Metastatic Renal Cell Carcinoma:
Treatment Landscape and Management of TKI Toxicity

September 28, 2018

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Faculty Disclosure

- Faculty: Christina Canil
- Advisory Boards: Pfizer, Eisai, Bayer, Janssen, Merck, Novartis, Bristol-Myer Squibb, Sanofi Genzyme, AstraZeneca and EMD Serono
- Educational travel grants: Sanofi Genzyme and Amgen
- Clinical trials: Bayer, Bristol-Myer Squibb, Janssen, Eisai, and Roche

Learning Objectives

- Discuss the evolving treatment landscape in metastatic Renal Cell Carcinoma (mRCC)
- Discuss the management of toxicities associated with Tyrosine Kinase Inhibitor (TKI) therapies used in mRCC
- Clinical scenarios

Met Renal Cell Cancer

CANIL Notes®

Question #1

How often do you see patients with metastatic renal cell carcinoma?

- **A** – all the time
- **B** – some of the time
- **C** – rarely
- **D** – never
- **E** – renal cell carcinoma? – I am just here for the food

Epidemiology and Etiology

- Renal Cell Carcinoma (RCC) is a basket term for kidney tumors but **clear cell carcinoma** is the most common at 85% of cases

- Localized disease can be cured with surgery or in non-surgical patients local therapy such as RFA, etc. In some cases – small renal masses can be observed

- Metastatic disease tends to be incurable except in situations where there is oligo-metastatic disease (<4 lesions) which can be surgically excised (or be subject to other local interventions)

- Patients who have advanced, incurable disease are offered drug therapy

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All RCC are not alike

- Metastatic disease can run very different courses - from indolent to highly aggressive

- Prognostic risk factors have been developed to try and categorize patients both to provide prognostic information but also to tailor treatment decisions

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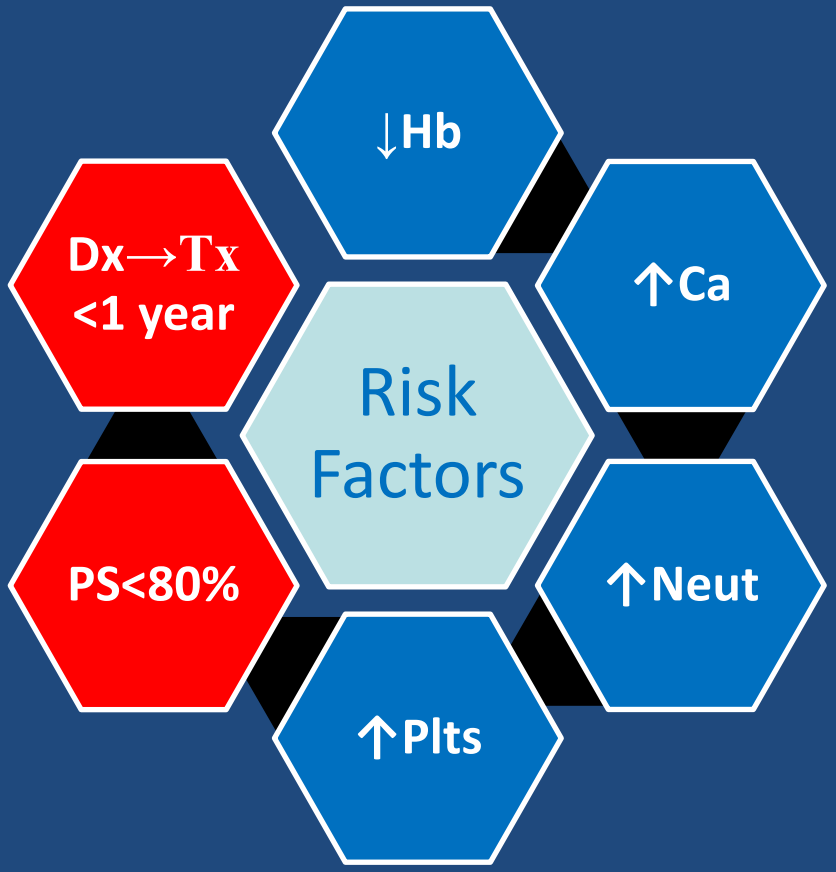
IMDC Prognostic Factors (Heng Criteria)



1 point for each

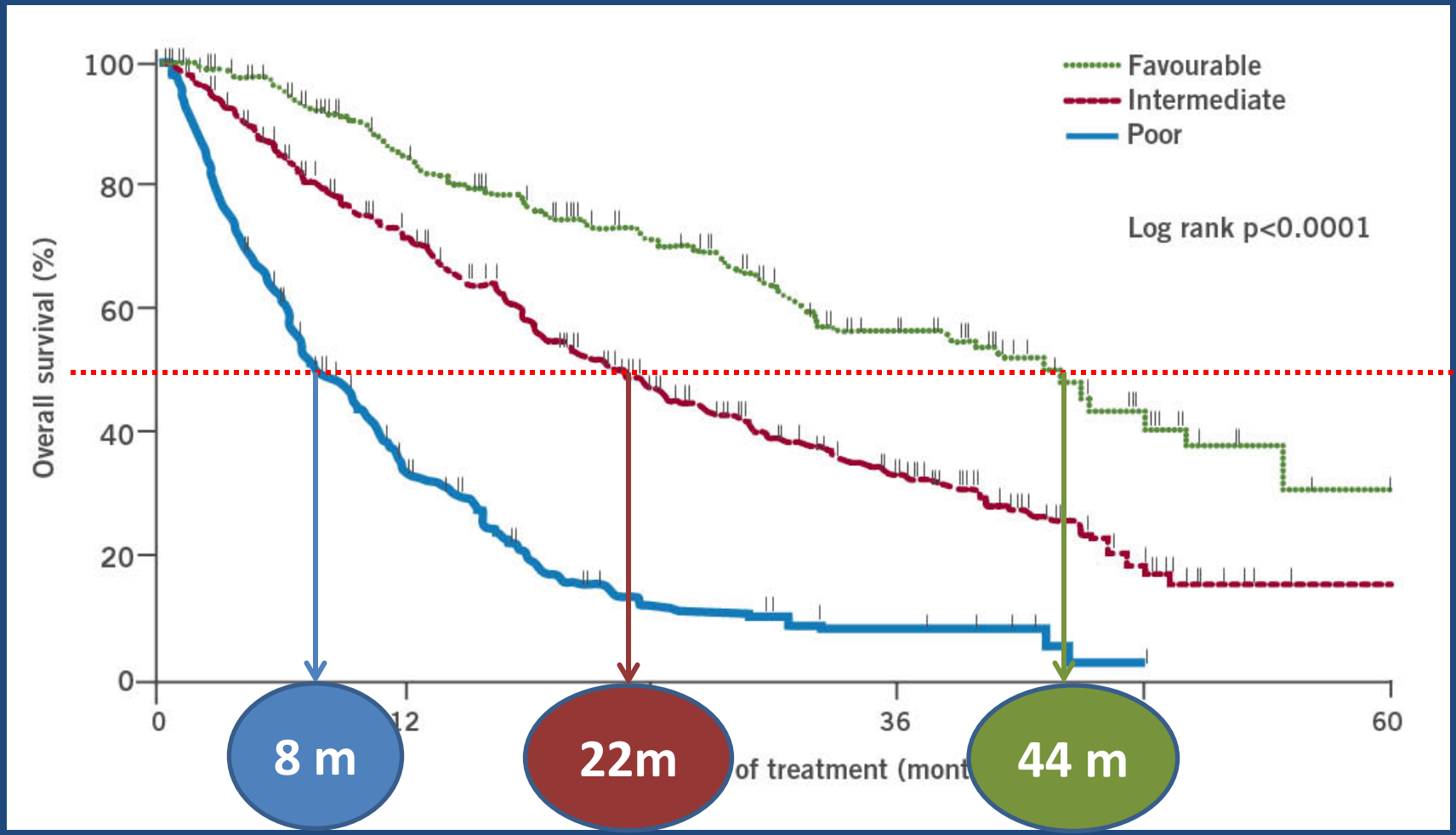
0 Risk Factors = Favourable

1 or 2 Risk Factors = Intermediate

3 or more Risk Factors = Poor

1. Heng DYC, Xie W, Regan MM, Warren MA, Golshayan AR, Sahi C, et al. Prognostic factors for overall survival in patients with metastatic renal cell carcinoma treated with vascular endothelial growth factor-targeted agents: Results from a large, multicenter study. J Clin Oncol. 2009 Dec 1; 27(34): 5794-5799. **2.** Heng DYC, Xie W, Regan MM, Harshman LC, Bjarnason GA, Vaishampayan UN, et al. External validation and comparison with other models of the International Metastatic Renal-Cell Carcinoma Database Consortium prognostic model: A population-based study. Lancet Oncol. 2013 Feb; 14(2): 141-148.

Overall Survival By Heng Criteria Score

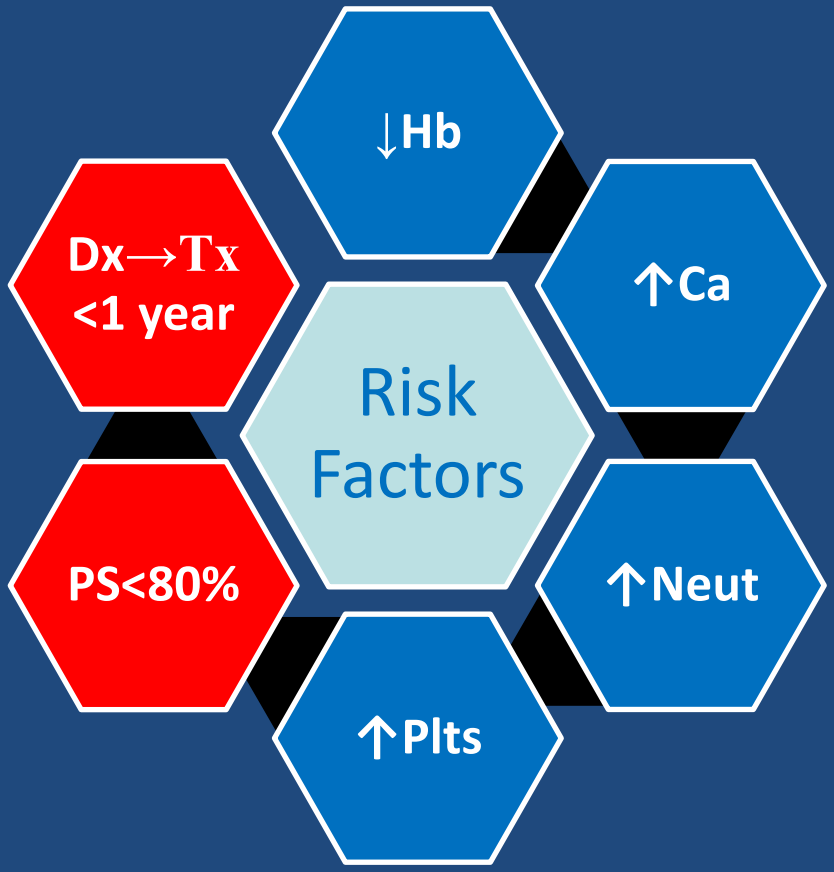


Heng DYC, Xie W, Regan MM, Harshman LC, Bjarnason GA, Vaishampayan UN, et al. External validation and comparison with other models of the International Metastatic Renal-Cell Carcinoma Database Consortium prognostic model: A population-based study. Lancet Oncol. 2013 Feb; 14(2): 141-148.

