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ORIGINAL ARTICLE

Avelumab plus sacituzumab govitecan versus avelumab monotherapy as first-line maintenance treatment in patients with advanced urothelial carcinoma: JAVELIN Bladder Medley interim analysis☆

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Background: Avelumab first-line maintenance is a recommended treatment option for patients with locally advanced or metastatic urothelial carcinoma (la/mUC) without progression following platinum-based chemotherapy (PBC). The JAVELIN Bladder Medley phase II trial is investigating the efficacy and safety of maintenance treatment with avelumab combined with other antitumor agents versus avelumab monotherapy. We report an interim analysis of avelumab plus sacituzumab govitecan (SG) versus avelumab monotherapy.

Patients and methods: Patients with la/mUC without progression after first-line PBC were randomized 2 : 1 to receive avelumab (800 mg every 2 weeks) plus SG (10 mg/kg on days 1 and 8 of 21-day cycles) or avelumab monotherapy (800 mg every 2 weeks). Primary endpoints are investigator-assessed progression-free survival (PFS) and safety. For PFS and overall survival (OS), data in the avelumab monotherapy arm were extended per protocol using propensity score-weighted JAVELIN Bladder 100 data.

Results: At data cut-off (16 September 2024), 38/74 patients (51.4%) in the avelumab plus SG arm and 10/37 patients (27.0%) in the avelumab monotherapy arm were still receiving study treatment. Median PFS with avelumab plus SG versus avelumab monotherapy was 11.17 versus 3.75 months, respectively [hazard ratio (HR) 0.49, 95% confidence interval (CI) 0.31-0.76; prespecified efficacy boundary: HR $\leq$ 0.60]. OS data were immature; median OS was not reached versus 23.75 months, respectively (HR 0.79, 95% CI 0.42-1.50). In patients treated with avelumab plus SG or avelumab monotherapy, any-grade treatment-related adverse events (TRAEs) occurred in 97.3% versus 63.9% (grade $\geq$3 in 69.9% versus 0%), respectively.

Conclusion: In patients with la/mUC without progression after first-line PBC, PFS was prolonged with avelumab plus SG versus avelumab monotherapy as maintenance treatment. TRAEs were more frequent with the combination and were consistent with known safety profiles of SG and avelumab. Combining avelumab with anti-Trop-2 antibody—drug conjugates may be a promising strategy to improve patient outcomes in la/mUC.

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Key words: advanced urothelial carcinoma, antibody—drug conjugate, immunotherapy, maintenance, phase II trial, randomized

INTRODUCTION

In the JAVELIN Bladder 100 trial, switch-maintenance treatment with avelumab [an anti-programmed death-ligand 1 (PD-L1) antibody] plus best supportive care (BSC) significantly prolonged overall survival (OS) and progression-free survival (PFS) versus BSC alone in patients with locally advanced or metastatic urothelial carcinoma (la/mUC) who were progression free following first-line (1L) platinum-based chemotherapy (PBC).[1,2] After $\geq$2 years of follow-up in all patients, the median OS from the start of maintenance was 23.8 versus 15.0 months, respectively [hazard ratio (HR) 0.76, 95% confidence interval (CI) 0.63-0.91, two-sided $P = 0.0036$], and the median investigator-assessed PFS was 5.5 versus 2.1 months (HR 0.54, 95% CI 0.46-0.64, two-sided $P < 0.0001$).[1] The long-term safety of avelumab 1L maintenance was demonstrated with no new safety concerns,[1] and no detrimental impact on quality of life and an increase in quality-adjusted time without symptoms or toxicity were observed with avelumab 1L maintenance treatment.[3,4] Results from the trial supported the inclusion of avelumab 1L maintenance in international guidelines as a recommended treatment for patients with la/mUC without progression following 1L PBC.[5-8]

Sacituzumab govitecan (SG) is a Trop-2-directed antibody and topoisomerase inhibitor drug conjugate that is being investigated as a treatment in several solid tumors.[9-12] SG is approved in the United States and European Union and in several other countries for the treatment of patients with unresectable locally advanced or metastatic triple-negative breast cancer who have received two or more prior systemic therapies with one or more for metastatic disease and unresectable locally advanced or metastatic hormone receptor-positive, human epidermal growth factor receptor 2-negative breast cancer who have received three or more prior systemic therapies including endocrine-based therapy.[13,14] In a cohort of the TROPHY-U-01 phase II trial, combination treatment with SG and pembrolizumab [an anti-programmed cell death protein 1 (PD-1) antibody] in patients with la/mUC who had progression after PBC and no prior anti-PD-(L)1 inhibitor treatment had encouraging efficacy and a manageable safety profile, supporting further investigation of SG plus immune checkpoint inhibitor combinations.[15]

JAVELIN Bladder Medley is a randomized phase II trial investigating combinations of avelumab with other agents as 1L switch-maintenance treatment. We hypothesized that combining avelumab with other antitumor agents that target different pathways could provide increased efficacy compared with avelumab monotherapy. In this article, we report the results of an interim analysis of avelumab plus SG versus avelumab monotherapy.

