Focus On Possibilities

For Treating Your Patients with Advanced RCC

KEYTRUDA® (pembrolizumab), in combination with **KISPLYX® (lenvatinib)**, is indicated for the first-line treatment of adult patients with advanced renal cell carcinoma (RCC).

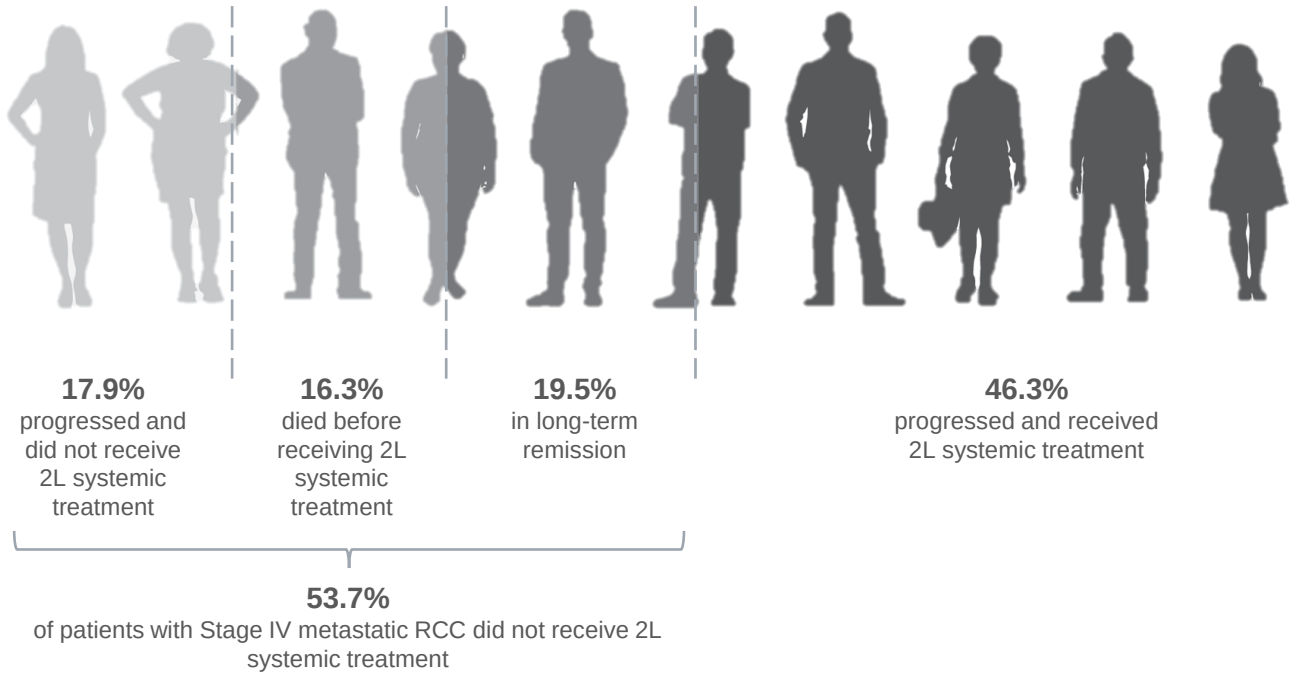
Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/ (please note that the MHRA Yellow Card link will redirect you to an external website, for which MSD does not review or control the content) or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Merck Sharp & Dohme (UK) Limited (Tel: 020 8154 8000).

Prescribing Information for KEYTRUDA and KISPLYX can be accessed via the 'PI' buttons at the bottom of this page and throughout.
Please consult the Summary of Product Characteristics and Risk Management Materials for further information before making any prescribing decisions.

Job code: GB-KLR-00327 Date of preparation: January 2025

2L systemic treatment in patients with metastatic RCC[1]

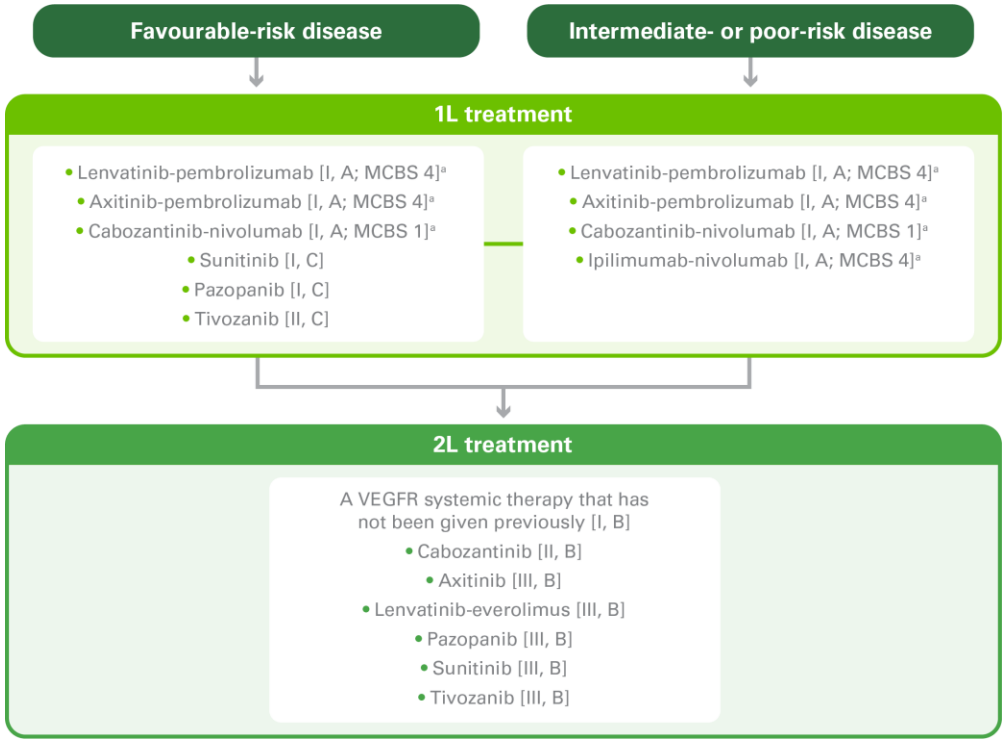
In a survey of 103 physicians who treated 4509 patients monthly in five European countries in 2020,[a] 46% of patients with Stage IV metastatic RCC received 2L systemic treatment



Adapted from Kantar Health 2020[1]

[a]France, Germany, Italy, Spain, UK.
2L, second-line; RCC, renal cell carcinoma.

ESMO guidelines for advanced and metastatic ccRCC treatment (May 2024)



Adapted from Powles T et al. 2024[2]

Level of evidence[2]

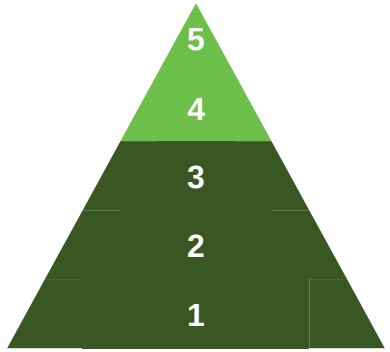
- **I:** At least one large randomised, controlled trial of good methodological quality (low potential for bias) or meta-analyses of well-conducted randomised trials without heterogeneity
- **II:** Small randomised trials or large randomised trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials with demonstrated heterogeneity
- **III:** Prospective cohort studies

Grades of recommendation[2]

- **A:** Strong evidence for efficacy with a substantial clinical benefit; strongly recommended
- **B:** Strong or moderate evidence for efficacy but with a limited clinical benefit; generally recommended
- **C:** Insufficient evidence of efficacy or benefit does not outweigh the risk or the disadvantages (AEs, costs, etc.); optional

MCBS in non-curative settings:[3,4]
Assessment of a treatment's clinical benefit based on survival, QoL and safety benefits compared with previous SoC

- **1–2:** Negligible benefit to patients
- **3:** Moderate benefit to patients
- **4–5:** Substantial benefit to patients



Adapted from ESMO-MCBS Evaluation Forms[5]

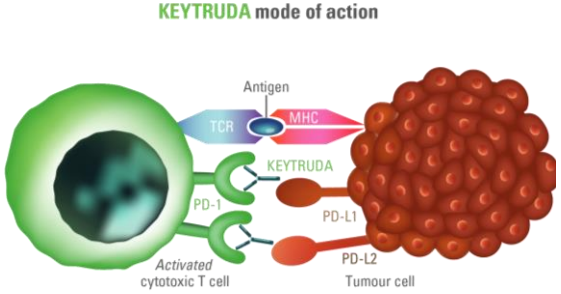
Note: The licensed indication for a product may vary from the patient group in which it is recommended in treatment guidelines. Refer to the Prescribing Information for the latest information about individual product indications.

Note that therapies not approved by the FDA or EMA have been removed from the treatment algorithm.

[a]ESMO-MCBS v1.1 was used to calculate scores for therapies/indications approved by the FDA or EMA. The scores have been calculated and validated by the ESMO-MCBS Working Group and reviewed by the authors.[5]

1L, first-line; 2L, second-line; AE, adverse event; ccRCC, clear-cell renal cell carcinoma; EMA, European Medicines Agency; ESMO, European Society for Medical Oncology; FDA, US Food and Drug Administration; MCBS, Magnitude of Clinical Benefit Scale; QoL, quality of life; SoC, standard of care; VEGFR, vascular endothelial growth factor receptor.

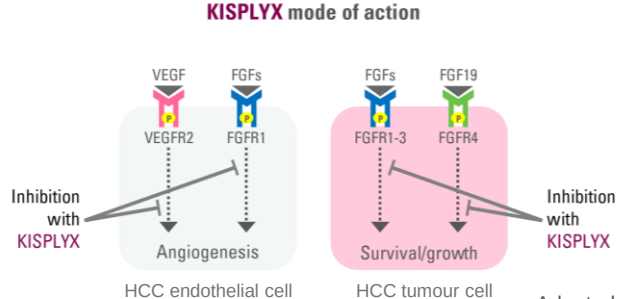
KEYTRUDA + KISPLYX has a dual MOA inhibiting two disease pathways



Adapted from Pardoll DM 2012[6]

The immune-stimulatory effect of **KEYTRUDA** (anti-PD-1)[6,7]

- **KEYTRUDA** is a selective, humanised, monoclonal antibody designed to block the interaction between PD-1 and its ligands, PD-L1 and PD-L2[7]
- By inhibiting PD-1 receptor binding, **KEYTRUDA** **reactivates tumour-specific cytotoxic T lymphocytes** in the tumour microenvironment, resulting in **anti-tumour immunity**[7]



Adapted from Kudo M 2018[8]

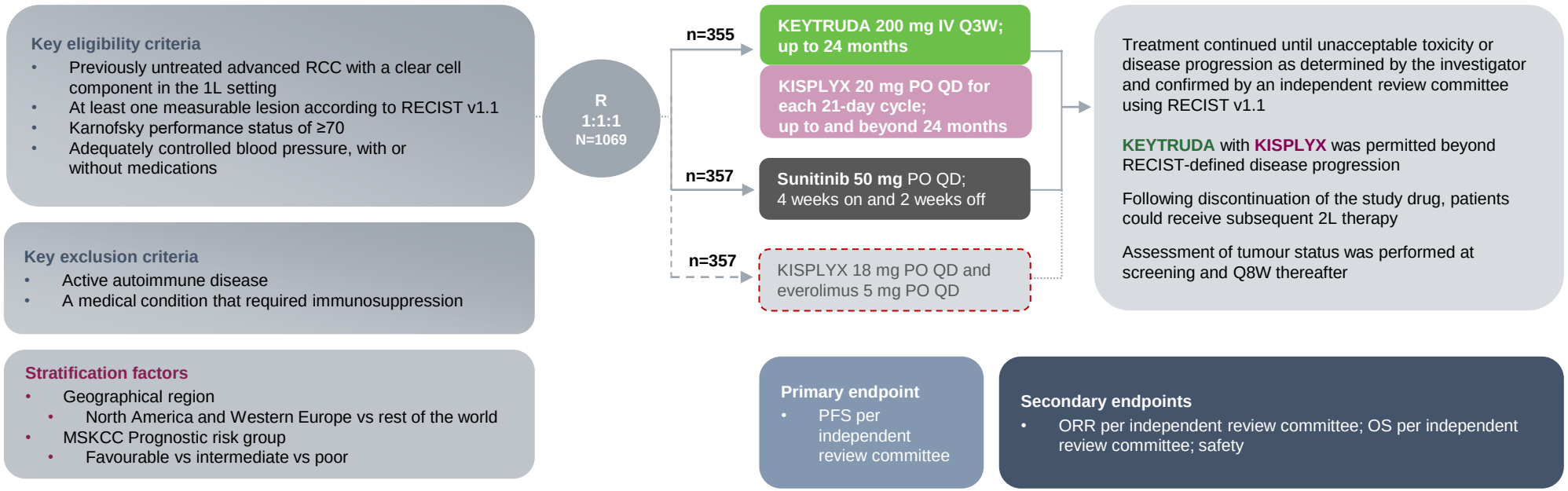
The anti-angiogenic effect of **KISPLYX** (anti-VEGFR/FGFR)[8,9]

- **KISPLYX** is a RTK inhibitor that selectively inhibits the kinase activities of VEGF receptors, VEGFR1 (FLT1), VEGFR2 (KDR), and VEGFR3 (FLT4), in addition to other proangiogenic and oncogenic pathway-related RTKs including FGF receptors FGFR1, 2, 3, and 4; the PDGF receptor, PDGFRα; KIT; and RET[8,9]

FGF, fibroblast growth factor; FGFR, fibroblast growth factor receptor; KIT, proto-oncogene c-KIT; MHC, major histocompatibility complex; MOA, mode of action; PD-1, programmed death receptor-1; PDGFR, platelet-derived growth factor receptor; PD-L1, programmed death ligand-1; PD-L2, programmed death ligand-2; RET, proto-oncogene RET; RTK, receptor tyrosine kinase; TCR, T-cell receptor; VEGF, vascular endothelial growth factor; VEGFR, vascular endothelial growth factor receptor.

The efficacy and safety of **KEYTRUDA** + **KISPLYX** vs sunitinib monotherapy were investigated in the CLEAR trial[10]

A randomised, multicentre, open-label, Phase 3 trial evaluating the efficacy and safety of **KEYTRUDA** + **KISPLYX** in patients with advanced RCC in the 1L setting (N=1069)



Adapted from Motzer R et al. 2021[10]

1L use of KISPLYX in combination with everolimus is not approved in the UK in patients with advanced RCC. This treatment arm has been included for transparency. Clinical data shown are from the KEYTRUDA + KISPLYX vs sunitinib arms only.[7,9]

Full eligibility and exclusion criteria are described in the trial protocol.

