

# Cancers Urologiques

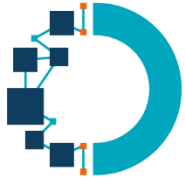
Mardi 21 novembre 2023

**Palais de la Bourse - Bordeaux**

**Dr Marine Gross-Goupil**

**CHU Bordeaux**

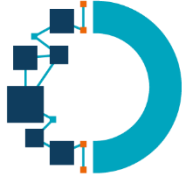
Les « Actus » de l'ESMO – Soirée Post-ESMO Bordeaux 2023



## Liens d'intérêts

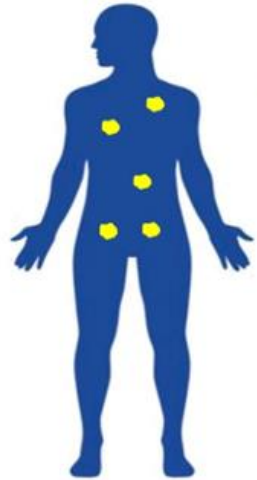
Amgen, Astellas, Astra Zeneca, BMS, Eisai, Gilead, Ipsen, MSD, Pfizer, Roche, Novartis





# Carcinome Urothélial

Métastatique ou avancé en 2023



## 1<sup>ère</sup> ligne

### Eligibles au cisplatine

- Cisplatine + gemcitabine
- Dose-dense méthotrexate + vinblastine + doxorubicine + cisplatine (ddMVAC)

### Inéligibles au cisplatine

- Carboplatine + gemcitabine

PD  
→

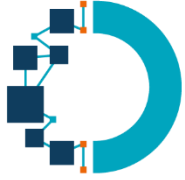
## 2<sup>ème</sup> ligne

Pembrolizumab

RC/RP/SD  
↓

### Entretien Avelumab

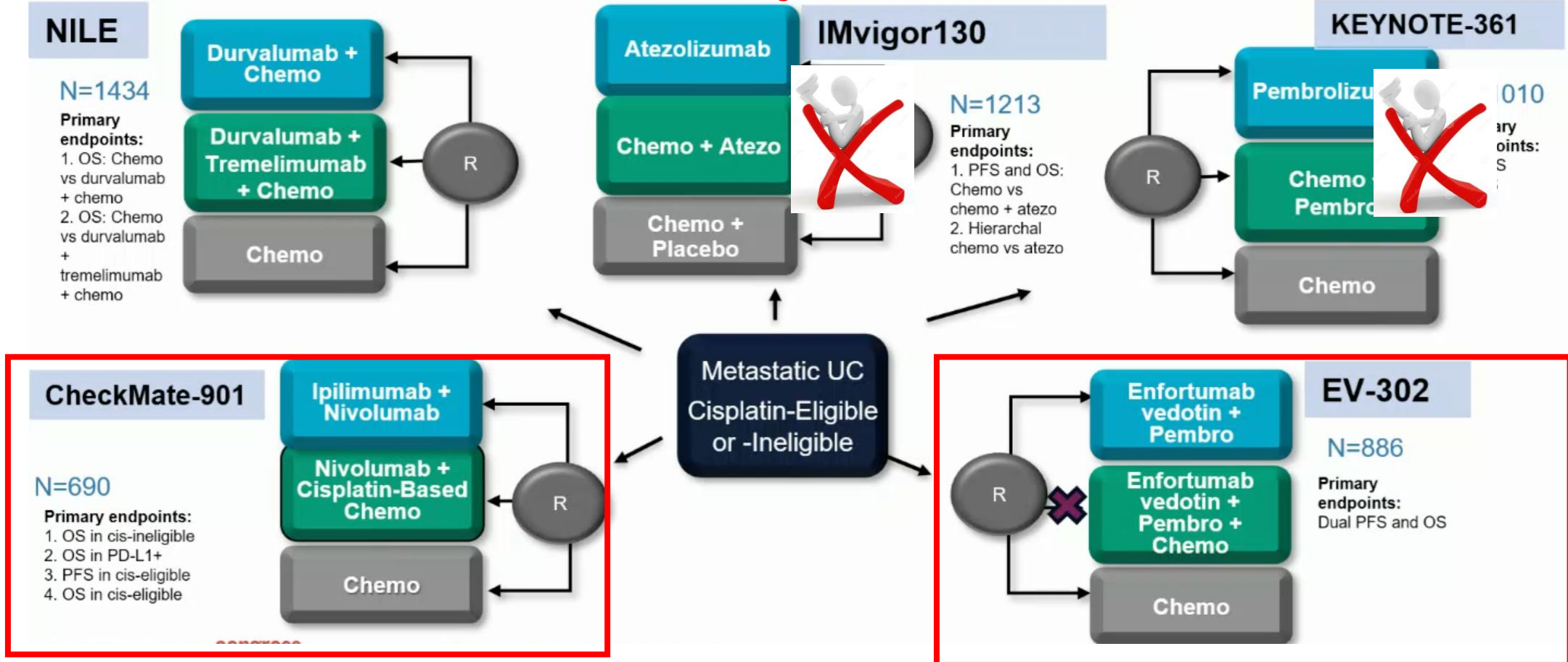
Si RC + RP + SD après une CT à base de platine

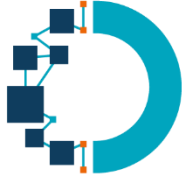


# Phase III- combinaison IO-chimiothérapie

SSP positive ESMO 2019  
SG Négative ASCO 2023

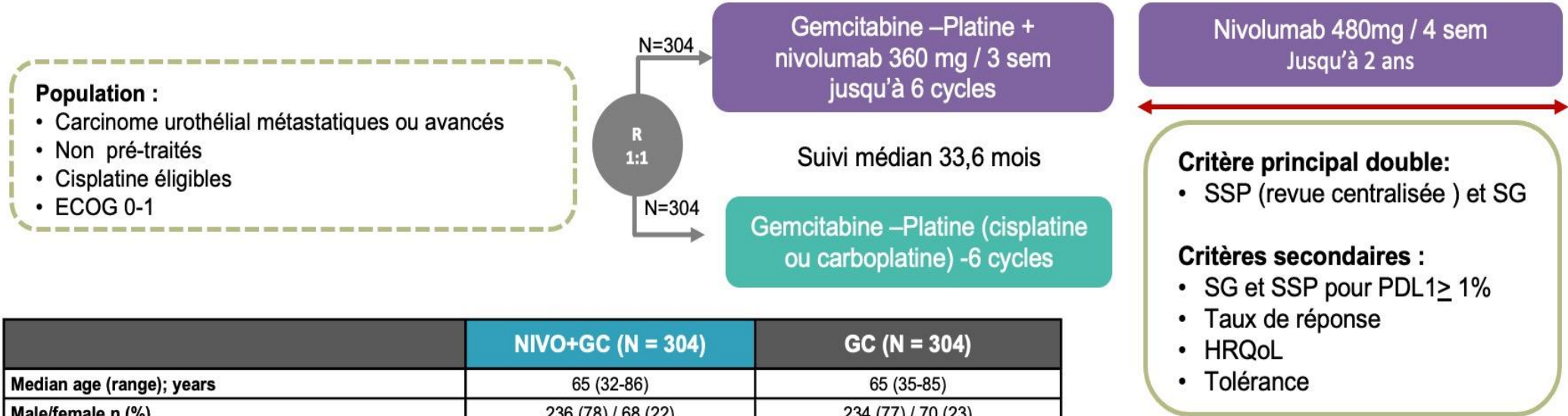
Négative SSP ESMO 2019





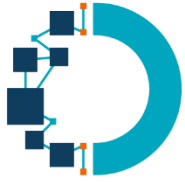
# Phase III- combinaison IO-chimiothérapie

