ASCO® Genitourinary Cancers Symposium

Nivolumab plus ipilimumab versus sunitinib for first-line treatment of advanced renal cell carcinoma: long-term follow-up data from the phase 3 CheckMate 214 trial

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Abstract number 363

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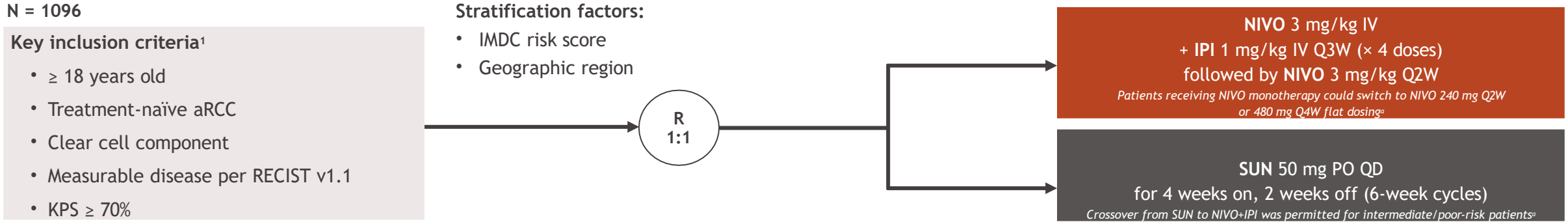
Background and study design

- NIVO+IPI is approved for first-line treatment of IMDC intermediate/poor-risk aRCC, based on superior OS and ORR over SUN in the randomized, phase 3 CheckMate 214 trial[1-3]
- NIVO+IPI has demonstrated durable survival and response benefits versus SUN across a broad range of patients, providing the opportunity to conduct long-term survival analyses[4-6]
- With a median follow-up of 8 years in the CheckMate 214 trial, we present updated efficacy and safety outcomes, and exploratory subgroup analyses in patients by organ sites of metastasis at baseline



Median (range) follow-up for OS, 99.1 (91.0-107.3) months

Primary endpoints: OS, PFS and ORR (both per IRRC) in IMDC intermediate/poor-risk patients
Secondary endpoints: OS, PFS and ORR (both per IRRC) in ITT patients; safety in all treated patients
Exploratory endpoints: OS, PFS and ORR (both per IRRC) in IMDC favorable-risk patients

Response was assessed using RECIST v1.1. [a]As of a November 2017 protocol amendment and protocol revision 04.

1. Motzer RJ, et al. *N Engl J Med* 2018;378:1277–1290. 2. OPDIVO (nivolumab) [package insert]. Princeton, NJ: Bristol Myers Squibb; 2023. 3. YERVOY (ipilimumab) [package insert]. Princeton, NJ: Bristol Myers Squibb; 2023. 4. Motzer RJ, et al. *Cancer* 2022;128:2085-2097. 5. Albiges L, et al. *Eur Urol* 2022; 81:266-271. 6. Tannir NM, et al. Poster presentation at the International Kidney Cancer Symposium (IKCS); November 5-6, 2021; Austin, TX. Abstract CTR11.

