

Section introduction

Introduction to sessions on Personalising treatment

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Survival rates in breast cancer continue to increase in most Western countries. This is undoubtedly underpinned in part by advances in breast cancer therapy and a wider range of treatments. Better surgical techniques and chemotherapeutic regimens, and more specific and potent targeted treatment have all combined to increase therapeutic efficacy while reducing morbidity in the general population of patients with breast cancer. Nevertheless, not all patients experience benefit. Tumours that respond to one form of treatment fail to respond to therapies that are effective in other breast cancers. Similarly, a treatment that overall might produce lower responses can still be extremely effective in a subset of breast cancer patients. Ideally, optimal management would offer the most effective treatment on an individual basis. Improving the tailoring or personalization of treatment, founded upon patient and tumour characteristics, is therefore a major objective of clinical practice and translational research. The current status of personalized treatment was the topic of two meeting sessions.

Professor Monica Morrow [1] considered surgical treatment. She reviewed changes in surgical practice that have occurred since the 1940s, selection criteria for breast-conserving treatment, the need for radiotherapy and individualized management of the axilla (focusing on the role of sentinel node biopsy). Surgery is the first treatment modality faced by the majority of patients. Tailoring surgical therapy is based largely on patient choice along with consideration of a number of mechanical/cosmetic issues that pertain to the size and location of the lesion. However, molecular predictors of risk for both local and systemic spread were identified as particular future needs; markers that indicate that the no surgery option was safe for the elderly/unfit would also be helpful. Postsurgical radiotherapy is currently under greater study in relation to molecular predictability, but this relates at least as much to predicting normal tissue damage as to the antitumour efficacy of the treatment.

Professor Mitch Dowsett and colleagues [2] addressed the topic of 'short-term preoperative treatment for all', in which

the approach is to use the interval between time of diagnosis and surgery to employ treatment, and to measure the effect on proliferation and/or other molecular markers in tumour biopsies. They identified advantages in terms of being able to identify on-treatment prognostic indices and biological responses that might be used to select subsequent adjuvant therapy. Conversely, there could be potential disadvantages relating to long-term detrimental effects, downgrading of disease (currently used to select treatment), and the extra workload for surgeons and pathologists (when equivalent information might be derived from pretreatment samples). The potential of presurgical treatment was illustrated by comparing results from the IMPACT (Immediate Preoperative Anastrozole Tamoxifen or Combined with Tamoxifen) and ATAC (Arimidex, Tamoxifen Alone or Combination) trials. Thus, the information from short-term neoadjuvant treatment in the IMPACT trial (involving hundreds of patients) would have predicted the results of long-term treatment in the ATAC adjuvant trial (involving thousands of patients). These results have provided the impetus for the POETIC (PeriOperative Endocrine Treatment for Individualising Care) prospective clinical trial, in which results from presurgical treatment are being used to stratify subsequent adjuvant therapy.

The topic covered by Professor Per Lonning [3] was 'the contribution of expression microarrays in personalizing adjuvant treatment'. He provocatively indicated that microarrays have yielded no advances in personalizing adjuvant treatment and that it will be a long time before they do so. This is because of wrong conceptual use. The need to apply technology and bioinformatics to biology rather than moulding observations to fit in with bioinformatic models was emphasized. However, there was hope in that we now have the tools with which to elucidate key mechanisms of cancer development and therapy. Furthermore, gene expression patterns from microarrays are providing useful tumour subclassification, most notably *Oncotype Dx*TM (Genomic Health Inc., Redwood City, CA, USA) and the *MammaPrint* (Agendia BV, Amsterdam, The Netherlands). Each of these is being tested in a large prospective clinical trial (TAILORx

[Trial Assigning Individualized Options for Treatment] and MINDACT [Microarray for Node-Negative Disease may Avoid Chemotherapy], respectively) to assess how much clinical benefit is derived from their application.

Professor Matt Ellis [4] considered progress made in personalized endocrine treatment. He identified the therapeutic choices available and key issues such as prediction of response, the role of neoadjuvant therapy as a test bed for adjuvant treatment, and combination of endocrine therapy with other signal transduction inhibitors. In terms of response prediction, the status of proliferation markers and *cerbB2* were evaluated as illustrative examples using findings from trials comparing aromatase inhibitors with tamoxifen. The potential of using endocrine therapy with drugs that influence phosphoinositol-3-kinase (PI3K) signalling was also highlighted. A major point from the presentation and a recurrent theme from other topics in the session was that studies conducted in the neoadjuvant setting would be particularly informative in validating translation research and progressing preliminary clinical observations toward the ultimate goal of personalizing treatment.

There is no doubt that substantial effort will be made to improve personalized therapy. The challenge of patients who respond to treatments that do not benefit the majority and *vice versa* must still be faced. However, with greater emphasis on targeted therapy and the ability to measure the target, tailored treatment may become rational and more easily achieved.

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