2nd Annual Southern California Genitourinary Cancer Research Forum

Key Updates from 2024 in Kidney Cancer

Alex Chehrazi-Raffle, MD

Assistant Professor, Division of Medical Oncology & Experimental Therapeutics

City of Hope Comprehensive Cancer Center

Disclosures

- Consultant for Eisai, Exelixis, and Pfizer.

This presentation and/or comments will be free of any bias toward or promotion of the above referenced companies or their product(s) and/or other business interests.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

This presentation has been peer-reviewed and no conflicts were noted.

Cultural Linguistic Competency (CLC) & Implicit Bias (IB)

STATE LAW:

The California legislature has passed Assembly Bill (AB) 1195, which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed AB 241, which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

EXEMPTION:

Business and Professions Code 2190.1 exempts activities which are dedicated solely to research or other issues that do not contain a direct patient care component.

This presentation is dedicated solely to research or other issues that do not contain a direct patient care component.

RCC Highlights from 2024

ASCO GU

- Overall survival results from the phase 3 KEYNOTE-564 study of adjuvant pembrolizumab versus placebo for the treatment of clear cell renal cell carcinoma

ASCO

- Circulating kidney injury molecule-1 (KIM-1) biomarker analysis in IMmotion010: A randomized phase 3 study of adjuvant atezolizumab vs placebo in patients with renal cell carcinoma at increased risk of recurrence after resection

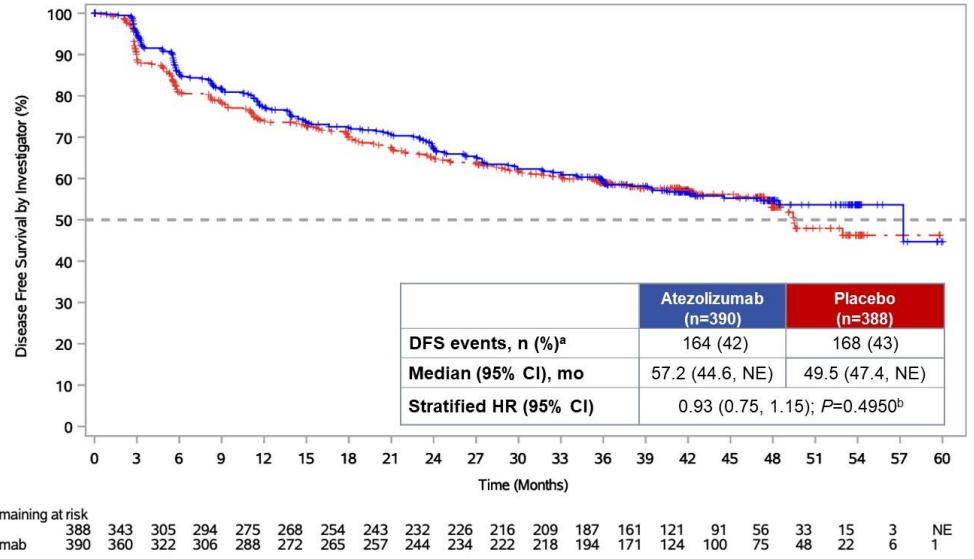
ESMO

- Tivozanib Plus Nivolumab vs Tivozanib Monotherapy in Patients with Metastatic Renal Cell Carcinoma Following an Immune Checkpoint Inhibitor: Results of the Phase III TiNivo-2 Study

RCC Highlights from 2024 – ASCO GU

Overall survival results from the phase 3 KEYNOTE-564 study of adjuvant pembrolizumab versus placebo for the treatment of clear cell renal cell carcinoma (ccRCC)

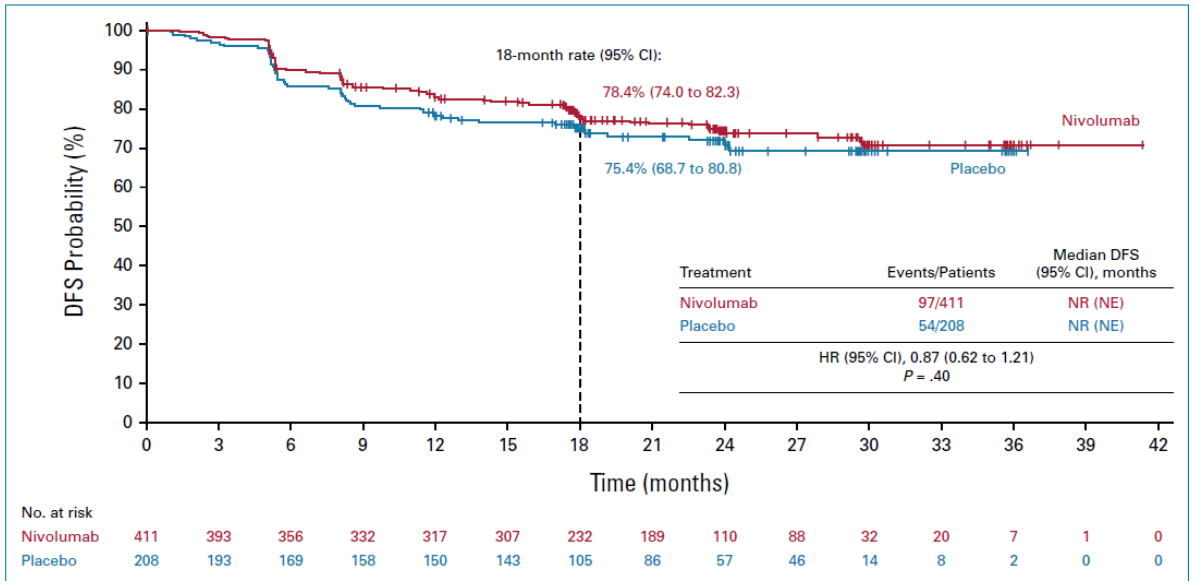
IMMotion010



	Atezolizumab (n=390)	Placebo (n=388)
DFS events, n (%)[a]	164 (42)	168 (43)
Median (95% CI), mo	57.2 (44.6, NE)	49.5 (47.4, NE)
Stratified HR (95% CI)	0.93 (0.75, 1.15); *P*=0.4950[b]	

Data cutoff, 03 May 2022. Minimum follow-up time was 38.6 months.
NE, not estimable.
[a] Stratified for disease status and PD-L1 status; [b] Not significant at α=0.05.

CheckMate 914

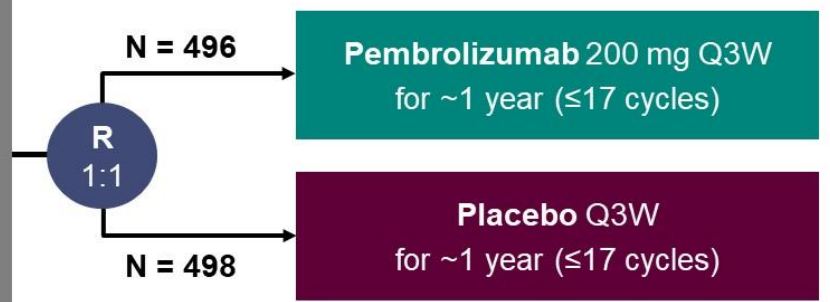


Treatment	Events/Patients	Median DFS (95% CI), months
Nivolumab	97/411	NR (NE)
Placebo	54/208	NR (NE)
HR (95% CI), 0.87 (0.62 to 1.21) *P* = .40		

KEYNOTE-564 Study (NCT03142334)

Key Eligibility Criteria

- Histologically confirmed clear cell RCC with no prior systemic therapy
- Surgery ≤12 weeks prior to randomization
- Postnephrectomy intermediate-high risk of recurrence (M0):
  - pT2, grade 4 or sarcomatoid, N0
  - pT3, any grade, N0
- Postnephrectomy high risk of recurrence (M0):
  - pT4, any grade, N0
  - Any pT, any grade, N+
- Postnephrectomy + complete resection of metastasis (M1 NED)
- ECOG PS 0 or 1



Stratification Factors

- M stage (M0 vs. M1 NED)
- M0 group further stratified:
  - ECOG PS 0 vs. 1
  - US vs. non-US

Primary Endpoint

- Disease-free survival by investigator

Key Secondary Endpoint

- Overall survival

Other Secondary Endpoints

- Safety

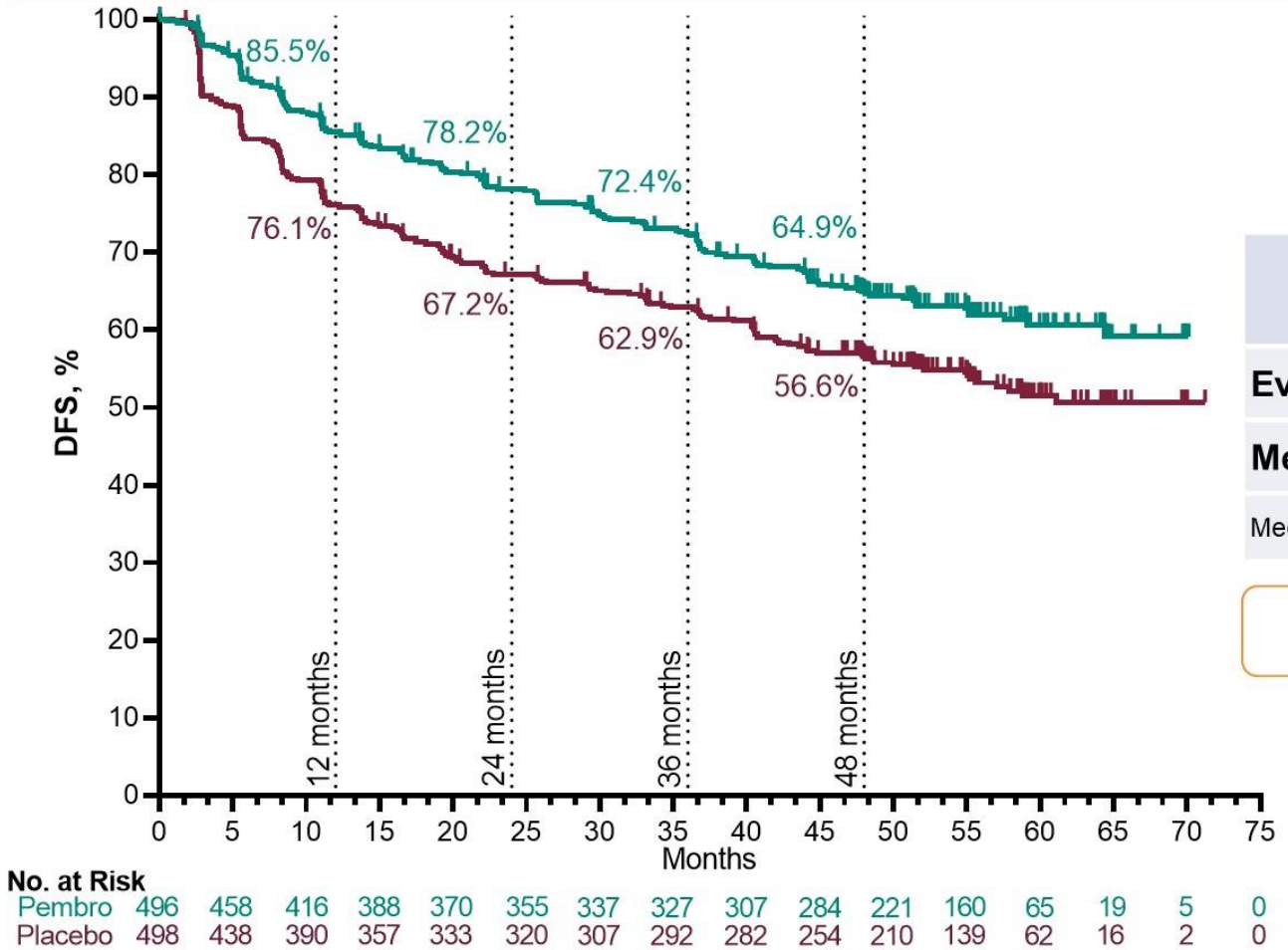
NED, no evidence of disease.

