Eastern Health

Estrogen and Progesterone Testing

Media Technical Briefing

December 11, 2006

Briefing Participants

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Technical Briefing Agenda

1. Chronology of events
2. Understanding the principles and practice of disclosure
3. Understanding the ER/PR Test
4. Reviewing our outcomes
5. Where to from here?

Photography and video are not permitted in the briefing however, interviews may be scheduled following the briefing. You may also take video and pictures in the laboratory. Tumor slide samples, charts and graphs have been provided for you on cd.

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CHRONOLOGY

April 2004: Eastern Health (then the Health Care Corporation of St. John's) installs a new Ventana system

May 2005: Index case

June 2005: 2002 case review

Early July 2005: Decision to retest all ER/PR negatives from 1997-2004 (internally)

Late July 2005: Stop reporting ER/PR in our laboratory; arrange for an independent, external laboratory to complete our retesting

August 2005: Mt. Sinai Hospital agrees to take on project; collecting, packaging and shipping all negative test results.

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CHRONOLOGY

October 2005: First results come in from Mt. Sinai.

Tumor Board begins reviewing and making treatment recommendations.

Organization conducts media interviews.

Phone contact with all individuals being retested.

External review process begins.

November/ December 2005: Mt. Sinai concerns

Late January 2006: Final samples arrive; forwarded to Mt. Sinai

February 2006: Last test results received

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CHRONOLOGY

February - May 2006: Tumor Board work continues.

June – November 2006: Quality review process; establish centre of excellence for breast cancer pathology; assign head pathologist for immunohistochemistry; prepare for continuation of ER/PR testing

September 2006: Statistical review begins: this work is continuing.

Late November 2006: Quality review completed

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DISCLOSURE

"Disclosure is the imparting, by health care workers to patients or their significant others, of information pertaining to any health-care event affecting (or liable to affect) the patient's interests."

The Canadian Patient Safety Dictionary, Davies et. al

Eastern Health is committed to candid and timely disclosure of adverse events, particularly those that may cause risk to a patient.

DISCLOSURE

Our Policy States:

(a) *Concentrate on what happened and the possible consequences. Avoid too much detail and technical language.*

(b) *Remain factual.*

(c) *Take the lead in disclosure*

(d) *Outline a plan of care to rectify the harm and prevent recurrence for this patient and others.*

(e) *Offer to obtain second opinions where appropriate.*

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DISCLOSURE

The Policy States:

(f) *Offer the option of a family meeting.*

(g) *Document the discussion in the patient's health record.*

(h) *Determine the need for follow-up meetings and who should attend.*

(i) *Be prepared for strong emotions and offer personal support and support from others.*

(j) *Accept responsibility for outcomes*

(k) *Apologies are appropriate.*

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A COMPLICATED DISCLOSURE

- Systems issue
- Oncology practice has changed
- Laboratory technology has changed
- No patient specific information to disclose
- National implications
- Class action lawsuit

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Understanding the ER/PR Test

- When a breast cancer is removed from the body, tests are used to determine if the cancer cells have estrogen or progesterone receptors.
- If estrogen receptors present on those cells, anti-estrogen therapy such as Tamoxifen is used to treat that cancer.
- Literature suggests about 75% of breast cancers are estrogen–receptor–positive (or "ER-positive"), "positive" meaning that a certain number of cancer cells have receptors present.
- When a cancer shows no estrogen receptors (when it is "ER-negative"), anti-estrogen therapy is not effective.

