Avelumab

RWE Field Deck

For Medical use with healthcare decision makers only.

For additional resources, please visit our US Medical Resources Website Oncology page at https://medical.emdserono.com/en_US/medinfo/therapeutic-areas/oncology.html

Important Notices

- Avelumab has been approved by the FDA and is under investigation for the treatment of various diseases. Efficacy and safety of avelumab are still under investigation for various indications. Regulatory approval is dependent on the completion of the study programs and review by the FDA. Clinical trial information is available at www.clinicaltrials.gov.
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FDA-Approved Indications

First-line maintenance treatment of urothelial carcinoma

BAVENCIO® (avelumab) is indicated for the maintenance treatment of patients with locally advanced or metastatic urothelial carcinoma (UC) that has not progressed with first-line platinum-containing chemotherapy.

Previously-treated urothelial carcinoma

BAVENCIO® is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma (UC) who:

- have disease progression during or following platinum-containing chemotherapy
- have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy

Please see the full BAVENCIO® (avelumab) US Prescribing Information available at https://www.emdserono.com/us-en/pi/bavencio-pi.pdf

Important Safety Information

Avelumab can cause **severe and fatal immune-mediated adverse reactions** in any organ system or tissue and at any time after starting treatment with a PD-1/PD-L1 blocking antibody, including after discontinuation of treatment.

Early identification and management of immune-mediated adverse reactions are essential to ensure safe use of PD-1/PD-L1 blocking antibodies. Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.

No dose reduction for avelumab is recommended. For immune-mediated adverse reactions, withhold or permanently discontinue avelumab depending on severity. In general, withhold avelumab for severe (Grade 3) immune-mediated adverse reactions. Permanently discontinue avelumab for life-threatening (Grade 4) immune-mediated adverse reactions, recurrent severe (Grade 3) immune-mediated reactions that require systemic immunosuppressive treatment, or an inability to reduce corticosteroid dose to 10 mg or less of prednisone or equivalent per day within 12 weeks of initiating corticosteroids. In general, if avelumab requires interruption or discontinuation, administer systemic corticosteroid therapy (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroid therapy. Toxicity management guidelines for adverse reactions that do not necessarily require systemic corticosteroids (eg, endocrinopathies and dermatologic reactions) are discussed in subsequent sections.

Avelumab can cause **immune-mediated pneumonitis**. Withhold avelumab for Grade 2, and permanently discontinue for Grade 3 or Grade 4 pneumonitis. Immune-mediated pneumonitis occurred in 1.1% (21/1854) of patients, including fatal (0.1%), Grade 4 (0.1%), Grade 3 (0.3%), and Grade 2 (0.6%) adverse reactions. Systemic corticosteroids were required in all (21/21) patients with pneumonitis.

Avelumab can cause **immune-mediated colitis**. The primary component of immune-mediated colitis consisted of diarrhea. Cytomegalovirus infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies. Withhold avelumab for Grade 2 or Grade 3, and permanently discontinue for Grade 4 colitis. Immune-mediated colitis occurred in 1.5% (27/1854) of patients, including Grade 3 (0.4%) and Grade 2 (0.8%) adverse reactions. Systemic corticosteroids were required in all (27/27) patients with colitis.

Avelumab can cause **hepatotoxicity and immune-mediated hepatitis**. Withhold or permanently discontinue avelumab based on tumor involvement of the liver and severity of aspartate aminotransferase (AST), alanine aminotransferase (ALT), or total bilirubin elevation. Immune-mediated hepatitis occurred with avelumab as a single agent in 1.1% (20/1854) of patients, including fatal (0.1%), Grade 3 (0.8%), and Grade 2 (0.2%) adverse reactions. Systemic corticosteroids were required in all (20/20) patients with hepatitis.

Avelumab can cause primary or secondary **immune-mediated adrenal insufficiency**. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement, as clinically indicated. Withhold avelumab for Grade 3 or Grade 4 endocrinopathies until clinically stable or permanently discontinue depending on severity. Immune-mediated adrenal insufficiency occurred in 0.6% (11/1854) of patients, including Grade 3 (0.1%) and Grade 2 (0.4%) adverse reactions. Systemic corticosteroids were required in all (11/11) patients with adrenal insufficiency.

Avelumab can cause **immune-mediated hypophysitis**. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field defects. Hypophysitis can cause hypopituitarism. Initiate hormone replacement, as clinically indicated. Withhold avelumab for Grade 3 or Grade 4 endocrinopathies until clinically stable or permanently discontinue depending on severity. Immune-mediated pituitary disorders occurred in 0.1% (1/1854) of patients, which was a Grade 2 (0.1%) adverse reaction.

Avelumab can cause **immune-mediated thyroid disorders**. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement for hypothyroidism or institute medical management of hyperthyroidism, as clinically indicated. Withhold avelumab for Grade 3 or Grade 4 endocrinopathies until clinically stable or permanently discontinue depending on severity. Thyroiditis occurred in 0.2% (4/1854) of patients, including Grade 2 (0.1%) adverse reactions. Hyperthyroidism occurred in 0.4% (8/1854) of patients, including Grade 2 (0.3%) adverse reactions. Systemic corticosteroids were required in 25% (2/8) of patients with hyperthyroidism. Hypothyroidism occurred in 5% (97/1854) of patients, including Grade 3 (0.2%) and Grade 2 (3.6%) adverse reactions. Systemic corticosteroids were required in 6% (6/97) of patients with hypothyroidism.

Avelumab can cause **immune-mediated type I diabetes mellitus**, which can present with diabetic ketoacidosis. Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Withhold avelumab for Grade 3 or Grade 4 endocrinopathies until clinically stable or permanently discontinue depending on severity. Immune-mediated type I diabetes mellitus occurred in 0.2% (3/1854) of patients, including Grade 3 (0.2%) adverse reactions.

Please see the full BAVENCIO® (avelumab) US Prescribing Information available at https://www.emdserono.com/us-en/pi/bavencio-pi.pdf

Important Safety Information, continued

Avelumab can cause **immune-mediated nephritis with renal dysfunction**. Withhold avelumab for Grade 2 or Grade 3, and permanently discontinue for Grade 4 increased blood creatinine. Immune-mediated nephritis with renal dysfunction occurred in 0.1% (2/1854) of patients, including Grade 3 (0.1%) and Grade 2 (0.1%) adverse reactions. Systemic corticosteroids were required all (2/2) patients with nephritis with renal dysfunction.

Avelumab can cause **immune-mediated dermatologic adverse reactions**, including rash or dermatitis. Exfoliative dermatitis including Stevens Johnson Syndrome (SJS), drug rash with eosinophilia and systemic symptoms (DRESS), and toxic epidermal necrolysis (TEN), has occurred with PD-1/PD-L1 blocking antibodies. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes. Withhold avelumab for suspected and permanently discontinue for confirmed SJS, TEN, or DRESS. Immune-mediated dermatologic adverse reactions occurred in 6% (108/1854) of patients, including Grade 3 (0.1%) and Grade 2 (1.9%) adverse reactions. Systemic corticosteroids were required in 25% (27/108) of patients with dermatologic adverse reactions.

