UNIVERSITÀ CATTOLICA del Sacro Cuore

Gemelli ART
Fondazione Policlinico Universitario Agostino Gemelli IRCCS
Università Cattolica del Sacro Cuore
Advanced Radiation Therapy

MRO . ART

Modern Radiation Oncology:
multidisciplinarity in the era
of OMICS and AI guided oncology
32° RESIDENTIAL COURSE

17 | 18 | 19 October 2022

Comprehensive Cancer Center

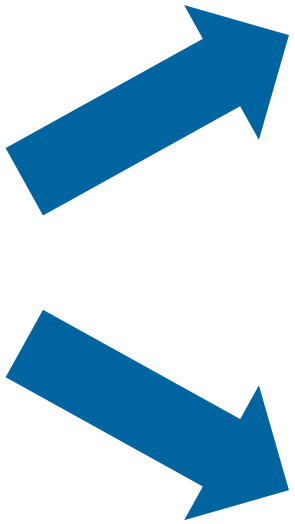
FOCUS ON

Immunotherapy approaches in the Omics Era: focus on Genitourinary cancer

G. Schinzari
Medical Oncology
FPG – UCCS
Rome Italy

clarification …

Omic Sciences



the scientific branches investigating every aspect of cell's biology, including structures, functions and dynamics pathways: genomics, epigenomics, proteomics, transcriptomics, metabolomics, radiomics ...

cover many issues that are not politically correct

Immunotherapy in GU cancer

Company sponsored trials → Checkpoint inhibitors approval

Is it really a patient-focused approach?

Immunotherapy in GU cancer

Trials that led to FDA/EMA approval

Trial	Agent(s)	Cancer Subtype and Disease Setting	Description	Original Food and Drug Administration Approval Date	Modifications
NCT02625961 (KEYNOTE-057)	Pembrolizumab monotherapy	Non-muscle-invasive bladder cancer	BCG refractory	January 2020	
NCT02632409 (CheckMate 274)	Nivolumab monotherapy	Muscle-invasive bladder cancer	Adjuvant therapy after radical resection	August 2021	
NCT02951767 (IMvigor210)	Atezolizumab monotherapy	Locally advanced or metastatic cisplatin-ineligible urothelial carcinoma	First-line metastatic	April 2017 (accelerated approval)	June 2018 (stricter guidelines including PD-L1 expression)
NCT02335424 (KEYNOTE-052)	Pembrolizumab monotherapy	Locally advanced or metastatic cisplatin-ineligible urothelial carcinoma	First-line metastatic	August 2021	
NCT03288545 (EV-103/KEYNOTE-869)	Pembrolizumab and enfortumab vedotin	Locally advanced or metastatic cisplatin-ineligible urothelial carcinoma	First-line metastatic	February 2020 (breakthrough designation)	
NCT02603432 (JAVELIN Bladder 100)	Avelumab monotherapy	Locally advanced or metastatic urothelial carcinoma	First-line maintenance after platinum-based chemotherapy	June 2020	
NCT02108652 (IMvigor210)	Atezolizumab monotherapy	Locally advanced or metastatic urothelial carcinoma after platinum therapy	Second-line metastatic	May 2016 (accelerated approval)	Withdrawal in March 2021
NCT02387996 (CheckMate 275)	Nivolumab monotherapy	Locally advanced or metastatic urothelial carcinoma after platinum therapy	Second-line metastatic	February 2017 (accelerated approval)	
NCT02256436 (KEYNOTE-045)	Pembrolizumab monotherapy	Locally advanced or metastatic urothelial carcinoma after platinum therapy	Second-line metastatic	May 2017	
NCT01772004 (JAVELIN Solid Tumor)	Avelumab monotherapy	Locally advanced or metastatic urothelial carcinoma after platinum therapy	Second-line metastatic	May 2017 (accelerated approval)	
NCT01693562 (Study 1108)	Durvalumab monotherapy	Locally advanced or metastatic urothelial carcinoma after platinum therapy	Second-line metastatic	May 2017 (accelerated approval)	Withdrawal in February 2021
NCT02853331 (KEYNOTE-426)	Pembrolizumab and axitinib	Metastatic renal cell carcinoma	First-line metastatic	April 2019	
NCT02684006 (JAVELIN Renal 101)	Avelumab and axitinib	Metastatic renal cell carcinoma	First-line metastatic	May 2019	
NCT0281186 (CLEAR)	Lenvatinib and pembrolizumab	Metastatic renal cell carcinoma	First-line metastatic	August 2021	
NCT03141177 (CheckMate 9ER)	Nivolumab and cabozantinib	Metastatic renal cell carcinoma	First-line metastatic	January 2021	
NCT02231749 (CheckMate 214)	Nivolumab and ipilimumab	Metastatic renal cell carcinoma	First-line metastatic	April 2018	
NCT01668784 (CheckMate 025)	Nivolumab	Metastatic renal cell carcinoma previously treated with angiogenic inhibitor	Second-line metastatic	November 2015	
NCT01876511	Pembrolizumab	Tumors with high microsatellite instability or deficiency in mismatch repair refractory to other treatments	Progression on at least one prior systemic therapy	May 2017 (accelerated approval)	
NCT02628067 (KEYNOTE-158)	Pembrolizumab	Tumors with high mutational burden refractory to other treatments	Progression on at least one prior systemic therapy	June 2020 (accelerated approval)	

Jang A, 2021

Renal cell carcinoma

Advanced disease

Second line after TKi:
IO monotherapy

First line:
IO-IO combination in intermediate/poor risk pts
IO-TKI (anti -VEGF) combination

Adjuvant setting

IO monotherapy
effective in high risk resected ccRCC
and in resected metastatic disease

IO-IO combination:
benefit not proven

Urothelial carcinoma

Advanced disease

Second line after TKi:
IO monotherapy

First line:
patients unfit for cisplatin with CPS ≥10

Perioperative setting

Promising result with IO monotherapy and IO-chemo combination

Renal cell carcinoma

advanced disease

Figure 4. Progression-free survival[a]

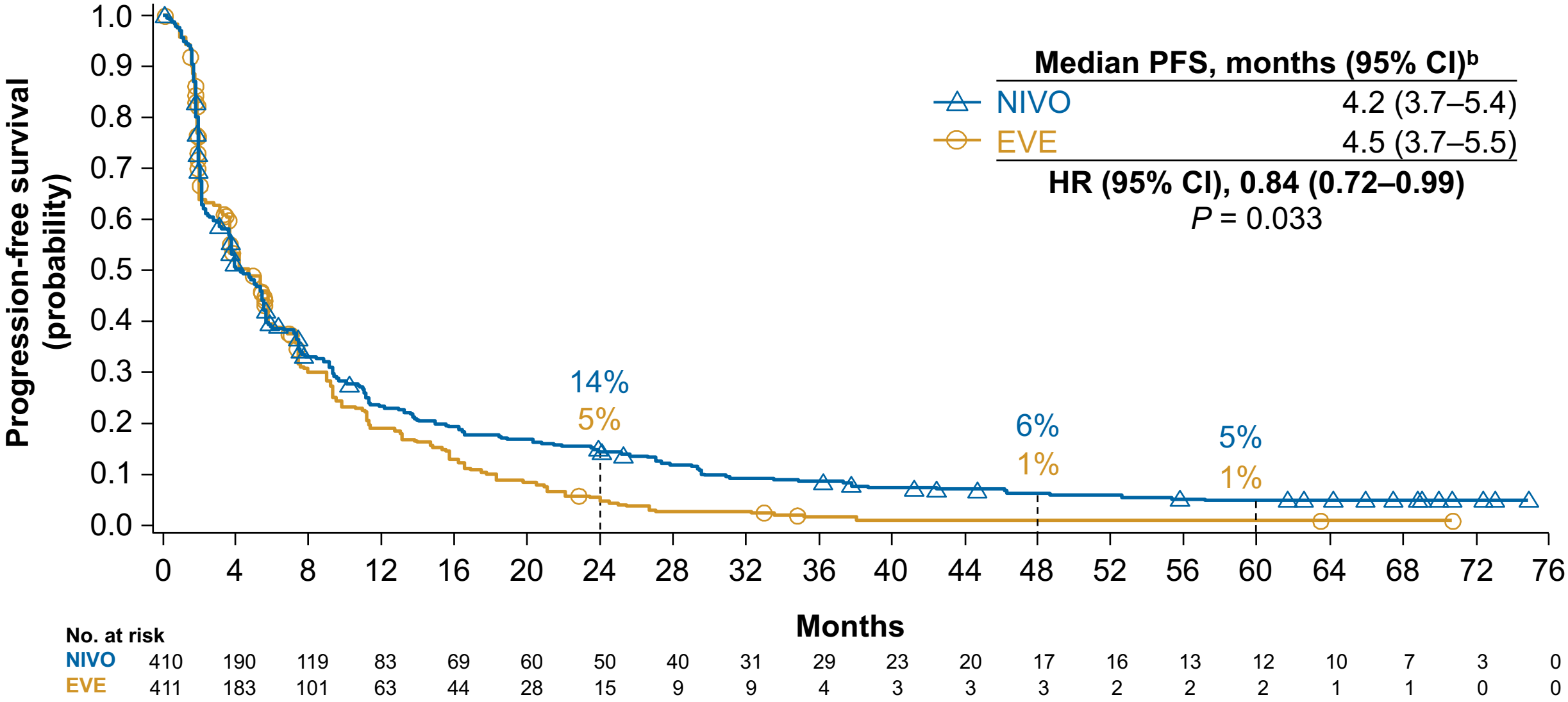
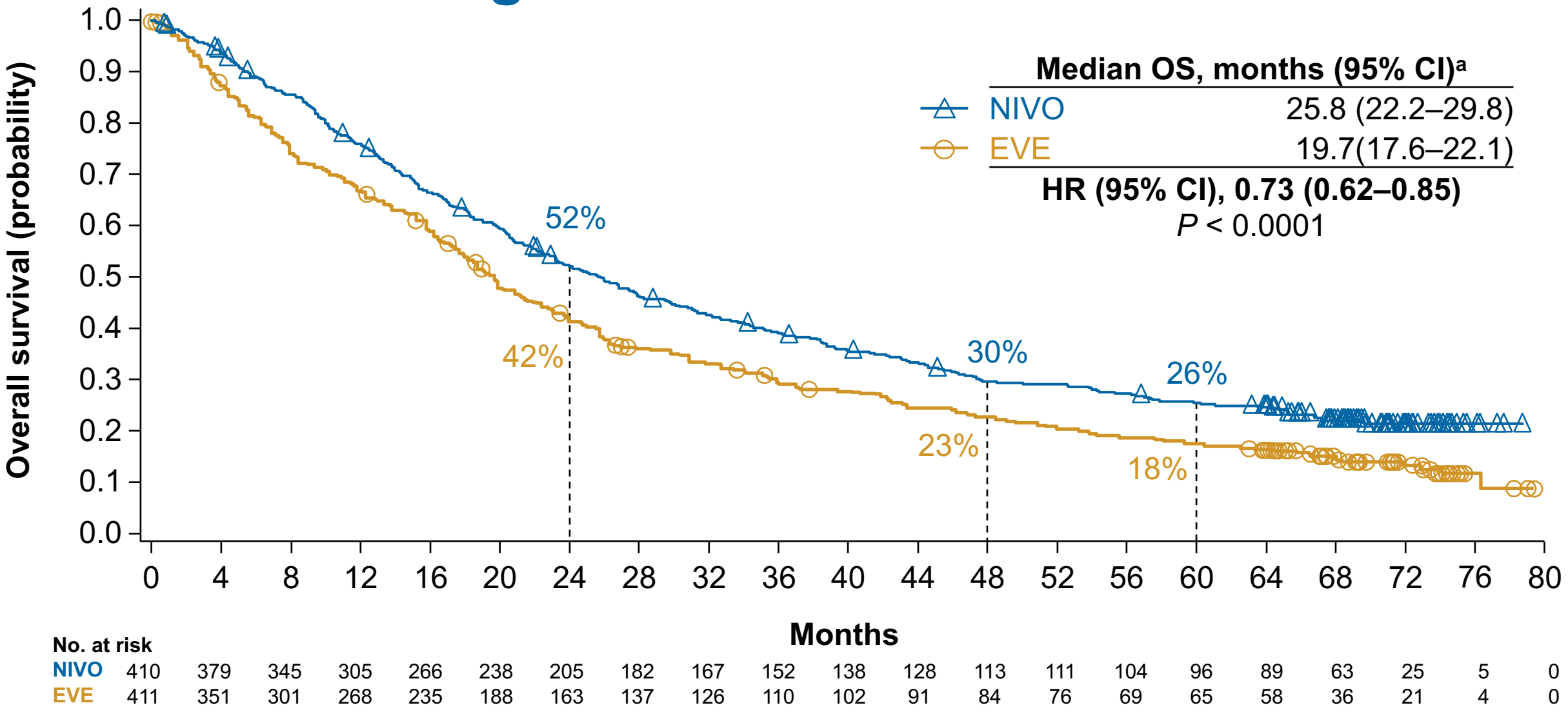


Figure 1. Overall survival

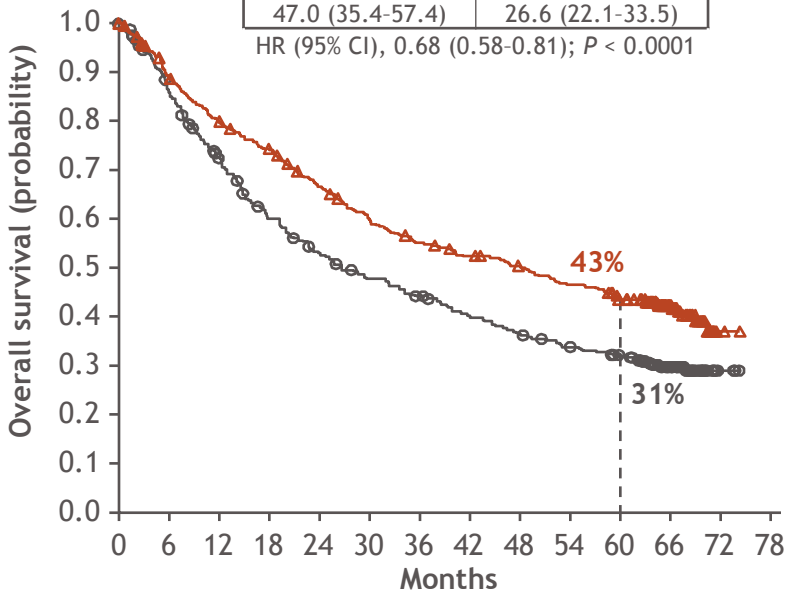


OS, PFS, and DOR in IMDC intermediate/poor-risk patients

Overall survival

Median OS (95% CI), months	
NIVO+IPI (N = 425)	SUN (N = 422)
47.0 (35.4-57.4)	26.6 (22.1-33.5)

HR (95% CI), 0.68 (0.58-0.81); *P* < 0.0001

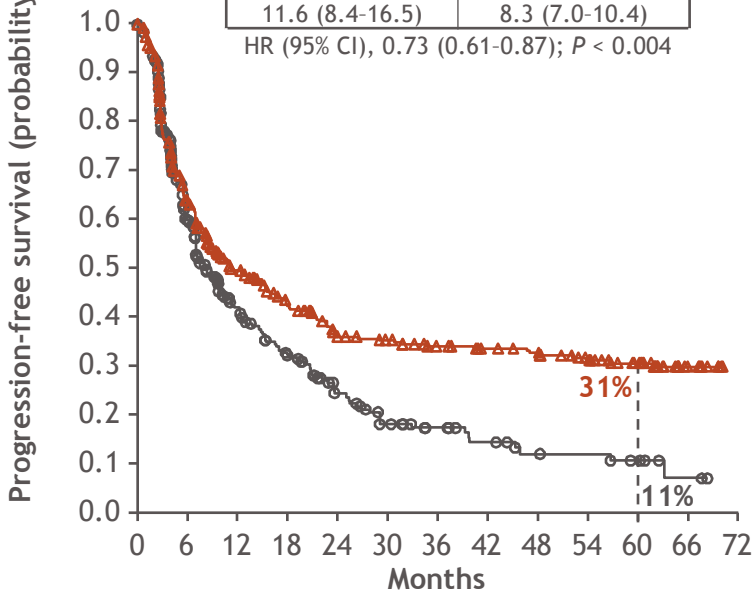


No. at risk														
NIVO+IPI	425	372	332	306	270	241	220	207	196	181	163	79	2	0
SUN	422	353	291	237	206	184	169	151	137	125	112	58	3	0

Progression-free survival

Median PFS (95% CI), months	
NIVO+IPI (N = 425)	SUN (N = 422)
11.6 (8.4-16.5)	8.3 (7.0-10.4)

HR (95% CI), 0.73 (0.61-0.87); *P* < 0.004

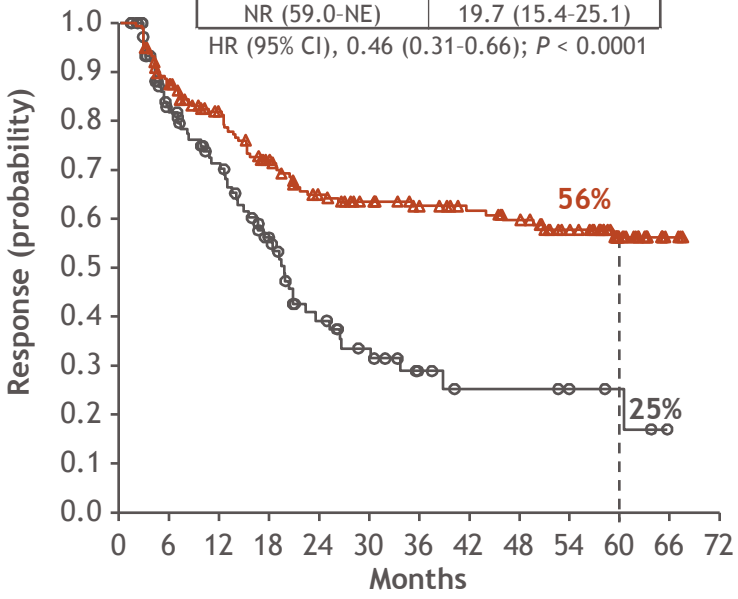


No. at risk														
NIVO+IPI	425	233	164	130	101	94	81	74	70	60	48	10	0	
SUN	422	188	106	74	46	29	21	15	10	9	6	2	0	

