



KCCNN

KIDNEY CANCER CANADA
NURSES NETWORK



RIACCR

RÉSEAU DES INFIRMIÈRES ET
INFIRMIERS DE
L'ASSOCIATION CANADIENNE
DU CANCER DU REIN

Update on the Management of Kidney Cancer

Kingston
May 21, 2013

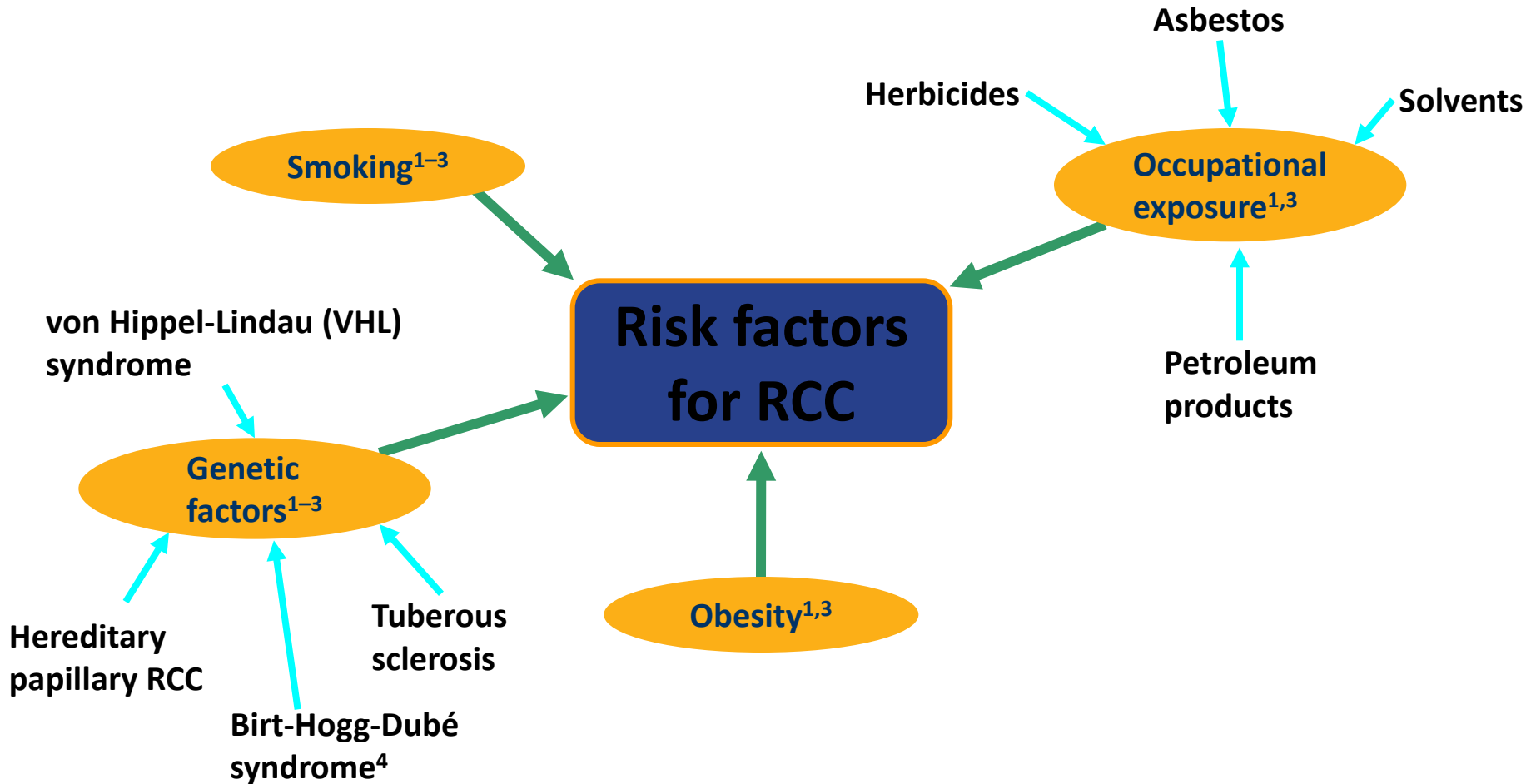
Renal Cell Carcinoma

- Overview
- Surgical Treatment
- Medical Treatment
- KCCNN

Incidence & Mortality

- 2012 estimates
 - 5600 new cases
 - 1700 deaths
 - Rise in male incidence of 2.6%
 - Mortality rates have decreased slightly

Risk Factors for RCC



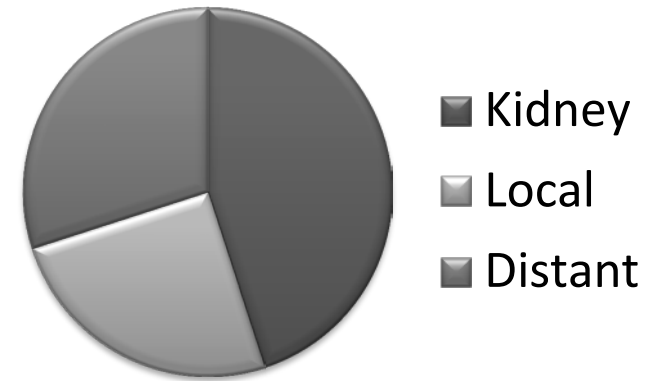
1. ACS Detailed Guide: Kidney Cancer. Available at: <http://www.cancer.org>.
2. NCI Renal Cell Cancer Treatment PDQ. Available at: <http://www.cancer.gov>.
3. McLaughlin & Liworth. *Semin Oncol* 2000; 27:115–123.
4. Rosner et al. *Urol Oncol* 2009;131-136.

Presentation

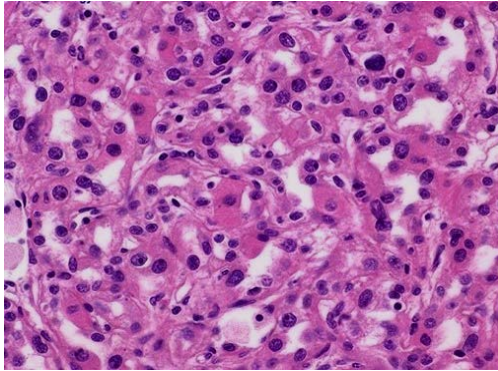
- Usually found incidentally with imaging for other causes
- Median tumour size is <4cm
- Classic “too late” triad -10%
 - Blood in urine (must be investigated as could arise from kidney or bladder)
 - Palpable mass
 - Flank pain

Extent of Renal Cell Carcinoma at Time of Diagnosis

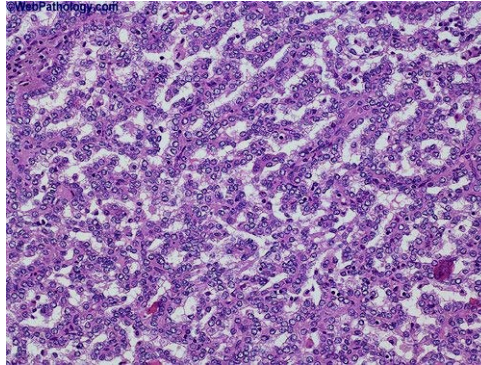
Stage	% of Patients
Localized	45%
Locally advanced	25%
Metastatic	30%