Baseline Characteristics

	Pembrolizumab (N = 496)	Placebo (N = 498)
Age, median (range), yrs	60 (27–81)	60 (25–84)
Male	70.0%	72.1%
ECOG performance status of 0	84.9%	85.5%
Region		
United States (US)	23.0%	23.5%
Outside US	77.0%	76.5%
M stage		
M0	94.2%	94.4%
M1	5.8%	5.6%
Disease risk category[a]		
M0 intermediate-high risk	85.1%	86.9%
M0 high risk	8.1%	7.4%
M1 NED	5.8%	5.6%
Sarcomatoid features		
Present	10.5%	11.8%
Absent	83.5%	83.3%
Unknown	6.0%	4.8%
PD-L1 status[b]		
CPS <1	25.0%	22.7%
CPS ≥1	73.6%	76.9%
Missing	1.4%	0.4%

[a]Another 1.0% of pts in the pembro group and 0% in the placebo group had T2 (grade ≤3) N0 M0 or T1 N0 M0 disease (protocol violations). [b]Assessed with PD-L1 IHC 22C3 pharmDx. PD-L1 combined positive score (CPS) is the # of PD-L1–staining cells (tumor cells, lymphocytes, and macrophages) divided by the total # of viable tumor cells, multiplied by 100. Data cutoff date: September 15, 2023.

Updated Disease-Free Survival by Investigator, Intention-to-Treat Population



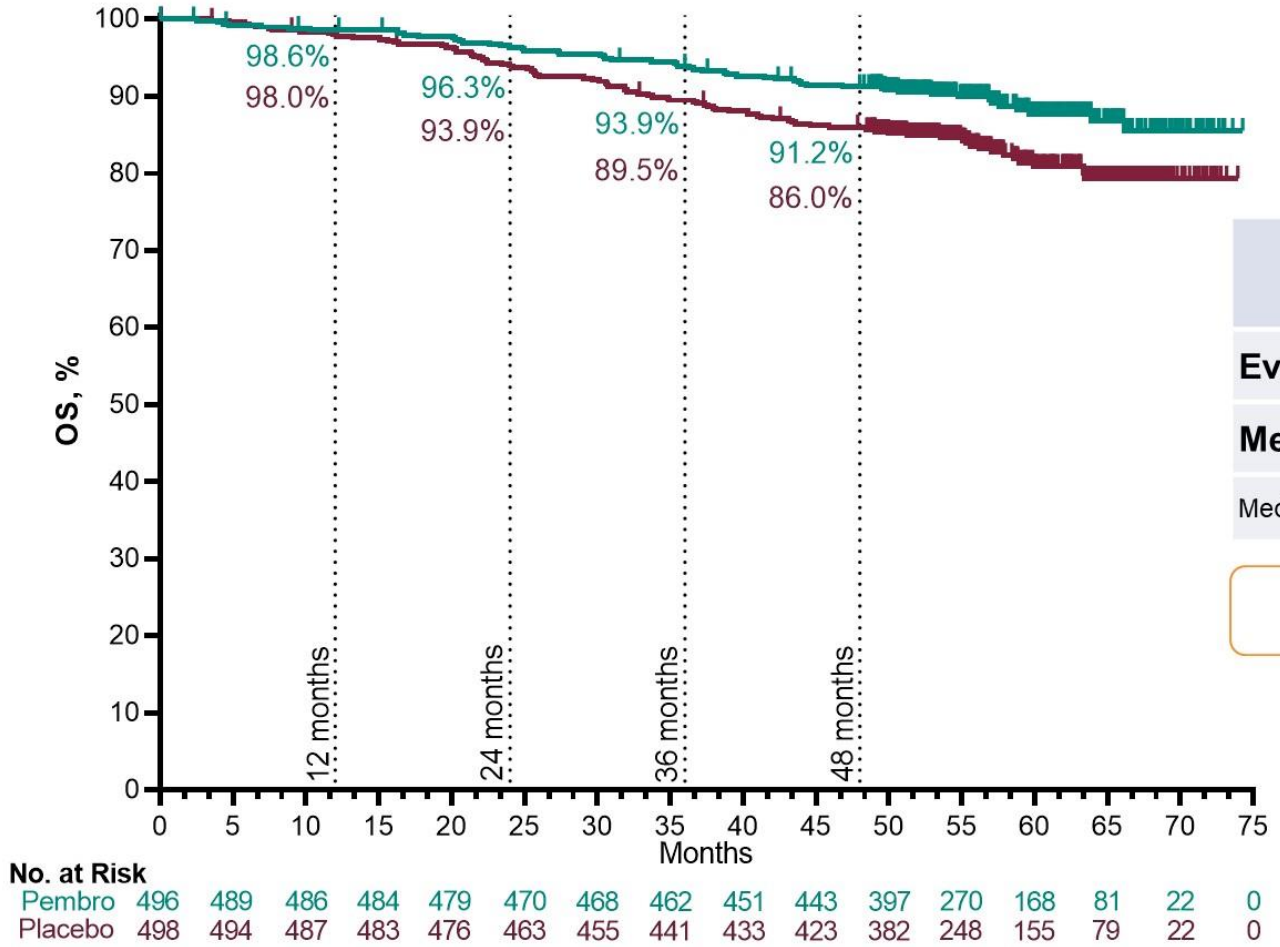
	Pembro (N = 496)	Placebo (N = 498)
Events, n	174	224
Median, mo (95% CI)	NR (NR–NR)	NR (54.9–NR)
Median follow-up was 57.2 months (range, 47.9–74.5)		

HR 0.72 (95% CI 0.59–0.87)

Primary DFS endpoint was met at IA1 and was not formally statistically tested thereafter.

Data cutoff date: September 15, 2023.

Overall Survival, Intention-to-Treat Population



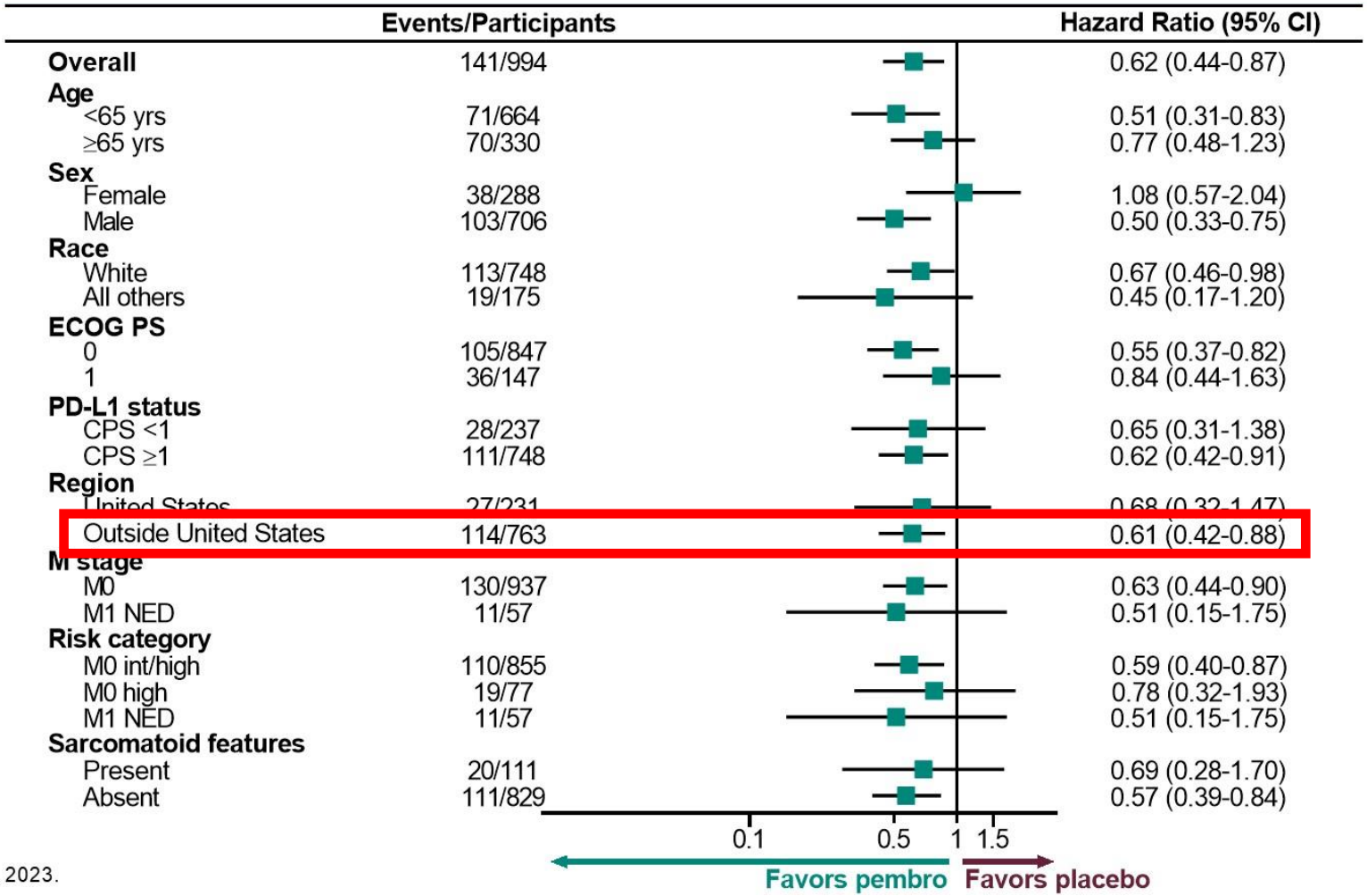
	Pembro (N = 496)	Placebo (N = 498)
Events, n	55	86
Median, mo (95% CI)	NR (NR–NR)	NR (NR–NR)
Median follow-up was 57.2 months (range, 47.9–74.5)		

HR 0.62 (95% CI 0.44–0.87); *P* =.002*

*** denotes statistical significance**. P-value boundary for OS at IA3 was 0.0072 (1-sided) per Lan-DeMets O'Brien-Fleming spending approximation α-spending function. As this key secondary endpoint was formally met, any future OS analyses will be descriptive only.

