Certainly! But it too will have to evolve. In this presentation the new multigene expression signatures will be reviewed. There are certainly signatures based on both protein and nucleic acid technologies that can refine estimates of patient prognosis beyond the estimates that can be made by classic pathologic information. Some of these signatures have also shown promise in making estimates of treatment efficacy. Adjuvant! was specifically designed so that estimates for prognosis and efficacy from other sources and can be entered either to be combined with or to override estimates based on newer technologies.

No tool can ever be claimed to be perfect. This is because many factors evolve with time. Screening, exogenous exposures, general medicine and salvage therapy all in a state of change. Much of what we "know" in terms or treatment efficacy is based on short term follow-up. We are inevitably developing new models for 10 year outcome based on population of patients from at least 10 years ago, and making projections of outcome for 10 years from now. Given the rapid evolution of technology these will always be approximations. Nonetheless prognostic and treatment efficacy tools that produce numerical estimates have moved us beyond the era of vague non-numerical statements to an era of shared decision making where patients and their health care team can discuss options in a more complete way.

443 Proffered paper oral

PARP is expressed in all subtypes of early breast cancer and is a predictive factor for response to neoadjuvant chemotherapy

G. von Minckwitz[1], B. Müller[2], S. Loibl[3], J.U. Blohmer[4], A. duBois[5], J. Huober[6], R. Kandolf[7], J. Budczies[2], C. Denkert[2]. *[1]GBG Forschungs GmbH, Managing Director, Neu-Isenburg, Germany; [2]Charité Universitätsmedizin Berlin, Institut für Pathologie, Berlin, Germany; [3]German Breast Group, Medicine & Research, Neu-Isenburg, Germany; [4]St. Gertrauden Krankenhaus, Gynecology, Berlin, Germany; [5]HSK Wiesbaden, Gynecology, Wiesbaden, Germany; [6]UFK Tübingen, Internal Medicine, Tübingen, Germany; [7]University of Tübingen, Institut für molekulare Pathologie, Tübingen, Germany*

Background: The polyadenosine diphosphate [ADP]-ribose polymerases (PARPs) are a large family of multifunctional enzymes. PARP-1 plays a key role in the genomic stability. Increased expression is considered to be associated with resistance to DNA damage-inducing therapeutic agents. Combining these cytotoxic agents with a PARP inhibitor showed improved activity in patients with triple negative metastatic breast cancer.

We investigated PARP expression in various hormone (HR)/HER2 receptor subtypes of early breast cancer and evaluated its predictive value for pathological complete response (pCR; defined as no invasive residuals in breast and nodes).

Methods: Tissue microarrays from core biopsies of 582 patients recruited to the phase III GeparTrio trial, who received neoadjuvant 6−8 cycles TAC/NX chemotherapy, were centrally stained immunohistochemically for PARP, ER, PgR and HER2 expression. Cytoplasmatic and nuclear staining of PARP was assessed with regard to intensity and percentage of positive cells and scored as low, medium or high expression.

Results: Overall, cytoplasmatic PARP expression was high in 24.4%, medium in 52.4% and low in 23.2% of patients. High expression was found in 19.9% of 286 HR+/HER2−, 20.2% of 129 HR+/HER2+, 36.0% of 50 HR−/HER2+ and 35.6% of 101 HR−/HER2− tumours ($p = 0.001$). High PARP expression was significantly correlated with undifferentiated tumour pattern ($p < 0.001$), non-lobular cancers ($p < 0.001$), negative HR ($p < 0.001$). Correlation was only of borderline significance for tumour size and nodal status, no correlations were found for HER2 status and age. Patients with high PARP expression showed a pCR rate of 25.7% compared to 18.8% and 6.1% in patients with medium or low expression ($p < 0.001$). In univariate logistic regression, pCR rate was different between PARP high and low expressing tumours with OR = 5.3 (95% CI 2.4–12.0). This result remained significant when corrected for tumour stage, nodal status, histological type, tumour grade, molecular subtype and age, OR = 2.6 (1.1−6.4). No such correlations were found regarding nuclear PARP staining.

Conclusions: Cytoplasmatic PARP expression can be detected by immunohistochemistry in all subtypes of early breast cancers and is correlated with an aggressive biological tumour pattern. Cytoplasmatic PARP expression predicts pCR to neoadjuvant taxane-anthracycline-based chemotherapy. Clinical investigation of PARP inhibitors should not be limited to triple negative tumours alone.

