Kidney Cancer 101

Note: The following summary notes are provided in detail for the education and benefit of kidney cancer patient organizations who were not able to be present for the IKCC Expanding Circles 2012 conference or the Kidney Cancer 101 sessions. Each of the three presentations highlighted here provides an excellent overview for patient group representatives who require greater familiarity with kidney cancer.

The three sessions comprising Kidney Cancer 101 included:

- ***Kidney Cancer Overview***
- ***Surgical Treatment***
- ***Treatment Options and Support***

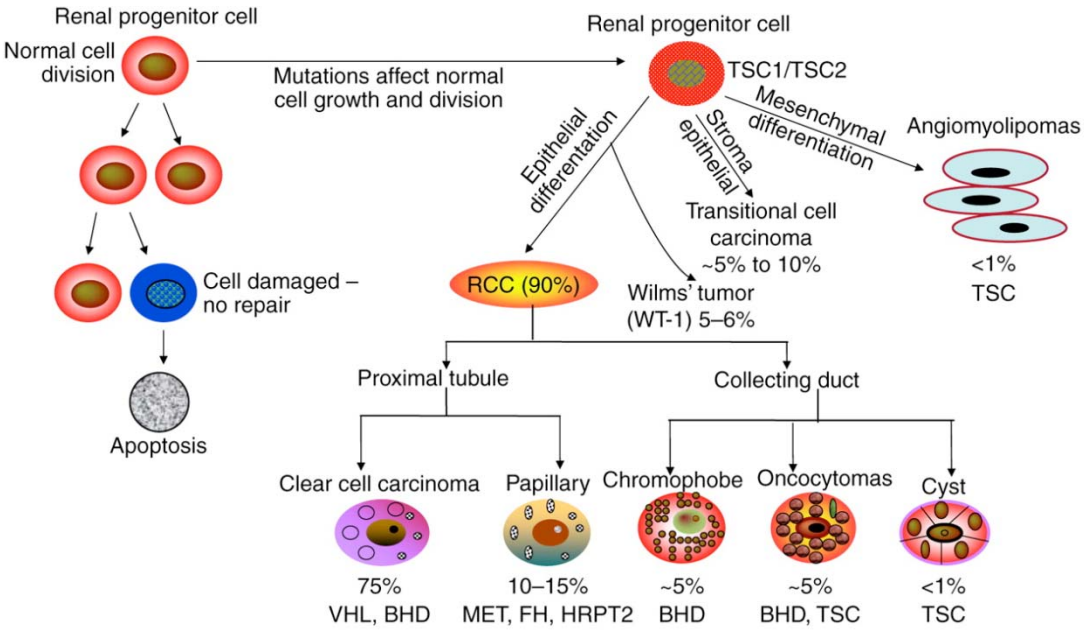
Kidney Cancer Overview

Rachel Giles, Professor of Nephrology and Medical Oncology at the University Medical Center, Utrecht, started the Kidney Cancer 101 session with an overview of kidney cancer. Kidney cancer is the 7th most common cancer in men, 10th most common in women and twice as many men are diagnosed with kidney cancer as women. Kidney cancer usually affects people older than 50 years. Kidney cancer patients younger than 40 years old need to be investigated for a familial history or genetic component of the disease. About 5-10% of kidney cancer runs in the family. Kidney cancer tumours are highly vascularlised and heterogeneous.

Smoking, obesity, high blood pressure and long-term dialysis are all risk factors for kidney cancer. Patients with von Hippel-Lindau syndrome are also at risk of developing the disease. There are also some occupational hazards that can increase the risk of developing kidney cancer, such as coke oven workers in the iron and steel industry and workers exposed to asbestos or cadmium. Moderate alcohol consumption has been shown to slightly reduce the risk of kidney cancer.

