Avelumab first-line maintenance in advanced urothelial carcinoma: conditional survival and long-term safety in patients treated for ≥1 or ≥2 years in JAVELIN Bladder 100

P. Grivas,[1] S. H. Park,[2] E. Voog,[3] W.-P. Su,[4] W. Demey,[5] P. C. Fong,[6] J. A. Garcia,[7] N. Jacob,[8] A. Gerhold-Ay,[8] K. Tyroller,[9] J. Hoffman,[5] J. Bellmunt,[10] T. Powles[11]

[1]University of Washington, Fred Hutchinson Cancer Center, Seattle, WA, USA; [2]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea; [3]Centre Jean Bernard Clinique Victor Hugo, Le Mans, France; [4]National Cheng Kung University Hospital, Tainan City, Taiwan; [5]AZ KLINA, Brasschaat, Belgium; [6]Auckland Hospital and the University of Auckland, Auckland, New Zealand; [7]University Hospitals Seidman Cancer Center, Cleveland, OH, USA; [8]Merck Healthcare KGaA, Darmstadt, Germany; [9]EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA; [10]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA; [11]Barts Cancer Institute, Experimental Cancer Medicine Centre, Queen Mary University of London, St Bartholomew's Hospital, London, UK

JAVELIN Bladder 100

CONCLUSIONS

- **This post hoc analysis from the JAVELIN Bladder 100 phase 3 trial examined the probability of additional overall survival (OS), progression-free survival (PFS), and safety in patients with advanced urothelial carcinoma (UC) that had not progressed with first-line (1L) platinum-based chemotherapy who received ≥1 or ≥2 years of avelumab 1L maintenance treatment**
- **In patients who had received 1 year of avelumab treatment (118/344 [34.3%] treated patients), the probability of an additional 1 or 2 years of OS was 93.2% and 79.6%, respectively**
- **In patients who had received 2 years of avelumab treatment (68/344 [19.8%]), the probability of an additional 1 or 1.5 years of OS was 95.8% and 90.3%, respectively**
- **Patients who had received 1 or 2 years of avelumab treatment also had a high probability (66.7%) of having an additional 1 year of PFS**
- **In patients still receiving treatment, rates of grade ≥3 treatment-related adverse events (TRAEs) occurring after 1 or 2 years were low (11.9% and 5.9%, respectively)**
- **Overall, these results inform prognosis and show that patients with advanced UC without progression after 1L platinum-based chemotherapy who survive for ≥1 or ≥2 years while receiving avelumab 1L maintenance treatment have a high probability of additional years of OS, with low rates of grade ≥3 TRAEs**

PLAIN LANGUAGE SUMMARY

- **The JAVELIN Bladder 100 clinical trial showed that avelumab maintenance treatment helps people with advanced urothelial cancer live longer**
  - **Maintenance treatment means treating people whose cancer has disappeared, shrank, or stopped growing with chemotherapy**
- **In this new analysis from the trial, researchers looked at survival in people who had lived for at least 1 or 2 years while receiving avelumab maintenance treatment**
  - **In people who had received 1 year of avelumab treatment, the likelihood of surviving for an additional 1 or 2 years was 93% and 80%, respectively**
  - **In people who had received 2 years of avelumab treatment, the likelihood of surviving for an additional 1 or 1.5 years was 96% and 90%, respectively**
  - **In people who received avelumab treatment for at least 1 or 2 years, severe side effects occurred after 1 year in 12% of patients and after 2 years in 6%**
- **Overall, these results suggest that people with advanced urothelial cancer who live for at least 1 year while receiving avelumab maintenance treatment have a high likelihood of surviving for another 1 or 2 years or longer, with a low frequency of severe side effects**

