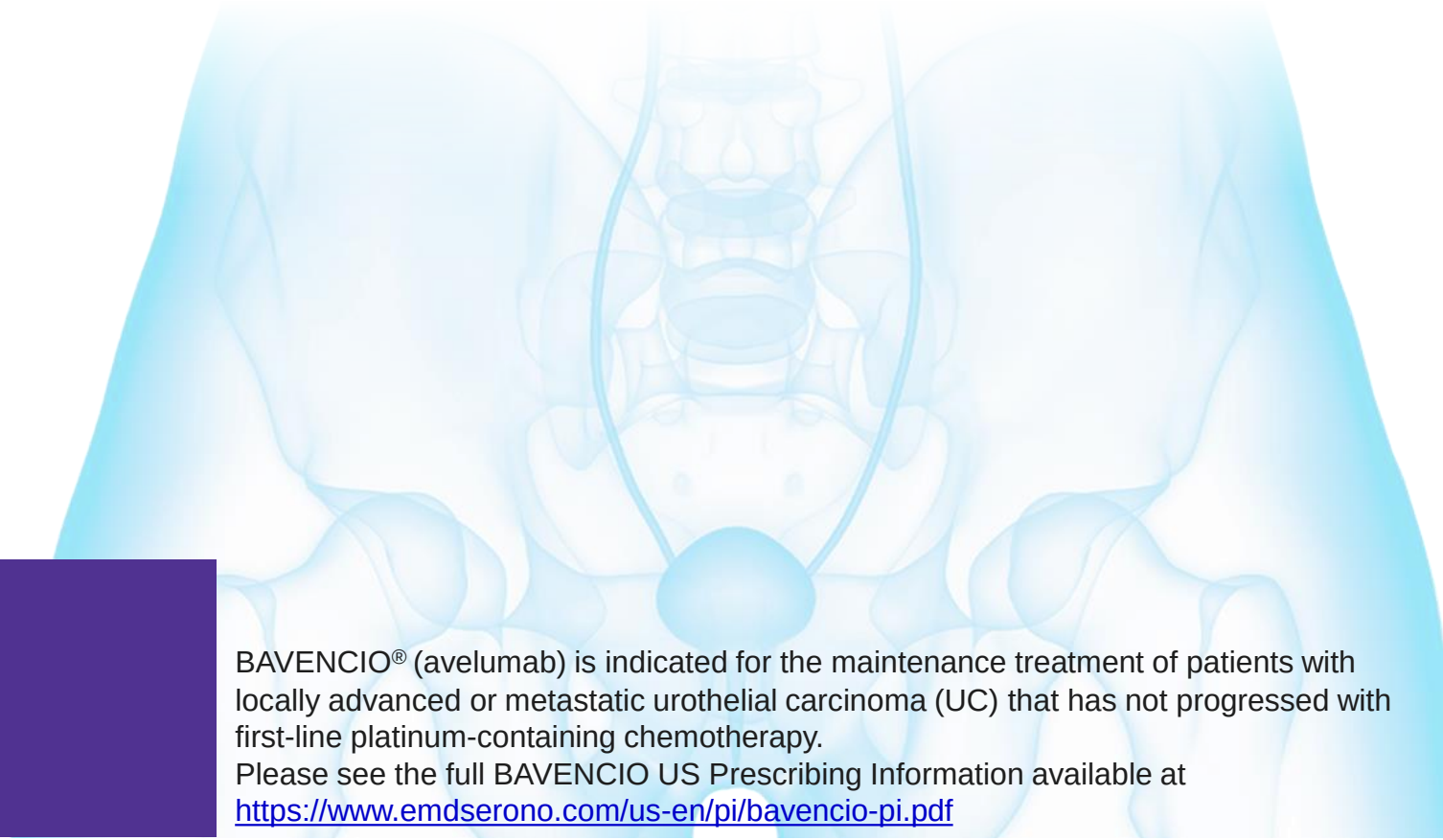
JAVELIN Bladder 100

Overview Deck



BAVENCIO® (avelumab) is indicated for the maintenance treatment of patients with locally advanced or metastatic urothelial carcinoma (UC) that has not progressed with first-line platinum-containing chemotherapy.
Please see the full BAVENCIO US Prescribing Information available at https://www.emdserono.com/us-en/pi/bavencio-pi.pdf

For additional resources, please visit our US Medical Resources Website Oncology page at https://medical.emdserono.com/en_US/medinfo/therapeutic-areas/oncology.html

Important Notices

- Avelumab has been approved by the FDA and is under investigation for the treatment of various diseases. Efficacy and safety of avelumab are still under investigation for various indications. Regulatory approval is dependent on the completion of the study programs and review by the FDA. Clinical trial information is available at www.clinicaltrials.gov.
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- This presentation is for discussion purposes only.

JAVELIN Bladder 100 Overview

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- Indications and ISI
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- JB100 Results
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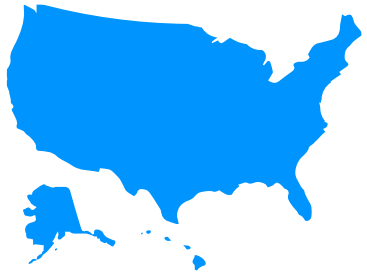
Bladder Cancer: Key US and Global Statistics



6th
Most common cancer in the US[1]

Estimated new cases in 2025[1]	Estimated deaths in 2025[1]	Median age at diagnosis[1,*]
84,870	17,420	73 y

9th
Most common cancer globally[2]

Estimated new cases in 2022[2]	Estimated deaths in 2022[2]
613,791	220,349

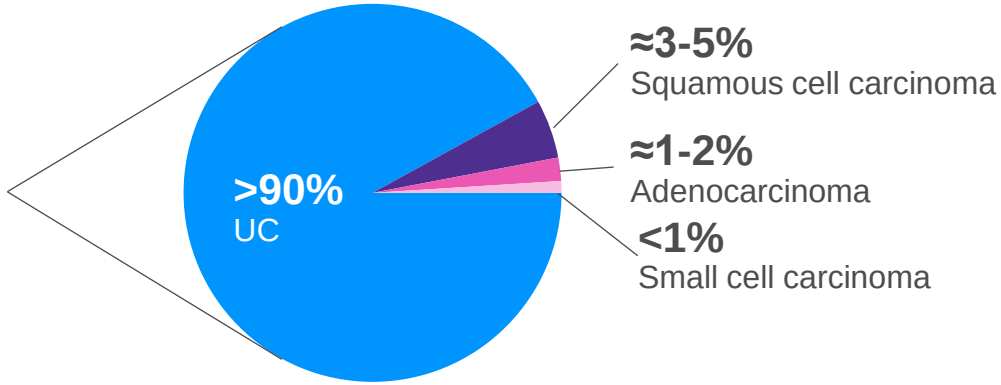
* Based on SEER 22 2016-2020, All Races, Both Sexes.

Key risk factors[3]:

- Smoking
- Age
- Sex
- Ethnicity
- Genetics
- Chemicals
- Chronic infections

Bladder cancer histologies[4-7]

>90%
of bladder cancers are UC[4-7]

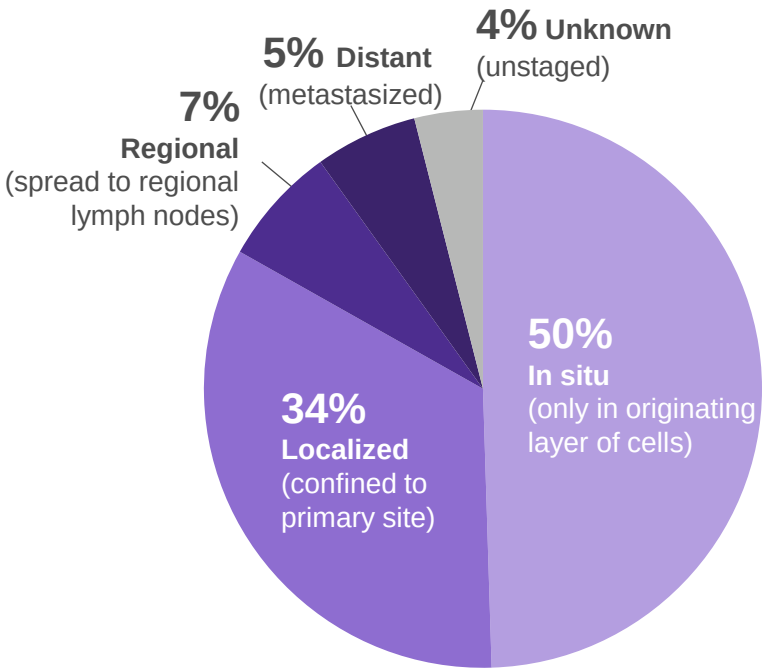


NCCN, National Comprehensive Cancer Network; UC, urothelial carcinoma.

1. National Cancer Institute, Surveillance, Epidemiology, and End Results Program. Cancer Stat Facts: Bladder Cancer. Accessed April 17, 2025. https://seer.cancer.gov/statfacts/html/urinb.html; 2. Bray F, et al. CA Cancer J Clin. 2024;74(3):229-263; 3. American Cancer Society. Bladder Cancer Risk Factors. Accessed April 1, 2025. https://www.cancer.org/cancer/bladder-cancer/causes-risks-prevention/risk-factors.html; 4. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Bladder Cancer Version 1.2025. © National Comprehensive Cancer Network, Inc. 2025. All rights reserved. March 25, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content or its use or application and disclaims any responsibility for its use or application in any way; 5. American Cancer Society. About Bladder Cancer. Accessed April 1, 2025. https://www.cancer.org/cancer/bladder-cancer/about/what-is-bladder-cancer.html; 6. Cancer Research UK. Bladder Cancer. Accessed April 1, 2025. https://www.cancerresearchuk.org/about-cancer/bladder-cancer/types-stages-grades/types; 7. Yousef PG and Gabril MY. Pathol Res Pract. 2018;214:1-6.

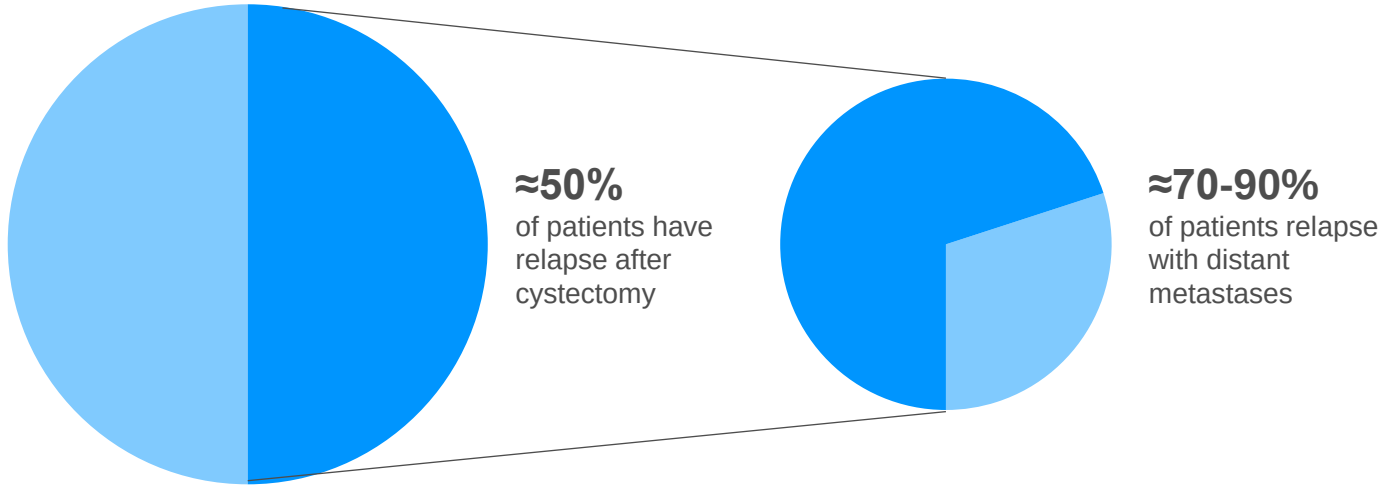
Bladder Cancer: Metastatic Disease

Percentage of bladder cancer cases by stage at diagnosis[1,*]



Approximately **5% of patients** have metastatic bladder cancer at diagnosis[1,*]

Relapse after cystectomy in bladder cancer[2]



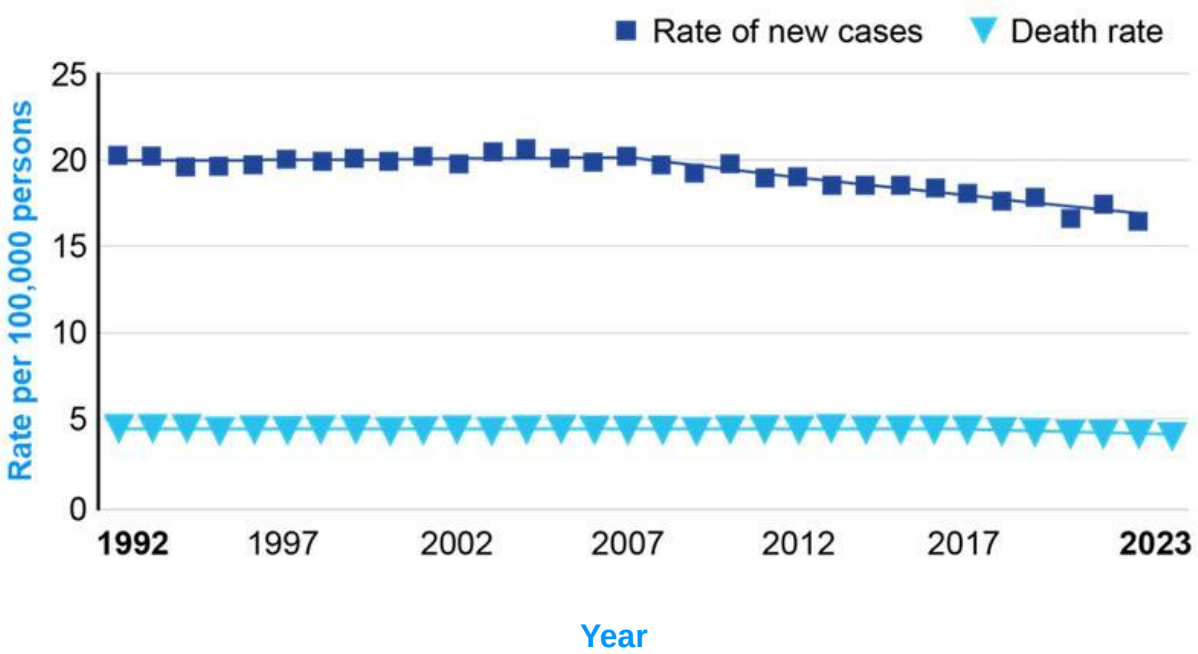
Relapse occurs after cystectomy in approximately half of patients, with distant metastasis accounting for **70-90% of relapses[2]**

* Based on SEER 21 (Excluding IL) 2015-2021, All Races, Both Sexes by SEER Combined Summary Stage.

1. National Cancer Institute, Surveillance, Epidemiology, and End Results Program. Cancer Stat Facts: Bladder Cancer. Accessed April 17, 2025. https://seer.cancer.gov/statfacts/html/urinb.html ; 2. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Bladder Cancer Version 1.2025. © National Comprehensive Cancer Network, Inc. 2025. All rights reserved. March 25, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content or its use or application and disclaims any responsibility for its use or application in any way.

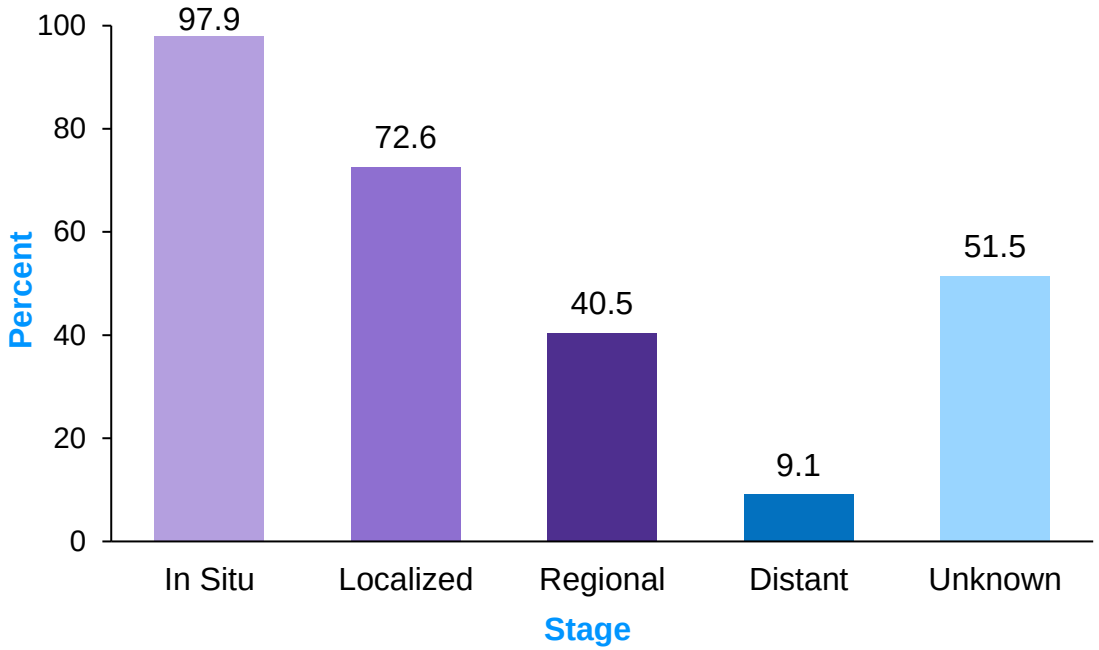
Bladder Cancer: US Survival

New cases of bladder cancer and deaths per 100,000 people in the US[1,*]



In the last 20 years, the death rate from bladder cancer has remained relatively unchanged[1]

5-year relative survival in the US by bladder cancer stage at diagnosis[1,†]



Patients diagnosed with metastatic disease have a 5-year relative survival rate of 9.1%[1,†]

* New cases come from SEER 12. Deaths come from US Mortality. All Races, Both Sexes. Rates are age-adjusted. Modeled trend lines were calculated from the underlying rates using the Joinpoint Trend Analysis Software

†Based on SEER 21 (Excluding IL) 2015-2021, All Races, Both Sexes by SEER Combined Summary Stage.

1. National Cancer Institute, Surveillance, Epidemiology, and End Results Program. Cancer Stat Facts: Bladder Cancer. Accessed April 17, 2025. https://seer.cancer.gov/statfacts/html/urinb.html.

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Bladder Cancer:

Preferred/Recommended Regimens for 1L Systemic Therapy for Locally Advanced or Metastatic UC[1]

Cisplatin-eligible

Preferred regimens

- Enfortumab vedotin-ejfv and pembrolizumab (NCCN category 1)

Other recommended regimens

- Gemcitabine and cisplatin (NCCN category 1) followed by avelumab maintenance therapy (NCCN category 1)*
- Gemcitabine, cisplatin, and nivolumab (NCCN category 1) followed by nivolumab maintenance therapy (NCCN category 1)
- DDMVAC with growth factor support (NCCN category 1) followed by avelumab maintenance therapy (NCCN category 1)*†

Cisplatin-ineligible

Preferred regimens

- Enfortumab vedotin-ejfv and pembrolizumab (NCCN category 1)

Useful in certain circumstances

- Gemcitabine and carboplatin followed by avelumab maintenance therapy (NCCN category 1)*
- Pembrolizumab (for the treatment of patients with la/mUC, who are not eligible for any platinum-containing chemotherapy)
- Atezolizumab (only for patients whose tumors express PD-L1‡ or who are not eligible for any platinum containing chemotherapy regardless of PD-L1 expression) (NCCN category 2B)

*Maintenance therapy with avelumab only if there is no progression on 1L platinum-containing chemotherapy. †The avelumab registrational study for this indication did not specifically investigate avelumab maintenance therapy following DDMVAC with growth factor support.[2] ‡Atezolizumab: SP142 assay, PD-L1–stained tumor-infiltrating immune cells covering ≥5% of the tumor area.

1L, first line; DDMVAC, dose-dense methotrexate, vinblastine, doxorubicin, cisplatin; NCCN, National Comprehensive Cancer Network; PD-L1, programmed death ligand-1; UC, urothelial cancer.

1. Adapted with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Bladder Cancer Version 1.2025. ©2025 National Comprehensive Cancer Network, Inc. All rights reserved. March 25 16, 2025. The NCCN Guidelines® and illustrations herein may not be reproduced in any form for any purpose without the express written permission of NCCN. To view the most recent and complete version of the NCCN guidelines, go online to NCCN.org. The NCCN Guidelines are a work in progress that may be refined as often as new significant data becomes available. NCCN makes no warranties of any kind whatsoever regarding their content or its use or application and disclaims any responsibility for its use or application in any way; 2. Bavencio®. First-Line Maintenance Therapy. Accessed April 1, 2025. https://www.bavencio.com/en_US/hcp/uc-home/maintenance.html.

Metastatic UC: Criteria for Platinum Eligibility

GALSKY CRITERIA FOR CISPLATIN INELIGIBILITY[1]

Patients who meet ≥1 of the following criteria are deemed unfit for cisplatin-based chemotherapy

- ECOG PS ≥2
- CrCl <60 mL/min
- Grade ≥2 hearing loss
- Grade ≥2 neuropathy
- NYHA Heart Failure Class ≥III

CRITERIA FOR PLATINUM INELIGIBILITY BASED ON A SURVEY OF 60 US GU MEDICAL ONCOLOGISTS[2]

- ECOG PS ≥3
- CrCl <30 mL/min
- Peripheral neuropathy grade ≥2
- NYHA Heart Failure Class ≥III
- Combined ECOG PS 2 and CrCl <30 mL/min

Although there are guidelines for cisplatin ineligibility, criteria are less clear for platinum ineligibility

2021 Updated European Association of Urology (EAU) Guidelines on metastatic UC[3]

PLATINUM ELIGIBLE

CISPLATIN ELIGIBLE

- ECOG PS 0-1
- GFR >50-60 mL/min
- Audiometric hearing loss grade <2
- Peripheral neuropathy grade <2
- Cardiac insufficiency NYHA Class <III

CARBOPLATIN ELIGIBLE

- ECOG PS 2 or GFR 30-60 mL/min
- Or not fulfilling other cisplatin-eligibility criteria

PLATINUM INELIGIBLE

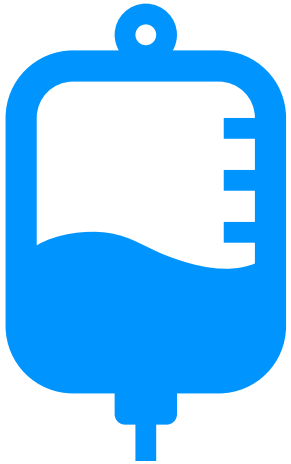
Any of the following:

- GFR <30 mL/min
- ECOG PS >2
- ECOG PS 2 and GFR <60 mL/min
- Comorbidities grade >2

CrCl, creatinine clearance; ECOG, European Cooperative Oncology Group; GFR, glomerular filtration rate; GU, genitourinary; NYHA, New York Heart Association; PS, performance status; UC, urothelial carcinoma.

1. Galsky MD, et al. J Clin Oncol 2011;29:2432-8; 2. Gupta S, et al. J Clin Oncol. 2022;40(16_suppl):4577; 3. Cathomas R, et al. Eur Urol. 2022 Jan;81(1):95-103.

Metastatic UC: Unmet Needs With 1L Platinum-Containing Chemotherapy



Most patients with locally advanced or metastatic UC who receive 1L platinum-containing chemotherapy have a response or disease control **(~75%)**[1-3,*]

However, survival outcomes are limited at this late stage[1-5]

Median PFS:

~4 to 9.5 months

Median OS:

~8 to 16 months

* Based on ITT analysis in all patients with measurable disease, using standard World Health Organization criteria (von der Maase et al) or RECIST criteria (De Santis et al).[1,2]

1L, first line; ITT, intent to treat; OS, overall survival; PFS, progression-free survival; RECIST, response evaluation criteria in solid tumors; UC, urothelial carcinoma.

1. von der Maase H, et al. J Clin Oncol. 2000;18:3068–3077; 2. De Santis M, et al. J Clin Oncol. 2012;30:191–199; 3. Bellmunt J, et al. J Clin Oncol. 2012;30:1107-1113; 4. von der Maase H, et al. J Clin Oncol. 2005;23:4602–4608; 5. Sternberg CN, et al. Eur J Cancer. 2006;42:50–54.

Metastatic UC: Outcomes With 1L Platinum-Containing Chemotherapy

Randomized trials of 1L platinum-containing chemotherapy for locally advanced or metastatic UC[1-5]

	PHASE 3 (N = 405)[1,3]		PHASE 2/3 EORTC (N = 263)[4]		PHASE 3 (N = 238)[2]		PHASE 3 (N = 626)[5]	
ARM	**CISPLATIN + GEMCITABINE**	**MVAC**	**DDMVAC**	**MVAC**	**CARBOPLATIN + GEMCITABINE**	**M-CAVI**	**CISPLATIN + GEMCITABINE**	**CISPLATIN/ GEMCITABINE/ PACLITAXEL**
Patients, n	182*	181*	134	129	119	119	314	312
Median chemotherapy cycles	6	4	6	4	4	5	6	6
ORR (ITT analysis)	**44.5%**	**38.1%**	**61.9%†**	**50.4%†**	**41.2%**	**30.3%**	**43.6%**	**55.5%**
Disease control rate (ITT analysis)	**78.0%†**	**70.7%†**	**-**	**-**	**73.9%‡**	**64.7%‡**	**74.5%**	**77.6%**
Median PFS, months	**7.7**	**8.3**	**9.5**	**8.1**	**5.8**	**4.2**	**7.6**	**8.3**
Median OS, months	**14.0**	**15.2**	**15.1**	**14.9**	**9.3**	**8.1**	**12.7**	**15.8**

Most patients with locally advanced or metastatic UC who receive 1L platinum-containing chemotherapy have a response or disease control (~75%)[1,2,5]; however, survival outcomes are limited at this late stage with median PFS of ~4 to 9.5 months and median OS of ~8 to 16 months[1-5]

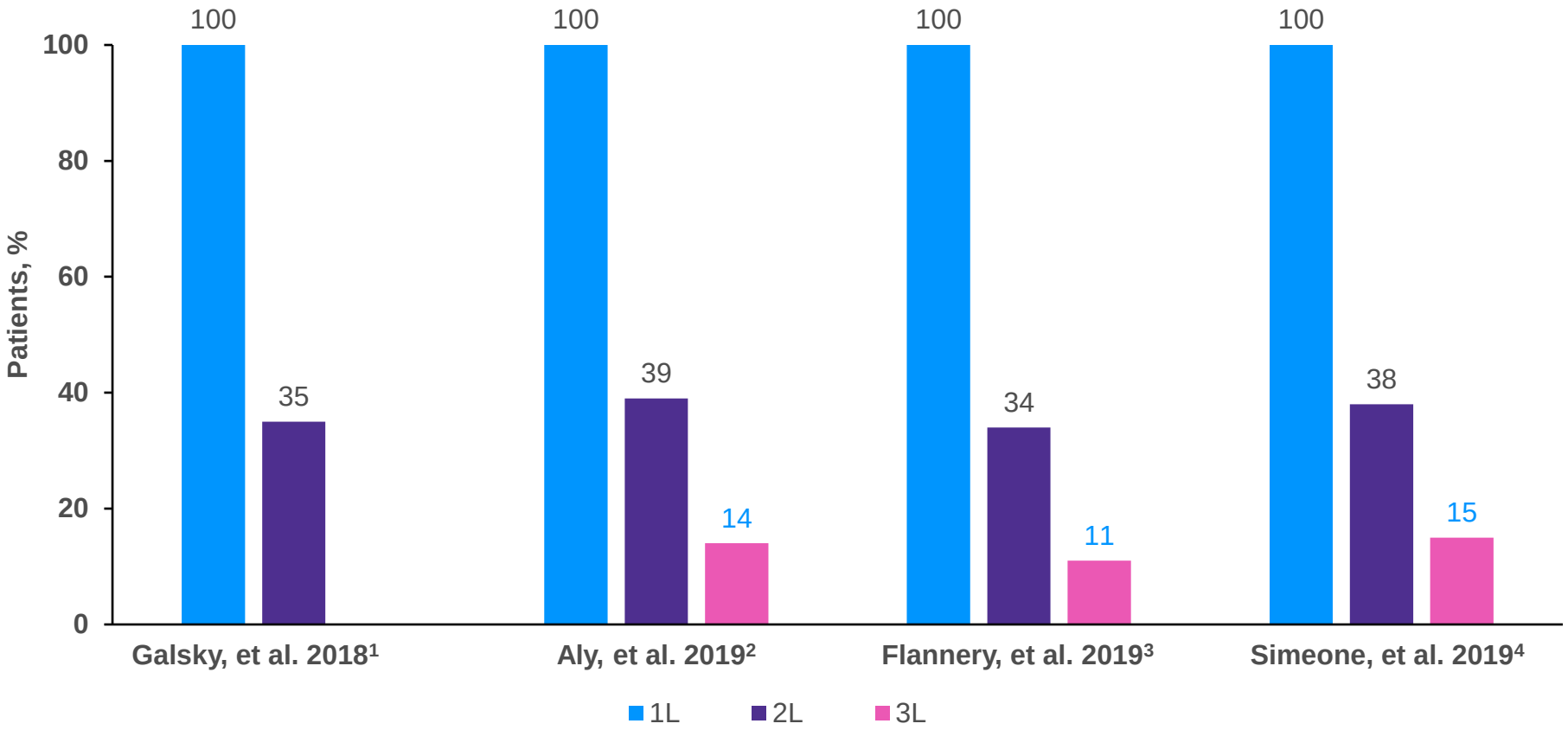
* Patients with measurable disease. † Derived rate based on ITT analysis in all patients with measurable disease, using World Health Organization criteria.
‡ Derived based on ITT analysis in all patients with measurable disease, using RECIST criteria.

1L, first line; ITT, intent to treat; DDMVAC, dose-dense methotrexate, vinblastine, doxorubicin, cisplatin; EORTC, European organization for research and treatment of cancer; M-CAVI, carboplatin, methotrexate, vinblastine; MVAC, methotrexate vinblastine doxorubicin cisplatin; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; RECIST, response evaluation criteria in solid tumors; UC, urothelial carcinoma.

1. von der Maase H, et al. J Clin Oncol. 2000;18:3068–3077; 2. De Santis M, et al. J Clin Oncol. 2012;30:191–199; 3. von der Maase H, et al. J Clin Oncol. 2005;23:4602–4608; 4. Sternberg CN, et al. Eur J Cancer. 2006;42:50–54; 5. Bellmunt J, et al. J Clin Oncol. 2012;30:1107-1113.

Bladder Cancer: Unmet Need After 1L Treatment

Patient attrition between 1L and later lines of therapy in real-world studies of patients with metastatic UC in the US



Data from real-world studies show that **34-39% of patients** who received 1L chemotherapy for metastatic UC received 2L treatment[5]

1L, first line; 2L, second line; 3L, third line; UC, urothelial cancer.

1. Galsky MC, et al. Bladder Cancer. 2018;4:227-238; 2. Aly A, et al. J Med Econ. 2019;22:662-670; 3. Flannery K, et al. Future Oncol. 2019;15:1323-1334; 4. Simeon JC, et al. Cancer Epidemiol. 2019;60:121-127; 5. Grivas P, et al. Cancer Treat Rev. 2021;97:102187.

Indication and Important Safety Information

FDA-Approved Indications

First-line maintenance treatment of urothelial carcinoma

BAVENCIO® (avelumab) is indicated for the maintenance treatment of patients with locally advanced or metastatic urothelial carcinoma (UC) that has not progressed with first-line platinum-containing chemotherapy.

Previously-treated urothelial carcinoma

BAVENCIO® is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma (UC) who:

- have disease progression during or following platinum-containing chemotherapy
- have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy

Please see the full BAVENCIO® (avelumab) US Prescribing Information available at https://www.emdserono.com/us-en/pi/bavencio-pi.pdf

Important Safety Information

Avelumab can cause **severe and fatal immune-mediated adverse reactions** in any organ system or tissue and at any time after starting treatment with a PD-1/PD-L1 blocking antibody, including after discontinuation of treatment.

Early identification and management of immune-mediated adverse reactions are essential to ensure safe use of PD-1/PD-L1 blocking antibodies. Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.

No dose reduction for avelumab is recommended. For immune-mediated adverse reactions, withhold or permanently discontinue avelumab depending on severity. In general, withhold avelumab for severe (Grade 3) immune-mediated adverse reactions. Permanently discontinue avelumab for life-threatening (Grade 4) immune-mediated adverse reactions, recurrent severe (Grade 3) immune-mediated reactions that require systemic immunosuppressive treatment, or an inability to reduce corticosteroid dose to 10 mg or less of prednisone or equivalent per day within 12 weeks of initiating corticosteroids. In general, if avelumab requires interruption or discontinuation, administer systemic corticosteroid therapy (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroid therapy. Toxicity management guidelines for adverse reactions that do not necessarily require systemic corticosteroids (eg, endocrinopathies and dermatologic reactions) are discussed in subsequent sections.

Avelumab can cause **immune-mediated pneumonitis**. Withhold avelumab for Grade 2, and permanently discontinue for Grade 3 or Grade 4 pneumonitis. Immune-mediated pneumonitis occurred in 1.1% (21/1854) of patients, including fatal (0.1%), Grade 4 (0.1%), Grade 3 (0.3%), and Grade 2 (0.6%) adverse reactions. Systemic corticosteroids were required in all (21/21) patients with pneumonitis.

Avelumab can cause **immune-mediated colitis**. The primary component of immune-mediated colitis consisted of diarrhea. Cytomegalovirus infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies. Withhold avelumab for Grade 2 or Grade 3, and permanently discontinue for Grade 4 colitis. Immune-mediated colitis occurred in 1.5% (27/1854) of patients, including Grade 3 (0.4%) and Grade 2 (0.8%) adverse reactions. Systemic corticosteroids were required in all (27/27) patients with colitis.

Avelumab can cause **hepatotoxicity and immune-mediated hepatitis**. Withhold or permanently discontinue avelumab based on tumor involvement of the liver and severity of aspartate aminotransferase (AST), alanine aminotransferase (ALT), or total bilirubin elevation. Immune-mediated hepatitis occurred with avelumab as a single agent in 1.1% (20/1854) of patients, including fatal (0.1%), Grade 3 (0.8%), and Grade 2 (0.2%) adverse reactions. Systemic corticosteroids were required in all (20/20) patients with hepatitis.

Avelumab can cause primary or secondary **immune-mediated adrenal insufficiency**. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement, as clinically indicated. Withhold avelumab for Grade 3 or Grade 4 endocrinopathies until clinically stable or permanently discontinue depending on severity. Immune-mediated adrenal insufficiency occurred in 0.6% (11/1854) of patients, including Grade 3 (0.1%) and Grade 2 (0.4%) adverse reactions. Systemic corticosteroids were required in all (11/11) patients with adrenal insufficiency.

Avelumab can cause **immune-mediated hypophysitis**. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field defects. Hypophysitis can cause hypopituitarism. Initiate hormone replacement, as clinically indicated. Withhold avelumab for Grade 3 or Grade 4 endocrinopathies until clinically stable or permanently discontinue depending on severity. Immune-mediated pituitary disorders occurred in 0.1% (1/1854) of patients, which was a Grade 2 (0.1%) adverse reaction.

Avelumab can cause **immune-mediated thyroid disorders**. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement for hypothyroidism or institute medical management of hyperthyroidism, as clinically indicated. Withhold avelumab for Grade 3 or Grade 4 endocrinopathies until clinically stable or permanently discontinue depending on severity. Thyroiditis occurred in 0.2% (4/1854) of patients, including Grade 2 (0.1%) adverse reactions. Hyperthyroidism occurred in 0.4% (8/1854) of patients, including Grade 2 (0.3%) adverse reactions. Systemic corticosteroids were required in 25% (2/8) of patients with hyperthyroidism. Hypothyroidism occurred in 5% (97/1854) of patients, including Grade 3 (0.2%) and Grade 2 (3.6%) adverse reactions. Systemic corticosteroids were required in 6% (6/97) of patients with hypothyroidism.

Avelumab can cause **immune-mediated type I diabetes mellitus**, which can present with diabetic ketoacidosis. Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Withhold avelumab for Grade 3 or Grade 4 endocrinopathies until clinically stable or permanently discontinue depending on severity. Immune-mediated type I diabetes mellitus occurred in 0.2% (3/1854) of patients, including Grade 3 (0.2%) adverse reactions.

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BAVENCIO® (avelumab). Prescribing information. https://www.emdserono.com/us-en/pi/bavencio-pi.pdf

Important Safety Information, continued

Avelumab can cause **immune-mediated nephritis with renal dysfunction**. Withhold avelumab for Grade 2 or Grade 3, and permanently discontinue for Grade 4 increased blood creatinine. Immune-mediated nephritis with renal dysfunction occurred in 0.1% (2/1854) of patients, including Grade 3 (0.1%) and Grade 2 (0.1%) adverse reactions. Systemic corticosteroids were required all (2/2) patients with nephritis with renal dysfunction.

Avelumab can cause **immune-mediated dermatologic adverse reactions**, including rash or dermatitis. Exfoliative dermatitis including Stevens Johnson Syndrome (SJS), drug rash with eosinophilia and systemic symptoms (DRESS), and toxic epidermal necrolysis (TEN), has occurred with PD-1/PD-L1 blocking antibodies. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes. Withhold avelumab for suspected and permanently discontinue for confirmed SJS, TEN, or DRESS. Immune-mediated dermatologic adverse reactions occurred in 6% (108/1854) of patients, including Grade 3 (0.1%) and Grade 2 (1.9%) adverse reactions. Systemic corticosteroids were required in 25% (27/108) of patients with dermatologic adverse reactions.

Avelumab can result in **other immune-mediated adverse reactions**. Other clinically significant immune-mediated adverse reactions occurred at an incidence of <1% in patients who received avelumab or were reported with the use of other PD-1/PD-L1 blocking antibodies. For **myocarditis**, permanently discontinue avelumab for Grade 2, Grade 3, or Grade 4. For **neurological toxicities**, withhold avelumab for Grade 2 and permanently discontinue for Grade 3 or Grade 4.

Avelumab can cause severe or life-threatening **infusion-related reactions**. Premedicate patients with an antihistamine and acetaminophen prior to the first 4 infusions and for subsequent infusions based upon clinical judgment and presence/severity of prior infusion reactions. Monitor patients for signs and symptoms of infusion-related reactions, including pyrexia, chills, flushing, hypotension, dyspnea, wheezing, back pain, abdominal pain, and urticaria. Interrupt or slow the rate of infusion for Grade 1 or Grade 2 infusion-related reactions. Permanently discontinue avelumab for Grade 3 or Grade 4 infusion-related reactions. Infusion-related reactions occurred in 26% of patients, including three (0.2%) Grade 4 and ten (0.5%) Grade 3 infusion-related reactions. Eleven (85%) of the 13 patients with Grade ≥3 reactions were treated with intravenous corticosteroids.

Fatal and other serious **complications of allogeneic hematopoietic stem cell transplantation (HSCT)** can occur in patients who receive HSCT before or after being treated with a PD-1/PD-L1 blocking antibody. Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/PD-L1 blocking antibody prior to or after an allogeneic HSCT.

Avelumab can cause **fetal harm** when administered to a pregnant woman. Advise patients of the potential risk to a fetus including the risk of fetal death. Advise females of childbearing potential to use effective contraception during treatment with avelumab and for at least 1 month after the last dose of avelumab. It is not known whether avelumab is excreted in human milk. Advise a lactating woman **not to breastfeed** during treatment and for at least 1 month after the last dose of avelumab due to the potential for serious adverse reactions in breastfed infants.

A **fatal adverse reaction** (sepsis) occurred in one (0.3%) patient with **locally advanced or metastatic urothelial carcinoma (UC)** receiving avelumab + best supportive care (BSC) as first-line maintenance treatment. In patients with previously treated locally advanced or metastatic UC, fourteen patients (6%) who were treated with avelumab experienced either pneumonitis, respiratory failure, sepsis/urosepsis, cerebrovascular accident, or gastrointestinal adverse events, which led to death.

The most common adverse reactions (all grades, ≥20%) in patients with **locally advanced or metastatic UC** receiving avelumab + BSC (vs BSC alone) as first-line maintenance treatment were fatigue (35% vs 13%), musculoskeletal pain (24% vs 15%), urinary tract infection (20% vs 11%), and rash (20% vs 2.3%). In patients with previously treated locally advanced or metastatic UC receiving avelumab, the most common adverse reactions (all grades, ≥20%) were fatigue, infusion-related reaction, musculoskeletal pain, nausea, decreased appetite, and urinary tract infection.

Selected laboratory abnormalities worsening from baseline (all grades, ≥20%) in patients with **locally advanced or metastatic UC** receiving avelumab + BSC (vs BSC alone) as first-line maintenance treatment were blood triglycerides increased (34% vs 28%), alkaline phosphatase increased (30% vs 20%), blood sodium decreased (28% vs 20%), lipase increased (25% vs 16%), aspartate aminotransferase (AST) increased (24% vs 12%), blood potassium increased (24% vs 16%), alanine aminotransferase (ALT) increased (24% vs 12%), blood cholesterol increased (22% vs 16%), serum amylase increased (21% vs 12%), hemoglobin decreased (28% vs 18%), and white blood cell decreased (20% vs 10%).

