Results: We have enrolled 13 men and 16 women, median age 65 years old. In 29 evaluable patients, only 1 episode of febrile neutropenia has been documented and was related to aspergillus pneumonia. Twenty of 29 patients have developed grade 3/4 neutropenia (only 4 grade 4), all requiring dose reductions. Ten of 29 patients have developed grade 3/4 thrombocytopenia, and an additional 11 of 29 had grade 1 or 2 thrombocytopenia. No significant bleeding episodes have been documented, though grade 1/2 hemorrhoidal bleeding was documented in 4/29 and grade 1 hematuria occurred in 4/29 patients. Anemia has been mild with grade 3 anemia in only 5 of 29 patients. Non-hematologic toxicity was generally minor, with fatigue being the principal toxicity; adverse events possible related to BV include grade 3 hypertension and angina (1 pt), grade 1 hypertension (1 pt), perforated ulcer (1 pt) and epistaxis (grade 3 in 1 pt, grade 1 in 11 pts). No thrombosis has been reported and grade 1 proteinuria in only 1 patient. There have been no fatal toxicities.

Conclusions: To date, the addition of BV to GC in pts with NSCLC is generally well tolerated, and toxicities have been expected and manageable. Enrollment is ongoing.

P3-108 NSCLC: Molecular Targeted Therapy Posters, Wed, Sept 5 – Thurs, Sept 6

Correlative genomics in a phase II clinical trial of first-line therapy of erlotinib for clinically selected patients with advanced non-small cell lung cancer

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Background: It is apparent that there is a cluster of clinical factors that predict for an increased rate of response and survival to the epidermal growth factor (EGFR) tyrosine kinase inhibitors. However, the current knowledge of EGFR DNA mutations and gene expression is insufficient to explain these observations. The purpose of this study is to enrich the population of patients more likely to respond to the EGFR inhibitor, erlotinib, and to perform extensive genomic screening to identify tumour-specific genome abnormalities to predict patterns of response and resistance.

Methods: Eligibility criteria: stage IIIB/IV NSCLC; chemo-naive; ≥ 1 measurable lesion; ECOG ≤2; adequate organ function; and at least 2 of the following 4 criteria: women, never-smokers, Southeast Asian extraction, adenocarcinoma (ACA) and/or bronchioloalveolar carcinoma. All patients must consent to a baseline fresh tumour biopsy and serum sample; biopsies during treatment and at disease progression are optional. Tumour cells are isolated by laser microdissection following a pathology review. Tumour genomic DNA is applied to high-resolution genomic microarrays to detect tumour-specific changes in copy number and/or genotype at multiple sites across the genome, including EGFR and exons encoding genes with altered copy number. Erlotinib 150mg p.o. daily is given on a continuous basis until disease progression.

Results: From Sept-06 to Feb-07, 20 patients (pts) have been enrolled. Median age 62 (range 43- 78); 17 females and 3 males; 18 never smokers, 2 former and 0 current smokers. PS 0-4; 1 - 13; 2 - 3. Ethnicity: 5 Caucasian and 15 Asian (including China-7 & Hong Kong-3). Pathology: 17 ACA; 1 squamous carcinoma; 2 NSCLC NOS. As of Feb-07, 16 pts have received >8 weeks of treatment or have been taken off study for progressive disease. Toxicities consist of expected rates of rash and diarrhea. Responses: PR - 5; SD - 6; PD - 5; 4 pts are too early to assess (4 weeks only). Thus 11 of 16 (69%) have not progressed at 8 weeks. All pts had fresh tumour samples collected. Laser microdissection and tumour DNA extraction was performed and genomic analysis is underway.

Summary: In this clinically selected population treated with first-line erlotinib, the rate of non-progression at 8 weeks is acceptable. A unique correlation of extensive molecular data obtained from fresh tumour samples, data on pre-drug genetic abnormalities and post-drug clinical response, time to progression, and survival will be performed in all patients enrolled in this study. This work represents an effort to go beyond EGFR analysis and uncover novel features of the lung cancer genome that may help predict drug response and further understanding of tumour biology.

P3-109 NSCLC: Molecular Targeted Therapy Posters, Wed, Sept 5 – Thurs, Sept 6

Survival benefit of gefitinib in patients with good performance status and never-smoker: Retrospectiveanalysis of 359 Korean non-small-cell lung cancer patients

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Background: Gefitinib is a selective inhibitor of the epidermal growth factor (EGFR) tyrosine kinase and approved for use as salvage therapy in advanced non-small cell lung cancer (NSCLC). We retrospectively analyzed 359 Korean NSCLC patients treated with gefitinib to identify clinicopathologic parameters predictive of response and survival benefit.

Methods: Data from NSCLC patients treated with gefitinib at Samsung Medical Center in Korea from Jan 2003 until Dec 2005 were collected. Patients were treated with gefitinib 250mg per day until progression or development of toxicity. Response evaluation with spiral CT scan was performed at 4-8 weeks after gefitinib treatment. Multivariate Cox regression hazards analysis was performed to determine the combined effects of clinicopathological variables in relation to tumor response and overall survival.

Results: For 331 evaluable patients the overall response rate was 25.1% (83/331; 3 CR, 80 PR) and disease control rate was 48.6%. Median age was 60 years (range 25-86). 236 patients (65.7%) were male and 154 patients (42.9%) were never-smokers. The most common histological subtype was adenocarcinoma (67.1%) and 183 patients(51.0%) had a PS≥2. In a large majority of case (90.0%), cytotoxic chemotherapy had been administered before treatment of gefitinib and most of them received platinum-based combination regimens(84.4%) as the first-line treatment. At a median follow-up of 30 months, the median survival for all the 359 patients from the date of gefitinib administration was 6.2 months with 1 year-survival rate of 32.2%. The median survival time calculated from the first diagnosis of advanced/metastatic or recurrent disease was 19.7 months. Good performance status (PS 0-1), never-smoker and development of skin rash after administration of gefitinib were statistically significant favorable predictive markers for tumor response by multivariate analysis. Significant predictors for favorable survival were good performance status