

Metastatik Mesane ve Üst Üriner Sistem Kanserlerinde Birinci Basamak Tedavi

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Tıbbi Onkoloji**

Ders Planı

- ❑ Mesane Kanseri İnsidans ve Mortalite

Metastatik Hastalık

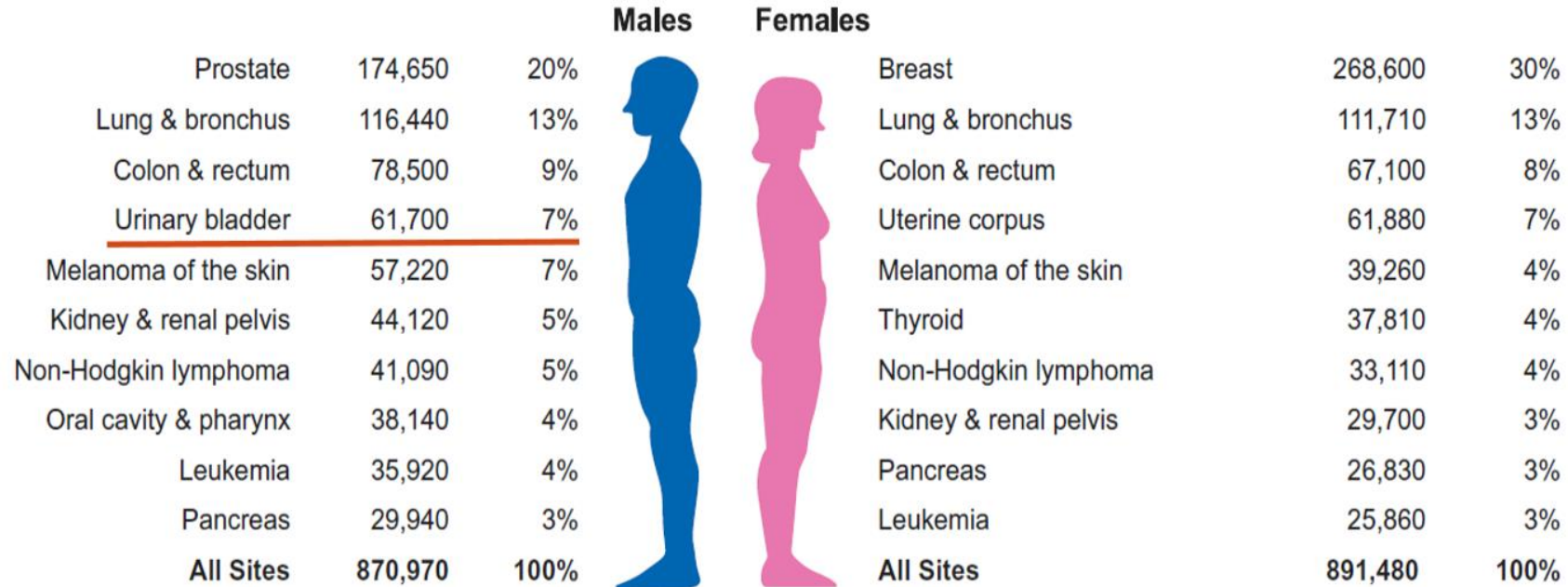
- ❑ Sisplatine uygun hastada birinci basamak

- ❑ Sisplatine uygun olmayan hastada birinci basamak

- ❑ Özet

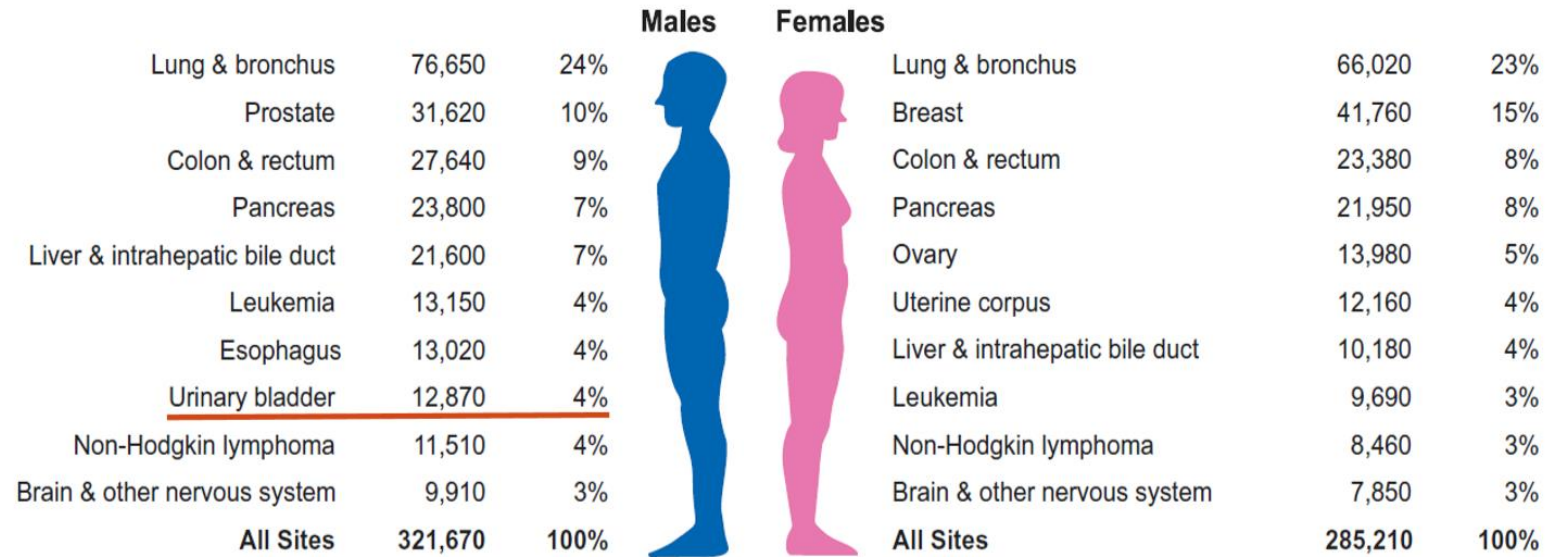
Mesane Kanseri İnsidans ve Mortalite

2019 ESTIMATED NEW CANCER CASES — US



Mesane Kanseri İnsidans ve Mortalite

2019 ESTIMATED CANCER DEATHS – US

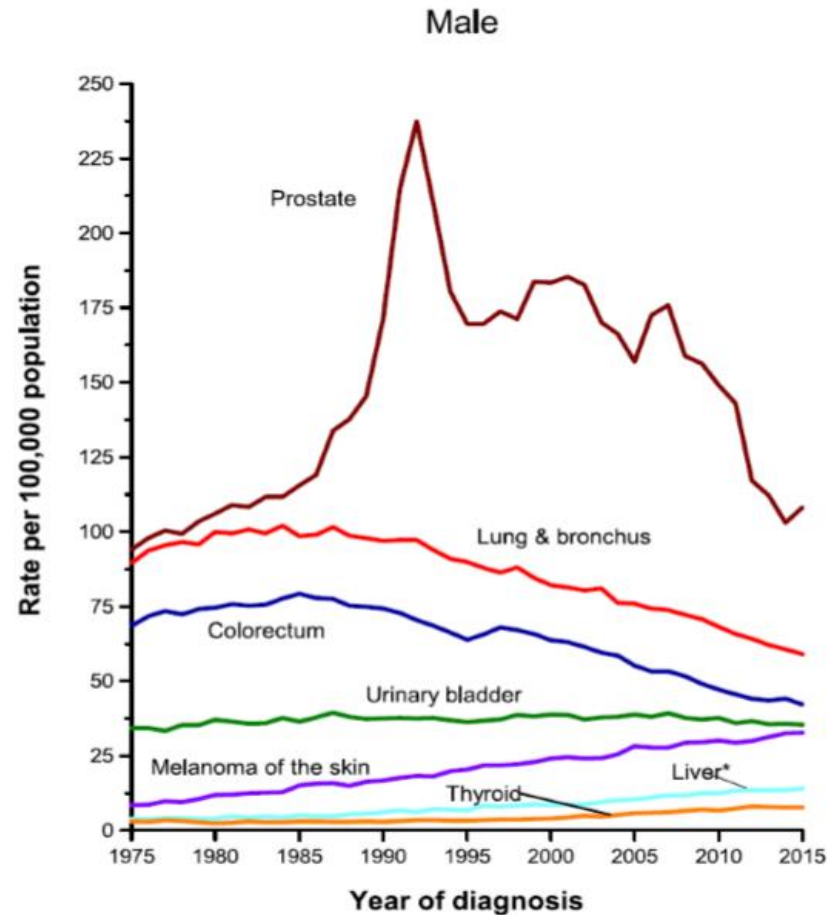


Mesane Kanseri İnsidans ve Mortalite

TEMPORAL TRENDS IN THE INCIDENCE OF BLADDER CANCER

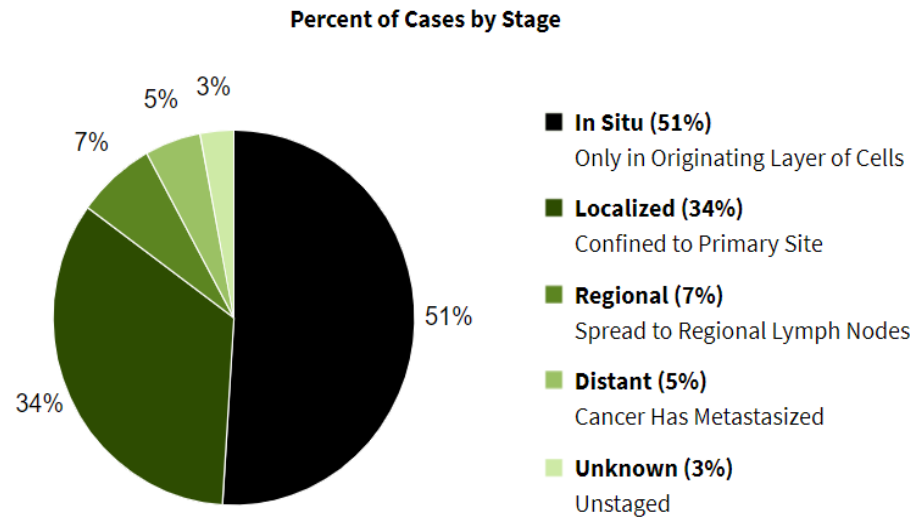
- The incidence of several major cancers has fallen over the last 40 years
 - There have been increased incidence in a few (melanoma and liver for example)
- No major changes in the incidence of bladder cancer in the last 40 years

CA CANCER J CLIN 2019;69:7-34

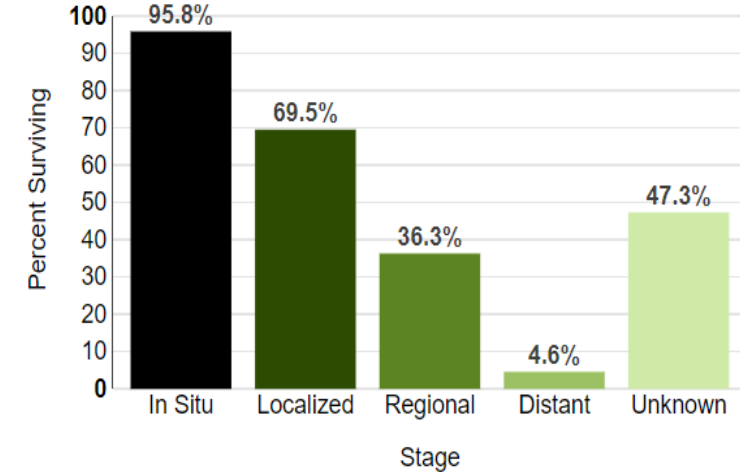


Mesane Kanseri İnsidans ve Mortalite

Percent of Cases & 5-Year Relative Survival by Stage at Diagnosis: Bladder Cancer



5-Year Relative Survival



SEER 18 2009-2015, All Races, Both Sexes by SEER Summary Stage 2000

Metastatik Mesane Kanseri

Birinci Basamak Kemoterapi

Selected randomized clinical trial comparisons of chemotherapy for metastatic bladder cancer

Study (year of publication)	<i>n</i>	Interventions	Response rate (%)	Median OS (months)	Toxicity
Logothetis <i>et al.</i> ³⁶ (1990)	110	MVAC versus CISCA	65 versus 46; $P<0.05$	15.5 versus 10.1; $P= 0.0003$	MVAC>CISCA
Loehrer <i>et al.</i> ³⁷ (1992)	269	MVAC versus cisplatin	39 versus 12; $P<0.0001$	12.5 versus 8.2; $P= 0.0002$	MVAC>cisplatin
Mead <i>et al.</i> ³⁹ (1998)	214	CMV versus MV	46 versus 19 (P value not reported)	7.0 versus 4.5; $P= 0.0065$	CMV>MV
von der Maase <i>et al.</i> ^{70,71} (2000,2005)	405	GC versus MVAC	49 versus 46; $P=0.51$	14.0 versus 15.2; $P=0.66$	MVAC>GC
Sternberg <i>et al.</i> ^{75,76} (2001, 2006)	263	ddMVAC versus MVAC	72 versus 58; $P=0.016$	15.1 versus 14.9 (P value not reported; 5-year OS was 21.8% versus 13.5%, $P= 0.04$)	MVAC>ddMVAC
Bamias <i>et al.</i> ⁸⁴ (2013)	130	ddGC versus ddMVAC	32 versus 27; $P= 0.67$	18 versus 19; $P= 0.98$	ddMVAC>ddGC

CISCA, cisplatin, cyclophosphamide, and doxorubicin; CMV, cisplatin, methotrexate, and vinblastine; ddGC, dose-dense gemcitabine and cisplatin; ddMVAC, dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin; GC, gemcitabine and cisplatin; MV, methotrexate and vinblastine; MVAC, methotrexate, vinblastine, doxorubicin, and cisplatin; *n*, number of patients; OS, overall survival.

Metastatik Birinci Basamak Kemoterapi Sonuçları

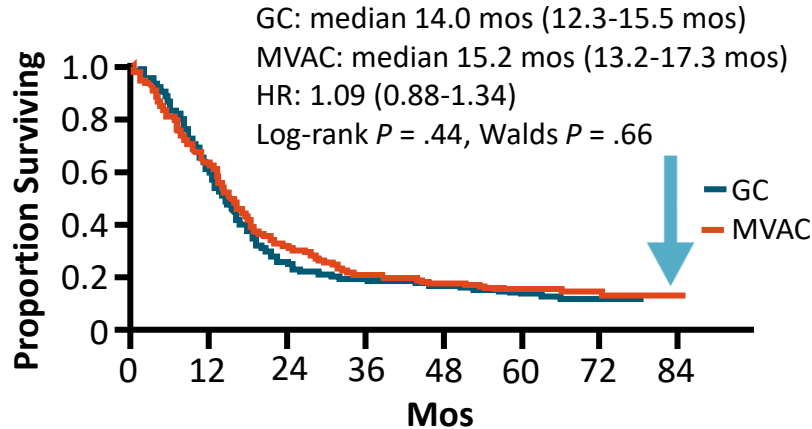
Sisplatin Uygun

Gemcitabine + Cisplatin^[1,2]

ORR: 49%

CR: 12%

Median OS: 14.0 mos



Patients at Risk, n

GC 203 118 50 36 30 23 7 0

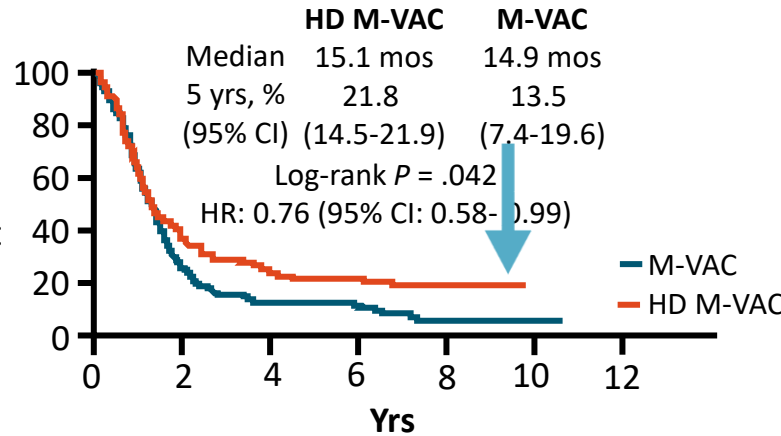
MVAC 202 125 62 40 34 29 9 1

Dose Dense MVAC^[3]

ORR: 72%

CR: 25%

Median OS: 15.1 mos



O N Patients at Risk, n

112 129 32 15 11 4 2 M-VAC

101 134 45 29 23 8 0 HD M-VAC

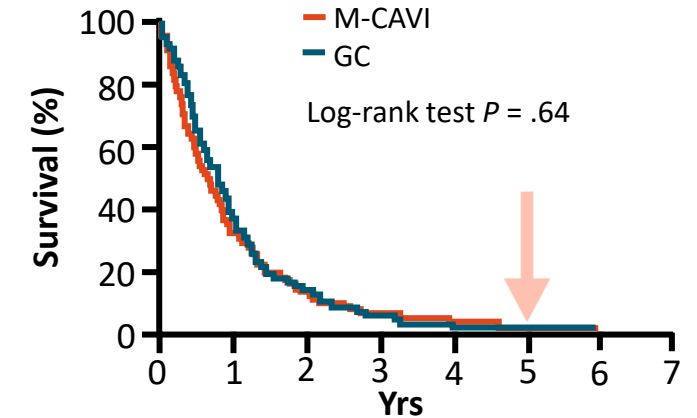
Sisplatin uygun değil

Gemcitabine + Carboplatin^[4]

ORR: 36%

CR: 3%

Median OS: 9.3 mos



O N Patients at Risk, n

M-CAVI 108 119 37 13 7 3 1 1

GC 110 119 44 15 5 2 2 1

1. von der Maase H, et al. J Clin Oncol. 2005;23:4602-4608. 2. von der Maase H, et al. J Clin Oncol. 2000;18:3068-3077.

3. Sternberg CN, et al. Eur J Cancer. 2006;42:50-54. 4. De Santis M, et al. J Clin Oncol. 2012;30:191-199.

Metastatik Birinci Basamak Kemoterapi Sonuçları

Cisplatin-based yields higher CR rates than carboplatin-based therapy in UC

Objective response

Source	Cisplatin-based		Carboplatin-based		Weight (%)	RR (95% CI)	P value
	Events	Total	Events	Total			
Petrioli et al. [15]	12	23	9	23	20.64	1.75 (1.05–2.93)	
Bellmunt et al. [13]	20	28	11	27	16.58	1.33 (0.70–2.54)	
Drecier et al. [2]	14	36	12	39	21.23	1.26 (0.68– 2.36)	
Dogliotti et al. [14]	27	41	22	39	41.55	1.17 (0.82–1.66)	
Overall (Mantel–Haenszel method)	73	128	54	128		1.34 (1.04–1.71)	0.02

Heterogeneity chi-square test = 1.68 (d.f. = 3); $P = 0.642$; I-squared test (variation in RR attributable to heterogeneity) = 0.0%.

RR, risk ratio; CI, confidence interval.

Complete response

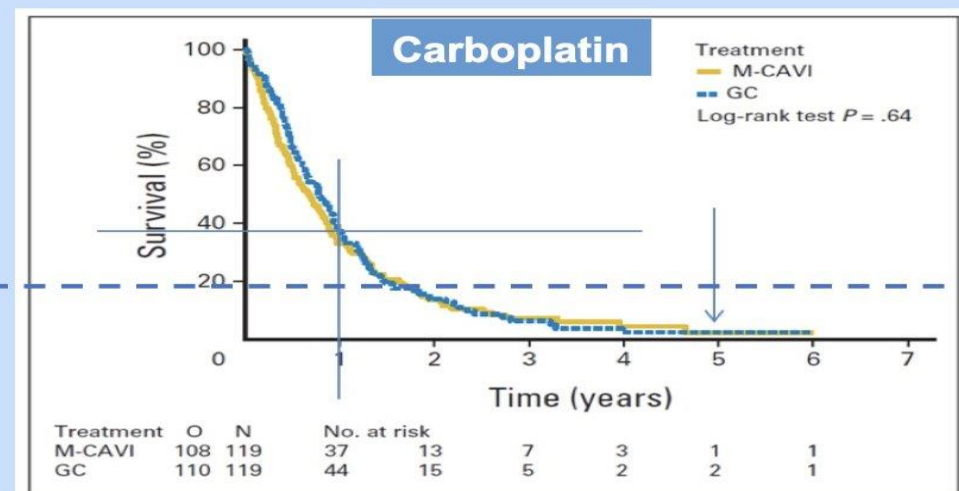
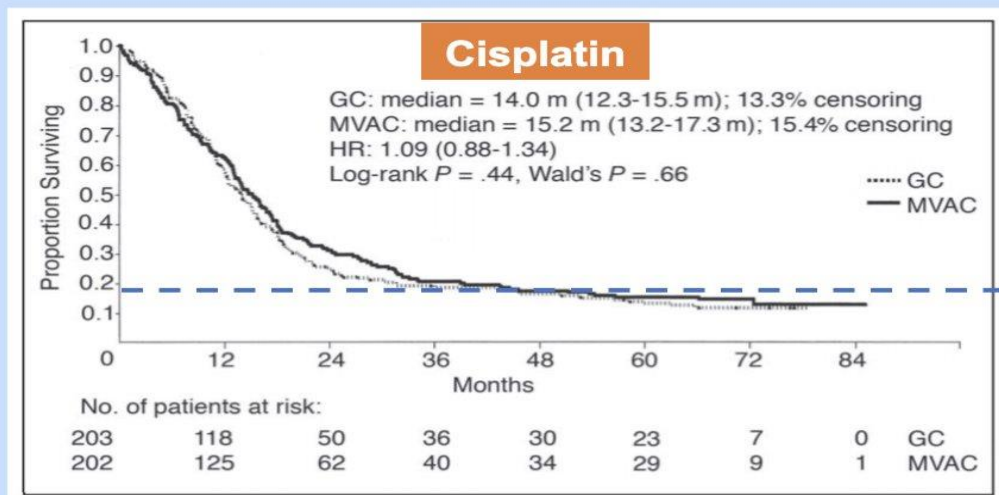
Source	Cisplatin-based		Carboplatin-based		Weight (%)	RR (95% CI)	P value
	Events	Total	Events	Total			
Petrioli et al. [15]	7	28	3	27	51.80	2.25 (0.65–7.18)	
Bellmunt et al. [13]	3	23	0	23	14.54	1.17 (0.07–18.58)	
Drecier et al. [2]	5	36	1	39	16.28	5.42 (0.66–44.12)	
Dogliotti et al. [14]	8	41	1	39	17.38	7.61 (0.10–58.06)	
Overall (Mantel–Haenszel method)	23	128	5	128		3.54 (1.48–8.49)	0.005

Heterogeneity chi-square test = 1.83 (d.f. = 3); $P = 0.609$; I-squared test (variation in RR attributable to heterogeneity) = 0.0%.

