particularly invasive LR. An overview of all four of the randomised trials that compared adjuvant whole breast radiotherapy (RT) vs no RT after breast-conserving surgery for DCIS showed that RT halved the LR rate [1]. It reduced the absolute 10-year intraductal or invasive LR risk by 15.2% (12.9% vs 28.1%, 2P < 0.00001). RT was effective irrespective of age, detection method, focality, tumour size, architecture, grade, comedonecrosis, margin status or tamoxifen use. However, there was no significant effect on breast cancer mortality or all-cause mortality.

Currently, there are no reliable predictors for invasive LR and published data is limited to identification of surrogate markers for clinical outcome. There is a consistent association between younger age and an increased LR risk. High nuclear grade and presence of comedonecrosis are strongly associated with LR and progression to invasive disease. In addition, large tumour size and involvement of surgical margin are associated with LR but the optimal margin size remains controversial. Molecular markers including oestrogen receptor status, HER2/neu oncogene over-expression and p53 tumour suppressor gene mutation have not been reliably associated with LR risk. Approaches derived from global molecular profiling are being investigated for predictive assessment of recurrence.

A principal aim of DCIS research is to determine robust biomarkers to identify women at high risk from those at lower risk of invasive LR, and enable individualised treatment. A single-arm prospective study reported a 5-year LR rate after breast-conserving surgery, without RT of 6.1% in patients with low or intermediate grade DCIS $\leqslant$25 mm in size and resected with margins $\geqslant$3 mm, and 15.3% in patients with high grade DCIS $\leqslant$10 mm [2] Further research on biomarkers may enable more reliable identification of patients who have low absolute risk of LR and for whom RT may provide little absolute gain. In contrast, patients at higher risk of LR may benefit from more extensive surgery and/or RT. The addition of a tumour bed boost to whole breast RT to further reduce LR rate is being investigated in a clinical trial.

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216 Invited

The Pathology of DCIS: Take it or Leave it

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Incidence rates of ductal carcinoma in situ (DCIS) have increased over the past decades largely due to population-based screening for breast cancer. However, data from 1987 to 1999 indicate that invasive ductal carcinoma incidence rates have remained essentially constant. On pathological examination, a subgroup of neoplastic low grade intraductal lesions is even more low risk than classical cribriform ductal carcinoma in situ grade 1 with a cumulative risk on progressive disease of 0.5−1.0% per year, a risk that is comparable to developing local recurrence after breast conserving therapy. These lesions share the same histogenetic alterations and are diagnosed by a variety of terms covering a spectrum of morphological slightly different lesions ranging from columnar cell change to cribriform ductal carcinoma In situ grade I. Within this spectrum, a variety of diagnostic definitions have been proposed like atypical ductal hyperplasia, flat epithelial atypia, columnar alterations with prominent snouts and secretions (CAPSS), etc., etc. Nevertheless, one of the major challenges remains, I.e. the substantial interobserver variation in diagnosing these low risk, low grade intraductal neoplastic lesions.

In current practice, most women undergo surgery to excise the high end of the risk spectrum, i.e. the unambigious DCIS grade I lesions, regardless of extensiveness and patient's features, such as age and co-morbidity, to exclude that the core biopsy was containing just the tip of the iceberg. For the more ambigious lesions, patient management can vary enormously due to different opinions and interpretations of the multidisciplinary breast team. Most likely, the majority of women with such a lesion would not benefit from surgery due to the low risk of developing extensive DCIS and/or invasive ductal carcinoma. In addition, if lesions do develop from a low grade in situ component, these are almost always well differentiated, small sized, hormone receptor positive, HER2 negative invasive carcinomas with an exceptionally favorable prognosis. In fact, the risk of dying due to the disease might not be significantly higher than in the non affected population. It is therefore unsure whether surgical excision (followed by radiotherapy in case of breast conserving treatment) of such lesions can be considered as adequate treatment or overtreatment. To solve this issue, proper follow-up of patients with such lesions without surgical intervention is required to justify either surgery or a watchful waiting policy.

217 Proffered paper oral

Adjuvant Radiotherapy After Breast-conserving Surgery for Ductal Carcinoma in Situ − Fifteen-year Results of the EORTC Randomized Phase III Trial 10853

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Background: The incidence of ductal carcinoma in situ (DCIS) has increased in the last decades due to mammographic screening and accounts currently for 25% of the new breast cancers. We present the 15-years results of a randomized controlled trial that investigated the role of adjuvant radiotherapy (RT) after a local excision (LE) for DCIS.

Patients and Methods: Between 1986 and 1996, 1010 patients with a complete excision of DCIS <5 cm were randomized to no further local treatment or RT (50 Gy in 25 fractions to the whole breast).

