Society for Immunotherapy of Cancer

ADVANCES IN Cancer IMMUNOTHERAPY™

Immunotherapy for the Treatment of Genitourinary Malignancies

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AAEM AMERICAN ACADEMY OF EMERGENCY MEDICINE CHAMPION OF THE EMERGENCY PHYSICIAN

ACCC Association of Community Cancer Centers

HOPA Hematology/Oncology Pharmacy Association

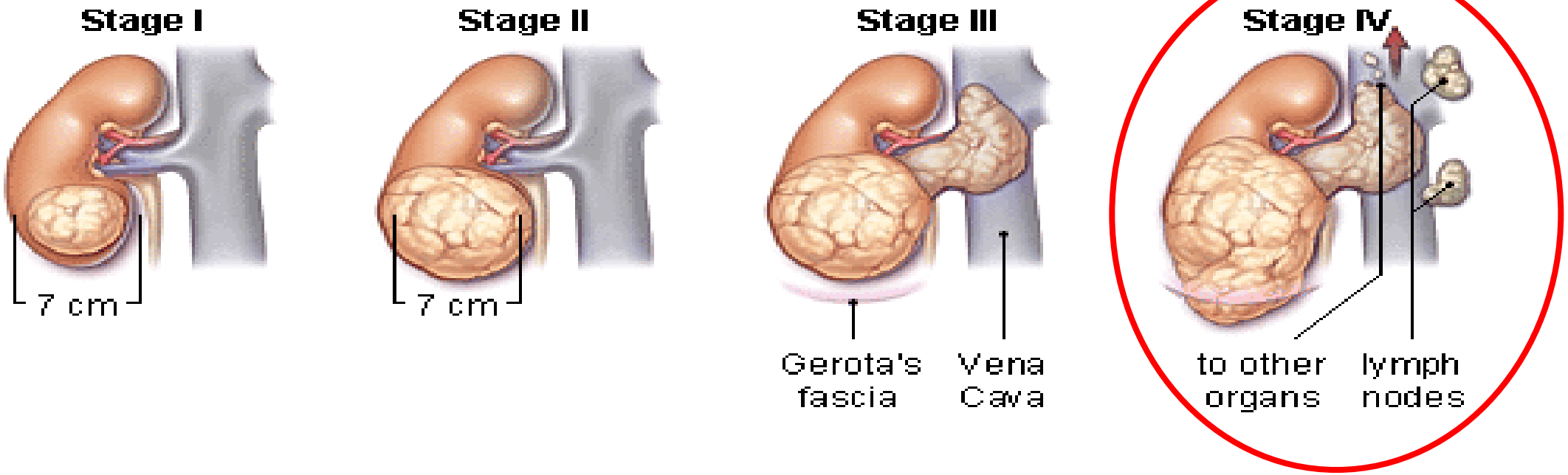
Society for Immunotherapy of Cancer

Michael B. Atkins: Disclosures

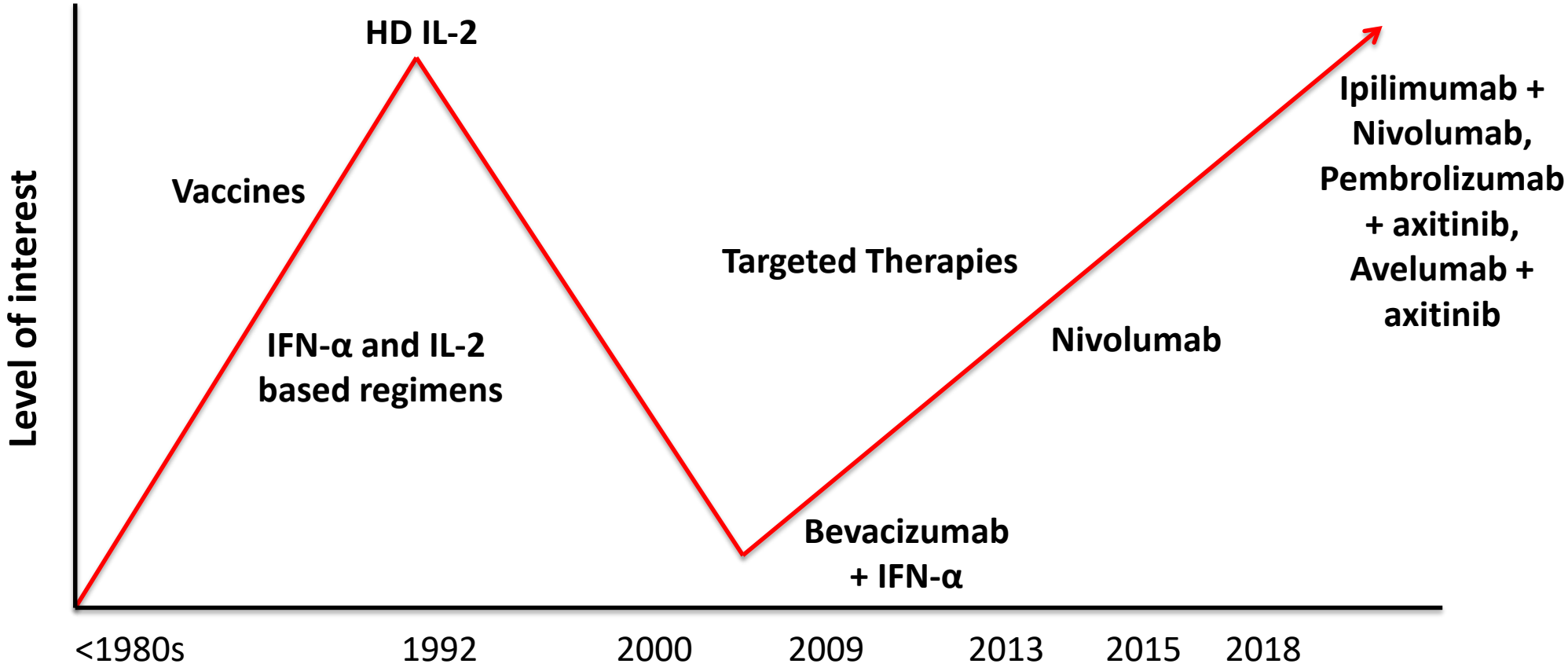
- Consulting Fees:Amgen, Aveo, BMS, Eisai, Exelixis, Genentech, Iovance, Merck, Novartis, Pfizer, Roche, Pyxis, Leads, Werewolf, TRV
- Ownership Interest Less Than 5 Percent: Werewolf, Pyxis
- I will be discussing non-FDA approved indications during my presentation.

Immunotherapy for Metastatic Kidney Cancer (Renal Cell Carcinoma; RCC)

Surgically resectable → Oligo-metastatic → Metastatic



History of Immunotherapy in mRCC



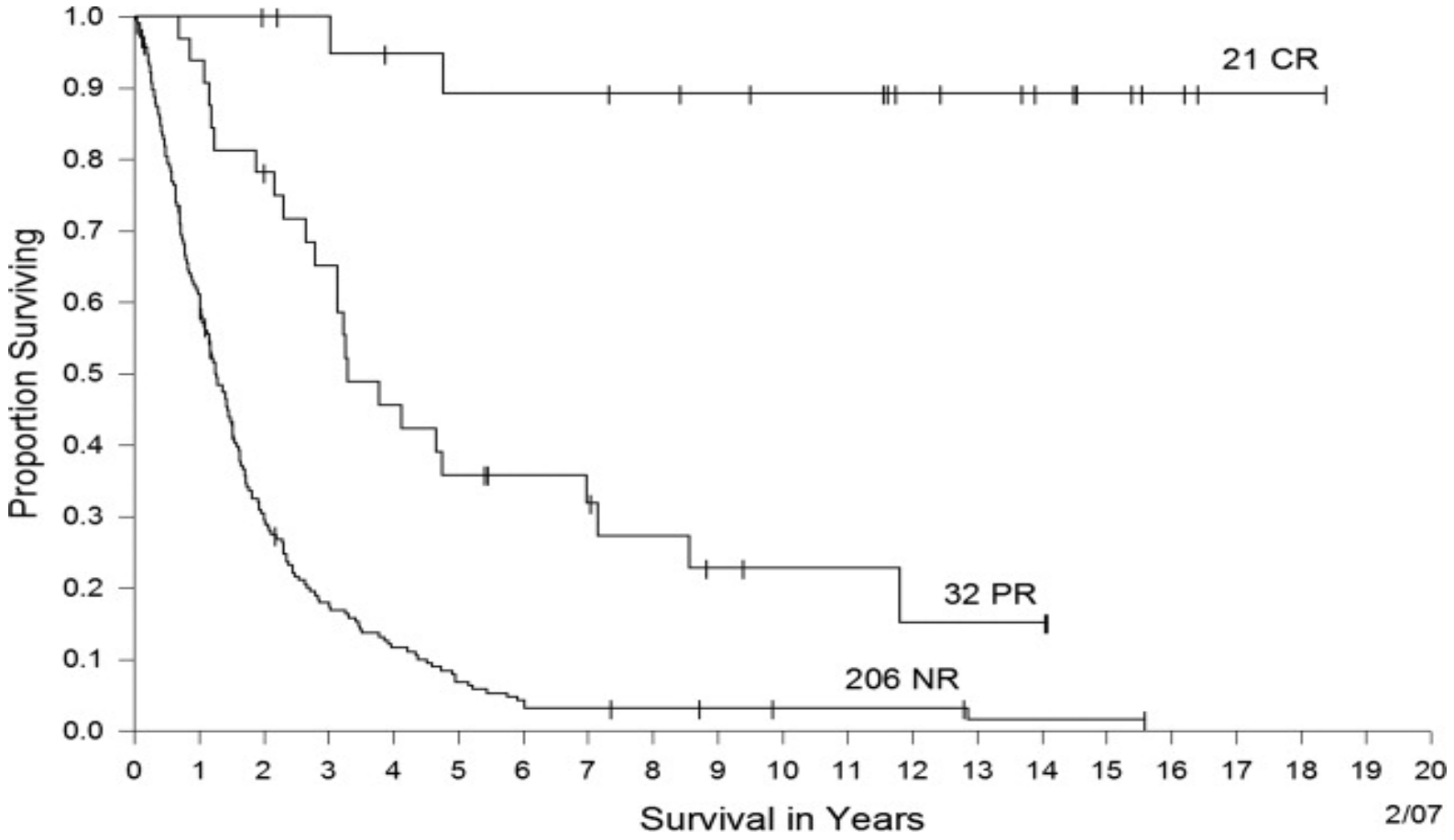
Resurgence of interest in immunotherapy

FDA-approved Immunotherapies for mRCC

Drug	Approved	Indication	Dose
High dose Interleukin-2	1992	Metastatic RCC	600,000 International Units/kg (0.037 mg/kg) IV q8hr infused over 15 minutes for a maximum 14 doses, THEN 9 days of rest, followed by a maximum of 14 more doses (1 course)
Interferon-a + bevacizumab	2009	Clear cell RCC	IFN 9 MIU s.c. three times a week + bev 10 mg/kg Q2W
Nivolumab	2015	Clear cell RCC refractory to prior VEGF targeted therapy	3mg/kg or 240mg IV Q2W or 480mg IV Q4W
Nivolumab +ipilimumab	2018	Clear cell RCC, treatment naïve	3mg/kg nivo plus 1mg/kg ipi Q3W x 4 doses then nivo maintenance at flat dosing
Pembrolizumab + axitinib	2019	Advanced RCC, Treatment naïve	200 mg pembro Q3W + 5 mg axitinib twice daily
Avelumab + axitinib	2019	Advanced RCC, Treatment naïve	800 mg avelumab Q2W + 5 mg axitinib twice daily

High Dose IL-2 in mRCC

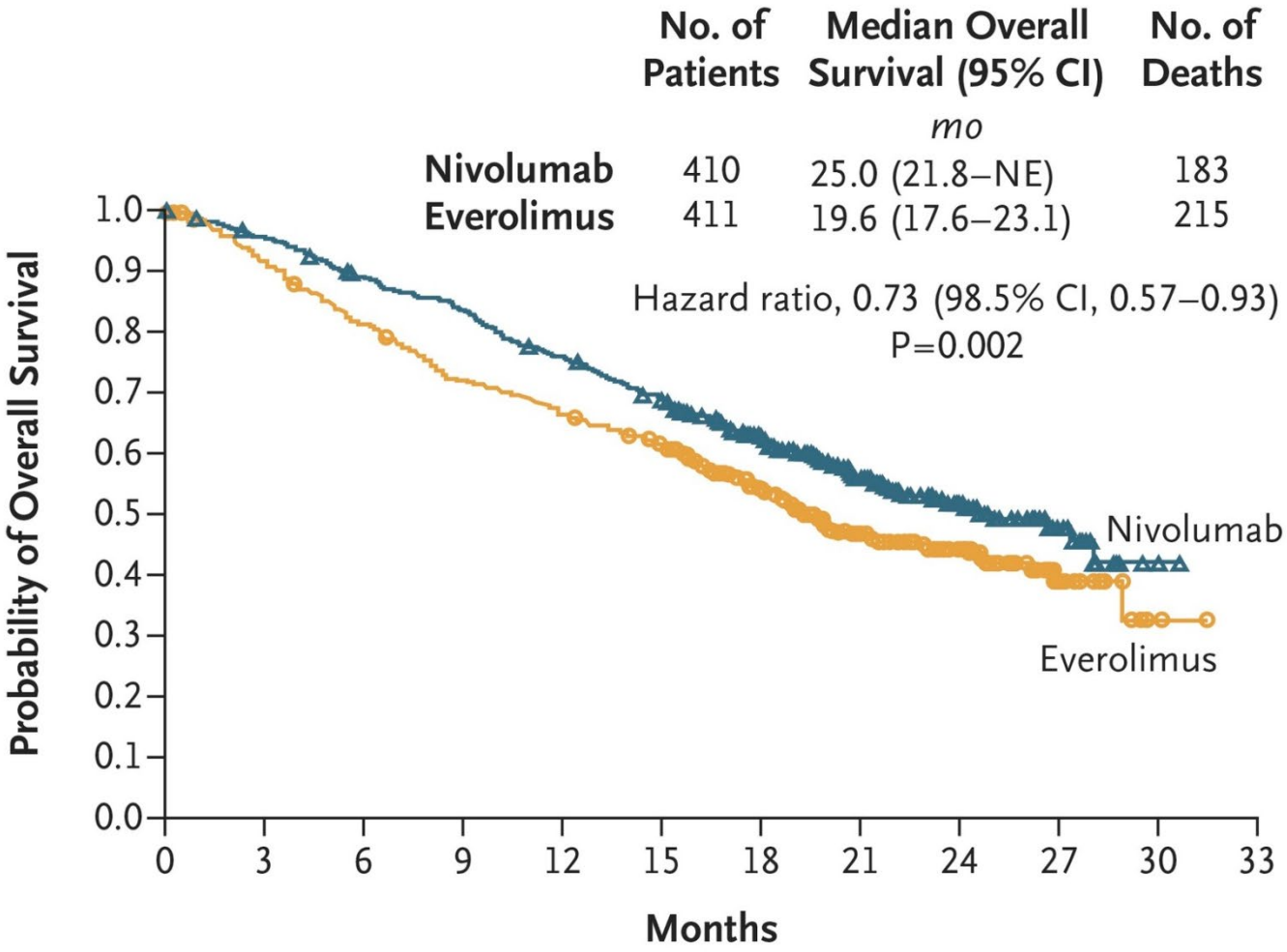
- 20 year analysis of 259 patients
- ORR = 20%
  - 9% CR (n = 23)
  - 12% PR (n = 30)
- Median duration of response = 15.5 months
- Median OS = 19 months



Klapper et al. Cancer 2008

Second-Line Nivolumab in mRCC

- CheckMate 025 Phase III trial
- Metastatic, clear-cell disease
- One or two previous antiangiogenic treatments
- Nivolumab (3 mg/kg IV Q2W) vs everolimus (10 mg daily)

