



November 2016

STRAIGHT TALK

A publication for those interested in prostate and urologic research, education and care at the University of Minnesota, brought to you by the Institute for Prostate and Urologic Cancers.

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From the Director

This issue of *Straight Talk* focuses on the community of patients, researchers, educators, and others who support the Institute for Prostate and Urologic Cancers' work. Without them, we could not do what we do.

Our patients and caregivers, for example, organized everything needed for this year's incredibly successful Donald Tremblay Walk for Bladder Cancer. It was the second year for the event, which attracted over 250 participants and raised \$45,000. We are the thankful recipients of the walk organizers' time, energy and generosity.

Our campus community is being expanded as we welcome our new post-docs and fellows, including Kojiro Tashiro, MD, from Tokyo, Japan, who is working with Dr. Anindya Bagchi. Their research is looking at a new gene broadly involved in cancer development and specifically altered in prostate and urologic cancers. They are determining ways to alter this gene to prevent the growth of the cancers.

In addition, we welcome our second Semmer Scholar, made possible by the Philip G. Semmer Fund for Prostate Cancer Research, Katherine Murphy, PhD. She is currently working with Thomas Griffith, PhD on using gene therapy to inhibit the growth of prostate and kidney cancer.

Medical oncologist Shilpa Gupta, MBBS, is a relatively new member of our community. She brings a wealth of expertise, ideas, and new clinical trials into the Institute. Thanks to her inspiration, we're exploring unique approaches to chemotherapy and immunotherapy for various cancers. Read more about her work on page 3.

Speaking of new approaches, we are actively enrolling participants in some clinical trials about which we are very excited. They cross the spectrum of urologic cancers, from kidney to bladder to prostate. We are extraordinarily grateful to the patients participating in these trials – they are as driven to discover as we are. Over the past year, we have almost doubled the number of clinical trials available and the number of patients who are enrolled in these studies. More information can be found on page 6.



Dr. Badrinath Konety

(continued on page 2)

OUR MISSION

is to provide all patients with individualized, comprehensive, innovative and efficient care based on advances in technology and research.

From the Director, continued

Members of our research community are continuing to develop exciting new approaches to treatment as well as enhancing our understanding of cancer. They have published over 70 articles in journals and presented at 15 conferences. They have also been key members of committees developing guidelines for cancer treatment such as those for bladder cancer and for prostate cancer diagnosis with MRI. A list of recent publications can be found on page 7.

Finally, we are proud to announce the official funding of the Dougherty Family Chair in Uro-Oncology. A celebration of the endowment was held at the Minikahda Club in Minneapolis. We humbly thank our community – no, family – of supporters who made it all possible.

All the different members of the IPUC community enable us to improve patient care, push the boundaries of the practice, and achieve things never thought possible. Thank you.

Sincerely,

Badrinath R. Konety, MD

Director of the Institute for Prostate and Urologic Cancers

Message from Dean Junkans

Bladder cancer support group facilitator, IPUC patient

There has been a lot of activity led by bladder cancer patients, survivors, caregivers, family, friends and medical staff in the IPUC family. Here are some highlights:

- We launched a Bladder Cancer Support Group in April 2015 that meets the third Thursday of each month at Hope Lodge near the U of M campus. This has developed into an active and passionate group around support, mentoring, education and outreach for anyone in the community dealing with bladder cancer. We have had a number of people newly diagnosed with bladder cancer who have stopped in simply to get connected with this group and to know there are others who have successfully walked the journey.
- We have seen steady activity in our peer-to-peer mentoring program for anyone newly diagnosed or going through treatment or recovery who wants to talk to a survivor one-on-one who has been through it.
- We had a good TV piece via KARE 11 on bladder cancer awareness discussing early warning signs of bladder cancer. This was filmed locally and syndicated across the country to NBC affiliates.
- In May, we completed our first U of M-sponsored Donald Tremblay Walk for Bladder Cancer with all funds raised going for bladder cancer research and education. Funds are used locally for research and education and if you would like to contribute anytime during the year, we now have a permanent fund set up. (See page 8)



Faculty Profile: Dr. Shilpa Gupta



Shilpa Gupta, MBBS, is an Assistant Professor in the Division of Hematology, Oncology and Transplantation. Dr. Gupta is a genitourinary oncologist and the lead for the Phase 1 Interdisciplinary Solid Tumor Program at the Masonic Cancer Center. She joined us from the H. Lee Moffitt Cancer Center and Research Institute/University of South Florida, Tampa, where she was Assistant Professor in the Departments of Genitourinary Oncology and Experimental Therapeutics since 2011. She obtained her medical degree at the Lady Hardinge Medical College in New Delhi, India, after which she did a fellowship through the Royal College of General Practitioners, in the UK. She pursued a master's in health informatics at the University of Minnesota and went on to do residency in internal medicine at the University of Connecticut Health