## Checkmate-901 – Gemcitabine Cisplatine +/- nivolumab



	NIVO+GC (N = 304)	GC (N = 304)
<b>Median age (range); years</b>	65 (32-86)	65 (35-85)
<b>Male/female,n (%)</b>	236 (78) / 68 (22)	234 (77) / 70 (23)
<b>ECOG PS, n (%)</b> 0 / 1	162 (53) / 140 (46)	162 (53) / 142 (47)
<b>Tumor type at initial diagnosis, n (%)</b>		
Urinary bladder	235 (77)	219 (72)
Renal pelvis	33 (11)	44 (14)
Other	36 (12)	41 (13)
<b>Tumor PD-L1 expression, n (%)<sup>b</sup></b>		
$\geq 1\%$	111 (37)	110 (36)
< 1% or indeterminate	193 (63)	194 (63)
<b>Liver metastases, n (%)<sup>b</sup></b>	64 (21)	64 (21)

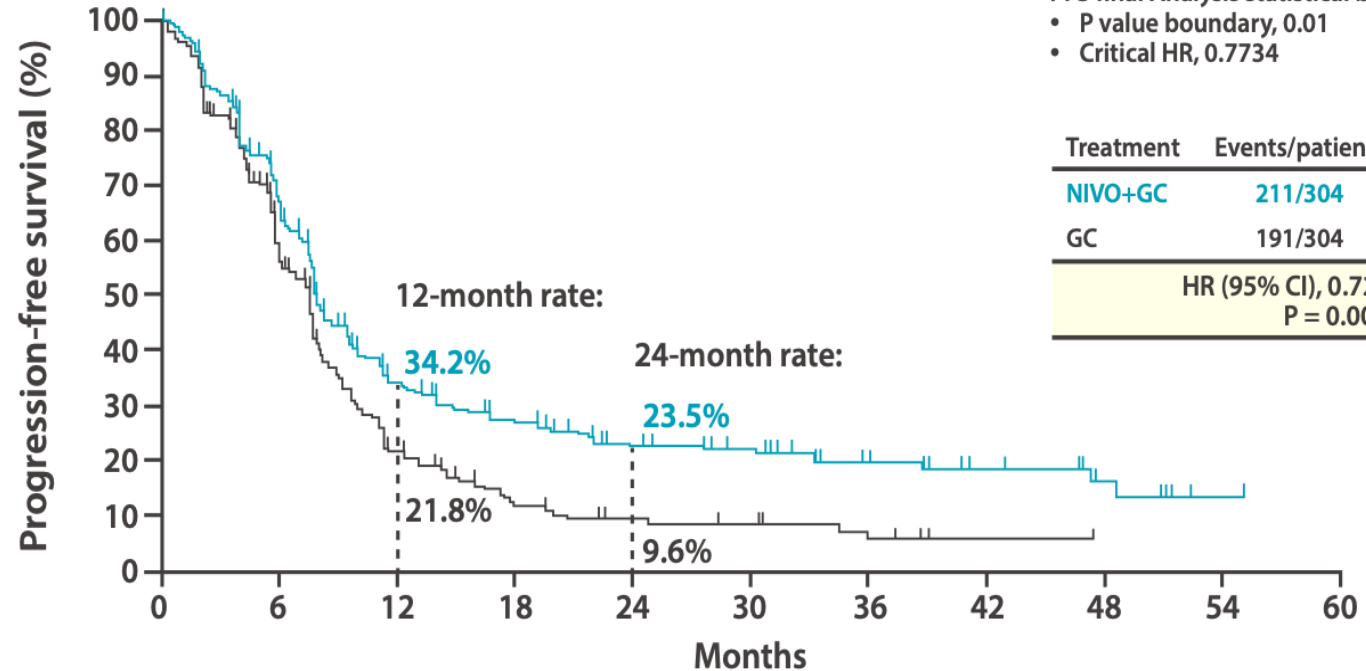
Van der Heijden MS, LBA7, ESMO 2023



# Phase III- combinaison IO-chimiothérapie

## Checkmate-901 – Gemcitabine Cisplatine +/- nivolumab

SSP (revue centralisée)

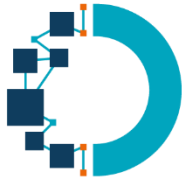


PFS final Analysis statistical boundaries:

- P value boundary, 0.01
- Critical HR, 0.7734

Treatment	Events/patients	Median PFS (95% CI), months
NIVO+GC	211/304	7.9 (7.6-9.5)
GC	191/304	7.6 (6.1-7.8)
HR (95% CI), 0.72 (0.59-0.88)		P = 0.0012

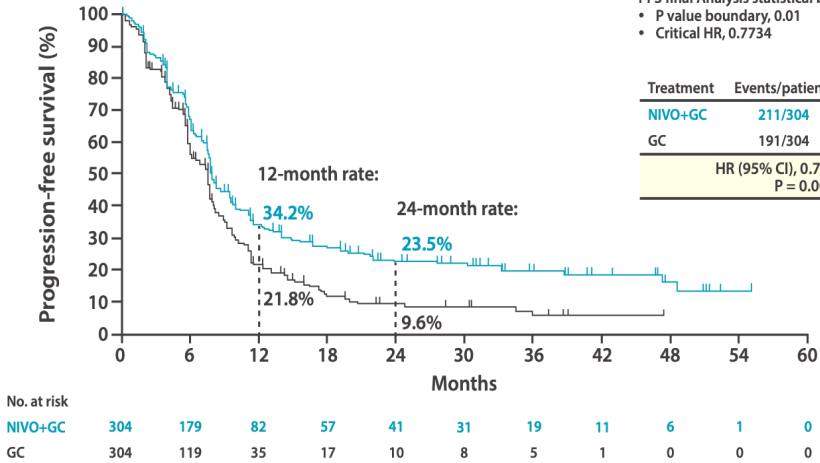
No. at risk	0	6	12	18	24	30	36	42	48	54	60
NIVO+GC	304	179	82	57	41	31	19	11	6	1	0
GC	304	119	35	17	10	8	5	1	0	0	0



