# Sequencing Therapies in Renal Cell Carcinoma

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Medical Oncology & Experimental Therapeutics

City of Hope Comprehensive Cancer Center

2018 JADPRO Live
THE ANNUAL APSHO MEETING

# Learning Objectives

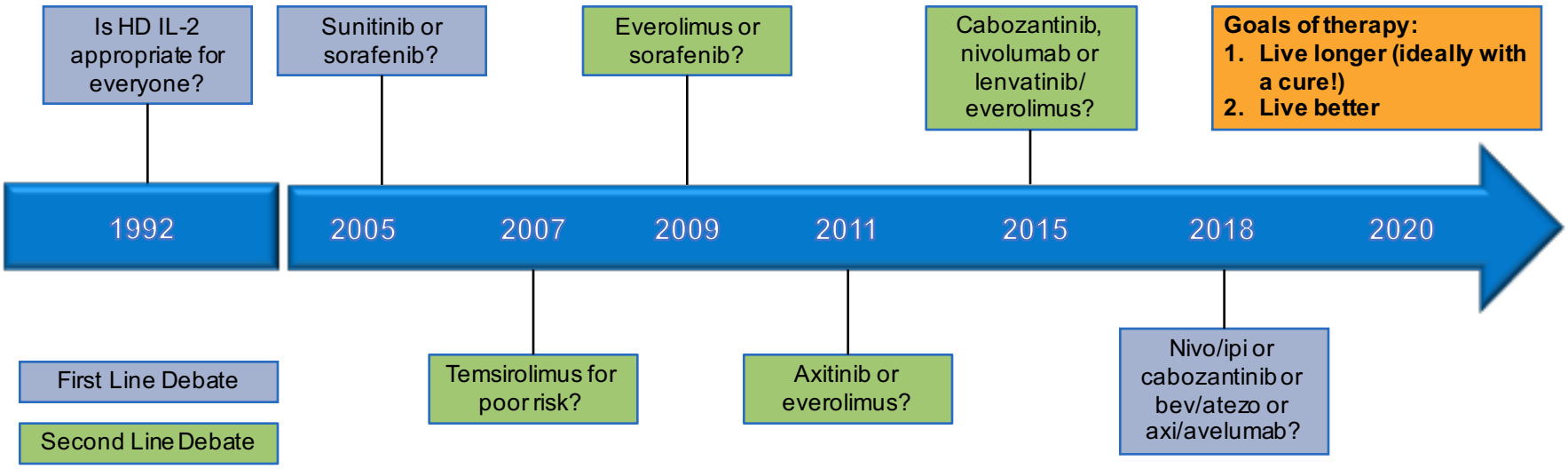
1. Plan how to best utilize immunotherapy in renal cell carcinoma (RCC)
2. Explain the use of tyrosine kinase inhibitors in the adjuvant setting in patients with advanced RCC

# Financial Disclosures

Relevant financial relationships in the past 12 months by presenter or spouse/partner:

- Sumanta Pal, MD
  - Consultant: Genentech, Aveo, Eisai, Roche, Pfizer, Novartis, Exelixis, Ipsen, BMS, Astellas
  - The speaker will directly disclose the use of products which are not labeled (e.g., off-label use) or if the product is still investigational.
- Kathy Burns, NP
  - Speakers Bureau: Pfizer, Astellas, Amgen

# Debates in RCC Therapy



# A Banner Year for Immunotherapy in RCC

**ESMO 2017: Nivolumab/Ipilimumab vs Sunitinib Primary Analysis**

**GUCS 2018: Bevacizumab/Atezolizumab vs Sunitinib Primary Analysis**

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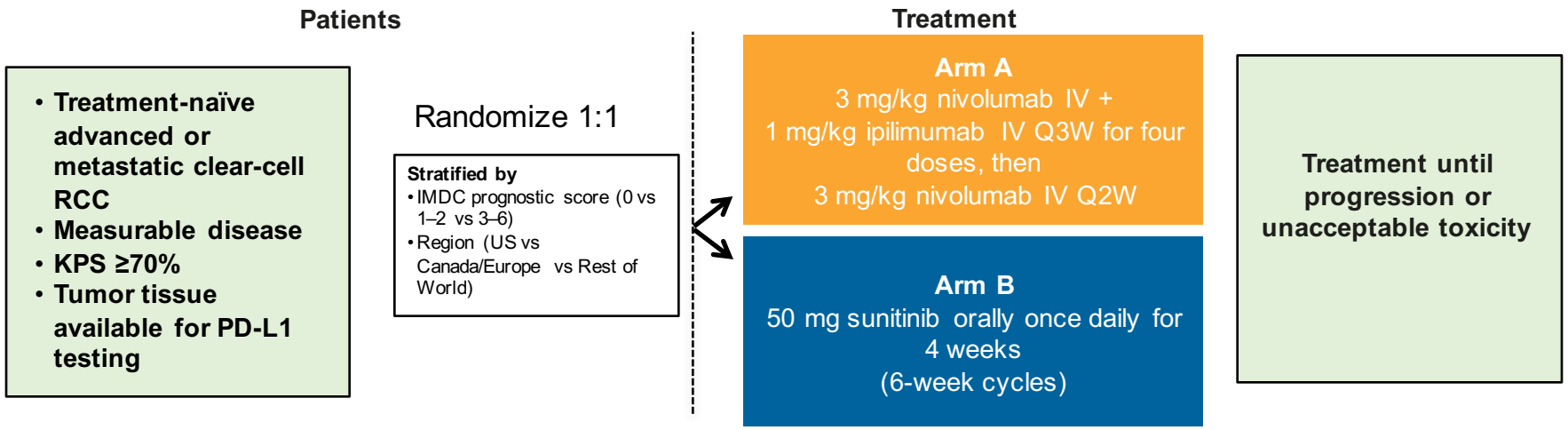
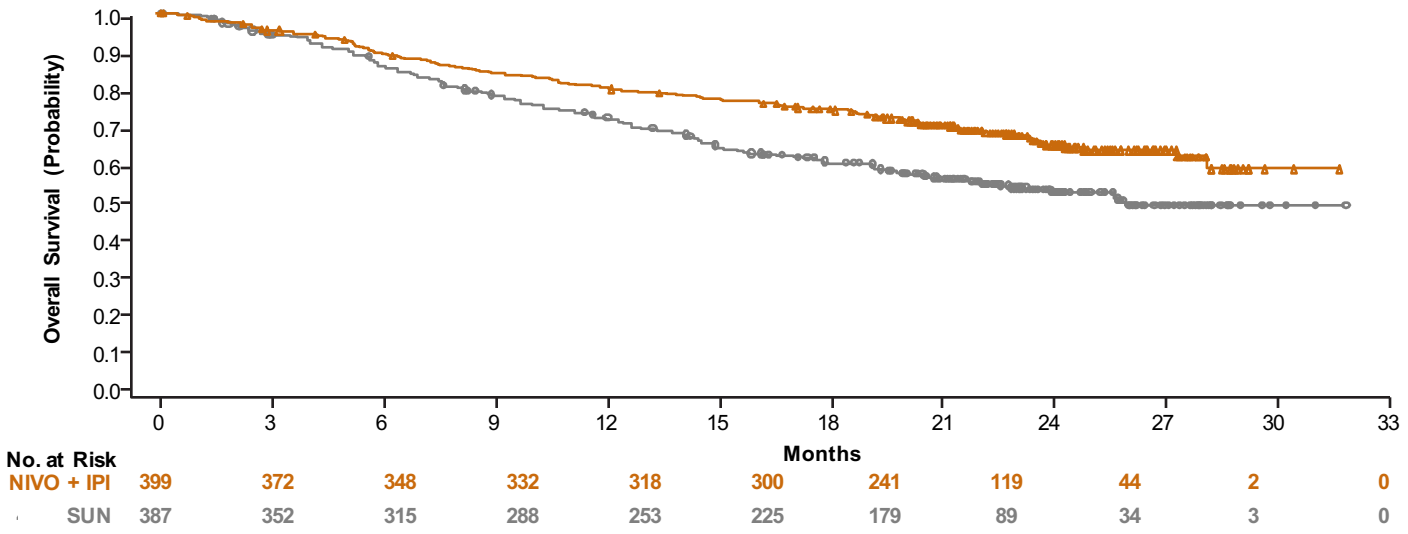
# CheckMate 214: Study Design




Escudier et al. ESMO 2017.

**Co-primary endpoint**

# CheckMate 214: Study Design




| Median OS, months (95% CI) | |
|---|---|
| NIVO + IPI | NR (28.2–NE) |
| SUN | 26.0 (22.1–NE) |

**Hazard ratio (99.8% CI), 0.63 (0.44–0.89)**
***P* < 0.0001**

| Outcome | N = 847 | |
|---|---|---|
| | NIVO + IPI N = 425 | SUN N = 422 |
| **Confirmed ORR,[a] % (95% CI)** | **42 (37–47)** | **27 (22–31)** |
| | *P* < 0.0001 | |
| **Confirmed BOR,[a] %** | | |
| **Complete response** | **9[b]** | **1[b]** |
| Partial response | 32 | 25 |
| Stable disease | 31 | 45 |
| Progressive disease | 20 | 17 |
| Unable to determine/not reported | 8 | 12 |

[a]IRRC-assessed ORR and BOR by RECIST v1.1.

[b]P< 0.0001.

Escudier et al. ESMO 2017.

Exploratory endpoint

# ORR and PFS: IMDC Favorable Risk

| Outcome | N = 249[a] | |
|---|---|---|
| | NIVO + IPI<br>N = 125 | SUN<br>N = 124 |
| **Confirmed ORR,[b] % (95% CI)** | **29 (21–38)** | **52 (43–61)** |
| | *P* = 0.0002 | |
| **PFS,[c] median (95% CI), months** | 15.3 (9.7–20.3) | 25.1 (20.9–NE) |
| | **HR (99.1% CI) 2.18 (1.29–3.68)**<br>***P* < 0.0001** | |

[a]11% pf patients in both arms had tumor PD-L1 expression ≥1%. [b]IRRC-assessed by RECIST v1.1. [c]IRRC-assessed.

Escudier et al. ESMO 2017.

# Patient Disposition: All Treated Patients

| | NIVO + IPI N = 547 | SUN N = 535 |
|---|---|---|
| **Treatment discontinuation, %** | 77 | 82 |
| **Reasons for treatment discontinuation, %** | | |
| Disease progression | 42 | 55 |
| **Study drug toxicity** | **24** | **12** |
| Adverse event unrelated to study drug | 6 | 6 |
| Other | 4 | 9 |
| **Median duration of therapy (95% CI), months** | 7.9 (6.5–8.4) | 7.8 (6.4–8.5) |
| **Median doses received (range), no.** | | |
| Nivolumab | 14 (1–63) | NA |
| Ipilimumab | 4 (1–4) | NA |
| **Median daily dose (range), mg/day** | NA | 31 (14–50) |

- In the NIVO + IPI arm, 79% of patients received all four doses of IPI
- Median follow-up was 25.2 months

Escudier et al. ESMO 2017.