Center and Hematology-Oncology Fellowship at Georgetown University and Thomas Jefferson University. She completed a genitourinary translational research fellowship in Dr. Marja Nevalainen's laboratory at Thomas Jefferson University. She has served as a panel member on NCCN committees for kidney and testicular cancers and is a member of several other committees, including: ASCO, AUA, AACR, SWOG, Alliance Genitourinary Cancers committees, Big Ten Cancer Research Consortium and Hoosier Cancer research Network.

Dr. Gupta's research interests are to develop novel targeted therapies and immunotherapies in prostate, bladder, testicular, kidney and penile cancers. Dr. Gupta is passionate about her research and has opened several early and late phase clinical trials in prostate, bladder and kidney cancers since her arrival at UMN. She is collaborating with our translational working group to explore the androgen-receptor pathway and efficacy of enzalutamide in ex-vivo model systems in bladder cancer as well as looking at gene mutations and patient outcomes in bladder cancer. She is leading several investigator-initiated trials, including brentuximab and bevacizumab in CD30+ germ cell tumors, enzalutamide and gemcitabine-cisplatin in 1st line metastatic bladder cancer, novel and VEGF-TKI and immunotherapy combination trials in refractory bladder cancer.

In her free time, she loves to spend time with her sons, Arash and Arav.

“Thanks to her inspiration, we're exploring some really unique approaches to chemotherapy and immunotherapy for various cancers.”

Dr. Badrinath Konety



SEMMER SCHOLAR AWARDEE EXPLORES INNOVATIONS IN PROSTATE CANCER TREATMENT

Dr. Katie Murphy graduated from the University of Iowa with a B.S. in Biochemistry and Microbiology and received her PhD from the University of Minnesota in Molecular, Cellular, Developmental Biology, and Genetics. She conducted her graduate research in the laboratory of Dr. John Ohlfest developing an effective immunotherapy for gliomas. She is currently a postdoctoral associate in Dr. Thomas Griffith's lab. Her research is focused on immunotherapy for renal cell carcinoma and prostate cancer among other things. She is also examining the role of the AdTRAIL gene therapy in prostate and kidney cancer.

New Guidelines on Management of Early Bladder Cancer

PRESENTATIONS

CK2 Regulation of Key Pathways in Prostate Cancer

Homburg, Germany
September 2016
Ahmed, Khalil, PhD

Patient Selection for Renal NSS

Durham, NC
June 2016
Anderson, J.K., MD

Point Counterpoint on Biopsy

Durham, NC
June 2016
Anderson, J.K., MD

Current Strategies in Penile Prosthetic Surgery

Mexico City, June 2016
Elliott, S.P., MD

Overview of Medical Device Concepts of Artificial Urinary Sphincters - New & Old

San Diego, CA
May 2016
Elliott, S.P., MD

Intravesical Salvage Intravesical Chemotherapy in Bladder Cancer

Chile
April 2016
Konety, B.R., MD
(continued on page 5)

The American Urologic Association recently released updated guidelines for management of early stage bladder cancer. Dr. Konety was one of the members of the panel that formulated the guidelines. The guideline formulation process is complex and comprehensive. It involves a complete and thorough analysis of all the information about this type of cancer that is available. Based on this analysis, the nationally known panel of experts formulates a set of principles or guidelines. These guidelines are published and generally used as the basis for management of patients by urologists all over the United States and the rest of the world. They significantly influence clinical practice, quality assessment and insurance regulation regarding payments. The guidelines were updated from those released in 2007 based on new information that has become available over that time. They emphasize the following:

- All patients need to have their bladder tumors completely resected as far as possible
- In cases with aggressive early stage cancer, the bladder muscle wall should be assessed for involvement with tumor even if that requires a second operation soon after the first one
- Bladder cancers have been categorized into a low, medium and high-risk category
- Low and medium risk cancers can be managed with bladder washings using chemotherapy
- Recurring medium risk cancers and all high risk cancers should be managed with bladder washings using BCG
- BCG washings should be repeated periodically as a booster for up to 3 years in patients as a maintenance therapy to maximize the prevention of recurrence

