weeks (5-31). Plasma pharmacokinetic analyses and pharmacodynamic analyses on buccal swabs are being performed.

The recommended phase II doses are ABT-751 125 mg twice daily for 7 days and carboplatin AUC 6 on a 21-day cycle. This regimen is well tolerated and shows preliminary evidence of activity for previously treated NSCLC.

**P2-250**

**NSCLC: Cytotoxic Chemotherapy Posters, Tue, Sept 4**

A Phase II Study of Gleevec (Imatinib Mesylate) Plus Taxotere (Docetaxel) in Patients with Advanced Non-Small Cell Lung Cancer

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**Background:** Docetaxel has been shown to improve overall survival in patients with recurrent NSCLC. Pre-clinical data suggests synergistic activity with the combination of docetaxel and imatinib. Paul Matthew, et al demonstrated the safety of this combination in the MD Anderson trial “Targeting the platelet-derived growth factor receptor in androgen-independent prostate cancer.” Therefore this combination was administered to patients with recurrent NSCLC to determine overall response rate.

**Methods:** This is a phase II study of the combination of Taxotere and Gleevec in refractory NSCLC to determine tumor activity, toxicity and recommendations for further studies of this combination. Patients must have received at least one prior regimen and experienced recurrence or have been refractory to the initial treatment. Taxotere was administered at 30 mg/M² on a weekly schedule for 3 weeks followed by one week rest. Gleevec was administered at a starting dose of 600 mg daily. Dose modifications to address toxicity were built in to the protocol.

**Results:** To date, a total of 10 patients have been enrolled on this study. Seven male and 3 female with a median age of 66 years (range 58 - 74). A total of 26 cycles were delivered to 10 patients (mean = 3).

Four patients experienced fatal adverse events while on study. Two with a non-study related fatal MI (both with history of heart disease). One patient developed GI perforation not related to study (history of ischemic bowel disease). One patient suffered a fatal pulmonary embolus not related to study (history of CAD and peripheral vascular disease).

Grade 4 toxicities included periordial edema (1 pt), pneumonia (2 pts), diarrhea (1 pt), dehydration (1 pt), dyspnea (1pt), anorexia (1 pt), bilateral pleural effusion (1 pt), and neutropenia (2 pts).

Grade 3 toxicities included hypotension, renal failure, hypotension, mental status changes, anorexia, azotemia, dyspnea, herpetic esophageal ulcer, pneumonitis, cough, neutropenia, shortness of breath, weakness, fatigue, and anemia.

**Results:** Responses were minimal. Four of 10 patients received only 1 cycle. Three of those 4 suffered a fatal adverse event and tumor assessment was not performed. The fourth developed herpetic esophageal lesions and was started on 2nd line therapy prior to tumor assessment. One patient had stable disease after 2 cycles but progressed after cycle 3. One patient received 3 cycles, had stable disease after cycle 2 but refused additional therapy after cycle 3 due to grade 2 nausea. One patient had stable disease after 6 cycles then experienced a fatal pulmonary embolus. An additional patient had a partial response after cycle 4 but CT after cycle 6 demonstrated progression. Two patients progressed after cycle 2.

**P2-251**

**NSCLC: Cytotoxic Chemotherapy Posters, Tue, Sept 4**

Phase I/II study evaluating the safety and efficacy of ABT-751 in combination with docetaxel vs docetaxel alone in subjects with advanced or metastatic non-small-cell lung cancer

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**Background:** ABT-751 is an orally bioavailable sulfonamide that binds to the colchicine site on β-tubulin and inhibits polymerization of microtubules. Docetaxel (Taxotere®) is an antineoplastic taxoid. Both compounds have been evaluated individually in advanced NSCLC subjects and in combination in preclinical xenograft models.

**Methods:** The Phase 1 open-label dose escalation portion of the study was designed to determine the maximum tolerated dose (MTD) and recommended Phase 2 dose (RPTD) of ABT-751 when administered with docetaxel. For each cycle, subjects received 75 mg/m² docetaxel IV on Day 1 and ABT-751 orally QD for 14 consecutive days followed by 7 days off drug. Dose levels of ABT-751 began at 200 mg and will escalate by 50 mg increments. Pharmacokinetic sampling was performed on Day 1 of Cycle 1. The Phase 2 portion of the study was designed to determine the effect of ABT-751 plus docetaxel on progression-free survival.

**Results:** The RPTD was determined to be 200 mg of ABT 751 QD for 14 days. To date, 7 subjects have been accrued into the Phase 1 portion of the study, and preliminary safety data are available for 5. One of the subjects in the 200 mg cohort experienced a dose-limiting toxicity of grade 4 thrombocytopenia. Two subjects experienced an adverse event (1 multiple sclerosis and 1 hiccup) rated grade 3 using the Common Terminology Criteria for Adverse Events (CTCAE) version 3.0. No grade 4 or 5 adverse events were reported. Preliminary results indicate that the pharmacokinetics of ABT-751 and its glucuronide and sulfate metabolites after concomitant administration of a single dose of ABT-751 (200 mg) with docetaxel were comparable to those after a single dose of ABT-751 (200 mg) alone in a previous study.

Pharmacokinetic parameters of ABT-751 after a 200 mg oral dose of ABT-751

| Pharmacokinetic parameters of ABT-751 after a 200 mg oral dose of ABT-751 |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| ABT-751 With Docetaxel | ABT-751 Alone# | ABT-751 Glucuronide with Docetaxel | ABT-751 Glucuronide Alone# | ABT-751 Sulfate with Docetaxel## | ABT-751 Sulfate Alone# |
| N | 3 | 23 | 3 | 23 | 3 | 23 |
| Tmax (h) | 2.3 ± 1.5 | 2.0 ± 1.3 | 5.0 ± 2.7 | 4.5 ± 2.2 | 5.0 ± 2.7 | 4.0 ± 2.4 |
| Cmax (μg/mL) | 9.1 ± 5.0 | 9.1 ± 4.5 | 6.1 ± 4.3 | 4.6 ± 1.7 | 8.0 ± 3.2 | 7.4 ± 3.2 |
| AUC0-8 (μg*h/mL) | 33.8 ± 15.1 | 33.0 ± 10.1 | 30.2 ± 22.5 | 26.6 ± 10.5 | 43.6 ± 21.3 | 39.5 ± 15.0 |

#Results from Phase 1 Study M01-303 were used as a historical reference.

**Conclusions:** The RPTD of the combination of ABT-751 and docetaxel has been determined. Coadministration of docetaxel with ABT-751 does not appear to affect the pharmacokinetics of ABT-751.