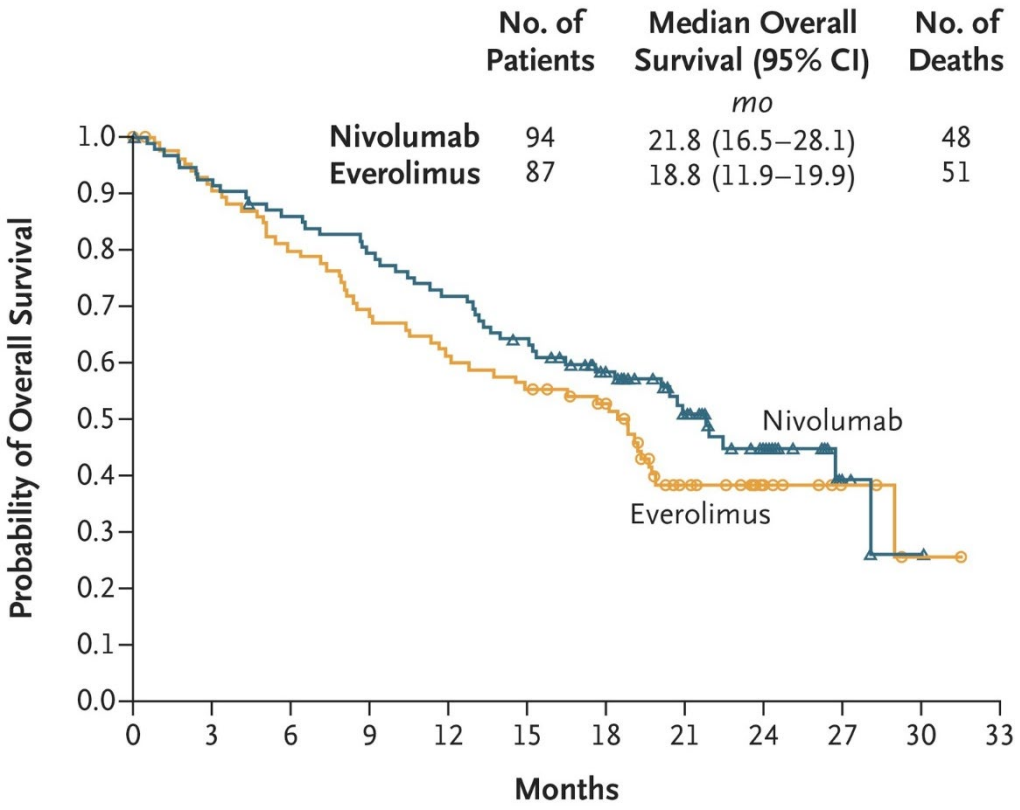


Motzer et al. NEJM 2015

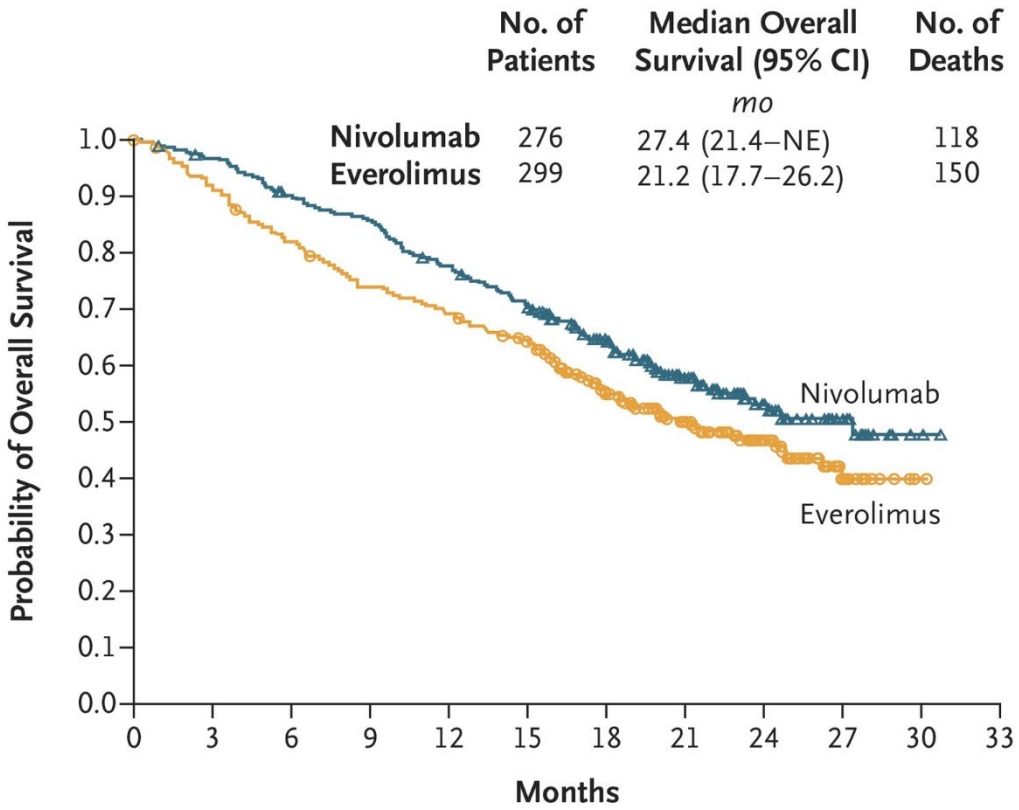
Second-Line Nivolumab in mRCC

PD-L1 subgroups

PD-L1 ≥ 1%



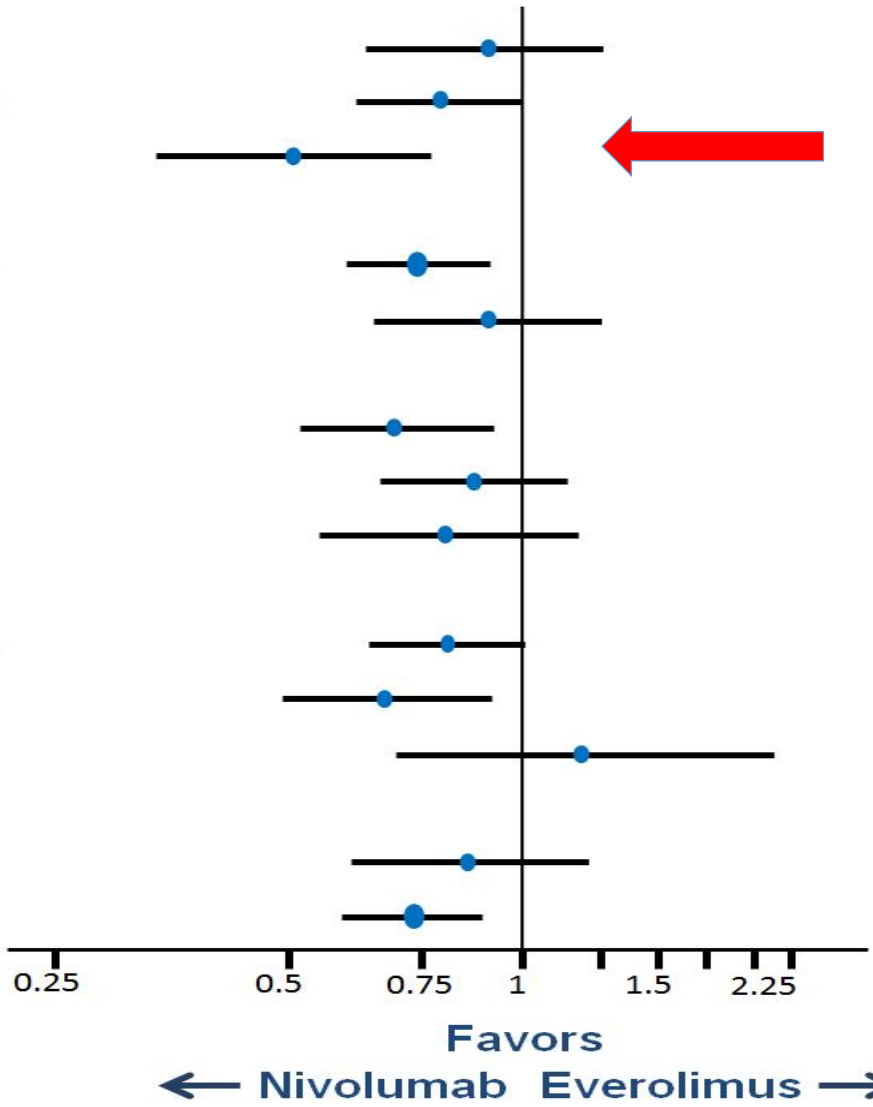
PD-L1 < 1%



Motzer et al. NEJM 2015

Overall survival by subgroup analyses

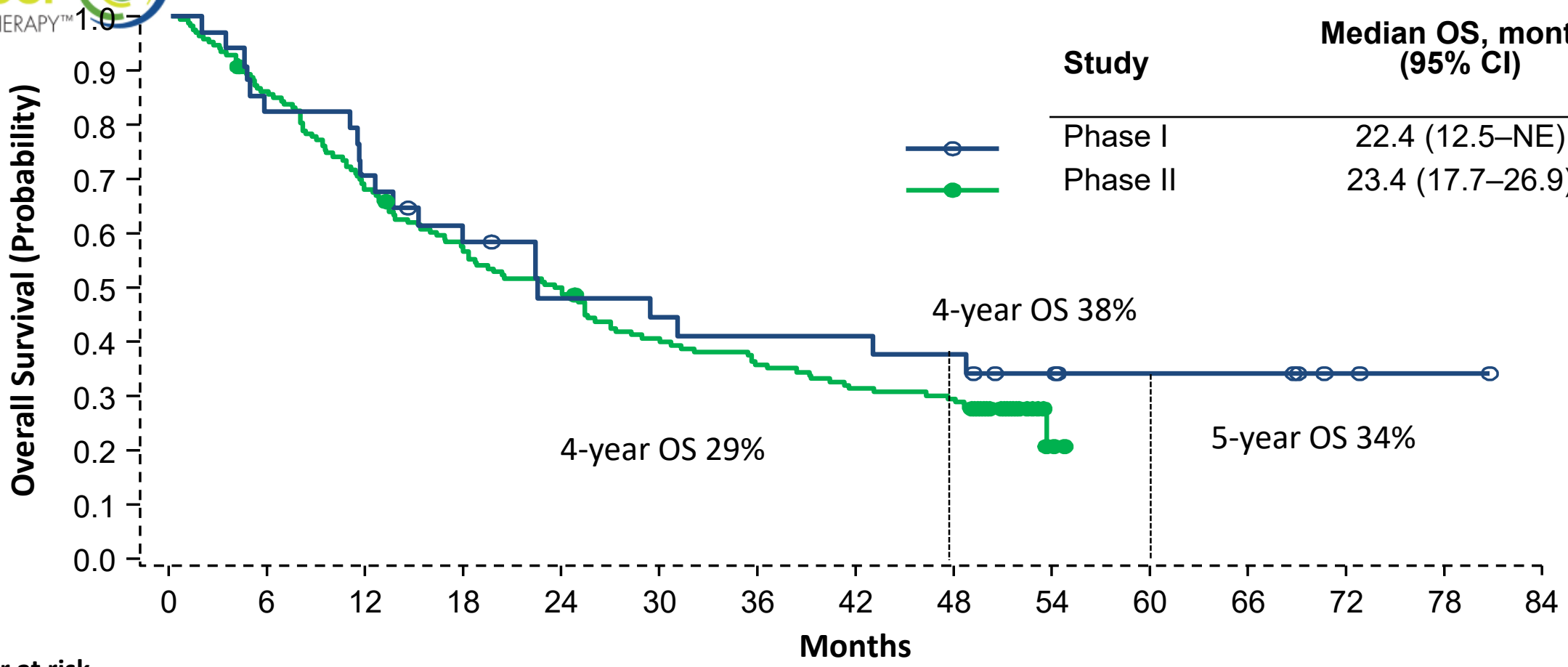
Subgroup	Nivolumab n/N	Everolimus n/N
MSKCC risk group		
Favorable	45/145	52/148
Intermediate	101/201	116/203
Poor	37/64	47/60
Prior anti-angiogenic regimens		
1	128/294	158/297
2	55/116	57/114
Region		
US/Canada	66/174	87/172
Western Europe	78/140	84/141
Rest of the world	39/96	44/98
Age, years		
<65	111/257	118/240
≥65 to <75	53/119	77/131
≥75	19/34	20/40
Sex		
Female	48/95	56/107
Male	135/315	159/304



Motzer R, et al. NEJM 2015.

Analyses based on interactive voice response system data.

Nivo Overall Survival in Phase I and II studies



Study	Median OS, months (95% CI)
Phase I	22.4 (12.5–NE)
Phase II	23.4 (17.7–26.9)

Number at risk

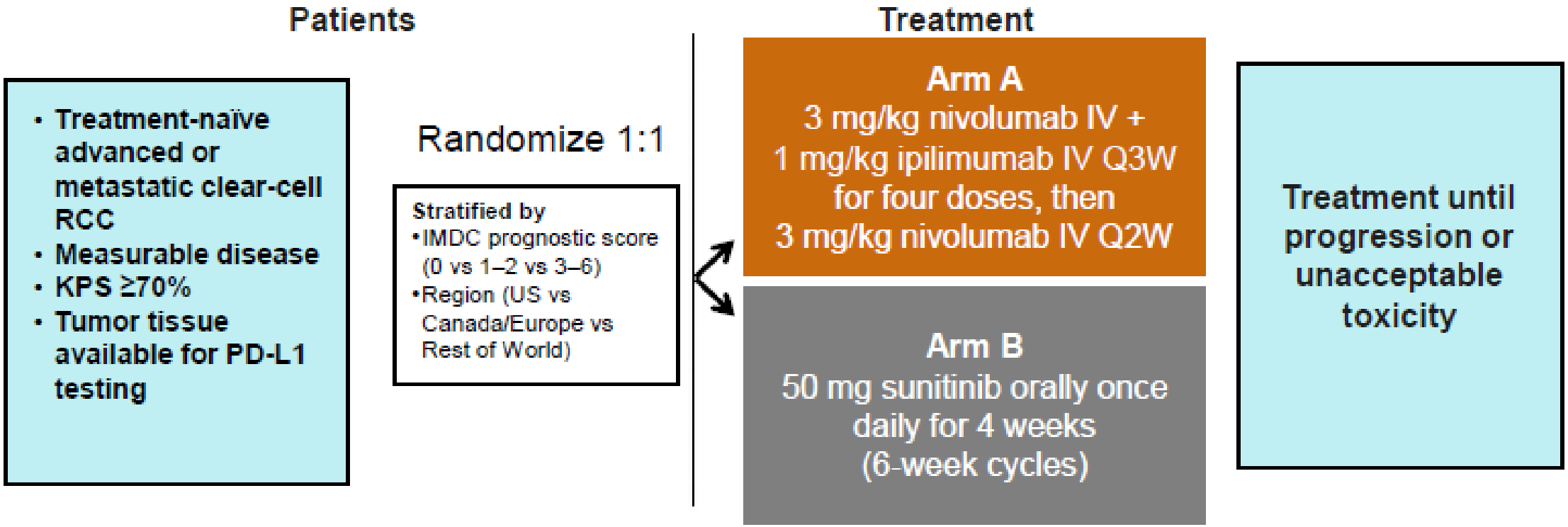
Phase I	34	28	24	18	14	13	12	12	11	8	6	6	2	1	0
Phase II	167	142	113	93	80	65	58	51	47	2	0	0	0	0	0

In phase I and II studies, min follow-up was 50.5 mos and 49.2 mos, respectively

NE, not estimable.

McDermott et al ASCO Abst 2016

First-line Nivolumab + Ipilimumab in mRCC

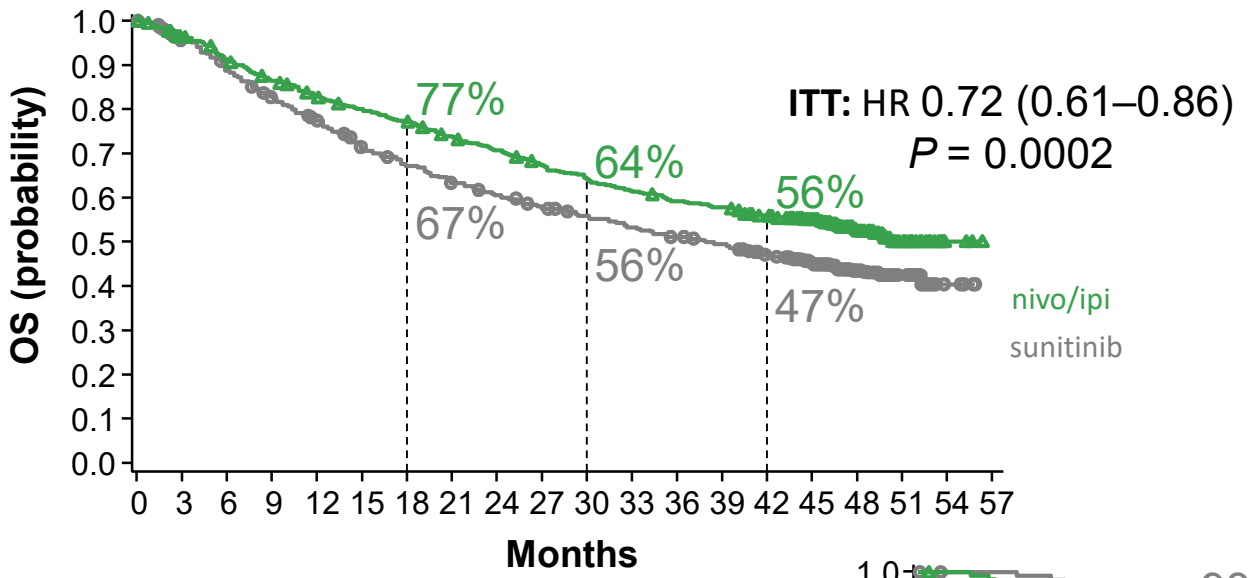


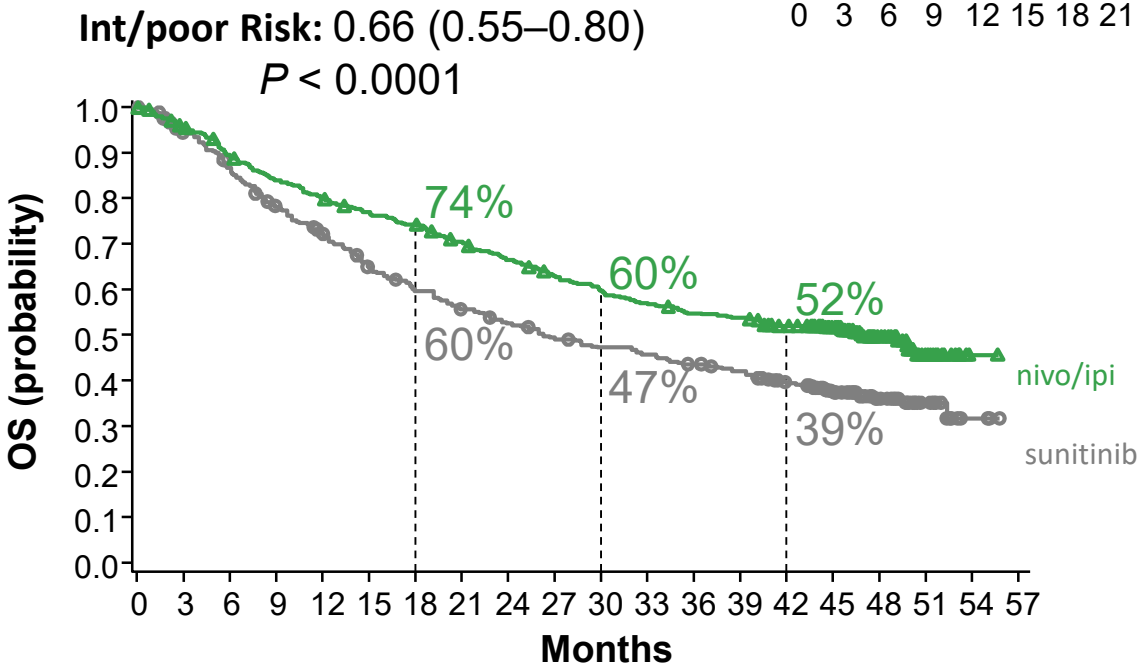
Nivolumab = anti-PD-1 antibody Ipilimumab = anti-CTLA-4 antibody