Data cutoff date: September 15, 2023.

Overall Survival by Subgroups



Data cutoff date: September 15, 2023.

Subsequent Therapies, Intention-to-Treat Population

	Participants with Documented Recurrence	
	Pembrolizumab (N = 161)	**Placebo (N = 210)**
Received any subsequent therapy[a,b]	128/161 (79.5%)	171/210 (81.4%)
Received systemic anticancer drug therapy	102/128 (79.7%)	145/171 (84.8%)
Anti–PD-(L)1 therapy[c]	42/102 (41.2%)	101/145 (69.7%)
VEGF/VEGFR inhibitor[d]	94/102 (92.2%)	123/145 (84.8%)
Other[e]	32/102 (31.4%)	60/145 (41.4%)
Received radiation therapy	31/128 (24.2%)	33/171 (19.3%)
Received surgery	35/128 (27.3%)	50/171 (29.2%)
No subsequent therapy	28/161 (17.4%)	28/210 (13.3%)
No subsequent therapy data available	5/161 (3.1%)	11/210 (5.2%)

[a]An additional 4 and 1 pts respectively in the pembro and placebo arms who are not included in the figure received subsequent therapy without documented recurrence. [b]Pts could have multiple subsequent anticancer therapies for RCC; each pt is counted once in each applicable category. [c]Atezolizumab, avelumab, durvalumab, nivolumab, pembrolizumab. [d]Axitinib, bevacizumab, cabozantinib, lenvatinib, pazopanib, sorafenib, sunitinib, tivozanib. [e]Included but was not limited to belzutifan, everolimus, and ipilimumab.
Data cutoff date: September 15, 2023.

RCC Highlights from 2024 – ASCO GU

- Adjuvant pembrolizumab prolonged OS vs placebo in ccRCC at increased risk of recurrence following surgery
    - 38% reduction in risk of death vs placebo
- Continued DFS with pembrolizumab was observed with further follow up
- KEYNOTE-564 is the first study to demonstrate a survival benefit with adjuvant therapy in RCC
- Questions remains about subsequent therapy availability, particularly outside the US

RCC Highlights from 2024 - ASCO

Circulating kidney injury molecule-1 (KIM-1) biomarker analysis in IMmotion010: A randomized phase 3 study of adjuvant atezolizumab vs placebo in patients with renal cell carcinoma at increased risk of recurrence after resection

Introduction

- In the Phase 3 IMmotion010 trial, adjuvant atezolizumab (anti–PD-L1) did not prolong investigator-assessed DFS vs placebo after resection in patients with RCC with increased risk of recurrence[1]
- Heterogeneity in outcomes across clinical trials evaluating checkpoint inhibitors as adjuvant therapy in RCC[1-4] suggests that there may be patient subpopulations that derive differential benefit from these agents
- Additionally, biomarkers are needed to identify patients with minimal residual disease (MRD) after resection who may have increased risk of recurrence

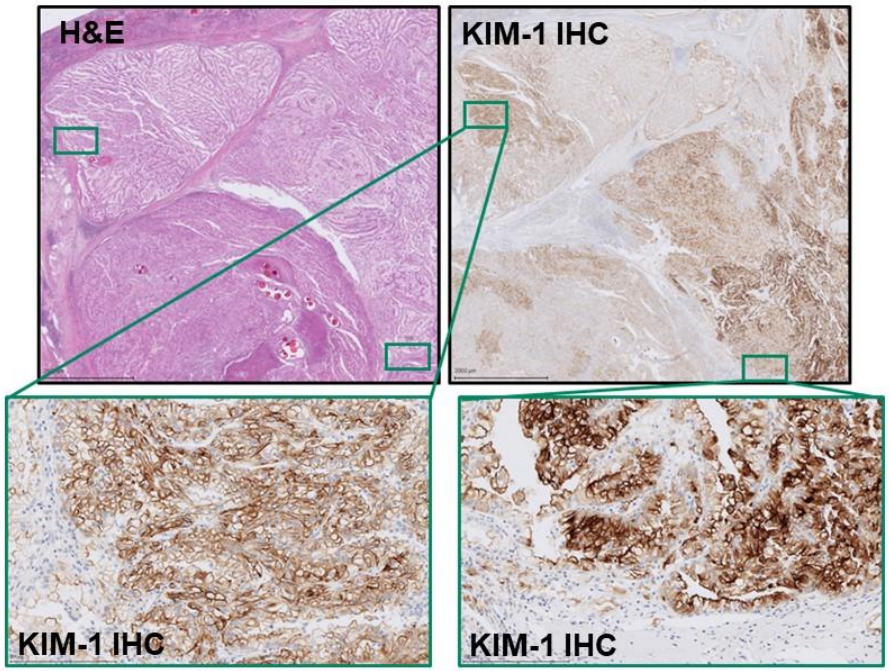
PD-L1, programmed death-ligand 1.

1. Pal S, et al Lancet 2022;400:359-68. 2. Choueiri T, et al. N Engl J Med 2021;385:683-94. 3. Motzer RJ, et al. Lancet 2023;401:821-32. 4. Choueiri T, et al. N Engl J Med 2024; 390:1359-71.

KIM-1 (Kidney injury molecule-1) is a tumor associated protein and may be a useful circulating biomarker in RCC

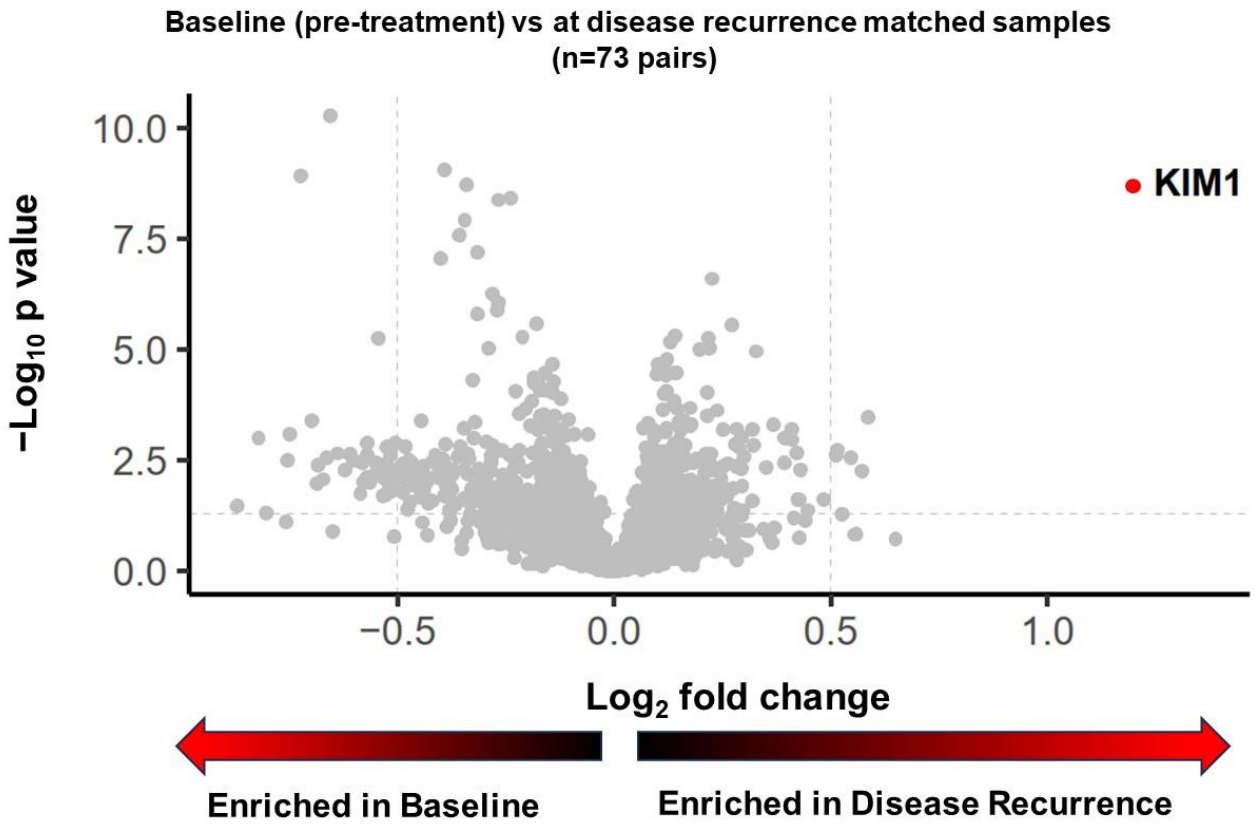
- KIM-1, a type 1 membrane glycoprotein, has been identified as a marker of unresected clear-cell RCC and as a marker for early detection of RCC[1,2,3]
- In the ASSURE trial of adjuvant sunitinib, sorafenib, or placebo, higher levels of KIM-1 in post-nephrectomy, pre-treatment **plasma samples** were associated with worse DFS and OS[4]
- KIM-1 can be measured **in plasma or serum** and is stable under different storage conditions, suggesting suitability to serve as a **peripheral blood circulating biomarker**[5]

KIM-1 IHC analysis in RCC Primary Tumor



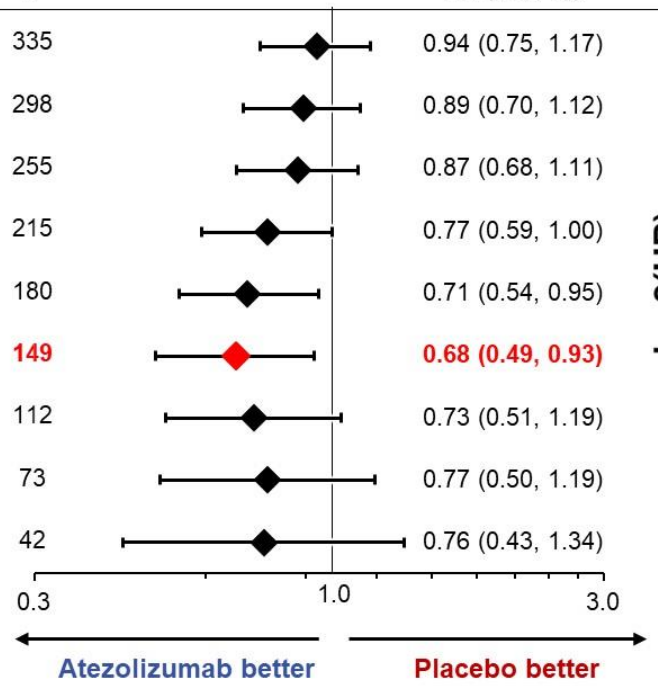
1. Kushlinskii NE, et al. Bull Exp Biol Med 2019; 167:388-92. 2. Scelo G, et al. Clin Cancer Res 2018;24:5594-601. 3. Xu W, et al. J Clin Oncol 2024; JCO2300699.
4. Xu W, et al. Clin Cancer Res 2021;27:3397-403. 5. Hou W, et al. Transpl Rev 2010; 24:143-6.

