Findings: As the extra cost of 2 yrs T + 3 yrs E over 5 yrs T (considering bone density scans) was £3,280, it cost £69,787.2 to prevent one women relapsing (£3,280/4.7%). Our analysis calculated that the average monthly cost of treating a relapse was £752.35. As the mean survival was 32.6 months the mean total cost/patient was £24,526.66. Subtracting this from the initial extra cost of E gives a mean extra cost of £45,260.54 to prevent one patient relapsing. As the median survival of the relapsed women in our analysis was 2.72 yrs and the expected survival if they don't relapse is 18 years, the cost per life year saved was £2,962/yr.
Discussion: Notwithstanding the humanitarian issues, these figures from a single institution suggest it is cost efficient to switch to E at 2 years. As these figures reflect the management of women over the last seven years they are likely to underestimate the future cost. Further modelling of the data in relation to the 25.5% who were HER2+ in terms of the extra cost of herceptin and the longer survival with relapsed disease, together with further detailed subset cost effectiveness analysis will be presented.

2134 POSTER

Clinical benefit of trastuzumab plus vinorelbine as second-line treatment for women with HER2-positive metastatic breast cancer beyond disease progression

P. Chollet[1], X. Durando[1], L. Mauriac[2], C. Delcambre[3], P. Maillart[4], C. Veyret[5], M.A. Mouret-Reynier[1], I. Van Praagh[1], T. Bachelot[6]. *[1]Centre Jean Perrin and UMR INSERM 484, Oncology, Clermont Ferrand, France; [2]Institut Bergonié, Oncology, Bordeaux, France; [3]Centre François Baclesse, Oncology, Caen, France; [4]Centre Paul Papin, Oncology, Angers, France; [5]Centre Henri Becquerel, Oncology, Rouen, France; [6]Centre Léon-Bérard, Oncology, Lyon, France*

Background: The benefits of multiple lines of trastuzumab (Herceptin®; H) therapy have been increasingly reported for women with HER2-positive metastatic breast cancer (MBC). We report the results from the first planned interim analysis of a Phase II, 2 step, multicentre trial evaluating second-line H + vinorelbine (N) in women who received first-line H + taxane therapy for HER2-positive MBC.
Materials and Methods: Women aged ⩾18 years with HER2-positive (IHC3+/2+ and FISH+) MBC who progressed following first-line H + taxane therapy were enrolled. All patients (pts) received H (8 mg/kg iv loading dose followed by 6 mg/kg q3w or 4 mg/kg iv loading dose followed by 2 mg/kg qw) + N (30 mg/m^2 days 1 and 8, q3w) until disease progression (PD). The primary end point was overall response rate (ORR); secondary end points included time to progression, time to treatment failure, overall survival and safety.
Results: To date 17 pts with HER2-positive (16 pts IHC 3+; 1 pt IHC 2+ and CISH+) MBC have been evaluated. Mean age was 54 years (range 42−70). Nine pts had hormone receptor-positive MBC (7 pts ER+/PgR−; 2 pts ER−/PgR+). Prior to enrolling, 12 pts had received previous chemotherapy in the neoadjuvant/adjuvant setting and 6 had undergone adjuvant hormonal therapy. All pts had previously received H in combination with paclitaxel (9 pts) or docetaxel (8 pts) as first-line therapy for MBC. In addition to these treatments for MBC, 3 pts had received hormonal therapy. A median of 6 H + N treatment cycles (range 2−14) were administered, with 2 pts receiving H q3w and 15 pts receiving H qw. The clinical benefit rate was 53% and ORR was 30%, with 2 pts (12%) showing a complete response, 3 pts (18%) experiencing a partial response and 4 pts (23%) achieving stable disease lasting 6 months. Fourteen pts withdrew from the study due to PD. The main serious adverse event was grade 3/4 neutropenia, leading to a delay and dose reduction of N in 4 pts. Only 2 asymptomatic grade 1 cardiac events were reported for the 9 pts for whom cardiac function data were available. No deaths were reported.
Conclusions: First planned interim results indicate that treatment with H + N in pts with MBC who progressed following first-line H + taxane therapy is active and well tolerated. These data provide further evidence for the clinical potential of multiple lines of H in pts with HER2-positive MBC.

