5th ANNUAL UC COURSE
Emerging personalized therapies for the management of urothelial carcinomas

V CURSO ANUAL DE UC
Terapias personalizadas emergentes en el manejo del carcinoma urotelial

Classic platinum-based chemo or new combination in 1st line mUC?

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DISCLOSURES

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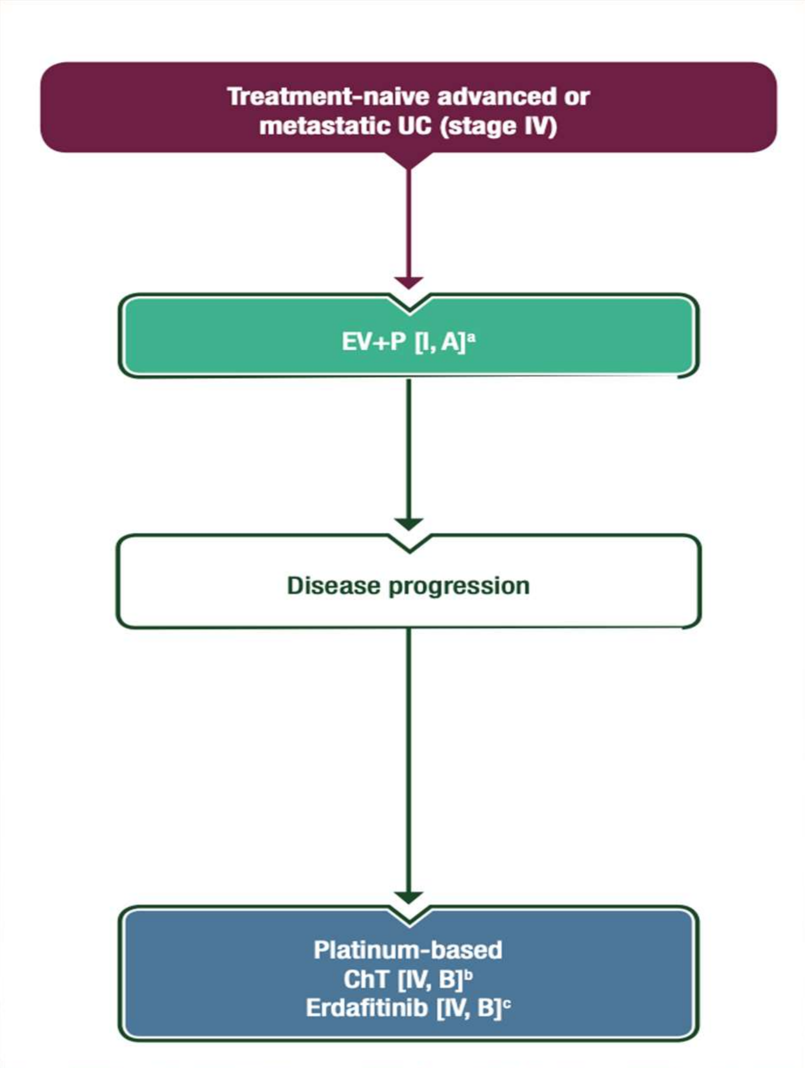
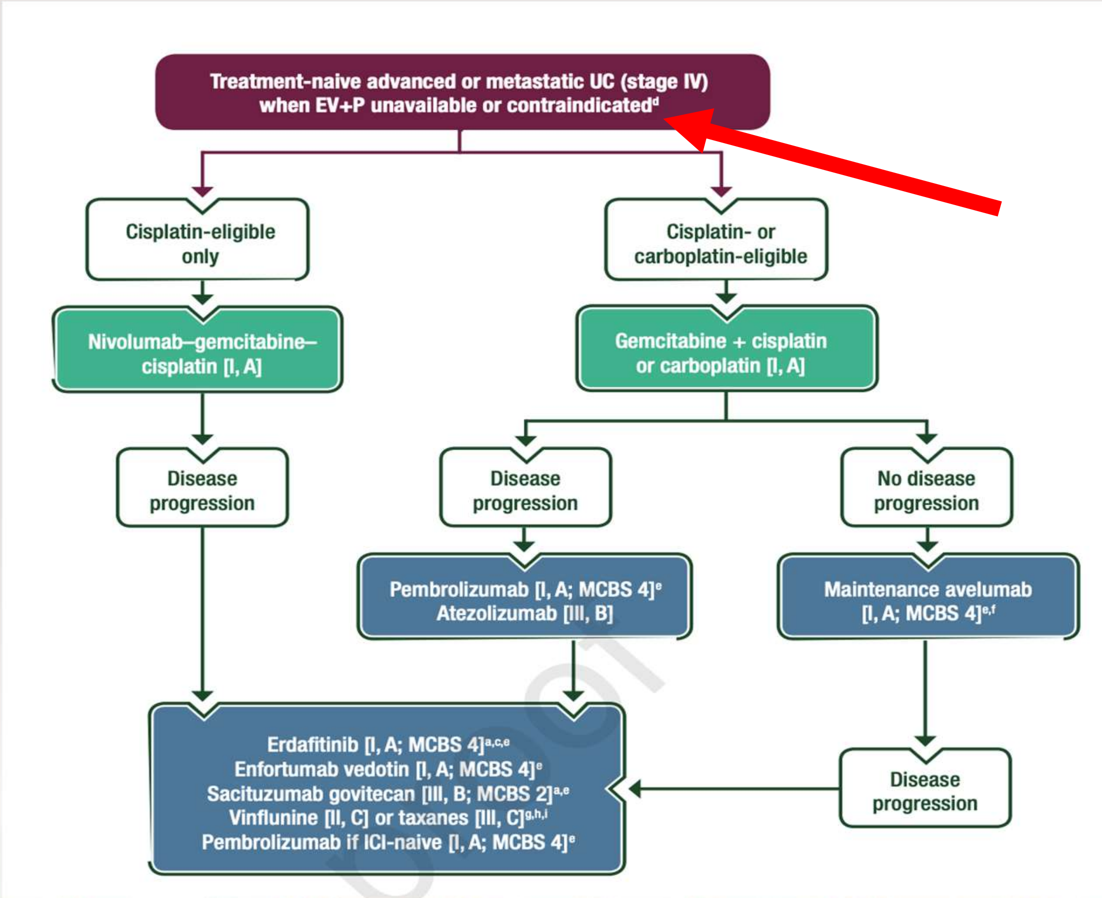
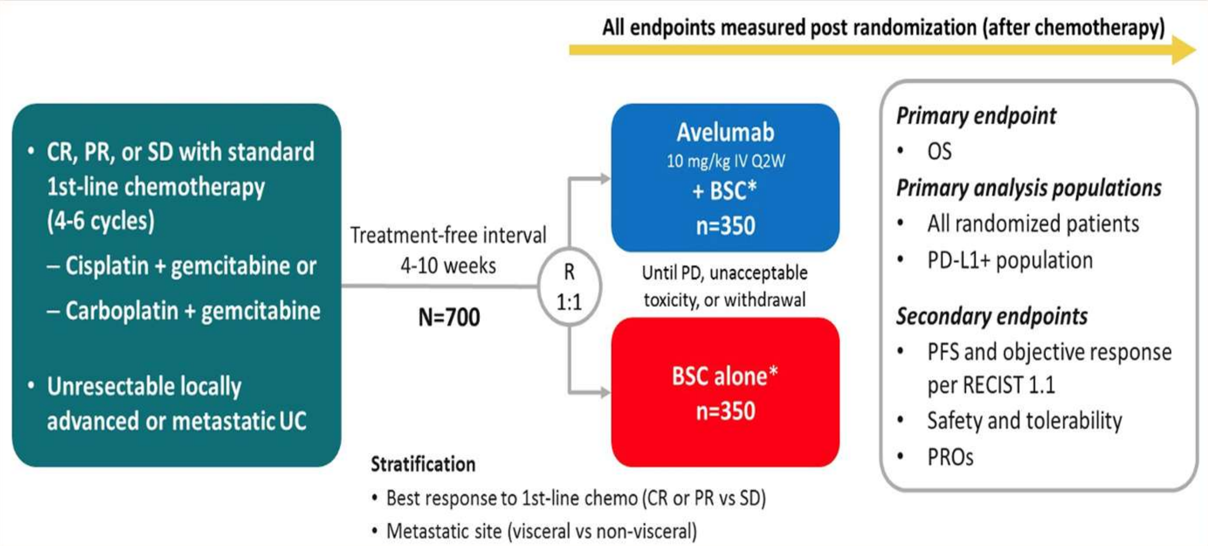
Travel arrangements: Janssen, Roche, Pfizer, BMS, Ipsen, MSD

