Presentaciones más destacadas en cáncer renal

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Dr. Alonso Gordoa financial interests:

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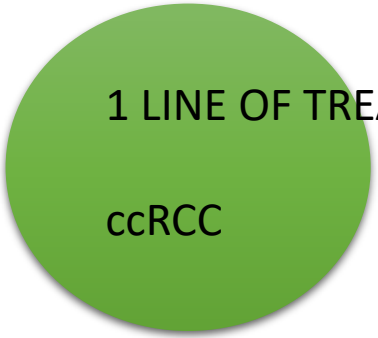
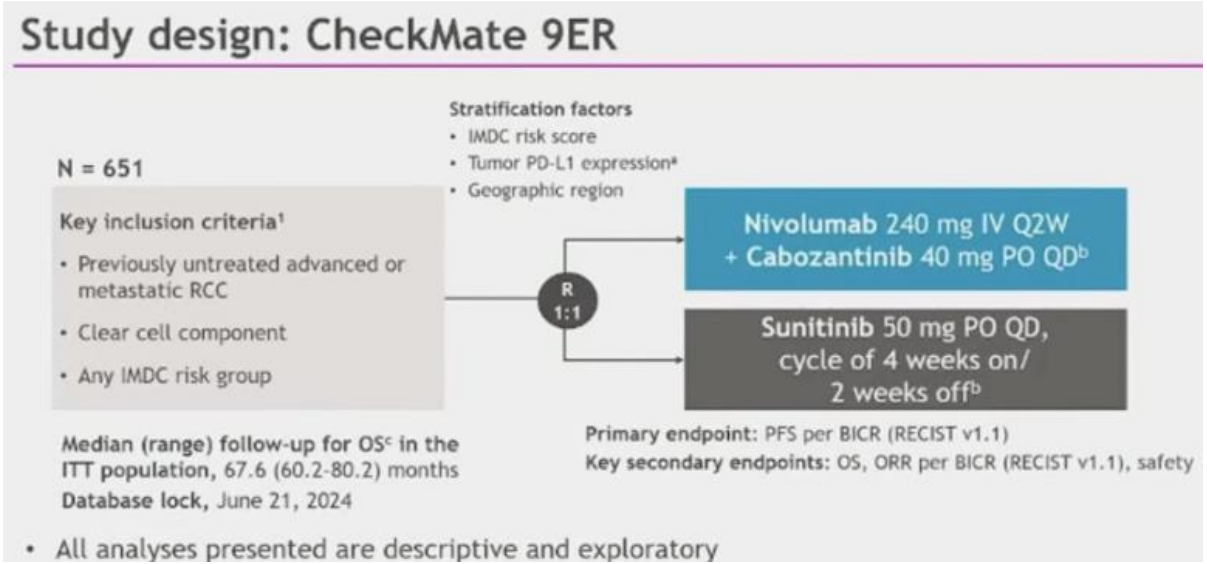

1 LINE OF TREATMENT IN ADVANCED DISEASE
ccRCC

Final Analysis Checkmate 9ER



Median FUP = 67.6 months

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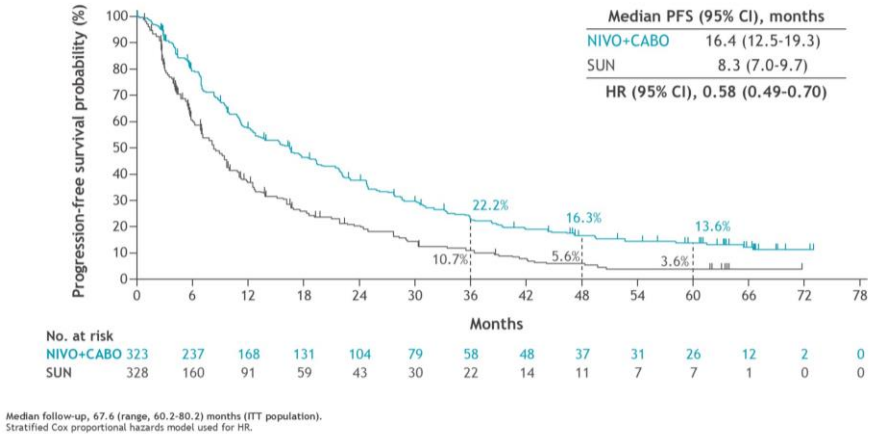
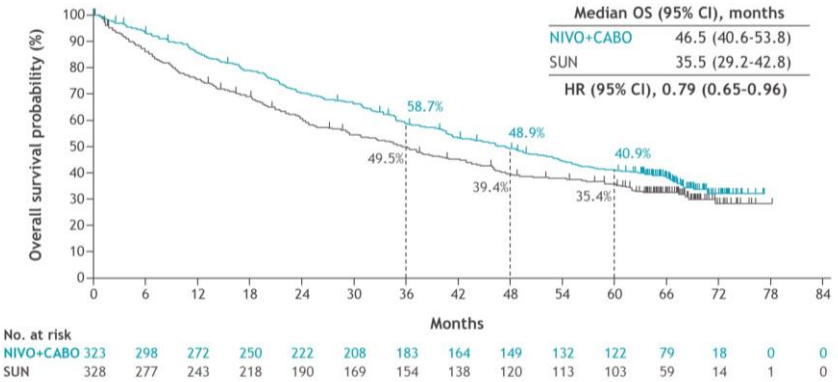
Final Analysis Checkmate 9ER

PFS per BICR in the *ITT population*



Median follow-up, 67.6 (range, 60.2-80.2) months (ITT population).
Stratified Cox proportional hazards model used for HR.

OS in the *ITT population*



Median follow-up, 67.6 (range, 60.2-80.2) months (ITT population).
Stratified Cox proportional hazards model used for HR.

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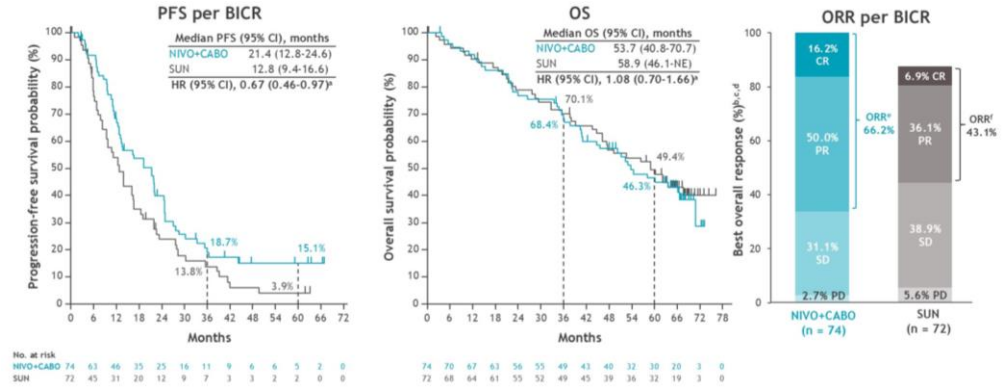
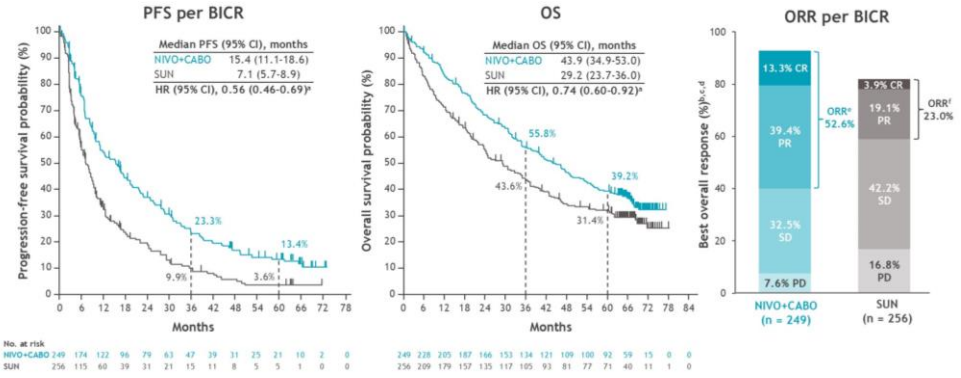
PFS per BICR, OS, and ORR per BICR in IMDC favorable risk



Good risk patients:

- Active surveillance
- Local treatment
- IO based combinations
- *TKI monotherapy*

PFS per BICR, OS, and ORR per BICR in IMDC intermediate/poor risk



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Final Analysis Checkmate 9ER

Efficacy outcomes by baseline organ sites of metastases all favored NIVO + CABO (HRs 0.43–0.75)