Question #2

- 70 yo woman - R radical nephrectomy Feb 2018 for *T3b clear cell, fuhrmans grade 3/4*
- **Now** - multiple bilateral pulmonary nodules
- N hemoglobin, platelets, calcium; ⬆ neuts
- KPS 100
- What is her prognostic category?
- **A** – favourable
- **B** – intermediate
- **C** – poor
- **D** – unable to determine

IMDC Prognostic Factors (Heng Criteria)



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B

1. Heng DYC, Xie W, Regan MM, Warren MA, Golshayan AR, Sahi C, et al. Prognostic factors for overall survival in patients with metastatic renal cell carcinoma treated with vascular endothelial growth factor-targeted agents: Results from a large, multicenter study. J Clin Oncol. 2009 Dec 1; 27(34): 5794-5799. **2.** Heng DYC, Xie W, Regan MM, Harshman LC, Bjarnason GA, Vaishampayan UN, et al. External validation and comparison with other models of the International Metastatic Renal-Cell Carcinoma Database Consortium prognostic model: A population-based study. Lancet Oncol. 2013 Feb; 14(2): 141-148.

FUTURE
PAST
PRESENT

In the Past - Limited Choices

- Biological agents to enhance immune system
  - Interleukin-2
  - Interferon
- Clinical trial
- Best supportive care

Von Hippel Lindau (vHL) gene

- vHL was known to be a genetic syndrome affecting families wherein they developed RCC amongst other tumors

- Sporadic ccRCC was known to have vHL mutations which were not inherited but rather developed over time and led to cancer

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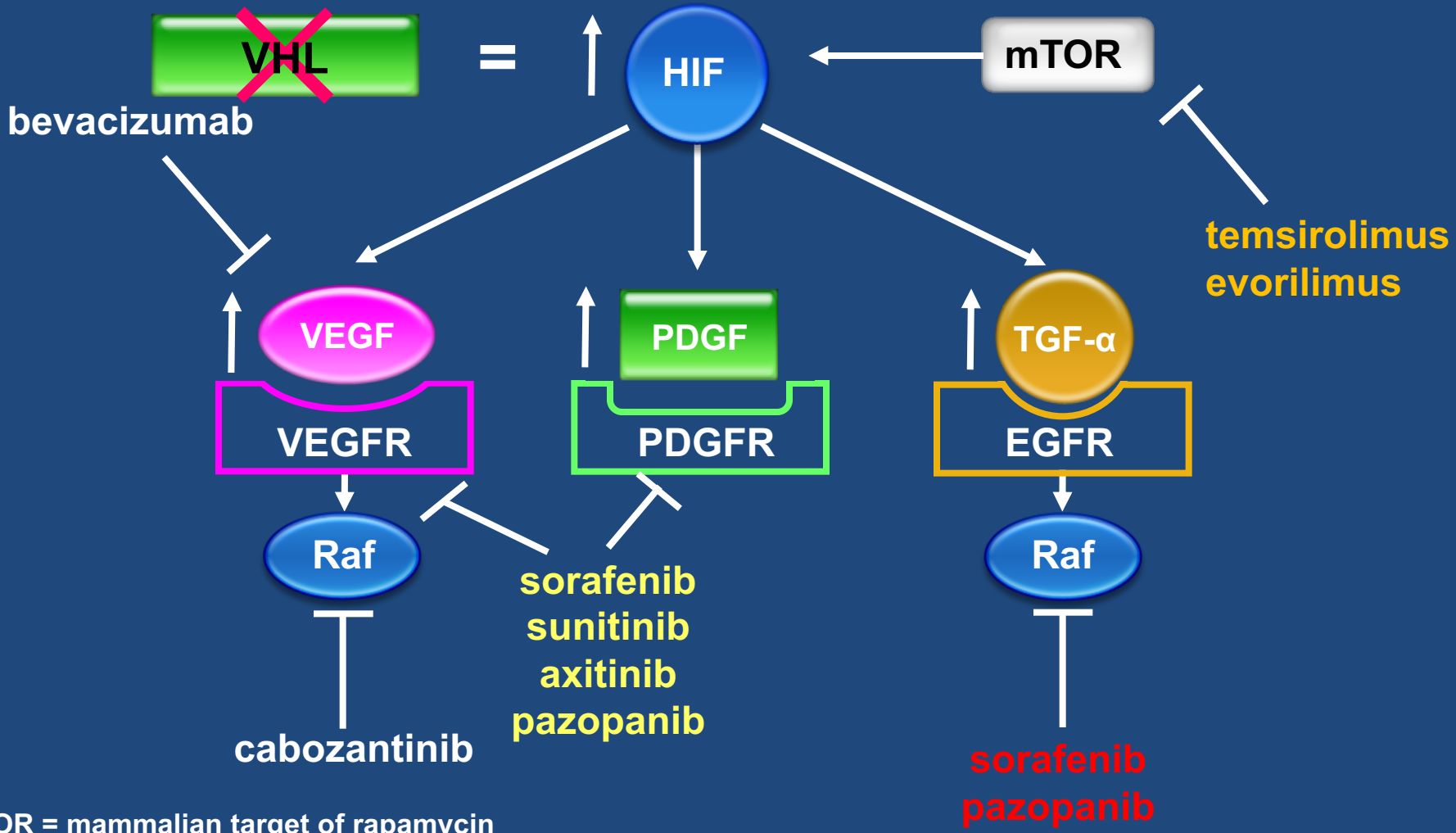
Renal cell carcinoma (RCC): Therapeutic targets



mTOR = mammalian target of rapamycin
EGFR = epithelial growth factor receptor
VEGFR = vascular endothelial growth factor receptor
PDGFR = platelet derived growth factor receptor

Kaelin WG. Nat Rev Cancer 2002;2:673–82

VEGF and c-MET pathways

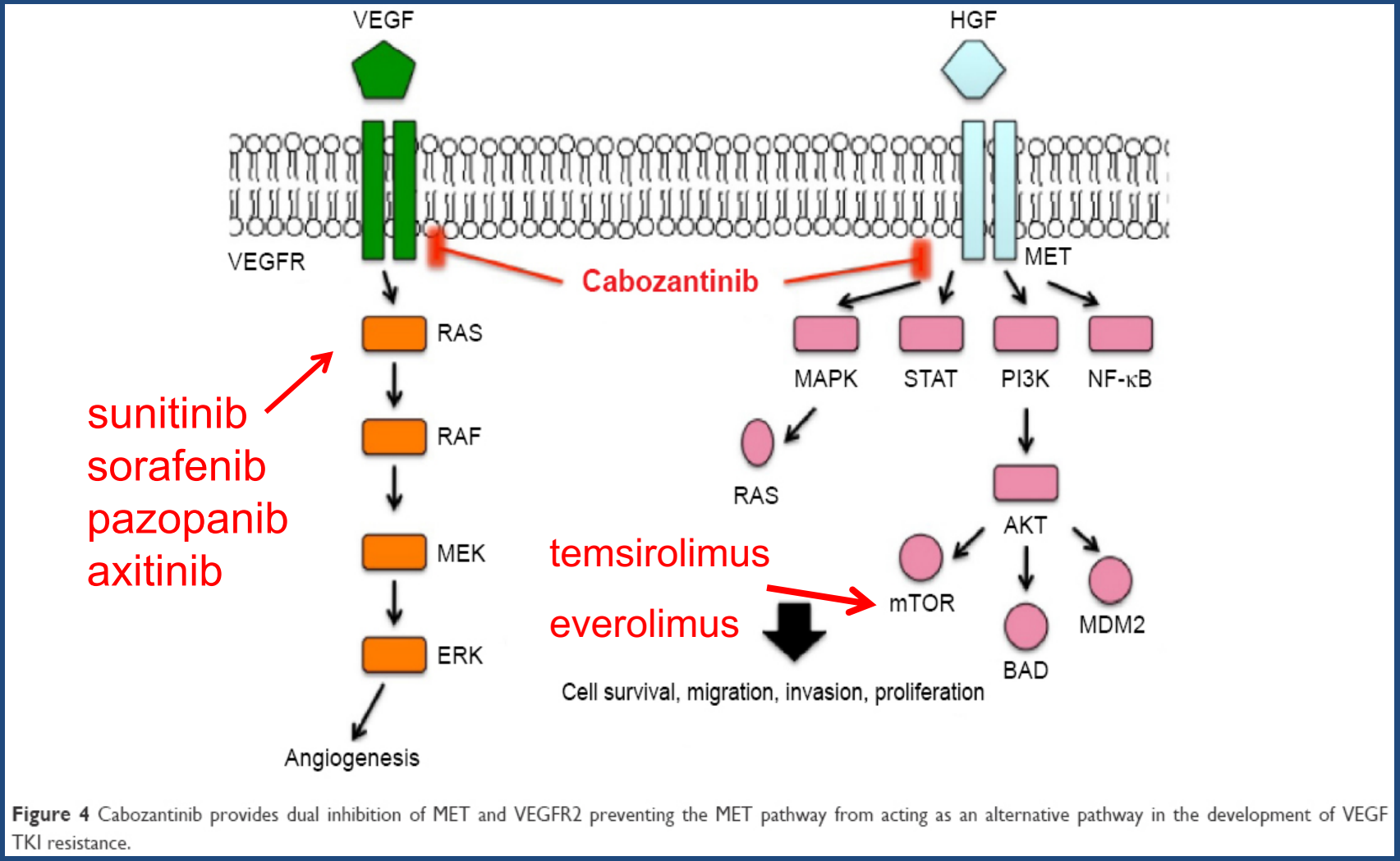


Figure 4 Cabozantinib provides dual inhibition of MET and VEGFR2 preventing the MET pathway from acting as an alternative pathway in the development of VEGF TKI resistance.

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How did this information change the landscape of RCC?