Secondary endpoint

# Treatment-Related Adverse Events: All Treated Patients

| | NIVO + IPI N = 547 | | SUN N = 535 | |
|---|---|---|---|---|
| Event, % | Any grade | Grade 3–5 | Any grade | Grade 3–5[a] |
| **Treatment-related adverse events in ≥25% of patients** | **93** | **46** | **97** | **63** |
| Fatigue | **37** | **4** | **49** | **9** |
| Pruritus | **28** | **<1** | **9** | **0** |
| Diarrhea | **27** | **4** | **52** | **5** |
| Na | | | | |
| Hy | | | | |
| De | | | | |
| Dy | | | | |
| Stomatitis | **4** | **0** | **28** | **3** |
| Hypertension | **2** | **<1** | **40** | **16** |
| Mucosal inflammation | **2** | **0** | **28** | **3** |
| Palmar-plantar erythrodysesthesia syndrome | **1** | **0** | **43** | **9** |
| **Treatment-related AEs leading to discontinuation, %** | **22** | **15** | **12** | **7** |
| **Treatment-related deaths** | **n = 7[b]** | | **n = 4[c]** | |

**60% of patients treated with NIVO + IPI required systemic corticosteroids for an adverse event**

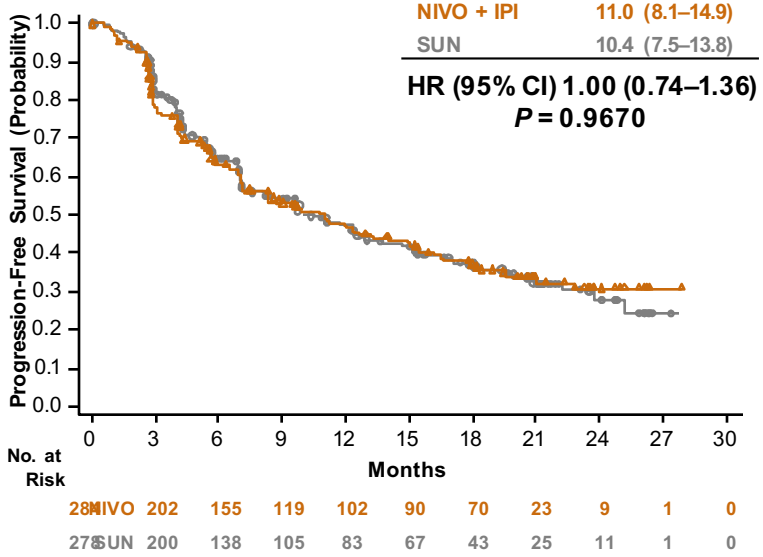
[a]Two patients had grade 5 cardiac arrest. [b]Pneumonitis, immune mediated bronchitis, lower GI hemorrhage, hemophagocytic syndrome, sudden death, liver toxicity, lung infection. [c]Cardiac arrest (n = 2), heart failure, multiple organ failure

Escudier et al. ESMO 2017.

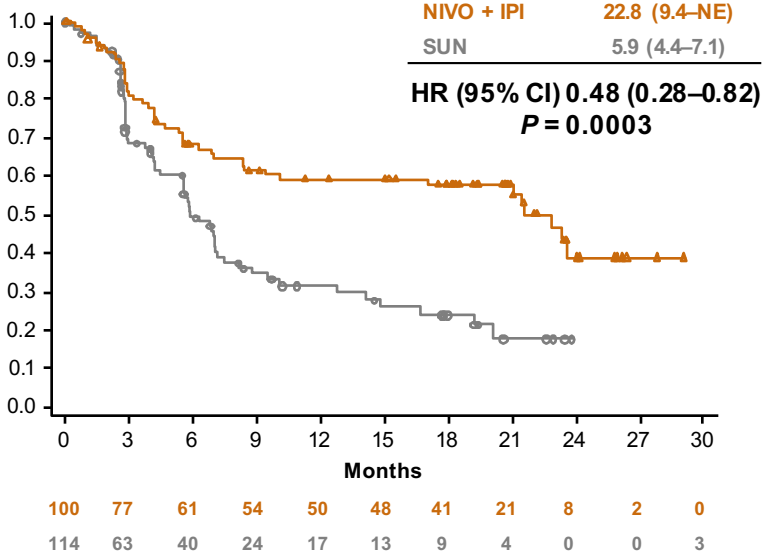
Exploratory endpoint

# PFS by PD-L1 Expression: IMDC Intermediate/Poor Risk

## PD-L1 <1% (n = 562)

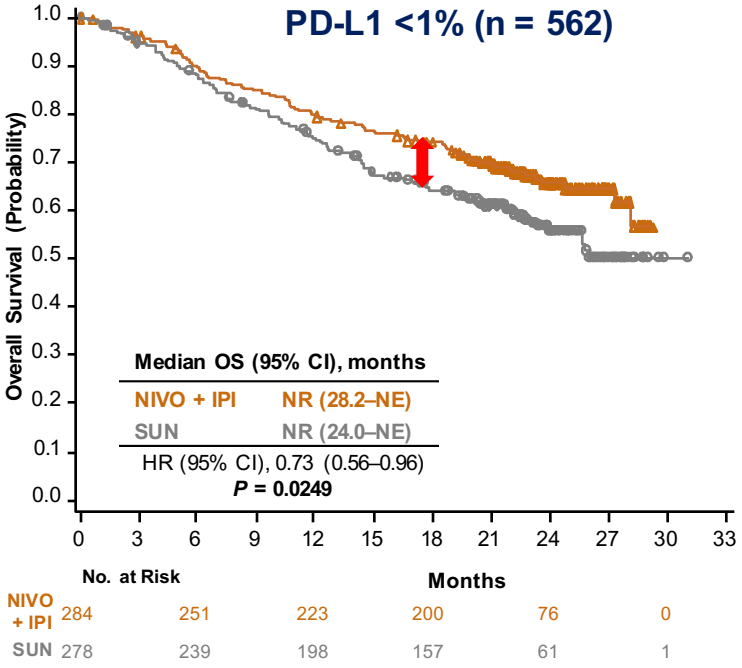


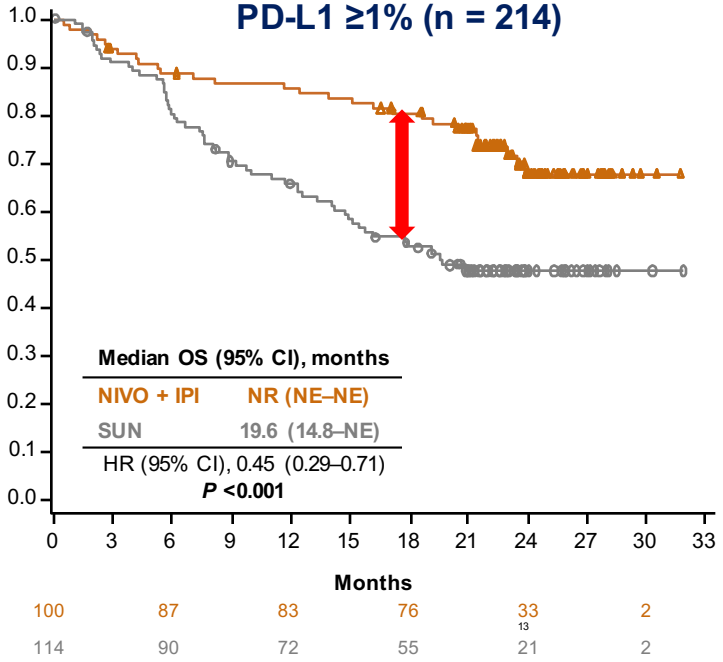

## PD-L1 ≥1% (n = 214)




Escudier et al. ESMO 2017.

# OS by Tumor PD-L1 Expression: IMDC Intermediate/Poor Risk

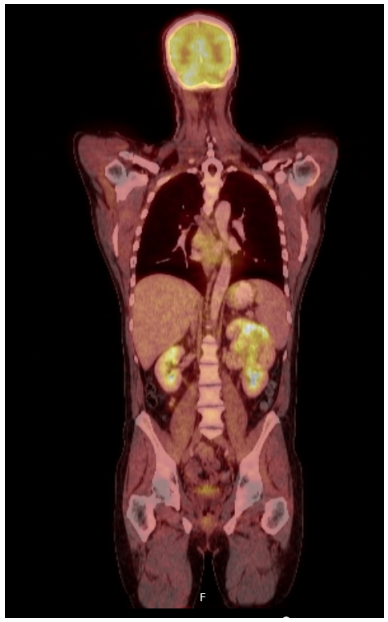



Motzer, et al. SITC 2017.

# Case Study 1

- 44-year-old male with no past medical history presents with headaches
- 1.6-cm cerebellar lesion and a 7.5-cm left renal mass
- Resection of CNS lesion followed by nephrectomy
- Progressive disease in the retroperitoneum
- Received IL-2, pazopanib, bevacizumab, and then enrolled in phase I clinical trial with nivo/ipi



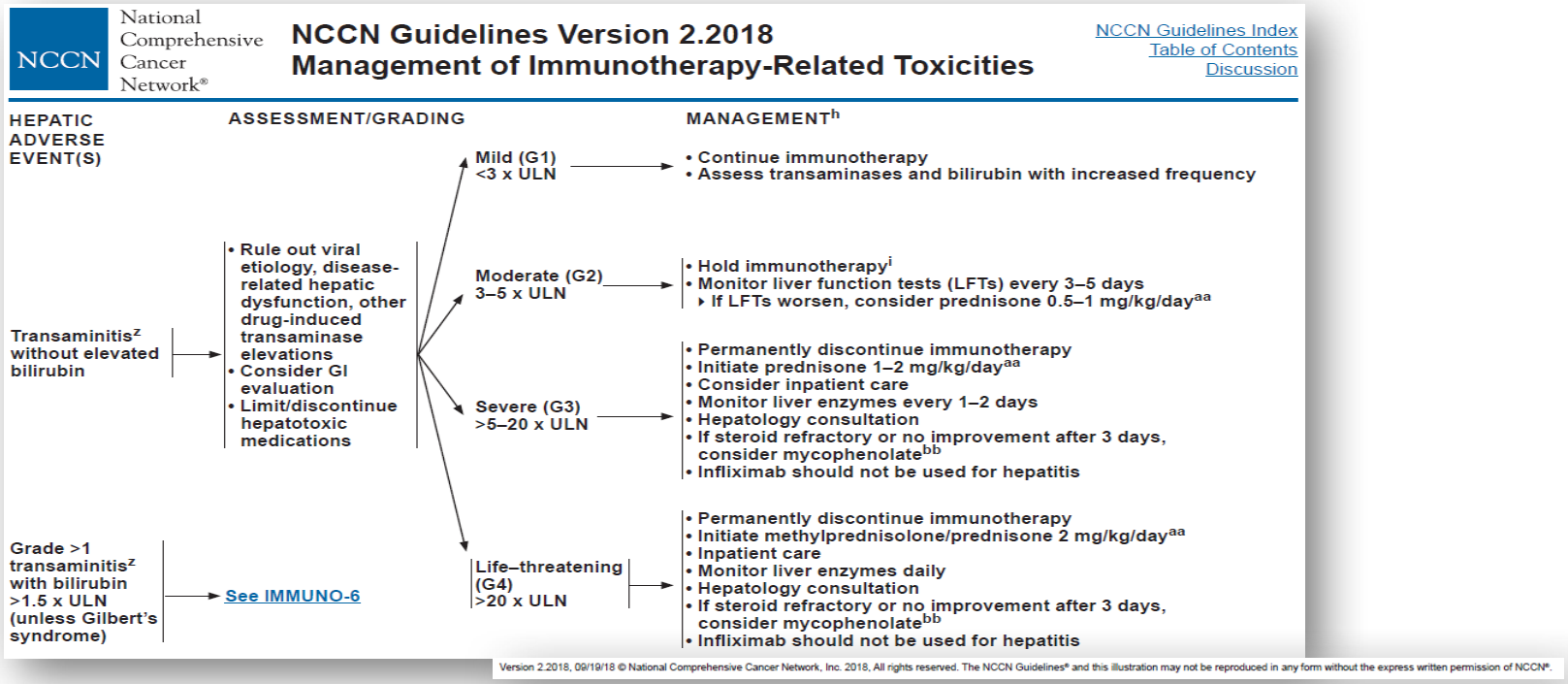
# Case Study 1

**Nivolumab/Ipilimumab begins:**

- Presents for C2, D1
- ALT 658 after one dose of nivo/Ipi (7-56 IU/L)
- No other symptoms

