BREAST CANCER

Anastrozole sets the STAGE for premenopausal women

Aromatase inhibitors are an effective and well tolerated neoadjuvant treatment with improved efficacy for postmenopausal women with breast cancer compared with tamoxifen. Moreover, neoadjuvant endocrine therapy provides an important treatment option to downstage tumors so mastectomy can be avoided in preference of breast-conserving surgery in postmenopausal women. The efficacy and safety of the aromatase inhibitor anastrozole, however, has not previously been assessed fully in premenopausal women. In Japan, tamoxifen and goserelin is the standard treatment for premenopausal women with breast cancer. Now, a phase III, randomized, double-blind study carried out in 27 centers in Japan has demonstrated that the combination of anastrozole and goserelin has a more favorable risk–benefit profile compared with tamoxifen and goserelin.

Preliminary clinical data in premenopausal women had indicated that anastrozole and goserelin may provide a greater reduction in mean estradiol concentrations, and results from the ABCSG-12 trial have shown similar disease-free survival rates for anastrozole plus goserelin and tamoxifen plus goserelin. This prompted the initiation of the Study of Tamoxifen or Arimidex, combined with Goserelin acetate, to compare Efficacy and safety (STAGE) trial, in which neoadjuvant

anastrozole and goserelin were compared with tamoxifen and goserelin in 197 premenopausal Japanese women (over 20 years of age) with estrogen receptor-positive, HER2-negative operable breast cancer. Tumor response (measured by a reduction in tumor size), was assessed with calliper and ultrasound every 4 weeks for 24 weeks, and MRI or CT at 12 and 24 weeks.

Shinzaburo Noguchi, senior investigator of the study highlights the key findings: “after 24 weeks of treatment, significantly more women in the anastrozole group achieved a complete or partial response than those in the tamoxifen group. Patients treated with anastrozole showed a higher tumor response rate (70%) than those treated with tamoxifen (51%). This resulted in a greater proportion (86%) of patients in the anastrozole group having breast-conserving surgery compared with those in the tamoxifen group (68%).”

Reductions in estrone and estradiol levels at 24 weeks were significantly greater in women treated with anastrozole. Most of the observed adverse events were mild or moderate in nature (grade 1 or 2), and musculoskeletal disorders were higher with the anastrozole combination compared with the tamoxifen group.

Expression levels of the cell proliferation marker Ki-67 have previously been correlated with treatment efficacy. In this trial, the reductions in Ki-67 levels

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were significantly greater for women treated with anastrozole compared with tamoxifen. Noguchi expands on future research plans, “Ki-67 is being evaluated for its ability to act as a predictive marker of therapeutic response. We are interested in assessing further the relationship between Ki-67 expression and anastrozole plus goserelin versus tamoxifen plus goserelin neoadjuvant therapy, as well as any correlation between Ki-67 and overall tumor response rate”.

The researchers conclude, “results from this study have shown for the first time that neoadjuvant treatment with anastrozole plus goserelin has a better risk–benefit profile than tamoxifen plus goserelin as neoadjuvant treatment for premenopausal women with early stage breast cancer”. Larger studies are required to confirm these encouraging results before clinical practice changes can be considered.

Lisa Hutchinson

Original article Masuda, N. *et al.* Neoadjuvant anastrozole versus tamoxifen in patients receiving goserelin for premenopausal breast cancer (STAGE): a double-blind, randomised phase 3 trial. *Lancet Oncol.* doi:10.1016/S1470-2045(11)70373-4