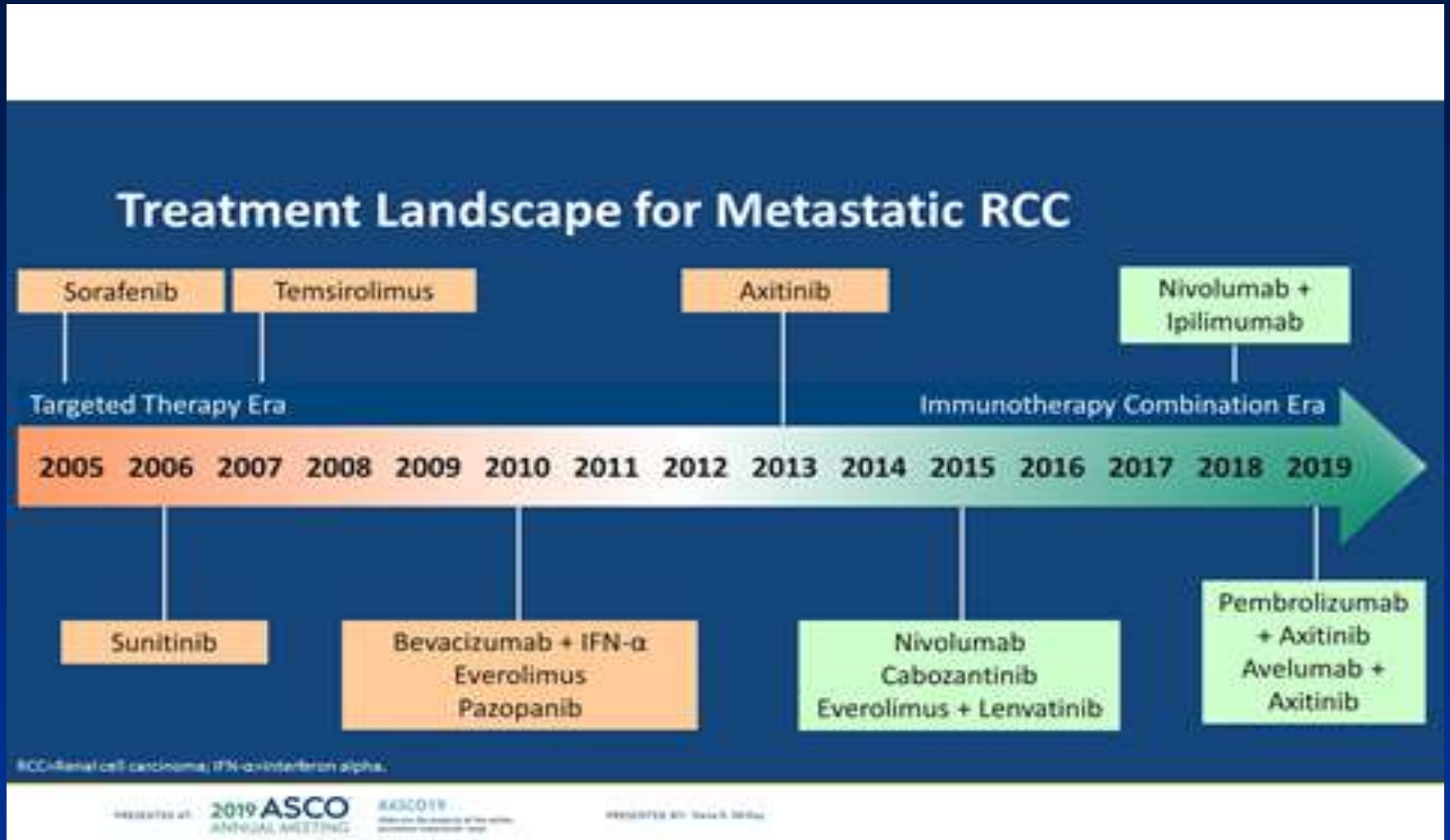
ASL Toscana Sud Est
U.O.C. Oncologia Medica
Grosseto

Carcinoma renale

Dr. Aldo Chioni

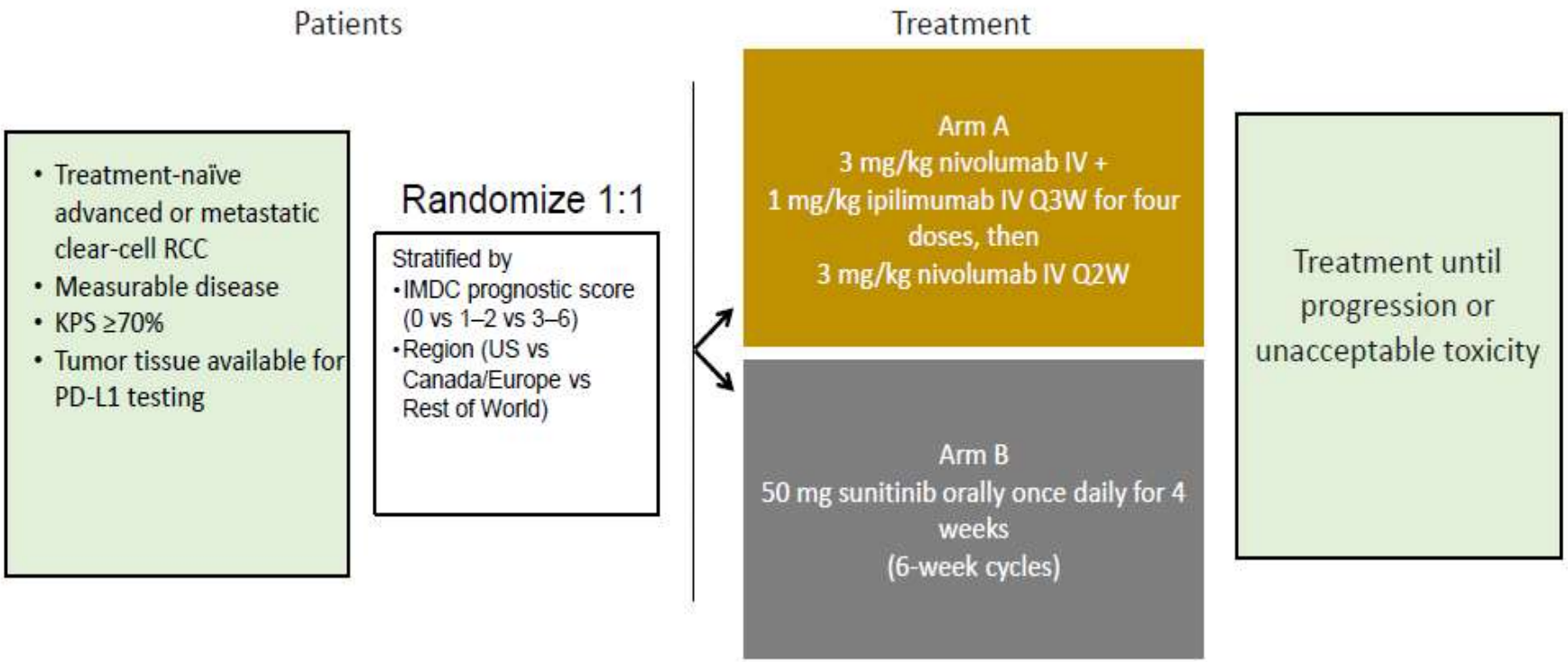
Supernovae in Oncologia
Pisa 19-20 settembre 2019



Presented By Rana McKay at 2019 ASCO Annual Meeting

Nel 2018

CheckMate 214: Study design



MADRID 2017 ESMO congress

Exploratory endpoint

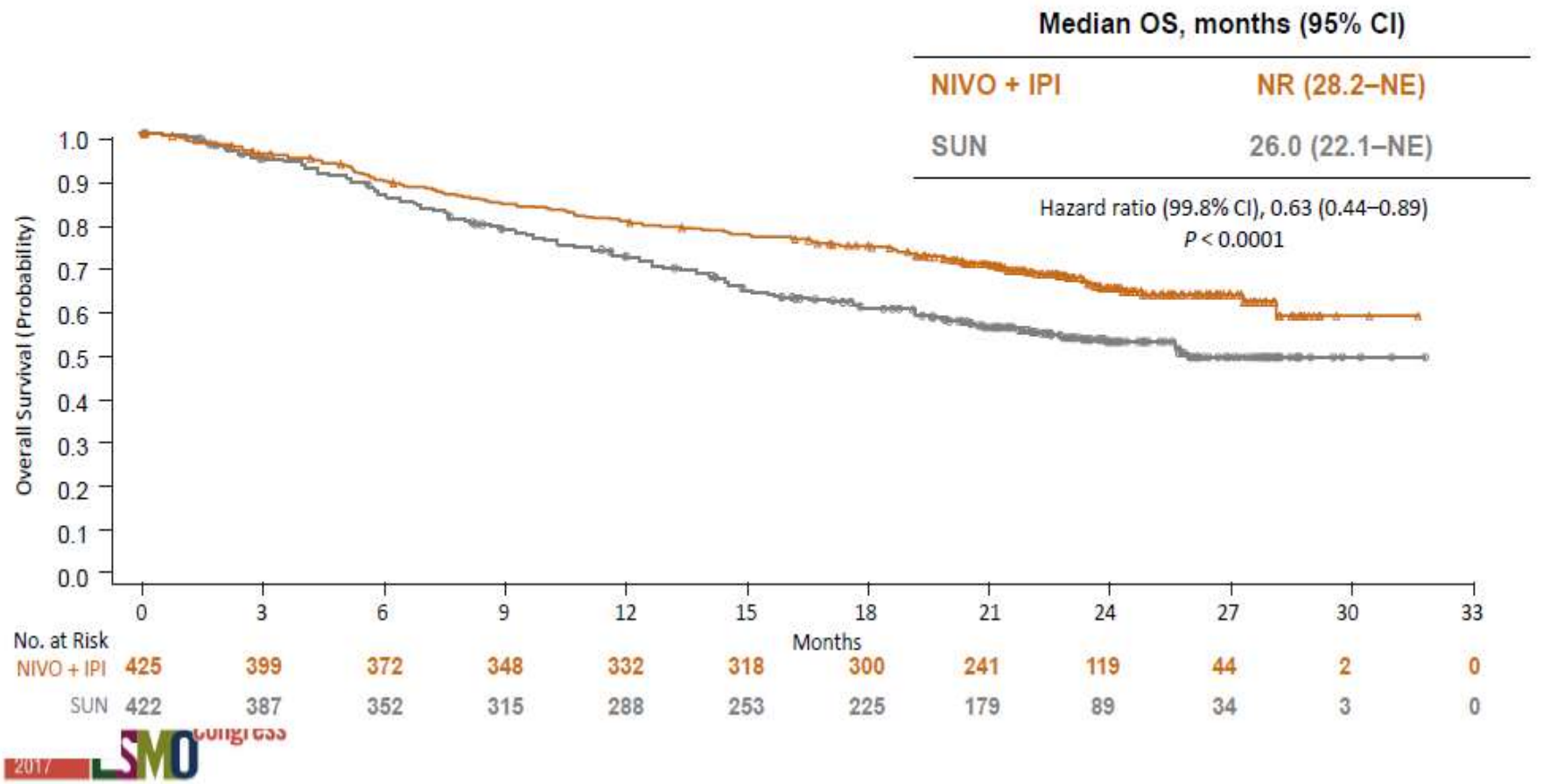
ORR and PFS: IMDC favorable risk

	N = 249[a]	
Outcome	NIVO + IPI N = 125	SUN 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) ***P* < 0.0001**	

MADRID 2017 ESMO congress

Co-primary endpoint

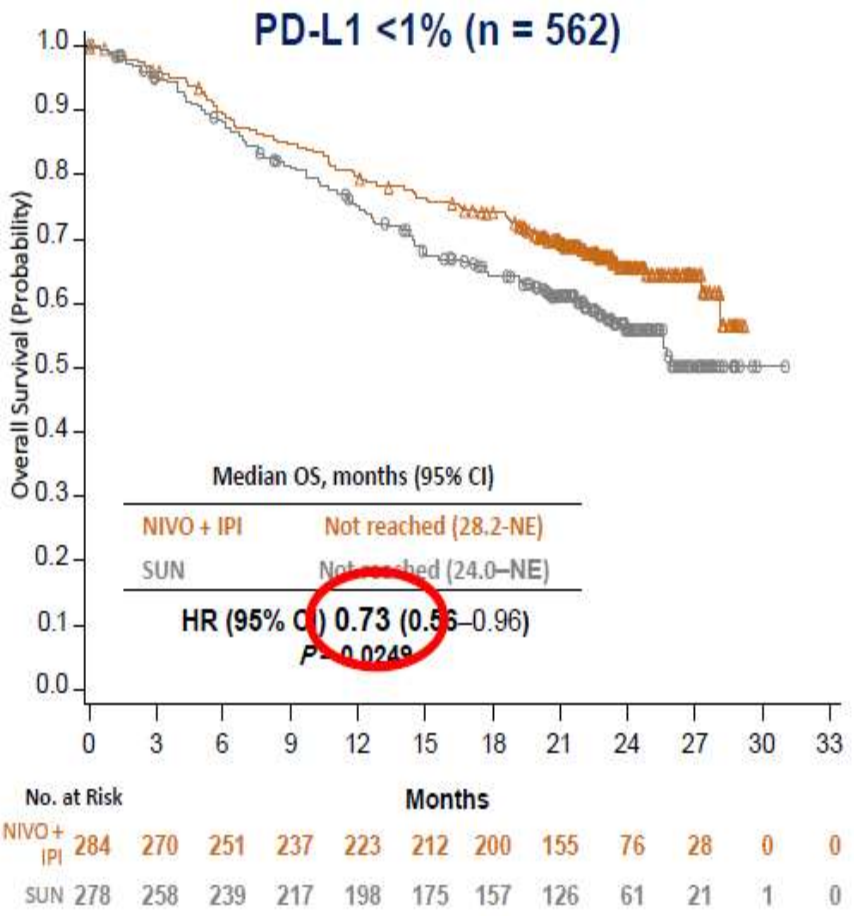
OS: IMDC intermediate/poor risk

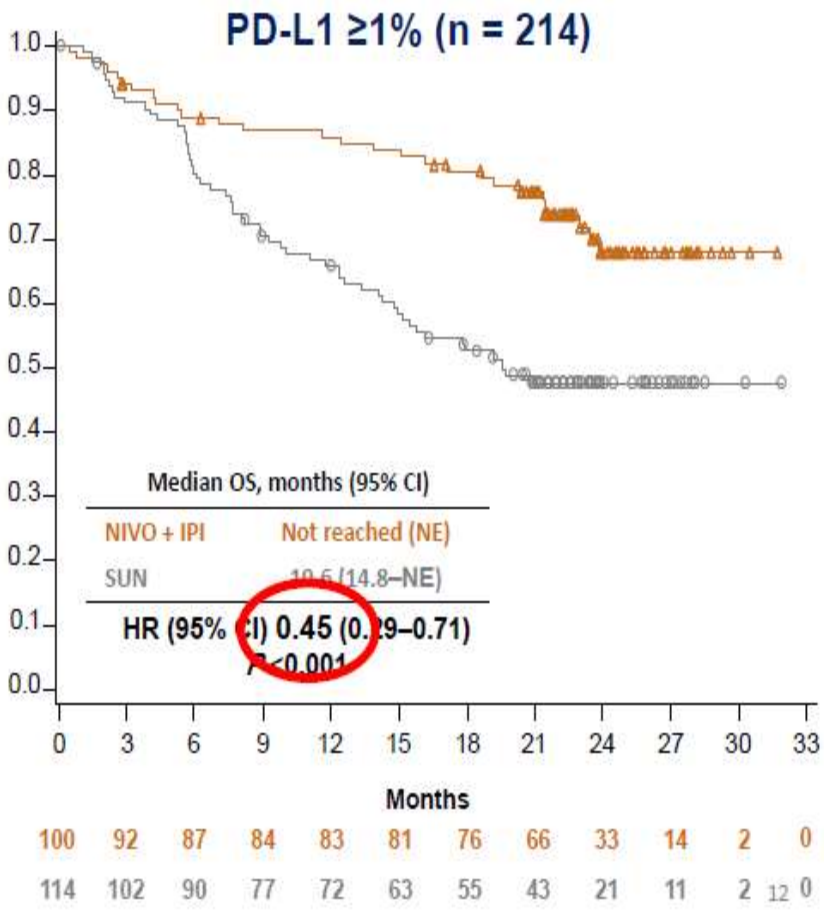


2017 SMO Congress

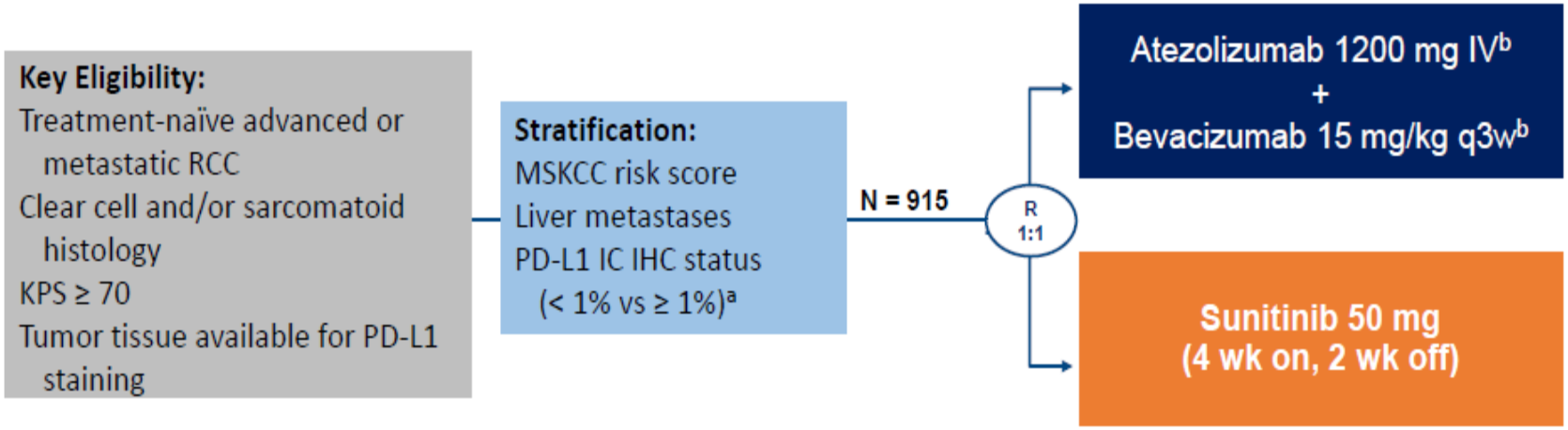
CheckMate 214, Motzer et al.