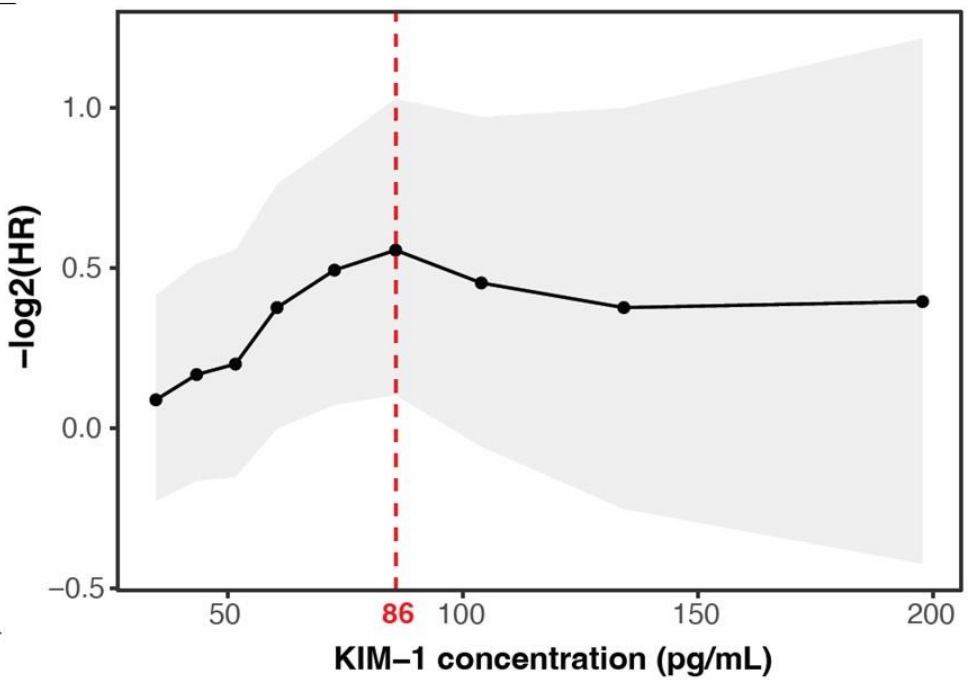
KIM-1 was identified as the most significantly enriched circulating protein in recurrence vs baseline serum samples in IMmotion010



Baseline KIM-1 level of 86 pg/mL was identified as the optimized threshold for defining KIM-1^{High} vs KIM1^{Low} subgroups

KIM-1 Threshold pg/mL (percentile)	Atezolizumab n	Placebo n	HR (95% CI)
≥35 (≥10%)	341	335	0.94 (0.75, 1.17)
≥43 (≥20%)	303	298	0.89 (0.70, 1.12)
≥52 (≥30%)	272	255	0.87 (0.68, 1.11)
≥60 (≥40%)	237	215	0.77 (0.59, 1.00)
≥73 (≥50%)	196	180	0.71 (0.54, 0.95)
≥86 (≥60%)	**151**	**149**	**0.68 (0.49, 0.93)**
≥104 (≥70%)	114	112	0.73 (0.51, 1.19)
≥134 (≥80%)	77	73	0.77 (0.50, 1.19)
≥198 (≥90%)	34	42	0.76 (0.43, 1.34)





Baseline characteristics by KIM-1 status

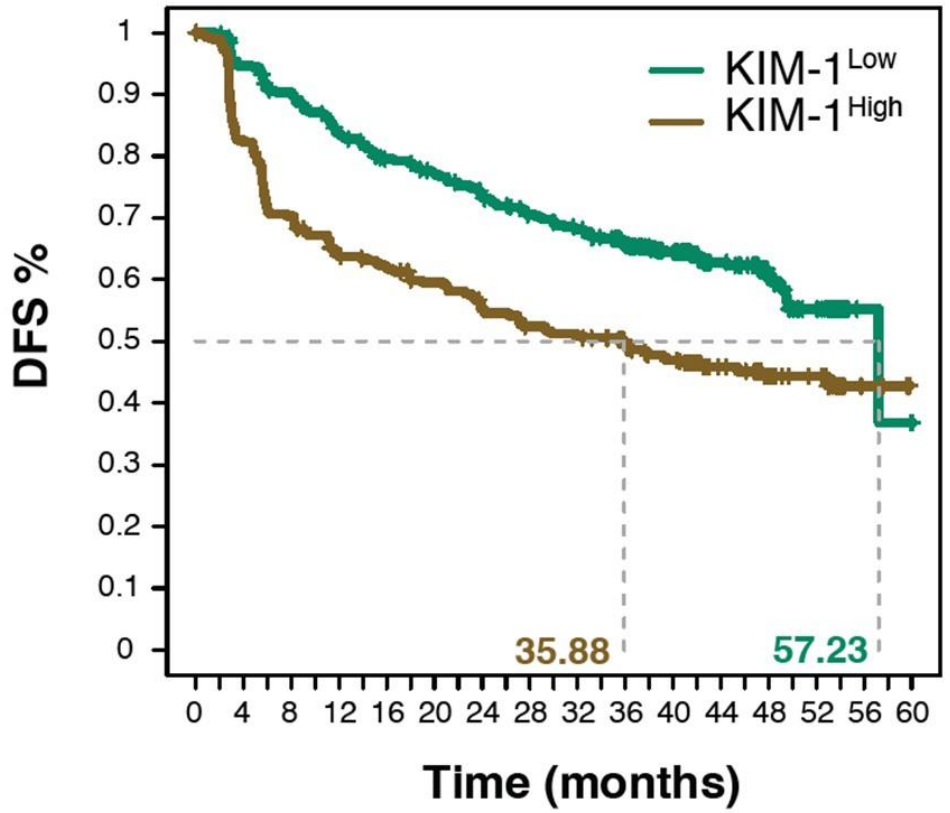
Baseline

Characteristic	KIM-1^{High} (n=300)	KIM-1^{Low} (n=452)
Age, median (range), y	64 (56-70)	58 (50-67)
Male, n (%)	232 (77)	314 (69)
Region, n (%)[a]		
Europe and Middle East	128 (43)	207 (46)
North America	102 (34)	172 (38)
Asia-Pacific	53 (18)	23 (5)
Central or South America	12 (4)	41 (9)
Australia	5 (2)	9 (2)
Pathologic disease stage, n (%)		
T2/T3a	171 (57)	313 (69)
T3b/c/T4/N+	81 (27)	82 (18)
M1 NED	48 (16)	57 (13)
Disease stage, n (%)		
I	16 (5)	14 (3)
II	21 (7)	26 (6)
III	249 (83)	388 (86)
IV	14 (5)	24 (5)
PD-L1 Status[a]		
PD-L1 positive	188 (63)	266 (59)
PD-L1 negative	112 (37)	186 (41)
Sarcomatoid component	48 (16)	51 (11)

PD-L1 evaluated using SP142 assay, PD-L1 positive was defined as ≥1% tumor infiltrating immune cells expressing PD-L1.

KIM-1^{High} status at baseline was associated with worse DFS in IMmotion010

Baseline

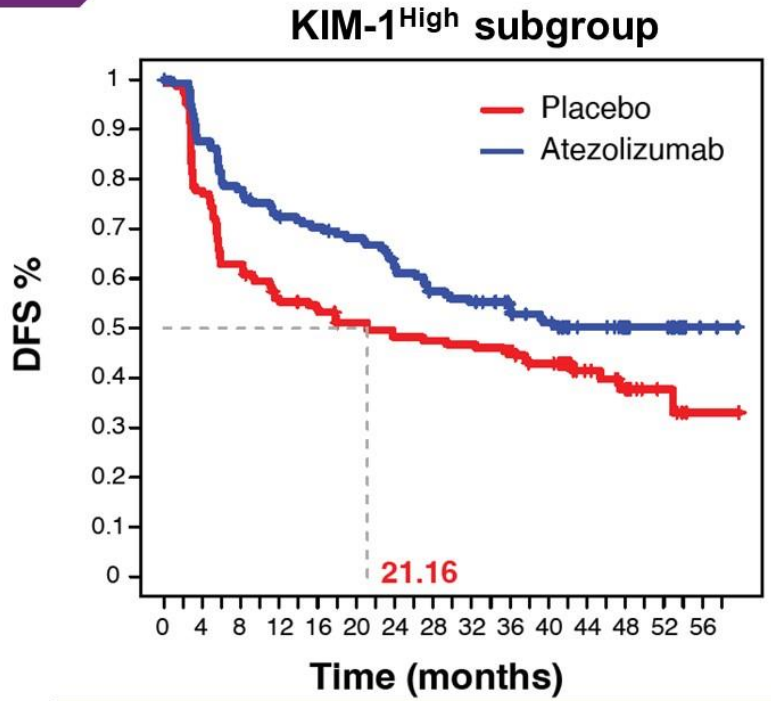


	n	Median DFS (months)	HR[a] (95% CI)
KIM-1^{High}	300	35.88	1.75 (1.40, 2.17)
KIM-1^{Low}	452	57.23	

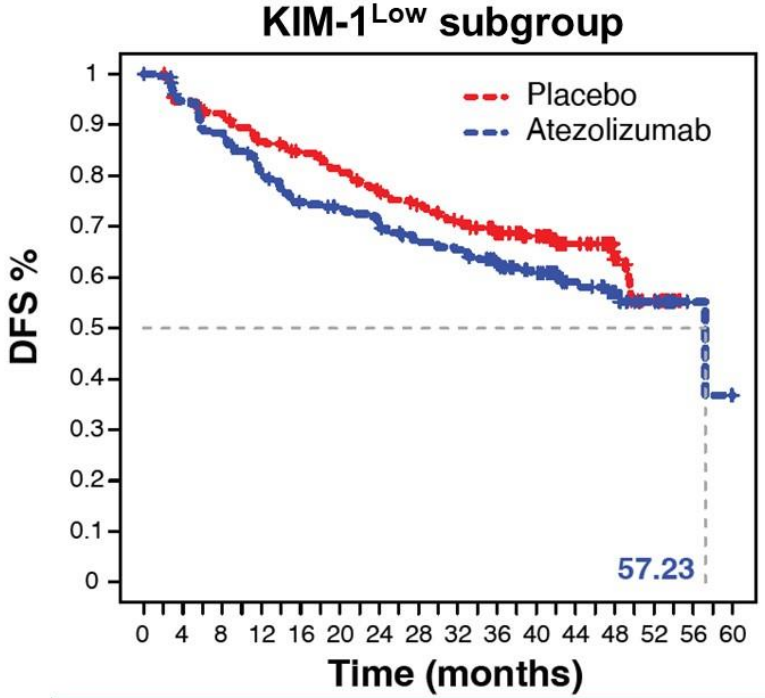
[a] HR stratified by pathologic disease stage and geographic region.

