Best of ASCO in Bladder and Kidney Cancer

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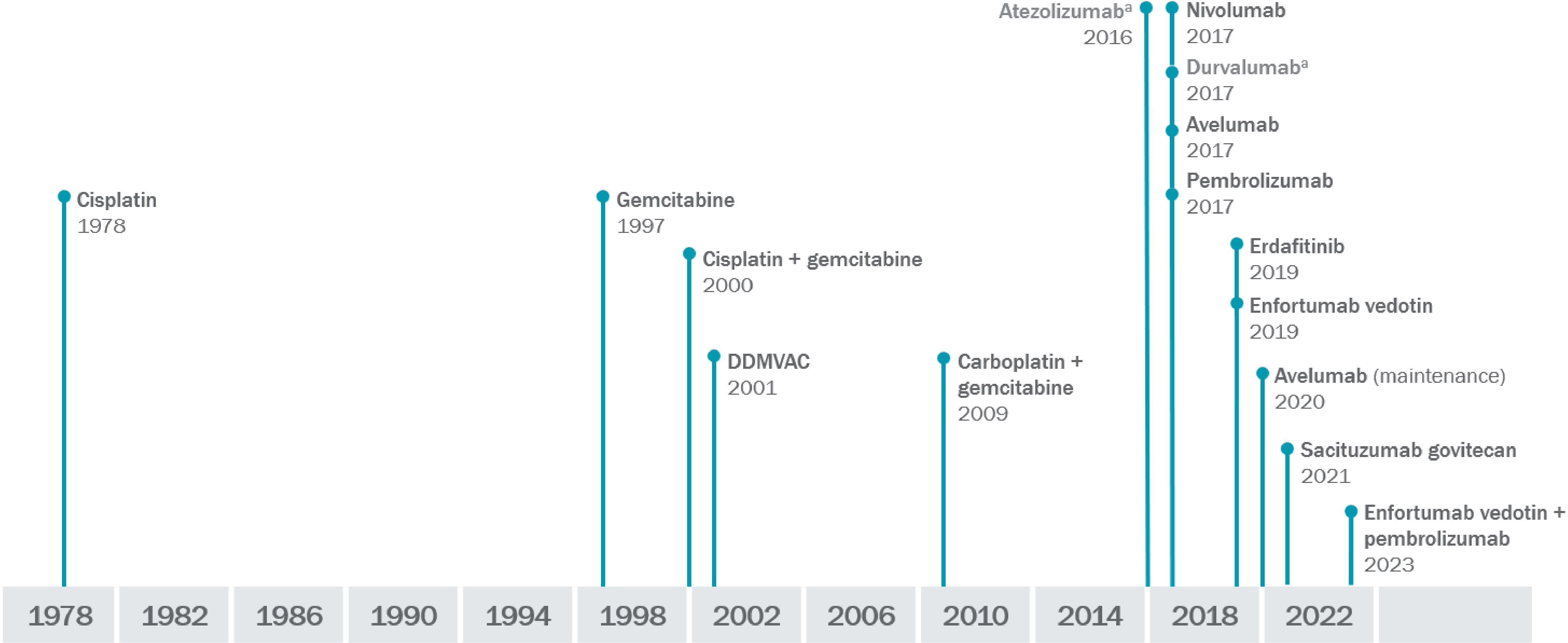
University of Iowa
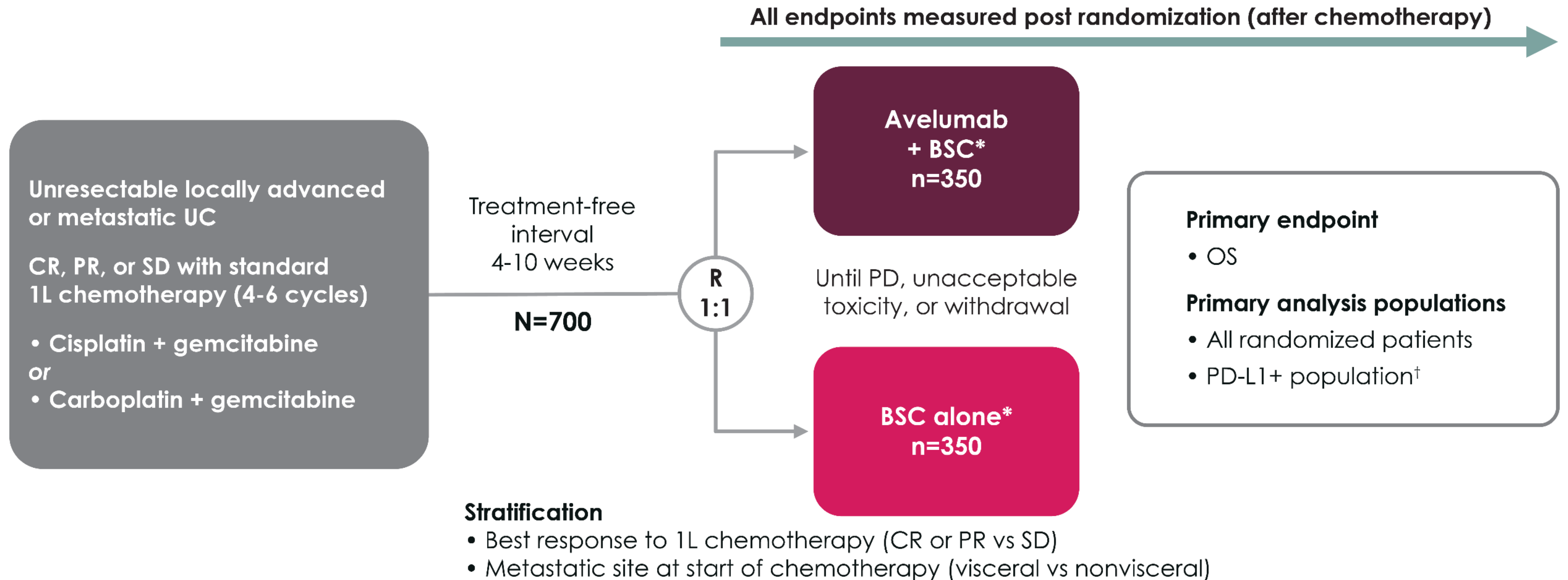Holden Comprehensive Cancer Center

Disclosure

- Advisory Board: Bristol Myers Squibb, Eisai, Exelixis, Pfizer, EMD serono, Seagen.

- DSMC: Janssen Research and Development

Treatment Landscape for la/mUC

JAVELIN Bladder 100 Phase III Study Design

All endpoints measured post randomization (after chemotherapy)

Unresectable locally advanced or metastatic UC

CR, PR, or SD with standard 1L chemotherapy (4-6 cycles)

- **Cisplatin + gemcitabine**
or
- **Carboplatin + gemcitabine**

Treatment-free interval 4-10 weeks

N=700

R 1:1

Avelumab + BSC*
n=350

Until PD, unacceptable toxicity, or withdrawal

BSC alone*
n=350

Primary endpoint
- OS

Primary analysis populations
- All randomized patients
- PD-L1+ population[†]

Stratification
- Best response to 1L chemotherapy (CR or PR vs SD)
- Metastatic site at start of chemotherapy (visceral vs nonvisceral)
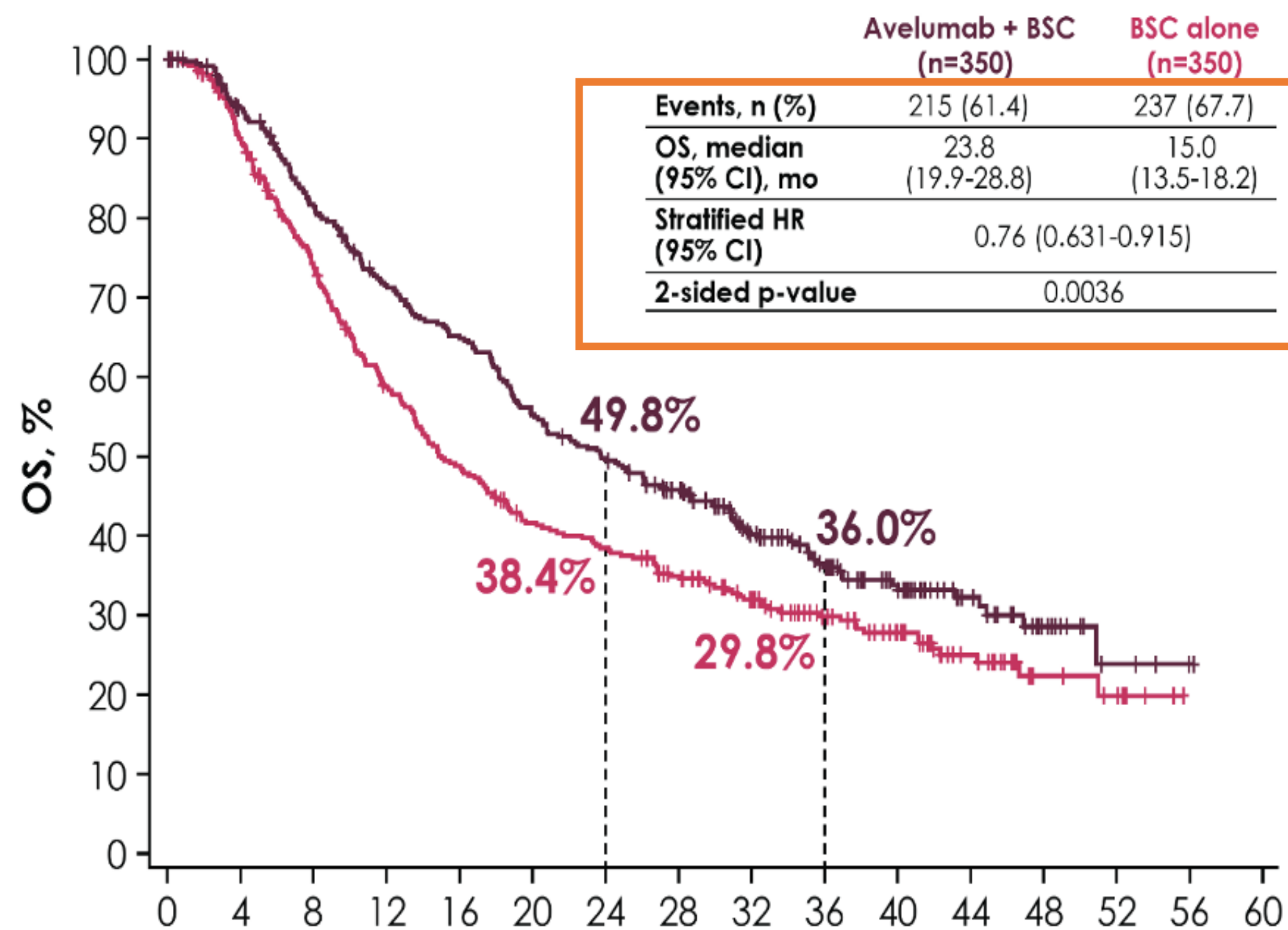
Data cutoff date: June 2021
*BSC (eg, antibiotics, nutritional support, hydration, or pain management) was administered per local practice based on patient needs and clinical judgment; other antitumor therapy was not permitted, but palliative local radiotherapy for isolated lesions was acceptable. †Assessed using the Ventana SP263 assay.
1L, first line; BSC, best supportive care; CR, complete response; PR, partial response; OS, overall survival; PD, progressive disease; R, randomization; SD, stable disease; UC, urothelial carcinoma.

Presented by Srikala Sridhar at ASCO 2021 Annual Meeting June 4-8, 2021. Abstract 4527.
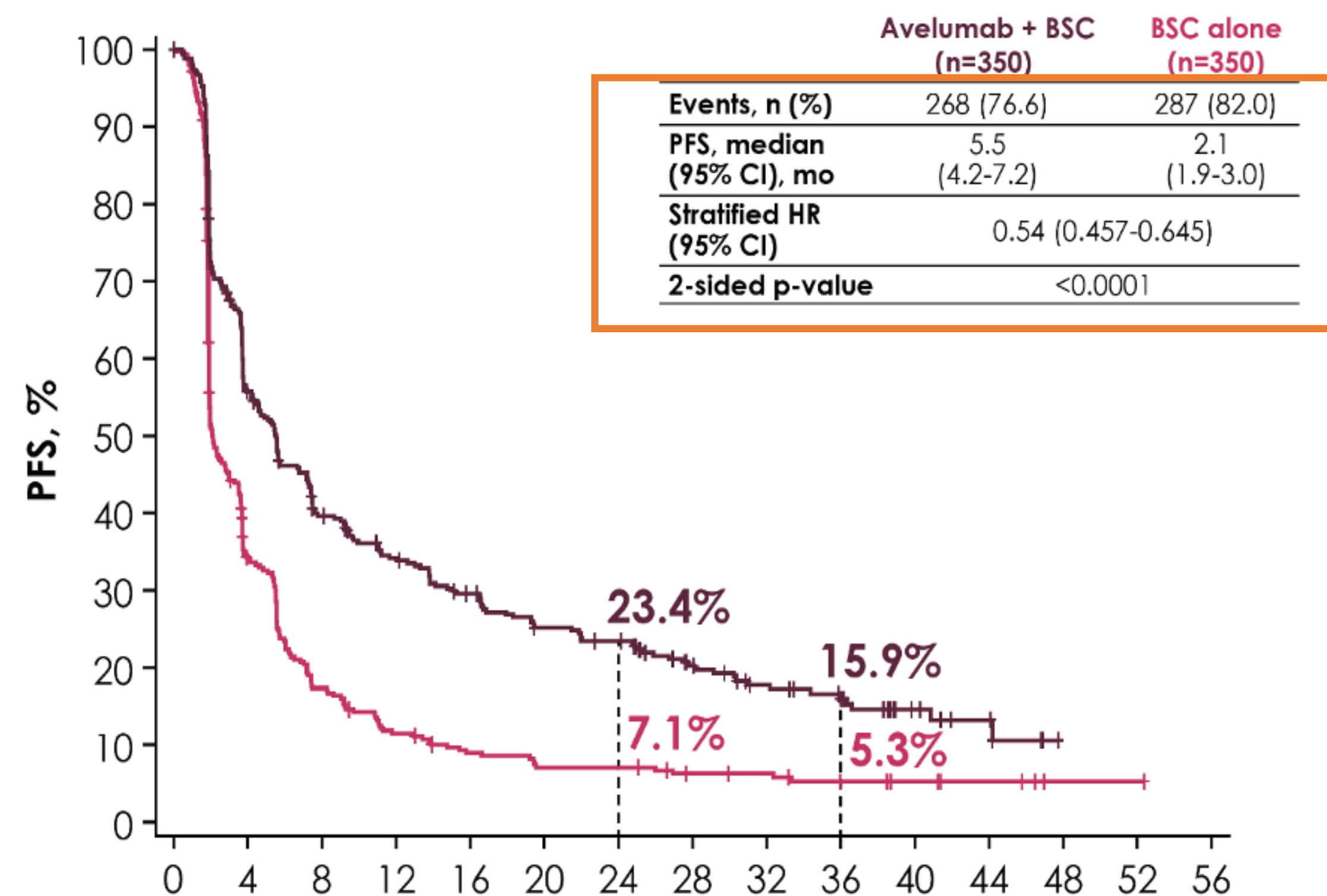
Iowa Oncology Society

OS and PFS in the Overall Population: 38m Follow-up

Presented by Srikala Sridhar at ASCO 2021 Annual Meeting June 4-8, 2021. Abstract 4527.

EV-302/KEYNOTE-A39 (NCT04223856)

Patient population (N=886)
- Previously untreated la/mUC
- Eligible for platinum, EV, and P
- PD-(L)1 inhibitor-naive
- GFR ≥30 mL/min[a]
- ECOG PS ≤2[b]

R 1:1

EV + Pembrolizumab
No maximum treatment cycles for EV, Maximum 35 cycles for P

Treatment until disease progression per BICR, clinical progression, unacceptable toxicity, or completion of maximum cycles

Chemotherapy
(Cisplatin or carboplatin + gemcitabine)
Maximum 6 cycles

Dual primary endpoints:
- PFS by BICR
- OS

Select secondary endpoints:
- ORR per RECIST v1.1 by BICR and investigator assessment
- Safety

Prespecified subgroups:
- Stratification factors
  - Cisplatin eligibility (eligible, ineligible)
  - PD-L1 expression (low, high)
  - Liver metastases (present, absent)
- Age (<65, ≥65 years old)
- Region (North America, Europe, Rest of World)
- Sex (female, male)
- Race (white, other)
- ECOG PS at baseline (0, 1-2)
- Visceral metastases vs. lymph node only metastases
- Primary disease site of origin (upper tract, lower tract)
- Renal function (normal, mild, moderate, severe)

Cisplatin eligibility and assignment/dosing of cisplatin vs carboplatin were protocol-defined; patients received 3-week cycles of EV (1.25 mg/kg; IV) on Days 1 and 8 and P (200 mg; IV) on Day 1

Statistical plan for analysis: the first planned analysis was performed after approximately 526 PFS (final) and 356 OS events (interim); if OS was positive at interim, the OS interim analysis was considered final

Maintenance therapy was permitted if deemed appropriate by the investigator following completion and/or discontinuation of platinum-containing therapy

[a]Measured by the Cockcroft-Gault formula, Modification of Diet in Renal Disease, or 24-hour urine
[b]Patients with ECOG PS of 2 were required to also meet additional criteria: hemoglobin ≥10 g/dL, GFR ≥50mL/min, may not have NYHA class III heart failure
BICR, blinded independent central review; ECOG PS, Eastern Cooperative Oncology Group performance status; GFR, glomerular filtration rate; NYHA, New York Heart Association; ORR, objective response rate; PFS, progression-free survival; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors

Data cutoff: 08 August 2023; FPI: 07 Apr 2020, LPI: 09 Nov 2022

Van der Heijden MS et al. Genitourinary Cancers Symposium 2024;Abstract LBA530.

