

groups, however pemetrexed appears to be more effective for non-squamous than for squamous histology. A possible explanation for this result is the previously observed overexpression of TS in squamous cell carcinoma.

	Non-squamous group		Squamous group	
	Pemetrexed (n = 205)	Docetaxel (n = 194)	Pemetrexed (n = 78)	Docetaxel (n = 94)
% ECOG PS 2	12.5	10.1	8.3	17.4
% TSPC <3 months	51.0	51.0	48.7	41.9
% Stage IV	81.5	78.9	57.7	66.0
% Male	60.5	69.1	89.7	88.3
Median OS, months	9.3	8.0	6.2	7.4
OS HR (95% CI)	0.778 (0.607, 0.997)		1.563 (1.079, 2.264)	
Median PFS, months	3.1	3.0	2.3	2.7
PFS HR (95% CI)	0.823 (0.664, 1.020)		1.403 (1.006, 1.957)	

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POSTER

EGFR mutations and response to TKIs therapy in NSCLC patients pre-treated with chemotherapy

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Background: The aim of this work was to study the association between EGFR mutations (mut) and response to conventional chemotherapy (CHT) and tyrosine kinase inhibitors (TKIs) in NSCLC pts of Caucasian origin.

Methods: This retrospective analysis was conducted on 103 consecutive stage I to IV NSCLC pts treated with TKIs (gefitinib or erlotinib) from July 2002 to November 2006 after failure of platinum-based CHT. Genomic DNA was isolated from paraffin-embedded tumor specimens, amplified for EGFR (exons 18 to 21) by touchdown hemi-nested PCR and sequenced in both sense and antisense directions. Response to CHT and TKIs was assessed according to RECIST criteria.

Results: Median age was 60 yrs (range 25–81.5); M/F: 59/44, ECOG-PS 0/1/2/3/68/30/4/1; stage: I/II/III/IV 4/5/35/59; adeno/bac/squamous/large-cells/other:66/9/20/3/5; never/former/current smokers: 26/20/36. EGFR mut were detected in 19 pts (18.5%); 13 (13.8%) deletions in exon 19, 3 (2.9%) point mut in exon 20 (one pt had 2 mutations) and 3 (2.9%) missense mut in exon 21. No associations were detected between EGFR mut and adeno/bac histotype (p=0.51), smoke (p=0.23) and gender (p=0.14). Disease control rate to TKIs therapy was 54.4%, including 1 CR (pt. with EGFR mutation), 21 PR and 34 SD and objective response rate (RR) was 42%. Median time to progression was 4.4 and median survival 23.7 months. EGFR mut had a significant impact on response (PR/CR, 42% p=0.015) to TKIs while they did not influence response to CHT. Cox's multivariate analysis including gender, smoke, stage and histotype showed that EGFR mut did not reach statistical significance for progression free survival (PFS) (p=0.52) and overall survival (OS) (p=0.50); only adeno/bac histotype was a prognostic factor for longer PFS (p=0.01) and OS (p=0.04).

Conclusions: In our experience EGFR mut seem to influence RR in pts treated with TKIs after platinum-based CHT. These data will be refined by FISH analysis of EGFR gene copy number, immunohistochemistry for EGFR and phosphorylated Akt (p-Akt) protein and KRAS mutations.

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POSTER

Clinical and potential prognostic significance of serum mesothelin and osteopontin in chemotherapy treated patients affected by malignant pleural mesothelioma

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Background: Malignant pleural mesothelioma (MPM) is a highly aggressive tumour for which no fully reliable serum tumour markers are available for diagnosis and monitoring treatment response. Candidate biomarkers

for MPM diagnosis include soluble serum mesothelin-related peptides and osteopontin, and novel ELISA systems have recently been developed for their detection in the sera of MPM patients. The aim of this work was to determine whether a correlation exists between these serum markers and clinical response.

Patients and Methods: serum of 15 patients (11 males, 4 female; median age 61 years) with histologically proven, inoperable MPM were tested; samples were collected before and after at least 2 cycles of chemotherapy. Chemotherapy was always pemetrexed and a platinum compound; only one patient received second line chemotherapy with gemcitabine and vinorelbine. Responses after chemotherapy were recorded according to RECIST criteria. Evaluations were always made by two independent physicians on spiral CT scans.

Results: 8 stable diseases, 2 partial response 1 complete response and 4 progressive diseases have been observed. A strong correlation was observed among Osteopontine and Mesothelin serum levels (R sq linear 0.83 p<0.001). No clear relationship resulted between clinical responses and the levels of the two markers. The patient with a partial response showed the lowest level of mesothelin before treatment, value that declined toward zero after chemotherapy, and a very low level of Osteopontine, which became again the lowest after chemotherapy. Mean level of mesothelin before treatment in responders was considerably lower than in non responders or in stable disease (1.46 vs 5.55).

Conclusions: Osteopontine and Mesothelin levels in serum of MPM are strongly correlated. Clinical response (progression and stable diseases) does not appear to be related to markers levels even if the only patient with partial response showed the lowest levels of the two markers. Other patients will be added to the study and the follow-up will prosecute to evaluate the predictive significance of these two markers and their relationship with patients' survival.

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POSTER

Primary tumour standardized uptake value (SUV max) measured on fluorodeoxyglucose positron emission tomography (FDG-PET) is of prognostic value for survival in non-small cell lung cancer (NSCLC): a systematic review and meta-analysis (MA) by the European Lung Cancer Working Party for the IASLC Staging Project

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Background: FDG-PET is an effective imaging technique for assessing cTNM in NSCLC. The prognostic role of SUV max, measured on the primary tumour, has been suggested in several studies of limited sample sizes. We aimed to assess more precisely its effect on survival by aggregating results of individual studies in a meta-analysis of the literature.

Methods: We searched for all studies assessing the prognostic role of SUV max on survival in NSCLC. We evaluated the methodology of each eligible study (using a non validated quantitative scale with 44 points for the clinical data and 40 points for the FDG-PET data, designed for the purpose of the review). For each publication, we extracted an estimate of the hazard ratio (HR) for comparing patients with a low or high SUV and aggregated the individual HRs into a combined HR, using a random-effects model.

Results: Eleven studies including NSCLC only, published between 1998 and 2006, were eligible. Most of them included patients with stages I to III/IV and used a SUV assessment corrected for weight. Numbers of patients ranged from 38 to 162 (total: 1108); 9 studies identified a high SUV as a poor prognostic factor for survival and 2 concluded to a non significant effect. The qualitative evaluation provided a median of 61% for the clinical data and of 50% for the FDG-PET data. SUV measurement and threshold for defining high SUV were study dependent, 7 studies looked for a "best" cut-off (maximizing the logrank test statistic) however without adjusting the p value for multiplicity.

	Number of patients	HR	95% CI
All studies (n = 11)	1108	2.13	1.54–2.95
"Best cut-off" excluded (n = 6)*	456	1.77	1.01–3.12
Stage IV excluded (n = 5)	558	2.22	1.38–3.58

*for two studies, it was possible to use median value of SUV max instead of the author's best cut-off