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Editorial

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Breast cancer, the most common cancer in women, is a chronic disease that has a major impact on the life of those who have this malignancy. Patients presenting with early breast cancer may be cured of detectable disease by surgery (plus radiotherapy, if given), but many remain at risk of relapse throughout their life. To reduce this risk of recurrence, these patients should receive adjuvant treatment. The exact treatment to be given will depend on patient and disease characteristics, including the hormone-receptor (HR) status of the primary tumor, and the patient's wishes. Earlier detection and more effective therapies have greatly improved prognosis and outcomes in breast cancer, but the appearance of breast cancer metastases still signals the development of mainly incurable disease, and prognosis for women with advanced breast cancer is poor, with a median survival of approximately 2 years [1]. The prevention of recurrences at distant sites is thus a key aim of adjuvant therapy. Treatment for metastatic disease is almost always palliative, and aims to prolong progression-free survival and overall survival while giving patients the best possible quality of life. As treatment for early disease is given with curative intent, the approach to treatment can differ considerably between metastatic and early disease.

Systemic chemotherapy and/or endocrine therapy form the backbone of anticancer therapy throughout the breast cancer continuum, along with treatments directed at specific receptors such as HER-2, and at the angiogenesis pathway. Patients who have large or inoperable tumors may receive neoadjuvant chemo- or endocrine therapy to shrink the tumor sufficiently to allow surgery, or to reduce the extent of surgery needed. At the most recent meeting of the St Gallen Expert Consensus Panel, the Panel supported the use of preoperative systemic therapy to improve resectability and thus cosmetic outcome [2]. The neoadjuvant setting also provides the ideal opportunity to assess potential tumor responsiveness to adjuvant therapy, or to identify potential predictive and prognostic factors.

Following surgery, and after consideration of the individual's risk of relapse, patients will receive adjuvant chemotherapy or endocrine therapy, as appropriate. In 2005, the St Gallen Expert Consensus Panel made a fundamental change to the algorithm for selection of systemic adjuvant therapy: risk of recurrence, previously the most important factor to influence treatment choice, was replaced by tumor endocrine-responsiveness as the primary consideration when selecting adjuvant treatment [3]. The 2007 guidelines continue to support this change, with risk playing a second role in treatment selection, guiding the selection of patients with endocrine-responsive tumors who require chemotherapy in addition to endocrine therapy. Other recent recommendations from the St Gallen Expert Panel include the classification of all HER2+ tumors as at least intermediate-risk, the use of trastuzumab plus chemotherapy for patients with HER2+ tumors, and sequential treatment with chemotherapy and endocrine therapy for intermediate/high-risk groups [2, 4].

The third-generation aromatase inhibitors (AIs), letrozole, anastrozole and exemestane, have recently challenged and often replaced tamoxifen as the recommended treatment for HR+ disease. These highly effective drugs have improved outcomes for women with early and advanced disease, and letrozole in particular has proved superior to the previous standard of care throughout the treatment continuum. In the neoadjuvant setting and as first-line treatment for advanced disease, AIs have demonstrated at

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least equivalent (anastrozole, exemestane) or superior (letrozole) efficacy to tamoxifen [5]. Perhaps the most noticeable effect of AIs has been in the adjuvant setting, where superior efficacy to tamoxifen has been demonstrated in large, randomized trials [6]. On the basis of these trial results, AIs are now the preferred adjuvant endocrine therapy for the treatment of most patients with early HR+ breast cancer, and are recommended by national and international treatment guidelines [3, 7, 8]. Letrozole is also recommended as extended adjuvant therapy in patients with HR+ disease who have completed 5 years of tamoxifen, to protect further against the risk of late relapse.

Tolerability and safety profiles of anticancer therapies are important considerations, both for patients with early disease, who may receive long-term therapy, and in the metastatic setting, where quality of life is a key issue. The AIs are a relatively well-tolerated class of drugs, associated with predictable and manageable side effects. Importantly for adjuvant therapy, where patients are clinically disease-free and the intended treatment duration is at least 5 years, the AIs have a better safety profile than tamoxifen [9].