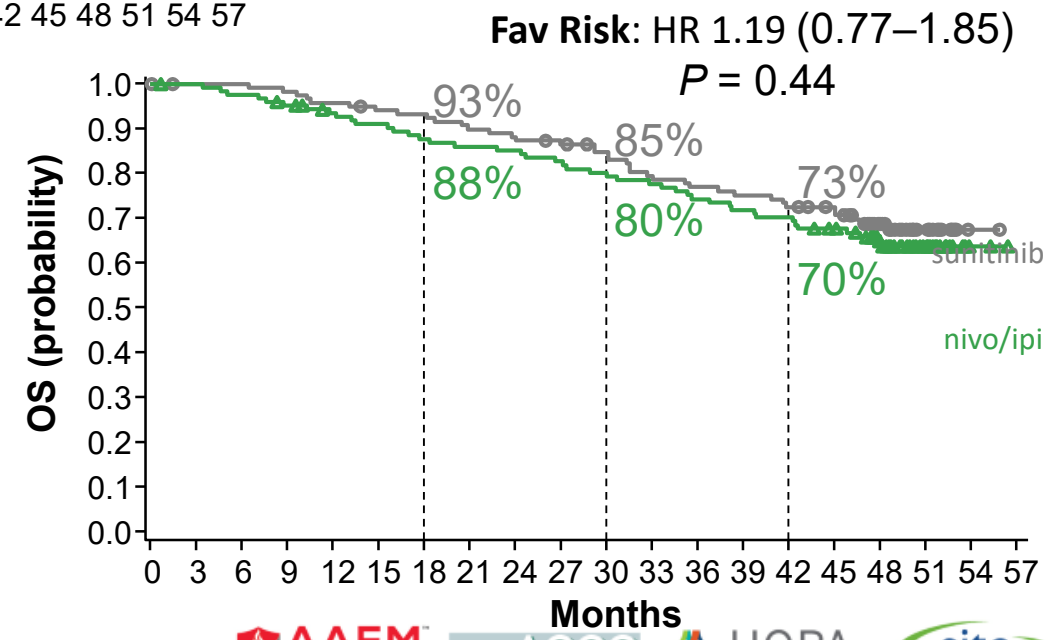
IMDC = International Metastatic RCC Database Consortium

Escudier et al. ESMO 2017

OS Results: 42 Months Follow-up Data

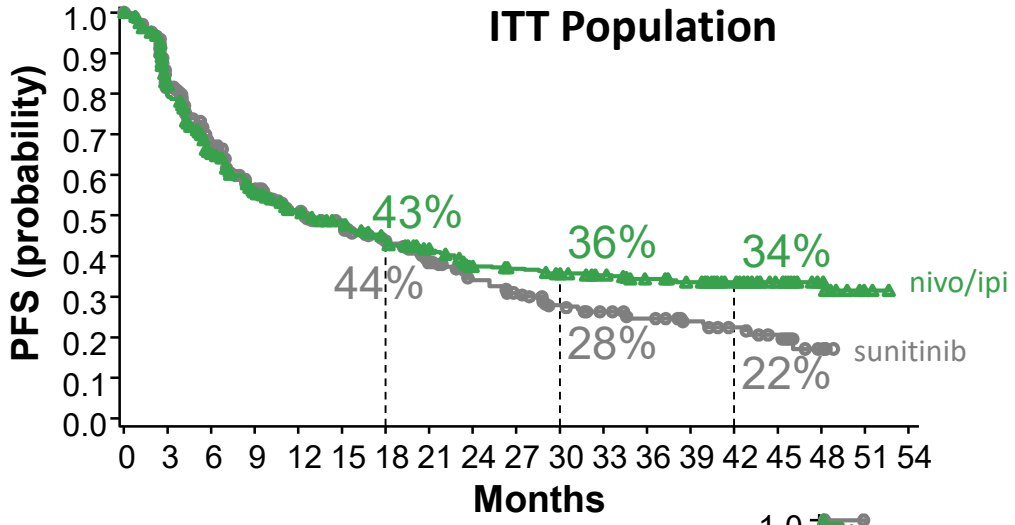


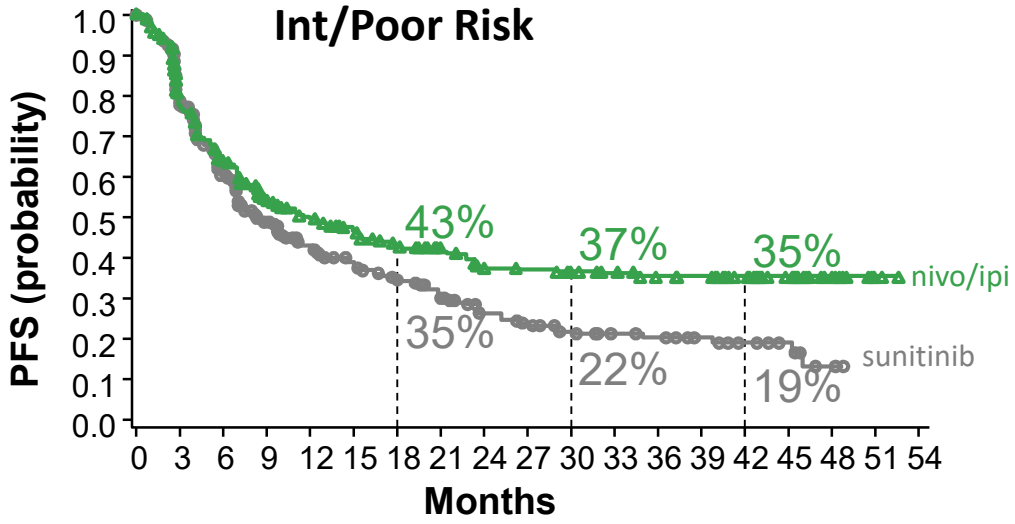


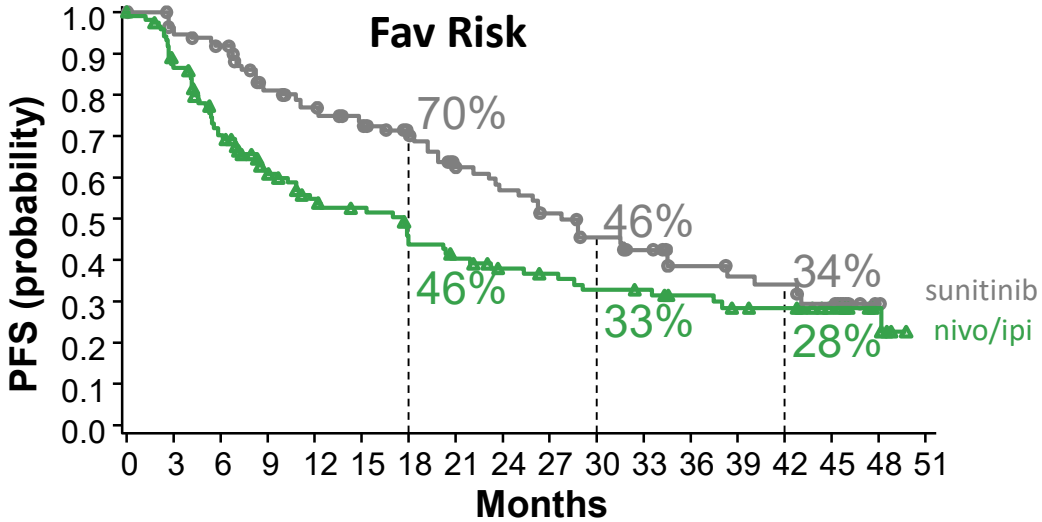


Tannir N et al. Presented at: ASCO GU 2020; February 13-15, 2020; San Francisco, CA. Abstract 609.

PFS Results: 42 Months Follow-up Data







Tannir N et al. Presented at: ASCO GU 2020; February 13-15, 2020; San Francisco, CA. Abstract 609.

Nivolumab/Ipilimumab Activity Based on IMDC Category

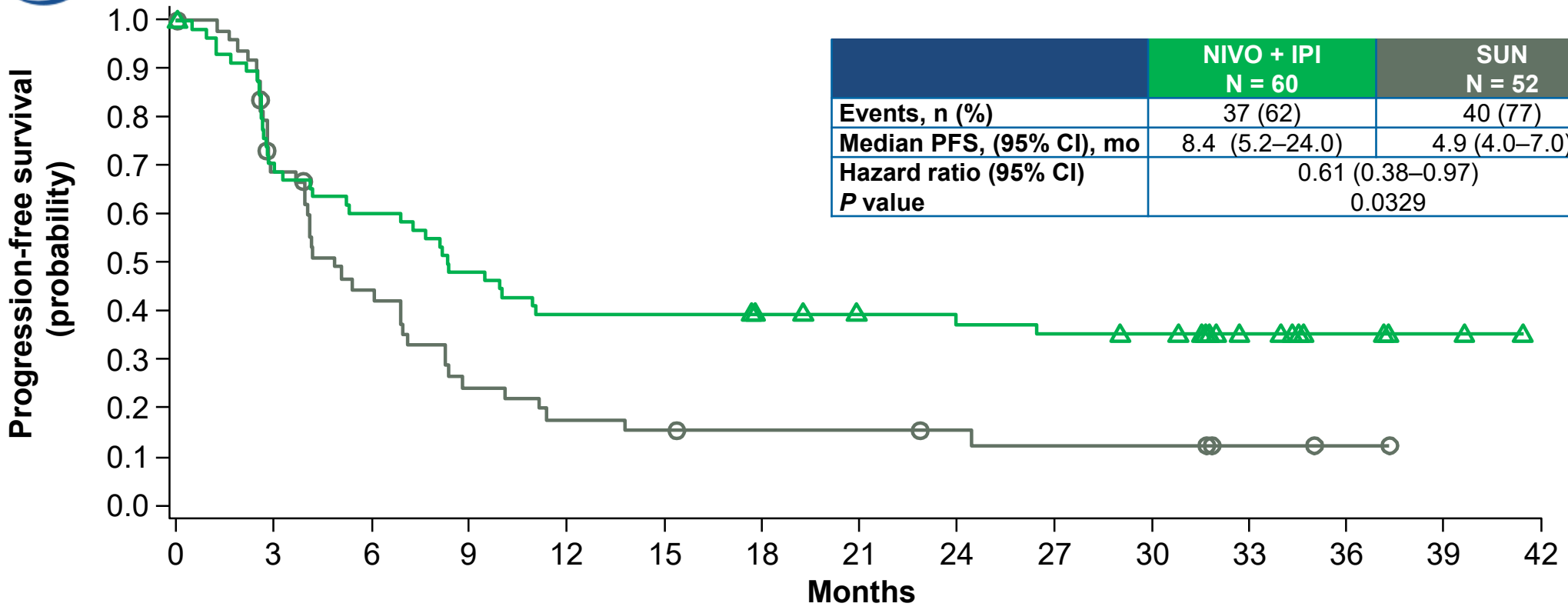
Property	Favorable	Intermediate/Poor
ORR	39%	42%
CR	8%	11%
42 mos DOR Rate	62%	60%
42 mos PFS Rate	28%	35%
42 mos OS Rate	70%	52%

Efficacy of nivolumab/ipilimumab similar across IMDC Categories
8 x more CRs than sunitinib, 28%-35% plateau on PFS curves

Tannir N et al. Presented at: ASCO GU 2020; February 13-15, 2020; San Francisco, CA. Abstract 609.

PFS per Investigator: Intermediate/Poor-Risk Sarcomatoid Patients

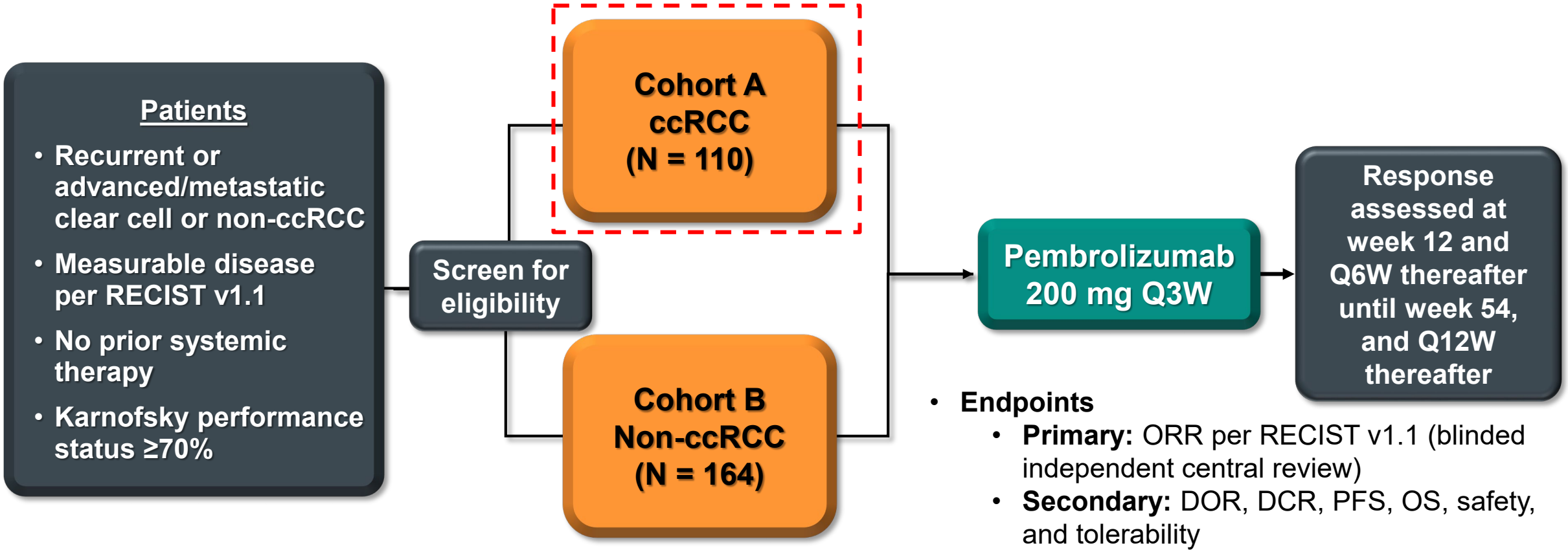
	NIVO + IPI N = 60	SUN N = 52
Events, n (%)	37 (62)	40 (77)
Median PFS, (95% CI), mo	8.4 (5.2–24.0)	4.9 (4.0–7.0)
Hazard ratio (95% CI)	0.61 (0.38–0.97)	
P value	0.0329	



No. at risk														
NIVO+IPI	60	41	35	28	23	23	21	19	19	17	16	10	4	2	0
SUN	52	32	20	11	8	7	6	6	5	4	4	2	1	0	0

What about anti-PD1 monotherapy? Can Nivo/ipi salvage anti-PD1 non-responders?

KEYNOTE-427: (NCT02853344)



- **Endpoints**
  - **Primary:** ORR per RECIST v1.1 (blinded independent central review)
  - **Secondary:** DOR, DCR, PFS, OS, safety, and tolerability
  - **Exploratory:** tissue based biomarkers (e.g. IHC, RNA sequencing)

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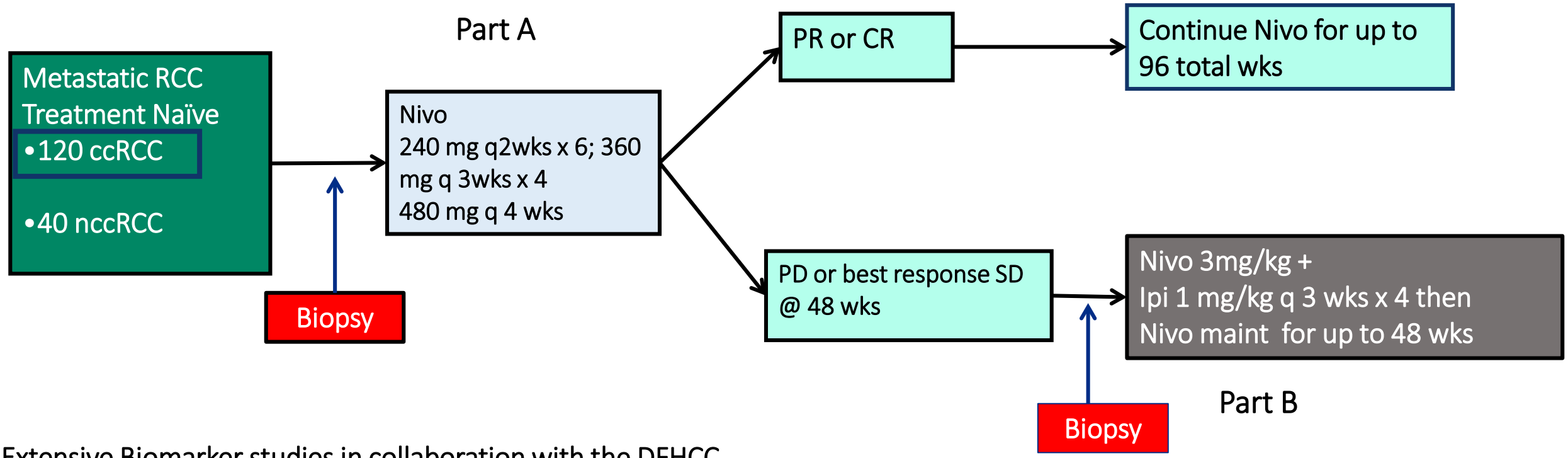
Pembrolizumab ORR in First line ccRCC

	N = 110		
	n	%	95% CI
ORR	**42**	**38.2**	**29.1-47.9**
DCR (CR + PR + SD ≥6 months)	**65**	**59.1**	**49.3-68.4**
Best overall response			
CR	3	2.7	
PR	39	35.5	
SD	35	31.8	
PD	31	28.2	
No assessment	2	1.8	

Database cutoff: March 12, 2018.

HCRN GU16-260: Study Design

IIT at 12 sites conducted through the HCRN GU Group
(CM209-669)



Extensive Biomarker studies in collaboration with the DFHCC
Kidney Cancer SPORE
DOD Translational Partnership Grant (Atkins, Wu)

Scans q12 weeks; Confirm response and PD;
Measurements by RECIST 1.1
Mandatory biopsies

Atkins M et al. Presented at: ASCO 2020; May 29-31, 2020; Virtual Meeting. Abstract 5006.

