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

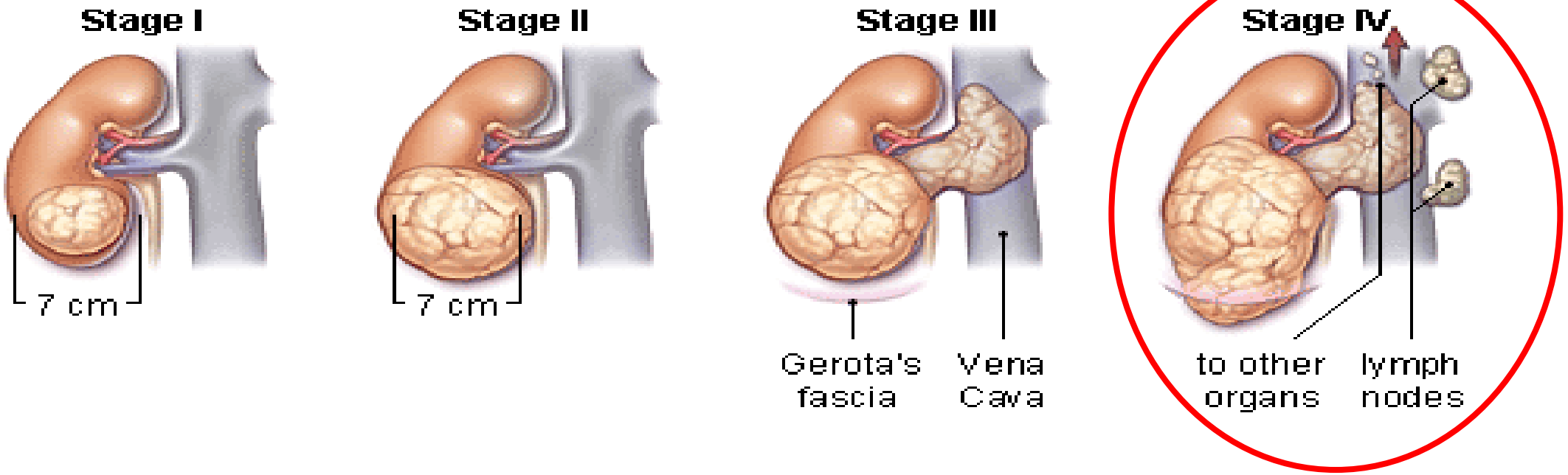
Disclosures

- Advisory role:
  - Genentech, Merck, Pfizer, GSK, BMS, Pierre-Fabre, Sanofi Aventis, Astellas, OncoGenex, Janssen
- Speaker role:
  - Pfizer, Merck, GSK, Novartis, Pierre-Fabre, Astellas
- Research funding:
  - Takeda, Pfizer, Novartis, Sanofi Aventis

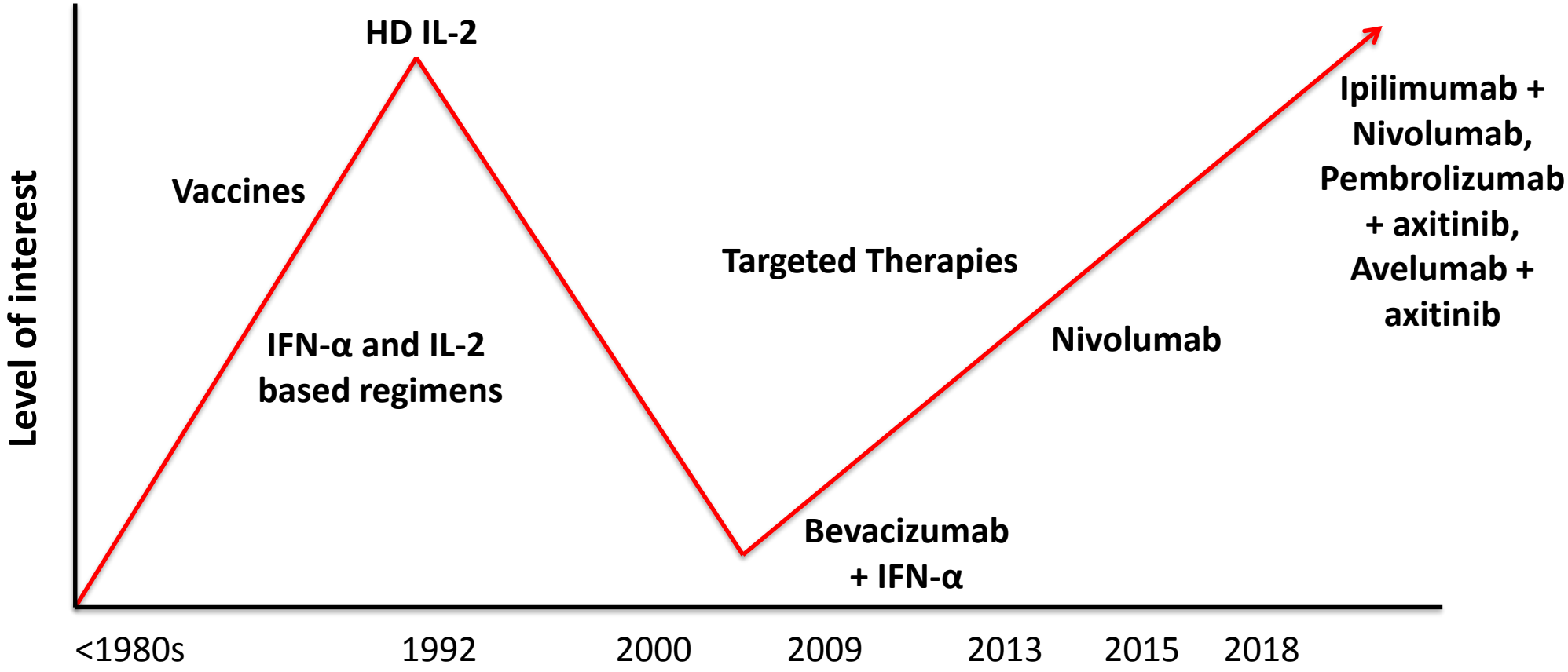
I will be discussing non-FDA approved indications during my presentation

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

Surgically resectable → Oligo-metastatic → Metastatic



History of Immunotherapy in mRCC



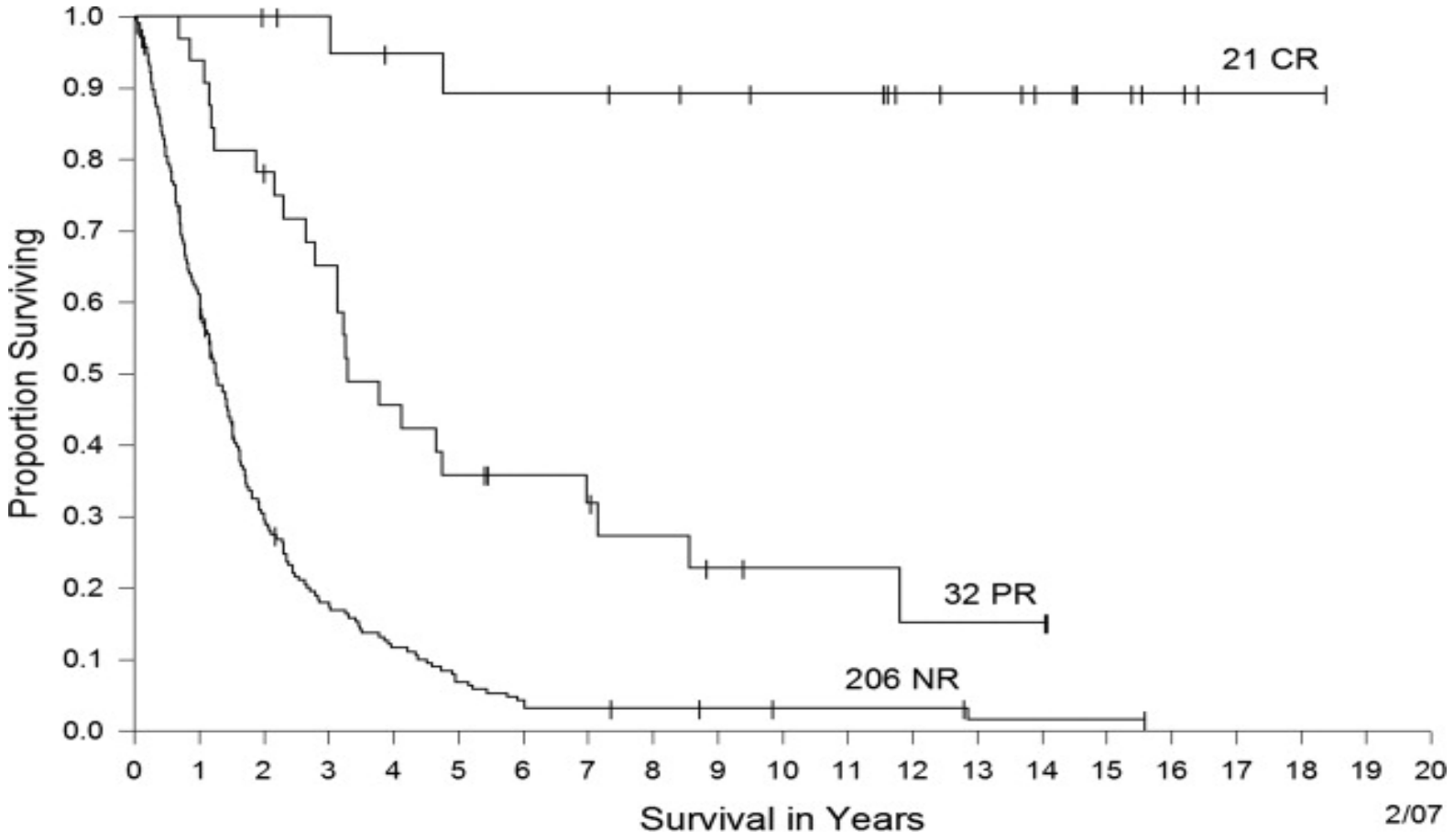
Resurgence of interest in immunotherapy

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

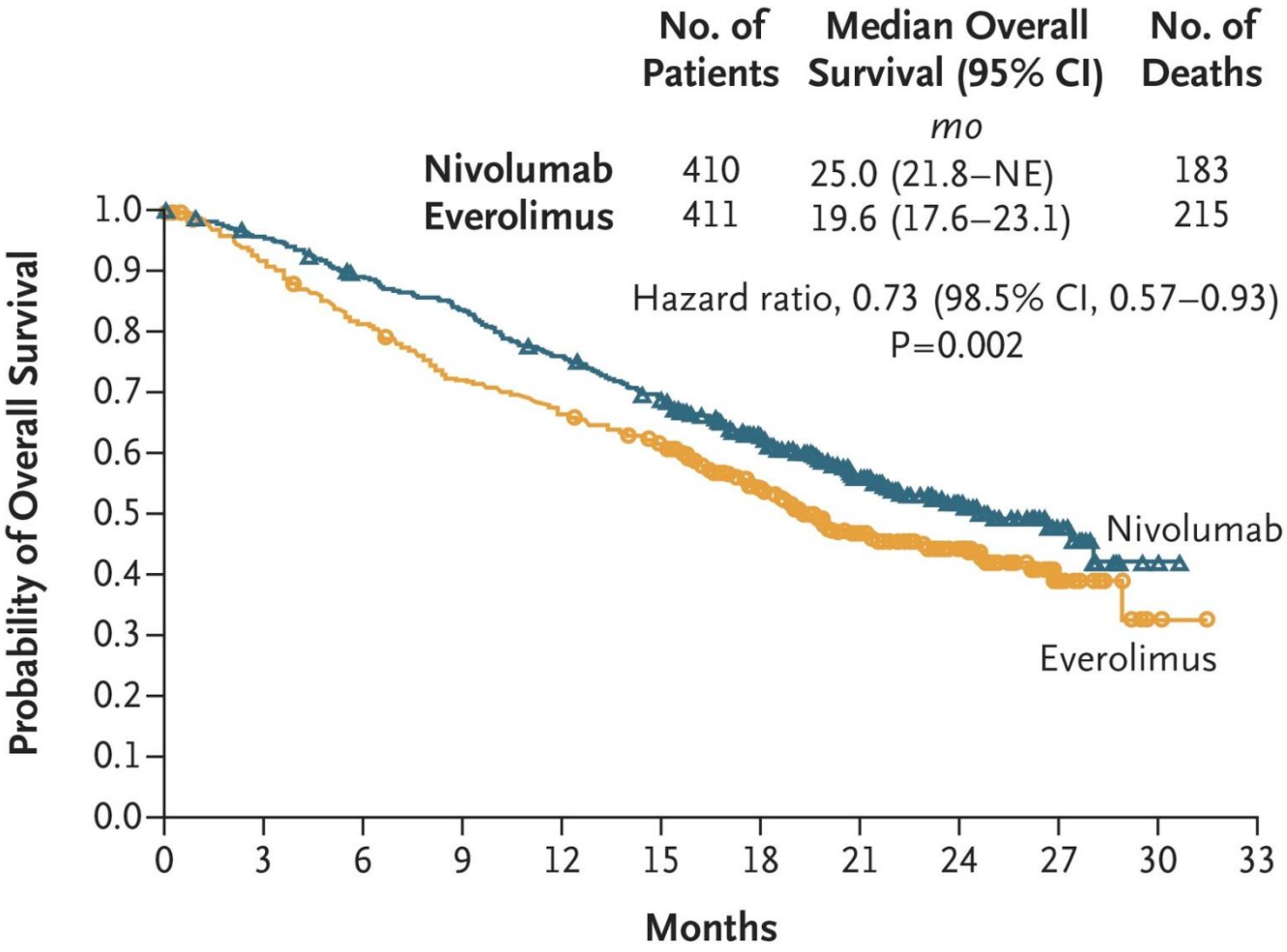
- 20 year analysis of 259 patients
- ORR = 20%
  - 9% CR (n = 23)
  - 12% PR (n = 30)
- Median duration of response = 15.5 months
- Median OS = 19 months



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)