# Phase III- combinaison IO-chimiothérapie

## Checkmate-901 – Gemcitabine Cisplatine +/- nivolumab

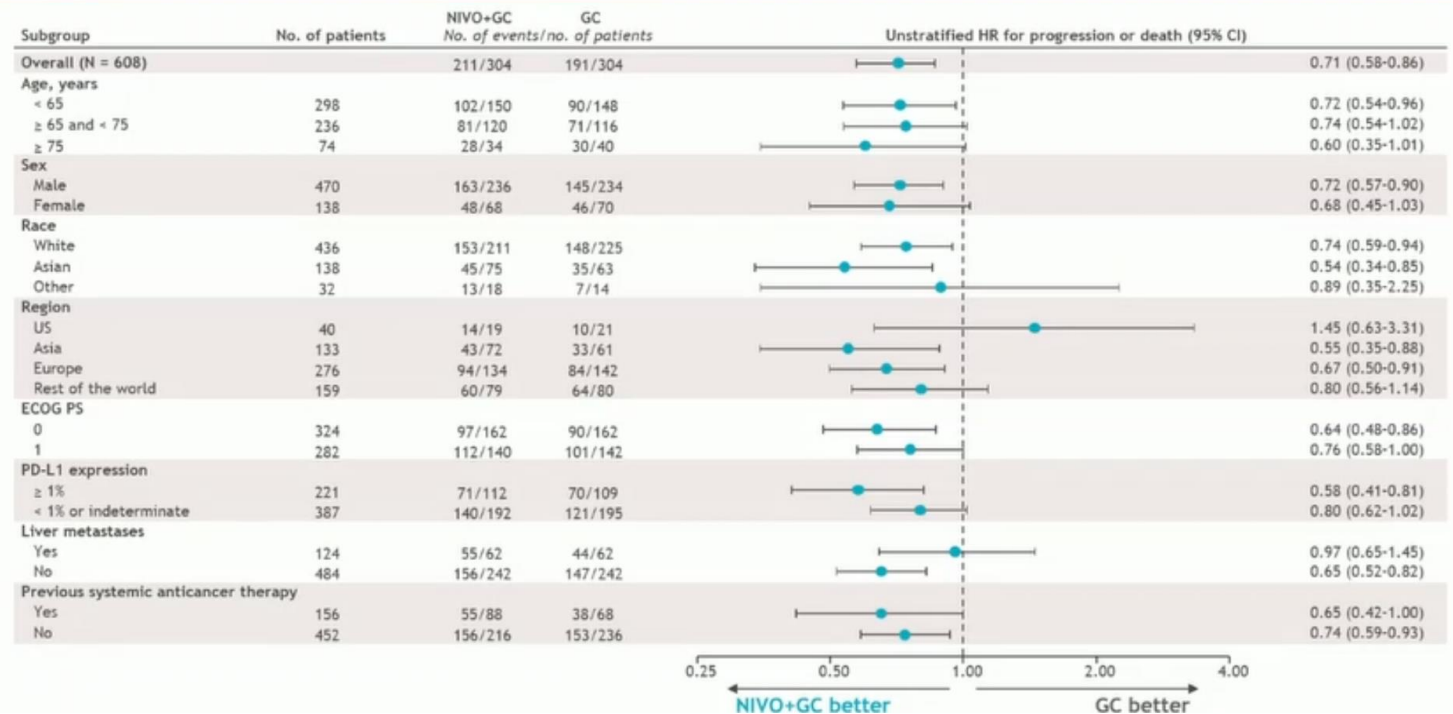
SSP (revue centralisée)

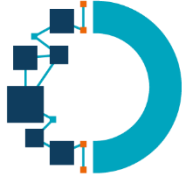


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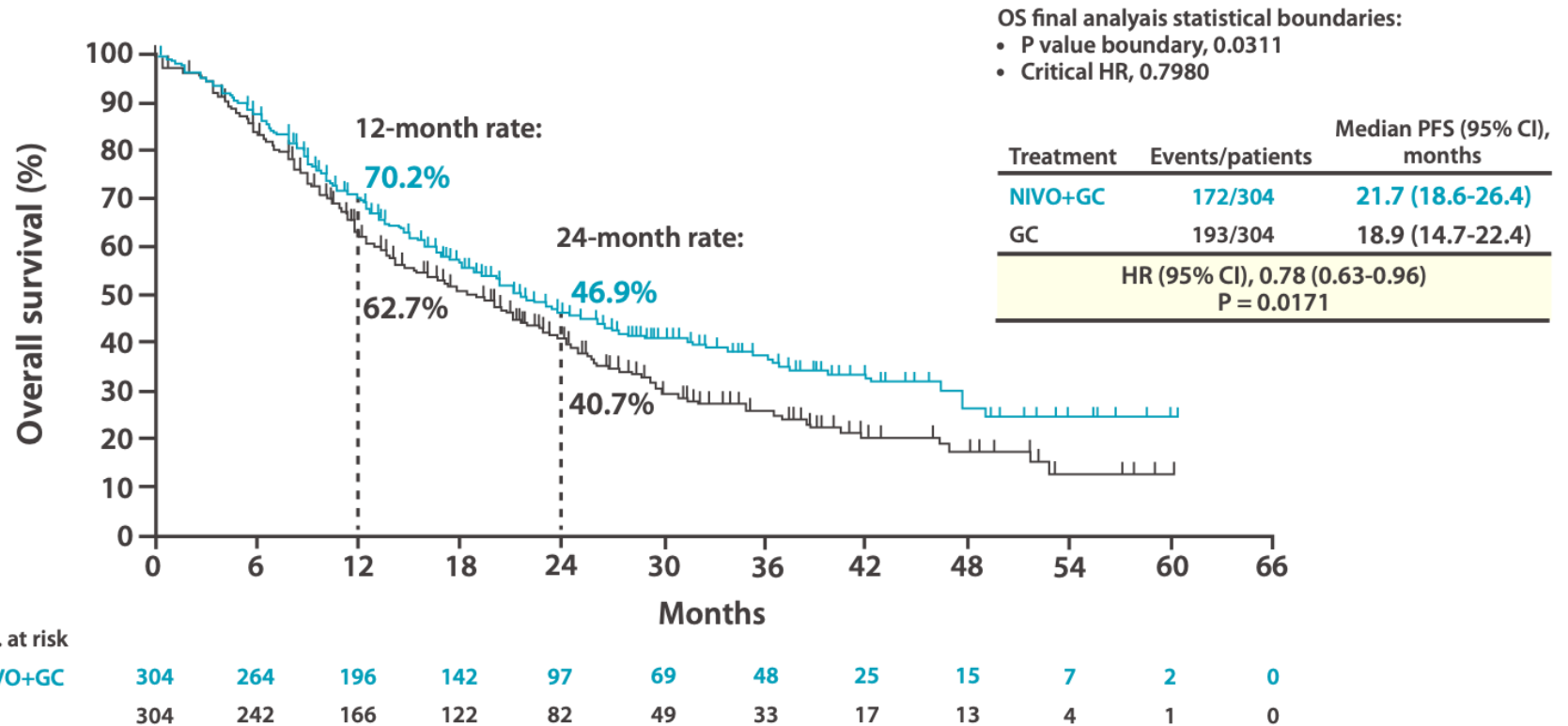




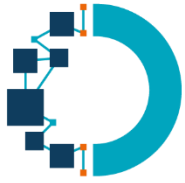
# Phase III- combinaison IO-chimiothérapie

## Checkmate-901 – Gemcitabine platine +/- nivolumab

Survie Globale







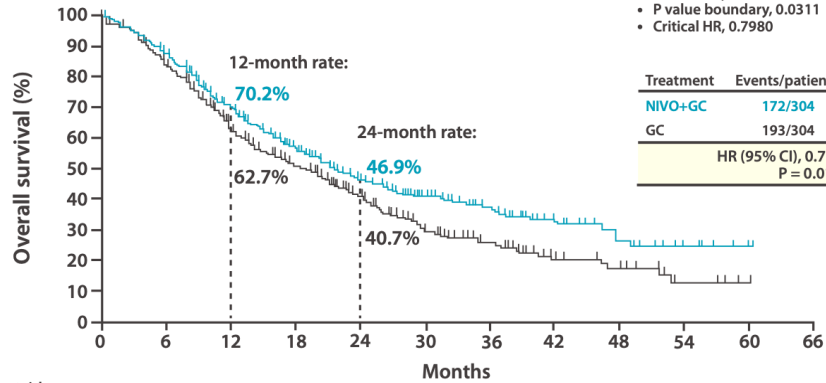
# Phase III- combinaison IO-chimiothérapie

