Updated results from AVENANCE: real-world effectiveness of avelumab first-line maintenance in patients with advanced urothelial carcinoma and analysis of subsequent treatment

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CONCLUSIONS

- We report updated data and analyses by subsequent (second-line [2L]) treatment from AVENANCE, an ongoing, real-world, ambispective
 (retrospective and prospective) study in France investigating avelumab first-line (1L) maintenance treatment in patients with advanced urothelial
 carcinoma (aUC) that has not progressed following 1L platinum-based chemotherapy
- Longer-term follow-up confirms the effectiveness and safety of avelumab 1L maintenance treatment in a real-world setting
- Median overall survival (mOS) from the start of avelumab 1L maintenance was 21.3 months
- In subgroup analyses, mOS from the start of avelumab 1L maintenance was 31.3 months in patients who received 2L antibody-drug conjugate (ADC) treatment (mostly enfortumab vedotin) after avelumab 1L maintenance, and 16.7 months in patients who received 2L platinum-based chemotherapy
- In an exploratory analysis, mOS measured from the start of 1L platinum-based chemotherapy in this population without disease progression was 26.5 months
- mOS from the start of 1L platinum-based chemotherapy was 40.8 months in patients who received 2L ADC treatment after avelumab 1L maintenance, and 24.5 months in patients who received 2L platinum-based chemotherapy
- At data cutoff, 21.0% of patients were still receiving avelumab 1L maintenance treatment, and 55.5% had received 2L treatment
 Thus, most patients (76.5%) were still receiving avelumab or had received 2L treatment, and only a minority had discontinued without receiving
- any 2L treatment
 Overall, these results support the recommendation of avelumab 1L maintenance as standard of care in patients with aUC that has not progressed with 1L platinum-based chemotherapy
- Results from exploratory analyses suggest that patients who receive 1L platinum-based chemotherapy without disease progression followed by avelumab 1L maintenance and 2L treatment with an ADC, such as enfortumab vedotin, may have a mOS >3 years

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 with platinum chemotherapy given as initial treatment
- In a French study called AVENANCE, researchers found that patient outcomes with avelumab maintenance treatment given outside of a clinical trial were similar to clinical trial results
- In this new analysis from AVENANCE, researchers looked at how long people lived after starting avelumab maintenance treatment depending on what type of treatment they received when avelumab was stopped
- Overall, people treated with avelumab lived for an average of 21 months
- People treated with avelumab followed by a type of drug called an antibody-drug conjugate lived for an average of 31 months
- People treated with avelumab followed by more platinum chemotherapy lived for an average of 17 months
- Researchers also looked at how long people lived when survival was measured from the start of chemotherapy
- Overall, people in the study, which only included people whose cancer disappeared, shrank, or stopped growing with chemotherapy, lived for
 an average of 26.5 months from the start of chemotherapy
- People treated with avelumab followed by an antibody-drug conjugate lived for an average of 41 months from the start of chemotherapy,
 whereas people treated with more platinum chemotherapy after avelumab lived for an average of 24.5 months
- Overall, these results provide more support for using avelumab maintenance treatment in people with advanced urothelial cancer
- Results from exploratory analyses suggest that people treated with platinum chemotherapy who then receive avelumab maintenance followed by an antibody-drug conjugate might live for longer than 3 years on average

BACKGROUND

- In the JAVELIN Bladder 100 phase 3 trial (NCT02603432), avelumab 1L maintenance + best supportive care (BSC) significantly prolonged OS and progression-free survival (PFS) vs BSC alone in patients with aUC that had not progressed with 1L platinum-based chemotherapy^{1,2}
- Trial results led to avelumab 1L maintenance being recommended as a standard of care in international treatment guidelines³⁻⁶
- After ≥2 years of follow-up in all patients, mOS (measured 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
- In a post hoc analysis, mOS with avelumab 1L maintenance measured from start of 1L platinum-based chemotherapy in this population without disease progression was 29.7 months⁷
- OS durations in the JAVELIN Bladder 100 trial were achieved despite only 9 patients receiving enfortumab vedotin as 2L treatment after discontinuing avelumab
 1L maintenance (2.9% of discontinuing patients), reflecting available options when the study was conducted⁸
- Given the evolving treatment landscape, studies to assess OS with different treatment sequences in patients with aUC are needed
- AVENANCE is an ongoing, real-world study evaluating the effectiveness and safety of avelumab 1L maintenance in patients with aUC in France
- Results from the overall population with a median follow-up of 15.2 months have been reported previously⁹
- Here, we report updated data from AVENANCE in addition to analyses by subsequent (2L) treatment, and exploratory analyses of OS measured from start of 1L platinum-based chemotherapy in this study population of patients without disease progression