Atezolizumab improved DFS vs Placebo in the baseline KIM-1^{High} subgroup

Baseline



	n	Median DFS	HR[a] (95% CI)
Atezolizumab	151	NE	0.72 (0.52, 0.99)
Placebo	149	21.16	

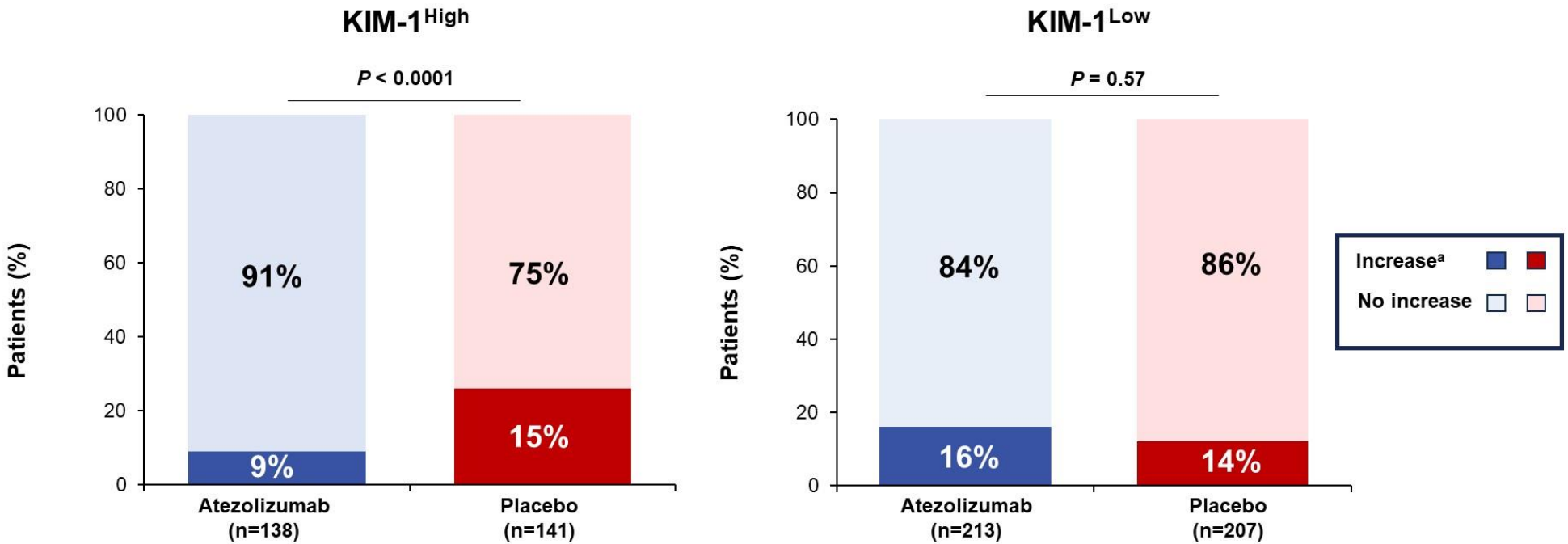


	n	Median DFS	HR[a] (95% CI)
Atezolizumab	229	57.23	1.12 (0.88, 1.63)
Placebo	223	NE	

[a] HR stratified by pathologic disease stage and geographic region.

In the KIM-1^{High} subgroup, patients were less likely to experience an on-treatment increase in KIM-1 levels with atezolizumab vs placebo treatment

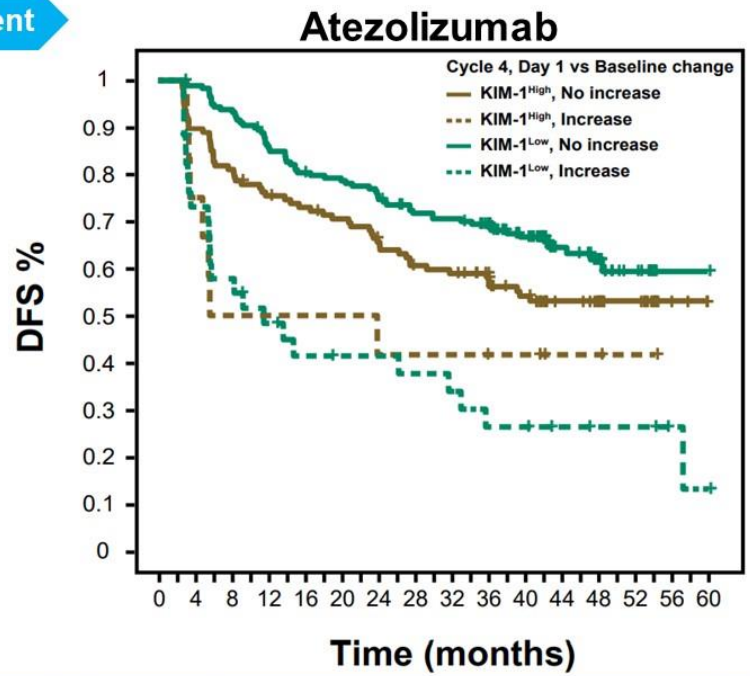
On Treatment

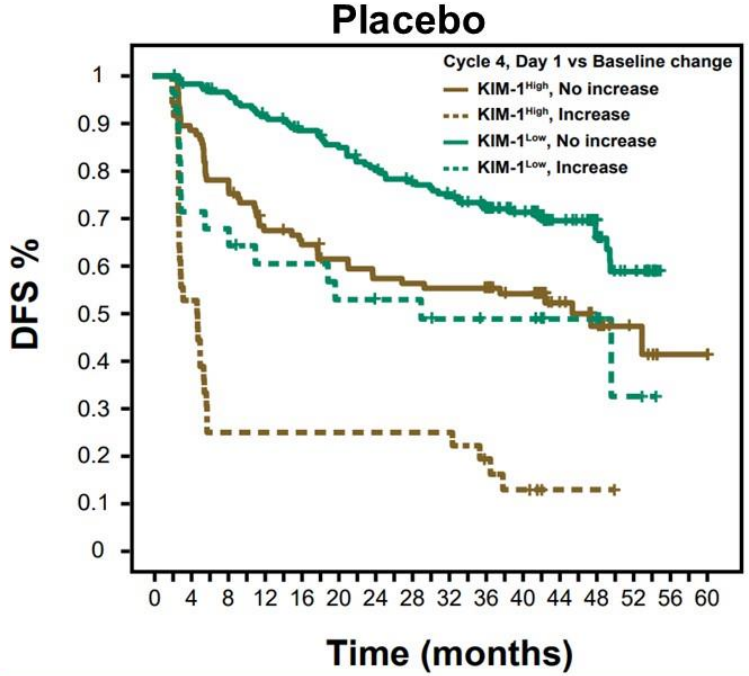


[a] Increase in KIM-1 was defined as a ≥30% increase from baseline to Cycle 4 Day 1 value.

On-treatment increase in KIM-1 was associated with worse DFS in both KIM-1^{High} and KIM-1^{Low} subgroups

On Treatment





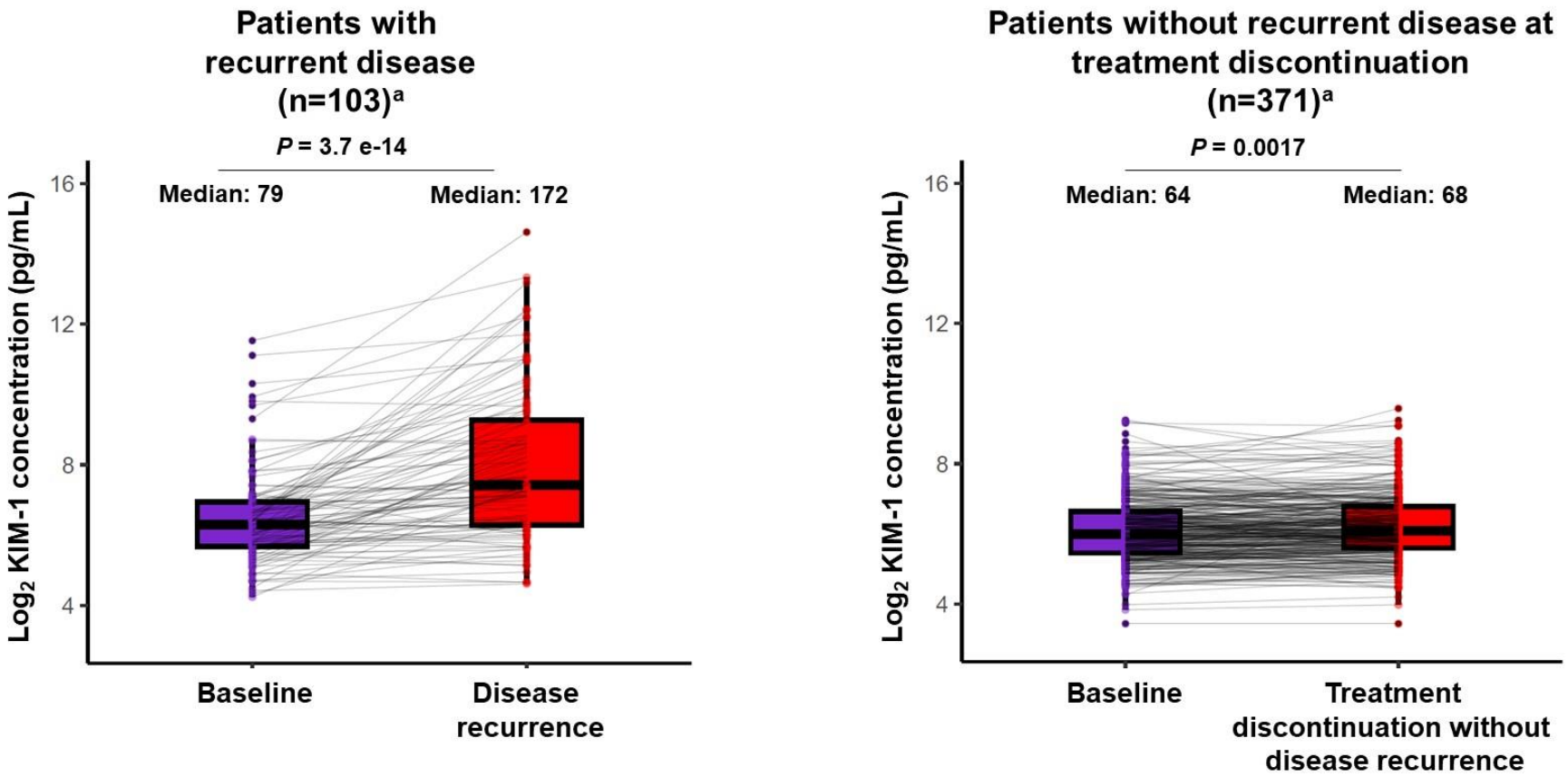
Baseline	On-treatment	n	Median DFS	HR (95% CI)
KIM-1^{High}	Increase[a]	12	14.8	1.68 (0.77, 3.69)
	No increase	126	NE	
KIM-1^{Low}	Increase[a]	34	11.5	3.56 (2.21, 5.75)
	No increase	179	NE	