Outcome	Liver[a,b]		Bone[a,b]		Lung[a,b]	
	NIVO+CABO (n = 73)	SUN (n = 56)	NIVO+CABO (n = 79)	SUN (n = 75)	NIVO+CABO (n = 241)	SUN (n = 251)
Median PFS (95% CI), mo	10.9 (7.0-15.2)	6.2 (2.9-8.3)	13.8 (8.3-20.1)	5.3 (3.9-8.2)	16.4 (12.3-21.4)	8.3 (6.9-9.7)
HR (95% CI)[c]	0.55 (0.37-0.82)		0.43 (0.30-0.64)		0.56 (0.46-0.69)	
Median OS (95% CI), mo	37.6 (23.5-49.9)	22.1 (9.9-29.3)	34.8 (21.4-58.9)	20.7 (12.7-29.2)	47.5 (40.6-55.8)	32.4 (24.6-38.0)
HR (95% CI)[c]	0.65 (0.43-0.97)		0.66 (0.45-0.95)		0.75 (0.60-0.94)	
ORR (95% CI), %	52.1 (40.0-63.9)	21.4 (11.6-34.4)	49.4 (37.9-60.9)	9.3 (3.8-18.3)	57.3 (50.8-63.6)	27.9 (22.4-33.9)

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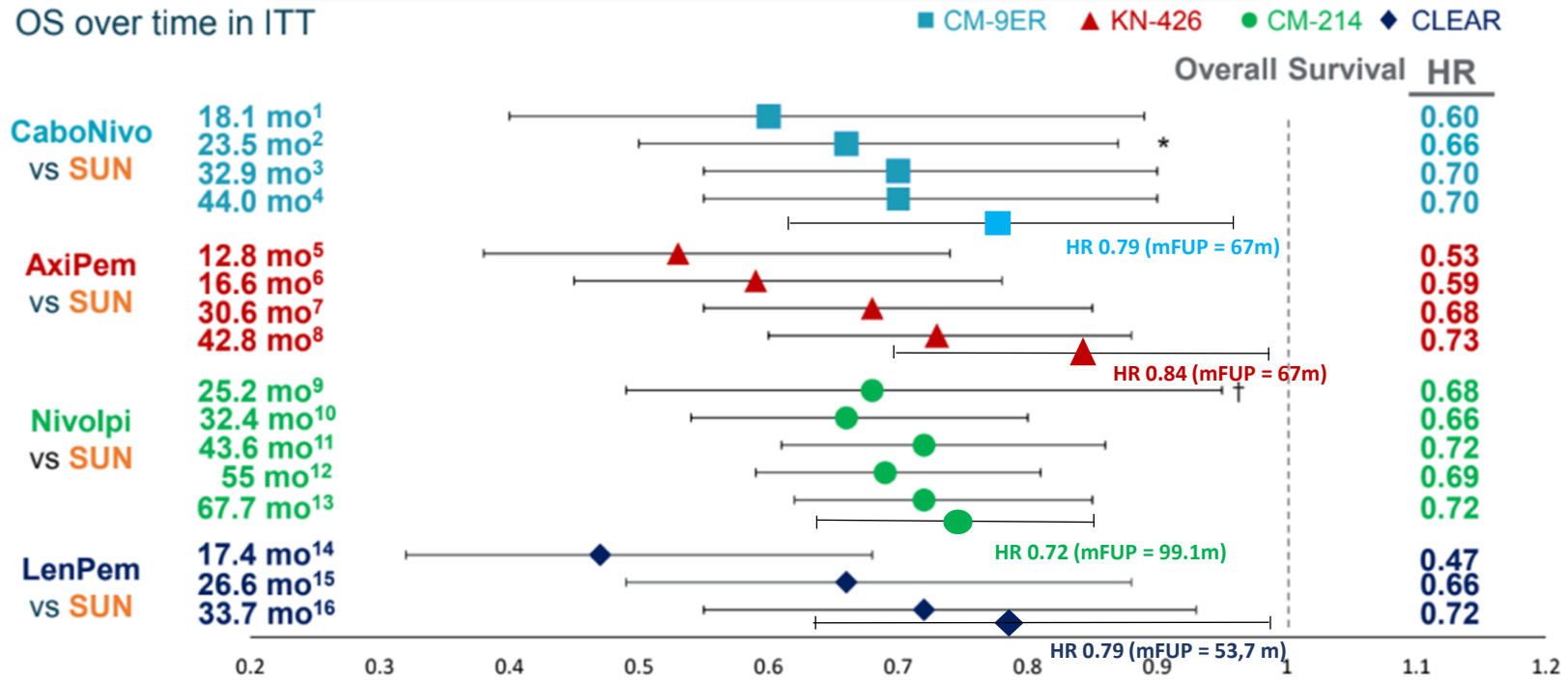
IO-BASED COMBINATIONS IN RCC



Courtesy of J. Molina-Cerrillo

Rini BI, et al. N Engl J Med. 2019 Mar 21;380(12):1116-1127; Motzer R, et al. N Engl J Med. 2021 Apr 8;384(14):1289-1300; Choueiri TK, et al. N Engl J Med. 2021 Mar 4;384(9):829-841.

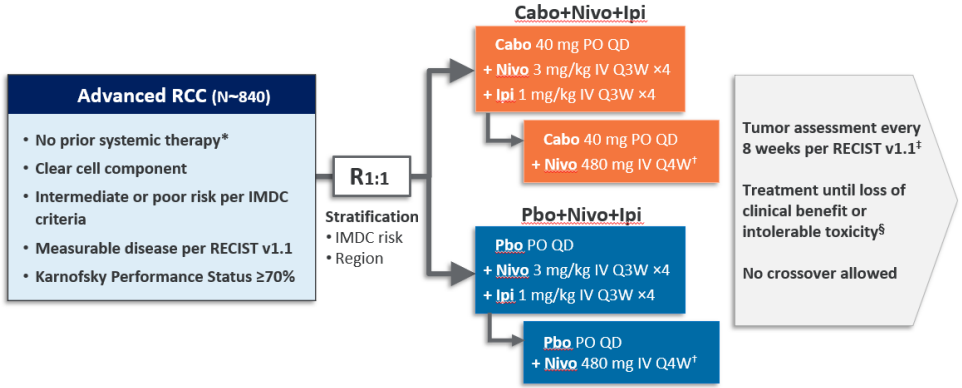
IO-BASED COMBINATIONS IN RCC

	KEYNOTE 426		CLEAR		CHECKMATE 9ER			CHECKMATE 214
Min FUP (m)	13	43	27	50	18	44	67	99
ORR (%)	59 vs 36	60 vs 40	71 vs 36	71 vs 37	56 vs 27	56 vs 28	56 vs 27	42 vs 28
CR (%)	6 vs 2	10 vs 3.5	16 vs 4	18 vs 5	8 vs 5	13 vs 5	14 vs 5	12 vs 3
PD (%)	11 vs 17	11 vs 17	5 vs 14	5 vs 14	6 vs 14	7 vs 14	6.5 vs 14	18 vs 14
mDoR (m)	NR vs 15	24 vs 15	26 vs 15	27 vs 15	20 vs 12	22 vs 16	22 vs 15	82.8 vs 19.8
mPFS (m)	15 vs 11	16 vs 11	24 vs. 9	24 vs 9	17 vs 8	17 vs 8	16 vs 8	8.3 vs 8.3
mOS (m)	NR vs NR	46 vs 40	NR vs NR	54 vs 54	NR vs NR	50 vs 36	46 vs 35	46.7 vs 26

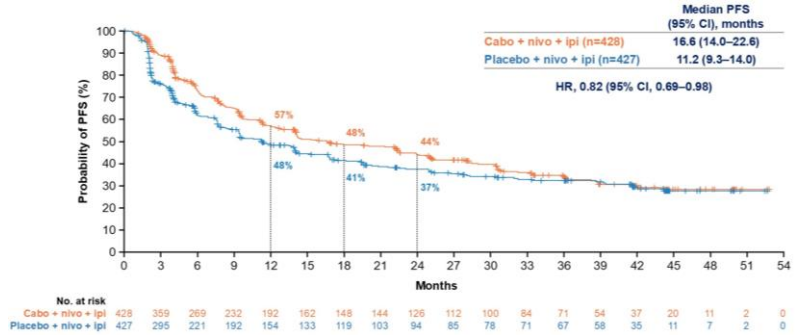
Rini BI, et al. N Engl J Med. 2019 Mar 21;380(12):1116-1127; Motzer R, et al. N Engl J Med. 2021 Apr 8;384(14):1289-1300; Choueiri TK, et al. N Engl J Med. 2021 Mar 4;384(9):829-841.

