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Management of Recurrent and Metastatic Bladder Cancer in first line setting

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Disclosures

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- Advisory board/Consultancy: Roche, MSD, AstraZeneca, BMS, Janssen, GSK, Astellas, Pfizer, Bayer, Merck, Gilead, Pierre Fabre, Sotio.

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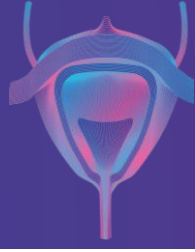
Over 20,000 people in the UK are diagnosed with bladder cancer each year[1]



- Bladder cancer is the **11th most common cancer** in the UK, with over 20,000 cases per year*[1,2]
- The majority of cases occur in people **>60 years of age**[3]
- The incidence and mortality of bladder cancer is greater in men than in women[2,4]
- Bladder cancer is associated with one of the **highest recurrence rates** of all cancers (up to 80%)[5]

In the UK, the **incidence and mortality** of bladder cancer is more than **2 times greater** in men than in women[2]

UK incidence and mortality of bladder cancer by sex

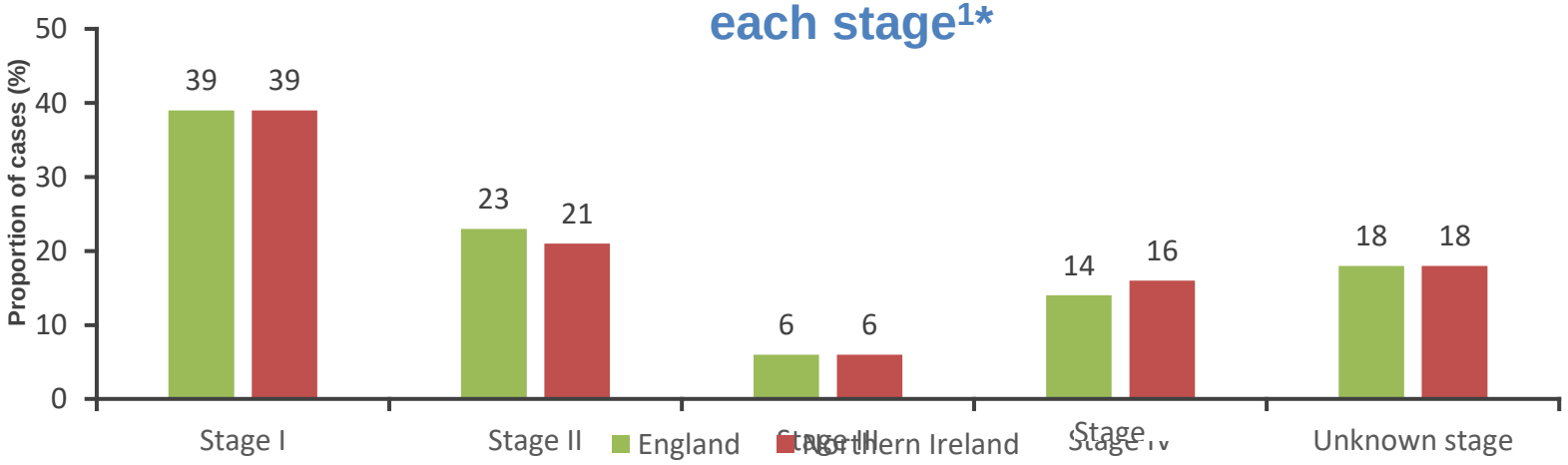
	Men	vs	Women
Incidence:[6]	**27.4 per 100,000**		**8.2 per 100,000**
Mortality:[7]	**14.0 per 100,000**		**4.9 per 100,000**

*According to data collected in 2015–2017.[2]

1. Fight bladder cancer. My diagnosis counts. https://fightbladdercancer.co.uk/downloads/my-diagnosis-counts (accessed May 2022); 2. Cancer Research UK. Bladder cancer statistics. https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/bladder-cancer (accessed May 2022); 3. National Institute for Health and Care Excellence. Bladder cancer: diagnosis and management (NG2). Published February 2015; 4. Bray F et al. *CA Cancer J Clin* 2018;68:394–424; 5. Action Bladder Cancer UK. The facts about bladder cancer. Available at https://actionbladdercanceruk.org/the-facts-about-bladder-cancer/ (accessed May 2022); 6. Cancer Research UK. Bladder cancer incidence statistics. https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/bladder-cancer/incidence#heading-Zero (accessed May 2022); 7. Cancer Research UK. Bladder cancer mortality statistics. https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/bladder-cancer/mortality#heading-Zero (accessed May 2022).

The majority of patients with bladder cancer are diagnosed with early-stage disease[1]

Proportion of bladder cancer cases diagnosed at each stage[1]*

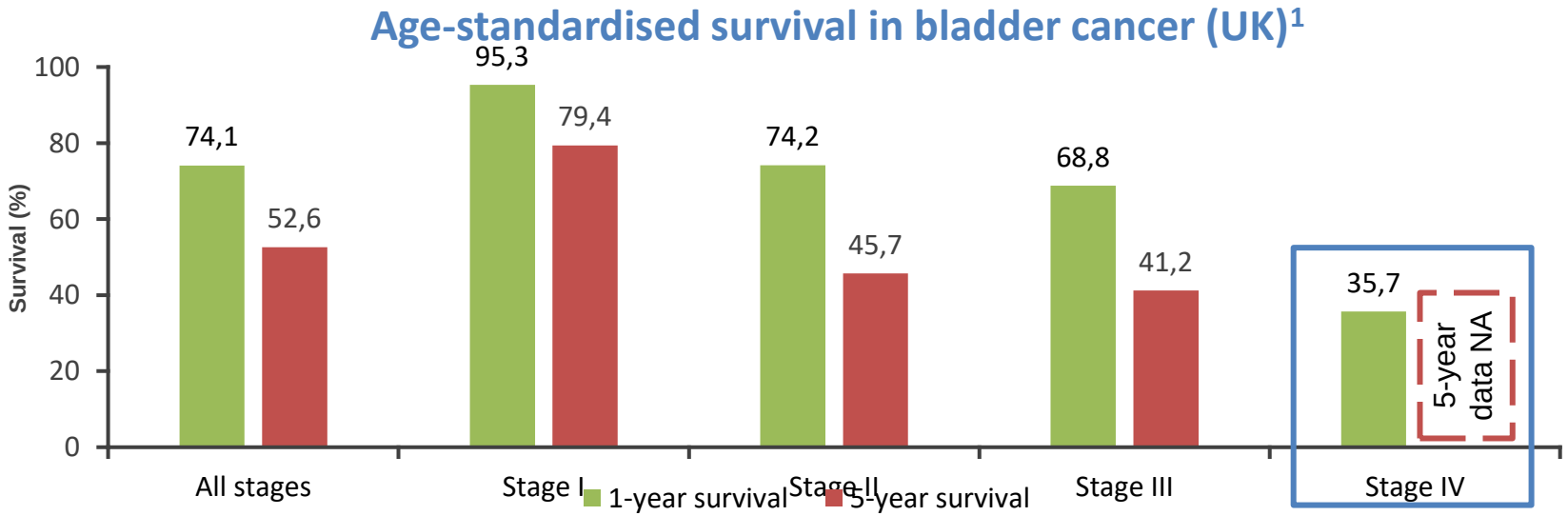


In the UK, the proportion of patients with advanced or metastatic disease at diagnosis is approximately 15%‡[1]

*According to data collected in 2014 for England, and 2010–2014 for Northern Ireland; †Locally advanced and metastatic disease; ‡Estimated from data for England and Northern Ireland.

1. Cancer Research UK. Bladder cancer (C67). https://www.cancerresearchuk.org/sites/default/files/cstream-node/inc_by_stage_bladder_0.pdf (accessed May 2022).

For patients with advanced stage bladder cancer, prognosis is poor with less than 46% of patients surviving 5 years with stage III cancer[1]



1-year survival is just 35.7% for patients with stage IV disease[1]

NA, not available.

1. Office for National Statistics. Cancer survival in England (2013–2017). https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/datasets/cancersurvivalratescancersurvivalinenglandadultsdiagnosed (accessed May 2022).

First-line platinum-based CT is associated with high disease control rates, but benefits are generally not durable[1–3]

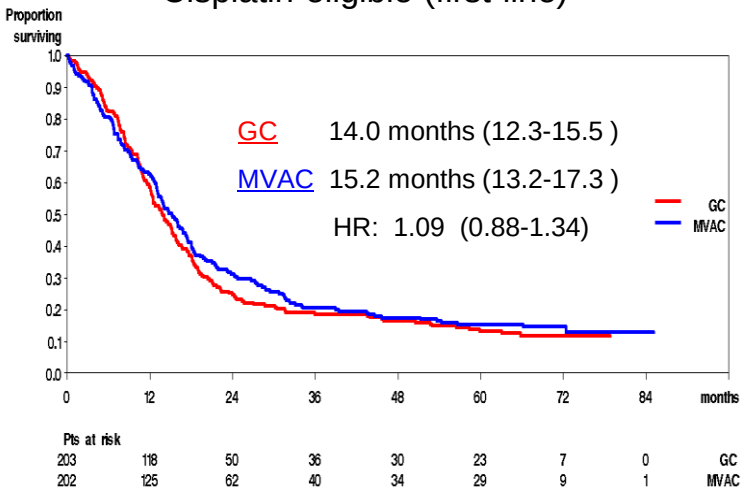
The safety and tolerability profile of first-line platinum-based CT for locally advanced or metastatic UC is well established; however, toxicities limit treatment durations[10]

1L, first line; 2L, second line; CT, chemotherapy; DCR, disease control rate; UC, urothelial carcinoma.

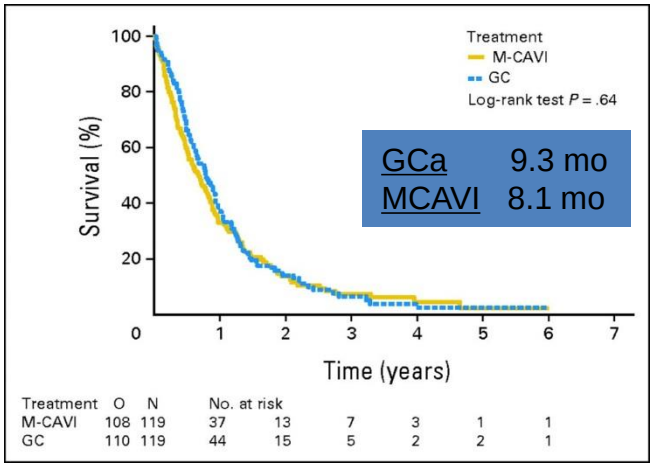
1. De Santis M et al. *J Clin Oncol* 2012;30:191–199; 2. von der Maase H et al. *J Clin Oncol* 2000;18:3068–3077; 3. Dogliotti L et al. *Eur Urol* 2007;52:134–141; 4. Cheeseman S et al. *Front Oncol* 2020;10:167; 5. Aly A et al. *J Med Econ* 2019;22:662–670; 6. Galsky MD et al. *Bladder Cancer* 2018;4:227–238; 7. Fisher MD et al. *Clin Genitourin Cancer* 2018;16:e1171–e1179; 8. Niegisch G et al. *J Cancer* 2018;9:1337–1348; 9. Flannery K et al. *Future Oncol* 2019;15:1323–1334; 10. Sonpavde G et al. *J Urol* 2018;200:1207–1214.

First-line chemotherapy for metastatic urothelial carcinoma (UC)

Cisplatin-eligible (first-line)



Cisplatin-ineligible



Von der Maase H, JCO 2005
De Santis M, et al, JCO 2012

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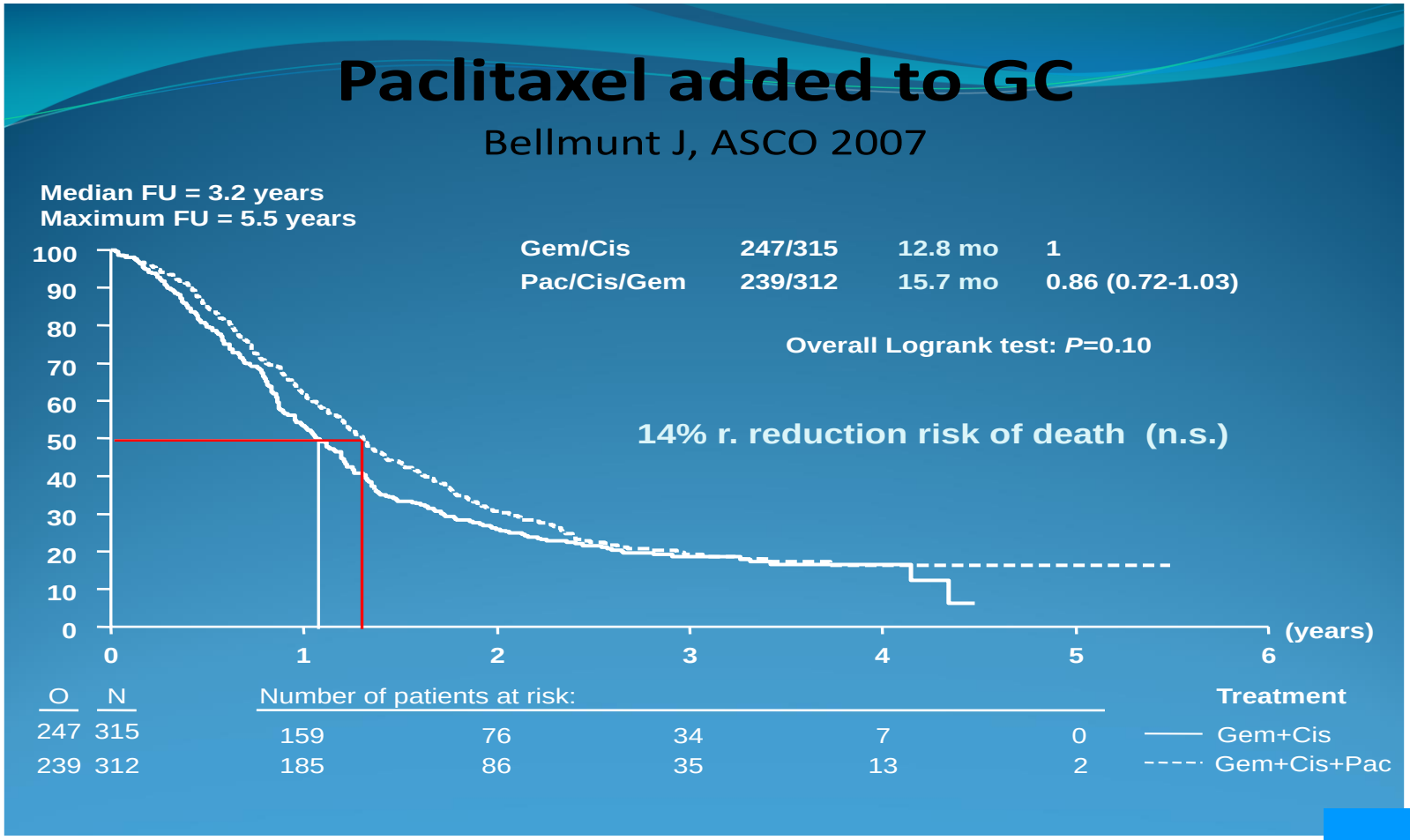
Paclitaxel plus GC



