The present report gives a scope on relevant abstracts presented at the 12th World Conference of Lung Cancer held in Seoul, South Korea, in September 2007. Some data will directly influence the daily routine of thoracic oncologists. The most important is the intention of the International Association for the Study of Lung Cancer IASLC to modify the staging system. For example, T4 tumours with satellite nodules will be reclassified as T3, and nodules in the ipsilateral lung from M1 to T4.

In the first-line treatment of stage IIIB/IV patients the combination of cisplatin/pemetrexed was equally effective as the control arm applying cisplatin/gemcitabine with a lower rate of side effects. Interestingly, patients with adenocarcinomas and large cell carcinomas showed a significant survival benefit using the new combination which might be explained by divergent enzymatic activity between the histological subtypes. Gefitinib, applied in the second line setting, showed similar efficacy when compared with docetaxel, even in a non-Asian population. Maybe, the gefitinib story has now to be discussed again. The knowledge on predictive markers for an individualised application of targeted therapies is improving, but at the moment this does not influence our daily practice.

The role of smoking in lung cancer was discussed in the presidential session. It was stated that the dramatic increase of adenocarcinomas in relation to other NSCLC subtypes is consistent with the hypothesis that changes in cigarette design and composition were the major factors responsible for this development. The use of filter vents reduced the resistance to draw allowing smokers to take bigger, deeper puffs thus facilitating the delivery of smoke particles deep into the airways.

In conclusion one can say that the international effort to improve lung cancer outcome is effective, however, the clinically relevant steps are still small.

Keywords: Lung cancer, staging system, smoking, pemetrexed

Abbreviations
Carbo Carboplatin
CCRT Combined chemoradiotherapy
CDDP Cisplatinum
CX Chemotherapy
DFS Disease-free survival
DXL Docetaxel
EGFR Epithelial growth factor receptor
Gem Gemcitabine
HR Hazard ratio
MST Median survival time
NSCLC Non-small cell lung cancer
OS Overall survival
ORR Overall response rate
Pem Pemetrexed
PFS Progression-free survival
PCI Prophylactic cranial irradiation
PXL Paclitaxel
QoL Quality of life
RR Response rate
RT Radiotherapy
SCLC Small cell lung cancer
TKI Tyrosine kinase inhibitor
TS Thymidylate synthase

Introduction
The 12th World Conference on Lung Cancer was held in Seoul, South Korea, from September 2nd to 6th. 4700 attendants joined the meeting, more than 400 posters and more than 200 oral presentations showed interesting findings relevant for daily practice. The selection of abstracts is arbitrary and represents a subjective view of the author. The original abstracts are available in a supplement to the Journal of Thoracic Oncology, Vol. 2, No. 8, 2007.

Combined modality therapy in NSCLC
The addition of induction chemotherapy (CDDP/Gem × 2) to CCRT failed to increase the survival of unresectable stage III
NSCLC over immediate CCRT. Moreover, the PFS was inferior to immediate CCRT in this phase III trial [1]. Similarly, the consolidation with DXL after CCRT does not further improve survival and was associated with significant toxicity including an increased rate of hospitalisation and premature death [2].

A large meta-analysis proved sequential (2.6% absolute benefit) and concomitant (3.2%) chemotherapy to be superior compared to RT alone concerning survival at three years [3]. Another meta-analysis compared concomitant CCRT with sequential CCRT and found an improved survival rate for the first one (24.8% vs. 18.2% at 3 years) mainly due to a decrease of loco-regional progression (HR 0.76). Concomitant CCRT increased acute oesophageal toxicity [4].

The question whether a tri-modality approach could improve the patients’ outcome was addressed by the German group. In a phase III trial including 112 patients using induction CT, CCRT plus surgery, they found out that survival was in favour of the trimodality therapy and that there was a trend supporting more limited surgical resections [5].

Patients fulfilling the following disease criteria are candidates for surgery after induction treatment for stage IIIA-pN2 NSCLC, when PET is included in staging procedures [6] (cave: recommendations based on low number of patients, n=30): Persistent minor pN2 disease following induction CX does not exclude favourable outcome after surgery.

Serial FDG-PET is able to select surgical candidates amongst patients with persistent minor pN2 disease or with mediastinal clearance.

Persistent major N2 disease has a poor prognosis and should not be considered for surgery.