OVERALL SURVIVAL DATA FROM THE 1st TRIPLET

COSMIC-313 Study Design



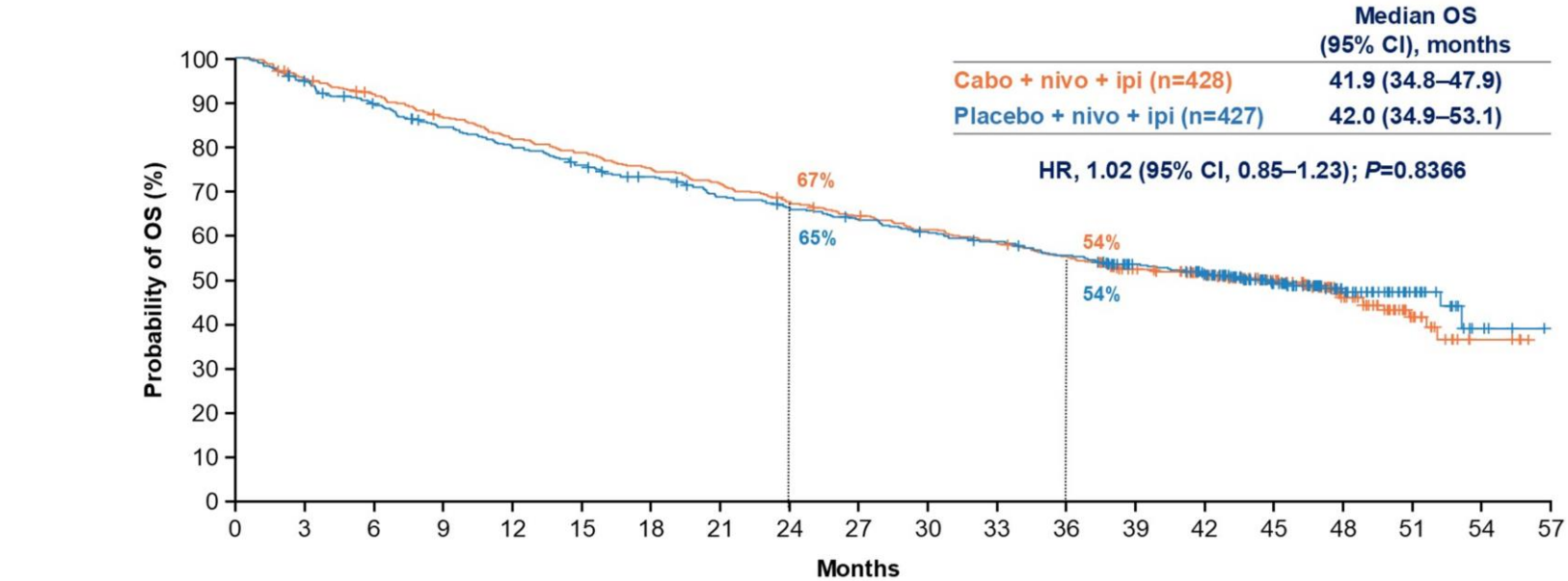
Progression-free Survival (updated analysis, mFUP = 45 months)



	Cabo+Nivo+Ipi	Pbo+Nivo+Ipi
ORR (95% CI), %	43 (37.2–49.2)	36 (30.1–41.8)
CR, n (%)	7 (3)	9 (3)
PR, n (%)	112 (41)	89 (32)
PD, n (%)	23 (8)	55 (20)

Choueiri TK, et al. N Engl J Med. 2023 May 11;388(19):1767-1778.
Albiges L, et al. ASCO GU 2025

OVERALL SURVIVAL DATA FROM THE 1st TRIPLET



Median follow-up of 45.0 months.

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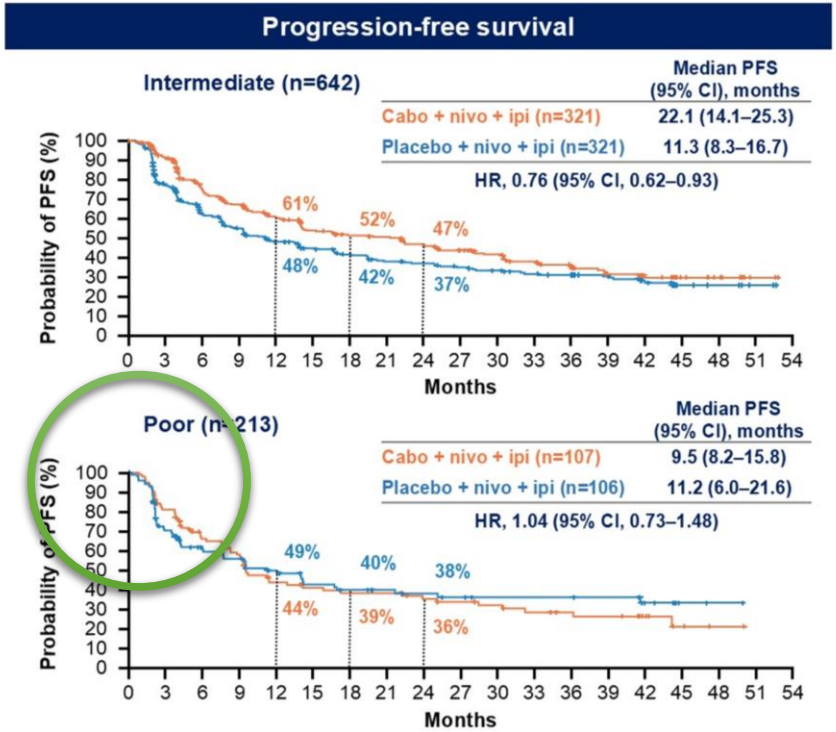
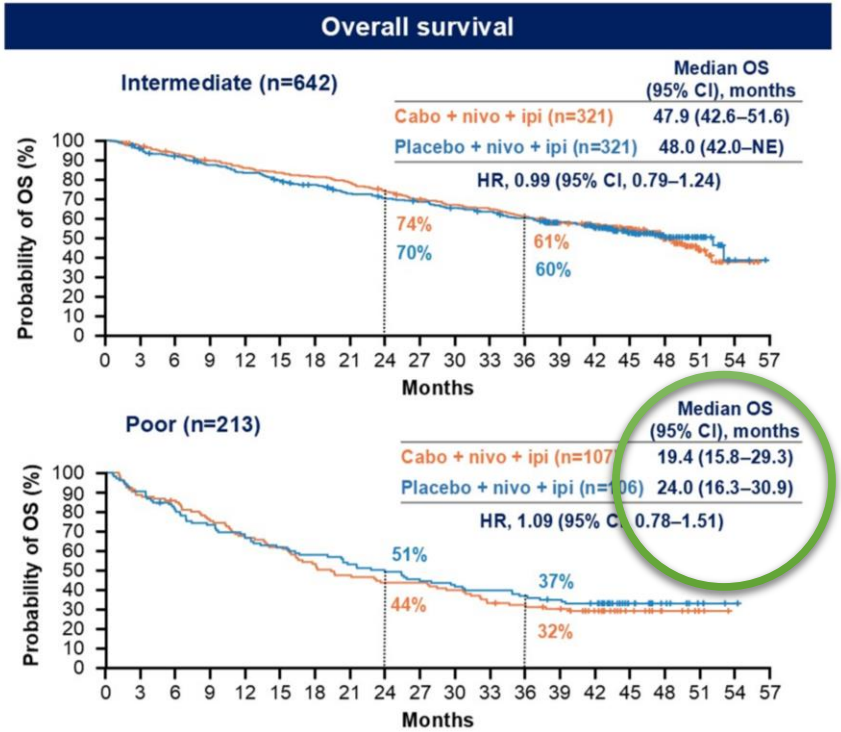
OVERALL SURVIVAL DATA FROM THE 1st TRIPLET





Median follow-up of 45.0 months.

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OVERALL SURVIVAL DATA FROM THE 1st TRIPLET

Treatment exposure and dose modifications

	Cabo + nivo + ipi (n=426)	Placebo + nivo + ipi (n=423)
Median duration of exposure of study treatment, months (range)	13.7 (0.2–53.4)	10.3 (0.1–55.3)
Median average daily dose of cabo/placebo, mg (range)	22.4 (3.6–40.0)	35.2 (0.8–40.0)
Median nivo infusions per patient, n (range)	11.0 (1–52)	9.0 (1–48)
1 / 2 / 3 / 4 cycles of ipi administered, %	7 / 22 / 13 / 58	6 / 7 / 13 / 74
Dose modification (any treatment component) due to AE, %	92	76
Treatment-related AE leading to discontinuation of ≥1 component, %	49	26

Most common treatment-related AEs (any grade in ≥25% of patients)

	Cabo + nivo + ipi (n=426)		Placebo + nivo + ipi (n=423)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Treatment-related AE, %	**99**	**75**	**91**	**43**
Alanine aminotransferase increased	46	26	19	6
Aspartate aminotransferase increased	44	19	17	5
Diarrhea	43	5	21	3
Palmar-plantar erythrodysesthesia syndrome	29	4	5	0
Hypothyroidism	26	<1	17	0
Hypertension	25	9	7	2
Pruritus	21	0	26	<1

- Use of systemic immune-modulating medications* for AE was 73.0% in the cabo + nivo + ipi arm and 56.7% in the control arm