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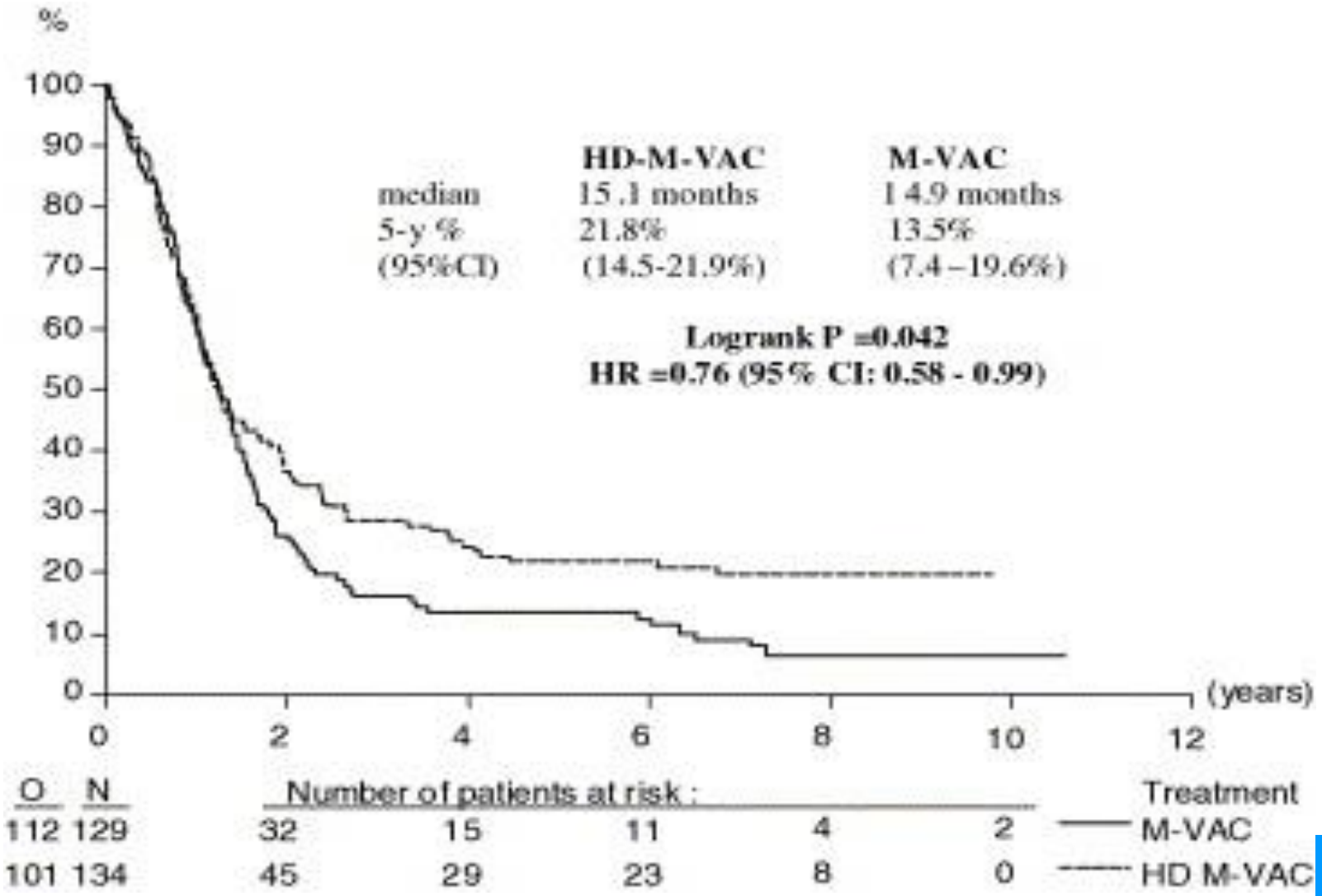
DD-MVAC vs. MVAC: Sternberg CN, JCO 2001, Eur J Cancer 2006



Cisplatin ineligible

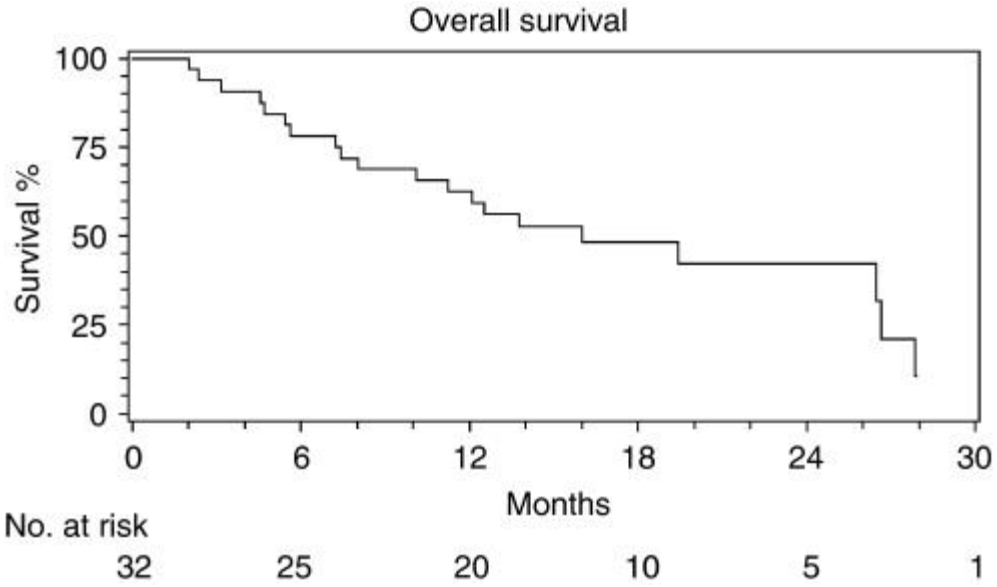
Table. Cisplatin vs. Platinum Ineligibility

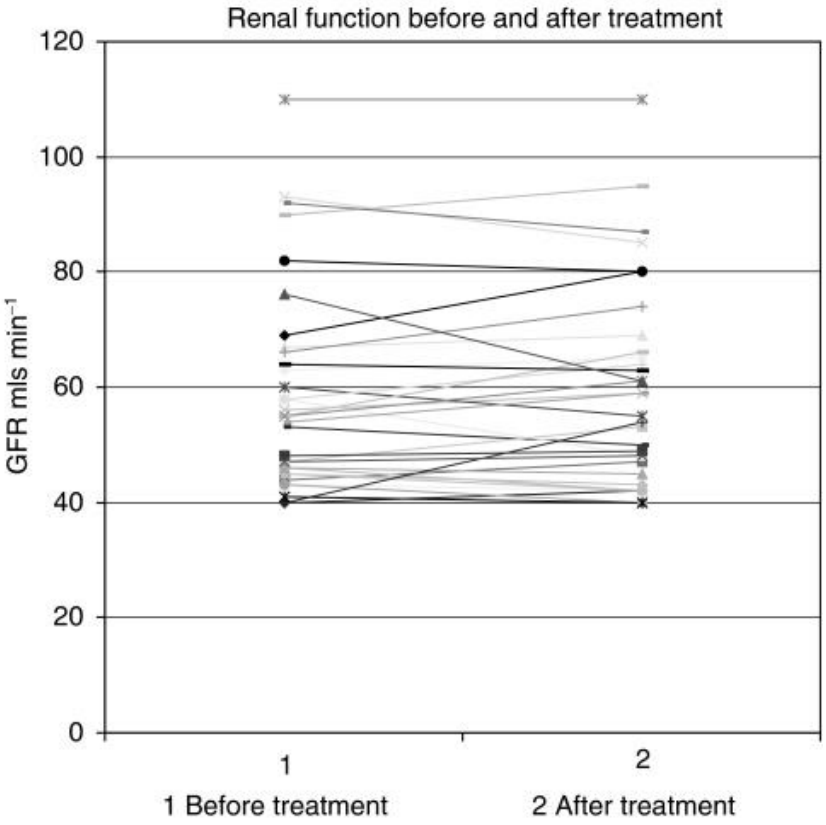
Parameters (Any one of the parameters would qualify as ineligibility)	Cisplatin Ineligibility	Platinum Ineligibility
ECOG Performance Status	≥ 2	> 2
NYHA Heart Failure	> 2	> 3
Creatinine Clearance (Cr Cl)	< 50 mL/min (split cisplatin could be used for Cr Cl < 60 mL/min)	< 30 mL/min
Peripheral Neuropathy	≥ 2 grade	> 2 grade
Presence of Solitary Kidney	Avoid in patients with suboptimal Cr Cl < 60 mL/min	Physician discretion should be used for patients with low Cr Cl
Others	Advanced age and other comorbidities that could compromise patient safety during chemotherapy	

Abbreviations: ECOG, Eastern Cooperative Oncology Group; NYHA, New York Heart Association.

Fractionated weekly cisplatin + gemcitabine (wGC) is safe and highly active in patients ineligible for conventional day 1 cisplatin.

Hussain SA et al, Br J Cancer 2004





MTD: Cis 35/m^2 + Gem 1000/m^2 D1,8

N=32; N=19 with Cr Cl 40-60

Overall response rate = 65.5%

Complete responses =12.5%

Median OS = 16 months

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Pooled analysis of phase II trials evaluating weekly or conventional cisplatin as first-line therapy for advanced urothelial carcinoma Clinic Genit cancer 2013; Agarwal, Vonder Masse, Hussain et al

Table

Study author Outcome	wGC		GC			p-values (wGC vs. GC)	
	Hussain	Von der Maase	Kaufman	Lorusso	Moore	Unadjusted (binomial model)	Adjusted (allows for heterogeneity between studies in the same Group)
Efficacy							
CR	4/32 12.5%	7/38 18%	10/46 22%	8/54 15%	6/31 19.3%	0.59	0.49
PR	17/32 53%	9/38 24%	9/46 19%	18/54 33%	10/31 32%	0.24	0.55
SD	6/32 19%	10/38 26%	18/46 39%	12/54 22%	11/31 35.4%	0.18	0.36
Toxicity (≥Grade 3)							
Anemia	4/32 13%	12/41 29%	12/46 26%	18/54 33%	10/31 32%	0.19	0.32
Neutropenia	9/32 28%	21/36 58%	17/46 37%	15/54 28%	12/31 39%	0.15	0.43
Thrombocytopenia	15/32 47%	32/41 76%	16/46 35%	11/54 20%	17/31 55%	0.0003	0.19
Renal	0/32 0%	2/42 5%	0/46 0%	4/54 7%	1/31 3%	0.68	0.77
Nausea, vomiting	6/32 19%	12/42 29%	8/46 17%	11/54 20%	6/31 19%	0.24	0.24

and wGC yielded similar responses and toxicities in advanced UC in this hypothesis-generating

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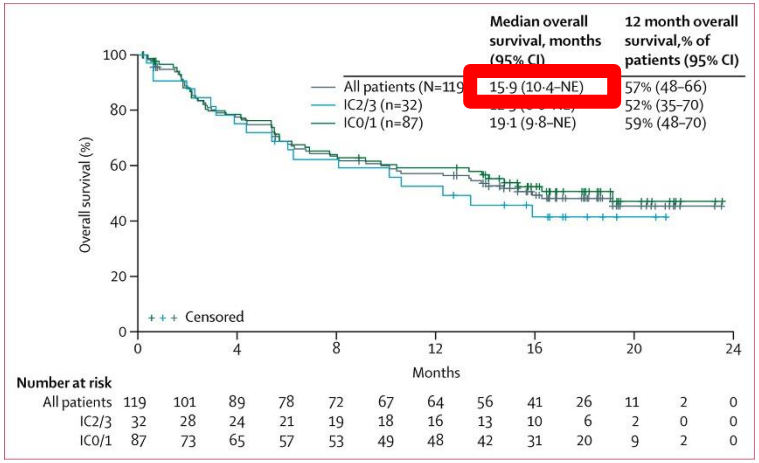
First-line PD1/PD-L1 inhibitors for cisplatin-ineligible UC:

Atezolizumab



ORR 23%

Median PFS 2·7 months

Balar AV, Lancet 2017

Pembrolizumab

	Total Population N = 370		
	n	%	95% CI
Objective response rate	108	**29**	25-34
Complete response	27	7	5-10
Partial response	81	22	18-27
Stable disease	67	18	14-22
Progressive disease	155	42	37-47

O'Donnell P, ASCO 2017

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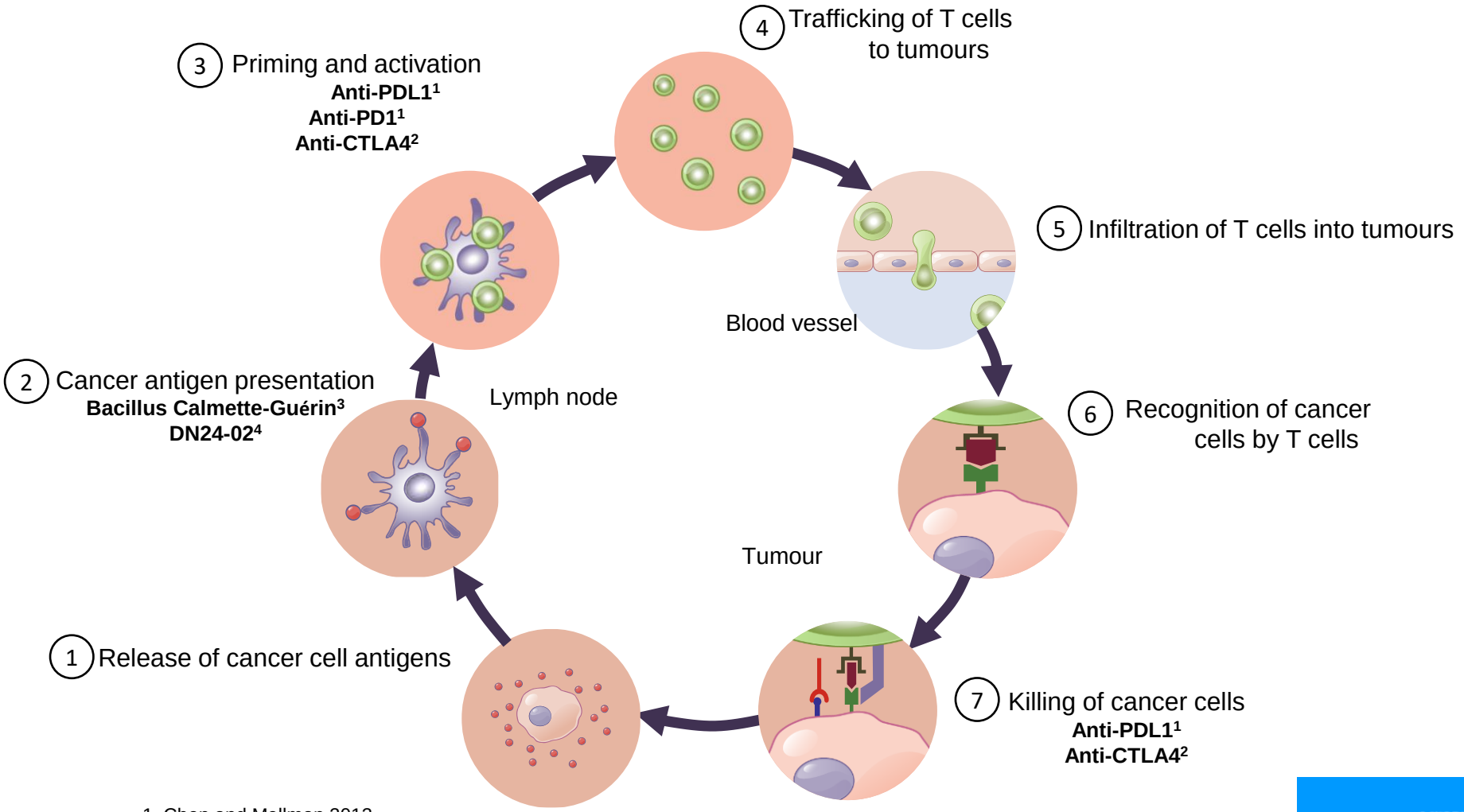
Immunotherapy in bladder cancer can target several steps in the cancer immunity cycle



1. Chen and Mellman 2013
2. Liakou, et al. 2008
3. Herr and Morales 2008
4. Bajorin, et al. 2014

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ESMO 2019: IMvigor130: Efficacy and Safety from a Phase 3 Study of Atezolizumab as Monotherapy or Combined with Platinum-based Chemotherapy vs Placebo + PBC in Previously Untreated Locally Advanced or Metastatic Urothelial Carcinoma

Enrique Grande et al

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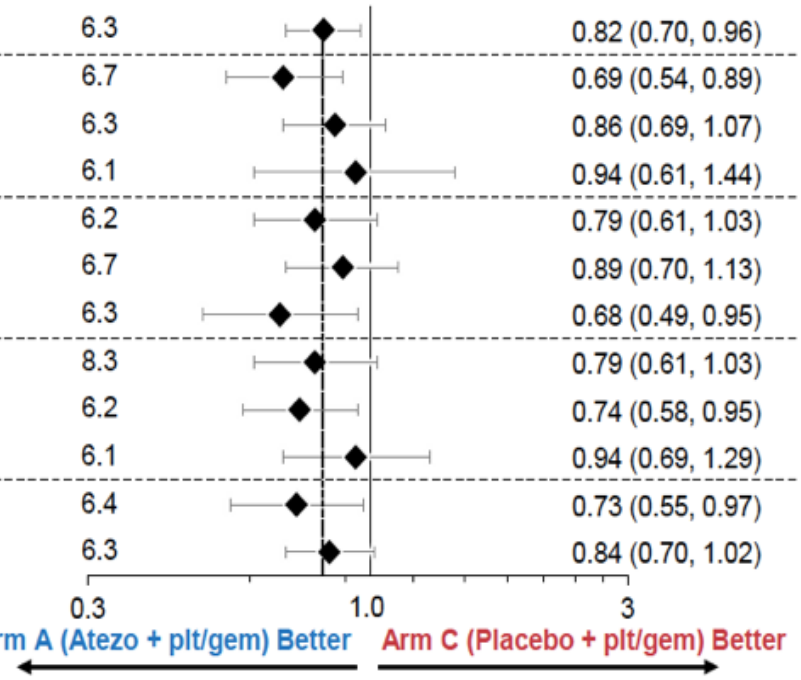
PFS subgroups: ITT (Arm A vs Arm C)

Characteristic		Patients (n)	Arm A mPFS, mo (n = 451)	Arm C mPFS, mo (n = 400)	HR (95% CI)[a]
All patients		851	8.2	6.3	0.82 (0.70, 0.96)
ECOG PS	0	355	9.4	6.7	0.69 (0.54, 0.89)
	1	396	6.8	6.3	0.86 (0.69, 1.07)
	2	100	4.8	6.1	0.94 (0.61, 1.44)
PD-L1 status	0	278	6.5	6.2	0.79 (0.61, 1.03)
	1	374	8.1	6.7	0.89 (0.70, 1.13)
	2/3	199	8.6	6.3	0.68 (0.49, 0.95)
Bajorin risk factor score	0	338	9.8	8.3	0.79 (0.61, 1.03)
	1	318	8.2	6.2	0.74 (0.58, 0.95)
	2 and/or liver mets	195	5.0	6.1	0.94 (0.69, 1.29)
Investigator choice of chemo	Cisplatin	273	8.8	6.4	0.73 (0.55, 0.97)
	Carboplatin	578	7.1	6.3	0.84 (0.70, 1.02)



[a] Unstratified HR shown for all characteristics except for 'All Patients', where stratified HR is shown.

IMvigor130 baseline characteristics

Characteristic	Atezo + plt/gem (n = 451)	Placebo + plt/gem (n = 400)[a]	Atezo (n = 362)
Median age (range), y	69 (31-87)	67 (33-89)	67 (36-87)
ECOG PS, n (%)			
0	182 (40)	173 (43)	157 (43)
1	209 (46)	187 (47)	174 (48)
2	60 (13)	40 (10)	31 (9)
Bajorin risk factor score, n (%)			
0	176 (39)	162 (41)	151 (42)
1	169 (37)	149 (37)	134 (37)
2 and/or liver mets	106 (24)	89 (22)	77 (21)
PD-L1 status on IC, n (%)			
IC2/3	108 (24)	91 (23)	88 (24)
IC1	195 (43)	179 (45)	160 (44)
IC0	148 (33)	130 (33)	114 (31)
Cisplatin ineligibility[b]	204 (45)	140 (35)	107 (30)
Renal impairment	113 (25)	94 (24)	65 (18)
Investigator choice of chemotherapy[c]			
Carboplatin	314 (70)	264 (66)	227 (63)
Cisplatin	137 (30)	136 (34)	135 (37)

[a] n = 359 for comparisons to atezo monotherapy arm. [b] Per Galsky criteria per protocol, excluding New York Heart Association functional classification.
[c] Of the patients considered cisplatin eligible at study entry, 52% received carboplatin, while 10% of patients who were cisplatin ineligible received cisplatin.

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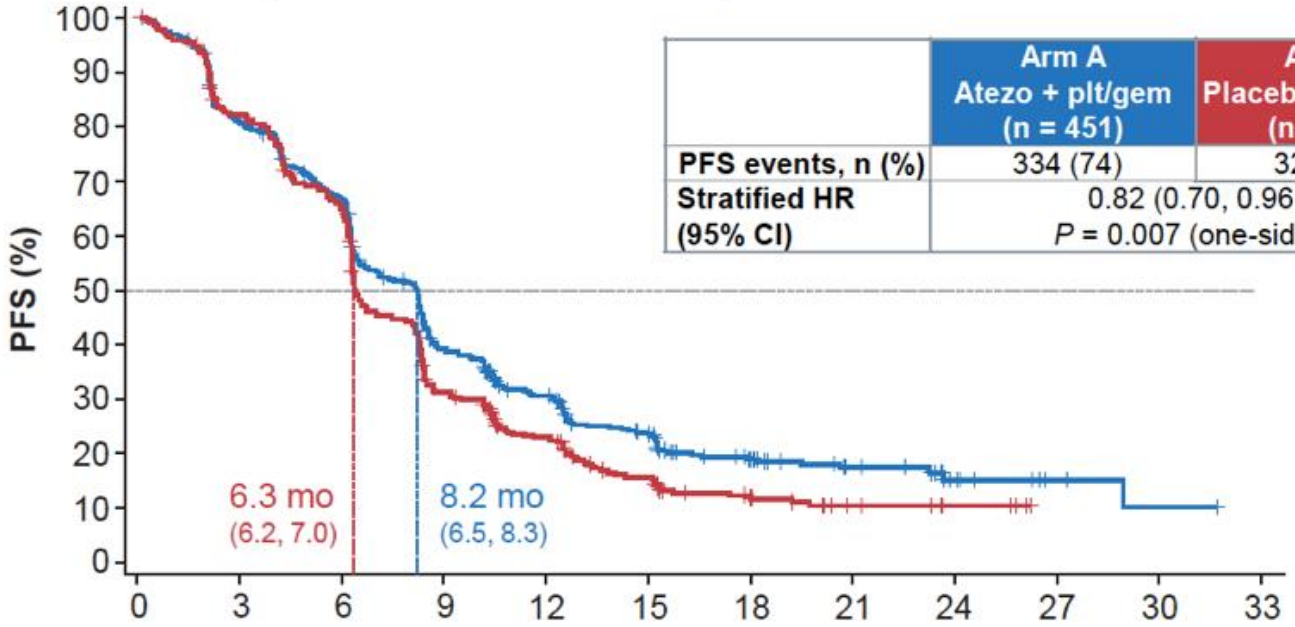
Final PFS: ITT (Arm A vs Arm C)



	Arm A Atezo + plt/gem (n = 451)	Arm C Placebo + plt/gem (n = 400)
PFS events, n (%)	334 (74)	326 (82)
Stratified HR (95% CI)	0.82 (0.70, 0.96) *P* = 0.007 (one-sided)	

No. at Risk												
Atezo + plt/gem	451	345	282	160	111	74	42	22	10	4	2	NE
Placebo + plt/gem	400	317	246	116	73	40	18	11	4	NE	NE	NE

NE, not estimable. Data cutoff 31 May 2019; median survival follow-up 11.8 months (all patients).

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DANUBE: DANUBE is a phase 3 study to evaluate Durvalumab, with or without Tremelimumab (an anti–CTLA-4 agent), as a first-line treatment for metastatic UC **; Powles et al ESMO 2020**

Results

A total of 1032 pts were randomized. Median OS was not significantly different between D and CT among pts with high PD-L1 expression, nor between D+T and CT in the ITT population. Treatment-related adverse events of grade 3–4 occurred in 14%, 28%, and 60% of pts in the D, D+T, and CT arms, with deaths possibly related to treatment in 0.6%, 0.6%, and 0.3% of pts, respectively.

Conclusions: While a trend towards improved OS was observed with D vs CT in the PD-L1 high population and with D+T vs CT in the ITT population, statistical significance was not reached. Additional analyses are ongoing to characterize D and D+T efficacy/safety in different pt subgroups.