BAVENCIO® (avelumab). Prescribing information. https://www.emdserono.com/us-en/pi/bavencio-pi.pdf

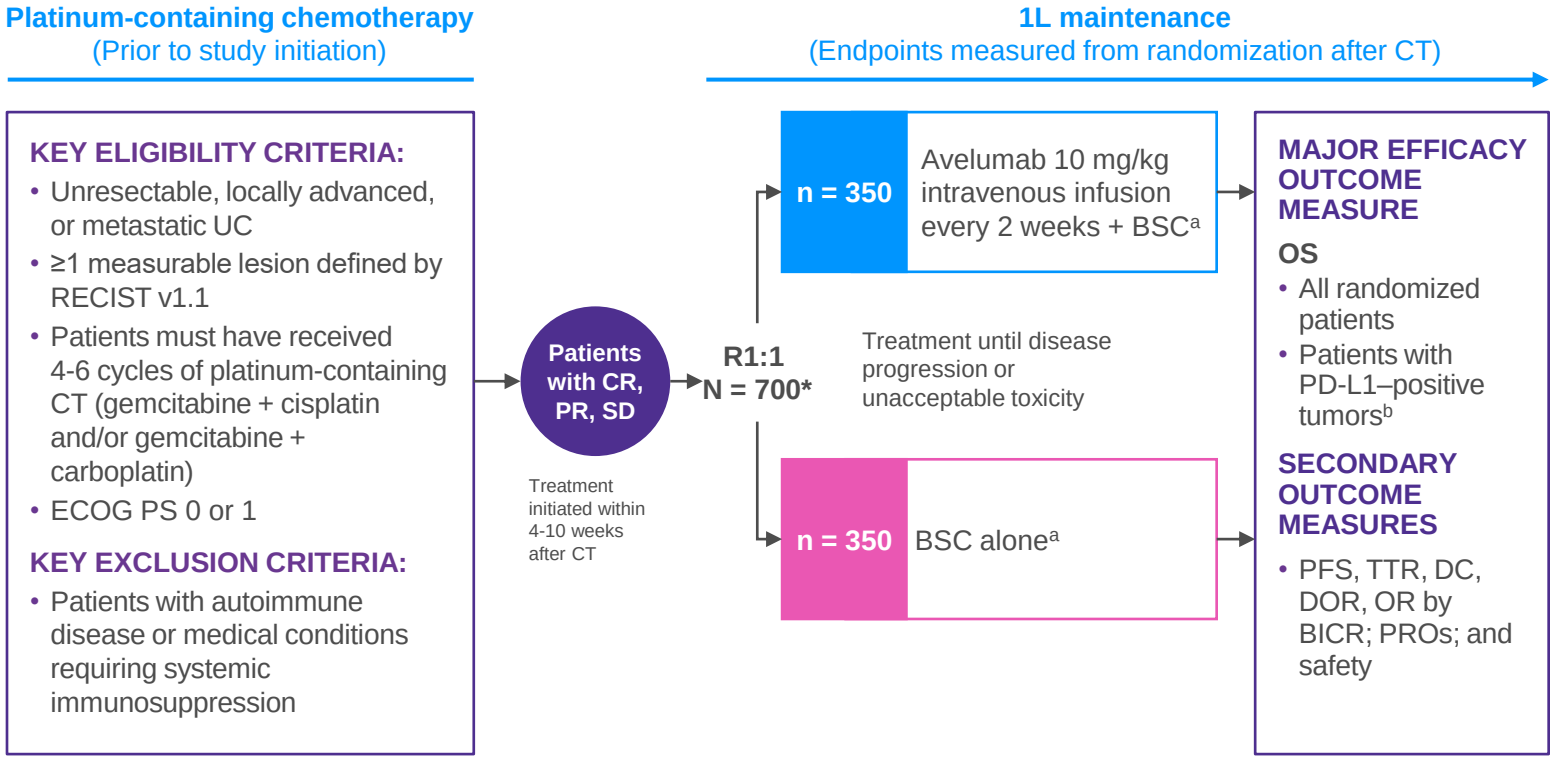
JAVELIN Bladder 100

Study Design

JAVELIN Bladder 100 (NCT02603432)

Phase III, randomized, open-label trial investigating 1L maintenance with avelumab in patients with locally advanced or metastatic UC that did not progress with platinum-containing CT[1,2]

JAVELIN Bladder 100 regimen with avelumab as 1L maintenance treatment[1,2]



- Stratified by best response to CT (CR/PR vs SD per RECIST v1.1) and site of metastasis (visceral vs non-visceral [including bone metastasis]) assessed at the time of initiating 1L platinum-containing chemotherapy[1,2]
- Administration of avelumab was permitted beyond RECIST-defined disease progression if the patient was clinically stable and considered to be deriving clinical benefit by the investigator[2]
- Assessment of tumor status was performed at baseline, 8 weeks after randomization, then every 8 weeks up to 12 months after randomization, and every 12 weeks thereafter until documented confirmed disease progression based on BICR assessment per RECIST v1.1[2]

* 1005 patients were screened with 305 deemed ineligible at screening; 267 screen failure, 21 no longer meet eligibility criteria, 11 withdrew consent, 3 deaths and 3 other reasons[3];
[a] BSC was administered as deemed appropriate by the treating physician, and could include treatment with antibiotics, nutritional support, and other patient management approaches with palliative intent (excludes systemic antitumor therapy); [b] PD-L1 expression was assessed in tumor samples using the VENTANA PD-L1 (SP263) assay.[1]

1L, first-line; BICR, blinded independent central review; BSC, best supportive care; CR, complete response; CT, chemotherapy; DC, disease control; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; OR, overall response; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PR, partial response; PROs, patient-reported outcomes; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; TTR, time to response; UC, urothelial cancer.

1. Powles T, et al. N Engl J Med. 2020;383(13):1218-1230; 2. BAVENCIO® (avelumab). Prescribing information. https://www.emdserono.com/us-en/pi/bavencio-pi.pdf; 3. Powles T, et al. N Engl J Med. 2020;383(13):1218-1230 (suppl).

JAVELIN Bladder 100

Results

Baseline Characteristics[1,2]

	ALL RANDOMIZED PATIENTS		PD-L1–POSITIVE PATIENTS	
	AVELUMAB + BSC (n = 350)	BSC ALONE (n = 350)	AVELUMAB + BSC (n = 189)	BSC ALONE (n = 169)
Age, median (range), years	68 (37-90)	69 (32-89)	70 (37-90)	70 (32-84)
ECOG PS at randomization, n (%)				
0	213 (60.9)	211 (60.3)	114 (60.3)	107 (63.3)
1	136 (38.9)	136 (38.9)	74 (39.2)	61 (36.1)
2	1 (0.3)	0	1 (0.5)	0
3	0	3 (0.9)	0	1 (0.6)
PD-L1 status, n (%)				
Positive	189 (54.0)	169 (48.3)	189 (100.0)	169 (100.0)
Negative	139 (39.7)	131 (37.4)	0	0
Unknown	22 (6.3)	50 (14.3)	0	0

	ALL RANDOMIZED PATIENTS		PD-L1–POSITIVE PATIENTS	
	AVELUMAB + BSC (n = 350)	BSC ALONE (n = 350)	AVELUMAB + BSC (n = 189)	BSC ALONE (n = 169)
Site of baseline metastasis (prior to CT), n (%)				
Visceral	191 (54.6)	191 (54.6)	88 (46.6)	79 (46.7)
Non-visceral	159 (45.4)	159 (45.4)	101 (53.4)	90 (53.3)
1L CT regimen, n (%)				
Gem + cis	183 (52.3)	206 (58.9)	101 (53.4)	98 (58.0)
Gem + carbo	147 (42.0)	122 (34.9)	74 (39.2)	54 (32.0)
Gem + cis/carbo	20 (5.7)	20 (5.7)	14 (7.4)	15 (8.9)
Not reported	0	2 (0.6)	0	2 (1.2)
Best response to 1L CT, n (%)				
CR	90 (25.7)	89 (25.4)	60 (31.7)	53 (31.4)
PR	163 (46.6)	163 (46.6)	79 (41.8)	75 (44.4)
SD	97 (27.7)	98 (28.0)	50 (26.5)	41 (24.3)

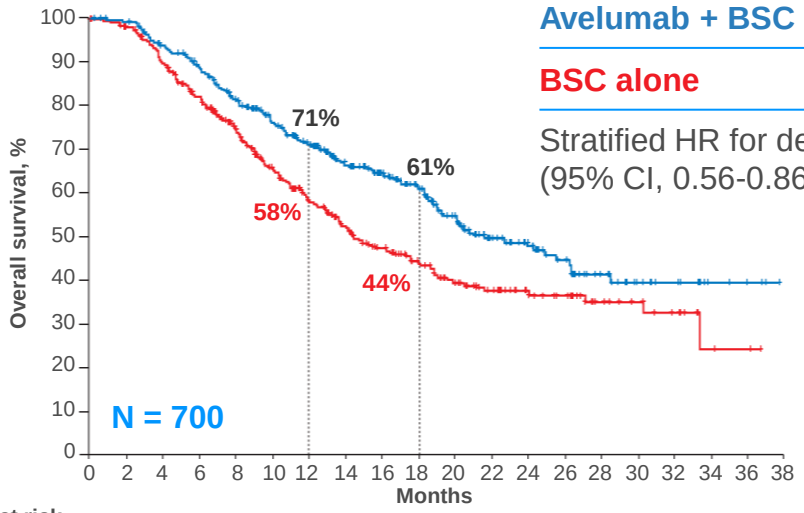
Baseline characteristics were balanced between the treatment arms, between all randomized and PD-L1–positive patient populations

For full definitions please refer to Powles T, et al. N Engl J Med. 2020;383(13):1218-1230.
1L, first-line; BSC, best supportive care; carbo, carboplatin; cis, cisplatin; CR, complete response; CT, chemotherapy; ECOG PS, Eastern Cooperative Oncology Group performance status; gem, gemcitabine; PD-L1, programmed death-ligand 1; PR, partial response; SD, stable disease.
1. Powles T, et al. Poster E7. Presented at: ASCO GU Symposium; February 17-19, 2022; San Fransisco, CA; 2. Powles T, et al. N Engl J Med. 2020;383(13):1218-1230 (suppl).

JAVELIN Bladder 100

OS Data

OS in All Randomized Patients[1-3]



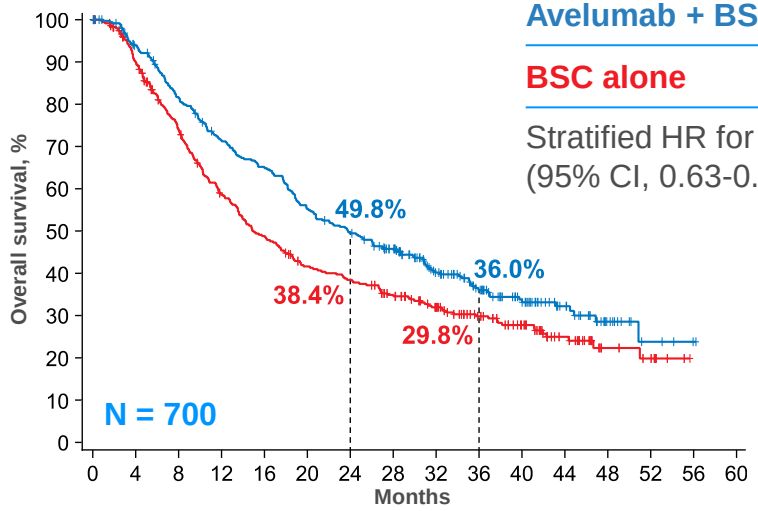
Median OS, months (95% CI)	
Avelumab + BSC	**21.4** (18.9-26.1)
BSC alone	**14.3** (12.9-17.9)

Stratified HR for death, **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

Median follow-up: avelumab + BSC: 19.6 months (95% CI, 18.0-20.6); BSC alone: 19.2 months (95% CI, 17.4-21.6)[3]

In the primary analysis, patients receiving avelumab + BSC had a **31% decrease** in the risk of death vs BSC alone



Median OS,* months (95% CI)	
Avelumab + BSC	**23.8** (19.9-28.8)
BSC alone	**15.0** (13.5-18.2)

Stratified HR for death, **0.76** (95% CI, 0.63-0.92); **p=0.0036**

No. at risk																
Avelumab + 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	

Median follow-up: avelumab + BSC: 38.0 months (95% CI, 36.1-40.5); BSC alone: 39.6 months (95% CI, 36.2-41.7)[3]

An updated OS analysis was conducted when 452 deaths were observed. The follow-up OS analysis was prespecified, but no formal hypothesis testing was performed given that the OS endpoint was met in the initial interim analysis

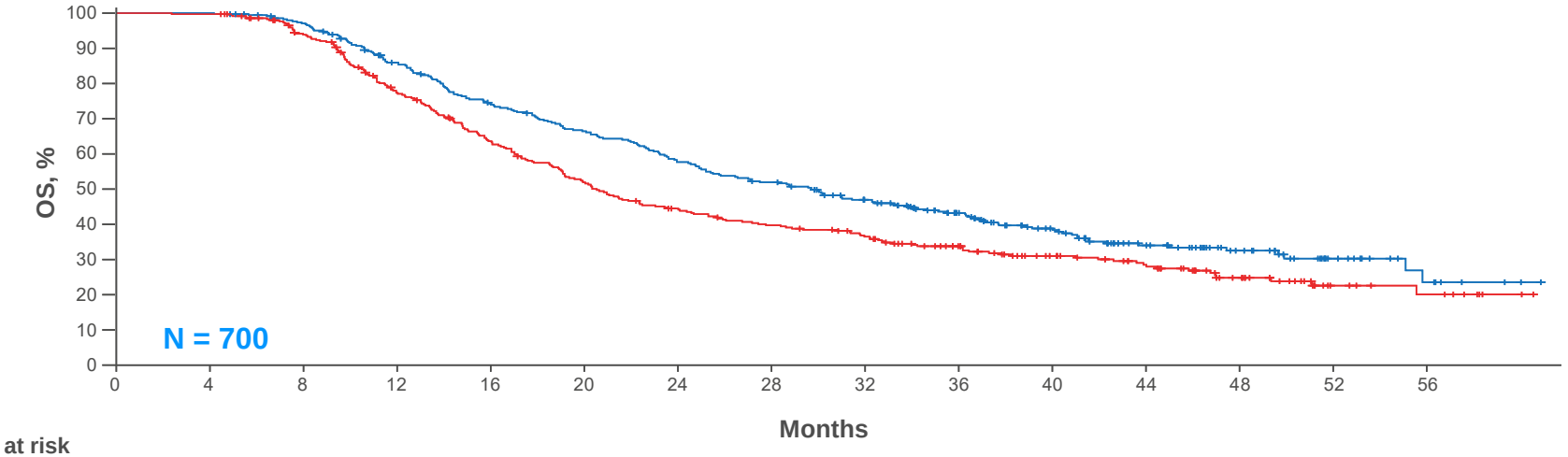
A pre-planned IA occurred with a data cut-off of October 21, 2019. The IA was considered as the primary analysis of the trial since the primary endpoint was met[3]; OS was measured post-randomization (after chemotherapy)[3]; the OS analysis crossed the prespecified efficacy boundary based on the alpha-spending function (p<0.0053).[2] * Follow-up OS analysis is investigator-assessed.[1]

BSC, best supportive care; CI, confidence interval; HR, hazard ratio; IA, interim analysis; OS, overall survival.

1. Powles T, et al. Poster E7. Presented at: ASCO GU Symposium; February 17-19, 2022; San Fransisco, CA; 2. Powles T, et al. N Engl J Med. 2020;383(13):1218-1230; 3. Data on File, B9991001; August 2, 2021.

OS From Start of 1L CT in All Randomized Patients[1]

Exploratory post hoc analysis



No. at risk															
Avelumab + BSC	350	350	334	288	247	220	191	171	145	114	86	58	36	17	7
BSC	350	349	317	255	207	168	141	125	111	89	68	54	33	12	8

Median OS, months (95% CI)	
Avelumab + BSC	**29.7** (25.2-34.0)
BSC alone	**20.5** (19.0-23.5)

HR **0.77** (95% CI, 0.64-0.92)

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])

Limitations

- This is an exploratory, post hoc analysis of OS data, inclusive of platinum-containing chemotherapy (4-6 cycles), treatment-free interval (4-10 weeks, per trial protocol), randomized study treatment with avelumab + BSC or BSC alone, and subsequent therapy
- This analysis only includes patients who did not progress on first-line platinum-containing chemotherapy and subsequently enrolled in the JAVELIN Bladder 100 trial
- Safety data are not available pre-randomization
- No conclusions can be drawn from this OS analysis

1L, first-line; BSC, best supportive care; CI, confidence interval; CT, chemotherapy; HR, hazard ratio; OS, overall survival.

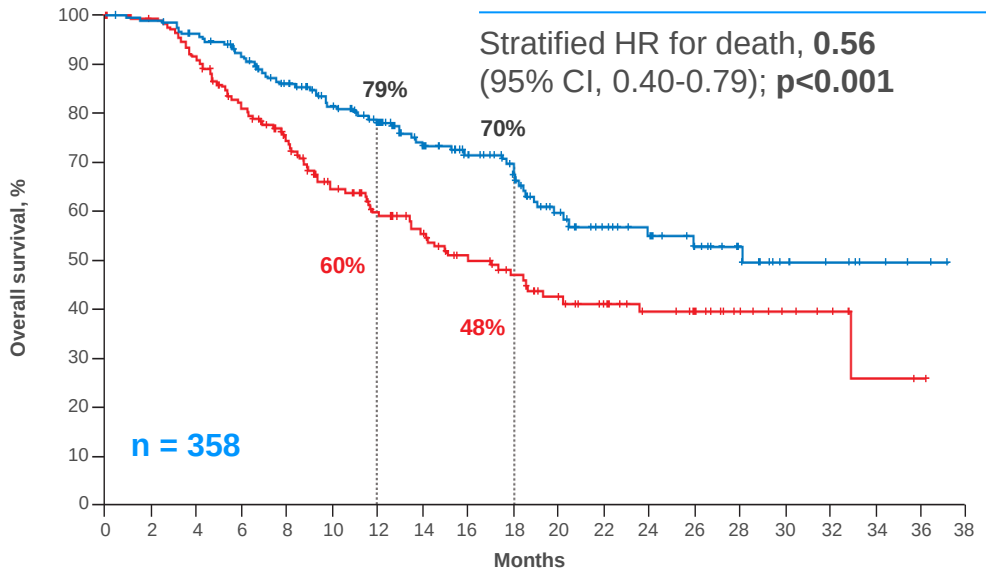
1. Sridhar SS, et al. Poster 508. Presented at: ASCO GU Symposium; February 16-18, 2023; San Fransisco, CA.

OS in PD-L1–Positive Populations[1-3]

Median OS, months (95% CI)

Avelumab + BSC	**NE** (20.3-NE)
BSC alone	**17.1** (13.5-23.7)

Stratified HR for death, **0.56** (95% CI, 0.40-0.79); **p<0.001**



No. at risk

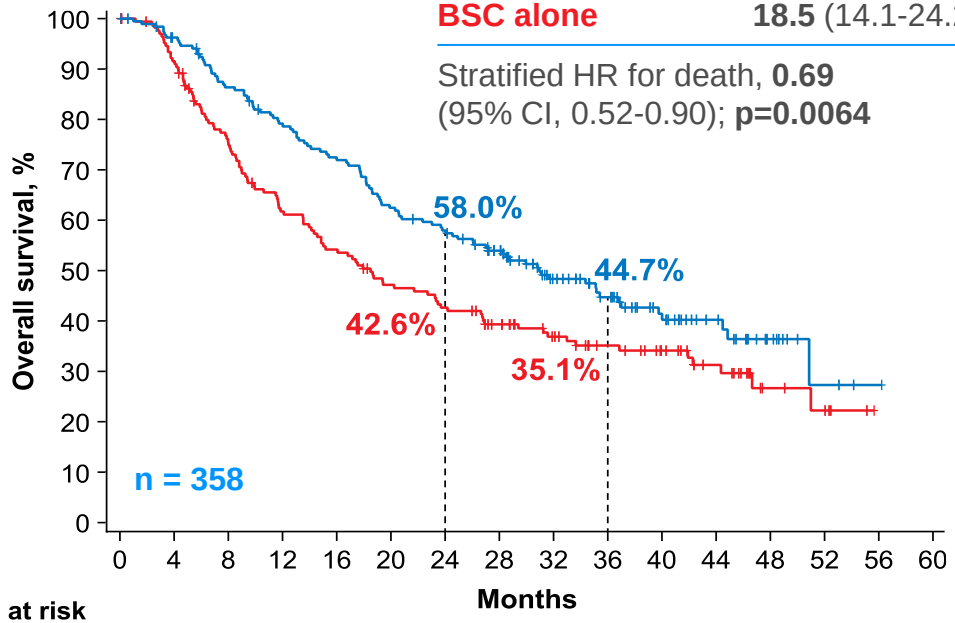
Avelumab + BSC	189	185	177	165	146	129	114	95	81	70	49	38	32	26	18	9	8	4	2	0
BSC	169	165	152	132	113	89	76	67	54	45	37	30	23	21	12	8	6	2	1	0

In the primary analysis, patients receiving avelumab + BSC had a **44% decrease** in the risk of death vs BSC alone

Median OS,* months (95% CI)

Avelumab + BSC	**30.9** (24.0-39.8)
BSC alone	**18.5** (14.1-24.2)

Stratified HR for death, **0.69** (95% CI, 0.52-0.90); **p=0.0064**



No. at risk

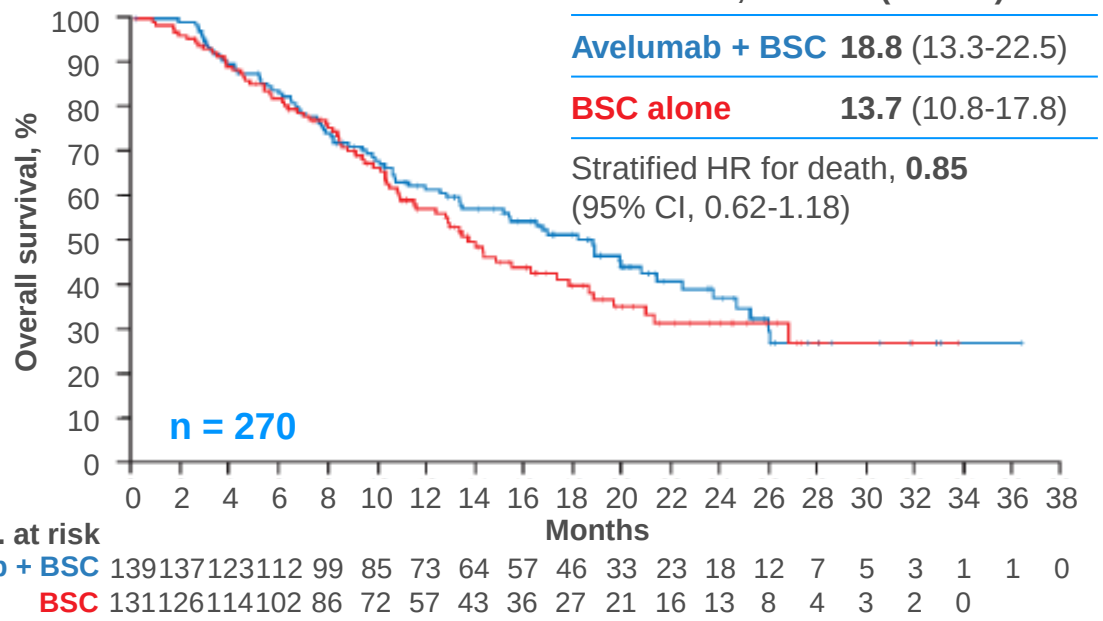
Avelumab + BSC	189	177	157	142	130	112	103	87	61	48	34	22	10	3	1	0
BSC	169	152	121	98	86	73	66	55	44	35	28	19	7	5	0	

The follow-up OS analysis was prespecified, but no formal hypothesis testing was performed given that the OS endpoint was met in the initial interim analysis

OS was measured post-randomization (after chemotherapy); the OS analysis crossed the prespecified efficacy boundary based on the alpha-spending function (p<0.0014). * Long-term follow-up OS analysis is investigator-assessed.
BSC, best supportive care; CI, confidence interval; HR, hazard ratio; NE, not estimable; OS, overall survival; PD-L1, programmed death-ligand 1.

1. Powles T, et al. Poster E7. Presented at: ASCO GU Symposium; February 17-19, 2022; San Fransisco, CA; 2. Powles T, et al. N Engl J Med. 2020;383(13):1218-1230; 3. Grivas P, et al. Abstract 704MO. Presented at: ESMO Virtual Congress; September 19-21, 2020.

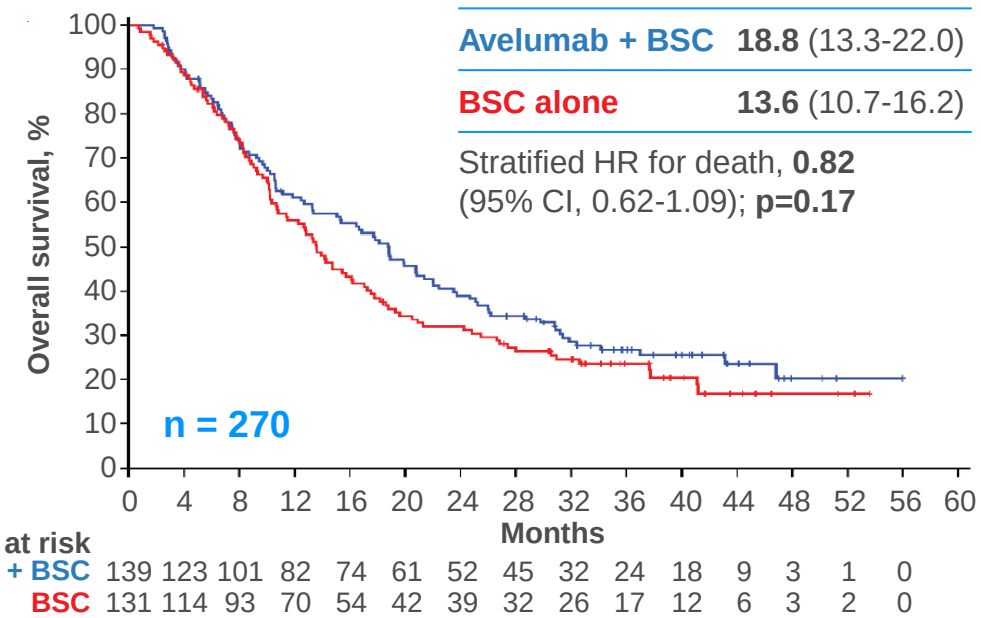
OS in PD-L1–Negative Populations[1-3]



Median OS, months (95% CI)	
Avelumab + BSC	**18.8** (13.3-22.5)
BSC alone	**13.7** (10.8-17.8)

Stratified HR for death, **0.85** (95% CI, 0.62-1.18)

No. at risk																			
Avelumab + BSC	139	137	123	112	99	85	73	64	57	46	33	23	18	12	7	5	3	1	1	0
BSC	131	126	114	102	86	72	57	43	36	27	21	16	13	8	4	3	2	0		



Median OS, months (95% CI)	
Avelumab + BSC	**18.8** (13.3-22.0)
BSC alone	**13.6** (10.7-16.2)

Stratified HR for death, **0.82** (95% CI, 0.62-1.09); **p=0.17**

No. at risk															
Avelumab + BSC	139	123	101	82	74	61	52	45	32	24	18	9	3	1	0
BSC	131	114	93	70	54	42	39	32	26	17	12	6	3	2	0

In the primary OS analysis in patients with PD-L1–negative tumors (exploratory analysis) (n = 270, 39%) the OS hazard ratio was 0.85 (95% CI, 0.62-1.18)

In the follow-up OS analysis in patients with PD-L1–negative tumors (exploratory analysis) (n = 270, 39%) the OS hazard ratio was 0.83 (95% CI, 0.63-1.10)

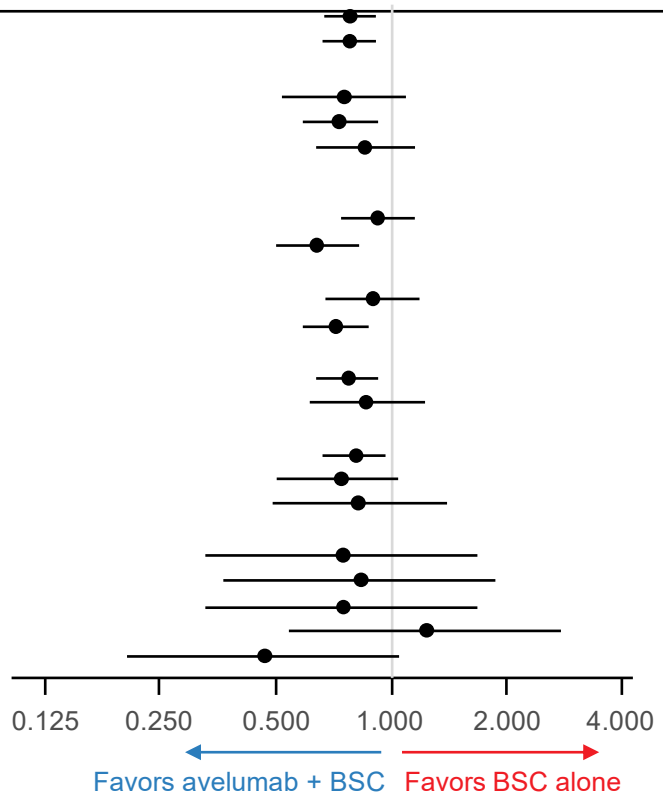
For full definitions please refer to Powles T, et al. N Engl J Med. 2020;383(13):1218-1230.
OS was measured post-randomization (after chemotherapy); the OS analysis crossed the prespecified efficacy boundary based on the alpha-spending function (p<0.0014).
BSC, best supportive care; CI, confidence interval; HR, hazard ratio; OS, overall survival; PD-L1, programmed death-ligand

1. Powles T, et al. *N Engl J Med.* 2020;383(13):1218-1230 (suppl); 2. Powles T, et al. Abstract LBA1. Presented at: ASCO Virtual Annual Meeting; May 29-31, 2020. 3. Powles T, et al. *J Clin Oncol.* 2023;41(19):3486-3492 (suppl).

OS: Select Subgroup Analysis[1]

Post hoc subgroups in all randomized patients

Subgroup	Avelumab + BSC	BSC alone	HR for OS (95% CI)*
	Number of events/number of patients		
All patients (stratified†)	215/350	237/350	0.76 (0.63 to 0.91)
All patients (unstratified)	215/350	237/350	0.75 (0.63 to 0.91)
Best response to 1L chemotherapy			
CR	43/90	54/89	0.72 (0.48 to 1.08)
PR	108/163	117/163	0.70 (0.54 to 0.91)
SD	64/97	66/98	0.84 (0.60 to 1.19)
Metastatic disease site when initiating 1L chemotherapy			
Visceral	130/191	130/191	0.91 (0.71 to 1.16)
Nonvisceral	85/159	107/159	0.60 (0.45 to 0.80)
Age			
<65	85/129	71/107	0.89 (0.65 to 1.22)
≥65	130/221	166/243	0.68 (0.54 to 0.86)
Sex			
Male	163/266	189/275	0.74 (0.60 to 0.91)
Female	52/84	48/75	0.84 (0.57 to 1.25)
Race			
White	151/232	162/238	0.78 (0.63 to 0.89)
Asian	41/75	55/81	0.70 (0.46 to 1.04)
Other	23/43	20/31	0.80 (0.44 to 1.47)
Pooled geographic region			
Europe	136/214	146/203	0.71 (0.56 to 0.89)
North America	7/12	14/22	0.82 (0.33 to 2.03)
Asia	40/73	49/74	0.73 (0.48 to 1.11)
Australasia	23/34	18/37	1.29 (0.70 to 2.40)
Rest of the world	9/17	10/14	0.42 (0.16 to 1.06)



OS analyses also favored avelumab across subgroups, including those defined by chemotherapy regimen and best response to chemotherapy

Limitations

Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

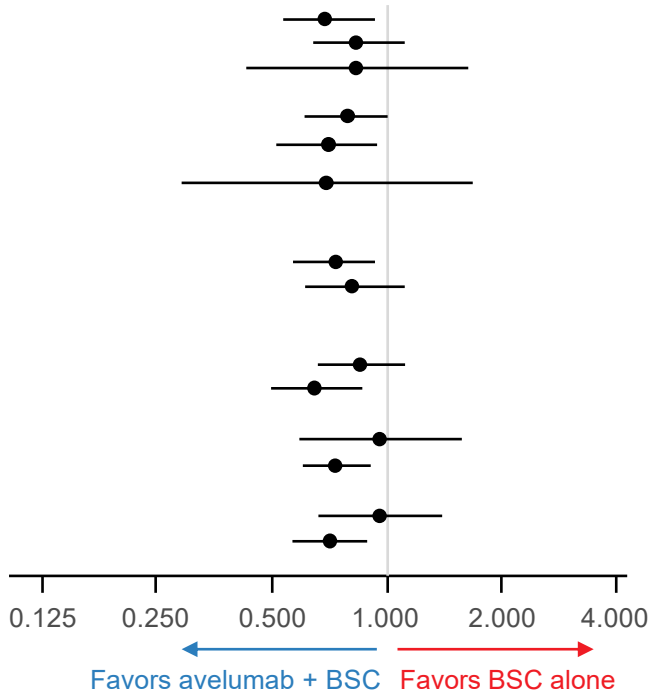
*HRs and CIs were calculated using Cox proportional hazard model. Unless otherwise stated, all analyses are unstratified. †Stratified by best response to 1L chemotherapy (CR or PR vs SD) and metastatic disease site when initiating 1L chemotherapy (visceral vs nonviseceral).
1L, first-line; BSC, best supportive care; CI, confidence interval; CR, complete response; HR, hazard ratio; OS, overall survival; PR, partial response; SD, stable disease.

1. Powles T, et al. *J Clin Oncol.* 2023;41(19):3486-3492.

OS: Select Subgroup Analysis[1]

Post hoc subgroups in all randomized patients

Subgroup	Number of events/number of patients: Avelumab + BSC	BSC alone	HR for OS (95% CI)*
PD-L1 status at baseline			
Positive	102/189	108/169	0.69 (0.53 to 0.91)
Negative	101/139	100/131	0.83 (0.63 to 1.10)
Unknown	12/22	29/50	0.82 (0.42 to 1.61)
1L chemotherapy regimen			
Gemcitabine plus cisplatin	108/183	134/206	0.78 (0.61 to 1.01)
Gemcitabine plus carboplatin	97/147	91/122	0.70 (0.52 to 0.93)
Gemcitabine plus carboplatin or cisplatin†	10/20	11/20	0.69 (0.29 to 1.64)
ECOG PS			
0	125/213	141/211	0.72 (0.56 to 0.91)
≥1	90/137	96/139	0.81 (0.61 to 1.08)
Creatinine clearance at baseline, mL/min			
≥60	113/181	125/196	0.84 (0.65 to 1.09)
<60	101/168	109/148	0.64 (0.49 to 0.85)
Liver lesions at baseline			
Yes	33/43	33/44	0.95 (0.58 to 1.54)
No	182/307	204/306	0.73 (0.60 to 0.89)
Lung lesions at baseline			
Yes	59/83	57/83	0.95 (0.66 to 1.36)
No	156/267	180/267	0.70 (0.56 to 0.87)



OS analyses also favored avelumab across subgroups, including those defined by chemotherapy regimen and best response to chemotherapy

Limitations

Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

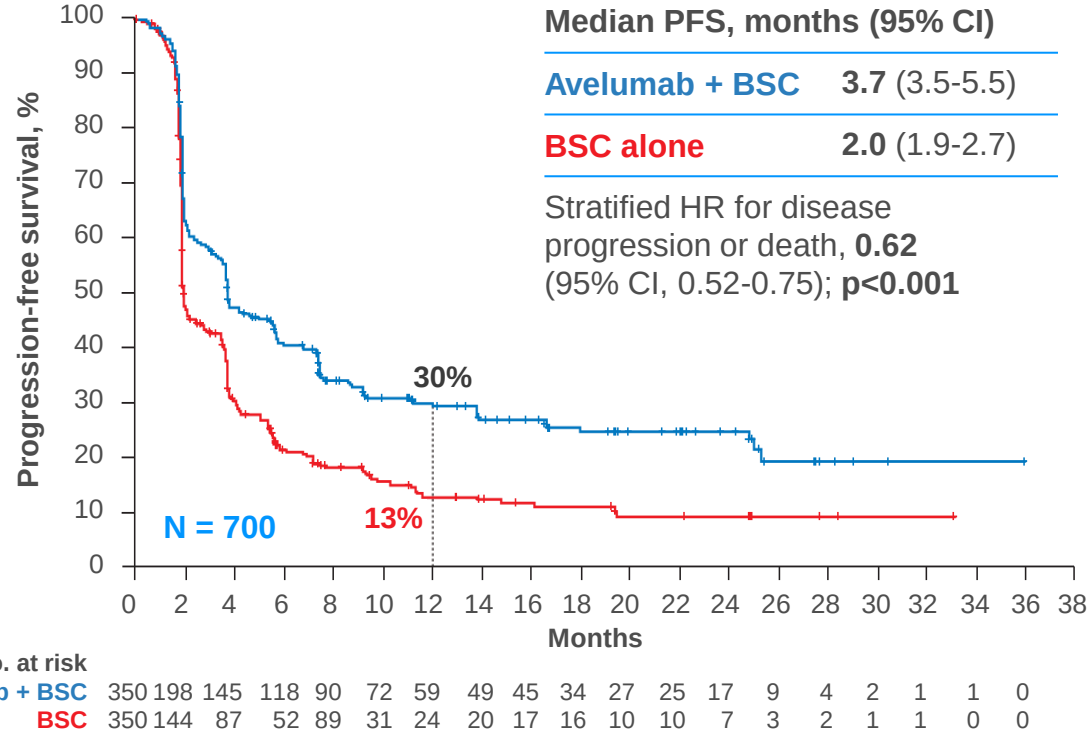
*HRs and CIs were calculated using Cox proportional hazard model. All analyses are unstratified. †Patients who switched platinum regimens while receiving 1L chemotherapy.
1L, first-line; BSC, best supportive care; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; OS, overall survival; PD-L1, programmed death-ligand 1.

1. Powles T, et al. *J Clin Oncol.* 2023;41(19):3486-3492.

JAVELIN Bladder 100

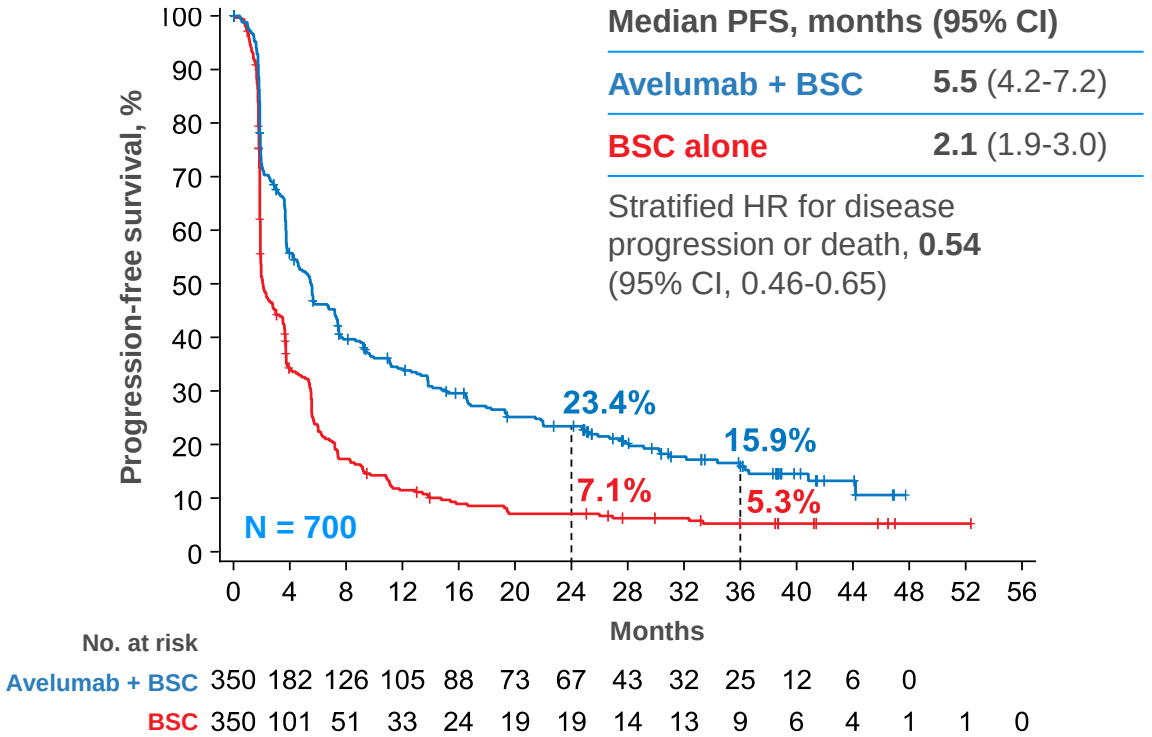
PFS Data

Secondary Endpoint: PFS in All Randomized Patients[1,2]



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

Stratified HR for disease progression or death, **0.62** (95% CI, 0.52-0.75); **p<0.001**



Median PFS, months (95% CI)	
Avelumab + BSC	**5.5** (4.2-7.2)
BSC alone	**2.1** (1.9-3.0)

Stratified HR for disease progression or death, **0.54** (95% CI, 0.46-0.65)

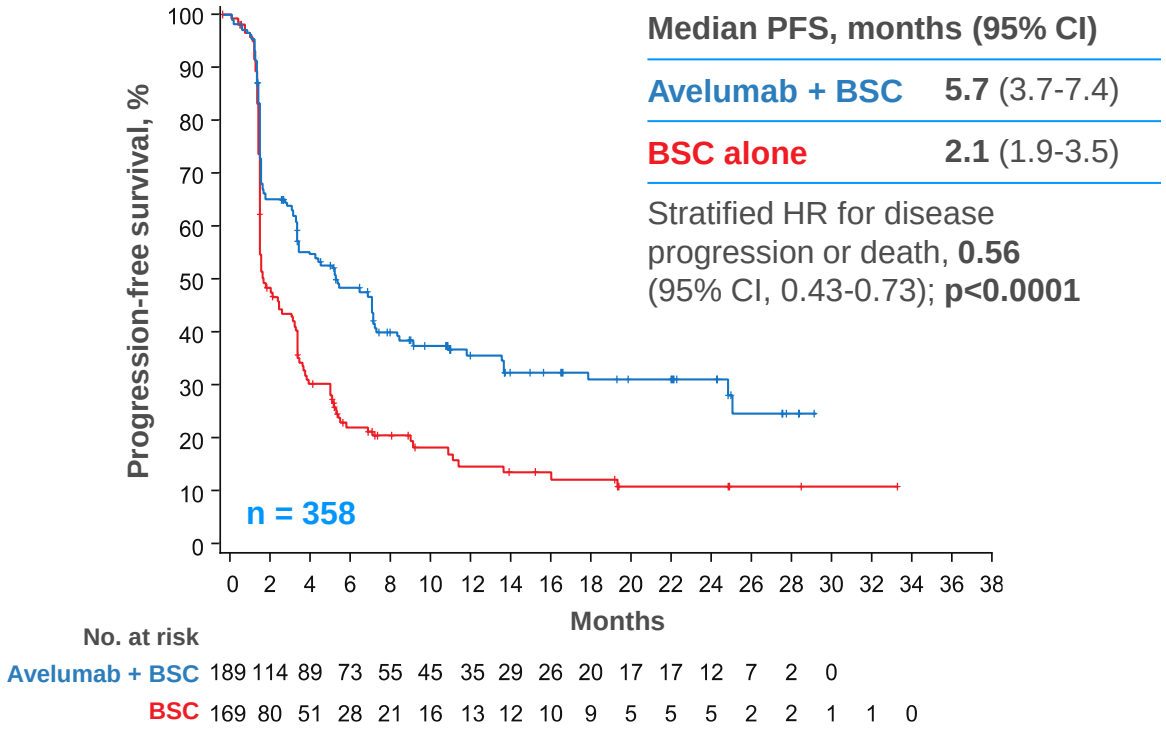
Patients receiving avelumab + BSC had a **38% decrease** in risk of progression vs BSC alone

The follow-up PFS analysis was prespecified, but no formal hypothesis testing was performed given that the PFS endpoint was met in the initial interim analysis

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(13):1218-1230; 2. Powles T, et al. Poster E7. Presented at: ASCO GU Symposium; February 17-19, 2022; San Francisco, CA.

