First-Line Ia/m UC Treatment under NHI: Clinical Value and Practical Challenges

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2025/07/26

Outline

- Current guidelines and their evidence
- Difference between EV-302, CM-901, JB-100
- Under NHI Situation
- Case sharing

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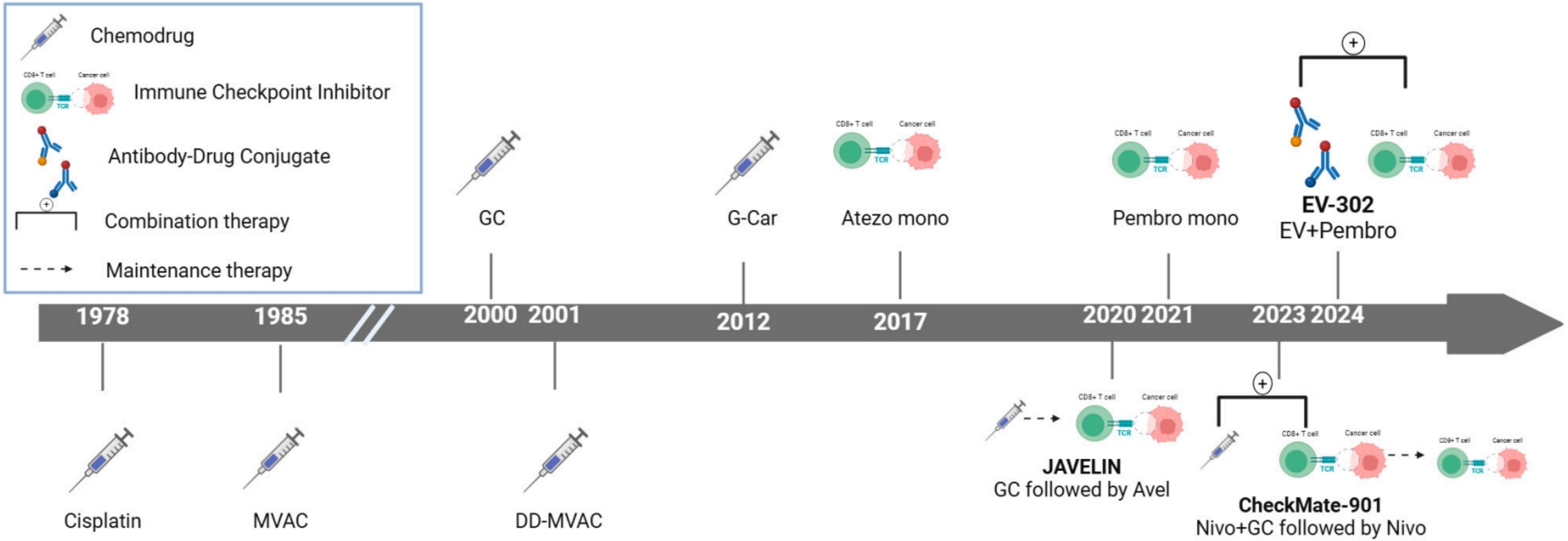
Evolution of Frontline Treatments for Metastatic Urothelial Carcinoma



In Past, chemotherapy was main treatment - Depending on the Cisplatin use

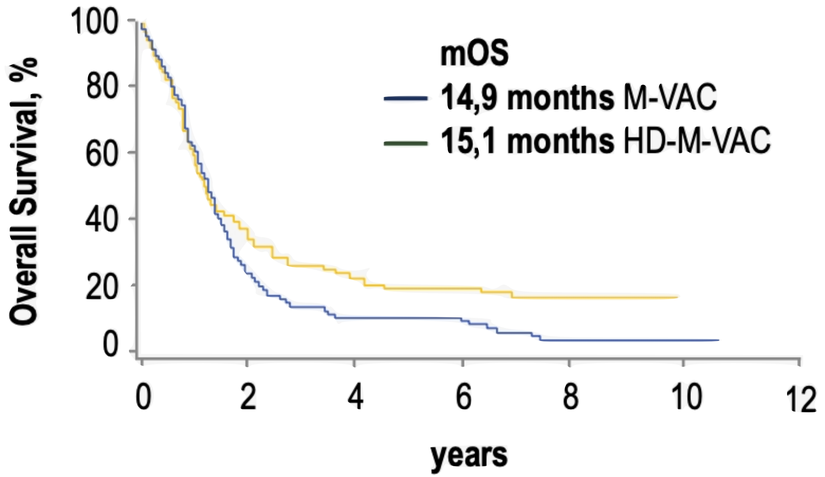
Cisplatin - Eligible

Dosedense M-VAC

ORR 72 %

CR 25 %

mOS 15,1 months



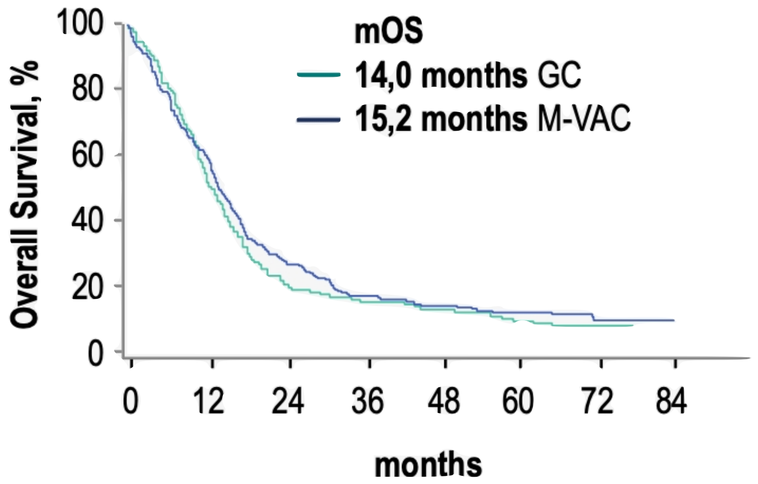
HR: 0,76 (CI: 0,58 – 0,99)
Log rank p = 0,042

Gemcitabin/Cisplatin

ORR 49 %

CR 12 %

mOS 14 Monate



HR: 1,09 (CI: 0,88 – 1,34),
Log rank p = 0,44; Wald´s *p* = 0,66

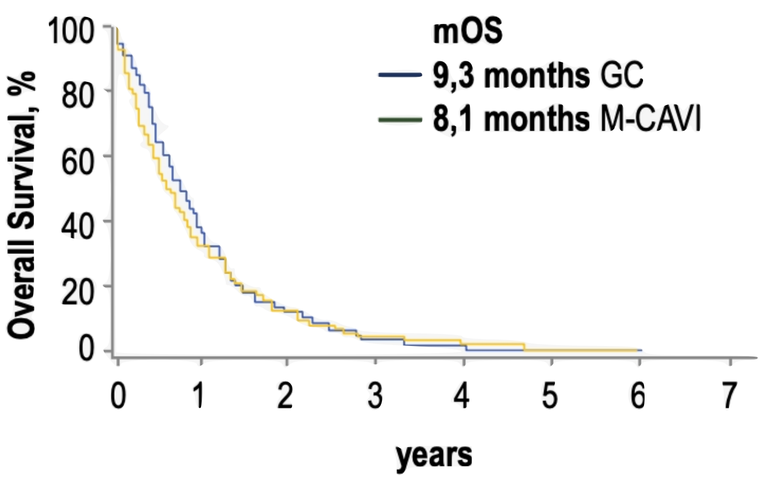
Cisplatin - Ineligible

Gemcitabin/ Carboplatin

ORR 36 %

CR 3 %

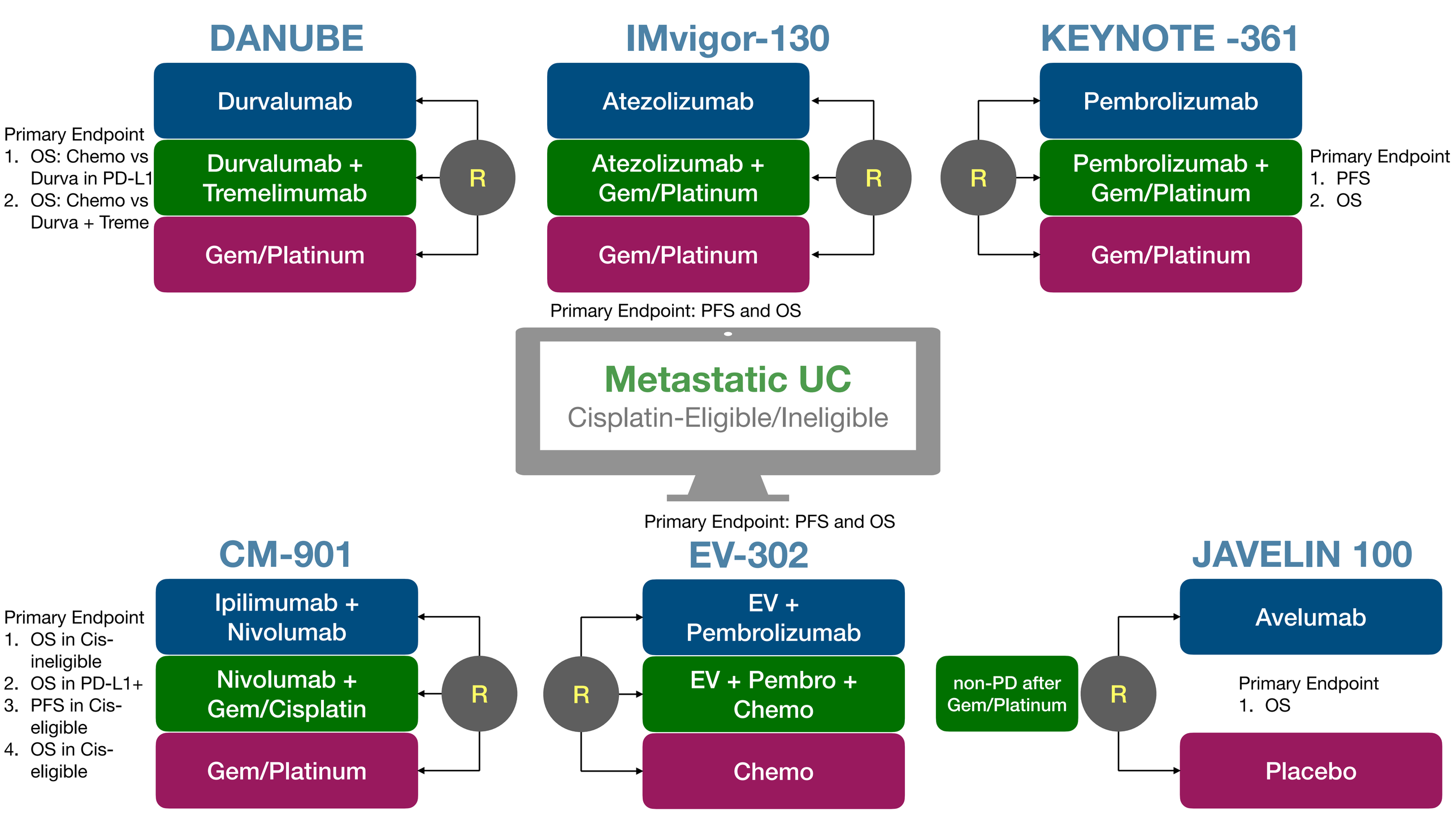
mOS 9,3 Monate

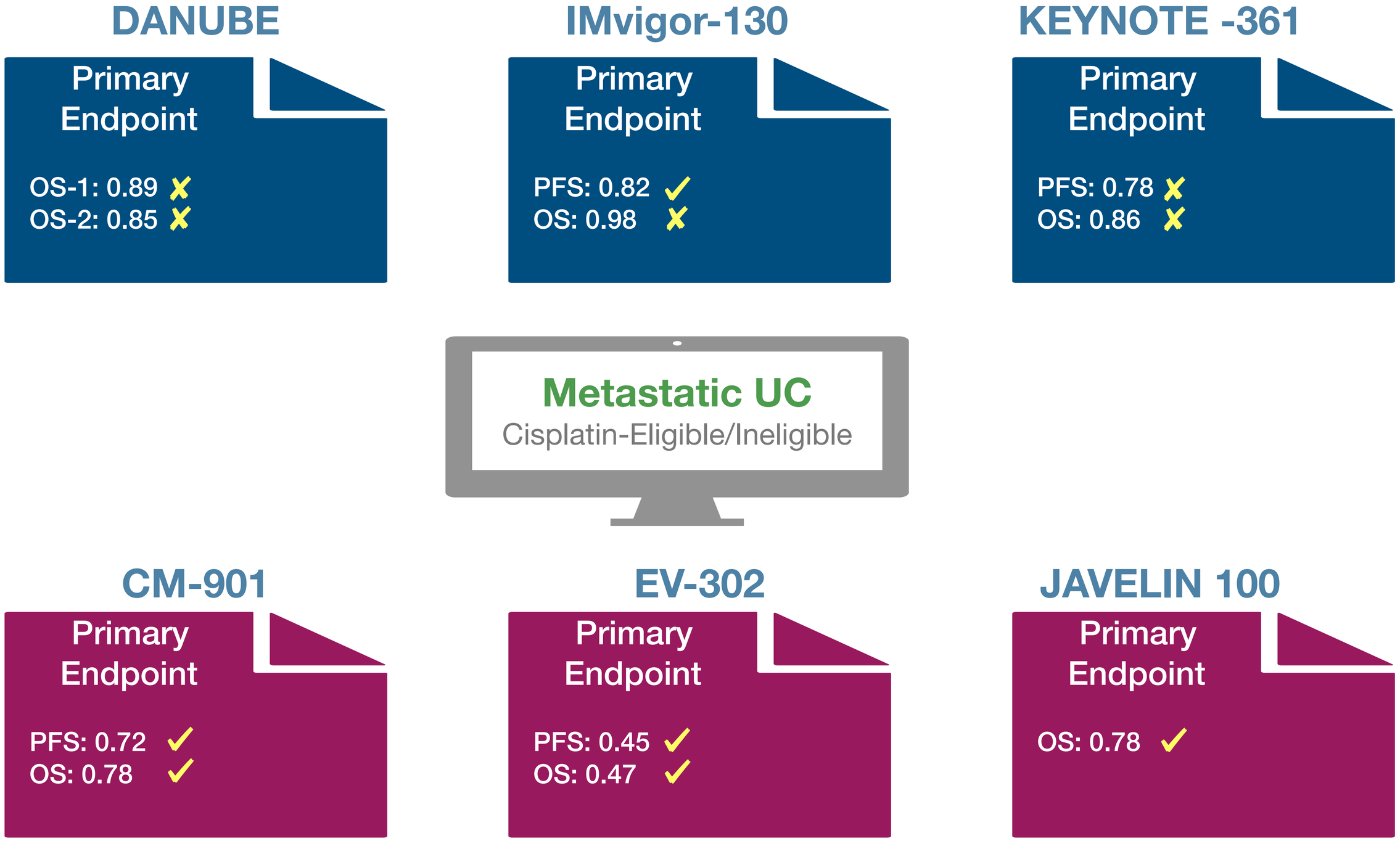


HR: 0,94
Log rank p = 0,64

CI = confidence intervall; CR = complete response; HR = hazard ratio; mOS = median overall survival; ORR = overall response rate

Plimack ER. ASCO 2020; Eur J Cancer 2006;42(1):50-54; J Clin Oncol 2005;23(21):4602-4608; J Clin Oncol 2012;30(2):191-199


DANUBE
Durvalumab
Durvalumab + Tremelimumab
Gem/Platinum
R
Primary Endpoint
1. OS: Chemo vs Durva in PD-L1
2. OS: Chemo vs Durva + Treme
IMvigor-130
Atezolizumab
Atezolizumab + Gem/Platinum
Gem/Platinum
R
Primary Endpoint: PFS and OS
KEYNOTE -361
Pembrolizumab
Pembrolizumab + Gem/Platinum
Gem/Platinum
R
Primary Endpoint
1. PFS
2. OS
Metastatic UC
Cisplatin-Eligible/Ineligible
Primary Endpoint: PFS and OS
CM-901
Ipilimumab + Nivolumab
Nivolumab + Gem/Cisplatin
Gem/Platinum
R
Primary Endpoint
1. OS in Cis-ineligible
2. OS in PD-L1+
3. PFS in Cis-eligible
4. OS in Cis-eligible
EV-302
EV + Pembrolizumab
EV + Pembro + Chemo
Chemo
R
JAVELIN 100
non-PD after Gem/Platinum
R
Avelumab
Placebo
Primary Endpoint
1. OS


DANUBE
Primary Endpoint
OS-1: 0.89 ✗
OS-2: 0.85 ✗
IMvigor-130
Primary Endpoint
PFS: 0.82 ✓
OS: 0.98 ✗
KEYNOTE -361
Primary Endpoint
PFS: 0.78 ✗
OS: 0.86 ✗
Metastatic UC
Cisplatin-Eligible/Ineligible
CM-901
Primary Endpoint
PFS: 0.72 ✓
OS: 0.78 ✓
EV-302
Primary Endpoint
PFS: 0.45 ✓
OS: 0.47 ✓
JAVELIN 100
Primary Endpoint
OS: 0.78 ✓

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2025
Bladder Cancer

NCCN Guidelines Index
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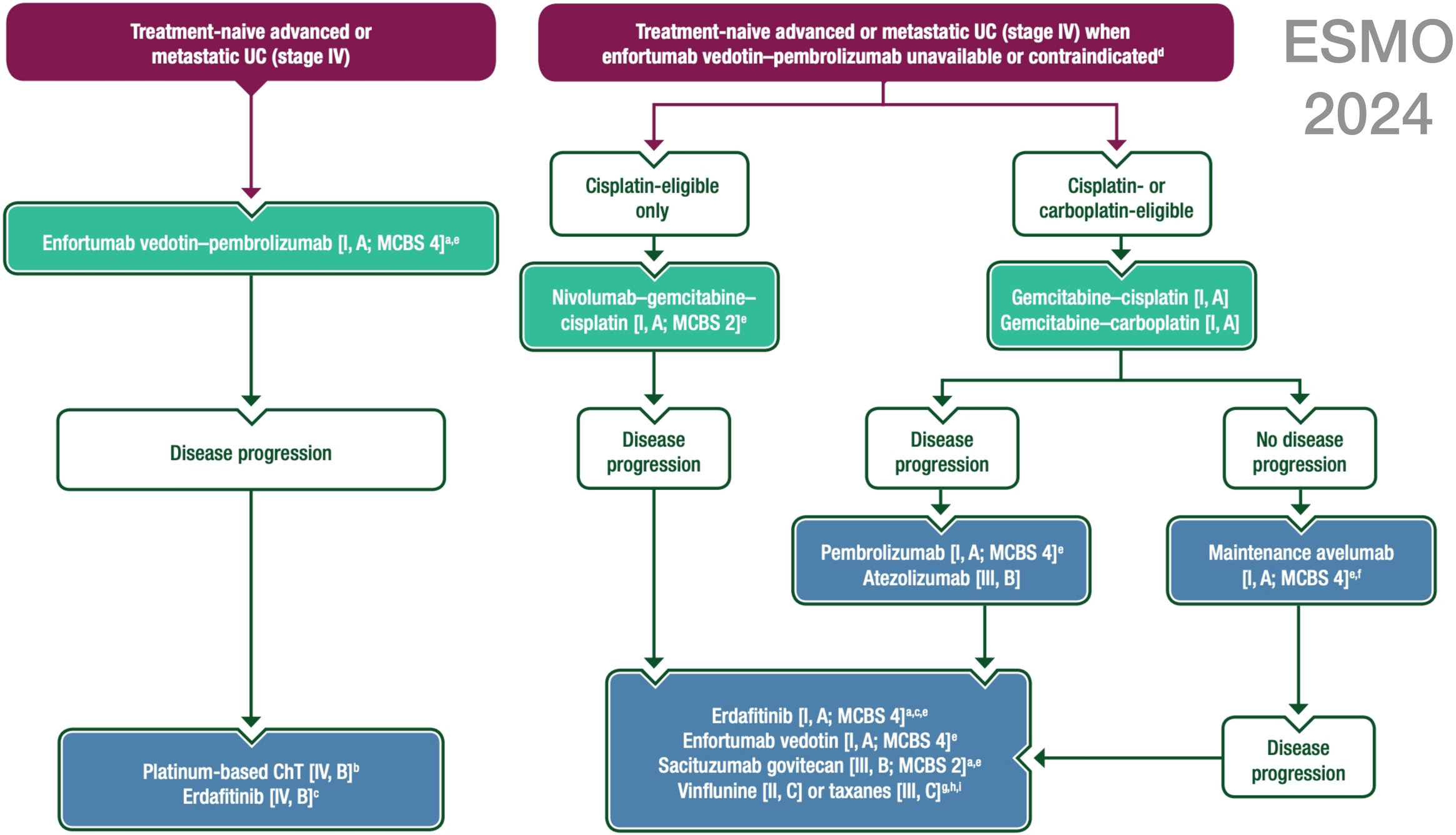
Discussion

PRINCIPLES OF SYSTEMIC THERAPY

First-Line Systemic Therapy for Locally Advanced or Metastatic Disease (Stage IV)		
Preferred regimen • Enfortumab vedotin-ejfv[15,16] and pembrolizumab (category 1)	**Other recommended regimens** • Gemcitabine and cisplatin[4] (category 1) followed by avelumab maintenance therapy (category 1)[a,17] • Gemcitabine, cisplatin, and nivolumab (category 1) followed by nivolumab maintenance therapy[18] (category 1) • DDMVAC with growth factor support[2,10] (category 1) followed by avelumab maintenance therapy (category 1)[a,17]	**Useful in certain circumstances (cisplatin-ineligible)** • Gemcitabine and carboplatin[19] followed by avelumab maintenance therapy (category 1)[a,17] • Pembrolizumab (for the treatment of patients with locally advanced or metastatic urothelial carcinoma who are not eligible for any platinum-containing chemotherapy)[20] • Atezolizumab[21] (only for patients whose tumors express PD-L1[b] or who are not eligible for any platinum-containing chemotherapy regardless of PD-L1 expression) (category 2B)

- Atezolizumab and hyaluronidase-tqjs subcutaneous injection may be substituted for IV atezolizumab. Atezolizumab and hyaluronidase-tqjs has different dosing and administration instructions compared to atezolizumab for IV infusion.
- Nivolumab and hyaluronidase-nvhy subcutaneous injection may be substituted for IV nivolumab. Nivolumab and hyaluronidase-nvhy has different dosing and administration instructions compared to IV nivolumab.



ESMO 2024

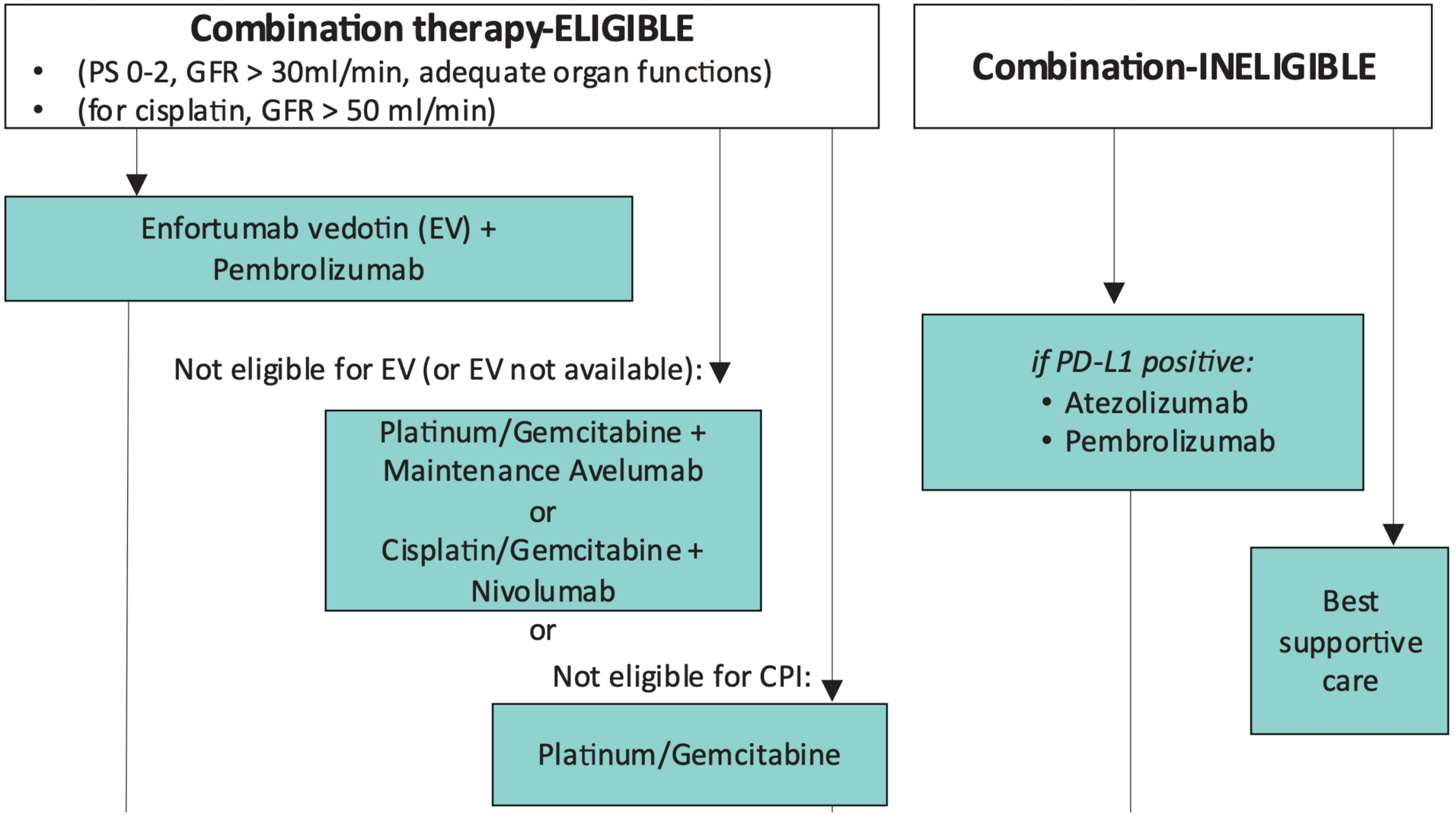
Ann Oncol . 2024 Jun;35(6):485-490

EUA Guideline
- Definitions of Platinum-eligibility for mUC

Platinum-eligible		Platinum-ineligible
Cisplatin-eligible	**Carboplatin-eligible**	
ECOG PS 0-1 *and*	ECOG PS 2 *or* GFR 30–60 mL/min	Any of the following:
GFR > 50–60 mL/min *and*	or not fulfilling other cisplatin-eligibility criteria	GFR < 30 mL/min
Audiometric hearing loss grade < 2 *and*		ECOG PS > 2
Peripheral neuropathy grade < 2 *and*		ECOG PS 2 *and* GFR < 60 mL/min
Cardiac insufficiency NYHA class < III		Comorbidites > Grade 2

ECOG = Eastern Cooperative Oncology Group; GFR = glomerular filtration rate; NYHA = New York Heart Association; PS = performance status.

