Interim results from the AVENUE study: real-world patient characteristics and safety with avelumab maintenance treatment for locally advanced or metastatic urothelial carcinoma

Peter J. Goebell,[1] Alexander Sultanbaev,[2] Simba-Joshua Oostdam,[3] Aurea Molina Diaz,[4] Rocio Garcia Dominguez,[5] Deborah Zihler,[6]* Sara Colli,[7] Jason Hoffman,[8] Laura Cremer,[9] Jürgen Gschwend[10]

[1]Department of Urology and Pediatric Urology, University Hospital Erlangen, Erlangen, Germany; [2]Department of Chemotherapy, Republican Clinical Oncology Dispensary, Ufa, Russia; [3]Department of Urology, Vincent Hospital Hannover, Hannover Germany; [4]Department of Medical Oncology, University Hospital of A Coruña, A Coruña, Spain; [5]Department of Medical Oncology, University Hospital of Salamanca, Salamanca, Spain; [6]Department of Medical Oncology, Hematology, and Transfusion Medicine, Cantonal Hospital Aarau, Aarau, Switzerland; [7]IQVIA, Real World Solutions, Milan, Italy; [8]Global Medical Unit Oncology, EMD Serono Research & Development Institute, Inc, Billerica, MA, USA, an affiliate of Merck KGaA; [9]Medical Affairs Oncology, Merck Healthcare Germany GmbH, Weiterstadt, Germany, an affiliate of Merck KGaA; [10]Department of Urology, Technical University of Munich, School of Medicine, Klinikum rechts der Isar, Munich, Germany

*Affiliation at the time the study was conducted

CONCLUSIONS

- Interim data from the AVENUE study provide insights into the characteristics of patients with locally advanced or metastatic urothelial carcinoma (la/mUC) receiving avelumab first-line (1L) maintenance treatment in clinical practice across several countries
- The study population is heterogeneous and includes patients with varying characteristics and comorbidities
- Most patients (86%) received 4-6 cycles of prior 1L chemotherapy, consistent with international guidelines[1-3]
- Data show the acceptable safety profile of avelumab 1L maintenance treatment in clinical practice, consistent with previous studies[4-7]
- Future analyses from AVENUE will provide data for effectiveness and safety in a larger population

PLAIN LANGUAGE SUMMARY

- Based on results from the JAVELIN Bladder 100 clinical trial, avelumab maintenance is considered a standard therapy for people with advanced urothelial cancer that disappeared, shrank, or stopped growing with chemotherapy
- In the AVENUE study, researchers looked at people in Germany, Spain, Switzerland, and Russia with advanced urothelial cancer who received avelumab maintenance therapy in routine clinical practice, outside of a clinical trial
- This analysis from AVENUE included 173 people with varying disease characteristics
- Most people (86%) were treated with 4-6 cycles of chemotherapy before avelumab maintenance, consistent with international guidelines
- Avelumab maintenance treatment was safe in people treated in clinical practice, consistent with results from clinical trials
- Future analyses from AVENUE will provide results for effectiveness and safety in a larger population

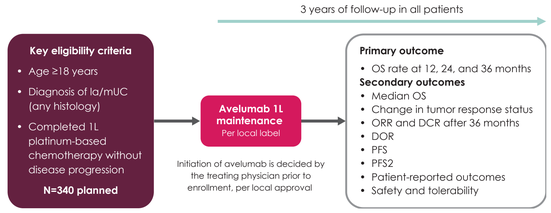
BACKGROUND

- In the phase 3 JAVELIN Bladder 100 trial, avelumab 1L maintenance treatment + best supportive care significantly prolonged overall survival (OS) and progression-free survival (PFS) vs best supportive care alone in patients with la/mUC without disease progression after 1L platinum-based chemotherapy[4,5]
  - After ≥2 years of follow-up, median OS from the start of avelumab 1L maintenance was 23.8 vs 15.0 months (HR, 0.76 [95% CI, 0.63-0.91]; p=0.0036) and median PFS was 5.5 vs 2.1 months (HR, 0.54 [95% CI, 0.46-0.64]; p<0.0001), respectively[5]
  - The long-term safety of avelumab 1L maintenance treatment was also demonstrated[5]
- Based on results from JAVELIN Bladder 100, avelumab 1L maintenance treatment is recommended in international guidelines as a standard of care for patients treated with platinum-based chemotherapy without disease progression[1-3]
  - Further studies to assess avelumab 1L maintenance treatment in routine clinical practice are needed
- AVENUE is a real-world study investigating avelumab 1L maintenance treatment in Germany, Spain, Switzerland, and Russia
  - An initial analysis reported baseline characteristics from the first 78 patients enrolled[8]
  - Here, we report updated baseline data and initial safety data in an expanded population