EV-302 Summary: PFS per BICR and OS in ITT

## mPFS and mOS were nearly doubled in the EV+P arm compared with chemotherapy

PFS
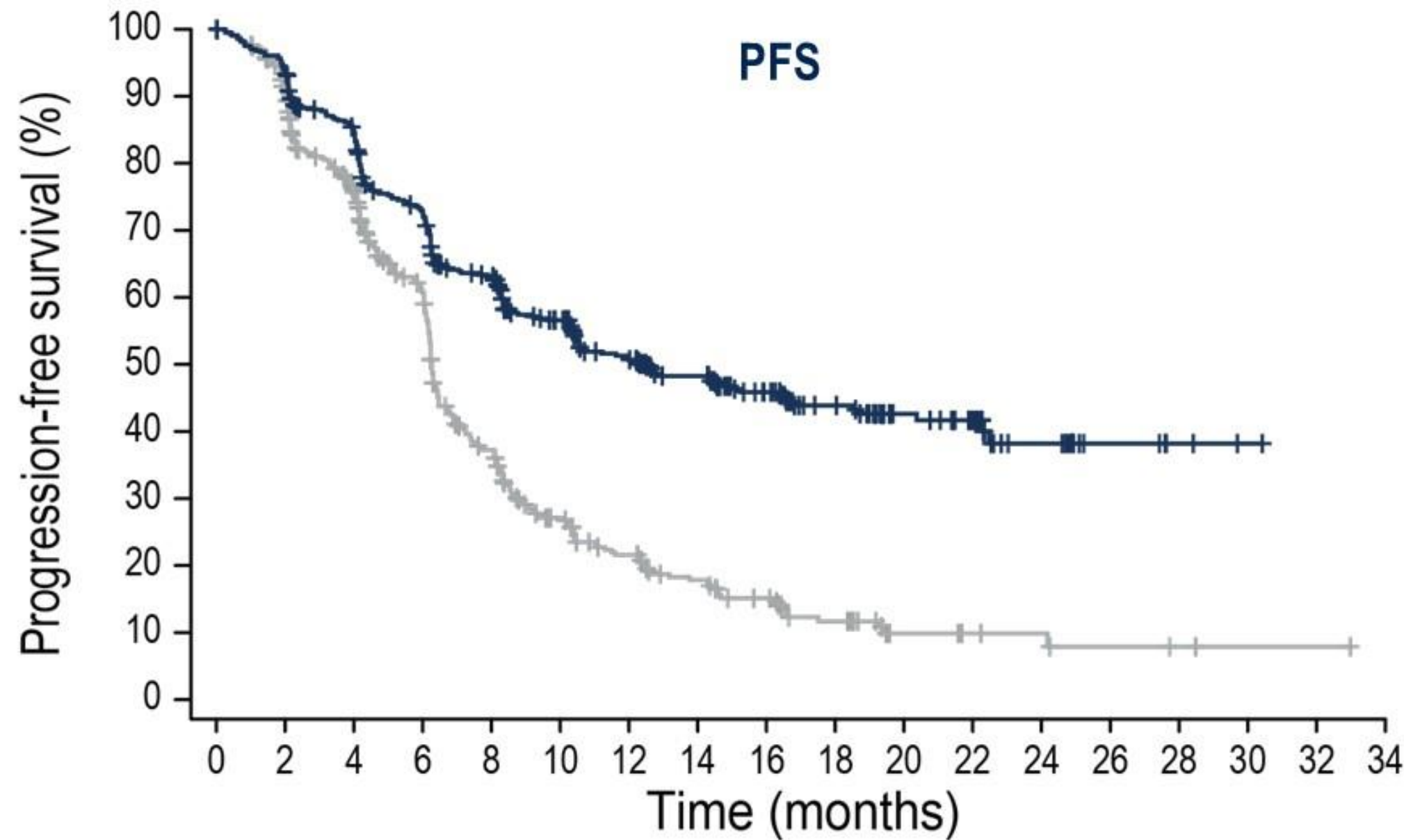
N at risk
EV+P	442	409	361	303	253	204	167	132	102	73	45	33	17	6	3	1
Chemotherapy	444	380	297	213	124	78	56	41	30	19	8	6	5	3	2	1	1

	HR[a] (95% CI)	2-sided P value	mPFS (95% CI), months
EV+P	0.45	<0.00001	12.5 (10.4-16.6)
Chemotherapy	(0.38-0.54)		6.3 (6.2-6.5)

Powles T. ESMO 2023: Oral presentation. Abstract LBA6.
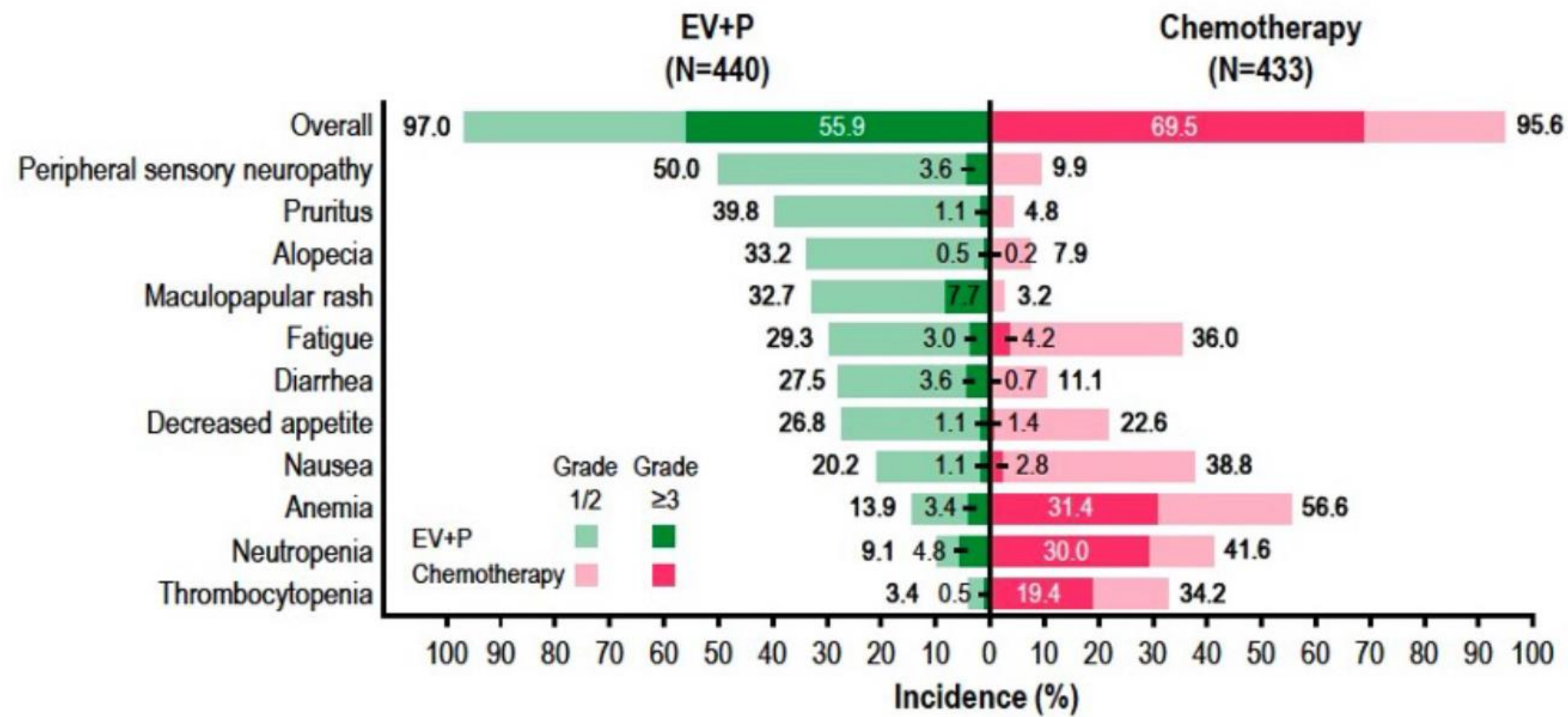Data cutoff: 08 August 2023

OS

Median survival follow-up: 17.2 months
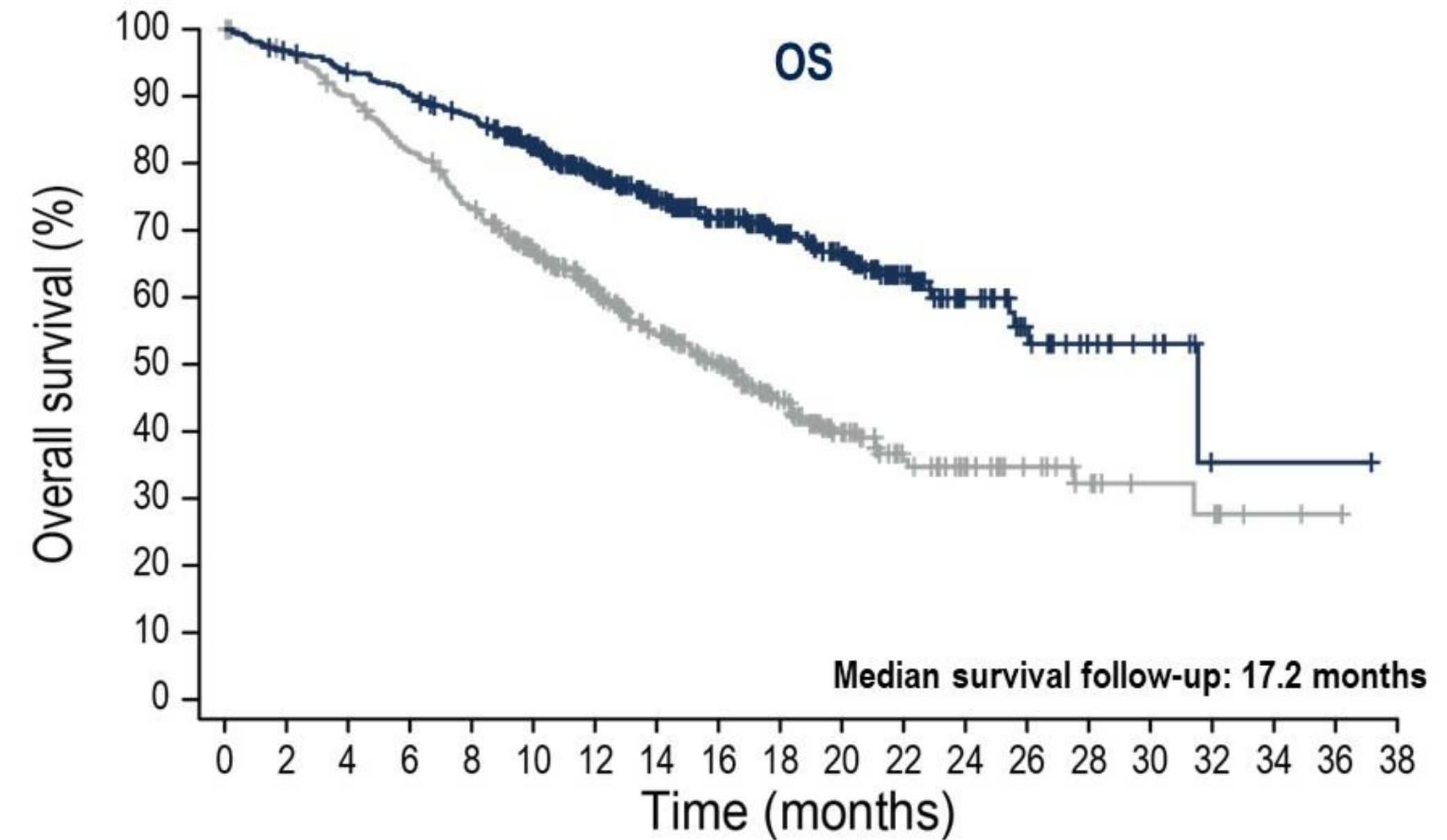
N at risk
EV+P	442	426	409	394	376	331	270	222	182	141	108	67	36	22	12	8	1	1	1
Chemotherapy	444	423	393	356	317	263	209	164	125	90	60	37	25	18	12	7	6	2	1

	HR[a] (95% CI)	2-sided P value	mOS (95% CI), months
EV+P	0.47	<0.00001	31.5 (25.4-NR)
Chemotherapy	(0.38-0.58)		16.1 (13.9-18.3)

[a]Calculated using stratified Cox proportional hazards model; a hazard ratio <1 favors the EV+P arm
HR, hazard ratio; ITT, intent-to-treat; mOS, median overall survival; mPFS, median progression-free survival; NR, not reached

Van der Heijden MS et al. Genitourinary Cancers Symposium 2024;Abstract LBA530.

Iowa Oncology Society

Grade ≥3 events were 56% in EV+P and 70% in chemotherapy

Serious TRAEs:
- 122 (27.7%) EV+P
- 85 (19.6%) chemotherapy
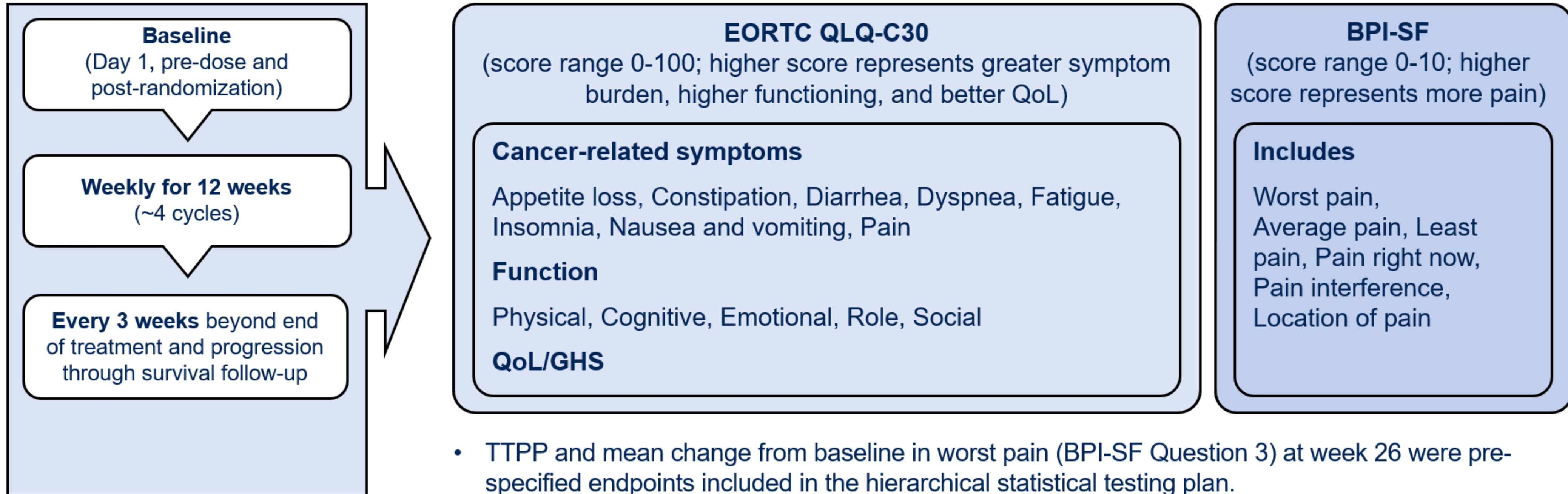
TRAEs leading to death (per investigator):
EV+P: 4 (0.9%)
- Asthenia
- Diarrhea
- Immune-mediated lung disease
- Multiple organ dysfunction syndrome

Chemotherapy: 4 (0.9%)
- Febrile neutropenia
- Myocardial infarction
- Neutropenic sepsis
- Sepsis

Van der Heijden MS et al. Genitourinary Cancers Symposium 2024;Abstract LBA530.