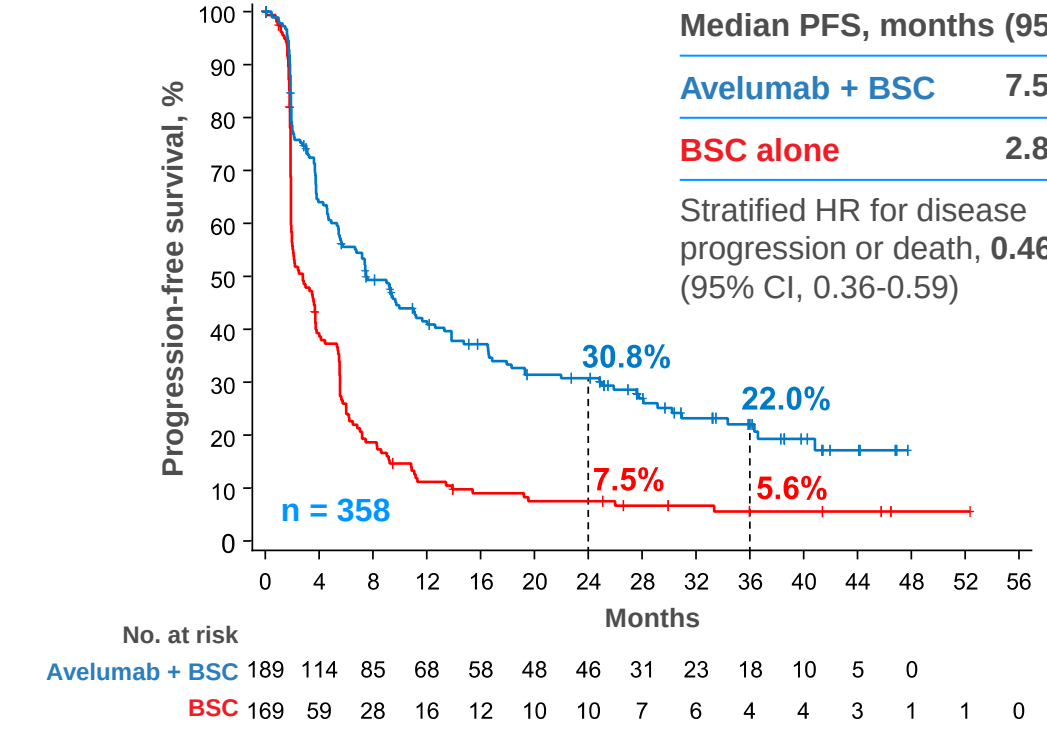
Secondary Endpoint: PFS in PD-L1–Positive Populations[1,2]



Median PFS, months (95% CI)

Avelumab + BSC	**5.7** (3.7-7.4)
BSC alone	**2.1** (1.9-3.5)

Stratified HR for disease progression or death, **0.56** (95% CI, 0.43-0.73); **p<0.0001**



Median PFS, months (95% CI)

Avelumab + BSC	**7.5** (5.5-11.1)
BSC alone	**2.8** (2.0-3.7)

Stratified HR for disease progression or death, **0.46** (95% CI, 0.36-0.59)

Patients receiving avelumab + BSC had a **44% decrease** in risk of progression vs BSC alone

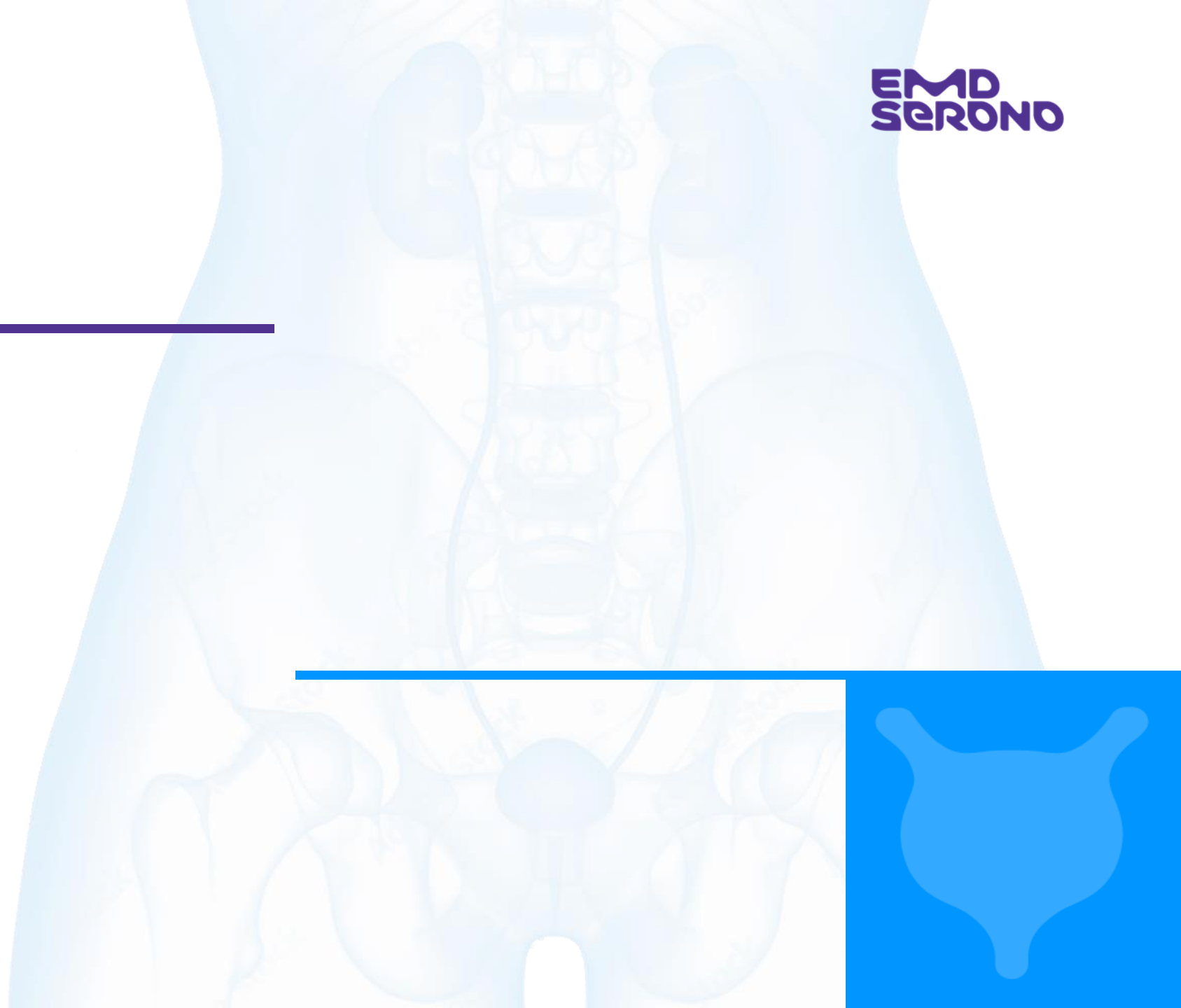
The follow-up PFS analysis was prespecified, but no formal hypothesis testing was performed given that the PFS endpoint was met in the initial interim analysis

BSC, best supportive care; CI, confidence interval; HR, hazard ratio; PD-L1, programmed death-ligand 1; PFS, progression-free survival.

1. Powles T, et al. N Engl J Med. 2020;383(13):1218-1230; 2. Powles T, et al. Poster E7. Presented at: ASCO GU Symposium; February 17-19, 2022; San Francisco, CA.

JAVELIN Bladder 100

Safety Data



Secondary Endpoint: Safety[1]

	AVELUMAB + BSC (n = 344) n (%)	BSC ALONE (n = 345) n (%)
Any TEAE*	337 (98.0)	268 (77.7)
Grade ≥3 TEAE	163 (47.4)	87 (25.2)
TRAE	266 (77.3)	4 (1.2)
Grade ≥3 TRAE	57 (16.6)	0
Serious TEAE	96 (27.9)	69 (20.0)
Serious TRAE	31 (9.0)	0
TEAE leading to dose reduction of avelumab	1 (0.3)	–
TEAE leading to interruption of avelumab	140 (40.7)	–
TEAE leading to discontinuation of study drug	41 (11.9)	0
TRAE leading to discontinuation of study drug	33 (9.6)	0
TEAE leading to death	4 (1.2)	24 (7.0)
TRAE leading to death	1 (0.3)	0
irAE	101 (29.4)	5 (1.4)
IRR	74 (21.5)	0

* AE of any causality occurring within 30 days after the last dose of study treatment.

- No new safety signal or concerns were identified[2]
- The safety profile of avelumab + BSC was similar between subgroups, irrespective of duration or cycles of 1L chemotherapy[3]

For full definitions please refer to Powles T, et al. N Engl J Med. 2020;383(13):1218-1230.
1L, first-line; AE, adverse event; BSC, best supportive care; irAE, immune-related AE; IRR, Infusion-related reaction; TEAE, treatment-emergent AE; TRAE, treatment-related AE.
1. Powles T, et al. N Engl J Med. 2020;383(13):1218-1230 (suppl); 2. Powles T, et al. N Engl J Med. 2020;383(13):1218-1230; 3. Loriot Y, et al. Abstract 438. Presented at: ASCO GU Virtual Symposium; February 11-13, 2021.

Secondary Endpoint: Safety[1]

	AVELUMAB + BSC (n = 344)		BSC ALONE (n = 345)	
ALL CAUSALITY TEAEs*	**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

* TEAEs of any grade occurring in ≥10% or grade ≥3 TEAEs occurring in ≥5% in either arm.

- TEAEs led to discontinuation of avelumab in 11.9% of patients
- 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)

For full definitions please refer to Powles T, et al. N Engl J Med. 2020;383(13):1218-1230.
AE, adverse event; BSC, best supportive care; IRR, Infusion-related reaction; TEAE, treatment-emergent AE; UTI, urinary tract infection.
1. Powles T, et al. Abstract LBA1. Presented at: ASCO Virtual Annual Meeting; May 29-31, 2020.

Secondary Endpoint: Safety[1]

	AVELUMAB + BSC (n = 344)	
IMMUNE-RELATED AEs*	**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
Pruritus	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 of any grade occurring in ≥1% or grade ≥3 irAEs occurring in ≥0.5% in either arm.

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

For full definitions please refer to Powles T, et al. N Engl J Med. 2020;383(13):1218-1230.
AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BSC, best supportive care.
1. Powles T, et al. Abstract LBA1. Presented at: ASCO Virtual Annual Meeting; May 29-31, 2020.

Select Baseline Characteristics of Patients Treated With Avelumab for ≥12 Months[1]

	AVELUMAB + BSC ARM (n = 350)	PATIENTS WITH ≥12 MONTHS OF AVELUMAB TREATMENT (n = 118)
Age, median (range), years	68 (37-90)	69 (43-86)
Sex, n (%)		
Male	266 (76.0)	91 (77.1)
Female	84 (24.0)	27 (22.9)
Pooled geographic region, n (%)		
Europe	214 (61.1)	61 (51.7)
North America	12 (3.4)	6 (5.1)
Asia	73 (20.9)	32 (27.1)
Australia	34 (9.7)	15 (12.7)
Rest of the world	17 (4.9)	4 (3.4)
ECOG PS at randomization, n (%)		
0	213 (60.9)	83 (70.3)
1	136 (38.9)	35 (29.7)
2	1 (0.3)	0
PD-L1 status, n (%)		
Positive	189 (54.0)	72 (61.0)
Negative	139 (39.7)	39 (33.1)
Unknown	22 (6.3)	7 (5.9)
1L CT regimen, n (%)		
Gem + cis	183 (52.3)	67 (56.8)
Gem + carbo	147 (42.0)	43 (36.4)
Gem + cis/carbo	20 (5.7)	8 (6.8)
Best response to 1L CT, n (%)		
CR	90 (25.7)	36 (30.5)
PR	163 (46.6)	51 (43.2)
SD	97 (27.7)	31 (26.3)
Site of metastasis at start of CT, n (%)		
Visceral	191 (54.6)	56 (47.5)
Non-visceral	159 (45.4)	62 (52.5)
Site of primary tumor, n (%)		
Upper tract	106 (30.3)	34 (28.8)
Lower tract	244 (69.7)	84 (71.2)

Baseline characteristics of patients treated with avelumab for ≥12 months were generally similar to those of all patients randomized to the avelumab + BSC arm

For full definitions please refer to Powles T, et al. N Engl J Med. 2020;383(13):1218-1230.
1L, first-line; BSC, best supportive care; carbo, carboplatin; cis, cisplatin; CR, complete response; CT, chemotherapy; ECOG PS, Eastern Cooperative Oncology Group performance status; gem, gemcitabine; PD-L1, programmed death-ligand 1; PR, partial response; SD, stable disease.
1. Bellmunt J, et al. Abstract 4516. Presented at: ASCO Annual Meeting; June 2-6, 2023; Chicago, IL.

Secondary Endpoint: Updated Safety[1]

EVENTS, n (%)	AVELUMAB + BSC (N = 344) ONSET AT ANY TIME (n = 344)	AVELUMAB + BSC (N = 344) ONSET AFTER ≥12 MONTHS OF TREATMENT (n = 118)
Any TEAE*	**338 (98.3)**	**102 (86.4)**
Grade ≥3 TEAE	185 (53.8)	56 (47.5)
Any TRAE	269 (78.2)	59 (50.0)
Grade ≥3 TRAE	67 (19.5)	14 (11.9)
Serious TEAE	105 (30.5)	28 (23.7)
Serious TRAE	35 (10.2)	6 (5.1)
TEAE leading to interruption of avelumab	156 (45.3)	43 (36.4)
TEAE leading to discontinuation of study drug	49 (14.2)	13 (11.0)
TRAE leading to discontinuation of study drug	40 (11.6)	12 (10.2)
TEAE leading to death	7 (2.0)	3 (2.5)
TRAE leading to death	2 (0.6)	1 (0.8)
IRR	75 (21.8)	4 (3.4)

* AE of any causality occurring within 30 days after the last dose of study treatment.

In patients with ≥12 months of treatment with avelumab + BSC (n = 118)

- Any-grade TEAEs with onset after ≥12 months occurred in 102 patients (86.4%), including grade ≥3 in 56 (47.5%)
- Any-grade TRAEs with onset after ≥12 months occurred in 59 patients (50.0%), including grade ≥3 in 14 (11.9%) with discontinuations occurring in 12 patients (10.2%)

For full definitions please refer to Powles T, et al. N Engl J Med. 2020;383(13):1218-1230.
AE, adverse event; BSC, best supportive care; IRR, Infusion-related reaction; TEAE, treatment-emergent AE; TRAE, treatment-related AE.
1. Powles T, et al. Poster E7. Presented at: ASCO GU Symposium; February 17-19, 2022; San Francisco, CA.

Secondary Endpoint: Updated Safety[1]

	ONSET AFTER ≥12 MONTHS OF TREATMENT (n = 118)	
EVENTS, n (%)	ANY GRADE	GRADE ≥3
Any TEAE	**102 (86.4)**	**56 (47.5)**
UTI	15 (12.7)	3 (2.5)
Diarrhea	15 (12.7)	1 (0.8)
Arthralgia	14 (11.9)	1 (0.8)
Back pain	14 (11.9)	0
Cough	14 (11.9)	0
Pruritus	14 (11.9)	0
Nasopharyngitis	12 (10.2)	0

The most common TEAEs with onset ≥12 months of treatment with avelumab + BSC were UTI and diarrhea (n = 15 [12.7%] each)

1 patient had a TRAE after ≥12 months of treatment with avelumab + BSC that led to death

- Attributed to immune-related nephritis by the treating investigator

For full definitions please refer to Powles T, et al. N Engl J Med. 2020;383(13):1218-1230.
AE, adverse event; BSC, best supportive care; TEAE, treatment-emergent AE; TRAE, treatment-related AE; UTI, urinary tract infection.
1. Powles T, et al. Poster E7. Presented at: ASCO GU Symposium; February 17-19, 2022; San Francisco, CA.

Secondary Endpoint: Updated Safety[1]

EVENTS, n (%)	AVELUMAB + BSC (N = 344)	
	ONSET AT ANY TIME (n = 344)	ONSET AFTER ≥12 MONTHS OF TREATMENT (n = 118)
Any-grade irAEs	**111 (32.3)**	**27 (22.9)**
Grade ≥3 irAEs	26 (7.6)	5 (4.2)
irAEs leading to discontinuation of study drug	21 (6.1)	5 (4.2)
NUMBER OF irAEs PER PATIENT, %		
1 irAE	17.7	15.3
2 irAEs	8.7	3.4
3 irAEs	3.2	2.5
≥4 irAEs	2.6	1.7

In patients with ≥12 months of treatment with avelumab + BSC (n = 118)

- Any-grade irAEs with onset after ≥12 months occurred in 27 patients (22.9%), including grade ≥3 in 5 (4.2%)
- Most patients had a single irAE
- No category of grade ≥3 irAEs was most common because none occurred in >1 patient
- irAEs led to death in 1 patient (immune-related nephritis/renal dysfunction)

For full definitions please refer to Powles T, et al. N Engl J Med. 2020;383(13):1218-1230.
BSC, best supportive care; irAE, immune-related adverse event.
1. Bellmunt J, et al. Abstract 4516. Presented at: ASCO Annual Meeting; June 2-6, 2023; Chicago, IL.

Secondary Endpoint: Most Common Categories of irAEs[1]

	ONSET AT ANY TIME (n = 344)		ONSET AFTER ≥12 MONTHS OF TREATMENT (n = 118)	
irAE CATEGORY	ANY GRADE*	GRADE ≥3	ANY GRADE*	GRADE ≥3
Any irAE, n (%)	**111 (32.3)**	**26 (7.6)**	**27 (22.9)**	**5 (4.2)**
Thyroid disorders	44 (12.8)	1 (0.3)	2 (1.7)	0
Immune-related rash	37 (10.8)	5 (1.5)	12 (10.2)	1 (0.8)
Immune-related nephritis/renal dysfunction	8 (2.3)	2 (0.6)	4 (3.4)	1 (0.8)
Immune-related pneumonitis	7 (2.0)	1 (0.3)	2 (1.7)	0
Immune-related colitis	6 (1.7)	3 (0.9)	2 (1.7)	1 (0.8)
Immune-related hepatitis	5 (1.5)	5 (1.5)	0	0
Type 1 diabetes	4 (1.2)	3 (0.9)	1 (0.8)	1 (0.8)
Other irAEs	10 (2.9)	1 (0.3)	4 (3.4)	0

- For irAEs occurring at any time, 7 patients had any-grade irAE, and 1 patient had a grade ≥3 irAE that had not been categorized at the time of analysis
- For irAEs with onset after ≥12 months of treatment, 2 patients had any-grade irAE that had not been categorized at time of analysis

* Any-grade irAEs occurring in ≥1% of the patients.

For full definitions please refer to Powles T, et al. N Engl J Med. 2020;383(13):1218-1230.
irAE, immune-related adverse event.
1. Bellmunt J, et al. Abstract 4516. Presented at: ASCO Annual Meeting; June 2-6, 2023; Chicago, IL.

JAVELIN Bladder 100

1L Chemotherapy Regimen Subgroup Data

Baseline Characteristics by 1L Chemotherapy Regimen[1]

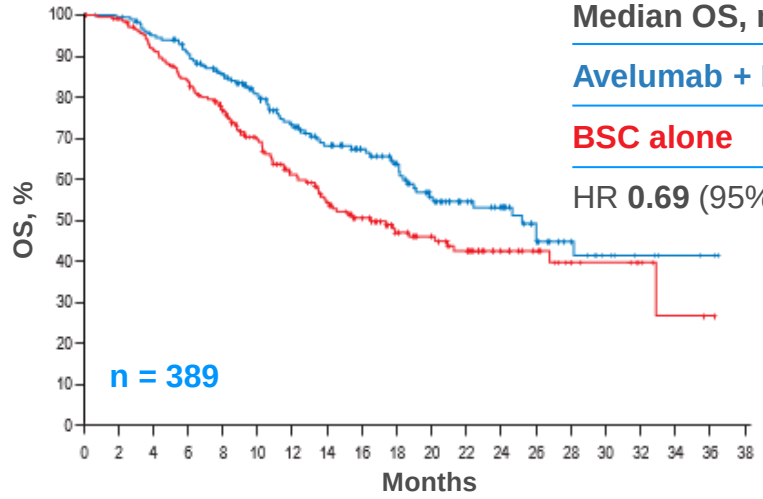
	CISPLATIN + GEMCITABINE		CARBOPLATIN + GEMCITABINE	
	AVELUMAB + BSC (n = 183)	BSC ALONE (n = 206)	AVELUMAB + BSC (n = 147)	BSC ALONE (n = 122)
Age, median (range), years	66.0 (37.0-86.0)	67.0 (32.0-84.0)	71.0 (46.0-90.0)	73.5 (46.0-89.0)
Sex, n (%)				
Male	138 (75.4)	158 (76.7)	115 (78.2)	98 (80.3)
Female	45 (24.6)	48 (23.3)	32 (21.8)	24 (19.7)
ECOG PS at randomization, n (%)				
0	124 (67.8)	135 (65.5)	75 (51.0)	65 (53.3)
1	58 (31.7)	71 (34.5)	72 (49.0)	54 (44.3)
≥2	1 (0.5)	0	0	3 (2.5)
Site of metastasis at start of 1L CT, n (%)				
Visceral	103 (56.3)	121 (58.7)	80 (54.4)	59 (48.4)
Non-visceral	80 (43.7)	85 (41.3)	67 (45.6)	63 (51.6)
PD-L1 status, n (%)				
Positive	101 (55.2)	98 (47.6)	74 (50.3)	54 (44.3)
Negative	69 (37.7)	74 (35.9)	65 (44.2)	53 (43.4)
Unknown	13 (7.1)	34 (16.5)	8 (5.4)	15 (12.3)
Best response to 1L CT, n (%)				
CR or PR	132 (72.1)	149 (72.3)	107 (72.8)	82 (67.2)
SD	51 (27.9)	57 (27.7)	40 (27.2)	40 (32.8)
Creatinine clearance, n (%)				
≥60 ml/min	118 (64.5)	132 (64.1)	53 (36.1)	54 (44.3)
<60 ml/min	65 (35.5)	69 (33.5)	93 (63.3)	67 (54.9)
Unknown	0	5 (2.4)	1 (0.7)	1 (0.8)

Patients who received carboplatin + gemcitabine were older and included a larger proportion of patients who had ECOG PS ≥1 or creatinine clearance <60 ml/min compared with patients who received cisplatin + gemcitabine

For full definitions please refer to Powles T, et al. N Engl J Med. 2020;383(13):1218-1230.
1L, first-line; BSC, best supportive care; CT, chemotherapy; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; PD-L1, programmed death-ligand 1; PR, partial response; SD, stable disease.
1. Sridhar SS, et al. Poster 508. Presented at: ASCO GU Symposium; February 16-18, 2023; San Fransisco, CA.

OS in All Randomized Patients Who Received 1L Cisplatin + Gemcitabine[1,2]

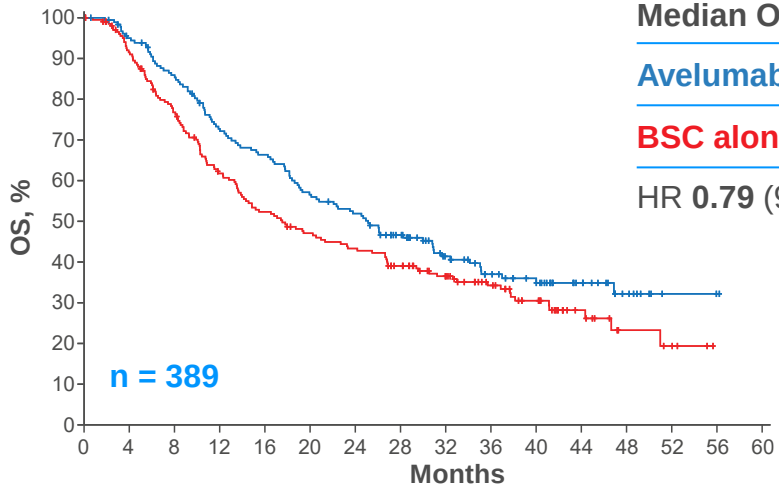
Protocol-specified subgroups



Median OS, months (95% CI)	
Avelumab + BSC	**25.3** (18.6-NE)
BSC alone	**16.5** (13.4-26.8)

HR **0.69** (95% CI, 0.51-0.94)

Exploratory post-hoc analysis



Median OS, months (95% CI)	
Avelumab + BSC	**25.1** (19.3-30.9)
BSC alone	**17.5** (13.7-24.2)

HR **0.79** (95% CI, 0.61-1.02)

OS was longer with avelumab + BSC vs BSC alone in patients who received 1L cisplatin + gemcitabine and maintained in the follow-up analysis

Limitations

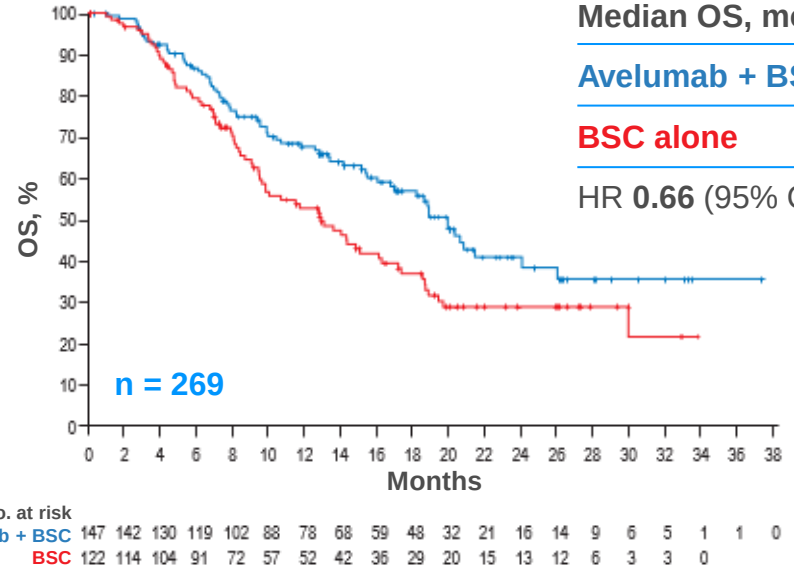
Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

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

1. Grivas P, et al. Abstract 704MO. Presented at: ESMO Virtual Congress; September 19-21, 2020; 2. Sridhar SS, et al. Poster 508. Presented at: ASCO GU Symposium; February 16-18, 2023; San Fransisco, CA.

OS in All Randomized Patients Who Received 1L Carboplatin + Gemcitabine[1,2]

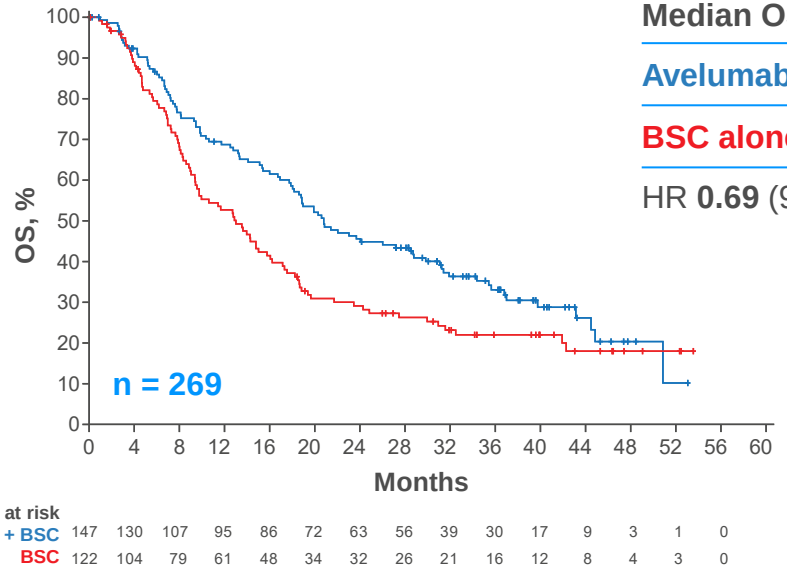
Protocol-specified subgroups



Median OS, months (95% CI)	
Avelumab + BSC	**19.9** (16.0-24.0)
BSC alone	**12.9** (9.4-16.2)

HR **0.66** (95% CI, 0.47-0.91)

Exploratory post-hoc analysis



Median OS, months (95% CI)	
Avelumab + BSC	**20.8** (17.9-28.7)
BSC alone	**13.0** (9.4-16.1)

HR **0.69** (95% CI, 0.52-0.93)

OS was longer with avelumab + BSC vs BSC alone in patients who received 1L carboplatin + gemcitabine and maintained in the follow-up analysis

Limitations

Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

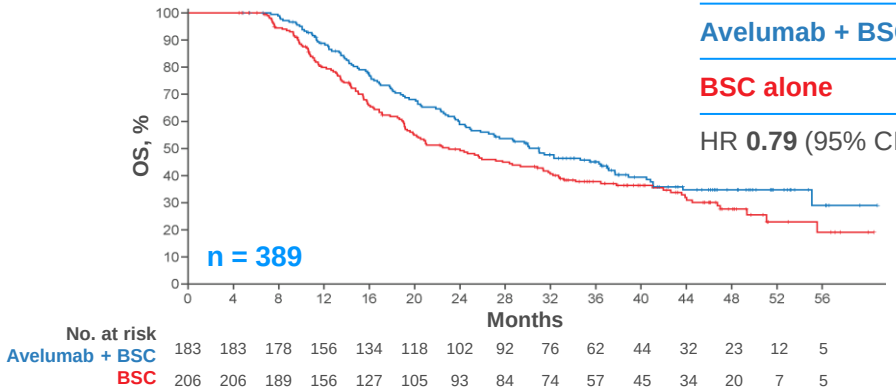
1L, first-line; BSC, best supportive care; CI, confidence interval; HR, hazard ratio; OS, overall survival.

1. Grivas P, et al. Abstract 704MO. Presented at: ESMO Virtual Congress; September 19-21, 2020; 2. Sridhar SS, et al. Poster 508. Presented at: ASCO GU Symposium; February 16-18, 2023; San Fransisco, CA.

OS From Start of 1L CT by 1L CT Regimen[1]

Exploratory post hoc analysis

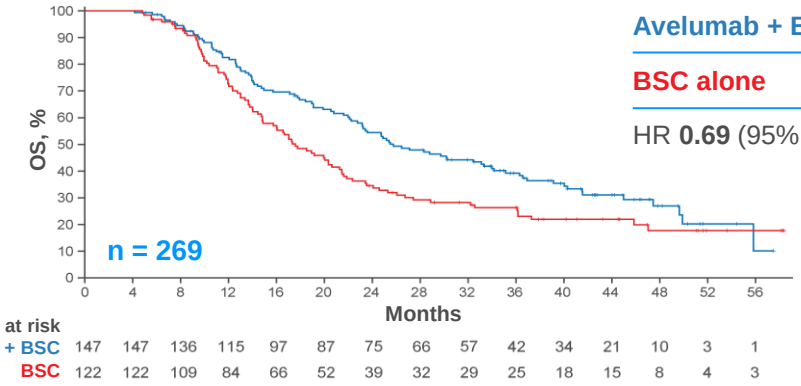
CISPLATIN + GEMCITABINE



Median OS, months (95% CI)	
Avelumab + BSC	**31.0** (24.9-37.1)
BSC alone	**23.0** (19.2-30.9)

HR **0.79** (95% CI, 0.61-1.02)

CARBOPLATIN + GEMCITABINE



Median OS, months (95% CI)	
Avelumab + BSC	**25.8** (22.8-33.3)
BSC alone	**17.6** (14.8-21.3)

HR **0.69** (95% CI, 0.51-0.92)

OS measured from the start of 1L chemotherapy was longer with avelumab + BSC vs BSC alone irrespective of 1L chemotherapy regimen received

Limitations

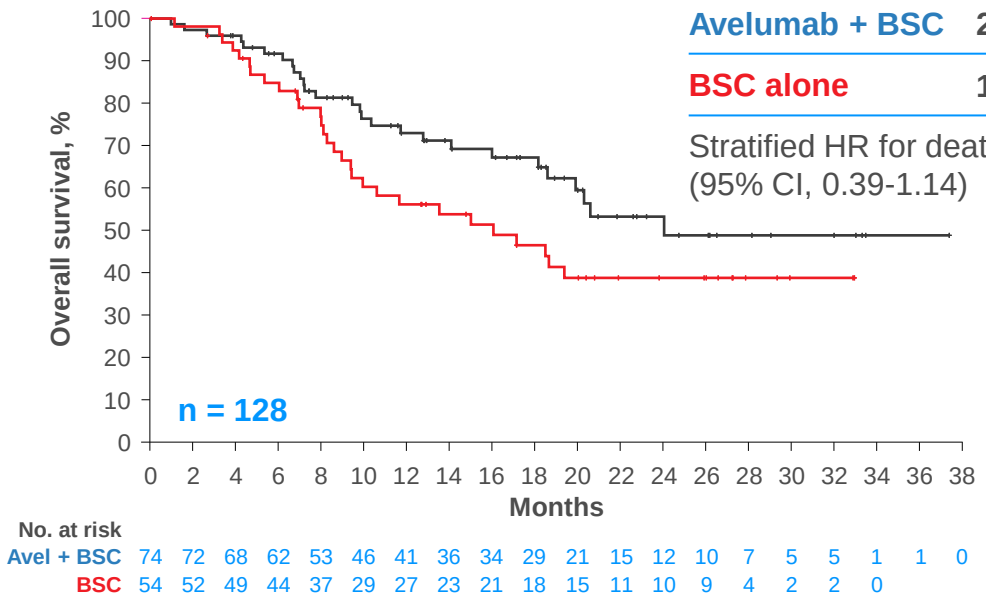
- This is an exploratory, post hoc analysis of OS data, inclusive of platinum-containing chemotherapy (4-6 cycles), treatment-free interval (4-10 weeks, per trial protocol), randomized study treatment with avelumab + BSC or BSC alone, and subsequent therapy
- This analysis only includes patients who did not progress on first-line platinum-containing chemotherapy and subsequently enrolled in the JAVELIN Bladder 100 trial
- Small patient numbers can be a limitation of subgroup analyses
- Safety data are not available pre-randomization
- No conclusions can be drawn from this OS analysis

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 Fransisco, CA.

OS and PFS Among Patients With PD-L1–Positive Tumors Who Received 1L Carboplatin + Gemcitabine[1,2]

Post hoc analysis

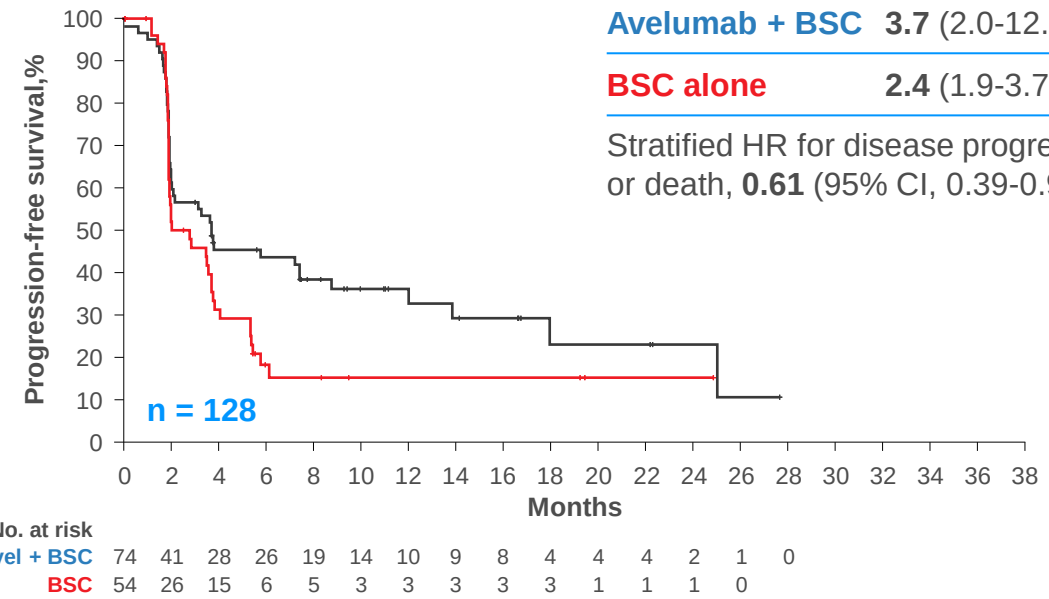


Median OS, months (95% CI)

Avelumab + BSC	**24.0** (18.6-NE)
BSC alone	**16.1** (9.4-NE)

Stratified HR for death, **0.67** (95% CI, 0.39-1.14)

No. at risk																				
Avel + BSC	74	72	68	62	53	46	41	36	34	29	21	15	12	10	7	5	5	1	1	0
BSC	54	52	49	44	37	29	27	23	21	18	15	11	10	9	4	2	2	0		



Median PFS, months (95% CI)

Avelumab + BSC	**3.7** (2.0-12.0)
BSC alone	**2.4** (1.9-3.7)

Stratified HR for disease progression or death, **0.61** (95% CI, 0.39-0.96)

No. at risk															
Avel + BSC	74	41	28	26	19	14	10	9	8	4	4	4	2	1	0
BSC	54	26	15	6	5	3	3	3	3	3	1	1	1	0	

Longer OS and PFS were observed with avelumab + BSC vs BSC alone in patients with PD-L1–positive tumors who received 1L carboplatin + gemcitabine, and findings were consistent with the overall JAVELIN Bladder 100 trial population

Limitations

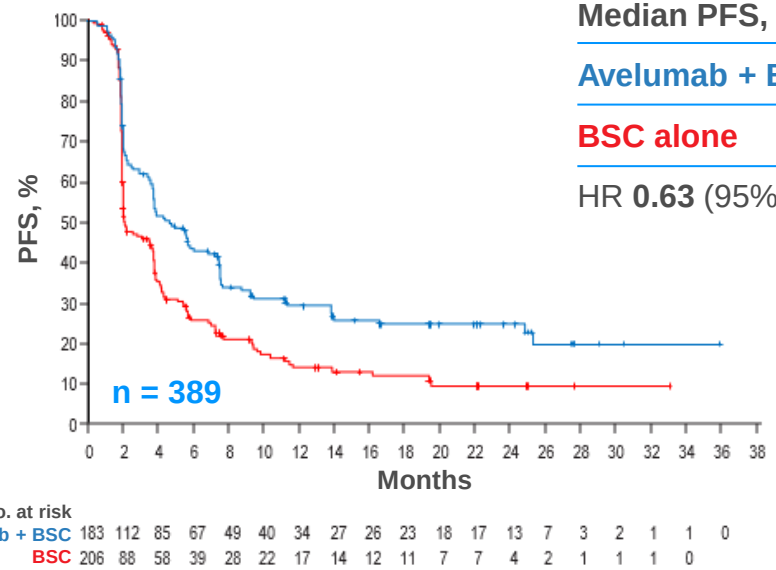
Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

1L, first line; Avel, avelumab; BSC, best supportive care; CI, confidence interval; HR, hazard ratio; NE, not estimable; OS, overall survival; PFS, progression-free survival.