EUA Guideline

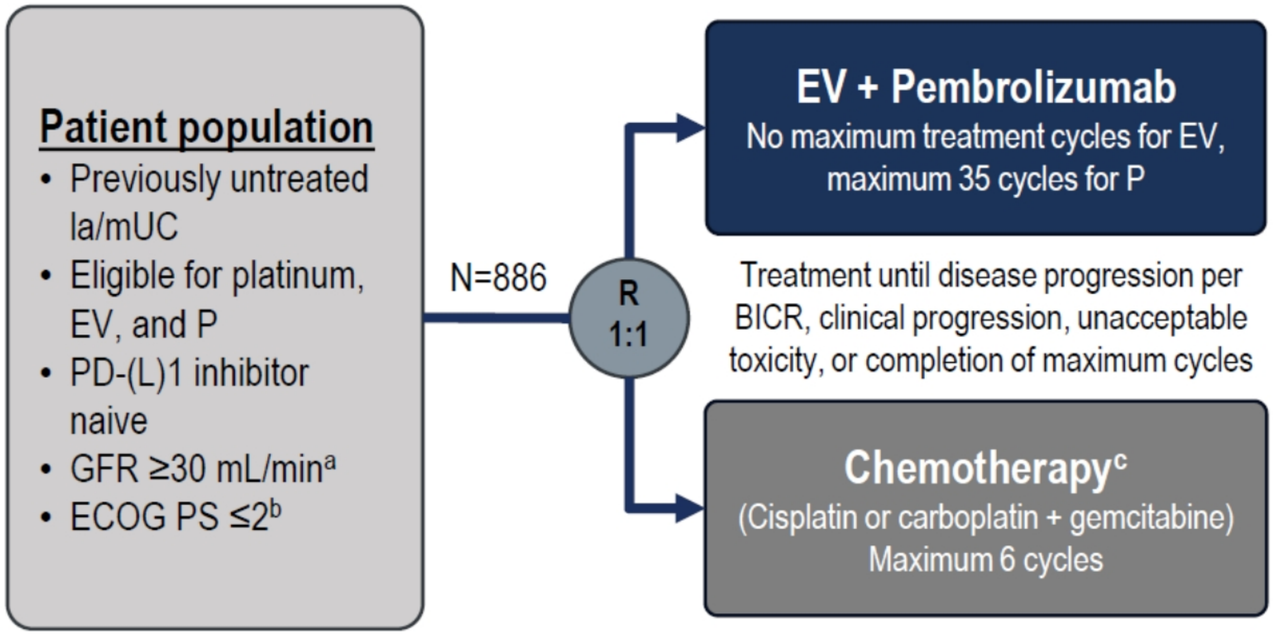


https://uroweb.org/guidelines/muscle-invasive-and-metastatic-bladder-cancer

Outline

- Current guidelines and their evidence
- **Difference between EV-302, CM-901, JB-100**
- Under NHI Situation
- Case sharing

EV-302: Ph3, Enfortumab Vedotin + Pembrolizumab vs Chemotherapy in la/mUC



Dual °1: endpoints: PFS by BICR; OS
°2: endpoints: ORR per RECIST v1.1 by BICR/IBA, safety

Exclusion Criteria of interest

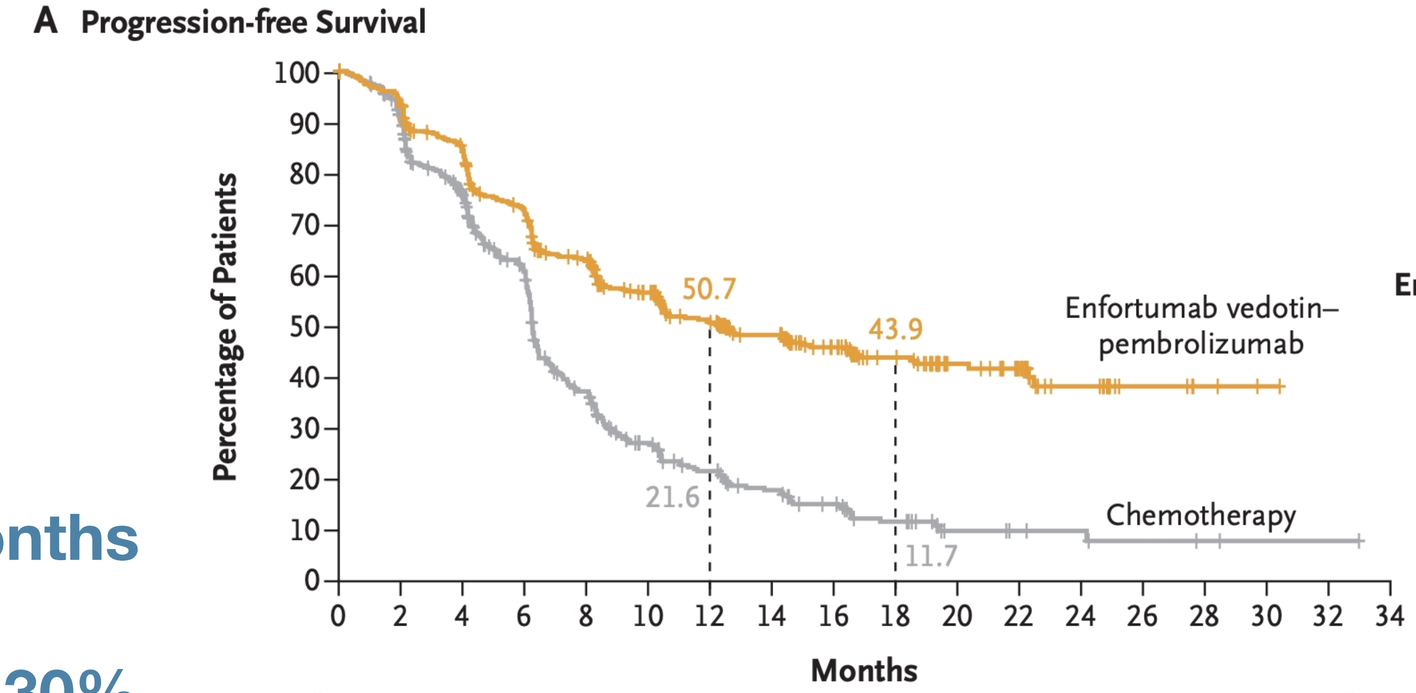
- ✓Currently receiving systemic antimicrobial treatment
- ✓High dose steroids
- ✓Uncontrolled diabetes
  - ✓HbA1c ≥8%
  - ✓HbA1c 7–8% + associated diabetes symptoms (polyuria or polydipsia)

Stratification factors:

Cisplatin eligibility
PD-L1 expression
Liver metastasis

	Age≥75	ECOG 0	ECOG 1	Mets	Visceral Mets	Upper Tract	Ccr<60	Cis-eligiable	CPS≥10
EVP	23.1	50.5	46.2	95.2	71.9	30.5	43.7	54.3	58.0
Chemo	24.3	48.4	48.6	94.6	71.6	23.4	42.1	54.5	57.9

PFS

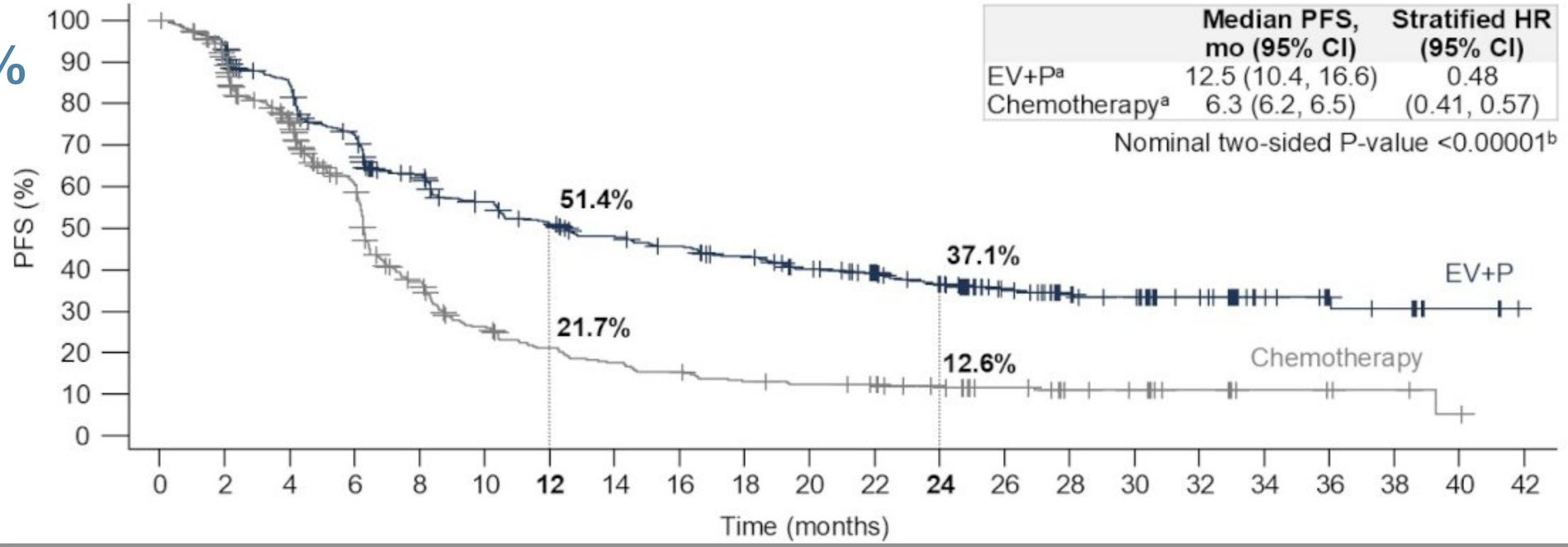


	No. of Events/ No. of Patients	Median Progression-free Survival (95% CI)
		mo
Enfortumab Vedotin–Pembrolizumab	223/442	12.5 (10.4–16.6)
Chemotherapy	307/444	6.3 (6.2–6.5)

Hazard ratio, 0.45 (95% CI, 0.38–0.54)
Two-sided P<0.001

ΔPFS = **6 months**

1-yr survival: **30%**
1.5-yr survival: **32%**
2-yr survival: **25%**

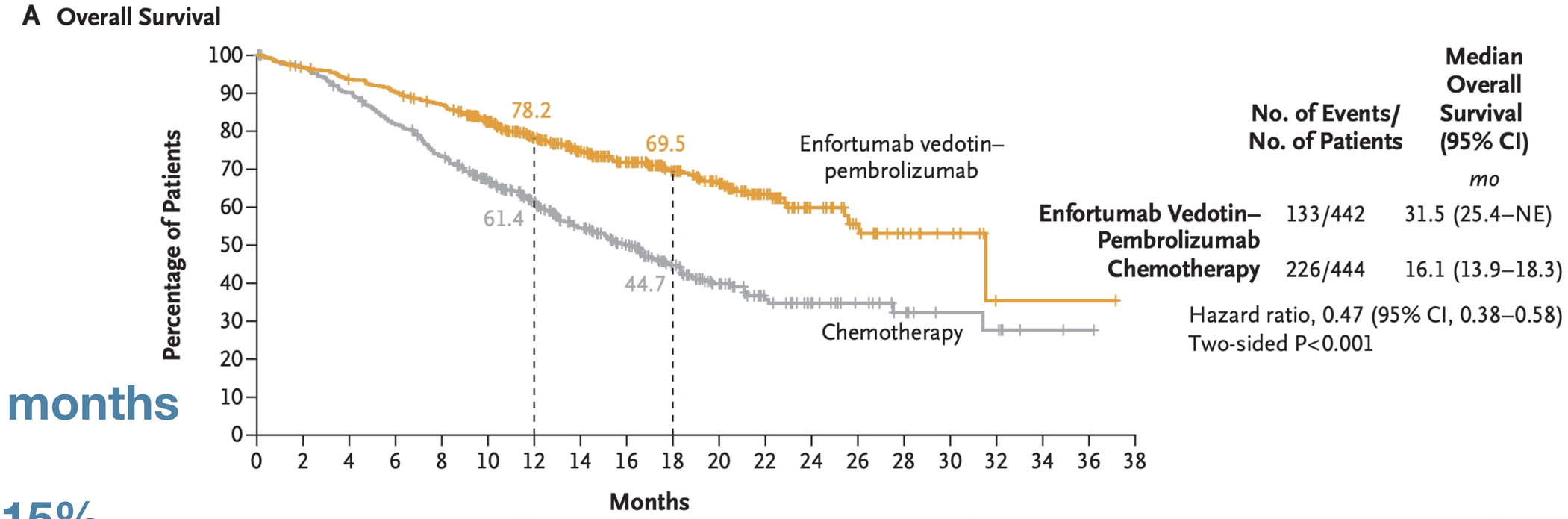


	Median PFS, mo (95% CI)	Stratified HR (95% CI)
EV+P[a]	12.5 (10.4, 16.6)	0.48
Chemotherapy[a]	6.3 (6.2, 6.5)	(0.41, 0.57)

Nominal two-sided P-value <0.00001[b]

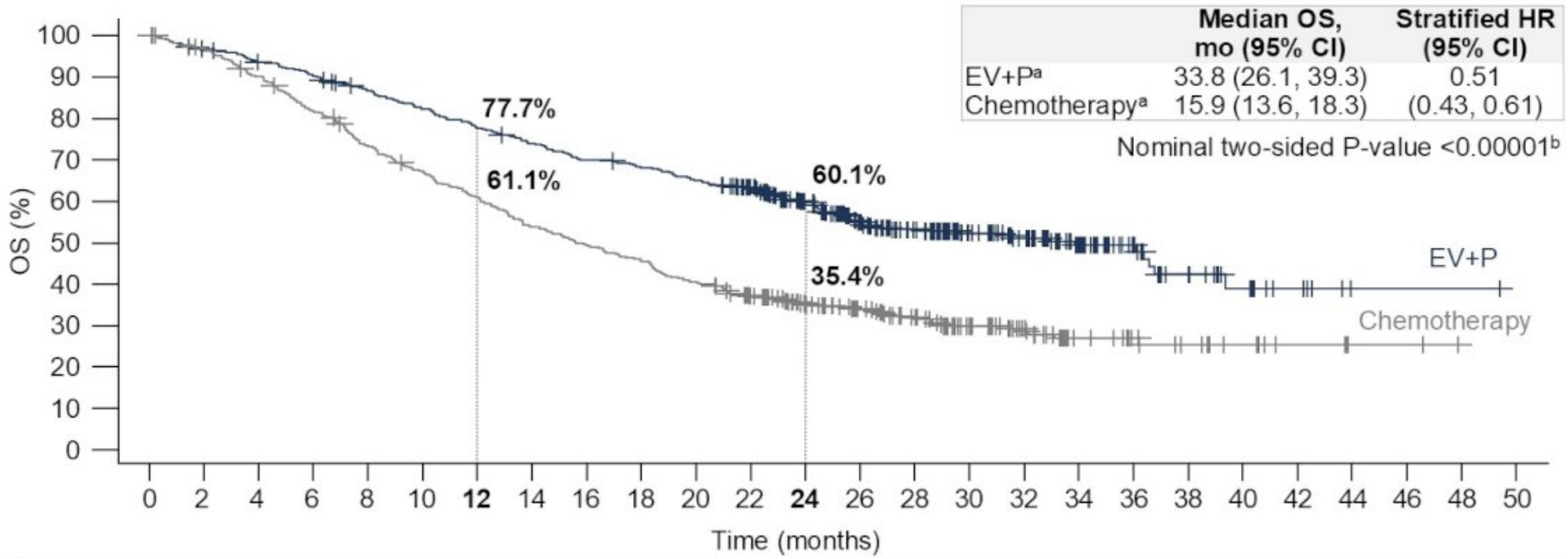
N Engl J Med 2024;390:875-888; ASCO GU 2025

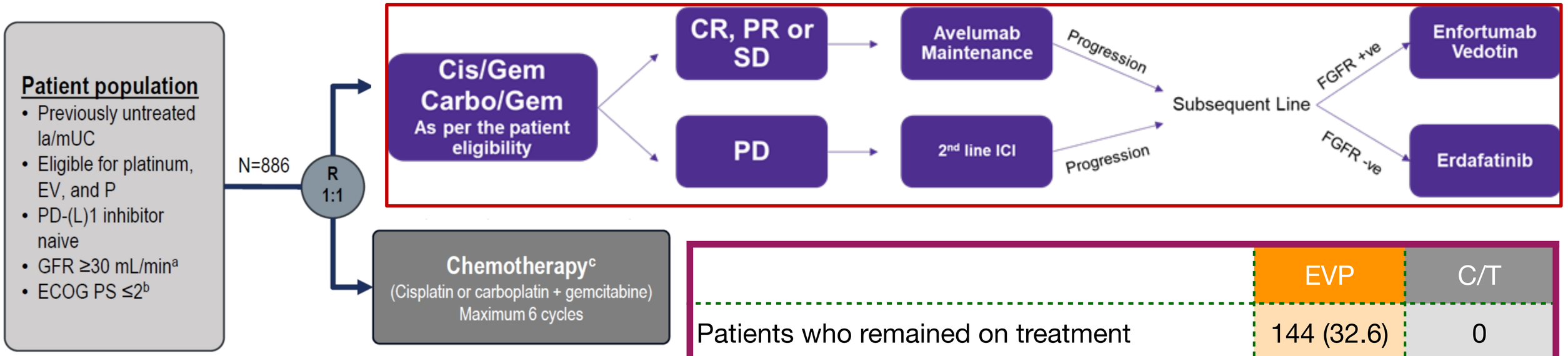
OS



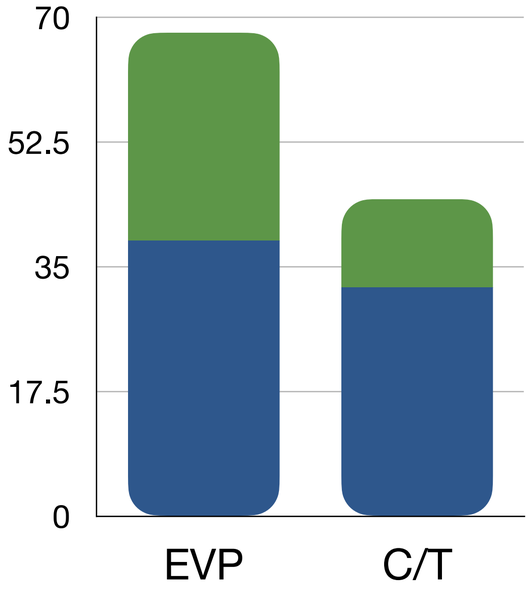
ΔOS = **15-18 months**

1-yr survival: **15%**
1.5-yr survival: **25%**
2-yr survival: **25%**





	EVP	C/T
CR	29.1	12.5
PR	38.7	32.0
SD	18.8	33.8
PD	8.7	13.6
ORR	67.7	44.4

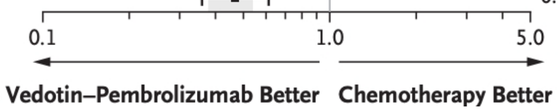


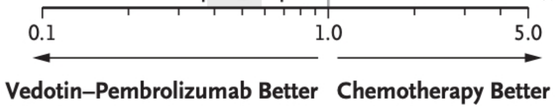
	EVP	C/T
Patients who remained on treatment	144 (32.6)	0
Patients who received subsequent anticancer therapies	140 (31.7)	313 (70.5)
First subsequent systemic therapy	128 (29.0)	294 (66.2)
Platinum-based therapy	110 (24.9)	17 (3.8)
PD-1/PD-L1 inhibitor-containing therapy	7 (1.6)	260 (58.6)
Maintenance therapy	0	143 (32.2)
Avelumab	0	135 (30.4)
Other therapy	7 (1.6)	117 (26.4)

PFS

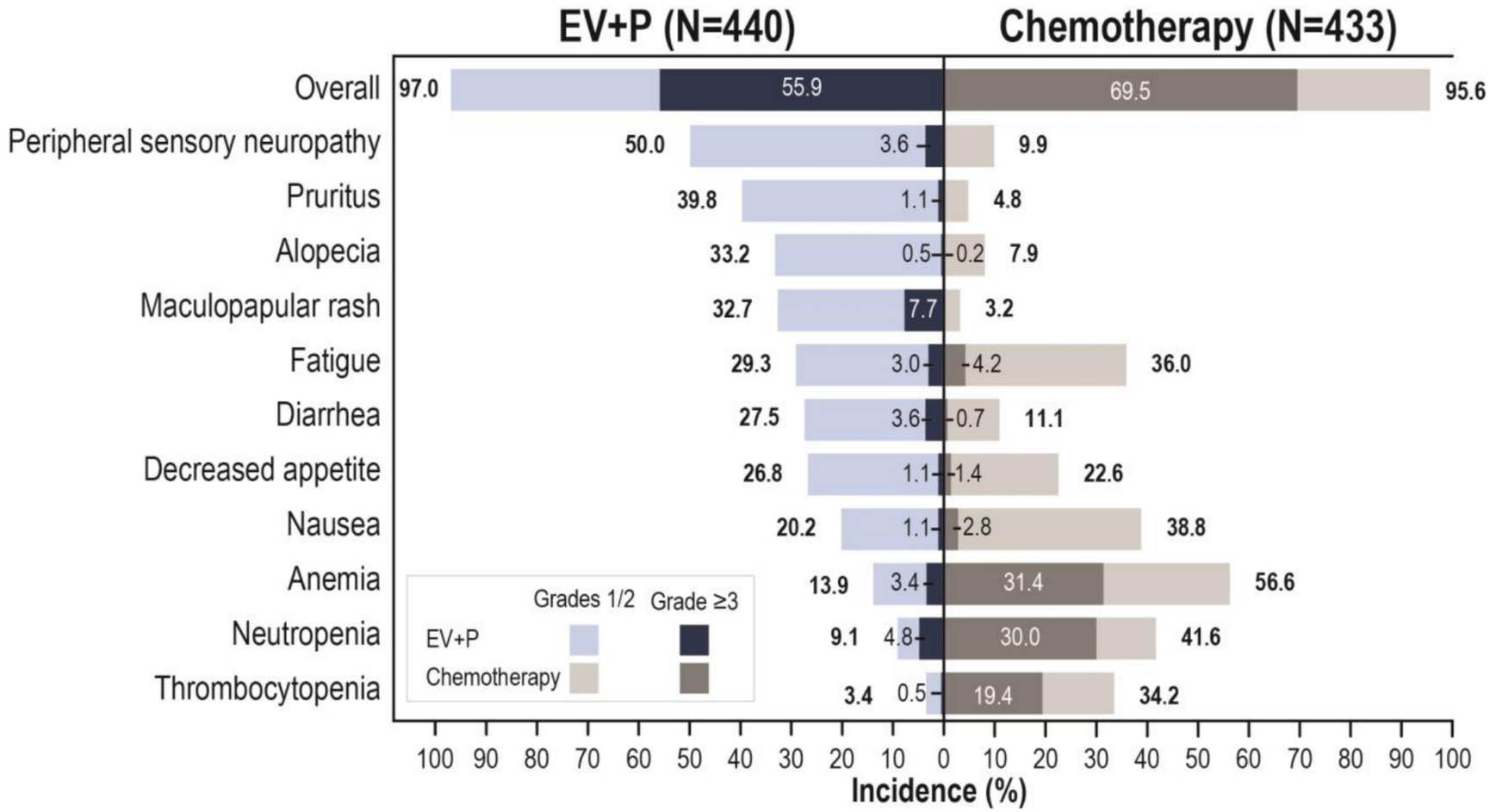
OS

Subgroup	Enfortumab Vedotin–Pembrolizumab	Chemotherapy	Hazard Ratio for Disease Progression or Death (95% CI)	Enfortumab Vedotin–Pembrolizumab	Chemotherapy	Hazard Ratio for Death (95% CI)
	mo (no. of events/no. of patients)			*mo (no. of events/no. of patients)*		
Overall	12.5 (223/442)	6.3 (307/444)	0.45 (0.38–0.54)	31.5 (133/442)	16.1 (226/444)	0.47 (0.38–0.58)
Age						
<65 yr	12.7 (75/144)	6.4 (88/135)	0.45 (0.32–0.62)	NE (39/144)	19.7 (58/135)	0.46 (0.30–0.71)
≥65 yr	12.0 (148/298)	6.2 (219/309)	0.45 (0.36–0.56)	31.5 (94/298)	14.6 (168/309)	0.48 (0.38–0.63)
Race						
White	10.4 (168/308)	6.2 (207/290)	0.48 (0.39–0.60)	26.1 (104/308)	15.3 (162/290)	0.47 (0.36–0.60)
Other	22.3 (55/134)	6.5 (100/154)	0.39 (0.27–0.55)	NE (29/134)	19.3 (64/154)	0.46 (0.29–0.72)
Geographic region						
North America	12.0 (58/103)	6.3 (55/85)	0.56 (0.38–0.82)	25.6 (40/103)	21.2 (42/85)	0.71 (0.44–1.12)
Europe	10.4 (94/172)	6.3 (144/197)	0.50 (0.38–0.66)	NE (56/172)	13.9 (110/197)	0.40 (0.28–0.56)
Rest of the world	NE (71/167)	6.2 (108/162)	0.35 (0.26–0.48)	NE (37/167)	16.4 (74/162)	0.41 (0.27–0.61)
Sex						
Female	10.4 (55/98)	6.1 (74/108)	0.49 (0.34–0.71)	25.4 (32/98)	14.6 (54/108)	0.51 (0.32–0.80)
Male	14.6 (168/344)	6.3 (233/336)	0.44 (0.36–0.54)	31.5 (101/344)	16.6 (172/336)	0.47 (0.36–0.60)
ECOG performance-status score						
0	22.3 (93/223)	6.7 (146/215)	0.36 (0.28–0.48)	NE (44/223)	18.4 (94/215)	0.36 (0.25–0.53)
1 or 2	9.3 (130/219)	6.1 (161/227)	0.53 (0.42–0.68)	25.4 (89/219)	13.1 (131/227)	0.54 (0.41–0.72)
Primary site of origin of disease						
Upper tract	12.7 (69/135)	6.2 (70/104)	0.50 (0.35–0.71)	NE (38/135)	18.4 (45/104)	0.53 (0.34–0.83)
Lower tract	12.5 (152/305)	6.3 (236/339)	0.44 (0.35–0.54)	31.5 (94/305)	15.6 (180/339)	0.46 (0.36–0.59)
Liver metastases						
Present	8.2 (66/100)	6.0 (78/99)	0.53 (0.38–0.76)	19.1 (43/100)	10.1 (67/99)	0.47 (0.32–0.71)
Absent	16.4 (157/342)	6.4 (229/345)	0.43 (0.35–0.52)	NE (90/342)	17.9 (159/345)	0.47 (0.36–0.61)
PD-L1 expression						
Low (CPS <10)	10.5 (105/184)	6.3 (127/185)	0.50 (0.38–0.65)	NE (53/184)	15.5 (99/185)	0.44 (0.31–0.61)
High (CPS ≥10)	18.5 (116/254)	6.2 (176/254)	0.42 (0.33–0.53)	31.5 (79/254)	16.6 (125/254)	0.49 (0.37–0.66)
Cisplatin eligibility status						
Eligible	14.6 (117/244)	6.5 (149/234)	0.48 (0.38–0.62)	31.5 (69/244)	18.4 (106/234)	0.53 (0.39–0.72)
Ineligible	10.6 (106/198)	6.1 (158/210)	0.43 (0.33–0.55)	NE (64/198)	12.7 (120/210)	0.43 (0.31–0.59)
Site of metastasis						
Visceral site	10.4 (176/318)	6.2 (238/318)	0.45 (0.37–0.55)	25.6 (108/318)	13.6 (182/318)	0.47 (0.37–0.60)
Lymph node only	NE (38/103)	8.3 (55/104)	0.40 (0.26–0.62)	NE (22/103)	27.5 (39/104)	0.46 (0.27–0.78)
Renal function						
Normal	18.7 (38/84)	6.7 (61/95)	0.46 (0.30–0.71)	26.1 (24/84)	18.4 (44/95)	0.51 (0.30–0.86)
Mild impairment	12.7 (79/165)	6.3 (114/162)	0.46 (0.34–0.62)	NE (42/165)	16.4 (78/162)	0.44 (0.30–0.65)
Moderate or severe impairment	10.5 (106/193)	6.2 (132/187)	0.47 (0.36–0.61)	31.5 (67/193)	13.3 (104/187)	0.50 (0.37–0.69)





Treatment-Related Adverse Events - Gr≥3 events were 56% in EVP and 70% in C/T



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

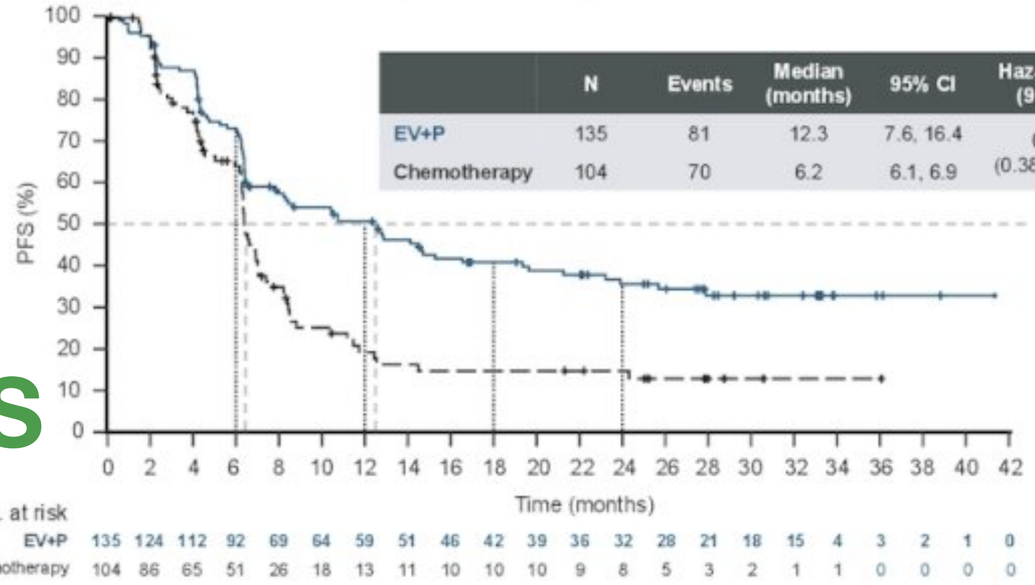
Chemotherapy: 4 (0.9%)
- Febrile neutropenia
- Myocardial infarction
- Neutropenic sepsis
- Sepsis

