started any treatment or not started any treatment -

DR. BRUFSKY:

A. And generally within three days I wouldn't, I mean, the way things usually work is that, at least in our institution, is that a patient has her surgery and usually if she has drains put in, they're pulled out usually seven to fourteen days later. At that visit, they'll come to see me or a medical oncologist in my group and at that point usually the ER and PR are done by then.

CHAYTOR, Q.C.:

Q. Yes, in this case the ER and PR appear to have been done, the specimen is negative.

DR. BRUFSKY:

A. They done and were negative but then they suddenly became positive, but they were three days later, so if it's only three days later, that would be okay. If it was three months

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later, that's a different story.

CHAYTOR, Q.C.:

Q. In terms of patient care, yes, okay. What about in terms of any concern that it would raise to you that the repeated due to quality insurance issues, would this be the subject of any discussion, for example, in your tumour board rounds?

DR. BRUFSKY:

A. Possibly or I would probably call, for example, if this addendum came three weeks later to me and I had already talked to the patient about what her therapy is going to be and even thought about initiating it, what I would do is I would call up and I would call the lab and I would say, well what is the quality assurance issue, what exactly happened. I would call and ask. Again, three days, I probably wouldn't because quality assurance issues on the three day time flow could be anything and I think that, you know, not knowingly the inner workings of my pathology lab, again, I leave that to the pathologist, you know, systematically things happen, I mean bathes of formalin are bad or

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the fixation is bad or whatever and as long as they have, I'm assuming or I have to assume in my pathology lab that the quality controls are already in place, and so I'm assuming that this is just one of those things that happens and it doesn't happen that often. If it kept happening on every specimen I had, I would say there's something wrong. But one that happened, say once a month or once every couple of months, I would probably not question it if it was this sort a time period, three days. But if it was three weeks, three months, I would definitely say what happened.

CHAYTOR, Q.C.:

Q. And if we could have please, C-0228? And in this case I'll take you to--the original addendum is done in--the original test is March 17th, 2003 and ER/PR, the ER is occasional and positive, less than one percent and PR is 15 positivity, no controls available; and then addendum two, as requested, repeat estrogen and progesterone receptors and the ER is 40 percent and the PR is 73 percent.

DR. BRUFSKY:

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A. Go back to the actual pathology of the patient because what I would do with this really depends on the pathology of this particular lady. Well differentiated one centimeter tumour--or one by two, so it's a two centimeter tumour. This is a woman who, first of all I'm scratching my head, how could it be well differentiated but ER negative, but on the other hand I would say and she's N1 as well. This woman likely, let's see, why is she N1, did she have--let's see, number of lymph nodes, 13, so she had one lymph node involved--okay, so this woman had lump node positive breast cancer. I mean, I forgot her age, do you have the age there as well?

CHAYTOR, Q.C.:

Q. I don't know that we have, no it's blocked.

DR. BRUFSKY:

A. Can't see the age, but in this woman, in this particular case, this is someone who being lymph node positive would likely have received chemotherapy in any event. So in this case what would happen is she like would be in the middle of her chemotherapy when I got this report three months later. So while

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questioning why it took three months, it wouldn't have affected this particular woman because I would have given her hormonal therapy after, based on this. But I likely would have given her chemo anyway because of her lymph node positivity.

CHAYTOR, Q.C.:

Q. And would the change in result be the subject of discussion then amongst your group?

DR. BRUFSKY:

A. Potentially, again, if there were a few of these--this particular case changing, this particular one, probably not because it would have occurred during her chemotherapy. The assumption is this woman would have likely had chemotherapy. Now, again, not knowing this woman, let's say this woman for some reason couldn't get chemotherapy and received no therapy at all, and I got this report, you know, I told her to go home, get radiation therapy, do what you were going to do, and I got this report two months later, yeah, then I would bring it to my tumour committee because then it would have truly changed her treatment.

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CHAYTOR, Q.C.:

Q. So in terms of dealing with treatment, yes.

DR. BRUFSKY:

A. Yes, in terms of dealing with treatment it would change.

CHAYTOR, Q.C.:

Q. Okay, if we don't not think of it in terms of the treatment of the patient as opposed to what may or may not be happening in the lab and if you're seeing a change in result and the other one that I had brought you to a few minutes ago occurred in May, as well, of 2003 and now we see a second one here with a changed result in May of 2003.

DR. BRUFSKY:

A. I would ask myself why are all these tumours changing in 2003, not knowing anything behind this, if I suddenly got a whole stack of reports that the tumours themselves have been changing, I would say what's wrong here, let's bring this to our breast cancer conference and discuss it, yes, that's what would have happened in our group.

CHAYTOR, Q.C.:

Q. And would any individual bring it forward,

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because, I mean, you may have had the first case and someone else, another oncologist may have had the second case -

DR. BRUFSKY:

A. Yeah, I think what would have happened was, right, this happens one of two ways, we have informal discussions among our colleagues and again we're lucky in that we're all geographically right in the same clinic. So someone could just walk over to me and say, "Gosh, Dr. Brufsky"--or "Adam, what's going on?" And we would say, yeah, let's go call the pathologist and find out what's going on and we would. But I think that the other way this would come out is that I would present this at the tumour conference and say, gosh, this is one of several I have had in the last three weeks or four weeks, you know, has anybody else had them? And then other people who were attending that breast cancer conference would say yes, I had one. And then suddenly we would realize and maybe go back and have to do some sort of quality control on all of the specimens or talk with pathologists about what's being done, yes.

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CHAYTOR, Q.C.:

Q. And if we could have, please, C-0174?

DR. BRUFSKY:

A. But again, the key is that the therapy of the patients are so individualized that sometimes it's hard to, in the context of a busy practice pick up one particular one as opposed to another.

CHAYTOR, Q.C.:

Q. Yes. And this one is a little bit different in that it's a year, I believe, between the two tests.

DR. BRUFSKY:

A. And it was a lymph node, I believe it was two centimeters lymph node, it was a two centimeter tumour well differentiated, I was just glancing at that.

CHAYTOR, Q.C.:

Q. That's right, here we go.

DR. BRUFSKY:

A. Two centimeters, well differentiated, lymph node negative.

CHAYTOR, Q.C.:

Q. And so what does that tell you, Doctor, in terms of your expectations?

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DR. BRUFSKY:

A. So, I mean, it depends how old the patient is, but this is someone who clearly could potentially get hormone therapy only and not chemotherapy. I think if this woman had an estrogen receptor negative tumour, I would have given her chemo. And if I got this back a year later, I would definitely would have brought this to our tumour board.

CHAYTOR, Q.C.:

Q. Okay, so this one in August 29th, 2002, she was immunohistochemical staining for progesterone receptors is positive in approximately 15 percent; immunohistochemical stain for estrogen is negative and at the request of Dr. Saidi and we know Dr. Saidi was a medical oncologist here at the time, immunohistochemical staining for ER and PR has been repeated and the ER showed faint staining now in approximately 10 to 15 and progesterone is 75 percent.

DR. BRUFSKY:

A. Yeah, faint in 10 to 15, I'm not sure I would have done, I mean, you're asking my opinion of what I would have in particular. Faint in

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about 10 to 15, I'm not sure that would have convinced me, but with a strong progesterone receptor staining there as a medical oncologist, I probably would have--I mean, this is clearly a lot more positive, I probably would have asked them to run this even again a third time, I would have asked to turn this a third time.

CHAYTOR, Q.C.:

Q. And if we could have, please, P-0489? And again, though, would that have been the subject of discussion, something that you would want to discuss amongst your group?

DR. BRUFSKY:

A. Yes.

CHAYTOR, Q.C.:

Q. And this is an e-mail exchange between Dr. Laing and Dr. Cliff Hudis from Sloan-Kettering.

DR. BRUFSKY:

A. Yes, I know Dr. Hudis well.

CHAYTOR, Q.C.:

Q. You know him well, okay.

DR. BRUFSKY:

A. Yes.

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CHAYTOR, Q.C.:
Q. And what happened here in 2005 is Dr. Laing contacted Dr. Hudis with Peggy Deane, I've showed you her pathology report and on April 9th, 2005, she contacted him and gave a summary of her treatment to date and I'm wondering if basically they would have anything else that could be offered to her at Sloan-Kettering?
DR. BRUFSKY:
A. Yes, I get these e-mails a lot as well, yeah, from people.
CHAYTOR, Q.C.:
Q. And, Doctor Hudis replied and said "ER and PR negative, invasive lobular? Very rare to say the least. If you are sure it is invasive lobular, I would repeat the ER/PR. If it is really ER/PR negative and she is -
DR. BRUFSKY:
A. Status (unintelligible) chemotherapies.
CHAYTOR, Q.C.:
Q. Thank you, and then he goes on from there.
DR. BRUFSKY:
A. Right.
CHAYTOR, Q.C.:

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Q. And he says he doesn't have a clinical trial option at this time.
DR. BRUFSKY:
A. Right. No, but he went through--you can read in his response he went through the decision tree that we would do, I mean, the first thing is that is it really lobular? One thing you can always ask is, yeah, it could be an ER/PR negative tumour, but how sure is the pathologist that it's lobular, so that's the first question. The next question was, well it could be metastatic rarely, very rarely you get metastatic ovarian cancer to the breast, this doesn't happen that often, but it could look like a lobular cancer and so that's why he suggests maybe use carbo plan. So he was at least thinking of other things, but there was clearly a lobular cancer as he said there, it's very uncommon for it to be ER/PR negative.
CHAYTOR, Q.C.:
Q. Yes. And then Dr. Laing responds, "ER was negative and PR was weakly positive in less than 10 percent, which we consider negative. Can get it rechecked."

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DR. BRUFSKY:
A. Right.
CHAYTOR, Q.C.:
Q. And his response then is "I'd try hormonal therapy. I have never seen an ER/PR negative invasive lobular. Signed Cliff." So even without having the repeat test or him having knowledge then that the test ultimately is repeated and apparently is strongly positive, he indicates that he would go with hormonal therapy because he's never seen an ER/PR negative in an invasive lobular.
DR. BRUFSKY:
A. Right, and very uncommonly when we have people who come to us for second or third opinions, and I'd see a lot of women like this with metastatic breast cancer that have been through a lot of different therapies, and, you know, one of the things if they really are ER/PR negative but you don't have very good access to their primary tumour or that we can't biopsy a metastatic lesion, I mean, I think you could try it, I mean I think just to try hormonal therapy anyway, you know, on someone who has been through all of these

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therapies wouldn't be a bad idea to do.
CHAYTOR, Q.C.:
Q. And if we could have, please, P-0046? And, Doctor, this is a report which was an independent review by a pathologist from British Columbia who came in, in the fall of 2005 and I just want to bring you to one part here under the "Incident Problem Case" which we understand to be the Peggy Deane case. He says, "The case is that of a patient with invasive lobular carcinoma whose tumour was tested in 2002 on the DAKO immunostainer and reported as negative for ER and PR and when retested in 2005 on the Ventana benchmark was strongly positive for both receptor proteins. It should be noted that invasive lobular carcinomas are frequently ER positive 92 percent, thus the initial negative result should have been questioned." When Dr. Banerjee when he was here giving evidence at the Commissioner, the reference that he gave was, the reference that he gave here is a 2005, I believe, reference, but he indicated that that would have been true as well in 2002.

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DR. BRUFSKY:
A. Yes.
CHAYTOR, Q.C.:
Q. And in his opinion that both the pathologist and the oncologist should have questioned the result in 2002. Do you agree with that?
DR. BRUFSKY:
A. I would, yes. Again, I think as a--but I would have to say that I look at this from the standpoint of someone who does nothing but breast cancer. I think if someone has a varied practice, say, maybe sees 10 or 20 breast cancer a year or 30, I'm not quite sure what the average oncologist in Newfoundland would see, but as someone who sees 350, I would question it. I clearly, at least the pathologist, I think should have questioned it.
CHAYTOR, Q.C.:
Q. Doctor, have you ever encountered a similar situation with your hormone receptor tests?
DR. BRUFSKY:
A. Yeah, I believe we had--there were a few tests that were not coming out correctly, this is maybe ten years ago at Magee.

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CHAYTOR, Q.C.:
Q. So pre Dr. Dabb's days -
DR. BRUFSKY:
A. Pre, definitely before Dr. Dabb's, yes. And I think we had a similar situation. It was on a lot few patients, but apparently there were probably 10 or 15 women who, at some point, you know, either the controls weren't being done properly, we investigated it but it wasn't making sense, very similar to this, where there is a group of patients with invasive lobular cancer that appeared to have ER negative tumours, but we caught this fairly quickly. I mean, in our group, we went back and looked and said, you know, it was a bunch that suddenly occurred, I believe, within a few months and we looked through this in our group and the medical oncologists brought this to the attention of the pathologists.
CHAYTOR, Q.C.:
Q. So it was the medical oncologists who discovered it?
DR. BRUFSKY:
A. Yeah, and we discussed this in our case conference actually, in one of our breast cancer conferences in 1999, I think, or 2000. You know, we discussed this and went back and retested the specimens, found that in these cases, some of them were positive.

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CHAYTOR, Q.C.:
Q. And so it was about 10 or 15 patients that you discovered?
DR. BRUFSKY:
A. I think so. I'm not--it was even less than that, but it was a small number. It was not anywhere near this number.
CHAYTOR, Q.C.:
Q. So it's something that was detected fairly quickly?
DR. BRUFSKY:
A. Yes, within a couple of months, yes.
CHAYTOR, Q.C.:
Q. And it was discovered through communication amongst the oncologists?
DR. BRUFSKY:
A. Correct, yes, that's what happened.
CHAYTOR, Q.C.:
Q. And Doctor, in terms of the patients in that case, were they informed beforehand that they were going to be retested?

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DR. BRUFSKY:
A. Yeah, what we did was we went through the list of patients to determine whether it would have made a difference in their care. We actually had a meeting of a group, very similar, I think, to the meetings that have been described here, to determine whether it would make a difference in their care. We were going to inform them anyway, but I think we really needed to kind of meet to say "well, would this have made a difference?" Because that was the first question out of most people's mouths was "well, would it have made a difference?" If it wasn't going to make a difference in someone's care, then it wouldn't have mattered, say someone who had a very tiny cancer, you know, five millimetres, who we probably wouldn't have treated with hormonal therapy anyway at that point or someone who, again, had a tumour that maybe on retesting was estrogen receptor positive for five percent or six percent, probably would not have made a difference, and so we did it on a case-by-case basis. But everybody was informed regardless, but I think we had to

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figure out what the next step would be in most of them.

