Immunohistochemistry determined expression of EGFR and phosphorylated protein kinase B (PKB)/Akt. *EGFR* amplification was determined using fluorescence *in situ* hybridization.

Response to erlotinib was unaffected by treatment group or pharmacokinetic parameters, but was associated with *EGFR* overexpression ($P = 0.03$) and gene amplification ($P = 0.02$) in the 29 patients with glioblastoma multiforme. Six patients with *EGFR* amplification were nonresponders to erlotinib, indicating involvement of additional mechanisms. Phosphorylated PKB/Akt was associated with a poor response to erlotinib and shorter time to progression in the entire cohort.

In patients with glioma, expression levels of EGFR and phosphorylated PKB/Akt were strong predictors of response to erlotinib. The authors plan a phase II trial, with treatment strategies formulated according to the status of these molecular markers.

Rebecca Ireland

Original article Haas-Kogan DA *et al.* (2005) Epidermal growth factor receptor, protein kinase B/Akt, and glioma response to erlotinib *J Natl Cancer Inst* **97:** 880–887

96-hour infusion of paclitaxel in advanced bronchioloalveolar carcinoma

Bronchioloalveolar carcinoma (BAC) is a histologic subgroup of non-small-cell lung cancer (NSCLC) that accounts for 2–5% of new NSCLC cases. The relative infrequency of BAC has meant that few clinical trials for this disease have been performed. Focal BAC can be cured by resection, but no optimal therapy for multilobar or recurrent disease has been established. Paclitaxel is one of the most commonly used agents for the treatment of NSCLC, and prolonged infusion of paclitaxel has demonstrated significant activity in *in vitro* studies, clinical studies in NSCLC, and in anecdotal cases of BAC.

The Southwest Oncology Group 9714 phase II trial set out to determine whether 96-hour infusion of paclitaxel would demonstrate promising survival and response rates in patients with previously untreated advanced BAC. Partial responses were confirmed in 9% of the 58 patients analyzed in the study, and 40% had stable disease. The median overall survival and median time to disease progression were 12 months and 5 months, respectively. Grade 3 or greater toxicities were seen with neutropenia/granulocytopenia (43%), febrile neutropenia (12%), infection (22%) and stomatitis/pharyngitis (10%); there were also five deaths, which were likely to be treatment related.

The authors conclude that although 96-hour paclitaxel infusion is active in BAC, the toxicity is considerable. This trial shows that BAC can be studied effectively in a multi-institutional setting and provides a benchmark for assessing response rate and efficacy data for ongoing and future trials of BAC.

Rachel Murphy

Original article West HL *et al.* (2005) Advanced bronchioloalveolar carcinoma: a phase II trial of paclitaxel by 96-hour infusion (SWOG 9714): a Southwest Oncology Group study. *Ann Oncol* **16:** 1076–1080

Promoter methylation reduces expression of *TGF-β* receptor type 2 gene in prostate cancer

Transforming growth factor-β (TGF-β) protein is a potent inhibitor of epithelial cell proliferation, and its action is mediated through type 1 (TGF-βRI) and type 2 (TGF-βRII) receptor proteins. Resistance to TGF-β signaling caused by loss of *TGF-βRII* gene expression has been implicated in prostate cancer, and methylation of promoter sequences leads to downregulation of tumor suppressor genes in various human cancers.

Zhao *et al.* investigated promoter methylation and expression levels of TGF-βRII in 67 human prostate cancer samples, 48 benign hyperplasia samples and 4 prostate cancer cell lines. The methylation status of binding site at position –140 within the promoter element of the *TGF-βRII* gene was assessed using a methylation-specific polymerase chain reaction. Levels of *TGF-βRII* mRNA and protein expression were compared using a semi-quantitative reverse transcriptase polymerase chain reaction and immunohistochemistry, respectively.

The level of methylation at binding site –140 was higher in prostate cancer tissues than in benign hyperplasia samples. Levels of *TGF-βRII* mRNA and protein were, however, significantly reduced in prostate cancer tissue compared with benign hyperplasia samples. In three out of four prostate cancer cell lines analyzed, treatment with a demethylating