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Summary of the 6th annual bladder cancer think tank: New directions in urologic research

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Abstract

The 6th Annual Bladder Cancer Think Tank brought together a multidisciplinary group of clinicians, researchers, and representatives from the National Cancer Institute and Industry in an effort to advance bladder cancer research efforts. This year's meeting comprised panel discussions and research involving 5 separate working groups, including the Survivorship, Clinical Trials, Standardization of Care, Data Mining, and Translational Science working groups. In this manuscript, the accomplishments and objectives of the working groups are summarized. Notable efforts include: (1) the development of a survivorship care plan for early and late-stage bladder

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cancer; (2) the development of consensus criteria for eligibility and endpoints for bladder cancer clinical trials; (3) an improved understanding of current practice patterns regarding the use of perioperative chemotherapy in an effort to standardize care; (4) creation of a comprehensive handbook to assist researchers with developing bladder cancer databases; and (5) identification of response to therapy of high-grade non muscle invasive disease through a collaborative exchange of expertise and resources.

The Bladder Cancer Advocacy Network (BCAN) is a recognized non-profit organization whose mission is to increase public awareness about bladder cancer; to advance bladder cancer research; and to provide educational and support services for the bladder cancer community.

1. Introduction

In 2006, the Bladder Cancer Think Tank held its first meeting, with an aim of establishing critical collaborations amongst several disciplines in order to improve the care of patients with bladder cancer. That meeting included urologists, medical oncologists, researchers, and patient advocates. The meeting has since expanded to include radiation oncologists, industry representatives, and representatives from the National Cancer Institute (see appendix for list of participants). Since 2008, BCAN has sponsored this annual meeting, which helps to shape its research agenda. One component of the think tank involves research activities of working groups that focus on various aspects of bladder cancer research. The working groups at the 6th annual meeting include survivorship, clinical trials, standardization of care, data mining and translational science. This report summarizes the 6th session and provides a review of the accomplishments and/or objectives of these working groups.

2. Survivorship working group

2.1. Co-chairs: Cheryl T. Lee and David M. Latini

The mission of the Survivorship Working Group (SWG) is to develop programs that improve the quality of life (QOL) of bladder cancer survivors, caregivers, and family through educational programs, research, and advocacy. The group is comprised of survivors, urologists, other physicians, and social scientists.

BCAN's pamphlet for newly diagnosed patients remains a highly useful and popular resource [1]. The SWG will be working with the rest of BCAN to develop a revised and expanded version of the pamphlet in English and then will develop a Spanish translation. In the previous year, the SWG developed several modules of a survivors' toolkit to provide information about common procedures such as cystoscopy and intravesical therapy. Other modules for later stage survivors are under development, including a module on managing incontinence. Likewise, in the coming year, this group intends to create a patient-centered video that will help survivors in their decision-making process for urinary diversion selection. Recently, a manuscript describing the dearth of resources available to bladder cancer survivors, even in large cancer centers, was accepted for publication [2].

Over the last year, the SWG used a consensus process to develop a bladder cancer survivorship care plan for early and late-stage disease. The SWG held focus groups with male and female survivors, physicians, and non-physician providers to obtain feedback on the care plan. In the coming year, the SWG will pilot the plan with 5 patients each in at least 10 urology and oncology practices to determine the feasibility of implementing the care plan. SWG members also will seek external funding to conduct a comparative trial to determine the utility of the care plan on the quality and process of bladder cancer care.

There exists a limited understanding of bladder cancer survivorship. Therefore, SWG members are trying to examine existing administrative data to look at patterns of health care utilization and clinical outcomes in large medical systems as they relate to survivorship issues. Few such papers have been written about bladder cancer and the limited numbers that exist have primarily focused on cystectomy patients. Projects are beginning to look at these national data sets available from the National Cancer Institute, Centers for Disease Control and Prevention, and private insurers. These projects will examine health care costs and patterns of utilization across different disease stages. In addition, the SWG will use administrative data to examine an important but rarely studied area in most cancers—how does bladder cancer affect a survivor's ability to continue working or return to work after treatment? This important issue is critical to designing effective interventions that can help survivors reintegrate into their communities, including their jobs.

