



Sixth Annual Bladder Cancer Think Tank

Identifying Obstacles and Creating Solutions in Bladder Cancer: Basic Science, Clinical Trials and Survivorship

On August 4-6, 2011, more than 100 leading clinicians, researchers, patient advocates, and industry representatives came together in Coronado, California, for the 6th annual Bladder Cancer Advocacy Network Think Tank. This year, for the first time, Think Tank participants included European physicians who expressed great interest in collaborating with their North American colleagues. In particular, they are eager to work with BCAN to develop bladder cancer patient education and advocacy efforts in their own countries. BCAN hopes this early outreach to European colleagues is the beginning of a broader collaboration with bladder cancer researchers, providers, and patient advocates worldwide.

The meeting convened with an opening keynote address from Jeffrey Trent, PhD, President and Research Director of the Translational Genomics Research Institute. Dr. Trent described the process by which genomics is transforming medical research by changing the paradigm from evidence-based medicine, in which experimental trials examine large groups of study participants, to intelligence-based medicine, in which specialized treatments are selected based on an individual patient's tumor characteristics. Advances in bladder cancer treatment may be possible through genomics, but issues of ethics, legality, practicality and cost must first be resolved.

As the meeting concluded, participants reflected on the totality of the Think Tank and articulated several themes that give direction for the coming year to the bladder cancer research community generally, and to BCAN in particular. Participants want to improve the visibility of bladder cancer and BCAN in relevant professional societies. They want to increase collaboration across Think Tank Working Groups and expand the Working Group efforts by funding new research projects. Furthermore, participants want to find ways to improve patient care, especially ways to help primary care providers be more proactive with their patients who present with bladder cancer symptoms so that patients can get into treatment early, when it may be more effective.

Session One: Utilizing the Neoadjuvant Paradigm for New Drug Development

Colin Dinney, MD, M.D. Anderson Cancer Center, Chair

Gary Steinberg, MD, University of Chicago, Facilitator

Rick Bangs, Patient Advocate

Robert Dreicer, MD, Cleveland Clinic

David McConkey, Ph.D, M.D. Anderson Cancer Center

Steven Smith, MD, Ph.D, University of Michigan

Walter Stadler, MD, University of Chicago

Neoadjuvant therapies, or treatments given before radical cystectomy, offer a unique opportunity for bladder cancer researchers. Tumors are clinically staged before radical cystectomy on the basis of a biopsy recovered during a trans-urethral resection of the bladder tumor. This ensures that a pre-treatment tissue sample is available. Then, when the bladder is removed the bladder and any remaining tumor tissue is available for pathological staging and examination. The neoadjuvant paradigm for new drug development utilizes the availability of tissue before radical cystectomy to test for markers that could indicate response or resistance to a given treatment, and then the availability of tissue following radical cystectomy for pathological staging to evaluate whether there was a correlating response or lack of response to the treatment.

While this paradigm offers an exciting opportunity for developing new and better therapeutic agents, considerable debate surrounds the best potential agents, the suitable endpoints, the most appropriate patients, and the optimal methods for conducting clinical trials to test potential agents. It is important to note that the use of pathological staging as an indicator of treatment response is still controversial. The most favored measure of response remains progression and survival endpoints, but given the lack of advances with those standards, pathological staging is an increasingly intriguing alternative. Continued research and collaboration is necessary to continue the development of agents available for study, the identification of standards for collecting, processing and analyzing the tissue, blood and urine specimens that are vital to the evaluation of predictive markers and response, and the enrollment of eligible patients in clinical trials.

