

# IKCS 2021: Moving Kidney Cancer Care Forward

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Austin, Texas served as the site for the Kidney Cancer Association’s International Kidney Cancer Symposium (IKCS 2021), with the option for virtual attendance and presentation due to the ongoing pandemic. Live attendants were thrilled to be back in-person for this important annual meeting that sets the standard for disease-specific conferences world-wide.

## DAY ONE

Sessions began with presentations and discussions around Multimodality Perspectives on Clinical Trial Development and included a discussion in health equity in clinical trials by Dr. Lola Fashoyin-Aje. She explored modernizing clinical trial eligibility criteria to allow for more diverse enrollment with the goal of achieving better understanding of drug effects and efficacy across heterogeneous populations. She also discussed the importance of decentralizing trials to make trials available to a diverse population as well as the importance for leveraging technology to allow for more efficient trials with improved access for patients. These might include utilizing remote assessments and electronic consenting for example.

Dr. Biren Saraiya gave a very provocative talk entitled Enhancing Patient-centered Care in Systemic Therapy and Clinical Trials. He began by reminding the audience of the importance of recognizing that each provider brings to each patient encounter a different personal experience, cultural background, knowledgebase and personal bias, and that patients and caregivers similarly bring these characteristics to each encounter as well. Understanding and recognizing these is a first step towards shared decision making. He suggested physician might consider asking patients, “What have you learned from



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Google about you condition?” He explained that patients need time to process information that they are given and to deal with the emotions that are attached, and this one of the many reasons that integration of early palliative care into the care of cancer patients can be greatly beneficial. He also noted the importance of providers recognizing their own emotions and approach, particularly in how they communicate the inherent uncertainty which exists in oncology practice.

An excellent panel discussion around neoadjuvant trials in locally advanced RCC prompted much discussion about this novel approach. The goal of such therapy would be to downstage tumors, hopefully leading to smaller surgeries to achieve full resection, and the eradication of micro-metastatic disease, while providing a window into the biology of individual patients’ cancer and the

mechanism of action of drugs used in this setting. Discussion around the optimal endpoints for neoadjuvant trials suggested that these would need to be individualized based on the mechanism of action of the drugs studied in a particular trial. The question of placebo in the neoadjuvant trials was also addressed, although given the wide variety of active agents in kidney cancer it was felt that placebo-controlled trials in the neoadjuvant setting would largely be unnecessary. Finally, a discussion around the important of considering combination therapy in the neoadjuvant setting was had.

Dr. Ivan Pedrosa gave a compelling lecture entitled “Phenotypic Characterization of Renal Masses – The Virtual Biopsy,” in which he delineated the characterization of kidney tumors using MRI. He explained the limitations of attempting tissue diagnosis of every renal mass and introduced the Clear Cell Likelihood Score, a Likert scale for

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interpretation of multiparametric MRI that allows for a non-invasive detection of clear cell RCC and helps predict likelihood of metastases.

The surgical management of non-clear cell RCC was explored in a presentation by Dr. Ronald Boris of Indiana University. The focus of this talk was on the importance of understanding histological subtypes of RCC and their differences in metastatic potential and surgical outcomes. Dr. Boris explained that the nature of the peritumoral pseudocapsule differs significantly and predictably based on histologic subtypes of disease and can be used to personalize surgical approach and planning.

Dr. Hassanpour discussed the use of artificial intelligence (AI) deep learning in histologic classification of kidney cancer. He and his colleagues have built a AI model to help pathologists accurately classify tissue specimens. Such a system can potentially aid in automatically pre-screening slides to reduce false-negative cases, highlight regions of importance on digitized slides, and provide second opinions.

The role of NF2 in tumorigenesis in RCC was explored by Dr. Kun-Liang Guan. NF2 is a tumor suppressor acting upstream of the Hippo pathway which when mutated increases risk of developing cancerous and benign tumors, and Dr. Guan explained that the novel compound VT103 is in clinical trials in NF2 mutated cancers

Dr. McGregor gave an excellent overview of systemic therapy for non-clear cell RCC and discussed current and future approaches. He discussed PARP inhibitor trials in FH/SDH-deficient RCC, as well as chemotherapy and immunotherapy combinations for non-clear cell RCCs.

The conference's keynote lecturer was delivered by Noble Laureate Dr. Jim Allison from MD Anderson Cancer Center, one of the world's most respected and well-known scientists and a father of immunotherapy. Allison reviewed the history of immune checkpoint blockade and noting that his early work in this area was not specific to cancer, but instead sought to better understand the function and control of T-cells. Of course, this work led to the approval of immune checkpoint inhibitors that have revolutionized system therapy

for most solid tumors over the several years. He reviewed work being done around learning why some cancers respond so well to immunotherapy, while others do not and search for biomarkers that might aid in therapy selection.

