## Friday, 2 October 1998 16:00-18:00

EUROPA DONNA SYMPOSIUM

# Clinical trials

600 INVITED

### Introduction to cancer clinical trials

P. Therasse. *EORTC Data Center, Date Center, Av. Mounier 83, Bte 11, B-1200 Brussels, Belgium*

In the field of cancer, scientists and doctors are constantly looking for new or improved treatments to help patients. Cancer clinical trials are studies with patients, which are generally designed to confirm the safety and effectiveness of a new promising treatment. Some clinical trials are aimed at discovering new drugs while others evaluate different therapeutic approaches including surgery, irradiation and combinations of drugs already on the market. The purpose of the trial may be to test different doses of the treatment or the route and the mode of administration, for example. The trial design will be different depending on whether the drug or the new regimen is in at early stage (phase I), intermediate (phase II) or late stage of development (phase III).

Clinical trials result in the generation of data which, hopefully, will answer the questions that have been raised in the design of the study and which have been fully elucidated in the protocol. The questions and the interpretation of answers can be viewed from three broad perspectives. The traditional, and most common, perspective is the research perspective. This involves a hypothesis, which is generated and then tested in the clinical trial. The data are interpreted as either supporting the hypothesis or invalidating it. The second perspective is the patient care perspective. This implies the evaluation of the study results from the point of view of their impact upon the care of individual patients. The third perspective is the regulatory and administrative perspective. The regulatory component assesses whether the data will be acceptable to a regulatory agency so that the new treatment can be approved for widespread usage and commercial sale.

In parallel to the evolution of the methodology, a full set of regulations has been developed to guarantee the respect of integrity and rights of patients included in clinical trials. Nowadays, clinical trials are still considered as the indispensable step to allow new discoveries being implemented in daily medical practice.

601 INVITED

### Breast cancer clinical trials in Europe – What has been done and what is currently underway

M. Castiglione-Gertsch. *SAKK/SIAK, Konsumstrasse, 13, CH-3010 Bern, Switzerland*

Several European groups have studied breast cancer both in the adjuvant setting, attempting to reduce risk of relapse after surgery, and in advanced disease, when palliation and quality of life of the patients is the most relevant aspect.

European research led to several major enhancing knowledge and improving treatment of the disease. Special attention was given to development of efficacious chemotherapy and endocrine regimens for the adjuvant treatment, to quality of life issues, and to improving the use of best available therapies. This enhanced knowledge on treatment effects and increased the potential of international cooperation significantly.

A selection of some of the most important results of adjuvant trials, as well as studies in the advanced disease setting will be presented together with description of some of the ongoing European trials.

The newly constituted Breast International Group (BIG), which includes most of the active research groups in the continent will allow to conduct larger clinical trials and in a more efficient way leading, we hope, to further improvement of cure and palliation for patients suffering from breast cancer.

602 INVITED

### The role of clinical trials and their impact on breast cancer management

Ian F. Tannock. *Dept. of Medical Oncology, Princess Margaret Hospital, Toronto, Canada*

For *adjuvant treatment*, overview analyses have demonstrated small but important levels of benefit for chemotherapy and/or tamoxifen. Current interest is in specifying more subtle differences (e.g. from different drug combinations). Problems include:

(i) Understanding levels of benefit (reduction in hazard ratio vs absolute increase in survival). (ii) Summing effects of treatment of variable intensity and quality. (iii) Applying uniform treatments to very heterogenous patients and tumours. Tests of heterogeneity applied in meta-analysis are insensitive.

It will be shown that cell kill from adjuvant treatment is limited ($\leq$2 logs), and that repopulation between treatments may limit the benefit of chemotherapy.

For *metastatic disease*, randomized trials have shown no consistent improvements in survival, and resources are being wasted on trials comparing many different drug combinations. Innovative mechanistically-based approaches are required which recognize tumour heterogeneity and problems related to drug penetration of tissue and repopulation between courses of treatment.

603 INVITED

### Isssues around informed consent – Why and when should women participate in clinical trials?

H. Goodare. *Counsellor, and Chair, Research Committee, UK Breast Cancer Coalition, UK*

Clinical trials cannot be done without patients, and the whole purpose of conducting trials is to benefit patients. So patients should be at the front of researchers' minds when they design, conduct, and report medical research. It follows that patients should help to decide which research is undertaken, help to plan the protocols and interpret the data, and help to disseminate the results.

If this is done, the matter of informed consent will fall into place. No longer will paternalistic researchers fail to give full information about the risks and benefits of a proposed trial: as joint investigators, women with personal experience of the disease will be involved from the start in designing patient information leaflets and consent forms.

But patients should never be coerced into taking part: as the Nuremberg Code stated 50 years ago, 'The voluntary consent of the human subject is absolutely essential.'