Michael B. Atkins, MD

Objective Response Rates: Nivo Monotherapy (Part A)

Best Response N (%)	IMDC Risk Category (N)			Total (N= 123) N (%)
	Favor (30) N (%)	Interm (80) N (%)	Poor (12) N (%)	
CR	4 (13.3)	3 (3.8)	0	7 (5.7)
PR*	11 (36.7)	17 (21.2)	3 (25)	32 (26.0)
SD	15 (50.0)	26 (32.5)	5 (42)	46 (37.4)
PD	0	34 (42.5)	4 (33)	38 (30.9)
ORR	15/30 (50)	20/80 (25)	3/12 (25)	39/123 (31.7)
(95% CI) %	(31.3, 68.7)	(16.6, 35.1)		(23.6, 40.7)

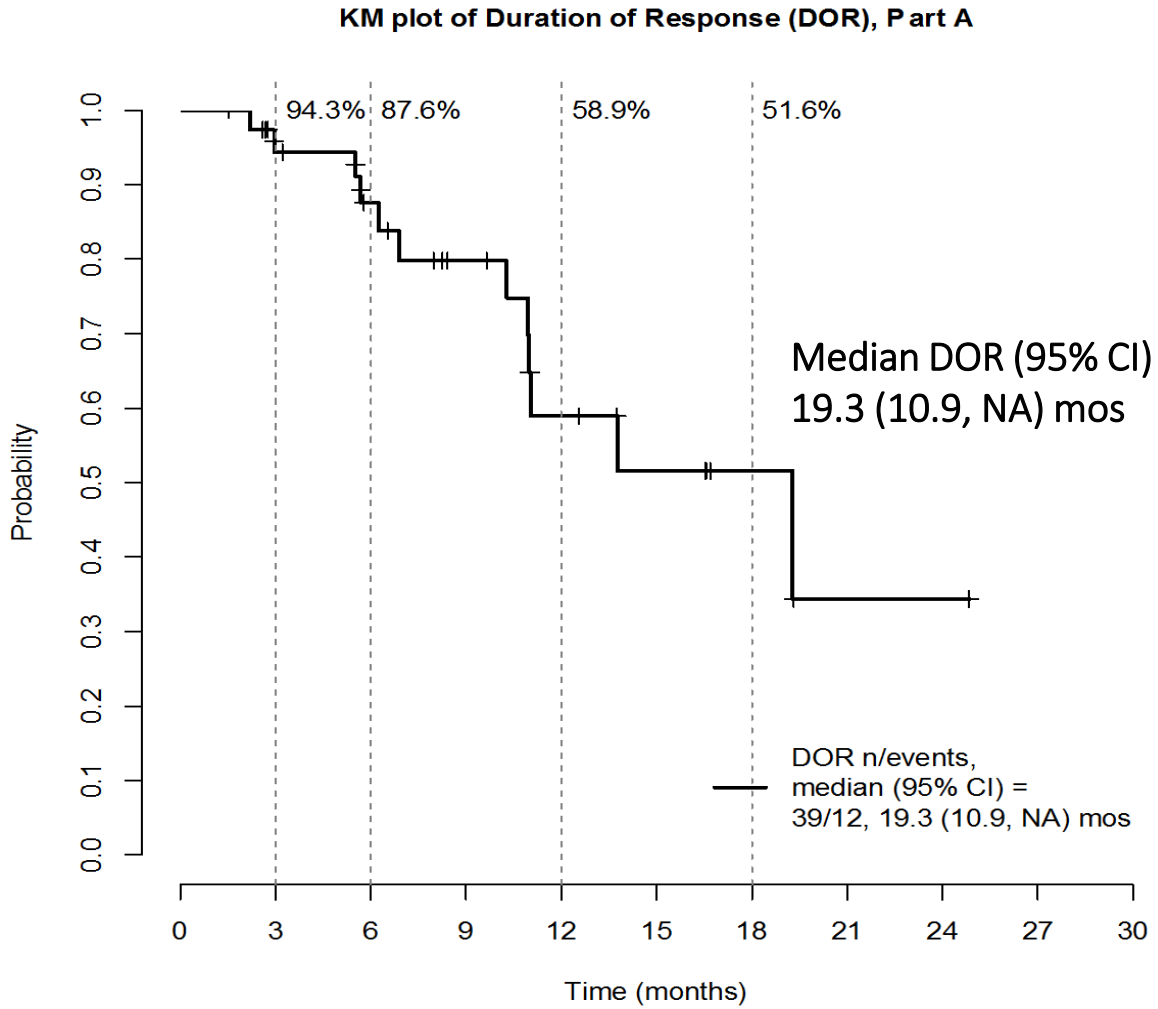
ORR: 39/123 = 31.7%
95% CI (23.6, 40.7%)

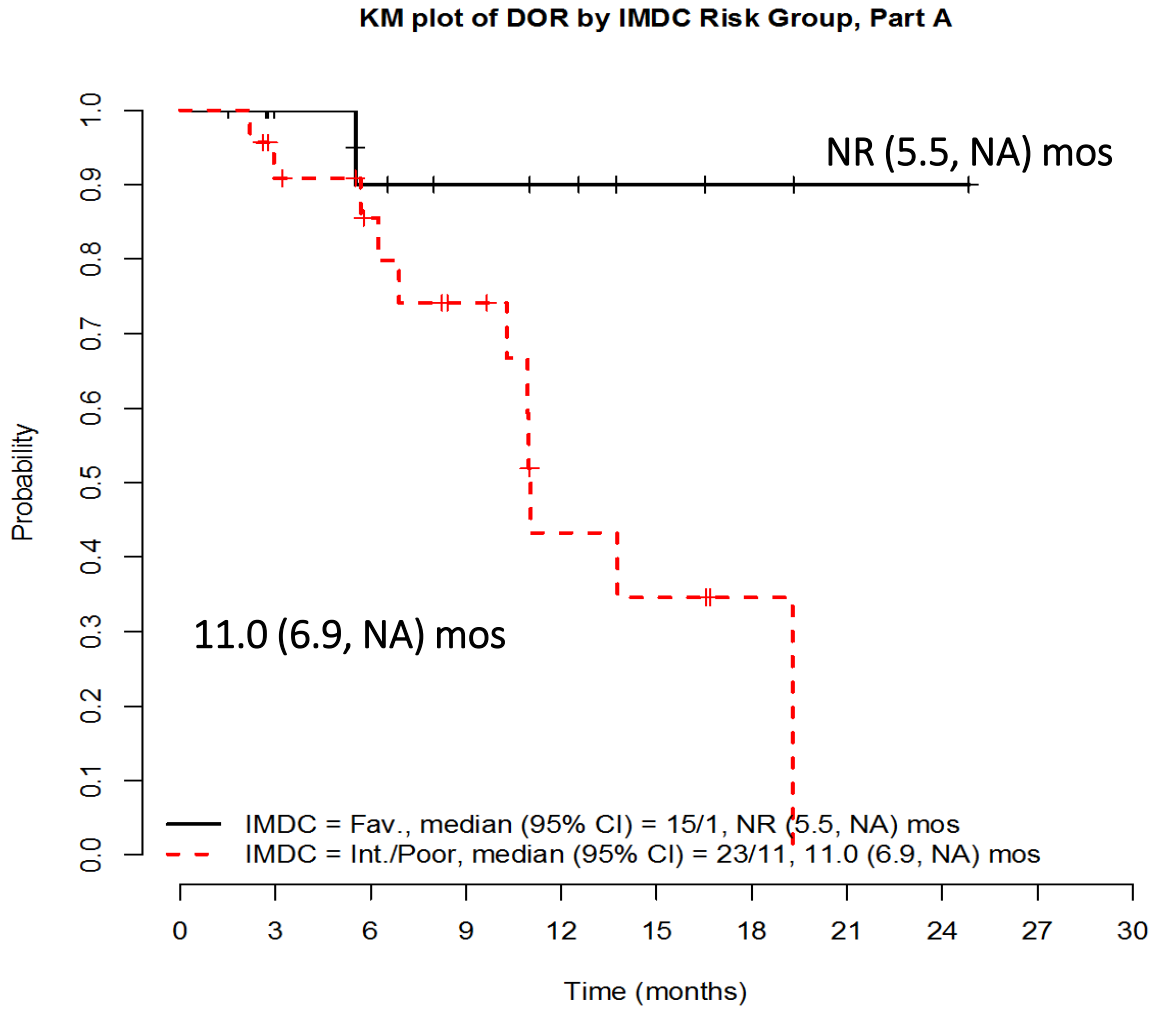
Sarcomatoid RCC ORR:
7/22 = 31.8% (all PRs)
95% CI (13.9, 54.9%)

* 1 PR with missing IMDC Risk Category

Atkins M et al. Presented at: ASCO 2020; May 29-31, 2020; Virtual Meeting. Abstract 5006.

Duration of Response: Nivo Monotherapy (Part A)





Atkins M et al. Presented at: ASCO 2020; May 29-31, 2020; Virtual Meeting. Abstract 5006.

Objective Response Rates: Nivo/Ipi Salvage (Part B)

Best Response N (%)	IMDC Risk Category (N=30)			Total N (%)
	Favor (4)	Interm (24)	Poor (2)	
CR	0	0	0	0
PR	2 (50)	2 (8.3)	0	4 (13.3)
SD	1 (25)	6 (25)	0	7 (23.3)
PD	1 (25)	16 (66.7)	2 (100)	19 (63.3)

ORR: 4/30 = 13.3%
95% CI (3.8, 30.7)

Atkins M et al. Presented at: ASCO 2020; May 29-31,2020; Virtual Meeting. Abstract 5006.

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Combination of Anti-PD1 and VEGF Pathway Blockade

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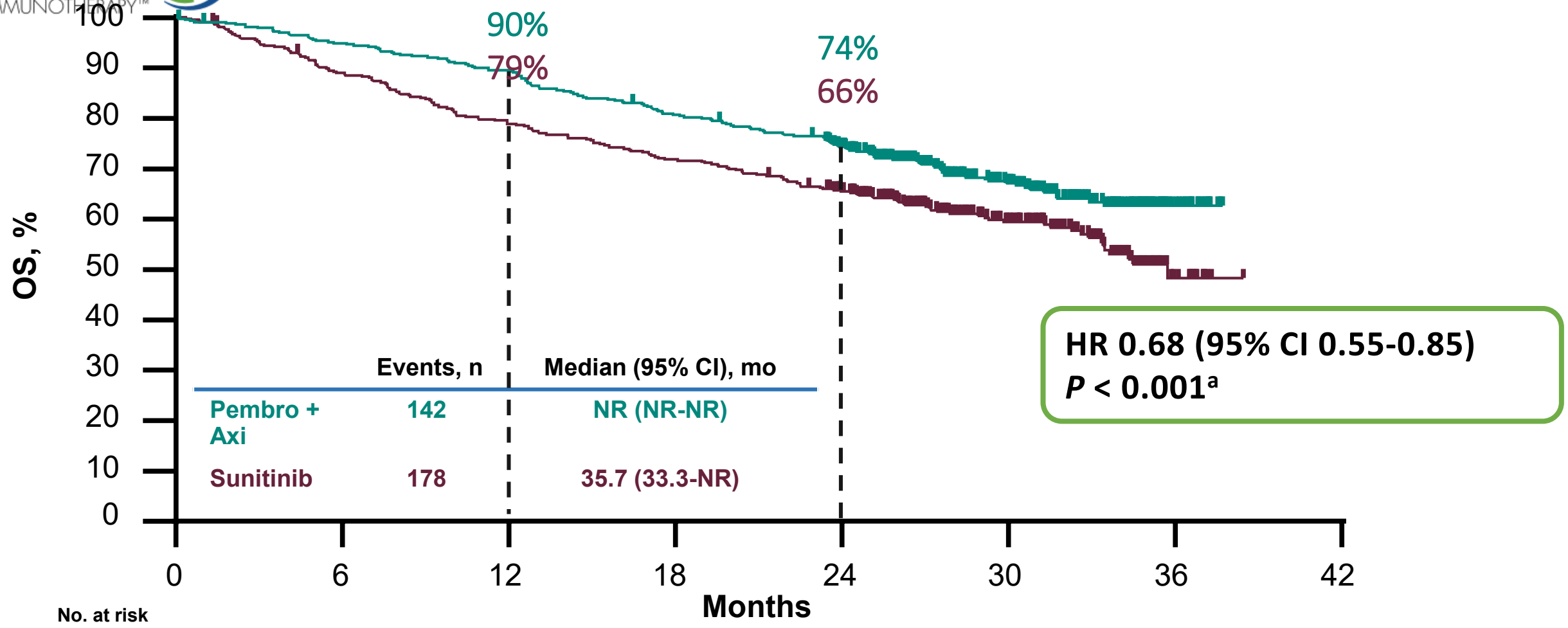
Randomized Phase III Study Designs for IO + VEGF

IMmotion151 Rini et al. Lancet	Treatment-naive advanced or metastatic RCC with clear cell and/or sarcomatoid histology; KPS ≥ 70; (N = 915)	**Atezolizumab** 1200 mg IV + **Bevacizumab** 15 mg/kg IV Q3W **Sunitinib** 50 mg PO QD for 4 wks on, 2 wks off	1º EP: PFS in PD-L1+ pts; OS in ITT pts
JAVELIN Renal 101 Motzer et al. NEJM	Treatment-naive advanced RCC with a clear cell component; ECOG PS 0 or 1; (N = 886)	**Avelumab** 10 mg/kg IV Q2W + **Axitinib** 5 mg PO BID in 6-wk cycles **Sunitinib** 50 mg PO QD for 4 wks on, 2 wks off	1º EP: PFS and OS in PD-L1+ pts
KEYNOTE-426 Rini et al. NEJM	Treatment-naive advanced clear-cell RCC; KPS ≥ 70%; (N = 861)	**Pembrolizumab** 200 mg IV Q3W + **Axitinib** 5 mg PO BID **Sunitinib** 50 mg PO QD for 4 wks on, 2 wks off	1º EP: PFS and OS in ITT

Rini BI et al. *Lancet*. 2019;393:2404-241. Motzer RJ et al. *N Engl J Med*. 2019;380:1103-1115. Rini BI et al. *N Engl J Med*. 2019;380:1116-1127.

KN 426: OS in the ITT Population

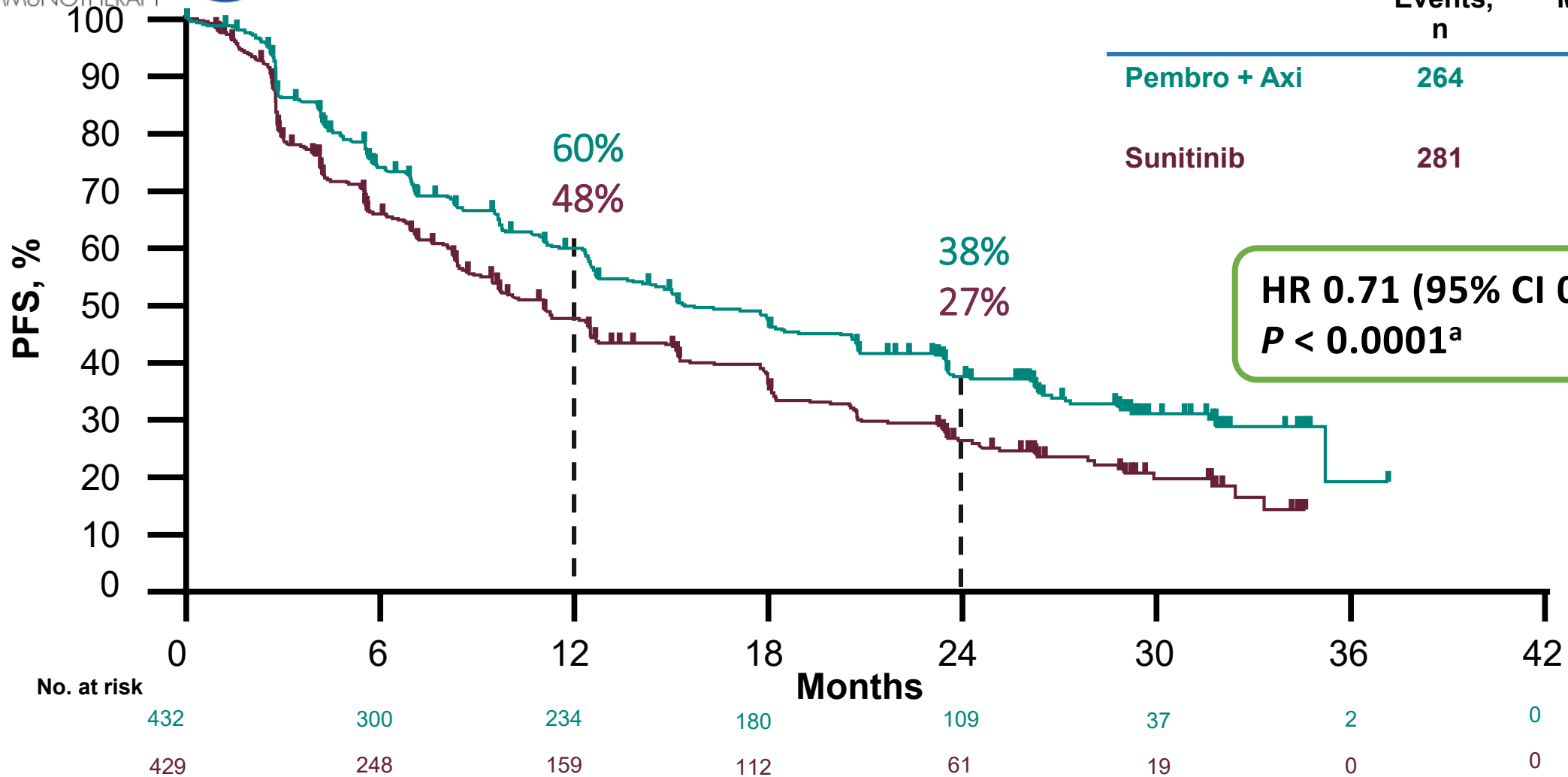


HR 0.68 (95% CI 0.55-0.85)
***P* < 0.001[a]**

[a]As superiority of pembrolizumab plus axitinib was demonstrated at the first interim analysis, no alpha was allocated to overall survival; only nominal p-values are reported. Data cutoff: January 6, 2020.

Plimack E et al. Presented at: ASCO 2020; May 29-31, 2020; Virtual Meeting. Abstract 5001.

