TAMOXIFEN: TO USE OR NOT TO USE

To the Editor:

I read with great interest the editorial by Wang and Chao [1]. The authors concluded that raloxifene prevails over tamoxifen and may face an easier road to acceptance.

The authors mentioned the following:

1. A rare case report of endometrial cancer in a 71-year-old breast cancer survivor treated with 10-year daily tamoxifen [2].
2. Tamoxifen was associated with increased risks of endometrial cancer, stroke, pulmonary embolism, deep vein thrombosis, and cataract.
3. No trial has shown improved survival with tamoxifen.

Therefore, the use of selective estrogen receptor modulators, other than tamoxifen, may be a better choice for breast cancer prevention.

The incidence of breast cancer in Taiwan has remarkably increased during the past decade. Advancements in screening and treatment have been associated with a reduction in mortality. Many breast cancer survivors may receive follow-up care at our outpatient department. Their concern about the long-term complications of therapy must be recognized and managed.

Tamoxifen, a triphenylethylene, was the first selective estrogen receptor modulator that has been approved as an adjuvant in patients with breast cancer for more than a quarter of a century. The use of tamoxifen to prevent breast cancer and decrease recurrence is not controversial. In postmenopausal hormone receptor-positive patients, 5 years of tamoxifen therapy has been the standard of care, and the addition of chemotherapy has a small effect on survival [3].

In 2004, Cykert et al performed a cost-effectiveness analysis by comparing women aged 50 years, who were treated with tamoxifen for 5 years, with an untreated cohort. The cost per quality-adjusted life-year gained was $43,300. They concluded that tamoxifen chemoprevention is cost effective for women aged 40–50 years [4]. Slomovitz et al reported a cohort of 89 patients with a history of breast cancer in whom endometrial cancer developed. Among tamoxifen users, the interval from breast cancer to endometrial cancer diagnosis was significantly shorter than that in non-users. In that cohort, a history of tamoxifen use was not associated with a worse overall or disease-specific survival [5].

Breast cancer survivors may have increased risks of some cancers, including angiosarcoma (after irradiation), myeloid leukemia (after chemotherapy) and uterine carcinoma (after tamoxifen). But the incidence is low and routine screening for these cancers is not recommended.

Raloxifene, a new selective estrogen receptor modulator, is approved for use in the prevention and treatment of osteoporosis. Although Eli Lilly and Company announced on September 4, 2007 that the US Food and Drug Administration had approved raloxifene for a new use to reduce the risk of breast cancer in postmenopausal women [6], their use is not without side effects. Premkumar et al [7] studied 30 women aged 35 to 47 years who were at high risk of breast cancer and had regular periods. After raloxifene 60 mg daily for 2 years, they found evidence of ovarian stimulation and benign asymptomatic endometrial polyps developing in some women.

Even in the RUTH (Raloxifene Use for The Heart) trial, there was a small increase in stroke mortality [8]; whereas in the STAR (Study of Tamoxifen and Raloxifene) trial, the number of *in situ* breast cancer with raloxifene was greater than that with tamoxifen (81/9,745 *vs.* 57/9,726). This greater increase with raloxifene use is disturbing [8].

Hayes [9] stated: "Raloxifene has not been shown to be equivalent to tamoxifen for the treatment of established breast cancer, and is generally not used in women with breast cancer. Raloxifene should not be substituted for tamoxifen in the adjuvant setting, nor should it be used with tamoxifen, given their similar effect".

Now, another new player in this field, aromatase inhibitors with greater efficacy and safety, will perform better in prevention trials. Third-generation non-steroidal (triazole) aromatase inhibitors, such as anastrozole and letrozole, and the steroidal aromatase inhibitor exemestane are being evaluated in clinical trials. I think it's too soon to jump on the raloxifene bandwagon. Thank you.

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