be pro-active in price adjustment and regulations so that new therapies introduced are economically viable for health systems.

As breast cancer treatments become more complex, more targeted and more tailored to each woman's particular needs, patient advocates need to be vigilant in seeing that new, potentially effective treatments are studied and made available to patients. We cannot walk away from health economics but effectiveness must remain the criterion for introducing new treatments. Breast cancer advocates need to keep a close watch on the economic decision making process utilised in each country setting.

6 Invited

The doctor's view

E. Winer[1]. [1]*Dana Farber Cancer Center, Harvard Medical School, Boston, USA*

The cost of cancer treatment continues to escalate and is a major problem around the world. In less developed countries, the cost of new treatments, such as monoclonal antibodies and targeted small molecules, is simply prohibitive. In other countries, these new treatments have been embraced but have placed a major strain on health care budgets and have led to unprecedented increases in medical expenditures for breast cancer. What is the role of the physician in this ever more complex and frequently frustrating economic environment? At a minimum, the physician plays three distinct and very important parts. First, on an individual level, the physician must be his own patient's advocate, attempting, whenever possible, to provide the best available evidence-based care. When one is sitting in the examining room with a patient, societal costs should not affect the treatment recommendation. Second, and on a broader scale, the physician must actively participate in a societal process that determines whether a particular treatment should be available to patients. The decision may well differ across countries and will be highly dependent on both resources and competing demands, but in all cases, physicians must play a pivotal role. Third, the physician must be a spokesperson for the development of cost-effective strategies to care for individuals with breast cancer. Breast cancer clinicians, working with scientists, advocates, and others, need to speak against costly and ineffective strategies, as well as excess profits. If, as doctors, we walk away from economics, we walk away from a set of responsibilities and increase the likelihood that both our patients and we will become the victims of the economic realities that lie ahead.

Wednesday, 16 April 2008 16:00–17:30

CLINICAL SCIENCE SYMPOSIUM

Towards a rational endocrine therapy treatment

7 Invited

Biomarkers to guide rational endocrine therapy of breast cancer

M. Dowsett[1]. [1]*Royal Marsden Hospital – NHS Trust, Academic Department of Biochemistry, London, United Kingdom*

Approximately 75−80% of breast cancer patients have oestrogen receptor positive (ER+) disease and all such patients should receive some form of endocrine therapy. Tamoxifen may be used in both pre and postmenopausal patients while GnRH agonists and aromatase inhibitors are confined to pre and postmenopausal women, respectively. Overall aromatase inhibitors show greater efficacy than tamoxifen but the difference is not so substantial to exclude the possibility that some patients derive equal benefit from tamoxifen. Despite major efforts being directed at identifying such patients at present there are no markers are usable with confidence. HER2 positive disease shows impeded response to tamoxifen in the neoadjuvant setting and aromatase inhibitors do not show this effect but in the adjuvant setting no distinction has been shown. The presurgical setting provides the opportunity to determine the biological response of individual patients to endocrine therapy based on molecular markers and to consider additional treatments to be considered in relation to this response.

8 Invited

Endocrine treatment of premenopausal breast cancer patients

M. Gnant[1]. [1]*Medical University Vienna, Department of Surgery, Vienna, Austria*

Premenopausal breast cancer patients face a particular challenge for the interdisciplinary team: The prognosis of breas young breast cancer patients is often considered worse due to the increased agressiveness of the tumor. In fact, young age is an independent risk factor in most epidemiologic studies. Also, the special social situation of young patients need to be taken into account for treatment planning. Younger patients have also different tolerabilities for treatment side effects. Chemotherapy is considered the mainstay of the advuvant treatment, even for endocrine responsive disease. This may not me necessarily true. Several trials have shown that adjuvant endocrine intervention alone can yield comparable or even improved results for premenopausal patients with endocrine responsive breast cancer. Tamoxifen is effective in premenopausal breast cancer patients, and several combinations of aromatase inhibitorswith ovarian function suppression (OFS) using GnRH analogues are tested in clinical trials.

