Signal Genetics Announces Publication of Meta-Analysis of its Colon Cancer Test-Previstage™ GCC Confirming Prognostic Capabilities in Patients with Colon Cancer.

New York, NY, January 23, 2012 – Signal Genetics, a privately held personalized medicine company focused on cancer, announced today the presentation of a paper entitled “Guanylyl Cyclase C (GCC) Lymph Nodes (LN) Classification as a Prognostic Marker in Patients with Stage II Colon Cancer: A Pooled Analysis” at the 2012 American Society of Clinical Oncology Gastrointestinal Cancer Symposium held in San Francisco, CA January 21, 2012. The data from the paper demonstrate the value of implementing Previstage testing in patients with colorectal cancer to identify those patients at risk of relapse.

The paper is the culmination of the work conducted by a team of researchers and collaborators from several centers, including: Rhode Island Hospital, Brown University, University of Massachusetts Medical School, University of North Carolina, Lahey Clinic, Brigham and Women's Hospital, British Columbia Cancer Agency and DiagnoCure Inc. These researchers conducted a pooled individual data analysis on 310 patients to confirm whether molecular detection of GCC in Lymph Nodes indicates high risk of disease recurrence and poor survival in untreated stage II colon cancer.

GCC is a colon-specific biomarker normally found in gastrointestinal epithelium whose expression is preserved in primary and metastatic colorectal cancer cells. Studies to date have suggested that the presence of GCC gene expression in lymph nodes increased the likelihood of disease recurrence in stage II colon cancer patients, independent of traditional high risk features. The results of this study suggest that detection of GCC mRNA in lymph nodes is associated with risk of disease recurrence in stage II colon cancer patients not treated with adjuvant chemotherapy. These findings are consistent with several other studies conducted over the past 10 years.

Based on GCC levels, the estimated 5 year recurrence risks were 11% and 32% for the low and high risk groups respectively, clearly showing that GCC is a strong prognostic marker that effectively stratifies patients between those that are essentially cured from those at risk of disease recurrence. Higher detection levels of GCC in lymph nodes is also significantly associated with increased risk of all-cause mortality, disease-specific survival, and disease-free survival.

According to Joe Hernandez, President and CEO of Signal Genetics, “This paper represents further validation of GCC as a strong prognostic test that provides physicians and their patients an important insight that helps them make critical treatment decisions.”
About Signal Genetics
Signal Genetics, the parent company of Myeloma Health, Respira Health, and CC Health, is a privately held personalized medicine genetic testing company focused on bringing novel insights to physicians and their patients with various types of cancer. The goal of Signal Genetics is to provide information regarding disease status, stage, odds of relapse, predicting response to therapy, and prognosis through an array of proprietary tools to help guide physicians to the optimal treatment for each individual patient. Additional information is available at www.signalgenetics.com.

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Guanylyl Cyclase C (GCC) Lymph Nodes (LN) Classification as a Prognostic Marker in Patients with Stage II Colon Cancer: A Pooled Analysis


Mayo Clinic, Rochester, MN; Rhode Island Hospital and Brown University, Providence, RI; UMass Medical School, Worcester, MA; UNC Chapel Hill; NC; Louisiana University, Baton Rouge, LA; Boston University School of Medicine, Boston, MA; BC Cancer Agency, Vancouver, BC, Canada; DiagnosCare Inc., Quebec, QC, Canada

Background

- Unmet need to risk of recurrence exists in stage II CC patients
- Molecular markers and gene signatures have been recently evaluated to identify patients with a higher risk of recurrence.

Objective

- We conducted a pooled individual data analysis to confirm whether molecular detection of GCC in LNs indicates high risk of disease recurrence and poor survival in unresected stage II CC.

Methods

- GCC expression
- GCC mRNA was quantified by RT-qPCR using formalin-fixed paraffin-embedded LNs samples from unresected stage II CC patients included in clinical trial
- Individual LNC GCC status was determined by relative quantification of GCC-normalized to housekeeping genes (GAPDH + GLUD) with a validated cut-off (6.5).
- Populations
- Sargent 2017: N = 241
- 5-year recurrence rate = 15.7
- Median age = 74 yrs, range = 24 - 96 yrs
- Male = 56%
- Surgery in 2004 – 2006: 85%
- Grade G1 = 9%, G2 = 24%, G3 = 15%
- T stage: T2 = 85%, T4 = 5%
- Disease-free survival (DFS) = 80% at 5 years
- LN failure (LNF): number of positive nodes by GCC divided by number of informatative nodes
- High risk group: LNF > 0.5
- Low risk group: LNF ≤ 0.5
- Stratified logrank test to examine the relationship between GCC LNF classification and primary and secondary outcomes.

Statistical Analyses

- Clinical outcomes:
  - Time to recurrence (TTR): time from surgery to first event of recurrence (local or distant) or death related to disease.
  - Overall Survival (OS): time from surgery to death due to any cause.
  - Event-free survival (EFS): time from surgery to death due to disease.
- Survival analysis (Kaplan-Meier) with C-index to evaluate the prognostic performance of the model.
- Univariate analysis to determine the association between GCC LNF classification and risk of disease recurrence.
- Multivariable Cox models (univariate and multivariate) used to estimate unadjusted and adjusted Hazard Ratios (HRs), controlling the risk of recurrence and death between risk groups defined by GCC LNF values.

Results

- ROC curve analysis for TTR: AUC = 0.73
- ROC curve analysis for OS: AUC = 0.69
- ROC curve analysis for DFS: AUC = 0.72

- In this pooled analysis, the prognostic value of the ratio of the number of GCC+ LNs over the total number of informative LNs was confirmed.
- High LNF significantly predicted higher disease recurrence risk. The estimated 5-year recurrence rates were 11% and 32% for the low and high risk group, respectively. Figure 1A (HR = 2.95, 95% CI: 1.63 - 5.42, p=0.0083).
- Higher GCC LNF (≥ 0.5) is also significantly associated with increased risk of all cause mortality (HR = 1.83), disease-specific survival (HR = 2.07), and disease-free survival (HR = 2.23).

- In a multivariate analysis adjusted for age, T stage, grade, number of LNs assessed, and LNI, the GCC LNF significantly predicted higher risk of death (HR = 2.04, 95% CI: 1.45-4.78, p=0.0014).

- The GCC LNF appears to have the greatest clinical utility for stage II patients with 12 LNs assessed, which constitute the majority of stage II CC patients.

Conclusions

- Our results suggest that detection of GCC mRNA in LNs is associated with risk of disease recurrence in stage II CC patients treated with adjuvant chemotherapy.

- The GCC LNF appears to be the most important factor for risk of disease recurrence in stage II CC patients treated with adjuvant chemotherapy.

References