CHAYTOR, Q.C.:

Q. And they were informed before they were retested and then offered the opportunity to be retested?

DR. BRUFSKY:

A. Well, I think we retested everybody regardless.

CHAYTOR, Q.C.:

Q. Okay.

DR. BRUFSKY:

A. But we just told them that they were going to be retested.

CHAYTOR, Q.C.:

Q. Okay, and that might be a good place then to ask you about current quality assurance and best practices in your own institution.

DR. BRUFSKY:

A. Sure.

CHAYTOR, Q.C.:

Q. And how issues such as what we're dealing with here and on a smaller scale you dealt with in the past in your institution can be detected and what safeguards are really in place to

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allow for that. So perhaps you could tell us what it is you do in your institution in terms of quality assurance from an oncology point of view?

DR. BRUFSKY:

A. Well, if I can put it more on a global perspective. So most of the breast programs in the United States, at least the larger ones, are accredited by the Council on Cancer of the American College of Surgeons, and to be accredited by the Council on Cancer, it's a three-year accreditation. There are about 25 to 30 percent of all cancer programs in the United States have this accreditation. You are reviewed on 36 criteria to meet this, and there are a variety of criteria. Some have to do with quality assurance and quality control. Some have to do with having a cancer committee. You have to have a cancer committee, multi-disciplinary cancer committee. It has to meet with some frequency, usually monthly. There has to be a tumour registry, where the characteristics of all the cancers that are seen in your institution, not only breast, but you know,

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ovarian, lung, etcetera, have to be registered in a registry and easily available for analysis and there has to be at least one quality assurance project yearly, based on the data in the registry, and that could be picked by the group, what that quality assurance project is. But there also have to be multi-disciplinary cancer conferences every week where, again, I think I discussed this earlier, where at least ten percent of all the cases need to be discussed, the analytic cases of your institution, and 75 percent of the cases have to be prospective discussion. That is, the discussion has to occur before the patient is treated. So in other words, so it's 75 percent of ten percent. So it's eight or nine percent of the cases totally have to be discussed prospectively.

So that's the framework that we use for our quality control. So aside from the quality control that the pathologists do, as medical oncologists, we have quality control by doing various projects on our data on a yearly basis. And again, they're not the same projects every year. They're always somewhat

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different, but it could be how many women who are--I'll give you one example that was in our--from a year or two ago. How many women with stage one and two breast cancer that was estrogen receptor positive received the recommendation for hormonal therapy? So that was a quality control project we did where we went back to our registry, which actually records what therapy people get also, we go a little bit further, and we basically saw who was ER positive stage one and two breast cancer in the year, I think, 2005, and how many of those patients received Tamoxifen or an aromatase inhibitor. So those are the sort of things that we do.

CHAYTOR, Q.C.:

Q. Okay, and in terms of your multi-disciplinary committee that you referred to, there's recently been here at Eastern Health has established a breast disease site group. Perhaps I'll just show you the terms of reference for that group.

DR. BRUFSKY:

A. Sure.

CHAYTOR, Q.C.:

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Q. It's P-2478, please, Registrar, and the purpose is to develop evidence-based practice guidelines for diagnosis, care and treatment of individuals with breast disease. The objective being to determine priorities for guideline development, review national and international guidelines and provide direction for local adaptation. Approve practice guidelines for local, provincial use. Provide direction for dissemination and evaluation of guidelines. Develop strategies for collection and analysis of breast cancer data within Eastern Health, and you can see that there's representatives from the Cancer Care Program, pathology, radiology, medical oncology, radiation, pharmacy, nursing, surgery and genetics. Is that the type of committee and the mandate of your committee?

DR. BRUFSKY:

A. This is the type of committee, but the mandate's a little bit different. This is more of a guidelines committee that sets treatment guidelines, which we have committees that do that also, but they're separate from this. But this composition is what a cancer

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committee would look like under the American College -

CHAYTOR, Q.C.:

Q. So the membership would be?

DR. BRUFSKY:

A. The member is very similar to what the membership of a cancer committee would look like.

CHAYTOR, Q.C.:

Q. And so what--well, how does your cancer committee differ? What exactly would your mandate be?

DR. BRUFSKY:

A. So our mandate is actually to review the--not exactly review the treatment. So this is actually a treatment committee, but this is actually--the committee that we would have would be more of a quality control committee. So in other words, our committee meets, I think, quarterly to review the registry, to go and do a spot check of the cases in the registry, to be sure they're being recorded properly, to discuss issues that arise of quality control among the various cancer programs that are specifically tied to the

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American College of Surgeons guidelines.

CHAYTOR, Q.C.:

Q. And so that committee is for more--that's for all cancers, all site groups?

DR. BRUFSKY:

A. Well, it's for--it's for GYN cancers, breast and ovarian, endometrial, but nonetheless, that cancer committee meets more not to establish treatment guidelines. We have separate committees that do that that are composed mostly of surgeons, medical oncologists, not so much geneticists and other people. It's mostly radiation therapists, medical oncologists, surgeons, geneticists. The nursing and pharmacy probably wouldn't be part of this. Pathology and radiology probably wouldn't be part of a guidelines committee, because a guidelines committee really is doing treatment guidelines. So that would be really people involved in treatment. This is mostly treatment, but I mean, I think that this is kind of--but there are some objectives that are good that are developed (unintelligible) and analogy of breast cancer data. So that's more of a cancer committee

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sort of focus.

I mean, I think that generally, with the exception of the treatment guidelines, I think that if you call it clinical practice, I guess clinical practice is different than treatment. So I guess this is kind of functioning like a cancer committee would in our institution.

CHAYTOR, Q.C.:

Q. Okay. So your committee that meets is clearly--the one that meets quarterly -

DR. BRUFSKY:

A. Yes.

CHAYTOR, Q.C.:

Q. - the cancer committee, it's clearly meant more for QA and for analysis of the data which is going into your database?

DR. BRUFSKY:

A. Correct.

CHAYTOR, Q.C.:

Q. Or your registry, as you call it, yes.

DR. BRUFSKY:

A. Right, and for deciding on, you know, being sure that the multi-disciplinary conferences are going, that they're well--that they're attended. Making sure that any--the quality

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projects that we're doing are ongoing.
CHAYTOR, Q.C.:
Q. So they oversee that as well?
DR. BRUFSKY:
A. They oversee that as well, yes.
CHAYTOR, Q.C.:
Q. Okay, and in terms of the data collection specifically for hormone receptor tests, what would you track? What would you be recording?
DR. BRUFSKY:
A. Well, again, that would be mostly in the pathology, okay, and we would do through the registry, we would say, one of the registry things that we would do is we would say "do all"--the question we would ask of the registry is if we look at all--you know, X number of cases from 2005, do they all have--what is the estrogen and progesterone receptor status of those cases? You know, if there are too many unknowns, then we have a problem, or if there are too many revised--I mean, for example, relevant to us, if there are too many--if there are multiple revised reports that would probably come up in a committee review like this.

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CHAYTOR, Q.C.:
Q. Okay, and would there be any analysis, for example, by types of cancers? Would you be looking for anything like that, in terms of what the hormone receptor status versus type of cancer?
DR. BRUFSKY:
A. Not necessarily, unless it came up, unless it was brought to our attention.
CHAYTOR, Q.C.:
Q. Unless that was your project for the year perhaps?
DR. BRUFSKY:
A. Correct, if that was a project for the year, right.
CHAYTOR, Q.C.:
Q. Okay, and what about in terms of correlations between ER positivity and PR positivity, would that be something that you could track through your registry?
DR. BRUFSKY:
A. We could track it through our database, yes, but again, that would--it's not something that we normally do. So unless it was brought to someone's attention. I mean, for example,

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again, if, like you said, there was suddenly a bolus of reports that were revised, it would come to the attention of the cancer committee.
CHAYTOR, Q.C.:
Q. And if you were seeing a number of patients who had ER negativity but PR positivity -
DR. BRUFSKY:
A. Yes.
CHAYTOR, Q.C.:
Q. - and seeing a lot of that, that's something again that might come to your -
DR. BRUFSKY:
A. That would come to one of the quarterly meetings of the cancer committee, correct.
CHAYTOR, Q.C.:
Q. Okay.
THE COMMISSIONER:
Q. Would you describe this committee as kind of having an audit function?
DR. BRUFSKY:
A. In some ways, yes. It does have an audit function, yes.
THE COMMISSIONER:
Q. So it's--but when the committee goes in to look at essentially a file which tells them

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how a particular patient was treated, and as I understand it, you would have there all of these experts looking presumably at the file from the perspective of that particular expertise. Then are they looking at whether or not the particular patient was treated or dealt with in the context of norms which were established or are they looking for this on a more global basis, having picked a percentage of the files and then trying to determine whether over the course of this percentage, these kinds of standards are being met?
DR. BRUFSKY:
A. Yeah, it's a more - the case of this particular committee it's global.
THE COMMISSIONER:
Q. Uh-hm, yes.
DR. BRUFSKY:
A. We have separate committees, though, that are cancer centre-wide where we have established clinical practice guidelines for the treatment of all stages of breast cancer.
THE COMMISSIONER:
Q. Uh-hm.
DR. BRUFSKY:

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A. It's web-based and we actually have a separate committee, separate from this, comprised mostly of medical oncologists and surgeons that actually looks to see whether a particular practitioner has deviated from the practice guidelines. So that's a different committee function than this, but there's a separate committee that actually does that, yes. So I think the answer is this sort of committee does it more on a global sense.

THE COMMISSIONER:

Q. All right, but there is another group that would - whose function is to determine whether or not guidelines having been established are being followed?

DR. BRUFSKY:

A. Correct, yes, that's a more recent committee, yes.

CHAYTOR, Q.C.:

Q. If we can look, please, at P-2601, and this is entitled Eastern Health Clinical Practice Guidelines in Oncology Breast Cancer, and I'll just take you down through part of this. "In DCIS and LCIS, what is the role of Tamoxifen in the management of DCIS, LCIS, and adjuvant

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hormone therapy, what constitutes a positive hormone receptor breast cancer", and there is reference to -

DR. BRUFSKY:

A. To 1 percent.

CHAYTOR, Q.C.:

Q. To the 1 percent right here, "Patients should be referred to medical oncology in a timely fashion to allow for assessment to take place 10 to 12 weeks post-surgery. The discussion will include the adjuvant treatments of choice, and for those patients who have ER/PR positive disease, adjuvant hormonal therapy will be discussed. The threshold for ER and PR positivity has been debated in the past, but the group decided the result of 1 percent or over will be considered positive". Now there has been another document, however, entered here, and I believe it might be 2599, where it discusses the 1 to 10 percent.

DR. BRUFSKY:

A. Uh-hm. Right there.

CHAYTOR, Q.C.:

Q. Here we go, right here. "So the breast group has decided to accept the St. Gallen's

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recommendations in which patients with hormone receptor staining found to be greater than 10 percent are considered positive and should be offered hormonal treatment. Those with 1 to 10 percent staining are deemed to be hormone response unknown and may still be offered hormone manipulation, while those under 1 percent exhibit no detectable hormone receptor staining are considered to be negative, and, therefore, do not derive benefit from hormonal therapy", and we've heard from the oncologists practising here in St. John's that anyone 1 to 10 percent now, their current practice is to bring those patients to their tumour board rounds and discuss them.

DR. BRUFSKY:

A. And that's very reasonable. I think that's an excellent way to do it. I mean, again, I think that we - because there is a lot of controversy still about that 1 to 10 percent, and even amongst my colleagues in my own institution, some will treat with 1 percent. I particularly will not. Everybody - I think it's a very reasonable thing to do.

CHAYTOR, Q.C.:

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Q. Okay. If we could have, please, P-2596. This is a guideline that's been developed for DCIS patients, and the group has decided to not recommend carrying out routine receptor testing on DCIS, however, if an individual physician requests it, the pathology department will provide testing on a case by case by case basis. Doctor, what's your current practice in terms of dealing with DCIS?

DR. BRUFSKY:

A. We test for DCIS and LCIS. Well, we don't test LCIS because we know (unintelligible) is 98 percent positive, but DCIS we do because that will affect our recommendations for Tamoxifen. Again that's - and I can understand this. This is kind of a more - there's still some debate country by country about the - it's based on one or two papers, one big presentation at the San Antonio Breast Conference in 2005 from Dr. Allred. There is a lot of - we particularly have adopted it, so we do ER/PR testing on all DCIS.