Median OS, mo (95% CI)	14.4 (10.4–17.3)	12.1 (10.4–15.0)
Hazard ratio (95% CI)	0.89 (0.71–1.11)	
Log-rank P value	0.3039	
ITT Population	D+T (n=342)	CT (n=344)
Median OS, mo (95% CI)	15.1 (13.1–18.0)	12.1 (10.9–14.0)
Hazard ratio (95% CI)	0.85 (0.72–1.02)	
Log-rank P value	0.0751	

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Maintenance avelumab + best supportive care (BSC) versus BSC alone after platinum-based first-line chemotherapy in advanced urothelial carcinoma: JAVELIN Bladder 100 phase III results

Thomas Powles,[1] Se Hoon Park,[2] Eric Voog,[3] Claudia Caserta,[4] Begoña P. Valderrama,[5] Howard Gurney,[6] Haralabos Kalofonos,[7] Sinisa Radulovic,[8] Wim Demey,[9] Anders Ullén,[10] Yohann Loriot,[11] Srikala S. Sridhar,[12] Norihiko Tsuchiya,[13] Evgeny Kopyltsov,[14] Cora N. Sternberg,[15] Joaquim Bellmunt,[16] Jeanny B Aragon-Ching,[17] Daniel P. Petrylak,[18] Alessandra di Pietro,[19] Petros Grivas[20]

[1]Barts Cancer Institute, Experimental Cancer Medicine Centre, Queen Mary University of London, St Bartholomew's Hospital, London, UK; [2]Sungkyunkwan University Samsung Medical Center, Seoul, Korea; [3]Centre Jean Bernard Clinique Victor Hugo, Le Mans, France; [4]Medical Oncology Unit, Azienda Ospedaliera S. Maria, Terni, Italy; [5]Department of Medical Oncology, Hospital Universitario Virgen del Rocío, Sevilla, Spain; [6]Department of Clinical Medicine, Macquarie University, Sydney, New South Wales, Australia; [7]Medical Oncology, University General Hospital of Patras, Patras, Greece; [8]Institute for Oncology and Radiology of Serbia, Belgrade, Serbia; [9]Department of Medical Oncology, AZ KLINA, Brasschaat, Belgium; [10]Patient Area Pelvic Cancer, Theme Cancer, Karolinska University Hospital and Department of Oncology-Pathology, Karolinska Institute, Solna, Sweden; [11]Gustave Roussy, INSERMU981, Université Paris-Saclay Villejuif, France; [12]Princess Margaret Cancer Center, University Health Network, Toronto, Ontario, Canada; [13]Department of Urology, Yamagata University Faculty of Medicine, Yamagata, Japan; [14]State Institution of Healthcare Regional Clinical Oncology Dispensary, Omsk, Russia; [15]Weill Cornell Medicine, Hematology/Oncology, New York, New York, USA; [16]Department of Medical Oncology, Beth Israel Deaconess Medical Center; Harvard Medical School, Boston, Massachusetts, USA; [17]Inova Schar Cancer Institute, Fairfax, Virginia, USA; [18]Yale Cancer Center, New Haven, Connecticut, USA; [19]Pfizer srl, Milano, Italy; [20]Department of Medicine, Division of Oncology, University of Washington; Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, Washington, USA

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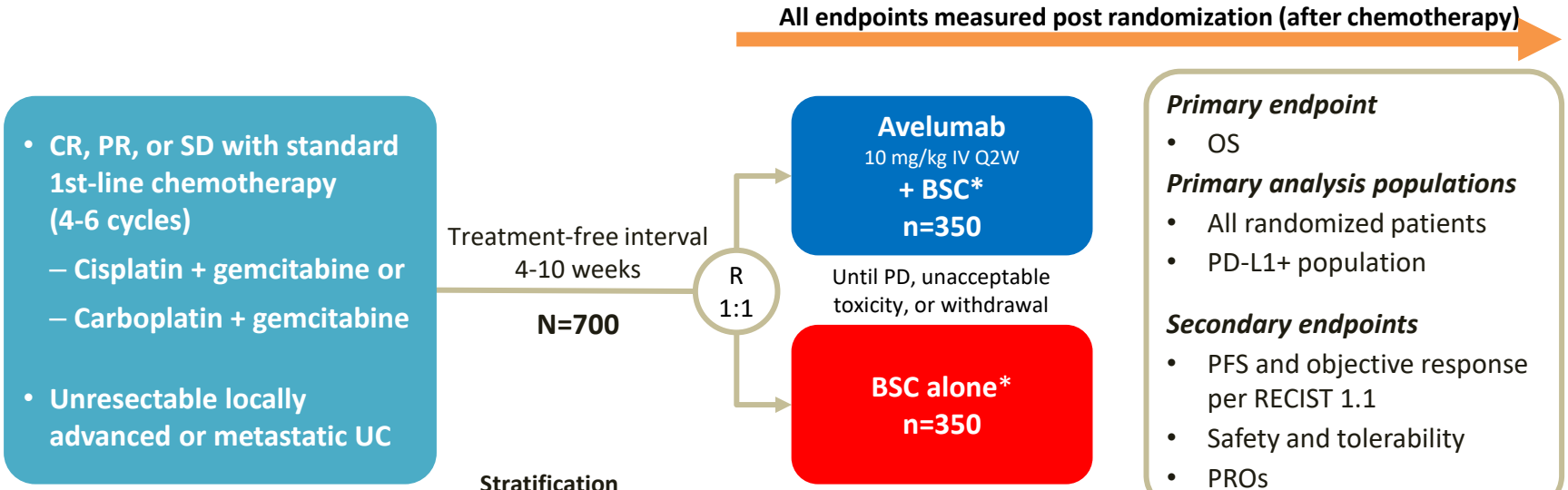
JAVELIN Bladder 100 study design (NCT02603432)



Stratification

- Best response to 1st-line chemo (CR or PR vs SD)
- Metastatic site (visceral vs non-visceral)

PD-L1+ status was defined as PD-L1 expression in ≥25% of tumor cells or in ≥25% or 100% of tumor-associated immune cells if the percentage of immune cells was >1% or ≤1%, respectively, using the Ventana 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

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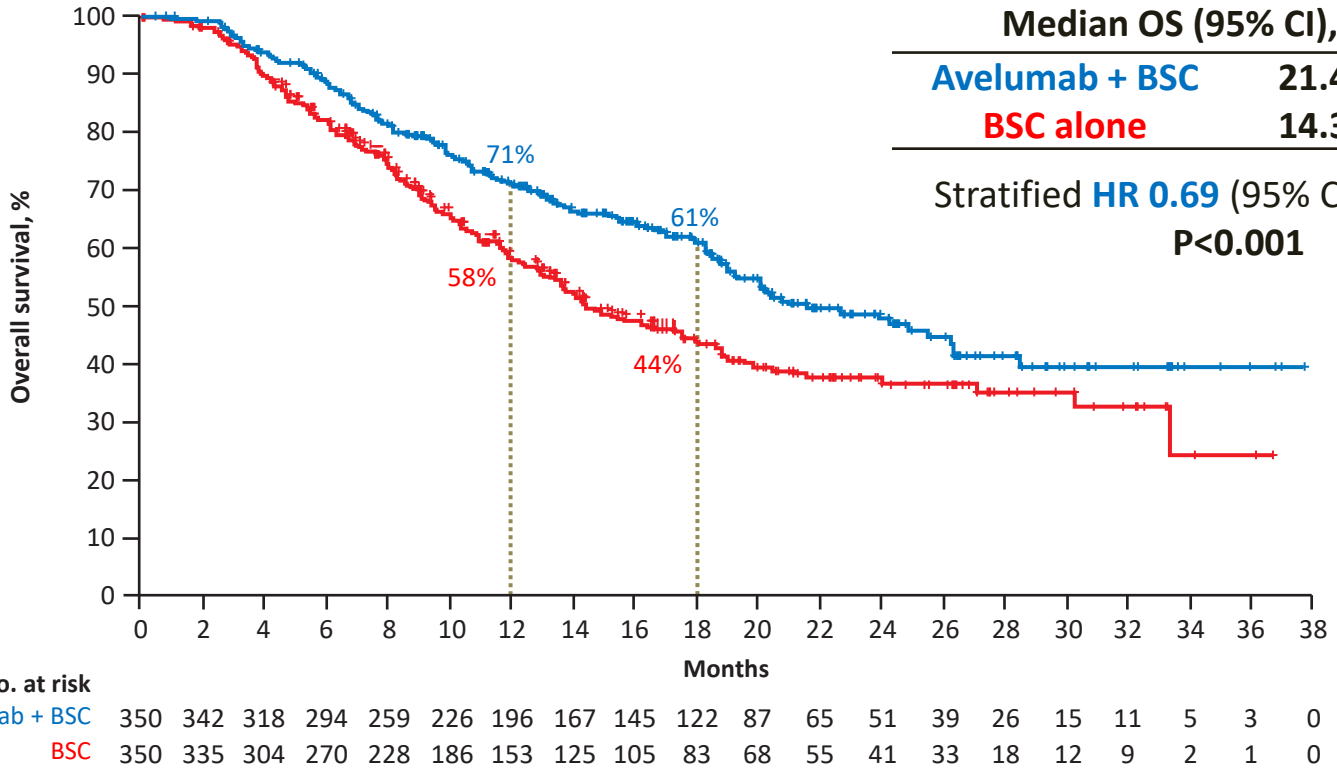
OS in the overall population



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

Stratified **HR 0.69** (95% CI, 0.56, 0.86)

P<0.001

No. at risk																				
Avelumab + BSC	350	342	318	294	259	226	196	167	145	122	87	65	51	39	26	15	11	5	3	0
BSC	350	335	304	270	228	186	153	125	105	83	68	55	41	33	18	12	9	2	1	0

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

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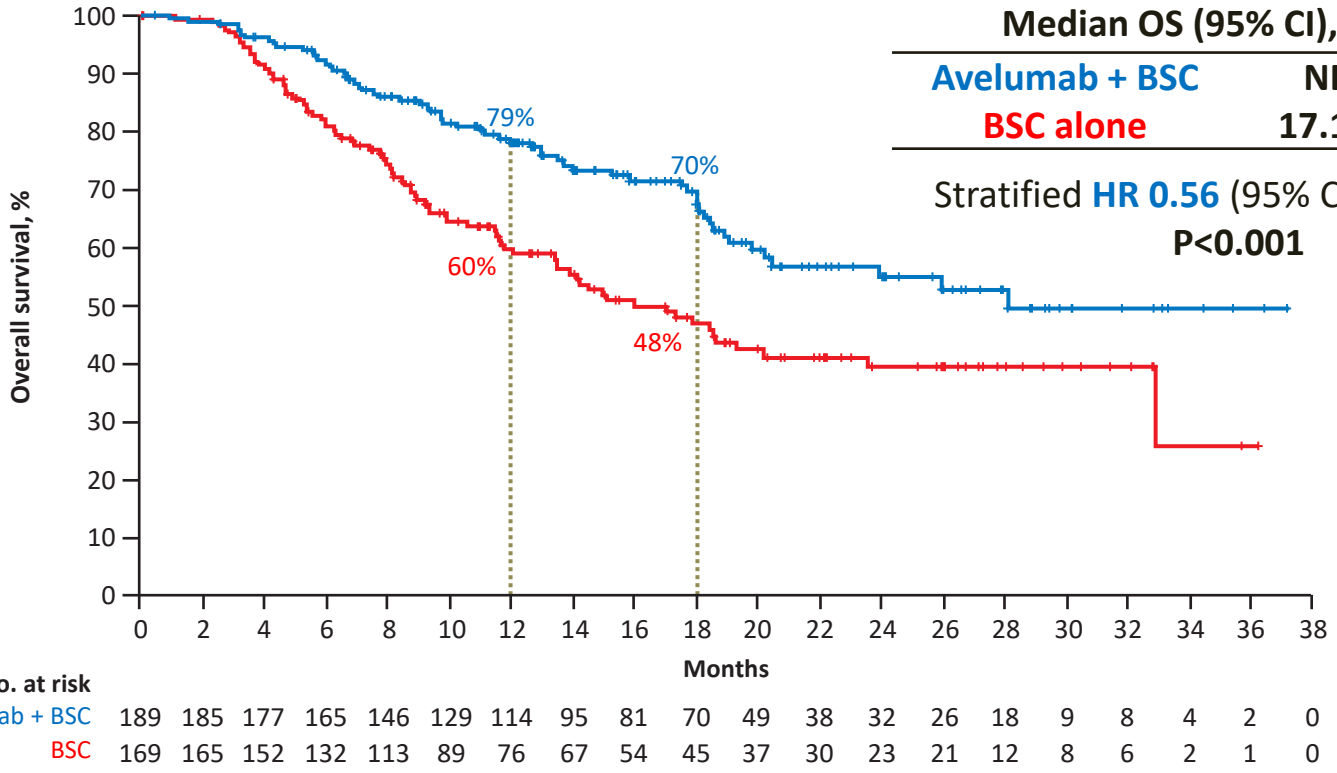
OS in the PD-L1+ population



Median OS (95% CI), months	
Avelumab + BSC	**NE** (20.3, NE)
BSC alone	**17.1** (13.5, 23.7)

Stratified **HR 0.56** (95% CI, 0.40, 0.79)

