Whole-Breast Irradiation: Worthwhile in Early Ca?

New data show that adding whole-breast irradiation to standard treatment may increase positive results.

BY BRUCE JANCIN
Denver Bureau

DENVER — Whole-breast irradiation coupled with breast-conserving surgery and hormone therapy remains the standard of care in women with favorable early breast cancer, Richard Poetter, M.D., said at the annual meeting of the American Society for Therapeutic Radiology and Oncology.

New data from a large multicenter randomized Austrian trial demonstrate that although lumpectomy plus 5 years of tamoxifen or an aromatase inhibitor provides "excellent" results in such patients, "we can do significantly better if we add whole-breast radiotherapy," said Dr. Poetter of the University of Vienna.

But this assertion was challenged by discussant Kevin S. Hughes, M.D., who argued that the benefits conferred by the addition of radiation therapy (RT), while statistically significant, are modest and do not rise to the level of clinical significance or warrant standard-of-care status.

He urged an individualized approach to breast RT, a treatment he said most elderly patients are best spared.

"Breast radiation therapy provides less and less benefit as women get older," said Dr. Hughes, surgical director of the Avon Foundation Comprehensive Breast Evaluation Center at Massachusetts General Hospital, Boston.

"Most radiation oncology colleagues I know would agree that in elderly patients, breast irradiation plus tamoxifen or an aromatase inhibitor is overkill and is seldom required. Where we disagree is in deciding who are the elderly."

Dr. Poetter reported on 826 postmenopausal women with favorable early breast cancer as defined by a tumor size less than 3 cm, negative lymph nodes, and positive tumor estrogen and/or progesterone receptor status. All underwent lumpectomy plus hormone therapy and were randomized to whole-breast RT or not in the Austrian Breast and Colorectal Cancer Study Group trial 8. Patients in the RT arm received 50 Gy to the breast; two-thirds of them got an additional 10-Gy boost.

After a median 42 months' follow-up, the 5-year local recurrence rate—the primary study end point—was 4.5% in controls, compared with 0.6% in the RT group. The risk of local relapse was increased 13.5-fold by lack of RT.

'We can do ... better if we add whole-breast radiotherapy' to treat women with early cancer.

DR. POETTER

Dr. Hughes, however, flipped those figures around, noting the Austrians had shown that more than 96% of study participants who were exposed to the cost, inconvenience, and potential toxicities of RT derived no benefit from it. "Perhaps a more intelligent way of looking at these older patients is to say 'lumpectomy plus radiation therapy' or 'lumpectomy plus tamoxifen.' Both give very good outcomes as patients age."

Dr. Poetter noted that four cases of contralateral breast cancer arose among controls, versus none in the RT group. However, RT had no significant impact upon distant metastasis or overall survival rates.

The 42-month follow-up in the Austrian trial is relatively brief, Dr. Hughes said. More mature 7-year data are now available from the similarly designed Cancer and Leukemia Group B trial 9343, in which he was the lead investigator. Five-year data already have been reported from the trial, in which 636 women aged 70 years or older with favorable early breast cancer treated by lumpectomy and tamoxifen were randomized to RT or not (N. Engl. J. Med. 2004;351:971-7).

At 7 years, 99% of women in the RT arm remain disease free, compared with 94.4% with lumpectomy and tamoxifen alone. "But whether you irradiate or not, essentially 98%-99% of those women will preserve their breast through the remainder of their lives," the surgeon said.

A total of 24% of study participants have died; 1% of breast cancer, the other 23% of other causes. ■

In Vitro Fertilization May Increase Breast Cancer Risk in Predisposed

BY KATE JOHNSON
Montreal Bureau

MONTREAL — Ovulation induction for in vitro fertilization may promote the growth of breast cancer in patients who are predisposed to the disease, results of a case series of seven IVF patients later diagnosed with the disease suggest.

"A breast cancer family history should be included in the pre-IVF work-up, and women with a positive history should be considered candidates for an alternate IVF stimulation protocol," recommended Kutluk Oktay, M.D., who reported the findings in a poster at the joint annual meeting of the American Society for Reproductive Medicine and the Canadian Fertility and Andrology Society.