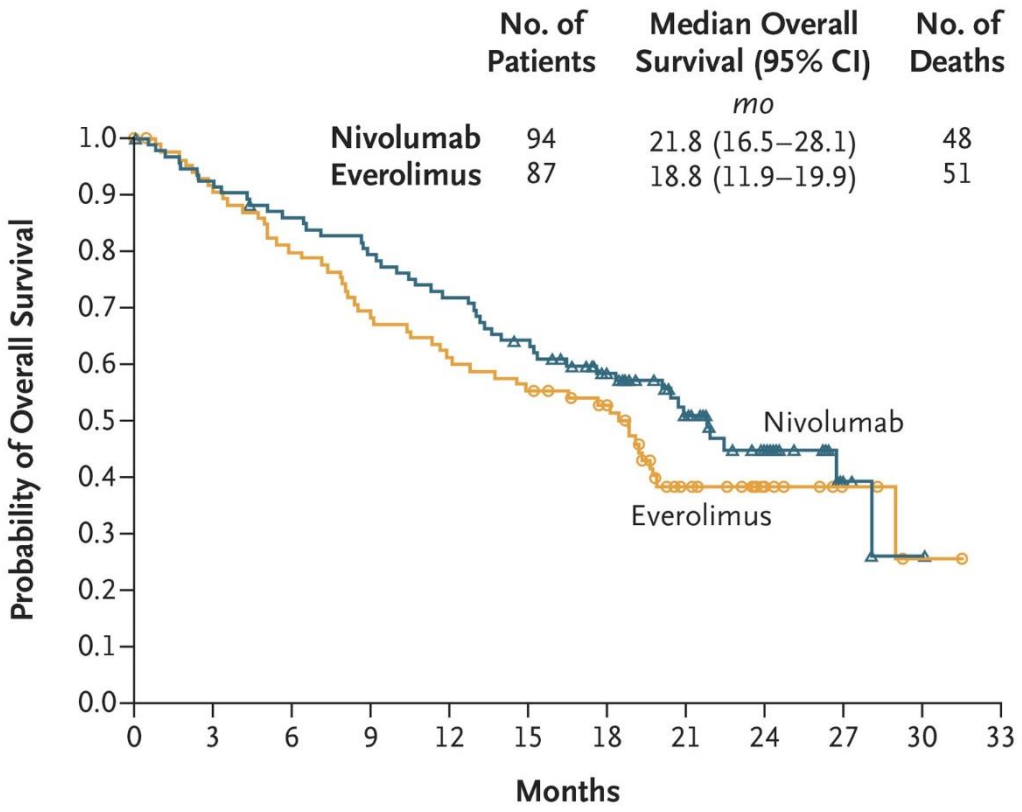


Motzer et al. NEJM 2015

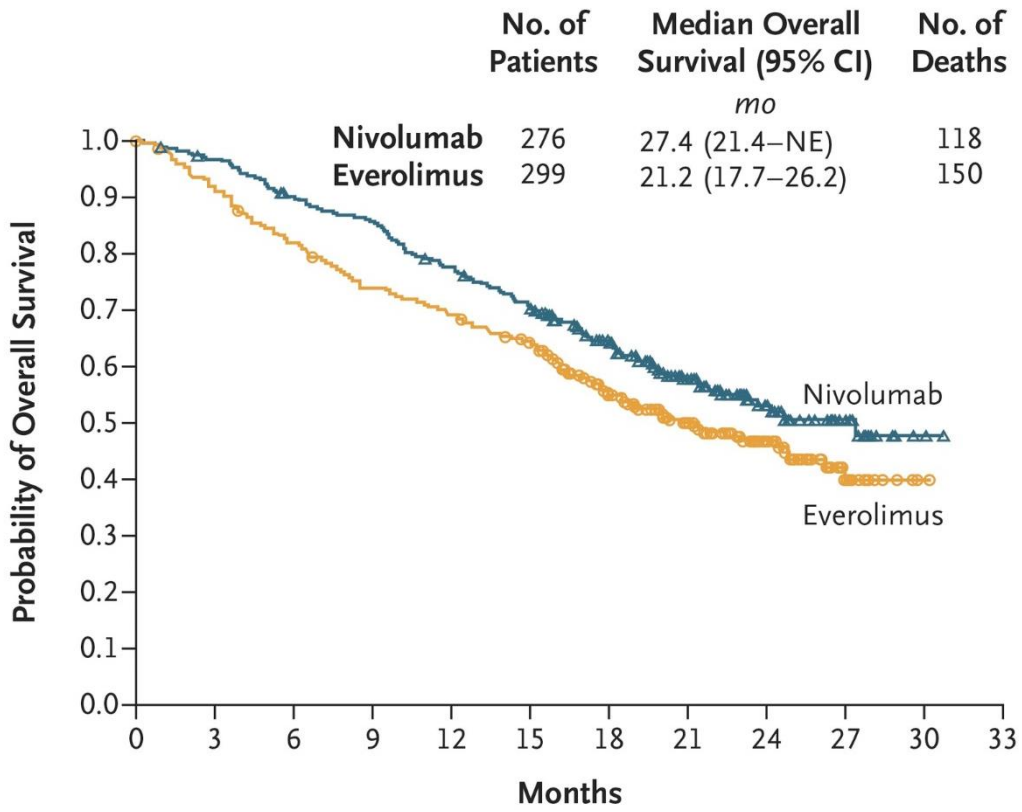
Second-Line Nivolumab in mRCC

PD-L1 subgroups

PD-L1 ≥ 1%

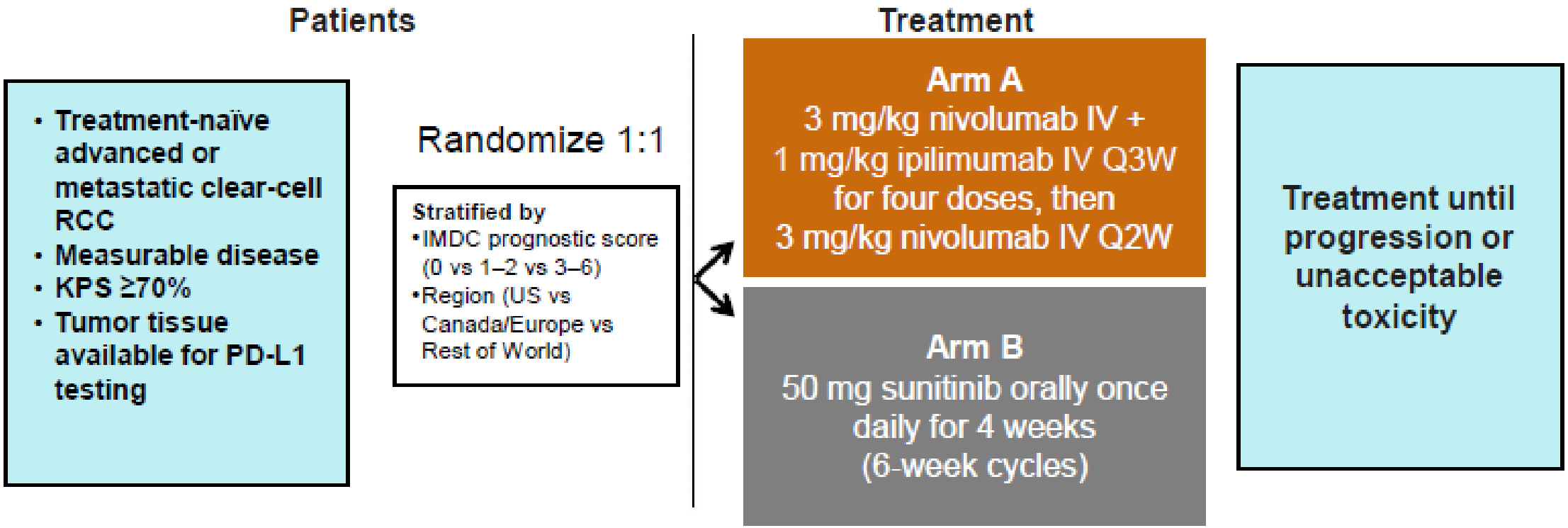


PD-L1 < 1%



Motzer et al. NEJM 2015

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

First-line Nivolumab + Ipilimumab in mRCC by IMDC Risk: overall survival

CheckMate 214

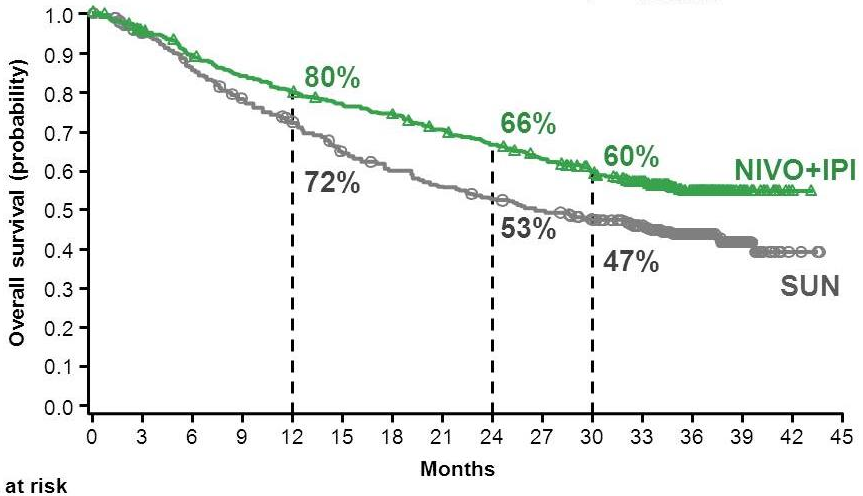
Follow-up
= 30 months

Intermediate/poor risk

Median OS, months (95% CI)

NIVO+IPI	NR (35.6–NE)
SUN	26.6 (22.1–33.4)

HR (95% CI), 0.66 (0.54–0.80)
P < 0.0001



No. at risk

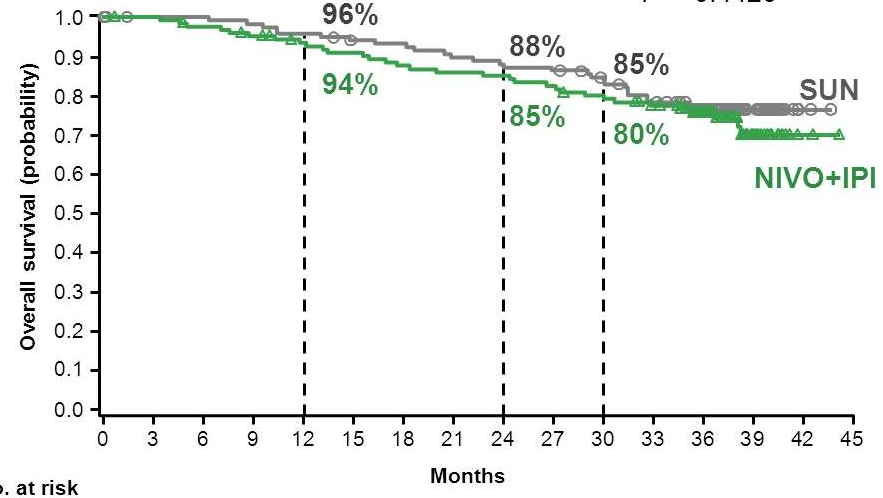
NIVO+IPI	425	399	372	348	332	317	306	287	270	253	233	183	90	34	2	0
SUN	422	388	353	318	290	257	236	220	207	194	179	144	75	29	3	0

Favorable risk

Median OS, months (95% CI)

NIVO+IPI	NR (NE)
SUN	NR (NE)

HR (95% CI), 1.22 (0.73–2.04)
P = 0.4426



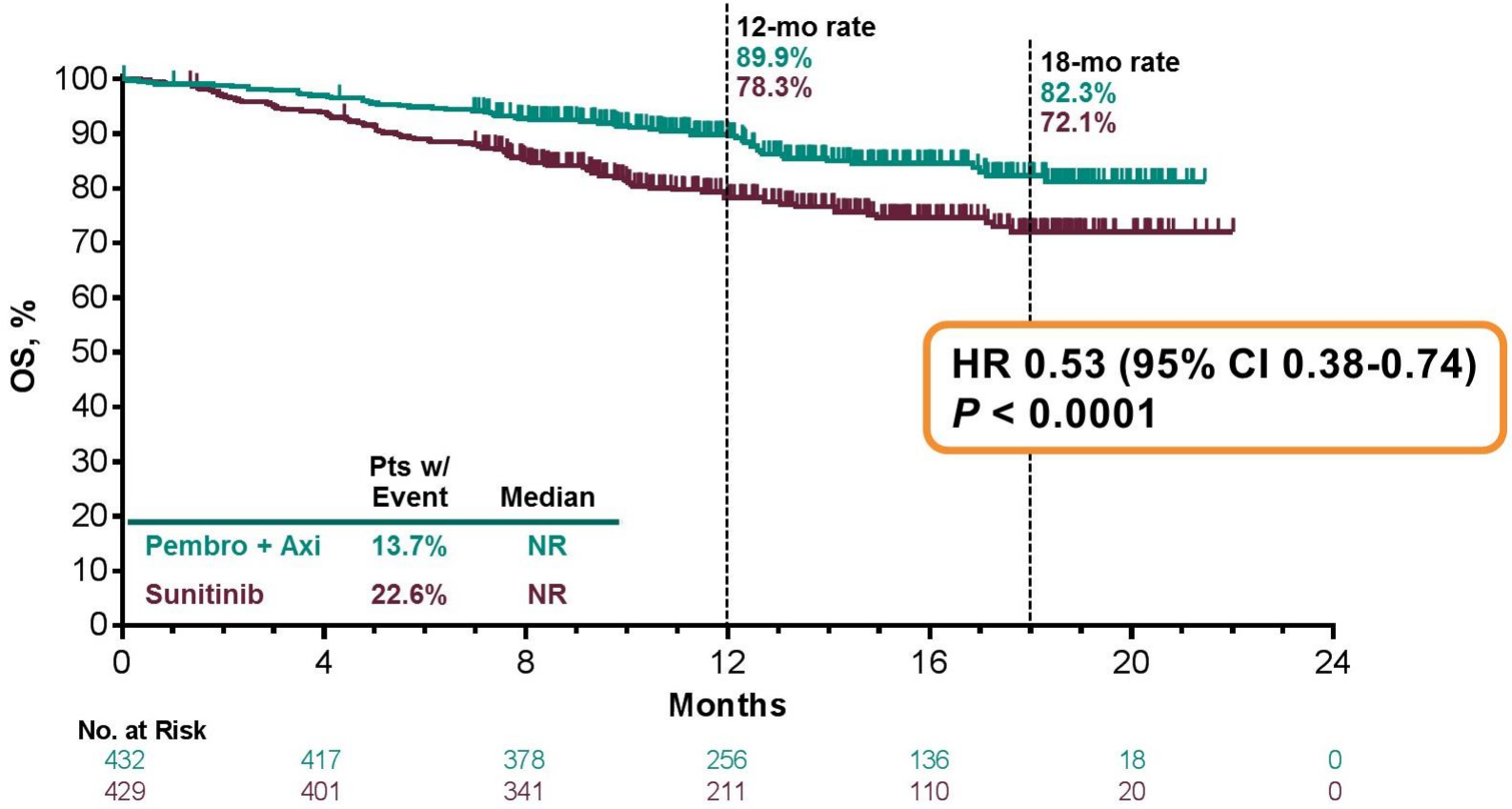
No. at risk

NIVO+IPI	125	124	120	116	111	108	104	102	101	98	94	88	71	24	2	0
SUN	124	119	119	117	114	110	109	105	103	101	96	88	70	26	2	0

Tannir et al. ASCO GU 2019/ Motzer RJ. NEJM April 2018

First-line Pembrolizumab + axitinib in advanced RCC: overall survival

KEYNOTE-426: OS in the ITT Population

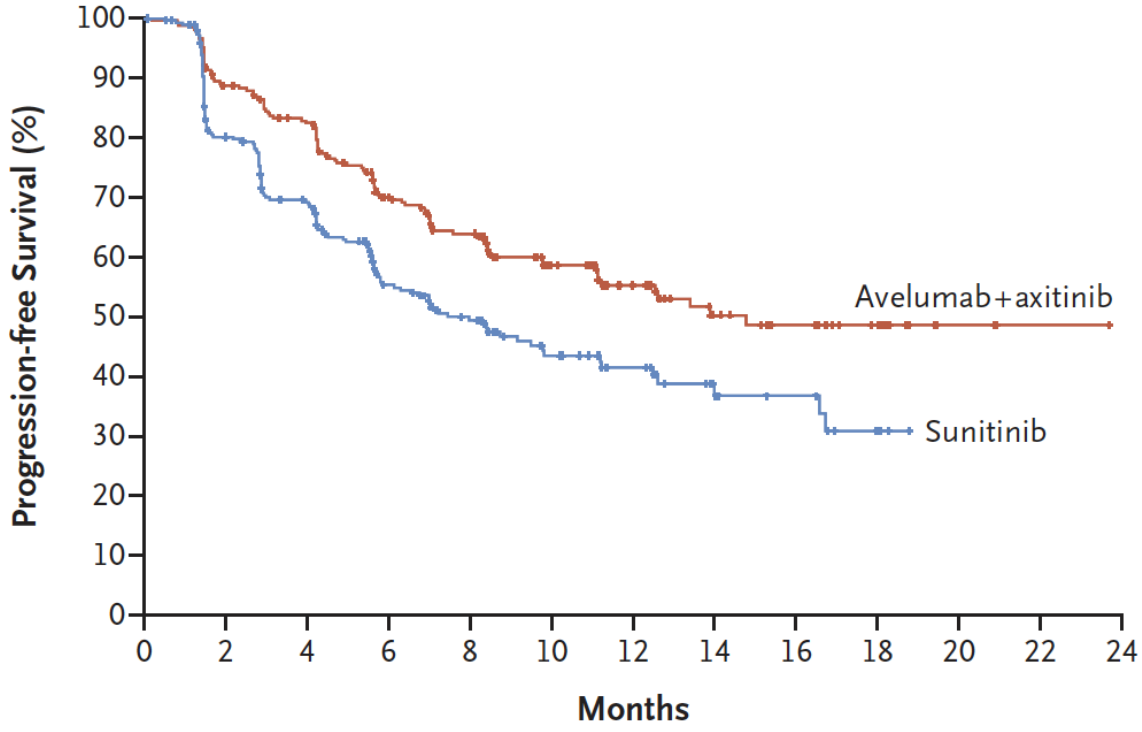


Rini, ASCO 2019/NEJM March 2019

First-line avelumab + axitinib in mRCC: progression-free survival

- Primary Endpoint: PFS and OS in PD-L1+
- Median PFS – 13.8 mo vs 7.2 mo (HR 0.61; 95% CI, 0.47–0.79)
- ORR: 61.9% vs 29.7
- OS data: immature

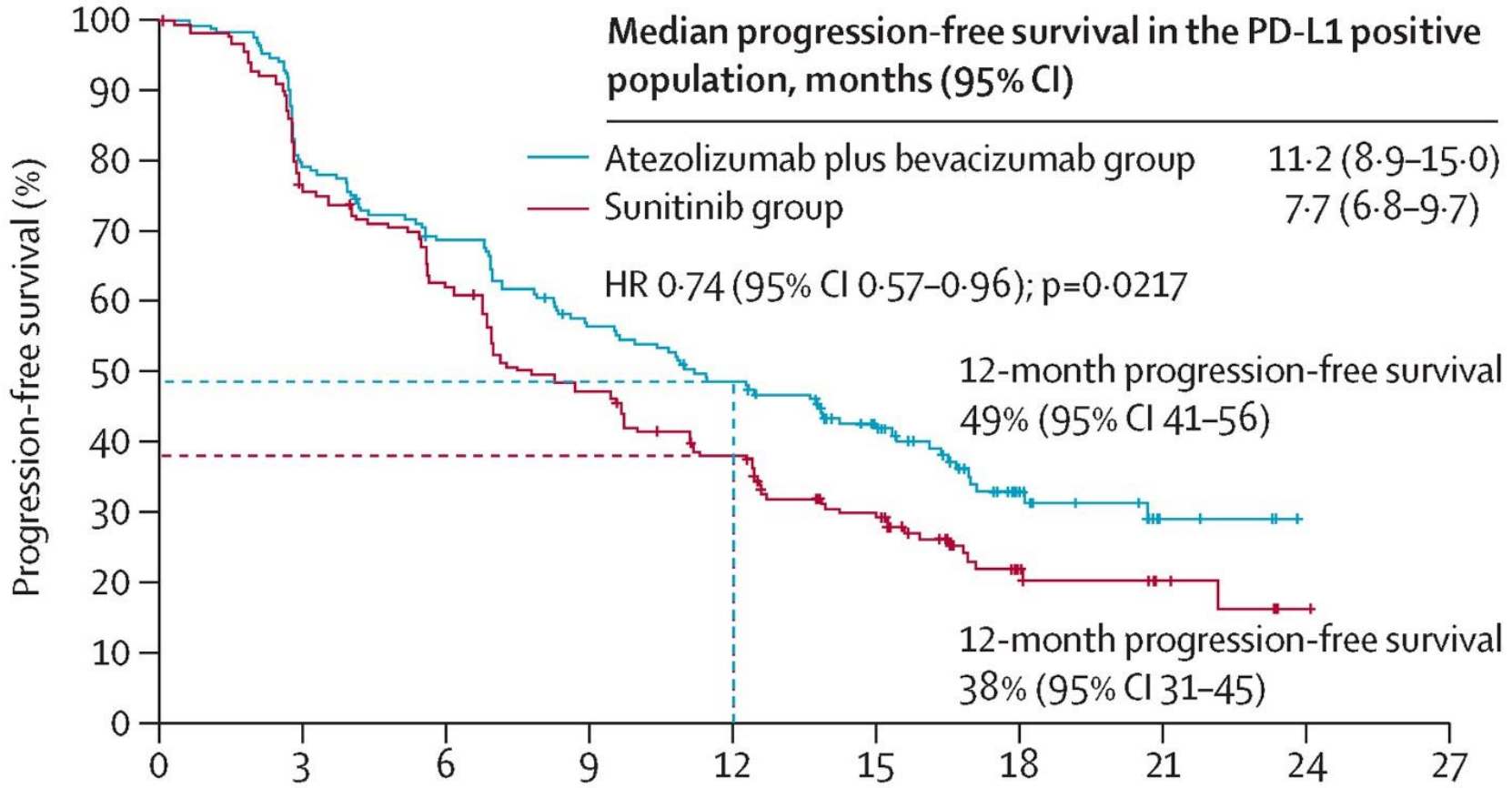
JAVELIN 101 : PFS in the PD-L1+ Population



Motzer, NEJM March 2019.

