

# Avelumab first-line maintenance for advanced urothelial carcinoma: long-term outcomes from JAVELIN Bladder 100 in subgroups defined by first-line chemotherapy regimen and analysis of overall survival from start of first-line chemotherapy

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## Disclosures for Dr Gupta

- Consulting or advisory roles for AVEO, Gilead Sciences, Guardant Health, Loxo/Lilly, Merck & Co., Kenilworth, NJ, Pfizer, and the healthcare business of Merck KGaA, Darmstadt, Germany
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# Background

- In the JAVELIN Bladder 100 trial, avelumab 1L maintenance + BSC significantly prolonged OS and PFS vs BSC alone in patients with advanced UC without PD following 1L platinum-based chemotherapy<sup>1,2</sup>
  - After ≥2 years of follow-up in all patients, median OS was 23.8 vs 15.0 months, respectively (HR, 0.76 [95% CI, 0.63-0.91]; p=0.0036)<sup>2</sup>
  - Long-term safety of avelumab 1L maintenance was demonstrated and no new safety concerns were identified<sup>2</sup>
- Results from this trial led to the approval of avelumab 1L maintenance in various countries worldwide
  - Avelumab 1L maintenance is recommended as a standard of care in international treatment guidelines for cisplatin-eligible and cisplatin-ineligible patients with advanced UC without PD after 1L platinum-based chemotherapy<sup>3-5</sup>

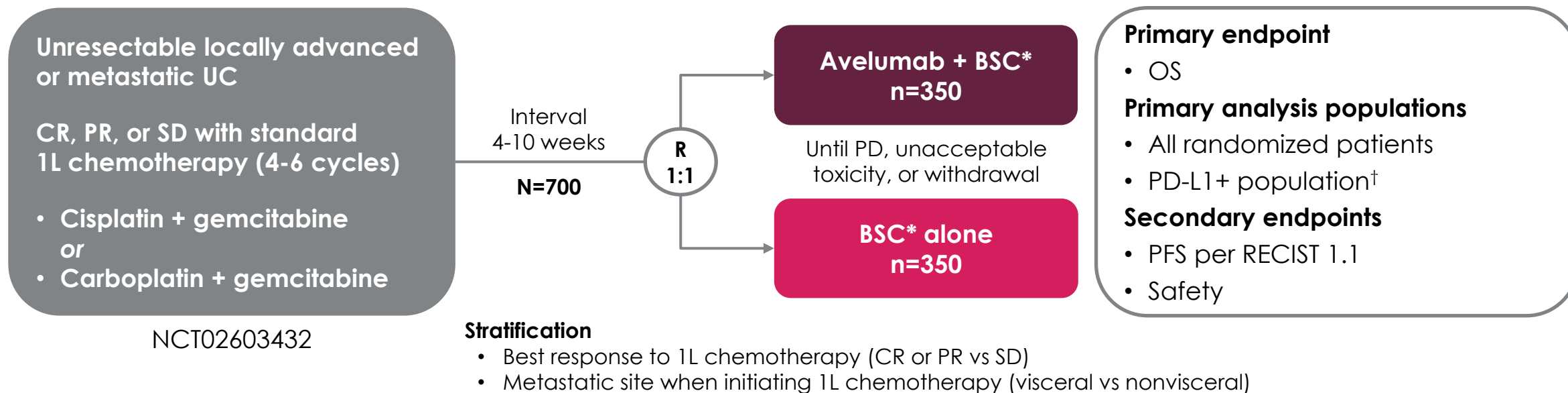
1L, first line; BSC, best supportive care; HR, hazard ratio; OS, overall survival; PD, progressive disease; PFS, progression-free survival; UC, urothelial carcinoma.

1. Powles T, et al. N Engl J Med. 2020;383(13):1218-30. 2. Powles T, et al. J Clin Oncol. 2023;41(19):3486-92. 3. NCCN Clinical Practice Guidelines: Bladder Cancer. V1.2024. 4. Powles T, et al. Ann Oncol. 2022;33(3):244-58; 5. Cathomas R, et al. Eur Urol. 2022;81(1):95-103.

