Methylation-Specific-PCR (qMSP) to characterize potential "field effect" markers in DNA samples from tissue prints obtained from diagnostic prostate biopsies and confirmed the technical validity of the assay design. Biopsy tissue print techniques allowed us to design DNA-M marker panels that include up to 6 candidate field effect markers. Tissue prints also simplify the development of tests that include both DNA and RNA based assays.
Conclusion: By getting the most from the least tissue, a tissue print "field effect" biomarker test might be used with prostate biopsies to predict the presence of an adjacent cancer while reserving the FFPE specimens for histology.

PP121

High coexpression of both the epidermal growth factor receptor (EGFR) and insulin-like growth factor receptor-1 (IGF-1R) correlates with a poor patient prognosis in resected non-small cell lung cancer (NSCLC).

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Background: Following the success of the EGFR inhibitors a renewed interest in IGF-1R inhibitors has emerged. IGF-1R overexpression has been identified in several tumour types and protects cancer cells from apoptosis. Currently, several different approaches are being investigated for targeting the IGF-1R, including small-molecule kinase inhibitors, IGF1R monoclonal antibodies, antisense oligonucleotides and RNA interference. To date, it is not clear what factors influence sensitivity to IGF-1R blockade but it is likely that tumours that respond well to treatment will be those where IGF-1R overexpression results in a poor patient prognosis. Initial data show that tumour type may also determine response to therapy with squamous non-small cell lung cancers responding well to a combination of a IGF-1R monoclonal antibody and chemotherapy. The aim of this study was to elucidate the EGFR and IGF-1R expression profile in a cohort of NSCLC patients and correlate the results to patient clinico-pathological data and prognosis.
Materials and Methods: EGFR and IGF-1R expression were evaluated in 197 NSCLC patients (92 − squamous, 87 − adenocarcinoma, 18 − others) using immunohistochemistry analysis and the results were scored by a pathologist as follows: 0 (negative), 1+ (weak), 2+ (moderate) and 3+ (strong). Expression of EGFR and IGF-1R were also examined in a panel of cell lines (SKMES1, A549, HCC827, H1819, H1299) and patient samples (10 squamous and 10 adenocarcinomas) using Western Blot analysis.
Results: The panel of 6 NSCLC cell lines examined showed variability in IGF-1R expression. In the fresh frozen resected NSCLC tumours IGF-1R was overexpressed relative to matched normal tissues. Furthermore squamous cell carcinomas had higher levels of expression than adeno-carcinomas. Immunohistochemistry analysis demonstrated that squamous cell tumours have higher IGF-1R expression levels than adenocarcinomas (3+/2+ Squamous [70/197] versus 3+/2+ Adenocarcinoma 27/197)] $p < 0.0001$). Patients with squamous cell carcinoma also had higher EGFR expression than those with adenocarcinoma ($p = 0.002$). Patients with EGFR and IGF-1R overexpression had a poorer survival ($p = 0.043$).
Conclusion: Our findings indicate that while EGFR and IGF-1R expression alone are not independent prognostic markers of survival in NSCLC. Taken together overexpression of both proteins correlates to a poor survival. This subset of patients may benefit from a combination of TKIs/monoclonal antibodies and chemotherapy.

PP81

18F-FDG PET/CT for early detection of relapse in head and neck squamous cell carcinoma