1. Powles T, et al. Poster 4520. Presented at: ASCO Virtual Annual Meeting; June 4-8, 2021.

PFS in All Randomized Patients Who Received 1L Cisplatin + Gemcitabine[1,2]

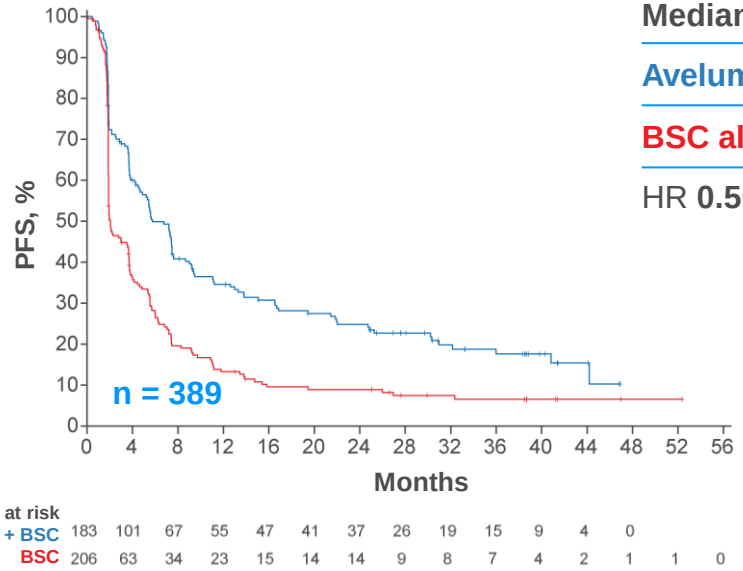
Protocol-specified subgroups



Median PFS, months (95% CI)	
Avelumab + BSC	**4.6** (3.6-6.8)
BSC alone	**2.0** (1.9-3.6)

HR **0.63** (95% CI, 0.50-0.81)

Exploratory post-hoc analysis



Median PFS, months (95% CI)	
Avelumab + BSC	**5.7** (4.6-7.5)
BSC alone	**2.0** (1.9-3.6)

HR **0.56** (95% CI, 0.45-0.71)

Investigator–assessed PFS was longer with avelumab + BSC vs BSC alone in patients who received 1L cisplatin + gemcitabine and maintained in the follow-up analysis

Limitations

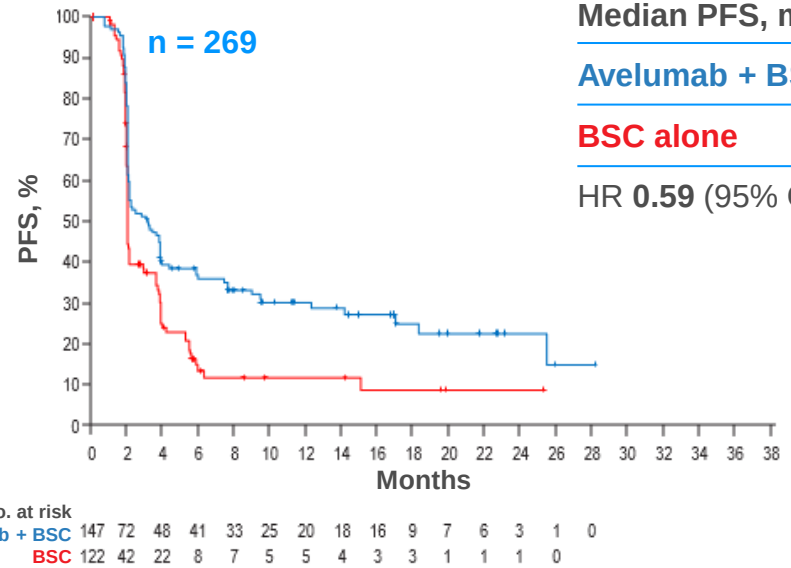
Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

1L, first-line; BSC, best supportive care; CI, confidence interval; HR, hazard ratio; PFS, progression-free survival.

1. Grivas P, et al. Abstract 704MO. Presented at: ESMO Virtual Congress; September 19-21, 2020; 2. Sridhar SS, et al. Poster 508. Presented at: ASCO GU Symposium; February 16-18, 2023; San Fransisco, CA.

PFS in All Randomized Patients Who Received 1L Carboplatin + Gemcitabine[1,2]

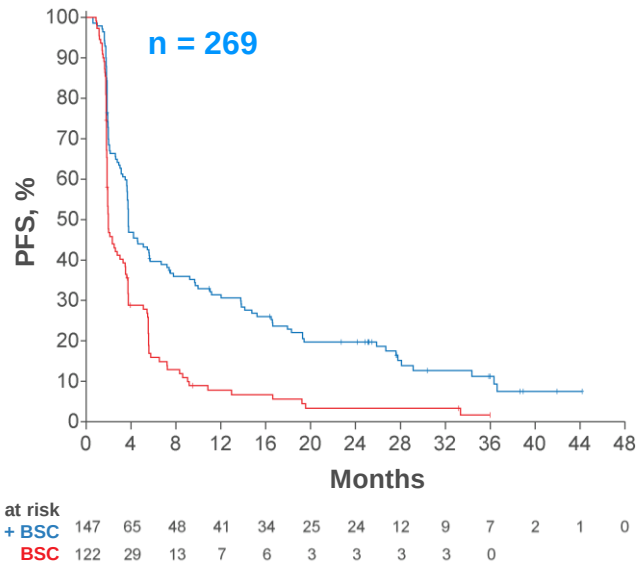
Protocol-specified subgroups



Median PFS, months (95% CI)	
Avelumab + BSC	**3.0** (2.0-3.7)
BSC alone	**1.9** (1.9-2.0)

HR **0.59** (95% CI, 0.44-0.80)

Exploratory post-hoc analysis



Median PFS, months (95% CI)	
Avelumab + BSC	**3.7** (3.6-5.6)
BSC alone	**2.0** (1.9-3.0)

HR **0.48** (95% CI, 0.36-0.64)

Investigator–assessed PFS was longer with avelumab + BSC vs BSC alone in patients who received 1L carboplatin + gemcitabine and maintained in the follow-up analysis

Limitations

Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

1L, first-line; BSC, best supportive care; CI, confidence interval; HR, hazard ratio; PFS, progression-free survival.

1. Grivas P, et al. Abstract 704MO. Presented at: ESMO Virtual Congress; September 19-21, 2020; 2. Sridhar SS, et al. Poster 508. Presented at: ASCO GU Symposium; February 16-18, 2023; San Fransisco, CA.

Patient Disposition by 1L CT Regimen[1]

	CISPLATIN + GEMCITABINE		CARBOPLATIN + GEMCITABINE	
	AVELUMAB + BSC (n = 183)	BSC ALONE (n = 206)	AVELUMAB + BSC (n = 147)	BSC ALONE (n = 122)
Study treatment ongoing at data cut-off, n (%)	28 (15.3)	7 (3.4)	10 (6.8)	1 (0.8)
Discontinued, n (%)	155 (84.7)	199 (96.6)	137 (93.2)	121 (99.2)
Progressive disease	109 (59.6)	164 (79.6)	91 (61.9)	93 (76.2)
Adverse event	19 (10.4)	2 (1.0)	26 (17.7)	0
Withdrew consent	14 (7.7)	17 (8.3)	8 (5.4)	13 (10.7)
Physician decision	6 (3.3)	4 (1.9)	4 (2.7)	3 (2.5)
Death	3 (1.6)	4 (1.9)	4 (2.7)	9 (7.4)
Global health deterioration	2 (1.1)	2 (1.0)	1 (0.7)	3 (2.5)
Other reason*	2 (1.1)	6 (2.9)	3 (2.0)	0

* Includes eligibility criteria no longer met, loss to follow-up, nonadherence to study drug, and other.

1L, first-line; BSC, best supportive care; CT, chemotherapy.

1. Sridhar SS, et al. Poster 508. Presented at: ASCO GU Symposium; February 16-18, 2023; San Fransisco, CA.

Secondary Endpoint: Updated Safety by Prior 1L CT Regimen[1]

EVENTS, n (%)	CISPLATIN + GEMCITABINE		CARBOPLATIN + GEMCITABINE	
	AVELUMAB + BSC (n = 182)	BSC ALONE (n = 204)	AVELUMAB + BSC (n = 142)	BSC ALONE (n = 119)
AE of any grade	**182 (100)**	**160 (78.4)**	**136 (95.8)**	**90 (75.6)**
Grade ≥3 AE	92 (50.5)	52 (25.0)	82 (57.7)	34 (28.6)
TRAE of any grade	147 (80.8)	5 (2.5)	107 (75.4)	1 (0.8)
Grade ≥3 TRAE	30 (16.5)	0	32 (22.5)	0
Serious AE	47 (25.8)	36 (17.6)	51 (35.9)	31 (26.1)
Serious TRAE	15 (8.2)	0	15 (10.6)	0
AE leading to interruption of avelumab	80 (44.0)	NA	69 (48.6)	NA
AE leading to discontinuation	19 (10.4)	0	27 (19.0)	0
TRAE leading to discontinuation	16 (8.8)	0	21 (14.8)	0
AE leading to death	3 (1.6)	9 (4.4)	4 (2.8)	12 (10.1)
TRAE leading to death	1 (0.5)	0	1 (0.7)	0
IRR of any grade	41 (22.5)	0	27 (19.0)	0

Long-term safety was similar in both the cisplatin + gemcitabine and carboplatin + gemcitabine subgroups, with no new safety concerns identified

For full definitions please refer to Powles T, et al. N Engl J Med. 2020;383(13):1218-1230.
1L, first line; AE, adverse event; BSC, best supportive care; CT, chemotherapy; IRR, infusion-related reaction; NA, not applicable; TRAE, treatment-related adverse event.
1. Sridhar SS, et al. Poster 508. Presented at: ASCO GU Symposium; February 16-18, 2023; San Fransisco, CA.

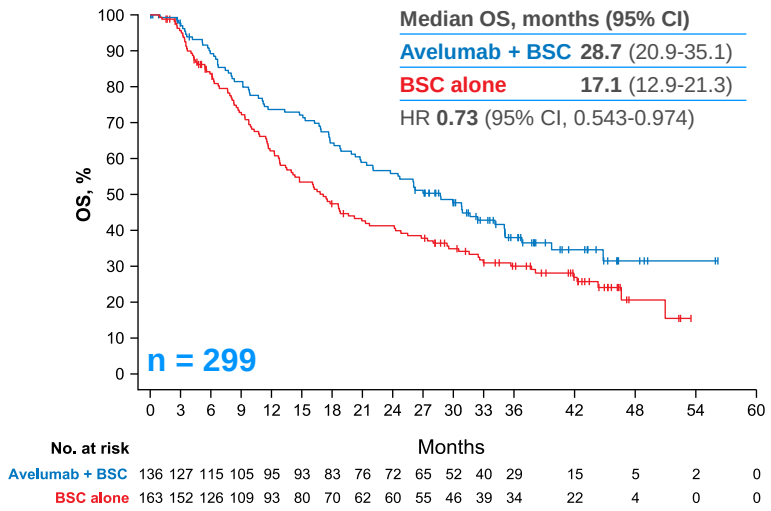
JAVELIN Bladder 100

Elderly Subgroup Data

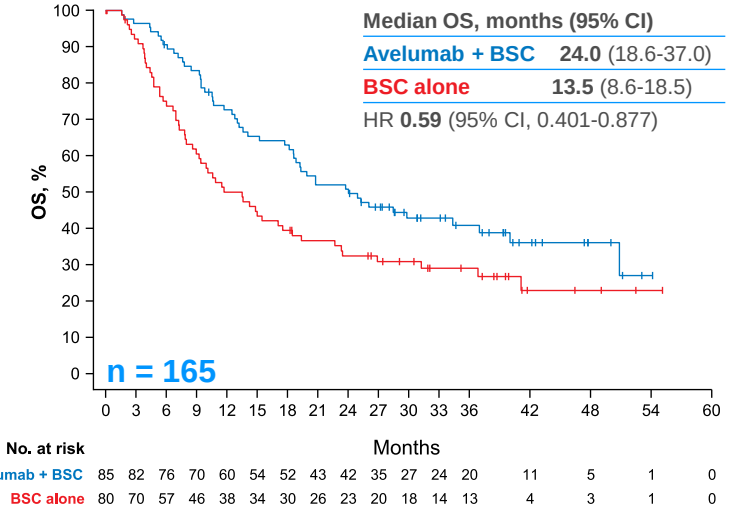
OS in Elderly Subgroups[1]

Exploratory post hoc analysis

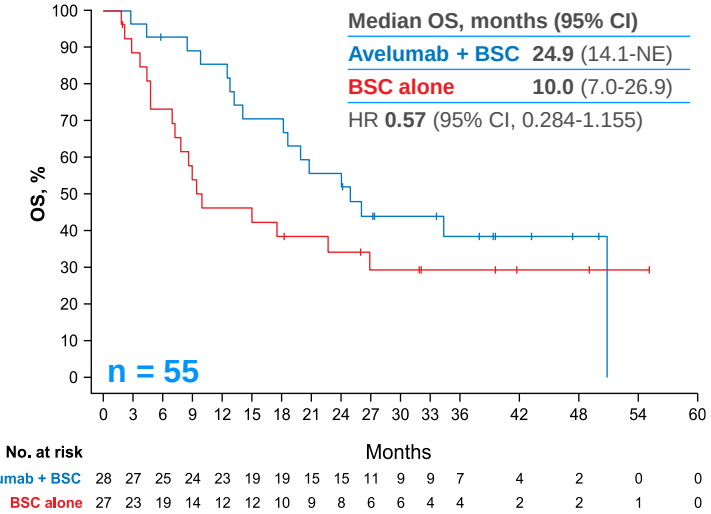
≥65 to <75 years



≥75 years



≥80 years



Limitations

Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

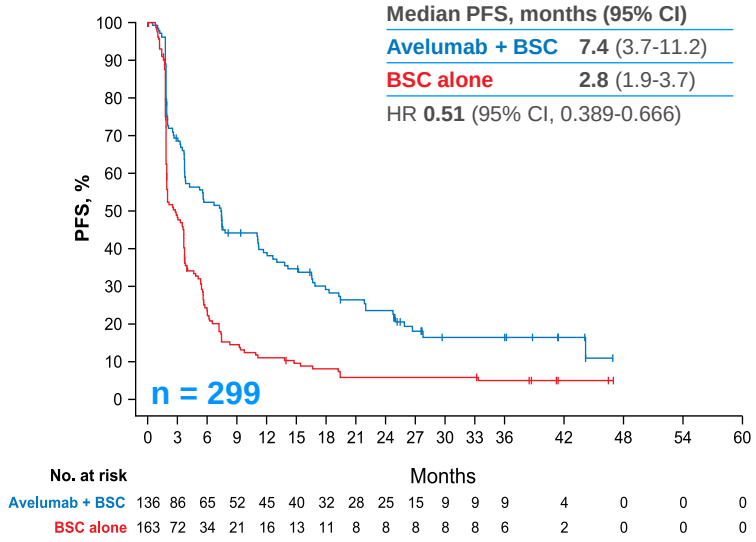
BSC, best supportive care; CI, confidence interval; HR, hazard ratio; OS, overall survival.

1. Gupta S, et al. Poster No. 2371P. Presented at: ESMO Congress 2023; October 20-24, 2023; Madrid, Spain.

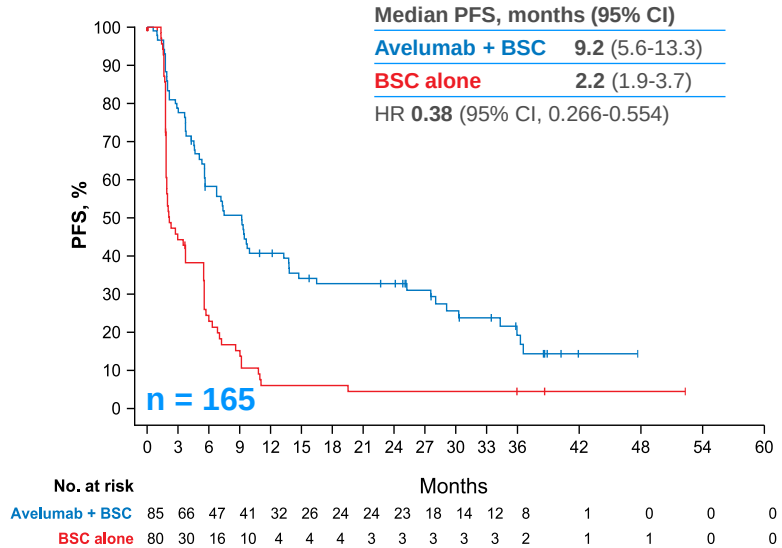
Secondary Endpoint: PFS in Elderly Subgroups[1]

Exploratory post hoc analysis

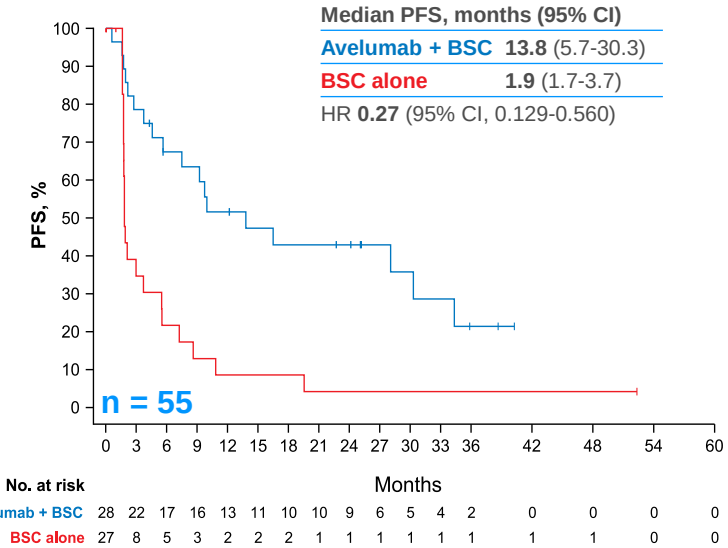
≥65 to <75 years



≥75 years



≥80 years



Limitations

Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

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

1. Gupta S, et al. Poster No. 2371P. Presented at: ESMO Congress 2023; October 20-24, 2023; Madrid, Spain.

Follow-up Analysis | Data Cut-off: June 4, 2021

Secondary Endpoint: Updated Safety by Age

Post hoc analysis

PATIENTS, N (%)	≥65 TO >75 YEARS		≥75 YEARS		≥80 YEARS	
	AVELUMAB + BSC (N = 130)	BSC ALONE (N = 162)	AVELUMAB + BSC (N = 85)	BSC ALONE (N = 77)	AVELUMAB + BSC (N = 28)	BSC ALONE (N = 27)
AE of any grade	**128 (98.5)**	**127 (78.4)**	**83 (97.6)**	**62 (80.5)**	**28 (100)**	**22 (81.5)**
Grade ≥3 AE	68 (52.3)	48 (29.6)	49 (57.6)	19 (24.7)	18 (64.3)	8 (29.6)
TRAE of any grade	103 (79.2)	2 (1.2)	70 (82.4)	2 (2.6)	24 (85.7)	0
Grade ≥3 TRAE	24 (18.5)	0	18 (21.2)	0	9 (32.1)	0
Serious AE	40 (30.8)	39 (24.1)	34 (40.0)	19 (24.7)	15 (53.6)	7 (25.9)
Serious TRAE	10 (7.7)	0	15 (17.6)	0	8 (28.6)	0
AE leading to discontinuation of study drug	17 (13.1)	0	18 (21.2)	0	7 (25.0)	0
TRAE leading to discontinuation of study drug	13 (10.0)	0	17 (20.0)	0	7 (25.0)	0
AE leading to death	2 (1.5)	9 (5.6)	3 (3.5)	10 (13.0)	1 (3.6)	4 (14.8)
TRAE leading to death	0	0	2 (2.4)	0	1 (3.6)	0
irAE of any grade	39 (30.0)	4 (2.5)	36 (42.4)	1 (1.3)	13 (46.4)	0
IRR of any grade	25 (19.2)	0	27 (31.8)	0	6 (21.4)	0

AE, adverse event; BSC, best supportive care; irAE, immune-related AE; IRR, infusion-related reaction; TRAE, treatment-related AE.

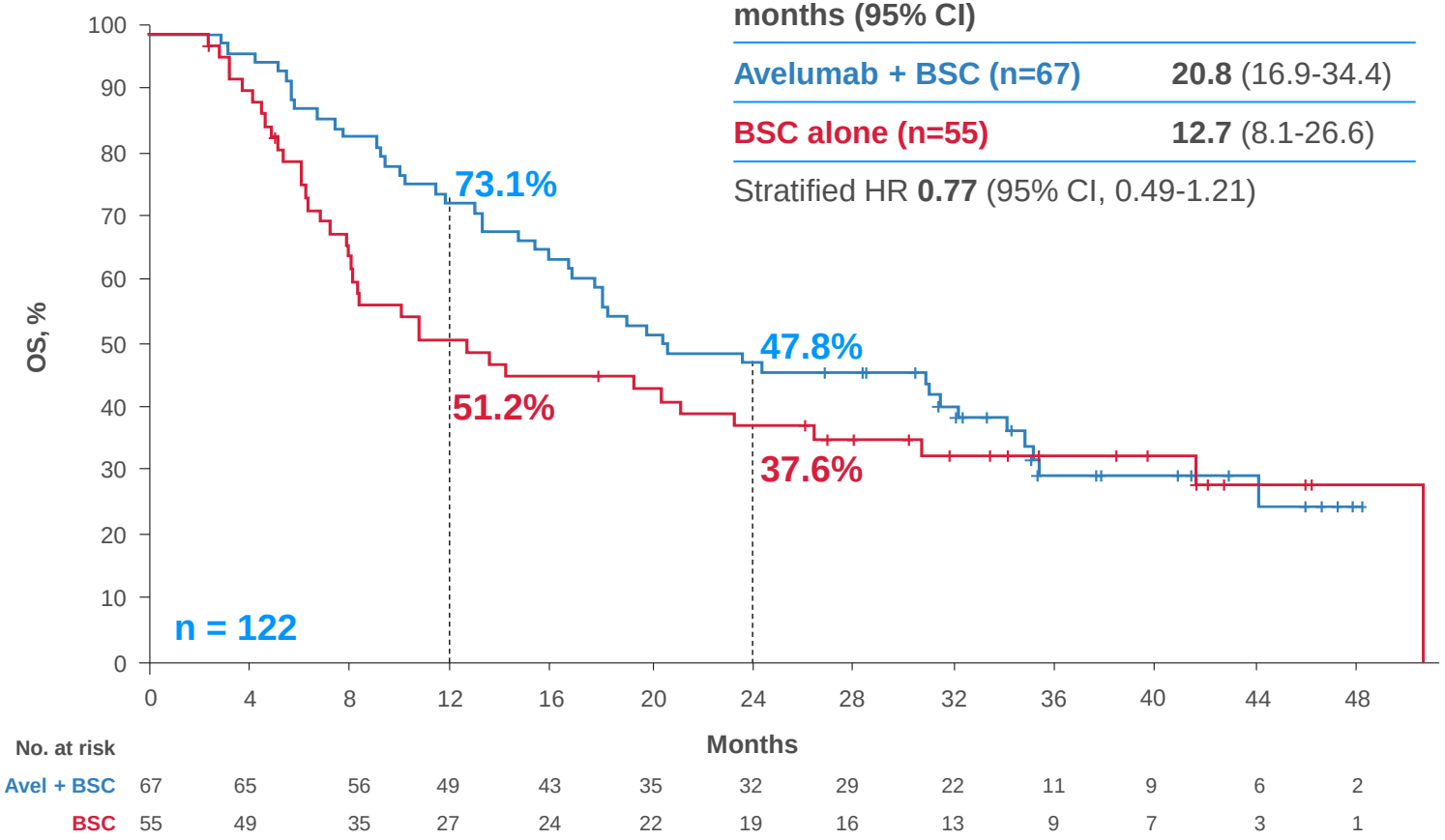
1. Gupta S, et al. Poster No. 2371P. Presented at: ESMO Congress 2023; October 20-24, 2023; Madrid, Spain.

JAVELIN Bladder 100

High BMI Subgroup Data

OS in Patients With High BMI[1]

Exploratory post hoc analysis



Median OS, months (95% CI)	
Avelumab + BSC (n=67)	**20.8** (16.9-34.4)
BSC alone (n=55)	**12.7** (8.1-26.6)

Stratified HR **0.77** (95% CI, 0.49-1.21)

Limitations

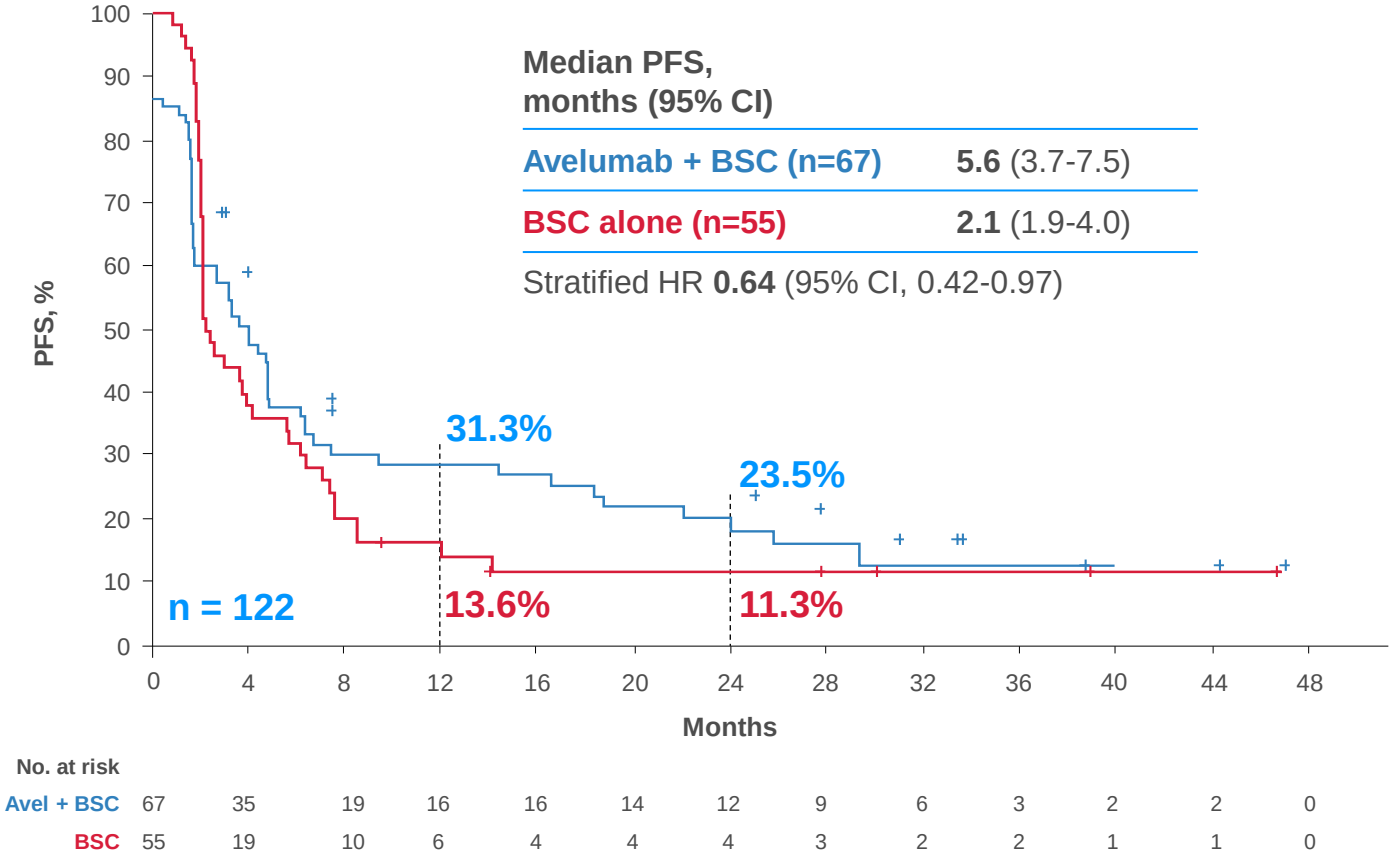
Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

BMI, body mass index; BSC, best supportive care; CI, confidence interval; HR, hazard ratio; OS, overall survival.

1. Aragon-Ching JB, et al. Abstract No. 600. Presented at: ASCO Genitourinary Cancers Symposium; January 25-27, 2024; San Francisco, CA.

Secondary Endpoint: PFS in Patients With High BMI

Exploratory post hoc analysis



Median PFS, months (95% CI)	
Avelumab + BSC (n=67)	**5.6** (3.7-7.5)
BSC alone (n=55)	**2.1** (1.9-4.0)

Stratified HR **0.64** (95% CI, 0.42-0.97)

No. at risk													
Avel + BSC	67	35	19	16	16	14	12	9	6	3	2	2	0
BSC	55	19	10	6	4	4	4	3	2	2	1	1	0

Limitations

Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

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

1. Aragon-Ching JB, et al. Abstract No. 600. Presented at: ASCO Genitourinary Cancers Symposium; January 25-27, 2024; San Francisco, CA.

Secondary Endpoint: Safety in Patients With High BMI[1]

Exploratory Post hoc analysis

	TREATED PATIENTS WITH HIGH BMI		OVERALL SAFETY POPULATION	
PATIENTS, n (%)	AVELUMAB + BSC (n = 67)	BSC ALONE (n = 54)	AVELUMAB + BSC (n = 344)	BSC ALONE (n = 345)
AE of any grade	**66 (98.5)**	**44 (81.5)**	**338 (98.3)**	**270 (78.3)**
Grade ≥3 AE	43 (64.2)	17 (31.5)	185 (53.8)	89 (25.8)
TRAE of any grade	54 (80.6)	2 (3.7)	269 (78.2)	6 (1.7)
Grade ≥3 TRAE	18 (26.9)	0	67 (19.5)	0
Serious AE	24 (35.8)	15 (27.8)	105 (30.5)	72 (20.9)
Serious TRAE	13 (19.4)	0	35 (10.2)	0
AE leading to discontinuation of study drug	8 (11.9)	0	49 (14.2)	0
TRAE leading to discontinuation of study drug	7 (10.4)	0	40 (11.6)	0
AE leading to death	3 (4.5)	7 (13.0)	7 (2.0)	24 (7.0)
TRAE leading to death	1 (1.5)*	0	2 (0.6)	0
irAE of any grade	24 (35.8)	0	111 (32.3)	6 (1.7)
IRR of any grade	15 (22.4)	0	75 (21.8)	0

*Attributed to immune-mediated nephritis by the investigator.

AE, adverse event; BMI, body mass index; BSC, best supportive care; irAE, immune-related adverse event; IRR, infusion-related reaction; TRAE, treatment-related adverse event.

1. Aragon-Ching JB, et al. Abstract No. 600. Presented at: ASCO Genitourinary Cancers Symposium; January 25-27, 2024; San Francisco, CA.

EMD SERONO

JAVELIN Bladder 100

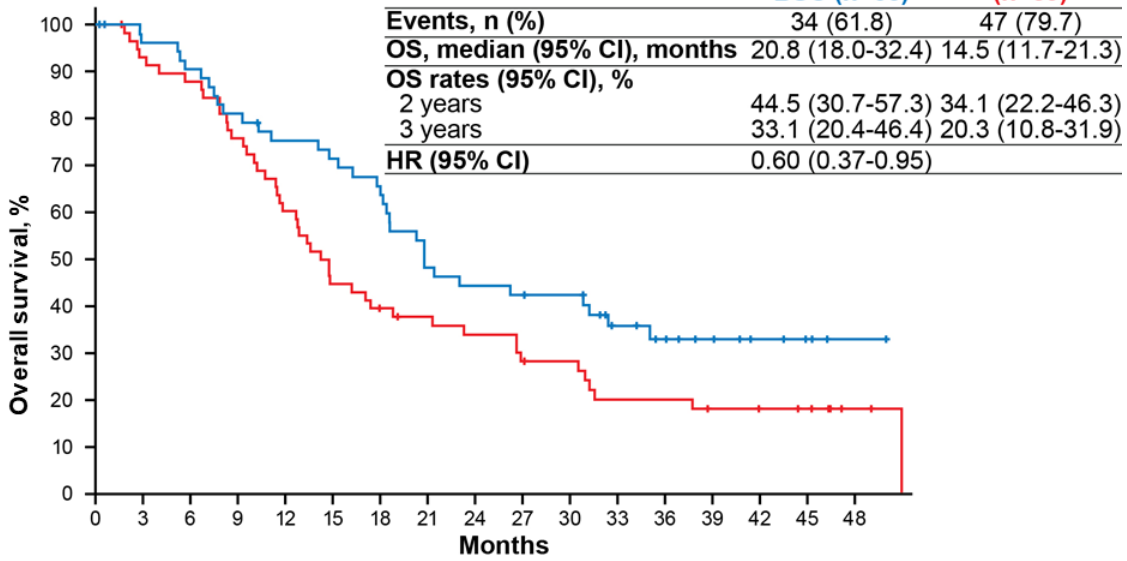
Diabetes Mellitus Subgroup Data

OS in Patients With or Without Diabetes Mellitus[1]

Post hoc analysis

Patients with controlled diabetes mellitus

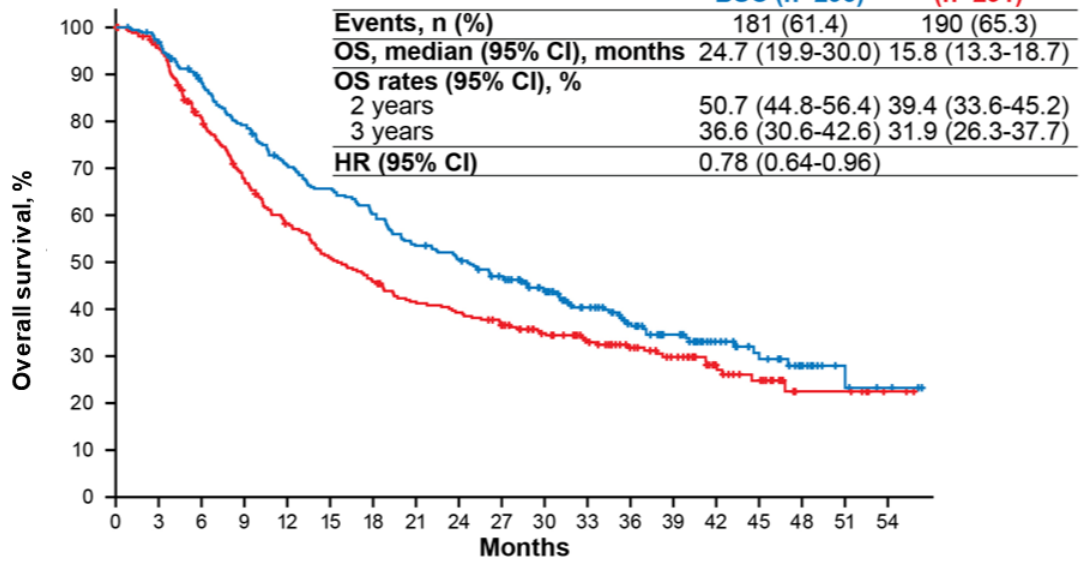
	Avelumab + BSC (n=55)	BSC alone (n=59)
Events, n (%)	34 (61.8)	47 (79.7)
OS, median (95% CI), months	20.8 (18.0-32.4)	14.5 (11.7-21.3)
OS rates (95% CI), %		
2 years	44.5 (30.7-57.3)	34.1 (22.2-46.3)
3 years	33.1 (20.4-46.4)	20.3 (10.8-31.9)
HR (95% CI)	0.60 (0.37-0.95)	



No. at risk																	
Avelumab + BSC	55	51	48	43	39	37	34	25	23	22	21	14	11	8	5	3	1
BSC	59	54	51	44	35	26	22	20	18	15	14	10	10	8	7	6	2

Patients without diabetes mellitus

	Avelumab + BSC (n=295)	BSC alone (n=291)
Events, n (%)	181 (61.4)	190 (65.3)
OS, median (95% CI), months	24.7 (19.9-30.0)	15.8 (13.3-18.7)
OS rates (95% CI), %		
2 years	50.7 (44.8-56.4)	39.4 (33.6-45.2)
3 years	36.6 (30.6-42.6)	31.9 (26.3-37.7)
HR (95% CI)	0.78 (0.64-0.96)	



No. at risk																		
Avelumab + BSC	295	280	250	224	198	184	169	150	141	127	98	80	63	50	34	23	12	5	3
BSC	291	268	220	182	155	136	122	108	103	92	78	64	52	42	27	18	8	8	2

Limitations

Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

In subgroups with or without diabetes mellitus, OS was prolonged with avelumab + BSC vs BSC alone

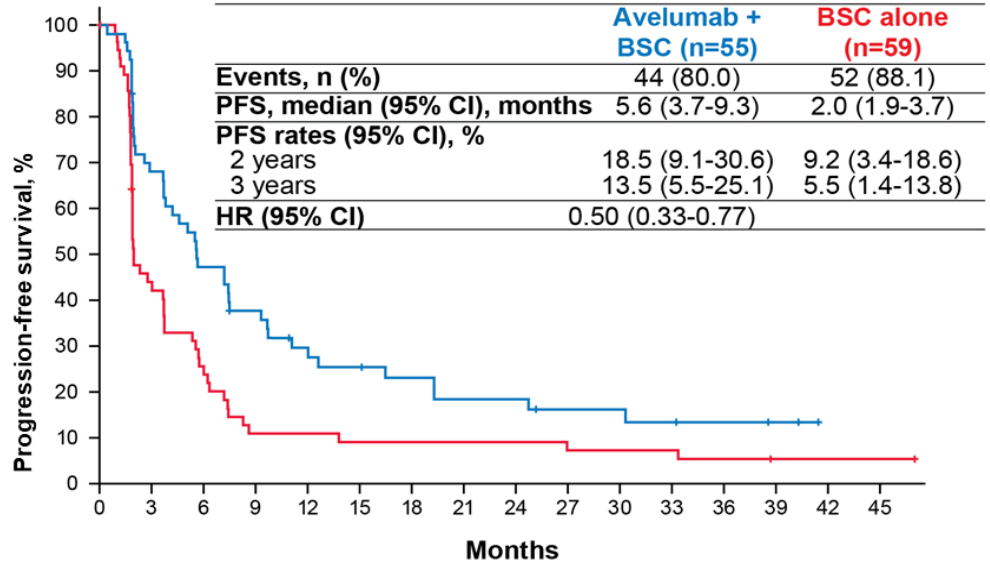
BSC, best supportive care; CI, confidence interval; HR, hazard ratio; OS, overall survival.

1. Gupta S, et al. Abstract No. 869. Presented at the ASCO Genitourinary Cancers Symposium, February 13-15, 2025; San Francisco, CA.

PFS in Patients With or Without Diabetes Mellitus[1]

Post hoc analysis

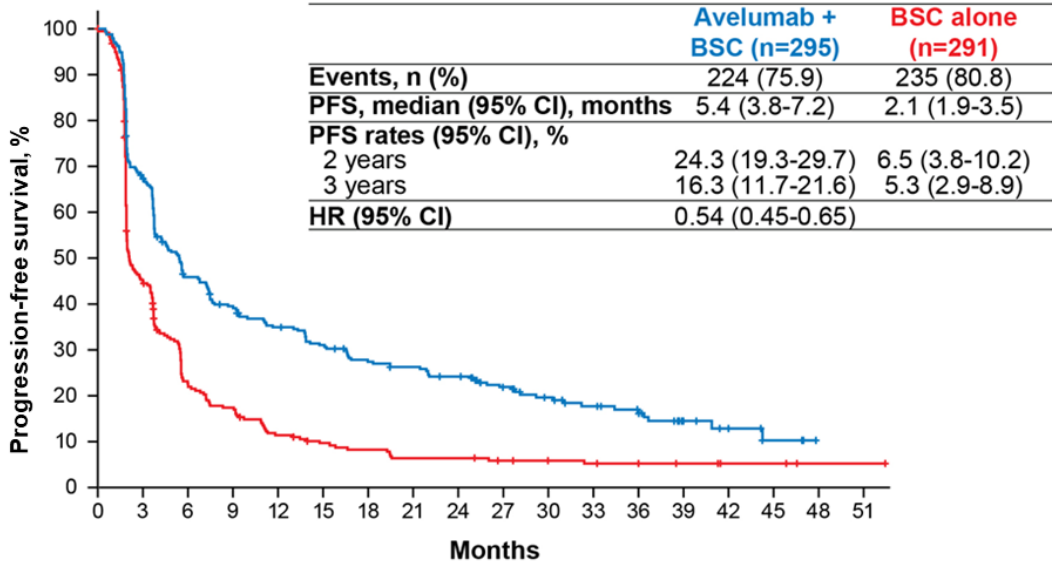
Patients with controlled diabetes mellitus



	Avelumab + BSC (n=55)	BSC alone (n=59)
Events, n (%)	44 (80.0)	52 (88.1)
PFS, median (95% CI), months	5.6 (3.7-9.3)	2.0 (1.9-3.7)
PFS rates (95% CI), %		
2 years	18.5 (9.1-30.6)	9.2 (3.4-18.6)
3 years	13.5 (5.5-25.1)	5.5 (1.4-13.8)
HR (95% CI)	0.50 (0.33-0.77)	

No. at risk																
Avelumab + BSC	55	36	25	19	14	12	10	8	8	6	6	5	4	3	0	0
BSC	59	24	14	6	6	5	5	5	5	4	4	4	3	1	1	1

Patients without diabetes mellitus



	Avelumab + BSC (n=295)	BSC alone (n=291)
Events, n (%)	224 (75.9)	235 (80.8)
PFS, median (95% CI), months	5.4 (3.8-7.2)	2.1 (1.9-3.5)
PFS rates (95% CI), %		
2 years	24.3 (19.3-29.7)	6.5 (3.8-10.2)
3 years	16.3 (11.7-21.6)	5.3 (2.9-8.9)
HR (95% CI)	0.54 (0.45-0.65)	

No. at risk																		
Avelumab + BSC	295	189	124	105	91	80	69	65	59	44	33	26	21	10	6	3	0	0
BSC	291	113	55	42	27	21	18	14	14	11	9	8	6	5	3	3	1	1

Limitations

Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

In subgroups with or without diabetes mellitus, PFS was prolonged with avelumab + BSC vs BSC alone

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

*

1. Gupta S, et al. Abstract No. 869. Presented at the ASCO Genitourinary Cancers Symposium, February 13-15, 2025; San Francisco, CA.