Duration of response

Median DOR (95% CI), months	
NIVO+IPI (N = 179)	SUN (N = 113)
NR (59.0-NE)	19.7 (15.4-25.1)

HR (95% CI), 0.46 (0.31-0.66); *P* < 0.0001



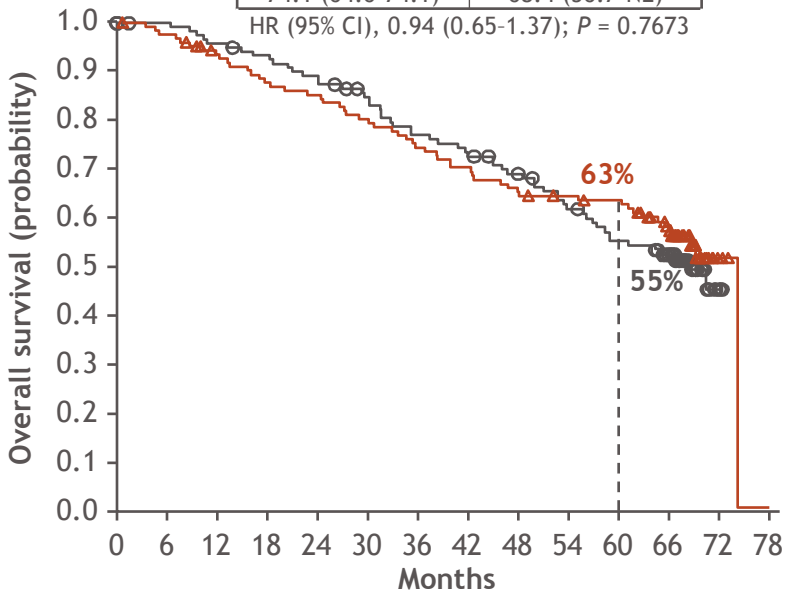
No. at risk														
NIVO+IPI	179	146	125	104	88	79	71	66	61	49	23	4	0	
SUN	113	75	58	39	23	16	9	6	6	4	3	0	0	

OS, PFS, and DOR in IMDC favorable-risk patients

Overall survival

Median OS (95% CI), months	
NIVO+IPI (N = 125)	SUN (N = 124)
74.1 (64.6-74.1)	68.4 (56.7-NE)

HR (95% CI), 0.94 (0.65-1.37); *P* = 0.7673



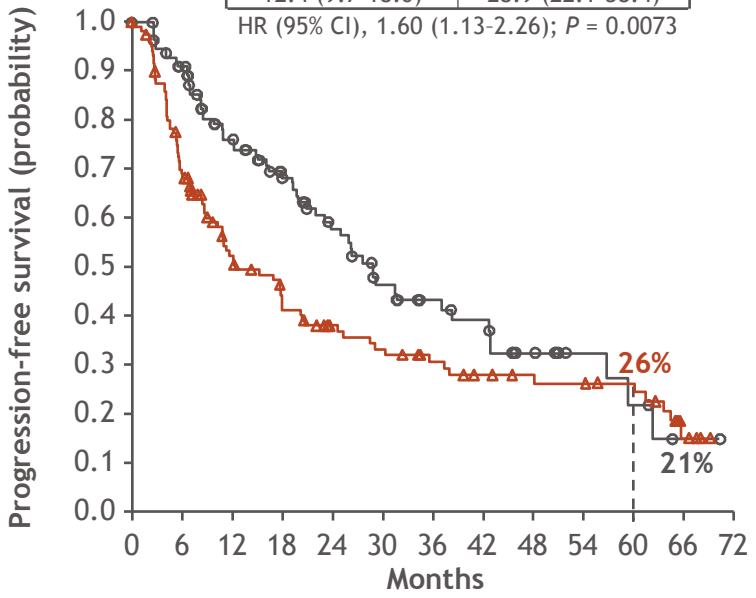
No. at risk

NIVO+IPI	125	121	112	105	102	96	89	84	78	75	73	59	3	0
SUN	124	119	114	110	104	97	88	83	76	67	59	50	3	0

Progression-free survival

Median PFS (95% CI), months	
NIVO+IPI (N = 125)	SUN (N = 124)
12.4 (9.7-18.0)	28.9 (22.1-38.4)

HR (95% CI), 1.60 (1.13-2.26); *P* = 0.0073



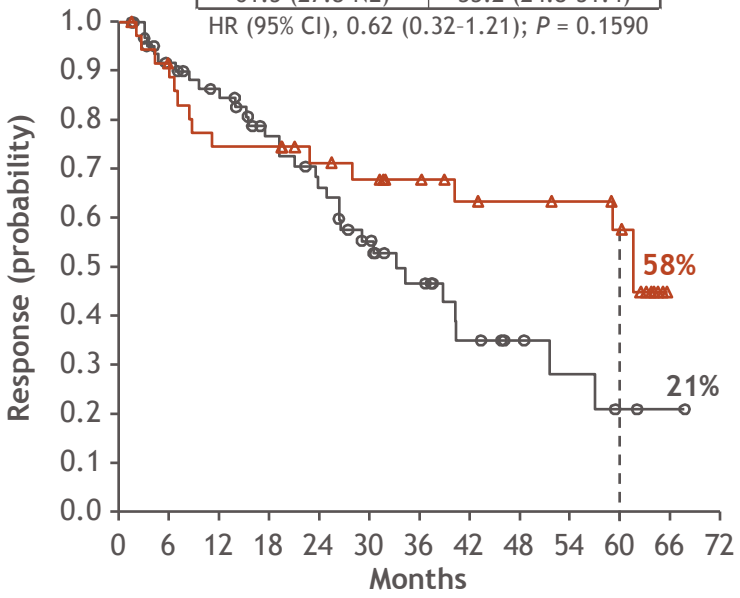
No. at risk

NIVO+IPI	125	82	53	41	31	27	22	18	16	15	14	4	0	
SUN	124	97	72	56	41	30	21	18	11	6	4	1	0	

Duration of response

Median DOR (95% CI), months	
NIVO+IPI (N = 37)	SUN (N = 64)
61.5 (27.8-NE)	33.2 (24.8-51.4)

HR (95% CI), 0.62 (0.32-1.21); *P* = 0.1590



No. at risk

NIVO+IPI	37	31	26	26	22	20	17	14	13	12	10	0	0	
SUN	64	53	46	37	31	23	15	9	6	4	2	1	0	

Rationale for IO–TKI combinations

IO and anti-VEGF TKIs have complementary MoAs

1 Normalize vasculature[1]

- Increase immune infiltration
- Improve delivery of anticancer therapies

2 Immune stimulation[1,2]

- Promote tumor infiltration by T cells
- Induce DC maturation and thus T-cell activation
- Reduce Treg cells
- Upregulated PD-L1 expression on both endothelial cells and tumor cells

Activity of anti–PD-(L)1 antibodies

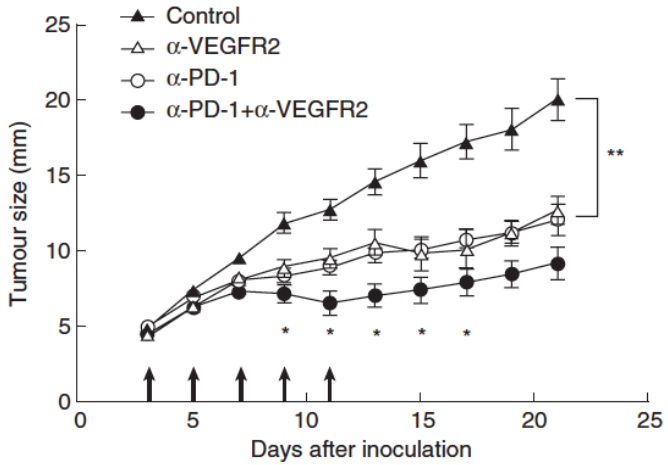
3 Reactivation of T cells[3]

- Reverse the PD-L1-mediated disabling of TILs by tumor cells, and enhance the ‘effector’ stage of the immune response

Preclinical model: anti-VEGF + immunotherapy

Murine colon cancer model[4]

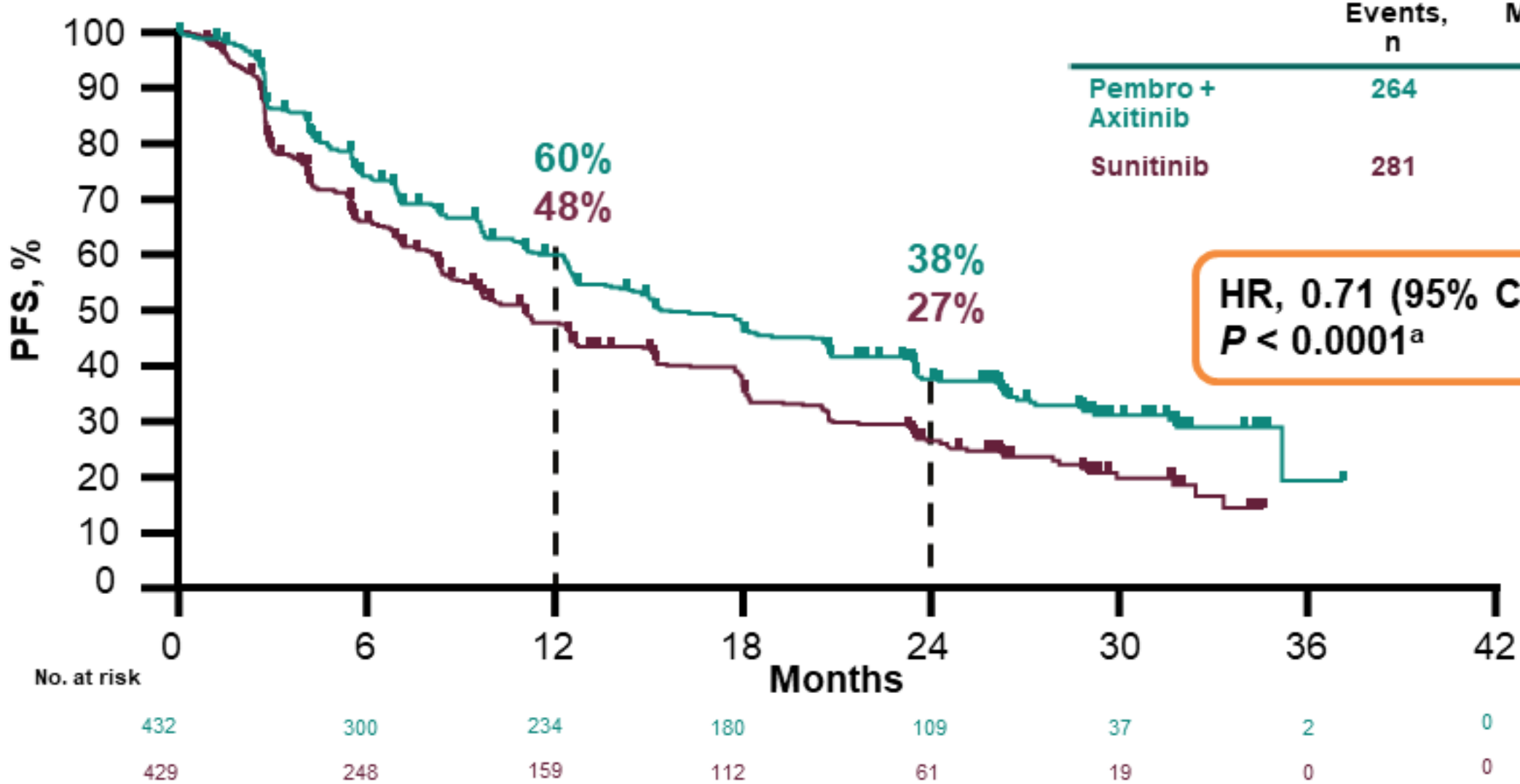
Simultaneous blockade of PD-1 and VEGFR in a murine colon cancer model significantly inhibited tumor growth



Simultaneous blockade of PD-1 and VEGFR2 *in vivo*[4]

1. Fukumura D, et al. Nat Rev Clin Oncol. 2018;15:325-40; 2. Einstein DJ, McDermott DF. Clin Adv Hematol Oncol. 2017;15:478-88; 3. Seidel JA, et al. Front Oncol. 2018;8:86;
4. Yasuda S, et al. Clin Exp Immunol. 2013;172:500-6.

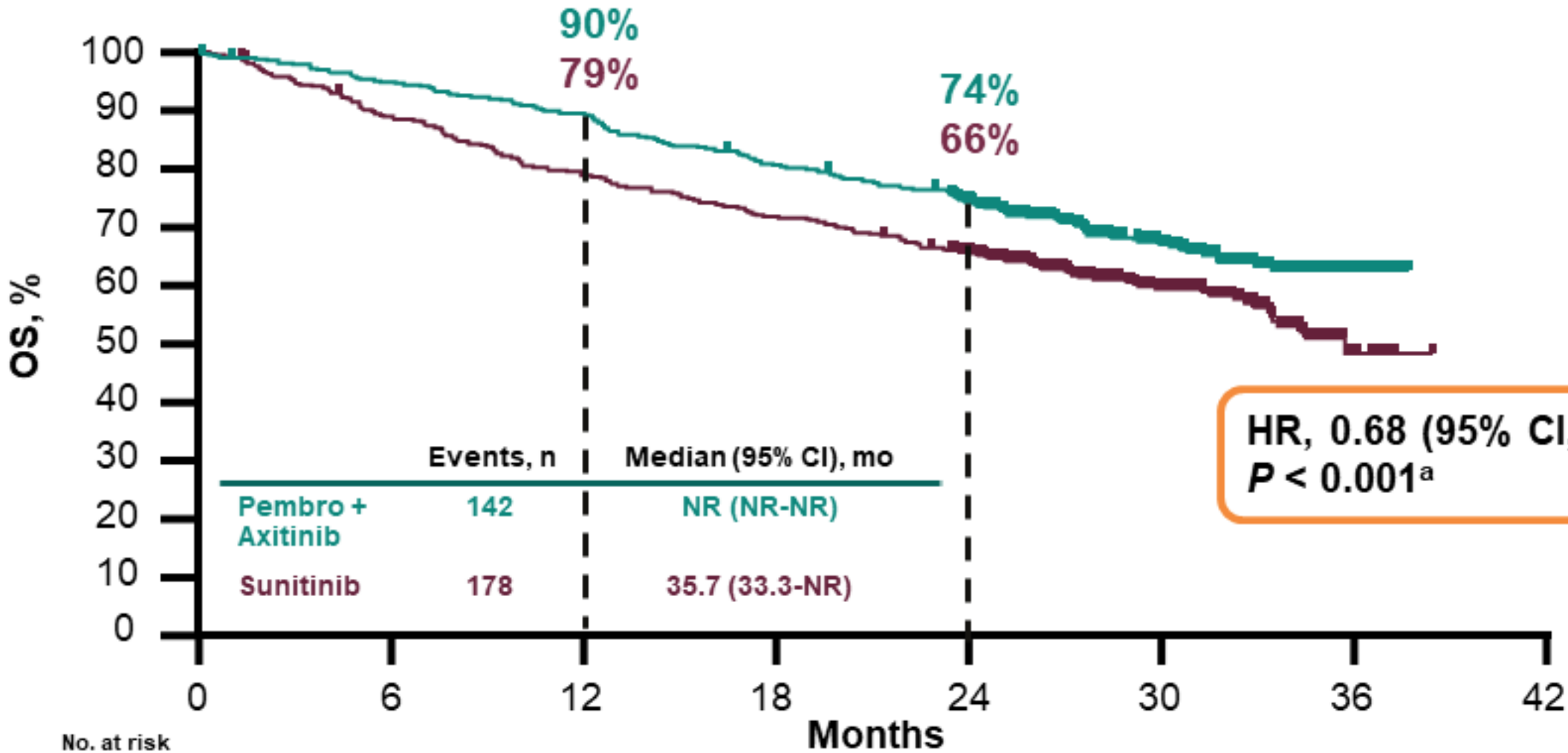
PFS in the ITT Population



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

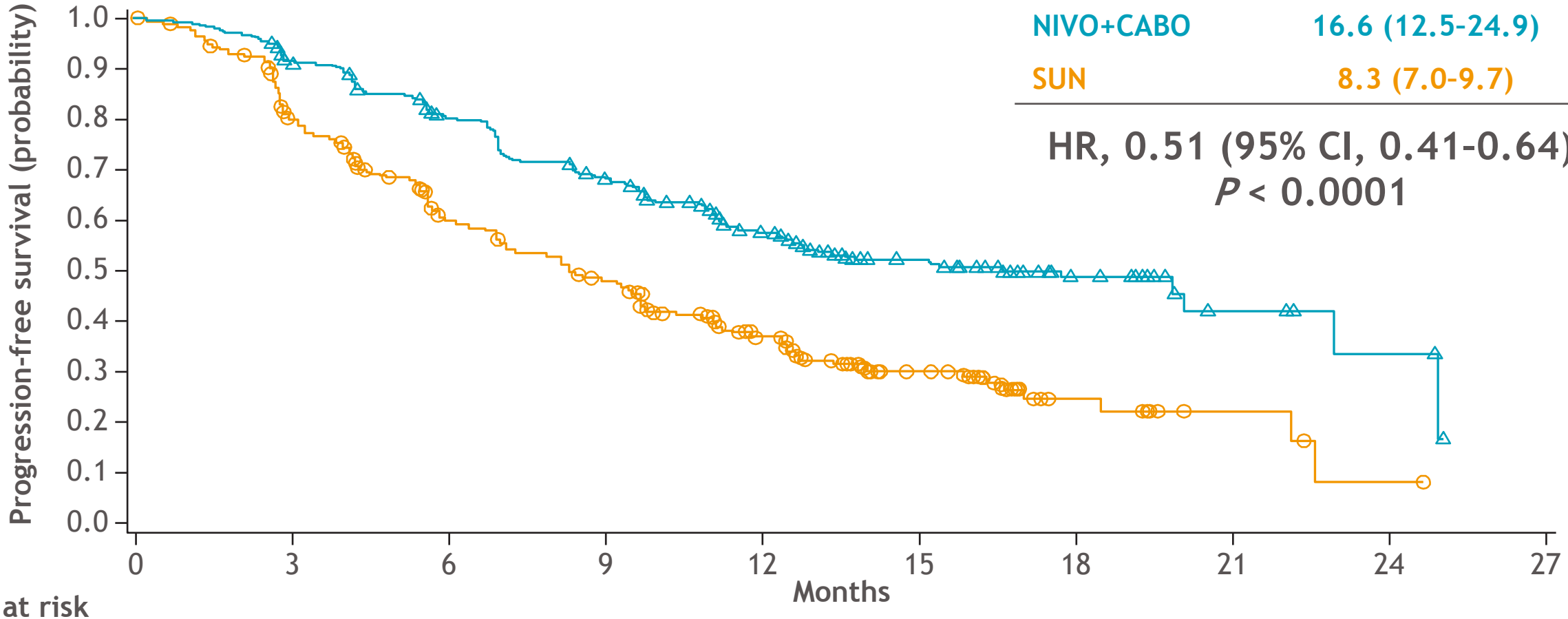
HR, 0.71 (95% CI, 0.60-0.84)
P < 0.0001[a]

