Panel Discussion

④ 75/M Bony Visit

⇒ Comorbidity ⇒ • DM (+)

• ↑ Cocaine (+)

• B.P ??? +

• No Cardiac issue

⇒ Surgery

⇒ RCC in 2016 / Clear cell Carcinoma

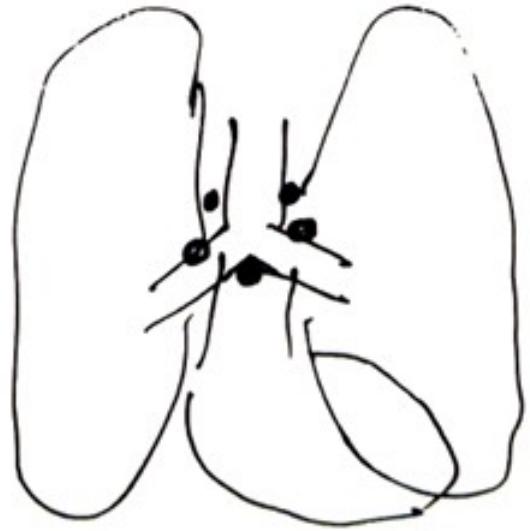
⇒ NU Sx

⇒ Habits ⇒ Occasional drink

⇒ Habits ⇒ Occasional drink

(8) Recurrence clear cell

⇒ Nearly after 9 years



. Sx ⇒ not possible

. RT ⇒ not possible

MMC Registration Number

Consultant's Signature

(c) Why in Intermediate risk group < LOH/Ca .?.?? >

(d) Multiple Rx option.

- Not Curable
- Control

- Goal → QOL
  → Symptom Control
  → S/E

- Response ↓↓↓

	Azithro + Pentoro	Cefix + Nitro	Ipl + Nitro	Levo + Pentoro
RR	59.3%	55.7%	42%	71.0 %
S/e	75.8%	75.3%	46%	82.4%
	HyT. 22.2%	12.5%		
long term Survival	2yr - 80%	80%	70%	2yr - 80%
	5yr ?	5yr - ?		5yr - 46%
Schedule	Oral + IV	Oral + IV	IV + IV	Oral + IV.

84r. 35%

⇒ (In your situation looking at need for resistance ⇒ Levofloxacin + Pentoprazole)

⇒ 1st 2 cycle will be in admission. After every cycle ⇒ See your doctor for 14 day.