2135 POSTER

Cost-effectiveness (CE) of lapatinib plus capecitabine (L+C) in women with ErbB2+ (HER2+) metastatic breast cancer (MBC) who have received prior therapy with trastuzumab (TZ) from the United Kingdom (UK) National Health Service (NHS) perspective

T.E. Delea[1], P. Tappenden[2], O. Sofrygin[1], J. Karnon[2], M. Amonkar[3], D. Browning[4], H. Rudge[4], M. Walker[5]. *[1]Policy Analysis Inc. (PAI), Brookline MA, USA; [2]University of Sheffield, School of Health and Related Research (ScHARR), Sheffield, United Kingdom; [3]GlaxoSmithKline, Global Health Outcomes, Collegeville PA, USA; [4]GlaxoSmithKline, Health Outcomes, London, United Kingdom; [5]GlaxoSmithKline, Global Health Outcomes, London, United Kingdom*

Background: Lapatinib (Tyverb®, Tykerb®) is an oral small molecule dual tyrosine kinase inhibitor that binds intracellularly to the ATP binding site of the EGFR and HER2 receptors. In EGF100151, L+C improved time to progression (TTP) and progression free survival (PFS) vs capecitabine monotherapy (C-only) in women with ErbB2+ (HER2+) MBC who have received prior therapy with TZ. CE of L+C has not been evaluated to date.
Methods: We evaluated CE (ΔCosts/ΔQuality Adjusted Life Years [QALYs]) of L+C vs C-only in women with ErbB2 (HER2+) MBC who have received prior therapy with TZ from the UK NHS perspective using an assumed acquisition cost. Because many patients such in typical clinical practice receive monotherapy with vinorelbine (V-only) or TZ-only or combination therapy with TZ and C (TZ+C) or TZ and V (TZ+V), we also assessed CE of L+C vs these strategies. PFS and overall survival (OS) with L+C and C-only were based on Weibull survival functions estimated using data from EGF100151. Post-progression survival (PPS) for L+C and C-only were calculated as OS − PFS. Lacking data from comparative trials in this population, PFS with TZ+C, TZ+V and TZ-only were estimated from published cohort studies of continued TZ±chemotherapy (TZ±CT) following progression; PPS was assumed to equal that with L+C. PFS and OS with V-only were assumed equal to that with C-only. Drug costs were from the British National Formulary; other costs from NHS reference costs and published studies. Utility values for PFS were from EQ-5D data collected in EGF100151; for PPS, from a UK community-based study of preferences for disease states in MBC. Costs and QALYs were discounted at 3.5% annually.
Results: Results are presented in the table. L+C is dominant (provides more QALYs at a lower cost) vs TZ+V, TZ+C, and TZ-only. In probabilistic sensitivity analyses, the probability (p) that L+C is CE given willingness to pay (WTP) for QALY of £30,000 ranged from. 05 vs C-only to. 95 vs TZ+V.

	L+C	C-only	V-only	TZ+V	TZ+C	TZ-only
Total costs (£)	25,678	11,805	14,094	30,131	27,864	26,753
Total QALYs	0.857	0.686	0.686	0.714	0.714	0.714
CE L+C (£/QALY)		81,129	67,743	Dominant	Dominant	Dominant
p L+C is CE (WTP = £30,000/QALY)		0.05	0.07	0.95	0.89	0.85

Conclusions: The efficacy of L+C has been demonstrated in women with Erb2+ (HER2+) MBC who have received prior therapy with TZ. This study, using indirect comparisons in the absence of head-to-head data, suggests that L+C is a cost effective therapeutic option vs TZ±CT from the UK NHS perspective.

2136 POSTER

Expression profile of TRAIL and its receptors in breast cancer patients with invasive ductal carcinoma

A.D. Sanlioglu[1], A.F. Korcum[2], E. Pestereli[3], G. Erdogan[3], S. Karaveli[3], B. Savas[4], T.S. Griffith[5], S. Sanlioglu[1]. *[1]Akdeniz University School of Medicine Human Gene Therapy Unit, Department of Medical Biology and Genetics, Antalya, Turkey; [2]Akdeniz University School of Medicine, Department of Radiation Oncology, Antalya, Turkey; [3]Akdeniz University School of Medicine, Department of Pathology, Antalya, Turkey; [4]Akdeniz University School of Medicine, Department of Medical Oncology, Antalya, Turkey; [5]University of Iowa, Department of Urology, Iowa City, USA*

Background: TNF-Related Apoptosis Inducing Ligand (TRAIL) selectively induces apoptosis in cancer cells but not in normal cells, and several clinical trials have been started to assess the safety and anticancer properties of TRAIL in patients with cancer. Four different receptors have been identified to bind to TRAIL: two are known as killer receptors [TRAIL-R1 (DR4) and TRAIL-R2 (DR5)], the other two [TRAIL-R3 (DcR1) and TRAIL-R4 (DcR2)] are decoy receptors which counteract TRAIL-induced cell death. Because high levels of DcR2 expression has recently been correlated with carcinogenesis in synoviocytes, prostate and lung, the significance of