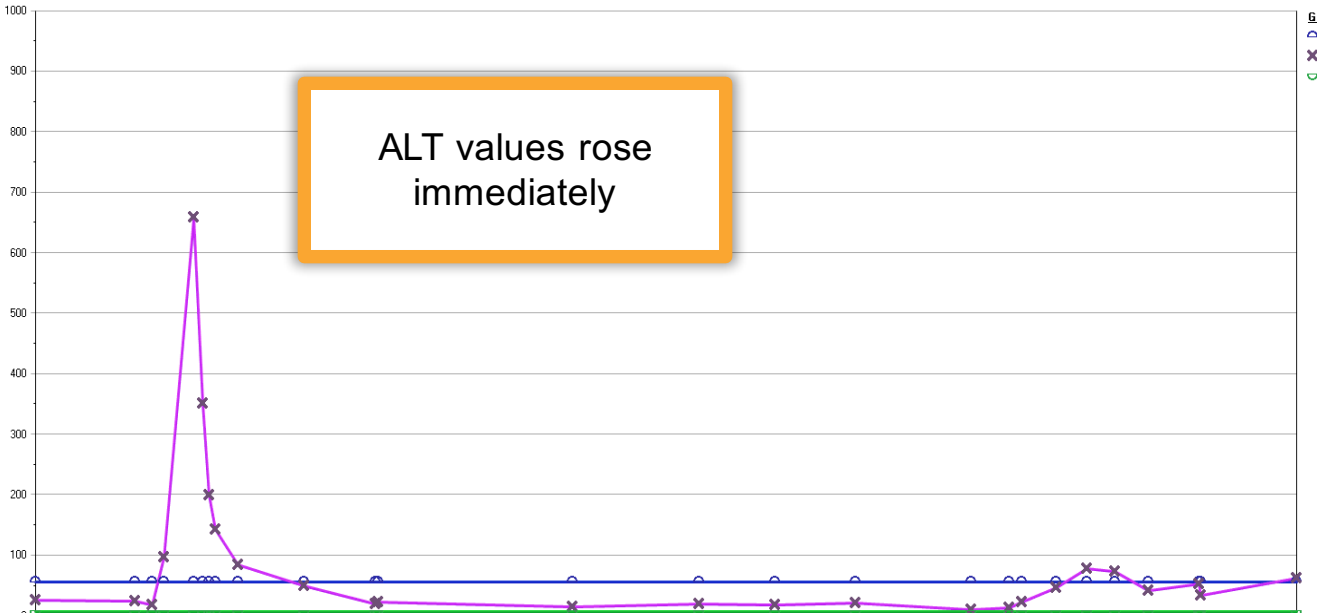
- Grade 3 transaminitis without elevation of bilirubin

# NCCN Immunotherapy Guidelines



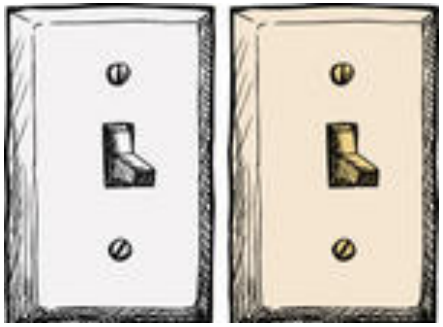
# Case Study 1

## Early toxicity

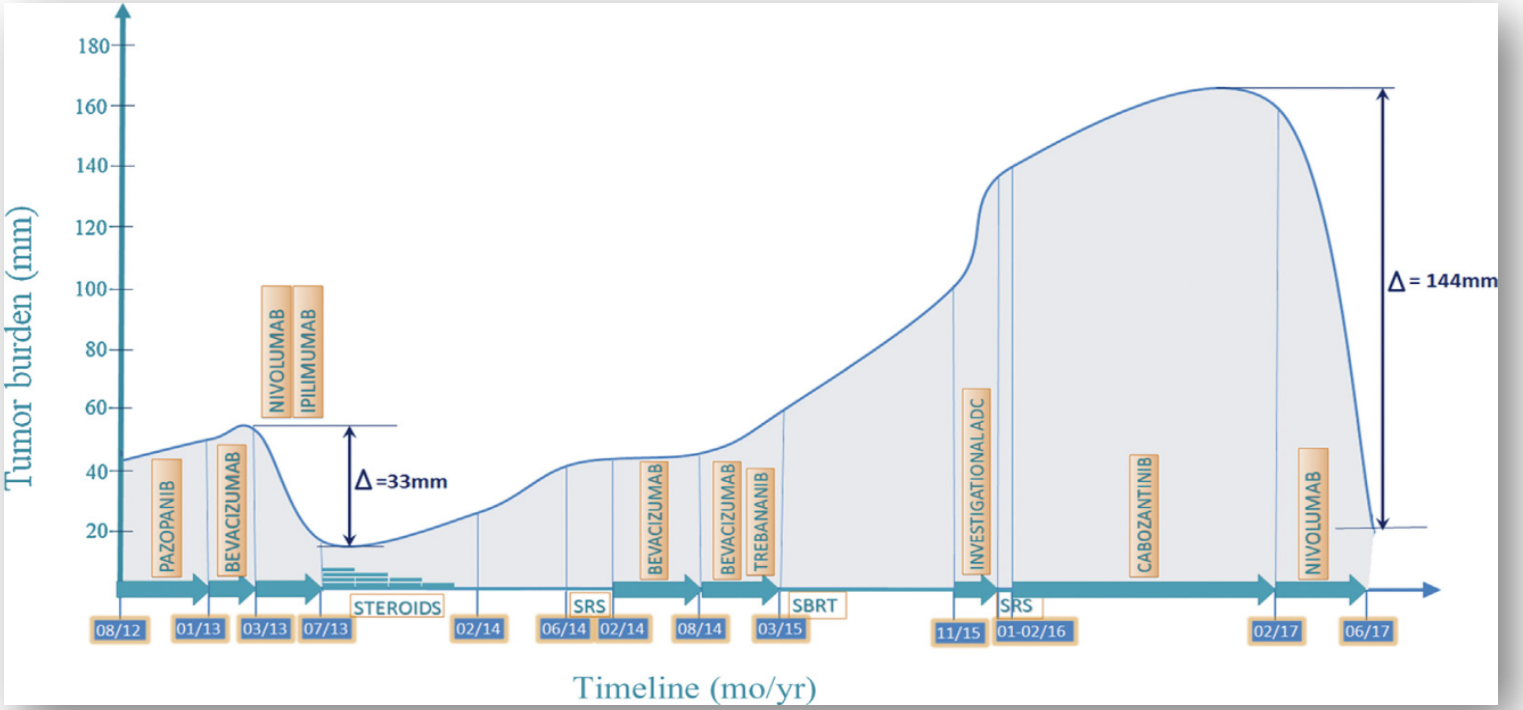


# Adverse Events FAQs

**Will taking steroids stop the treatment's response against the tumor?**



# Case Study 1: Subsequent Treatments

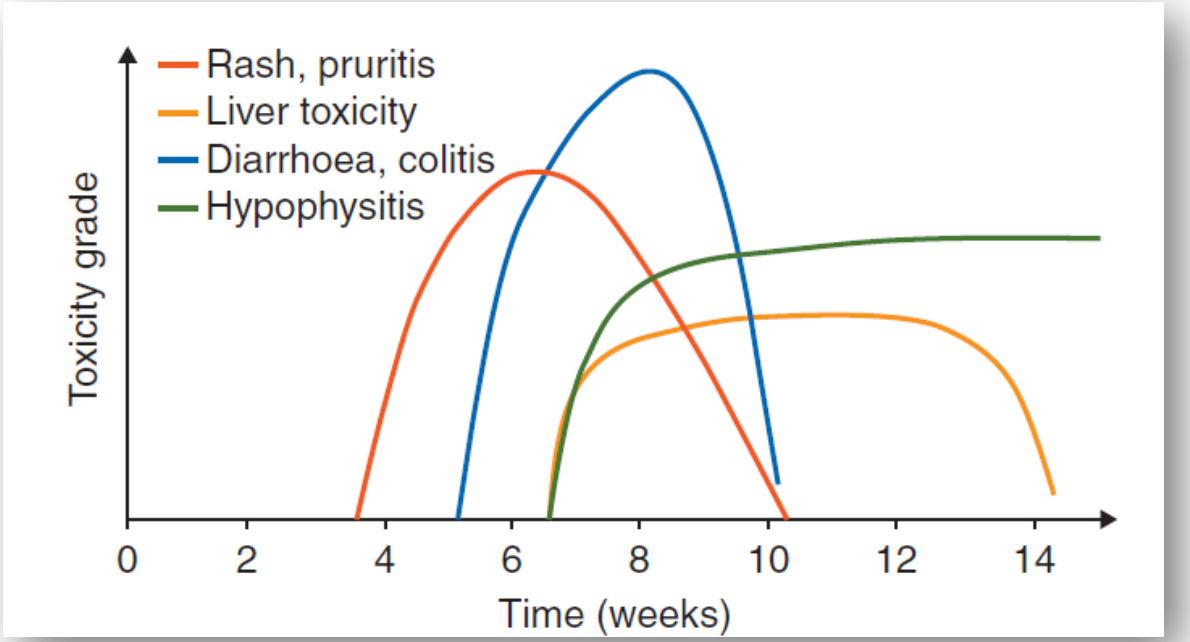



Dizman et al. Eur Urol 2017.

# Immunotherapy FAQs

- Endocrine, thyroid adverse events are the only class that may not need steroids. Generally only replacement is necessary
- Remember that if your steroid dose is > 20 mg/day for 4 weeks, pneumonia prophylaxis is advised
- If it is > 20 mg for >6-8 weeks fungal prophylaxis is recommended
- PPIs are advised for steroid induced gastritis

# Immunotherapy Side-Effect Timing



# A Banner Year for Immunotherapy in RCC

ESMO 2017: Nivolumab/Ipilimumab vs Sunitinib Primary Analysis

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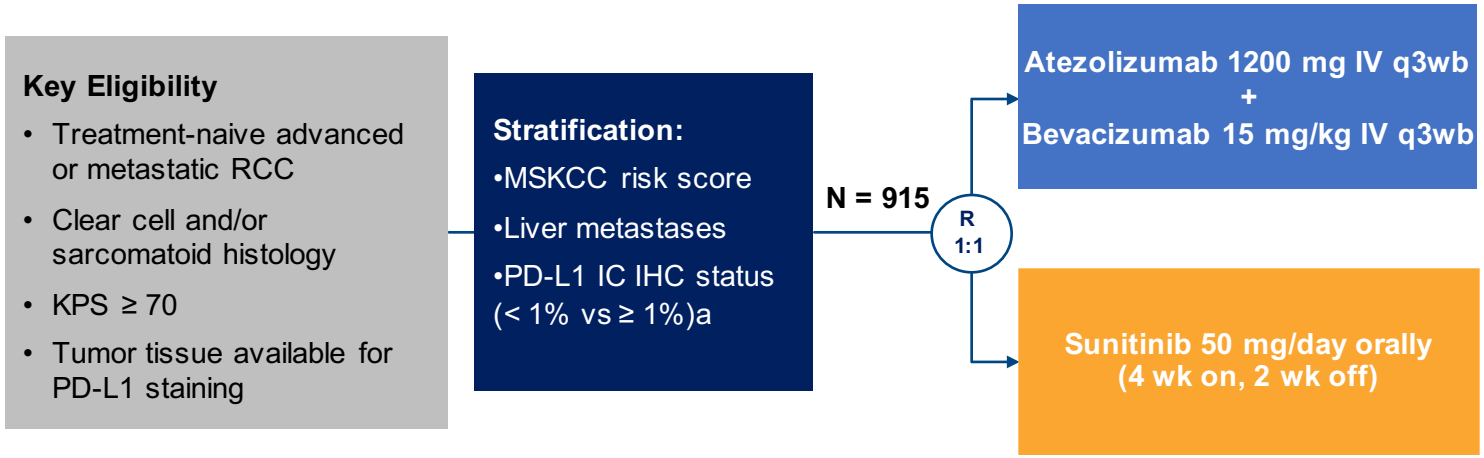
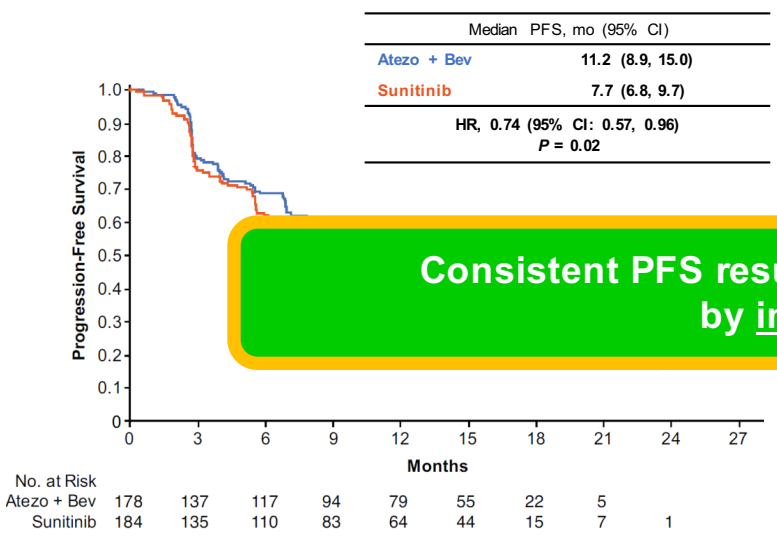
# Study Design

