

could indicate that hormone receptor negative cancers are less likely to spread lymphogenously.

4N Invited Disease-free survival in breast cancer patients with minimal lymph node involvement: results in 241 isolated tumour cells or micrometastases in the sentinel lymph node with negative complementary axillary dissection

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Background: Sentinel lymph node (SLN) biopsy has led to an increase in the detection of minimal lymph node involvement (micrometastases-pN1mi and isolated tumor cells-pN0i+). The outcome may be different between patients with minimal lymph node involvement (MLNI) in the SLN with negative complementary axillary dissection (CAD) and those with negative SLN without CAD. The aim of this study was to determine the disease free survival (DFS) of breast cancer patients with MLNI in SLNs.

Patients and Methods: The Institut Curie SLN Database was used to identify all patients who underwent a SLNB for invasive breast cancer between January 2000 and December 2006 and had MLNI (pN0i+ and pN1mi) with a negative CAD or negative SLN (pN0) without CAD. The primary endpoint, DFS, was estimated using Kaplan-Meier method. The log-rank test was used to determine differences in DFS of patients from different groups.

Results: The whole series of 1701 patients was divided into three groups according to axillary status, pN0i+ with a negative CAD (n=104), pN1mi with a negative CAD (n=137) and pN0 without CAD (n=1460). With a median follow-up of 52 months (range 1–110 months), there was no statistical difference in axillary recurrence rates between pN0, pN1mi and pN0i+, respectively 0.48%, 0%, and 0% (p=0.753). MLNI in SLN was not associated with a significantly shorter DFS, compared with negative SLN without CAD, respectively 94.1% for pN0, 92.5% for pN1mi and 96.3% for pN0i+ (p=0.599).

Conclusions: In this series, MLNI with negative CAD was not associated with a worse DFS compared to negative SLN. It seems therefore important to distinguish MLNI followed by a negative CAD, from MLNI without CAD performed. However, longer follow-up is needed to confirm these results, as well as the impact of MLNI on overall survival.

5N Invited Elective irradiation of Internal Mammary Chain (IMC) after mastectomy has no impact on 10y overall survival in breast cancer – results of a randomized phase III study in France

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Background: Post operative radiotherapy after mastectomy for breast cancer includes the supraclavicular area and usually the chest wall. In some institutions, the target volume is extended to the internal mammary chain (IMC). There was however no proof that this elective irradiation was efficacious. Moreover, this irradiation could be responsible of some of fatal coronary events occurring after irradiation. The objective of this randomized trial was to evaluate the impact of internal mammary chain irradiation (IMC-RT) on 10y overall survival in breast cancer patients treated with mastectomy.

Methods: Multicentric randomized phase III trial comparing chest wall, axillary and supra-clavicular irradiation with or without IMC-RT in newly diagnosed stage I and II breast cancers. Inclusion criteria: Patients under 76-years-old with positive axillary nodes or internal/central tumor location, whatever pN. Stratification was done by center, nodal status and tumor location (internal/central vs. external). IMC-RT consisted in a combination of photons (12.5 Gy in five fractions) and electrons (32.5 Gy in 13 fractions) over 5 weeks. The target field included the first five intercostal spaces. Adjuvant chemotherapy or hormonal treatment was at the discretion of the physician. We planned to include 1200 pts that allowed us to detect 10% difference in survival (observed arm: 40% versus 50% RT-arm).

Results: A total of 1334 patients (in 12 centers) have been randomized. Mean age was 56.5 yrs, 1003 (75%) pts had positive lymph no, 1147 (86%) received chemotherapy or/and hormonotherapy. With a median follow-up of

10 yrs, we observed 535 deaths. 10-yr survival was 62.57% in case of IMC-RT and 59.55% without IMC-RT (p = 0.8762 by log-rank test). No difference was obtained in the different subgroups: positive or negative axillary nodes, external vs central/internal tumors, or according the adjuvant chemotherapy or hormonotherapy. Causes of death are known in 422 Pts: most of these deaths were due to breast cancer (371); no increase in cardiac toxicity was observed in the IMC-RT group with a median FU of 5y. The late toxicity will be update at the time of the meeting.

Conclusion: There are no clear beneficial effects of the IMC specific irradiation on the overall survival most probably because the scarcity of the invasion and several other factors such as chemotherapy and hormonotherapy.

6N Invited Irradiation of the internal mammary and medial supraclavicular lymph node chain in stage I to III breast cancer: state of the day of EORTC phase III trial 22922/10925 with 4004 patients

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Background: Postmastectomy locoregional radiotherapy is known to improve disease free and overall survival in patients with involved axillary lymph nodes. Our trial was designed to investigate the contribution of IM-MS lymph node irradiation to this effect.

Material and Methods: Eligible patients had involved axillary lymph nodes and/or a medially located primary tumour. Based on randomisation, half received IM-MS radiotherapy to a dose of 50 Gy in 25 fractions. The original trial design aimed at detecting a 5% increase in 10-year overall survival (from 50 to 55%, HR=0.86). After reviewing the patient characteristics and in view of new data in the literature, the objectives of the trial were updated in April 2003 to target a 10-y overall survival benefit from 75% to 79% (HR = 0.82). Three analyses are planned, at respectively 10, 15 and 20 years median follow-up, each at the 0.022 significance level. The first analysis will be done after 1000 deaths have been observed. At each annual visit, data on survival, recurrences, second tumours, toxicity and performance score are recorded. At 5 and at 10 years, an additional late toxicity evaluation form is completed for cardiac, pulmonary and other diseases.

Results: Between July 1996 and January 2004, a total of 4004 patients entered this study. Of all patients, 59% were postmenopausal; 33.8%, 52.1% and 14.1% had stage I, stage II and stage III respectively. A majority of the patients (76.1%) was treated with breast conserving therapy of which 85.1% received a boost. After mastectomy, 73.2% of the patients in both randomisation arms received chest wall irradiation. 6.8% in the no IM-MS and 7.8% in the IM-MS group received axillary radiotherapy. Nearly all node-positive and over 2/3 of node-negative patients received adjuvant systemic treatment. The evaluation of the dummy run and the individual case review confirmed a positive influence of the quality assurance program on protocol compliance. At 3 years of follow-up, an additional 57 cases of lung toxicity in the IM-MS arm were recorded, translating into a significant higher rate of "any lung" toxicities after IM-MS treatment (4.3% vs. 1.3%; p < 0.0001). Other toxicity was the same in both treatment arms and no significant worsening of the performance score was observed, suggesting that treatment-related toxicity did not impair patient's daily activities.

Currently, median follow-up is 7.3 years and 558 patients have died, giving an estimated overall 10-y OS within 79.1%-82.5% (95% confidence interval), close to the anticipations. Data maturity for the first analysis is expected to be reached in 3 to 4 years.

Conclusions: Toxicity at 3 years was limited, obviating the need for early disclosure of the results. For the evaluation of the primary endpoint at 10 years, we need to wait for 2012. As IM-MS irradiation seems well tolerated with limited toxicity and no impairment on performance score at 3 years, it can in the meantime still be considered as a treatment option, especially in high-risk patients.