## Checkmate-901 – Gemcitabine Cisplatine +/- nivolumab

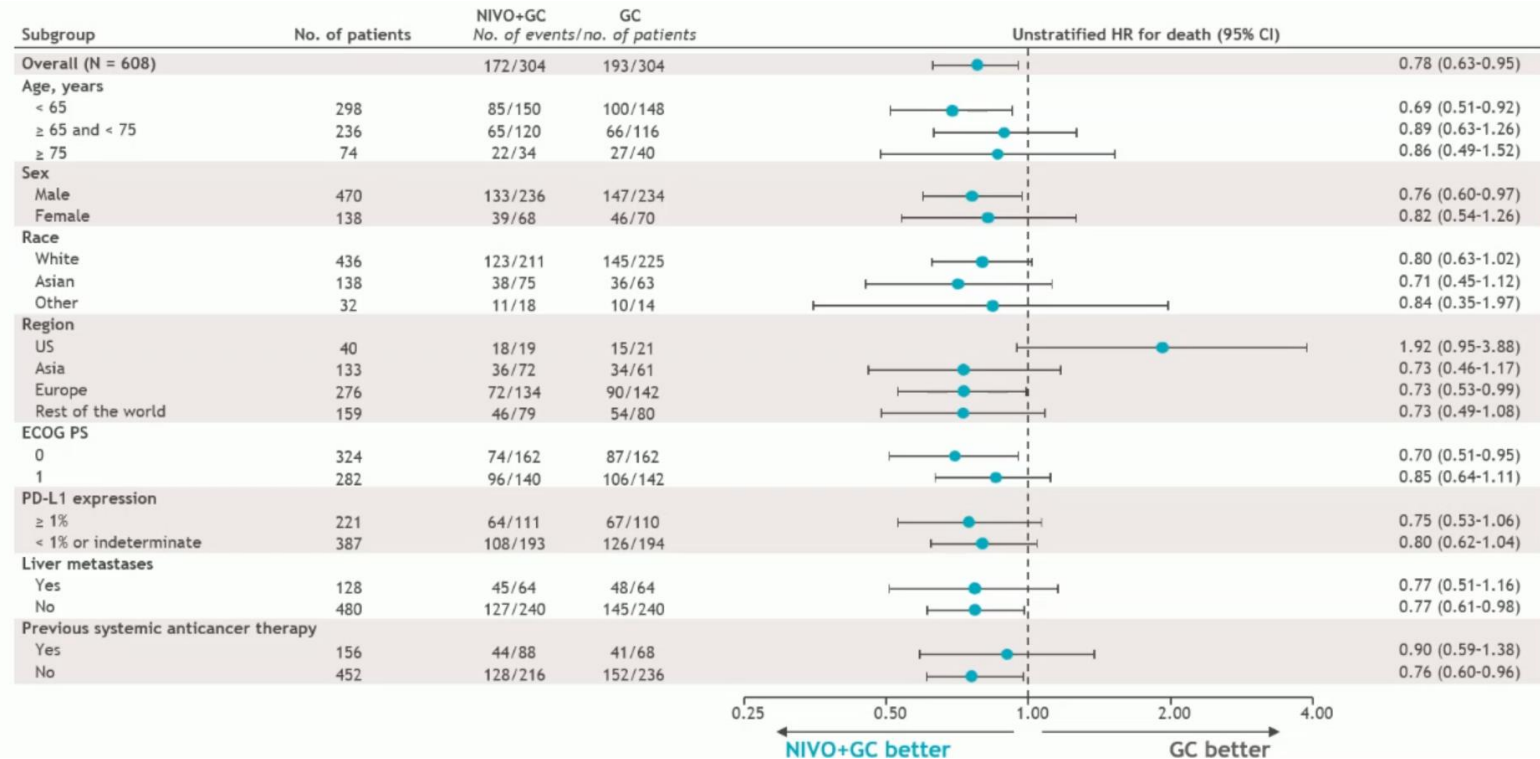
Survie Globale

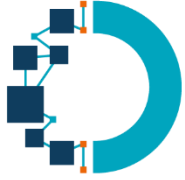
OS final analysis statistical boundaries:  
 • P value boundary, 0.0311  
 • Critical HR, 0.7980

Treatment	Events/patients	Median PFS (95% CI), months
NIVO+GC	172/304	21.7 (18.6-26.4)
GC	193/304	18.9 (14.7-22.4)
HR (95% CI), 0.78 (0.63-0.96)		P = 0.0171



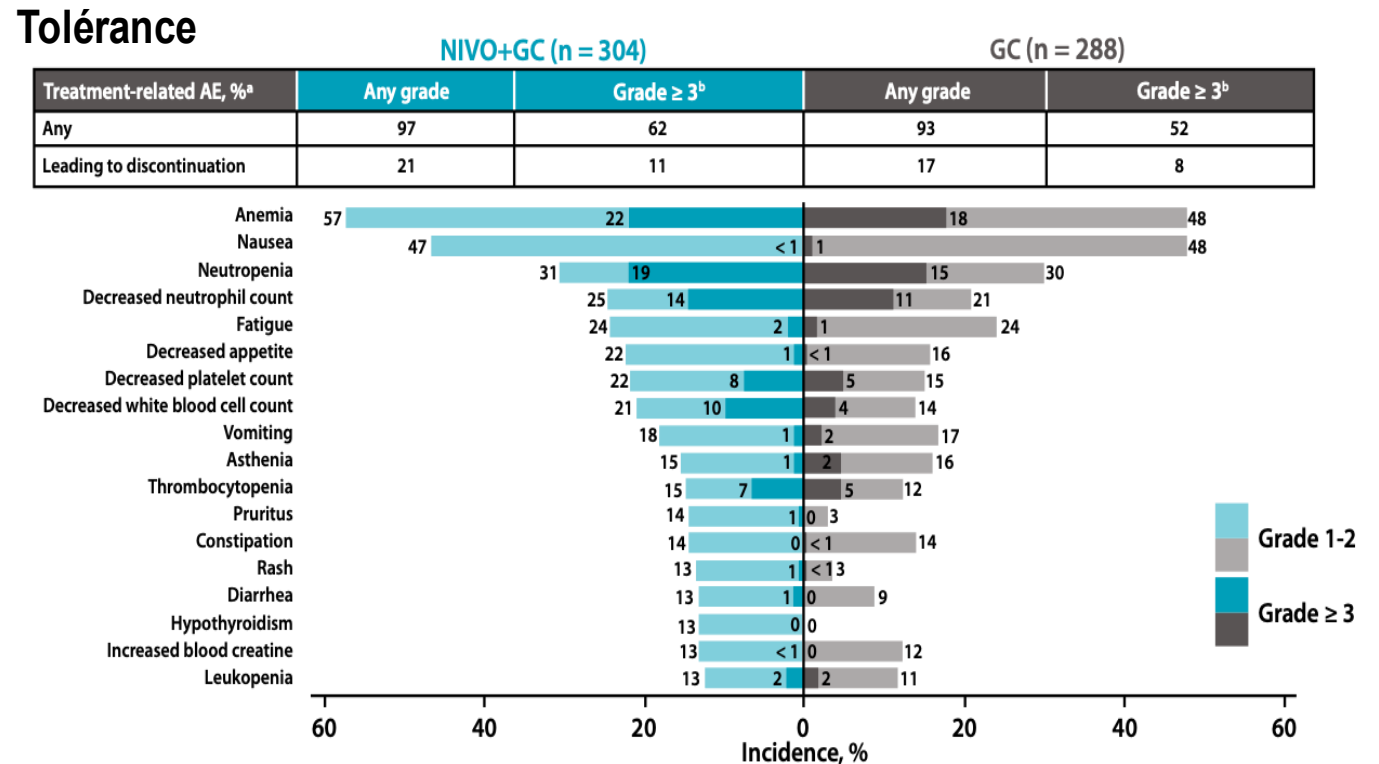
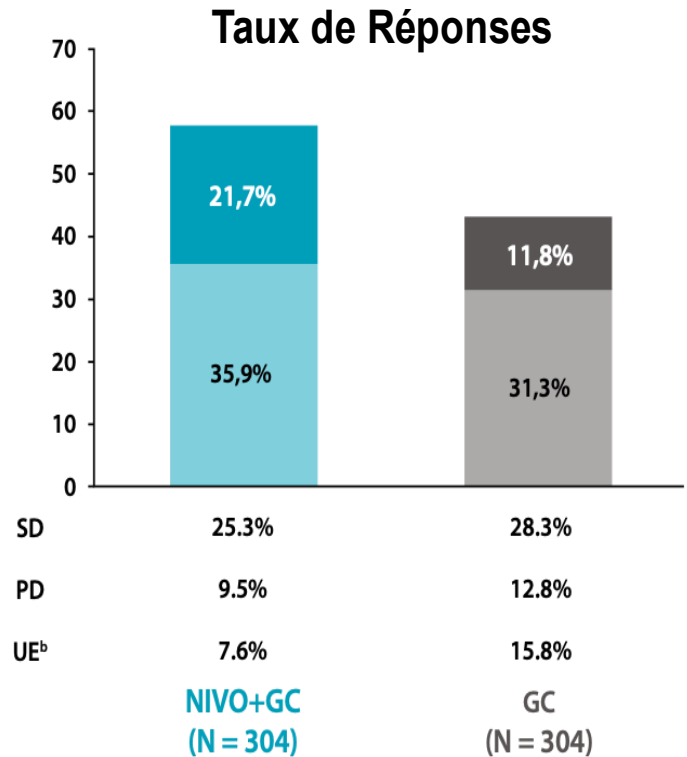
No. at risk	0	6	12	18	24	30	36	42	48	54	60	66
NIVO+GC	304	264	196	142	97	69	48	25	15	7	2	0
GC	304	242	166	122	82	49	33	17	13	4	1	0



