Preliminary results from AVENANCE, an ongoing, noninterventional real-world, ambispective study of avelumab first-line maintenance treatment in patients with locally advanced or metastatic urothelial carcinoma

P. Barthélémy,[1] C. Thibault,[2] E. Voog,[3] J. C. Eymard,[4] A. Ravaud,[5] A. Fléchon,[6] C. Abraham,[7] W. Hilgers,[8] S. Le Moulec,[9] M. Chasseray,[10] D. Pouessel,[11] E. Amela,[12] V. Lorgis,[13] E. Nicolas,[14,15] E. Kazan,[16] G. Denechere,[17] M.-N. Solbes,[18] P. Lambert,[17] Y. Loriot[19]

[1]Medical Oncology, Institut de Cancérologie Strasbourg Europe, Strasbourg, France; [2]Department of Medical Oncology, Hôpital Européen Georges Pompidou, Institut du Cancer Paris CARPEM, AP-HP Centre, Université de Paris Cité, Paris, France; [3]LC Groupe/Clinique Victor Hugo, Le Mans, France; [4]Department of Medical Oncology, Institut de Cancérologie Jean-Godinot, Reims, France; [5]Department of Medical Oncology, Bordeaux University Hospital, Bordeaux University, Bordeaux, France; [6]Department of Medical Oncology, Centre Léon Bérard, Lyon, France; [7]Medical Oncology, Foch Hospital, Suresnes, France; [8]Department of Medical Oncology, Avignon-Provence Cancer Institute, Avignon, France; [9]Medical Oncology, Groupe de Radiothérapie et d'Oncologie des Pyrénées, Clinique Marzet, Pau, France; [10]Centre Finistérien de Radiothérapie et d'Oncologie- Clinique Pasteur, Brest, France; [11]Medical Oncology Department, Institut Claudius Régaud–IUCT Oncopole, Toulouse, France; [12]Centre de Cancérologie Bourgogne, Hôpital Privé Le Bois, Lille, France; [13]Medical Oncology, Institut de Cancérologie de Bourgogne, Dijon, France; [14]Department of Medical Oncology, University Hospital of Nîmes, Nîmes, France; [15]Institute Desbrest of Epidemiology and Public Health, Research Unit INSERM, University of Montpellier, Montpellier, France; [16]Department of Medical Oncology, Ramsay Health Group–Private Hospital Villeneuve d'Ascq, Villeneuve-d'Ascq, France; [17]Pfizer Oncology, Paris, France; [18]Merck Santé S.A.S., Lyon, France, an affiliate of Merck KGaA; [19]Department of Cancer Medicine, DITEP, Gustave Roussy, Université Paris-Saclay, Villejuif, France

SCOPE

- This preliminary analysis reports efficacy and safety outcomes from AVENANCE, an ongoing, real-world, ambispective (retrospective and prospective) study evaluating avelumab first-line (1L) maintenance treatment in patients with locally advanced or metastatic urothelial carcinoma (Ia/mUC) in France

CONCLUSIONS

- These first real-world data for avelumab 1L maintenance in patients with Ia/mUC from the ongoing AVENANCE study support the findings of the JAVELIN Bladder 100 trial[1,2]
- These early results (median follow-up, 13.5 months) confirm the clinical activity and acceptable safety profile of avelumab in a heterogeneous population outside of a clinical trial setting
  - The 12-month overall survival (OS) rate was 66.9%
  - Median progression-free survival (PFS) from the start of avelumab treatment was 5.7 months (95% CI, 5.0-7.9 months) comparable to results from the JAVELIN Bladder 100 trial[2]
  - The safety profile was consistent with that observed in other studies of avelumab monotherapy, and no new safety concerns were identified[3]
- These results further support the recommendation of avelumab 1L maintenance as standard of care for patients with Ia/mUC that has not progressed with 1L platinum-based chemotherapy

Correspondence: **Philippe Barthélémy, p.barthelemy@icans.eu**

GET PLAIN LANGUAGE SUMMARY

Please scan this quick response (QR) code with your smartphone app to view a plain language summary of the accepted scientific abstract.