METHODS

- AVENANCE (NCT04822350) is an ongoing, multicenter, ambispective, noninterventional 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 July 13, 2021
- 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, and secondary endpoints include PFS, duration of treatment, and safety
- 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
- An exploratory analysis of OS from start of 1L chemotherapy was also performed, which excluded patients whose start date for chemotherapy was not provided or was recorded as being on or after the date of avelumab initiation
- Here, detailed analyses were performed in the overall population and in subgroups defined by 2L treatment received after discontinuing avelumab 1L maintenance
 Patients may have received 2L treatment within standard clinical practice, early access programs, or clinical trials
- Additional follow-up and analysis is ongoing

RESULTS

- Of 604 screened patients, 595 were included in the effectiveness population and 596 were included in the safety population
- Excluded patients had no avelumab treatment data, were missing safety data, or did not meet study eligibility criteria
- At data cutoff (December 7, 2023), median follow-up since avelumab initiation (by reverse Kaplan-Meier estimation) in the effectiveness population was 26.3 months (range, 0.6-43.7)
- 125 patients (21.0%) were still receiving avelumab treatment
- Reasons for discontinuation (reported in 469/470 patients) were disease progression (n=340; 72.5%), adverse events (n=53; 11.3%), death (n=44; 9.4%), and other reasons (n=32; 6.8%)
- Median duration of avelumab treatment was 5.6 months (95% CI, 4.9-6.9)
- 330 patients (55.5%) received 2L treatment after avelumab (70.2% of patients who discontinued avelumab); of these 330 patients:
- 244 (73.9%) received chemotherapy, including platinum-based chemotherapy in 81 (24.5%) and other chemotherapy in 163 (49.4%)
- 62 (18.8%) received an ADC, including enfortumab vedotin in 56 (17.0%) and sacituzumab govitecan in 6 (1.8%)
 24 (7.3%) received other treatments
- Baseline characteristics are shown in Table 1