In addition to projects carried out by the larger SWG, smaller collaborations among clinicians and researchers in the SWG are ongoing and have resulted in several applications for external funding in the past two years. SWG collaborators have submitted requests for internal and external funding to begin moving bladder cancer survivorship to intervention studies that range from transition visits to navigation programs to symptom management education. As part of the growing interest in survivorship across cancers, the SWG is building a strong foundation that will sustain longer-terms programs in education, research, and advocacy necessary to support those whose lives have been touched in profound ways by bladder cancer.

3. Clinical trials working group

3.1. Co-chairs: Jonathan E. Rosenberg, Robert S. Svatek, and Matthew D. Galsky

A new working group was created for this 6th annual BCAN meeting. The Clinical Trials Working Group was charged with the task of addressing challenges in bladder cancer clinical trial availability and patient accrual to active bladder cancer trials. Prior to the meeting, a survey was distributed to the meeting's attendees in an effort to gain insights into the troubled clinical trial track record in bladder cancer, and to identify key areas in which the Working Group could focus. Survey results were largely obtained from urologists (55.4%) and medical oncologists (32.1%). Accrual barriers were categorized into 1 of 4 categories, including patient-related, physician-related, protocol-related, and funding-related. Key barriers to accrual to trials in non-muscle-invasive tumors were primarily physician-related, including "lack of exciting agents" or "lack of interesting trials" as principal barriers identified among the group. For patients with advanced disease, both physician-related barriers (lack of access to patients) and funding-related barriers (lack of

available trials) were cited as important barriers to patient accrual to bladder cancer trials.

In a series of small group meetings, members of the Clinical Trials Working Group contributed a variety of ideas regarding mechanisms to improve the process of clinical trial design, implementation, and accrual, across the spectrum from non-muscle invasive disease to advanced bladder cancer. Education, of both physicians and patients, was identified as a potential method to address several of these barriers, and several educational initiatives were proposed for completion over the next year.

The group discussed in detail the fragmented approach to bladder cancer clinical trials in the United States. A consequence of this fragmentation is lack of knowledge among physicians regarding the availability of trials at other centers, lack of uniform trial design preventing cross trial comparisons, and lack of an agreed upon agenda of high priority future bladder cancer research. While the NCI sponsored cooperative groups and associated Steering Committees may serve some of these roles, additional efforts from key stakeholders will be necessary to complement existing strategies. Therefore, an initial task identified by the group was a comprehensive cataloging of currently available clinical trials to provide a survey of the current landscape of the field, discover variability in trial design, pinpoint areas of synergy among investigators, facilitate collaboration with other clinical investigators, and translational investigators, and allow a central repository of available trials that can be easily searched by patients. Posting of this trials repository on www.bcan.org was proposed as a strategy to fulfill this latter goal.

One of the greatest assets of BCAN is the collective knowledge of its members, and therefore the Working Group identified several ways to capitalize on this resource. Focus groups and interviews will be carried out with principal investigators of previous bladder cancer clinical trials to solicit “lessons learned,” namely, mistakes or advice pertaining to particular aspects of trial design. The group also identified heterogeneity in trial design as a barrier to effective trial implementation and interpretation. Therefore, over the next year, the group plans to begin the process of developing consensus criteria for eligibility and endpoints for advanced/metastatic bladder cancer clinical trials. The development of similar consensus criteria for non-muscle invasive disease and muscle-invasive will subsequently be considered.

4. Standardization of Care Working Group

4.1. Co-chairs: Bernie Bochner, Andrea B. Apolo, Alon Weizer, and Srikala Sridhar

The goal of the Standardization of Care Working group (SOCWG) is to promote a standardized multidisciplinary approach to the management of bladder cancer. The SOCWG discussed two ongoing projects and initiated two new projects. The first ongoing project aims to evaluate and standardize the use of perioperative chemotherapy for patients with muscle invasive bladder cancer (MIBC), where despite Level 1 evidence demonstrating a benefit of neoadjuvant chemotherapy (NC) for patients undergoing radical cystectomy, NC has not been widely adopted.