International Guidelines on Prostate Biopsy Techniques

The Societe Internationale d'Urologie in conjunction with the International Consultation of Urologic Diseases recently published a comprehensive review and guidelines for the use of image-guided therapies for prostate and kidney cancers. This tremendous undertaking resulted in a 674 page document summarizing the published literature on a comprehensive range of topics ranging from the use of biomarkers and advanced imaging techniques in the diagnosis of prostate cancer, to the application of focal therapy approaches. A similar range of topics was included for kidney cancers as well. Drs. Warlick and Konety were among the authors on the chapter entitled, "Prostatic Biopsies: Available Techniques and Approaches". This chapter summarized the numerous techniques currently available to perform image-guided prostate biopsies which offer certain advantages over traditional transrectal ultrasound systematic (TRUS) prostate biopsies. Key findings and guideline statements from this chapter include:

- MRI guided biopsies can lead to fewer biopsies
- MRI guided biopsies can detect cancers missed by TRUS biopsies including anterior tumors
- MRI-TRUS fusion guided biopsies can detect more high-risk and fewer low-risk prostate cancers

Immunotherapy in Genitourinary Cancers, Offering a Glimmer of Hope

Immunologic checkpoint blockade with drugs that target the PD-1/PD-L1 checkpoint pathway have demonstrated significant promise in a variety of malignancies. These drugs block the PD-1/PD-L1 between our immune system and its interaction with cancer cells, thus helping to fight cancer. The harnessing of one's own immune system has shown a tremendous scope for a variety of cancers and has revolutionized the way we approach cancer treatment.

The initial clinical trials with anti-PD-1 therapies, pembrolizumab (Keytruda) and nivolumab (Opdiva) demonstrated a significant activity and durability of response in a variety of cancers, and the FDA granted approval of these therapies for melanoma in 2014. Subsequently, pembrolizumab and nivolumab were approved for lung cancer in 2015. Nivolumab also received approval for treatment of metastatic renal cancer in 2015.

In several completed and ongoing clinical trials, pembrolizumab, nivolumab, darvalumab and atezolizumab have shown promising activity in advanced/metastatic **bladder cancer**. In May 2016, the FDA approved the atezolizumab (Tecentriq), an anti-PD-L1 antibody. This is a very exciting development in treatment of bladder cancer as it is after almost 30 years, that a new drug has been approved for this indication, with results that are superior to any historical chemotherapy. Tecentriq is approved for the treatment of patients with locally advanced or metastatic urothelial carcinoma whose disease has worsened during or following platinum-containing chemotherapy, or within 12 months of receiving platinum-containing chemotherapy, either before (neoadjuvant) or after (adjuvant) surgical treatment. This approval was based on the Imvigor210 trial and atezolizumab demonstrated remarkable response rates and durability of response. The response rates seen with atezolizumab, including partial and complete response are very promising and better than any we have seen with salvage chemotherapy in this setting. In addition, Tecentriq is very well tolerated, which makes it an attractive option for patients who are previously treated with chemotherapy.

This approval has paved the way for many more clinical trials and exciting immunotherapy drug combinations in bladder cancer. This is an exciting era for us and our patients and these novel immunotherapy drugs offer a glimmer of hope like never before.

At UMN, we are at the forefront of clinical trials for bladder, prostate, kidney and testicular cancers. We have several ongoing and planned clinical trials with immunotherapy agents as well as targeted therapies. We have clinical trials for various stages of bladder cancer, including advanced bladder cancer, superficial bladder cancer, as well as post cystectomy for high-risk cases. We also have clinical trials for metastatic prostate and kidney cancers and plan novel therapy trials in testicular cancer for salvage treatment.

PRESENTATIONS, continued

Role of Lymphadenectomy in Bladder Cancer MRI and Prostate Biopsy

Chile
April 2016
Konety, B.R., MD

Update on Penile Cancer, and Infiltrating Bladder Cancer, When to Indicate Surgery and Factors Affecting Survival

Chile
April 2016
Konety, B.R., MD

Robotic versus Open Radical Cystectomy

Lima, Peru
August 2016
Konety, B.R., MD

Present and Future Chemohyperthermia in Bladder Cancer and Surgical Techniques in Urology

Panama City, Panama
October 2016
Konety, B.R., MD

Evaluation of the Oncotype DX Test in African-American Men with Prostate Cancer

Minneapolis, MN
March 2016
Warlick, C.A., MD
(continued on page 6)

Current Clinical Trials

PRESENTATIONS, continued

Vapor Therapy for Prostate Cancer

Durham, NC

June 2016

Warlick, C.A., MD

Chemoradiation for Bladder Cancer

Puebla, Mexico

April 2016

Weight, C.J., MD

Neoadjuvant vs. Adjuvant chemotherapy for bladder cancer

Puebla, Mexico

April 2016

Weight, C.J., MD

Chemoradiation for Bladder Cancer

Puebla, Mexico

April 2016

Weight, C.J., MD

Current trials:

