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?

A.N.J. Tutt[1], J.S. Reis-Filho[2]. [1]*Breakthrough Breast Cancer Research Unit, Kings College London School of Medicine, London, United Kingdom;* [2]*Breakthrough Breast Cancer Research Centre, Institute of Cancer Research, London, United Kingdom*

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.

Materials and Methods: Established in 2002, the Breast Health Global Initiative (BHGI) created an international health alliance to develop evidence-based guidelines for LMCs to improve breast health outcomes. The BHGI held two Global Summits in October 2002 (Seattle) and January 2005 (Bethesda) and using an expert consensus, evidence-based approach developed resource-sensitive guidelines that define comprehensive pathways for step-by-step quality improvement in health care delivery. The BHGI guidelines, now published in English and Spanish, stratify resources into four levels (basic, limited enhanced and maximal), making the guidelines simultaneously applicable to countries of differing economic capacities.

Results: The 3rd BHGI Global Summit in October 2007 (Budapest, Hungary) addressed guideline implementation in LMCs. 82 selected international experts working on four panels (Early Detection, Diagnosis, Treatment, Health Care Systems) discussed situation analysis tools and quality indicators to facilitate pilot project development in LMCs. Funded pilot projects have begun in Colombia and Indonesia. The BHGI guidelines provide a hub for linkage among clinicians and alliance among governmental agencies and advocacy groups to translate guidelines into policy and practice.

Conclusions: The breast cancer problem in LMCs can be improved through practical interventions that are realistic and cost-effective. Early breast cancer detection and comprehensive cancer treatment play synergistic roles in facilitating improved breast cancer outcomes. The most fundamental interventions in early detection, diagnosis, surgery, radiation therapy, and drug therapy can be integrated and organized within existing health care schemes in LMCs. Future research will study what implementation strategies can most effectively guide health care system reorganization to help countries that are motivated to provide better care to women in their country afflicted with breast disease and to improve breast cancer outcome among their populations.

390 Invited

Breast cancer in emerging countries: The status of breast care in South Africa

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The apartheid system, which created an extremely efficient, high quality health service for a minority of the population, became untenable by 1990. Resources were then redirected to primary care at the expense of tertiary care. “Transformation” of the health service to allow “previously disadvantaged” population groups access to management positions denuded the service of experienced managers and was compounded by a succession of ineffective top officials. Deteriorating working and life circumstances and increasingly inadequate salaries led to emigration of professionals: A third of all South African nurses work abroad and half of all medical graduates emigrate upon graduation. In the underresourced public sector about 10% of medical doctors cater for about 80% of the population; breast cancer, despite being the most common female cancer, does not appear in the top 10 causes of women life years lost; the first 5 places are taken by AIDS, homicide, TB, diarrheal diseases and pulmonary infections. The incomplete statistics available generate the perception, that breast cancer is largely a “white womens’ disease” pushing it further down the list of priorities. Currently the country experiences about 8000 new cases of breast cancer, of which only about 2000 are catered for in 4 multidisciplinary centres offering in varying degrees state of the art diagnostics and therapy from BRCA testing, digital mammography to oncoplastic surgery, free tissue transfer reconstruction, neoadjuvant therapy with antracyclin-taxane regimens and MeV radiation. To prevent further deterioration and reverse the trend, where there is still expertise is left it must be maximally exploited; public–private and South2South partnerships of apex institutions are to be formed. The North should accept an obligation to prevent uncoupling of 3rd world countries by maintaining active relations with apex institutions, sponsoring congress participation and support trial participation.

391 Proffered Paper Oral

A health economic evaluation of follow up after breast cancer surgery – result from of an rct study

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Introduction: We studied the costs of following 264 breast cancer patients, stage I and II, randomised to two different follow-up programmes in a prospective trial, involving, on the one hand, routine follow-up visits to the physician with follow-up visits twice a year or more over five years (PG = physician group), and on the other, specialist nurse intervention with check-ups on demand (NG = nurse group). The trial period was 5 years. The women in the two intervention groups did not differ in anxiety and depression, their satisfaction with care, their experienced accessibility to the medical centre or their medical outcome as measured by recurrence or death.