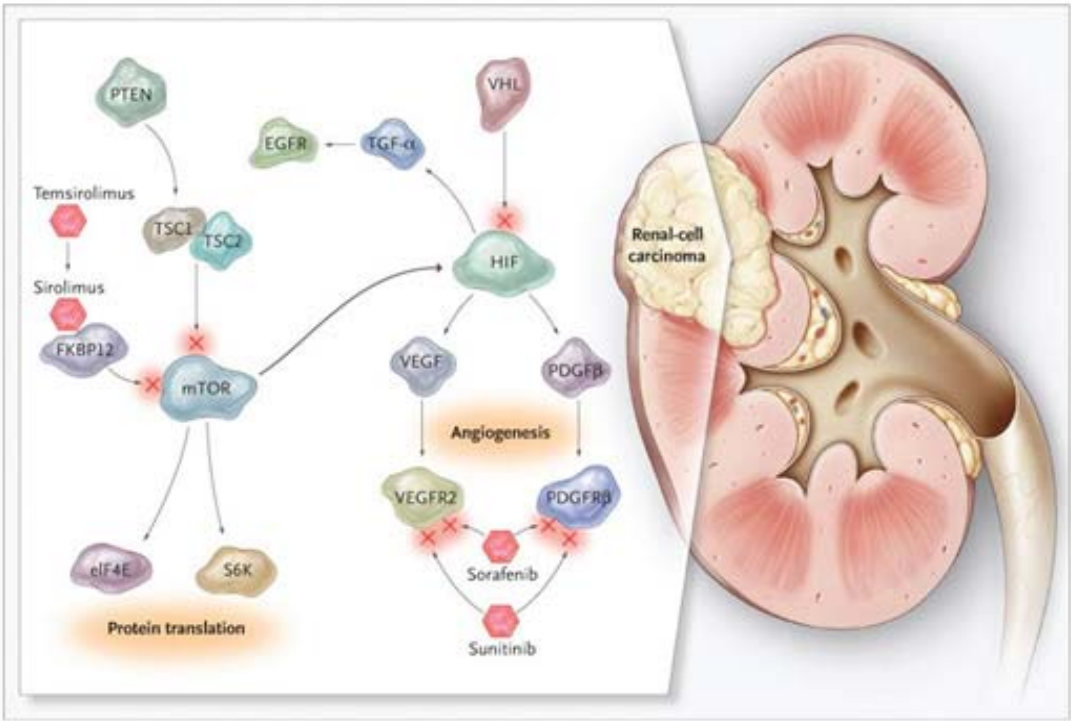
Common symptoms of kidney cancer include blood in the urine, persistent side or back pain, a lump or mass in the side of the abdomen, weight loss, testicular pain (in men), fever and feeling very tired.

There are 4 main sub-types of renal cell carcinoma (RCC); clear cell (75%), papillary (10-15%), chromophobe (approx. 5%) and oncocytoma (approx. 5%). Dr. Giles went on to explain the genetics involved in the development of the different RCC sub-types and how mutations affect the normal cell growth and division of renal progenitor cells resulting in the RCC sub-types. RCC contributes to about 90% of all kidney cancers. The remaining 10% consists of transitional cell carcinomas (approx. 5-10%), Wilms' tumour (5-6%) and angiomyolipomas (<1%).



Angiogenesis is a common theme in all carcinomas. Angiogenesis is the process of new blood vessel formation from existing blood vessels and occurs during embryonic development, wound healing and endometrial blood vessel formation during the menstrual cycle in women. However, angiogenesis can also occur during tumour growth, metastasis (cancer spread) and airway remodeling in asthma.

Modern targeted therapies, such as sunitinib or sorafenib exert their action through their affects on angiogenesis in tumours and metastases. These drugs act on the VEGF and PDGF pathways to influence vascular permeability, cell survival, proliferation and growth, and the formation and maturation of blood vessels. Treatment of advanced RCC patients with sunitinib results in a median progression-free survival of 11 months, compared to a median progression-free survival of 5 months with interferon-α (IFN-α) treatment.