OS in the ITT Population



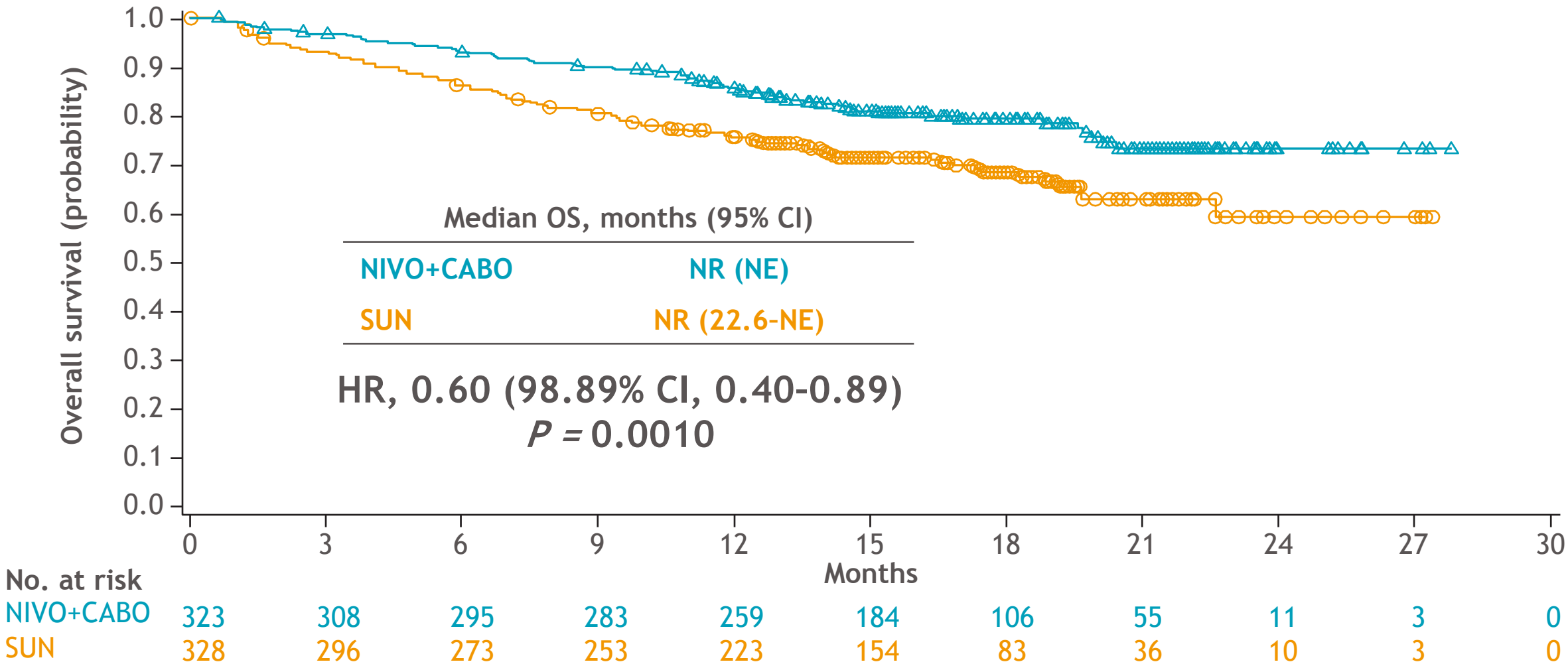
HR, 0.68 (95% CI, 0.55-0.85)
P < 0.001[a]

Progression-free survival per BICR



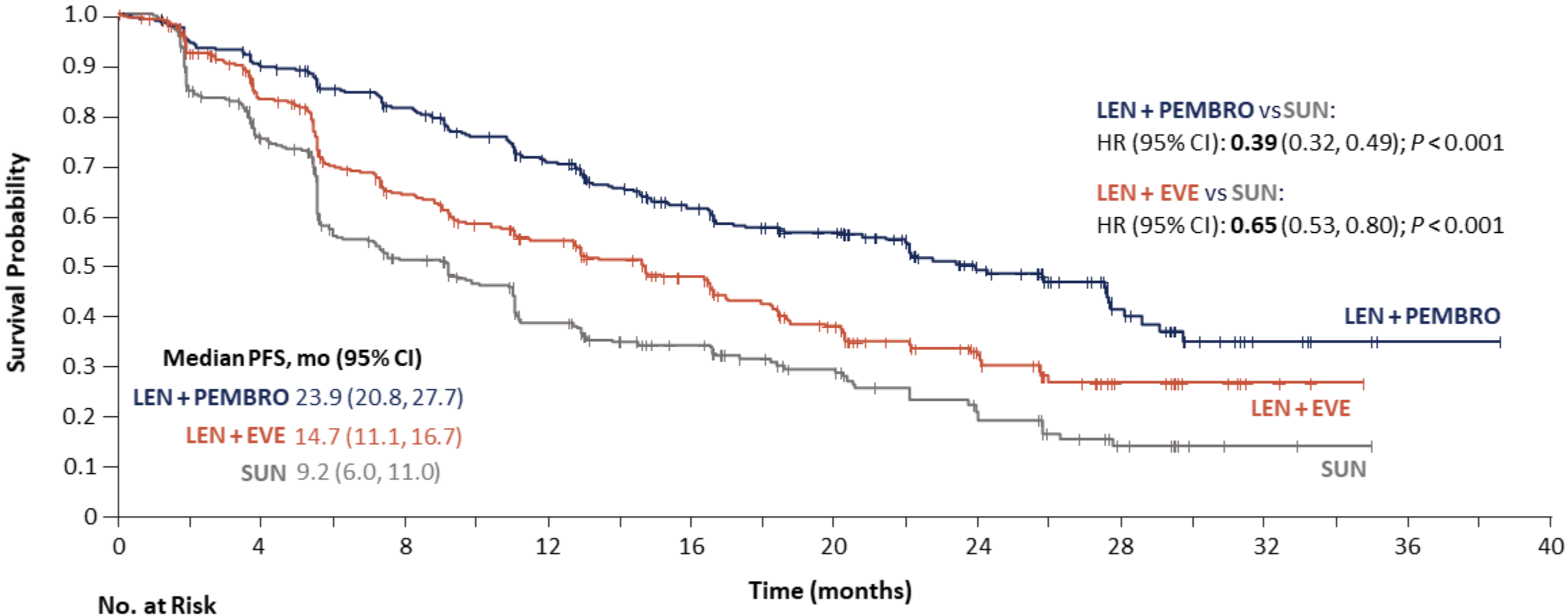
Minimum study follow-up, 10.6 months.

Overall survival



Minimum study follow-up, 10.6 months.
NE, not estimable; NR, not reached.

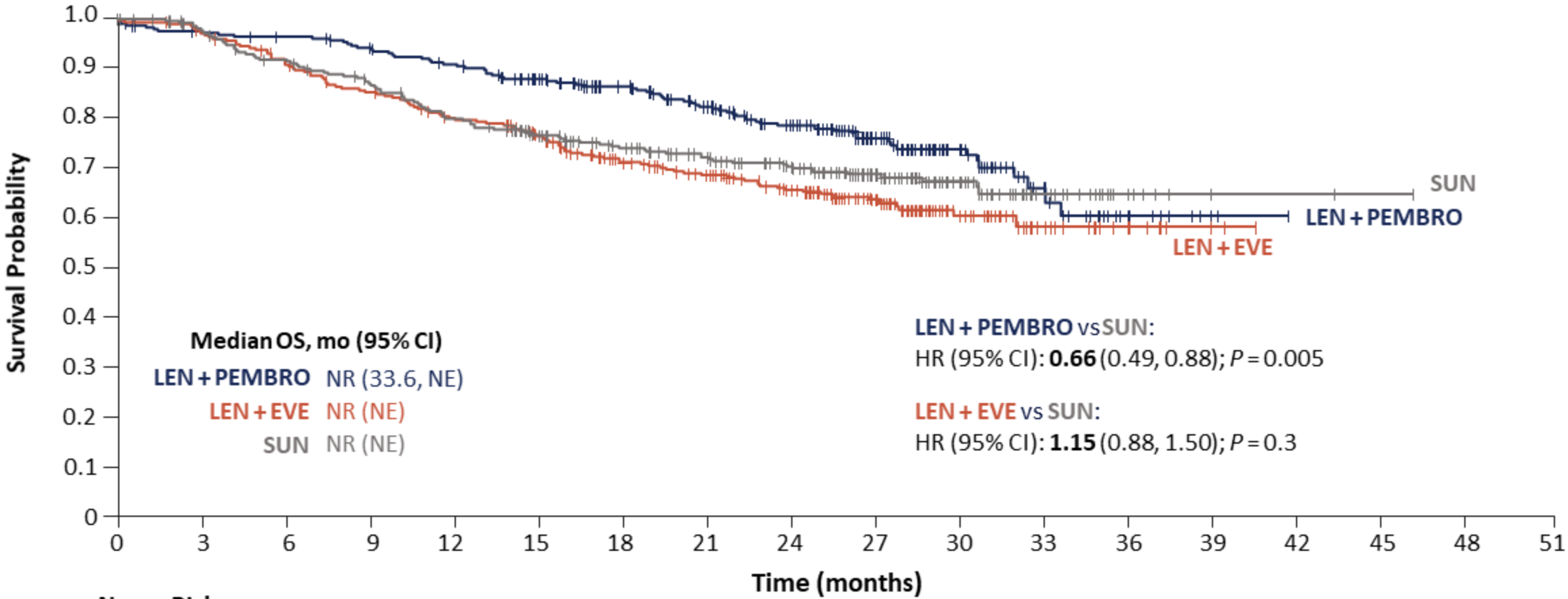
Progression-free Survival



No. at Risk										
355	300	259	213	160	126	80	30	6	1	0
357	259	185	149	105	70	37	13	3	0	
357	218	124	85	62	42	25	9	2	0	

Overall Survival

pembrolizumab + lenvatinib *vs* everolimus + lenvatinib vs sunitinib



No. at Risk

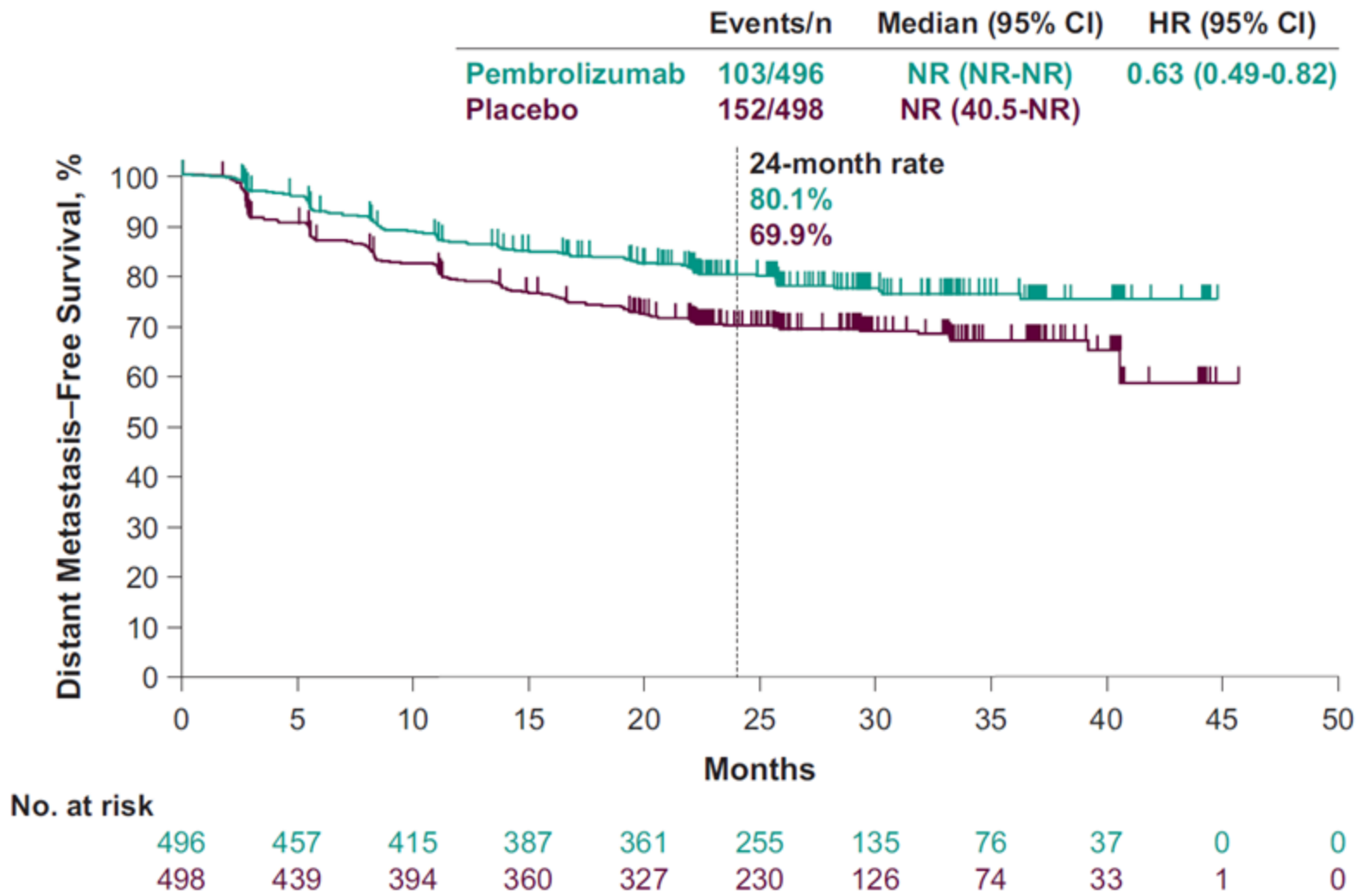
355	342	338	327	313	280	253	222	188	129	66	26	10	2	0	
357	346	321	299	277	246	205	183	154	109	46	22	8	2	0	
357	332	307	289	264	236	207	186	160	112	60	25	7	2	2	1	0

NE, not estimable; NR, not reached.

