Friday 18 April 11:00–13:00

KEYNOTE SYMPOSIUM

Late breaking session

1LB Late Breaking

Neoadjuvant treatment of HER2 overexpressing primary breast cancer with trastuzumab given concomitantly to epirubicin/ cyclophosphamide followed by docetaxel ± capecitabine. First analysis of efficacy and safety of the GBG/AGO multicenter intergroup-study "GeparQuattro"

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Background: Trastuzumab has shown high efficacy in combination with neoadjuvant chemotherapy (NACT). We have prospectively investigated the efficacy of trastuzumab in a large controlled multicenter study.

Material: Patients (pts) were eligible in whom adjuvant chemotherapy would be considered otherwise and received 4 cycles of epirubicin/cyclophosphamide (EC) (90 mg/m^2/600 mg/m^2) and were then randomized to either 4 cycles of docetaxel (D) (100 mg/m^2), standard arm or 4 cycles of D-capecitabine (DX), (75 mg/m^2/1800 mg/m^2), combination arm or 4 cycles of D (75 mg/m^2) followed by 4 cycles of X (1800 mg/m^2) (D $\rightarrow$ X), sequential arm. Pts with HER2-positive tumors received trastuzumab 6 (8) mg/kg every 3 weeks concomitantly with all NACT before surgery and for up to 1 year after surgery. The second co-primary aim of this trial was to compare the pathologic complete response (pCR) rate in pts with HER2-positive tumors receiving NACT plus trastuzumab to the response rate in pts with HER2-negative tumors receiving the same NACT without trastuzumab.

Results: Within 15 months 1510 pts (453 HER2-positive) entered and after receiving 4 cycles EC, 1421 (427 HER2-positive) were randomized to D (N = 471; 147 HER2-positive), or DX (N = 471; 144 HER2-positive), or D $\rightarrow$ X (N = 479; 136 HER2 positive). Safety interim analysis of the HER2 positive pts revealed no increase in toxicity for NACT + trastuzumab compared to NACT alone. In 97% of HER2 positive and 96% of HER2 negative pts LVEF was >55%. No patients developed a loss in LVEF below 45%. During simultaneous treatment with trastuzumab and chemotherapy no CTC grade 4 cardiac event occurred, CTC grade 3 cardiac events were observed in two HER2 positive pts and in two HER2 negative pts. There were no congestive heart failures and no cardiac related deaths. The pathologic complete response rates (pCR) including residues of carcinoma in situ was 19.5% without trastuzumab and 41.3% with trastuzumab ($p < 0.001$); the rates of breast conserving surgery (BCS) were 63.1% without trastuzumab and 61.8% with trastuzumab (not significant).

Conclusions: The addition of trastuzumab to epirubicin/cyclophosphamide followed by docetaxel with and without capecitabine is feasible without clinically relevant cardiotoxicity. The pathologic complete response rate in patients with Her 2 neu overexpressing tumors was significantly increased by the addition of trastuzumab. Further follow up of this study will analyse the correlation of this result to patient outcome.

2LB Late Breaking

Breast conservative surgery with and without radiotherapy in patients aged 55−75 with early stage breast cancer – a prospective randomised multi-centre trial

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Breast conserving therapy (BCT) including postoperative irradiation of the remaining breast tissue is generally accepted as the treatment of choice for the vast majority of patients with early stage breast cancer, resulting in advantages of improved cosmesis and quality of life (QOL) as compared to mastectomy (MX). The question whether post operative irradiation is mandatory in all patients and, herewith, over-treating almost a half of them, remains one of the most controversial issues in BCT. To properly answer this question a randomised prospective multi-centre study was launched in January 2001 based on long-term follow-up data of the Milan III trial comparing BCT with or without postoperative irradiation. Those data demonstrated a significant lower risk of local recurrence in patients older than 55 years in comparison to the younger age group. Moreover, in patients older than 65 years the risk of local recurrence was similar in the irradiated and the control group.