Long-term Safety in Patients With or Without Diabetes Mellitus[1]

Post hoc analysis

	PATIENT WITH CONTROLLED DIABETES MELLITUS		PATIENT WITHOUT DIABETES MELLITUS	
PATIENTS, n (%)	AVELUMAB + BSC (n = 54)	BSC ALONE (n = 59)	AVELUMAB + BSC (n = 290)	BSC ALONE (n = 286)
AE of any grade	52 (96.3)	45 (76.3)	286 (98.6)	225 (78.7)
Grade ≥3 AE	32 (59.3)	18 (30.5)	153 (52.8)	71 (24.8)
TRAE of any grade	41 (75.9)	1 (1.7)	228 (78.6)	5 (1.7)
Grade ≥3 TRAE	13 (24.1)	0	54 (18.6)	0
Serious AE	20 (37.0)	14 (23.7)	85 (29.3)	58 (20.3)
Serious TRAE	5 (9.3)	0	30 (10.3)	0
AE leading to discontinuation of avelumab	6 (11.1)	–	43 (14.8)	–
TRAE leading to discontinuation of avelumab	5 (9.3)	–	35 (12.1)	–
AE leading to death	1 (1.9)	6 (10.2)	6 (2.1)	18 (6.3)
TRAE leading to death	0	0	2 (0.7)	0
irAE of any grade	17 (31.5)	2 (3.4)	94 (32.4)	4 (1.4)

The long-term safety of avelumab 1L maintenance was similar in patients with or without diabetes mellitus at randomization

AE, adverse event; BSC, best supportive care; irAE, immune-related AE; IRR, infusion-related reaction; TRAE, treatment-related AE; UC, urothelial carcinoma.

1. Loriot Y, et al. Abstract No. 4567. Presented at the 2024 ASCO Annual Meeting, May 31-June 4, 2024; Chicago, IL.

Most Common TRAEs in Patients With or Without Diabetes Mellitus[1]

Post hoc analysis

PATIENTS, n (%)	PATIENTS WITH CONTROLLED DIABETES MELLITUS (n=54)	PATIENTS WITH CONTROLLED DIABETES MELLITUS (n=290)	OVERALL AVELUMAB + BSC ARM (n=344)
TRAE of any grade	41 (75.9)	228 (78.6)	269 (78.2)
Pruritus	6 (11.1)	45 (15.5)	51 (14.8)
Hypothyroidism	4 (7.4)	34 (11.7)	38 (11.0)
Fatigue	3 (5.6)	34 (11.7)	37 (10.8)
Asthenia	5 (9.3)	31 (10.7)	36 (10.5)
Diarrhea	4 (7.4)	32 (11.0)	36 (10.5)
Infusion-related reaction	3 (5.6)	31 (10.7)	34 (9.9)
Rash	7 (13.0)	20 (6.9)	27 (7.8)
Arthralgia	2 (3.7)	23 (7.9)	25 (7.3)
Nausea	5 (9.3)	20 (6.9)	25 (7.3)
Grade ≥3 TRAE	13 (24.1)	54 (18.6)	67 (19.5)
Lipase increased	2 (3.7)	10 (3.4)	12 (3.5)
Amylase increased	1 (1.9)	7 (2.4)	8 (2.3)
Anemia	2 (3.7)	3 (1.0)	5 (1.5)

Most common TRAEs that occurred in patients with or without diabetes mellitus at randomization were consistent with those observed in the overall population

Any-grade and grade ≥3 TRAEs that occurred in >7% and >1% of patients in the overall avelumab + BSC arm, respectively, are shown.
BSC, best supportive care; TRAE, treatment-related adverse event.

1. Gupta S, et al. Abstract No. 869. Presented at the ASCO Genitourinary Cancers Symposium, February 13-15, 2025; San Francisco, CA.

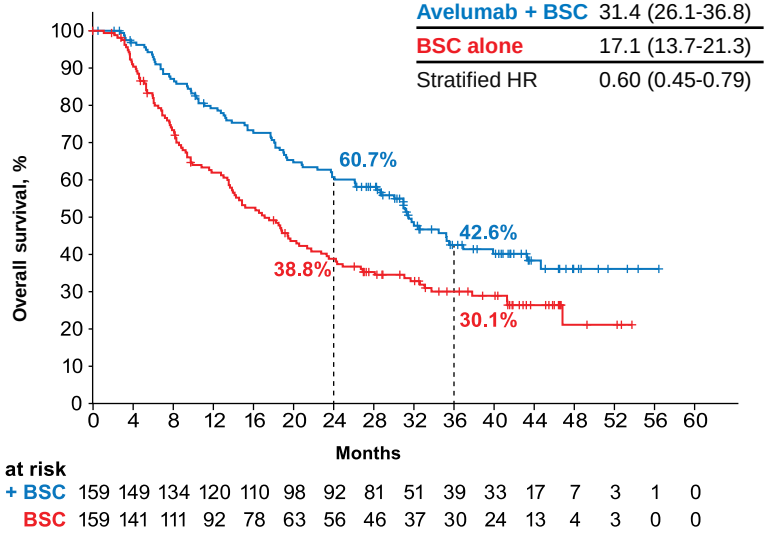
JAVELIN Bladder 100

Low Tumor Burden Subgroup Data

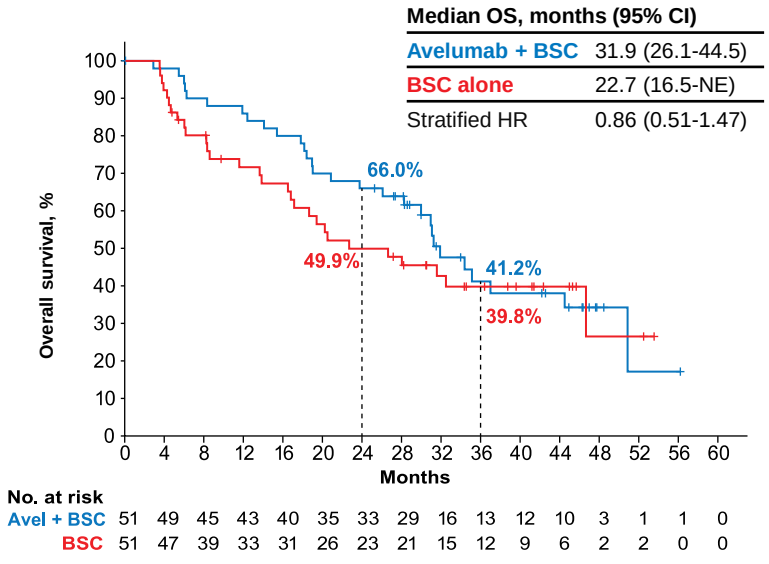
OS in Patients With Low Tumor Burden[1]

Post hoc analysis

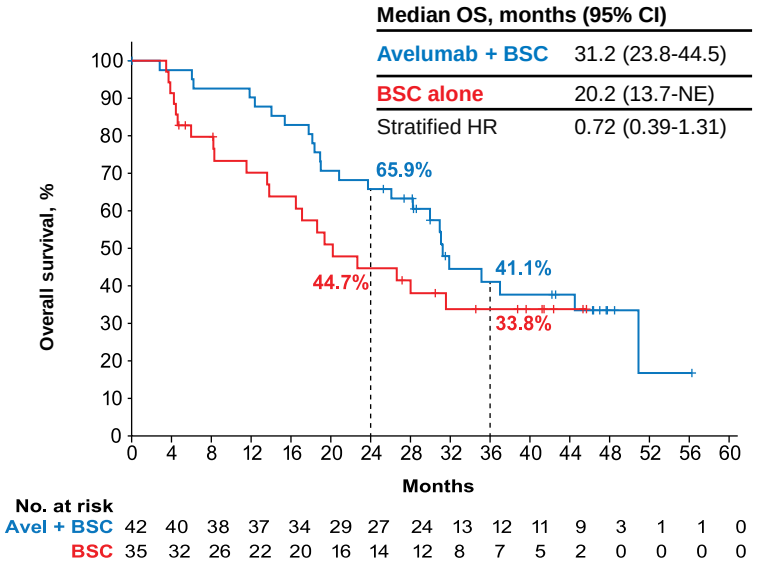
Nonvisceral metastases



Lymph node-only disease



Pelvic/retroperitoneal lymph node-only disease



In patients with low tumor burden, OS was prolonged in the avelumab + BSC arm vs the BSC alone arm

Limitations

Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

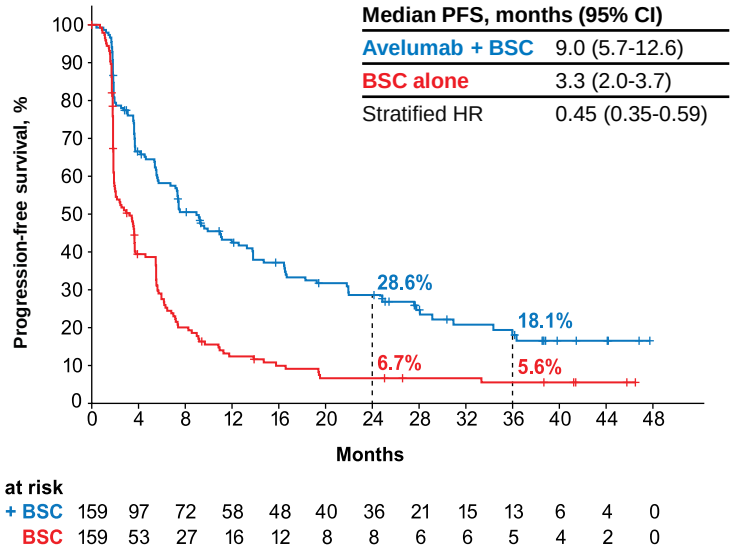
BSC, best supportive care; HR, hazard ratio; NE, not evaluable; OS, overall survival

1. Bellmunt J , et al. Abstract No. 4566. Presented at the 2024 ASCO Annual Meeting, May 31-June 4, 2024; Chicago, IL.

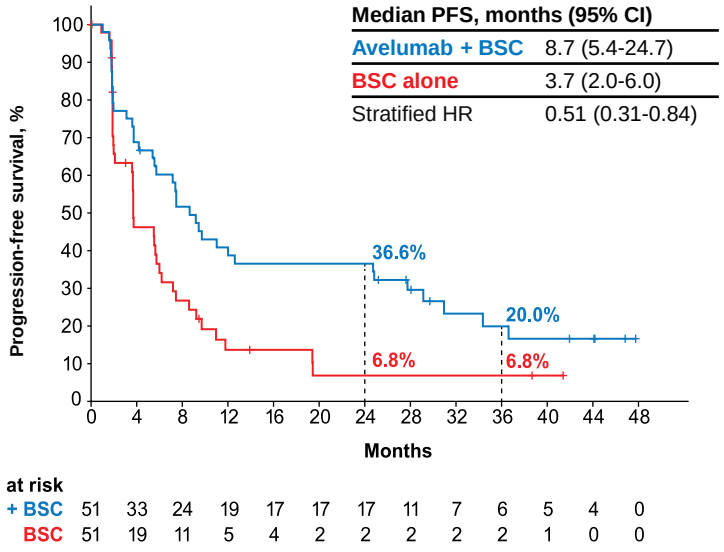
Secondary Endpoint: PFS in Patients With Low Tumor Burden[1]

Post hoc analysis

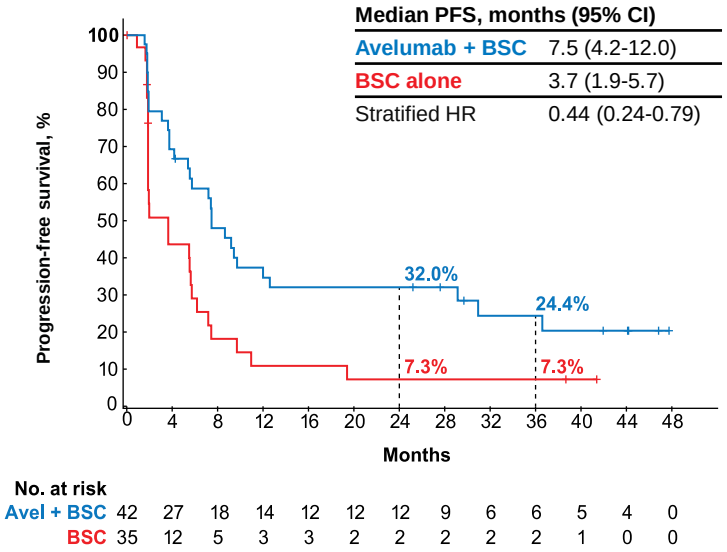
Nonvisceral metastases



Lymph node-only disease



Pelvic/retroperitoneal lymph node-only disease



In patients with low tumor burden, investigator-assessed PFS was prolonged in the avelumab + BSC arm vs the BSC alone arm

Limitations

Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

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

1. Bellmunt J , et al. Abstract No. 4566. Presented at the 2024 ASCO Annual Meeting, May 31-June 4, 2024; Chicago, IL.

Secondary Endpoint: Safety in Patients With Low Tumor Burden[1]

Post hoc analysis

	NONVISCERAL METASTASES		LYMPH NODE–ONLY DISEASE		PELVIC/RETROPERITONEAL LYMPH NODE–ONLY DISEASE	
PATIENTS, n (%)	AVELUMAB + BSC (n = 158)	BSC ALONE (n = 157)	AVELUMAB + BSC (n = 50)	BSC ALONE (n = 50)	AVELUMAB + BSC (n = 41)	BSC ALONE (n = 34)
AE of any grade	156 (98.7)	133 (84.7)	50 (100)	37 (74.0)	41 (100)	24 (70.6)
Grade ≥3 AE	93 (58.9)	43 (27.4)	33 (66.0)	11 (22.0)	29 (70.7)	7 (20.6)
TRAE of any grade	122 (77.2)	2 (1.3)	44 (88.0)	0	36 (87.8)	0
Grade ≥3 TRAE	30 (19.0)	0	8 (16.0)	0	6 (14.6)	0
Serious AE	55 (34.8)	40 (25.5)	20 (40.0)	12 (24.0)	18 (43.9)	9 (26.5)
Serious TRAE	18 (11.4)	0	7 (14.0)	0	5 (12.2)	0
AE leading to discontinuation of study drug	24 (15.2)	0	5 (10.0)	0	4 (9.8)	0
TRAE leading to discontinuation of study drug	21 (13.3)	0	3 (6.0)	0	2 (4.9)	0
AE leading to death	2 (1.3)	11 (7.0)	3 (6.0)	4 (8.0)	2 (4.9)	2 (5.9)
TRAE leading to death	2 (1.3)	0	1 (2.0)	0	0	0
irAE of any grade	52 (32.9)	5 (3.2)	17 (34.0)	3 (6.0)	15 (36.6)	3 (8.8)
IRR of any grade	33 (20.9)	0	12 (24.0)	0	9 (22.0)	0

AE, adverse event; BSC, best supportive care; irAE, immune-related AE; IRR, infusion-related reaction; TRAE, treatment-related AE.

1. Bellmunt J , et al. Abstract No. 4566. Presented at the 2024 ASCO Annual Meeting, May 31-June 4, 2024; Chicago, IL.

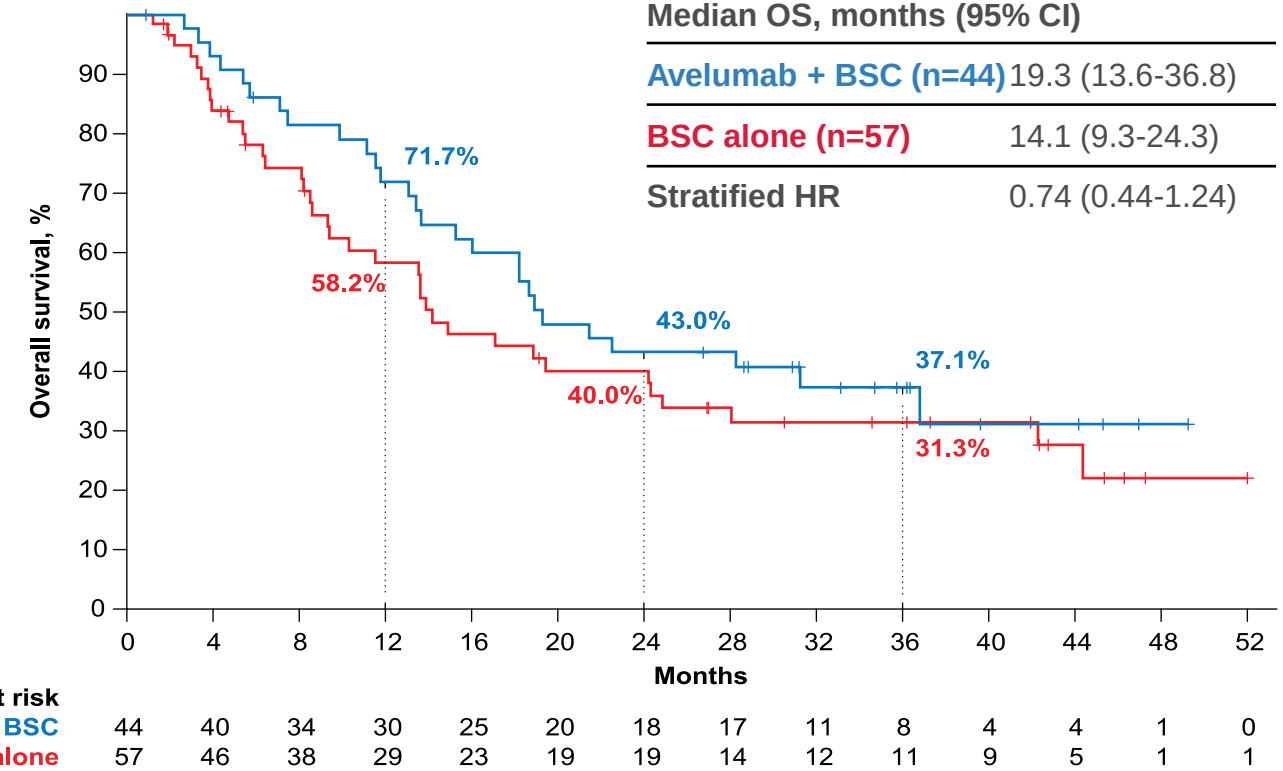
JAVELIN
Bladder 100

Mixed Variant Histological Subtypes Data

OS in Patients With UC Mixed With Histological Subtypes[1]

Exploratory post hoc analysis

In patients with histological subtypes, OS was prolonged in the avelumab + BSC vs the BSC alone arm



Median OS, months (95% CI)	
Avelumab + BSC (n=44)	19.3 (13.6-36.8)
BSC alone (n=57)	14.1 (9.3-24.3)
Stratified HR	0.74 (0.44-1.24)

Limitations

Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

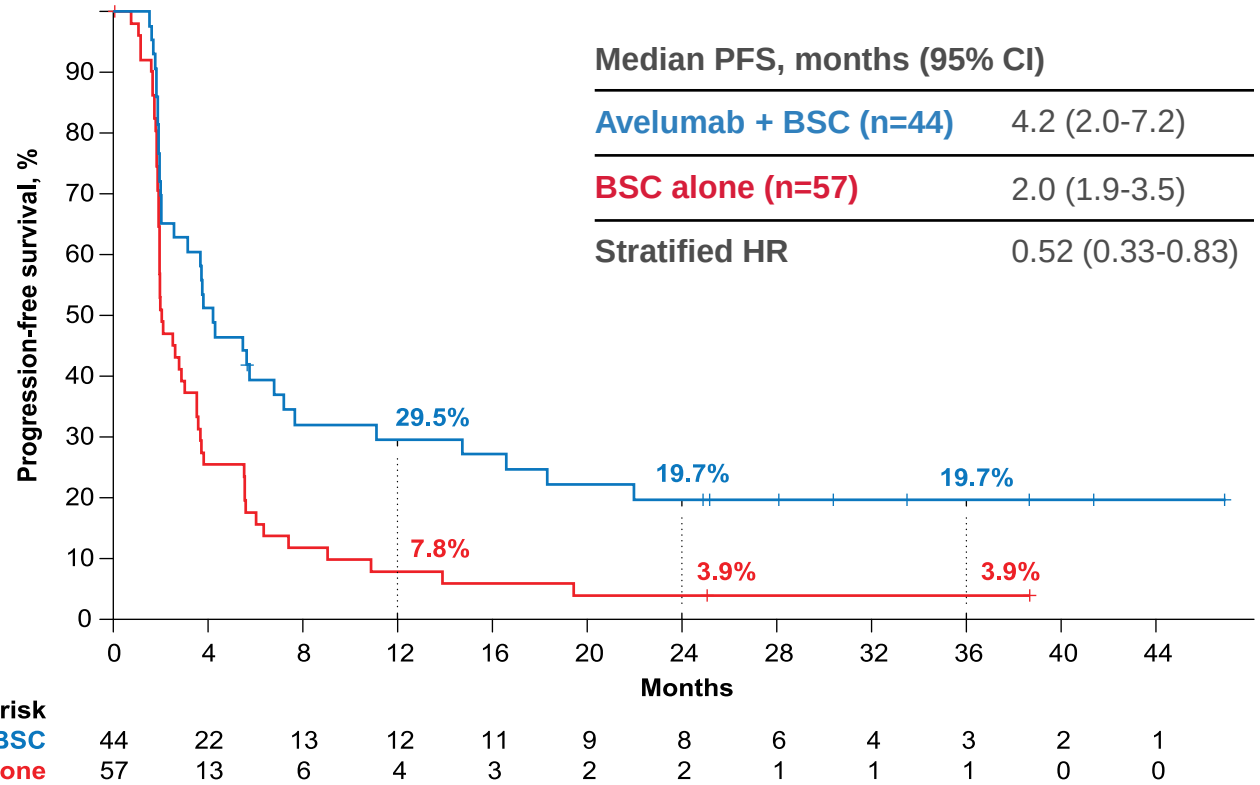
BSC, best supportive care; HR, hazard ratio; OS, overall survival; UC, urothelial carcinoma.

1. Loriot Y, et al. Abstract No. 4567. Presented at the 2024 ASCO Annual Meeting, May 31-June 4, 2024; Chicago, IL.

Secondary Endpoint: PFS in Patients With UC Mixed With Histological Subtypes[1]

Exploratory post hoc analysis

In patients with histological subtypes, investigator-assessed PFS was prolonged in the avelumab + BSC vs the BSC alone arm



Median PFS, months (95% CI)	
Avelumab + BSC (n=44)	4.2 (2.0-7.2)
BSC alone (n=57)	2.0 (1.9-3.5)
Stratified HR	0.52 (0.33-0.83)

Limitations

Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

BSC, best supportive care; HR, hazard ratio; PFS, progression-free survival; UC, urothelial carcinoma.

1. Loriot Y, et al. Abstract No. 4567. Presented at the 2024 ASCO Annual Meeting, May 31-June 4, 2024; Chicago, IL.

Secondary Endpoint: Safety in Patients With UC Mixed With Histological Subtypes[1]

Exploratory post hoc analysis

	TREATED PATIENTS WITH UC MIXED WITH HISTOLOGICAL SUBTYPES		OVERALL SAFETY POPULATION	
PATIENTS, n (%)	AVELUMAB + BSC (n = 43)	BSC ALONE (n = 57)	AVELUMAB + BSC (n = 344)	BSC ALONE (n = 345)
AE of any grade	43 (100)	51 (89.5)	338 (98.3)	270 (78.3)
Grade ≥3 AE	24 (55.8)	18 (31.6)	188 (54.7)	90 (26.1)
TRAE of any grade	36 (83.7)	1 (1.8)	272 (79.1)	5 (1.4)
Grade ≥3 TRAE	9 (20.9)	0	69 (20.1)	0
Serious AE	13 (30.2)	15 (26.3)	111 (32.3)	73 (21.2)
Serious TRAE	3 (7.0)	0	35 (10.2)	0
AE leading to discontinuation of study drug	7 (16.3)	0	50 (14.5)	0
TRAE leading to discontinuation of study drug	6 (14.0)	0	40 (11.6)	0
AE leading to death	0	6 (10.5)	7 (2.0)	24 (7.0)
TRAE leading to death	0	0	2 (0.6)	0
irAE of any grade	15 (34.9)	0	113 (32.8)	7 (2.0)
IRR of any grade	10 (23.3)	0	74 (21.5)	0

AE, adverse event; BSC, best supportive care; irAE, immune-related AE; IRR, infusion-related reaction; TRAE, treatment-related AE; UC, urothelial carcinoma.

1. Loriot Y, et al. Abstract No. 4567. Presented at the 2024 ASCO Annual Meeting, May 31-June 4, 2024; Chicago, IL.

JAVELIN Bladder 100

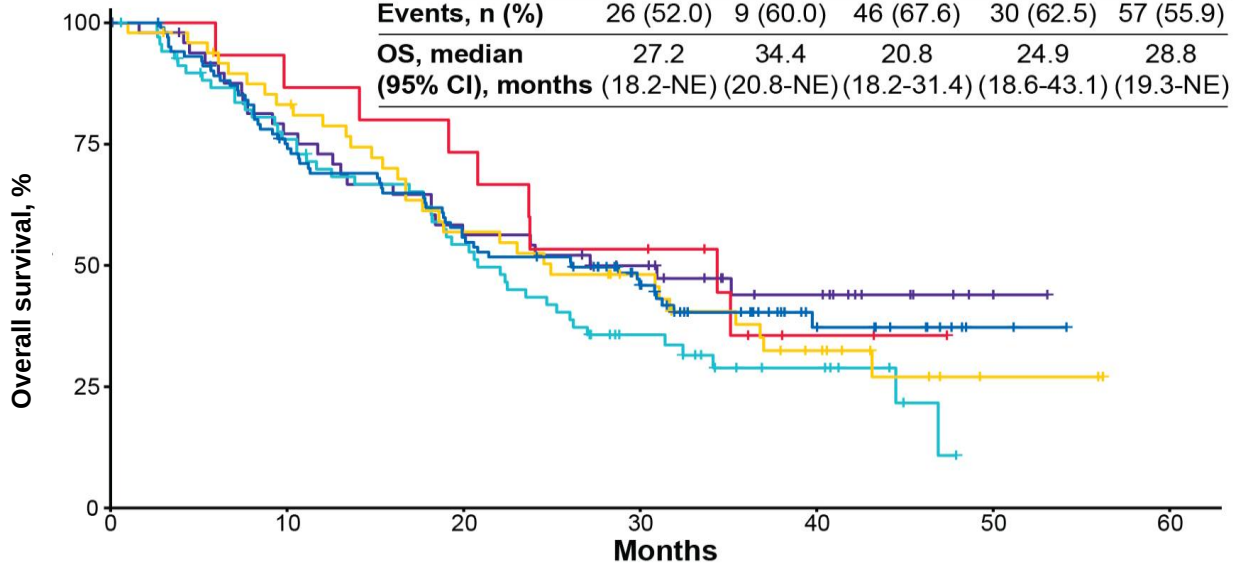
Molecular Subtypes Data

OS in Subgroups Defined by Molecular Subtype[1]

Post hoc analysis

No significant difference in OS was noted across molecular subtypes

	Ba/Sq (n=50)	LumNS (n=15)	LumP (n=68)	LumU (n=48)	SR (n=102)
Events, n (%)	26 (52.0)	9 (60.0)	46 (67.6)	30 (62.5)	57 (55.9)
OS, median (95% CI), months	27.2 (18.2-NE)	34.4 (20.8-NE)	20.8 (18.2-31.4)	24.9 (18.6-43.1)	28.8 (19.3-NE)



No. at risk							
Ba/Sq	50	37	27	21	12	2	0
LumNS	15	13	11	8	2	0	0
LumP	69	50	35	17	8	0	0
LumU	49	39	26	19	10	2	0
SR	103	74	55	35	12	2	0

Limitations

Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

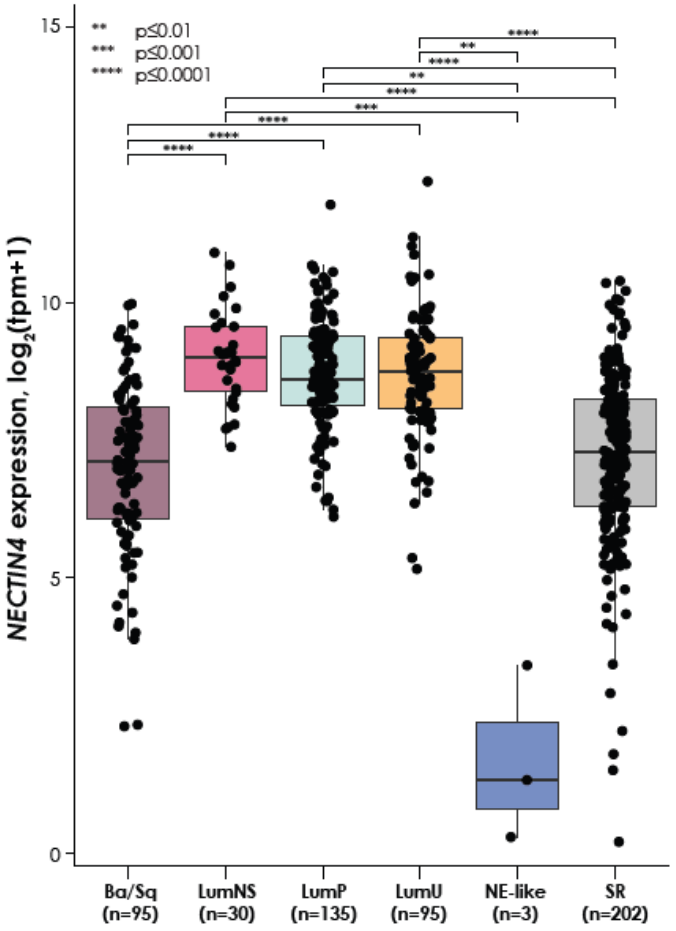
Ba/Sq, basal/squamous; CI, confidence interval; LumNS, luminal nonspecified; LumP, luminal papillary; LumU, luminal unstable; NE, not evaluable; OS, overall survival; SR, stroma rich.

1. Eckstein M., et al. Abstract No. 828. Presented at the ASCO Genitourinary Cancers Symposium, February 13-15, 2025; San Francisco, CA.

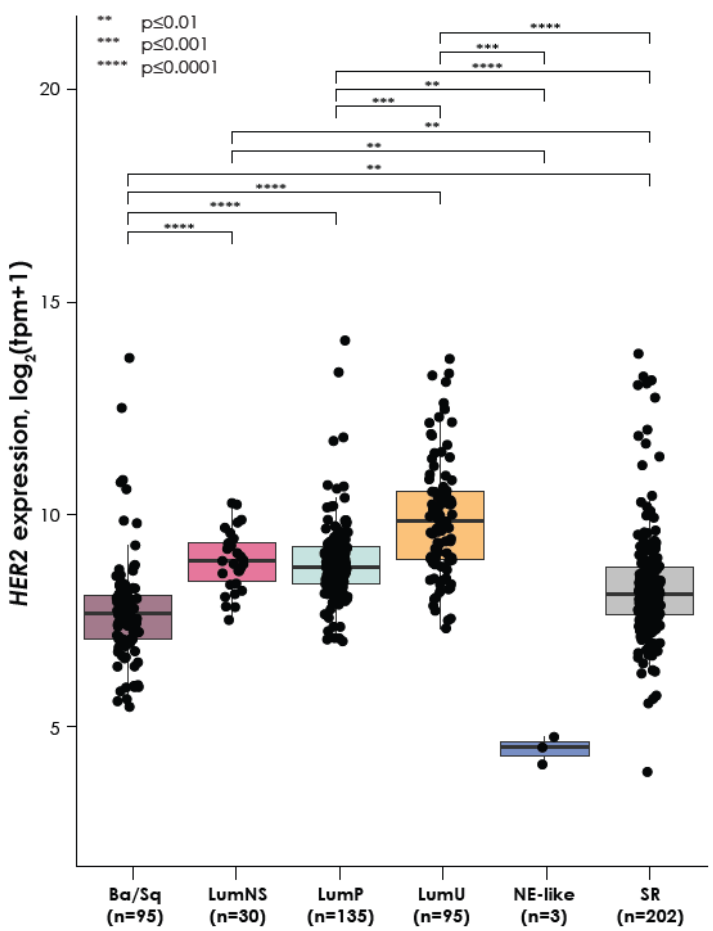
NECTIN4 and *HER2* RNA Expression Defined by Molecular Subtype[1]

Post hoc analysis

NECTIN4 RNA expression



HER2 RNA expression



NECTIN4 and *HER2* RNA expression were heterogeneous across molecular subtypes

- Expression patterns across subtypes were highly similar for both biomarkers, with highest *NECTIN4* and *HER2* RNA expression in the LumU, LumP and LumNS subtypes, and lowest expression in the NE-like subtype

Limitations

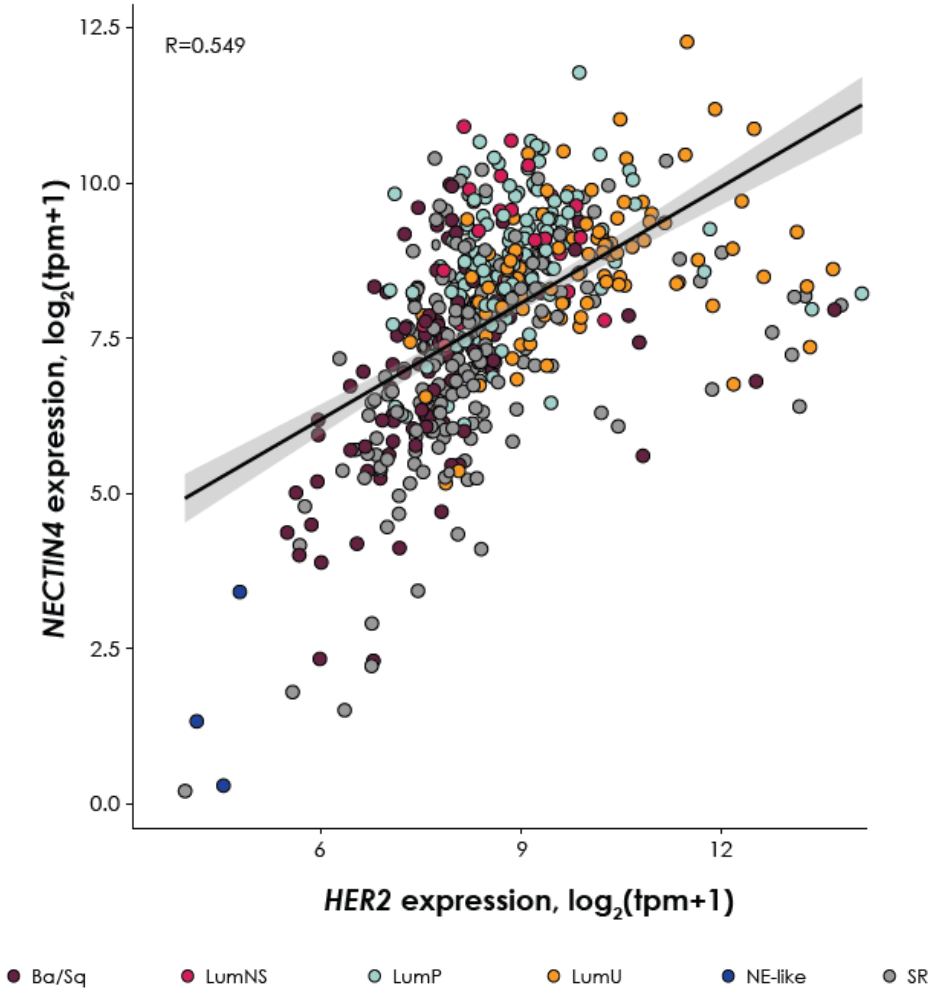
Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

Ba/Sq, basal/squamous; LumNS, luminal nonspecified; LumP, luminal papillary; LumU, luminal unstable; NE-like, neuroendocrine-like; SR, stroma rich, tpm, transcripts per million.

1. Eckstein M., et al. Abstract No. 828. Presented at the ASCO Genitourinary Cancers Symposium, February 13-15, 2025; San Francisco, CA.

Correlation Between *NECTIN4 and HER2* RNA Expression[1]

Post hoc analysis



A strong correlation between *NECTIN4* and *HER2* RNA expression was observed overall

- 57% of tumors had high (≥ median) expression of both *NECTIN4* and *HER2*
- Expression of only one marker (*NECTIN4* or *HER2*) within a tumor sample was rarely observed

Limitations

Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

*Ba/Sq, basal/squamous; LumNS, luminal nonspecified; LumP, luminal papillary; LumU, luminal unstable; NE-like, neuroendocrine-like; SR, stroma rich, tpm, transcripts per million.

1. Eckstein M., et al. Abstract No. 828. Presented at the ASCO Genitourinary Cancers Symposium, February 13-15, 2025; San Francisco, CA.

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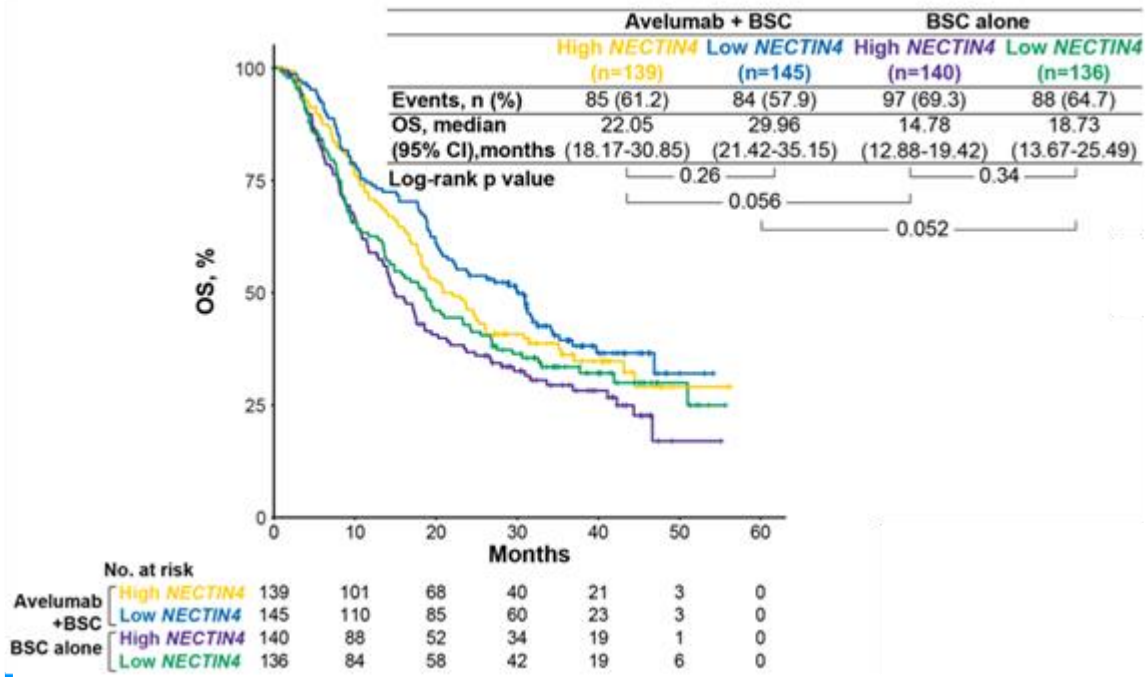
Subgroups with *NECTIN4* RNA expression

OS in Subgroups with *NECTIN4* RNA expression[1]

Post hoc analysis

Median Split

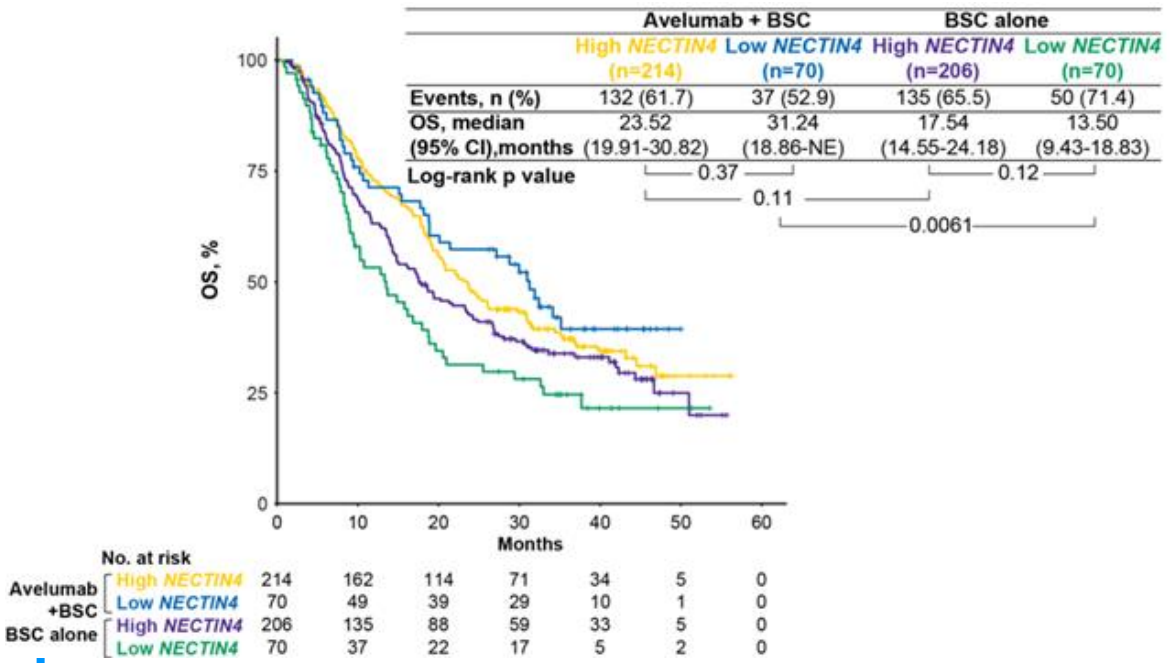
('high' refers to patients with expression levels ≥ the median (in relation to the overall population); 'low' refers to patients with < median expression)



In subgroups with high or low *NECTIN4* RNA expression, OS improvements with avelumab + BSC vs BSC alone were consistent with those observed in the overall population

Lower quartile Split

('high' refers to patients with expression levels ≥25% of the overall population; 'low' patients with expression levels <25% of the overall population)



Within the avelumab + BSC and BSC alone arms, no significant differences in OS were observed between subgroups with high or low *NECTIN4* RNA expression; OS was more pronounced in the low *NECTIN4* subset with avelumab + BSC treatment

Limitations

Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

BSC, best supportive care; CI, confidence interval; NE, not evaluable; OS, overall survival.