1L, first-line; 2L, second-line; DOR, duration of response; IV, intravenous; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PO, orally; Q3W, every 3 weeks; Q8W, every 8 weeks; QD, once daily; R, randomisation; RCC, renal cell carcinoma; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

Patient baseline demographics and disease characteristics[10]

Characteristic[a]	KEYTRUDA + KISPLYX (n=355)	Sunitinib (n=357)
Median age (range), years	64 (34–88)	61 (29–82)
Aged <65 years, n (%)	194 (54.6)	225 (63.0)
Sex, n (%)		
Male	255 (71.8)	275 (77.0)
Female	100 (28.2)	82 (23.0)
Geographical region, n (%)		
Western Europe or North America	198 (55.8)	199 (55.7)
Rest of the world	157 (44.2)	158 (44.3)
Karnofsky performance status, n (%)[b]		
100–90	295 (83.1)	294 (82.4)
80–70	60 (16.9)	62 (17.4)
MSKCC prognostic risk group, n (%)		
Favourable	96 (27.0)	97 (27.2)
Intermediate	227 (63.9)	228 (63.9)
Poor	32 (9.0)	32 (9.0)
IMDC prognostic risk group, n (%)		
Favourable	110 (31.0)	124 (34.7)
Intermediate	210 (59.2)	192 (53.8)
Poor	33 (9.3)	37 (10.4)
Could not be evaluated	2 (0.6)	4 (1.1)

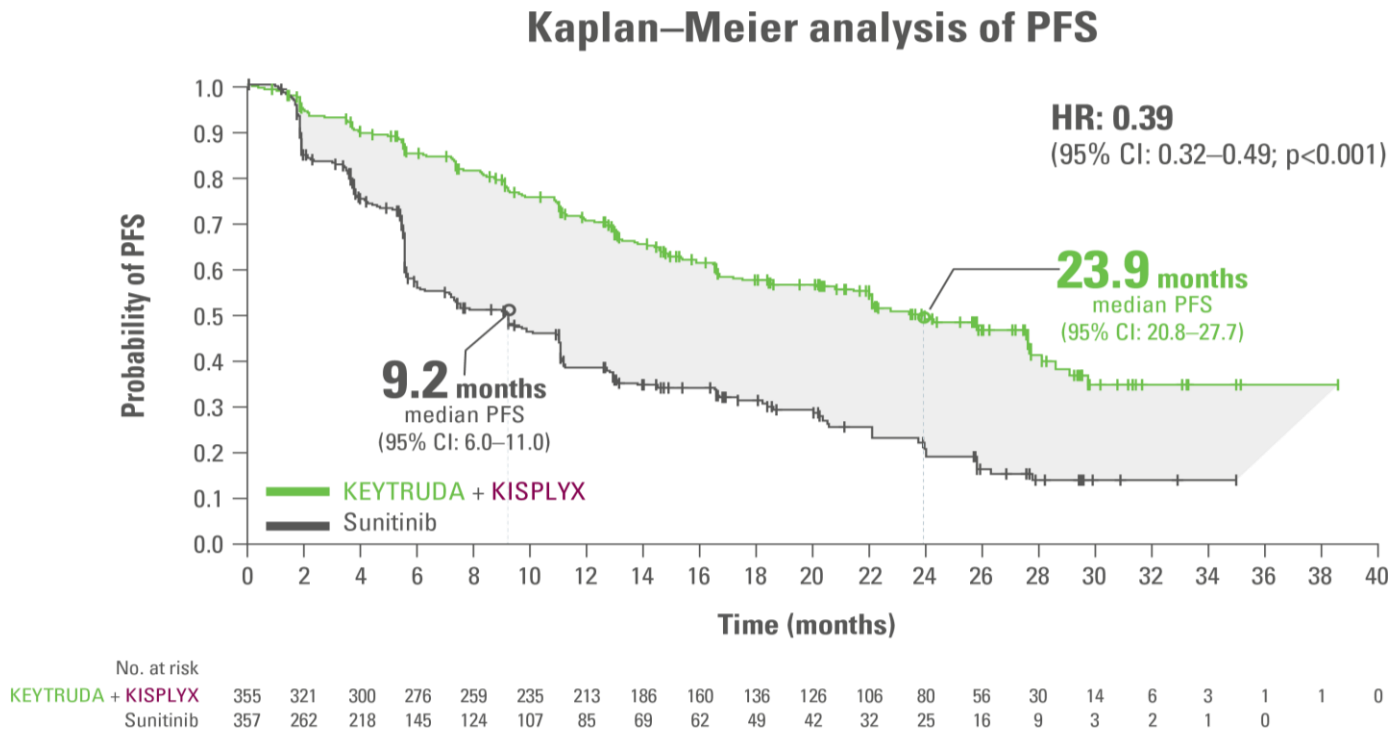
Characteristic[a]	KEYTRUDA + KISPLYX (n=355)	Sunitinib (n=357)
Sarcomatoid features, n (%)	28 (7.9)	21 (5.9)
PD-L1 combined positive score, n (%)		
≥1	107 (30.1)	119 (33.3)
<1	112 (31.5)	103 (28.9)
Not available	136 (38.3)	135 (37.8)
Number of metastatic organs or sites, n (%)[c]		
1	97 (27.3)	108 (30.3)
≥2	254 (71.5)	246 (68.9)
Site of metastasis, n (%)[d]		
Lung	249 (70.1)	239 (66.9)
Lymph node	170 (47.9)	159 (44.5)
Bone	85 (23.9)	97 (27.2)
Liver	60 (16.9)	61 (17.1)
Previous nephrectomy, n (%)	262 (73.8)	275 (77.0)

Adapted from Motzer R et al. 2021[10]

[a]One patient in the KEYTRUDA + KISPLYX group had carcinoma without a clear cell component; [b]Karnofsky performance status was missing for one patient in the sunitinib group; [c]Kidney was not included in the number of metastatic organs or sites; [d]Four common sites of metastasis are shown. Patients may have had metastasis at more than one site.
IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; MSKCC, Memorial Sloan Kettering Cancer Center; PD-L1, programmed death ligand-1.

Primary endpoint — KEYTRUDA + KISPLYX more than doubled median PFS vs sunitinib[a,10]

PFS was significantly longer in the **KEYTRUDA** + **KISPLYX** group compared with the sunitinib group

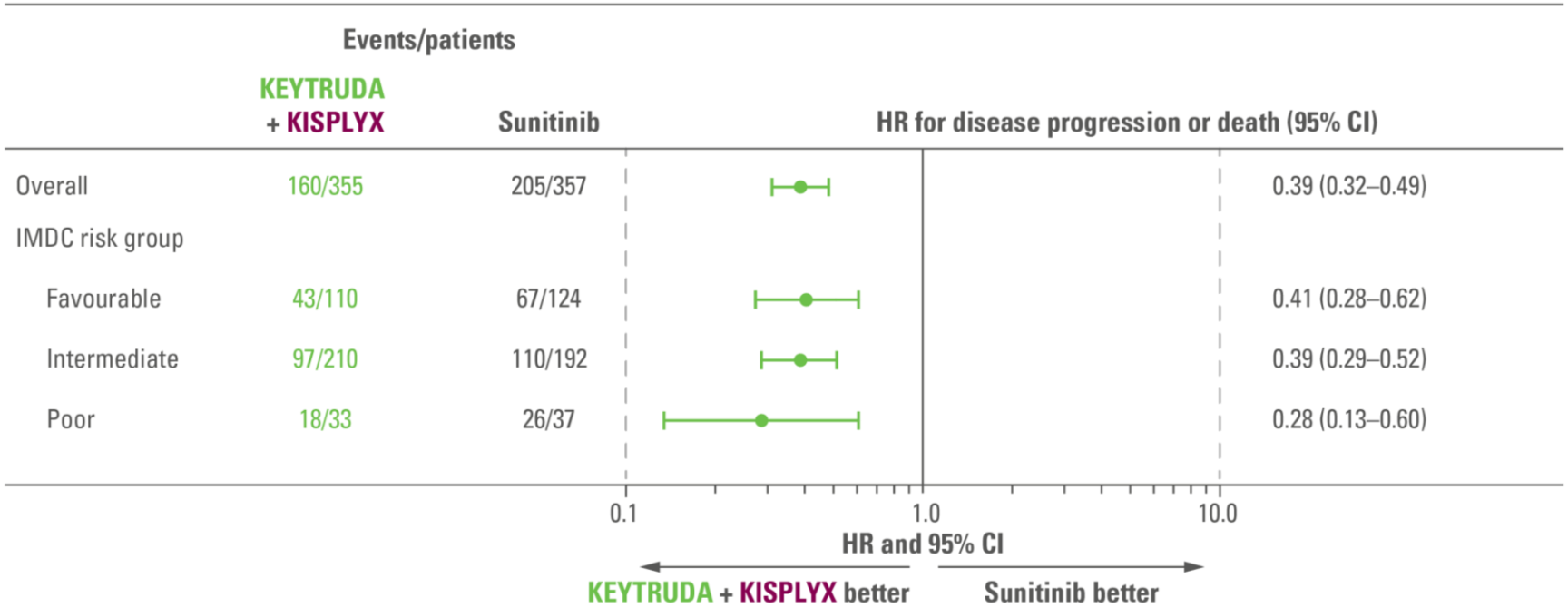


61%
reduction in risk of disease progression with **KEYTRUDA + KISPLYX** vs sunitinib

Adapted from Motzer R et al. 2021[10]

Analysis cutoff date: 28 August 2020. Median follow-up: 26.6 months.
[a]Assessed using RECIST v1.1 by an independent review committee.
CI, confidence interval; HR, hazard ratio; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; PFS, progression-free survival; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

Subgroup analysis — PFS in IMDC risk groups[a,10]



Adapted from Motzer R et al. 2021[10]

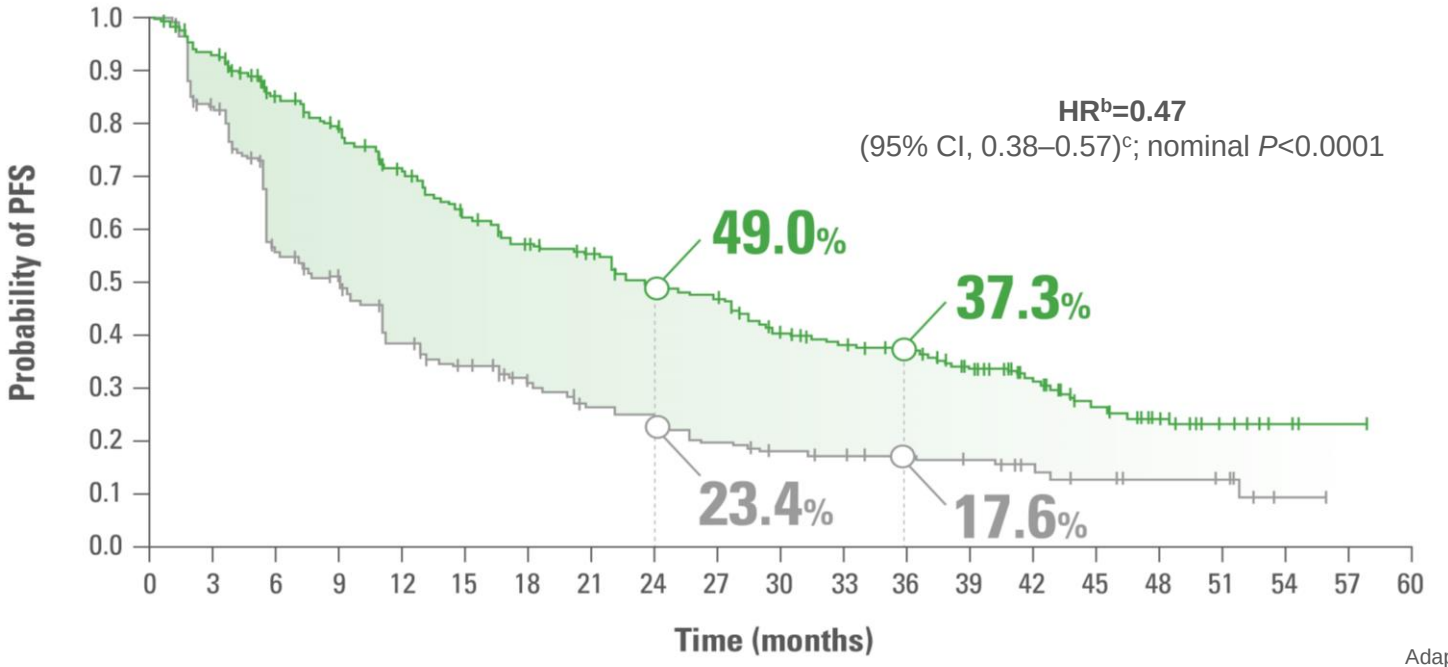
This study was not powered to detect differences in the treatment effect between these subgroups. Results from exploratory analyses should be interpreted with caution due to modest patient numbers and potential imbalances in baseline characteristics between subgroups

Analysis cutoff date: 28 August 2020. Median follow up: 26.6 months.
[a]Patients were stratified by MSKCC risk group but not by IMDC risk group.
CI, confidence interval; HR, hazard ratio; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; MSKCC, Memorial Sloan Kettering Cancer Center; PFS, progression-free survival.

