BC Cancer Protocol Summary for Neoadjuvant or Adjuvant Therapy for Breast Cancer using Exemestane in Postmenopausal Women

Protocol Code	*BRAJEXE*
Tumour Group	*Breast*
Contact Physician	*Dr. Angela Chan*

ELIGIBILITY:
Patients must be:

- Postmenopausal women (no menses for greater than 12 months; check FSH, LH, estradiol levels if less than 55 and prior hysterectomy or uncertain menopausal status due to young age or other factors) with hormone receptor positive invasive breast cancer, and
- Receiving aromatase inhibitor for one of the following scenarios:
  - Upfront: aromatase inhibitor for 5 years*,
  - Early switch: after 2 to 3 years of adjuvant tamoxifen to complete 5 years of endocrine therapy*,
  - Late switch: if remaining disease free, and within 12 months of the end of 4.5 to 6 years of adjuvant tamoxifen, may receive 5 years of aromatase inhibitor therapy to complete a total of 10 years of adjuvant endocrine therapy, or
  - Preoperatively in patients unsuitable for immediate surgery or preoperative chemotherapy

* Patients may continue an additional 5 years of aromatase inhibitor to complete up to a total of 10 years of adjuvant endocrine therapy if:

- Disease free after first 5 years of adjuvant endocrine therapy which included at least 2 years of aromatase inhibitor, and
- Less than 12 months since last dose of aromatase inhibitor
- Prescribers determined that patients have:
  - Stage IIA to IIIA disease if 5-10 year recurrence risk at least 10% (as assessed with CTS5 score calculator), or stage IIIB and C disease, and
  - Estimated life expectancy 10 years

EXCLUSIONS:

- Premenopausal women
- DCIS only

TESTS:

- Baseline (optional): bone density before or after 2 to 3 month trial of therapy
- Follow up every 3 years or as clinically indicated: bone density
- If clinically indicated: serum cholesterol, triglycerides

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
exemestane	25 mg daily	PO
Duration of Adjuvant Aromatase Inhibitor Therapy		
Upfront Therapy		Initially x 5 years, then may receive 5 additional years of aromatase inhibitor to complete a total of 10 years of endocrine therapy**
Early switch after 2 to 3 years of tamoxifen		Initially x 2 to 3 years to complete 5 years of initial therapy, then may receive 5 additional years of aromatase inhibitor to complete a total of 10 years of endocrine therapy**
Late switch after 4.5 to 6 years of tamoxifen		x 5 years, which completes a total of 10 years of endocrine therapy

** As outlined in Eligibility

PRECAUTIONS:

1. Hepatic dysfunction: Aromatase inhibitors are considered safe in mild-to-moderate hepatic dysfunction but have not been studied in severe hepatic dysfunction.
2. Bone density: The long-term effects of aromatase inhibitors on bone density in adjuvant therapy patients are known to reduce bone density and increase risk for osteoporosis. Supplementation with calcium and vitamin D and regular weight bearing exercise is recommended. A bone modifying agent should be considered if clinically indicated. Caution in patients with an already established diagnosis of clinically significant osteoporosis.
3. Hyperlipidemia: An increase in cholesterol or triglyceride levels may occur when an aromatase inhibitor is initiated.

Contact Dr. Angela Chan or tumour group delegate at 604-877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References

1. Coombes RC, Hall E, Gibson LJ, et al. A randomized trial of exemestane after two to three years of tamoxifen therapy in postmenopausal women with primary breast cancer. N Engl J Med 2004;350(11):1081-92.
2. The ATAC Trialists' Group. Anastrozole Alone or in Combination with Tamoxifen versus Tamoxifen Alone for Adjuvant Treatment of Postmenopausal Women with Early-Stage Breast Cancer. Cancer 2003;98:1802-10.
3. The ATAC Trialists' Group. Anastrozole alone or in combination with tamoxifen versus tamoxifen alone for adjuvant treatment of postmenopausal women with early breast cancer: first results of the ATAC randomised trial. Lancet 2002;359(9324):2131-39.

4. The ATAC Trialists' Group. Results of the ATAC (Arimidex, Tamoxifen, alone or in combination) trial after completion of 5 years' adjuvant treatment for breast cancer. Lancet Published online December 8, 2004;364(9451).
5. Winer EP, Hudis C, Burstein HJ, et al. American Society of Clinical Oncology technology assessment on the use of aromatase inhibitors as adjuvant therapy for postmenopausal women with hormone receptor-positive breast cancer: status report 2004. J Clin Oncol 2005;23(3):619-29.
6. Goss PE, Ingle JN, Martino S, et al. A randomized trial of letrozole in postmenopausal women after five years of tamoxifen therapy for early-stage breast cancer. N Engl J Med 2003;349(19):1793-802.
7. Mamounas EP, Bandos H, Lembersky BC, et al. Use of letrozole after aromatase inhibitor-based therapy in postmenopausal breast cancer (NRG Oncology/NSABP B-42): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol 2019;20(1):88-99