PFS in the ITT Population



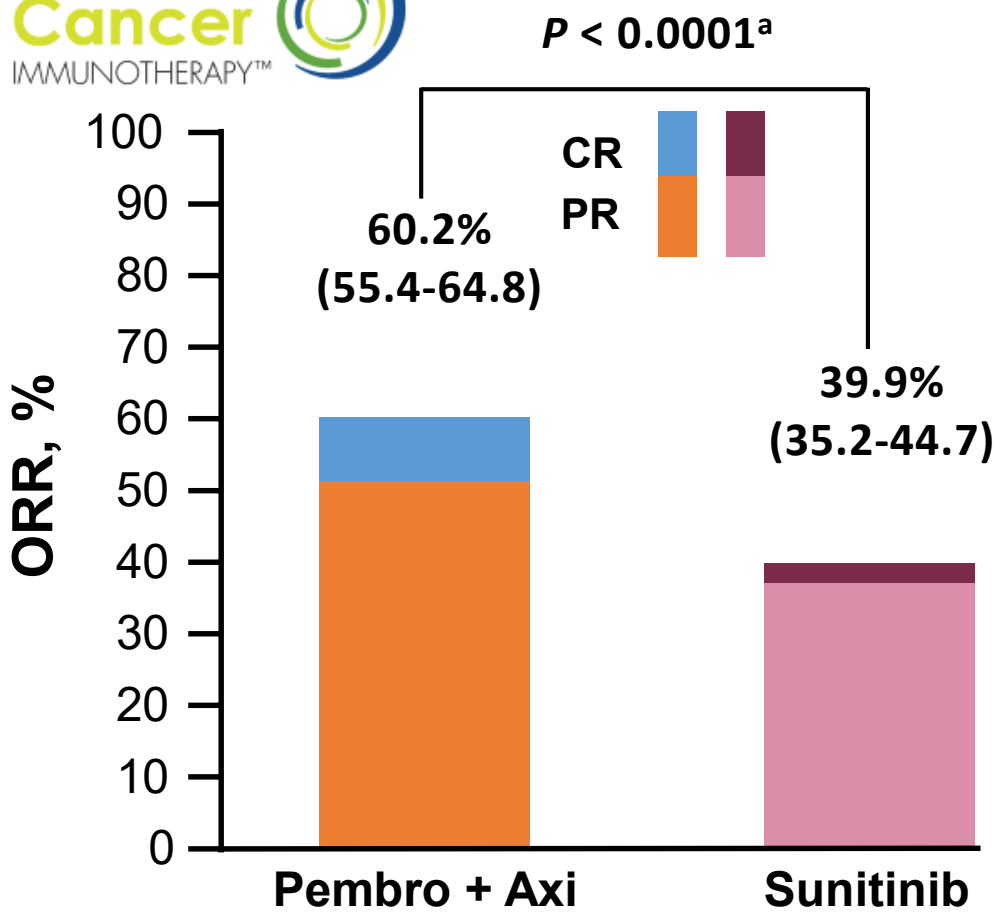
	Events, n	Median (95% CI), mo
Pembro + Axi	264	15.4 (12.7-18.9)
Sunitinib	281	11.1 (9.1-12.5)

HR 0.71 (95% CI 0.60-0.84)
***P* < 0.0001[a]**

[a]As superiority of pembrolizumab plus axitinib was demonstrated at the first interim analysis, no alpha was allocated to PFS; only nominal p-values are reported. Data cutoff: January 6, 2020.

Plimack E et al. Presented at: ASCO 2020; May 29-31, 2020; Virtual Meeting. Abstract 5001.

Confirmed Objective Response Rate ITT Population



	Pembro + Axi n = 432	Sunitinib n = 429
Best Response, n (%)		
CR	38 (8.8)	13 (3.0)
PR	222 (51.4)	158 (36.8)
SD	100 (23.1)	150 (35.0)
PD	49 (11.3)	74 (17.2)
NE[b]	16 (3.7)	28 (6.5)
NA[c]	7 (1.6)	6 (1.4)
Median (range) duration of response, mo	23.5 (1.4+ to 34.5+)	15.9 (2.3 to 31.8+)

[a]As superiority of pembrolizumab plus axitinib was demonstrated at the first interim analysis, no alpha was allocated to confirmed objective response; only nominal p-values are reported. [b]Post-baseline assessment(s) available however not being evaluable (i.e., all post-baseline assessment(s) with insufficient data for assessment of response per RECIST 1.1. or CR/PR/SD <6 weeks from randomization). [c]No post-baseline assessment available for response evaluation; + indicates an ongoing response at time of last disease assessment.
Data cutoff: January 6, 2020.

Plimack E et al. Presented at: ASCO 2020; May 29-31, 2020; Virtual Meeting. Abstract 5001.

Phase III TKI/IO-based Combinations in RCC-Current Status

Control	Comparator(s)	Median Follow-up	PFS (HR)	OS (HR)
Sunitinib	Axitinib + Pembrolizumab[1,2*]	12.8 mo	Yes (0.69)	Yes (0.53)
		27.0 mo	Yes (0.71)	Yes (0.68)
Sunitinib	Bevacizumab + Atezolizumab[3]	15 mo	Yes (0.88)	TE (0.93)*
Sunitinib	Axitinib + Avelumab[4]	10.8 mo	Yes (0.69)*	TE (0.78)*
Sunitinib	Cabozantinib + Nivolumab[5]	18.1 mo	Yes (0.51)	Yes (0.60)
Sunitinib	(Lenvatinib + Eve) vs (Len + Pembro)[6]	TE	TE	TE

1. Rini BI et al. *N Engl J Med*. 2019;380:1116-1127. 2. Plimack E et al. Presented at: ASCO 2020; May 29-31, 2020; Virtual Meeting. Abstract 5001. 3. Rini BI et al. *Lancet*. 2019;393:2404-241. 4. Motzer RJ et al. *N Engl J Med*. 2019;380:1103-1115. 5. Grünwald V, Calvo E. *Ann Oncol*. 2020;S0923-7534(20)39838-0. 6. https://clinicaltrials.gov/ct2/show/NCT02811861

* ITT populations

Efficacy Results by Prior Anticancer Therapy Subgroup[a]

Parameter	Anti-PD-1/ PD-L1[b] (N = 104)	Anti-PD-1/PD-L1 and Anti-VEGF[c] (n = 68)	Nivolumab + Ipilimumab (n = 38)
ORR, % (95% CI)	55 (45–65)	59 (46–71)	47 (31–64)
Best objective response, %			
Partial response	55	59	47
Stable disease	36	31	42
Progressive disease	5	6	8
Not evaluable	5	4	3
Median duration of response, months (95% CI)	12 (9–18)	9 (7–17)	NR (7–NR)

[a] By irRECIST per investigator assessment. Patients can belong to > 1 category; [b] in combination or as monotherapy; [c] in combination or sequentially.

First-Line Therapy for RCC: Conclusions (1)

- IO based doublets represent current SOC
  - No clear role for IMDC classification
  - VEGFR TKIs only indicated in patients who can't get IO therapy
  - PDL1 expression too inexact to select pts
- Nivo + ipi represents a current SOC for treatment naïve patients with intermediate and poor risk advanced RCC
  - Exclusion of good risk patients doesn't take into consideration IO endpoints
  - Durable response (TFS) possible in 30-35% of patients
- Anti-PD1 monotherapy may play a role in TKI/Ipi averse pts, particularly those with favorable risk

First-Line Therapy for RCC: Conclusions (2)

- Anti-PD1/PDL1 + anti-VEGF represents an alternative SOC
- Efficacy may relate to efficacy of TKI component/study design (bevacizumab < axitinib < cabozantinib < lenvatinib)/(early OS HR > late)
  - Axi/Pembro produces best OS HR (could be early reporting)
  - Cabo/Nivo results encouraging for stage of reporting
  - Len/Pembro promising 2nd line data; 1st line pending
- On the other hand
  - Unclear if activity is synergistic or merely additive
  - Expense and likely toxicity exceed sequential treatments
  - Ability to produce durable TFS yet to be established

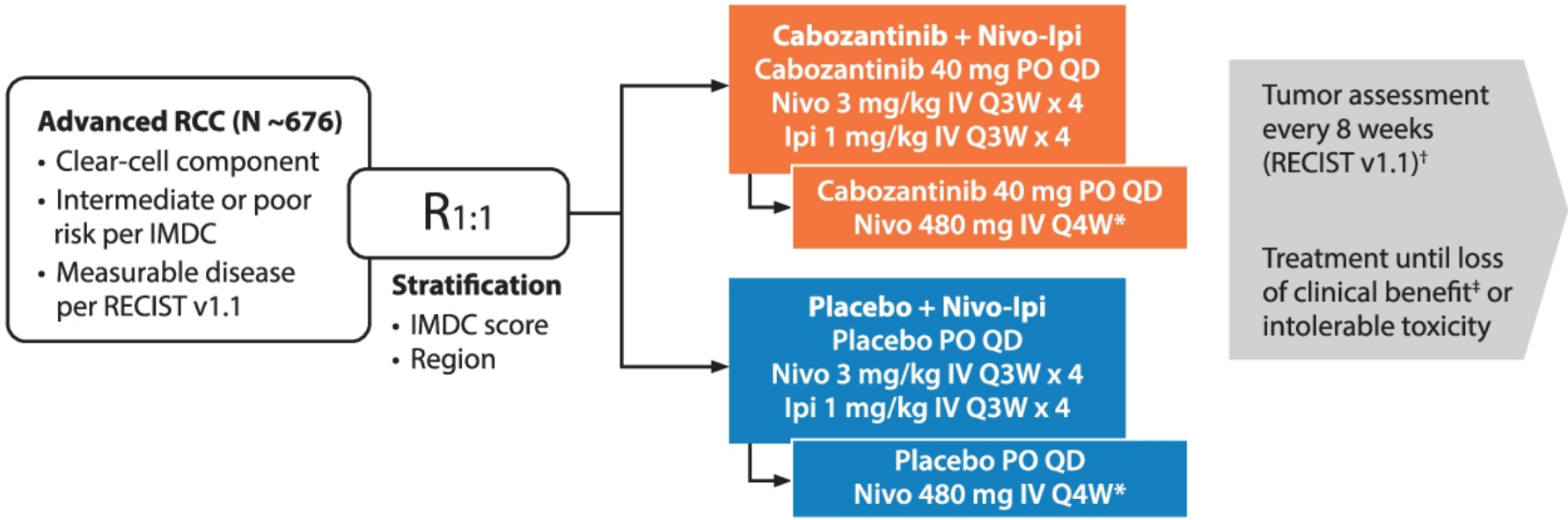
Ipi/Nivo vs VEGF/PD1 Blockade?

- Need longer follow-up and appropriate phase III trials with IO endpoints, standardized biomarkers, and universally available crossover to be able to make rational treatment decisions

- Need biomarker studies to help us sort out who should get which therapy, rather than focusing on clinical variables
  - Biomarkers should be tied to IO endpoints

Cosmic-313 Trial Design

Figure 2. Study Design



*Nivolumab administered for a maximum of 2 years

†Tumor assessment (RECIST v1.1) at week 10, then every 8 weeks for the first 50 weeks, then every 12 weeks thereafter

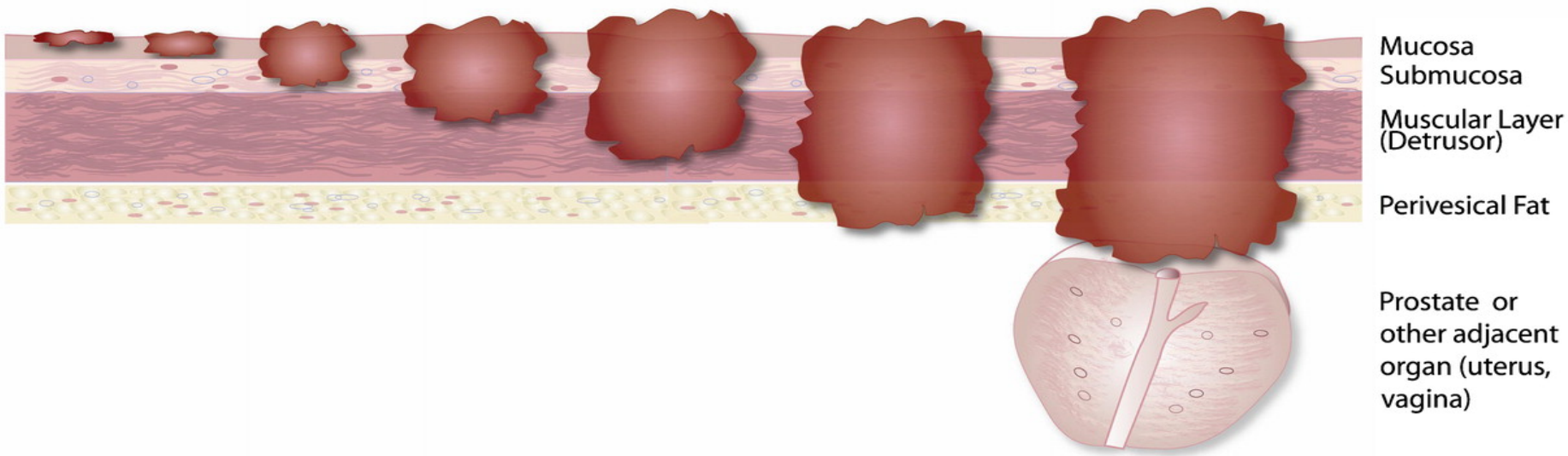
‡Patients may be treated beyond progression if there is clinical benefit in the opinion of the investigator

Choueiri et al. Presented at: ASCO 2020; May 29-31, 2020; Virtual Meeting. Abstract 5102.

Immunotherapy for Metastatic Bladder Cancer (Urothelial Carcinoma; UC)

Non-Muscle Invasive → Muscle Invasive → Metastatic

TNM	TIS	T_a	T_1	T_{2A}	T_{2B}	T_{3B}	T_{4A}
JSM	0	0	A	B_1	B_2	C	D_1



Approved checkpoint inhibitor for non-muscle invasive bladder cancer

Drug	Approved	Indication	Dose
Pembrolizumab	January 2020	BCG-unresponsive, high-risk NMIBC, with or without papillary tumors and ineligible for cystectomy	200 mg Q3W

Response, n (%)	KEYNOTE-057 cohort A (n=97)
Complete response	40 (41.2)
Non-complete response	56 (57.7)
Persistent	40 (41.2)
Recurrent	6 (6.2)
NMIBC stage progression	9 (9.3)
Progression to T2	0
Extravesical disease	1 (1.0)
Non-evaluable	1 (1.0)

FDA Advisory Committee Briefing Document, 2019.

Approved checkpoint inhibitors for mUC – *cisplatin refractory*

Drug	Approved	Indication	Dose
Atezolizumab	2016 (2018)	Advanced/metastatic UC	1200 mg Q3W
Avelumab	2017	Advanced/metastatic UC	10 mg/kg Q2W
Durvalumab	2017	Advanced/metastatic UC	10 mg/kg Q2W
Nivolumab	2017	Advanced/metastatic UC	240 mg Q2W or 480 mg Q4W
Pembrolizumab	2017 (2018)	Advanced/metastatic UC	200 mg Q3W

Approved checkpoint inhibitors for mUC – *cisplatin ineligible*

Drug	Approved	Indication	Dose
Atezolizumab	2017 (2018)	Advanced/metastatic UC (PD-L1 ≥5%)	1200 mg Q3W
Pembrolizumab	2017 (2018)	Advanced/metastatic UC (PD-L1 CPS ≥10)	200 mg Q3W

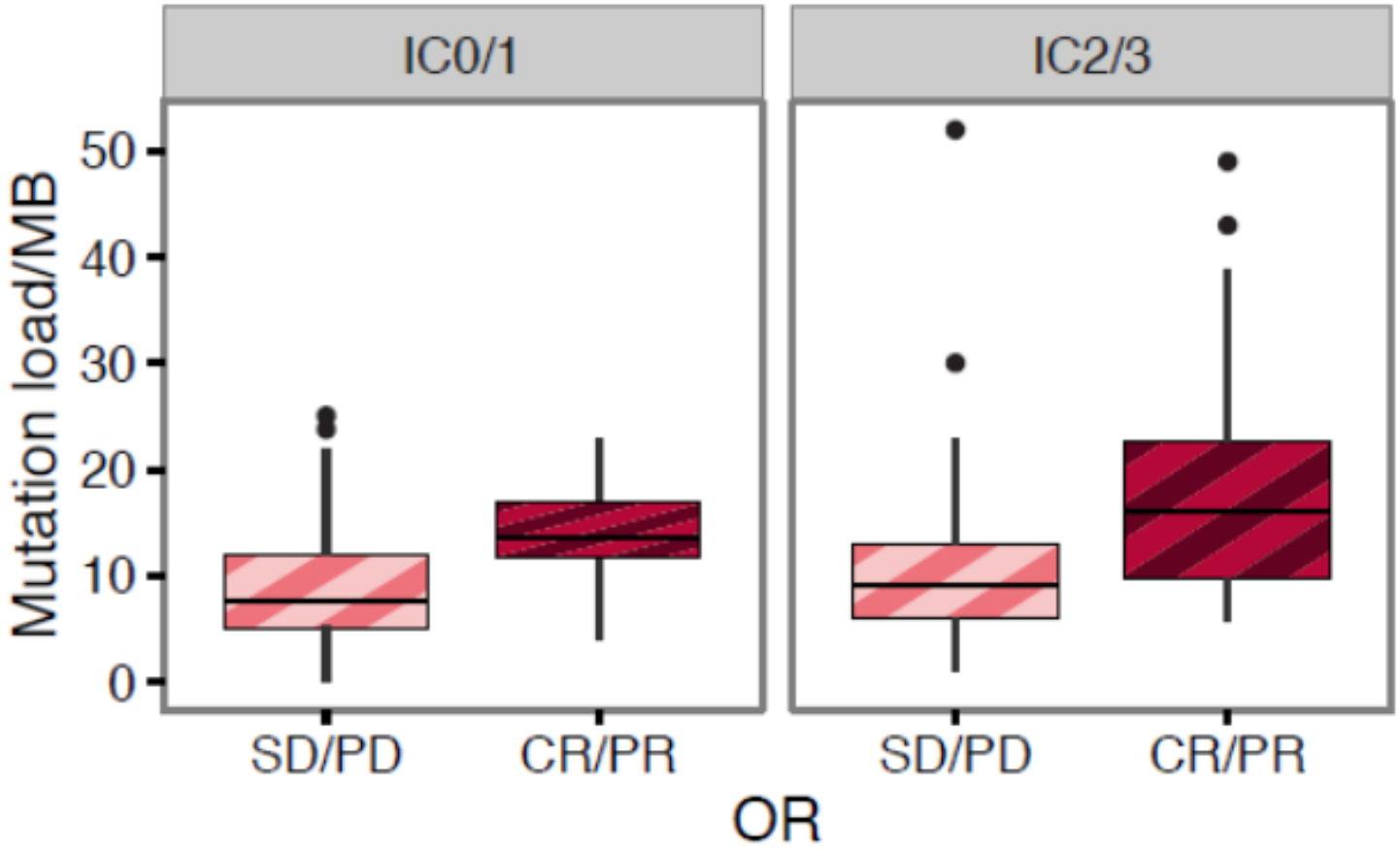
June 2018

FDA limits the use of Atezolizumab and Pembrolizumab for some urothelial cancer patients