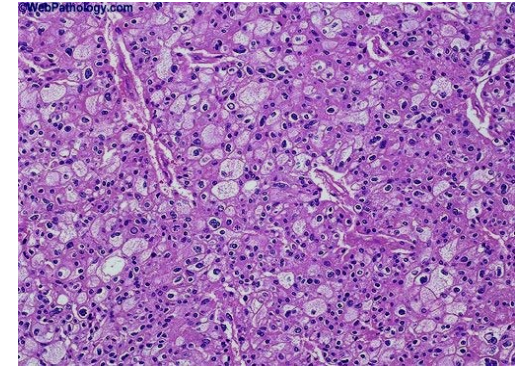
Histology



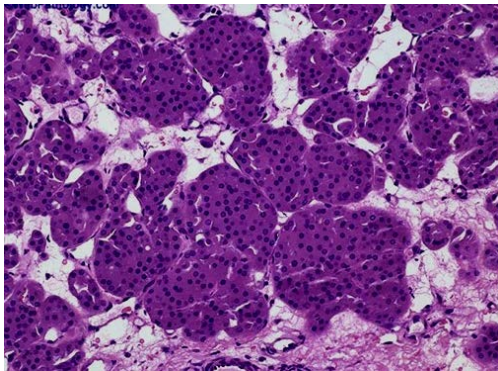
Clear cell 75-80%



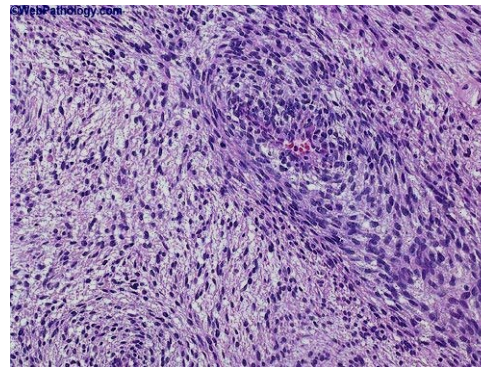
Papillary (7-14%)



Chromophobe 5-8%



Oncocytoma 2-5%



Sarcomatoid / Others 1-2%



**Heterogeneous
group**

**Clear cell most
frequent type**

Staging

- Staging includes
 - Bloodwork
 - Chest x-ray or CT chest
 - Abdominal CT scan with IV contrast
 - MRI

Prognosis

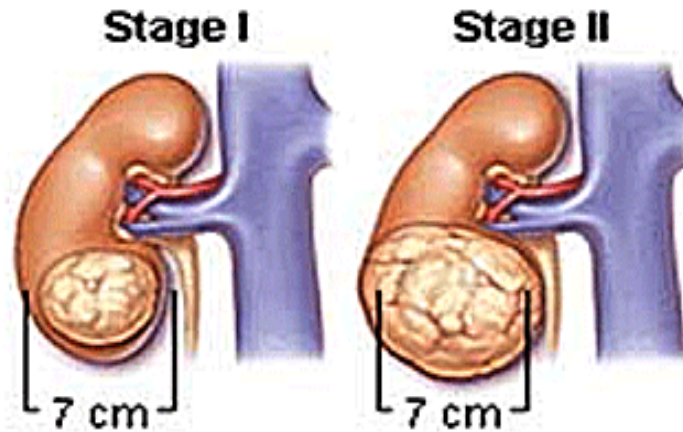
5 year survival

- T1: 90 – 100%
- T2-3: 60%
- Mets: 0 – 20%

Metastasis

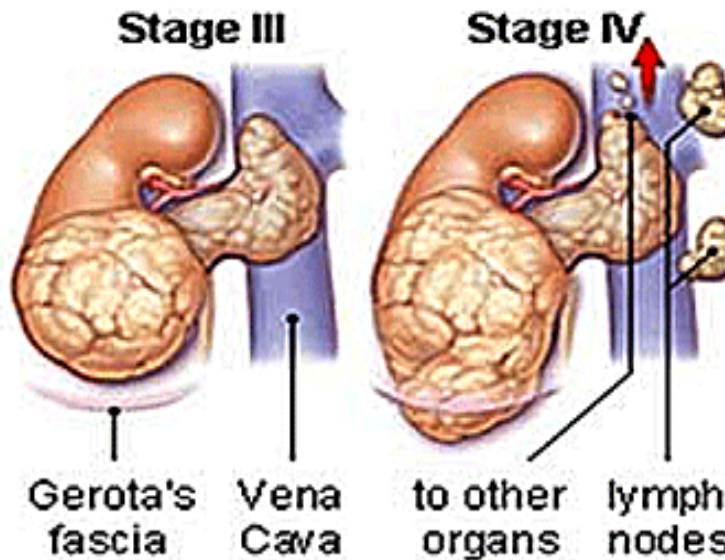
- Lung- 60%
- Lymph nodes- 40%
- Liver- 40%
- Bone- 30%
- Adrenal- 20%
- Contralateral kidney- 10%
- Brain- 5%

Stages of Kidney Cancer



Stage I – inside, <7cm

Stage II – inside, >7cm



Stage III – outside

Stage IV – distant

How is Kidney Cancer Treated?

Treatment depends on stage of cancer

- Surgery
- Active Observation
- Targeted therapy
- Immunotherapy
- Radiation therapy