Understanding the Role of Risk in the Treatment of Metastatic RCC

IMDC Criteria for Metastatic RCC

Karnofsky performance score <80%

Time from initial diagnosis to targeted tx <1 yr

Hemoglobin < LLN

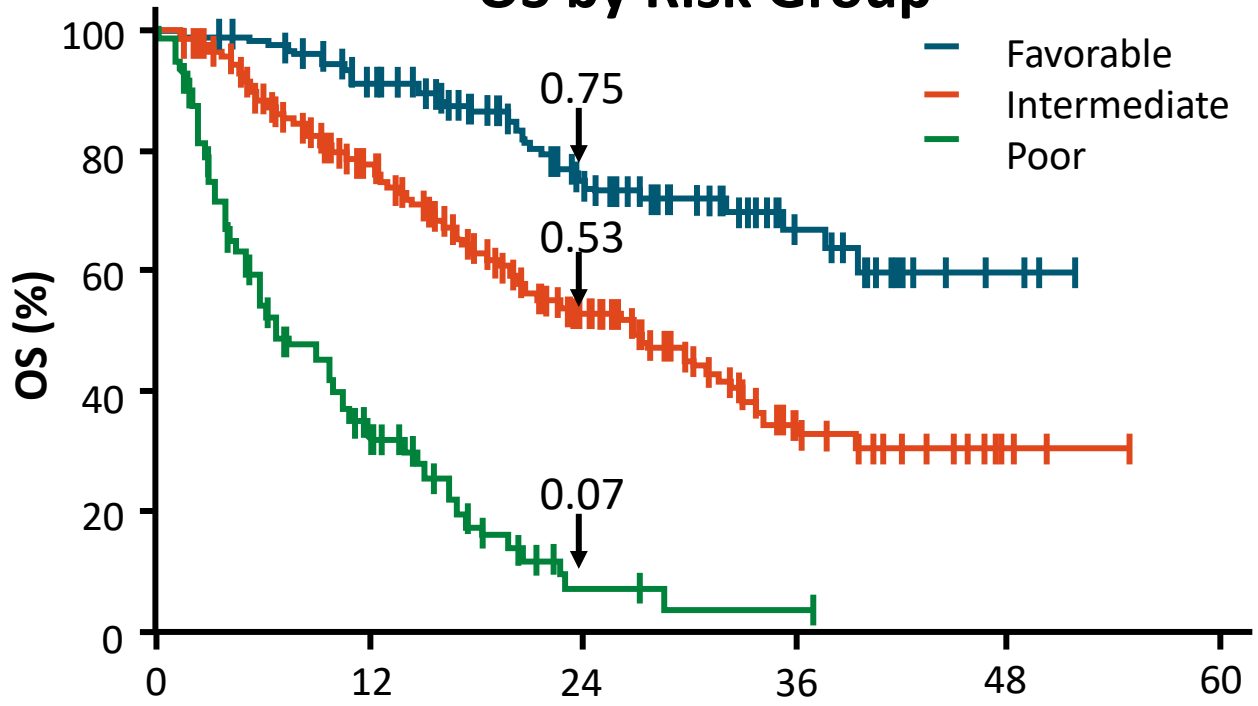
Calcium >10 mg/dL

Platelet count > ULN

Neutrophil count > ULN

- Favorable: 0 risk factors
- Intermediate: 1-2 risk factors
- Poor: 3+ risk factors

OS by Risk Group



No. of Events/No. at Risk

Favorable	11/133	16/110	4/62	2/22	0/3
Intermediate	61/301	50/182	17/82	2/18	0/3
Poor	94/152	19/36	1/3	0/1	0/0

International Kidney Cancer Coalition. Heng. JCO. 2009;27:5794.