CHAYTOR, Q.C.:

Q. And what is it that you've adopted?

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DR. BRUFSKY:
A. Testing for - estrogen receptor testing on DCIS.
CHAYTOR, Q.C.:
Q. Okay.
DR. BRUFSKY:
A. Where here they have not, and - which is okay right now, but I think that within the next year or two, they probably will end up adopting it, but that's the reason people have meetings for guidelines is to sit and discuss the literature and have a take of whatever expert committee you put together. I mean, I think in the United States if you put together 15 expert committees, determining whether to test DCIS or LCIS - DCIS for the estrogen receptor, I think you probably would have six that would say do it, you'd have four that would say not. So, I mean, I think that's reasonable, although at our institution we do it.
CHAYTOR, Q.C.:
Q. And why, who do you do it at your institution?
DR. BRUFSKY:
A. Because our pathologists believe that the

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receptor testing can be done, they believe the results, and the medical oncologists in our institution believe that DCIS that's estrogen receptor negative will not respond to Tamoxifen. So, therefore, it does change what hormonal therapy we offer the patient.
CHAYTOR, Q.C.:
Q. Okay. In terms of the types of guidelines that you see here, are there any - I know you've had a chance to look over those somewhat before coming here.
DR. BRUFSKY:
A. Yes.
CHAYTOR, Q.C.:
Q. Are there any other guidelines that you would recommend in terms of hormone receptor testing?
DR. BRUFSKY:
A. Well, I think they've done a fairly good job. Again I think one thing they will have to do in the near future, if it becomes available in Canada and in Newfoundland, is determine how to integrate the Oncotype DX test into it. I think that's going to be an important - because that clearly - outside of the United

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States it really has not been widely integrated, but I suspect within the next three to five years it will be.
CHAYTOR, Q.C.:
Q. Okay.
DR. BRUFSKY:
A. But generally these are pretty good. I mean, understanding that there's some local differences between Newfoundland and Pittsburg.
CHAYTOR, Q.C.:
Q. Yes. I believe, Doctor, you said in answering my questions earlier this morning that you don't currently have what we call mortality or morbidity rounds. What do you have instead?
DR. BRUFSKY:
A. What we - again our tumour board, cancer board that we have, or breast cancer committee -
CHAYTOR, Q.C.:
Q. It's the committee that we just spoke about, is it?
DR. BRUFSKY:
A. Not the - not the cancer committee, but our multidisciplinary rounds every week serves as an M & M as well. So if - because again

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thankfully complications of breast surgery are somewhat rare, but we will discuss them and how to prevent them in the future, which is really the function of a surgical M & M, by and large, at our breast cancer conference. So we - even though it's got the tumour board name on it, it really is a conference where a lot of different issues in our institution come up like this.
CHAYTOR, Q.C.:
Q. Okay. If we could have then, please, P-3354. Doctor, perhaps you can just tell us what this document is and take us through the relevant portions?
DR. BRUFSKY:
A. Sure, I could take you through some of this. This is actually - this is the Commission on Cancer, cancer program standards that you have to meet, and the guideline is widely available on the internet for cancer programs in the United States that want to receive American College of Surgeons accreditation, which again is a plus for that program because it indicates that it meets certain quality control standards, and if I can just briefly

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go through some of these pages of this document. Where are we here? I mean, I'll just kind of go through - you need to meet 36 criteria that are divided, I think, into nine different sections, and let me just see if I can kind of see - it's a long document, and I don't want to go through all of this, but - so, for example, these are the standards, so these are a variety of standards that you have to meet. So this is the standard, 1.1, the faculty is accredited by a recognized authority, and depending on what kind of cancer program - there's six different kinds of cancer programs they would accreditate, but depending on, and these are the organizations that you can see on the left hand side, like the JCAHO, or the American Osteopathic Association, if it's an osteopathic hospital or there's various health licensure agencies. So you have to meet that. Then you have to have cancer program leadership. So you have to have organization structure that has a cancer committee, that has someone leading the cancer committee, and again there's all these sorts of names for it; Cancer Centre Board,

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Executive Committee, etc, but you have to have all these committees and there's various standards that you're rated on. Then Chapter Three really describes that you have to have a cancer data management and tumour registry, and it goes through the various specifications for this. There's all sorts of requirements that are in here. You have to have a registrar, they have to be specifically trained, etc, and it also describes the registry operations here. You know, there's a policy and procedure manual for the cancer registry, how the cases are reported, how they're adjudicated, how there's case finding, and what you have to have in the index. Chapter Four really has to do more with the treatment services that are offered by a cancer program, and the three major ones are surgery, radiation, and systemic therapy, but you also have to have rehabilitation services, social services, high risk programs for people who don't have cancer, but believe they are at high risk for cancer. Chapter Five is going through this, the kind of research, about disseminating research during clinical trials.

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You have to have clinical trials program information at your institution. You have to have community out-reach, so supportive care of various support groups, and then this is the important issue - well, there's cancer conferences that you have to have, but you also have to have one big cancer educational opportunity for local physicians, and finally, Chapter Eight has to do with quality improvement, and you have to have various quality outcomes that they require and you're rated on all of these. Again it turns out that within these eight criteria there are sub-criteria, and you're rated on all 36, and you have to receive at least a passing score on all 36 to get accreditation. If you don't, it depends on how many you failed, you're given three years or a year to fix whatever you need to fix.

CHAYTOR, Q.C.:

Q. Okay.

DR. BRUFSKY:

A. But this serves as a very nice framework, I think, for quality control in the cancer program, and the reason I brought this with me

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is that this is kind of how our cancer program is organized, at least in terms of its quality improvement and quality control.

CHAYTOR, Q.C.:

Q. Okay.

DR. BRUFSKY:

A. From the medical leadership standpoint, not internally within the pathology department, which is a separate quality control entirely.

CHAYTOR, Q.C.:

Q. Yes. Commissioner -

THE COMMISSIONER:

Q. I was just going to remind you of the morning break at any point you want to take it.

CHAYTOR, Q.C.:

Q. Perhaps this would be a good point. I'm just about finished with the doctor, so I'll just look over my notes.

THE COMMISSIONER:

Q. When we come back, just because I happen to be interested in it, could we perhaps get the opinion of the witness on the value of the data management aspect.

CHAYTOR, Q.C.:

Q. Yes.

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THE COMMISSIONER:
Q. Thank you.
CHAYTOR, Q.C.:
Q. Thank you.
THE COMMISSIONER:
Q. Take fifteen minutes.
(BREAK)
THE COMMISSIONER:
Q. Ms. Chaytor, before you begin, I think I should interrupt the proceedings for just a moment to convey some congratulations which are in order to Ms. Brazil, Mr. Pike, and Mr. Browne on attaining their QC's. We look forward to seeing you all in silk in due course.
CHAYTOR, Q.C.:
Q. Congratulations.
BRAZIL, Q.C.:
Q. Thank you, Commissioner.
BROWNE, Q.C.:
Q. Thank you, Commissioner.
PIKE, Q.C.:
Q. Commissioner, thank you very much. Thank you.
CHAYTOR, Q.C.:
Q. Doctor, I'd just like to ask - the area that

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the Commissioner would like to have some more information on in terms of the value of data management for your group that--the committee that you told us about that collects the data. Who mandates what data has to be collected?
DR. BRUFSKY:
A. So the American College of Surgeons as part of their Council on Cancer, as part of being one of the certified institutions, they mandate very specific data elements that at a minimum have to be collected. It's our choice to collect more if we so desire.
CHAYTOR, Q.C.:
Q. And do you do that, do you collect -
DR. BRUFSKY:
A. We do, yes.
CHAYTOR, Q.C.:
Q. - more than what -
DR. BRUFSKY:
A. We collect on data on treatments, which is not necessarily required.
CHAYTOR, Q.C.:
Q. And what types--what are--what types of data are included in the minimum of what has to be collected?

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DR. BRUFSKY:
A. Oh, it's in there, it's actually in the standards. There's a very nice list, believe it or not.
CHAYTOR, Q.C.:
Q. Perhaps we can bring that up again then, please, Registrar, 3354?
DR. BRUFSKY:
A. Let me see if I can find you the exact elements.
CHAYTOR, Q.C.:
Q. Okay, and is there a particular page then, Doctor?
DR. BRUFSKY:
A. Try pages 48 and 49 of this document. Let's see. I don't know if that's the right page. Hold on. It's actually, standard 3.8, so I would keep going. Go down a few more.
CHAYTOR, Q.C.:
Q. Yeah, you just scroll down there. 3.7 so, here we go, 3.8 "Special Studies"?
DR. BRUFSKY:
A. Yeah. No, go down, go back one. Let me see if it's the right one. Let me see if I'm on the right page. Yeah, it's in the special

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studies. It kind of says at least the minimum sort of things that are collected.
CHAYTOR, Q.C.:
Q. Okay.
COMMISSIONER:
Q. Now is this data then communicated some place or is it available to others?
DR. BRUFSKY:
A. Oh, it's available to anybody who wants it, yes. So it's a whole listing. I mean, you'll see if you go down through this, there's a whole series of material. And it's not all of them, there's a whole policy and procedure manual that has a bunch of other things that are collected. Keep going.
CHAYTOR, Q.C.:
Q. Keep going?
DR. BRUFSKY:
A. But most of them, this just tells you how--keep going. Index. These are the sort of things--you can go back a little bit. If you look at the index, there's a whole listing of things there that you collect. Then you collect data diagnosis. Keep going. You can go down a little bit further. And then you

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actually abstract it. So there's actually a form, I don't have the form on me, but there's a form that basically stages--the biggest one of all is staging the cancer. So the most important things are data diagnosis, the T stage, the N stage, the M stage. Those are the most important parts of the registry that have to be done and the follow-up, whether the patient is alive or dead. Those are really the requirements, because they all have to be submitted in a particular format to a national database. They have to be submitted, I think, every six months to a national database of all cancers in the United States that are participating in the ACS Registry. But what people do on top of that, there are actually computer registry, computer programs that are commercially available that allow you to collect additional data if you so desire on treatments, etcetera, and we've done that in our database.

CHAYTOR, Q.C.:

Q. Yes. And what's the purpose then of collecting this data, what benefit can it have?

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DR. BRUFSKY:

A. So (a) there is a variety of things. (a), it's one group of many throughout the United States that provides bulk data on cancer incidents and mortality in the United States, so that's one function. The second function is a local function where you compare your incidences and mortality rates to national standards. That's probably the two biggest ones that we use. And there's a third one, obviously, to look at various trends in the data. Especially if you're collecting some of these other additional data elements, you can look at trends in your data and see if anything is kind of skewing differently than national norms.

CHAYTOR, Q.C.:

Q. And that's the purpose for which your organization uses the data?

DR. BRUFSKY:

A. Would be for quality control a lot of times, yeah.

CHAYTOR, Q.C.:

Q. Okay. Now, I think that there have been some updates to this document just recently. And

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you'd be aware, I take it, of that, the updates in -

DR. BRUFSKY:

A. Yeah, I am. The updates, at least a lot of them are not relevant, I think, to our discussion.

CHAYTOR, Q.C.:

Q. Okay.

DR. BRUFSKY:

A. The only one is that the staging systems for various cancers have changed over the last couple of--especially breast cancer in 2006.

CHAYTOR, Q.C.:

Q. Yes.

DR. BRUFSKY:

A. The staging symptom for lymph nodes changed quite a bit, and as a result they've added, over time, various new staging systems.

CHAYTOR, Q.C.:

Q. Okay. And we have another exhibit, Commissioner, if we could have entered, please, is P-3355?

COMMISSIONER:

Q. Thank you. Entered.

EXHIBIT P-3355 ENTERED INTO EVIDENCE.

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CHAYTOR, Q.C.:

Q. And if we could bring up, please, P-3355? And this is the new standard updates, actually, for 2009.

DR. BRUFSKY:

A. Um-hm.

CHAYTOR, Q.C.:

Q. So that would be the document that you're referring to in terms of the updates? There's--have a blank page. So basically most of what's relevant to our discussion we would find in the original document, 3354, I take it -

DR. BRUFSKY:

A. Yes.

CHAYTOR, Q.C.:

Q. - is that right, Doctor?

DR. BRUFSKY:

A. Um-hm.

CHAYTOR, Q.C.:

Q. Okay. Doctor, unless there's anything else that you would like to add in term of any recommendations on a go forward basis that might be useful, other than what we've covered -

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DR. BRUFSKY:
A. No, I'd just like to summarize, I think that having a cancer committee very similar to the design of a commission on cancer, cancer committee, I think, that meets at least monthly or at least quarterly, would be a very important step. I mean, I think that clearly it's a characteristic of some of the top cancer centres, the best practices in the United States to have such committees, number one, to have a weekly multidisciplinary tumour board, clearly, would be a major best practice. I think another best practice would be to have a cancer committee comprised of this group of people which could also serve as a guidelines committee for dissemination of best practices in cancer. I noticed on this committee that you have surgeons and you have geneticists and radiation therapists, but most of the--and radiologists. But most of the recommendations are surrounding treatment. I think it would be important going forward, you know, again, to promulgate guidelines about screening, about various--which radiologic techniques to use, a la, you know, mammograms

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versus digital mammograms, versus breast MRI, these sort of--this is one example of many. But, I mean, this sort of committee that you've formed could serve all of those functions, which would be very useful, as well.
CHAYTOR, Q.C.:
Q. Okay.
DR. BRUFSKY:
A. Not just treatment.
CHAYTOR, Q.C.:
Q. Thank you. Thank you, Doctor, for your time.
DR. BRUFSKY:
A. You're welcome.
CHAYTOR, Q.C.:
Q. And some of my colleagues will have questions, perhaps, for you. Thank you, Commissioner.
COMMISSIONER:
Q. Ms. Brazil?
BRAZIL, Q.C.:
Q. No questions, Commissioner.
COMMISSIONER:
Q. Mr. Simmons?
DR. ADAM BRUFSKY, EXAMINATION BY MR. DANIEL SIMMONS
MR. SIMMONS:

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Q. Thank you, Commissioner. Good morning, Dr. Brufsky.
DR. BRUFSKY:
A. Good morning.
MR. SIMMONS:
Q. My name is Dan Simmons and I'm here representing Eastern Health, which is the health authority that now operates the cancer centre here and laboratory services, as well. I was very interested in your evidence this morning, I found it very informative. And I note that you've given us a number of examples of the way things work at your institution in Pittsburgh, and I want to ask you just a little bit more background about your institution there.
DR. BRUFSKY:
A. Sure.
MR. SIMMONS:
Q. I understand it's Magee Women's Hospital?
DR. BRUFSKY:
A. Yes.
MR. SIMMONS:
Q. And I apologize if I don't get these names exactly right.

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DR. BRUFSKY:
A. No, no, that's okay. Now, that institution is affiliated with the University of Pittsburgh?
DR. BRUFSKY:
A. Correct.
MR. SIMMONS:
Q. Okay. And what the portion of the institution that you're the director of is the Comprehensive Breast Cancer Centre?
DR. BRUFSKY:
A. Yes, of all of the UPMC, so Magee is the main obstetrics hospital of the entire UPMC system.
MR. SIMMONS:
Q. Yes.
DR. BRUFSKY:
A. And the breast centre is located at the University of Pittsburgh. We have a comprehensive free-standing cancer centre called the Hillman Cancer Centre.
MR. SIMMONS:
Q. Um-hm.
DR. BRUFSKY:
A. Which is attached to a hospital called Shadyside.
MR. SIMMONS:

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Q. Um-hm.
DR. BRUFSKY:
A. When we built that, we had just built the Comprehensive Breast Centre at Magee and we did not want to spend another $10 million so we decided to leave the Comprehensive Breast Cancer Centre at Magee. But it's for the entire system, though.
MR. SIMMONS:
Q. Okay, and you've said that you see about 100 new breast cancer patients?
DR. BRUFSKY:
A. The entire practice, yes, of about three FTE medical oncologists sees about 1000.
MR. SIMMONS:
Q. Okay. Which works out to about 300 or so patients each -
DR. BRUFSKY:
A. Actually, well, we have five people total. I see the most, I see 350.
MR. SIMMONS:
Q. Yes.
DR. BRUFSKY:
A. And then my colleagues see anywhere from 100 to probably 200 each, depending on the person.