Key baseline characteristics

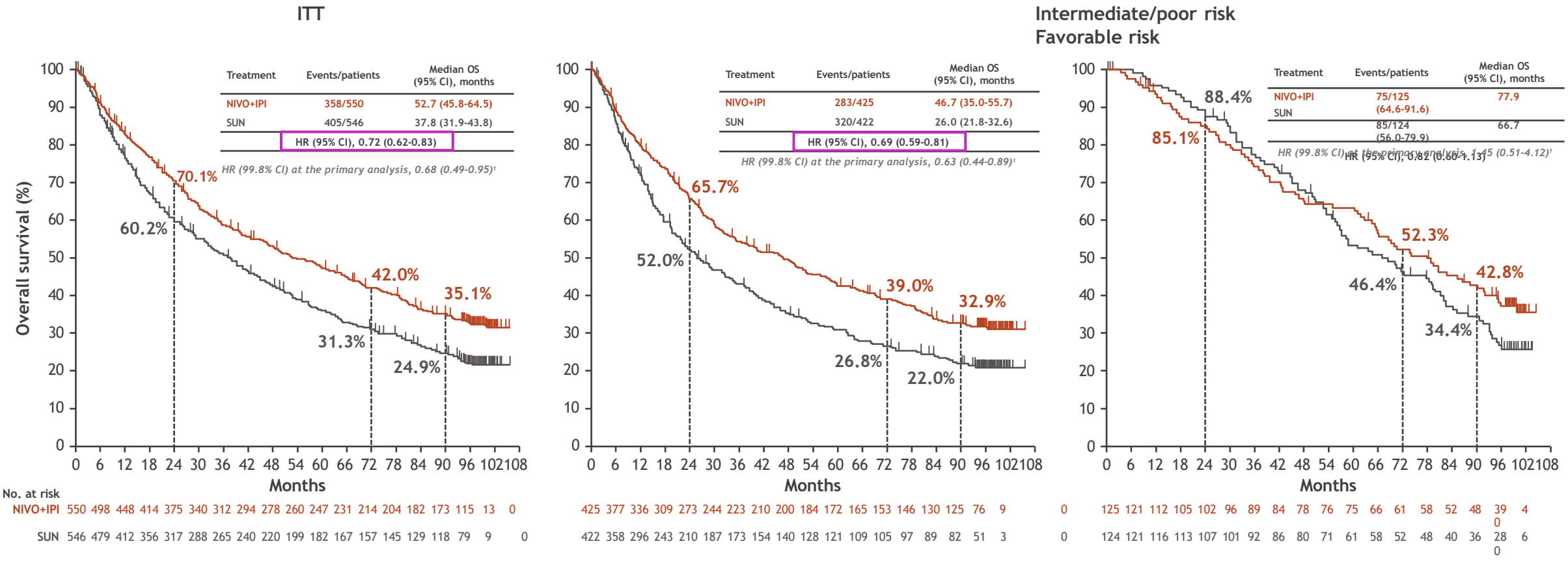
- Key baseline characteristics by IMDC risk groups, published previously,[1] were generally similar between treatment arms and consistent with the ITT population

Characteristic[a]	ITT patients[1]		All patients with lung metastases[b]		All patients with liver metastases[b]		All patients with bone metastases[b]	
	NIVO+IPI (N = 550)	SUN (N = 546)	NIVO+IPI (n = 382)	SUN (n = 373)	NIVO+IPI (n = 99)	SUN (n = 107)	NIVO+IPI (n = 98)	SUN (n = 109)
IMDC prognostic score, %[c]								
Favorable (0)	23	23	22	18	10	17	14	17
Intermediate (1–2)	61	61	59	63	58	54	60	55
Poor (3–6)	17	16	19	19	32	29	26	28
Geographic region, %								
Europe and Canada	37	36	37	35	38	36	38	27
United States	28	28	29	27	25	26	23	31
Rest of the world	35	36	34	37	36	38	39	42

[a]Data collected via interactive voice-response system. [b]Within each subgroup, all patients had metastasis within the specified site but may have had lesions in more than 1 site.
[c]IMDC prognostic score was not reported for 1 SUN patient with baseline lung metastasis. 1. Motzer RJ, et al. *N Engl J Med* 2018;378:1277–1290.

Overall survival

- The HR for OS has been stable over 8 years of median follow-up in ITT and intermediate/poor-risk patients and has improved over time in favorable risk patients