Table 1. Baseline characteristics

	(N=595)	(n=244)	7.55 (52)	
Age, median (IQR), years	73.0 (67.0-78.2)	72.8 (66.7-78.1)	71.3 (64.7-77.5)	72.6 (67.8-75.0)
Sex, n (%)			,	
Male	491 (82.5)	198 (81.1)	49 (79.0)	20 (83.3)
Female	104 (17.5)	46 (18.9)	13 (21.0)	4 (16.7)
Location of primary tumor, n (%)	n=593	n=243	n=62	n=24
Bladder	444 (74.9)	180 (74.1)	46 (74.2)	15 (62.5)
Upper tract	117 (19.7)	48 (19.8)	14 (22.6)	8 (33.3)
Urethra	32 (5.4)	15 (6.2)	2 (3.2)	1 (4.2)
Tumor histology, n (%)	n=587	n=240	n=62	n=24
Pure urothelial carcinoma	542 (92.3)	222 (92.5)	56 (90.3)	23 (95.8)
Urothelial carcinoma with variant	29 (4.9)	11 (4.6)	3 (4.8)	1 (4.2)
Epidermoid carcinoma	5 (0.9)	2 (0.8)	1 (1.6)	0
Other	11 (1.9)	5 (2.1)	2 (3.2)	0
Tumor status at start of 1L chemotherapy, n (%)	n=593	n=242	n=62	n=24
Locally advanced	48 (8.1)	12 (5.0)	2 (3.2)	2 (8.3)
Metastatic	545 (91.9)	230 (95.0)	60 (96.8)	22 (91.7)
Visceral metastasis at start of 1L chemotherapy, n (%)	n=545	n=230	n=60	n=22
Yes	462 (84.8)	205 (89.1)	46 (76.7)	14 (63.6)
No	83 (15.2)	25 (10.9)	14 (23.3)	8 (36.4)
Metastasis sites at start of 1L chemotherapy, n (%)	n=462	n=205	n=46	n=14
Lymph nodes	288 (62.3)	122 (59.5)	33 (71.7)	9 (64.3)
Liver	86 (18.6)	48 (23.4)	5 (10.9)	3 (21.4)
Lung	153 (33.1)	73 (35.6)	16 (34.8)	5 (35.7)
Bone	164 (35.5)	75 (36.6)	13 (28.3)	2 (14.3)
Brain	2 (0.4)	2 (1.0)	0	0
Other	91 (19.7)	39 (19.0)	6 (13.0)	5 (35.7)
ECOG performance status at start of 1L chemotherapy, n (%)	n=473	n=186	n=49	n=20
O O	147 (31.1)	53 (28.5)	13 (26.5)	7 (35.0)
<u> </u>	251 (53.1)	100 (53.8)	27 (55.1)	13 (65.0)
≥2	75 (15.9)	33 (17.7)	9 (18.4)	0
1L chemotherapy regimen, n (%)	n=592	n=242	n=61	n=24
Carboplatin + gemcitabine	364 (61.5)	154 (63.6)	38 (62.3)	16 (66.7)
Cisplatin + gemeitabine	165 (27.9)	58 (24.0)	18 (29.5)	4 (16.7)
Cisplatin or carboplatin + gemcitabine*	11 (1.9)	3 (1.2)	2 (3.3)	0
ddMVAC	25 (4.2)	12 (5.0)	2 (3.3)	2 (8.3)
Other	27 (4.6)	15 (6.2)	1 (1.6)	2 (8.3)
1L chemotherapy cycles received, median (range)	5 (1-15)	5 (1-10)	5 (3-10)	6 (3-6)
Response to 1L chemotherapy, n (%)	n=590	n=241	n=62	n=24
Complete response	116 (19.7)	42 (17.4)		5 (20.8)
Partial response	332 (56.3)	` '	16 (25.8)	
•		140 (58.1)	32 (51.6)	12 (50.0) 7 (29.2)
Stable disease Disease progression	136 (23.1)	57 (23.7)	11 (17.7)	
Disease progression	4 (0.7)	1 (0.4)	3 (4.8)	0
Nonevaluable Time forms about a fill a least a fill a fill a fill a least a fill a least a fill a fill a least a fill a least a fill a least a fill a fill a least a fill a least a fill a f	2 (0.3)	1 (0.4)	0	0
Time from start of 1L chemotherapy to start of avelumab 1L maintenance, median (IQR), months	4.5 (3.4-5.3)	4.5 (3.6-5.3)	4.6 (3.4-5.2)	4.6 (4.2-5.1)

1L, first line; 2L, second line; ADC, antibody-drug conjugate; ddMVAC, dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin; IQR, interquartile range.
*Includes patients who switched platinum-based regimens while receiving 1L chemotherapy.

- In the overall effectiveness population, mOS from the start of avelumab 1L maintenance treatment was 21.3 months (95% CI, 17.6-24.6) (**Figure 1A**)
- 1- and 2-year OS rates were 66.52% (95% CI, 62.53%-70.19%) and 45.89% (95% CI, 41.55%-50.12%), respectively
- A subgroup analysis of OS is shown in Table 2

In patients who received 2L ADC treatment after discontinuing avelumab, mOS from start of avelumab 1L maintenance was 31.3 months (95% CI, 29.1-not estimable) (Figure 1B)

- 1- and 2-year OS rates were 86.71% (95% CI, 75.16%-93.12%) and 70.06% (95% CI, 55.42%-80.70%), respectively
 In patients who received 2L chemotherapy, mOS from start of avelumab 1L maintenance was 14.4 months
- In patients who received 2L chemotherapy, mOS from start of avelumab 1L maintenance was 14.4 months (95% CI, 13.2-15.9)
- In patients who received 2L platinum-based or nonplatinum-based chemotherapy, mOS was 16.7 months (95% CI, 13.6-22.8) and 13.6 months (95% CI, 12.3-15.2), respectively (Figure 1B)