PATIENTS AND METHODS

Study design and patients

JAVELIN Bladder Medley (NCT05327530) is an ongoing, international, randomized, open-label, parallel-arm, phase II trial. The study design has been reported.[16] Briefly, eligible patients were aged $\geq$18 years; had unresectable la/mUC and no progressive disease following four to six cycles of 1L PBC (cisplatin and/or carboplatin plus gemcitabine); and had Eastern Cooperative Oncology Group performance status (ECOG PS) of 0/1. In the avelumab plus SG and avelumab monotherapy arms reported in this paper, after a 4- to 10-week interval from last chemotherapy dose, patients were randomized 2 : 1 to receive avelumab (800 mg every 2 weeks) plus SG (10 mg/kg on days 1 and 8 of 21-day cycles) or avelumab monotherapy (800 mg every 2 weeks), stratified by the presence of visceral metastases at the start of 1L chemotherapy. Protocol guidance for dose modification and management was provided for specified adverse reactions; guidance for SG-related neutropenia is described in the Supplementary Material, available at https://doi.org/10.1016/j.annonc.2025.05.010. Treatment continued until disease progression (per investigator assessment), unacceptable toxicity, withdrawal of consent, initiation of new anticancer treatment, or any other prespecified reason for permanent discontinuation occurred.

The trial was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines defined by the International Council of Harmonisation. All procedures were carried out in compliance with relevant laws and institutional guidelines. The protocol, amendments, and informed consent forms were approved by the institutional review board or independent ethics committee at each trial site. All patients provided written consent.

Outcomes and statistical analysis

The primary endpoints were PFS (time from randomization until progression or death) by investigator assessment and safety. Secondary endpoints included OS (time from randomization until death due to any cause), objective response (change versus baseline assessment at randomization), and duration of response per investigator assessment. For analyses of PFS and OS, data in the avelumab monotherapy arm (control arm) were extended per protocol using propensity score-weighted data from the avelumab plus BSC arm of the JAVELIN Bladder 100 trial. Specifically, all patients from the avelumab plus BSC arm of JAVELIN Bladder 100 who met the inclusion and exclusion criteria of the JAVELIN Bladder Medley trial ($n = 313$) were included in the analyses. Data from individual patients were weighted using propensity scores based on predefined

baseline characteristics (age, visceral metastases, liver lesions, lung lesions, ECOG PS, PD-L1 status) to account for any population differences.[17,18] The propensity score-weighted data from JAVELIN Bladder 100 was additionally down-weighted so that the overall weight of the JAVELIN Bladder 100 data was 37 patients, which corresponds to the number of patients randomized to the JAVELIN Bladder Medley control arm. For the PFS analysis, investigator-assessed data from the JAVELIN Bladder 100 trial were used. PFS and OS were analyzed using the Kaplan—Meier method, and stratified HRs and associated 95% CIs were calculated using a Cox proportional hazards model. Tumor response was evaluated by investigators according to the Response Evaluation Criteria in Solid Tumors version 1.1. Safety was assessed in all patients who received one or more dose of trial treatment. Adverse events (AEs) were graded according to the National Cancer Institute Common Terminology Criteria for AEs version 5.0. An interim analysis was triggered when 56 PFS events were observed in the treatment—control comparison; the primary analysis is planned at 65 PFS events. The efficacy boundary for PFS in the interim analysis was HR $\leq$ 0.60. *P* values are not reported because of the exploratory nature of the study.

RESULTS

Patients

In total, 111 patients were randomized to receive avelumab plus SG ($n = 74$) or avelumab monotherapy ($n = 37$). Baseline characteristics were generally similar between the arms (Table 1); however, a smaller proportion of patients had an ECOG PS of 1 in the avelumab plus SG arm than in the avelumab monotherapy arm (31.1% versus 54.1%).