- Understanding that VEGF, c-MET, and mTOR pathways were important led to new drugs targeting these pathways
- Multiple clinical trials were conducted to get new therapies approved
- Survival for patients with mRCC improved dramatically

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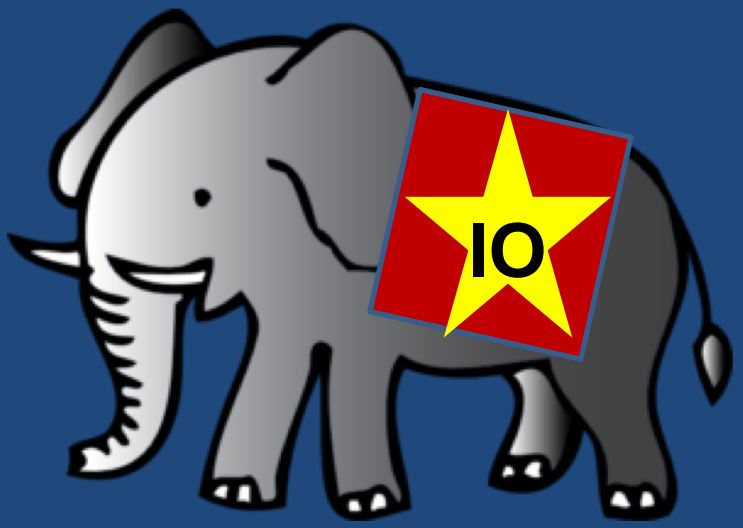
Targeted Therapy for mRCC approved in Canada

- <u>Oral TKI – VEGF-R inhibitors</u>
  - sunitinib (sutent)
  - sorafenib (nexavar)
  - pazopanib (votrient)
  - axitinib (inlyta)
  - cabozantinib (cabometyx)

- <u>Oral and IV m-TOR inhibitors</u>
  - temsorlimus (torsel) IV
  - everolimus (afinitor) oral



1st line therapy

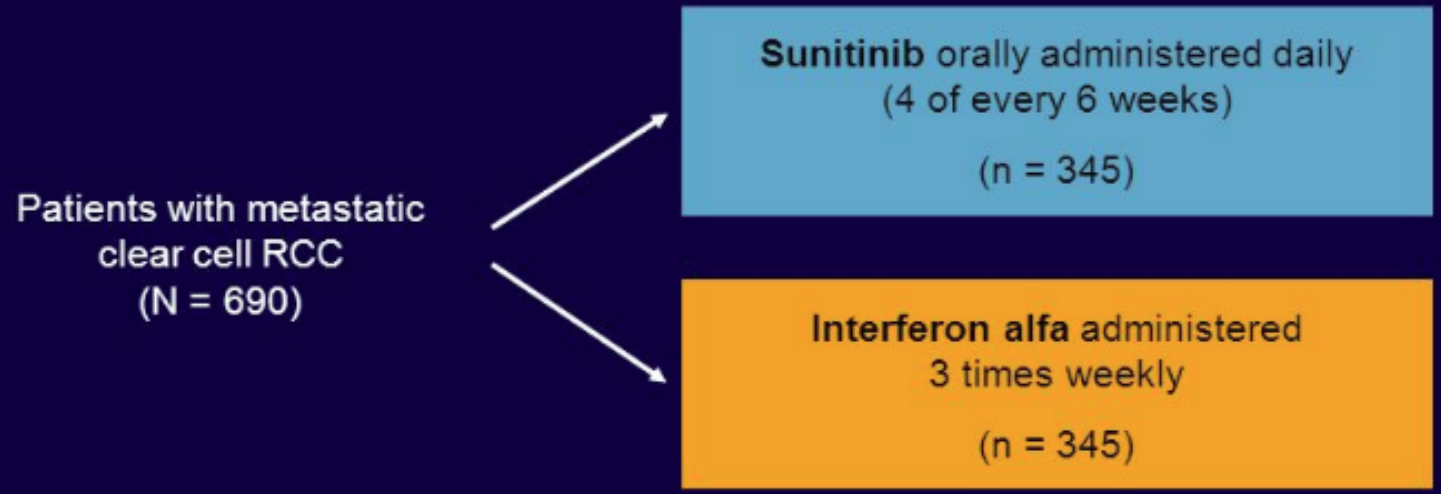
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 11, 2007 VOL. 356 NO. 2

Sunitinib versus Interferon Alfa in Metastatic Renal-Cell Carcinoma

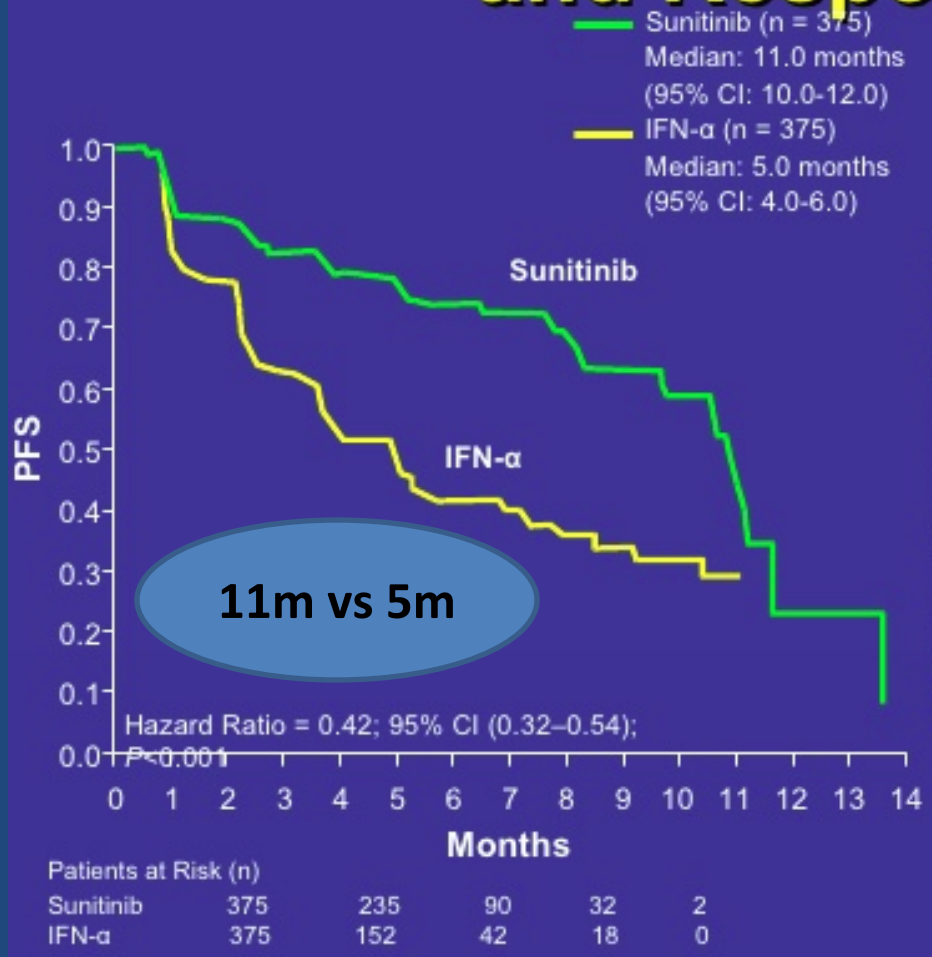
Robert J. Motzer, M.D., Thomas E. Hutson, D.O., Pharm.D., Piotr Tomczak, M.D., M. Dror Michaelson, M.D., Ph.D., Ronald M. Bukowski, M.D., Olivier Rixe, M.D., Ph.D., Stéphane Oudard, M.D., Ph.D., Sylvie Negrier, M.D., Ph.D., Cezary Szczylik, M.D., Ph.D., Sindy T. Kim, B.S., Isan Chen, M.D., Paul W. Bycott, Dr.P.H., Charles M. Baum, M.D., Ph.D., and Robert A. Figlin, M.D.*

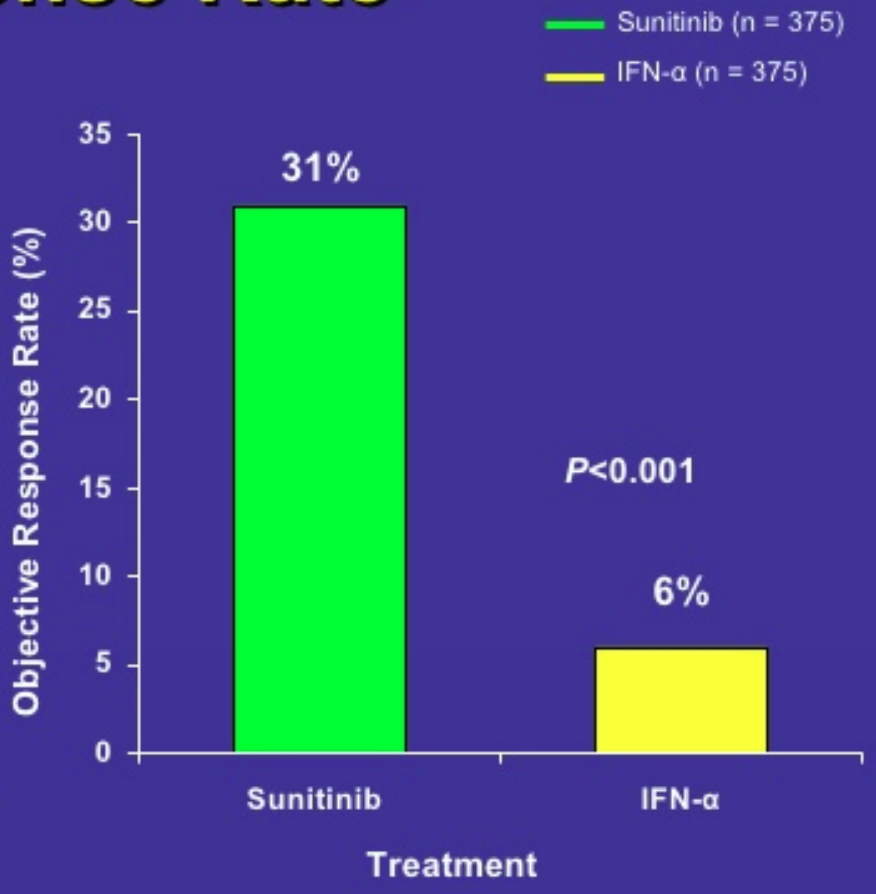
Phase III Trial of Sunitinib vs Interferon alfa in Metastatic RCC



- Randomized, open-label, multicenter trial
  - 100 Sites (US, Canada, Europe, Australia, Brazil)
- Endpoints
  - Primary: PFS
  - Secondary: TTP, OS, RR, QoL, safety, cost-effectiveness