In a case series of seven breast cancer patients who had undergone ovarian stimulation for in vitro fertilization (IVF), Dr. Oktay's team found more than half (57%) had a family history of breast cancer. It is normally expected that only about 10% of breast cancer patients will have a family history of the disease.

All women had estrogen- and progesterone-receptor-positive breast cancer, when normally it is expected that about 40% of breast cancer patients will have this type of disease, said Dr. Oktay, of Cornell University in New York.

Ovulation induction exposes women to supraphysiologic levels of estrogen, which may be problematic in women with a family history of breast cancer, Dr. Oktay suggested. "Not that IVF necessarily causes their cancer, but it may promote it," he said. "Counseling should include the fact that if you have a family history of breast cancer, this may increase your risk—but it may simply facilitate the appearance of the disease and so patients should be closely examined before IVF and followed after."

The mean age of the patients was 40, and the mean duration from the time of their IVF treatment until their breast cancer diagnosis was 8.5 months.

One patient had a breast lesion biopsied before undergoing IVF, and it was initially negative for malignancy. However, after her IVF treatment, the mass grew, and a second biopsy revealed stage I invasive ductal carcinoma.

'A breast cancer family history should be included in the pre-IVF work-up.'

DR. OKTAY

One other patient had stage I invasive ductal carcinoma, three had stage IIA disease, and two had carcinoma in situ. Tumor size was less than or equal to 1.5 cm in all except one patient.

Dr. Oktay, also of the Center for Reproductive Medicine and Infertility of New York–Presbyterian Hospital/Weill Cornell Medical Center, recommends that IVF patients who face an elevated risk of breast cancer based on their family history should undergo ovulation induction with a letrozole/FSH protocol instead of standard ovulation induction, which exposes patients to high levels of estrogen.

Letrozole, an aromatase inhibitor that also is used to treat breast cancer, can stimulate oocyte production without raising estrogen levels, making it ideal for this patient population. "Obviously, if they conceive, they are going to be exposed to high levels of estrogen anyway … and the studies so far don't suggest that pregnancy necessarily increases the risk of cancer." ■

Gabapentin May Help Hot Flashes in Breast Cancer

BY DOUG BRUNK
San Diego Bureau

A 900-mg daily dose of gabapentin was associated with significant decreases in hot flash severity and frequency, but a 300-mg daily dose of the drug was not, results from a randomized, double-blind, placebo-controlled trial have found.

"We believe gabapentin can be added to the list of nonhormonal agents for the control of hot flashes in women with breast cancer, and the effects of doses higher than 900 mg/day merit further study," wrote the investigators, led by Kishan J. Pandya, M.D., of the University of Rochester (N.Y.).

In a study funded by the National Cancer Institute, he and his associates randomized 420 women with a mean age of 55 years to receive placebo, 300 mg/day of gabapentin, or 900 mg/day of gabapentin.

The women, the majority of whom were white, were enrolled at 18 different sites of the university's community clinical oncology program. They recorded the severity level of hot flashes and 10 other symptoms in a 1-week self-report diary at baseline and during the fourth and eighth weeks of treatment (Lancet 2005;366:818-24).

Posttreatment analysis revealed that the reduction in hot flash severity score was only 15% for those in the placebo group, compared with 31% for those in the 300-mg/day gabapentin group and 46% for those in the 900-mg/day gabapentin group. The differences between groups were statistically significant, but only the 900-mg/day dose of gabapentin was associated with significant decreases in hot flash frequency and severity.

No differences were observed among the three treatment groups with respect to the 10 other symptoms, suggesting that gabapentin was well tolerated.

"Our study was designed to test the intervention for 8 weeks; therefore, we cannot comment on long-term use of gabapentin," the investigators wrote.

While the drug's mechanism of action in the reduction of hot flashes in women with breast cancer remains unclear, the investigators speculate that "upregulation of the gabapentin binding site could be involved in the hypothalamus as a result of estrogen withdrawal, leading to increased activity of the neurotransmitters in the hypothalamus."

Gabapentin is approved for the treatment of epileptic seizures but it is also used for the treatment of migraines, restless legs syndrome, and bipolar disorder.

Pfizer Inc. provided the gabapentin and placebo used in the study. ■