New O-Glycan Gene Signature for Improved Ovarian Cancer Therapy and Prediction of Response to Gemcitabine

This technology is a new gene-based diagnostic assay based on the O-glycan pathway that can be used to assist physicians with determining whether ovarian cancer patients would benefit from first-line optimal (or aggressive/ultradical) cytoreductive surgery. Physicians currently use clinical parameters to decide whether to perform aggressive surgery, but those parameters don't inform them about which patients are likely or not likely to benefit from this high-cost treatment that has a high incidence of perioperative morbidities. Based on gene expression data from a tumor biopsy, our diagnostic could help physicians clearly identify patients with no increased survival benefit from optimal cytoreductive surgery who could therefore receive less costly chemotherapy instead. Preclinical data also suggest that this signature may be useful as a predictive diagnostic for response to second-line gemcitabine.

COMMERCIAL OPPORTUNITY

- In 2012, over 22,000 women were diagnosed with ovarian cancer in the US with over 15,000 patients dying in that same time frame. Cytoreductive surgery + adjuvant chemotherapy is the most common first-line therapy.
- Currently, the standard of care for these women is to use clinical presentations of the disease and overall health status to make decisions about who is a good candidate for initial surgery with adjuvant chemotherapy—however, here are no reliable biomarkers available to assist the physician.
- In a retrospective study of patient data, our gene signature has shown utility in identifying patients for whom aggressive cytoreductive surgery brings no additional survival benefit over non-aggressive surgery. Since survival outcomes of non-aggressive primary surgery equal those of chemotherapy, our signature could be developed to help guide patient selection for surgery vs. chemotherapy.
- Standard primary chemotherapy (paclitaxel+carboplatin) for ovarian cancer costs about $5000 for six cycles, whereas cytoreductive surgery can cost over $86,000. A diagnostic that could aid physicians in selecting patients for first-line chemotherapy without surgery, would save payers over $80,000/patient.
- Gemcitabine is frequently prescribed as a second-line chemotherapeutic agent for relapsed patients and can cost over $12,000 for a full course of therapy (Gemzar, Lilly Pharmaceuticals). However, only approximately 20% of patients with recurrent ovarian cancer have shown responses in clinical trials.

TECHNOLOGY

The molecular basis of ovarian cancer response to gemcitabine was studied by treating 41 cell lines with increasing doses of gemcitabine, and gene expression data were used to identify an O-glycan pathway gene signature (OGBPS) that correlated with gemcitabine sensitivity ($p=0.001$). From the cell line data, low OGBPS expression is associated with gemcitabine sensitivity. Studies on tumor samples from patients with advanced-stage ovarian cancer showed that low expression of a 34-gene OGBPS in patients demonstrating a complete clinical response to primary platinum therapy was significantly associated with reduced survival ($p = 0.003$). Patients with low OGBPS also receive no significant survival benefit from cytoreductive surgery.

PUBLICATION/PATENT

- NB Zgheib, et al., (2012) *Int J Oncol*. 41(1):179-88
- PCT patent application filed on 4/5/2013 for Drs. Lancaster and Marchion and Yin Xiong

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