Subgroup analyses of patients with advanced urothelial carcinoma who had long-term progression-free survival or overall survival with avelumab first-line maintenance in the AVENANCE real-world study

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CONCLUSIONS

- **Previous analyses from AVENANCE, an ongoing noninterventional study in France, demonstrated the effectiveness and safety of avelumab first-line (1L) maintenance treatment in a real-world population of patients with advanced urothelial carcinoma (UC) that had not progressed following 1L platinum-based chemotherapy**
- **Here, we report analyses of subgroups with long-term progression-free survival (PFS; defined as ≥12 months from start of avelumab 1L maintenance) or long-term overall survival (OS; defined as ≥3 years from start of 1L chemotherapy)**
  - **In this selected population of patients without disease progression after 1L chemotherapy who were treated with avelumab 1L maintenance, 29.1% had long-term PFS and 23.4% had long-term OS**
  - **Subgroups with long-term PFS and OS included patients with varying demographic and disease characteristics, and treatment sequences**
- **These findings support the use of avelumab 1L maintenance as a standard of care for patients with advanced UC who are progression free after 1L platinum-based chemotherapy**

PLAIN LANGUAGE SUMMARY

- **Based on clinical trial results, avelumab maintenance is considered a standard treatment for people with advanced urothelial cancer whose cancer disappeared, shrank, or stopped growing after chemotherapy was given as the first treatment**
  - **Maintenance treatment is given to help keep cancer from growing again**
- **In a French study called AVENANCE, researchers found that real-world results (ie, not part of a clinical trial) with avelumab maintenance treatment were similar to clinical trial results**
- **In this new analysis from AVENANCE, researchers looked at people who received avelumab maintenance treatment and lived for a long time**
  - **29% of people whose cancer disappeared, shrank, or stopped growing with chemotherapy lived without their cancer getting worse for longer than 1 year after starting avelumab maintenance treatment**
  - **23% of people whose cancer disappeared, shrank, or stopped growing with chemotherapy were still alive 3 years after starting chemotherapy**
  - **Overall, people who received avelumab and lived for a long time had varying characteristics**
- **These results provide more support for giving avelumab maintenance treatment to people with advanced urothelial cancer that disappears, shrinks, or stops growing with chemotherapy who have different characteristics**

BACKGROUND

- In the JAVELIN Bladder 100 phase 3 trial (NCT02603432), 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 in all patients, median OS (from start of maintenance) was 23.8 months with avelumab 1L maintenance + BSC vs 15.0 months with BSC alone (hazard ratio, 0.76 [95% CI, 0.63-0.91]; 2-sided p=0.0036)[2]
  - Avelumab 1L maintenance is approved worldwide and is a recommended treatment option in international guidelines[3-6]
- AVENANCE, an ongoing noninterventional study, has shown the real-world effectiveness and safety of avelumab 1L maintenance in patients with advanced UC in France
  - In a previously reported analysis in the overall effectiveness population, with a median follow-up of 26.3 months[7]:
    - Median OS from the start of avelumab 1L maintenance treatment was 21.3 months (95% CI, 17.6-24.6 months)
    - Median PFS was 5.7 months (95% CI, 5.2-6.5 months)
- Here, we report analyses from AVENANCE in subgroups defined by duration of PFS or OS

METHODS

- AVENANCE (NCT04822350) is a multicenter, noninterventional, ambispective (retrospective and prospective) study
- Eligible patients have locally advanced or metastatic UC that has not progressed with 1L platinum-based chemotherapy (ie, ongoing complete response, partial response, or stable disease) and previous, ongoing, or planned avelumab 1L maintenance treatment
- Data collection started on 13 July 2021, and additional follow-up and analyses are ongoing
- No study-specific visits are required, and patients are assessed and followed up per standard clinical practice
- The primary endpoint is OS measured from the start of avelumab treatment
  - The effectiveness population includes all patients who received ≥1 dose of avelumab and met all eligibility criteria, and the safety population includes all patients who received ≥1 dose of avelumab
  - Duration of follow-up was estimated using the reverse Kaplan-Meier method
- Here, detailed analyses were performed in subgroups with short PFS (≤3 months from start of avelumab), long PFS (≥12 months from start of avelumab), or long OS (≥3 years from start of 1L chemotherapy)
  - Subgroup definitions were based on unadjusted analyses of PFS and OS
  - Subgroups were not mutually exclusive (ie, patients could be in >1 subgroup)
  - Descriptive statistics were used, and no statistical tests to compare subgroups were conducted