TRAIL and TRAIL receptor expression was investigated in breast cancer patients with invasive ductal carcinoma.
Methods and Materials: Patients were selected from a cohort of 133 consecutive patients with nonmetastatic invasive ductal carcinoma treated at the Department of Radiation Oncology at the Akdeniz University Faculty of Medicine. Of these 133 patients, 90 (67.6%) had paraffin-embedded breast cancer tissue samples available for examination and immunohistochemical staining, and for subsequent evaluation in terms of various characteristics, including age, menopausal status, tumor size, axillary lymph node involvement, histological grade, lymphovascular invasion (LVI), perineural invasion, extracapsular extension (ECE), presence of an extensive intraductal component (EIC), multicentricity, estrogen and progesterone receptor status, CerbB2 (HER2/neu) oncogene status, and adjuvant radiotherapy and/or systemic treatment. Of these patients, 25 patients (27.7%) were treated with breast-conserving surgery (BCS), and 65 patients (72.2%) were treated with modified radical mastectomy and level I-II axillary dissection. All patients underwent postoperative external beam radiation therapy (RT) as a component of their treatment.
Results: DR4 expression was significantly higher compared to TRAIL, DR5, DcR1, and DcR2 expression. While progesterone receptor positive patients exhibited lower DR5 expression, CerbB2 positive tissues displayed higher levels of both DR5 and TRAIL expressions.
Conclusions: DR4 was the highest TRAIL receptor expressed in patients with invasive ductal carcinoma. DR4 expression might be important for the transition from a low grade to a high grade tumor.

2137 POSTER

Post-mastectomy breast reconstruction complications – ten years experience

D. Stojiljkovic, M. Inic, R. Dzodic, N. Miletic, M. Prekajski, O. Kosovac, I. Markovic, A. Celebic, S. Jokic. *Institute of Oncology and Radiology, surgery, Belgrade, Serbia*

Background: Complications of reconstructive procedures after mastectomy are divided into early (infection) and late (endoprosthesis prolapse, capsular contracture, iatrogenic damage of endoprosthesis, local recurrence). Skin flap necrosis or musculocutaneous lobe necrosis can be both early and late complication and it occurs as sequela of compromised vascularization or influence of certain factors (radiotherapy, infection).
Materials and Methods: During 1997 and 2006, 682 reconstructive procedures in 593 patients were performed at Institute of Oncology and Radiology of Serbia.Primary reconstruction was performed in 484 (71%) cases, postponed reconstruction in 109 (16%) cases and correction of healthy breasts because of symmetralization in 89 (13%) cases. From 484 primary reconstructions, 376 were positioned subpectorally, 104 subcutaneously, while 2 of them were performed as a combination of endoprosthesis and m. latissimus dorsi flap. Postponed reconstructions were performed in 72 cases by implanting endoprosthesis, in 30 cases by combining latissimus dorsi musculo-cutaneous flap and endoprosthesis and in 7 cases TRAM method was used. Most of the patients were treated with postoperative adjuvant chemotherapy and some of them with combined radio chemotherapy too.
Results: Out of 682 reconstructive operational procedures, complications occurred in 66 (9.7%) cases (28 prostheses prolapses, 26 in primary reconstructions and 2 in postponed). Capsular contracture occurred in 26 (3.8%) (25 after primary reconstruction and 1 after postponed reconstruction). Other complications, which were 12 (1.8%), occurred in 10 cases (infection), in one case (iatrogenic damage of endoprosthesis) and in one case (pseudo cyst). Prolapse of primary reconstructions occurred in 10 (2.7%) cases of subpectorally positioned endoprosthesis and in 16 (15.4%) cases of subcutaneously positioned endoprosthesis. Out of 26 prolapses of primary reconstructions in 3 cases the cause was post operational chemotherapy, adjuvant chemotherapy in 4 cases, skin necrosis in 15 cases, and among 4 women the rejection of implant occurred.
Conclusion: Number of complications is smaller if the implant is positioned subpectorally. Post operational radio and chemotherapy increase the risk of complications. Number of complications was reduced as the operational technique improved which shows that operational skill is an important factor for complications occurrence.

