Nivolumab plus cabozantinib versus sunitinib for first-line treatment of advanced renal cell carcinoma: extended follow-up from the phase III randomised CheckMate 9ER trial

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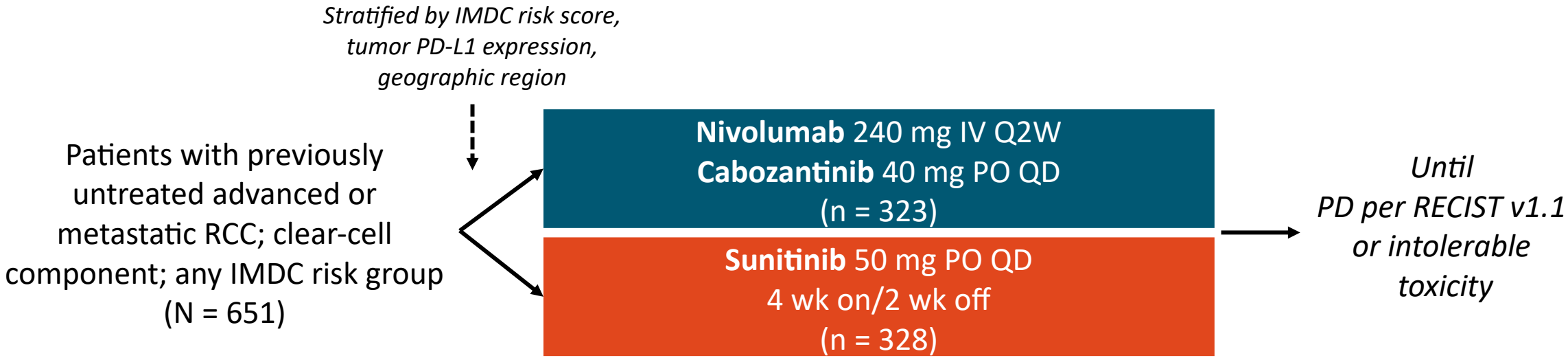
Background

- Results from phase III CheckMate 9ER trial demonstrated superior efficacy with nivolumab + cabozantinib vs sunitinib as first-line treatment in patients with advanced or metastatic RCC.
  - PFS, OS, and ORR benefits were seen at primary analysis and subsequent follow-up (median follow-up: 18.1 and 32.9 mo)

- Current analysis reported outcomes from CheckMate 9ER after median follow-up of 44 mo (range: 36.5-56.5 mo)[3]
  - Includes subgroup analyses by IMDC risk category and **among patients completing 2 yr of nivolumab treatment**

CheckMate 9ER 3-Yr Update: Study Design

- 3-yr follow-up of randomized phase III **open-label** trial (data cutoff: May 27, 2022)



- Primary endpoint: PFS (BICR)
- Secondary endpoints: OS, ORR (BICR), safety

Choueiri. NEJM. 2021;384:829. Motzer. Lancet Oncol. 2022;23:888. Burotto. ASCO GU 2023. Abstr 603.

