Controversies in endocrine treatment: effective utilization of steroidal and nonsteroidal aromatase inhibitors: now and in the future

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Foreword

In the past few years, the paradigm of breast cancer adjuvant treatment, as discussed at the St. Gallen 2007 Breast Cancer conference [1], has shifted from focusing on risk to focusing on responsiveness. When selecting systemic therapy, it is important to initially determine the endocrine responsiveness of the cancer. Breast cancer endocrine-responsiveness is divided into three categories: highly responsive – high expression of both oestrogen receptors and progesterone receptors in most tumour cells; incompletely responsive – lower expression of oestrogen receptors and/or progesterone receptors in tumour cells; and nonresponsive – complete absence of both hormone receptors. Tamoxifen has traditionally been the standard adjuvant endocrine therapy for women with hormone-receptor-positive breast cancer. It remains the only one recommended in premenopausal women. Third-generation aromatase (oestrogen synthetase) inhibitors (AIs), exemestane, letrozole and anastrozole have been initially shown to be superior to tamoxifen in the metastatic setting. Owing to their effect on the ovaries, they cannot be used in premenopausal women, and indeed caution has to be taken when they are introduced in women with a recent menopause, especially if the latter is chemotherapy-induced. Prolonged therapy with tamoxifen has been suggested to induce resistance and such treatment has therefore been limited to an initial 5 years following diagnosis. AIs have therefore been explored in various modalities in the adjuvant treatment of postmenopausal women. Promising results have thus led to their acceptance as the only or sequential adjuvant treatment choice for most of these women.

This journal supplement brings together papers from a symposium on 'Controversies in Endocrine Treatment', held in St. Gallen, Switzerland, in March 2007. During the biannual 'Consensus Meeting', it brought together experts in oncology to discuss their viewpoints on current controversies in the management of women with breast cancer. This satellite symposium tackled the issue of whether the similarities between steroidal and nonsteroidal AIs outweigh the differences or whether the lack of cross-resistance between the AIs provides evidence to suggest that there is a difference between these agents. The potential mechanisms of *de novo* and acquired resistance to endocrine therapy are discussed along with treatment options which may offer alternative therapeutic options in these patients.

One of the unanswered questions frequently encountered in the clinic is whether greater benefits are observed with up-front AI monotherapy or whether it is better to begin with tamoxifen and then switch to AI therapy after a number of years. At least most concur that prolonged treatment beyond the old 5-year limit is of benefit for many women. For patients who have completed 5 years of tamoxifen treatment, the majority of the St Gallen panel supported the addition of an AI for a further period of time, although restricting it for patients with node-positive disease, based on presently available results on impact on survival. As expected, measurement of bone mineral density before use of an AI was recommended, and use of bisphosphonates discussed according to existing guidelines. Calcium, vitamin D and especially physical exercise (to reduce the risk of bone loss and treatment-related symptoms) were advocated.

Conflicts of interest: M. Aapro has received honoraria as speaker from Novartis, AstraZeneca and Pfizer.

Reference

1 Goldhirsch A, Wood WC, Gelber RD, Coates AS, Thurlimann B, Senn HJ and panel members. Progress and promise: highlights of the International Expert Consensus on the Primary Therapy of Early Breast Cancer. *Ann Oncol* 2007; **18**:1133–1144.