

A Letter from The Director

Dear friends:

We want to provide an update on our progress at the Johns Hopkins Greenberg Bladder Cancer Institute (JHGBCI), as we approach our 6th year of being of service to our bladder cancer patients, families, and community.

This year, 2020, has been one like no other, but we want to assure you that we have not stopped nor paused our efforts to provide care and continue our rigorous research efforts to more fully understand and treat bladder cancer, and to find cures.

The ongoing pandemic has forced us to find ways to work intelligently and more efficiently. From March 14 until mid-June we could only access our laboratories to preserve critical ongoing experiments, and much of elective patient care had to be curtailed (except for those with urgent needs) when the Johns Hopkins Hospital devoted itself almost entirely

to treating COVID-19 patients. Gradually, we were able to re-open the Bladder Cancer clinics for in-person and telehealth visits and get back to the levels of care we had experienced before we had to shut down in March 2020.

I am happy to report that on the clinical side, patient volumes are robustly back to normal levels, patients who had to defer care are now in our clinics, and telemedicine has become a convenient option for patients when appropriate. On the research side we have slowly increased our density of personnel to the point where we are now almost at pre-COVID-19 levels of activity. We have surprised ourselves at what we could jointly accomplish with a phone, a computer and Zoom calls. All of our national working group meetings – BCAN, ASCO, AUA and even our international meetings pivoted to a virtual format, the silver lining being that our international research, discovery, and collaboration efforts in bladder cancer are stronger than ever. Attendance at meetings has significantly increased, given that we attend from the comfort of our own homes at all hours of the day and night. Here we highlight some of our JHGBCI colleagues' contributions to bladder cancer research and clinical trials.

In this newsletter, we are pleased to welcome two new faculty members to the Johns Hopkins Greenberg Bladder Cancer Institute: Medical Oncologist Dr. Rusty Johnson and Urologic Surgeon Dr. Nirmish Singla. We highlight a new and important JHGBCI initiative focused on

identifying new therapeutic targets in and caring for patients with Upper Tract Urothelial Cancer ("UTUC"). You can read about "UTUC" here and meet our team.

We have launched a new virtual JHGBCI Educational outreach program with our faculty for you and everyone to join, with monthly webinars on different topics relevant to bladder cancer patients and survivors. (The talks are recorded and can be viewed anytime). Of special interest is our focus on Women and Bladder Cancer with our women's Bladder Cancer Program at our partner hospital, Sibley Hospital in Washington DC. The December 1, 2020 Educational Webinar will be on women and bladder cancer exclusively.

As always, our work continues and we are here to make as much progress for bladder cancer patients as we can. No pandemic will stop us. We hope you and your families remain safe and healthy. Know that we are here for you.

Please stay well,



David J. McConkey, PhD

Director, Johns Hopkins Greenberg Bladder Cancer Institute



The Brady Urological Institute is growing:

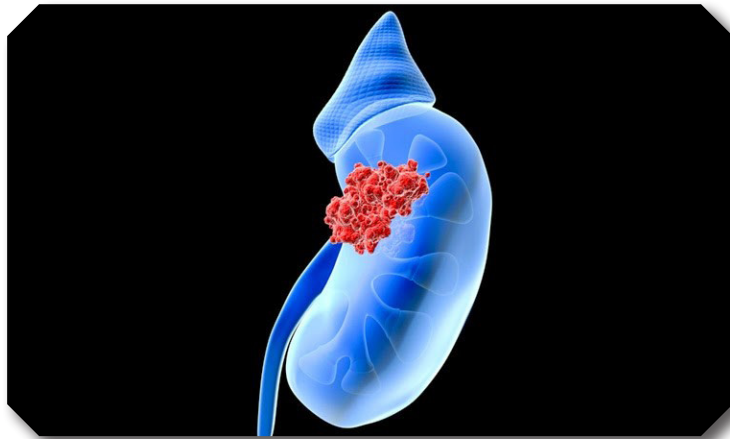
Located at the newly-completed **Johns Hopkins Greenspring Station Pavilion 3**, a brand new state-of-the-art building housing the Brady Urological Institute, it offers a convenient location in Baltimore County for clinic visits, procedures and follow-up visits, staffed by the JHGBCI faculty who rotate between the downtown Johns Hopkins campus and Greenspring Station.