RR, risk ratio; CI, confidence interval.

Metastatik Birinci Basamak Kemoterapi Sonuçları

Where is the tail of the curve with carboplatin-based chemotherapy?



1. von der Maase H, et al. J Clin Oncol. 2005. PMID: 16034041
2. De Santis M, et al. EORTC 30986. J Clin Oncol. 2011. PMID: 19786668

Metastatik Birinci Basamak Kemoterapi Sonuçları

Supplementary Table S3. Multivariate Cox Regression Analysis for Overall Survival in the Overall Population.

Variable*	Levels	Parameter Estimate	Standard Error	Wald Chi-Square Statistic	P-Value (2-sided)	HR (95% CI)
Treatment group	Avelumab plus BSC	-0.370	0.1143	10.46	0.0012	0.69 (0.552-0.865)
	BSC alone					
Best response to first-line chemotherapy	Stable disease					
	Complete or partial response	-0.079	0.1241	0.41	0.5242	0.92 (0.724-1.179)
Site of baseline metastasis	Nonvisceral					
	Visceral	0.188	0.1221	2.36	0.1244	1.21 (0.950-1.533)
Age	<65 years					
	≥65 years	-0.215	0.1225	3.07	0.0796	0.81 (0.635-1.026)
Race	White					
	Asian	-0.252	0.1466	2.95	0.0857	0.78 (0.583-1.036)
	Other	-0.589	0.2207	7.11	0.0076	0.56 (0.360-0.855)
PD-L1 status	Positive					
	Negative	0.294	0.1212	5.87	0.0154	1.34 (1.058-1.701)
	Unknown	0.256	0.1981	1.68	0.1956	1.29 (0.876-1.905)
First-line chemotherapy regimen	Gemcitabine plus cisplatin					
	Gemcitabine plus carboplatin	0.262	0.1218	4.64	0.0312	1.30 (1.024-1.651)
	Gemcitabine plus cisplatin/carboplatin	-0.314	0.2927	1.15	0.2840	0.73 (0.412-1.297)
ECOG performance status	0					
	≥1	0.462	0.1149	16.18	<0.0001	1.59 (1.267-1.988)
Liver metastasis	Yes					
	No	-0.421	0.1621	6.73	0.0095	0.66 (0.478-0.902)

BSC, best supportive care; ECOG, Eastern Cooperative Oncology Group; PD-L1, programmed cell death ligand 1.

* Explanatory variables were selected using a stepwise selection procedure. The level of significance for a variable to enter the model was 0.15 and the significance level for removal was 0.04.

Hangi Kemoterapi Rejimi ?

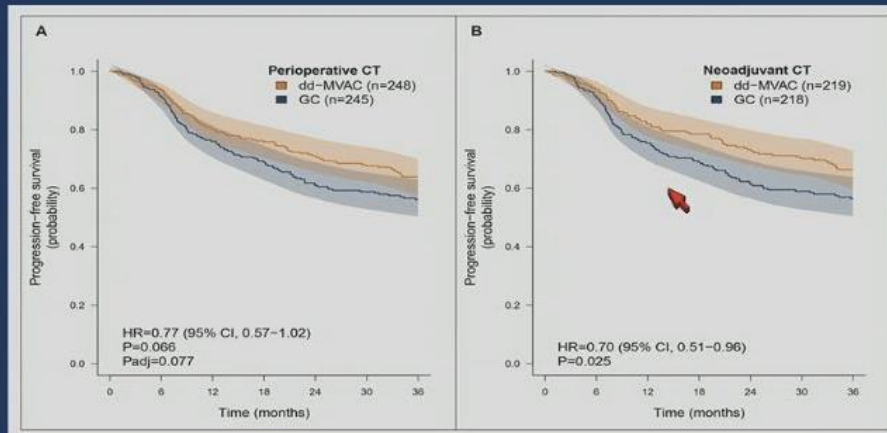
Trial design (3)

- 500 patients included in 28 centers from 2013 to 2018
(493 patients available for intent-to-treat analysis)
- Adjuvant (n=56) and Neoadjuvant (n=437) (88%)
- Primary end-point : Progression Free Survival at 3 years
- Final analysis : Overall and Specific Survival at 5 years



Hangi Kemoterapi Rejimi ?

PFS at 3 years



Perioperative dd-MVAC improved 3-y PFS over GC

In the **neoadjuvant group**, better bladder tumor local control with a **significant improvement on 3-y PFS** in the dd-MVAC arm

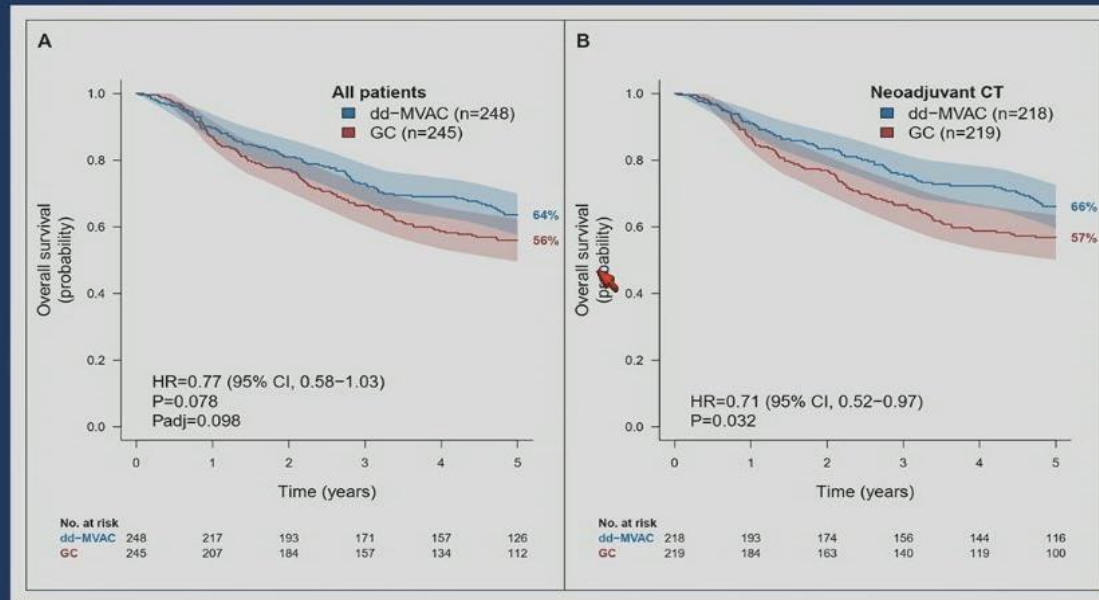
Pfister et al. J Clin Oncol 2022



Hangi Kemoterapi Rejimi ?

Results (1)

Overall Survival at 5 years



Metastatik Mesane Kanseri Birinci Basamak Tedavi Seçimi



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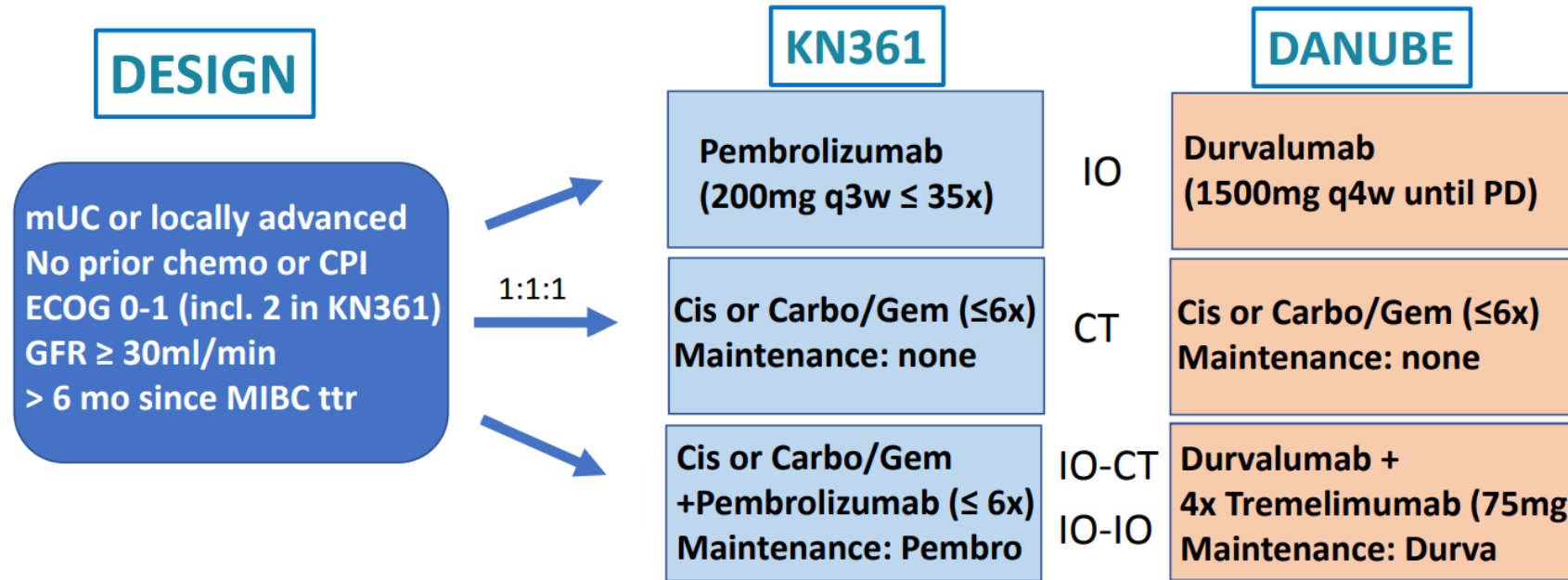
PRINCIPLES OF SYSTEMIC THERAPY

First-Line Systemic Therapy for Locally Advanced or Metastatic Disease (Stage IV)	
Cisplatin eligible	Preferred regimens • Gemcitabine and cisplatin⁴ (category 1) followed by avelumab maintenance therapy (category 1)^{a,11} • DDMVAC with growth factor support (category 1)^{2,8} followed by avelumab maintenance therapy (category 1)^{a,11}
Cisplatin ineligible	Preferred regimens • Gemcitabine and carboplatin¹² followed by avelumab maintenance therapy (category 1)^{a,11} • Pembrolizumab¹⁴ (for the treatment of patients with locally advanced or metastatic urothelial carcinoma who are not eligible for any platinum-containing chemotherapy) • Pembrolizumab and enfortumab vedotin-ejfv¹⁷ Other recommended regimens • Gemcitabine¹⁵ • Gemcitabine and paclitaxel¹⁶ • Atezolizumab¹³ (only for patients whose tumors express PD-L1^b) (category 2B) Useful under certain circumstances • Ifosfamide, doxorubicin, and gemcitabine¹⁸ (for patients with good kidney function and good performance status) • Atezolizumab¹³ (only for patients who are not eligible for any platinum-containing chemotherapy regardless of PD-L1 expression) (category 3)

Sisplatin Kombinasyonlu Kemoterapiye Uygun Olmayan Hasta Grubu

- ❑ ECOG PS ≥ 2
- ❑ Kreatinin klirensi $< 60\text{ml/dk}$
- ❑ İşitme kaybı olması grade2>
- ❑ Periferik nöropati grade2>
- ❑ KKY olması (NYHA class III)

Metastatik Mesane Kanseri Birinci Basamak Platin bazlı kemoterapi+ İmmün kontrol noktası inhibitörleri



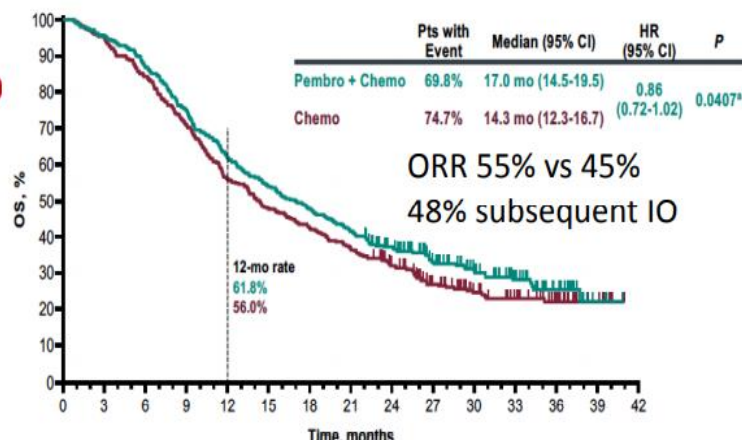
	KEYNOTE 361 (N=1010)	DANUBE (N=1032)
Stratification	Cis/Carbo investigator choice PD-L1: CPS ≥10	Cisplatin eligibilty PD-L1: ≥25% IC and/or TC positive Liver and/or lung metastases
Primary endpoints	PFS and OS: IO-CT vs CT (total) OS: IO vs CT (total and PD-L1 +) Sequential testing!	OS: IO-IO vs CT (ITT) OS: IO vs CT (PD-L1 +)
Minimum follow up	22 months (median 31.7)	34 months (median 41.2)

Metastatik Mesane Kanseri Birinci Basamak Platin bazlı kemoterapi+ İmmün kontrol noktası inhibitörleri

Overall survival

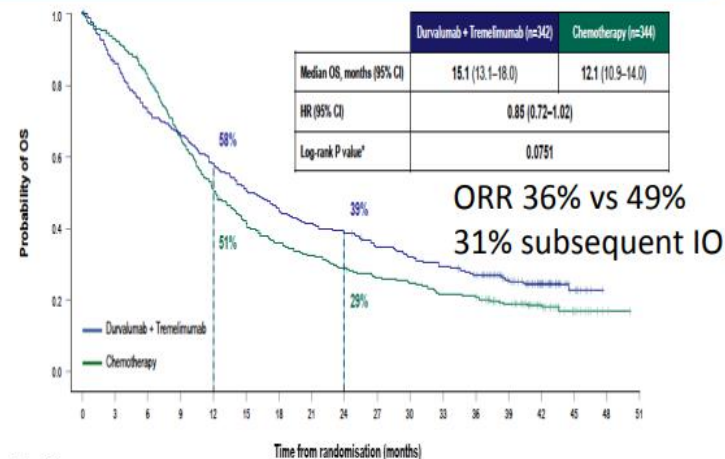
Combination vs Chemo

TOTAL population (ITT)



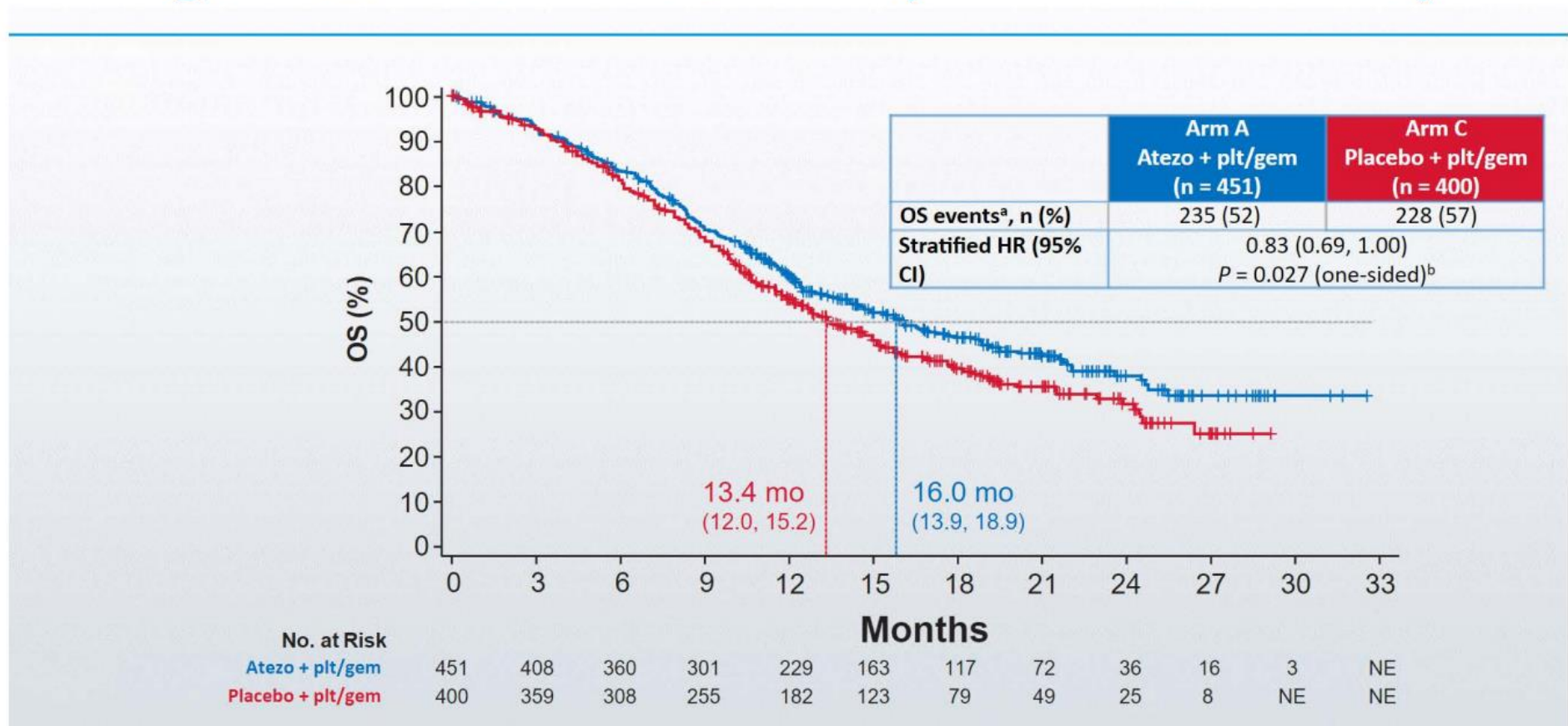
KEYNOTE 361 –IO-CT vs CT (1°EP)

DANUBE – IO-IO vs CT (1°EP)

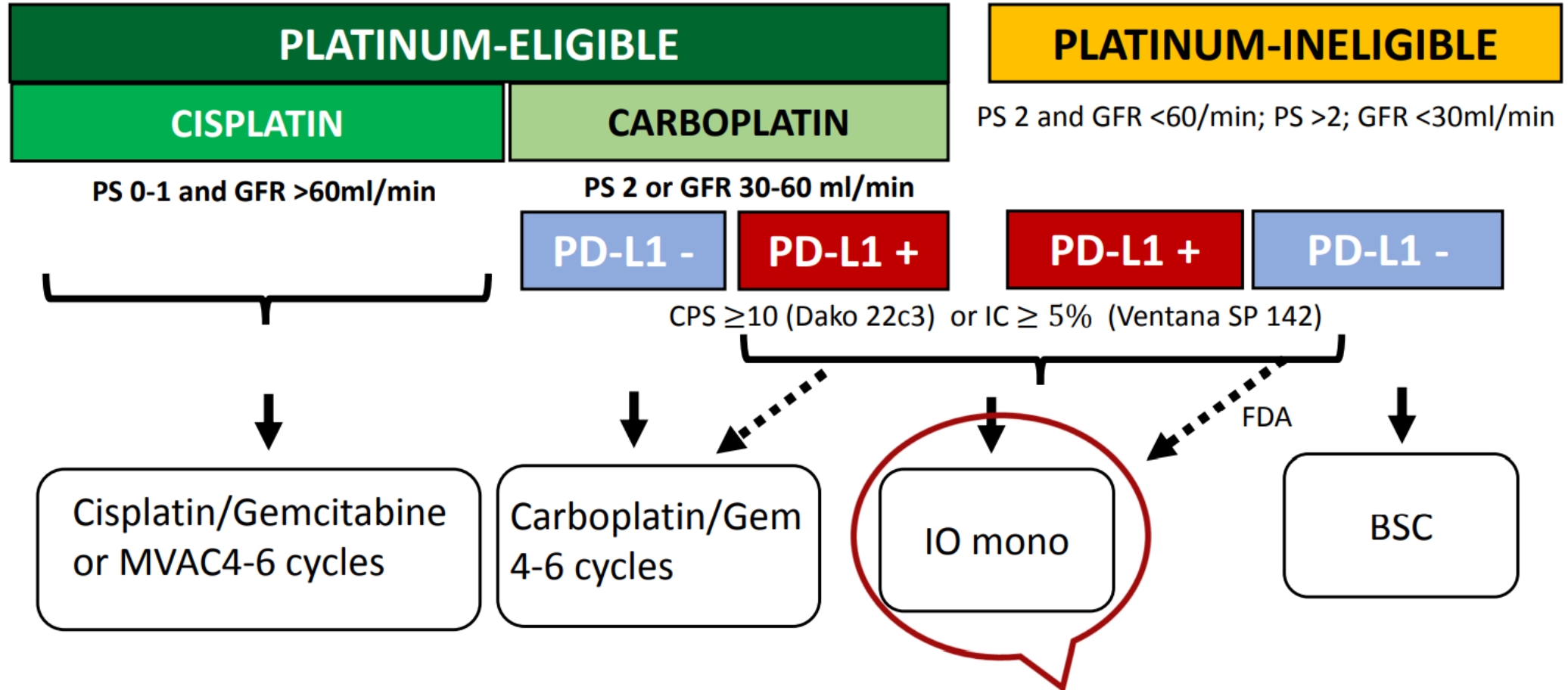


Metastatik Mesane Kanseri Birinci Basamak Platin bazlı kemoterapi+ İmmün kontrol noktası inhibitörleri

IMvigor130 Interim OS: ITT (Arm A vs Arm C)



