

recent phase III study has shown efficacy of pemetrexed (Pem) as a maintenance therapy. This is a prospective multicenter study of Pem combined with carboplatin (Cb) as an induction therapy followed by Pem maintenance. Trial sponsor is Eli Lilly Japan K.K. (ClinicalTrials.gov identifier NCT01020786).

**Materials and Methods:** Eligible patients (pts) had chemo-naïve, unresectable stage IIIB, IV or postoperative recurrent non-squamous NSCLC, and ECOG Performance Status (PS) of 0–1. Pts received Cb AUC 6 and Pem 500 mg/m<sup>2</sup> on Day 1 of each 21-day cycle for 4 cycles as induction therapy. Pts who achieved CR/PR/SD by the end of induction phase, could continue on Pem as maintenance therapy until PD or unacceptable toxicity. Written informed consent was obtained from all enrolled pts.

**Results:** Pem and Cb were administered as induction therapy to 109 pts. Patients backgrounds were; median age 63 years (range 38–78), male/female (63%/37%), PS 0/1 (34%/66%), and stage IIIB/IV/recurrent disease (30%/66%/4%). Seventy-five pts (69%) were completed induction therapy, and 60 pts (55%) entered into the maintenance therapy. In the induction phase, dose reduction was required in 20% of pts, and dose delay in 68%. The relative dose intensities for Pem and Cb were 89% and 90%, respectively. The most frequently reported grade  $\geq 3$  toxicity was neutropenia (54%). Other grade  $\geq 3$  toxicities were also hematologic, including thrombocytopenia (41%) and anemia (28%). Red blood cells transfusion, platelet transfusion and G-CSF administration were required in 10%, 7% and 9% of the pts. Serious adverse events including thrombocytopenia, anemia, or gastric ulcer were reported in 12 pts (11%). There were no treatment related deaths.

Of 109 pts evaluable for response, 42 pts (38.5%) achieved a partial response (including unconfirmed) in the induction phase.

**Conclusions:** This prospective multicenter study suggested that Pem plus Cb combination chemotherapy was well tolerated and more than half of pts could be received maintenance therapy. This combination is active as a first-line treatment for advanced non-squamous NSCLC. Overall safety and efficacy results will be presented at the conference.

## 9129

## POSTER

# **Safety Profile and Efficacy of Erlotinib in a Japanese Post-marketing Surveillance Study of 10,708 Non-small-cell Lung Cancer (NSCLC) Patients (pts) – Interim Analyses From the First 3,488 Pts**

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**Background:** Erlotinib is approved in Japan for the treatment of nonresectable, recurrent and advanced NSCLC, following failure of at least one prior chemotherapy regimen. A large scale surveillance study has been implemented to investigate erlotinib safety and efficacy in Japanese pts, focusing on the incidence of interstitial lung disease (ILD), which had been highlighted in previous studies as an adverse drug reaction (ADR) of particular concern in this population.

**Methods:** Enrolment: Dec 2007–Oct 2009; observation period: 12 months. ADRs were defined as adverse events (AEs) where causality to erlotinib could not be ruled out and all events resembling ILD were assessed by an independent committee. Overall survival (OS) and progression-free survival (PFS) were also assessed. These interim data are for pts registered prior to 30 Jun 2008.

**Results:** From a total of 10,708 enrolled pts, 3743 were enrolled by 30 Jun 2008 and data were available for 3488 (255 pts unavailable for CRF or not treated with erlotinib or registered more than once). Baseline characteristics included: male (51%), median age (65 years), any smoking history (52%), adenocarcinoma (83%), ECOG PS 0–1 (74%), patients who received more than three lines of treatment (56%). Previous first-line chemotherapy included platinum-based doublets (73.2%), of which the majority were carboplatin based (52.9%; predominantly carboplatin/paclitaxel, 39%), non-platinum single agents (20.7%), and non-platinum doublets (2.8%). Gefitinib, mainly second line, had been received by 55%. ADRs were reported in 82% of pts and the most common were skin disorders (69%), including rash (63%), and gastrointestinal disorders (32%), including diarrhoea (24%). 189 pts experienced 'ILD-like' events and ILD was confirmed by the independent ILD review committee in 158 pts (4.5% of population), with a mortality rate of 1.6%. Smoking status (hazard ratio

[HR]=3.0), history of ILD (HR=4.1), history of lung infection (HR=2.0) and ECOG PS 2–4 (HR=1.6) were identified as risk factors for ILD by multivariate analysis. No new safety signals were identified. Median OS and PFS were 260 days and 64 days, respectively. Data collection and analysis are continuing.