Median number of cycles (range): 12.0 (1,46) for EV+P; 6.0 (1,6) for chemotherapy

Powles et al. ESMO 2023, Data cutoff: 08 Aug 2023

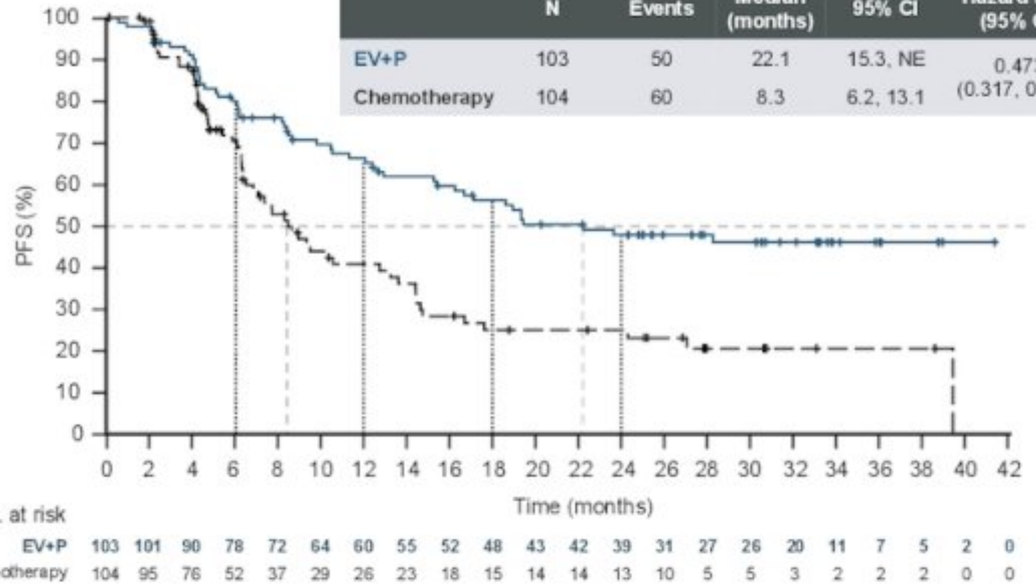
PFS

(A) Primary Disease Site of Origin in the Upper Tract



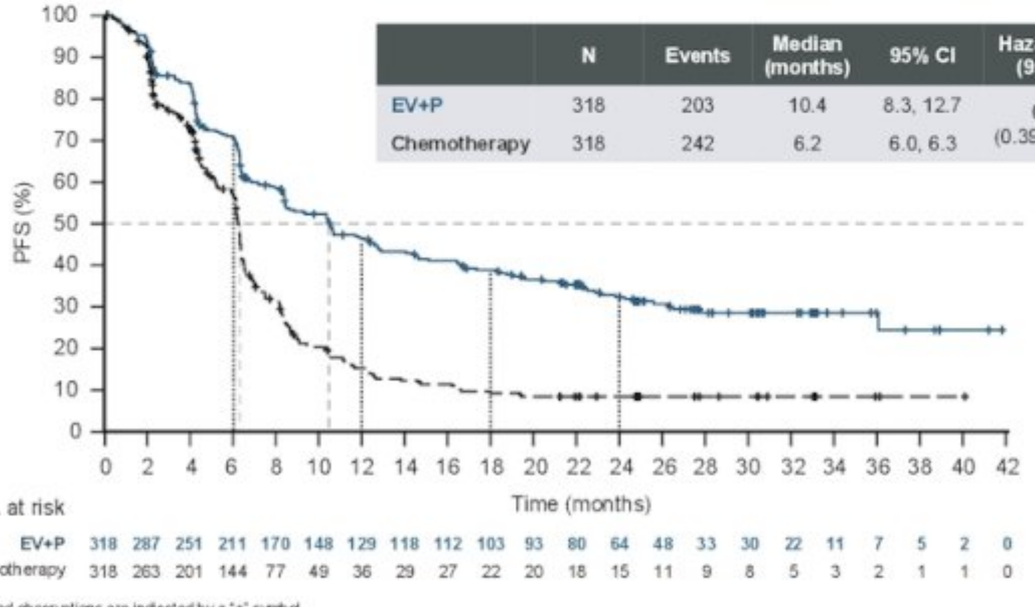
	N	Events	Median (months)	95% CI	Hazard ratio (95% CI)
EV+P	135	81	12.3	7.6, 16.4	0.542 (0.384, 0.763)
Chemotherapy	104	70	6.2	6.1, 6.9	

(B) LN-Only Metastases



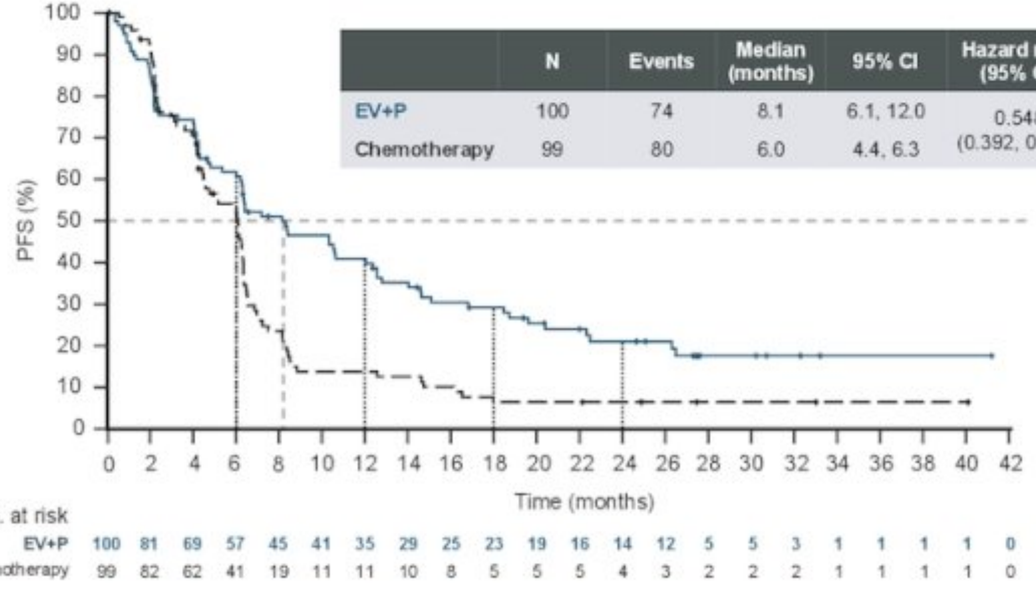
	N	Events	Median (months)	95% CI	Hazard ratio (95% CI)
EV+P	103	50	22.1	15.3, NE	0.473 (0.317, 0.704)
Chemotherapy	104	60	8.3	6.2, 13.1	

(C) Presence of Visceral Metastases



	N	Events	Median (months)	95% CI	Hazard ratio (95% CI)
EV+P	318	203	10.4	8.3, 12.7	0.477 (0.393, 0.579)
Chemotherapy	318	242	6.2	6.0, 6.3	

(D) Presence of Liver Metastases

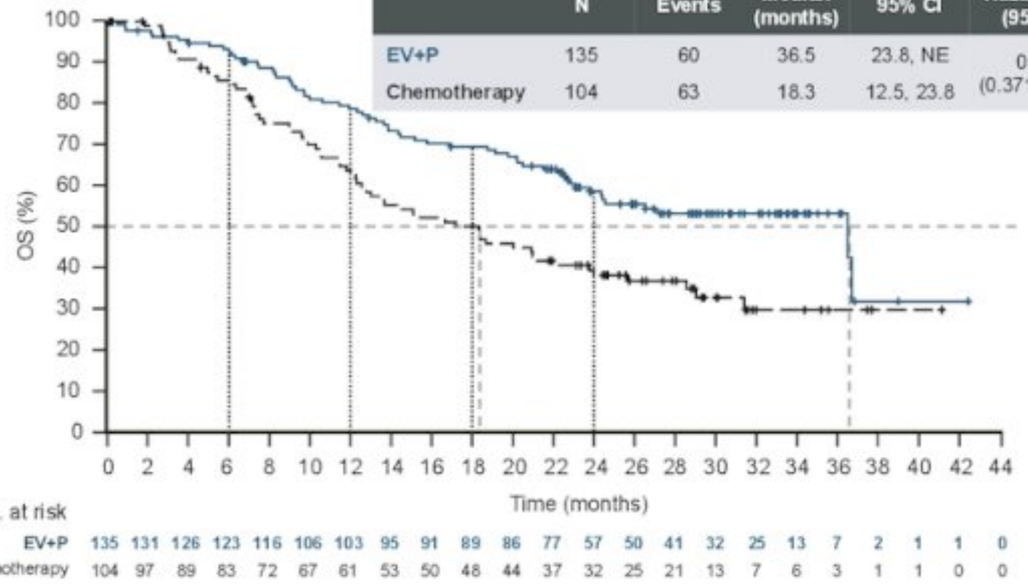


	N	Events	Median (months)	95% CI	Hazard ratio (95% CI)
EV+P	100	74	8.1	6.1, 12.0	0.548 (0.392, 0.766)
Chemotherapy	99	80	6.0	4.4, 6.3	

OS

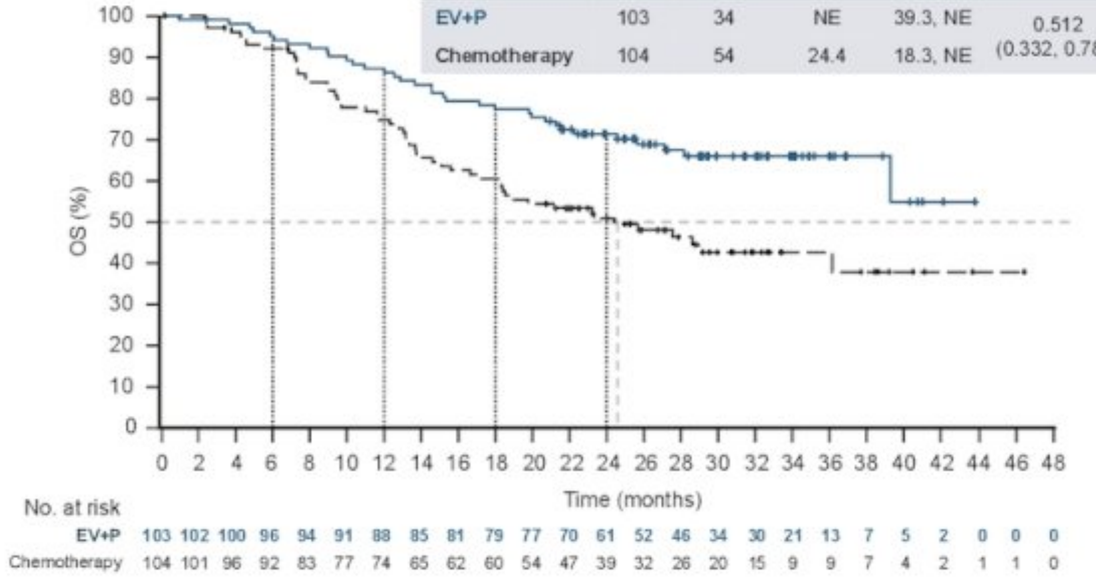
(A) Primary Disease Site of Origin in the Upper Tract

	N	Events	Median (months)	95% CI	Hazard ratio (95% CI)
EV+P	135	60	36.5	23.8, NE	0.538 (0.371, 0.781)
Chemotherapy	104	63	18.3	12.5, 23.8	



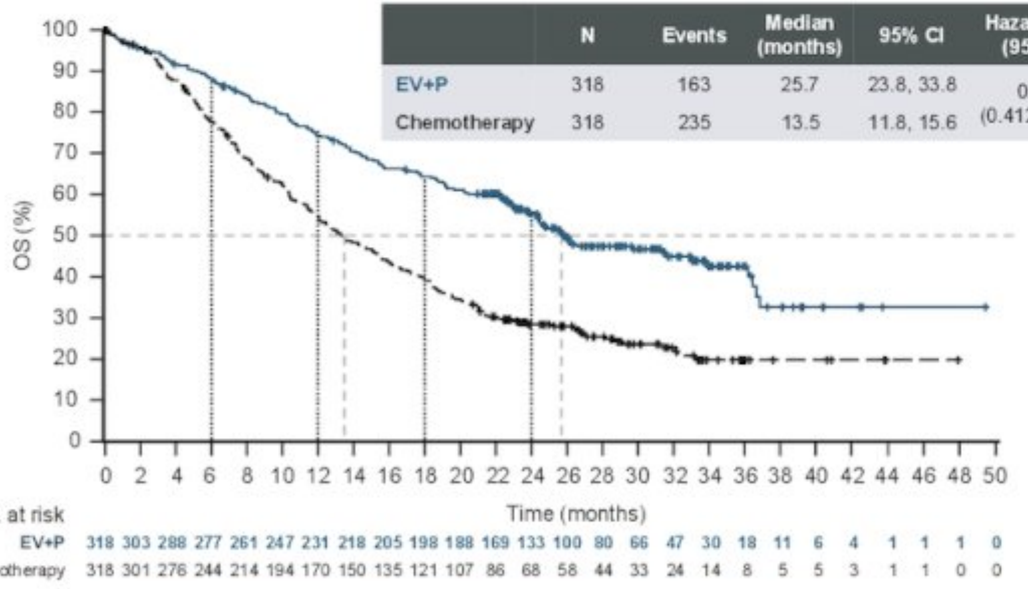
(B) LN-Only Metastases

	N	Events	Median (months)	95% CI	Hazard ratio (95% CI)
EV+P	103	34	NE	39.3, NE	0.512 (0.332, 0.789)
Chemotherapy	104	54	24.4	18.3, NE	



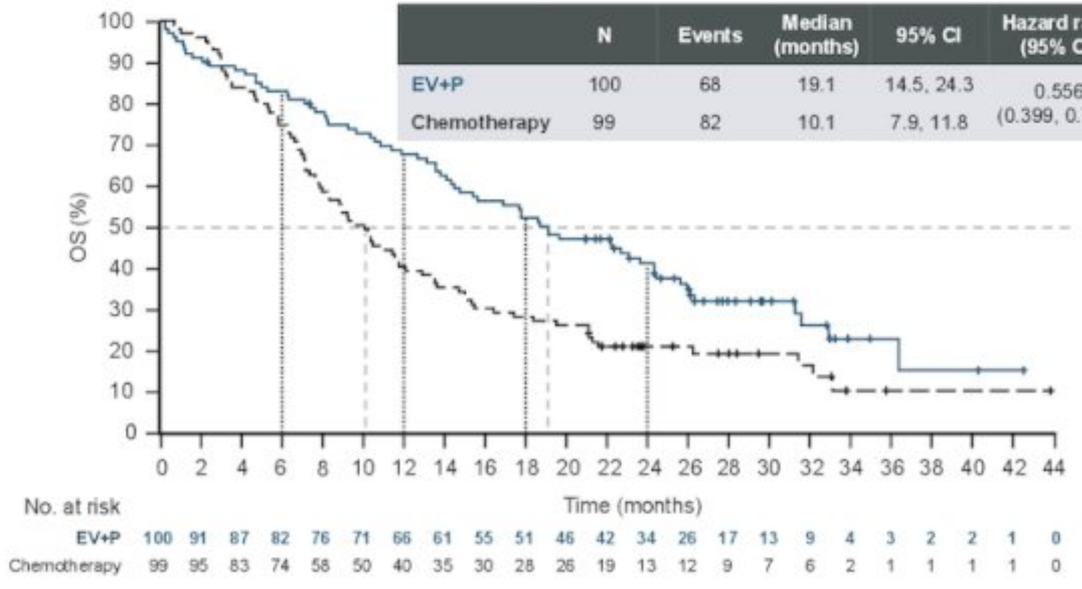
(C) Presence of Visceral Metastases

	N	Events	Median (months)	95% CI	Hazard ratio (95% CI)
EV+P	318	163	25.7	23.8, 33.8	0.505 (0.412, 0.619)
Chemotherapy	318	235	13.5	11.8, 15.6	

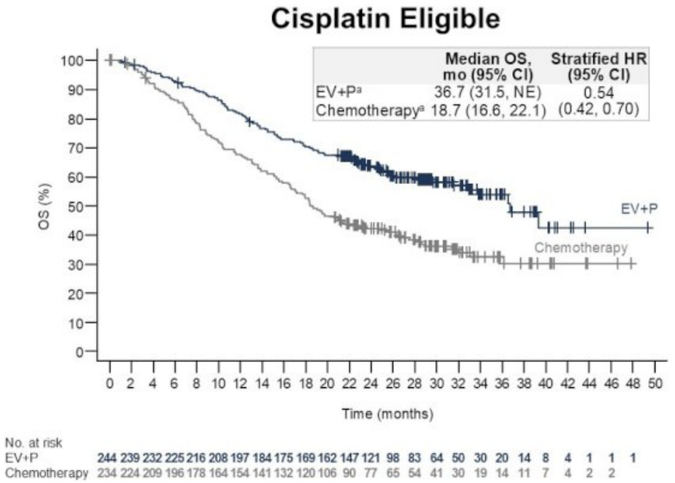


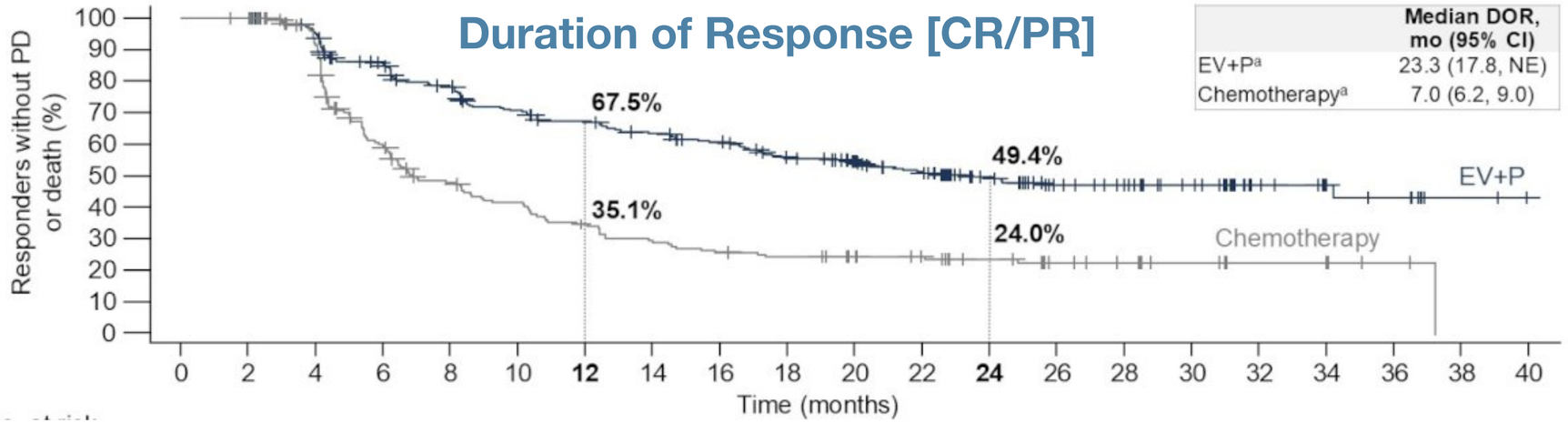
(D) Presence of Liver Metastases

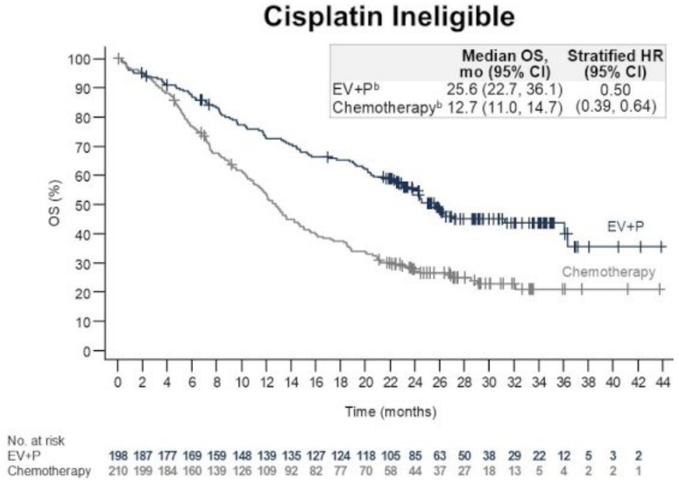
	N	Events	Median (months)	95% CI	Hazard ratio (95% CI)
EV+P	100	68	19.1	14.5, 24.3	0.556 (0.399, 0.776)
Chemotherapy	99	82	10.1	7.9, 11.8	

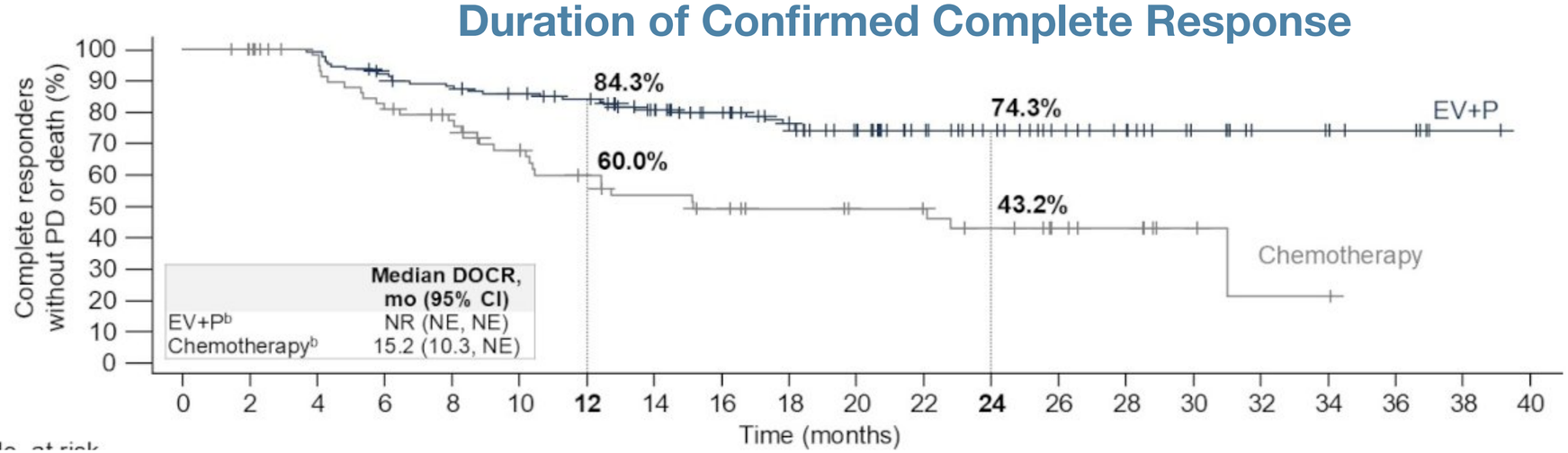


Survival Analysis:
Update with 1 year of additional follow-up







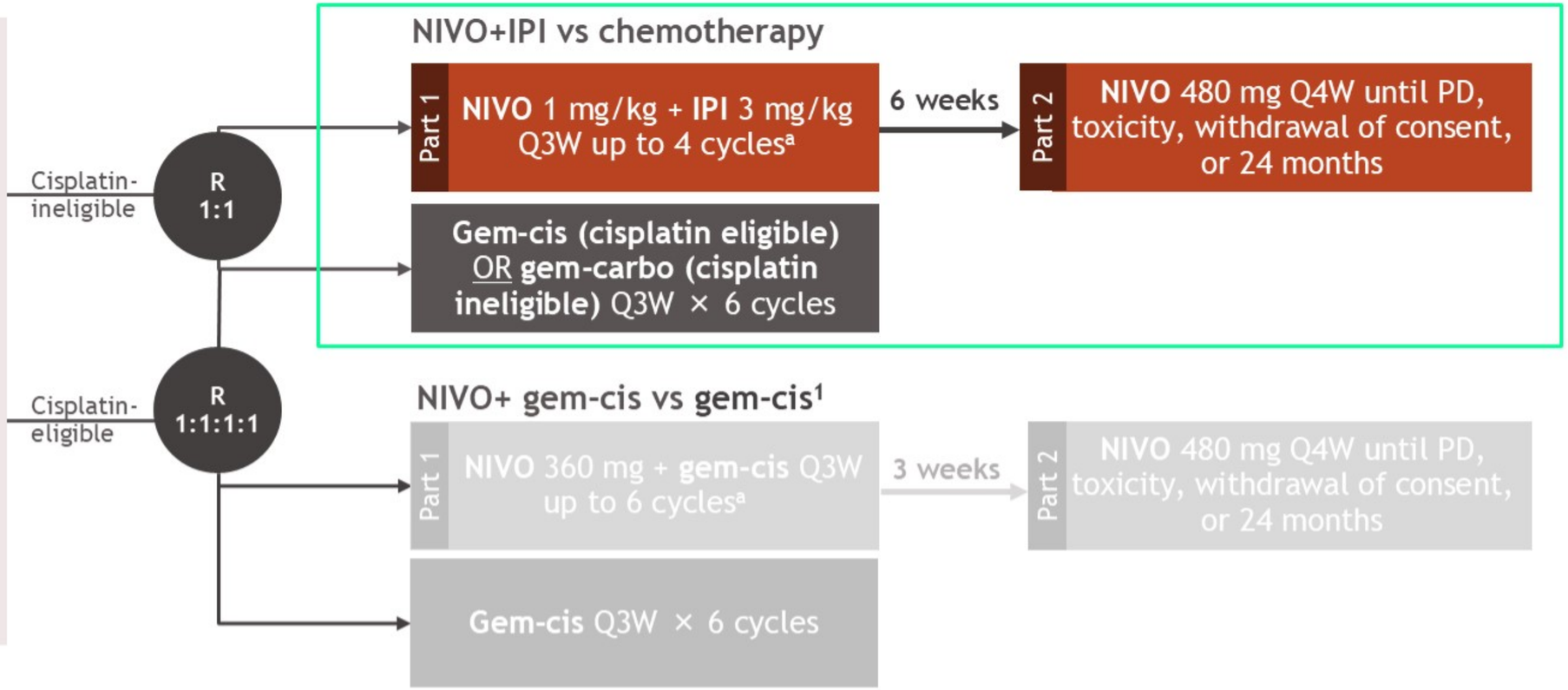


CheckMate 901: Ph3, Nivolumab + Gem/Cis vs Gem/Cis in la/mUC

Overall study population
- Patients with untreated, unresectable, or metastatic UC enrolled

Treatment assignment
- Cisplatin-ineligible randomized 1:1 to NIVO+IPI and gem-platinum arms *only*
- Cisplatin-eligible randomized 1:1:1:1 across all 4 arms

Stratification factors
- Tumor PD-L1 expression (≥ 1% vs <1%)
- Cisplatin eligibility
- Liver metastasis



Database locks:
- OS for cisplatin-ineligible and all randomized patients: July 9, 2021 (interim analysis); September 30, 2024 (final analysis)
- OS for PD-L1 ≥ 1% patients: October 22, 2020 (interim analysis); April 20, 2022 (final analysis)

Key endpoints for NIVO+IPI vs chemotherapy

Primary endpoints: OS in cisplatin-ineligible patients and in patients with tumor PD-L1 ≥ 1%

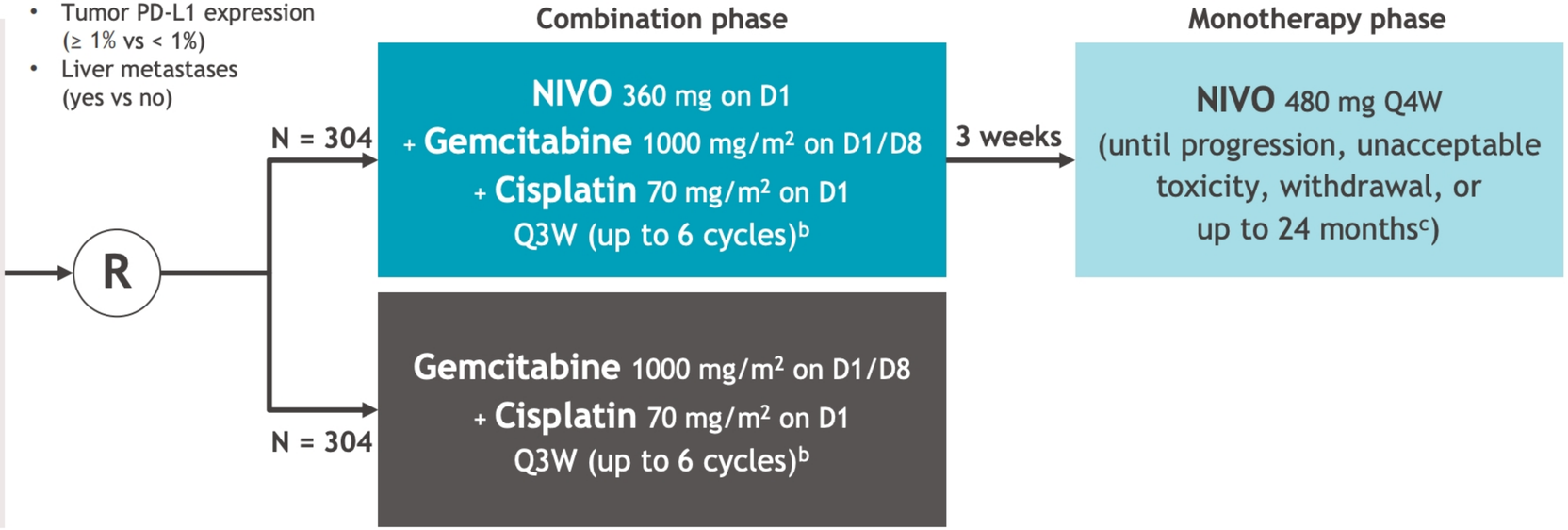
Key secondary endpoints: OS in all randomized patients, PFS by BICR in cisplatin-ineligible patients

CheckMate 901: Ph3, Nivolumab + Gem/Cis vs Gem/Cis in la/mUC with Cisplatin-eligible

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)

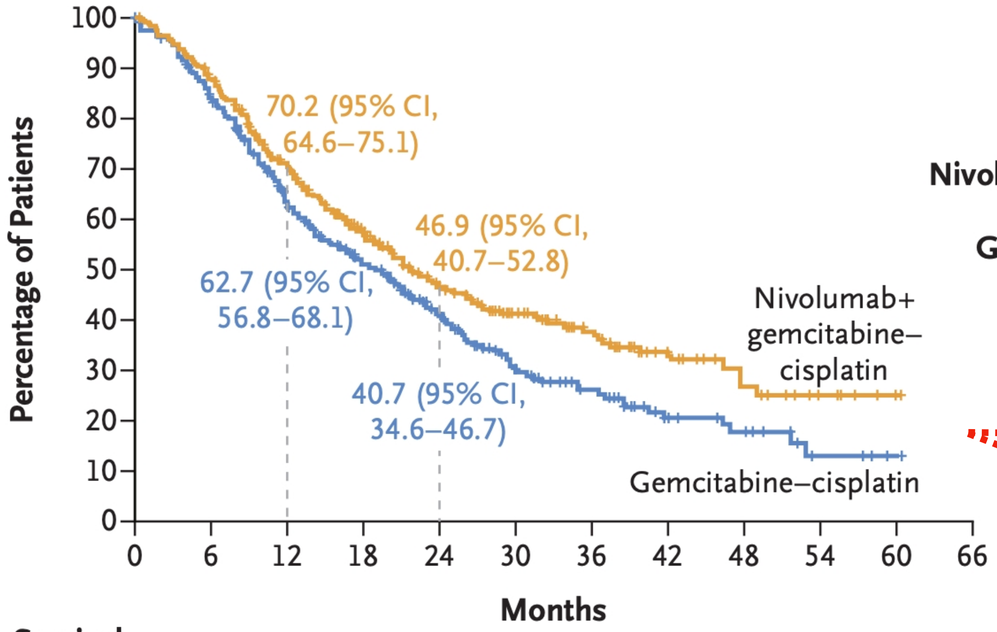


	Age≥65	Asian	ECOG 0	ECOG 1	Mets	Liver Mets	Upper Tract	PD-L1<1%
Nivo	50.7	23.7	53.3	46.1	85.9	21.1	10.9	63.5
Chemo	51.3	20.1	53.3	46.7	88.5	21.1	14.5	63.8

N Engl J Med . 2023 Nov 9;389(19):1778-1789.