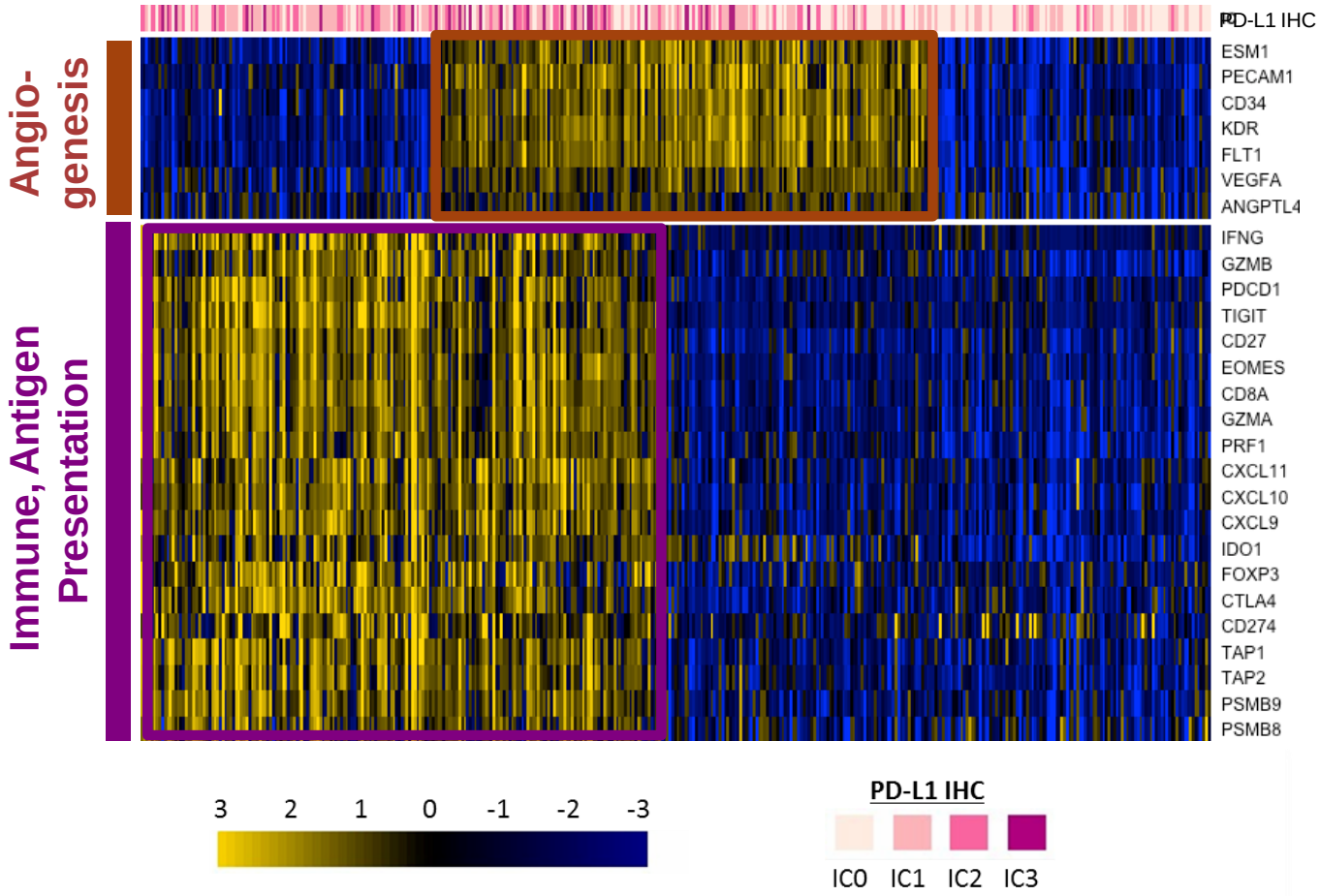
In Development: First-line atezolizumab + bevacizumab in PD-L1+ mRCC

Immotion151



Rini, The Lancet 2019.

In Development: First-line atezolizumab + bevacizumab: molecular signatures



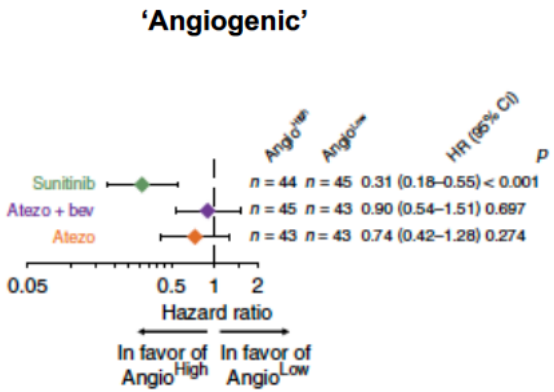
Identification of gene signatures based on association with clinicaloutcome

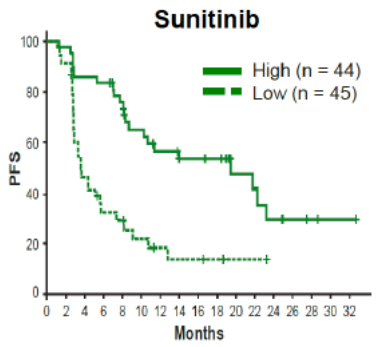
- T_{eff}: *CD8a*, *IFNG*, *PRF1*, *EOMES*, *CD274*
- Angio: *VEGFA*, *KDR*, *ESM1*, *PECAM1*, *CD34*, *ANGPTL4*

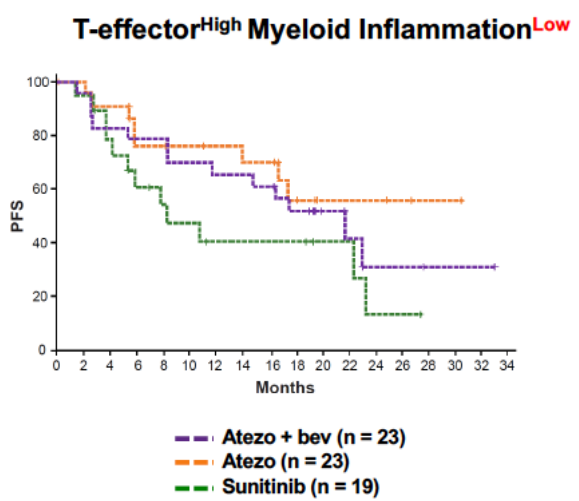
Rini et al, ESMO 2018

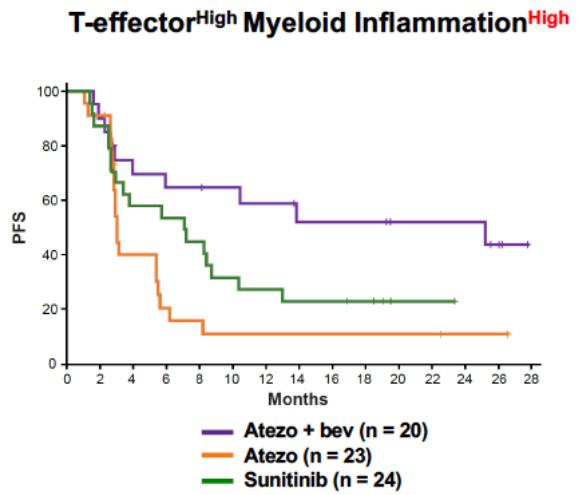
In Development: First-line atezolizumab + bevacizumab: molecular signatures

Predictive biomarkers – gene expression profiling









McDermott et al. Nat Med 2018

Rini et al, ESMO 2018/McDermott et al, Nat Med 2018

Front-line phase 3 trials with immunotherapy agents (efficacy summary)

	CheckMate 214	KEYNOTE-426	JAVELIN 101	IMmotion151
Intervention	Ipilimumab + Nivolumab	Pembrolizumab + Axitinib	Avelumab + Axitinib	Atezolizumab + Bevacizumab
Comparator	Sunitinib	Sunitinib	Sunitinib	Sunitinib
Primary Endpoint	OS, PFS, ORR in int/poor risk	OS, PFS	PFS, OS in PD-L1+	PFS in PD-L1+; OS
mOS, months	NR vs 37.9 (30 mo min followup)	NR vs NR (median 12.8 mo followup)	Not reported	33.6 vs 34.9 (median 24 mo followup)
PFS, months	9.7 vs 9.7	15.1 vs 11.1	13.8 vs 7.2	11.2 vs 7.7
ORR (ITT), %	41% vs 34%	59.3% vs 35.7%	51.4% vs 25.7%	37% vs 33%
CR rate (ITT)	10.5% vs 1.8%	5.8% vs 1.9%	3.4% vs 1.8%	5% vs 2%

IIT: Intent-to-Treat; PFS: progression-free survival; ORR: overall response rate; OS: overall survival

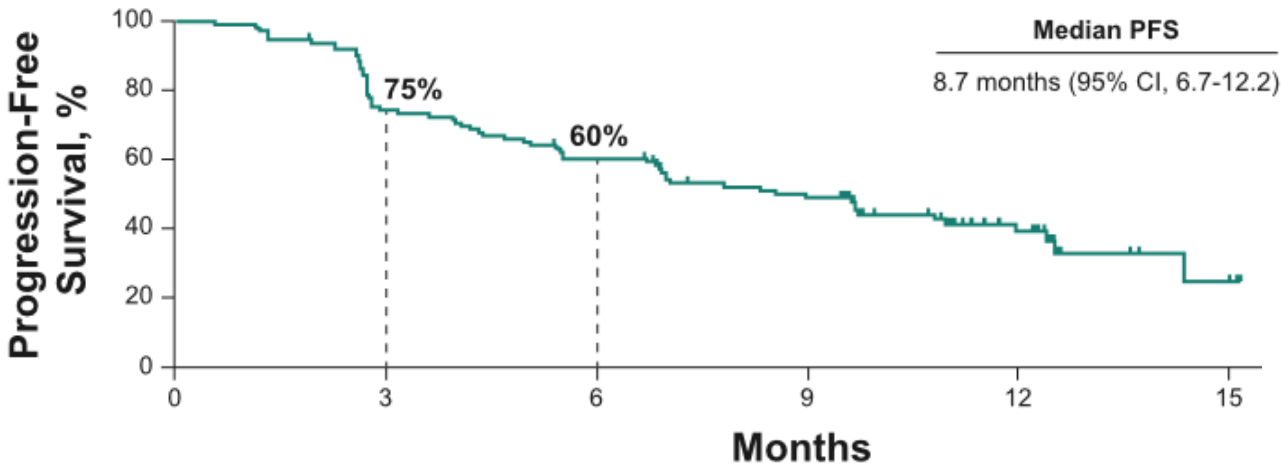
Tannir, ASCO GU 2019.
Rini, NEJM 2019.
Motzer, NEJM 2019.
Rini, Lancet 2019.

Ongoing front-line phase 3 trials with immunotherapy agents for front-line ccRCC

Trial number	Trial Name	Treatment Arm	Comparator Arm	Population Size	Primary End Point
NCT03141177	CheckMate 9ER	Cabozantinib + Nivolumab	Sunitinib	630	PFS
NCT02811861	CLEAR	Lenvatinib + Pembrolizumab or Everolimus	Sunitinib	1050	PFS
NCT03729245	CA045002	NKTR-214 + Nivolumab	Sunitinib	600	ORR, OS
NCT03937219	COSMIC-313	Cabozantinib + Ipilimumab + Nivolumab	Sunitinib	676	PFS

PFS: progression-free survival; ORR: overall response rate; OS: overall survival

In Development: First-line pembrolizumab monotherapy in ccmRCC KEYNOTE - 427



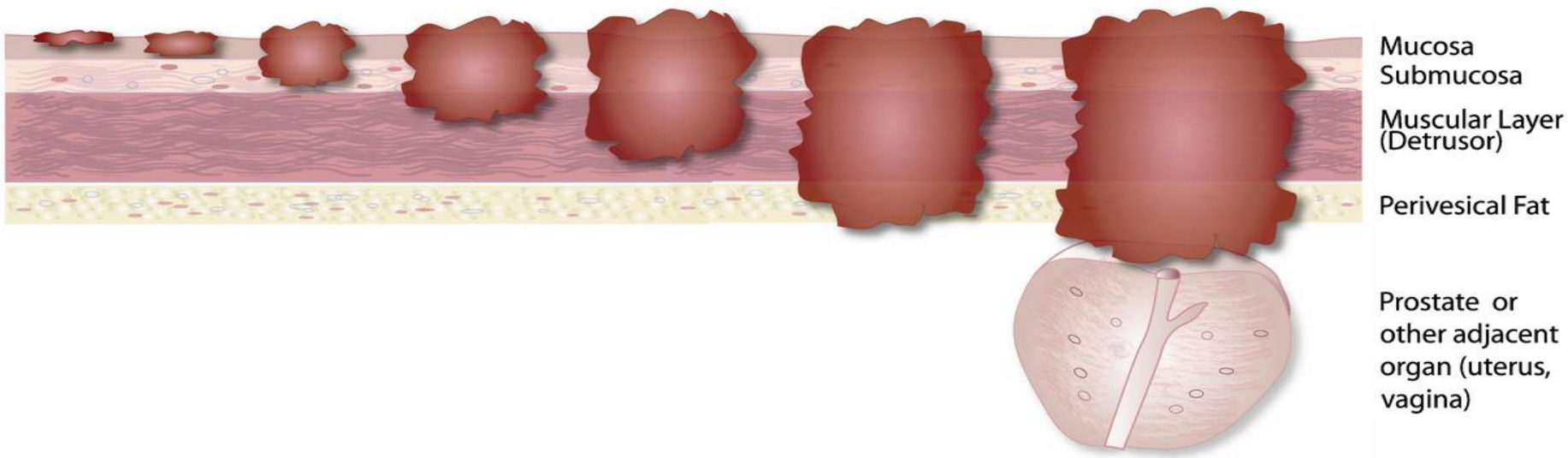
	N = 110
Confirmed ORR, % (95% CI)	36.4
CR, %	3 (3)
PR, %	37 (34)
DCR, %	57 (47-67)
DOR, median (range), mo	Not Reported
DOR ≥ 6 mo (responders), %	77

Donskov et al. ESMO 2018
Tykodi et al, ASCO 2019
McDermott et al ASCO 2019

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 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 Tecentriq and Keytruda 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

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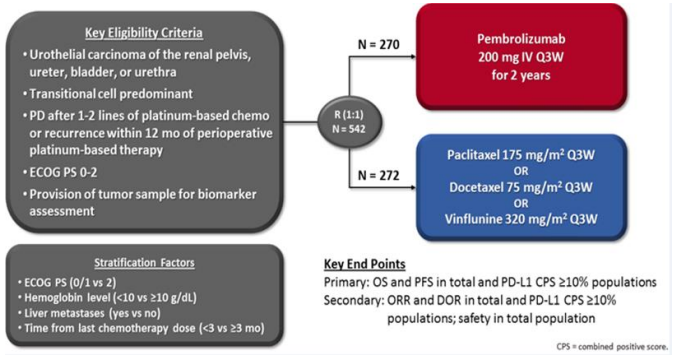
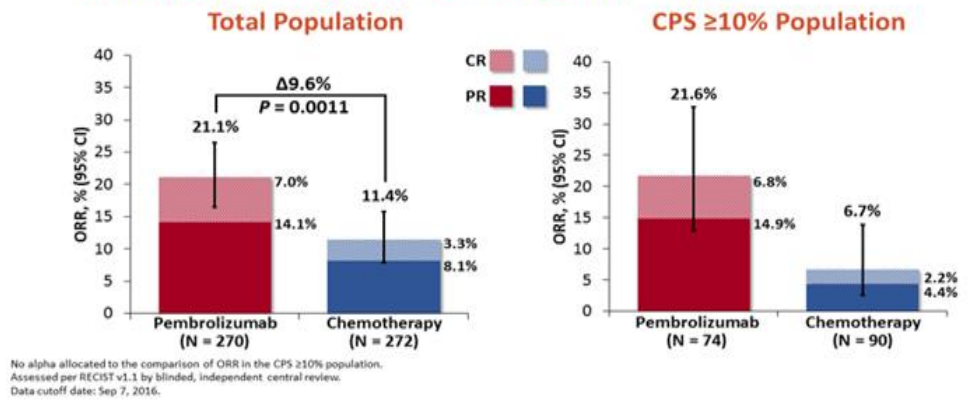
The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 MARCH 16, 2017 VOL. 376 NO. 11

