BC Cancer Protocol Summary for Adjuvant Treatment of postmenopausal Women Using 6-Monthly Zoledronic Acid

Protocol Code BRAJZOL5

Tumour Group Breast

Contact Physician Dr. Stephen Chia

ELIGIBILITY:

- Initial stage II or III only (pT2-4 pN0-3; pT0-4pN1-3), or
- Post neo-adjuvant chemotherapy stage ypT2-4 ypN0-3; ypT0-4 ypN1-3
- Biomarkers: ER any PR any
- Adequate renal function (CrCl ≥ 30 mL/min)
- Bisphosphonate therapy must begin within 1 year of diagnosis

TESTS:

- Completion of necessary dental assessment and dental work is recommended prior to starting zoledronic acid
- Baseline and prior to each treatment: serum creatinine
- If clinically indicated: serum calcium* and albumin (or ionized calcium)
 *corrected calcium (mmol/L) = total calcium (mmol/L) + (0.02 x [40 albumin in g/L])

PREMEDICATIONS:

None

TREATMENT:

| Drug | Dose | BCCA Administration Guideline |
|-----------------|------|---------------------------------|
| zoledronic acid | 4 mg | IV in 100 mL NS over 15 minutes |

Repeat once every 6 months (24 weeks) for 5 years

DOSE MODIFICATIONS:

1. Renal dysfunction: Zoledronic acid

| Creatinine clearance (mL/min) | Dose |
|-------------------------------|-----------------|
| >60 | 4 mg |
| 50-60 | 3.5 mg |
| 40-49 | 3.3 mg |
| 30-39 | 3 mg |
| < 30 | not recommended |

 There is limited experience with zoledronic acid in patients with serum creatinine greater than 440 micromol/L; caution is required.

PRECAUTIONS:

- 1. Zoledronic acid should NEVER be given as a bolus since severe local reactions and thrombophlebitis may result from high concentrations.
- 2. **Symptomatic hypocalcemia** (e.g., muscle spasms, irritability) may occur and may require calcium supplement. Avoid concomitant use of other calcium lowering agents such as corticosteroids and loop diuretics.
- After the use of bisphosphonates, there is a persistent risk of jaw osteonecrosis.
 Patients in whom bisphosphonates are planned should have prophylactic assessment and management by a dentist and all later dental work should be undertaken cautiously by dental specialists experienced in the recognition and management of jaw osteonecrosis

Call Dr. Stephen Chia or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References:

- 1. Ben-Aharon I, Vidal L, Rizel S, et al. Bisphosphonates in the adjuvant setting of breast cancer therapy-effect on survival: a systematic review and meta-analysis. PLoS One 2013 Aug 26;8(8):e70044.
- 2. Coleman R, Cameron D, Dodwell D, et al.; AZURE investigators. Adjuvant zoledronic acid in patients with early breast cancer: final efficacy analysis of the AZURE (BIG 01/04) randomized open-label phase 3 trial. Lancet Oncol 2014;15(9):997-1006.
- 3. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Adjuvant bisphosphonate treatment in early breast cancer: meta-analyses of individual patient data from randomised trials. Lancet 2015;386(10001):1353-61. Erratum in: Lancet 2016;387(10013):30.
- 4. Gnant M, Mlineritsch B, Stoeger H, et al.; Austrian Breast and Colorectal Cancer Study Group, Vienna, Austria. Zoledronic acid combined with adjuvant endocrine therapy of tamoxifen versus anastrozole plus ovarian function suppression in premenopausal early breast cancer: final analysis of the Austrian Breast and Colorectal Cancer Study Group Trial 12. Ann Oncol 2015;26(2):313-20.
- 5. Paterson AH, Anderson SJ, Lembersky BC, et al. Oral clodronate for adjuvant treatment of operable breast cancer (National Surgical Adjuvant Breast and Bowel Project protocol B-34): a multicentre, placebo-controlled, randomised trial. Lancet Oncol 2012;13(7):734-42.
- 6. Powles T, Paterson A, McCloskey E, et al. Reduction in bone relapse and improved survival with oral clodronate for adjuvant treatment of operable breast cancer [ISRCTN83688026]. Breast Cancer Res 20068(2):R13. Erratum in: Breast Cancer Res 2006;8(3):406.