# Design of JAVELIN Bladder 100: an international phase 3 trial<sup>1</sup>

Endpoints measured post randomization (after chemotherapy)

OS measured from the start of 1L chemotherapy



- We report post hoc analyses to evaluate:
  - OS from start of avelumab 1L maintenance in subgroups defined by 1L chemotherapy regimen
  - OS from the start of 1L chemotherapy

1L, first line; BSC, best supportive care; CR, complete response; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease; UC, urothelial carcinoma.

\*BSC (eg, antibiotics, nutritional support, hydration, and pain management) was administered per local practice based on patient needs and clinical judgment; other antitumor therapy was not permitted, but palliative local radiotherapy for isolated lesions was acceptable. <sup>†</sup>PD-L1+ status was defined as PD-L1 expression in ≥25% of tumor cells or in ≥25% or 100% of tumor-associated immune cells if the percentage of immune cells was >1% or ≤1%, respectively (Ventana SP263 assay).

1. Powles T, et al. N Engl J Med. 2020;383(13):1218-30.

# Baseline characteristics by 1L chemotherapy regimen

	Cisplatin + gemcitabine		Carboplatin + gemcitabine	
	Avelumab + BSC (n=183)	BSC alone (n=206)	Avelumab + BSC (n=147)	BSC alone (n=122)
<b>Age, median (range), years</b>	<b>66.0 (37.0-86.0)</b>	<b>67.0 (32.0-84.0)</b>	<b>71.0 (46.0-90.0)</b>	<b>73.5 (46.0-89.0)</b>
<b>ECOG PS, n (%)</b>				
0	124 (67.8)	135 (65.5)	75 (51.0)	65 (53.3)
1	<b>58 (31.7)</b>	<b>71 (34.5)</b>	<b>72 (49.0)</b>	<b>54 (44.3)</b>
≥2	<b>1 (0.5)</b>	<b>0</b>	<b>0</b>	<b>3 (2.5)</b>
<b>Site of metastasis*, n (%)</b>				
Visceral	103 (56.3)	121 (58.7)	80 (54.4)	59 (48.4)
Nonvisceral	80 (43.7)	85 (41.3)	67 (45.6)	63 (51.6)
<b>PD-L1 status, n (%)†</b>				
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)
<b>Best response to 1L chemotherapy, n (%)</b>				
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)
<b>CrCl, n (%)</b>				
≥60 mL/min	118 (64.5)	132 (64.1)	53 (36.1)	54 (44.3)
<60 mL/min	<b>65 (35.5)</b>	<b>69 (33.5)</b>	<b>93 (63.3)</b>	<b>67 (54.9)</b>
Unknown	0	5 (2.4)	1 (0.7)	1 (0.8)

- Patients in the carboplatin subgroup were older and included a larger proportion with ECOG PS ≥1 or CrCl <60 mL/min

Data of note in these subgroups are highlighted.

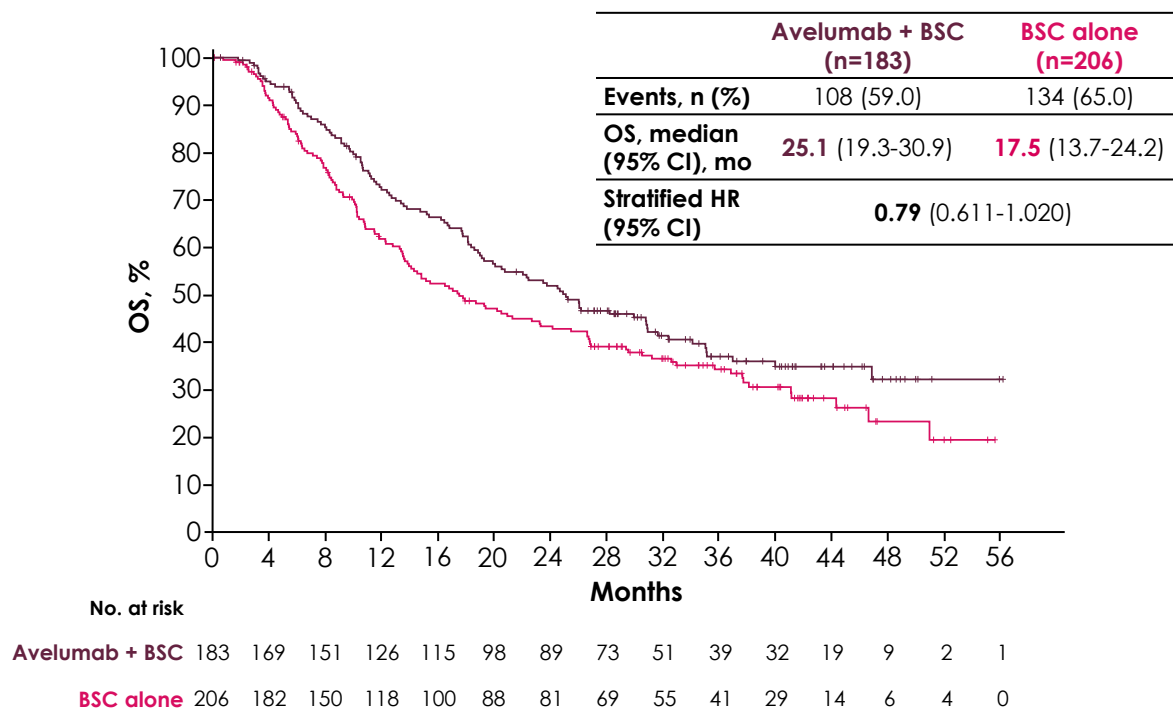
**1L**, first line; **BSC**, best supportive care; **CR**, complete response; **CrCl**, creatinine clearance; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **PR**, partial response; **SD**, stable disease.