KEYNOTE-045: OS and ORR

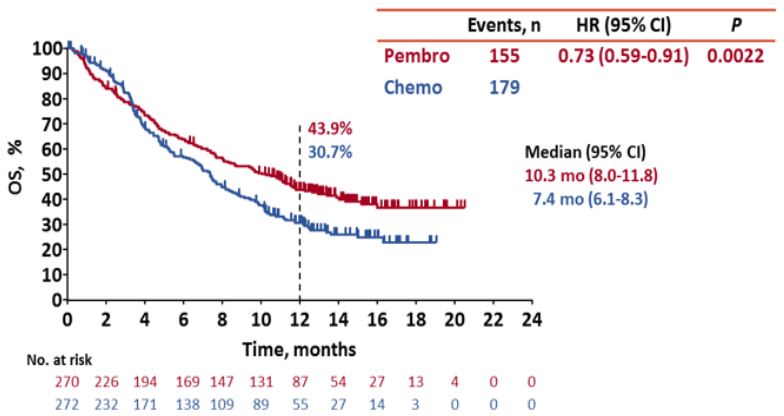
Pembrolizumab as Second-Line Therapy for Advanced Urothelial Carcinoma

J. Bellmunt, R. de Wit, D.J. Vaughn, Y. Fradet, J.-L. Lee, L. Fong, N.J. Vogelzang, M.A. Climent, D.P. Petrylak, T.K. Choueiri, A. Necchi, W. Gerritsen, H. Gurney, D.I. Quinn, S. Culine, C.N. Sternberg, Y. Mai, C.H. Poehlein, R.F. Perini, and D.F. Bajorin, for the KEYNOTE-045 Investigators*





Overall Survival: Total

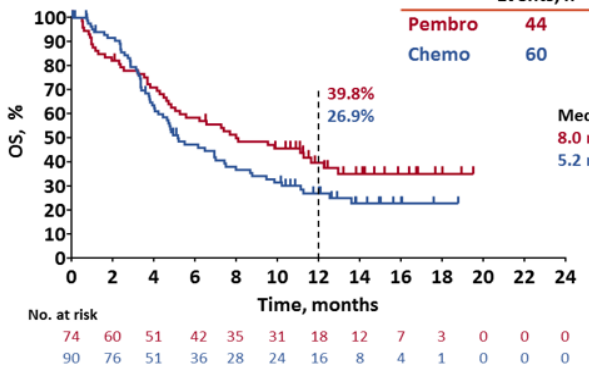


	Events, n	HR (95% CI)	P
Pembro	155	0.73 (0.59-0.91)	0.0022
Chemo	179		

Median (95% CI)
10.3 mo (8.0-11.8)
7.4 mo (6.1-8.3)

Data cutoff date: Sep 7, 2016.

Overall Survival: CPS ≥10%



	Events, n	HR (95% CI)	P
Pembro	44	0.57 (0.37-0.88)	0.0048
Chemo	60		

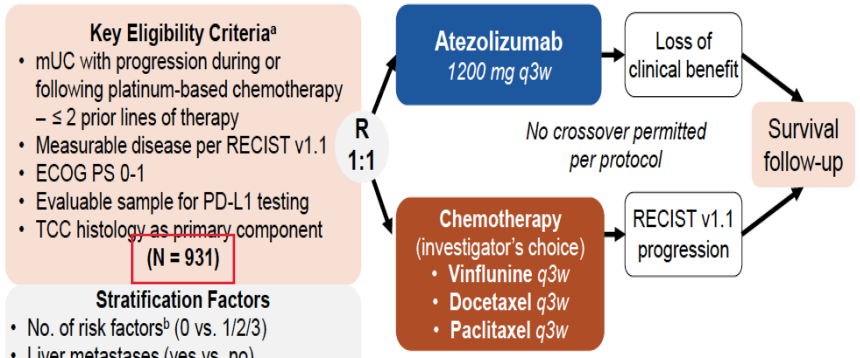
Median (95% CI)
8.0 mo (5.0-12.3)
5.2 mo (4.0-7.4)

Data cutoff date: Sep 7, 2016.

Bellmunt, J.; De Wit, R.; Vaughn, D.J.; Fradet, Y.; Lee, J.L.; Fong, L.; Vogelzang, N.J.; Climent, M.A.; Petrylak, D.P.; Choueiri, T.K.; et al. Pembrolizumab as Second-Line Therapy for Advanced Urothelial Carcinoma. N Engl J Med 2017;376:1015-26.

Atezolizumab

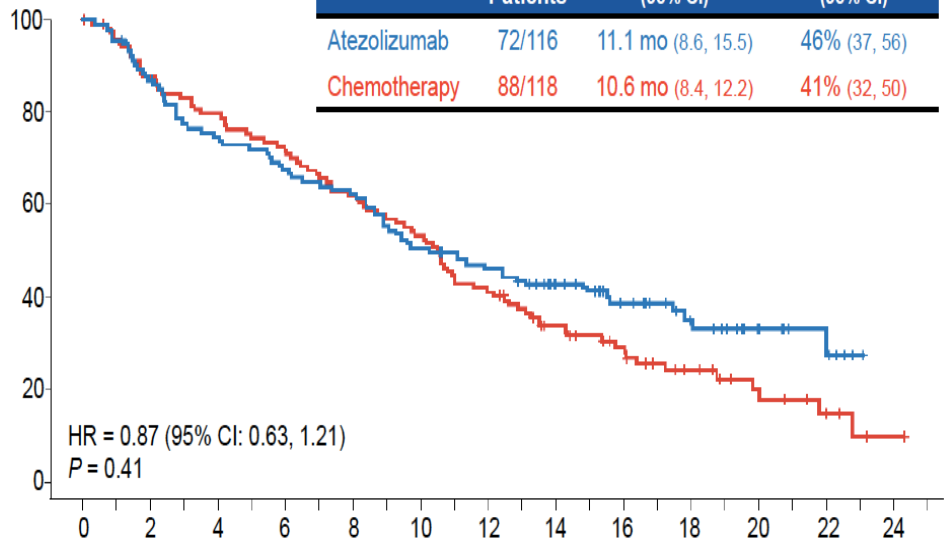
- **IMvigor 211: fase III.**



Media F/U: 17.3 mo

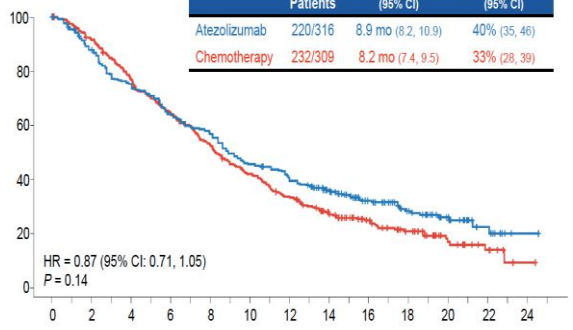
OS in PD-L1 IC2/3.

	Events/ Patients	Median OS (95% CI)	12-mo OS Rate (95% CI)
Atezolizumab	72/116	11.1 mo (8.6, 15.5)	46% (37, 56)
Chemotherapy	88/118	10.6 mo (8.4, 12.2)	41% (32, 50)



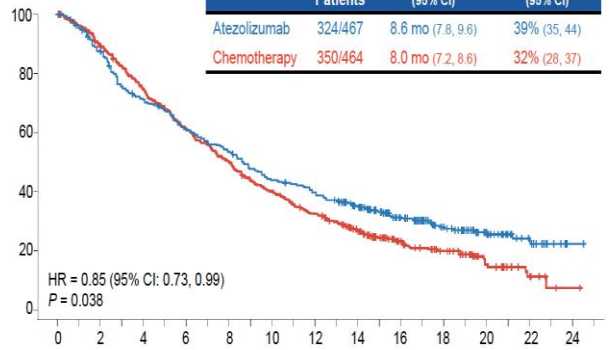
OS in patients PD-L1 IC 1/2/3.

	Events/ Patients	Median OS (95% CI)	12-mo OS Rate (95% CI)
Atezolizumab	220/316	8.9 mo (8.2, 10.9)	40% (35, 46)
Chemotherapy	232/309	8.2 mo (7.4, 9.5)	33% (28, 39)



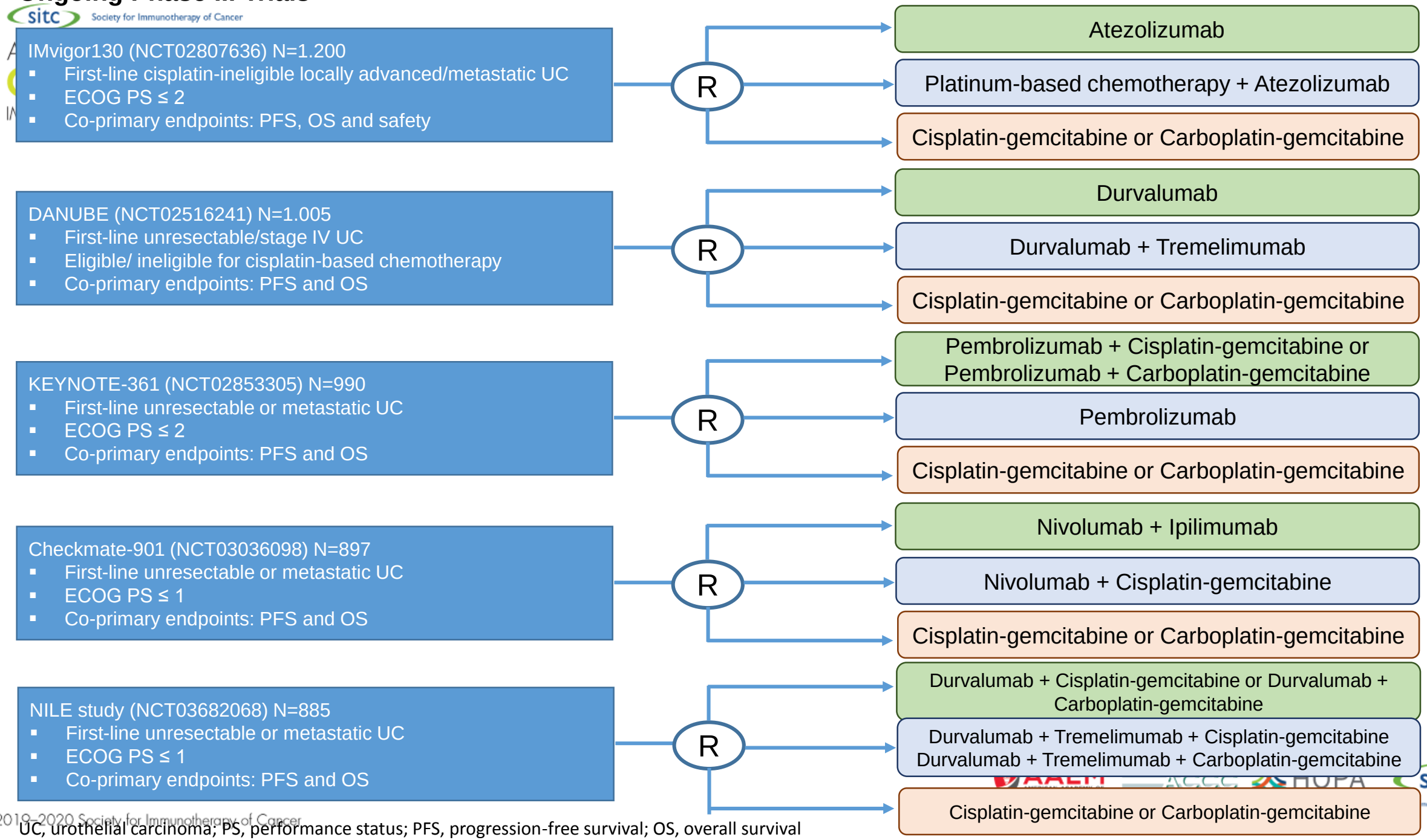
OS in ITT

	Events/ Patients	Median OS (95% CI)	12-mo OS Rate (95% CI)
Atezolizumab	324/467	8.6 mo (7.8, 9.6)	39% (35, 44)
Chemotherapy	350/464	8.0 mo (7.2, 8.6)	32% (28, 37)



Powles T, et al. Lancet 2017 Dec 18 [epub ahead of print].

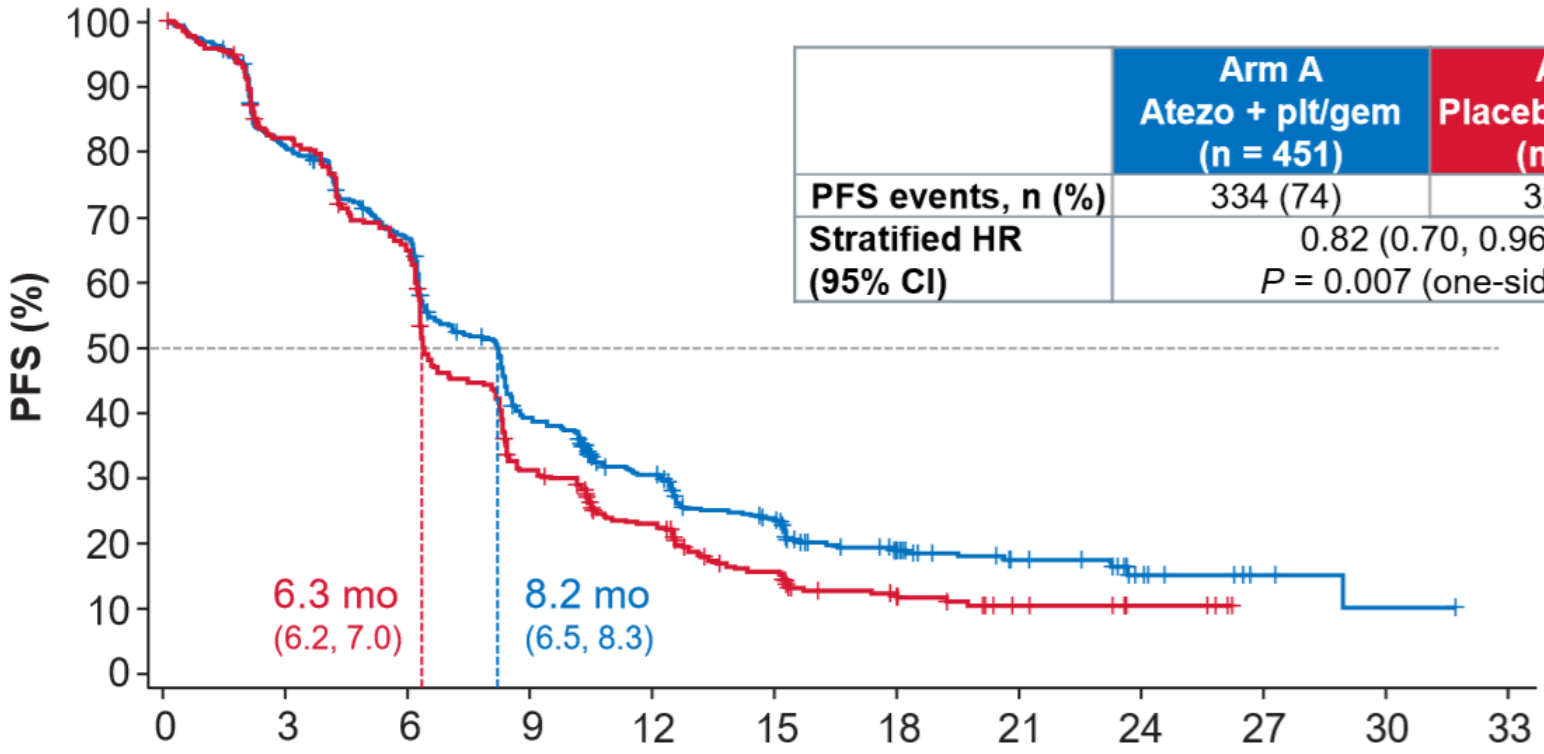
Ongoing Phase III Trials



UC, urothelial carcinoma; PS, performance status; PFS, progression-free survival; OS, overall survival

IMvigor130 (NCT02807636) N=1.200

Final PFS: ITT (Arm A vs Arm C)



	Arm A Atezo + plt/gem (n = 451)	Arm C Placebo + plt/gem (n = 400)
PFS events, n (%)	334 (74)	326 (82)
Stratified HR (95% CI)	0.82 (0.70, 0.96) *P* = 0.007 (one-sided)	

No. at Risk												
Atezo + plt/gem	451	345	282	160	111	74	42	22	10	4	2	NE
Placebo + plt/gem	400	317	246	116	73	40	18	11	4	NE	NE	NE

NE, not estimable. Data cutoff 31 May 2019; median survival follow-up 11.8 months (all patients).

