**High prevalence of concomitant oncogene mutations in prospectively identified patients with ROS1-positive metastatic lung cancer**

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**Purpose:** We report clinical outcomes and genomic findings of patients with ROS1-positive lung cancer that were prospectively identified within a multiplex biomarker profiling program at the West German Cancer Center.

**Patients and Methods:** Standardized immunohistochemistry, FISH and mutation analyses were prospectively conducted in 665 patients with metastatic lung adenocarcinoma. Clinical and epidemiological data were retrieved from the institutional database.

**Results:** ROS1 positivity by immunohistochemistry was detected in 22 lung cancer patients (5.6%), including 12 patients (3.1%) with FISH positivity using ≥15% events as cut-off. 32% of ROS1-positive cases presented with concomitant oncogenic driver mutations involving EGFR (4 cases), KRAS (2 cases), PIK3CA and BRAF. Five patients had sustained responses to crizotinib. Three cases which were initially classified as ROS1 FISH-negative passed the threshold of 15% positive events when tumor biopsies were analyzed at progression. Median overall survival of 22 ROS1-positive lung cancer patients (not reached) was significantly prolonged as compared to 261 pemetrexed-treated patients with EGFR/ALK-negative lung adenocarcinoma (24.4 months, p = 0.039). Overall survival of 12 ROS1-positive lung cancer patients from initiation of pemetrexed-based chemotherapy was significantly prolonged compared to 169 pemetrexed-treated patients with EGFR/ALK-negative adenocarcinoma (p = 0.011).

**Conclusion:** ROS1-positive metastatic lung adenocarcinomas frequently harbor concomitant oncogenic driver mutations. Levels of ROS1 FISH-positive events are variable over time. This heterogeneity provides additional therapeutic options if discovered by multiplex biomarker testing and repeat biopsies.

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**Molecular Pathology**

**ID0597**

**Viral-cellular DNA junctions are ideal molecular markers for assessing intra-tumor heterogeneity and for the detection of cell-free tumor DNA in serum**

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**Aim:** Integration of HPV DNA into the host genome is frequently observed during cervical carcinogenesis and can confer a selective growth advantage to the affected cell. The resulting viral-cellular junction sequences are highly tumor specific. By using viral-cellular junctions as tumor cell markers we addressed the question of intra-tumor heterogeneity and their use for the detection of circulating tumor DNA (ctDNA) in the serum of cervical cancer patients.

**Methods:** For intra-tumor heterogeneity analyses tumors of 8 patients displaying up to 5 viral-cellular junctions per tumor were included. From cryosections of tumor sub-blocks representing different tumor regions, tumor islands were micro-dissected and directly analyzed in junction-specific PCR assays. For the detection of circulating tumor DNA junction-specific PCR assays were applied to sera of 21 patients. Sera were collected preoperatively and during follow up.

**Results:** Intra-tumor heterogeneity was evident in only one tumor. Seven of 8 tumors showed remarkable homogeneity. In five of 21 analyzed preoperative serum samples junction fragments could be specifically amplified. No correlation was found between the detection of viral-cellular junction fragments and TNM-stage. However, Kaplan Meier analyses of the patients with primary tumors revealed a significant association between the detection of junction fragments in pre-operative sera and a reduced recurrence free survival (p = 0.003)

**Conclusions:** Viral-cellular junction fragments are representative tumor cell markers and thus comprise highly specific novel biomarkers which may prove to be of value for disease monitoring and prognostication.
pared to placebo, NSAIDs and morphine, the incidence of adverse effects (AEs) was not increased.

**Conclusion:** Dipyrone can be recommended for the treatment of cancer pain as an alternative to other non-steroids either alone or in combination with opioids. It can be preferred over NSAIDs due to the presumably favorable side effect profile in long-term use, but comparative studies are not available for long-term use.

**Questions:**
- a) What influence does advanced breast cancer disease have on family life?
- b) What needs arise in families?
- c) What resources do these families fall back on?

**Method:** The Grounded Theory qualitative research approach was used for this study. Data was collected by means of guideline-supported interviews. The 29 interviews were transcribed and systematically analysed in order to develop the concepts. The application to the Ethics Committee was approved.

**Results:** Not only the individual family members are influenced by the approaching decease of the wife/mother and the end of existence as a family, but also the complete family system. The emotional strain on the family members is high. The importance of the disease and the approach to it differ for each individual person. The existential threat to family life, the specific approach to the woman's last phase of life in the present and the outlook on the future situation are important themes for all of the family members.

**Summary:** The results of this study give an indication of how specially trained care experts could provide continuous support for the family members in their approach to the illness and death of the wife/mother.

**ID0577**

**Can a pathological complete response after neoadjuvant chemotherapy in breast cancer patients be diagnosed by minimal invasive biopsy?**

J. Heiß1, B. Schäfgen1, P. Sinn1, H. Richter1, A. Harcos1, C. Gomezi1, A. Stieber1, A. Hennigs1, G. Rauch1, A. Schneeveis1, F. Schuetz1, C. Sohn1, M. Golatta1

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**Background:** Neoadjuvant chemotherapy (NACT) is increasingly used and pathological complete response (pCR = ypT0) in the breast is a achievable result. As breast imaging does not accurately predict a pCR, this study aimed to systematically explore the ability of a minimal invasive biopsy to diagnose pCR after NACT.

**Methods:** 50 patients were included in this review-board approved prospective, monocenter cohort study between Aug. 2014 and Feb. 2015. Ultrasound guided, vacuum-assisted, minimal-invasive biopsy (VAB) was performed after NACT and before surgery. To assess the possible sampling error, representativeness the sample was evaluated during the VAB by the performing physician, and afterwards by radiography and histopathology. Breast conserving surgery or mastectomy was performed in every case after VAB. Residual cancer in VAB and surgical specimen was defined a positive result. Negative predictive values (NPV) and false negative rates (FNR) to predict a pCR (= ypT0) in surgical specimen were calculated for the whole study cohort and different subgroups defined by the evaluation of the representativeness.

**Findings:** Differentiating VAB specimen with and without vital tumor cells (ignoring the evaluation of representativeness) yielded a NPV of 76.7% and an FNR of 25.9%. Given the pathologically diagnosed representativeness of the VAB specimen (n = 38), the NPV was 94.4% (95% CI 87.1–100.0) and the FNR 4.8% (95% CI 0.0–11.6). Non-representative VABs were mainly due to a bad visibility of the target lesion in ultrasound.

**Interpretation:** Given a representative (according to the pathologist’s evaluation) VAB minimal invasive biopsy can accurately diagnose a pCR. A confirmative, multi-center, diagnostic trial to validate the results is warranted.

**ID0584**

**Families and breast cancer: Needs and coping in the final phase of life**

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To date, there are only very few research findings dealing with the families of patients with advanced breast cancer. Not only do the women themselves suffer but also the members of their families. In order to widen the knowledge on this phenomenon, we examined how the families experienced the palliative phase of breast cancer, how they coped with it and what their own needs were.

**Poster**

**Breast Cancer**

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