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MR. SIMMONS:
Q. So you have five medical oncologists available for that volume of new breast cancer patients?
DR. BRUFSKY:
A. Correct, yes.
MR. SIMMONS:
Q. And those five oncologists, do they do almost exclusively breast cancer or do they do a variety of other types of cancer treatment, as well?
DR. BRUFSKY:
A. One does all types. One works--see, again, this being an academic practice, I work three days a week in clinic, I have someone that works two days a week and we have two oncologists who work two days a week in clinic, I have some works a week, day and a half in clinic, and then I have one medical, and they all see nothing but breast cancer.
MR. SIMMONS:
Q. Um-hm.
DR. BRUFSKY:
A. The fifth person sees breast cancer one day and then all types of cancers on the other four days.

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MR. SIMMONS:
Q. And I presume that that level of staffing of medical oncologists you'd consider appropriate and in line with any guidelines that are out there for the number of oncologists you need for that volume of patients that you see?
DR. BRUFSKY:
A. Probably because we're academic oncologists on the low side. I would say the national norms are about 300 patients, 200 to 300 patients per medical oncologist.
MR. SIMMONS:
Q. Now, we've heard in this Inquiry, as you may or may not be aware, considerable evidence about difficulties in recruiting specialist positions here. Pathologists, we've heard a lot about, but we've heard about medical oncologists, as well. And I wonder if you can give me any--your view on your experience over the last five, six, eight, ten years in your ability to recruit and retain medical oncologists for your institution?
DR. BRUFSKY:
A. It's actually going down. I think that there is in the US a national--there will be by 2020

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a predicted national shortage of medical oncologists, and it has become more difficult in the Pittsburgh area to recruit people. Generally people want to live, at least in the US, on one of the coasts. They don't necessarily want to move into the interior as much. That's been hard. But in general the supply, actually, has gone down. And most medical--especially in the academic setting and most groups in the US have a substantial proportion of foreign medical graduates because of that.
MR. SIMMONS:
Q. Okay. How does your current staffing level of medical oncologists compare to, say, five years ago in your program?
DR. BRUFSKY:
A. We're probably the same or slightly lower.
MR. SIMMONS:
Q. Right. And compared to ten years ago?
DR. BRUFSKY:
A. A bit bigger.
MR. SIMMONS:
Q. Okay.
DR. BRUFSKY:

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A. Well, to ten--at least in the Magee--let me rephrase that because I think I know what question you're asking. We have grown at Magee, for example, from one medical oncologist seeing 50 patients a year to, I mean, we clearly have grown in terms of the breast medical oncology.

MR. SIMMONS:

Q. Right.

DR. BRUFSKY:

A. But I think in terms of the overall medical oncology group, it's kind of remained stable.

MR. SIMMONS:

Q. Right.

DR. BRUFSKY:

A. Maybe slightly increased.

MR. SIMMONS:

Q. So your numbers have remained relatively stable. What about your turnover of medical oncologists, what has your experience been in how frequently people will come to your institution, stay a short period of time and then move on somewhere else?

DR. BRUFSKY:

A. Actually, thankfully less than at most

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institutions. I think that generally we've had very good retention. We're a little bit different than a typical practice in that we're academic and for whatever reasons people find a job, an academic sometimes you have to move to get promoted or change, you know, whatever focus of research you're doing, and so there academic reasons why people move, but in general until very recently because we're actually changing the leadership of our cancer centre, we've had a fairly stable group of medical oncologists.

MR. SIMMONS:

Q. Okay. Now, you've told us about the types of committees you've been able to have in place, the multidisciplinary committees, the quality control work that you're able to do. I wonder do you have any view on whether or not your relative stability in numbers of medical oncologists and in turnover has been a positive or negative factor in being able to do that sort of work?

DR. BRUFSKY:

A. Absolutely. I would have to say that the stability of--the stability has been an

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important factor, that you have people who are the institutional memory, and that's very important to have people there who have been there for a number of years and understand how things have been done over an extensive period of time.

MR. SIMMONS:

Q. Okay. Ms. Chaytor asked you some questions about whether the relative percent of a positive estrogen test would play any role in deciding whether or not a particular patient would start hormone replacement therapy. And I think I understood you to say that as long as the percentage is ten percent, which is the threshold to trigger consideration, higher percentages don't necessarily tell you much more about what the prognosis will be for that patient--is that fair?

DR. BRUFSKY:

A. It tells more--I think it's a fair statement to say it doesn't predict response to estrogen therapy.

MR. SIMMONS:

Q. Okay.

DR. BRUFSKY:

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A. I think those with a higher percentage of estrogen receptors probably have a slightly better prognosis. Again, how much weight someone puts on the degree of estrogen receptors really depends on the individual medical oncologist.

MR. SIMMONS:

Q. Yes.

DR. BRUFSKY:

A. So I put some weight on it, but not as much as others. Some oncologists put no weight in it.

MR. SIMMONS:

Q. Um-hm.

DR. BRUFSKY:

A. But in terms of a predictive response, I would say that generally over ten percent, there's slightly higher response, but the ten percent threshold, at least for me, is a good cutoff.

MR. SIMMONS:

Q. Is enough to trigger the consideration of the other factors that you take into account -

DR. BRUFSKY:

A. Correct.

MR. SIMMONS:

Q. - when you decide if you're going to recommend

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hormone therapy. Now, that's one of a number of examples I think you gave us where there are differing views among different medical oncologists about how to take factors into consideration. A lay person looking at this from the outside would tend to think there's a right way and there's a wrong way to do a lot of these things.

DR. BRUFSKY:

A. Right.

MR. SIMMONS:

Q. But I gather that's not the case when it comes to making these sorts of decisions?

DR. BRUFSKY:

A. Correct. And I think that, you know, there-- in general what tends to happen is that there is agreement on certain parameters that you can use. I mean, there are certain boundaries that you try to stay within. I mean, there are clearly certain things that are, no one would agree with. So if someone comes in with an estrogen receptor that's 100 percent with, say, a two centimetre breast cancer and doesn't receive hormonal therapy, I think you would get agreement on with most medical

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oncologists that that woman should be treated.

MR. SIMMONS:

Q. Right.

DR. BRUFSKY:

A. Whereas a woman comes in with one percent estrogen receptor positive tumour, I would say that there's a little bit less agreement about how that woman should be treated.

MR. SIMMONS:

Q. Okay, good. Now, oncologists' views on issues like this and the sort of acceptance in the profession of where those limits are, has that been something that has evolved and changed over the last five or ten years, many of these issues?

DR. BRUFSKY:

A. Yes, and in many different ways. There's new literature that comes out.

MR. SIMMONS:

Q. Yes.

DR. BRUFSKY:

A. There are experts in the field like myself that--that disseminate guidelines, etcetera, for other oncologists, perhaps, who are too busy to kind of keep up with every single item

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of the medical literature. They serve more as shorthand for those medical oncologists.

MR. SIMMONS:

Q. You've spent quite a few years now concentrating on this area and you're obviously quite knowledgable in the treatment of breast cancer. I'm going to put you a little bit on the spot now. My impression is that this is still an area where there's a lot to learn and we're far from being at the point where we know what all the answers are about how to-about the best ways to treat breast cancer.

DR. BRUFSKY:

A. Oh, I -

MR. SIMMONS:

Q. I wonder if you can give me some idea where you think we are in what we need to learn in order to know the optimal way to treat breast cancer?

DR. BRUFSKY:

A. I think we've gotten much better in the last ten or fifteen years. In fact, there's a lot of literature to support that. I mean, I think 15 years ago maybe 60 percent of women

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would have survived ten years with a breast cancer. It's now over 80 to 85 percent.

MR. SIMMONS:

Q. Um-hm.

DR. BRUFSKY:

A. And it's only getting better. And I think that we have achieved agreement that women who are estrogen receptor positive should receive Tamoxifen, women who are positive for the HER2/neu protein should receive Herceptin. There's now a drug called Avastin, there's a whole class of drugs called Biphosphonates I kind of hinted at that probably are going to benefit women with breast cancer. But the issue is a lot of what happens with this is that like in anything in medicine, you know, you're sure of one thing and then all of a sudden you explore it a little bit more deeply and you realize it's a lot more complex than you thought. So, you know, back to your- there's no black and white, it's more kind of greyer or whiter or blacker. And I think it's always, medicine is always an evolution, but I think in general we've done much better than we have 15 or 20 years ago.

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MR. SIMMONS:
Q. Yeah. You were asked some questions about the effect of delaying the start of hormone therapy. And I understood you to say that a matter of weeks might not have any significant impact, but if it were months or years, then the potential for an impact is greater. And I think I took from what you were saying that, and I may be wrong on this, that you were thinking in terms of the time from the surgery and the initial presentation at diagnosis when you were using those time frames?
DR. BRUFSKY:
A. Yes, yes.
MR. SIMMONS:
Q. Okay. And I take it then that there is some research available that you're familiar with that you can use to support that conclusion that from the time of surgery there is kind of an optimal time -
DR. BRUFSKY:
A. You know, there's not a lot of research, actually, interestingly enough.
MR. SIMMONS:
Q. Yes, okay.

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DR. BRUFSKY:
A. Most of the--the reason I say this is that most of the clinical trials, we've gone through this, it's a question that my fellows ask all the time, it's a socratic question that we get all the time.
MR. SIMMONS:
Q. Um-hm.
DR. BRUFSKY:
A. How do we know that starting adjuvant therapy within eight to 12 weeks is appropriate, I mean, why don't we start later or sooner. And the reason most of us say that eight to 12 week period is that most of the clinical trials of adjuvant therapy in cancer have used that eight to 12 weeks window, so most of the trials have started the therapy within eight to 12 weeks. So that's really where we obtained that number from.
MR. SIMMONS:
Q. So the-so there is research and knowledge about what the benefit is if it is started within that window, but not necessarily research out there to say what the effect is if it's started at some different time?

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DR. BRUFSKY:
A. Correct.
MR. SIMMONS:
Q. Would that be a fair statement?
DR. BRUFSKY:
A. The only trials we have, really, that speak to that, at least with hormonal therapy, are a series of trials that were done about 15 or 20 years ago where women received chemotherapy with their Tamoxifen concurrently.
MR. SIMMONS:
Q. Yeah.
DR. BRUFSKY:
A. Or received chemotherapy--or received Tamoxifen after their chemotherapy.
MR. SIMMONS:
Q. Yes.
DR. BRUFSKY:
A. And that chemotherapy was about probably four to six months. So in other words, these were a group of women who had Tamoxifen immediately or four to six months later. And there was no difference in their survival, interestingly enough. But, the problem was all of these women received chemotherapy so you have no

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idea--that's a confounding issue.
MR. SIMMONS:
Q. Right.
DR. BRUFSKY:
A. There was another series of trials where women received Tamoxifen before, with radiation or after radiation. The initial results of those trials showed that the women who received their hormonal therapy at the start of their radiation did better than the women who received it after the radiation, which is a period of about eight weeks. However, on long-term follow up, the initial follow up on that trial was five years, there appeared to be a difference in the people who got it upfront versus out back, is how we called the trial, was the upfront out back trial. But the thing was at 11 years of follow up, at long-term follow up on that trial there was no difference.
MR. SIMMONS:
Q. Um-hm.
DR. BRUFSKY:
A. So, in fact, what we believed upfront, we believed initially turned out not to be the

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case. So in the end of the day I would say that these are the only studies that we really have that, you know, give us any inkling about using therapies sooner as opposed to later in the treatment of cancer.

MR. SIMMONS:

Q. And here we're looking into what I gather to be a fairly unique circumstance where there were retests done in some cases eight years after the original test was done and treatment decisions then made to institute Tamoxifen at that point. Are you aware of any research that's been done that would help us assess the degree of benefit to be expected as a result of the instituting the treatment at that-as late as that?

DR. BRUFSKY:

A. Eight years, no. But in terms of eight years, no, but, in the trial that we kind of quoted in one of these exhibits, I think it's been quoted before -

MR. SIMMONS:

Q. Yeah.

DR. BRUFSKY:

A. We'll just find that. That's the Delozier

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Trial from the Annals of Oncology, I think, if I'm not mistaken.

BROWNE, Q.C.:

Q. 2582.

DR. BRUFSKY:

A. Yeah, 2582. That trial was done with Tamoxifen and I believe that was a delay of a few years.

MR. SIMMONS:

Q. Yes.

DR. BRUFSKY:

A. But more importantly, the MA17 follow-up trial informs us that you can have a delay of up to three years and still have benefit in your hormonal therapy. So the--and the question that I raise is you can have benefit, but the issue that is unresolved right now, is that benefit the same as if you started it upfront.

MR. SIMMONS:

Q. Um-hm.

DR. BRUFSKY:

A. That's the question I think no one can answer right now.

MR. SIMMONS:

Q. So aside from those studies which look at

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starting Tamoxifen up to three years after the original surgery, there is no other research out there to judge the relative effectiveness after -

DR. BRUFSKY:

A. No.

MR. SIMMONS:

Q. - any later than three years and whether starting the Tamoxifen at any particular time after that is more beneficial than the other regime?

DR. BRUFSKY:

A. Correct, no. No.

MR. SIMMONS:

Q. It would seem intuitive that it would be of benefit to do it?

DR. BRUFSKY:

A. Right. But -

MR. SIMMONS:

Q. But the work hasn't been done?

DR. BRUFSKY:

A. - there's just no, there's no studies of women, say, who are eight years out receiving Tamoxifen, no.

MR. SIMMONS:

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Q. No, right, okay. You were shown, I think, three different pathology reports where there were reports from pathologists of having repeated an ER and PR test and some change in results. Now, did I gather correctly that in your experience, in your practice, it's not unknown to repeat an ER and PR test?

DR. BRUFSKY:

A. No, it's not.

MR. SIMMONS:

Q. No. What kinds of circumstances, in your experience, would you normally find the tests to be repeated or even asked for to be repeated?