OS by tumor PD-L1 expression: IMDC intermediate/poor risk



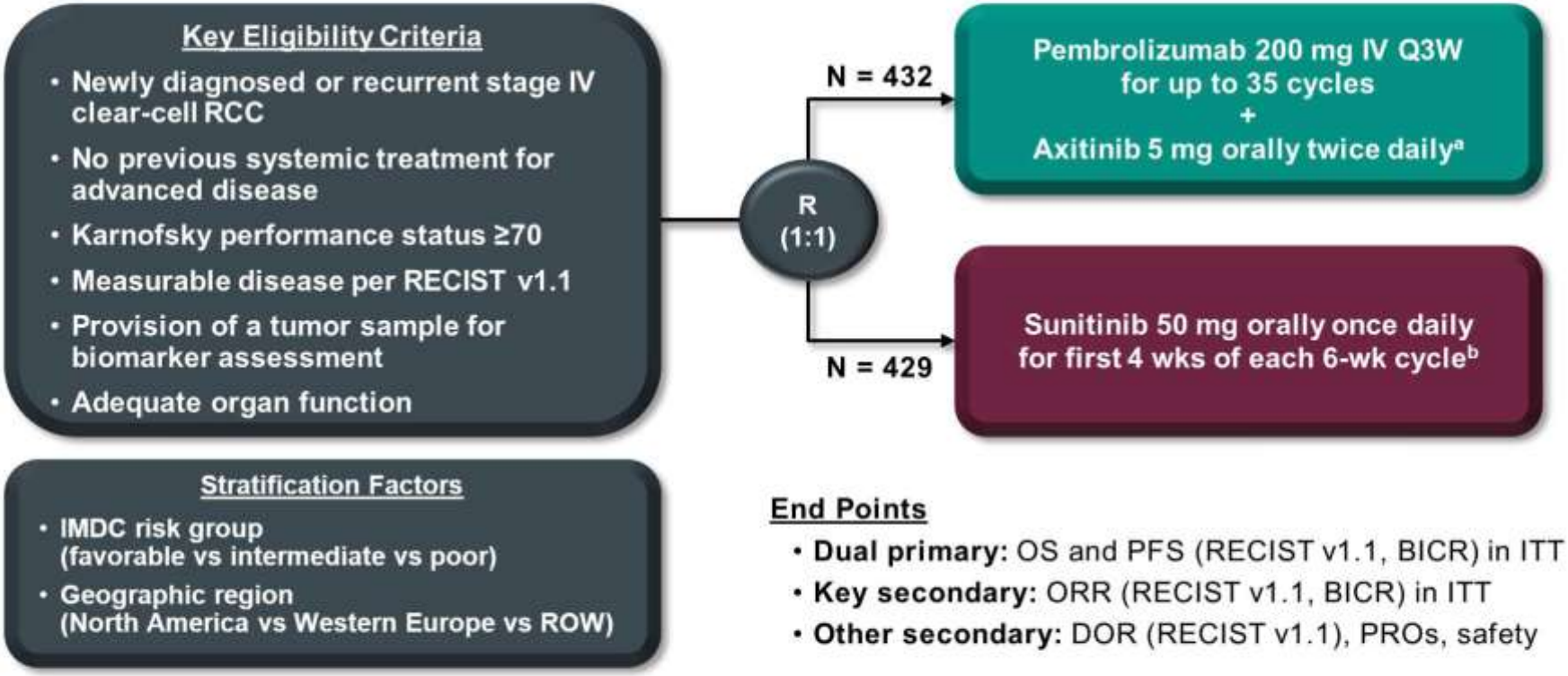


Immotion 151 study



Novità 2019

KEYNOTE-426 Study Design



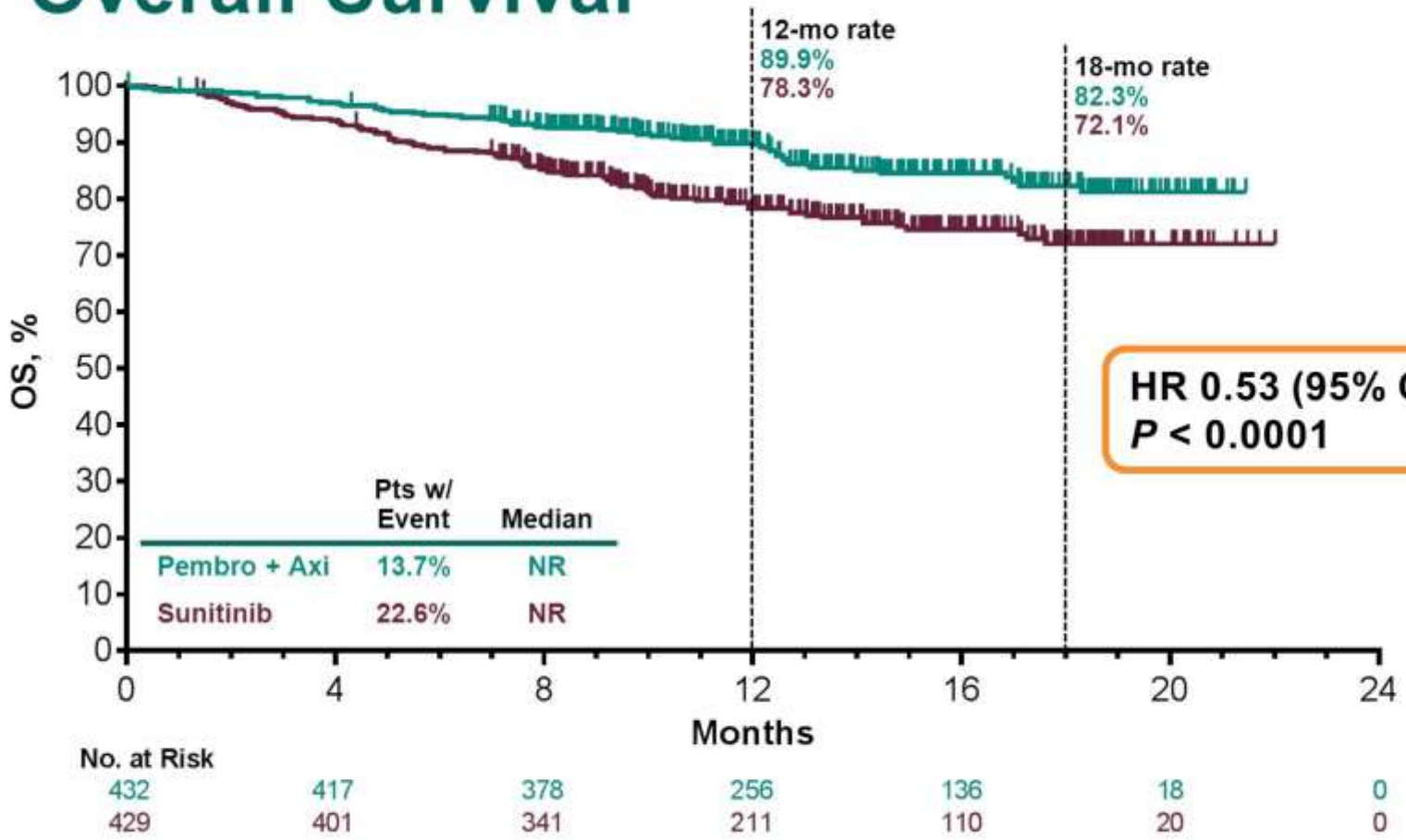
[a]Axitinib dose could be increased to 7 mg, then 10 mg, twice daily if safety criteria were met; dose could be reduced to 3 mg, then 2 mg, twice daily to manage toxicity.
[b]Sunitinib dose could be decreased to 37.5 mg, then 25 mg, once daily for the first 4 wks of each 6-wk cycle to manage toxicity.
BICR, blinded independent central radiologic review; DOR, duration of response; PROs, patient-reported outcomes; ROW, rest of world.
KEYNOTE-426 is a randomized, open-label, phase 3 study (ClinicalTrials.gov identifier NCT02853331).

Baseline Characteristics

	Pembrolizumab + Axitinib N = 432	Sunitinib N = 429
Age, median (range)	62 yrs (30-89)	61 yrs (26-90)
Male	308 (71.3%)	320 (74.6%)
Region of enrollment		
North America	104 (24.1%)	103 (24.0%)
Western Europe	106 (24.5%)	104 (24.2%)
Rest of world	222 (51.4%)	222 (51.7%)
IMDC risk category		
Favorable	138 (31.9%)	131 (30.5%)
Intermediate	238 (55.1%)	246 (57.3%)
Poor	56 (13.0%)	52 (12.1%)
Sarcomatoid features	51/285 (17.9%)	54/293 (18.4%)
PD-L1 CPS ≥1[a]	243/410 (59.3%)	254/412 (61.7%)
≥2 metastatic organs	315 (72.9%)	331 (77.2%)
Previous nephrectomy	357 (82.6%)	358 (83.4%)

[a]Assessed at a central laboratory using the PD-L1 IHC 22C3 pharmDx assay. CPS = combined positive score = number of PD-L1–positive cells (tumor cells, lymphocytes, macrophages) divided by total number of tumor cells × 100.
Data cutoff date: Aug 24, 2018.

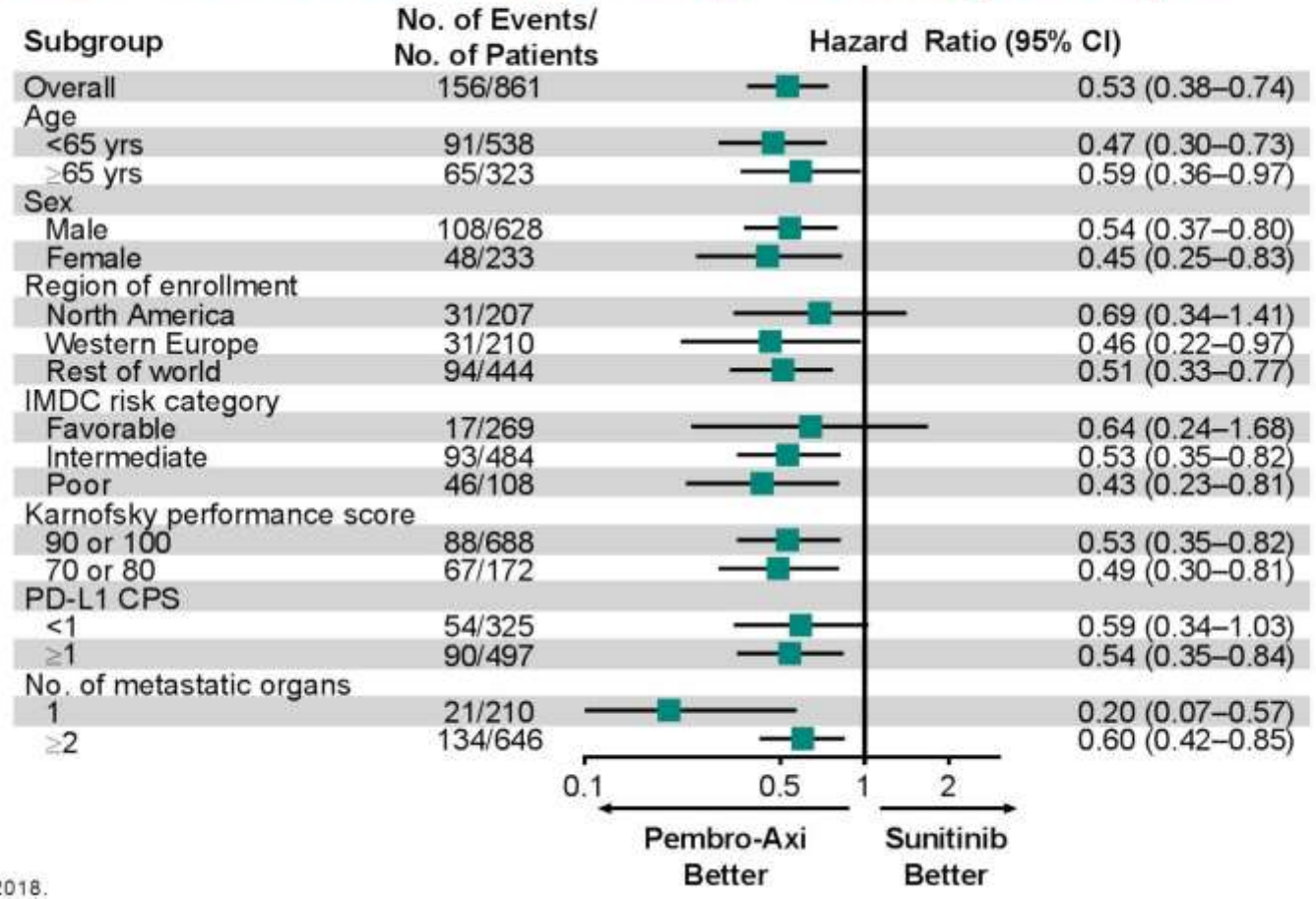
Overall Survival



HR 0.53 (95% CI 0.38-0.74)
P < 0.0001

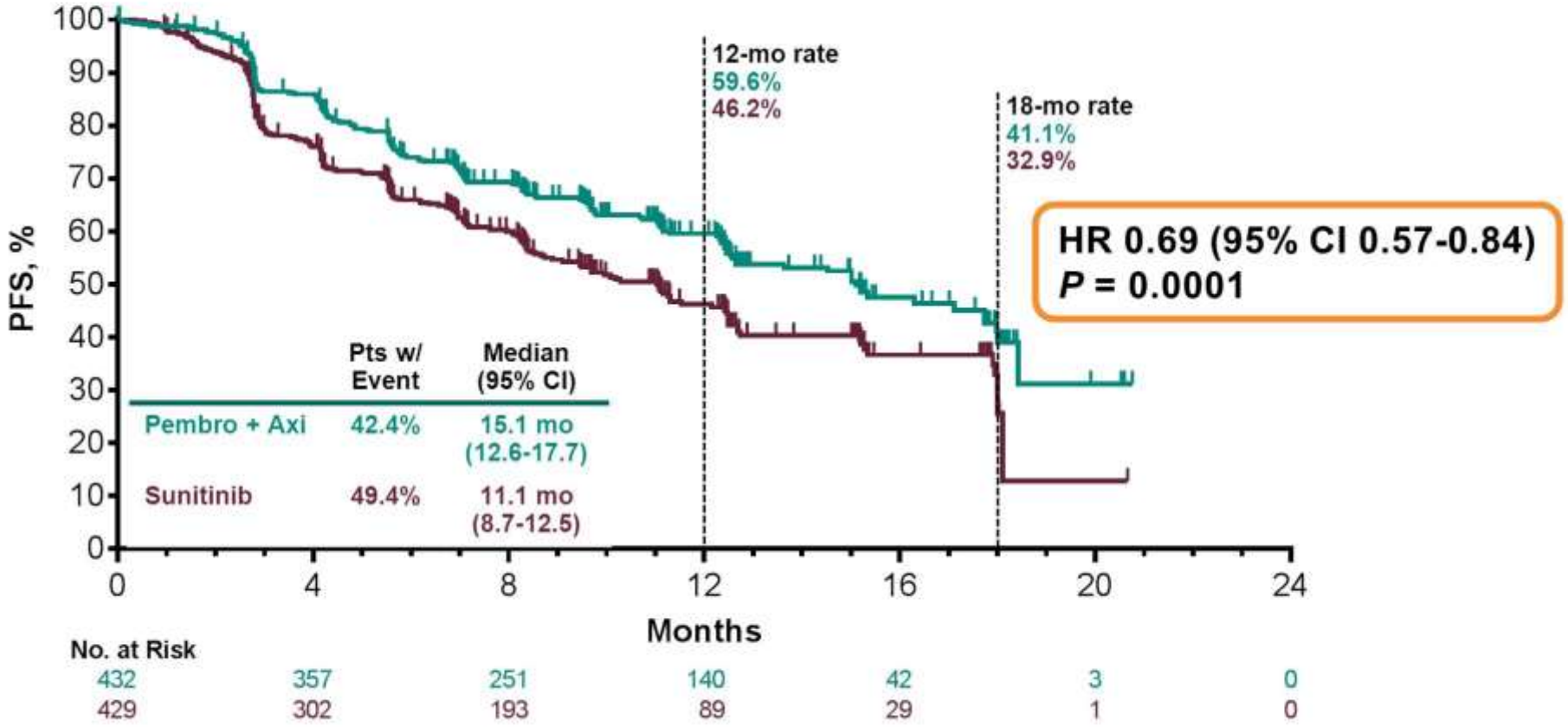
Data cutoff date: Aug 24, 2018.