RESULTS

- Of 604 screened patients, 595 were included in the effectiveness population, and 596 were included in the safety population
- At data cutoff (15 July 2024) in the overall effectiveness population:
  - Median follow-up since avelumab initiation was 33.2 months (95% CI, 31.7-34.2 months)
  - 86 patients (14.5%) were still receiving avelumab 1L maintenance treatment
  - Median duration of avelumab treatment was 5.6 months (95% CI, 5.1-6.9 months)
- Subgroups of interest defined by treatment outcome were identified
  - 187 patients (31.4%) had short PFS (≤3 months from start of avelumab 1L maintenance)
  - 173 patients (29.1%) had long PFS (≥12 months from start of avelumab 1L maintenance)
  - 139 patients (23.4%) had long OS (≥3 years from start of 1L chemotherapy)
- Within these subgroups, 90 patients (15.1%) had both long PFS and long OS (ie, were included in both subgroups)
- Patient characteristics in subgroups defined by treatment outcome were heterogeneous (**Table 1**)
  - Compared with the short PFS subgroup, long PFS and long OS subgroups had slightly higher proportions of patients with Eastern Cooperative Oncology Group performance status of 0, prior 1L cisplatin, and no visceral disease at start of 1L chemotherapy
- In the short PFS, long PFS, and long OS subgroups, respectively, best response to 1L platinum-based chemotherapy, was:
  - Complete response in 22 (11.9%), 39 (22.7%), and 37 (26.6%) patients
  - Partial response in 114 (61.6%), 102 (59.3%), and 81 (58.3%) patients
  - Stable disease in 48 (25.9%), 30 (17.4%), and 21 (15.1%) patients

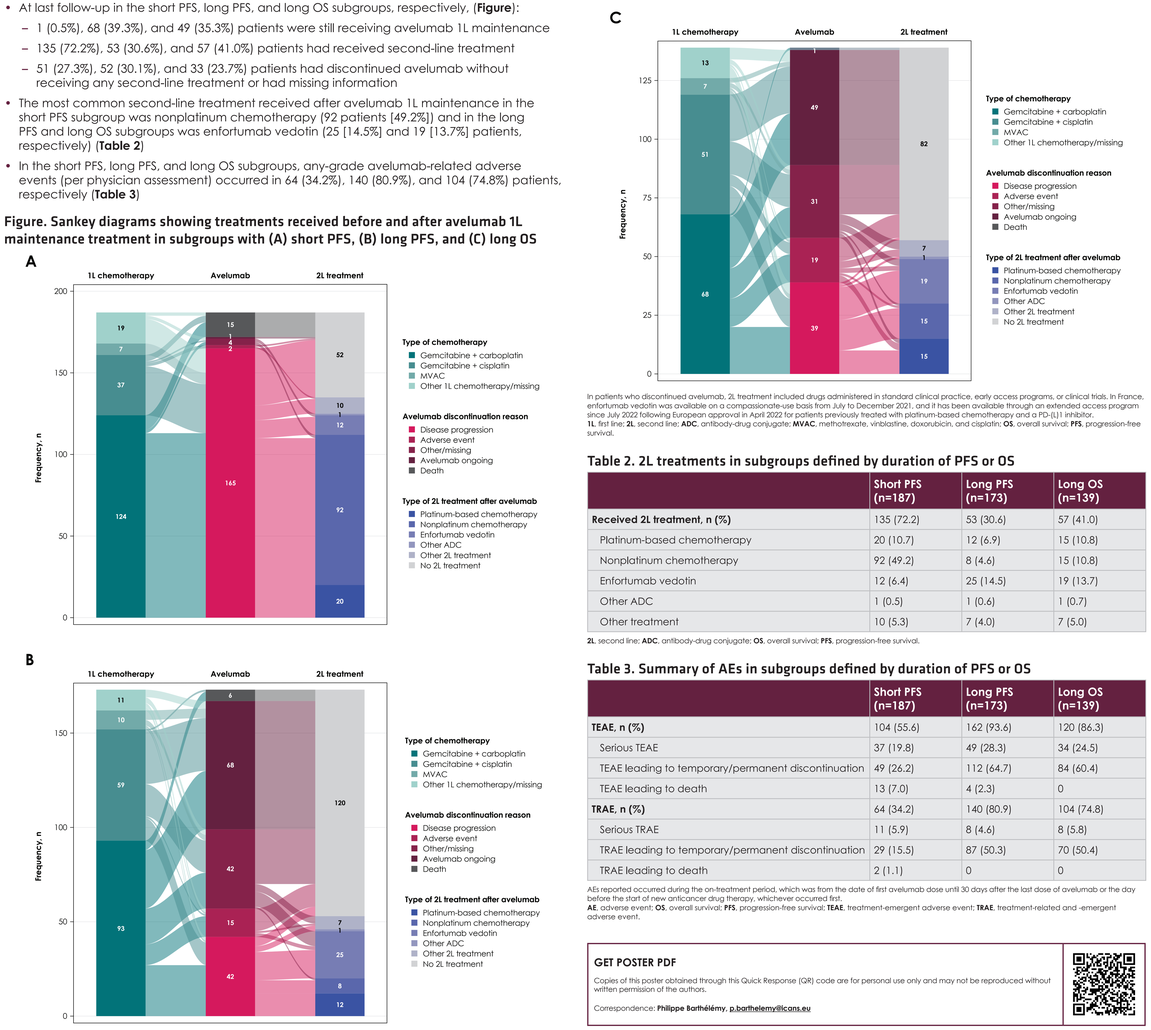
Table 1. Patient and disease characteristics