EV-302 PRO Collection

Baseline
(Day 1, pre-dose and post-randomization)

Weekly for 12 weeks
(~4 cycles)

Every 3 weeks beyond end of treatment and progression through survival follow-up

EORTC QLQ-C30
(score range 0-100; higher score represents greater symptom burden, higher functioning, and better QoL)

Cancer-related symptoms

Appetite loss, Constipation, Diarrhea, Dyspnea, Fatigue, Insomnia, Nausea and vomiting, Pain

Function

Physical, Cognitive, Emotional, Role, Social

QoL/GHS

BPI-SF
(score range 0-10; higher score represents more pain)

Includes

Worst pain, Average pain, Least pain, Pain right now, Pain interference, Location of pain

- TTPP and mean change from baseline in worst pain (BPI-SF Question 3) at week 26 were pre-specified endpoints included in the hierarchical statistical testing plan.
- Pre-specified descriptive analyses included change from baseline and time to confirmed deterioration (TTCD).
- Patients with moderate/severe pain at baseline were a pre-specified subgroup of interest.

BPI-SF, Brief Pain Inventory-Short Form

Gupta S et al. ASCO 2024;Abstract 4502.

Baseline QoL and Pain Scores

Parameter	EV+P (n=376)	Chemotherapy (n=355)
BPI-SF		
Worst pain, mean (SD)	3.1 (2.8)	3.3 (3.0)
Patients with moderate to severe pain at baseline, n (%)	128 (34)	128 (36)
EORTC QLQ-C30, mean (SD)		
GHS/QoL	62.4 (22.5)	60.3 (25.4)
Functioning scales		
Cognitive functioning	84.3 (19.6)	83.9 (19.9)
Social functioning	77.3 (27.4)	76.3 (26.3)
Emotional functioning	75.5 (20.7)	74.6 (22.0)
Physical functioning	76.5 (22.7)	72.8 (24.3)
Role functioning	75.8 (28.3)	73.2 (29.4)

- Baseline scores were balanced between treatment arms in the PRO full analysis set.[a]

- Approximately one-third of patients had moderate to severe pain (pain score of 5 or greater on a scale of 1–10) at baseline.

Gupta S et al. ASCO 2024;Abstract 4502.

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Change in Worst Pain (BPI-SF)

"Please rate your pain from 0 (no pain) to 10 (pain as bad as you can imagine) that best describes your pain at its worst in the last 24 hours."

- Although pre-defined clinically meaningful thresholds were not met in either treatment arm:
  - Patients in the EV+P arm reported improved pain compared to baseline.
  - Larger improvements in pain were demonstrated in the EV+P arm than in the CT arm.

LS mean (95% CI)	-0.58 (-1.05, -0.11)
Two-sided P value[a]	0.015

No. at Risk																		
EV+P	368	321	333	311	315	303	300	307	302	307	298	297	295	288	277	261	251	242
Chemotherapy	345	306	293	301	294	298	282	296	279	278	271	260	256	239	241	204	179	172
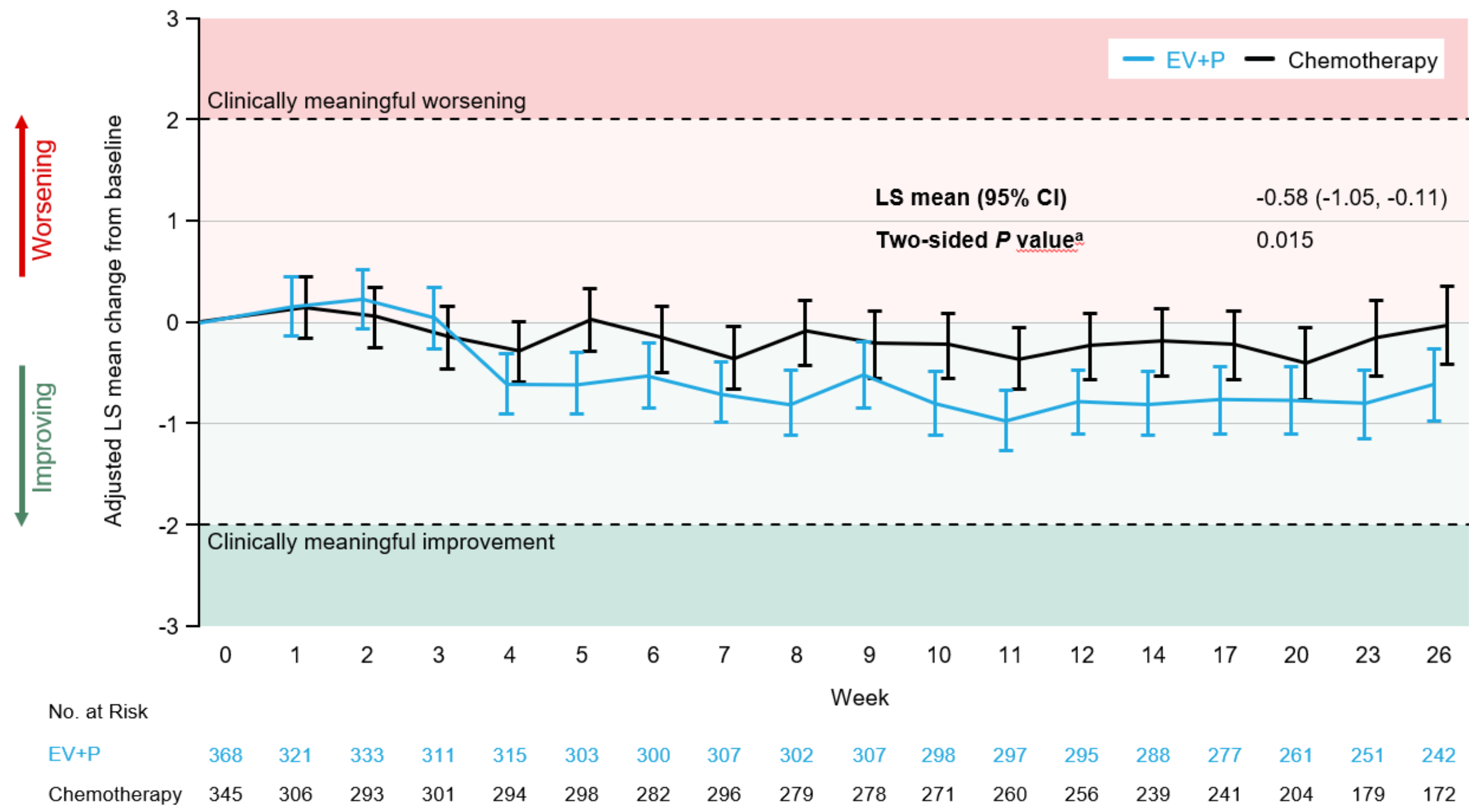
Gupta S et al. ASCO 2024;Abstract 4502.

Change in EORTC QLQ-C30 Global Health Status/QoL Score

> "How would you rate your overall health during the past week?"
> "How would you rate your overall quality of life during the past week?"

- Patients in the EV+P arm had a transient worsening in GHS/QoL score at week 3, followed by a return to baseline at week 4.

- Patients in the CT arm had a worsening from week 1 through week 17; scores returned to baseline from week 20.

- Median time to confirmed deterioration (mTTCD) was 5.9 months with EV+P and 3.2 months with CT, (HR 0.98 [95% CI: 0.79, 1.2]).
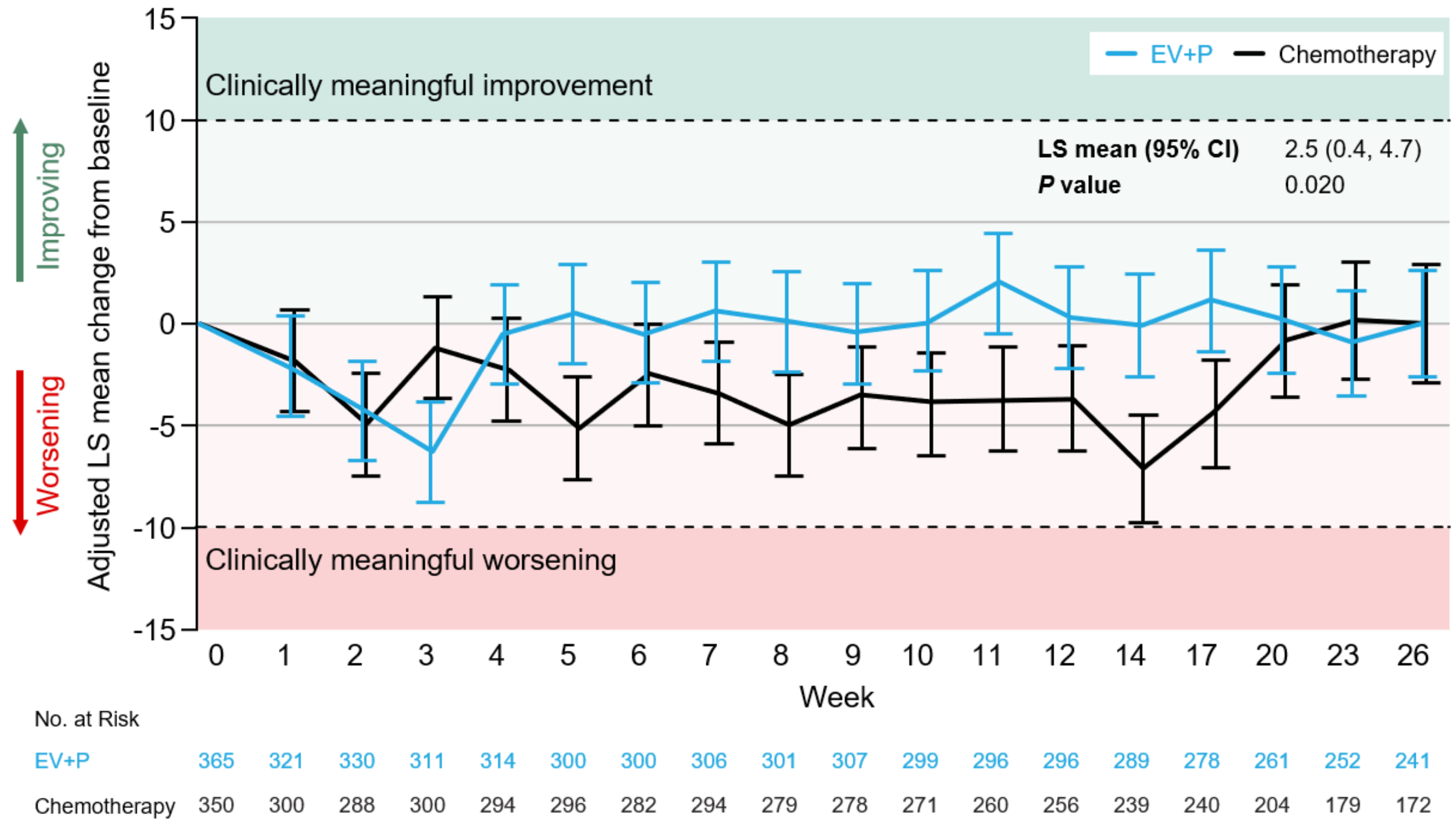
Gupta S et al. ASCO 2024;Abstract 4502.

2021

UTUC
Neoadjuvant gem cis
Nephro U T3N1
Nivolumab adjuvant
Progression liver mets
Single agent EV

2021

2024

Significant neuropathy refusing to stop treatment.
Improved with reducing dose.

Phase III CheckMate 901

- NIVO + gemcitabine-cisplatin vs gemcitabine-cisplatin in cisplatin-eligible patients[a]

Key inclusion criteria

- Age ≥ 18 years
- Previously untreated unresectable or mUC involving the renal pelvis, ureter, bladder, or urethra
- Cisplatin eligible
- ECOG PS of 0-1

Stratification factors:
- Tumor PD-L1 expression (≥ 1% vs < 1%)
- Liver metastases (yes vs no)

R

N = 304

Combination phase

NIVO 360 mg on D1
+ **Gemcitabine** 1000 mg/m² on D1/D8
+ **Cisplatin** 70 mg/m² on D1
Q3W (up to 6 cycles)[b]

3 weeks

Monotherapy phase

NIVO 480 mg Q4W (until progression, unacceptable toxicity, withdrawal, or up to 24 months[c])

N = 304

Gemcitabine 1000 mg/m² on D1/D8
+ **Cisplatin** 70 mg/m² on D1
Q3W (up to 6 cycles)[b]

Median (range) study follow-up, 33.6 (7.4-62.4) months

Primary endpoints: OS, PFS per BICR
Key secondary endpoints: OS and PFS by PD-L1 ≥ 1%,[d] HRQoL
Key exploratory endpoints: ORR per BICR, safety

[a]Further CheckMate 901 trial design details are available at https://clinicaltrials.gov/ct2/show/NCT03036098. [b]Patients who discontinued cisplatin could be switched to gemcitabine-carboplatin for the remainder of the platinum doublet cycles (up to 6 in total). [c]A maximum of 24 months from first dose of NIVO administered as part of the NIVO + gemcitabine-cisplatin combination. [d]PD-L1 status was defined by the percentage of positive tumor cell membrane staining in a minimum of 100 tumor cells that could be evaluated with the use of the PD-L1 IHC 28-8 pharmDx immunohistochemical assay (Dako, Santa Clara, CA, USA).
BICR, blinded independent central review; D, day; ECOG PS, Eastern Cooperative Oncology Group performance status; HRQoL, health-related quality of life; ORR, objective response rate; PD-L1, programmed death ligand 1; PFS, progression-free survival; QxW, every x weeks; R, randomization.

Van der Heijden MS et al. ESMO 2023;Abstract LBA7.

Phase III CheckMate 901

Van der Heijden MS et al. ESMO 2023;Abstract LBA7.

Select characteristics for all patients with complete response

	All randomized patients		Patients with CR	
	NIVO+GC (N = 304)	GC (N = 304)	NIVO+GC (N = 66)	GC (N = 36)
Median age (range), years	65.0 (32-86)	65.0 (35-85)	65.0 (33-81)	63.5 (36-80)
Male sex, n (%)	236 (78)	234 (77)	53 (80)	31 (86)
Race				
White	211 (69)	225 (74)	47 (71)	27 (75)
Black or African American	0	2 (< 1)	0	0
American Indian or Alaska Native	1 (< 1)	1 (< 1)	0	1 (3)
Asian	75 (25)	63 (21)	16 (24)	6 (17)
Other	17 (6)	13 (4)	3 (5)	2 (6)
LN only disease,ᵃ n (%)	54 (18)	56 (18)	34 (52)	19 (53)
Disease stage at study entry, n (%)				
Stage III	37 (12)	28 (9)	9 (14)	5 (14)
Stage IV	265 (87)	274 (90)	56 (85)	31 (86)
Not reported	2 (< 1)	2 (< 1)	1 (2)	0
PD-L1 status, n (%)				
≥ 1%	112 (37)	109 (36)	28 (42)	11 (31)
< 1%	192 (63)	195 (64)	38 (58)	25 (69)
Subsequent anticancer therapy received	108 (36)	156 (51)	23 (35)	15 (42)

- Of the 608 total patients randomized, 102 (16.8%) achieved a CR

- Approximately 50% of patients with CR had LN only mUC vs approximately 20% of all randomized patients

ᵃLN only disease as defined per BICR. There may not be full concordance with investigator assessment.

Galsky M et al. ASCO 2024;Abstract 4509.

Select characteristics for all patients with complete response

	All randomized patients		Patients with CR	
	NIVO+GC (N = 304)	GC (N = 304)	NIVO+GC (N = 66)	GC (N = 36)
Median age (range), years	65.0 (32-86)	65.0 (35-85)	65.0 (33-81)	63.5 (36-80)
Male sex, n (%)	236 (78)	234 (77)	53 (80)	31 (86)
Race				
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[a]LN only disease as defined per BICR. There may not be full concordance with investigator assessment.

Galsky M et al. ASCO 2024;Abstract 4509.

