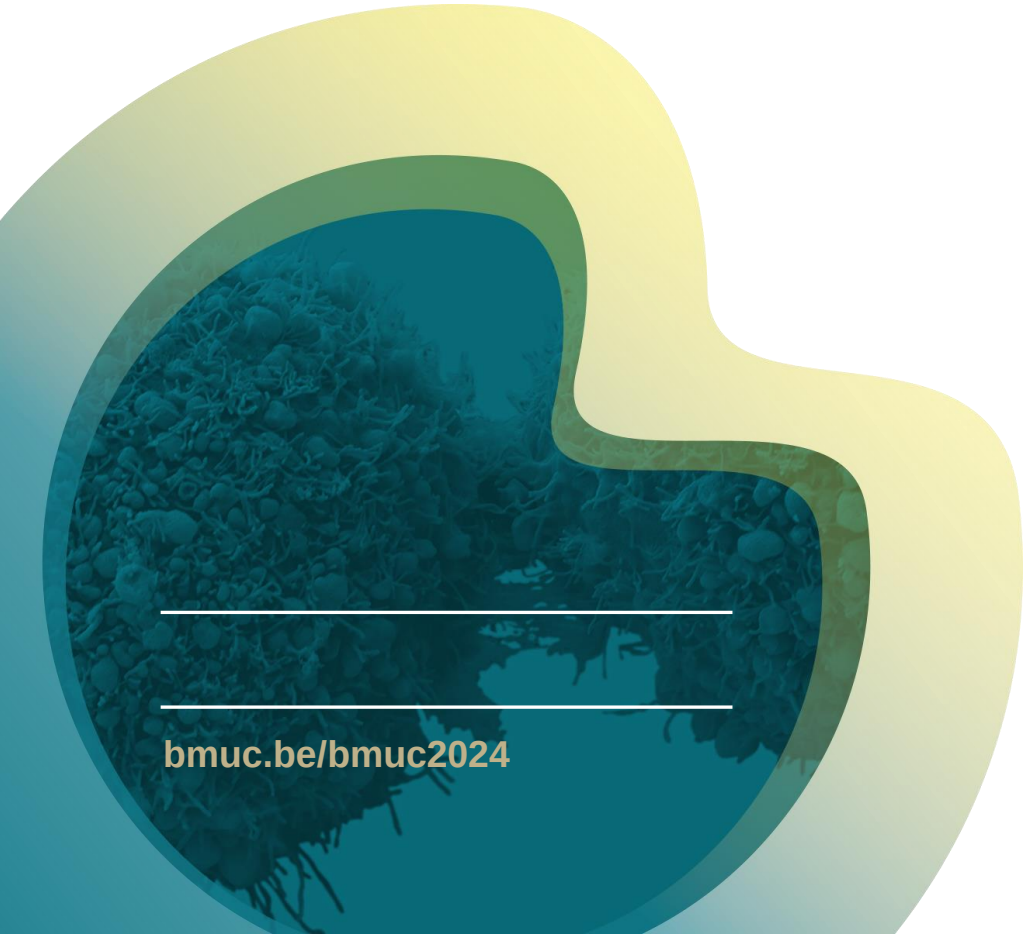
Do we still need chemo in 1st line metastatic bladder cancer ?

Sylvie Rottey, MD, PhD



bmuc.be/bmuc2024

BMUC
UROLOGY - RADIATION ONCOLOGY - MEDICAL ONCOLOGY

11th Belgian Multidisciplinary Meeting on Urological Cancers

Conflicts of interest

Research Grants from Roche, MSD, BMS

Speakers fee from BMS, MSD, Ipsen, Astellas

Advisory Board with Astellas, J&J, MSD, BMS, Ipsen

President of Pfizer Onco Award

Member of the Jury of Gilead Award

PI of clinical trials with > 30 different sponsors

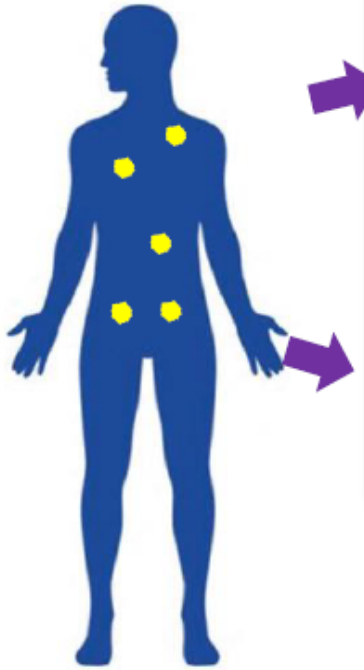
ESMO – Madrid

BMUC
UROLOGY - RADIATION ONCOLOGY - MEDICAL ONCOLOGY
11th Belgian Multidisciplinary Meeting on Urological Cancers

- October 2023
- Excitement
- The first time in 30 y with a positive ph III trial in first line M+ disease
- EAU : Standing ovation for EV302

  Not for the CheckMate 901

Standard of Care Management of Advanced/Metastatic Urothelial Carcinoma (pre-ESMO 2023)



First-Line

Cisplatin-eligible

- **Cisplatin + gemcitabine[2]**
- **Dose-dense methotrexate + vinblastine + doxorubicin + cisplatin (ddMVAC)[3]**

Cisplatin-ineligible[1]

- **Carboplatin + gemcitabine[4]**

Platinum-ineligible

Pembrolizumab

Maintenance

For patients who achieve a response (CR/PR/SD) to platinum-based chemotherapy

- **Avelumab[5]**
- **Pembrolizumab[6]**

or Second-Line

- **Pembrolizumab[7]**
- **Nivolumab**
- **Avelumab**

Beyond-Second-Line

- **Enfortumab Vedotin[8]**
- **Erdafitinib[9] (if tumor +FGFR 2/3 genetic alterations)**
- **Sacituzumab govitecan[10]**
- **Clinical trial**
- **Paclitaxel, docetaxel, or vinflunine**

1. Galsky, et al. JCO 2011 Jun 10;29(17):2432-8
2. von der Maase, et al. JCO 2000 Sep 18;(17):3068-77
3.Sternerg, et al. JCO 2001 May 15;19(10):268-46
4. De Santis, et al. JCO 2012 Jan 10;30(2):191-9
5. Powles, et al., N Engl J Med 2020 Sep 24;383(13):1218-1230
6. Galsky et al., JCO. 2020 Jun 1;38(16):1797-1806.
7. Bellmunt et al., N Engl J Med 2017; 376:1015-1026
8. Powles T et al., N Engl J Med 2021;384:1125-35
9. Loriot Y, et al. N Engl J Med. 2019;381:338-348;
10. Tagawa CT et al., JCO 2021 Aug 1;39(22):2474-2485

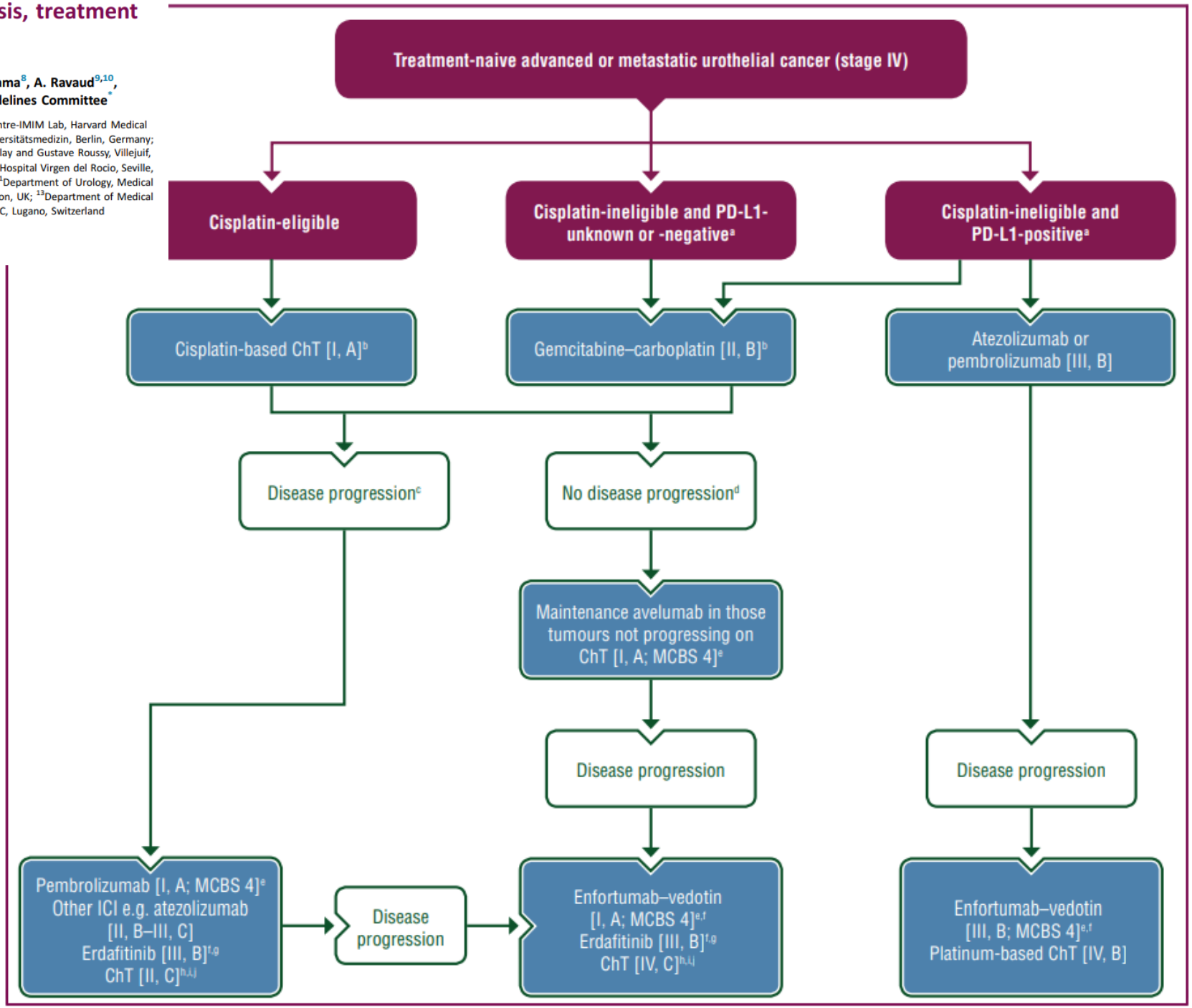
Presented by Andrea B. Apolo, MD
@apolo_andrea