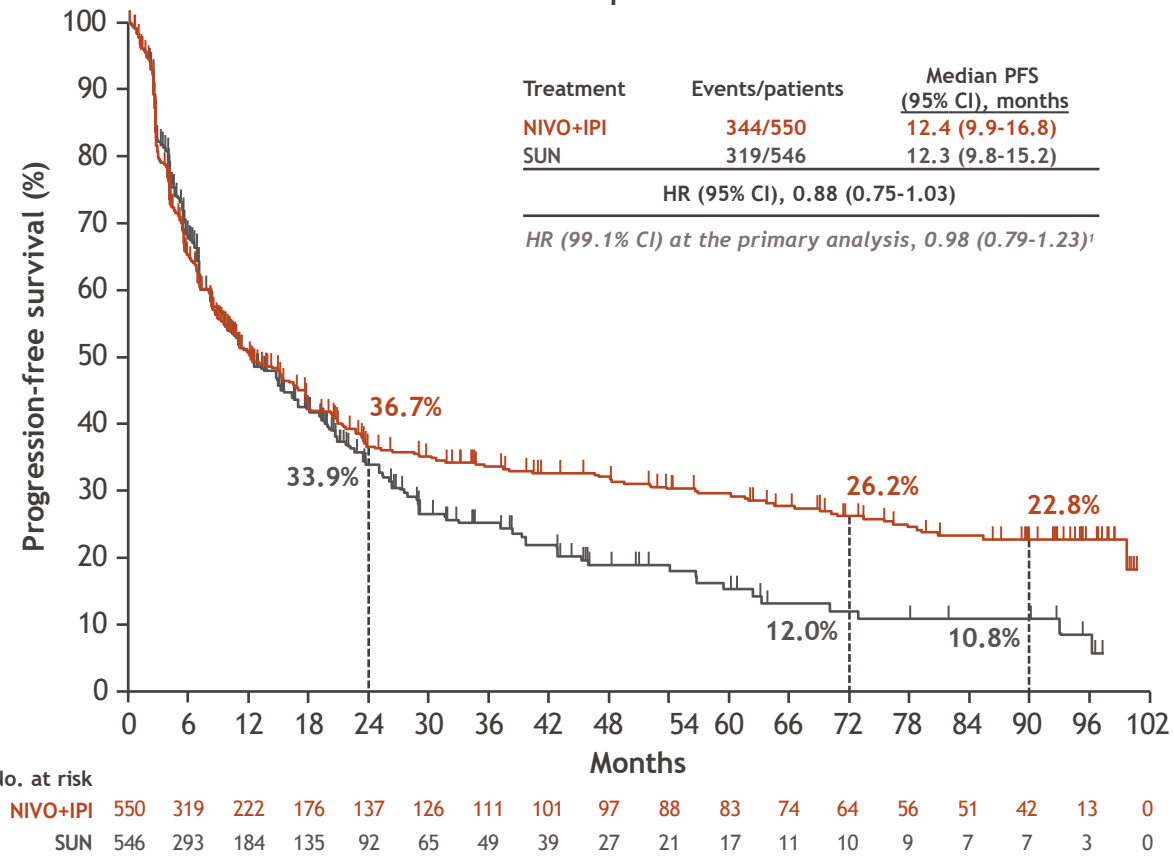


Stratified Cox proportional hazards model.

1. Motzer RJ, et al. *N Engl J Med* 2018;378:1277–1290.

PFS in the ITT population

PFS per IRRC



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)