More than one treatment may be used

Surgical Options

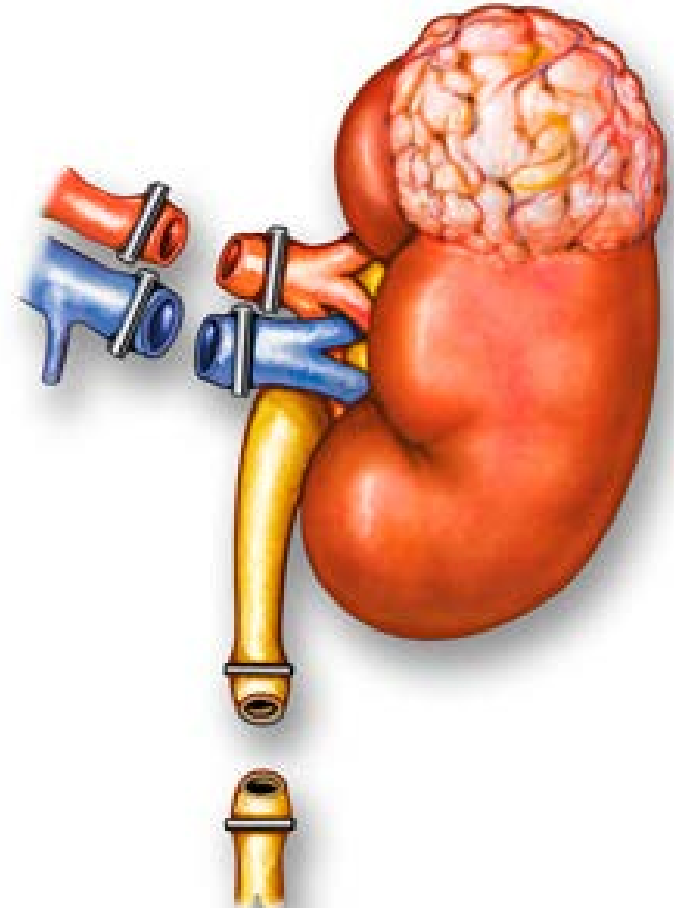
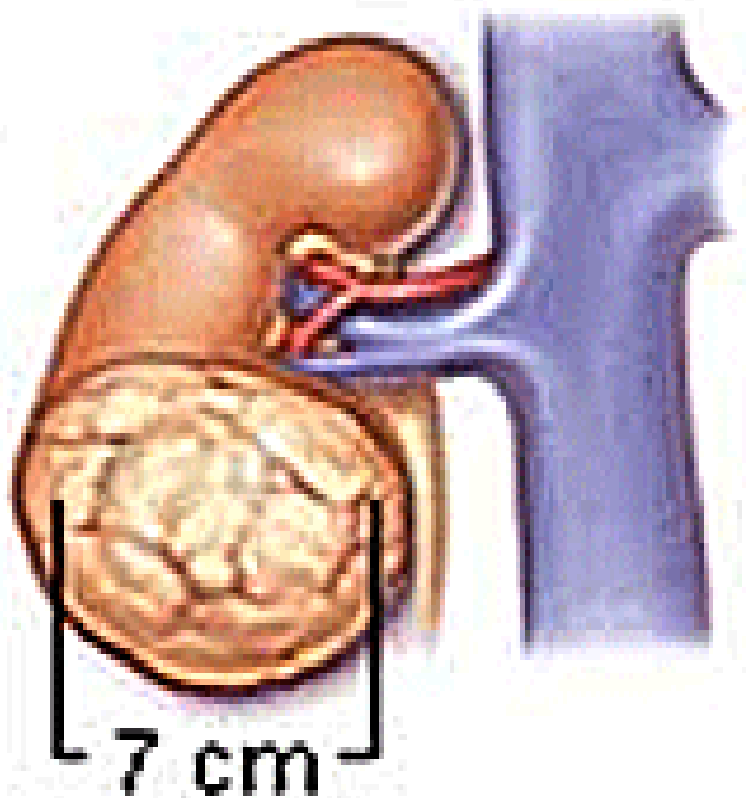
- Excision
 - Open vs Laparoscopic
 - Partial vs Radical
- Ablation
 - Cryotherapy
 - Radiofrequency Ablation
- Active Surveillance

Surgery: Organ Confined Lesion <7cm

	Nephron Sparing	Radical Nephrectomy
Laparoscopic	1 (if amenable & trained surgeon)	3
Open	2 (1 st choice in EAU)	4

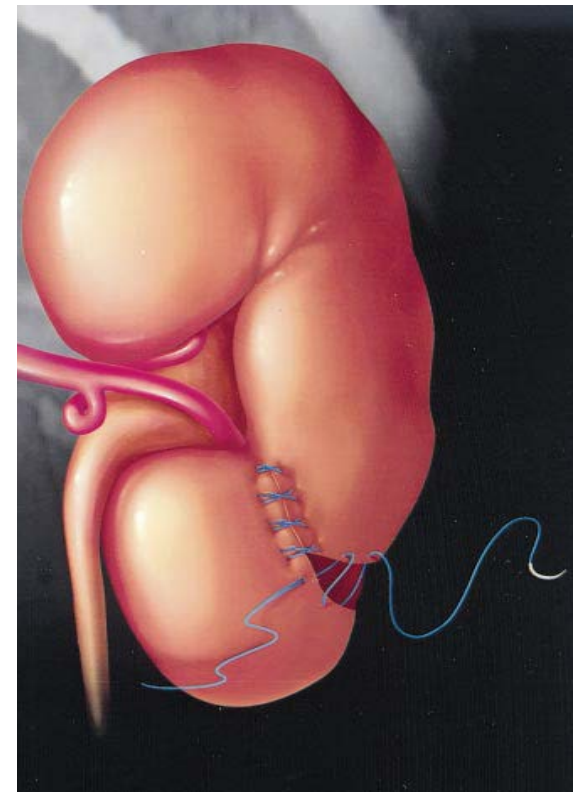
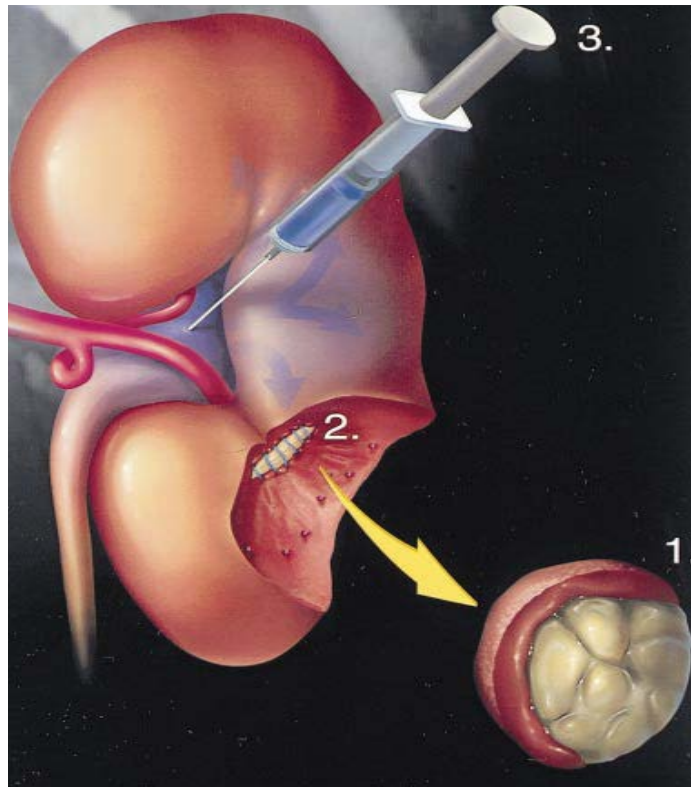
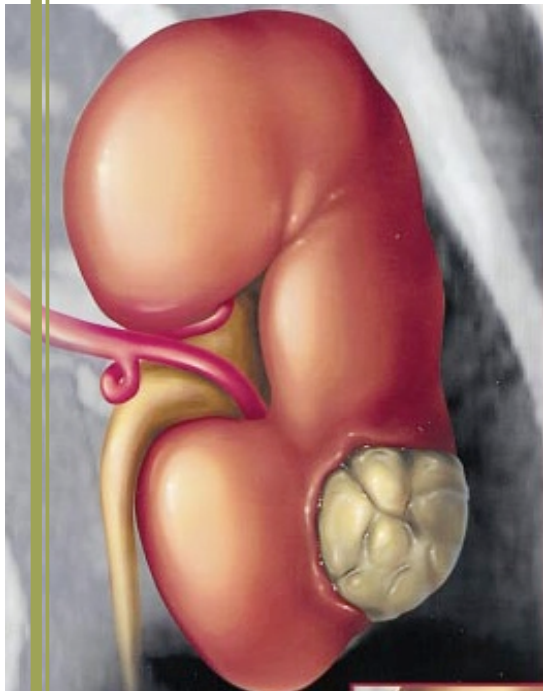
Treatment of RCC – surgery – large stage I, stage II