P<0.001

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

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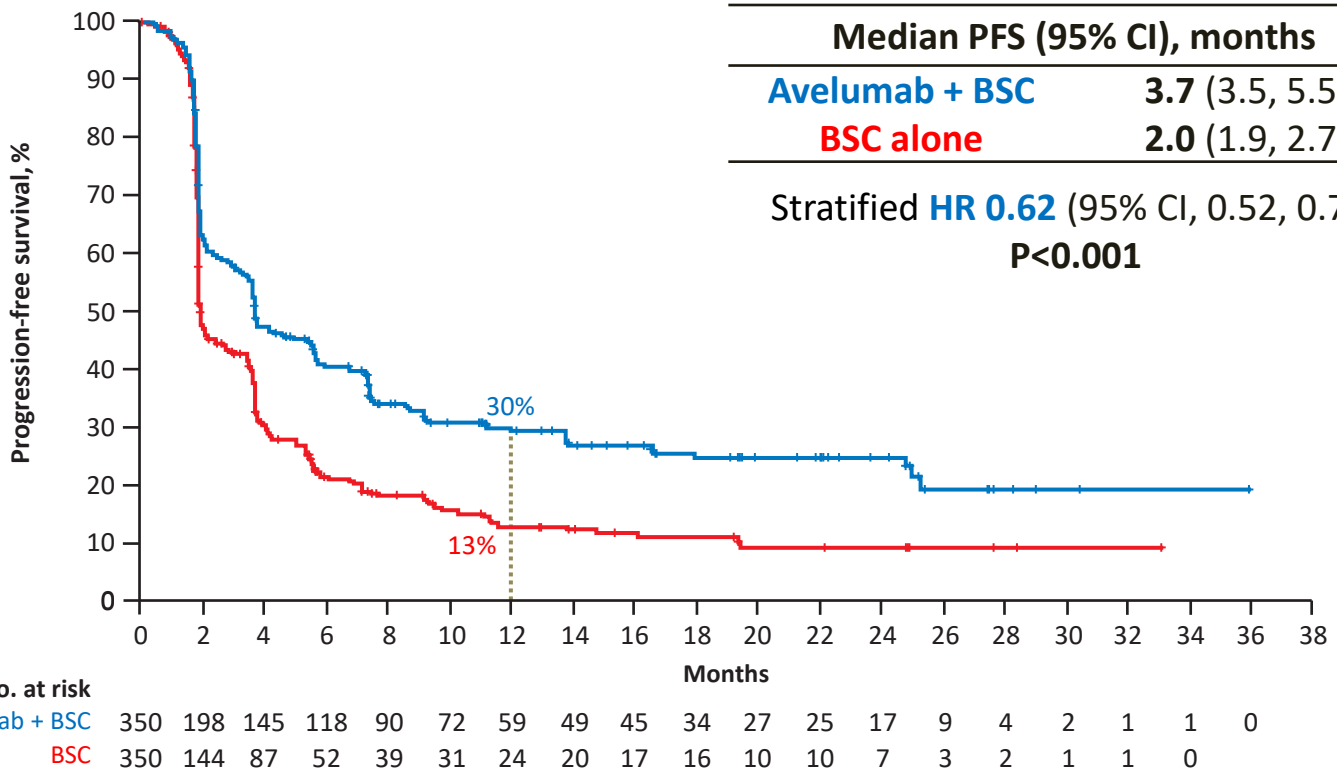
PFS by independent radiology review in the overall population



Median PFS (95% CI), months	
Avelumab + BSC	**3.7** (3.5, 5.5)
BSC alone	**2.0** (1.9, 2.7)

Stratified **HR 0.62** (95% CI, 0.52, 0.75)
P<0.001

No. at risk																			
Avelumab + BSC	350	198	145	118	90	72	59	49	45	34	27	25	17	9	4	2	1	1	0
BSC	350	144	87	52	39	31	24	20	17	16	10	10	7	3	2	1	1	0	

PFS was measured post randomization (from end of chemotherapy)

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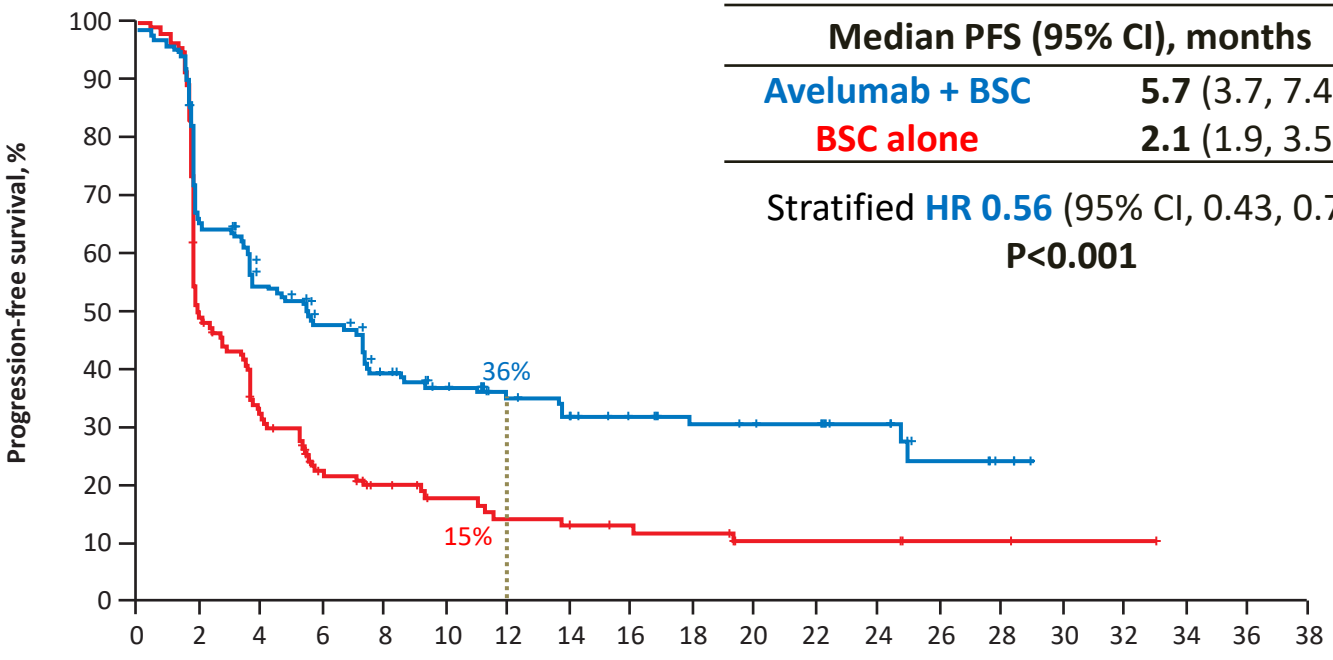
PFS by independent radiology review in the PD-L1+ population

Median PFS (95% CI), months	
Avelumab + BSC	**5.7** (3.7, 7.4)
BSC alone	**2.1** (1.9, 3.5)

Stratified **HR 0.56** (95% CI, 0.43, 0.73)
P<0.001



No. at risk																	
Avelumab + BSC	189	114	89	73	55	45	35	29	26	20	17	17	12	7	2	0	
BSC	169	80	51	28	21	16	13	12	10	9	5	5	5	2	2	1	1	0

PFS was measured post randomization (from end of chemotherapy)

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Subsequent anticancer therapy

	Overall population		Subgroup who discontinued study therapy due to PD	
	Avelumab + BSC (N=350)	BSC alone (N=350)	Avelumab + BSC (N=189)	BSC alone (N=263)
Discontinued and received subsequent drug therapy, %	**42.3**	**61.7**	**70.4**	**75.3**
PD-L1/PD-1 inhibitor	**6.3**	**43.7**	**9.0**	**52.9**
Fibroblast growth factor receptor inhibitor	2.6	2.3	4.8	3.0
Any other drug	40.0	34.0	67.2	41.8
Discontinued with no subsequent drug therapy, %	33.4	30.9	29.6	24.7
Study treatment ongoing, %	24.3	7.4	–	–

All percentages were calculated using the denominator of all patients in the treatment arm within each population; some patients received >1 category of subsequent therapy

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Treatment-emergent AEs (any causality)

	Avelumab + BSC (N=344)		BSC alone (N=345)	
	Any grade	**Grade ≥3**	**Any grade**	**Grade ≥3**
Any TEAE, %	**98.0**	**47.4**	**77.7**	**25.2**
Fatigue	17.7	1.7	7.0	0.6
Pruritus	17.2	0.3	1.7	0
UTI	17.2	4.4	10.4	2.6
Diarrhea	16.6	0.6	4.9	0.3
Arthralgia	16.3	0.6	5.5	0
Asthenia	16.3	0	5.5	1.2
Constipation	16.3	0.6	9.0	0
Back pain	16.0	1.2	9.9	2.3
Nausea	15.7	0.3	6.4	0.6
Pyrexia	14.8	0.3	3.5	0
Decreased appetite	13.7	0.3	6.7	0.6
Cough	12.8	0.3	4.6	0
Vomiting	12.5	1.2	3.5	0.6
Hypothyroidism	11.6	0.3	0.6	0
Rash	11.6	0.3	1.2	0
Anemia	11.3	3.8	6.7	2.9
Hematuria	10.5	1.7	10.7	1.4
IRR	10.2	0.9	0	0

AE, adverse event; **IRR**, infusion-related reaction; **TEAE**, treatment-emergent adverse event; **UTI,** urinary tract infection
Safety was assessed in all patients who received ≥1 dose of avelumab in the avelumab arm, or who completed the cycle 1 day 1 visit in the BSC arm (N=689)

- TEAEs led to discontinuation of avelumab in 11.9%
- Death was attributed by the investigator to study treatment toxicity in 2 patients (0.6%) in the avelumab + BSC arm
  - Due to sepsis (in Cycle 10) and ischemic stroke (100 days after a single dose of avelumab)

Table shows TEAEs of any grade occurring in ≥10% or grade ≥3 TEAEs occurring in ≥5% in either arm

Immune-related AEs

	Avelumab + BSC (N=344)	
	Any grade	**Grade 3**
Any irAE, %	**29.4**	**7.0**
Hypothyroidism	10.2	0.3
Rash	4.9	0.3
Hyperthyroidism	4.7	0
Rash maculopapular	2.3	0.3
Pruritis	2.0	0
Pneumonitis	1.5	0.3
Colitis	0.9	0.6
Increased ALT	0.9	0.9
Increased AST	0.6	0.6
Hyperglycemia	0.9	0.9
Myositis	0.6	0.6

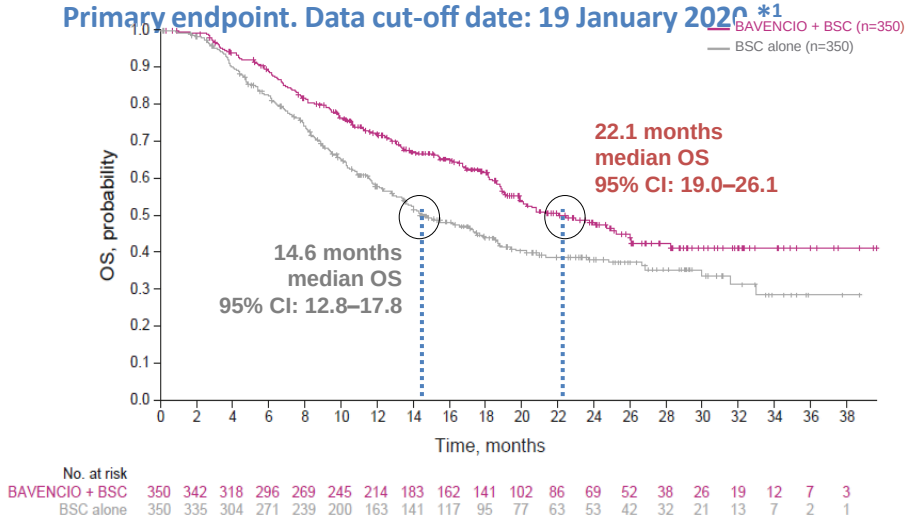
irAEs were identified according to a prespecified case definition
ALT, alanine aminotransferase; **AST**, aspartate aminotransferase; **irAE,** immune-related adverse event

- No grade 4/5 irAEs occurred
- High-dose corticosteroids (≥40 mg total daily prednisone or equivalent) were administered following irAE in 9.0% of avelumab-treated patients

Table shows irAEs of any grade occurring in ≥1% or grade ≥3 irAEs occurring in ≥0.5% in either arm

In the overall population, patients treated with BAVENCIO (avelumab) + BSC continued to achieve a significantly improved median OS compared with those treated with BSC alone[1,2]

Overall population (N=700): Primary endpoint. Data cut-off date: 19 January 2020.*[1]



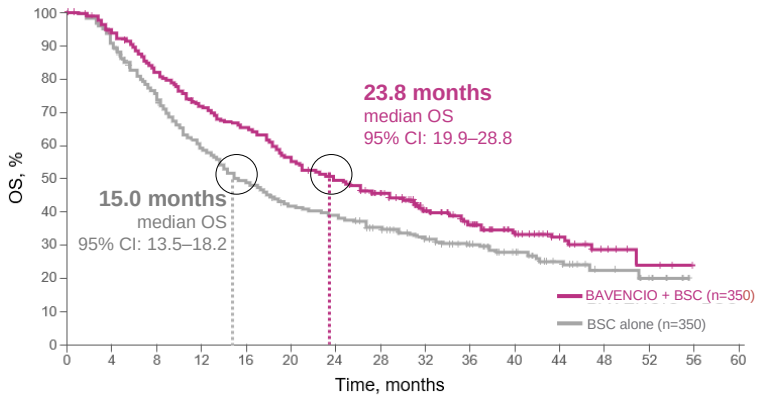
No. at risk

BAVENCIO + BSC	350	342	318	296	269	245	214	183	162	141	102	86	69	52	38	26	19	12	7	3
BSC alone	350	335	304	271	239	200	163	141	117	95	77	63	53	42	32	21	13	7	2	1