New strategies of radiotherapy are able to improve efficacy and to reduce toxicity. For example, stereotactic radiotherapy using four-dimensional target definition achieved a local control rate of > 90% making it an effective alternative in patients not fit for surgery [7].

Cytotoxic chemotherapy

(Neo-)adjuvant chemotherapy

A meta-analysis conclusively demonstrated a benefit of adjuvant CX, both in the presence or absence of adjuvant RT (8). In a large phase III study 528 patients with stage I-II NSCLC were randomised to 4 arms [9]: (A) 2 × CDDP/Gem, in responders 2 × CDDP/Gem, then S; (B) 2 × CDDP/Gem, S; in responders 2 × CDDP/Gem; (C) 2 × PXL/Carbo, in responders 2 × PXL/Carbo, then S; (D) 2 × PXL/Carbo, S, in responders 2 × PXL/Carbo; as a result they found that both protocols were effective and that the results of pathological responses suggested that 2 preoperative cycles might be as effective as 4 cycles and that dose intensity was higher when CX was given before surgery.

Second-line

Pemetrexed 900 mg/m² did not improve overall survival, PFS or RR over 500 mg/m² in second-line NSCLC. Toxicities and sequelae were more frequent if the higher dose was given [10].

Another phase III study examined vinflunine, a novel microtubule inhibitor, in comparison to docetaxel. In terms of efficacy, both therapies were comparable, the toxicity profile was divergent with a higher rate of constipation and injection site reaction with vinflunine [11].

First-line treatment

In the first-line treatment of NSCLC the carboplatin/pemetrexed combination was equally effective to the carboplatin/gemcitabine combination. However, the toxicity profile with respect to leucopenia, granulocytopenia and thrombocytopenia was in favour of the pemetrexed combination [12].

At the presidential session Giorgio Scagliotti presented the first analysis of a randomised trial comparing pemetrexed/cisplatin with gemcitabine/cisplatin in previously untreated stage IIB/IV NSCLC patients (n = 1725) [13]. The primary endpoint of this study was met successfully: Cisplatin/pemetrexed is not inferior to cisplatin/gemcitabine in terms of RR, PFS and OS (OS, HR 0.94). Applying Cis/Pem the rate of platelet transfusions (1.8% vs. 4.5%, p = 0.002), of red blood cell transfusions (16.1% vs. 27.3%, p = 0.001), the use of erythropoiesis stimulating agents (10.4% vs. 18.1%) and of G-CSF/GM-CSF (3.1% vs. 6.1%, p = 0.004) was significantly lower when compared with the standard arm. Concerning drug related grade 3 and 4 toxicities, considerable differences were observed: neutropenia 15.1% vs. 26.7%, anaemia 5.6% vs. 9.9%, thrombocytopenia 4.1% vs. 12.7%, febrile neutropenia 1.3% vs. 3.7%, alopecia (any grade) 11.9% vs. 21.4% with Cis/Pem and Cis/Gem respectively. Only nausea was seen more often in the experimental arm (7.2% vs. 3.9%). Interestingly, concerning overall survival in patients with adenocarcinomas or large cell carcinomas, the new combination was significantly more effective when compared with the Cis/Gem combination (MST 11.8 vs. 10.4 months, HR 0.81, p = 0.03). Based on previous publications (14–16) it is known that baseline expressions of TS genes and proteins are higher in squamous cell carcinomas when compared with adenocarcinomas and that a high expression of TS correlated with reduced sensitivity to pemetrexed. Therefore the authors concluded that the differential activity may be related to a differential expression of TS in different histological subtypes.

In the discussion following the presidential session, L. Einhorn stressed that this new regimen could be a preferred preferable one and he also stated that data comparing Cis/Pem with and without bevavizumab are urgently needed.

Molecular targets – novel therapeutics

The addition of L-BLP25 (or Stimuvax®), a liposome vaccine, as a maintenance therapy in a randomised phase IIB study with 171 patients with stable disease or response after first-line therapy showed a 17.3 months difference in survival and a 45% reduction in mortality in the subgroup of stage IIB patients receiving the vaccine. Based on these optimistic results a phase III study is now planned [17].

Another immunotherapeutic substance, MAGE-A3, was added in the adjuvant setting in stage IB/II patients. This randomised phase II study revealed a beneficial effect of this new strategy with a HR of MST of 0.66 and DFS of 0.73. Treatment was well tolerated, a phase III evaluation will be initiated [18].