Predictive Oncology—Second Conference of the International Society for Chemosensitivity Testing in Oncology

Ian A. Cree[a]

Anti-Cancer Drugs 15:301–302 © 2004 Lippincott Williams & Wilkins.

Anti-Cancer Drugs 2004, **15**:301–302

[a]Local Conference Organizer and President, ISCO.

Correspondence to I. A. Cree, Translational Oncology Research Centre, Queen Alexandra Hospital, Portsmouth PO6 3LY, UK.
Tel: +44 2392 286378; fax: +44 2392 286379;
e-mail: ian.cree@port.ac.uk

Oncology is currently an empirical discipline in which all patients with a particular type of cancer are treated as though they were the same. The weight of evidence from genetic, molecular, cell pathology and clinical studies suggests that this is incorrect: patients' tumors differ from each other. As new drugs come onto the market so oncologists and patients are faced with a bewildering array of choices. Which patients need treatment? How long do they need it for, and at what dose?

'Predictive Oncology' allowed delegates from Japan, Korea, Europe and North America involved in predictive testing to meet and discuss the amazingly large variety of methods capable of tailoring treatment to the circumstances of individual patients and their tumors. We began with a discussion of HER2, the target of Herceptin, by Dr Tim Gulliford (Portsmouth, UK), an oncologist with an interest in breast cancer. Immunocytochemistry is the one method of predictive testing that has made it into practice—very few oncologists would now treat a patient with breast cancer unless they knew their estrogen receptor (ER) and progesterone receptor status and HER2 can now be added to that list. The potential relevance of HER2 positivity to resistance to Tamoxifen in patients that are also ER-positive highlights the potential for patient profiling. Measuring large numbers of different molecular targets may improve patient management. The ultimate in such multiplex assays is the DNA expression array. Dr James Brenton (Cambridge, UK) gave an excellent lecture highlighting the technical and analytical problems of such assays. Such assays have a tendency to suffer from considerable problems of reproducibility and this must be addressed before they are used clinically. Indeed, the need for rigorous attention to issues of reproducibility and external quality assurance was a theme of the meeting. Unlike the DNA expression arrays, quantitative reverse-transcriptase polymerase chain reaction (RT-PCR) already meets the needs of diagnostic laboratories with excellent reproducibility—CoVs of $< 1.5\%$ are routine. The need to show relative increases or decreases in target gene expression requires the use of housekeeping genes, which should stable within the cell under varying conditions. Stuart Mercer (Portsmouth, UK) showed that various chemotherapy agents can affect expression of these genes—GAPDH was particularly variable. However, assessment of several such genes provides a mean against which changes in target genes can be assessed with considerable accuracy. Appreciation of the role of various mechanisms of gene silencing in cancer, and in particular the effect of DNA methylation on chemosensitivity to platinum and other DNA-damaging agents was covered by Professor Bob Brown (Glasgow, UK). These changes in tumor-derived DNA may have predictive value.

The International Society for Chemosensitivity Testing in Oncology (ISCO) grew from meetings of those involved in cell-based assays of chemosensitivity and three of the seven sessions were devoted to advances in these methods. The latest generation of chemosensitivity assays are much more robust and better validated. A number of methods are available and probably differ in their suitability for use in particular clinical situations. All laboratory assays have their limitations, but within these it is clear that cell-based assays have much to offer oncology. One of the most intriguing presentations was from Dr Angela Otto who is able to measure pH change oxygen tension and electrical impedance simultaneously within cell cultures. These biosensor wells still require quite large instruments, but such sensor technologies may have much to offer. Other methods included a variation of the ATP-based tumor chemosensitivity assay (ATP-TCA) suitable for small cell numbers a two-chamber assay suitable for assessment of angiogenesis and several presentations using the MTT assay.

One session was devoted to imaging technologies as predictive assays. Dr Eric Aboagye covered the advances in molecular imaging using positron emission tomography and this was followed by a presentation from Dr Neil

0959-4973 © 2004 Lippincott Williams & Wilkins DOI: 10.1097/01.cad.0000117273.59571.81

Steinmetz of the use of Annexin-V to label dead and dying cells within tumors shortly after the first dose of chemotherapy. Several of these methods appear to be able to predict subsequent clinical response, and would be very useful as surrogates of clinical response speeding up clinical trials and allowing simple assessment of sequential regimens. Clinical trials of this methodology are well advanced and likely to enter clinical practice soon.

A further session looked at the issues of immunotherapy, with a plenary lecture by Dr Antonella Romanini (Pisa). Immunotherapy should work! There are many documented occurrences of immune-mediated spontaneous regression of tumors, particularly for melanoma. However, cancer vaccines and less-specific approaches using cytokines have been disappointing, despite their increasing sophistication. Response rates remain low and there are still no methods to choose patients for this type of intervention in preference to other modalities.

The final session dealt with the practicalities of introducing predictive methods into oncology practice. Professor Doug Altman gave a particularly useful plenary lecture emphasizing the need for rigorously designed prospective clinical studies with clearly defined protocols including entry criteria and endpoints for exploratory as well as confirmatory studies. At some point in the development of predictive tests, patients have to be treated according to the test. A series of presentations from Japan covered the clinical use of the Collagen Gel Droplet embedded culture sensitivity test (CD-DST). This assay is now being used to direct patient treatment in lung cancer (Dr M. Kawamura) and other tumors in pilot and phase II clinical trials. The results are encouraging, but there is a need for randomized clinical trials to be performed with this and other assays to ensure that the test really does add to the efficacy of treatment. To date, few such studies have been performed. A randomized study of ATP-TCA directed treatment versus physician's choice has recently been completed in recurrent ovarian cancer and interim data are encouraging. The full analysis of these data is awaited with some interest!

In conclusion, the next 10 years are set to be an exciting time in oncology, but as drugs improve, tests must improve too. The delegates at this conference had a unique opportunity to get to grips with what our patients will require from us. The abstracts are available on the conference website at www.predictiveoncology.co.uk and those interested in coming to the next one are encouraged to join ISCO—further details are available from the author.