Renal cell carcinoma

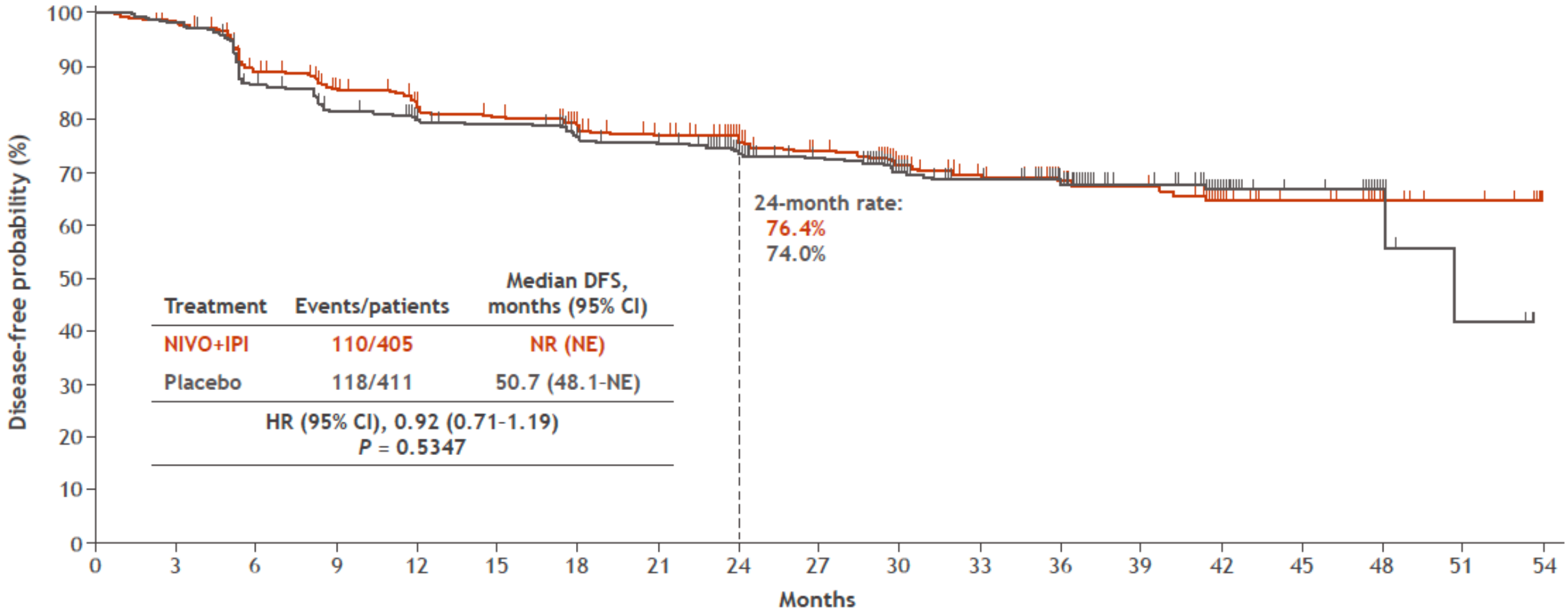
adjuvant setting

Distant Metastasis–free Survival in the Intention-to-treat Population

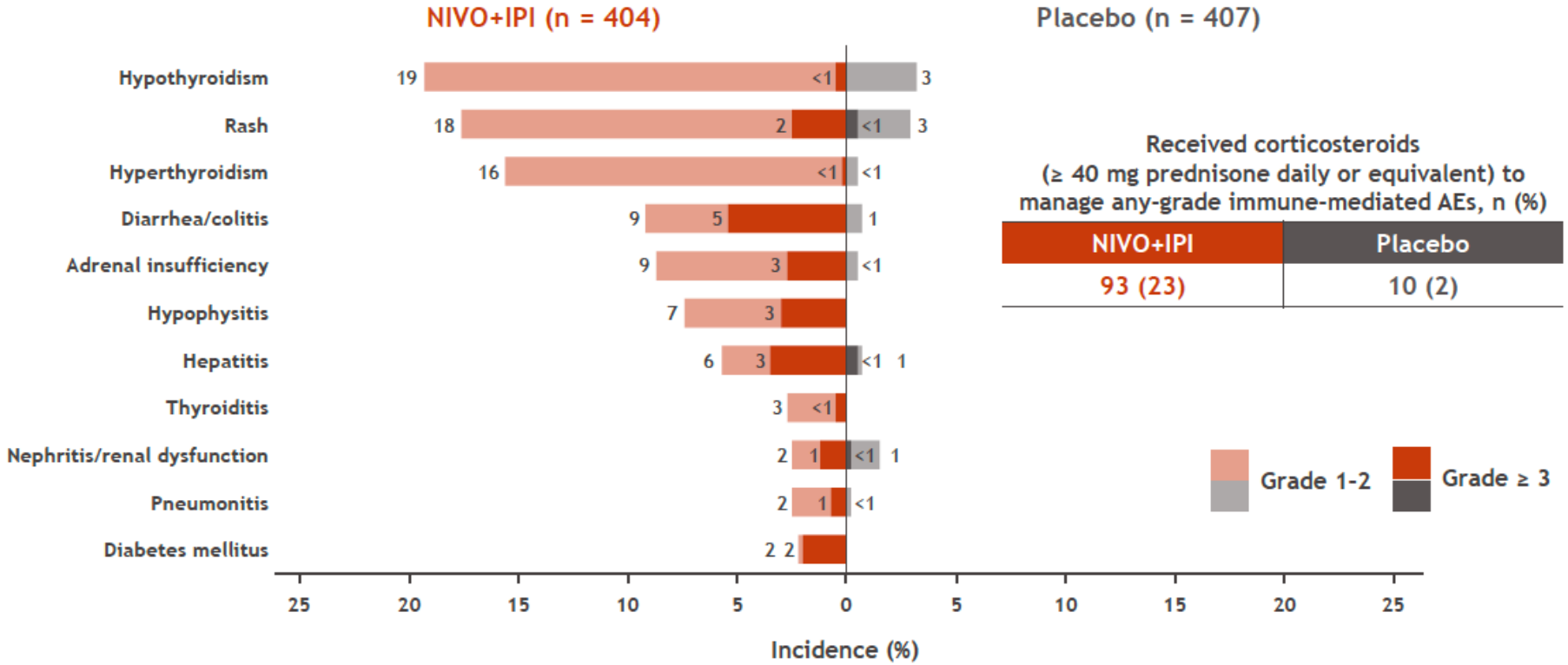


NR, not reached.

Primary endpoint: disease-free survival per BICR



Immune-mediated AEs in all treated patients[a]



Received corticosteroids (≥ 40 mg prednisone daily or equivalent) to manage any-grade immune-mediated AEs, n (%)

NIVO+IPI	Placebo
93 (23)	10 (2)

- Safety of NIVO+IPI in this population was consistent with the known profile for this combination in advanced RCC
- The rate of discontinuation due to treatment-related AEs was considerable with NIVO+IPI in the adjuvant setting
- Further analyses are underway to understand the outcome of CheckMate 914 Part A, and Part B investigating adjuvant nivolumab monotherapy is ongoing

Urothelial carcinoma

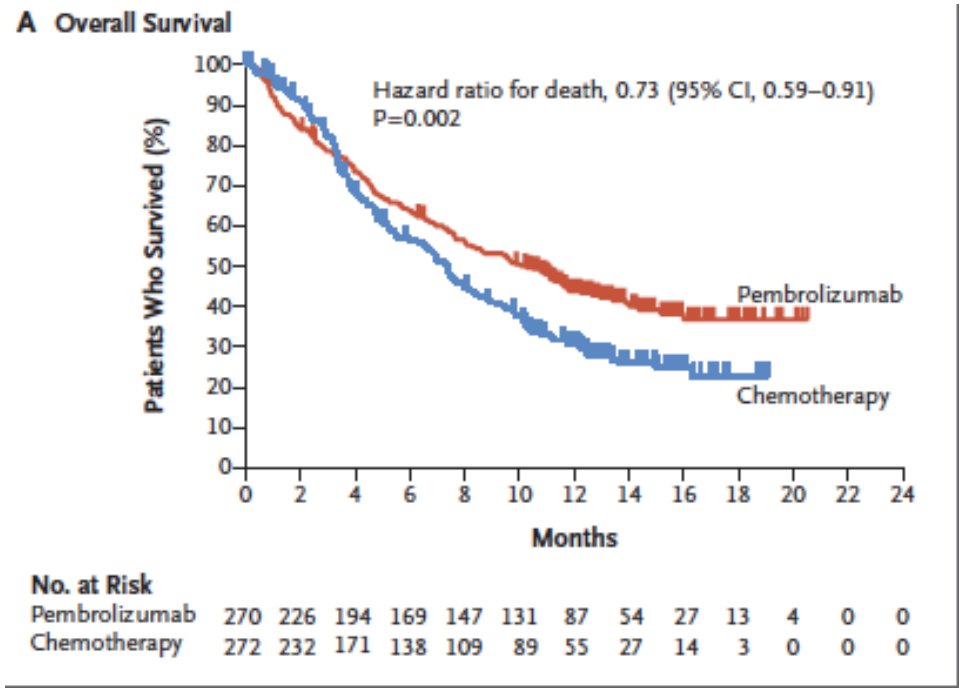
advanced disease

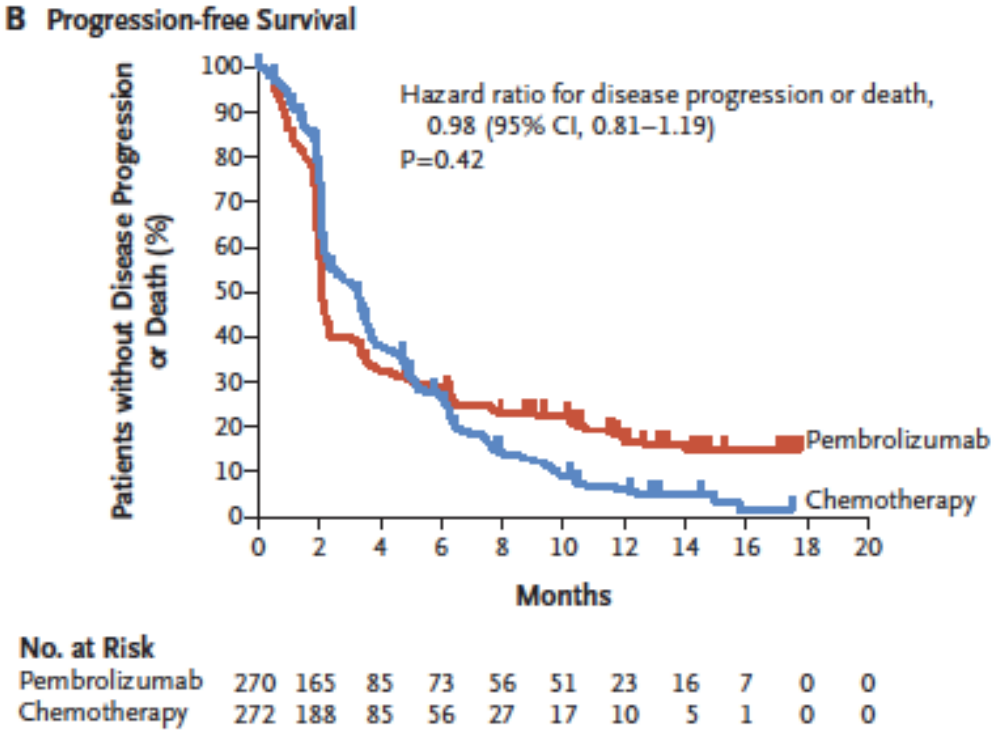
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 16, 2017 VOL. 376 NO. 11

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*

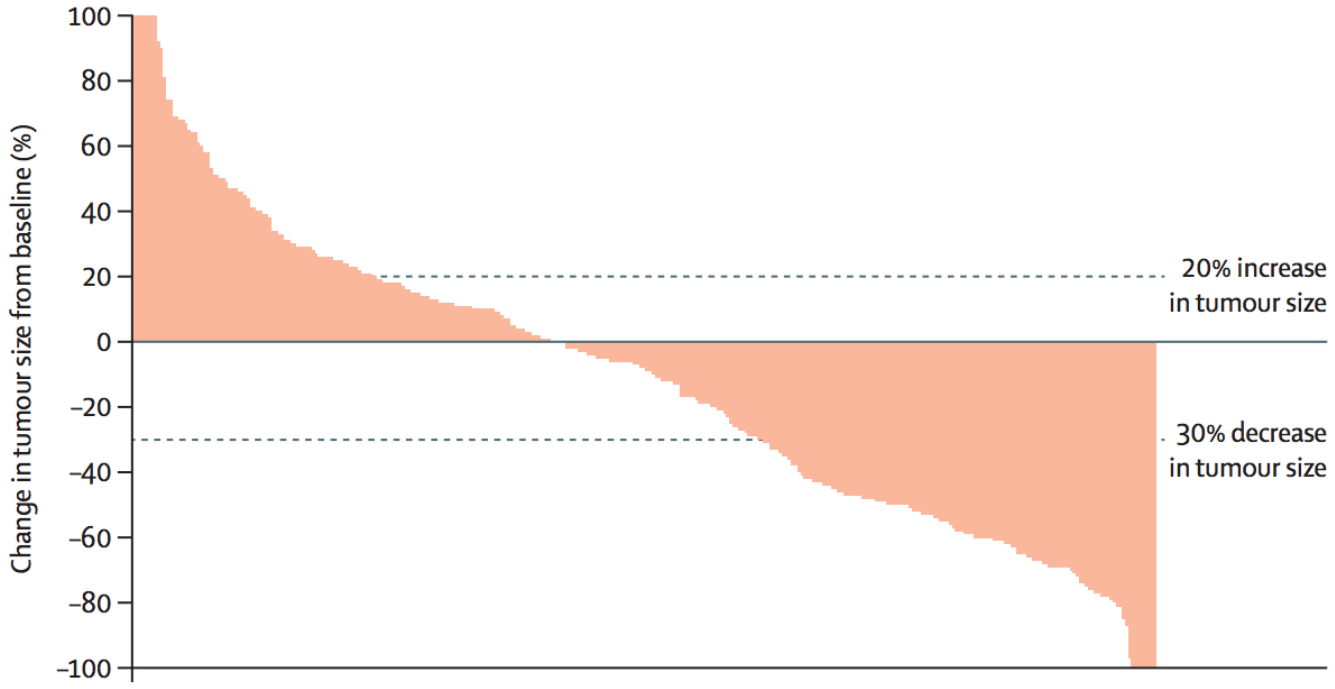




First-line pembrolizumab in cisplatin-ineligible patients with locally advanced and unresectable or metastatic urothelial cancer (KEYNOTE-052): a multicentre, single-arm, phase 2 study

Arjun V Balar, Daniel Castellano, Peter H O'Donnell, Petros Grivas, Jacqueline Vuky, Thomas Powles, Elizabeth R Plimack, Noah M Hahn, Ronald de Wit, Lei Pang, Mary J Savage, Rodolfo F Perini, Stephen M Keefe, Dean Bajorin, Joaquim Bellmunt

Lancet Oncol 2017; 18: 1483–92

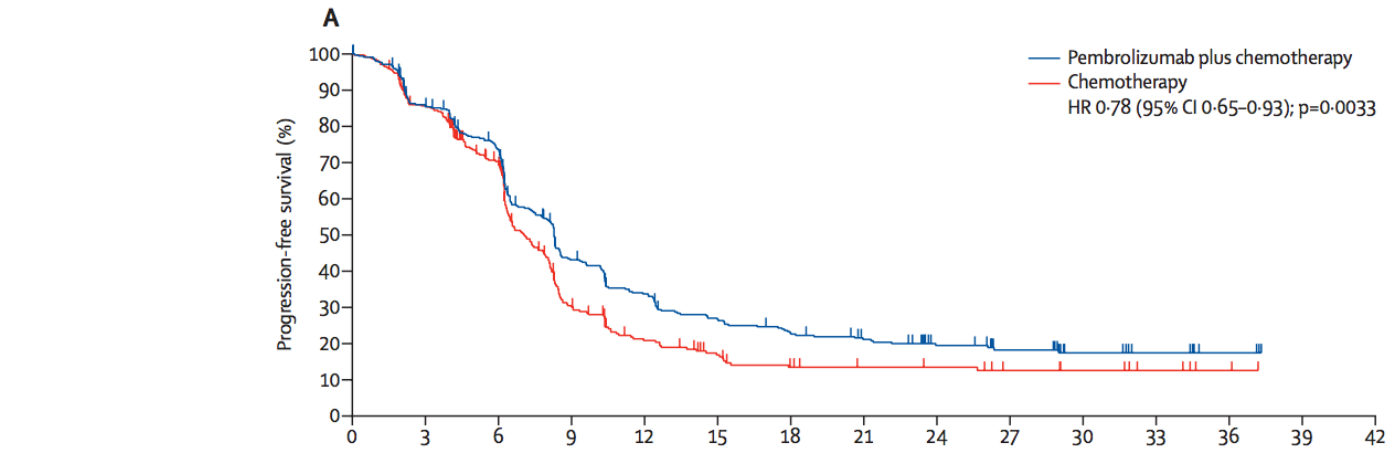


CPS (%)	RR
<1	11
1-9	20
≥10	39

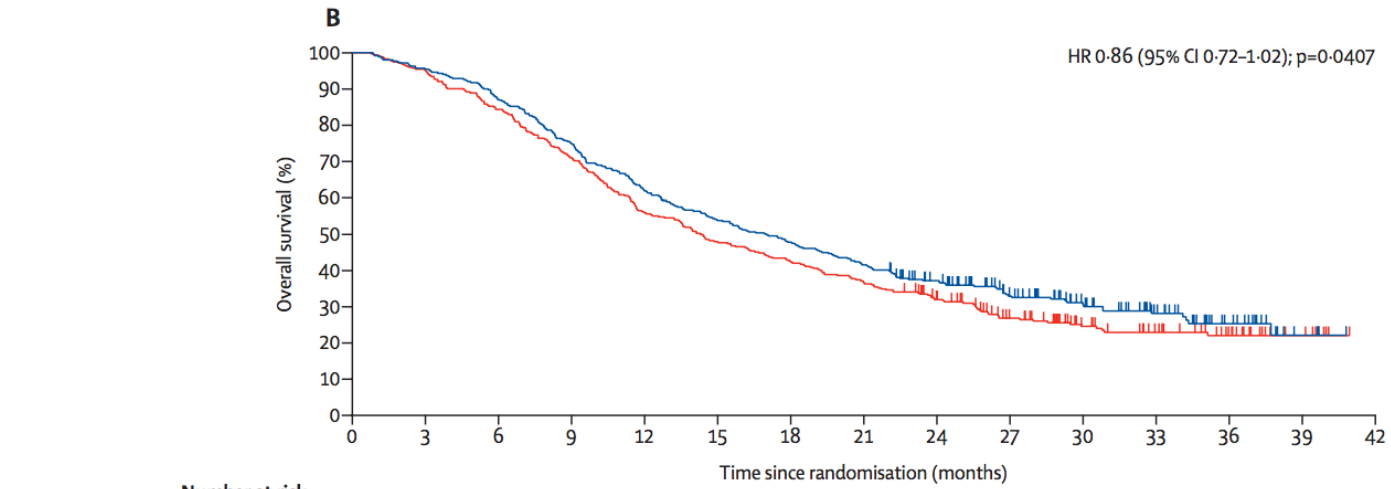
Pembrolizumab alone or combined with chemotherapy versus chemotherapy as first-line therapy for advanced urothelial carcinoma (KEYNOTE-361): a randomised, open-label, phase 3 trial

*Thomas Powles, Tibor Csőszi, Mustafa Özgüroğlu, Nobuaki Matsubara, Lajos Géczi, Susanna Y-S Cheng, Yves Fradet, Stephane Oudard, Christof Vulsteke, Rafael Morales Barrera, Aude Fléchon, Seyda Gunduz, Yohann Loriot, Alejo Rodriguez-Vida, Ronac Mamtani, Evan Y Yu, Kijoeng Nam, Kentaro Imai, Blanca Homet Moreno, Ajjai Alva, for the KEYNOTE-361 Investigators**

