**Results:** A total of 7 RCTs were identified (2,867 patients). IPD analyses are still pending for one trial. The pooled estimate for overall survival showed an improvement in favor of docetaxel whatever the source data used:

<table>
<thead>
<tr>
<th>Trial</th>
<th>No. of pts</th>
<th>Design</th>
<th>Published data Hazard ratio [95% CI]</th>
<th>Study report data Hazard ratio [95% CI]</th>
<th>IPD Hazard ratio [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>fosseila et al. j clin oncol 2003</td>
<td>1218</td>
<td>DC vs VC</td>
<td>0.85 [0.70, 1.01] 0.85 [0.72, 0.99]</td>
<td>0.89 [0.76, 1.04]</td>
<td></td>
</tr>
<tr>
<td>DC vs VC</td>
<td>0.95 [0.80, 1.16] 0.95 [0.81, 1.12]</td>
<td>1.02 [0.88, 1.20]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>douillard et al. Ann Oncol 2005</td>
<td>233</td>
<td>DC vs VC</td>
<td>0.89 [0.68, 1.16]</td>
<td>0.89 [0.66, 1.19]</td>
<td>0.87 [0.66, 1.13]</td>
</tr>
<tr>
<td>KUBOTA K et al. J Clin Oncol 2004</td>
<td>311</td>
<td>DC vs VC</td>
<td>0.73 [0.57, 0.94]</td>
<td>0.75 [0.58, 0.97]</td>
<td>0.71 [0.56, 0.91]</td>
</tr>
<tr>
<td>georgoulis et al. J clin oncol 2005</td>
<td>413</td>
<td>DG vs VS</td>
<td>1.00 [0.80, 1.26]</td>
<td>1.00 [0.80, 1.26]</td>
<td>1.02 [0.81, 1.27]</td>
</tr>
<tr>
<td>papul et al. Ann Oncol 2005</td>
<td>311</td>
<td>DG vs VS</td>
<td>0.90 [0.70, 1.16]</td>
<td>0.90 [0.70, 1.16]</td>
<td>pending</td>
</tr>
<tr>
<td>KODUH S et al. J Clin Oncol 2006</td>
<td>180</td>
<td>D vs VS</td>
<td>0.78 [0.56, 1.08]</td>
<td>0.78 [0.56, 1.08]</td>
<td>0.78 [0.56, 1.08]</td>
</tr>
<tr>
<td>Monnier A et al. Proc ASCO 2003</td>
<td>201</td>
<td>D vs V</td>
<td>NA (abstract)</td>
<td>0.95 [0.70, 1.20]</td>
<td>0.96 [0.70, 1.31]</td>
</tr>
<tr>
<td>Overall HR</td>
<td></td>
<td></td>
<td>0.88 [0.81, 0.96]</td>
<td>0.89 [0.82, 0.96]</td>
<td>0.90 [0.82, 0.98]</td>
</tr>
</tbody>
</table>

Dr docetaxel, C: cisplatin, O: carboplatin, G: gemcitabine, V: vinorelbine, Vd: vindesine

**Conclusions:** For this meta-analysis of survival, IPD confirmed the results found with either study report or data published. The meta-analysis is currently on-going for other less objective endpoints such as tumour response and progression-free survival. Pending data will be available and presented at the meeting.

**B3-06**  
**Molecular Targeted Therapy: EGFR Inhibitors, Tue, 13:45 - 15:30**

**Interim safety results from TRUST, a global open-label study of erlotinib in patients with advanced non-small-cell lung cancer (NSCLC)**

Arbidzoni, Andrea1 Razis, Evangelia2 Lichninster, Mikhail3 Yilmaz, Ugar4 Griogrescu, Alexandru C.5 Morero, José Luis5 Skrickova, Jana7 Cervantes, Guadalupé7 Gottfried, Maya9 Van Meerbeeck, Jan10 1 University of Parma, Parma, Italy 2 Hygeia Hospital, Athens, Greece 3 NN Blochin Russian Oncology Research Center, Moscow, Russia 4 Dokaz Eylul University Medical Faculty, Izmir, Turkey 5 Bucharest Oncology Institute, Bucharest, Romania 6 Hospital Maria Ferrer, Buenos Aires, Argentina 7 University Hospital Brno, Brno, Czech Republic 8 Hospital 20 de Noviembre Centro Medico ISSSTE, Mexico City, Mexico 9 Meir-Sapir Medical Center, Kfar-Saba, Israel 10 University Hospital, Gent, Belgium., Ghent, Belgium