Prespecified final analysis

Exploratory analysis — **KEYTRUDA** + **KISPLYX** PFS consistent with primary analysis at 39.2 months median follow up[a,11]

Median (IQR) follow-up for PFS: 39.2 (22.1–48.5) months with **KEYTRUDA** + **KISPLYX** and 20.6 (5.5–41.2) months with sunitinib



HR[b]=0.47
(95% CI, 0.38–0.57)[c]; nominal *P*<0.0001

	Median PFS, months (95% CI)
Pembrolizumab + lenvatinib (n=355)	23.9 (20.8–27.7)
Sunitinib (n=357)	9.2 (6.0–11.0)

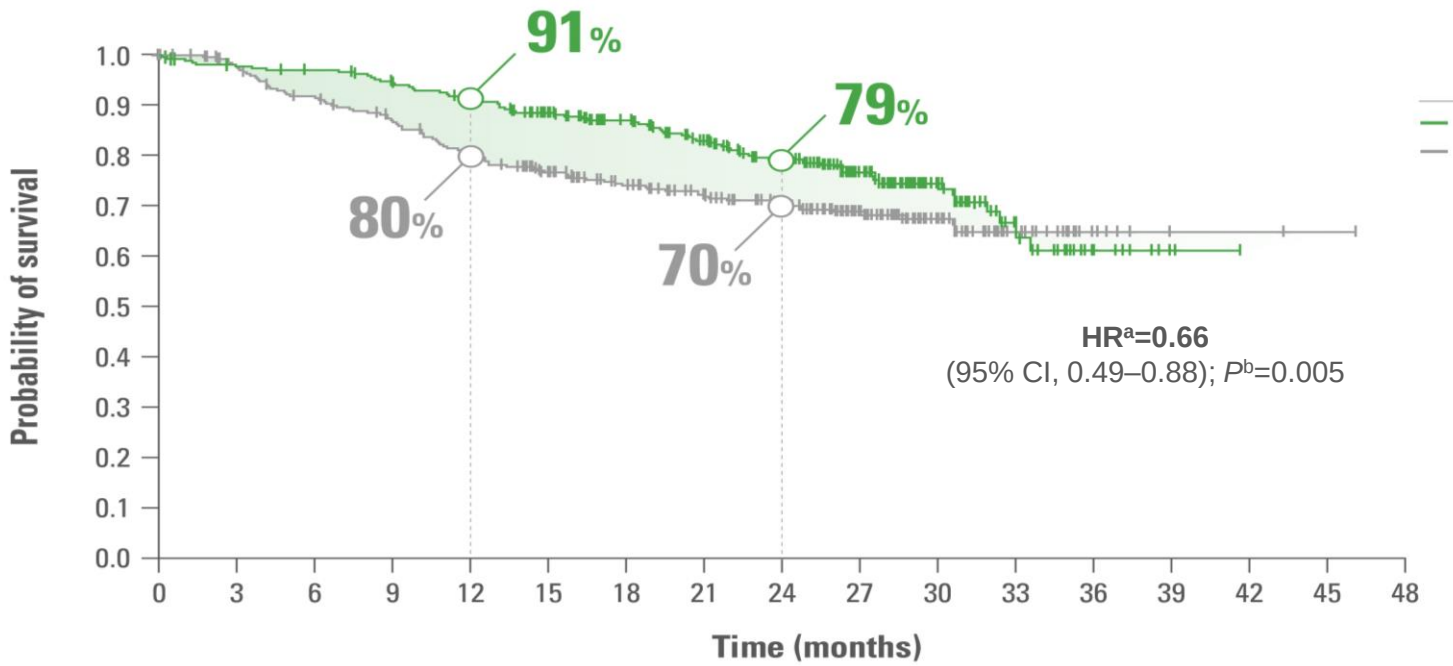
No. at risk											
Pembrolizumab + lenvatinib	355	276	213	161	128	99	81	49	25	4	0
Sunitinib	357	145	85	59	41	30	23	12	7	1	0

LIMITATION: No formal statistical testing was performed for this analysis, and, therefore, no conclusions can be drawn.

Adapted from Motzer R et al. ASCO 2023[11]

Analysis cutoff date: 31 July 2022.
[a]Assessed using RECIST v1.1 by an independent review committee; [b]HR based on a Cox proportional hazards model including treatment group as factor. Efron method used for ties and stratified by geographic region and MSKCC prognostic groups by IxRS factors; [c]The 95% CIs are estimated with a generalised Brookmeyer and Crowley method. IQR, interquartile range; IxRS, Interactive Voice/Web Response System.

Secondary endpoint — Superior OS with **KEYTRUDA** + **KISPLYX** vs sunitinib[10]



	Events	Median OS, months (95% CI)
Pembrolizumab + lenvatinib (n=355)	80/355 (23%)	NR (33.6–NE)
Sunitinib (n=357)	101/357 (28%)	NR (NE–NE)

No. at risk																	
Pembrolizumab + lenvatinib	355	342	338	327	313	280	253	222	188	129	66	26	10	2	0	0	0
Sunitinib	357	332	307	289	264	236	207	186	160	112	60	25	7	2	2	1	0

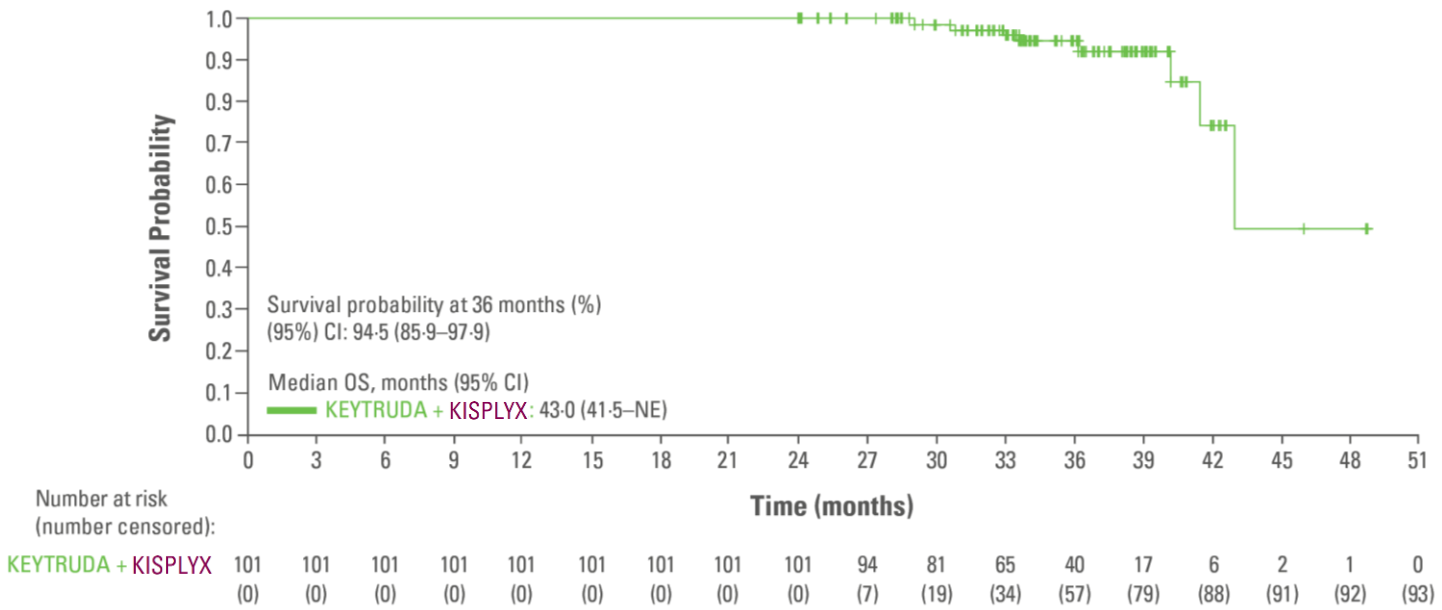
34%
reduced risk of death vs sunitinib

- **KEYTRUDA + KISPLYX** superior OS vs sunitinib: Reduced the risk of death by 34% (HR:[a] 0.66; 95% CI: 0.49–0.88; p=0.005[b])
- **Median OS**: NR in both arms
- OS may be confounded by the difference in subsequent therapies

Adapted from Motzer R et al. 2021[10]

Analysis cutoff date: 28 August 2020. Median follow up: 26.6 months.
[a]Based on the stratified Cox proportional-hazards model; [b]Two-sided p-value based on stratified log-rank test.
CI, confidence interval; HR, hazard ratio; NE, not estimable; NR, not reached; OS, overall survival.

Exploratory analysis - OS in patients who completed 2 years of KEYTRUDA and continued on KISPLYX monotherapy[12]



- Of patients who completed 2 years of **KEYTRUDA** and continued with **KISPLYX** monotherapy (101/355 patients), exploratory OS rate was 94.5% at 36 months based on Kaplan–Meier estimate
  - Of the 101 patients, 65 had IMDC intermediate/poor-risk disease and 36 had favourable-risk disease

Results from exploratory analyses should be interpreted with caution due to modest patient numbers and potential imbalances in baseline characteristics between subgroups

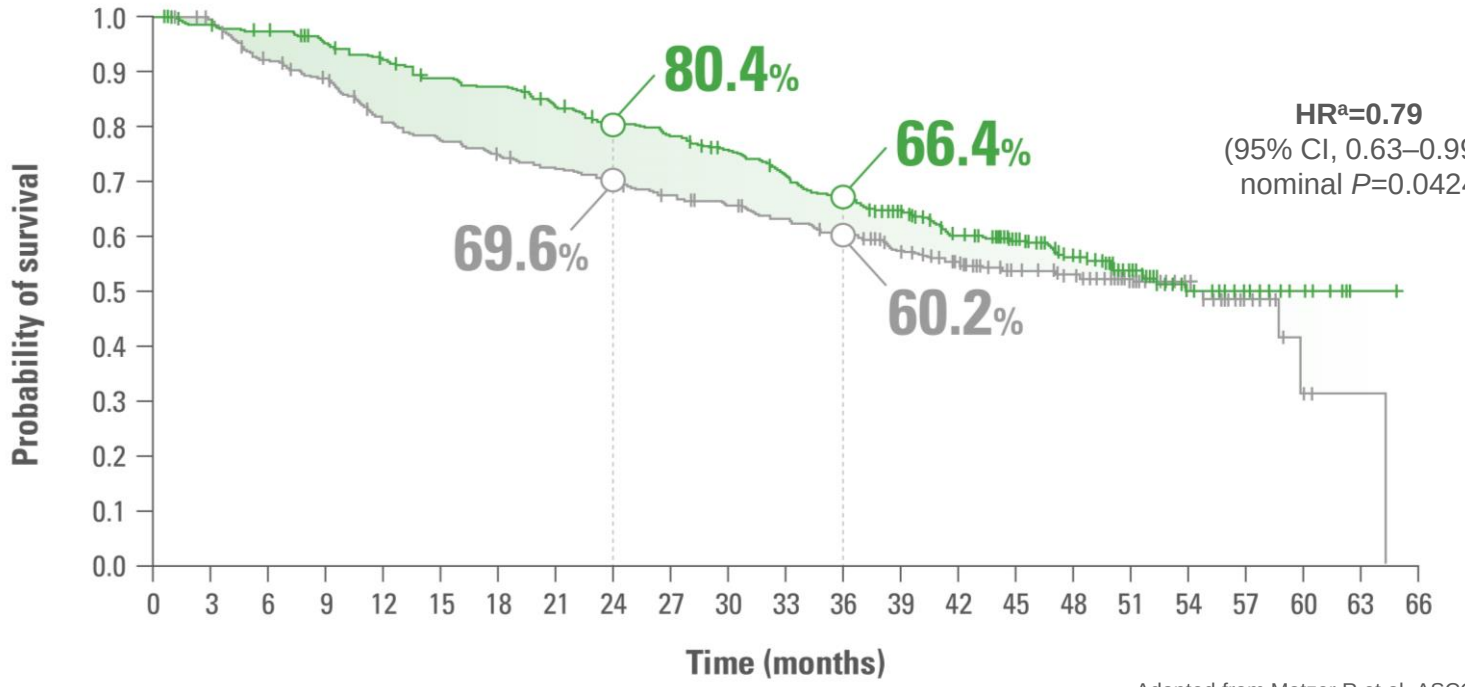
Adapted from Choueiri et al. 2023[12]

Analysis cut-off date: 31 March 2021.
CI, confidence interval; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; NE, not estimable; OS, overall survival.

Prespecified final analysis

Exploratory analysis — **KEYTRUDA** + **KISPLYX** OS at 49.8 months median follow up[11]

Median (IQR) follow-up for OS: 49.8 (41.4–53.1) months with **pembrolizumab** + **lenvatinib** and 49.4 (41.6–52.8) months with sunitinib



HR[a]=0.79
(95% CI, 0.63–0.99);
nominal *P*=0.0424

	Median OS, months (95% CI)
Pembrolizumab + lenvatinib (n=355)	53.7 (48.7–NE)
Sunitinib (n=357)	54.3 (40.9–NE)

No. at risk												
Pembrolizumab + lenvatinib	355	338	313	296	269	245	216	158	117	34	5	0
Sunitinib	357	308	264	242	226	208	188	145	108	33	3	0

Adapted from Motzer R et al. ASCO 2023[11]

The OS analysis was not adjusted to account for subsequent therapies; 54.6% of patients in the sunitinib arm subsequently received a PD-1/PD-L1 checkpoint inhibitor vs 15.8% in the **KEYTRUDA** + **KISPLYX** arm

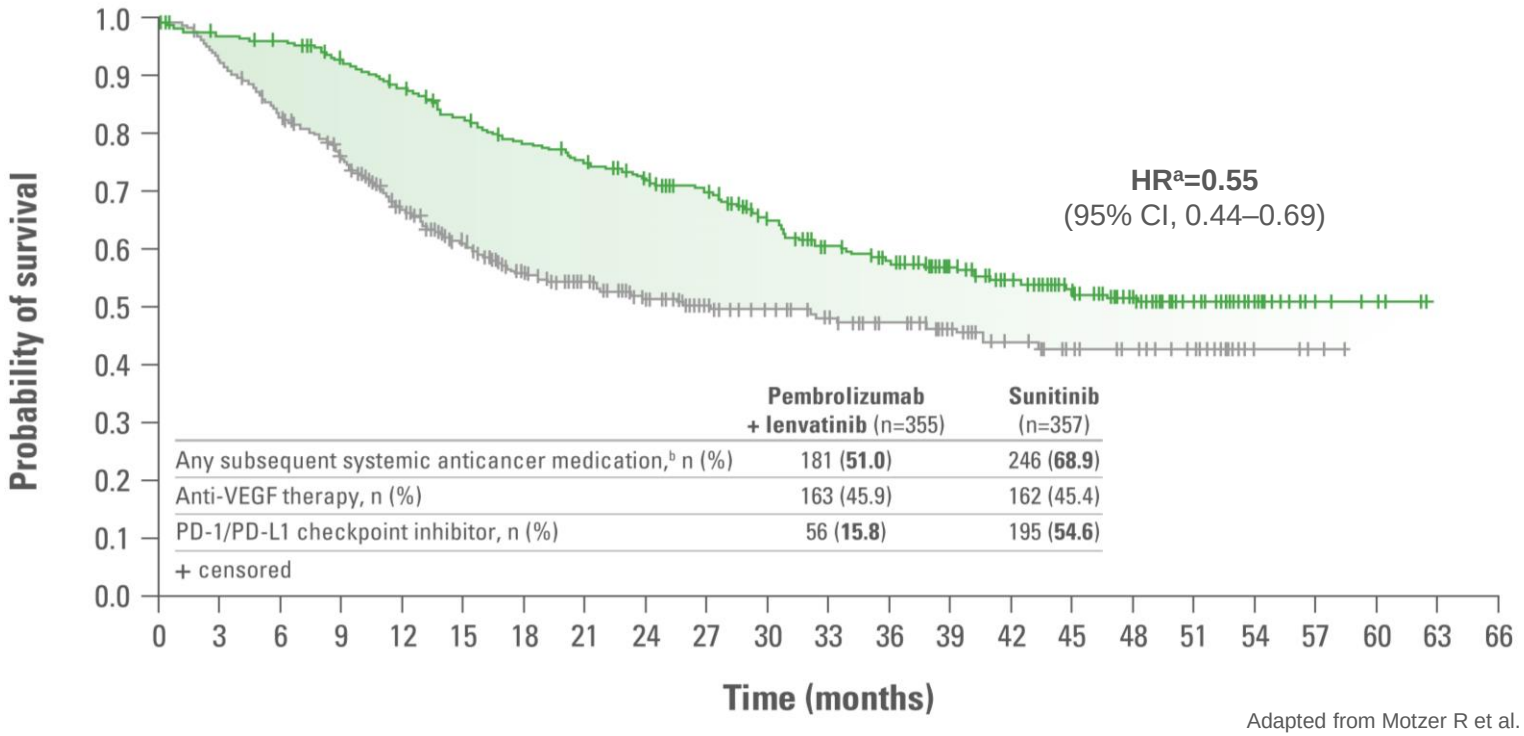
LIMITATION:
This was a protocol-pre-specified analysis. No formal statistical testing was performed for this analysis, and, therefore, no conclusions can be drawn.
OS results after 36 months of follow-up should be interpreted with caution due to the number of censored patients.