Avelumab can result in **other immune-mediated adverse reactions**. Other clinically significant immune-mediated adverse reactions occurred at an incidence of <1% in patients who received avelumab or were reported with the use of other PD-1/PD-L1 blocking antibodies. For **myocarditis**, permanently discontinue avelumab for Grade 2, Grade 3, or Grade 4. For **neurological toxicities**, withhold avelumab for Grade 2 and permanently discontinue for Grade 3 or Grade 4.

Avelumab can cause severe or life-threatening **infusion-related reactions**. Premedicate patients with an antihistamine and acetaminophen prior to the first 4 infusions and for subsequent infusions based upon clinical judgment and presence/severity of prior infusion reactions. Monitor patients for signs and symptoms of infusion-related reactions, including pyrexia, chills, flushing, hypotension, dyspnea, wheezing, back pain, abdominal pain, and urticaria. Interrupt or slow the rate of infusion for Grade 1 or Grade 2 infusion-related reactions. Permanently discontinue avelumab for Grade 3 or Grade 4 infusion-related reactions. Infusion-related reactions occurred in 26% of patients, including three (0.2%) Grade 4 and ten (0.5%) Grade 3 infusion-related reactions. Eleven (85%) of the 13 patients with Grade ≥3 reactions were treated with intravenous corticosteroids.

Fatal and other serious **complications of allogeneic hematopoietic stem cell transplantation (HSCT)** can occur in patients who receive HSCT before or after being treated with a PD-1/PD-L1 blocking antibody. Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/PD-L1 blocking antibody prior to or after an allogeneic HSCT.

Avelumab can cause **fetal harm** when administered to a pregnant woman. Advise patients of the potential risk to a fetus including the risk of fetal death. Advise females of childbearing potential to use effective contraception during treatment with avelumab and for at least 1 month after the last dose of avelumab. It is not known whether avelumab is excreted in human milk. Advise a lactating woman **not to breastfeed** during treatment and for at least 1 month after the last dose of avelumab due to the potential for serious adverse reactions in breastfed infants.

A **fatal adverse reaction** (sepsis) occurred in one (0.3%) patient with **locally advanced or metastatic urothelial carcinoma (UC)** receiving avelumab + best supportive care (BSC) as first-line maintenance treatment. In patients with previously treated locally advanced or metastatic UC, fourteen patients (6%) who were treated with avelumab experienced either pneumonitis, respiratory failure, sepsis/urosepsis, cerebrovascular accident, or gastrointestinal adverse events, which led to death.

The most common adverse reactions (all grades, ≥20%) in patients with **locally advanced or metastatic UC** receiving avelumab + BSC (vs BSC alone) as first-line maintenance treatment were fatigue (35% vs 13%), musculoskeletal pain (24% vs 15%), urinary tract infection (20% vs 11%), and rash (20% vs 2.3%). In patients with previously treated locally advanced or metastatic UC receiving avelumab, the most common adverse reactions (all grades, ≥20%) were fatigue, infusion-related reaction, musculoskeletal pain, nausea, decreased appetite, and urinary tract infection.

Selected laboratory abnormalities worsening from baseline (all grades, ≥20%) in patients with **locally advanced or metastatic UC** receiving avelumab + BSC(vs BSC alone) as first-line maintenance treatment were blood triglycerides increased (34% vs 28%), alkaline phosphatase increased (30% vs 20%), blood sodium decreased (28% vs 20%), lipase increased (25% vs 16%), aspartate aminotransferase (AST) increased (24% vs 12%), blood potassium increased (24% vs 16%), alanine aminotransferase (ALT) increased (24% vs 12%), blood cholesterol increased (22% vs 16%), serum amylase increased (21% vs 12%), hemoglobin decreased (28% vs 18%), and white blood cell decreased (20% vs 10%).

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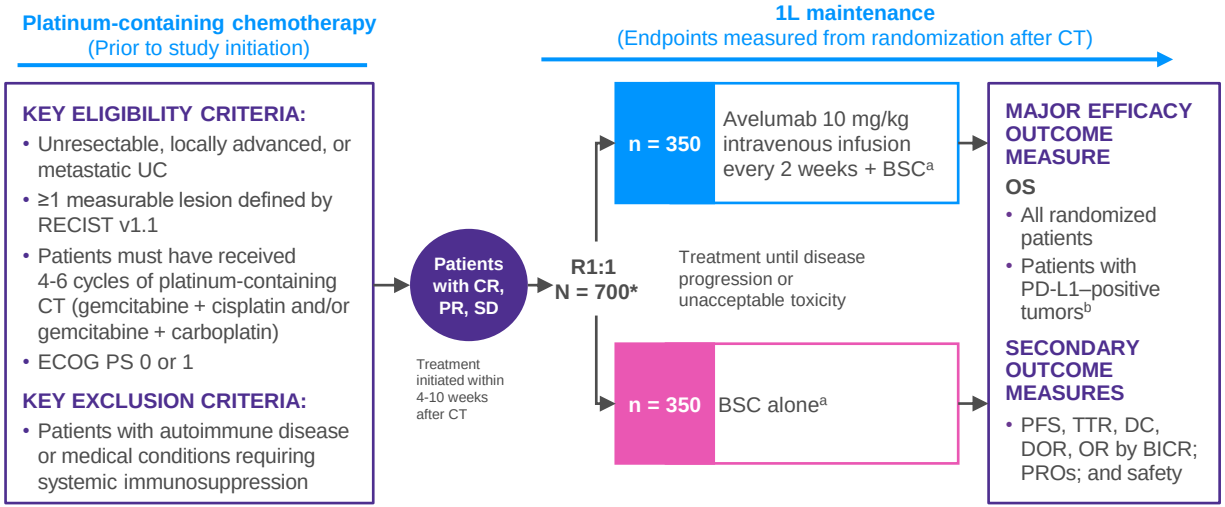
JAVELIN Bladder 100

JAVELIN Bladder 100 (NCT02603432)

Phase III, randomized, open-label trial investigating 1L maintenance with avelumab in patients with locally advanced or metastatic UC that did not progress with platinum-containing CT[1,2]

JAVELIN Bladder 100 regimen with avelumab as 1L maintenance treatment[1,2]