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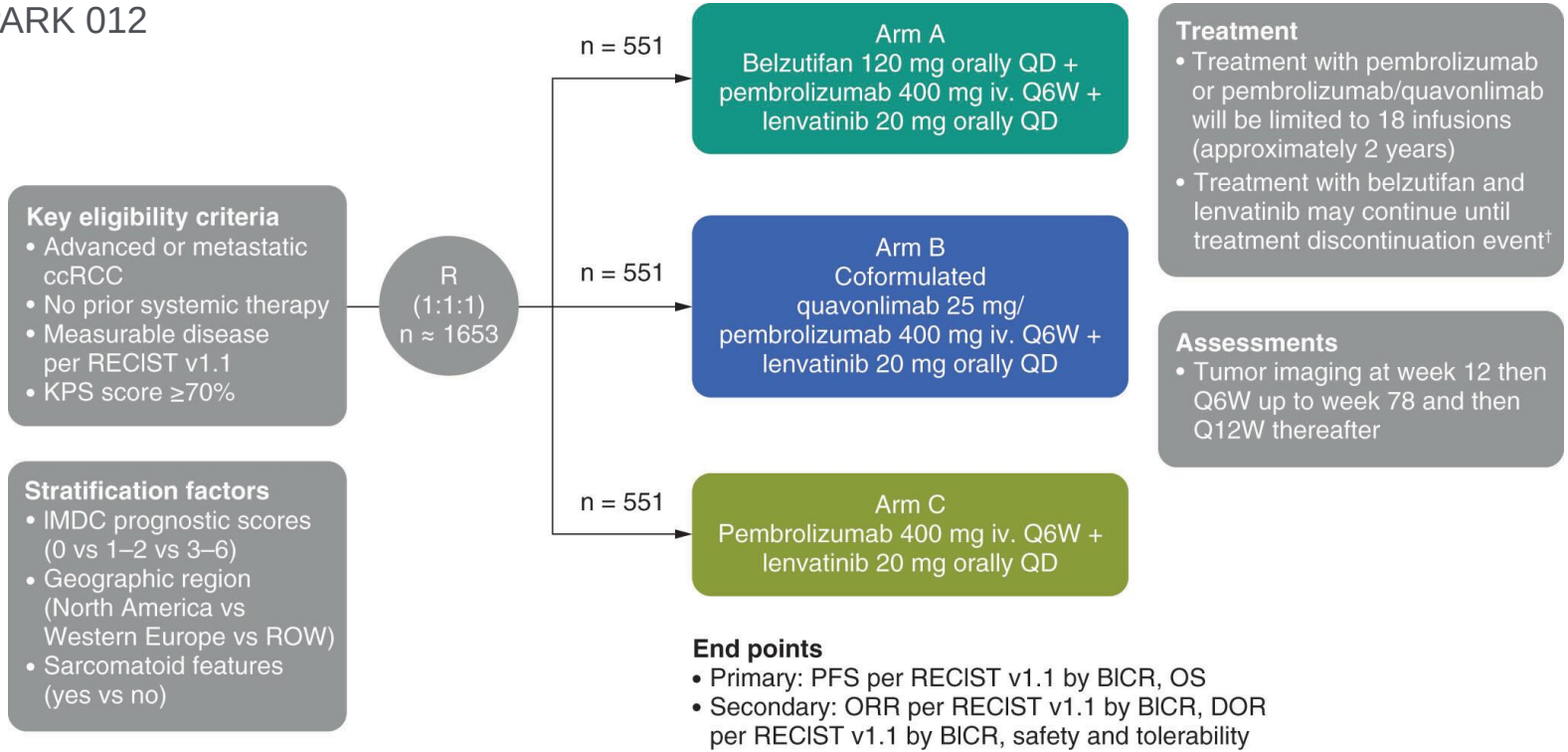
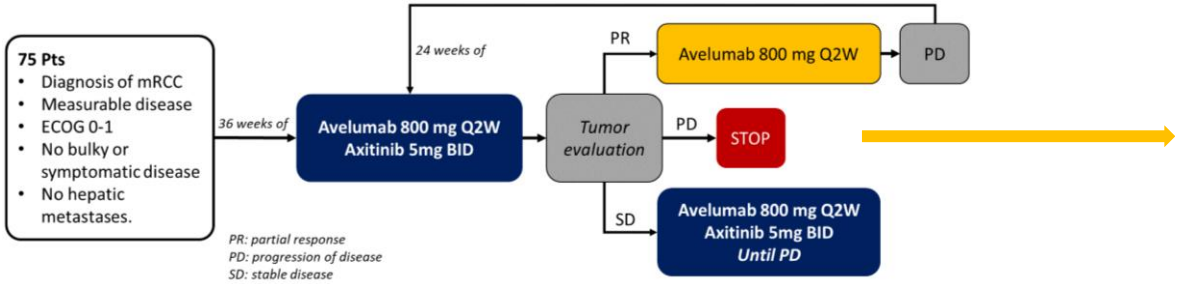
LITESPARK 012



www.clinicaltrials.gov

TIDE-A STUDY (Adapting treatment/response)

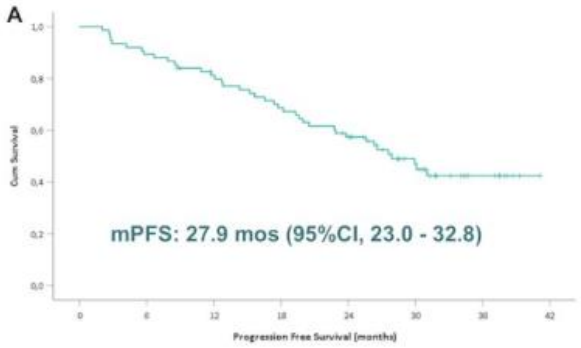


N=29 patients (stop axitinib at W36).

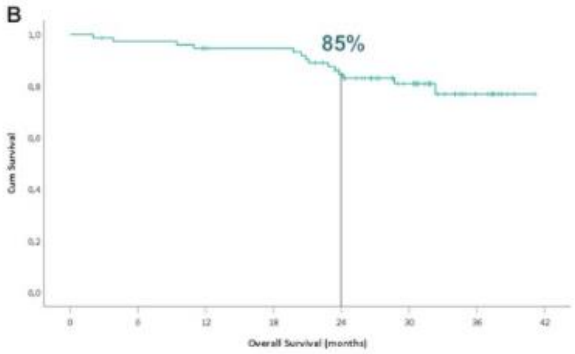
- median PFS = NR (24m PFS rates 58%)
- median OS = NR (24-m OS rates 82%)

mFUP = 31.7 months

Progression Free Survival

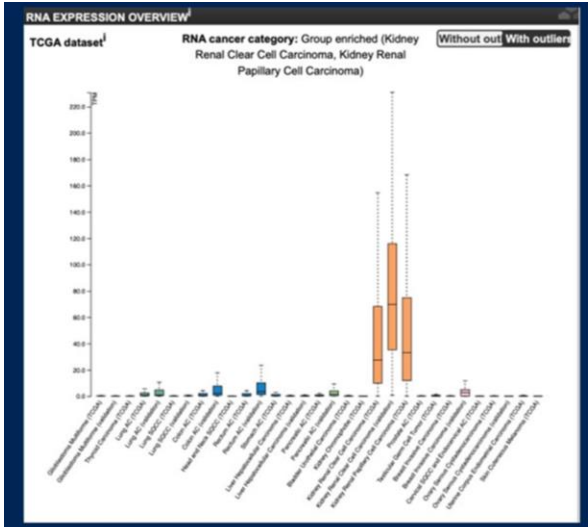


Overall Survival



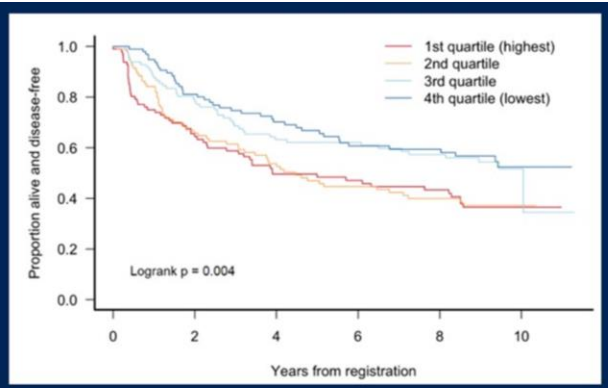
Tumor response of axitinib reintroduction (N=21)

KIM1 AS DIAGNOSTIC AND PROGNOSTIC BIOMARKER



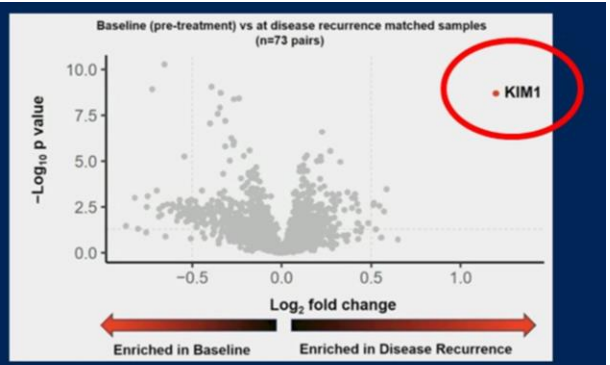
Kidney Injury Molecule-1

↑↑↑ ccRCC, pRCC, chRCC (TCGA)