METHODS

- AVENUE is a prospective, noninterventional study of avelumab 1L maintenance in patients with la/mUC without disease progression after 1L platinum-based chemotherapy (**Figure 1**)
  - The study is enrolling patients receiving treatment at centers in Germany, Spain, Switzerland, and Russia
  - Initiation of avelumab 1L maintenance is decided by the treating physician prior to enrollment per local approval
- The primary objective is to evaluate the OS rate at 12, 24, and 36 months
  - Secondary endpoints include median OS and PFS, and safety
- This report includes updated baseline data and initial safety data from the preplanned interim analysis, which occurred when 50% of patients had been enrolled

Figure 1. AVENUE study design



1L, first line; **DCR**, disease control rate; **DOR**, duration of response; **la/mUC**, locally advanced/metastatic urothelial carcinoma; **ORR**, objective response rate; **OS**, overall survival; **PFS**, progression-free survival; **PFS2**, time until disease progression on second-line treatment or death.

RESULTS

- At data cutoff (September 15, 2023), 173 patients had received avelumab 1L maintenance
- Most patients were men (77.5%) and had an ECOG PS of 0-1 (88.4%) (**Table1**)
  - 24.3% of patients were aged >75 years
- Median time since first cancer diagnosis was 1.2 years (range, 0.3-23.1 years) (**Table 2**)
- The primary tumor location was the upper or lower urinary tract in 71.1% and 28.9%, respectively (**Table 3**)
- Patient comorbidities are shown in **Table 3**

Table 1. Patient characteristics

	N=173
Sex, n (%)	
Male	134 (77.5)
Female	39 (22.5)
Age	
Median (range), years	70 (43-89)
<65 years, n (%)	53 (30.6)
65-75 years, n (%)	78 (45.1)
>75 years, n (%)	42 (24.3)
Hispanic or Latino ethnicity, n (%)	
Yes	19 (11.0)
No	153 (88.4)
Not available	1 (0.6)
ECOG PS, n (%)	
0	63 (36.4)
1	90 (52.0)
≥2	9 (5.2)
Not available	11 (6.4)
Smoking status, n (%)	
Never	64 (37.0)
Current	32 (18.5)
Former	77 (44.5)

*Some patients are included in >1 row.
ECOG PS, Eastern Cooperative Oncology Group performance status.

Table 2. Disease characteristics

	N=173
Time since first cancer diagnosis, years	
Median (range)	1.2 (0.3-23.1)
Primary tumor site, n (%)	
Lower urinary tract	123 (71.1)
Upper urinary tract	50 (28.9)
Primary tumor subsite(s), n (%)*	
Bladder	103 (59.5)
Ureter	30 (17.3)
Urethra	26 (15.0)
Renal pelvis	24 (13.9)
Histopathologic classification, n (%)	
Urothelial carcinoma	169 (97.7)
Other	4 (2.3)
Location of metastasis, n (%)*	
Lymph nodes	110 (63.6)
Liver	32 (18.5)
Lung	45 (26.0)
Bone	33 (19.1)
Other	26 (15.0)
Not reported	2 (1.2)
PD-L1 status, n (%)	
Positive	56 (32.4)
Negative	45 (26.0)
Not assessed	72 (41.6)

*Some patients are included in >1 row.

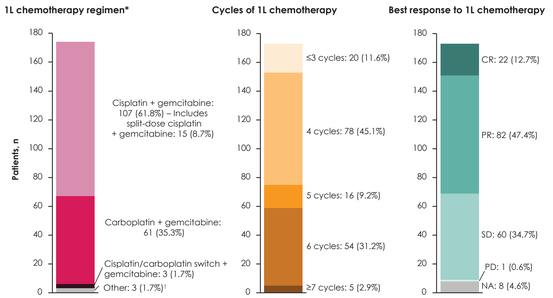
Table 3. Comorbidities

	N=173
Any comorbidity, n (%)	**159 (91.9)**
Vascular disorder	100 (57.8)
Metabolism or nutrition disorder	61 (35.3)
Renal or urinary disorder	38 (22.0)
Cardiac disorder	37 (21.4)
Surgical or medical procedure	36 (20.8)
Musculoskeletal or connective tissue disorder	31 (17.9)
Neoplasm	31 (17.9)
Respiratory, thoracic, or mediastinal disorder	30 (17.3)
Gastrointestinal disorder	28 (16.2)
Nervous system disorder	25 (14.5)
General disorder or administration site condition	22 (12.7)
Endocrine disorder	18 (10.4)

Categories of comorbidities present in ≥10 patients are shown.