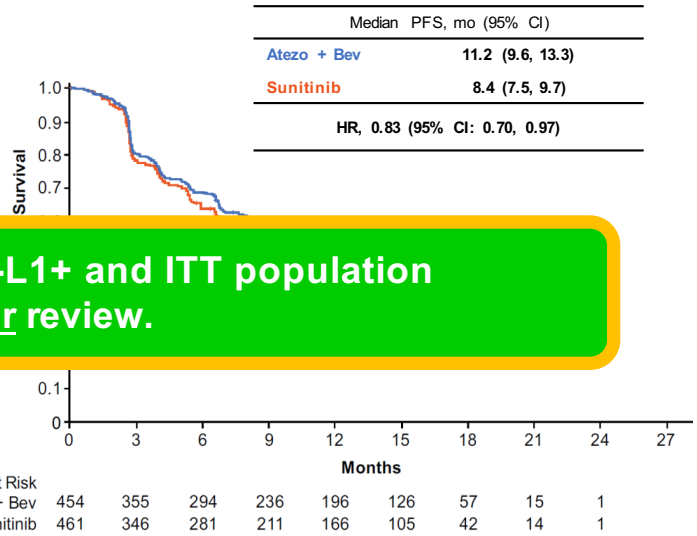



- ≥ 1% IC: 40% prevalence using SP142 IHC assay
- No dose reduction for atezolizumab or bevacizumab

Co-Primary Endpoint

# PFS: PD-L1+ and ITT




**Consistent PFS results in PD-L1+ and ITT population by investigator review.**

PFS assessed by investigators. Minimum follow-up, 12 mo. Median follow-up, 15 mo.

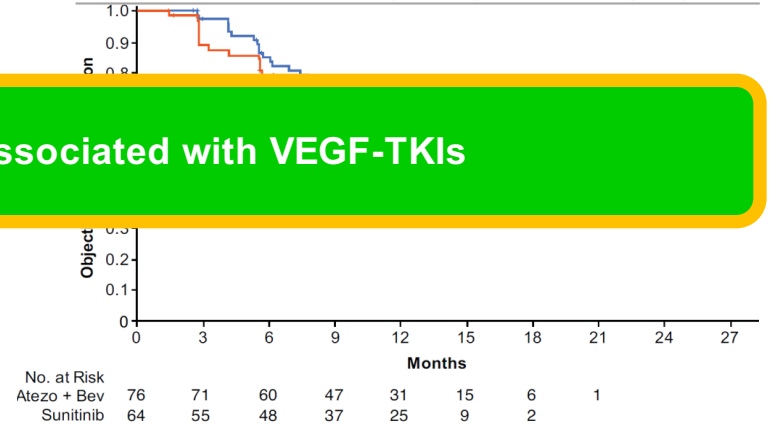
Secondary Endpoint

# Objective Response Rate

| | PD-L1+ | |
|---|---|---|
| | Atezo + Bev n = 178 | Sunitinib n = 184 |
| Confirmed ORR, % 95% CI | 43% (35, 50) | 35% (28, 42) |
| Progressive disease | 19% | 21% |
| Not evaluable[a] | 7% | 10% |

**Higher CR rates than associated with VEGF-TKIs**

| PD-L1+ | Median DOR, mo (95% CI) | Ongoing Responders, n (%) |
|---|---|---|
| Atezo + Bev | NR (12.4, NR) | 49 (65%) |
| Sunitinib | 12.9 (9.8, NR) | 34 (53%) |

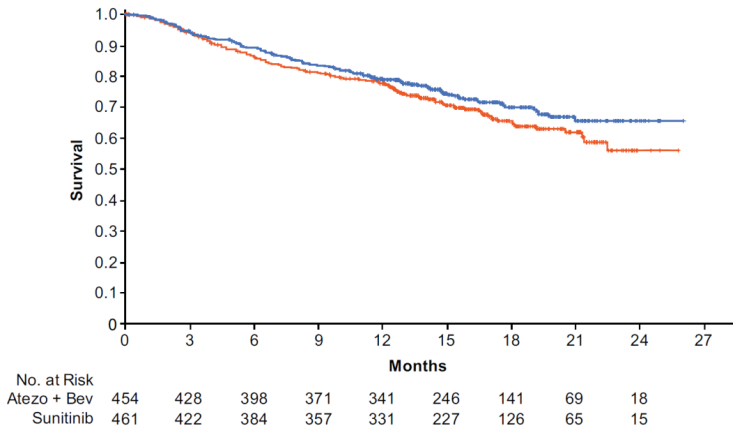



NR, not reached. [a] Including patients with no post-baseline tumor assessment. ORR assessed by investigators in patients with measurable disease at baseline. Minimum follow-up, 12 mo. Median follow-up, 15 mo.

Co-Primary Endpoint

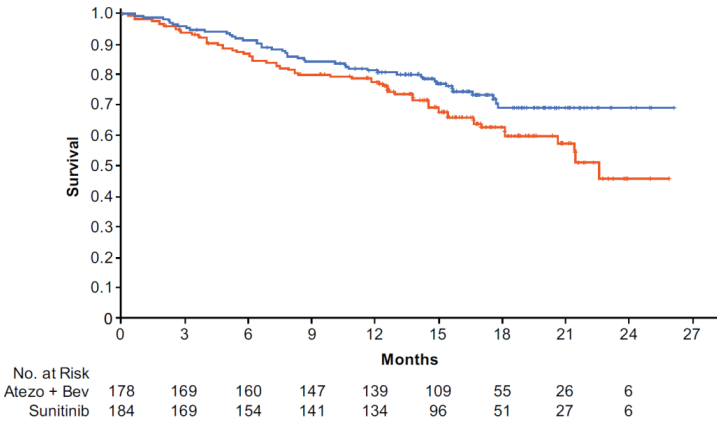
# Overall Survival in ITT and PD-L1+

| ITT Median OS, mo (95% CI) | |
|---|---|
| Atezo + Bev | Not reached |
| Sunitinib | Not reached |
| | HR, 0.81 (95% CI: 0.63, 1.03) P = 0.09 |




| No. at Risk | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Atezo + Bev | 454 | 428 | 398 | 371 | 341 | 246 | 141 | 69 | 18 |
| Sunitinib | 461 | 422 | 384 | 357 | 331 | 227 | 126 | 65 | 15 |

| PD-L1+ Median OS, mo (95% CI) | |
|---|---|
| Atezo + Bev | Not reached |
| Sunitinib | 23.3 (21.3, NR) |
| | HR, 0.68 (95% CI: 0.46, 1.00) |



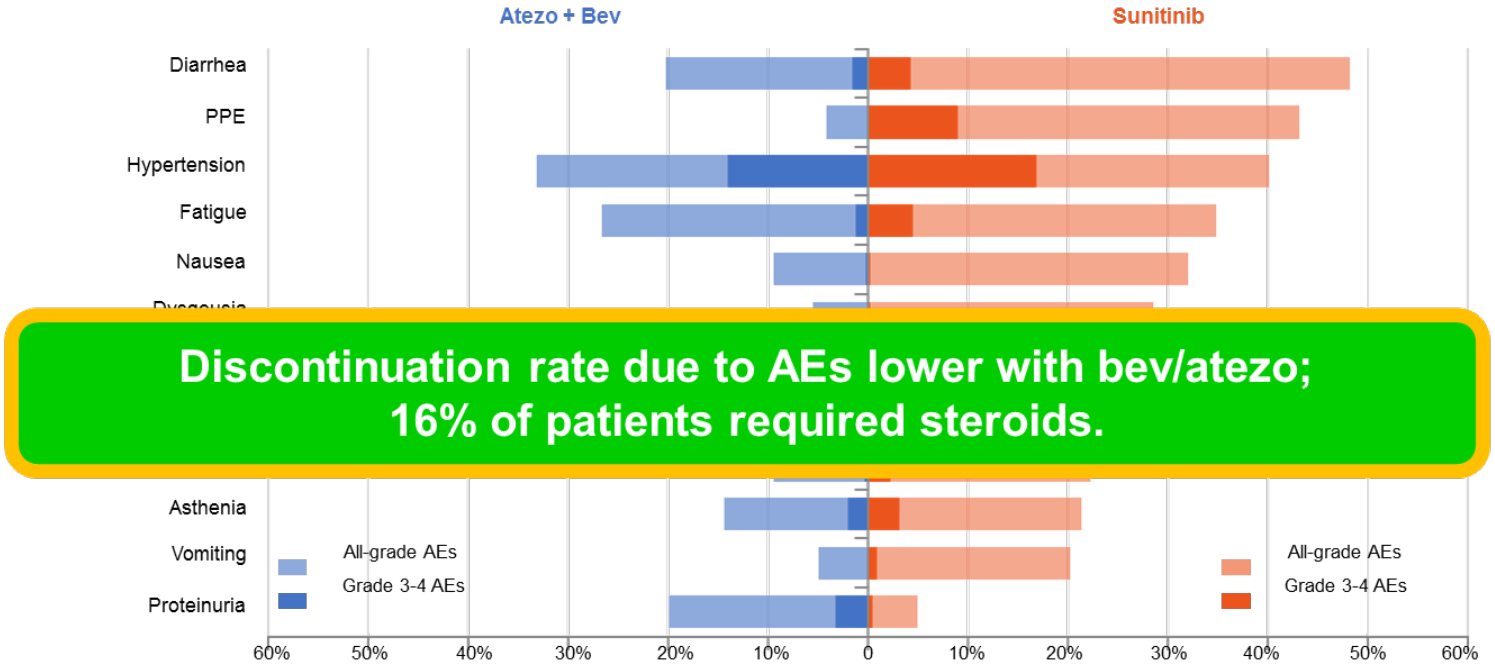

| No. at Risk | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Atezo + Bev | 178 | 169 | 160 | 147 | 139 | 109 | 55 | 26 | 6 |
| Sunitinib | 184 | 169 | 154 | 141 | 134 | 96 | 51 | 27 | 6 |

Minimum follow-up, 12 mo. Median of follow-up, 15 mo. Event/patient ratio: 27% for atezo + bev, 31% for sunitinib
The OS analysis did not pass the *P* value boundary of alpha = 0.0009 at the first interim analysis.