The first project is a quality care initiative, consisting of 2 phases. The first phase was a retrospective analysis of perioperative chemotherapy use among 16 academic centers [3] including data on 4,450 patients. The rate of perioperative chemotherapy use was 34%, with significant inter-institutional variability (12%–58%) [3]. The second phase of this project aims to prospectively understand the reasons for variations in practice patterns. Four quality care indicators for the management of operable muscle-invasive bladder cancer were established by the working group. These included (1) whether a referral was made to medical oncology for consideration of perioperative chemotherapy, (2) whether neo-adjuvant or adjuvant chemotherapy was recommended, (3) whether at least 3 cycles of cisplatin-based chemotherapy was used, and (4) whether a bilateral pelvic lymph node dissection with at least external iliac, hypogastric, and obturator lymph nodes was performed. A Web based survey tool was completed for this study. Patient data enrollment was started in a pilot design to evolve the WEB tool with an anticipated completion of enrollment by late 2012.

The second project entitled, “Examining the Management of Muscle-Invasive Bladder Cancer by Medical Oncologists,” was aimed at understanding current practice patterns of medical oncologists practicing in the US. An electronic 26 question survey was distributed and completed by 61 medical oncologists. Perioperative chemotherapy, equally distributed between neoadjuvant and adjuvant, is offered by the majority of respondents; however, overall referral rate remains low. Despite the evidence, non-cisplatin containing regimens are being used in the perioperative setting. The main reason for not giving neoadjuvant chemotherapy was poor performance status. Final data analysis for this project will be completed in early 2012.

Two new projects were discussed this year. The first is the development of a multi-institutional clinical registry for all T2-T4N0–3/M0 patients. The goal of this project is to capture accurate prospective real world data on the multidisciplinary care of patients with muscle invasive bladder cancer. The data obtained from this registry will be critical in providing us with a better understanding of the current management of bladder cancer. It will also help to determine where educational programs should be directed to standardize management and ultimately improve performance across institutions.

The second new initiative is an educational effort for patients and practitioners. An educational program will be developed via the BCAN website. This program will outline the diagnostic procedures, treatments, and follow-up recommended for patients with muscle invasive bladder cancer. The patient educational program will be developed in collaboration with the “survivorship” working group. The practitioner educational program will outline principles of care, available evidence, recommended quality care indicators, and provide power point slides that would be available for download. The ultimate goal is to provide a bladder cancer comprehensive educational resource for both patients and physicians. In addition to these efforts, BCAN members are working towards establishing consensus statements for management of bladder cancer patients at all stages. In many instances, high-quality prospective studies have not been performed to address clinical dilemma but we feel that it is important that a consensus on the best management should be provided to physicians based on the existing data.

5. Data Mining Working Group

5.1. Co-chairs: Yair Lotan and Norm Smith

The Data Mining Working Group for 6th annual meeting was comprised of academic urologists, traveling fellows, and representatives from industry. Our main objectives for the meeting were to review progress from projects established at Bladder Cancer Think Tank 2010 as well as to develop new goals for 2011–2012. The primary goal for the Data Mining Working Group from Bladder Cancer Think Tank 2010 was to create and publish a comprehensive handbook for the development of bladder cancer databases. The group sought to determine the most critical data points regarding demographics, clinical variables such as comorbidities, laboratory studies, preoperative clinical staging, perioperative chemotherapy, radical cystectomy, operative and pathologic details, postoperative recovery, complications, cancer outcomes, and quality of life measurements. Not only did the group seek to determine the most important variables but also to provide a literature review to support the necessary critical data elements. This comprehensive handbook was completed and accepted for publication in *Urologic Oncology*.

Secondary goals from Bladder Cancer Think Tank 2010 were to evaluate current practice patterns for management of non-muscle-invasive bladder cancer via both online surveys and development of a prospective study. Online surveys were sent to members of the American Urologic Association, Society of Urologic Oncology, and certain Large Urology Group Practice Associations regarding practice patterns concerning use of intravesical therapy, urinary markers and risk-specific surveillance patterns. The data from the surveys have been collected, analyzed, and three distinct scientific reports are in various stages of preparation. The group also developed a prospective, multi-institutional study to evaluate surveillance of patients with non-muscle-invasive bladder cancer collecting both patient and surgeon demographics, as well as a brief patient history to include smoking, exposures, intravesical therapy, TURBT and pathology data, details of cystoscopy and use of ancillary tests at the time of cystoscopy like cytology, urinary markers, and upper tract imaging. This prospective study is in the process of approval by local Institutional Review Committees.