Bladder cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up☆

T. Powles[1], J. Bellmunt[2], E. Comperat[3], M. De Santis[4], R. Huddart[5], Y. Loriot[6], A. Necchi[7], B. P. Valderrama[8], A. Ravaud[9,10], S. F. Shariat[11], B. Szabados[1,12], M. S. van der Heijden[13] & S. Gillessen[14], on behalf of the ESMO Guidelines Committee*

[1]Barts Cancer Centre, Barts Health NHS Trust, Queen Mary University of London, London, UK; [2]Beth Israel Deaconess Medical Centre-IMIM Lab, Harvard Medical School, Boston, USA; [3]L'Assistance Publique-Hôpitaux de Paris, Hôpital Tenon, Paris, France; [4]Department of Urology, Charité Universitätsmedizin, Berlin, Germany; [5]Royal Marsden Hospital, Institute of Cancer Research, London, UK; [6]Département de Médecine Oncologique, Université Paris-Saclay and Gustave Roussy, Villejuif, France; [7]Vita-Salute San Raffaele University, Department of Medical Oncology, IRCCS San Raffaele Hospital, Milan, Italy; [8]University Hospital Virgen del Rocio, Seville, Spain; [9]Hôpital Saint-André CHU, Bordeaux; [10]Department of Medical Oncology, Bordeaux University Hospital, Bordeaux, France; [11]Department of Urology, Medical University of Vienna, Vienna General Hospital, Vienna, Austria; [12]Department of Urology, University College London Hospital, London, UK; [13]Department of Medical Oncology, The Netherlands Cancer Institute, Amsterdam, The Netherlands; [14]Oncology Institute of Southern Switzerland (IOSI), EOC, Lugano, Switzerland

Available online 30 November 2021



Journal Pre-proof

ESMO Clinical Practice Guideline interim update on first-line therapy in advanced urothelial carcinoma

T. Powles, J. Bellmunt, E. Comperat, M. De Santis, R. Huddart, Y. Loriot, A. Necchi, B.P. Valderrama, A. Ravaud, S.F. Shariat, B. Szabados, M.S. van der Heijden, S. Gillessen, on behalf of the ESMO Guidelines Committee

PII: S0923-7534(24)00075-9

DOI: https://doi.org/10.1016/j.annonc.2024.03.001

Reference: ANNONC 1449

To appear in: *Annals of Oncology*

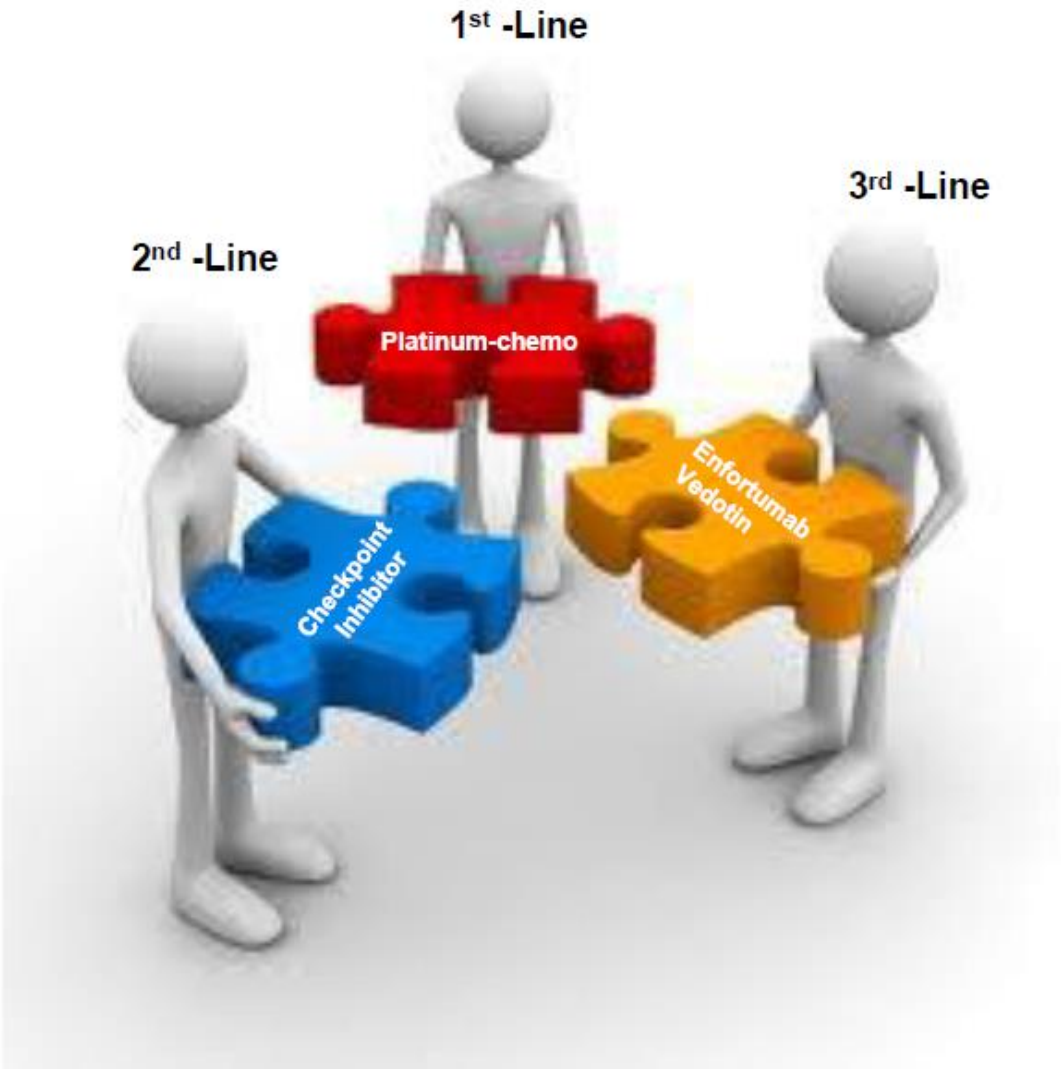
Received Date: 9 January 2024

Revised Date: 29 February 2024

Accepted Date: 1 March 2024

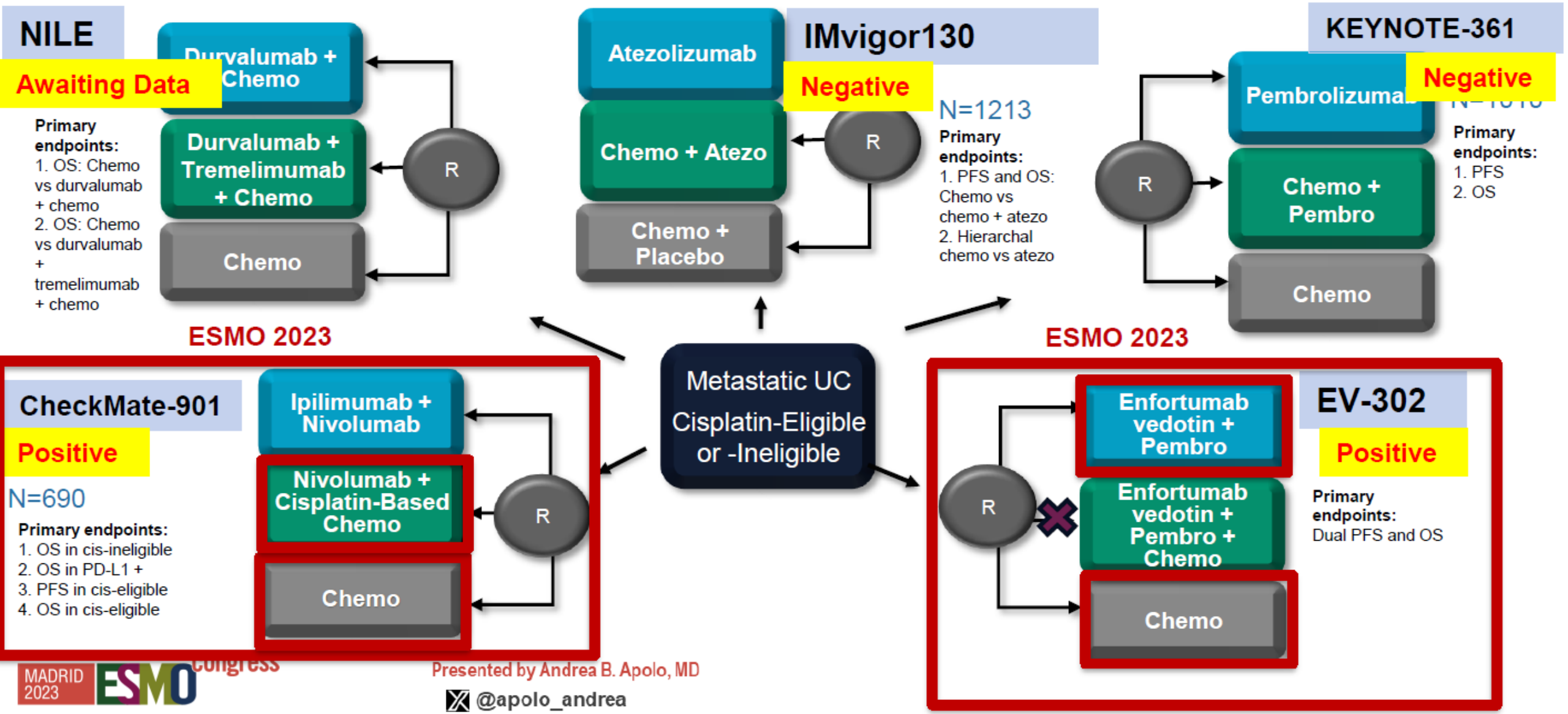
Goals of Treatment in the First-line Setting in Urothelial Carcinoma

- Early tumor shrinkage
- Durable responses
- Longer overall survival
- Minimal treatment toxicity



Presented by Andrea B. Apolo, MD
@apolo_andrea

First-line Phase 3 Trials with Checkpoint-Inhibitor Combinations vs Platinum-based Chemo for Metastatic Urothelial Carcinoma