Stage II



Radical nephrectomy

Treatment of RCC – surgery – small stage I



Partial nephrectomy

Indications for Partial Nephrectomy

- **Absolute**
 - Solitary kidney
 - Bilateral tumours
 - Severe renal insufficiency
- **Relative** - Contralateral kidney threatened by:
 - Local conditions: (eg. stones, infection)
 - Systemic conditions: (eg. DM, HTN)
 - Genetic conditions: (eg. vHL)
- **Elective** (Normal contralateral kidney)
 - Small tumour (<4 cm; ? <7 cm)
 - Young

Nephron Sparing

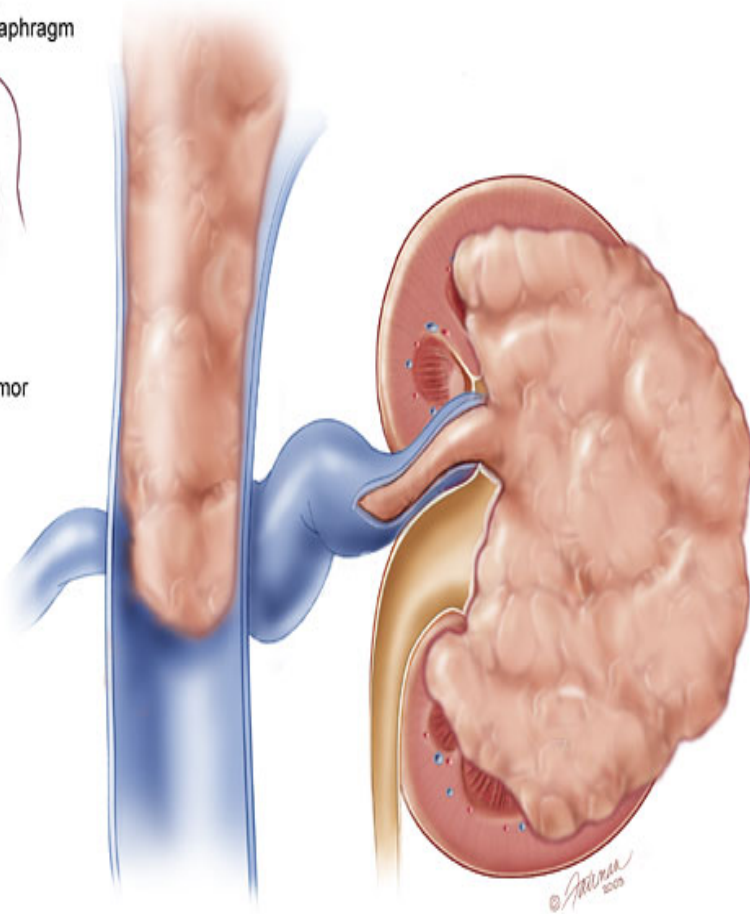
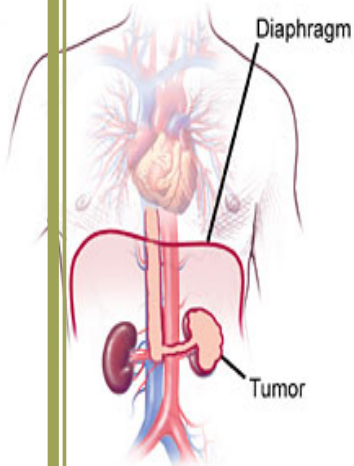
	Radical	Nephron Sparing
Short Term Complications:		
Technical Challenge		More Demanding
Severe Bleeding	1.2%	3.1%
Urine Leak	0%	4.4%
Re-Operation	2.4%	4.4%
Tumours > 7cm	Superior	
Local Recurrence	Superior	Very low rate
Long Term Complications:		
Renal Function		Superior
Quality of Life		Superior
Risk of Mortality		Superior

Laparoscopic Vs Open Surgery

	Laparoscopic	Open
Recovery Time	3-4 weeks	2-3 months
Hernia Incidence		Higher
Cosmesis	Better	
Hospital Stay	2-3 days	4-5 days
Difficult Anatomy		Superior