Slide credit: clinicaloptions.com

CCO powered by cea

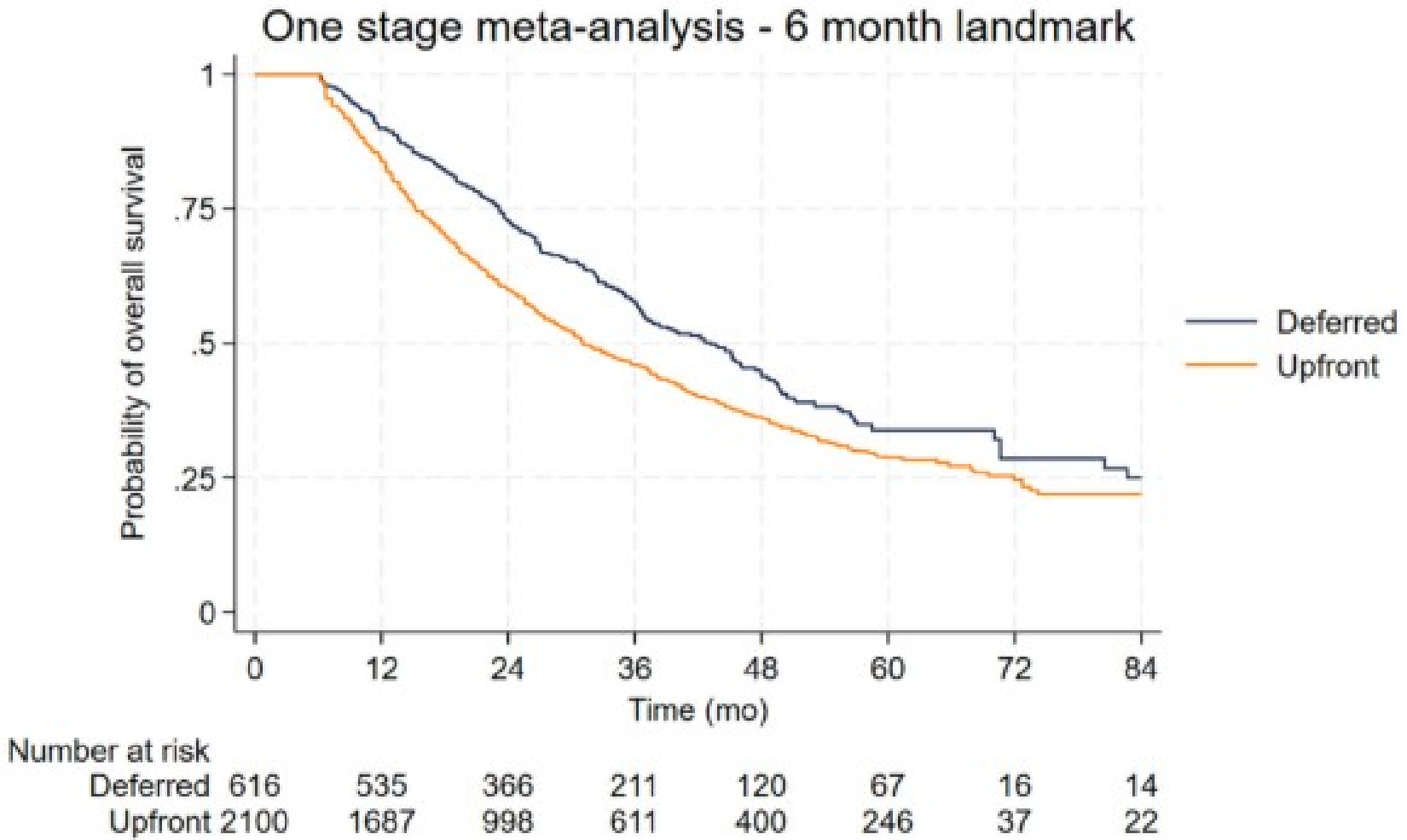


Fig. 2 – Kaplan-Meier survival curve of overall survival derived from one-stage meta-analysis of reconstructed individual patient data using a 6-mo landmark to account for immortal time bias.

#529 Efficacy and safety of SABR with TKI and IO therapy in patients with mRCC

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Background

- Metastatic RCC is a deadly disease and TKI in combination with IO has become a standard therapy for most patients.
- Some of the patients may present with oligo-metastasis and some with metastatic sites related symptoms.
- SABR (Stereotactic Ablative Body Radiotherapy) has been proved to be highly effective for RCC in some studies and with potential immune-enhancing ability.
- The purpose of this study is to investigate the efficacy and safety of SABR with TKI and IO therapy in patients with mRCC.

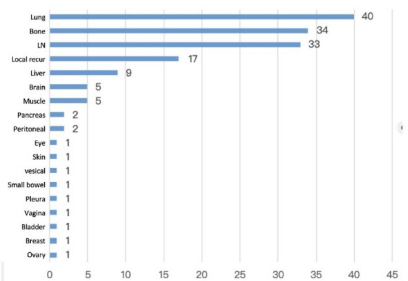
Methods

- This is an ambispective cohort study including pts receiving SABR with TKI and IO at the same time.
- The primary endpoint was PFS. Secondary endpoints included OS, ORR, DCR and TTTC (Time to treatment change). We also analyzed some of the patients' gene alteration characteristics to investigate the relationship between gene alterations and prognosis. Adverse events were evaluated according to CTCAE 5.0.

Results

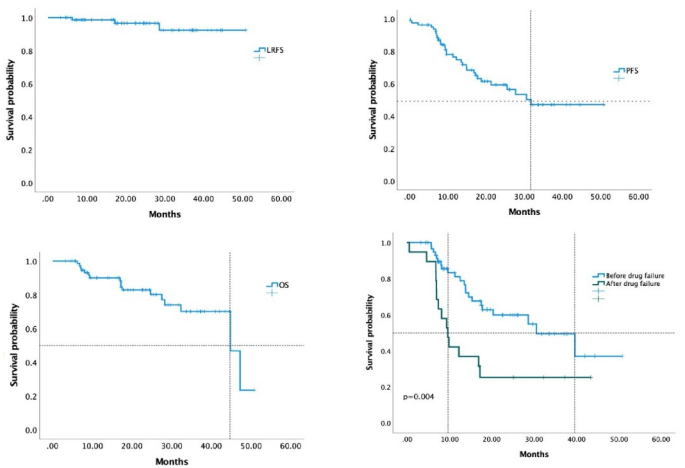
Until Aug 2024, we retrospectively analyzed patients from Mar 2020 to Mar 2024, and prospectively from Mar 2024 to May 2024. A total of 79 patients were included, of whom 72.2% were with ccRCC, 68.4% were with oligo-metastases (≤5 meta sites), and 83.5% were combined with SABR before 1st-line systemic therapy failure.