Figure 1. OS from the start of avelumab 1L maintenance treatment

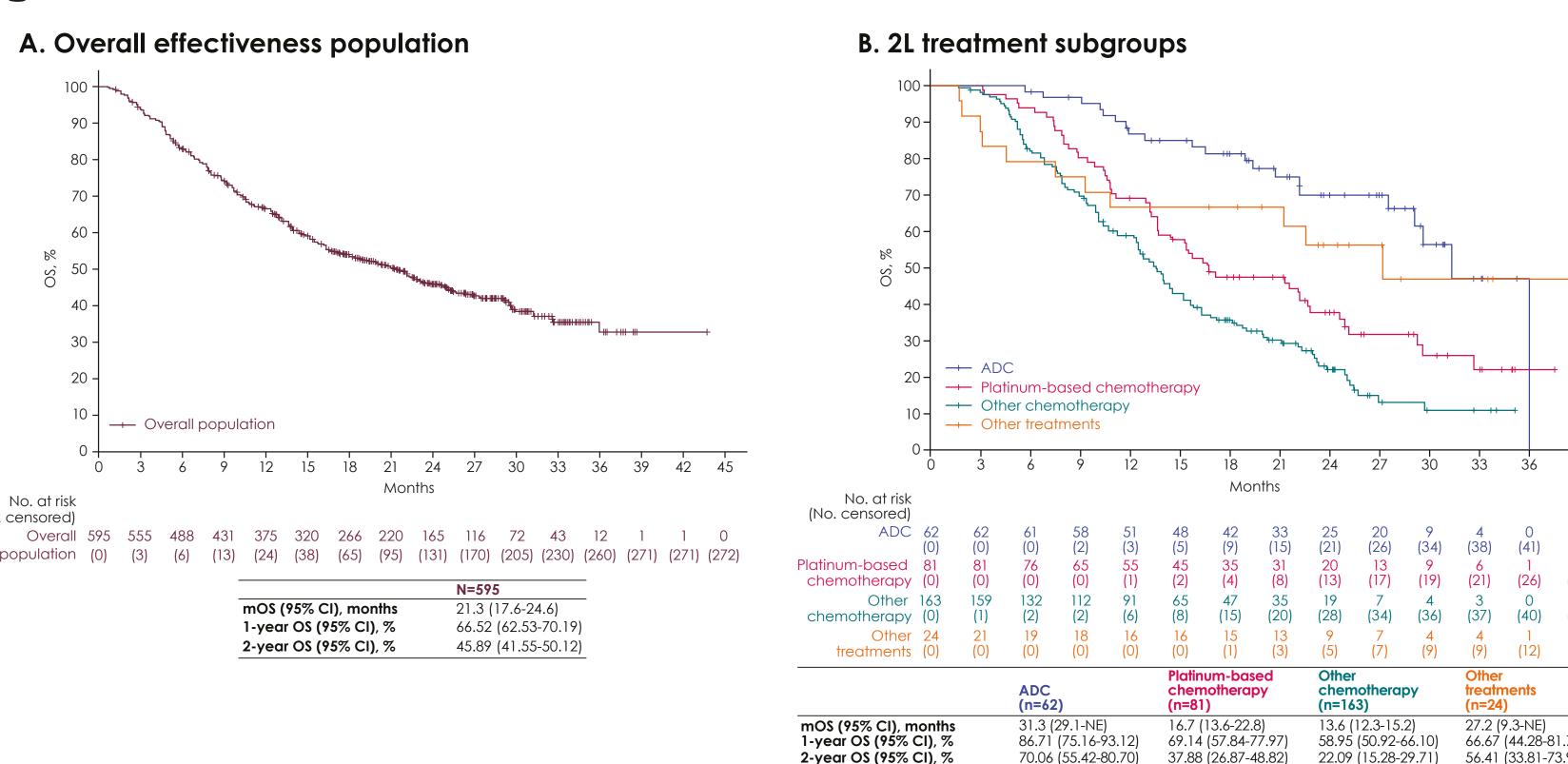




Table 2. Subgroup analysis of OS from the start of avelumab 1L maintenance treatment