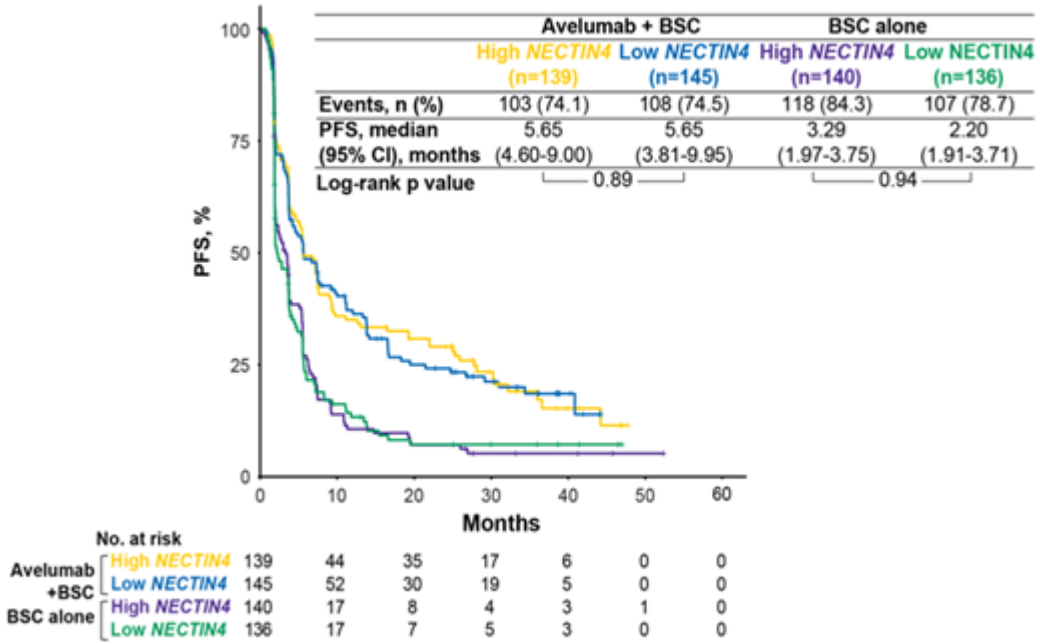
1. Klümper N, et al. Abstract No. 827. Presented at the ASCO Genitourinary Cancers Symposium, February 13-15, 2025; San Francisco, CA.

PFS in Subgroups with *NECTIN4* RNA expression[1]

Post hoc analysis

Median Split

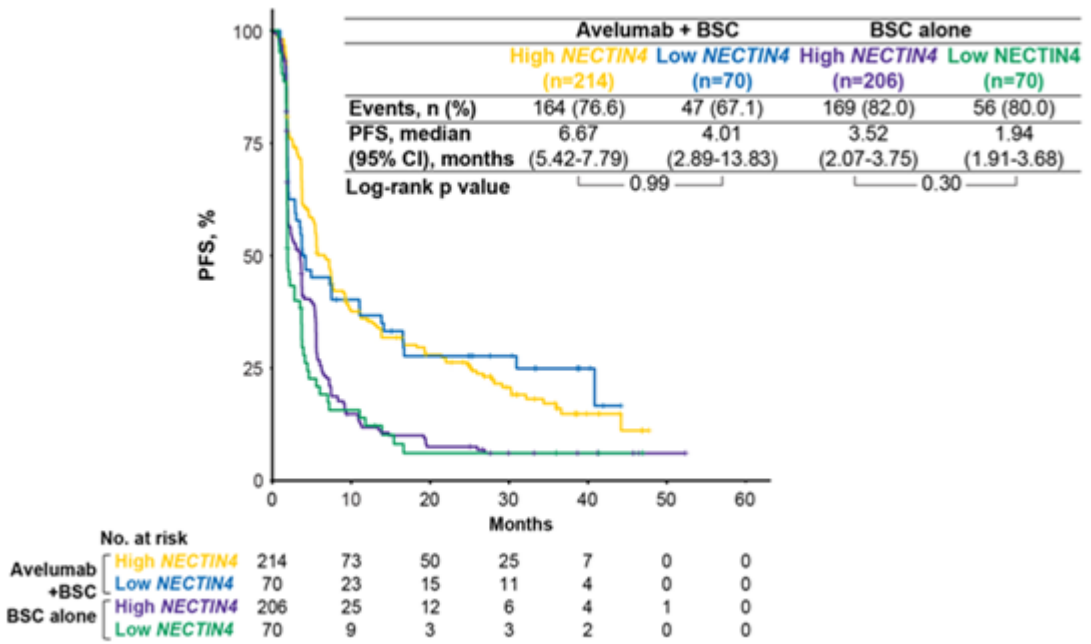
('high' refers to patients with expression levels ≥ the median (in relation to the overall population); 'low' refers to patients with < median expression)



In subgroups with high or low *NECTIN4* RNA expression, PFS improvements with avelumab + BSC vs BSC alone were consistent with those observed in the overall population

Lower quartile Split

('high' refers to patients with expression levels ≥25% of the overall population; 'low' patients with expression levels <25% of the overall population)



Within the avelumab + BSC and BSC alone arms, no significant differences in PFS were observed between subgroups with high or low *NECTIN4* RNA expression

Limitations

Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

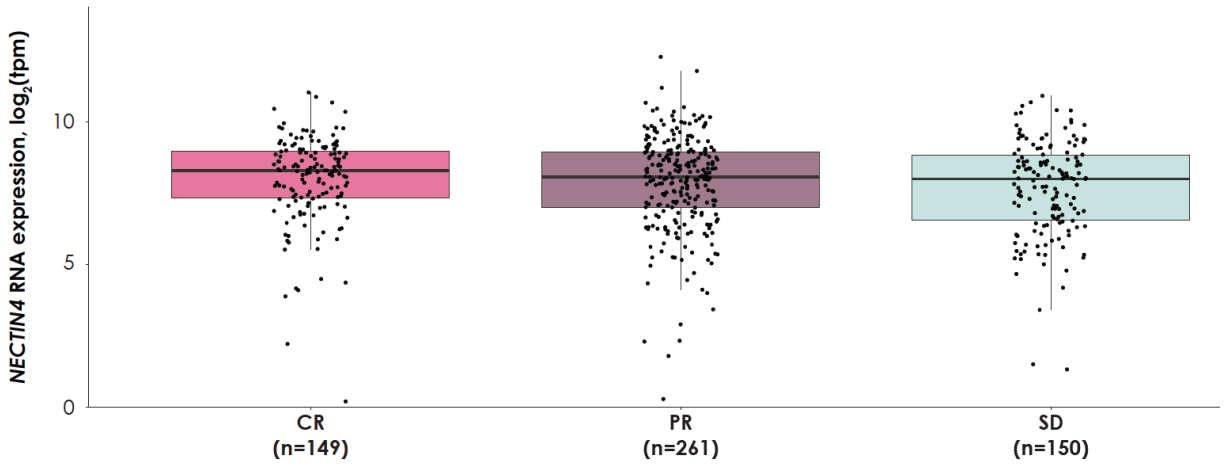
BSC, best supportive care; CI, confidence interval; NE, not evaluable; PFS, progression-free survival.

1. Klümper N, et al. Abstract No. 827. Presented at the ASCO Genitourinary Cancers Symposium, February 13-15, 2025; San Francisco, CA.

NECTIN4 RNA Expression in Subgroups Defined by Response to 1L PBC and Tumor Location[1]

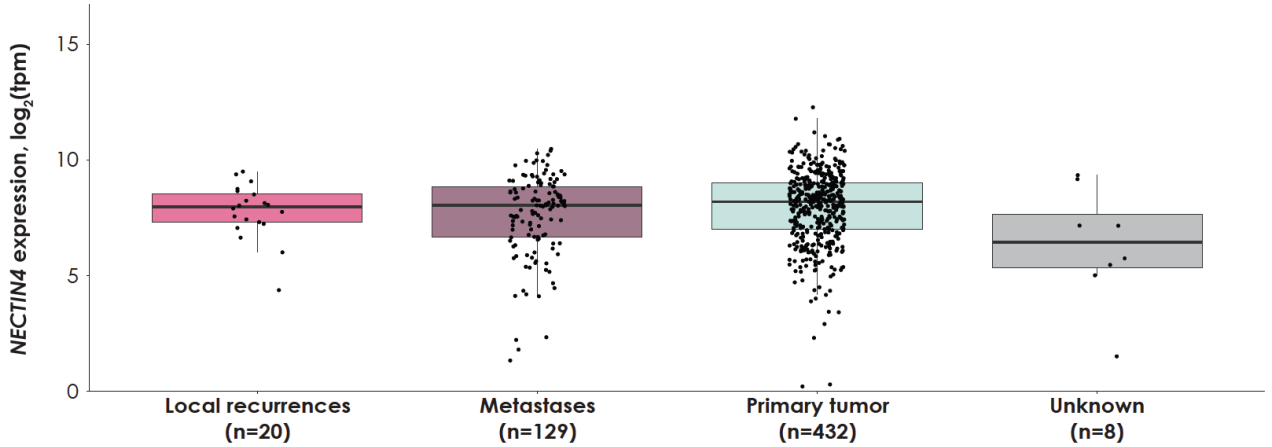
Post hoc analysis

NECTIN4 RNA expression in subgroups defined by response to 1L PBC



In biomarker-assessable patients from both arms combined, no significant differences were observed in tumor *NECTIN4* RNA expression between patients who had CR, PR, or SD with 1L PBC

NECTIN4 RNA expression in subgroups defined by tumor location



No significant differences were observed in tumor *NECTIN4* RNA expression between samples taken from different tumor locations

Note: The tumor samples were taken prior 1L CT.

1L, first line; CR, complete response; PBC, platinum-based chemotherapy; PR, partial response; SD, stable disease; tpm, transcripts per million.

1. Klümper N, et al. Abstract No. 827. Presented at the ASCO Genitourinary Cancers Symposium, February 13-15, 2025; San Francisco, CA.

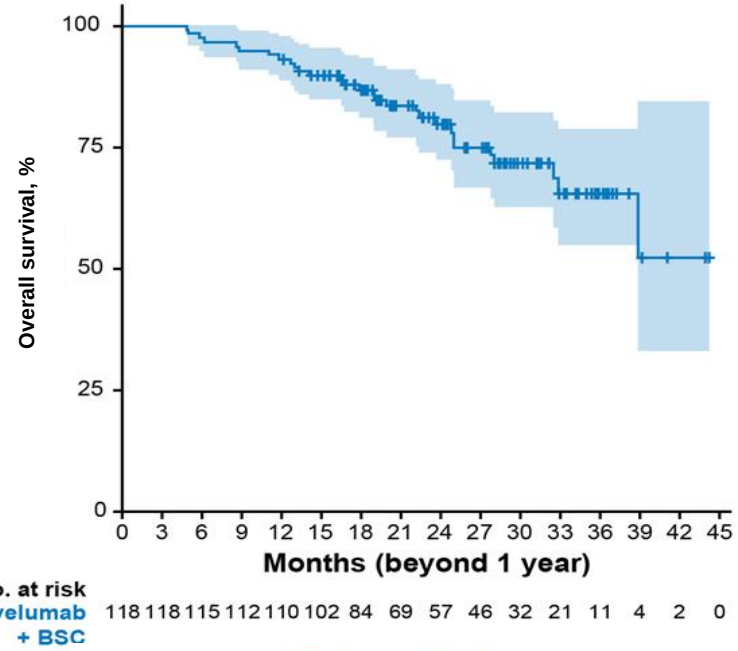
JAVELIN Bladder 100

Patients who received ≥1 or ≥2 Years of Avelumab

OS in Patients Who Received ≥1 or ≥2 Years of Avelumab[1]

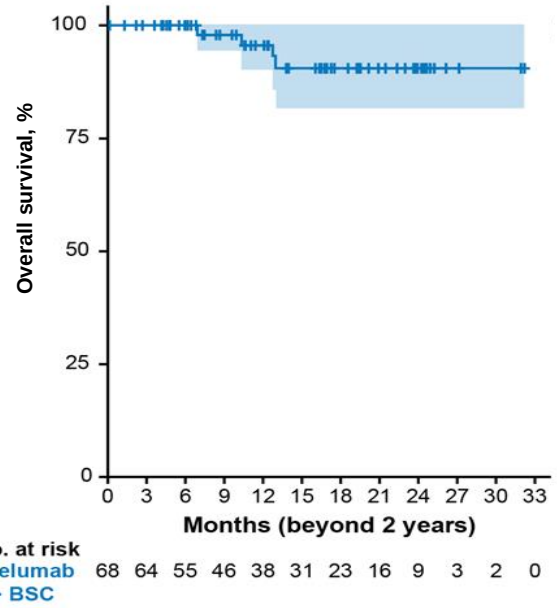
Post hoc analysis

OS beyond 1 year



	Patients with ≥1 year of avelumab treatment (n=118)
Probability of additional OS beyond 1 year (95% CI), %	
6 months	97.5 (94.7-100)
1 year	93.2 (88.8-97.9)
1.5 years	86.8 (80.8-93.3)
2 years	79.6 (72.0-88.0)

OS beyond 2 years



	Patients with ≥2 years of avelumab treatment (n=68)
Probability of additional OS beyond 2 years (95% CI), %	
6 months	100 (100-100)
1 year	95.8 (90.2-100)
1.5 years	90.3 (81.6-99.9)

Patients who had received 1 or 2 years of avelumab treatment have a high probability of additional years of survival

Limitations

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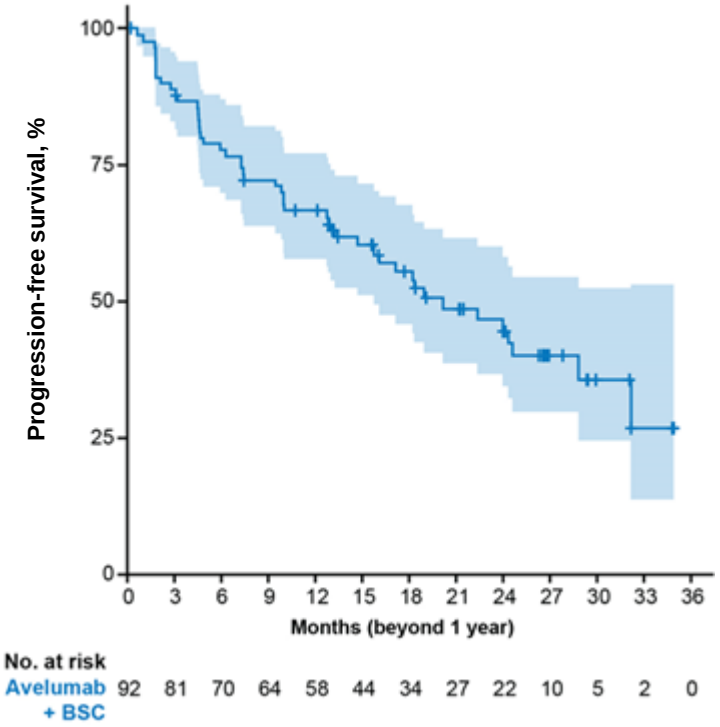
BSC, best supportive care; CI, confidence interval; OS, overall survival.

1. Grivas P, et al. Poster No. 1975P. Presented at the ESMO Congress 2024, 13-17 September 2024; Barcelona, Spain.

PFS in Patients Who Received ≥1 or ≥2 Years of Avelumab[1]

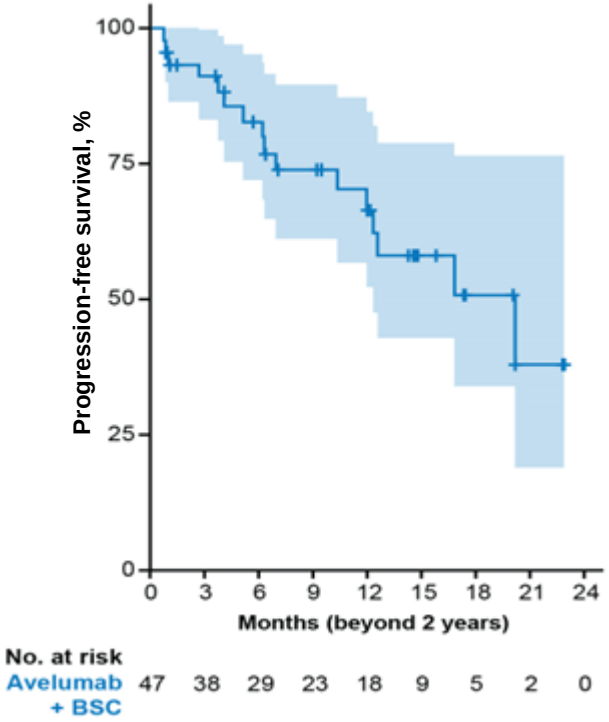
Post hoc analysis

PFS beyond 1 year



	Patients with ≥1 year of avelumab treatment (n=118)
Probability of additional PFS beyond 1 year (95% CI), %	
6 months	77.9 (69.8-86.9)
1 year	66.7 (57.6-77.2)

PFS beyond 2 years



	Patients with ≥2 years of avelumab treatment (n=68)
Probability of additional PFS beyond 2 years (95% CI), %	
6 months	82.9 (72.0-95.4)
1 year	66.7 (52.5-84.7)

Patients who had received 1 or 2 years of avelumab treatment have a high probability of additional years of survival

Limitations

Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

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

1. Grivas P, et al. Poster No. 1975P. Presented at the ESMO Congress 2024, 13-17 September 2024; Barcelona, Spain.

Safety in Patients at Any Time and After ≥1 or ≥2 Years of Avelumab Treatment[1]

PATIENTS, n (%)	OCCURRED AT ANY TIME (all treated patients; n=344)	OCCURRED AFTER ≥1 year (patients with ≥1 year of treatment; n=118)	OCCURRED AFTER ≥2 years (patients with ≥2 years of treatment; n=68)
AE of any grade	338 (98.3)	102 (86.4)	48 (70.6)
Grade ≥3 AE	185 (53.8)	56 (47.5)	21 (30.9)
TRAEs of any grade	269 (78.2)	59 (50.0)	24 (35.3)
Grade ≥3 TRAE	67 (19.5)	14 (11.9)	4 (5.9)
Serious AE	105 (30.5)	28 (23.7)	9 (13.2)
Serious TRAE	35 (10.2)	6 (5.1)	2 (2.9)
AE leading to discontinuation of avelumab	49 (14.2)	13 (11.0)	3 (4.4)
TRAE leading to discontinuation of avelumab	40 (11.6)	12 (10.2)	2 (2.9)
AE leading to death	7 (2.0)	3 (2.5)	2 (2.9)
TRAE leading to death	2 (0.6)	1 (0.8)*	1 (1.5)*
irAE of any grade	111 (32.3)	27 (22.9)	9 (13.2)
Grade ≥3 irAE	26 (7.6)	5 (4.2)	3 (4.4)

In patients who were still receiving avelumab treatment at specified time points, rates of ≥3 TRAEs occurring after 1 or 2 years were low

*Attributed to immune-mediated nephritis by the investigator

AE, adverse event; irAE, immune-related AE; TRAE, treatment-related AE.

1. Grivas P, et al. Poster No. 1975P. Presented at the ESMO Congress 2024, 13-17 September 2024; Barcelona, Spain.

Safety in Patients at Any Time and After ≥1 or ≥2 Years of Avelumab Treatment[1]

	OCCURRED AT ANY TIME (all treated patients; n=344)		OCCURRED AFTER ≥1 year (patients with ≥1 year of treatment; n=118)		OCCURRED AFTER ≥2 years (patients with ≥2 years of treatment; n=68)	
PATIENTS, n (%)	ANY GRADE*	GRADE ≥3	ANY GRADE*	GRADE ≥3	ANY GRADE*	GRADE ≥3
Any TRAE	269 (78.2)	67 (19.5)	59 (50.0)	14 (11.9)	24 (35.3)	4 (5.9)
Pruritus	51 (14.8)	1 (0.3)	13 (11.0)	0	4 (5.9)	0
Fatigue	37 (10.8)	1 (0.3)	8 (6.8)	0	3 (4.4)	0
Rash	27 (7.8)	2 (0.6)	8 (6.8)	1 (0.8)	3 (4.4)	0
Diarrhea	36 (10.5)	0	7 (5.9)	0	3 (4.4)	0
Asthenia	36 (10.5)	0	4 (3.4)	0	2 (2.9)	0
Blood creatinine increased	7 (2.0)	0	4 (3.4)	0	1 (1.5)	0
Anemia	14 (4.1)	5 (1.5)	3 (2.5)	0	1 (1.5)	0
Arthralgia	25 (7.3)	1 (0.3)	3 (2.5)	0	2 (2.9)	0
Constipation	13 (3.8)	0	3 (2.5)	0	2 (2.9)	0
Hypothyroidism	38 (11.0)	1 (0.3)	3 (2.5)	0	1 (1.5)	0
Lipase increased	15 (4.4)	12 (3.5)	3 (2.5)	2 (1.7)	1 (1.5)	1 (1.5)
Muscle spasms	4 (1.2)	0	3 (2.5)	0	1 (1.5)	0
Musculoskeletal pain	4 (1.2)	0	3 (2.5)	0	1 (1.5)	0
Myalgia	14 (4.1)	0	3 (2.5)	0	0	0

Types of TRAEs that occurred after 1 or 2 years of treatment were consistent with those observed in the overall population

*TRAEs of any grade that occurred in ≥2% of patients who were treated for ≥1 or ≥2 years are shown.

TRAE, treatment-related adverse event.

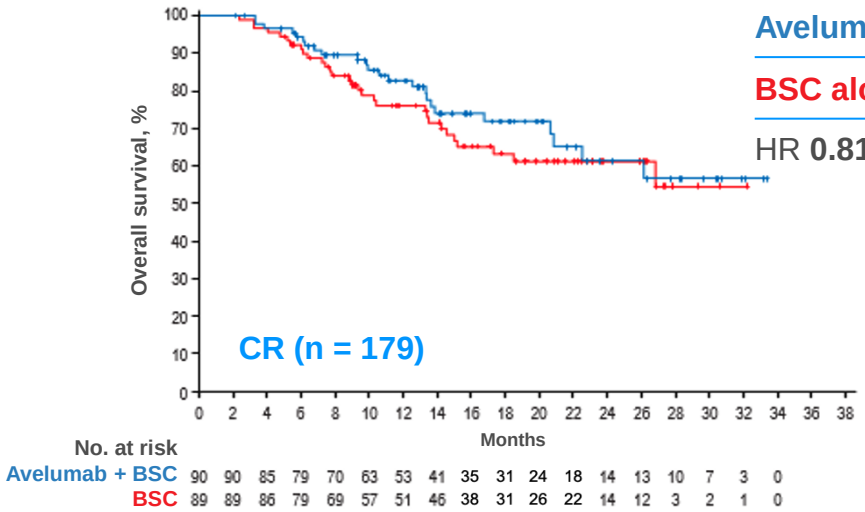
1. Grivas P, et al. Poster No. 1975P. Presented at the ESMO Congress 2024, 13-17 September 2024; Barcelona, Spain.

JAVELIN
Bladder 100

Response to 1L Chemotherapy Subgroup Data

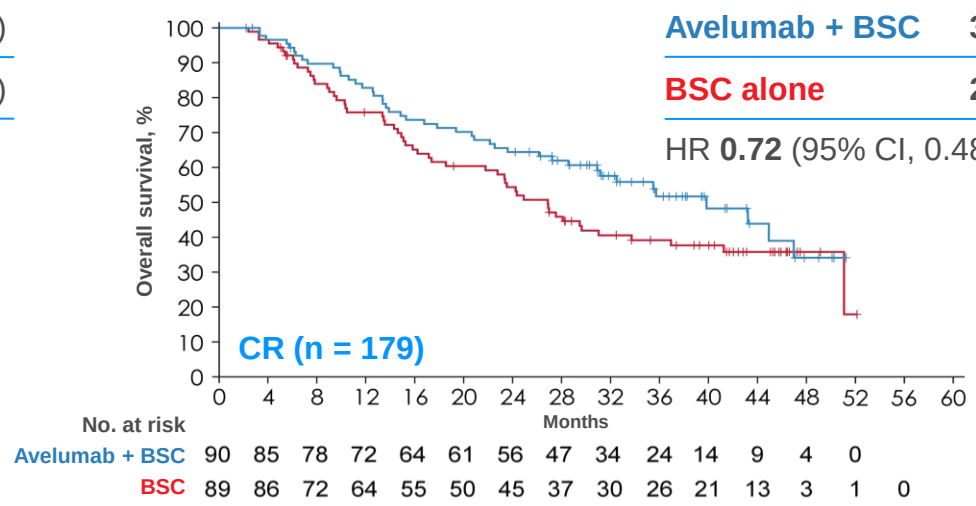
OS by Complete Response to 1L Platinum-Containing CT[1,2]

Protocol-specified subgroups in all randomized patients



Median OS, months (95% CI)	
Avelumab + BSC	**NE** (20.8-NE)
BSC alone	**NE** (18.5-NE)

HR **0.81** (95% CI, 0.47-1.38)



Median OS, months (95% CI)	
Avelumab + BSC	**39.8** (28.5-NE)
BSC alone	**26.8** (18.5-33.6)

HR **0.72** (95% CI, 0.48-1.08)

OS was longer with avelumab + BSC vs BSC alone in patients with a CR to 1L platinum-containing CT regimen in both primary and follow-up analyses

Limitations

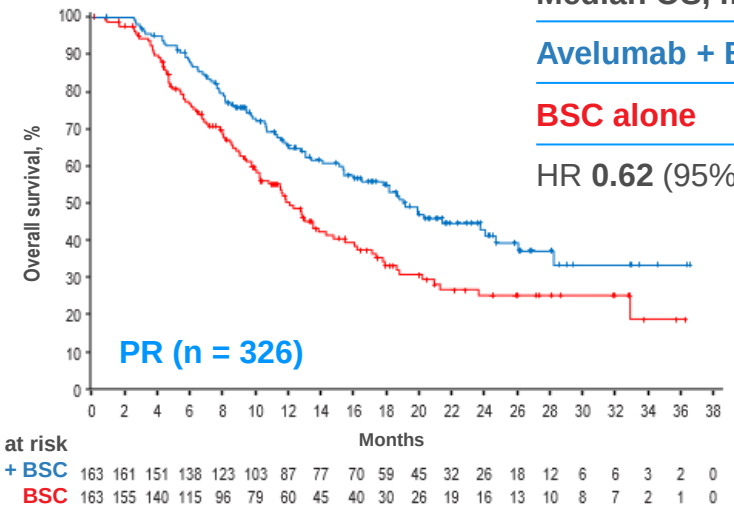
Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

1L, first-line; BSC, best supportive care; CI, confidence interval; CR, complete response; CT, chemotherapy; HR, hazard ratio; NE, not estimable; OS, overall survival.

1. Grivas P, et al. Abstract 704MO. Presented at: ESMO Virtual Congress; September 19-21, 2020; 2. Valderrama BP, et al. Poster 4559. Presented at: ASCO Hybrid Annual Meeting; June 3-7, 2022; Chicago, IL.

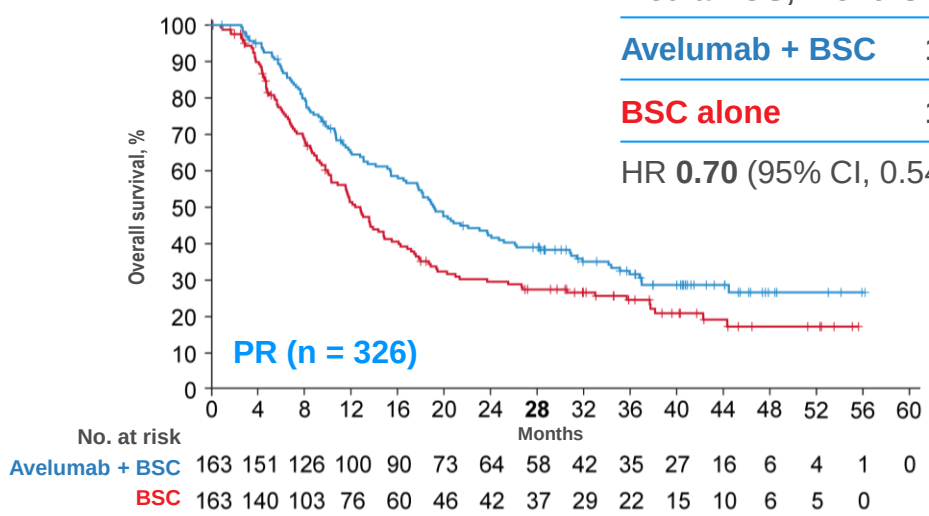
OS by Partial Response to 1L Platinum-Containing CT[1,2]

Protocol-specified subgroups in all randomized patients



Median OS, months (95% CI)	
Avelumab + BSC	**19.2** (15.4-24.7)
BSC alone	**12.1** (10.1-14.3)

HR **0.62** (95% CI, 0.46-0.83)



Median OS, months (95% CI)	
Avelumab + BSC	**19.2** (16.0-23.8)
BSC alone	**12.8** (10.3-14.8)

HR **0.70** (95% CI, 0.54-0.91)

OS was longer with avelumab + BSC vs BSC alone in patients with a PR to 1L platinum-containing CT regimen in both primary and follow-up analyses

Limitations

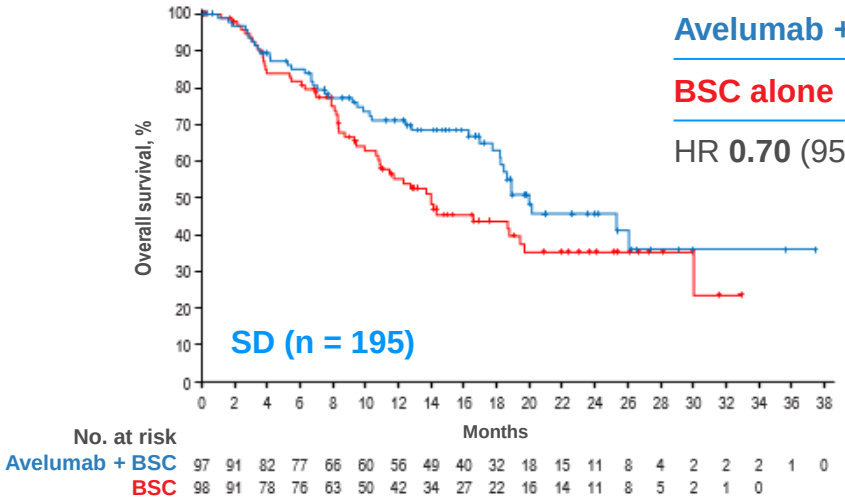
Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

1L, first-line; BSC, best supportive care; CI, confidence interval; CT, chemotherapy; HR, hazard ratio; OS, overall survival; PR, partial response.

1. Grivas P, et al. Abstract 704MO. Presented at: ESMO Virtual Congress; September 19-21, 2020; 2. Valderrama BP, et al. Poster 4559. Presented at: ASCO Hybrid Annual Meeting; June 3-7, 2022; Chicago, IL.

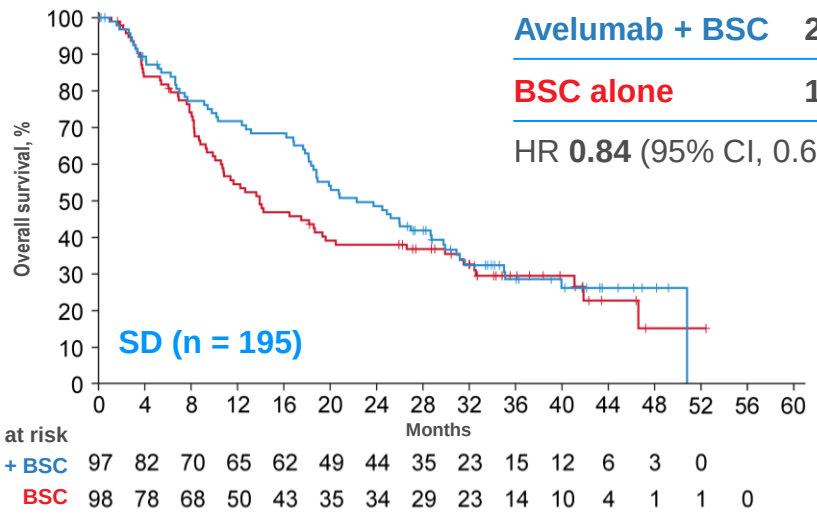
OS by Stable Disease to 1L Platinum-Containing CT[1,2]

Protocol-specified subgroups in all randomized patients



Median OS, months (95% CI)	
Avelumab + BSC	**19.9** (18.2-NE)
BSC alone	**14.0** (10.7-19.4)

HR **0.70** (95% CI, 0.46-1.05)



Median OS, months (95% CI)	
Avelumab + BSC	**22.3** (18.2-28.8)
BSC alone	**14.0** (10.6-19.6)

HR **0.84** (95% CI, 0.60-1.19)

OS was longer with avelumab + BSC vs BSC alone in patients with a SD to 1L platinum-containing CT regimen in both primary and follow-up analyses

Limitations

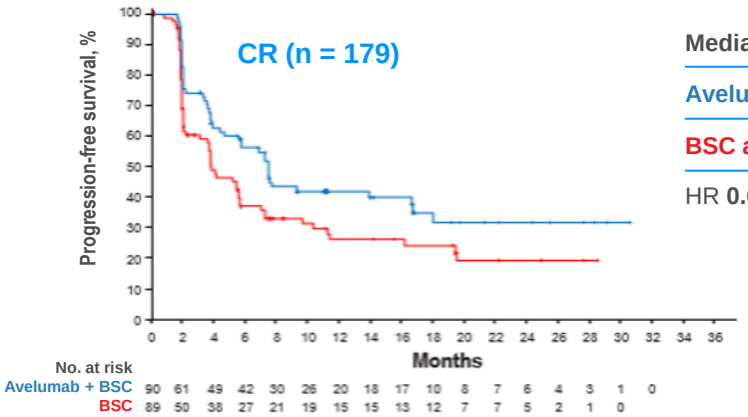
Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

1L, first-line; BSC, best supportive care; CI, confidence interval; CT, chemotherapy; HR, hazard ratio; NE, not estimable; OS, overall survival; SD, stable disease.

1. Grivas P, et al. Abstract 704MO. Presented at: ESMO Virtual Congress; September 19-21, 2020; 2. Valderrama BP, et al. Poster 4559. Presented at: ASCO Hybrid Annual Meeting; June 3-7, 2022; Chicago, IL.

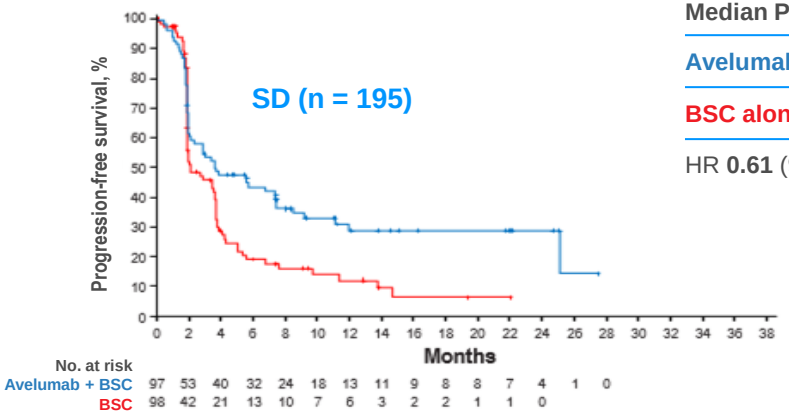
PFS by Best Response to 1L Platinum-Containing CT[1]

Protocol-specified subgroups in all randomized patients



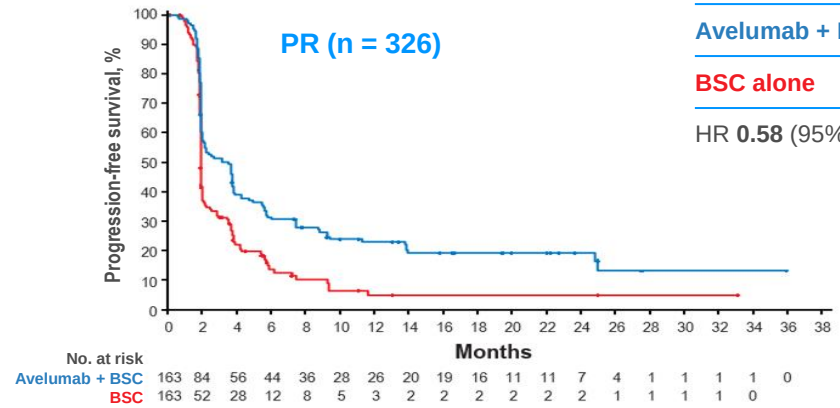
Median PFS, months (95% CI)	
Avelumab + BSC	**7.4** (4.3-16.5)
BSC alone	**3.8** (2.1-5.6)

HR **0.65** (95% CI, 0.45-0.96)



Median PFS, months (95% CI)	
Avelumab + BSC	**3.7** (2.0-7.4)
BSC alone	**2.1** (1.9-3.6)

HR **0.61** (95% CI, 0.42-0.87)



Median PFS, months (95% CI)	
Avelumab + BSC	**3.1** (2.0-3.7)
BSC alone	**1.9** (1.9-1.9)

HR **0.58** (95% CI, 0.44-0.75)

PFS was prolonged with avelumab + BSC vs BSC alone irrespective of best response to 1L platinum-containing CT regimen

Limitations

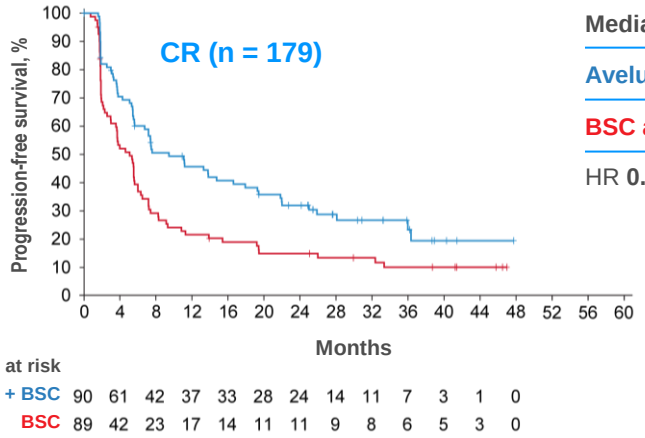
Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

1L, first-line; BSC, best supportive care; CI, confidence interval; CR, complete response; CT, chemotherapy; HR, hazard ratio; PFS, progression-free survival; PR, partial response; SD, stable disease.

1. Grivas P, et al. Abstract 704MO. Presented at: ESMO Virtual Congress; September 19-21, 2020.

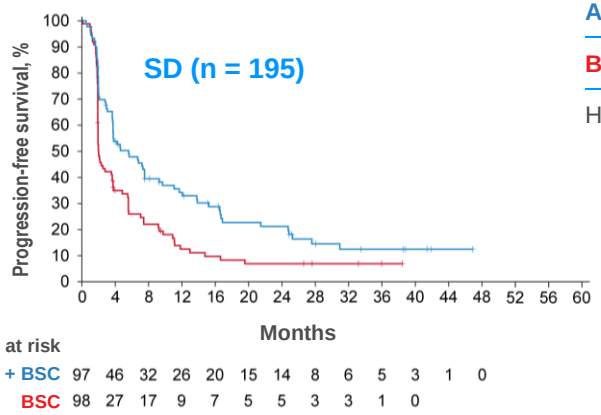
PFS by Best Response to 1L Platinum-Containing CT[1]

Protocol-specified subgroups in all randomized patients



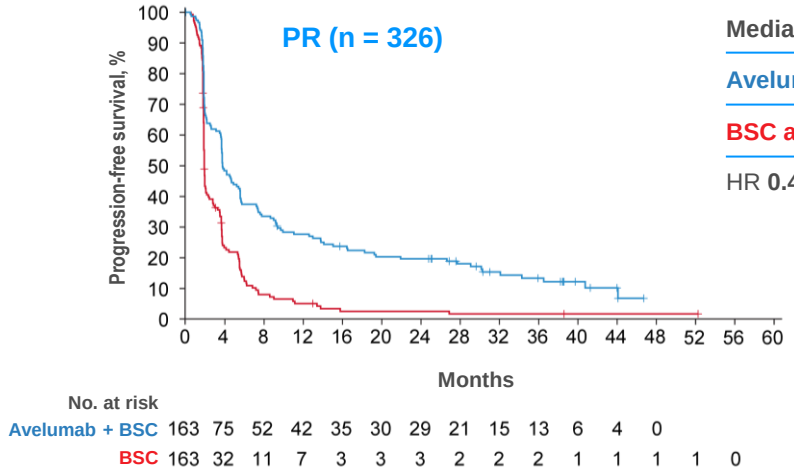
Median PFS, months (95% CI)	
Avelumab + BSC	**9.5** (5.7-16.6)
BSC alone	**5.1** (3.0-5.7)

HR **0.58** (95% CI, 0.41-0.82)



Median PFS, months (95% CI)	
Avelumab + BSC	**5.6** (3.7-7.5)
BSC alone	**2.0** (1.9-3.6)

HR **0.59** (95% CI, 0.42-0.82)



Median PFS, months (95% CI)	
Avelumab + BSC	**3.8** (3.7-5.6)
BSC alone	**1.9** (1.9-2.1)

HR **0.47** (95% CI, 0.37-0.61)

Limitations

Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of observed treatment effect over several subgroups

1L, first-line; BSC, best supportive care; CI, confidence interval; CR, complete response; CT, chemotherapy; HR, hazard ratio; PFS, progression-free survival; PR, partial response; SD, stable disease.