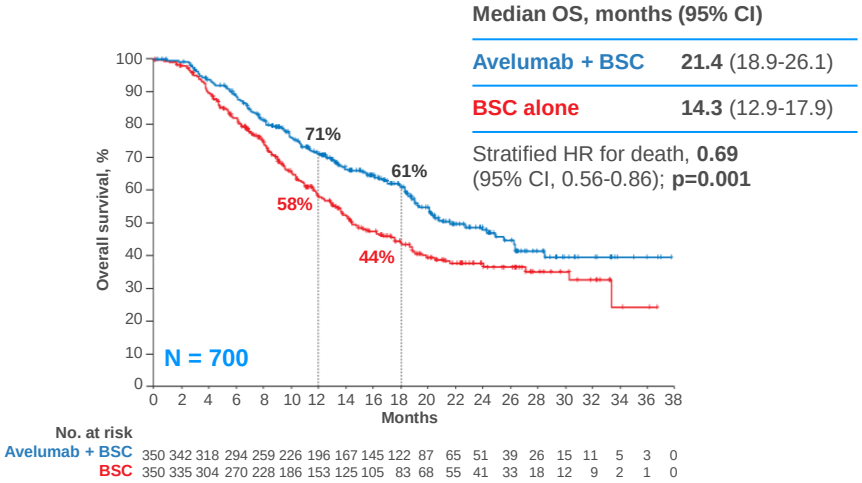
- Stratified by best response to CT (CR/PR vs SD per RECIST v1.1) and site of metastasis (visceral vs non-visceral [including bone metastasis]) assessed at the time of initiating 1L platinum-containing chemotherapy[1,2]
- Administration of avelumab was permitted beyond RECIST-defined disease progression if the patient was clinically stable and considered to be deriving clinical benefit by the investigator[2]
- Assessment of tumor status was performed at baseline, 8 weeks after randomization, then every 8 weeks up to 12 months after randomization, and every 12 weeks thereafter until documented confirmed disease progression based on BICR assessment per RECIST v1.1[2]

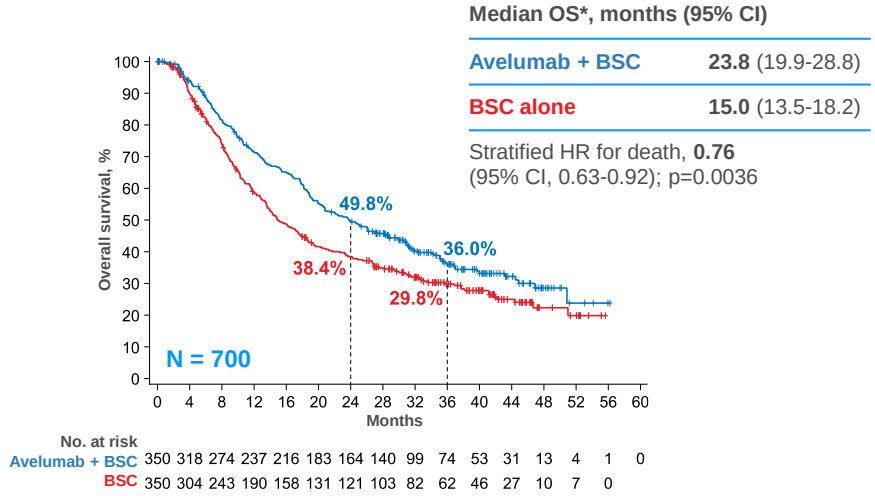
*1005 patients were screened with 305 deemed ineligible at screening; 267 screen failure, 21 no longer meet eligibility criteria, 11 withdrew consent, 3 deaths, and 3 other reasons[3]
[a] BSC was administered as deemed appropriate by the treating physician, and could include treatment with antibiotics, nutritional support, and other patient management approaches with palliative intent (excludes systemic antitumor therapy); [b] PD-L1 expression was assessed in tumor samples using the VENTANA PD-L1 (SP263) assay.[1]

1L, first-line; BICR, blinded independent central review; BSC, best supportive care; CR, complete response; CT, chemotherapy; DC, disease control; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; OR, overall response; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PR, partial response; PROs, patient-reported outcomes; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; TTR, time to response; UC, urothelial cancer.

1. Powles T, et al. N Engl J Med. 2020;383(13):1218-1230; 2. BAVENCIO® (avelumab). Prescribing information. Rockland, MA: EMD Serono, Inc. https://www.emdserono.com/us-en/pi/bavencio-pi.pdf; 3. Powles T, et al. N Engl J Med. 2020;383(13):1218-1230 (suppl).

OS in all Randomized Patients[1-3]





Median follow-up: avelumab + BSC: 19.6 months (95% CI, 18.0-20.6); BSC alone: 19.2 months (95% CI, 17.4-21.6)[3]

Median follow-up: avelumab + BSC: 38.0 months (95% CI, 36.1-40.5); BSC alone: 39.6 months (95% CI, 36.2-41.7)[3]

In the primary analysis, patients receiving avelumab + BSC had a **31% reduction** in the risk of death vs. BSC alone

An updated OS analysis was conducted when 452 deaths were observed. The follow-up OS analysis was prespecified, but no formal hypothesis testing was performed given that the OS endpoint was met in the initial interim analysis

A pre-planned IA occurred with a data cut-off of October 21, 2019. The IA was considered as the primary analysis of the trial since the primary endpoint was met[3]; OS was measured post-randomization (after chemotherapy)[3]; the OS analysis crossed the prespecified efficacy boundary based on the alpha-spending function (p<0.0053).[2]

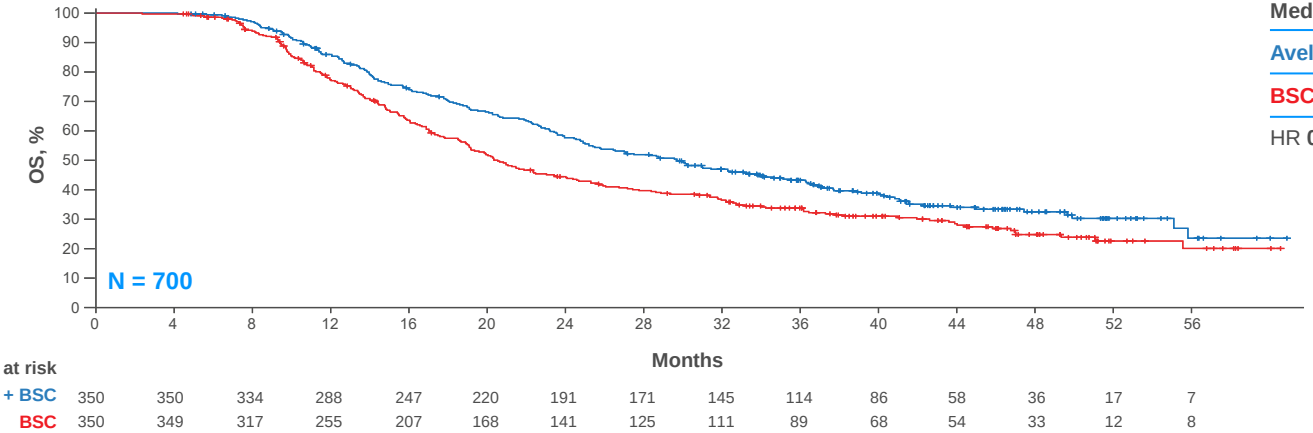
* Follow-up OS analysis is investigator-assessed.[1]

BSC, best supportive care; CI, confidence interval; HR, hazard ratio; IA, interim analysis; OS, overall survival.