IMvigor130—ESMO 2019 (LBA14): presented by Dr Enrique Grande http://bit.ly/2Z1bPbD

rapid communication

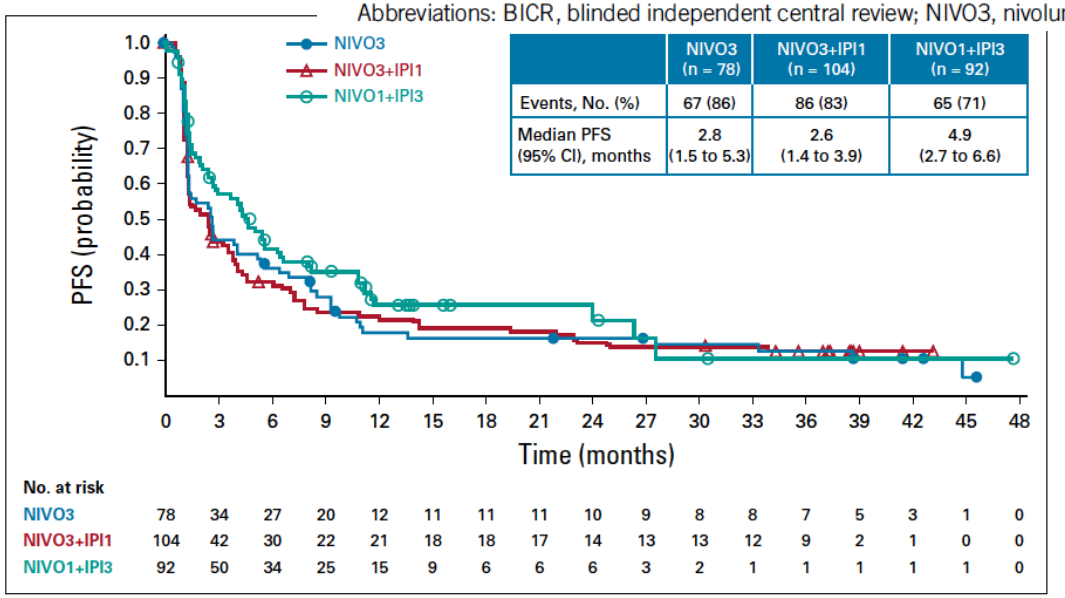
Nivolumab Alone and With Ipilimumab in Previously Treated Metastatic Urothelial Carcinoma: CheckMate 032 Nivolumab 1 mg/kg Plus Ipilimumab 3 mg/kg Expansion Cohort Results

Padmanee Sharma, MD, PhD[1]; Arlene Siefker-Radtke, MD[1]; Filippo de Braud, MD[2]; Umberto Basso, MD[3]; Emiliano Calvo, MD, PhD[4]; Petri Bono, MD, PhD[5,6]; Michael A. Morse, MD[7]; Paolo A. Ascierto, MD[8]; Jose Lopez-Martin, MD, PhD[9]; Peter Brossart, MD[10]; Kristoffer Rohrberg, MD, PhD[11]; Begoña Mellado, MD, PhD[12]; Bruce S. Fischer, MD[13]; Stephanie Meadows-Shropshire, PhD[13]; Abdel Saci, PhD[13]; Margaret K. Callahan, MD, PhD[14,15]; and Jonathan Rosenberg, MD[14,15]

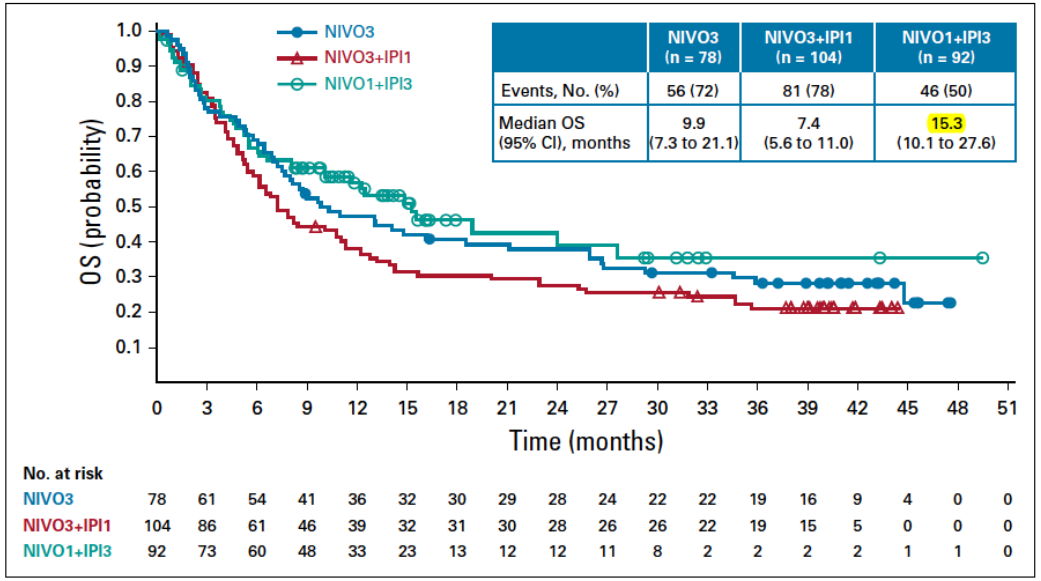
Nivolumab Alone and With Ipilimumab in Previously Treated Metastatic Urothelial Carcinoma: CheckMate 032 Nivolumab 1 mg/kg Plus Ipilimumab 3 mg/kg Expansion Cohort Results

	Per Investigator			Per BICR	
Response	NIVO3 (n = 78)	NIVO3+IPI1 (n = 104)	NIVO1+IPI3 (n = 92)	NIVO3 (n = 78)	NIVO1+IPI3 (n = 92)
ORR, No. (%)	20 (25.6)	28 (26.9)	35 (38.0)	16 (20.5)	34 (37.0)
95% CI	16.4 to 36.8	18.7 to 36.5	28.1 to 48.8	12.2 to 31.2	27.1 to 47.7
Best overall response, No. (%)					
Complete response	8 (10.3)	8 (7.7)	6 (6.5)	9 (11.5)	14 (15.2)
Partial response	12 (15.4)	20 (19.2)	29 (31.5)	7 (9.0)	20 (21.7)
Stable disease	21 (26.9)	24 (23.1)	23 (25.0)	27 (34.6)	24 (26.1)
Progressive disease	30 (38.5)	44 (42.3)	20 (21.7)	31 (39.7)	21 (22.8)
Unable to determine/not reported	7 (9.0)	8 (7.7)	14 (15.2)	4 (5.1)	13 (14.1)

Abbreviations: BICR, blinded independent central review; NIVO3, nivolumab 3 mg/kg monoth



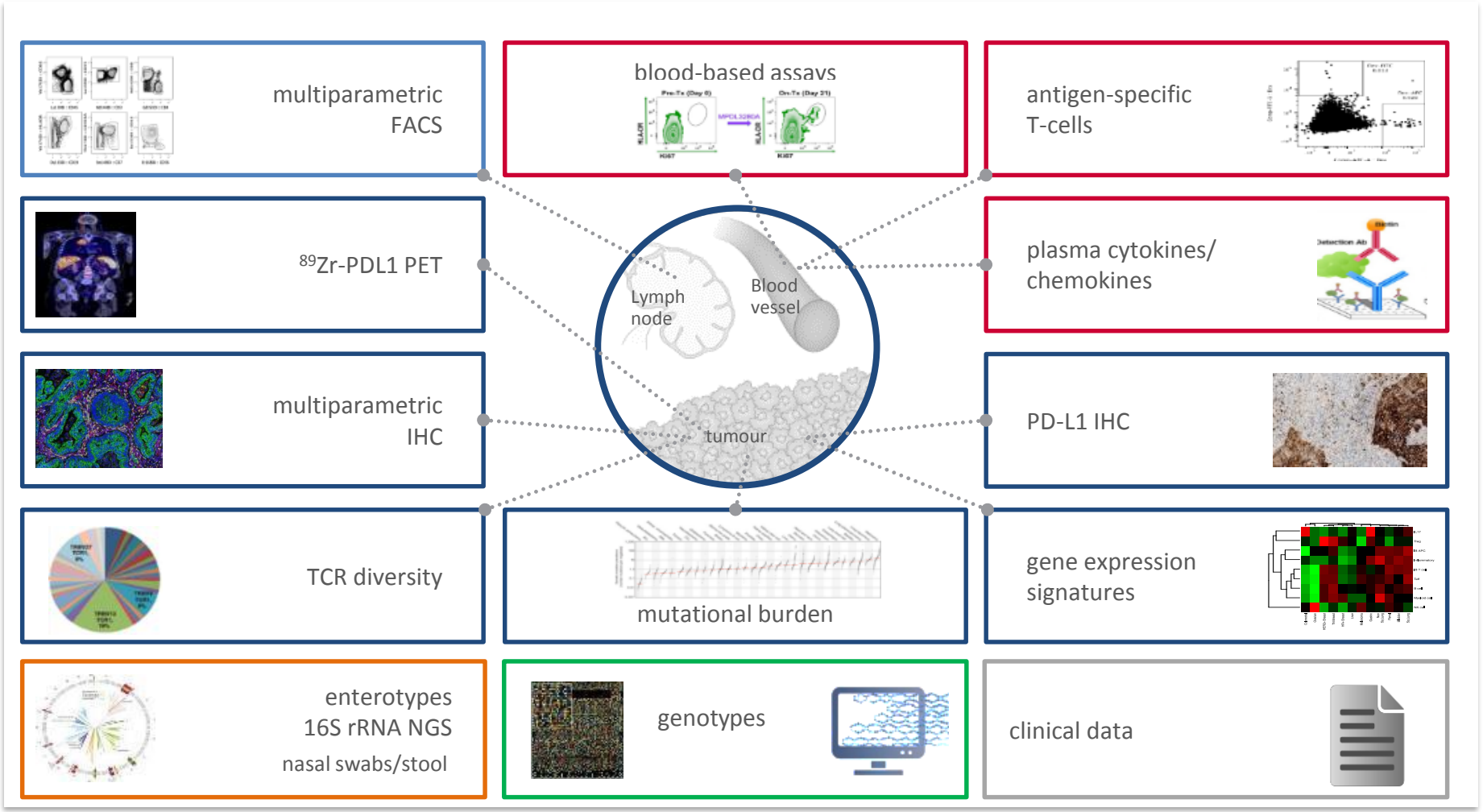
	NIVO3 (n = 78)	NIVO3+IPI1 (n = 104)	NIVO1+IPI3 (n = 92)
Events, No. (%)	67 (86)	86 (83)	65 (71)
Median PFS (95% CI), months	2.8 (1.5 to 5.3)	2.6 (1.4 to 3.9)	4.9 (2.7 to 6.6)



	NIVO3 (n = 78)	NIVO3+IPI1 (n = 104)	NIVO1+IPI3 (n = 92)
Events, No. (%)	56 (72)	81 (78)	46 (50)
Median OS (95% CI), months	9.9 (7.3 to 21.1)	7.4 (5.6 to 11.0)	15.3 (10.1 to 27.6)

Accepted on March 29, 2019 and published at jco.org on May 17, 2019: DOI https://doi.org/10.1200/JCO.19.00538

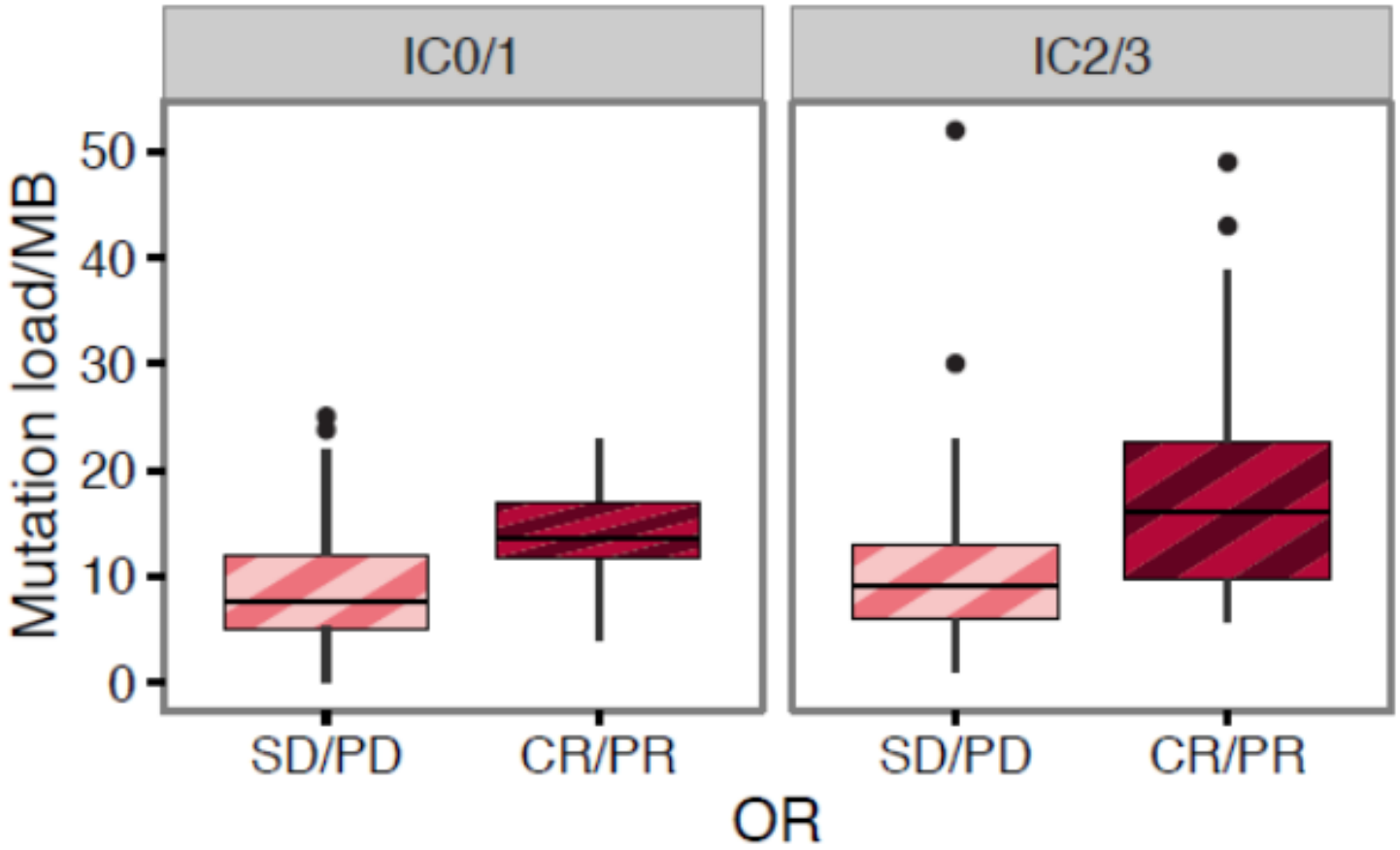
Multidimensional Prediction of Benefit to Immunotherapy



Adapted from Yuan et al. J Immunother Cancer 2016.

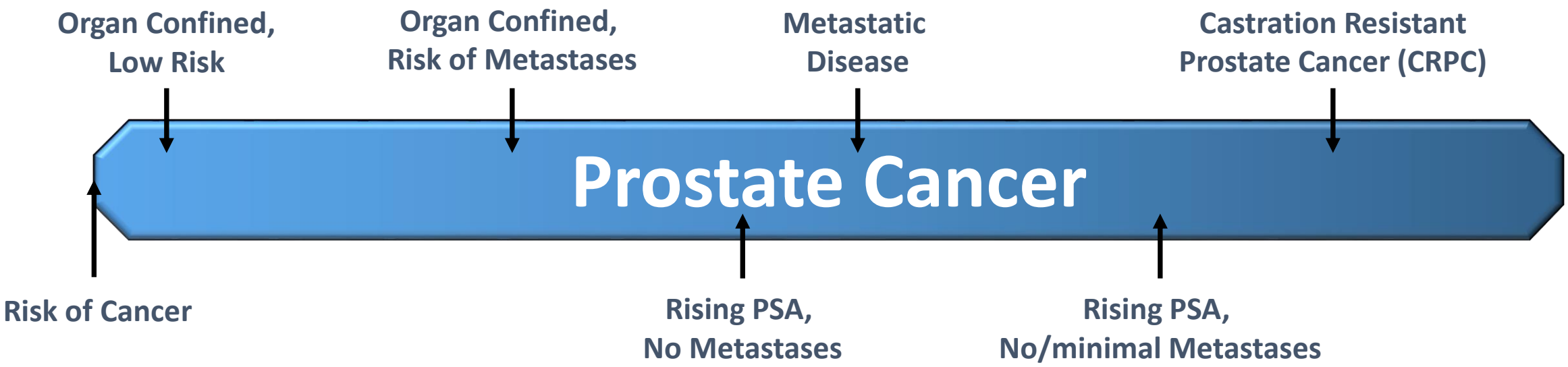
Tumor Mutational Burden (TMB) May Signal Responses with PD-1 Blockade