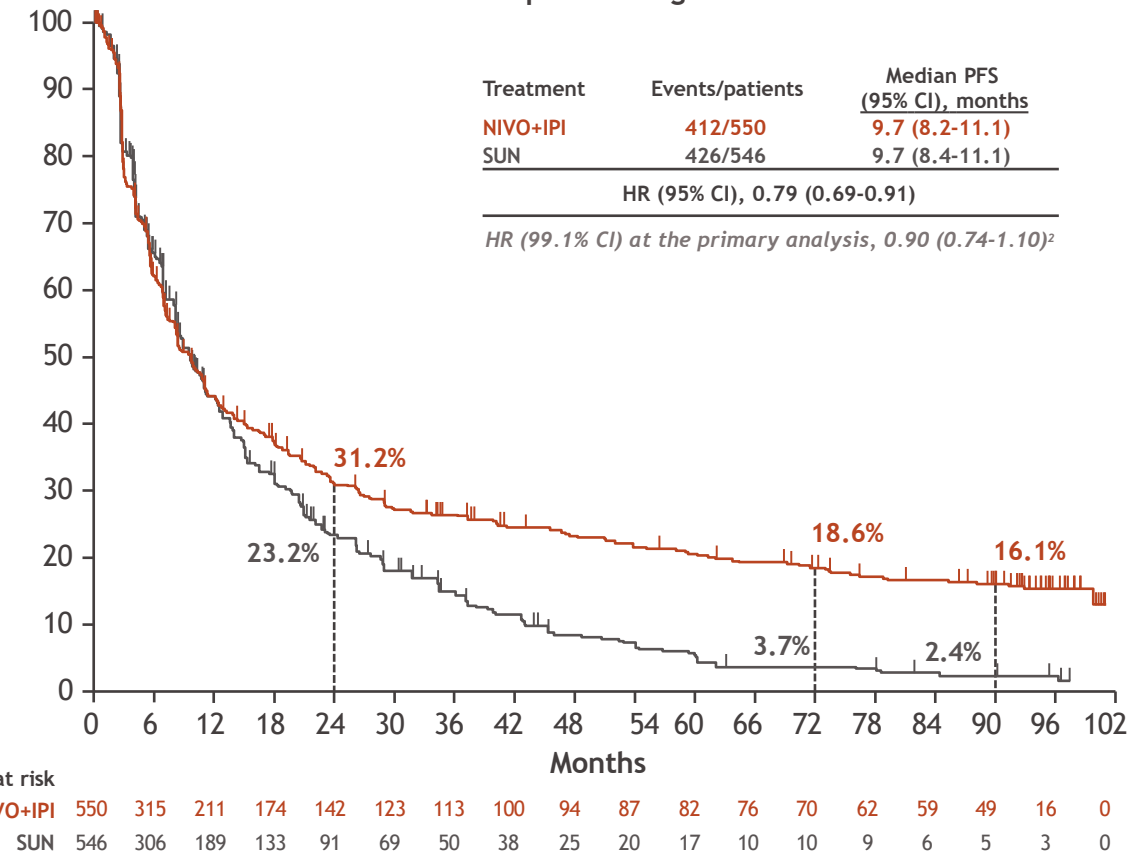
HR (95% CI), 0.88 (0.75-1.03)

HR (99.1% CI) at the primary analysis, 0.98 (0.79-1.23)[1]

No. at risk

NIVO+IPI	550	319	222	176	137	126	111	101	97	88	83	74	64	56	51	42	13	0
SUN	546	293	184	135	92	65	49	39	27	21	17	11	10	9	7	7	3	0

PFS per investigator



Treatment	Events/patients	Median PFS (95% CI), months
NIVO+IPI	412/550	9.7 (8.2-11.1)
SUN	426/546	9.7 (8.4-11.1)

HR (95% CI), 0.79 (0.69-0.91)

HR (99.1% CI) at the primary analysis, 0.90 (0.74-1.10)[2]