Stratified HR for death: 0.70[1]
(95% CI: 0.56–0.86)
p=0.0008

7.5 months
improvement in median OS in patients receiving BAVENCIO® (avelumab) + BSC vs BSC alone[1]

Overall population (N=700): Primary endpoint. Data cut-off date: 4 June 2021.†[2]



No. at risk

BAVENCIO + BSC	350	318	274	237	216	183	164	140	99	74	53	31	13	4	1	0
BSC	350	304	243	190	158	131	121	103	82	62	46	27	10	7	0	

Stratified HR for death: 0.76[2]
(95% CI: 0.631–0.915)
p=0.0036

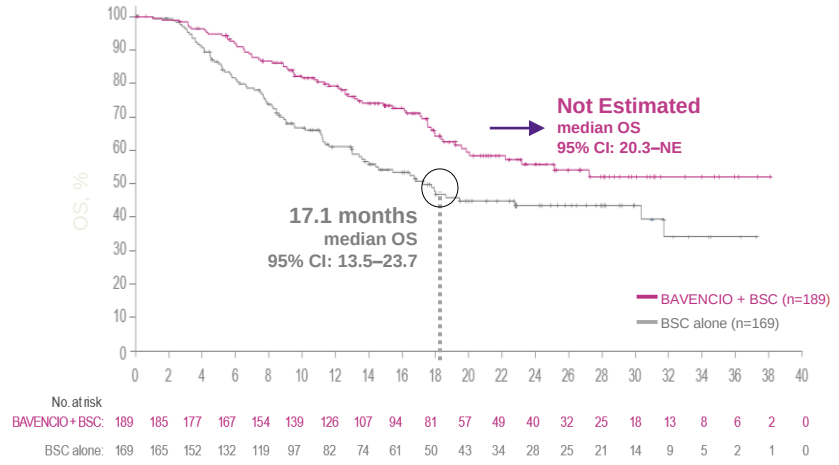
8.8 months[2]
improvement in median OS in patients receiving BAVENCIO (avelumab) + BSC vs BSC alone

*Data cut-off date: 19 January 2020. Median duration of treatment in the BAVENCIO (avelumab) + BSC group was 25.3 weeks (range: 2.0–173.9); in the BSC alone group it was 13.1 weeks (range: 0.1–168.4);[3] †Data cut-off 4 June 2021. Median duration of treatment in the BAVENCIO + BSC group was 25.3 weeks (range: 2.0–216.0).[2] Median duration of treatment in the BSC alone arm was 13.1 weeks (range 0.1–231.7 weeks).[4]
BSC, best supportive care; CI, confidence interval; HR, hazard ratio; OS, overall survival.

1. BAVENCIO (avelumab). SPC (GB: www.medicines.org.uk; NI: www.emcmedicines.com/en-gb/northernireland/ accessed May 2022); 2. Powles T et al. Abstract No. 487. Presented at the 2022 ASCO Genitourinary Cancers Symposium, 17–19 February 2022; 3. Merck. Data on file AVE008; 4. Pfizer. Data on file.

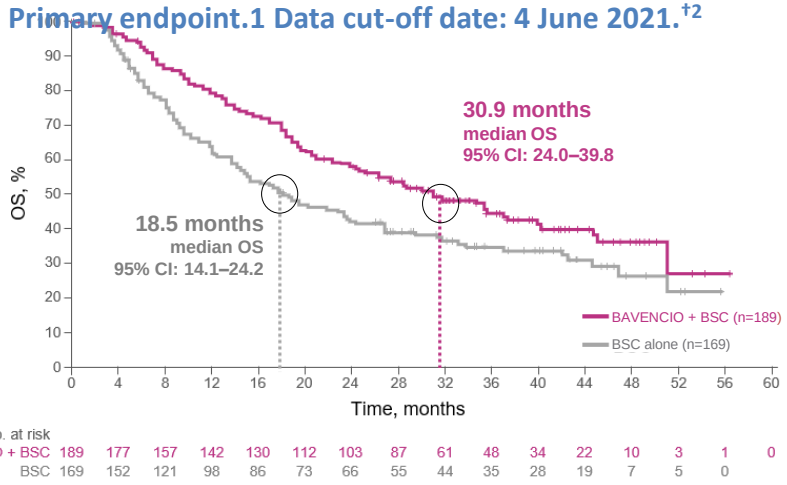
In the PD-L1+ subgroup, patients treated with BAVENCIO (avelumab) + BSC achieved a significantly improved median OS compared with those treated with BSC alone[1,2]

PD-L1-positive tumour population (n=358): Primary endpoint. Data cut-off date: 19 January 2020.*[1]



Stratified HR for death: 0.60[1]
(95% CI: 0.44–0.83)
p<0.001

PD-L1-positive tumour population (n=358): Primary endpoint.1 Data cut-off date: 4 June 2021.[†2]



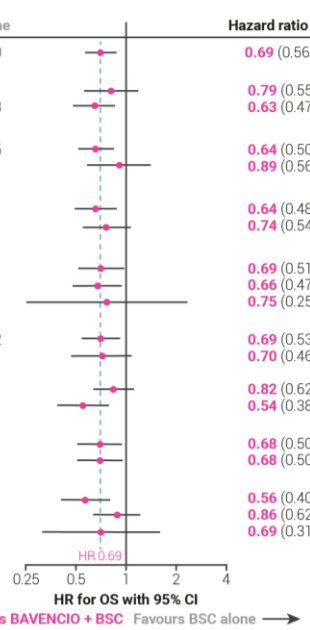
Stratified HR for death: 0.69[2]
(95% CI: 0.521–0. 901)
p=0.0064

*Data cut-off date: 19 January 2020. Median duration of treatment in the BAVENCIO (avelumab) + BSC group was 25.3 weeks (range: 2.0–173.9); in the BSC alone group it was 13.1 weeks (range: 0.1–168.4);[3] †Data cut-off 4 June 2021. Median duration of treatment in the BAVENCIO + BSC group was 25.3 weeks (range: 2.0–216.0).[2] Median duration of treatment in the BSC alone arm was 13.1 weeks (range 0.1–231.7 weeks).[4]
BSC, best supportive care; CI, confidence interval; HR, hazard ratio; NE, not estimable; OS, overall survival; PD-L1, programmed death-ligand 1.
1. BAVENCIO (avelumab). SPC (GB: www.medicines.org.uk; NI: www.emcmedicines.com/en-gb/northernireland/ accessed May 2022); 2. Powles T et al. Abstract No. 487. Presented at the 2022 ASCO Genitourinary Cancers Symposium, 17–19 February 2022; 3. Merck. Data on file AVE008; 4. Pfizer. Data on file.

BAVENCIO (avelumab) + BSC demonstrated favourable OS trends compared with BSC alone across almost all protocol-specified subgroups[1]

OS (protocol-specified subgroup analysis: 2019 cut off)*[1]

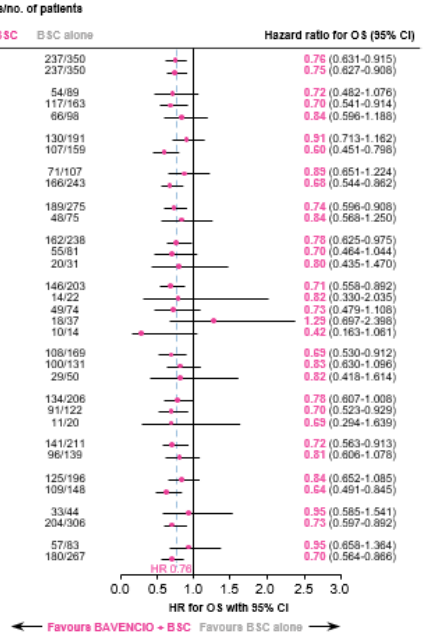
Subgroup	Events/patients, n: BAVENCIO + BSC	BSC alone	Hazard ratio (95% CI)
All patients	145/350	179/350	0.69 (0.56–0.86)
Age			
<65 years	61/129	53/107	0.79 (0.55–1.15)
≥65 years	84/221	126/243	0.63 (0.47–0.83)
Sex			
Male	105/266	145/275	0.64 (0.50–0.83)
Female	40/84	34/75	0.89 (0.56–1.41)
ECOG performance status score			
0	77/213	101/211	0.64 (0.48–0.86)
≥1	68/137	78/139	0.74 (0.54–1.03)
1L chemotherapy regimen			
Gemcitabine + cisplatin	71/183	98/206	0.69 (0.51–0.94)
Gemcitabine + carboplatin	68/147	73/122	0.66 (0.47–0.91)
Gemcitabine + cisplatin/carboplatin†	6/20	7/20	0.75 (0.25–2.25)
Best response to 1L chemotherapy			
CR or PR	104/253	127/252	0.69 (0.53–0.89)
SD	41/97	52/98	0.70 (0.46–1.05)
Site of baseline metastasis			
Visceral	93/191	101/191	0.82 (0.62–1.09)
Non-visceral	52/159	78/159	0.54 (0.38–0.76)
Creatinine clearance			
≥60 mL/min	74/181	97/196	0.68 (0.50–0.92)
<60 mL/min	71/168	81/148	0.68 (0.50–0.94)
PD-L1 status			
Positive	61/189	82/169	0.56 (0.40–0.78)
Negative	76/139	72/131	0.86 (0.62–1.18)
Unknown	8/22	25/50	0.69 (0.31–1.53)



Amended from Powles et al. 2020

OS (protocol-specified subgroup analysis: 2021 cut off)‡[2]

Subgroup	No. of events/no. of patients: BAVENCIO + BSC	BSC alone	Hazard ratio for OS (95% CI)
All patients (stratified)	215/350	237/350	0.76 (0.631-0.915)
All patients (unstratified)	215/350	237/350	0.75 (0.627-0.908)
Best response to IL chemotherapy			
CR	43/90	54/89	0.72 (0.482-1.076)
PR	108/163	117/163	0.70 (0.541-0.914)
SD	64/97	66/98	0.84 (0.596-1.188)
Metastatic disease site when initiating 1L chemotherapy			
Visceral	130/191	130/191	0.91 (0.713-1.162)
Nonvisceral	85/159	107/159	0.60 (0.451-0.798)
Age			
<65 years	85/129	71/107	0.83 (0.651-1.224)
≥65 years	130/221	166/243	0.68 (0.544-0.862)
Sex			
Male	163/266	189/275	0.74 (0.596-0.908)
Female	52/84	48/75	0.84 (0.568-1.250)
Race			
White	151/232	162/238	0.78 (0.625-0.975)
Asian	41/75	55/81	0.70 (0.464-1.044)
Other	23/43	20/31	0.80 (0.435-1.470)
Pooled geographic region			
Europe	136/214	146/203	0.71 (0.558-0.892)
North America	7/12	14/22	0.82 (0.330-2.035)
Asia	40/73	49/74	0.73 (0.479-1.108)
Australasia	23/34	18/37	1.29 (0.697-2.396)
Rest of the World	9/17	10/14	0.42 (0.163-1.081)
PD-L1 status at baseline			
Positive	102/189	108/169	0.69 (0.530-0.912)
Negative	101/139	100/131	0.83 (0.630-1.096)
Unknown	12/22	29/50	0.82 (0.418-1.614)
IL chemotherapy regimen			
Gemcitabine + cisplatin	108/183	134/206	0.78 (0.607-1.008)
Gemcitabine + carboplatin	97/147	91/122	0.70 (0.523-0.929)
Gemcitabine + carboplatin + cisplatin‡	10/20	11/20	0.65 (0.294-1.439)
ECOG performance status			
0	125/213	141/211	0.72 (0.563-0.913)
≥1	90/137	98/139	0.81 (0.606-1.078)
Creatinine clearance at baseline			
≥60 mL/min	113/181	125/196	0.84 (0.652-1.085)
<60 mL/min	101/168	109/148	0.64 (0.491-0.845)
Liver lesions at baseline			
Yes	33/43	33/44	0.95 (0.585-1.541)
No	182/307	204/306	0.73 (0.597-0.892)
Lung lesions at baseline			
Yes	59/83	57/83	0.95 (0.658-1.364)
No	156/267	180/267	0.70 (0.564-0.866)



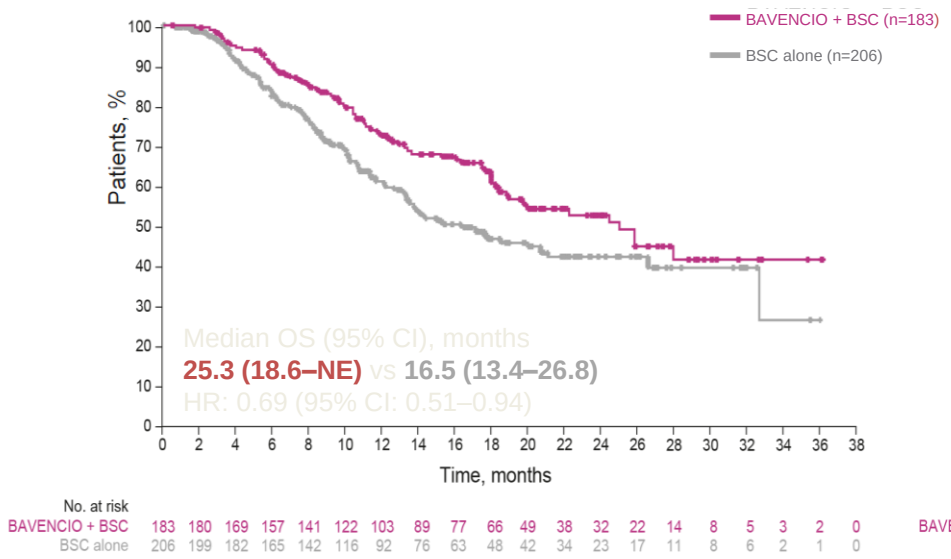
Amended from Powles et al. 2022

*Supplementary appendix to include HR 0.69 for all patients.[1] Data cut-off: 21 October 2019. Median duration of treatment in the BAVENCIO (avelumab) + BSC group was 24.9 weeks (range: 2.0–159.9); in the BSC alone group it was 13.1 weeks (range: 0.1–155.6).[1] Error bars show 95% CI. All analyses shown are unstratified except for the analysis in all patients. †This category includes patients who switched platinum regimens while receiving first-line chemotherapy; ‡Data cut-off 4 June 2021. Median duration of treatment in the BAVENCIO + BSC group was 25.3 weeks (range: 2.0–216.0).[2] Median duration of treatment in the BSC alone arm was 13.1 weeks (range 0.1–231.7 weeks).[3] 1L, first line; BSC, best supportive care; CI, confidence interval; CR, complete response; ECOG, Eastern Cooperative Oncology Group; HR, hazard ratio; OS, overall survival; PD-L1, programmed death-ligand 1; PR, partial response; SD, stable disease.