MADRID 2023 ESMO Congress

Presented by Andrea B. Apolo, MD

@apolo_andrea

MADRID 2023 ESMO congress

Nivolumab plus gemcitabine-cisplatin versus gemcitabine-cisplatin alone for previously untreated unresectable or metastatic urothelial carcinoma: results from the phase 3 CheckMate 901 trial

Michiel S. van der Heijden,[1] Guru Sonpavde,[2a] Thomas Powles,[3] Andrea Necchi,[4b] Mauricio Burotto,[5] Michael Schenker,[6] Juan Pablo Sade,[7] Aristotelis Bamias,[8] Philippe Beuzeboc,[9] Jens Bedke,[10c] Jan Oldenburg,[11] Yüksel Ürün,[12] Dingwei Ye,[13] Zhisong He,[14] Begoña P. Valderrama,[15] Yoshihiko Tomita,[16] Jeiry Filian,[17] Daniela Purcea,[18] Federico Nasroulah,[17] Matthew D. Galsky[19]

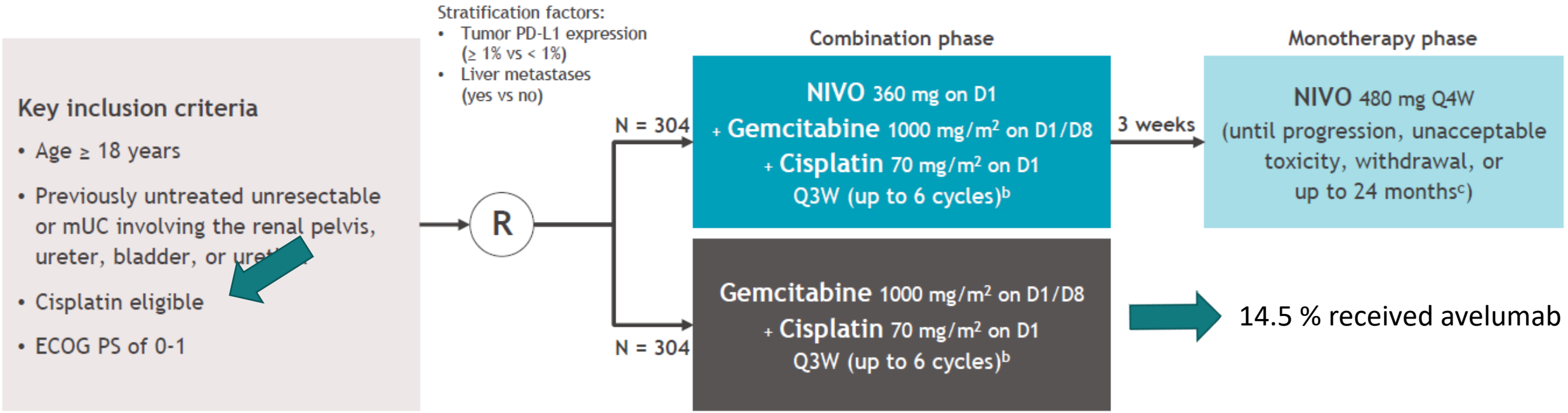
[1]Netherlands Cancer Institute, Amsterdam, the Netherlands; [2]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA; [3]Barts Cancer Institute, Queen Mary University of London, London, UK; [4]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [5]Bradford Hill Clinical Research Center, Santiago, Chile; [6]University of Medicine and Pharmacy, Craiova, Romania; [7]Alexander Fleming Institute, Buenos Aires, Argentina; [8]National and Kapodistrian University of Athens, ATTIKON University Hospital, Athens, Greece; [9]Hopital Foch, Suresnes, France; [10]Eberhard Karls University Tübingen, Tübingen, Germany; [11]Akershus University Hospital (Ahus), Lørenskog, Norway; [12]Ankara University, Ankara, Turkey; [13]Fudan University Shanghai Cancer Center, Shanghai, China; [14]Peking University First Hospital, Beijing, China; [15]Hospital Universitario Virgen del Rocío, Sevilla, Spain; [16]Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan; [17]Bristol Myers Squibb, Princeton, NJ, USA; [18]Bristol Myers Squibb, Boudry, Switzerland; [19]Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA

[a]Current affiliation is AdventHealth Cancer Institute and University of Central Florida, Orlando, FL, USA. [b]Current affiliation is IRCCS San Raffaele Hospital, Vita-Salute San Raffaele University, Milan, Italy. [c]Current affiliation is Klinikum Stuttgart, Katharinenhospital, Stuttgart, Germany.

Presentation number LBA7

Study design

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

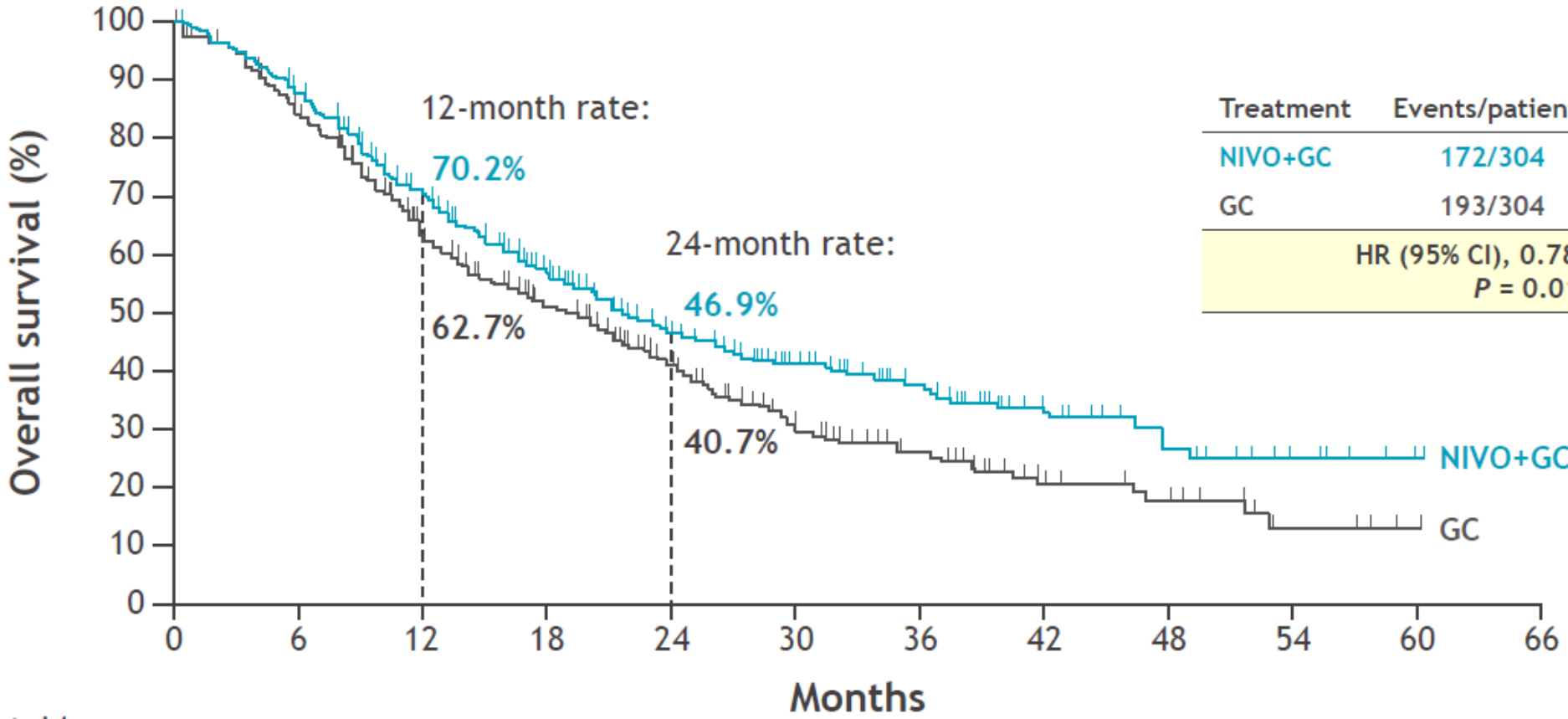


Median (range) study follow-up, 33.6 (7.4-62.4) months

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; Q×W, every × weeks; R, randomization.

OS (primary endpoint)