At data cut-off (16 September 2024), 38 patients (51.4%) in the avelumab plus SG arm and 10 patients (27.0%) in the avelumab monotherapy arm were still receiving study treatment; 35 (47.3%) and 26 patients (70.3%) had discontinued all study treatment, respectively, and one patient in each arm (1.4% and 2.7%, respectively) had not received any study treatment. Avelumab treatment was discontinued by 36 patients (48.6%) in the avelumab plus SG arm and 26 patients (70.3%) in the avelumab monotherapy arm; the most common reason for avelumab discontinuation in both arms was disease progression [avelumab plus SG, 21/36 (58.3%); avelumab monotherapy, 21/26 (80.8%)]. SG treatment was discontinued in 42 patients (56.8%); the most common reasons for SG discontinuation were disease progression [20/42 (47.6%)] and AEs [9/42 (21.4%)]. The median duration of avelumab treatment was 6.67 months (range 0.46-23.92 months) in the avelumab plus SG arm and 3.35 months (range 0.46-21.62 months) in the avelumab monotherapy arm. The median duration of SG treatment was 5.75 months (range 0.23-23.69 months).

Table 1. Baseline characteristics

	Avelumab plus SG ($n = 74$)	Avelumab monotherapy ($n = 37$)
Age, median (range), years	70 (42-85)	67 (53-89)
Sex, *n* (%)		
Male	61 (82.4)	28 (75.7)
Female	13 (17.6)	9 (24.3)
Pooled geographic region, *n* (%)		
Asia	20 (27.0)	10 (27.0)
Europe	38 (51.4)	22 (59.5)
North America	10 (13.5)	2 (5.4)
Rest of the world	6 (8.1)	3 (8.1)
ECOG performance status, *n* (%)		
0	51 (68.9)	17 (45.9)
1	23 (31.1)	20 (54.1)
PD-L1 status, *n* (%)		
Positive	20 (27.0)	13 (35.1)
Negative	51 (68.9)	22 (59.5)
Unknown	3 (4.1)	2 (5.4)
Primary tumor location, *n* (%)		
Bladder	56 (75.7)	26 (70.3)
Ureter/renal pelvis	17 (23.0)	11 (29.7)
Urethra	1 (1.4)	0
Site of metastasis at start of 1L chemotherapy, *n* (%)		
Visceral	37 (50.0)	19 (51.4)
Nonvisceral	37 (50.0)	18 (48.6)
Liver lesions at randomization, *n* (%)		
Yes	20 (27.0)	9 (24.3)
No	54 (73.0)	28 (75.7)
Lung lesions at randomization, *n* (%)		
Yes	17 (23.0)	11 (29.7)
No	57 (77.0)	26 (70.3)
1L chemotherapy regimen, *n* (%)		
Cisplatin plus gemcitabine	41 (55.4)	25 (67.6)
Carboplatin plus gemcitabine	33 (44.6)	12 (32.4)
Best response to 1L chemotherapy, *n* (%)		
CR or PR	54 (73.0)	29 (78.4)
SD	19 (25.7)	8 (21.6)
Not reported	1 (1.4)	0

1L, first-line; CR, complete response; ECOG, Eastern Cooperative Oncology Group; PD-L1, programmed death-ligand 1; PR, partial response; SD, stable disease; SG, sacituzumab govitecan.

Efficacy

The interim analysis was carried out when 56 PFS events were reported across the avelumab plus SG and avelumab monotherapy arms. Median follow-up for PFS was 10.94 months in the avelumab plus SG arm and 19.25 months in the avelumab monotherapy arm (extended with propensity score-weighted data from JAVELIN Bladder 100). At last follow-up, 52 patients (70.3%) in the avelumab plus SG arm and 27 patients (73.0%) in the avelumab monotherapy arm were alive. Investigator-assessed PFS was prolonged with avelumab plus SG versus avelumab monotherapy (Figure 1A); median PFS was 11.17 months [95% CI 7.43 months-not estimable (NE)] versus 3.75 months (95% CI 3.32-6.77 months), respectively (HR 0.49, 95% CI 0.31-0.76). Thus, the prespecified efficacy boundary for PFS (HR $\leq$ 0.60) was crossed. PFS analyses favored avelumab plus SG across subgroups, including those defined by age and 1L chemotherapy regimen (Figure 1B). In a sensitivity analysis that did not include the extended control arm data (i.e. only patients enrolled in this trial), the median PFS in the avelumab monotherapy arm ($n = 37$) was 3.56 months (95% CI 1.91-9.23 months; HR for avelumab plus SG versus avelumab monotherapy 0.43, 95% CI 0.25-0.75) (Supplementary Figure S1, available at https://doi.org/10.1016/j.annonc.