Motzer et al. ASCO GU 2018.

Secondary Endpoint

# Overall Survival in ITT and PD-L1+




**Discontinuation rate due to AEs lower with bev/atezo; 16% of patients required steroids.**

Motzer et al. ASCO GU 2018.

# Case Study 2: Bev/Atezo

- 91 years young female diagnosed in 2011 – radical nephrectomy
- Comorbidities of hypertension and osteoporosis
- She initiated a front-line study of bevacizumab with MPDL3280A (atezolizumab) on 11/25/14
- Fatigue and proteinuria – over the course of her treatment
- 3-year durable PR
- Able to maintain her QOL and her work as a museum docent

# CTCAE 5.0 Toxicity Grading for Proteinuria

| Adverse event | Grade 1 | Grade 2 | Grade 3 | Grade 4 | Grade 5 |
|---|---|---|---|---|---|
| Proteinuria | 1+ proteinuria on dipstick; urinary protein <1.0 g/24 hours | Adult: 2+ and 3+ proteinuria on dipstick; urinary protein 1.0 to 3.4 g/24 hours | Adult: Urinary protein ≥3.5 g/24 hours | | |
| | | Pediatric: Urine protein/creatinine (P/C) ratio 0.5 to 1.9 | Pediatric: Urine protein/creatinine (P/C) ratio >1.9 | | |

Renal injury and proteinuria (bevacizumab package insert):

- Monitor urine protein
- Discontinue for nephrotic syndrome
- Withhold until less than 2 g of protein in urine

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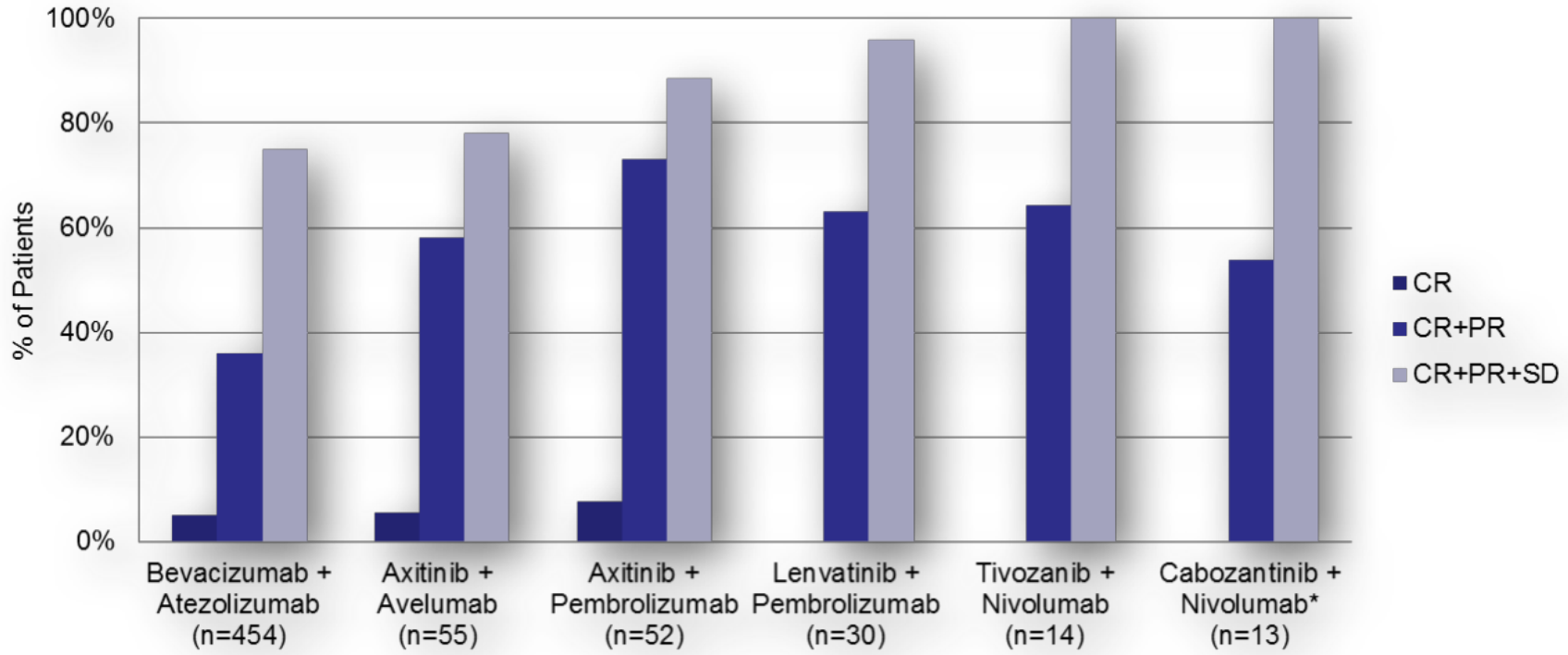
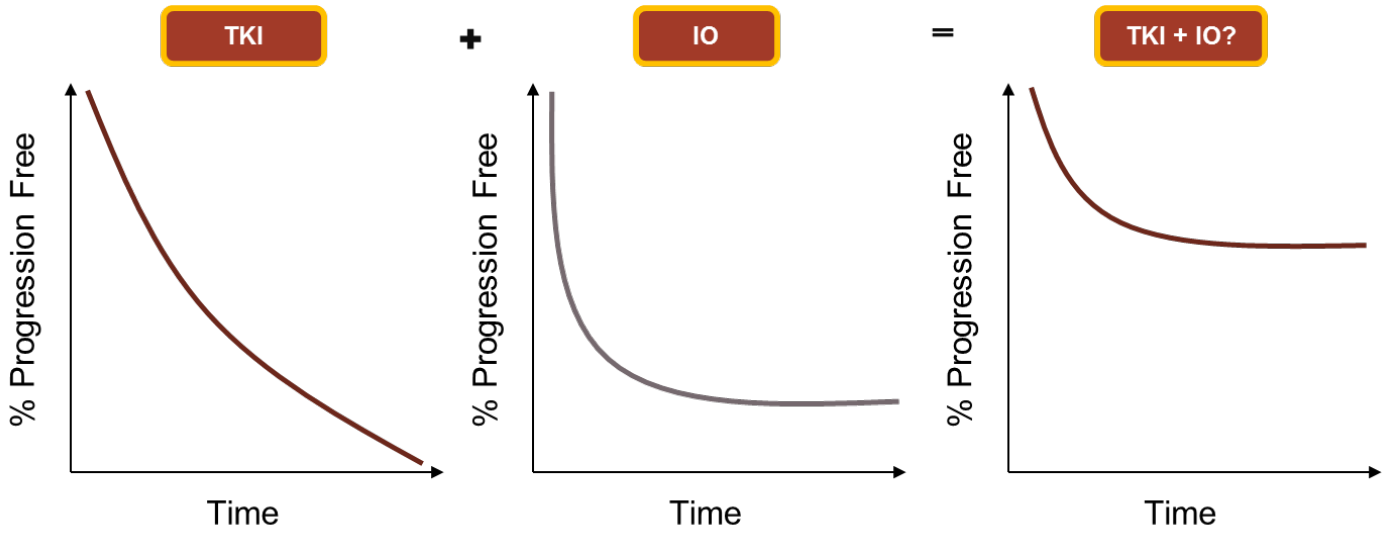
**ESMO 2018: Axitinib/Avelumab vs Sunitinib Primary Analysis**

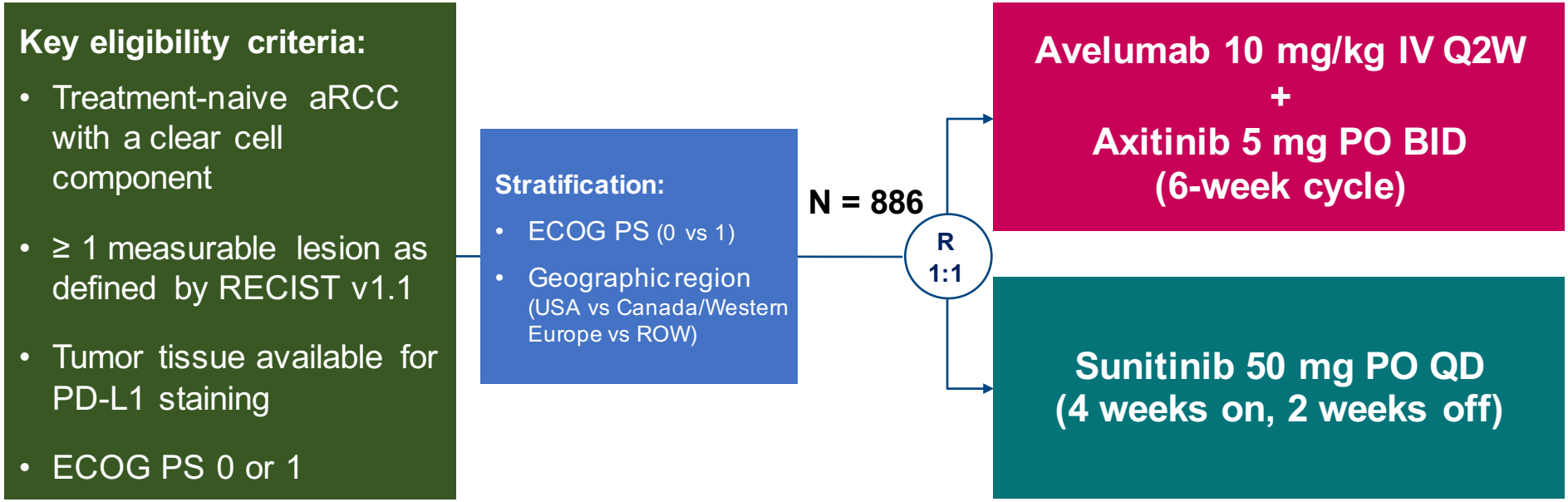
# The Current Landscape…



# Objective of Combination Therapy



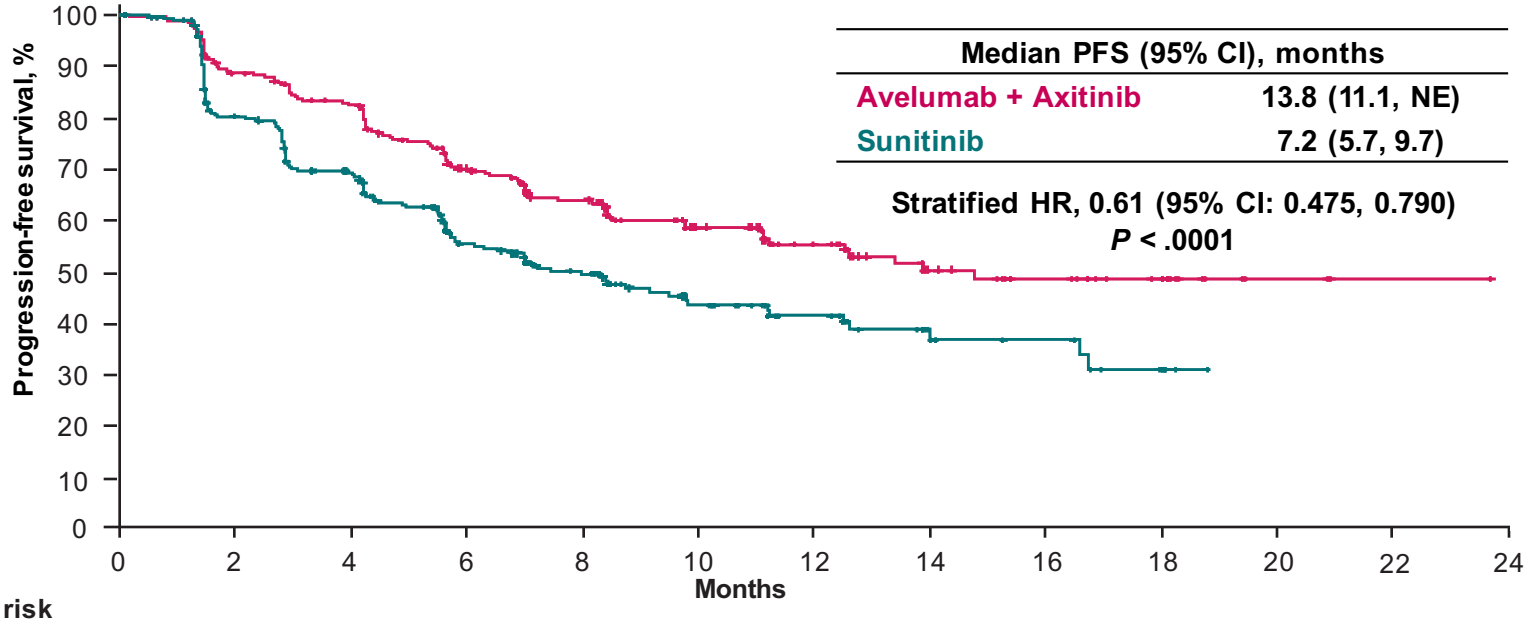
# JAVELIN Renal 101: Study Design




BID, twice per day; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; PO, orally; Q2W, every 2 weeks; QD, once per day; ROW, rest of the world.

