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Avelumab first-line maintenance for advanced urothelial carcinoma in the JAVELIN Bladder 100 trial: subgroup analysis by duration of treatment-free interval from end of chemotherapy to start of maintenance

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JAVELIN Bladder 100

SCOPE

- We report post hoc analyses from the JAVELIN Bladder 100 phase 3 trial assessing outcomes with avelumab first-line (1L) maintenance + best supportive care (BSC) vs BSC alone by duration of the treatment-free interval (TFI; ie, time from completion of chemotherapy to start of 1L maintenance) in patients with advanced urothelial carcinoma (UC)

CONCLUSIONS

- In these post hoc analyses, overall survival (OS) and progression-free survival (PFS) were prolonged with avelumab 1L maintenance + BSC vs BSC alone irrespective of the TFI assessed in this study (4-10 weeks)
- The safety profile of avelumab was similar across TFI subgroups and consistent with the overall population[1]
- The results support the use of avelumab 1L maintenance as a standard of care for patients with advanced UC who remain progression free after varying intervals from completion of 1L platinum-containing chemotherapy (4-10 weeks)
- These findings suggest that timing for starting maintenance can be based on individual patient considerations (eg, resolution of chemotherapy-related toxicity, patient preference, scheduling logistics, etc.)

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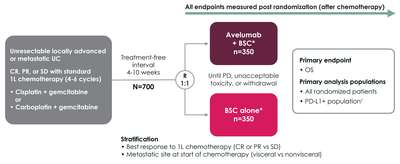
BACKGROUND

- In the phase 3 JAVELIN Bladder 100 trial, avelumab 1L maintenance + BSC significantly prolonged OS vs BSC alone in patients with advanced UC that had not progressed with 1L platinum-based chemotherapy
  - Median OS was 21.4 vs 14.3 months, respectively (hazard ratio [HR], 0.69 [95% CI: 0.56, 0.86]; 1-sided p=0.0005)[1]
  - The trial demonstrated the benefits of starting avelumab as 1L maintenance in patients who had disease control with 1L chemotherapy instead of waiting until disease progression
- Based on results from the trial, avelumab 1L maintenance was approved in the US, Europe, Japan, and several other countries for the treatment of patients with locally advanced or metastatic UC who are progression free following platinum-based chemotherapy[2,3]
- Avelumab 1L maintenance is recommended as a standard of care in US and European guidelines for both cisplatin-eligible and -ineligible patients, irrespective of PD-L1 status, based on level 1 evidence[4-6]
- In the trial, patients received avelumab + BSC or BSC alone after a TFI of 4 to 10 weeks from completion of 1L therapy
  - The TFI allowed for resolution of any chemotherapy-related toxicities and tumor assessment to confirm eligibility[1]
- However, the optimal timing for starting avelumab after completion of 1L chemotherapy is unknown

METHODS

- JAVELIN Bladder 100 (NCT02603432) enrolled patients with locally advanced or metastatic UC that had not progressed with 1L chemotherapy (4-6 cycles of gemcitabine + cisplatin or carboplatin)
- After a TFI of 4 to 10 weeks, patients were randomized to receive 1L maintenance avelumab + BSC or BSC alone until disease progression, unacceptable toxicity, or withdrawal (**Figure 1**)
- The primary endpoint was OS, assessed in all randomized patients and in patients with PD-L1+ tumors
- In this post hoc analysis, subgroups were defined based on a TFI of 4 to <6 weeks (ie, <42 days), 6 to <8 weeks (ie, 42 to <56 days), or 8 to 10 weeks (ie, ≥56 days) from last dose of chemotherapy
- Treatment arms were compared within subgroups using a stratified Cox proportional hazards model

Figure 1. JAVELIN Bladder 100 phase 3 study design



Data cutoff date: October 21, 2019.

1L, first line; **BSC**, best supportive care; **CR**, complete response; **PR**, partial response; **OS**, overall survival; **PD**, progressive disease; **R**, randomization; **SD**, stable disease; **UC**, urothelial carcinoma.