Baseline	On-treatment	n	Median DFS	HR (95% CI)
KIM-1^{High}	Increase[a]	36	4.8	3.53 (2.24, 5.58)
	No increase	105	45.4	
KIM-1^{Low}	Increase[a]	28	29.0	2.51 (1.42, 4.44)
	No increase	179	NE	

[a] Increase in KIM-1 was defined as a ≥30% increase from baseline to Cycle 4 Day 1 value.

Serum KIM-1 levels increased at time of disease recurrence vs baseline

Disease Recurrence/ Treatment Discontinuation



[a] Analysis conducted in patients with matched samples at baseline and at disease recurrence or at treatment discontinuation without disease recurrence (approximately 1 year or 16 treatment cycles)

RCC Highlights from 2024 - ASCO

- In IMmotion010, elevated post-nephrectomy KIM-1 serum levels showed potential as a circulating protein biomarkers for minimal residual disease and disease recurrence in the adjuvant setting
  - High post-nephrectomy KIM-1 serum levels were associated with worse DFS
  - An increase in post-treatment KIM-1 levels was associated with worse DFS
- Atezolizumab showed improved DFS vs placebo in patients with high baseline KIM-1
- Standardized cutoffs are needed before KIM-1 can be used in clinical decision making

RCC Highlights from 2024 - ESMO

Tivozanib Plus Nivolumab vs Tivozanib Monotherapy in Patients with Metastatic Renal Cell Carcinoma Following an Immune Checkpoint Inhibitor: Results of the Phase III TiNivo-2 Study

Background

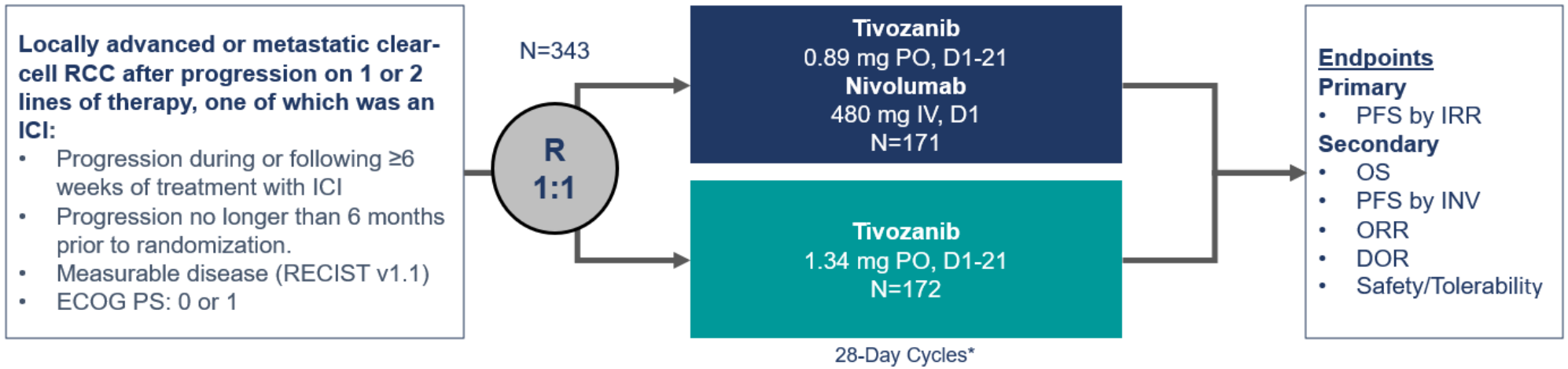
- The optimal sequence in patients whose disease progressed after treatment with ICI is uncertain, leaving several unanswered questions:
  - Can ICI rechallenge improve clinical outcomes?
  - Can outcomes be impacted if non-ICI drugs were used before ICI rechallenge (ICI break)?
  - Any differences between anti–PD-1 or anti–PD-L1 therapies in the rechallenge setting?
- Evidence supports the value of VEGFR TKI use, including tivozanib, in patients previously treated with ICI-based regimens[1,2]
- Tivozanib was evaluated in combination with nivolumab in the phase 1/2 TiNivo study showing promising antitumor efficacy with an expected adverse event profile in patients with mRCC[3]

BARCELONA 2024 ESMO congress

ICI, immune checkpoint inhibitor; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; mRCC, metastatic renal cell carcinoma; VEGFR-TKI, vascular endothelial growth factor receptor tyrosine kinase inhibitor.

1. Pal SK, et al. *Lancet*. 2023;402:185-195. 2. Rini BI, et al. *Lancet Oncol*. 2020;21:95-104. 3. Albiges L, et al. *Ann Oncol*. 2021;32:97-102.

TiNivo-2: Phase 3 Study Design



Stratification Factors
- IMDC risk category
- Prior therapy (ICI as most recent therapy or not)

Key Considerations
- Reduced dose of tivozanib in combination arm was agreed with regulatory authorities due to potential risk of higher rate of grade 3/4 hypertension
- Prior therapy (ICI as most recent therapy or not)
  - Test if ICI break impacts outcome (reset the immune system?)

*Treatment was continued until progression or unacceptable toxicity, nivolumab discontinued in all subjects after 2 years of treatment.
DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ICI, immune checkpoint inhibitor; IMDC, International mRCC Database Consortium; INV, investigator; IRR, independent radiology review; IV, intravenous; ORR, objective response rate; OS, overall survival; PO, by mouth; PFS, progression-free survival; RCC, renal cell carcinoma; RECIST, Response Evaluation Criteria in Solid Tumors

1. ClinicalTrials.gov. Accessed May 20, 2024. https://clinicaltrials.gov/study/NCT04987203.

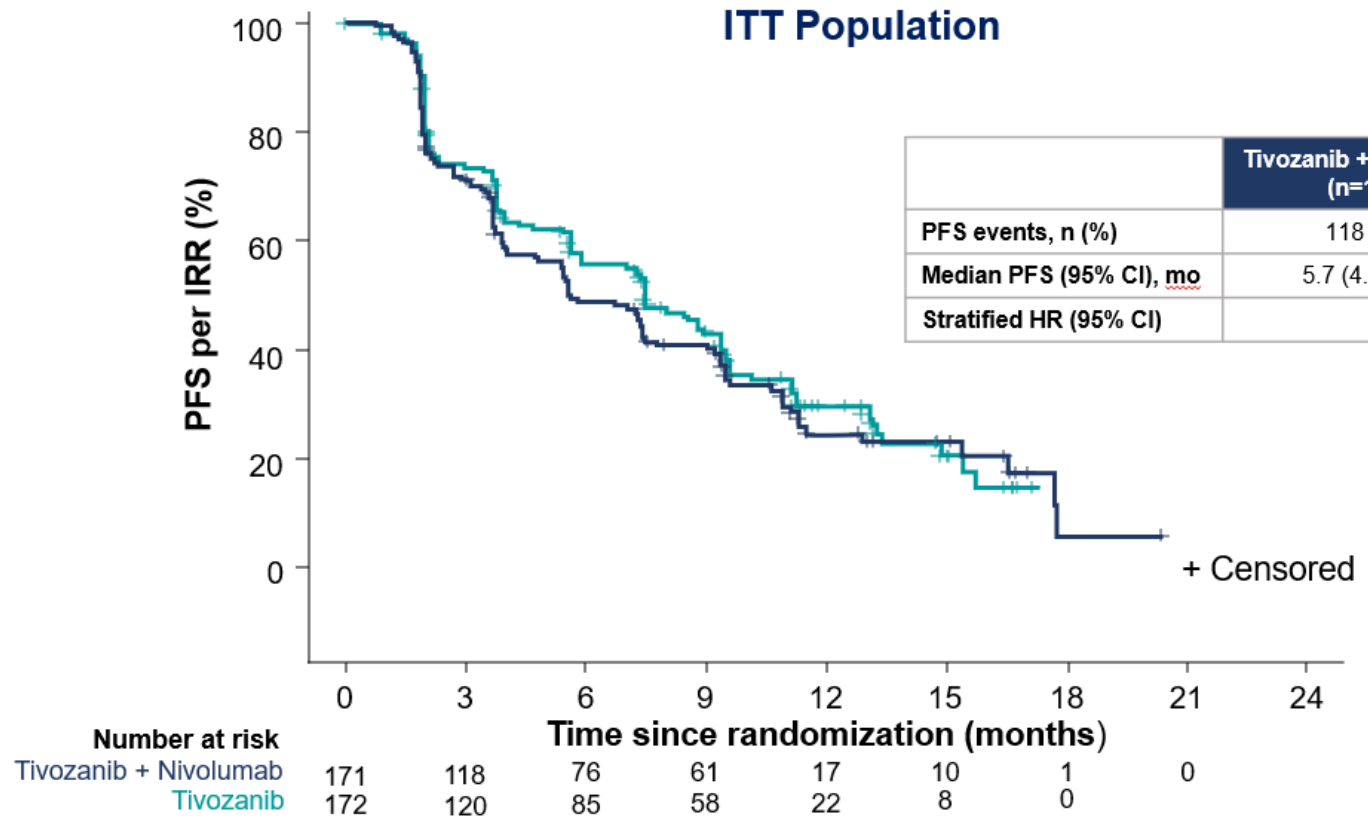
Baseline Demographics and Disease Characteristics

