Northern Alberta Breast Cancer Program

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This is the first issue of the Northern Alberta Breast Cancer Program Newsletter. Our goal is to provide you, our colleagues, with valuable resources to help you care for patients with breast cancer.

www.albertabreast.com

is an easy-to-use, up-to-date, and accurate website created to provide both physicians and patients with important information about the Cancer Centres in Alberta as well as

- Peer-reviewed management guidelines,
- Information about radiation therapy and chemotherapy,
- Suggestions for symptom management,
- Coping with cancer, and
- Standard treatments and the available clinical trials.

It was implemented in October 2000 and presently receives up to 1,000 "hits" per day. It is maintained without industry sponsorship and, as a result, no pharmaceutical company advertisements will be seen.

Future issues of this newsletter will discuss other hot topics such as the controversy over breast self-examination and screening mammography.

OTHER RECOMMENDED RESOURCES

www.albertadoctors.org provides many clinical resources and practice guidelines, as well as access to the benefits and services offered by the Alberta Medical Association.

www.cancer.gov is an excellent site developed by the National Cancer Institute in the United States. It provides comprehensive cancer treatment summaries for both physicians and patients.

The Canadian Breast Cancer Initiative's "Care and Treatment of Breast Cancer" Clinical Practice Guidelines are available on-line at **www.cma.ca/cmaj**. There you will find all of the consensus statements on the management of palpable lumps or mammographic lesions, guidelines for follow-up after breast cancer treatment, and information on chronic pain, lymphedema, and sentinel lymph node biopsy.

HOT TOPIC 1: THE "ATAC" TRIAL

Release of the preliminary results of the ATAC trial results has created much controversy in the treatment of early breast cancer. Many patients are asking how this affects them.

Background Information:

Tamoxifen is a non-steroidal estrogen receptor modulator with the capacity to alter the signal transduction pathways required for cellular growth and proliferation. In patients whose breast cancer expresses estrogen and/or progesterone (hormone) receptors, the administration of tamoxifen for five years reduces the relative risk of recurrence by 47%, the relative risk of contralateral breast cancer by 47%, and the relative risk of death by 26%, irrespective of age and menopausal status. Despite its benefits, tamoxifen predispose to hot flushes, weight gain, vaginal bleeding, and a small risk of venous thromboembolic events (e.g.: deep vein thrombosis), endometrial cancer, and ischemic cerebrovascular events.

Anastrozole (Arimidex®) is a non-steroidal agent that specifically inhibits the peripheral conversion of adrenal androgens to estrogen by the enzyme aromatase. Pre-menopausal ovaries produce estrogen in amounts that far exceed that produced by peripheral synthesis. As a result, anastrozole has no benefit in this population. In post-menopausal women with estrogen receptor-positive and non-visceral metastatic breast cancer, anastrozole dramatically reduces estrogen levels and significantly prolongs the time to progression over tamoxifen (10.7 months *versus* 6.4 months) with less risk of thromboembolic events and vaginal bleeding. No change in overall survival has yet been reported.

The "ATAC" Trial Design:

This trial enrolled 9,366 women with breast cancer and either a positive or unknown estrogen receptor status between July 1996 and March 2000. It then randomized them to five years of

Anastrozole 1 mg PO QD and Placebo
or
Tamoxifen 20 mg PO QD and Placebo
or
Anastrozole 1 mg PO QD and Tamoxifen 20 mg PO QD

The preliminary results (after a median follow-up of 33.3 months) were presented at the San Antonio Breast Cancer Symposium in December 2001.

Comparing all patients (irrespective of estrogen receptor status), anastrozole reduced the relative risk of recurrence by 17% more than did tamoxifen. In patients with estrogen-receptor positive disease, the relative risk of recurrence was decreased by 22% more than tamoxifen. Anastrozole was associated with a 58% greater reduction in the risk of contralateral breast cancer than tamoxifen.