What do the guidelines say?

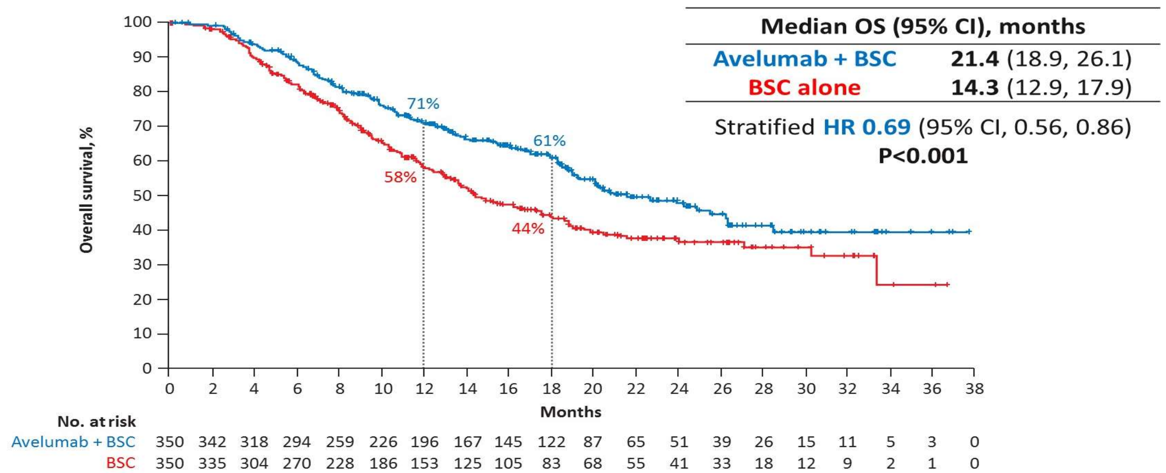




Powles et al. Ann Oncol 2024



OS in the overall population



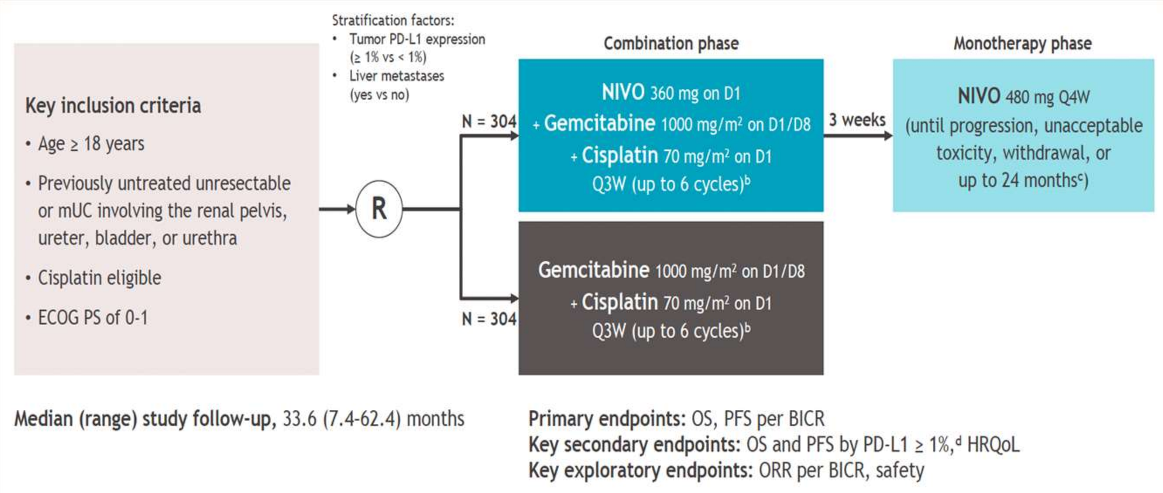
State-of-the-art

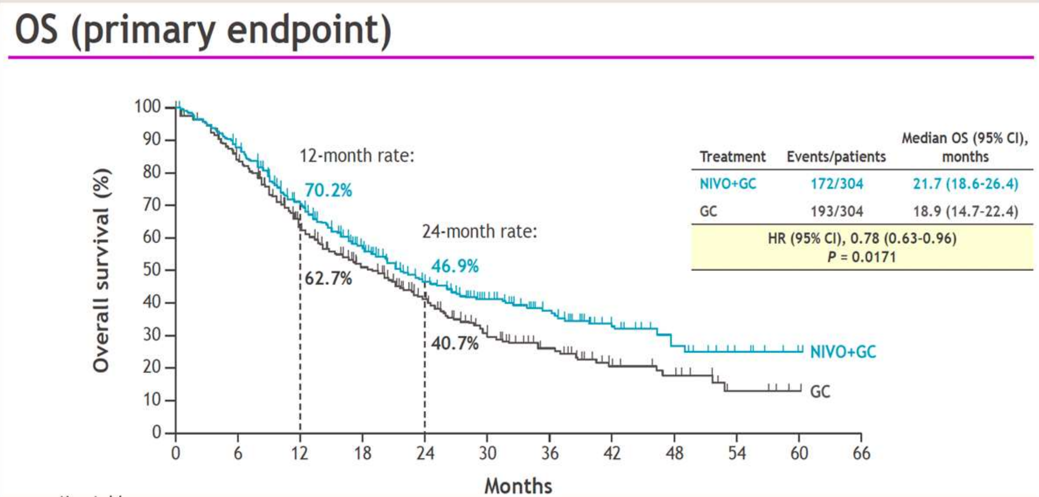
OS improvement regardless:
- PD-L1 expression
- Cis- o Carbo- as 1st line chemo
- Quality of response (CR,PR,SD)