Analysis cutoff date: 31 July 2022. A total of 308 target OS events had occurred, of which 149 were with pembrolizumab + lenvatinib and 159 with sunitinib.
[a]HR and 2-sided 95% CI for lenvatinib + pembrolizumab vs sunitinib were estimated by a stratified Cox Proportional Hazards Model with Efron's method for ties, stratified by geographic region and MSKCC prognostic groups.
CI, confidence interval; HR, hazard ratio; NE, not estimable; NR, not reached; OS, overall survival.

Prespecified final analysis

Exploratory analysis — Final OS analysis adjusted for subsequent anticancer medications[11]

Median (IQR) follow-up for OS: 49.8 (41.4–53.1) months with **pembrolizumab** + **lenvatinib** and 49.4 (41.6–52.8) months with sunitinib



Median OS, months (95% CI)	
Pembrolizumab + lenvatinib	NR (40.9–NE)
Sunitinib	32.0 (18.7–NE)

LIMITATION: No formal statistical testing was performed for this final pre-specified analysis and, therefore, no conclusions can be drawn.

Adapted from Motzer R et al. ASCO 2023[11]

No. at risk												
Pembrolizumab + lenvatinib	355	336	303	266	240	193	159	107	68	19	3	0
Sunitinib	357	282	212	140	100	72	56	37	26	4	0	0

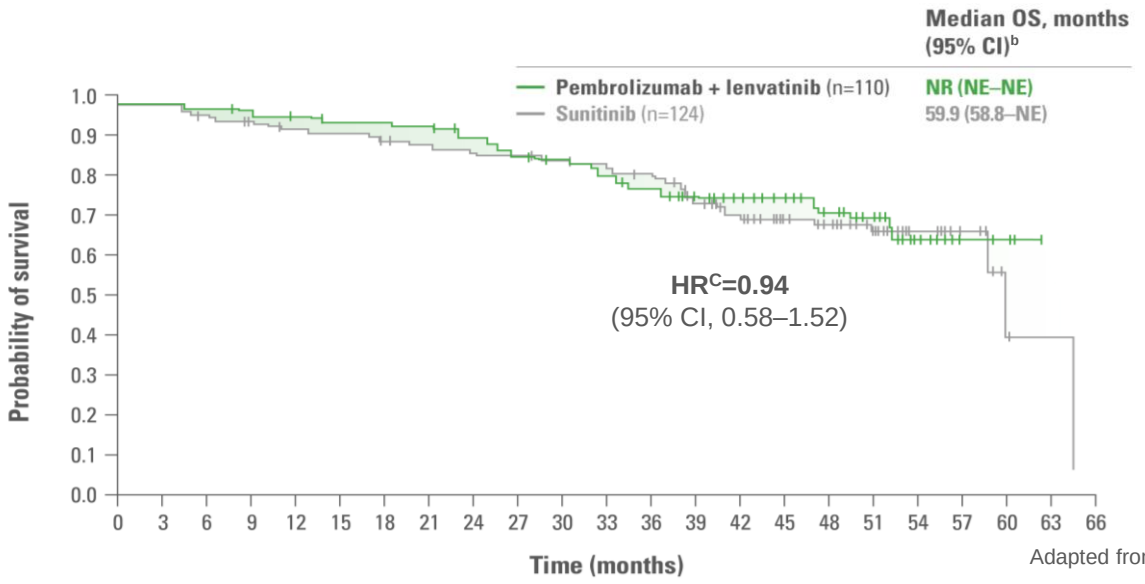
Analysis cutoff date: 31 July 2022. [a]A 2-stage estimation method was used for the post-hoc analysis of OS to adjust for the impact of imbalance in subsequent anticancer medications between treatment groups; [b]During survival follow–up.

Prespecified final analysis

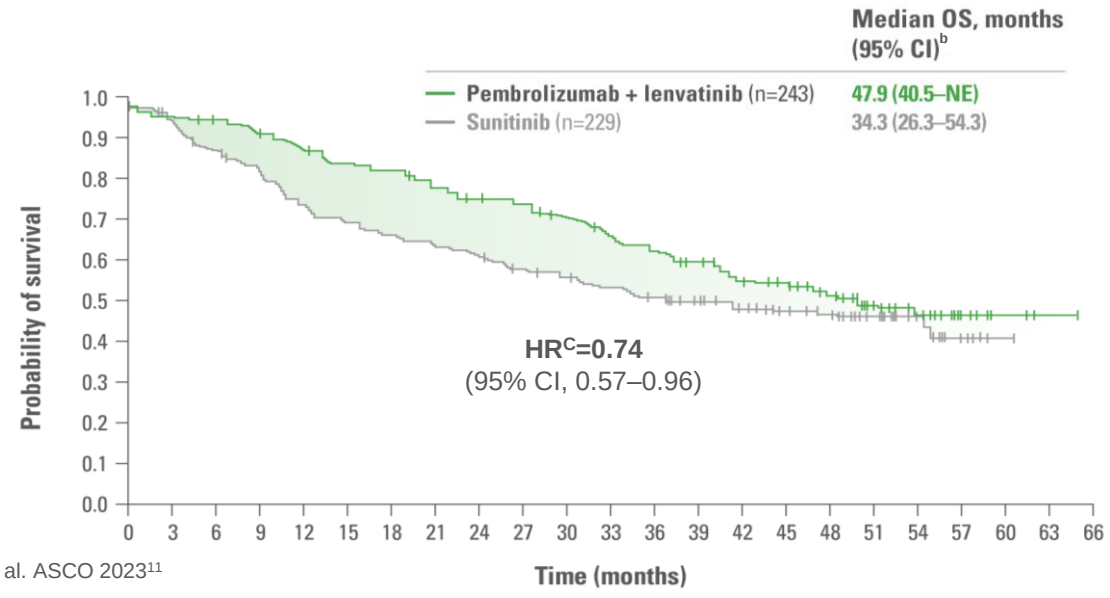
Exploratory analysis — Kaplan-Meier estimates of OS by IMDC risk subgroup[a,11]

Median (IQR) follow-up for OS: 49.8 (41.4–53.1) months with **pembrolizumab** + **lenvatinib** and 49.4 (41.6–52.8) months with sunitinib

Favourable



Intermediate + poor



Adapted from Motzer R et al. ASCO 2023[11]

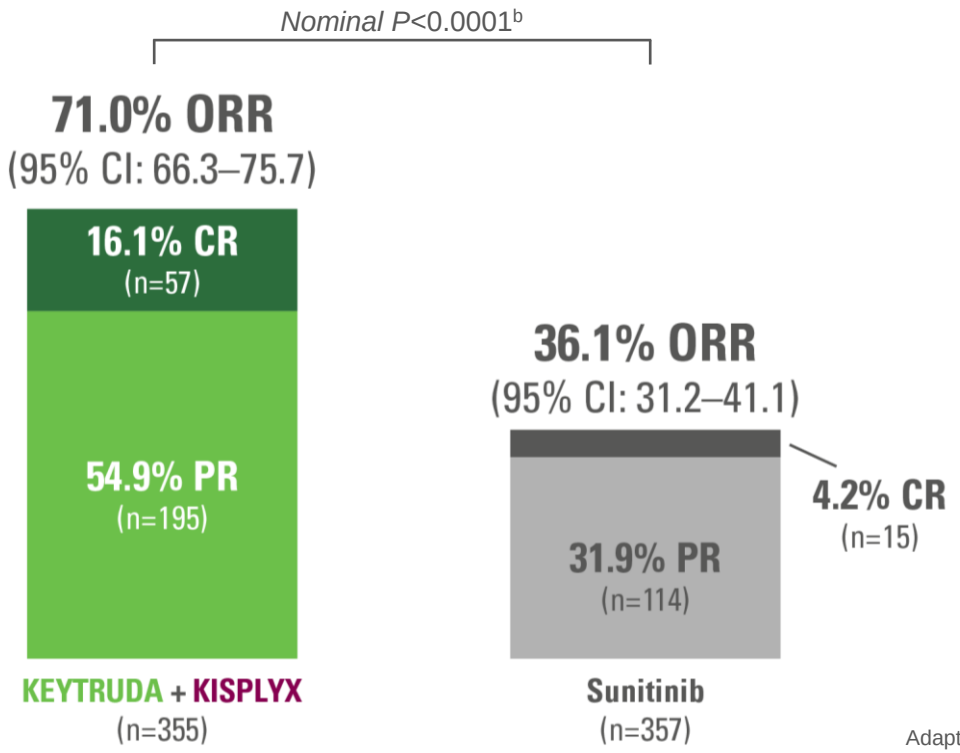
LIMITATION: This trial was not powered to detect differences between subgroups. No formal statistical testing was planned for this exploratory analysis and, therefore, no conclusions can be drawn.

Analysis cutoff date: 31 July 2022.

[a]IMDC risk group was not a stratification factor and relevant data were derived programmatically; [b]Medians were estimated by the Kaplan–Meier method, and 95% CIs were estimated with a generalised Brookmeyer and Crowley method; [c]HR was based on a Cox regression model with treatment as a factor and with Efron's method used for correction of tied events.

Secondary endpoint — ORR[a] nearly double with **KEYTRUDA** + **KISPLYX** vs sunitinib[7,9,10]

Superior ORR vs sunitinib



- Progressive disease was observed in 5.4% of patients who received **KEYTRUDA** + **KISPLYX** vs 14% of patients with sunitinib
- Stable disease was observed in 19.2% of patients who received **KEYTRUDA** + **KISPLYX** vs 38.1% of patients with sunitinib
- The median time to first response for **KEYTRUDA** + **KISPLYX** compared with sunitinib was 1.94 (1.41–20.14) and 1.99 (1.51–16.56) months, respectively
- The median duration of response for **KEYTRUDA** + **KISPLYX** compared with sunitinib was 25.8 (22.1–27.9) and 14.6 (9.4–16.7) months, respectively

Adapted from Motzer R et al. 2021[10]

Analysis cutoff date: 28 August 2020. Median follow-up: 26.6 months.

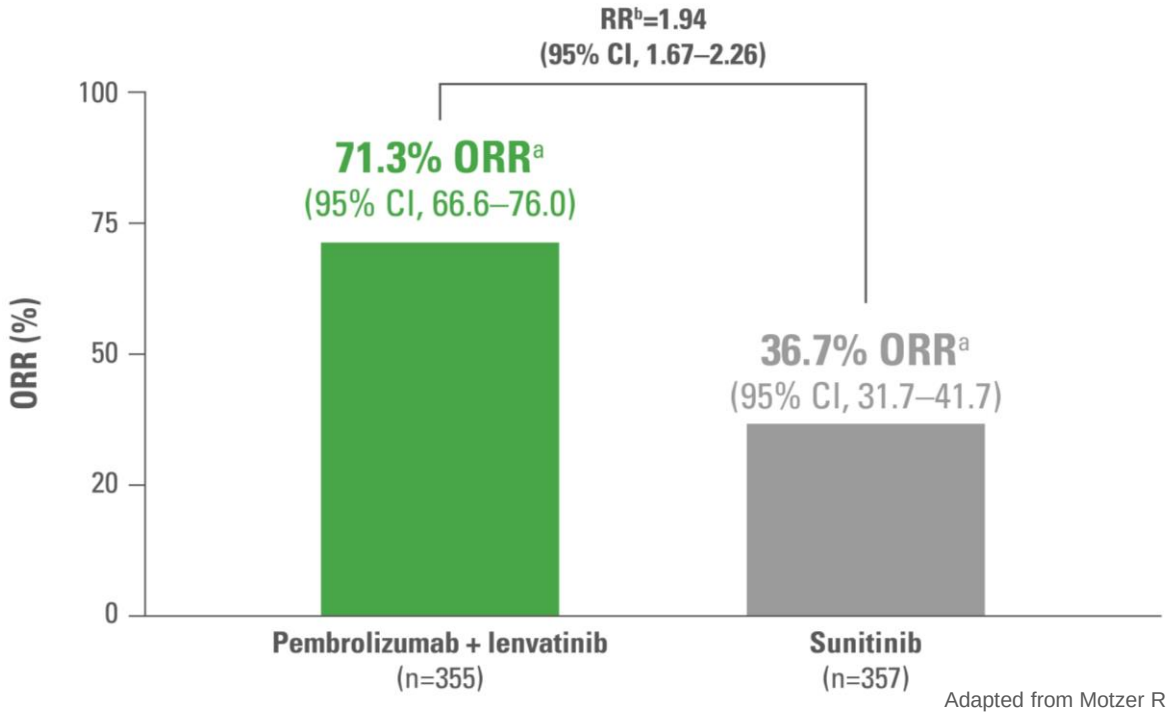
[a]Assessed using RECIST v1.1; [b]Nominal P-value. At the Interim Analysis 2 prespecified final analysis of ORR (median follow-up time of 17.3 months), statistically significant superiority was achieved for ORR comparing KEYTRUDA + KISPLYX with sunitinib (odds ratio: 3.84 [95% CI: 2.81, 5.26], nominal P-value <0.0001).[7,9]