Response per BICR
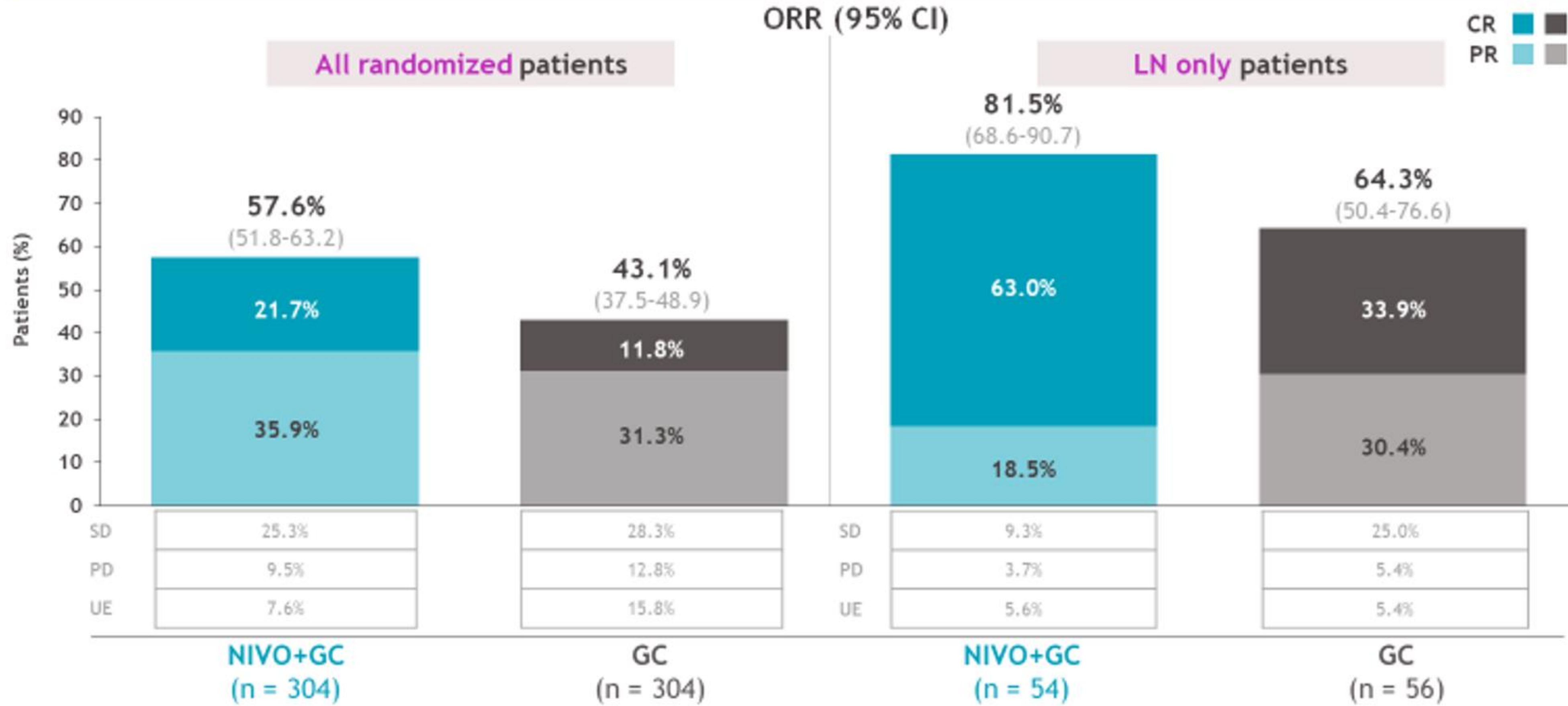
CheckMate 901

Galsky M et al. ASCO 2024;Abstract 4509.
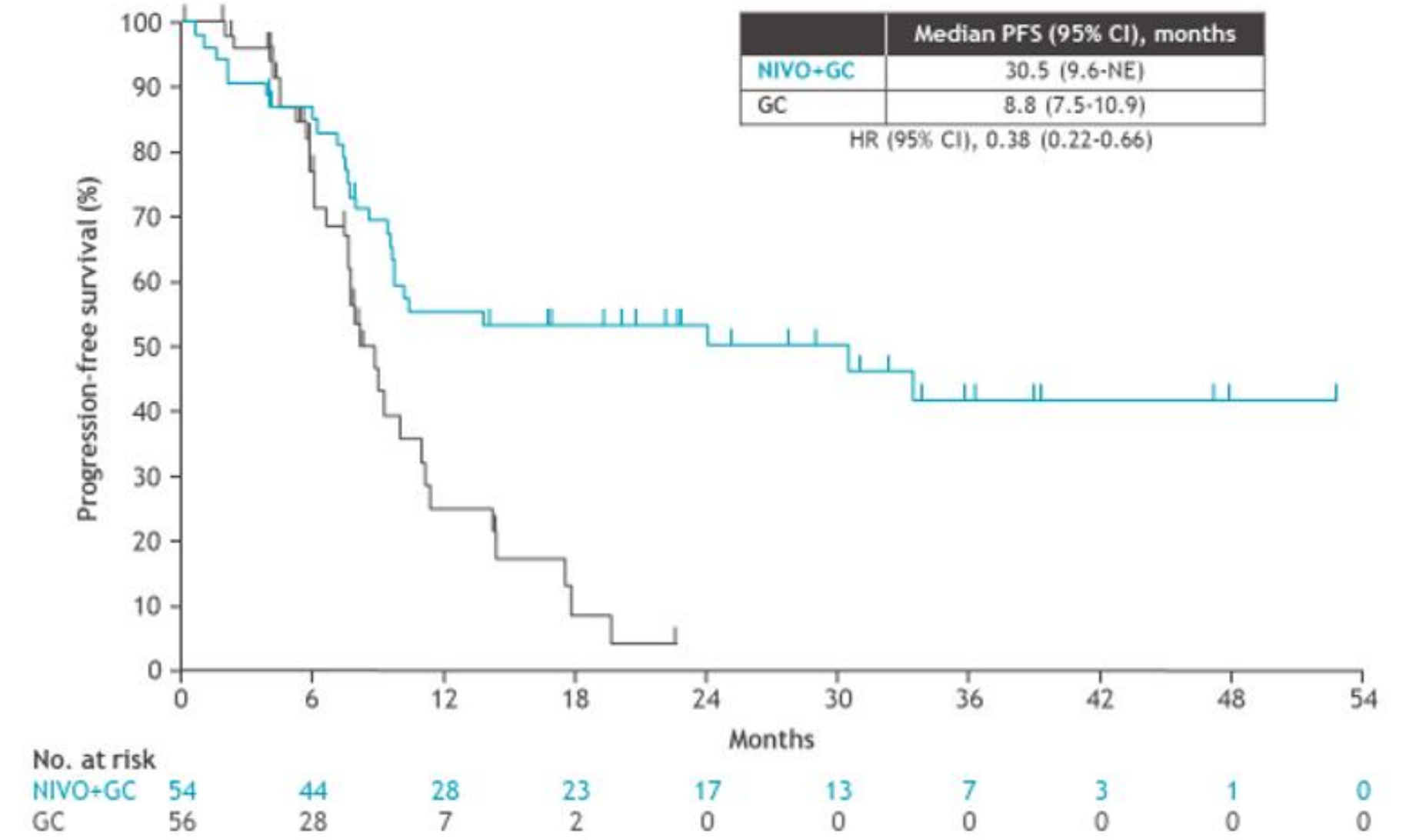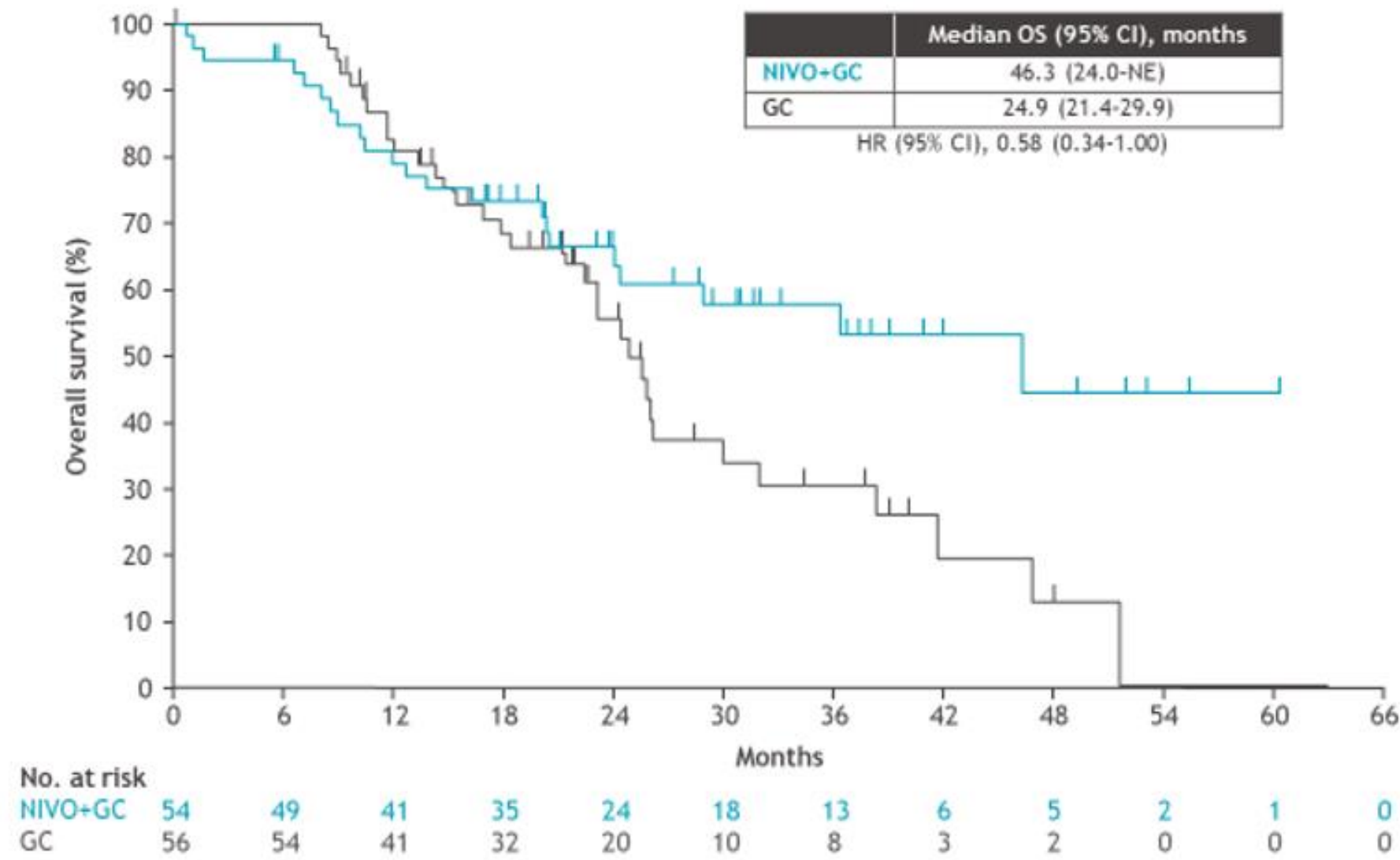
Galsky M et al. ASCO 2024;Abstract 4509.

Take Home

- Exciting time for UC, but still a lot of unanswered questions.

- Antibody drug conjugates appear to have favorable efficacy /toxicity profile in refractory mUC patients.

- Enfortumab Vedotin plus pembrolizumab combination changed the paradigm of how we treat.

- Optimal sequencing remains unclear.

How About Renal Cancer

N = 1096

Key inclusion criteria[1]

- ≥ 18 years old
- Treatment-naïve aRCC
- Clear cell component
- Measurable disease per RECIST v1.1
- KPS ≥ 70%

Stratification factors:

- IMDC risk score
- Geographic region

R
1:1

**NIVO 3 mg/kg IV
+ IPI 1 mg/kg IV Q3W (× 4 doses)
followed by NIVO 3 mg/kg Q2W**
*Patients receiving NIVO monotherapy could switch to NIVO 240 mg Q2W
or 480 mg Q4W flat dosing[a]*

**SUN 50 mg PO QD
for 4 weeks on, 2 weeks off (6-week cycles)**
Crossover from SUN to NIVO+IPI was permitted for intermediate/poor-risk patients[a]

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

Nizar Tannir, ASCO GU 2024, #363

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Checkmate-214 (8 Year Follow Up; GU ASCO 2024)
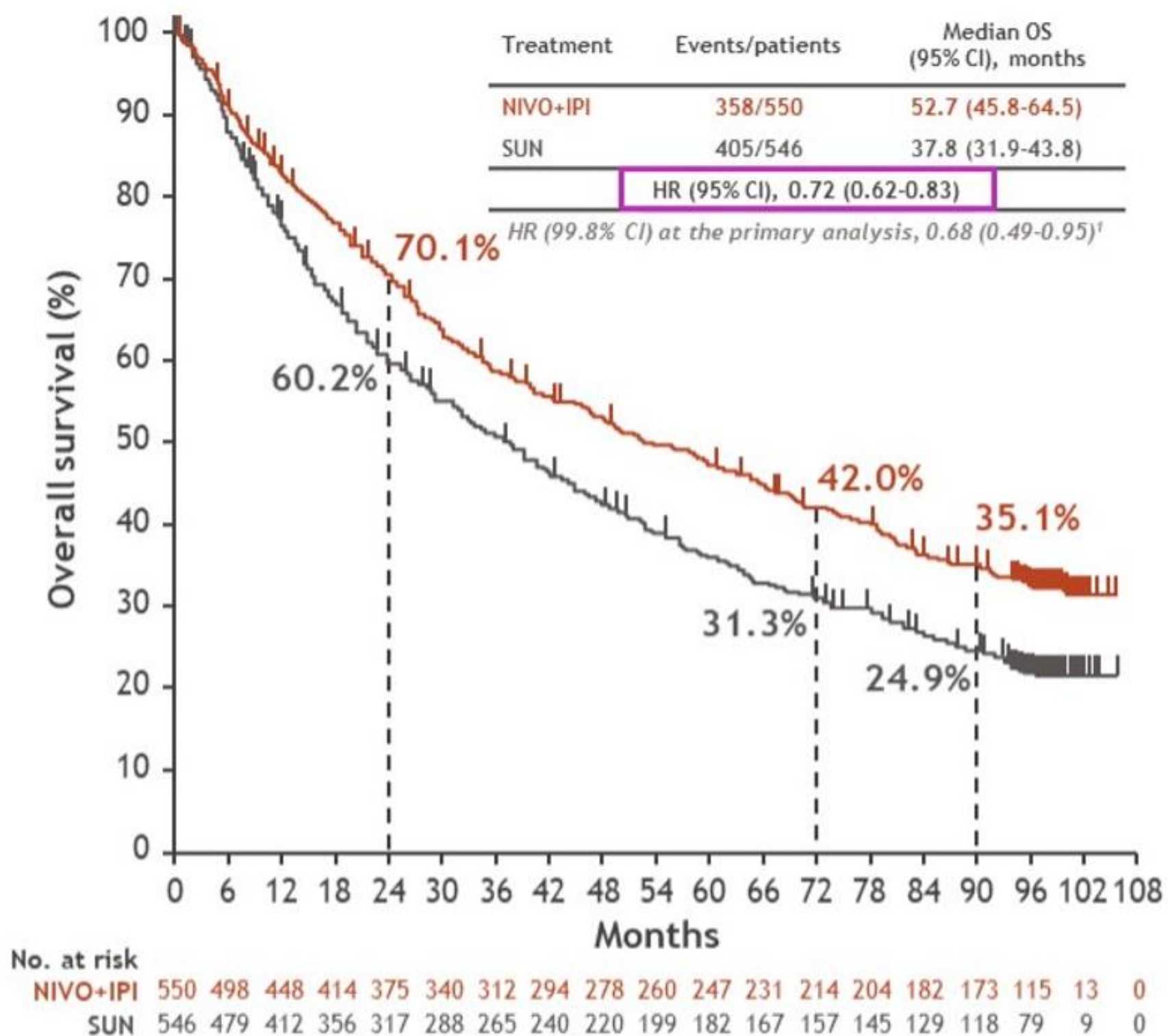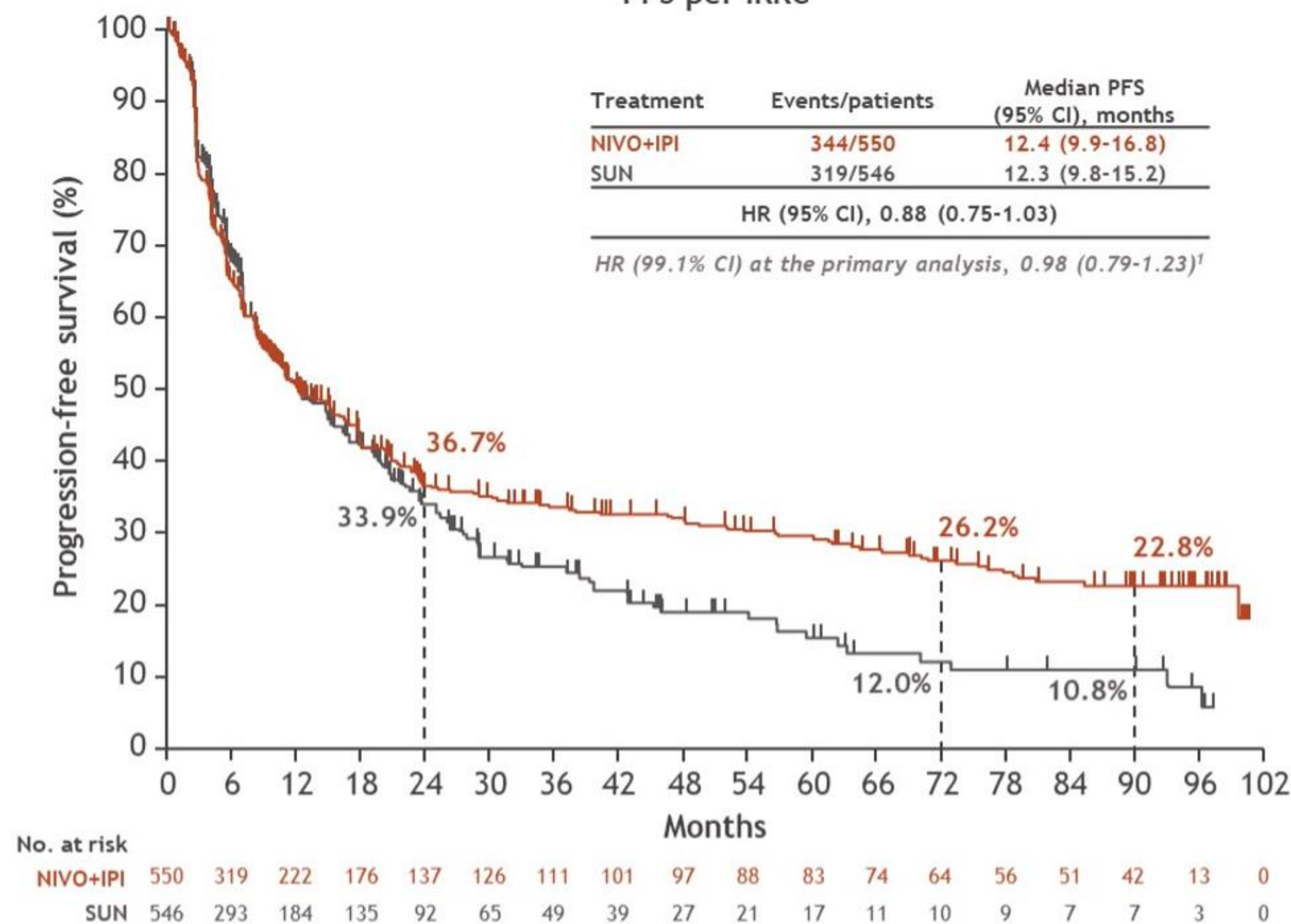
Nizar Tannir, ASCO GU 2024, #363

