

ASCO Breast: Implants May Quell Hormone Deficiency

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October 04, 2010

MedPage Today Action Points

- Note that this study was published as an abstract and presented at a conference. These data and conclusions should be considered to be preliminary until published in a peer-reviewed journal.
- Explain that subcutaneous implants of a combination of testosterone and the aromatase inhibitor anastrozole in postmenopausal breast cancer survivors improved menopausal symptoms without increasing estradiol levels.
- Note that this proof-of-concept study has set the stage for a randomized, controlled phase III trial, according to the investigators.

Review

NATIONAL HARBOR, Md. -- A subcutaneous testosterone implant has shown potential to reduce hormone-deficiency symptoms without raising estradiol levels in breast cancer survivors, data from a small clinical series showed.

Combined with the aromatase inhibitor anastrozole (Arimidex), the implant maintained an average testosterone level of 281 ng/dL with associated estradiol levels <30 pg/mL in 43 breast cancer patients.

Implants containing testosterone alone were associated with estradiol levels >30 pg/mL in 50 of 119 postmenopausal women without breast cancer. That compared with five of 75 (6.7%) combination implants in the breast cancer patients, Rebecca L. Glaser, MD, of Wright State University in Dayton, Ohio, reported here at the Breast Cancer Symposium.

"We believe testosterone is beneficial to breast tissue, and, in fact, most of my referrals are from oncologists," Glaser told *MedPage Today*. "The downside is that testosterone can be aromatized into estradiol, which may stimulate breast tissue.

"So, we came up with the combination of testosterone with an aromatase inhibitor, delivering it subcutaneously. It is extremely well tolerated, there are no compliance issues, and it takes care of the symptoms."

Breast cancer survivors often have severe menopausal-like symptoms owing to treatment-induced hormone deficiency. Clinical and preclinical evidence suggests androgens inhibit mammary epithelial proliferation and breast growth, leading researchers to wonder if adding testosterone to hormone therapy will reduce the breast cancer risk associated with estrogen/progestin treatment.

Glaser and colleagues have evaluated subcutaneous testosterone implants for treatment of hormone deficiency symptoms in pre- and postmenopausal women without breast cancer. In an article currently in press, they have reported that the implants relieve a variety of symptoms, including hot flashes, sleep disturbance, depressed mood, irritability, and fatigue.

Each combination implant contains 60 mg of testosterone and 4 mg of anastrozole, and patients receive two of the implants every 90 days.

Glaser reported findings from a proof-of-concept study to evaluate the combination pellets' effect on estradiol levels in breast cancer survivors. The study involved 43 patients, 38 of whom were more than five years out from diagnosis. The study population consisted of eight patients with initial diagnoses of ductal carcinoma in situ, one with lobular carcinoma in situ, 19 patients with stage I invasive cancer, 10 with stage II, one with stage III, and four with stage IV.

The 43 patients have undergone a total of 75 subcutaneous insertion procedures. In 70 of 75 procedures, serum estradiol levels were ≤ 30 pg/mL in association with therapeutic levels of testosterone (range 120 to 518 ng/dL). The highest estradiol measured was 53 pg/mL, which occurred on one occasion in a postmenopausal woman with estrogen receptor-negative breast cancer. Subsequent measurements in this same patient were all < 30 pg/mL.

No significant adverse effects have occurred in any of the breast cancer survivors who received the testosterone-anastrozole implants, Glaser said. The total number of insertions had increased to 150 by the end of August.

No breast cancer patient has had disease recurrence during treatment with the implants for as long as three years. Additionally, three patients with metastatic breast cancer have had no evidence of disease progression since beginning treatment with the testosterone-anastrozole pellets.

The findings have set the stage for a randomized, placebo-controlled clinical trial of the implants in breast cancer survivors, according to Glaser.

Glaser reported that she had no relevant disclosures.

Primary source: ASCO Breast Cancer Symposium

Source reference:

Glaser RL "Subcutaneous testosterone-anastrozole therapy in breast cancer survivors" *ASCO Breast 2010*; Abstract 221.
