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In this issue

New challenges in conducting clinical trials

In this issue of *EJC*, Therasse and colleagues present an update on the methodology and conduct of cancer clinical trails. They comment on RECIST in practice, simple methods for interim analysis, and the EU Clinical Trial Directive. RECIST is now widely adopted in clinical research in patients with advanced or metastatic disease, where there is a need to assess changes in solid tumour sizes in response to drug regimen. The challenge of applying RECIST to measure progression in randomized trials that enrol patients with non-measurable disease, and how best to incorporate the use of functional imaging in the future are discussed by the authors. Interim analyses are increasingly planned in clinical trials to stop them as soon as a treatment effect/s emerges. During long trials, interim safety and efficacy analyses are performed at regular intervals for review by an Independent Data Monitoring Committee (IDMC). The authors argue that although interim analyses can be complex, simple measures of treatment effects can be calculated and assessed for statistical significance at any time during a clinical trial. They also assert that IDMCs can fulfil their role adequately based on such simple statistics. Lastly, the authors speculate on the impact of the EU Clinical Trial directive on maintaining high-quality academic 'non-commercial' clinical research in Europe.

Two-pronged attack with tyrosine kinase inhibitors

Recent insights into the role of receptor tyrosine kinase function in cancer cells have culminated in the design of highly selective tyrosine kinase inhibitors. It is now accepted that most tumours will depend on more than one signalling pathway for their growth and survival. As a consequence, different strategies have been pursued to inhibit multiple signalling pathways or multiple steps in the same pathway. This goal has been realised by the development of multi-targeted agents and/or the use of combinations of single-targeted drugs. In this issue of *EJC*, Jonge and Verweij discuss advantages and disadvantages of using multi-targeted agent vs combinational single-target therapy in cancer treatment. The authors note that the use of a combination of different tyrosine kinase inhibitor compounds will be less convenient to the patient and that dosing mistakes and possible drug-drug interactions should be anticipated. However, this approach will enable the titration of the dose of either agent to optimize target inhibition. The use of multi-targeted kinase inhibitors will circumvent several of the problems of combinational therapy, but optimal inhibition of several targets might not be feasible at a dose with acceptable toxicity.

Mammographic surveillance in high-risk women increases survival

In women with a family history of breast cancer, the risk of disease can be substantially increased and starts at an earlier age than in the general population. Recognition of this, along with the identification of the high-risk susceptibility genes *BRCA1* and *BRCA2*, has led to the emergence and subsequent expansion of breast cancer Family History Clinics. Such centres offer accurate assessment of the increased risk by virtue of family history and advice on preventative measures. In a study reported in this issue of *EJC*, Maurice and colleagues compared the survival of 62 breast cancer patients diagnosed in the context of a family history clinic offering 12–18 monthly mammographic screening with that of 1108 patients of the same age range but having no exposure to screening. The authors found that survival (less breast cancer death and longer disease-free survival) was significantly better in the family history group with mammographic surveillance. The large prospective study that is currently underway to further evaluate mammographic surveillance services, in women between the ages of 40 and 49 with a family history of breast cancer, should hopefully also clarify the benefits further in the future.

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