Atezolizumab in mUC



Rosenberg et al. Lancet 2016

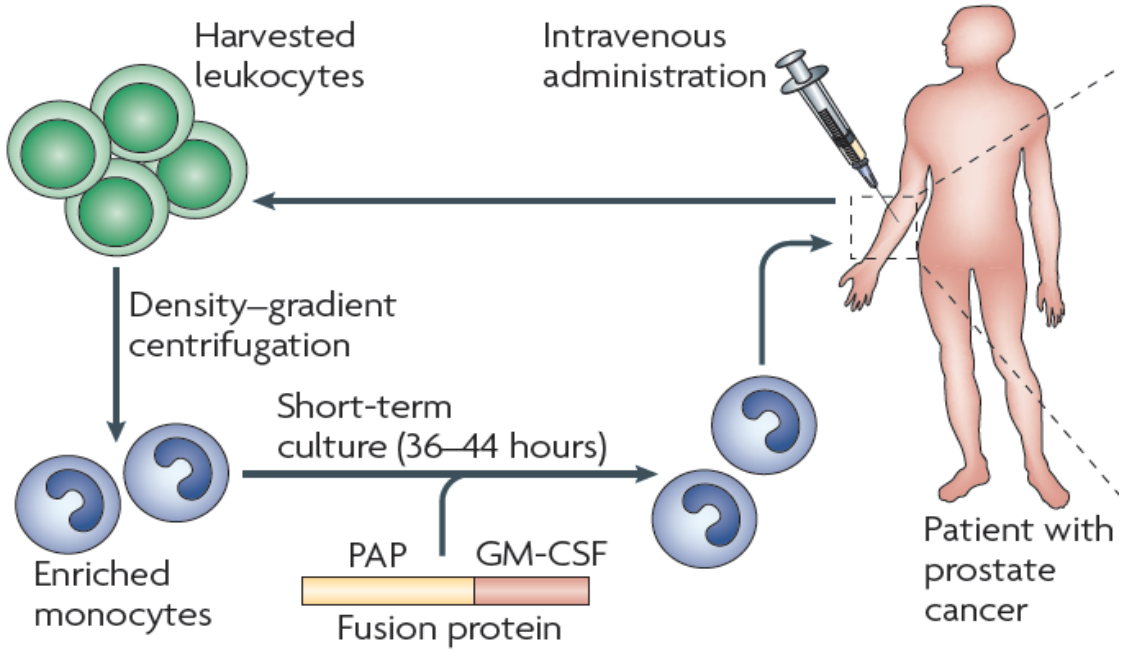
The Spectrum of Prostate Cancer

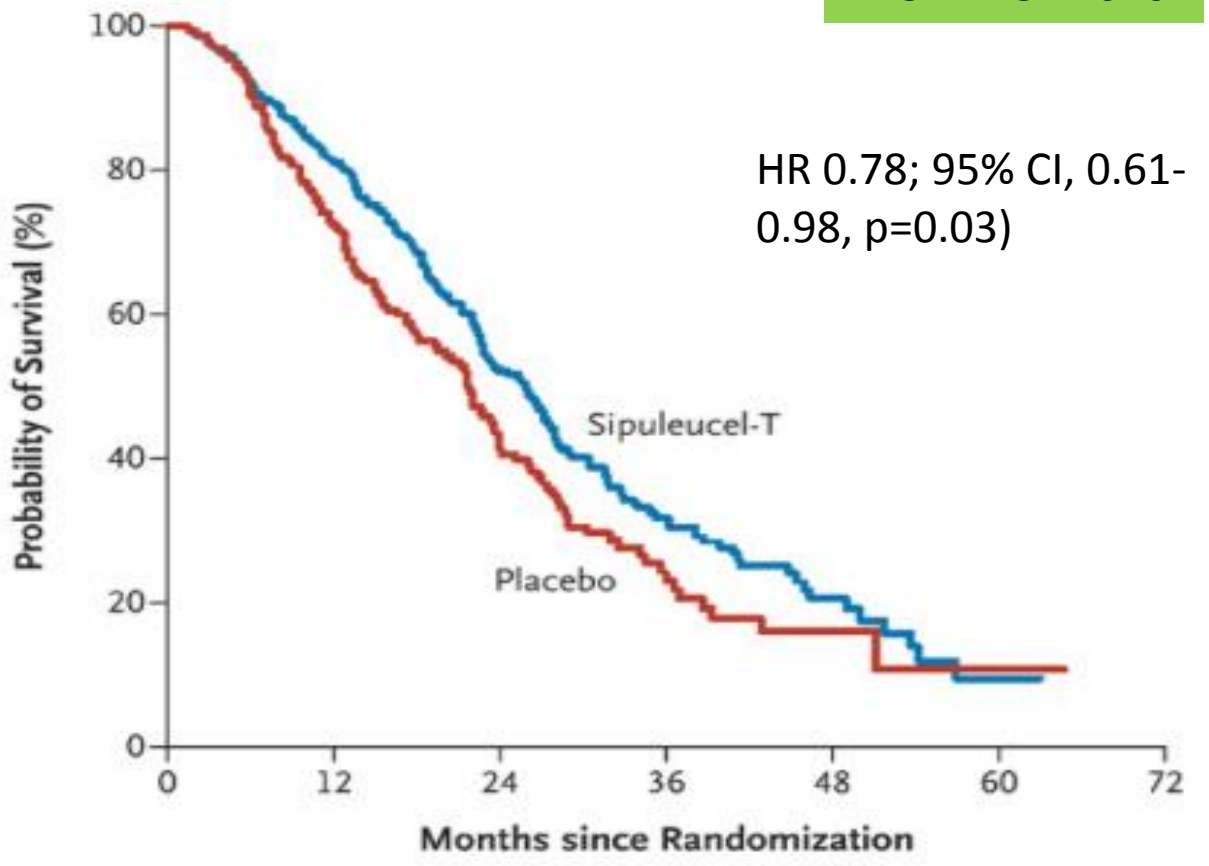


Sipuleucel-T in mCRPC

PROVENGE 2010

First anti-cancer therapeutic vaccine





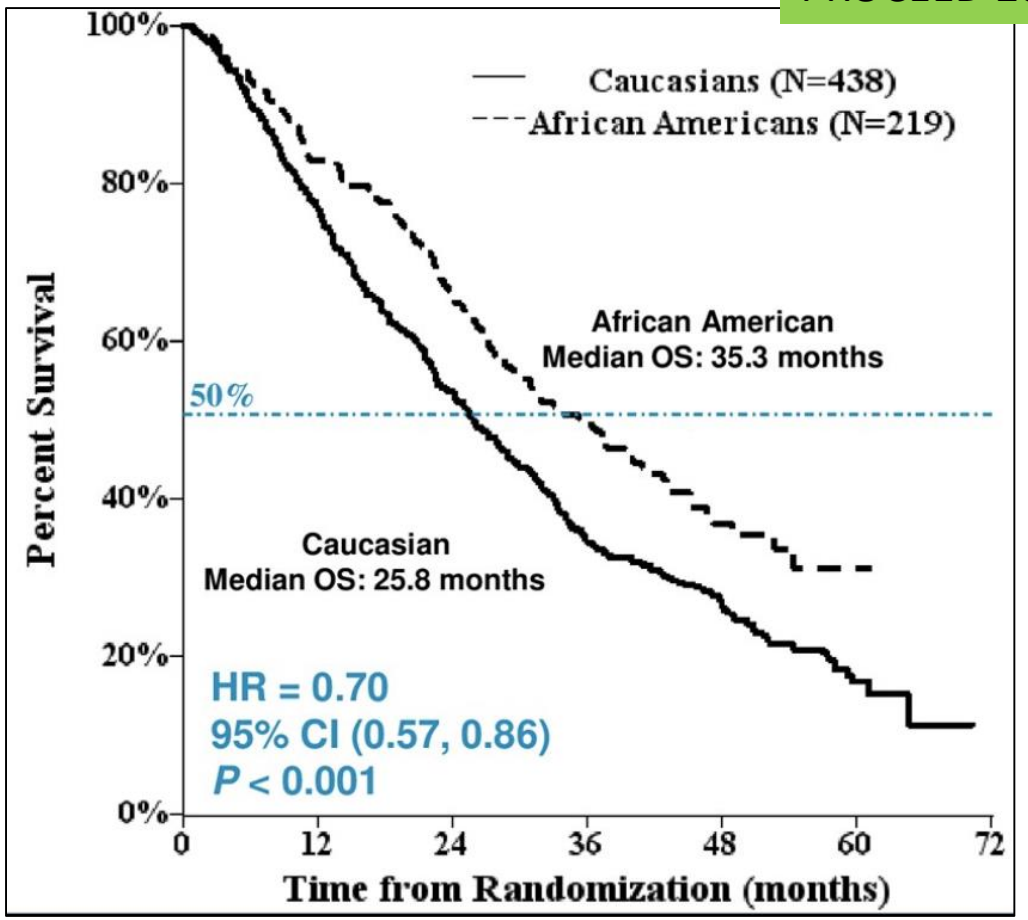
HR 0.78; 95% CI, 0.61-0.98, p=0.03)

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)

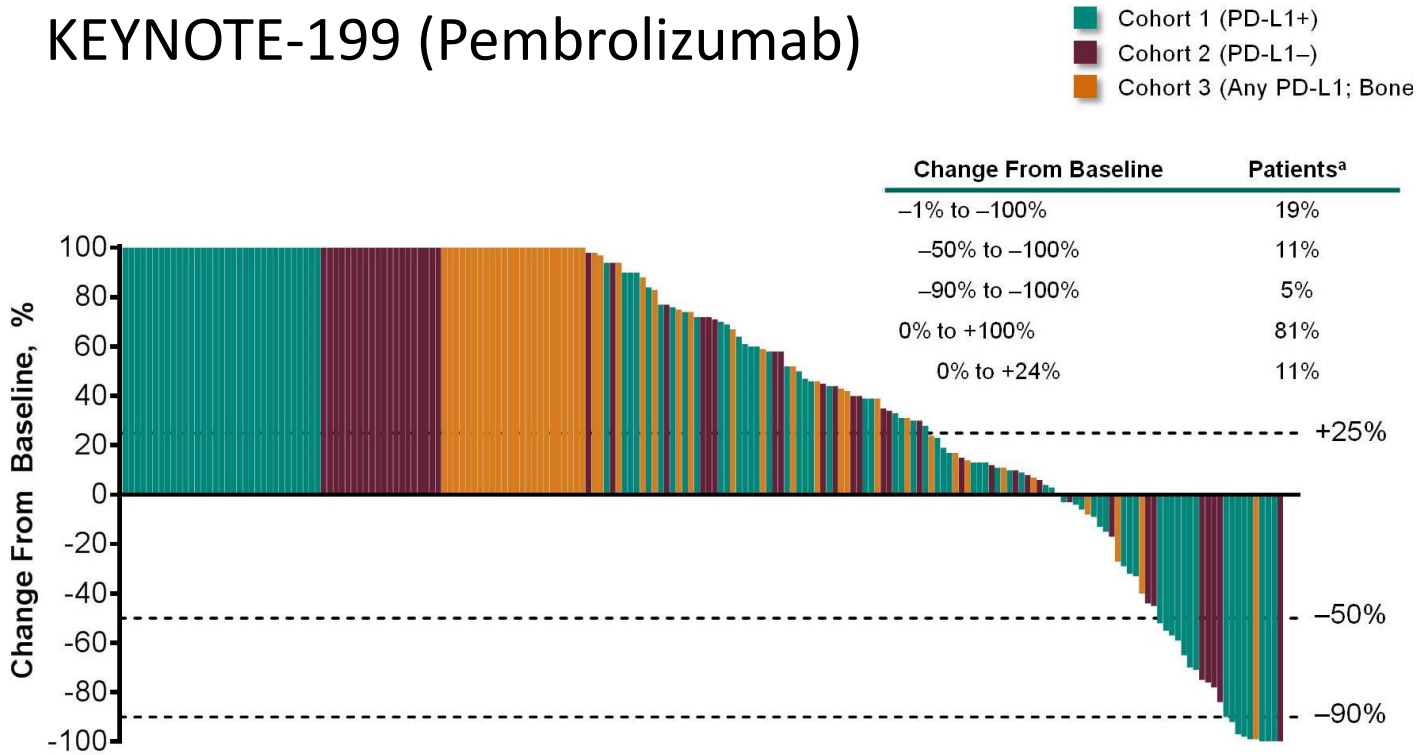


Sartor et al. ASCO 2019

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

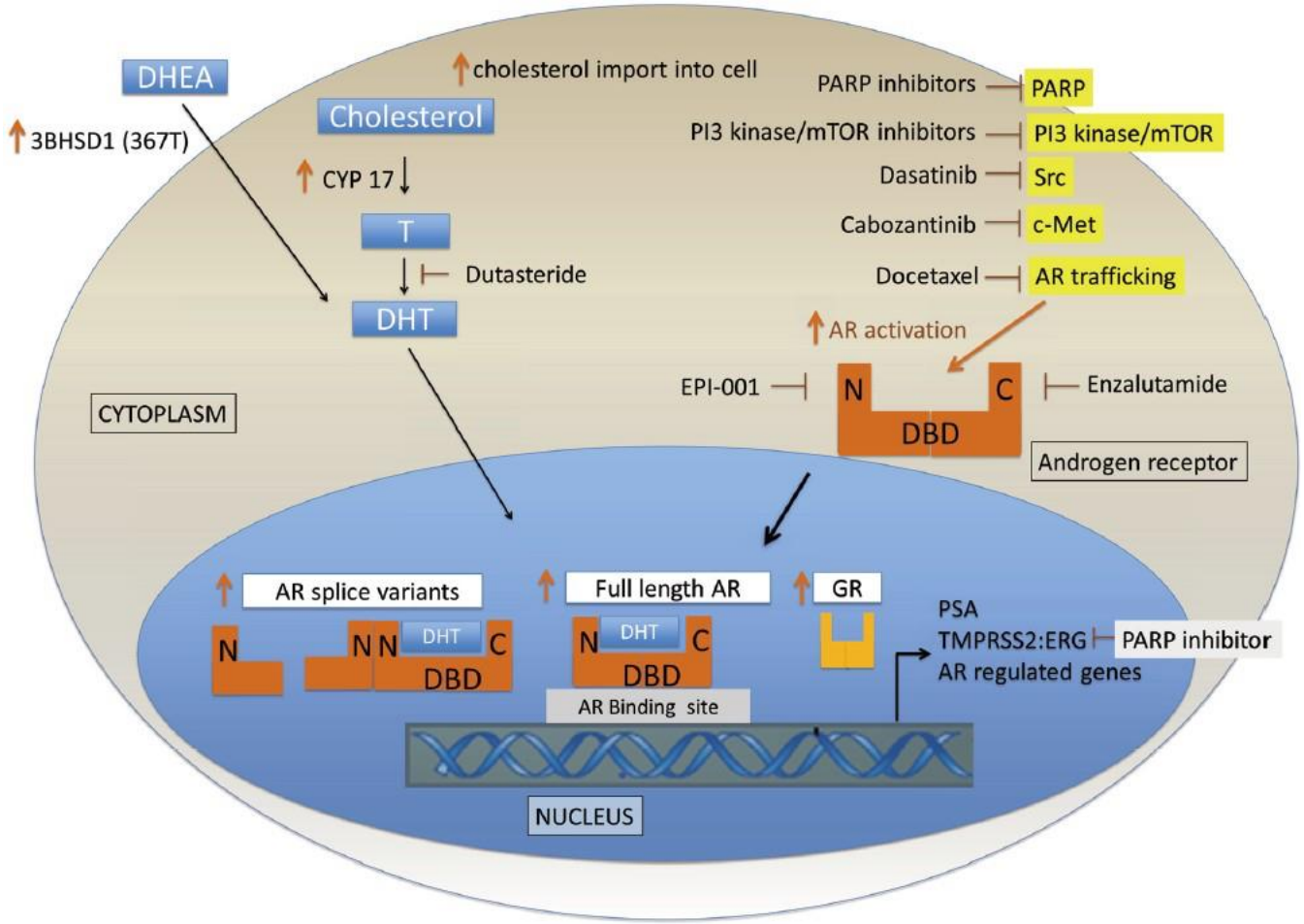
In development: nivolumab + ipilimumab in mCRPC

- 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

irAEs with Immune Checkpoint Inhibitors in GU Cancers - Meta-analysis of 8 studies

Similar incidence overall

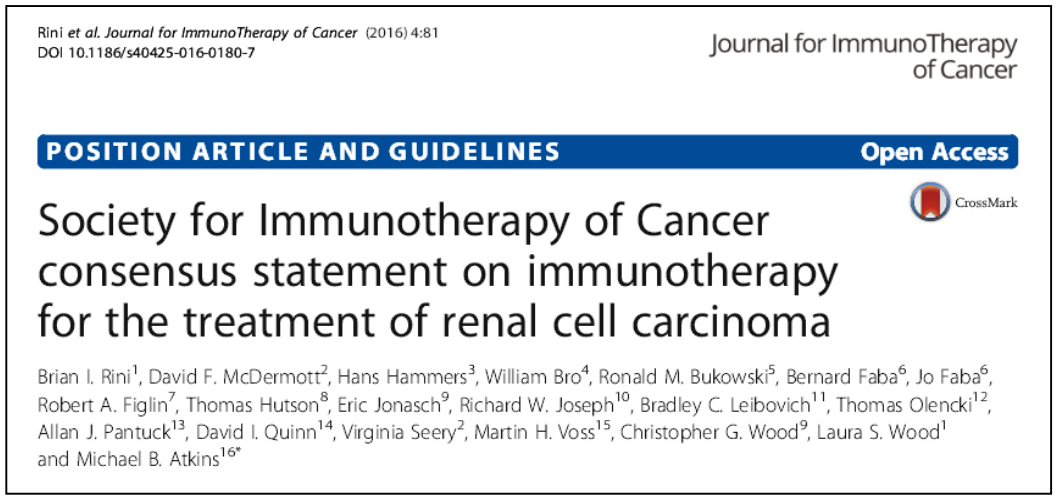
Adverse event	Incidence, any grade (GU only trials) (%)	Incidence, grades 3–5 (GU only trials) (%)	Incidence any grade (non-GU clinical trials) (%)	Incidence, grades 3–5 (non-GU clinical trials) (%)
Hypothyroid/ thyroiditis	0.8–9	0–0.6	3.9–12	0–0.1
Diabetes/DKA	0–1.5	0–0.7	0.8–0.8	0.4–0.7
LFT changes/ hepatitis	1.5–5.4	1–3.8	0.3–3.4	0.3–2.7
Pneumonitis	2–4.4	0–2	1.8–3.5	0.25–1.9
Encephalitis	NR	NR	0.2–0.8	0.0–0.2
Colitis/diarrhea	1–10	1–10	2.4–4.1	1.0–2.5
Hypophysitis	0–0.5	0–0.2	0.2–0.9	0.2–0.4
Renal Dysfunction/ nephritis	0.3–1.6	0–1.6	0.3–4.9	0.0–0.5
Myositis	0.8–5	0–0.8	NR	NR