*BSC (eg, antibiotics, nutritional support, hydration, or 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

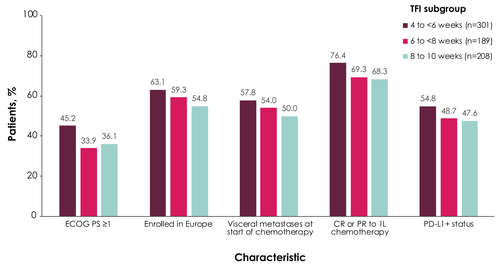
- Baseline characteristics in subgroups defined by TFI were generally well balanced between treatment arms (**Table 1**)
  - For both arms combined, the TFI 4 to <6 weeks subgroup vs the other 2 subgroups included more patients with visceral metastases, an objective response with 1L chemotherapy, and an ECOG PS of ≥1 (**Figure 2**)

Table 1. Selected baseline characteristics in TFI subgroups

	TFI 4 to <6 weeks		TFI 6 to <8 weeks		TFI 8 to 10 weeks	
	Ave + BSC (n=143)	BSC alone (n=158)	Ave + BSC (n=109)	BSC alone (n=80)	Ave + BSC (n=98)	BSC alone (n=110)
Median age, years	70	69	69	68.5	67	69
ECOG PS, %						
0	55	55	70	61	60	67
≥1	45	45	30	39	40	33
Pooled geographic region, %						
North America	1	8	4	4	7	6
Europe	66	61	63	54	52	57
Asia	24	23	21	24	16	16
Australasia	9	5	7	15	13	15
Rest of the world	1	3	5	4	11	5
Site of advanced disease at start of chemotherapy, %						
Visceral	58	58	52	56	52	48
Nonvisceral	42	42	48	44	48	52
1L chemotherapy regimen, %						
Gemcitabine + cisplatin	51	59	52	56	54	61
Gemcitabine + carboplatin	46	34	41	40	37	33
Gemcitabine + cisplatin or carboplatin*	3	6	6	4	9	6
Best response to 1L chemotherapy, %						
CR or PR	78	75	67	73	69	67
SD	22	25	33	28	31	33
PD-L1 status, %						
Positive	59	51	51	45	50	45
Negative	36	37	43	41	42	36
Not evaluable	6	12	6	14	8	18

1L, first line; **Ave**, avelumab; **BSC**, best supportive care; **CR**, complete response; **PR**, partial response; **SD**, stable disease; **TFI**, treatment-free interval.
*Patients who switched platinum regimens while receiving 1L chemotherapy.

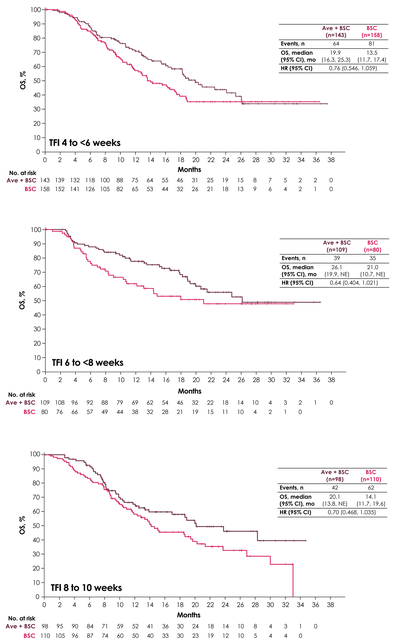
Figure 2. Selected baseline characteristics in TFI subgroups (both arms combined)



1L, first line; **CR**, complete response; **PR**, partial response; **TFI**, treatment-free interval.