1. Valderrama BP, et al. Poster 4559. Presented at: ASCO Hybrid Annual Meeting; June 3-7, 2022; Chicago, IL.

Patient Disposition by Response to 1L Platinum-Containing CT[1]

	CR (n = 179)		PR (n = 326)		SD (n = 195)	
	AVELUMAB + BSC (n = 90)	BSC ALONE (n = 89)	AVELUMAB + BSC (n = 163)	BSC ALONE (n = 163)	AVELUMAB + BSC (n = 97)	BSC ALONE (n = 98)
Study treatment ongoing, n (%)	12 (13.3)	6 (6.7)	21 (12.9)	1 (0.6)	10 (10.3)	3 (3.1)
Discontinued, n (%)	78 (86.7)	83 (93.3)	142 (87.1)	162 (99.4)	87 (89.7)	95 (96.9)
Progressive disease	45 (50)	69 (77.5)	110 (67.5)	134 (82.2)	54 (55.7)	72 (73.5)
Adverse event	23 (25.6)	1 (1.1)	14 (8.6)	1 (0.6)	11 (11.3)	0
Withdrew consent	8 (8.9)	5 (5.6)	4 (2.5)	14 (8.6)	11 (11.3)	12 (12.2)
Death	0	3 (3.4)	4 (2.5)	6 (3.7)	4 (4.1)	5 (5.1)
Physician decision	1 (1.1)	2 (2.2)	5 (3.1)	2 (1.2)	5 (5.2)	3 (3.1)
Global health deterioration	0	0	2 (1.2)	3 (1.8)	1 (1.0)	2 (2.0)
Other reason*	1 (1.1)	3 (3.4)	3 (1.8)	2 (1.2)	1 (1.0)	1 (1.0)
Median duration of study treatment (range), months†	7.8 (0.5-49.3)	5.5 (0.02-38.7)	5.1 (0.5-49.0)	2.8 (0.02-53.3)	5.8 (0.5-49.7)	2.8 (0.02-37.7)

* Includes eligibility criteria no longer met, loss to follow-up, noncompliance with study drug, and other. † In treated patients.

BSC, best supportive care; CR, complete response; PR, partial response; SD, stable disease.

1. Valderrama BP, et al. Poster 4559. Presented at: ASCO Hybrid Annual Meeting; June 3-7, 2022; Chicago, IL.

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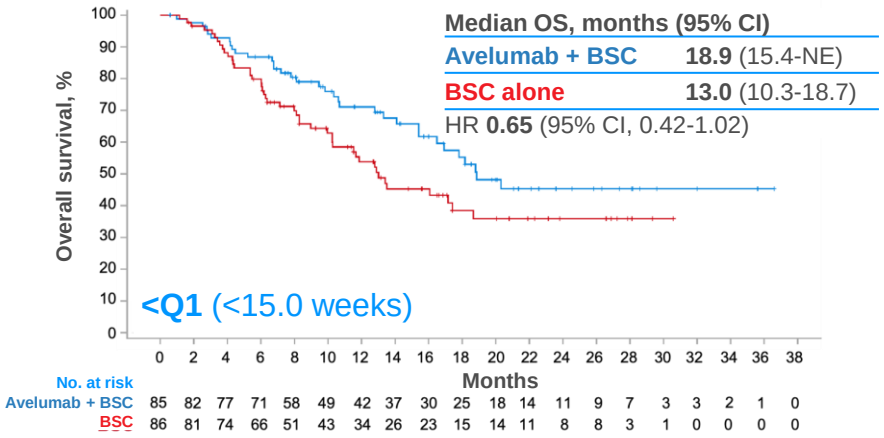
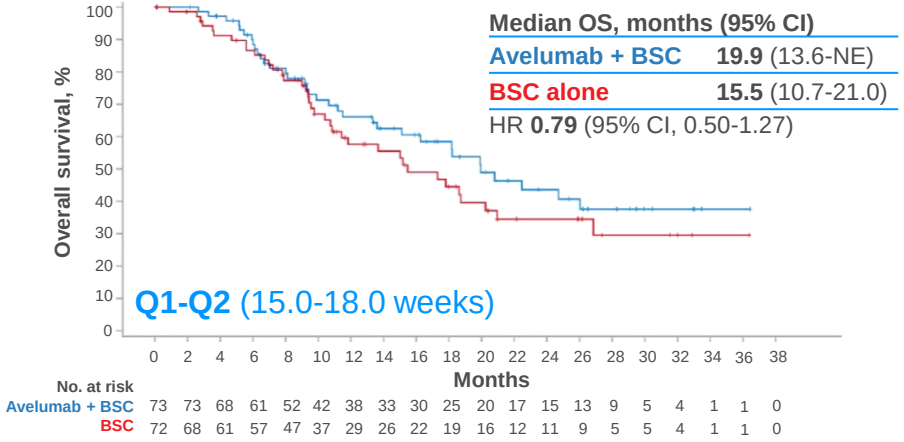
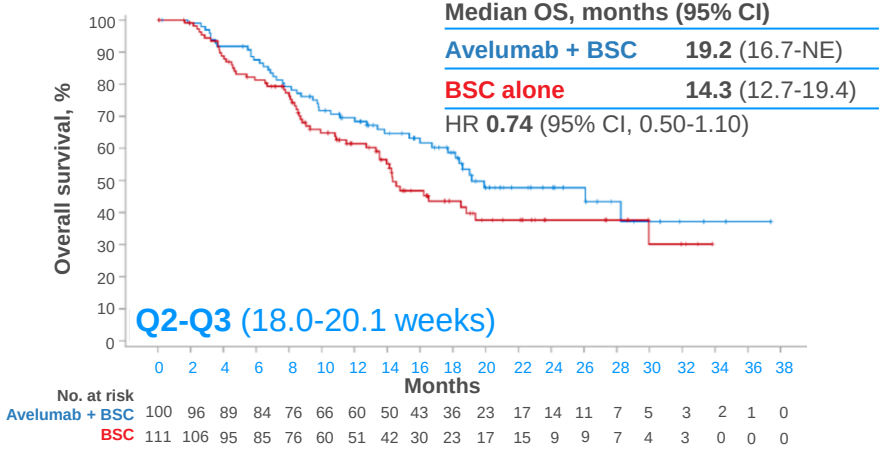
Chemotherapy Cycles and Treatment-free Interval Subgroup Data

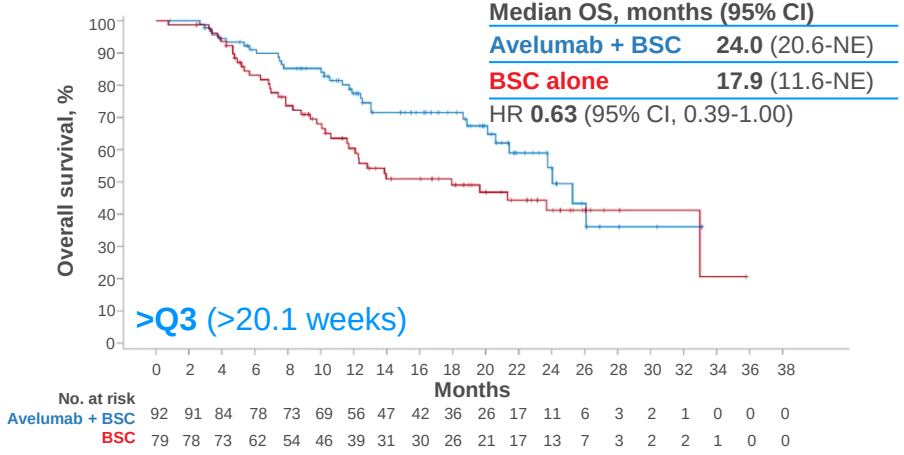
OS by Duration of 1L Platinum-Containing CT[1]

Post hoc analysis









OS was prolonged with avelumab + BSC vs BSC alone across subgroups with differing durations of 1L CT

Limitations

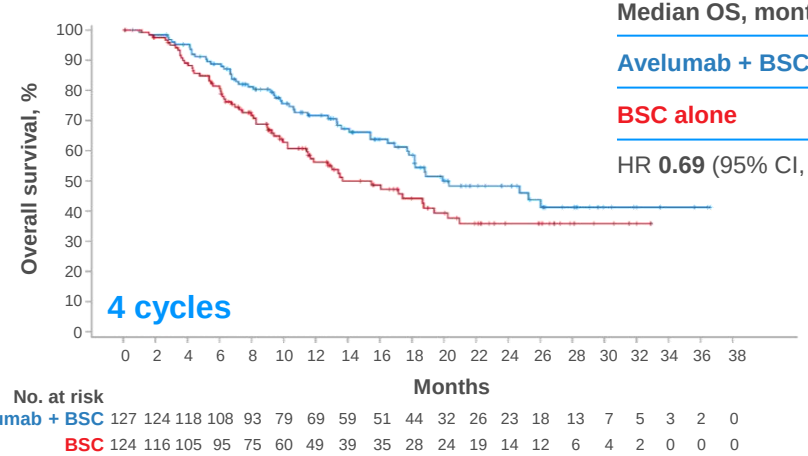
Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

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

1. Loriot Y, et al. Abstract 438. Presented at: ASCO GU Virtual Symposium; February 11-13, 2021.

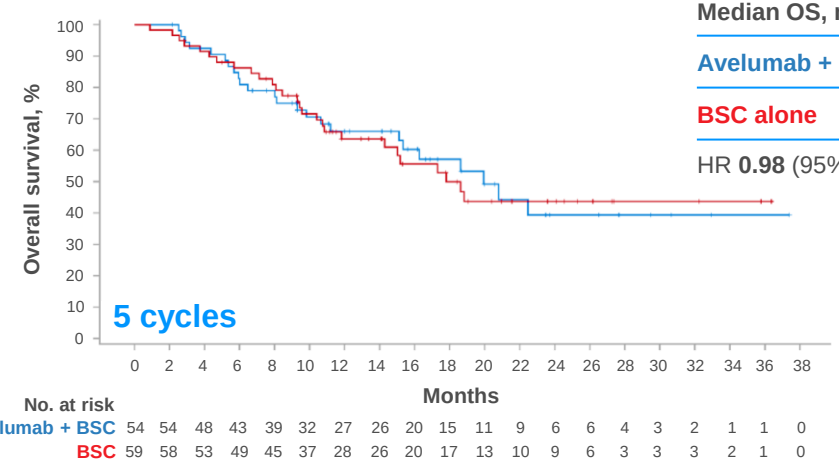
OS by Number of 1L Platinum-Containing CT Cycles[1]

Exploratory post hoc analysis



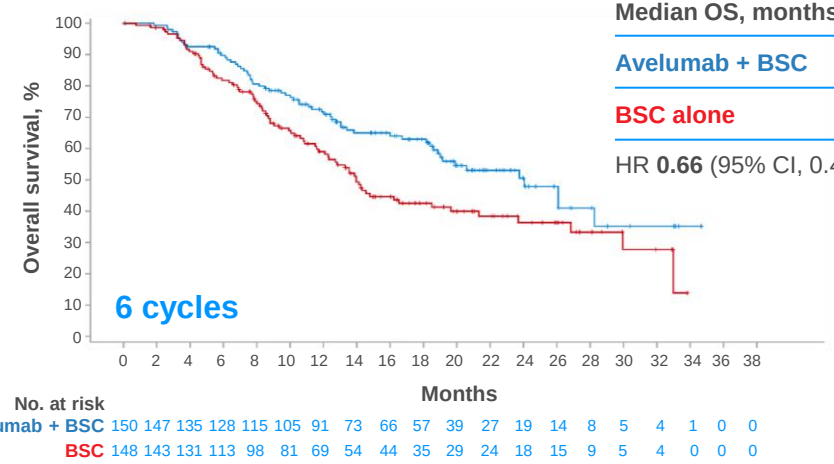
Median OS, months (95% CI)	
Avelumab + BSC	**19.9** (17.7-NE)
BSC alone	**13.7** (11.4-19.4)

HR **0.69** (95% CI, 0.48-1.00)



Median OS, months (95% CI)	
Avelumab + BSC	**19.9** (15.1-NE)
BSC alone	**17.8** (11.8-NE)

HR **0.98** (95% CI, 0.57-1.71)



Median OS, months (95% CI)	
Avelumab + BSC	**24.0** (18.9-NE)
BSC alone	**14.0** (12.1-19.6)

HR **0.66** (95% CI, 0.47-0.92)

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

Limitations

Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

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

1. Loriot Y, et al. Abstract 438. Presented at: ASCO GU Virtual Symposium; February 11-13, 2021.

OS and PFS by Duration of TFI Before Maintenance[1]

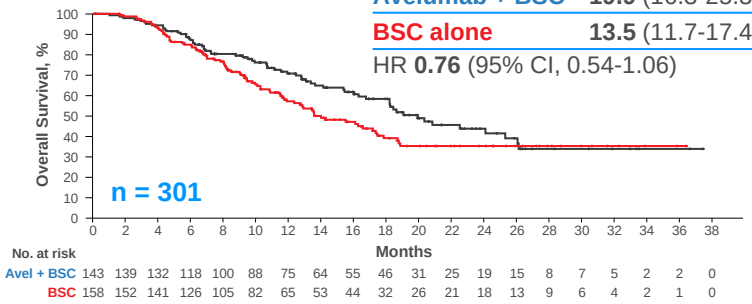
Post hoc analysis

TFI 4 to <6 Weeks

Median OS, months (95% CI)

Avelumab + BSC	**19.9** (16.3-25.3)
BSC alone	**13.5** (11.7-17.4)

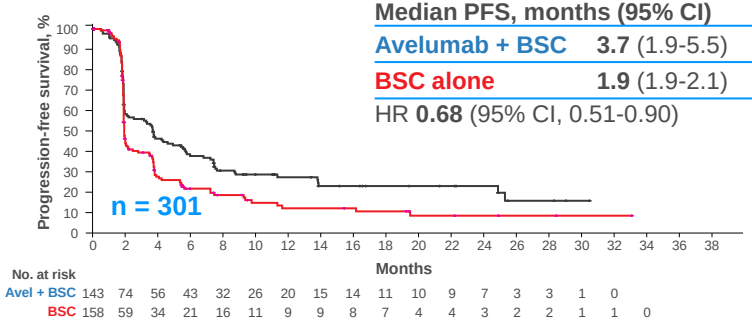
HR **0.76** (95% CI, 0.54-1.06)



Median PFS, months (95% CI)

Avelumab + BSC	**3.7** (1.9-5.5)
BSC alone	**1.9** (1.9-2.1)

HR **0.68** (95% CI, 0.51-0.90)

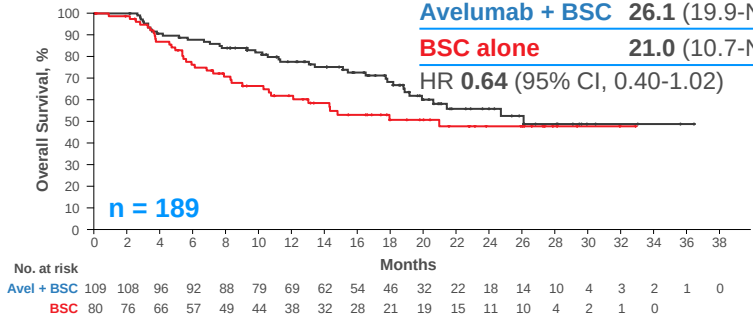


TFI 6 to <8 Weeks

Median OS, months (95% CI)

Avelumab + BSC	**26.1** (19.9-NE)
BSC alone	**21.0** (10.7-NE)

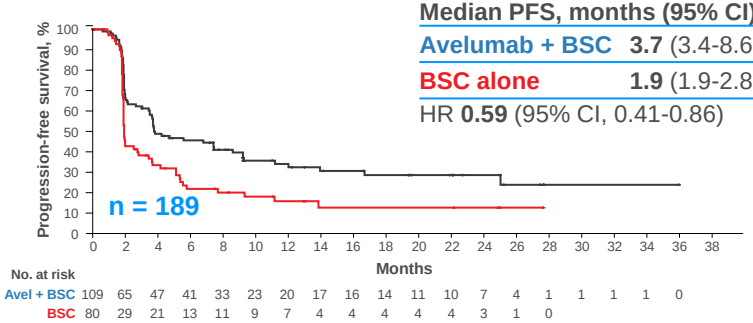
HR **0.64** (95% CI, 0.40-1.02)



Median PFS, months (95% CI)

Avelumab + BSC	**3.7** (3.4-8.6)
BSC alone	**1.9** (1.9-2.8)

HR **0.59** (95% CI, 0.41-0.86)

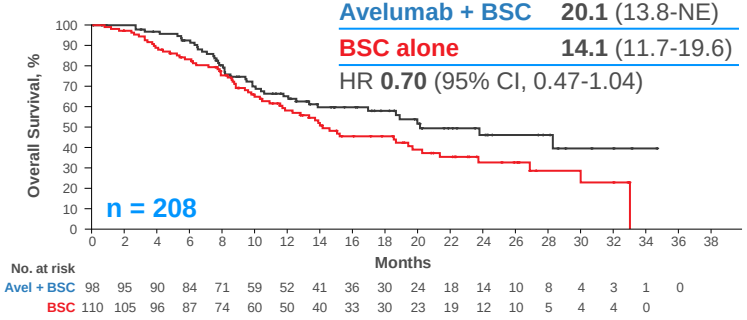


TFI 8 to 10 Weeks

Median OS, months (95% CI)

Avelumab + BSC	**20.1** (13.8-NE)
BSC alone	**14.1** (11.7-19.6)

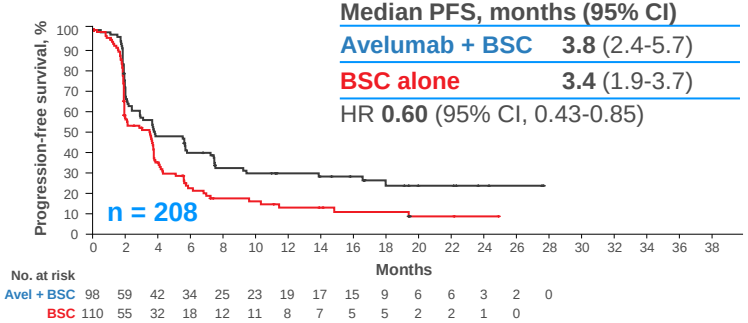
HR **0.70** (95% CI, 0.47-1.04)



Median PFS, months (95% CI)

Avelumab + BSC	**3.8** (2.4-5.7)
BSC alone	**3.4** (1.9-3.7)

HR **0.60** (95% CI, 0.43-0.85)



Prolonged OS and PFS were observed with avelumab + BSC vs BSC alone in all TFI subgroups

- OS and PFS benefits with avelumab + BSC vs BSC alone were similar across all TFI subgroups

The safety profile of avelumab 1L maintenance was generally similar between subgroups, irrespective of the length of TFI before starting maintenance

Limitations

Small patient numbers can be a limitation of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup. The results show the variability of the observed treatment effect over several subgroups

1L, first-line; avel, avelumab; BSC, best supportive care; CI, confidence interval; HR, hazard ratio; NE, not estimable; OS, overall survival; PFS, progression-free survival; TFI, treatment-free interval.

1. Sridhar SS, et al. Abstract 4527. Presented at: ASCO Virtual Annual Meeting; June 4-8, 2021.

JAVELIN Bladder 100

Tumor Response Data

Secondary Endpoints: Responses in All Randomized Patients Following 1L Platinum-Containing CT[1]

VARIABLE	ALL RANDOMIZED PATIENTS: AVELUMAB + BSC (n = 350)	ALL RANDOMIZED PATIENTS: BSC ALONE (n = 350)	PD-L1–POSITIVE POPULATION: AVELUMAB + BSC (n = 189)	PD-L1–POSITIVE POPULATION: BSC ALONE (n = 169)
Confirmed ORR* (95% CI), %	9.7 (6.8-13.3)	1.4 (0.5-3.3)	13.8 (9.2-19.5)	1.2 (0.1-4.2)
Stratified odds ratio (95% CI)	7.46 (2.82-24.45)		12.70 (3.16-114.12)	
Confirmed best overall response, n (%)				
CR	21 (6.0)	3 (0.9)	18 (9.5)	1 (0.6)
PR	13 (3.7)	2 (0.6)	8 (4.2)	1 (0.6)
SD	44 (12.6)	46 (13.1)	19 (10.1)	23 (13.6)
Non–CR/non–PD†	66 (18.9)	45 (12.9)	38 (20.1)	22 (13.0)
PD	130 (37.1)	169 (48.3)	59 (31.2)	82 (48.5)
NE	76 (21.7)‡	85 (24.3)§	47 (24.9)¶	40 (23.7)‖
Disease control, n (%)**	144 (41.1)	96 (27.4)	83 (43.9)	47 (27.8)
Median time to response (range), months	2.0 (1.7-16.4)	2.0 (1.8-7.0)	2.0 (1.7-16.4)	2.8 (1.8-3.8)

Disease control was achieved by more patients receiving **avelumab + BSC (41.1%)** than patients receiving **BSC alone (27.4%)**

* An objective response was defined as a CR or PR. Objective responses were assessed by BICR according to the RECIST v1.1 and indicated the change in tumors as compared with baseline at randomization (ie, the change during chemotherapy was not considered). In patients with a CR after chemotherapy, the BOR was noted as "could not be evaluated" if no evidence of disease at baseline was detected after randomization or as "progressive disease" if disease progression occurred after randomization; these patients could not have had a BOR of CR, PR, SD, or non–CR or non–PD after randomization. Percentages may not total 100 because of rounding. † This category of response is defined by RECIST v1.1. and refers to persistence of one or more nontarget lesions in patients with nontarget lesions only. ‡ Reasons that the response could not be evaluated were the following: no evidence of disease at baseline (in 52 patients), no postbaseline assessments owing to other reasons (in 18), SD occurring less than 6 weeks after randomization (in 2), PD occurring more than 12 weeks after randomization (in 2), no postbaseline assessments owing to early death (in 1), and new anticancer therapy started before the first postbaseline assessment (in 1). § Reasons that the response could not be evaluated were the following: no evidence of disease at baseline (in 50 patients), no postbaseline assessments owing to other reasons (in 17), SD occurring less than 6 weeks after randomization (in 8), no postbaseline assessments owing to early death (in 4), new anticancer therapy started before the first postbaseline assessment (in 3), PD occurring more than 12 weeks after randomization (in 2), and all postbaseline assessment had an overall response of "could not be evaluated" (in 1). ¶ Reasons that the response could not be evaluated were the following: no evidence of disease at baseline (in 31 patients), no postbaseline assessments owing to other reasons (in 12), SD occurring less than 6 weeks after randomization (in 1), no postbaseline assessments owing to early death (in 1), new anticancer therapy started before the first postbaseline assessment (in 1), and PD occurring more than 12 weeks after randomization (in 1). ‖ Reasons that the response could not be evaluated were the following: no evidence of disease at baseline (in 28 patients), no postbaseline assessments owing to other reasons (in 5), SD occurring less than 6 weeks after randomization (in 3), PD occurring more than 12 weeks after randomization (in 2), no postbaseline assessments owing to early death (in 1), and new anticancer therapy started before the first postbaseline assessment (in 1). ** Disease control was defined as a BOR of CR, PR, SD, or non–CR or non–PD.

For full definitions please refer to Powles T, et al. N Engl J Med. 2020;383(13):1218-1230.

BICR, blinded independent central review; BOR, best overall response, BSC, best supportive care; CI, confidence interval; CR, complete response; CT, chemotherapy, NE, not estimable; ORR, objective response rate; PD, progressive disease; PD-L1, programmed death-ligand 1; PR, partial response; RECIST, response evaluation criteria in solid tumors; SD, stable disease.

1. Powles T, et al. N Engl J Med. 2020;383(13):1218-1230.

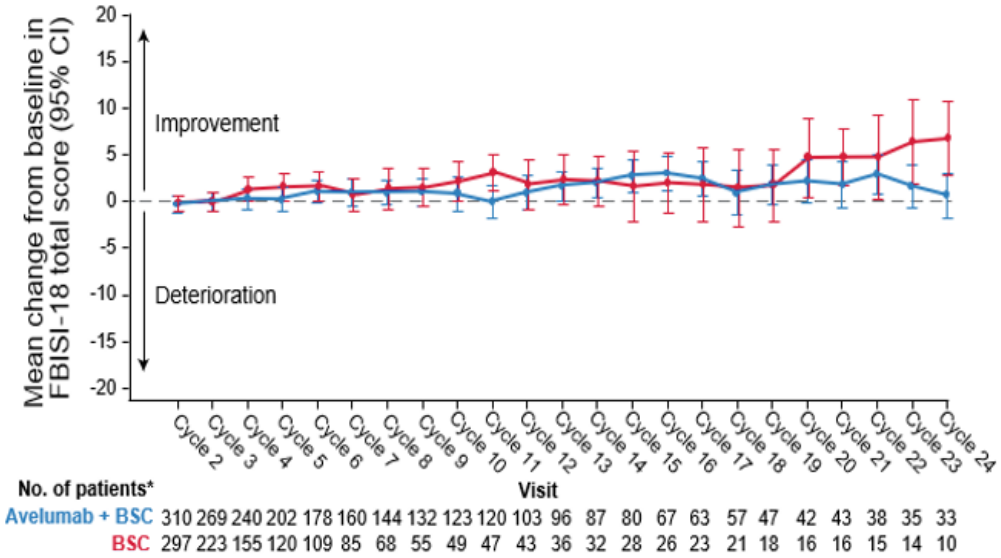
JAVELIN Bladder 100

Patient-reported Outcomes

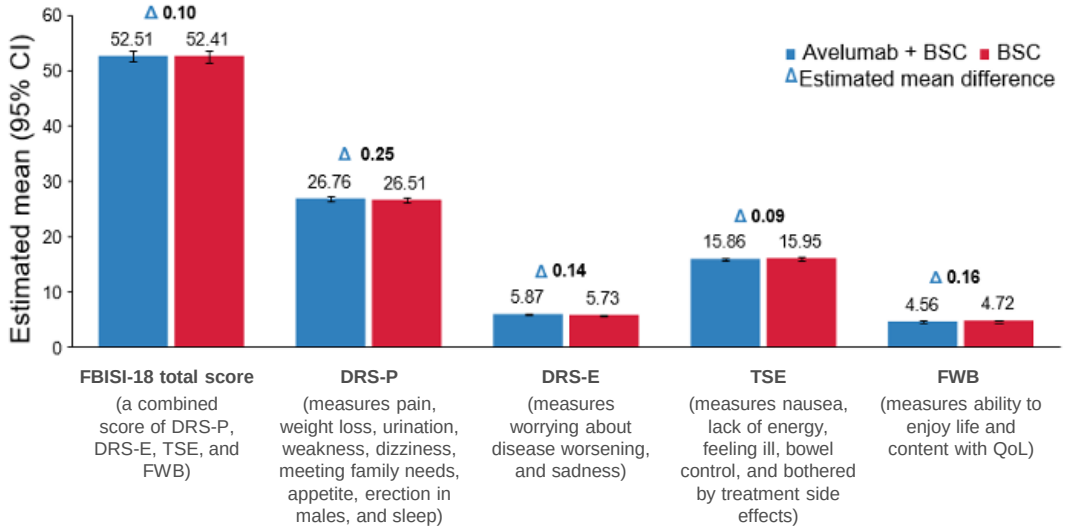
Secondary Endpoints: PROs in All Randomized Patients[1]

FBISI-18: a validated, bladder cancer-specific tool that measures symptoms and QoL in the past 7 days

Changes from baseline in FBISI-18 total score†



Mixed-model analysis of FBISI-18 total score and subscales prior to end of treatment



Limitations

- Open-label trial design and the limited number of patients providing data at later time points
- The limited number of patients at later cycles was prominent in the control arm, mainly due to progression events, which may limit interpretation of longer-term PRO
- The FBISI-18 instrument was validated in patients with bladder cancer, but some items may be less relevant for advanced disease in the maintenance setting
- All analyses were not adjusted for multiple testing, hindering their overall interpretation
- The methodology of this assessment does not allow conclusions based on this data

* Number of patients who completed the baseline assessment and the assessment at the respective cycle. † Includes data for on-treatment visits that had ≥10 patients in each arm.

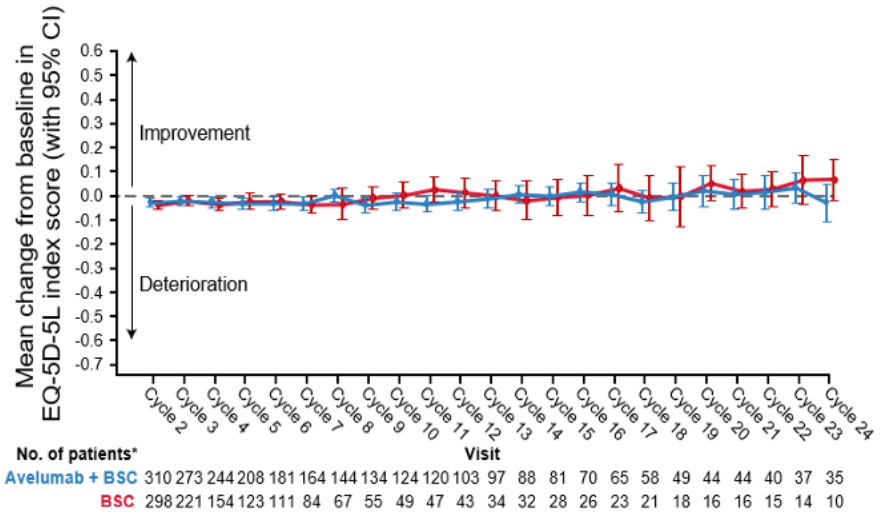
BSC, best supportive care; CI, confidence interval; DRS-E, disease-related symptoms–emotional; DRS-P, disease-related symptoms–physical; FBISI-18, Functional Assessment of Cancer Therapy – Bladder Symptom Index; FWB, general function/functional and well-being; OS, overall survival; PROs, patient-reported outcomes; QoL, quality of life; TSE, treatment side effects.

1. Grivas P, et al. Eur Urol. 2023;83(4):320-328.

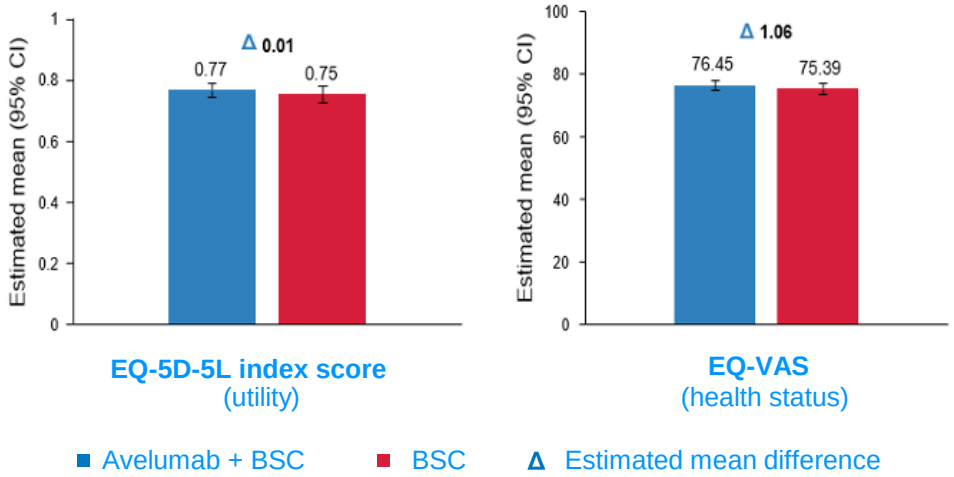
Secondary Endpoints: PROs in All Randomized Patients[1]

EQ-5D-5L: assesses general health status based on mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, on the day of assessment

Changes from baseline in EQ-5D-5L index score†



Mixed-model analysis of EQ-5D-5L index score and EQ-VAS prior to end of treatment



Limitations

- Open-label trial design and the limited number of patients providing data at later time points
- The limited number of patients at later cycles was prominent in the control arm, mainly due to progression events, which may limit interpretation of longer-term PRO
- All analyses were not adjusted for multiple testing, hindering their overall interpretation
- The methodology of this assessment does not allow conclusions based on this data

* Number of patients who completed the baseline assessment and the assessment at the respective cycle. † Includes data for on-treatment visits that had ≥10 patients in each arm.

BSC, best supportive care; CI, confidence interval; EQ-5D-5L, euroqol group 5-descriptors-5-levels; EQ-VAS, euroqol group visual analogue scale; OS, overall survival; PROs, patient-reported outcomes.

1. Grivas P, et al. Eur Urol. 2023;83(4):320-328.

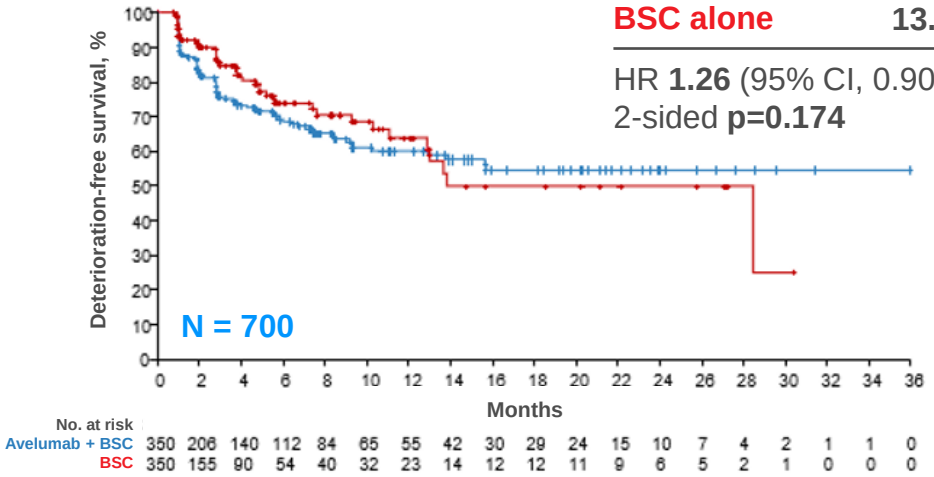
Secondary Endpoints: PROs in All Randomized Patients[1]

TTD: time-to-deterioration

TTD in FBISI-18 DRS-P scores*

Median TTD, months (95% CI)	
Avelumab + BSC	**NE** (13.9-NE)
BSC alone	**13.8** (12.9-NE)

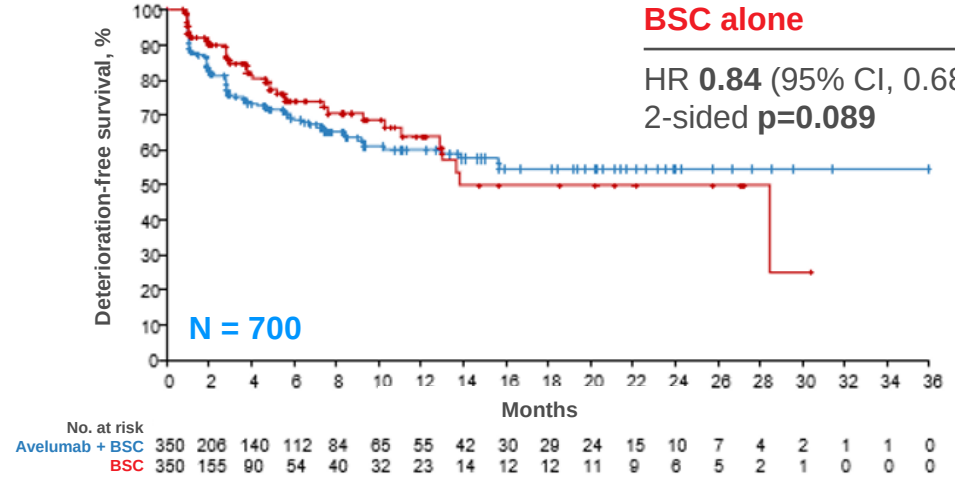
HR **1.26** (95% CI, 0.90-1.77);
2-sided **p=0.174**



TTD in FBISI-18 DRS-P scores or death*

Median TTD, months (95% CI)	
Avelumab + BSC	**9.2** (7.4-11.7)
BSC alone	**8.8** (7.9-9.9)

HR **0.84** (95% CI, 0.68-1.03);
2-sided **p=0.089**



Limitations

- Open-label trial design and the limited number of patients providing data at later time points
- The limited number of patients at later cycles was prominent in the control arm, mainly due to progression events, which may limit interpretation of longer-term PRO
- Crossing of curves and inconsistency between HRs and differences in median TTD suggest that HRs may be nonproportional
- Death and disease progression were not included in the prespecified event definition, and from Cycle 2, substantially fewer patients were eligible to complete PRO assessments in the control arm
- The methodology of this assessment does not allow conclusions based on this data

* TTD was defined as a ≥3-point decrease from baseline in the FBISI-18 DRS-P subscale for 2 consecutive assessments using the Kaplan-Meier method.

BSC, best supportive care; CI, confidence interval; DRS-P, disease-related symptoms–physical; FBISI-18, Functional Assessment of Cancer Therapy – Bladder Symptom Index; HR, hazard ratio; NE, not estimable; PRO, patient-reported outcome; TTD, time to deterioration.

1. Grivas P, et al. Eur Urol. 2023;83(4):320-328.

JAVELIN Bladder 100

Subsequent Therapy Data

Subsequent Anticancer Therapies in Patients Who Discontinued Study Treatment Due to Disease Progression[1,2]

	ALL PATIENTS (N = 700)		SUBGROUP THAT RECEIVED SUBSEQUENT THERAPY AFTER DISCONTINUING STUDY TREATMENT DUE TO DISEASE PROGRESSION (n = 383)	
	AVELUMAB + BSC (n = 350)	BSC ALONE (n = 350)	AVELUMAB + BSC (n = 158)	BSC ALONE (n = 225)
Discontinued* and received subsequent drug therapy, n (%)	185 (52.9)	252 (72.0)	158 (100)	225 (100)
PD-1 or PD-L1 inhibitor	40 (11.4)	186 (53.1)	27 (17.1)	166 (73.8)
FGFR inhibitor	10 (2.9)	13 (3.7)	10 (6.3)	11 (4.9)
Any other drug	177 (50.6)†	156 (44.6)‡	151 (95.6)	139 (61.8)
Study treatment ongoing, n (%)	43 (12.3)	10 (2.9)	–	–

74% of patients in the BSC arm received subsequent PD-1 or PD-L1 inhibitor therapy after discontinuing study treatment due to disease progression (vs 17% in avelumab + BSC arm)[1,2]

* Patients discontinued treatment due to progressive disease (59.7%, avelumab; 78.6%, BSC), adverse events (13.7%, avelumab; 0.6%, BSC), consent withdrawal (6.6%, avelumab; 8.9%, BSC), death (2.3%, avelumab; 4%, BSC), physician decision (3.1%, avelumab; 2%, BSC), global health deterioration (0.9%, avelumab; 1.4%, BSC), no longer meeting eligibility criteria (0.9%, avelumab), lost to follow-up (0.3%, avelumab; 0.3%, BSC), non-compliance with study drug (0.3%, avelumab) and other (1.4%, BSC).[2]
† The most common other drugs received were gemcitabine (n = 87), carboplatin (n = 66), paclitaxel (n = 60), vinflunine (n = 46), and cisplatin (n = 37). ‡ The most common other drugs received were gemcitabine (n = 67), paclitaxel (n = 59), carboplatin (n = 48), cisplatin (n = 28) and vinflunine (n = 22).

BSC, best supportive care; FGFR, fibroblast growth factor receptor; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1.

1. Powles T, et al. Poster E7. Presented at: ASCO GU Symposium; February 17-19, 2022; San Fransisco, CA. 2. Data on File, B9991001, August 2, 2021.