1. Powles T, et al. Poster E7. Presented at: ASCO GU Symposium; February 17-19, 2022; San Fransisco, CA; 2. Powles T, et al. [illegible] Data on File, B9991001; August 2, 2021.

OS From Start of 1L CT in All Randomized Patients[1]

Post hoc analysis



No. at risk															
Avelumab + BSC	350	350	334	288	247	220	191	171	145	114	86	58	36	17	7
BSC	350	349	317	255	207	168	141	125	111	89	68	54	33	12	8

Median OS, months (95% CI)	
Avelumab + BSC	**29.7** (25.2-34.0)
BSC alone	**20.5** (19.0-23.5)

HR **0.77** (95% CI, 0.64-0.92)

In the overall population, median OS measured from the start of 1L chemotherapy was 29.7 months (95% CI, 25.2-34.0) in the avelumab + BSC arm and 20.5 months (95% CI,19.0-23.5) in the BSC alone arm (HR, 0.77 [95% CI, 0.636-0.921])

Limitations

- This is an exploratory, post hoc analysis of OS data, calculated from the start of chemotherapy (based on investigator-reported data) to death
- This analysis only includes patients who did not progress on 1L platinum-containing chemotherapy and subsequently enrolled in the JAVELIN Bladder 100 trial
- Safety data are not available pre-randomization
- This analysis is inclusive of platinum-containing chemotherapy,* treatment-free interval,† randomized study treatment with avelumab + BSC or BSC alone, and subsequent therapy
- Therefore, no conclusions can be drawn from this OS analysis

* Patients were treated with platinum-containing chemotherapy for 4 to 6 cycles.[2] †The treatment-free interval was 4 to 10 weeks, per trial protocol.[2]

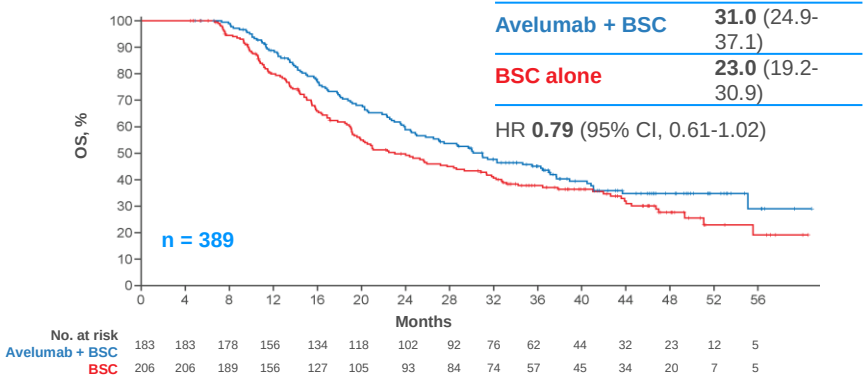
1L, first-line; BSC, best supportive care; CI, confidence interval; CT, chemotherapy; HR, hazard ratio; OS, overall survival.

1. Sridhar SS, et al. Poster 508. Presented at: ASCO GU Symposium; February 16-18, 2023; San Fransisco, CA; 2. Powles T, et al. N Engl J Med. 2020;383(13):1218-1230.

OS From Start of 1L CT by 1L CT Regimen[1]

Post hoc analysis

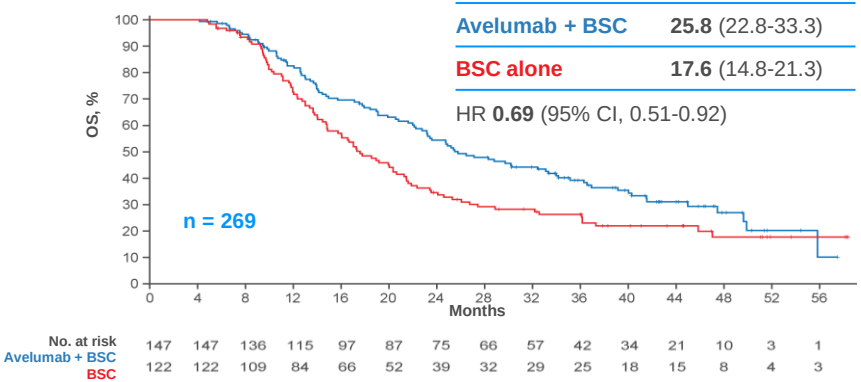
Cisplatin + gemcitabine



Median OS, months (95% CI)	
Avelumab + BSC	**31.0** (24.9-37.1)
BSC alone	**23.0** (19.2-30.9)

HR **0.79** (95% CI, 0.61-1.02)

Carboplatin + gemcitabine



Median OS, months (95% CI)	
Avelumab + BSC	**25.8** (22.8-33.3)
BSC alone	**17.6** (14.8-21.3)

HR **0.69** (95% CI, 0.51-0.92)

OS measured from the start of 1L chemotherapy was longer with avelumab + BSC vs BSC alone, irrespective of 1L chemotherapy regimen received

Limitations

- This is an exploratory, post hoc analysis of OS data, inclusive of platinum-containing
- chemotherapy (4-6 cycles), treatment-free interval (4-10 weeks, per trial protocol), randomized study treatment with avelumab + BSC or BSC alone, and subsequent therapy.
- This analysis only includes patients who did not progress on first-line platinum-containing chemotherapy and subsequently enrolled in the JAVELIN Bladder 100 trial.
- Safety data are not available pre-randomization.
- No conclusions can be drawn from this OS analysis.

Limitations

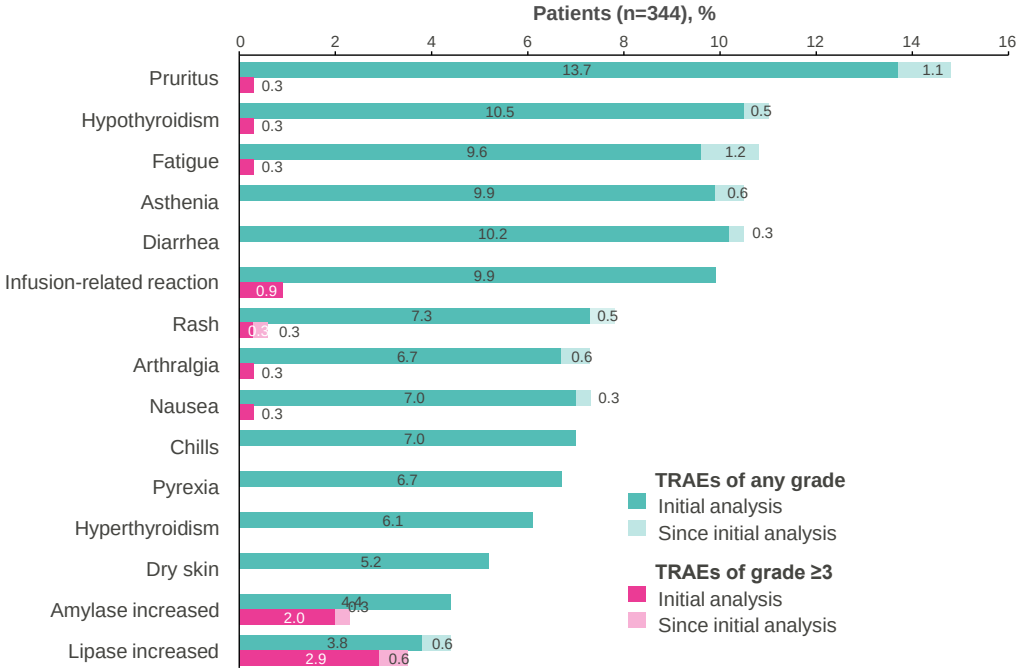
- Small patient numbers can be a Limitations of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup
- The results show the variability of the observed treatment effect among several subgroups
- No adjustments were made for multiple comparisons in the subgroup analyses

