prognostic/predictive value of several biomarkers (BM): epidermal growth factor receptor (EGFR) immunohistochemistry (IHC), EGFR fluorescence in situ hybridization (FISH), and *EGFR* and *Kras* mutation status.
**Methods:** 743 pts with advanced NSCLC whose disease had not progressed following 4 cycles of 1st-line chemotherapy with B were randomized by the interim analysis data cut-off to receive B+E or B+P. B dosing was 15 mg/kg every 3 weeks; E dosing was 150 mg daily. Maintenance therapy continued until unacceptable toxicity or disease progression.
Archival tumor tissue was collected for BM analysis. EGFR FISH and IHC analyses were performed using the PathVysion® and PharmDx kits™ from Abbott-Vysis and DAKO. Analyses of *EGFR* tyrosine kinase mutations in exons 18−21 and *Kras* mutations in exons 2 and 3 were performed using DHPLC (denaturing high-performance liquid chromatography) and mutations were validated by sequencing.
**Results:** Biomarker assay results were available for 49.4% of randomized patients. Their demographics were similar to the overall trial population.
The PFS HRs for the BM defined subgroups are presented in the table.

Overall survival data for the ATLAS trial remains immature.

| BM status | n = 367 (49.4%)[a] | HR[b] (95% CI) for PFS |
|---|---|---|
| EGFR IHC+ | 191 (25.7%) | 0.92 (0.64, 1.32) |
| EGFR IHC− | 67 (9.0%) | 1.00 (0.55, 1.82) |
| *EGFR* FISH+ | 87 (11.7%) | 0.66 (0.39, 1.13) |
| *EGFR* FISH− | 109 (14.7%) | 1.40 (0.86, 2.28) |
| *EGFR* mut+ | 52 (7.0%) | 0.44 (0.22, 0.86) |
| *EGFR* wt | 295 (39.7%) | 0.85 (0.64, 1.13) |
| *KRAS* mut+ | 93 (12.5%) | 0.93 (0.55, 1.56) |
| *KRAS wt* | 239 (32.2%) | 0.67 (0.49, 0.91) |

[a]Denominator for % is number of patients in ITT population (n = 743).
[b]HR for B+E, compared with B+P.

**Conclusions:** Pts with assay results for BM analysis were representative of the overall population. The PFS results of the BM defined subgroups were consistent with the overall PFS benefit seen in the trial. These results suggest that EGFR FISH +, *EGFR* mutated, and *Kras* wildtype pts could derive the greatest improvement in PFS with B+E.

**9LBA** LATE BREAKING ABSTRACT

**A randomized phase III study comparing gefitinib with carboplatin (CBDCA) plus paclitaxel (TXL) for the first-line treatment of non-small cell lung cancer (NSCLC) with sensitive EGFR mutations: NEJ002 study**

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**Background:** Based on our promising results of phase II studies estimating gefitinib for NSCLC with sensitive EGFR mutations, this multicenter phase III study comparing gefitinib with standard chemotherapy, i.e. CBDCA plus TXL, for the first-line treatment of advanced NSCLC with EGFR mutations was conducted.
**Materials and Methods:** Peptide nucleic acid-locked nucleic acid PCR clamp test (Cancer Res 2005) was employed to detect EGFR mutations from cytological or histological samples. NSCLC patients (pts) having sensitive EGFR mutations, measurable lesion, ECOG PS 0−1, age of 20−75 years, and no prior chemotherapy were randomized (balanced for institution, sex, and clinical stage) to receive arm A: gefitinib (250 mg/day) daily, or arms B: CBDCA AUC 6 and TXL 200 mg/m2 in 21-day cycles. The primary endpoint was progression-free survival (PFS) and secondary endpoints were overall survival, response rate, quality of life, time to PS 3, and toxicity profiles. The sample size was calculated to be 320 in total (alpha = 5%, power = 80%) to confirm the PFS superiority of arm A (hazard ratio = 0.69). Per protocol, an interim analysis was performed 4 months after 200 pts entered.
**Results:** From April 2006 to December 2008, 200 pts were enrolled, and according to the study protocol, the interim analysis was performed at the end of May 2009 on 198 pts except for 2 ineligible pts (arm A, 98; arm B, 100). Patients' characteristics were well balanced between arms: median age = 63/63 years; 63%/64% female; 79%/75% stage IV; 90%/96% adenocarcinoma, respectively. Significantly higher response rate was obtained in arm A (74.5% vs. 29.0%, $p < 0.001$). There were several differences in toxicities between arms: grade 4 neutropenia 1% vs. 33%, grade 3−4 liver dysfunction 25% vs. 1%, and grade 3 neuropathy 0% vs. 5%, respectively, $p < 0.01$. An interim analysis clearly showed a significantly longer PFS in arm A than arm B (10.4 months vs. 5.5 months, hazard ratio = 0.357, $p < 0.001$). Therefore, the independent safety committee recommended terminating accumulation of pts at the end of May 2009. Preliminary results of median survival time were 28.0 months in arm A and 23.6 months in arm B ($p = 0.353$).
**Conclusions:** The NEJ002 study met its primary endpoint with high statistical significance. Gefitinib as the first-line treatment for advanced NSCLC harboring EGFR mutations significantly improves PFS with favorable toxicity profiles against CBDCA plus TXL, thus should be considered as the new standard treatment for sensitive EGFR mutation-positive NSCLC pts.