Maughan et al. Front Oncol 2017

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

Additional Resources



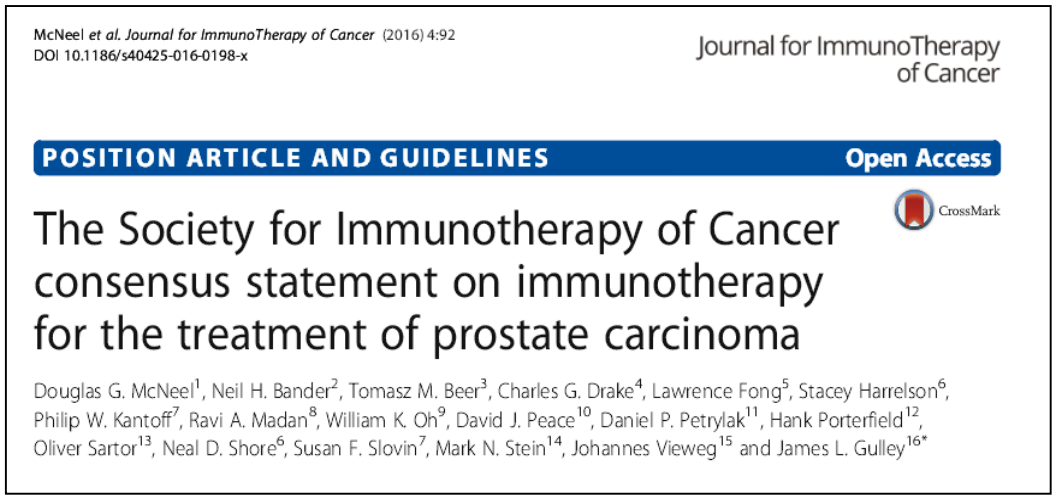
Rini *et al. Journal for ImmunoTherapy of Cancer* (2016) 4:81
DOI 10.1186/s40425-016-0180-7

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*]



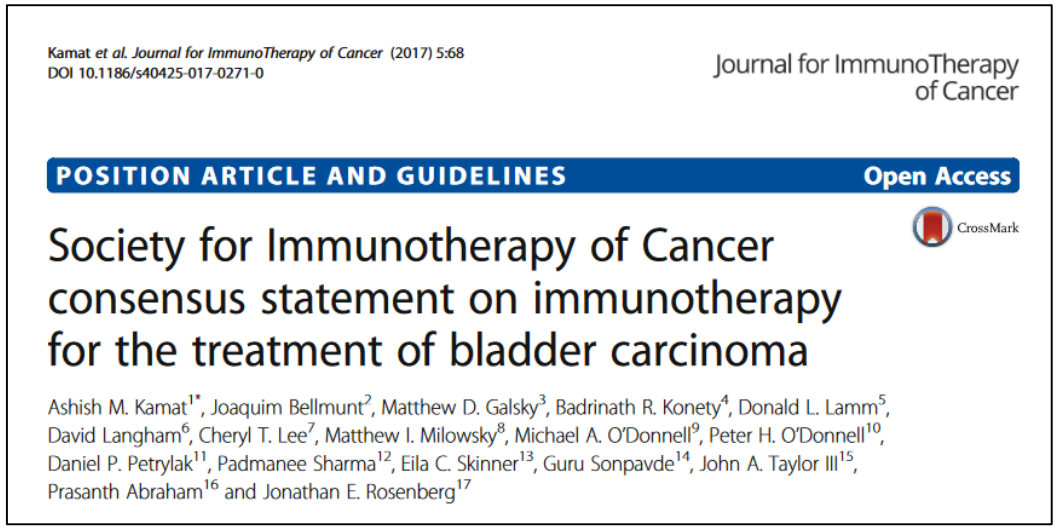
McNeel *et al. Journal for ImmunoTherapy of Cancer* (2016) 4:92
DOI 10.1186/s40425-016-0198-x

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]

Case Studies

Society for Immunotherapy of Cancer
ADVANCES IN Cancer IMMUNOTHERAPY™

Clinical Case 1- Bladder Cancer

Clinical Case- Bladder Cancer

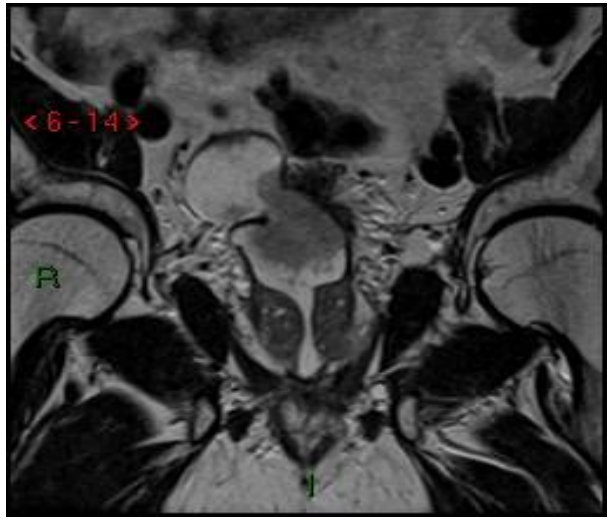
- ESG, male, 65 years old, Engineer, Married, 2 sons
- No smoke or drinking history
- Comorbidities: Mild hypertension (ACE inhibitor), Diabetes II (Oral Antidiabetics), well controlled
- 02/2012: History of painless macrohematuria
- TURB: Transitional cell carcinoma, low grade, no muscle invasion- cT1N0M0
- No adjuvant treatment

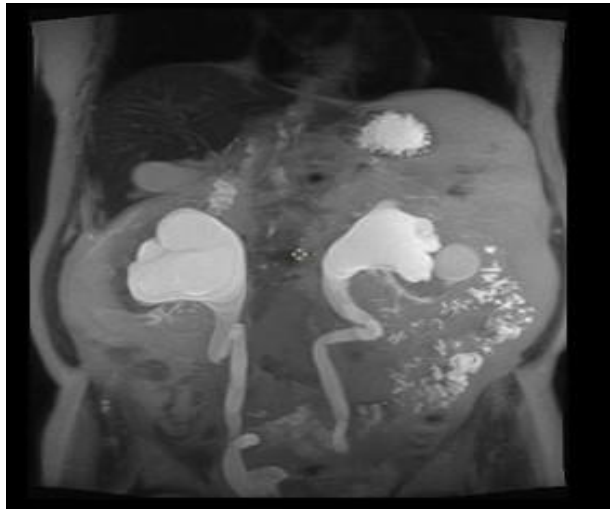
Clinical Case- Bladder Cancer

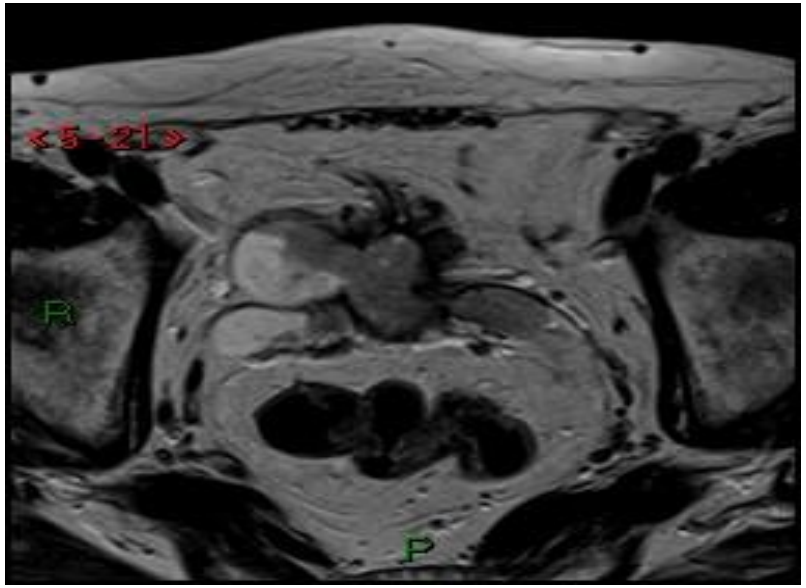
- 10/2013: Cystoscopy- Tumor recurrence HGT1->> TURBT >>> BCG
- 12/2015: Cystoscopy- Tumor recurrence.>> TURB- T1N0M0 - Patient refused intra vesical therapy
- 10/2017: Tumor recurrence >> HGT1 . MRI: Multiple vegetative bladder lesions
- Cystoprostatectomy was indicated- Patient refused
- Abandoned treatment

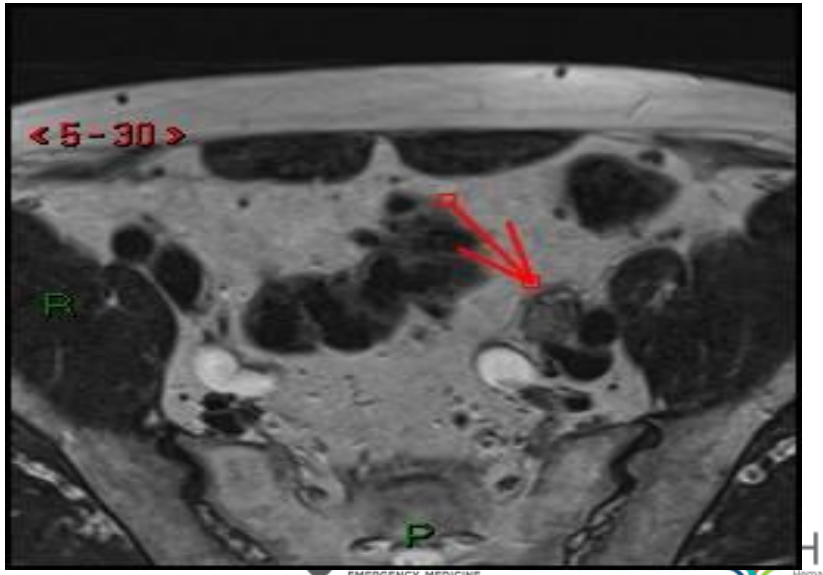
02/2019: Acute renal failure due to bilateral ureteral obstruction

MRI- 19/01/19







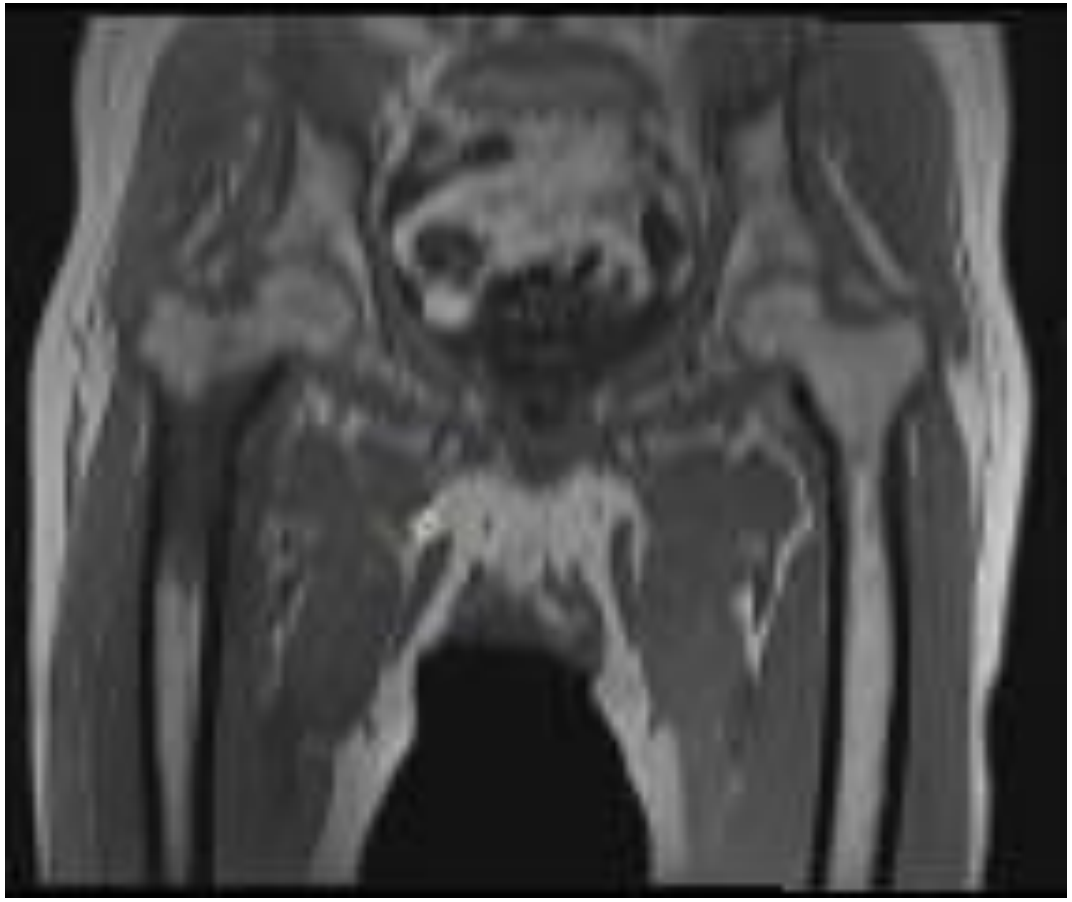


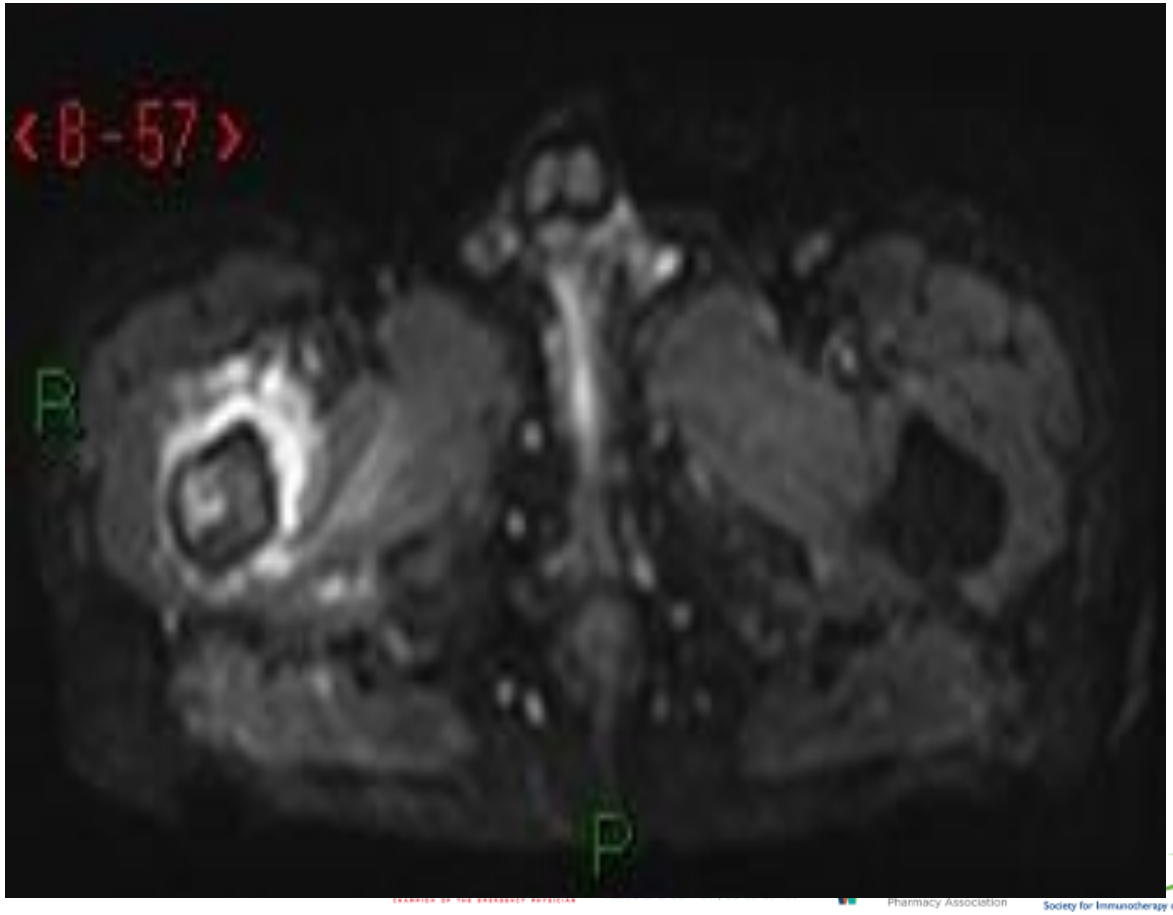
Clinical Case- Bladder Cancer

- Cystoprostatectomy and bilateral lymphadectomy, Brickers conduit (02/2019)
- Transitional cell carcinoma- pT3bN1M0
- Adenocarcinoma of the prostate, Gleason 6 (3+3)-T2cN0
- 03/2019: Pain in right femur

Clinical Case- Bladder Cancer

MRI- 28/03/19





Clinical Case- Bladder Cancer

- 03/2019: Pain in right femur
- Whole body MRI: lytic lesion in right femur, no other metastatic lesions
- Biopsy: Metastatic transitional cell carcinoma.
- Renal Function Impairment - GFR 34 ml/min
- ECOG 2

What is next ?

1.- Palliative radiation therapy only and wait for further PD?

2.- Palliative radiation therapy followed by chemotherapy CBDCA/Gem o Gem monotherapy ?

3- Palliative radiation therapy followed by IO ?

4.- Supportive care ?

Any specific requirement for a decission ?

Clinical Case- Bladder Cancer

- Status PD-L1= Positive, CPS ≥10
- 04/2019- Pembrolizumab 200 mg, IV, every 3 weeks
- 07/2019- Clinical Response, ECOG 1. Still on treatment

Questions ?

