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A genomic strategy to refine prognosis in early stage non-small cell lung cancer

Reviewed by Dr. Charles Butts

Potti A *et al.* NEJM 2006; 355:570-80

This paper by Potti et al. from the Duke Lung Group uses the lung metagene model to prognosticate outcomes for patients with early stage non-small cell lung cancer. They initially analyzed 198 tumor samples from 3 cohorts of patients with non-small cell lung cancer. These were divided into a training cohort of 89 patients and 2 independent validation cohorts of 25 and 84 patients. RNA was extracted from tumor tissue, the RNA quality assessed and microray assays carried out using AFFYMETRIX gene chips. Metagene represented the dominant average pattern of expression the gene clusters across the tumor samples. High risk of recurrence is classified as the probability greater than .5 while low risk was probably a recurrence of .5 or less. The metagene model was compared to a clinical model which includes stage, age, sex, tumor diameter, histology and smoking history. The metagene model was significantly more accurate in predicting outcome than the clinical model and addition to the metagene model added no improvement in prognostic ability. This was confirmed in the two validation cohorts. The overall accuracy of the metagene model in the ACOSOG validation core was 72% and in the CALGB it was 78%. When focusing on 68 patients with stage IA disease they were able to be separated into a risk. Those classified at high risk based on a metagene profile had a 4 year survival rate of less than 10%. In addition, the metagenes with the greatest discriminatory capability included genes known to have relevance in non-small cell lung cancer suggesting that the metagene model truly does predict the biology of the early lung cancer. In the future, such models may be used to help design randomized trials of adjuvant therapy in patients who would otherwise be considered to be at low risk of recurrence such as the stage IA patients. Those patients could be randomized to observation or chemotherapy based on risk as defined by the metigene model. In addition, further enhancement of such prognostic models may in the future help define which therapies may be beneficial in sub-group patients.