

42–77). Fifteen pts had mutations in exon 19 and 9 in exon 21. Eight pts had ECOG 0, 14 ECOG 1 and 2 ECOG 2. Most common sites of metastases were bone (37.5%), liver (33.3%) and brain (20.8%). Median time since diagnosis was 26.9 months and the median of previous administered treatments was 3. The median number of cycles of E and V administered per pt were two (range 1–9). No objective antitumour responses were observed. Seven pts experienced stable disease, of whom two lasted more than 9 months. Median TTP was 2.0 months and 29% of pts were free of disease progression at 12 weeks. The most common toxicities were mild or moderate (grade I-II) and include anaemia (75.0%), diarrhoea (62.5%), rash (45.9%), asthenia (45.9%), nausea (41.7%), vomiting (37.5%), anorexia (37.5%), dry skin (33.3%), xerostomia (20.8%). The most common grade III-IV adverse events were asthenia (20.9%), diarrhoea (12.5%) and anorexia (8.3%).

Conclusions: Concurrent administration of E 150 mg PO daily plus oral V 400 mg QD on days 1–7 and 15–21 is feasible. No objective antitumour activity was detected with the addition of V to E treatment; however, some prolonged stabilizations have been observed in this group of advanced NSCLC pts with EGFR mutations after E progression.

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POSTER

MRNa Levels and Genetic Status of Genes Involved in the Epidermal Growth Factor Receptor (EGFR) and the Nuclear Factor κ B (NF- κ B) Pathways in Metastatic Non-Small-Cell Lung Cancer (NSCLC) Patients (P)

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Background: Little is known about the potential effect of genetic alterations in the NF κ B and Notch pathways on NSCLC p. Musashi 2 activates HES-1 in the Notch pathway, and HES-1 can abrogate CYLD. A20, AEG-1, EZH2 and TRAF6 are also involved in NF κ B activation. BRCA1 and RAP80 are modulators of cisplatin-based chemotherapy. Mutations in NF κ BIA and DUSP22, which prevent NF κ B activation, were described in the sequencing exome of a single NSCLC p, together with K-ras mutations.

Material and Methods: mRNA expression of Musashi 2, CYLD, HES-1, A20, EZH2, AEG-1, TRAF6, NF κ BIA, RelA, BRCA1 and RAP80 was analyzed by quantitative RT-PCR in tumour samples from 60 advanced NSCLC p. Expression levels by terciles were correlated with clinical characteristics and outcome to chemotherapy. Mutations in NF κ BIA and DUSP22 were sequenced in 28 and 21 patients, respectively, and in 12 cancer cell lines.

Results: Patient characteristics: 36 male; 39 adenocarcinomas; 22 smokers; 23 bone metastases; 9 EGFR mutations; 10 K-ras mutations. No NF κ BIA or DUSP22 mutations were observed in any of the p or cell lines. PFS was 12.3 months (m) for p in the lowest tercile of AEG-1 expression vs 9.3 m for p in the intermediate tercile and 4.8 for p in the highest tercile ($P = 0.002$). The multivariate analysis showed that only AEG-1 expression was associated with shorter PFS (HR, 1.43; $P = 0.006$). Expression levels of the other genes did not correlate with outcome. In patients with low levels of both BRCA1 and AEG-1, PFS was 13.02 months, compared to 5.4 months in those with high levels of both genes and 7.7 months for those with other combinations ($P = 0.025$). The multivariate analysis for PFS confirmed the role of high BRCA1/AEG-1 expression (HR, 3.1; $P = 0.01$).

Conclusions: The present study helps to improve our understanding of the clinical relevance of genetic factors in metastatic NSCLC. AEG-1 and BRCA1 mRNA expression could be a useful prognostic model for the management of NSCLC p.

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POSTER

Expressions of IGF-1R and IGFBP3 in Advanced Non-small Cell Lung Cancer (NSCLC)

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Background: The insulin-like growth factor (IGF) pathway plays an important role in cell proliferation, differentiation, and apoptosis, and

IGF induces those effects mainly through IGF receptor-1 (IGF-1R). The activities of IGF are strictly regulated by a family of IGF binding proteins (IGFBP), especially IGFBP3, a major serum carrier protein for IGF. To date, however, insufficient data have been accumulated concerning the expressions of IGF and IGFBP3 in advanced NSCLC.