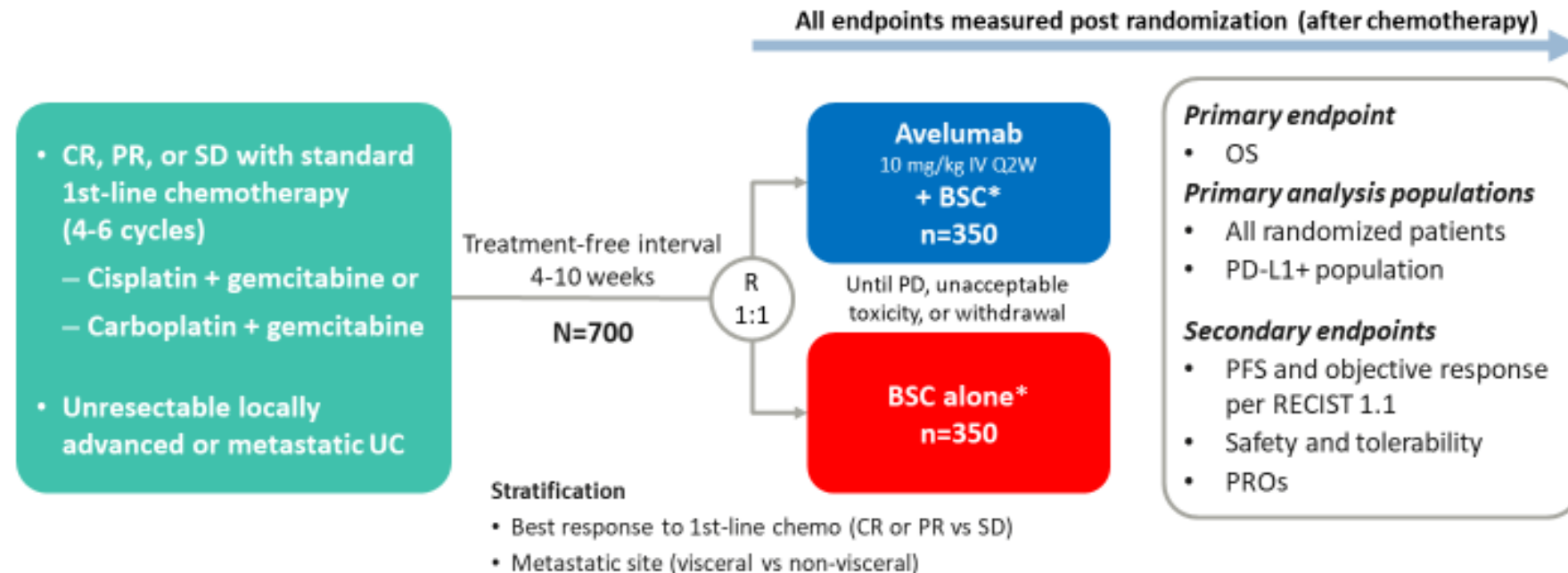
Metastatik Mesane Kanseri Birinci Basamak Tedavi Seçimi



Pembrolizumab Lancet Oncology 2017/JCO 2020
Atezolizumab Lancet 2017

Metastatik Mesane Kanseri Birinci Basamak Tedavi Platin bazlı kemoterapi Sonrası İdame Avelumab

JAVELIN Bladder 100 study design (NCT02603432)



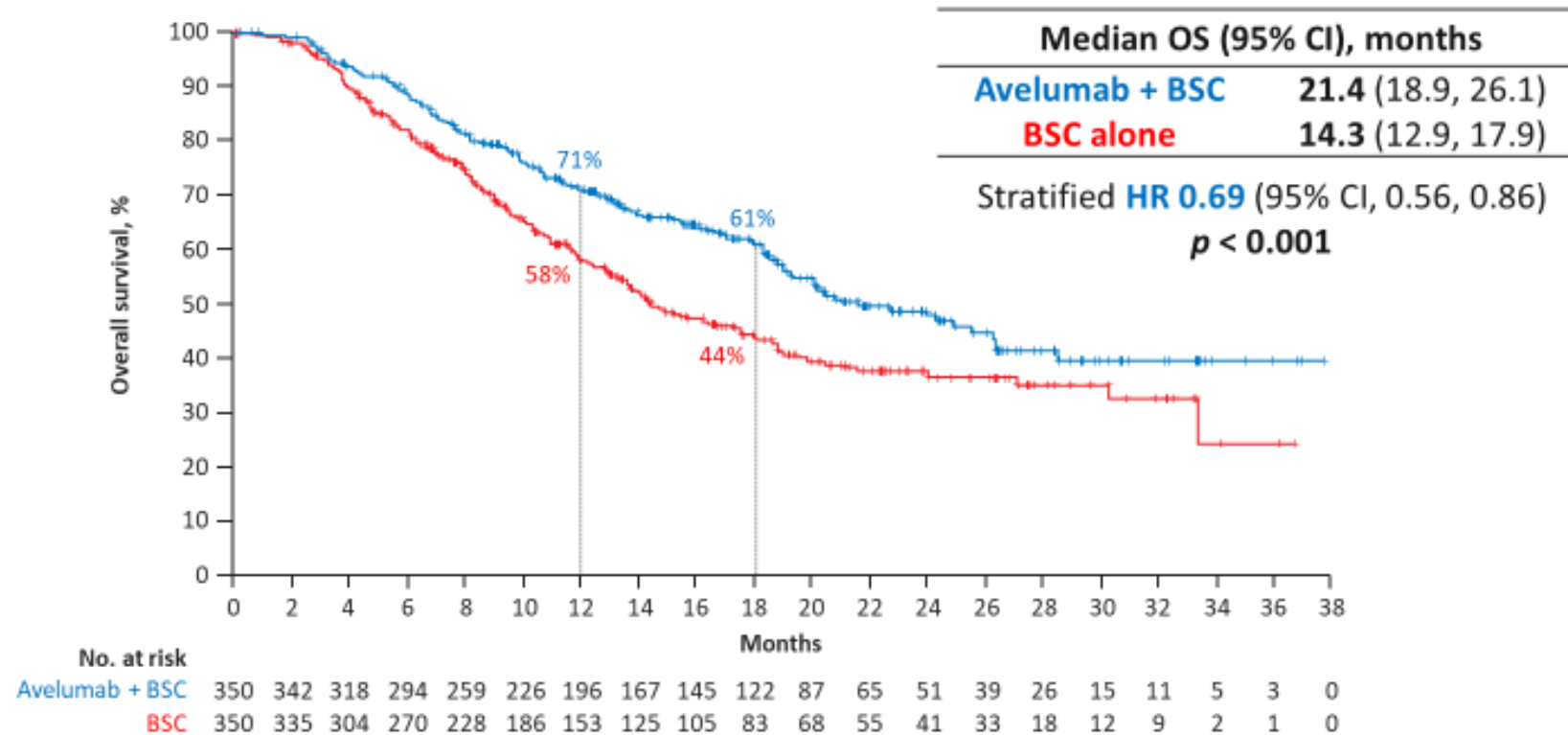
PD-L1+ status was defined as PD-L1 expression in $\geq 25\%$ of tumor cells or in $\geq 25\%$ or 100% of tumor-associated immune cells if the percentage of immune cells was $>1\%$ or $\leq 1\%$, respectively, using the SP263 assay; 358 patients (51%) had a PD-L1-positive tumor

BSC, best supportive care; CR, complete response; IV, intravenous; PR, partial response; PRO, patient reported outcome; Q2W, every 2 weeks; R, randomization; RECIST 1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease

*BSC (eg, antibiotics, nutritional support, hydration, or pain management) was administered per local practice based on patient needs and clinical judgment; other systemic antitumor therapy was not permitted, but palliative local radiotherapy for isolated lesions was acceptable

Metastatik Mesane Kanseri Birinci Basamak Tedavi Platin bazlı kemoterapi Sonrası İdame Avelumab

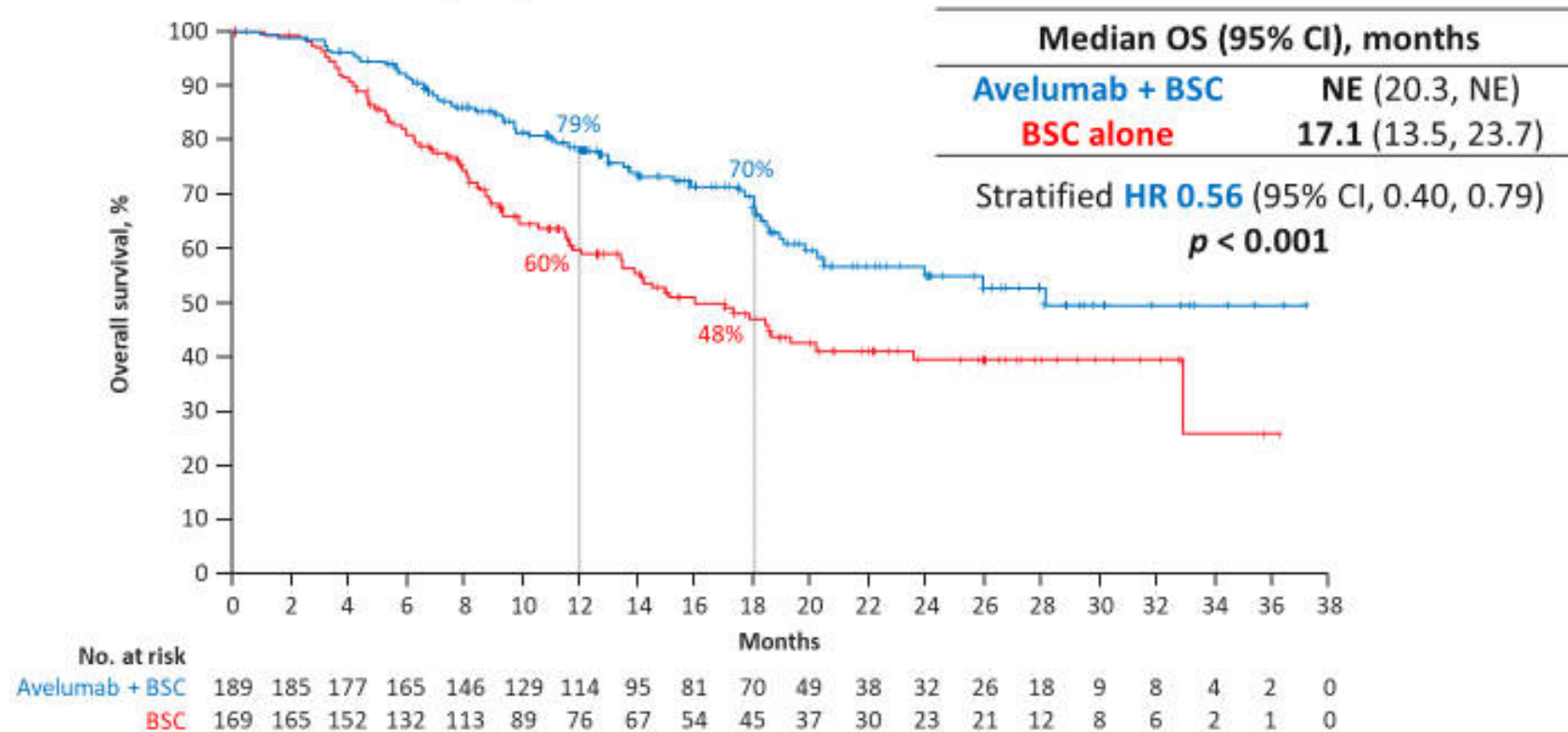
OS in the overall population



OS was measured post randomization (after chemotherapy); the OS analysis crossed the prespecified efficacy boundary based on the alpha-spending function ($P < 0.0053$)

Metastatik Mesane Kanseri Birinci Basamak Tedavi Platin bazlı kemoterapi Sonrası İdame Avelumab

OS in the PD-L1+ population



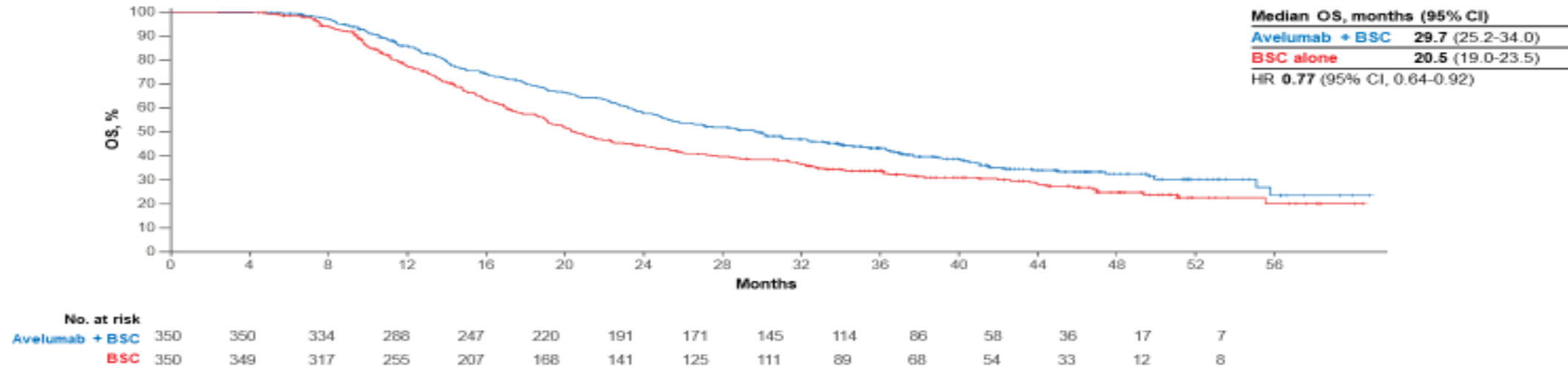
OS was measured post randomization (after chemotherapy); the OS analysis crossed the prespecified efficacy boundary based on the alpha-spending function ($P < 0.0014$). NE, not estimable

Metastatik Mesane Kanseri Birinci Basamak Tedavi Platin bazlı kemoterapi Sonrası İdame Avelumab

Long-term Analysis Data Cut-off: 4th June 2021

OS From the Start of 1L CT in All Randomized Patients¹

Post hoc analysis



In the overall population, median OS measured from the start of 1L chemotherapy was 29.7 months (95% CI, 25.2-34.0) in the avelumab + BSC arm and 20.5 months (95% CI, 19.0-23.5) in the BSC alone arm (HR, 0.77 [95% CI, 0.636-0.921])

1L, first-line; BSC, best supportive care; CI, confidence interval; CT, chemotherapy; HR, hazard ratio; OS, overall survival.
1. Sridhar SS, et al. Poster 508. Presented at: ASCO GU Symposium; February 16-18, 2023; San Francisco, CA.

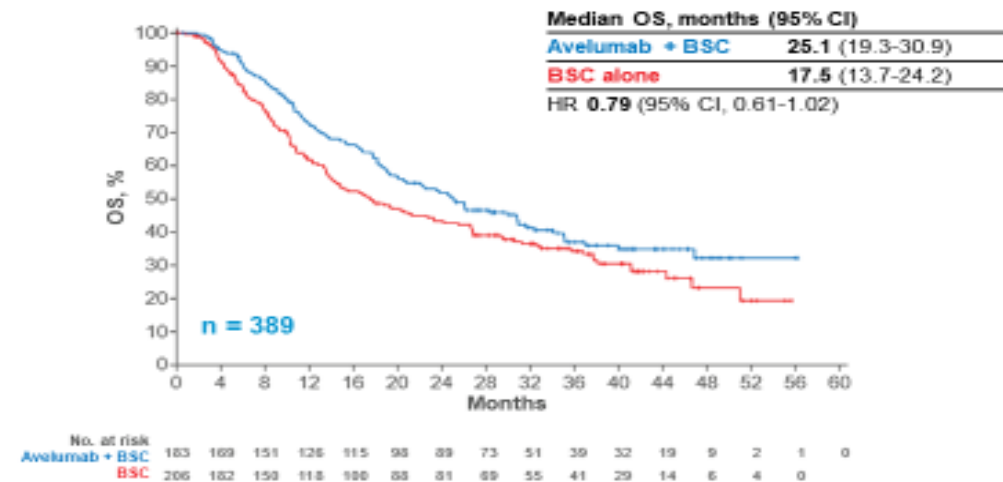
Metastatik Mesane Kanseri Birinci Basamak Tedavi Platin bazlı kemoterapi Sonrası İdame Avelumab

Long-term Analysis Data Cut-off: 4th June 2021

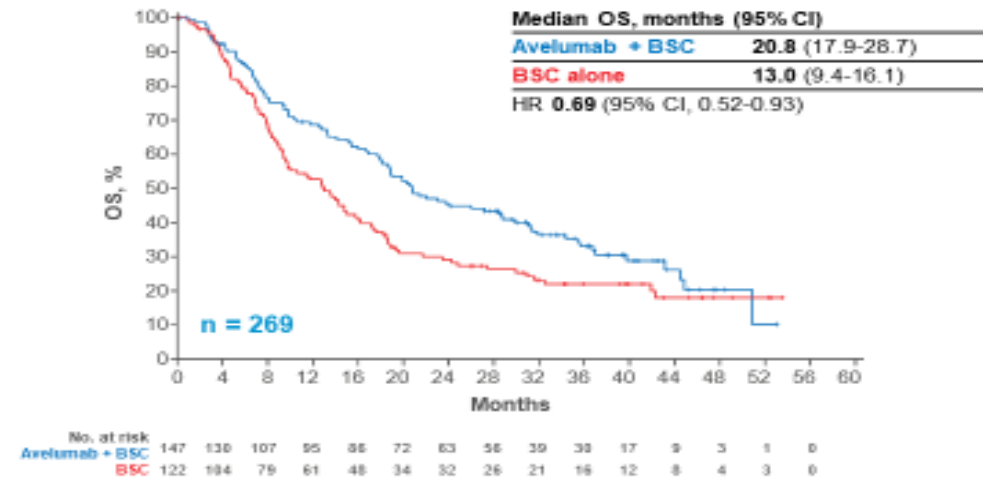
OS From the Start of Randomization by 1L CT Regimen¹

Post hoc analysis

Gemcitabine + cisplatin



Gemcitabine + carboplatin



OS was longer with avelumab + BSC vs BSC alone in patients irrespective of 1L chemotherapy regimen received

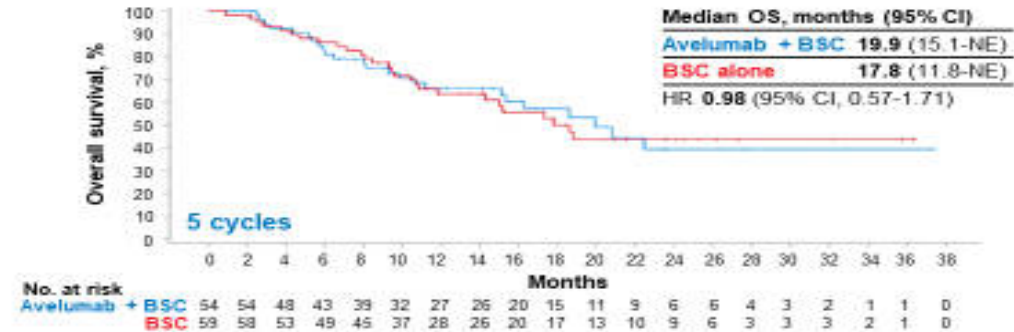
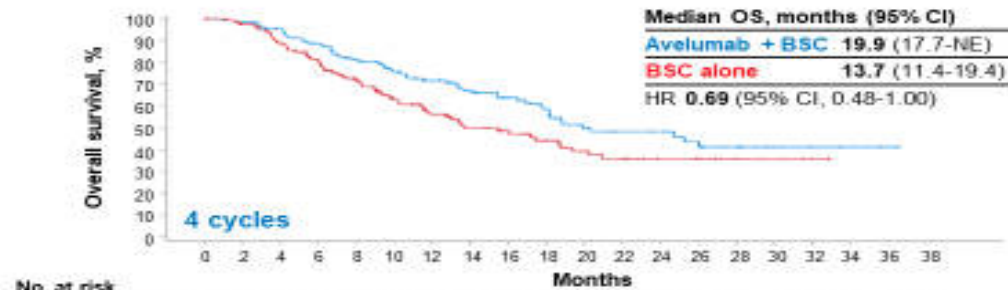
1L, first-line; BSC, best supportive care; CI, confidence interval; HR, hazard ratio; OS, overall survival.
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Metastatik Mesane Kanseri Birinci Basamak Tedavi Platin bazlı kemoterapi Sonrası İdame Avelumab

Primary Analysis Data Cut-off: 21st October 2019

Survival by Number of 1L Platinum-Containing CT Cycles¹

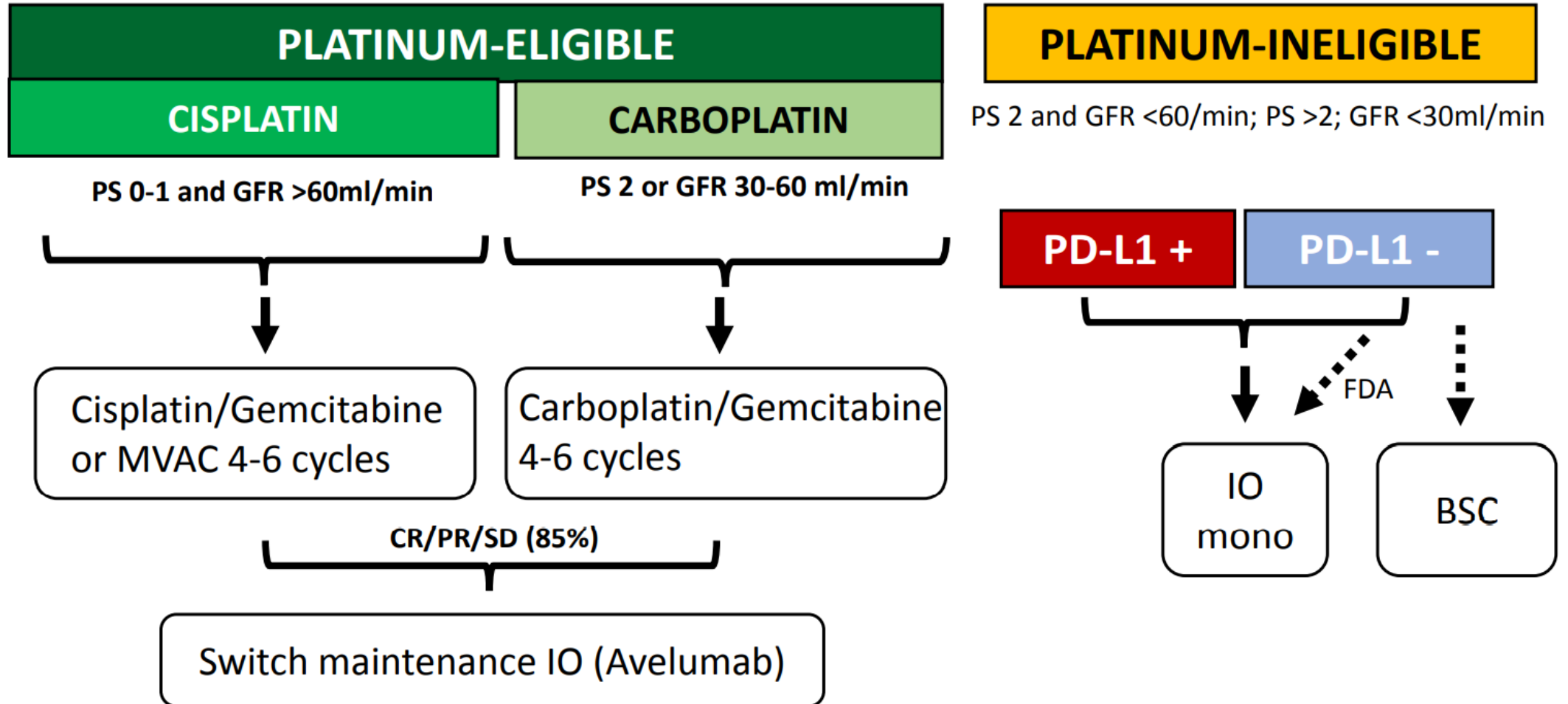
Post hoc analysis



OS was prolonged with avelumab + BSC vs BSC alone across subgroups with differing cycles of 1L CT
No significant treatment-by-cycle interaction (at $p < 0.05$ level) was observed

¹1L, first line; BSC, best supportive care; CI, confidence interval; HR, hazard ratio; NE, not estimable; OS, overall survival; PD-L1, programmed death ligand-1; PFS, progression-free survival.
1. Powles T, et al. Poster 4520. Presented at ASCO Virtual Annual Meeting, June 4-8, 2021.