PFS
OS

A Overall Survival

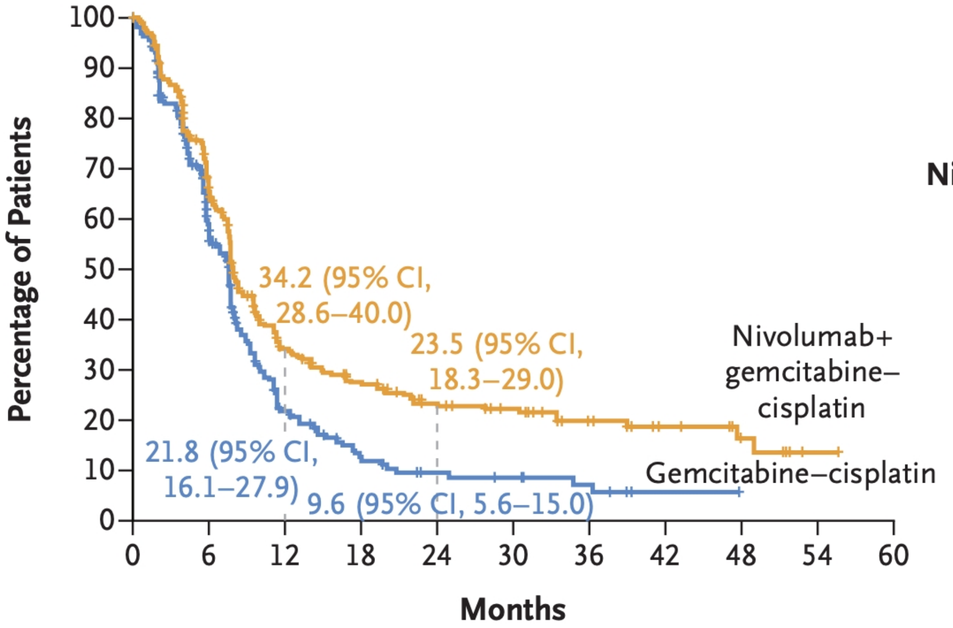


	No. of Events/ No. of Patients	Median Overall Survival (95% CI)
		mo
Nivolumab+Gemcitabine–Cisplatin	172/304	21.7 (18.6–26.4)
Gemcitabine–Cisplatin	193/304	18.9 (14.7–22.4)

Hazard ratio for death, 0.78 (95% CI, 0.63–0.96)
P=0.02

Only 9% received Avelumab maintenance of potential 71.3% (CR/PR/SD)

B Progression-free Survival



	No. of Events/ No. of Patients	Median Progression-free Survival (95% CI)
		mo
Nivolumab+Gemcitabine–Cisplatin	211/304	7.9 (7.6–9.5)
Gemcitabine–Cisplatin	191/304	7.6 (6.1–7.8)

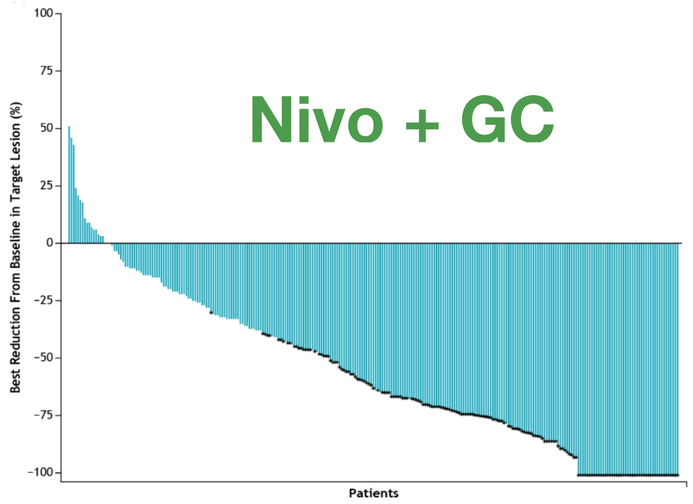
Hazard ratio for disease progression or death, 0.72 (95% CI, 0.59–0.88)
P=0.001

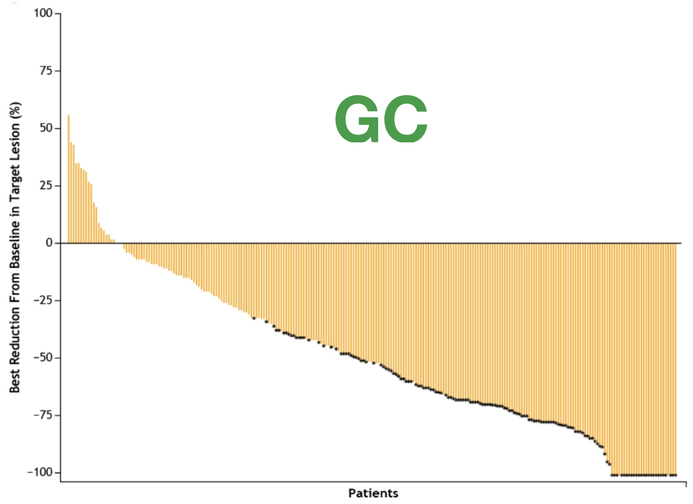
N Engl J Med . 2023 Nov 9;389(19):1778-1789.

Objective Response Rate

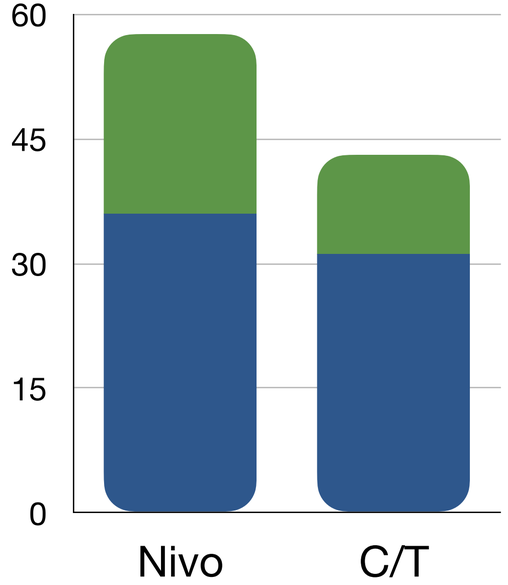
	Nivo + GC N=304	GC N=288
Completed 6 cycles per protocol, n	225 (74)	157 (55)
Discontinued treatment, n (%)		
Any reason	79 (26)	131 (45)
Disease progression	20 (7)	50 (17)
Study drug toxicity	23 (8)	22 (8)

	Nivo + GC	GC
Any objective response	N=175	N=131
Median TTR (Q1-Q3), months	2.1 (2.0–2.3)	2.1 (2.0–2.2)
Median DoR (95% CI),	9.5 (7.6–15.1)	7.3 (5.7–8.9)
Complete response	N=66	N=36
Median TTR (Q1-Q3), months	2.1 (1.9-2.2)	2.1 (1.9-2.2)
Median DoR (95% CI),	37.1 (18.1-NE)	13.2 (7.3-18.4)





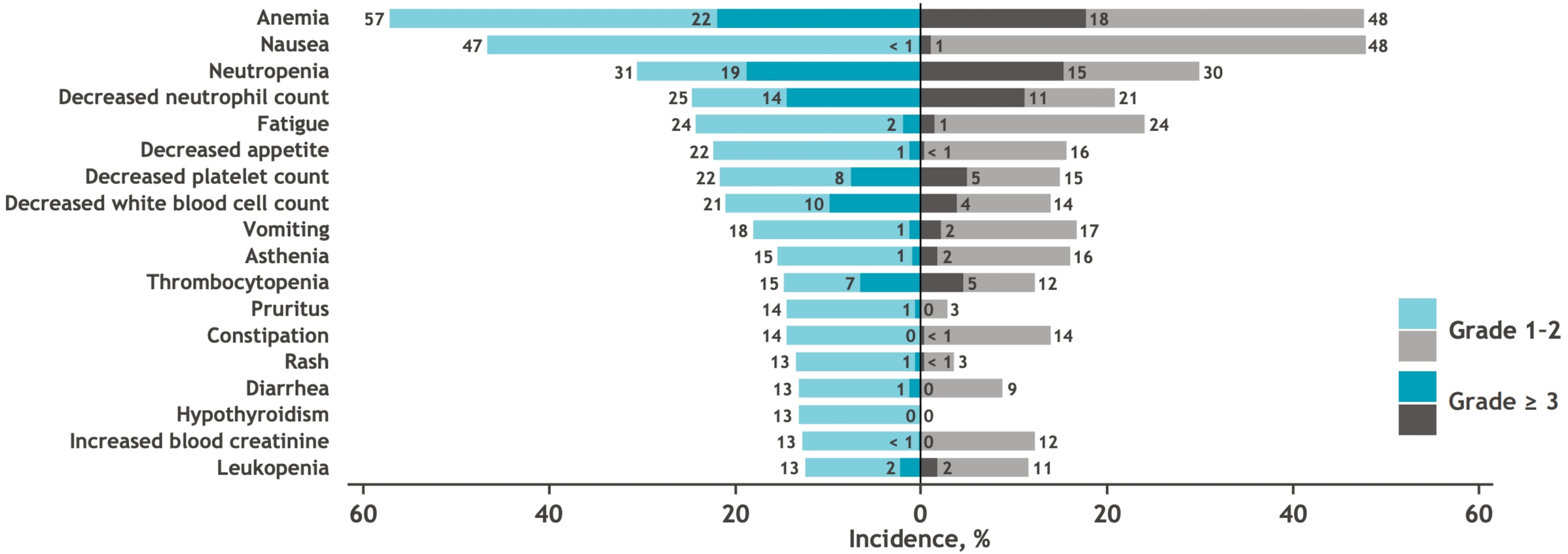
	Nivo	GC
CR	21.7	11.8
PR	35.9	31.2
SD	25.3	28.3
PD	9.5	12.8
ORR	57.6	43.1



ESMO 2023 LBA7, N Engl J Med . 2023 Nov 9;389(19):1778-1789.

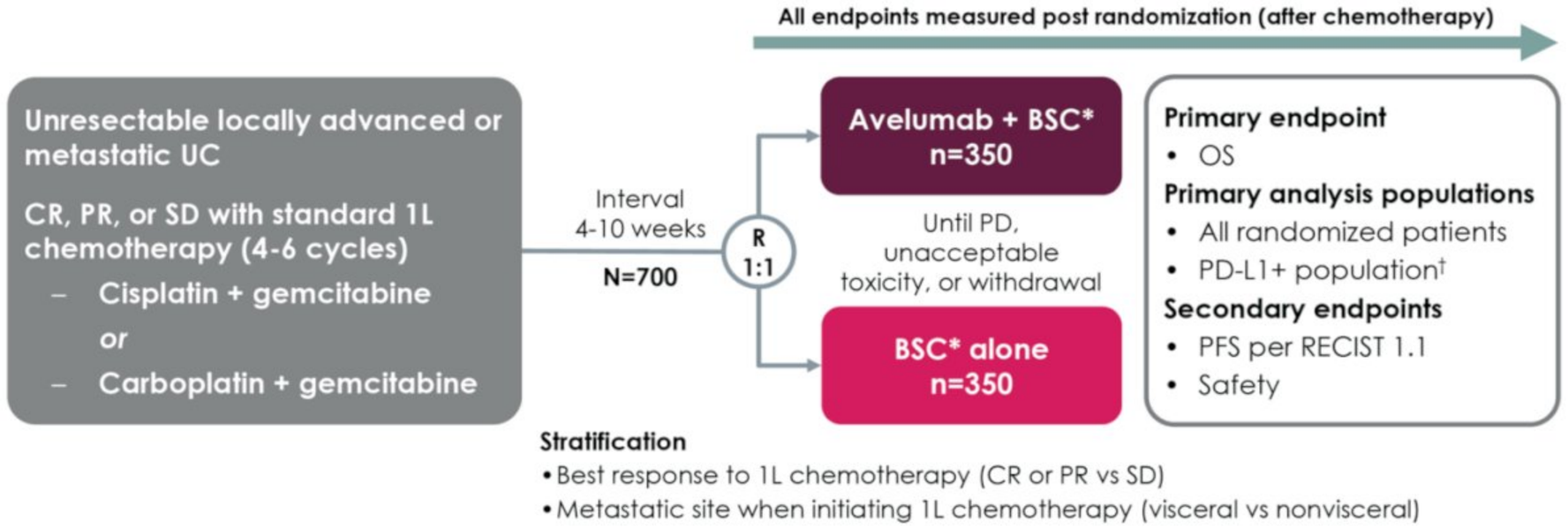
Treatment-related AEs in all treated patients

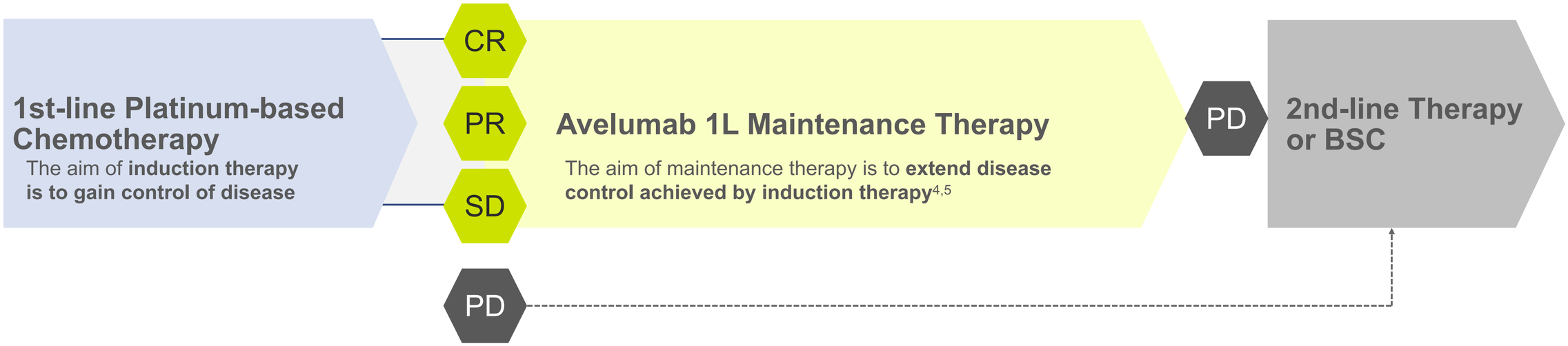
	NIVO+GC (n = 304)		GC (n = 288)	
Treatment-related AE, %[a]	Any grade	Grade ≥ 3[b]	Any grade	Grade ≥ 3[b]
Any	97	62	93	52
Leading to discontinuation	21	11	17	8



[a]Includes events that occurred in treated patients between first dose and 30 days after last dose of study therapy. Tornado plot displays individual treatment-related AEs occurring at any grade in ≥ 10% of treated patients in either arm. [b]One grade 5 event occurred in each arm (sepsis in the NIVO+GC arm and acute kidney injury in the GC arm).
AE, adverse event.

JAVELIN 100: Ph3, Avelumab as maintenance after Platinum-based regimen with CR/PR/SD in mUC





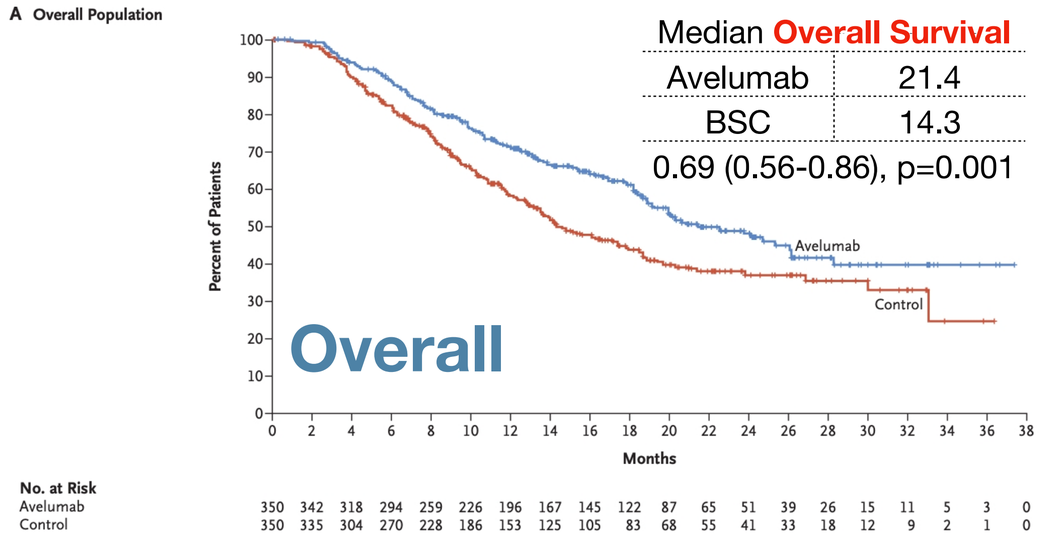
N Engl J Med . 2020 Sep 24;383(13):1218-1230

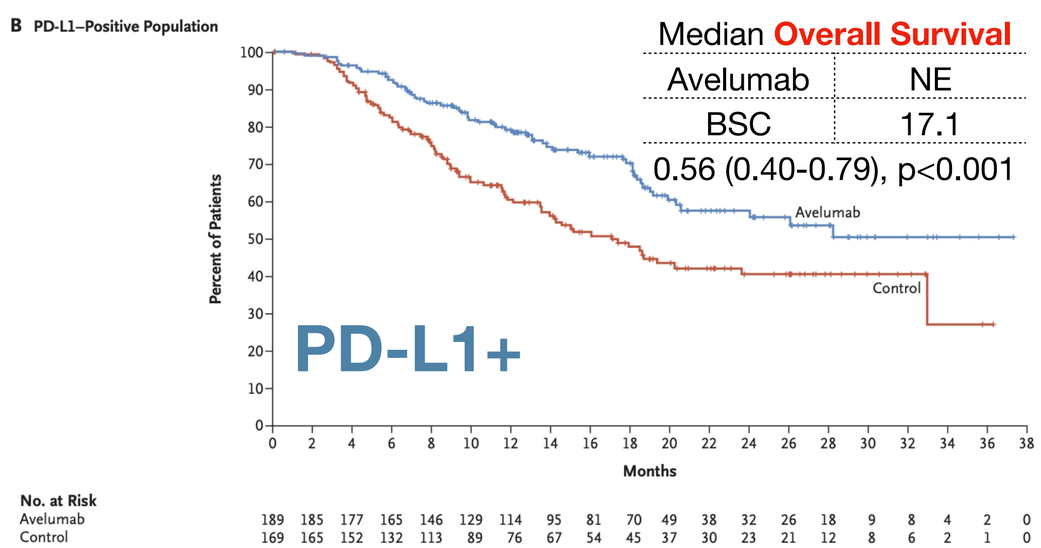
Characteristics of the Patients at Baseline

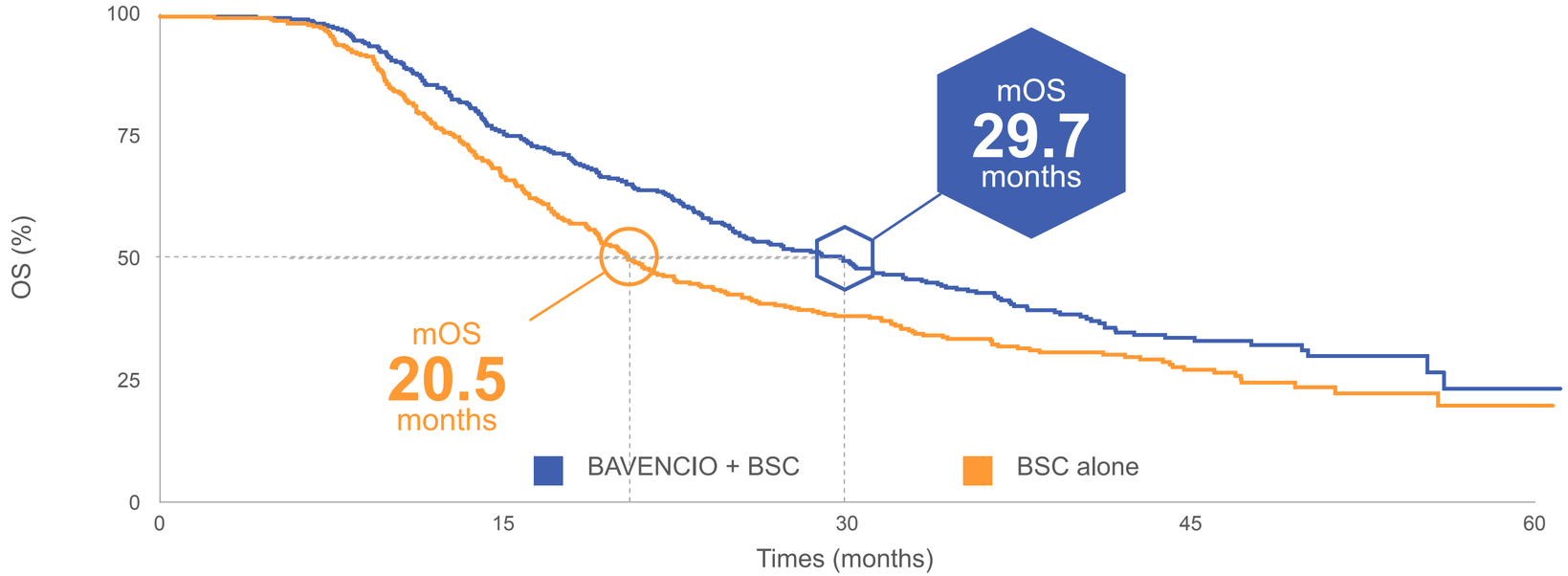
	Overall population		PD-L1-Positive population	
	Avelumab (n=350)	BSC (n=350)	Avelumab (n=189)	BSC alone (n=169)
Age – yr				
Median	68	69	70	70
Range	37–90	32–89	37–90	32–84
Site of primary tumor – no. (%)				
Upper tract	106 (30.3)	81 (23.1)	44 (23.3)	35 (20.7)
Lower tract	244 (69.7)	269 (76.9)	145 (76.7)	134 (79.3)
Site of baseline metastasis before chemotherapy – no.(%)				
Visceral site	191 (54.6)	191 (54.6)	88 (46.6)	79 (46.7)
Non-visceral site	159 (45.4)	159 (45.4)	101 (53.4)	90 (53.3)
PD-L1 status – no. (%)				
Positive	189 (54.0)	169 (48.3)	189 (100)	169 (100)
Negative	139 (39.7)	131 (37.4)	0	0
Unknown	22 (6.3)	50 (14.3)	0	0
First-line chemotherapy regimen – no. (%)				
Gemcitabine plus cisplatin	183 (52.3)	206 (58.9)	101 (53.4)	98 (58.0)
Gemcitabine plus carboplatin	147 (42.0)	122 (34.9)	74 (39.2)	54 (32.0)
Gemcitabine plus cisplatin or carboplatin	20 (5.7)	20 (5.7)	14 (7.4)	15 (8.9)
Not reported	0	2 (0.6)	0	2 (1.2)
Best response to first-line chemotherapy – no. (%)				
Complete response or partial response	253 (72.3)	252 (72.0)	139 (73.5)	128 (75.7)
Stable disease	97 (27.7)	98 (28.0)	50 (26.5)	41 (24.3)

N Engl J Med . 2020 Sep 24;383(13):1218-1230

Post-hoc exploratory analysis: **OS** from start of 1L CT





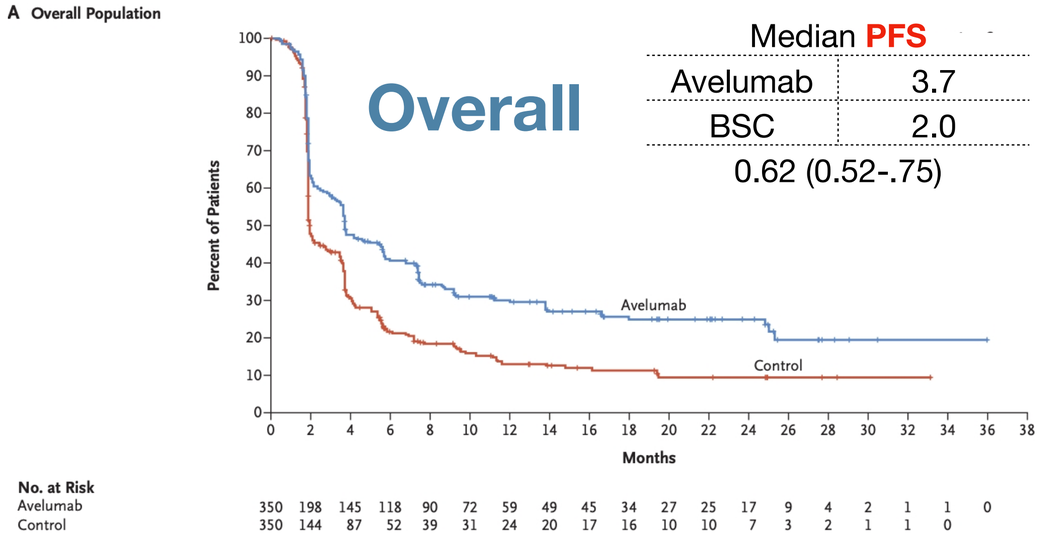


BAVENCIO + BSC (n=350)	BSC alone (n=350)
mOS, months (95% CI)	
29.7 (25.2, 34.0)	20.5 (19.0, 23.5)
HR (95% CI)	
0.77 (0.636, 0.921)	

This is a *post-hoc* exploratory analysis of OS data calculated from the start of 1L CT in patients who were progression-free following 1L CT, and there are limitations to the interpretation of these data.