\*Site of metastasis at the start of 1L chemotherapy.

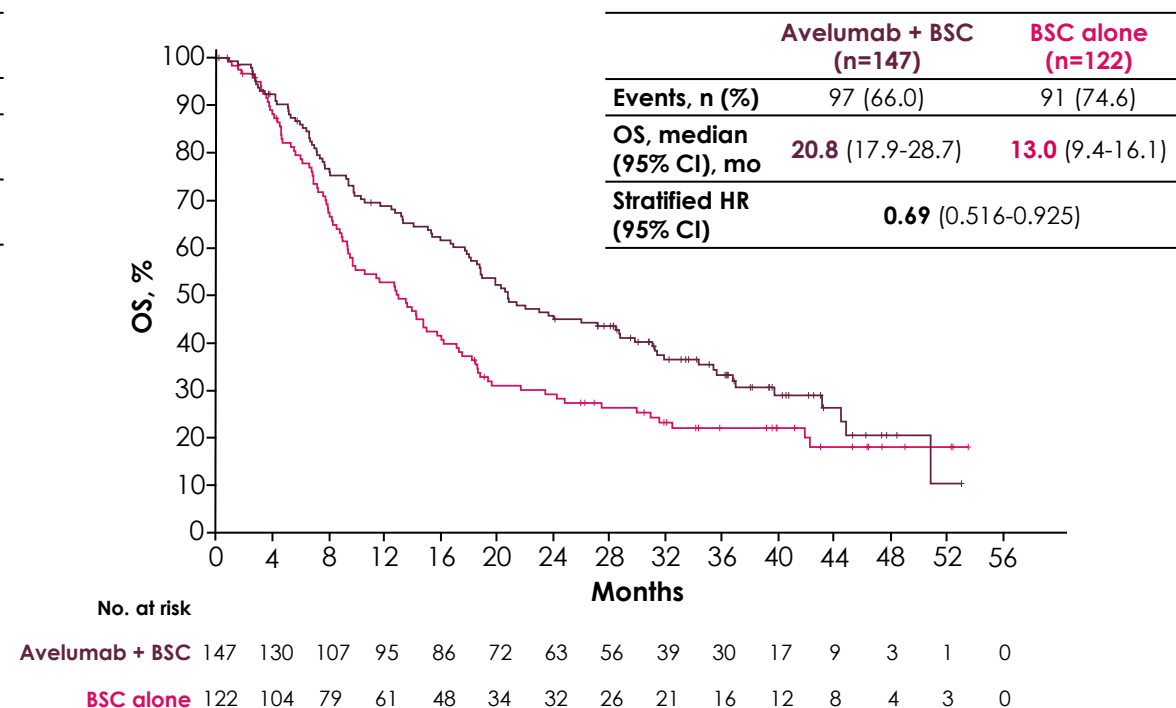
†PD-L1+ status was defined as PD-L1 expression in ≥25% of tumor cells or in ≥25% or 100% of tumor-associated immune cells if the percentage of immune cells was >1% or ≤1%, respectively (Ventana SP263 assay).

