phenotype might contribute to define this issue. Several potential treatment targets have been identified. Among those, EGF-R overexpression, DNA repair deficit, hyperproliferation, and angiogenesis, seem to be the most promising. Tumor biology may change during the course of advanced disease. Ideally, a biological characterization of each tumor should be performed immediately before activating a new line of treatment.

386 Invited

The molecular pathology of ER, PR HER2 negative breast cancers: finding novel biomarkers

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Breast cancer is a heterogeneous disease that encompasses several distinct entities with remarkably different biological characteristics and clinical behaviour. Currently, breast cancer patients are managed according to algorithms based on a constellation of clinical and histopathological parameters in conjunction with assessment of hormone receptors (oestrogen and progesterone receptor) and HER2 status. Although effective tailored therapies have been developed for patients with hormone receptor positive or HER2 positive disease, chemotherapy is the only modality of systemic therapy for patients with breast cancers lacking the expression of these markers (triple negative cancers, TN). Recent microarray expression profiling analyses have demonstrated that breast cancers can be systematically characterised into biologically and clinically meaningful groups. These studies have led to the re-discovery of basal-like breast cancers, which preferentially show a TN phenotype. TN and basal-like cancers preferentially affect young and African-American women, are of high histological grade and have a more aggressive clinical behaviour. A significant overlap between the biological and clinical characteristics of sporadic TN and basal-like cancers has been demonstrated. TN and basal-like cancers are remarkably similar to tumours arising in BRCA1 mutation carriers. We have shown that a substantial proportion of sporadic TN tumours have a dysfunctional BRCA1 pathway and that inactivation of Brca1 and p53 in an engineered mouse model leads to the development of tumours whose morphological features recapitulate those of sporadic TN cancers. It should be noted, however, that TN and basal-like cancers are heterogeneous groups of tumours at the histopathological, phenotypic and genetic levels. Novel approaches for unravelling the complexity of these cancers and for the identification of biomarkers and therapeutic targets in TN and basal-like cancers through a combination of high throughput techniques, including microarray-based comparative genomic hybridisation, expression arrays, RNAi screening and tissue microarrays, will be discussed.

387 Invited

How should we best target the biology of ER PR HER2 negative breast cancer?

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Breast cancer comprises a diverse collection of diseases with distinct biological features and clinical behaviour. Both pre-clinical and clinical research now commonly targets specific sub-groups of breast cancer with the aim of identifying biological markers or genetic phenotypes, which reveal specific therapeutic targets or indicators of prognosis for each of these groups. Examples include the targeting of oestrogen receptor (ER) driven breast cancers with endocrine therapies, and sub-group of breast cancers driven by the receptor tyrosine kinase ErbB2 (HER2) by targeting this receptor using the monoclonal antibody (e.g. trastuzumab) or the small molecule inhibitor lapatinib. In each case, extensive preclinical research followed by large, multi-centre, randomised controlled trials has led to improved disease free survival and overall survival. These novel targeted agents are, however, of no benefit to a substantial number of women whose breast cancers lack ER, PR and HER2 receptors; the so called "triple negative" sub-group. In the previous paper a dissection of the molecular pathology of and relationships between "triple negative" and "basal-like" breast cancers reveals some recurrent genetic, epigenetic and gene expression changes associated with these sub-types. These are now being used to inform early phase clinical trials in "triple negative" and "basal-like" breast cancer subtypes. Initial targets considered worthy of investigation in "triple negative" and "basal-like" cancers include the following: The EGF receptor, which is expressed in more than 50% and amplified in up to 5% of these cancers; c-Kit, which is overexpressed in the majority of these tumours; and VEGF, given the high vascularity noted in some "basal-like" cancers. Src inhibitors have also been shown to have preclinical efficacy in cell lines with a triple negative phenotype. Furthermore, our group has explored the concept of targeting abnormal DNA repair associated with abnormal BRCA1 function. Given that cancer cells with a dysfunctional BRCA1 pathway have been shown to display an exquisite sensitivity to DNA cross-linking agents and PARP inhibitors, clinical trials are now testing whether these agents can be used for the management of patients with hereditary BRCA cancers and sporadic carcinomas with "triple negative" and "basal-like" phenotypes. The rationale for, and nature of, clinical trials examining targeted approaches will be discussed in the context of the molecular pathology data outlined in the preceding paper.

Friday, 18 April 2008 16:00–17:30

CLINICAL SCIENCE SYMPOSIUM

Delivering optimal breast cancer care in all circumstances

388 Invited

Organisation of breast units

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In October 1998 the First European Breast Cancer Conference took place, jointly organised by the EORTC Breast Cancer Cooperative Group, EUSOMA and Europa Donna.

Delegates agreed a consensus on research, genetic predisposition, psycho-social status, treatment and notably quality of care. "The Florence statement" demanding that all women have access to multidisciplinary breast clinics based on populations of around 250,000; also it called for mandatory quality assurance programmes for breast services. With the intention of assuring a high quality specialist service Europe-wide, a working party was established to consider what should comprise a specialist service. These resulted in the publication of the "Requirements of a Specialist Breast Unit" which describe the standards required for forming high quality Breast Unit across Europe (European Journal of Cancer 2000; 36: 2288–2293).

These guidelines have been generally well received, have been influential in the introduction of the multidisciplinary working teams in several Countries (see www.eusoma.org and www.senonetwork.org) and considerable attention was drawn to the approval given to this approach by the European Parliament (2004).

The key requirements to establish a proper Breast Unit are a relevant critical mass (at least 150 new cases per year and at least 5,000 mammographies), development of individual skills (at least 50 operations per surgeon and 500 mammographies per radiologist), dedicated specialist from all the relevant specialties (pathology, medical oncology, nursing, etc.).

389 Invited

The Breast Health Global Initiative: a catalyst for cancer control in limited resource countries

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Background: Breast cancer is the most common cancer among women around the globe, and is the most likely reason a woman will die of cancer. Of the 411,000 breast cancer deaths around the world in 2002, 221,000 (54%) occurred in low- and middle-income countries (LMCs). Incidence rates of breast cancer are increasing in most countries, with increases that are greatest where rates were previously low. Guidelines for breast health care (early detection, diagnosis and treatment) that were developed in high resource countries cannot be directly applied in LMCs, because these guidelines do not consider real world resource constraints, nor do they prioritize which resources are most critically needed in specific countries for care to be most effectively provided.