Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) as a biomarker for the effect of PTK787/ZK 222584 as second-line mono-therapy in patients with stage IIIB or stage IV non-small-cell lung cancer (NSCLC).

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Background: Over expression of vascular endothelial growth factor receptor (VEGF-R) in NSCLC-tumors is linked to poor prognosis. PTK787/ZK 222584 (PTK/ZK) is an orally active, potent and selective inhibitor of VEGF-R tyrosine kinases. DCE-MRI, which measures early changes in tumor-associated vasculature in response to treatment, has been successfully used as a biomarker for assessment of biological activity of PTK/ZK in liver metastases from colorectal cancer [Morgan et al., 2003, J Clin Oncol 21: 3955-3964].

Methods: This is a prospective, single-arm, multi-center, phase-II study of PTK/ZK in pretreated patients with advanced stage NSCLC. All patients (pts) received 1250 mg of PTK/ZK once daily (qd) until disease progression or unacceptable toxicity occurred. Response evaluation was based on RECIST criteria. Disease stabilization of at least 12 weeks based on CT/MRI-imaging was defined as clinically relevant drug activity. DCE-MRI was performed prior to PTK/ZK administration, on day 2 and at day 28. Contrast enhancement for the whole tumour was assessed by calculating the transfer constant ($K_{trans}$) using a two-compartment model.

Results: DCE-MRI imaging was performed successfully in 35 pts on day 2 and 29 pts at day 28. Thirty-two pts with day 2 DCE-MRI were evaluable for response assessment, 11 (34%) achieving stable disease (SD) at 12 weeks and 18 classified as progressive disease (PD). Response assessment for the whole group so far (56 pts) is 56% stable disease. There was a statistically significant average reduction in $K_{trans}$ at day 2 of 35.2 % (p<0.0001, paired ‘t’ test) and 36.8 % at day 28 (p<0.0001). Pts with SD at 12 weeks had a greater reduction in enhancement at day 2 (44.8%) as compared to those with PD (34.6%), but this did not reach statistical significance (p=0.3).

Conclusions: These results suggest that DCE-MRI may be useful in predicting biological response of VEGF inhibition in lung tumours, and studies are ongoing using this approach to aid dose scheduling. The study is currently recruiting for twice daily treatment.