

## Living Longer and Living Better

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### Letter to the Editor

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It was with great enthusiasm that we have seen the results published by Francis et al. about the 8-year updates of the key modern trials of ovarian function suppression after local treatment for young women with resected breast cancer. In the SOFT (Suppression of Ovarian Function Trial) study, the 8 year disease-free survival rate was 78.9% in patients who did only tamoxifen, 83.2% with tamoxifen and ovarian suppression, and 85.9% with exemestane and ovarian suppression <sup>[1]</sup>.

The history of hormone therapy dates back more than a century (more precisely to 1896) when George Beatson, a British surgeon, describes surgical castration as a therapeutic option in some patients diagnosed with breast cancer <sup>[2]</sup>. Until the late 1960s, this along with bilateral adrenalectomy, were the only therapeutic options in hormone-sensitive disease. It was at this time that tamoxifen was discovered by Arthur Walpole <sup>[3]</sup>. Since then to date, aromatase inhibitors and LHRH analogs have emerged. These along with tamoxifen have been tested in different combinations resulting in the progressive increase in disease-free survival and overall survival.

However, there is something that has not improved since 1896 which are the side effects of hormone therapy and the negative impact on the quality of life of our patients. Side effects of endocrine treatments have been described during the last several decades, usually focusing on the fact that such therapies are associated with less subjective toxicity than cytotoxic drugs. In the work published by Dr. Prudence Francis, grade 3 or higher adverse effects are reported in 24.6% in the tamoxifen-only group, 31% in the tamoxifen group and ovarian suppression, and 32.3% in the exemestane group and ovarian suppression <sup>[1]</sup>.

Actually, we have increased survival at the expense of side effects that greatly diminish the quality of life and this issue becomes more worrisome considering that it has increased the number of young patients, and, therefore, they will live many years with these effects. We cannot forget the negative consequences that early menopause has on a woman in her 30s or 40s. These consequences act not only physically and emotionally, but also affect family and social life and can interfere with compliance. Nearly 50% of breast cancer survivors are non-adherent and 70% discontinue therapy before the recommended 5 years <sup>[4,5]</sup>.

We think there are two ways to reduce the side effects of endocrine therapy:

First, we have to tailor the appropriate adjuvant therapy. Not all patients will benefit of the combination of ovarian suppression and an aromatase inhibitor or tamoxifen. A sophisticated analysis of SOFT and TEXT (Tamoxifen and Exemestane Trial) study further supports the option of adjuvant tamoxifen alone without chemotherapy for some premenopausal women with hormone receptor-positive, HER2-negative disease at low risk of recurrence (tumors <2 cm in size that do not have nodal involvement) <sup>[6]</sup>.

In our institution we are currently studying the effect of hormone therapy in young women in concerning quality of life. Together with the Gynecology department, we want to understand what really concerns these women so that we can draw strategies in order to improve their quality of life. It is not enough to think about how to make our patients live longer, we also have to think how they will live that time. Future trials should evaluate how to reduce side effects and thus improve tolerance.

So, we have to put many factors on the balance to think what the best is for our patients. Appropriate adjuvant systemic therapy involves choosing treatments tailored to individual patients according to assessments of patient risk, co-morbidities and preference. Quality-of-life issues related to endocrine therapies, which might affect their acceptance, should also guide in the selection of endocrine therapies in patients.

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