Plasma KIM-1

ASSURE Trial DFS



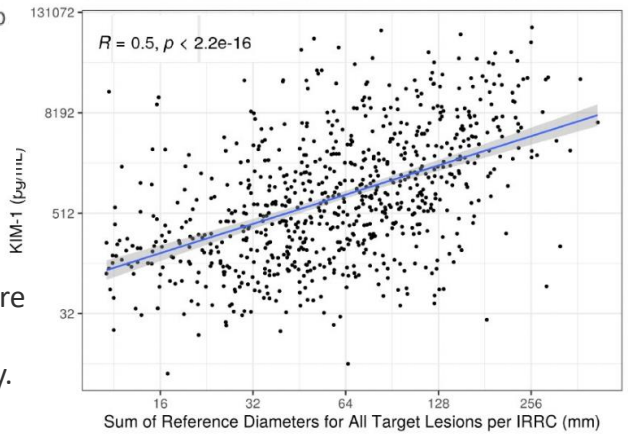
Plasma KIM-1

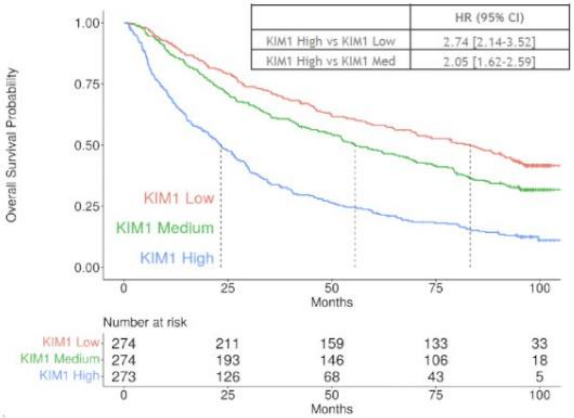
IMMOTION010

Han et al, 2002, Xu et al 2021

KIM1 AS DIAGNOSTIC AND PROGNOSTIC BIOMARKER (CM 214)

High baseline KIM-1 levels were associated with worse IMDC risk and no prior nephrectomy.

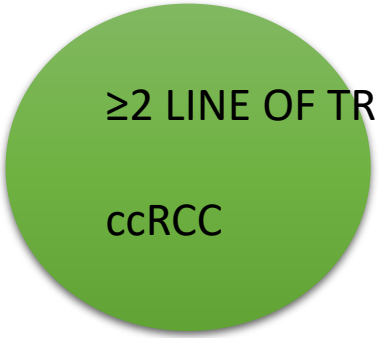




Higher baseline KIM-1 was associated with worse OS

KIM1 decrease associated with response to Nivo Ipi

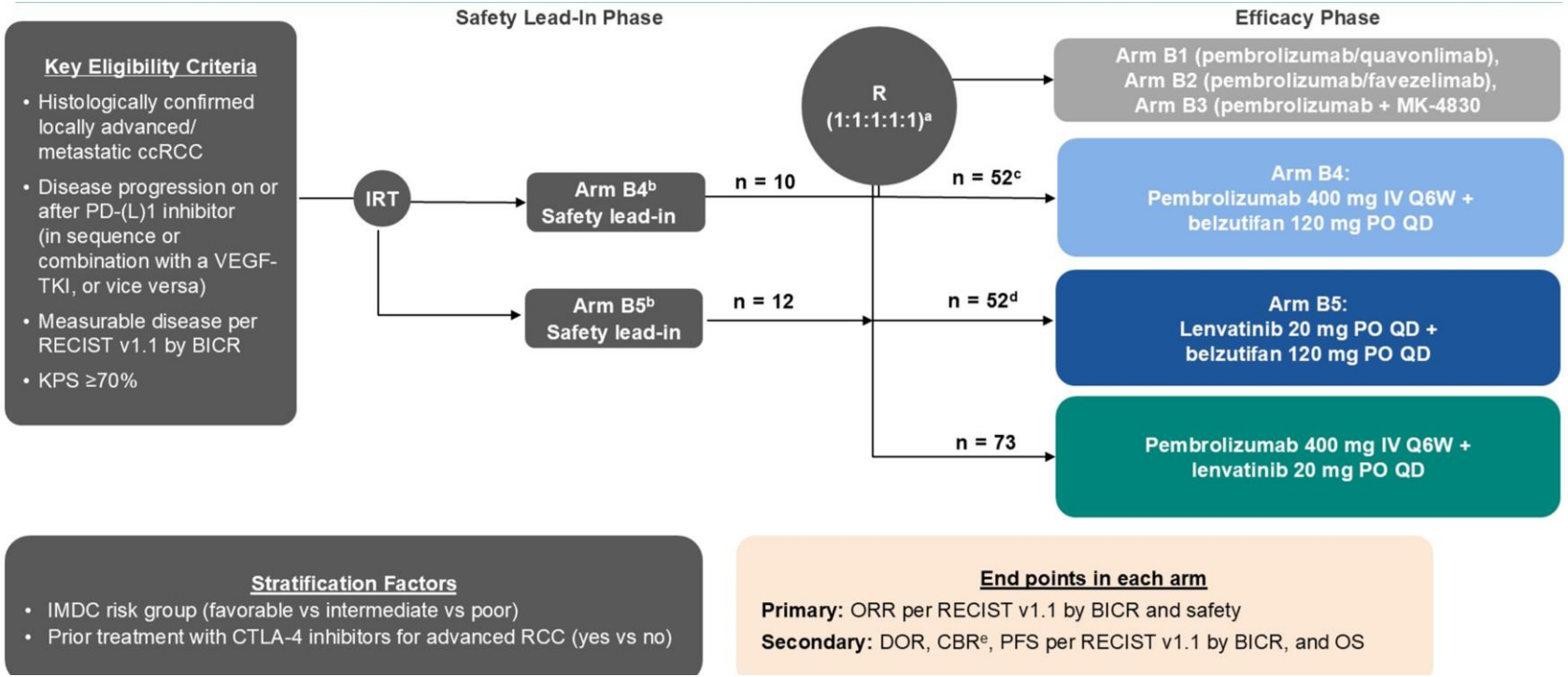
3 wks KIM-1 change	N (%)	ORR, % (95% CI)	mPFS, months	mOS, months
>30% Decrease	140 (31.7)	69.3 (60.9-76.8)	70.8 (17.8- NR)	85.4 (63.1-NR)
>10-30% Decrease	87 (19.7)	36.8 (26.4-47.8)	11.4 (6.3-18.2)	66.1 (40.4-80.1)
<10% Change	86 (19.5)	30.2 (20.8-41.1)	15.4 (10.3-20.7)	52.7 (30.3-70.7)
>10-30% Increase	56 (12.7)	23.2 (13.0-36.4)	7.1 (4.2-16.8)	40.3 (23.8-58.4)
>30% Increase	72 (16.3)	13.9 (6.9-24.1)	4.2 (3.0-8.1)	26.6 (18.8-38.4)



≥2 LINE OF TREATMENT IN ADVANCED DISEASE

ccRCC

KEYMAKER – U03B Substudy 03B Study Design



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KEYMAKER – U03B Substudy

	Arm B4 Pembrolizumab + belzutifan n = 62	Arm B5 Lenvatinib + belzutifan n = 64	Pembrolizumab + lenvatinib n = 73
Age, median (range), years	62 (32-86)	60 (33-80)	63 (36-85)
Sex, n (%)			
Male	47 (75.8)	49 (76.6)	57 (78.1)
Female	15 (24.2)	15 (23.4)	16 (21.9)
ECOG PS, n (%)			
0	20 (32.3)	30 (46.9)	33 (45.2)
1	40 (64.5)	34 (53.1)	40 (54.8)
IMDC risk category, n (%)			
Favorable	14 (22.6)	15 (23.4)	15 (20.5)
Intermediate	41 (66.1)	38 (59.4)	50 (68.5)
Poor	7 (11.3)	11 (17.2)	8 (11.0)
Sarcomatoid features, n (%)			
Yes	4 (6.5)	3 (4.7)	13 (17.8)
No	29 (46.8)	30 (46.9)	28 (38.4)
Unknown/missing	29 (46.8)	31 (48.4)	32 (43.8)
Prior first-line CTLA-4 inhibitor use, n (%)	23 (37.1)	23 (35.9)	26 (35.6)
Number of prior lines of therapy, n (%)			
1	5 (8.1)	14 (21.9)	10 (13.7)
2	22 (35.5)	23 (35.9)	27 (37.0)
≥3	35 (56.5)	27 (42.2)	36 (49.3)

Data cutoff date: March 22, 2024.

