

KCRNC

KIDNEY CANCER RESEARCH
NETWORK OF CANADA

RRCRC


RÉSEAU DE RECHERCHE SUR LE
CANCER DU REIN DU CANADA




Living with Chronic Toxicities: Healthcare Teams and Patients Working Together

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Disclosures

- ▶ Ad boards: no financial compensation
 - ▶ Research: with lots of companies
 - Pfizer, BMS, AZ, Roche, Merck, Novartis
 - Financial compensation to my institute
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Topics


- ▶ Chronic Toxicities
 - Targeted therapies
 - CPI
 - Steroids
 - Combinations
 - ▶ Safety of drug sequencing
 - ▶ A few other things to ponder!
 - ▶ Need a team approach
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Chronic Targeted Therapy Toxicities

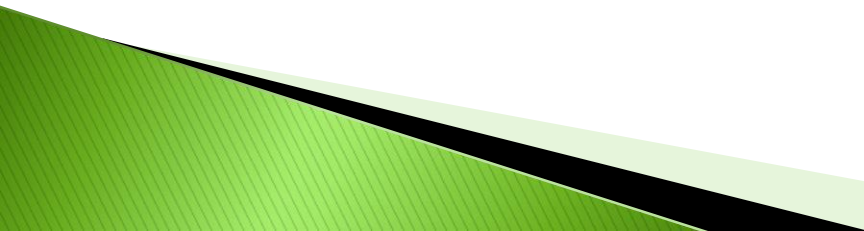
- ▶ Patients are the best to give us advice about this topic...
 - Fatigue
 - Abnormal Taste
 - Diarrhea

- ▶ Kidney Cancer Canada website
 - Managing side effects

Chronic CPI Toxicities

- ▶ Endocrinopathies
 - ▶ Dermatitis / Pruritis
 - ▶ Colitis
 - ▶ Pneumonitis
 - ▶ Myocarditis
 - ▶ Rheumatological
 - ▶ Neurological
- 

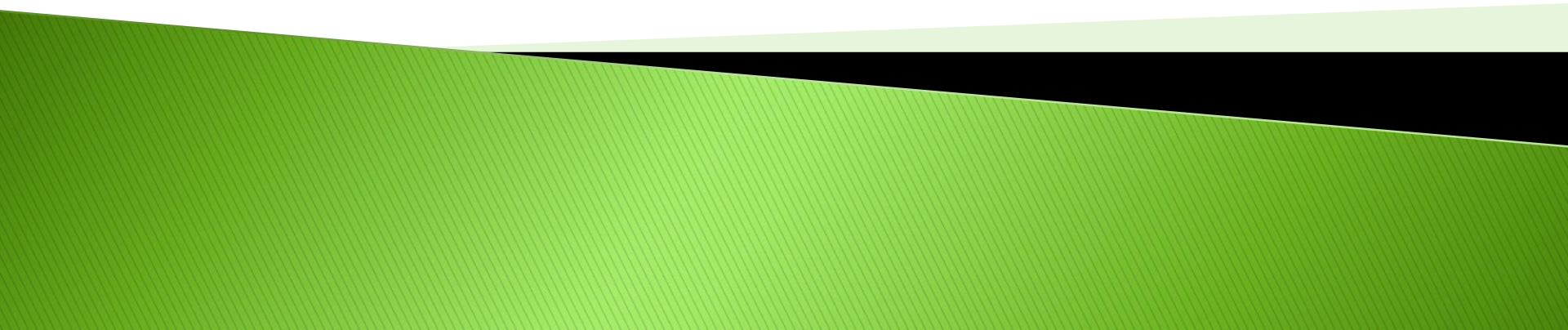
Chronic Steroid Toxicities

- ▶ Can be months on steroids
 - ▶ Weight gain
 - Obstructive Sleep Apnea
 - ▶ Infection Risk
 - PCP: ?Septra if > 30 days of steroids
 - Zoster: live vaccine
 - ▶ Hyperglycemia
 - Need for Insulin
 - ▶ Osteoporosis
 - Vit D, Calcium, +/- Bisphosphonates
 - ▶ Psychological/Cognitive Changes
- 

Chronic VEGF/CPI Combo Toxicities

- ▶ Can potentially be a double whammy!

Overlapping Chronic Toxicities with Sequencing Treatments




CPI to Targeted Therapy

▶ Case 1:


- Ipi/Nivo X 4- mixed response but clinically bone pain worse and grade 2 pneumonitis. Steroids.
- Waited 8 weeks → Pazopanib
- Very quick decline and worsening pneumonitis

▶ Case 2:

- Ipi/Nivo X 4 – progression, ECOG 0
- Waited 5 weeks → Sunitinib
- 14 days later:
 - diarrhea, renal failure (Creatinine >1300)
 - myocarditis (troponin >5000), hepatotoxicity (AST >700)
 - severe mucositis, severe myelosuppression (platelets 11)

- ▶ VEGF to VEGF
 - ▶ VEGF to Nivolumab
 - ▶ Nivolumab to Targeted Therapy
 - ▶ Ipi/Nivo to Targeted therapy
 - ▶ Axitinib/CPI to Targeted therapy
- 

So...questions to ponder...

- ▶ How long after stopping CPI can the toxicities appear?
 - ▶ How long do you wait between Ipi/Nivo and targeted therapy?
 - ▶ Post Ipi/Nivo, what is the best second line therapy from a minimization of toxicities point of view
- 

How long after CPI stop can toxicities appear?

- ▶ BCCA:

- “symptoms may be delayed and can develop months after your last dose”


- ▶ ESMO:

- Anytime...and “sometimes as long as **1 year** after treatment has finished”

Not just a question we are asking

- ▶ Also need to know this answer to inform:
 - Patients
 - Family doctors
 - Palliative care doctors

How long between Ipi/Nivo and Sunitnib/Pazopanib?

- ▶ Long enough to avoid overlapping toxicities
 - ▶ Not too long where patients have clinically progressive disease
 - ▶ Note: there will be a cohort of Ipi/Nivo pts who have such severe CPI toxicities that they don't get second line therapy
- 

CPI and Sunitinib/Pazopanib

- ▶ Checkmate 016: Safety and efficacy of nivolumab in combination with sunitinib or pazopanib in mRCC
- ▶ Conclusion: You cannot combine these drugs at standard doses

	Nivo/Sunitinib	Nivo/Pazopanib
N	33	19
TRAE	100%	100%
Gr 3,4 TRAE	82%	70%
TRAE → D/C drug	39%	25%

What is the best therapy post Ipi/Nivo?

- ▶ If a VEGF Targeted therapy is the next therapy
 - I would argue Axitinib has the most safety data

- ▶ Do these questions influence our decision regarding first line therapy
 - With CPI/Axitinib – at least you are guaranteed to get both drugs

An issue we sometimes forget....

▶ Sexual health:

- Intercourse
 - **Interest/Ability**
 - Sexual life of male patients with advanced renal cancer treated with angiogenesis inhibitors
 - Semen/Vaginal fluids with targeted therapies
- Fertility
- Breastfeeding

Medical Oncologists cannot manage all of these issues on own..

- ▶ Definitely need a team approach
- ▶ Education, monitoring and delivering care
 - Medical Oncologists
 - Clinic RNs
 - Phone toxicities
 - Triageing phone calls/need for visits
 - Chemotherapy RNs
 - Pharmacists
 - Family Doctors/Palliative Care Doctors
 - **PATIENTS**
 - **FAMILIES**

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Questions?