DR. BRUFSKY:

A. Me asking for a repeat test -

MR. SIMMONS:

Q. Yes.

DR. BRUFSKY:

A. - or them repeating them on their own?

MR. SIMMONS:

Q. Well, both -

DR. BRUFSKY:

A. There's two separate -

MR. SIMMONS:

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Q. - both, you can try both.
DR. BRUFSKY:
A. I think in the circumstance at least what I've been able to find out, because again, I'm not a pathologist, but what I've been able to find out is that again some--occasionally, just like with any system, you know, a buffer was wrong, you know, a buffer was mixed incorrectly or went bad.
MR. SIMMONS:
Q. Um-hm.
DR. BRUFSKY:
A. And their internal controls that they have showed that it wasn't working and so they had to repeat it on a batch of specimens. That happens occasionally. When I want to repeat it, the times I want to repeat it generally are when the clinical picture doesn't fit, so the pathology doesn't fit with the clinical picture, such as someone with lobular cancer having ER negative tumour or someone with a tubular cancer having ER negative tumour, those sort of things. I would ask the test to be repeated in that case.
MR. SIMMONS:

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Q. Yeah. I'll go back to sort of the layman's conception. Looking at this from the outside, people may think looking at a test like this that it should be right the first time and if you repeated it, you should get exactly the same results every time you repeat it. Is--but where you sit as a medical oncologist is that the kind of absolute expectation you have from this test?
DR. BRUFSKY:
A. I would expect it to be 100 percent, but I understand that it's not, like anything, like any system and I know there's going to be a certain level of--there's going to be a certain error rate of any test. No test is 100 percent. You know, I would hope that the rate is 95 percent or above, I would hope that, you know, I get no more than one in 20 or one in 50 like this and that I have to deal with it. And generally from my pathologists it's generally what happens. And if something in my mind--again, because I just see so much breast cancer, and if I suddenly get a string, you know, of five or ten things that suddenly have to be repeated, that's a red flag in my

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mind.
MR. SIMMONS:
Q. Right.
DR. BRUFSKY:
A. That something has to be done.
MR. SIMMONS:
Q. Now, aside from the ten or 15 repeats of the lobular cases that you told us about earlier, have you had other experience with requesting that an ER and PR test be repeated and finding a change in the result that would affect
DR. BRUFSKY:
A. Yes.
MR. SIMMONS:
Q. - the clinical treatment of the patient?
DR. BRUFSKY:
A. Yes. And again, where that happens mostly is in specimens that come from second opinions. So someone that was tested in the lab that maybe has a lower volume comes to me and the clinical picture doesn't fit the test and I'll ask for that to be retested. So you know, for example, someone who comes in very similar in a slightly different way from this case that you talked about with Dr. Hudis before,

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someone comes in with a cancer that just hasn't responded to the therapies like we thought they would and I ask that the--and the tissue block was done, say, five years ago or seven years ago or something, I'll ask for that tissue block to be retrieved and I'll have our pathologist repeat it. And I found occasionally that the test is ER positive where it was negative in the past.
MR. SIMMONS:
Q. And I presume in those cases you would have to report back to the referring institution that there had been a retest and a -
DR. BRUFSKY:
A. Absolutely.
MR. SIMMONS:
Q. - changed result and then it's up to them to determine what they do to investigate from that point, is it?
DR. BRUFSKY:
A. Absolutely, yes.
MR. SIMMONS:
Q. Okay. Now, Ms. Chaytor asked you a number of questions about this already when looking at numbers of retests and changes. And I recall

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you saying this morning that if there was one a month or so that you saw that was a changed result, that wouldn't necessarily raise any alarm bells with you, but if there was a cluster of them, then that might be something you would want -

DR. BRUFSKY:

A. Yeah.

MR. SIMMONS:

Q. - to have looked at further?

DR. BRUFSKY:

A. Yes.

MR. SIMMONS:

Q. But an occasional one here and there wouldn't necessarily trigger any greater concern for you -

DR. BRUFSKY:

A. No, unless they were in something that just made absolutely no sense. I mean, I think that, you know, if I see a test repeated every so often, that's okay. But if I see a test that's negative, even if it's--that should really be positive, that's something that will make me call the pathologist up and ask it to be redone.

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MR. SIMMONS:

Q. So that would be the circumstance that would cause, be more likely to cause you to make an inquiry?

DR. BRUFSKY:

A. Yes.

MR. SIMMONS:

Q. Where it's a case that you expected to be positive and turned out negative, then just to report from the lab that we've redone it, it was -

DR. BRUFSKY:

A. Yes, one that's redone -

MR. SIMMONS:

Q. - originally one thing and the other -

DR. BRUFSKY:

A. - every couple of months or whatever, no, I would not have a problem with it. But if suddenly there are four or five that the test was redone, I would get on the phone and call the pathologist, yes.

MR. SIMMONS:

Q. Okay. Now, you did tell us about the retesting that was done at, I gather, at your institution for these lobular cases about ten

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years ago, you say?

DR. BRUFSKY:

A. They weren't only lobular, they were a bunch of different kind of cases besides lobular, but, yeah.

MR. SIMMONS:

Q. Okay.

DR. BRUFSKY:

A. Again, I don't recall the details precisely. It was a long time ago.

MR. SIMMONS:

Q. And did I understand correctly that there was only ten or 15 cases that were retested?

DR. BRUFSKY:

A. There wasn't a lot, that's correct.

MR. SIMMONS:

Q. Okay. And what was it that triggered the decision to do a retest of that?

DR. BRUFSKY:

A. I think there were a number of cases actually brought to our attention by a pathologist who had recently been hired who said, gosh, you know, these are lobular, this is a lobular cancer, this is a tubular, shouldn't these be positive, let's go back and recheck some

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things.

MR. SIMMONS:

Q. Right. So the retesting then that was done was of the specific cases that were called into question, was it?

DR. BRUFSKY:

A. Correct.

MR. SIMMONS:

Q. Was there any consideration given then to the possibility of there being some broader underlying reason why these tests were changing?

DR. BRUFSKY:

A. Yes, there were.

MR. SIMMONS:

Q. And any exploration of doing any broader retesting of cases

DR. BRUFSKY:

A. Yes, and I believe there had been--again, I was not as involved in that back then.

MR. SIMMONS:

Q. Yes.

DR. BRUFSKY:

A. But there was some broader analysis of the lab.

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MR. SIMMONS:
Q. Yes.
DR. BRUFSKY:
A. It was felt that it was a limited, it was a situation limited to a particular point in time.
MR. SIMMONS:
Q. Okay. I'm just curious, I have to ask you, was there any public announcement at the time?
DR. BRUFSKY:
A. No, there was-of this, no. There was not of this particular thing, I don't think so. I don't recall off the top of my head.
MR. SIMMONS:
Q. Okay. And you have told us that the patients whose samples were retested were notified of that fact?
DR. BRUFSKY:
A. Yes.
MR. SIMMONS:
Q. I gather you said that before they were notified, the cases were considered to assess the potential for there to be impact on their treatment?
DR. BRUFSKY:

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A. Yes, only for the reason that was done was that, again, the question someone would--we wanted to kind of have a plan for each individual patient before we told them -
MR. SIMMONS:
Q. Right.
DR. BRUFSKY:
A. - whether they needed to be retested or not.
MR. SIMMONS:
Q. So you wanted to be in a position to answer the questions you'd expect them to have
DR. BRUFSKY:
A. Correct.
MR. SIMMONS:
Q. - before you went to them first and raised the issue?
DR. BRUFSKY:
A. Correct.
MR. SIMMONS:
Q. Yeah. Now, was there ever any--did anyone ever figure out what had happened to cause the tests to be changed once they were redone?
DR. BRUFSKY:
A. I think they did. I think--again, I don't remember off the top of my head because I'm not a pathologist.
MR. SIMMONS:
Q. Right.
DR. BRUFSKY:
A. But I do recall that there were some things that were found in the system.
MR. SIMMONS:
Q. Yes, okay.
DR. BRUFSKY:
A. That were altered.
MR. SIMMONS:
Q. Do you know if there was anything done then to contact those patients and explain to them what had happened and why the test results were changed or would you know?
DR. BRUFSKY:
A. I don't know off the top of my head. All I remember, because my role in it was to contact the patient, so that was my, that's what I remember of it.
MR. SIMMONS:
Q. Right. Do you have any recollection of making any follow-up contact with them once any investigation -
DR. BRUFSKY:

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A. Well, the vast majority of them were my own patients, so they kept coming to see me.
MR. SIMMONS:
Q. Okay. You've given us a very good explanation of how you use your cancer registry data for quality control purposes in doing a study, a mandated study each year in which you identify a topic and go in and look at your statistics. Aside from that is there anything done in your institution on an annual or other basis to track and report things like the percentage of ER/PR tests that are positive -
DR. BRUFSKY:
A. Yes, we've had -
MR. SIMMONS:
Q. - and those sorts of things?
DR. BRUFSKY:
A. It's not--we do these projects on our own, so we've been doing the percent of tests that are ER positive, just in general, you know, positive, just--yeah, we do that on our own.
MR. SIMMONS:
Q. Yes. Okay, thank you, very much. That's all the questions I have for you.
DR. BRUFSKY:

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A. You're welcome. Thank you.
COMMISSIONER:
Q. Mr. Browne?
BROWNE, Q.C.:
Q. Thank you, Commissioner.
DR. ADAM BRUFSKY, EXAMINATION BY PETER BROWNE, Q.C.
BROWNE, Q.C.:
Q. Thank you, Commissioner. Good afternoon, Doctor. My name is Peter Browne. I represent a number of the individual physicians, both pathologists and oncologists who have testified here. Just to follow up on some of the questions both Mr. Simmons just asked you and earlier Ms. Chaytor. Firstly, Registrar, if we could have Exhibit P-2617, please? You had mentioned that in your training you, I guess, generally use ten percent?
DR. BRUFSKY:
A. Yes.
BROWNE, Q.C.:
Q. And that was your understanding?
DR. BRUFSKY:
A. Correct.
BROWNE, Q.C.:
Q. This is an article, I'm not sure if you've

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seen this article previously, by Dr. Layfield.
DR. BRUFSKY:
A. Um-hm.
BROWNE, Q.C.:
Q. And others. And it's a survey of, you'll just see here now in the abstract portion, they surveyed 300 laboratories within the United States. And I've actually put this out previously to Dr. Dabbs. Now, he thought they may have included some labs within Canada, but it clearly indicates the -
DR. BRUFSKY:
A. Oh, yes, the United States.
BROWNE, Q.C.:
Q. United States. And if we go to--I'll just scroll down here now. Just bear with me here. It's actually highlighted. You'll see the highlighted areas there, Doctor, and it shows--just trying to see now where this indicates. And there's probably an earlier comment. But it does indicate cutoff points.
DR. BRUFSKY:
A. Right.
BROWNE, Q.C.:
Q. Of 30 percent in some of the labs. Let me

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just see what my copy here--I'll just find one, ninety-three here. Just bear with me, I'm just trying to--oh, here it is lower down. I don't seem to have the section here. Let me just--oh, here we go. And there's earlier points here. He says, "The oncologists vary significantly in the threshold they use to classify specimens as positive. The reported cutoff for positivity vary from any staining to a cutoff point of at least 30 percent of nuclei."
DR. BRUFSKY:
A. Um-hm.
BROWNE, Q.C.:
Q. So at least some of the responses here, and there is, you think, if you look back at Table 7, an indication, as well, albeit a--and I don't think there was actually a very good response rate from all the--I think they surveyed 300 and I think -
DR. BRUFSKY:
A. Right.
BROWNE, Q.C.:
Q. - in total they only got -
DR. BRUFSKY:

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A. Twenty-seven.
BROWNE, Q.C.:
Q. - 80 responses in total. But nevertheless, it does indicate that some of the labs, at least one of the respondents here, not--shouldn't say labs. Some of the oncologists were using a 30 percent cutoff within the United States.
DR. BRUFSKY:
A. Right, seven of--two of 27.
BROWNE, Q.C.:
Q. Yeah. So again, while it's -
DR. BRUFSKY:
A. Oh, there's some distribution, absolutely. Because again, this was done when the tests were negative and the paper from Allred, which I think really -
BROWNE, Q.C.:
Q. Yes.
DR. BRUFSKY:
A. - this paper, really which established the ten percent for most people had just really been--had come out, I think, in '99. Actually, let's take a look.
BROWNE, Q.C.:
Q. Yes, I think Allred and Harvey -

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DR. BRUFSKY:
A. Allred paper came out in '99. And again, the rate-it was a new test. The Allred paper came out in '99. The way that medical oncology information percolates down through most oncologists is not--most oncologists are really conservative and so--you know, but that's not surprising that a couple of oncologists would say 30 percent.
BROWNE, Q.C.:
Q. It wouldn't be surprising that this move towards ten percent occurred much later, say, 2000, 2001 in terms of -
DR. BRUFSKY:
A. I would say that's about right, I would say in that area. I mean, again, but very--I mean, when I trained, and again, I trained around the time this was done, we thought it was ten percent. We never thought it was 30.
BROWNE, Q.C.:
Q. Thank you. Again just to go back on a question Mr. Simmons asked you about the retest of these 10 to 15 patients, and you mentioned some of these patients were lobulars and tubulars, and you mentioned in response

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that you were - because most of these patients were your patients that the pathologist had identified. Did you have the results in hand when you contacted the patients to inform them?
DR. BRUFSKY:
A. The new result?
BROWNE, Q.C.:
Q. Yes, the retest result.
DR. BRUFSKY:
A. The retest result. I don't remember off the top of my head. I can't remember, obviously. I'd have to really think about it and go back to the list. I think what I had was - I did not have the retesting, but I had - when we talked to them, I had the fact that their tests were not - I'm trying to think off the top of my head. I just don't remember. I can't really tell you one way or the other.
BROWNE, Q.C.:
Q. What was the general response of the patients, do you recall, in terms of -
DR. BRUFSKY:
A. They were happy that they were told. The vast majority - if I recall this correctly, there

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was maybe one person out of, like, the 10 or 15 that I recall that would have had her treatment changed. So the rest of them were, like, thanks for doing this, you know, and we explained to them it would have made no difference in their therapy. One or two we couldn't find, they'd moved out of the area, so it was hard to find the people.
BROWNE, Q.C.:
Q. And again there was some questioning, both from the Commissioner and from Ms. Chaytor, on data collection and you had mentioned that, I guess, you compile your own data within -
DR. BRUFSKY:
A. Over and above that data that's required by the American College of Surgeons.
BROWNE, Q.C.:
Q. But within sort of the oncology side, you had mentioned, I think, that there is sort of data collection on the pathology side as well.
DR. BRUFSKY:
A. Yes.
BROWNE, Q.C.:
Q. Is there any linkages that occur to sort of say, okay, to compile all this information to

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use - I'm sure the pathologists are collecting information that would be of use to you and vice versa. Is there sort of that interchange that occurs as well at some point?
DR. BRUFSKY:
A. Well, we're actually trying - you know, that's a very interesting question. We have - data is collected at the tumour registry, and data is collected by the pathologists on their pathology report. Theoretically, that data should be merged.
BROWNE, Q.C.:
Q. Right.
DR. BRUFSKY:
A. We have spent the last five years negotiating to try to figure out how to merge it because there are two separate computer systems, and I think that's the - even if they're two separate computer systems, it seems like a fairly trivial exercise to merge two datasets.
BROWNE, Q.C.:
Q. We've heard a lot about that. The Commissioner has heard a lot about that here.
DR. BRUFSKY:
A. Right, it's a lot more - it's a lot less of a

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trivial exercise than you think when you start thinking about doing it.

