Clinical Practice Guideline for the Use of Hormonal Therapy in the Treatment of Breast Cancer in the Metastatic Setting

Eastern Health Breast Cancer Disease Site Group

Questions:

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

2. What is the potential list of hormone therapies that could be used in the treatment of pre and post-menopausal, hormone receptor positive, and metastatic breast cancer?

Target Population:

These recommendations apply to pre and postmenopausal patients with Stage IV (metastatic) breast cancer, who have hormone receptor positive disease.

Recommendations and Supporting Evidence:

Treatment of metastatic breast cancer is not considered curative. Rather, the goals of treatment are to prolong survival, alleviate or prevent tumor-related symptoms or complications, and improve quality of life. In the case of hormone receptor sensitivity and in the absence of visceral, life-threatening disease, endocrine manipulation is the treatment of choice. Where patients' performance status allows and chemotherapy is deemed to be the optimal initial treatment, hormonal therapy still remains an important and frequently effective treatment option once the chemotherapy regimen is completed.

The selection of endocrine therapies for patients with hormone receptor positive breast cancer is strongly influenced by the menopausal status of the patient. For premenopausal patients, antiestrogen therapy, such as tamoxifen would be an appropriate first-line hormonal therapy. Other options include the use of the progestin, megestrol acetate [1,2,3], as well as the suppression of ovarian function. Ovarian ablation can be achieved by surgery, radiotherapy, or the use of a luteinising hormone-releasing hormone analogue, such as goserelin [11,18]. In turn, for those who undergo ovarian ablation, a class of drugs referred to as aromatase inhibitors becomes another alternative treatment option.

For postmenopausal patients, the non-steroidal aromatase inhibitors, such as anastrozole and letrozole, represent the preferred first line hormonal treatment for metastatic breast cancer. The results of a combination phase III clinical trial (conducted in both North America and Europe),

known as the TARGET trial [9] (the Tamoxifen or Arimidex Randomized Group Efficacy and Tolerability), and a large phase III study of letrozole versus tamoxifen [19] as first-line therapy of advanced breast cancer provides evidence for this treatment choice. For second-line therapy, a number of options exist including tamoxifen, the steroidal aromatase inhibitor exemestane [20], an estrogen receptor antagonist fulvestrant [21,29], and megestrol acetate. Though aromatase inhibitors are the most active agents, the choice and sequence of endocrine therapies for metastatic disease are dictated by prior adjuvant treatments received and specific patient-related disease factors.