Results: Median time between CT scan and surgery was 18 days (range 1-48). The analysis revealed a moderate correlation between CT tumor volume and weight (p=0.001, correlation coefficient 0.58, CT volume and tumor volume at surgery showed strong correlation (p=0.001, correlation coefficient 0.65). No significant correlation was observed between cT stage and tumor weight (p=0.1, correlation coefficient 0.31), but a moderate correlation between cT stage and CT volume (p=0.001, correlation coefficient 0.58) as well as specimen volume (p=0.008, correlation coefficient 0.58). There was a moderate correlation of tumor weight with pT stage (p=0.02, correlation coefficient 0.42), but no correlation of CT volume (p=0.1, correlation coefficient 0.31) as well as specimen volume with the pT stage (p=0.2, correlation coefficient 0.32).

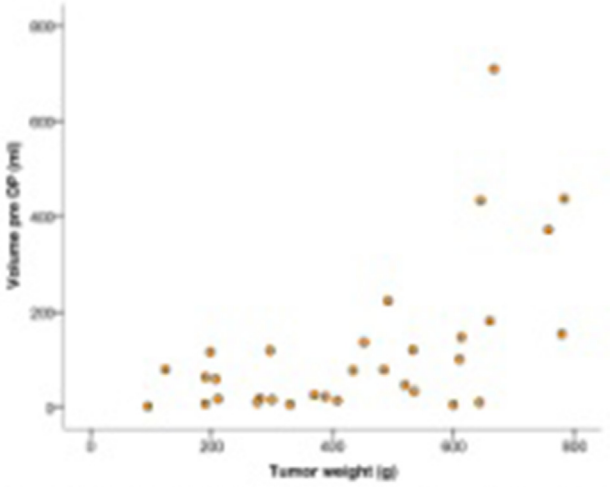

Figure 1: Spearman correlation of CT volume and specimen volume (n=21): correlation coefficient 0.65, p=0.001

Conclusion: The correlation between preoperatively assessed CT tumor volume and volume of the resected specimen showed a strong correlation. To assess the prognostic role of CT measured tumor volume a correlation to prognosis has to be performed before implementation as a new T-factor.

Keywords: Tumor weight, Tumor volume, Mesothelioma, TNM staging

OA23.01
Anti-EGFR Monoclonal Antibodies plus Chemotherapy in the First-Line Treatment of Advanced NSCLC: A Meta-Analysis

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Background: Monoclonal Antibodies (mAbs) against the Epidermal Growth Factor Receptor (EGFR) in association with platinum-based doublet chemotherapy have emerged as a potential first-line treatment option for advanced non-small cell lung cancer (NSCLC). This study was conducted to systematically review available data and evaluate the efficacy and toxicity of anti-EGFR mAbs plus chemotherapy vs chemotherapy alone for advanced NSCLC.

Methods: We carried out a search on network databases and oncology conference abstracts for studies between 1990 and January 2016. Only prospective randomized clinical trials were included. Primary endpoints were overall survival (OS) and toxicity frequency. Secondary endpoints were progression-free survival (PFS) and overall response rate (ORR). Subgroup analysis was performed assessing histological subtypes, EGFR protein expression by immunohistochemistry (IHC), EGFR gene copy number by fluorescence in-situ hybridization (FISH), EGFR mutation status, and smoking status.

Results: Seven studies (2 with necitumumab and 5 with cetuximab) were included with 5,057 patients. Compared to chemotherapy alone, significant benefits were demonstrated by the addition of anti-EGFR mAb to chemotherapy in OS (HR 0.90; 95%CI 0.84-0.95), PFS (HR 0.93; 95%CI 0.87-0.98), and ORR (OR 1.27; 95%CI 1.06-1.51). In subgroup analyses, the association of anti-EGFR mAb was associated with improved OS among patients with squamous histology (HR 0.84; 95%CI 0.76-0.92), tumours with high EGFR expression by IHC (HR 0.83; 95%CI 0.70-0.98), and smokers (HR 0.87; 95%CI 0.79-0.96). Patients with squamous histology and high EGFR expression by IHC achieved the highest benefit with the association (HR 0.71; 95%CI 0.59-0.86). The OS with the association also seemed to be higher in EGFR FISH negative and in EGFR wild-type tumours, but without statistical significance. Chemotherapy plus anti-EGFR mAb caused more grade 3 or worse adverse events (OR 1.73; 95%CI 1.50-2.00), remarkedly these known to be associated with anti-EGFR therapy, such as acne-like rash (OR 34.13; 95%CI 16.40-71.00) and hypomagnesemia (OR 6.23; 95%CI 3.04-12.77).