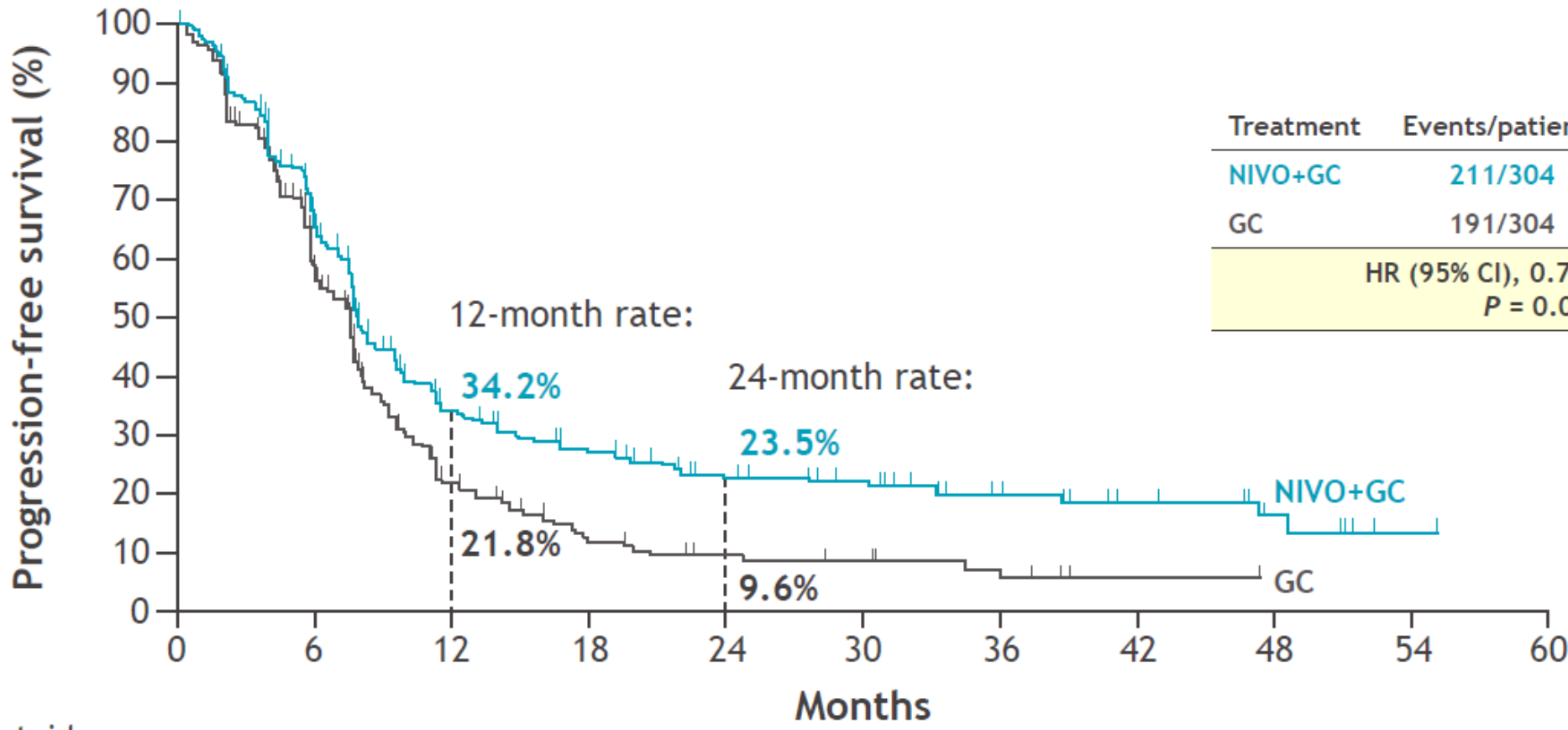


Treatment	Events/patients	Median OS (95% CI), months
NIVO+GC	172/304	21.7 (18.6-26.4)
GC	193/304	18.9 (14.7-22.4)
HR (95% CI), 0.78 (0.63-0.96) *P* = 0.0171		

No. at risk												
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

Median (range) study follow-up was 33.6 (7.4-62.4) months. OS was estimated in all randomized patients and defined as time from randomization to death from any cause. For patients without documented death, OS was censored on the last date the patient was known to be alive. For randomized patients with no follow-up, OS was censored at randomization.

PFS per BICR (primary endpoint)



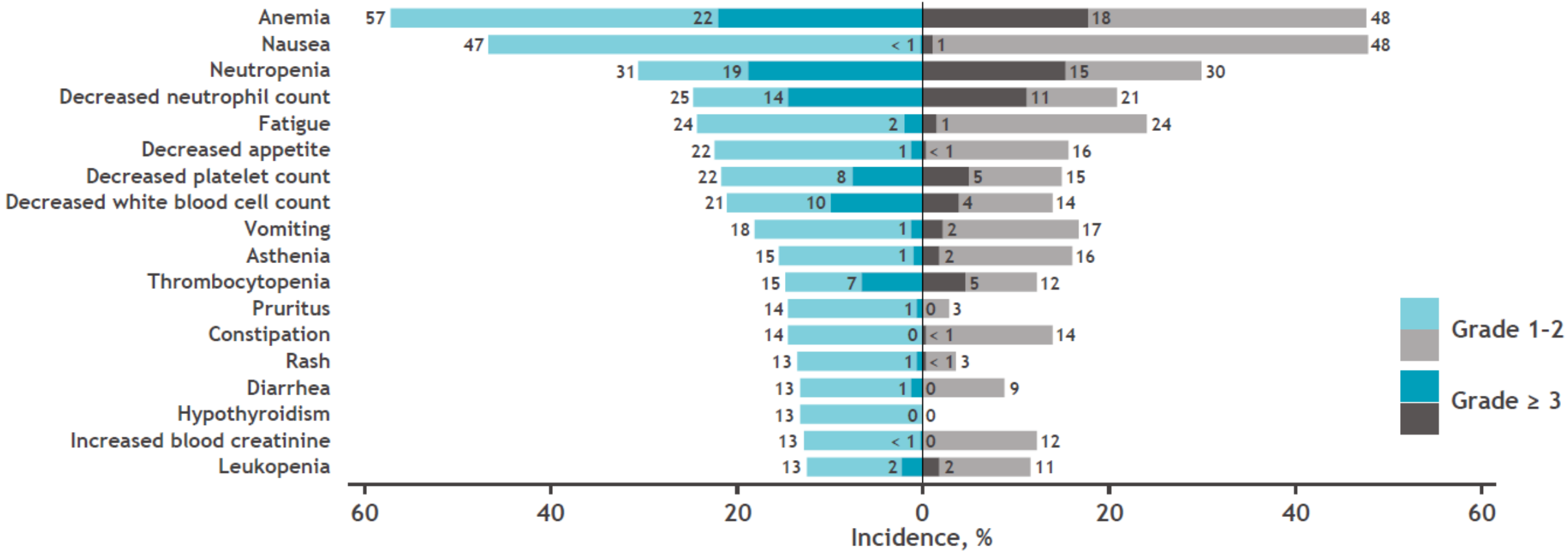
Treatment	Events/patients	Median PFS (95% CI), months
NIVO+GC	211/304	7.9 (7.6-9.5)
GC	191/304	7.6 (6.1-7.8)
HR (95% CI), 0.72 (0.59-0.88) *P* = 0.0012		

No. at risk											
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

Median (range) study follow-up was 33.6 (7.4-62.4) months. PFS was estimated in all randomized patients and defined as time from randomization to first documented disease progression (per BICR assessments using RECIST v1.1) or death due to any cause, whichever occurred first. Patients who did not progress or die were censored at last evaluable tumor assessment. Patients without on-study tumor assessments who did not die were censored at randomization. **Patients who started any subsequent anticancer therapy without prior reported progression were censored at last evaluable tumor assessment before initiation of subsequent therapy.**

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.

Summary

- NIVO+GC demonstrated statistically significant and clinically meaningful improvements in OS and PFS versus GC alone as first-line treatment for unresectable or mUC
- ORR and CR rates were notably higher with NIVO+GC and the concurrent ICI and chemotherapy combination was associated with deep and durable responses
  - The CR rate was nearly doubled (21.7% vs 11.8%) and the DoCR almost 3 times longer (37.1 vs 13.2 months) with NIVO+GC, despite a maximum of 2 years of NIVO treatment
- The combination of NIVO+GC resulted in no new toxicity signals, and the safety profile was consistent with the established safety of these agents in prior UC trials
- HRQoL was maintained with addition of NIVO to GC
- NIVO+GC is the first frontline concurrent ICI plus chemotherapy combination to improve OS in this setting, with results supporting NIVO plus cisplatin-based chemotherapy as a new SOC for patients with unresectable or mUC

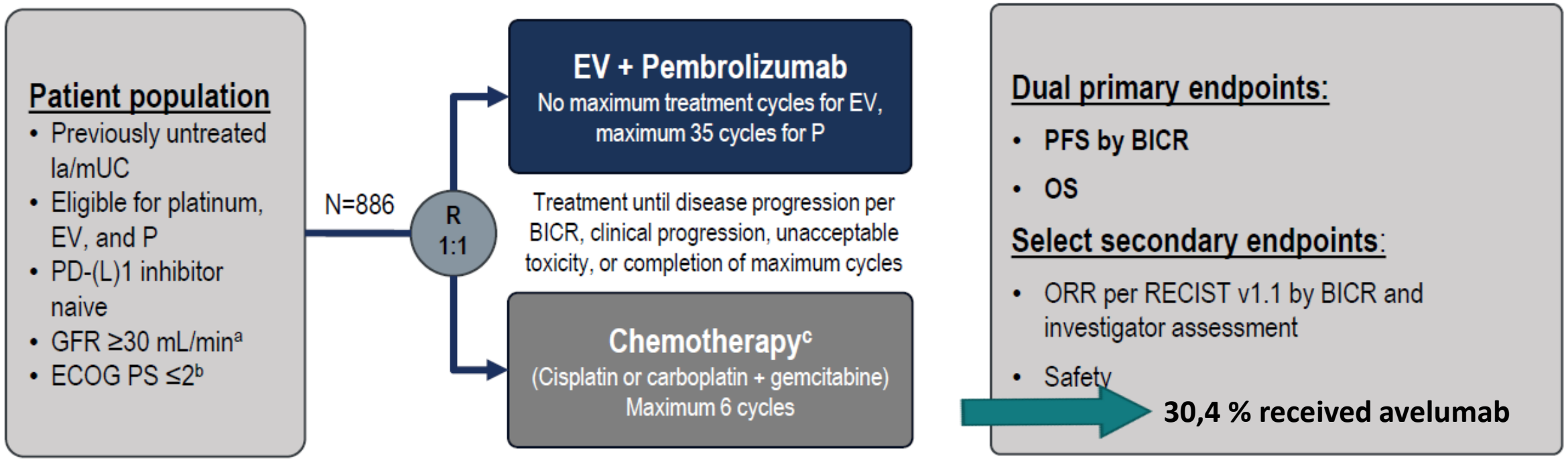
MADRID 2023 ESMO congress

EV-302/KEYNOTE-A39: Open-Label, Randomized Phase 3 Study of Enfortumab Vedotin in Combination with Pembrolizumab vs Chemotherapy in Previously Untreated Locally Advanced or Metastatic Urothelial Carcinoma

Thomas Powles, Begona Perez-Valderrama, Shilpa Gupta, Jens Bedke, Eiji Kikuchi, Jean Hoffman-Censits, Gopa Iyer, Christof Vulsteke, Se Hoon Park, Sang Joon Shin, Daniel Castellano Gauna, Giuseppe Fornarini, Jian-Ri Li, Mahmut Gumus, Nataliya Mar, Sujata Narayanan, Xuesong Yu, Seema Gorla, Blanca Homet Moreno, Michiel Van der Heijden

FPN: LBA6

EV-302/KEYNOTE-A39 (NCT04223856)



Stratification factors: cisplatin eligibility (eligible/ineligible), PD-L1 expression (high/low), liver metastases (present/absent)

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

BICR, blinded independent central review; ECOG PS, Eastern Cooperative Oncology Group performance status; GFR, glomerular filtration rate; ORR, overall response rate; PFS, progression-free survival; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors
[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 the additional criteria: hemoglobin ≥10 g/dL, GFR ≥50mL/min, may not have NYHA class III heart failure
[c]Maintenance therapy could be used following completion and/or discontinuation of platinum-containing therapy