Primary endpoint

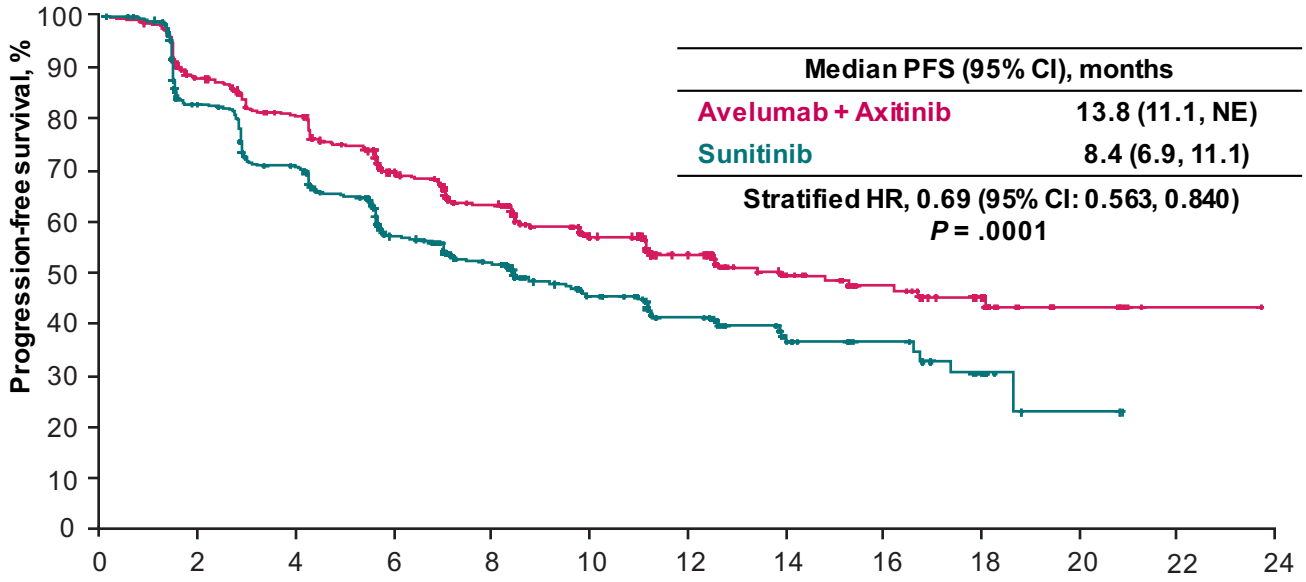
# PFS per IRC in the PD-L1+ Group




Minimum follow-up, 6 months. Median follow-up, 9.9 months (avelumab + axitinib) and 8.4 months (sunitinib). The PFS analysis crossed the prespecified efficacy boundary based on the alpha-spending function ($P = .001$)

Key Secondary endpoint

# PFS per IRC in the Overall Population




Minimum follow-up, 6 months. Median follow-up, 10.8 months (avelumab + axitinib) and 8.6 months (sunitinib). The PFS analysis crossed the prespecified efficacy boundary based on the alpha-spending function (*P* = .001)

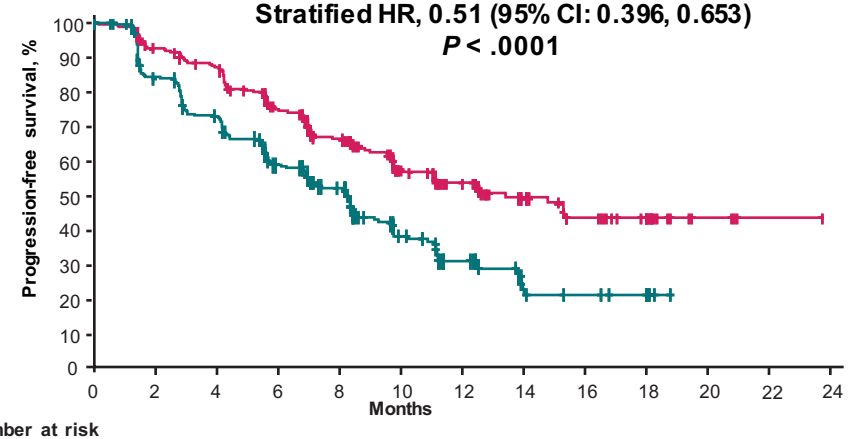
Secondary endpoint

# PFS per Investigator Assessment

## PD-L1+ group

| Median PFS (95% CI), months | |
|---|---|
| Avelumab + Axitinib | 13.3 (9.8, NE) |
| Sunitinib | 8.2 (6.9, 8.5) |

Stratified HR, 0.51 (95% CI: 0.396, 0.653)
*P* < .0001



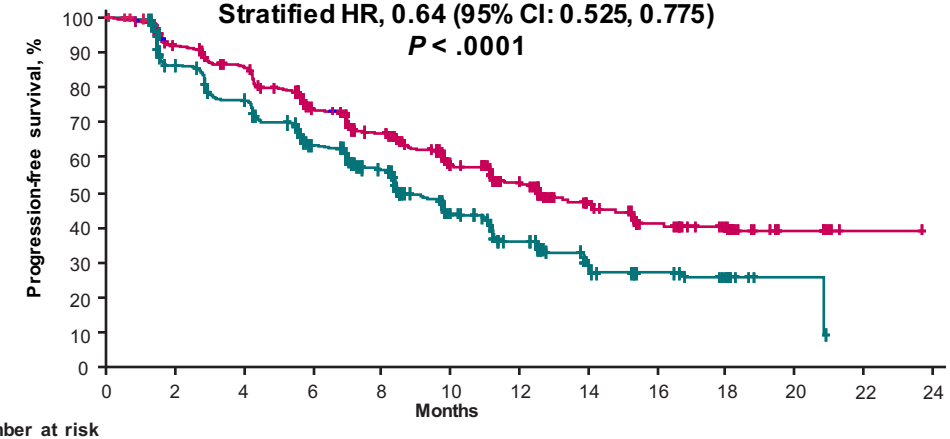

Number at risk

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Avel + Axit: | 270 | 235 | 216 | 166 | 127 | 78 | 57 | 36 | 25 | 15 | 4 | 1 | 0 |
| Sunitinib: | 290 | 227 | 191 | 138 | 100 | 51 | 32 | 12 | 10 | 5 | 0 | | |

## Overall population

| Median PFS (95% CI), months | |
|---|---|
| Avelumab + Axitinib | 12.5 (11.1, 15.2) |
| Sunitinib | 8.4 (8.2, 9.7) |

Stratified HR, 0.64 (95% CI: 0.525, 0.775)
*P* < .0001



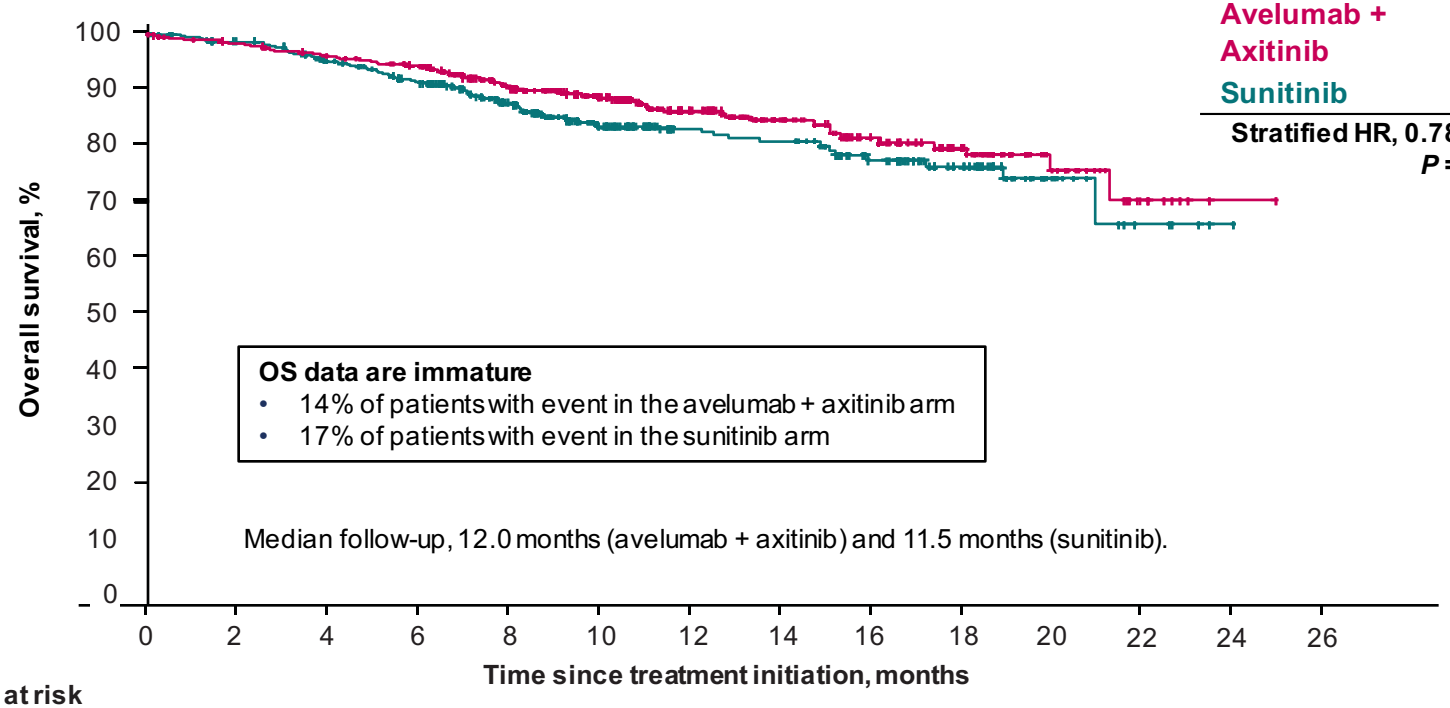

Number at risk

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Avel + Axit: | 442 | 380 | 344 | 270 | 211 | 140 | 104 | 64 | 45 | 26 | 8 | 1 | 0 |
| Sunitinib: | 444 | 348 | 299 | 225 | 170 | 95 | 62 | 26 | 20 | 10 | 3 | 0 | |

# OS in the Overall Population

| Median OS (95% CI), months | |
|---|---|
| Avelumab + Axitinib | Not reached |
| Sunitinib | Not reached |

