WEB EXCLUSIVES

House Call

BY AMAN BUZDAR

Question: What are the latest trends in adjuvant hormonal treatment with aromatase inhibitors?

Answer: Adjuvant therapy is treatment received after surgery with the goal of reducing the risk of recurrence, particularly for early-stage breast cancer. Breast cancer can recur many years following initial surgery and treatment, but a woman's risk of recurrence is highest during the five years immediately following diagnosis, peaking in the first three years. Tumor size, hormone receptor status, menopausal status and whether cancer was detected in the lymph nodes can provide information regarding risk of recurrence and what therapy is best to prevent it.

Adjuvant therapies for breast cancer can include radiation, chemotherapy and/or hormonal therapies, such as tamoxifen and aromatase inhibitors, or AIs, which are prescribed particularly for postmenopausal women with hormone receptor-positive breast cancer. Two-thirds of women with breast cancer have hormone receptor-positive disease—where breast cancer cells have a significant number of estrogen or progesterone receptors that bind to the hormones and promote cancer growth.

AIs, which include Arimidex (anastrozole), Femara (letrozole), and Aromasin (exemestane), block aromatase, an enzyme needed to make estrogen, which leads to a lower availability of the hormone to fuel breast cancer cell growth. AIs, which are available as a daily pill, have become the preferred treatment over tamoxifen because several studies have consistently shown their superior ability to reduce the risk of breast cancer recurrence in postmenopausal women. Tamoxifen is still the preferred treatment for premenopausal women.

The ATAC study (Arimidex, Tamoxifen Alone or in Combination), one of the largest early-stage breast cancer treatment studies ever conducted, compared Arimidex with tamoxifen. The latest results show that treatment with Arimidex reduced the risk of breast cancer recurrence in postmenopausal women with early-stage hormone receptor-positive breast cancer. After 68 months, patients treated with Arimidex experienced a 26 percent reduction in the risk of recurrence compared with patients on tamoxifen.

Clinical studies have also shown that Femara may be a better option than tamoxifen. Taken in lieu of the five-year tamoxifen regimen, five years of Femara reduced recurrence an additional 19 percent, lowering it from 10.7 percent to 8.8 percent. Another study found that five years of Femara taken after five years of tamoxifen can further reduce the risk of recurrence by 43 percent. A trial

comparing Femara with Arimidex, known as the FACE study (Femara versus Anastrozole Clinical Evaluation), is currently enrolling 4,000 patients internationally. The trial will be the first to compare the two AIs in the post-surgery setting to see which drug is better suited for patients who had breast cancer spread to the lymph nodes.

Another strategy puts postmenopausal patients on tamoxifen and then switches them to an AI after two to three years. Switching to Aromasin, the third AI, has shown superiority over five years of tamoxifen in a large trial of more than 4,500 women. Women who received tamoxifen for five years had a 9 percent risk of recurrence compared with 6 percent for women taking two to three years of tamoxifen followed by Aromasin to complete five years of adjuvant hormonal therapy.

A common side effect of all three AIs is bone loss, which can result in bone thinning and fractures because of lower levels of estrogen in the body. Most postmenopausal women on AIs should have their bone density checked before treatment and then annually while on therapy. Bone-strengthening drugs called bisphosphonates, such as Fosamax (alendronate), Boniva (ibandronate) and Actonel (risedronate), are commonly given with AIs to decrease the risk of bone loss and fractures. Other studies have found that Femara taken with another bisphosphonate called Zometa (zoledronic acid) can improve bone density. Joint and muscle pain is another common AI side effect that can be bothersome to patients.

Ongoing AI studies of different combinations, various treatment durations and treatment given before surgery may add to the wide range of indications AIs now offer postmenopausal women with hormone receptor-positive breast cancer. Femara and Aromasin have been shown to shrink large breast cancer tumors before surgery (called neoadjuvant therapy), but larger trials are needed. Researchers are also trying to locate biomarkers that may help doctors choose the most appropriate AI for each patient.

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