Indicators of hereditary kidney cancer include a young age at kidney cancer diagnosis, a family history of kidney cancer and multifocal (multiple tumours) or bilateral disease (tumours in both kidneys). If kidney cancer is known to be hereditary, there are a number of implications: treatment options must be nephron-sparing; the patient and their family should undergo genetic testing for hereditary syndromes such as von Hippel-Lindau (VHL), Birt-Hogg-Dubé (BHD), hereditary leiomyomatosis and renal cell carcinoma (HLRCC), hereditary papillary renal carcinoma and hereditary renal carcinoma (HRC); the patient should undergo annual screening for other tumour types; and children and adolescents require different medical attention.

Prof. Giles concluded by mentioning that the same genes and pathways are involved in hereditary RCC as in sporadic RCC. Multiple tumours within one individual allow the opportunity for researchers to study the growth patterns of the tumours. Patient organizations need to learn to recognize the 5-10% of RCC that is hereditary since they require different care and have different needs to those patients with sporadic RCC.

Surgical Treatment Options

Joan Basiuk is a registered nurse with many years of urology and uro-oncology experience. Prior to retirement, she was a Clinical Research Coordinator and actively involved in kidney cancer research at the Princess Margaret Hospital in Toronto, Canada. She has been volunteering with Kidney Cancer Canada (KCC) since 2008 and is their Vice-Chair and Director of Medical Relations. In this role she is responsible for building relationships with the Canadian medical and nursing community and providing educational support to patients and caregivers across Canada.

Joan gave a comprehensive overview of the surgical techniques used to treat kidney cancer, including radical and partial nephrectomy, ablation techniques, surgery for metastatic disease and active surveillance.

About 70% of renal masses are detected incidentally when a patient is having a scan for an unrelated condition. Median tumour size is approximately 4 cm when discovered incidentally and 20% of masses less than 4 cm are discovered to be benign after surgical resection. A further 25% are indolent tumours with limited metastatic potential e.g. papillary and chromophobe carcinoma
Surgeons have a number of options for the surgical treatment of kidney cancer. To determine the best option for a patient, they need to consider the morbidity of the patient, the size and spread of the tumour (the grade and stage) and the expertise on hand to determine the approach to take: for example, laparoscopic versus open nephrectomy, partial versus radical nephrectomy, ablative techniques, such as cryotherapy and radiofrequency ablation, cytoreductive nephrectomy, resection of local tumour recurrence and metastectomy (from the lung, brain or bone).

Pre-operative work-up of kidney cancer patients will include staging of the tumour – assessing the current tumour mass, if the tumor has been followed over time growth rate will be determined, and possible spread will be examined. As a minimum, patients should have a CT scan of the abdomen and pelvis (and sometime the head), a chest X-ray or CT scan of the chest, kidney and liver function tests and possibly a bone scan if abnormal levels of calcium or alkaline phosphatase are detected in the blood.

For small tumours less than 4 cm, laparoscopic nephrectomy, open partial nephrectomy or ablative techniques are often employed to preserve kidney function, especially if there is underlying kidney disease, a solitary kidney or hereditary syndrome. For tumours between 4 and 7 cm in size, surgeons try to preserve kidney function with partial nephrectomy or ablation, if possible. If not possible because the tumour is too deep inside the kidney, radical nephrectomy is used and the whole kidney is removed. For more complex tumours involving the renal vein or local lymph nodes and of more than 7 cm in size a radical nephrectomy is needed, usually conducted using open surgery. Joan then showed some photographs of post-surgery torsos with open surgery scars and laparoscopic scars.

The benefits of laparoscopic surgery:

- Shorter hospital stays
- Less post-operative pain
- Earlier resumption of diet
- Shorter convalescence
- Quicker return to work
- Smaller incisions (cosmetic appeal) and
- Quicker recovery to start systemic therapy if the cancer has spread.

Radical nephrectomy is the complete removal of the kidney, the lymph nodes and fat around the kidney, and possibly the adrenal gland on top of the kidney.