1L, first-line; BSC, best supportive care; CI, confidence interval; CT, chemotherapy; HR, hazard ratio; OS, overall survival.

1. Sridhar SS, et al. Poster 508. Presented at: ASCO GU Symposium; February 16-18, 2023; San Fransisco, CA;

JAVELIN Bladder 100 Long-term Safety[1]

Most common TRAEs observed with avelumab + BSC in initial analysis and ≥2-year follow-up



	Onset after ≥12 months of treatment (n=118)	Onset at any time (n=344)
TRAE of any grade, %	50.0	78.2
Grade ≥3 TRAE, %	11.9	19.5
TRAE leading to discontinuation, %	10.2	11.6
Any-grade irAE, %	22.9	32.3

BSC, best supportive care; irAE, immune-related adverse event; TRAE, treatment-related adverse event.

1. Powles T, et al. J Clin Oncol. 2023;41:3486–92(Suppl).

Avelumab 1L maintenance treatment can be tailored according to practical considerations and patient needs[1-3]

Premaintenance factor	HR (unstratified) for OS with avelumab + BSC vs BSC alone in key subgroups
1L chemotherapy regimen	Cisplatin + gemcitabine: 0.78 (95% CI 0.61-1.01)* Carboplatin + gemcitabine: 0.70 (95% CI 0.52-0.93)*
Duration of 1L chemotherapy	4 cycles: 0.69 (95% CI 0.48-1.00)† 6 cycles: 0.66 (95% CI 0.47-0.92)†
Response to 1L chemotherapy	CR: 0.72 (95% CI 0.482-1.08)* PR: 0.70 (95% CI 0.54-0.91)* SD: 0.84 (95% CI 0.60-1.19)*
Interval from end of chemotherapy to start of maintenance	4 to <6 weeks: 0.76 (95% CI 0.55-1.06)† 6 to <8 weeks: 0.64 (95% CI 0.40-1.02)† 8 to 10 weeks: 0.70 (95% CI 0.47-1.04)†

Limitations

- Small patient numbers can be a Limitations of subgroup analyses. These results are presented for descriptive purposes and cannot be interpreted as a demonstration of efficacy in any particular subgroup
- The results show the variability of the observed treatment effect among several subgroups
- No adjustments were made for multiple comparisons in the subgroup analyses

*Data cutoff, June 4, 2021; †Data cutoff, October 21, 2019.
1L, first line; BSC, best supportive care; CR, complete response; HR, hazard ratio; OS, overall survival; PR, partial response; SD, stable disease.
1. Powles T, et al. J Clin Oncol. 2023;41:3486-92; 2. Loriot Y, et al. J Clin Oncol. 2021;39(6_Suppl):Abstract 438 (ASCO-GU 2021 poster presentation);
3. Sridhar SS, et al. J Clin Oncol. 2021;39(15_Suppl):Abstract 4527 (ASCO 2021 poster presentation).

Real-world Evidence – Study Limitations

- Results of real-world studies are limited by lack of randomization, which can reduce internal validity of data (i.e., limit the ability to discern whether the difference between control and intervention groups is due to the intervention or due to other factors)
- Individual studies may have additional limitations such as small sample size, lack of control group, participants and investigators not being blinded, limited follow-up duration, poor quality of data collection, missing data, and exploratory nature of the data
- Retrospective studies may also be limited by sampling bias, recall bias, confounding bias, and changes in disease management practices
- The data presented are real-world analyses that reflect an observational analysis that may be still ongoing and do not meet the reliability and accuracy afforded by randomized controlled trials; data for patients may be missing due to patients not being fully compliant with follow up visits or other factors
- There are no head-to-head, controlled studies comparing avelumab to other anticancer therapies in locally advanced or metastatic UC
- **Therefore, no conclusions should be drawn, and no treatment decisions should be made based on real-world analyses**

UC, urothelial carcinoma.

Summary of Real-World Evidence (RWE) Sources

	AVENANCE (France)	READY CUP (Italy)	JAVEMACS (Japan)
Data source	Ambispective Study: retrospective (Early Access Program) or prospective enrollment	READY: prospective, noninterventional, multicentre compassionate use program (CUP)	JAVEMACS chart review: multicenter, noninterventional, retrospective review based on data from medical charts of patients in Japan
Community vs Academic Medical Centers		140 centres in Italy	University hospitals and cancer institutes in Japan

ASCO, American Society of Clinical Oncology; US, United States.

Summary of Real-World Evidence (RWE) Sources cont'd.

	Bakaloudi et al (US)	Tempus (US)	Flatiron (US)	PATRIOT-II (US)	IMPACT UC-II (US)	IMPACT UC-III (US)	SPEAR Bladder II (US)
Data source	• ~14 centers of cancer care • Longitudinal Electronic Health Record (EHR) database	Longitudinal Electronic Health Record (EHR) database	• ~800 unique sites of care • Longitudinal Electronic Health Record (EHR) database	Retrospective multicenter chart review	Optum Research Database (ORD) / claims data	Carelon Research's Healthcare Integrated Research Database (HIRD) / clinical and claims data	US Oncology Network iKnowMed™ (iKM) Electronic Health Record (EHR) data system
Community vs Academic Medical Centers	Academic centers in the US and Europe	26% community, 40% academic, 33% others (ASCO CancerLinq)	89% community, 8% academic	37 community and academic oncology centers	~8% commercial insurance, 18% Medicare Advantage		500 healthcare centers in US

ASCO, American Society of Clinical Oncology; US, United States.

Please choose a section

Topics of interest →

RWE Studies →

Topics of interest

Pre-avelumab 1LM

Unmet needs

Study details
- Flatiron I
- Tempus I

Baseline characteristics

Treatment patterns

Post-avelumab 1LM

Study details
- AVENANCE
- AVENANCE Low Tumor Burden Subgroups
- READY CUP
- JAVEMACS Chart Review
- Tempus I
- Tempus II
- Flatiron II
- Flatiron III
- Flatiron III Tumor Burden
- Flatiron Safety
- PATRIOT-II
- SPEAR Bladder II
- IMPACT UC III
- Bakaloudi et al

Baseline characteristics

Treatment patterns and sequencing

Effectiveness
- OS & PFS
- OS from start of 1L chemotherapy
- ORR
- Subgroup analysis: OS

Safety

Overview

1LM, first-line maintenance, CUP, compassionate use program; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; UC, urothelial carcinoma.