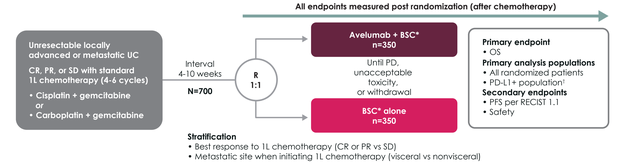
BACKGROUND

- In the JAVELIN Bladder 100 trial, avelumab 1L maintenance + best supportive care (BSC) significantly prolonged OS and PFS vs BSC alone in patients with advanced UC that had not progressed with 1L platinum-based chemotherapy[1,2]
  - After ≥2 years of follow-up, median OS was 23.8 vs 15.0 months, respectively (hazard ratio, 0.76 [95% CI, 0.63-0.91]; 2-sided p=0.0036)[1]
  - OS rates at 2 years were 49.8% with avelumab + BSC vs 38.4% with BSC alone
  - Avelumab 1L maintenance was associated with acceptable long-term safety, including a low rate of discontinuations due to TRAEs and preserved health-related quality of life[1,3]
- Results from the trial supported the inclusion of avelumab 1L maintenance in updated international treatment guidelines as a recommended treatment option for patients with advanced UC[4,5]
- Here, we report post hoc analyses from the JAVELIN Bladder 100 trial that assessed the probability of additional OS, PFS, and safety in patients treated with avelumab for ≥1 or ≥2 years

METHODS

- JAVELIN Bladder 100 (NCT02603432) is an international, randomized, phase 3 trial that enrolled patients with unresectable locally advanced or metastatic UC who were progression free after 4-6 cycles of 1L platinum-based chemotherapy (**Figure 1**)
  - Patients were randomized 1:1 to receive avelumab + BSC or BSC alone until disease progression, unacceptable toxicity, or patient withdrawal
  - The primary endpoint was OS, measured from randomization after chemotherapy
- In this post hoc analysis, subgroups of patients who had been treated with avelumab for ≥1 or ≥2 years were analyzed

Figure 1. JAVELIN Bladder 100 study design[1]



1L, first line; **BSC**, best supportive care; **CR**, complete response; **OS**, overall survival; **PD**, progressive disease; **PFS**, progression-free survival; **PR**, partial response; **R**, randomization; **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. †Assessed using the Ventana SP263 assay.

RESULTS

- At data cutoff (4 June 2021), median follow-up in the avelumab + BSC arm (n=350) was 38.0 months (≥2 years in all patients)
- Among all patients who received ≥1 dose of avelumab (n=344), duration of avelumab treatment was ≥1 year in 118 patients (34.3%) and ≥2 years in 68 (19.8%)
- Compared with the overall avelumab arm, subgroups with ≥1 or ≥2 years of treatment included higher proportions of patients who had received 1L cisplatin + gemcitabine (56.8%-64.7% vs 52.3%), had nonvisceral metastases at the start of chemotherapy (52.5%-58.8% vs 45.4%), and had PD-L1+ tumors (61.0%-64.7% vs 54.0%) (**Table 1**)

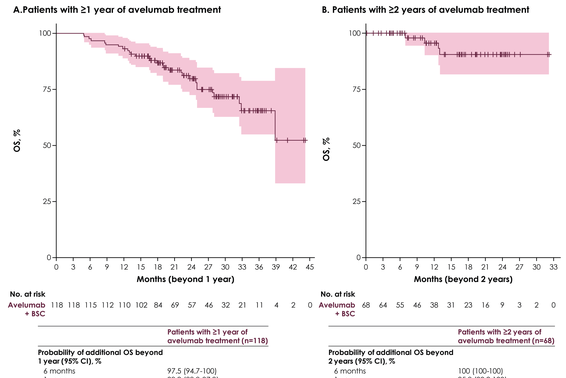
Table 1. Baseline characteristics in the overall avelumab arm and subgroups with ≥1 or ≥2 years of avelumab treatment