BACKGROUND

- In the phase 3 JAVELIN Bladder 100 trial (NCT02603432), avelumab 1L maintenance therapy + best supportive care (BSC) significantly prolonged OS vs BSC alone in patients with Ia/mUC that had not progressed after 1L platinum-based chemotherapy[1,2]
  - Results from this trial led to the approval of avelumab 1L maintenance in various countries worldwide, and it is now recommended as standard of care in international treatment guidelines, based on level 1 evidence[4-7]
- Longer-term follow-up from JAVELIN Bladder 100 (≥2 years in all patients) continued to show prolonged OS and investigator-assessed PFS in patients treated with avelumab 1L maintenance + BSC vs BSC alone[2]
  - Median OS was 23.8 vs 15.0 months, respectively (hazard ratio [HR], 0.76 [95% CI, 0.631-0.915]; 2-sided p=0.0036), and 2-year OS rates were 49.8% vs 38.4%
  - Median PFS was 5.5 vs 2.1 months, respectively (HR, 0.54 [95% CI, 0.457-0.645]; 2-sided p<0.0001), and 2-year PFS rates were 23.4% vs 7.1%
  - Avelumab 1L maintenance also demonstrated an acceptable long-term safety profile
- AVENANCE is an ongoing, real-world study investigating efficacy and safety in patients with Ia/mUC treated with avelumab 1L maintenance in France

METHODS

- AVENANCE (NCT04822350) is a multicenter, ambispective, noninterventional study of patients with Ia/mUC treated with avelumab 1L maintenance in France
- In this ongoing study, eligible patients have previous, ongoing, or planned avelumab 1L maintenance treatment for Ia/mUC that did not progress after 1L platinum-based chemotherapy (ie, ongoing complete response, partial response, or stable disease)
  - Data collection started on 13 July 2021
- The primary endpoint is OS from start of avelumab treatment
- Secondary endpoints include OS from start of 1L chemotherapy, PFS, duration of treatment, and safety
- In this preliminary analysis, patients who started avelumab ≥6 months prior to data cutoff (31 January 2022) were analyzed
  - Efficacy and safety were analyzed in patients who had received ≥1 dose of avelumab

RESULTS

- This analysis included 267 patients (of 500 planned); baseline characteristics are detailed in **Table 1**
- At data cutoff (31 January 2022), median follow-up since avelumab initiation (by reverse Kaplan-Meier estimation) was 13.5 months (95% CI, 12.8-14.7 months)
- Treatment was ongoing in 92 patients (34.5%)
  - Among the 174/175 patients for whom the reason for discontinuing avelumab was reported, the most common reason was disease progression (n=138 [79.3%])

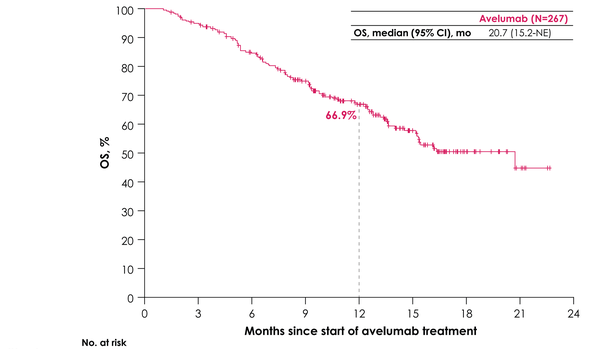
Table 1. Baseline characteristics

	N=267
Age, median (interquartile range), years	73.1 (66.7-77.9)
Sex, n (%)	
Male	217 (81.3)
Female	50 (18.7)
Location of primary tumor, n (%)	
Bladder	197 (74.1)
Upper urinary tract	52 (19.5)
Urethra	17 (6.4)
Missing data	1
Tumor histology, n (%)	
Pure urothelial carcinoma	243 (93.1)
Urothelial carcinoma with variant (eg, squamous cell, adenocarcinoma, neuroendocrine)	12 (4.6)
Squamous cell carcinoma	5 (1.9)
Other	1 (0.4)
Missing data	6
Tumor status at start of 1L chemotherapy, n (%)	
Locally advanced	26 (9.8)
Metastatic	238 (90.2)
Missing data	3
ECOG PS at start of 1L chemotherapy, n (%)	
0	74 (35.9)
1	103 (50.0)
2	26 (12.6)
3	3 (1.5)
Missing data	61
Type of 1L chemotherapy, n (%)	
Carboplatin + gemcitabine	152 (57.6)
Cisplatin + gemcitabine	84 (31.8)
Other (including MVAC)	28 (10.6)
Missing data	3
No. of 1L chemotherapy cycles, median (range)	5 (1-10)
Response to last chemotherapy, n (%)	
Complete response	57 (21.8)
Partial response	146 (55.9)
Stable disease	53 (20.3)
Disease progression	1 (0.4)
Non-evaluable	4 (1.5)
Missing data	6
Presence of visceral metastasis at start of 1L chemotherapy, n (%)	**n=238**
No	41 (17.3)
Yes	196 (82.7)
Missing data	1
Metastasis sites at start of 1L chemotherapy, n (%)	**n=196**
Lymph nodes	114 (58.2)
Liver	35 (17.9)
Lung	57 (29.1)
Bone	71 (36.2)
Brain	1 (0.5)
Other	38 (19.4)