9 Invited

Are there any difference between third-generation aromatase inhibitors?

P.E. Lønning[1]. [1]*Section of Oncology Institute of Medicine, University of Bergen, Bergen, Norway*

Third-generation aromatase inhibitors (anastrozole, letrozole and exemestane) have been successfully implemented for treatment of early breast cancer. These drugs all inhibit in vivo aromatization effectively (>98%). Based on head-to-head comparison, letrozole (2.5 mg daily) was found superior to anastrozole (1 mg daily) inhibiting in vivo aromatization. While each compound has been revealed to improve relapse-free survival in early breast cancer, we are awaiting the results of head-to-head comparisons between individual compounds regarding clinical efficacy. Steroidal (exemestane) and non-steroidal (anastrozole and letrozole) compounds differ with respect to several important aspects.

First, steroidal compounds like exemestane binds to the substrate pocket of the aromatase enzyme while the non-steroidal compounds (anastrozole and letrozole) bind to the heme part. Second, steroidal compounds bind irreversibly, destroying the aromatase protein. Third, and probably of most importance to the clinic, steroidal compounds express light androgen agonistic activity, revealed by a significant suppression of sex hormone binding globulin, an androgen parameter in vivo. Notably, most breast cancers which express the estrogen receptor will express the androgen receptor in concert, and androgens may cause anti-tumour effects in experimental system as well as in clinical breast cancer. Clinically, several studies now confirm lack of cross-resistance between steroidal and non-steroidal compounds, in as much as patients progressing on non-steroidal compounds including anastrozole and letrozole may subsequently benefit from treatment with exemestane. In addition, a large randomized study recently confirmed for metastatic breast cancer exemestane to be as effective as faslodex among patients failing anastrozole therapy. While anecdotic evidence suggest patients becoming resistant to steroidal compounds may subsequently respond to a non-steroidal third-generation inhibitor, more data are needed to address this issue.

10 Proffered Paper Oral

A randomised study of the impact of endocrine therapy for breast cancer on bone turnover and quality of life

F.M. McCaig[1], L. Renshaw[1], R. Hannon[2], L. Williams[3], L. Fallowfied[4], O. Young[1], J. Murray[1], E.J. Macaskill[1], M. McHugh[1], J.M. Dixon[1]. [1]*Western General Hospital, Edinburgh Breast Unit, Edinburgh, United Kingdom;* [2]*Metabolic Bone Centre, Northern General Hospital, Unit of Bone Metabolism, Sheffield, United Kingdom;* [3]*Edinburgh University Medical School, Medical Statistics Unit, Edinburgh, United Kingdom;* [4]*Brighton and Sussex Medical School, Cancer Research UK Psychosocial Oncology Group, Falmer, Sussex, United Kingdom*

Background: Letrozole (L) decreases circulating oestrogen levels to a greater degree than anastrozole (A). The aim of this study was to compare the effects of L and A on musculoskeletal symptoms and bone turnover.

Patients and Methods: 182 postmenopausal women with invasive oestrogen receptor (ER) positive breast cancer were randomised as part of their adjuvant hormone therapy to receive: "12 weeks of L followed by 12 weeks of A or" 12 weeks of A followed by 12 weeks of L as initial upfront adjuvant or delayed adjuvant therapy after 5 years of tamoxifen (T). 84 had fasting blood and urine samples for the markers N-terminal telopeptides (NTx), C-terminal telopeptides (CTx), bone alkaline phosphatase (ALP) and parathyroid hormone (PTH). 170 patients had sufficient data on musculoskeletal side effects collected by a nurse after 4, 8 and 12 weeks of each drug for analysis.

Results: Tamoxifen Effect: Baseline PINP 37.5 (32.1−42.9) vs. 46.2 (41.0−51.3 and serum CTx 0.49 (0.42−0.57) vs. 0.62 (0.55−0.70), both $p < 0.025$ were lower in the prior T group. Letrozole vs. Anastrozole: L and A had similar effects on markers at all time point (all $p > 0.10$). 131 had