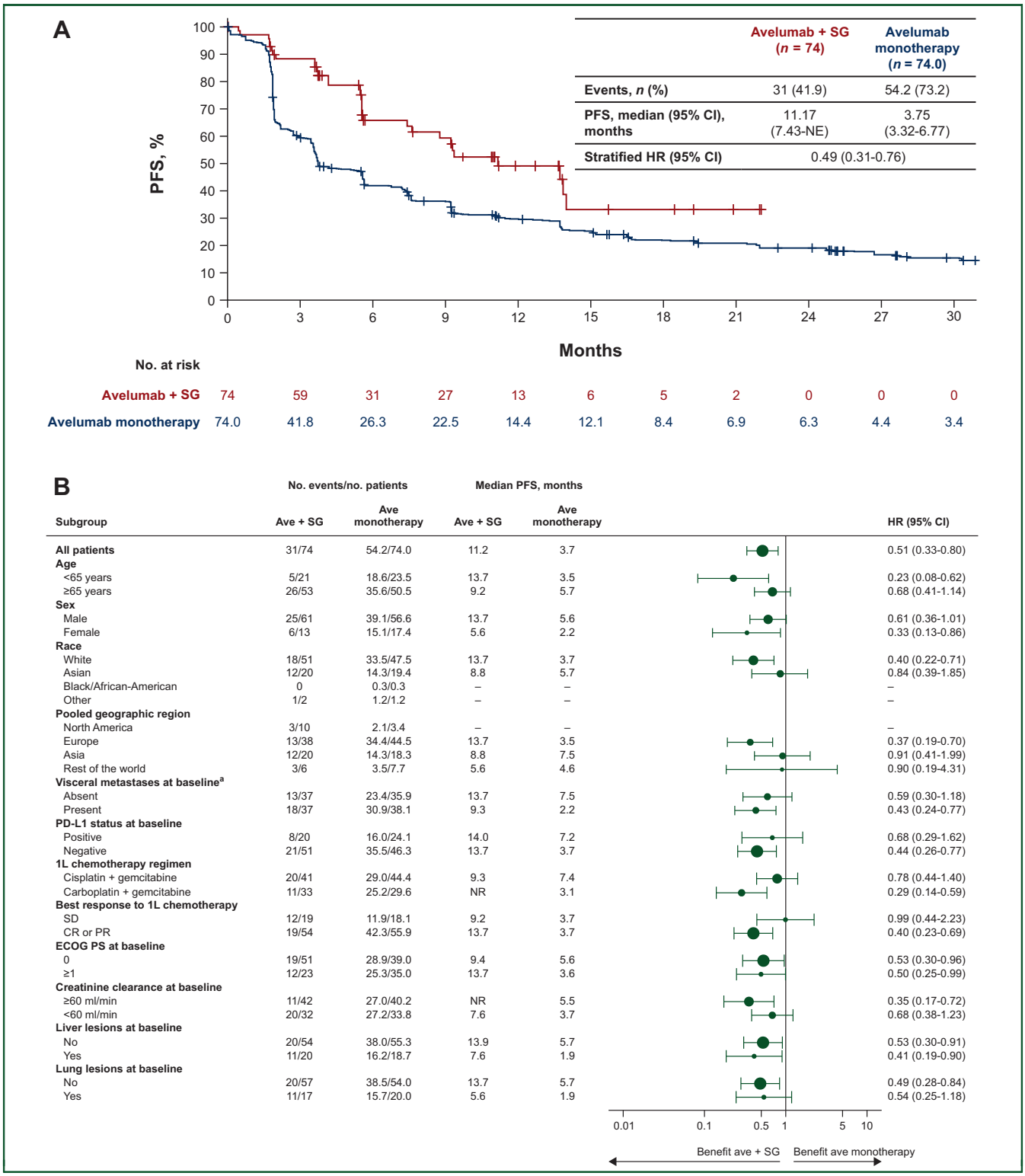

Figure 1. Efficacy analyses. (A) Investigator-assessed PFS in the overall population. (B) Subgroup analyses of investigator-assessed PFS. (C) OS in the overall population. Data in the avelumab monotherapy arm (control arm) were extended per protocol using propensity score-weighted data from the avelumab plus BSC arm of the JAVELIN Bladder 100 trial. For subgroup analyses, categories with <5 patients in one or both treatment arms were not included.
1L, first-line; BSC, best supportive care; CI, confidence interval; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; NE, not estimable; NR, not reached; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PR, partial response; SD, stable disease; SG, sacituzumab govitecan.
[a]Reported at the time of randomization, refers to the presence of visceral metastases at first diagnosis of locally advanced or metastatic urothelial carcinoma.