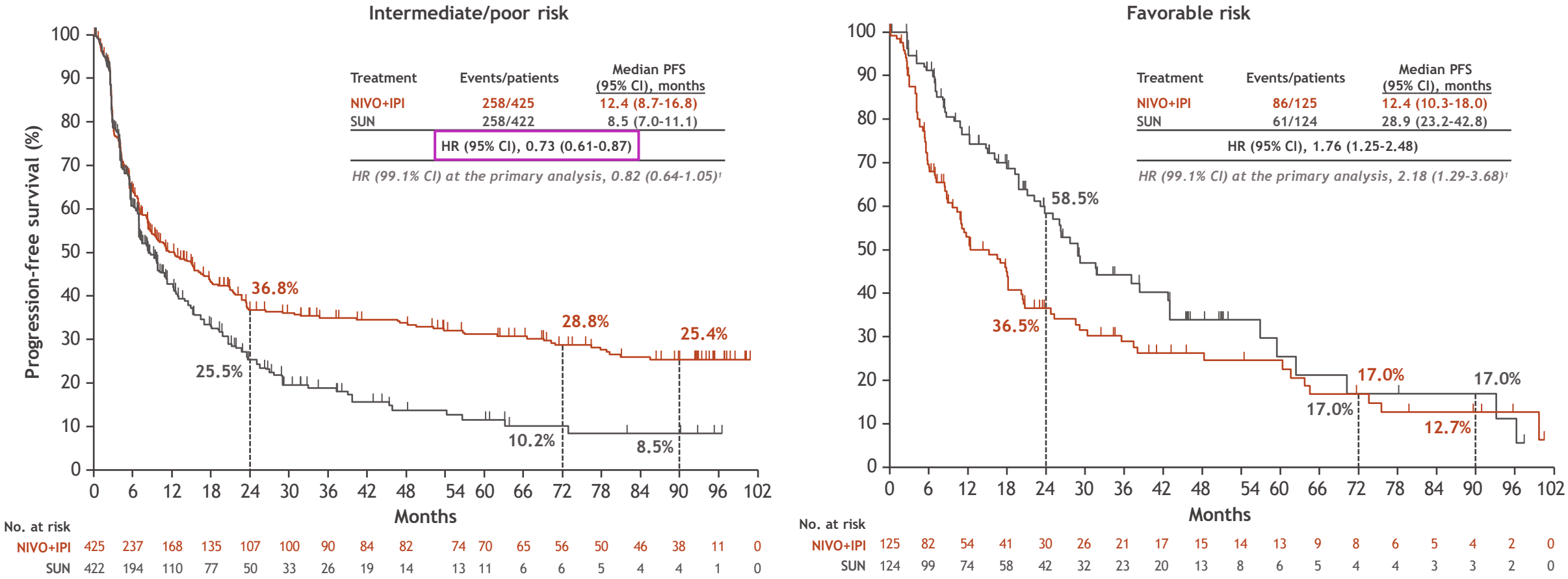
No. at risk

NIVO+IPI	550	315	211	174	142	123	113	100	94	87	82	76	70	62	59	49	16	0
SUN	546	306	189	133	91	69	50	38	25	20	17	10	10	9	6	5	3	0

Stratified Cox proportional hazards model.

1. Motzer RJ, et al. *N Engl J Med* 2018;378:1277–1290. 2. Bristol Myers Squibb. Data on file. NIVO 260. 2017.

PFS per IRRC by IMDC risk

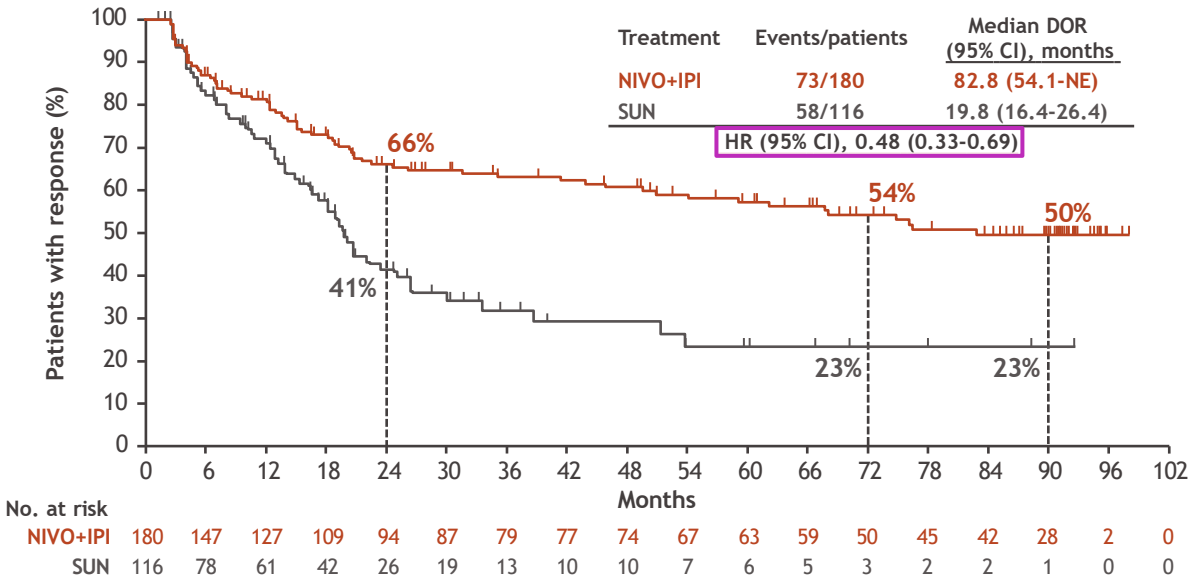


Stratified Cox proportional hazards model.