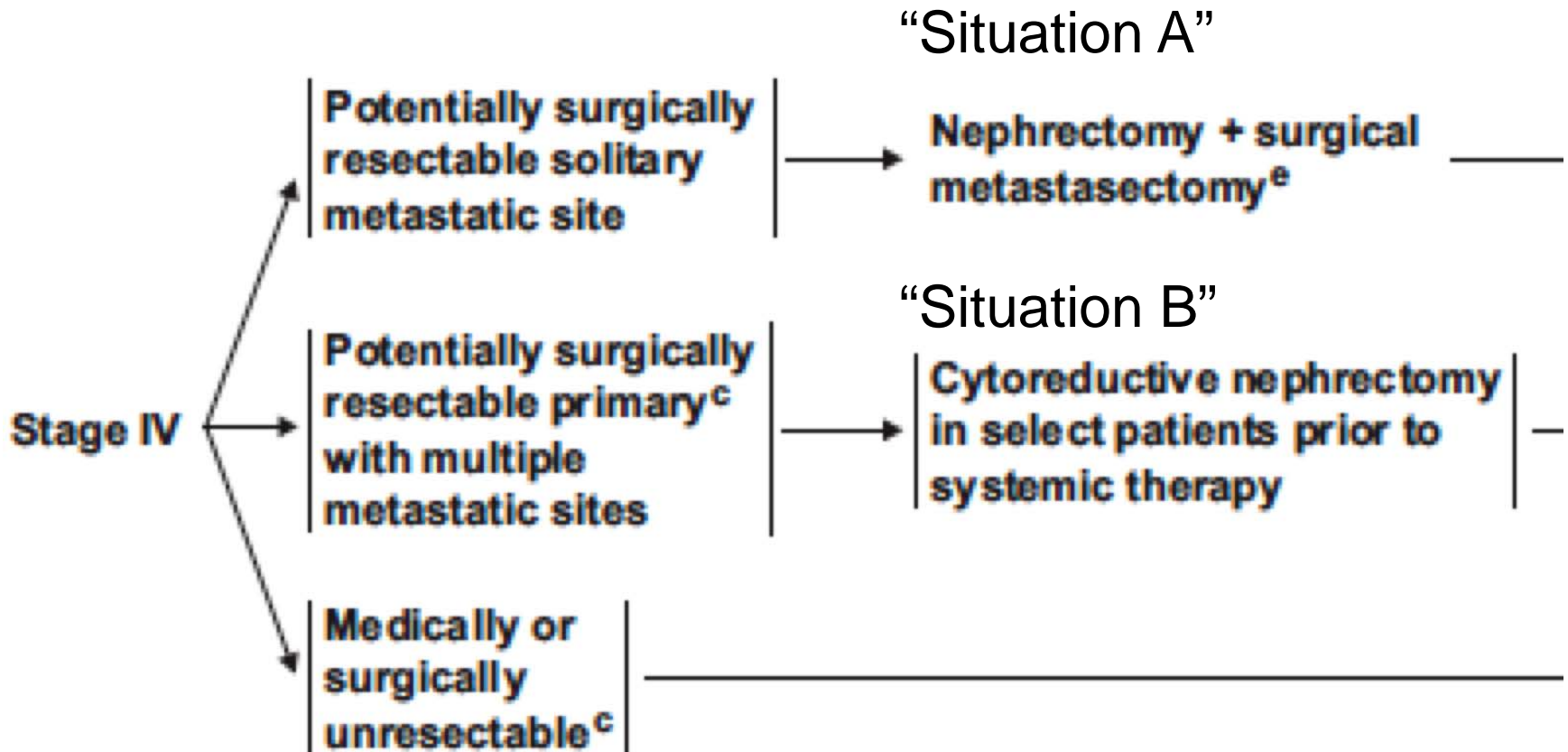


Stage 3 kidney cancer



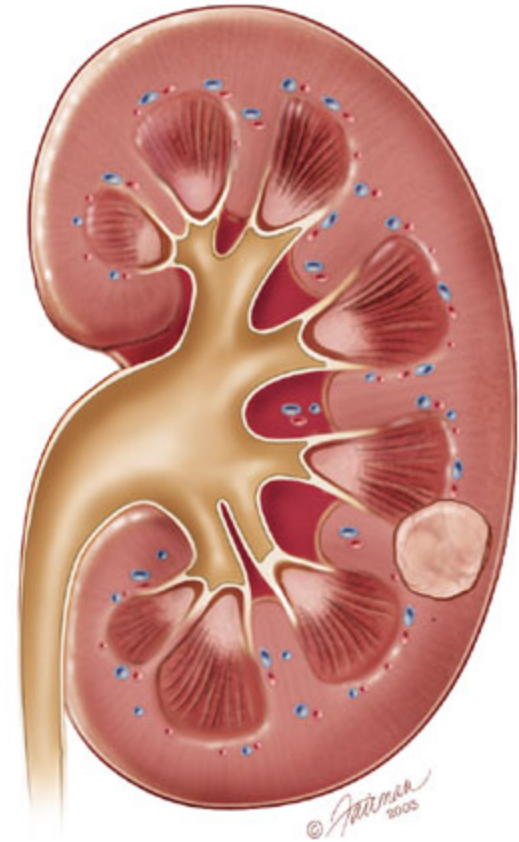
- 5-10% of kidney cancer
- Open surgery required
- May require heart bypass
- Still curable with surgery even though very locally advanced
- * Not laparoscopic*

Nephrectomy in Stage 4

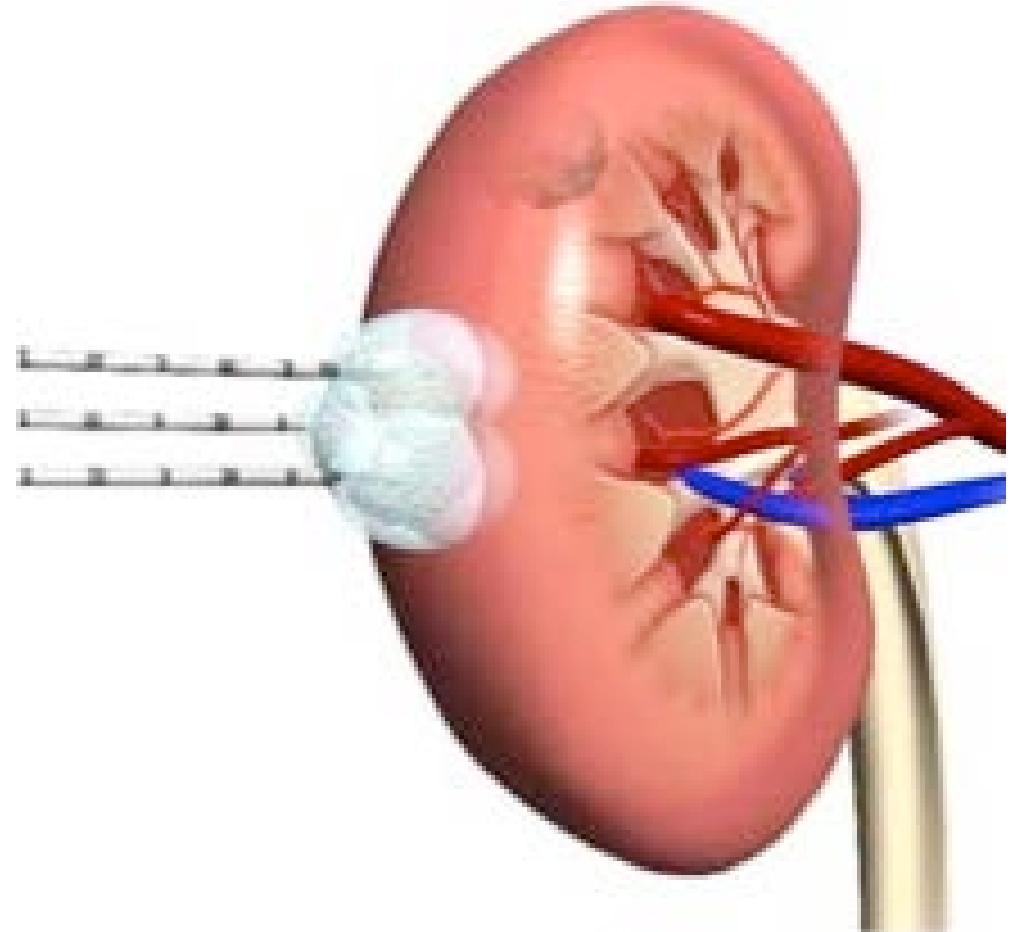
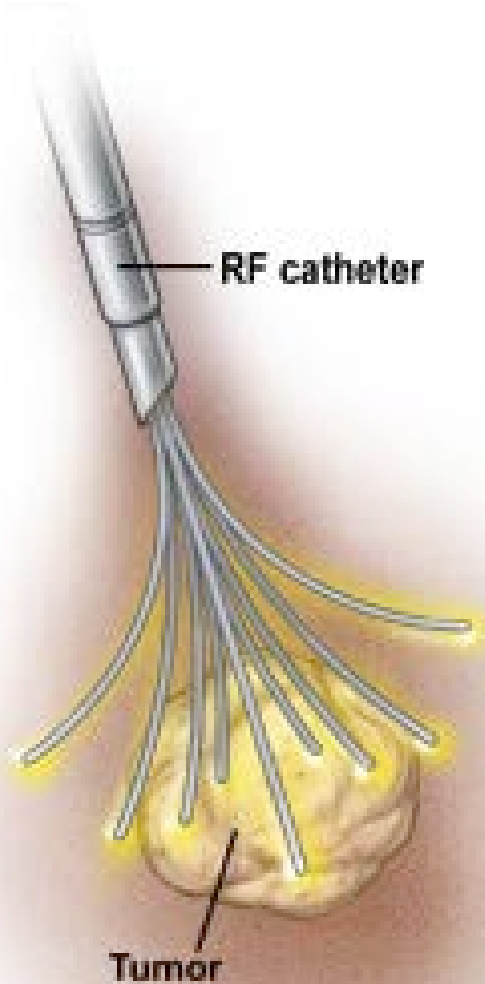