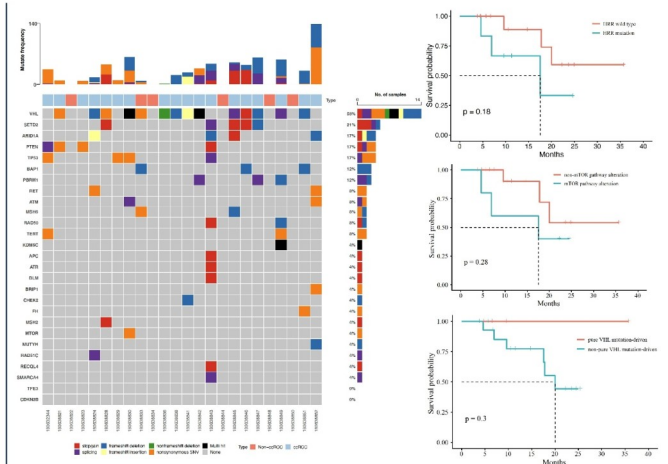
Characters	Total(n=79)
Age(yr)	
Median (range)	57(12-83)
Sex，n(%)	
female	21(26.6%)
IMDC score, n(%)	
0	23(29.1%)
1	36(45.6%)
2	10(12.7%)
3	8(10.1%)
4	2(2.5%)
Pathology	
Clear-cell carcinoma	57(72.2%)
Papillary renal carcinomas	11(14.0%)
TFE3	5(6.3%)
Chromophobe renal carcinoma	2(2.5%)
Others	4(5.0%)
Metastatic status	
Oligo-	54(68.4%)
extensive	25(31.6%)



Targeted therapy combined with immunotherapy and stereotactic radiotherapy has achieved satisfactory survival results for mRCC, and early intervention by SABR may lead to a better PFS.

- All patients were categorized to IMDC intermediate or poor prognosis group and TKI and IO combination was used in all pts. All patients with oligo-metastases received SABR for all tumor sites and others were for cytoreductive purpose.The median follow-up was 20.3 mo.
- The mPFS was 28.6 mo and TTTC was 31.8 mo. The ORR was 68.4% and the DCR was 89.9%. The DCR of radiation-treated lesions was 96.2%. The mOS was 44.8 mo. Grade 3 or above AE was 50.2%, and there was no treatment-related death.
- For patients received SABR before or after 1st-line systemic therapy failure, the mPFS were 30.6 mo vs. 9.6 mo, respectively (p=0.004).
- In addition, The NGS analysis was performed in 25 pts tumor samples. The most frequent genes mutated were VHL (60%), SETD2 (24%), ARID1A (24%), TP53 (20%), PTEN (20%), TEF3 (16%), BAP1 (12%), RET (12%), and PBRM1 (12%). We discovered a favorable trend in the prognosis for PFS in pts with tumors purely driven by VHL loss. Mutations in the mTOR pathway genes, PTEN and HRR-related genes appeared to lead to poorer PFS.





Future Directions for Research

SABR has a satisfactory local control ability for ccRCC and can prolong time to treatment change and PFS in selected patients.
Early intervention for mRCC patients covering comprehensively all lesions in IO+TKI response patients may eventually prolong PFS and OS

