Soy Strikes Out for Breast Cancer Risk Reduction

ARTICLES BY BRUCE JANCIN

SAN ANTONIO — Six months on a mixed soy isoflavone dietary supplement produced no significant change in breast epithelial cell proliferation in healthy women at high risk for breast cancer in a phase IIb randomized trial.

"These results argue against the efficacy of soy isoflavones supplementation of the adult Western diet for purposes of breast cancer prevention, but also do not suggest an adverse effect on the breast," Dr. Seema A. Khan declared at the San Antonio Breast Cancer Symposium.

The study included 99 women with an elevated breast cancer risk score or a history of completely treated unilateral breast cancer. They were randomized to 6 months of placebo or the soy isoflavone supplement, each serving containing 150 mg of genistein, 74 mg of daidzein, and 11 mg of glycitein.

The primary study end point was change over time in Ki-67, a measure of breast epithelial cell proliferation that reflects cancer risk. The samples were obtained by random fine-needle aspiration.

Among the 43 postmenopausal participants there was no difference in Ki-67 between the treatment and control arms at 6 months. Among the premenopausal women there was actually an unwelcome but nonsignificant trend for greater Ki-67 labeling in the soy supplement group, especially in samples obtained during the luteal phase, reported Dr. Khan, professor of surgery at Northwestern University, Chicago.

Plasma genistein concentrations at 6 months averaged 269.8 mg/mL in the treatment arm, compared with 2.5 ng/mL in the control group.

The phase IIb study was undertaken in response to epidemiologic evidence that consumption of soy isoflavones confers protection against development of breast cancer in Asian populations (Br. J. Cancer 2008; 98:9-14), among whom soy isoflavone–rich food products such as miso soup, tofu, and natto are popular.

However, a Japanese study presented at the San Antonio meeting suggested that it is consumption of soy isoflavones early in life that's the key to possible reduction of breast cancer risk decades later in middle-aged Japanese women.

Dr. Masakazu Toi of Kyoto (Japan) University presented a population-based case-control study involving 355 breast cancer patients aged 40-55 years and 710 age- and region-matched controls. They underwent structured interviews by blinded interviewers regarding their past consumption of soy isoflavone–containing foods during three specific periods of their life: age 10-12 years, around age 20, and 10-15 years prior to the interview.

Combining consumption during the three periods, 29% of all subjects with breast cancer fell into the lowest quartile for average daily soy consumption, as did 20% of controls. In a multivariate logistic regression analysis, women in the top quartile for average daily soy consumption during the three time periods of interest were 55% less likely to have breast cancer than those in the lowest quartile.

This study was funded by the Japanese Public Health Research Foundation.

Dr. Khan's study was funded by the Bluhm Family Program for Breast Cancer Early Detection and Prevention and the National Cancer Institute. ■

Stellate Ganglion Block May Ease Severe Hot Flashes

SAN ANTONIO — Stellate ganglion block may be an option for severe, treatment-refractory hot flashes and sleep disturbances in breast cancer patients.

In a prospective study, stellate ganglion block procedures led to significant improvements in 17 of 24 breast cancer patients with severe hot flashes despite pharmacotherapy with venlafaxine (Effexor) and/or clonidine, Dr. Patrick Neven reported at the San Antonio Breast Cancer Symposium.

The ganglion block is performed as an outpatient procedure and takes about 5 minutes. An anesthetist uses fluoroscopic guidance to inject 10 cc of anesthetic at the anterolateral aspect of the C-6 vertebra.

Benefits endured 12 or more weeks in 12 of the 17 responders. A single right-sided stellate ganglion block was effective in five patients. Following a second block placed on the opposite side, 5 of 10 patients had responses. Benefits also were seen in two of three patients who got a third block 2-3 months after the first, according to Dr. Neven of the University of Leuven (Belgium).

Stellate ganglion block was associated with no side effects other than the temporary Horner syndrome, which merely indicates the block has been successful. Horner syndrome involves pupillary changes, a droopy eyelid, and a one-sided decrease in facial sweating, typically lasting for about 20 minutes.

Stellate ganglion blocks have been used for at least 6 decades to treat a variety of pain conditions, including chronic regional pain syndrome, migraine, and angina. The notion of using the procedure to treat severe hot flashes in postmenopausal women and in breast cancer patients is credited to Dr. Eugene G. Lipov, director of pain research at Northwest Community Hospital, Arlington Heights, Ill. In his 13-patient pilot study, the mean number of hot flashes per week plummeted from 79 at baseline to 7 at 42 weeks of follow-up. Ten patients needed additional blocks after a mean of 11 weeks (Lancet Oncology 2008;9:819-20).