- Locally advanced or metastatic urothelial carcinoma and ineligible for cisplatin-based chemo and tumor PD-L1 (CPS ≥ 10, pembro; IC ≥ 5% tumor area, atezo)
- Patients ineligible for any platinum-containing chemotherapy regardless of PD-L1 status

Tumor Mutational Burden (TMB) May Signal Responses with PD-1 Blockade

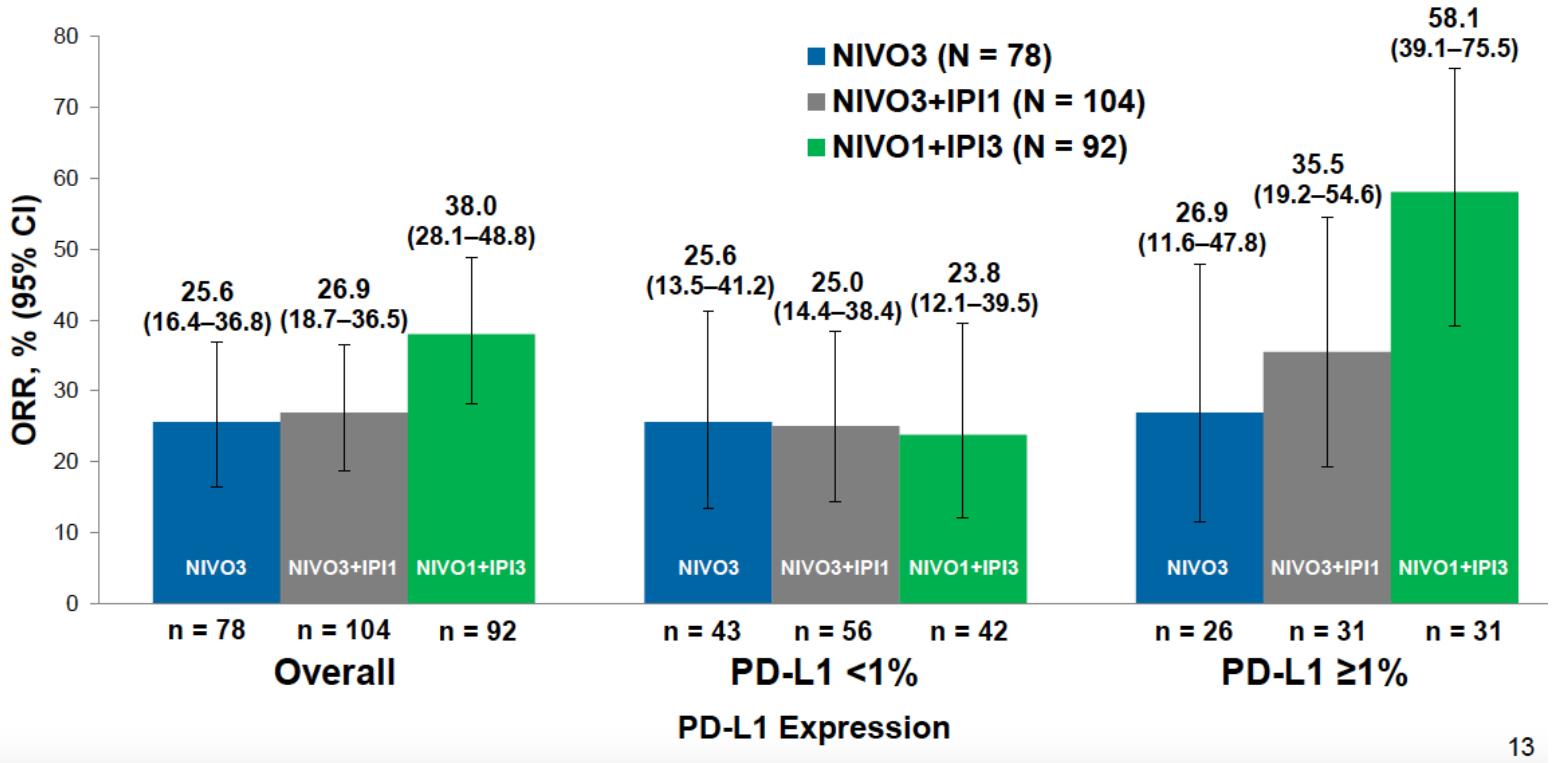
Atezolizumab in mUC



Rosenberg et al. Lancet 2016

In development: Ipilimumab + Nivolumab CheckMate 032

ORR by Baseline Tumor PD-L1 Expression per Investigator



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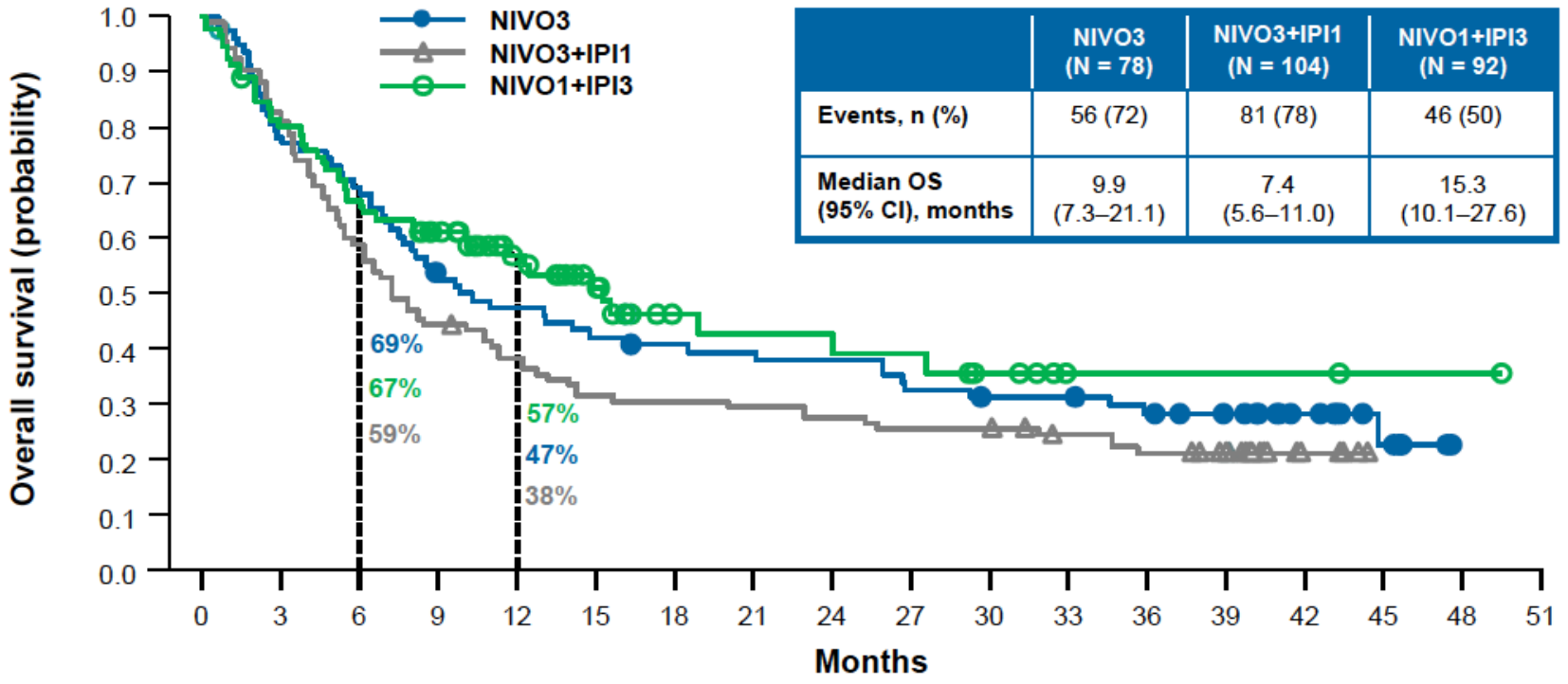
Rosenberg, ESMO 2018

In development: Ipilimumab + Nivolumab CheckMate 032



	NIVO3 (N = 78)	NIVO3+IPI1 (N = 104)	NIVO1+IPI3 (N = 92)
Events, n (%)	56 (72)	81 (78)	46 (50)
Median OS (95% CI), months	9.9 (7.3–21.1)	7.4 (5.6–11.0)	15.3 (10.1–27.6)

Number at risk

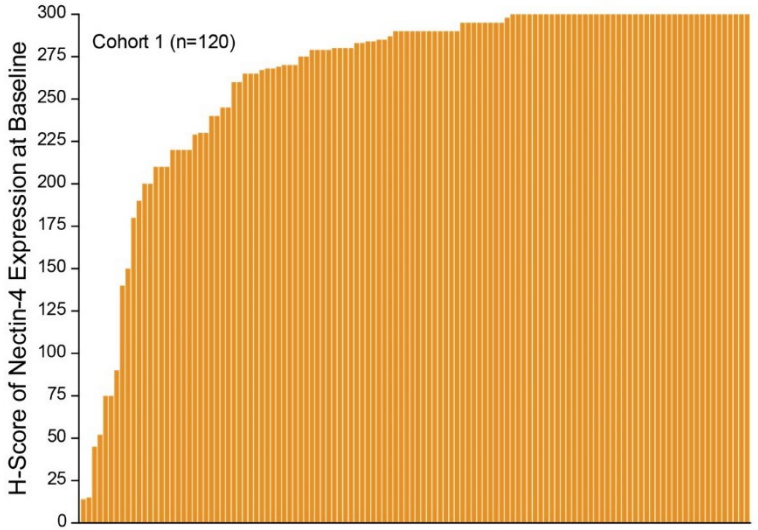
NIVO3	78	61	54	41	36	32	30	29	28	24	22	22	19	16	9	4	0	0
NIVO3+IPI1	104	86	61	46	39	32	31	30	28	26	26	22	19	15	5	0	0	0
NIVO1+IPI3	92	73	60	48	33	23	13	12	12	11	8	2	2	2	2	1	1	0

Rosenberg, ESMO 2018

Approved antibody-drug conjugate for mUC

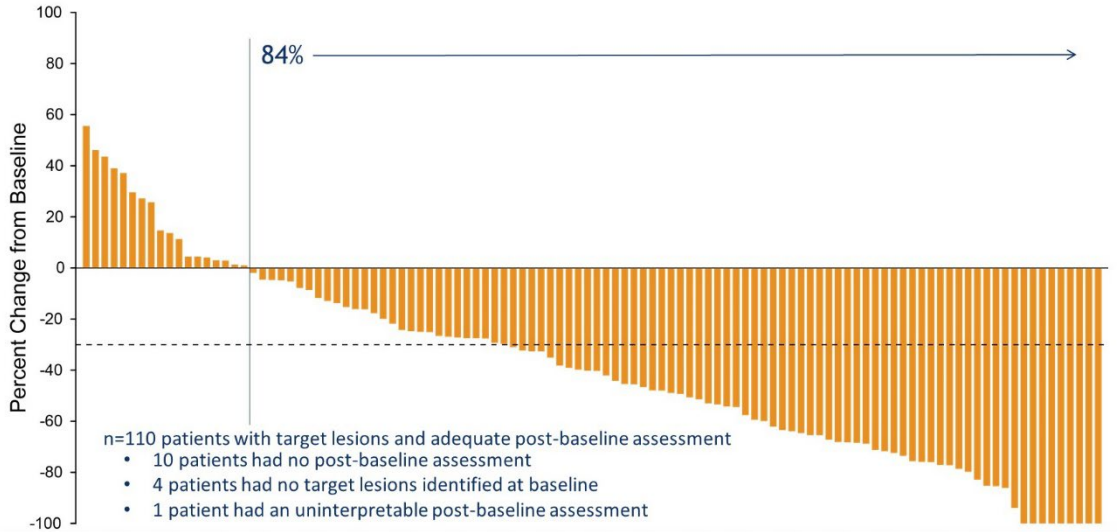
Drug	Approved	Indication	Dose
Enfortumab vedotin	December 2019	Locally advanced/metatstatic UC with previous αPD-1/PD-L1 and Pt-based chemotherapy	1.25 mg/kg IV on days 1, 8, and 15 of each 28-day cycle

EV-201: Cohort 1 Nectin-4 Expression



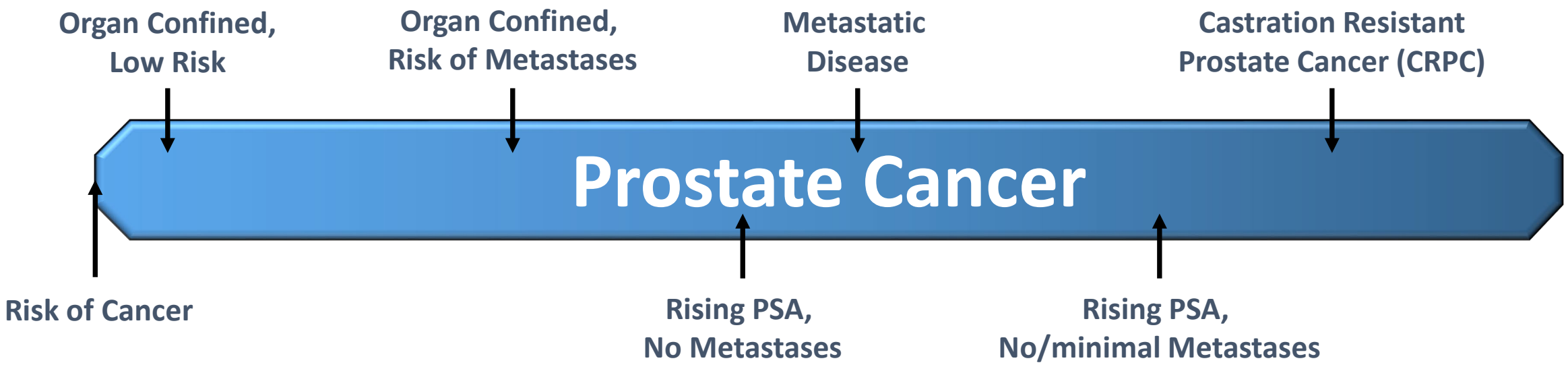
[1] Five patients did not have adequate tissue for Nectin-4 testing

EV-201: Cohort 1 Change in Tumor Measurements per BICR



Petrylak, ASCO 2019.

