



22 August 2005

SUBJECT: NEW TREATMENT GUIDELINES IN BREAST CANCER (JUNE 2005)

The British Columbia Cancer Agency Breast Tumour Group wishes to advise you of another new change in treatment guidelines for postmenopausal women with early breast cancer. The new advice is summarized at bottom for quick reference.

You will recall that, earlier, you received a letter regarding the use of letrozole, an aromatase inhibitor (AI), for postmenopausal women already completing 5 years of adjuvant tamoxifen therapy. This was based on the results of a large randomized trial showing a 6% absolute reduction in breast cancer recurrences for postmenopausal women treated with letrozole after completion of 5 years of tamoxifen. In women with node positive disease, there was also a modest survival advantage. A similar large study has established that an earlier switch in therapy from tamoxifen to an AI after 2-3 years may be an optimal strategy for most postmenopausal women with ER+ breast cancer. We are writing now to inform you that we are recommending most women in this category be offered **an earlier switch to an AI, after 2-3 years of tamoxifen**, for 3-2 years, to complete a total of 5 years of adjuvant hormone therapy. We hope that you can assist us in rolling out this new program to your patients who are earlier in their tamoxifen therapy.

We are recommending an earlier switch to an AI be considered **after 2-3 years** of tamoxifen for most postmenopausal women with breast cancer. The available medications include: anastrozole 1 mg daily or letrozole 2.5 mg daily or exemestane 25 mg daily. (Exemestane would be preferred for women with lactose intolerance.) The prescriptions may be filled through the BC Cancer Agency (BCCA) pharmacy, as per usual.

- Eligible women
 - Are postmenopausal
 - Have received 2-3 years of tamoxifen only
 - Have remained free of recurrence
 - Have had ER+ invasive breast cancer (node negative or positive)
 - not approved for DCIS only
 - not recommended for low risk breast cancer**

**As was the case with extended adjuvant therapy with letrozole after 5 years of tamoxifen, we are not making a recommendation that women with very low risk tumours, defined as <2 cm, node negative AND low grade (grade 1) make a switch in therapy if they are doing well on tamoxifen. This is again because these low risk tumours have an excellent prognosis for cure already with tamoxifen monotherapy.



We are writing to women whom we have identified as being on adjuvant tamoxifen, and suggesting they may contact you. As well, you may have other patients in your practice who may meet the criteria. Please discuss this new policy with patients who may be eligible and may want to consider this option. If you and your patient decide to proceed, you may write the prescription for one of the above listed AI's and it will be filled by a BCCA pharmacy. You are invited to call your patient's oncologist to discuss their situation before making the switch, if there are any issues which concern you.

In general, women who have not menstruated for more than 1 year would be considered postmenopausal. However, some women who are premenopausal prior to the use of tamoxifen may stop menstruating while on tamoxifen, and yet have hormone levels in the premenopausal range. It is important for you to know that aromatase inhibitors do not work in premenopausal women. Therefore, if your patient was premenopausal prior to their therapy for breast cancer, it may be prudent to check FSH, LH, and estradiol levels prior to initiating a switch in therapy, particularly in younger women. If, despite these measures, your patient resumes menstruating after starting an AI, they must discontinue this.

Side effects of AI's are similar to those from tamoxifen. Menopausal symptoms such as hot flashes and vaginal dryness may occur with slightly reduced frequency. Arthralgias and myalgias and diarrhea, usually mild, may occur with greater frequency than with tamoxifen. The low risks of deep venous thrombosis, endometrial cancer, and strokes with AI's are lower than with tamoxifen, due to absence of estrogen-like activity. However, there is a potential increased risk of bone thinning (osteoporosis) and altered lipid levels (usually mild). To decrease the effect on bones, we recommend women should take in 1500mg of calcium from food sources and supplements, and 800IU of vitamin D daily. If you are concerned that your patient may have established osteoporosis, a baseline and 24-month follow up bone mineral density exam may be considered. If the bone density scan suggests osteoporosis, you should talk with your patient about whether she needs treatment or more follow-up for this. If she has particularly significant osteoporosis, it may be best for her to remain on tamoxifen, which tends to increase or preserve bone density. Women with prior significant lipid abnormalities would benefit from monitoring of lipid levels in the first few months of therapy.

We would also like to advise you that some postmenopausal women with features of very aggressive cancer, at high risk for early relapse, may be offered by their oncologist, treatment with an AI from the outset of their adjuvant hormonal therapy. There would be no plan for them to switch therapy part way through, unless they developed relapse. At that point, those patients should be re-referred to their oncologist.

More information can be found in support of this issue on the BCCA website, www.bccancer.bc.ca located in the following section – Health Professionals Info/CancerManagementGuidelines/Breast/Management/Adjuvant Hormonal Therapy.

Please contact the BCCA if you have any questions, if you would like to speak to an oncologist or if you would like your patient seen by their oncologist for a further consultation. As well, if you have a patient who does not fit the guideline but you think would benefit, please contact their



oncologist for a further discussion. Thank you for participating in this new policy and in the care of our breast cancer patients.

Yours sincerely,

Karen Gelmon MD FRCPC
Chair, Breast Tumour Group

Susan Ellard MD FRCPC
Head, Breast Systemic Committee

QUICK SUMMARY

Patient on adjuvant tamoxifen:

If completed 2-3 years AND postmenopausal AND invasive breast cancer*:

Switch to one of:

Letrozole 2.5 mg od

Anastrozole 1. mg od, or

Exemestane 25 mg od

To complete 5 years of total hormone therapy (tam plus AI)

***UNLESS:**

DCIS only, **or**

T1 (<2 cm tumour) **and** N0 (no lymph nodes involved) **and** grade 1 (low grade), **or**

Still pre or perimenopausal (if unsure, check FSH, LH, estradiol)

(in which case continue tamoxifen to complete 5 years)

If postmenopausal between 3 and 5 years of tamoxifen, can prescribe an AI at the end of therapy for 3 years, except for above exclusions.

If intolerant of AI, or resume menstruating, can resume tamoxifen to complete 5 years.

If tolerant of AI, ensure adequate calcium and vitamin D intake and obtain BMD test.

If osteoporotic, consider bisphosphonate therapy and repeat BMD q 2 years during therapy.

If difficult lipid control at baseline, check lipids within 2 months of start of AI.

Patient on AI already from oncologist, make no changes.

Contact your patient's oncologist if need to discuss, or if relapse occurs despite therapy.