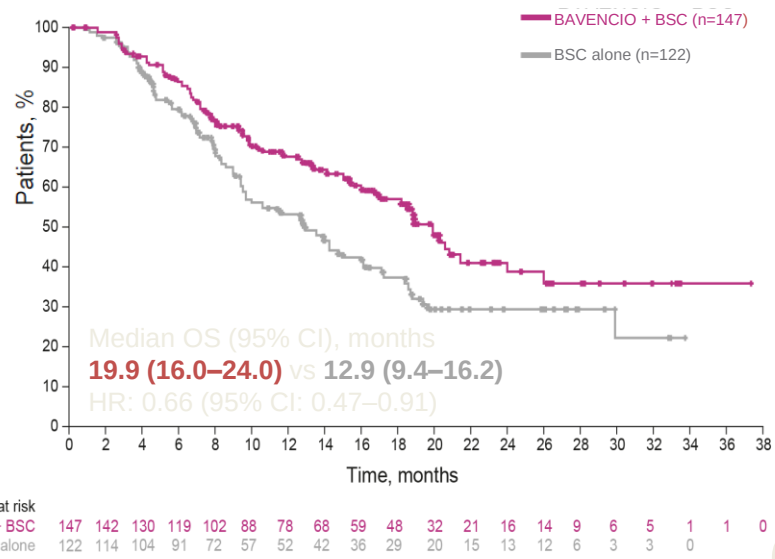
1. Powles T et al. *N Engl J Med* 2020;383:1218–1230(Supplementary appendix); 2. Powles T et al. Abstract No. 487. Presented at the 2022 ASCO Genitourinary Cancers Symposium, 17–19 February 2022; 3. Pfizer. Data on file.

OS benefit with BAVENCIO + BSC first-line maintenance therapy occurred irrespective of first-line CT regimen[1]

OS in patients who received 1L gemcitabine + cisplatin (n=389)



OS in patients who received 1L gemcitabine + carboplatin (n=269)



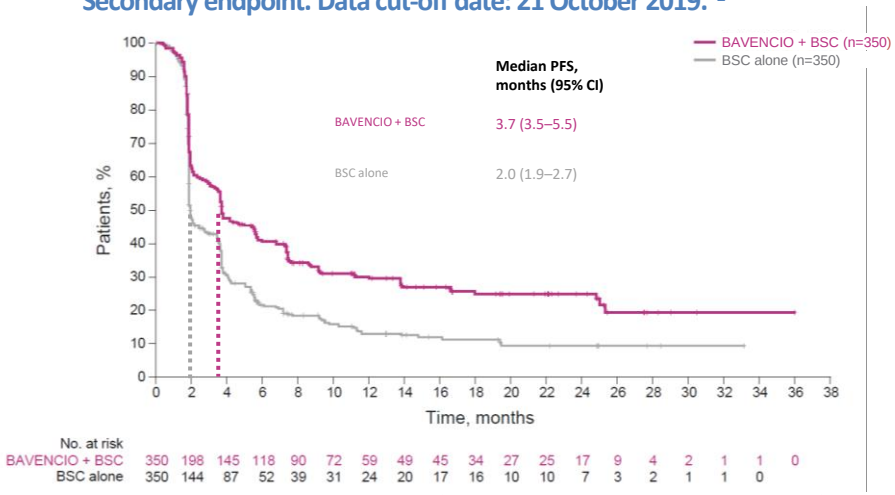
Data cut-off date: 21 October 2019. Median duration of treatment in the BAVENCIO + BSC group was 24.9 weeks (range: 2.0–159.9)[1,2]

1L, first line; BSC, best supportive care; CI, confidence interval; HR, hazard ratio; NE, not estimable; OS, overall survival.

1. Grivas P et al. ESMO Virtual Congress 2020. Abstract #704MO; 2. Powles T et al. *N Engl J Med* 2020;383:1218–1230.

In the overall population, patients treated with BAVENCIO (avelumab) + BSC continued to achieve a longer median PFS compared with those treated with BSC alone*[1,2]

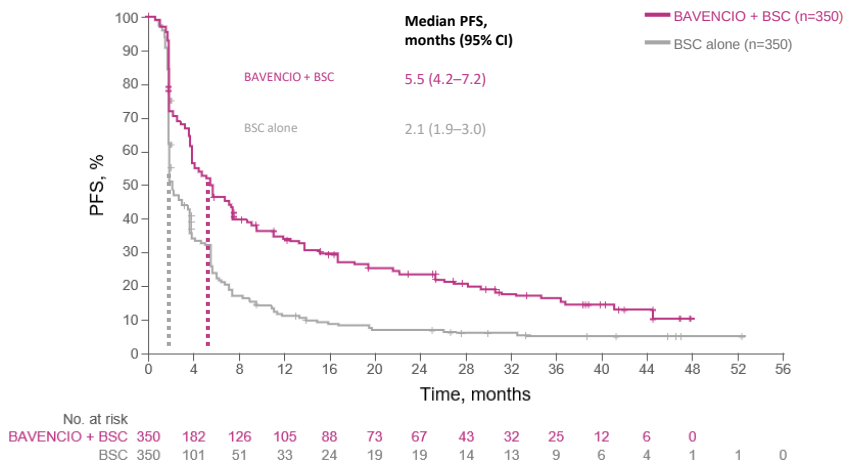
Overall population (N=700): Secondary endpoint. Data cut-off date: 21 October 2019.[†1]



1.7 months[1]
improvement in median PFS in patients receiving BAVENCIO (avelumab) + BSC vs BSC alone*

Stratified HR for disease progression of death: 0.62[1]
(95% CI: 0.52–0.75)*

Overall population (N=700): Secondary endpoint. Data cut-off date: 4 June 2021.[‡2]



3.4 months[2]
improvement in median PFS in patients receiving BAVENCIO (avelumab) + BSC vs BSC alone*

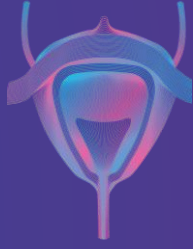
Stratified HR for disease progression of death: 0.54[2]
(95% CI: 0.457–0.645)*

*PFS was a secondary endpoint of the study; as such, median PFS data may not be defined as statistically significant; [†]Data cut-off date: 21 October 2019. Median duration of treatment in the BAVENCIO + BSC group was 24.9 weeks (range: 2.0–159.9). In the BSC alone group it was 13.1 weeks (range: 0.1–155.6);[1] [‡]Data cut-off 4 June 2021. Median duration of treatment in the BAVENCIO + BSC group was 25.3 weeks (range: 2.0–216.0).[2] Median duration of treatment in the BSC alone arm was 13.1 weeks (range 0.1–231.7 weeks).[3]

BSC, best supportive care; CI, confidence interval; HR, hazard ratio; PFS, progression-free survival.

1. Powles T et al. *N Engl J Med* 2020;383:1218–1230; 2. Powles T et al. Abstract No. 487. Presented at the 2022 ASCO Genitourinary Cancers Symposium, 17–19 February 2022; 3. Pfizer. Data on file.

OS was longer with BAVENCIO + BSC vs BSC alone, despite the more frequent use of subsequent treatment in the control group, including immune checkpoint inhibitors*[1]



Subsequent cancer therapy†[2,3]

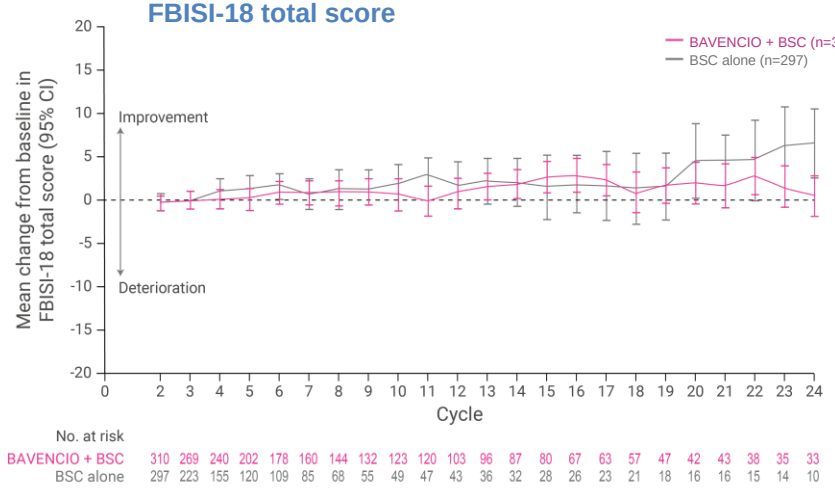
Therapy	Overall population		Subgroup who discontinued study therapy due to PD	
	BAVENCIO + BSC (n=350)	BSC alone (n=350)	BAVENCIO + BSC (n=189)	BSC alone (n=263)
Discontinued and received subsequent drug therapy, %	**42.3**	**61.7**	**70.4**	**75.3**
PD-L1/PD-1 inhibitor	6.3	43.7	9.0	52.9
Fibroblast growth factor receptor inhibitor	2.6	2.3	4.8	3.0
Any other drug	40.0	34.0	67.2	41.8
Discontinued with no subsequent drug therapy, %	**33.4**	**30.9**	**29.6**	**24.7**
Study treatment ongoing, %	**24.3**	**7.4**	**–**	**–**

*Please note that this refers to the overall population; †All percentages were calculated using the denominator of all patients in the treatment arm within each population; some patients received >1 category of subsequent therapy.
Data cut-off date: 21 October 2019. Median duration of treatment in the BAVENCIO + BSC group was 24.9 weeks (range: 2.0–159.9); in the BSC alone group it was 13.1 weeks (range: 0.1–155.6). Median follow-up for each group was more than 19 months.[1,3]
BSC, best supportive care; PD, progressive disease; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; OS, overall survival.
1. Powles T et al. *N Engl J Med* 2020;383:1218–1230; 2. Powles T et al. *N Engl J Med* 2020;383:1218–1230. Supplementary appendix; 3. Powles T et al. ASCO Virtual Annual Meeting 2020. *J Clin Oncol* 2020;38(suppl; abstr LBA1). Presentation.

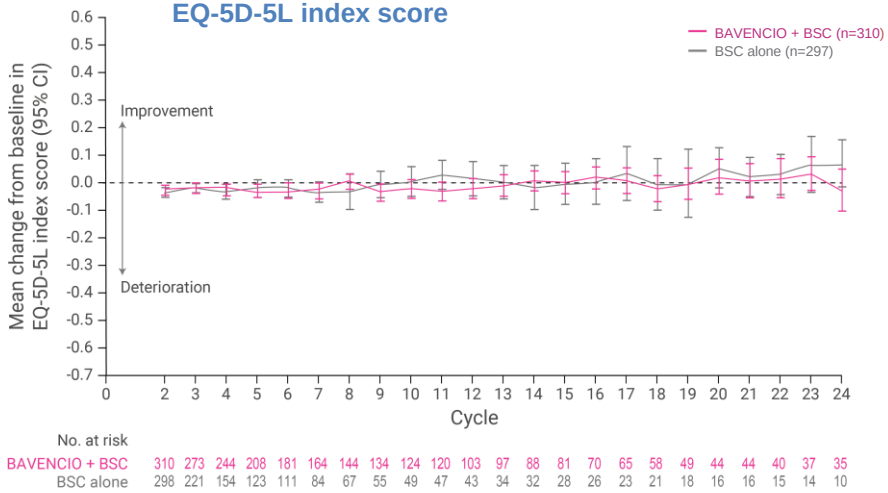
BAVENCIO + BSC first-line maintenance therapy prolongs median OS compared with BSC alone, with no detrimental impact on clinically relevant PROs[1]

Patient-reported outcomes: secondary endpoint

FBISI-18 total score



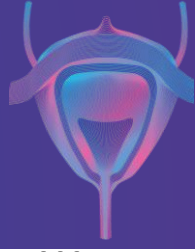
EQ-5D-5L index score



Mean changes from baseline in FBISI-18 and EQ-5D-5L were similar between patients receiving BAVENCIO + BSC and those receiving BSC alone[1]

Data cut-off date: 21 October 2019. Median duration of treatment in the BAVENCIO + BSC group was 24.9 weeks (range: 2.0–159.9); in the BSC alone group it was 13.1 weeks (range: 0.1–155.6).[1,2] BSC, best supportive care; CI, confidence interval; EQ-5D-5L, EuroQoL 5 Dimensions 5 Level; FBISI-18, National Comprehensive Cancer Network – Functional Assessment of Cancer Therapy Bladder Symptom Index-18; OS, overall survival; PRO, patient-reported outcome.