Acknowledgements

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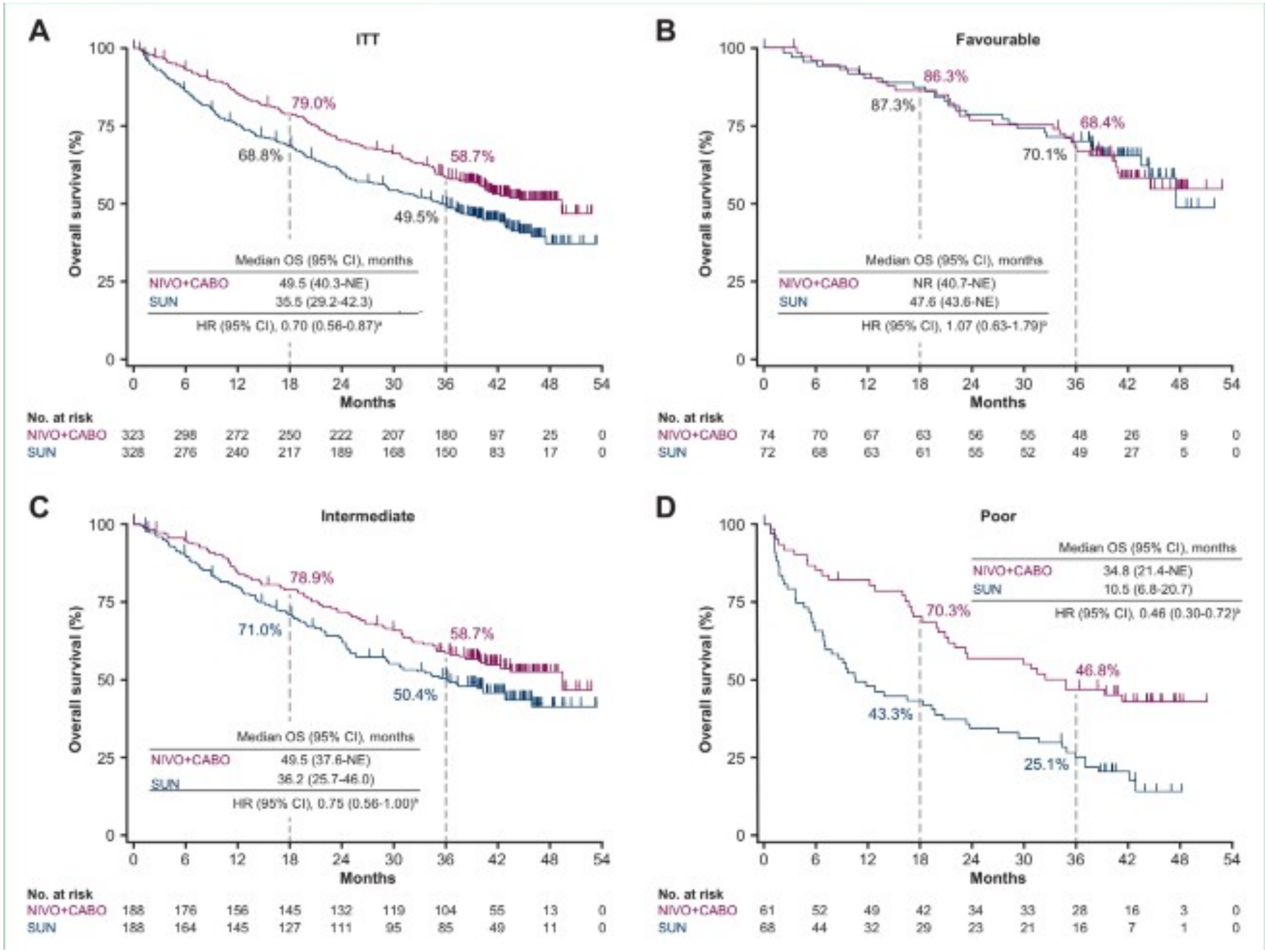
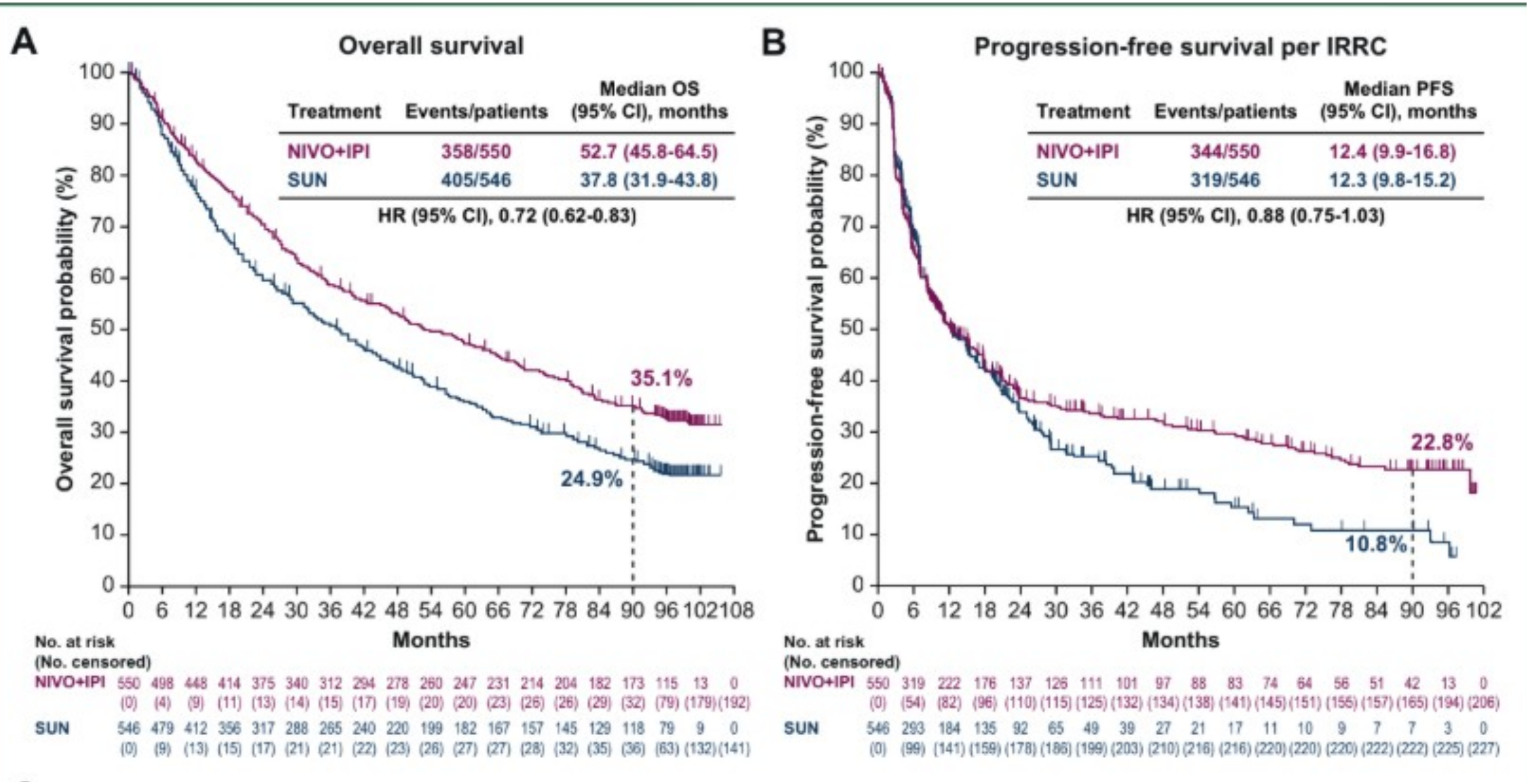
Phase 3 Trials of Front-Line Therapies for aCC-RCC