2138 POSTER

Age-related methylation pattern of ESR1 in patients with breast cancer

B.J. Song[1], H.M. Jeon[1], J.S. Kim[1], S.T. Oh[1], S.S. Jung[1]. [1]*Kang Nam St. Mary's Hospital, Department of Surgery, Seoul, Korea*

Background: The methylation of some genes increases or decreases as acquired with age in different tissues. These age-dependent methylation changes of some genes can have pathologic processes and causing to the progressive growth of tumor. The purpose of this study was to evaluate the effects of aging on the methylation of specific genes in breast cancer.
Materials and Methods: Thirty-nine paired samples of human breast cancer and adjacent normal tissues were collected. The breast cancer tissue was performed immunohistochemical staining for ESR1, PgR, HER-2 and P53. Genomic DNA from paired cancer and normal tissues were isolated. To perform bisulfite sequencing analysis of ESR1, PgR, RASSF1A, CDH13 and CYP 1B1, 25 ng of bisulfite-modified DNA was amplified with primer sets which were designed using MethPrimer program. PCR products were randomly chosen for sequencing. Three CpG sites in the 5′-upstream region of genes were selected for quantitation of methylation. Bisulfite-modified DNA was amplified by PCR; the PCR was modified for pyrosequencing based methylation analysis. Pyrosequencing was completed automatically by using a PSQ HS 96A system (Biotage AB). Methylation patterns of ESR1, PgR, RASSF1A, CDH13 and CYP 1B1 were analyzed according to age above and below 50 years old.
Results: Below 50 years old, mean of methylation frequencies of the gene tested in the normal tissue and tumor tissue was 88.29% and 83.23% for ESR1, 3.75% and 5.72% for PgR, 5.45% and 20.94% for RASSF1A, 4.31% and 8.51% for CDH13 and 2.07% and 2.39% for CYP1B1. Above 50 years old, mean of methylation frequencies of the gene tested in the normal tissue and tumor tissue was 87.71% and 74.36% for ESR1, 4.08% and 5.96% for PgR, 7.17% and 19.34% for RASSF1A, 4.26% and 9.53% for CDH13 and 1.75% and 2.44% for CYP1B1. Hypomethylation of ESR1 over the age of 50 years in breast cancer showed strong correlation with age and statistical significance was noted. PgR, RASSF1A and CDH13 showed hypermethylation pattern with aging, but statistical significance was not noted. Hypomethylation of ESR1 showed strong correlation with over the age of 50 years in breast cancer. CYP1B1 does not show methylation change with aging.
Conclusions: Hypomethylation of ESR1 in breast cancer showed strong correlation with age. ESR1 expression reflects the change of DNA methylation with age and the methylation related to the aging may contribute to the hypomethylation in breast cancer.

2139 POSTER

Validation of a nomogram to predict the risk of non-sentinel lymph node metastasis in breast cancer patients with a positive sentinel node biopsy

R. van la Parra[1], M.F. Ernst[1], P.C. Barneveld[2], J. Broekman[3], K. Bosscha[1]. [1]*Jeroen Bosch Hospital, Surgery, 's-Hertogenbosch, The Netherlands;* [2]*Jeroen Bosch Hospital, Nuclear Medicine, 's-Hertogenbosch, The Netherlands;* [3]*Jeroen Bosch Hospital, Pathology, 's-Hertogenbosch, The Netherlands*

Background: Completion axillary lymph node dissection (ALND) remains, according to the Dutch guidelines, the standard of care for patients with a positive sentinel lymph node (SLN). However, approximately 40−60% of patients with positive SLNs will have no additional positive nodes. To identify the individual patient's risk for non-SLN metastases, the Memorial Sloan-Kettering cancer Center (MSKCC) developed a nomogram currently available as an online tool. The purpose of this study was to validate the nomogram in a Dutch population of breast cancer patients.
Methods: The medical records of 193 breast cancer patients who underwent sentinel lymph node biopsy examination and ALND were selected from a prospectively collected database and were reviewed for multiple clinicopathologic variables. A receiver operating characteristic (ROC) curve was drawn and the area under the curve was calculated to assess the discriminative power of the nomogram. Also, data of the index and test populations were compared.
Results: The area under the ROC curve was 0.693 (range 0.614−0.773), as compared to 0.76 in the MSKCC study. When the tool was applied solely to macrometastases, the area under the ROC curve was 0.688 (range 0.595−0.781).
Conclusions: The MSKCC-nomogram seems to be a useful tool to predict the individual patient's risk for positive axillary non-sentinel lymph nodes in a Dutch population of breast cancer patients. Further analysis, however, has to be performed to identify subgroups, in which the nomogram is even more predictive. Predicting the risk of additional nodal metastases will allow the surgeon and the patient to make an individualized decision regarding the need for completion axillary lymph node dissection.