Percentages reported were calculated using the denominator of patients with available data for each characteristic.
1L, first line; **MVAC**, methotrexate, vinblastine, doxorubicin, and cisplatin.

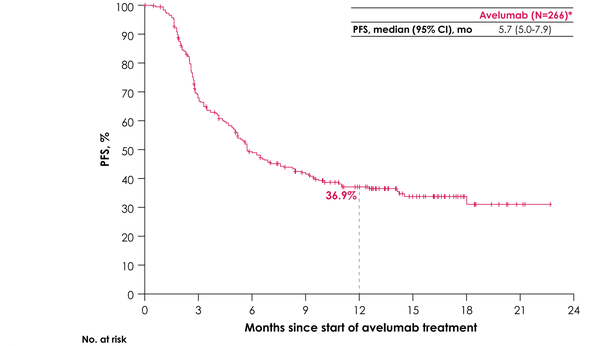
- The 12-month OS rate from start of avelumab was 66.9% (95% CI, 60.5%-72.5%) (**Figure 1**) and from start of 1L chemotherapy was 79.1% (95% CI, 73.5%-83.6%; n=262 evaluable)
- Median PFS from start of avelumab was 5.7 months (95% CI, 5.0-7.9 months), and the 12-month PFS rate was 36.9% (95% CI, 30.8%-43.1%) (**Figure 2**)
- Median duration of avelumab treatment was 5.8 months (95% CI, 4.9-7.4 months)

Figure 1. OS from start of avelumab treatment



NE, not estimable; **OS**, overall survival.

Figure 2. PFS from start of avelumab treatment



PFS, progression-free survival.
*1 patient has been excluded from this analysis because of an incorrect date of first injection.

- 112 patients (41.9%) reported receiving subsequent anticancer treatment (including second-line and later) (**Table 2**)
- Safety data are summarized in **Table 3**
  - Treatment-emergent adverse events (TEAEs) occurred in 170 patients (63.7%), with serious TEAEs in 75 patients (28.1%)
  - The most common TEAEs (in >5% of patients) were asthenia (n=35 [13.1%]) and pruritus (n=29 [10.9%])

Table 2. Subsequent treatment (second-line and later)

Subsequent treatment, n (%)	n=112
Non–platinum-based chemotherapy	71 (63.4)
Paclitaxel monotherapy	59 (52.7)
Paclitaxel + gemcitabine	4 (3.6)
Gemcitabine monotherapy	5 (4.5)
Docetaxel monotherapy	1 (0.9)
Vinflunine monotherapy	2 (1.8)
Platinum-based chemotherapy	24 (21.4)
Carboplatin + gemcitabine	12 (10.7)
Carboplatin monotherapy	4 (3.6)
Carboplatin + paclitaxel	4 (3.6)
Carboplatin + etoposide	1 (0.9)
Cisplatin + paclitaxel	1 (0.9)
Cisplatin + gemcitabine	1 (0.9)
MVAC	1 (0.9)
Enfortumab vedotin*	12 (10.7)
Sacituzumab govitecan*	3 (2.7)
Pembrolizumab	2 (1.8)

MVAC, methotrexate, vinblastine, doxorubicin, and cisplatin.
*Not approved for use in the EU at the time of study.

Table 3. Summary of AEs

Events, n (%)	N=267
TEAE	170 (63.7)
Serious TEAE	75 (28.1)
TEAE leading to temporary/permanent discontinuation	72 (27.0)
TEAE leading to death	31 (11.6)
TRAE	102 (38.2)
Serious TRAE	14 (5.2)
TRAE leading to temporary/permanent discontinuation	26 (9.7)
TRAE leading to death	1 (0.4)

AE, adverse event; **TEAE**, treatment-emergent adverse event; **TRAE**, treatment-related adverse event.