2025.05.010). OS data were immature at data cut-off. Median follow-up for OS was 11.40 months in the avelumab plus SG arm and 18.04 months in the avelumab monotherapy arm (extended with propensity score-weighted data from JAVELIN Bladder 100). Median OS was not reached (95% CI 15.51 months-NE) in the avelumab

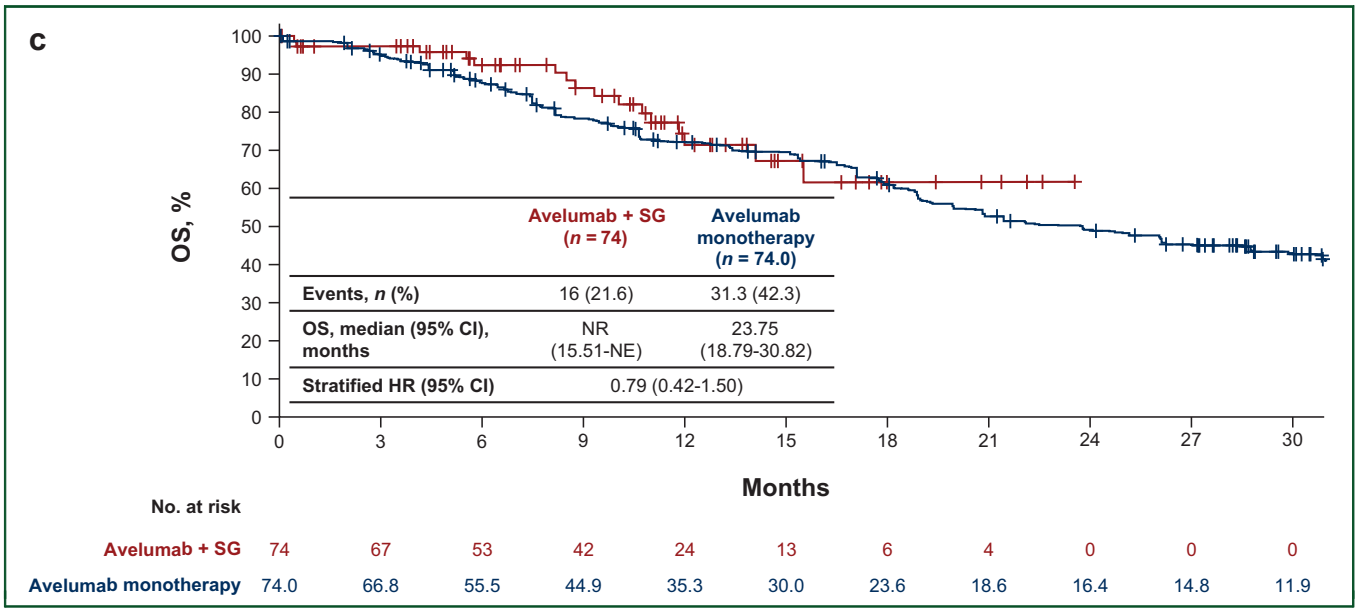

Figure 1. Continued.

plus SG arm versus 23.75 months (95% CI 18.79-30.82 months) in the avelumab monotherapy arm (HR 0.79, 95% CI 0.42-1.50) (Figure 1C). Sensitivity analyses of OS without extended data were not conducted in this interim analysis because OS data were immature.

Objective response rates in the avelumab plus SG and avelumab monotherapy arms (change compared with baseline post 1L PBC; not extended with JAVELIN Bladder 100 data) were 24.3% (95% CI 15.1% to 35.7%) versus 2.7% (95% CI 0.1% to 14.2%), respectively (Supplementary Table S1, available at https://doi.org/10.1016/j.annonc.2025.05.010). Disease control rates were 68.9% versus 43.2%, respectively. Among responders, the median duration of response was 11.9 months (95% CI 5.7 months-NE) in the avelumab plus SG arm ($n = 18$) and NE in the avelumab monotherapy arm ($n = 1$).