Lancet Oncol 2021; 22: 931–45

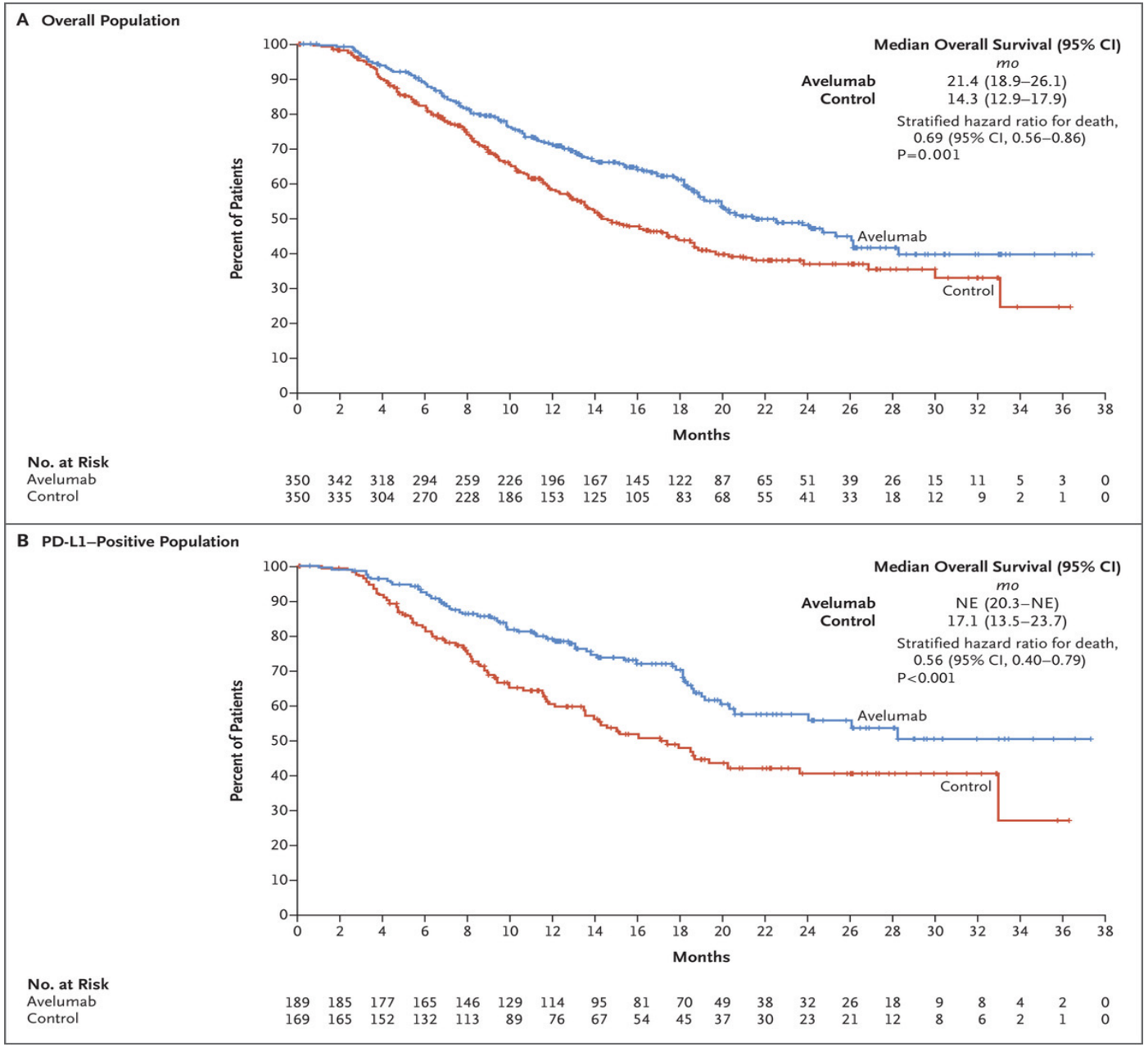


Number at risk (number censored)															
Pembrolizumab plus chemotherapy	351 (0)	288 (13)	243 (19)	135 (29)	102 (33)	79 (35)	67 (36)	55 (43)	36 (58)	27 (65)	18 (73)	9 (82)	3 (88)	0 (91)	0 (91)
Chemotherapy	352 (0)	274 (30)	191 (67)	75 (81)	44 (90)	31 (95)	22 (98)	17 (103)	15 (105)	11 (108)	8 (111)	5 (114)	2 (117)	0 (119)	0 (119)



Number at risk (number censored)															
Pembrolizumab plus chemotherapy	351 (0)	335 (0)	306 (0)	263 (0)	217 (0)	189 (0)	168 (0)	146 (0)	118 (13)	84 (35)	56 (58)	36 (74)	17 (90)	3 (103)	0 (106)
Chemotherapy	352 (0)	335 (0)	297 (0)	250 (0)	197 (0)	169 (0)	150 (0)	129 (0)	104 (9)	71 (27)	46 (47)	33 (57)	20 (69)	7 (82)	0 (89)

Maintenance therapy with a immune checkpoint inhibitor



Powles T, 2020

Urothelial carcinoma

perioperative setting

VOLUME 36 · NUMBER 34 · DECEMBER 1, 2018

JOURNAL OF CLINICAL ONCOLOGY

RAPID COMMUNICATION

Pembrolizumab as Neoadjuvant Therapy Before Radical Cystectomy in Patients With Muscle-Invasive Urothelial Bladder Carcinoma (PURE-01): An Open-Label, Single-Arm, Phase II Study

Andrea Necchi, Andrea Anichini, Daniele Raggi, Alberto Briganti, Simona Massa, Roberta Lucianò, Maurizio Colecchia, Patrizia Giannatempo, Roberta Mortarini, Marco Bianchi, Elena Farè, Francesco Monopoli, Renzo Colombo, Andrea Gallina, Andrea Salonia, Antonella Messina, Siraj M. Ali, Russell Madison, Jeffrey S. Ross, Jon H. Chung, Roberto Salvioni, Luigi Mariani, and Francesco Montorsi

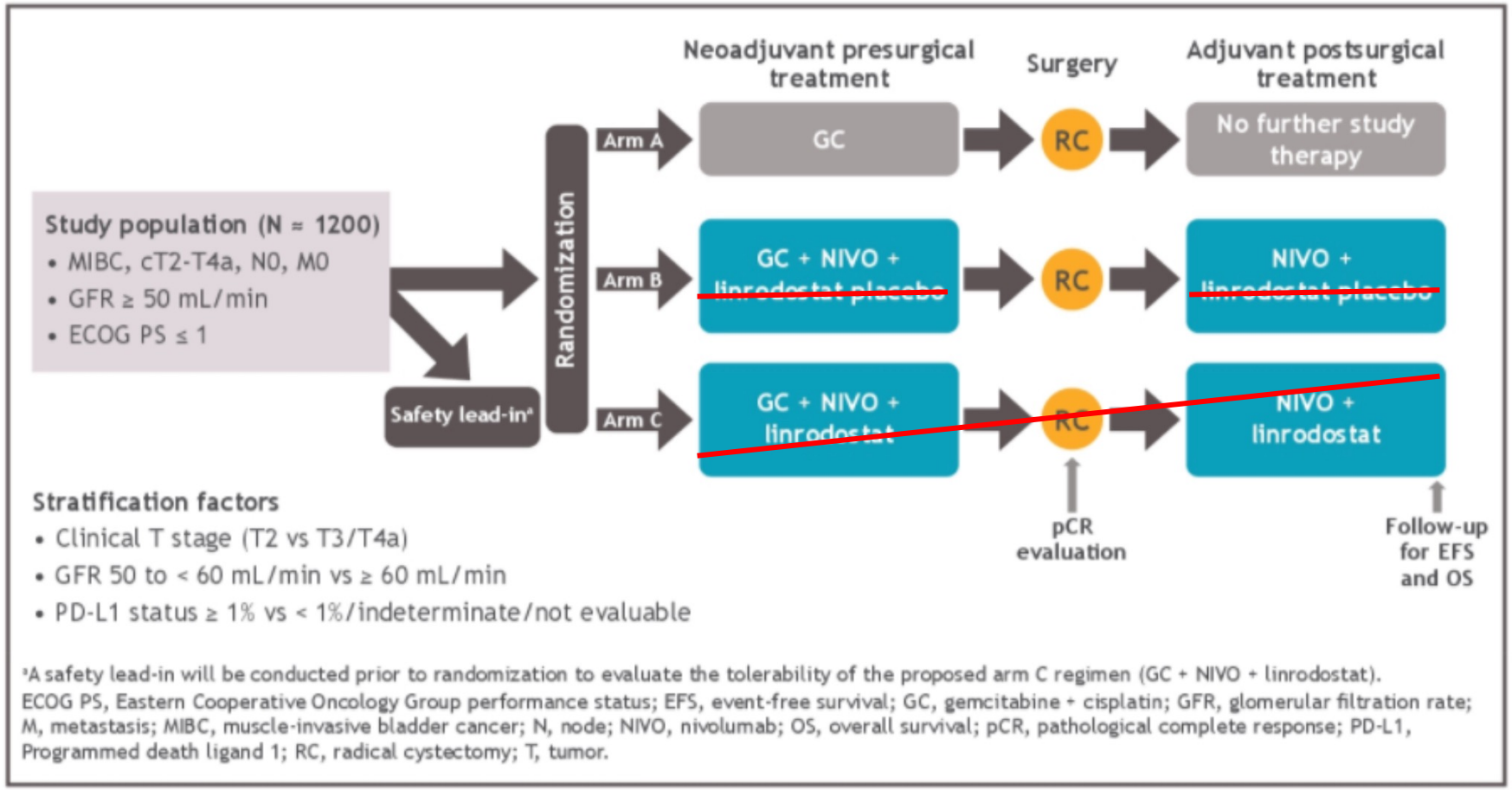
Table 3. Pathologic Response to Pembrolizumab

Response	All Treated Patients (N = 50)	PD-L1 CPS ≥ 10% (n = 35)	PD-L1 CPS < 10% (n = 15)
Primary end point			
Pathologic complete response, No. (%)	21 (42)	19 (54.3)	2 (13.3)
95% CI	28.2 to 56.8		
Secondary end point			
Pathologic downstaging to pT<2, No. (%)	27 (54)	23 (65.7)	4 (26.7)
95% CI*	39.3 to 68.2		

A Study to Compare Chemotherapy Alone Versus Chemotherapy Plus Nivolumab or Nivolumab and BMS-986205, Followed by Continued Therapy After Surgery With Nivolumab or Nivolumab and BMS-986205 in Participants With Muscle Invasive Bladder Cancer

ClinicalTrials.gov Identifier: NCT03661320

Figure 2. CA017-078 study design



[a]A safety lead-in will be conducted prior to randomization to evaluate the tolerability of the proposed arm C regimen (GC + NIVO + linrodostat).
ECOG PS, Eastern Cooperative Oncology Group performance status; EFS, event-free survival; GC, gemcitabine + cisplatin; GFR, glomerular filtration rate; M, metastasis; MIBC, muscle-invasive bladder cancer; N, node; NIVO, nivolumab; OS, overall survival; pCR, pathological complete response; PD-L1, Programmed death ligand 1; RC, radical cystectomy; T, tumor.

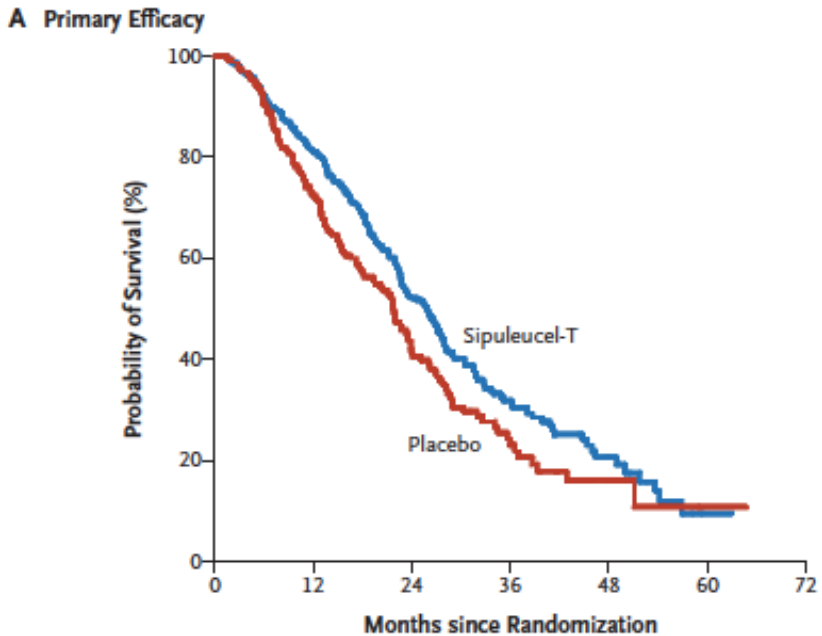
Prostate adenocarcinoma

The NEW ENGLAND JOURNAL of MEDICINE

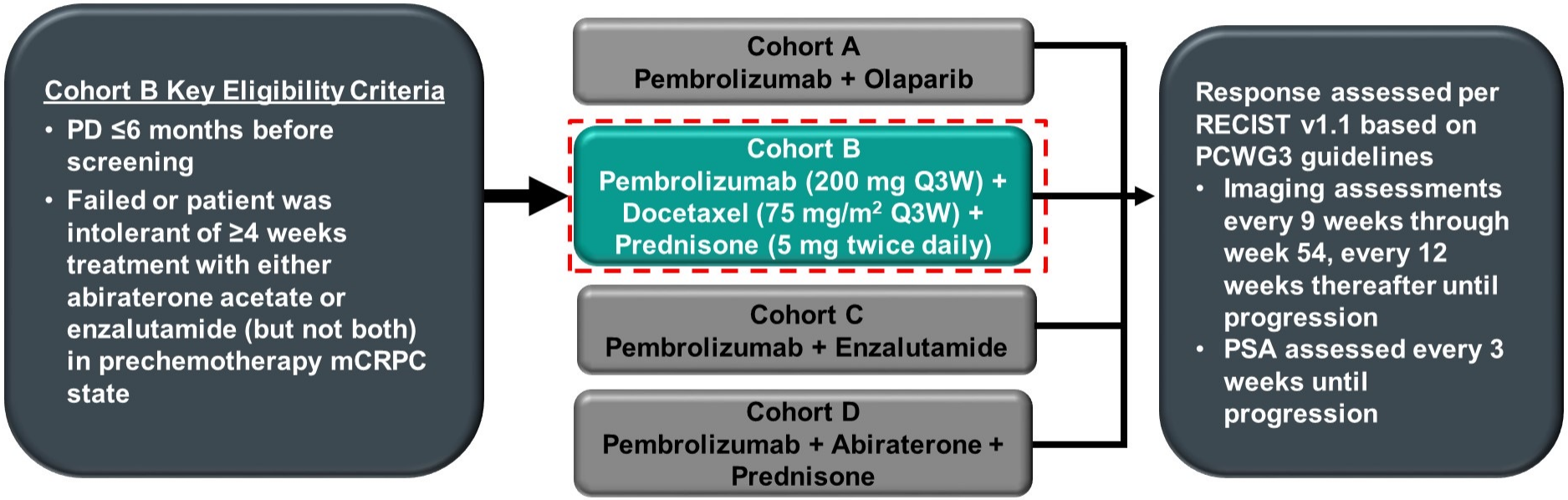
ESTABLISHED IN 1812 JULY 29, 2010 VOL. 363 NO. 5

Sipuleucel-T Immunotherapy for Castration-Resistant Prostate Cancer

Philip W. Kantoff, M.D., Celestia S. Higano, M.D., Neal D. Shore, M.D., E. Roy Berger, M.D., Eric J. Small, M.D., David F. Penson, M.D., Charles H. Redfern, M.D., Anna C. Ferrari, M.D., Robert Dreicer, M.D., Robert B. Sims, M.D., Yi Xu, Ph.D., Mark W. Frohlich, M.D., and Paul F. Schellhammer, M.D.,



KEYNOTE-365 Study Design



Median Time From Enrollment to Data Cutoff in Cohort B

- **All patients**: 32.4 months (range, 13.9-40.3)

Primary End Points

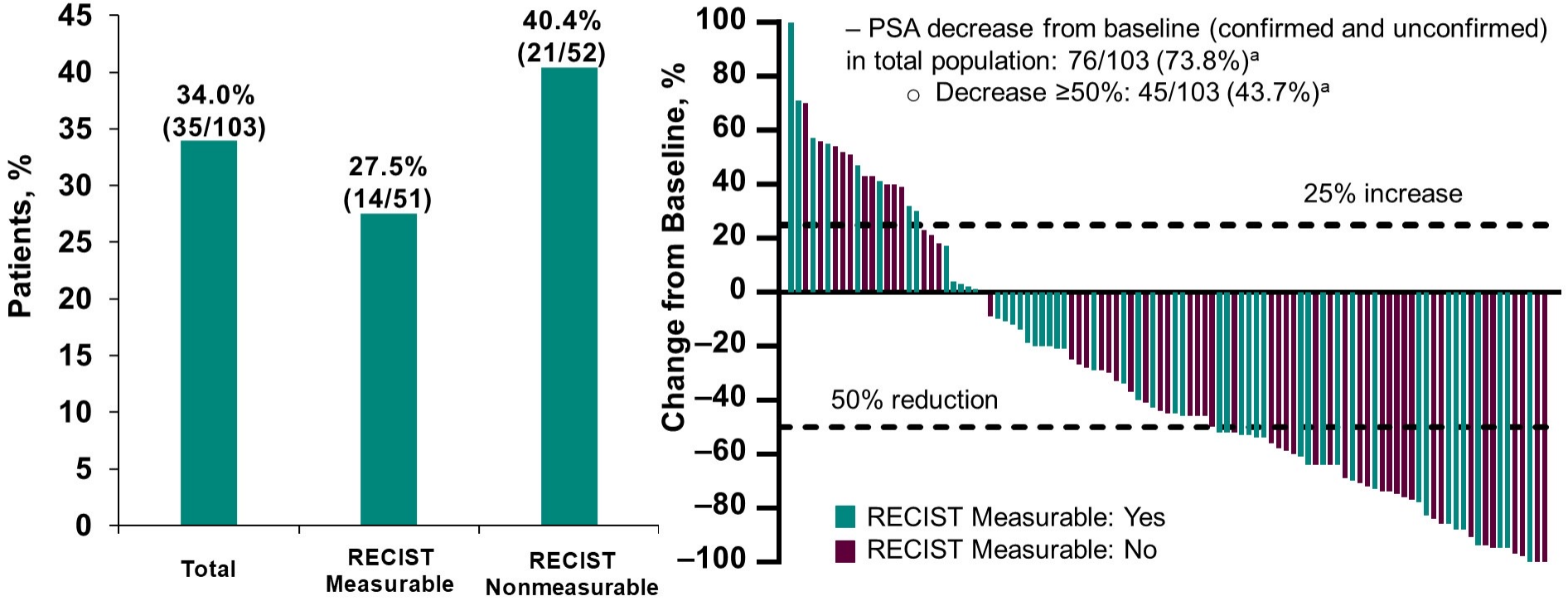
- Safety
- PSA response rate
- ORR by RECIST v1.1 (BICR)