Session Two: Developing the Next Generation of Bladder Cancer Trials—Paths to Success

Jonathan Rosenberg, MD, Dana-Farber Cancer Institute, Chair

Joaquim Bellmunt, MD, PhD, Medical Oncology Service, Hospital del Mar, Barcelona, Spain

Susan Dickerman, Patient Advocate

Robert Svatek, MD, University of Texas Health Science Center, San Antonio

Jake Vinson, MHA, Prostate Cancer Clinical Trials Consortium

Enhancing the involvement of eligible patients in bladder cancer clinical trials is essential to evaluating the effectiveness of new treatment developments and determining which agents are best for which patients. Unfortunately, many trials close prematurely because too few patients enroll or complete the trial. Barriers to the accrual of patients to any clinical trials are complex and varied, and include the fears of patients regarding randomization and treatment with placebos and the unwillingness of providers to lose patients to trial sites, as well as more systematic issues such as restrictive protocol designs and referral timings. Members of the newly formed Clinical Trials Working Group surveyed Think Tank registrants and found that, more specifically, issues preventing engagement in bladder cancer clinical trials include the lack of exciting agents and trials, as well as lack of awareness among patients and providers. Similar clinical trials issues persist in Europe.

Panelists and participants agreed that the current system had not produced significant advances in the last two decades, and sought to find key areas of improvement. To succeed in the future, researchers must improve both enrollment and design of bladder cancer clinical trials. Areas to target include improving awareness and collaboration among participating physicians, finding new ways to reach out to and educate eligible patients, experimenting with novel trial designs and approaches, and, perhaps most importantly, dedicating research to new and more interesting agents. Also important is recognition of how financial burdens associated with running and participating in trials disincentivize provider and patient participation.

Session Three: Quality of Cystectomy Care and Partnerships with Payers

John Gore, MD, MS, University of Washington, Seattle, Co-Chair

Seth Strobe, MD, Washington University, Co-Chair

Ronald Kaufman, MD, Albany Medical College

The decision to recommend a particular course of treatment is all too often influenced by an awareness of reimbursement policies. Since 1992, Medicare and most HMOs have based physician reimbursement on the Resource Based Relative Value Scale. This scale calculates the amount the payer will allow for a procedure based on the physician work, the practice expense, and the malpractice expense. The relative value of the procedure is then adjusted for geographic location. The values used for each procedure are based on surveys from practicing doctors, input from professional organizations, and approval from the Centers for Medicare & Medicaid Services (CMS). When a new diagnostic or therapeutic procedure is developed, it must be proven to substantially differ from current procedures and be scientifically validated before being assigned a Current Procedural Terminology code and, ultimately, Relative Value Units. While this system restricts reimbursement to scientifically validated procedures, it does not reward outcomes or restrict the use to patients for whom the procedure is expected to be beneficial. This incentivizes a greater quantity of care without emphasizing quality.

CMS seeks to improve payment and care models across all patients with several new initiatives, three of which have particular implications for bladder cancer: prioritizing coordination of care which is a key issue in bladder cancer patients who may deal with a primary care physician, urologist and oncologist, bundling payments for acute care episodes such as radical cystectomy, and penalizing hospitals for readmissions which could especially affect the high rate of readmissions after cystectomy. At the same time, private payers and purchasers are developing their own innovative initiatives to contain costs and improve healthcare quality. While none of these goals are new, the increasing awareness of rising healthcare costs gives such projects a greater importance. The bladder cancer community must become more involved in the development and implementation of such initiatives to ensure that high quality care for bladder cancer patients is defined appropriately.

Supporting Young Investigators

Four young investigators were awarded John Quale Travel Fellowships to present at the 2011 Think Tank Meeting:

Meng Chen, PhD, University of Texas M.D. Anderson Cancer Center, presented on a potential genetic marker indicative of susceptibility to bladder cancer.

Kenneth Nepple, MD, Washington University, St. Louis, discussed factors such as XYZ that might affect hospital readmission rates for patients after a radical cystectomy.

Sandip Prasad, MD, University of Chicago, described the use of XYZ software to identify geographic areas that are "hot spots" for bladder cancer, and how those hot spots are being studied for correlations to environmental carcinogen levels.