- The 1L platinum-based chemotherapy regimen was gemcitabine + cisplatin in 61.8% (split dose in 8.7%) and gemcitabine + carboplatin in 35.3% (**Figure 2**)
  - The number of cycles of 1L platinum-based chemotherapy received was ≤3, 4-6, and ≥7 in 11.6%, 85.5%, and 2.9%, respectively (**Figure 2**)
- Median duration of avelumab 1L maintenance treatment was 16 weeks (IQR, 8-28) (**Table 4**)
- At data cutoff, 84 patients (48.6%) remained on avelumab treatment (**Table 4**)
  - Reasons for discontinuation are shown in **Figure 3**
- 54.3% of patients had a treatment-related adverse event of any grade, which was grade ≥3 in 14.5% and led to discontinuation in 7.5% (**Table 5**)
  - The most common treatment-related adverse events of any grade are shown in **Figure 4**

Figure 2. 1L platinum-based chemotherapy prior to avelumab 1L maintenance (N=173)



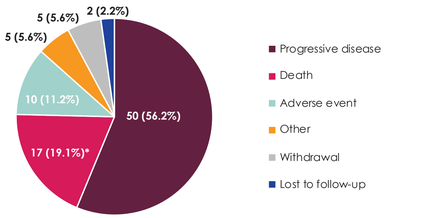
1L, first line; **CR**, complete response; **NA**, not available; **PD**, progressive disease; **PR**, partial response; **SD**, stable disease.
*Patients may have received ≥1 1L chemotherapy regimen. †3 patients received a different platinum-based chemotherapy regimen.

Table 4. Avelumab treatment

	N=173
Time from last dose of chemotherapy to start of avelumab 1L maintenance, median (IQR), weeks	4.7 (2.3-7.7)
Duration of avelumab treatment, median (IQR), weeks	16 (8-28)
Avelumab treatment ongoing, n (%)	84 (48.6)
Avelumab treatment discontinued, n (%)	89 (51.4)

1L, first line; **IQR**, interquartile range.
*Reasons for death: 11 patients due to disease progression or a disease related condition, 4 patients due to events unrelated to study treatment (biliary pancreatitis, septic shock, sepsis, pneumonitis), and 2 patients due to unknown causes.

Figure 3. Reasons for discontinuation (n=89)



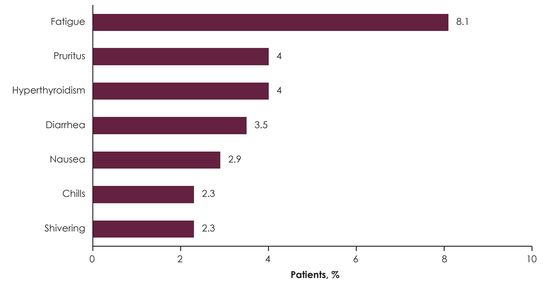
*Reasons for death: 11 patients due to disease progression or a disease related condition, 4 patients due to events unrelated to study treatment (biliary pancreatitis, septic shock, sepsis, pneumonitis), and 2 patients due to unknown causes.

Table 5. Summary of safety

Patients, n (%)	N=173
AE of any grade	133 (76.9)
Grade ≥3	60 (34.7)
TRAE of any grade	94 (54.3)
Grade ≥3	25 (14.5)
Serious AE	57 (32.9)
Serious TRAE	25 (14.5)
AE leading to discontinuation of avelumab	22 (12.7)
TRAE leading to discontinuation of avelumab	13 (7.5)
AE leading to death	12 (6.9)
TRAE leading to death	3 (1.7)*
irAE	36 (20.8)
Grade ≥3	8 (4.6)
Infusion-related reaction†	40 (23.1)
Grade ≥3	6 (3.5)

AE, adverse event (treatment-emergent); **irAE**, immune-related adverse event; **TRAE**, treatment-related adverse event.
*2 TRAEs leading to death had an unknown relationship to avelumab, per investigator.
†Infusion-reaction reactions were identified as specified AEs (infusion-related reaction, [drug/type I] hypersensitivity, anaphylactic reaction) with onset on the day of or day after study drug infusion (irrespective of resolution date) or specified signs/symptoms (pyrexia, chills, flushing, hypotension, dyspnea, wheezing, back pain, abdominal pain, or urticaria) with onset on the day of study drug infusion that resolved on the day of onset or the following day.

Figure 4. Most common TRAEs of any grade (>2% of patients)



TRAE, treatment-related adverse event.

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Correspondence: **Peter J. Goebell**, **Peter.Goebell@uk-erlangen.de**

REFERENCES 1. NCCN Clinical Practice Guidelines: Bladder Cancer. V.4.2024. **2.** Powles T, et al. Ann Oncol. 2024;35(6):485-90. **3.** Cathomas R, et al. Eur Urol. 2022;81(1):95-103. **4.** Powles T, et al. N Engl J Med. 2020;383(13):1218-30. **5.** Powles T, et al. J Clin Oncol. 2023;41(19):3486-92. **6.** Barthelemy P, et al. J Clin Oncol. 2024;42(5upp 4):Abstract 561. **7.** Grivas P, et al. J Clin Oncol. 2024;42(5uppl 4):Abstract 497. **8.** Schlack K, et al. Congress of the German Society of Urology 2023. Abstract 229.

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