KEYNOTE-426: Trial Design

Key Eligibility Criteria

- Newly diagnosed or recurrent stage IV clear cell RCC
- No previous systemic treatment for advanced disease
- Measurable disease per RECIST v1.1

Stratification Factors

- IMDC risk group (favorable vs intermediate vs poor)
- Geographic region (North America vs Western Europe vs ROW)

R (1:1)
N = 861

n = 432
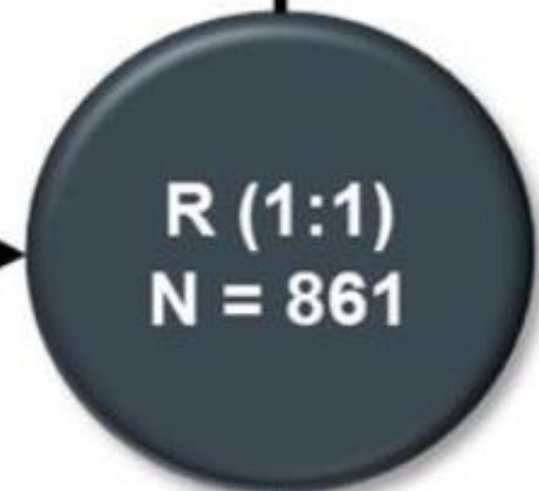
Pembrolizumab 200 mg IV Q3W for up to 35 cycles (approximately 2 years) + Axitinib 5 mg orally twice daily[a]

n = 429

Sunitinib 50 mg orally once daily for first 4 weeks of each 6-week cycle[b]

End Points
- **Dual primary:** PFS (RECIST v1.1, BICR) and OS in ITT
- **Key secondary:** ORR (RECIST v1.1, BICR) in ITT
- **Other secondary:** DOR (RECIST v1.1, BICR), safety

Rini et al, ASCO 2023 #LBA4501

KEYNOTE-426: Efficacy in Favorable Risk RCC
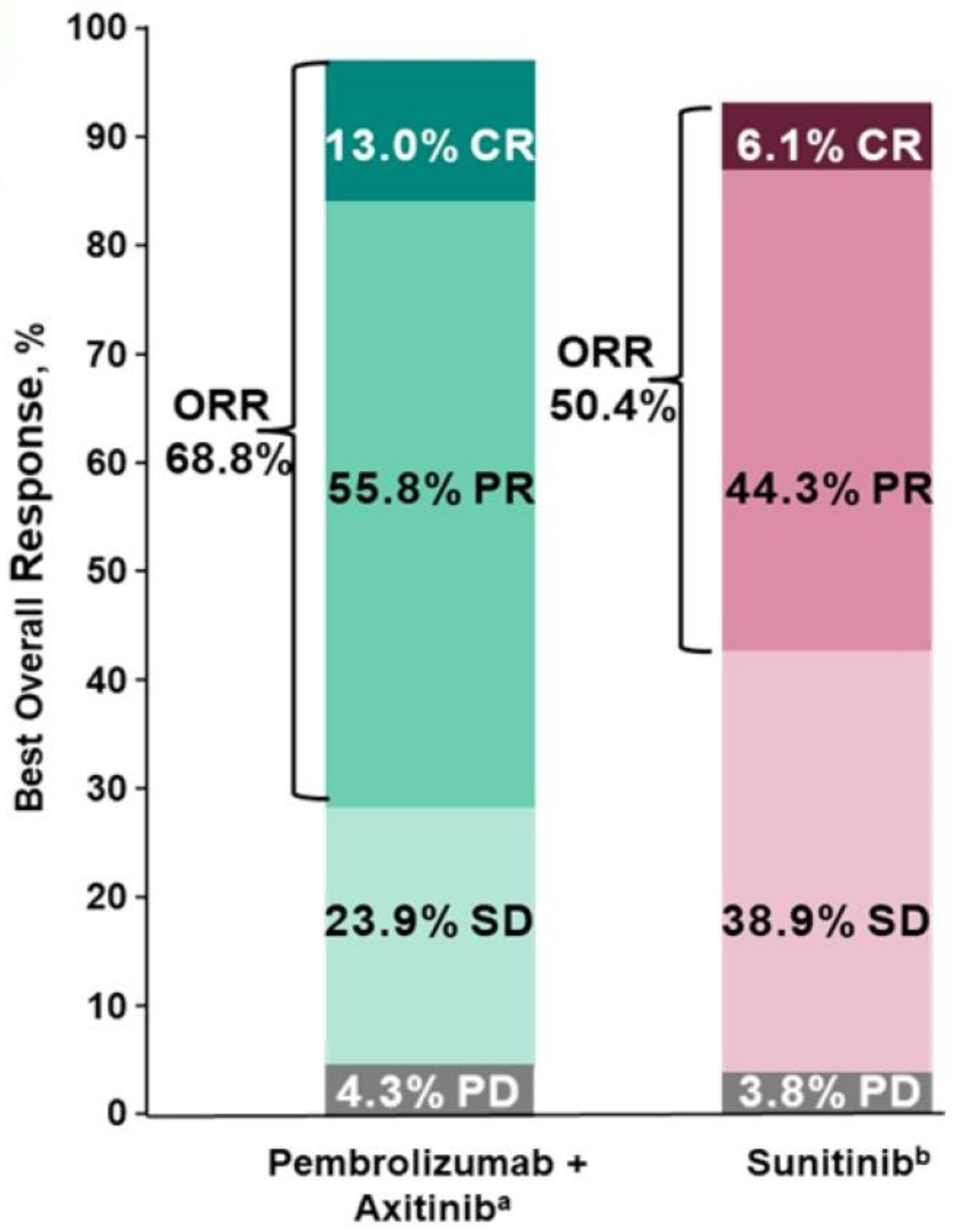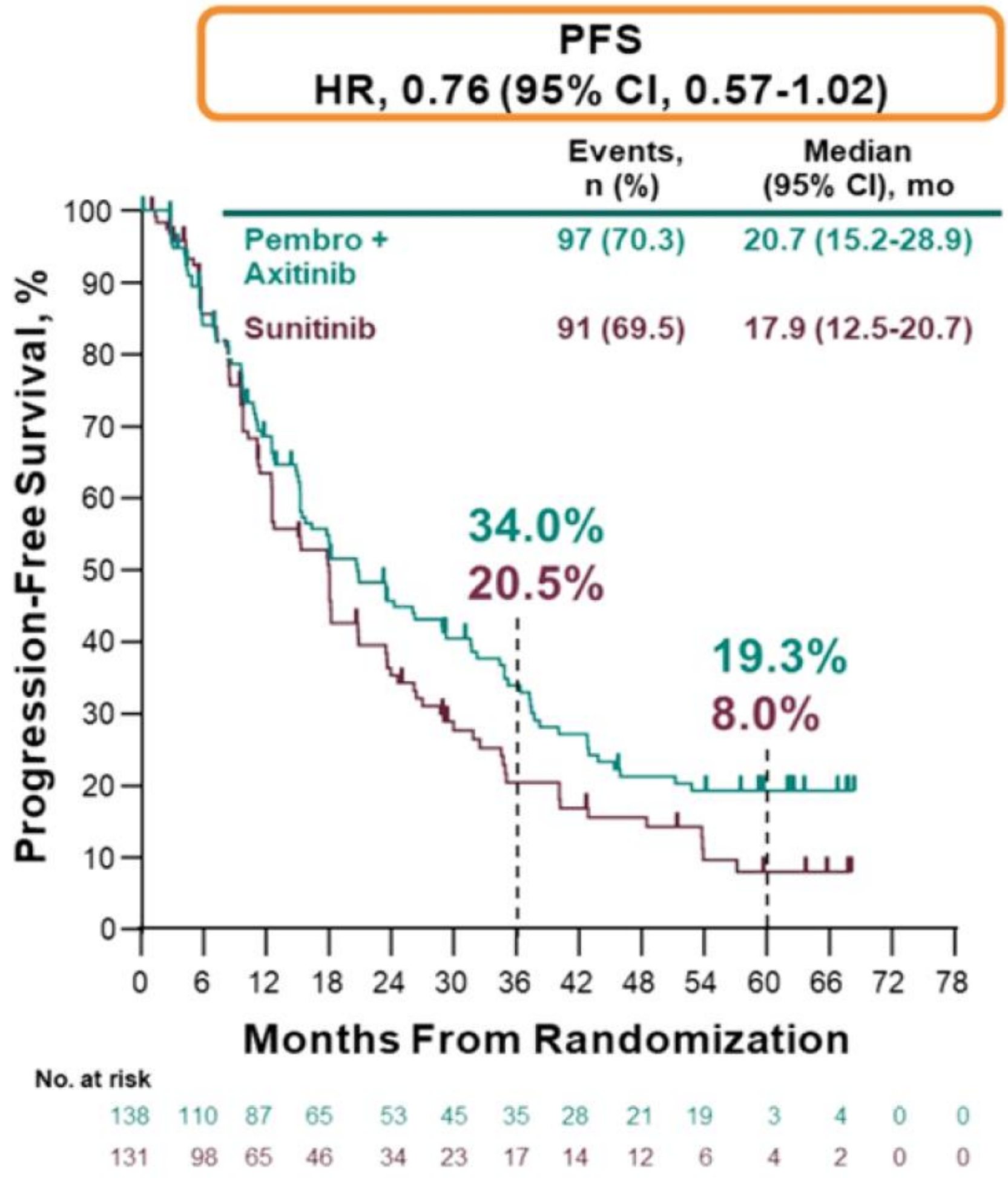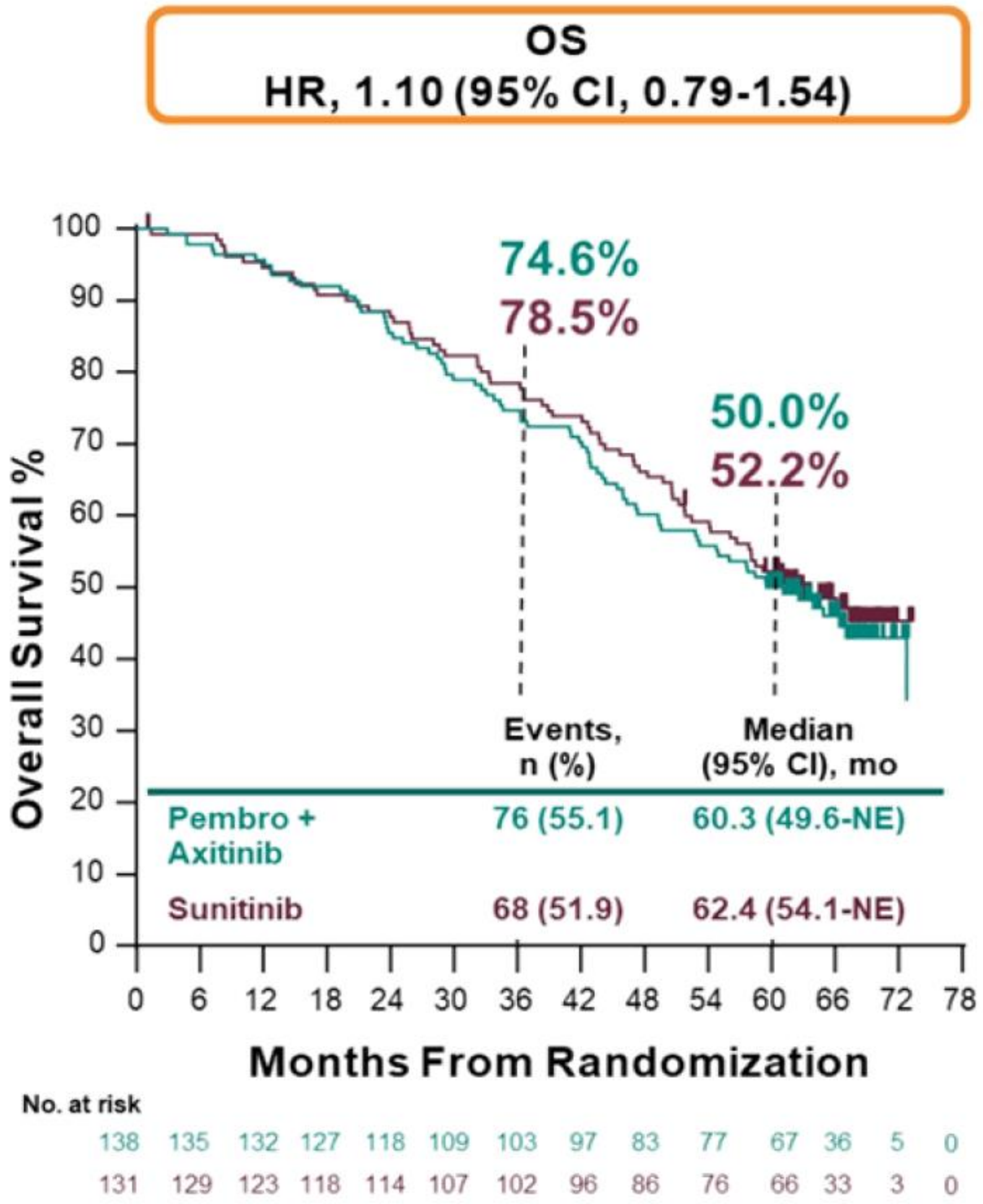
Rini et al, ASCO 2023 #LBA4501

KEYNOTE-426: Efficacy in Intermediate/Poor Risk RCC

Rini et al, ASCO 2023 #LBA4501
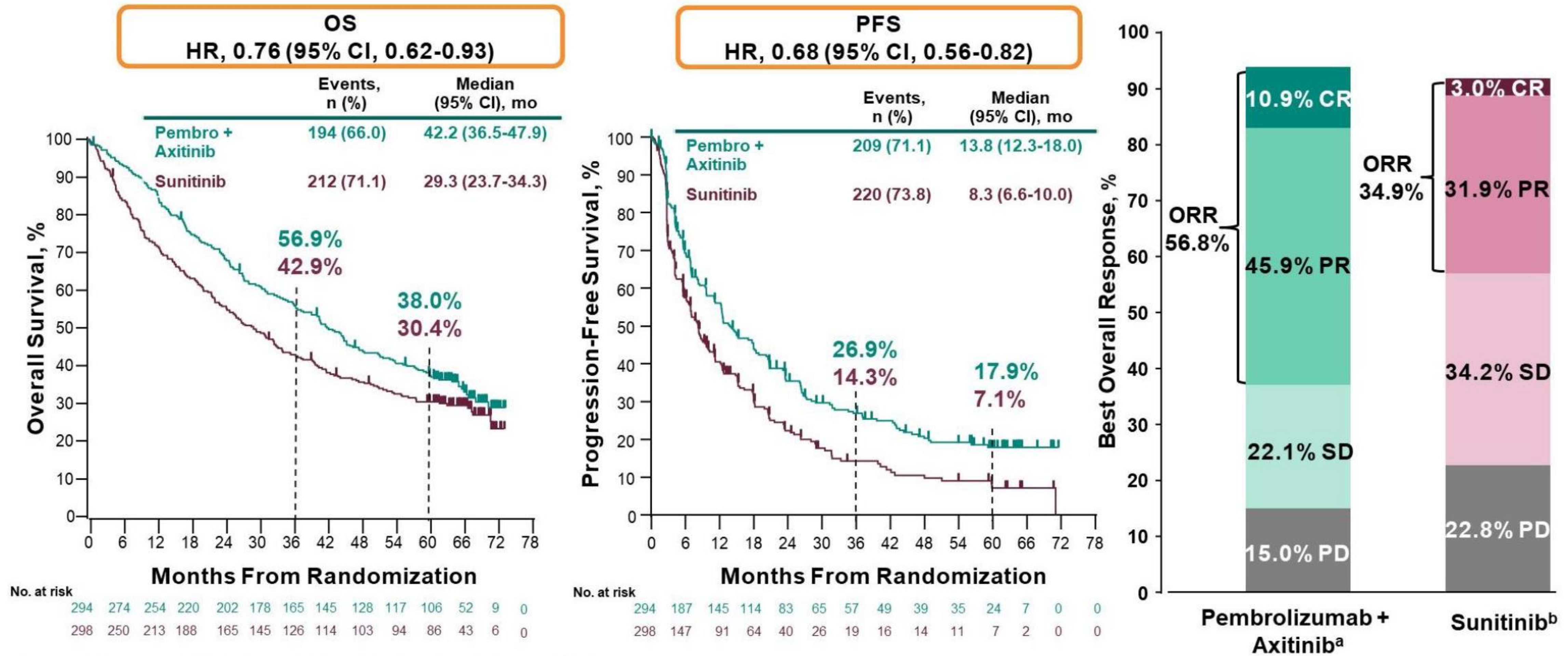
KEYNOTE-426: Exploratory Biomarker Analysis

