

Outlook

President's Message - Fall 2008

As our country is in a period of transition, so is BCAN. We welcome three new members to our Board of Directors: David Pulver, Jared Sher and Mace Rosenstein. Bios for each of these new directors can be found on our website. In addition, we welcome David Latini, PhD, Assistant Professor of Urology at Baylor College of Medicine, to our Scientific Advisory Board. More information about Dr. Latini can be found on our website.

We are pleased to announce the availability of our new publication, Bladder Cancer Basics for the Newly Diagnosed. As its name suggested, this booklet is intended to provide information about the disease and available treatment options to those who have recently begun their bladder cancer journey. The booklet can be downloaded from our website or you can order a hard copy by emailing us at info@bcan.org. This publication was made possible by an unrestricted educational grant from GE Healthcare.

BCAN was in Boston in October for another successful patient forum, "Understanding Bladder Cancer" at the Harvard Medical Center. It was a very informative and interactive program. Many thanks to Dr. Kevin Loughlin, our faculty chair and to all of our faculty members: Dr. David Wang, Dr. John Feldman, Dr. Jerome Richie, Dr. Shahin Tabatabaei, Dr. Marsha Moses, Donna Loehner, RN and Linda Martin.

Our educational offerings continue on January 8, 2009, from 8-9:30 p.m. Eastern time, as we partner once again with the AUA Foundation to present a Bladder Cancer webinar. More information about how to register can be found at the BCAN website.

BCAN proudly hosted the Third Annual Bladder Cancer Think Tank last August in Mont Tremblant, Quebec. This meeting was attended by biomedical experts in the field of bladder cancer, including urologists, pathologists and scientists. The scientific sessions focused on the cause, detection and prevention of bladder cancer. We are grateful to the companies that provided unrestricted grants to support BCAN's hosting of this important meeting: Abbott Molecular, Bioniche, GE Healthcare and Indevus.

Attendees at Think Tank Meeting were treated to a reading from a new book of poetry, Bladderville. Bladderville was written by poet Kendra Kopelka, wife of Jonathon Shorr, a bladder cancer survivor. You can find a sample of Kendra's poetry on our website and the book is available for purchase from our online store.

My sincere gratitude to the many people who sent support to me and my family following my husband's death from bladder cancer in June. Our family is not alone in suffering a loss, and I want to acknowledge those families and friends who have generously made donations to BCAN in memory of their loved one during the past 12 months. BCAN is truly honored to continue its work in memory of: Jack Aregood, Ben Astley, Robert Barnard, Judith Beier, Arelena Bernard, Fred Emerson Browning, Esther C. Bush, Clemente Cohen, Joseph Florio, Bob Green, Clifton Charles Gregory, Brian Haefele, Cecilia Anne Hayes, Harry Hileman, Julian Hoffar, John Larkin, Clara MacCastle Self, Matthew A. McClellan, James P. Meeks, Sr., Ann Morris, Francine Perrine Wittkamp, Helen Phillips, Helen Remsing, Paula Smith, Sidney William Schwartz, Harry Solomon, James Taubenheim, Ronnie Thomson.

Diane Zipursky Quale
BCAN President

On Trial

We thank Dr. Michael O'Donnell, Holden Cancer Center at the University of Iowa, for providing this description of "A Safety and Tolerability Study of SCH 721015 (Recombinant Interferon Producing Adenovirus) in Patients With Transitional Cell Carcinoma of the Bladder."

The purpose of this first-in-human study is to determine the safety and tolerability of SCH 721015 in subjects with non-muscle-invasive transitional cell carcinoma of the bladder who have previously failed at least two cycles of BCG immunotherapy. SCH 721015 is a form of the common cold virus that has been genetically modified to cause exposed cells of the body to produce excess amounts of a natural anti-cancer substance called interferon. Upon bladder administration, SCH 721015 infects nearby tumor cells causing them to produce interferon alpha-2b which activates multiple genes whose products mediate antiviral, antiproliferative, antitumor, and immune-modulating effects. The gene therapy drug is administered as a single dose into the bladder for a 1-hour dwell time. Subjects who at 3 months post administration demonstrate a complete response on cystoscopy/biopsy and cytology and who did not experience dose-limiting toxicity are allowed to receive a second intravesical administration at the same dose level. Five escalating dose levels are planned together with serial collections of blood and urine to determine the amount and durability of the interferon production.