Safety

Among treated patients, treatment-related AEs (TRAEs) occurred in 71 patients (97.3%) in the avelumab plus SG arm and 23 patients (63.9%) in the avelumab monotherapy arm, including grade ≥3 TRAEs in 51 patients (69.9%) and 0 patients, respectively (Table 2). The most common avelumab- and SG-related AEs are detailed in Table 3. The most common avelumab-related AEs were fatigue [avelumab plus SG arm: 21 (28.8%), grade ≥3: 3 (4.1%); avelumab monotherapy arm: 2 (5.6%), none grade ≥3] and diarrhea [avelumab plus SG arm: 16 (21.9%), grade ≥3: 2 (2.7%); avelumab monotherapy arm: 2 (5.6%), none grade ≥3]. The most common SG-related AEs were alopecia [43 (58.9%)], diarrhea [36 (49.3%); grade ≥3: 9 (12.3%)], and neutropenia [35 (47.9%); grade ≥3: 29 (39.7%)]. Febrile neutropenia occurred in eight patients (11.0%). In the avelumab plus SG arm, TRAEs led to dose reduction of SG in 39 patients (53.4%), and led to permanent discontinuation of avelumab in 3 patients (4.1%), SG in 9 patients (12.3%), and both study drugs in 3 patients (4.1%). In the avelumab monotherapy arm, TRAEs led to permanent discontinuation of avelumab in one patient (2.8%). One patient in the avelumab plus SG arm had an SG-related AE that led to death (acute subarachnoid hemorrhage in the setting of sepsis and pancytopenia). Concomitant granulocyte colony-stimulating factor (G-CSF) administration was reported in 36 patients (48.6%) in the avelumab plus SG arm and one patient (2.7%) in the avelumab monotherapy arm.

DISCUSSION

Avelumab maintenance following disease control with 1L PBC is a recommended 1L treatment option for patients with la/mUC,[5-8] and its effectiveness and safety has been confirmed in multiple real-world studies in several countries.[19-24] The JAVELIN Bladder Medley phase II trial sought to increase the benefits of switch-maintenance treatment by investigating novel combinations of avelumab with other antitumor agents. In this interim analysis, avelumab plus SG prolonged PFS versus avelumab monotherapy (median 11.17 versus 3.75 months). A PFS benefit was also observed across various subgroups. OS data were immature at cut-off (HR 0.79, 95% CI 0.42-1.50), and longer follow-up is required.

As expected with combination treatment, TRAEs were more frequent in the avelumab plus SG arm than in the avelumab monotherapy arm, including grade ≥3 TRAEs. However, no new safety signals were observed, and individual TRAEs were consistent with the known safety profiles of SG and avelumab.[1,2,25-27] The incidence of grade 3/4 neutropenia was 39.7% in this study and 34%-37% in previously reported studies of SG monotherapy or SG plus pembrolizumab in patients with la/mUC.[15,25,27] SG-related neutropenia was managed with SG dose reduction and early detection through protocol-defined monitoring

Table 2. Summary of safety

Patients, *n* (%)	Avelumab plus SG (*n* = 73)	Avelumab monotherapy (*n* = 36)
Treatment-emergent AE of any grade	73 (100)	33 (91.7)
Grade ≥3 treatment-emergent AE	58 (79.5)	13 (36.1)
Treatment-related AE of any grade	71 (97.3)	23 (63.9)
Grade ≥3 treatment-related AE	51 (69.9)	0
Serious treatment-emergent AE	27 (37.0)	8 (22.2)
Serious avelumab-related AE	6 (8.2)	0
Serious SG-related AE	15 (20.5)	—
Treatment-emergent AE leading to dose reduction of SG	39 (53.4)	—
Treatment-related AE leading to dose reduction of SG	39 (53.4)	—
Treatment-emergent AE leading to discontinuation of avelumab	6 (8.2)	2 (5.6)
Treatment-related AE leading to discontinuation of avelumab	3 (4.1)	1 (2.8)
Treatment-emergent AE leading to discontinuation of SG	10 (13.7)	—
Treatment-related AE leading to discontinuation of SG	9 (12.3)	—
Treatment-emergent AE leading to discontinuation of both study drugs	3 (4.1)	—
Treatment-related AE leading to discontinuation of both study drugs	3 (4.1)	—
Treatment-emergent AE leading to death	2 (2.7)	2 (5.6)
Treatment-related AE leading to death	1 (1.4)	0
irAE of any grade	14 (19.2)	5 (13.9)
IRR of any grade	7 (9.6)	4 (11.1)

AE, adverse event; irAE, immune-related adverse event; IRR, infusion-related reaction; SG, sacituzumab govitecan.