IN THIS ISSUE:

- Meet our new team members
- Upper tract urothelial cancer
- Women's Bladder Cancer Program
- Research update

What is Upper Tract Urothelial Cancer?

Urothelial cancer refers to a cancer of the lining of the urinary system. While the majority of urothelial cancers (approximately 90-95%) arise in the bladder, upper tract urothelial cancers (UTUCs) correspond to a subset of urothelial cancers that arise in the lining of the kidney (called the renal pelvis) or the ureter (the long, thin tube that connects that kidney to the bladder). There are many similarities and some differences between UTUCs and bladder cancers. For instance, both bladder cancers and UTUCs can present with hematuria (blood in the urine). However, UTUCs can block the ureter or kidney, causing swelling (known as hydronephrosis) and frequent infections, and it can also adversely affect kidney function in some patients.



Similar to bladder cancers, UTUCs can develop as low or high-grade tumors. In general, low-grade tumors are not invasive and rarely spread from the kidney or ureter. However, they often recur. Management involves treating visible tumors and trying to preserve the urinary tract, because these tumors are more likely to recur in the urinary system than they are to spread. High-grade tumors have an aggressive appearance under a microscope and are assumed

invasive into the kidney or ureter. In the bladder, a thick bladder muscle (called the detrusor) acts as a barrier to confine invasive cancers, but in the kidney and ureter, this muscle does not exist. High-grade UTUC has the potential to spread from the kidney or ureter and is most often treated with surgical removal of the kidney and ureter – an operation called radical nephroureterectomy. High-grade UTUC can be aggressive and an expert may recommend systemic therapy (such as chemotherapy) before or after surgery to reduce the risk of recurrence elsewhere in the body. An expert pathologist is often

enlisted to distinguish low- and high-grade urothelial cancers, as this distinction can dramatically impact management choices.

At the JHGBCI, we now have a specialized multidisciplinary team focused on UTUC. Treatment plans are tailored to each patient's needs, based on their genetic profile. The JHGBCI team works to understand the variabilities of UTUC and explores ways to properly treat it to improve the lives of patients with this particular strain of cancer. Members of the UTUC team include oncologist Dr. Jean Hoffman-Censits, urologists Dr. Nirmish Singla and Dr. Philip Piorozazio, and others.



Meet Dr. Burles (Rusty) Johnson, MD, PhD

Dr. Burles (Rusty) Johnson, MD, PhD has joined the faculty of the JHGBCI as a medical oncologist and scientist following the completion of his hematology/oncology fellowship at Johns Hopkins. He is an award-winning researcher with a keen interest in understanding how bladder cancer evades the immune system. He is the recipient of a Conquer Cancer Foundation grant as well as a BCAN New Discoveries Research Young Investigator Award in 2019. Dr. Johnson's area of focus is the often underexplored "B" cells which play an important role in bladder cancer immunity. Dr. Johnson studies the mechanisms of "B" cells, also called lymphocytes, a type of white blood cell, which, when activated, produce antibodies. Sometimes "B" cells misbehave, and play a negative role in accelerating bladder cancer and can be resistant to immunotherapy. His work seeks to target B cells and reverse their negative behaviors.



Meet Dr. Nirmish Singla, MD, MSCS

Dr. Nirmish Singla, MD, MSCS joins the Brady Urological Institute and the JHGBCI as Assistant Professor of Urology and Oncology, having completed his residency at the University of Texas Southwestern Medical Center and a fellowship in urologic oncology at Memorial Sloan Kettering in New York. His specific area of interest within the GBCI is Upper Tract Urothelial Disease, and he takes care of patients with adrenal, kidney, prostate and other genitourinary cancers. Dr. Singla has a robust research agenda, and we are delighted to welcome him to our ever-expanding team.

JHGBCI Research Update

Here are some highlights from the JHGBCI team:

Dr. Jean Hoffman-Censits has discovered that patients with pre-existing auto-immune diseases (such as diabetes, anemia or rheumatoid arthritis) who also have urothelial cancer, who have been historically excluded from participating in clinical trials of immune checkpoint blockades (PD-1 and PDL-1), now finds that, when looking at large data sets, immune-related adverse events may in fact be manageable. While more studies need to be done, it may mean that patients with pre-existing auto-immune diseases may no longer be disqualified from participating in immune checkpoint clinical trials. (ESMO European Society for Medical Oncology Conference September 2020).