Secondary End Points

- DCR
- rPFS by PCWG-modified RECIST v1.1
- OS

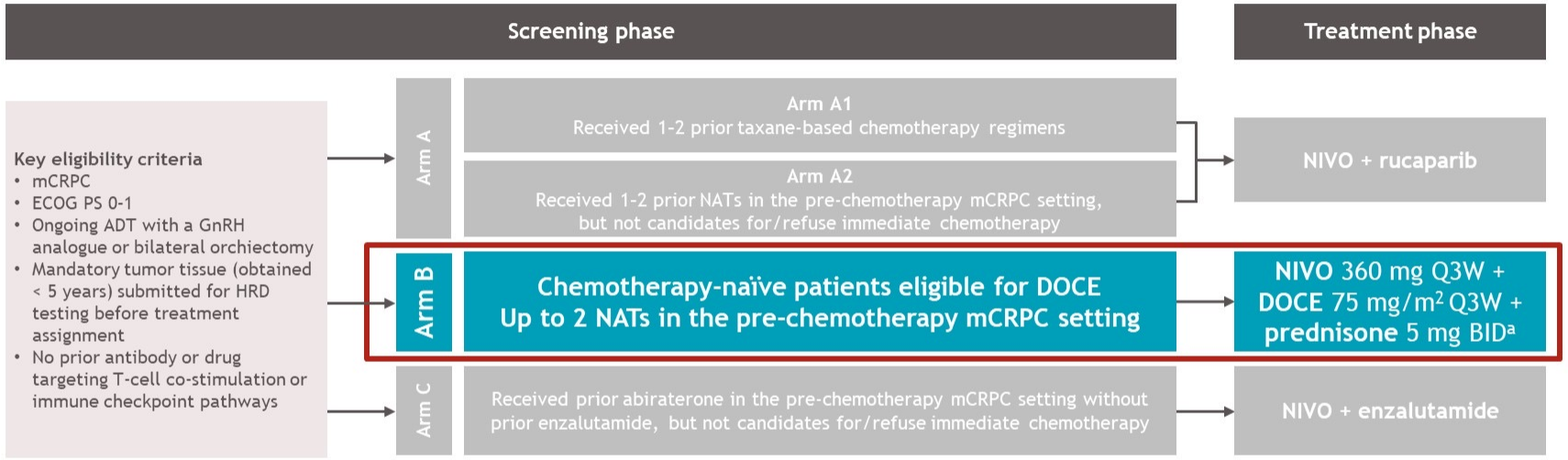
Data cutoff: July 9, 2020.

Confirmed PSA Response Rate (≥50% Reduction)[a] and Percentage Change From Baseline[b]



[a]Calculation is based on patients who had nonmissing PSA measurements at baseline; ≥50% PSA decline confirmed by subsequent value ≥3 weeks later. [b]Plot is based on patients who had a PSA measurement at baseline and ≥1 postbaseline PSA measurement (n = 103).
Data cutoff: July 9, 2020.

CheckMate 9KD: study design



Co-primary endpoints: ORR per investigator,[b] PSA response rate (response: ≥ 50% decrease from baseline PSA)[c]

Secondary endpoints: rPFS,[d] OS, time to and duration of response,[d] time to PSA progression,[d] and safety

[a]DOCE was given up to a maximum of 10 cycles; NIVO was administered as monotherapy (480 mg Q4W) after cycle 10 for up to 2 years. [b]Assessed using PCWG3 criteria in treated patients with measurable disease at baseline. [c]Represents the proportion of treated patients with a ≥ 50% decrease in PSA from baseline to the lowest post-baseline PSA result; a second consecutive value obtained ≥ 3 weeks later was required for confirmation of PSA response. [d]Assessed using PCWG3 criteria in relevant populations.
ADT, androgen deprivation therapy; ECOG PS, Eastern Cooperative Oncology Group performance status; GnRH, gonadotropin-releasing hormone; HRD, homologous recombination deficiency; NAT, novel antiandrogen therapy (eg, abiraterone, enzalutamide, etc.); ORR, objective response rate; OS, overall survival; PCWG3, Prostate Cancer Clinical Trials Working Group 3; PSA, prostate-specific antigen; rPFS, radiographic progression-free survival.

Objective and PSA response outcomes

Objective response[a]	All patients (N = 45)	No prior NAT (n = 14)	Prior NAT (n = 31)
ORR, % (95% CI)	40.0 (25.7-55.7)	42.9 (17.7-71.1)	38.7 (21.8-57.8)
Best overall response, n (%)			
Complete response	1 (2.2)	0	1 (3.2)
Partial response	17 (37.8)	6 (42.9)	11 (35.5)
Stable disease	24 (53.3)	7 (50.0)	17 (54.8)
Progressive disease	3 (6.7)	1 (7.1)	2 (6.5)
PSA response[b]	**All patients (N = 81)**	**No prior NAT (n = 28)**	**Prior NAT (n = 53)**
Confirmed PSA response rate, % (95% CI)	46.9 (35.7-58.3)	60.7 (40.6-78.5)	39.6 (26.5-54.0)

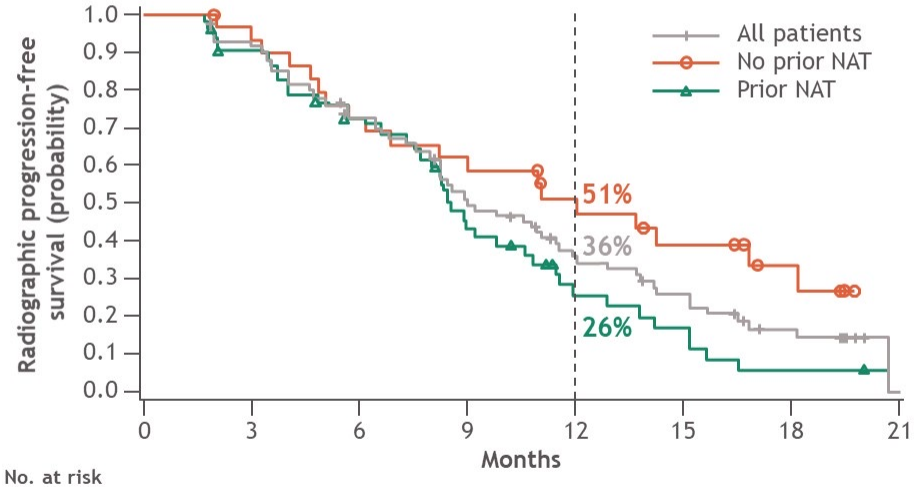
- For the 18 objective responders
  - Median time to response (range) was 2.0 (1.6-7.3) months
  - Median duration of response (95% CI) was 7.0 (6.4-12.4) months
- Among 81 PSA-evaluable patients, median time to PSA progression (95% CI) was 8.7 (7.3-10.4) months

[a]Represents confirmed complete or partial response per PCWG3 in patients with measurable disease at baseline. [b]Represents the proportion of treated patients with a ≥ 50% decrease in PSA from baseline to the lowest postbaseline PSA result; a second consecutive value obtained ≥ 3 weeks later was required for confirmation of PSA response.

Survival outcomes

rPFS

	All patients (N = 84)	No prior NAT (n = 30)	Prior NAT (n = 54)
Events, n	61	19	42
Median (95% CI), months	9.0 (8.0-11.6)	12.0 (6.2-18.2)	8.5 (7.5-10.8)

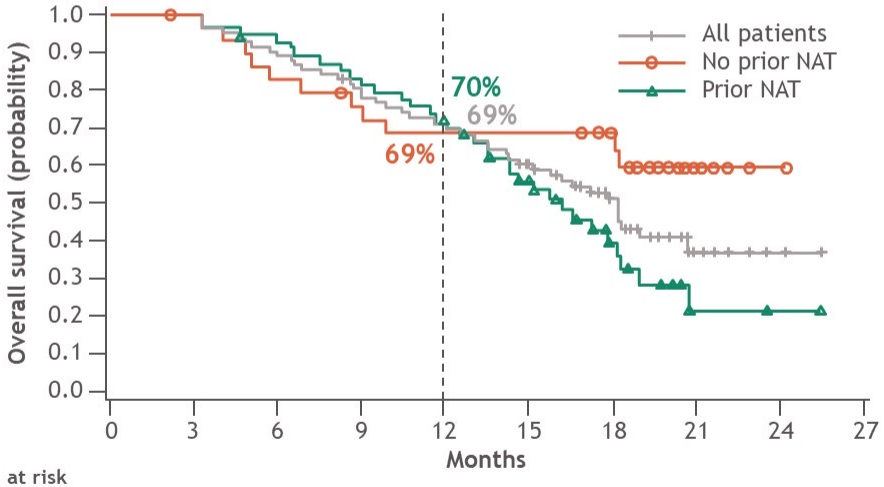


No. at risk

All patients	84	73	54	37	22	15	7	0
No prior NAT	30	27	21	18	13	9	5	0
Prior NAT	54	46	33	19	9	6	2	0

OS

	All patients (N = 84)	No prior NAT (n = 30)	Prior NAT (n = 54)
Events, n	44	11	33
Median (95% CI), months	18.2 (14.6-20.7)	NR (9.9-NE)	16.2 (13.5-18.3)



No. at risk

All patients	84	83	73	64	55	44	26	7	2	0
No prior NAT	30	29	24	21	19	19	15	5	1	0
Prior NAT	54	54	49	43	36	25	11	2	1	0

NE, not estimable; NR, not reached.

Renal cell carcinoma

Advanced disease

Second line after TKi:
IO monotherapy

First line:
IO-IO combination in intermediate/poor risk pts
IO-TKI (anti -VEGF) combination

Adjuvant setting

IO monotherapy
effective in high risk resected ccRCC
under investigation in resected metastatic disease

IO-IO combination:
benefit not proven

Some critical issues not addressed in trials for FDA/EMA approval

- primary refractory patients
- patients at risk for serious adverse events
- patient who may benefit from a TKi monotherapy or IO monotherapy

Urothelial carcinoma

Advanced disease

Second line after TKi:
IO monotherapy

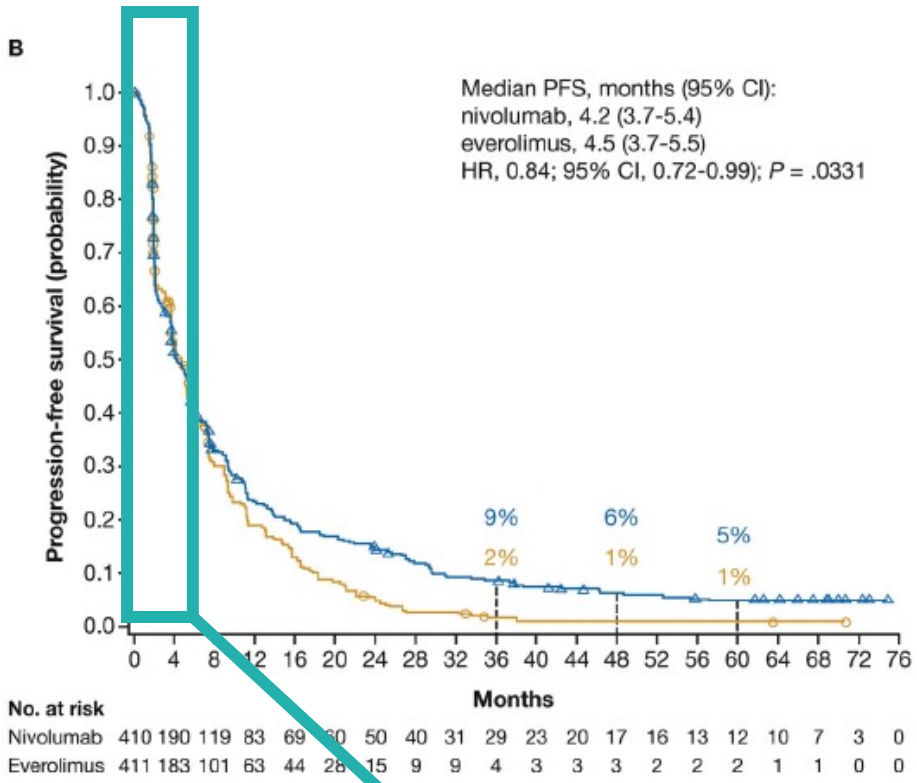
First line:
patients unfit for cisplatin with CPS ≥10

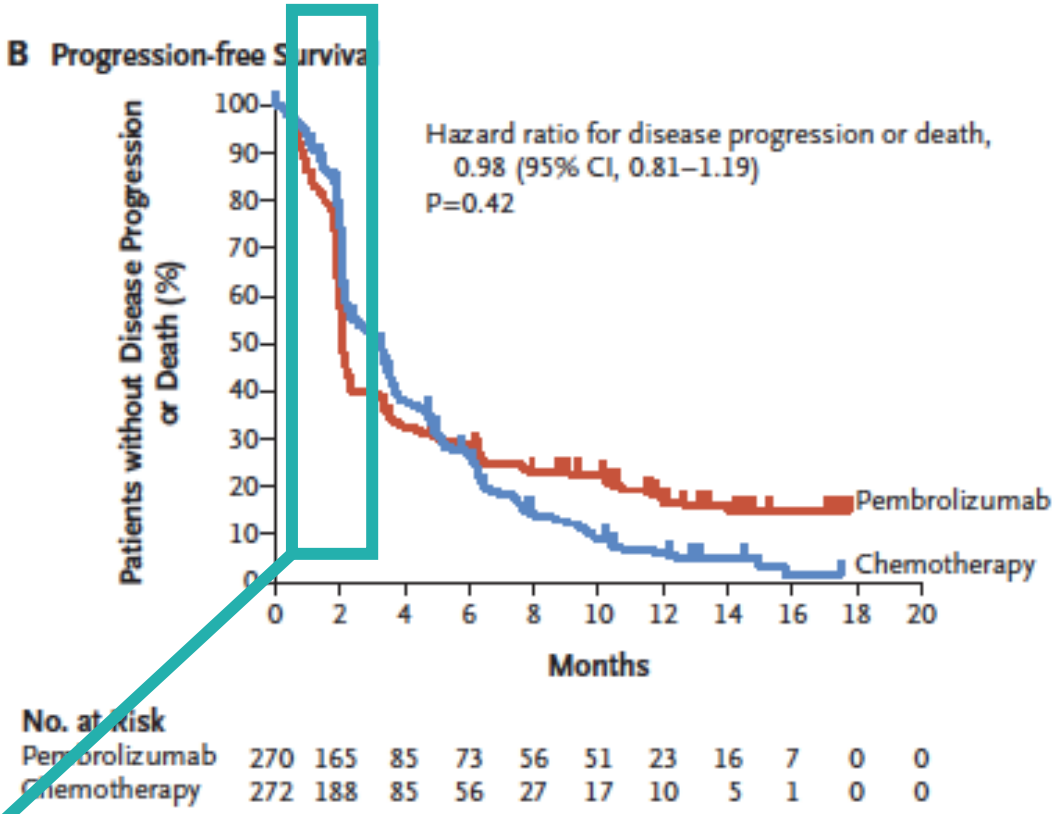
Perioperative setting

Promising result with IO monotherapy and IO-chemo combination

Some critical issues not addressed in trials for FDA/EMA approval

- predictive factors for efficacy (IO effectiveness despite PD-L1 status)
- predictive factors for toxicity