Selecting the best treatment for an individual patient involves careful evaluation of the risk:benefit profile of a given therapy. An increasing number of treatment options are now available for early and metastatic disease, and it is important that patients receive the most appropriate treatment to achieve the best possible outcome. Where possible, overtreatment should also be avoided to spare patients from unnecessary exposure to cytotoxic agents and the associated side effects, which can affect daily quality of life considerably. It is therefore important that physicians keep up to date with the findings of clinical trials, developments in treatment decision-making, and recommended disease/patient management strategies. These issues were the focus of the 2007 Educational Breast Care meeting, "Optimizing breast cancer patient care today and tomorrow: implications for clinicians", held in Barcelona, Spain, the presentations from which form the basis of this supplement.

A diagnosis of breast cancer is a distressing experience, and dealing with information about prognosis and treatment options can be a daunting task for patients. Healthcare professionals play a vital role in ensuring patients are informed about therapeutic options, the risks and benefits of different treatment, management of side effects, and the potential impact of the disease and treatment on their quality of life. Dr Lesley Fallowfield (*University of Sussex, Brighton, UK*) discusses the importance of the doctor–patient relationship, highlighting the value of effective communication skills for involving patients in the treatment decision-making process.

Although the outlook for patients diagnosed with early breast cancer has improved greatly in recent years, disease recurrences remain commonplace, highlighting the ongoing need for newer, improved treatments. Changing clinical practice in the treatment of early disease is reviewed by Dr Antonio Llombart Cussac (*Hospital Universitario Arnau Vilanova, Lleida, Spain*), including new approaches to the identification of predictive and prognostic factors in breast cancer. Such advances might help oncologists to better tailor treatment to the individual patient, although truly individualized therapy remains an elusive goal. Current therapeutic options available for patients with early HR+ disease are considered and the optimization of treatment strategies to improve outcomes for individual patients is discussed.

One of the most significant changes in the treatment of HR+ early breast cancer is the acceptance of the third-generation AIs as a standard adjuvant endocrine therapy. Dr Rowan Chlebowski (*UCLA, CA, USA*) presents the evidence from clinical trials showing that letrozole, anastrozole and exemestane are superior to tamoxifen alone in the adjuvant setting, and discusses the optimum adjuvant treatment strategy for AIs. Although direct comparative data are not yet available, evidence from cross-trial comparisons suggests that, from both an efficacy and a safety perspective, upfront AI therapy will enable patients with HR+ disease to achieve the best possible outcome.

The discussion of adjuvant AIs is continued by Dr Kimberly Blackwell (*Duke Comprehensive Cancer Center, Durham, NC, USA*), who examines whether efficacy and safety differences exist between the different AIs. No direct comparative data are currently available on AIs in the adjuvant setting, but letrozole is the only AI to demonstrate clear superiority over tamoxifen throughout the treatment continuum. Furthermore, only letrozole significantly reduces the risk of early distant metastases in patients with HR+ early breast cancer. Ongoing head-to-head trials will help us to understand the efficacy and safety differences between these three agents.

Starting adjuvant letrozole therapy after 5 years of adjuvant tamoxifen improved outcomes in HR+ disease in the pivotal MA.17 trial, which defined the 'extended adjuvant' treatment period. Professor Paul Goss (*Harvard Medical School, Boston, MA, USA*) provides a comprehensive review of the latest updates from the MA.17 trial, which continues to demonstrate the benefits of extended adjuvant letrozole. Importantly, starting letrozole has now been shown to benefit patients even after a prolonged period without active therapy.

In the final article, Dr Joseph Gligorov (*Tenon Hospital, Paris, France*) discusses optimal treatment of metastatic breast cancer, with a focus on expanding treatment options and improving outcomes. The treatment of metastatic disease varies widely, and therapy is usually chosen after consideration of patient and disease characteristics and patient preference. Treatment of metastatic disease may

include chemotherapy, radiotherapy, bisphosphonates, and endocrine and/or biological therapy. Evidence supporting the efficacy of novel therapies and the use of cardioprotective agents to allow anthracycline retreatment is also considered.

Advances in diagnosis and treatment have dramatically improved the outlook for patients with breast cancer, and treatment for early disease is now given with curative intent. Despite expanding therapeutic options, and increasingly complex regimens, disease recurrence and deaths from breast cancer remain all too common. Treatment is moving towards an individualized approach, and correctly used scientific techniques are helping to bring this closer to reality. However, treatment decision-making remains a challenge for the physician, particularly in the rapidly changing field of breast cancer. Maintaining awareness of current developments and ensuring effective communication with patients will help physicians to provide the best care for their patients.

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