Patients and Methods: The analyses were done from different lists representing costs at three hospitals in Sweden according to the principles of a cost minimization study.

Result: The cost per person year of follow-up differed between the groups, with €630 per person year in PG compared to €495 per person year in NG. Thus, specialist nurse intervention with check-ups on demand was 20% less expensive than routine follow-up visits to the physician. The main difference in cost between the groups was explained by the numbers of visits to the physician in the respective study arms. There were 21% more primary contacts in PG than NG.

Discussion: The difference in cost per year and patient by study arm is modest, but transforms to nearly €9,000 per patient and 5-year period, offering a substantial opportunity for reallocating resources since breast cancer is the most prevalent tumour worldwide.

392 Proffered Paper Oral

Does working in a multidisciplinary breast unit have any impact on surgical treatment?

B. Merck[1], J.M. Ramos-Rincón[2], M.J. Giménez Climent[1], M.P. Cansado[3], I.T. Rubio[4], M. Ramos-Boyero[5], C. Vázquez-Albaladejo[1]. [1]*Fundacion Instituto Valenciano de Oncologia, Surgery, Valencia, Spain;* [2]*Hospital GU de Elche, Medicine, Elche, Spain;* [3]*Hospital GU de Elche, Surgery, Elche, Spain;* [4]*Hospital Valle d’Hebrón, Surgery, Barcelona, Spain;* [5]*Hospital Clínico, Surgery, Salamanca, Spain*

Background: Multidisciplinary treatment is the optimal approach to breast cancer. When it is performed in specialized units, it benefits patients and leads to more rational resource use. The European Society of Mastology (EUSOMA) published in 2000 their recommendations designed to provide a model for European high quality breast units (BU).

Methods: We analyze the results concerning surgical treatment, obtained from the survey about BU performed by the Breast Diseases Group of the Spanish Association of Surgeons, in 247 Spanish hospitals. Data of 167 (69.3%) answers were obtained. Analysis was undertaken using the Kruskal–Wallis test for cuantitative and the chi-squared and Fisher exact tests for cathegorical variables; p-values of 0.05 or less were considered significant.

Results: Most BU (82) were managed by general surgeons, 70% of them specifically dedicated to breast diseases and near 40% with a postgraduate training in mastology. Clinical guidelines about diagnosis and treatment were used in 97.7% of BU. More breast cancer patients were diagnosed (112.6 vs. 69.4; $p = 0.004$) and surgically treated yearly (96.8 vs. 55.5; $p < 0.001$) in BU compared with hospitals with no BU. Breast conservation was performed in 55% of cases without differences concerning the presence of BU.

Sentinel node biopsy was more frequently adopted in the presence of breast unit (55 vs. 23; $p < 0.001$), specially dedicated surgeon (54 vs. 18; $p < 0.001$) and nuclear medicine facilities (40 vs. 33; $p < 0.001$). In 90.3% isotopic or combined injection was used. Intraoperative evaluation of sentinel node was possible in 32.9%.

Postmastectomy reconstruction was performed by general surgeons in 41 BU. In most cases (37 vs. 13; $p < 0.001$) reconstruction was immediately done as part of the initial treatment of breast cancer and by means of an implant (48.9%). Other reconstructive procedures as musculocutaneous flap techniques or oncoplastic approaches were less frequently completed.

Conclusions: Surgeons specially dedicated to breast diseases, working in multidisciplinary BU do more frequently use diagnostic and treatment protocols and guidelines, perform sentinel lymph node biopsy and postmastectomy reconstruction. These aspects are considered of high quality in breast cancer management and confirm the usefulness of establishing breast units.