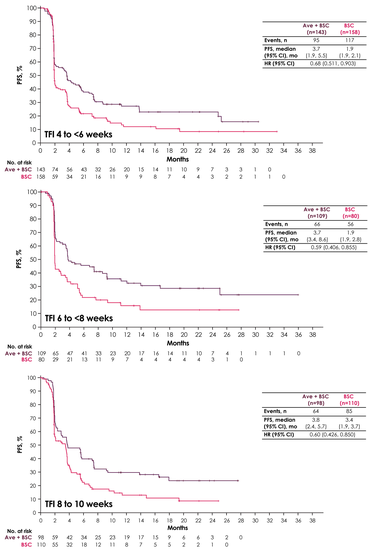
- Prolonged OS was observed with avelumab + BSC vs BSC alone in all TFI subgroups (**Figure 3**)
- PFS was also prolonged with avelumab + BSC vs BSC alone across subgroups (**Figure 4**)
- OS and PFS benefits with avelumab + BSC vs BSC alone were similar across all TFI subgroups
- The safety profile of avelumab 1L maintenance was generally similar between subgroups, irrespective of the length of TFI before starting maintenance (**Table 2**)

Figure 3. OS by duration of TFI before maintenance



Ave, avelumab; **BSC**, best supportive care; **HR**, hazard ratio; **NE**, not estimable; **OS**, overall survival; **TFI**, treatment-free interval.

Figure 4. PFS by duration of TFI before maintenance



Ave, avelumab; **BSC**, best supportive care; **HR**, hazard ratio; **PFS**, progression-free survival; **TFI**, treatment-free interval.

Table 2. Safety summary by duration of TFI before maintenance

Events, %	TFI 4 to <6 weeks		TFI 6 to <8 weeks		TFI 8 to 10 weeks	
	Ave + BSC (n=142)	BSC alone (n=157)	Ave + BSC (n=106)	BSC alone (n=78)	Ave + BSC (n=96)	BSC alone (n=108)
TEAE of any grade	97	72	98	83	99	81
Grade ≥3 TEAE	50	22	43	28	48	27
TRAE of any grade	77	0	80	1	74	3
Grade ≥3 TRAE	18	0	11	0	21	0
Serious TEAE	32	13	27	22	22	29
Serious TRAE	10	0	10	0	6	0
TEAE leading to interruption of avelumab	39	–	43	–	40	–
TEAE leading to discontinuation	18	0	5	0	11	0
TRAE leading to discontinuation	14	0	4	0	9	0
TEAE leading to death	1	2	0	12	2	10
TRAE leading to death	0	0	0	0	1	0
IrAE of any grade	27	1	33	3	28	2
Infusion-related reaction* of any grade	20	0	24	0	21	0

Ave, avelumab; **BSC**, best supportive care; **IrAE**, immune-related adverse event; **TEAE**, treatment-emergent adverse event; **TFI**, treatment-free interval; **TRAE**, treatment-related adverse event.
*Composite term, including several prespecified preferred terms, in addition to signs and symptoms of infusion-related reaction.

REFERENCES 1. Powles T, et al. N Engl J Med. 2020;383(13):1218-30. **2.** Bavencio (avelumab). Summary of product characteristics. Merck KGaA; 2021. **3.** Bavencio (avelumab). Prescribing information. EMD Serono Inc; 2020. **4.** NCCN Clinical Practice Guidelines. Bladder Cancer. V3.2021. **5.** European Society for Medical Oncology. eUpdate—bladder cancer treatment recommendations. Accessed April 28, 2021. https://www.esmo.org/guidelines/genitourinary-cancers/bladder-cancer/eupdate-bladder-cancer-treatment-recommendations4 **6.** European Association of Urology. Muscle-invasive and metastatic bladder cancer. Accessed April 28, 2021. https://uroweb.org/guideline/bladder-cancer-muscle-invasive-and-metastatic/ **DISCLOSURES S. S. Sridhar** has received personal fees from and served in consultancy or advisory roles for Astellas, AstraZeneca, Bristol Myers Squibb, Immunomedics, Janssen, Merck KGaA, Pfizer, and Roche. **T. 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