Stratified HR, 0.78 (95% CI: 0.554, 1.084)
*P* = .0679




| Number at risk | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Avel + Axit: | 442 | 426 | 412 | 396 | 319 | 252 | 187 | 121 | 93 | 70 | 27 | 8 | 1 | 0 |
| Sunitinib: | 444 | 426 | 401 | 373 | 295 | 224 | 175 | 113 | 84 | 59 | 17 | 5 | 1 | 0 |

Secondary endpoint

# TRAEs in All Treated Patients (N = 873)

| | Avelumab + Axitinib (N = 434) | | Sunitinib (N = 439) | |
|---|---|---|---|---|
| | All grades | Grade 3 (4) | All grades | Grade 3 (4) |
| **All TRAEs, %** | **95** | **51 (4)** | **96** | **48 (7)** |
| Diarrhea | 54 | 5 (0) | 45 | 3 (0) |
| Hypertension | 48 | 24 (0) | 32 | 15 (0) |
| Fatigue | 36 | 3 (0) | 36 | 4 (0) |
| Hand-foot syndrome | 33 | 6 (0) | 34 | 4 (0) |
| Dysphonia | 27 | 1 (0) | 3 | 0 (0) |
| Nausea | 25 | 1 (0) | 34 | 1 (0) |
| Hypothyroidism | 24 | < 1 (0) | 13 | < 1 (0) |
| Stomatitis | 22 | 2 (0) | 23 | 1 (0) |
| Decreased appetite | 20 | 2 (0) | 26 | 1 (0) |
| Dysgeusia | 13 | 0 (0) | 32 | 0 (0) |
| Increased alanine aminotransferase | 13 | 4 (1) | 10 | 2 (0) |
| Thrombocytopenia | 3 | < 1 (0) | 18 | 5 (1) |
| Anemia | 2 | < 1 (0) | 17 | 5 (< 1) |
| Neutropenia | 1 | < 1 (0) | 18 | 7 (1) |
| **TRAEs leading to discontinuation of all study drugs, %*** | **4** | | **8** | |
| **TRAEs leading to death, %†** | **1** | | **< 1** | |

Treatment-related adverse events (TRAEs) of any grade occurring in ≥ 20% of patients or grade 3-4 in ≥ 3% of patients are shown. * No events occurred in ≥ 1% of patients. † Grade 5 events occurred in 3 patients in the avelumab + axitinib arm (myocarditis, necrotizing pancreatitis, sudden death; n = 1 each); in 1 patient in the sunitinib arm (intestinal perforation).

Secondary endpoint

# AEs of Special Interest in All Treated Patients

| | Avelumab + Axitinib (N = 434) | |
|---|---|---|
| | **All grades** | **Grade 3 (4)** |
| **All immune-related AEs, %** | **38** | **8 (1)** |
| Hypothyroidism | 21 | < 1 (0) |
| Liver function test abnormalities | 5 | 4 (< 1) |
| Adrenal insufficiency | 2 | 1 (0) |
| Diarrhea | 2 | 1 (0) |
| Acute kidney injury | 1 | 1 (0) |
| Colitis | 1 | 1 (0) |
| Hepatotoxicity | 1 | 1 (0) |
| **Infusion-related reaction, %** | **12** | **1 (0)** |

High-dose corticosteroids* were administered to 11% of patients who experienced an immune-related AE.

Immune-related AEs of any grade occurring in ≥ 5% of patients or grade 3 in ≥ 1% of patients are shown. * ≥40 mg total daily prednisone or equivalent.

# Case Study 3: Avelumab/Axitinib

- 77-year-old male diagnosed in 11/14 – had nephrectomy and developed med LN's and lung mets
- 6/21/18 started avelumab/axitinib
- 8/16/18 developed left sided facial droop with no other neuro symptoms – Treatment held
- Differential dx: thrombosis, stroke r/t axitinib

# Neuro Workup

- Head CT negative
- Brain MRI negative; neurology referral
- Suspected myasthenia gravis (autoimmune disorder of the proteins in the post synaptic membrane of the NMJ)
- Marked improvement in symptoms with physostigmine 60 mg TID over 3 months and resumed therapy with lenvatinib/everolimus

# A Banner Year for Immunotherapy in RCC

ESMO 2017: Nivolumab/Ipilimumab vs Sunitinib Primary Analysis

GUCS 2018: E rimary Analysis

ESMO 20 ry Analysis

**Is there a role for TKI monotherapy?**

# CABOSUN

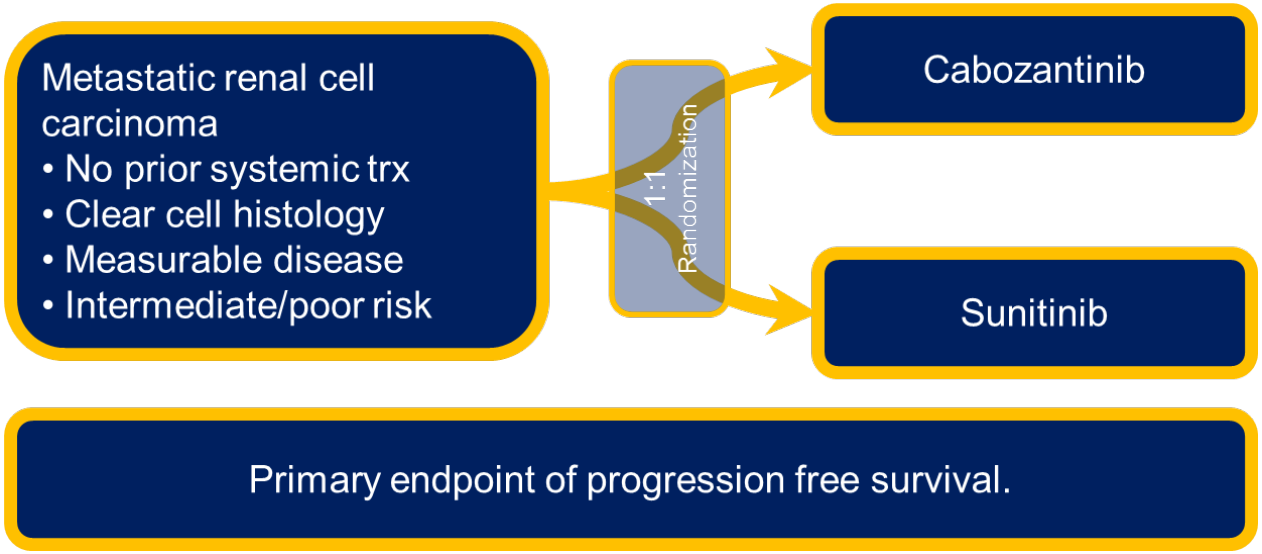
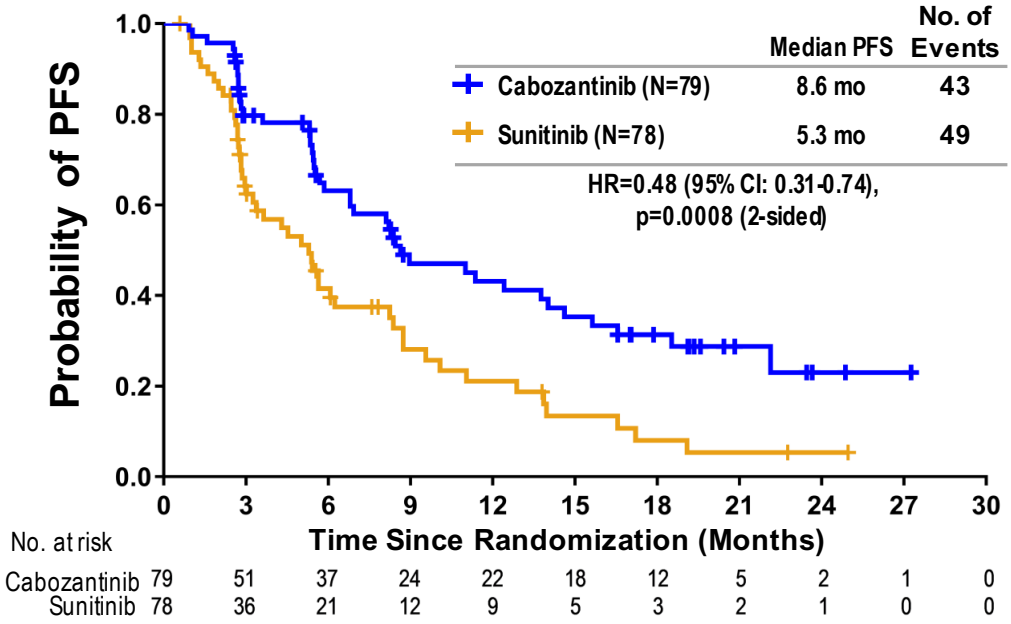
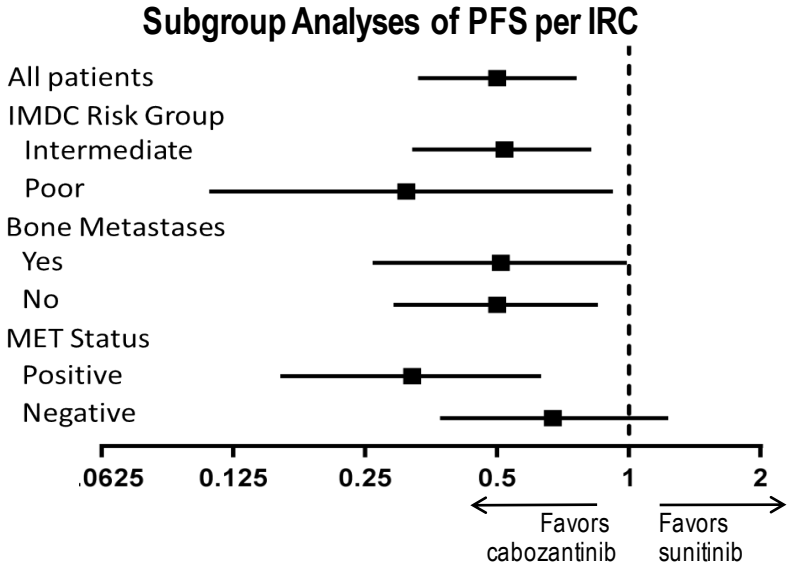

Metastatic renal cell carcinoma
• No prior systemic trx
• Clear cell histology
• Measurable disease
• Intermediate/poor risk
1:1 Randomization
Cabozantinib
Sunitinib
Primary endpoint of progression free survival.

**Table 1. Adverse Reactions Occurring in ≥ 10% Patients Who Received Cabozantinib in METEOR**

| Adverse Reaction | CABOMETYX(n=331) | | Everolimus(n=322) | |
|---|---|---|---|---|
| | All Grades | Grade 3-4 | All Grades2 | Grade 3-4 |
| | Percentage (%) of Patients | | | |
| **Gastrointestinal Disorders** | | | | |
| Diarrhea | 74 | 11 | 28 | 2 |
| Nausea | 50 | 4 | 28 | <1 |
| Vomiting | 32 | 2 | 14 | <1 |
| Stomatitis | 22 | 2 | 24 | 2 |
| Constipation | 25 | <1 | 19 | <1 |
| Abdominal pain | 23 | 4 | 13 | 2 |
| Dyspepsia | 12 | <1 | 5 | 0 |
| **General Disorders and Administration Site Conditions** | | | | |
| Fatigue | 56 | 9 | 47 | 7 |
| Mucosal inflammation | 19 | <1 | 23 | 3 |
| Asthenia | 19 | 4 | 16 | 2 |
| **Metabolism and Nutrition Disorders** | | | | |
| Decreased appetite | 46 | 3 | 34 | <1 |
| **Skin and Subcutaneous Tissue Disorders** | | | | |
| Palmar-plantar erythrodysesthesia | 42 | 8 | 6 | <1 |
| Rash4 | 23 | <1 | 43 | <1 |
| Dry skin | 11 | 0 | 10 | 0 |

# PFS per IRC and Overall Survival




Data cutoff : PFS, Sep 15, 2016; OS, July 1, 2017; **IRC**, Independent Review Committee; **IMDC**, International Metastatic RCC Database Consortium.