Metastatik Mesane Kanseri Birinci Basamak Tedavi Seçimi



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Cisplatin ineligible	Preferred regimens • Gemcitabine and carboplatin¹² followed by avelumab maintenance therapy (category 1)^{a,11} • Atezolizumab¹³ (only for patients whose tumors express PD-L1¹⁰ or who are not eligible for any platinum-containing chemotherapy regardless of PD-L1 expression) • Pembrolizumab¹⁴ (for the treatment of patients with locally advanced or metastatic urothelial carcinoma who are not eligible for any platinum-containing chemotherapy) Other recommended regimens • Gemcitabine¹⁵ • Gemcitabine and paclitaxel¹⁶ Useful under certain circumstances • Ifosfamide, doxorubicin, and gemcitabine¹⁷ (for patients with good kidney function and good PS)

Metastatik Mesane Kanseri Birinci Basamak Tedavi Seçimi

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İmmün kontrol noktası inhibitörleri

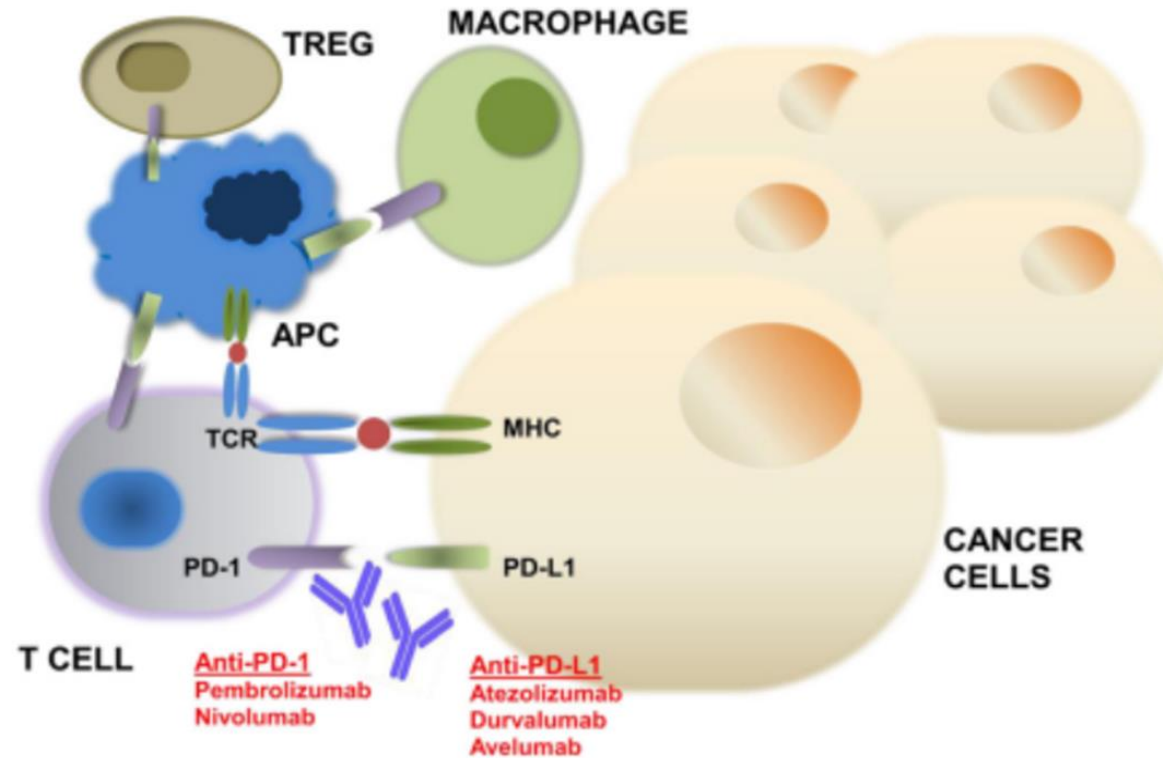
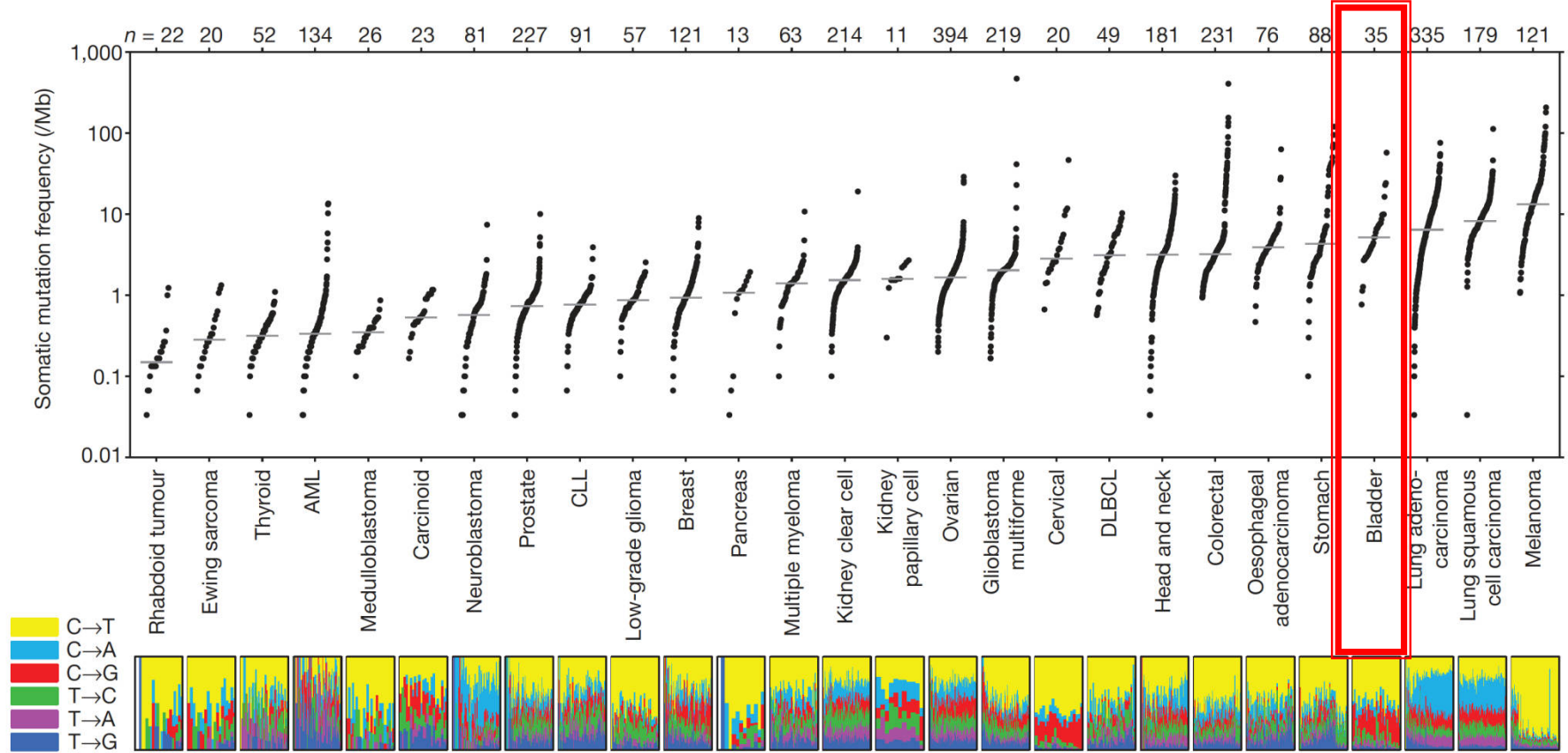


Fig. 1 Mechanism of action of PD-1 and PD-L1 inhibitors. The programmed cell death 1 (PD-1) receptor is expressed on activated T cells, B cells, macrophages, regulatory T cells (Tregs), and natural killer (NK) cells. Binding of PD-1 to its B7 family of ligands, programmed death ligand 1 (PD-L1 or B7-H1) or PD-L2 (B7-DC) results in suppression of proliferation and immune response of T cells. Activation of PD-1/PD-L1 signaling serves as a principal mechanism by which tumors evade antigen-specific T-cell immunologic responses. Antibody blockade of PD-1 or PD-L1 reverses this process and enhances antitumor immune activity. TCR, T-cell receptor; MHC, major histocompatibility complex; APC, antigen-presenting cell

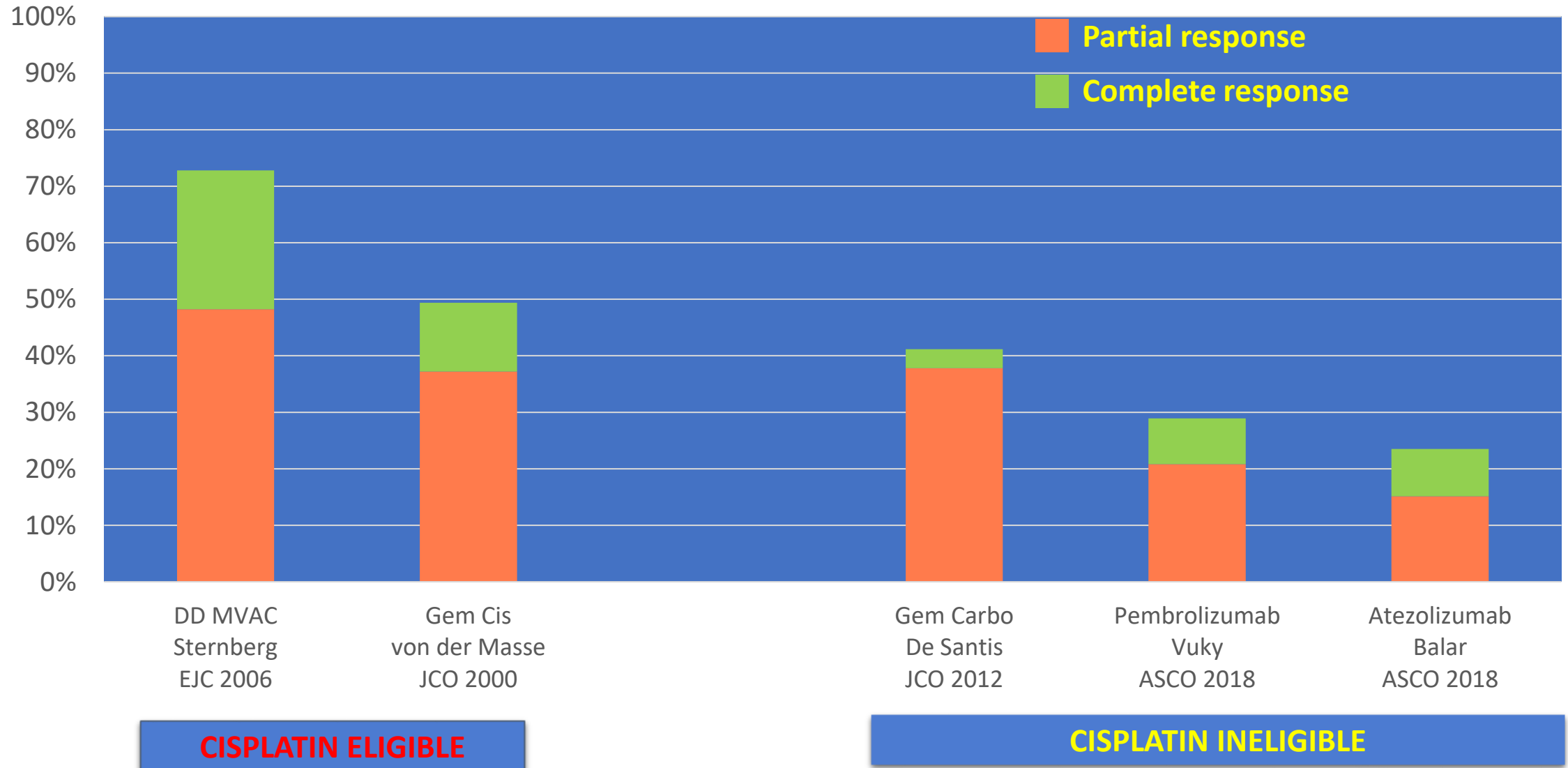
Mesane Kanserinde Tümör Mutasyon Yüğü



Lawrence et al. Nature 2013

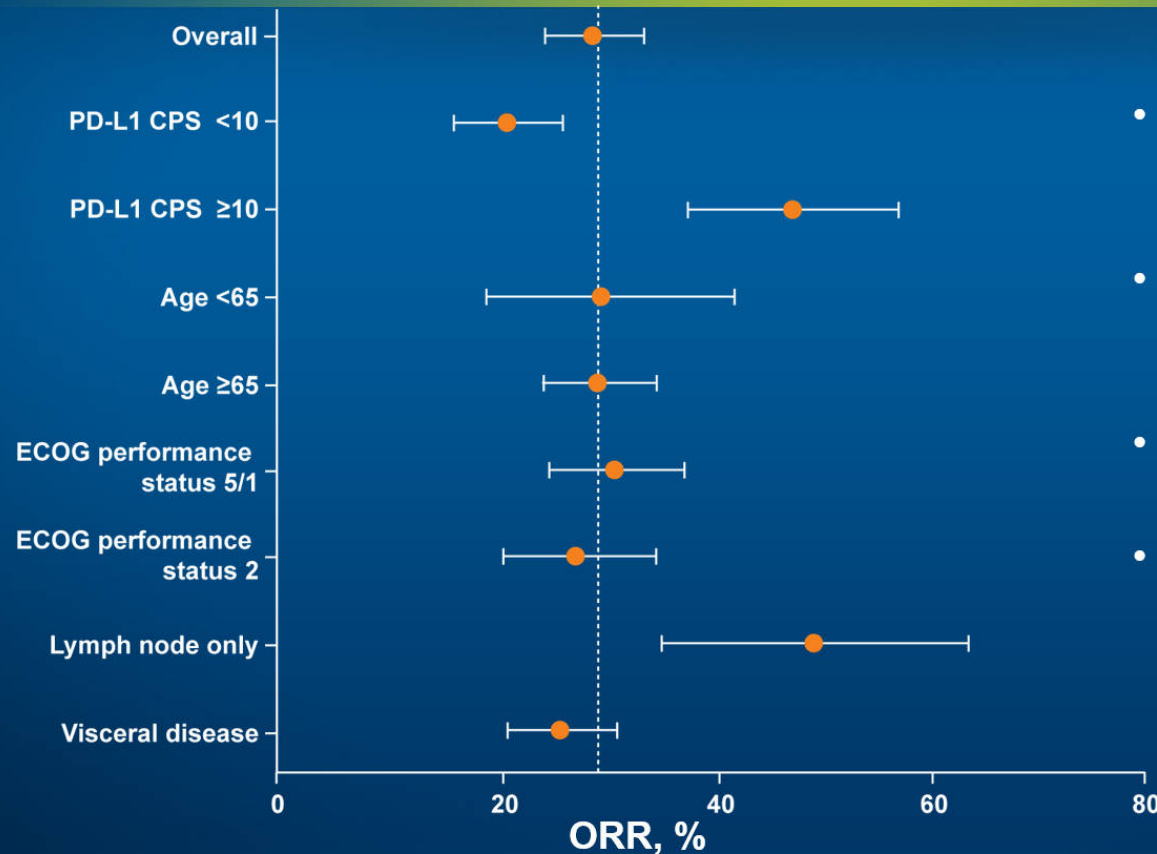
- ☐ Yüksek kompleks mutasyon durumu bütün ve diğer kanserojenlere maruz kalma ile benzer
- ☐ Bir çok neoantijen konakçı immün sistemi tarafından potansiyel olarak yabancı gibi görünür

Metastatik Mesane Kanseri Birinci Basamak Tedavi Yanıtları



Sisplatin Tedavisine Uygun Olmayan Grupta Birinci Basamak Tedavi İmmün kontrol noktası inhibitörleri

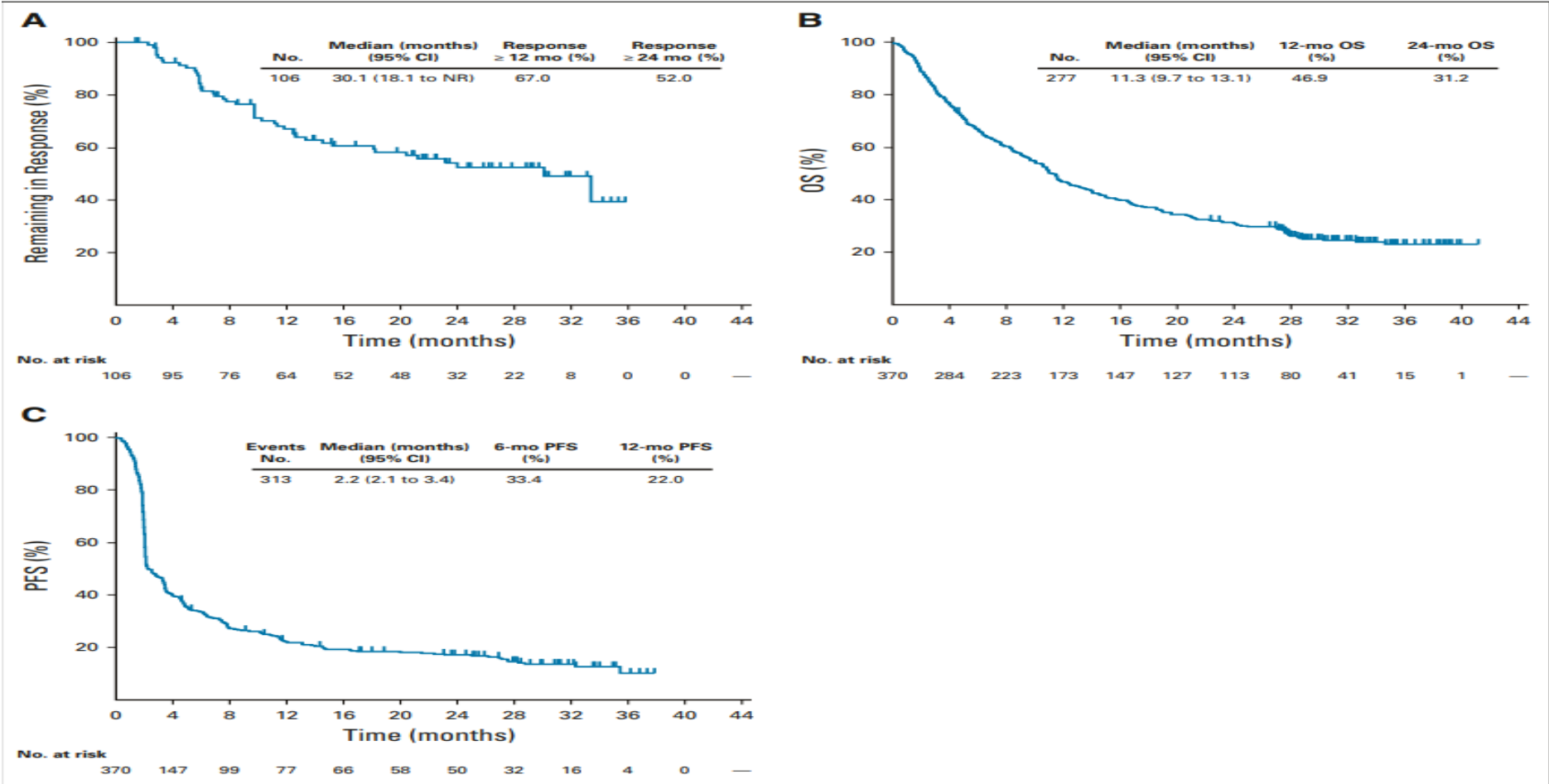
KEYNOTE-052: Objective Response Rate with First-Line Pembrolizumab by Subgroup in Cisplatin-Ineligible Advanced UC



- Treatment-related adverse events (AEs) occurred in 67.6% of patients.
- Most common were:
 - Fatigue (18.1%)
 - Pruritus (17.8%)
- Grade ≥3 AEs occurred in 20.3% of patients.
- Immune-mediated AEs occurred in 24.6% of patients.