CI, confidence interval; CR, complete response; ORR, objective response rate; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

Prespecified final analysis

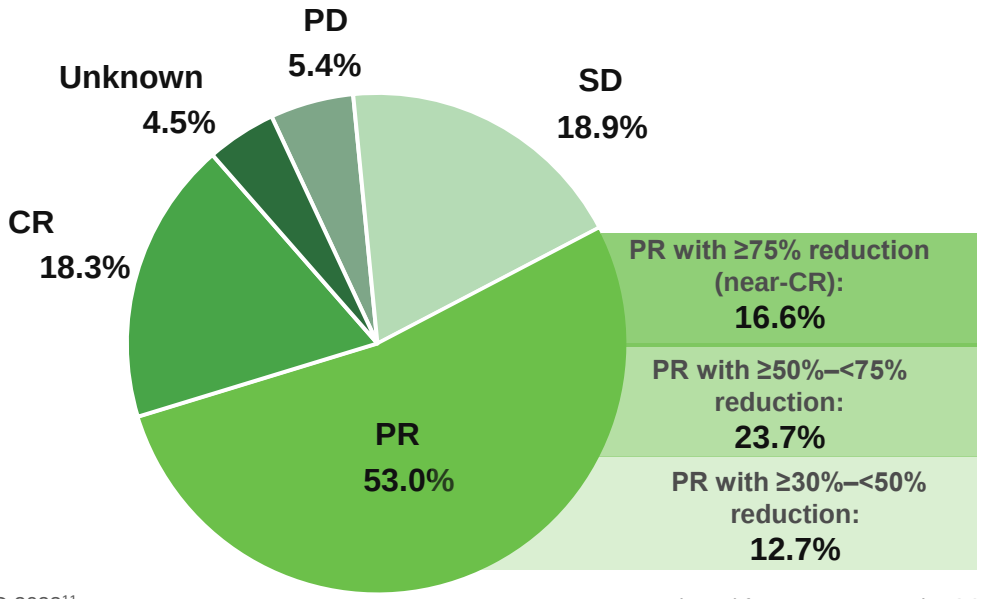
Exploratory analysis — ORR consistent with primary analysis at 49.8 months median follow up[a,11]

Median (IQR) follow-up for OS: 49.8 (41.4–53.1) months with **KEYTRUDA** + **KISPLYX** and 49.4 (41.6–52.8) months with sunitinib



Adapted from Motzer R et al. ASCO 2023[11]

Best overall response[c] with KEYTRUDA + KISPLYX



Adapted from Motzer R et al. ASCO 2023[11]

LIMITATION: No formal statistical analysis was performed for this analysis; therefore, no conclusions can be drawn.

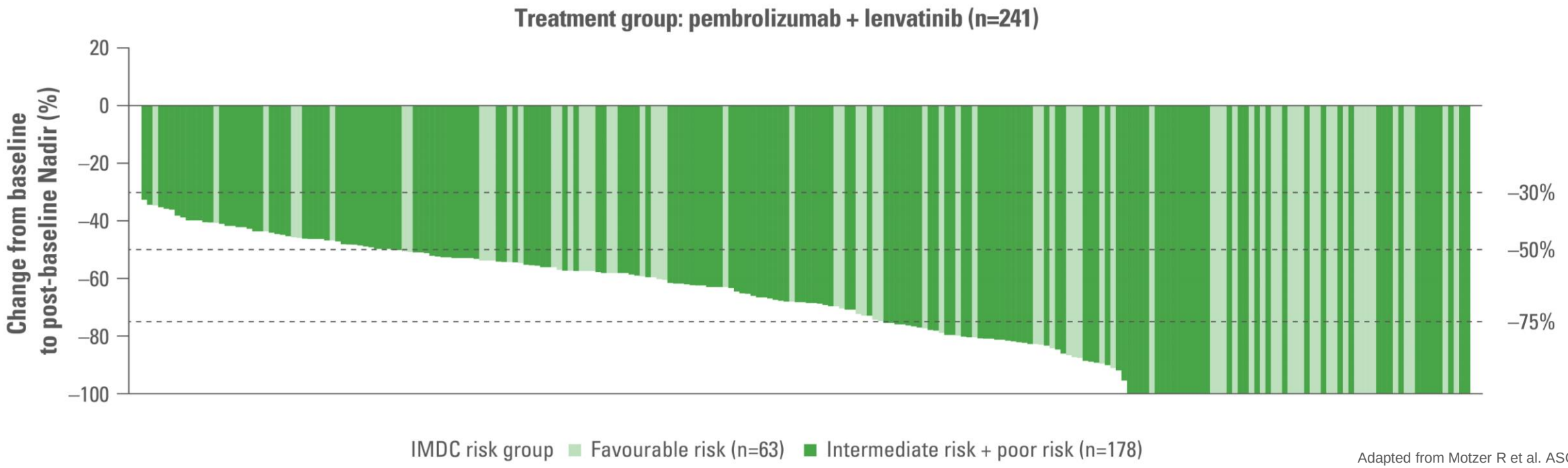
Analysis cutoff date: 31 July 2022. When median follow-up time was not specified for an endpoint, median follow-up for OS is presented in the slide. [a]As determined by independent review committee using RECIST v1.1; [b]RR, Relative Risk was calculated using the Cochran-Mantel-Haenzel methods stratified by IxRS factors, and the 95% CIs were calculated using the method of normal approximation; [c]Best overall response categories (SD, PD, CR, PR or unknown) were determined based on RECIST v1.1 at the time of analysis. SD must occur ≥49 days after randomization. If a patient best overall response was non-CR/non- PD, it was grouped with the SD category.[13]

RR, relative risk.

Prespecified final analysis

Exploratory analysis — Change in target lesion size[a] in patients who responded to treatment with KEYTRUDA + KISPLYX[11]

Median (IQR) follow-up for OS: 49.8 (41.4–53.1) months with **KEYTRUDA** + **KISPLYX** and 49.4 (41.6–52.8) months with sunitinib



Adapted from Motzer R et al. ASCO 2023[11]

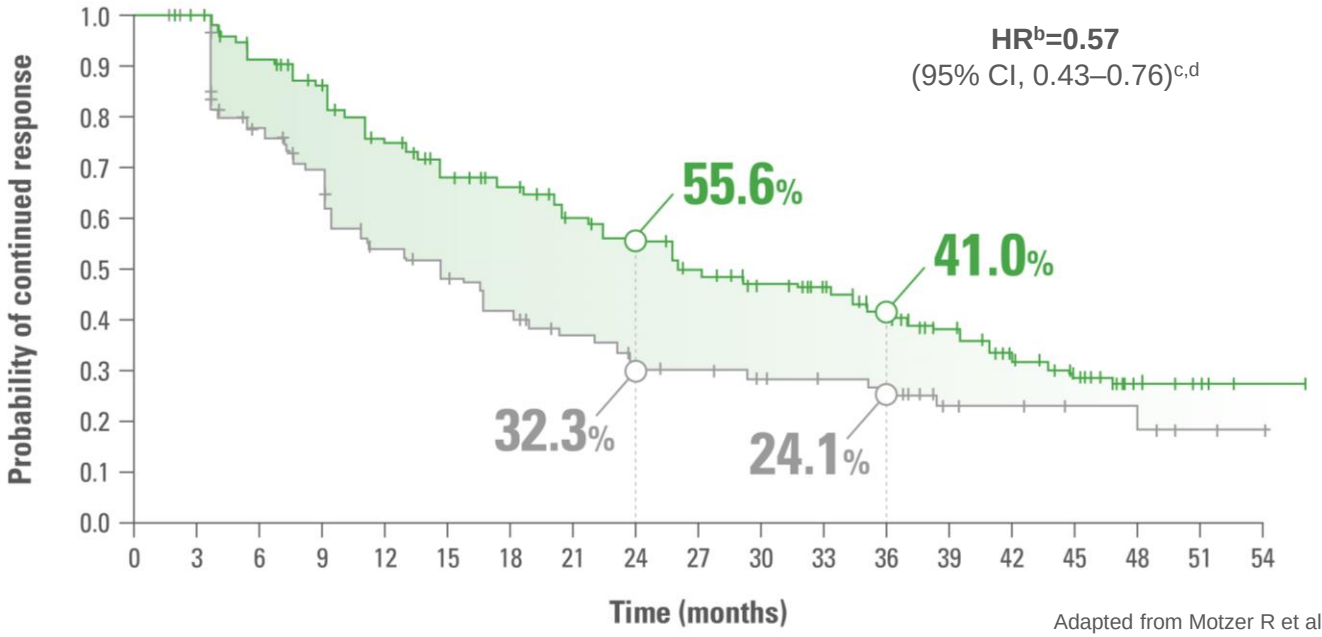
LIMITATION: No formal statistical analysis was performed for this analysis; therefore, no conclusions can be drawn.

Analysis cutoff date: 31 July 2022. When median follow-up time was not specified for an endpoint, median follow-up for OS is presented in the slide.
[a]Changes in size of the target lesion were determined as per independent review. Patients included in the analysis had both baseline and ≥1 post-baseline target lesion assessment.

Prespecified final analysis

Exploratory analysis — Duration of response (DOR)[a,11]

Median (IQR) follow-up for OS: 49.8 (41.4–53.1) months with **KEYTRUDA** + **KISPLYX** and 49.4 (41.6–52.8) months with sunitinib



Adapted from Motzer R et al. ASCO 2023[11]

	Median DOR, months (95% CI)
Pembrolizumab + lenvatinib (n=253)	26.7 (22.8–34.6)
Sunitinib (n=131)	14.7 (9.4–18.2)

- In the **pembrolizumab** + **lenvatinib** group, median DOR (95% CI) for CR was **43.7** (39.2–NE) months
- Median DOR (95% CI) for near-CR[e] with **pembrolizumab** + **lenvatinib** was **30.5** (22.4–NE) months

LIMITATION: This analysis was a protocol pre-specified descriptive analysis. No formal statistical analysis was performed for this analysis; therefore, no conclusions can be drawn.

Analysis cutoff date: 31 July 2022. When median follow-up time was not specified for an endpoint, median follow-up for OS is presented in the slide.
[a]As determined by independent review committee using RECIST v1.1; [b]HR is based on a Cox Proportional Hazards Model including treatment group as a factor. Efron method is used for ties and stratified by geographic region and MSKCC prognostic groups by IxRS; [c]The 95% CIs were estimated using the method of normal approximation; [d]The 95% CIs are estimated with a generalised Brookmeyer and Crowley method; [e]Near-CR refers to individuals who presented a PR with a maximum tumour reduction of ≥75%.
NE, not estimable.

Subgroup analysis — Tumour responses across subgroups of interest[14]

Median follow-up: 26.6 months with **KEYTRUDA** + **KISPLYX** and with sunitinib[6]

Parameter	Sarcomatoid features				Bone metastases			
	Yes		No		Yes		No	
	Pembrolizumab + lenvatinib (n=28)	Sunitinib (n=21)	Pembrolizumab + lenvatinib (n=327)	Sunitinib (n=336)	Pembrolizumab + lenvatinib (n=85)	Sunitinib (n=97)	Pembrolizumab + lenvatinib (n=270)	Sunitinib (n=260)
ORR,[a] n (%)	17 (60.7)	5 (23.8)	235 (71.9)	124 (36.9)	55 (64.7)	22 (22.7)	197 (73.0)	107 (41.2)

Parameter	Liver metastases				Previous nephrectomy			
	Yes		No		Yes		No	
	Pembrolizumab + lenvatinib (n=60)	Sunitinib (n=61)	Pembrolizumab + lenvatinib (n=295)	Sunitinib (n=296)	Pembrolizumab + lenvatinib (n=262)	Sunitinib (n=275)	Pembrolizumab + lenvatinib (n=93)	Sunitinib (n=82)
ORR, [a] n (%)	40 (66.7)	21 (34.4)	212 (71.9)	108 (36.5)	193 (73.7)	110 (40.0)	59 (63.4)	19 (23.2)

Parameter	Lung metastases			
	Yes		No	
	Pembrolizumab + lenvatinib (n=249)	Sunitinib (n=239)	Pembrolizumab + lenvatinib (n=106)	Sunitinib (n=118)
ORR, [a] n (%)	186 (74.7)	87 (36.4)	66 (62.3)	42 (35.6)

Adapted from Grünwald V et al 2023[14]

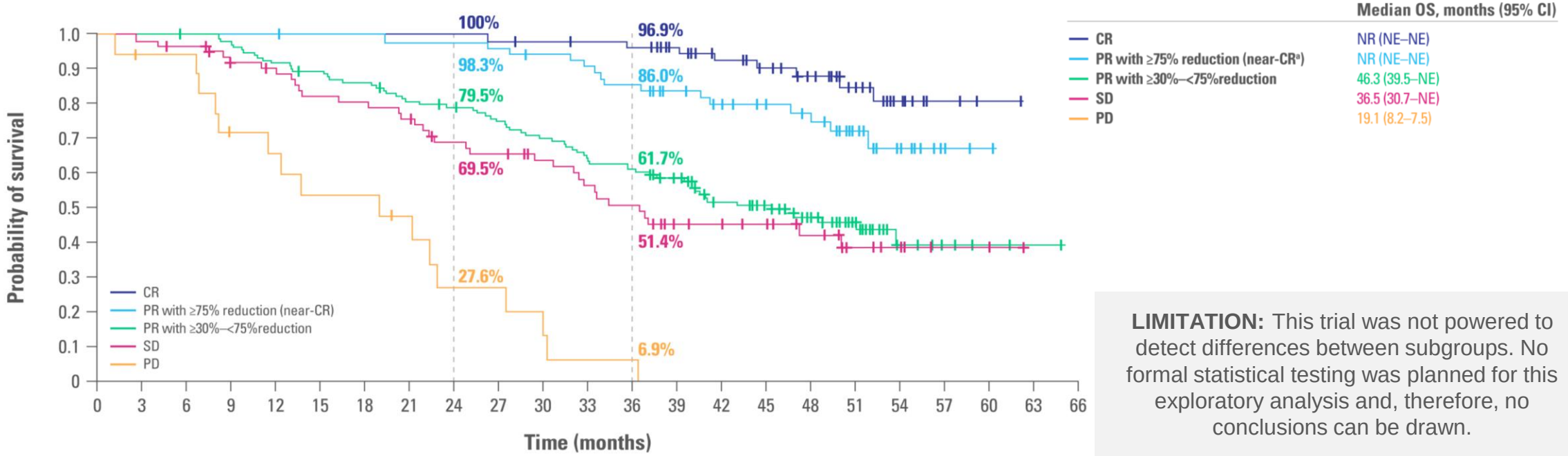
This study was not powered to detect differences in the treatment effect between these subgroups. Results from exploratory analyses should be interpreted with caution due to modest patient numbers and potential imbalances in baseline characteristics between subgroups

Analysis cutoff date: 28 August 2020.[a]Assessed using RECIST v1.1.
CI, confidence interval; ORR, objective response rate; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

Prespecified final analysis

Exploratory analysis — Final OS analysis by best overall response in patients treated with **KEYTRUDA** + **KISPLYX**[11]

Median (IQR) follow-up for OS: 49.8 (41.4–53.1) months with **KEYTRUDA** + **KISPLYX** and 49.4 (41.6–52.8) months with sunitinib



No. at risk																							
CR	65	65	65	65	65	65	65	65	65	64	63	62	61	53	46	40	35	24	12	4	1	0	0
PR with ≥75% reduction (near-CR[a])	59	59	59	59	59	58	58	57	57	56	54	52	49	44	40	33	30	19	9	2	1	0	0
PR with ≥30%–<75%reduction	129	129	128	126	118	114	110	102	99	93	87	80	76	66	51	46	37	24	8	4	2	1	0
SD	67	66	64	60	56	51	50	47	41	39	35	31	28	21	20	18	14	8	5	2	1	0	0
PD	19	17	17	12	11	9	9	7	4	4	3	1	1	0	0	0	0	0	0	0	0	0	0

Analysis cutoff date: 31 July 2022.