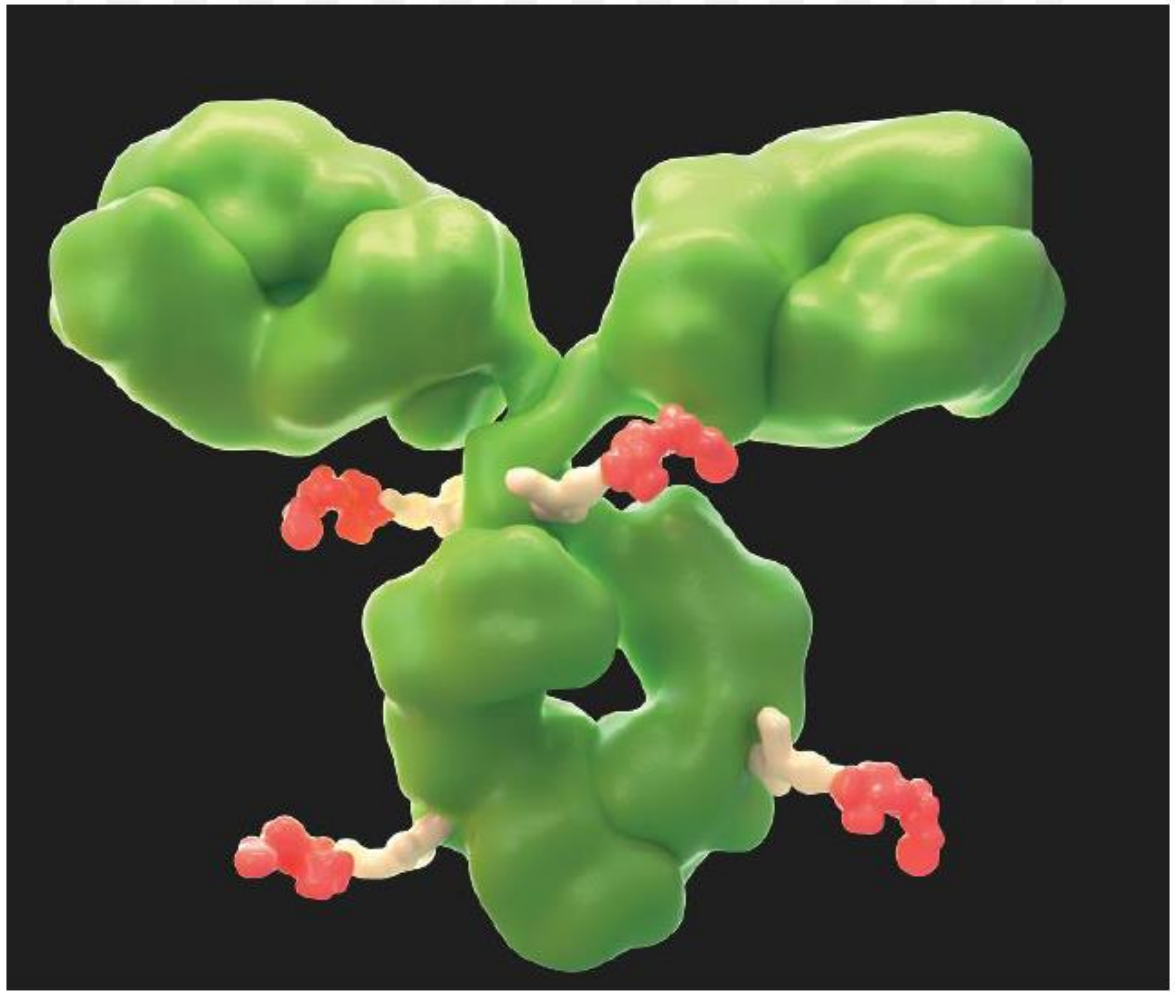
Data cutoff: 08 Aug 2023; FPI: 7 Apr 2020, LPI: 09 Nov 2022

Enfortumab Vedotin (EV), an Antibody-Drug Conjugate Targeting Nectin-4

Is it a chemo-free regimen ???

- Antibody-drug conjugates are made up of 3 parts:
  - **The antibody: Anti-nectin-4**
  - **The payload: MMAE**
  - **The linker (stable in circulation, but releases the cytotoxic agent in the target cell)**

- Nectin-4 is highly expressed in metastatic urothelial cancer patients not necessitating tumor screening
- The payload MMAE (plus linker) is vedotin, a microtubule-disrupting agent (200x more potent than vinblastine)
- December 2019, FDA granted accelerated approval of EV for 2 indications 1]Platinum and PD-1/PD-L1 refractory metastatic urothelial carcinoma; 2] cisplatin-ineligible and have previously received PD-1/PD-L1 therapy

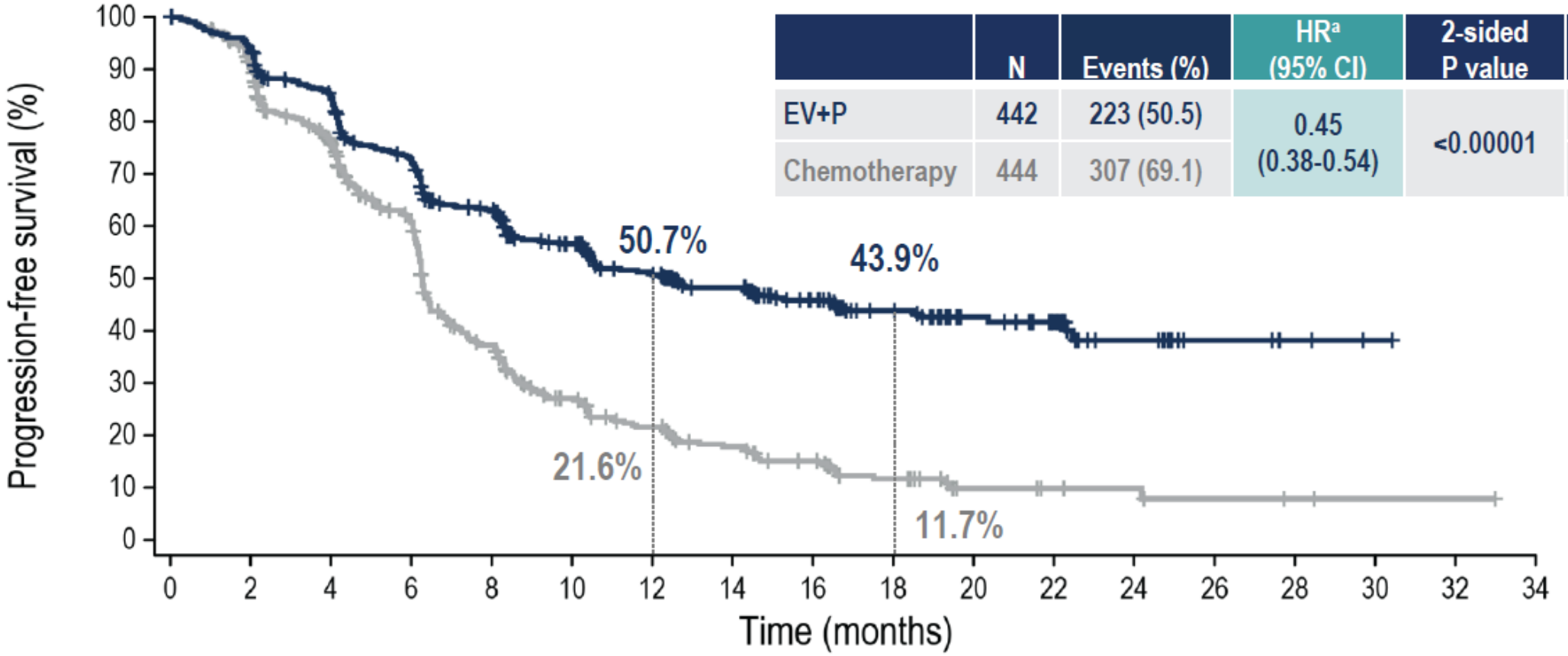


Rosenberg, J et al., J Clin Oncol. 2019 10;37(29):2592-2600

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)



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

Data cutoff: 08 Aug 2023

PFS at 12 and 18 months as estimated using Kaplan-Meier method
HR, hazard ratio; mPFS, median progression-free survival
[a]Calculated using stratified Cox proportional hazards model; a hazard ratio <1 favors the EV+P arm

MADRID 2023 ESMO congress

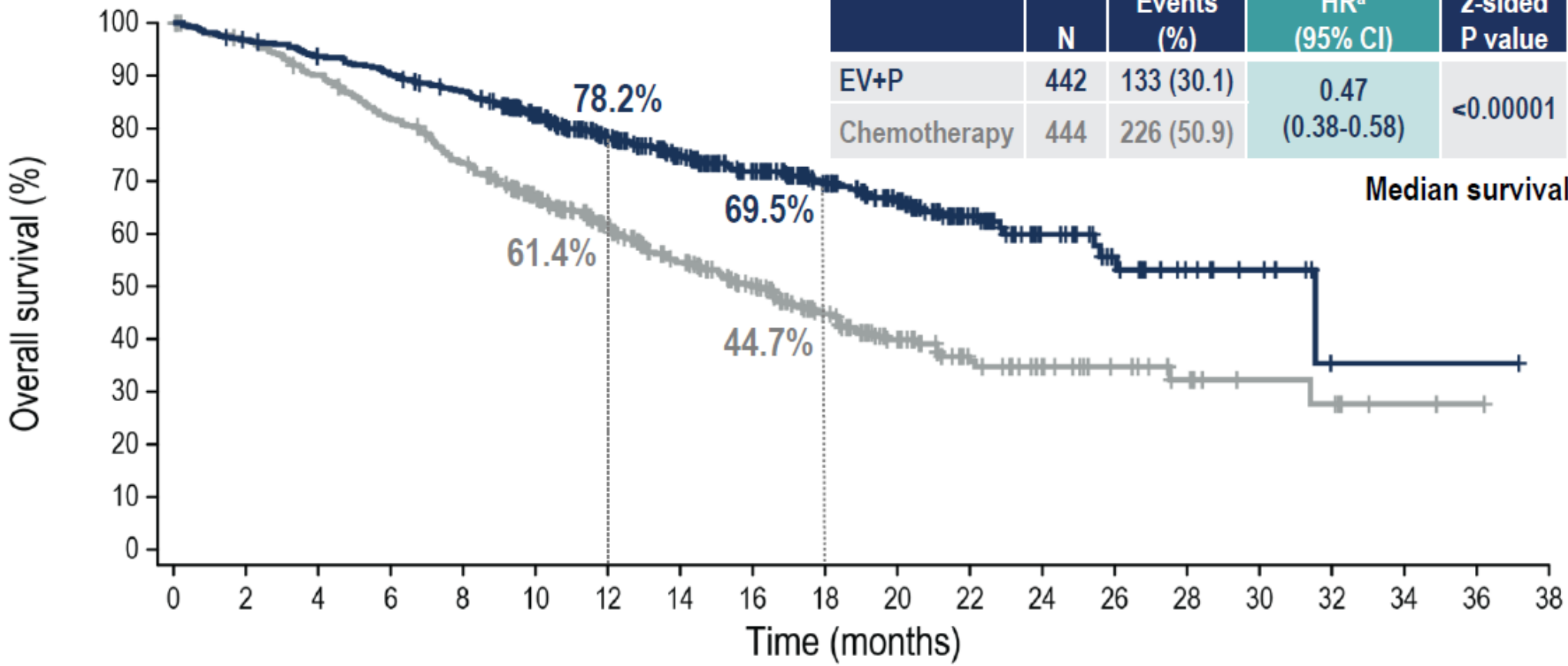
Powles et al.

