

Unfortunately, one of the two large American sentinel node trials has been suspended because of low accrual: the ACOSOG trial Z0011 was designed to address the question of further treatment to the axilla in, on H&E staining, sentinel node positive patients. So far, 595/1900 (31%) patients were randomly assigned to radiation of the breast only, without specific treatment of the axilla, or to radiation of the breast accompanied with ALND.

The NSABP B-32 has a similar design as the Italian study: SLNB followed by ALND versus SLNB and ALND only if tumour is found in the SLNB. Primary endpoints of this multi-centre study are the long term control of regional disease, disease-free and overall survival of patients who underwent a SLNB alone and its morbidity compared with ALND. This study has completed accrual with 5611 patients randomized between May 1999 and February 2004. Preliminary results demonstrated an overall sentinel node identification rate of 97%, 26% of whom were sentinel node positive and a 10% false negative rate [6].

In the previous St. Gallen consensus discussion meeting [7], it was concluded that sentinel lymph node biopsy (SLNB) is considered standard for lymphatic staging in patients with invasive breast cancer <3 cm, and no clinical involvement of ipsilateral axillary lymph nodes. Although there is not yet data on the effect of SLNB on long-term survival of patients with breast cancer, the available evidence from randomized clinical trials demonstrates that this technique is safe and accurate if performed by experienced surgeons.

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## 231 Proffered Paper Oral Improved outcome of breast cancer patients with internal mammary lymph node metastases by use of tailored treatment

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**Introduction:** Staging of the internal mammary (IM) nodal basin is not performed routinely and subsequent treatment generally is not influenced. The IM lymph node status is, however, a major independent prognostic factor in breast cancer. If positive, prognosis is less favourable.

Since the introduction of the sentinel node procedure for staging in breast cancer, we routinely perform IM sentinel node biopsy as visualized on lymphoscintigraphy, in order to improve nodal staging and to adjust adjuvant treatment accordingly.

**Patients and Methods:** Between April 1997 and July 2004, a total of 794 consecutive patients with stage T1–3 breast cancer were enrolled into a prospective study on SN biopsy. Adjuvant treatment algorithms were according to Dutch national guidelines. In case of IM metastases internal mammary radiotherapy was added and systemic treatment was adjusted when appropriate. Data with regard to demographics, diagnostic procedures, therapy and follow up were gathered from all patients. Patients treated after July 2004 were excluded from this study to permit at least one year of follow-up.

**Results:** Data from 788 patients were available for follow-up, six patients were lost for follow-up.

A total of 425 patients proved to have no lymph node metastases (group 1), 336 patients had axillary metastases (group 2) and 27 patients had IM metastases (group 3). Mean follow-up was 46 months. Overall survival was 94% in group 1, 85% in group 2 and 87% in group 3, respectively. Disease free survival was 90% in group 1, 81% in group 2 and 86% in group 3. The differences between group 2 and group 3 were statistically not significant.

**Discussion:** With positive IM nodes a survival disadvantage is expected. However, after adjuvant local treatment (parasternal radiotherapy) and adjusting chemotherapy in therapeutic schedules, treatment outcome of patients with proven IM nodal metastases, after a mean follow-up of 46 months, was comparable to patients with axillary metastases only.

**Conclusion:** Our results suggest that high risk patients with IM metastases benefit from improved staging and tailored adjuvant treatment algorithms.

## 232 Proffered Paper Oral Recurrences and survival after sentinel node biopsy with mandatory axillary node dissection versus sentinel node biopsy followed by axillary node dissection only for positive sentinel nodes – a retrospective analysis of 3159 cases from the Austrian Sentinel Node Study Group

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The purpose of this analysis was to determine the influence of sentinel node biopsy followed by axillary node dissection only in cases of positive sentinel nodes as opposed to sentinel node biopsy (SNB) with obligatory axillary dissection in all cases, on axillary lymph node recurrence, disease free survival and over all survival.

3564 patients are registered in the Austrian sentinel node data base. 3159 patients with unilateral, unicentric, non metastatic invasive breast cancer were analysed for axillary recurrence. 50 sentinel node biopsies with obligatory axillary dissection (phase I) (n658) were obligatory before performing SNB as standard procedure (phase II).

Blue dye, technetium<sup>99</sup> or a combination of both were applied to identify the sentinel node.

473 out of 658 SNB were identified in phase I with a false negative rate of 6.4%. The median follow up in phase I is 50.1 (±28.3) months, in phase II 29.5 (±19.3) months

The axillary recurrence rate was 1% in phase I and 0.3% in phase II. There was no significant difference in disease free and over all survival although the follow up time interval is still short.

