

Gene Signature Predicts Recurrence and Benefit From Adjuvant Chemotherapy in Colorectal Cancer



This gene signature can differentiate between the stage 2 colorectal cancer patients that are at a high vs. low risk for recurrence within five years following surgery. Adjuvant chemotherapy is currently not recommended for stage 2 patients; however approximately 10% of stage 2 patients will recur, and could therefore benefit from adjuvant chemotherapy. The test may also benefit stage 3 patients who currently all receive chemotherapy by identifying the patients who will not recur or who at least do not benefit from certain combination regimens. A similar test called Oncotype DX Colon Cancer Assay is marketed for stage 2 patients to determine who should receive chemotherapy and for stage 3 patients to determine which patients would benefit from oxaliplatin in addition to 5-FU/LV. On multiple datasets, the Moffitt signature had lower p-values suggesting it was a better predictor of recurrence than the Oncotype DX Colon Cancer Assay signature.

COMMERCIAL OPPORTUNITY

- Over 135,000 new colorectal cancer cases are estimated to occur in the US in 2014. Currently stage 2 patients (about 28% of all patients) are generally treated by surgical resection alone whereas stage 3 patients (about 38%) is treated with 6 months of adjuvant chemotherapy.
- The attractiveness of the market is evident from the Oncotype DX Colon Cancer Assay gene signature for stage 2 patients that was launched in January 2010 and is currently listed at \$4,030. The Oncotype DX signature is targeted to the 70% of patients for whom MMR/MSI and T-stage are uninformative. The Moffitt signature however performed more strongly regarding Recurrence-Free Survival in the ALMAC stage 2 dataset than did Oncotype DX ($p=0.0064$ vs. 0.8).
- The Oncotype DX Signature is also used to help predict which Stage 3 patients would benefit from Oxaliplatin. The addition of oxaliplatin to 5FU/LV benefits only 6-7% of treated patients and comes with significant toxicity, including long-term peripheral neuropathy. The 5FU/LV + oxaliplatin regimen is expected to add approximately \$38,000 in costs to the 5FU/LV treatment alone.
- The Moffitt Colon Cancer Signature was a better predictor of recurrence and overall survival in eight different analyses with five different datasets with multiple stages of disease, suggesting that it might also be superior to Oncotype DX with regard to Stage 3 patients receiving oxaliplatin—if the same dataset were used of 892 stages 2 and 3 patients randomized between 5FU/LV and 5FU/LV + oxaliplatin.

TECHNOLOGY

The Moffitt test consists of 1204 probesets from 508 genes derived from the difference between the PC1 and EMT signatures. PC1 includes expression of 243 genes in colorectal tumors, while EMT is obtained from 310 genes in the lung tumors. The final gene set is predictive of recurrence ($HR=1.31$; $p=0.0064$) and overall survival ($HR=1.38$; $p=0.0012$) in stage 2 colorectal patients. The test is also highly predictive of progression free survival in 644 stage 3 patients ($HR=1.69$; $p=3.99 \times 10^{-8}$). Additionally, the test predicted overall survival ($p=8.22 \times 10^{-9}$) and survival after relapse ($p=0.015$) in stage 3 patients. The test showed statistically significant p-values in five colorectal datasets: PETACC3 (OS and PFS), ALMAC (OS and PFS), French (PFS), GEO41258 (OS and PFS), and GSE14333 (PFS).

PUBLICATION/PATENT

- Manuscript submitted
- US provisional patent application filed on 7/30/2013 for Drs. Schell and Yeatman

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LICENSING OPPORTUNITY



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