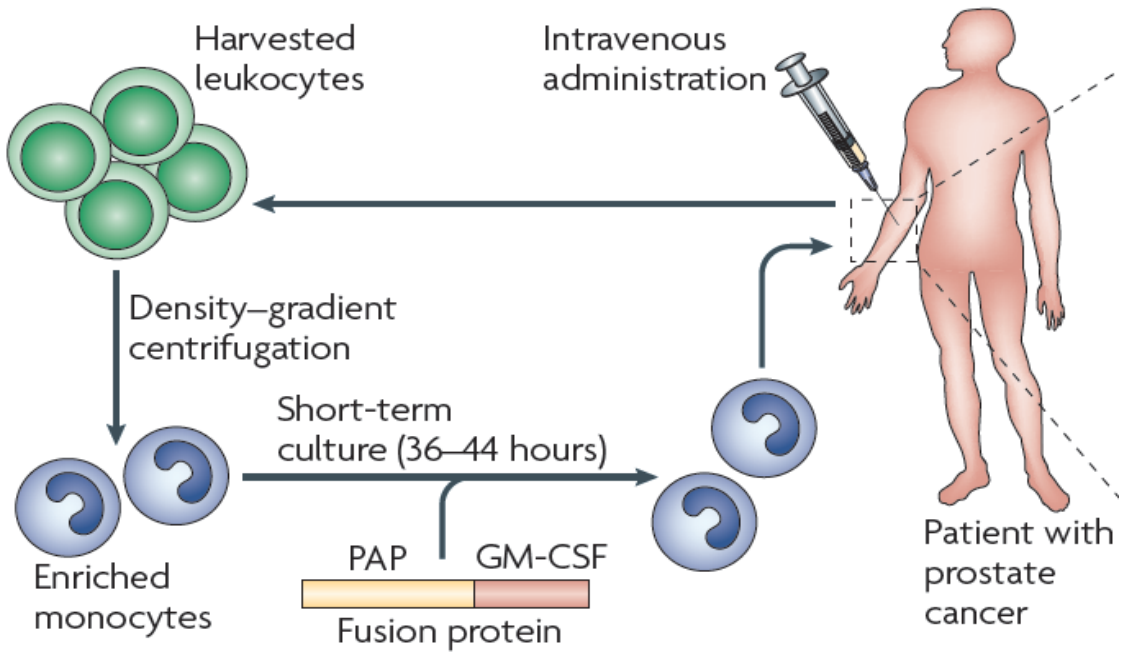
The Spectrum of Prostate Cancer

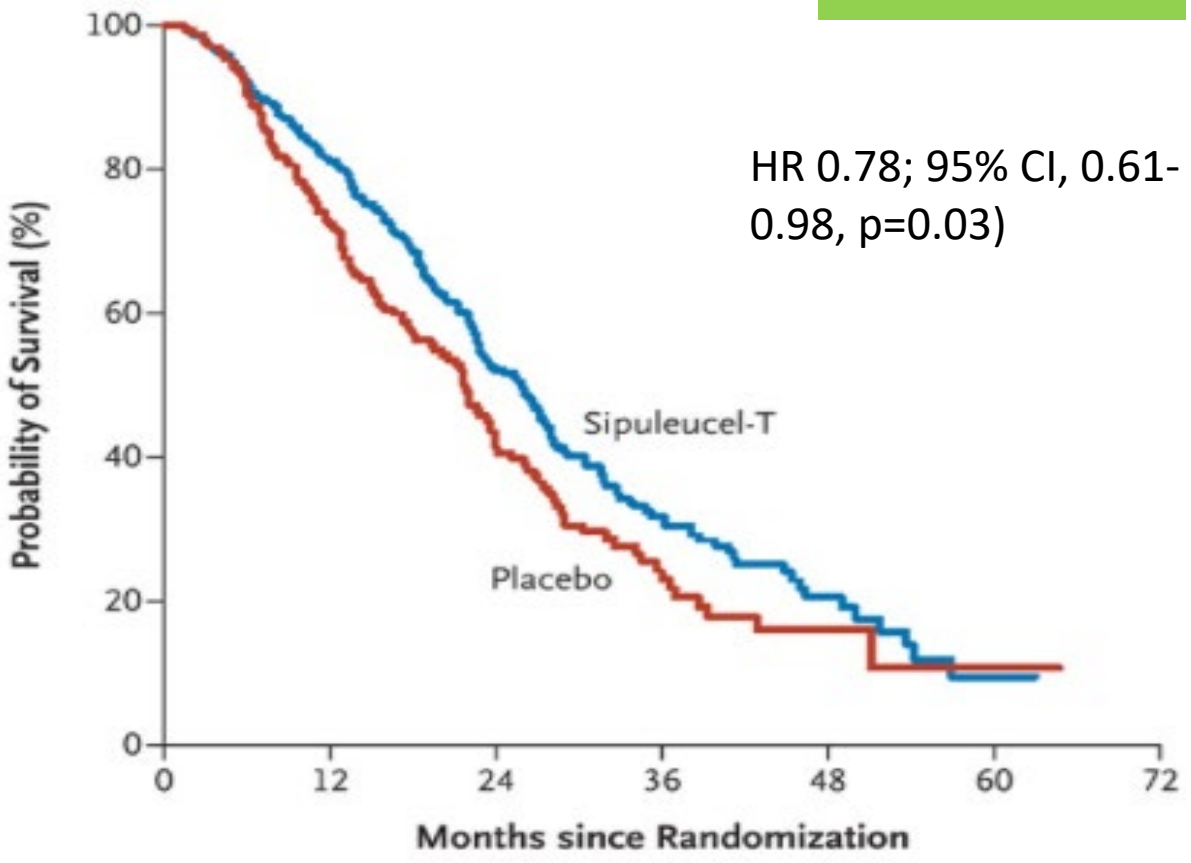


Sipuleucel-T in mCRPC

PROVENGE 2010

First anti-cancer therapeutic vaccine





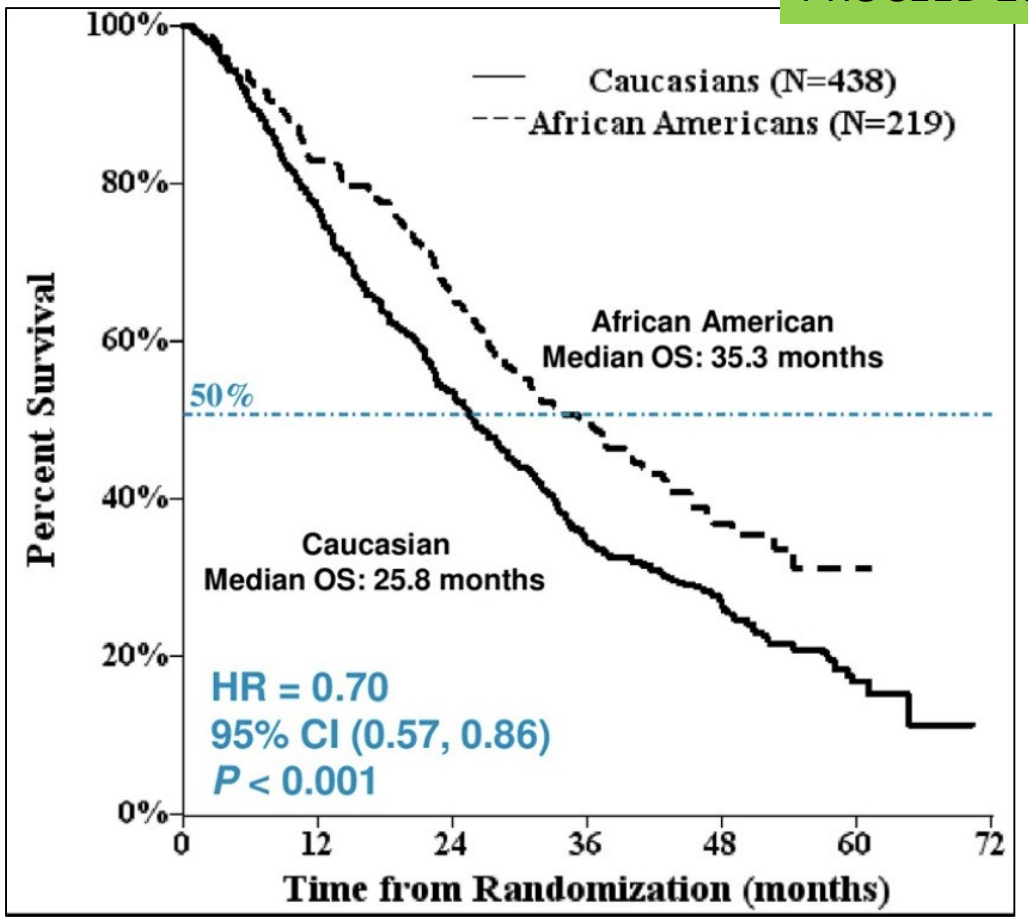
HR 0.78; 95% CI, 0.61-0.98, p=0.03)

Drake et al. Curr Opin Urol 2010
Kantoff et al. NEJM 2010

Sipuleucel-T in mCRPC

PROCEED 2019

- Post-hoc analysis of Phase 3 trial PROCEED (N = 1902 mCRPC patients)
- African-Americans (AA) = 438; Caucasians (CAU) = 219
- Median OS = 35.2 (AA) vs 29.9 mo (CAU); HR 0.81, 95% CI 0.68–0.97; p = 0.03.
- AA race was independently associated with prolonged OS on multivariate analysis (HR 0.60, 95% CI 0.48–0.74; p < 0.001)

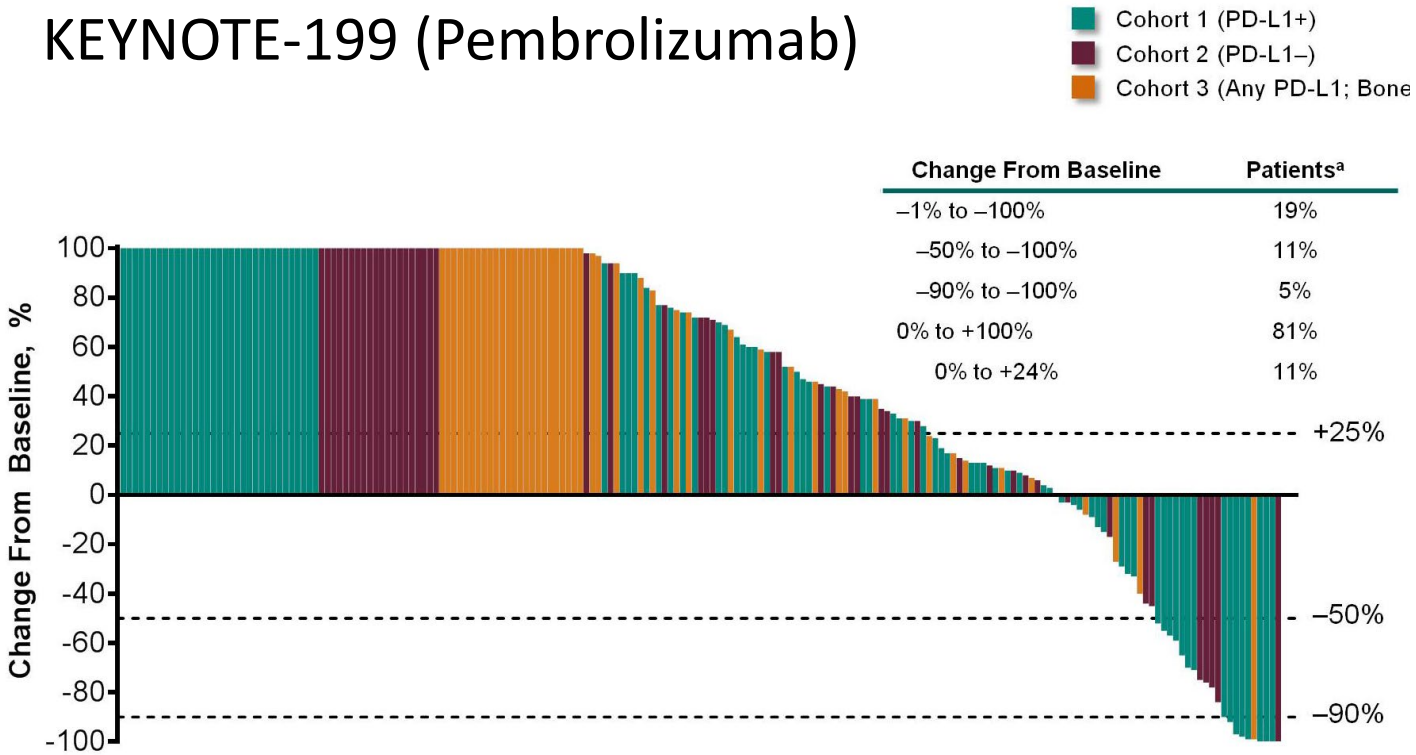


Sartor et al. ASCO 2019

Limited efficacy of Checkpoint Inhibitors in mCRPC

No FDA-approved CIs for mCRPC

KEYNOTE-199 (Pembrolizumab)



- Pembrolizumab is approved for all Microsatellite Instability-High (MSI-H) solid tumors
- MSI-H incidence is low in PC
  - Localized PC ~2%
  - Autopsy series of mCRPC ~12%
- MSI testing may offer pembrolizumab as an option

DeBono et al. ASCO 2018

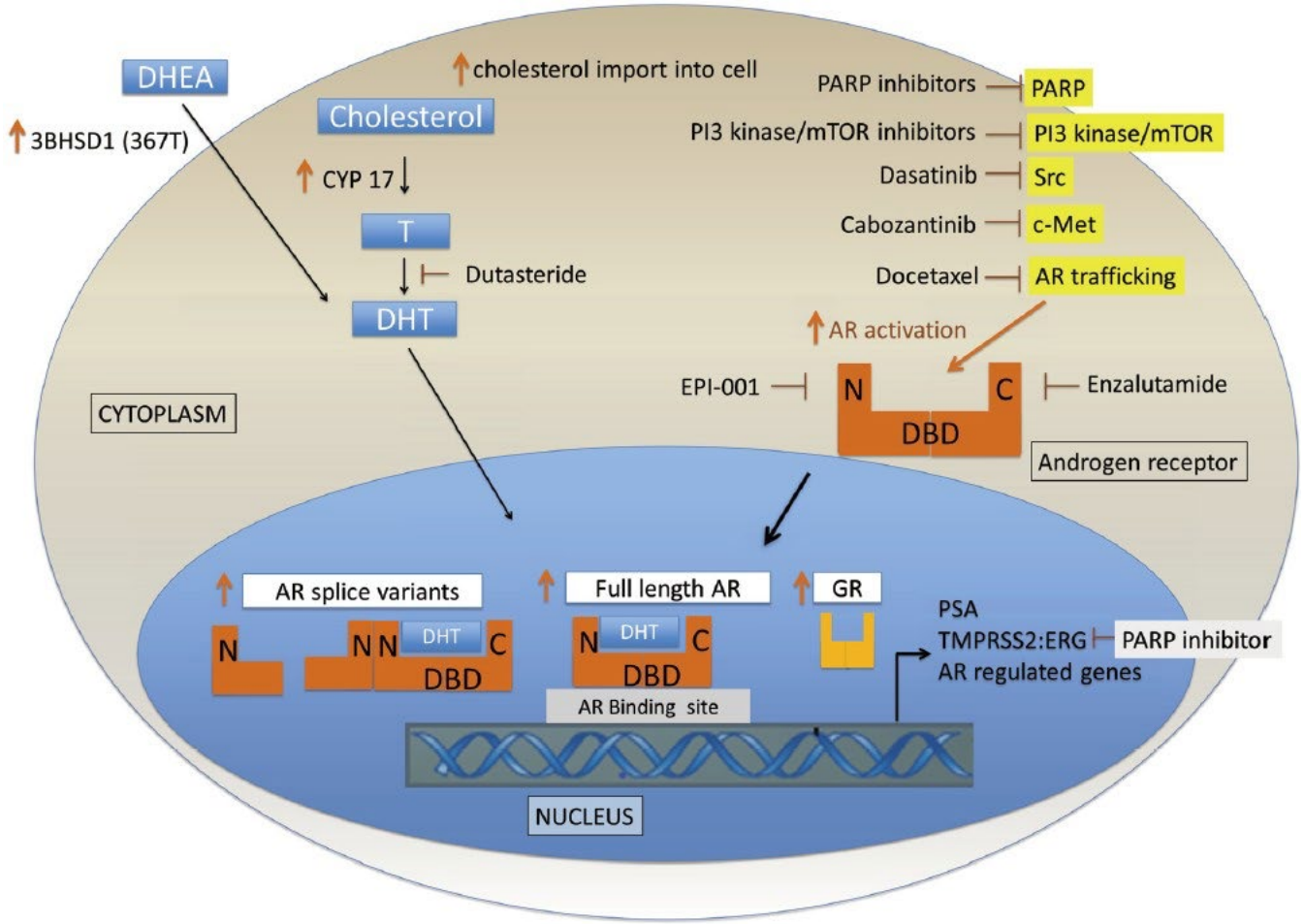
In development: nivolumab + ipilimumab in mCRPC

- Checkmate 650
- Nivo 1 mg/kg + Ipi 3 mg/kg Q3W for 4 doses, then Nivo 480 mg Q4W
- Progressed after 2nd-gen hormonal: 26% response @ 11.9 mo, 2 CR
- Progressed after chemo+hormonal: 10% response @ 13.5 mo, 2 CR
- Higher ORR in:
  - PD-L1 > 1%
  - DNA damage repair deficient
  - homologous recombination deficiency
  - high tumor mutational burden

Sharma, GU Cancer Symp 2019.

Future Combinations in mCRPC to Engage Immune System

- Hormonal therapy
- Radiation
- Radium-223
- PARP inhibitors
- Chemotherapy
- New targets



Stein et al. Asian J Andrology 2014

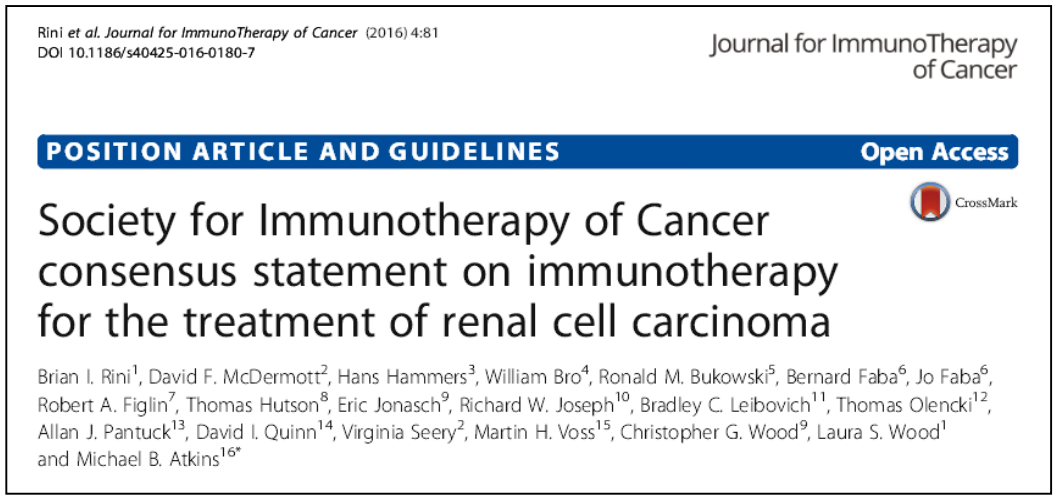
Conclusions

- The role of immunotherapy in GU malignancies is increasing
- In RCC, many front-line checkpoint inhibitor options are approved
- Multiple checkpoint inhibitors approved for advanced/metastatic urothelial carcinoma
- Low immune engagement in prostate cancer has limited the application of immunotherapy in this disease

Society for Immunotherapy of Cancer
ADVANCES IN Cancer IMMUNOTHERAPY™

Additional Resources

Society for Immunotherapy of Cancer
Cancer Immunotherapy GUIDELINES

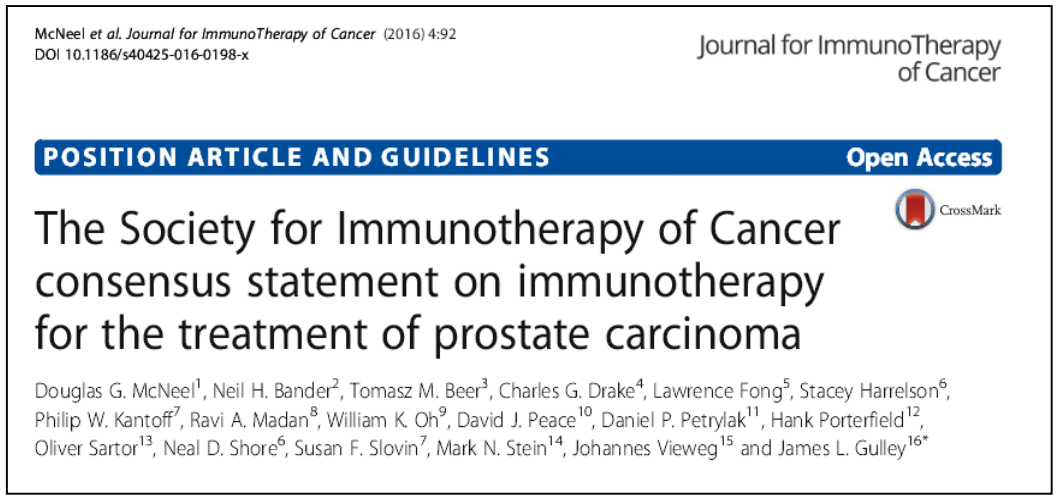

Rini et al. Journal for ImmunoTherapy of Cancer (2016) 4:81
DOI 10.1186/s40425-016-0180-7