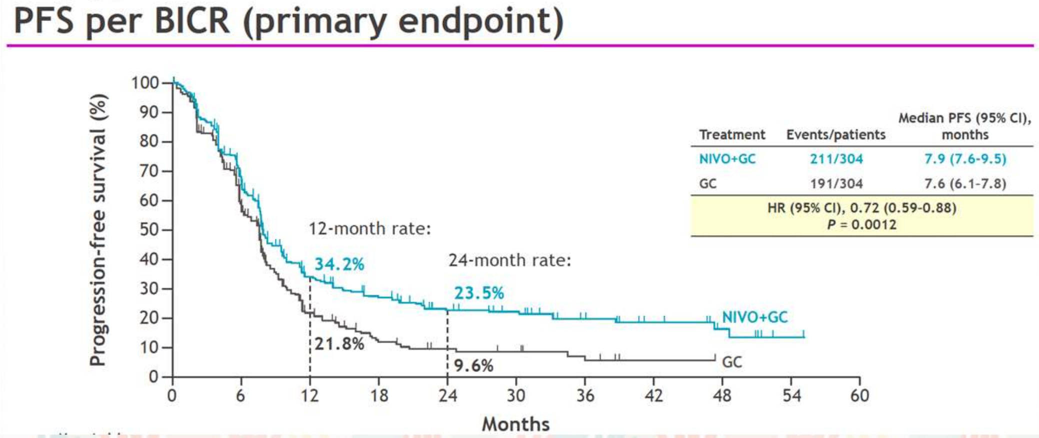
Several controversies:
- Selected population (responders)
- Number of chemo cycles
- Are we wasting lines of therapy?

Powles et al. N Engl J Med 2020

A new option for 1st line therapy

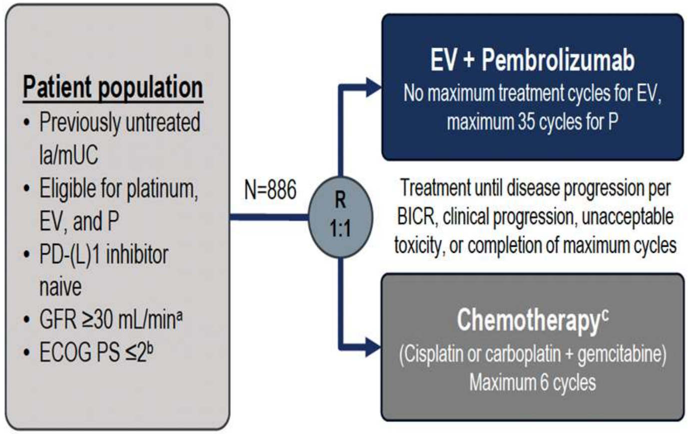






Van der Heijden et al. N Engl J Med 2023

…AND A NEW STANDARD THERAPY



Dual primary endpoints:

- PFS by BICR
- OS

Select secondary endpoints:

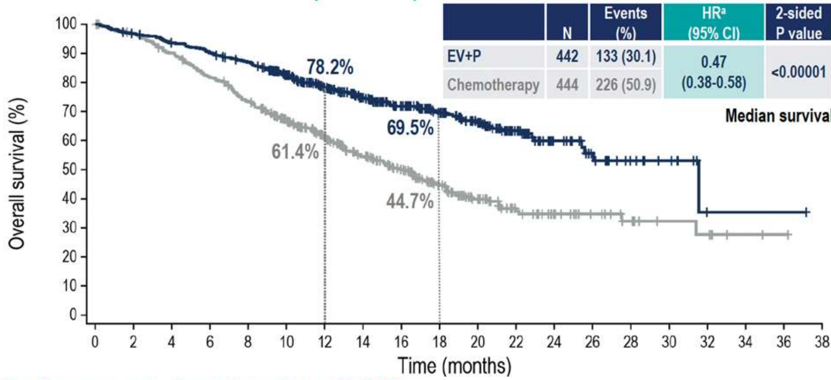
- ORR per RECIST v1.1 by BICR and investigator assessment
- Safety

Overall Survival

Risk of death was reduced by 53% in patients who received EV+P

	N	Events (%)	HR[a] (95% CI)	2-sided P value	mOS (95% CI), months
EV+P	442	133 (30.1)	0.47 (0.38-0.58)	<0.00001	31.5 (25.4-NR)
Chemotherapy	444	226 (50.9)			16.1 (13.9-18.3)

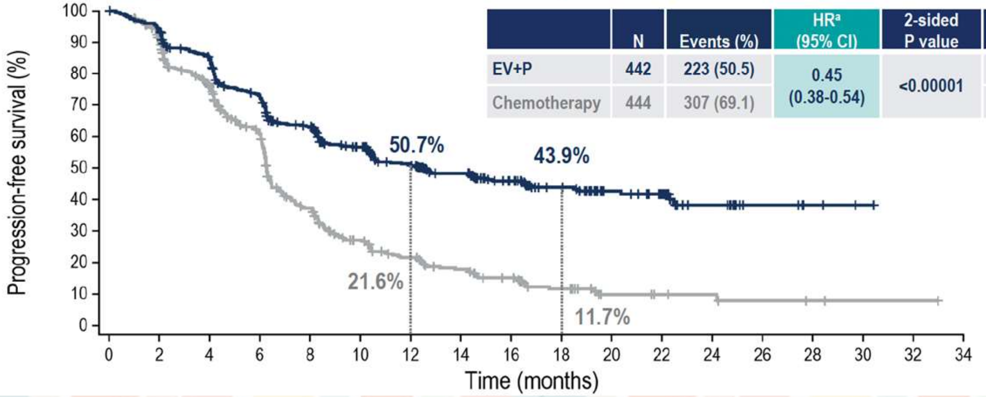
Median survival follow-up: 17.2 months



Progression-Free Survival per BICR

Risk of progression or death was reduced by 55% in patients who received EV+P

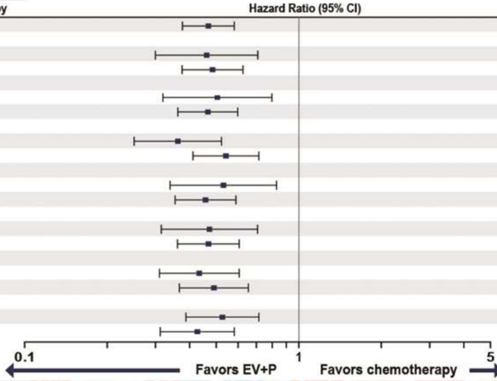
	N	Events (%)	HR[a] (95% CI)	2-sided P value	mPFS (95% CI), months
EV+P	442	223 (50.5)	0.45 (0.38-0.54)	<0.00001	12.5 (10.4-16.6)
Chemotherapy	444	307 (69.1)			6.3 (6.2-6.5)



