# The 9th European Breast Cancer Conference (EBCC-9) – Highlights of the Late-breaking Abstracts

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The 9th European Breast Cancer Conference (EBCC-9) was held in Glasgow, Scotland from 19 to 21 March 2014. The conference is the largest breast cancer (BC) conference outside the US, and is unique in that its organiser, the European Breast Cancer Council (EBC Council) includes patient advocates within its framework, providing a platform for advocates to collaborate with BC professionals. The aim of the conference was to disseminate information directly to patient advocates and enable healthcare professionals to implement new findings in daily practice. Late-breaking abstracts provide an opportunity to communicate the most recent clinical and scientific breakthroughs. This article will focus on late-breaking abstracts from the conference that focus on a number of major areas of interest in BC research.

## Late-breaking Abstracts

### Radiotherapy

Radiotherapy (RT) is applied to the breast after breast-conserving surgery (BCT) and may be given to the chest wall following mastectomy. The nodal areas, particularly the supraclavicular fossa and axilla, may also be treated in patients at risk of regional relapse.[1] Post-operative RT for BC is known to reduce the rate of local recurrence in around two-thirds of cases.[2] Two late-breaking abstracts presented new data on RT. Dr Henk Struikmans of The Netherlands presented 10-year data from the European Organisation for Research and Treatment of Cancer (EORTC) BC group and the Radiation Oncology Group (ROG) phase III clinical trial 22922/10925, which demonstrated the benefit of locoregional radiation therapy of the internal mammary and medial supraclavicular (IM-MS) lymph nodes in stage I–III BC. Post-operative RT to the IM-MS lymph nodes improved overall, disease free and distant metastases-free survival without any increase in non BC-related mortality.[3]

In addition, Dr V Skvortsov of St Petersburg presented the first data on the use of intra-operative RT in the treatment of early-stage BC. Intra-operative RT allows accurate delivery of radiation to the tumour bed rather than conventional post-operative whole breast irradiation, giving the same equivalent dose during surgery. Patients (n=150) with early stage (T1-2N0-1M0) BC underwent BCT with sentinel node biopsy using the Intrabeam system, followed by adjuvant chemotherapy or endocrinotherapy. At 18-month follow up, 99.3 % of patients were recurrence free and 98.7 % had no distant metastases. In 2 % of patients, lymphocysts were observed in the area of radiation exposure that required prolonged puncturing. The treatment was well-tolerated, was convenient to use and the disadvantages associated with external beam RT are eliminated, and therefore warrants further investigation.[4]

### Targeted Therapy

Targeted therapy remains an active area of BC research, and Dr Martine Piccart presented the latest data from the phase III BC trials of OraL EveROlimus-2 (BOLERO-2). This study had previously demonstrated that the addition of the mammalian target of rapamycin (mTOR) inhibitor everolimus (EVE) to the aromatase inhibitor exemestane (EXE) more than doubled progression-free survival (PFS) in patients (n=724) with hormone-receptor positive (HR+) human epidermal growth factor receptor-2-negative (HER-) advanced BC following disease recurrence or progression with nonsteroidal aromatase inhibitors.[5] Dr Piccart announced that although the primary endpoint of PFS was clinically meaningful and statistically significant, the secondary endpoint of the study, that of overall survival, did not reach statistical significance.[6] Further studies are needed to refine the clinical benefits of mTOR inhibitors and combinations of targeted agents in this patient population.

### Predicting Response to Therapy

Following the advent of new therapeutic options in BC, identification of patients most likely to benefit from individual therapies is essential. Dr Fatima Cardoso of the Champalimaud Cancer Centre in Lisbon, Portugal, presented data from the phase III Microarray In Node negative and 1–3 positive lymph node Disease may Avoid ChemoTherapy (MINDACT) trial, which investigated the clinical utility of the genomic microarray assay MammaPrint in 6,698 patients with early BC in selecting patients for adjuvant chemotherapy.[7] Gene-expression data for the oestrogen receptor (OR), progesterone receptor (PgR) and human epidermal growth factor 2 (HER2) obtained by TargetPrint were compared with central pathology assessment. Positive agreement with central assessment of 98 %, 85 % and 72 % was reported for OR, PgR and HER2, respectively. Negative agreements were 95 %, 94 % and 99 %, respectively. However, a difference between mRNA and protein assessment for PgR and HER2 requires further investigation. These data will be crucial to the interpretation of the primary endpoint data of the MINDACT trial.[8]