Following Allison's keynote lecture, Dr. Hakimi discussed immunological consequences of obesity in clear cell RCC.

\* The role of the microbiome in cancer was addressed by Dr. Dizman.

\* Dr. Vitaly Margulis discussed the role of metabolomics in RCC.

\* Novel Immunotherapy Targets – Dr. Ornstein

\* Dr. Divya Bezwada delivered a talk entitled, *“Assessing Human Kidney Cancer Metabolism with Intraoperative Isotope Tracing.”*

A session focused on mentoring including a presentation by Dr. Brian Rini on the Academy of Kidney Cancer Investigators, a formalized organization providing research direction and career guidance to early-career investigators. This was followed by presentations by three mentees regarding ongoing research projects. Dr. Rini's presentation as followed by a mentorship roundtable consisting of medical oncologists, urologists, and translational researchers. The panelists gave brief descriptions of their own career journeys and answered a multitude of questions regarding the importance of mentorship, institutional diversity, and other topics. The roundtable was followed by a panel on networking hot topics presented by Drs. Nizar Tannir, Jeff Yorio, W. Kimryn Rathmell, and Brian Shuch. The panel addressed topics such as community oncology and community-based research, grantsmanship, networking, and other topics. An excellent poster walk was hosted by Drs. Eric Kauffman, Ritesh Kotecha, Nizar Tannir, and Stephen Culp.

## DAY 2

Day two of the conference, brought lectures on adjuvant therapies and advocacy, an award lecture, and abstracts. Dr. Toni Choueiri spoke on the Future of Adjuvant Therapy in RCC. He reviewed data on adjuvant sunitinib, which while approved in this setting in the US, has had largely disappointing outcomes especially with regards to overall survival. He then described results of the KEYNOTE-564 study which randomizes patients at high-risk of

recurrence to pembrolizumab vs placebo after complete resection of RCC (including 5.8 percent of patient with completely resected metastatic disease). The study achieved a disease-free survival (DFS) of 68.1% in placebo arm vs 77.3% in the pembrolizumab arm at 24 months, and while overall survival is still not mature, it trended towards favoring the pembrolizumab arm. He also reviewed data using circulating tumor DNA to predict who might have residual disease and benefit most from an adjuvant therapy approach. This has been challenging as RCC does not shed ctDNA at high rates. Choueiri described cfMedIP-sequencing that may help improve this approach. He finally mentioned the lack of data on adjuvant strategies of non-clear cell histologies and the need to explore whether strategies giving longer or short durations of adjuvant immunotherapy are appropriate. Dr. Choueiri talk was followed by a panel exploring adjuvant approaches in RCC via an interactive case-based discussion.

The next session of IKCS 2021 focused on advocacy, funding, and the patient experience, starting with a talk by Gretchen E. Vaughan, President and CEO of the Kidney Cancer Association. She reviewed programmatic initiatives including the organization's progress, projects, and goals. Theresa Miller spoke on Congressionally Directed Medical Research Programs (a program of the Department of Defense) and specifically the Kidney Cancer Research Program (KCRP). The KCRP received \$50 million in funding in 2021 and funding has increased each year since 2017. She also described the funding opportunities that include concept awards, idea development awards (for early career investigators and established investigators), translational research partnership awards, clinical trial awards, clinical research nurse development award, early career development awards for the Academy of Kidney Cancer Investigators, and postdoctoral and clinical fellowship awards. A legislative advocacy roundtable followed that included Bruce Hill and Ryan Natzke, both patient advocates, who encouraged physicians and researchers to meet with their elected representatives and their legislative/congressional staffers.

The Andrew C. Novick Award

Lecture was given by Dr. Brian Lane on the topic of the management of T1 renal masses. He reviewed the history and data behind robotic partial nephrectomies that have become the goal standard for most T1 renal masses. He reviewed concepts around loss of renal function following partial nephrectomy, noting that loss of renal function is rare following surgery with those who has underlying chronic kidney disease are at greater risk. He also shared data that showed renal functional outcomes after partial nephrectomy are better than open nephrectomy even with partial nephrectomy is associated with prolonged ischemia. He also discussed the concept of surgical chronic kidney disease, as a distinct entity from other forms of kidney disease and its impact on overall survival. He noted that open nephrectomies may not be as bad as once thought and described a randomized trial. He also introduced MUSIC, the Michigan Urological Surgery Improvement Collaborative, an umbrella that include many quality improvement projects. He finally noted that with greater and appropriate use of high-quality imaging, renal mass biopsy, and surveillance we can better identify patients who can safely avoid intervention. He concluded his presentation by sharing his own personal story of being a patient with two simultaneous types of cancer including kidney cancer.

