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Introduction

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The symposium *Innovations in the Management of Metastatic Breast Cancer* was held during the European Society of Medical Oncology congress in Hamburg, 13 October 2000. Its aim was to provide clinicians with an update on new drugs that are expected to have a significant impact on their ability to provide women with breast cancer with the opportunity for improved survival and quality of life. Both of these are important to women and society as a whole due to the profound effects of breast cancer.

Current therapies for metastatic breast cancer have produced some improvement in outcomes, but often at the cost of debilitating side effects that patients can find unacceptable. Therefore, the development of strategies that improve outcomes while maintaining or improving quality of life is a particularly important goal in this population. This has stimulated the research that has produced a number of novel, effective and better-tolerated agents, including the tumor-selective oral fluoropyrimidine Xeloda® and the potent bisphosphonate Bondronat®. However, one of the most interesting developments in anticancer therapy is the introduction of biological agents. The first of these to become clinically available for the treatment of solid tumors is the oncogene-targeted humanized anti-epidermal growth factor receptor-2 (HER2) monoclonal antibody Herceptin®, the focus of the articles in this supplement.

Herceptin® is now widely approved in Europe, North America and elsewhere for the treatment of women with HER2-positive metastatic breast cancer. Generally, it is indicated as first-line therapy in combination with 3-weekly paclitaxel or as second/third-line therapy as a single agent. These indications are based on the results of pivotal clinical trials indicating the ability of Herceptin® to improve the outcomes of women treated, extending median survival by as much as 45%, while also being well tolerated and maintaining quality of life. However, this can be viewed as just the beginning of the development of Herceptin® as an essential part of therapy for women with HER2-positive breast cancer. The ongoing and extensive program of clinical trials of Herceptin® is now beginning to extend our knowledge of the use of this drug in such women. In this context, this supplement provides information on:

- Selection of patients for Herceptin® therapy, particularly in terms of defining the patient population most likely to benefit from treatment in order to optimize clinical benefit.
- The most recent analysis of pivotal trial data showing that adding Herceptin® to paclitaxel increases median survival duration by as much as 40%.
- The best time to initiate Herceptin® therapy in the metastatic setting, focusing on new data on the use of Herceptin® monotherapy first line, and examination of the effect of cross-over between the chemotherapy and chemotherapy plus Herceptin® groups in the pivotal phase III trial.
- The efficacy and safety of new Herceptin® regimens, including an attractive 3-weekly regimen of equivalent dose intensity (8 mg/kg i.v. followed by 6 mg/kg i.v. every 3 weeks until progression), and combinations with chemotherapeutic agents such as vinorelbine, weekly paclitaxel and epirubicin.

This outline of the wider discussions featured in these articles indicates the continuing progress that is being made in refining the use of Herceptin®. Importantly, these studies also appear to be providing the data that will ultimately provide patients with HER2-positive metastatic breast cancer with increased choice regarding how they receive Herceptin®, whether weekly or 3-weekly, or with one or more of a variety of chemotherapeutic and hormonal agents. This has the potential to allow increasing individualization of therapy for metastatic breast cancer while optimizing patient outcomes.

While improving therapy for metastatic breast cancer is a major goal, the ultimate goal would be to prevent the recurrence of primary breast cancer by providing improved therapies in the adjuvant setting. With HER2 amplification/overexpression being observed early in breast cancer development and its effects on disease aggressiveness

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occurring from the onset of invasive disease, the effect of targeting this oncogene with customized therapy is a logical area for clinical trials. To this end, four major clinical trials in over 12 000 patients will examine the efficacy and safety of Herceptin® used as part of various adjuvant approaches. These trials are described in detail, indicating that they cover the range of adjuvant therapies used worldwide. Data from these trials, while taking some years to accrue, will provide the evidence necessary to demonstrate the contribution that Herceptin® can make to achieving the goal of preventing breast cancer recurrence.

This supplement, therefore, provides a full update of recent results from the Herceptin® clinical trials program, while also looking to the future development of this biological therapy. As Herceptin® promises to be only the first of a new generation of targeted biological agents, these developments promise to have wide implications for the introduction of future agents. It should also be remembered that Herceptin® has proved the principle that targeting cellular factors known to be implicated in tumor development can produce clinical benefit while improving tolerability. Thus, with the variety of approaches currently being examined for targeting, including monoclonal antibodies, gene therapies and cancer vaccines, Herceptin® is potentially at the forefront of a research effort that will revolutionize how cancer is treated. Individualized therapeutic regimens that are tailored to produce optimal effects against individual tumors based on their intrinsic characteristics, while at the same time minimizing side effects, are likely to be the major advance resulting from this.