Steven Smith, MD, PhD, University of Michigan, presented on the potential use of molecular biology to identify which patients are likely to respond to chemotherapy.

Elizabeth Guancial, MD, a fellow at the Dana-Farber Cancer Institute, was the recipient of the 2010 **BCAN Award for Bladder Cancer Research** and presented on her results. With the help of the award, Dr. Guancial identified two microRNA biomarkers that correlated with longer survival time in patients with metastatic bladder cancer who received chemotherapy containing platinum. She will continue to study whether the biomarkers have a causal relationship with cisplatin sensitivity and if they could be used to predict whether patients with advanced bladder cancer will respond to platinum-based chemotherapy.

Ongoing Collaboration

Attendees at the 2011 Think Tank participated in working groups ranging from three well-established groups that were formed in 2009 to two newly-formed groups meeting in person for the first time. The Working Groups met in small-group sessions to discuss their ongoing work and to develop their goals and plans for the coming year. Each group presented on their activities to the full Think Tank.

Standardization of Treatment for Advanced Disease

As it enters its third year, the goal of this working group remains the promotion of a standardized multidisciplinary approach to the management of bladder cancer. Ongoing projects include a Quality of Care Initiative analyzing rates of perioperative chemotherapy use in sixteen academic centers and the reasons given for variations in its use, as well as an examination of perioperative chemotherapy regimens offered by medical oncologists. Preliminary data from these studies have been presented and additional analyses and manuscripts will be prepared for publication. New efforts being considered include the creation of a multi-institutional clinical registry for all T2-T4N0-3/M0 patients with the goal of capturing accurate prospective real world data on the multi-disciplinary care of patients with muscle invasive bladder cancer, as well as the development, in conjunction with the Survivorship working group, of a patient educational program outlining the diagnostic procedures, treatments, and follow-up recommended for patients with muscle invasive bladder cancer.

Survivorship: How to Measure and Improve Patient Outcomes

The central project of this ongoing working group has been the development of a Bladder Cancer Patient Care Plan, which provides a record for providers and patients of all treatments received, doctors seen, and available treatment resources. The care plan has been tested in focus groups, and plans for testing it in clinical settings are underway. Smaller collaborations include ongoing work on a Patient Education Toolkit, revision of BCAN's handbook for bladder cancer patients, and other efforts to better support those whose lives have been touched in profound ways by bladder cancer.

Multi-Institutional, Multi-Investigator Collaboration: Data Mining

Members of the Data Mining group worked in the past year to compile a handbook establishing standards for the collection of data, including patient information and tissue samples, for bladder cancer. To conduct analyses of samples from multiple institutions, researchers must be certain that the samples were collected in standardized ways. In the coming year, the group plans to transition to a focus on improving care for non-muscle invasive bladder cancer patients.

Enhancing Enrollment and Design of Bladder Cancer Clinical Trials

This new Working Group identified increasing awareness and education among patients and physicians as a key actionable step toward improving clinical trials completion rates. Efforts to educate patients about common trial misconceptions and the benefits of trial participation will include additional information on the BCAN website and in BCAN's patient handbook, *Bladder Cancer Basics for the Newly Diagnosed*. Improved patient education regarding clinical trials will hopefully enhance enrollment, but the best way to ensure the successful completion of protocols for bladder cancer remains the careful conception and design of trials. The group plans to develop a series of trial design resources for bladder cancer investigators, to include advice culled from successful trials and consensus eligibility criteria.

Translational Science

This new Working Group was formed to facilitate the exchange of expertise and resources among bladder cancer researchers, beginning with the development of a catalog of bladder cancer assay expertise, tissue holdings, and novel biomarkers in development. The group hopes that such a catalog will be the basis for a cooperative tissue exchange between interested investigators. They plan to assess the feasibility of an inter-institution tissue exchange via a pilot project collecting clinically annotated, high grade T1 samples to examine for insight into resistance mechanisms to intravesical therapy in non-muscle invasive disease.