207 Proffered paper oral

70-Gene Signature Prospectively Predicts Prognosis of Patients with Node-negative Breast Cancer: 5 Year Follow-up of the RASTER Study

S.C. Linn[1], C.A. Drukker[2], V.P. Retel[3], J.M. Bueno-de-Mesquita[4], W.H. van Harten[3], H. van Tinteren[5], J. Wesseling[4], L.J. van 't Veer[6], E.J.T. Rutgers[2], M.J. van de Vijver[4]. *[1]Netherlands Cancer Institute − Antoni van Leeuwenhoek hospital, Department of Medical Oncology, Amsterdam, The Netherlands; [2]Netherlands Cancer Institute − Antoni van Leeuwenhoek hospital, Department of Surgical Oncology, Amsterdam, The Netherlands; [3]Netherlands Cancer Institute − Antoni van Leeuwenhoek hospital, Division of Psychosocial Research and Epidemiology, Amsterdam, The Netherlands; [4]Netherlands Cancer Institute − Antoni van Leeuwenhoek hospital, Department of Pathology, Amsterdam, The Netherlands; [5]Netherlands Cancer Institute − Antoni van Leeuwenhoek hospital, Biometric Department, Amsterdam, The Netherlands; [6]Agendia, Amsterdam, The Netherlands*

Background: The 70-gene signature (MammaPrint®) has been developed to predict the risk of distant metastases in the first 5 years after diagnosis.

Methods: Clinical follow-up was updated for 427 patients with primary breast carcinoma (clinical T1−3N0) who had participated in the microarRAy prognoSTics in breast cancER study and for whom a 70-gene signature had been obtained. Concordance between risk predicted by the 70-gene signature and risk predicted by Adjuvant! Online (AOL) (10-year survival probability <90% was defined as high risk) has been assessed previously. Other endpoints of the RASTER study reported here were distant disease-free survival (DDFS) and distant recurrence free interval (DRFI). Adjuvant systemic treatment decisions were based on the restrictive 2004 Dutch guidelines, the 70-gene signature outcome, and doctors' and patients' preferences.

Findings: The median follow-up was 62 months. In the 70-gene signature low risk group 15% (33/219) of the patients had received adjuvant chemotherapy, versus 81% (169/208) in the 70-gene signature high risk group. In 161 patients the result of the 70-gene signature and AOL were discordant. The 5-years follow-up results defined by the MammaPrint, AOL risk groups and adjuvant systemic therapy use are shown in the table.

70-gene signature	AOL	Endocrine therapy	Chemotherapy	5-year DDFS (%) (95% CI)	5-year DRFI (%) (95% CI)
Low	Low	7/95 (7%)	3/95 (3%)	94.3 (90−99)	95.3 (90–100)
High	Low	29/37 (78%)	21/37 (57%)	94.6 (88–100)	100 (100–100)
Low	High	53/124 (43%)	30/124 (24%)	97.6 (95–100)	98.4 (96–100)
High	High	93/171 (54%)	148/171 (87%)	88.7 (84−94)	89.8 (85−95)

In the group that did not receive any adjuvant systemic treatment (chemotherapy nor endocrine therapy) the 70-gene signature low risk − AOL low risk group (n = 88) had a DDFS of 95.0% (95% CI 90–100) The 70-gene signature low risk − AOL high risk group (n = 70) had a DDFS of 100%.

Interpretation In a prospective community-based observational study, the 5-year DDFS and 5-year DRFI probabilities confirmed the additional prognostic value of the 70-gene signature to clinico-pathologic factors used in AOL risk estimations. If in a comparable cohort diagnosed today the 70-gene signature would be added to standard guidelines used to select patients for adjuvant systemic therapy, a reduction of 29% in the use of adjuvant chemotherapy would be seen. Omission of chemotherapy as judged appropriate by doctors and patients and supported by a low risk 70-gene signature test appeared indeed safe.

Thursday, 22 March 2012 15:30–17:00

CLINICAL SCIENCE SYMPOSIUM

Controversies on Breast Cancer Treatment/Breast Conservation

208 Invited

Imaging in Breast Conservation

Abstract not received.