Overall Survival in Key Subgroups



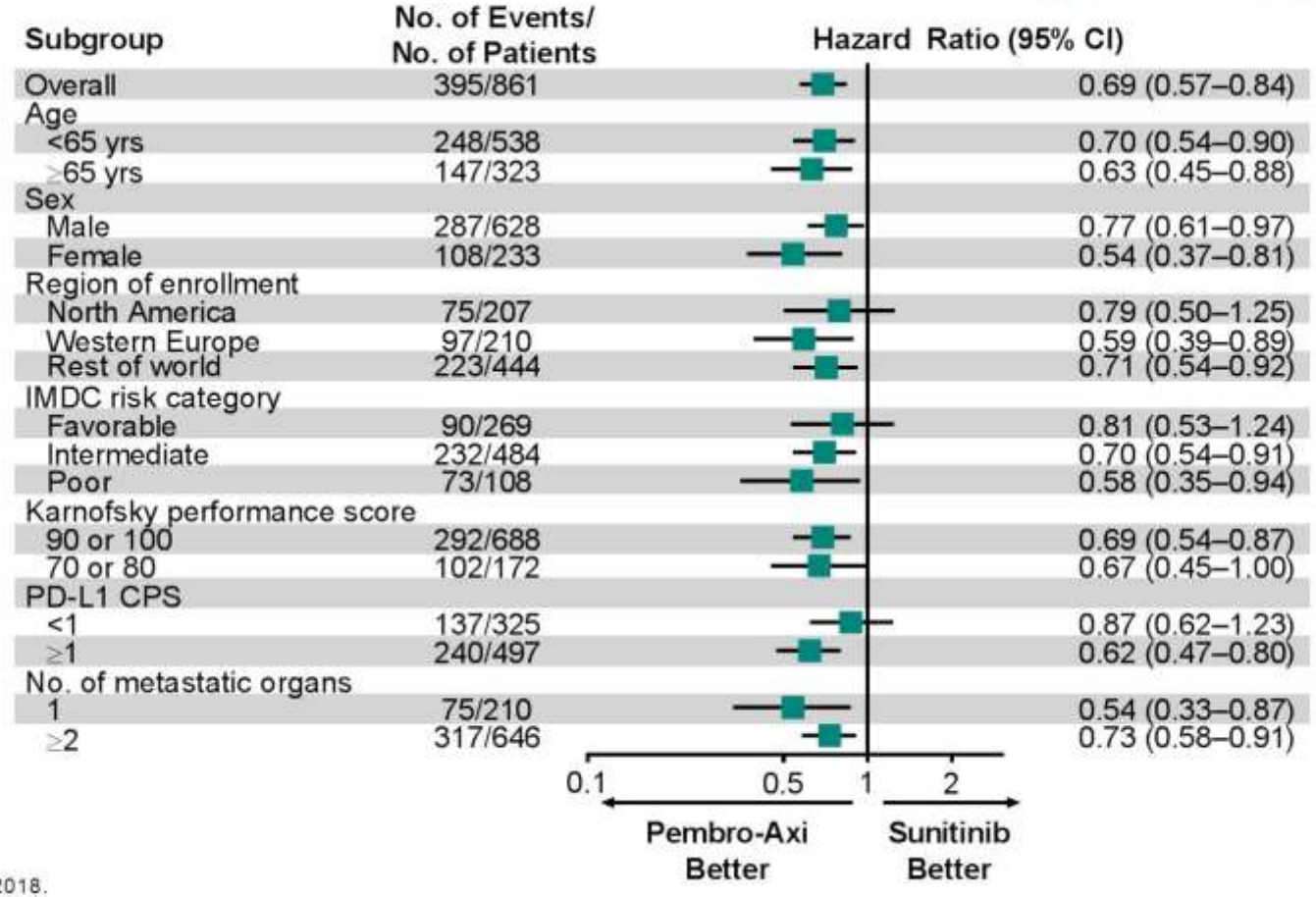
Data cutoff date: Aug 24, 2018.

Progression-Free Survival



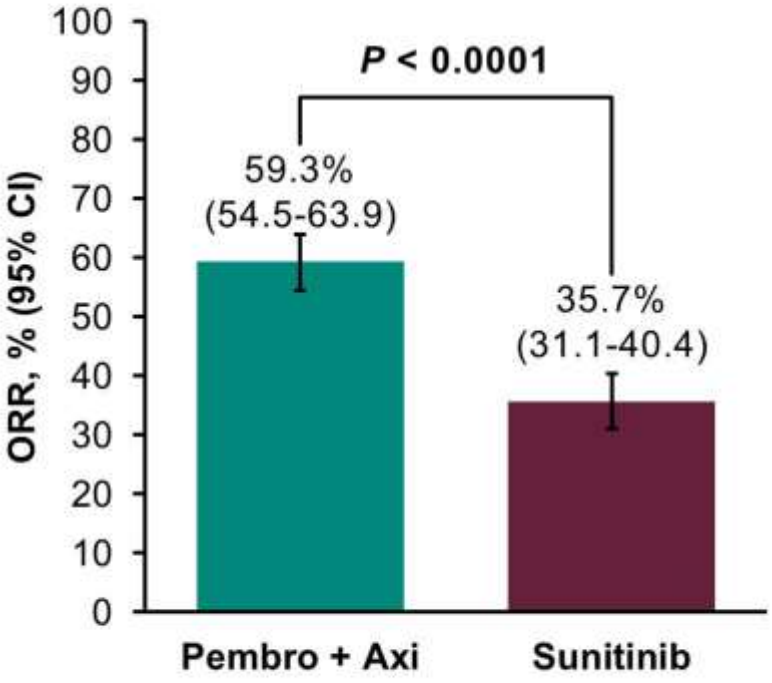
Data cutoff date: Aug 24, 2018.

Progression-Free Survival in Key Subgroups



Data cutoff date: Aug 24, 2018.

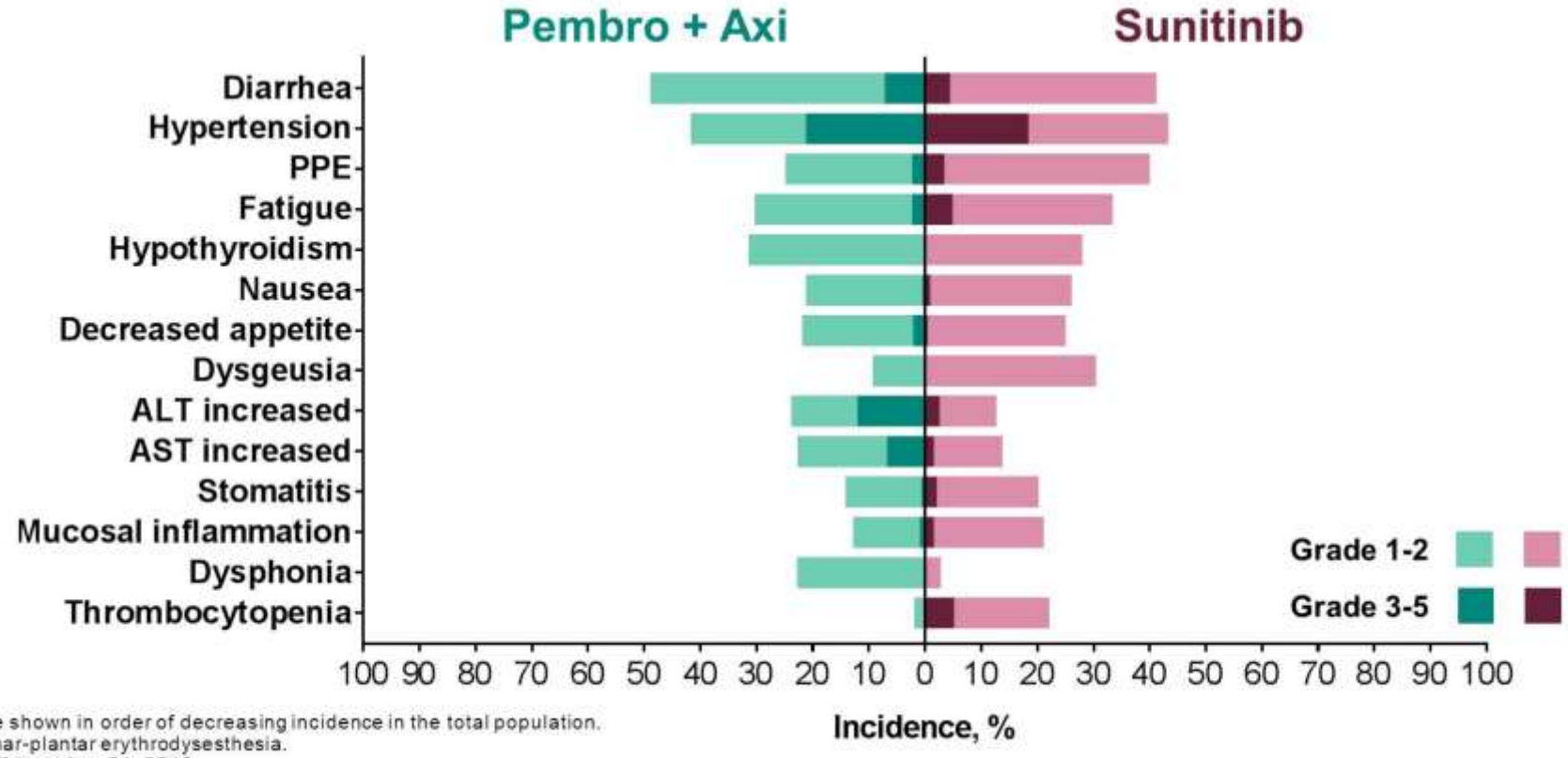
Confirmed Objective Response Rate



Best Response	Pembro + Axi N = 432	Sunitinib N = 429
CR	25 (5.8%)	8 (1.9%)
PR	231 (53.5%)	145 (33.8%)
SD	106 (24.5%)	169 (39.4%)
PD	47 (10.9%)	73 (17.0%)
NE[a]	8 (1.9%)	6 (1.4%)
NA[b]	15 (3.5%)	28 (6.5%)
Response Duration	**N = 256**	**N = 153**
Median (range), mo	NR (1.4+ to 18.2+)	15.2 (1.1+ to 15.4+)

[a]Patients who had ≥1 post-baseline imaging assessment, none of which were evaluable per RECIST v1.1 by BICR. [b]Patients who did not have ≥1 post-baseline imaging assessment.
Data cutoff date: Aug 24, 2018.

Treatment-Related Adverse Events: Incidence ≥20%



Events are shown in order of decreasing incidence in the total population.
PPE, palmar-plantar erythrodysesthesia.
Data cutoff date: Aug 24, 2018.

Pembrolizumab plus Axitinib as First-Line Therapy for mRCC: Outcomes in the Combined IMDC Intermediate/Poor Risk and Sarcomatoid Subgroups of KEYNOTE-426

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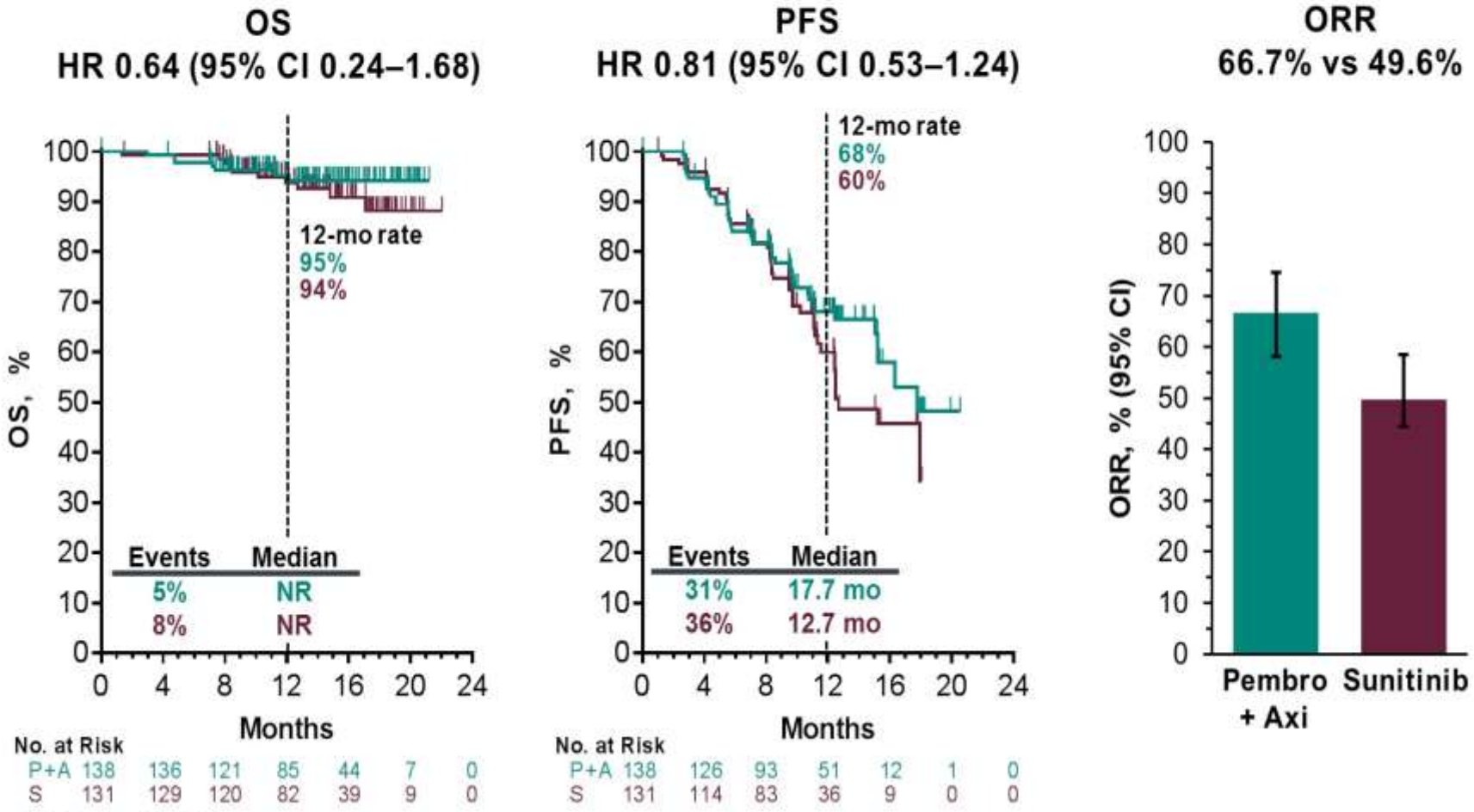
[1]Cleveland Clinic Taussig Cancer Institute, Cleveland, OH, USA; [2]Fox Chase Cancer Center, Philadelphia, PA, USA; [3]Dnipropetrovsk Medical Academy of Ministry of Health of Ukraine, Dnipro, Ukraine; [4]Russian Scientific Center of Roentgenoradiology, Moscow, Russia; [5]The Christie NHS Foundation Trust, Manchester, UK; [6]Central Clinical Hospital with Outpatient Clinic, Moscow, Russia; [7]CHU de Québec and Université Laval, Quebec City, QC, Canada; [8]Centre Hospitalier de l'Universitaire de Montréal, Montréal, QC, Canada; [9]Palacky University Medical School and Teaching Hospital, Olomouc, Czech Republic; [10]Sumy State University, Sumy Regional Oncology Center, Sumy, Ukraine; [11]Hospital de Clinicas de Porto Alegre, Porto Alegre, Brazil; [12]Centre Antoine Lacassagne, Université Côte d'Azur, Nice, France; [13]Adelaide and Meath Hospital and University College Dublin, Dublin, Ireland; [14]Department of Urology, Eberhard-Karls University Tübingen, Tübingen, Germany; [15]Osaka City University Hospital, Osaka, Japan; [16]Merck & Co., Inc., Kenilworth, NJ, USA; [17]Georgetown–Lombardi Comprehensive Cancer Center, Washington, D.C., USA; [18]Barts Health and the Royal Free NHS Trusts, Barts Cancer Institute, and Queen Mary University of London, London, UK