**Background:** In the BR.21 phase III placebo-controlled study (Shepherd et al. NEJM 2005;353:123-132), erlotinib (Tarceva®) was well tolerated and significantly improved survival, delayed symptomatic progression and improved quality of life in patients with relapsed advanced NSCLC. The multicentre, open-label TRUST study was initiated to provide erlotinib access for patients with stage III/IV advanced NSCLC.

**Methods:** Eligible patients had failed prior chemotherapy, or were unsuitable for chemotherapy. Erlotinib was administered orally 150mg/day until disease progression or unacceptable toxicity. The NCI-CTC v3.0 was used to grade toxicities, including: incidence and grade of erlotinib-related rash; serious adverse events (SAEs) and treatment-related SAEs; and adverse events (AEs) leading to treatment withdrawal. Other treatment-related AEs were reported if they were not included on a list of 15 pre-specified AEs in the study protocol (rash; pruritis; dry skin; diarrhea; nausea; vomiting; stomatitis; abdominal pain; fatigue; dyspnoea; cough; anorexia; infection; conjunctivitis; and keratoconjunctivitis sicca). Dose reductions (50mg increments) were allowed as required.

**Results:** 5,015 patients from 51 countries were included in the analysis at the data cut-off (20/11/06). Median age was 63 years (range 19–95). Patient characteristics: male 62%, female 38%; stage IIB 22%, stage IV 78%; ECOG PS 0 21%, PS 1 53%, PS 2 20%, PS 3 6%; Caucasian 76%, Oriental 19%, other 5%; non-smoker 28%, ever-smoker 71% (no data 1%); adenocarcinoma 53%, squamous-cell carcinoma 25%, other 21% (no data <1%); erlotinib 1st line 14%, 2nd line 48%, 3rd line 37%, other 1%. Data on the occurrence of rash were available for 4,965 patients, of whom 70% experienced rash, which was mainly mild or moderate (among those with rash, 84% of cases were grade 1/2 and 16% were grade 3/4). AE safety data were available for 4,423 patients, of whom, 55% experienced at least one AE. Erlotinib-related SAEs were experienced by 5% of patients, the most common of these being gastrointestinal (GI) disorders (2% all grades, 1% ≥ grade 3). Lung-related SAEs occurred in <1% of patients. 10% of patients had at least one treatment-related AE that was not pre-specified (3% had at least one grade 3/4 event), but no single such event occurred in more than 1% of patients. Treatment discontinuation due to erlotinib-related AEs occurred in 6% of patients, mainly due to GI disorders (2% all grades, 1% ≥ grade 3) and skin disorders (2% all grades, 1% ≥ grade 3). Lung-related AEs led to erlotinib withdrawal in <1% of patients. Among 4,405 patients with available data, 577 patients (13%) required dose reductions due to erlotinib-related events, mostly commonly related to rash (n=416) or diarrhea (n=72). Safety results for the subgroup of patients who received erlotinib second-line were similar to the overall results. Efficacy data will be presented.

**Conclusions:** The safety data obtained in the TRUST study of erlotinib in advanced NSCLC confirm a wider clinical setting the favourable safety profile of erlotinib observed in previous clinical trials. Erlotinib was generally well tolerated, thus enabling the majority of patients to receive the full therapeutic dose.

**B3-07**  
**Molecular Targeted Therapy: EGFR Inhibitors, Tue, 13:45 - 15:30**

**A phase II study of Cetuximab (C225) in combination with chemoradiation**

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**Background:** Cetuximab (C225) is a chimerized monoclonal antibody that targets the epidermal growth factor receptor (EGFR). NSCLC commonly expresses the EGFR, which is associated with aggressive tumor behavior and poor clinical outcome. Preclinical model systems
demonstrate radiosensitization following molecular inhibition of EGFR signaling.