Subsequent Anticancer Therapies in Patients Who Discontinued Study Treatment for Any Reason[1,2]

	ALL PATIENTS (N = 700)		SUBGROUP THAT RECEIVED SUBSEQUENT THERAPY AFTER DISCONTINUING STUDY TREATMENT FOR ANY REASON (n = 437)	
	AVELUMAB + BSC (n = 350)	BSC ALONE (n = 350)	AVELUMAB + BSC (n = 185)	BSC ALONE (n = 252)
Discontinued* and received subsequent drug therapy, n (%)	185 (52.9)	252 (72.0)	185 (100)	252 (100)
PD-1 or PD-L1 inhibitor	40 (11.4)	186 (53.1)	40 (21.6)	186 (73.8)
FGFR inhibitor	10 (2.9)	13 (3.7)	10 (5.4)	13 (5.2)
Any other drug	177 (50.6)†	156 (44.6)‡	177 (95.7)	156 (61.9)
Study treatment ongoing, n (%)	43 (12.3)	10 (2.9)	–	–

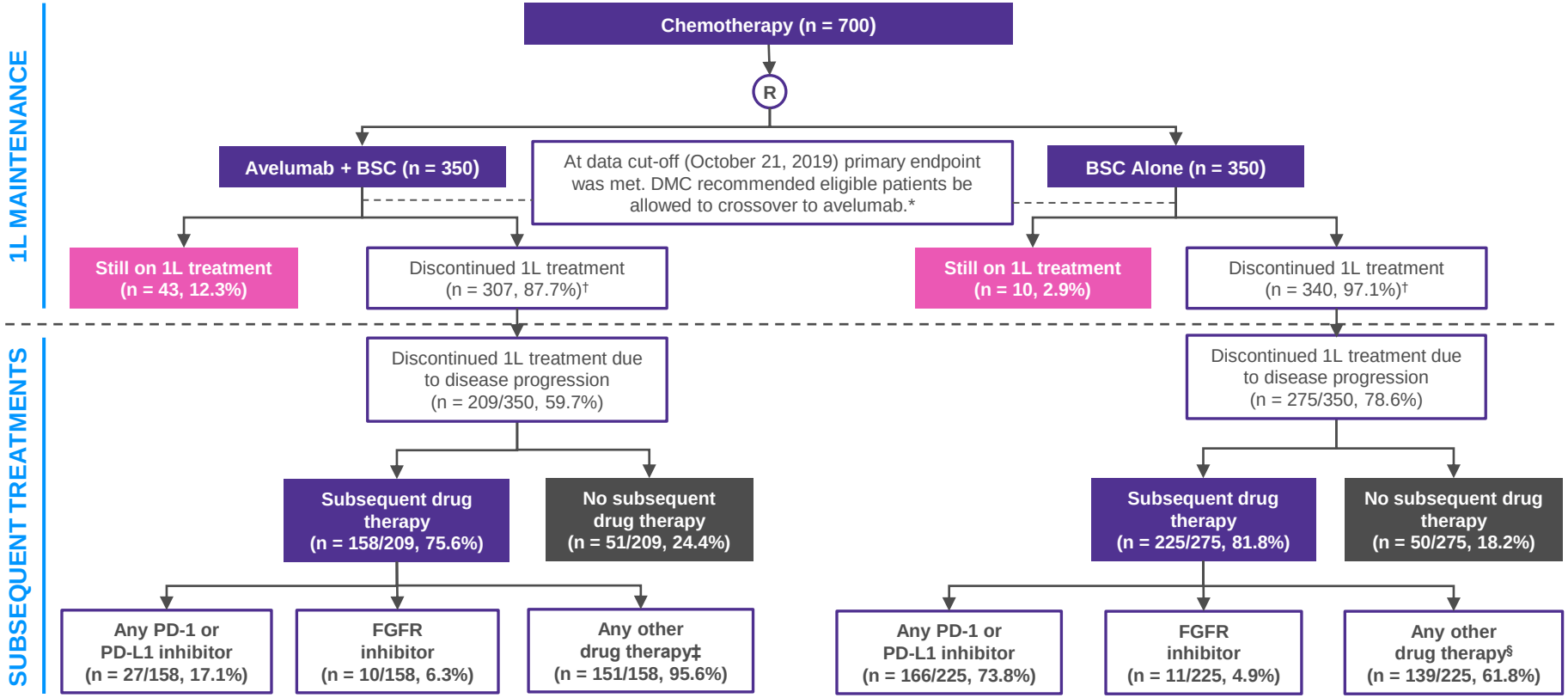
74% of patients in the BSC arm received subsequent PD-1 or PD-L1 inhibitor therapy after discontinuing study treatment for any reason* (vs 22% in avelumab + BSC arm)[1,2]

* Patients discontinued treatment due to progressive disease (59.7%, avelumab; 78.6%, BSC), adverse events (13.7%, avelumab; 0.6%, BSC), consent withdrawal (6.6%, avelumab; 8.9%, BSC), death (2.3%, avelumab; 4%, BSC), physician decision (3.1%, avelumab; 2%, BSC), global health deterioration (0.9%, avelumab; 1.4%, BSC), no longer meeting eligibility criteria (0.9%, avelumab), lost to follow-up (0.3%, avelumab; 0.3%, BSC), non-compliance with study drug (0.3%, avelumab) and other (1.4%, BSC).[2]
† The most common other drugs received were gemcitabine (n = 87), carboplatin (n = 66), paclitaxel (n = 60), vinflunine (n = 46), and cisplatin (n = 37). ‡ The most common other drugs received were gemcitabine (n = 67), paclitaxel (n = 59), carboplatin (n = 48), cisplatin (n = 28) and vinflunine (n = 22).

BSC, best supportive care; FGFR, fibroblast growth factor receptor; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1.

1. Powles T, et al. Poster E7. Presented at: ASCO GU Symposium; February 17-19, 2022; San Fransisco, CA. 2. Data on File, B9991001, August 2, 2021.

Subsequent Anticancer Therapies in Patients Who Discontinued Study Treatment Due to Disease Progression[1,2]



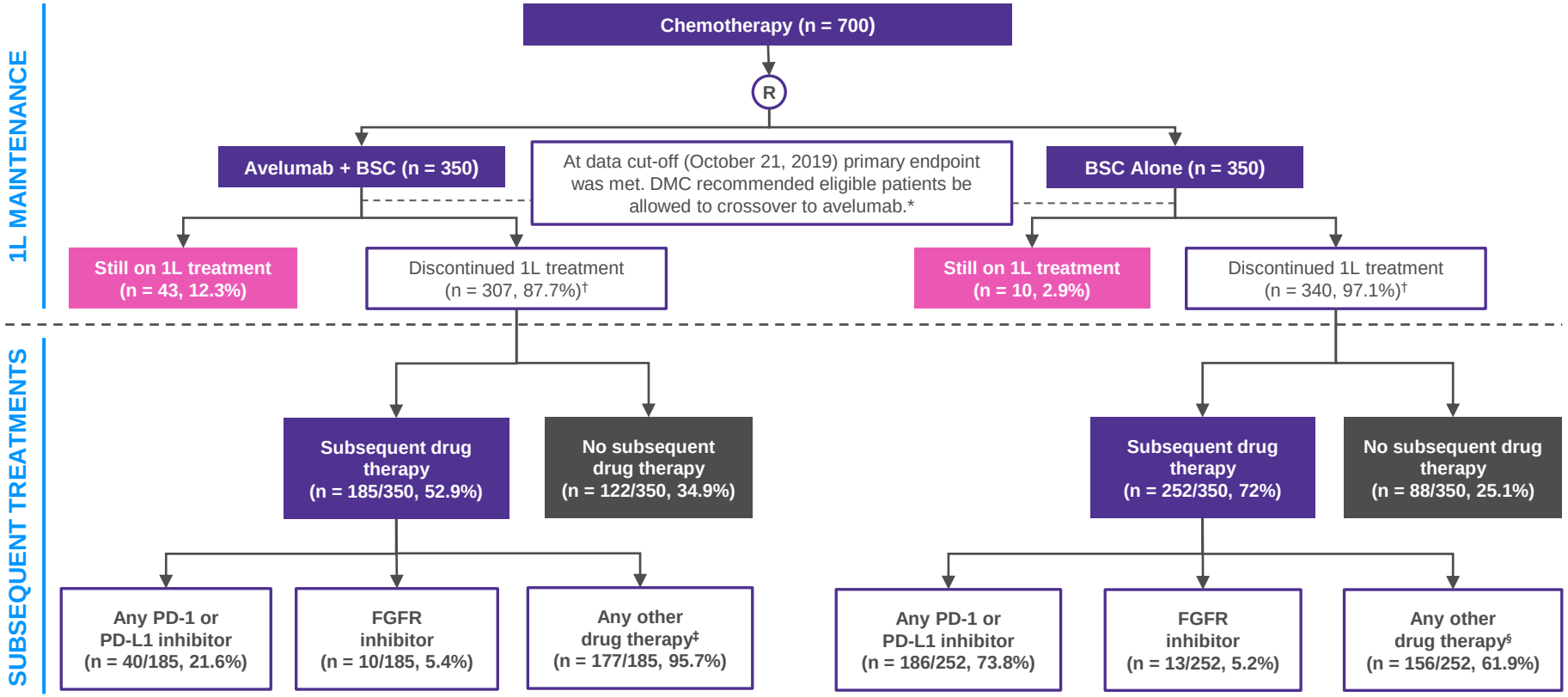
74% of patients in the BSC arm received subsequent PD-1 or PD-L1 inhibitor therapy after discontinuing study treatment due to disease progression (vs 17% in avelumab + BSC arm)[1,2]

* As of June 4, 2021, three patients crossed over from the BSC arm to the avelumab + BSC arm.[2] † Patients discontinued treatment due to progressive disease (59.7%, avelumab; 78.6%, BSC), adverse events (13.7%, avelumab; 0.6%, BSC), consent withdrawal (6.6%, avelumab; 8.9%, BSC), death (2.3%, avelumab; 4%, BSC), physician decision (3.1%, avelumab; 2%, BSC), global health deterioration (0.9%, avelumab; 1.4%, BSC), no longer meeting eligibility criteria (0.9%, avelumab), lost to follow-up (0.3%, avelumab; 0.3%, BSC), non-compliance with study drug (0.3%, avelumab) and other (1.4%, BSC).[2] ‡ The most common other drugs received were gemcitabine (n = 87), carboplatin (n = 66), paclitaxel (n = 60), vinflunine (n = 46), and cisplatin (n = 37). § The most common other drugs received were gemcitabine (n = 67), paclitaxel (n = 59), carboplatin (n = 48), cisplatin (n = 28) and vinflunine (n = 22).

1L, first-line; BSC, best supportive care; DMC, Data Monitoring Committee; FGFR, fibroblast growth factor receptor; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; R, randomized.

1. Powles T, et al. Poster E7. Presented at: ASCO GU Symposium; February 17-19, 2022; San Francisco, CA; 2. Data on File, B9991001, August 2, 2021.

Subsequent Anticancer Therapies in Patients Who Discontinued Study Treatment for Any Reason[1,2]



74% of patients in the BSC arm received subsequent PD-1 or PD-L1 inhibitor therapy after discontinuing study treatment for any reason* (vs 22% in avelumab + BSC arm)[1,2]

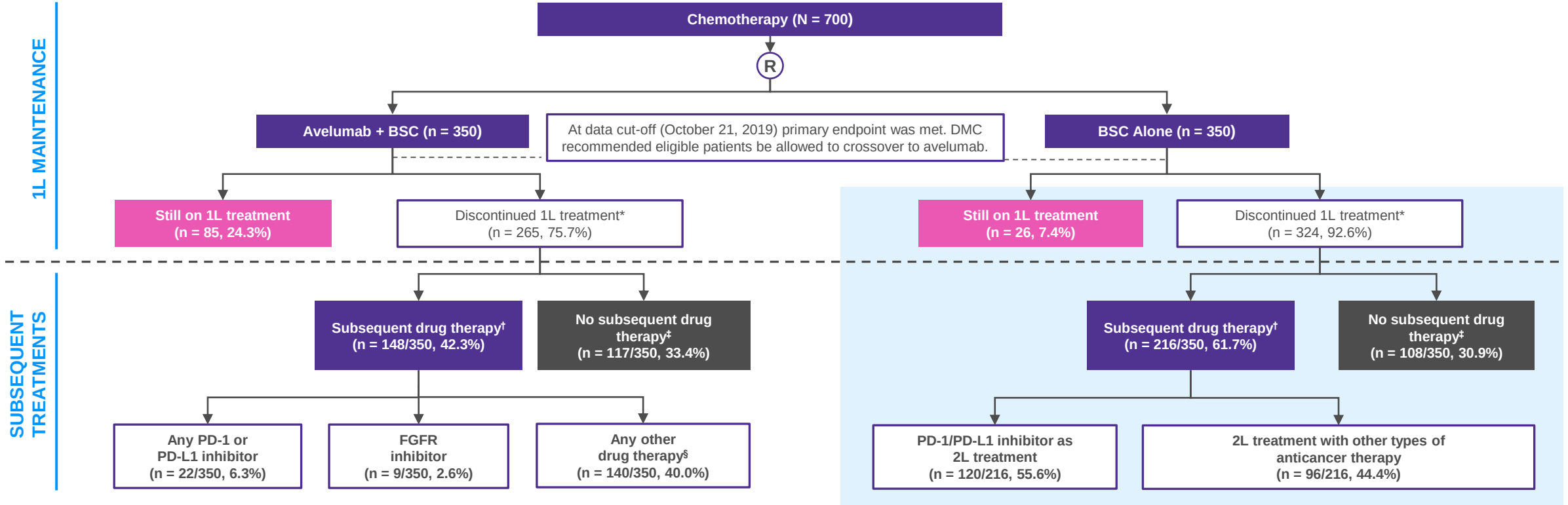
***** As of June 4, 2021, three patients crossed over from the BSC arm to the avelumab + BSC arm.[2] † Patients discontinued treatment due to progressive disease (59.7%, avelumab; 78.6%, BSC), adverse events (13.7%, avelumab; 0.6%, BSC), consent withdrawal (6.6%, avelumab; 8.9%, BSC), death (2.3%, avelumab; 4%, BSC), physician decision (3.1%, avelumab; 2%, BSC), global health deterioration (0.9%, avelumab; 1.4%, BSC), no longer meeting eligibility criteria (0.9%, avelumab), lost to follow-up (0.3%, avelumab; 0.3%, BSC), non-compliance with study drug (0.3%, avelumab) and other (1.4%, BSC).[2] ‡ The most common other drugs received were gemcitabine (n = 87), carboplatin (n = 66), paclitaxel (n = 60), vinflunine (n = 46), and cisplatin (n = 37). § The most common other drugs received were gemcitabine (n = 67), paclitaxel (n = 59), carboplatin (n = 48), cisplatin (n = 28) and vinflunine (n = 22).

1L, first-line; BSC, best supportive care; DMC, Data Monitoring Committee; FGFR, fibroblast growth factor receptor; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; R, randomized.

1. Powles T, et al. Poster E7. Presented at: ASCO GU Symposium; February 17-19, 2022; San Francisco, CA; 2. Data on File, B9991001, August 2, 2021.

Exploratory Ad-hoc Analysis of Overall Survival by 2L Therapy in the Best Supportive Care Arm

Subsequent Anticancer Therapies in All Randomized Patients[1-4]



***** Patients discontinued treatment due to progressive disease (54%, avelumab arm; 75%, BSC), adverse events (11%, avelumab; 1%, BSC), consent withdrawal (5%, avelumab; 8%, BSC), death (1%, avelumab; 4%, BSC), physician decision (1%, avelumab; 2%, BSC), global health deterioration (1%, avelumab; 2%, BSC), or other reasons (2%, avelumab; 1%, BSC). Other reasons included no longer meeting eligibility criteria (1%, avelumab), lost to follow-up (0.6%, avelumab; 0.6%, BSC), non-compliance with study drug (0.3%, avelumab) and other (0.3%, avelumab; 0.3%, BSC).[3]

† Some patients received >1 category of subsequent therapy. All percentages were calculated using the denominator of all patients in the treatment arm within each population.[2]

‡ Some patients who did not receive subsequent drug therapy received anticancer radiotherapy and/or anticancer surgery (n = 19, avelumab; n = 12, BSC).[6]

§ Other drug therapies included single agent or combination chemotherapies, TKI, antibody-drug conjugates, IDO1 inhibitors, PARP inhibitors, mTOR inhibitors, monoclonal antibodies, immune-stimulating vaccines or investigational agents.[7]

1L, first-line; 2L, second-line; BSC, best supportive care; DMC, Data Monitoring Committee; FGFR, fibroblast growth factor receptor; IDO, indoleamine 2,3-dioxygenase; IO, immunotherapy; mTOR, mammalian target of rapamycin; PARP, poly ADP-ribose polymerase; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; TKI, tyrosine kinase inhibitor.

1. Powles T, et al. N Engl J Med. 2020;383(13):1218-1230; 2. Powles T, et al. Abstract LBA1. Presented at: ASCO Virtual Annual Meeting; May 29-31, 2020; 3. Powles T, et al. N Engl J Med. 2020;383(13):1218-1230 (suppl); 4. PBS. Avelumab (urothelial carcinoma): solution concentrate for I.V. infusion 200 mg in 10 mL; Bavencio®. Accessed June 29, 2023. https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2021-03/files/avelumab-urothelial%20carcinoma-psd-mar-2021.pdf; 5. Data on File, B9991001, August 2, 2021; 6. Data on File, B9991001_adcm_s0010, January 14, 2020; 7. Data on File, B9991001_adcm_s009c_pdl1c, January 14, 2020.

EMD SERONO

Exploratory Ad-hoc Analysis: Overall Survival by 2L Therapy in the BSC Arm

	2L PD-1/PD-L1 INHIBITOR (n = 120)	2L NON–PD-1/ PD-L1 INHIBITOR (n = 96)	NO SUBSEQUENT ANTICANCER DRUG THERAPY* (n = 134)
OS, median (95% CI), months	16.5 (13.5-30.0)	14.0 (11.4-17.8)	13.3 (10.3-26.8)

* Including those who discontinued from the BSC arm with no subsequent therapy (n = 108) or who were still receiving BSC within the study (n = 26).[2]

Limitations

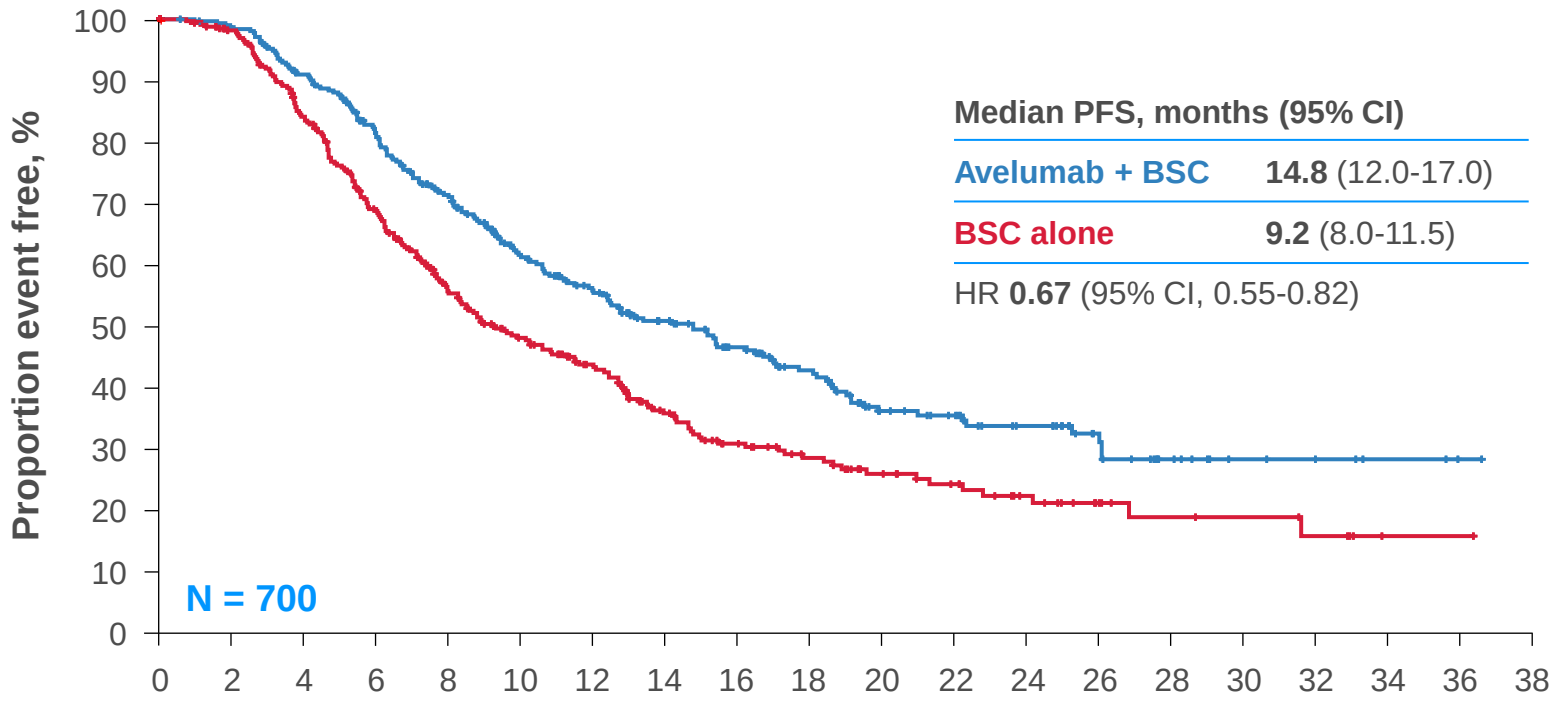
This ad-hoc analysis was an exploratory analysis and results need to be taken with caution. These results have not been published or presented and represent the BSC arm for descriptive purposes only and cannot be interpreted as a demonstration of efficacy.

2L, second-line; BSC, best supportive care; CI, confidence interval; OS, overall survival; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1.

1. PBS. Avelumab (urothelial carcinoma): solution concentrate for I.V. infusion 200 mg in 10 mL; Bavencio®. Accessed June 29, 2023. https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2021-03/files/avelumab-urothelial%20carcinoma-psd-mar-2021.pdf; 2. Powles T, et al. N Engl J Med. 2020;383(13):1218-1230.

Time to End of Next-line Therapy* in All Randomized Patients[1]

Post hoc analysis



No. at risk																				
Avelumab + BSC	350	307	279	243	204	162	138	112	92	74	51	45	34	23	13	7	6	3	1	0
BSC	350	315	266	211	157	125	102	74	57	46	34	27	19	12	8	7	5	1	1	0

Among all randomized patients, time to end of next-line therapy was prolonged in the avelumab + BSC arm vs the BSC alone arm

* Time to end of next-line therapy was defined in all patients as the time from randomization until discontinuation of next treatment received after first progression, as assessed by investigator, or death from any cause, whichever occurred first; patients who did not die or receive next-line therapy were censored at last follow-up.

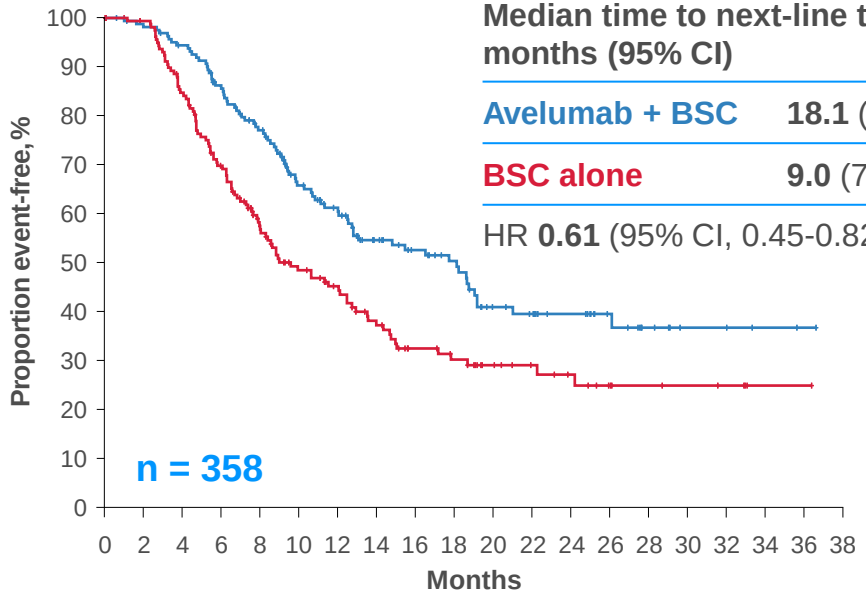
BSC, best supportive care; CI, confidence interval; HR, hazard ratio.

1. Grivas P, et al. Abstract 4525. Presented at: ASCO Virtual Annual Meeting; June 4-8, 2021.

Time to End of Next-line Therapy* by Tumor PD-L1 Status[1]

Post hoc analysis

PD-L1–positive



Median time to next-line therapy, months (95% CI)

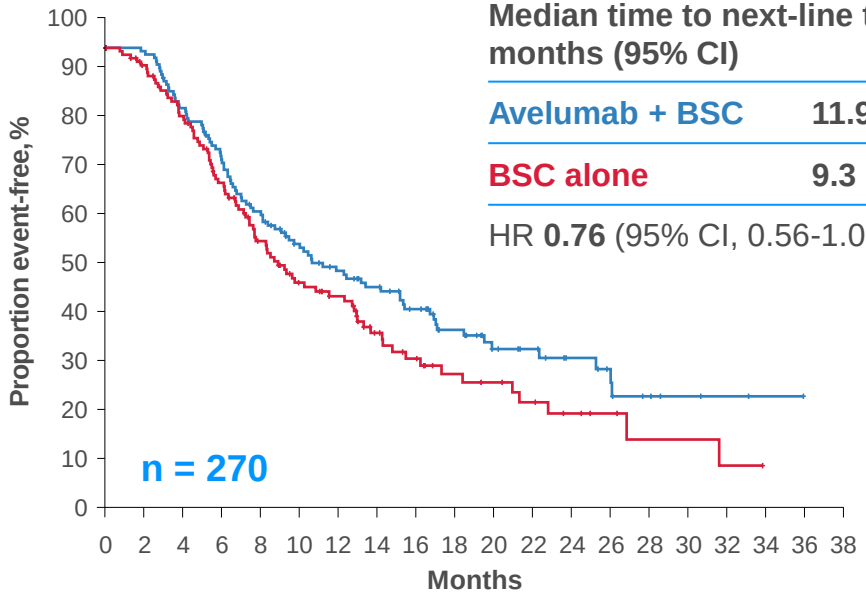
Avelumab + BSC	**18.1** (12.5-19.2)
BSC alone	**9.0** (7.9-12.5)

HR **0.61** (95% CI, 0.45-0.82)

No. at risk

Avel + BSC	189	158	150	132	114	89	75	57	49	43	30	27	22	14	8	4	4	2	1	0
BSC	169	156	132	105	77	61	52	40	30	26	19	15	12	8	6	5	4	1	1	0

PD-L1–negative



Median time to next-line therapy, months (95% CI)

Avelumab + BSC	**11.9** (9.1-15.4)
BSC alone	**9.3** (7.6-12.8)

HR **0.76** (95% CI, 0.56-1.04)

No. at risk

Avel + BSC	139	132	114	96	80	65	56	49	40	29	20	17	12	9	5	3	2	1	0	
BSC	131	119	103	82	62	47	40	26	20	14	12	9	6	4	2	2	1	0		

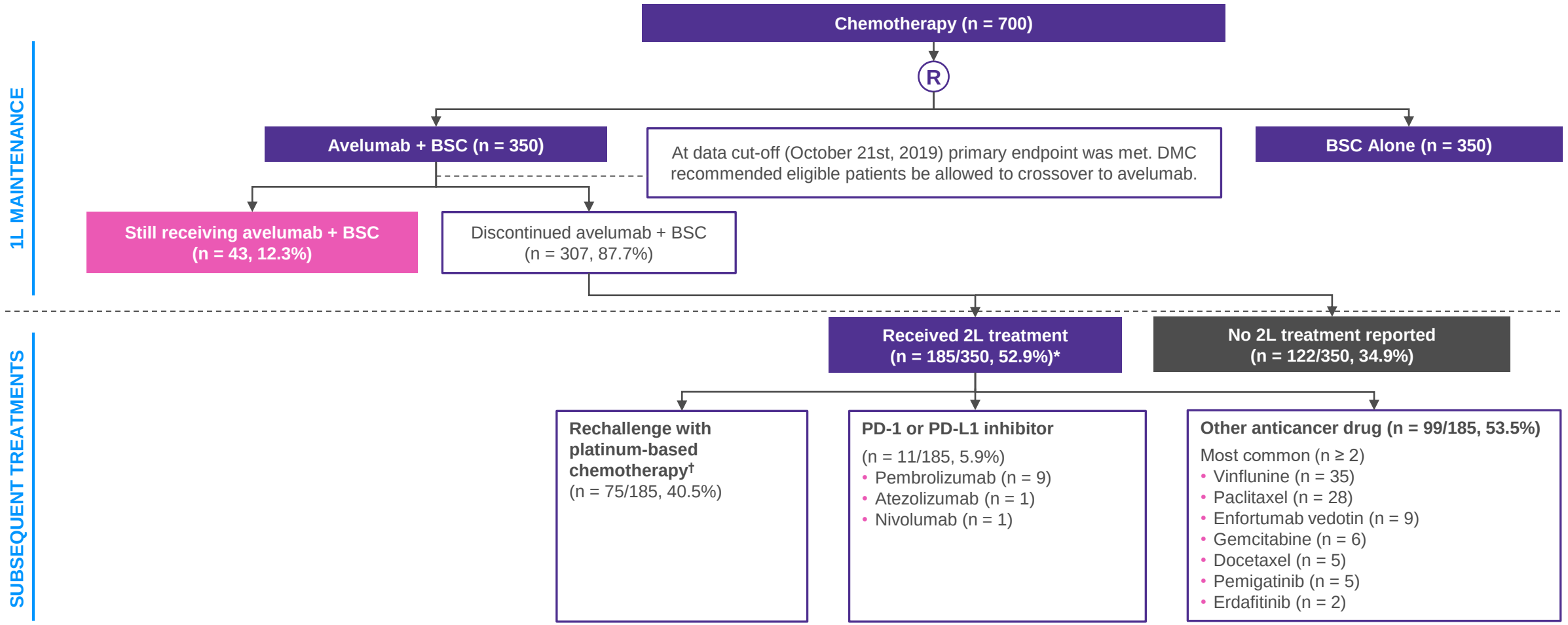
Time to end of next-line therapy was also longer in the avelumab + BSC arm vs the BSC alone arm in patients with PD-L1–positive or PD-L1–negative tumors

***** Time to end of next-line therapy was defined in all patients as the time from randomization until discontinuation of next treatment received after first progression, as assessed by investigator, or death from any cause, whichever occurred first; patients who did not die or receive next-line therapy were censored at last follow-up.

Avel, avelumab; BSC, best supportive care; CI, confidence interval; HR, hazard ratio; mo, months; PD-L1, programmed death ligand 1.

1. Grivas P, et al. Abstract 4525. Presented at: ASCO Virtual Annual Meeting; June 4-8, 2021.

Summary of Treatment Sequencing in the Avelumab + BSC Arm[1]



* Some patients also received third-line or later treatment. † Readministration of chemotherapy regimens administered as first-line treatment (gemcitabine + cisplatin or gemcitabine + carboplatin).

2L, second line; BSC, best supportive care; DMC, Data Monitoring Committee; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; R, randomized.

1. Bellmunt J, et al. Poster 4560. Presented at: ASCO Hybrid Annual Meeting; June 3-7, 2022; Chicago, IL.

Time From Randomization to End of 2L Treatment* in the Avelumab + BSC Arm[1]

Post hoc analysis

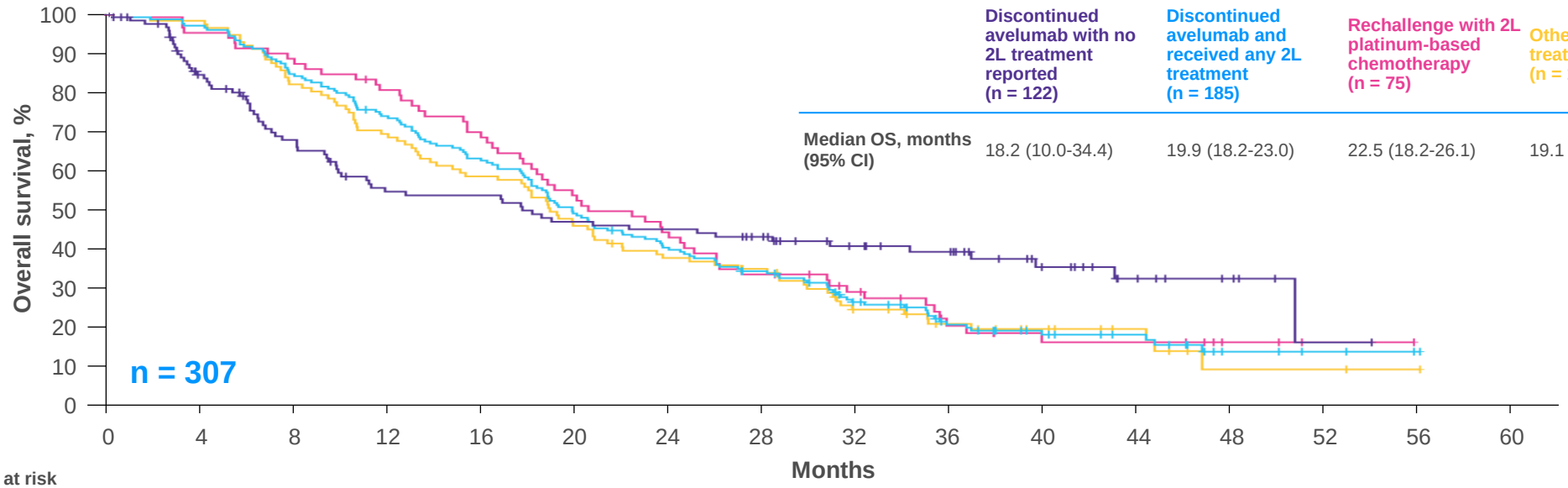
	N = 350	MEDIAN TIME FROM RANDOMIZATION TO END OF 2L TREATMENT* (95% CI), MONTHS
Discontinued avelumab and received any 2L treatment, n (%)	185 (52.9)	11.7 (9.7-13.8)
Rechallenge with 2L platinum-based chemotherapy	75 (21.4)	13.2 (9.3-16.7)
Other 2L anticancer treatment	110 (31.4)	10.8 (8.8-13.0)

* Time to end of 2L therapy was defined as the time from the date of randomization to discontinuation of 2L treatment after first objective disease progression by investigator assessment, or death from any cause, whichever occurred first.

2L, second-line; BSC, best supportive care; CI, confidence interval.

1. Bellmunt J, et al. Poster 4560. Presented at: ASCO Hybrid Annual Meeting; June 3-7, 2022; Chicago, IL.

Exploratory Analysis: Overall Survival by 2L Therapy in the Avelumab + BSC Arm[1]



	Discontinued avelumab with no 2L treatment reported (n = 122)	Discontinued avelumab and received any 2L treatment (n = 185)	Rechallenge with 2L platinum-based chemotherapy (n = 75)	Other 2L anticancer treatment (n = 110)
Median OS, months (95% CI)	18.2 (10.0-34.4)	19.9 (18.2-23.0)	22.5 (18.2-26.1)	19.1 (15.3-22.0)

No. at risk															
Discontinued avelumab with no 2L treatment reported	122	94	73	57	56	49	47	42	31	27	17	9	5	1	0
Discontinued avelumab and received any 2L treatment	185	181	158	137	117	91	74	60	41	27	19	14	5	3	1	0
Rechallenge with 2L platinum-based chemotherapy	75	72	67	60	52	40	33	25	19	11	8	7	3	1	0
Other 2L anticancer treatment	110	109	91	77	65	51	41	35	22	16	11	7	2	2	1	0

Limitations

Although the follow-up OS analysis was prespecified, no formal hypothesis testing was performed given that the OS endpoint was met in the initial interim analysis (primary analysis). Therefore, this analysis is exploratory and results need to be taken with caution and cannot be interpreted as a demonstration of efficacy

2L, second-line; CI, confidence interval; OS, overall survival.

1. Bellmunt J, et al. Poster 4560. Presented at: ASCO Hybrid Annual Meeting; June 3-7, 2022; Chicago, IL.

JAVELIN Bladder 100: Summary

1° endpoint

JAVELIN Bladder 100 met its primary objective of prolonging OS with avelumab + BSC vs BSC alone, both among all randomized patients and those with PD-L1–positive tumors in the primary analysis[1]

OS was longer with avelumab + BSC vs BSC alone across prespecified subgroups[2]

- Includes subgroups defined by cisplatin-based or carboplatin-based CT, or response or SD with 1L platinum-containing CT
- Small patient numbers can be a limitation of subgroup analyses and results presented for each subgroup are for descriptive purposes only

In post hoc analyses, OS was longer with avelumab + BSC vs BSC alone

- Irrespective of duration or number of cycles of 1L chemotherapy received prior to randomization[3]; and
- Among patients with PD-L1–positive tumors who received 1L carboplatin + gemcitabine[4]

2° endpoint

The safety profile of avelumab as 1L maintenance was consistent with previous studies of avelumab monotherapy[2,5]

In all subgroups defined by older age (≥65 to ≥80 years), OS and PFS were prolonged in the avelumab + BSC arm vs the BSC alone arm and no new safety concerns were identified[6]

1L, first-line; BSC, best supportive care; CT, chemotherapy; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; SD, stable disease; UC, urothelial carcinoma.

1. Powles T, et al. N Engl J Med. 2020;383(13):1218-1230; 2. Powles T, et al. N Engl J Med. 2020;383(13):1218-1230 (suppl); 3. Loriot Y, et al. Presented at ASCO GU 2021. Abstract 438; 4. Powles T, et al. Poster presentation at ASCO 2021. Abstract 4520; 5. Kelly K, et al. Cancer 2018;124:2010–2017; 6. Gupta S, et al. Poster No. 2371P. Presented at the ESMO Congress 2023, 20-24 October 2023; Madrid, Spain.

JAVELIN Bladder 100: Summary

In patients with high BMI (BMI ≥30 kg/m^2 at baseline), OS and investigator-assessed PFS was prolonged in the avelumab + BSC arm vs the BSC alone arm. Long-term safety in these patients was generally consistent with that in the overall safety population[1]

In subgroups with or without diabetes mellitus, OS and PFS were prolonged with avelumab + BSC vs BSC alone. The long-term safety of avelumab 1L maintenance was similar in patients with controlled or without diabetes mellitus at randomization. Most common TRAEs that occurred in patients with or without diabetes mellitus were consistent with those observed in the overall population[2]

In patients with low tumor burden, OS and investigator-assessed PFS were prolonged in the avelumab + BSC arm vs the BSC alone arm. Long-term safety of avelumab 1L maintenance was acceptable in all subsets of patients with low tumor burden[3]

In patients with histological subtypes (<50% histological subtype component, including squamous, glandular, and variant differentiation), OS and investigator-assessed PFS were prolonged in the avelumab + BSC vs the BSC alone arm. Long-term safety in these patients were generally consistent with that in the overall safety population[4]

No significant difference in OS was noted across molecular UC subtypes (Ba/Sq, LumNS, LumP, LumU, SR)[5]

In subgroups with high or low *NECTIN4* RNA expression, OS and PFS improvements with avelumab + BSC vs BSC alone were not significantly different with those observed in the overall population[6]

1L, first-line; Ba/Sq, basal/squamous; BMI, body mass index; BSC, best supportive care; CT, chemotherapy; LumNS, luminal nonspecified; LumP, luminal papillary; LumU, luminal unstable; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; SD, stable disease; SR, stroma rich; TRAE, treatment-related adverse events; UC, urothelial carcinoma.

1. Aragon-Ching JB, et al. Abstract No. 600. Presented at: ASCO Genitourinary Cancers Symposium; January 25-27, 2024; San Francisco, CA. 2. Gupta S, et al. Abstract No. 869. Presented at the ASCO Genitourinary Cancers Symposium, February 13-15, 2025; San Francisco, CA. 3. Bellmunt J , et al. Abstract No. 4566. Presented at the 2024 ASCO Annual Meeting, May 31-June 4, 2024; 4. Loriot Y, et al. Abstract No. 4567. Presented at the 2024 ASCO Annual Meeting, May 31-June 4, 2024; Chicago, IL. 5. Eckstein M., et al. Abstract No. 828. Presented at the ASCO Genitourinary Cancers Symposium, February 13-15, 2025; San Francisco, CA. Chicago, IL.6. Klümper N, et al. Abstract No. 827. Presented at the ASCO Genitourinary Cancers Symposium, February 13-15, 2025; San Francisco, CA.

JAVELIN Bladder 100: Summary

Patients who had received 1 or 2 years of avelumab treatment have a high probability of additional years of survival. Types of TRAEs that occurred after 1 or 2 years of treatment were consistent with those observed in the overall population[1]

- Avelumab maintenance in patients whose disease has not progressed with 1L platinum-containing CT represents a treatment option in the 1L setting for patients with advanced UC[2]
- These results further support the recommendation of avelumab 1L maintenance as standard of care for patients with advanced UC that has not progressed with 1L platinum-containing chemotherapy.[3] Long-term safety data and the high percentage of patients on treatment at 2 years indicate the good tolerability and feasibility of the regimen as treatment until progression

- An exploratory analysis with ≥2 years of follow-up (additional 19 months of median follow-up from the initial analysis), enabling assessment of longer-term efficacy and safety[4]

A plain language summary (PLS) of the initial JB100 data was published in *Future Oncology* (doi: 10.2217/fon-2021-1631)[5]

1L, first-line; CT, chemotherapy; TRAE, treatment related adverse events; UC, urothelial carcinoma.

1. Grivas P, et al. Poster No. 1975P. Presented at the ESMO Congress 2024, 13-17 September 2024; Barcelona, Spain. 2. Powles T, et al. Oral presentation at ASCO 2020. Abstract LBA1. 3. Powles T, et al. Poster E7. Presented at: ASCO GU Symposium; February 17-19, 2022; San Francisco, CA; 4. Powles T, et al. Poster E7. Presented at: ASCO GU Symposium; February 17-19, 2022; San Francisco, CA; 5. Powles T, et al. Future Oncol. 2022; 18(19):2361-2371.