First-Line Sunitinib vs IFN-α: PFS and Response Rate

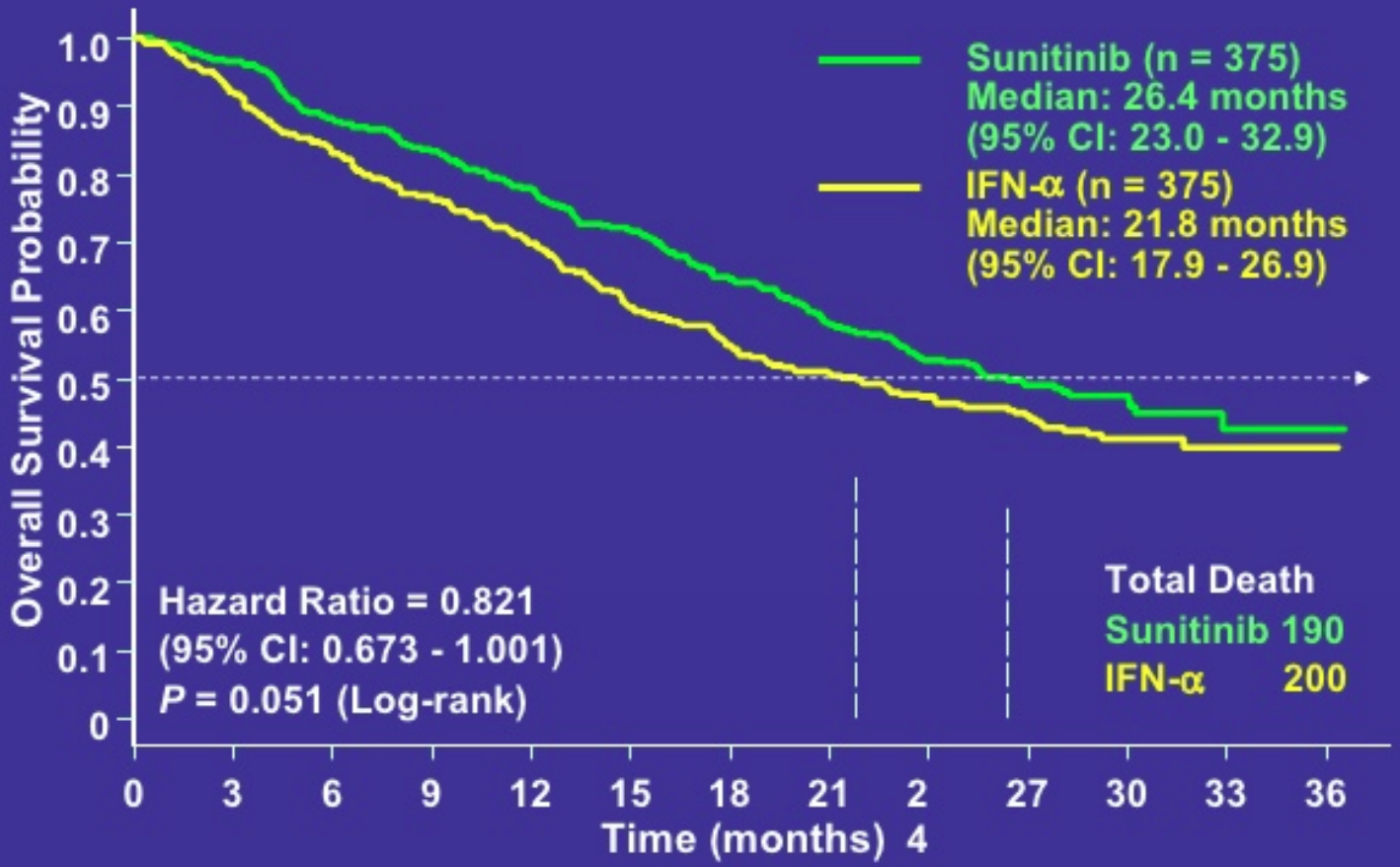




PFS = progression-free survival.

Motzer RJ, et al. *N Engl J Med.* 2007;356:115-124.
Motzer RJ, et al. 2007 ASCO Annual Meeting; Abstract 5024.

Sunitinib vs IFN-α: Final Overall Survival



Figlin RA, et al. 2008 ASCO Annual Meeting; Abstract 5024.

Sunitinib became the 1st line treatment for metastatic RCC

The NEW ENGLAND JOURNAL of MEDICINE

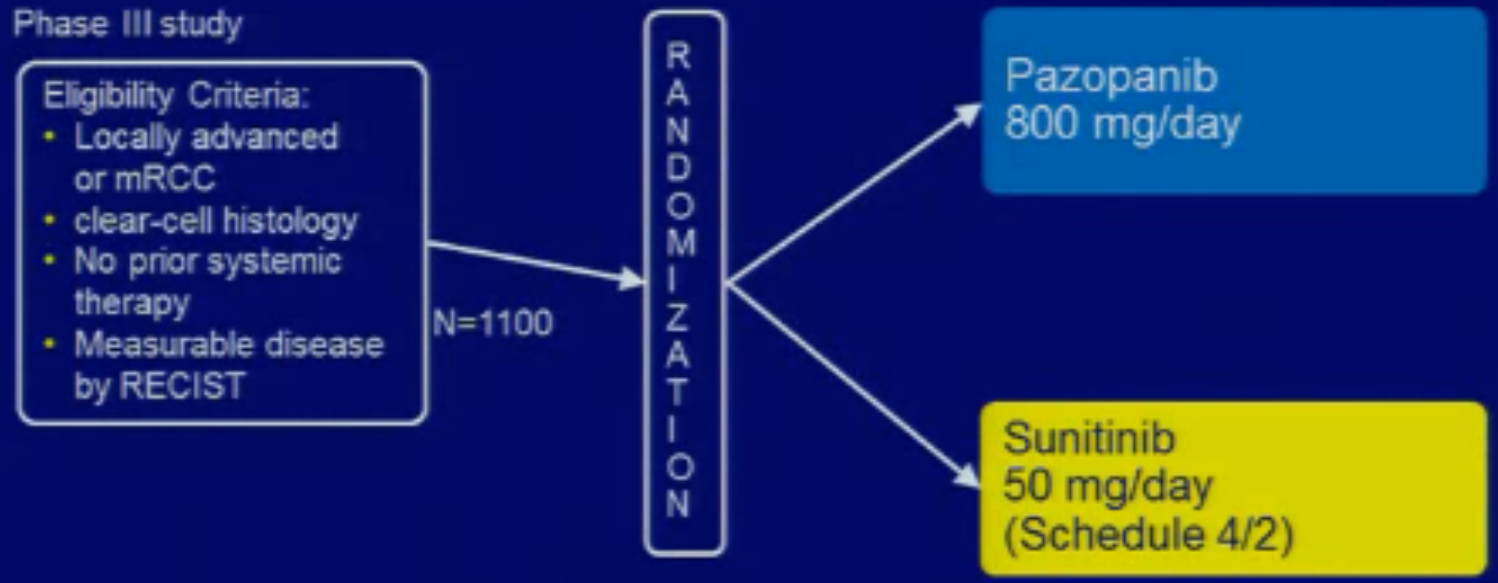
ORIGINAL ARTICLE

Pazopanib versus Sunitinib in Metastatic Renal-Cell Carcinoma

Robert J. Motzer, M.D., Thomas E. Hutson, D.O., David Cella, Ph.D., James Reeves, M.D., Robert Hawkins, M.B., B.S., Ph.D., Jun Guo, Ph.D., Paul Nathan, M.B., B.S., Ph.D., Michael Staehler, M.D., Paul de Souza, M.B., B.S., Ph.D., Jaime R. Merchan, M.D., Ekaterini Boleti, M.D., Ph.D., Kate Fife, M.D., Jie Jin, M.D., Robert Jones, Ph.D., Hirotsugu Uemura, M.D., Ph.D., Ugo De Giorgi, M.D., Ulrika Harmenberg, M.D., Ph.D., Jinwan Wang, M.D., Cora N. Sternberg, M.D., Keith Deen, M.S., Lauren McCann, Ph.D., Michelle D. Hackshaw, Ph.D., Rocco Crescenzo, D.O., Lini N. Pandite, M.D., and Toni K. Choueiri, M.D.

2013

Pazopanib vs Sunitinib for 1st-line Treatment of Clear-Cell mRCC (COMPARZ)

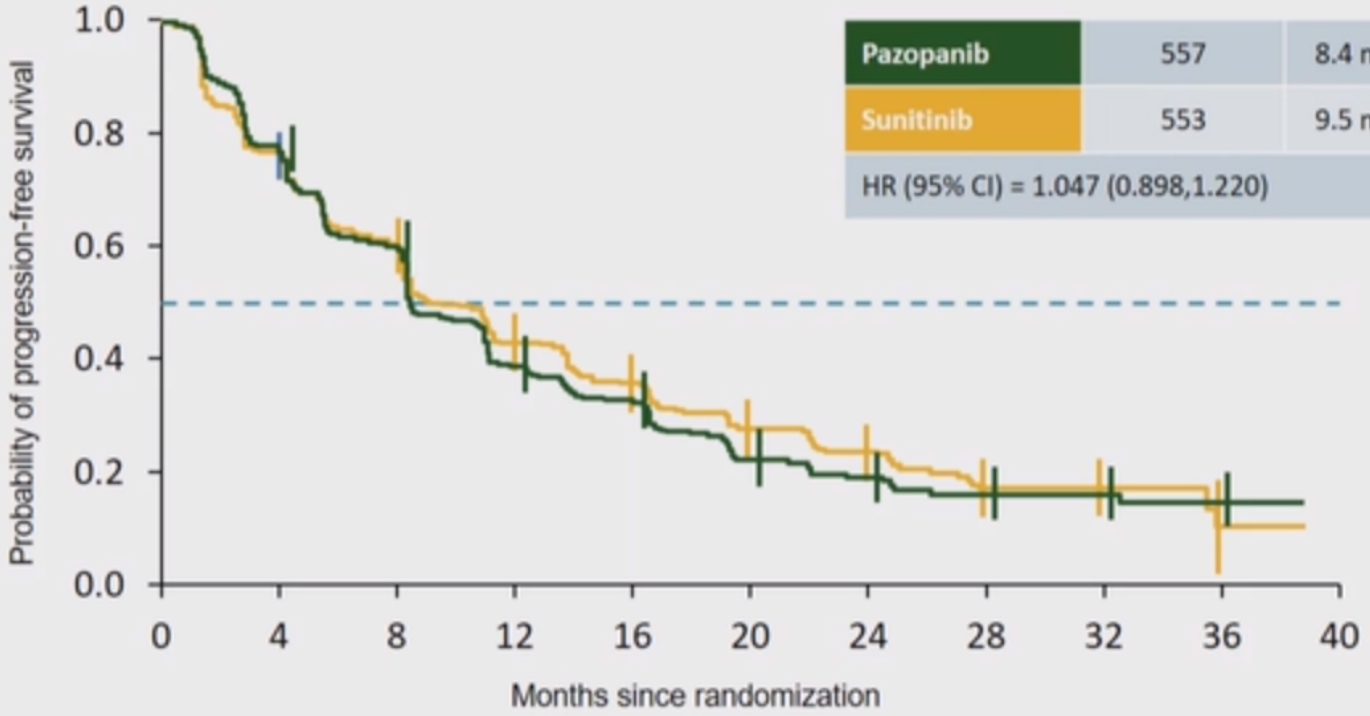


Primary Endpoint: PFS

Secondary Endpoints: OS, ORR, time to response, duration of response, safety, QoL

Available at: http://www.clinicaltrials.gov. NCT00720941.