After reviewing progress of previously established goals during 2010–2011, the group then worked to determine goals for 2011–2012. The first goals concerned completing unfinished business from last year, including publishing manuscripts reporting the online survey data for current practice patterns regarding utilization of intravesical therapy, urinary markers, and risk-specific surveillance, as well as to launch the multi-institutional prospective study as previously described. Another goal for 2011–2012 is to create and publish a comprehensive handbook on utilization of secondary data sets for bladder cancer research like SEER, SEER-Medicare, NHANES, etc. Finally, as the working group sessions from Bladder Cancer Think Tank 2011 progressed, it became apparent that the Data Mining Working Group was clearly evolving into an “Early Bladder Cancer Working Group” focused on screening/early detection, prevention/reduction of environmental exposures, surveillance, and intravesical therapy/management of non-muscle-invasive disease. This new agenda will be addressed at the future meeting in 2012.

6. Translational Science Working Group

6.1. Co-Chairs: Ashish Kamat, Thomas Flaig, and Donna Hansel

The translational science working group was a new addition to the BCAN think tank meeting this year. The group's membership consisted of an international panel of urologists, medical oncologists, pathologists, basic scientists, and industry representatives with a research focus on bladder cancer. Being an inaugural session, much of the discussion focused on the identification of important and practical translational science issues in the treatment of bladder cancer.

As a prelude, the group discussed the general needs of the field. One area of widely recognized need was that of facilitating collaborations between investigators across institutions and countries. It was appreciated that many individual institutions and groups possess bladder cancer-related expertise in various areas, as well as have biological samples. However, there has not been a wide-scale effort to assess and quantify these talents and holdings. Additionally, there was a clear recognition that new biomarkers in bladder cancer, both prognostic and predictive, are needed and their development has been stunted due to lack of a common marketplace or "exchange." To this end, the first project is to develop a survey tool to catalog the bladder cancer assay expertise, tissue holdings, and any novel biomarkers in development among the members of BCAN. The availability of bladder samples, including formalin-fixed tissue, fresh-frozen tissue, as well as blood samples and urine samples will be catalogued. The importance of clinical annotation and the future need to standardize the collection of the most relevant clinical data points was emphasized. With the results of the survey, an "exchange" will be established, in which new collaborations between bladder cancer investigators could be facilitated. For example, if a researcher was seeking preoperative bladder cancer biopsy tissue to validate the prognostic value of a new biomarker, the "exchange" would potentially identify several such samples in the holdings of other BCAN members. This could also occur in the reverse direction with someone becoming interested in a new biomarker through the "exchange" and then provide the needed tissue for a secondary validation of the marker.

In seeking a clinical bladder cancer project, several areas of clinical need were identified. Recognizing a relative void, the group decided to focus the second project on high grade, non-muscle-invasive disease with a special emphasis on resistance mechanisms to intravesical therapy. In a first step to assess feasibility, each collaborating institution will be asked to look into their resources and commit to provide a small number of clinically annotated samples from patients with high grade, T1 tumors treated in a uniform manner and in accordance with standard of care in 2011. This will provide both a feasibility check with regard to sharing actual tissue samples across institutions and will also provide a multi-center tissue collection for immediate use. Based on this experience, additional cross-institutional efforts would be pursued.

In summary, the inaugural Translational Science Bladder Cancer Working Group identified several pressing areas of need. The group set forth its main priority for this year to facilitate an exchange of expertise and resources and use this unique opportunity of collaboration to

translate our collective efforts in identifying markers of response/nonresponse in the therapy of high-grade non-muscle-invasive disease.

7. Conclusions

The bladder cancer Think Tank meeting represents an opportunity for open discussion and collaboration among clinicians from multiple disciplines, patients, and patient advocates, as well as industry. The goal of the Think Tank is to advance the care of patients with bladder cancer and promotes research that is carried out during the year between meetings.