Sisplatin Tedavisine Uygun Olmayan Grupta Birinci Basamak Tedavi İmmün kontrol noktası inhibitörleri

First-Line Pembrolizumab in Advanced/Metastatic Urothelial Cancer



Sisplatin Tedavisine Uygun Olmayan Grupta Birinci Basamak Tedavi İmmün kontrol noktası inhibitörleri

IMvigor210: Efficacy of Atezolizumab in First-Line Cisplatin-Ineligible or Platinum-Treated Locally Advanced or Metastatic UC

	Cohort 1 (cisplatin ineligible)	Cohort 2 (platinum treated)
Median follow-up, months	29.3	32.9
Response		
ORR	24%	16%
CR	8%	7%
Median DOR (range), months	NR (30.4-NE)	24.8 (13.8-30.4)
Survival		
Median OS, months	16.3	7.9
1-year OS	58%	37%
2-year OS	41%	23%

Sisplatin Tedavisine Uygun Olmayan Grupta Birinci Basamak Tedavi İmmün kontrol noktası inhibitörleri

Atezolizumab Monotherapy in Cisplatin-Ineligible Patients With Previously Untreated Metastatic Urothelial Carcinoma: 5-Year Response and Survival Analysis From the Phase II IMvigor210 Study (Cohort 1)

Jonathan E. Rosenberg,¹ Matthew D. Galsky,² Arjun V. Balar,³ Yohann Loriot,⁴ Andrea Necchi,⁵ Jean Hoffman-Censits,⁶ Sandy Srinivas,⁷ Alexandra Drakaki,⁸ Apurva Javery,⁹ Yi Shi,¹⁰ Hannah (Xinhui) Huang,¹⁰ Xiaodong Shen,¹⁰ Michiel S. van der Heijden¹¹

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BACKGROUND

- Cisplatin-based chemotherapy is the standard of care for first-line (1L) treatment of metastatic urothelial carcinoma (mUC), although many patients are ineligible for cisplatin
- Atezolizumab (anti-PD-L1) is recommended for the treatment of several types of locally advanced or mUC, including cisplatin-ineligible patients whose tumours express PD-L1 (PD-L1-expressing immune cells [IC] covering ≥5% of the tumour area [IC2/3])¹⁻³
- Cohort 1 of the pivotal, single-arm, Phase II, IMvigor210 study demonstrated the tolerability of and durable responses to 1L atezolizumab in patients with cisplatin-ineligible mUC, with sustained responses observed with additional follow-up⁴
- The ongoing Phase III IMvigor130 study has also demonstrated prolonged efficacy with 1L atezolizumab monotherapy vs platinum-based chemotherapy in exploratory analyses in patients with PD-L1 IC2/3 tumours, including those ineligible for cisplatin^{5,7}
- To evaluate the long-term efficacy of atezolizumab in patients with cisplatin-ineligible previously untreated mUC, here, we report updated data from IMvigor210 Cohort 1, based on over 5 years of follow-up

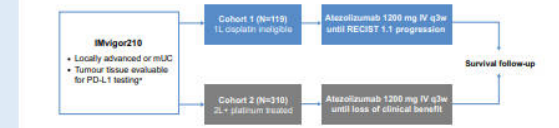
Abstract 4282
Poster 689P



METHODS

IMvigor210 is an ongoing, global, single-arm, Phase II trial investigating the efficacy and safety of atezolizumab monotherapy in 1L cisplatin-ineligible mUC and previously platinum-treated mUC

Figure 1. IMvigor210 study design⁴



ClinicalTrials.gov ID: NCT02031767 (Cohort 1), NCT02080222 (Cohort 2).
2L, second-line; q3w, every 3 weeks; RECIST 1.1, Response Evaluation Criteria in Solid Tumours 1.1.
*PD-L1 status was prospectively and centrally evaluated using the VENTANA SP142 IHC assay. The study enrolled an all-comer population (patients were eligible regardless of PD-L1 status).

- Primary endpoint (Cohort 1) was objective response rate (ORR) per RECIST 1.1 as assessed by independent review facility (IRF)
- Key secondary endpoints reported here: duration of response (DOR) as assessed by IRF and overall survival (OS)
- In this poster, efficacy was descriptively evaluated in the all-comer patients and subgroups defined by PD-L1 status on IC (IC2/3 or PD-L1-expressing IC covering <5% of the tumour area [IC0/1])



RESULTS

Durable responses and long-term survival with 1L atezolizumab monotherapy were observed in this 5-year clinical update

Table. Efficacy summary	All comers (N=119)	PD-L1 IC0/1 (n=87)	PD-L1 IC2/3 (n=32)
Objective response^a			
ORR, n (%)	28 (23.5)	19 (21.8)	9 (28.1)
[95% CI]	[16.2, 32.2]	[13.7, 32.0]	[13.8, 46.8]
CR, n (%)	12 (10.1)	7 (8.0)	5 (15.6)
Ongoing responses, n/n (%) ^b	15/28 (53.6)	9/19 (47.4)	6/9 (66.7)
Median DOR (95% CI), mo	59.1 (44.2, NE)	53.5 (30.4, NE)	NE (11.1, NE)
OS			
OS events, n (%)	92 (77.3)	68 (78.2)	24 (75.0)
Median OS (95% CI), mo	16.3 (10.4, 24.5)	19.1 (10.4, 25.2)	12.3 (6.0, 49.8)
24-mo OS (95% CI), %	41.1 (32.1, 50.2)	41.8 (31.1, 52.5)	39.3 (22.1, 56.5)
60-mo OS (95% CI), %	21.6 (13.7, 29.5)	19.6 (10.8, 28.5)	27.0 (10.3, 43.7)

Clinical cutoff, 31 January 2021.

NE, not estimable.

^aResponse was per IRF in objective response-evaluable patients.

^bPatients to no death or progressive disease only in patients who achieved an objective response.

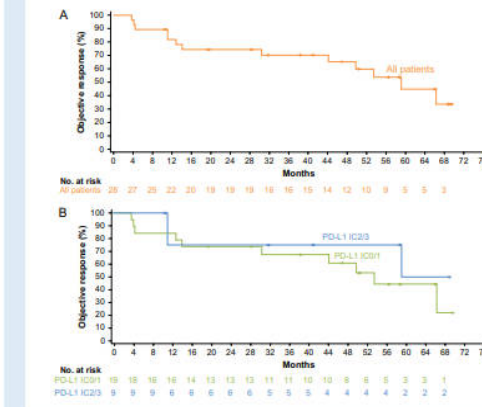
- As of the data cutoff, the median follow-up duration was 70.8 months (range, 0.2-77.5)
- There were no new responders since the 14 March 2016 data cutoff

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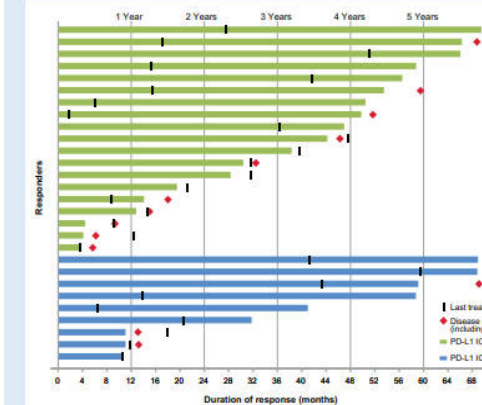
Median DOR has not been reached in the PD-L1 IC2/3 subgroup of patients

Figure 2. Kaplan-Meier curves for DOR (A) in all comers and (B) by PD-L1 status



Clinical cutoff, 31 January 2021.

Figure 3. Duration of treatment and response by PD-L1 status



Clinical cutoff, 31 January 2021.

ACKNOWLEDGEMENTS

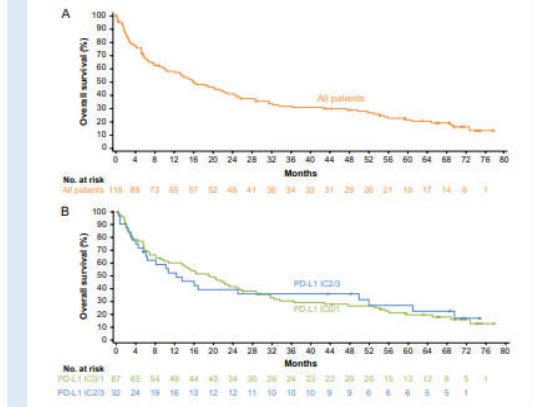
- The patients and their families
- The investigators and clinical study sites
- This study is sponsored by F. Hoffmann-La Roche Ltd
- Betty Nelson of Genentech Inc for contributions to the statistical analyses
- Medical writing assistance for this poster was provided Priscilla Hong, PhD, of Health Interactions and funded by F. Hoffmann-La Roche Ltd

DISCLOSURES

- Dr Rosenberg is an advisor to Astellas, AstraZeneca, Bayer, Boehringer Ingelheim, BMS, EMD Serono, GlaxoSmithKline, GSK, Janssen, Lilly, Merck, Miral, Pfizer, QED, Roche/Genentech, Seattle Genetics and Tysa Biosciences and received research funding support from Roche, Genentech, AstraZeneca, Ziyang, Seattle Genetics, Astellas and QED
- For author disclosures, please refer to published abstract

Prolonged survival was seen in the all-comer population, including patients with PD-L1 IC0/1 and IC2/3 tumours

Figure 4. Kaplan-Meier curves for OS (A) in all comers and (B) by PD-L1 status



Clinical cutoff, 31 January 2021.



CONCLUSIONS

Durable responses and long-term survival with 1L atezolizumab monotherapy in cisplatin-ineligible mUC were observed in this 5-year clinical update from the Phase II IMvigor210 study (Cohort 1)

Median DOR was not reached in patients with PD-L1 IC2/3 mUC

The 5-year OS rate seen in the overall all-comer population (≈22%) compares favourably with historic data,⁸ including gemcitabine/carboplatin in cisplatin-ineligible patients⁹

AUTHOR EMAIL

For questions or comments on this poster, please contact Dr Jonathan E. Rosenberg at jrosenberg@mskcc.org



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Metastatik Mesane Kanseri

İkinci Basamak Tedavi Seçenekleri

Bladder cancer is composed of multiple tumors:
Subtypes within subtypes

	24%	8%	15%	15%	35%	3%
	Luminal Papillary	Luminal Non-Specified	Luminal Unstable	Stroma-rich	Basal/Squamous	Neuroendocrine-like
						
Differentiation	Urothelial / Luminal				Basal	Neuroendocrine
Oncogenic mechanisms	FGFR3 ++ CDKN2A-	PPAR-γ ++	PPAR-γ ++ E2F3 +, ERBB2 + Genomic instability		EGFR +	TP53 --, RB1 --, Cell cycle +
Mutations	FGFR3 (40%), KDM6A (38%), STAG2 (22%)	ELF3 (35%)	TP53 (76%), ERCC2 (22%) TMB +, APOBEC +		TP53 (61%), RB1 (25%)	TP53 (94%) RB1 (39%)
Stromal infiltrate		Fibroblasts		Smooth muscle Fibroblasts Myofibroblasts	Fibroblasts Myofibroblasts	
Immune infiltrate				B cells	CD8 T cells NK cells	
Histology	Papillary morphology	Micropapillary variants			Squamous differentiation	Neuroendocrine differentiation
Clinical	T2 stage +	Older patients + (80+)			Women + T3/T4 stage +	
Median overall survival (years)	4	1.8	2.9	3.8	1.2	1

APOBEC, apolipoprotein B mRNA-editing enzyme, catalytic polypeptide-like; CDKN2A, cyclin-dependent kinase Inhibitor 2A; E2F3, E2F transcription factor 3; NK, natural killer; TMB, tumour mutation burden.

Kamoun A, et al. 2019. Epub ahead of print date.

Courtesy of Arlene O. Siefker-Radtke, MD

Metastatik Mesane Kanseri Sisplatin Uygun Olmayanlarda Birinci Basamak Tedavi Yanıtları

EV-103: Phase 1b/2 Trial of Enfortumab + Pembrolizumab

Patients With 1L Cisplatin-Ineligible
la/mUC (N=45)

Dose escalation

EV + Pembro
(n=5)

Dose expansion cohort A

EV + Pembro
(n=40)

EV 1.25 mg/kg days 1 and 8
of a 3-week cycle
+
Pembrolizumab 200 mg on day 1
of a 3-week cycle

- 84% of patients had visceral disease and 31% had liver metastasis
- 31% of patients had PD-L1 CPS ≥ 10

Confirmed ORR
95% CI

73% (33/45)
(58.1, 85.4)

- 57% confirmed ORR in patients with liver metastases

Complete response

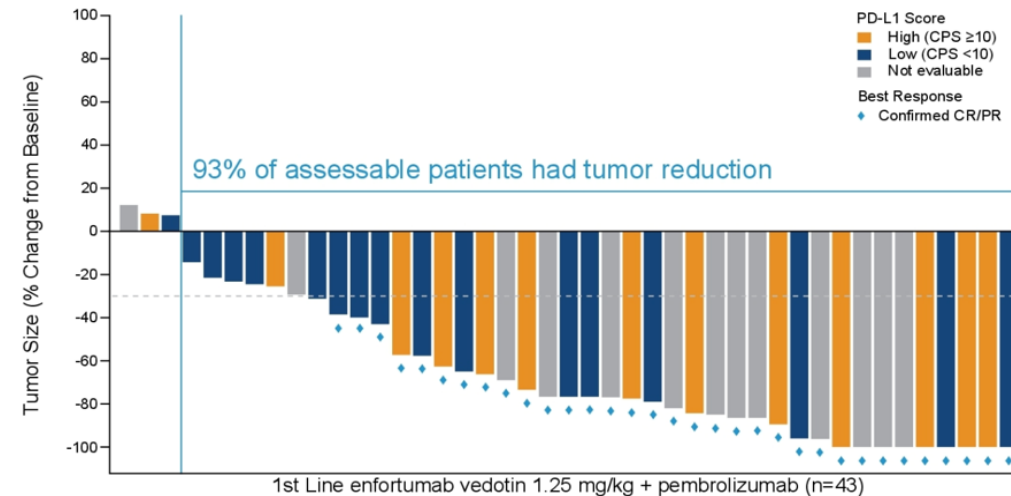
16% (7/45)

Partial response

58% (26/45)

Maximum Target Lesion Reduction From Baseline by PD-L1 Status

Best Overall Response per RECIST v1.1 by Investigator (N=45)



Metastatik Mesane Kanseri Sisplatin Uygun Olmayanlarda Birinci Basamak Tedavi Yanıtları

EV-103 Cohort K: Phase 1b/2 Trial

Cohort K

- Unresectable Ia/mUC
- Cisplatin ineligible
- No prior treatment for Ia/mUC

N=149
R
1:1

n=76
EV 1.25 mg/kg days 1 and 8 of a 3-week cycle
+
Pembrolizumab 200 mg on day 1 of a 3-week cycle

n=73
EV 1.25 mg/kg days 1 and 8 of a 3-week cycle

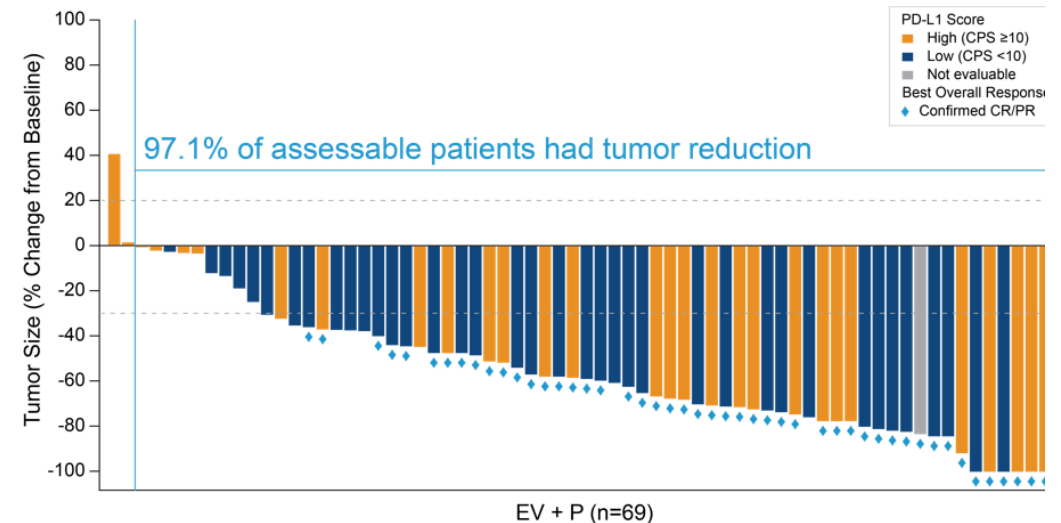
Primary Endpoint

- ORR per BICR

Secondary Endpoints

- ORR per investigator assessment
- DOR
- Disease control rate
- PFS
- OS
- Safety

	EV+P (N=76)	EV Mono (N=73)
Confirmed ORR, n (%) (95% CI)	49 (64.5) (52.7, 75.1)	33 (45.2) (33.5, 57.3)
Best overall response, n (%)		
Complete Response	8 (10.5)	3 (4.1)
Partial Response	41 (53.9)	30 (41.1)
Stable Disease	17 (22.4)	25 (34.2)
Progressive Disease	6 (7.9)	7 (9.6)
Not Evaluable	3 (3.9)	5 (6.8)
No Assessment	1 (1.3)	3 (4.1)
Median time to objective response (range), mos	2.07 (1.1, 6.6)	2.07 (1.9, 15.4)
Median number of treatment cycles (range)	11.0 (1, 29)	8.0 (1, 33)



Data cutoff: 10Jun2022

BICR: Blinded Independent Central Review; cORR: Confirmed Objective Response Rate; NR: Not Reached

BICR: Blinded Independent Central Review; CPS: Combined Positive Score; CR: Complete Response; PD-L1: Programmed Death-Ligand 1 PR: Partial Response

Rosenberg JE, et al. ESMO 2022. Abstract 2895/LBA73.

Metastatik Mesane Kanseri Birinci Basamak Tedavi Yanıtları EV103 -EV/pembrolizumab

Overall Objective Response Rates by BICR

High confirmed ORR (73.3%) with high concordance rate between BICR and INV assessments

	Dose Escalation + Cohort A (N = 45)
Objective Response Rate, n (%)	33 (73.3)
95% CI ^a for ORR	58.1-85.4
Best Overall Response, n (%)	
Complete response	7 (15.6)
Partial response	26 (57.8)
Stable disease	5 (11.1)
Progressive disease	5 (11.1)
No assessment ^b	2 (4.4)
Disease Control Rate, n (%)	38 (84.4)
95% CI ^a for DCR	70.5-93.5
Concordance rate of BOR between BICR and INV^c assessment	95.3%

BICR = blinded independent central review; BOR = best overall response; CI = confidence interval; DCR = disease control rate; INV = investigator; ORR = objective response rate

^aCI was computed using the Clopper-Pearson method (Clopper 1934)

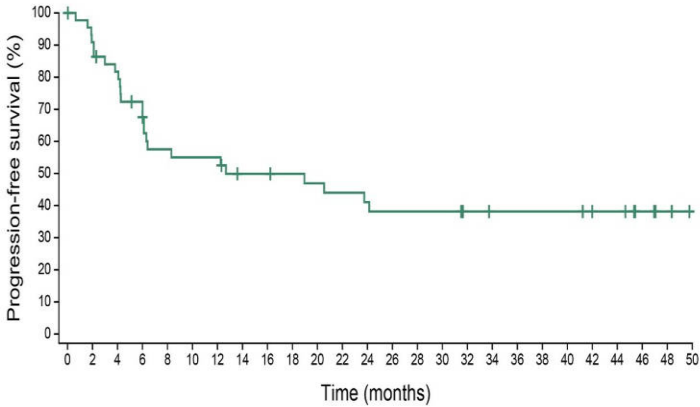
^bPatients had no response assessment post-baseline

^cORR per INV assessment was 33/45 (73.3%)

Metastatik Mesane Kanseri Birinci Basamak Tedavi Yanıtları EV103 -EV/pemrolizumab

Progression-Free Survival by BICR

41.1% of patients were progression-free at 24 months



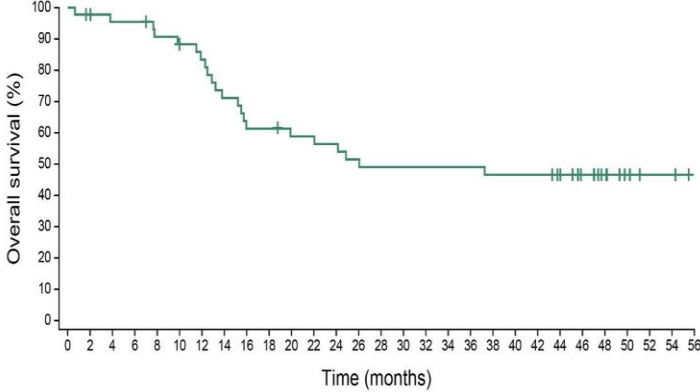
No. at risk 45 40 35 30 22 22 18 17 16 15 13 13 11 10 10 10 8 8 4 2

Dose Escalation + Cohort A (N = 45)	
PFS events, n	25
Median PFS (95% CI) ^a	12.7 months (6.11-NE)
PFS rate ^b at:	
6 months, % (95% CI) ^a	72.4 (56.47-83.26)
12 months, % (95% CI) ^a	55.0 (38.84-68.58)
24 months, % (95% CI) ^a	41.1 (25.69-55.88)

BICR = blinded independent central review; CI = confidence interval; NE = not estimable;
PFS = progression-free survival
^aCI was calculated using the complementary log-log transformation method (Collett, 1994)
^bAs estimated using Kaplan-Meier method

Overall Survival

Median survival exceeds 2 years



No. at risk 45 43 41 38 36 34 29 25 25 24 23 21 20 20 20 20 19 19 17 12 8 4 2 2

Dose Escalation + Cohort A (N = 45)	
OS events, n	22
Median OS (95% CI) ^a	26.1 months (15.51-NE)
OS rate ^b at:	
6 months, % (95% CI) ^a	95.4 (83.00-98.84)
12 months, % (95% CI) ^a	83.4 (68.25-91.72)
24 months, % (95% CI) ^a	56.4 (40.03-69.91)
Median follow-up time	47.0 months