The study is currently underway at MD Anderson Cancer Center (Houston) and the University of Iowa (Iowa City). Fourteen patients have been recruited with another five expected to be enrolled to complete the study. Already there have been no dose-limiting toxicity and some complete clinical responses obtained. The study is under the medical directorship of David Cutler, MD, FRCPC at Schering-Plough Research Institute. To obtain more information contact the Schering-Plough Clinical Trial Registry Call Center at 1-888-772-8734.

Ask the Doctor

Our questions for this issue of Outlook were answered by Dr. Donna Hansel, Assistant Professor, Department of Pathology and Laboratory Medicine at Taussig Cancer Center at Cleveland Clinic. We sincerely appreciate her sharing her expertise with us.

Q. In reviewing a urine cytology report, the terms "negative" or "positive" are easy to understand. Sometimes, however, the results are not so definitive, and the terms "atypical" or "suspicious for TCC" are used. What do these terms mean, and how should such results be interpreted by the patient and his/her doctor?

A. Urine cytology is commonly used in patients who have hematuria (blood in the urine) or other urinary tract symptoms that raise the suspicion for urothelial cancer. The cytologic examination is a microscopic examination performed by a pathologist with subspecialty training in cytopathology and is extremely useful for identifying a variety of conditions ranging from inflammation to cancer. The general cytopathologic evaluation considers cells that are shed from the lining of the bladder into the urine and generally includes either single cells or small groups of cells.

Urine cytology is most useful in the diagnosis of high-grade papillary urothelial carcinoma, flat urothelial carcinoma in situ (CIS) or invasive urothelial carcinoma; these forms of high-grade bladder cancer are often characterized by loss of cell adhesion molecules - factors that normally allow cells to maintain binding to the bladder surface and to one another - resulting in cancer cells shed into the urine. In contrast, low-grade tumors present more of a challenge due to their ability to cytologically resemble normal urothelial cells and lower incidence in the urine.

On occasion, atypical cells are present in the urine that defy further characterization, either due to low numbers of cells to examine or lack of definitive features for high-grade malignancy. In addition, a variety of non-cancerous conditions can cytologically mimic high-grade cancer, including viral infection, reactive changes due to urinary tract stones or infection, radiation treatment, among many others. As a good example, human polyoma virus (BK virus) cytologically resembles cells of flat CIS and these cells have been termed “decoy” cells for obvious reasons. Fortunately, for many of the mimickers specific microscopic features or additional tests will lead to a definitive diagnosis. Yet despite this, there are still a small number of cases that share some - but not all - of the features of high-grade urothelial cancer that cannot be definitively diagnosed. These cases are termed “atypical cells” that may be “suspicious for urothelial carcinoma.” Patients with this diagnosis are often followed closely for the development of urothelial carcinoma, often with repeated urine cytologies. Although several molecular tests for urothelial cancer on urine cytology currently exist (one of the most common is the UroVysion test), these are typically used in a supporting role to the microscopic urine cytology rather than in lieu of it. Ongoing research in this field will hopefully yield more specific tests that will reduce the percentage of “atypical” cases and provide a more complete and detailed picture of the underlying changes in the urothelial lining.

Q: Please explain the difference between the “stage” and “grade” of a bladder tumor. Why is it possible for two different pathologists to arrive at different conclusions as to the stage and grade of one specific bladder tumor?

A. Over the past several decades, the terminology of bladder tumors has undergone tremendous changes based on our improved knowledge of the molecular changes that define this group of entities. The most recent classification scheme is based on the 1998 World Health Organization/International Society of Urologic Pathology, which outlines microscopic criteria for the classification of urothelial (formerly, “transitional”) tumors. In this classification scheme, urothelial tumors are defined by both stage (pT) and grade (e.g., low- and high-grade), among other features.

Stage represents the depth of invasion into the bladder wall, including (in order of increasing stage) lamina propria, muscularis propria (detrusor muscle), perivesical fat and adjacent organs. Typically, there is fairly good concordance between different pathologists in the identification of pathologic stage, with the caveat that there is occasional difficulty in the distinction of the muscularis propria (detrusor muscle) layer. This layer of the bladder wall consists of large bundles of smooth muscle that are readily identifiable in normal bladder

specimens, but can become markedly distorted and disrupted when invaded by urothelial carcinoma. In addition, smaller bundles of smooth muscle (“muscularis mucosa”) are present in the superficial layers of the bladder that may also be difficult to distinguish from muscularis propria in small biopsy material. The identification of the muscularis propria is critically important in the setting of transurethral resection specimens and biopsies, where invasion into the muscularis propria indicates the need for radical cystectomy in most cases. Due to the critical importance of recognizing this part of the bladder wall, many researchers have recently focused on identifying markers specific for the muscularis propria, with the hope that within the next several years new techniques to aid in the diagnosis of this layer of the bladder wall will be developed.