Upper Track Urothelial Cancer (UTUC) accounts for 5-10% of all urothelial cancers, affecting a median age of 69-73 years. One of the challenges of intravesical therapy (instilling an agent such as BCG in the bladder or upper track ureter) is that agents don't "stick" to the epithelial linings of the bladder or ureters and are most often flushed out of the body. Working with biomedical engineers, using nanoparticles, a new chemotherapy delivery drug is being tested that, when instilled, takes on a gel like consistency, and "sticks" to the bladder or upper track lining. **Dr. Philip Pierorazio** and **Dr. Max Kates** have played a role in developing this new drug delivery system (called UGN-101), also called a "chemo-ablative" treatment. Dr. Hoffman-Censits, who specializes in Upper Track Urothelial Disease, allows that this new compound could be practice changing. She reviewed the results of the Olympus Trial at the American Society of Clinical Oncologists meeting earlier this year.

Dr. Philip Pierorazio, a surgeon-scientist, has expertise in malignancies of the urinary tract whose specialty includes kidney, bladder, prostate and testicular cancer. Within the GCBI, Dr. Phil has created a UTUC working group that coordinates weekly tissue acquisition from the OR for research, and is developing a kidney sparing protocol for patients who cannot or do not want to undergo nephroureterectomy (removal of the kidney and ureter). He was also instrumental in the approval of the new drug, Jelmyto, a mitomycin gel, the first drug approved to treat cancer that grows in the upper part of the urinary system known as upper tract urothelial cancer. It is now approved and being used to treat patients.

BCG has been the standard of care for patients with non-muscle invasive bladder cancer (NIMBC) since it was introduced in the late 1970's. While it can be effective, it also has

its limitations relating to its effectiveness for patients, as studies reveal that within 5 years, about 50% of tumors treated with BCG recur, and 20% of tumors progress. **Dr. Woonyoung Choi MS, PhD** has devoted her career to understanding the mechanisms of BCG's therapeutic effect by classifying the differing genetic and molecular variations within tumors to better predict their response – and resistance – to BCG. Long term, this genetic knowledge will guide treatment plans for patients, knowing, in advance if a patient's own tumor subtype will respond well (or not) to BCG as a therapy. Dr. Choi presented her recent findings at the BCAN Think Tank in August 2020.

Dr. Max Kates, a surgeon-scientist, also studies BCG, gene expression and BCG resistance. His most recent presentation to the BCAN 2020 Think Tank was on the role of PD-1/PDL-1 therapy for those who do not respond to BCG, seeking to unlock the reasons why BCG works for some, and not for others.

Noah Hahn, MD is an oncologist who specializes in bladder cancer and also serves as Deputy Director of the JHGBCI. He is an internationally recognized authority on bladder cancer clinical trials and translational investigations. Dr. Hahn maintains a busy clinical practice who sees patients at all stages of urothelial cancer, including non-muscle invasive disease. In 2019, Noah was awarded a \$3.2 million NIH grant for early stage Bladder Cancer Research. The grant supports efforts to participate in novel multidisciplinary clinical trials, specifically the "ADAPT-BLADDER" trial which offers patients with non-muscle invasive disease the chance to enroll and receive immunotherapy, BCG and radiation therapy, the first trial to offer patients all three modalities. The trial, designed with several arms and phases, is expandable to include other drugs and combinations at a future date without having to start a new trial. The ADAPT trial is being offered at Johns Hopkins and other centers across the US.

Dr. Trinity Bivalacqua, a surgeon-scientist, has long been involved in the development of a new gene therapy called Adstiladrin (also called nadofaragene firadenovec) a treatment option for patients with high-grade, BCG unresponsive NIMBC. It is a type of gene therapy consisting of an adenovirus which contains interferon (IFN-1) which is known to have anti-tumor effects against urothelial carcinoma. Preliminary

data suggest that Adstiladrin may be a promising alternative treatment for patients who do not respond to BCG. Phase 2 and 3 multi-center clinical trials have tested the treatment, which is administered to patients via a catheter, directly into the bladder. It was found that the medication helps the body produce high quantities of a protein that fights the cancer. It is now in a Phase 3 clinical trial and pending review by the FDA for approval. Dr. Bivalacqua presented his findings at the recent International Bladder Cancer Network's (IBCNC's) Annual Meeting in October, 2020.