Primary Endpoint: Progression-free-Survival (independent review)



Pazopanib	557	8.4 mo (8.3, 10.9)
Sunitinib	553	9.5 mo (8.3, 11.1)
HR (95% CI) = 1.047 (0.898,1.220)		

No. at Risk										
Pazopanib	557	361	245	136	105	61	46	19	13	1
Sunitinib	553	351	249	147	111	69	48	18	10	3

COMPARZ Trial Summary

	Pazopanib (months)	Sunitinib (months)
Treatment duration	8.0	7.6
PFS	8.4	9.5
OS	28.4	29.3

- Pazopanib found to be non-inferior to sunitinib

Comparative Data: COMPARZ

	Pazopanib (n=554), %		Sunitinib (n=548), %	
	All grades	Grade 3/4	All grades	Grade 3/4
Any event*	>99	59 / 15	>99	57 / 17
Diarrhoea	63	9 / 0	57	7 / <1
Fatigue	55	10 / <1	63	17 / <1
Thrombocytopaenia	41	3 / <1	78	6 / 0
Hypertension	46	15 / <1	41	15 / <1
Nausea	45	2 / 0	46	2 / 0
Decreased appetite	37	1 / 0	37	3 / 0
ALT increased	31	10 / 2	18	2 / <1
Hair colour changes	30	0 / 0	10	<1 / 0
Hand–foot syndrome	29	6 / 0	50	11 / <1
Taste alteration	26	<1 / 0	36	0 / 0

First line therapy (2017)

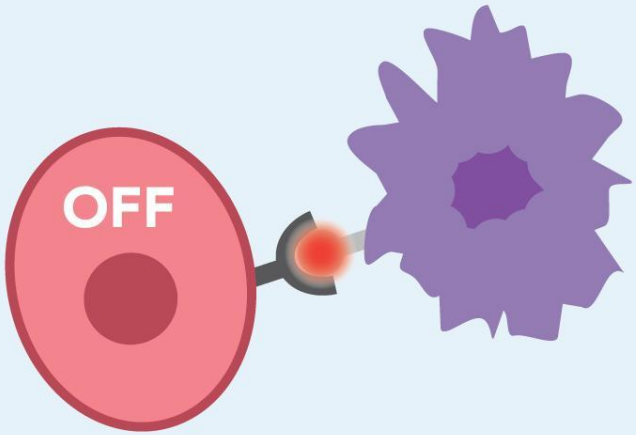
- sunitinib, pazopanib

Other options one might consider:

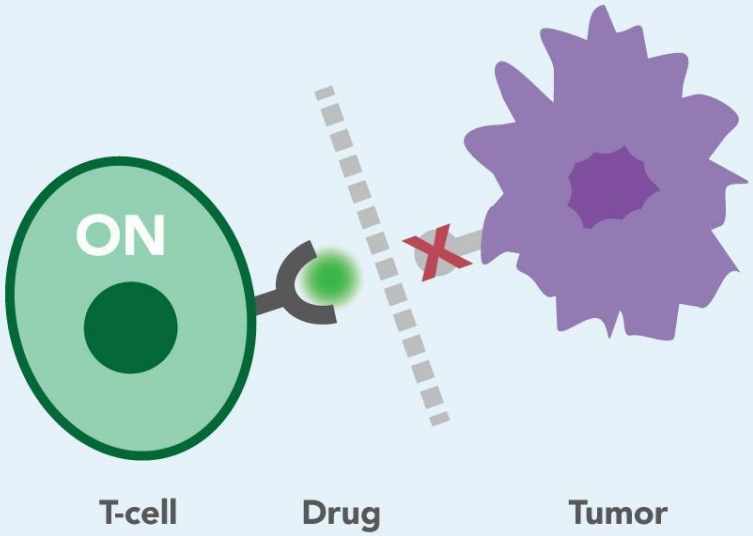
- Favourable
  - Observation/Active surveillance
  - High dose IL-2
- Poor
  - Temsorlimus
  - Best supportive care

How Does Immunotherapy Work?

Tumor cells bind to T-cells to deactivate them



Immunotherapy drugs can block tumor cells from deactivating T-cells



Columbia University Medical Center

Immunotherapy

- In recent years there has been a focus on immunotherapy to treat various cancers, such as malignant melanoma

- We already knew that RCC had something to do with the immune system based on previous experience

- Nivolumab studied in 2nd line setting in mRCC – survival benefit

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ORIGINAL ARTICLE FREE PREVIEW

Nivolumab plus Ipilimumab versus Sunitinib in Advanced Renal-Cell Carcinoma

Robert J. Motzer, M.D., Nizar M. Tannir, M.D., David F. McDermott, M.D., Osvaldo Arén Frontera, M.D., Bohuslav Melichar, M.D., Ph.D., Toni K. Choueiri, M.D., Elizabeth R. Plimack, M.D., Philippe Barthélémy, M.D., Ph.D., Camillo Porta, M.D., Saby George, M.D., Thomas Powles, M.D., Frede Donskov, M.D., Ph.D., et al., for the CheckMate 214 Investigators*

Abstract

BACKGROUND Nivolumab plus ipilimumab produced objective responses in patients with advanced renal-cell carcinoma in a pilot study. This phase 3 trial compared nivolumab plus ipilimumab with sunitinib for previously untreated clear-cell advanced renal-cell carcinoma.

METHODS We randomly assigned adults in a 1:1 ratio to receive either nivolumab (3 mg per kilogram of

April 5, 2018
N Engl J Med 2018; 378:1277-1290
DOI: 10.1056/NEJMoa1712126

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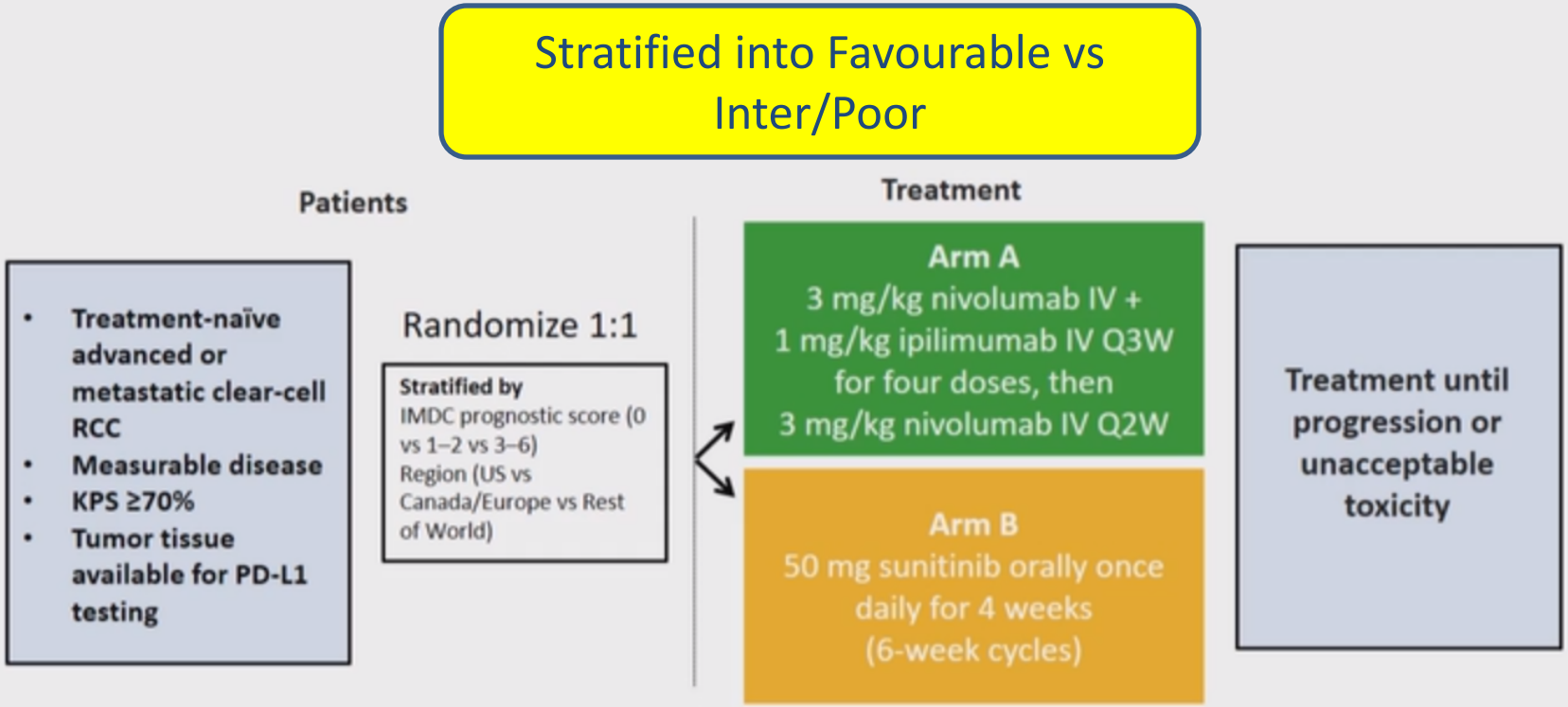
CheckMate 214: Study design

