ed with palliative chemotherapy at Samsung Medical Center, Seoul, Korea were retrospectively reviewed. According to a case-match-control study design, 334 patients matched by age, sex, and histology for each treatment period; pre-gefitinib era (1999-2001) and post-gefitinib era (2002-2005) were selected and compared for overall survival. For each group, 69.5% were male, 53.3% were < 60 years, and 66.5% of patients had adenocarcinoma.

Results: With the median follow-up of 68 and 30 months in pre- and post-gefitinib eras, the median overall survival (OS) from the date of first diagnosis of advanced/metastatic or recurrent disease were 11.5 (95% CI, 10.0-12.9 months) and 19.3 (95% CI, 17.2-21.3 months) months, respectively, which was significantly different (p<0.001). The overall response rate and disease control rate were 24.7% (3 complete response, 73 partial response) and 48.7% for 308 evaluable post-gefitinib era patients, respectively. By multivariate analysis for all the 668 patients, gefitinib treatment (HR 0.64, P<0.001), Stage III (HR 0.64, P<0.001), PS ≤1 (HR 0.57, P<0.001), adenocarcinoma histology (HR 0.80, P=0.025), and prior chemotherapy ≥2 (HR 0.66, P<0.001) were significant favorable predictors for survival. Exploratory subgroup analyses also showed a prolonged overall survival for patients in post-gefitinib era in almost all subgroups: age ≥60 (12.7 vs 20.6 M, P<0.001), age ≥60 (10.6 vs 18.1 M, P<0.001), male (11.4 vs 16.5 M, P<0.001), female (12.4 vs 21.5 M, P<0.001), never-smokers (12.6 vs 24.9 M, P<0.001), smokers (10.9 vs 15.7 M, P<0.001), stage III (14.2 vs 24.7 M, P<0.001), stage IV (9.9 vs 17.6 M, P<0.001), adenocarcinoma histology (12.6 vs 24.2 M, P<0.001), performance status (PS) ≤1 (12.7 vs 20.4, P<0.001), prior chemotherapy ≥1 (11.7 vs 20.0 M, P<0.001), and previous platinum based chemotherapy (11.7 vs 20.3 M, P<0.001).

Conclusions: This historical control study shows significant improvement of overall survival with the introduction of gefitinib in clinic to the treatment of advanced/metastatic NSCLC patients. These results strongly suggest the efficacy as well as the survival advantage of EGFR tyrosine kinase inhibitor in Asian population for the treatment of advanced NSCLC.

Methods: A 2-part study was initiated to escalate erlotinib to the Maximum Tolerated Dose (MTD) in current smokers and evaluate pharmacokinetics (PK) at this MTD versus 150 mg/d. Part I: sequential cohorts of advanced NSCLC patients (pts) that were current smokers received escalating doses of erlotinib for 14 days until MTD was defined. Part II: pts were randomized between the MTD and 150 mg/d erlotinib and PK assessed at D14.

Results: Twenty-two pts were enrolled in Part I at 4 dose levels; 200, 250, 300 and 350 mg/d. Dose limiting toxicities were observed in 1/6 MTD-evaluable pts at 300 mg/d (G3 rash) and 2/5 pts at 350 mg/d (G3 acniform dermatitis and G3 fatigue/decreased ECOG PS). Thirteen pts have been entered into Part II to date, 7 randomized to 300 mg/d and 6 to 150 mg/d. Median age is 59 yrs (range 52-74) with 7 males and 6 females. Histology: Adenocarcinoma (7/13), Squamous (5/13) and other (1/13). Median/range number of cigarettes smoked and duration of smoking is 15/d (10-25) and 42 yrs (20-63), respectively. Erlotinib dose of 300 mg/d has been well tolerated to date, with a single case of G3 diarrhea. Other toxicity among all 13 pts has been grade 4 (46%) and diarrhea (31%). Preliminary PK data (n=10) show median plasma Cmax of erlotinib was 1.77 (range 0.85-4.58) versus 3.48 (range 1.14-4.88) ug/mL for 150 and 300 mg/d dose cohorts, respectively. The median AUC of erlotinib was 29.3 (range 19.8-50.9) versus 46.2 (range 23.7-95.2) ug.hr/mL for 150 and 300 mg/d dose cohorts, respectively. PK of the main metabolite of erlotinib, OSI-420, mirrored erlotinib PK. The median trough plasma concentration at steady state (CminSS) of erlotinib was 0.42 and 1.84 ug/mL for 150 and 300 mg/d dose cohorts, respectively.

Conclusions: The MTD of erlotinib in NSCLC pts who continue to smoke was 300 mg/d. Early data indicate that there is a dose-dependent increase in the systemic erlotinib exposure in current smokers. Enrollment in to Part II continues and updated data will be presented.

PD3-2-4 Molecular Targeted Therapy: EGFR inhibitors, Thu, 12:30 - 14:15
Third-line erlotinib therapy versus best supportive care for advanced non-small cell lung cancer (NSCLC) in British Columbia (BC), Canada. Is it cost effective?
Melosky, Barb L.1 Taylor, Suzanne C.1 Peacock, Stuart J.2 Johnston, Karissa2 van der Hoek, Kim2
1 BC Cancer Agency, Vancouver, BC, Canada 2 Centre for Health Economics in Cancer, BC Cancer Agency, Vancouver, BC, Canada
Erlotinib was approved for funding as a systemic therapy treatment for third line management of advanced NSCLC by the BC Cancer Agency (BCCA) in April 2004. BCCA patient outcome and cost data are routinely collected to verify the therapeutic effectiveness and cost-effectiveness of systemic treatment policies. This was a pragmatic retrospective analysis of all patients who received third line erlotinib compared to a historical group treated with second line docetaxel then no further active treatment, both according to BCCA protocol. The primary end-point was cost-effectiveness, measured in terms of cost-per-life-year-gained. Secondary end-points included: median overall survival (MOS); overall survival (OS) at one year; and comparison to phase III efficacy results. Data was retrieved from the Cancer Agency Information System (CAIS) and Systemic Therapy Data Warehouse. Life-years-gained were calculated from the area under the survival function curve. CEA took the BCCA perspective and costs included all direct drug costs for treatment of advanced disease. Sensitivity analyses included varying life expectancy across its 95% CI, cost