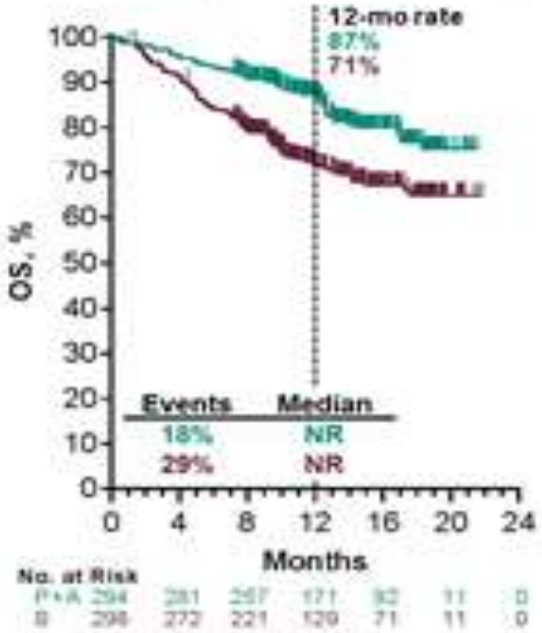
IMDC Favorable Risk: OS, PFS, and ORR



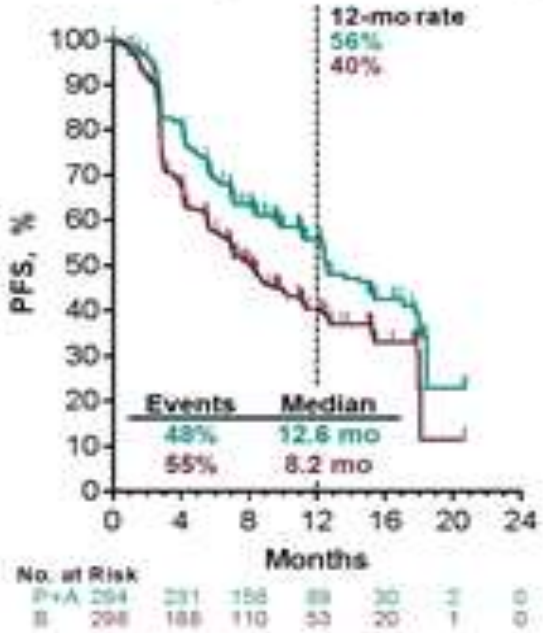
Data cutoff date: Aug 24, 2018.

IMDC Intermediate/Poor Risk: OS, PFS, and ORR

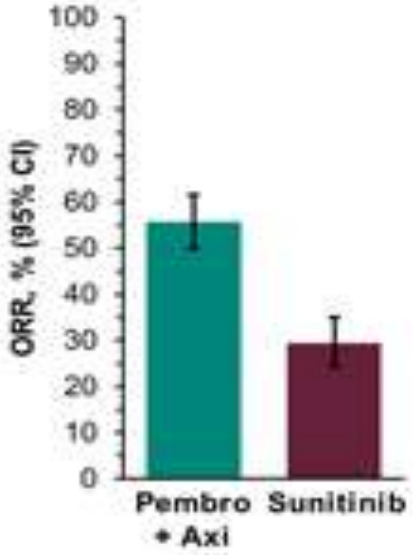
OS
HR 0.52 (95% CI 0.37–0.74)



PFS
HR 0.67 (95% CI 0.53–0.85)



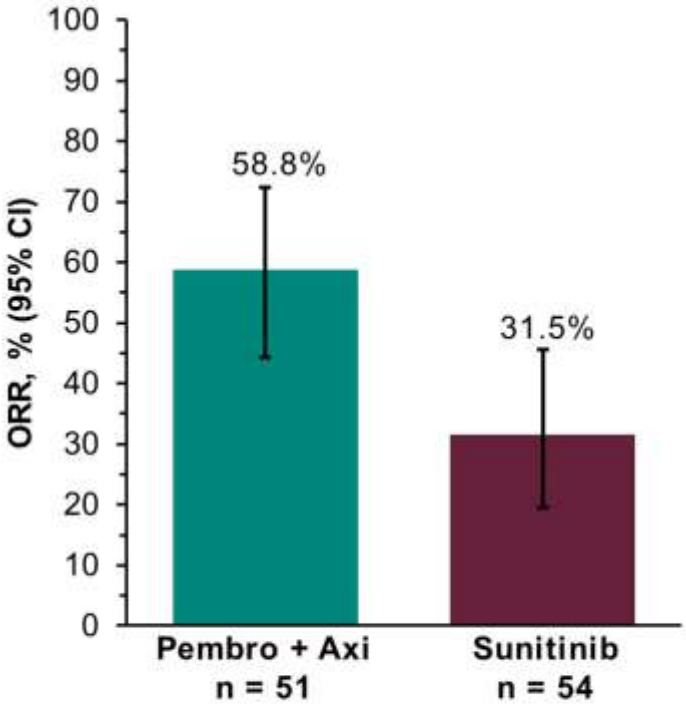
ORR
55.8% vs 29.5%

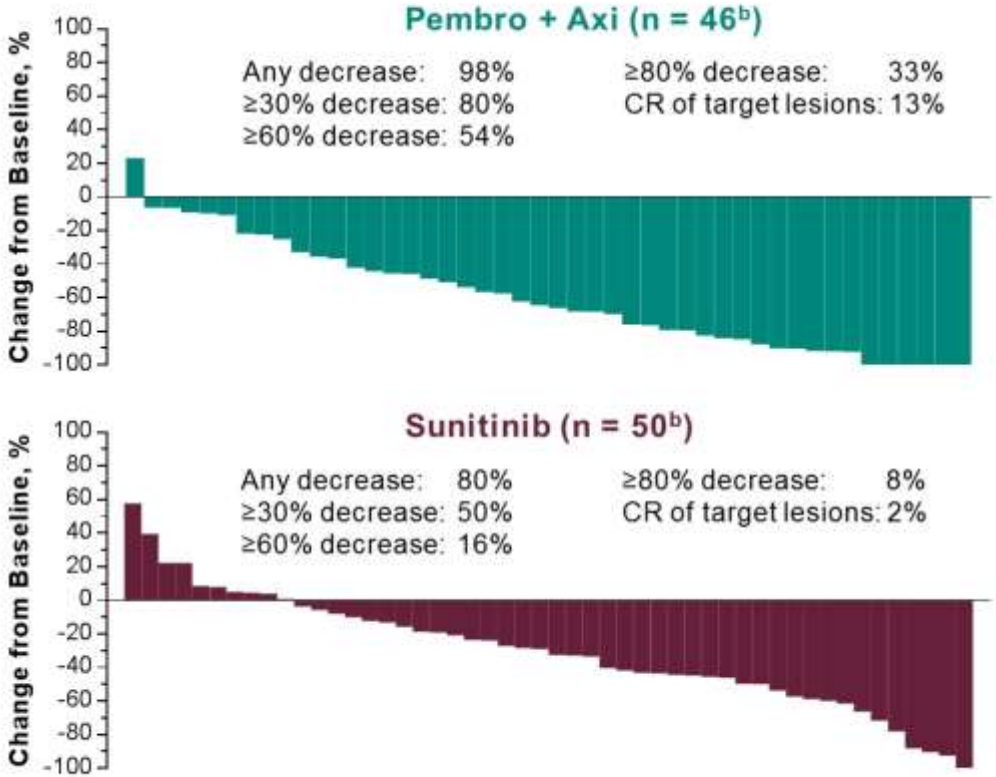


Data cutoff date: Aug 24, 2018.

Presented By Brian Rini at 2019 ASCO Annual Meeting

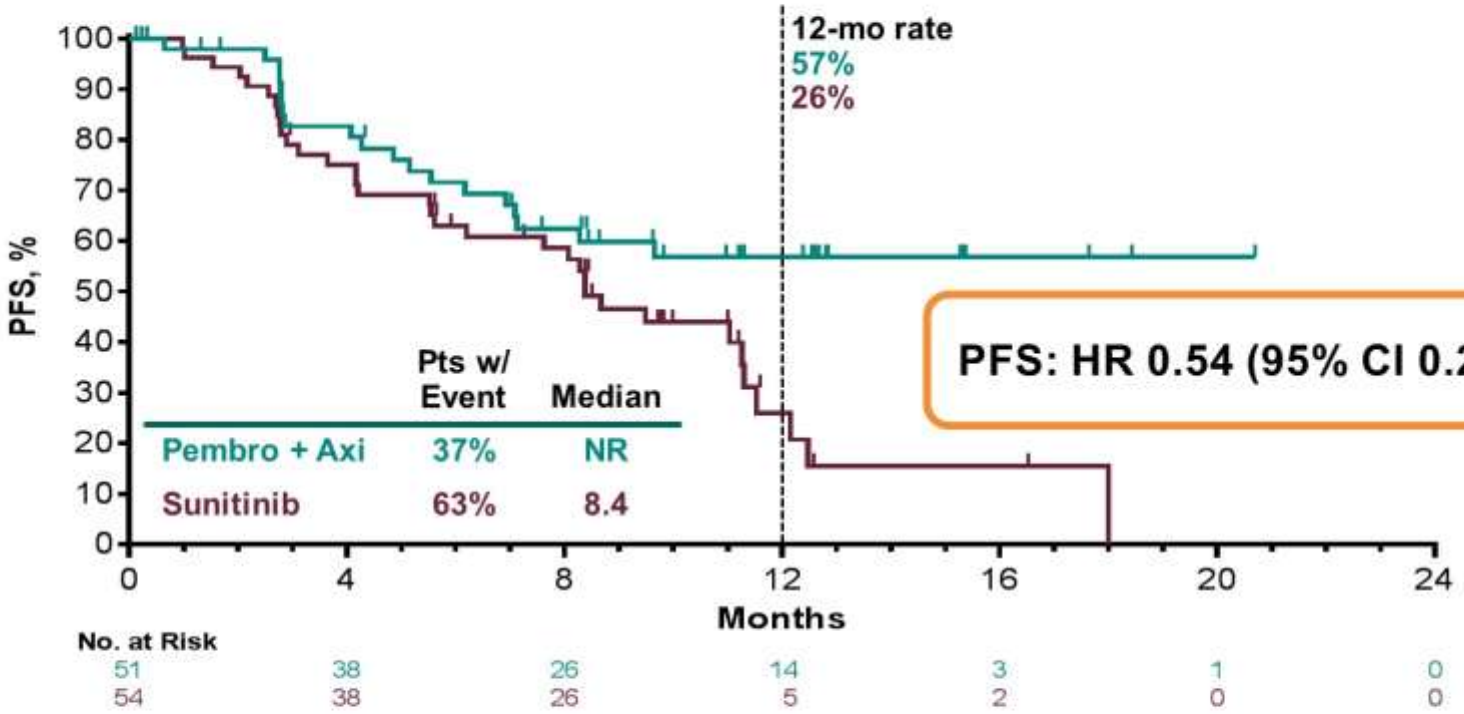
Response: Presence of Sarcomatoid Features[a]





[a]Among the 578 participants with known status assessed by local pathology review and as indicated on the eCRF. [b]Pts with ≥1 measurable lesion per RECIST v1.1 by BICR at baseline and ≥1 post-baseline imaging assessment evaluable per RECIST v1.1 by BICR. Data cutoff date: Aug 24, 2018.

PFS: Presence of Sarcomatoid Features[a]



PFS: HR 0.54 (95% CI 0.29–1.00)

OS: HR 0.58 (95% CI 0.21–1.59); median NR in either arm[b]

[a]Among the 578 participants with known status assessed by local pathology review and as indicated on the eCRF. [b]Pts who died: 16% in the pembro + axi arm, 20% in the sunitinib arm. Data cutoff date: Aug 24, 2018.

JAVELIN Renal 101: study design

Key eligibility criteria

- Treatment-naive aRCC with a clear cell component
- ≥ 1 measurable lesion as defined by RECIST v1.1
- Tumor tissue available for PD-L1 staining
- ECOG PS 0 or 1

Stratification

- ECOG PS (0 vs 1)
- Geographic region (USA vs Canada/Western Europe vs ROW)

N = 886

R 1:1

Avelumab 10 mg/kg IV Q2W + Axitinib 5 mg PO BID (6-week cycle)

Sunitinib 50 mg PO QD (4 weeks on, 2 weeks off)

- **Primary objective**
  - To demonstrate the superiority of avelumab + axitinib compared with sunitinib for either PFS or OS in patients with PD-L1+ tumors

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

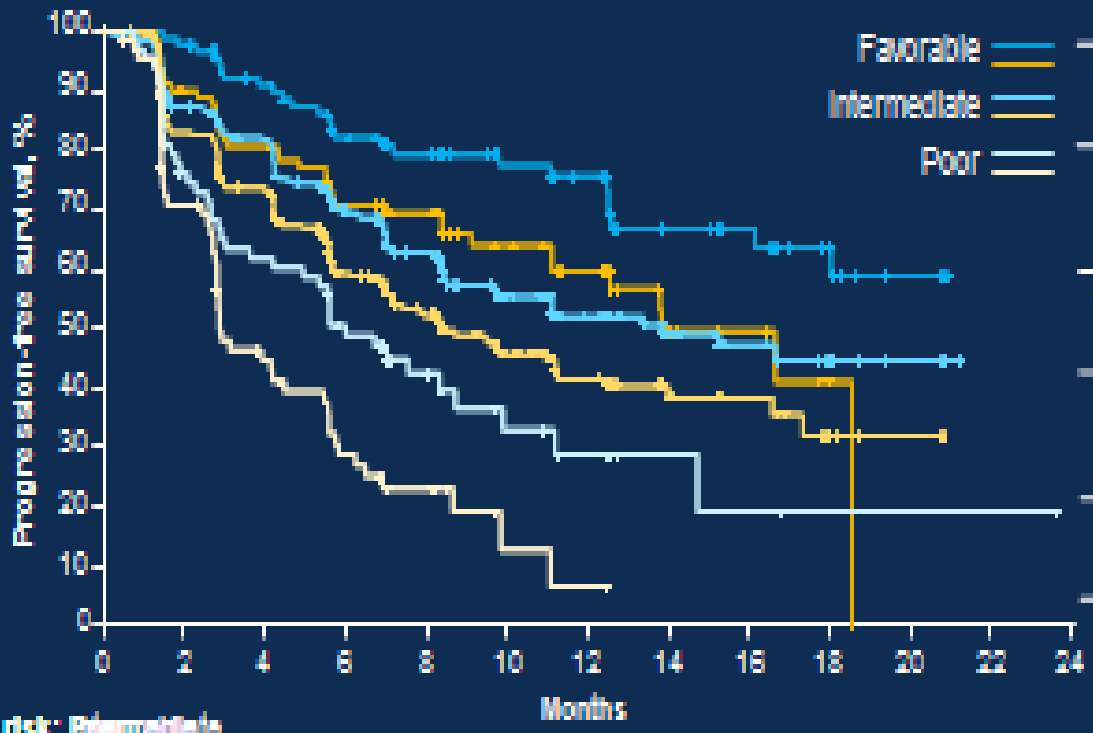
Baseline characteristics in the overall population

Characteristic	Overall population (N = 886) Avelumab + axitinib (N = 442)	Sunitinib (N = 444)
Median age, years	62	61
Male, %	72	78
Prior nephrectomy, %	80	80
ECOG PS, %		
0/1	63/37	63/37
IMDC prognostic risk, %*		
Favorable	21	22
Intermediate/poor	61/16	62/16
MSKCC prognostic risk, %†		
Favorable	22	23
Intermediate/poor	64/12	66/10
Geographic region, %		
United States	29	29
Canada/Western Europe	29	29
Rest of the world	42	42

Characteristic	Overall population (N = 886) Avelumab + axitinib (N = 442)	Sunitinib (N = 444)
BMI, %		
< 25	32	29
≥ 25	67	70
Smoking status, %		
Never	50	48
Current/former	50	52
RECIST-defined tumor sites at baseline per Independent review, %		
0	3	4
1	41	39
2	34	34
3	15	18
≥ 4	8	5

BMI, body mass index; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; MSKCC, Memorial Sloan Kettering Cancer Center.
Values may not sum to 100% due to rounding. *Not reported in < 1% of patients. †Not reported in < 5% of patients.