**10LBA** LATE BREAKING ABSTRACT

**Randomized phase 3 study of panitumumab with FOLFOX4 compared to FOLFOX4 alone as 1st-line treatment (tx) for metastatic colorectal cancer (mCRC): the PRIME trial**

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**Background:** Panitumumab (pmab) is a fully human anti-epidermal growth factor receptor (EGFR) monoclonal antibody (mAb) approved as monotherapy for patients (pts) with mCRC. The PRIME trial was designed to evaluate the efficacy and safety of pmab with FOLFOX4 vs FOLFOX4 alone as 1st-line tx for mCRC (clinicaltrials.gov identifier: NCT00364013; sponsor: Amgen Inc).
**Methods:** This was a randomized, multicenter, phase 3 study. Pts were randomized 1:1 to receive pmab 6.0 mg/kg Q2W + FOLFOX4 (Arm 1) vs FOLFOX4 (Arm 2). Pts had metastatic adenocarcinoma of the colon or rectum; no prior chemotherapy for mCRC; no prior oxaliplatin; ECOG 0−2; and available tumor tissue for biomarker testing. Randomization was stratified by ECOG 0−1 vs 2 and region. The primary endpoint was progression-free survival (PFS). Originally designed to compare the tx effect in the all randomized population, the study was amended to focus hypothesis testing in the wild-type (WT) *KRAS* subset. *KRAS* status was determined by a blinded central laboratory using allele-specific PCR prior to the primary analysis.
**Results:** From Aug 2006 to Feb 2008, a total of 1,183 pts were randomized after signing an informed consent, and received tx: 593 Arm 1, 590 Arm 2. Demographics were generally well-balanced and included 63% men, median age 62 years [range: 24−85]; ECOG 0 or 1; 95%. 1096/1183 pts (93%) had *KRAS* results: 656 (60%) WT, 440 (40%) mutant (MT). For pts with WT *KRAS,* median PFS was 9.6 months for Arm 1 and 8.0 months for Arm 2; HR (95% CI) = 0.80 (0.66, 0.97); $p = 0.0234$ and response rate (by blinded central review) was 55% (Arm 1) and 48% (Arm 2). For pts with MT *KRAS*, median PFS was 7.3 months for Arm 1 and 8.8 months for Arm 2; HR (95% CI) = 1.29 (1.04, 1.62); $p = 0.0227$. Adverse event rates were comparable across arms with the exception of known toxicities associated with anti-EGFR therapy such as rash, diarrhea, and hypomagnesemia. Pmab-related grade 3 infusion reactions were reported for 2 patients in Arm 1 (<1%).
**Conclusions:** Pmab significantly improves PFS and is well tolerated when added to FOLFOX4 for 1st-line tx of pts with WT *KRAS* mCRC. PFS was inferior in the pts with MT *KRAS* tumors who received pmab. This study confirms the importance of *KRAS* as a predictive biomarker in the setting of 1st-line mCRC tx with an anti-EGFR mAb in combination with chemotherapy.