Pre-avelumab 1LM UC

Unmet needs

Study details
- Flatiron I
- Tempus I

Baseline characteristics
- Tempus I
- Flatiron I

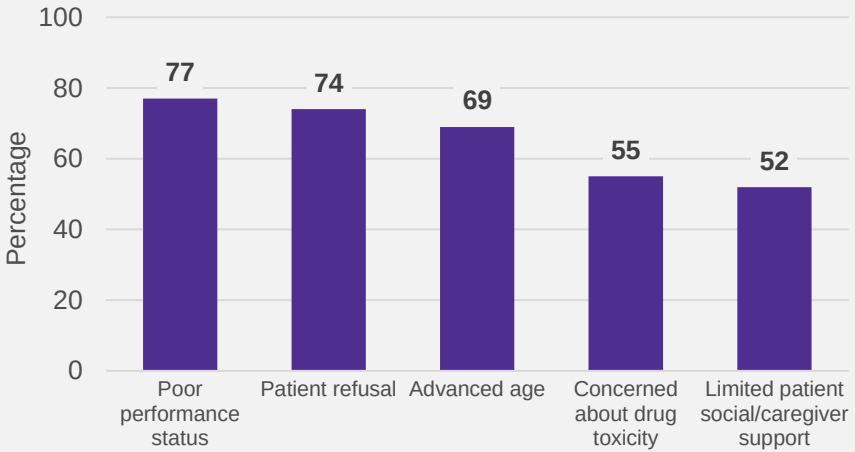
Treatment patterns
- Flatiron I
- Tempus I

Unmet treatment needs: real-world studies on rates of 1L therapy use

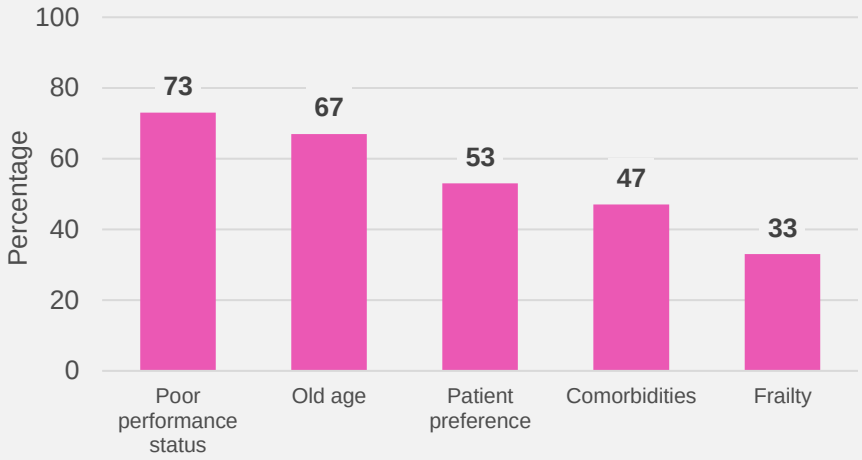
Across several real-world studies, 23%-69% of patients with advanced UC did not receive any 1L drug therapy[1-8]

Most common reasons for not prescribing systemic drug therapies[9]

Cross-sectional survey of 150 US oncologists in 2021



Qualitative interviews of 15 US oncologists/urologists in 2021

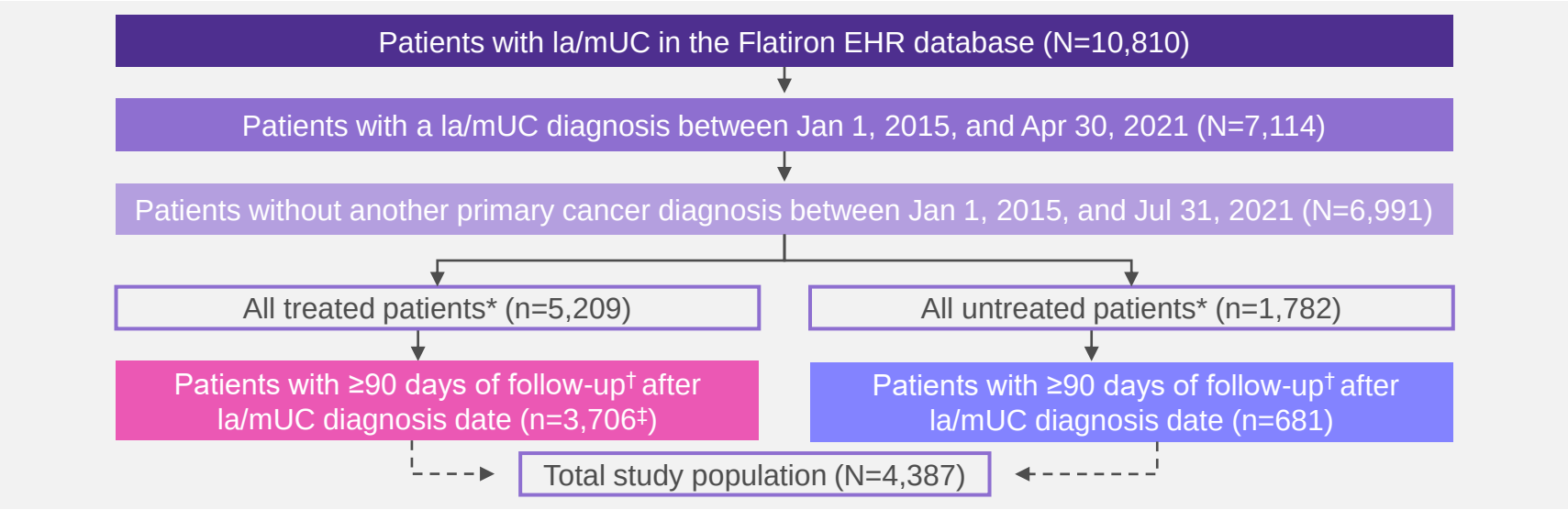


1L, first line; 1LM, first line maintenance; UC, urothelial carcinoma; US, United States.

1. Bilen M, et al. Presented at: ESMO; September 16-21, 2021; ESMO Congress 2021; 2. Geynisman DM, et al. *Urol Oncol.* 2022;40(5):195.e1-11; 3. Kearney M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA; 4. Niegisch G, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA; 5. Knott C, et al. Poster presented at: ESMO; September 9-13, 2022; Paris, France; 6. Jensen JB, et al. Presented at: ESMO; September 16-21, 2021; ESMO Congress 2021; 7. Maraz AC, et al. Poster presented at: ESMO; September 9-13, 2022; Paris, France; 8. Richters A, et al. *Cancer Treat Res Commun*. 2020;25:100266; 9. Gupta S, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 17-19, 2022; San Francisco, CA.