Material and Methods: Between January 2006 and February 2009, 191 patients were histologically diagnosed as having non-small cell lung cancer (NSCLC) in our hospital, and 74 patients were treated by chemotherapy alone. We examined immunohistochemical expression of both IGF-1R and IGFBP3 in 68 patients who were definitively diagnosed as having adenocarcinoma or squamous cell carcinoma among the 74 patients. We also investigated the association of IGF-1R and IGFBP3 expression and clinical background, including histology, and survival. Staining of each antibody was considered positive if >10% of the tumour cells were stained.

Results: Clinical characteristics of the included patients were as follows: median age was 68 (range, 29–86), male/female=40/28, stage III/IV=18/50, PS 0–1/2–4=58/10, smoker/non-smoker=44/24, Sq/Ad=13/55. Expression of IGF-1R and IGFBP3 was observed in 37 (54%) and 11 patients (11%), respectively. IGF-1R expression was detected more frequently in Sq patients (100%) than Ad patients (44%, $p < 0.001$), while IGFBP3 expression was not significantly associated with histology ($p = 0.356$). Both IGF-1R and IGFBP3 expression were not significantly associated with the response to chemotherapy ($p = 0.196$ and $p = 0.846$, respectively). Among all factors, including IGF-1R and IGFBP3 expression, only PS was significantly associated with OS ($p < 0.001$).

Conclusions: IGF-1R expression, not IGFBP3 expression, was significantly associated with histology; however, neither of these was correlated with chemo-sensitivity or survival in advanced NSCLC patients treated by chemotherapy.

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POSTER

EGFR Mutation Testing and First Line Treatment of Patients With Advanced NSCLC and Positive EGFR Mutation Status – Results From a German Registry

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Background: In patients diagnosed with advanced non-small-cell lung cancer (NSCLC), somatic mutations in the epidermal growth factor receptor (EGFR) gene are predictors of sensitivity to EGFR tyrosine kinase inhibitors (TKIs). With effective TKIs available the EGFR mutation analysis is becoming increasingly integrated into the diagnostic routine.

Methods: REASON is an AstraZeneca sponsored registry (ClinTrials ID: NCT00997230) being conducted in Caucasian patients in Germany. Between Nov 2009 and Mar 2011, 150 sites recruited 4,300 patients with histologically confirmed locally advanced/metastatic NSCLC stage IIIB/IV for whom an EGFR mutation analysis was planned. Data collected include demographic information, tumour anamnesis, result of EGFR gene mutation analysis and therapeutic agents selected for the intended first-line palliative therapy. Furthermore, clinical outcomes for patients with positive EGFR mutation status (EGFR mut+) were correlated with the applied treatment regimen.

Results: To date, information covering the period up to the first-line treatment is available on 3,155 patients. The rate of sensitizing EGFR mutations was 9.8% (all histologies, 12.8% adenocarcinoma), with the majority analysed in the primary tumour tissue (84%). The median turnaround time for testing was 11 days. Among those patients with EGFR mutations, there was a similar proportion of non-smokers and smokers (47% vs 53%), and approx. twice as many females as males (62% vs 38%). The rate of female EGFR mutation positive patients was twice as high as the respective rate of male patients (62% vs 38%). 274 out of all 310 EGFR mutation positive patients had adenocarcinoma histology (88%). Mutation analyses were performed locally at 67 pathology laboratories. 88% of EGFR mutation positive patients ($n = 273$) received a first-line therapy, with either gefitinib (45%), platinum-based combinations (39%), Bevacizumab containing triple combinations (9%), Erlotinib (3%) other combinations (4%).

Conclusion: The REASON data base allows a thorough analysis of epidemiological parameters in correlation with clinico-pathological characteristics in patients with advanced NSCLC and will contribute further insight into this frequent disease. Providing information on EGFR mutation status influences treatment decisions regarding first-line TKI application.