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# Chairman's Introduction

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MILLIONS OF cancer patients in Europe still develop metastatic disease and die. The early breakthrough in, for example, ways of treating Hodgkin's disease and teratoma, and the use of adjuvant therapy for breast cancer, have not subsequently been matched. Indeed, improvements in patient outcome and survival rates have plateaued over the last 10–15 years. Oncologists still currently face high failure rates in the clinic. This is frustrating for the whole management team and fatal for the patient. The need for new and more effective treatment is, therefore, urgent for all cancer specialists.

Following a period with few developments, exciting, new anticancer agents are now in the pipeline. The fact that an audience of almost 1000 delegates was attracted into a satellite debate discussing anticancer drug evaluation methodology is reassuring evidence that clinical research is again creating enthusiasm within the oncology community. With this burst of new activity, the need has become evident for clarification of the efficacy criteria used in drug evaluation in order to allow informed treatment comparison and clinical decision-making.

## POSSIBLE REASONS FOR THE POOR CORRELATION OF SURVIVAL AND RESPONSE RATE

In recent years, it seemed that objective response had little or no impact on overall patient survival rates, even when a clear improvement was seen after drug treatment [1]. Results from the analysis of trials in which survival and response were significantly correlated suggested that very large improvements in the clinical response rate were needed for there to be any meaningful effect on median patient survival [2].

A variety of factors contribute to the apparent failure of currently available chemotherapeutic agents to improve both survival and response rate among cancer patients. A number of suggestions have been put forward.

- The responses achieved may be of insufficient duration to influence survival significantly.
- The accessible lesions measured in trials represent only a minor component of the overall tumour burden.
- 'Partial' responses (i.e. most responses in solid tumours) involve only minimal killing of tumour cells [1].

Alternatively, the reason for the poor correlation between response rate and survival may be less obvious; a drug which fails to demonstrate an objective response, but achieves stabilisation of disease, may also slow tumour growth sufficiently to influence survival [1].

Another possible explanation for the lack of evidence for improved survival is that the statistical power of the trials conducted to date has been inadequate to demonstrate a difference in survival if that difference is small [1]. Attention has, therefore, been drawn to the specific issue of methodology and the need for randomised studies with evaluation of survival as the endpoint [2–4].

## THE NEED TO ADDRESS QUALITY OF LIFE AND PATIENT WELL-BEING

In the light of poor treatment outcomes, the high economic costs of treatment and the toxicity problems still associated with most chemotherapeutic regimens, one of the most important questions asked by oncologists today is "when is a treatment worthwhile?" [5]. The responses to a Canadian questionnaire circulated 10 years ago showed that only 5% of doctors involved in the management of patients with locally advanced non-small cell lung cancer would opt for chemotherapy [6]. What should be their view in 1997? How can physicians evaluate evidence from clinical trial reports and use this to make informed decisions and appropriate choices for their patients?

In addressing this issue, some researchers have focused as much attention on measures relating to their patients' quality of life as on those relating to survival alone. Ways of estimating quality of life are becoming more sophisticated. For example, a methodology allowing prediction of long-term results for mean Quality-adjusted Time Without Symptoms of disease and Toxicity of treatment (Q-TWiST) from shorter-term, median, follow-up data was published in 1993 [7]. When this technique was applied in node-positive breast cancer, it suggested that patients continued to obtain greater benefit from long-duration than from short-duration adjuvant chemotherapy, in terms of quality of life-adjusted survival, for 5–10 years after treatment [7].

## THE DEBATE

The possible reasons for the poor correlation of survival and response rate are explored in more depth by two of the contributors to this debate. However, each speaker approaches the matter from a different perspective. E. Cvitkovic argues for the motion that 'current methods of assessing the efficacy of new anticancer drugs have failed', while W. ten Bokkel Huinink presents new trial data in his role as proposer against it.

The seconder for the motion, K. Redmond, argues strongly

*J.G. McVie, from the Cancer Research Campaign, was Chairman of a stimulating debate held at a satellite at the 19th Meeting of the European Society for Medical Oncology (ESMO) held in Lisbon in November 1994. The motion addressed at the satellite was "Current methods of assessing the efficacy of new anti-cancer drugs have failed—or have they?"

from the perspective that current methods of drug evaluation have failed to take sufficient account of patient well-being or of the economic cost of treatment. The strengths of rigorous statistical analysis, together with some of the potential pitfalls, are reviewed by K. MacRae, seconder against the motion.

The current level of interest in the topics raised during this debate is such that the lively and informative discussion following this meeting may well continue for much of the remainder of this century.

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