Rini et al, ASCO 2024 #4505
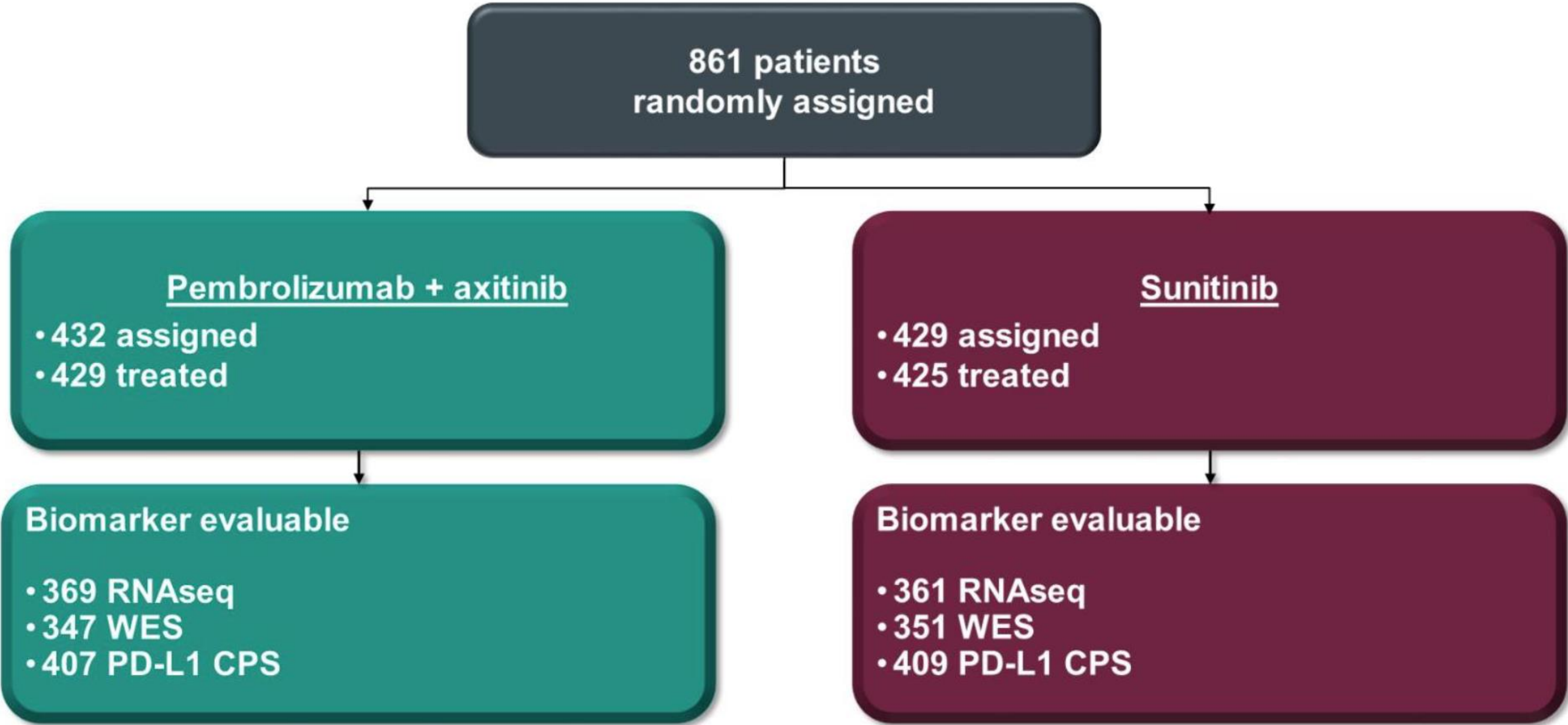
KEYNOTE-426: $Tcell_{inf}GEP$, Angiogenesis, PD-L1

Biomarker	Pembrolizumab + axitinib			Sunitinib		
	ORR	PFS	OS	ORR	PFS	OS
$Tcell_{inf}GEP$	<0.0001(+)	<0.0001(+)	0.002(+)	NS	NS	NS
Angiogenesis	NS	NS	0.004(+)	0.002(+)	<0.001(+)	<0.0001(+)
PD-L1 CPS	NS	NS	NS	NS	NS	0.025(-)

- Higher $Tcell_{inf}GEP$ was associated with improved clinical outcome within the pembrolizumab + axitinib arm

- Higher angiogenesis gene expression was associated with improved clinical outcome within the sunitinib arm

- PD-L1 CPS was negatively associated with OS within the sunitinib arm

Rini et al, ASCO 2024 #4505

KEYNOTE-426: ORR by Molecular Subtype

- Pembro + axitinib showed improved ORR across molecular subtypes
- Within pembro + axitinib arm, ORR highest in immune/proliferative subtype
- Within sunitinib arm, ORR highest in angiogenic subtype
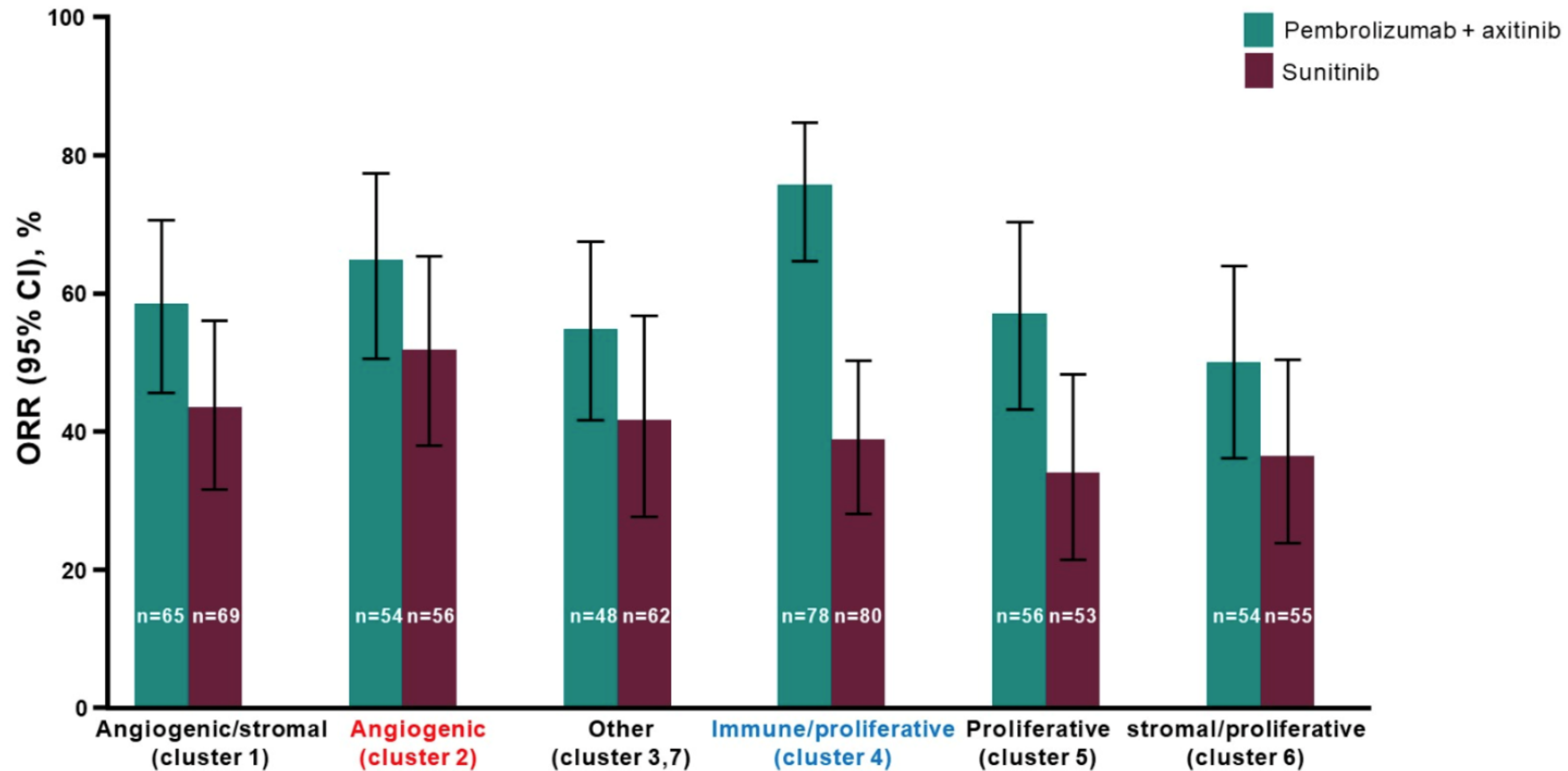
Rini et al, ASCO 2024 #4505

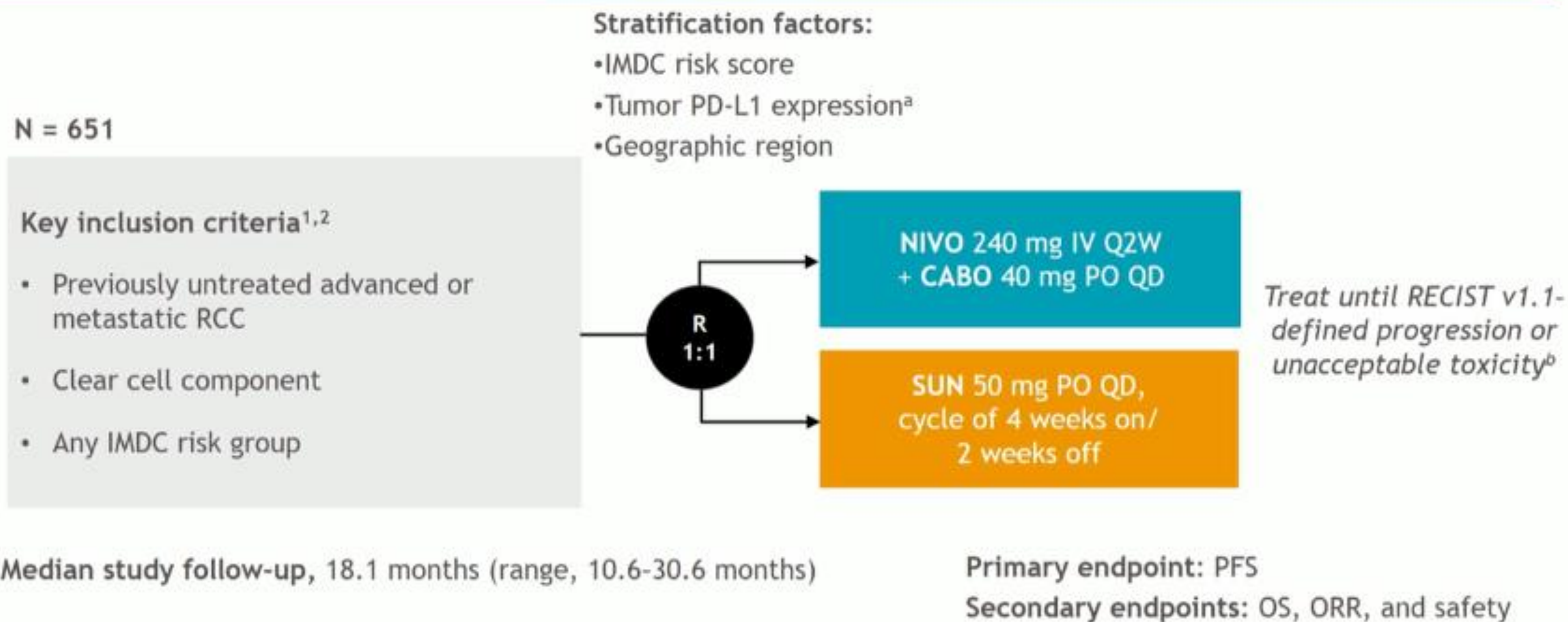# KEYNOTE-426: ORR by Mutational Status
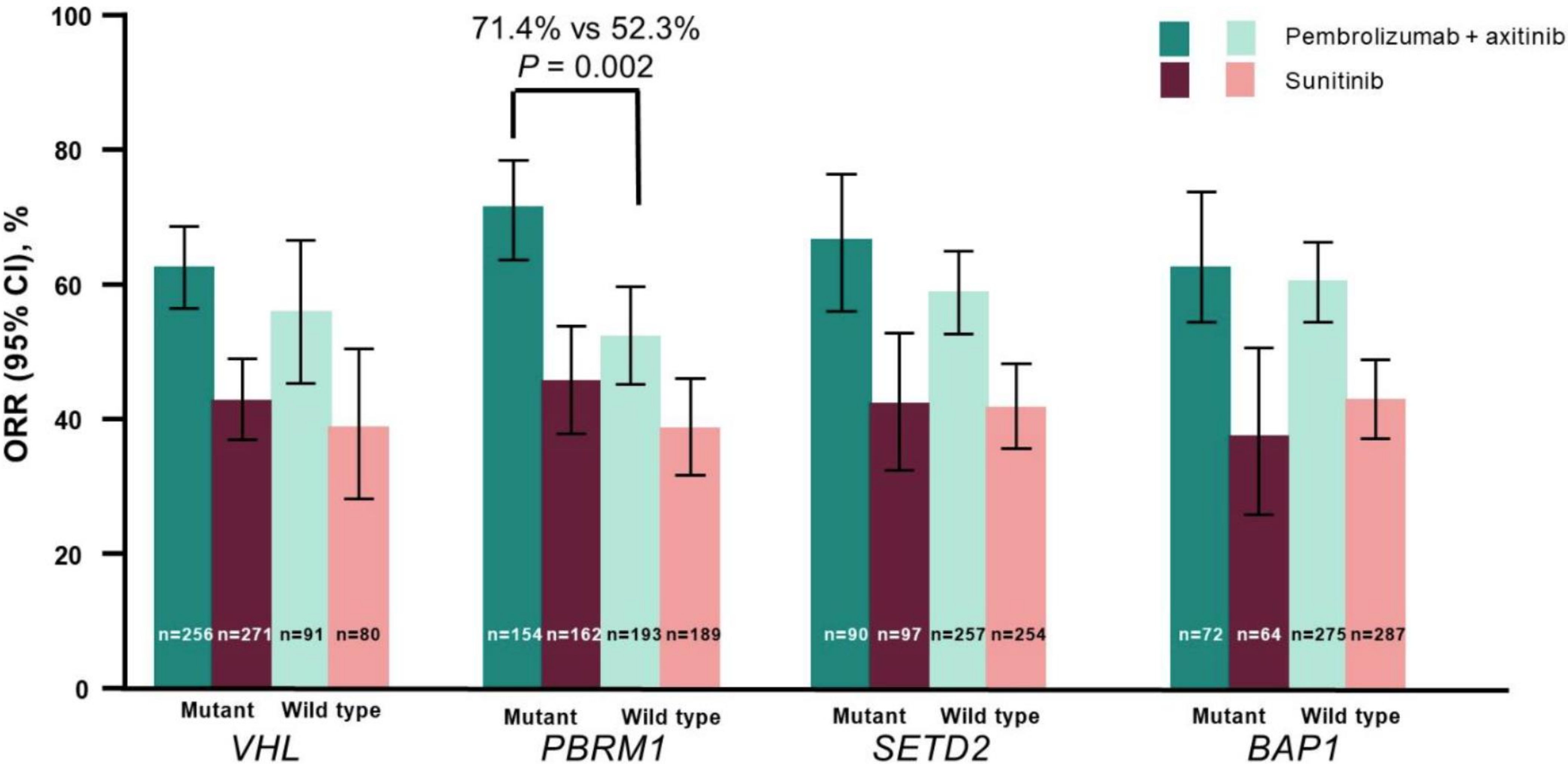
Rini et al, ASCO 2024 #4505

