

NCCN Offers Updated Breast Cancer Guidelines

Genetic counseling is now advised for women with DCIS and a high risk for hereditary breast cancer.

BY DAMIAN McNAMARA

HOLLYWOOD, FLA. — New recommendations in breast cancer guidelines rank preferred adjuvant chemotherapy regimens and offer guidance on local therapy for women who present with stage IV breast cancer, according to an update presented at the annual conference of the National Comprehensive Cancer Network, an alliance of 21 leading cancer centers.

The revised guidelines also make optional a radiation boost after lumpectomy for early invasive disease, and call for a mammogram between surgery and radiotherapy for women with ductal carcinoma in situ (DCIS). Furthermore, they say that women with DCIS or early invasive disease should be referred for genetic counseling if they are at high risk for hereditary breast cancer.

For women who initially present with metastatic breast cancer, a new guideline says that local breast surgery and/or radiation therapy may be beneficial. These “generally palliative” treatments should be considered after a patient responds to initial systemic treatment.

“There is some evidence for an impact on survival for stage IV disease in some large registries,” Dr. Stephen B. Edge said, noting that, historically, local therapy was reserved for palliation of patients with local tumor progression.

Partial mastectomy improved median survival for women with stage IV disease at initial diagnosis, according to a National Cancer Data Base study (Surgery 2002;132:620-6). With clear margins, these women lived a median of 23 months, compared with 12 months for women with no surgery.

However, the data to support surgery vs. systemic therapy in stage IV disease are all retrospective, Dr. Edge said. The surgery benefit may be best in the setting of minimal metastatic burden, he added. “This will be best addressed by a controlled trial, which has been proposed but not yet initiated” in the United States.

Exclusive locoregional radiation therapy improved survival among 581 women with synchronous metastasis at the time of diagnosis, and might be an alternative to surgery (J. Clin. Oncol. 2009;27:1375-81). Overall survival at 3 years was 43% with exclusive locoregional radiotherapy, compared with 27% without.

“Interestingly, [women with] visceral metastasis ... fared better vs. those with bone metastasis,” said Dr. Edge, chair of breast surgery at Roswell Park Cancer Institute in Buffalo, N.Y.

Another new recommendation calls for mammography following surgery in women with DCIS. This is a “very important footnote,” Dr. Beryl McCormick said. “A postexcision mammogram should be performed when there is uncertainty about margins.” She copresented the updates with Dr. Edge; neither disclosed any relevant conflicts of interest.

The radiation boost was previously “recommended for all women having breast conservation therapy. This year, we changed the guidelines to say [the boost] could be omitted in older women,” as well as in some other scenarios, such as in a patient who has a re-excision—for example, in the case of close initial margins—and the specimen is large and contains no cancer, said Dr. McCormick, clinical director of the department of radiation oncology at the Memorial Sloan-Kettering Cancer Center in New York.

The boost is an option for women with stage I, IIA, IIB, or T3 N1 M0 cancer following lumpectomy with surgical axillary staging. Significantly less local recurrence at 5 years among women who received additional radiation to their tumor bed, compared with those who did not, was reported in a key study (N. Engl. J. Med. 2001;345:1378-87).

The data out to 8 years still support a significant benefit, particularly for younger women, Dr. McCormick said. The decrease in local recurrence was “highly significant” for women younger

than 40 years who had the boost, compared with those who did not ($P = .0019$). The benefit remained significant, with P values of .0096 in women aged 41-50 years, .0012 in women aged 51-60, and .029 in women older than age 60. “The biological benefit was really insignificant for women over 60,” she noted.

The guideline panel also reorganized adjuvant chemotherapy regimens in invasive disease. “This year, we ranked the relative value of adjuvant chemotherapy—a list of ‘preferred regimens’ and

erately or poorly differentiated, or have unfavorable features.

Although it was added to the guidelines, the recommendation is not as strong as the unanimous category 1 recommendation for use of trastuzumab in combination with adjuvant endocrine therapy and adjuvant chemotherapy for women with tumors larger than 1 cm or who have node-positive disease with one or more axillary node metastases larger than 2 mm.

Genetic counseling of women with DCIS “if they are at high risk for hereditary breast cancer or early invasive disease” is a new recommendation. “In high-risk women, genetic testing can often lead to a decision that leads to treatment of both the affected breast and the unaffected breast,” Dr. McCormick said, citing a study that notes the increase in prophylactic bilateral mastectomy rates from 4% in 1998 to 11% in 2003 (J. Clin. Oncol. 2007;25:5203-9). “And I suspect if we look again, it would be even higher.”