REFERENCES 1. Powles T, et al. N Engl J Med. 2020;383(13):1218-30. **2.** Powles T, et al. J Clin Oncol. 2022;40(6 Suppl). Abstract 487. **3.** Kelly K, et al. Cancer. 2018;124(9):2010-17. **4.** NCCN Clinical Practice Guidelines. Bladder Cancer. V2.2022. **5.** Powles T, et al. Ann Oncol. 2022;33(3):244-58. **6.** Cathomas R, et al. Eur Urol. 2022;81(1):95-103. **7.** Japanese Urological Association. Supplemental to Clinical Practice Guidelines for Bladder Cancer (2019). Accessed August 15, 2022. https://www.urol.or.jp/lib/files/other/guideline/39_bladder_cancer_2019_rev2021_info.pdf.
DISCLOSURES P. Barthélémy has served in advisory roles for Amgen, Astellas, Bayer, Bristol Myers Squibb, Ipsen, Janssen Cilag, Merck, MSD, Novartis, and Pfizer and reports speaker services for AstraZeneca and Seagen. **C. Thibault** has received institutional research funding from AstraZeneca and Sanofi; has served in advisory roles for AstraZeneca, Bristol Myers Squibb, Ipsen, Merck, MSD, and Pfizer; and reports speaker services for Astellas, AstraZeneca, Bristol Myers Squibb, Ipsen, Janssen, MSD, and Sanofi. **E. Voog** has nothing to declare. **J. C. Eymard** has received personal and institutional research funding from Bristol Myers Squibb, Ipsen, and Pfizer and has served in advisory roles for Astellas, Ipsen, Janssen, and Sanofi. **A. Ravaud** has received institutional research funding from Ipsen, Merck, and Pfizer; has served in advisory roles for AstraZeneca, Bristol Myers Squibb, Eisai, Ipsen, Merck, and Pfizer; and has received travel and accommodation expenses from AstraZeneca, Bristol Myers Squibb, Eisai, Ipsen, Merck, and Pfizer. **A. Fléchon** has received honoraria from Gilead Sciences, Janssen, Merck, MSD, and Pfizer. **C. Abraham** has nothing to declare. **W. Hilgers** has nothing to declare. **S. Le Moulec** has nothing to declare. **M. Chasseray** has nothing to declare. **D. Pouessel** has received institutional research funding from MSD; has served in advisory roles for Astellas, AstraZeneca, Merck, MSD, and Pfizer; reports speaker services for Astellas, AstraZeneca, Bristol Myers Squibb, Ipsen, Janssen, MSD, and Pfizer; and has received travel and accommodation expenses from MSD and Pfizer. **E. Amela** has nothing to declare. **V. Lorgis** has nothing to declare. **E. Nicolas** has served in an advisory role for Merck. **E. Kazan** has nothing to declare. **G. Denechere** reports employment with Pfizer. **M.-N. Solbes** reports employment with Merck Santé S.A.S., Lyon, France, an affiliate of Merck KGaA. **P. Lambert** reports employment with Pfizer. **Y. Loriot** has served in consulting or advisory roles for Astellas, AstraZeneca, Bristol Myers Squibb, Gilead Sciences, Janssen, Merck, MSD, Pfizer, Roche, Seagen, and Taiho; has served as a steering committee member for Astellas, Basilea, Gilead Sciences/Immunomedics, Janssen, MSD, and Taiho; has served as a clinical principal investigator for Astellas, AstraZeneca, Bristol Myers Squibb, Exelixis, Gilead Sciences, Incyte, Janssen, Merck, MSD, and Pfizer; has served as a coordinating principal investigator for Janssen; and has received institutional research funding from Celsius, Janssen, MSD, Roche, and Sanofi. **ACKNOWLEDGMENTS** The authors thank the patients and their families, investigators, co-investigators, and the study teams at each of the participating centers. This study was sponsored by Pfizer as part of an alliance between Pfizer and Merck (CrossRef Funder ID: 10.13039/100009945). Medical writing support was provided by Eleanor Bishop of ClinicalThinking and was funded by Pfizer and Merck.

Poster No. 1757P. Presented at the ESMO Congress 2022, 9-13 September 2022; Paris, France; Hybrid.