[a]Near-CR refers to individuals who presented a PR with a maximum tumour reduction of ≥75%.

LIMITATION: This trial was not powered to detect differences between subgroups. No formal statistical testing was planned for this exploratory analysis and, therefore, no conclusions can be drawn.

Adapted from Motzer R et al. ASCO 2023[11]

Secondary endpoint — AE summary for **KEYTRUDA** + **KISPLYX** compared with sunitinib[a,10]

	KEYTRUDA + KISPLYX (n=352)	Sunitinib (n=340)
Median duration of treatment, months (range)	17.0 (0.1–39.1)	7.8 (0.1–37.0)
AEs of any grade, any cause, %	99.7	98.5
Grade ≥3	82.4	71.8
Death during treatment (Grade 5 AE)[b]	4.3	3.2
Patients with any grade TEAEs leading to discontinuation vs sunitinib, %		
Pembrolizumab, lenvatinib, or both drugs	37.2	14.4
Pembrolizumab	28.7	
Lenvatinib	25.6	
Pembrolizumab + lenvatinib	13.4	
Patients with any grade TEAEs leading to dose interruption (pembrolizumab, lenvatinib, or both drugs) vs sunitinib, %	78.4	53.8
Patients with any grade TEAEs leading to dose reduction (for lenvatinib ONLY) vs sunitinib[c], %	68.8	50.3

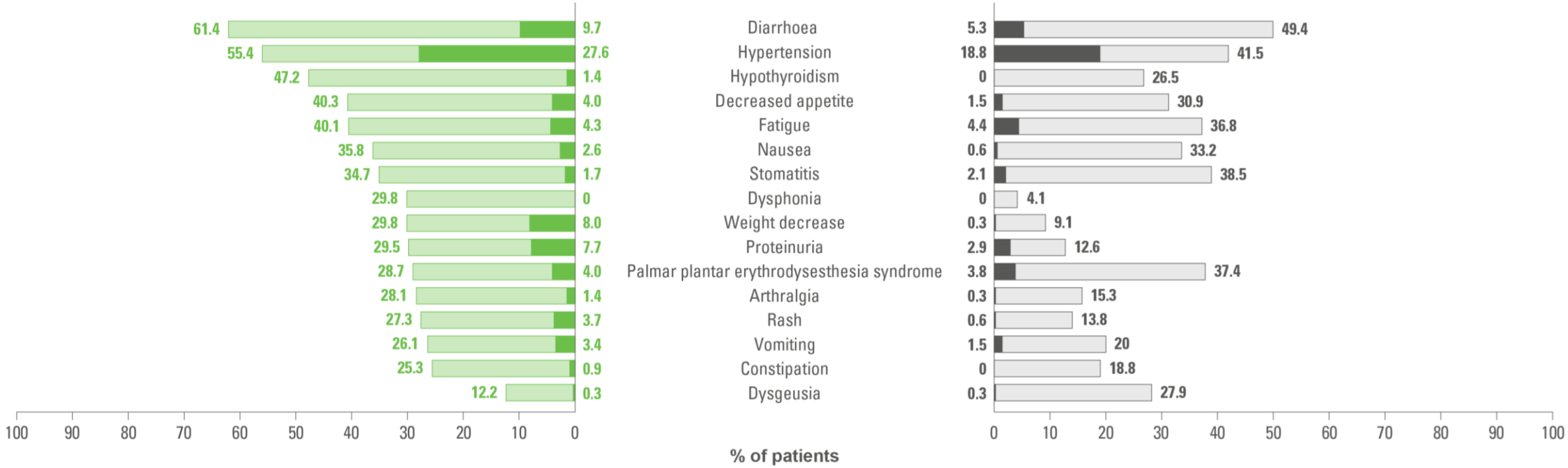
Analysis cutoff date: 28 August 2020.

[a]Safety assessment was based on an as-treated principle and consisted of monitoring and recording all AEs and serious AEs using the Common Terminology Criteria for AEs, version 4.03, in the group of patients who received at least one dose of the study drug; [b]Of the 15 patients in the KEYTRUDA + KISPLYX group who had grade 5 AEs during treatment, 11 had fatal AEs not attributed to disease progression (acute renal failure, uncontrolled hypertension, complications from myasthenic syndrome, complications from autoimmune hepatitis, cardiac arrest, and death–cause not specified in 1 patient each; haemorrhagic events in 2 patients; and sepsis in 3 patients). Among the 11 patients in the sunitinib group with grade 5 AEs during treatment, fatal AEs not attributed to disease progression occurred in 2 patients (respiratory failure and acute kidney injury in 1 patient and death–cause not specified in 1 patient); [c]Dose reduction in KISPLYX only. Dose reductions for KEYTRUDA are not recommended.

AE, adverse event; TEAE, treatment-emergent adverse event.

CLEAR study primary analysis

Secondary endpoint — AEs of any cause that emerged or worsened during treatment in ≥25% of patients in either treatment group[a,10]



Adapted from Motzer R et al. 2021[10]

Analysis cutoff date: 28 August 2020.

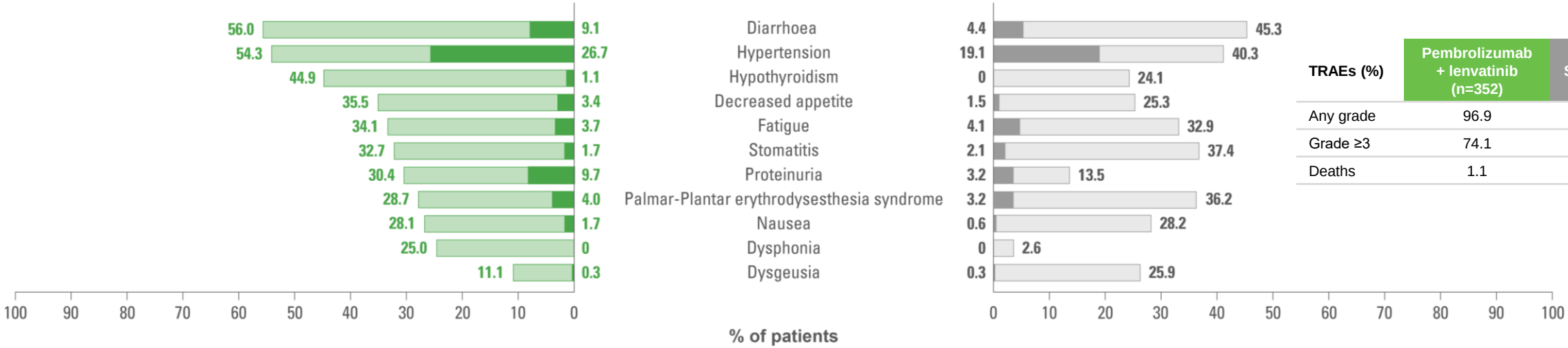
[a]Safety assessment was based on an as-treated principle and consisted of monitoring and recording all AEs and serious AEs using the Common Terminology Criteria for AEs, version 4.03, in the group of patients who received at least one dose of the study drug. Hypothyroidism is an AE of interest associated with KEYTRUDA.

AE, adverse event.

Prespecified final analysis

Exploratory analysis — TRAEs in ≥25% of patients in any treatment group[11]

Median (IQR) follow-up for OS: 49.8 (41.4–53.1) months with **KEYTRUDA** + **KISPLYX** and 49.4 (41.6–52.8) months with sunitinib



TRAEs (%)	Pembrolizumab + lenvatinib (n=352)	Sunitinib (n=340)
Any grade	96.9	92.1
Grade ≥3	74.1	60.3
Deaths	1.1	0.3

Adapted from Motzer R et al. ASCO 2023[11]

- There were no new safety signals identified at 49.8 months median follow up

LIMITATION: This was a protocol-pre-specified analysis. No formal statistical testing was performed for this analysis, and, therefore, no conclusions can be drawn.

Analysis cutoff date: 31 July 2022. When median follow-up time was not specified for an endpoint, median follow-up for OS is presented in the slide. The median duration of treatment (IQR) was 22.6 (9.4–37.1) months with pembrolizumab + lenvatinib and 7.8 (3.7–19.4) months with sunitinib.

Secondary endpoint — summary of TEAEs of interest for **KEYTRUDA**[a,10]

Click for TEAEs of interest for **KISPLYX**

TEAE	KEYTRUDA + KISPLYX (n=352)		Sunitinib (n=340)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Any	214 (60.8)	52 (14.8)	105 (30.9)	4 (1.2)
Adrenal insufficiency	18 (5.1)	4 (1.1)	0 (0.0)	0 (0.0)
Colitis	9 (2.6)	4 (1.1)	2 (0.6)	0 (0.0)
Encephelitis	2 (0.6)	2 (0.6)	0 (0.0)	0 (0.0)
Hepatitis	7 (2.0)	5 (1.4)	0 (0.0)	0 (0.0)
Hyperthyroidism	28 (8.0)	0 (0.0)	12 (3.5)	0 (0.0)
Hypophysitis	3 (0.9)	2 (0.6)	0 (0.0)	0 (0.0)
Hypothyroidism	166 (47.2)	5 (1.4)	90 (26.5)	0 (0.0)
Infusion reactions	5 (1.4)	1 (0.3)	2 (0.6)	0 (0.0)
Myasthenic syndrome	1 (0.3)	1 (0.3)	0 (0.0)	0 (0.0)

TEAE	KEYTRUDA + KISPLYX (n=352)		Sunitinib (n=340)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Myocarditis	4 (1.1)	3 (0.9)	0 (0.0)	0 (0.0)
Myositis	3 (0.9)	2 (0.6)	0 (0.0)	0 (0.0)
Nephritis	6 (1.7)	4 (1.1)	0 (0.0)	0 (0.0)
Pancreatitis	10 (2.8)	6 (1.7)	2 (0.6)	1 (0.3)
Pneumonitis	19 (5.4)	7 (2.0)	0 (0.0)	0 (0.0)
Severe skin reactions	18 (5.1)	18 (5.1)	5 (1.5)	3 (0.9)
Thyroiditis	2 (0.6)	0 (0.0)	2 (0.6)	0 (0.0)
Type 1 diabetes mellitus	2 (0.6)	1 (0.3)	0 (0.0)	0 (0.0)
Uveitis	1 (0.3)	1 (0.3)	0 (0.0)	0 (0.0)

Adapted from Motzer et al. 2021[10]

Analysis cutoff date: 28 August 2020.
[a]No cases of Guillain-Barré syndrome, myelitis, or sarcoidosis were reported in any group.
AE, adverse event, TEAE, treatment-emergent adverse event.

Secondary endpoint — summary of clinically significant TEAEs for **KISPLYX**[10]

Click for TEAEs of interest for **KEYTRUDA**

TEAE	KEYTRUDA + KISPLYX (n=352)		Sunitinib (n=340)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Any	331 (94.0)	188 (53.4)	289 (85.0)	118 (34.7)
Arterial thromboembolic events	19 (5.4)	13 (3.7)	7 (2.1)	2 (0.6)
Cardiac dysfunction	9 (2.6)	6 (1.7)	7 (2.1)	4 (1.2)
Fistula formation	2 (0.6)	0 (0.0)	2 (0.6)	1 (0.3)
Gastrointestinal perforation	5 (1.4)	4 (1.1)	3 (0.9)	1 (0.3)
Haemorrhage	96 (27.3)	18 (5.1)	90 (26.5)	13 (3.8)
Hepatotoxicity	96 (27.3)	35 (9.9)	82 (24.1)	18 (5.3)
Hypertension	198 (56.3)	101 (28.7)	145 (42.6)	66 (19.4)
Hypocalcaemia	5 (1.4)	1 (0.3)	9 (2.6)	1 (0.3)

