occurred among the first 3 pts. Treatment response was assessed after every second cycle. In case of disease progression, treatment was stopped. EGFR expression was determined by immunohistochemistry.

**Results:** All 29 pts screened thus far were found to be positive for EGFR expression. Seventeen pts with metastatic NSCLC (4x squamous cell, 12x adenocarcinoma, 1x mixed) and a median age of 61 [29-73] years were included in the study. Sixteen pts have received at least two cycles [range 2-11] of P/EMD72000 and are eligible. Seven pts had been pretreated [median number of 2 prior chemotherapy regimens (range 1-3)]. A total of 71 cycles have been applied. EMD 72000 related skin toxicity did not exceed NCI-CTC grade 2. Flush (grade 1) and bronchospasm (grade 2) were observed in one pt after the 3rd EMD 72000 application, which did not recur after premedication upon re-exposure. P applications had to be postponed due to toxicity in 2 pts and withdrawn due to allergic reactions in 4 pts. Recruitment at the highest dose level (800mg) is completed and the MTD has not been reached. One complete and 6 partial responses (3 pts pretreated) as well as 4 disease stabilizations (>12 weeks) have been thus far achieved in 16 eligible pts.

**Conclusions:** The monoclonal EGFR-antibody EMD 72000 given in combination with P appears to be well tolerated. Final results and pharmacokinetic data will be presented.

54 ORAL

## The epidermal growth factor receptor tyrosine kinase inhibitor, erlotinib (TarcevaTM, OSI-774), is an active agent in bronchioloalveolar carcinoma (BAC) and its variants: interim results of a Phase II Trial

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**Background:** Erlotinib has shown promising activity in the treatment of advanced non-small cell lung cancer. Anecdotally, some of the most dramatic results have occurred in patients with BAC. BAC is an increasingly common subtype of non-small cell lung cancer [Read, Proc Am Soc Clin Oncol, 2002], and has been felt to be chemoresistant by most clinicians. We chose to conduct a Phase II trial of erlotinib in BAC to define the activity of this agent in this patient population.

**Methods:** Patients with clinical presentations or pathologic findings consistent with BAC were screened for trial entry. Those who tumors' consist of pure BAC, BAC with focal invasion, or adenocarcinoma with BAC features [Ebright, Ann Thor Surg, 2002;74:1640-6] were deemed eligible and were then screened for treatment.

**Results:** Between 6/02 and 4/03, 95 patients underwent pathologic review. Of these, 64 were felt to have BAC or a variant and were eligible for treatment. 54 patients have been treated to date. Patient characteristics: Men-17/Women-37; KPS: 100-1, 90-16, 80-34, 70-3; Prior chemotherapy regimens: None-42; One-12; Smoking history: Never-14; Former or current-40. 47 patients have completed at least 4 weeks of therapy and are therefore assessable for response; 12 patients have achieved a partial response, major response rate 25% (95% CI 14-41). Of the responding patients: Men-2/Women-10; KPS: 100-1, 90-2, 80-9; Prior chemotherapy regimens: None-11; One-1; Smoking history: Never-7; Former or current-5.

**Conclusions:** Erlotinib is an active agent in BAC. Given this level of activity, a Phase III trial of erlotinib in BAC and its variants is warranted. We are prospectively constructing a tissue microarray to evaluate differences in the EGFR and related signaling pathways in sensitive and resistant tumors.

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55 ORAL

## Randomized phase II clinical trial of cetuximab in combination with cisplatin (C) and vinorelbine (V) or CV alone in patients with advanced Epidermal Growth Factor Receptor (EGFR)-expressing non-small-cell lung cancer (NSCLC)

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**Background:** Cetuximab (Erbitux) is a chimeric monoclonal antibody targeting the EGFR, which is highly expressed in patients with NSCLC. Combinations of cetuximab and chemotherapy have shown to be safe and active in combination in several EGFR-expressing tumor types including NSCLC. CV is a standard treatment for advanced NSCLC.

**Objective:** The primary objective was to determine the response rates for the combination of cetuximab and CV and for CV alone in chemotherapy-naïve patients with EGFR-expressing stage IIIb/IV NSCLC.

**Regimens:** All patients received C 80 mg/m$^2$ d1 and V 25 mg/m$^2$ d1 and 8, q3 weeks. Patients in arm A also received cetuximab 400 mg/m$^2$ week 1 and 250 mg/m$^2$ weekly thereafter.

**Results:** 84/93 (90,3%) of patients screened had EGFR-expressing tumors. 68 patients (63: stage IV, 5: IIIb) have been enrolled to date. Of these 34 patients (9 female (F), 25 male (M), median age 58 years) were randomized to arm A and 34 to arm B (10 F, 24 M, median age 58.5 years). 45 serious adverse events were observed so far, 27 in arm A (including 2 considered related to cetuximab), and 18 in arm B. 55 patients (27 in arm A and 28 in arm B) are currently evaluable for response. The overall response rates to date are 59% [16 PR (13 confirmed), 10 SD, 1 PD] in arm A and 36% [10 PR (8 confirmed), 12 SD, 6 PD] in arm B. The trial is ongoing with a target recruitment of 40 patients per arm.

**Conclusion:** Cetuximab can safely be added to the regimen of cisplatin and vinorelbine, with preliminary evidence suggesting enhancement of activity.

56 ORAL

## An epidemiological survey for interstitial lung disease induced by gefitinib in patients with advanced non-small cell lung cancer. West Japan Thoracic Oncology Group (WJTOG)

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Gefitinib is an orally active, selective epidermal growth factor receptor tyrosine kinase inhibitor, which blocks signal transduction pathways implicated in the proliferation and survival of cancers. IDEAL 1 and 2 were both randomized, double-blind, phase II trials designed to evaluated gefitinib at two dose levels (250 and 500 mg/day) for the treatment of patients in whom advanced non-small cell lung cancer (NSCLC) had not responded to platinum-based and docetaxel-based combination chemotherapy regimens. Gefinitib has been proven to have activity in heavily pretreated and very sick patients. It has clearly shown a clinical benefit to patients, many of whom had improvement in symptoms within two weeks after the start of treatment gefitinib at 250 mg/day had results equivalent to those of the higher dose, with less toxicity.

Gefitinib was approved by the regulatory at July 5, 2002, which was the world's first, in Japan. From August 2002 to December 2002, 19,000 and over patients with advanced NSCLC had received gefitinib in all of