Feasibility Study For Large-Scale, Population-Based Validation of a Molecular Staging Tool For Bladder Cancer

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Lay Summary

The American Cancer Society estimates that 69,000 new cases of bladder cancer will be diagnosed in the U.S. this year. For patients diagnosed with early stage bladder cancer, 5 year survival rates are high. However, about one third of bladder cancer patients present with advanced disease, and 5 year survival rates are much lower for these cases. Treatment for advanced bladder cancer includes radical cystectomy and lymphadenectomy (complete removal of the bladder and associated lymph nodes) or a combination of chemotherapy and radiation. Despite these treatments, cancer will still spread in up to half of these patients, and is nearly always fatal when it does. One treatment option for advanced bladder cancer patients is the addition of chemotherapy prior to removal of the bladder. This is done in the hopes of eradicating the cancer which has spread locally prior to the surgery. **Previous studies have shown that a subset of patients who receive 3 months of chemotherapy before cystectomy have significantly better survival than patients with cystectomy only**. Unfortunately, only a subset of patients derives benefit from this approach, and it is not possible using current methodologies to reliably identify those individuals who will benefit.

Finding the right treatment for cancer patients is a constant challenge; sometimes a cancer responds to a specific drug, and sometimes the treatment is not effective and the cancer continues to grow and spread. The concept behind “personalized medicine” is to use specific markers in the cancer itself to identify the best drugs for treatment. Personalized medicine can be used to spare patients from treatments that will be ineffective for their specific tumor, as well as identifying the patients most likely to respond to specific therapies. Recently, such tools have been developed for advanced bladder cancer. These tools, called Gene Expression Modeling (or GEM) takes information on specific gene combinations within the tumor and uses that information to predict whether patients are are at high or low risk of local disease spread, and whether the tumor is likely to respond to chemotherapy. One particular benefit to this approach is that GEM testing can be done on biopsy specimens which are taken before cystectomy. Thus, GEM testing could be used to identify patients most likely to have disease spread and most likely to respond to therapy before the cystectomy is performed, and thus greatly improve their chances of survival.

This proposal describes a feasibility study that, if successful, would be used to develop a large, national study to validate the use of three GEMs to predict who are the patients at risk for developing metastatic bladder cancer after cystectomy, and which patients with established metastatic disease will respond to specific chemotherapy treatments. We will first identify all bladder cancer patients that have been diagnosed and treated at Kaiser Permanente Colorado (KPCO) between 2000-2010. From those patients, we will select a subset of patients who were 1) diagnosed with advanced bladder cancer, 2) who have a sample of their tumor stored in the KPCO pathology department, and 3) who have follow-up information to determine how they were treated, whether their cancer progressed, and whether they died of bladder cancer. We will use the GEM profiles to determine whether this approach could have been used to predict who are the patients at risk for developing metastatic bladder cancer, and for patients with established metastatic disease, who best would respond to treatment.

Testing the GEM in a sample of KPCO patients is ideal, because KPCO is a member of the Cancer Research Network (CRN) consortium. The CRN includes 14 health plans across the U.S. that provide care to over 11 million individuals. If this proposed pilot study is successful, we will launch a large, national study across the CRN to validate the use of these GEMs to predict treatment response and survival in bladder cancer patients. GEM has the promise of providing bladder cancer patients and their doctors the ability to make informed decisions about which treatment options will give them the best chance for long term survival.