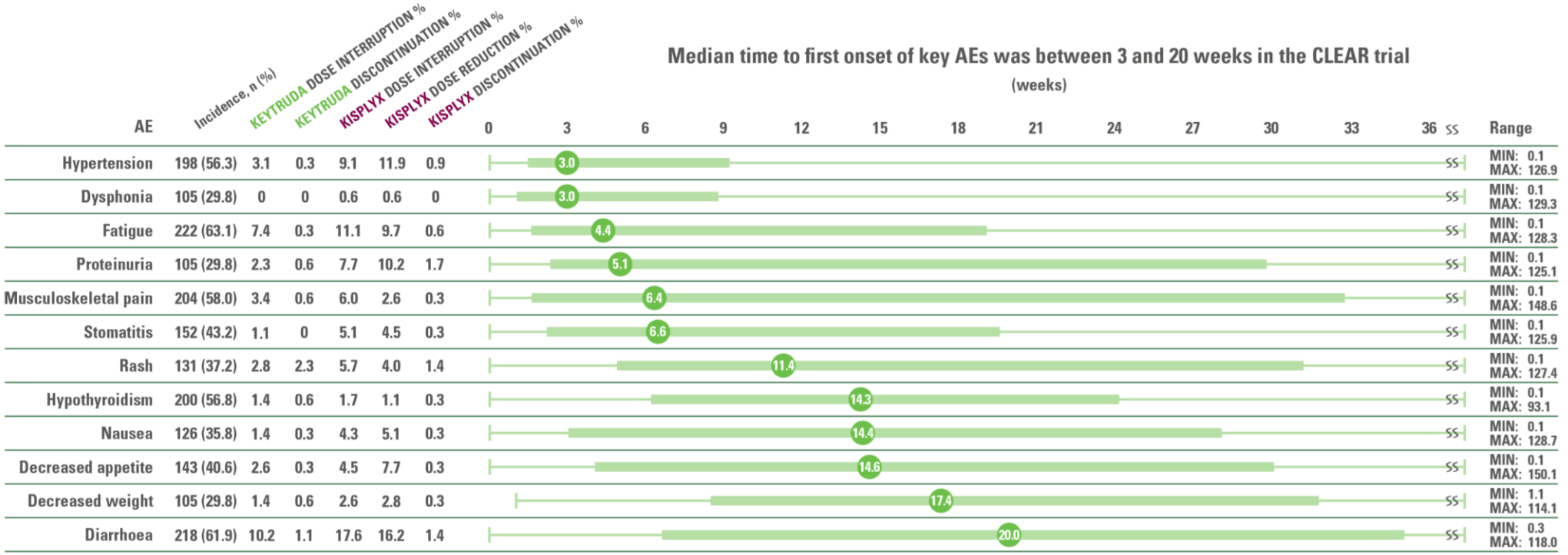
TEAE	KEYTRUDA + KISPLYX (n=352)		Sunitinib (n=340)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Hypothyroidism	200 (56.8)	5 (1.4)	109 (32.1)	0 (0.0)
Palmar–Plantar erythrodysesthesia syndrome	104 (29.5)	14 (4.0)	129 (37.9)	13 (3.8)
Posterior reversible encephalopathy syndrome	2 (0.6)	2 (0.6)	1 (0.3)	0 (0.0)
Proteinuria	104 (29.5)	27 (7.7)	43 (12.6)	10 (2.9)
QT prolongation	23 (6.5)	10 (2.8)	13 (3.8)	4 (1.2)
Renal events	78 (22.2)	20 (5.7)	60 (17.6)	8 (2.4)

Adapted from Motzer et al. 2021[10]

Analysis cutoff date: 28 August 2020.
AE, adverse event, TEAE, treatment-emergent adverse event.

Exploratory analysis — Median time to first onset of key AEs[a] (all grades) and dose management for KEYTRUDA + KISPLYX[b,13]

Median follow-up: 26.6 months with **pembrolizumab** + **lenvatinib** and with sunitinib



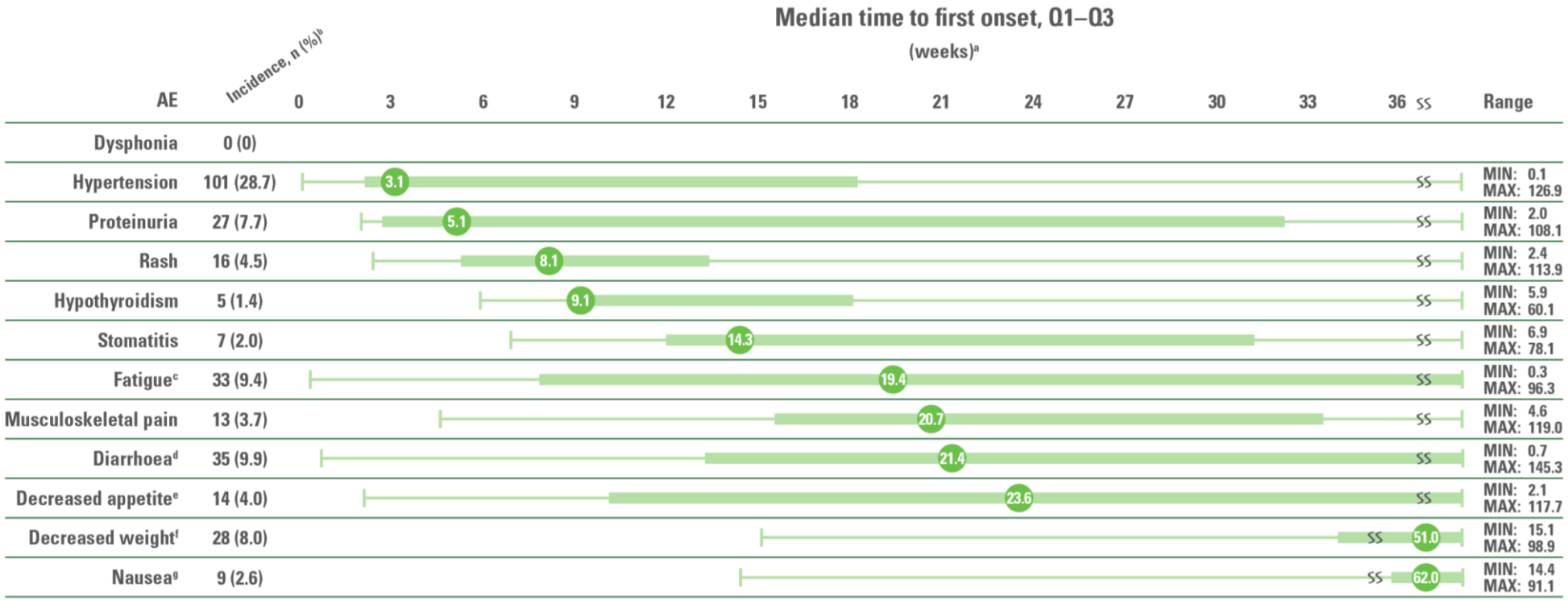
Adapted from Motzer R et al. 2023[13]

LIMITATION:
This was a post-hoc exploratory analysis based on data from the CLEAR trial. No formal statistical testing was planned for this exploratory analysis and, therefore, no conclusions can be drawn.

[a]Key AEs: AEs with incidence ≥30% in the KEYTRUDA + KISPLYX group that occurred either while receiving treatment or within the protocol-defined follow-up period of 30 days after the patient's last dose. The safety population included all patients who received at least one dose of any study drug and percentages presented in the figure were based on the safety population of the pembrolizumab + lenvatinib group (n=352). Coloured boxes represent Q1–Q3 and lines represent the range;
[b]Median time to first onset in patients who experienced the AE.
AE, adverse event; max, maximum; min, minimum; Q, Quartile.

Exploratory analysis — Median time to first onset of Grade ≥3 AEs in patients treated with KEYTRUDA + KISPLYX[a,13]

Median follow-up: 26.6 months with **pembrolizumab** + **lenvatinib** and with sunitinib



Adapted from Motzer R et al. 2023[13]

LIMITATION:
This was a post-hoc exploratory analysis based on data from the CLEAR trial. No formal statistical testing was planned for this exploratory analysis and, therefore, no conclusions can be drawn.

[a]Median time to first onset in patients who experienced the Grade ≥3 adverse reaction. Coloured boxes represent Q1–Q3. Lines represent the range; [b]Any grade. Percentages are based on the safety population of the KEYTRUDA + KISPLYX group (n=352). The safety population included all patients who received at least one dose of any study drug; [c]Q1=7.86, Q3=42.29; [d]Q1=13.29, Q3=56.71; [e]Q1=10.14, Q3=69.14; [f]Q1=34.00, Q3=64.71; [g]Q1=42.57, Q3=74.00.
AE, adverse event; max, maximum; min, minimum; Q, Quartile.

HRQoL — patient reported outcomes[a,15]

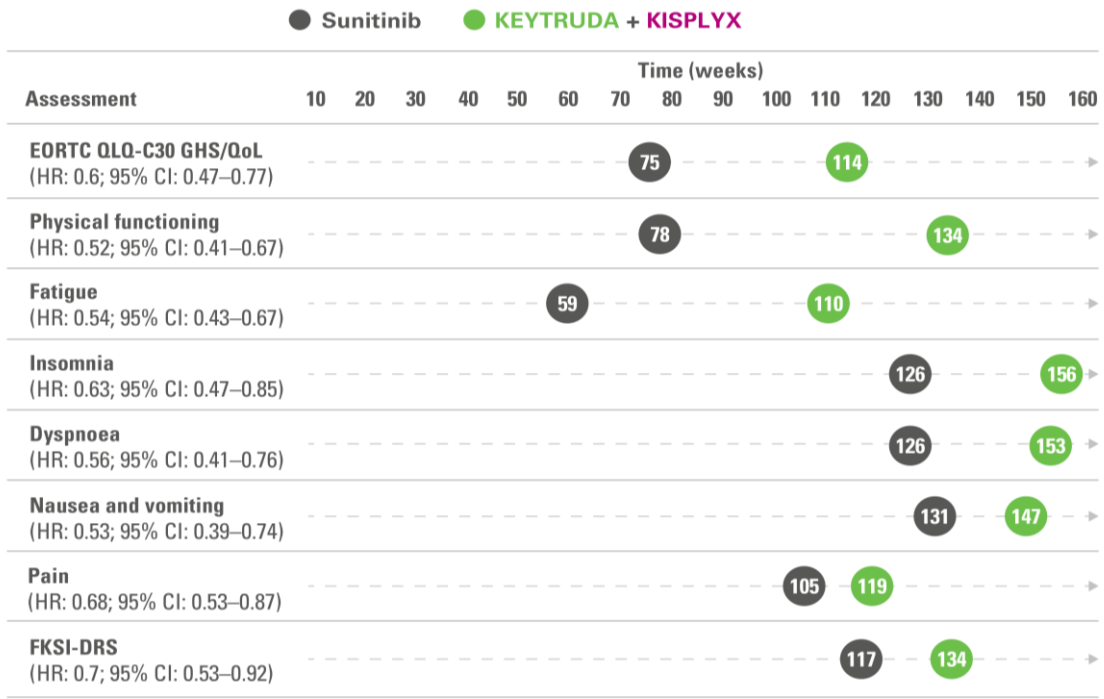
Median (IQR) follow-up: 12.9 (5.6–22.3) months with **pembrolizumab** + **lenvatinib** and with sunitinib

- **KEYTRUDA + KISPLYX** showed a **more than 12-week delay** in median time to worsening in GHS, physical functioning, and patient reported symptoms with no subsequent recovery vs sunitinib[b]

>12-week
delay in median time to worsening symptoms vs sunitinib group

LIMITATION: These results should be interpreted in the context of the open-label study design and therefore taken cautiously.

Time to definitive deterioration in selected HRQoL scales for KEYTRUDA + KISPLYX vs sunitinib



Adapted from Motzer R et al. 2022[15]

Analysis cutoff date: 24 July 2019.

[a]**Patient-reported outcomes (PROs) were assessed using the EORTC QLQ-C30 and the FKSI-DRS;** [b]**Measured from baseline to a mean follow-up time of 46 weeks.**

AE, adverse event; CI, confidence interval; EQ-5D-3L, European Quality of Life 5 Dimensions 3 Levels; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire–Core 30; FKSI-DRS, Functional Assessment of Cancer Therapy Kidney Cancer Symptom Index – Disease Related Symptoms; GHS, Global Health Status; HR, hazard ratio; HRQoL, health-related quality of life; QoL, quality of life; VAS, visual analogue scale.

KEYTRUDA and KISPLYX are administered via IV infusion and oral capsules, respectively

KEYTRUDA offers flexibility of dosing[7]

Administered as an IV infusion[7]

Over 30 minutes[7]

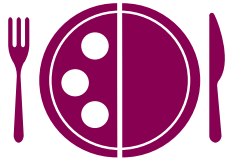
200 mg Q3W or 400 mg Q6W[7]

The 200 mg Q3W (once every 3 weeks) regimen has been assessed in Phase 2 and 3 registration studies across a multitude of indications of KEYTRUDA. An exposure-response evaluation, using modelling and simulation, led to the approval of the 400 mg Q6W (once every 6 weeks) dosing for monotherapy and combination therapy[7]

What does flexibility mean to you and your patients?

KISPLYX[9]

20 mg orally QD at the same time each day[9]



Administered with or without food[9]

Swallowed whole with water. For patients unable to swallow capsules, please refer to the SmPC for alternative methods of preparation[9]

- Continue treatment with **KISPLYX** for as long as there is clinical benefit or until unacceptable toxicity occurs
- For AEs thought to be related to **KISPLYX**, upon resolution/improvement of an AE to Grade 0–1 or baseline, treatment should be resumed at a reduced dose of **KISPLYX**
  - Please refer to the **KISPLYX** SmPC for the management of AEs
- **PLEASE REFER TO THE FOLLOWING SLIDE FOR INFORMATION ON DOSE MODIFICATIONS AND ALTERNATIVE STARTING DOSES FOR KISPLYX IN COMBINATION WITH KEYTRUDA**

AE, adverse event; IV, intravenous; QD, once daily; Q3W, every three weeks; Q6W, every six weeks; SmPC, Summary of Product Characteristics.

Dose modification for **KISPLYX** in combination with **KEYTRUDA**

- The recommended starting daily dose of **KISPLYX** is 20 mg. Dose modification can be used to manage adverse reactions as appropriate[9]
- When administering **KISPLYX** in combination with **KEYTRUDA**, interrupt, reduce or discontinue **KISPLYX** as appropriate. Withhold or discontinue **KEYTRUDA** in accordance with the instructions in the SmPC for **KEYTRUDA**. No dose reductions are recommended for **KEYTRUDA**[7,9]

Recommended dose modification for KISPLYX in advanced RCC[9]

Recommended starting dose	10 10	**20 mg** orally once daily
1st dose reduction to	10 4	**14 mg** orally once daily
2nd dose reduction to	10	**10 mg** orally once daily
3rd dose reduction to	4 4	**8 mg** orally once daily

- If a **KISPLYX** dose is missed and cannot be administered within 12 hours, skip that dose and take the next dose at the usual time of administration[9]
- Continue treatment with **KEYTRUDA** + **KISPLYX** until disease progression, unacceptable toxicity or, for **KEYTRUDA**, up to 24 months[7,9]
- The recommended starting dose of **KISPLYX** for patients with advanced RCC and severe renal impairment is 10 mg administered orally QD[9]
- The recommended starting dose of **KISPLYX** for patients with advanced RCC and severe hepatic impairment (Child–Pugh C) is 10 mg administered orally QD[9]

QD, once daily; RCC, renal cell carcinoma.