Dr. Lipov demonstrated that the stellate ganglion has second- and third-order neuronal connections to key areas of the brain involved in temperature regulation and other functions. His proposed mechanism of benefit is that stellate ganglion block causes a prolonged reduction in brain nerve growth factor levels, resulting in decreased brain norepinephrine (Med. Hypotheses 2009;72:657-61).

Dr. Neven reported that sleep quality improved significantly in 14 of the 24 Belgian breast cancer patients, although the effect was temporary in 2 of them.

Session chair Charles L. Loprinzi said he found the Belgian study particularly interesting because, after speaking with Dr. Lipov, he too has undertaken a prospective pilot study of stellate ganglion block for hot flashes, with data available on eight breast cancer patients.

"Let me just say that similar results are being observed. We gave only one block and we've seen a drastic decrease in hot flashes in the first 1-3 weeks. With follow-up out to 6 weeks, some women have their hot flashes come back, others don't," commented Dr. Loprinzi, professor of oncology at the Mayo Clinic, Rochester, Minn.

A parallel improvement in sleep disturbances was seen.

"Sleep problems in patients with hot flashes are often due to night sweats. Get rid of the hot flashes and the patients often sleep better," Dr. Loprinzi said.

Dr. Neven had no disclosures in regard to the study. ■

MRI Detected Breast Cancer Earlier in High-Risk Women

VITALS

Major findings: In a sample of women with BRCA1 and -2 mutation, 13% of invasive cancers in an MRI surveillance group were node positive, compared with 40% in controls.

Source of data: The nonrandomized study involved 1,275 women with BRCA and -2 mutations; 445 received annual MRI and mammography along with twice-yearly clinical breast examination. A control group of 830 women was screened by annual mammography and twice-yearly clinical breast exams.

Disclosures: The investigator served as a consultant to Berlex and Bayer.

SAN ANTONIO — Adding MRI surveillance to conventional mammography in women with BRCA1 or BRCA2 mutations results in a favorable stage shift, with breast cancers being detected at an earlier, more curable stage, according to a prospective cohort study.

This finding is consistent with the notion that MRI surveillance reduces distant recurrence rates and breast cancer mortality, although definitive proof must await another 5-10 years of study follow-up, Dr. Ellen Warner said at the San Antonio Breast Cancer Symposium.

In the meantime, these encouraging interim results will hopefully convince very-high-risk women and their physicians that surveillance with yearly MRI and mammography is a reasonable alternative to prophylactic mastectomy, added Dr. Warner of the University of Toronto.

A randomized controlled trial comparing MRI surveillance to mammography will never happen for ethical as well as practical reasons, she asserted. The next-best study design would be a prospective cohort study. Such a study is underway in Toronto. It involves 1,275 women with BRCA1 or -2 mutations who to date have been followed for a mean of 3.2 years for incident breast cancer.

The nonrandomized study involves 445 women in a Toronto surveillance program involving annual MRI and mammography along with twice-yearly clinical breast examination and a control group comprising 830 women screened by annual mammography and twice-yearly clinical breast exams.

There have been 41 cases of invasive breast cancer detected in the MRI group and 77 in controls. The incidence in the two groups was nearly identical. However, there was a marked difference in cancer stage. Only 13% of invasive cancers in the MRI group were node positive, compared with 40% in controls.

The mean 9-mm tumor size in the MRI group was one-half that in controls. Only 3% of invasive tumors in the MRI group exceeded 20 mm, compared with 29% in controls.

Ductal carcinoma in situ (DCIS) was detected in 2.2% of the MRI group and 1.1% of controls.

After controlling for baseline differences in menopausal status, tamoxifen therapy, and other potential confounders, the MRI cohort was 5.7-fold more likely than controls to be diagnosed with DCIS, threefold more likely to be diagnosed with stage 1 breast cancer, and one-quarter as likely to have stage 2 or higher breast cancer.

This study probably underestimates the true benefit of MRI surveillance, Dr. Warner said. Major advances in MRI technology have occurred since the study began roughly a decade ago, with resultant markedly improved diagnostic sensitivity. ■