Efficacy Endpoints	**CheckMate 214*[1] Ipi/Nivo (N = 1096)**	**KEYNOTE-426[2] Axi/Pembro (N = 861)**	**CheckMate 9ER[3] Cabo/Nivo (N = 651)**	**CLEAR[4] Len/Pembro (N = 1069)**	COSMIC-313[5] Cabo/Nivo/Ipi (N = 855)	RENOTORCH
Median PFS, mo HR (95% CI)	12.3 0.86 (0.73-1.01)	15.7 0.68 (0.58-0.80)	16.6 0.58 (0.48-0.71)	23.3 0.42 (0.34-0.52)	NR 0.73 (0.57-0.94))	18.0
Median OS, mo HR (95% CI)	55.7 0.72 (0.62-0.85)	45.7 0.73 (0.60-0.88)	49.5 0.70 (0.56-0.87)	NR 0.72 (0.55-0.93)	- -	NE
ORR/CR, %	**42/12**	**60.4/10**	**55.7/12.4**	**71/17**	**43/3**	**56.7/4.8**
Sarcomatoid Features, %	13	12	11.5	7.9	NA	NR
AEs leading to d/c	23	10.7	7	37.2	45	5.8
IMDC or MKSCC Risk F/I/P, %	23/61/17	31.9/55.1/13	22.6/57.6/19.7	31/59.2/9.3	0/75/25	81.5/18.5
Median follow-up, mo	67.7	42.8	44.0	33.7	14.9	14.6