Methods: We report a phase II trial testing the combination of C225 with CRT in unresectable stage III NSCLC with a planned sample size of 84 PTS. Eligibility criteria included Zubrod performance status (PS) ≤ 1, weight loss ≤ 5% over past 3 months, FEV1 ≥ 1.2 L, adequate hematologic, hepatic, and renal function. PTS received an initial dose of C225 (400 mg/m²) on day 1 of week 1, then weekly doses of C225 (250 mg/m²) until completion of therapy (weeks 2 – 17). During week 2, PTS started CRT (63 Gy/35 fractions) with weekly carboplatin (C) AUC 2 and paclitaxel (P) 45 mg/m² x 6 doses followed by C (AUC 6) and P (200 mg/m²) x 2 cycles (weeks 12-17). Interim monitoring for severe (grade ≥ 3) or excessive non-hematologic toxicities occurred after PTS had been treated and followed for at least 90 days after RT. Primary endpoints include safety and compliance of concurrent C225 and CRT.

Results: 93 PTS were enrolled with 87 evaluable PTS. PTS characteristics: 57% male, median age 64 years (range 42-85), 47% PS 0, 46% stage IIIA. Median follow-up is 17.6 months. Response rate is 62% (n=54) and 18 month overall survival (OS) is 54.7%(# at risk=39). Adverse events related to treatment include 20%(n=17) of PTS with grade 4 hematologic toxicities and 7 PTS who had grade 3 esophagitis. There was 1 infection related death, 1 death NOS, and 3 PTS who died of pulmonary complications (adult respiratory distress syndrome, pneumonitis, and hypoxia).

Conclusions: The combination of C225 with CRT is feasible. Further study will be needed to determine whether the addition C225 to CRT enhances toxicity or efficacy. Complete compliance and toxicity data along with median survival will be reported.

Session B4: Prevention & Early Detection + Epidemiology
Tuesday, September 4

B4-02 Prevention & Early Detection + Epidemiology, Tue, 13:45 - 15:30
Incidence of occupational lung cancer in Tehran-Iran
Kolahi, Ali A.; Mosavi-Jarrahi, Alireza
Shaheed Beheshti University of Medical Sciences, Tehran, Iran

Background: Occupational carcinogens occupy a special place among the different classes of human carcinogens. The aim of this study was to estimate the fraction of lung cancer incidence attributed to occupational exposures to Silica, Cadmium, Nickel, Arsenic, Chromium, Diesel Fumes, Beryllium, and Asbestos (the best established lung cancer carcinogens in the workplace).

Methods: Exposure to each of the mentioned carcinogens at national level was estimated using workforce data estimated by the population census 1995 and obtained from the ILO. The prevalence of exposure for each industry/carcinogen was estimated using exposure data from the CAREX database (CAREX is an international information system on occupational exposure to known and suspected carcinogens kept and maintained by EU). The magnitude of relative risk of lung cancer for each carcinogen of interest was estimated from local and international literatures. The Levin modified population attributable risk (incidence) fraction was utilized to estimate the fraction of lung cancer incidence attributed to occupational exposure as estimated by the Tehran Population Based Cancer Registry that could be attributed to workplace exposure of carcinogens of interest.

Results: The investigated burden of disease from mortality attributable to smoking was based on analysis of data from the National Statistics Institute for the year 2004. There were 6,565 DALYs lost per 100,000. The group of diseases related to smoking is responsible for 50% of the deaths and 39% of the DALYs. Twelve percent of the total disease burden due to mortality and DALYs is attributable to smoking, being higher for men (16% of DALYs) than for women (4%). If smoking was abandoned, the burden of disease would be reduced by 53% (54% in men; 65% in women).

Conclusions: Twelve percent of the overall disease burden and mortality is attributable to smoking. The health gains obtained by reducing tobacco consumption could reach 50%. This highlights the importance of smoking cessation as a priority in health policies.