Journal for ImmunoTherapy of Cancer

POSITION ARTICLE AND GUIDELINES Open Access

Society for Immunotherapy of Cancer consensus statement on immunotherapy for the treatment of renal cell carcinoma

Brian I. Rini[1], David F. McDermott[2], Hans Hammers[3], William Bro[4], Ronald M. Bukowski[5], Bernard Faba[6], Jo Faba[6], Robert A. Figlin[7], Thomas Hutson[8], Eric Jonasch[9], Richard W. Joseph[10], Bradley C. Leibovich[11], Thomas Olencki[12], Allan J. Pantuck[13], David I. Quinn[14], Virginia Seery[2], Martin H. Voss[15], Christopher G. Wood[9], Laura S. Wood[1] and Michael B. Atkins[16*]

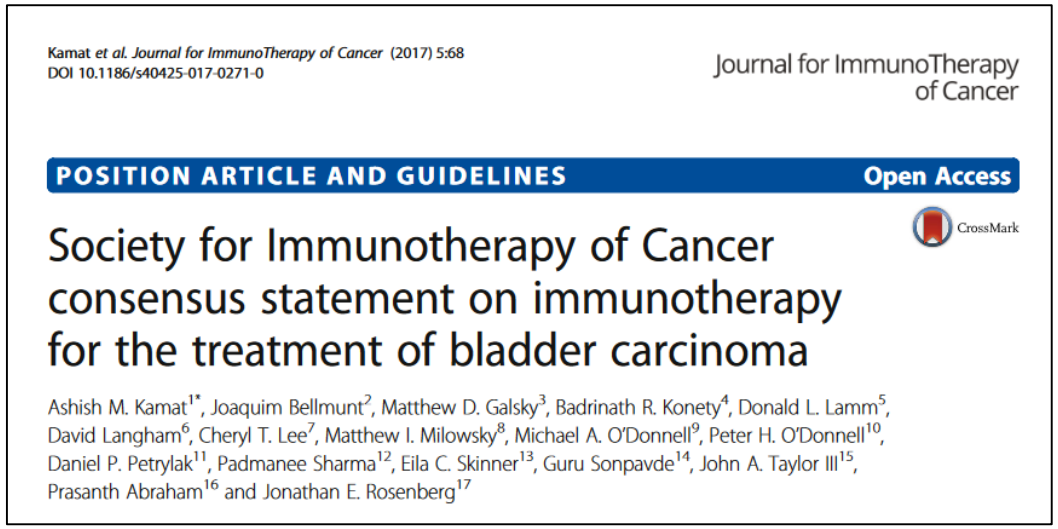

McNeel et al. Journal for ImmunoTherapy of Cancer (2016) 4:92
DOI 10.1186/s40425-016-0198-x

Journal for ImmunoTherapy of Cancer

POSITION ARTICLE AND GUIDELINES Open Access

The Society for Immunotherapy of Cancer consensus statement on immunotherapy for the treatment of prostate carcinoma

Douglas G. McNeel[1], Neil H. Bander[2], Tomasz M. Beer[3], Charles G. Drake[4], Lawrence Fong[5], Stacey Harrelson[6], Philip W. Kantoff[7], Ravi A. Madan[8], William K. Oh[9], David J. Peace[10], Daniel P. Petrylak[11], Hank Porterfield[12], Oliver Sartor[13], Neal D. Shore[6], Susan F. Slovin[7], Mark N. Stein[14], Johannes Vieweg[15] and James L. Gulley[16*]


Kamat et al. Journal for ImmunoTherapy of Cancer (2017) 5:68
DOI 10.1186/s40425-017-0271-0

Journal for ImmunoTherapy of Cancer

POSITION ARTICLE AND GUIDELINES Open Access

Society for Immunotherapy of Cancer consensus statement on immunotherapy for the treatment of bladder carcinoma

Ashish M. Kamat[1*], Joaquim Bellmunt[2], Matthew D. Galsky[3], Badrinath R. Konety[4], Donald L. Lamm[5], David Langham[6], Cheryl T. Lee[7], Matthew I. Milowsky[8], Michael A. O'Donnell[9], Peter H. O'Donnell[10], Daniel P. Petrylak[11], Padmanee Sharma[12], Eila C. Skinner[13], Guru Sonpavde[14], John A. Taylor III[15], Prasanth Abraham[16] and Jonathan E. Rosenberg[17]

AAEM American Academy of Emergency Medicine
ACCC Association of Community Cancer Centers
HOPA Hematology/Oncology Pharmacy Association
sitc Society for Immunotherapy of Cancer

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Case Study

Case Study 1

- 62 yo man with 7 year h/o Crohn's Disease rx'ed with intermittent azathioprine and steroids with response, presented with abd pain, weight loss and fatigue
- Abd MRI: 12 cm R upper pole renal mass with paracaval adenopathy
- R radical nephrectomy revealed a 12 cm ccRCC with 90% sarcomatoid features; 2/6 LNs + (T3a N1a M0); declined adjuvant Rx
- 2 mos post-op: he has night sweats, anorexia; CT CAP showed 4.4 cm mass in R nx bed, sub-cm pulm nodules and abd LNs

- How would you treat?

How would you treat?

A) Sunitinib/Pazopanib

B) Cabozantinib

C) Ipilimumab/Nivolumab

D) Axitinib/Pembrolizumab

E) Other

Case Study (History 2)

- Patient started on cabozantinib 60 mg daily by outside oncologist
- Symptoms persisted and CT scan 12 weeks into treatment showed significant interval progression

How would you treat now?

A) Ipi/Nivo

B) Axi/Pembro

C) Nivolumab monotherapy

D) Lenvatinib/everolimus

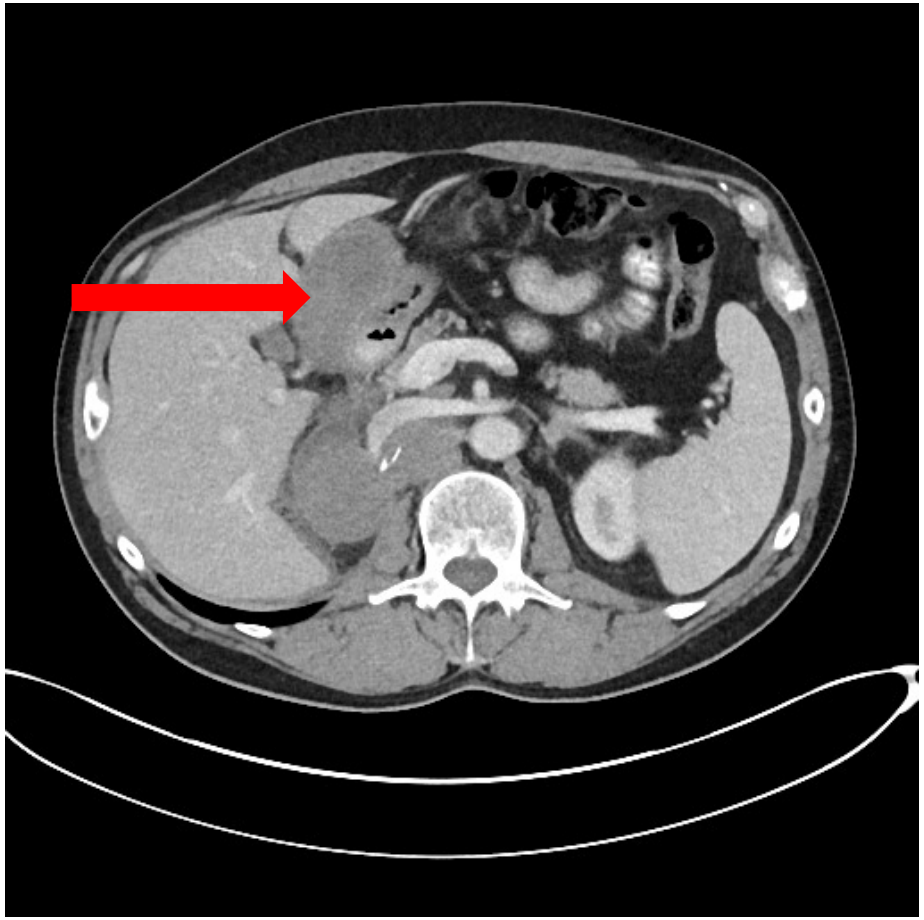
E) Other

Case Study (History 3)

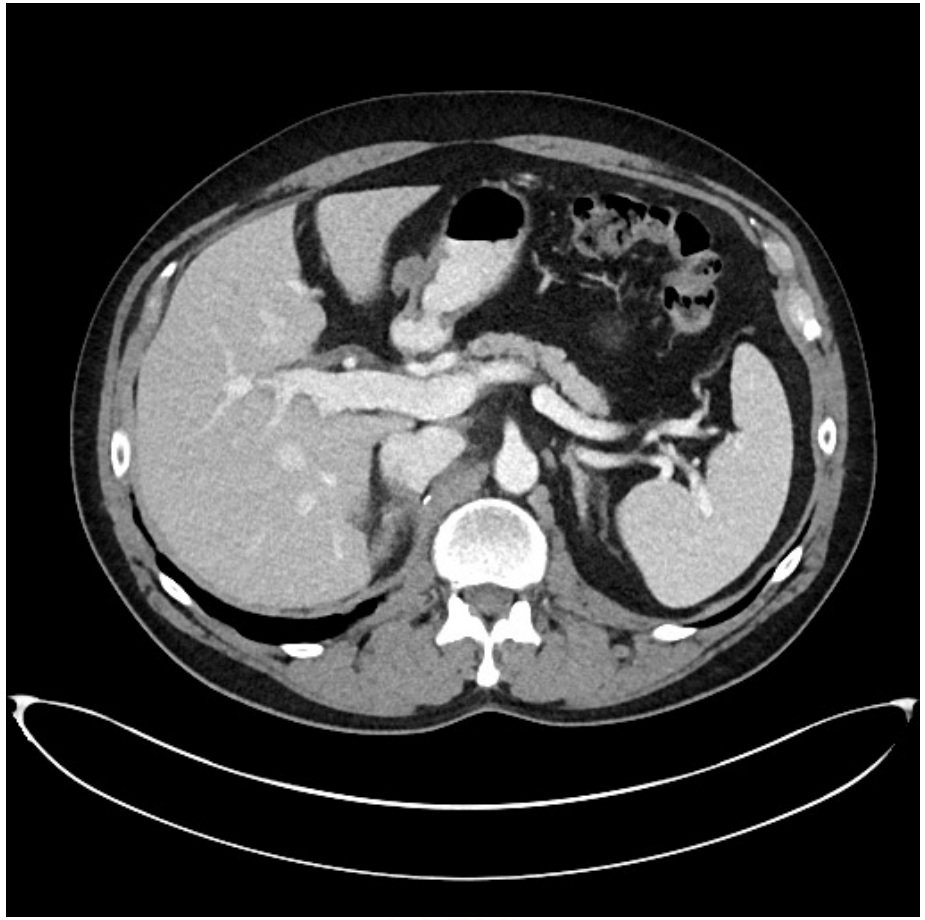
- He was begun on nivo monotherapy
- Symptoms rapidly improved, he regained energy and lost weight
- He experienced rash and joint pains, but no Crohn's flare
- Scans showed major response

Case Study Image- Abdominal Nodes

4/2018

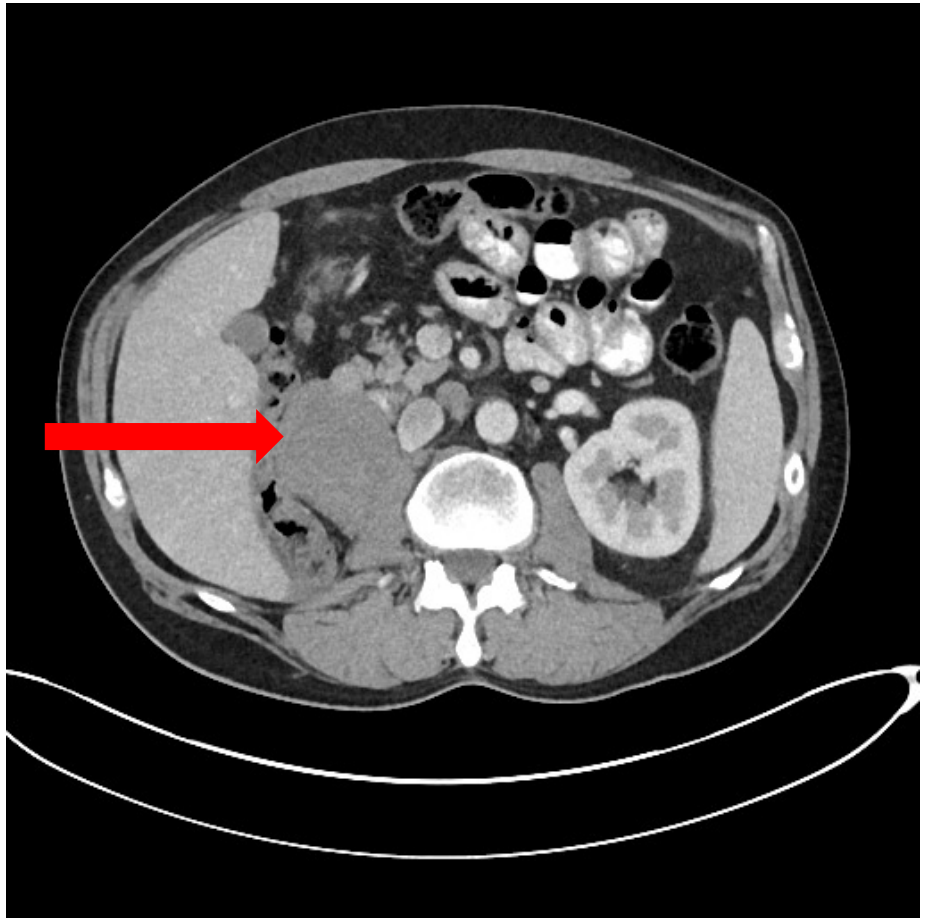


4/2019

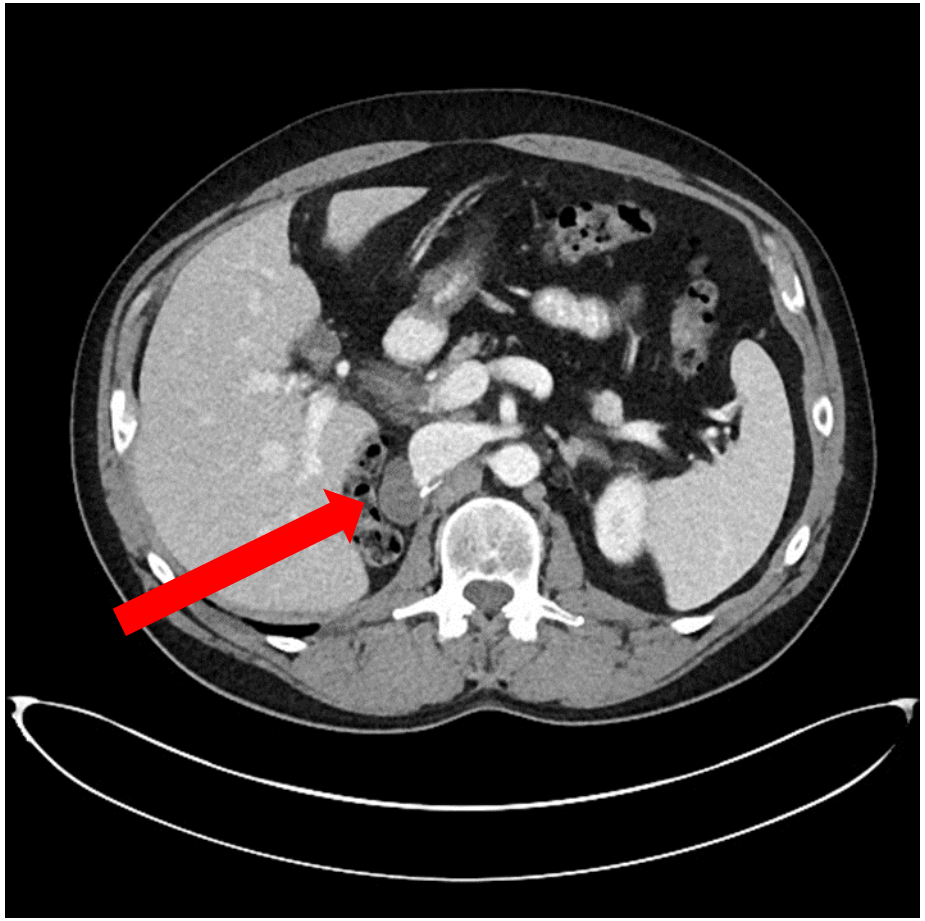


Case Study Image 2: R Nx Bed Lesion

4/2018



4/2020



What would do now?

A) Continue Nivo Monotherapy

B) Switch to Axi/pembro

C) Add Ipilimumab

D) Switch to Lenvatinib/everolimus

E) Evaluate for stopping therapy

Case Study 1 (History 4)

- PET-CT showed uptake only in the R Nx bed lesion.
- Biopsy of residual Nx bed lesion after 2 years of Rx showed no cancer.
- Treatment stopped; patient continues to do well off therapy now 6 months after treatment cessation.

Case Study 1: Take Home Messages

1) Immunotherapy works particularly well relative to VEGFR TKIs in patients with RCC and sarcomatoid histology
2) Anti-PD1 monotherapy represents an option for patients where it is risky to give nivo/ipi
3) Anti-PD1 monotherapy doesn't always exacerbated underlying autoimmune conditions
4) Many residual radiographic abnormalities may not represent active cancer in patients responding to immunotherapy
5) Anti-PD1 therapy can be safely stopped in patients without active cancer turning survivors into "thrivers".