Results: After a median follow up of 15.8 years, radiotherapy continued to reduce the risk of a local recurrence (LR) (HR = 0.52; 95% CI = 0.40–0.68): the LR free rate was 69% in the LE arm, which was increased to 82% in the LE+RT arm. There were comparable reductions in the incidence of a *DCIS* LR (HR = 0.49; 95% CI = 0.33–0.73) and an *invasive* LR (HR = 0.49; 95% CI = 0.33–0.73). The 15-years cumulative incidence for LE alone compared to LE+RT for *DCIS* LR was 14.9% versus 7.5% respectively, and for an *invasive* LR this was 15.5% vs. 9.8% respectively.

When the hazard rate of a LR was analysed within three time windows (0−5, 5−10 and from 10 year onwards), this was estimated as 2.0% (95% CI = 1.4−2.6) during the first 5 years in the group receiving RT and 4.0% (95% CI = 3.2−4.8) in the group treated only with LE, 1.2% (95% CI = 0.8−1.7) and 2.0% (95% CI = 1.4−2.8) respectively in the next five years, and 0.6% (95% CI = 0.4−1.0) and 1.3% (95% CI = 0.8−1.9) respectively from 10 year onwards. The protecting effect of RT on a *DCIS* LR was similar throughout all time frames, the effect of RT on an *invasive* LR was observed mainly in the first 5 years after treatment.

The differences in LR in both arms did not lead to a difference in distant metastasis (HR = 0.99, 95% CI = 0.61–1.61) or death (HR = 1.02; 95% CI = 0.71–1.44).

Women with a *DCIS* LR had a similar survival prognosis after the event as compared to those without a LR. However, after an *invasive* LR their prognosis was significantly worse as compared to the non-recurring patients; this is reflected by a HR of 5.2 (95% CI = 3.1−8.7) for overall mortality and a HR of 17.7 (95% CI = 8.9–35.2) for breast cancer related mortality.

Conclusion: At 15 years, almost 1 in 3 women developed a LR after LE for DCIS. RT reduced this risk by 50%, equally divided over *invasive* or *DCIS* recurrences. The majority of the LRs occurred within five years after treatment; radiotherapy seemed to have a continuous protecting effect with respect to *DCIS* recurrence; but only a temporary protecting effect with respect to *invasive* recurrences in the first 5 years after treatment. Although no survival difference was seen between the two treatment groups, women who experienced an invasive recurrence had a significant worse survival compared to women who had a DCIS recurrence or no recurrence at all.

Thursday, 22 March 2012 15:30–17:00

CLINICAL SCIENCE SYMPOSIUM

Barriers to Effective Care

218 Invited

External Barries to Effective Care in Clinical Research

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Therapeutic drug development in oncology has reached new heights in recent years with the emergence of targeted agents. More than 20 years on from the development of trastuzumab to treat HER2+ breast cancer, clinicians still only have limited registered therapeutics for treatment i.e. trastuzumab and lapatinib. This phenomenon is not specific to breast

cancer but why is this the case, where are the obstacles and what needs to change to move forward efficiently?

The answers to these questions are complex in nature and the solutions involve establishing sincere partnerships. Future targeted and non-targeted therapy trials hold the key. Integral is the uptake of tissue sampling for biomarker analyses and translational research to progress the understanding of cancer biology.

A change in direction of trial design is required. Inherent difficulties with conventional trial design and drug evolution stratagems in their application to targeted therapeutics exist. These nuances are part of the reasons why such drugs fail at the costly phase III stage. Options include using validated alternative clinical endpoints and the neoadjuvant setting to test early drug signals.

The explosion of targeted agent trials and advances in genomics has meant that vast amounts of data are generated (i.e. clinical, pathology, imaging and complex molecular signatures). However, optimal exploitation of this data to improve standards in patient outcomes has lagged behind research efforts. Data sharing environments involving co-operation with industry and academia for re-use of data to test hypotheses, generate new biomarkers and clinical trials and set contemporary benchmarks in cancer therapy are called for.

Collaboration must exist between pharmaceutical companies and academia. The pharmaceutical industry is facing mounting pressures in drug development. The substantial investment required for drug maturity, limited drug pipelines, difficulty with traditional drug development paradigms and loss of patents have all been sited as causes. The fallout from this pressure to produce the new 'blockbuster' targeted therapy is abandoning many drugs that may have a niche therapeutic indication due to limited potential market share.

The progress of clinical trials in the future will strongly rely on the co-operation of governments/regulatory bodies with the research industry to break down administrative barriers, assist in the acquisition of knowledge of standards of care in different countries, provide flexibility of drug registration and establish a partnered cost relationship for expensive targeted therapies.

These new streamlined drug development methods and partnerships need to be adopted by the academic, pharmaceutical industry, regulatory bodies and government in order to progress effective clinical research.