The SNB became standard in many breast cancer centres in Austria. The axillary recurrence rate is very low. The impact of axillary dissection or irradiation of the axilla after pos SNB is still unclear.

## 233 Proffered Paper Oral Determination of axillary sentinel lymph node status in primary breast cancer by prospective use of immunohistochemistry increases the rate of micrometastases and intratumour cells without prognostic information

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**Background:** Axillary node status is today determined by the sentinel lymph node (SLN) biopsy avoiding axillary lymph node dissection (ALND) in patients without metastatic involvement. In patients with SLN micrometastases the risk of non SLN metastases is about 15% making ALND standard procedure, whereas in patients with intratumour cells (ITC) the risk for additional nodal involvement is not defined.

**Patients and Methods:** 174 patients with invasive breast cancer <3 cm were enrolled consecutively during 2001–2002. SLN's were examined by frozen section perioperatively and on formalin fixed, paraffin-embedded tumours using hematoxylin and eosin (H&E) as well as immunohistochemistry (IHC) with cytokeratin antibodies for definitive histopathological diagnosis. Patients with macrometastases (>2 mm in size), micrometastases (>0.2 mm ≤2 mm) and ITC (≤0.2 mm) in SLN had ALND enabling examination of axillary nodes in all patients irrespective of SLN tumour burden. The follow-up was 3 years (0–4 years).

**Results:** Macrometastatic SLN was found in 29 patients and could be diagnosed by H&E in all cases, micrometastatic SLN was identified in 16 patients (3 diagnosed by IHC) and ITC in 6 patients (4 diagnosed by IHC).

No non SLN metastasis was found by ALND in the ITC group, but two of the patients with micrometastatic SLN diagnosed by H&E had non SLN metastases and for patients with macrometastatic SLN 54% had additional nodal involvement. After this short period of follow-up, micrometastatic SLN or ITC did not yield any prognostic information for breast cancer recurrence or death in contrast to macrometastatic SLN, size of SLN metastases in mm, non SLN metastases as well as the total number of involved nodes which were all significantly correlated with outcome by univariate analysis.

**Conclusion:** In this consecutive single institution cohort, micrometastatic involvement of SLN was associated with 12.5% risk of non SLN metastases but for ITC the risk was null for further axillary involvement and ALND did not add any further prognostic information. The use of prospective IHC increased the number of patients diagnosed with minor tumour burden but did not identify any patient at risk for non SLN metastases. After a median of three years of follow-up neither micrometastases or ITC increased the risk of breast cancer events.

**234** Proffered Paper Oral  
**Multimodal management of early breast cancer without any treatment at axilla. Early results of a randomised clinical trial comparing quadrantectomy and axillary dissection vs quadrantectomy alone**

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**Background:** Since NSABP B-04 trial, more than thirty years ago, the need for axillary treatment remains controversial. Several findings underscore the fact that, in clinically node-negative patients, treatment of regional lymph node metastases does not seem to be a determining factor in the outcome of breast cancer. Nevertheless axillary dissection, which is nowadays performed only in case of positive sentinel node, has maintained its role in prevention of regional relapse and as a staging procedure. The integration of additional tumour features with those commonly used may allow a more reliable selection of patients for adjuvant treatments without performing axillary surgery.

**Study design:** Toward this end, a randomised clinical trial comparing surgical staging of axillary lymph nodes at primary treatment (control arm) with a surgical treatment only in case of relapse (study arm) is currently in progress at the National Cancer Institute in Milan. Adjuvant treatment of patients who received quadrantectomy alone was determined through a prognostic panel including morphological and biological features of the primary tumour while traditional criteria was applied to the control arm. The primary end point of this study was to verify if the Overall Survival of the patients enrolled in the study arm is equal or improved when compared with the control group.

**Results:** From May 1998 to May 2003 516 patients with T1, clinically node negative, breast cancer were enrolled. 250 and 266 patients were assigned to the study and control arm respectively. According to the prognostic panel, in the first group 84 patients (33.6%) were eligible for adjuvant chemotherapy compared to 136 (51.1%) of the control group by means of traditional criteria. Ten patients of the study group (4.0%) developed axillary lymph node relapse and was subsequently operated. Analysis of first unfavourable event (regardless of axillary relapse) did not show any significant difference between the two groups.

**Conclusion:** Axillary relapse was lower than expected in the group treated without axillary dissection. Rescue surgery was feasible in all cases without major morbidity. According to the protocol applied, the study arm received less adjuvant chemotherapy than the control group and, at this time, we can't appreciate any difference in outcome.

