# Eastern Health
# Clinical Practice Guidelines in Oncology

# BREAST CANCER

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# SYSTEMIC THERAPY

## HORMONAL THERAPY

### Clinical Practice Guideline in the Use of Hormonal Therapy in the Clinic Setting

Breast Cancer Disease Site Group

#### CHEMOPREVENTION

Question : What is the optimal chemoprevention management offered to high risk patients?

Target Population : These recommendations apply to patients who are deemed high risk for the development of breast cancer.

Recommendations and Supporting Evidence

Patients are currently referred to medical oncology by their family physicians, surgeons, or the medical genetics department for a risk assessment. The medical oncologist will see the patient in consultation and determine risk assessment, using a tool such as the Gail Model (which takes into account patient's own personal medical history, reproductive history and history of breast cancer among her first degree relatives), to determine the patients risk of developing breast cancer. If the medical oncologist deems that the risk warrants, chemoprevention will be offered to the patient in the form of hormonal therapy. The current standard of treatment would be Tamoxifen as per the National Surgical Breast and Bowel Project (NSABP) P-1 clinical trial. An alternative to Tamoxifen would be Raloxifene, as per the STAR trial ( Study of Tamoxifen and Raloxifene ). However, currently there isn't enough evidence to offer Raloxifene over Tamoxifen based on side effect profile, and Raloxifene does not prevent DCIS .

Examples of high risk patients would include genetic carriers of the BRCA1 and 2 mutations, and those with E-Cadherin. There are other patients who meet the criteria for high risk status but who may not carry

these known mutations. The medical oncologist will decide whether these patients require followup in the cancer clinic or have them followed by their family or referring physicians.

Currently, there is no evidence to support a role for aromatase inhibitors in chemoprevention.

## DCIS/LCIS

Question : What is the role of Tamoxifen in the management of DCIS/LCIS?

Target Population : These recommendations apply to women with DCIS.

Recommendations and Supporting Evidence

These patients are generally referred by their surgeons and assessed by medical oncology, but have commonly been seen by radiation oncologists as well when a discussion regarding breast radiation is required. During the consultation, a discussion will ensue regarding the individual need for hormonal manipulation with each patient. Presently, it is unclear whether or not testing for estrogen and progesterone receptors should be performed routinely on DCIS/LCIS specimens. The group recommended that testing should not be performed on LCIS, since 99% are known to be estrogen and progesterone receptor positive. Currently, testing for hormone receptors status on LCIS/DCIS specimens is not standard in most centres in the country, and there is no evidence to suggest that knowing this result will affect the outcome. Therefore, 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 basis following referral.

The oncologist will discuss the treatment option of Tamoxifen with those patients deemed to be candidates, especially those with high grade disease. Patients with low or moderate grade disease including those under the age of 50 should be considered for Tamoxifen. Patients who have undergone bilateral mastectomies do not require Tamoxifen. Those who have undergone a unilateral mastectomy could derive a small benefit for the remaining breast, thus a discussion with the patient should include the potential thromboembolic and endometrial carcinoma risks associated with Tamoxifen.

ADJUVANT HORMONE THERAPY

Questions : What constitutes a positive hormone receptor breast cancer?

How will hormonal treatment options be affected by the patient's menopausal state?

Target Population : These recommendations will apply to patients who have been diagnosised with early-stage, hormone receptor positive breast cancer.

Recommendations and Supporting Evidence

Patients should be referred to medical oncology in a timely fashion to allow first assessment to take place within 10-12 weeks post surgery. The discussion will include the adjuvant treatment(s) of choice, namely chemotherapy and/or hormonal therapy. For those patients who have estrogen &/or progesterone positive disease, adjuvant hormonal therapy will be discussed. The threshold for ER and PR positivity has been debated in the past but the group has decided that any result of 1% or over will be considered positive, and could indicate eligibility for hormonal manipulation.

Premenopausal patients are to be offered Tamoxifen but where applicable, a clinical trial is also to be offered if available. Higher risk patients could also be offered ovarian ablation plus or minus hormonal therapy as well, but currently there is not enough evidence to reccommend this as standard of care.

Postmenopausal patients can be subdivided into three groups – low, moderate and high risk. High risk patients would be those that include node positive disease and some node negative patients with high risk features. Those high risk patients, with no contraindications, will be offered an aromatase inhibitor upfront, such as letrozole (2.5 mg/day for five years) as per the Breast International Group (BIG) 1-98 study or anastrozole (1mg/day for five years) as per the ATAC clinical trial. The low to moderate risk patients will be offered the switch option, which consists of Tamoxifen for the initial 2-3 years followed by a switch to an aromatase inhibitor, namely Aromasin as per the Intergroup Exemestane Study (IES).

For post menopausal patients, who received five years of Tamoxifen treatment, they will be offered letrozole for five years in the extended adjuvant setting, as per MA 17.

## HORMONE THERAPY IN METASTATIC SETTING

Questions : What is the optimal hormonal therapy management of pre and post menopausal patients with hormone receptor positive, metastatic breast cancer?

What are the potential list of hormone therapies that could be used in the treatment of post menopausal, hormone receptor positive metastatic breast cancer?

Target Population : These recommendations apply to pre and post menopausal patients with Stage IV (metastatic) breast cancer, who have hormone receptor positive disease.

Recommendations and Supporting Evidence

In the treatment of metastatic breast cancer, again the menopausal state of the patient plays an important role . In the premenopausal patient, the first line treatment option is Tamoxifen, or ovarian ablation plus an aromatase inhibitor which in this case would be letrozole. For postmenopausal patients, the first line treatment would be letrozole with Tamoxifen as the second line treatment option. In the case of those patients who develop metastatic disease while on a letrozole, then the next treatment choice would be Tamoxifen. For those who develop metastatic disease while on Tamoxifen, then first line of treatment would be letrozole. If the patient presents de-novo , then first line would be letrozole. The potential lines of hormonal treatments would begin with letrozole ( depending on whether patient began with Tamoxifen or the letrozole in the adjuvant setting), and with each subsequent failure would be as follows : Tamoxifen (or letrozole if Tamoxifen had been used initially), followed by exemestane and then Faslodex. If these patients have responded to more than all or most of these hormonal therapies then Megestrol Acetate could be offered has fourth or fifth line hormonal treatment in the metastatic setting.