ER and PgR negativity, HER2 positivity, high nuclear grade, lymph node metastasis and large pathological tumour size as significant variables associated with HOXB9 expression. Notably, 12 (92.3%) out of 13 triple negative breast cancer showed HOXB9 expression. The disease-free survival (DFS) and the overall survival were significantly different between the HOXB9 positive and negative group (HR = 20.714, p = 0.001, HR 9.206, p = 0.003, respectively). A Multivariate analysis indicated that HOXB9 expression was the independent prognostic factor for DFS (HR = 15.532, p = 0.009). In subgroup analysis, HOXB9 positive breast tumours showed a significant increase in the number of micro vessel density and the Ki-67 ratio in comparison with HOXB9 negative.
Conclusions: Our results suggest that HOXB9 expression promoting the tumour proliferation and angiogenesis in tumour microenvironment is a significant prognostic biomarker for clinical outcomes in breast cancer patients.

1446 POSTER

Evaluation of CTL Antigen 4 (CTLA-4) Expression as Prognostic Factor in Non-small Cell Lung Cancer (NSCLC)

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Background: CTLA-4, a close homologue to CD28, is a vital negative regulator of T-cell activation and proliferation. Preclinical studies and clinical trials have demonstrated that the administration of antibodies that block CTLA-4 can provoke the elimination or reduction of established tumours. We previously reported that CTLA-4 is expressed by NSCLC cell lines providing evidence of its involvement in apoptosis induction upon engagement with soluble CTLA-4 ligands (Contardi E, Int J Cancer 2005). The present study examined the expression of CTLA-4 on tumour tissues of patients (pts) with radically resected stage I-IIIA NSCLC.
Materials and Methods: Tumour tissue samples from 82 pts who underwent surgery between 7/2005−3/2007 were analyzed for expression of CTLA-4 using immunohistochemistry (IHC). Viable tumour was sampled in triplicate for tissue microarray analysis, and slides were stained by IHC with 14D3 mAb (eBioscence, San Diego, CA, USA). All tissue arrays were independently scored by two observers (M.T. and S.S.), blinded to the patients. CTLA-4 score was calculated using the following formula: $(1+I)\times PC$, where I is the staining intensity and PC the percentage of tumour cells that stained at each intensity, respectively. The score median value was a priori chosen as the cutoff point for classifying tumours as CTLA-4-negative (score $\leqslant$20) and positive (>20). Results: The median follow-up time was 41 months (range 28−54), and 27 deaths were observed. CTLA-4 expression was positive in 48% of tumours and similar in males and females (47 vs 47%), age $\leqslant$70 and >70 (46 vs 49%), ex-never smokers and current smokers (46 vs 47%), whereas was higher in non-squamous than in squamous carcinoma (53 vs 36%). Cox's multiple regression analysis identified stage and CTLA-4 expression as the only variables associated with survival. The hazard ratio (HR) was 2.76, (95% CI, 0.9−8.3; p = 0.07) and 6.61 (95% CI, 2.6–16.8; $p \leqslant 0.001$) for tumour stage II and III compared to stage I respectively, and 0.39 (95% CI, 0.2−0.9; p = 0.03) for CTLA-4 score >20. Conclusions: Our results demonstrate an association between CTLA-4 expression and increased overall survival in NSCLC pts suggesting a prognostic role for CTLA-4 in NSCLC. An increased CTLA-4 expression may contribute to NSCLC progression by modulating the interaction of microscopic disease with CTLA-4 ligand-expressing cells leading to NSCLC cell death.