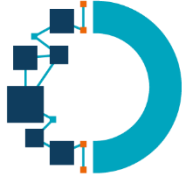


# Phase III- combinaison IO-chimiothérapie

## Checkmate-901 – Gemcitabine platine +/- nivolumab



Bénéfice de l'adjonction du nivolumab au doublet à base platine dès l'induction du traitement  
Nouveau standard



# Phase III- combinaison IO-chimiothérapie

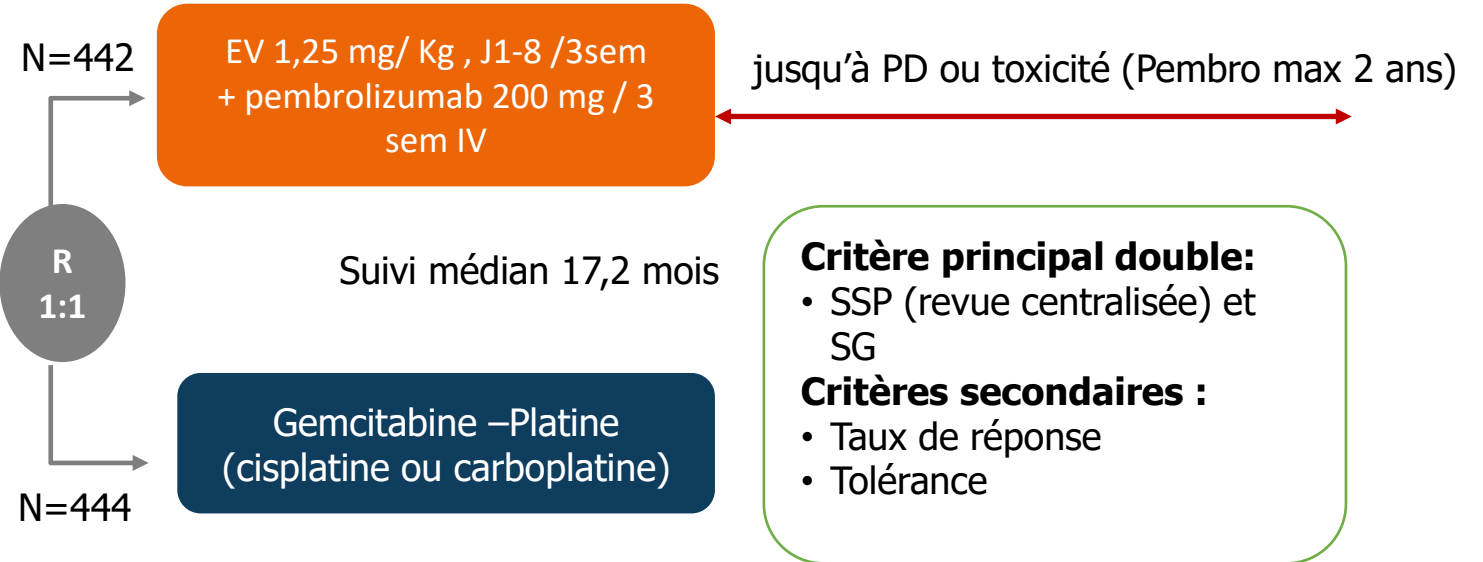
EV-302/ Keynote A 39 – Enfortumab vedotin -pembrolizumab vs Gem-Platine

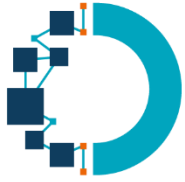
## Population :

- Carcinome urothélial métastatiques ou avancés
- Non pré-traités

## Stratification :

- ECOG 0-1 vs 2
- Site métastatique (viscéral vs autre)
- Site (USA vs Europe vs autre)