Flatiron I

Study details: retrospective cohort study of patients with la/mUC using data from the Flatiron Health EHR database from January 1, 2015, to July 31, 2021, to understand treatment patterns and real-world outcomes in patients with la/mUC in the US, including the early implementation of avelumab 1LM since its US FDA approval in June 2020.



*All patients were aged ≥18 years; †Unless in the case of death; ‡To reach this patient number, additional eligibility criteria were met: (1) no systemic treatment for la/mUC in the baseline period (n=5118); (2) <180 days between la/mUC diagnosis date and administration of 1L treatment (n=4634); (3) no clinical study drug during the study period (n=4532).
1L, first-line; 1LM, first-line maintenance; EHR, electronic health record; FDA, Food and Drug Administration; la/mUC, locally advanced/metastatic urothelial carcinoma; US, United States.
Kirker M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Tempus I

Study details: retrospective, observational study based on deidentified patient-level structured and unstructured data from the Tempus database, a US longitudinal electronic health record (EHR) database, to describe baseline demographic and clinical characteristics, real-world treatment patterns, and treatment sequencing in patients with la/mUC.

- Patients aged 18 years and older and diagnosed with la/mUC (T4b, N2/3, and/or M1 or overall cancer stage 3/4) between January 1, 2016, and February 23, 2022, were included

- Patients who completed 1L PBC and then received an IO therapy were categorized as 1LM or 2L
- 1LM was differentiated from 2L treatment based on a stated clinical intent of 1LM or initiation of IO therapy within 180 days of 1L PBC completion without disease progression

- Patients were then split into pre- and post-avelumab based on when they completed their 1L PBC treatment in relation to avelumab's 1LM US approval (June 30, 2020)

1L maintenance definition

If a patient…

- Received an IO therapy within 180 days of completing PBC

and

- Did not have a progression event in the same period, this IO therapy will be classified as 1LM
  - Permits CR, PR, and SD in period

2L therapy (subsequent)

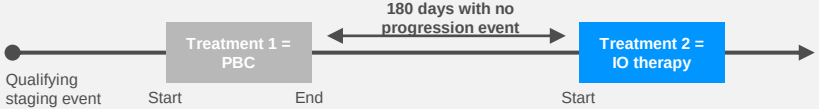
If a patient…

- Received an IO therapy >180 days after completing PBC

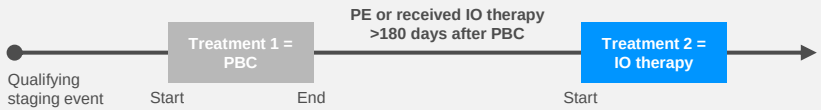
or

- Had a progression event between PBC and IO therapy

Defining 1L maintenance



2L therapy (subsequent)



1LM, first-line maintenance; 2L, second-line; CR, complete response; IO, immuno-oncology; la/mUC, locally advanced/metastatic urothelial carcinoma; PBC, platinum-based chemotherapy; PR, partial response; SD, stable disease; US, United States.

Kearney M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Flatiron I: Baseline Characteristics (1/4)

Retrospective cohort study of patients with la/mUC using data from the Flatiron Health database (N= 4387). Study period: January 1, 2015, to July 31, 2021.

	All treated, n (%)	Cisplatin-based, n (%)	Carboplatin-based, n (%)	IO monotherapy, n (%)	Other, n (%)	Avelumab 1LM, n (%)
	3706 (100.0)	1235 (33.3)	1147 (30.9)	1038 (28.0)	286 (7.7)	89 (2.4)
Age at la/mUC diagnosis, mean (SD), years	71.0 (9.0)	67.0 (8.9)	72.1 (8.0)	74.6 (8.2)	71.6 (8.9)	69.2 (10.1)
Sex						
Female	984 (26.6)	335 (27.1)	284 (24.8)	290 (27.9)	75 (26.2)	20 (22.5)
Male	2721 (73.4)	899 (72.8)	863 (75.2)	748 (72.1)	211 (73.8)	69 (77.5)
Unknown	1 (<0.1)	1 (0.1)	0	0	0	0
Race						
White	2585 (69.8)	867 (70.2)	796 (69.4)	716 (69.0)	206 (72.0)	54 (60.7)
Black	168 (4.5)	57 (4.6)	53 (4.6)	39 (3.8)	19 (6.6)	2 (2.3)
Hispanic or Latino	5 (0.1)	1 (0.1)	4 (0.3)	0	0	0
Asian	48 (1.3)	22 (1.8)	13 (1.1)	11 (1.1)	2 (0.7)	0
Other	596 (16.1)	192 (15.5)	183 (16.0)	185 (17.8)	36 (12.6)	23 (25.8)
Unknown	304 (8.2)	96 (7.8)	98 (8.5)	87 (8.4)	23 (8.0)	10 (11.2)

1LM, first-line maintenance; IO, immuno-oncology; la/mUC, locally advanced/metastatic urothelial carcinoma; SD, standard deviation.
Kirker M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Flatiron I: Baseline Characteristics (2/4)

Retrospective cohort study of patients with la/mUC using data from the Flatiron Health database (N= 4387). Study period: January 1, 2015, to July 31, 2021.

	All treated, n (%)	Cisplatin-based, n (%)	Carboplatin-based, n (%)	IO monotherapy, n (%)	Other, n (%)	Avelumab 1LM, n (%)
Region of residence						
Northeast	492 (13.3)	172 (13.9)	136 (11.9)	144 (13.9)	40 (14.0)	14 (15.7)
Midwest	464 (12.5)	157 (12.7)	147 (12.8)	123 (11.8)	37 (12.9)	14 (15.7)
South	1723 (46.5)	552 (44.7)	554 (48.3)	489 (47.1)	128 (44.8)	41 (46.1)
West	511 (13.8)	174 (14.1)	164 (14.3)	144 (13.9)	29 (10.1)	13 (14.6)
Other territories	41 (1.1)	10 (0.8)	13 (1.1)	14 (1.3)	4 (1.4)	0
Unknown	475 (12.8)	170 (13.8)	133 (11.6)	124 (11.9)	48 (16.8)	7 (7.9)

Of 4,387 patients included in the study, 3,706 (84.5%) received systemic anticancer treatments

1LM, first-line maintenance; IO, immuno-oncology; la/mUC, locally advanced/metastatic urothelial carcinoma;
Kirker M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Flatiron I: Baseline Characteristics (3/4)

Retrospective cohort study of patients with la/mUC using data from the Flatiron Health database (N= 4387). Study period: January 1, 2015, to July 31, 2021.

