BC Cancer Protocol Summary for Neoadjuvant or Adjuvant Therapy for Breast Cancer Using Tamoxifen

Protocol Code	*BRAJTAM*
Tumour Group	*Breast*
Contact Physician	*Dr. Susan Ellard*

ELIGIBILITY:

- May be given preoperatively in hormone receptor positive breast cancer patients who are unsuitable for immediate surgery or preoperative chemotherapy
- Adjuvant hormonal treatment for breast cancer, initiated up to 10 years after diagnosis and treatment
  - All premenopausal hormone receptor-positive women: upfront tamoxifen for up to a total of 10 years only (eligible if completed 5 years of therapy within last 12 months)
- Options for postmenopausal hormone receptor positive invasive breast cancer:
  - Upfront tamoxifen for up to a total of 10 years only (eligible if completed 5 years of therapy within last 12 months)
    - Consider aromatase inhibitor options below if disease higher than T1N0 low grade tumours
    - Any postmenopausal hormone receptor positive invasive breast cancer in patients intolerant to aromatase inhibitors
  - Early switch: 2 to 3 years of adjuvant tamoxifen to begin 5 to 10 years of hormone blockade (except T1N0 low grade disease)
  - Late switch: 5 years of adjuvant tamoxifen, followed by up to 5 additional years of aromatase inhibitor (except T1N0 low grade)
- See Cancer Management Guidelines for current guidelines.

EXCLUSIONS:

- Hormone receptor-negative
- Patients with a history of significant thromboembolic disease

TESTS:

- Annually: gynecological exam (postmenopausal patients with an intact uterus)
- If clinically indicated (see PRECAUTIONS, below): CBC and diff, platelets, serum cholesterol and triglycerides, bilirubin, alk phos, ALT, GGT, ophthalmologic exam

TREATMENT:
Upfront:
tamoxifen 20 mg PO daily x up to a total of 10 years

Early Switch:
tamoxifen 20 mg PO daily x 2 to 3 years, followed by aromatase inhibitor to complete up to a total of 10 years (see BRAJANAS, BRAJEXE, or BRAJLET)

Late Switch:
tamoxifen 20 mg PO daily x 5 years, followed by aromatase inhibitor x 5 years (see BRAJANAS, BRAJEXE, or BRAJLET)

MODIFICATIONS:
1. Intolerant or serious complications during tamoxifen therapy
   - Post-menopausal patients may be switched to aromatase inhibitor to complete adjuvant hormonal therapy (see BRAJANAS, BRAJEXE, BRAJLET)

PRECAUTIONS:
1. **Myelosuppression:** Mild myelosuppression with transient thrombocytopenia may occur rarely. The association with tamoxifen is uncertain.
2. **Endometrial Cancer:** Annual gynecological examinations are recommended. Pelvic complaints, such as unusual vaginal bleeding, require prompt evaluation.
3. **Ocular Toxicity:** Ocular toxicity is rare and may occur after only a few weeks of therapy, although it is more common with prolonged treatment. Ophthalmologic examination is recommended if visual disturbances occur.
4. **Thromboembolism:** Tamoxifen is associated with an increased risk of thromboembolism that is comparable to estrogen replacement therapy.
5. **Hepatotoxicity:** While hepatotoxicity is rare and usually presents as elevated hepatic enzymes, more serious liver abnormalities have been reported.
6. **Ovulation Induction:** Tamoxifen may induce ovulation in pre- and peri-menopausal women. Barrier forms of contraception are recommended.
7. **Hyperlipidemia:** Elevations in cholesterol and triglycerides may occur in patients with pre-existing hyperlipidemias.

Call Dr. Susan Ellard or tumour group delegate at (250) 712-3900 or 1-888-563-7773 with any problems or questions regarding this treatment program.

References:

1. Early Breast Cancer Trialists' Collaborative Group. Tamoxifen for early breast cancer: an overview of the randomised trials. Lancet 1998;351:1451-67.
2. Delozier T, Switsers O, Genot JY et al. Delayed adjuvant tamoxifen: ten-year results of a collaborative randomized controlled trial in early breast cancer (TAM-02 trial). Ann Oncol 2000;11:515-9.
3. Coombes, RC 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
4. 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):1793-02.
5. Davies C, Pan H, Godwin J, et al. Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years after diagnosis of oestrogen receptor-positive breast cancer: ATLAS, a randomised trial. Lancet 2013;381(9869):805-16.