Adjuvant Systemic Therapy for Early-Stage Breast Cancer

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INTRODUCTION

Over the past 20 years, substantial progress has been achieved in our understanding of breast cancer and in breast cancer treatment, with mortality from breast cancer declining by more than 25% over this time.1–3 This progress has been characterized by a greater understanding of the molecular biology of breast cancer, rational drug design, development of agents with specific cellular targets and pathways, development of better prognostic and predictive multigene assays, and marked improvements in supportive care. Specifically, 4 main factors have brought us closer to using the term “cure” for early breast cancer and led to a significant improvement in the quality of life of patients: (1) early detection through mammography;4 (2) a better understanding of breast cancer as both a local and a systemic disease leading to the demonstration that breast-conserving surgery (lumpectomy) followed by radiation therapy is unequivocally comparable to mastectomy;5,6 (3) the implementation of early systemic therapy;7–9 and (4) the understanding that breast cancer is a heterogeneous disease.10 These advances have led to the development of newer systemic chemotherapies, hormonal therapies, and targeted (biologic) therapies. One of the great advances made during this time, and in the history of breast cancer, was the recognition of the crucial role played by amplification of the human epidermal growth factor receptor 2 (HER2) gene for a subset of breast cancer patients and the implementation of anti-HER2 therapies in early breast cancer.11–14 However, important questions remain regarding how to further tailor therapy based on better predictive and prognostic markers. In this manual, we review the current approach to systemic therapy for early-stage disease (stages 0, I, II, III) in the adjuvant setting.

PRINCIPLES OF SYSTEMIC THERAPY

The improvement in breast cancer mortality over the past 2 decades has been a direct result of both advances in early detection through screening and advances in adjuvant treatment.9 Depending on the model of risk reduction, adjuvant therapy has been estimated to be responsible for 35%