This can be conducted laparoscopically or through open surgery. In open surgery, the patient lies on their side on a table with the side with the affected kidney uppermost. The table can bend in the middle at the level of the patient's waist so that the legs and head are lower than the abdomen making it easier to reach the kidney. An incision of about 8-10 cm is made in the flank to access the kidney.

Partial nephrectomy or nephron-sparing surgery reduces the risks associated with radical nephrectomy. The kidney is cooled by surrounding it in ice to reduce blood flow and thereby facilitate dissection of the portion of the kidney containing the tumour. The tumour is removed with a margin of normal kidney tissue surrounding it. Outcomes are similar to radical nephrectomy in terms of cancer cure for tumours up to 7 cm. However, laparoscopic partial nephrectomy is a more complicated operation than open partial nephrectomy requiring specialist intervention. Partial nephrectomy is indicated for patients with only one kidney, bilateral tumours and renal insufficiency. It is also indicated for patients with conditions that threaten the contralateral kidney e.g. kidney stones, infection, systemic conditions such as diabetes mellitus and hypertension, and genetic syndromes such as von Hippel-Lindau.

The outcome after radical or partial nephrectomy is dependent on the stage of the cancer at diagnosis, the grade of the cancer (how aggressive the cancer is) and the histology (chromophobe and papillary cancers have the best prognosis, collecting duct and sarcomatoid, the worst).

Patients are always anxious about what happens next after surgery. Unlike other cancers, such as breast and colon cancer, there is usually no treatment for kidney cancer patients, unless the disease has spread outside the kidney. Ongoing clinical trials are assessing the benefits of adjuvant treatment (treatment after surgery) to determine whether adjuvant treatment improves recurrence-free survival and overall survival of kidney cancer patients. Close follow-up by the urologist after surgery is recommended for at least five years. The interval between follow-up visits and the tests done are determined by the stage of the cancer.

Older patients with limited life expectancy, those with high operative risk or who refuse surgery, patient's with multifocal RCC (or risk thereof e.g von Hippel-Lindau syndrome), a solitary kidney or very small tumours (<1-3 cm) may be offered alternative treatment to nephrectomy. Experience has shown that the rate of growth of small tumours is variable and tumours that are destined to grow and possibly metastasize do so early. Most small tumours grow slowly or not at all. These patients may undergo a period of 'active surveillance' when the tumour is monitored closely for any signs of change. They may also undergo treatment by radiofrequency ablation (RFA) or cryoablation using a percutaneous or laparoscopic approach.

The role of surgery for metastatic disease is still under investigation. Cytoreductive nephrectomy and neo-adjuvant treatment are both used to treat metastatic disease. Cytoreductive nephrectomy is the removal of the kidney despite the presence of metastases to reduce the burden of the tumour on the body and hopefully enhance the response to systemic therapy. This operation is only done in otherwise relatively fit patients, especially with small numbers of metastases preferably in the lung. This surgery is not curative but may prolong survival in selected patients. Neo-adjuvant treatment is systemic treatment before surgery to shrink the tumour making it easier for removal. Neo-adjuvant treatment is currently undergoing clinical trials and is used for patients with advanced disease and low volume metastases.

Joan concluded her presentation by mentioning that the role of the urologist is paramount in the management of patients with kidney cancer. Observation or active surveillance of small tumours is appropriate for elderly or morbid patients that are either not suitable for surgery or who refuse surgery. In her presentation, she described the role of surgery for all stages of the disease; local, locally advanced and metastatic. Laparoscopic or keyhole surgery is growing in popularity and is important for stage 1 and 2 disease and partial nephrectomy or ablation of small early stage tumours helps to preserve kidney function. Surgery can provide a cure for kidney cancer, even if the tumours are large or locally advanced.

Treatment Options and Support

Robin Martinez

As listowner for ACOR's Kidney-Onc listserv (mailing list), Robin Martinez has provided support to thousands of kidney cancer patients from all over the world.