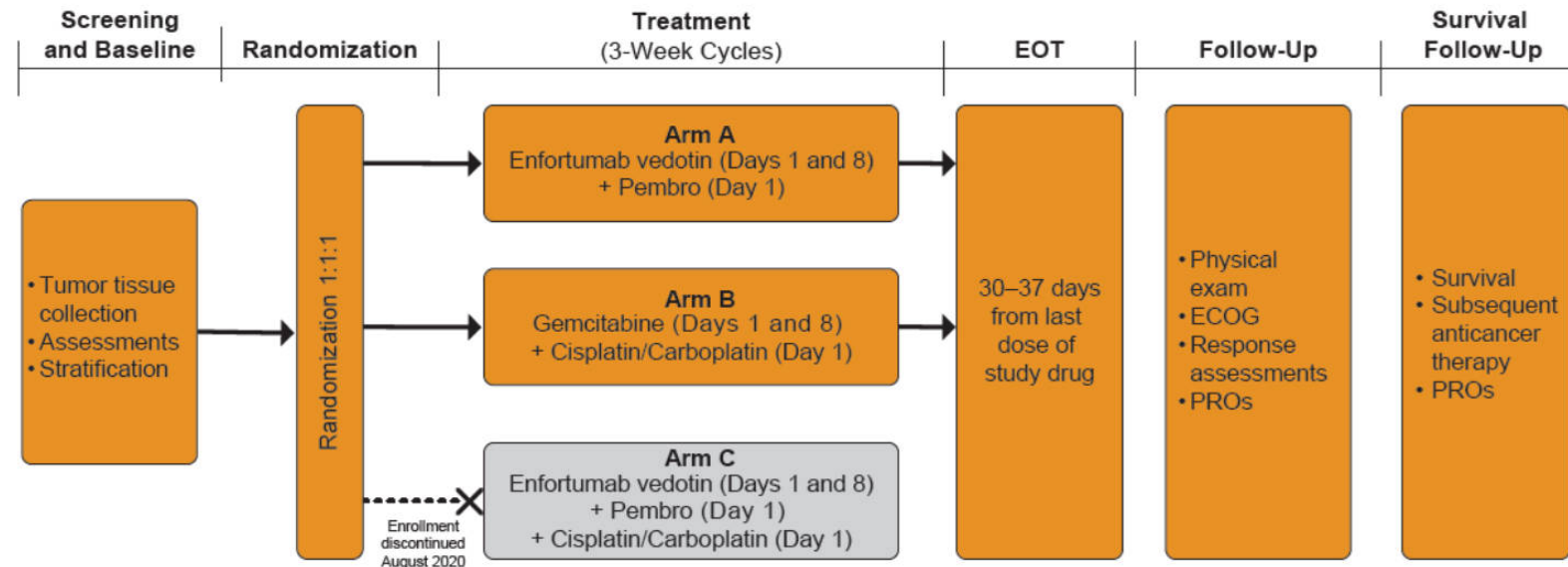
CI = confidence interval; NE = not estimable; OS = overall survival
^aCI was calculated using the complementary log-log transformation method (Collett, 1994)
^bAs estimated using Kaplan-Meier method

Gelecek Perspektif

EV-302 Randomized Phase 3 Trial Schema

Eligibility

- Locally advanced or metastatic urothelial carcinoma
- 1st line systemic therapy
- Platinum-eligible



EOT= End of Treatment; Pembro=pembrolizumab; PROs=patient reported outcomes

- Stratification Factors for Randomization: cisplatin eligibility (eligible/ineligible), liver metastases (present/absent), PD-L1 expression (high/low)
- Follow-up until disease progression, death, consent withdrawal, or study closure

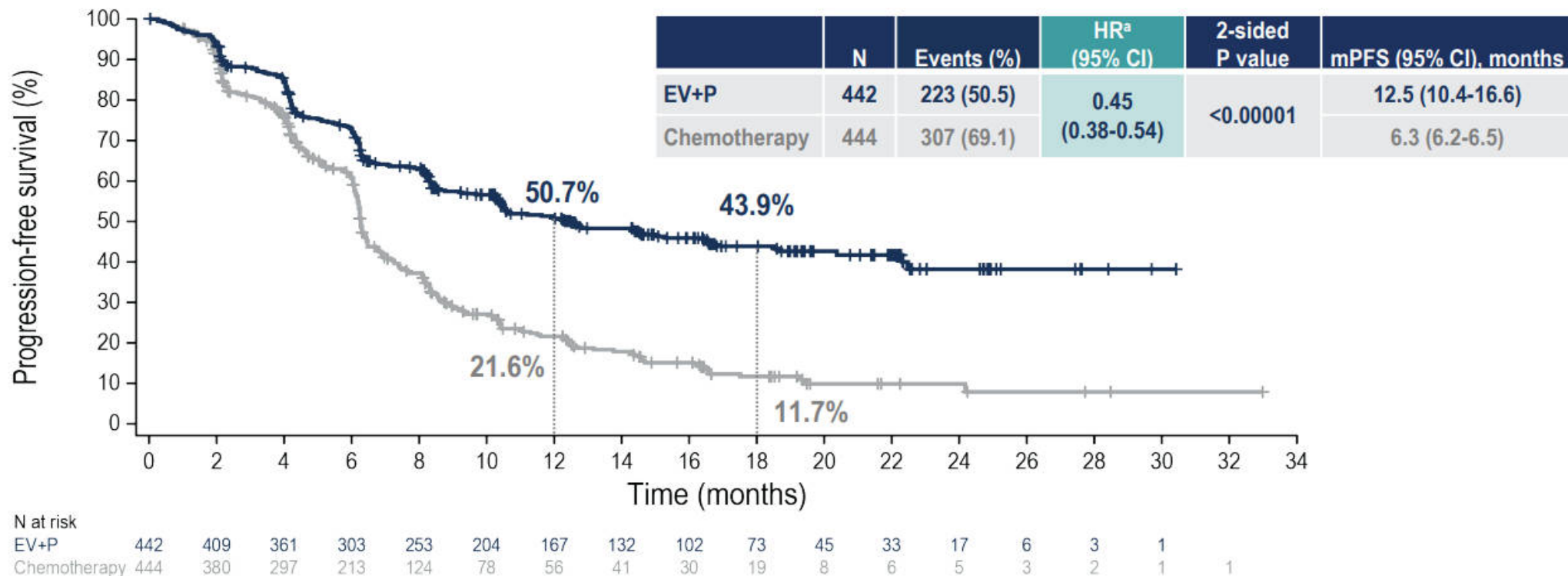
Primary Endpoints: PFS, OS
Secondary Endpoints: ORR, DOR, DCR, QOL, PRO, Safety

Metastatik Mesane Kanseri Birinci Basamak Tedavi Yanıtları

EV103 -EV/pembrolizumab

Progression-Free Survival per BICR

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



Data cutoff: 08 Aug 2023



Powles et al.

PFS at 12 and 18 months as estimated using Kaplan-Meier method

HR, hazard ratio; mPFS, median progression-free survival

^aCalculated using stratified Cox proportional hazards model; a hazard ratio <1 favors the EV+P arm

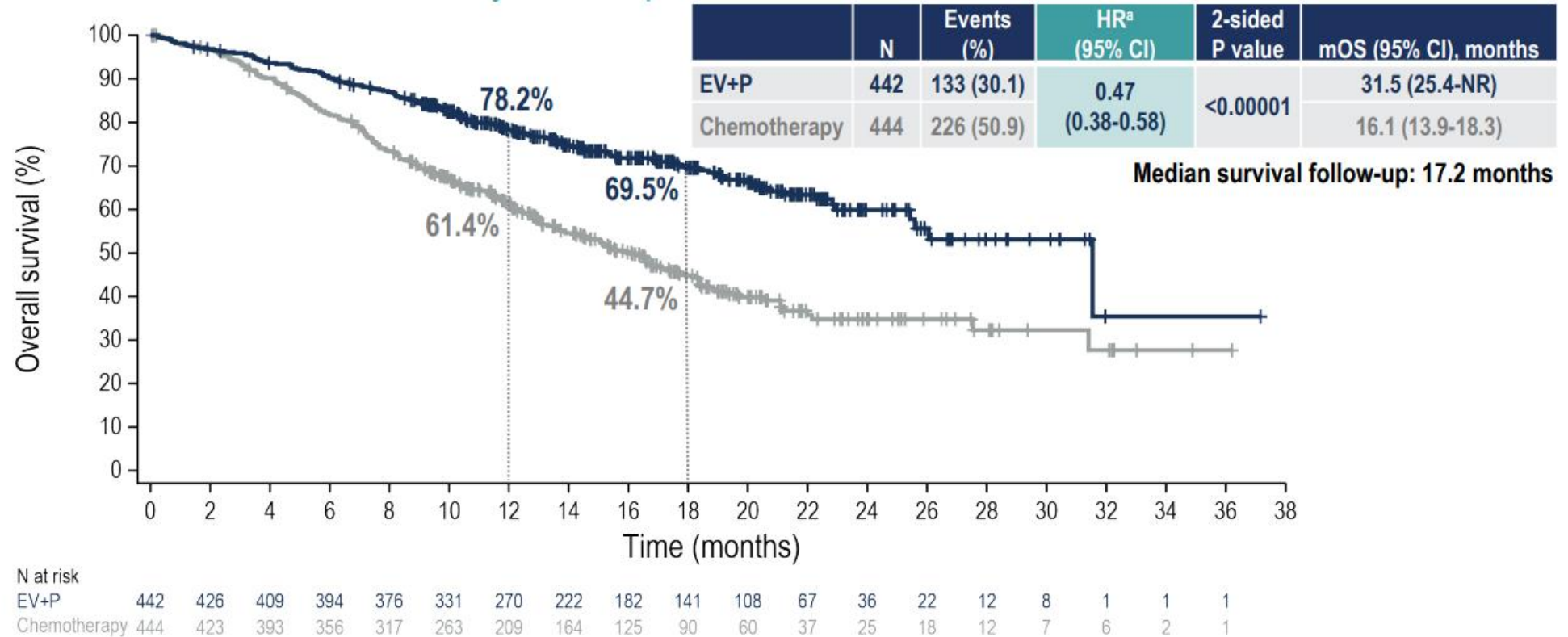
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Metastatik Mesane Kanseri Birinci Basamak Tedavi Yanıtları

EV103 -EV/pemrolizumab

Overall Survival

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



Data cutoff: 08 Aug 2023



Powles et al.

OS at 12 and 18 months was estimated using Kaplan-Meier method

mOS, median overall survival; NR, not reached

^aCalculated using stratified Cox proportional hazards model. A hazard ratio <1 favors the EV+P arm

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OS Subgroup Analysis: Cisplatin Eligibility

Cisplatin-eligible

Overall survival (%)

Time (months)



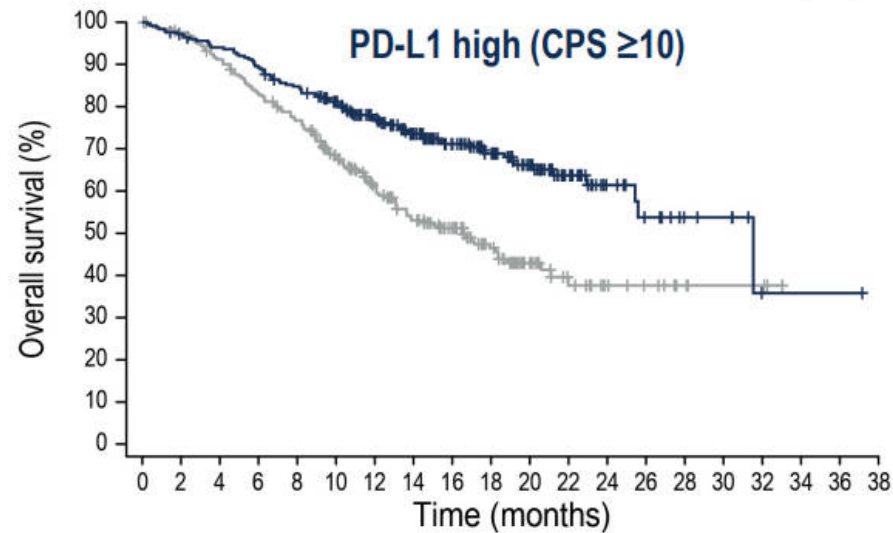
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Metastatik Mesane Kanseri Birinci Basamak Tedavi Yanıtları

EV103 -EV/pemrolizumab

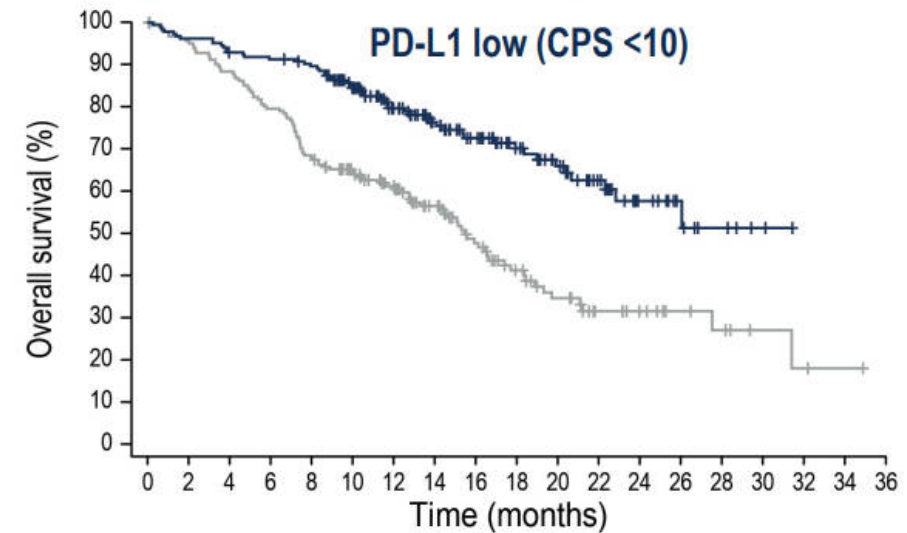
OS Subgroup Analysis: PD-L1 Expression

OS benefit was consistent with overall population regardless of PD-L1 expression status



N at risk	254	245	235	223	210	189	162	136	111	87	65	37	20	13	7	6	1	1	1
EV+P	254	245	235	223	210	189	162	136	111	87	65	37	20	13	7	6	1	1	1
Chemotherapy	254	245	228	207	189	155	122	97	76	54	33	19	12	9	5	3	3		

	Events, n	HR (95% CI)	mOS (95% CI), months
EV+P	79	0.49	31.5 (25.4-NR)
Chemotherapy	125	(0.37-0.66)	16.6 (13.1-20.6)



N at risk	184	177	170	167	162	139	106	86	71	54	43	30	16	9	5	2
EV+P	184	177	170	167	162	139	106	86	71	54	43	30	16	9	5	2
Chemotherapy	185	173	160	144	123	103	84	65	47	34	25	16	12	8	6	3

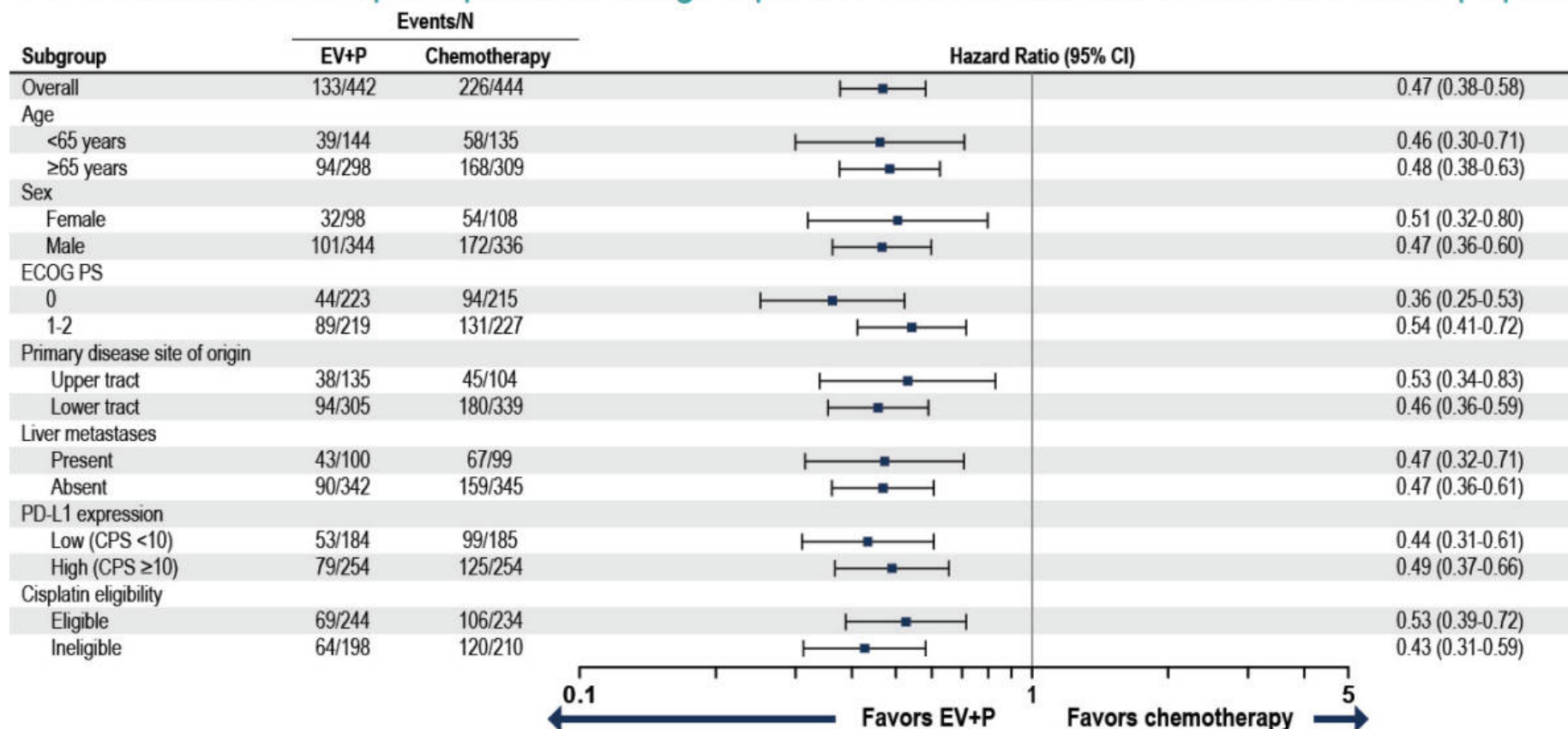
	Events, n	HR (95% CI)	mOS (95% CI), months
EV+P	53	0.44	NR (22.3-NR)
Chemotherapy	99	(0.31-0.61)	15.5 (12.9-17.7)

Data cutoff: 08 Aug 2023

Metastatik Mesane Kanseri Birinci Basamak Tedavi Yanıtları EV103 -EV/pembrolizumab

Subgroup Analysis of OS

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

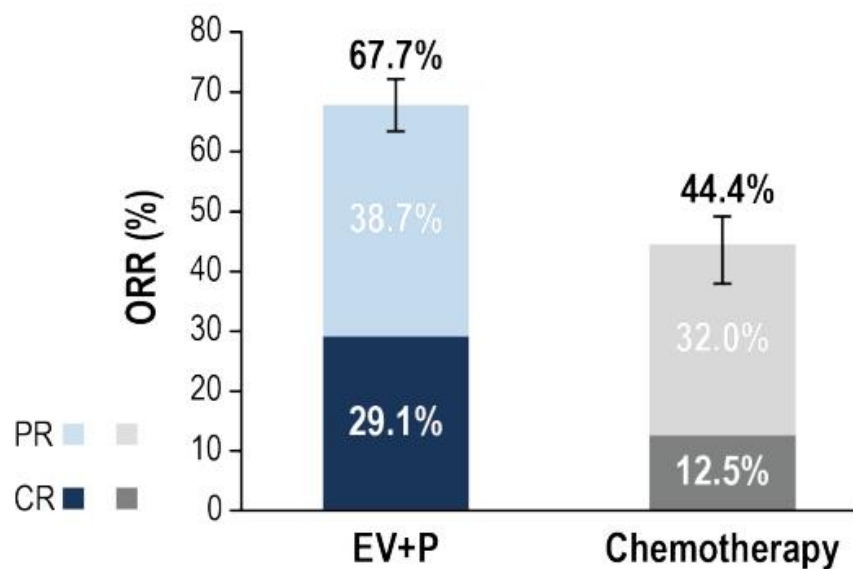


Data cutoff: 08 Aug 2023

Metastatik Mesane Kanseri Birinci Basamak Tedavi Yanıtları EV103 -EV/pembrolizumab

Confirmed Overall Response per BICR

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



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

	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)

CR, complete response; DOR, duration of response; PR, partial response

^aBest overall response according to RECIST v1.1 per BICR. CR or PR was confirmed with repeat scans ≥28 days after initial response

^bPatients 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



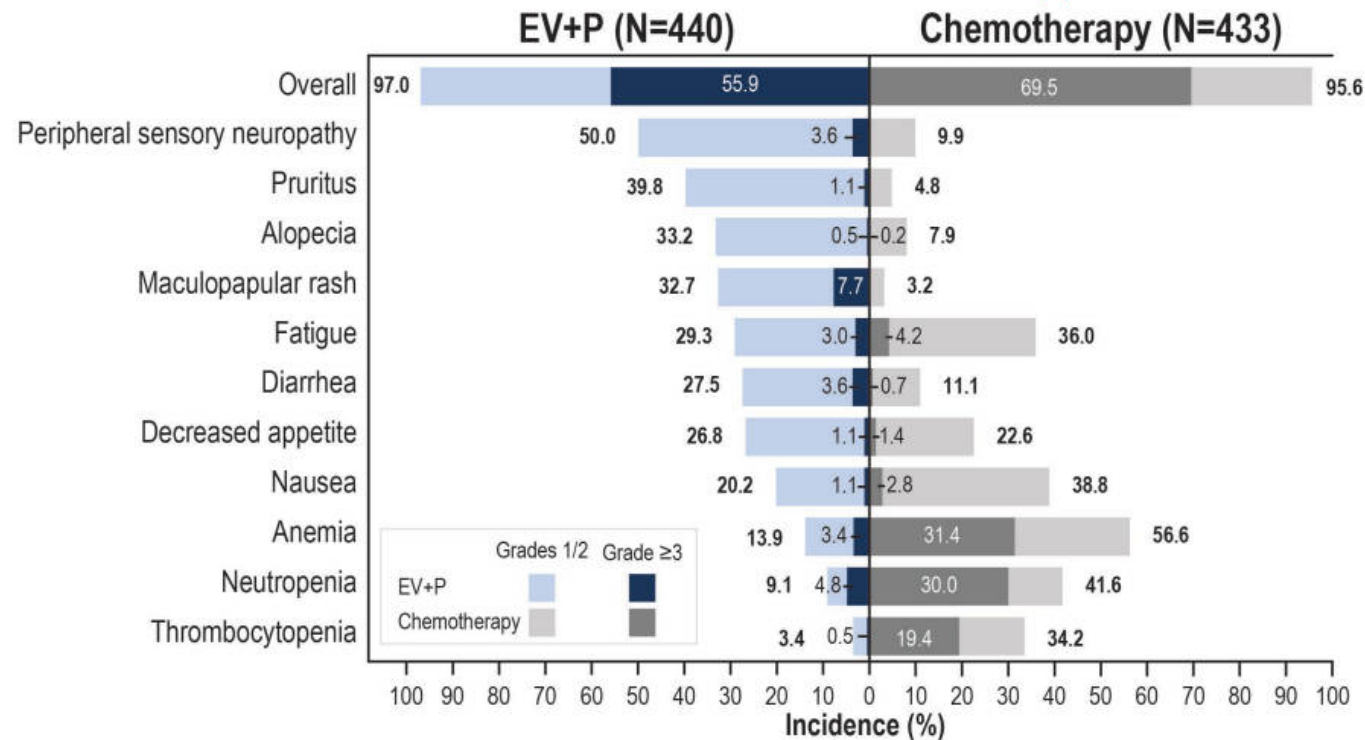
Powles et al.