Active Surveillance

- Well adopted in specific circumstances
 - Non surgical candidates
 - Older or ill pts
 - Pt declines surgery
 - Hereditary syndrome
- Many active surveillance series in literature



Ablation— Radio-frequency or cryo-ablation



Summary of Surgical Treatment

- Renal Cell Carcinoma is a primarily surgical disease
- For organ confined disease, usually nothing else is required
- Even with metastases, there can be a role for surgery
- Surgical Priorities:
 1. Complete resection
 2. Nephron Sparing
 3. Laparoscopic Approach

Medical Treatment

- Targeted Therapies
- Immunotherapy

Evolution of Treatment Options for Advanced RCC

Canadian

IV bolus
interleukin 2

Sorafenib

Sunitinib

Temsirolimus

Everolimus

Pazopanib

Axitinib

1992-2004

2005

2006

2007

2008

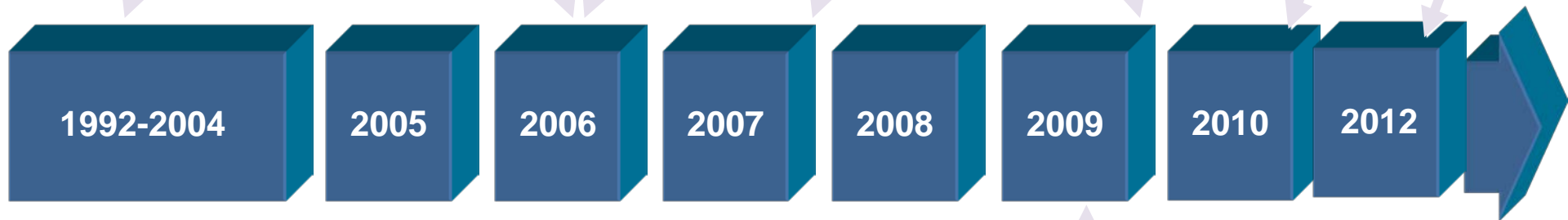
2009

2010


2012

Bevacizumab
+ IFN- α 2a

US

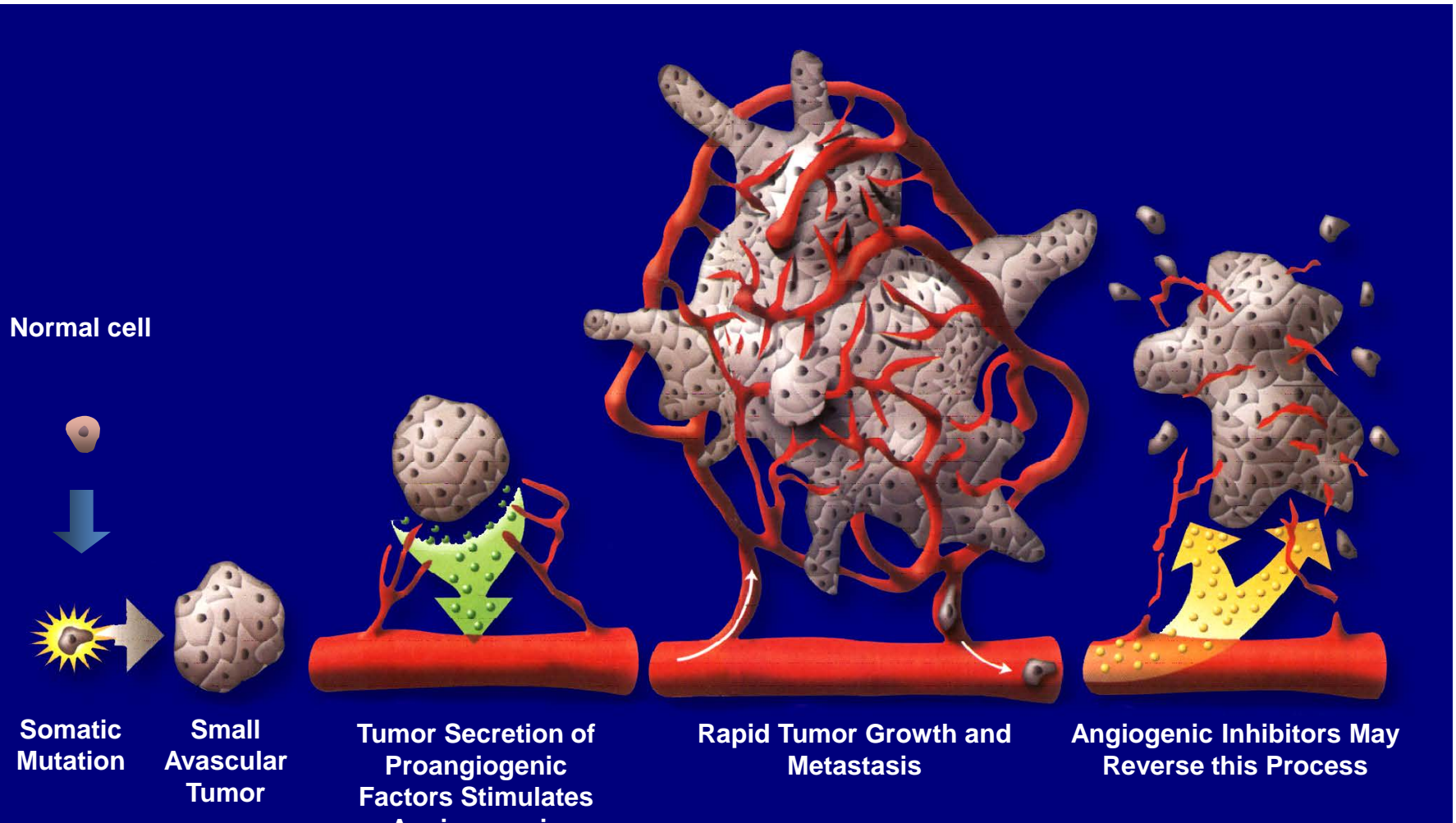


Targeted Therapies

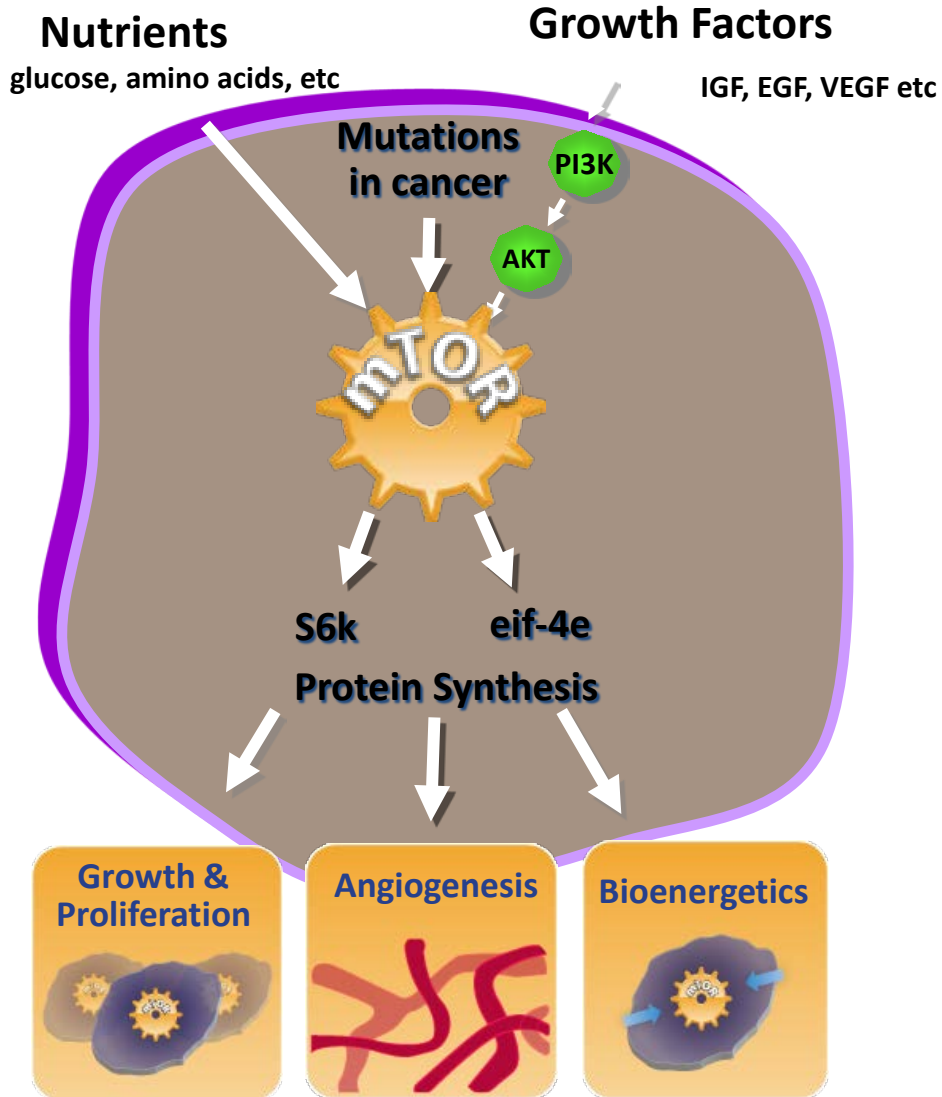
 **“target” and interfere (inhibit) with specific mechanisms in or outside the tumor which are important for the survival, growth and spread of the tumor**

- ❑ Anti-angiogenesis (anti-new blood vessel)
stop the uncontrolled formation of blood vessels
- ❑ mTOR Inhibitor (anti-tumor growth effect)
interfere with blood vessel formation and other cell function
- ❑ Many others in development.....

The Angiogenic Switch and Antiangiogenic Therapy



mTOR - A Novel Cancer Target



mTOR

- Regulates Glucose and lipids
- Regulates angiogenesis
- Regulates cell growth

Treatment with Targeted Agents



- Almost all of them are pills
- Treatment is usually given continuously as chronic , long-term therapy
- Treatment can usually be given as outpatient
- Treatment needs close surveillance because of potential side effects