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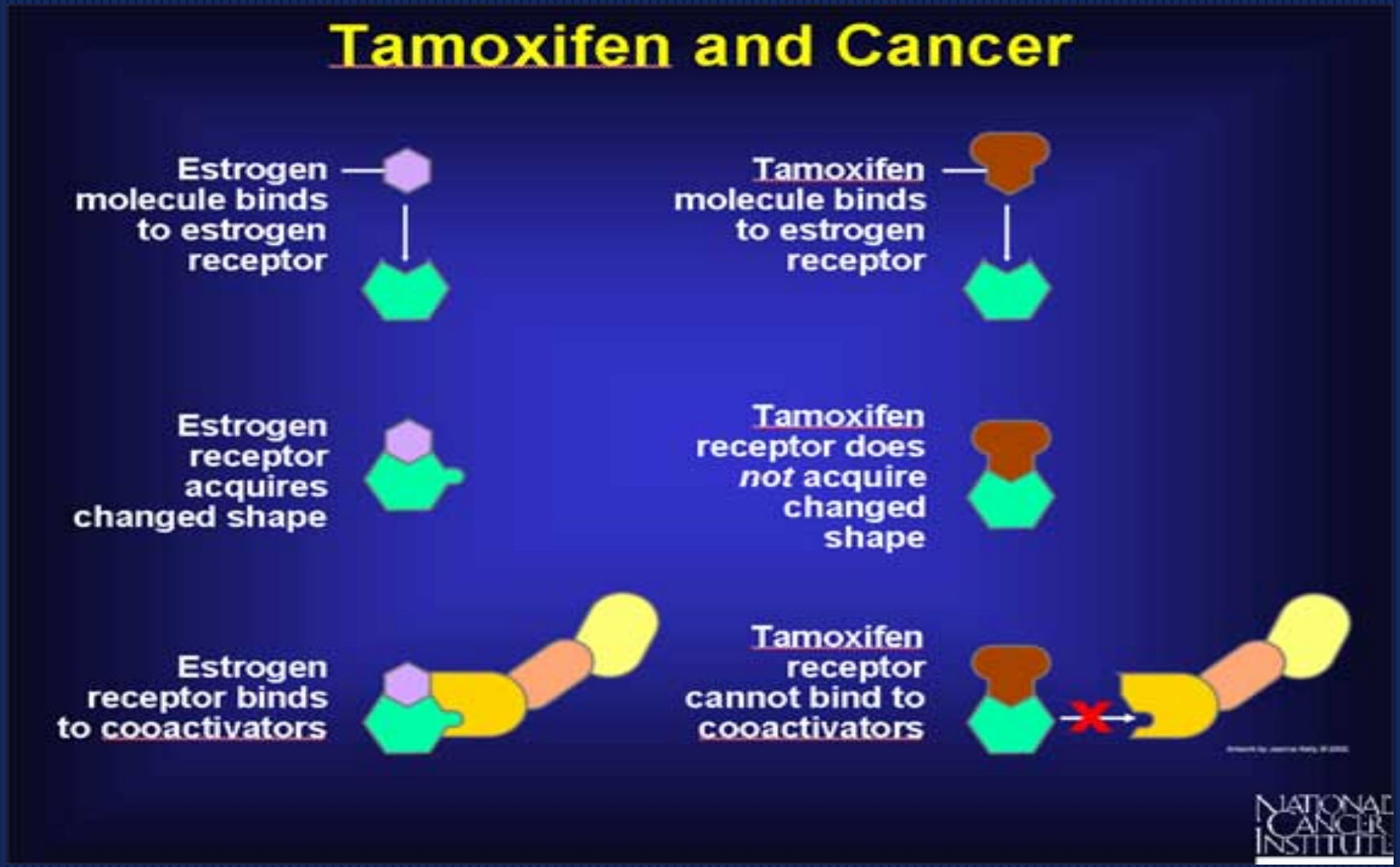
Tamoxifen and Cancer
Estrogen molecule binds to estrogen receptor
Tamoxifen molecule binds to estrogen receptor
Estrogen receptor acquires changed shape
Tamoxifen receptor does *not* acquire changed shape
Estrogen receptor binds to cooactivators
Tamoxifen receptor cannot bind to cooactivators
NATIONAL CANCER INSTITUTE

Understanding the ER/PR Test

Hormonal Therapy is considered to be an adjuvant therapy, which means that it is additional treatment given after potentially curative surgery.

Adjuvant therapies include:

- Radiation Therapy
- Chemotherapy
- Targeted Therapy
- Hormonal Therapy

The aim is to get rid of residual cancer cells in the body.

The goal is to:

- Decrease recurrence rates; and
- Improve overall survival.

However, a significant number of patients with breast cancer have recurrent disease despite advances in adjuvant therapy.

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Understanding the ER/PR Test

Tamoxifen:

"Gold standard" for years

Optimal duration 5 years

Side effects:

- Vasomotor (hot flashes)
- Uterine cancer
- Thromboembolic (blood clots)

	Relative Reduction In Odds Of…	
	Recurrence	Death
Age <50 years	45% (± 8%)	31% (±10%)
Age 50–59 years	37% (± 7%)	11% (± 8%)
Age 60–69 years	54% (± 5%)	33% (± 6%)
Age >70 years	54% (± 13%) p=0.00001	34% (± 13%) p=0.00001

Understanding the ER/PR Test

Aromatase Inhibitors:

- Used in post-menopausal patients
- May be given instead of or after Tamoxifen
- Side Effects:
  - Osteoporosis
  - Joint and Muscle Pain

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Understanding the ER/PR Test

Prior to April 2004: The Dako testing technique was used in our laboratories. This technique required the manual boiling of tissue and precise measuring of mixtures of immunohistochemical reagents.

After April 2004: The Ventana system was installed, which automates some of this process removing as much human manipulation as possible. In addition, there are significant advances in the development and use of reagents (such as antibodies).

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Understanding the ER/PR Test