CheckMate 9ER: Study design

Stratification factors:
- IMDC risk score
- Tumor PD-L1 expression[a]
- Geographic region

N = 651

Key inclusion criteria[1,2]

- Previously untreated advanced or metastatic RCC
- Clear cell component
- Any IMDC risk group

R 1:1

NIVO 240 mg IV Q2W + CABO 40 mg PO QD

SUN 50 mg PO QD, cycle of 4 weeks on/ 2 weeks off

Treat until RECIST v1.1-defined progression or unacceptable toxicity[b]

Median study follow-up, 18.1 months (range, 10.6-30.6 months)

Primary endpoint: PFS
Secondary endpoints: OS, ORR, and safety

[a]Defined as the percent of positive tumor cell membrane staining in a minimum of 100 evaluable tumor cells per validated Dako PD-L1 immunohistochemistry 28-8 pharmDx assay.
[b]NIVO dosing may not exceed a total of 2 years (from cycle 1); CABO and SUN treatment may continue beyond 2 years in the absence of progression or unacceptable toxicity. Patients may be treated beyond progression.
IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; IV, intravenously; ORR, objective response rate; PD-L1, programmed death ligand 1; PFS, progression-free survival; PO, orally; Q2W, every 2 weeks; QD, once daily; RECIST, Response Evaluation Criteria in Solid Tumors.
1. Clinicaltrials.gov/ct2/show/NCT03141177. Accessed June 8, 2020; 2. Choueiri TK et al. Poster presented at the American Society of Clinical Oncology Annual Meeting 2018. TPS4598. 4
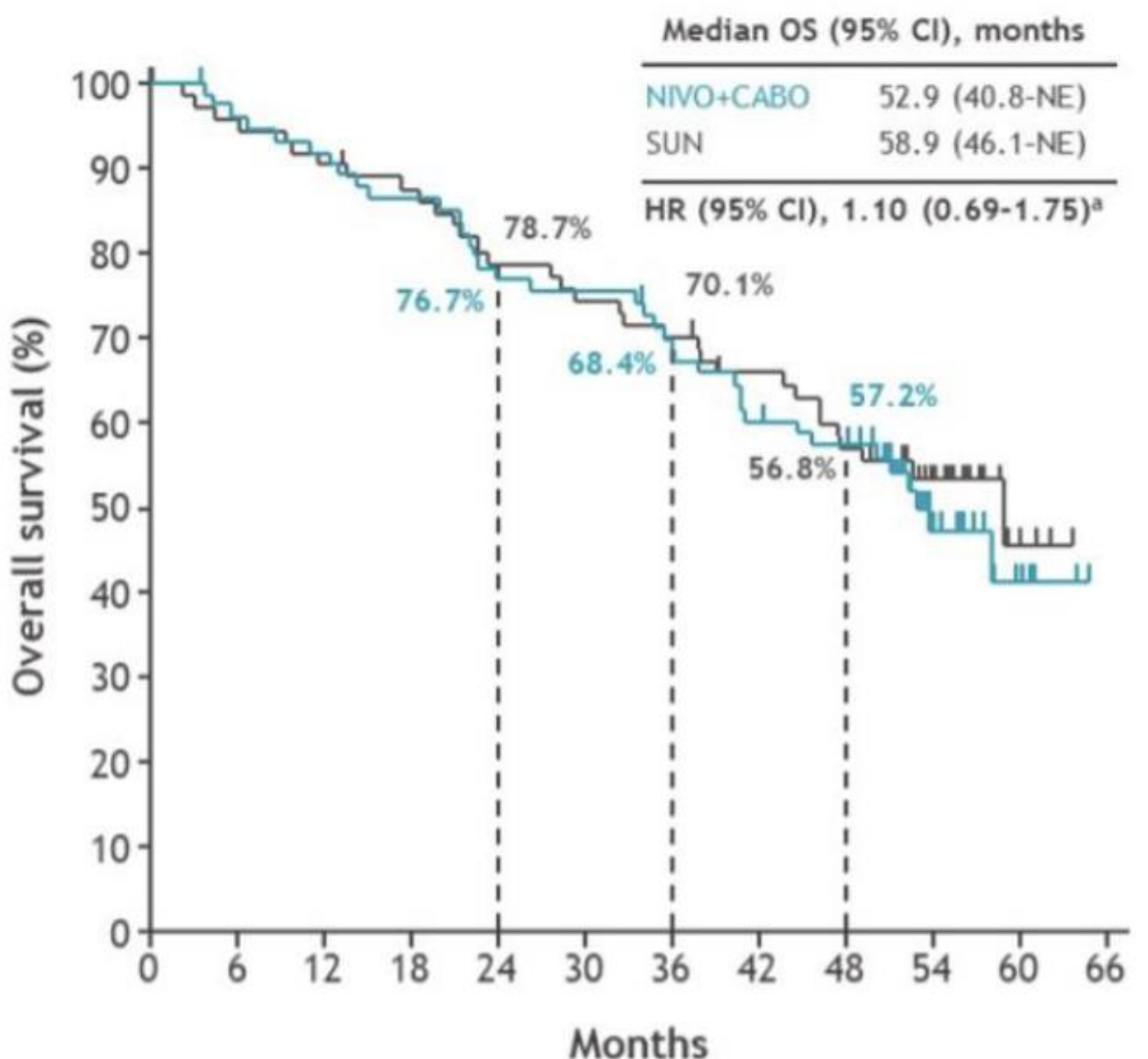
Maria Bourlon, ASCO GU 2024, Abstract #362

CheckMate 9ER: Efficacy in Favorable Risk RCC

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CheckMate 9ER: Efficacy in Intermediate/Poor Risk RCC

CheckMate 9ER: Efficacy by Baseline Organ Metastases

- PFS, OS, and ORR favored NIVO+CABO versus SUN in subgroups by baseline organ sites of metastases shown here

Outcome	Liver[a,b]		Bone[a,b]		Lung[a,b]	
	NIVO+CABO (n = 73)	SUN (n = 55)	NIVO+CABO (n = 79)	SUN (n = 73)	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)	4.4 (3.8-8.2)	16.4 (12.3-21.4)	8.3 (6.9-9.7)
HR (95% CI)[c]	0.54 (0.36-0.81)		0.45 (0.30-0.66)		0.56 (0.46-0.69)	
Median OS (95% CI), mo	37.6 (23.5-49.9)	22.1 (9.8-29.3)	34.8 (21.4-NE)	20.7 (12.5-25.7)	47.5 (40.6-56.1)	32.6 (24.9-39.7)
HR (95% CI)[c]	0.62 (0.41-0.95)		0.57 (0.38-0.84)		0.73 (0.58-0.92)	
ORR (95% CI), %	52.1 (40.0-63.9)	21.8 (11.8-35.0)	49.4 (37.9-60.9)	9.6 (3.9-18.8)	57.3 (50.8-63.6)	28.3 (22.8-34.3)

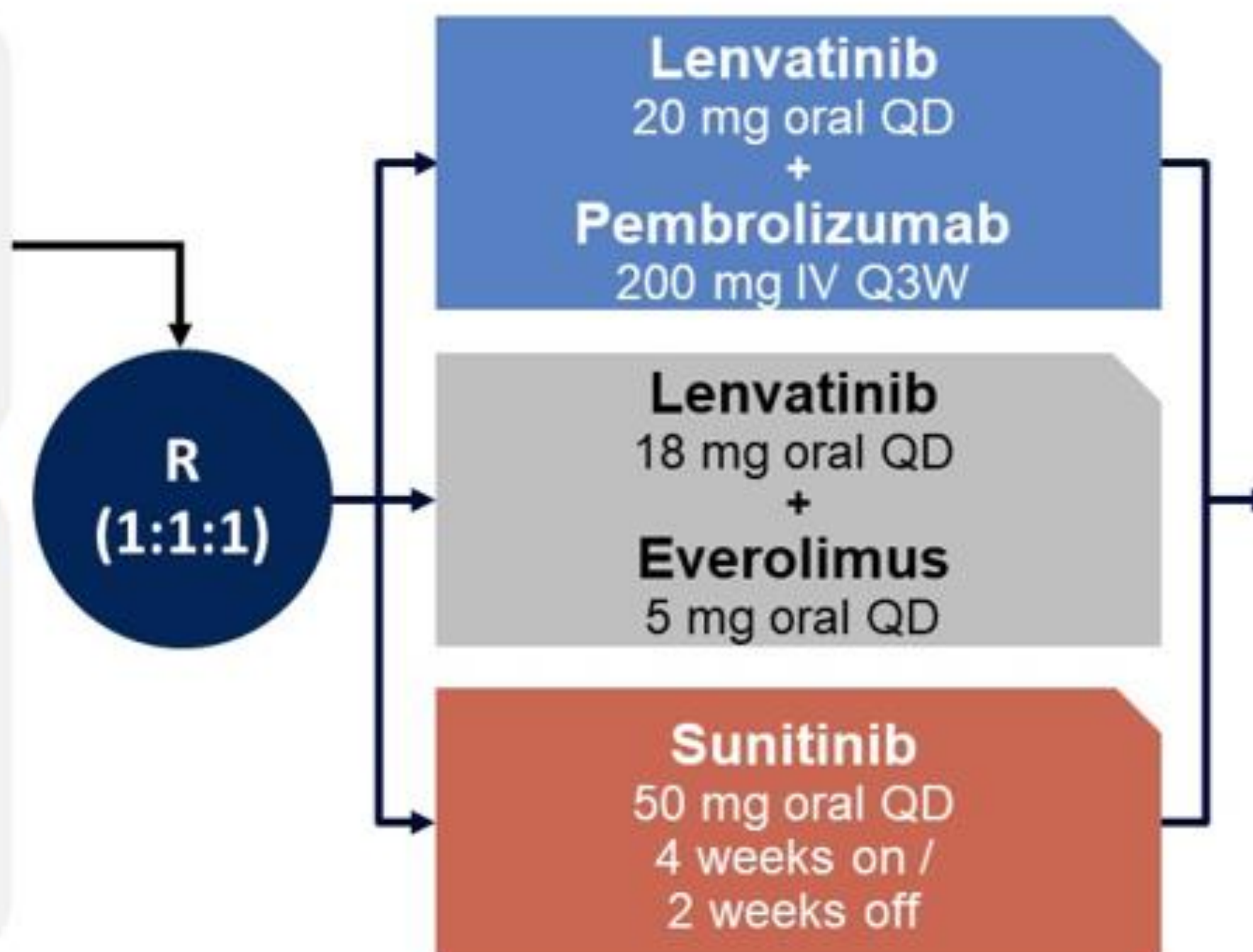Maria Bourlon, ASCO GU 2024, Abstract #362

CLEAR Trial

Key eligibility criteria
- Age ≥ 18 years
- Advanced clear-cell RCC
- No prior systemic anticancer therapy for RCC
- Karnofsky performance status ≥70

Stratification factors
- **Geographic region:** Western Europe and North America vs Rest of the World
- **MSKCC risk category:** Favorable, Intermediate, or Poor

R (1:1:1)

Lenvatinib
20 mg oral QD
+
Pembrolizumab
200 mg IV Q3W

Lenvatinib
18 mg oral QD
+
Everolimus
5 mg oral QD

Sunitinib
50 mg oral QD
4 weeks on /
2 weeks off

Primary endpoint
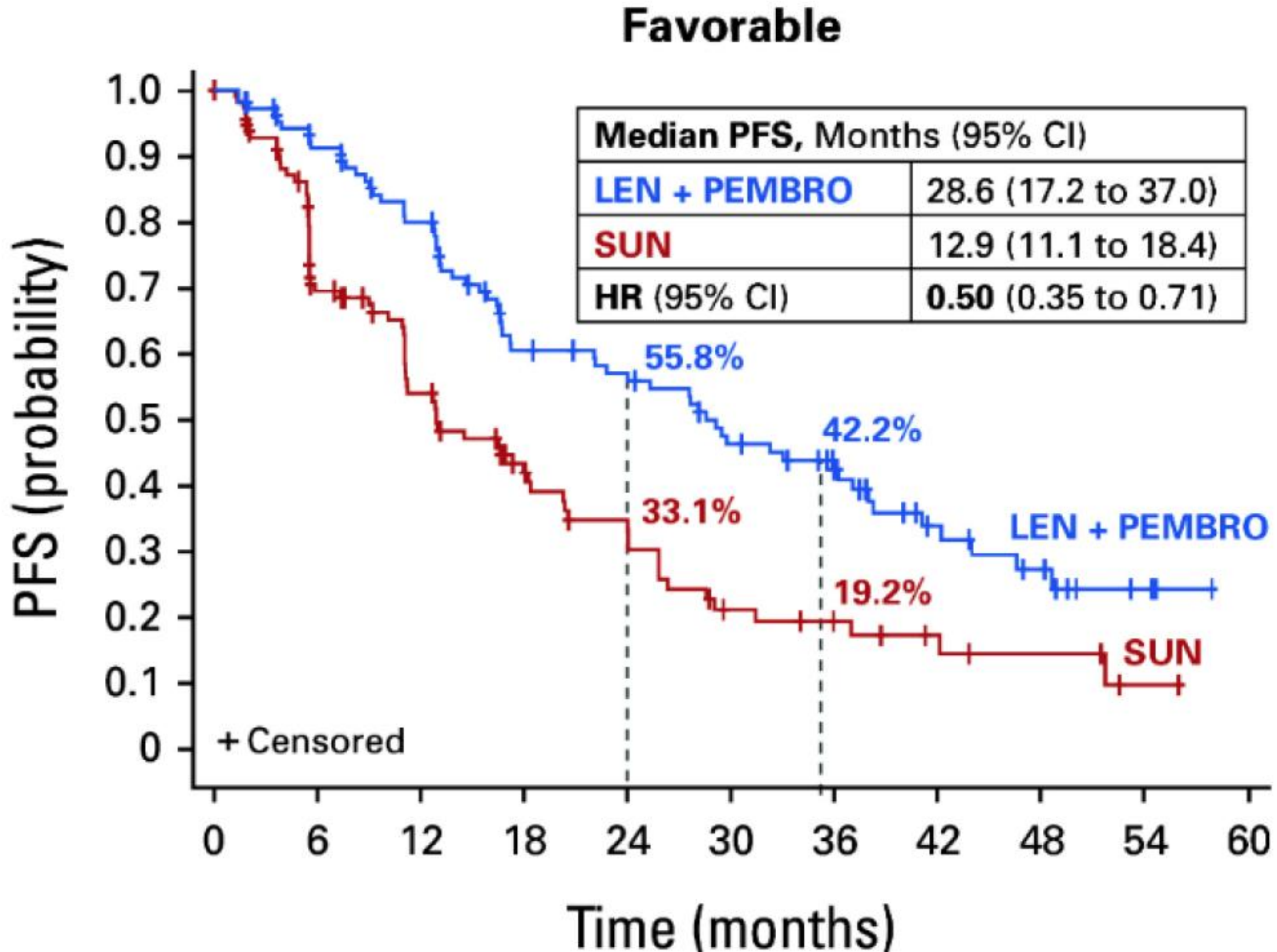- PFS by IRC per RECIST v1.1

