P3-133 NSCLC: Molecular Targeted Therapy Posters, Wed, Sept 5 – Thurs, Sept 6

**Bortezomib for advanced Bronchioloalveolar Carcinoma (BAC): a California-Pittsburgh Cancer Consortium multicenter phase II study**

Ramalingam, Suresh S.[1] Davies, Angela M.[2] Longmate, Jeff[3] Vokes, Everett E.[4] Wright, John[5] Gandara, David R.[2] Belani, Chandra P.[1]

*[1] University of Pittsburgh Cancer Institute, Pittsburgh, PA, USA [2] University of California Davis Cancer Center, Sacramento, CA, USA [3] City of Hope National Medical Center, Duarte, CA, USA [4] University of Chicago Cancer Center, Chicago, IL, USA [5] National Cancer Institute, Bethesda, MD, USA*

**Background:** BAC accounts for approximately 3-5% of all cases of non-small cell lung cancer (NSCLC). An additional 20% of patients with adenocarcinoma have a BAC component. The optimal treatment of advanced BAC is yet to be defined, though inhibitors of the epidermal growth factor receptor pathway (EGFR) have demonstrated promising efficacy. Bortezomib, a novel proteosome inhibitor, has demonstrated single agent activity against NSCLC. We conducted a phase II study to evaluate the efficacy of bortezomib for patients with advanced BAC or adenocarcinoma with BAC features. A novel weekly schedule of bortezomib was utilized for the study.

**Methods:** Eligibility criteria were: histological confirmation of diagnosis, ≤ 1 prior chemotherapy regimen, ECOG PS 0-2, presence of measurable disease, adequate bone marrow, hepatic and renal function and willingness to sign informed consent. Prior EGFR inhibitor therapy was permitted (not considered as a chemotherapy regimen for eligibility). Bortezomib (1.6 mg/m$^2$) was administered intravenously on days 1 and 8 of every 3 week cycle. Treatment was continued until disease progression or unacceptable toxicity. The primary endpoint was determination of the response rate. Secondary endpoints included survival and toxicity assessment.

**Results:** Twenty four patients have been enrolled to date: females-12; PS 0-9; PS 1-13; never smokers-8; prior therapy-16. Treatment was tolerated well and a median of 3 cycles of therapy were administered. Nine patients are still on treatment. Salient toxicities (grades 2/3) (N) attributable to treatment are: neutropenia-2/0; fatigue-4/2; diarrhea-2/2; nausea-1/0; emesis-1/0 and sensory neuropathy-1/0. One patient experienced partial response (4.5%) and 14 had stable disease (64%) out of 22 evaluable patients (clinical benefit rate - 69%). The median survival is 9.4 months. Most patients were censored at a median follow up of 5 months for the purposes of this analysis. Accrual to the study continues.

**Conclusions:** The preliminary results of our study demonstrate modest anti-cancer activity with bortezomib in patients with advanced BAC, including those who had disease progression with an EGFR inhibitor.

P3-134 NSCLC: Molecular Targeted Therapy Posters, Wed, Sept 5 – Thurs, Sept 6

**Sunitinib in combination with gemcitabine plus cisplatin for advanced non-small cell lung cancer (NSCLC): preliminary results from a phase I dose escalation study**

Reck, Martin[1] Frickhofen, Norbert[2] Gatzemeier, Ulrich[1] Fuhr, Heinz-Georg[2] Lanzalone, Silvana[3] Lechuga, Maria J.[3] Wang, Erjian[4] Chao, Richard[4] Felip, Enriqueta[5]

*[1] Hospital Grosshansdorf, Grosshansdorf, Germany [2] HSK, Dr. Horst Schmidt, Wiesbaden, Germany [3] Pfizer Italia srl, Milan, Italy [4] Pfizer Global Research and Development, La Jolla, CA, USA [5] Vall d'Hebron University Hospital, Barcelona, Spain*