Subgroup Analysis of OS

OS benefit in select pre-specified subgroups was consistent with results in overall population

Subgroup	Events/N EV+P	Events/N Chemotherapy	Hazard Ratio (95% CI)
Overall	133/442	226/444	0.47 (0.38-0.58)
Age			
<65 years	39/144	58/135	0.46 (0.30-0.71)
≥65 years	94/298	168/309	0.48 (0.38-0.63)
Sex			
Female	32/98	54/108	0.51 (0.32-0.80)
Male	101/344	172/336	0.47 (0.36-0.60)
ECOG PS			
0	44/223	94/215	0.36 (0.25-0.53)
1-2	89/219	131/227	0.54 (0.41-0.72)
Primary disease site of origin			
Upper tract	38/135	45/104	0.53 (0.34-0.83)
Lower tract	94/305	180/339	0.46 (0.36-0.59)
Liver metastases			
Present	43/100	67/99	0.47 (0.32-0.71)
Absent	90/342	159/345	0.47 (0.36-0.61)
PD-L1 expression			
Low (CPS <10)	53/184	99/185	0.44 (0.31-0.61)
High (CPS ≥10)	79/254	125/254	0.49 (0.37-0.66)
Cisplatin eligibility			
Eligible	69/244	106/234	0.53 (0.39-0.72)
Ineligible	64/198	120/210	0.43 (0.31-0.59)



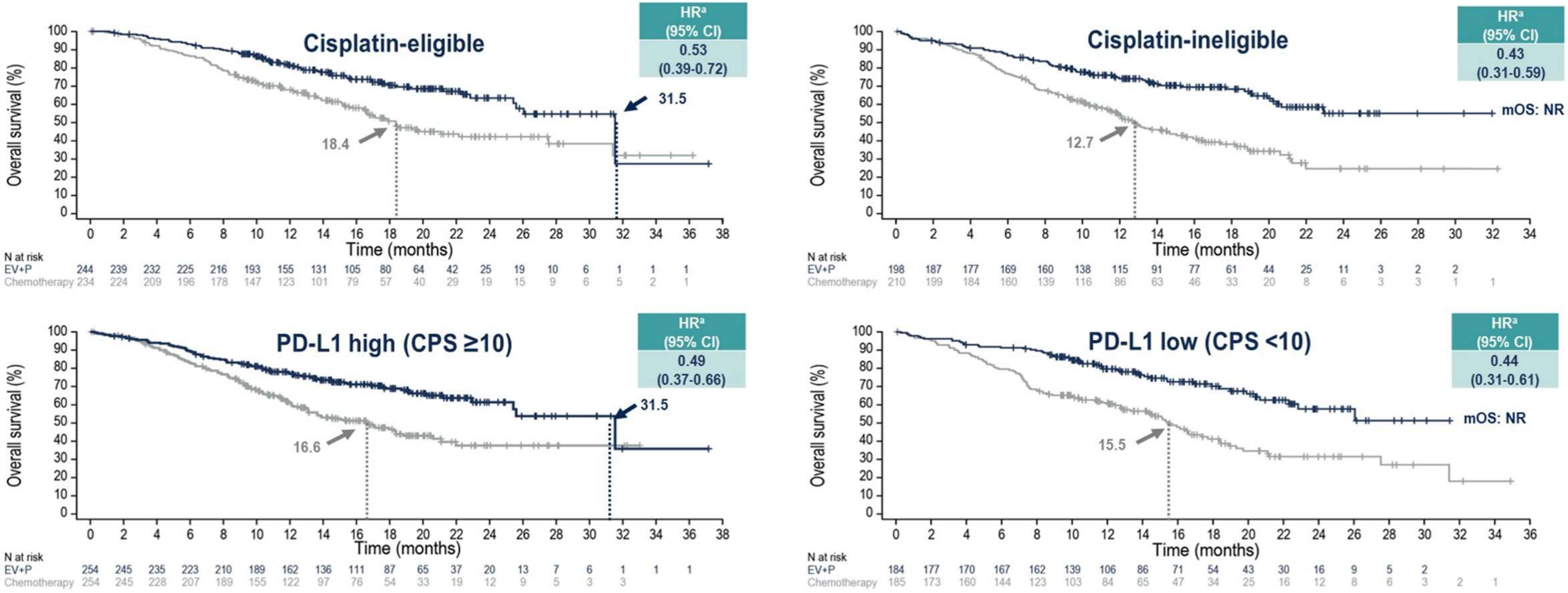
Powles T et al. N Engl J Med 2024

…AND A NEW STANDARD THERAPY

OS Subgroup Analysis: Cisplatin Eligibility and PD-L1 Expression

9

OS benefit was consistent with the overall population regardless of cisplatin eligibility or PD-L1 expression status



Powles T et al. N Engl J Med 2024

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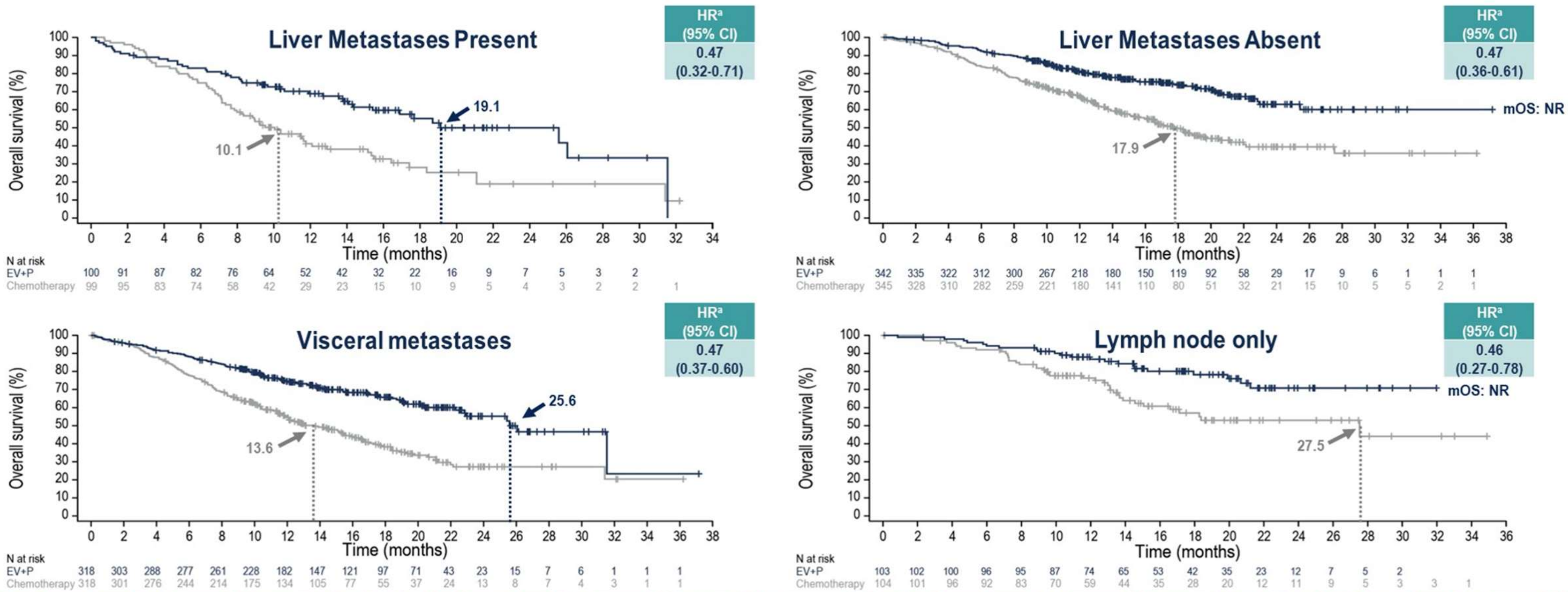
OS Subgroup Analysis: Liver Metastases and Metastatic Disease Site