N Engl J Med . 2020 Sep 24;383(13):1218-1230; Sridhar SS, et al. Abstract No. 508. Presented at the 2023 ASCO GU

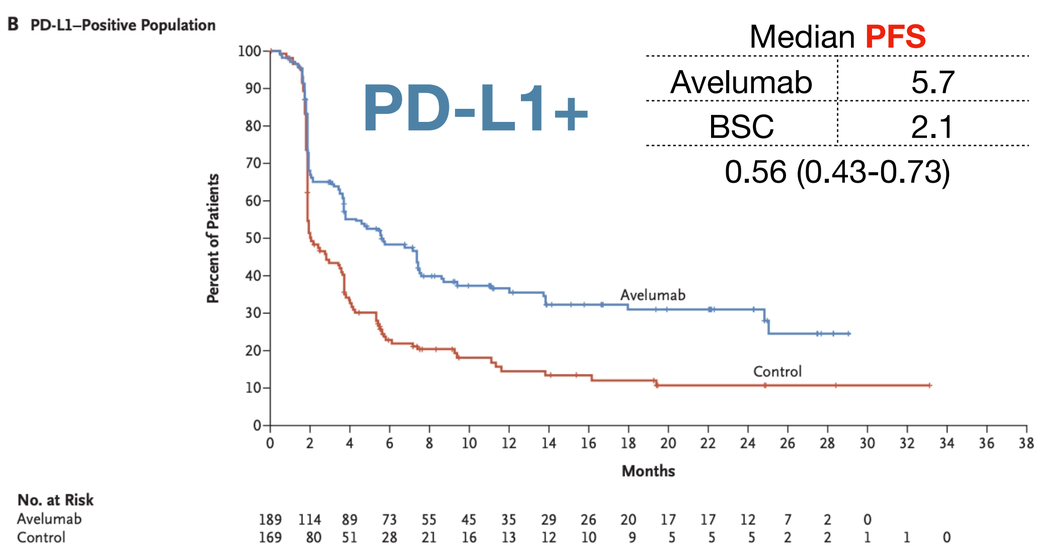
Long-term exploratory analysis: **PFS** from randomization



Overall

Median **PFS**	
Avelumab	3.7
BSC	2.0

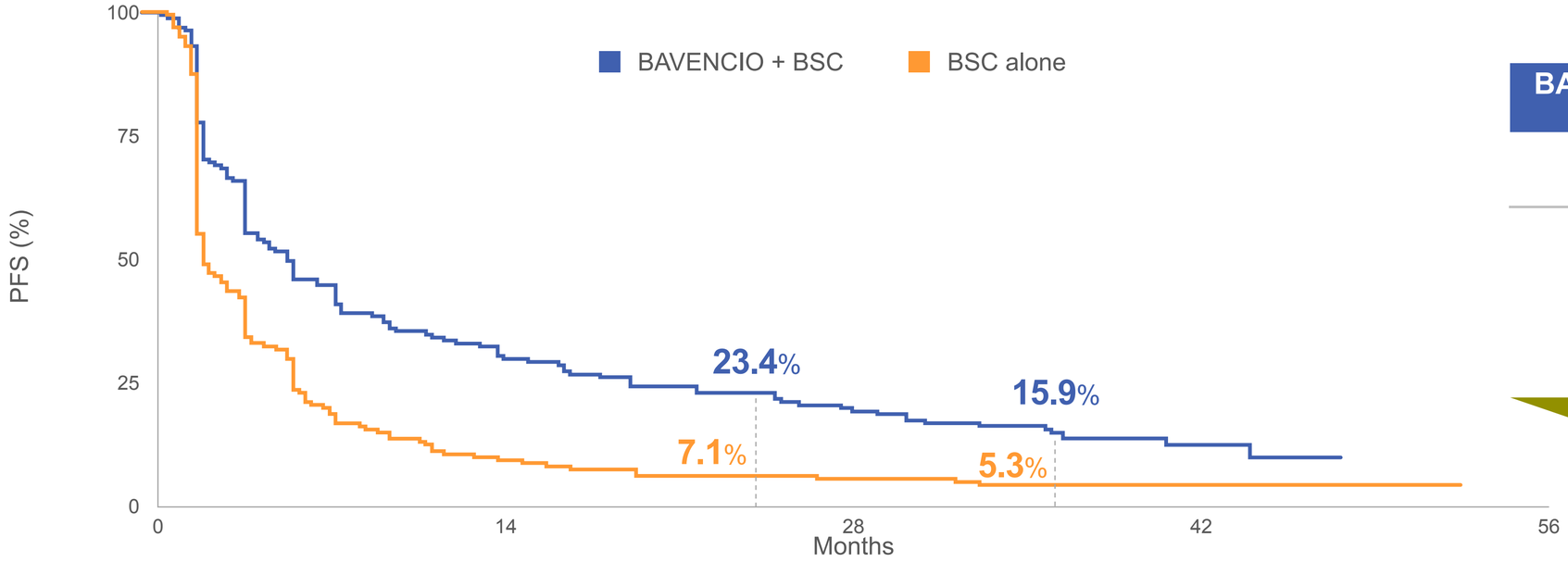
0.62 (0.52-.75)



PD-L1+

Median **PFS**	
Avelumab	5.7
BSC	2.1

0.56 (0.43-0.73)



BAVENCIO + BSC (n=350)	**BSC alone** (n=350)
mPFS, months (95% CI)	
5.5 (4.2, 7.2)	2.1 (1.9, 3.0)
Stratified HR (95% CI)	
0.54 (0.46, 0.64)	

reduction in risk of disease progression or death

46%

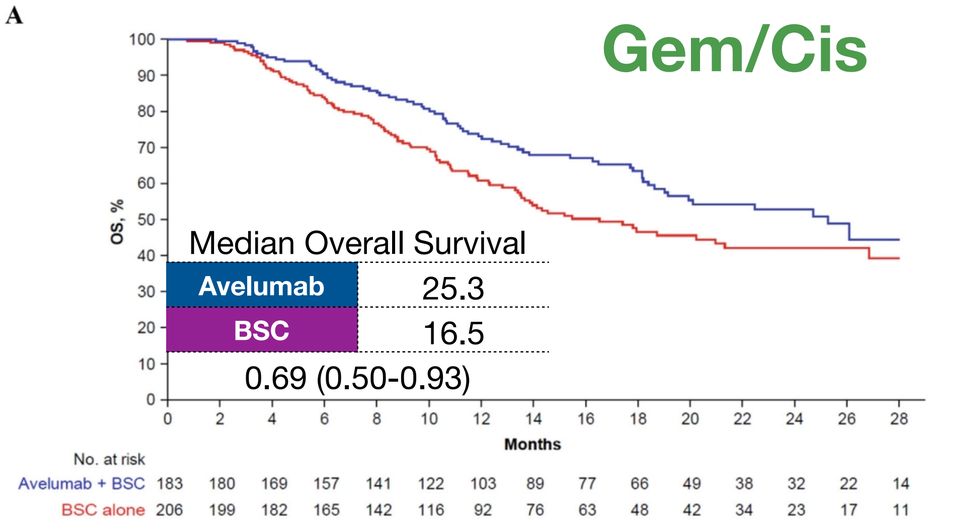
N Engl J Med . 2020 Sep 24;383(13):1218-1230; J Clin Oncol. 2023;41(19):3486-3492.

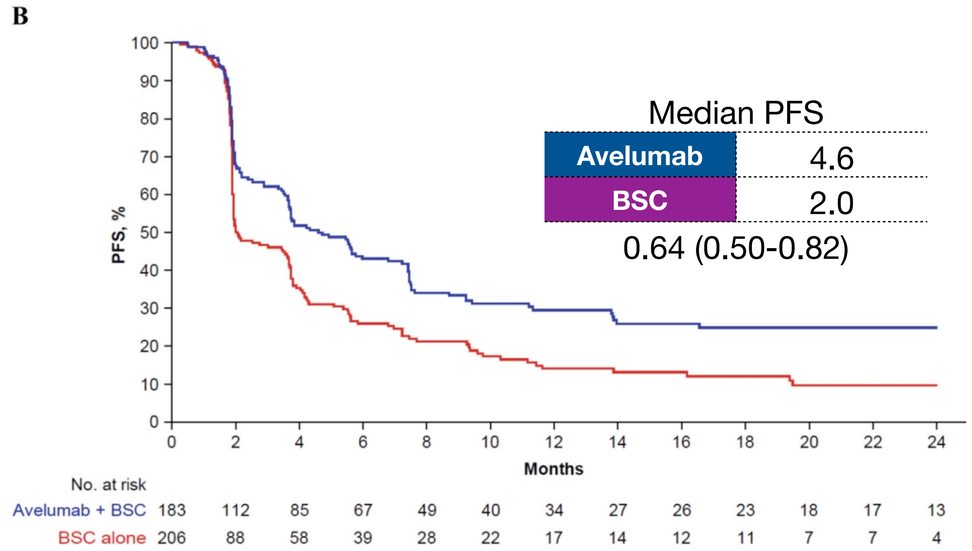
OS and PFS by 1L Platinum - Gem/Cis vs Gem/Carbo

OS

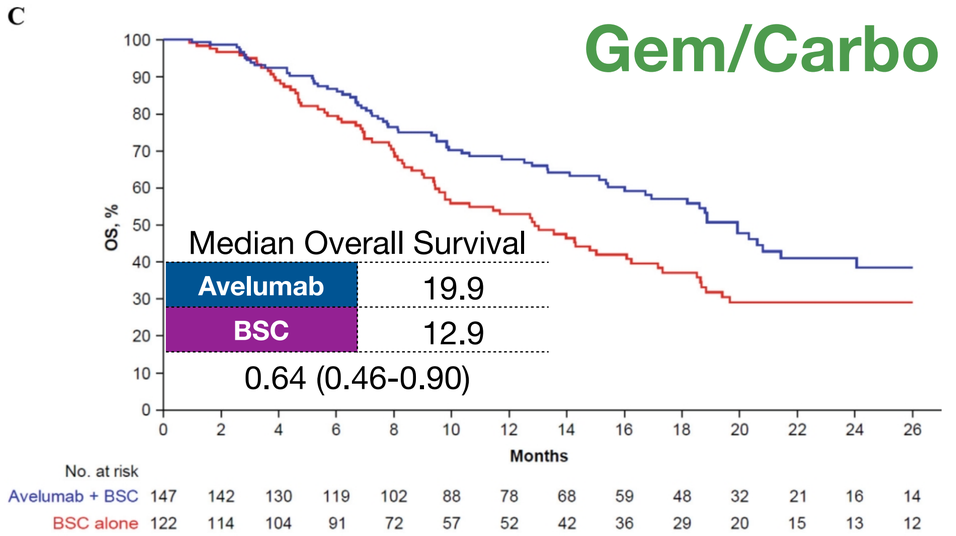
PFS

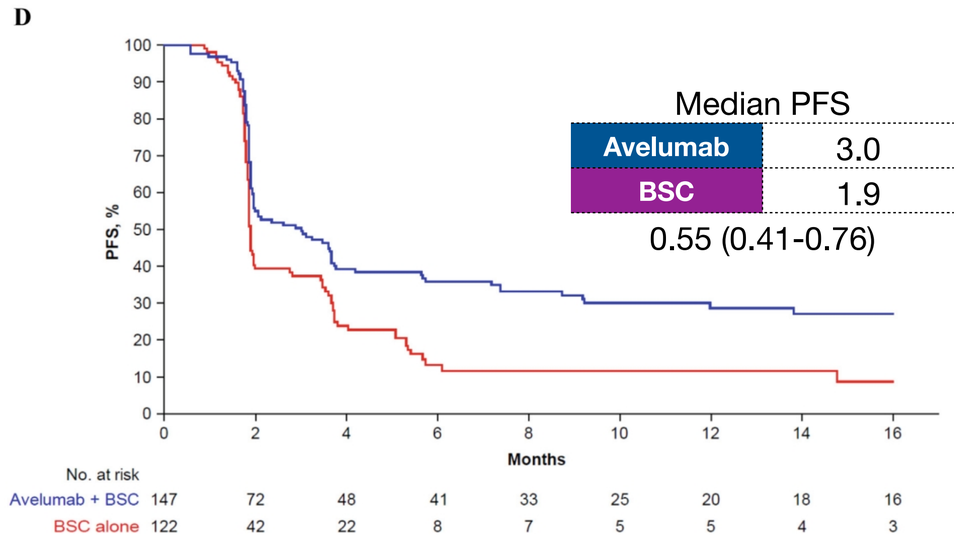
Gem/Cis





Gem/Carbo



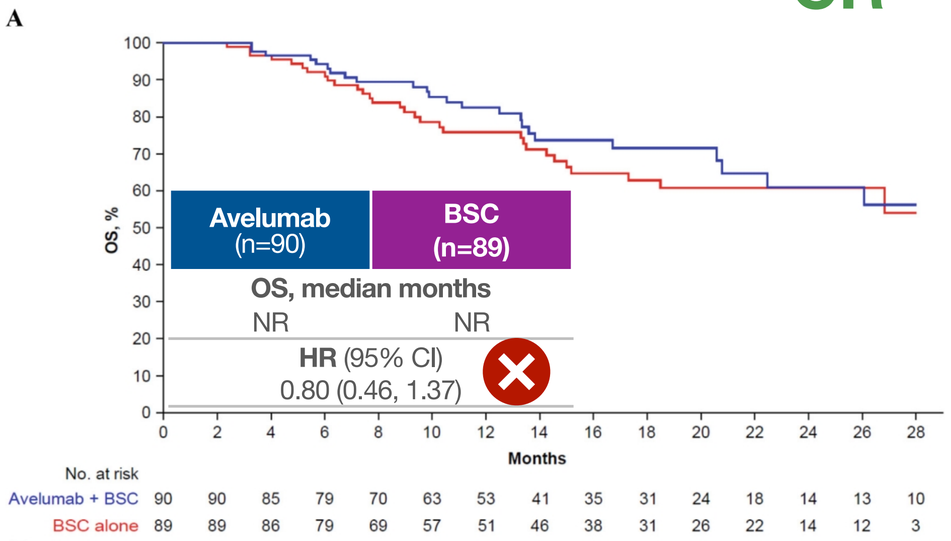


Eur Urol . 2023 Jul;84(1):95-108

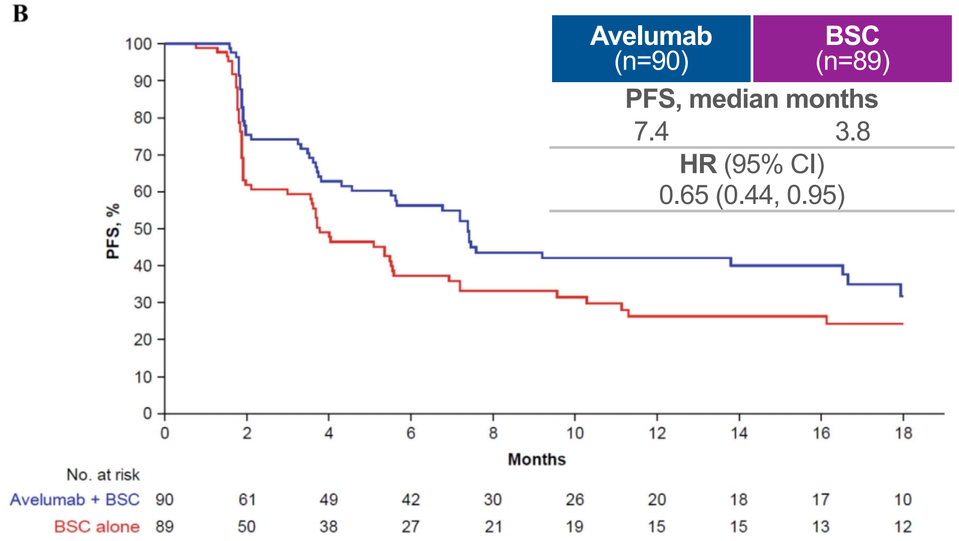
OS and PFS by Response - CR vs PR

CR

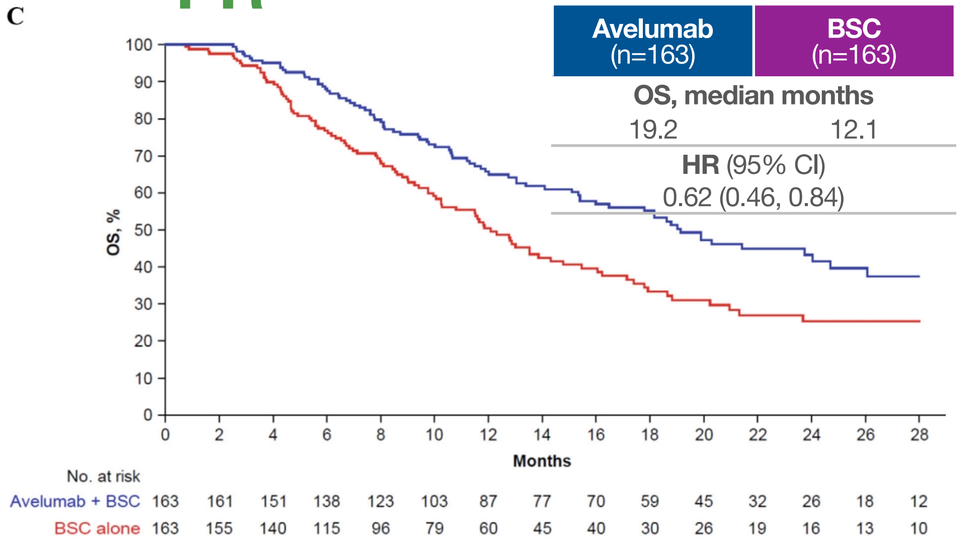
OS

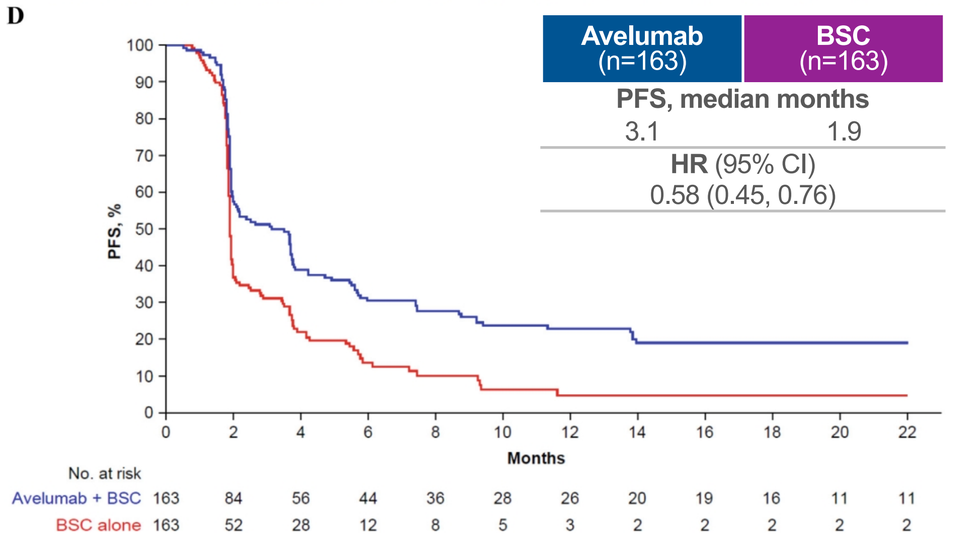


PFS

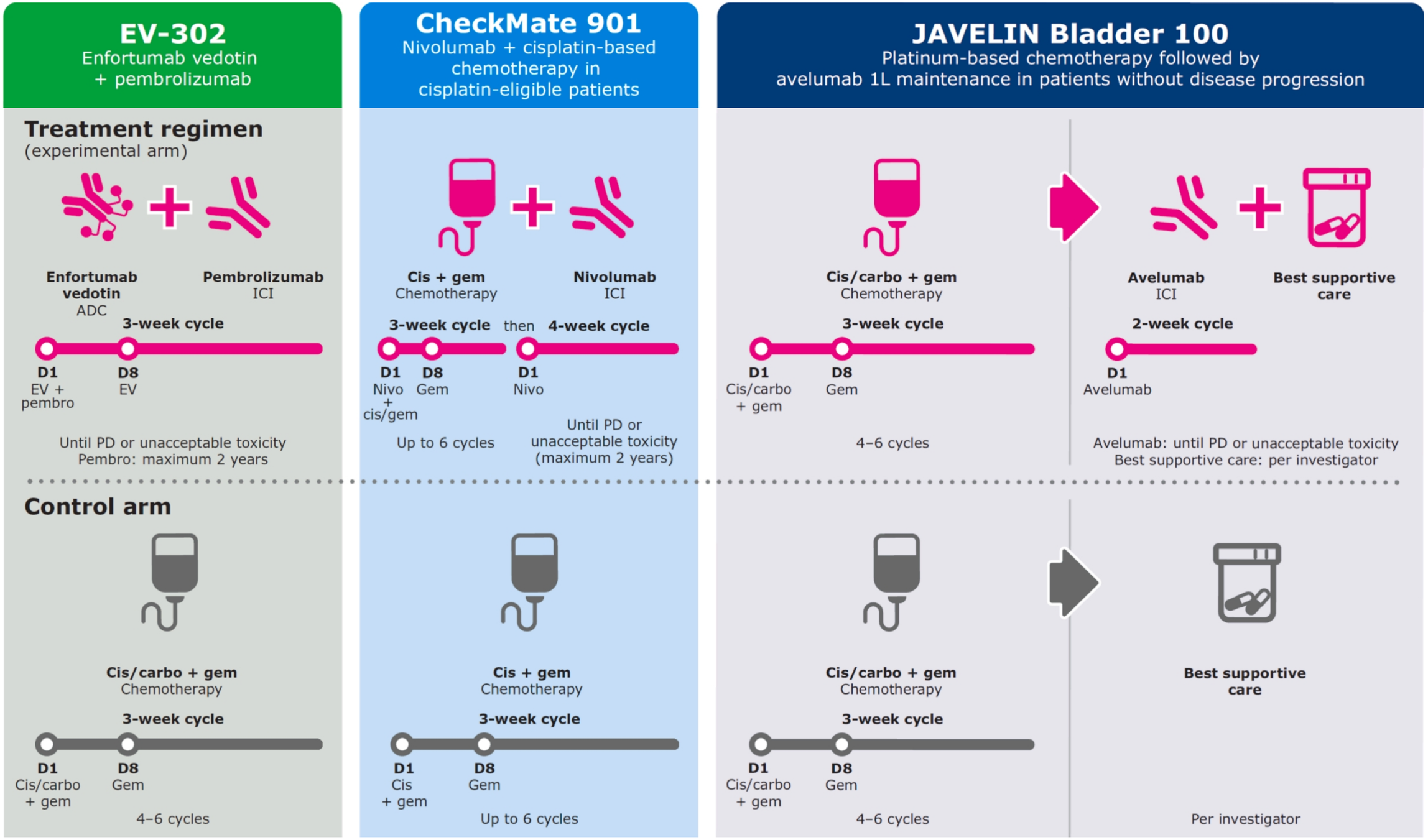


PR





Eur Urol . 2023 Jul;84(1):95-108


EV-302
Enfortumab vedotin + pembrolizumab
CheckMate 901
Nivolumab + cisplatin-based chemotherapy in cisplatin-eligible patients
JAVELIN Bladder 100
Platinum-based chemotherapy followed by avelumab 1L maintenance in patients without disease progression
Treatment regimen
(experimental arm)
Enfortumab vedotin
ADC
Pembrolizumab
ICI
3-week cycle
D1
EV + pembro
D8
EV
Until PD or unacceptable toxicity
Pembro: maximum 2 years
Cis + gem
Chemotherapy
Nivolumab
ICI
3-week cycle
then
4-week cycle
D1
Nivo + cis/gem
D8
Gem
D1
Nivo
Up to 6 cycles
Until PD or unacceptable toxicity (maximum 2 years)
Cis/carbo + gem
Chemotherapy
3-week cycle
D1
Cis/carbo + gem
D8
Gem
4–6 cycles
Avelumab
ICI
Best supportive care
2-week cycle
D1
Avelumab
Avelumab: until PD or unacceptable toxicity
Best supportive care: per investigator
Control arm
Cis/carbo + gem
Chemotherapy
3-week cycle
D1
Cis/carbo + gem
D8
Gem
4–6 cycles
Cis + gem
Chemotherapy
3-week cycle
D1
Cis + gem
D8
Gem
Up to 6 cycles
Cis/carbo + gem
Chemotherapy
3-week cycle
D1
Cis/carbo + gem
D8
Gem
4–6 cycles
Best supportive care
Per investigator

Difference in Study Population Criteria

不同試驗間不能直接比較
Slide僅方便闡述

EV-302	CheckMate-901	JAVELIN Bladder 100

✓ GFR ≧ 30 ml/min^2
✓ ECOG ≦ 2
✓ Eligible for Platinum
✓ For Carboplatin
  ✓ GFR ≧ 30 to <60 ml/min^2
  ✓ ECOG =2
  ✓ Hearing loss ≧ Gr2
  ✓ NYHA Fc III
	✓ GFR ≧ 60 ml/min^2
	✓ ECOG ≦ 1
	✓ Eligible for Cisplatin
		✓ ECOG ≦ 1
		✓ Eligible for Platinum
		✓ CR/PR/SD after 4-6 cycles of Gemcitabine/ Cisplatin or Carboplatin

Special Exclusion Criteria		
✓Neuropathy ≧ Gr2 ✓Uncontrolled diabetes ✓Receiving systemic antibiotic for active infection	✓Uncontrolled adrenal insufficiency ✓NYHA Fc III/IV	✓In previous 6 months: MI, symptomatic CHF, stroke, DVT, or symptomatic pulmonary embolism

N Engl J Med . 2024 Mar 7;390(10):875-888; N Engl J Med . 2023 Nov 9;389(19); N Engl J Med . 2020 Sep 24;383(13):1218-1230.

Difference in Study Population Criteria

不同試驗間不能直接比較
Slide僅方便闡述

EV-302

	EV N=442	CT N=444
Age ≥75 yr	102 (23.1)	108 (24.3)
Asian	99 (22.4)	92 (20.7)
ECOG=0	223 (50.5)	215 (48.4)
ECOG=1	204 (46.2)	216 (48.6)
Upper Tract	135 (30.5)	104 (23.4)
LN Only	103 (23.3)	104 (23.4)
Visceral	318 (71.9)	318 (71.6)
Liver Mets	100 (22.6)	99 (22.3)
Ccr ≥60	240 (54.3)	242 (54.5)

CheckMate-901

	Nivo N=304	CT N=304
Age ≥75 yr	34 (11.2)	40 (13.2)
Asian	72 (23.7)	61 (20.1)
ECOG=0	162 (53.3)	162 (53.3)
ECOG=1	140 (46.1)	142 (46.7)
Renal Pelvis	33 (10.9)	44 (14.5)
LN Only	54 (17.8)	56 (18.4)
Visceral		
Liver Mets	64 (21.1)	64 (21.1)
Ccr ≥60	304 (100)	304 (100)

JAVELIN Bladder 100

	Ave N=350	CT N=350
Median age	68	69
Asian	75 (21.4)	81 (23.1)
ECOG=0	213 (60.9)	211 (60.3)
ECOG=1	136 (38.9)	136 (38.9)
Upper Tract	106 (30.3)	81 (23.1)
LN Only	51 (14.6)	51 (14.6)
Visceral	191 (54.6)	191 (54.6)
Liver Mets		
Ccr ≥60	181 (51.7)	196 (56.0)

N Engl J Med . 2024 Mar 7;390(10):875-888; N Engl J Med . 2023 Nov 9;389(19); N Engl J Med . 2020 Sep 24;383(13):1218-1230.

