

Endocrine Therapy in the COVID-19 Pandemic

Introduction

The following is an adaptation of our [full document](#) on Endocrine Therapy for use during this pandemic. It also serves as an additional resource to the [Executive Summary](#) for COVID-19 Recommendations for Breast Cancer Care (pending full manuscript publication). This document is to assist with triaging breast cancer patients during this unprecedented global pandemic. Refer to the full endocrine therapy resource guide for detail and references.

Medications Utilized for Endocrine Therapy

Selective Estrogen Receptor Modulators (SERMS)

- Tamoxifen is effective in both pre- and post-menopausal women for hormonal receptive (HR+) breast cancer and is also effective in the management of HR+ breast cancer in men.
- Tamoxifen – 20 mg/day (breast cancer treatment and also prevention, side effects include uterine cancer and thromboembolic events)

Aromatase Inhibitors (AIs)

There are two categories of aromatase inhibitors (AIs): 1) non-steroidal AIs (anastrozole and letrozole), which bind reversibly to the aromatase enzyme, and 2) steroidal AIs (exemestane) which are androgen substrate analogues and bind irreversibly to the aromatase enzyme.

- Anastrozole (Arimidex) – 1 mg daily
- Letrozole (Femara) – 2.5 mg daily
- Exemestane (Aromasin) – 25 mg daily

Summary

- Anastrozole achieved a better breast cancer free interval and disease-free survival compared to tamoxifen in women younger than age 60 years. There was no difference between the two drugs in women older than age 60 years.
- Anastrozole achieved a significant reduction in contralateral invasive breast cancer compared to tamoxifen.
- There was no difference in overall survival between the two arms.

- Anastrozole was associated with a higher rate of osteoporotic fractures; while tamoxifen was associated with a higher risk of thromboembolic events.

Neoadjuvant Endocrine Therapy

The use of Neoadjuvant Endocrine Therapy (NET) is highly recommended for first line therapy of newly diagnosed HR+, HER2- invasive tumors and DCIS patients during this COVID-19 Pandemic. Confirm the strength of Estrogen Receptor Positivity. Genomic evaluation on a core biopsy may also be helpful to determine NET vs. neoadjuvant chemotherapy. (Table 4 Executive Summary)

There is limited data on the use of NET in premenopausal women, and it should only be done in the setting of a clinical study or under extenuating circumstances (**COVID-19 Pandemic**) where access to standard of care may be delayed.

AI's are preferred over tamoxifen for postmenopausal NET (LHRH agonists should be used in premenopausal women taking AI's).

Clinical Management of Patients Treated with Neoadjuvant Endocrine Therapy

Once therapy is initiated, the tumor's response should be assessed periodically by clinical examination (and ultrasound or other imaging if conditions allow) or at any time when there is clinical concern for tumor growth. Traditionally, NET is given for 3-6 months; however, endocrine treatments (tamoxifen, AI, LHRH agonists) are safe and if needed, can be continued for longer throughout the COVID-19 pandemic.

NET achieves high clinical response rates (20-76% across all studies) although is unlikely to result in a pCR. Optimal duration of NET is not clearly defined, but responses may take longer than chemotherapy. Most studies have evaluated 3-6 months of treatment and maximal responses may take up to 1 year. Of note, downstaging occurred more often at 6 months over 3 months duration of treatment.

Endocrine Therapy in the Elderly

The geriatric patient population needs special consideration when selecting treatment both in terms of their breast cancer and also their risks from COVID-19. Multiple comorbidities and functional issues may be present and can impact treatment tolerance and outcomes. However, mortality rate from COVID-19 for patients over age 70 is likely higher than from their breast cancer. After the age of 70 years, the percent of breast cancers that are estrogen positive and will respond to endocrine therapy rises. **In patients older than 75 years with comorbid conditions and poor functional status, it may be best to treat with endocrine therapy as the primary therapy with surgical intervention only for clinical progression of disease.** Patients older than 80 years have a higher percentage

presenting with locally advanced breast cancer as they have stopped screening and having routine breast exams. Primary endocrine therapy for many would be preferable to downstage disease.

As in all times, multidisciplinary patient management is ideal. Many of your decisions for the use of NET will depend on your institutional resources and the regional severity of the COVID-19 pandemic. These are recommendations and are not intended to supersede individual physician judgement or hospital policies and guidelines.