Methods: 228 pts with HER2-positive LABC randomly received neoadjuvant chemotherapy [CT] (3 cycles of doxorubicin–paclitaxel [AT], A 60 mg/m^2, T 150 mg/m^2 q3w, 4 cycles of T [175 mg/m^2 q3w], and 3 cycles of cyclophosphamide/methotrexate/5 fluoracil [CMF]: C 600 mg/m^2, M 40 mg/m^2, F 600 mg/m^2 q4w on days 1 and 8) plus concomitant Herceptin®; H (8 mg/kg loading dose then 6 mg/kg q3w for 1 year) before surgery [115 pts] or the same chemotherapy only [113 pts]. In parallel 99 pts with HER2-negative LABC received the same CT. The primary end point is event-free survival (data maturing); secondary end points included overall response rate (ORR), pathological complete response (pCR) and overall survival. We report here updated ORR and the percentage of pts in whom breast conserving surgery (BCS) became feasible after primary neoadjuvant treatment.

Results: Improvement of pCR with H (43% vs 23%) in NOAH trial was already reported (ASCO 2007, abstr. 532). In the intent-to-treat population the updated ORR was 89% for the trastuzumab+CT group vs 76% for the CT alone group ($p = 0.012$). After 10 cycles of neoadjuvant therapy, 96 pts (83.4%) from H+AT/T/CMF group and 88 (77.8%) from CT-alone group underwent surgery. Adding H to AT/T/CMF improved rate of BCS (23% vs 12.5%, $p = 0.07$). Furthermore, in the subgroup of patients who achieved a clinical response (>50% tumour size reduction), this improvement was significant (24.7% vs 10.8%, $p = 0.02$).

Conclusion: Addition of H to neoadjuvant CT significantly increased ORR, led to downsizing of HER-positive LABC, thus allowing for more surgical options, and doubled the rate of BCS compared with CT alone.

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External validation of a piecewise effect model of axillary lymph node involvement in elderly breast cancer patients

H. Wildiers[1], B. Van Calster[2], L.V. van de Poll-Franse[3], W. Hendrickx[4], S. Van Huffel[2], A. Smeets[4], R. Paridaens[4], K. Deraedt[5], M.R. Christiaens[4], P. Neven[4]. *[1]U.Z. Gasthuisberg, Multidisciplinary Breast Centre, Leuven, Belgium; [2]K.U. Leuven, Department of Electrical Engineering, Leuven, Belgium; [3]Eindhoven Cancer Registry, Comprehensive Cancer Centre South, Eindhoven, The Netherlands; [4]U.H. Leuven, Multidisciplinary Breast Centre, Leuven, Belgium; [5]U.H. Leuven, Pathology Department, Leuven, Belgium*

Background: Conflicting data exist on the correlation between the presence of axillary lymph node metastasis (LN+) and increasing age in breast cancer. In a large database of a single center of 2227 consecutively treated patients with early breast cancer, a piecewise effect of age on lymph node involvement was found with an increase in lymph node involvement after age 70 mainly in smaller tumors (St-Gallen 2007). The statistical model was now prospectively investigated in an external database.

Patients and Methods: The population-based Eindhoven Cancer Registry was used to validate the prediction model. It contains data from 11061 women with early breast cancer diagnose between 1-1-2000 and 1-1-2006, and for 3448 pts data on age, tumor size and lymph node status were available.

Results: The piecewise effect and tumor size dependence was confirmed. Lymph node involvement decreases up to age 70 (OR per decade increase in age = 0.764, 95% CI = 0.732−0.797) while for age $\geqslant$70, there is an increase with increasing age (OR 1.554, 95% CI = 1.371−1.761). There was a significant interaction with tumor size ($p = 0.0182$) where this increase in lymph node involvement after age 70 was only seen in smaller tumors ($\leqslant$20 mm).

Conclusion: Axillary lymph node involvement decreases with increasing age until the age of 70y, but then increases again. This increase after age 70 is only seen in the smaller tumors and suggests a different behavior of small breast cancers in elderly patients.

We hypothesize that on the one hand, breast tumors may metastasize less frequently to lymph nodes with increasing age due to the decreased biological aggressiveness in these tumors. On the other hand, if the tumors have the potential to metastasize to lymph nodes in elderly, this occurs more rapidly in smaller tumors and this may be related to decreased immune defense mechanisms in elderly patients.

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Elderly breast cancer patients treated by conservative surgery alone and adjuvant tamoxifen: 15 years results of a prospective study

R. Giovanazzi[1], G. Martelli[1], R. Miceli[1], D. Piromalli[1], G. Vetrella[1], M. Greco[1]. *[1]Istituto Nazionale Tumori, Breast Surgery, Milano, Italy*

Background: In elderly patients with early breast cancer and clinically clear axilla, axillary surgery, sentinel node biopsy and post operative radiotherapy to the residual breast may not be necessary because of reduced life expectancy, effectiveness of hormone therapy in achieving long-term disease control and generally favourable biological behaviour of breast cancer in elderly patients.