OS benefit was consistent with the overall population regardless of the presence or absence of liver or visceral metastases



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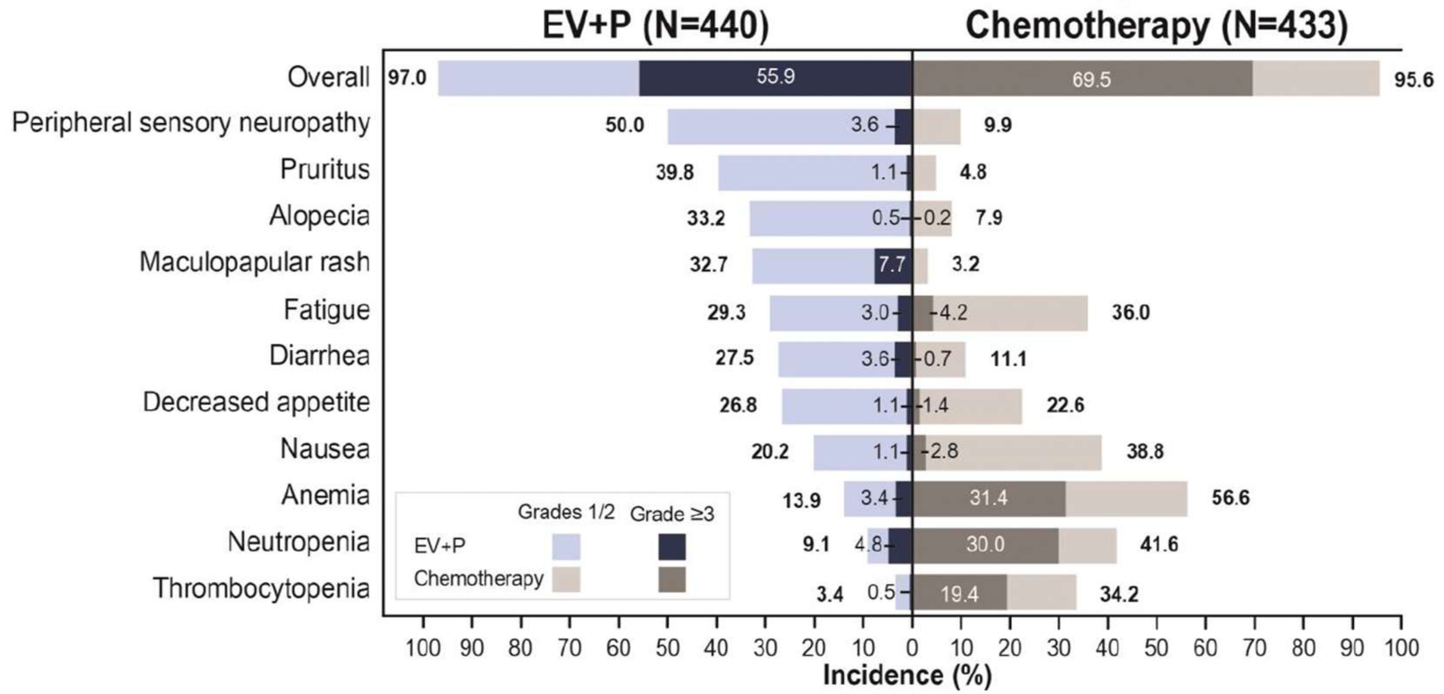
Treatment-Related Adverse Events

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

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

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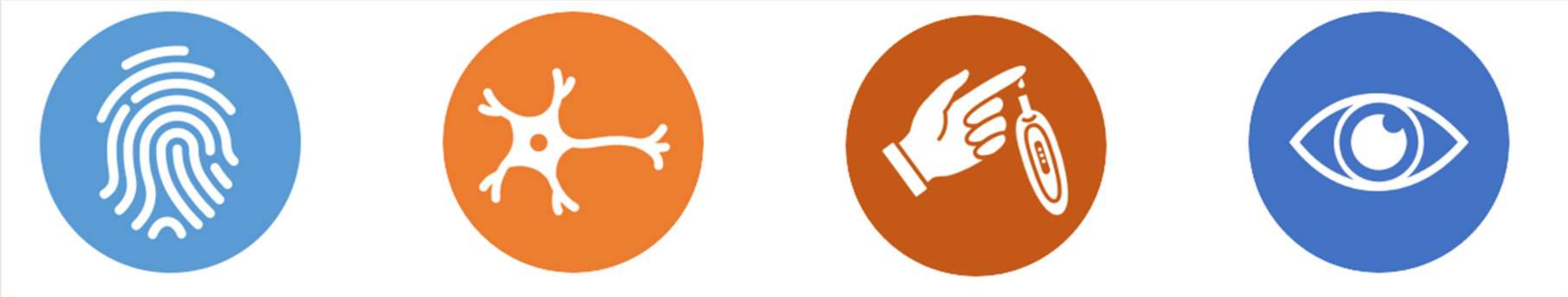