Table 3. Summary of most common treatment-related AEs

Patients, *n* (%)	Avelumab plus SG (*n* = 73)		Avelumab monotherapy (*n* = 36)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Avelumab-related AE				
Fatigue	21 (28.8)	3 (4.1)	2 (5.6)	0
Diarrhea	16 (21.9)	2 (2.7)	2 (5.6)	0
Asthenia	12 (16.4)	0	4 (11.1)	0
Pruritus	11 (15.1)	0	6 (16.7)	0
Hypothyroidism	8 (11.0)	0	0	0
Nausea	7 (9.6)	0	1 (2.8)	0
Infusion-related reaction	6 (8.2)	0	4 (11.1)	0
Rash	6 (8.2)	0	0	0
SG-related AE				
Alopecia	43 (58.9)	0	—	—
Diarrhea	36 (49.3)	9 (12.3)	—	—
Neutropenia	35 (47.9)	29 (39.7)	—	—
Fatigue	29 (39.7)	6 (8.2)	—	—
Nausea	26 (35.6)	0	—	—
Anemia	23 (31.5)	8 (11.0)	—	—
Neutrophil count decreased	23 (31.5)	17 (23.3)	—	—
Asthenia	17 (23.3)	0	—	—
Decreased appetite	13 (17.8)	0	—	—
Constipation	10 (13.7)	0	—	—
Vomiting	10 (13.7)	0	—	—
Febrile neutropenia	8 (11.0)	8 (11.0)	—	—
Pruritus	7 (9.6)	0	—	—
Thrombocytopenia	6 (8.2)	0	—	—

AEs occurring in ≥7.5% of patients in either arm are listed.
AE, adverse event; SG, sacituzumab govitecan.

of absolute neutrophil count. Concomitant G-CSF administration was reported in approximately half of patients in the avelumab plus SG arm. The role of G-CSF use in primary versus secondary prophylaxis or neutropenia management was not evaluated in this interim analysis, but investigation is planned for the primary analysis.

The JAVELIN Bladder Medley trial reconfirmed the efficacy and safety of avelumab 1L maintenance treatment. To minimize patient exposure to the avelumab monotherapy arm, PFS and OS data in this arm were extended with external control data from the avelumab plus BSC arm of the JAVELIN Bladder 100 trial. Limitations of this extended analysis include potential differences in patient characteristics, subsequent treatment, and follow-up time between the trials. However, data from JAVELIN Bladder 100 were weighted using propensity scores to mitigate differences in baseline characteristics between the trials. Furthermore, a sensitivity analysis of PFS that did not include extended control arm data had similar findings to the main PFS analysis. A similar sensitivity analysis of OS is planned for the primary analysis. Because of the exploratory nature of this study, central radiology review was not conducted, and disease progression/response was assessed by investigators. Although investigator assessment has limitations, such as greater potential for bias and variability, it enables faster data collection and improved cost-effectiveness versus central radiology review.

SG monotherapy was previously an option in the United States for patients with la/mUC following PBC and anti-PD-(L)1 inhibitor treatment based on single-arm studies.[15,25,28] However, accelerated approval was voluntarily withdrawn by the manufacturer in October 2024 because the TROPiCS-04 phase III trial did not show a significant improvement in OS with SG monotherapy versus physician's choice of single-agent chemotherapy (taxane or vinflunine). None the less, the activity of SG was demonstrated by a higher objective response rate versus single-agent chemotherapy.[27] The authors concluded that early toxicity-related complications with SG may have impacted efficacy outcomes. Specifically, in TROPiCS-04, 14 patients had fatal infections in the setting of neutropenia within the first month of SG treatment; all 14 patients had multiple risk factors for which primary prophylaxis with G-CSF is recommended, but none received prophylactic G-CSF. The authors stated that stronger protocol recommendations regarding use of G-CSF as primary prophylaxis might have mitigated the risk of early fatal events in the SG group that are likely to have affected efficacy outcomes.[27] Further studies to optimize the use of SG in UC are needed.

In conclusion, avelumab plus SG as 1L switch-maintenance treatment improved PFS versus avelumab monotherapy in patients with la/mUC without progression following 1L PBC. Combining avelumab with anti-Trop-2

antibody—drug conjugates may be a promising strategy to improve patient outcomes in la/mUC.