Characteristic	Tivozanib + Nivolumab (N=171)	Tivozanib (N=172)
Age, years		
Median (range)	63 (37-87)	62 (33-82)
Sex, n (%)		
Female	46 (27)	38 (22)
Male	125 (73)	134 (78)
Race, n (%)		
White	112 (65)	107 (62)
Asian	1 (<1)	0
Black or African American	2 (1)	8 (5)
Not reported	56 (33)	57 (33)
ECOG PS, n (%)		
0	76 (44)	85 (49)
1	94 (55)	87 (51)
Missing	1 (<1)	0

Characteristic	Tivozanib + Nivolumab (N=171)	Tivozanib (N=172)
IMDC Risk Category, n (%)		
Favorable	30 (18)	31 (18)
Intermediate	114 (67)	113 (66)
Poor	27 (16)	28 (16)
Prior Lines of Therapy, n (%)		
1	111 (65)	105 (61)
2	60 (35)	67 (39)
Most recent therapy, n (%)		
ICI	119 (71)	122 (71)
Non-ICI	49 (29)	50 (29)
Prior VEGF-TKI Use, n (%)		
0	51 (30)	53 (31)
1	95 (57)	100 (58)
2	22 (13)	18 (11)

BARCELONA 2024 ESMO congress

Primary Analysis of Centrally Reviewed PFS (primary endpoint)



	Tivozanib + Nivolumab (n=171)	Tivozanib (n=172)
PFS events, n (%)	118 (69)	112 (65)
Median PFS (95% CI), mo	5.7 (4.0, 7.4)	7.4 (5.6, 9.2)
Stratified HR (95% CI)	1.10 (0.84, 1.43); p=0.49	

Median follow up was 11.8 months for the tivozanib + nivolumab cohort and 12.5 months for tivozanib monotherapy

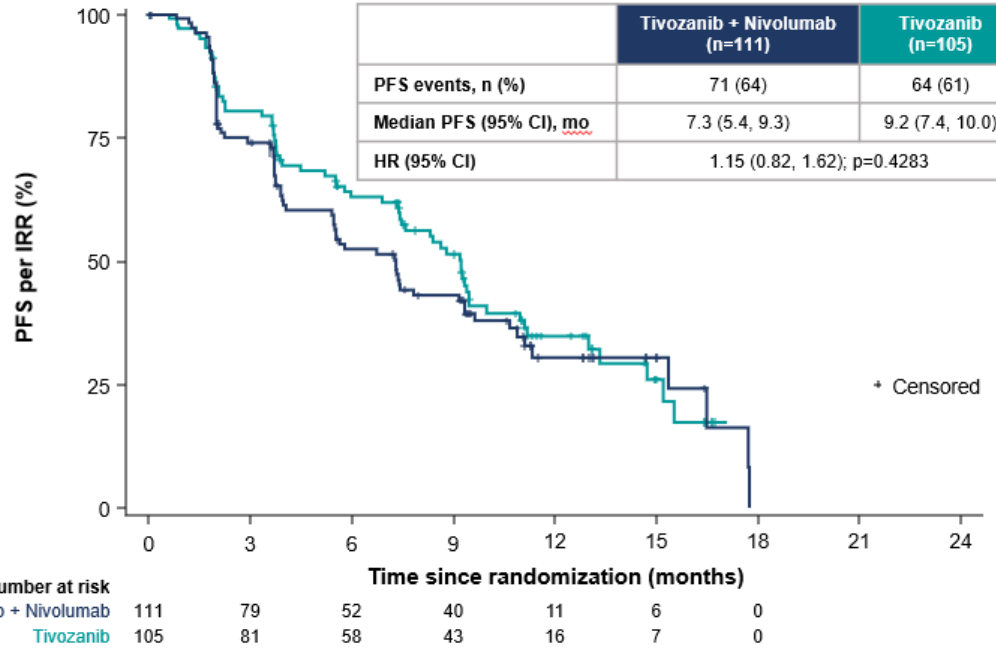
BARCELONA 2024 ESMO congress

HR, hazard ratio; IRR, independent radiology review; ITT, intent to treat.

Centrally Reviewed PFS by Line of Therapy

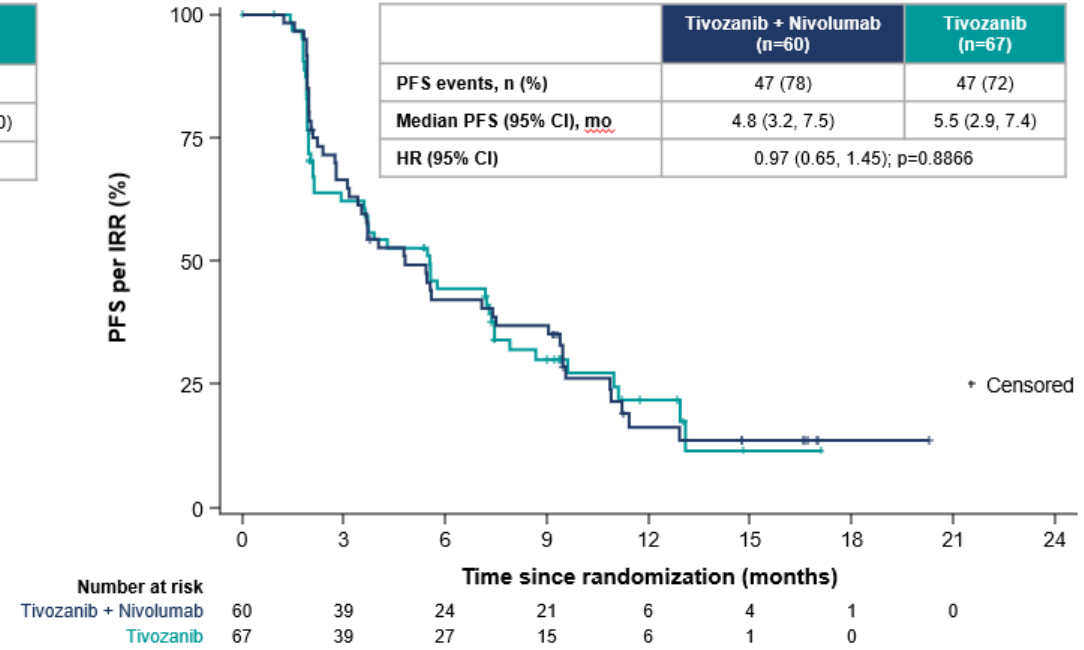
Second Line Therapy

	Tivozanib + Nivolumab (n=111)	Tivozanib (n=105)
PFS events, n (%)	71 (64)	64 (61)
Median PFS (95% CI), mo	7.3 (5.4, 9.3)	9.2 (7.4, 10.0)
HR (95% CI)	1.15 (0.82, 1.62); p=0.4283	



Third Line Therapy

	Tivozanib + Nivolumab (n=60)	Tivozanib (n=67)
PFS events, n (%)	47 (78)	47 (72)
Median PFS (95% CI), mo	4.8 (3.2, 7.5)	5.5 (2.9, 7.4)
HR (95% CI)	0.97 (0.65, 1.45); p=0.8866	



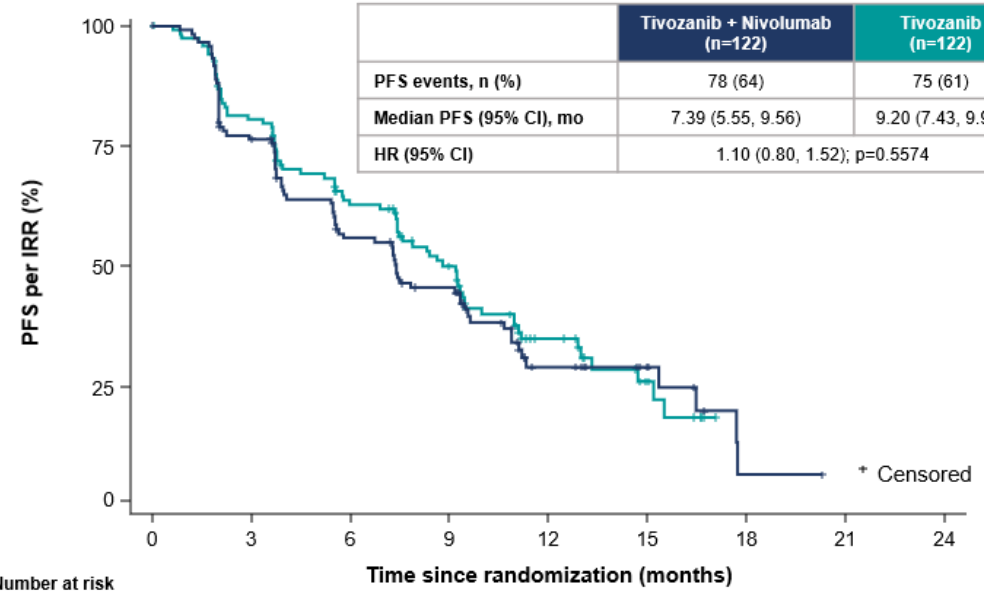
BARCELONA 2024 ESMO congress

By independent radiology review.

