
Treatment-induced amenorrhea improves prognosis of early, ER/PR-positive breast cancer

Premenopausal women with early-stage, hormone receptor-positive breast cancer have better relapse-free survival if they become amenorrheic during adjuvant hormonal therapy or chemotherapy; this was among the key findings presented by Michael Gnant, MD, and his colleagues from Austria.

“Treatment-induced amenorrhea occurs after both ovarian ablation and suppression treatment and chemotherapy in premenopausal breast cancer patients,” said Dr. Gnant. “The association of amenorrhea with improved prognosis in CMF (cyclophosphamide, methotrexate, and fluorouracil)-treated premenopausal patients supports the hypothesis of indirect endocrine effects of cytotoxic chemotherapy.”

The investigators analyzed data from the Austrian Breast and Colorectal Study Group (ABCSCG) 05 trial, a prospective randomized trial that enrolled premenopausal

women with stage I or II breast cancer positive for estrogen receptors, progesterone receptors, or both. After surgery, with or without adjuvant radiation therapy, the women were randomized in equal numbers to receive either hormonal therapy—goserelin (Zoladex) for 3 years plus tamoxifen for 5 years—or chemotherapy—6 cycles of CMF.

Analyses were based on 1,017 patients with a median follow-up of 11 years. At baseline, their median age was 45 years. “It’s a relatively good-prognosis patient group: 56% had a tumor size less than 2 cm, 50% had node-negative disease, and about 50% had high estrogen and/or progesterone receptor-positive tumors,” Dr. Gnant noted.

In the study population overall, 77% of patients experienced treatment-induced amenorrhea (an absence of periods for at least 4 months starting the third month of adjuvant therapy); the incidence was 100% in the hormonal

therapy group but only 53% in the chemotherapy group. In the latter group, the incidence increased with age, with amenorrhea occurring in 30% of patients aged 40 years or younger, 57% of those aged 41 to 50 years, and 66% of those older than age 50.

Benefit may depend on age and HER2 status

Estimated relapse-free survival was significantly better in patients who experienced treatment-induced amenorrhea than in those who did not, Dr. Gnant said, adding that the eventual converging of the curves was likely due to the onset of natural menopause. Overall survival also favored the amenorrheic group, although not significantly so.

In a multivariate model, treatment-induced amenorrhea was associated with a significant reduction in the risk of relapse (hazard ratio [HR], 0.58) and a nonsignificant reduction in the risk of death (HR, 0.82). In a model

restricted to the chemotherapy group, treatment-induced amenorrhea also conferred a significant reduction in the risk of relapse (HR, 0.56) and a nonsignificant reduction in the risk of death (HR, 0.79).

Treatment-induced amenorrhea interacted with age marginally among patients overall and significantly within the CMF group, in which there was a 44% reduction in the risk of relapse among amenorrheic women 40 years old or younger. Treatment-

induced amenorrhea did not interact with HER2 status among all patients but did within the CMF group, in which patients with HER2-negative tumors had a reduced risk with amenorrhea but those with HER2-overexpressing tumors did not. In contrast, there were no interactions between treatment-induced amenorrhea and quantitative hormone receptor level.

In conclusion, “The prognostic impact of treatment-induced amenorrhea is particularly present in patients

younger than 40 years of age and patients with HER2/*neu*-negative tumors. Conversely, such patients treated with CMF who did not experience amenorrhea are at increased risk of relapse.”

Gnant M, Greil R, Kubista E, et al. The impact of treatment-induced amenorrhea on survival of premenopausal patients with endocrine-responsive breast cancer: 10-year results of ABCSG-05 (CMF vs goserelin-tamoxifen). Paper presented at the 29th Annual San Antonio Breast Cancer Symposium; December 14–17, 2006; San Antonio, Tex. Abstract 17.