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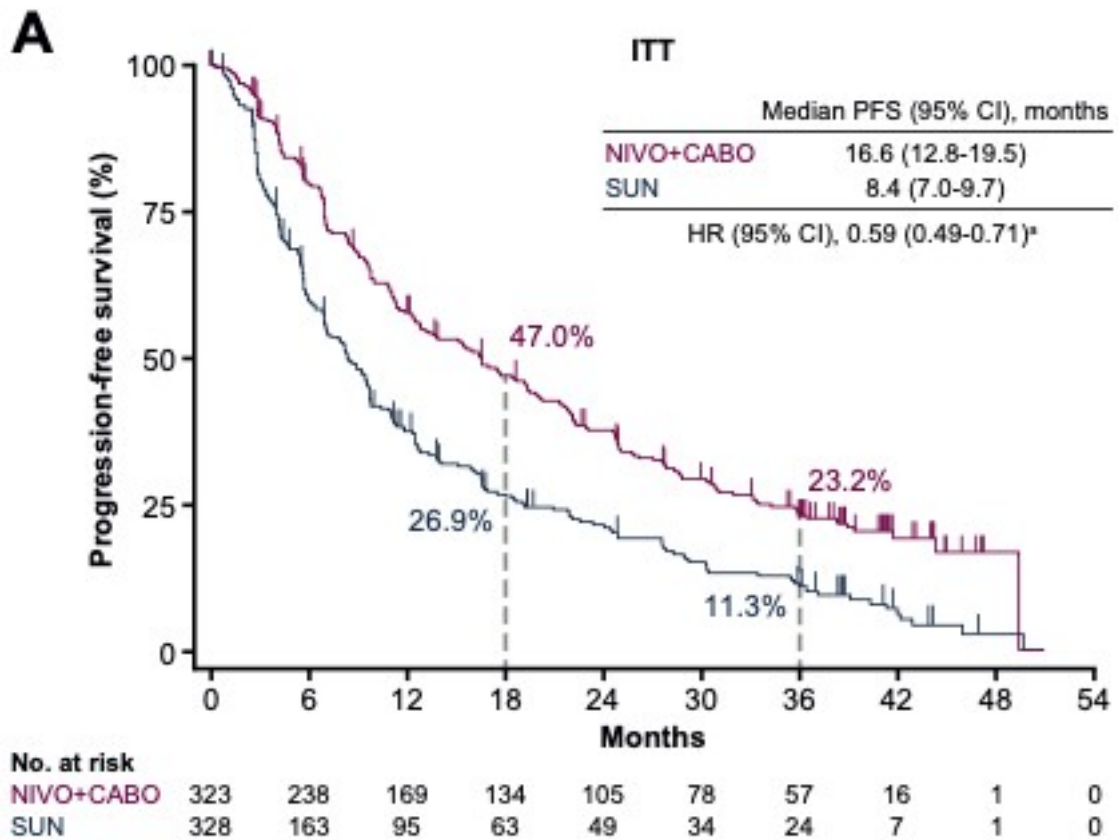
CheckMate 9ER 3-Yr Update: PFS and OS in ITT Population and by IMDC Risk Subgroup