Characteristic	Short PFS (n=187)	Long PFS (n=173)	Long OS (n=139)
Age, years			
Median (IQR)	73.9 (67.5-79.0)	71.9 (66.3-76.7)	72.2 (66.5-76.9)
Range	43.0-89.3	41.3-88.5	50.6-84.6
Sex, n (%)			
Female	41 (21.9)	30 (17.3)	21 (15.1)
Male	146 (78.1)	143 (82.7)	118 (84.9)
ECOG PS at start of avelumab, n (%)	**n=160**	**n=147**	**n=120**
0	41 (25.6)	56 (38.1)	50 (41.7)
≥1	119 (74.4)	91 (61.9)	70 (58.3)
Primary tumor site, n (%)	**n=187**	**n=171**	**n=138**
Lower tract	144 (77.0)	138 (80.7)	110 (79.7)
Upper tract	43 (23.0)	33 (19.3)	28 (20.3)
Disease stage at start of 1L chemotherapy, n (%)	**n=186**	**n=173**	**n=139**
Metastatic	178 (95.7)	154 (89.0)	120 (86.3)
Locally advanced	8 (4.3)	19 (11.0)	19 (13.7)
Visceral metastasis at start of 1L chemotherapy, n (%)	**n=178**	**n=154**	**n=120**
Yes	164 (92.1)	127 (82.5)	97 (80.8)
No	14 (7.9)	27 (17.5)	23 (19.2)
1L chemotherapy regimen, n (%)	**n=186**	**n=173**	**n=139**
Carboplatin + gemcitabine	124 (66.7)	93 (53.8)	68 (48.9)
Cisplatin + gemcitabine	37 (19.9)	59 (34.1)	51 (36.7)
Methotrexate, vinblastine, doxorubicin, and cisplatin	7 (3.8)	10 (5.8)	7 (5.0)
Other or switched	18 (9.7)	11 (6.4)	13 (9.4)
No. of 1L chemotherapy cycles, median (range)	5 (1-10)	5 (2-10)	6 (1-15)
Response to 1L chemotherapy, n (%)	**n=185**	**n=172**	**n=139**
Complete response	22 (11.9)	39 (22.7)	37 (26.6)
Partial response	114 (61.6)	102 (59.3)	81 (58.3)
Stable disease	48 (25.9)	30 (17.4)	21 (15.1)
Other	1 (0.5)	1 (0.6)	0

1L, first line; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **IQR**, interquartile range; **OS**, overall survival; **PFS**, progression-free survival.