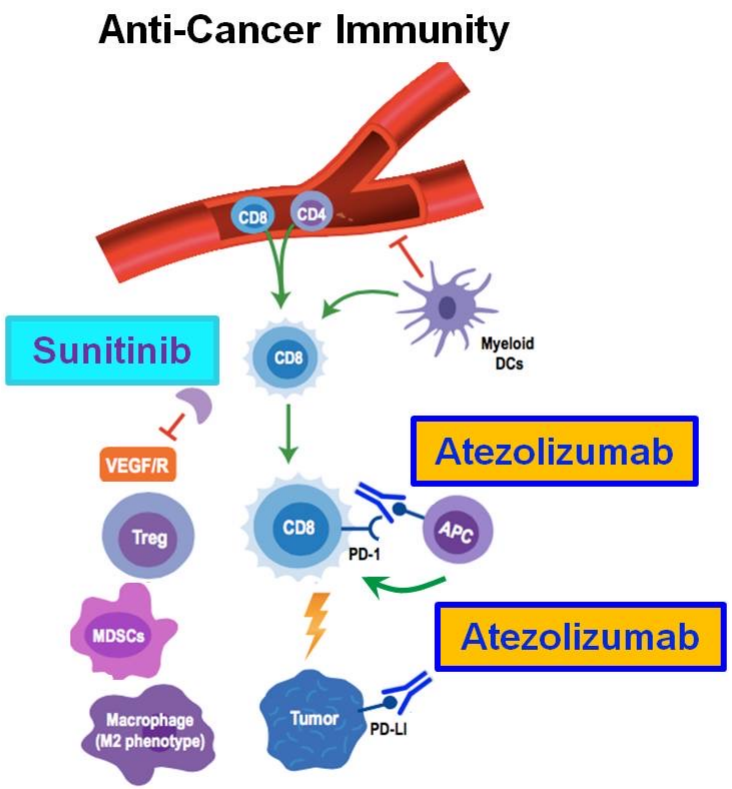


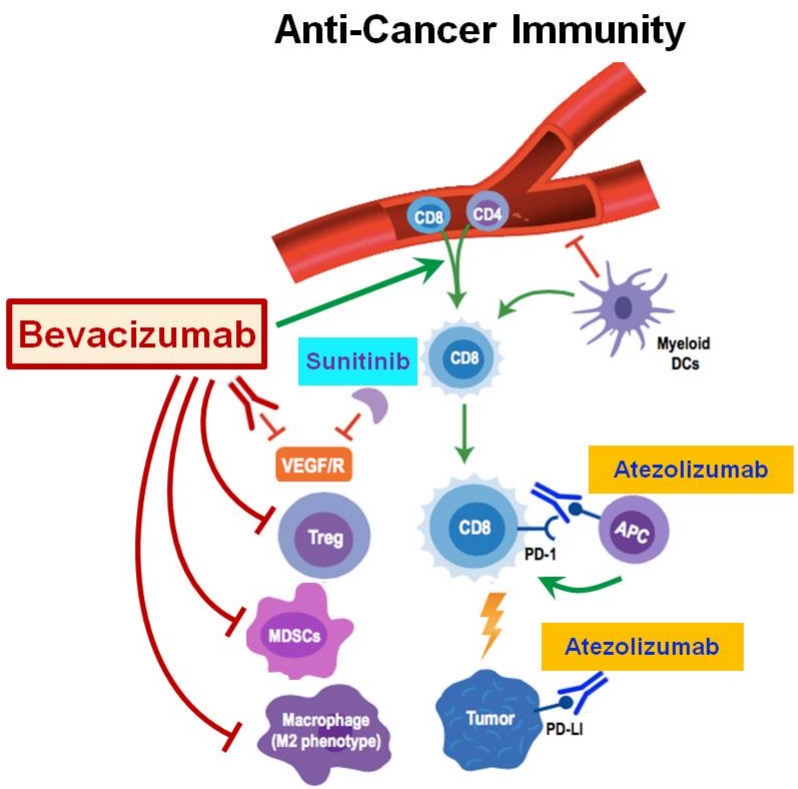


pts progressed at the first tumor assessment

Can the omic sciences help answer some clinically relevant issues?

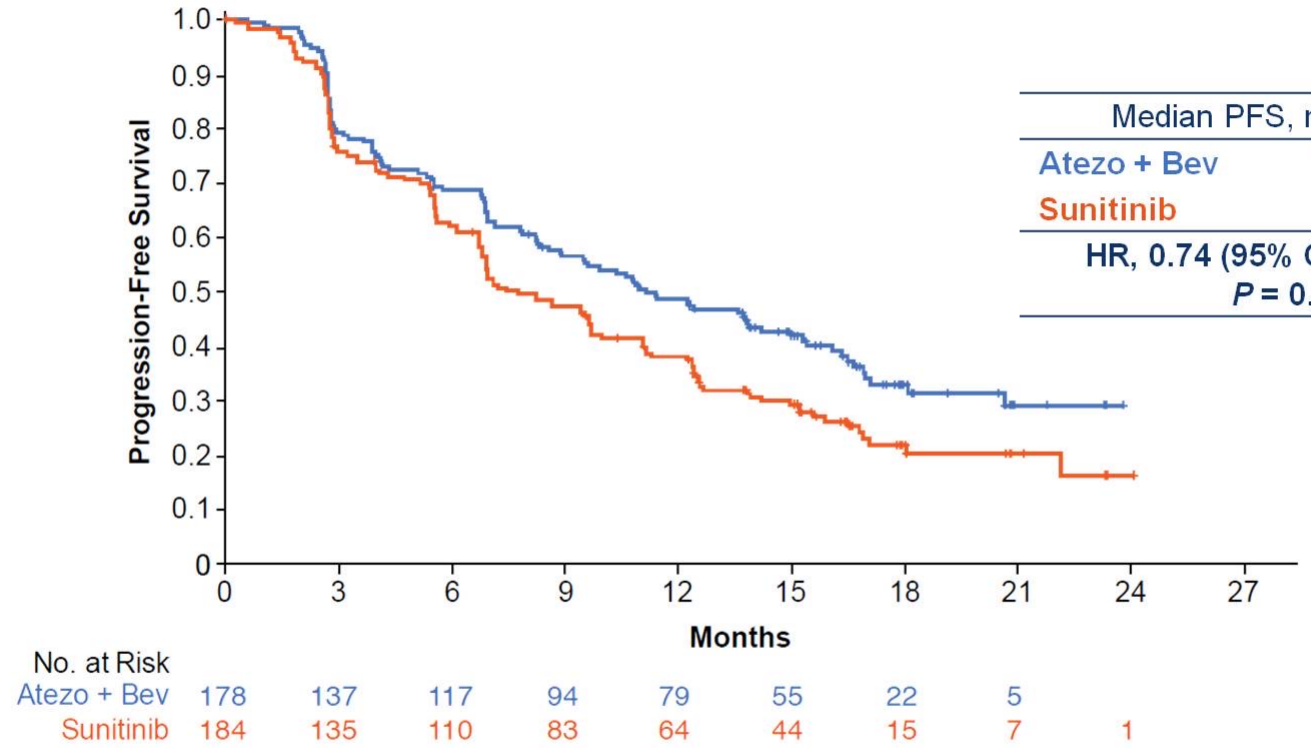
Bevacizumab + Atezolizumab





IMmotion 151:
Atezolizumab + Bevacizumab vs Sunitinib

Progression-Free Survival in the PD-L1+ Population



Median PFS, mo (95% CI)	
Atezo + Bev	11.2 (8.9, 15.0)
Sunitinib	7.7 (6.8, 9.7)

HR, 0.74 (95% CI: 0.57, 0.96)
P = 0.02[a]

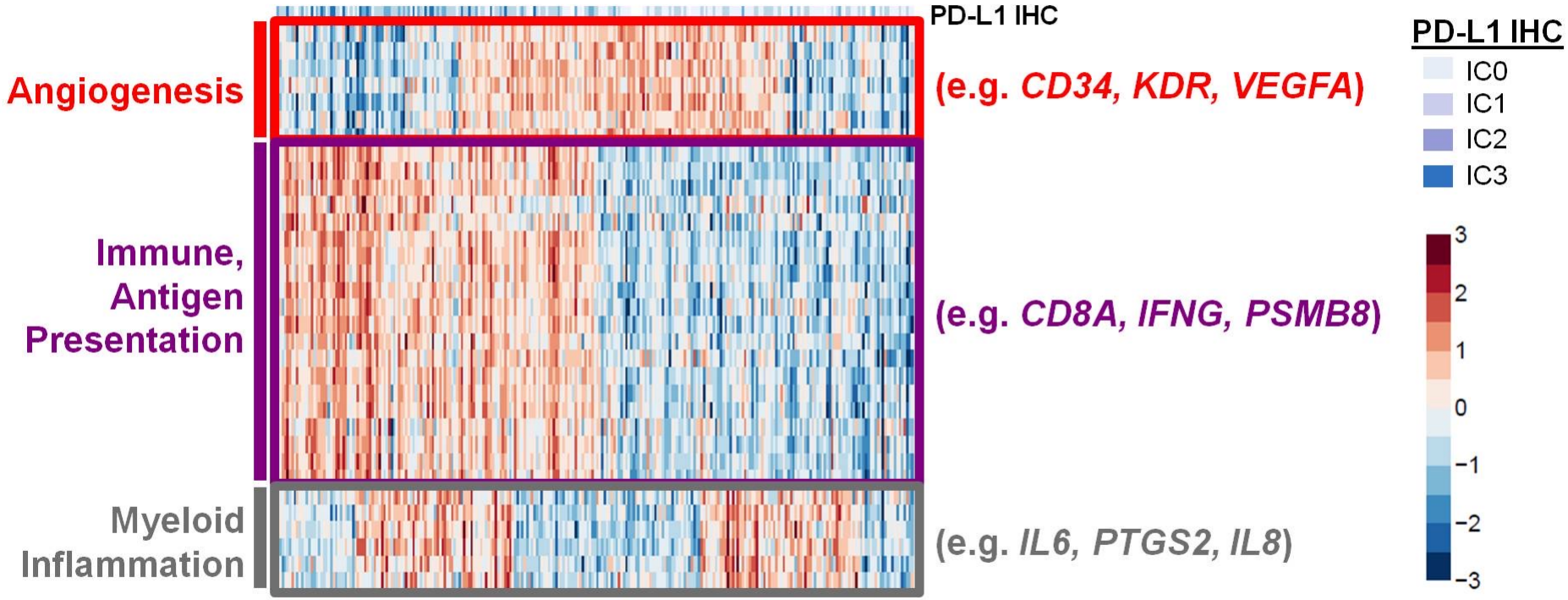
Escudier B, 2018

IMmotion 150:
Atezolizumab +/- Bevacizumab vs Sunitinib

Setting:	**First line**
Study:	**Phase II**
Patients:	**305**
Primary objectives:	**PFS in ITT**
	PFS in PD-L1+

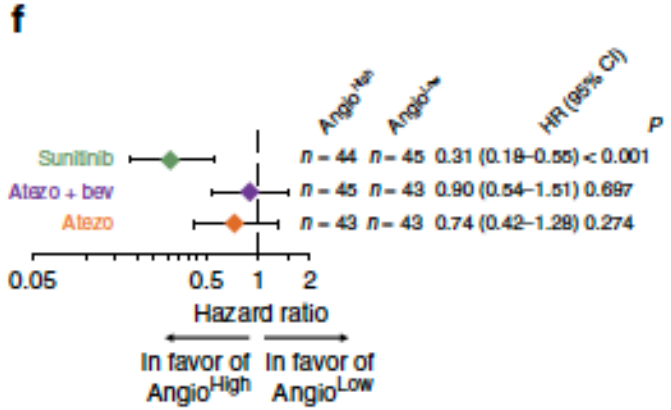
IMmotion 150:
Atezolizumab +/- Bevacizumab vs Sunitinib

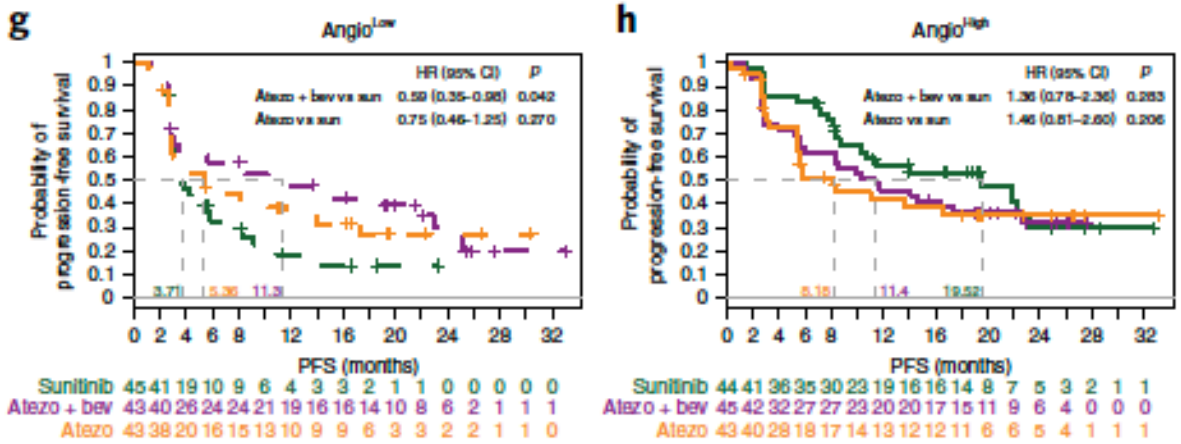
Transcriptome Map of Angiogenesis and Immune-Associated Genes in RCC Tumors

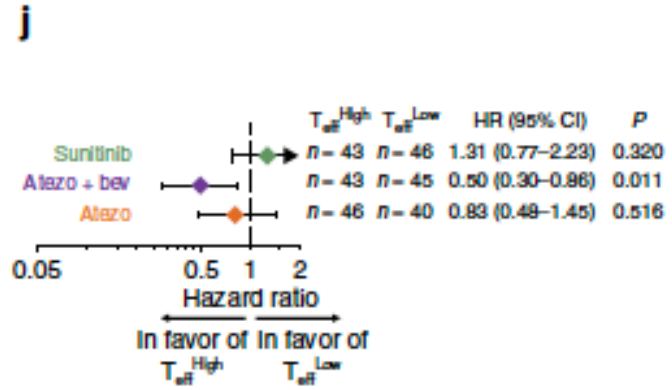


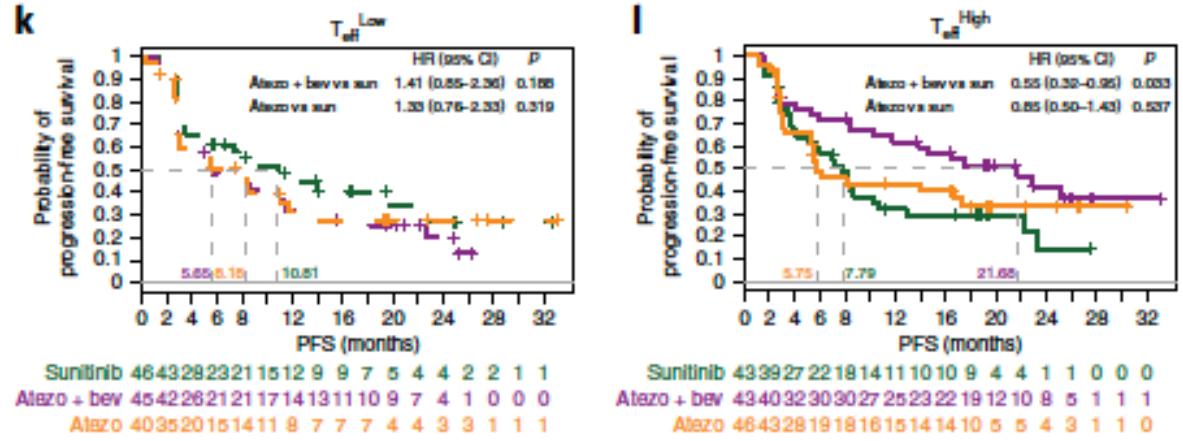
Atkins M, 2017

IMmotion 150:
Atezolizumab +/- Bevacizumab vs Sunitinib





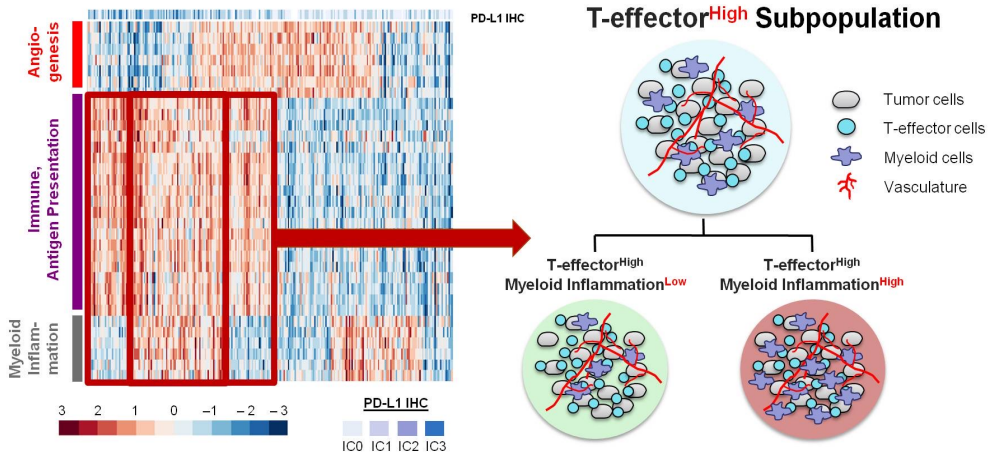




McDermott DF, 2018

IMmotion 150:
Atezolizumab +/- Bevacizumab vs Sunitinib

Angiogenic tumor: **anti-VEGF better**



"Inflammed" tumor: **anti-VEGF may confer sensitivity to checkpoint inhibitors**

Pembrolizumab as 2nd/3rd line for advanced ccRCC: a radiomic approach

pts:	60
RR:	28%
pts on treatment >12 m:	35%

Rossi E, Boldrini L, preliminary data

Pembrolizumab as 2nd/3rd line for advanced ccRCC: a radiomic approach

min_L_minor
max_L_minor
min_F_cm_2.5D.joint.entr
max_F_cm_2.5D.joint.entr
min_F_cm.2.5Dmerged.sum.avg
max_F_cm.2.5Dmerged.sum.avg
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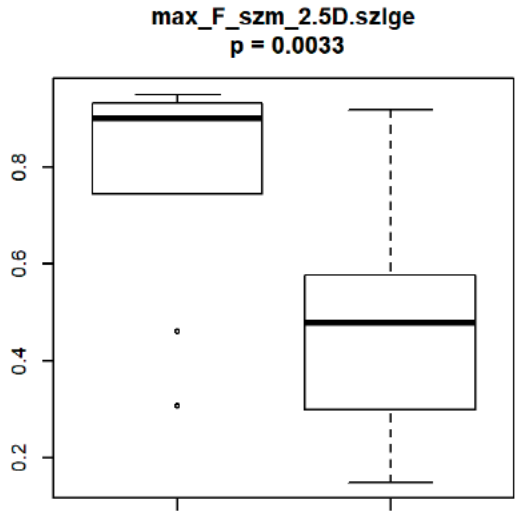
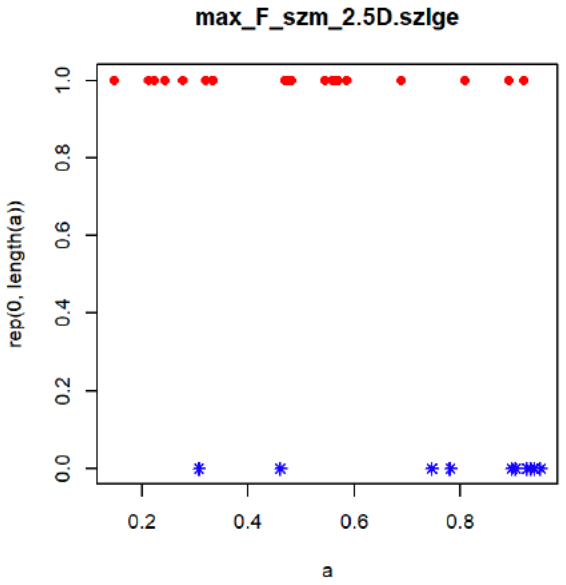
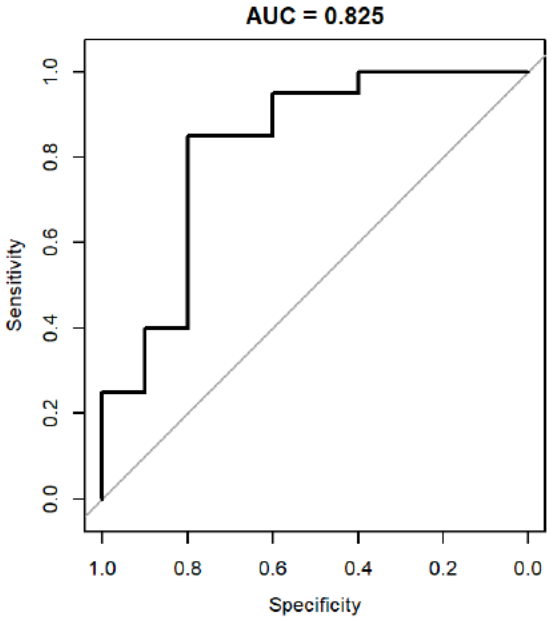
max_F_szm_2.5D.szlge