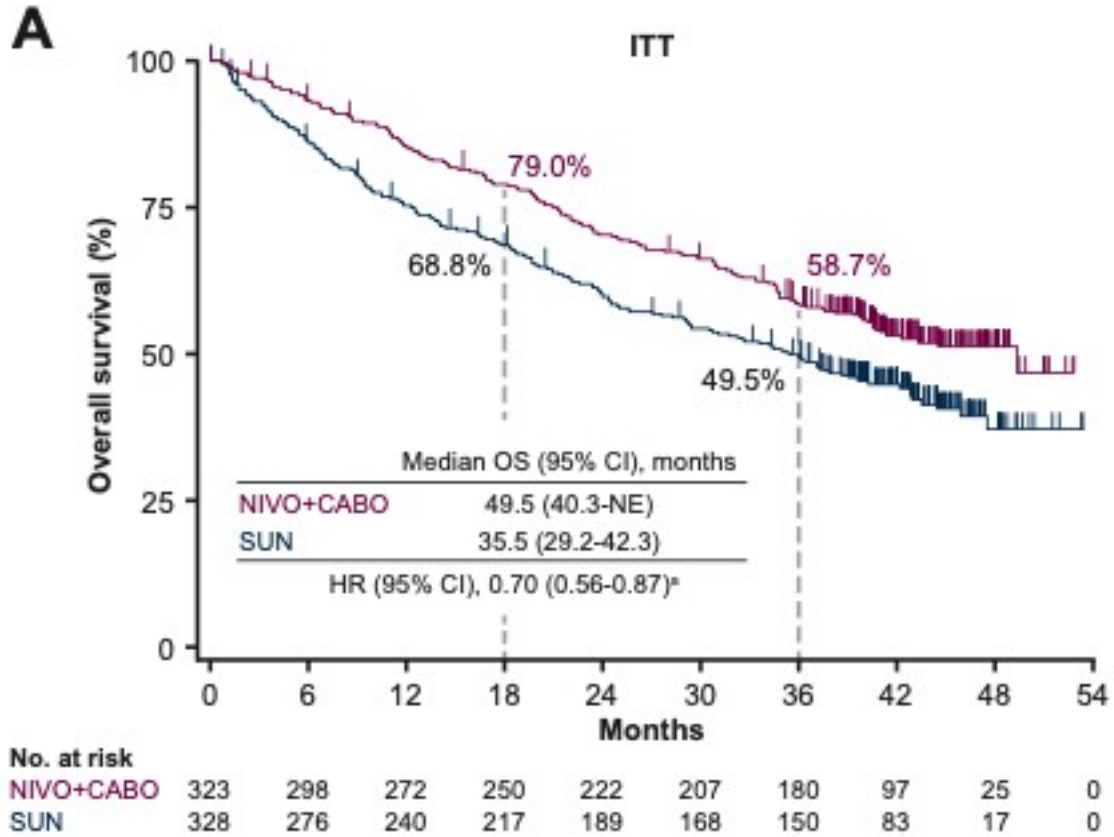
- Outcomes after median follow-up for OS in ITT population: 44.0 mo (range: 36.5-56.5 mo)