% ALL GRADE AEs	32.7%	50%	6.8%	21.3%
% G3-4	7.7%	3.6%	4.4%	0.7%

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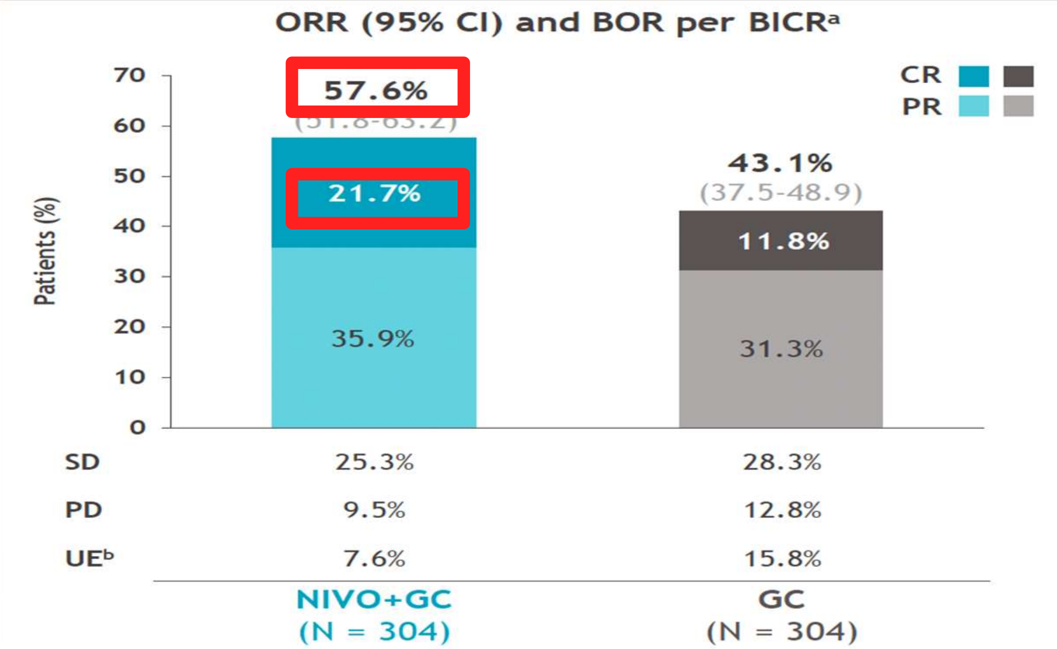
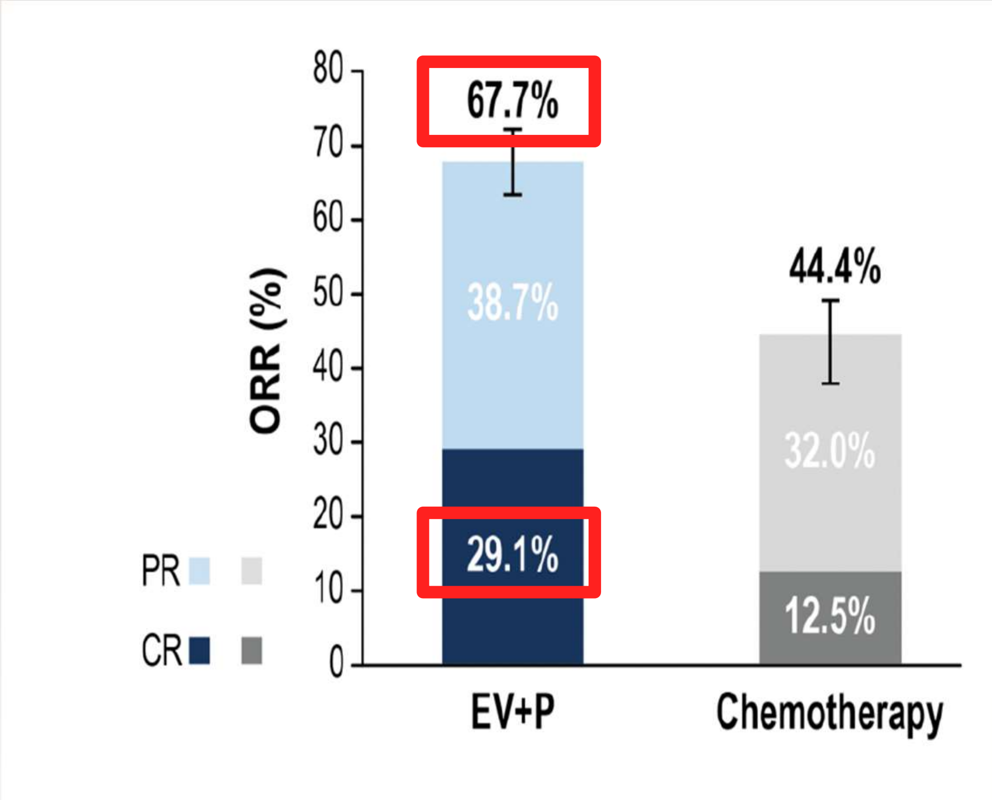
CIS-GEM-NIVO



Any objective response[c]	NIVO+GC (n = 175)	GC (n = 131)
Median TTR (Q1-Q3), months	2.1 (2.0-2.3)	2.1 (2.0-2.2)
Median DoR (95% CI), months	9.5 (7.6-15.1)	7.3 (5.7-8.9)

EV + PEMBRO



Median DOR (95% CI)	NR (20.2, NR)	7.0 (6.2, 10.2)