BROWNE, Q.C.:

Q. But for effective patient care, do you think that that would be a very useful exercise?

DR. BRUFSKY:

A. Absolutely, yes, and I've fought for that in our institution for many years, yes.

BROWNE, Q.C.:

Q. Because Dr. Dabbs talked about on his side the use of metrics and so on in terms of tracking. That again would be something very useful for oncology.

DR. BRUFSKY:

A. Oh, absolutely, I agree, and we tried to get metrics from our registry data, but the problem is the registry data is always at least a couple of months behind, so it's not in real time.

BROWNE, Q.C.:

Q. Again I think both Mr. Simmons and Ms. Chaytor asked you about your tumour board, how that operates and so on. When patients are discussed there, are they discussed with - I guess, their clinical histories reviewed, the

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tumour, the tumour size, staging, and all that is discussed. Are there recommendations that come out to the particular oncologists?

DR. BRUFSKY:

A. Yes.

BROWNE, Q.C.:

Q. And those are recommendations, and is the purpose of the recommendations then for the oncologist to meet with the patient -

DR. BRUFSKY:

A. Yes.

BROWNE, Q.C.:

Q. And discuss what sort of treatment should be given?

DR. BRUFSKY:

A. Yes, but again we can't - because of our volumes, we can't do it for everybody.

BROWNE, Q.C.:

Q. Correct.

DR. BRUFSKY:

A. So we can only do it for a certain percentage of our patients, but, yes.

BROWNE, Q.C.:

Q. And I guess you have some general familiarity with what occurred here at Eastern Health in

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terms of the offering of both Tamoxifen and aromatase inhibitors to patients. Would it be useful, do you think, in this setting to as well have - if the data would be compiled, information regarding outcomes? There are oncologists who have talked about that -

DR. BRUFSKY:

A. Yes.

BROWNE, Q.C.:

Q. As being an important feature of this whole exercise is to know what sort of -

DR. BRUFSKY:

A. I think that would be an incredibly important feature.

BROWNE, Q.C.:

Q. Because it will address this whole issue, this question that remains unanswered, you said, in terms of what effect does this have on patients?

DR. BRUFSKY:

A. Correct, and I think that it's a very - the absolute effect would be a very - I think, a very useful item, not only for you here in Newfoundland, but everybody who studies breast cancer, we would really like to know what

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those results were.

BROWNE, Q.C.:

Q. Thank you, doctor. That's all my questions.

DR. BRUFSKY:

A. You're welcome.

THE COMMISSIONER:

Q. Mr. Pritchett, any questions?

MR. PRITCHETT:

Q. No questions, Commissioner.

THE COMMISSIONER:

Q. Ms. Newbury.

DR. ADAM BRUFSKY - EXAMINATION BY MS. JENNIFER NEWBURY

MS. NEWBURY:

Q. Good afternoon, Doctor. My name is Jennifer Newbury, and I represent the Newfoundland and Labrador Division of the Canadian Cancer Society. I want to ask you first of all about statistics for ER and PR results, and in particular if you are familiar with the breakdown of percentages of ER negative, PR positive, ER negative, PR positive, etc. Is that something that you -

DR. BRUFSKY:

A. I think I can give a general idea.

MS. NEWBURY:

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Q. Okay, starting with ER negative, PR positive?
DR. BRUFSKY:
A. Probably 5 percent or less.
MS. NEWBURY:
Q. And ER negative, PR negative?
DR. BRUFSKY:
A. Okay, so of all - okay, I've got to think about this. It depends if you're pre or post menopausal, but I'll just give you a general idea.
MS. NEWBURY:
Q. Sure.
DR. BRUFSKY:
A. It's probably about 35 to 40 percent.
MS. NEWBURY:
Q. 35 to 40 percent would be -
DR. BRUFSKY:
A. In my practice.
MS. NEWBURY:
Q. ER negative and PR negative?
DR. BRUFSKY:
A. Both negative.
MS. NEWBURY:
Q. Okay, and is there a difference? You just indicated that it would depend on pre or post

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menopausal.
DR. BRUFSKY:
A. Generally post-menopausal women have a lower proportion of ER/PR positives. Probably again with my practice, just looking at my practice off the top of my head, probably 20 percent.
MS. NEWBURY:
Q. Okay, and ER positive, PR negative?
DR. BRUFSKY:
A. ER positive, PR negative, probably - again overall, the total percentage of ER positives completely - because I tend to not use the PR any more.
MS. NEWBURY:
Q. Okay.
DR. BRUFSKY:
A. But ER positive probably in my practice, pre-menopausal, 50 percent, post-menopausal, 60 percent, and of those maybe 20 percent are ER positive, PR negative.
MS. NEWBURY:
Q. 20 percent of those are ER positive, PR negative, regardless of whether pre or post menopausal?
DR. BRUFSKY:

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A. Yes, yeah.
MS. NEWBURY:
Q. And is that something that your institution monitors just to see if your rates are in line with -
DR. BRUFSKY:
A. Yes.
MS. NEWBURY:
Q. And what group within your institution would monitor that?
DR. BRUFSKY:
A. It would be the cancer committee that I had discussed, the ACS Cancer Committee.
MS. NEWBURY:
Q. And you were just mentioning that there are two datasets, I think, between the cancer registry and the pathologists?
DR. BRUFSKY:
A. Correct.
MS. NEWBURY:
Q. They each keep a - is there a duplication of the data?
DR. BRUFSKY:
A. There is.
MS. NEWBURY:

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Q. Okay, and are there any instances where neither keeps data on significant -
DR. BRUFSKY:
A. Generally, between one or the other, we get most of the significant data points we want. The issues that we run into are that the pathology data tends to be more accurate in general when we do audits of it.
MS. NEWBURY:
Q. Okay.
DR. BRUFSKY:
A. Than the registry data.
MS. NEWBURY:
Q. And would oncologists have access to the information for the pathologists?
DR. BRUFSKY:
A. Yes.
MS. NEWBURY:
Q. That they collect, and the cancer registry as well, obviously?
DR. BRUFSKY:
A. Yes.
MS. NEWBURY:
Q. You just mentioned, and you'd mentioned earlier this morning, that in your view ER

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positivity is not a predictive marker with respect to response to Tamoxifen?

DR. BRUFSKY:

A. Not as much as I think it was previously believed to be.

MS. NEWBURY:

Q. Okay, and when did that learning -

DR. BRUFSKY:

A. Within the last two years, especially the data that I showed you from the San Antonio Breast Symposium last year.

MS. NEWBURY:

Q. Okay, and that applies to other types of hormonal treatments as well?

DR. BRUFSKY:

A. Yes.

MS. NEWBURY:

Q. Okay, and does this mean that generally an ER negative PR positive patient would not be offered hormonal therapy?

DR. BRUFSKY:

A. It depends on the degree of PR positivity. I think that if a woman comes in like I - say, she's PR positive 5 percent, I personally would not offer her hormonal therapy. There

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would be oncologists who would, and again there's a lot of debate, but if I were presented that sort of patient in the tumour board, I would say do not offer her hormonal therapy.

MS. NEWBURY:

Q. And that's perhaps consistent with how you would treat an ER positive patient as well? I think your evidence is that -

DR. BRUFSKY:

A. Correct.

MS. NEWBURY:

Q. Even at ER 5 percent, you wouldn't necessarily offer -

DR. BRUFSKY:

A. Right. Where the question becomes is the very rare patient, and I think Dr. Dabbs may have talked about in our institution.

MS. NEWBURY:

Q. Uh-hm.

DR. BRUFSKY:

A. The very rare patient who is ER negative and PR, say, 30 or 40 percent, that is a patient that, I think, not a lot of us know what to do with.

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MS. NEWBURY:

Q. And you say rare because it's not a frequent occurrence?

DR. BRUFSKY:

A. It's not a very frequent occurrence at all.

MS. NEWBURY:

Q. And how would you typically respond if you came across such a patient?

DR. BRUFSKY:

A. I probably would want the test - I probably would want her ER/PR retested.

MS. NEWBURY:

Q. Okay, and if you did that, and found out that the results were valid, is there any guideline as to how that particular patient would be treated?

DR. BRUFSKY:

A. I think some - there are guidelines. I'm not sure how much I trust them. I probably - if that were the case, I probably would give that particular woman an anti-hormonal treatment, yes.

MS. NEWBURY:

Q. Okay.

THE COMMISSIONER:

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Q. Excuse me, but while we're on the topic, you indicate that this - not just your evidence, but evidence of other people here, have suggested - at least I'm taking that evidence to suggest that the question of PR positivity has been somewhat like the pendulum swinging.

DR. BRUFSKY:

A. Yes.

THE COMMISSIONER:

Q. Back and forth over time. So what you have been responding, I take it, is in light of the research that has become available over the last couple of years. So can I also take it that, say, in 2002 or 2003, then the likelihood of being treated for an ER negative PR positive would be higher than it is now?

DR. BRUFSKY:

A. Yes, that is exactly correct.

MS. NEWBURY:

Q. And can you indicate sort of the general trends that you're familiar with in the United States or elsewhere, if you're familiar, when would the ER negative PR positive patient have first been offered typically hormonal treatment?

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DR. BRUFSKY:
A. Probably around the time anti-hormonal - IHCs were being done. So even in the days of hormone binding assays, I think.
MS. NEWBURY:
Q. So mid to late 1990s for sure this was being done.
DR. BRUFSKY:
A. Yeah.
MS. NEWBURY:
Q. And it wasn't until a couple of years ago that that -
DR. BRUFSKY:
A. And it's still - in the minds of some people, it's still not totally - I mean, in my mind it is, but in the minds of other prominent oncologists, they still treat PR positive patients.
MS. NEWBURY:
Q. Yes, and again this is a small group because you've indicated --
DR. BRUFSKY:
A. It us.
MS. NEWBURY:
Q. Less than 5 percent would fall into that

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category?
DR. BRUFSKY:
A. Yes.
MS. NEWBURY:
Q. So there's not a whole lot of opportunity, I guess, to -
DR. BRUFSKY:
A. Correct.
MS. NEWBURY:
Q. Continually deal with these patients. In terms of the hormonal treatment for positive - ER positive patients, I think it's your evidence that the rate of positivity wouldn't affect whether or not hormonal treatment is offered?
DR. BRUFSKY:
A. No, I think as long as - at least in my mind, if it's over 10, it should be offered.
MS. NEWBURY:
Q. And I think you were commenting this morning on whether or not the rate of positivity would affect other forms of treatment, such as chemotherapy.
DR. BRUFSKY:
A. Yes.

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MS. NEWBURY:
Q. I wonder if you could just review what the characteristics are of a patient who would receive hormonal therapy but would not receive chemotherapy?
DR. BRUFSKY:
A. A typical patient in the days before Oncotype DX, because now we have this Oncotype DX test, which is making a lot of the decisions for us, but I would say that generally a woman who walks in, 60 years old, 1.2 centimetre breast cancer, kind of small in our business, has an ERH score of 250, has a Nottingham score of six, five or six, that is lymph node negative, that's a typical patient I would give hormonal therapy only to.
MS. NEWBURY:
Q. And would such a patient receive any radiation?
DR. BRUFSKY:
A. If she did not have a mastectomy, yes.
MS. NEWBURY:
Q. Okay.
DR. BRUFSKY:
A. Almost all women receive radiation.

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MS. NEWBURY:
Q. And would an ER negative PR positive patient be in the same category of if they meet the, you know, 60 years of age as an example?
DR. BRUFSKY:
A. Sixty years of age, ER negative, PR 5 percent, low PR, I would say that woman would likely get chemotherapy. We'd talk about it, but she may get chemotherapy.
MS. NEWBURY:
Q. How about if that same patient was ER negative PR 60 or 40?
DR. BRUFSKY:
A. What I would do in that case - thankfully we have Oncotype DX in the United States. I would do an Oncotype DX on her to make my decision, but assuming she did not - we did not have that test, that would be a very tough question, and I think - you know, I remember the kinds of - I've had a few of those in my career, and I would sit and I would - I mean, there's a lot of other instances that will go into this. I would tell the patient of the uncertainty concerning the benefit of hormonal therapy in her case, and it is likely that

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that woman would get both. I would probably treat her with chemo and hormonal therapy.

MS. NEWBURY:

Q. Okay, and would there be any other differences in, for example, the types of chemotherapy or the duration of chemotherapy based on the rate of positivity, either ER positivity or PR positivity, or some combination of that?

DR. BRUFSKY:

A. If it's over 10 percent, I consider it ER positive for the sake of discussion. I would not necessarily change someone's chemotherapy. Chemotherapy changes for me have more to do with the type and number of cycles, for example, have more to do with the size of the cancer and the number of lymph nodes involved.

MS. NEWBURY:

Q. Dr. Brufsky, you've indicated that, I believe, it's the Cancer Program Standards require that 10 percent of cases be reviewed by the tumour board?

DR. BRUFSKY:

A. Correct.

MS. NEWBURY:

Q. Or multidisciplinary committee.

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DR. BRUFSKY:

A. Uh-hm.

MS. NEWBURY:

Q. That's one and the same, I take it, is it?

DR. BRUFSKY:

A. Yes.

MS. NEWBURY:

Q. Okay, and of those, 75 percent would be reviewed prospectively. I'm wondering are there any criteria for how exactly those cases are brought to the tumour board?