Centrally Reviewed PFS by Most Recent Line of Therapy

ICI as Most Recent Therapy

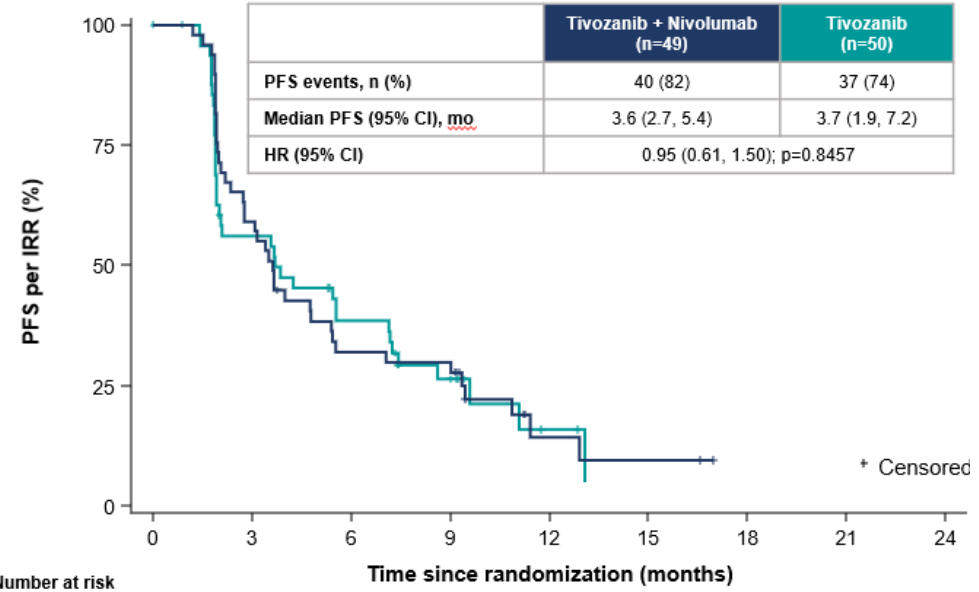
	Tivozanib + Nivolumab (n=122)	Tivozanib (n=122)
PFS events, n (%)	78 (64)	75 (61)
Median PFS (95% CI), mo	7.39 (5.55, 9.56)	9.20 (7.43, 9.99)
HR (95% CI)	1.10 (0.80, 1.52); p=0.5574	



Number at risk								
Tivozanib + Nivolumab	122	89	61	47	14	8	1	0
Tivozanib	122	94	68	49	20	8	0	

Non-ICI as Most Recent Therapy

	Tivozanib + Nivolumab (n=49)	Tivozanib (n=50)
PFS events, n (%)	40 (82)	37 (74)
Median PFS (95% CI), mo	3.6 (2.7, 5.4)	3.7 (1.9, 7.2)
HR (95% CI)	0.95 (0.61, 1.50); p=0.8457	



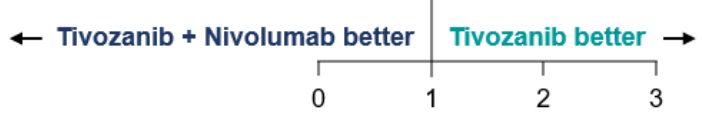
Number at risk								
Tivozanib + Nivolumab	49	29	15	14	3	2	0	
Tivozanib	50	26	17	9	2	0		

BARCELONA 2024 ESMO congress

*Analysis by strata

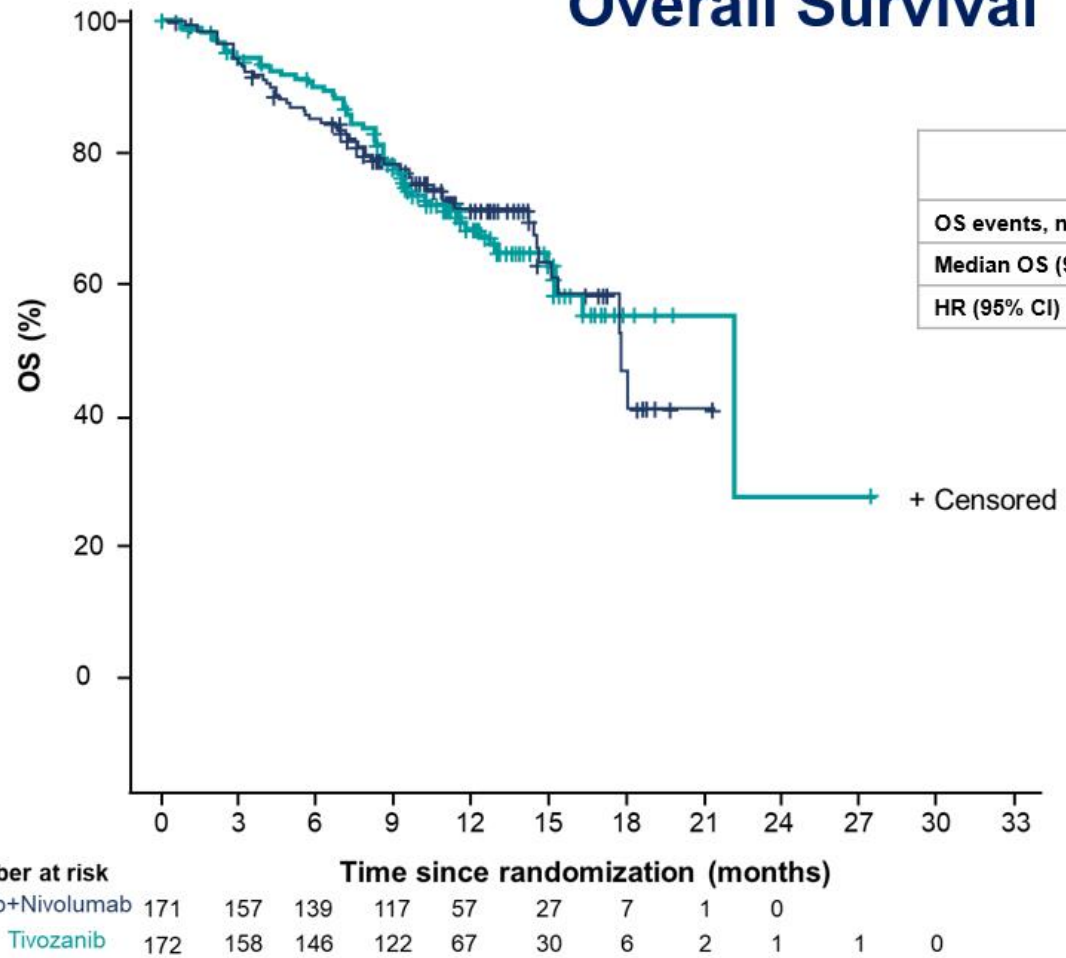
Centrally reviewed PFS by subgroup

Category	Tivozanib + Nivolumab Event/N	Tivozanib + Nivolumab Median PFS, Months (95% CI)	Tivozanib Event/N	Tivozanib Median PFS, Months (95% CI)	PFS HR (95% CI)
Age					
< 65 years	68/89	4.8 (3.4–7.3)	65/97	7.4 (5.5–9.2)	1.25 (0.89–1.76)
≥ 65 years	50/82	9.2 (5.5–9.6)	47/75	7.6 (5.2–10.0)	0.92 (0.61–1.37)
Gender					
Male	86/125	5.6 (3.9–7.5)	88/134	7.4 (5.5–9.2)	1.01 (0.75–1.36)
Female	32/46	6.7 (3.7–10.9)	24/38	7.4 (5.6–12.9)	1.27 (0.75–2.16)
ECOG					
0	52/76	7.3 (4.0–9.4)	53/85	8.8 (7.2–11.1)	1.15 (0.78–1.69)
1	66/94	5.5 (3.7–9.0)	59/87	6.0 (3.7–8.6)	0.95 (0.67–1.36)
IMDC Risk Category					
Favorable	18/30	9.3 (4.0–11.4)	15/31	11.2 (9.3–13.1)	1.37 (0.69–2.73)
Intermediate	78/114	5.7 (4.0–9.4)	75/115	7.4 (4.5–8.4)	0.99 (0.72–1.36)
Poor	22/27	3.7 (2.7–7.4)	22/26	5.7 (2.3–9.2)	1.35 (0.73–2.50)
Use of VEGFR-TKI in recent line					
Yes	37/45	3.4 (2.2–4.8)	37/50	3.7 (1.9–7.2)	0.96 (0.61–1.52)
No	37/66	9.6 (7.5–11.2)	36/65	9.3 (7.4–14.7)	0.95 (0.60–1.51)
Previous use of VEGFR-TKI (any prior line)					
0 VEGFR-TKI	29/53	9.6 (7.4–15.3)	28/53	9.4 (7.4–15.5)	1.03 (0.61–1.74)
1 VEGFR-TKI	69/96	5.4 (3.7–6.7)	70/101	7.4 (5.5–8.8)	1.04 (0.74–1.45)
2 VEGFR-TKI	20/22	3.1 (2.1–4.0)	14/18	3.8 (1.9–7.2)	1.33 (0.67–2.65)



BARCELONA 2024 ESMO congress

Overall Survival



	Tivozanib+Nivolumab (n=171)	Tivozanib (n=172)
OS events, n (%)	53 (31)	57 (33)
Median OS (95% CI), mo	17.7 (15.1, NR)	22.1 (15.2, NR)
HR (95% CI)	1.00 (0.68, 1.46); p=0.9868	

Overall survival data are not mature.
At data cutoff, 33% of events had occurred.

NR, not reached.

Safety Summary

Adverse Event, n (%)	Tivozanib 0.89 mg + Nivolumab (n=168)	Tivozanib 1.34 mg (n=171)
Any-cause TEAE, n (%)	**163 (97)**	**167 (98)**
Related TEAE	137 (82)	144 (84)
Tivozanib	135 (80)	144 (84)
Nivolumab	119 (71)	0
Grade 3 or 4 AE, n (%)	**102 (61)**	**103 (60)**
Related	54 (32)	60 (35)
Serious AE, n (%)	**54 (32)**	**64 (37)**
Related	14 (8)	15 (9)
Death due to AE, n (%)	**7 (4)**	**5 (3)**
Related	0	1 (<1)
TEAE leading to discontinuation, n (%)	**27 (16)**	**33 (19)**
Due to tivozanib	19 (11)	33 (19)
Due to nivolumab	22 (13)	0
TEAE leading to dose interruption, n (%)	**82 (49)**	**93 (54)**
Due to tivozanib	79 (47)	93 (54)
Due to nivolumab	35 (21)	0
TEAE leading to dose reduction of tivozanib, n (%)	**18 (11)**	**38 (22)**
Median duration of treatment, months (range)	**6.3 (0.0, 20.7)**	**7.4 (0.1, 17.9)**

BARCELONA 2024 ESMO congress

TEAE, treatment-emergent adverse event.

RCC Highlights from 2024 - ESMO

- The addition of nivolumab to tivozanib did not result in improved clinical outcomes in patients with mRCC who progressed on or after prior ICI treatment
- Tivozanib with or without nivolumab was tolerated and consistent with the established safety profiles of these agents
- Meaningful results were observed in the tivozanib monotherapy arm with a 9.2 months mPFS immediately following ICI and as a second line treatment following ICI combinations.
- This trial confirms the key conclusion from CONTACT-03 – ICI re-challenge in mRCC should be discouraged regardless of treatment sequence

Thank you!