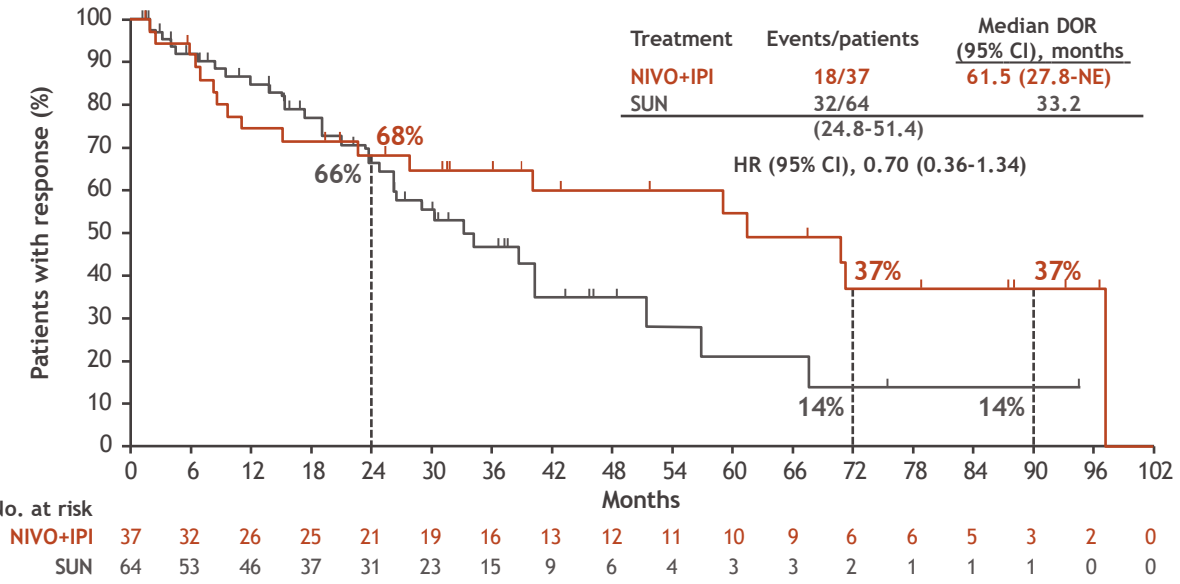
1. Motzer RJ, et al. *N Engl J Med* 2018;378:1277–1290.

DOR, ORR, and BOR (all per IRRC)

Intermediate/poor risk



Favorable risk



	ITT population		Intermediate/poor risk		Favorable risk	
	NIVO+IPI N = 550	SUN N = 546	NIVO+IPI N = 425	SUN N = 422	NIVO+IPI N = 125	SUN N = 124
ORR (95% CI), %	39 (35-44)	33 (29-37)	42 (38-47)	27 (23-32)	30 (22-38)	52 (43-61)
Best overall response, n (%)						
Complete response	66 (12)	19 (3)	50 (12)	11 (3)	16 (13)	8 (6)
Partial response	151 (27)	161 (29)	130 (31)	105 (25)	21 (17)	56 (45)
Stable disease	197 (36)	230 (42)	130 (31)	186 (44)	67 (54)	44 (35)
Progressive disease	97 (18)	77 (14)	82 (19)	71 (17)	15 (12)	6 (5)
UTD/NR	39 (7)	59 (11)	33 (8)	49 (12)	6 (5)	10 (8)
Ongoing response, % (n/N)	58 (126/217)	50 (90/180)	59 (107/180)	50 (58/116)	51 (19/37)	50 (32/64)
Ongoing complete response, % (n/N)	80 (53/66)	89 (17/19)	84 (42/50)	91 (10/11)	69 (11/16)	88 (7/8)

RECIST v1.1 response criteria. Stratified Cox proportional hazards model.
In the ITT population, median (95% CI) DOR was 76.2 (59.1-NE) months with NIVO+IPI and 25.1 (19.8-33.2) months with SUN (HR, 0.52; 95% CI, 0.38-0.72).