Woonyoung Choi, MS, PhD

What are Immune Checkpoint Inhibitors?

An important function of the immune system is its ability to tell the difference between "normal" cells (good cells) and cells it perceives to be "foreign" (bad cells). The immune system will attack the foreign (bad) cells while leaving the normal (good) cells alone. To do this, it uses "checkpoints". These are proteins on the surface of the cells that need to be activated (turned on) to start an immune response against the foreign (bad) cells to make them go away.

Cancer cells (unfortunately) are very clever. They sometimes find ways to trick these checkpoints to avoid being attacked by the immune system (that's bad). Again, the checkpoints are proteins that need to be turned on, like a light switch, to start an immune response. Immune Checkpoint Inhibitors are a type of immunotherapy whose only function is to target the checkpoints and turn them on. These drugs don't work on the tumor directly, they only work on the checkpoint and have the effect of turning on the immune system at full throttle to attack the "foreign" (bad) cancer cells.

What is PD-1 and PD-L1?

PD-1 and PDL-1 are the checkpoint proteins which lay on the surface of immune cells, called T cells. PD-1 is a protein which acts as a type of "off switch" that helps keep normal cells from attacking other cells in the body. That's a good thing unless there is a cancer cell lurking. PD-1 stays in the "off" position as it attaches to another protein, PD-L1, present on normal (and some cancer) cells. When PD-1 binds to PD-L1, it basically tells the T cell to leave the cell alone – don't attack it – even if it's a cancer cell (that's bad). Since some cancer cells have large amounts of PD-L1, they can hide from an immune attack. Checkpoint inhibitors – a new class of drugs – target PDI and PD-L1 causing them to reverse course and turn the immune system ON to attack the cancer cells. Keytruda (Pembrolizumab) and Opdivo (nivolumab) are just two of several new drugs developed and FDA approved that target PD-1 inhibitors. Examples of drugs that target PD-L1 inhibitors are Tencentric (Atezolizumab), Bavenco (Avelumab) and Imfinzi (Durvalmab). The past five years have seen a significant uptick in approvals of molecular and targeted therapies for the treatment of bladder cancer. Because of robust clinical trials taking place nationally and internationally, new drugs and combination immunotherapy drugs are being developed like never before to treat bladder cancer. Since 2016, more than 6 new drugs and treatments have been FDA approved for the treatment of bladder and Upper Track Urothelial Cancer and many are in the pipeline to receive approvals shortly.

Johns Hopkins Medicine Greenberg Bladder Cancer Institute

Fall Virtual Grand Rounds for the Bladder Cancer Community

WHAT:

Hear important updates from Greenberg Bladder Cancer Institute leaders, hosted by Dr. David McConkey, through our virtual Zoom series focused on engaging the broader bladder patient/family/advocacy community.

HOW:

One-hour Zoom webinar (20-25 minutes with slides / 40 minute conversational Q & A) with opportunity to “chat” with experts.

Register for any of our sessions here:

<https://events.jhu.edu/form/GBCIGrandRounds>



Tuesday, Sept. 15 – 4:00 p.m.

BCG in Short Supply: New Alternatives and Options for Patients

Max Kates, M.D.

Assistant Professor of Urology and Oncology
James Buchanan Brady Urological Institute
Johns Hopkins Kimmel Cancer Center

Tuesday, Oct. 13 – 4:00 p.m.

Clinical Trials and Immunotherapy

Jean Hoffman-Censits, M.D.

Co-Director, Women's Bladder Cancer Program
Assistant Professor of Oncology and Urology
Johns Hopkins Kimmel Cancer Center
James Buchanan Brady Urological Institute

Tuesday, Nov. 17 – 4:00 p.m.

Bladder Cancer Staging and Standards of Care

Trinity J. Bivalacqua, M.D., Ph.D.

R. Christian B. Evensen Professor of Urology and Oncology
Director of Urologic Oncology
James Buchanan Brady Urological Institute
Johns Hopkins Kimmel Cancer Center

Tuesday, Dec. 15 – 4:00 p.m.

Advances in Upper Tract Urothelial Cancer

Phillip M. Pierorazio, M.D.