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Metastatik Mesane Kanseri Birinci Basamak Tedavi Yan etki EV103 -EV/pembrolizumab

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

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

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Metastatik Mesane Kanseri Birinci Basamak Tedavi Yanıtları EV103 -EV/pembrolizumab

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



Powles et al.

*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

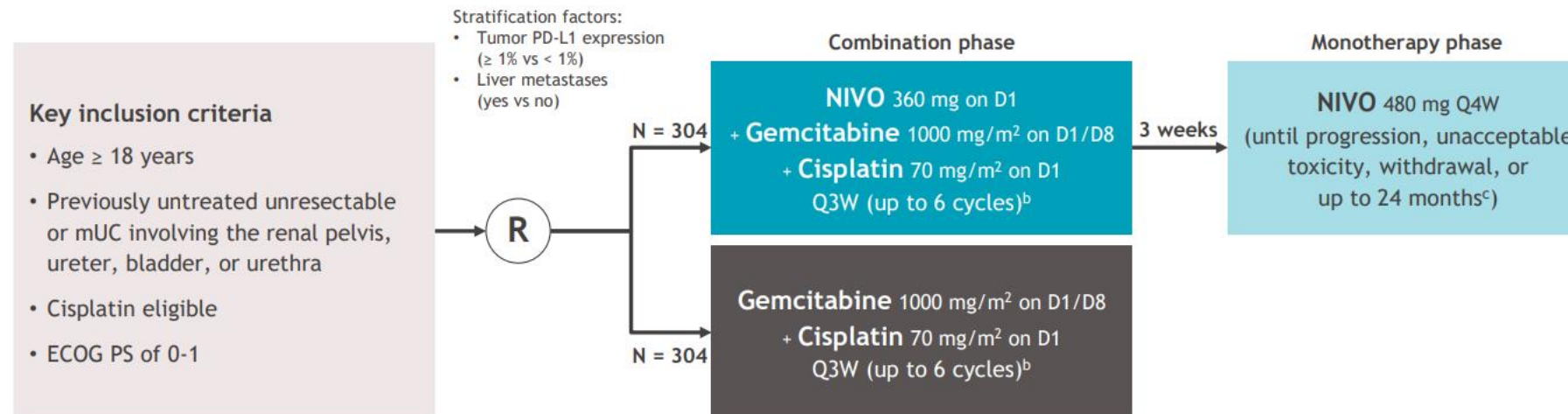
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Sisplatine uygun hastalarda KT+İmmünoterapi

CheckMate 901

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 $\geq 1\%$,^d HRQoL

Key exploratory endpoints: ORR per BICR, safety

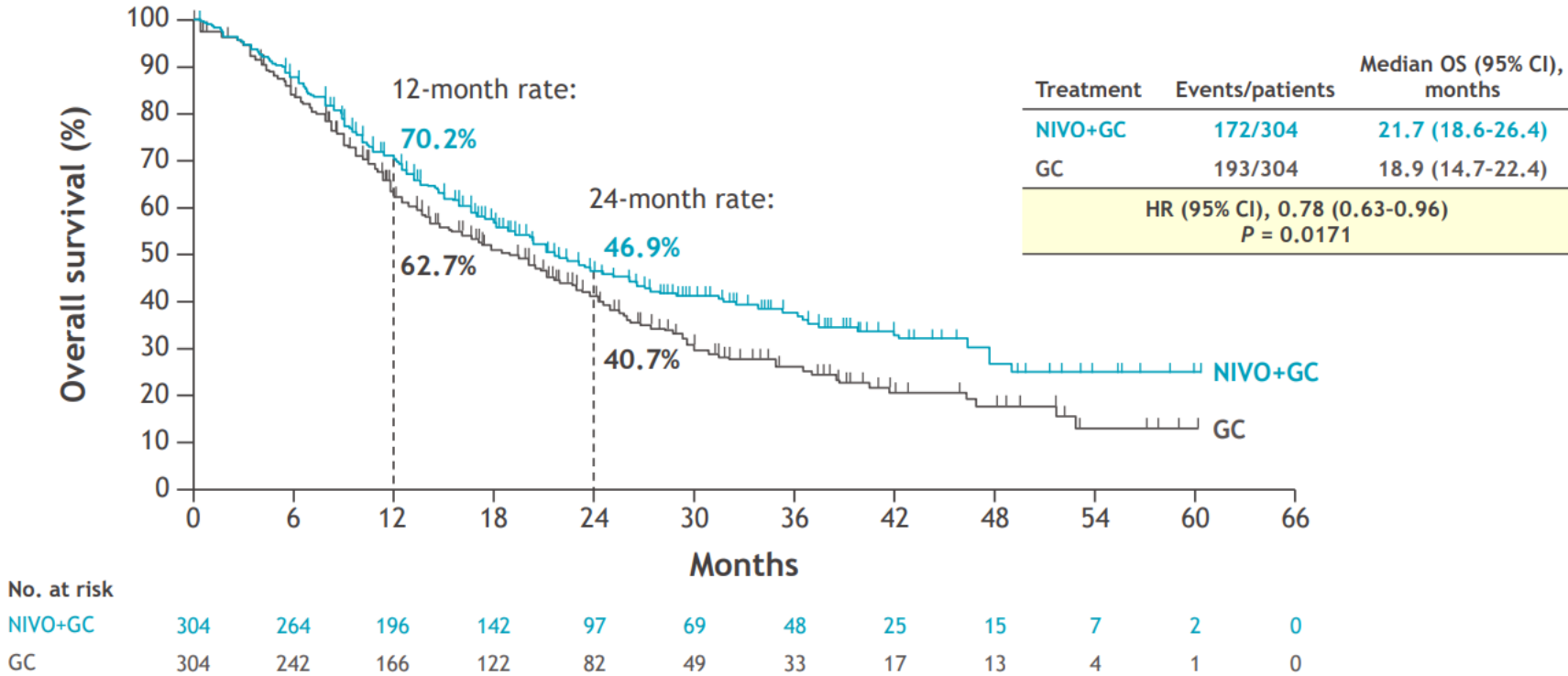
^aFurther CheckMate 901 trial design details are available at <https://clinicaltrials.gov/ct2/show/NCT03036098>. ^bPatients who discontinued cisplatin could be switched to gemcitabine-carboplatin for the remainder of the platinum doublet cycles (up to 6 in total). ^cA maximum of 24 months from first dose of NIVO administered as part of the NIVO + gemcitabine-cisplatin combination. ^dPD-L1 status was defined by the percentage of positive tumor cell membrane staining in a minimum of 100 tumor cells that could be evaluated with the use of the PD-L1 IHC 28-8 pharmDx immunohistochemical assay (Dako, Santa Clara, CA, USA).

BICR, blinded independent central review; D, day; ECOG PS, Eastern Cooperative Oncology Group performance status; HRQoL, health-related quality of life; ORR, objective response rate; PD-L1, programmed death ligand 1; PFS, progression-free survival; QxW, every x weeks; R, randomization.

Sisplatine uygun hastalarda KT+İmmünoterapi

CheckMate 901

OS (primary endpoint)

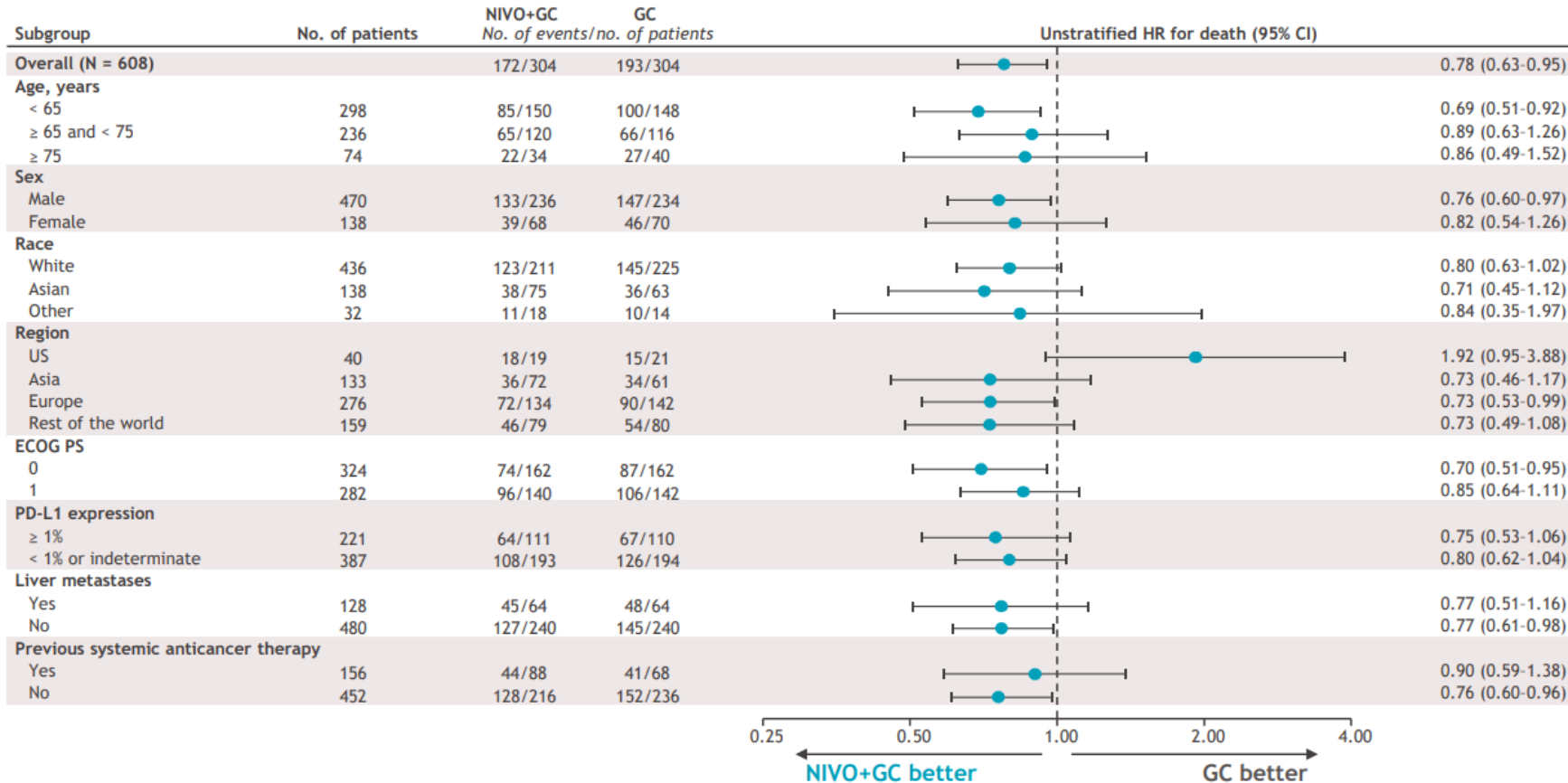


Median (range) study follow-up was 33.6 (7.4-62.4) months. OS was estimated in all randomized patients and defined as time from randomization to death from any cause. For patients without documented death, OS was censored on the last date the patient was known to be alive. For randomized patients with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

Sisplatin uygun hastalarda KT+İmmünoterapi

CheckMate 901

OS in subgroups

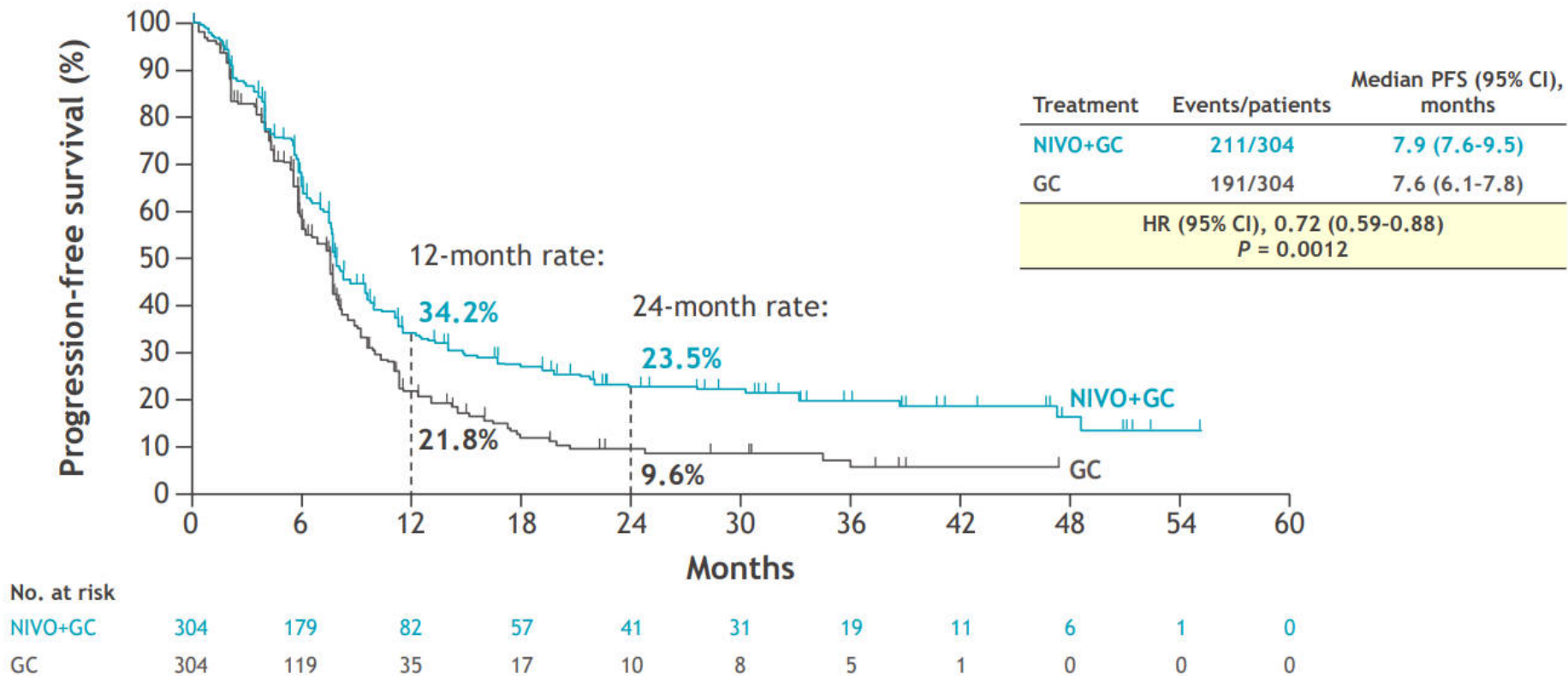


All randomized patients. HRs were not computed for subgroup categories (except for age, sex, race, and region) with < 10 patients per treatment group. Categories without a meaningful estimate of the HR are not shown. PD-L1 expression and liver metastases are per interactive response technology. There were no patients with indeterminate PD-L1 status. Previous systemic anticancer therapy refers to neoadjuvant/adjuvant treatments for patients undergoing radical resection or as part of a bladder-sparing approach in muscle-invasive bladder cancer.

Sisplatine uygun hastalarda KT+İmmünoterapi

CheckMate 901

PFS per BICR (primary endpoint)

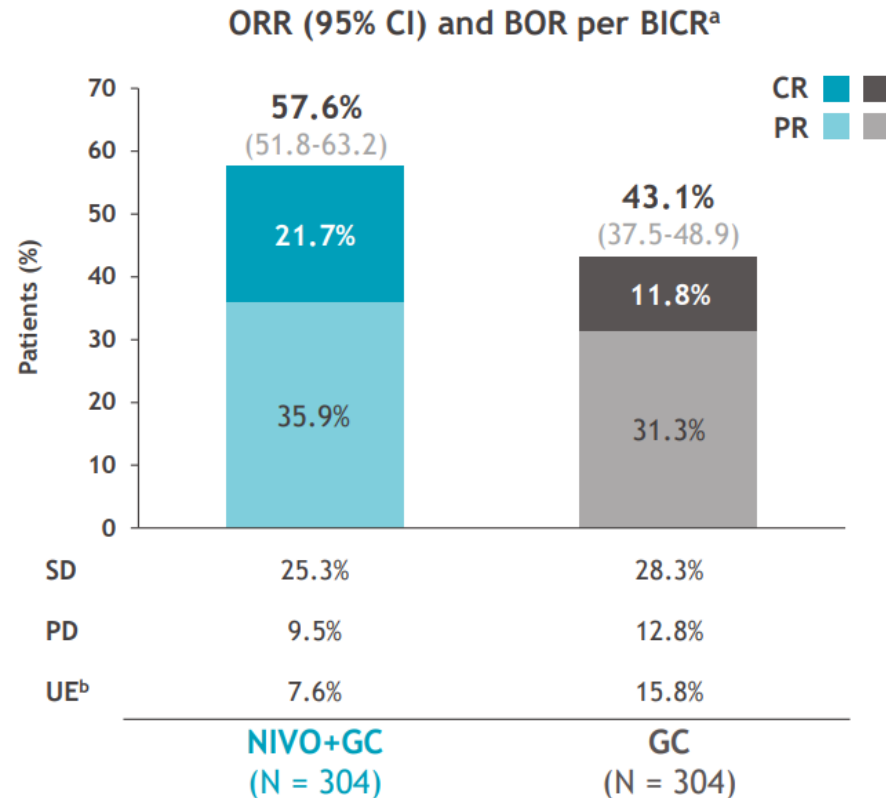


Median (range) study follow-up was 33.6 (7.4-62.4) months. PFS was estimated in all randomized patients and defined as time from randomization to first documented disease progression (per BICR assessments using RECIST v1.1) or death due to any cause, whichever occurred first. Patients who did not progress 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.

Sisplatine uygun hastalarda KT+İmmünoterapi

CheckMate 901

Objective response outcomes (exploratory endpoints)



Time to and duration of responses

	NIVO+GC (n = 175)	GC (n = 131)
Any objective response ^c		
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)

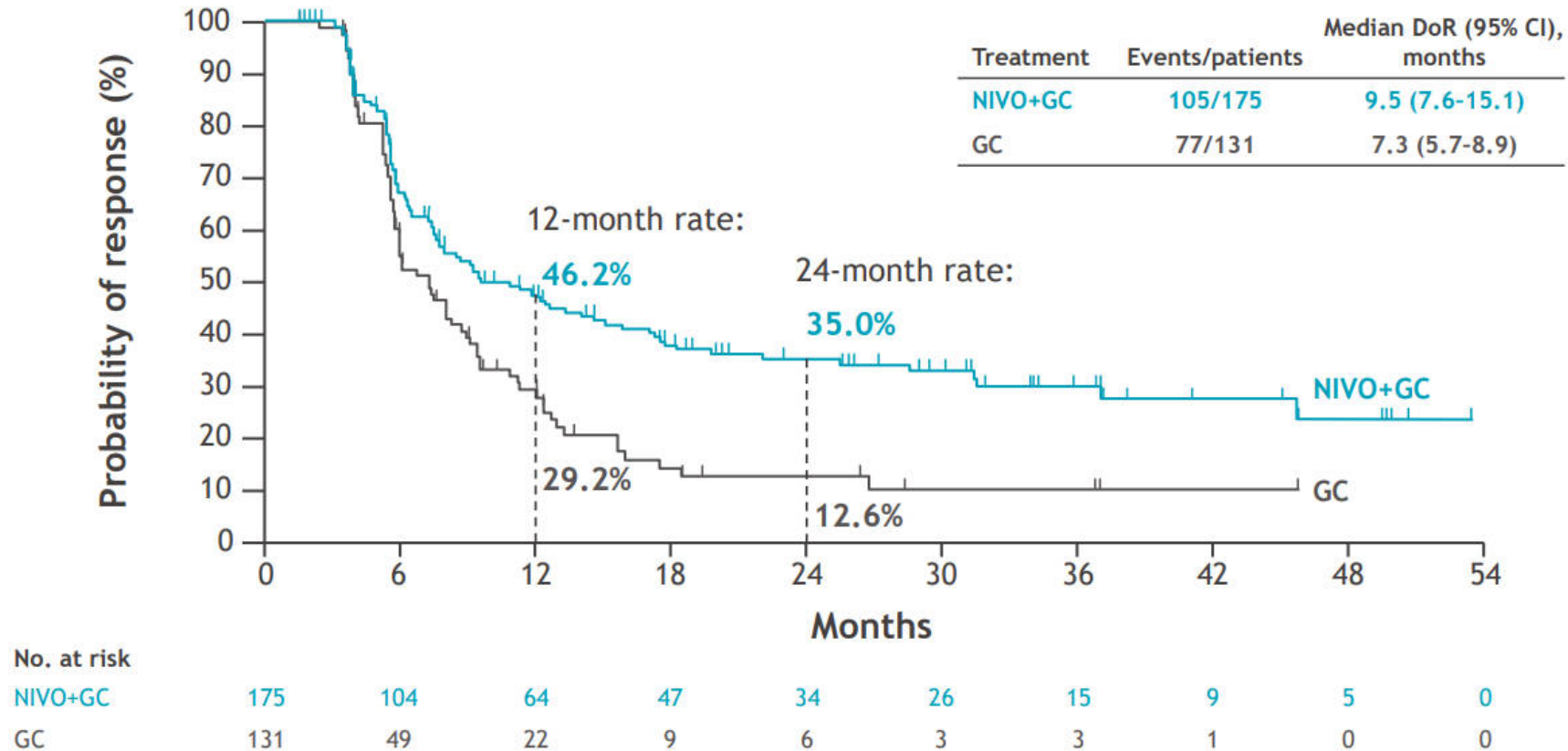
	NIVO+GC (n = 66)	GC (n = 36)
Complete response ^d		
Median TTCR (Q1-Q3), months	2.1 (1.9-2.2)	2.1 (1.9-2.2)
Median DoCR (95% CI), months	37.1 (18.1-NE)	13.2 (7.3-18.4)

^aIn all randomized patients. ^bThe most common reasons for UE response included death before first tumor assessment, withdrawal of consent, treatment stopped due to toxicity, patient never treated, and receipt of subsequent anticancer therapy before first tumor assessment. ^cBased on patients with an objective response per BICR (PR or CR as BOR). ^dBased on patients with a CR per BICR. BOR, best overall response; CR, complete response; DoCR, duration of complete response; DoR, duration of objective response; NE, not estimable; PD, progressive disease; PR, partial response; Q, quartile; SD, stable disease; TTCR, time to complete response; TTR, time to objective response; UE, unevaluable.