Aims of the study: The main aim was to assess the cumulative incidence of local recurrence after conservative surgery with (CS+RT) vs without breast irradiation (CS). Added values of the study were to avoid the inconvenience and the risk of side-effects of radiation therapy and to prevent unnecessary mastectomies in hospitals where the facilities for radiation treatment are not available.

Patients and Methods: From January 2001 until December 2005 749 patients from 11 centres in Italy were randomly assigned to CS+RT (radiotherapy: homogenous breast irradiation 50 Guy +10 Guy boost) or to CS. Main patients and tumours characteristics were fairly well balanced between treatment groups. Adjuvant systemic therapy in patients at moderate-high risk of distant recurrence were allowed as per participating center policy.

Results: After a median follow-up of 53 months, the cumulative incidence of local recurrence was 0.7%±0.4 after CS+RT vs 2.5%±0.9 after CS (HR: 4.01, 95% confidence limits 0.85−18.89; P = 0.07). Distant disease-free survival was 96% after CS+RT and 96.5% after CS. Overall survival was 95% vs 96%, respectively. Local-regional treatment was well tolerated and devoid of major side effects.

Conclusion: Present data indicate that breast irradiation after conservative surgery can be avoided in patients aged 55−75 years without exposing them to an increased risk of local recurrence and death. Prolonged follow-up will further clarify possible late sequelae potentially induced by breast irradiation in these patient population. Participating centres:

1. Division of Surgery and Senology, The Maugeri Foundation Pavia, Italy
2. Italian School of Senology, Milano, Italy
3. Division of Surgery General Hospital Alba, Italy
4. Division of Surgery and Senology General Hospital Bergamo, Italy
5. Division of Senology General Hospital Ortona, Italy
6. Division of Surgery Arcispedale Santa Maria Reggio Emilia, Italy
7. Division of Surgical Science and Medical Technology University La Sapienza Roma, Italy
8. Division of Surgery Casa Sollievo della Sofferenza Hospital S. Giovanni Rotondo, Italy
9. Division of Surgery S. Orsola Malpighi Hospital Bologna, Italy
10. Division of Surgery S. Maria della Misericordia Hospital Udine, Italy
11. Division of Gynaecology Cancer Research Centre Torino, Italy
12. Division of Gynaecology General Hospital Cirié, Italy
13. Division of Psychology, The Maugeri Foundation Pavia, Italy
14. Statistical Centre National Cancer Institute, Milano, Italy

3LB Late Breaking

UK TACT trial results – does everyone need adjuvant taxanes?

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Introduction: Initial reports from several trials suggested a modest survival benefit favouring taxanes over anthracyclines for women with early breast cancer (BC). Other trials failed to show such a benefit and uncertainty remains where taxanes are compared with anthracycline regimens of similar duration. The UK TACT Trial, a multicentre phase III randomised trial comparing sequential FEC – docetaxel (FEC-T) to UK anthracycline chemotherapy (CT), provides further evidence with regard to overall benefit, as well as which sub-groups, if any, have more or less to gain.

Materials and Methods: Between Feb 2001 and July 2003 4162 women with node positive or high risk node negative early BC were recruited from 104 centres (103-UK, 1-Belgium). Centres chose FEC (600/60/600 mg/m^2 q3wk $\times$ 8) or E-CMF (Epirubicin 100 mg/m^2 q3wk $\times$ 4 CMF 100 mg/m^2 PO d1−14 or 600 mg/m^2 IV d1&8/40/600 mg/m^2 q4wk $\times$ 4) as the control arm, reflecting standard UK practice. Patients (pts) were randomised to FEC-T (FEC q3wk $\times$ 4 docetaxel 100 mg/m^2 q3wk $\times$ 4) or control. 2523 pts were from FEC centres (FEC = 1265: FEC-T = 1258) and 1639 from E-CMF centres (E-CMF = 824; FEC-T = 815). Tumor blocks were collected prospectively for central HER2 testing and creation of