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Background: A key prognostic factor in head and neck squamous cell carcinoma (HNSCC) is the loco-regional control of the disease. Early detection of relapse by selected imaging modalities is therefore of upmost importance. We evaluated the diagnostic accuracy of 18F-FDG PET/CT and MRI for the assessment of HNSCC relapse. Since early treatment might anticipate on inoperable relapse, we also evaluated if early 18F-FDG PET/CT might help in residual tumor detection despite treatment-related changes.
Materials and Methods: The study was prospectively performed on 32 patients with 36 primary HNSCC who underwent 18F-FDG PET/CT and MRI before treatment and at 4 and 12 mo after treatment completion. 18F-FDG PET/CT was also performed 2 weeks after the end of radiotherapy. All images were blindly and independently interpreted and graded on a 5-point scale. Histopathology or a minimum of 18 mo follow-up were used as gold standard.
Results: Before treatment 18F-FDG PET/CT and MRI detected all primary tumors except for 2 limited vocal fold lesions (sensitivity: 94%). MRI was more sensitive than 18F-FDG PET/CT for the detection of precise local extension sites (sensitivity: 75% versus 58%, $P < 0.05$) but at the cost of a higher rate of false positive results (positive predictive value: 74% versus 86%, $P < 0.05$). For relapse detection at 4 mo, sensitivity was significantly higher for 18F-FDG PET/CT (92%) than for MRI (73%) ($P < 0.05$), but the diagnostic performances were not significantly different at 12 mo post-treatment. For the detection of residual malignant tissue at 2 weeks post-radiotherapy, sensitivity and specificity of 18F-FDG PET/CT were respectively 86% and 85%, when using an SUV cut-off value of 5.8.
Conclusion: This study demonstrates that 18F-FDG PET/CT is effective in the differentiation between residual tumor and radiation-induced changes, as early as 2 weeks after treatment of a primary HNSCC. For follow-up, accuracy of 18F-FDG PET/CT and MRI are similar except for a higher sensitivity of 18F-FDG PET/CT at 4 mo.

PP14

RRM1 expression in muscle invasive, locally advanced urothelial cancer is associated with survival in younger patients

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Background: RRM1, the regulatory subunit of ribonucleotide reductase, plays an important role in DNA repair after chemotherapy damage and in regulation of tumor progression. Prior studies demonstrated a survival benefit to high expression in resected early stage lung cancer and a trend to longer time to progression in patients with low expression in unresectable advanced bladder cancer treated with gemcitabine-cisplatin therapy. We undertook this study to assess whether patients with resected locally advanced (T2−4NxM0) urothelial carcinoma (UC) whose tumors had higher RRM1 expression would have longer overall survival (OS).
Materials and Methods: 84 radical cystectomy specimens with muscle invasive UC were identified from existing tissue microarrays. The medical records of these patients were retrospectively reviewed to confirm pathology and stage. Specimens were analyzed for RRM1 expression using automated quantitative analysis (AQUA). The median value of RRM1 was established a priori as the cutoff for high and low expression. Older patients were defined as having an age $\geqslant$70 years.
Results: Median age was 69.3 years. 43 patients were <70 years; 41 were $\geqslant$70 years. There was near equal distribution of stages: 30%, 38%, and 32% for stage II, III, and IV respectively. The majority were high grade (99%) with no nodal involvement (69%). Median OS was 2.0 years (0−13.1). Tumoral RRM1 expression levels did not correlate with OS. However, when adjusted for age, high tumoral RRM1 expression in younger patients (<70 years) correlated with increased survival. Younger patients with high RRM1 had a median OS of 10.6 years compared to 1.6 years in older patients ($p = 0.0013$). No difference in survival was seen among low RRM1 expressors: 2.3 vs. 1.6 years in younger and older patients respectively, ($p = 0.215$). 40% of younger patients were high expressors. 32% of younger patients had nodal involvement compared to 29% of the older subset. In terms of T stage, 33% of younger patients had T3 disease compared to 54% of older patients and 33% of younger patients had T4 disease compared to only 15% of older patients.
Conclusion: Our results suggest that high RRM1 expression may be prognostic for improved survival in locally advanced UC patients less than 70 years old. This novel finding suggests that the biology of bladder cancer in "younger" patients is inherently different than their older cohort such that RRM1 gene expression should be the target of a larger investigation in this subset of patients.

PP16

Metronomic weekly use of zoledronic acid for breast cancer with bone metastases has more potent antitumor and bone-preserving effects than conventional zoledronic acid given every-four-weeks

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Background: Zoledronic acid (ZOL) has direct and indirect antitumor effects, however, the pharmacokinetics of the drug in breast cancer patients remain to be elucidated and optimized. The main study objectives were