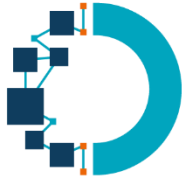


# Phase III- combinaison IO-chimiothérapie

## EV-302/ Keynote A 39 – Enfortumab vedotin -pembrolizumab vs Gem-Platine

- Caractéristiques cliniques

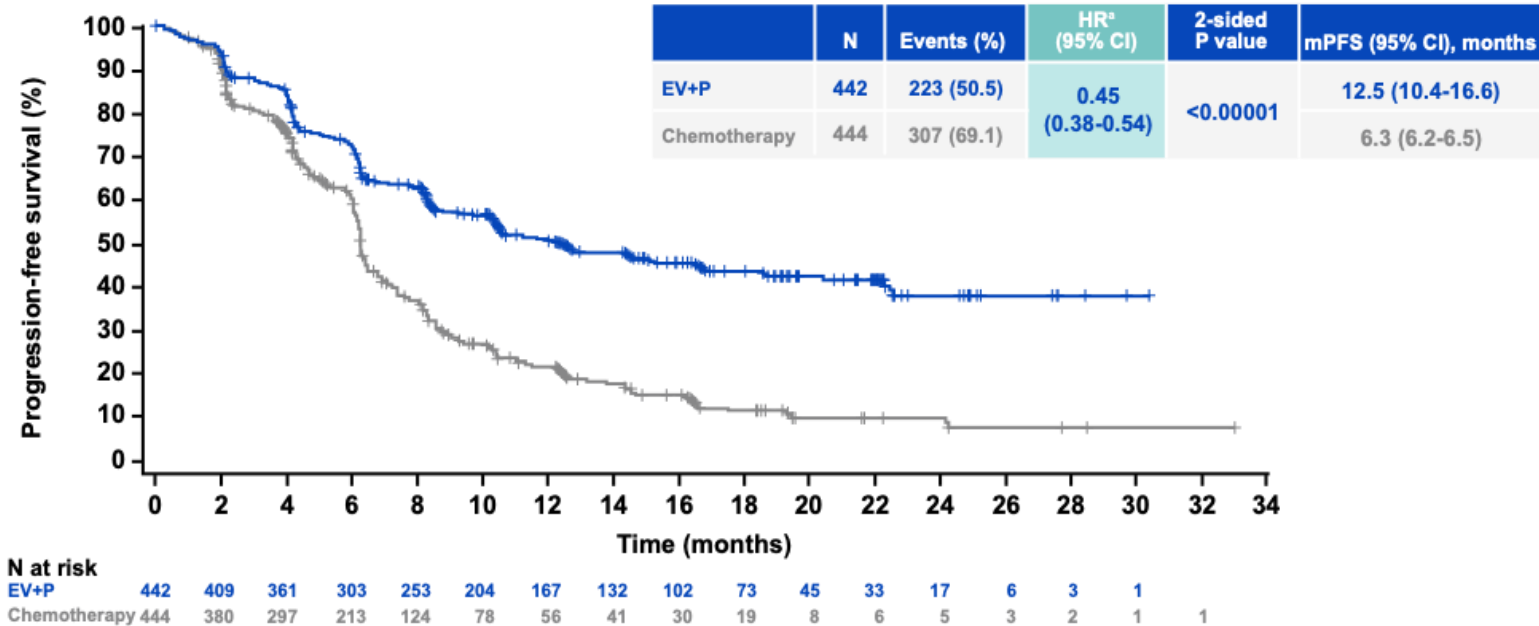
	EV+P (N=442)	Chemotherapy (N=444)
<b>Male sex, n (%)</b>	344 (77.8)	336 (75.7)
<b>Age (yrs), median (range)</b>	69.0 (37.87)	69.0 (22.91)
<b>ECOG PS, n (%)</b>		
0	223 (50.5)	215 (48.4)
1	204 (46.2)	216 (48.6)
2	15 (3.4)	11 (2.5)
<b>Primary tumor location, n (%)</b>		
Upper tract	135 (30.5)	104 (23.4)
Lower tract	305 (69.0)	339 (76.4)
<b>Cisplatin eligible, n (%)</b>	240 (54.3)	242 (54.5)
<b>Metastatic category, n (%)</b>		
Visceral metastases	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)
Lymph node only disease	103 (23.3)	104 (23.4)
<b>PD-L1 expression, n/N (%)</b>		
High (CPS ≥10)	254/438 (58.0)	254/439 (57.9)
Low (CPS < 10)	184/438 (42.0)	185/439 (42.1)



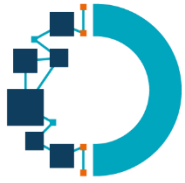
# Phase III- combinaison IO-chimiothérapie

EV-302/ Keynote A 39 – Enfortumab vedotin -pembrolizumab vs Gem-Platine

Survie Sans Progression (BICR).



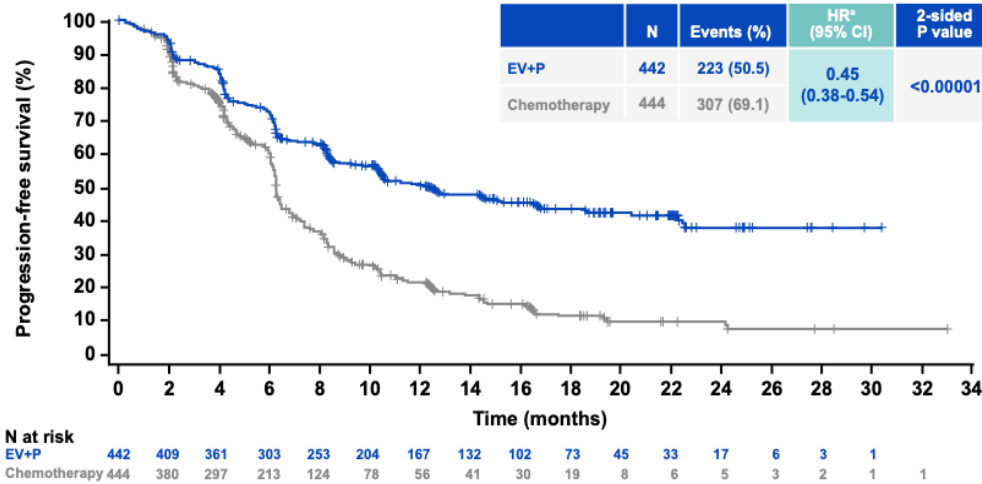
→ Le risque de progression ou de décès est réduit de 55 % chez les patients ayant reçu EV+P.



# Phase III- combinaison IO-chimiothérapie

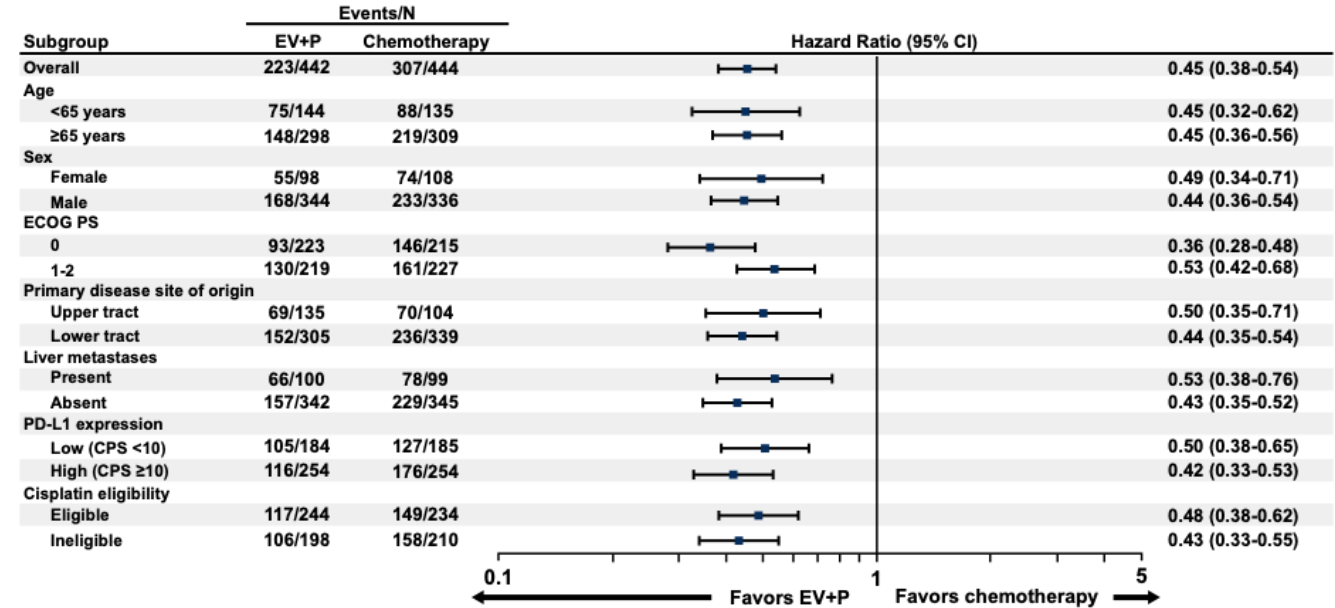
## EV-302/ Keynote A 39 – Enfortumab vedotin -pembrolizumab vs Gem-Platine

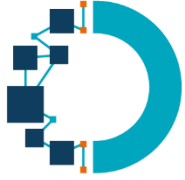
### Survie Sans Progression (BICR).