Overall Survival (OS)

HR=0.80 (95% CI: 0.53-1.21); p=0.29 (2-sided)

Median OS: Cabozantinib **26.6 mo**, Sunitinib **21.2 mo**

# Case Study 4: Managing TKI Toxicity

- 64-year-old male auto mechanic with met RCC; pT3a clear cell RCC had a laparoscopic nephrectomy on 6/2015
- 12/2017 he presented with progression to brain, mediastinum, bone
- Cabozantinib: oral inhibitor of TKs including VEGF, MET, AXL
- Started 1/18 at 60 mg and was decreased to 40 mg for fatigue
- 5/18 developed PPE/HFS, which was maintained as a grade 1 with good hand care

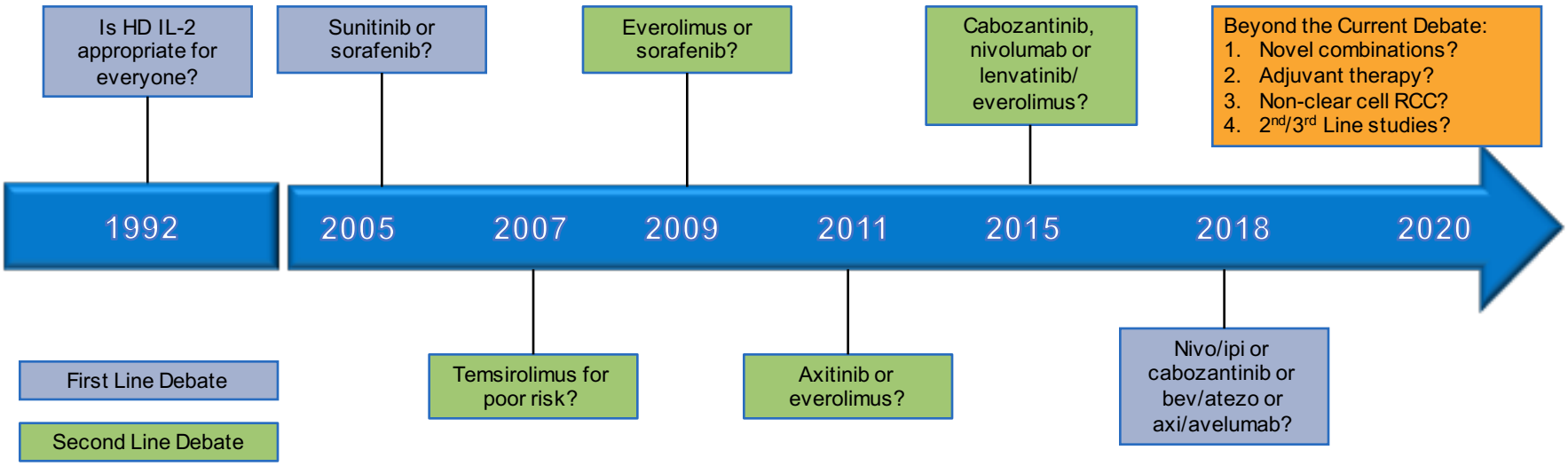
# Palmar-Plantar Erythrodysesthesia (PPE)

- In RCC trials, PPE occurred in 42% of cabozantinib patients; grade 3 PPE occurred in 8% of cabozantinib patients
- Withhold cabozantinib in patients who develop intolerable grade 2 PPE or grade 3 PPE until improvement to grade 1
- Resume cabozantinib at a reduced dose

# Management Strategies for Keeping Patients on TKIs

- Start strong and provide a close system of patient feedback
- Manage patient and family expectation around dose adjustment and reassure them that we want to maintain QOL while getting the most of the treatment as possible
- Oral therapies can require as much teaching/support as IV

# Beyond the Current Debate …



# Adjuvant Therapy With Atezolizumab

## Kidney Cancer

Key Eligibility (n=664)
- High risk OR limited metastasis s/p metastasectomy
- s/p nephrectomy ≤ 12 weeks
- No evidence of residual disease
- Clear cell or **sarcomatoid histology**

Stratification Factors
- Disease stage (T2/T3a vs. T3b/c/T4/N+ vs metastasectomy)
- PD-L1 (IC0 vs IC1/2/3)
- Region (US/Canada vs ROW)

1:1 Randomization

Atezolizumab 1200 mg IV q3wk x 16 cycles

Placebo q3wk x 16 cycles

**We need you!**

City of Hope

NCT02450331: A Phase III, Open-Label, Multicenter, Randomized Study of Atezolizumab (Anti-PD-L1 Antibody) Versus Observation as Adjuvant Therapy in Patients With High-Risk Muscle-Invasive Urothelial Carcinoma After Surgical Resection

# Novel Combinations

## Cabozantinib with Atezolizumab

**Dose Expansion**

Dose escalation
- UC (including renal pelvis, ureter, bladder, urethra) after prior platinum-based therapy, or
- RCC (clear cell, **non-clear cell**) with or without prior systemic anticancer therapy

Define Recommend Dose

- RCC with clear cell histology who have not received prior systemic anticancer therapy
- UC with progression on or after platinum-containing chemotherapy
- UC not eligible for cisplatin-based chemo and no prior platinum-based chemotherapy
- UC eligible for cisplatin-based chemotherapy with no prior platinum-based chemotherapy

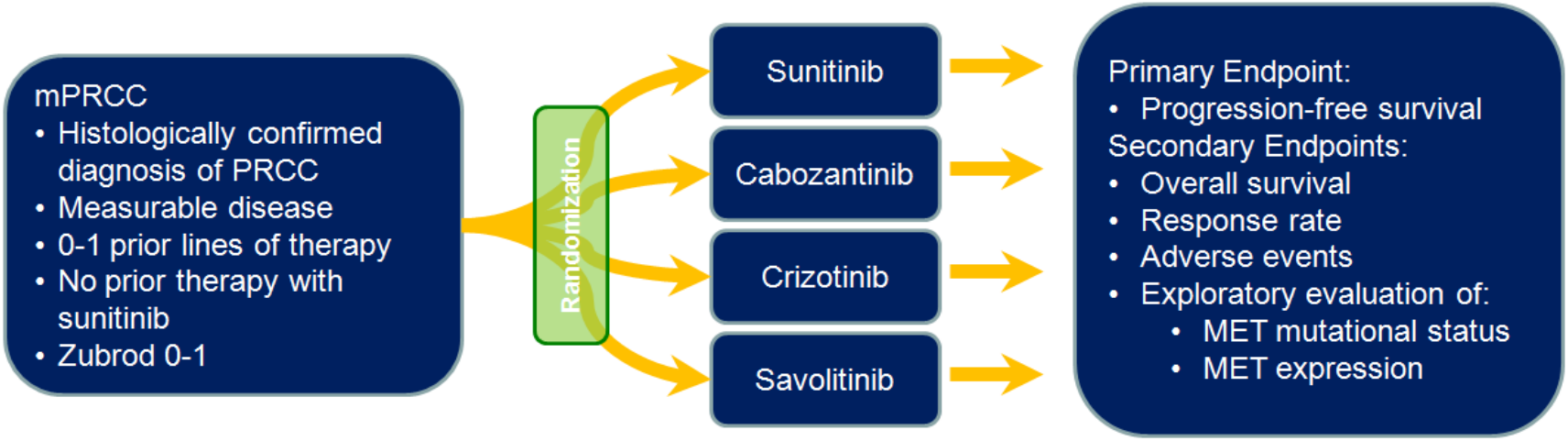
**Now expanding to 18 different tumor types**

**Dose Escalation in ncRCC Planned**

NCT03170960: A Phase 1b Dose-Escalation Study of Cabozantinib (XL184) Administered in Combination With Atezolizumab to Subjects With Locally Advanced or Metastatic Solid Tumors

City of Hope

# Papillary Kidney Cancer




- Tackles a rare subtype of kidney cancer called papillary
- **Supported by NCI grants**

**We need you!**

City of Hope

NCT02761057: A Randomized, Phase II Efficacy Assessment of Multiple MET Kinase Inhibitors (Cabozantinib [NSC #761968], Crizotinib [NSC #749005], Savolitinib [NSC #785348], and Sunitinib [NSC #736511]) in Metastatic Papillary Renal Carcinoma (PAPMET)

# Second- and Third-Line Therapy Trial

**N = 306**

**Key Inclusion Criteria**
- Advanced clear cell RCC
- Progression on/after 1 prior VEGF-targeted treatment
- Prior PD-1/PD-L1 inhibitor treatment is allowed
- Measurable disease
- KPS ≥ 70

R 1:1

- **Lenvatinib 18 mg qd + Everolimus 5 mg qd**
- **Lenvatinib 14 mg qd★ + Everolimus 5 mg qd**


Pal (COH)


Heng (Calgary)

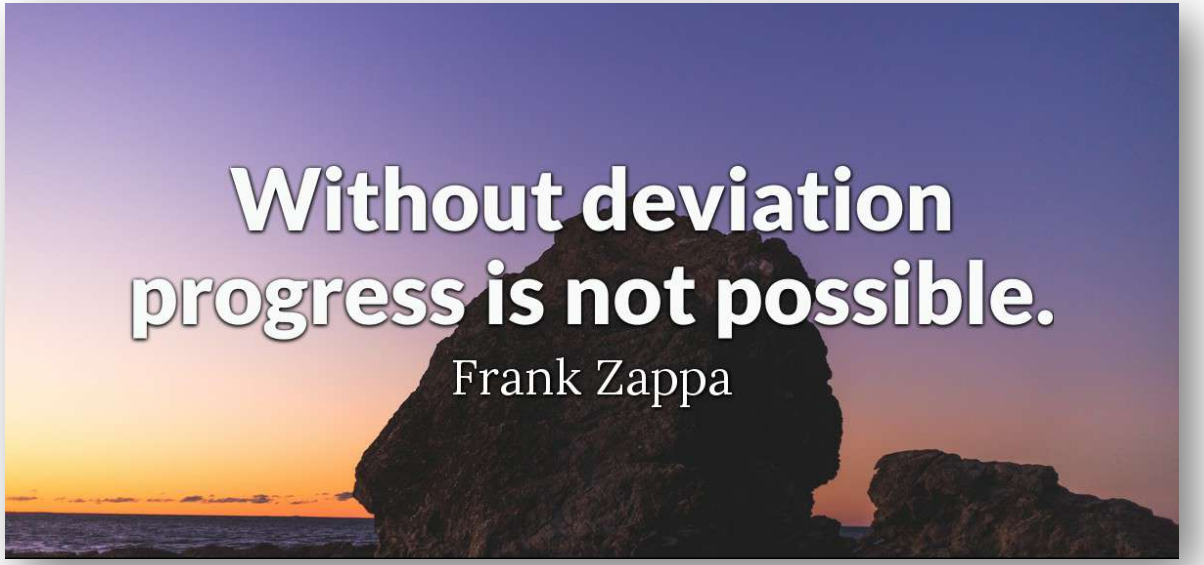

Puente (Spain)

★On Cycle 2 Day 1: Lenvatinib will be escalated to 18 mg qd if no intolerable G2 or G3/G4 AEs or SAEs are observed in the first 28 days

City of Hope

**International study:**
- Lead sites in US, Korea, Europe
- FDA mandated study that may change dosing of an approved regimen

# Thank you to our patients and their families for their continuing interest in progress




@montypal

@kanurkkooo

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