Treatment with Targeted Agents

These agents can lead to:

- Improved tumor shrinkage (“response rate”)
- Prolonged interval without tumor growth (“progression-free survival”)
- Prolonged life span (“overall survival”)

BUT:

All of them can have side effects

Side effects with Targeted Agents

- Fatigue
- Hypertension
- Stomatitis / mucositis
- Indigestion
- Diarrhea
- Skin rash
- Hand-foot syndrome
-

Coping with Side Effects

- ❑ Side effects can happen, BUT they don't have to happen
- ❑ Every patient is different, and side effects cannot be predicted
- ❑ Side effects are treatable; talk with the doctor or nurse
- ❑ Medications may help with various side effects
- ❑ High blood pressure is treatable
- ❑ Pain is treatable; non-narcotic pain-relievers are available

There are lots of things patients can do to prevent or relieve side effects

Nurses play an important role with this!

Coping with Side Effects

- ❑ Dose interruptions / treatment breaks
- ❑ Dose reductions
- ❑ Schedule changes
- ❑ Switch to a different drug

There are lots of things doctors can do to prevent or relieve side effects



*"I stopped taking the medicine because I prefer
the original disease to the side effects."*

Treatment with Targeted Agents

First-line Therapy

- Sunitinib
- Pazopanib
- Sorafenib

Choice depends on:

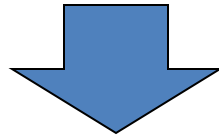
- Co-existing illnesses
- Experience of the treating physician
- Functional status of the patient
- Age of the patient
-

Can we better predict who will benefit and who will not ?

Second line therapy

- Everolimus (mTOR inhibitor)

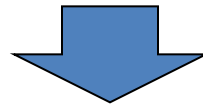
- Axitinib (TKI)



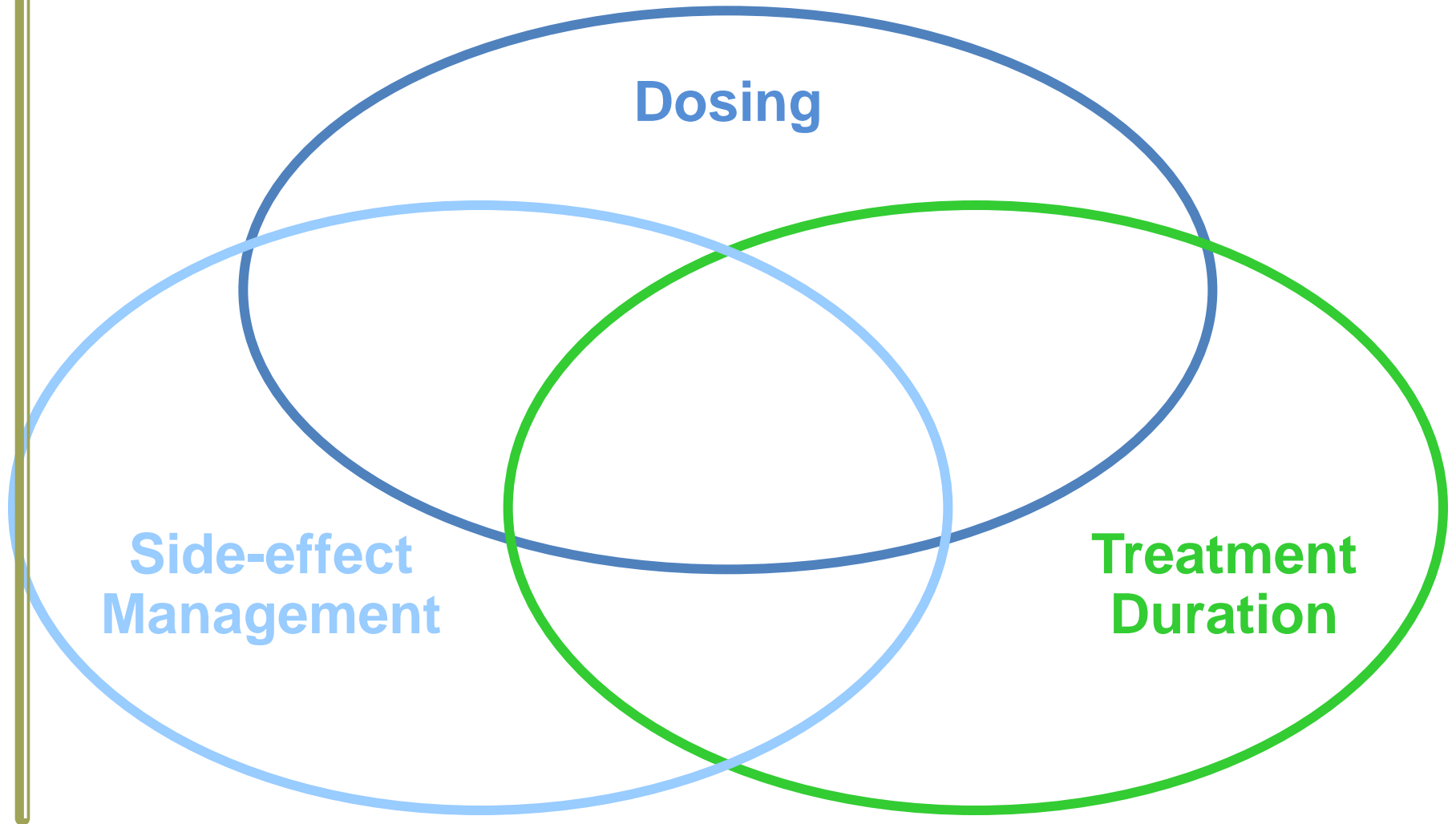
- Mostly stabilize the disease
- Keep patients free of progression for a prolonged period of time