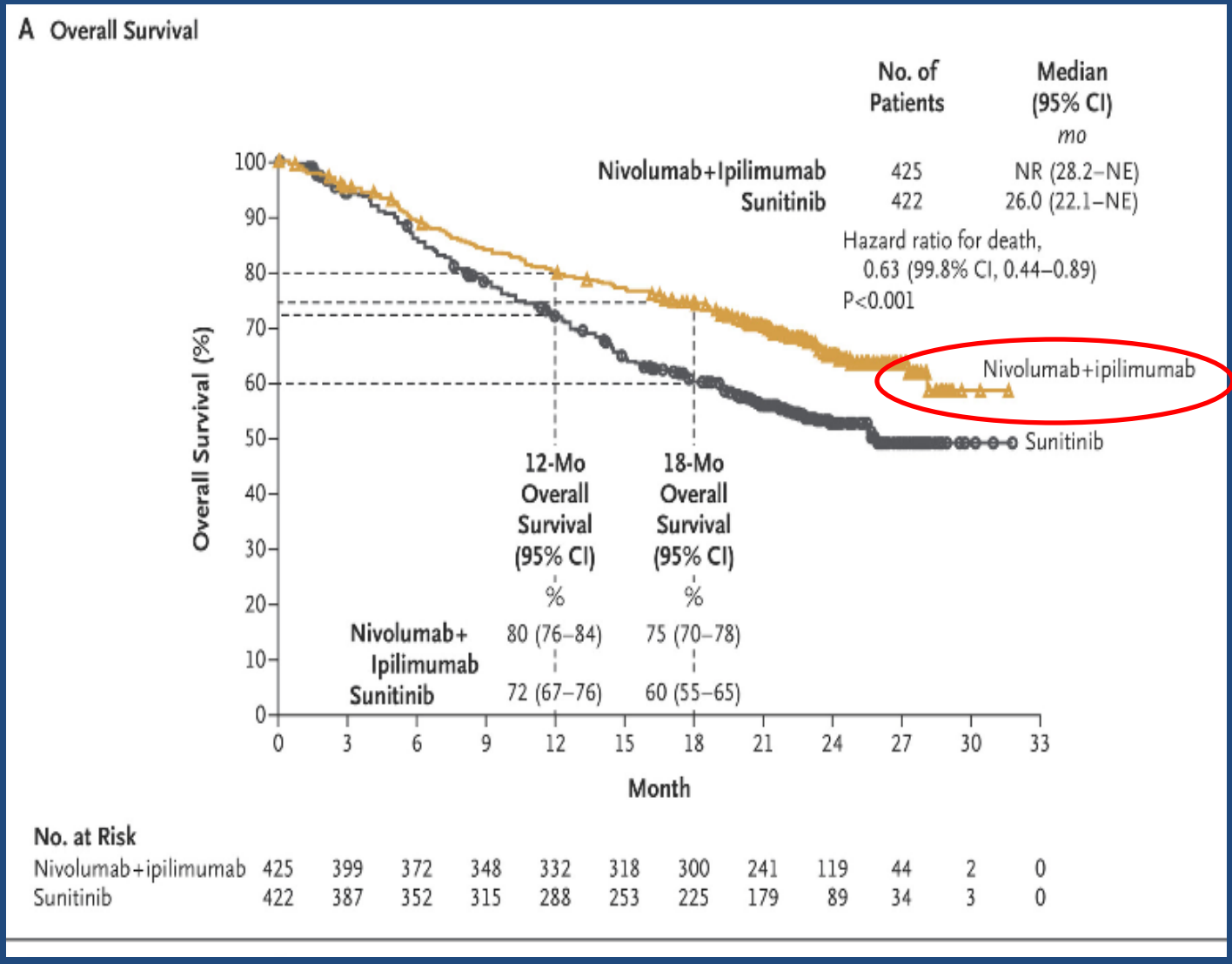


IMDC, International Metastatic RCC Database Consortium; KPS, Karnofsky performance status; Q2W, every 2 weeks; Q3W, every 3 weeks

Results – Checkmate 214

	Ipi/Nivo	Sunitinib
Poor/intermediate		
ORR	42%	27%
CR	9%	1%
PFS	11.6 months	8.4 months
OS	NR	26 months
Favourable		
ORR	29%	52%
PFS	15 months	25 months

Ipilimumab/nivolumab vs. sunitinib



Improvement in OS compared to sunitinib for **intermediate and poor risk patients**

Toxicity

- Ipi/nivo – fatigue, pruritus, diarrhea
- Sunitinib – diarrhea, fatigue and hand foot

- Approx 60% of pts on ipi/nivo required steroids due to toxicity
- Despite this – quality of life index favoured ipi/nivo

Systemic Treatment First-Line Options (2018)

BOTTOM LINE		
Patients Risk	**Therapy (Level 1 evidence)**	**Other options**
Good	**Sunitinib Pazopanib**	**Observation/Active Surveillance**
Intermediate/ Poor risk	**Ipilimumab/ Nivolumab**	**Sunitinib Pazopanib**

Second line treatment and beyond

- Data has existed for a while in support of multiple different second line and beyond agents post TKI
  - Everolimus
  - Axitinib
  - Nivolumab monotherapy
  - Cabozantinib

Comparison of current therapies beyond first line

Drug	Trial	Population	ORR	PFS Benefit	OS Benefit
Everolimus Motzer et al 2008 Lancet Oncol	RECORD 1 Everolimus vs Placebo	Prior VEGFR TKI	No	Yes	No*
Axitinib Motzer et al 2013 Lancet Oncol	AXIS Axitinib vs Sorafenib	2nd line post cytokines or TKI	Yes	Yes	No
Nivolumab Motzer et al 2015 New Engl J Med	CHECKMATE 025 Nivolumab vs Everolimus	Post 1 or 2 TKIs	Yes	No	Yes
Cabozantinib Choueiri et al 2015 New Engl J Med	METEOR Cabozantinib vs Everolimus	At least 1 prior TKI (can have prior Nivo)	Yes	Yes	Yes

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Systemic Treatment Second Line and beyond (2018)

BOTTOM LINE		
Prior treatment	**Proposed Therapy**	
Sutininib **Pazopanib**	**Axitinib** **Nivolumab** **Cabozatinib** everolimus	**Level 1 data**
Ipilimumab/Nivolumab	**Sutininib** **Pazopanib** **Axitinib** **Cabozatinib**	**Not so robust data** **No Health Canada approval**

Case scenario

- 70 yo woman - R radical nephrectomy Feb 2018 for *T3b clear cell, fuhrmans grade 3/4*
- **Now** - multiple bilateral pulmonary nodules
- N hemoglobin, platelets, calcium; ⬆ neuts
- KPS 100
- Intermediate prognosis
- PMHx: DM, HTN

Question #3

- What treatment would you recommend?
- **A** – observation
- **B** – sunitinib
- **C** – pazopanib
- **D** – ipilimumab/nivolumab
- **E** – everolimus

Question #3

- What treatment would you recommend?
- **A** – observation
- **B** – sunitinib
- **C** – pazopanib
- **D** – ipilimumab/nivolumab
- **E** – everolimus

D

Case scenario

- 80 yo man - L radical nephrectomy Dec 2010 for clear cell RCC
- 2016 – metastatic disease to pancreas
- Treated with sunitinib for 2 years, with radiological stability
- Side effects: diarrhea and mucositits
- Dose adjusted to 2 weeks on, 1 week off
- Restaging CTs show multiple new lung metastases

Question #4

- What treatment would you recommend?
- **A** – axitinib
- **B** – cabozantinib
- **C** – nivolumab
- **D** – clinical trial
- **E** – all of the above are reasonable options

Question #4

- What treatment would you recommend?
- **A** – axitinib
- **B** – cabozantinib
- **C** – nivolumab
- **D** – clinical trial
- **E** – all of the above are reasonable options

E

Not too distant Future

- Predictive markers:
  - PDL1 for IPI/NIVO in first line

- Drug combinations
  - VEGF-R + immunotherapy
    - Atezoluzumab + bevacuzimab
  - VEGF-R + mTOR
    - Everolimus + lenvatinib

Toxicity

- Focus on side effects TKIs used in mRCC
- Immunotherapy toxicity deferred

Why is it important?

- Incurable cancer – Quality of life
- Want to reach maximum tolerated dose to achieve best effect/best outcomes
- Limited treatment options
- Also knowledge of side effects may influence treatment selection

Who manages toxicity?

- Multidisciplinary team
- Pharmacy teach (call back)
- Clinic nurses are the front line for toxicity management
- More frequent visits initially
- Patient (and caregiver) education
  - Cope better with symptoms
  - Less likely to minimize symptoms
  - Use of diaries may lead to earlier ID and Mx

How?

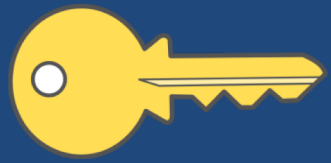
Principles of managing side effects

2 pronged approach

Prevention & Early Intervention

Management & dose/schedule adjustment

Patient education is key



Fatigue

Fatigue

- ***R/O alternative causes such as anemia, hypothyroidism, depression**
- ***Regular light exercise**
- ***Prioritize activities**
- Encouraged to pursue hobbies and interests to distract from fatigue
- Maintain normal sleeping habits
- Healthy diet
- Pharmacologic interventions: methylphenidate, prednisone

Hypertension

- Mechanism may be associated with ⬇ nitric oxide leads to ⬇ endothelial permeability and increase in vasoconstriction
- Ideal BP is <140/90
- Establish baseline BP – ideally normalize before starting TKI
- Ask patient to monitor BP and keep a log that they bring in to clinic

Hypertension

- Consider starting antihypertensive agent if persistent or symptomatic >/20 mmHg (diastolic) or >150/100
- Avoid non-dihydropyridine calcium channel blockers (ex verapamil, diltiazem)
- If BP still high on 2 agents – consider cardiology referral
- Often do not stop or hold drug for HTN (unless hypertensive crisis) as it can usually be managed with appropriate therapy
- Add lifestyle modifications such as diet and exercise

Other Cardiac Toxicity

- Decreased LVEF less common side effect
  - Consider baseline ECHO in pts with underlying cardiac history before starting TKI (sunitinib)
  - Consider ECHO if pt has shortness of breath, leg swelling etc where you are concerned of CHF

Hand-Foot Syndrome

Grade 3 hand-foot syndrome including acral erythema, hyperkeratotic areas, and desquamation. Considered grade 3 due to pain interfering with function.

Figure 2 Grade 2 hand-foot syndrome including erythema, desquamation, and skin discoloration. Considered grade 2 because mild discomfort did not interfere with function.

Hyperkeratotic hand-foot skin reaction

Autier, J. et al. Arch Dermatol 2008;144:886-892.