DR. BRUFSKY:

A. No. It used to be every case, but again as we got bigger, it couldn't be. What we try to do is have people bring their most difficult cases to the board or cases that present a conundrum.

MS. NEWBURY:

Q. Uh-hm.

DR. BRUFSKY:

A. For example, something that's just unusual, doesn't happen all the time, and really people - cases that people need advice for.

MS. NEWBURY:

Q. Okay.

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DR. BRUFSKY:

A. That is out of the ordinary.

MS. NEWBURY:

Q. Is there any component for bringing some randomly selected cases?

DR. BRUFSKY:

A. We don't bring randomly selected cases, but what we've tried to do over the years is that when - because I help run the tumour board, and so - with the surgeon, and so what we try to do over time is if the cases get too esoteric, is go back and always have some that are garden variety that we just selected.

MS. NEWBURY:

Q. Okay.

DR. BRUFSKY:

A. That we have a fellow - one of the fellows pick.

MS. NEWBURY:

Q. So you try to at least cover off the different bases there?

DR. BRUFSKY:

A. Right, but it's not random which is - we've really debated that, actually, whether they should be random to get a random sampling, but

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they're not - I have to admit it's not a random sample.

MS. NEWBURY:

Q. And is the purpose for trying to get some of the more garden variety cases to make sure that quality control for those types of cases?

DR. BRUFSKY:

A. There's not only a quality control function, but there's educational function for the staff as well.

MS. NEWBURY:

Q. Right, okay, and when a case is brought to the tumour board, how does that work, how does the case get presented to the board?

DR. BRUFSKY:

A. So we have a listing that goes out to everybody, the four to five cases per week that we do.

MS. NEWBURY:

Q. Uh-hm.

DR. BRUFSKY:

A. It obviously doesn't list the patient's name for privacy reasons, but it lists the case and what the question that we want discussed is.

MS. NEWBURY:

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Q. Uh-hm.
DR. BRUFSKY:
A. Then what happens is that it goes to the radiologist, the pathologist, the medical oncologist, and the surgeon that's involved in the case.
MS. NEWBURY:
Q. Okay.
DR. BRUFSKY:
A. The pathology is pulled and computerized, so there's photo micrographs taken. The mammograms are digitized, or whatever films we have, be they MRIs, are digitized, and then they're presented. Usually we try to get one of the junior faculty or the fellows to present the cases, but occasionally the senior people do it as well, and you'll present the case. You'll do a case history and you'll present the pathology, or you'll present the mammography or whatever, MRIs, and then we'll discuss the MRIs. Then we'll go to the pathology and present a photo micrograph and we'll discuss that. Then we'll have a discussion of whatever issue has come up. If the issue involves the pathology, we'll

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discuss the pathology, or some strange thing that happened with that - you know, just an example of some acute quality controls that happen, just to give you an example of what happens. One thing that we've tried to do is - this used to happen, doesn't happen as much any more, when someone repots micro-calcifications in a breast, will stick a wire in and the surgeon will cut around the wire and then the specimen will be mammogrammed to make sure the calcifications are in the specimen. So there will be cases where occasionally the wire will come out, or occasionally, you know, how often are we really getting all the micro calcifications, the mammogram - we'll present a case - even though the radiologists do their own quality control on that, we'll bring one of those cases to everybody just to make sure that everybody is aware of this sort of thing.
MS. NEWBURY:
Q. Right.
DR. BRUFSKY:
A. So the information is spread across all disciplines.

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MS. NEWBURY:
Q. And that's the educational component?
DR. BRUFSKY:
A. That's the educational component, which is also a quality component as well.
MS. NEWBURY:
Q. Right, sure, and in terms of the people participating in the presentation of the case, you indicated that usually a junior fellow would present the case?
DR. BRUFSKY:
A. Or whoever the doctor who takes care of the patient is, the senior fellow, or me, or whatever.
MS. NEWBURY:
Q. And is there a practice that at least one of the actual treating physicians for the patient be present?
DR. BRUFSKY:
A. Oh, absolutely, yes, the treating physician has to be there or we won't present their case.
MS. NEWBURY:
Q. Okay, and what is the rationale for that?
DR. BRUFSKY:

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A. Again because the recommendations have to be given to the patient, so they have to be given by the treating physician.
MS. NEWBURY:
Q. Okay, and would, say, if that primary treating physician or one of the treating physicians for the patient is not there, would there be any other appropriate means of communicating that with the patient.
DR. BRUFSKY:
A. We wouldn't present the case that day.
MS. NEWBURY:
Q. Okay.
DR. BRUFSKY:
A. The rare times when - say, there are two treating physicians, say, a medical oncologist and a surgeon.
MS. NEWBURY:
Q. Uh-hm.
DR. BRUFSKY:
A. And the medical oncologist is there, but the surgeon isn't, so the surgeon will communicate with the medical oncologists.
MS. NEWBURY:
Q. So the purpose -

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DR. BRUFSKY:
A. There has to be - somebody there who takes care of the patient has to be present, or we don't present that case.
MS. NEWBURY:
Q. Right, and is it often the case that more than one of the patient's treating physician would be at the tumour board?
DR. BRUFSKY:
A. You mean, one of the patient's treating physicians has to be at the tumour board? Yes.
MS. NEWBURY:
Q. I'm just saying - I'm wondering if there are instances or whether there's a -
DR. BRUFSKY:
A. Where a patient is presented where there's nobody treating the patient at the tumour board?
MS. NEWBURY:
Q. No, I'm just wondering if there's ever a situation or a practice or a guideline that more than one of the patient's physicians be at that? Do you try to get -
DR. BRUFSKY:

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A. We don't have formal guidelines, but we definitely - we, the leaders of the tumour board, are not happy when a treating physician is not there, okay.
MS. NEWBURY:
Q. Okay, so -
DR. BRUFSKY:
A. We generally - it's not a formal rule.
MS. NEWBURY:
Q. Right.
DR. BRUFSKY:
A. But generally more often than not, all the treating physicians involved with the patient's care are there.
MS. NEWBURY:
Q. So that's encouraged, I guess?
DR. BRUFSKY:
A. Oh, it's very strongly encouraged, yes
MS. NEWBURY:
Q. Strongly encouraged, okay, thank you. At the time the case is presented to the tumour board, is there an expectation that all sort of up to date information pertaining to the patient, the current, I guess, comorbidity is the term that's used -

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DR. BRUFSKY:
A. Yes.
MS. NEWBURY:
Q. All of that information is available at that time?
DR. BRUFSKY:
A. Yes, and if we do not have, for example, the photo micrographs, or the pathology, or the reproductions of the radiology, we won't present the case until that's done.
MS. NEWBURY:
Q. And in terms of the prospective cases, and that would be 75 percent of the 10 that are reviewed by the tumour board, are there any timelines considering that it's dealing with how the patient will be treated in the future?
DR. BRUFSKY:
A. There are guidelines. That's why -
MS. NEWBURY:
Q. As to how quickly that has to be brought?
DR. BRUFSKY:
A. Right, and so that's always been an issue. Again, when we have a breast evaluation centre and we can do 10 or 15 cases quickly every week, like some breast programs, we did them

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all, whatever came in that week. But as we got bigger--as we got larger, we had to go away from the totally prospective way of doing it. So in other words, again, if the pathologists and radiologists--not pathologists, but for example, if you do a prospective case and something is missing, either the attendings or the pathology radiology, that just would not be one of the prospective ones we did that day.
MS. NEWBURY:
Q. Okay.
DR. BRUFSKY:
A. So for the prospective ones, they have to be done within, you know, the time of the treatment, for example, you know, a patient's two weeks post-operative. She sees me in my clinic. I'll present her that next Thursday at our breast conference. So that's within three weeks basically and we try to encourage that for prospective cases at least.
MS. NEWBURY:
Q. So ultimately, if for whatever reason the physician treating the patient or all information wasn't available for the tumour

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board, it would not cause any delay in the treatment of that patient? You would just not deal with that case as a prospective quality review?

DR. BRUFSKY:

A. We just wouldn't deal with it as a prospective--we'd present it another week, but it wouldn't be considered one of our prospective cases.

MS. NEWBURY:

Q. So in the interim, the patient would have met with his or her treating physicians and would have been treated accordingly and then in a couple of weeks when you do bring the case to the board, you will review perhaps the -

DR. BRUFSKY:

A. Correct, or occasionally we won't have time to get to the case and so all the physicians will be there and will discuss it kind of on the side anyway.

MS. NEWBURY:

Q. Okay. You were giving evidence just a few minutes ago about whether or not you would see a red flag if there was a repeat test for ER/PR once every couple of months and you

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didn't see that that would really be a problem, and I think your number of cases per year is about 350. I'm just wondering if there would be any one monitoring those same types of trends, taking into account all of the 1,000 cases per year that are seen at your institution?

DR. BRUFSKY:

A. So the people that would be responsible for that would be the pathologists generally.

MS. NEWBURY:

Q. Okay.

DR. BRUFSKY:

A. So it wouldn't be the medical oncologists. We would do that on an individual basis.

MS. NEWBURY:

Q. Okay, and would they be doing that in a formal sort of manner?

DR. BRUFSKY:

A. The pathologists do. The medical oncologists do not.

MS. NEWBURY:

Q. Okay.

DR. BRUFSKY:

A. Outside of--again, if there were a trend that

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was seen in either the cancer registry or by some QA that the cancer committee had done, that's how these things would be picked up.

MS. NEWBURY:

Q. Okay. So the cancer registry might be monitoring such trends in addition to what the pathologists are doing?

DR. BRUFSKY:

A. Yes.

MS. NEWBURY:

Q. Okay, and who within the cancer registry would have the knowledge and expertise to know what to look for?

DR. BRUFSKY:

A. Right, and so that's a good point, so what would happen is that, again, we would go over certain--it would depend if that were the QA section of that year. So there was--if we decided to look at breast cancer that year, we would have one of the chief registrars, who's familiar with the registry, as well as one of the members of the cancer committee do the project together.

MS. NEWBURY:

Q. Okay.

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DR. BRUFSKY:

A. And so they would--the person, the member of the cancer committee who have the expertise to help out the tumour registrar.

MS. NEWBURY:

Q. Okay. So you would perhaps have an oncologist there who could -

DR. BRUFSKY:

A. Correct.

MS. NEWBURY:

Q. - help to define what the parameters are for that -

DR. BRUFSKY:

A. Or if it was a surgical outcome, it would be a surgeon, etcetera.

MS. NEWBURY:

Q. Right, okay, and the person in the cancer registry that would be involved in this project, what is the--typically, what are the qualifications for that individual?

DR. BRUFSKY:

A. So there is a specific registrar's program. I think it's a -

MS. NEWBURY:

Q. Okay.

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DR. BRUFSKY:
A. There's a specific registrar's program. It's actually outlined in the exhibit.
MS. NEWBURY:
Q. Okay.
DR. BRUFSKY:
A. So it determines the qualifications of this person.
MS. NEWBURY:
Q. Okay, and that's outlined in the cancer program requirements?
DR. BRUFSKY:
A. Manual, yeah.
MS. NEWBURY:
Q. Thank you. I think you mentioned earlier that you might, on occasion, repeat a retest of a pathology test result that may have initially been done about five years ago, if the patient wasn't responding as expected. First of all, is that sort of an example, does that relate to an ER/PR--well, breast cancer patient?
DR. BRUFSKY:
A. It could be ER/PR breast cancer or it could be HER2/neu for breast cancer. Those are the ones that are most common that we repeat.

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MS. NEWBURY:
Q. Right, and could you elaborate on what you mean by the patient doesn't respond as expected?
DR. BRUFSKY:
A. So like the example that was shown before in the exhibit, say somebody had been on chemotherapy and just was not responding, most women with breast cancer, with metastatic breast cancer, would generally respond to something for a little bit of time.
MS. NEWBURY:
Q. Right.
DR. BRUFSKY:
A. And if they respond to nothing, then you have to question, at least I do and I teach my fellows too as well, sometimes you have to question the underlying assumptions.
MS. NEWBURY:
Q. Okay.
DR. BRUFSKY:
A. Because you're trying to do what's best for the patient.
MS. NEWBURY:
Q. Sure.

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DR. BRUFSKY:
A. And again, occasionally, not commonly, you will get a result that just was not correct, and I'll repeat the test, and occasionally it would be positive and we'll treat someone and they will respond.
MS. NEWBURY:
Q. And what types of patients, in terms of ER/PR, may not respond to chemotherapy?
DR. BRUFSKY:
A. If you're strongly ER/PR positive. So if you're, you know, ER, your A score is 260-270, something like that.
MS. NEWBURY:
Q. So then a positive--an ER, strong ER/PR positive patient may not respond as expected to chemotherapy?
DR. BRUFSKY:
A. Correct.
MS. NEWBURY:
Q. And what sort of a time frame would you start to notice those trends? I mean, how long would you be looking at -
DR. BRUFSKY:
A. It really depends on the patient. I mean, I

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think that if someone, you know, had disease in her lungs or liver, like the--I mean, this was a good example. I mean, this woman took several years or several different regiments of chemo, I think four or five.
MS. NEWBURY:
Q. This is Ms. Deane, is it, the case that Dr. Hudis was -
DR. BRUFSKY:
A. Yes, Peggy Deane.
MS. NEWBURY:
Q. Yes.
DR. BRUFSKY:
A. And this is when her oncologist finally e-mailed somebody, a colleague of hers at Sloan-Kettering, you know, and said, you know, "what else is there available?" and that's when this kind of came up.
MS. NEWBURY:
Q. Okay. So potentially, in that case, it may have been noted at some point that the patient wasn't responding to chemotherapy as she might -
DR. BRUFSKY:
A. Should have.

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MS. NEWBURY:
Q. - otherwise have been expected?
DR. BRUFSKY:
A. Right. It also comes out in HER2/neu testing, which is similar to this in some ways. In HER2/neu testing, someone could also not respond to chemotherapy and, you know, this is a women, say, who was estrogen receptor negative, supposedly HER2/neu negative, and I've tested women and occasionally they're really HER2/neu positive, and I give them Herceptin with--Herceptin and exactly the same chemo they didn't respond to and they respond to it. So I've had that happen frequently enough in my practice that again, if someone doesn't fit the clinical picture, you know, and is still looking for something else, we try, we try.
MS. NEWBURY:
Q. Thank you. You'd mentioned that you were primarily involved with regard to the 10 to 15 patients whose initial ER/PR results were inaccurate.
DR. BRUFSKY:
A. Those were my patients, yeah.