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



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

Data cutoff: 08 Aug 2023

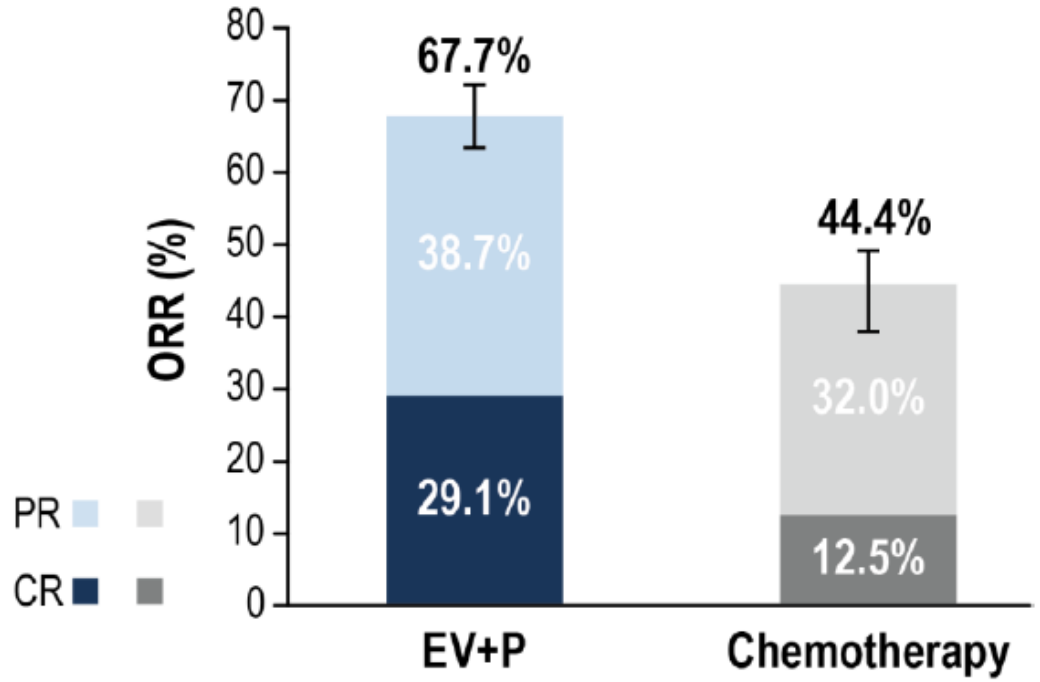
OS at 12 and 18 months was estimated using Kaplan-Meier method
mOS, median overall survival; NR, not reached
[a]Calculated using stratified Cox proportional hazards model. A hazard ratio <1 favors the EV+P arm

MADRID 2023 ESMO congress

Powles et al.

Confirmed Overall Response per BICR

Significant improvement in objective response rate was observed with EV+P



	EV+P (N=437)	Chemotherapy (N=441)
Confirmed ORR, n (%) (95% CI)	**296 (67.7) (63.1-72.1)**	**196 (44.4) (39.7-49.2)**
2-sided P value	<0.00001	
Best overall response[a], n (%)		
Complete response	127 (29.1)	55 (12.5)
Partial response	169 (38.7)	141 (32.0)
Stable disease	82 (18.8)	149 (33.8)
Progressive disease	38 (8.7)	60 (13.6)
Not evaluable/No assessment[b]	21 (4.8)	36 (8.2)

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

CR, complete response; DOR, duration of response; PR, partial response
[a]Best overall response according to RECIST v1.1 per BICR. CR or PR was confirmed with repeat scans ≥28 days after initial response
[b]Patients had either post-baseline assessment and the best overall response was determined to be not evaluable per RECIST v1.1 or no response assessment post-baseline

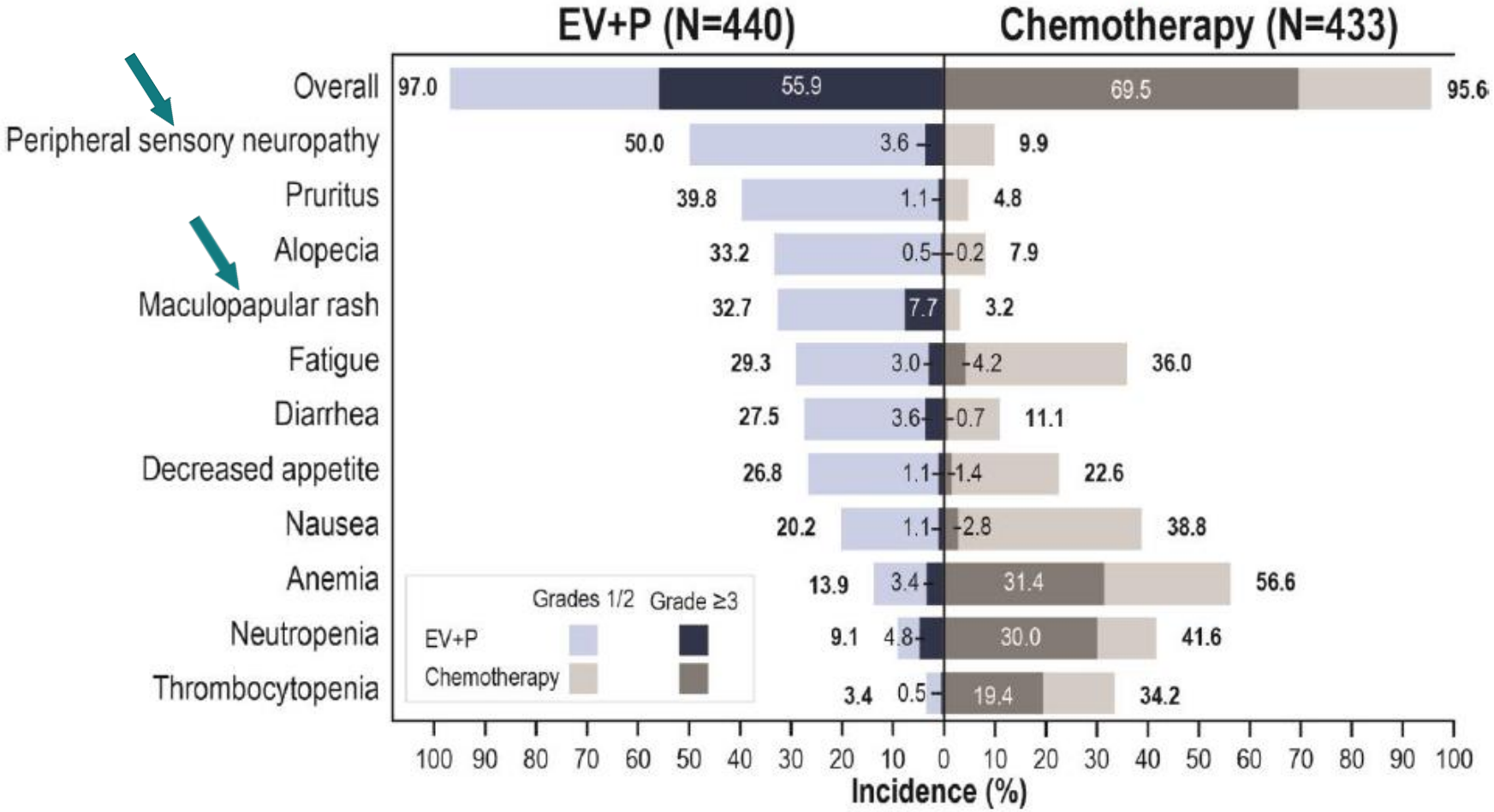
Data cutoff: 08 Aug 2023

MADRID 2023 ESMO congress

Powles et al.

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

Data cutoff: 08 Aug 2023

MADRID 2023 ESMO congress

Powles et al.

TRAEs shown in figure are any grade by preferred term in ≥20% of patients for any grade in either arm
TRAEs, treatment-related adverse events

EV Treatment-Related Adverse Events of Special Interest*

Majority of treatment-related AESIs were low grade

	EV+P (N=440) n (%)		Chemotherapy (N=433) n (%)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Skin reactions	294 (66.8)	68 (15.5)	60 (13.9)	1 (0.2)
Peripheral neuropathy	278 (63.2)	30 (6.8)	53 (12.2)	0 (0.0)
Sensory events	260 (59.1)	19 (4.3)	51 (11.8)	0 (0.0)
Motor events	44 (10.0)	12 (2.7)	5 (1.2)	0 (0.0)
Ocular disorders	94 (21.4)	0 (0.0)	12 (2.8)	0 (0.0)
Dry eye	82 (18.6)	0 (0.0)	8 (1.8)	0 (0.0)
Hyperglycemia	57 (13.0)	27 (6.1)	3 (0.7)	0 (0.0)
Infusion-related reactions	9 (2.0)	0 (0.0)	9 (2.1)	0 (0.0)

Data cutoff: 08 Aug 2023

*There are differences in the rates of skin reactions reported for EV treatment-related AESIs and P TEAEs of special interest because these adverse events were reported via different methodologies developed for EV and P monotherapies, respectively
AESI, adverse event of special interest

Summary & Conclusions

- EV-302/KEYNOTE-A39 is the first time that platinum-based chemotherapy has been surpassed in OS in patients with previously untreated la/mUC

- EV+P showed statistically significant and clinically meaningful improvement in efficacy over chemotherapy
  - PFS HR: 0.45; OS HR: 0.47
  - mPFS and mOS were nearly doubled in the EV+P arm compared with chemotherapy
  - Benefit in prespecified subgroups and stratification factors was consistent with the overall population

- The safety profile of EV+P was generally manageable, with no new safety signals observed

- These results support EV+P as a potential new standard of care for 1L la/mUC

ESMO Clinical Practice Guideline interim update on first-line therapy in advanced urothelial carcinoma

T. Powles, J. Bellmunt, E. Comperat, M. De Santis, R. Huddart, Y. Loriot, A. Necchi, B.P. Valderrama, A. Ravaud, S.F. Shariat, B. Szabados, M.S. van der Heijden, S. Gillessen, on behalf of the ESMO Guidelines Committee

Highlights (online only):

- This ESMO Clinical Practice Guideline eUpdate addresses developments in first-line therapy in advanced urothelial carcinoma.
- EV+P is the new standard of care in first-line advanced urothelial carcinoma.
- Nivolumab–cisplatin–gemcitabine or platinum-based ChT and maintenance avelumab are alternatives if EV+P is not possible.