PFS per IRC in IMDC prognostic risk groups in the overall population



Median PFS (95% CI), months	
Avelumab + axitinib	NE (18.1, NE)
Sunitinib	13.8 (11.1, 18.8)
Unstratified HR, 0.54 (95% CI: 0.321, 0.907)	

Median PFS (95% CI), months	
Avelumab + axitinib	13.8 (8.7, NE)
Sunitinib	8.4 (7.0, 11.2)
Unstratified HR, 0.74 (95% CI: 0.570, 0.960)	

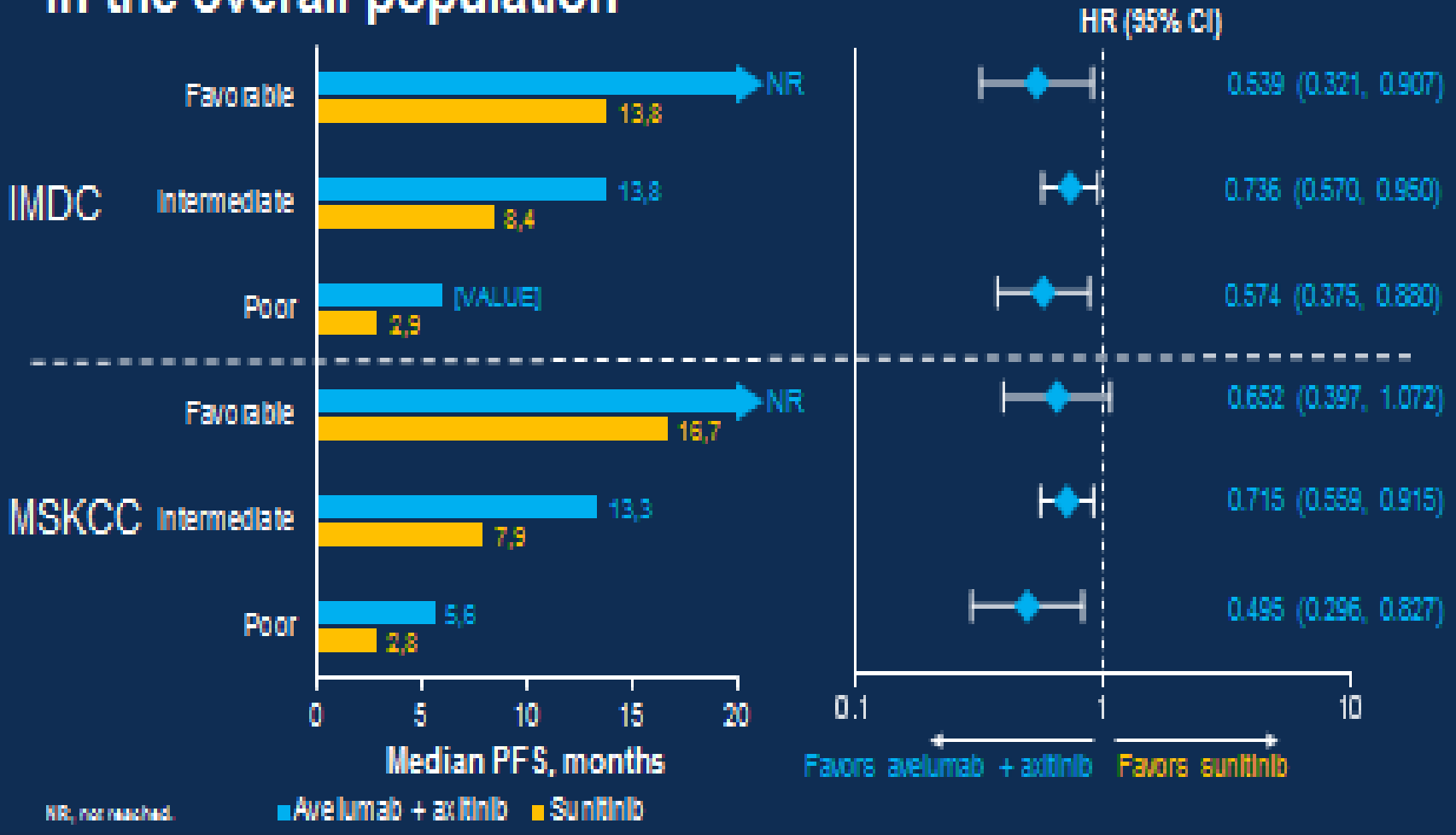
Median PFS (95% CI), months	
Avelumab + axitinib	8.0 (5.6, 8.7)
Sunitinib	2.9 (2.7, 5.5)
Unstratified HR, 0.67 (95% CI: 0.376, 0.889)	

JAVELIN Renal 101 efficacy summary[1]

	PD-L1+ group (N = 560)		Overall population (N = 886)	
	Avelumab + axitinib (N = 270)	Sunitinib (N = 290)	Avelumab + axitinib (N = 442)	Sunitinib (N = 444)
PFS per IRC				
Median, months	13.8	7.2	13.8	8.4
95% CI	11.1, NE	5.7, 9.7	11.1, NE	6.9, 11.1
Benefit vs sunitinib (HR; P value)	0.61; P < .0001	-	0.69; P = .0001	-
ORR per IRC, %	55.2	25.5	51.4	25.7
95% CI	49.0, 61.2	20.6, 30.9	46.6, 56.1	21.7, 30.0
PFS per investigator assessment				
Median, months	13.3	8.2	12.5	8.4
95% CI	9.8, NE	6.9, 8.5	11.1, 15.2	8.2, 9.7
Benefit vs sunitinib (HR; P value)	0.51; P < .0001	-	0.64; P < .0001	-
ORR per investigator assessment, %	61.9	29.7	55.9	30.2
95% CI	55.8, 67.7	24.5, 35.3	51.1, 60.6	25.9, 34.7

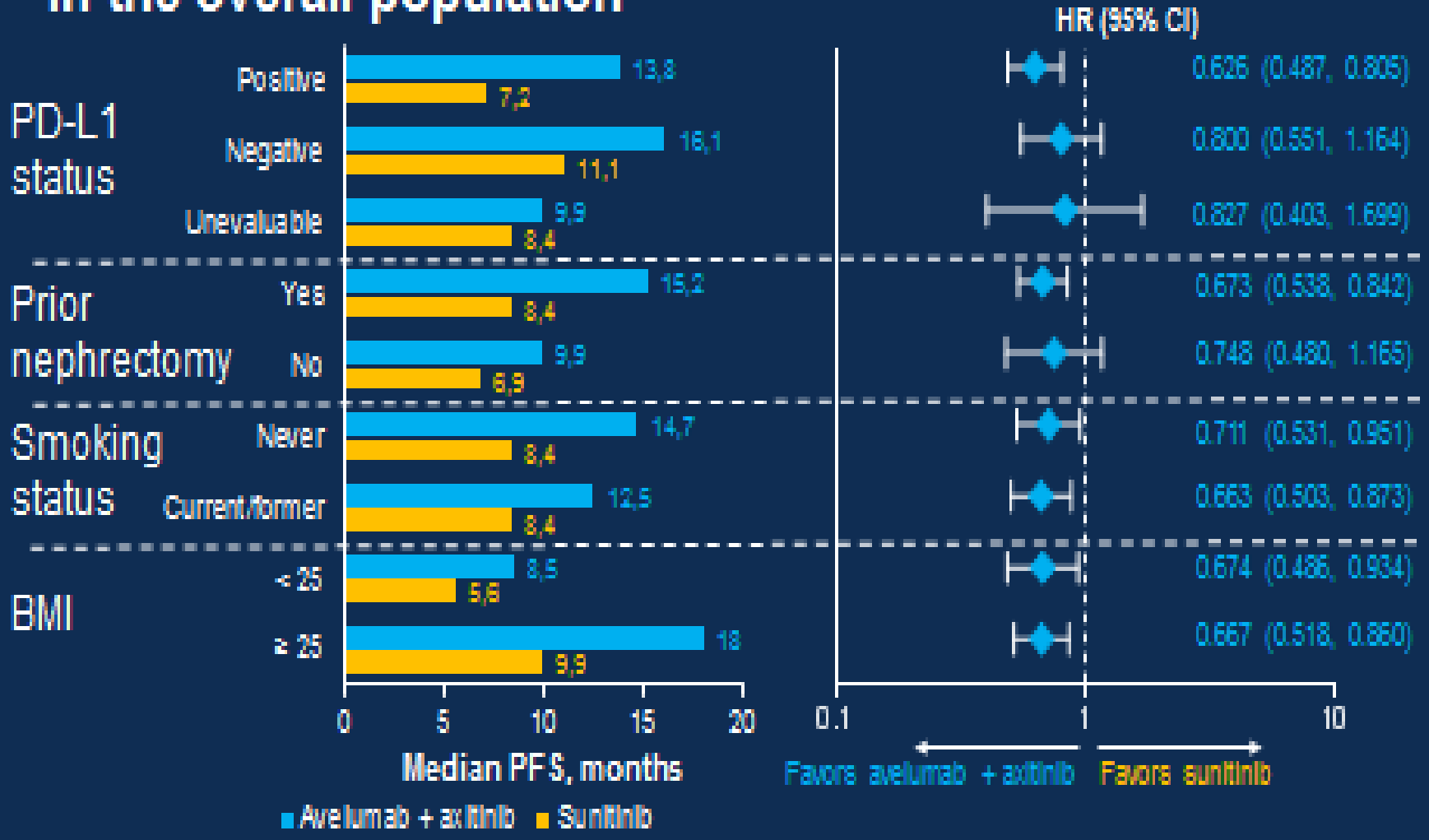
IRC, independent review committee; NE, not estimable; ORR, objective response rate.
Data cutoff date: June 30, 2018; median follow-up, 12.9 months (avelumab + axitinib) and 11.2 months (sunitinib).
1. Motzer RJ, et al. ESMO 2018;ESMO_PR.

PFS per IRC in prognostic risk groups in the overall population



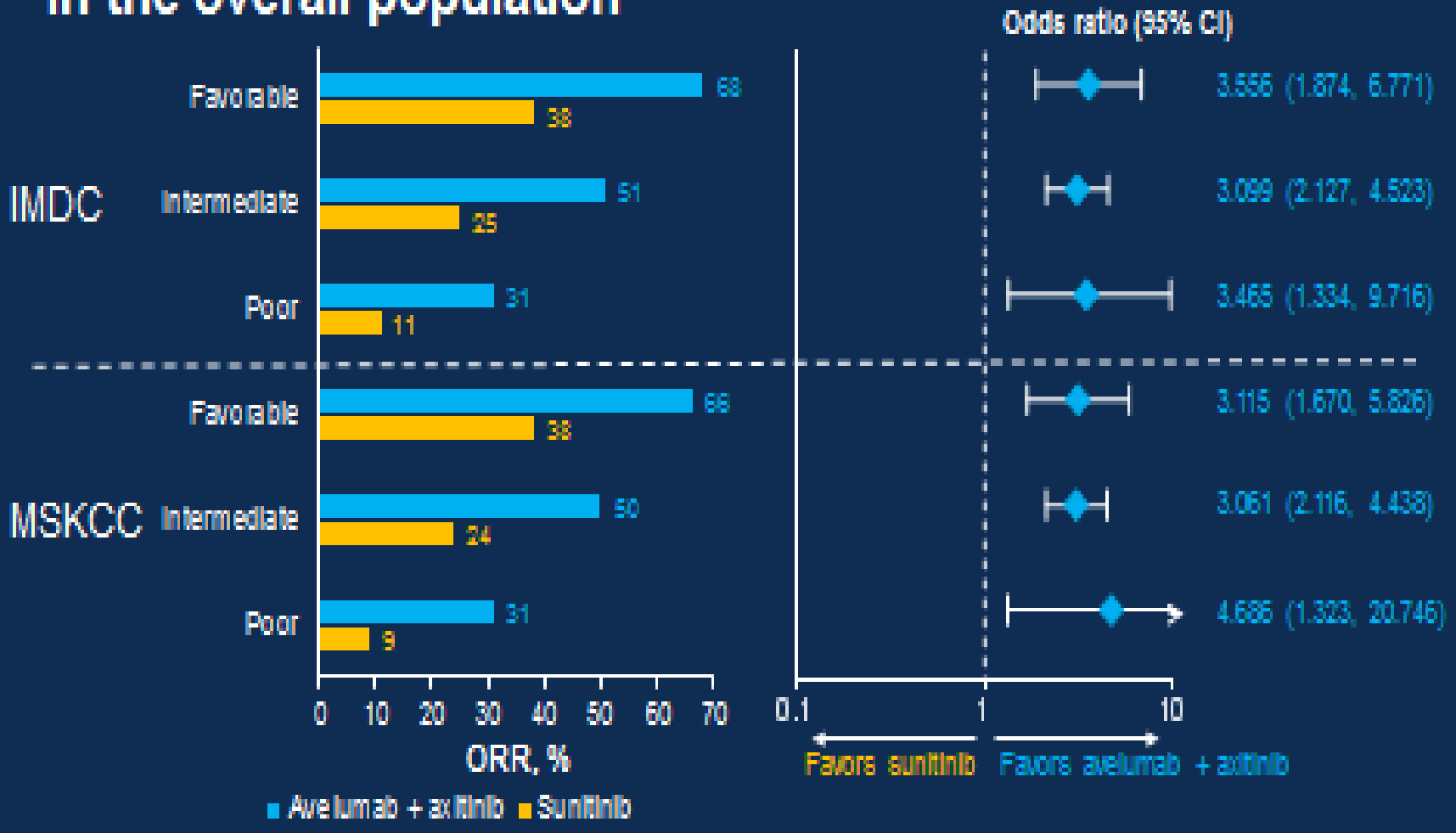
Presented by: Toni K. Choueiri, MD

PFS per IRC in other key subgroups in the overall population



Presented by: Toni K. Choueiri, MD

ORR per IRC in prognostic risk groups in the overall population



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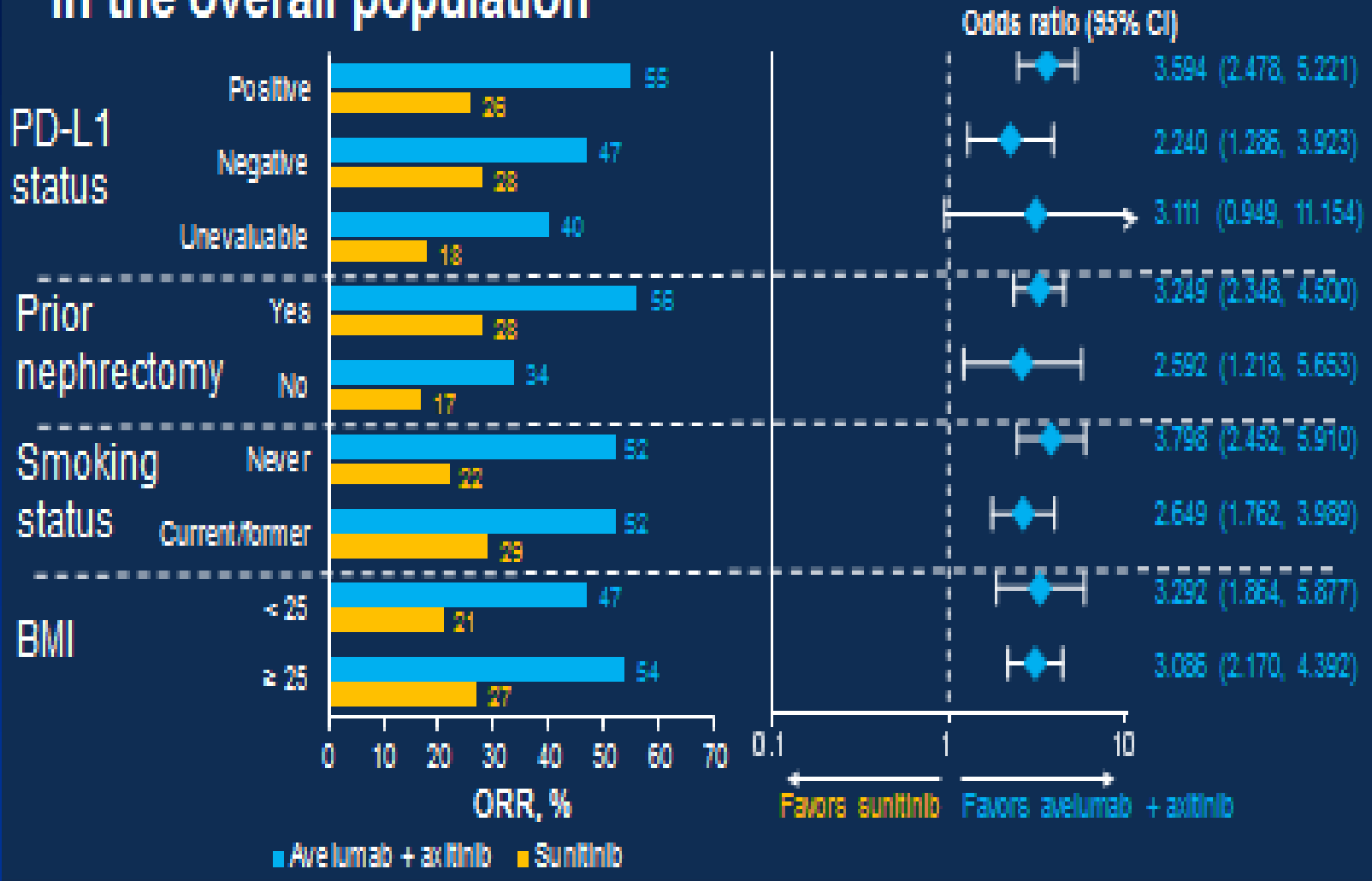
ORR per IRC in other key subgroups in the overall population



TRAEs in all treated patients (N = 873)[1]

	Avelumab + axitinib (N = 434)		Sunitinib (N = 438)	
	All grades	Grade 3 (4)	All grades	Grade 3 (4)
All TRAEs, %	86	61 (4)	88	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 ≥ 5% of patients are shown. * No events occurred in ≥ 1% of patients. † Grade 5 events occurred in 2 patients in the avelumab + axitinib arm (myocarditis, necrotizing pancreatitis, sudden death; n = 1 each); in 1 patient in the sunitinib arm (intestinal perforation).