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MS. NEWBURY:
Q. They were your patients, and you communicated the results to them. How long a period of time had elapsed between finding out that the results were unreliable or inaccurate -
DR. BRUFSKY:
A. Several months.
MS. NEWBURY:
Q. - and actually making the communication?
DR. BRUFSKY:
A. Several months.
MS. NEWBURY:
Q. Several months, okay, and are there any guidelines as to sort of a time frame which would be acceptable for communicating any such -
DR. BRUFSKY:
A. You know, I don't have any guidelines per se, but I think the--I think what you need to do, at least upfront, is you need to figure out the scope of the problem and get a sense of how much it's going to affect the individual patient. I think that's the important thing, before you inform them, because I think one of the most important things when you tell

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somebody is what you want to know is what's going to happen to me next. You know, yeah, people will be upset that--they say "look, you know, you should have been right the first time. Why weren't you right the first time?" But then the next question is "how is this going to affect me? What's going to happen to me?" and I think it's important to have that, as best as you can, before you tell them. I mean, you don't necessarily have to have the result per se, but at least you have to like have a plan in place for the individual person.
MS. NEWBURY:
Q. Okay, and would that plan look at perhaps the other characteristics of that patient which might suggest that, you know, in conjunction with the unreliability of the results that perhaps this patient's treatment might change, so -
DR. BRUFSKY:
A. Yes, I mean, the only time it would be kind of difficult is if someone had had chemotherapy that perhaps didn't need it.
MS. NEWBURY:

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Q. Right.
DR. BRUFSKY:
A. I mean, that's--but, again, you always get some benefit from chemotherapy. You'll always get some benefit. It's just some people will get very little benefit, but there's still going to be some benefit. So it's not like you're not getting any benefit at all.
MS. NEWBURY:
Q. Okay. Would there be a risk benefit analysis component of that?
DR. BRUFSKY:
A. Oh, absolutely, but I mean, but if you've given someone chemo in error, it's already done.
MS. NEWBURY:
Q. Yes, you can't undo it.
DR. BRUFSKY:
A. So you'll have to say--that's already been done, so you'll get some benefit already.
MS. NEWBURY:
Q. And in terms of the one patient for whom a treatment change was determined necessary, was that patient communicated or was that communicated to the patient more quickly than

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the other -
DR. BRUFSKY:
A. That woman had received chemotherapy already and the only issue was whether she should get hormonal therapy as well, and she did. We just added hormonal therapy to her treatment, probably two to three months later than we should have.
MS. NEWBURY:
Q. Okay, and the diagnosis of that particular patient, can you recall how much earlier the diagnosis had been?
DR. BRUFSKY:
A. She had node positive breast cancer, so she was going to get chemo anyway, this particular woman.
MS. NEWBURY:
Q. But I guess there was a particular day that you called this patient and said "we've made a -
DR. BRUFSKY:
A. Yeah, I mean, that was a long time ago. I have to really think through the date on that.
MS. NEWBURY:
Q. Okay, you don't know off the top of your head.

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That's fine. You'd mentioned earlier this morning that social workers attended tumour board rounds?
DR. BRUFSKY:
A. Yes, they do.
MS. NEWBURY:
Q. Just curious what the role of those individuals would be?
DR. BRUFSKY:
A. So we have support groups, women run support groups for breast cancer, so it's very useful to have--we actually have--they're called patient navigators. We've taken the social workers away and called them patient navigators now, but they attend the meetings and they're very helpful in kind of helping us figure out how things should be communicated to patients. Breast cancer is a very emotional disease, you know. The issues surrounding it are very emotional. And they're very useful because they're very in tune, from the support groups, for what the issues really are, at least in how things are communicated to women.
MS. NEWBURY:

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Q. Okay, and do these patient navigators or social workers assist the medical oncologists in how the information would be relayed or do they -
DR. BRUFSKY:
A. Very much so, yes.
MS. NEWBURY:
Q. Okay. Are they actually involved in the communication?
DR. BRUFSKY:
A. Yeah, very much so. They are. I mean, we have books, we have whole huge binders of information, I think a lot of cancer centres do this, about breast cancer and their treatment in general, and then we have a navigator if there are more questions. We have many different levels that patients can access to get information about their cancer.
MS. NEWBURY:
Q. Okay, and in your institution, how many patient navigators do you typically have?
DR. BRUFSKY:
A. Currently, we have three. We're probably going to get more.
MS. NEWBURY:

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Q. And they are employees of the institution?
DR. BRUFSKY:
A. Employees of the institution, yes.
MS. NEWBURY:
Q. Okay, and are they ever used or relied upon to help, I guess, track the timing of patients treatment, to help them, you know, make sure that they're being followed?
DR. BRUFSKY:
A. They're more advocates for the patients.
MS. NEWBURY:
Q. Okay.
DR. BRUFSKY:
A. So is that kind of--I don't know if you're asking the question -
MS. NEWBURY:
Q. I'm just wondering, trying to flesh out, I guess, what types of activities they might be involved in in connection -
DR. BRUFSKY:
A. Yeah, they're really--I mean, the best way to look at them is kind of as a patient advocate.
MS. NEWBURY:
Q. Yes.
DR. BRUFSKY:

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A. So as an information--I mean, they advocate for the patient throughout the system. So if the patient does not understand something, they know where to find the information and help them.

MS. NEWBURY:

Q. Okay. So they can call the patient navigator and said "I had a visit with my medical oncologist yesterday -

DR. BRUFSKY:

A. "I'm not sure what he said."

MS. NEWBURY:

Q. - I was overwhelmed by the information.

DR. BRUFSKY:

A. Correct.

MS. NEWBURY:

Q. Where can I go?"

DR. BRUFSKY:

A. Correct.

MS. NEWBURY:

Q. And how about following up on perhaps a patient is waiting for certain results and -

DR. BRUFSKY:

A. Yes, the patient -

MS. NEWBURY:

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Q. - wants to know what the time lines will be down the road?

DR. BRUFSKY:

A. Yes, and if a patient feels--the way I personally handle that in my practice, we were discussing this beforehand, is I use e-mail, which has its whole other set of issues, but the bottom line, I've decided in a risk benefit analysis for my own practice that using e-mail, the risks of e-mail and the privacy concerns are outweighed by the rapidity with which information could be conveyed to the patient and so I give all of my patients my e-mail address, and even here in St. John's, Newfoundland, I'm e-mailing people back and forth to Pittsburgh about their care, but generally, if you don't have that access to your doctor, you have things like navigators or clinic nurses that relay that information, yes.

MS. NEWBURY:

Q. On the issue of the benefits of Tamoxifen or hormonal therapy if it's delayed, in terms of being administered to the patient or recommended to the patient, I believe your

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evidence earlier this morning is that there would be a higher risk of recurrence of the cancer, particularly in the period of time that the patient was not receiving the drug and I just want to make sure I understand clearly. Say for example a patient was diagnosed in 2002, that was the initial diagnosis and the treatment wasn't started until 2006, for whatever reason, say treatment with Tamoxifen, does this mean that if there was a recurrence in the interim, that this might have been due to the delayed -

DR. BRUFSKY:

A. Yes.

MS. NEWBURY:

Q. - provision of Tamoxifen?

DR. BRUFSKY:

A. Yes.

MS. NEWBURY:

Q. And is there literature to support that or is that an inference drawn from -

DR. BRUFSKY:

A. It's an inference drawn from literature, because one of the peaks of recurrence is about two to three years after diagnosis.

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MS. NEWBURY:

Q. Sure.

DR. BRUFSKY:

A. And generally, you know, that's one of the areas in which early hormonal therapy may be of benefit.

MS. NEWBURY:

Q. So I guess it stands to reason that if Tamoxifen or other hormonal therapy prevents a recurrence of cancer and if recurrence of cancer peaks at two to three years, and if you didn't get it until the fifth year, then you may have missed out on that opportunity?

DR. BRUFSKY:

A. Correct.

MS. NEWBURY:

Q. Okay, and I guess the other aspect of that, if the patient doesn't receive Tamoxifen until say 2006, but had no recurrence in the interim, the risk of recurrence after 2006, is that the issue for which there's no literature?

DR. BRUFSKY:

A. That is the issue for which there's no good literature. I mean, clearly, her risk is

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reduced, but is it the same as if she had had Tamoxifen for that entire time? No one can really answer that right now. You can indirectly try to answer it through some statistical analysis of various trials, which people, I think, are trying to do right now, but to my knowledge, in 2008, we just don't have that answer.

MS. NEWBURY:

Q. Okay. Thank you, Dr. Brufsky, those are all my questions.

DR. BRUFSKY:

A. You're welcome.

THE COMMISSIONER:

Q. Thank you. Mr. Pike?

PIKE, Q.C.:

Q. No questions, thank you very much.

THE COMMISSIONER:

Q. Anything arising, Ms. Chaytor? We seem to have lost--did you have a message? Okay.

DR. ADAM BRUFSKY, EXAMINATION BY SANDRA CHAYTOR, Q.C.

CHAYTOR, Q.C.:

Q. Okay, just one issue that you were talking about the differences in opinion in oncology with Mr. Simmons in his line of questioning

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and the shades of grey, black and white. On the issue of you said you treat at ten percent is your cut off, and whether or not the positivity of ER makes any difference. I'm wondering, does it make any difference to your colleagues whether or not somebody is ten percent or 80 percent when you're making the decision as to whether or not to offer hormonal therapy?

DR. BRUFSKY:

A. Not the absolute difference. I mean, I think that some of my colleagues probably, I think, most of the real grey zone in this is between one and ten percent. I think most colleagues would agree that if you're over ten percent, you should be treated. The issue that becomes is if you're ten percent, should you get Tamoxifen and chemotherapy versus if you're 50 percent, should you get Tamoxifen and chemotherapy. The real issue between ten percent and 100 percent is really should you add additional therapy to the Tamoxifen and on what level.

CHAYTOR, Q.C.:

Q. So does the issue of then the strength of your

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positivity weighs into deciding what other -

DR. BRUFSKY:

A. More in the chemo decision, but not into the hormonal therapy decision.

CHAYTOR, Q.C.:

Q. Okay, thank you. That's it.

DR. BRUFSKY:

A. Thank you very much.

DR. ADAM BRUFSKY, EXAMINATION BY MADAME COMMISSIONER

THE COMMISSIONER:

Q. So just wait now, make sure I understand that. While the strength of positivity is relevant to treatment, it's not relevant to the kind of treatment that we have been concerned about as much?

DR. BRUFSKY:

A. Correct, not to the hormonal therapy treatment, at least in my opinion, but to whether you add chemotherapy to it. There are some oncologists who would use that to determine whether to give chemo or not.

THE COMMISSIONER:

Q. All right.

DR. BRUFSKY:

A. Not a lot, but some.

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THE COMMISSIONER:

Q. And are you in the sort of larger camp on the business of whether or not the strength of the positivity is a factor in hormonal therapy, in your view, or is there another view out there, I guess I wanted to -

DR. BRUFSKY:

A. In other words--so in other words, would some -

THE COMMISSIONER:

Q. Would other oncologists use the strength of positivity in making a determination about treatment with hormonal therapy, for example, when there are contraindications to hormonal therapy? Would that -

DR. BRUFSKY:

A. Oh, I see. Now I understand the question.

THE COMMISSIONER:

Q. - would that be a factor there?

DR. BRUFSKY:

A. That's a good question. There are some oncologists that would. I am not one of them.

THE COMMISSIONER:

Q. Okay.

DR. BRUFSKY:

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A. I think that I would use ten percent as my cut off. I think that I would use ten percent as my cut off, I'll leave it at that. I think that's a good way to say that.

THE COMMISSIONER:

Q. Okay. So for you, make sure I understand, for you, if you have a patient where there are some contraindications to hormonal therapy, on the one side of the scales, there is positivity, whether it be 11 percent or 50 percent, and then on the other side of the scales are whatever those things are that suggest that maybe hormonal therapy may not be necessarily a good thing for this particular patient. Where there are other people who, when they're weighing this, might have the scales tip a little heavier if it was 50 percent rather than 11 percent?

DR. BRUFSKY:

A. Yes. Some people would use that, yes.

THE COMMISSIONER:

Q. Okay.

DR. BRUFSKY:

A. Some oncologists would use that in making their decision.

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THE COMMISSIONER:

Q. Okay, thank you very much.

DR. BRUFSKY:

A. You're welcome.

THE COMMISSIONER:

Q. Anything else, Ms. Chaytor?

CHAYTOR, Q.C.:

Q. Thank you. No, that's it. Thanks, Commissioner. Thank you, Dr. Brufsky.

THE COMMISSIONER:

Q. Thank you very much for coming all this way and assisting us in our task. We very much appreciate it.

DR. BRUFSKY:

A. Thank you for having me. Thank you very much.

THE COMMISSIONER:

Q. Ms. Chaytor, do we have somebody for this afternoon?

CHAYTOR, Q.C.:

Q. Commissioner, we're seeing if we can have another witness come this afternoon, but Mr. Simmons is going to check and see if that can happen.

THE COMMISSIONER:

Q. All right.

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CHAYTOR, Q.C.:

Q. I don't know -

THE COMMISSIONER:

Q. I'm just thinking in terms of communicating with others.

CHAYTOR, Q.C.:

Q. Yes.

THE COMMISSIONER:

Q. Can we use our office as a central clearing house of the information?

MR. SIMMONS:

Q. I can--if I can get on the telephone for a little while, I may be able to answer the question of whether someone is available on short notice or not.

THE COMMISSIONER:

Q. Okay. Well, in that case, I suggest you all stay around for another five minutes while Mr. Simmons makes his telephone call. Thank you.

Upon conclusion.

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CERTIFICATE

I, Judy Moss, hereby certify that the foregoing is a true and correct transcript in the matter of the Commission of Inquiry on Hormone Receptor Testing, heard on the 6th day of October, A.D., 2008 before the Honourable Justice Margaret A. Cameron, Commissioner, at the Commission of Inquiry, St. John's, Newfoundland and Labrador and was transcribed by me to the best of my ability by means of a sound apparatus.

Dated at St. John's, Newfoundland and Labrador this 6th day of October, A.D., 2008

Judy Moss

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