tumors had a significantly higher miRNA risk-score than subjects with benign nodules or healthy controls (p-value <0.0001). MiRNA signature had an higher sensitivity than CT/PET (63% versus 53%), particularly among subjects with non-solid nodules (64% versus 18%). The combination of CT/PET and miRNA test correctly classified 83% of tumors. MiRNA and CT/PET specificity was 100% and 92%, respectively. We did not found any statistically significant association between the miRNA risk-score and clinical or radiological characteristics both for tumors and benign nodules.

Conclusions: MiRNA risk-score had a higher sensitivity than CT/PET in screen-detected lung cancers. A combination of miRNA test and CT/PET should be prospectively evaluated to optimize the workup for suspicious screen-detected nodules and to reduce the false positive cases at surgery.

Disclosure: All authors have declared no conflicts of interest.

24PD | METABOLIC PROFILE OF LUNG CANCER PATIENTS

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Lung cancer (LC) is the most common cause of cancer death worldwide. The lack of techniques for effective early diagnosis results in a very poor prognosis as the disease is frequently diagnosed at late stages. Thus, it is of therapeutic significance to develop fast and accurate diagnosis methods for lung cancer so that patients can be treated timely and properly. Metabolomics, a technique based on the measurement of metabolic profiles of biofluids, could represent a very powerful approach for the identification of potential biomarkers and metabolic pathways associated with lung cancer onset and progression. As a proof of principle, the potential of metabolomics by 1H-NMR to characterize the serum metabolic profile of LC patients has been evaluated. Serum metabolic profiles from early stage (n = 71) and advanced stage (n = 70) LC patients were acquired using 1H-NMR spectroscopy. A matched control set of 71 serum samples from healthy subjects was also included. Multivariable statistical modeling of the data showed that LC patients exhibit a specific serum metabolic profile (R² = 0.884; Q² = 0.813) characterized by lower concentrations of different lipids and some amino acids. A similar analysis was performed by comparison of LC patients at early and advanced stages of the disease (R² = 0.604; Q² = 0.507), reflecting that the evolution of the disease is also reflected in the serum metabolic profile of patients. Our results highlight the potential of metabolomics by 1H-NMR for identifying LC biomarkers that could be used for early diagnosis of the disease. Furthermore, the results associated with the differences found between early and advances stages of disease, if validated in proper cohorts of patients, could represent an objective and accurate method for patients follow up.

Disclosure: All authors have declared no conflicts of interest.

25PD | CIRCULATING MICRO-RNA PROFILING IN PATIENTS WITH ADVANCED NON-SQUAMOUS NON SMALL-CELL LUNG CANCER RECEIVING BEVACIZUMAB/ERLOTINIB FIRST-LINE TREATMENT FOLLOWED BY PLATINUM-BASED CHEMOTHERAPY AT DISEASE PROGRESSION (SAKK 19/05)

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Background: This study examined circulating miRNA profiles in peripheral blood from patients with non-squamous non small-cell lung cancer (NSCLC) receiving 1st-line bevacizumab/erlotinib followed by platinum-based chemotherapy at the time of progression [Swiss Group for Clinical Cancer Research (SAKK) 19/05].

Patients and Methods: We included 50 patients with baseline and 24 hours blood samples. The primary and secondary objectives of the study were to identify prognostic (overall survival, OS) and predictive (percentage of tumor shrinkage and time-to disease progression) miRNA’s. Following confirmation of RNA content and quality, patient samples were analyzed with Agilent human miRNA 8×60K microarrays, each glass slide formatted with eight high-definition 60K arrays. Each array contained 40 probes targeting each of the 1,347 miRNAs. Data preprocessing included quantile normalization using robust multi-array average (RMA) algorithm. Predictive and prognostic miRNA expression profiles were identified by using Spearman’s rank correlation test (percentage tumor shrinkage) or log-rank testing (for time-to-event endpoints).

Results: Data preprocessing kept 49 patients and 424 miRNAs for further analysis. Ten miRNAs significantly predicted OS (p <0.05), including mir-29a (HR = 6.44, 95%-CI 2.39–17.33, p = 0.0002). Six miRNA candidates (hsa-mir-29a, hsa-mir-542–5p, hsa-mir-502–3p, hsa-mir-376a, hsa-mir-500a, hsa-mir-424) were found to be insensitive to perturbations according to internal cross-validation (jackknifing) on their HR for OS. The respective principal component analysis defined a meta-miRNA signature including these 6 miRNA candidates that significantly predicted OS in the study population (HR = 0.66, 95%-CI 0.53–0.82, p = 0.0001). MicroRNA-665 significantly correlated with the percentage tumor shrinkage following 1st-line bevacizumab/erlotinib (rho = 0.62, p = 0.0002).

Conclusions: Circulating miRNA-profiling successfully identified a prognostic 6-gene signature in patients with advanced non-squamous NSCLC. This technique should be further evaluated for treatment selection and monitoring in patients with advanced NSCLC.

Disclosure: All authors have declared no conflicts of interest.

26PD | FORETINIB (GSK1363089), A MULTIKINASE INHIBITOR OF MET AND VEGF-S, OVERCOMES RESISTANCE TO BEVACIZUMAB IN AN IN VIVO MODEL OF ACQUIRED BEVACIZUMAB RESISTANCE

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Background: Bevacizumab, a monoclonal antibody targeting vascular endothelial growth factor (VEGF), has promising therapeutic