In another presentation, Professor Mike Dixon of the Breakthrough Breast Cancer Research Team at the University of Edinburgh introduced a four-gene model that could predict clinical response to neoadjuvant endocrine therapy in OR+/HER+ BC. This molecular subtype occurs

in 10 % of OR+ BC cases and has a poor prognosis compared with OR+/HER2- tumours. In a study of 89 post-menopausal women with OR+ BC treated with neoadjuvant letrozole, OR+/HER2+ and OR+/HER- responsive tumours showed similar gene changes following neoadjuvant letrozole, suggesting that OR rather than HER2 is affecting tumour growth. The four-gene model showed 96 % accuracy in a training dataset (n=73) and 91 % accuracy in an independent validation dataset (n=44).[9] These findings may allow the selection of OR+/HER2+ tumours that are unlikely to benefit from endocrine therapy but may respond to HER2 or mitogen-activated protein kinase (MAPK)-targeted therapies.

## Definition of Clinical Endpoints

An important requirement for future BC clinical studies is consistent definition of clinical endpoints in classifying disease recurrence. Currently, many different endpoints are used. Definitions are often not provided or they vary between studies. There are even disparities in the definitions of components of BC study endpoints such as local event, second primary BC, regional event and distant event, which may lead to unjustified conclusions in clinical studies. Dr Martine Moossdorff of the Maastricht University Medical Centre, The Netherlands, provided consensus definitions of these parameters, based on the opinions of 24 international BC experts comprising the Maastricht Breast Cancer Endpoint Consensus Group (see *Table 1*).[10]

## Assessing Individual Breast Cancer Risk

Professor Gareth Evans of St Mary's Hospital, Manchester, UK, presented 10-year data assessing BC risk in women participating in the Predicting Risk of Cancer At Screening (PROCAS) study. Of 53,467 women recruited, 1.4 % had a 10-year risk ≥8 % (high risk); 8.6 % had a risk of 5–8 % (moderately high risk) and 4.1 % had a low (<1 %) risk. Among women with 10-year risks above 3.5 %, 1.7 % had developed BC. Proportions of higher-stage cancers were higher in above-average risk women compared with those at average risk or below (32 % versus 19 %). The study concluded that 3-year screening was appropriate for average/low risk women, but that in the population at above-average risk, the higher rates of advanced cancers justify a reduced screening interval.[11]

## Summary and Concluding Remarks

Late-breaking abstracts at EBCC-9 have demonstrated the benefit of locoregional radiation therapy as well as intra-operative RT in early stage BC. Although OS in BOLERO-2 did not achieve statistical significance, the significant increase in PFS achieved by the combination of EVE and EXE in HR+/HER- advanced BC will ensure continued interest in this combined targeted approach. However, it is vital that future clinical studies show consistency in defining clinical endpoints: the consensus definitions provided by Maastricht Breast Cancer Endpoint Consensus Group represent a valuable reference. Continued advances in gene expression profiling should ultimately allow the selection of tumours that may benefit from specific therapeutic approaches. Finally, data from a large epidemiological cohort in the UK suggest that 3-year screening may be insufficient for women at above-average risk. These abstracts have presented data that are relevant to the entire BC community and should be directly applicable to clinical practice. ■

**Table 1: Consensus Definitions of Clinical Endpoints in Breast Cancer Studies**

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| Local event | Epithelial BC or DCIS in ipsilateral breast, surgical scar, biopsy tract and skin and subcutaneous nodules on the (former) ipsilateral breast and ipsilateral thoracic wall<br>*Should NOT include: LCIS, phyllodes tumours or any benign breast lesion and breast cancer event involving the sternal bone* |
| Second primary BC | Epithelial BC in contralateral breast |
| Regional event | BC in ipsilateral lymph node (axillary, infraclavicular, supraclavicular, internal mammary, intramammary) |
| Distant event | Breast cancer localisation anywhere else than listed above<br>including events involving the sternal bone<br>including contralateral lymph nodes (axillary, infraclavicular, supraclavicular internal mammary)<br>Tissue sampling<br>Confirmation (histology, cytology of suspected first solitary metastasis is highly recommended if feasible<br>If impossible, unconfirmed metastasis is acceptable at discretion of treating physician<br>Multiple metastases on imaging are acceptable without pathology confirmation |

*BC = breast cancer; DCIS = ductal carcinoma* in situ*; LCIS = lobular carcinoma* in situ.


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10. Moossdorff M, Van Roozendaal LM, Strobbe LJA, et al., Maastricht consensus on the definition of local event, second primary breast cancer, regional event and distant event for classifying recurrence in breast cancer research., Presented at the 9th European Breast Cancer Conference (EBCC-9), 19–21 March 2014, Glasgow, Scotland, abstract no 5LBA.
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