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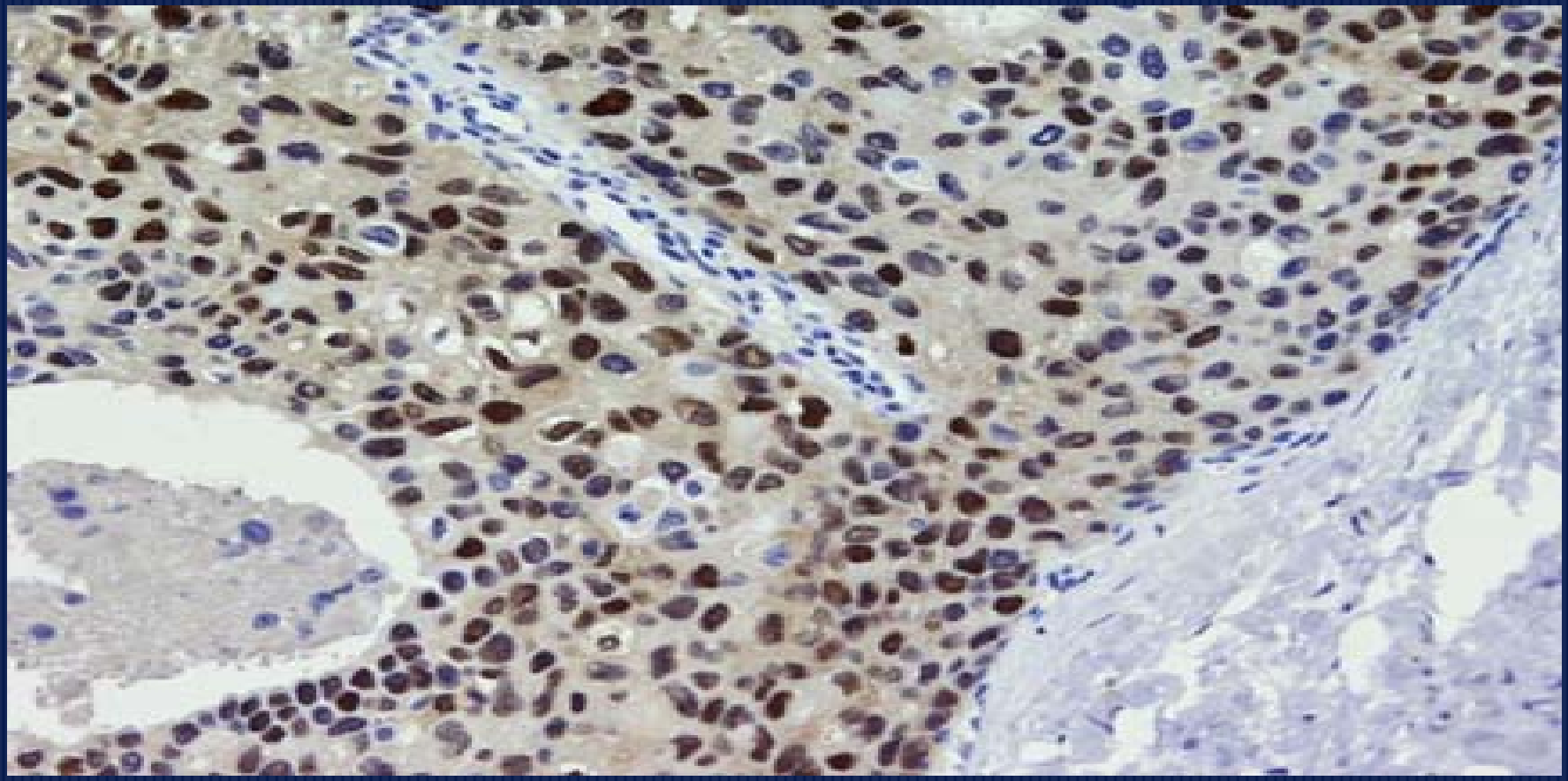
Immunohistochemistry:

- In order to determine whether a tumor has ER or PR receptors, laboratory technicians must expose cellular constituents so that pathologists can see them and count them to determine the percentage of positivity.
- Antibodies are used to visualize cellular proteins. An antibody is “a molecule that has the property of combining specifically to another molecule, termed an antigen.”
- Antibodies are made to specifically match the cellular antigen of interest. During the testing, the antibody is exposed to the tissue and binds to the antigen.
- Using good antigen retrieval methods are critical to the success of the test.



Understanding the ER/PR Test

- There are **no standardized immunohistochemistry testing** methodologies worldwide.
- Currently there is **no national laboratory accreditation process** for immunohistochemical labs.
- "**Immunohistochemistry tests are probabilistic, not accurate**." *Dr. Anthony Magliocco, Associate Professor of Oncology, Pathology and Laboratory Medicine, University of Calgary, at the U of T Pathology Update Course November 2005*
- In tumors with low expressors it is difficult to retrieve the antigen.

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Eastern Health Outcomes

- From 1997 to 2005, Eastern Health conducted 2760 ER/PR tests.
- 939 individual samples were sent to Mt. Sinai for retesting
- 117 individuals had recommended treatment changes.

  (Of these 117 individuals, some of the changes were related to ER/PR conversion while others were as a result of the panel reviewing their charts.)

Where to From Here?

For the last six months, Eastern Health has been focused on completing the disclosure process and a quality review. Within the next two months we will be reinstating ER/PR testing at our laboratory.

QUALITY ASSURANCES

- All recommendations from our external reviews have been implemented or are in progress
- Designated IHC Lab as separate department, including 3 designated IHC technologists, IHC Lab director and dedicated cutter
- Our technologists and pathologists have received specialized training in immunohistochemistry
- Consolidated all breast cases for examination and reporting to a designating group of pathologists
- Improved Quality Management Program.
- Seeking accreditation for entire laboratory.
- Involved in proficiency testing

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