2010), BO18279 MERIT (Tan et al. 2010), BO18602 TITAN (Ciuleanu et al. 2010), MO18109 TRUST (Heigener et al. 2011)).
Results: In total EGFR mutation status could be obtained from 970 samples out of the 4 studies. 26 (3%) of those had 'other' mutations, 6 in exon 18, 4 in exon 19, 10 in exon 20 and 7 in exon 21. One sample had a double mutation in exon 18 and 21. A detailed breakdown of the single mutations with clinical outcome will be shown and discussed.
Conclusion: The clinical implications of 'other' EGFR mutations cannot be categorized easily mainly due to low incidence rates of each single mutation. However, some patients respond well to Tarceva treatment, others have long PFS and OS which seems not necessarily linked to treatment, but rather to the molecular status of the underlying disease. Collection of more clinical data on 'other' EGFR mutations is warranted.

PP 3

S-100B concentrations predict disease specific survival in AJCC Stage III melanoma patients

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Background: S100-B is a tumor marker used in melanoma patients but its role in AJCC stage III melanoma patients is still undefined. Elevation of S-100B in AJCC stage III can be highly specific indicator for recurrence. The role of S-100B was evaluated as a pre-operative tumor marker in FDG-PET staged stage III melanoma patients undergoing a therapeutic lymph node dissection.
Materials and Methods: All patients with melanoma Stage III between January 2004 and August 2010 were included. There were 53 males and 47 females with a median age 54.5 (range 21.8–90.6). S-100B was measured pre-operative and recorded as elevated when S-100B $\geqslant 0.15\,\mu g/l$. Univariate and multivariable Cox Proportional Hazard Models were used to assess the association of S-100B with Disease Free Period (DFP) and Disease Specific Survival (DSS).
Results: Overall, 100 patients were included. S-100B was elevated in 50% of the patients. Patients with a normal S-100B value had a 5-years DFP of 40.6% (23.0–57.5) versus 15.3% (5.6–29.4) in patients with an elevated S-100B (Hazard Ratio (HR) 2.3 (95% CI 1.4−4.0); p = 0.002). S-100B was an independent prognostic factor (HR 2.6; p = 0.002). Patients with a normal S-100B had a 5-years DSS of 46.2% (27.1–63.3) while patients with an elevated S-100B had a 5-years DSS of 28.1% (14.9–42.9); HR 2.4 (95% CI 1.3−4.3; p = 0.003). In multivariable analysis, S-100B was an independent prognostic factor (HR 2.2 (95% CI 1.2−4.0); p = 0.01).
Conclusion: Preoperative elevated S-100B is strongly correlated with a reduced survival. S100-B should be used as a prognostic marker in the stratification in trials for adjuvant systematic treatment and should be considered to be added to the AJCC melanoma staging system.

PP 21

Gene expression module biomarkers to stratify multiple clinical and therapeutic endpoints for universal breast cancer companion diagnostic

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Background: Gene expression patterns are increasingly capable of stratifying patients based on prognosis and response to therapy. Given the limited availability of sample tissue, however, it is not feasible to run many tests, suggesting the need for a universal companion diagnostic assay that is informative with respect to multiple clinical and therapeutic endpoints. Key challenges are identification of appropriate gene expression biomarkers, translation of biomarkers to clinical assays, and development of reliable gene expression profiling of formalin-fixed clinical specimens. Here, we describe a meta-analysis approach that identifies novel biomarker modules that results in multiple clinical and therapeutic read-outs.
Materials and Methods: A co-expression meta-analysis of 5,339 breast tumors from 56 microarray datasets identified highly co-expressed sets of genes (modules) across multiple datasets. And these module based biomarkers were tested for their ability to associate with prognostic and predictive targets in published datasets. In addition, each module was reduced from 10–1000 genes to top performing 2−3 genes based on degree of co-expression across the meta-analysis and validation by quantitative PCR in an independent panel of FFPE tumor samples.
Results: This study demonstrates that a single 96 gene qPCR test utilizing multiple module biomarkers is not only capable of stratifying patients by standard histopathological parameters (ER, PR and Her2), but also stratifies by other diverse elements of the disease (cell lineage, dysregulated core biological functions, factors of cell growth, underlying genomic aberrations and the tumor microenvironment). Taken together, these biological variables represent the major biological diversity present within the breast cancer population. A series of retrospective analyses demonstrated that different single module and combinations of modules were capable of predicting a variety of clinical endpoints, including 5-year survival, neoadjuvant chemotherapy response in ER− patients and targeted therapy response in model systems.
Conclusion: The molecular heterogeneity of breast cancer can be summarized by discrete gene expression modules that individually represent distinct biological pathways, and that collectively can be represented by as few as 96 genes. These breast cancer modules, together with outlier genes, allow for summation of the entire transcriptional program and provide a universal assay with broad application to companion diagnostics development.

PP 12

Evidence of Galectin-1 involvement in glioma pro-angiogenic and pro-migratory effects and chemoresistance

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Background: Despite the advances in the management of malignant gliomas of which glioblastomas represent the ultimate grade of malignancy, they remain characterized by dismal prognoses. Glioblastoma patients have a median survival expectancy of 14 months on the current standard treatment of surgical resection to the extent feasible, followed by radiotherapy plus temozolomide chemotherapy, given concomitantly with and after radiotherapy. This prognosis can be at least partly explained by the fact that glioma cells diffusely infiltrate the brain parenchyma making them elusive targets for effective surgical management and exhibit decreased levels of apoptosis and are thus resistant to cytotoxic drugs [1]. We have previously reported that progression of malignancy in patients bearing astrocytic tumors correlates with increased tumor levels of Galectin-1 [2], that Galectin-1 is involved in the modulation of the migration of tumor astrocytes [3] and that Galectin-1, the expression of which is stimulated by hypoxia [4], is also a pro-angiogenic molecule [4,5].
Materials and Methods: We investigated whether decreasing Galectin-1 expression (by means of a siRNA approach) in human Hs683 glioblastoma cells increases their chemosensitivity.
Results: Temozolomide increases Galectin-1 expression in the Hs683 glioblastoma model both in vitro and in vivo [6]. Consequently, reducing Galectin-1 expression in this model increases the anti-tumor effects of various chemotherapeutic agents, in particular temozolomide [5,6]. Reducing Galectin-1 expression in glioblastoma cells does not induce apoptotic or autophagic features, but rather modulates p53 transcriptional activity and decreases p53-targeted gene expression. The decrease in Galectin-1 expression also impairs the expression levels of several genes implicated in chemoresistance: ORP150, HERP, GRP78/Bip, TRA1, BNIP3L, GADD45B and CYR61 [6].
Conclusion: The involvement of Galectin-1 in different steps of glioma malignant progression [7], such as migration, angiogenesis or chemoresistance, makes it a potential target for the development of new drugs to combat these malignant tumors [8].

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PP 10

Biomarker discovery by pharmacological studies in a population based tumor model for VEGFR inhibitors

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Background: VEGF pathway inhibitors have been shown to elicit broad activity in traditional preclinical models, yet clinical development thus far has met with significant variation in response due to the complexity of human genetics and tumor microenvironment. Since empirical biomarker discovery in the clinic is both challenging and time consuming, preclinical models that provide variation of genetic context and complex microenviroment and therefore variation in drug response will greatly facilitate predictive biomarker discovery, especially for drugs in development.
Materials and Methods: Using chimeric murine model technology, we generated over one hundred primary breast tumors driven by HER2