# OS measured from start of avelumab maintenance in subgroups defined by 1L chemotherapy regimen

**Cisplatin + gemcitabine**

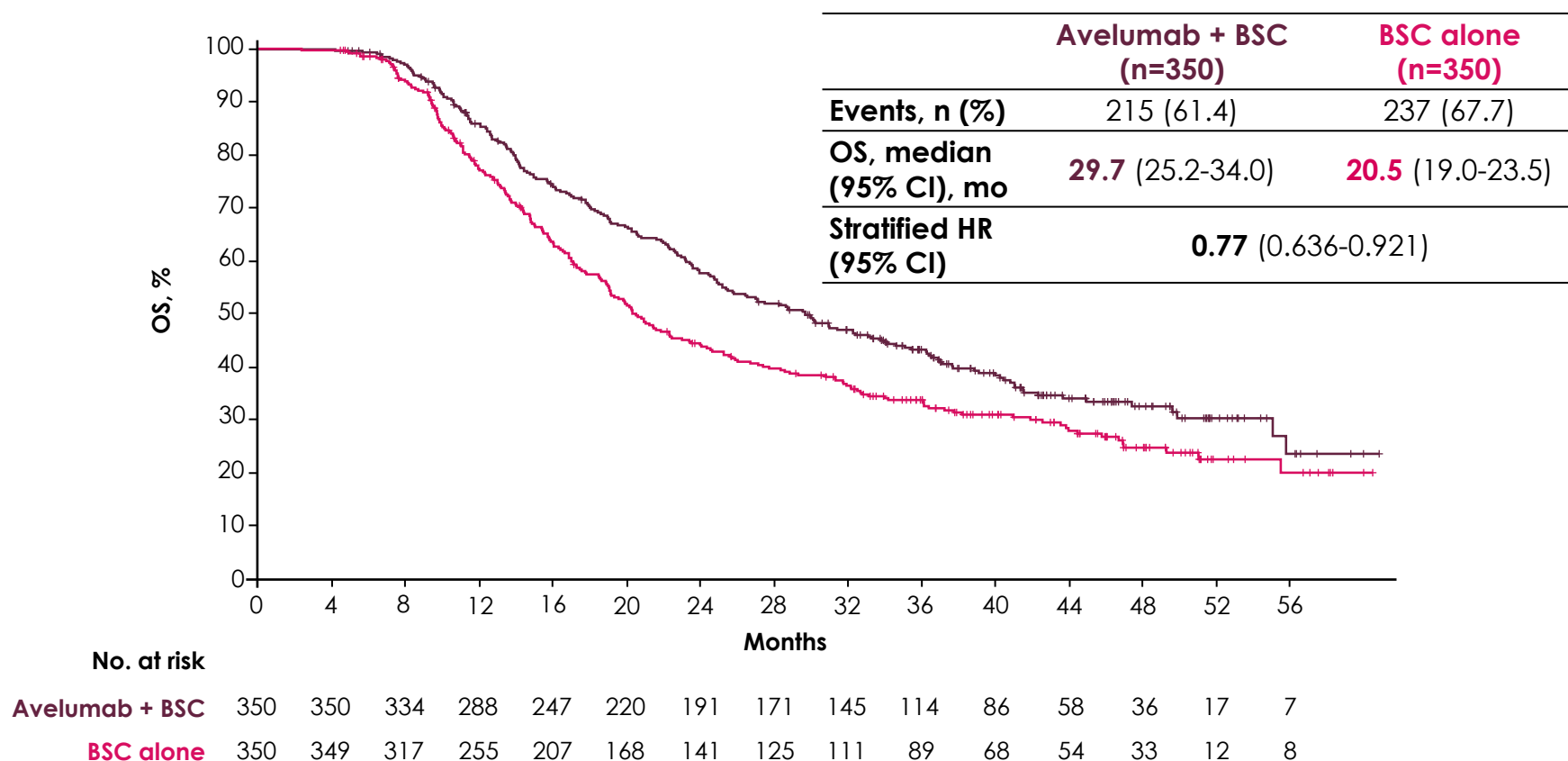


**Carboplatin + gemcitabine**



- OS was longer with avelumab + BSC vs BSC alone in both subgroups
- Investigator-assessed PFS was also longer in the avelumab + BSC arm vs the BSC alone arm in both subgroups
