Method for Measuring MRE11 in Muscle –Invasive Bladder Cancer to Predict Chemoradiation Response Using AQUA

Chemoradiation is one of the treatment options for muscle-invasive bladder cancer (MIBC). By determining a patient's MRE11 level, it might be possible to identify radio-resistant patients who would benefit from increased radiation treatment. MRE11 is a member of the MRN complex that regulates DNA double-strand breaks repair. Using Automated Quantitative Image Analysis (AQUA), a method was developed to quantify MRE11 levels and identify MIBC patients who might be resistant to chemoradiation treatment. With this additional information, physicians could make more informed decisions about how aggressively to manage the disease.

COMMERCIAL OPPORTUNITY

- The American Cancer Society estimates nearly 79,030 patients will be diagnosed with bladder cancer in 2017. About 23,000 patients will have MIBCs, and up to 50% of these MIBC patients will have metastatic recurrence with a median survival of about 14 months.

- The standard care for MIBC is cystectomy, but only 42.9% patients received this treatment due to their age, preference to preserve the bladder, and eligibility for surgery. Chemotherapy, radiotherapy or chemoradiation provides additional choices determined by patient preference and physician discretion.

- Using immunohistochemistry staining, a recent study found low MRE11 protein levels correlate with worse survival following radical radiotherapy for MIBC. The AQUA method is a more precise method to quantify MRE11 level.

- There are 11 radiotherapy studies in clinical trials involves in predictive marker validation, none of which is related to bladder cancer. The market is attractive for this technology because identifying patients who are radio-resistant might result in radiotherapy regimens that are more efficacious.

TECHNOLOGY

The invention is a quantitative method for accessing MRE11 level in MIBC samples. 465 MIBC tissues from six Radiation Therapy Oncology Group clinical trials were selected and stained with anti-MRE11 antibody. The slides were scanned and analyzed by automated quantitative image analysis. An MRE11 score was calculated as a ratio of nuclear to cytoplasmic (N/C) MRE11 levels in urothelial cells. After quality control, 135 samples were further analyzed for the association between chemoradiation and patients' outcomes. Patients with MRE11 N/C ≤1.49 were found associated with higher disease-specific mortality (4-year mortality: 41% N/C ≤ 1.49 vs. 21% >1.49, *p=0.03, n=135*).

PUBLICATION/PATENT

- A provisional patent application was filed on February 10, 2017 for Dr. Magliocco.

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