209 Invited

Radiotherapy in Breast Conservation

J. Yarnold[1]. *[1]The Institute of Cancer Research, Academic Unit of Radiotherapy, Sutton, United Kingdom*

The 2011 systematic overview of radiotherapy effects by the Early Breast Cancer Trialists' Collaborative Group reported retrospective analyses that identify women >60 years with pT1G1ER+pN- invasive carcinomas treated by breast conservation surgery and tamoxifen without radiotherapy as a subgroup with <10% local relapse at 10 years. This raises the question whether the benefits of standard whole breast radiotherapy outweigh the late adverse effects in this subgroup that is well represented in mammographically screened populations. A second controversial issue relates to 2010 guidelines for partial breast radiotherapy (PBRT) developed by professional bodies in North America and Europe that identify subgroups of women regarded as suitable for PBRT in a non-research context mainly on the basis of single arm studies. A third controversy relates to women at high local relapse risk after breast conservation surgery despite current standard therapies, especially young women with high grade (often ER−) tumours, for whom more effective dose escalation is needed. In this group, intensity modulated radiotherapy may be capable of matching dose intensity more effectively to the risk and location of local relapse. One approach involves combining reduced fraction size and reduced dose intensity outside the index quadrant with larger fraction sizes and higher dose intensities inside the index quadrant. Stratification of dose intensity based on predictive biomarkers of tumour response to radiotherapy represents a fourth controversial topic, based on suggestions that ER+ tumours are more likely to be controlled by radiation than ER− tumours. Finally, residual controversies in hypofractionation focus on its suitability for subgroups under-represented in current randomised trials. There is a risk that beneficial treatments are withheld on the basis of spurious concerns about the generalisability of trial results. If a particular hypofractionated schedule is proven safe and effective after breast conservation surgery, why should it need independent testing before it is used for post-mastectomy radiotherapy?

210 Invited

Breast Conservation in Controversial Cases − Surgical Techniques

Abstract not received.

211 Proffered paper oral

Phase III Trial (EORTC 10801) Comparing Breast-conserving Therapy with Radical Mastectomy − Twenty Year Follow-up Results

S. Litière[1], G. Werutsky[1], I.S. Fentiman[2], E. Rutgers[3], M.R. Christiaens[4], E. Van Limbergen[4], M.H.A. Baaijens[5], J. Bogaerts[1], H. Bartelink[3]. *[1]EORTC Headquarters, Brussels, Belgium; [2]Guy's and St. Thomas' NHS Foundation Trust, London, United Kingdom; [3]The Netherlands Cancer Institute, Amsterdam, The Netherlands; [4]University Hospital Gasthuisberg, Leuven, Belgium; [5]Erasmus MC-Daniel den Hoed Cancer Center, Rotterdam, The Netherlands*

Background: The EORTC 10801 trial compared Breast Conserving Therapy (BCT), comprising of lumpectomy and complete axillary clearance followed by whole breast irradiation and a tumor bed boost, with Modified Radical Mastectomy (MRM) in patients with tumors up to 5 cm and both positive and negative axillary nodes. At 13 years follow up MRM demonstrated better local control, but this did not affect Overall Survival (OS) or time to distant metastases (TDM) as compared with BCT. This analysis reports on the 20-year follow-up results.

Materials and Methods: The trial accrued 868 eligible patients between 1980 and 1986, with 448 randomized to BCT and 420 to MRM. Tumors were 2.1−5 cm in 80% of the patients, and 40% of the patients presented with positive lymph nodes. Microscopic margin involvement was observed in 217 of the 448 patients in the BCT arm. Median follow-up was 22.1 years.

Results: Patients' clinicopathological features were similar within the treatment arms. There was no significant difference in the TDM ($P = 0.23$). Rates of distant metastases at 20 years were 42.6% (95% CI = 37.8–47.5%) and 46.9% (95% CI = 42.2–51.6%) in the MRM and BCT arms respectively. Similarly, there was no significant difference in OS ($P = 0.23$), estimated at 20 years as 44.5% (95% CI = 39.3–49.5%) and 39.1% (34.4–43.9%) respectively. After adjusting for clinicopathological features in a Cox proportional hazards model no significant difference in TDM (HR = 1.09; 95% CI = 0.89–1.33) or OS (HR = 1.11; 95% CI = 0.93–1.33) was found. Forty percent of the patients were aged less than 50. There was no indication of a difference by age group (<50 versus $\geqslant$ 50 years) in terms of TDM or OS for the 2 arms.