Secondary endpoints
- OS
- ORR by IRC per RECIST v1.1
- Safety
- HRQoL
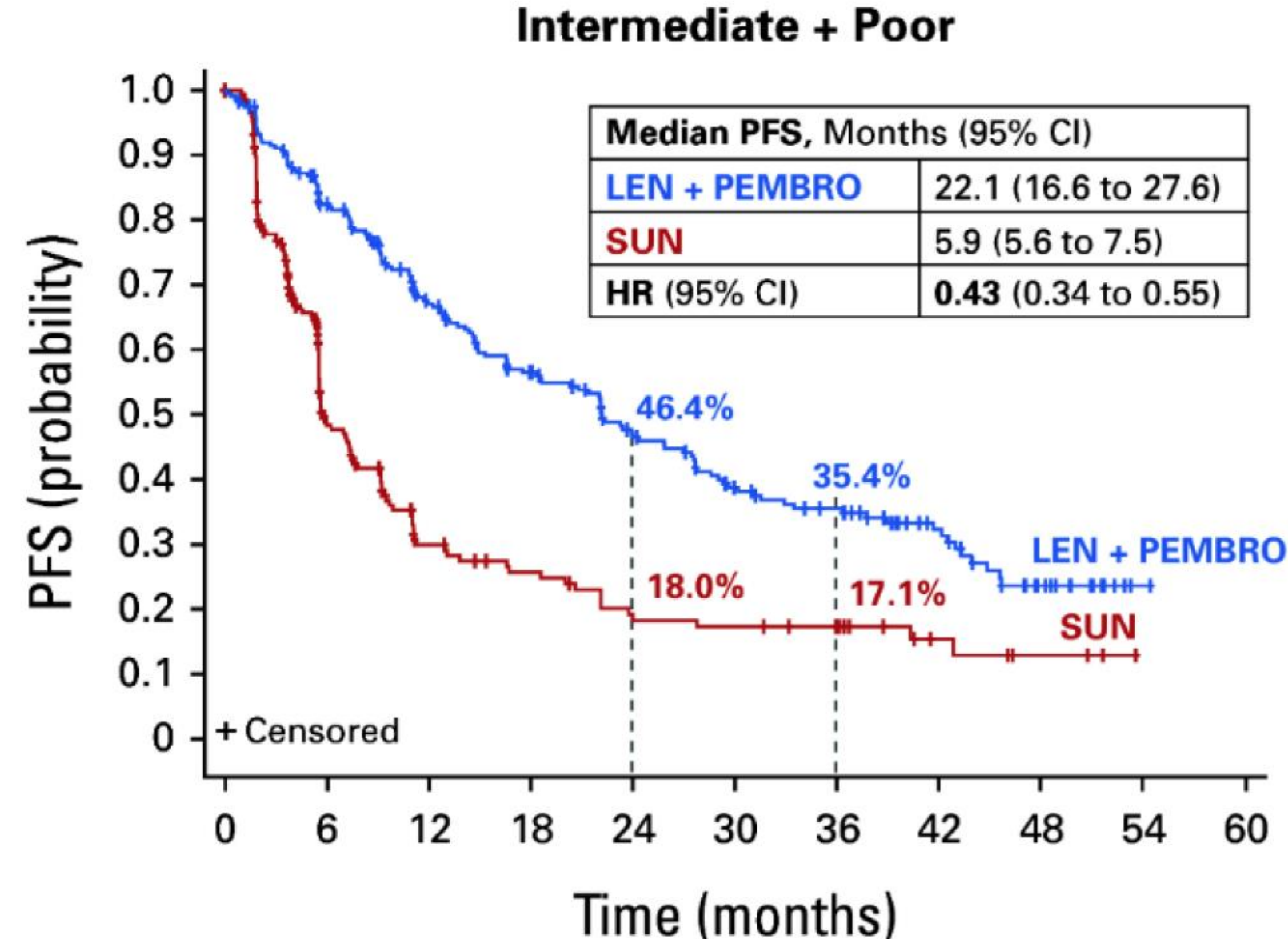
Key exploratory endpoints
- DOR
- Biomarkers

Choueiri TK, et al; ASCO 2024, Abstract 4504

CLEAR: Progression Free Survival by IMDC Subgroup

Favorable

Median PFS, Months (95% CI)	
LEN + PEMBRO	28.6 (17.2 to 37.0)
SUN	12.9 (11.1 to 18.4)
HR (95% CI)	**0.50** (0.35 to 0.71)

55.8%
42.2%
33.1%
19.2%
LEN + PEMBRO
SUN
+ Censored

No. at risk:

| 110 | 91 | 77 | 54 | 48 | 38 | 29 | 16 | 11 | 3 | 0 |
| 124 | 68 | 48 | 30 | 22 | 12 | 9 | 6 | 4 | 1 | 0 |

Intermediate + Poor

Median PFS, Months (95% CI)	
LEN + PEMBRO	22.1 (16.6 to 27.6)
SUN	5.9 (5.6 to 7.5)
HR (95% CI)	**0.43** (0.34 to 0.55)

46.4%
35.4%
18.0%
17.1%
LEN + PEMBRO
SUN
+ Censored

No. at risk:

| 243 | 184 | 136 | 107 | 80 | 61 | 52 | 33 | 14 | 1 | 0 |
| 229 | 75 | 37 | 29 | 19 | 18 | 14 | 6 | 3 | 0 | 0 |

CLEAR: Overall Survival by IMDC Subgroup
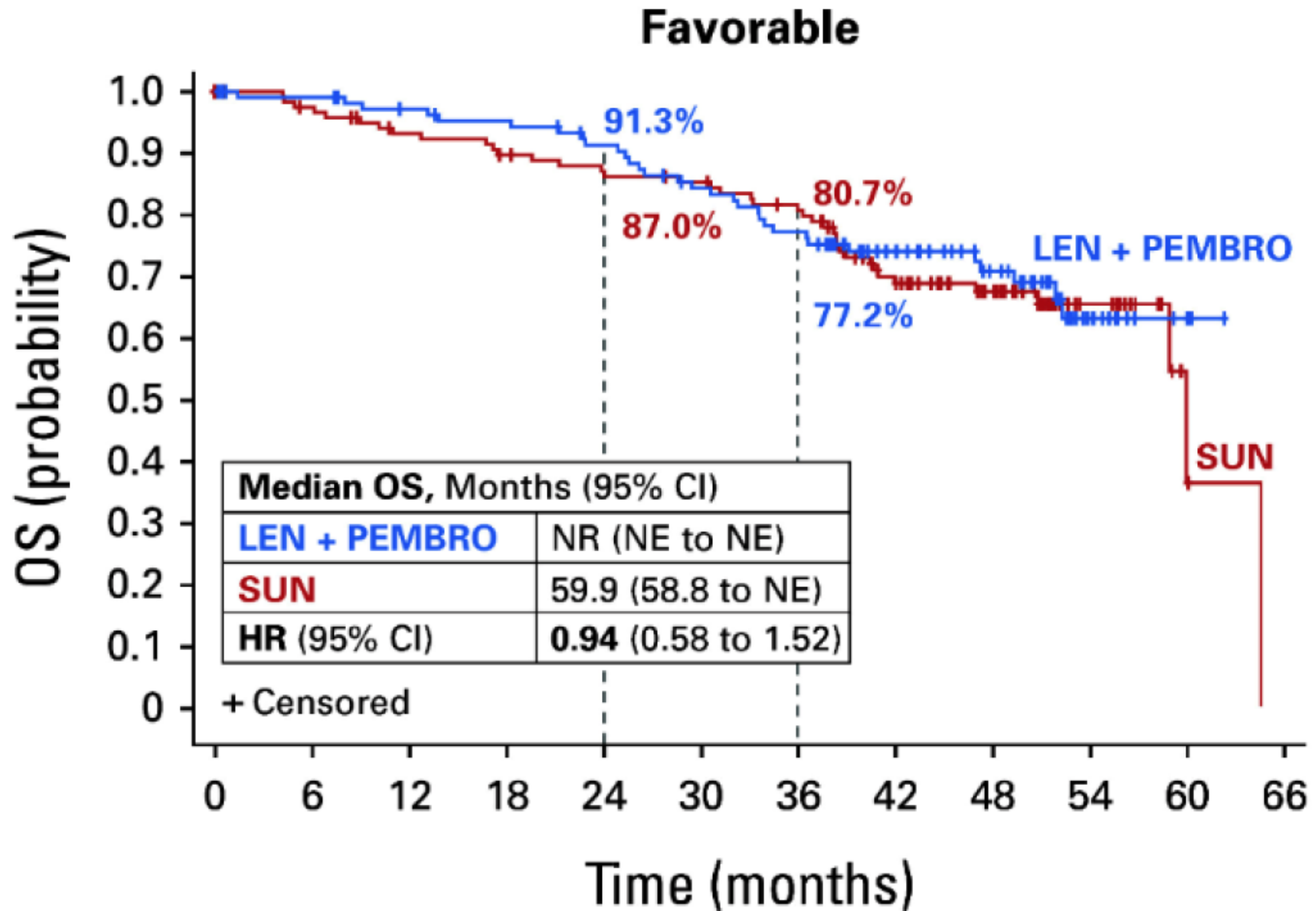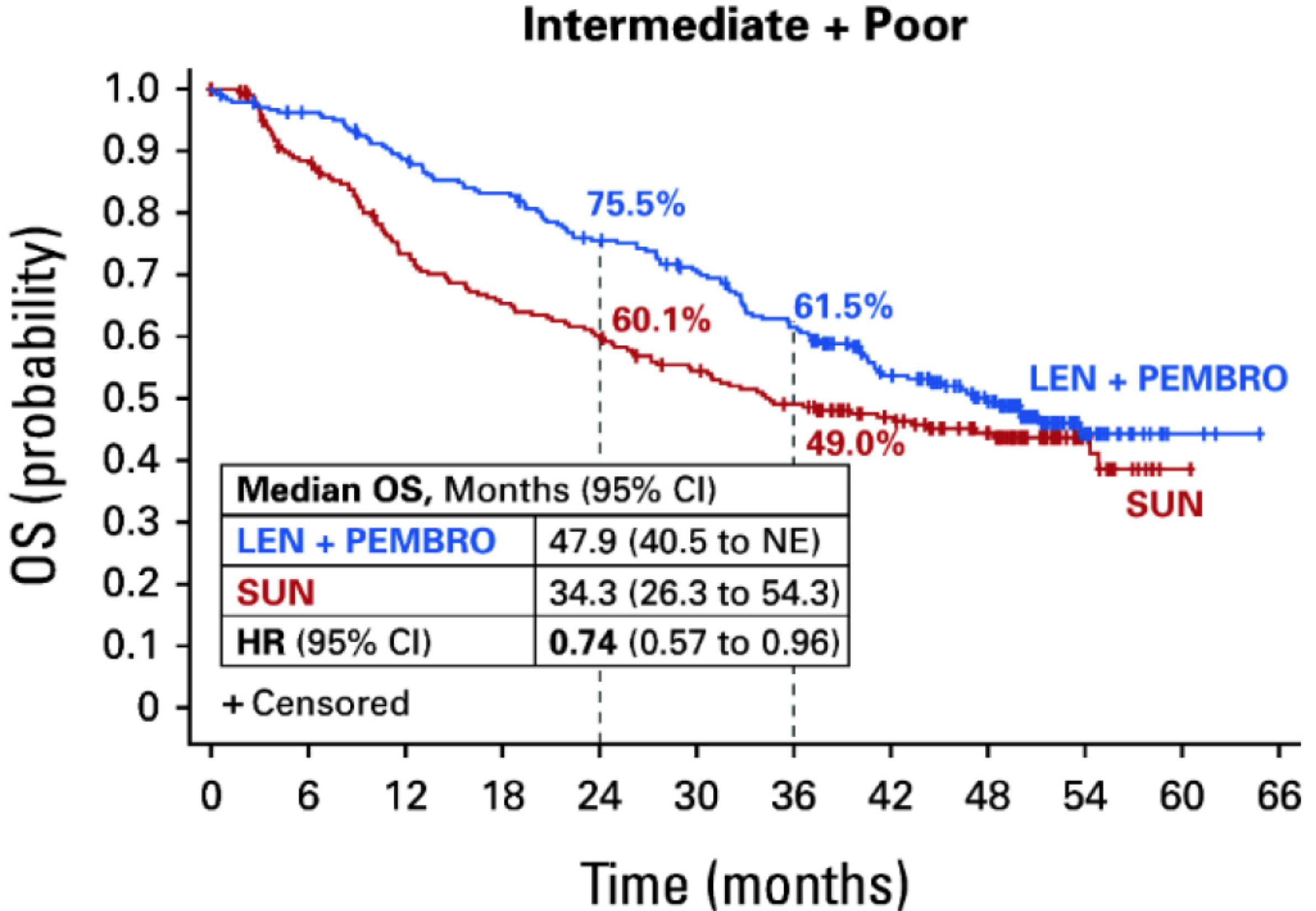
Motzer et al. *JCO.* 2024;42(11):1222-1228

Abstract 4504 (Choueiri TK, et al; CLEAR Trial)

Analysis (Baseline)	Assay
✗ **PD-L1 expression** n=441	**IHC:** 22C3 pharmDx
✗ **Gene alteration** n=380	**Whole-exome sequencing:** ImmunoID NeXT Platform
✗ **Gene expression** n=388	**RNA-seq:** ImmunoID NeXT Platform

	Association with PFS (*p*-value)	
PD-L1 IHC (CPS)	**Lenvatinib + pembrolizumab** n=219	**Sunitinib** n=222
	0.2301	0.0670

Statistical testing for L+P arm: one-sided test; for S arm: two-sided test. Analysis with KPS score group-adjusted PFS was performed using the Cox regression model.
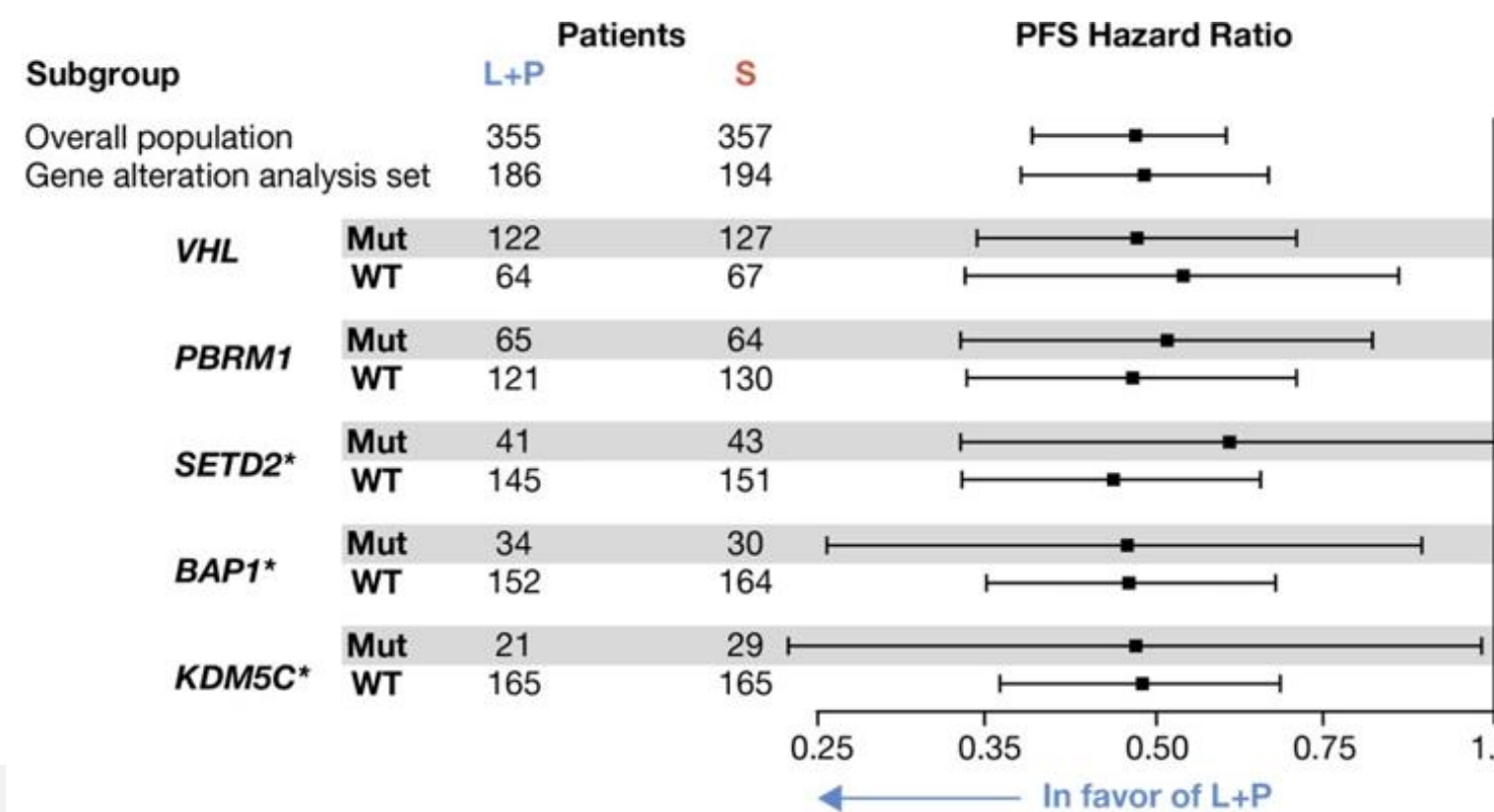
Signature type	Signature	L+P n=192	S n=196
		P-value*	
T-cell inflamed	GEP	0.36	0.95
Immuno-oncology	Monocytic myeloid-derived suppressor cells	0.86	0.84
	Granulocytic myeloid-derived suppressor cells	0.81	0.31
Angiogenesis	**Angiogenesis**	0.16	**< 0.1****
	Microvessel density	0.42	**< 0.1****
	Angio36	0.81	0.31
Pan-cancer	**Proliferation**	0.42	**< 0.1****
	MYC	0.19	**< 0.1****
	RAS	0.86	0.84
	WNT	0.81	0.31
	Stroma/Epithelial-mesenchymal transition/*TGFß*	0.81	0.43
	Glycolysis	0.68	0.19
	Hypoxia	0.42	0.31

Gene signature scores were not associated with PFS outcomes for the L+P arm

Choueiri TK, et al; ASCO 2024, Abstract 4504

Iowa Oncology Society

Take Home

- Long-term follow up for CLEAR, 9ER, KEYNOTE-426 and CM-214 all confirm that combination therapy is the optimal strategy for patients with metastatic clear cell RCC

- Biomarkers are being developed to help with first-line treatment selection. Currently the choice is dependent on clinical factors not molecular features