Efficacy by baseline organ sites of metastases

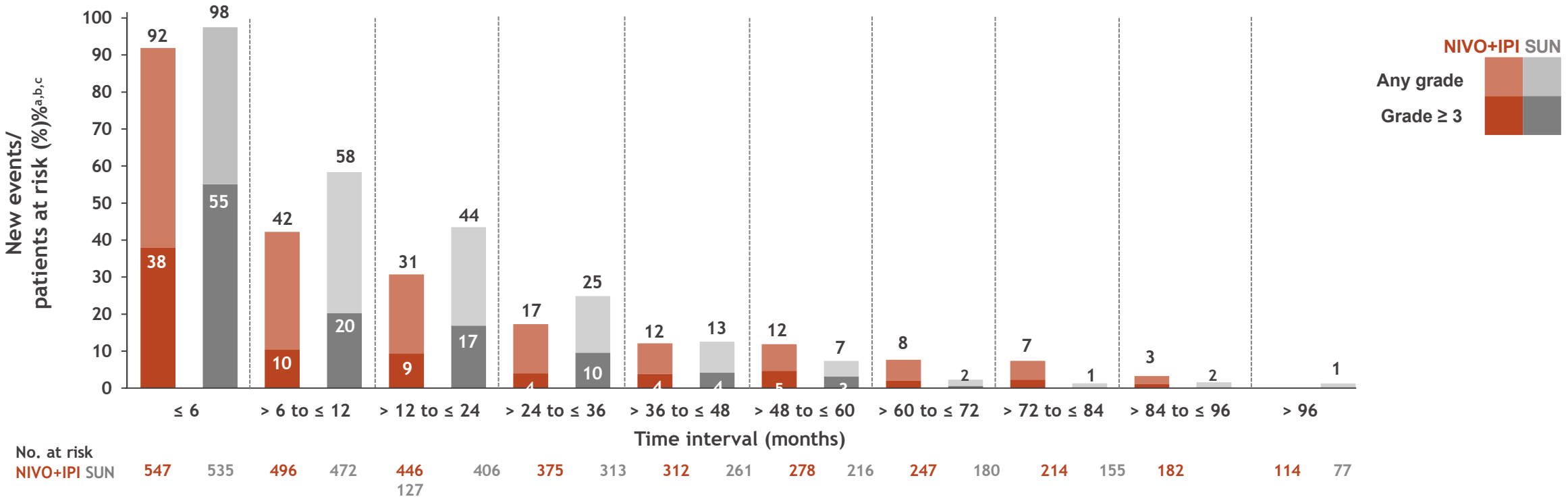
- OS, PFS and ORR outcomes favored NIVO+IPI versus SUN in patients with lung metastases at baseline

Outcome[a]	Lung[b]		Liver[b]		Bone[b,c]	
	NIVO+IPI (n = 382)	SUN (n = 373)	NIVO+IPI (n = 99)	SUN (n = 107)	NIVO+IPI (n = 98)	SUN (n = 109)
Median OS (95% CI), mo	49.8 (40.4-65.4)	32.2 (25.8-39.3)	27.3 (18.7-41.2)	17.8 (12.3-26.3)	26.3 (20.4-30.8)	20.0 (17.5-29.2)
HR (95% CI)	0.70 (0.59-0.83)		0.73 (0.54-1.00)		0.82 (0.61-1.11)	
Median PFS (95% CI), mo	14.0 (9.8-17.8)	10.8 (8.3-14.1)	6.9 (5.4-8.4)	7.1 (4.2-12.5)	8.3 (6.1-12.4)	9.7 (7.0-15.2)
HR (95% CI)	0.77 (0.64-0.93)		0.85 (0.61-1.18)		1.07 (0.76-1.51)	
ORR (95% CI), %	42.1 (37.1-47.3)	30.0 (25.4-35.0)	32.3 (23.3-42.5)	28.0 (19.8-37.5)	26.5 (18.1-36.4)	28.4 (20.2-37.9)