**Background:** Sunitinib malate is an oral, multitargeted tyrosine kinase inhibitor of VEGFRs, PDGFRs, KIT, RET, and FLT3, approved internationally for the treatment of advanced renal cell carcinoma and imatinib-resistant or -intolerant gastrointestinal stromal tumor. Single-agent sunitinib is also active in advanced NSCLC after failure of platinum-based therapy, resulting in an objective response rate of 11% (Socinski, ESMO 2006). We report preliminary results from a phase I dose-finding study assessing the safety, tolerability, and pharmacokinetics of sunitinib in combination with gemcitabine and cisplatin as first-line treatment of advanced NSCLC.

**Methods:** Patient eligibility criteria included histologically proven, stage IIIB or IV NSCLC not amenable to curative treatment; no prior chemotherapy except for adjuvant therapy completed more than 6 months before study start; ECOG performance status 0 or 1; and adequate organ function. Planned dose levels include: oral sunitinib (37.5 or 50 mg/day for 2 weeks followed by 1 week off treatment [2/1 schedule], in repeated three-week cycles) plus gemcitabine (1000 or 1250 mg/m$^2$ iv on days 1 and 8 of a 21-day cycle) and cisplatin (80 mg/m$^2$ iv on day 1 of each cycle). Sunitinib administered daily on a continuous dosing schedule will also be tested. Sunitinib doses are escalated in serial patient cohorts to determine the maximum tolerated dose for both schedules. Other endpoints include pharmacokinetics and antitumor efficacy.

**Results:** As of October 2006, 13 patients were treated on the 2/1 schedule, including 9 male and 4 female patients, median age 59 (range 48-68). Six patients received sunitinib 37.5 mg + gemcitabine 1000 mg/m$^2$ + cisplatin 80 mg/m$^2$, and 7 patients were treated with sunitinib 50 mg + gemcitabine 1000 mg/m$^2$ + cisplatin 80 mg/m$^2$. No dose-limiting toxicities were observed with sunitinib 37.5 mg, but 2 patients treated with sunitinib 50 mg experienced dose-limiting neutropenia and infection, and neutropenia, infection and thrombocytopenia, respectively. Grade 3/4 hematological adverse events included neutropenia (n=3 at sunitinib 37.5 mg/day and n=5 at sunitinib 50 mg/day dose levels), thrombocytopenia (n=1 and n=5) and anemia (n=2 and n=0). Three patients treated at the sunitinib 50 mg/day dose level achieved a partial tumor response. There were no apparent drug-drug interactions between sunitinib and gemcitabine or cisplatin based on their systemic exposures in this study.

**Conclusions:** The combination of sunitinib (37.5 mg) given on schedule 2/1 with gemcitabine (1000 mg/m$^2$) and cisplatin (80 mg/m$^2$) appears safe and tolerable in this patient population with advanced NSCLC. The trial continues with gemcitabine escalated to 1250 mg/m$^2$ and with sunitinib administered on a continuous dosing schedule.

P3-135 NSCLC: Molecular Targeted Therapy Posters, Wed, Sept 5 – Thurs, Sept 6

**Results of an open-label, Phase II trial of nanoparticle albumin bound paclitaxel (nab-paclitaxel), carboplatin, and bevacizumab as first-line therapy in patients with advanced non-squamous non-small cell lung cancer (NSCLC)**

Reynolds, Craig[1,7] Barrera, David[1,2] Vu, Duy Quoc[1,3] Jotte, Robert[1,4] Spira, Alexander I.[1,5] Weissman, Charles[1,6] Boehm, Kristi A.[1] Pritchard, Sharon[8] Asmar, Lina[1]

*[1] US Oncology Research, Inc., Houston, TX, USA [2] Texas Cancer Center, Ft. Worth, TX, USA [3] New York Oncology Hematology, Albany, NY, USA [4] Rocky Mountain Cancer Centers, Denver, CO, USA [5] Fairfax Northern Virginia Hematology - Oncology, Fairfax, VA, USA [6] New*