1. Motzer RJ, et al. ESMO 2018;LBA6_PR.

Subsequent anticancer therapy in the overall population

	Overall population (N = 888)	
	Avelumab + axitinib (N = 442)	Sunitinib (N = 444)
Patients with ≥1 type of follow-up anticancer therapy, n (%)	100 (22.6)	180 (40.5)
Drug therapy	92 (20.8)	174 (39.2)
Radiotherapy	26 (5.9)	36 (8.1)
Surgery	8 (1.8)	16 (3.6)

	Overall population (N = 888)	
	Avelumab + axitinib (N = 442)	Sunitinib (N = 444)
Follow-up anticancer drug therapies, n (%)		
ICI		
Nivolumab	14 (3.2)	107 (24.1)
Ipilimumab	3 (0.7)	7 (1.6)
Atezolizumab	0	2 (0.5)
Durvalumab	0	6 (1.4)
Pembrolizumab	0	1 (0.2)
TKI/VEGFI		
Cabozantinib	42 (9.5)	28 (6.3)
Axitinib	15 (3.4)	17 (3.8)
Sunitinib	15 (3.4)	23 (5.2)
Lenvatinib	11 (2.5)	16 (3.6)
Pazopanib	7 (1.6)	12 (2.7)
Bevacizumab	3 (0.7)	1 (0.2)
mTORI		
Everolimus	19 (4.3)	19 (4.3)
Investigational drug	2 (0.5)	23 (5.2)

- In the sunitinib arm, 277 patients discontinued treatment
  - Of the 174 patients who received subsequent anticancer drug therapy, 116 of 174 (66.7%) were known to have been treated with an anti–PD-1/PD-L1 agent

ICI, immune checkpoint inhibitor; mTORI, mechanistic target of rapamycin kinase inhibitor; VEGFI, vascular endothelial growth factor inhibitor.

Biomarker analyses from JAVELIN Renal 101: avelumab + axitinib vs sunitinib in advanced renal cell carcinoma

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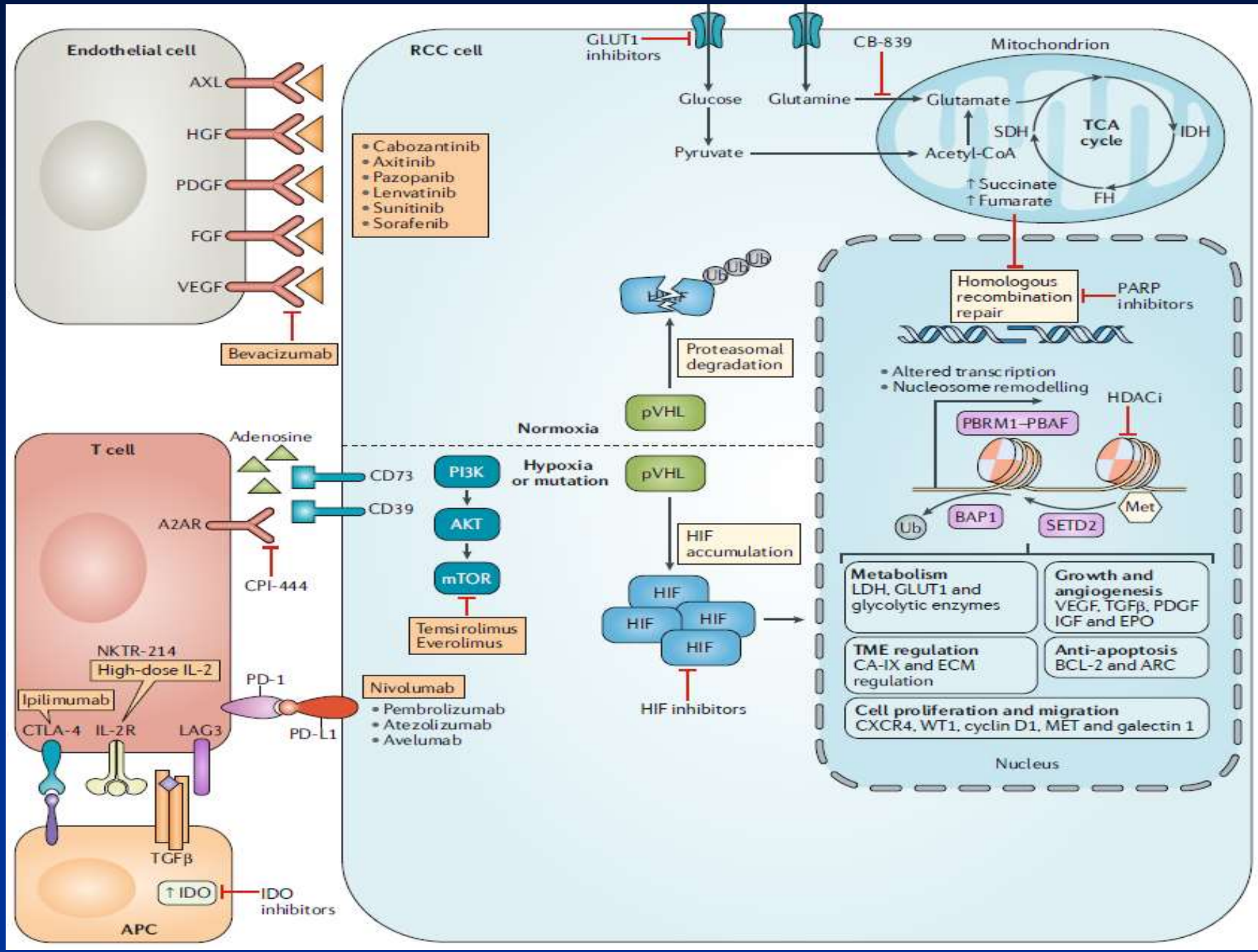

Endothelial cell
AXL
HGF
PDGF
FGF
VEGF
Bevacizumab
RCC cell
GLUT1 inhibitors
Glucose
Glutamine
CB-839
Mitochondrion
Glutamate
SDH
TCA cycle
IDH
Pyruvate
Acetyl-CoA
↑ Succinate
↑ Fumarate
FH
• Cabozantinib
• Axitinib
• Pazopanib
• Lenvatinib
• Sunitinib
• Sorafenib
Ub
Proteasomal degradation
pVHL
Normoxia
Homologous recombination repair
PARP inhibitors
• Altered transcription
• Nucleosome remodelling
HDACi
PBRM1–PBAF
Met
Ub
BAP1
SETD2
T cell
Adenosine
CD73
CD39
A2AR
CPI-444
PI3K
AKT
mTOR
Hypoxia or mutation
pVHL
HIF accumulation
Temsirolimus
Everolimus
HIF
HIF
HIF
HIF
HIF inhibitors
Metabolism
LDH, GLUT1 and glycolytic enzymes
Growth and angiogenesis
VEGF, TGFβ, PDGF IGF and EPO
TME regulation
CA-IX and ECM regulation
Anti-apoptosis
BCL-2 and ARC
Cell proliferation and migration
CXCR4, WT1, cyclin D1, MET and galectin 1
Nucleus
NKTR-214
High-dose IL-2
Ipilimumab
CTLA-4
IL-2R
LAG3
PD-1
PD-L1
Nivolumab
• Pembrolizumab
• Atezolizumab
• Avelumab
TGFβ
↑ IDO
IDO inhibitors
APC

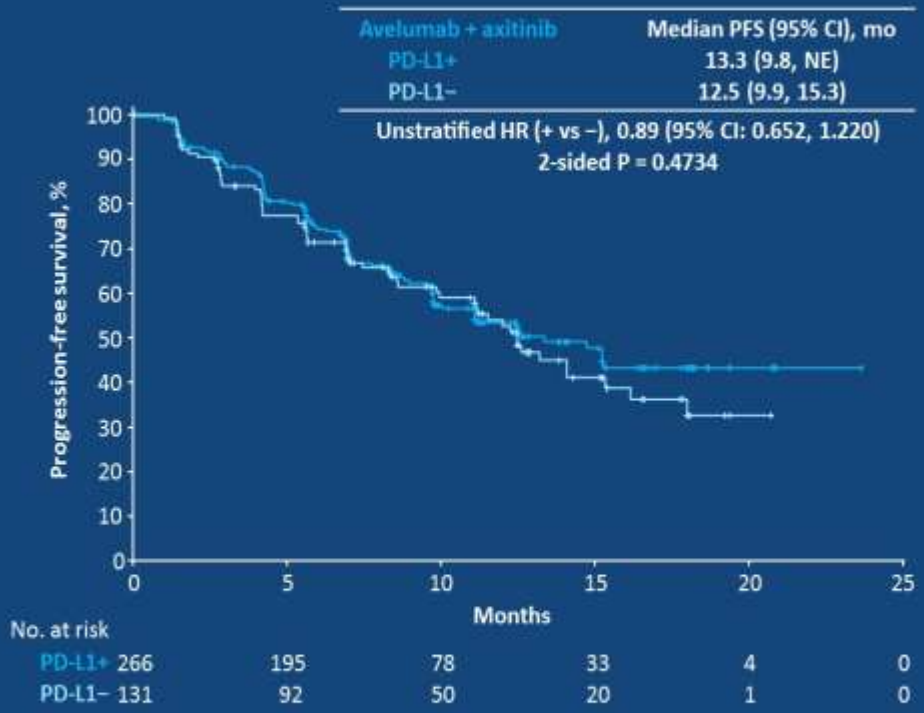
Biomarker assessments and methodology

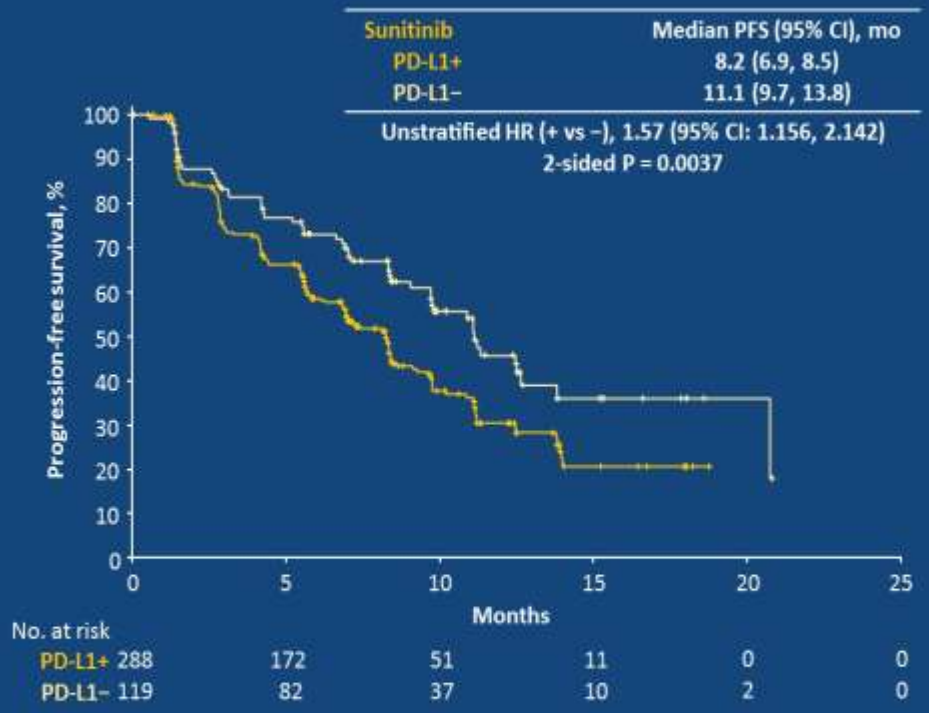
Analysis	Assay	Threshold
PD-L1 expression n=804	• IHC: Ventana SP263	• ≥1% PD-L1+ IC for IHC (+ vs –)
CD8 expression n=795	• IHC: clone C8/144B	• Median value (≥ vs <)
Gene expression profiling n=720	• RNA-seq: Illumina NovaSeq	• Median value (≥ vs <)
Mutations and polymorphisms n=733	• Whole-exome sequencing: Illumina NovaSeq	• Presence of protein-altering somatic mutations • Polymorphisms in Fcγ receptor genes that alter the affinity for IgG1

All analyses were performed on baseline tumor biopsies collected within 1 year of screening and prior to systemic therapy.

IC, immune cell; **IHC**, immunohistochemistry; **RNA-seq**, RNA sequencing.

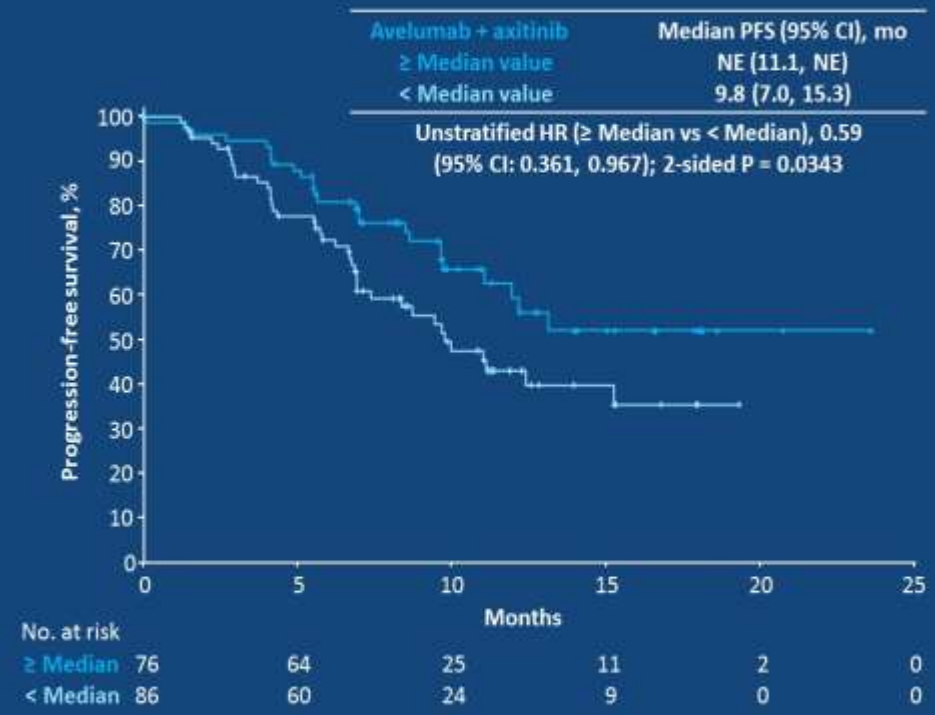
PFS according to PD-L1 IHC

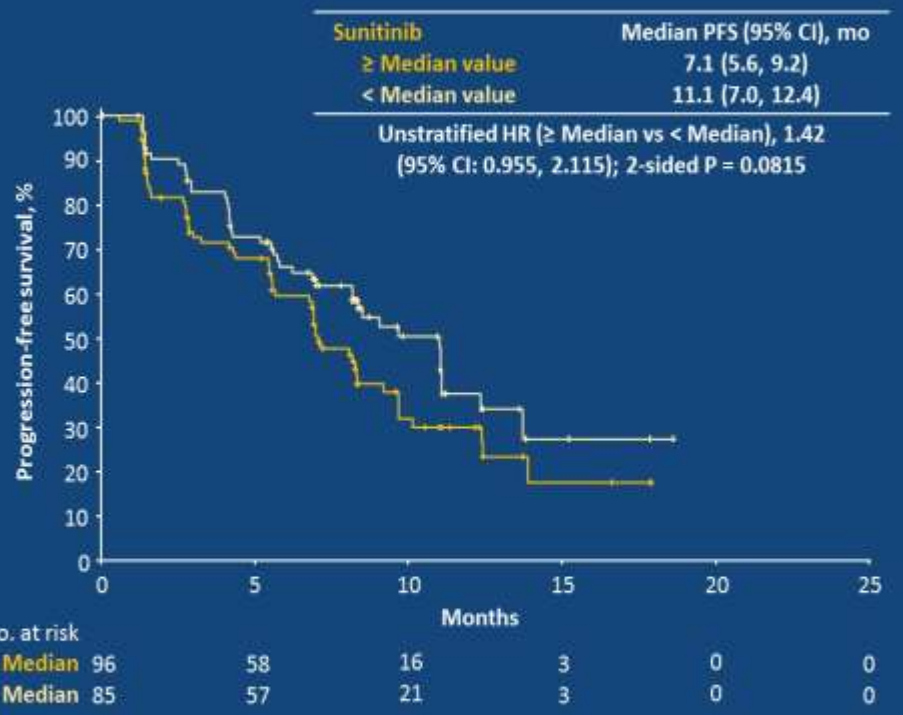




IHC, immunohistochemistry; NE, not estimable; PFS, progression-free survival.