Methods: We followed 354 prospectively recruited women aged 70 years or more with primary operable breast cancer and no palpable axillary nodes treated by conservative surgery and adjuvant tamoxifen, without axillary dissection or postoperative radiotherapy. Cases with resection margins in tumor tissue were excluded.

Endpoints were cumulative incidence of axillary disease, cumulative incidence of ipsilateral breast tumor recurrence (IBTR) and breast cancer mortality.

Results: Pathological stage at presentation showed pT1 size in 274 (77.4%) patients, pT2 ($\leqslant$3 cm) in 59 patients (16.7%) and pT4 b ($\leqslant$2.5 cm) accounted for 6% of cases. Infiltrating ductal carcinoma represented more than 65% of all histological types. ER and PgR receptor status was available for 331 patients; of these, 310 (94%) patients were ER +, 227 (69%) were PgR +, 224 (68%) were ER + and PgR + and 18 (5%) were ER − and PgR −.

After a median follow up of 15 years (interquartile range 14−17) crude cumulative incidences were: 4.2% (4.0% in pT1) for axillary disease, 8.3% (7.3% in pT1) for IBTR, and 17.0% for breast cancer mortality. Of the 268 patients who died during follow up, 222 (83%) died from causes unrelated to breast cancer.

Conclusions: Elderly patients with early breast cancer and no palpable axillary nodes may be safety treated by conservative surgery without axillary dissection and without postoperative radiotherapy, provided that surgical margins are in tumor free tissue and hormonal therapy is administered. Sentinel node biopsy is also unnecessary due to the low cumulative incidence of axillary disease and axillary surgery can be reserved for the small proportion of patients who later develop overt axillary disease.

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China multicenter study of sentinel node biopsy substituting axillary node dissection: CBCSG-01 trial

Y.S. Wang[1], T. Ouyang[2], Q.T. Wang[3], F.X. Su[4], S.G. Zhu[5], J. Wu[6], C.Z. Yu[7], S.S. Cao[8], S. Wang[9], J.Y. Li[1]. *[1]Shandong Cancer Hospital and Institute, Breast Cancer Center, Jinan, China; [2]Beijing University Cancer Hospital, Department of Breast Surgery, Beijing, China; [3]Qingdao University 2nd Hospital, Department of Breast Surgery, Qingdao, China; [4]Zhongshan University 2ndHospital, Department of Breast Surgery, Guangzhou, China; [5]Yantai Yuhuangding Hospital, Department of Breast Surgery, Yantai, China; [6]Shanghai Cancer Hospital, Department of Breast Surgery, Shanghai, China; [7]Beijing 307 Hospital, Department of Breast Surgery, Beijing, China; [8]Xuzhou Central Hospital, Department of Breast Surgery, Xuzhou, China; [9]Jiangsu People's Hospital, Department of Breast Surgery, Nanjing, China*

Background: China multicenter study of sentinel lymph node biopsy (SLNB) substituting axillary lymph node dissection (ALND) in breast cancer – CBCSG-01 trial was conducted from Jan. 2002 to Jun. 2007, with 1,970 SLNB pts recruitment. The primary objectives were 5ys DFS and complications between SLNB and ALND. The second objectives included 5ys OS, SLN intraoperative diagnosis, micrometastasis detection and prognosis, and radiologic safety.

Materials and Methods: Combined methylene blue dye and 99mTc-sulfur colloid or 99mTc-IT-Rituximab were used as tracers for SLNB. Preoperative lymphscintigraphy was mandatory for all pts. Pts with negative SLN did not receive ALND.

Results: The median age was 46ys. The median number of SLN was 2. Tumor size was less than 5 cm, with mean size as 1.9 cm. With the increase of the size and advance of the histopathology of the primary tumor, the positive rates of the SLN increased significantly ($p = 0.000$, both). The surgical types were as follows: BCS+SNLB 51.4%, Mastectomy+SLNB 26.1%, BCS+ALND 8.9%, and Mastectomy +ALND 13.6%, respectively. Mainly due to the difference of primary tumor sizes, the rates of BCS, SLNB substituting ALND, and the positive rate of SLN were different among different centers. With a median fellow-up of 42 months in one early center – Shandong Cancer Hospital, two cases of axillary relapse (0.82%) were found in 244 SLNB cases ($p > 0.05$), while the complications of SLNB were significantly lower than that of ALND ($p < 0.001$).