	N	Events (%)	HR* (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)

### Analyse en sous-groupe de la SSP (BICR)

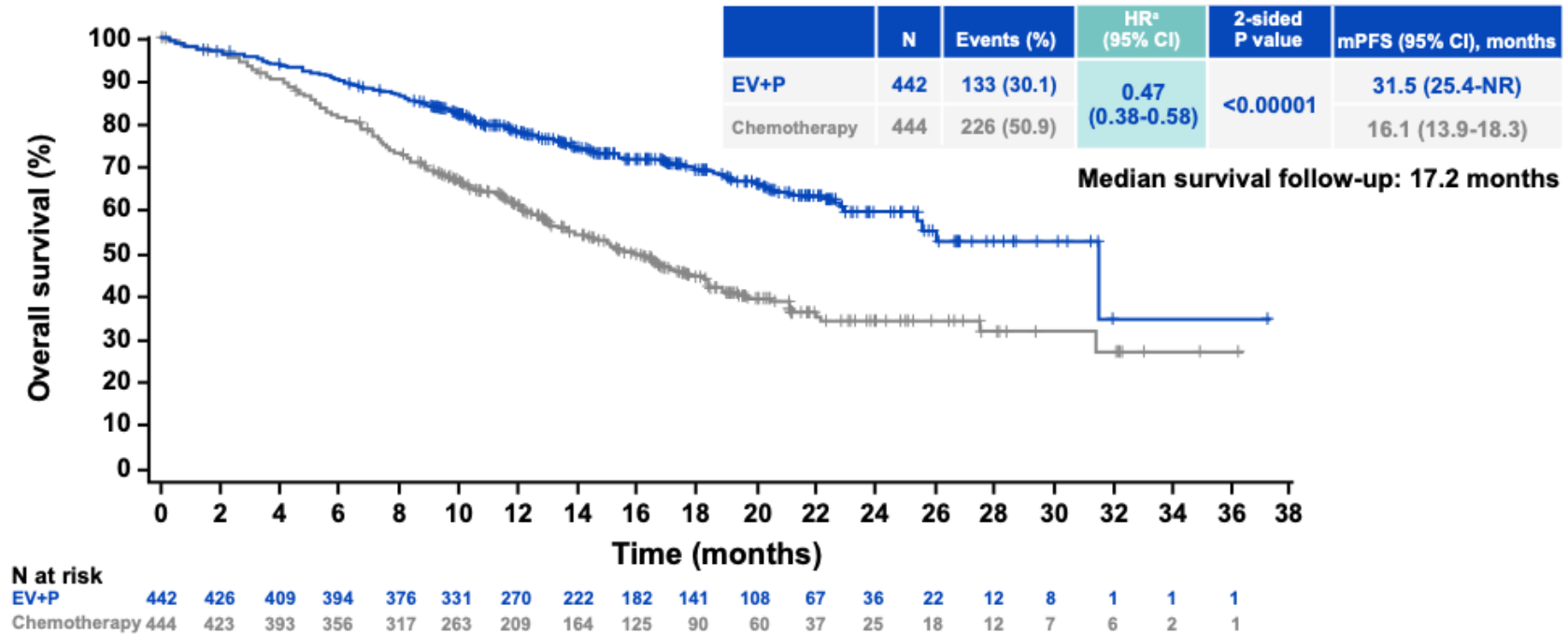




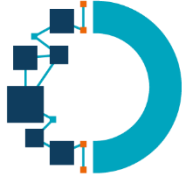
# Phase III- combinaison IO-chimiothérapie

EV-302/ Keynote A 39 – Enfortumab vedotin -pembrolizumab vs Gem-Platine

## Survie Globale



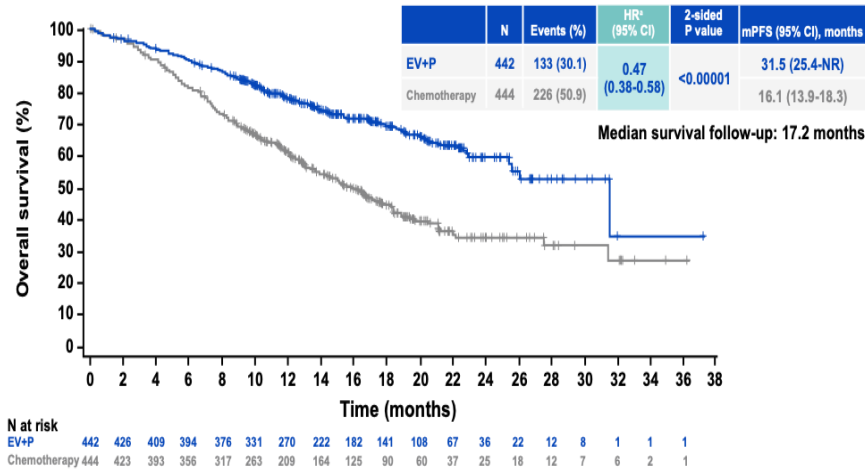
→ Le risque de décès est réduit de 53 % chez les patients ayant bénéficié d'une EV+P.



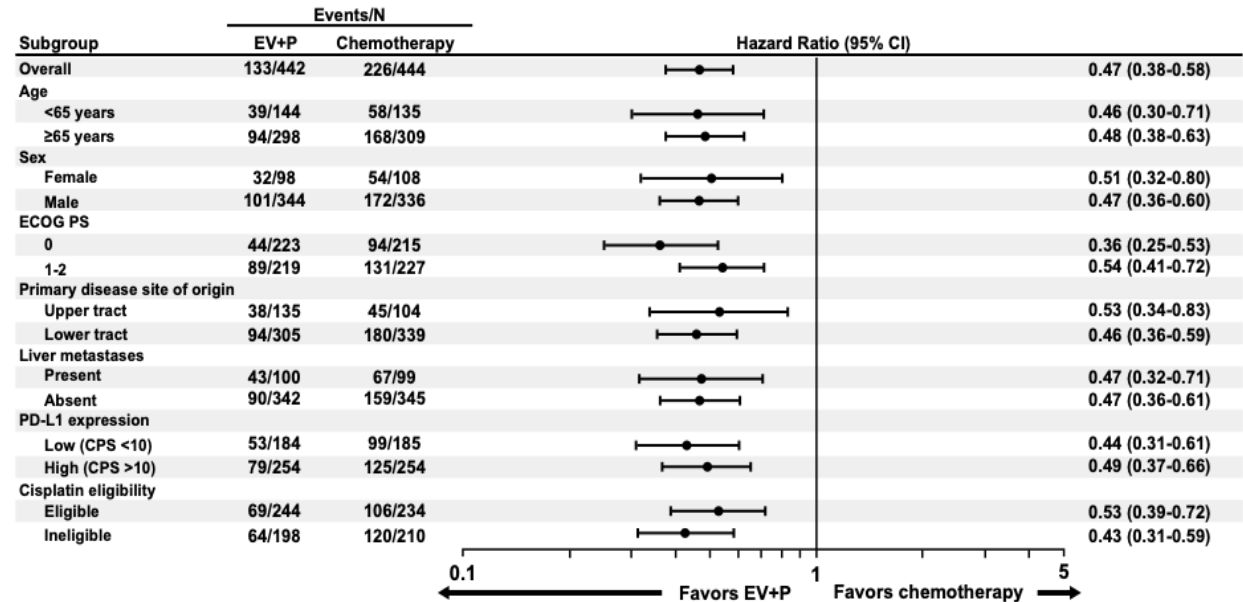
# Phase III- combinaison IO-chimiothérapie

## EV-302/ Keynote A 39 – Enfortumab vedotin -pembrolizumab vs Gem-Platine

Survie Globale



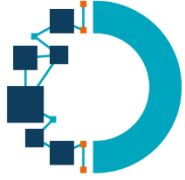
### Analyse en sous-groupe de la SG



→ Le risque de décès est réduit de 53 % chez les patients ayant bénéficié d'une EV+P.