1. Powles T et al. ESMO Virtual Congress 2020. Abstract #2653; 2. Powles T et al. *N Engl J Med* 2020;383:1218–1230.



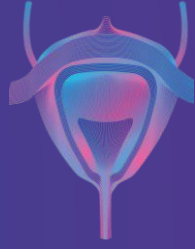
- JAVELIN Bladder 100 is an international, open-label, Phase III trial investigating whether BAVENCIO as **first-line maintenance therapy** improved outcomes vs BSC alone in patients whose disease had not progressed following platinum-based CT for locally advanced or metastatic UC[1,2]
- In the overall population, a significant increase in median OS by 8.8 months (HR=0.762 [95% CI: 0.631–0.915] p=0.0036)* was observed with BAVENCIO + BSC vs BSC alone[3]
- Consistent OS benefits were observed across prespecified subgroups with BAVENCIO + BSC vs BSC alone, including type of first-line CT regimen and best response to first-line CT[4]
- BAVENCIO + BSC demonstrated a generally well-tolerated safety profile, with no detrimental impact on clinically relevant PROs vs BSC alone[1,4,5]

*Updated OS results: 4 June 2021. Median duration of treatment in the BAVENCIO + BSC group was 25.3 weeks (range: 2.0–216.0).[3] Median duration of treatment in the BSC alone arm was 13.1 weeks (range 0.1–231.7 weeks).[6]

BSC, best supportive care; CT, chemotherapy; OS, overall survival; PRO, patient-reported outcome; UC, urothelial carcinoma.

1. Powles T et al. *N Engl J Med* 2020;383:1218–1230; 2.NCT02603432. https://clinicaltrials.gov/ct2/show/NCT02603432 (accessed May 2022); 3. Powles T et al. Abstract No. 487. Presented at the 2022 ASCO Genitourinary Cancers Symposium, 17–19 February 2022; 4. Powles T et al. *N Engl J Med* 2020;383:1218–1230. Supplementary appendix; 5. Powles T et al. ESMO Virtual Congress 2020. Abstract #2653; 6. Pfizer. Data on file.

Real world USA data; GRIVAS et al; ASCO GU 2023



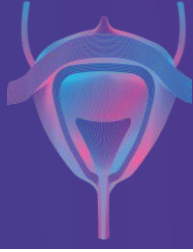
- Ongoing retrospective data:

- 160 patients received Avelumab in 1st line maintenance setting
- 100- post Cisplatin (62.5%)
- 60- post Carboplatin (37.5%)
- 13% had CR/ 68% had PR, 11% had stable disease 8% unknown best response.

Real world data ; Hussain et al

- 17 patients received Avelumab at Sheffield Teaching Hospitals
- Total of 220 cycles (range 4- 61) given till 3rd May 2023.
- Initially under EAMS and then NICE funded.
- Toxicity and efficacy data shows excellent tolerability and efficacy.
-

ESMO guidelines recommend platinum-based CT as first-line treatment for eligible patients – 2021 Update



First line

Patient	Treatment recommendation
Cisplatin eligible	Cisplatin-based CT followed by maintenance BAVENCIO (avelumab) for tumours that have not progressed on CT
Cisplatin ineligible and PD-L1 unknown or negative	Gemcitabine/carboplatin followed by maintenance avelumab for tumours that have not progressed on CT
Cisplatin ineligible and PD-L1 positive	Gemcitabine/carboplatin followed by maintenance avelumab for tumours that have not progressed on CT *OR* Atezolizumab* or pembrolizumab[†‡]

Second line

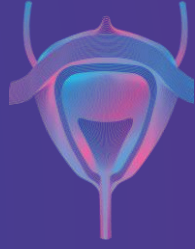
Patient	Standard therapy	When standard therapy not possible
Platinum refractory	ICI	CT ADC[‡]
Platinum refractory, with *FGFR* DNA alterations	ICI Investigational FGFR inhibitor[§]	CT
>1 year from first-line CT	ICI	Cisplatin-based CT rechallenge
ICI refractory, CT naïve	Platinum-based CT	

*PD-L1 expression on immunohistochemistry ≥5%; [†]In patients with tumour expressing PD-L1 with a CPS ≥10; [‡]Not licensed in the UK for use in UC; [§]Not UK licensed in UC as of May 2021.

ADC, antibody-drug conjugate; CPS, combined positive score; CT, chemotherapy; ESMO, European Society for Medical Oncology; FGFR, fibroblast growth factor receptor; ICI, immune checkpoint inhibitor; PD-L1, programmed death-ligand 1; UC, urothelial carcinoma.

Powles T et al. *Ann Oncol* 2022;33:244-258.

NICE guidelines for the treatment of locally advanced or metastatic UC[1]



First line

ECOG PS 0–1 + adequate renal function[1]

✓ Cisplatin + gemcitabine[3,4]

HD-MVAC + G-CSF

Cisplatin unsuitable + ECOG PS 0–2[1]

Carboplatin + gemcitabine*

Cisplatin unsuitable + PD-L1 positive

✓ Atezolizumab†[5,6]

Maintenance

✓ **BAVENCIO (avelumab)[2]**

✓ Licenced within the UK

Second line

ECOG PS 0–1 + adequate renal function[1]

✓ Cisplatin + gemcitabine[3,4]

HD-MVAC + G-CSF

Cisplatin unsuitable or declined:[1]

Carboplatin + paclitaxel

Gemcitabine + paclitaxel*

Prior platinum-based CT:

✓ Atezolizumab†[5,7]

- Pembrolizumab is indicated for the treatment of locally advanced or metastatic UC in adults who are not eligible for cisplatin-containing chemotherapy, whose tumours express PD-L1,and in those who have received prior platinum-containing chemotherapy,[8] but **it is no longer recommended by NICE** in the first-line or second-line treatment settings[9]
- Nivolumab is indicated for the treatment of locally advanced unresectable or metastatic UC in adults after failure of prior platinum-containing therapy;[10] but it is not recommended by NICE[11]
- Vinflunine is indicated for the treatment of adult patients with advanced or metastatic transitional cell carcinoma of the urothelial tract after failure of a prior platinum-containing regimen;[12] but it is not recommended by NICE[13]

*This is an off-label use of carboplatin in combination with gemcitabine and gemcitabine in combination with paclitaxel.

†PD-LPD-L1 expression on immunohistochemistry ≥5%. ECOG PS, Eastern Cooperative Oncology Group performance status; G-CSF, granulocyte-colony stimulating factor; HD-MVAC, high-dose methotrexate, vinblastine, doxorubicin and cisplatin; PD-L1, programmed death-ligand 1.

1. NICE. Bladder cancer: diagnosis and management. Available at: https://www.nice.org.uk/guidance/ng2 (accessed May 2022); 2. NICE. Avelumab for maintenance treatment of locally advanced or metastatic urothelial cancer after platinum-based chemotherapy (TA788). Available at: https://www.nice.org.uk/guidance/ta788 (accessed May 2022); 3. Cisplatin. SPC (www.medicines.org.uk accessed May 2022); 4. GEMZAR (gemcitabine). SPC (www.medicines.org.uk accessed May 2022); 5. TECENTRIQ (atezolizumab). SPC (GB: www.medicines.org.uk; NI: www.emcmedicines.com/en-gb/northernireland/ accessed May 2022); 6. NICE. Atezolizumab for untreated PD-L1-positive advanced urothelial cancer when cisplatin is unsuitable (TA739). October 2021. Available at: https://www.nice.org.uk/guidance/ta739 (accessed May 2022); 7. NICE. Atezolizumab for treating locally advanced or metastatic urothelial carcinoma after platinum-containing chemotherapy (TA525). June 2018 Available at: https://www.nice.org.uk/guidance/ta525 (accessed May 2022); 8. KEYTRUDA (pembrolizumab). SPC (GB: www.medicines.org.uk; NI: www.emcmedicines.com/en-gb/northernireland/ accessed May 2022); 9. Pembrolizumab NICE technology appraisal guidance (TA692). April 2021. Available at: https://www.nice.org.uk/guidance/ta692/ (accessed May 2022); 10. OPDIVIO (nivolumab). SPC (GB: www.medicines.org.uk; NI: www.emcmedicines.com/en-gb/northernireland/ accessed May 2022); 11. NICE. Nivolumab for treating locally advanced unresectable or metastatic urothelial cancer after platinum-containing chemotherapy (TA530). July 2018. Available at: https://www.nice.org.uk/guidance/ta530 (accessed May 2022); 12. JAVLOR (vinflunine) SPC (www.medicines.org.uk accessed May 2022); 13. NICE. Vinflunine for the treatment of advanced or metastatic transitional cell carcinoma of the urothelial tract (TA272). January 2013. Available at: https://www.nice.org.uk/guidance/ta272 (accessed May 2022).

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Changing landscape in bladder cancer Sequencing treatments ; A small window of opportunity when treating these patients

- Cisplatin eligible group
- Gemcitabine plus cisplatin.
- Adjuvant Nivolumab
- Maintenance Avelumab.
- Those unsuitable for maintenance IO or decline treatment in maintenance setting Consider 2nd line IO at progression.
- Enfortumab Vedotin
- EV Plus I-O in trials.
- Taxanes /Vinflunine
- ?Gemcitabine plus Cisplatin plus I-O in 1st Line (await further mature data)
- With multiple treatment options it is important to do regular scans to assess disease progression rather than finding it on symptomatic progression

- In cisplatin ineligible group;
- If PDL1 positive consider 1st line I-O.
- Gemcitabine plus split dose cisplatin
- Gemcitabine carboplatin
- Adjuvant Nivolumab
- Maintenance Avelumab
- Enfortumab vedotin.
- EV plus I-O in trials
- Taxanes /Vinflunine
- In symptomatic patients with visceral metastases Gemcitabine plus Carboplatin or Gemcitabine plus split dose cisplatin may be an option in 1st line setting or an early switch in pdl+ve patients in case of clinical or radiological progression from I-O to gemcitabine plus carboplatin or Split dose cisplatin should be considered.

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Window of opportunity studies

- This provides opportunity to test hypothesis and generate data that may help in moving treatments forward.
- Primary end point must be well defined.
- Multidisciplinary team work is key
- Needs close safety monitoring and careful patient selection.

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INVEST

Phase I study of Intravesical immunotherapy for bladder cancer patients undergoing radical cystectomy

Chief investigator: Professor Syed A Hussain CO-CI: Professor James Catto
University of Sheffield, United Kingdom.

Main inclusion criteria

- Patients for whom radical cystectomy is planned treatment for bladder urothelial cell carcinoma (UCC).
- Both MIBC and high-grade NMIBC tumours
- Performance status 0-2

Sample size

Between 6-42 DLT evaluable patients in the dose confirmation stages and a further 20 (10 per treatment route) in the dose expansion stages. Across the whole trial: up to 62 evaluable patients.

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Primary endpoints

Dose confirmation stages:

- To determine the toxicity and recommended dose (RD) for further investigation of atezolizumab by passively instilled intravesical administration.
- To determine the toxicity and RD for further investigation of atezolizumab when injected directly into the tumour/bladder wall via the intravesical route.

Dose expansion stages:

- To evaluate the safety and toxicity of passively instilled intravesical atezolizumab at the RD.
- To evaluate the safety and toxicity of directly injected atezolizumab into the tumour/bladder wall at the RD.

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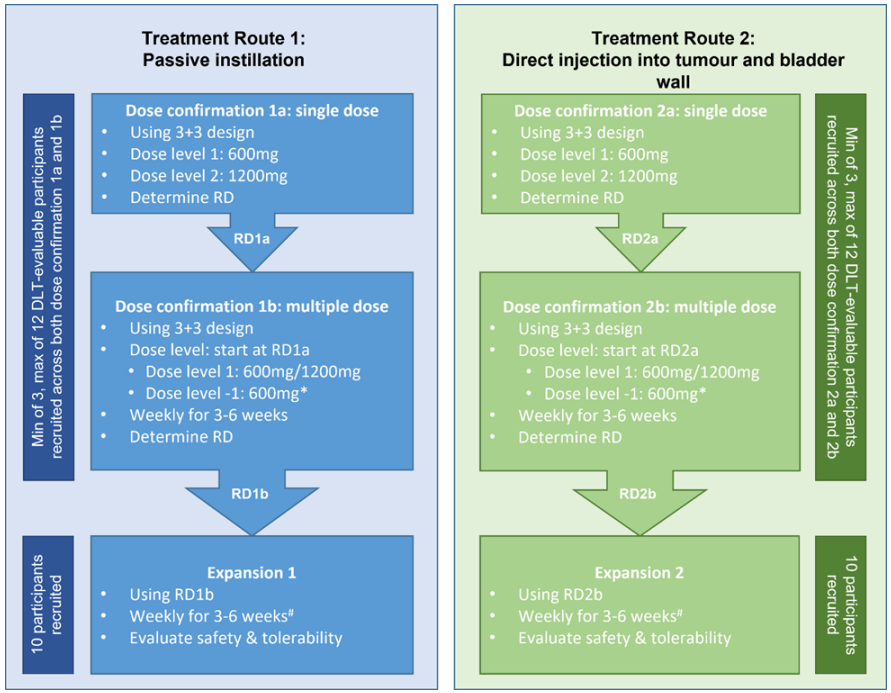
INVEST study



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Invest Translational Science

- Measure bladder wall penetration of atezolizumab by imaging mass spectrometry .
- Correlate gene expression signatures and mutational profiles with response to intra-vesical atezolizumab.
- Quantify changes in the tumour immune microenvironment following intra-vesical atezolizumab.
- Determine the effect of intra-vesical atezolizumab on circulating tumour DNA dynamics

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Joint uro-oncology clinic

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