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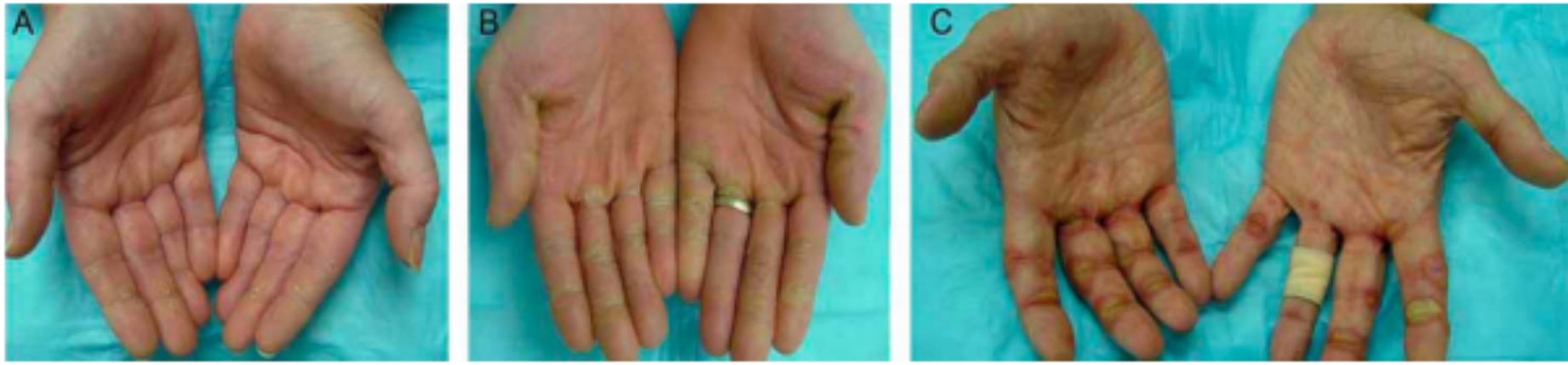
Hand Foot Syndrome

- Prevention
  - Prior to starting treatment - Manicure/pedicure to remove calluses and hyperkeratotic areas
  - Not wearing tight fitting shoes
  - Avoiding heat exposure
  - Emollients and creams containing urea can soften skin with hard calluses, reduce skin cracking
  - Sunscreen SPF >/30

Different Grades

Figure 2. Example of Grades 1 (A), 2 (B), and 3 (C) Hand-foot Skin Reaction (HFSR) with Multikinase Inhibitors. [7]



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Hand Foot Syndrome

- Usually occurs within 45 days of tx
- Grade 2
  - Topical steroid cream BID (clobetasol 0.05%)
  - Oral analgesia
  - Cotton gloves
  - If not better in 1 week – hold til grade 1
- Grade 3
  - As above, but stop right away
  - Wait till settle to grade 1 and dose adjust

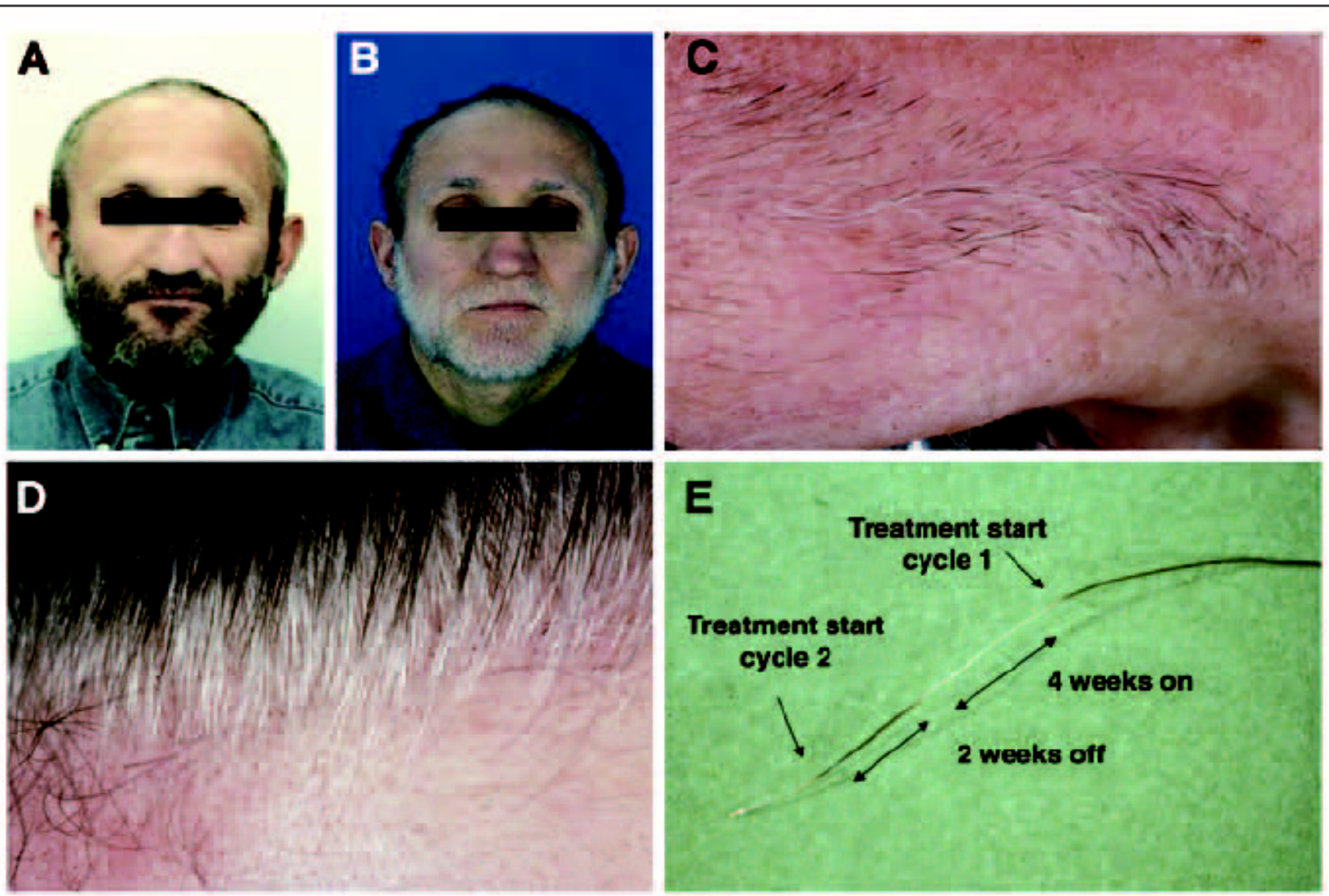
Other Skin Toxicity

- Yellowish pallor
- Depigmentation of hair
- Periorbital edema

- Poor wound healing

  -hold drug day of surgery and resume 14-28 days after if uneventful

A

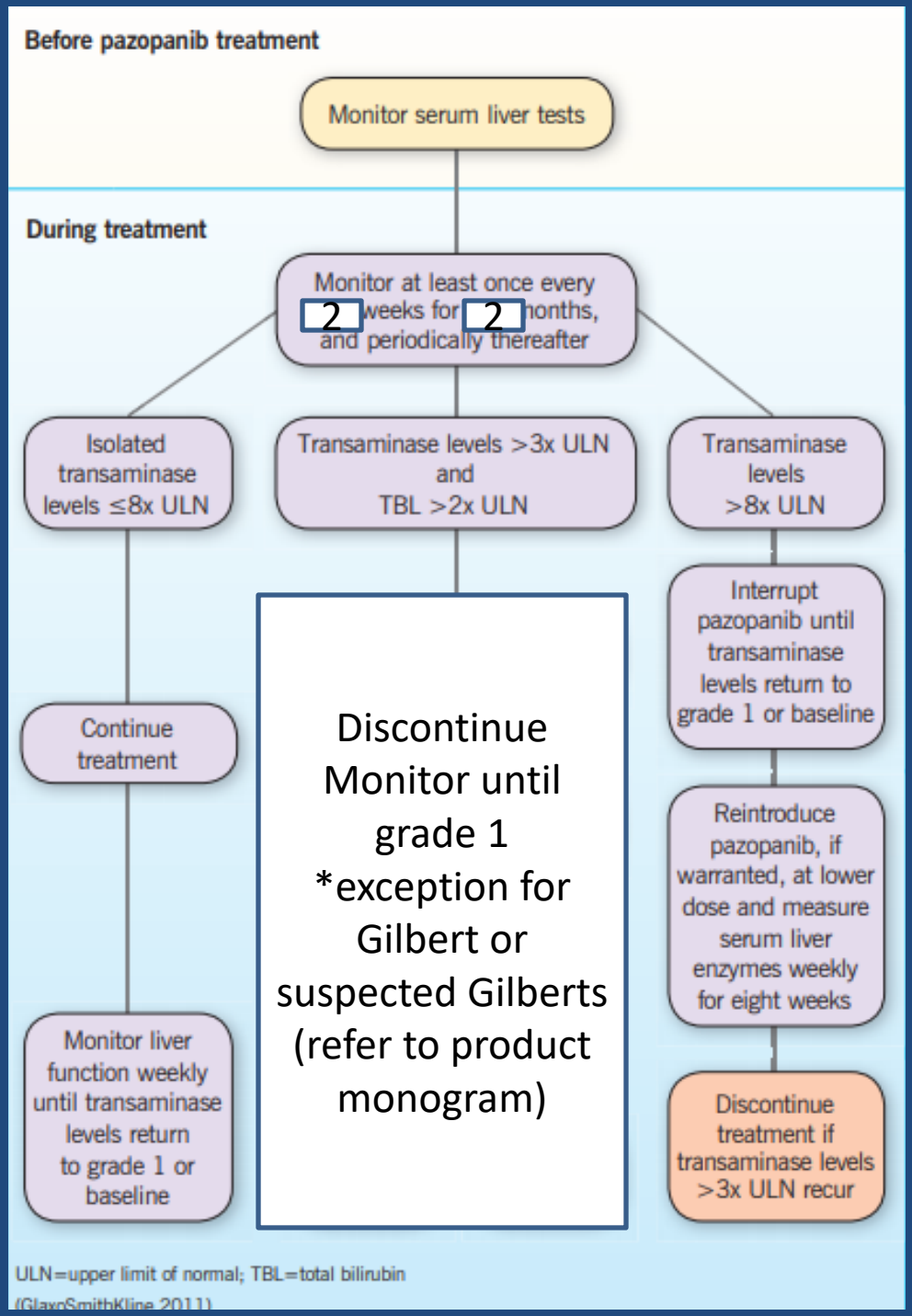

A
B
C
D
E
Treatment start
cycle 1
Treatment start
cycle 2
4 weeks on
2 weeks off

Hepatitis

- Pazopanib especially
- Rise in ALT/AST in first 18 weeks

- Close monitoring of liver enzymes
- Pazopanib q 2 weeks for first 2 months, then q 4 weeks

Pazopanib



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Diarrhea

- In advance – document baseline bowel pattern
- Provide script for loperamide (imodium)
- Adequate fluid intake
- Probiotics – live yoghurt
- Avoid spicy or greasy food

Diarrhea

- Grade 2 (incr 4-6 bm) – BRAT diet
  - start with loperamide (can add diphenoxylate)
  - Aggressive hydration

- Grade 3 (incr >7 bm)
  - Consider IV hydration
  - Octreotide 100 – 150 mcg SC TID
  - r/o other causes
  - Hold drug til grade 1 and dose interruption

Other GI Toxicity

Stomatitis

- Can be with or without ulceration
- Good oral hygiene – brushing after eating with soft toothbrush, alcohol free mouthwash
- Avoid spicy foods or citrus
- If painful, may require oral analgesia or topical lidocaine
- r/o thrush