IMDC Risk at Baseline	Treatment	Median PFS, Mo (95% CI)	PFS HR (95% CI)	Median OS, Mo (95% CI)	OS HR (95% CI)
Any (ITT)	▪ **Nivo + cabo (n = 323)** ▪ **Sunitinib (n = 328)**	**16.6 (12.8-19.8)** **8.4 (7.0-9.7)**	0.58 (0.48-0.71)	**49.5 (40.3-NE)** **35.5 (29.2-42.3)**	0.70 (0.56-0.87)
Favorable	▪ Nivo + cabo (n = 74) ▪ Sunitinib (n = 72)	21.4 (13.1-24.8) 13.9 (9.6-18.5)	0.75 (0.50-1.13)	NR (40.7-NE) 47.6 (43.6-NE)	1.07 (0.63-1.79)
Intermediate	▪ Nivo + cabo (n = 188) ▪ Sunitinib (n = 188)	17.5 (12.3-20.3) 8.5 (7.0-10.4)	0.61 (0.48-0.79)	49.5 (37.6-NE) 36.2 (25.7-46.0)	0.75 (0.56-1.00)
Poor	▪ Nivo + cabo (n = 61) ▪ Sunitinib (n = 68)	9.9 (5.9-17.7) 4.2 (2.9-5.6)	0.38 (0.25-0.58)	34.8 (21.4-NE) 10.5 (6.8-20.7)	0.46 (0.30-0.72)
Intermediate /poor	▪ **Nivo + cabo (n = 249)** ▪ **Sunitinib (n = 256)**	**16.4 (11.2-19.3)** **7.1 (5.7-8.9)**	0.55 (0.45-0.69)	**49.5 (34.9-NE)** **29.2 (23.7-36.0)**	0.65 (0.51-0.83)

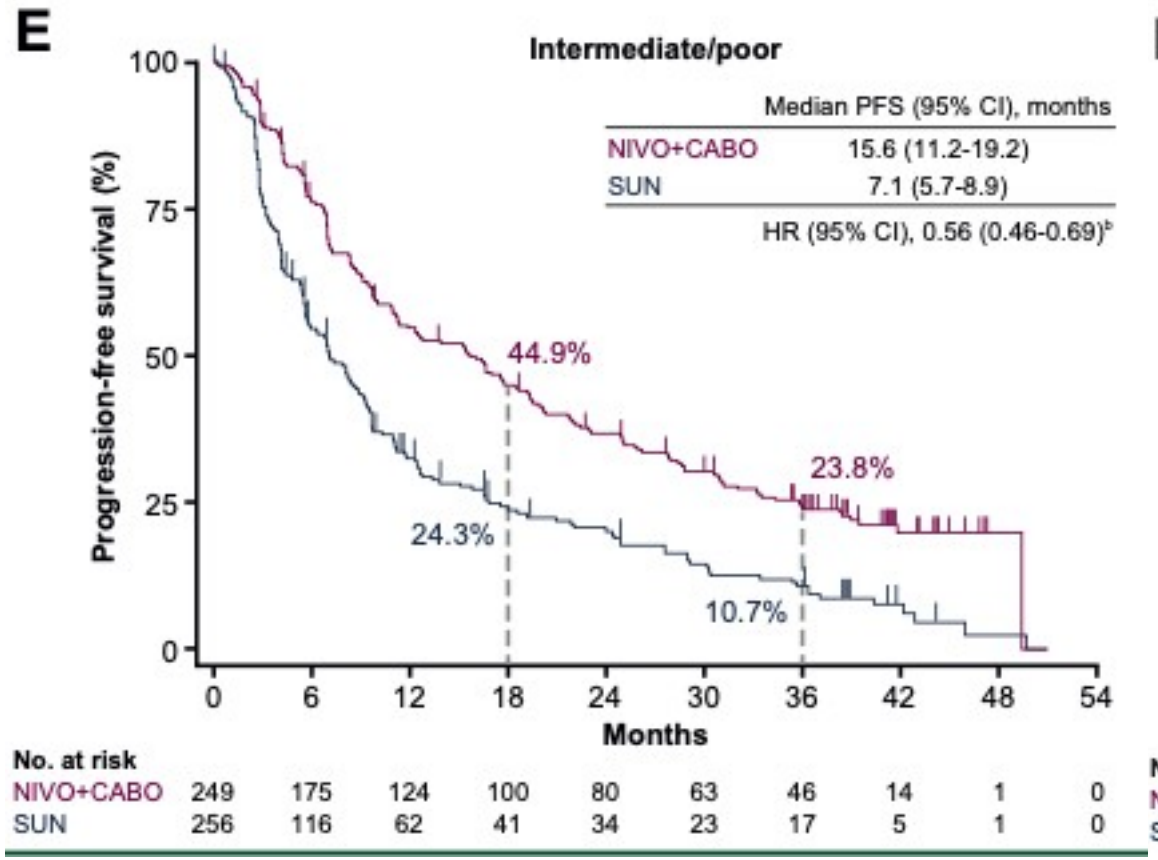
Burotto. ASCO GU 2023. Abstr 603.