1447 POSTER

First-line Treatment of Non-Small Cell Lung Cancer Under Routine Conditions: Observational Study (FRAME)

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Background: FRAME is a non-interventional, prospective observational study of first-line treatment (FLT) of advanced non-small cell lung cancer (NSCLC) in routine disease management. This analysis of baseline data provides insights to what extent histological sub-typing and the use of additional prognostic or predictive biomarkers are currently considered for differential therapeutic decisions.
Material and Methods: 1569 patients diagnosed with stage IIIB/IV NSCLC who initiated FLT with any platinum-based doublet chemotherapy, with or without targeted agents, were observed in routine practice. Patients' baseline characteristics, first-line treatment and all diagnostic procedures were collected upon study enrolment.
Results: FRAME was performed in 11 EU countries; baseline characteristics reflect this geographic location with a predominance of Caucasian patients (1.3% Asian origin) and smokers (84%). Median age was 64 yrs (33−87), females: 29%, stage IV: 77%, performance status 0−1: 82%.
Histological diagnosis was obtained in 80% while only cytological was obtained in 20% of patients. Not Otherwise Specified (NOS) was final diagnosis for 11% of patients. Most common reasons for NOS diagnosis were: 'Sub-typing technically not possible' (43%) and 'Not important for treatment decision' (40%).
At least one of the IHC markers was used in 54% of cases (p63−9%, ck14−2%, ck7−39%, ck5/6−18%, TTF-1−48%, cd56−4%, others-24%). EGFR, ERCC1, TS, or other predictive biomarkers were assessed in 21% of pts. EGFR mutation was positive in 12% of 308 tested patients.
FLTs were platinum-based therapy plus one of: pemetrexed 36%, gemcitabine 23%, taxanes 19%, vinorelbine 19%, others 3%. Ninety-seven percent of patients treated with pemetrexed and 97% with bevacizumab had a diagnosis of non-squamous NSCLC. Concurrent targeted agents were administered in 8% of cases (mostly bevacizumab, *7%).* Key factors identified by physicians for choice of FLT were 'Histopathological/cytological diagnosis' 77%, 'Performance status' 63% and 'Age' 53%.
Conclusions: In this large non-interventional study of FLT for NSCLC, a relatively high level of histological testing was observed (80%), likely resulting in low NOS (11%) diagnosis. In addition, IHC (54%) and predictive biomarkers (21%) were routinely assessed.

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Correlation of Topoisomerase IIα and MIB-1 Expression on Tissue Microarray of Breast Carcinomas

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Background: Breast cancer is the most common malignancy in females. Measurement of cell proliferation in breast carcinomas was shown to have prognostic importance, primarily measured by MIB-1 labelling index. A nucleic enzyme, topoisomerase IIα (TopIIa) expression was reported to be linked to cell proliferation that estimated the number of proliferative cells in actively cycling cells of both normal and neoplastic cells. The aim of this study was to evaluate TopIIa protein expression in breast carcinomas and compare with MIB-1 expression. We also analyzed TopIIa correlation with known outcome variables.
Materials and Methods: Using tissue microarray (TMA), we immunostained 70 breast carcinomas for TopIIa and MIB-1. A TopIIa staining index (TI) was calculated by the mean number of positive cells per high power magnification and was interpreted as positive (TI > 1) and negative (TI < 1) while MIB-1 was considered positive if 10% or more of the nuclei were stained.
Results: Forty-one of 70 breast carcinomas (59%) were TI positive (mean, 15.04 ± 18.09; range, 1.12 to 85.24) and 29 (41%) cases were TI negative (mean, 0.04 ± 0.12; range, 0–0.46). Our data demonstrated 64.7% concordance between TopIIa with MIB-1 expression (kappa = 0.239, p = 0.042). There were no significant association observed in this study between TopIIa overexpression and other known outcomes including lymph node metastases (46%, p = 0.467), low tumour grade (42%, p = 0.353), tumour size greater than 2 cm (71%, p = 0.634), ER positive (78%, p = 0.145), PR positive (76%, p = 0.093) and HER-2 overexpression (22%, p = 0.899).
Conclusions: A significant association between TopIIa and MIB-1 overexpression suggests that TopIIa maybe a potential proliferative marker that is similar or better than MIB-1.