Robin gave a short overview of treatments available in the USA for RCC. Even before the development of the new targeted therapies, the prognosis for Stage IV RCC was not as bad as for most other Stage IV cancers. Eliminating all visible metastases with surgery or non-invasive surgical alternatives (cryoablation, radiofrequency ablation, embolisation, or radiosurgery) can prevent the need for drug treatment for years.

Interleukin-2 is the oldest drug approved to treat RCC; for many years it was the only approved drug. This immunotherapy can extend or save lives, but it is expensive and difficult treatment and the response rate is not very high. However, IL-2 is still the only drug we know of which causes a significant percentage of complete and durable remissions.

Targeted therapies are not cures, but they help to control RCC. The following targeted therapies are approved in the US as of mid-2012:

- Sutent (sunitinib)
- Nexavar (sorafenib)
- Avastin (bevucizamab)
- Torisel (temsirolimus)
- Afinitor (everolimus)
- Votrient (pazopanib)
- Inlyta (axitinib)

Several promising treatments are currently in clinical trials -- an immunotherapy called MDX-1106 and two targeted therapies, XL-184 (Cabozantinib, Cabo) and Tivozanib (Tivo). Many others are in development.

Less common treatments for RCC include yttrium-90 microspheres for liver metastases, cancer vaccines and stem cell transplants, but none of these is widely available.

Most targeted therapies are pills, so they are the easiest metastatic treatment to deliver. Because treatment with targeted therapy continues as long as the cancer is responding to the drug, managing the side effects is crucial to the success of the treatment and the quality of life of the patients.

Management of side effects of targeted therapies:

Modifying the targeted therapy's dosage schedule can reduce the frequency and severity of side effects. This requires approval from the physician.

Nausea: Over-the-counter remedies. Prescription drugs – if your prescription doesn't work, be sure to report back to the physician because other drugs are available to try. Ginger capsules or ginger in the diet. Other folk remedies must be approved by the physician to make sure there will be no bad interaction.

Diarrhoea: Over-the-counter medications, often at a higher-than-normal dose (ask physician). Prescription medications. Coconut works very well; coconut macaroons are one way to gain that benefit.

Hand-foot syndrome (pain, redness, blisters, sores): Aim for prevention. Wear thick socks and larger, comfortable shoes. Use urea cream or other skin ointment or lotion constantly, even before problems appear. Before bedtime apply a heavy layer of cream. Put on cotton gloves and socks to keep cream in place. Henna as a remedy: http://xelodasideeffects.blogspot.com/

Mouth sores: Prevention is better than treatment. Use non-mint toothpaste. Rinse mouth frequently with lukewarm water and baking soda or a non-irritating mouthwash like Biotene. If mouth sores develop, get a product such as GelClair to cover and protect the sores. Ask physican for an anesthetic mouthwash mixed by the pharmacist: 1/3 Lidocaine local anesthetic, 1/3 Maalox thick antacid to coat the mouth, and 1/3 Benedryl (diphenhydramine) to reduce inflammation. Anti-fungal medication can be added to the mouthwash if thrush infection is a problem. Swish in mouth for 30 seconds. Mixture can be swallowed if the esophagus is also affected.

Rash: Stay out of the sun as much as possible. See doctor for prescription ointment, often containing an antibiotic. Over-the-counter lotions and creams usually will not help.

Hypothyroidism (low thyroid function): Test for missing thyroid hormones. Physician will order replacement hormone if needed. Note: Low thyroid is a good sign showing the therapy is attacking the cancer.

*High blood pressur*e: Get a prescription drug. Check blood pressure regularly to make sure it is controlled. High blood pressure will damage the kidney, so this issue is very important.

In conclusion:

RCC patients with no visible evidence of disease must be vigilant about the ever-present possibility of recurrence. When new symptoms occur -- digestive difficulties, cough, breathing problems, bone pain, fever, any kind of problem – and if those symptoms are not easily and quickly relieved by normal treatment, the patient must insist on a prompt and thorough examination including scans to rule out RCC as a possible cause. Often the vigilance of well-informed and persistent patients is one of the best treatments of all.