The grade of a urothelial tumor is determined at the microscopic level by a defined set of criteria. In general, the distinction has been made between low-grade and high-grade tumors, with the latter representing entities with an increased propensity for invasive and metastatic disease on numerous patient follow-up studies. The non-invasive neoplastic entities are divided into flat lesions (urothelial dysplasia, flat urothelial carcinoma in situ) and papillary lesions (papilloma, papillary urothelial neoplasm of uncertain malignant potential, low-grade papillary urothelial carcinoma, high-grade papillary urothelial carcinoma). Invasive urothelial carcinomas are typically considered high-grade lesions. The new classification scheme has been validated in part by molecular evidence suggesting different oncogenic pathways in these microscopically defined entities, including FGFR3 mutations in low-grade lesions and p53 mutations in high-grade lesions.

Despite the rigorous microscopic criteria set forth in the definition of these numerous forms of bladder cancer, the diagnosis often is challenging for a number of common reasons that include small size of some biopsy specimens, procedural artifact in obtaining the biopsy and limited orientation of specimens received for analysis. In some instances, these additional factors impact the interpretation of biopsy material, thus leading to discrepancy in staging and grading. Fortunately, with careful clinical follow-up and discussion with the consulting pathologist, proper patient care is ensured.

Volunteer Corner



Gene and his wife Gillian

In October of 2007, BCAN was fortunate to discover a very special person. Gene Breslow, a bladder cancer survivor, was attending our Patient Forum in Chicago where he enthusiastically signed up to be a volunteer. Since our medical outreach program was just getting underway, this was the perfect time to assign him to our Midwest team. Gene was asked to develop a database of large urology practices in Indiana and contact each one for the purpose of generating awareness of BCAN and bladder cancer in general. As soon as Gene finished up Indiana, he was assigned Wisconsin. But the Midwest simply couldn't hold Gene and he was soon helping our coordinator in the east with the state of Massachusetts.

Today, Gene still wants to do more, even volunteering to travel to both coasts to help with Patient Forums. You gotta love this guy!! Like many of us, Gene wanted to get involved as a BCAN volunteer to educate others about bladder cancer. His medical journey included visiting with many top urologists before finding the right treatment for himself. In July of 2006, Gene underwent a partial cystectomy at Memorial Sloan Kettering in New York and he has been cancer-free ever since. This active father and grandfather is enjoying life in Lake Forest, Illinois and his many hobbies which include skiing, tennis, golf, hiking and bike riding. Gene, a huge thank you for your energy and tireless efforts on our behalf!

We would also like to thank Urology Association Wisconsin for placing a BCAN link on their website - this is a great way for patients to find out about all that we offer to bladder cancer survivors, their families and the medical community.

It's Complementary

Is massage safe for people with cancer?

In a recent article in Prevention magazine, Dr. Andrew Weil reported that there is a lack of credible evidence to suggest that massage may spread cancer cells around the body, saying that the notion was simply untrue. In fact, says Dr. Weil, there is proof that massage can be helpful in a variety of ways for people who have cancer. He references several studies that show that manipulation of the body's muscles and other soft tissue can reduce nausea, pain, fatigue and anxiety in people with the disease.

Studies at Memorial Sloan-Kettering Cancer Center support his conclusions, reporting that clinical trials have shown that massage therapy helps reduce pain, mood disturbance and fatigue in cancer patients undergoing chemotherapy. Studies there have also shown that massage helps to improve sleep and reduce depression in patients with advanced cancer. According to The Mayo Clinic web site, "many cancer centers now have massage therapists on staff." MD Anderson Cancer Center, for example, offers massage therapy through its Wellness Center. Memorial Sloan-Kettering Cancer Center offers classes for massage therapists and massage services for patients through its Integrative Medicine Services. The Cancer Center at the University of Michigan offers hand and foot massage for patients getting chemotherapy.

When looking for a massage therapist, it's important to choose one that has specific training and experience in the special needs of cancer patients. While massage is becoming a recognized benefit for cancer patients, and those with a wide variety of other diseases, there are still precautions that should be taken, particularly for people with cancer.

- Don't have a massage if your blood counts are low.
- Avoid massage near surgical scars, radiation treatment areas or areas with tumors
- If you have cancer in your bones or other bone diseases, like osteoporosis, ask your therapist to use light pressure rather than deep massage.

For more information about massage therapy, visit the National Center for Complementary and Alternative Medicine web site at <http://nccam.nih.gov/health/massage>. As always, check with your physician before starting any complementary or alternative medicine therapy.