  - **Cisplatin + gemcitabine:** 5.7 months (95% CI, 4.6-7.5) vs 2.0 months (95% CI, 1.9-3.6); HR, 0.56 (95% CI, 0.446-0.713)
  - **Carboplatin + gemcitabine:** 3.7 months (95% CI, 3.6-5.6) vs 2.0 months (95% CI, 1.9-3.0); HR, 0.48 (95% CI, 0.362-0.640)

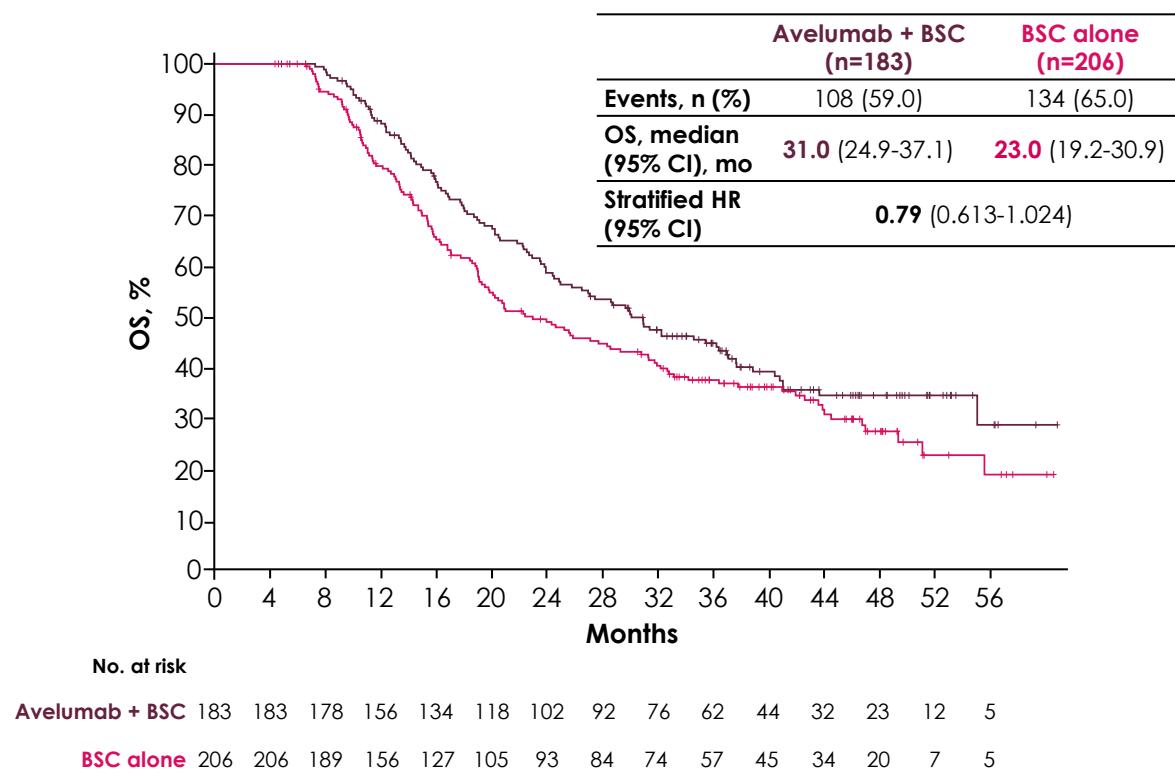
# Exploratory analysis of OS measured from the start of 1L chemotherapy in the overall population