For the first time, the guidelines also feature a section on principles of breast reconstruction after surgery. Breast implants, autologous tissue, or a combination are identified as options.

These principles say that skin-sparing mastectomy is “probably equivalent” to standard mastectomy, and “should be performed by an experienced breast surgery team that works in a coordinated, multidisciplinary fashion.” Dr. McCormick said at the meeting that reconstruction “most importantly” should be “performed by an experienced team of breast surgeons and plastic surgeons.”

Reconstruction can be done at the same time or after completion of cancer treatment. When postmastectomy radiation is required, however, the general preference is to delay autologous-tissue reconstruction until after the completion of radiation therapy, Dr. McCormick said. This is a category 2B recommendation, which means it was not unanimous, she noted. “We have had great experience [with delayed reconstruction] at Memorial Sloan-Kettering, but other colleagues on the panel, especially at [the University of Texas M.D. Anderson Cancer Center in Houston], have not, so it remains 2B,” she said. ■



A postexcision mammogram should be performed when there is uncertainty about margins.

DR. McCORMICK

‘other regimens’ that have been used,” Dr. Edge said.

The NCCN identifies the following “preferred” trastuzumab-containing adjuvant regimens for invasive breast cancer:

- ▶ Doxorubicin (Adriamycin) and cyclophosphamide (AC) followed by paclitaxel plus trastuzumab (Herceptin).
- ▶ Docetaxel (Taxotere), carboplatin, trastuzumab (TCH).

In terms of nontrastuzumab-containing adjuvant regimens, the NCCN designates the following as “preferred”:

- ▶ Docetaxel, doxorubicin, cyclophosphamide (TAC).
- ▶ Dose-dense AC followed by paclitaxel every 2 weeks.
- ▶ AC followed by weekly paclitaxel.
- ▶ Docetaxel and cyclophosphamide (TC).
- ▶ AC.

Another guideline change, which has achieved the status of the rarely used category 3 recommendation (reflecting “major disagreement”) is the use of trastuzumab for systemic adjuvant therapy in HER2 (human epidermal growth factor 2)-positive disease for women with small tumors, Dr. Edge said. This option was added for women with tumors measuring 0.6-1.0 cm that are mod-

Aromatase Inhibitors May Hasten Bone Loss in Osteopenia

BY MICHELE G. SULLIVAN

WASHINGTON — Aromatase inhibitors are associated with small but significant levels of additional bone loss in osteopenic women who take the drugs for hormone-sensitive breast cancer, according to a study of 104 women.

After just 1 year of aromatase inhibitor therapy, these women lost a mean of 1.5% in bone mineral density (BMD) at the lumbar spine and 2% at the femoral neck; two of the subjects progressed from osteopenia to osteoporosis, Dr. Pamela Taxel reported in a poster session at an international symposium sponsored by the National Osteoporosis Foundation.

Expected bone loss associated with natural progres-

sion generally would be about 0.5%-1% per year, according to Dr. Taxel of the University of Connecticut Health Center, Farmington.

She and her colleagues performed a chart review of 104 women who were taking the drugs for breast cancer and were evaluated for bone health. Of these, 61 (58%) had osteopenia. The patients’ mean age was 58 years; they had been on aromatase inhibitor therapy for up to 2 years. At baseline, 18% (11 patients) were taking a bisphosphonate. They were followed for an additional year.

Lumbar spine BMD measurements were available at baseline and at 1 year for 39 women. After 1 year, the women had lost a mean of 1.5% in BMD at this site; 18 women had lost more than 3%. Baseline and

1-year femoral neck BMD measurements were available for 36 women.

After 1 year, there was a mean BMD decrease of 2% at this site. Four women lost more than 3% at the spine and more than 5% at the femoral neck.

Two of the 36 women with both lumbar spine and femoral neck data progressed to osteoporosis during the follow-up period.

The progression in bone loss occurred despite increased patient compliance with vitamin D supplements. At baseline, 74% of the women were taking at least 1,000 mg/day of vitamin D, although 41% were still deficient. At the end of the follow-up period, vitamin D intake had significantly increased, with only 25% of the women still deficient, Dr. Taxel noted. ■