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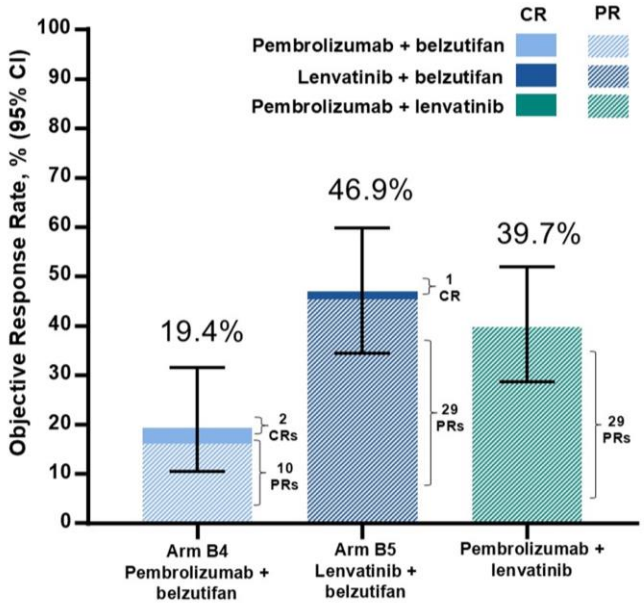
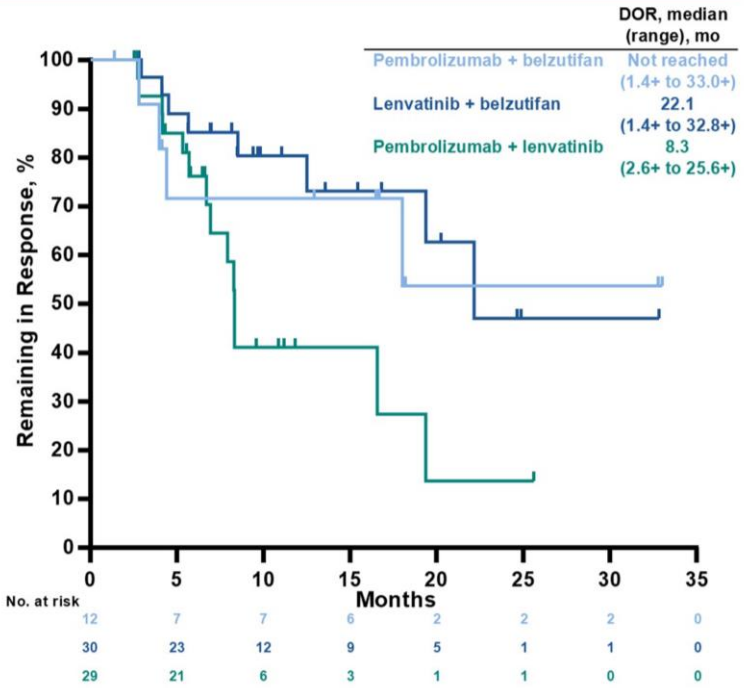
KEYMAKER – U03B Substudy 03B

Objective Response Rate per RECIST v1.1 by BICR



Data cutoff date: March 22, 2024.



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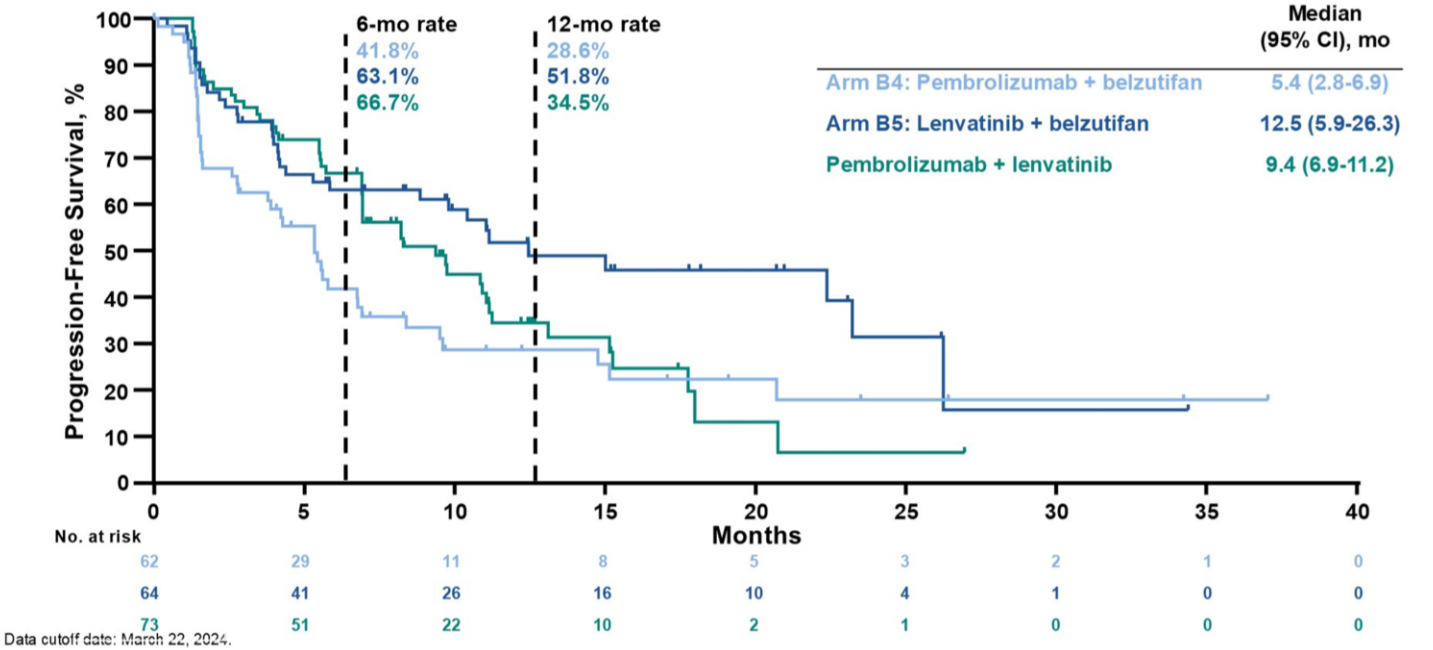
KEYMAKER – U03B Substudy 03B

Progression-Free Survival per RECIST v1.1 by BICR



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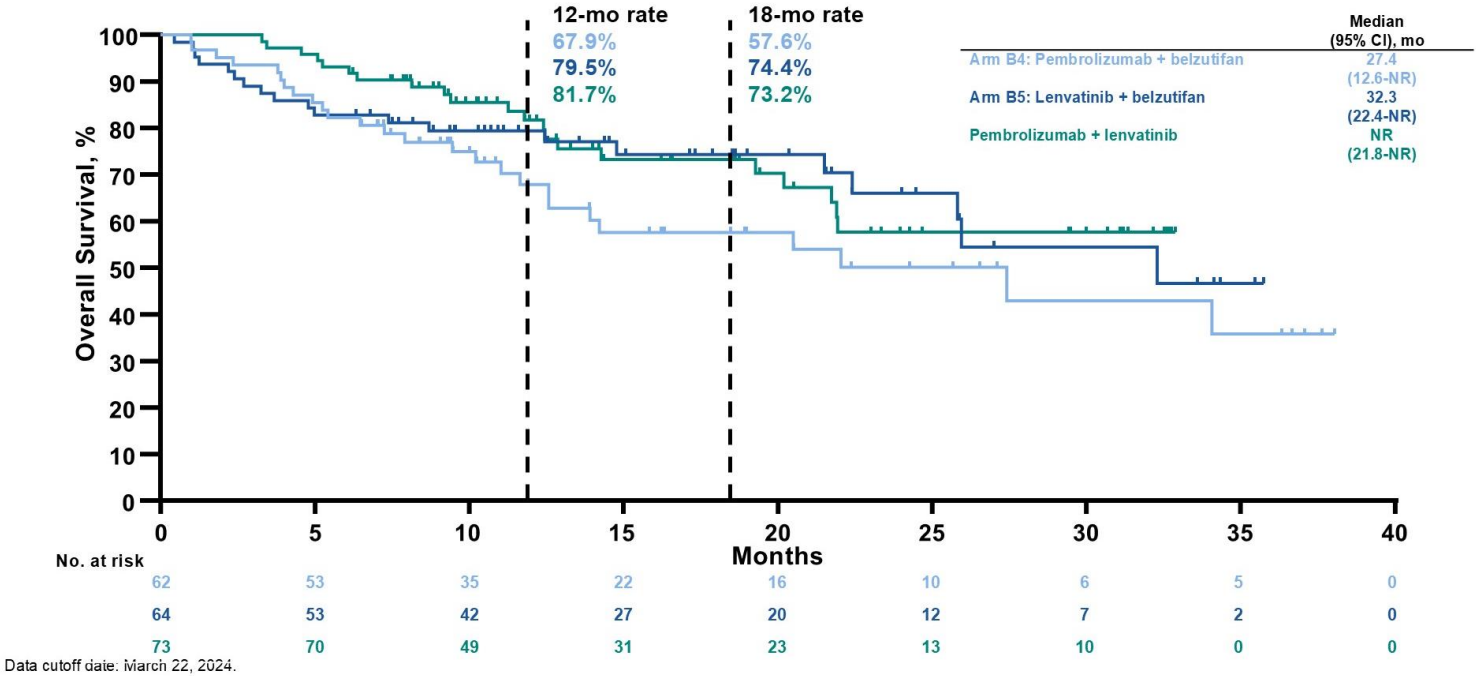
KEYMAKER – U03B Substudy

Overall Survival



Data cutoff date: March 22, 2024.