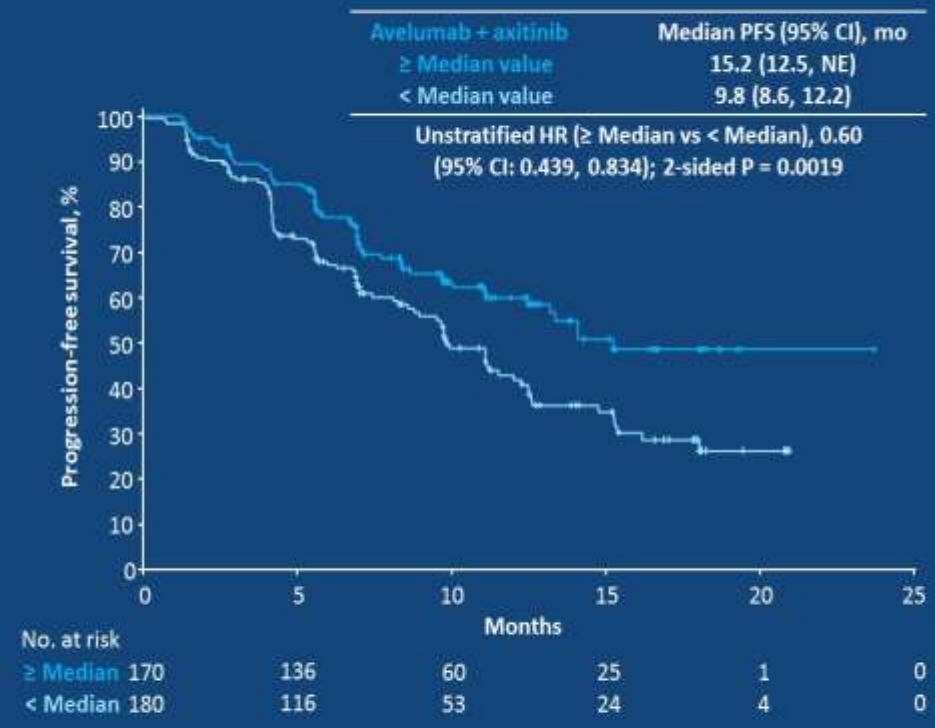
PFS according to CD8+ cells at the invasive margin (IHC)

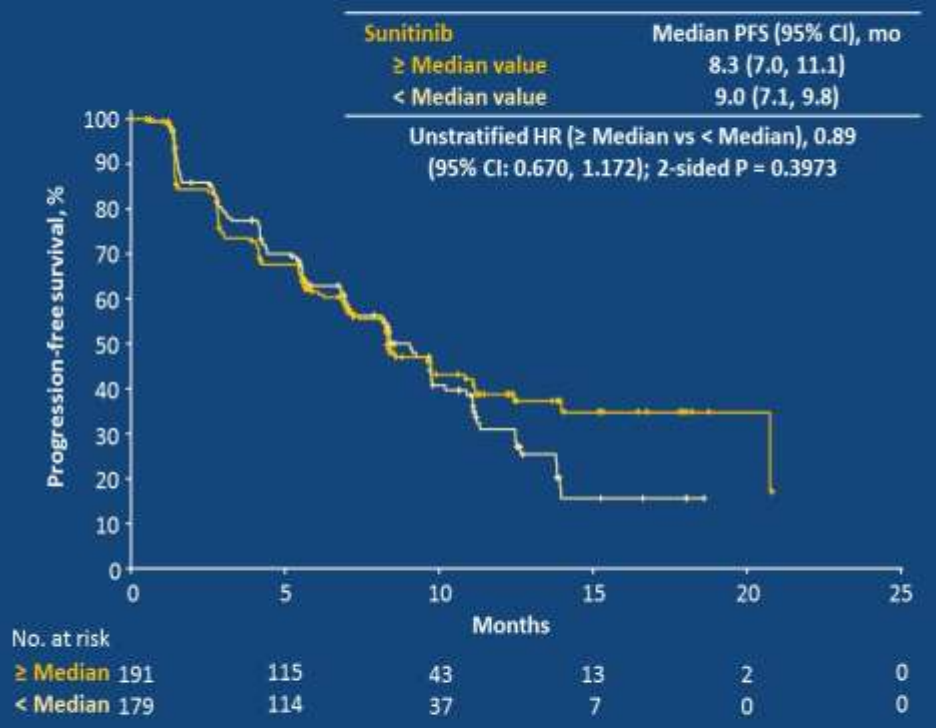




IHC, immunohistochemistry; NE, not estimable; PFS, progression-free survival.

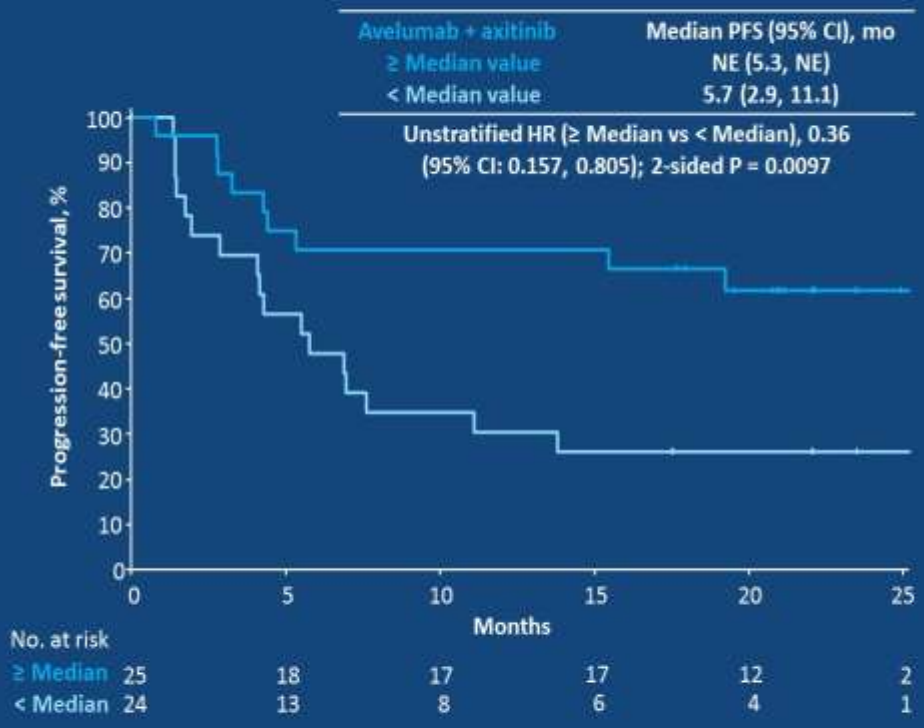
PFS according to 26-gene JAVELIN Renal 101 signature





NE, not estimable; PFS, progression-free survival.

Verification of the 26-gene JAVELIN Renal 101 signature in an independent data set



The 26-gene JAVELIN Renal 101 signature also enriched for responders to avelumab + axitinib when tested in an independent data set derived from the single-arm, phase 1b JAVELIN Renal 100 clinical trial[1]


THE LANCET
Oncology

Articles

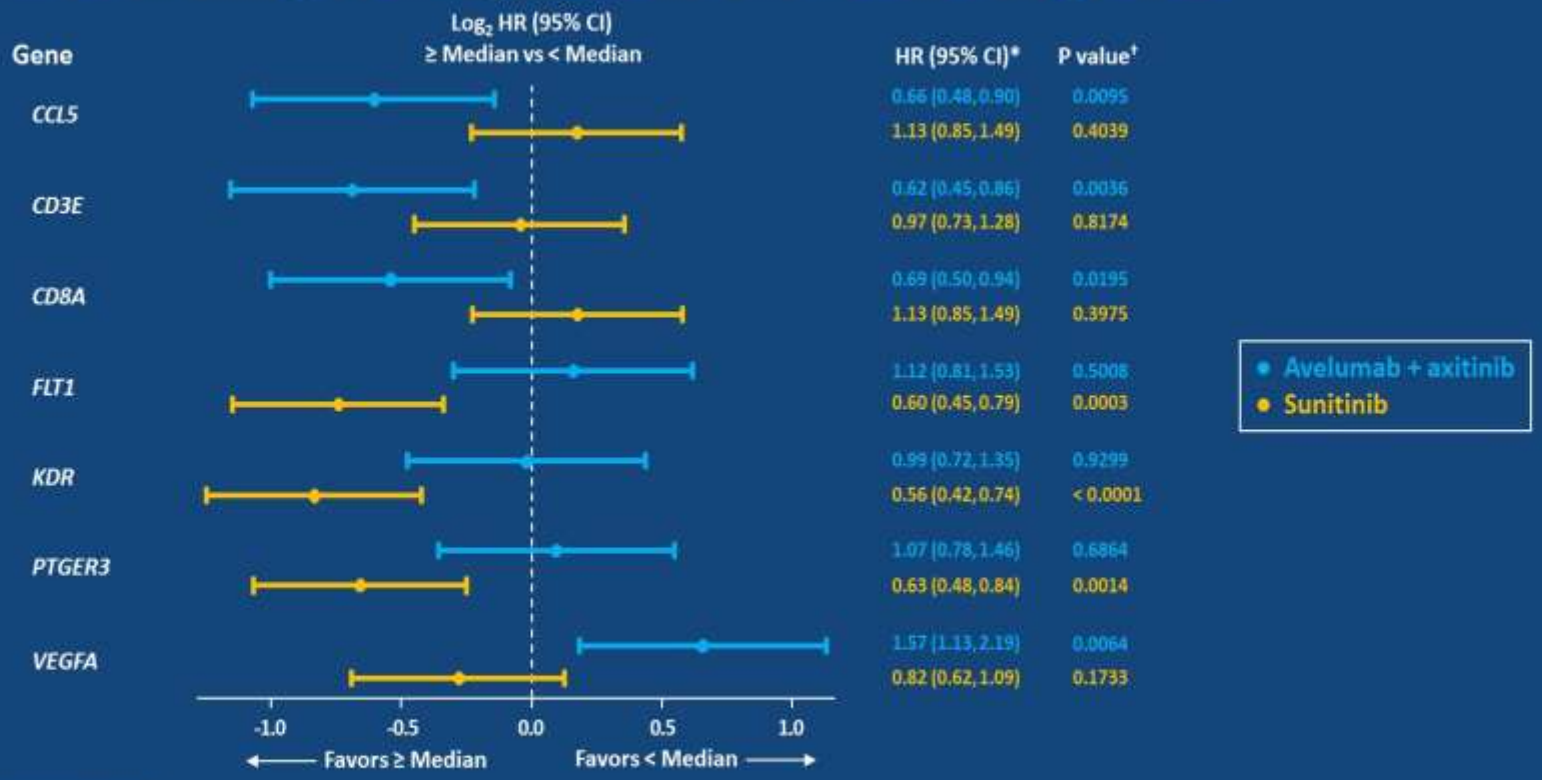
Preliminary results for avelumab plus axitinib as first-line therapy in patients with advanced clear-cell renal-cell carcinoma (JAVELIN Renal 100): an open-label, dose-finding and dose-expansion, phase 1b trial

Toni K Choueiri, James Larkin, Motohiro Oya, Fiona Thistlethwaite, Marcello Martignoni, Paul Nathan, Thomas Powles, David McDermott, Paul B Robbins, David D Chism, Daniel Cho, Michael B Atkins, Michael S Gordon, Sumati Gupta, Hirotsugu Uemura, Yoshihiko Tomita, Anna Compagnoni, Camilla Foust, Alessandro di Pietro, Brian I Rini

NE, not estimable; PFS, progression-free survival.

1. Choueiri TK, et al. Lancet Oncol. 2018;19(4):451-60.

PFS according to expression of select genes

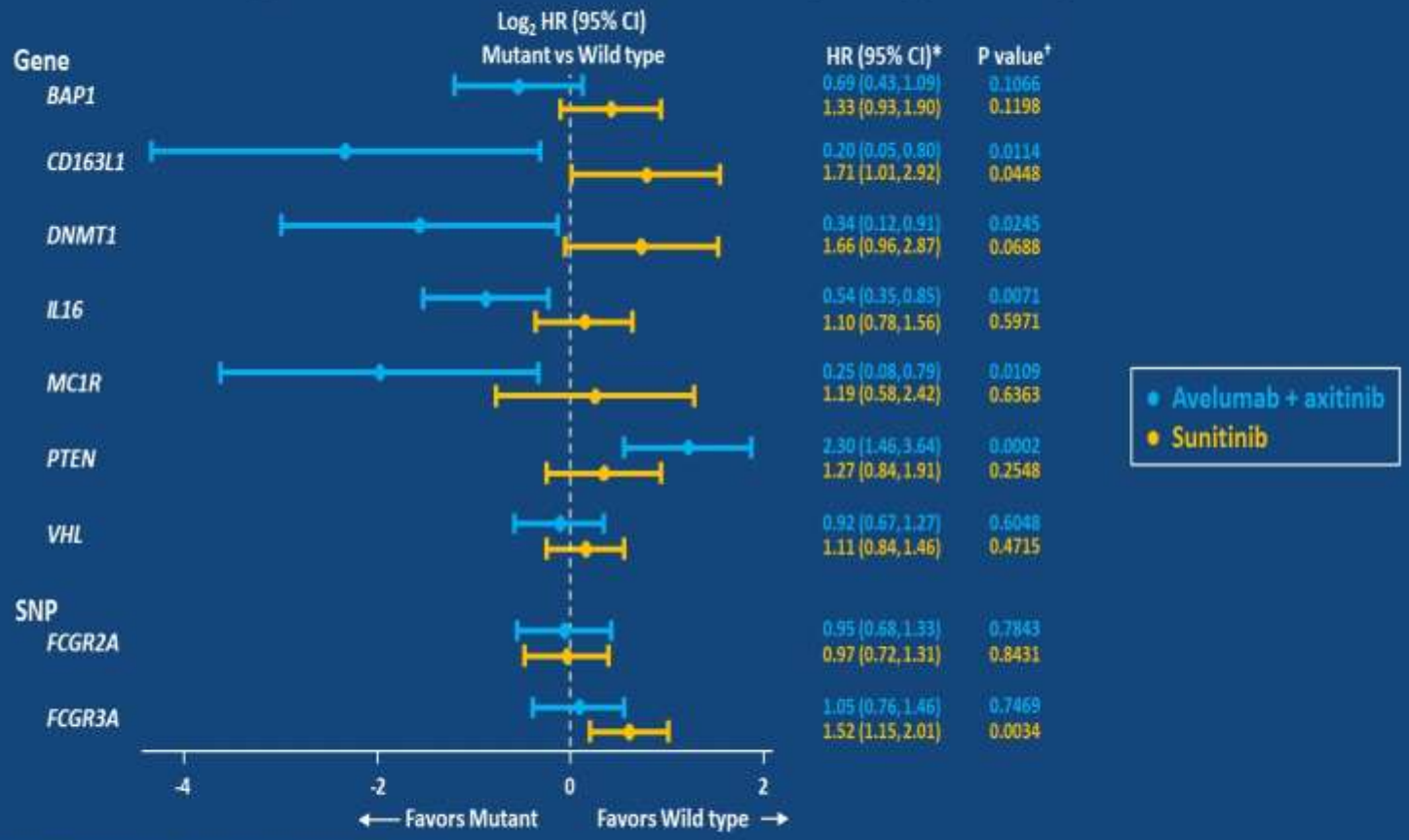


PFS, progression-free survival.