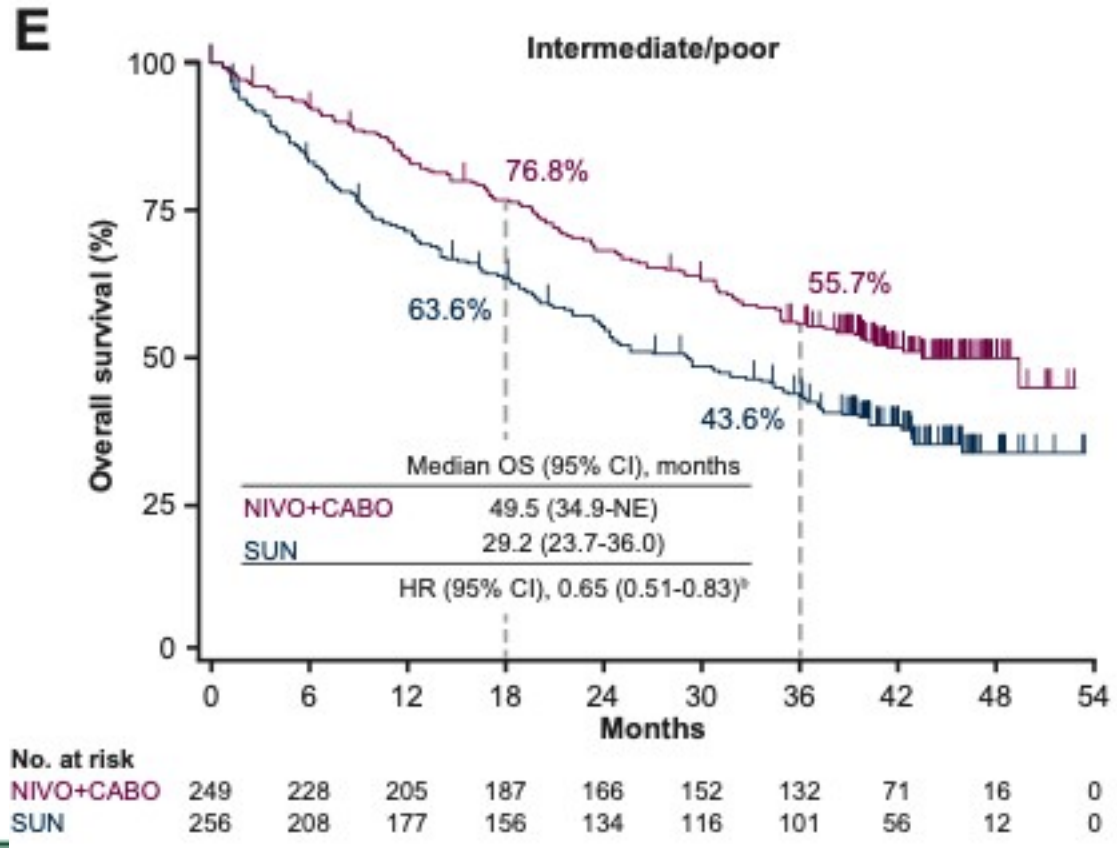
PFS and OS in ITT





PFS and OS in Intermediate + Poor IMDC Groups





CheckMate 9ER 3-Yr Update: Response in ITT Population

Outcome	Nivolumab + Cabozantinib (n = 323)	Sunitinib (n = 328)
ORR by BICR, % (95% CI)	55.7 (50.1-61.2)	28.4 (23.5-33.6)
▪ Odds ratio estimate (95% CI)	3.3 (2.4-4.6)	
Best overall response, n (%)		
▪ CR	**40 (12.4)**	**17 (5.2)**
▪ PR	140 (43.3)	76 (23.2)
▪ SD	105 (32.5)	134 (40.9)
▪ PD	20 (6.2)	45 (13.7)
▪ Unable to determine	18 (5.6)	56 (17.1)
Median TTR, mo (range)	2.8 (1.0-22.3)	4.2 (1.7-30.4)
Median DoR, mo (95% CI)	**23.1 (20.2-27.9)**	**15.2 (9.9-20.7)**

Burotto. ASCO GU 2023. Abstr 603.

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Subsequent Therapies

	Nivolumab + Cabozantinib (N=323)	Sunitinib (N=328)
Median Duration of treatment (Months)	23.1 (8.8-24)	8.9 (2.9-10.7)
Any Subsequent systemic therapy	25%	41%
PD1/PDL1 (Nivolumab/ Pembro/ Ipi)	7%	31%
TKI (Axitinib/ Cabozantinib/ Everolimus)	21%	19%

Time to Subsequent therapies	Months
Nivo + Cabo	4 (2.6-6.8)
Sunitinib	2.1 (1.4-2.8)
Nivo-2 (N=115)	20.6 (7.9-NE)

Nivo-2

Supplementary Table S2. Baseline demographic and clinical characteristics in patients who completed per-protocol 2 years of NIVO treatment

Characteristic	Patients who completed 2 years of NIVO treatment (*n* = 115)
Median age (range), years	59 (35-79)
Male	94 (81.7)
Region	
North America/Europe	56 (48.7)
Rest of the world	59 (51.3)
Karnofsky performance status	
90 or 100	98 (85.2)
70 or 80	17 (14.8)
IMDC prognostic score	
Favourable (0)	30 (26.1)
Intermediate (1-2)	71 (61.7)
Poor (3-6)	14 (12.2)
Prior nephrectomy	93 (80.9)
Tumour PD-L1 expression[a]	
≥1%	27 (23.5)
<1% or indeterminate	87 (75.7)
Sarcomatoid features	*n* = 113
Yes	10 (8.8)
No	103 (91.2)
Most common sites of metastasis	
Lung	85 (73.9)
Lymph node	38 (33.0)
Bone	23 (20.0)
Liver	23 (20.0)
Adrenal gland	15 (13.0)