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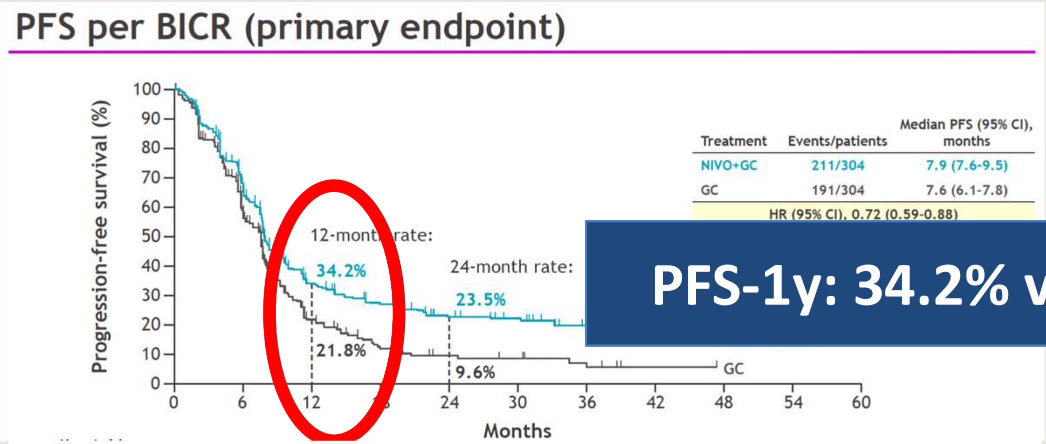
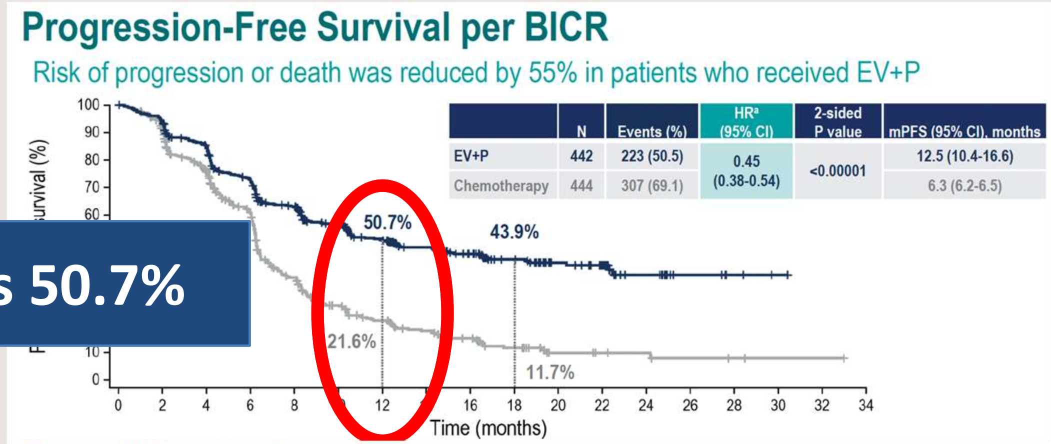
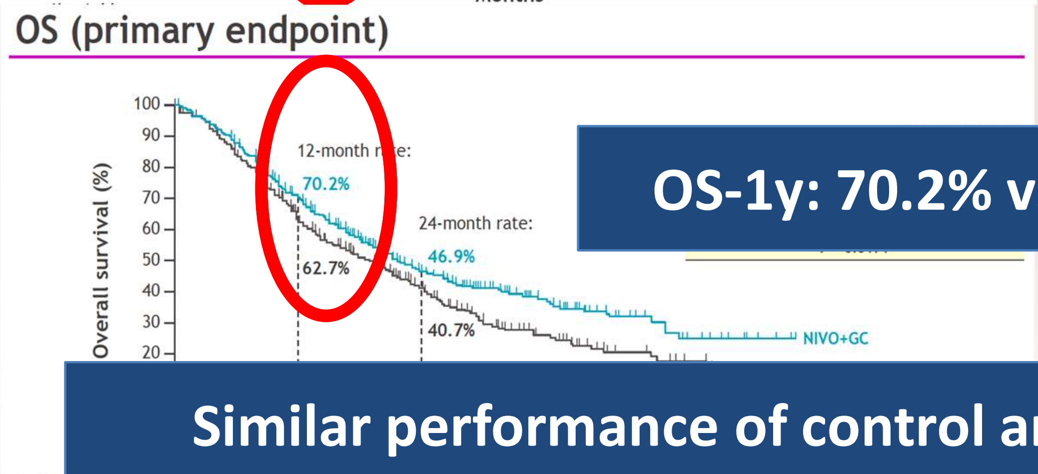
CIS-GEM-NIVO

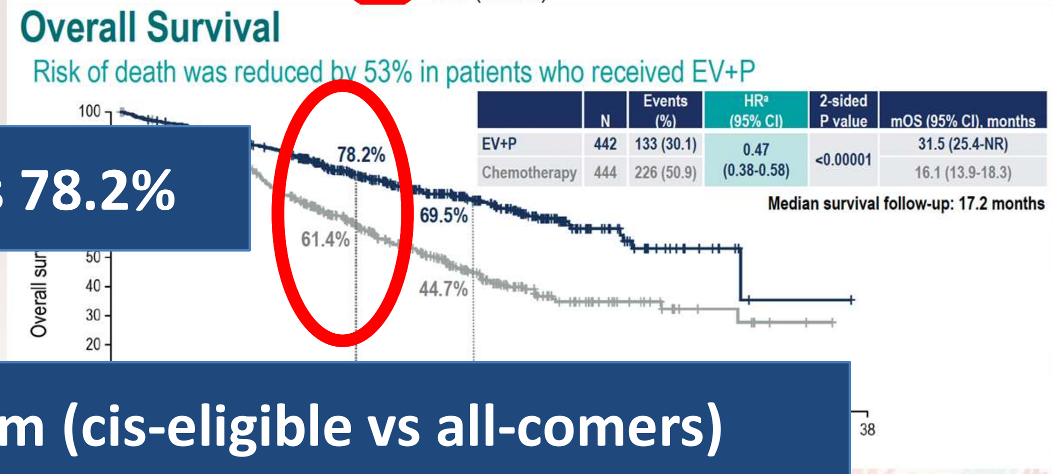
EV + PEMBRO





PFS-1y: 34.2% vs 50.7%





OS-1y: 70.2% vs 78.2%

Similar performance of control arm (cis-eligible vs all-comers)

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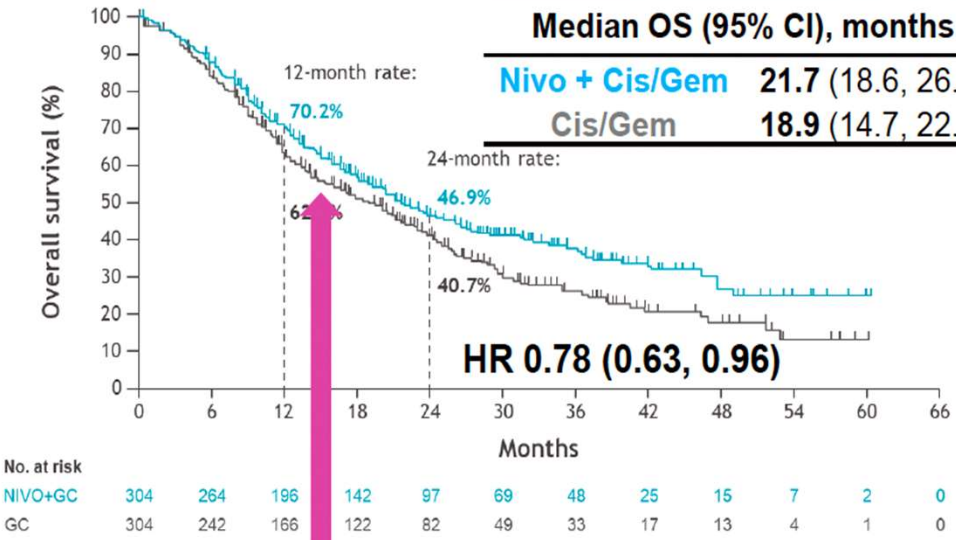
Nivo+Cis/Gem vs Cis/Gem

CheckMate 901 Study

Median OS (95% CI), months	
Nivo + Cis/Gem	**21.7** (18.6, 26.4)
Cis/Gem	**18.9** (14.7, 22.4)

