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Breast Cancer RESEARCH

SECTION INTRODUCTION

Introduction: are current drug development programmes realising the full potential of new agents?

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Just like the 2009 Edinburgh Controversies meeting, the final two sessions addressed the question of whether current drug development programmes for new agents in breast cancer are realising their full potential. However, this time the approach was to assess how various different clinical studies/novel drugs are prioritised by either the pharmaceutical industry or by academic groups and investigators, and in addition how clinical trials in breast cancer are evolving in an era of targeted therapeutics. As in previous years, this was followed by an expert panel of representatives who debated the issues in an interactive fashion with the audience.

Dr Maria Koehler from Pfizer Oncology gave her own perspective of how the pharmaceutical industry is meeting the challenge of developing targeted therapeutics in an era of escalating costs and increasing regulatory requirements. Recognition that breast cancer contains a group of heterogeneous diseases with distinctive molecular profiles has already led to notable success with endocrine therapy and trastuzumab. Increasingly, biomarker-directed subsets will be identified for development of the next generation of targeted therapeutics, and closer collaboration will be required than ever before between the pharmaceutical industry who have the novel drugs, molecular diagnostic companies who can develop biomarker testing, and academia/clinical investigators who have access to patients and their tissue samples. Dr Koehler described some recent examples where results from translational studies modified the development of novel targeted therapeutics, and emphasised that increasing collaboration and partnership will be required to develop the next generation of anti-cancer therapies.

Professor David Cameron discussed some of the issues around how clinical and translational research is conducted within the UK's National Cancer Research Network (NCRN). One of the fundamental principles behind the NCRN is that research should map onto the delivery of clinical service within the National Health Service, and that with appropriate infrastructure in place it should then be feasible for most cancer patients to be considered for clinical trials within the NCRN's portfolio of nationally run studies. Recruitment into cancer trials within the UK has been steadily increasing in recent years, and for breast cancer over 10% of patients are now being recruited into a randomised controlled trial, with an additional 15% recruited into non-randomised controlled trials. Commercial studies are increasingly being added to the NCRN portfolio, and opportunities exist to enhance the link with Experimental Cancer Medicine Centres (ECMCs) so that greater access can be made to early phase clinical trials. In addition, partnerships with major pharmaceutical companies have been initiated to facilitate further investigator developed studies with targeted therapies.

Mr Alistair Thompson discussed how priorities are decided upon within the Breast Cancer Clinical Studies Group (CSG) of the National Cancer Research Institute (NCRI). The three active subgroups cover the development of trials in the adjuvant/neoadjuvant setting, initiatives in advanced/metastatic disease, and translational or biomarker/imaging-based studies. Individuals with good ideas, often with links to industry, can develop their concept through the Breast Cancer CSG and work up their protocol through engagement with a recognised accredited Clinical Trials Unit. The Breast Cancer CSG then coordinates the overall strategy to ensure that there is no overlap of competing studies, at all times aiming to develop a broad-based portfolio of studies across the various subtypes and different stages of breast cancer. There has been an increasing drive for industry studies to be included and adopted onto the portfolio. Through the Breast Cancer CSG there has been a significant rise in the number of patients recruited into studies, with more than 16,000 recruited in 2009/2010 alone, which represents 30 to 45% of the UK's incident breast cancer population.

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Professor Per Lonning form Bergen, Norway then addressed drug development in breast cancer from his own European perspective. He outlined that while previous trials in breast cancer over the past few decades have attempted to identify prognostic factors in breast cancer, modern studies in Europe are focussing on predictive biomarkers that will identify optimal benefit from defined therapeutic regimens. Progress in breast cancer has been made with proliferation markers, growth factor receptors, and more recently gene expression profiling, such that several ongoing international trials are now testing these concepts in prospective randomised studies. Translational research and biomarker substudies should become an integral part of most phase I to III clinical trials. While in clinical practice we remain someway off utilising all of this predictive molecular information in deciding an individualised or stratified medicine strategy for each patient, the vision amongst academia and industry alike is that this should be achievable in the very near future.

There then followed an open discussion session in which the speakers were joined by other senior representatives from academia (Judith Bliss, Institute of Cancer Research; Bob Clarke, Washington), clinical investigation (John Robertson, Nottingham) and the pharmaceutical industry (Graham Ross, Roche), all of whom have been involved in development of novel therapies for breast cancer. Issues discussed included optimal trial design for targeted therapeutics, together with target validation in early studies. It remains clear that close collaboration between the pharmaceutical industry, academic institutions and clinical investigators will remain crucial if the new era of targeted therapies is to be translated into significant gains in clinical outcome for women with breast cancer.

The session concluded with a plenary lecture from Dr Larry Norton, Memorial Sloane Kettering Cancer Centre, New York. He addressed where the field of drug development in breast cancer might be heading in relation to molecular profiling and targeted therapies. Complex issues include the mathematics around the sheer number of genes of potential interest in molecular profiling studies, including the number of interactions that can occur. Furthermore, systems biology means that intracellular signalling networks have many redundant and compensatory pathways, making targeting of any single component potentially a futile approach. Robust systems in biology may be hard to perturb, but this could be overcome by smart combinations targeting multiple pathways or immunological approaches. Our optimism for the future might need to be tempered by the realisation that targeted therapies might not cure breast cancer, that 100% predictive molecular response criteria may not be possible to generate, and that the next generation of modern therapeutics may be hard to afford.

Abbreviations

CSG, Clinical Studies Group; NCRN, National Cancer Research Network.

Competing interests

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