Although few, if any prospective randomised trials comparing local therapy modalities after ICT are available, appropriate individual options can be offered, based on what evidence does exist.

ICT for *non-inflammatory, inoperable LABC* may result in operable clinical partial response (cPR) or complete response (cCR). In cPR there is fair evidence that breast conservative treatment (BCT; lumpectomy followed by radiotherapy) can be used selectively (small residual unifocal tumor, no extensive microcalcifications, tumor free margins, no contra indications for radiotherapy). Surgical excision of the residual tumor (tumor site in cases of cCR) has to be performed to optimize local control. In cases the tumor remains inoperable, radiotherapy may or may not result in operable disease. In the first case surgery followed by adjuvant chemotherapy, in the latter an other chemotherapy scheme possibly followed by surgery will complete treatment. When ICT in *inflammatory LABC* results in operable disease (no residual inflammation), a MRM or BCT may be considered on individual bases taking in to account the residual tumor mass. There is high evidence that ICT can be used to shrink *large operable tumors* to allow breast conservation.

Evaluation of the *extent of residual disease* may be tricky. In addition to physical examination, mammogram and ultra sound tools like multiple CNB/ FNAC, MRI and PET/CT may be used but evaluation and prediction of pathological response remains difficult. The way *tumors respond* (shrink or fragmentise) may alter the value of pathological 'free margins' and may result in a higher rate of in breast recurrences compared to BCT for early breast cancer. Even when cCR is obtained, excision of the tumor site (tattoo or daps before the start of ICT) is recommended since pathological complete remission (pCR) is uncommon. Furthermore, proven pCR bears important prognostic information since it is correlated with better disease free and overall survival.

After ICT most patients will undergo an *axillary lymph node dissection* (ALND) to provide good regional control. However, it is unclear how lymph node status will influence further systemic treatment. The role of *sentinel lymph node mapping* (SLN) remains unclear at this moment. In selected cases (cN0 at the moment of diagnosis) SLN mapping can be considered and by preference before starting ICT.

**Conclusion:** ICT allows in vivo study of tumor chemosensitivity and early control of distant micrometastases. Often, the tumor bulk decreases sufficiently and allows individualised local surgical treatment options based on the response obtained.

**236** Invited  
**Can radiotherapy for locally advanced breast cancer be individualised?**

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Locally advanced breast cancer requires a multidisciplinary treatment, hampering assessment of the specific role of each component. It is attempted to describe the specific role of radiotherapy in relation to surgery and systemic treatment from a historical perspective, followed by the authors' view concerning possibilities to individualize treatment.

In the 1980's locally advanced breast cancer was confined to stage IIIB disease (T4 and/or N2; irresectable). Locoregional radiotherapy was the sole treatment, achieving >85% complete response, ±60% local control and 35–40% 5-year survival. Later, the definition of locally advanced disease was extended to large but operable primary tumours (T3, stage IIIA), nowadays the majority of patients. Meanwhile neo adjuvant chemotherapy became an important tool to improve long term local control, to achieve resectability of stage IIIB disease and enable breast conservation in stage IIIA. Improvement of overall survival could be shown for stage IIIA disease but not for stage IIIB. Adding surgery as a standard procedure, where possible, had the advantage that pathological response rates of chemotherapy could be objectively assessed, which is a scientific, rather than a patient care advantage. In addition, extensive or limited surgery diminishes the tumour load for locoregional radiotherapy and hence improves local control. In the Oxford locoregional treatment overview it was clearly shown that in the higher tumour stages omitting (locoregional) radiotherapy from the multidisciplinary treatment would diminish locoregional control and 15 year survival.

In view of these developments and the available evidence, the author considers locoregional radiotherapy as the basis of treatment. Neo adjuvant systemic treatment and surgery diminish the tumour load and hence improve long-term locoregional control. Surgery may well be limited to removal of the residual tumour. It is likely that axillary dissection alone or axillary radiotherapy alone is equally effective as the combination in terms of axillary control but less toxic. So probably, axillary treatment may be individualized, for instance omitting axillary dissection in case of axillary remission, and choosing axillary dissection alone when axillary disease is still present after systemic treatment.

Thursday, 23 March 2006 14:15–16:00

SCIENTIFIC SESSION

**Locally advanced disease**

**235** Invited  
**Individualised surgery after induction chemotherapy**

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The use of more potent induction chemotherapy (ICT) regimens for locally advanced breast cancer (LABC) resulting in better local response and improved survival, has renewed the interest in local treatment issues.