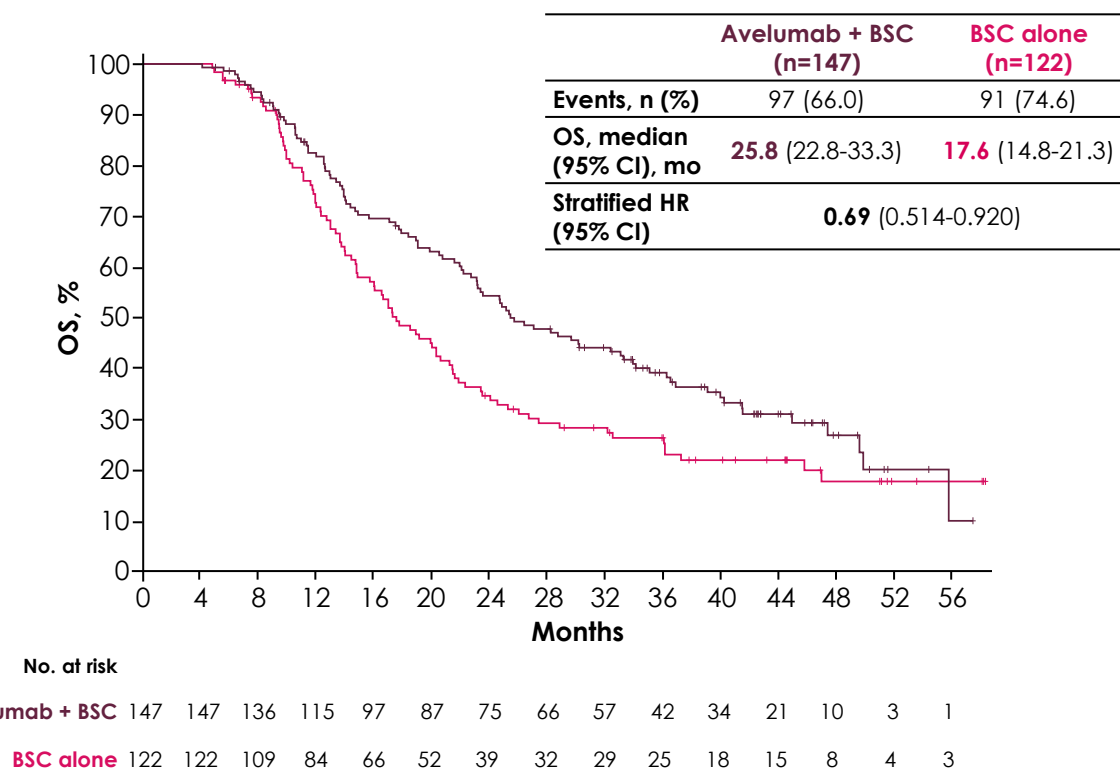
- The JAVELIN Bladder 100 trial only enrolled patients without disease progression following 1L platinum-based chemotherapy (ie, patients with CR, PR, or SD)

# Exploratory analysis of OS measured from the start of 1L chemotherapy in subgroups defined by 1L chemotherapy regimen

Cisplatin + gemcitabine



Carboplatin + gemcitabine



- OS measured from start of 1L chemotherapy was longer with avelumab + BSC vs BSC alone irrespective of 1L chemotherapy regimen
  - The JAVELIN Bladder 100 trial only enrolled patients without disease progression following 1L platinum-based chemotherapy (ie, patients with CR, PR, or SD)



# Exploratory analysis of long-term safety in subgroups defined by 1L chemotherapy regimen

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

- Long-term safety with avelumab was similar in subgroups that had received 1L cisplatin or carboplatin

Data of note in these subgroups are highlighted.

1L, first line; AE, adverse event; BSC, best supportive care; IRR, infusion-related reaction; N/A, not applicable; TRAE, treatment-related adverse event.

# Conclusions

- Long-term follow-up from the JAVELIN Bladder 100 trial (median follow-up,  $\geq 38.0$  months) confirmed that avelumab 1L maintenance provided similar OS and PFS benefits in patients treated with prior 1L cisplatin- or carboplatin-based chemotherapy
  - The JAVELIN Bladder 100 trial only enrolled patients without disease progression following 1L platinum-based chemotherapy (ie, patients with CR, PR, or SD)
- In the overall population, median OS from the start of 1L platinum-based chemotherapy (exploratory analysis) was 29.7 months
- Long-term safety of avelumab 1L maintenance was similar in patients who had received 1L cisplatin- or carboplatin-based chemotherapy
- These results further support avelumab 1L maintenance as the standard of care in patients with advanced UC without PD following 1L platinum-based chemotherapy

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