Appendix

2011 Bladder Cancer Think Tank Attendees' names, institutions

Dr. Hikmat Al-Ahmadie, Memorial Sloan-Kettering

Dr. Gilad Amiel, Baylor College of Medicine

Dr. Andrea Apolo, National Cancer Institute

Dr. Joaquim Bellmunt, Universitat Pompeu Fabra

Dr. Trinity Bivalacqua, Johns Hopkins

Dr. Peter Black, University of British Columbia

Dr. Bernie Bochner, Memorial Sloan-Kettering

Dr. William Brandt, Johns Hopkins

Dr. Keith Chan, Baylor College of Medicine

Dr. Sam Chang, Vanderbilt University

Dr. Ananya Choudhury, The Christie NHS Foundation Trust

Dr. John Colberg, Yale University School of Medicine

Dr. Sia Daneshmand, Keck USC Institute of Urology

Dr. Colin Dinney, M. D. Anderson

Dr. Tracy Downs, University of Wisconsin

Dr. Robert Dreicer, Cleveland Clinic

Dr. Jason Efstathiou, Massachusetts General Hospital

Dr. Andrew Feifer, Memorial Sloan-Kettering

Dr. Tom Flaig, University of Colorado, Denver

Dr. Matt Galsky, Mount Sinai

Dr. Scott Gilbert, University of Florida

Dr. Jeff Gingrich, University of Pittsburgh

Dr. Peter Goebell, University Clinic Erlangen

Dr. Heather Goltz, Houston VA HSR&D Center of Excellence

Dr. Mark Gonzalgo, Stanford University

Dr. John Gore, University of Washington

Dr. Elizabeth Guancial, Dana-Farber Cancer Institute

Dr. Kilian Gust, JW Goethe University

Dr. Noah Hahn, Indiana University

Dr. Jean Hoffman-Censits, Thomas Jefferson University

Dr. M'Liss Hudson, Washington University

Dr. Brant Inman, Duke University

Dr. Matthew Kaag Penn State Hershey

Dr. Ashish Kamat, M. D. Anderson

Dr. Lawrence Karsh, The Urology Center of Colorado

Dr. Wassim Kassouf, McGill University

Dr. Ronald Kaufman, Community Care Physicians

Dr. Theresa Koppie, Oregon Health & Science University

Dr. Donald Lamm, BCG Oncology

Dr. David Latini, Baylor College of Medicine

Dr. Cheryl Lee, University of Michigan

Dr. Seth Lerner, Baylor College of Medicine

Dr. David McConkey, M. D. Anderson

Dr. Ed Messing, University of Rochester

Dr. Adam Metwalli, National Cancer Institute

Dr. Matthew Milowsky, Memorial Sloan-Kettering

Dr. Nihal Mohamed, Mount Sinai

Dr. Matt Nielsen, University of North Carolina

Dr. Peter O'Donnell, University of Chicago

Dr. Mike O'Donnell, University of Iowa

Dr. Patricia Parker, M. D. Anderson

Dr. Amit Patel, University of Chicago

Dr. Daniel Petrylak, Columbia University

Dr. Elizabeth Plimack, Fox Chase Cancer Center

Dr. Kamal Pohar, Ohio State University

Dr. Michael Porter, University of Washington

Dr. Jonathan Rosenberg, Dana-Farber Cancer Institute

Dr. Art Sagalowsky, UT Southwestern

Dr. Mark Schoenberg, Johns Hopkins

Dr. Jay Shah, M. D. Anderson

Dr. Neal Shore, Carolina Urologic Research Center

Dr. Arlene Siefker-Radtke, M. D. Anderson

Dr. Carolyn Smith, Baylor College of Medicine

Dr. Norm Smith, University of Chicago

Dr. Guru Sonpavde Texas Oncology

Dr. Kala Sridhar, Princess Margaret Hospital

Dr. Walt Stadler, University of Chicago

Dr. Gary Steinberg, University of Chicago

Dr. Andrew Stephenson, Cleveland Clinic

Dr. Seth Strobe Washington University

Dr. Robert Svatek, UT Health Science Center

Dr. Jeffrey Trent, Translational Genomics Research Institute

Dr. Bas Van Rhijn, Netherlands Cancer Institute, Jake Vinson Memorial Sloan-Kettering

Dr. Alon Weizer, University of Michigan

Dr. Steven Wong, UCLA

Dr. Jingsong Zhang, Moffitt

Dr. Alex Zlotta, Mount Sinai

2011 John Quale Travel Fellowship Awardees

Meng Chen, Ph.D., M. D. Anderson

Sandip Prasad, M.D., University of Chicago

Kenneth Nepple, M.D., Washington University

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

2011 Patient Advocates

Janice Ashley

Rick Bangs

Susan Dickerman

Lynda Haworth

Dan Haworth

Al Krizelman

David Pulver

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