Recommendations

- EV+P is recommended as the preferred first-line therapy for advanced or metastatic UC, irrespective of platinum eligibility [I, A; FDA approved; not EMA approved].

- After progression on EV+P, standard platinum-based ChT without maintenance avelumab in unselected patients or erdafitinib in selected *FGFR*-altered tumours can be recommended [IV, B].

- Rechallenge with a single-agent ICI is not encouraged without further evidence [V, D].

- Patients not able to receive EV+P should be treated with nivolumab plus up to six cycles of gemcitabine–cisplatin (if cisplatin-eligible only) [I, A] (awaiting FDA and EMA decision) or up to six cycles of platinum-based ChT (gemcitabine plus cisplatin or carboplatin) [I, A], followed by maintenance avelumab (for non-progressing tumours) [I, A; ESMO-Magnitude of Clinical Benefit Scale (ESMO-MCBS) v1.1 score: 4].

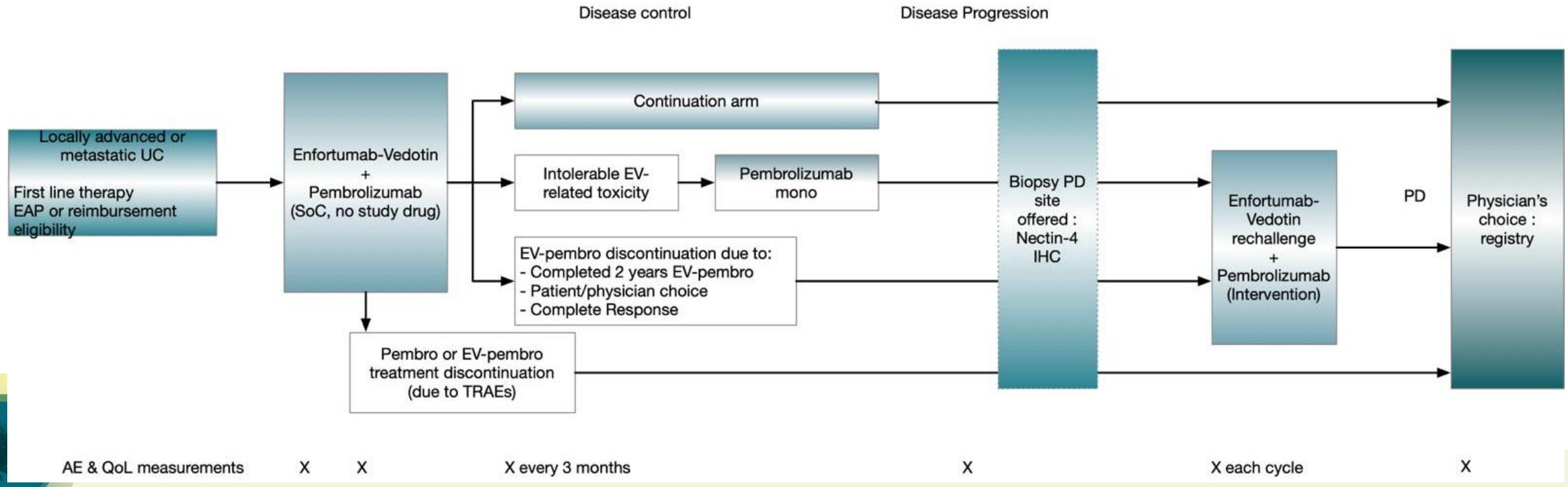
- Single-agent ICIs have a limited role in first-line advanced disease and should not be given

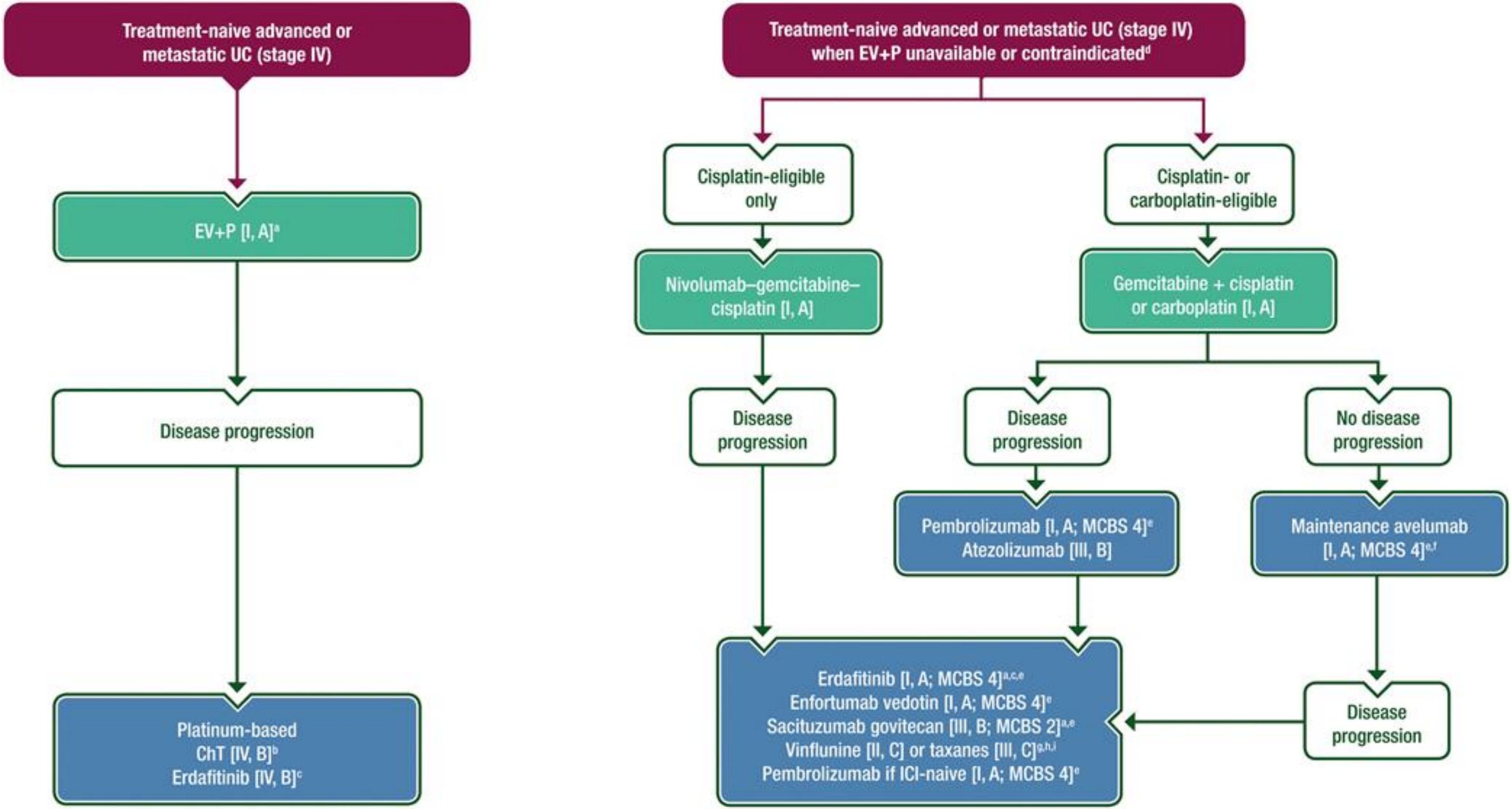
- There are two changes for treatment after first-line platinum-based ChT and an ICI (given concurrently, sequentially or as second-line therapy):
  - Erdafitinib is recommended in patients with selected *FGFR* DNA fusions and mutations who have previously been treated with ChT and an ICI [I, A; ESMO-MCBS v1.1 score: 4; Food and Drug Administration (FDA) approved, not European Medicines Agency (EMA) approved].
  - Sacituzumab govitecan can be recommended in patients previously treated with ChT and an ICI [III, B; ESMO-MCBS v1.1 score: 2; FDA approved, not EMA approved].

- For patients with progression after EV+P, treatments not previously given may be considered for third- and fourth-line therapy [V, C].