444 Proffered paper oral

The EORTC 10041/BIG 03−04 MINDACT trial is feasible: first results of the pilot phase

E. Rutgers[1], M. Piccart[2], S. Delaloge[3], L. Van 't Veer[4], I. Rubio[5], G. Viale[6], J. Bogaerts[7], F. Cardoso[2]. *[1]The Netherlands Cancer Institute, Department of Surgery, Amsterdam, The Netherlands; [2]Institut Jules Bordet, Department of Medical Oncology, Brussels, Belgium; [3]Institut Goustave Roussy, Department of Surgery, Villejuif, France; [4]Netherlands cancer institute, Department of Molec. pathology, Villejuif, The Netherlands; [5]Hospital Vall d'Hebrón, Department of Breast Pathology, Barcelona, Spain; [6]European Institute of Oncology, Department of Pathology, Milano, Italy; [7]EORTC, EORTC Breast Cancer Group, Brussels, Belgium*

The MINDACT trial (Micro array In Node negative and 1 to 3 positive lymph node Disease may Avoid ChemoTherapy) investigates whether the 70-gene profile (Mammaprint™) selects the right pts for adjuvant chemotherapy (CT) as compared to standard clinicopathological criteria. All pts have the 70-gene test (genomic high vs low risk) and clinical-pathological prognostic risk, the latter assessed through a modified version of Adjuvant! Online (low risk defined as >88% 10-years breast cancer specific survival for ER-positive and >92% for ER-negative disease). Genomic (G) and clinical (C) high risk pts are proposed adjuvant CT and may be randomized between an anthracycline-based regimen and the combination docetaxel-capecitabine. G-low and C-low risk patients do not receive CT. All ER-positive pts are offered an endocrine therapy randomization between 7 years of letrozole and 2 years of tamoxifen followed by 5 years of letrozole. Discordant patients (G-low/C-high or G-high/C-low) are randomized between decision of adjuvant CT based on G or C risk assessment. The study aims to enroll 6000 pts and has a predefined "pilot phase" of 800 pts to ensure its feasibility. The first pt was enrolled in March 2007, and in November 2008 accrual passed the 800 enrolled pts (i.e. pts with treatment assigned); these first pts are all node negative. The IDMC reviewed data from this pilot phase and endorsed communication of these results:

- The accrual is currently around 140 enrolled pts/month.
- 46% of screened pts were enrolled; 73% of screened pts had their sample shipped; of the shipped samples, 67% went through successful hybridization and testing by the 70-gene array.
- Reasons for non-eligibility: 28% of cases node positivity (before amendment), 29% for sample quality problems, 43% for failure to enrol within timelines or other reasons.
- C/G risk allocation: C/G low risk: 386 pts (48%); C/G high risk 198 pts (24.8%); C low risk/G high risk: 75 pts (9.4%); C high risk/G low risk 141 pts (17.6%). Total proportion of discordant cases: 27%.
- A statistically significant difference of 8.25% (C. I 4.7–11.8) is observed between pts that have a high C risk (42%) and those with a high G risk (34%) showing that, in the accrued population, more pts are assigned low risk by the G test than the C one.
- Compliance to randomization: within the key group of 69 pts with high C risk/low G risk assigned to no CT, 3 pts still received CT. In the 39 pts C low/G high risk assigned to CT, 5 pts did not receive it. Overall compliance >92%.

Conclusions: (1) The logistically complex MINDACT trial is feasible in an multinational setting. (2) The proportion of discordant pts, the expected reduction in CT in the 70-gene low risk group, and the compliance to treatment assignment in the discordant groups are according to plan. (3) The trial continues to accrue with new centers joining, and it was amended to include node positive disease, decreased tumor cellularity needed and increased timelines; these measures have already substantially decreased the number of ineligible pts.

445 Proffered paper oral

Beta-blocker treatment is associated with a reduction in tumour metastasis and an improvement in specific survival in patients with breast cancer

D.G. Powe[1], M.J. Voss[2], H.O. Habashy[3], K.S. Zänker[2], A.R. Green[3], I.O. Ellis[1], F. Entschladen[2]. *[1]Nottingham University Hospitals Trust, Cellular Pathology, Nottingham, United Kingdom; [2]University of Witten/Herdecke, Institute of Immunology, Witten, Germany; [3]University of Nottingham, Molecular Medical Sciences, Nottingham, United Kingdom*

Background: Breast cancer (BC) is the most common cause of cancer death in women and usually results from metastatic events. Recent studies suggest that neurotransmitters induce cancer cell migration mediated by beta2-adrenergic receptors (β_2AR). Therapeutic treatment with beta-blockers could protect against metastasis development giving improved clinical outcome in BC.

Materials and Methods: An epidemiologic study of beta-blocker treatment and its associations with metastasis and BC-specific survival