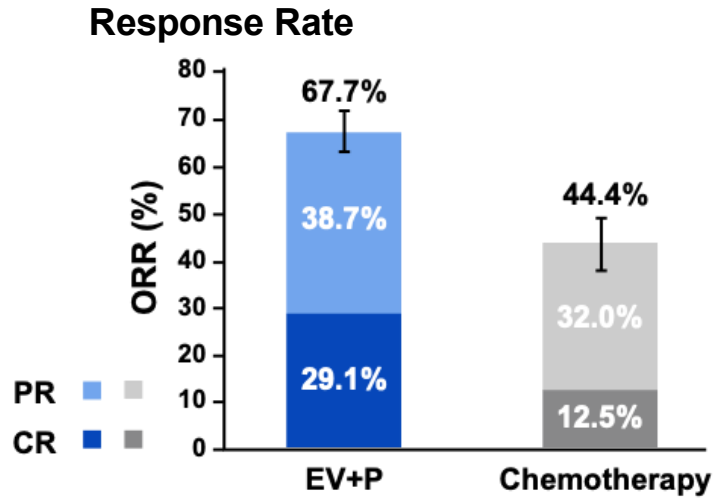
Powles T, LBA6, ESMO 2023





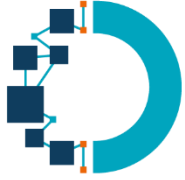
# Phase III- combinaison IO-chimiothérapie

EV-302/ Keynote A 39 – Enfortumab vedotin -pembrolizumab vs Gem-Platine



Median DOR (95% CI)	EV+P	Chemotherapy
	NR (20.2, NR)	7.0 (6.2, 10.2)

	EV+P (N=437)	Chemotherapy (N=441)
Stable disease	82 (18.8)	149 (33.8)
Progressive disease	38 (8.7)	60 (13.6)



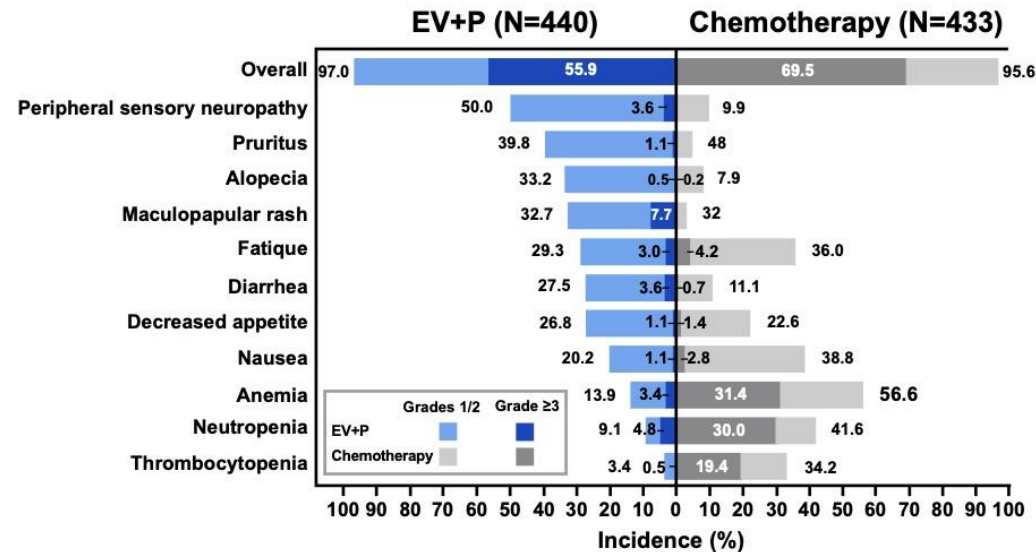
# Phase III- combinaison IO-chimiothérapie

## EV-302/ Keynote A 39 – Enfortumab vedotin -pembrolizumab vs Gem-Platine

### Tolérance

#### Effets indésirables liés au traitement

Les événements de grade ≥3 étaient de 56% pour l'EV+P et de 70% pour la chimiothérapie.



#### Serious TRAEs:

- 122 (27.7%) EV+P
- 85 (19.6%) chemotherapy

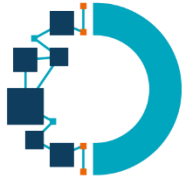
#### TRAEs leading to death (per investigator):

- EV+P: 4 (0.9%)
- Asthenia
- Diarrhea
- Immune-mediated lung disease
- Multiple organ dysfunction syndrome

#### Chemotherapy: 4 (0.9%)

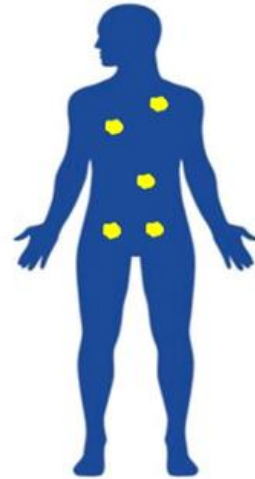
- Febrile neutropenia
- Myocardial infarction
- Neutropenic sepsis
- Sepsis

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



# Conclusions

**Nouveau standard de traitement de 1<sup>ère</sup> Ligne - actualisations recommandations en cours**



**1<sup>ère</sup> ligne**

- EV+ pembrolizumab

\* Sous réserve de l'AMM et du remboursement

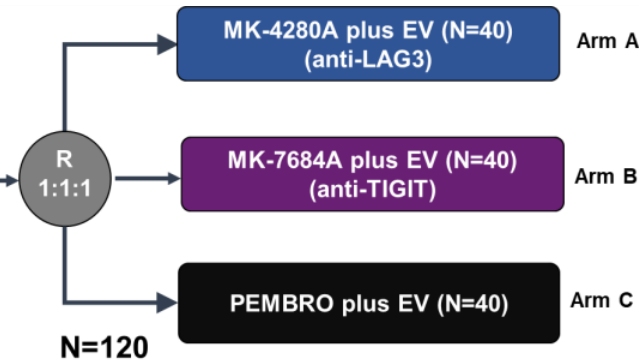
**Essai thérapeutique**

**Patient Population:**

- Previously untreated for locally advanced/ unresectable or mUC
- ECOG 0-1
- No restrictions regarding PD-L1 CPS

**Stratification Factor:**

Liver metastases (Yes vs No)



**After 120 total patients enrolled:**

- *Interim Analysis*
- *Consider expansion of Arm A and/or Arm B (and comparator Arm C)*

**Primary Endpoint (Arm A, Arm B vs Arm C)**

- ORR per RECIST 1.1 by BICR
- Safety

**Secondary Endpoints (Arm A, Arm B vs Arm C)**

- DOR and PFS per RECIST 1.1 by BICR
- PRO (patient reported outcomes)