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DISCLOSURE

JHC has received grants from Genentech; has received institutional research funding from Astellas Pharma, Daiichi Sankyo, Ikena Oncology, LOXO, Merck, Pfizer, and Seagen; has served in consulting or advisory roles for Gilead Sciences and Pfizer; and is a member of guideline committees for NCCN, AUA, and ASCO GU. MT has received honoraria from AstraZeneca, Bayer, GlaxoSmithKline, Ipsen, Janssen, Merck, MSD, and Pfizer; has served in a consulting or advisory role for Astellas Pharma, Bayer, Ipsen, Janssen, Merck, MSD, and Novartis; has received research funding from AstraZeneca, Bristol Myers Squibb, Daiichi Sankyo, Exelixis, Gilead Sciences, Janssen, Merck, MSD, and Pfizer; and has received travel and accommodation expenses from AstraZeneca, Ipsen, Janssen, MSD, and Pfizer. PMHC has served in consulting or advisory roles for AstraZeneca, Astellas Pharma, Bristol Myers Squibb/Ono Pharmaceutical, Ipsen, Merck, MSD, and Roche. MK has received honoraria from Astellas Pharma, Merck, Novartis, and Yuhan; and has served in a consulting or advisory role for Astellas Pharma, Bayer, Boryung, Bristol Myers Squibb/Ono Pharmaceutical, Eisai, Ipsen, Janssen, Merck, MSD, Pfizer, Roche, and Yuhan. GG has received honoraria from AstraZeneca, Bristol Myers Squibb, CEA Alliance, Ipsen, Janssen-Cilag, Leo Pharma, Medac Pharma, Merck, MSD, and Roche; and has served in consulting or advisory roles for Astellas Pharma, Bristol Myers Squibb, Bayer, Ipsen, Janssen-Cilag, Johnson & Johnson, Leo Pharma, Medac Pharma, Merck, MSD, Photocure, and QED Therapeutics. NB has served in consulting or advisory roles for AstraZeneca, Bristol Myers Squibb, Janssen Oncology, Merck, Novartis, Pfizer, Roche Canada, Sanofi, and Takeda; and has received institutional research funding from AstraZeneca. SHK has served in a consulting or advisory role for Guardant Health and Yuhan. JAAA has served in a consulting or advisory role for Astellas Pharma, AstraZeneca, Bayer, Bristol Myers Squibb, EUSA Pharma, Ipsen, Merck, MSD, Novartis, and Pfizer; has participated in a speakers' bureau for Merck and Pfizer; and has received institutional research funding from Bristol Myers Squibb. FZ has received honoraria from AstraZeneca, Daiichi Sankyo, Genesis Pharma, Gilead Sciences, Lilly, Merck, MSD, Novartis, Pfizer, and Roche; has served in consulting or advisory roles for AstraZeneca, Daiichi Sankyo, Genesis Pharma, Gilead Sciences, Lilly, Merck, MSD, Novartis, Pfizer, and Roche; and has received travel and accommodation expenses from AstraZeneca, Daiichi Sankyo, Genesis Pharma, Gilead Sciences, Lilly, Merck, MSD, Novartis, Pfizer, and Roche. MM has served in consulting or advisory roles for Astellas Pharma, Bristol Myers Squibb, Ipsen, Janssen, Merck, and MSD. CT has served in consulting or advisory roles for Bayer; has received institutional research funding from Bayer; and has other relationships with Fondation AP-HP (Inst). FF has received travel and accommodation expenses from Ipsen, Merck, and Teva Pharmaceuticals. A Schneider reports employment by Merck. KT reports employment by EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA, and stock or other ownership in Merck. NJ reports employment by Merck. PG (in the last 2 years) has served in consulting or advisory roles for AbbVie, Asieris Pharmaceuticals, Astellas Pharma, AstraZeneca, Bicycle Therapeutics, Bristol Myers Squibb, Daiichi Sankyo, Eli Lilly, Foundation Medicine, Fresenius Kabi, Gilead Sciences, ImmunityBio, Janssen, Merck, MSD, Pfizer, Replimune, Roche, and Strata Oncology; and has received institutional research funding from Acrivon Therapeutics, ALX Oncology, Bristol Myers Squibb, Genentech, Gilead Sciences, Merck, MSD, and QED Therapeutics. BPV has served in consulting or advisory roles for AAA, Astellas Pharma, AstraZeneca, Bayer, Bristol Myers Squibb, Ipsen, Janssen, Merck, MSD, Novartis, Pfizer, Recordati, and Roche; has received speaking honoraria from AAA, Almirall Pharma, Astellas Pharma, AstraZeneca, Bayer, Bristol Myers Squibb, Janssen, Merck, MSD, Novartis, Pfizer, and Roche; and has received travel and accommodation expenses from Astellas Pharma, Bristol Myers Squibb, Merck, MSD, Pfizer, and Roche. All other authors have declared no conflicts of interest.

DATA SHARING

Any requests for data by qualified scientific and medical researchers for legitimate research purposes will be subject to Merck's Data Sharing Policy. All requests should be submitted in writing to Merck's data-sharing portal (https://www.merckgroup.com/en/research/our-approach-to-research-and-development/healthcare/clinical-trials/commitment-responsible-data-sharing.html). When Merck has a co-research, co-development, or co-marketing or co-promotion agreement, or when the product has been out-licensed, the responsibility for disclosure might be dependent on the agreement between parties. Under these circumstances, Merck will endeavor to gain agreement to share data in response to requests.

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