*Intermediate/poor risk group only

1. Motzer. Cancer. 2022;128:2085. 2. Rini. ASCO 2021. Abstr 4500. 3. Burotto. ASCO GU 2023. Abstr 603. 4. Choueiri. Lancet Oncol. 2023;24:228. 5. Choueiri. Lancet Oncol. 2023;24:228.


A
ITT
Overall survival (%)
100
75
50
25
0
79.0%
68.8%
58.7%
49.5%
Median OS (95% CI), months
NIVO+CABO 49.5 (40.3-NE)
SUN 35.5 (29.2-42.3)
HR (95% CI), 0.70 (0.56-0.87)a
0 6 12 18 24 30 36 42 48 54
Months
No. at risk
NIVO+CABO 323 298 272 250 222 207 180 97 25 0
SUN 328 276 240 217 189 168 150 83 17 0
B
Favourable
86.3%
87.3%
68.4%
70.1%
Median OS (95% CI), months
NIVO+CABO NR (40.7-NE)
SUN 47.6 (43.6-NE)
HR (95% CI), 1.07 (0.63-1.79)b
No. at risk
NIVO+CABO 74 70 67 63 56 55 48 26 9 0
SUN 72 68 63 61 55 52 49 27 5 0
C
Intermediate
78.9%
71.0%
59.7%
50.4%
Median OS (95% CI), months
NIVO+CABO 49.5 (37.6-NE)
SUN 36.2 (25.7-46.0)
HR (95% CI), 0.75 (0.56-1.00)a
No. at risk
NIVO+CABO 188 176 156 145 132 119 104 55 13 0
SUN 188 164 145 127 111 95 85 49 11 0
D
Poor
Median OS (95% CI), months
NIVO+CABO 34.8 (21.4-NE)
SUN 10.5 (6.8-20.7)
HR (95% CI), 0.46 (0.30-0.72)b
70.3%
46.8%
43.3%
25.1%
No. at risk
NIVO+CABO 61 52 49 42 34 33 28 16 3 0
SUN 68 44 32 29 23 21 16 7 1 0


A
Overall survival
Overall survival probability (%)
Treatment
Events/patients
Median OS (95% CI), months
NIVO+IPI 358/550 52.7 (45.8-64.5)
SUN 405/546 37.8 (31.9-43.8)
HR (95% CI), 0.72 (0.62-0.83)
35.1%
24.9%
Months
No. at risk (No. censored)
NIVO+IPI 550 498 448 414 375 340 312 294 278 260 247 231 214 204 182 173 115 13 0
(0) (4) (9) (11) (13) (14) (15) (17) (19) (20) (20) (23) (26) (26) (29) (32) (79) (179) (192)
SUN 546 479 412 356 317 288 265 240 220 199 182 167 157 145 129 118 79 9 0
(0) (9) (13) (15) (17) (21) (21) (22) (23) (26) (27) (27) (28) (32) (35) (36) (63) (132) (141)
B
Progression-free survival per IRRC
Progression-free survival probability (%)
Treatment
Events/patients
Median PFS (95% CI), months
NIVO+IPI 344/550 12.4 (9.9-16.8)
SUN 319/546 12.3 (9.8-15.2)
HR (95% CI), 0.88 (0.75-1.03)
22.8%
10.8%
Months
No. at risk (No. censored)
NIVO+IPI 550 319 222 176 137 126 111 101 97 88 83 74 64 56 51 42 13 0
(0) (54) (82) (96) (110) (115) (125) (132) (134) (138) (141) (145) (151) (155) (157) (165) (194) (206)
SUN 546 293 184 135 92 65 49 39 27 21 17 11 10 9 7 7 3 0
(0) (99) (141) (159) (178) (186) (199) (203) (210) (216) (216) (220) (220) (220) (222) (222) (225) (227)