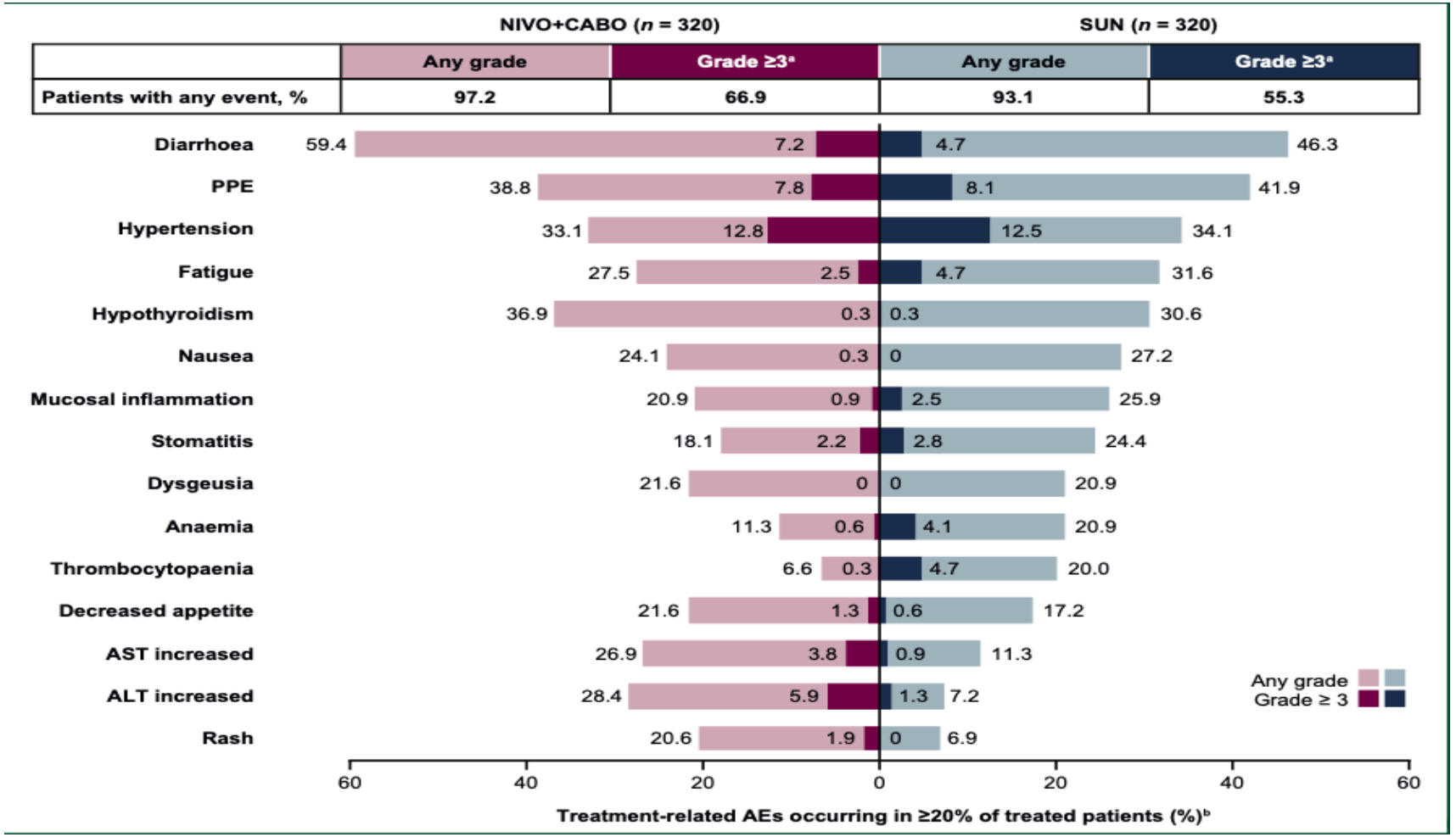
Subsequent Therapies in Nivo-2

Supplementary Table S3. Summary of subsequent cancer therapy in patients who completed the per-protocol 2 years of NIVO treatment

Therapy[a]	*n* = 115
Any subsequent therapy[b]	23 (20.0)
Any subsequent systemic therapy	12 (10.4)
Any PD-(L)1 inhibitor	5 (4.3)
Nivolumab	5 (4.3)
Pembrolizumab	1 (0.9)
Any CTLA-4 inhibitor	2 (1.7)
Ipilimumab	2 (1.7)
Any VEGF(R) inhibitor	7 (6.1)
Axitinib	3 (2.6)
Lenvatinib	3 (2.6)
Cabozantinib	1 (0.9)
Pazopanib	1 (0.9)
Sunitinib	1 (0.9)
Other	6 (5.2)
Everolimus	4 (3.5)
Belzutifan	1 (0.9)
Investigational antineoplastic drugs	1 (0.9)

Most Common Subsequent Therapy:
VEGFR -6.1%
Nivo – 4.3%

Treatment Related Adverse Effects



Treatment Discontinuation because of TRAE:

Nivo Cabo: 27.5%
Sunitinib: 10.6%

21.8% patients on Nivo Cabo arm received steroids for iRAEs

Conclusion:

- In the phase III CheckMate 9ER trial, after a median follow-up of 44.0 mo, first-line nivolumab + cabozantinib maintained superior OS over sunitinib in patients with advanced or metastatic RCC
  - Median OS with nivolumab + cabozantinib: 49.5 vs 35.5 mo with sunitinib (HR: 0.70)
  - **Median OS in nivolumab + cabozantinib arm improved by 11.8 mo since last analysis**

- Response rates with nivolumab + cabozantinib were higher vs sunitinib across IMDC risk groups

- No new safety signals reported

- Use of subsequent therapies after discontinuation was higher with sunitinib vs nivolumab + cabozantinib.


Thank
you