* Cox proportional hazards model with < Median as the reference group was used to calculate HR and 95% CI. An HR < 1 indicates better survival in the ≥ Median group, while an HR > 1 indicates better survival in the < Median group.

† Log-rank 2-sided test was performed to compare between overall median cutoff groups.

PFS according to mutations and polymorphisms



PFS, progression-free survival; SNP, single nucleotide polymorphism.

* Cox proportional hazards model with Wild type as the reference group was used to calculate HR and 95% CI. An HR < 1 indicates better survival in the Mutant group, while an HR > 1 indicates better survival in the Wild type group.

† Log-rank 2-sided test was performed to compare between Wild type/Mutant groups.

Summary

- PD-L1 expression did not distinguish PFS benefit in the avelumab + axitinib arm. However, in the sunitinib arm, patients with PD-L1+ tumors showed reduced PFS
- Patients whose tumors contained greater numbers of CD8+ cells had extended PFS in the combination arm and reduced PFS in the sunitinib arm
- The novel JAVELIN Renal 101 signature comprised immune-related genes most significantly associated with PFS in the avelumab + axitinib arm and was verified in an independent data set (single-arm, phase 1b JAVELIN Renal 100 trial of avelumab + axitinib[1])
- Elevated expression of the published angiogenesis gene signature and other related genes was associated with improved PFS in the sunitinib arm, but did not differentiate PFS in the avelumab + axitinib arm
- Significant treatment arm–specific differences in PFS were observed relative to wild type when mutations in genes such as *CD163L1*, *DNMT1*, or *PTEN* were present

IHC, immunohistochemistry; **PFS**, progression-free survival; **TMB**, tumor mutational burden.

1. Choueiri TK, et al. Lancet Oncol. 2018;19(4):451-60.

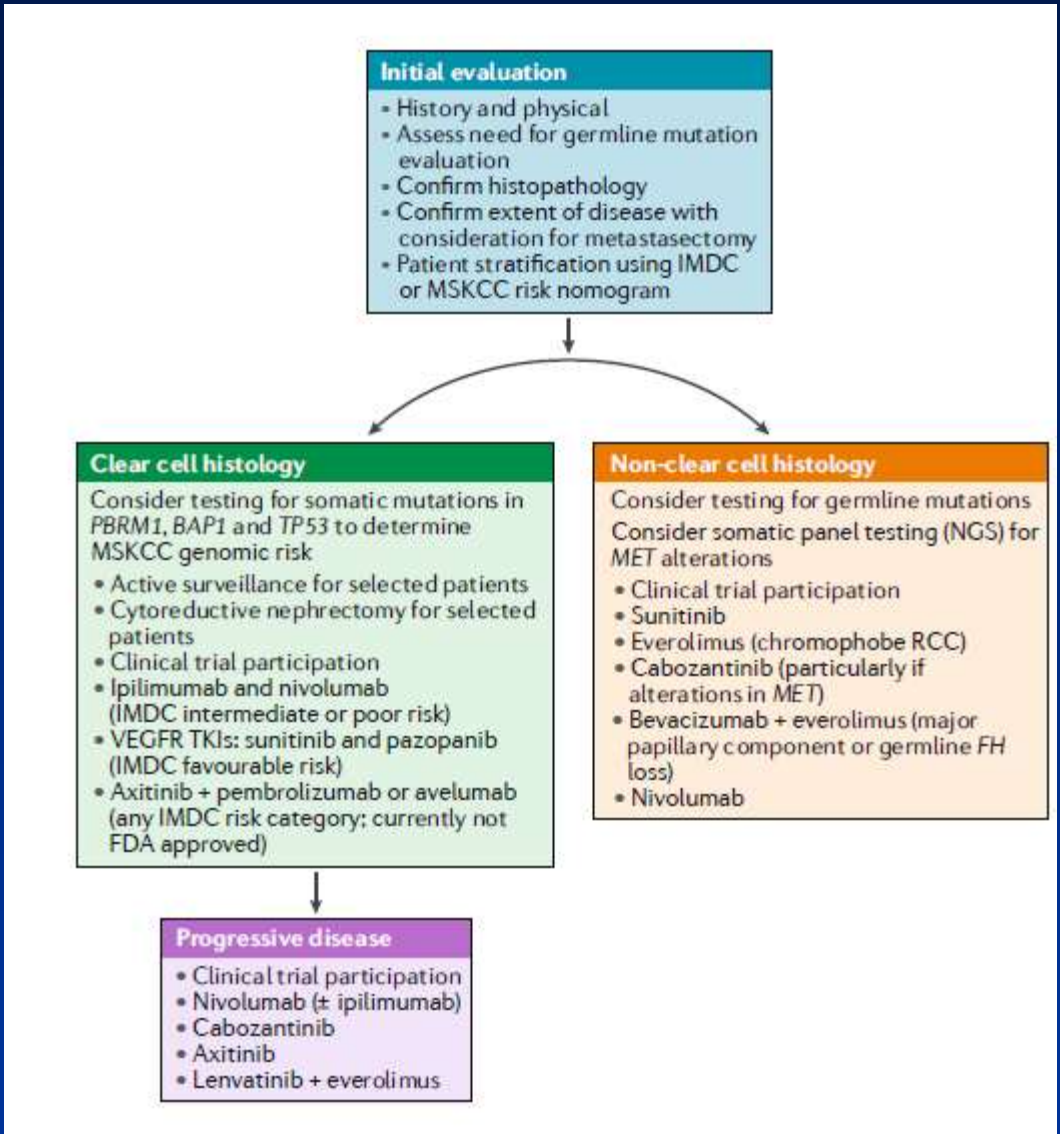
Combination Therapy as First-Line Treatment in Metastatic Renal-Cell Carcinoma

Bernard Escudier, M.D.

Table 1. Comparisons among Trials of Combination Therapy vs. Sunitinib for Patients with Metastatic Renal-Cell Carcinoma.*

Variable	Trial of Pembrolizumab plus Axitinib vs. Sunitinib[5] (N=861)	Trial of Avelumab plus Axitinib vs. Sunitinib[4] (N=886)	Trial of Nivolumab plus Ipilimumab vs. Sunitinib[3] (N=1096)
IMDC prognostic risk (% of patients)†			
Favorable	31.2	21.4	23
Intermediate	56.2	61.8	61
Poor	12.6	16.2	17
Quantifiable tumor PD-L1 expression ≥1% (% of patients)	60.5	63.2	24
Overall survival			
Hazard ratio for death	0.53	0.78	0.68
CI	95% CI, 0.38–0.74	95% CI, 0.55–1.08	99.8% CI, 0.49–0.95
P value	<0.0001	0.14	<0.001
Median progression-free survival (mo)			
Combination therapy group	15.1	13.8	12.4
Sunitinib group	11.1	8.4	12.3
Objective response in combination-therapy group (% of patients)	59.3	51.4	39.0
Complete response in combination-therapy group (% of patients)	5.8	3.4	10.2
Median follow-up (mo)	12.8	11.6	25.2

Possibile algoritmo decisionale



Nature Clin Oncol Rev 2019

Risk Factor Criteria for Advanced RCC

Parameters	
Karnofsky PS	<80%
Time from diagnosis to treatment	<12 mos
Hemoglobin	<LLN
Calcium	>ULN
Neutrophil count	>ULN
Platelet count	>ULN

Risk Level	Number of Factors
Favorable	0
Intermediate	1-2
Poor	≥3

LLN=lower limit of normal; ULN=upper limit of normal.

Heng. *J Clin Oncol.* 2009;27:5794.

Linee guida EAU 2019

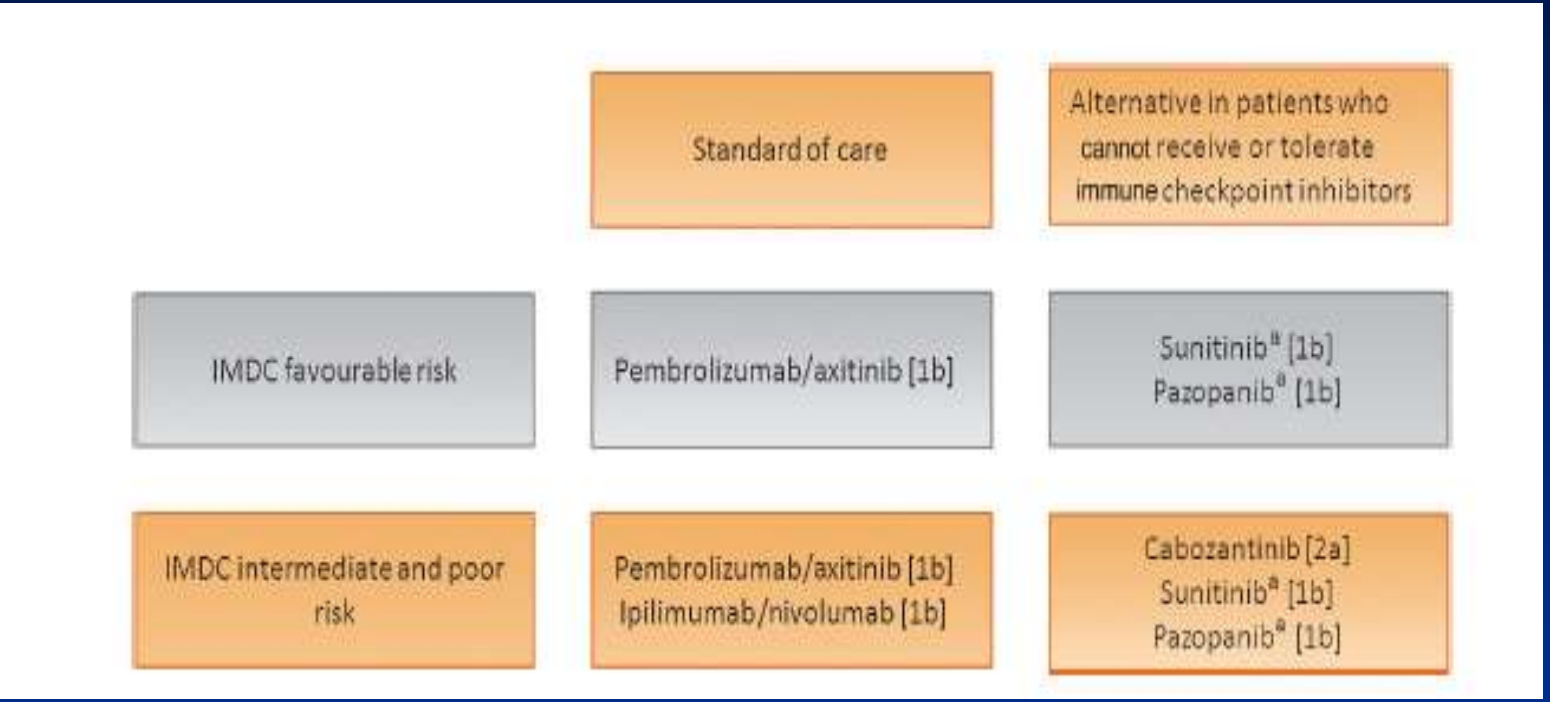
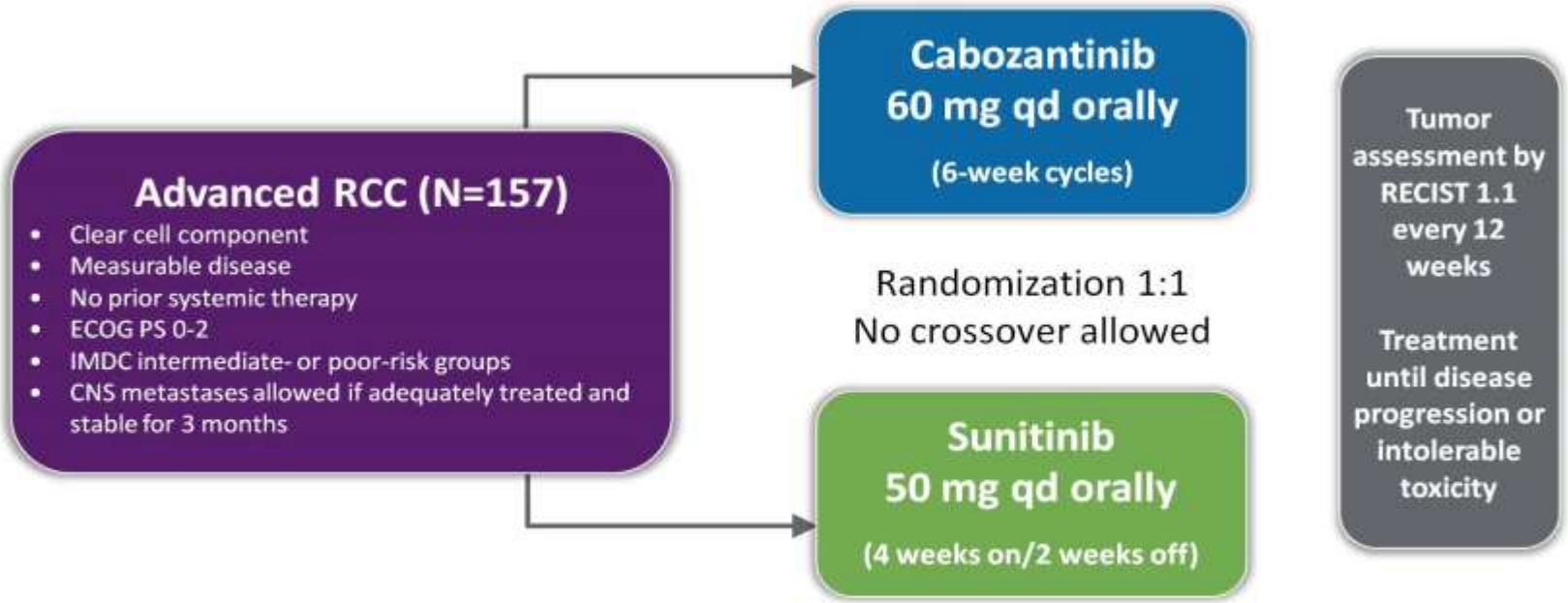


Table 2 – New recommendations for front-line treatment of metastatic clear-cell RCC

Recommendation	Strength rating
Offer pembrolizumab plus axitinib to treatment-naïve patients with any IMDC risk metastatic clear-cell RCC.	Strong
Offer ipilimumab plus nivolumab to treatment-naïve patients with IMDC intermediate- and poor-risk metastatic clear-cell RCC.	Strong
Offer sunitinib and pazopanib to treatment-naïve patients with IMDC favourable-, intermediate-, and poor-risk metastatic clear-cell RCC who cannot receive or tolerate immune checkpoint inhibition.	Strong
Offer cabozantinib to treatment-naïve patients with IMDC intermediate- and poor-risk metastatic clear-cell RCC who cannot receive or tolerate immune checkpoint inhibition.	Strong[a]

IMDC = International Metastatic Renal Cell Carcinoma Database Consortium; RCC = renal cell carcinoma.
[a] While this is based on a randomised phase II trial, cabozantinib (weak) looks at least as good as sunitinib in this population. This justified the same recommendation under exceptional circumstances.

Alliance A031203/CABOSUN: Randomized Phase II Trial of First-line Cabozantinib vs Sunitinib in Intermediate- or Poor-Risk Patients With mRCC[1]



Primary endpoint
- PFS by investigator assessment

Secondary endpoints
- OS, ORR, safety

Stratification
- IMDC risk group[2]: intermediate, poor
- Bone metastases: yes, no

ECOG=Eastern Cooperative Oncology Group; IMDC=International Metastatic Renal Cell Carcinoma Database Consortium; qd=once daily; RECIST=Response Evaluation Criteria in Solid Tumors.

1. Choueiri TK, et al. *J Clin Oncol*. 2017;35:591-597. 2. Heng DY, et al. *J Clin Oncol*. 2009;27:5794-5799.

Conclusioni
Possibili criteri di scelta

- Valutazione multidisciplinare del paziente
- Importanza dei fattori prognostici
- Sedi di malattia/urgenza di risposta
- istologia
- Età e comorbidità
- Richiesta del paziente/distanza dal DH
- Valutazione dei costi/indicazioni AIFA
- Possibili sequenze terapeutiche

GRAZIE PER L'ATTENZIONE!