Conclusions: 1) First in China to conduct prospective, multicenter study for SLNB substituting ALND for clinically early stage breast cancer, with 1970 cases enrolled; 2) Combined methylene blue dye and 99mTc were used as tracers for SLN, with the successful rate of 99.5%; 3) SLNB technique could avoid ALND for SLN negative pts (77.8% of clinically axillary negative cases in our study); 4) SLN positive rates increased significantly with the increase of the primary tumor size, which indicated that pts with small tumor should be selected first for SLNB substituting ALND in fresh hands; 5) The SLN positive rate was 3.5% in DCIS, which

indicated that SLNB should be performed in pts with DCIS if they would receive mastectomy or breast reconstruction; 6) With short-term follow-up of 42 months in one center, SLNB could replace ALND for SLN negative pts with low axillary recurrence; 7) SLNB could decrease postoperative complications significantly, and improve the quality of life for breast cancer pts.

Friday, 18 April 2008 12:30–14:30

POSTER SESSION

Metastatic disease

404 Poster

The prognostic significance of discordant receptor results and the progesterone receptor in metastatic breast cancer

R. Stuart-Harris[1], B. Shadbolt[2], H.A. Chaudri Ross[3]. [1]*The Canberra Hospital, Medical Oncology Unit, Canberra, Australia;* [2]*The Canberra Hospital, Centre for Advances in Epidemiology & Information Technology, Canberra, Australia;* [3]*Novartis Pharma AG, Oncology Biostatistics, Basel, Switzerland*

Background: In metastatic breast cancer (MBC), both the oestrogen receptor (ER) and the progesterone receptor (PgR) are usually analysed. If either is positive, the patient is classed as having a receptor positive tumour and may be offered endocrine therapy, if clinically appropriate. However, in the presence of a positive ER, the prognostic significance of the PgR is unknown.

Materials and Methods: We have performed a retrospective analysis of the data from a total of 1870 patients entered on to three, international, randomised phase 3 studies of letrozole or anastrozole in MBC. Data were analysed using SPSS, V12.0.1. The main outcomes were assessed using Kaplan–Meier analysis, with log rank tests and associated probabilities.

Results: Both receptors were analysed in 1010 patients. 31 patients had tumours that were both ER and PgR negative (−) and were excluded. Of the remaining 979, 726 (74.2%) had tumours that were both ER and PgR positive (+), 213 (21.8%) had tumours that were ER+PgR− and 40 (4.1%) had tumours that were ER−PgR+.

919 patients were assessable for response. There were no significant differences in objective response or median duration of response between patients with ER+PgR+ tumours and those with discordant receptor results. However, the median overall survival (OS) was significantly longer for those with tumours that were ER+PgR+ (800 days) than those with discordant receptor results (600 days, $p = 0.01$). For patients with ER+ tumours that were also PgR+, the median OS was significantly longer (800 days) than for those with tumours that were PgR− (625 days, $p = 0.02$).

Conclusions: In patients with MBC, the median OS was significantly longer in those with tumours that were both ER and PgR positive than those with tumours with discordant receptor results. In patients with ER positive tumours, those who also had a positive PgR had a significantly longer median OS than those with PgR negative tumours. The PgR status provides important prognostic information for overall survival and should continue to be assessed routinely in patients with MBC.

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French (lapatinib) authorization for temporary use (ATU) – design, operation and initial safety data

M. Campone[1], C. El-Kouri[2], P. Cottu[3], D.R. Otmezguine[4], J.P. Guastalla[5], J. Gligorov[6], E.C. Antoine[7], T. Petit[8], J.P. Ferrière[9], A. Goncalves[10]. [1]*Institut René Gauducheau, Département D'oncologie Médicale, Saint-Herblain, France;* [2]*Clinique Catherine De Sienne, Département D'oncologie Médicale, Paris, France;* [3]*Institut Curie, Département D'oncologie Médicale, Paris, France;* [4]*Clinique De La Porte De Saint-Cloud, Département D'oncologie Médicale, Boulogne, France;* [5]*Centre Léon Bérard, Département D'oncologie Médicale, Lyon, France;* [6]*Hospital Tenon, Département D'oncologie Médicale, Paris, France;* [7]*Clinique Hartmann, Département D'oncologie Médicale, Neuilly Sur Seine, France;* [8]*Centre Paul Strauss, Département D'oncologie Médicale, Strasbourg, France;* [9]*Centre Jean Perrin, Département D'oncologie Médicale, Clermont Ferrand, France;* [10]*Institut Paoli Calmette, Département D'oncologie Médicale, Marseille, France*

Background: ATU is a specific process established by the French Medical Agency (AFSSAPS) to allow early access to drugs in development under specific circumstances (rare disease, unmet medical need). The Lapatinib (Tyverb®) ATU started in January 2007, after the interim analysis and subsequent closure of the pivotal study EGF100151 pivotal study comparing capecitabine+lapatinib vs capecitabine in the ErbB2+ (HER2+) metastatic breast cancer setting (NEJM 355:2733, 2006).