[a]Efficacy outcomes by baseline organ sites of metastases were conducted in the ITT population. [b]Within each subgroup, all patients had metastasis within the specified site but may have had lesions in more than 1 site. [c]Patients with bone metastases with and without a soft tissue component at baseline were counted a single time, resulting in fewer total patients compared with those counted in the baseline characteristics table where patients with and without a soft tissue component were counted once in each category.

Safety

Treatment-related AEs over time



- Comparable overall rates of treatment-related AEs of any grade occurred with NIVO+IPI (94%) versus SUN (98%); however, fewer grade ≥ 3 treatment-related AEs were reported with NIVO+IPI (48%) compared with SUN (64%)[d,e]
  - Treatment-related AEs leading to discontinuation of therapy occurred in 24% of patients with NIVO+IPI and 13% with SUN[d]
  - Deaths due to study drug toxicity occurred in 8 patients in the NIVO+IPI arm and 5 patients in the SUN arm[f]

[a]Bar chart shows the occurrence or onset of new treatment-related AEs over time. Rates were calculated as new events out of all patients at risk at the beginning of each interval. The same preferred AE term may be included at different intervals if collected at different start dates. [b]N = patients at the beginning of each interval. [c]Patients may be counted more than once across intervals. Incidence of grade ≥ 3 treatment-related AEs in all intervals after 60 months was ≤ 2.3%. [d]Includes events reported in all treated patients between first dose and 30 days after the last dose of study drug. [e]Among all treated patients with 8 years of follow-up, zero patients had a grade 5 event with NIVO+IPI and 2 patients had a grade 5 event with SUN. [f]One death assigned to the SUN arm occurred in a patient after crossover from SUN to NIVO+IPI.

Summary

- The HR for OS with NIVO+IPI versus SUN has remained stable over 8 years (99.1 months) of median follow-up in ITT and intermediate/poor-risk patients and has improved over time in favorable-risk patients
- PFS probabilities were higher with NIVO+IPI versus SUN in ITT and intermediate/poor risk patients, with 90-month PFS probabilities ranging ~23-25% in the NIVO+IPI arm
- Responses to NIVO+IPI were deep and durable in the overall study population; patients had notably improved DOR and more complete responses with NIVO+IPI over SUN regardless of IMDC risk
- Long-term safety with NIVO+IPI continues to be manageable
- These results represent the longest follow-up in a phase 3 trial of a checkpoint inhibitor combination therapy in first-line aRCC and continue to support NIVO+IPI as standard of care

Thanks

Acknowledgments

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- The clinical study teams and the global trial manager
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- All the investigators of the CheckMate 214 study
- All authors contributed to and approved the presentation; writing and editorial assistance were provided by Rachel Maddente, PhD, of Parexel, funded by Bristol Myers Squibb

Abbreviations

AE, adverse event

aRCC, advanced renal cell carcinoma

BOR, best overall response

CI, confidence interval

DOR, duration of response

HR, hazard ratio

IMDC, International Metastatic Renal Cell Carcinoma Database Consortium

IPI, ipilimumab

IRRC, independent radiology review committee

ITT, intent-to-treat

IV, intravenous

KPS, Karnofsky performance status

NE, not estimable

NIVO, nivolumab

NR, not reached

ORR, objective response rate

OS, overall survival

PFS, progression-free survival

PO, orally

Q×W, every × weeks

QD, once daily

R, randomization

RECIST, Response Evaluation Criteria in Solid Tumors

SUN, sunitinib

UTD, unable to determine