- Any role for “Adjuvant” post local radical treatment of oligometastatic disease ?
  - No data (chemo/IO)
  - XRT/RFA/ + IO is under clinical trial
- For how long do we need to treat the patient ? (non PD status)
  - Data in NSCLC. One year and stop vs continue therapy.

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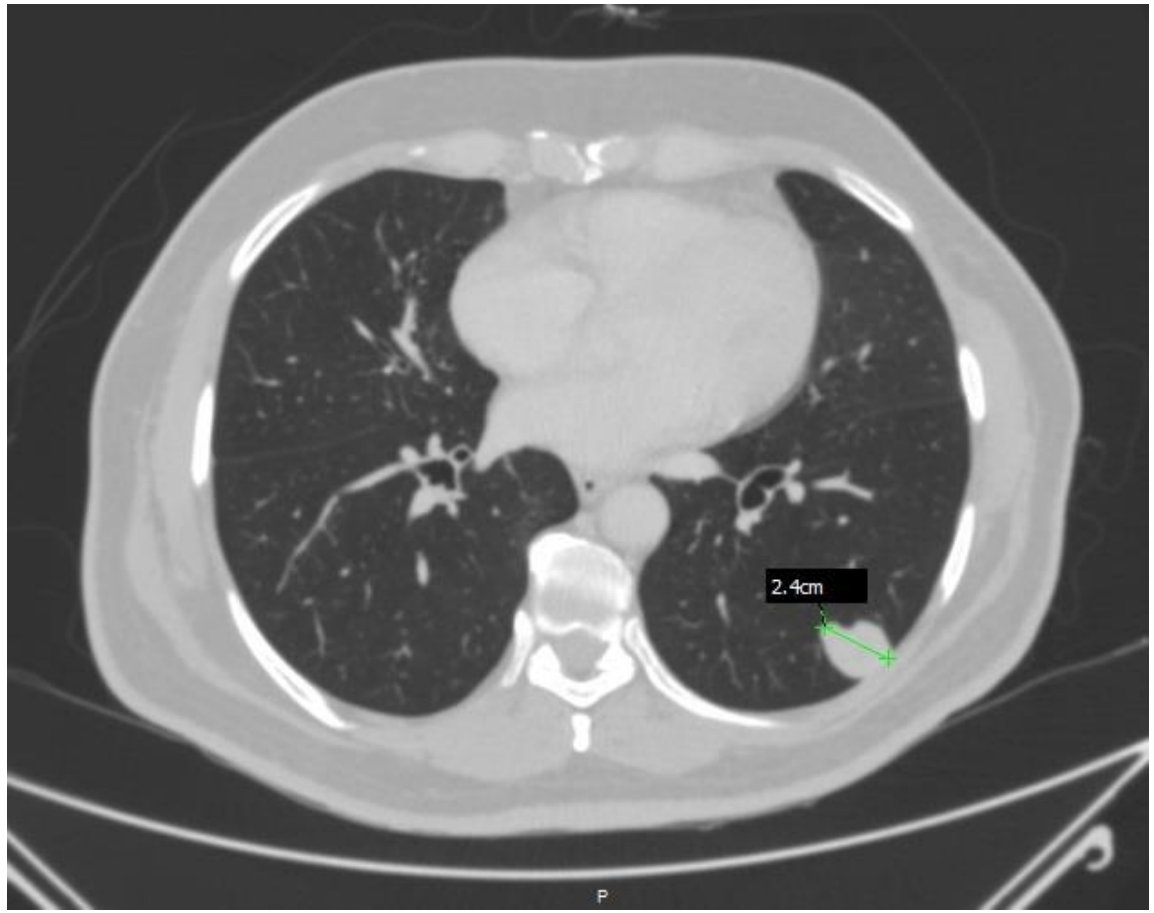
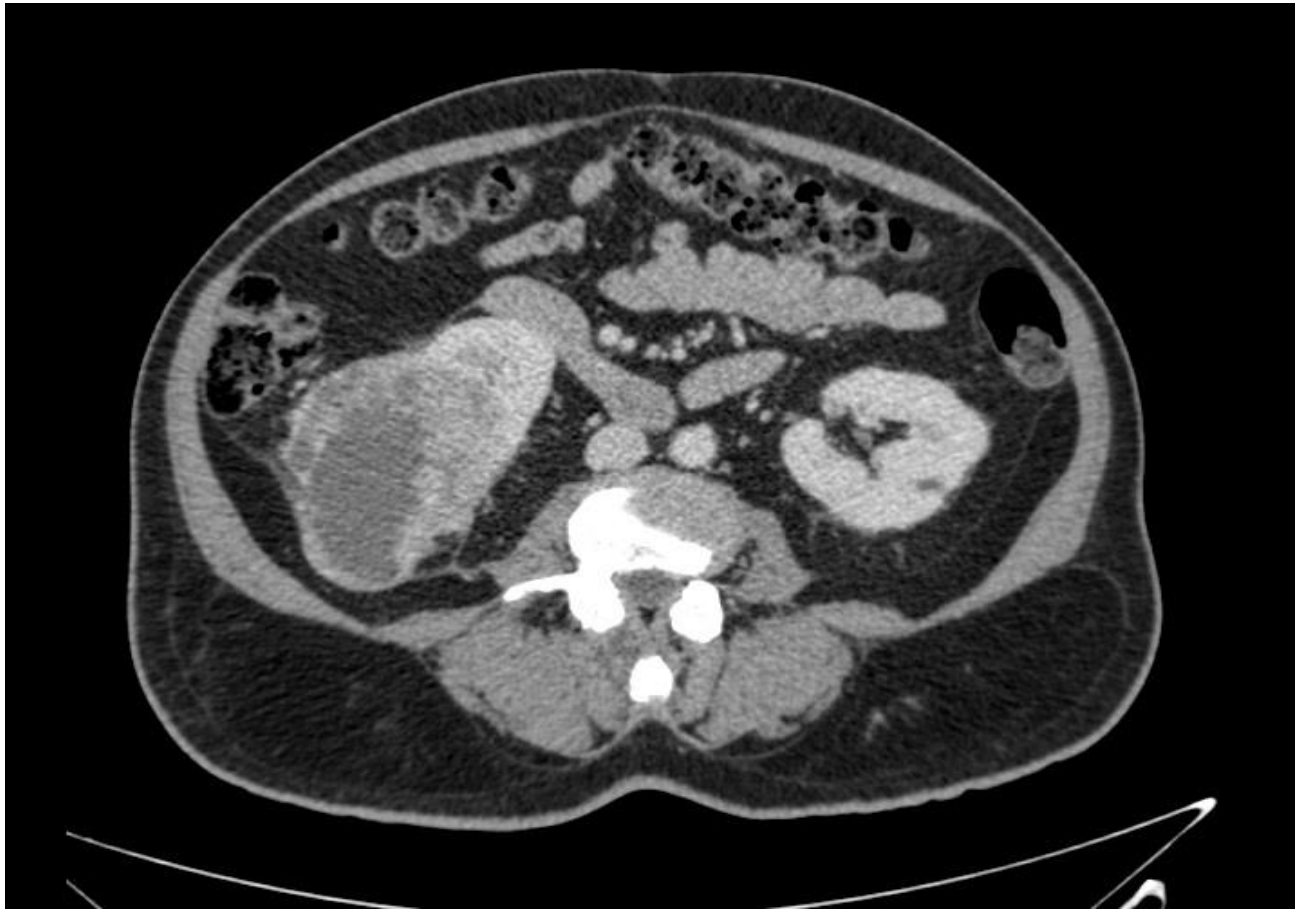
Clinical Case 2- Kidney Cancer

Clinical Case- Kidney Cancer

- 75 years old, retired, Married, 2 sons
- No relevant FH, no relevant PMH. Quit smoking 15 years ago
- Comorbidities: Mild hypertension (ACE inhibitor).
- Complaining of non specific symptoms (loss of appetite and loss of weight), cough and astenia. Right quadrant discomfort.
- CT chest, abdomen and pelvis 09/2018: large right renal mass (80x76 mm) with lung nodules (largest 24x19 mm)

Clinical Case- Kidney Cancer





09/2018

Clinical Case- Kidney Cancer

- Biopsy 10/2018: Clear Cell Renal Cell Carcinoma
- KPS: 70%, Anemia, Hypercalcemia, less than 1 year from time of diagnosis to systemic therapy
- Poor Risk IMDC Risk

Clinical Case- Kidney Cancer

- Options ?
- Ipilimumab (1mg/kg) + Nivolumab (3mg/kg) every 3 weeks, for 3 cycles

Clinical Case- Kidney Cancer

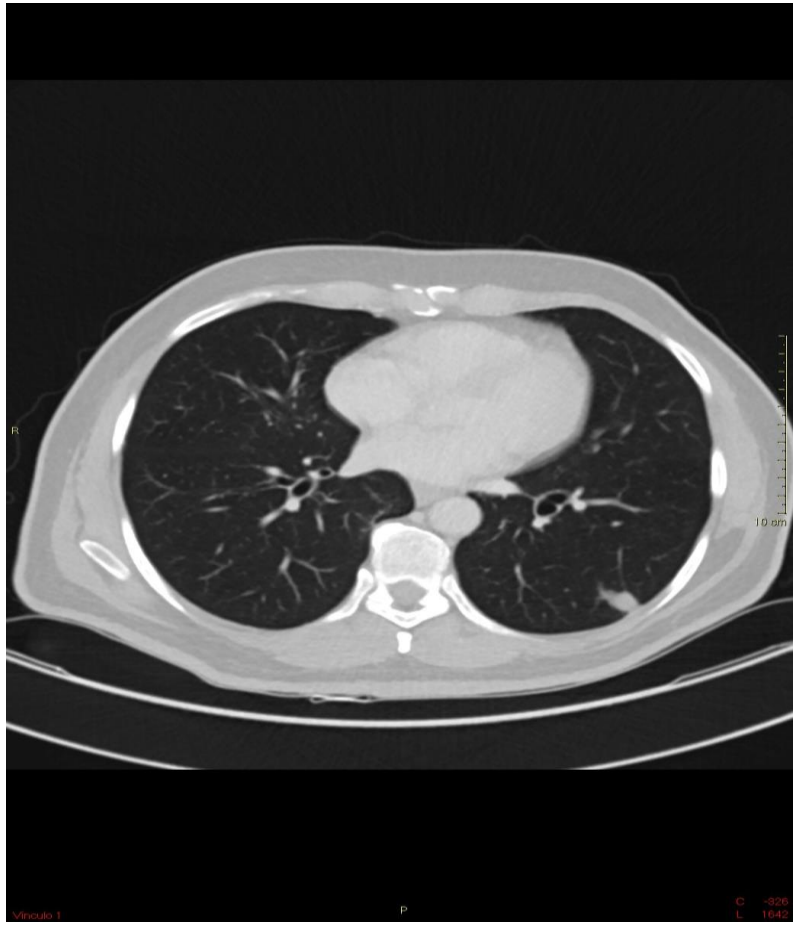
- Toxicity: - Skin Toxicity G2 after first cycle- Topical steroids cream + oral antihistamines

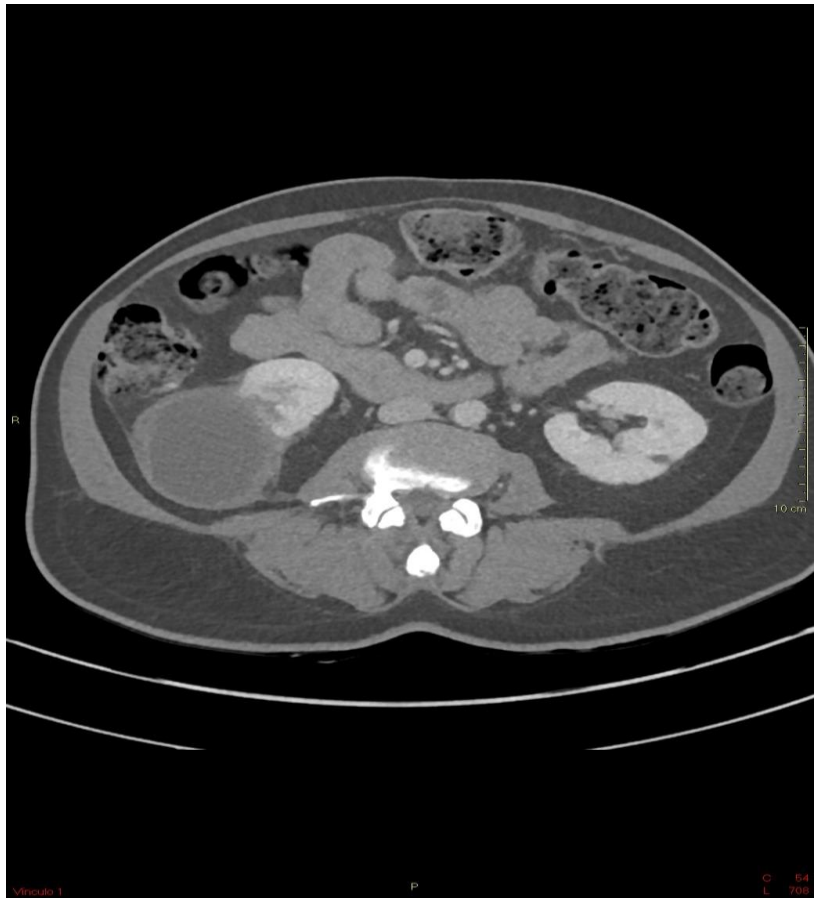
  - Diarrhea G3 after third cycle-

  Steroids (Methylprednisolone 2mg/Kg, IV) and Tt stopped

- KPS 90%, His symptoms subsided

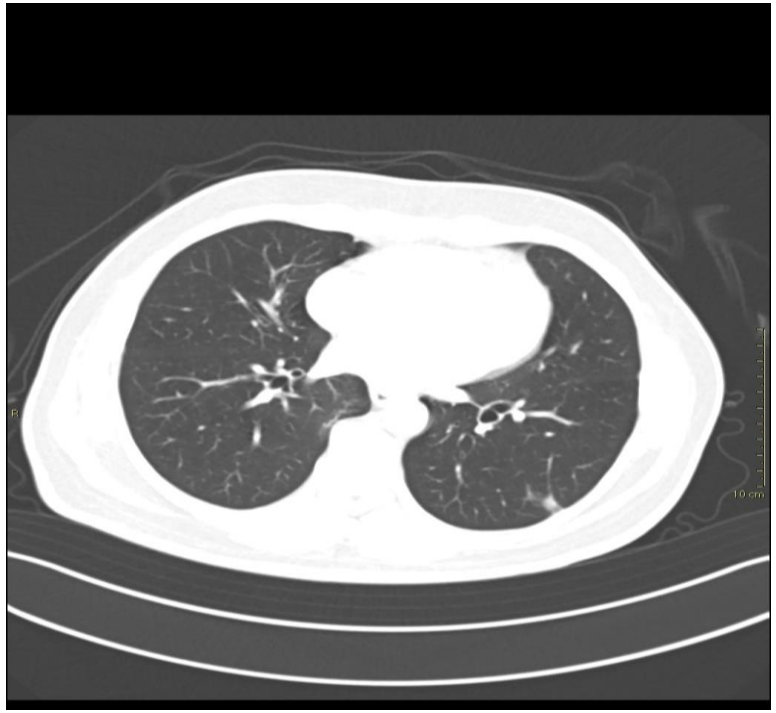
Clinical Case- Kidney Cancer

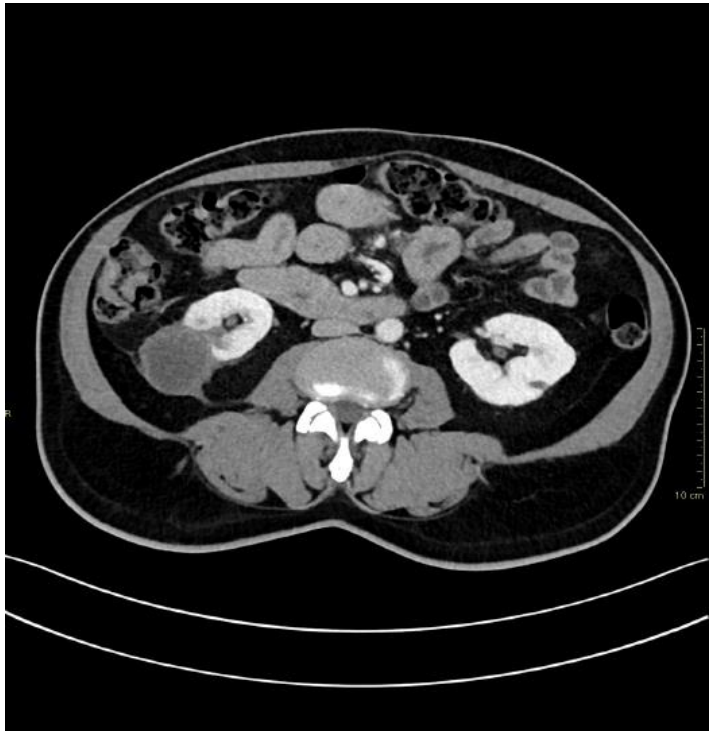




Clinical Case- Kidney Cancer IO

- Nivolumab (3 mg/Kg) every 2 weeks
- CT chest, abdomen and pelvis 04/19: Lung nodules (largest 8x6 mm) and the renal mass (42 x 39 mm) did reduce in size.





- Any role for nephrectomy ?

Clinical Case- Kidney Cancer

- Right Nefrectomy 05 /2019: Renal cell carcinoma with tumor size of 37x35 mm. It was infiltrating the capsule and involving perinephric fat but not exceeds the Gerota fascia. T3N0

- Still in Nivolumab treatment

- SBRT in lung nodule