It was with great interest that I read the new guidelines [1] from the St Gallen ‘International Consensus Conference on the Optimal Primary Therapy of Early Breast Cancer’ which include timely and fundamental changes to the recommendations for treatment selection. The new guidelines
The new St Gallen consensus has moved away from the previously recommended approach of starting with risk assessment by naming endocrine responsiveness as the first and most important consideration for treatment selection. A number of trials comparing AIs to tamoxifen or placebo have reported since the 2003 publication of the St Gallen guidelines and have had an appropriately influential role in shaping this revised version. The recommendation of specific AIs represents a change to the previous St Gallen guidelines. For the first time, 5 years’ treatment with an AI alone (anastrozole or letrozole) is listed as one of the best options for postmenopausal women with hormone-sensitive disease. Similarly, AIs (anastrozole or exemestane) are also recommended following 2–3 years of tamoxifen to complete 5 years of adjuvant therapy. Thus, the guidelines support the principle that it is not too late for a woman already partway through a 5-year course of tamoxifen to benefit by switching to an AI. However, it is worth noting that, when selecting a treatment schedule post-surgery, consideration should be given to data presented at the ASCO annual meeting in May 2005, which showed the importance of starting adjuvant therapy with the most effective treatment available [3, 4]. Ideally, an AI should be used as early as possible in the treatment course, as the risks associated with tamoxifen cannot be offset by later AI use and as yet no data are available to support a prospective sequencing strategy of starting treatment with tamoxifen with the specific intention of switching to an AI.

Important tolerability data on AIs have also been considered in the panel’s updated recommendations. The guidelines state that ‘treatment with AIs compared with tamoxifen is associated with a decreased risk of endometrial cancer and thromboembolic events, but with increased cardiovascular events as well as bone fractures, muscle and osteoarticular pain’ [1]. However, this broad statement deserves further consideration.

While I would concur that, as a group, AIs are associated with a greater risk of bone fractures than tamoxifen, the latest data suggest that the increased risk of cardiovascular events is not a class effect of all the AIs. Important differences are emerging in the toxicity profiles of AIs, with exemestane and letrozole—but not anastrozole—showing early signs of cardiac side effects when compared with tamoxifen. For example, in the BIG 1-98 trial, treatment with letrozole resulted in an increased number of cerebrovascular (7 versus 1) and cardiovascular (13 versus 6) deaths compared with tamoxifen [5]. An increased incidence of cardiac ischemic events (1.6% versus 0.6%) and cardiac deaths (5 versus 2) was also seen with exemestane compared with tamoxifen in the IES study: these data are now detailed in the updated exemestane prescribing information [6]. In the ATAC trial, which reported longer-term tolerability data than the BIG 1-98 trial (median follow-up >2.5 times longer in ATAC, 68 months versus 26 months, respectively), anastrozole was not associated with a significant increase in ischemic cardiovascular disease compared with tamoxifen and the numbers of cardiovascular deaths were similar (49 versus 46, respectively) [7, 8].

Since anastrozole has the most extensive efficacy and safety data and is the only AI with confirmed superiority to tamoxifen extending over the full 5-year treatment period we can be confident in its use and evidence-based medicine suggests that anastrozole may be the preferred AI to replace tamoxifen after breast cancer surgery. Overall, however it is pleasing to see that the St Gallen guidelines now recognize AIs as valuable treatment options for postmenopausal women with early breast cancer.

A. U. Buzdar
Department of Breast Medical Oncology, The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA
(E-mail: abuzdar@mdanderson.org)

References
doi:10.1093/annonc/mdj093