Survival Result in 3 Trials

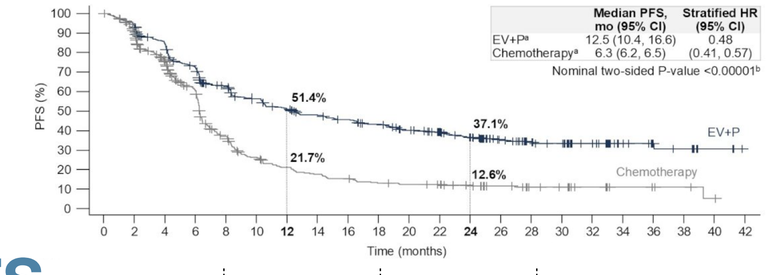
不同試驗間不能直接比較
Slide僅方便闡述

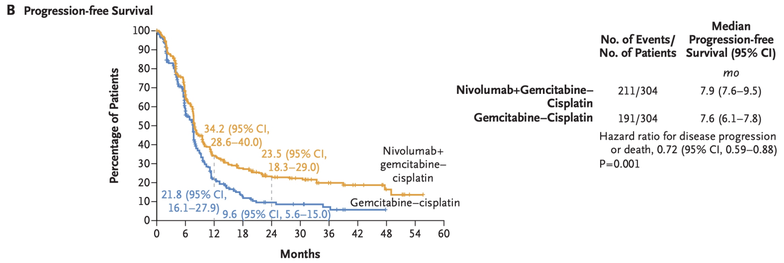
EV-302

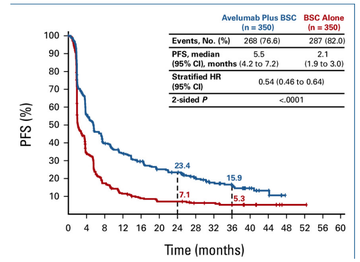
CheckMate-901

JAVELIN Bladder 100

PFS





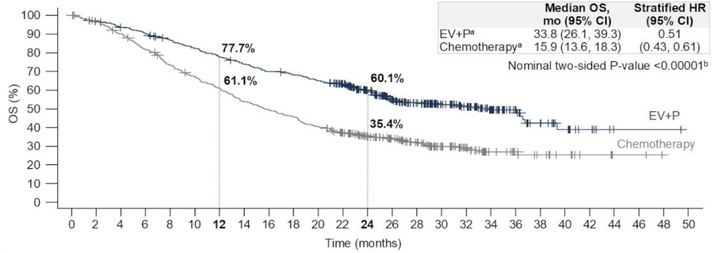


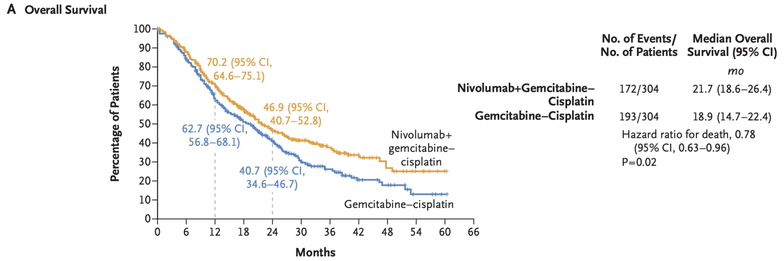
	Median	1-yr	2-yr
EV	12.5	51.4%	37.1%
GC	6.3	21.7%	12.6%

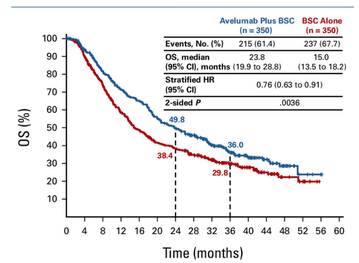
	Median	1-yr	2-yr
Nivo	7.9	34.2%	23.5%
GC	7.6	21.5%	9.6%

	Median	2-yr	3-yr
Ave	5.5	23.4%	15.9%
GC	2.1	7.1%	5.3%

OS







	Median	1-yr	2-yr
EV	33.8	77.7%	60.1%
GC	15.9	61.1%	35.4%

	Median	1-yr	2-yr
Nivo	21.7	70.2%	46.9%
GC	18.9	62.7%	40.7%

	Median	2-yr	3-yr
Ave	23.8	49.8%	36.0%
GC	15.0	38.4%	29.8%

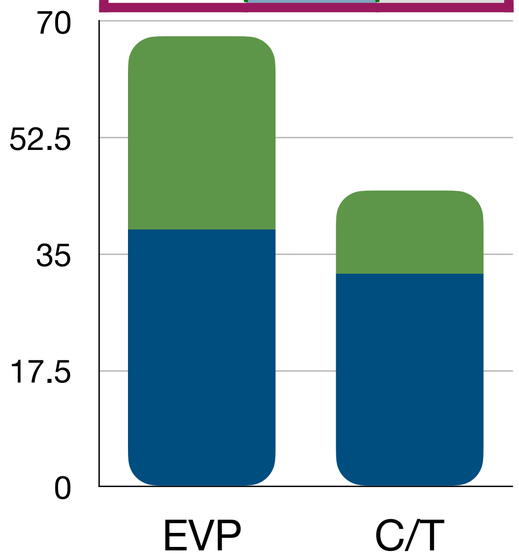
ASCO GU 2025; N Engl J Med . 2023 Nov 9;389(19):1778-1789; J Clin Oncol . 2023 Jul 1;41(19):3486-3492.

Treatment Response in 2 Trials

不同試驗間不能直接比較
Slide僅方便闡述

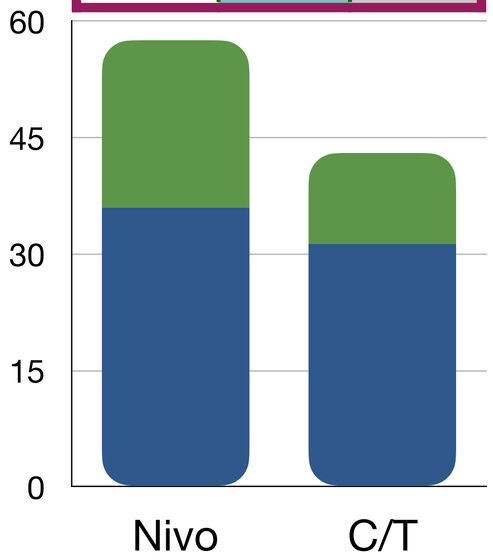
EV-302

	EVP	C/T
CR	29.1	12.5
PR	38.7	32.0
SD	18.8	33.8
PD	8.7	13.6
ORR	67.7	44.4



CheckMate-901

	Nivo	GC
CR	21.7	11.8
PR	35.9	31.2
SD	25.3	28.3
PD	9.5	12.8
ORR	57.6	43.1



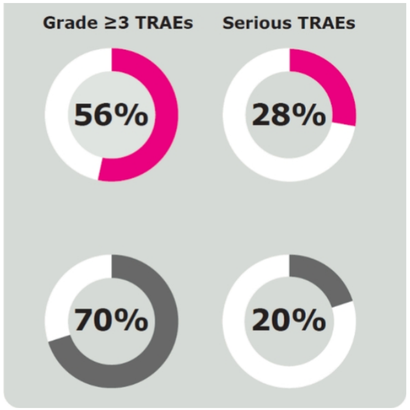
JAVELIN Bladder 100

Difference in Study Adverse Events

不同試驗間不能直接比較
Slide僅方便闡述

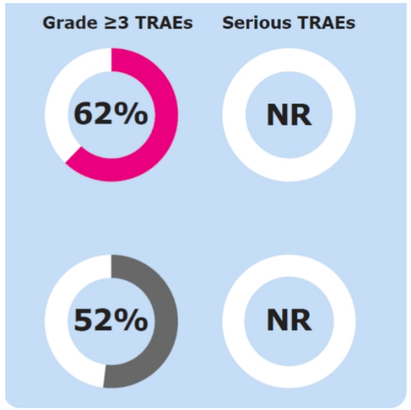
EV-302

- ✓Skin reaction
- ✓Peripheral neuropathy
- ✓Fatigue
- ✓Gastrointestinal AE
- ✓Ocular disorder
- ✓Hematologic AE
- ✓Hyperglycemia
- ✓Hypothyroidism
- ✓Pneumonitis



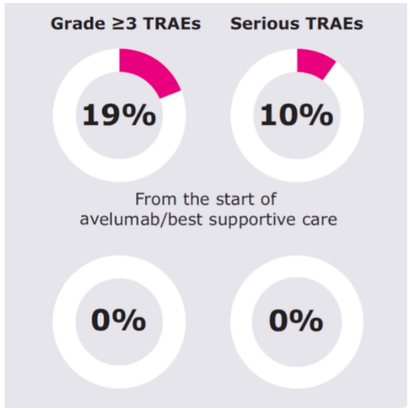
CheckMate-901

- ✓Hematologic AE
- ✓Gastrointestinal AE
- ✓Fatigue
- ✓Skin reaction
- ✓Hypothyroidism



JAVELIN Bladder 100

- ✓Skin reaction
- ✓Hypothyroidism
- ✓Fatigue
- ✓Gastrointestinal AE



Cancer Treat Rev . 2025 Mar:134:102900

Outline

- Current guidelines and their evidence
- Difference between EV-302, CM-901, JB-100
- **Under NHI Situation**
- Case sharing

泌尿上皮癌免疫檢查點抑制劑 (PD-1/PD-L1)藥品給付規定

BAVENCIO® avelumab 20 mg/mL Concentrate for solution for infusion

中央健康保險署藥品給付規定 (112.10.01)

1. 不適合接受化學治療之轉移性泌尿道上皮癌成人患者，且需符合下列條件之一:
   1) CTCAE(the common terminology criteria for adverse events) v4.0 grade ≥ 2 audiometric hearing loss
   2) CTCAE v4.0 grade ≥ 2 peripheral neuropathy
   3) CIRS(the cumulative illness rating scale) score >6

2. 先前已使用過 platinum 類化學治療失敗後疾病惡化的局部晚期無法切除或轉移性泌尿道上皮癌成人患者。

3. **限 avelumab 用於接受第一線含鉑化學治療 4 至 6 個療程後，疾病未惡化， 且達部分緩解 (PR)或疾病呈穩定狀態者 (SD) 之無法手術切除局部晚期 (stage III) 或轉移性泌尿上皮癌 (stage IV)成人患者之維持療法。**

IO使用條件

1. 病人身體狀況良好 (ECOG 1) 。
2. 病人之心肺與肝腎功能須符合下列所有條件：
   1) NYHA(the New York Heart Association) Functional Class I或II
   2) GOT<60U/L 及 GPT<60U/LGPT<60U/L，且，且T-bilirubin<1.5mg/dL (晚期肝細胞癌病人可免除此條件)
   3) 腎功能：(晚期腎細胞癌病人可免除此條件) (109/4/1)(109/4/1)
      - 泌尿道上皮癌第一線用藥： eGFR>30mL/min/1.73 m^2 且 <60mL/min/1.73 m^2 。
      - 泌尿道上皮癌第二線用藥： eGFR>30mL/min/1.73 m^2 。
      - **泌尿道上皮癌維持治療(112/10/1) eGFR>30mL/min/1.73m^2 。**
      - 其他癌別： Creatinine<1.5mg/dL 且 eGFR>60mL/min/ 1.73m^2 。
3. 病人之生物標記表現：除 avelumab 用於默克細胞癌 外，依個別藥品使用其 對應之第三等級體外診斷醫療器材 (class III 所檢測之 PD L1 表現量需符合下表

泌尿上皮癌藥品給付PD-L1檢測規定

BAVENCIO® avelumab 20 mg/mL Concentrate for solution for infusion

給付範圍	Pembrolizumab (Dako 22C3)	Atezolizumab (Ventana SP142) *僅適用於2024/08前申請通過者	Nivolumab (Dako 28-8)	Avelumab (Ventana SP263)
泌尿上皮癌 第一線	CPS ≥ 10 無法接受 化學治療患者	IC ≥ 5% 無法接受 化學治療患者	未給付	• TC ≥ 25% • IC ≥ 25% (若IC佔腫瘤區域>1%) • IC = 100% (若IC佔腫瘤區域≤ 1%) 維持療法
泌尿上皮癌 第二線	CPS ≥ 10	IC ≥ 5%	TC ≥ 5%	未給付

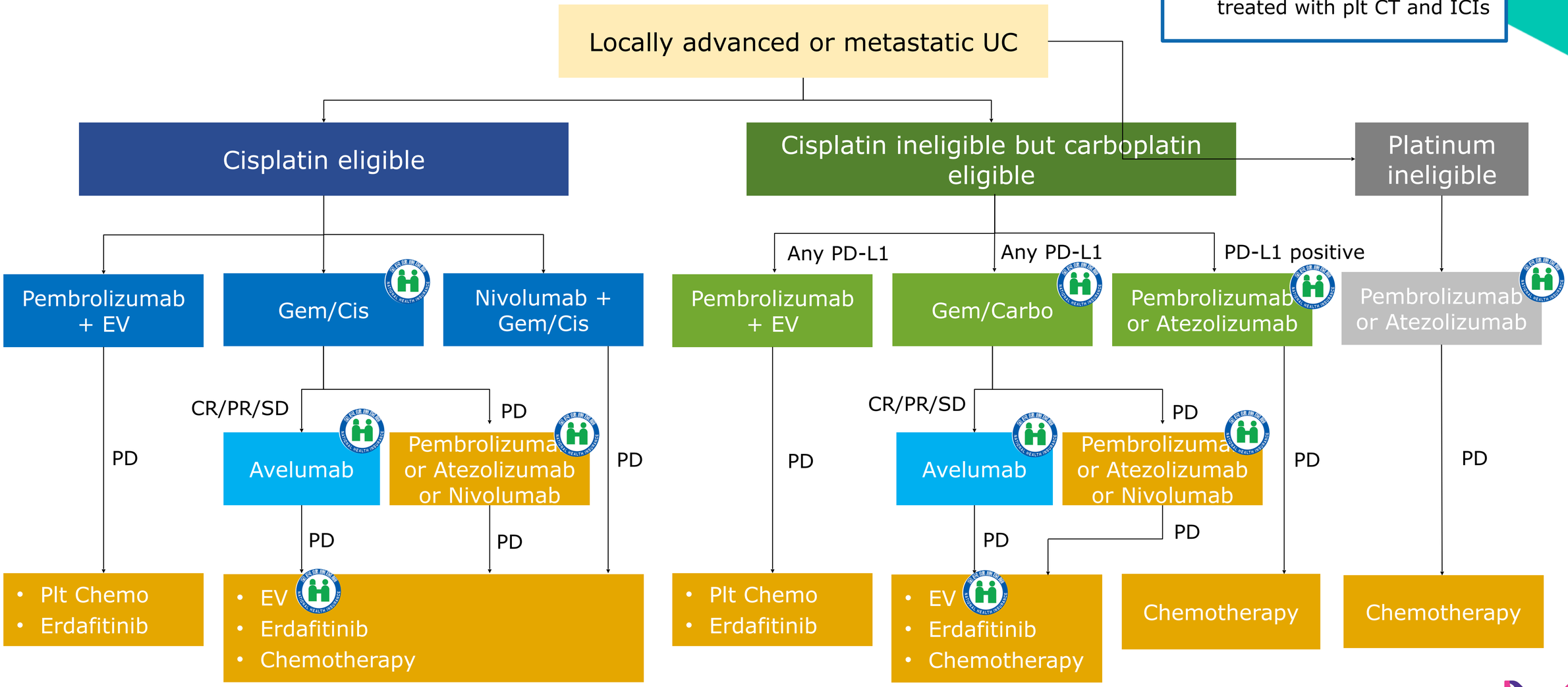
CPS, combined positive score; TC, tumor cell; IC, immune cell; ICP, immune cell presence

中央健康保險署藥品給付規定 (112.10.01)

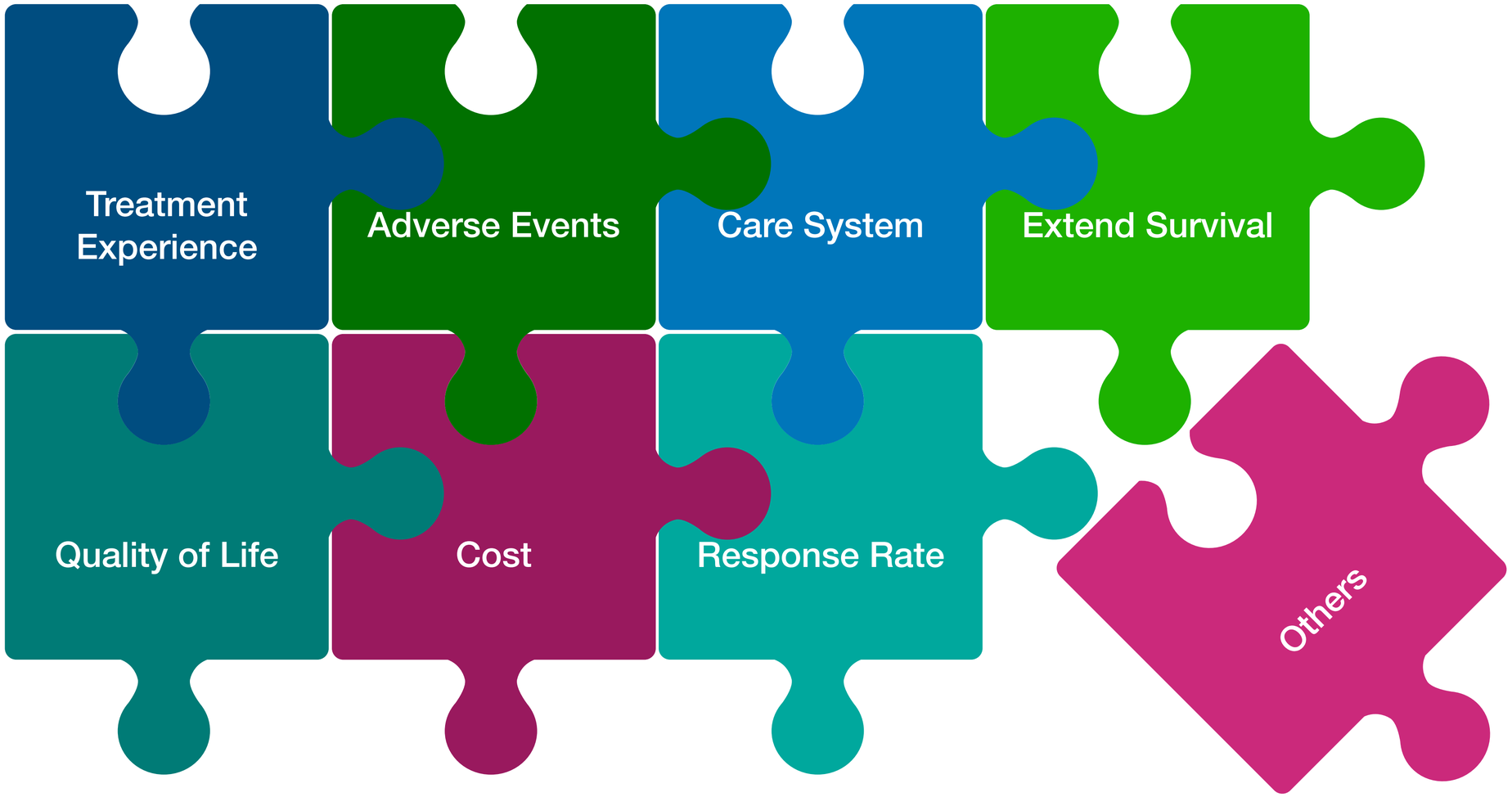
Treatment Landscape in a/mUC in Taiwan

BAVENCIO® 20 mg/mL ution for infusion

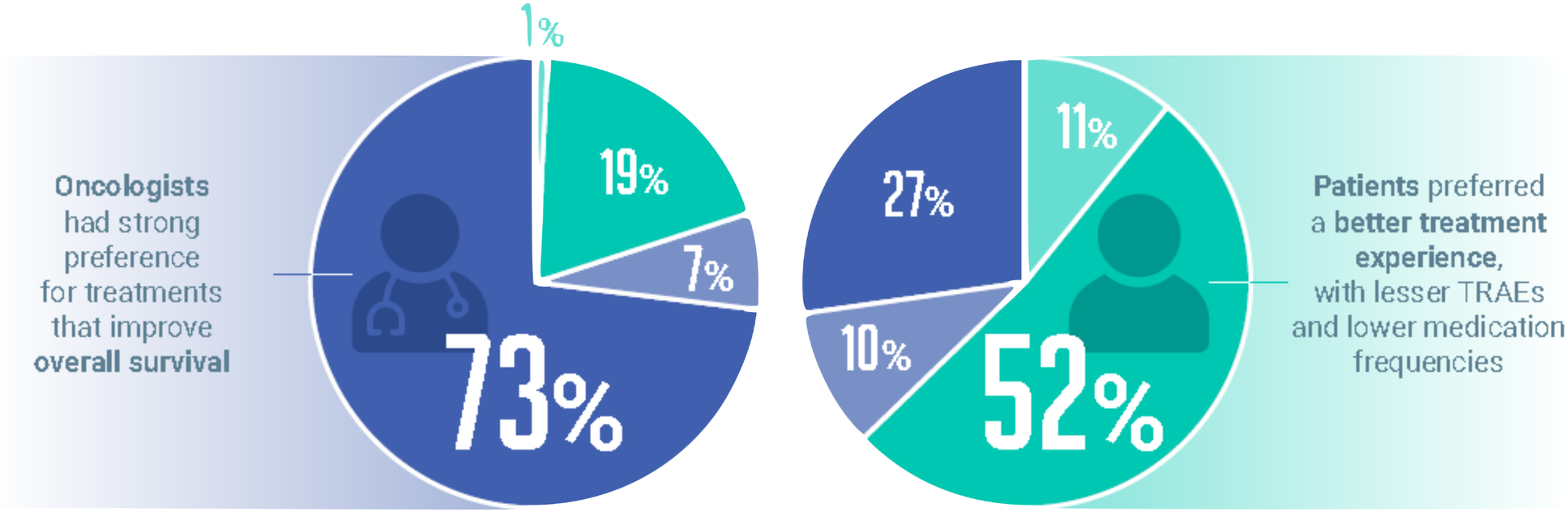
Reimbursement
- ICIs: only for PD-L1+ pts
- EV: only for pts who had treated with plt CT and ICIs



What treatment would you choose for your patients with la/m UC? What **Goal** do you prefer?



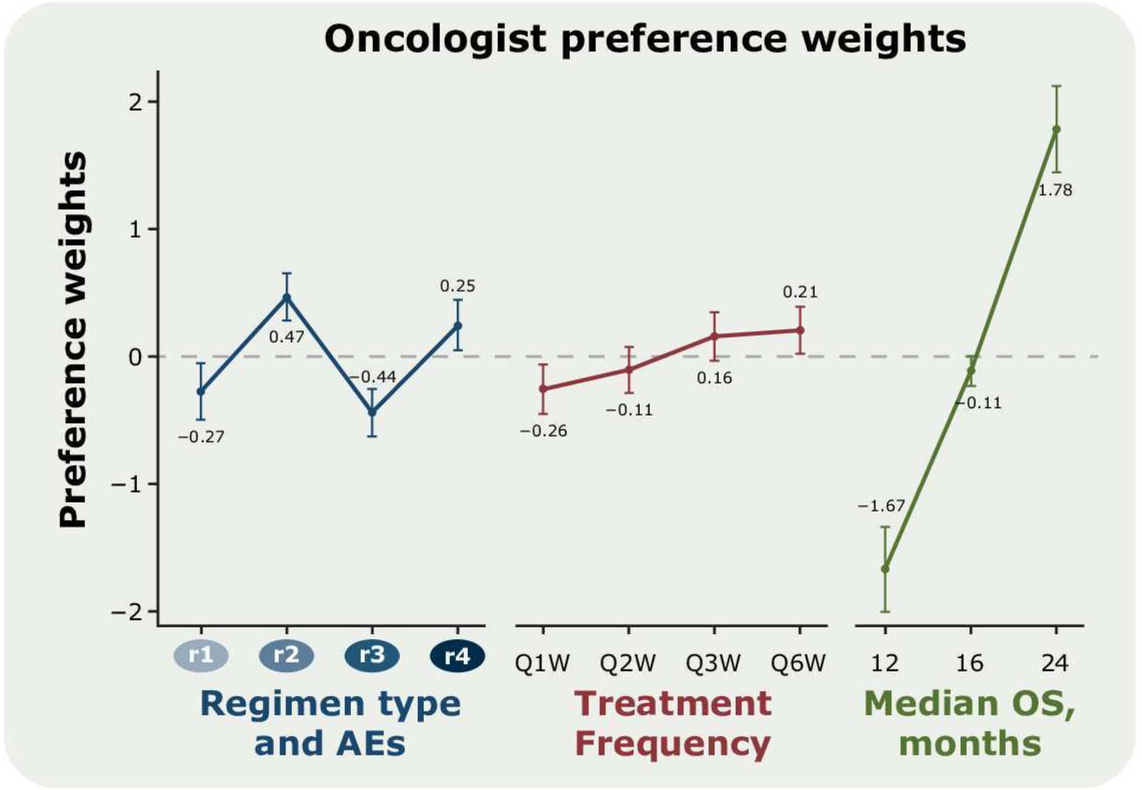
Preference of **Patients / Oncologist** in US

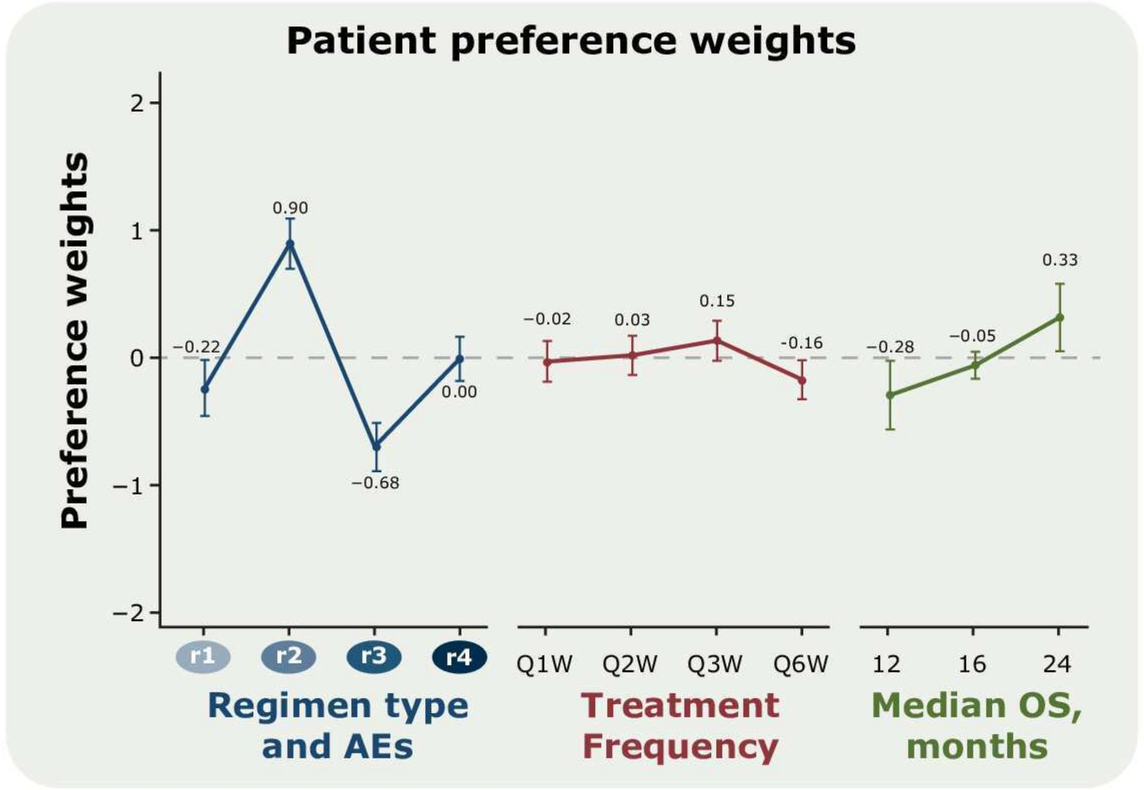


Regimen label	Regimen profile	Composite treatment experience	Frequency	Overall survival (months)
1L chemotherapy	Treatment like 1L chemotherapy	r1) One medication taken for 4 months with moderate grade 3/4 TRAEs	Q1W	12
1L ICI monotherapy	Treatment like 1L ICI monotherapy	r2) One medication until disease progression or unacceptable toxicity with low grade 3/4 TRAEs	Q3W	16
1L ICI combination therapy	Treatment like 1L ICI and chemotherapy together followed by ICI maintenance	r3) Two medications for 4 months → one medication until disease progression or unacceptable toxicity with high → low grade 3/4 TRAEs	Q1W → Q3W	16
1L ICI maintenance therapy	Treatment like 1L chemotherapy followed by 1L ICI maintenance therapy	r4) One medication for 4 months → one medication until disease progression or unacceptable toxicity with moderate → low grade 3/4 TRAEs	Q1W → Q2W	24

