Gene Expression Signature to Determine the Benefit of Adjuvant Chemotherapy in Early Stage Non-Small Cell Lung Cancer

80% of the 30,000 patients annually diagnosed with early stage non-small cell lung cancer (NSCLC) will be recommended for adjuvant chemotherapy (ACT) after surgical resection of their tumor. However, the five-year survival advantage of ACT is only 4-15%, suggesting that many patients receive little to no benefit. This technology is a diagnostic gene expression signature composed of transcripts involved in the Retinoblastoma-E2F pathway, and is predictive of the benefit of ACT. This diagnostic would identify stage II and III patients for whom adjuvant chemotherapy, post surgical resection of their primary tumor, would improve their median progression free survival and overall survival. It would also identify patients who would not benefit.

COMMERCIAL OPPORTUNITY

- There are approximately 230,000 new cases per year of lung cancer in the U.S. and about 85%-90% of all lung cancers are NSCLC. Of these, 15% are early stage (indicating that the tumor has not metastasized) leading to a market size of approximately 30,000 new early-stage NSCLC patients per year.

- This signature distinguishes between two groups: an E2F High Score group which does statistically significantly better with ACT vs. observation (median PFS 79.6 months vs. 8.7 months; $p=0.02$), and an E2F Low Score group that receives little to no benefit from ACT vs. observation (median PFS 44.2 months vs. 30.9 months; $p=0.62$).

- This technology is similar to Life Technologies' Pervenio Lung, a diagnostic based on a 25 gene signature, that stratifies NSCLC patients into risk groups, and currently sells for $3,600 per test. However, Pervenio Lung does not have the predictive power demonstrated by the Moffitt assay with respect to ACT response.

- A Markov model of Life Technologies' Pervenio Lung has demonstrated that including diagnostics to predict a patient's response to ACT is cost effective in 68% of cases. Moreover, this diagnostic could help patients avoid the cost ($10,000 - $30,000) of platinum based chemotherapy and additional money associated with ACT toxicity, approximately $3,000-$7000 per episode.

TECHNOLOGY

This 75-gene signature is derived from a comprehensive analysis of the E2F pathway in vitro using siRNA. In two separate randomized trials (JBR10 and NATCH), looking at different forms of platinum based ACT, the E2F signature was predictive of ACT benefit, as high E2F score patients showed a statistically significant increase in the median of progression free survival with ACT versus observation (JBR10: >60m vs. 37m; $p=0.03$ and NATCH: 79.6 m vs. 8.7 m; $p=0.02$), while the Low E2F score patients showed similar survival rates ($p=0.26$ & 0.62, respectively. Additionally, it has proven strongly prognostic of overall survival in five independent cohorts (MCLA, TCGA, JBR10, LCBRN, and NATCH), with patients that have a low E2F score having a median overall survival that was between 2.3 and 3.7 times as long as those patients with a high E2F score (all p values <0.03). Originally, the assay was based on microarray, but has now been fully optimized and validated for utilization of NanoString™ technology, which enables the evaluation of a smaller amount of a clinically relevant, pathologically confirmed sample, and reduces the cost and amount of time required.

PUBLICATION/PATENT

- US Patent Application was filed on 02/03/2014 for Drs. Cress and Chen.

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