Subgroup	Patients, n	mOS (95% CI), months
Location of primary tumor		
Bladder	444	20.4 (16.8-24.6)
Upper tract	117	23.3 (15.7-31.3)
Urethra	32	15.3 (9.1-NE)
Tumor histology		
Pure UC	542	21.3 (17.1-24.9)
Mixed UC with variant	29	16.5 (7.9-24.9)
Extent of disease at start of 1L chemotherapy		
Metastatic	545	20.7 (16.6-23.2)
Locally advanced	48	NR (18.0-NE)
Visceral metastases at start of 1L chemotherapy		
Yes	462	20.0 (15.6-23.1)
No	83	25.1 (16.5-NE)
1L chemotherapy regimen		
Cisplatin+ gemcitabine	165	25.2 (19.0-NE)
Carboplatin + gemcitabine	364	18.9 (15.4-22.3)
ddMVAC	25	25.4 (14.4-NE)
No. of 1L chemotherapy cycles		
<4	41	12.2 (7.8-16.8)
4-6	530	22.1 (18.1-25.2)
>6	22	22.1 (15.7-NE)
Response to 1L chemotherapy		
Complete response	116	29.6 (21.1-NE)
Partial response	332	22.8 (17.6-29.1)
Stable disease	136	13.6 (9.9-20.0)
Time from end of 1L chemotherapy to start of avelumab		
<4 weeks	215	23.3 (18.9-29.7)
≥4 weeks	377	19.9 (15.4-22.8)
2L treatment		
ADC	62	31.3 (29.1-NE)
Platinum-based chemotherapy	81	16.7 (13.6-22.8)
Other chemotherapy	163	13.6 (12.3-15.2)
Other treatments	24	27.2 (9.3-NE)

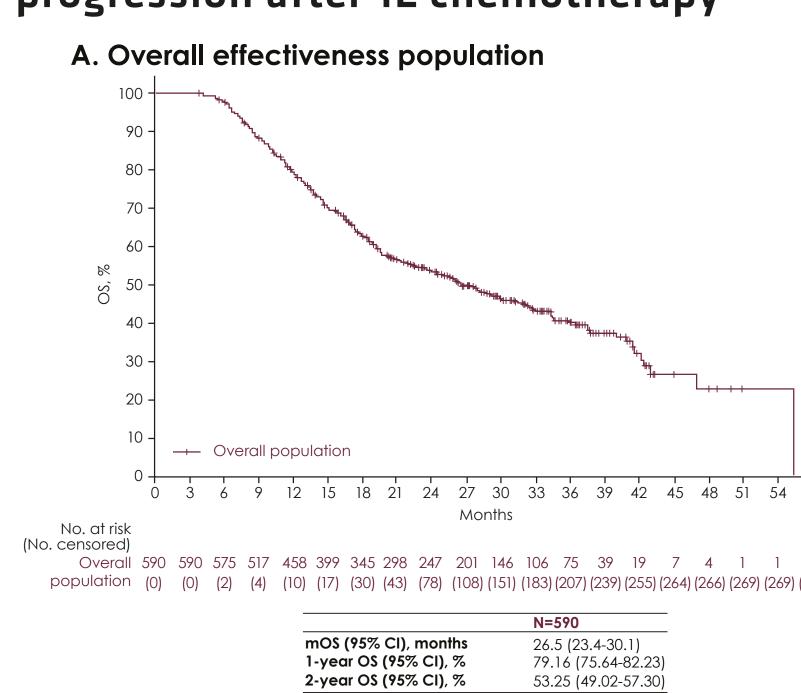
Subgroups with <20 patients are not shown. 1L, first line; 2L, second line; ADC, antibody-drug conjugate; ddMVAC, dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin; mOS, median overall survival; NE, not estimable; NR, not reached; UC, urothelial carcinoma.