Patients and Method: Women with HER2-positive, locally advanced or metastatic breast cancer who progressed after treatment with regimens that included an anthracycline, a taxane, and trastuzumab were eligible to receive the combination of Lapatinib-Capecitabine combination via the ATU, after central review of such criteria. Unlike EGF100151, the ATU allows enrollment of patients without measurable disease, with ECOG PS 2, and with brain metastasis. The preliminary safety results are presented.

Results: Between January 2007 and January 2008, 1018 patients have been approved to receive Lapatinib+capecitabine in the ATU, in 233 French centers. Safety data are presented for 693 patients involved as of September 30 2007. Non Serious Adverse Events (AE) and Serious Adverse Events (SAE) that were possibly or not related to the treatments were reported spontaneously by the physicians. A total of 126 cases were reported (88 AE, 38 SAE). The most common AE during therapy with lapatinib plus capecitabine were gastrointestinal (diarrhoea, nausea, and vomiting), dermatologic (palmar-plantar erythrodysesthesia and rash) and linked to general disorders (progressive disease). No new safety signals were identified. Apart from progressive disease, which is not reported as an AE in clinical trials, the reported AE are consistent with the known safety profile of lapatinib and capecitabine. Among non serious cardiac adverse events, asymptomatic decreases in LVEF were reported in 2 patients and retrosternal pain was reported in 1 patient. 18/38 SAE, including 3/22 deaths (1 septic shock, 1 disease progression with pulmonary disorders and one cardiac disorder), were reported as possibly related to the drugs.

Conclusion: The safety profile seen in this preliminary analysis of 693 patients receiving Lapatinib + capecitabine for breast cancer was consistent with that observed in study EGF100151. The ATU will continue until lapatinib launch in France. Updated data will be available at the time of presentation.

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Lapatinib plus paclitaxel versus paclitaxel alone for first line metastatic breast cancer (MBC) in ErbB2+ patients – Quality of Life (QOL) results

Y. Wu[1], A. Segreti[1], D. Cella[2], A. DiLeo[3], M. Amonkar[4], M. Koehler[4], M. Arbushites[4], M. Walker[5]. [1]*RTI-Health Solutions, Health Outcomes, Research Triangle Park, USA;* [2]*Evanston Northwestern Healthcare, Core, Evanston, USA;* [3]*"Sandro Pitigliani" Medical Oncology Unit, Oncology, Prato, Italy;* [4]*GlaxoSmithKline, Oncology, Collegeville, USA;* [5]*GlaxoSmithKline, Oncology, London, United Kingdom*

Background: A Phase III randomized, multicenter, double-blind, placebo-controlled study compared lapatinib and paclitaxel (L+P) versus paclitaxel alone (P) for 1st line MBC in adult women. In a sub-group analysis of ErbB2+ patients, time to tumor progression for L+P was significantly improved, with an emerging trend for survival benefit. This analysis focuses on the impact on QOL in the subset of the randomized ITT population that overexpressed ErbB2.

Methods: QOL was assessed using the Functional Assessment of Cancer Therapy-Breast (FACT-B) questionnaire. Outcome measures included FACT-B total score, FACT-general (FACT-G) score and trial outcome index (TOI) score. Higher scores indicate better QOL. Patients completed the FACT-B at the screening visit, week 9, every 12 weeks thereafter, and at discontinuation of therapy. Changes from baseline scores were analyzed for the ErbB2-positive subset (FISH+ or IHC3+) using analysis of covariance with baseline value as a covariate. Missing post-baseline data were imputed using the LOCF method for scheduled visits. No imputation was applied to the assessment at discontinuation.

Results: Of 579 randomized patients, 86 were ErbB2+ and 85 completed at least one item from the FACT-B ($n = 48$ L+P; $n = 37$ P). More than 70% of ErbB2-positive patients had QOL information at study discontinuation. Overall, the L+P arm showed improvement compared to the P arm for FACT-B total scores, FACT-G scores, and TOI scores at all scheduled visits. The treatment difference increased over time. These group differences in mean change from baseline, although not statistically significant, increased in favor of L+P from 2.9 to 6.3 (FACT-B), 1.1 to 3.5 (FACT-G), 1.8 to 5.3 (TOI) from week 9 to week 45, respectively. For the assessment at discontinuation, treatment differences were statistically significant for FACT-B total score (10.6, $p = 0.039$, 95% CI = 0.5, 20.6) and TOI score (7.4, $p = 0.032$, 95% CI = 0.6, 14.2), and they approached statistical significance for the FACT-G score (7.7, $p = 0.066$, 95% CI = −0.5, 16.0).

Conclusions: While not all differences were statistically significant, lapatinib plus paclitaxel demonstrated consistently better QOL compared to paclitaxel alone for ErbB2-positive patients.