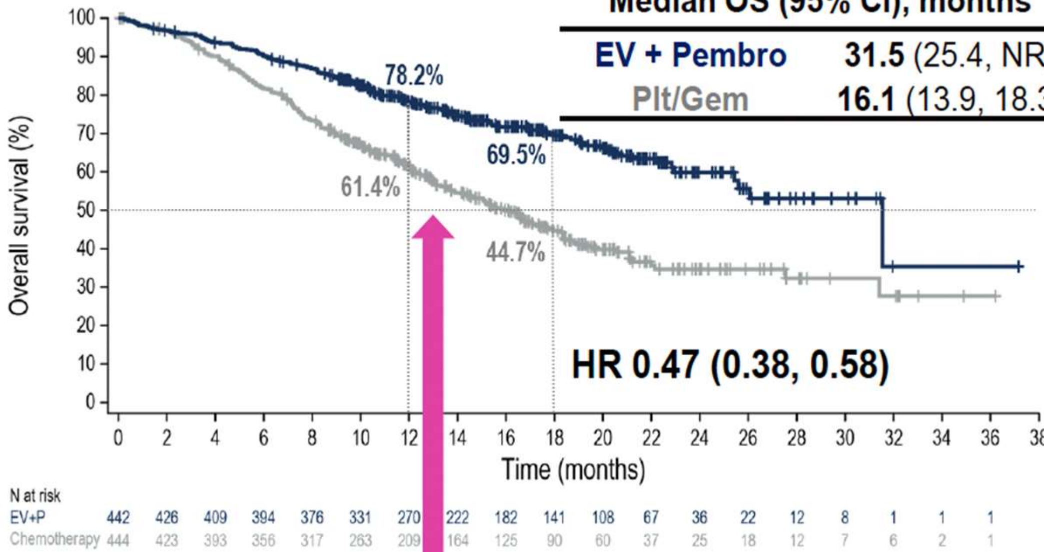


CONTROL ARM
20% received maintenance CPI (before PD)
40% received any subsequent CPI

EV+Pembro vs Plt/Gem

EV-302 Study

Median OS (95% CI), months	
EV + Pembro	**31.5** (25.4, NR)
Plt/Gem	**16.1** (13.9, 18.3)



CONTROL ARM
32% received maintenance CPI (before PD)
59% received any subsequent CPI

Presented by A.Apolo at ESMO 2023

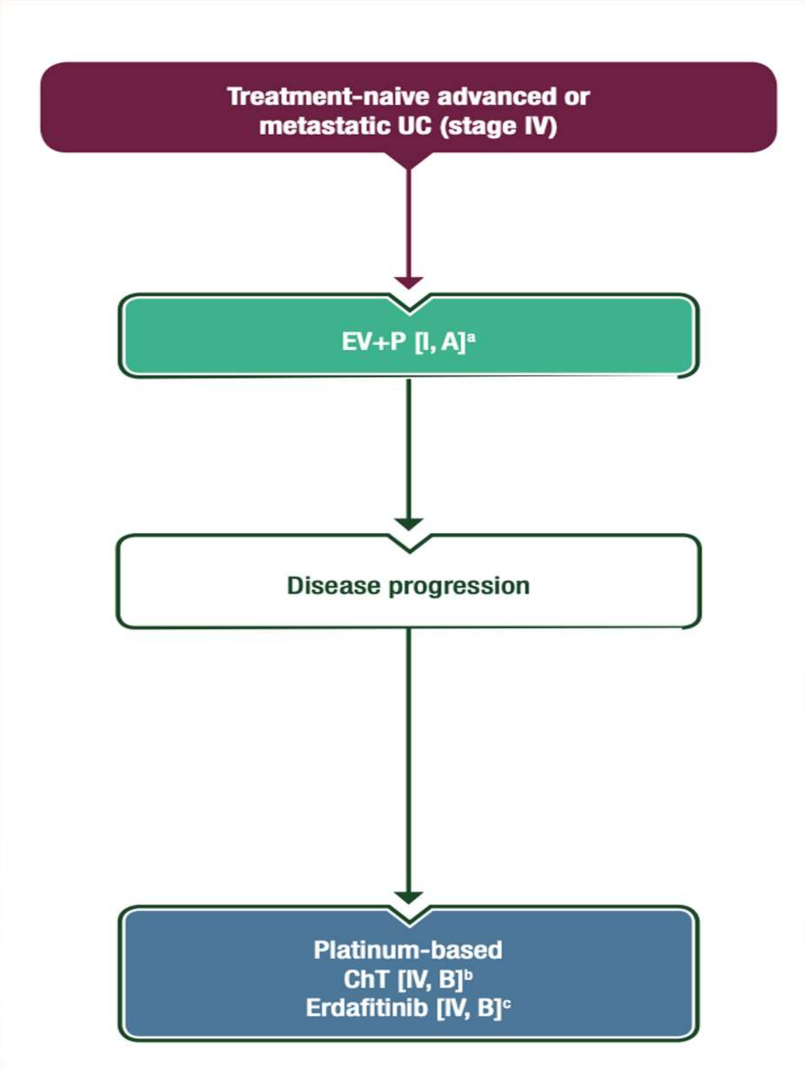
CIS-GEM-NIVO

ECOG performance-status score — no. (%)		
0	162 (53.3)	162 (53.3)
1	140 (46.1)	142 (46.7)
>1	2 (0.7)	0
Tumor type at initial diagnosis — no. (%)		
Urinary bladder	235 (77.3)	219 (72.0)
Renal pelvis	33 (10.9)	44 (14.5)
Other	36 (11.8)	41 (13.5)
Disease stage — no. (%)		
Metastatic	261 (85.9)	269 (88.5)
Locally unresectable or nonmetastatic	41 (13.5)	33 (10.9)
Not reported	2 (0.7)	2 (0.7)
Liver metastasis — no. (%)		
Yes	64 (21.1)	64 (21.1)
No	240 (78.9)	240 (78.9)

EV + PEMBRO

ECOG performance-status score — no. (%)§		
0	223 (50.5)	215 (48.4)
1	204 (46.2)	216 (48.6)
2	15 (3.4)	11 (2.5)
Data missing	0	2 (0.5)
Primary site of origin of disease — no. (%)		
Upper tract	135 (30.5)	104 (23.4)
Lower tract	305 (69.0)	339 (76.4)
Unknown	2 (0.5)	1 (0.2)
Disease status at randomization — no. (%)		
Locally advanced	21 (4.8)	24 (5.4)
Metastatic	421 (95.2)	420 (94.6)
Sites of metastasis — no. (%)		
Lymph node only	103 (23.3)	104 (23.4)
Visceral site	318 (71.9)	318 (71.6)
Bone	81 (18.3)	102 (23.0)
Liver	100 (22.6)	99 (22.3)
Lung	170 (38.5)	157 (35.4)

Van der Heijden et al. N Engl J Med 2023, Powles et al. N Engl J Med 2024



Classic platinum-based chemo or new combination in 1st line mUC?

EV+P IS THE NEW STANDARD FOR 1L mUC

SEQUENTIAL THERAPY AFTER EV+P?

DEFINITION OF EV+P ELEGIBILITY?

DE-ESCALATION STRATEGIES?

HOW LONG WILL IT TAKE TO HAVE A NEW STANDARD FOR 1L mUC?

Thank you for your attention

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