The award lecture was followed by presentations of the conference's top abstracts. Dr. Pedro Barata of Tulane University spoke on his abstract "Gene Expression Profiling (GEP) of non-clear cell renal cell carcinoma (nccRCC) identifies a unique spectrum of transcriptional signature with potential clinical relevance." Dr. Barata explained that 657 patient samples were sequenced including papillary (9.6%), chromophobe (4.6%), medullary (1.2%), collecting duct (0.9%), and mixed (6.2%) nccRCC subtypes. While most ccRCC samples were classified as 'Angiogenic' or 'Angio/stromal' (50%), these molecular subgroups comprised < 10% of nccRCC samples, which were predominantly classified as 'Proliferative' (49%). Defective MMR/MSI-H and TMB-High ( $\geq 10$  mutations/Mb) rates were highest (33.3%) in collecting duct carcinoma and rarely observed (< 3.5%) in all other histological subgroups. These observations provide a new understanding for personalized treatment of nccRCC, warranting further evaluation in prospective trials.

Dr. Sari Khaleel presented "Outcomes of cytoreductive nephrectomy followed by active surveillance in metastatic renal cell carcinoma." He presented data on 97 systemic-therapy-naïve mRCC patients who underwent cytoreductive nephrectomy followed by active surveillance between 1989 – 2020. Median follow-up was 31.8 months with an intervention-free survival of 11.6 months. Overall survival was 52.3 months in these patients. Of note, IMDC risk categories did not correlate with outcomes on multivariate analysis.

Dr. Charlotte Spencer spoke on her abstract entitled, "Machine learning predicts BAP1/PBRM1 in clear cell renal cell carcinoma: TRACERx Renal," which described a proof of principle study which showed that mutational status of two ccRCC driver genes, PBRM1 and BAP1 can be accurately predicted with a high degree of accuracy from digital histological images alone.

Dr. Nizar Tannir from MD Anderson spoke on "First-line nivolumab plus ipilimumab (NIVO+IPI) versus sunitinib (SUN) in patients with long-term survival of  $\geq 5$  years in the CheckMate 214 trial." Of 550 patients randomized to the immunotherapy arm, long-term survival of greater than 5 years was reported in 236 (43%) patients compared to 171 of 546 (31%) patients in the sunitinib arm. Baseline demographic and clinical characteristics generally did not distinguish which patients would achieve long-term survival, except for lower target lesion burden, IMDC poor risk disease, and bone metastases at baseline.

Dr. Akash Kaushik presented "Glutamine metabolism in clear cell Renal Cell Carcinoma," in which he described metabolic reprogramming in ccRCC, and suggested that mechanisms beyond glutaminase-dependent metabolism may fuel the TCA cycle in ccRCC, such as nitrogen-dependent glutamine and aspartate, suggesting that inhibiting glutaminase and aspartate simultaneously may be a useful therapeutic approach.

The final session of the conference focused on the role of perioperative therapy in RCC, with Dr. Christopher Wright speaking on the use of artificial intelligence for RCC diagnosis with CT scans. Dr. Wright introduced the

concept of "segmentation" or having a computer cluster parts of an image together that belong to the same object class. Such segmentation could be used to increase diagnostic certainty, predict best treatment approaches and outcomes, and better estimate post-operative renal function. He asked in artificial intelligence could be used to independently generate an unambiguous nephrometry score. Through crowd sourcing, hundreds of teams were able to generate programs that were able to complete these tasks in ways that were comparable to humans and were able to predict clinical outcomes. Dr. Wright concluded by suggesting broader future uses of this type of technology.

Dr. Hannan explored of stereotactic radiation (SBRT) for RCC inferior vena cava (IVC) thrombosis. He discussed a phase II trial of neoadjuvant SBRT for RCC IVC thrombus to evaluate whether this technique may reduce the risk of RCC recurrence. Results of the safety lead-in were encouraging, with 2 of 3 patients with metastatic disease at diagnosis having a response (1 complete response and 1 partial abscopal response). The study continues to enroll.

Dr. Mohamad Allaf spoke of surgical consideration with perioperative therapy. He reviewed small previous studies of neoadjuvant axitinib and pazopanib which suggested some role to help downstage patients prior to surgery but will increase risk of surgical complications. He reviewed pre-clinical data and data in other cancer types for neoadjuvant immunotherapy. Finally, he reviewed results of a small study (n=17) of non-metastatic, high-risk RCC patients who 3 cycles of nivolumab prior to partial or radical nephrectomy. Although some patients achieved tumor shrinkage all except one had statistically stable disease after treatment. He also described EA8143:PROSPER RCC trial, a large randomized study of perioperative nivolumab which has completed enrollment, but whose results are forthcoming.

The 2021 Kidney Cancer Association IKCS Meeting not only provided researchers and providers a terrific venue for networking and collaboration but also disseminated a great deal of knowledge as progress in the fight against kidney cancer marches on.