	Overall avelumab arm (n=350)	≥1 year of treatment (n=118)	≥2 years of treatment (n=68)
Age, median (range), years	68 (37-90)	69 (43-86)	69 (44-86)
Sex, n (%)			
Male	266 (76.0)	91 (77.1)	53 (77.9)
Female	84 (24.0)	27 (22.9)	15 (22.1)
Geographic region, n (%)			
Europe	214 (61.1)	61 (51.7)	38 (55.9)
North America	12 (3.4)	6 (5.1)	2 (2.9)
Asia	73 (20.9)	32 (27.1)	19 (27.9)
Australasia	34 (9.7)	15 (12.7)	7 (10.3)
Rest of the world	17 (4.9)	4 (3.4)	2 (2.9)
ECOG PS, n (%)			
0	213 (60.9)	83 (70.3)	44 (64.7)
≥1	137 (39.1)	35 (29.7)	24 (35.3)
PD-L1 status, n (%)			
Positive	189 (54.0)	72 (61.0)	44 (64.7)
Negative	139 (39.7)	39 (33.1)	20 (29.4)
Unknown	22 (6.3)	7 (5.9)	4 (5.9)
Site of metastasis at start of 1L chemotherapy, n (%)			
Visceral	191 (54.6)	56 (47.5)	28 (41.2)
Nonvisceral	159 (45.4)	62 (52.5)	40 (58.8)
1L chemotherapy regimen, n (%)			
Cisplatin + gemcitabine	183 (52.3)	67 (56.8)	44 (64.7)
Carboplatin + gemcitabine	147 (42.0)	43 (36.4)	18 (26.5)
Cisplatin + carboplatin + gemcitabine*	20 (5.7)	8 (6.8)	6 (8.8)
Best response to 1L chemotherapy, n (%)			
CR or PR	253 (72.3)	87 (73.7)	52 (76.5)
SD	97 (27.7)	31 (26.3)	16 (23.5)

1L, first line; **CR**, complete response; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **PR**, partial response; **SD**, stable disease.
*Patients who switched platinum regimens while receiving 1L chemotherapy.

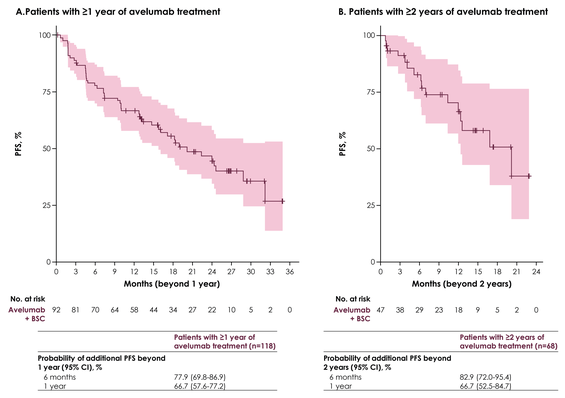
- In patients who had received 1 year of avelumab treatment, the probability of an additional 1 or 2 years of OS was 93.2% and 79.6%, respectively (**Figure 2A**)
  - In this subgroup, the probability of an additional 6 months or 1 year of PFS was 77.9% and 66.7%, respectively (**Figure 3A**)
- In patients who had received 2 years of avelumab treatment, the probability of an additional 1 or 1.5 years of OS was 95.8% and 90.3%, respectively (**Figure 2B**)
  - In this subgroup, the probability of an additional 6 months or 1 year of PFS was 82.9% and 66.7%, respectively (**Figure 3B**)

Figure 2. Additional OS in patients who had received 1 or 2 years of avelumab



BSC, best supportive care; **OS**, overall survival.

Figure 3. Additional PFS in patients who had received 1 or 2 years of avelumab



BSC, best supportive care; **PFS**, progression-free survival.

- In patients who were still receiving avelumab treatment at specified time points, rates of AEs and TRAEs decreased over time (**Table 2**)
  - Any-grade TRAEs occurred after 1 year in 50.0% of patients and after 2 years in 35.3%, including grade ≥3 TRAEs in 11.9% and 5.9%, respectively
- In general, types of TRAEs that occurred after 1 or 2 years of treatment were consistent with those observed in the overall population (**Table 3**)

Table 2. Summary of AEs occurring at any time and after ≥1 or ≥2 years of avelumab treatment

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)
TRAE 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)

AE, adverse event; **irAE**, immune-related AE; **TRAE**, treatment-related AE.
*Attributed to immune-mediated nephritis by the investigator.

Table 3. Most common TRAEs occurring after ≥1 or ≥2 years of avelumab treatment

	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

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.

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Correspondence: **Petros Grivas, pgrivas@uw.edu**

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