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KEYMAKER – U03B Substudy

Adverse Event Summary

	Arm B4 Pembrolizumab + belzutifan n = 62	Arm B5 Lenvatinib + belzutifan n = 64	Pembrolizumab + lenvatinib n = 73
All-cause AEs			
Any grade	62 (100)	63 (100)	73 (100)
Grades 3-5	40 (64.5)	49 (77.8)	56 (76.7)
Led to dose reduction of belzutifan	13 (21.0)	8 (12.7)	-
Led to dose reduction of lenvatinib	-	38 (60.3)	41 (56.2)
Led to treatment interruption of any drug	34 (54.8)	45 (71.4)	43 (58.9)
Led to treatment discontinuation of any drug	10 (16.1)	9 (14.3)	12 (16.4)
Death	2 (3.2)	3 (4.8)	2 (2.7)
Treatment-related AEs			
Any grade	59 (95.2)	60 (95.2)	72 (98.6)
Grades 3-5	26 (41.9)	38 (60.3)	36 (49.3)
Led to treatment discontinuation of any drug	7 (11.3)	6 (9.5)	9 (12.3)
Death	0	2 (3.2)[a]	1 (1.4)[b]

[a]Intracerebral hemorrhage and intracranial hemorrhage. [b]Esophageal perforation. Data cutoff date: March 22, 2024.

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KEYMAKER – U03B Substudy

	Pembrolizumab/ quavonlimab n = 20	Pembrolizumab/ favezelimab n = 20	Pembrolizumab + MK-4830 n = 24	Pembrolizumab + lenvatinib n = 73
ORR (95% CI), %	30.0 (11.9-54.3)	0 (0.0-16.8)	0 (0.0-14.2)	39.7 (28.5-51.9)
CBR (95% CI), %	35.0 (15.4-59.2)	5.0 (0.1-24.9)	0 (0.0-14.2)	57.5 (45.4-69.0)
Best response, n (%)				
CR	0	0	0	0
PR	6 (30.0)	0	0	29 (39.7)
SD	7 (35.0)	9 (45.0)	5 (20.8)	32 (43.8)
SD ≥6 months	1 (5.0)	1 (5.0)	0	13 (17.8)
PD	7 (35.0)	10 (50.0)	18 (75.0)	12 (16.4)
Not available	0	1 (5.0)	1 (4.2)	0
DOR, median (range), months	NR (5.6+ to 19.4+)	—	—	8.3 (2.6+ to 25.6+)
Participants with response duration ≥18 months, n (%)	1 (100)	—	—	2 (27.4)

"+" indicates ongoing response at the last assessment. NR, not reached.

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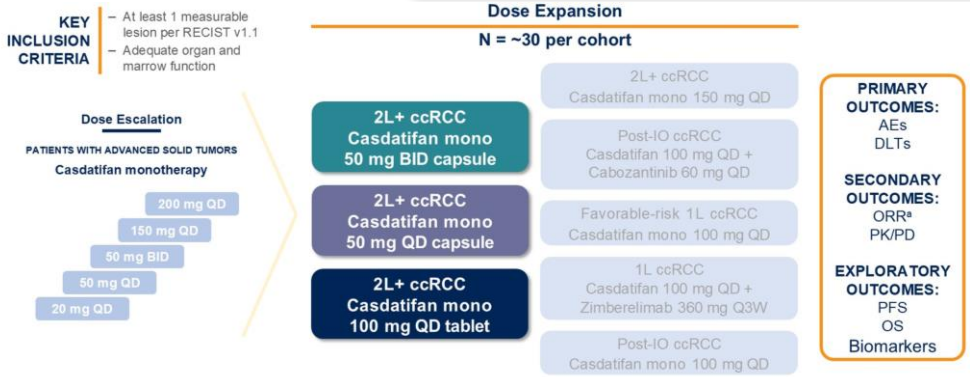
ARC-20 TRIAL



1L, first-line treatment setting; 2L+, second-line treatment setting or greater; DLT, dose-limiting toxicity; IO, immunotherapy.
[a]Assessed by the investigator according to RECIST v1.1.

Efficacy-Evaluable Population[a]	50 mg BID (n = 32)	50 mg QD (n = 28)	100 mg QD (n = 27)
Median follow-up, mo (range)	15 (7–19+)	12 (9–14+)	5 (2–6+)
Confirmed ORR, % (n) (95% CI)	**25% (8) (11.5, 43.4)**	**29% (8) (13.2, 48.7)**	**33% (9) (16.5, 54.0)**
Best Overall Response[b], n (%)	10 (31%)	9 (32%)	9 (33%)
CR	0	1 (4%)	0
PR	10 (31%)	8 (29%)	9 (33%)
SD	16 (50%)	15 (54%)	14 (52%)
PD	6 (19%)	4 (14%)	2[c] (7%)

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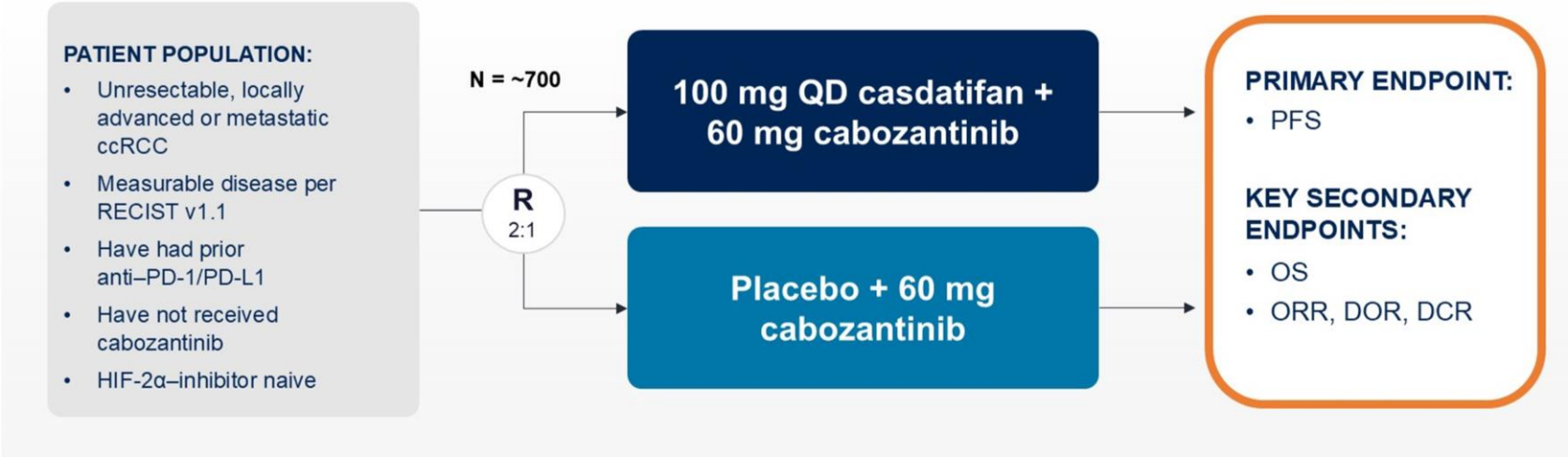
ARC-20 TRIAL

Anticipated first half 2025

PEAK-1



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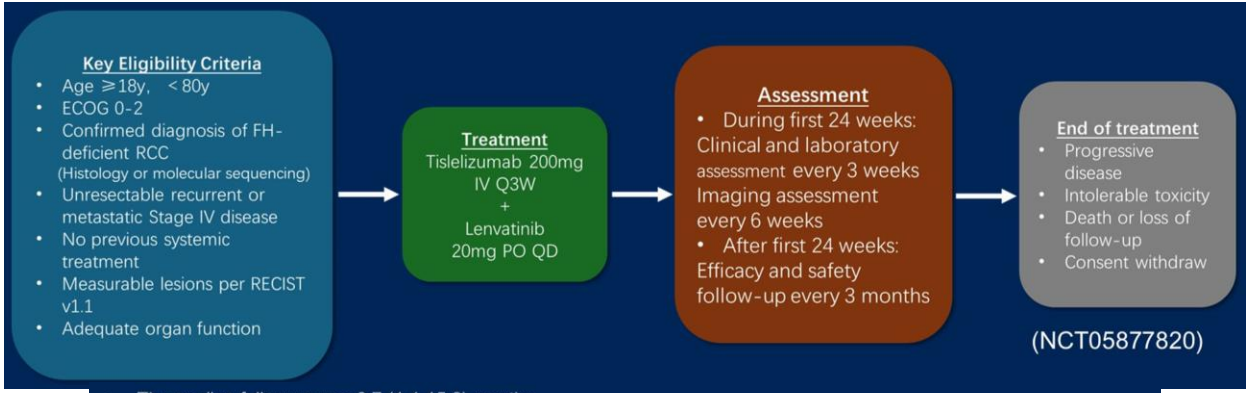
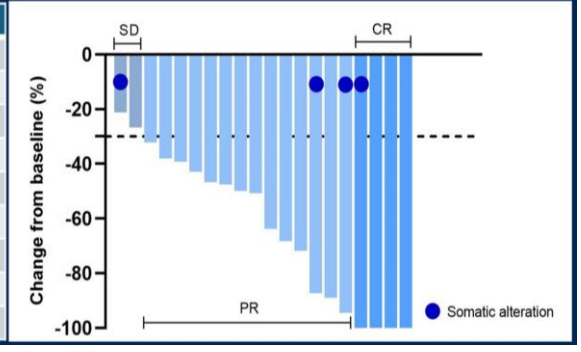
LENVATINIB + TISLELIZUMAB FH-RCC



Single arm
Single center

- The median follow up was 9.7 (1.4-15.2) months.
- ORR：90% (18/20)； DCR: 100%.
- Both hereditary and sporadic FH-RCC benefited from the treatment.