Exploratory subgroup analysis of efficacy outcomes by baseline tumour size[16]

Patient characteristics

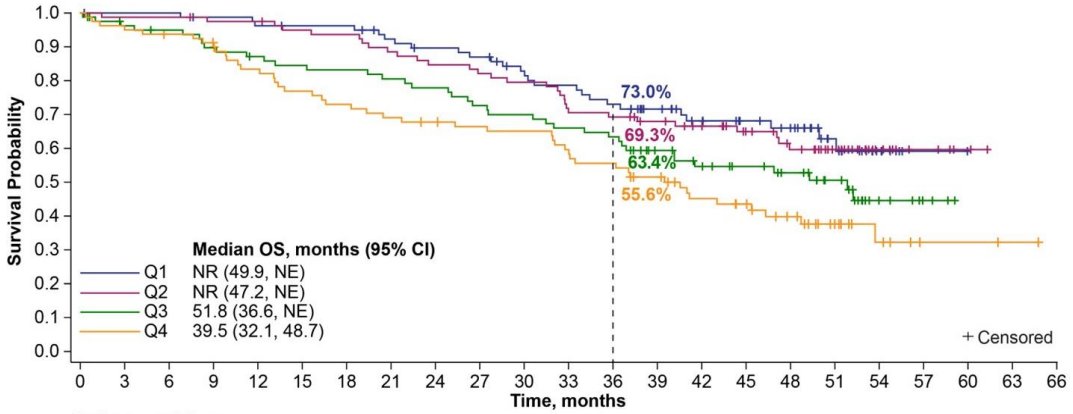
Characteristic	Baseline sums of diameters of target lesions[a] (N=355)			
	Q1 81 patients (22.8%)	Q2 80 patients (22.5%)	Q3 81 patients (22.8%)	Q4 80 patients (22.5%)
	Defined as ≤34.72 mm	Defined as >34.72 mm to ≤60.06 mm	Defined as >60.06 mm to ≤108.56 mm	Defined as >108.56 mm
Age, median (range), years	63.0 (34–78)	64.0 (36–84)	64.0 (39–80)	64.5 (38–88)
IMDC risk group,[b] % Favourable / Intermediate + Poor / Not evaluable	40.7/ 58.0 / 1.2	30.0/ 68.8 / 1.3	34.6 / 65.4 / 0	6.3 / 93.8 / 0
Sarcomatoid features, %	9.9	8.8	4.9	6.3
PD-L1 expression,[c] % ≥1 / <1 / Not available	25.9 / 32.1 / 42.0	37.5 / 28.8 / 33.8	37.0 / 34.6 / 28.4	23.8 / 33.8 / 42.5
Prior nephrectomy, %	87.7	88.8	76.5	38.8

Adapted from Grünwald V et al. ASCO GU 2024[16]

Percentages may not total 100 due to rounding. One patient in the KEYTRUDA + KISPLYX group had carcinoma without a clear-cell component.
[a]Includes patients in the full analysis set within the KEYTRUDA + KISPLYX group with baseline target lesion assessments by independent imaging review per RECIST v1.1; [b]IMDC scores: 0 indicates favourable risk, 1 or 2 intermediate risk, and 3 to 6 poor risk. IMDC risk group was not a stratification factor and relevant data were derived programmatically; [c]PD-L1 expression was assessed with the PD-L1 immunohistochemistry 22C3 pharmDx assay (Agilent Technologies) and reported as the combined positive score (number of PD-L1–staining cells [tumour cells, lymphocytes and macrophages] divided by the total number of viable tumour cells), then multiplied by 100.
IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; PD-L1, programmed death ligand-1; Q, Quartile; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

Exploratory subgroup analysis[16]

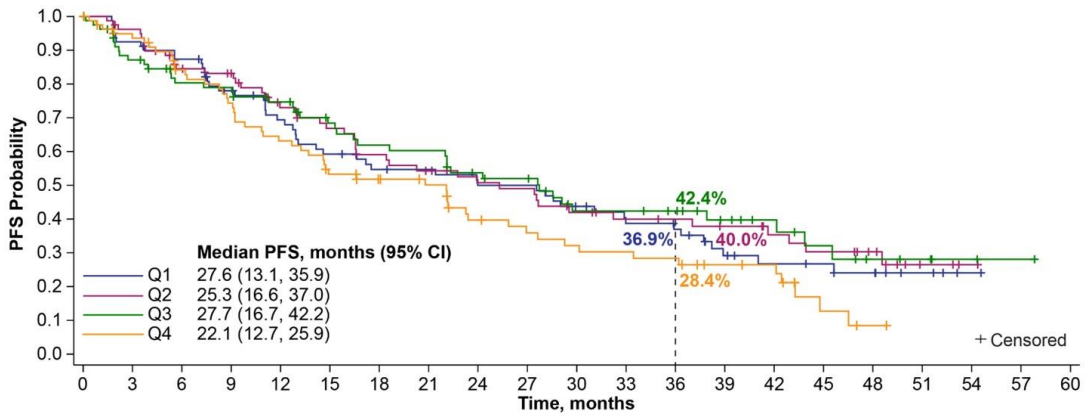
OS by baseline tumour size[a]



Patients at risk, n

Q1 (≤ 34.72 mm)	81	80	80	78	76	75	75	70	67	65	59	56	52	45	38	33	30	17	7	1	0	0	0
Q2 (> 34.72 to ≤ 60.06 mm)	80	79	79	77	77	74	73	69	66	64	62	55	54	50	46	39	33	24	11	5	2	0	0
Q3 (> 60.06 to ≤ 108.56 mm)	81	75	73	69	66	64	63	61	59	55	53	50	48	39	34	30	26	19	7	3	0	0	0
Q4 (> 108.56 mm)	80	76	74	71	64	59	56	53	51	49	48	44	41	35	28	25	19	11	6	2	2	1	0

PFS by baseline tumour size[b]



Patients at risk, n

Q1 (≤ 34.72 mm)	81	73	68	56	48	41	36	35	32	32	27	23	21	14	11	10	8	4	1	0	0	0
Q2 (> 34.72 to ≤ 60.06 mm)	80	75	63	60	48	43	37	33	29	28	23	20	19	17	14	12	9	3	1	0	0	0
Q3 (> 60.06 to ≤ 108.56 mm)	81	67	58	57	50	42	38	37	31	29	21	21	19	14	11	8	5	4	2	1	0	0
Q4 (> 108.56 mm)	80	71	60	53	45	37	33	30	22	19	17	16	15	11	10	3	1	0	0	0	0	0

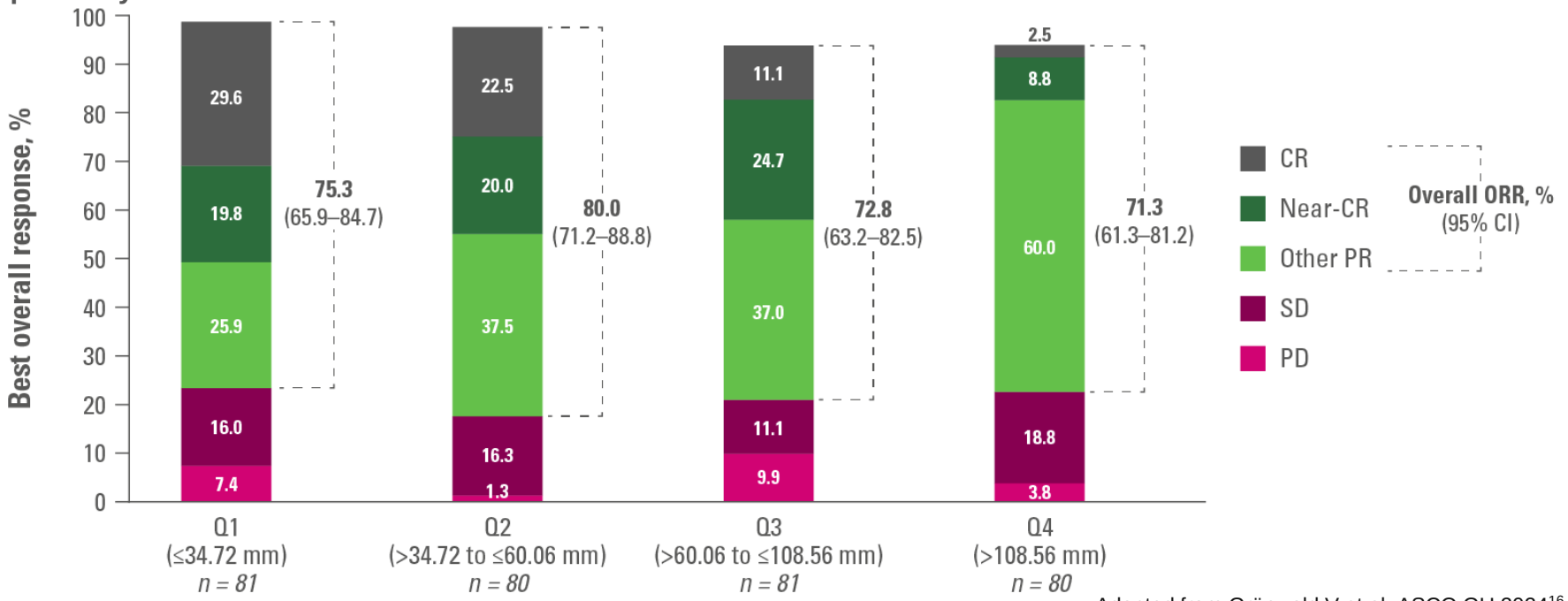
Adapted from Grünwald V et al. ASCO GU 2024[16]

LIMITATION: This study was not powered to detect differences in the treatment effect between these subgroups. Results from exploratory analyses should be interpreted with caution due to modest patient numbers and potential imbalances in baseline characteristics between subgroups.

Medians were estimated by the Kaplan–Meier method, and 95% CIs were estimated with a generalised Brookmeyer and Crowley method. Survival rate at 36 months was calculated using the Kaplan–Meier product-limit method.
[a]The number of patients with OS events (deaths) were: Q1=26, Q2=30, Q3=38, Q4=46; [b]Independent imaging review by RECIST v1.1. The number of patients with PFS events (death or progressive disease) were: Q1=50, Q2=45, Q3=42, Q4=54.
CI, confidence interval; NE, not estimable; NR, not reached; OS, overall survival; PFS, progression-free survival; Q, Quartile; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

Exploratory subgroup analysis[16]

Best overall response by baseline tumour size[a]



Adapted from Grünwald V et al. ASCO GU 2024[16]

LIMITATION: This study was not powered to detect differences in the treatment effect between these subgroups. Results from exploratory analyses should be interpreted with caution due to modest patient numbers and potential imbalances in baseline characteristics between subgroups.

Includes patients with baseline target lesion assessments, 95% CIs were calculated using asymptotic normal distribution. 'Near-CR' refers to individuals who presented a PR with a maximum tumour reduction of ≥75%. 'Other PR' refers to PRs with maximum tumour shrinkage <75%. The proportion of patients with unknown/not evaluable responses were: Q1=1.2%, Q2=2.5%, Q3=6.2%, Q4=6.3%. Percentages are based on the total number of patients in the full analysis set within the KEYTRUDA + KISPLYX group. Percentages may not total 100 due to rounding.

[a]Includes patients with baseline target lesion assessments by independent imaging review per RECIST v1.1.

CI, confidence interval; CR, complete response; ORR, objective response rate; PD, progressive disease; PR, partial response; Q, Quartile; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease.

Pembrolizumab + lenvatinib: Outcomes in 1L advanced RCC[10]

Superior PFS:
- A **61% reduction** in the risk of progression or death for **KEYTRUDA** + **KISPLYX** vs sunitinib (HR=0.39 [95% CI, 0.32–0.49]; *P*<0.0001)[a]

Superior OS:
- A **34% reduction** in risk of death for **KEYTRUDA** + **KISPLYX** vs sunitinib (HR=0.66 [95% CI, 0.49–0.88]; *P*=0.005)[a]

Superior ORR:
- ORR was **71.0%** with **KEYTRUDA** + **KISPLYX** vs 36.1% with sunitinib (*P*<0.0001)[b]
  - CR: **16.1%** with **KEYTRUDA** + **KISPLYX** vs 4.2% with sunitinib

Safety:
- The safety profile of **KEYTRUDA** + **KISPLYX** was consistent with the profiles for the individual drugs

[a]**Analysis cutoff date: 28 August 2020 and median follow-up: 26.6 months for pembrolizumab + lenvatinib and sunitinib[10]; [b]At the Interim Analysis 2, prespecified final analysis of ORR (median follow-up time of 17.3 months), statistically significant superiority was achieved for ORR comparing pembrolizumab + lenvatinib with sunitinib (odds ratio: 3.84 [95% CI: 2.81, 5.26], *P*<0.0001).[7,9]**

1L, first-line; CI, confidence interval; CR, complete response; HR, hazard ratio; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; RCC, renal cell carcinoma.

Prespecified final analysis

Pembrolizumab + lenvatinib: Outcomes in 1L advanced RCC[11,16]

Prespecified final analysis (exploratory data; no conclusions can be drawn):

- The pre-specified final OS analysis continues to support **KEYTRUDA** + **KISPLYX** as a standard of care in 1L advanced RCC

PFS:

- Median PFS was 23.9 months with **KEYTRUDA** + **KISPLYX** and 9.2 months with sunitinib (HR [95% CI]=0.47 [0.38–0.57]; nominal *P*<0.0001)

OS:

- Median OS was 53.7 months with **KEYTRUDA** + **KISPLYX** and 54.3 months with sunitinib (HR [95% CI]=0.79 [0.63–0.99); nominal *P*=0.0424)

ORR and DOR:

- ORR was 71.3% with **KEYTRUDA** + **KISPLYX** and 36.7% with sunitinib (RR [95% CI]=1.94 [1.67–2.26])
  - CR was 18.3% with **KEYTRUDA** + **KISPLYX** and 4.8% with sunitinib
- Median DOR was 26.7 months with **KEYTRUDA** + **KISPLYX** and 14.7 months with sunitinib (HR [95% CI]=0.57 [0.43–0.76])

Safety:

- No new safety signals were identified at the final prespecified analysis

Outcome by baseline tumour size:

- With extended follow-up (median ~4 years) of the CLEAR study, PFS, OS and ORR outcomes with **KEYTRUDA** + **KISPLYX** were observed across patients with advanced RCC, irrespective of baseline tumour size

Analysis cutoff date: 31 July 2022.

1L, first-line; CI, confidence interval; CR, complete response; DOR, duration of response; HR, hazard ratio; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; RCC, renal cell carcinoma; RR, relative risk.

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