219 Invited

Advocacy Perspective on Barriers to Effective Care

B. Borisch[1]. [1]*Institut de Médecine Sociale et Préventive, Geneva 4, Switzerland*

(1) There is a large amount of energy put into the improvement of care in breast cancer. Both from the medical as well as from the political side. In addition to the European guidelines for quality assurance in breast cancer screening and diagnosis a large number of guidelines exist. The work of specialists, politicians and patients together has established evidence based ways that will lead to more effective care for breast cancer patients. Data clearly indicate that multidisciplinary work and breast units are the cornerstones to improved care and more efficiency in European health care systems.

(2) Studies on the implementation of guidelines were reviewed (PubMed, HSTAT, HSRR/NLM). Data from qualitative and quantitative research on barriers in care and prevention were reviewed. In addition, the experience of patient advocates pushing for the implementation of European guidelines in three European countries was evaluated.

(3) The studies collected from the scientific literature indicate that several barriers to effective care exist: most often cited are structural, psychological, cultural, financial and bureaucracy levels as well as health inequalities. From the patients perspective all these barriers exist; in addition, the health care providers themselves are sometimes perceived as barriers to changes on the existing system. The local medical specialty organisations, the organisation of the health care system, interplay between private and public sector are a very frequently mentioned obstacle.

(4) In conclusion: patient advocates have been instrumental for getting the EU resoution on breast cancer adopted by the Parliament. Advocates work in their respective countries and encounter − in addition to the well documented (in the scientific literature) barriers − resistance from some of the health professionals. These kind of oppositions are less well documented in the literature. The barriers to change are common to many health care systems. Integration, innovation and values have to be challenged and improved. The system needs continous control and adaptation to patients needs.

References

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220 Invited

Internal Barriers to Effective Care (Staff Dynamics)

L. Fallowfield[1], V. Jenkins[1]. [1]*University of Sussex, SHORE-C, Brighton East Sussex, United Kingdom*

The delivery of good quality cancer care is now a serious team business demanding effective collaboration from numerous healthcare professionals from a variety of different disciplines. Ideally each member of these multi-disciplinary teams should contribute independently from their own area of expertise enabling appropriate treatment plans to be made and then offered to a patient.

The increasing complexity of cancer management means that large numbers of healthcare are involved so there is considerable potential for miscommunication and poor co-ordination. The putative benefits of working in collaborative groups should lead to consistency, continuity and cost-effectiveness of care that might enhance patient outcomes, provide better opportunities for audit and clinical trial recruitment and contribute to the satisfaction and psychological well-being of patients. There should also be other benefits including more educational opportunities for team members, support from a collegial working environment leading to increased job satisfaction and psychological well-being.

Crucial to the achievement of these aspirations are positive team dynamics and good leadership. Unfortunately teams do not automatically function well. The best team leaders are also not always the most senior member of the team. Without encouragement of full participation, some specialties may feel that they are without a voice. There is often a lack of clarity about shared objectives and little mutual respect or appreciation of the role of others.

Health service research demonstrating the benefits of effective team working is difficult to conduct given the numerous variables that impact on outcomes. Historical enmities, hierarchical boundaries and personality styles can be difficult to change and a lack of respect for different viewpoints is not conducive to harmonious exchanges that leave healthcare professionals feeling satisfied that they have contributed to optimal management plans for their patients. There is a need to invest in team training and support. In this talk examples will be shown of educational initiatives aimed at improving team functioning.

221 Invited

Political Barriers to Effective Care

V. Mazeau Woynar[1]. [1]*Institut National du Cancer, Boulogne-Billancourt cedex, France*

Approximately 360 000 new patients are diagnosed with cancer in France every year. It is the first mortality cause in our country. Since 2003, the fight against cancer has been supported by two consecutive national cancer plans which have guaranteed substantial funding to specific actions for almost 10 years.

Years can pass between the recognition of a public health problem and the implementation of a policy. It is strongly linked to the many political barriers that policy makers have to lift. The two cancer plans demonstrated a strong political will in the fight against cancer that has undoubtedly helped French policy makers in the cancer field to address many issues in a relatively short timeframe.

Some successful policies can be used as illustrations. In terms of access to innovation, the development of regional platforms for molecular diagnostic tests provides access for all to the adequate molecular test as soon as a new targeted therapy is available on the market. In terms of access to medical information, a personal cancer electronic medical record should be launched at the national level by 2013 to improve information exchange between healthcare professionals and thereby improve efficiency of care.

Some issues remain challenging because they generate important political barriers. In terms of access to more personalized pathways, France is experimenting organizations to implement survivorship care plans. Recommended organizations should reinforce the role of the primary care sector during and after cancer treatment. However, it can already be anticipated that the organizational and cultural change will take several more years and may imply various policies such as fee changes, new medical training, and more precise clinical guidelines. Policies promoted by the cancer plans have also addressed issues concerning life plans of cancer patients. Negotiation with insurers to increase access to loans for patients with cancers is an emblematic example of policies that are much hindered by politics.