- At last follow-up in the short PFS, long PFS, and long OS subgroups, respectively, (**Figure**):
  - 1 (0.5%), 68 (39.3%), and 49 (35.3%) patients were still receiving avelumab 1L maintenance
  - 135 (72.2%), 53 (30.6%), and 57 (41.0%) patients had received second-line treatment
  - 51 (27.3%), 52 (30.1%), and 33 (23.7%) patients had discontinued avelumab without receiving any second-line treatment or had missing information
- The most common second-line treatment received after avelumab 1L maintenance in the short PFS subgroup was nonplatinum chemotherapy (92 patients [49.2%]) and in the long PFS and long OS subgroups was enfortumab vedotin (25 [14.5%] and 19 [13.7%] patients, respectively) (**Table 2**)
- In the short PFS, long PFS, and long OS subgroups, any-grade avelumab-related adverse events (per physician assessment) occurred in 64 (34.2%), 140 (80.9%), and 104 (74.8%) patients, respectively (**Table 3**)

Figure. Sankey diagrams showing treatments received before and after avelumab 1L maintenance treatment in subgroups with (A) short PFS, (B) long PFS, and (C) long OS



In patients who discontinued avelumab, 2L treatment included drugs administered in standard clinical practice, early access programs, or clinical trials. In France, enfortumab vedotin was available on a compassionate-use basis from July to December 2021, and it has been available through an extended access program since July 2022 following European approval in April 2022 for patients previously treated with platinum-based chemotherapy and a PD-(L)1 inhibitor. **1L**, first line; **2L**, second line; **ADC**, antibody-drug conjugate; **MVAC**, methotrexate, vinblastine, doxorubicin, and cisplatin; **OS**, overall survival; **PFS**, progression-free survival.

Table 2. 2L treatments in subgroups defined by duration of PFS or OS

	Short PFS (n=187)	Long PFS (n=173)	Long OS (n=139)
Received 2L treatment, n (%)	135 (72.2)	53 (30.6)	57 (41.0)
Platinum-based chemotherapy	20 (10.7)	12 (6.9)	15 (10.8)
Nonplatinum chemotherapy	92 (49.2)	8 (4.6)	15 (10.8)
Enfortumab vedotin	12 (6.4)	25 (14.5)	19 (13.7)
Other ADC	1 (0.5)	1 (0.6)	1 (0.7)
Other treatment	10 (5.3)	7 (4.0)	7 (5.0)

2L, second line; **ADC**, antibody-drug conjugate; **OS**, overall survival; **PFS**, progression-free survival.

Table 3. Summary of AEs in subgroups defined by duration of PFS or OS

	Short PFS (n=187)	Long PFS (n=173)	Long OS (n=139)
TEAE, n (%)	104 (55.6)	162 (93.6)	120 (86.3)
Serious TEAE	37 (19.8)	49 (28.3)	34 (24.5)
TEAE leading to temporary/permanent discontinuation	49 (26.2)	112 (64.7)	84 (60.4)
TEAE leading to death	13 (7.0)	4 (2.3)	0
TRAE, n (%)	64 (34.2)	140 (80.9)	104 (74.8)
Serious TRAE	11 (5.9)	8 (4.6)	8 (5.8)
TRAE leading to temporary/permanent discontinuation	29 (15.5)	87 (50.3)	70 (50.4)
TRAE leading to death	2 (1.1)	0	0

AEs reported occurred during the on-treatment period, which was from the date of first avelumab dose until 30 days after the last dose of avelumab or the day before the start of new anticancer drug therapy, whichever occurred first.
AE, adverse event; **OS**, overall survival; **PFS**, progression-free survival; **TEAE**, treatment-emergent adverse event; **TRAE**, treatment-related and -emergent adverse event.

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