Response	Cohort (n=20)
ORR, % (95% CI)	90 (66.9-98.3)
Best response, No. (%)	
CR	4 (20)
PR	14 (70)
SD	2 (10)
PD	0 (0)
Disease control rate, % (95% CI)	100 (80.0-100)
Clinical benefit rate, % (95% CI)	85 (61.1-96.0)
Median PFS, months	NR



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BRAIN METASTASES

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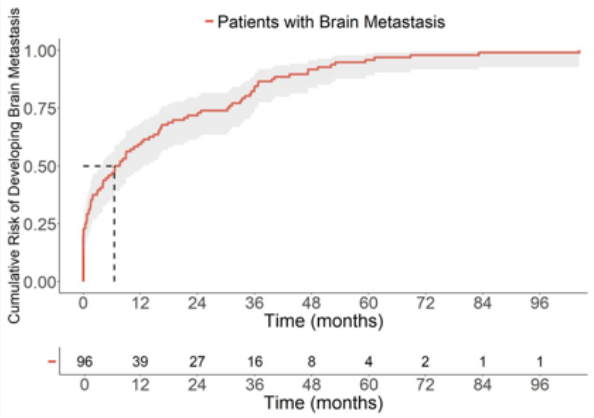
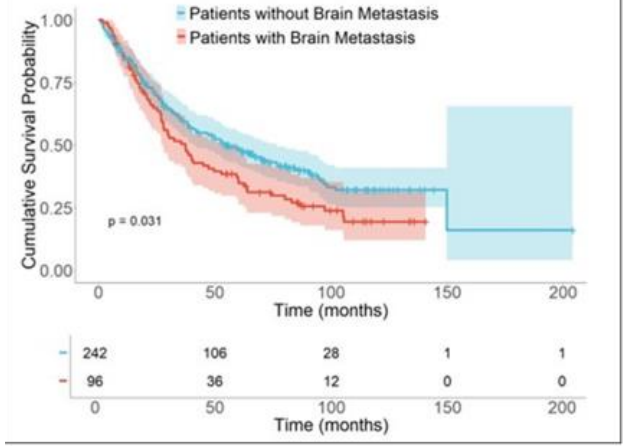
Figure 1. Timing of development of BM after diagnosis of metastatic disease



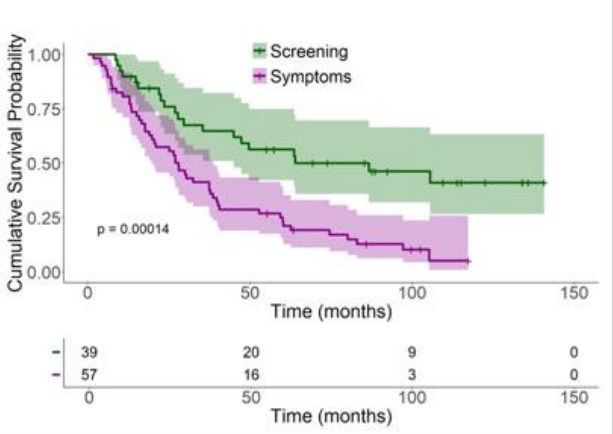
32.2% of patients had BM discovered when metastatic disease was first found. BM continued to develop >5 years after the development of metastatic disease (Figure 1).
mOS of patients was 17.0 mo after the development of BM.

Figure 2. OS of patients with or without BM



OS from the time of development of metastatic disease was worse for patients with BM than for those without BM (37.3 vs 54.3 mo, p=0.03) (Figure 2).

Figure 4. OS with BM discovered by screening or symptoms



Median OS from time of initial metastatic disease was 86.7 mo (95% CI: 44.9-NR mo) versus 27.9 mo (95% CI: 19.8-38.5 mo) for those who underwent screening versus those who did not (p=0.00016) (Figure 4).

- BM detected on screening were smaller (mean 11.0 vs 18.5 mm, p=0.0029).

- ❑ 28% of patients with BM
- ❑ 32% BM discovered at M1 diagnosis
- ❑ Median OS from BM development = 17.0 months
- ❑ Better OS in patients without BM vs BM
- ❑ Trend to better OS in patients with later BM presentation vs at dx
- ❑ **Better OS in patients with BM discovered by symptoms vs screening (86.7 vs 27.9 months)**

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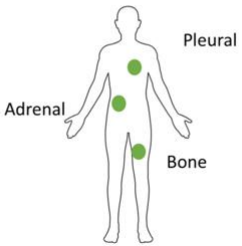
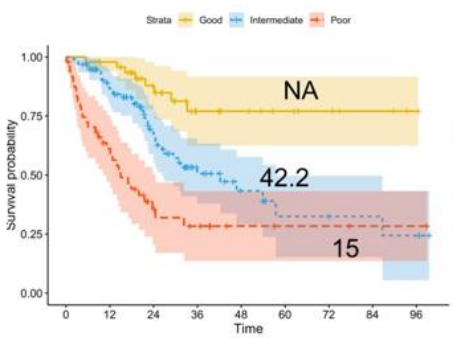
SITE OF METASTASES + IMDC (WITH IO TREATMENT)



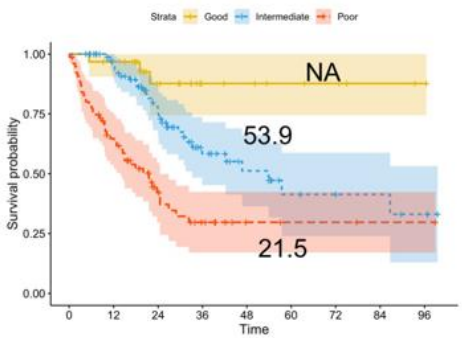
IMDC factors	Score
<1 year from time of diagnosis to start of systemic treatment	+1
KPS < 80%	+1
Hemoglobin < LLN	+1
Corrected calcium > ULN	+1
Neutrophils > ULN	+1
Platelets > ULN	+1
Site of metastasis	
• Pleural	+1
• Liver	+1
• Adrenal	+1
• Any other site of metastasis	0

	IMDC N (%)	IMDC-sm N (%)
1st Line		
Good	47 (25)	31 (16)
Intermediate	96 (50)	84 (44)
Poor	48 (25)	76 (40)
≥2nd Line		
Good	60 (18)	28 (8)
Intermediate	198 (59)	164 (49)
Poor	76 (23)	142 (43)

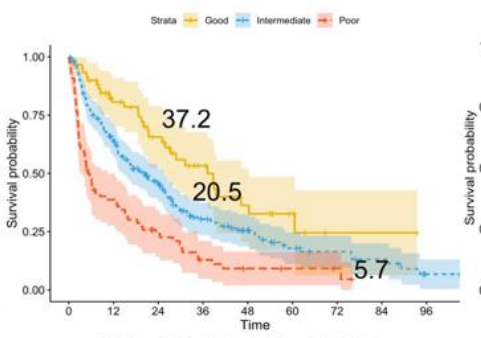
Table 3. Risk groups distribution with both prognostic scores



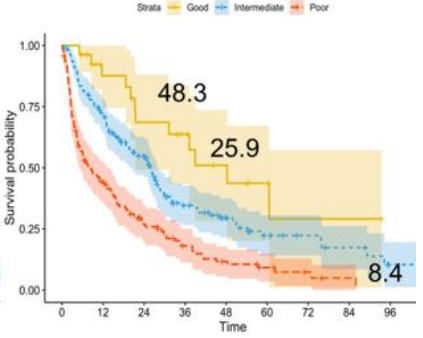
AIC: 691.5; BIC 696.2



AIC: 686.22; BIC 690.91



AIC: 2404.7; BIC: 2411.7



AIC: 2397.5; BIC: 2404.5

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CONCLUSIONS

- The final analysis from the Checkmate 9ER continues supporting the significant impact of IO-based combinations in the first line setting.
- How can we improve these data? Triplets Will be the answer? Not yet.
- Adaptive trials according to response (ideally molecularly based) Will be helpful for clinical practice.
- Promising results in pretreated patients, but based in the same strategies, we need novel MoA in kidney cancer.

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