Tamoxifen Alone Discouraged as Adjuvant Tx

BY DIANA MAHONEY
New England Bureau

HOLLYWOOD, FLA. — An aromatase inhibitor, either alone or after tamoxifen therapy, is better than tamoxifen alone for the long-term prevention of breast cancer in postmenopausal women with invasive breast cancer, according to updated treatment guidelines from the National Comprehensive Cancer Network.

Several recent clinical trials have shown that adjuvant endocrine therapy with the aromatase inhibitors anastrozole (Arimidex), letrozole (Femara), and exemestane (Aromasin), can significantly improve disease-free survival in postmenopausal women, compared with tamoxifen as a single agent.

Consequently, “tamoxifen alone [in this patient population] has fallen off the radar screen,” said Robert Carlson, M.D., chair of the NCCN panel that revised the guidelines for adjuvant hormonal therapy reinitiated,” Dr. Carlson said.

The guidelines for adjuvant hormonal therapy reinitiated,” Dr. Carlson said.

Anastrozole prevents one in four of the relapses experienced by patients on tamoxifen. The aromatase patients also had fewer hot flashes.

Guidelines Define Menopause

Critical to the appropriate clinical administration of the revised NCCN breast cancer treatment recommendations is a standardized definition of menopause.

“You wouldn’t think a definition of menopause would be needed, but just about all studies that have been done in postmenopausal women define [menopause] differently,” Dr. Carlson said. This can cause problems and confusion, particularly with respect to treatment with aromatase inhibitors, which are most effective in postmenopausal women.

Menopause is generally the permanent cessation of menses. “As the term is used in breast cancer management, it includes a period and permanent decrease in ovarian estrogen synthesis,” the revised guidelines state.

Reasonable criteria for determining menopause include any of the following:

► Prior bilateral oophorectomy.

► Age 60 years or older.

► Age younger than 60 years and amenorrhea for at least 12 months in the absence of chemotherapy, tamoxifen, toremifene, or ovarian suppression, and FSH and estradiol in the postmenopausal range.

► Age younger than 60 years and FSH and plasma estradiol levels in postmenopausal range in women taking tamoxifen or toremifene.

It is not possible to assign menopausal status to women receiving an LH-RH agonist or antagonist, the guidelines state. Amenorrhea is not a reliable indicator of menopausal status in women who are premenopausal at the outset of adjuvant chemotherapy.

Women who undergo chemotherapy treatments that permanently stop menses may still produce estradiol at levels that are premenopausal,” commented Dr. Carlson, stressing that premenopausal estrogen levels can influence treatment with aromatase inhibitors.

Study Identifies Novel Breast Cancer Prognostic Markers

BY PATRICIE WENDLING
Chicago Bureau

ATLANTA — New data suggest that the Notch signaling genes—Notch1 and Jagged1—are potential novel prognostic markers for breast cancer, Michael Reedijk, M.D., FACS, reported at a symposium sponsored by the Society of Surgical Oncology.

“Patients expressing high levels of Jagged1 or Notch1 demonstrated significantly poorer overall survival than patients expressing low levels,” said Dr. Reedijk of University Health Network, Princess Margaret Hospital in Toronto.

Abnormal Notch signaling has been observed in a number of malignancies, but this is the first report of direct evidence linking high-level Notch1 and Jagged1 expression with poorer outcomes in women with breast cancer.

The data also suggest a mechanism by which Notch is activated in aggressive breast cancer that may be targeted with drugs currently under development for Alzheimer’s disease, Dr. Reedijk said.

Dr. Reedijk and colleagues at Toronto’s Hospital for Sick Children and the University Health Network analyzed tumor samples from 184 breast cancers using in situ hybridization. One-third of the cancers were node-positive, one-third were node-negative, and one-third had metastasized at presentation. Notch2 was expressed at high levels in most tumors.

In contrast, high levels of Notch1, Jagged1, and Notch3 were found in the tumors of a subset of patients with poor prognostic pathological features.

Patients with tumors expressing high levels of these genes showed lower overall survival than those expressing low levels of these genes, although the association was not statistically significant for Notch3.

The 5-year survival rate for women expressing high levels of Jagged1 was 42%, with a median survival of 50 months, compared with 65% and 83 months for patients with low levels of Jagged1.

The 5-year survival rate was 49% for women expressing high levels of Notch1, with a median survival of 33 months, compared with 64% and 91 months for patients with low levels of Notch1, he said at the meeting.

For patients expressing high levels of both Jagged1 and Notch1, the 5-year survival rate and median survival time were approximately half of those seen for tumors without Jagged1 and/or Notch1 expression.

The 5-year survival rate was just 14%, with a median survival of 43 months.

“This suggests that there is a ligand and receptor circuit that is functioning in these tumors and may identify a signaling pathway that can be therapeutically targeted using newly developed secretase inhibitors, which block Notch signaling,” Dr. Reedijk said.