Conclusion: Anti-EGFR therapy plus platinum-based doublet chemotherapy as first-line treatment demonstrated significant efficacy benefits with acceptable toxicity for advanced NSCLC. This benefit is more expressive among squamous histology with high EGFR

expression. EGFR protein expression by IHC seems to be a predictive marker for survival in the association group. Further research is needed to corroborate these findings.

Keywords: anti-EGFR, biomarker, Targeted therapy, Individual Medicine

OA23.02

Efficacy and Safety of Necitumumab Continuation Monotherapy in Patients with EGFR-Expressing Tumors in SQUIRE, a Phase 3 Study

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Background: SQUIRE (NCT00981058) demonstrated adding necitumumab (N) to gemcitabine/cisplatin (GC) improved survival in patients with Stage IV squamous NSCLC (SQ-NSCLC). Retrospective analysis revealed consistent treatment effect in favor of patients receiving N monotherapy as continuation after chemotherapy (CT) (GC+N continuation patients) versus continuation therapy-eligible GC arm patients (GC non-progressors). In the EU, N is approved for patients with EGFR-expressing tumors. We repeated the analysis in this patient population.

Methods: Patients with Stage IV SQ-NSCLC were randomized 1:1 for ≤6 cycles of G (1250 mg/m^2 iv, Days [d] 1,8) and C (75 mg/m^2 iv, d1) either with or without N (800 mg iv, d1,8). Patients in GC+N without progression continued N until progressive disease (PD). SQUIRE included mandatory tissue collection. EGFR protein expression was assessed by IHC in a central lab (Dako EGFR PharmDx kit). Analyses were done in EGFR-expressing patients (EGFR >0). Patients who received ≥4 cycles of CT without PD were included. Overall survival (OS) and progression-free survival (PFS) were calculated by Kaplan-Meier method. 95% CIs and hazard ratios estimated using stratified Cox proportional hazards model.

Results: Of 1093 patients (ITT population), 982 patients (89.8%) had evaluable IHC assay results; 935/982 (95.2%) had EGFR>0. GC+N arm continuation therapy patients included 228 patients with EGFR>0 and 194 patients (EGFR>0) were GC arm non-progressors. Baseline characteristics were similar except gender (Males: 81% in GC+N vs 91% in GC arm). CT exposure was balanced. Median OS from randomization in GC+N vs GC was 16.1 vs 14.9 months; HR 0.76 (95% CI, 0.61, 0.95). Median PFS in GC+N vs GC was 7.4 vs 6.9 months; HR 0.81 (95% CI, 0.66, 1.00).

Selected Treatment Emergent Adverse Events (TEAEs)

Category	GC+N N = 228, %		GC N = 194, %		Necitumumab N = 228, %	
	Chemotherapy Phase				Continuation Phase	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Neutropenia	54.8	33.3	55.2	32.0	0.4	0.4
Febrile neutropenia	0.4	0.4	1.5	1.5	0.9	0.4
Anemia	43.0	9.6	50.5	8.8	13.2	1.3
Thrombocytopenia	25.4	9.6	28.9	11.9	0.9	0
Fatigue	38.2	4.8	41.2	4.1	9.6	0.9
Hypomagnesemia	39.9	14.5	17.5	0.5	15.4	2.2
Rash	86.0	5.3	10.3	0.5	26.3	4.4
Hypersensitivity/IRR	0.4	0	3.1	0	0	0
Conjunctivitis	7.9	0	3.6	0	5.3	0.4
Interstitial lung disease (pneumonitis)	0.9	0.4	0	0	0.4	0.4
Arterial thromboembolic event	3.9	1.3	0.5	0	2.2	1.8
Venous thromboembolic event	8.3	2.6	4.6	1.0	2.6	1.8

Conclusion: In patients with EGFR-expressing tumors, a consistent treatment effect in favor of GC+N continuation maintenance compared to GC non-progressors was observed, similar to ITT population with no unexpected increases in AEs.

Keywords: NSCLC, EGFR, squamous, Necitumumab

OA23.03

Second-Line Afatinib for Advanced Squamous Cell Carcinoma of the Lung: Analysis of Afatinib Long-Term Responders in the Phase III LUX-Lung 8 Trial

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