EAU in press – concerns

- Post – protocol therapies ?
- Extending duration of therapy - 2 years of EV needed?
- Toxicity – skin reactions, diabetes, neuropathy … **No QOL data**
- Cost : 127 individuals 1 cycle of chemo VERSUS 1 individual EV + Pem



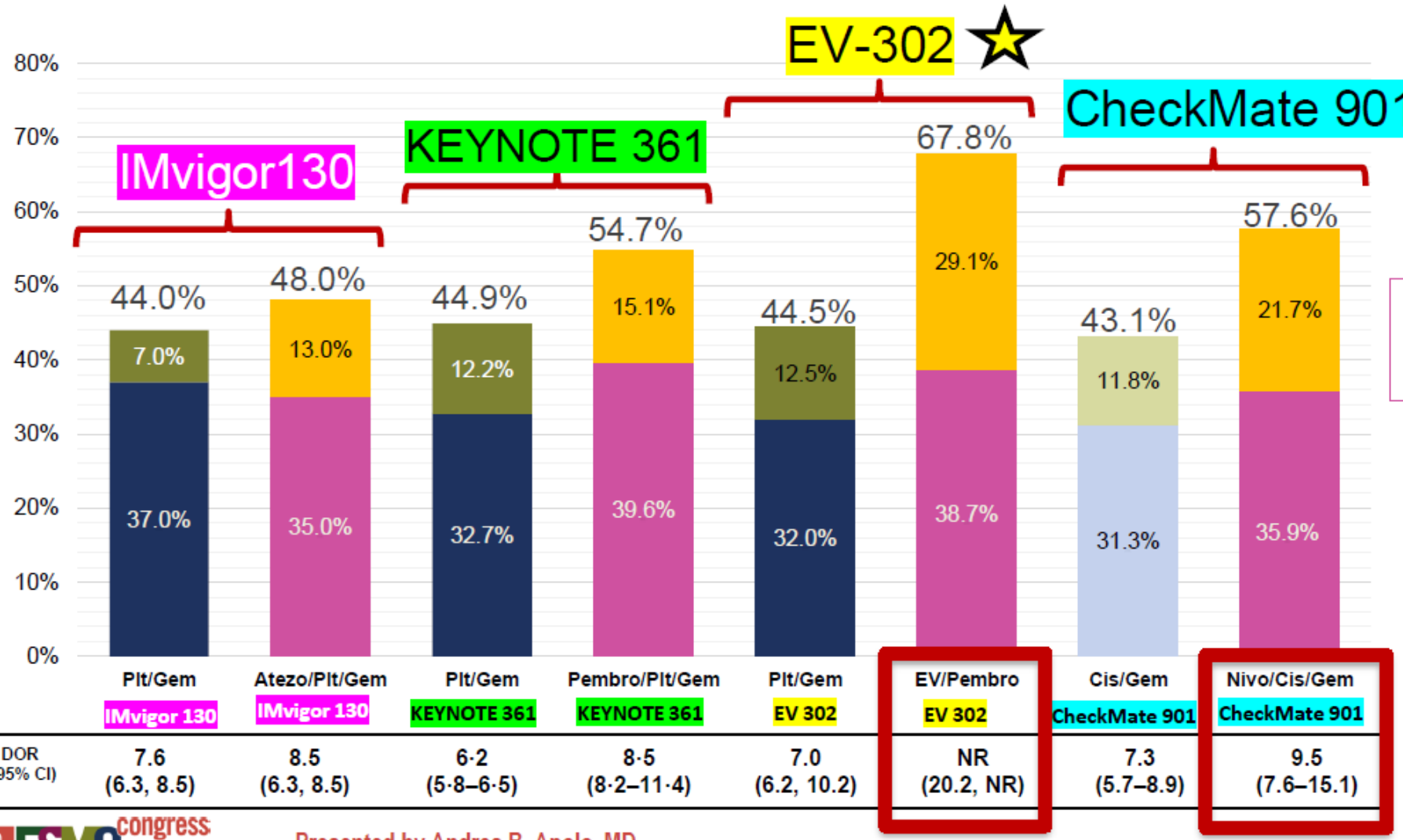


Pre-proof ESMO guideline 2024

Cross-trial comparison on display

WARNING

EV + Pembro's Duration of Response is longer



	Plt/Gem IMvigor 130	Atezo/Plt/Gem IMvigor 130	Plt/Gem KEYNOTE 361	Pembro/Plt/Gem KEYNOTE 361	Plt/Gem EV 302	EV/Pembro EV 302	Cis/Gem CheckMate 901	Nivo/Cis/Gem CheckMate 901
Median DOR Months, (95% CI)	7.6 (6.3, 8.5)	8.5 (6.3, 8.5)	6·2 (5·8–6·5)	8·5 (8·2–11·4)	7.0 (6.2, 10.2)	NR (20.2, NR)	7.3 (5.7–8.9)	9.5 (7.6–15.1)

EV302 and CM901:
Time to response was ~2 months or first restaging scan

MADRID 2023 ESMO congress

Presented by Andrea B. Apolo, MD

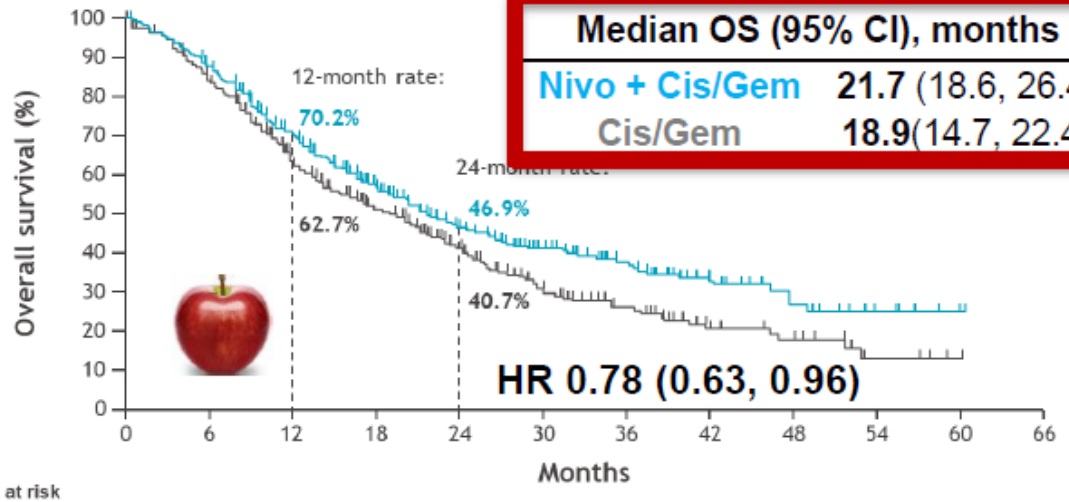
@apolo_andrea

Both sequential and combination chemo and CPI have efficacy

Nivo+Cis/Gem vs Cis/Gem

CheckMate 901 Study

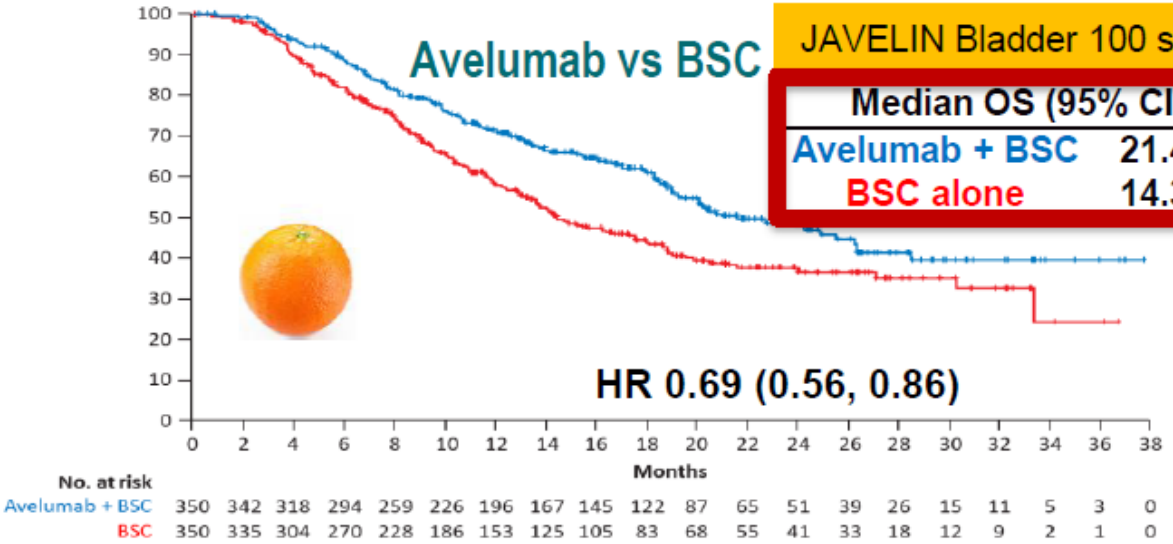
Median OS (95% CI), months	
Nivo + Cis/Gem	**21.7** (18.6, 26.4)
Cis/Gem	**18.9**(14.7, 22.4)



Avelumab vs BSC

JAVELIN Bladder 100 study

Median OS (95% CI), months	
Avelumab + BSC	**21.4** (18.9, 26.1)
BSC alone	**14.3** (12.9, 17.9)



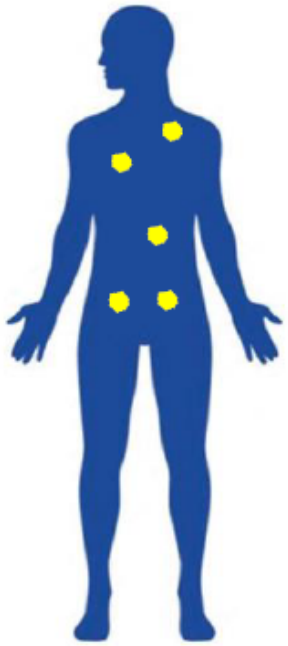
- We cannot directly compare these studies
- Different patient populations
- Avelumab maintenance study included only responders to 1L chemo
- Length of maintenance CPI therapy was similar: ~6 months for both

MADRID 2023 ESMO congress

Powles T, et al. NEJM 2020 Sep 24;383(13):1218-1230

Presented by Andrea B. Apolo, MD
@apolo_andrea

What would be the best 2nd line therapy?



First-Line

- **Enfortumab vedotin + Pembrolizumab**

Second-Line?

Cisplatin-eligible

- **Cisplatin + gemcitabine**
- **Dose-dense methotrexate + vinblastine + doxorubicin + cisplatin (ddMVAC)**

Cisplatin-ineligible

- **Carboplatin + gemcitabine**

Beyond-Second -Line

- **Erdafitinib (if tumor + FGFR 2/3 genetic alterations)**
- **Sacituzumab govitecan**
- **Clinical trial**
- **Paclitaxel, docetaxel, or vinflunine**

BMUC
UROLOGY - RADIATION ONCOLOGY - MEDICAL ONCOLOGY

11th Belgian Multidisciplinary Meeting on Urological Cancers

PLATINUM CORPORATE SPONSORS

astellas ONCOLOGY

Johnson&Johnson

MSD

CORPORATE SPONSORS

accord We make it better

IPSEN Innovation for patient care

NOVARTIS

GOLD SPONSORS

AstraZeneca

MERCK Marketing Authorisation Holder

Pfizer

Bristol Myers Squibb™

SILVER SPONSORS

RECORDATI

BRONZE SPONSORS

Telix Innovations

BAYER

FERRING PHARMACEUTICALS