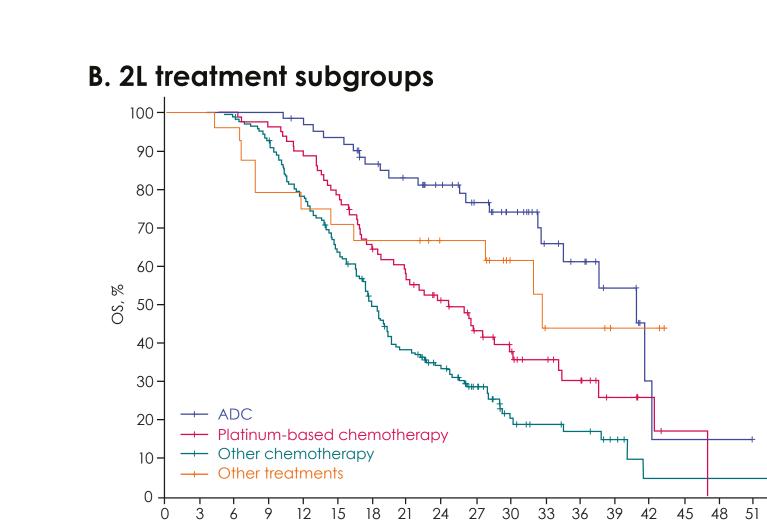
mOS measured from the start of 1L chemotherapy in this population of patients without disease progression after 1L chemotherapy was 26.5 months (95% CI, 23.4-30.1) (Figure 2A) In patients who received 2L ADC treatment after discontinuing avelumab, mOS from start of 1L

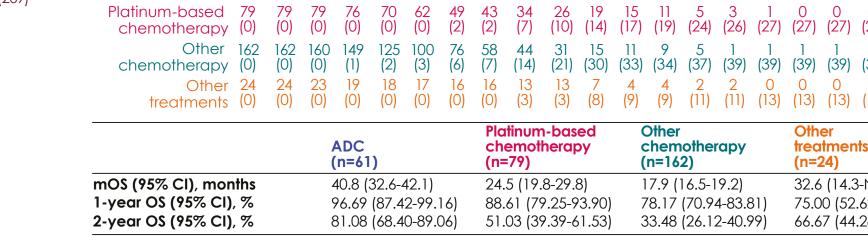
- platinum-based chemotherapy was 40.8 months (95% CI, 32.6-42.1) (**Figure 2B**)
- In patients who received 2L platinum-based chemotherapy after avelumab, mOS from start of 1L
 platinum-based chemotherapy was 24.5 months (95% CL 19.8-29.8) (Figure 2B)
- platinum-based chemotherapy was 24.5 months (95% CI, 19.8-29.8) (**Figure 2B**)

 Median PFS from start of avelumab treatment in the overall effectiveness population was 5.7 months
- (95% CI, 5.2-6.5)

Figure 2. OS from the start of 1L chemotherapy in this study population without disease progression after 1L chemotherapy







These exploratory analyses of OS measured from the start of 1L platinum-based chemotherapy in this population of patients without disease progression or platinum-based chemotherapy should be interpreted with caution. Patients without a start date for 1L platinum-based therapy were not included.

1L, first line; 2L, second line; ADC, antibody-drug conjugate; mOS, median overall survival; NE, not estimable.

Safety findings with avelumab 1L maintenance treatment in the overall safety population and in subgroups
defined by 2L treatment are summarized in Table 3

Table 3. Summary of AEs

	Overall safety population (N=596)	2L treatment: chemotherapy (n=244)	2L treatment: ADC (n=62)	2L treatment: other (n=24)
TEAE, n (%)*	507 (85.1)	201 (82.4)	55 (88.7)	20 (83.3)
Serious TEAE	305 (51.2)	147 (60.2)	36 (58.1)	12 (50.0)
TEAE leading to temporary/permanent discontinuation	299 (50.2)	100 (41.0)	25 (40.3)	13 (54.2)
TEAE leading to death	199 (33.4)	107 (43.9)	18 (29.0)	6 (25.0)
TRAE, n (%)	352 (59.1)	115 (47.1)	42 (67.7)	14 (58.3)
Serious TRAE	37 (6.2)	12 (4.9)	5 (8.1)	3 (12.5)
TRAE leading to temporary/permanent discontinuation	208 (34.9)	61 (25.0)	22 (35.5)	9 (37.5)
TRAE leading to death	4 (0.7)	1 (0.4)	0	0

2L, second line; **ADC**, antibody-drug conjugate; **AE**, adverse event; **TEAE**, treatment-emergent adverse event; **TRAE**, treatment-related and -emergent adverse event. *AEs were considered treatment emergent if their start date was on or after avelumab initiation.

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