Sisplatin uygun hastalarda KT+İmmünoterapi

CheckMate 901

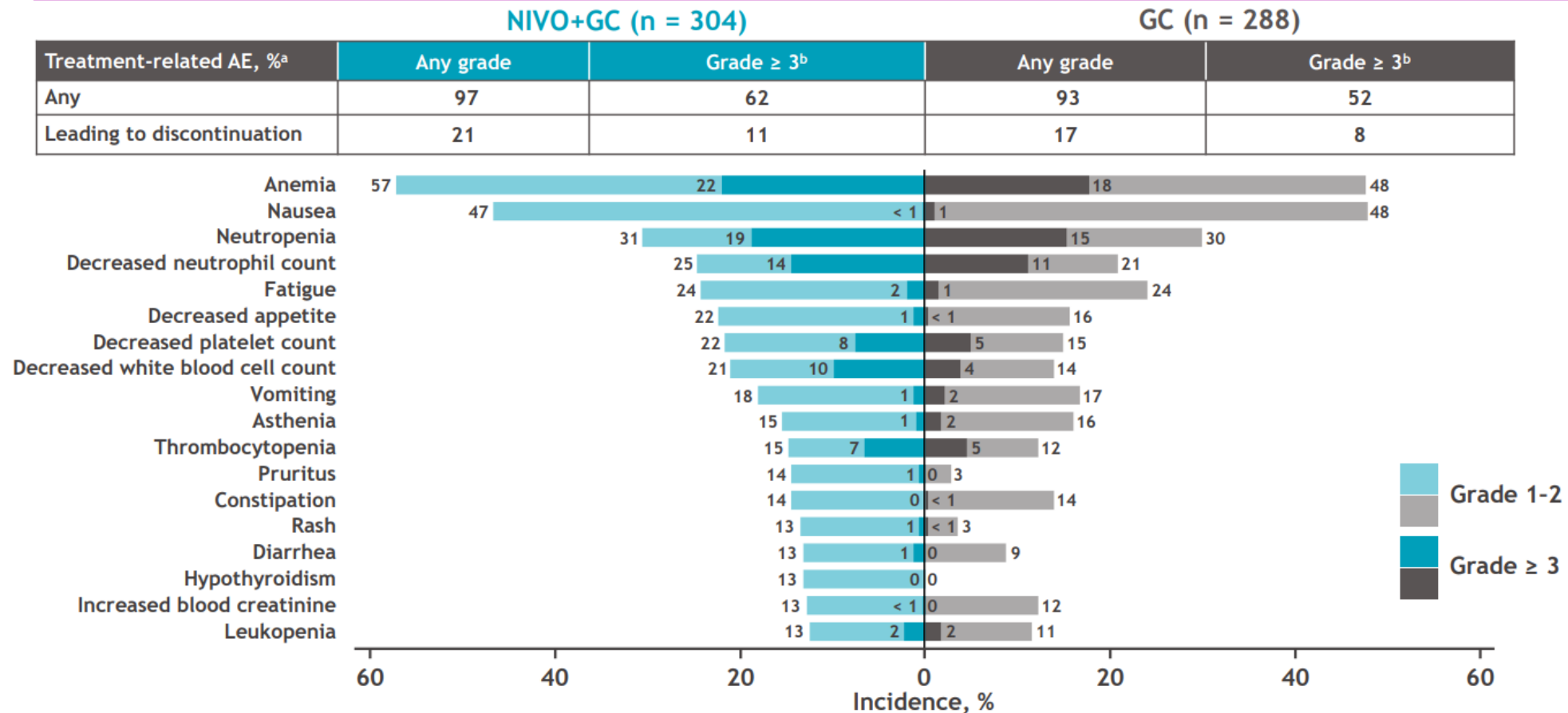
Duration of objective response per BICR



Sisplatin uygun hastalarda KT+İmmünoterapi

CheckMate 901

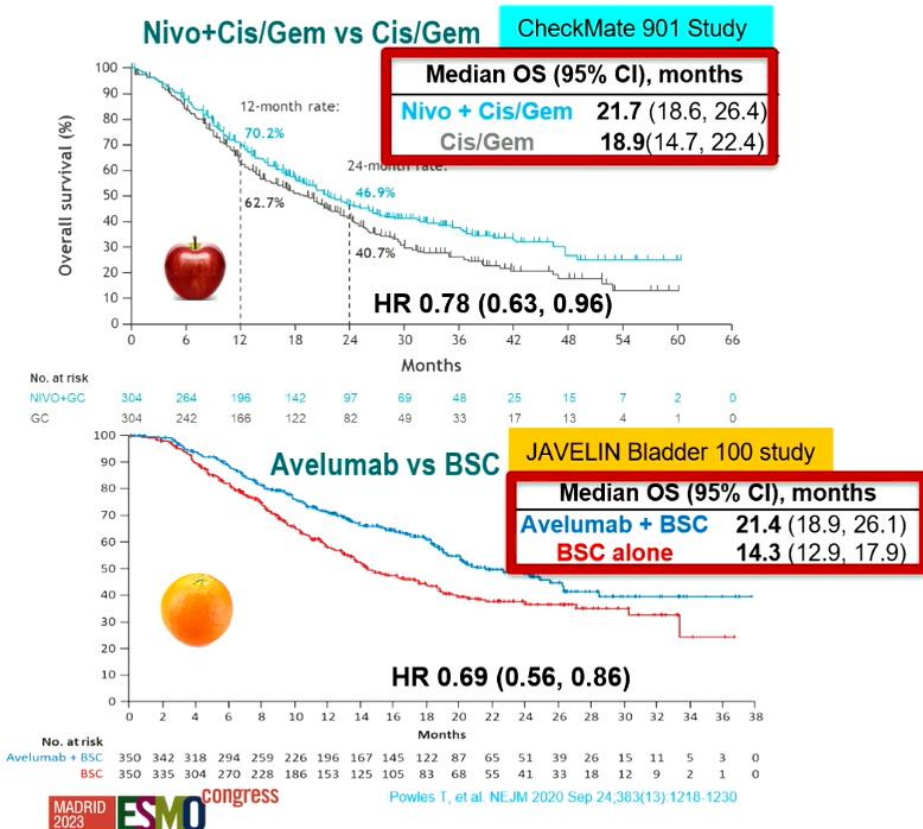
Treatment-related AEs in all treated patients



^aIncludes 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. ^bOne grade 5 event occurred in each arm (sepsis in the NIVO+GC arm and acute kidney injury in the GC arm). AE, adverse event.

Evre IV mesane birinci basamak tedavi seçeneği

Both sequential and combination chemo and CPI have efficacy



- 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



Andrea Apolo

Invited Discussant LBA6 and LBA7

Presented by Andrea B. Apolo, MD

Gelecek Perspektif

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

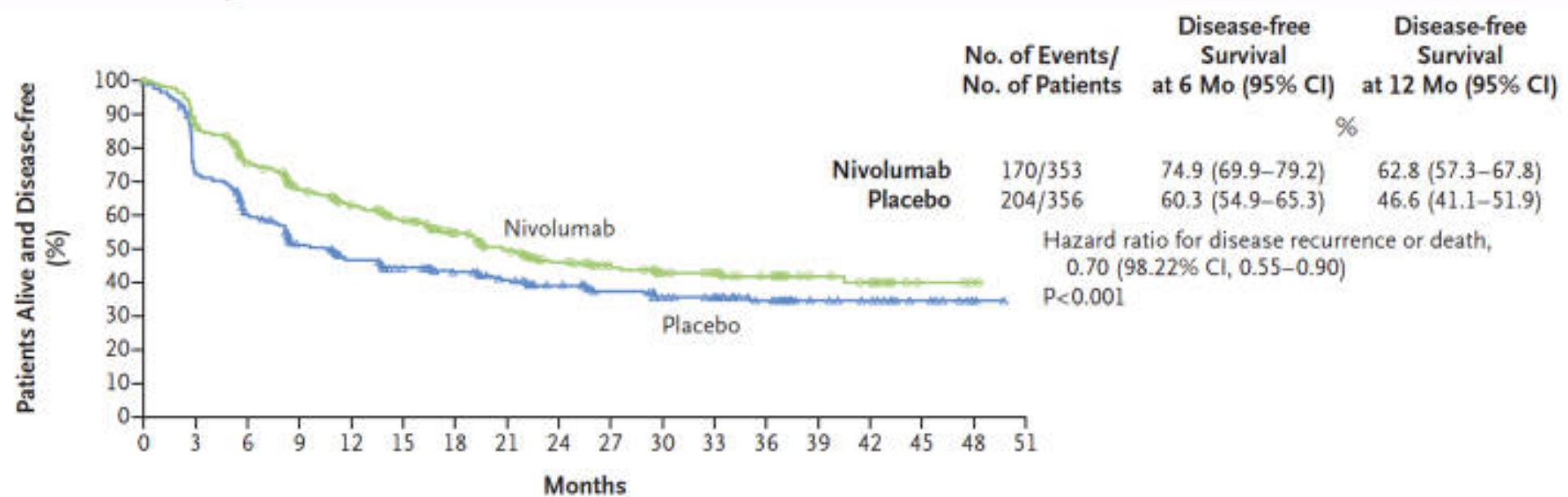
Adjuvant Nivolumab versus Placebo in Muscle-Invasive Urothelial Carcinoma

D.F. Bajorin, J.A. Witjes, J.E. Gschwend, M. Schenker, B.P. Valderrama, Y. Tomita, A. Bamias, T. Lebrecht, S.F. Shariat, S.H. Park, D. Ye, M. Agerbaek, D. Enting, R. McDermott, P. Gajate, A. Peer, M.I. Milowsky, A. Nosov, J. Neif Antonio, Jr., K. Tupikowski, L. Toms, B.S. Fischer, A. Qureshi, S. Collette, K. Unsal-Kacmaz, E. Broughton, D. Zardavas, H.B. Koon, and M.D. Galsky

N Engl J Med 2021 June 3;384:2102-14.

Gelecek Perspektif

CheckMate 274: Disease-Free Survival in the ITT Population



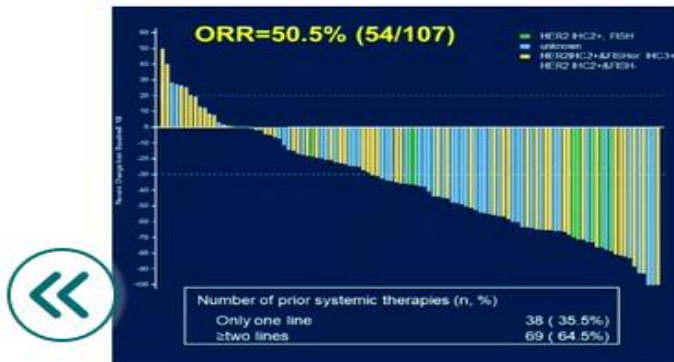
Gelecek Perspektif

Does CPI combine best with ADCs with MMAE payloads?

Disitamab vedotin in HER2 2/3+ Metastatic Urothelial Carcinoma

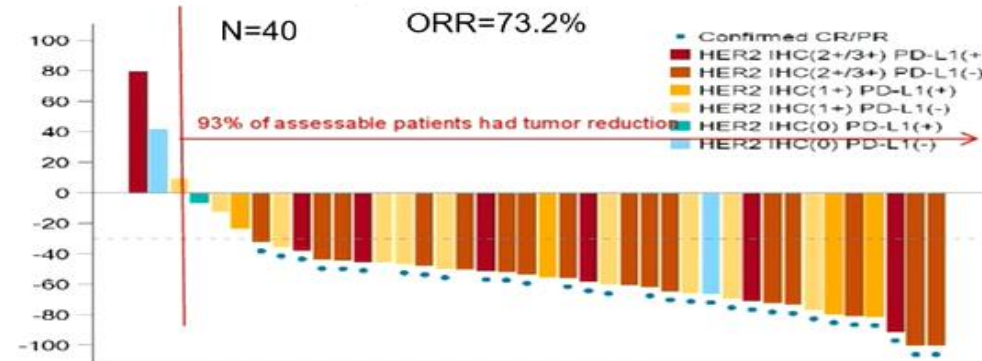
Disitamab vedotin

N=107 In the Second or Third-line setting



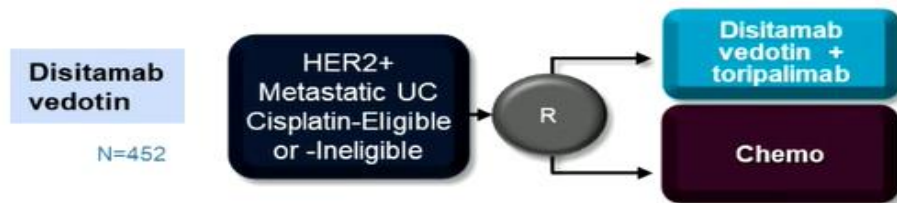
Sheng, et al. ASCO 2022 abstract 4518

Disitamab vedotin + toripalimab

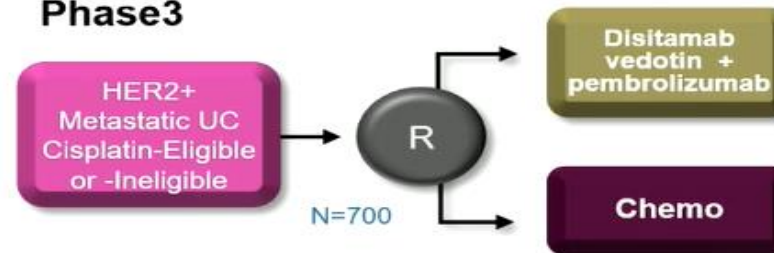


Sheng, X., et al. ASCO 2023

Phase 3



Phase3

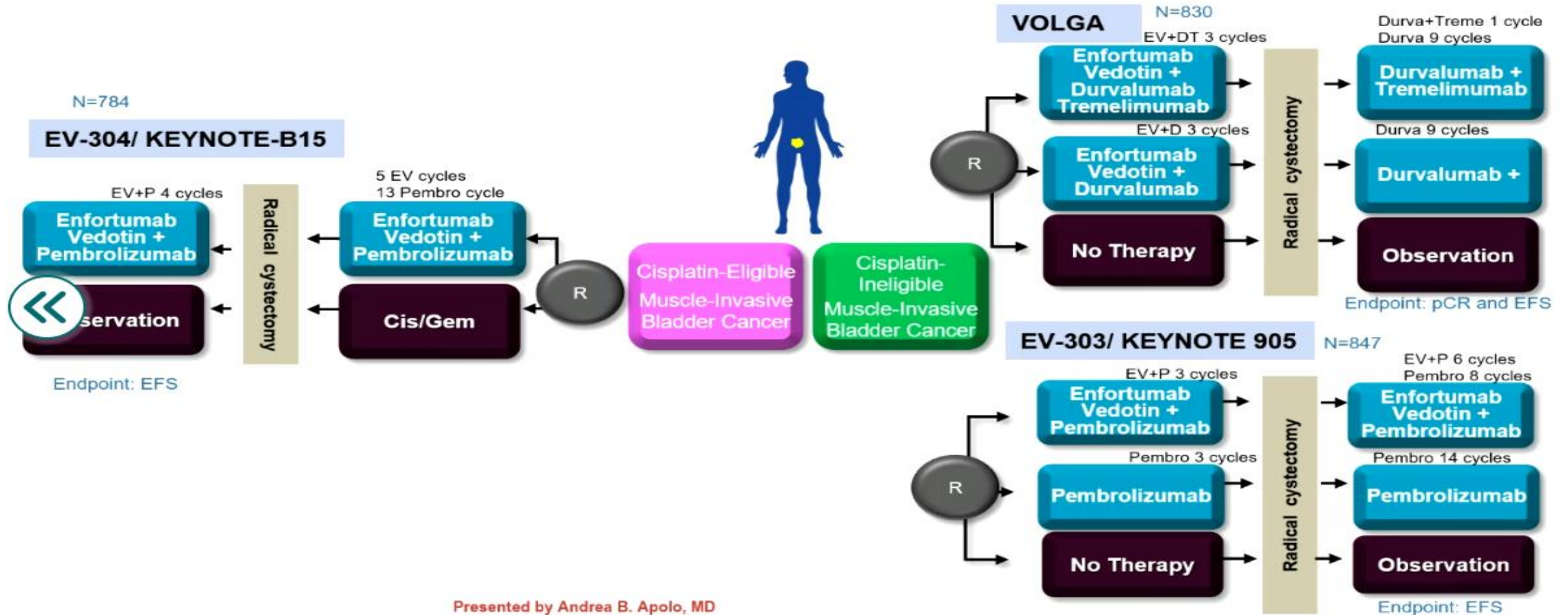


Presented by Andrea B. Apolo, MD

@apolo_andrea

Gelecek Perspektif

What is the efficacy of EV+CPI as Neoadjuvant or Adjuvant Therapy for MIBC?

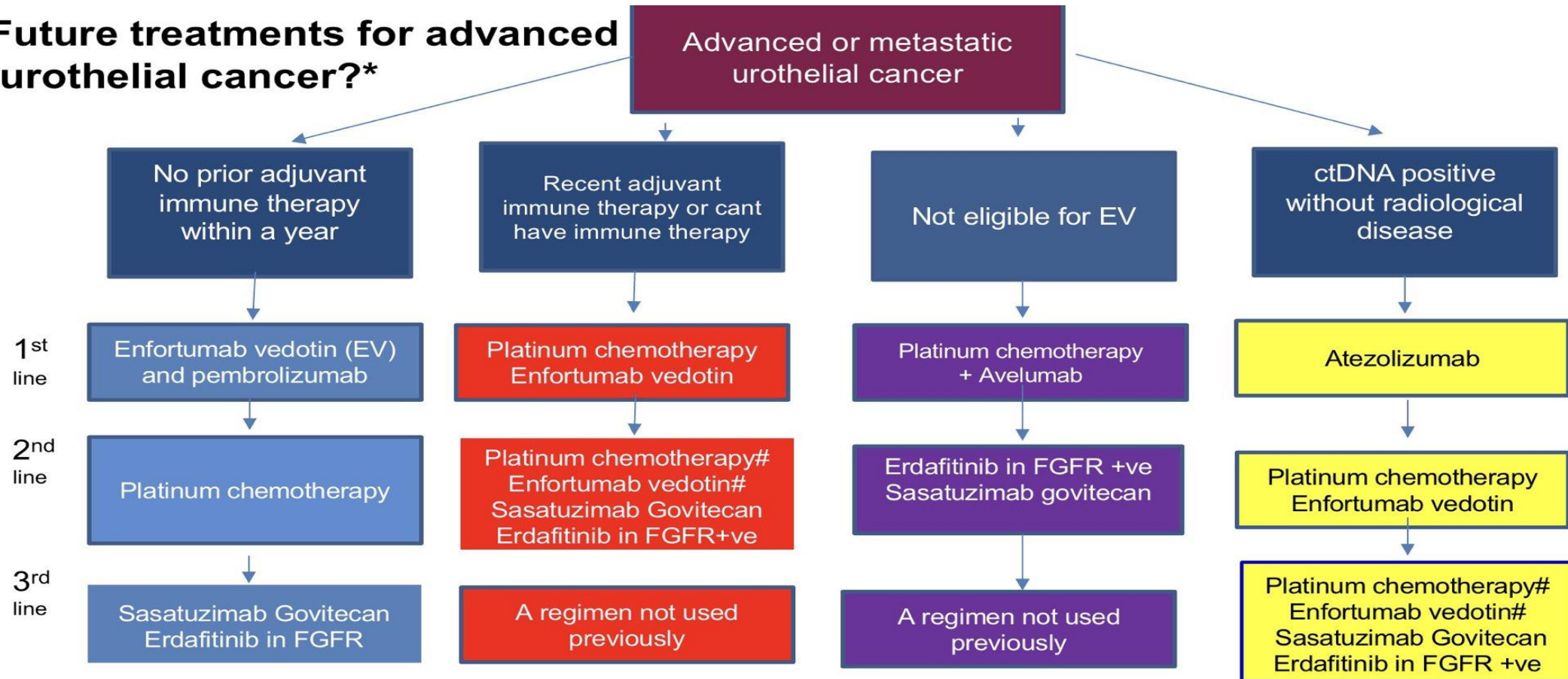


Presented by Andrea B. Apolo, MD

@apolo_andrea

Gelecek Perspektif

Future treatments for advanced urothelial cancer?*



*Assuming EV302 (EV/pembro), TROPICs (SG), IM011 (ctDNA+ve), THOR are +ve for OS
 # unless given previousl

Sonuç

- ❑ Enfortumab vedotin +pembrolizumab standart tedavi
- ❑ Evre IV mesane kanserinde birinci basamak tedavide sisplatin+gemsitabin+nivolumab bir seçenek
- ❑ Platin bazlı kemoterapi sonrası klinik yarar(CR/PR/SD) gören hastalarda idame tedavi olarak Avelumab bir seçenek
- ❑ Sisplatin alamayacak hastalarda carboplatin+ gemsitabin kemoterapi kombinasyonu klinik yarar alanlarda Avelumab idame tedavi olarak bir seçenek
- ❑ Platin bazlı kemoterapi alamayacak hastalarda birinci basamak tedavide (ECOG PS $\geq$ 2, komorbidite vs.) PD-L1 düzeyinden bağımsız Pemrolizumab önerilebilir