Future Oncol. 2023;19:369-383

ATTRIBUTES AND LEVELS IN THE DCE

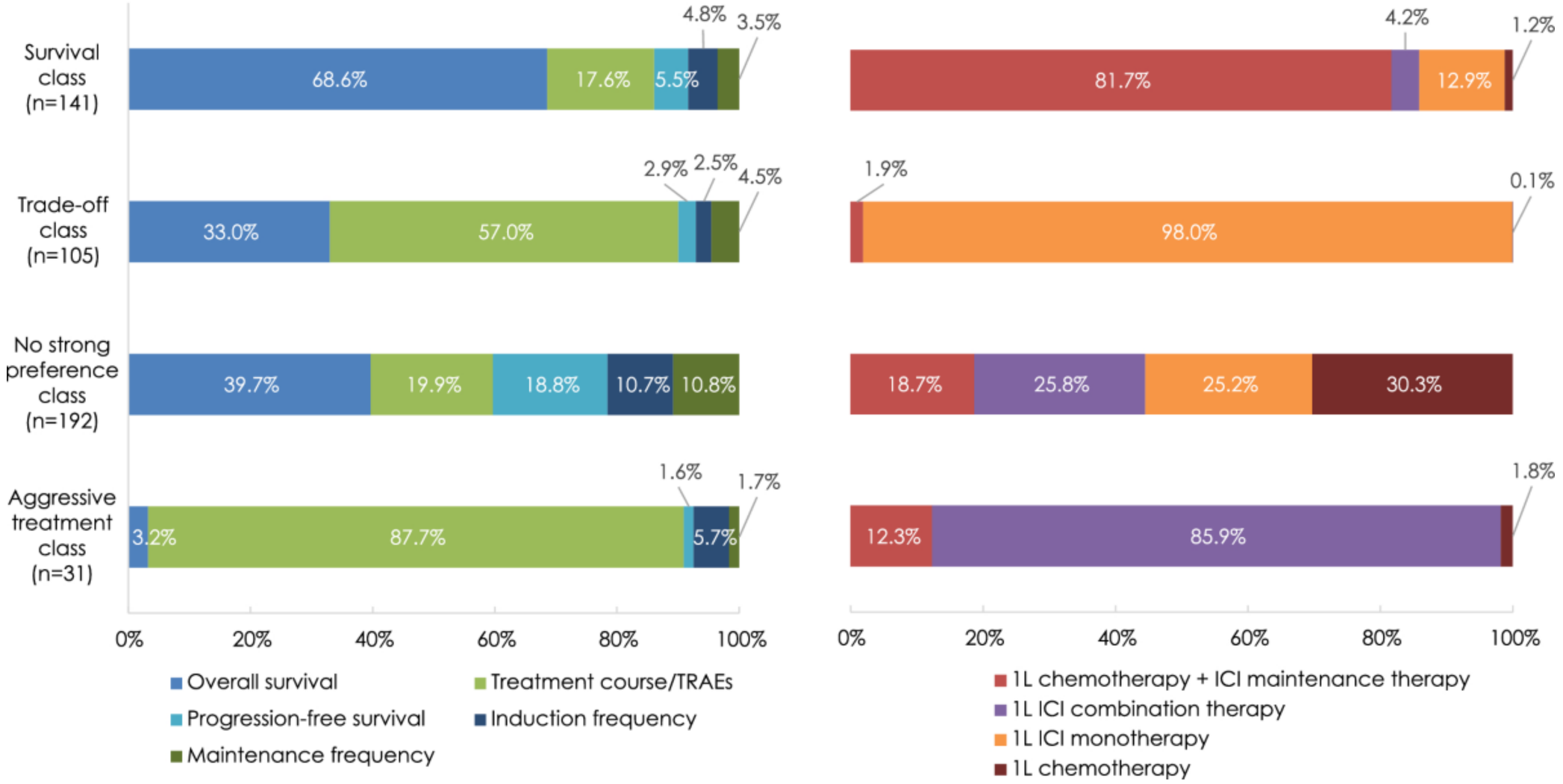




	Administration	Median OS, months	Incidence of grade 3/4 TRAEs
r1	Q1W	12	Moderate
r2	Q3W	16	Low
r3	Q1W → Q3W	16	High → low
r4	Q1W → Q2W	24	Moderate → low

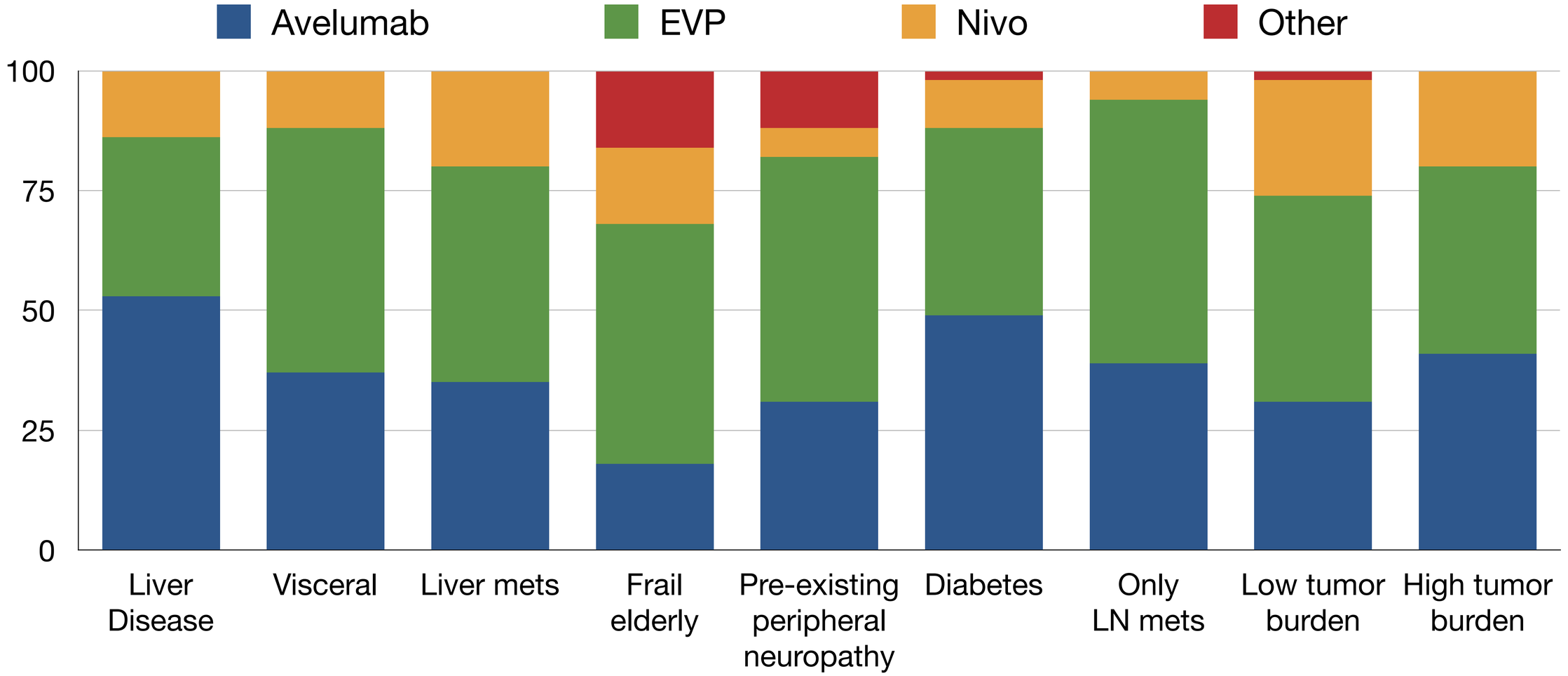
Future Oncol. 2023;19:369-383

Clinician Preferences in Five European Countries - 498 clinicians(343 oncologists / 155 urologists)

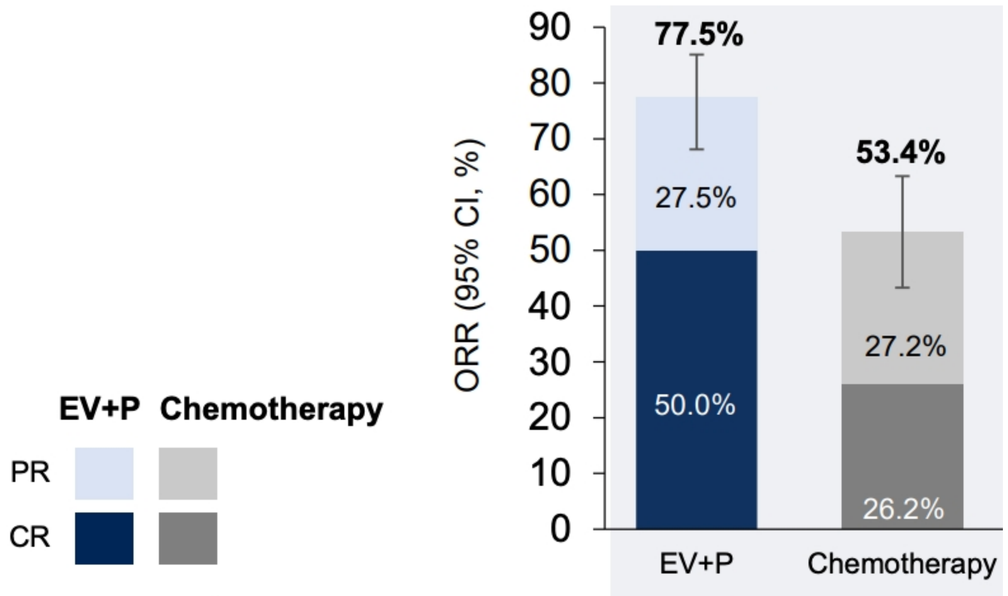


Pharmacoeconomics . 2024 Aug;42(8):895-909.

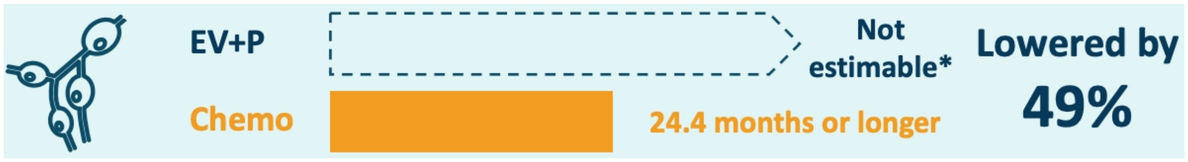
Patient profiles as drivers of **physician** choice for 1st-line Tx in la/mUC: perspectives from a US study



EV-302



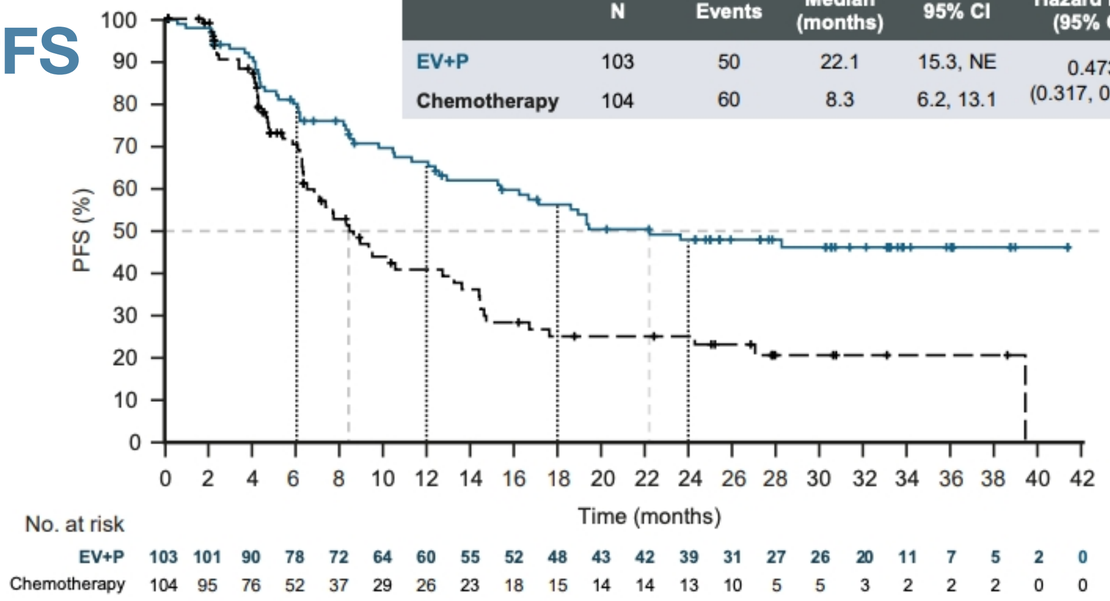
	LN-only mets	
	EV+P n=102	Chemotherapy n=103
ORR, n (%)	79 (77.5)	55 (53.4)
DOR, median (95% CI), months	NE (19.9, NE)	12.4 (8.6, 24.9)



PFS

(B) LN-Only Metastases

	N	Events	Median (months)	95% CI	Hazard ratio (95% CI)
EV+P	103	50	22.1	15.3, NE	0.473 (0.317, 0.704)
Chemotherapy	104	60	8.3	6.2, 13.1	



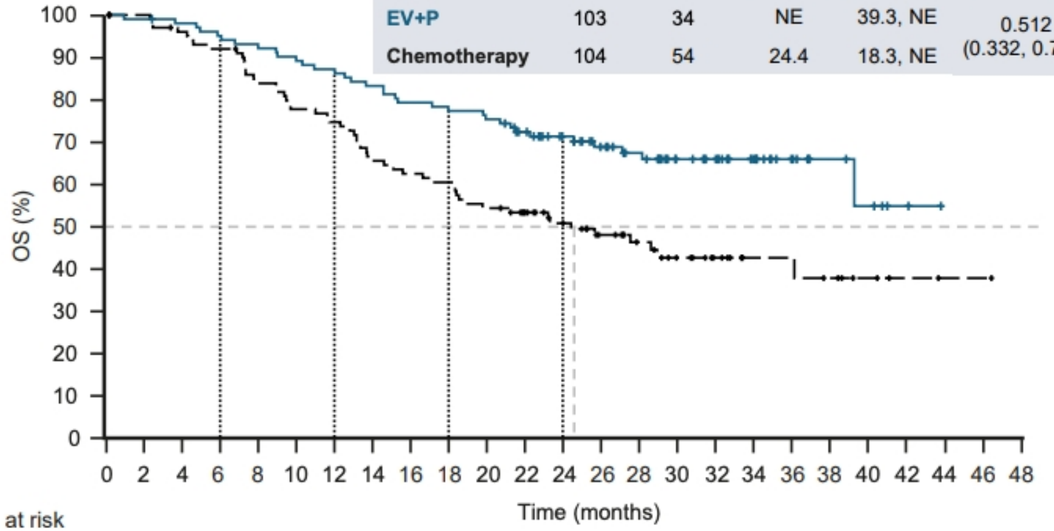
No. at risk

EV+P	103	101	90	78	72	64	60	55	52	48	43	42	39	31	27	26	20	11	7	5	2	0
Chemotherapy	104	95	76	52	37	29	26	23	18	15	14	14	13	10	5	5	3	2	2	2	0	0

OS

(B) LN-Only Metastases

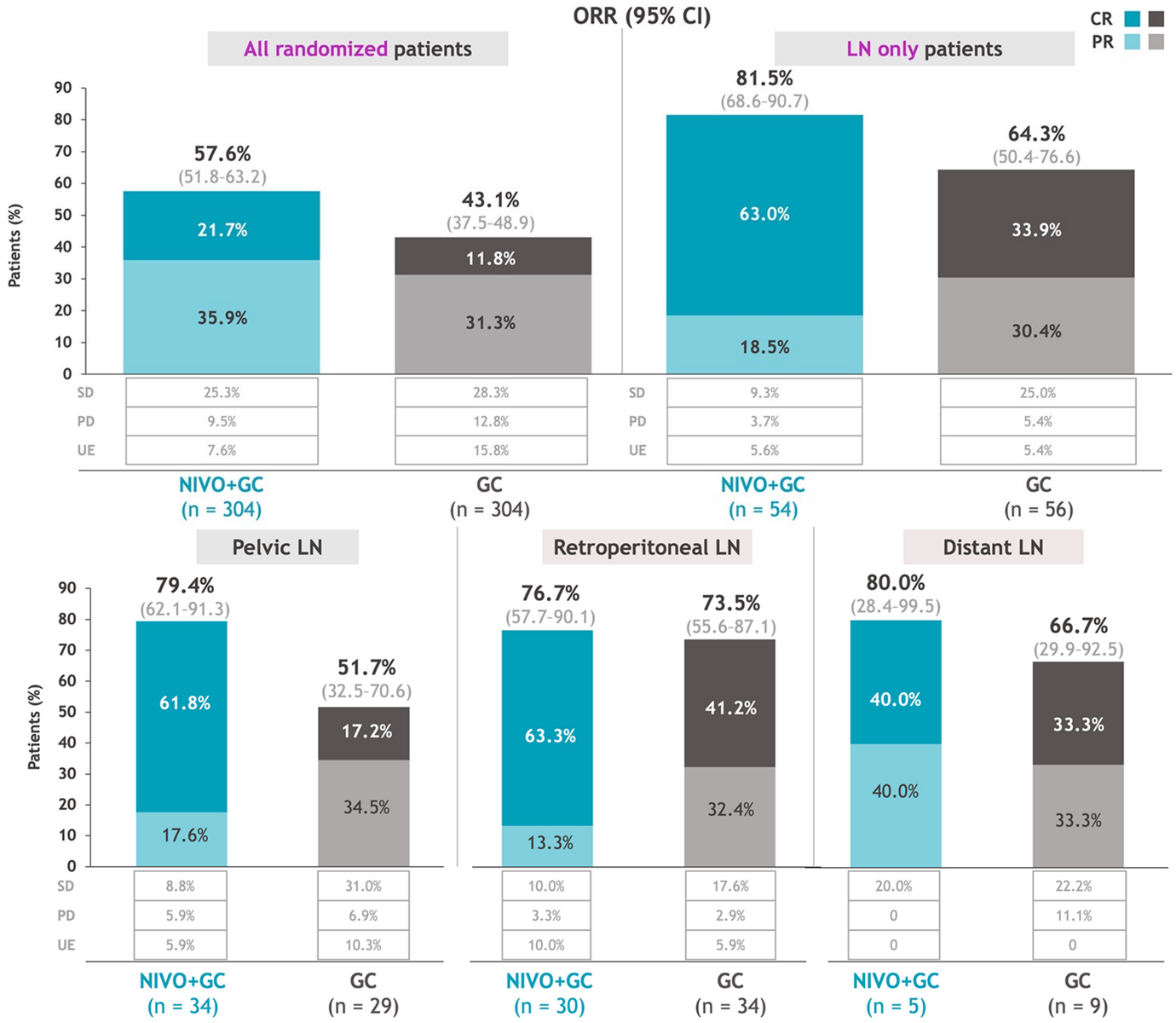
	N	Events	Median (months)	95% CI	Hazard ratio (95% CI)
EV+P	103	34	NE	39.3, NE	0.512 (0.332, 0.789)
Chemotherapy	104	54	24.4	18.3, NE	



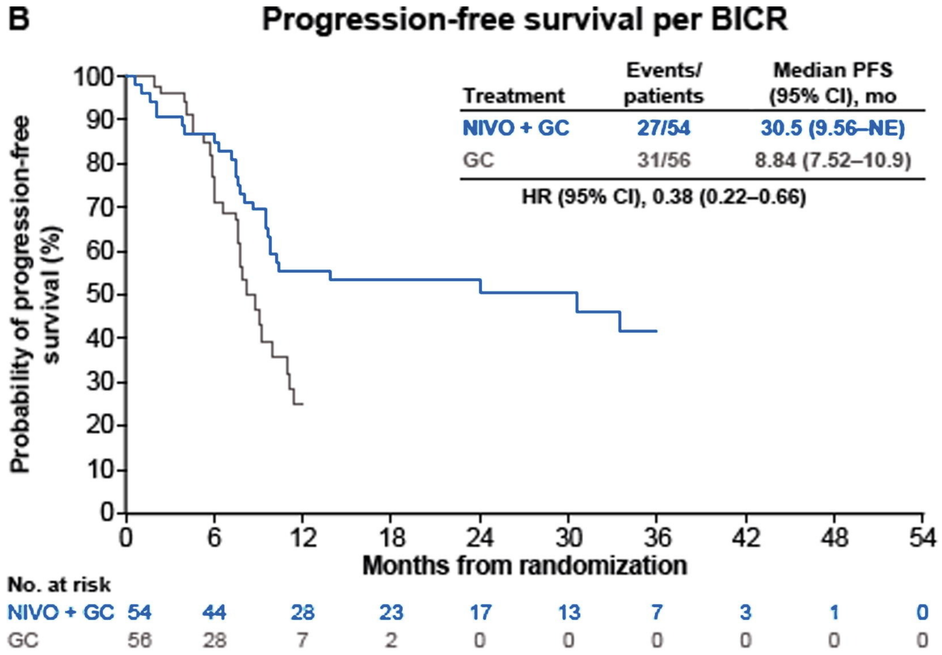
No. at risk

EV+P	103	102	100	96	94	91	88	85	81	79	77	70	61	52	46	34	30	21	13	7	5	2	0	0	0
Chemotherapy	104	101	96	92	83	77	74	65	62	60	54	47	39	32	26	20	15	9	9	7	4	2	1	1	0

CheckMate-901



B



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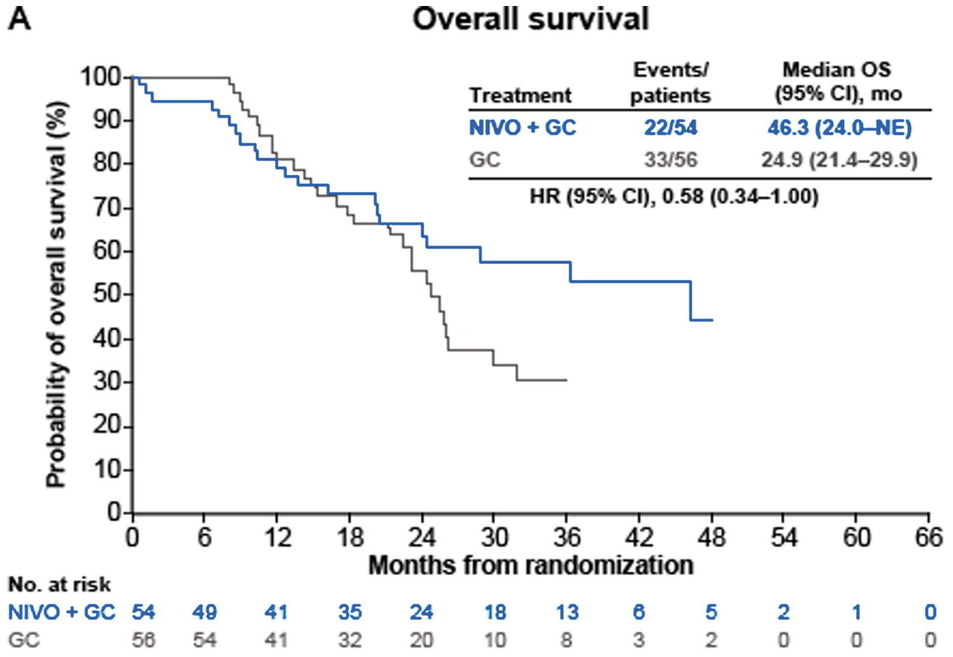
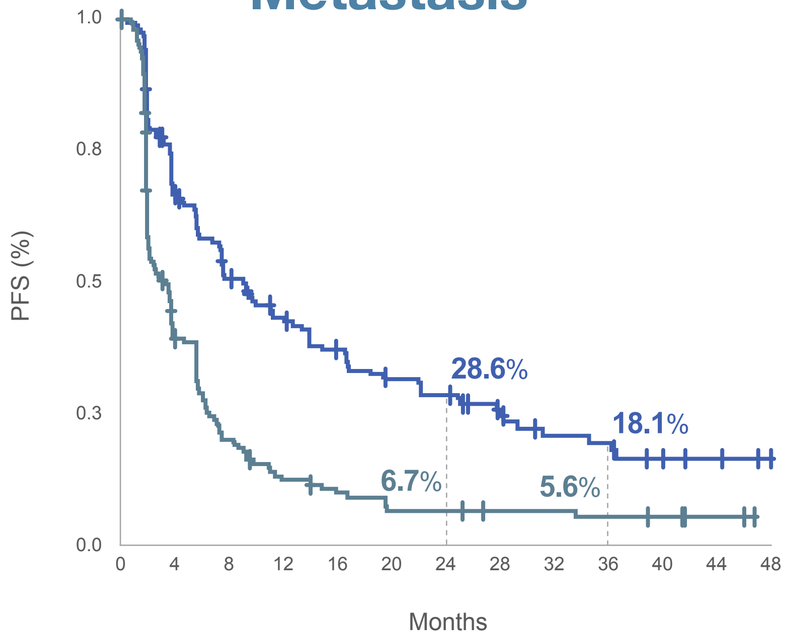


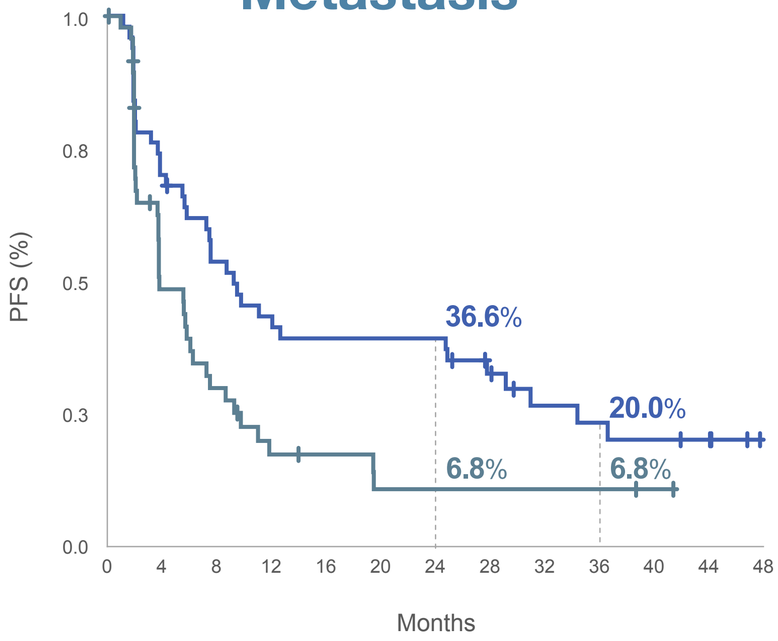
JAVELIN Bladder 100: Progression-Free Survival

Non-Visceral Metastasis



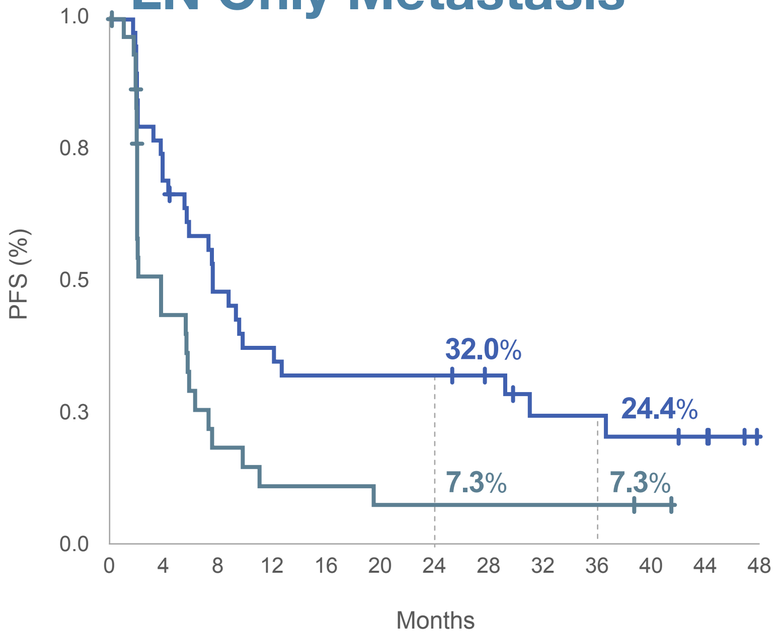
Avelumab (n=159)	BSC (n=159)
Median PFS, months (95% CI)	
9.0 (5.7, 12.6)	3.3 (2.0, 3.7)
Stratified HR (95% CI)	
0.45 (0.35, 0.59)	