Associate Professor of Urology and Oncology
James Buchanan Brady Urological Institute
Johns Hopkins Kimmel Cancer Center

Questions? Please email bladdercancer@jhmi.edu



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MEDICINE

JHGBCI Women's Bladder Program: Drs. Jean Hoffman-Censits and Armine Smith have established a joint clinic at the JHGBCI's Washington DC Sibley Memorial Hospital Campus for women who prefer the counsel of women physicians for their care. Working together, Dr. Armine Smith, a urologic oncologist, and Dr. Hoffman-Censits, a genitourinary medical oncologist, are leading a research program aimed at understanding gender-related differences in outcomes, and they have created a clinic that brings a unique understanding of the needs of women with bladder cancer to patient care. To schedule an appointment for the JHGBCI Women's Bladder Cancer Program at Sibley Memorial Hospital, call 202-660-5561.

JHGBCI Telemedicine Visits for Current Patients: Because the COVID-19 pandemic continues to affect our communities, telemedicine visits remain a critical component of patient care a great option for current patients who must travel great distances, or even those who prefer to be seen in the comfort and privacy of their own home. At this time, new patient telemedicine consults are limited. Current patients can review telemedicine options in your Johns Hopkins MyChart. If you have questions about new patient consults, please speak to our team in scheduling at 410-955-6100 or email us direct at bladdercancer@jhmi.edu.

HELP SUPPORT THE JHGBCI!

Your support of the JHGBCI is invaluable and helps serve those with bladder cancer. We hope that you will consider, among many needs, helping the JHGBCI underwrite the cost of our tumor sequencing program (not otherwise reimbursed). The cost of sequencing is approximately \$400 per sample, and contributes greatly to our understanding of bladder cancer and to the discovery of new treatment protocols.

We appreciate your partnership and belief in our mission.

To make an online gift to the Johns Hopkins Greenberg Bladder Cancer Institute, please Google:

JHGBCI CHARITABLE GIVING

Or click the image below:



For gifts of CASH, please make your check payable to Johns Hopkins and send it to the following address:

**The Brady Urological Institute
Development Office
600 North Wolfe Street, CMSC 130
Baltimore, MD 21287**

Please reference the Johns Hopkins Greenberg Bladder Cancer Institute or the faculty member to be supported by your gift on the memo line of the check.

Recordings of Past Virtual Grand Rounds

BCG IN SHORT SUPPLY

Max Kates, M.D., Assistant Professor of Urology and Oncology at the Johns Hopkins University School of Medicine and member of the Greenberg Bladder Cancer Institute, provides an important update on the BCG shortage, providing alternatives and options for bladder cancer patients. (Recorded 9/15/2020)

[View the recording here.](#)

CLINICAL TRIALS & IMMUNOTHERAPY

Jean Hoffman-Censits, M.D., Assistant Professor of Oncology and Urology at the Johns Hopkins University School of Medicine and member of the Greenberg Bladder Cancer Institute, provides an important update about clinical trials and immunotherapy for bladder cancer patients. (Recorded 10/13/2020)

[View the recording here.](#)



Register for upcoming Virtual Grand Rounds [here.](#)

Johns Hopkins Greenberg Bladder Cancer Institute
600 N. Wolfe Street | Park 2 | Baltimore, MD 21287

Request an appointment: (410) 955-6100

<https://www.hopkinsmedicine.org/greenberg-bladder-cancer-institute/>

You are Not Alone: Women with Bladder Cancer Sharing Their Stories Together



Bladder Cancer Support Group & Educational Forum for Women Only

Tuesday, December 1st, 2020
4:00 - 5:30 pm

via Zoom

To register, please visit
<https://events.jhu.edu/form/GBCIWomensGroup>



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Greenberg Bladder Cancer Institute



BCAN
Bladder Cancer Advocacy Network

Details

Please join us on Zoom on December 1st for the inaugural meeting of our **Women's Bladder Cancer Support Group**.

Our December 1st virtual meeting will feature supportive educational discussions facilitated by Dr. Armine Smith, M.D., and Dr. Jean Hoffman-Censits, M.D., co-directors of the Women's Bladder Cancer Program. Social workers will also be available.

You will receive the Zoom link via email after registering for the group.

Questions?

Please email us at bladdercancer@jhmi.edu or call 410-502-1807

Facilitators



JEAN HOFFMAN-CENSITS, M.D.
Assistant Professor of Oncology and Urology



ARMINE SMITH, M.D.
Assistant Professor of Urology

Questions? Email us at bladdercancer@jhmi.edu