**Application of kinase activity profiles to predict response to erlotinib in a neoadjuvant setting in early stage non-small cell lung cancer (NSCLC).**


*PamGene International BV, ‘s-Hertogenbosch, The Netherlands
*Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands.

**Study Design**
NSCLC patients (stage IA-IIIA) with resectable tumor (cT1-3, N0-1) from the M06NEL phase II study were treated in a neo-adjuvant setting with daily erlotinib for three weeks. At day 24 surgery was performed and histological assessment was performed to determine response. Fresh frozen tumor biopsies from the resected material, of 6 responders and 8 non-responders, based on histological assessment, were tested on PamChip arrays for kinase activity in the presence and absence of spiked in erlotinib. Multivariate analysis was used to classify samples.

**Key Findings**
Kinase activity profiles in the presence of erlotinib could establish a difference between erlotinib responders and non-responders (figure 1). Multivariate unsupervised analysis with leave-one-out cross validation resulted in misclassification of 1 sample (responder) (figure 2).

**“Author Quote”**
The present study suggests that kinase inhibition profiles are able to predict response to erlotinib based on results of this test. This means that more patients may be eligible for erlotinib treatment - since the test assesses the effect of a TKI directly at its target.

**Background**
Subcategories of NSCLC patients may benefit from epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKI’s), notably those with cancers that harbor mutated EGFR. However, certain patients lacking such mutations might also benefit from TKI treatment. At present, there are no reliable diagnostic tests to identify this patient subset.

**Conclusion**
This is the first prospective phase II biomarker study to show that kinase activity profiles of tumor tissue exposed ex vivo to a kinase inhibitor may be used to identify (early stage) NSCLC patients who are likely to respond to TKI treatment.