1. SWOG S1216- A Phase III Randomized Trial Comparing Androgen Deprivation Therapy + TAK-700 in Patients with Newly Diagnosed Metastatic Sensitive Prostate Cancer
2. Investigator-Initiated Trial: A Phase I/1b Study of Enzalutamide in Combination with Gemcitabine and Cisplatin in Bladder Cancer
3. A Phase 1B, Open Label, Dose Escalation Study to Evaluate Safety, Pharmacokinetics and Pharmacodynamics of Axitinib in Combination with Crizotinib in Patients with Advanced Solid Tumors (Kidney Cancer)
4. A Single-Arm, Phase 2 Study to Evaluate the Safety and Efficacy of VT-464 in Patients with Castration-Resistant Prostate Cancer Progressing on Enzalutamide or Abiraterone
5. A Phase I, First-Time-in-Human Study of MEDI9197, a TLR 7/8 Agonist, Administered Intratumorally in Subjects with a Solid Tumor Cancer
6. A Phase III, Randomized, Open-Label, Controlled, Multicenter, Global Study of First-Line MEDI4736 Monotherapy and MEDI4736 in Combination with Tremelimumab Versus Standard of Care Chemotherapy in Patients with Unresectable Stage IV Urothelial Bladder Cancer
7. A Phase II Study of Provenge and Indoximod for Patients with Refractory Metastatic Prostate CA

We are also in the process of opening:

1. Investigator-Initiated Trial: A Phase 2 Investigator Initiated Study of Brentuximab Vedotin and Bevacizumab In Refractory CD-30 Positive Germ Cell Tumors
2. A Phase II Clinical Trial to Study the Efficacy and Safety of Pembrolizumab (MK-3475) in Subjects with High Risk Non-muscle Invasive Bladder Cancer (NMIBC) Unresponsive to Bacillus Calmette-Guerin (BCG) Therapy
3. A Phase 3, Multicenter, Multinational, Randomized, Open-Label, Parallel-Arm Study Of Avelumab* (MSB0010718C) Plus Best Supportive Care Versus Best Supportive Care Alone as a Maintenance Treatment in Patients With Locally Advanced or Metastatic Urothelial Cancer Whose Disease Did Not Progress After Completion of First-Line Platinum-Containing Chemotherapy
4. A Randomized, Double-Blinded, Phase II Study of Maintenance Pembrolizumab versus Placebo After First-line Chemotherapy in Patients with Metastatic Urothelial Cancer
5. A Multicenter, Open Label, Randomized Phase 2 Study of AGS-16C3F vs. Axitinib in Metastatic Renal Cell Carcinoma
6. A Phase 1/2, Open Label, Dose-Escalation/Dose-Expansion, Safety and Tolerability Study of INCB057643 in Subjects with Advanced Malignancies
7. A Phase III Study of Atezolizumab Treatment Versus Observation as Adjuvant Therapy in Patients With PD-L1 Positive, High Risk Muscle Invasive Bladder Cancer After Cystectomy (IMvigor010)

2015/2016 Faculty Publications

Anderson JK, et al. Vasc Endovascular Surg. 2015

Chrouser K, et al. BJU Int. 2015

Chrouser K, et al. J Urol. 2015

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Jarosek SL, et al. Int J Radiat Oncol Biol Phys. 2015

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Konety B, et al. Nat Rev Urol. 2015

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Konety BR, et al. Clin Genitourin Cancer. 2015

Konety BR, et al. J Urol. 2015

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Konety BR, et al. BJU Int. 2015

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Ordonez MA, et al. F1000Res. 2016

Risk MC, et al. Indian J Urol. 2015

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Rosser S, et al. International Academy of Sex. 2015

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Warlick CA, et al. J Urol. 2015

Weight CJ, et al. Urology. 2015

Weight CJ, et al. J Urol. 2015

Weight CJ, et al. Cancer. 2015

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The Donald Tremblay Walk for Bladder Cancer

To give to the Bladder Cancer Research and Education Fund, visit: <https://give.umn.edu/giveto/bladdercancerfund>

The fifth annual Donald Tremblay Walk for Bladder Cancer was a huge success! We had 250 participants and volunteers in attendance and raised over \$45,000. The Institute for Prostate and Urologic Cancers at University of Minnesota Health partnered with the University of Minnesota Foundation to raise proceeds to benefit bladder cancer research and education.



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To find out how your gift can make a difference, please contact:

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