No additional benefits were achieved from the combination of anastrozole and tamoxifen.

When compared to anastrozole, tamoxifen was associated with fewer fractures and arthralgias but more hot flashes and weight gain plus a marginally higher risk of endometrial cancer, venous thromboembolism, and ischemic cerebrovascular events. Please see the www.albertabreast.com website for details about the actual frequency of these adverse effects.

Although it is tempting to apply these encouraging results to our current practice, changes must await more mature survival data, quality of life analyses, and both regulatory and funding approval.

For now, we recommend that anastrozole be considered only for patients intolerant to, or inappropriate for, tamoxifen. A switch should only be made after a careful discussion with the oncologist involved in the patient's care.

HOT TOPIC 2: THE USE OF MAGNETIC RESONANCE IMAGING IN BREAST CANCER SCREENING

by Tim Terry, MB, FRCPC, FRCR(UK)
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We occasionally receive requests to perform MRI of the breasts as the primary imaging modality for both symptomatic and asymptomatic women. Indications given by referring physicians include young women with mammographically dense breasts and a strong family history of breast cancer, the patient's fear of radiation, or patients who find that the compression of mammography is too painful. There are many reasons why breast MRI is unsuitable as a screening tool. These include:

1. **Limited cancer yield**
   The incidence of breast cancer increases with age. For women between fifty and sixty-nine years of age, we expect to find two to four cancers per 1,000 women screened. The incidence of breast cancer in women between 40 and 49 years of age is less than half of this number.

2. **Limited specificity**
   Although breast MRI is highly sensitive for detecting invasive cancers, it has a relatively low specificity. Benign disease may show an enhancement pattern indistinguishable from that of an invasive cancer and lead to a false positive result. The etiology of most mammographic abnormalities can be determined by additional views, ultrasound, and/or image-guided needle core biopsy.

   Although the sensitivity of breast MRI is high, some cancers will show a benign pattern of enhancement. MRI remains unable to differentiate between an abscess and an inflammatory breast carcinoma.

3. **MRI cannot detect microcalcifications**
   Microcalcifications represent an important sign of DCIS (ductal carcinoma *in situ*). Up to 20% of cancers found through mammography screening are DCIS.

4. **Difficulty localizing lesions found only by MRI**
   Some mammographically occult breast cancers may be visible with high-resolution ultrasound. As a result, they can be localized and biopsied under ultrasound guidance. Although pre-operative MRI-guided needle wire localization devices have been developed, they are cumbersome to use.

5. **Breasts change with the menstrual cycle**
   Normal breast tissue enhancement peaks one week prior to menstruation. Ideally, pre-menopausal patients should be scanned between the sixth and sixteenth day of their cycle, and not in the second half ("proliferative phase") as this increases the number of false positive scans. More than half of pre-menopausal women show focal areas of enhancement which resolve during follow-up studies.

6. **Limited technical resources**
   Of the nine MRI machines in clinical use in Edmonton, only four have the coils necessary to perform breast imaging.

   The examination requires the patient to remain in the magnet bore for forty-five minutes. Thirty minutes of processing time is required, as is ten to fifteen minutes of a radiologists' reading time. A screening mammogram takes ten minutes to obtain and only one to two minutes to read.

Together with annual clinical breast examination, mammography remains the most cost-effective imaging tool to screen for breast cancer.

At the Cross Cancer Institute, we use breast MRI to assess areas of mammographic or sonographic uncertainty. This includes the differentiation of tumor recurrence from scar, and looking for a breast cancer in women with axillary lymphadenopathy, no other known primary tumor, and a negative mammogram. Other uses of breast MRI include pre-operative staging looking for multifocal breast cancer and the assessment of the integrity of silicone breast implants.

FEEDBACK

Feedback about the utility and contents of both the website and this newsletter is always appreciated and will help us provide you with resources that meet your needs. Please forward your comments to newsletter@albertabreast.com.

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