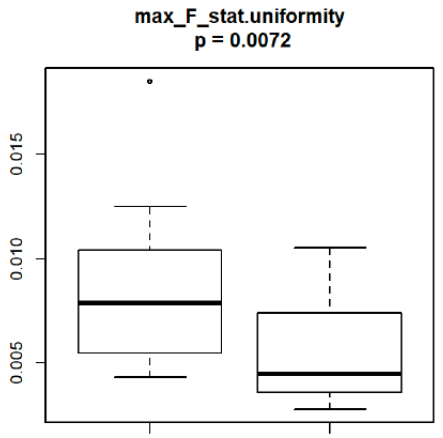


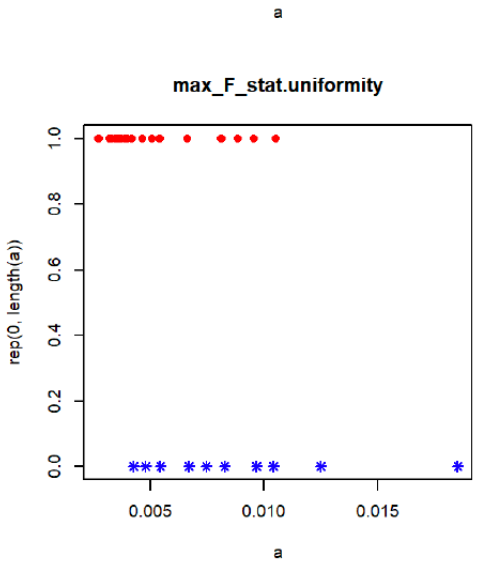


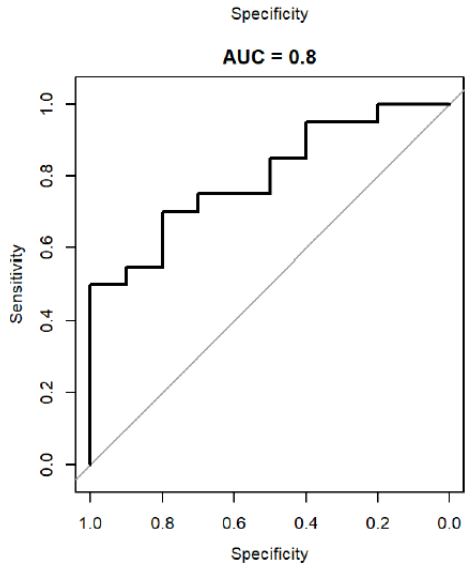
Rossi E, Boldrini L, preliminary data

Pembrolizumab as 2nd/3rd line for advanced ccRCC: a radiomic approach

min_F_stat.var
max_F_stat.var
min_F_stat.90thpercentile
max_F_stat.90thpercentile
min_F_stat.max
max_F_stat.max
min_F_stat.range
max_F_stat.range
min_F_stat.uniformity
max_F_stat.uniformity







Rossi E, Boldrini L, preliminary data

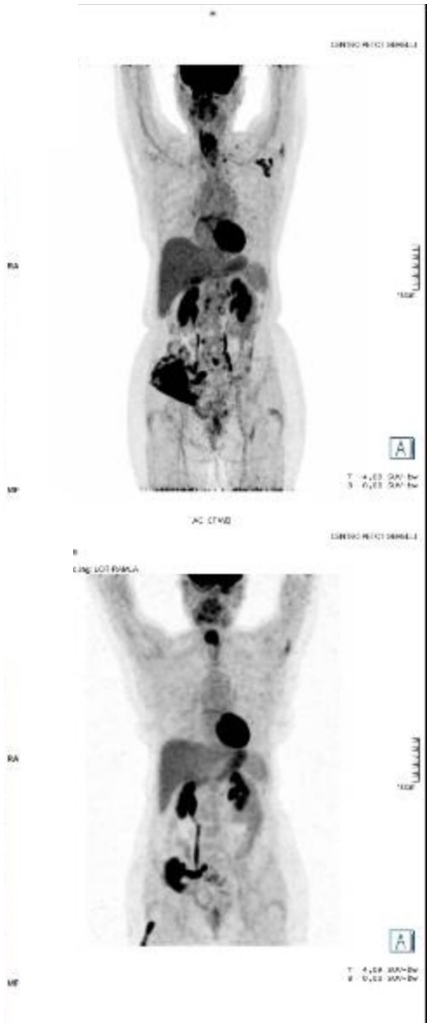
“Immunomics”:
the study of immune system regulation and response to pathogens

Practical application in immuno-oncology (IO)

study of circulating immune factor:
cytokines and soluble immune checkpoints

Multiple lymph-nodes metastasis from bladder urothelial carcinoma resistant to cisplatin-gemcitabine chemotherapy

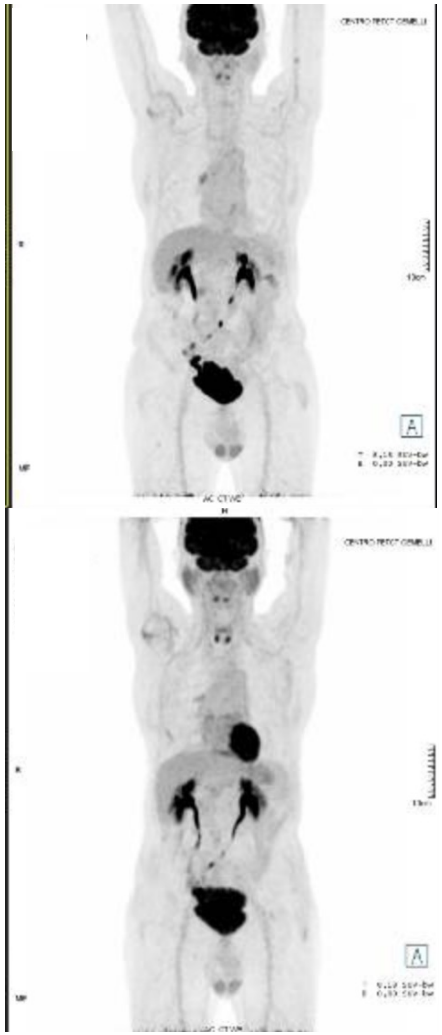
pt #22



Baseline

After 3 months with pembrolizumab

pt #9



Multiple lymph-nodes metastasis from bladder urothelial carcinoma resistant to cisplatin-gemcitabine chemotherapy

CPS 30%	pt #22 complete response to pembro	Soluble IC	pt #9 primary refractory to pembro	CPS 35%
	stable	BTLA	stable	
	lower	CD137	higher	
	lower	GITR	higher	
	higher	HVEM	lower	
	higher	IDO	lower	
	higher	TIM3	lower	

Schinzari G, in press

Microbiomic

nature COMMUNICATIONS

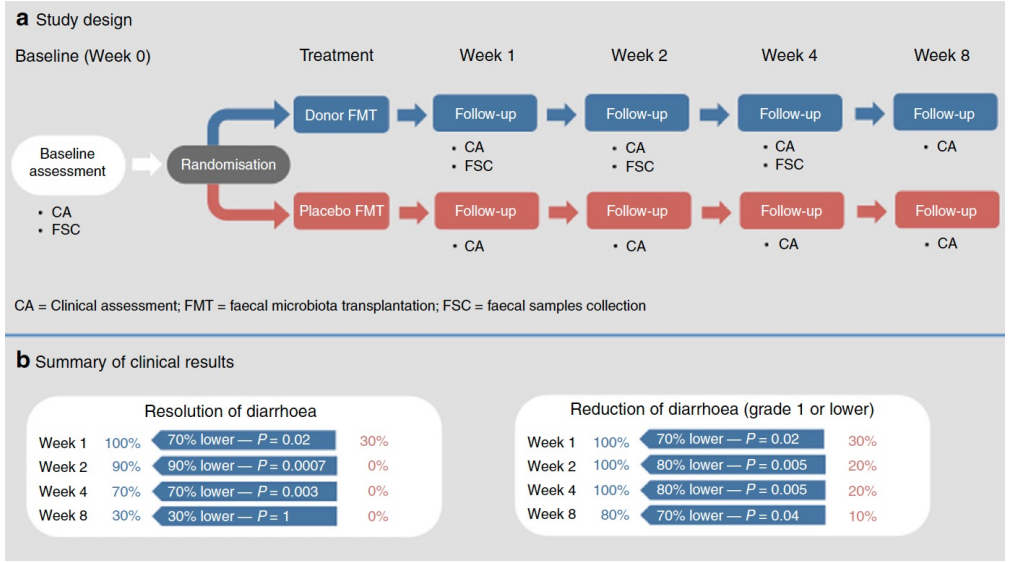
ARTICLE

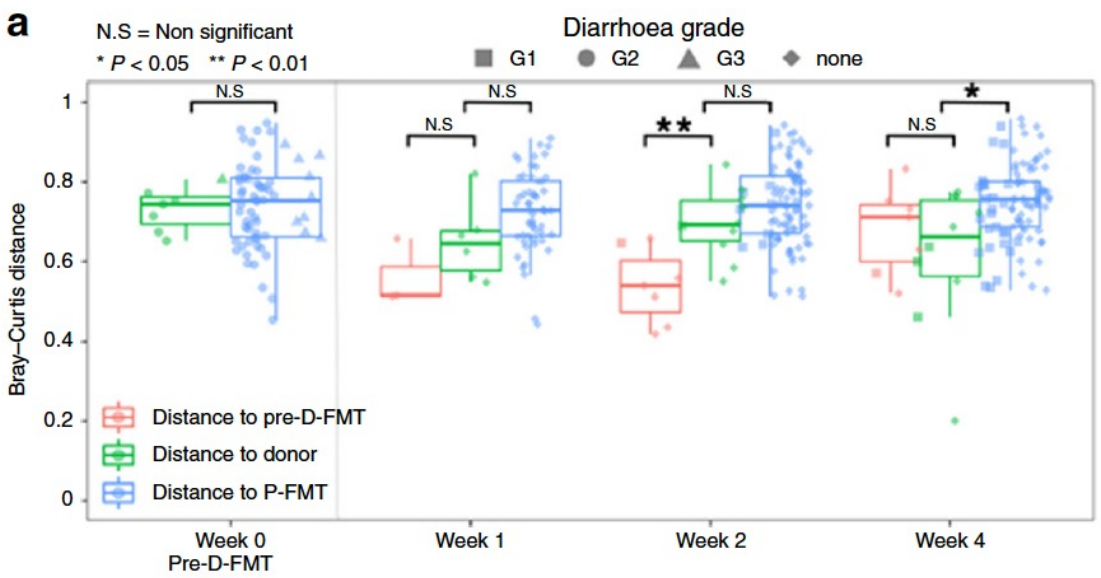
https://doi.org/10.1038/s41467-020-18127-y OPEN

Check for updates

Faecal microbiota transplantation for the treatment of diarrhoea induced by tyrosine-kinase inhibitors in patients with metastatic renal cell carcinoma

Gianluca Ianiro[1,7], Ernesto Rossi[2,7], Andrew M. Thomas[3], Giovanni Schinzari[2], Luca Masucci[4], Gianluca Quaranta[4], Carlo Romano Settanni[1], Loris Riccardo Lopetuso[1], Federica Armanini[3], Aitor Blanco-Miguez[3], Francesco Asnicar[3], Clarissa Consolandi[5], Roberto Iacovelli[2], Maurizio Sanguinetti[4], Giampaolo Tortora[2], Antonio Gasbarrini[1], Nicola Segata[3,6,7] & Giovanni Cammarota[1,7]✉





Immunotherapy approaches in the Omics Era: focus on Genitourinary cancer

Immunotherapy improved clinical outcome for GU cancer patients
Other benefit are expected in the next years

Immunotherapy approaches in the Omics Era: focus on Genitourinary cancer

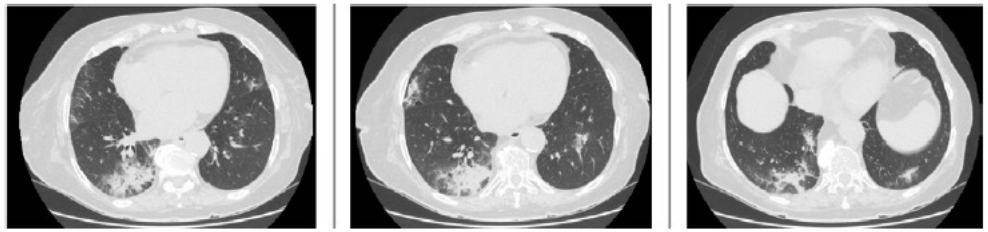
Many factors can influence the results with immunotherapy:

concomitant drugs (antibiotics), infections (viral), diet, comorbidities, gender…

Journal for ImmunoTherapy of Cancer

Pneumonitis from immune checkpoint inhibitors and COVID-19: current concern in cancer treatment

Ernesto Rossi,[1] Giovanni Schinzari,[1,2] Giampaolo Tortora[1,2]



Omic sciences can enrich the knowledge of factors influencing immunotherapy efficacy

Immunotherapy approaches in the Omics Era: focus on Genitourinary cancer

Immunotherapy improved clinical outcome for GU cancer patients
Other benefit are expected in the next years

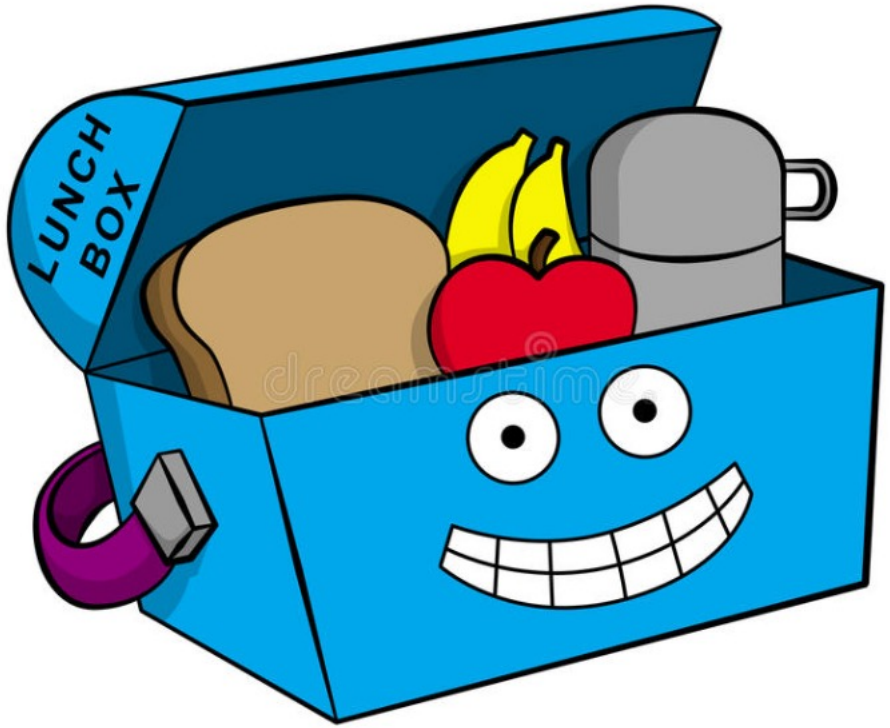
Many factors can influence the results obtaining with immunotherapy

Criteria for patient selection are needed to achieve a really patient – focused approach (“personalized oncology”)

Omic sciences can allow patient selection

Patient selection should be feasible in clinical practice

I hope you enjoyed the lunch



Thank you
for your attention!