Lymph Node Only Metastasis



Avelumab (n=51)	BSC (n=51)
Median PFS, months (95% CI)	
8.7 (5.4, 24.7)	3.7 (2.0, 6.0)
Stratified HR (95% CI)	
0.51 (0.31, 0.84)	

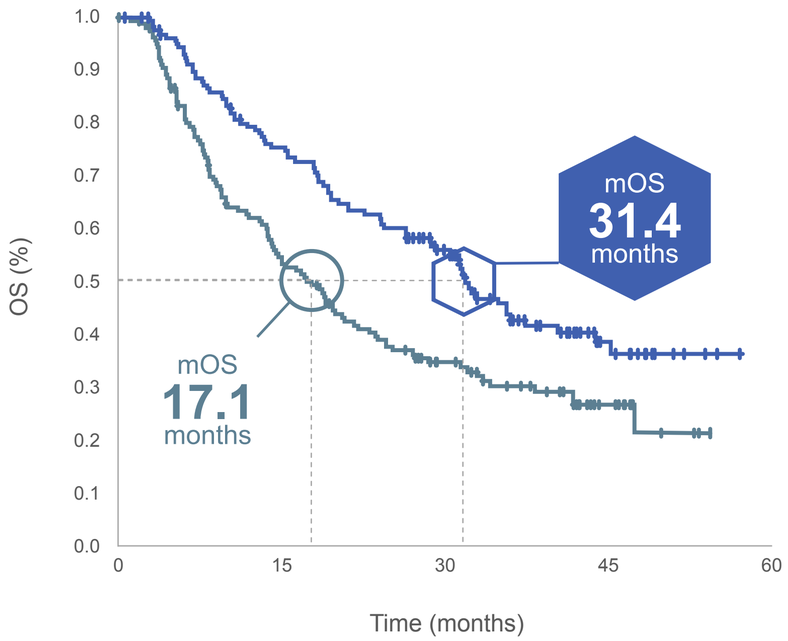
Pelvic/Retroperitoneal LN Only Metastasis



Avelumab (n=42)	BSC (n=35)
Median PFS, months (95% CI)	
7.5 (4.2, 12.0)	3.7 (1.9, 5.7)
Stratified HR (95% CI)	
0.44 (0.24, 0.79)	

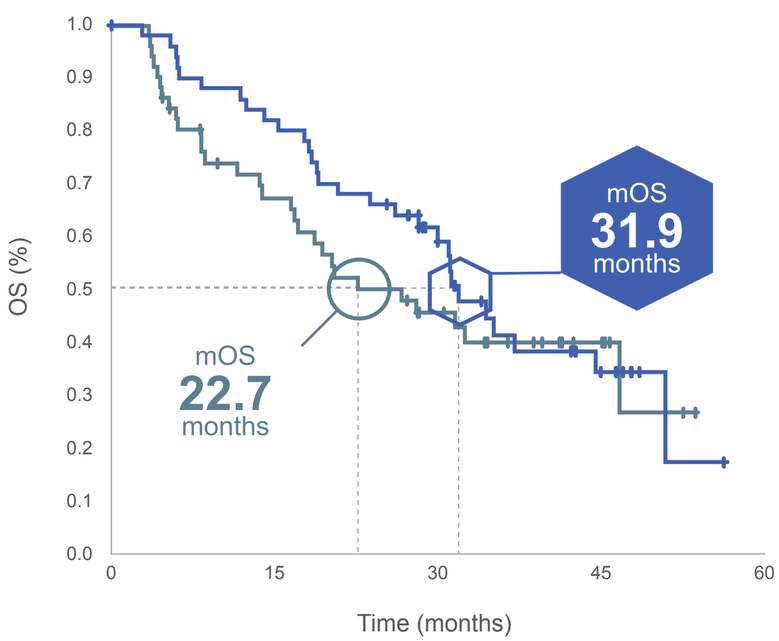
JAVELIN Bladder 100: Overall Survival

Non-Visceral Metastasis



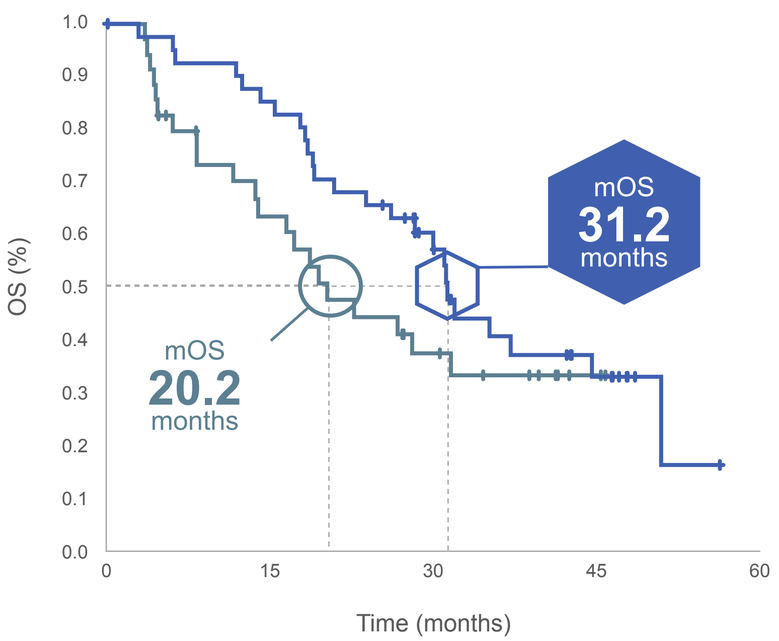
Avelumab (n=159)	BSC (n=159)
Median OS, months (95% CI)	
31.4 (26.1, 36.8)	17.1 (13.7, 21.3)
Stratified HR (95% CI)	
0.60 (0.45, 0.79)	

Lymph Node Only Metastasis



Avelumab (n=51)	BSC (n=51)
Median OS, months (95% CI)	
31.9 (26.1, 44.5)	22.7 (16.5, NE)
Stratified HR (95% CI)	
0.86 (0.51, 1.47)	

Pelvic/Retroperitoneal LN Only Metastasis



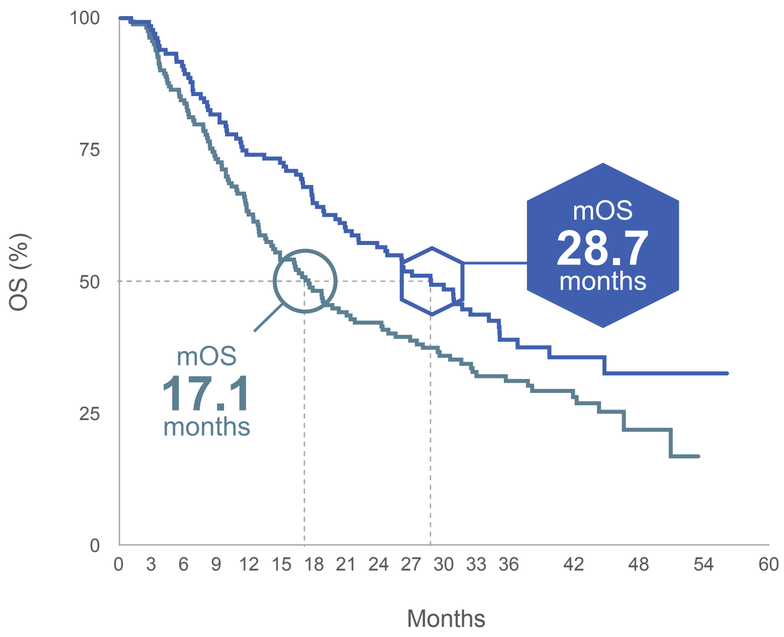
Avelumab (n=42)	BSC (n=35)
Median OS, months (95% CI)	
31.2 (23.8, 44.5)	20.2 (13.7, NE)
Stratified HR (95% CI)	
0.72 (0.39, 1.31)	

Pt with Age ≥75 y/o had less favorable ECOG PS at baseline compared with younger Pts and overall population

	≥65 to <75 years		≥75 years		≥80 years		Overall population	
	BAVENCIO + BSC (n=136)	BSC alone (n=163)	BAVENCIO + BSC (n=85)	BSC alone (n=80)	BAVENCIO + BSC (n=28)	BSC alone (n=27)	BAVENCIO + BSC (n=350)	BSC alone (n=350)
Age, median (range), **years**	70.0 (65.0-74.0)	70.0 (65.0-74.0)	77.0 (75.0-90.0)	78.0 (75.0-89.0)	81.0 (80.0-90.0)	82.0 (80.0-89.0)	68.0 (37.0-90.0)	69.0 (32.0-89.0)
Sex, n (%)								
Male	108 (79.4)	137 (84.0)	67 (78.8)	62 (77.5)	21 (75.0)	21 (77.8)	266 (76.0)	275 (78.6)
Female	28 (20.6)	26 (16.0)	18 (21.2)	18 (22.5)	7 (25.0)	6 (22.2)	84 (24.0)	75 (21.4)
Pooled geographic region, n (%)								
Europe	83 (61.0)	96 (58.9)	46 (54.1)	42 (52.5)	14 (50.0)	15 (55.6)	214 (61.1)	203 (58.0)
North America	5 (3.7)	7 (4.3)	4 (4.7)	4 (5.0)	0	2 (7.4)	12 (3.4)	22 (6.3)
Asia	30 (22.1)	39 (23.9)	18 (21.2)	16 (20.0)	5 (17.9)	4 (14.8)	73 (20.9)	74 (21.1)
Australasia	14 (10.3)	14 (8.6)	13 (15.3)	14 (17.5)	7 (25.0)	4 (14.8)	34 (9.7)	37 (10.6)
Rest of the world	4 (2.9)	7 (4.3)	4 (4.7)	4 (5.0)	2 (7.1)	2 (7.4)	17 (4.9)	14 (4.0)
ECOG performance status, n (%)								
0	84 (61.8)	100 (61.3)	47 (55.3)	44 (55.0)	12 (42.9)	12 (44.4)	213 (60.9)	211 (60.3)
≥1	52 (38.2)	63 (38.7)	38 (44.7)	36 (45.0)	16 (57.1)	15 (55.6)	137 (39.1)	139 (39.7)
PD-L1 status, n (%)								
Positive	72 (52.9)	73 (44.8)	55 (64.7)	47 (58.8)	20 (71.4)	15 (55.6)	189 (54.0)	169 (48.3)
Negative	57 (41.9)	63 (38.7)	27 (31.8)	28 (35.0)	8 (28.6)	11 (40.7)	139 (39.7)	131 (37.4)
Unknown	7 (5.1)	27 (16.6)	3 (3.5)	5 (6.3)	0	1 (3.7)	22 (6.3)	50 (14.3)
Best response to 1L chemotherapy, n (%)								
CR or PR	96 (70.6)	118 (72.4)	61 (71.8)	55 (68.8)	20 (71.4)	20 (74.1)	253 (72.3)	252 (72.0)
SD	410 (29.4)	45 (27.6)	24 (28.2)	25 (31.3)	8 (28.6)	7 (25.9)	97 (27.7)	98 (28.0)
Site of metastasis at start of 1L chemotherapy, n (%)								
Visceral	78 (57.4)	95 (58.3)	45 (52.9)	38 (47.5)	16 (57.1)	12 (44.4)	191 (54.6)	191 (54.6)
Non-visceral	58 (42.6)	68 (41.7)	40 (47.1)	42 (52.5)	12 (42.9)	15 (55.6)	159 (45.4)	159 (45.4)

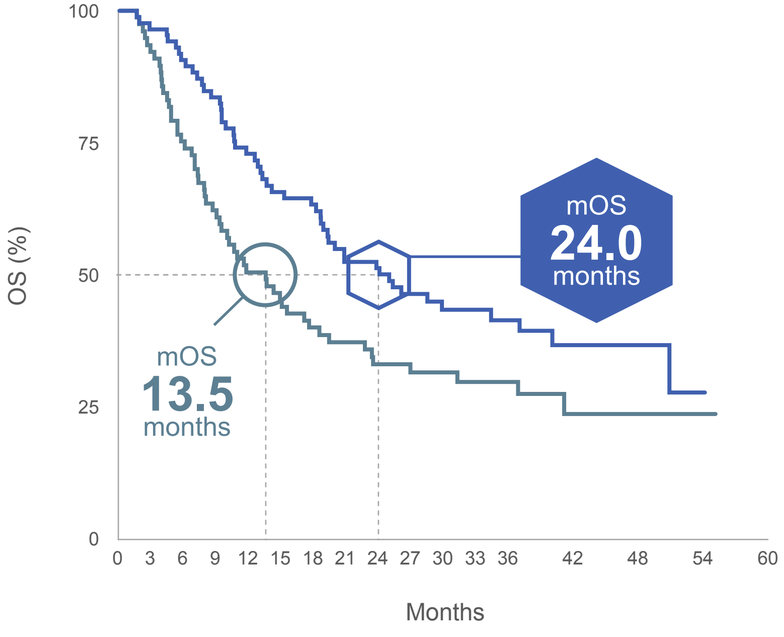
OS from randomization in older age subgroups - The trend to old age

≥65 to <75 years



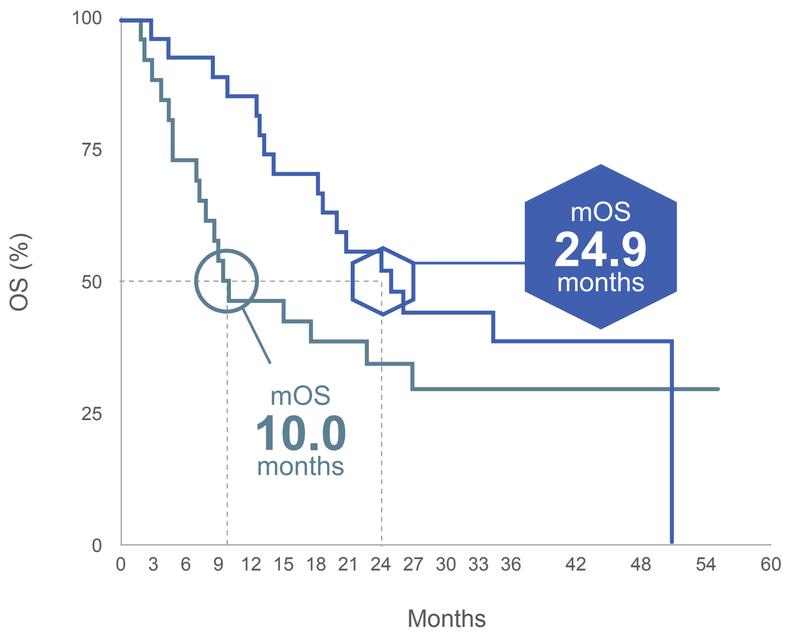
Avelumab (n=136)	BSC (n=163)
mOS, months (95% CI)	
28.7 (20.9, 35.1)	17.1 (12.9, 21.3)
Stratified HR (95% CI)	
0.73 (0.543, 0.974)	

≥75 to <80 years



Avelumab (n=85)	BSC (n=80)
mOS, months (95% CI)	
24.0 (18.6, 37.0)	13.5 (8.6, 18.5)
Stratified HR (95% CI)	
0.59 (0.401, 0.877)	

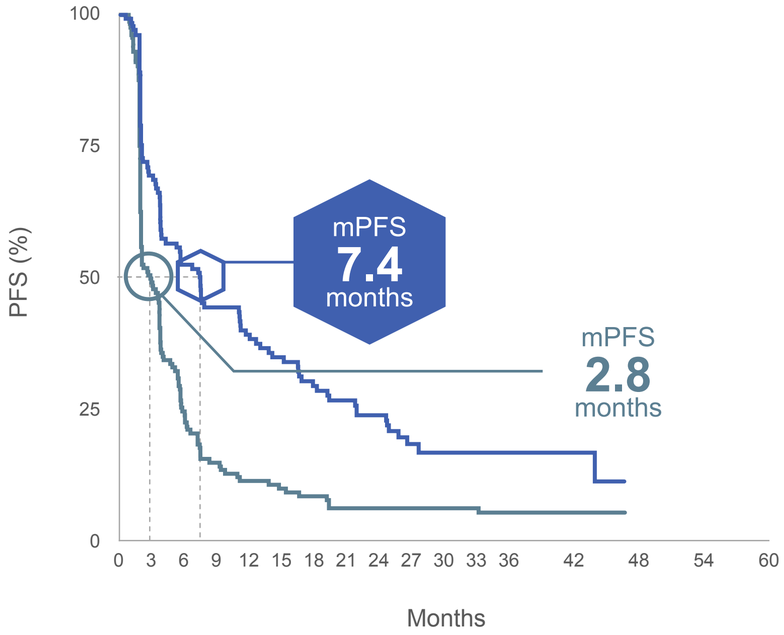
≥80 years



Avelumab (n=28)	BSC (n=27)
mOS, months (95% CI)	
24.9 (14.1, NE)	10.0 (7.0, 26.9)
Stratified HR (95% CI)	
0.57 (0.284, 1.155)	

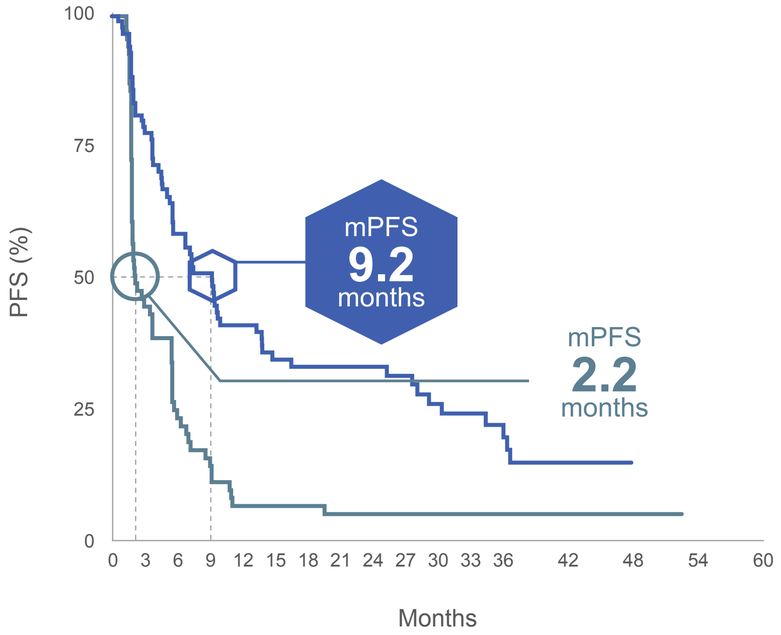
PFS from randomization in older age subgroups - The trend to old age

≥65 to <75 years



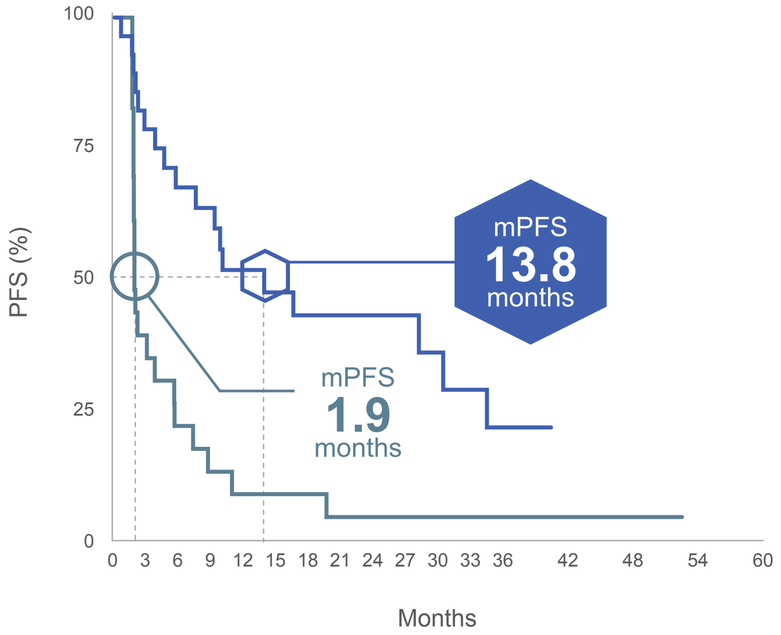
Avelumab (n=136)	BSC (n=163)
mOS, months (95% CI)	
7.4 (3.7, 11.2)	2.8 (1.9, 3.7)
Stratified HR (95% CI)	
0.51 (0.389, 0.666)	

≥75 to <80 years



Avelumab (n=85)	BSC (n=80)
mOS, months (95% CI)	
9.2 (5.6, 13.3)	2.2 (1.9, 3.7)
Stratified HR (95% CI)	
0.38 (0.266, 0.554)	

≥80 years

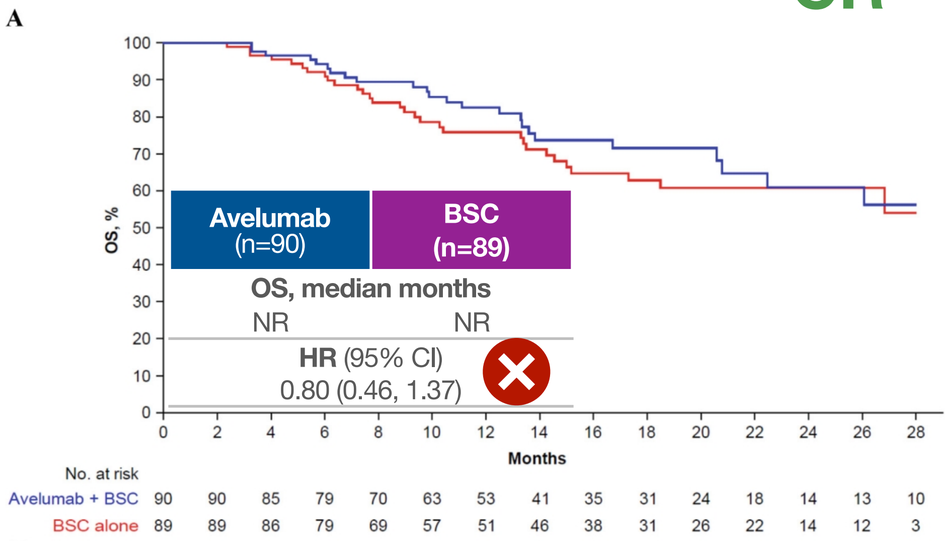


Avelumab (n=28)	BSC (n=27)
mOS, months (95% CI)	
13.8 (5.7, 30.3)	1.9 (1.7, 3.7)
Stratified HR (95% CI)	
0.27 (0.129, 0.560)	

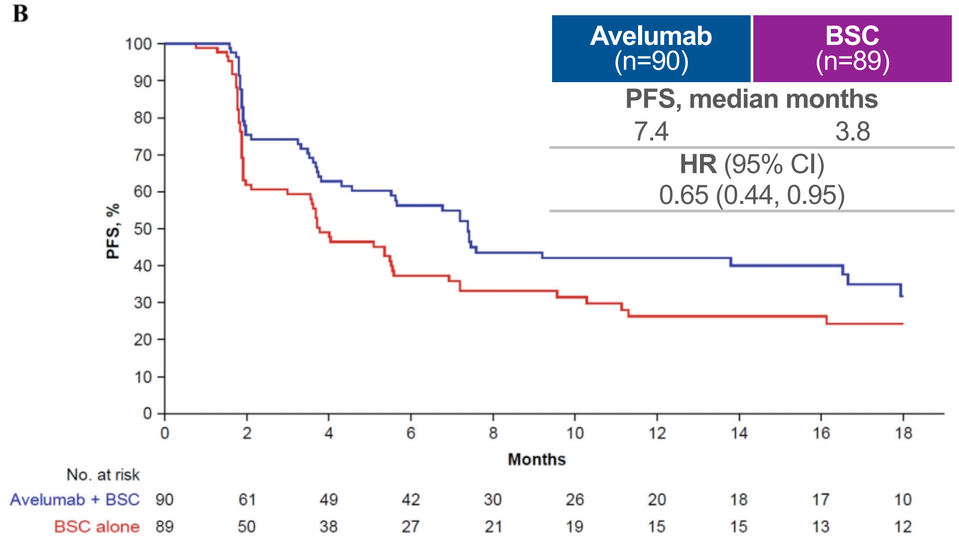
OS and PFS by Response - CR vs PR

CR

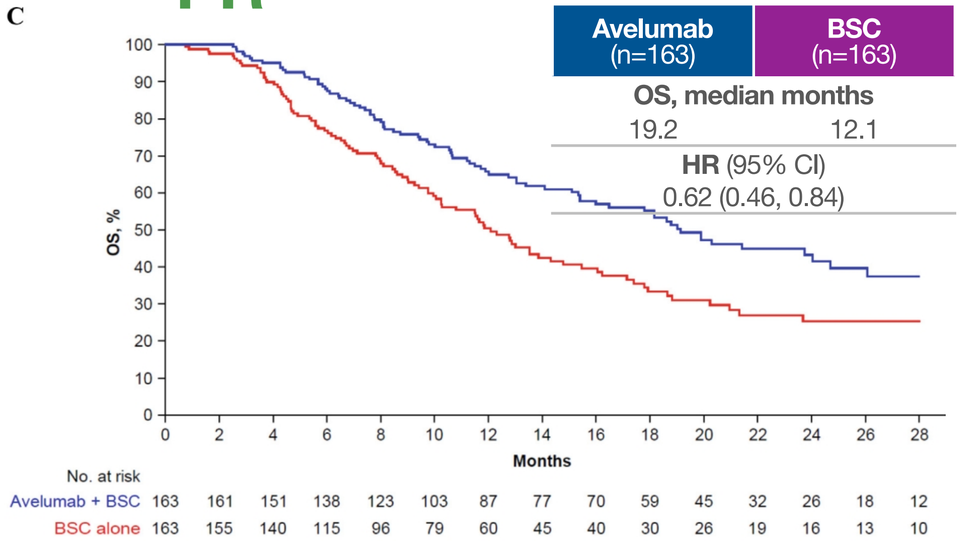
OS

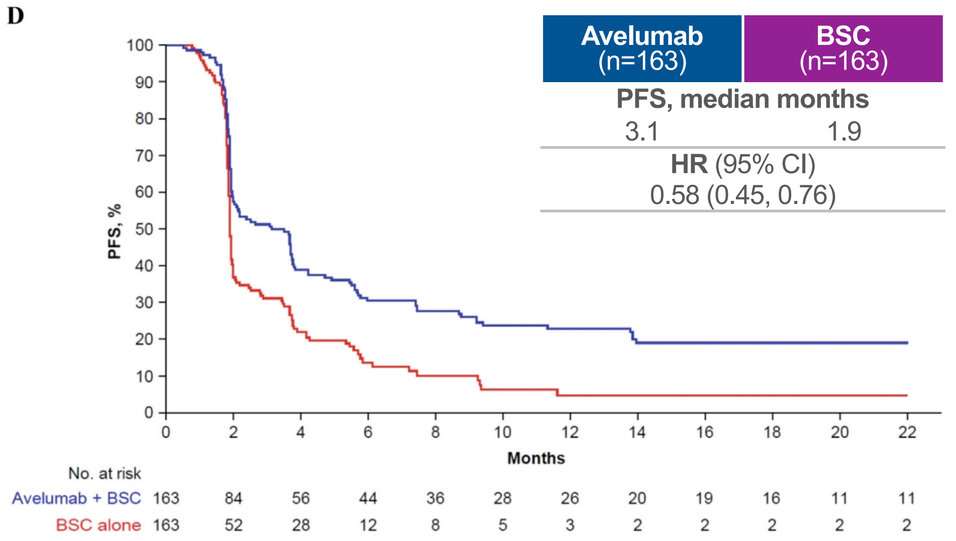


PFS



PR





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Outline

- Current guidelines and their evidence
- Difference between EV-302, CM-901, JB-100
- Under NHI Situation
- **Case sharing**

Take Home Message

- 1st-line treatment for la/mUC , we can choose regimen as below:
  - Enfortumab Vedotin/Pembrolizumab (EV-302)
  - Nivolumab/Gemcitabine/Cisplatin (CM-901)
  - Avelumab maintenance (JB-100)
- Under NHI, Avelumab maintenance is only choice in la/mUC with PD-L1+
- Who was feasible for Avelumab
  - Contra-indication for EV-302: Diabetes with poor control…
  - Old age, Lymph node only
- Well discussion with patient/family is very important