Other GI toxicities

- Nausea and vomiting
- Provide script of antiemetic (prochlorperazine, metoclopramide – 2nd line ondansetron)
- Small frequent meals
- Aggressive rehydration
- Avoid nausea triggers

Hypothyroidism

- Can be preceded by thyroiditis
- Risk increased with longer duration
- Mechanism not clearly understood

- Check TSH at baseline then q 4-12 weeks
- Treat with thyroid replacement for symptomatic pts and/or TSH >/10
- Usually do not need to dose adjust or discontinue TKI

Hematologic

- Anemia – r/o other causes
- Neutropenia – hold if neuts <1
- Thrombocytopenia – hold if <50-75
- Risk of bleeding

Before starting TKI…

- Baseline BP (and bowel habits) – optimize BP if high
- Hx of cardiac disease – baseline ECHO for sunitinib
- Script for loperamide
- Script for anti-nauseant such as prochlorperazine
- Encourage to apply moisturizing cream to hands and feet bid, wear comfortable shoes
- Precautions re spicy foods, soft toothbrush

Take away message

Before starting TKI…

- Educate pt (and family) re toxicity and low threshold to start supportive meds
- Call with any toxicity – reassurance
- Pt to record BP daily and symptom diary chart – bring with them to f/u appointments
- Return to clinic in 2 weeks for assessment with bloodwork (CBC, lytes, Cr, lytes, LFTs (esp Pazopanib), TSH)

Take away message

How to dose adjust

- **Sunitinib** (sutent) – 50 mg po daily;4 wks ON, 2 wks OFF
  - Maintain dose but shorten treatment length
  - Decrease dose

- Rest of TKIs are continuous:
- **Pazopanib** (votrient) – 800 mg daily
- **Axitinib** (inlyta) – 5 mg po bid (can dose escalate)
- **Cabozantinib** (cabametyx) – 60 mg po daily
  - Decrease dose or treatment breaks

How to dose adjust

- If pt has toxicity…
  - Have you/pt maximized supportive measures?
  - If so…need to change something

- Ask when does toxicity occur when the pt starts taking? Early or late?
  - Early – decrease dose
  - Later – consider altering schedule for sunitinib or short treatment break

Case scenario

- 60 yo woman, met RCC
- Started on sunitinib 50 mg daily – 4 weeks on, 2 weeks off
- Assessed at 2 weeks – mild fatigue, BP 140/80
- No diarrhea or skin toxicity, bw ok
- Week 3 – loose BMs, 3/day, starts loperamide, calls in – further teaching from nurses
- Week 4 – 7 watery bowel movements – calls in – not hypotensive, good fluid intake – instructed to stop sunitinib (around day 24)
- She returns to see you prior to start of cycle #2 – bowel movements are back to baseline

Question #5

- **A** – stop sunitinib and switch to another therapy as she is clearly not tolerating
- **B** – dose reduce sunitinib to 37.5 mg po daily 4 weeks on, 2 weeks off
- **C** – change scheduling to sunitinib 50 mg po daily – 2 weeks on, 1 week off
- **D** – you want to keep her on full doses, so give some more education and arrange for home IV hydration

C

- Doing well until 2 week mark
- Still maintaining dose intensity
- I would be concerned that she would run into problems if you maintain full doses
- Dose reducing right away may result in decreased efficacy
- Too early to bail on sunitinib

Case Scenario

- 87 yo man met RCC to lung and adrenal
- ECOG 2
- PMHx: BPH, incr cholesterol, bilateral hernia repair, ?MI – cath was ok
- BW all normal – including liver enzymes
- Started on pazopanib – 600 mg po daily (75% dose)
  - March 31st
- Returns to clinic at 2 weeks – hypertensive – amlodipine 2.5 mg po daily
- Repeat liver enzymes q 2 weeks, RTC in 4 weeks

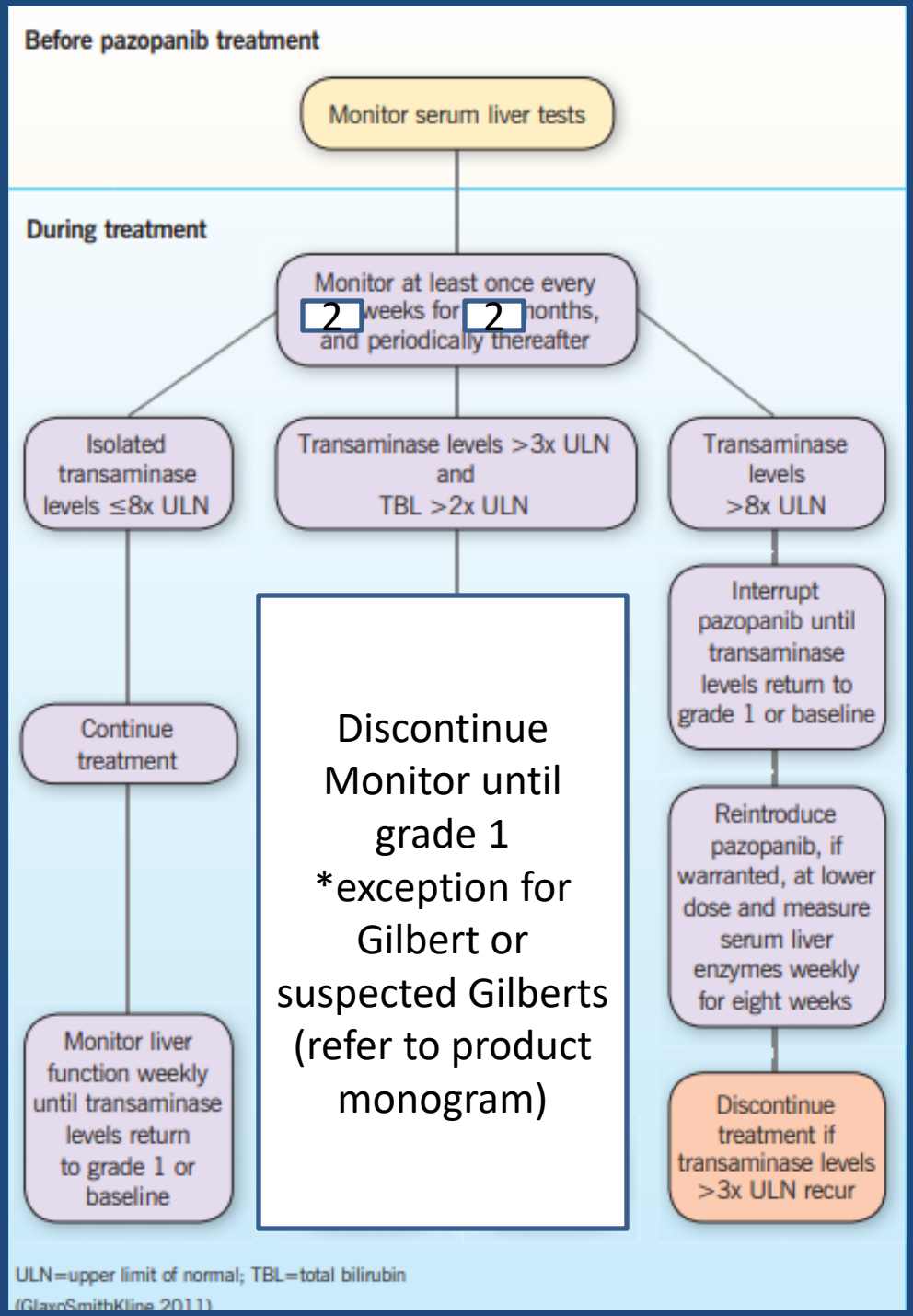
Normal bilirubin

	AST	ALT
April 10	N	N
April 26	127 <40	129 <50
May 8	117	213

Question #6

- **A** – stop pazopanib and discuss switching to sunitinib as he is clearly having liver toxicity
- **B** – hold the pazopanib and wait until the liver enzymes drop to normal and re-challenge at same dose
- **C** – hold the pazopanib and wait til the liver enzymes drop to normal and reduce dose
- **D** – continue with current doses and monitor liver enzymes closely

Pazopanib



D

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Normal bilirubin

	AST	ALT
April 10	N	N
April 26	127 <40	129 <50
May 8	117	213
May 22	73	112
May 28	63	94
June 13	54	76

Case scenario

- 66 yo man, met RCC
- Multiple lines of tx
- axitinib 5 mg po daily
- could not tolerate dose reduction
- felt relatively well, radiological response
- after being on drug for several months
- discomfort on walking

ARCHIVES OF DERMATOLOGY

Autier, J. et al. Arch Dermatol 2008;144:886-892.

Hold drug and return to clinic in 2 weeks
Skin toxicity resolves

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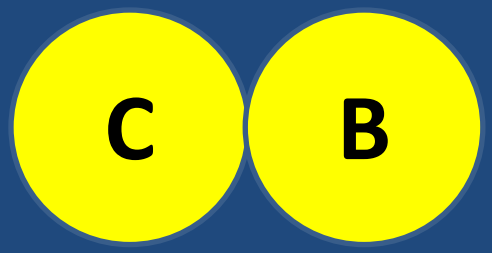
Question #7

- **A** – discontinue axitinib and discuss possibility of switching to different systemic therapy
- **B** – decrease dose of axitinib to 3 mg po daily
- **C** – continue with current doses but educate the patient to hold the drug when he begins to experience skin discomfort



- Motivated patients can take ownership for toxicity management

In Summary…

- Metastatic renal cell cancer has a variable course
- mRCC prognosis can be subdivided into favourable, intermediate and poor prognostic groups based on 2 clinic and 4 laboratory factors
- These prognostic groups can help guide drug therapy choices

In Summary…

- Drug therapy has been shown to improve overall survival

First line therapy

- Favourable prognostic group
  - Observation
  - Sunitinib
  - Pazopanib
- Intermediate/Poor prognostic group
  - Immunotherpy with ipilimumab and nivolumab has overall survival compared to sunitinib
  - Sunitinib and pazopanib considered for patient who are not candidates for immunotherapy

In Summary…

Second line and beyond therapy

- If treated with immunotherapy
  - Sunitinib
  - Pazopanib
  - Axitinib
  - Cabozantinib
- If treated with TKI
  - Nivolumab
  - Axitinib
  - Cabozantinib
  - Less so with everolimus

In Summary…

- Toxicity of TKIs
  - Multidisciplinary team
  - Education of patient
  - Prevention and early intervention is key
  - Ideally want to keep patient on maximum tolerated dose

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News

CANADIAN UROLOGICAL ASSOCIATION GUIDELINE

The Canadian Urological Association published the guideline for followup of patients after treatment of non-metastatic renal cell carcinoma. View guideline on this link.

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