**Conclusions:** Interim data from this large surveillance study in Japanese pts with recurrent and advanced NSCLC are favourable towards the risk/benefit balance for the use of erlotinib and provide further information on the risk of ILD and the treatment profile of this population.

## 9130

## POSTER

# **The Prognostic Role of Myeloid-derived Suppressor Cells Related Markers in Peripheral Blood From Advanced Non-small Cell Lung Cancer Patients**

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**Background:** Myeloid-derived suppressor cells (MDSC) are found in most patients with advanced cancers, and are potent inhibitors of innate and adaptive immunity. Marker genes associated with the presence of MDSC are CD11b, CD18, CD115, GR1, IL-4R $\alpha$  and IL-13. The aim of this study was to determine the expression level of these genes by qRT-PCR in patients with advanced non-small cell lung cancer (NSCLC) and to correlate them with clinico-pathological and prognostic variables.

**Methods:** RNA was isolated from peripheral blood collected from NSCLC patients (n = 50) and controls (n = 54). qRT-PCR was performed to analyze the expression of CD11b, CD18, CD115, GR1, IL-4R $\alpha$  and IL-13. Relative expression was normalized by endogenous genes (GAPDH and  $\beta$ -actin) using the Pfaffl formulae. Statistical analyses were considered significant at p < 0.05.

**Results:** We found significant differences in the expression levels of 3 analyzed genes (CD115, GR1 and IL4a) and in other two differences were borderline (CD11b, p = 0.061; and IL13, p = 0.068) between patients and controls. Pair-matched samples comparing pre and post-treatment expression levels of CD18, GR1 and IL4Ra showed that they were significantly reduced after chemotherapy. Lower levels of expression of CD11b were related with progressive disease (p = 0.005). The prognostic impact of the studied variables was assessed by Cox univariate analysis (see Table) and Kaplan–Meier plots. We found that those patients with baseline CD11b expression below the median had significant worse progression-free (p = 0.005) and overall survival (p = 0.013).

**Conclusion:** This study shows that it is possible to detect and quantified MDSC-related markers in peripheral blood samples of advanced NSCLC patients. The expression of the analyzed genes, especially CD11b, could have prognostic value in advanced NSCLC.

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## 9131

## POSTER

# **Relative Expression of Regulatory T-lymphocyte Associated Markers Inperipheral Blood Samples From Advanced NSCLC – Analysis of the Prognostic Role**

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**Background:** T-cell tolerance is an important mechanism for tumour escape. An imbalance of regulatory T-lymphocytes (Treg) could promote peripheral immune tolerance to tumour cells. Marker genes associated with the presence of Treg are CD127, CD8a, Foxp3, CD4, CD25 and TGF- $\beta$ 1. The aim of this study was to determine the expression level of these marker genes by qPCR in patients with non-small cell lung cancer (NSCLC) in advanced stages and to correlate them with clinico-pathological and prognostic variables.

**Methods:** 54 control individuals and 50 patients with advanced-NSCLC (IIIB-IV) treated with cisplatin and docetaxel were studied. Blood samples were collected at baseline and after 3 cycles of chemotherapy in PAXgene Blood RNA Tubes and stored at –80°C until RNA isolation. mRNA was reverse transcribed and RT-PCR was performed to analyze the expression of CD127, CD8a, Foxp3, CD4, CD25 and TGF- $\beta$ 1. Relative expression was normalized by endogenous genes (GAPDH and  $\beta$ -actin) using the Pfaffl formulae. Statistical analyses were considered significant at p < 0.05.

**Results:** The characteristics of the studied patients were: median age: 57.8 years [37.7–75.1], 89% males, 55% adenocarcinomas. We found significant differences in the expression levels of CD4 (p < 0.0001), CD8