

Chairperson's introduction

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Introduction

Despite significant advances in the diagnosis and treatment of breast cancer, approximately one third of patients still develop, and subsequently die from metastatic breast disease. Globally, half a million deaths each year are attributable to metastatic breast cancer, and the median survival time from diagnosis of secondary disease is approximately three years. The range is very wide, however, with some patients having more indolent disease living for 10–15 years in some cases, whilst in others survival from diagnosis of metastatic disease can be only a matter of months. In part this reflects the biological diversity of the disease, with some women who have oestrogen receptor (ER)-positive tumours that show extreme sensitivity to hormonal treatments, while in others with so-called triple-negative breast cancer the secondary sites of disease can display relative resistance to all therapies. In addition, the disease may be manifest as different patterns of metastatic spread, ranging from limited bone metastases to widespread and life-threatening metastases in visceral organs such as the liver, lung and brain. Both of these factors will influence the broad range of expected survival for an individual patient.

While recent years have witnessed substantial developments in various therapies that have improved the outlook for many women with breast cancer, the fact remains that at present secondary breast cancer cannot be cured. As such, the socioeconomic and psychological impact of the condition and its management is a major health problem for various reasons. The high prevalence of the disease, together with the relatively long natural history for many patients, means that in the UK approximately 100,000 women are living with a diagnosis of secondary breast cancer each year. However, for these women the true impact of living with an incurable condition and coping with an uncertain future is something that often goes unrecognised by health care professionals. The diagnosis of metastatic breast cancer is always a devastating event for any patient who has received

previous therapy for early breast cancer that was given with the hope and expectation of cure. Therefore, when secondary disease returns this is associated with the realisation that “cure” is no longer possible, and that by and large one day most women will die from their disease.

So the question that every patient inevitably asks when faced with this scenario is “how long do I have to live?” This is not a question that can be readily answered at the point of diagnosis of metastatic disease, as many factors will influence subsequent survival, including sites and distribution of secondary disease, the biological subtype of breast cancer, host co-morbidities and organ function, and most importantly the response of the metastatic breast cancer to the individual therapies. When treating metastatic breast cancer, however, the primary aim is to palliate disease-related symptoms and maintain quality of life. This is achieved by utilising systemic anti-cancer therapies such as endocrine therapy, biological approaches and chemotherapy, and also loco-regional therapies such as radiotherapy and surgery in certain circumstances. Each of these therapies can impact on tumour growth, thus relieving tumour-related symptoms and inducing disease control due to some form of partial remission. Indeed, it is well recognised that quality of life in advanced breast cancer is clearly linked to the likelihood of treatment response. While metastatic breast cancer cannot be cured, modern systemic and loco-regional treatment can be very effective in maximising a patient's duration of quality time without disease-related symptoms, which, if significant in itself, will often be manifest as prolonged survival. In this setting it is always important that this gain in quality time and life expectancy is achieved without any significant treatment-related toxicities.

With the introduction of more effective therapies over the last two decades, there have been substantial improvements in clinical outcomes for women with metastatic breast cancer compared with 30 years ago. Indeed, many patients can now expect to live with metastatic secondary breast cancer for several years. However, many challenges remain in the development

of novel therapies in proving that a given intervention on its own impacts on overall survival – this is because with so many effective therapies to offer patients with advanced disease, randomised trials against no therapy or “best supportive care” are impossible and indeed unethical to conduct in this disease. Furthermore, because breast cancer in general is relatively sensitive to the various drug- and radiation-based therapies that are available, with multiple lines of treatment often being used during the course of a patient's illness, subsequent therapies given in sequence will undoubtedly have a major impact on patient outcome. This makes the likelihood of a novel therapy in the first-line setting having a significant impact on overall survival almost impossible to demonstrate. Because of this, “progression-free survival” (PFS) has become in some instances a recognised primary end-point that is utilised to demonstrate to regulatory authorities the clinical utility of any given novel therapeutic. As such, overall survival has become a secondary end-point in large randomised trials, and most oncologists

accept that while improved survival is desirable, it is not always the most important end-point to focus upon in breast cancer studies in the advanced disease setting.

This chapter will review the role of each individual treatment modality that is used in the treatment of metastatic disease (i.e. endocrine therapy, radiotherapy, surgery, together with cytotoxic and targeted therapies), and highlight some of the recent developments with each approach, in particular with evidence of any impact that these therapies may have on overall survival. Ultimately, it is the sum of all of these approaches taken together, rather than any individual approach alone, that has contributed to the substantial improvements seen in the management of metastatic breast cancer.

Conflict of interest statement

The author has no conflict of interest to report.