Treatment

- First-line: Sunitinib, Pazopanib, Sorafenib
- Second line: Everolimus or Axitinib
- Third line: ??????????????????????????????



Three Key Factors for Successful Therapy Management in mRCC

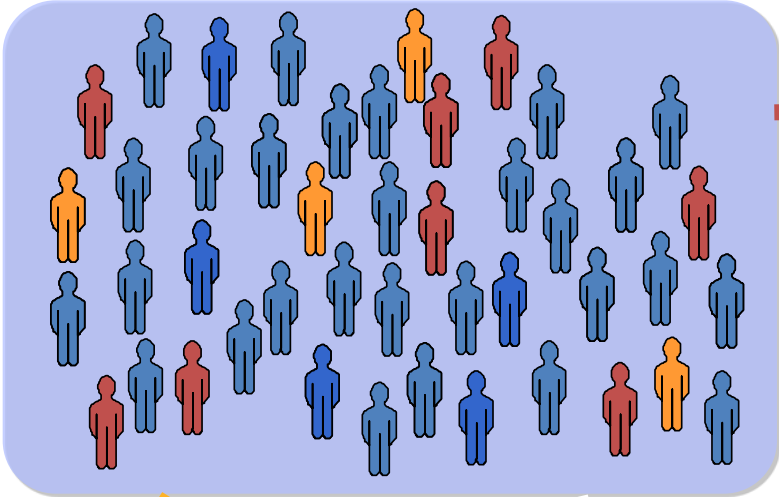


Role of Immunotherapy

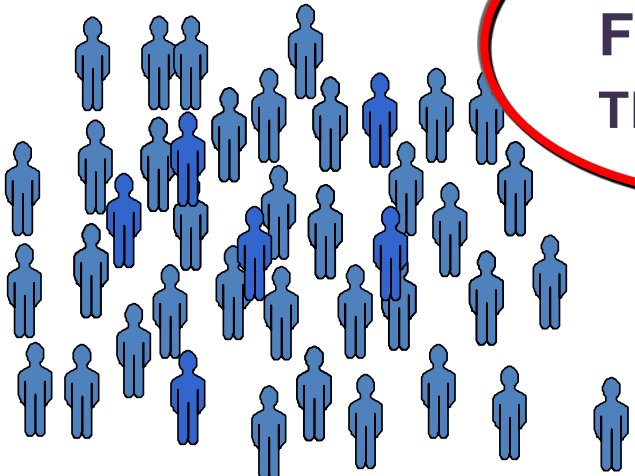
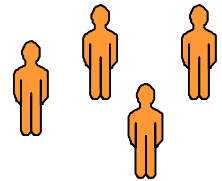
- Interferon-alpha
- High-dose interleukin-2
- Vaccines

Can we predict whether a patient will benefit ?

Patients with RCC



Factor Z:
High-dose IL-2



Predictive factors for targeted therapy in RCC

Patients who develop side effects seems to have a better chance to benefit from therapy

Demonstrated for : hypertension, hand-foot syndrome, thyroid dysfunction, fatigue.....



Onset of side effects as a indicator for a effective dose
("right dose", dose which causes effects in the body)

What's next with these new drugs?

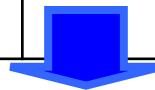
Many more questions

- Which are the best drugs?
- Can the drugs be used in combinations?
- What is the best sequences?
- How best to use the drugs in different clinical situations?
- How to make patients' disease control more durable?
- Could we cure more patients if used after kidney surgery without metastatic disease?
- Can we predict which patients respond best to these drugs and to which one?
-

Many trials ongoing and in preparation

Novel targets, novel agents overcoming resistance?

Agent	Main Targets	Med. Prior Tx	ORR	PFS (mo, 95% CI)	Comments
Cabozantinib (n=25)	VEGFR2 c-Met	2	28%	14.7 mo (7.3,--)	<ul style="list-style-type: none"> • VEGF TT refractory • Bone metastasis!
AMG 386 (combined with sunitinib n=43)	Angiopoietin/ Tie2 axis	0	58%	13.9 mo	<ul style="list-style-type: none"> • Combination tolerable
BMS-936558* (n=16 RCC)	PD-1*	2	31%	56% at 6mo	<ul style="list-style-type: none"> • Primary TT refractory



Active new agents / combinations

*PD-1 inhibitor: programmed death-1 is an inhibitory receptor expressed on T cells after activation

Role of Radiotherapy

- Traditionally thought not to play a role except in bone & brain metastases
- New role for SBRT in oligo-progression

Conclusions

- Multiple new agents are currently in clinical development
- Resistance to treatments develops
- We need to find out why
- We need to find drugs to treat resistance
- May be new role for radiotherapy

Kidney Cancer Canada Nurses Network

- **WHY** the need for a nurses' network in kidney cancer nursing
- **WHO** can join the nurses' network
- **WHAT** the nurses' network can do to help you
- **WHERE** you access the nurses' network
- **WHEN** you can use the nurses' network

Why ?

“As treatment options for patients with RCC become more numerous and complex, it is critical that nurses have a way to network with their colleagues to improve best practices. A virtual nurses network helps achieve this goal and will lead to better patient outcomes as we all learn from each other.”

Dr. Scott North
Medical Oncologist, Edmonton
Past-Chair, KCC Medical Advisory Board

Any Questions





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Thank you

Merci.