	All treated, n (%)	Cisplatin-based, n (%)	Carboplatin-based, n (%)	IO monotherapy, n (%)	Other, n (%)	Avelumab 1LM, n (%)
	3706 (100.0)	1235 (33.3)	1147 (30.9)	1038 (28.0)	286 (7.7)	89 (2.4)
Site of disease						
Bladder	2825 (76.2)	990 (80.2)	832 (72.5)	794 (76.5)	209 (73.1)	73 (82.0)
Renal pelvis	485 (13.1)	141 (11.4)	175 (15.3)	127 (12.2)	42 (14.7)	9 (10.1)
Ureter	366 (9.9)	91 (7.4)	128 (11.2)	116 (11.2)	31 (10.8)	7 (7.9)
Urethra	30 (0.8)	13 (1.1)	12 (1.0)	1 (0.1)	4 (1.4)	0
Disease grade						
High grade (grades 2-4)	3185 (85.9)	1093 (88.5)	951 (82.9)	890 (85.7)	251 (87.8)	70 (78.7)
Low grade (grade 1)	174 (4.7)	50 (4.0)	58 (5.1)	52 (5.0)	14 (4.9)	4 (4.5)
Unknown/not documented	347 (9.4)	92 (7.4)	138 (12.0)	96 (9.2)	21 (7.3)	15 (16.9)
Smoking status						
History of smoking	2717 (73.3)	908 (73.5)	850 (74.1)	747 (72.0)	212 (74.1)	59 (66.3)
No history of smoking	975 (26.3)	322 (26.1)	292 (25.5)	287 (27.6)	74 (25.9)	29 (32.6)
Unknown/not documented	14 (0.4)	5 (0.4)	5 (0.4)	4 (0.4)	0	1 (1.1)

1LM, first-line maintenance; IO, immuno-oncology; la/mUC, locally advanced/metastatic urothelial carcinoma;
Kirker M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Flatiron I: Baseline Characteristics (4/4)

Retrospective cohort study of patients with la/mUC using data from the Flatiron Health database (N= 4387). Study period: January 1, 2015, to July 31, 2021.

	All treated, n (%)	Cisplatin-based, n (%)	Carboplatin-based, n (%)	IO monotherapy, n (%)	Other, n (%)	Avelumab 1LM, n (%)
Stage at initial diagnosis						
0	13 (0.4)	5 (0.4)	4 (0.3)	4 (0.4)	0	1 (1.1)
I	66 (1.8)	20 (1.6)	22 (1.9)	20 (1.9)	4 (1.4)	3 (3.4)
II	286 (7.7)	52 (4.2)	54 (4.7)	149 (14.4)	31 (10.8)	6 (6.7)
III	335 (9.0)	139 (11.3)	68 (5.9)	103 (9.9)	25 (8.7)	3 (3.4)
IV	1415 (38.2)	593 (48.0)	480 (41.8)	246 (23.7)	96 (33.6)	40 (44.9)
Unknown/not documented	1591 (42.9)	426 (34.5)	519 (45.2)	516 (49.7)	130 (45.5)	36 (40.5)
PD-L1 testing status						
Yes						
Negative	342 (9.2)	107 (8.7)	115 (10.0)	94 (9.1)	26 (9.1)	15 (16.9)
Positive	393 (10.6)	117 (9.5)	107 (9.3)	144 (13.9)	25 (8.7)	20 (22.5)
Unknown	365 (9.8)	106 (8.6)	97 (8.5)	127 (12.2)	35 (12.2)	15 (16.9)
No	2606 (70.3)	905 (73.3)	828 (72.2)	673 (64.8)	200 (69.9)	39 (43.8)
GFR (mL/min/1.73m²) at la/mUC diagnosis date (±30 days)						
30-60	128 (3.5)	6 (0.5)	53 (4.6)	57 (5.5)	12 (4.2)	20 (22.5)
<30	845 (22.8)	171 (13.8)	319 (27.8)	279 (26.9)	76 (26.6)	0
>60	800 (21.6)	363 (29.4)	221 (19.3)	163 (15.7)	53 (18.5)	30 (33.7)
Unknown	1933 (52.2)	695 (56.3)	554 (48.3)	539 (51.9)	145 (50.7)	39 (43.8)

1LM, first-line maintenance; la/mUC, locally advanced/metastatic urothelial carcinoma; GFR, glomerular filtration rate; IO, immuno-oncology; PD-1, programmed cell death protein 1.
Kirker M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Tempus I: Baseline Characteristics (1/2)

Retrospective, observational study based on deidentified patient-level structured and unstructured data from the Tempus database, a US longitudinal EHR database (N= 821). Study period: January 1, 2016 to February 23, 2022.

	Overall cohort, N=821
Race, n (%)	
American Indian or Alaska Native	1 (0.1)
Black or African American	53 (6.5)
Other	48 (5.8)
Unknown	200 (24)
White	519 (63)
Region, n (%)	
Midwest	214 (46)
Northeast	33 (7)
South	108 (23)
West	115 (24)
Unknown	351 (43)
Data source, n (%)	
Academic centers	221 (27)
Community centers	169 (21)
Other	426 (52)
Unknown	5 (1)

	Overall cohort, N=821
Systemic treatment, n (%)	
Treated, curated	634 (77)
Untreated	187 (23)
Follow-up from la/mUC diagnosis, median (range), months	9.20 (3.71-18.80)
Age at la/mUC diagnosis, median (IQR), years	69 (62-76)
Year of la/mUC diagnosis, n (%)	
2016	90 (11)
2017	95 (12)
2018	110 (13)
2019	182 (22)
2020	207 (25)
2021	129 (16)
2022	8 (1)
Sex, n (%)	
Male	600 (73)
Female	221 (27)

EHR, Electronic health record; IQR, interquartile range; la/mUC, locally advanced/metastatic urothelial carcinoma; PD-L1, programmed death ligand 1.

Kearney M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Tempus I: Baseline Characteristics (2/2)

Retrospective, observational study based on deidentified patient-level structured and unstructured data from the Tempus database, a US longitudinal EHR database (N= 821). Study period: January 1, 2016 to February 23, 2022.

	Overall cohort, N=821
Smoking status, n (%)	
History of smoking	361 (63)
Never	212 (37)
Unknown	248
Histology type, n (%)	
Ambiguous carcinoma	131 (16)
Other	30 (3.7)
Squamous	2 (0.2)
Transitional	658 (80)
Histopathology grade, n (%)	
Grade 2 (moderately differentiated)	8 (1.6)
Grade 3 (poorly differentiated)	67 (14)
Grade 4 (undifferentiated)	1 (0.2)
High	416 (84)
Low	1 (0.2)
Unknown	328

	Overall cohort, N=821
Comorbidities, n (%)	
1	147 (37)
2	86 (22)
3	54 (14)
4+	106 (27)
Unknown	428
Death records, n (%)	305 (37)
PD-L1 status, n (%)	
Negative	123 (64)
Positive	70 (36)
Unknown	628

IQR, interquartile range; la/mUC, locally advanced/metastatic urothelial carcinoma; PD-L1, programmed death ligand 1.
Kearney M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

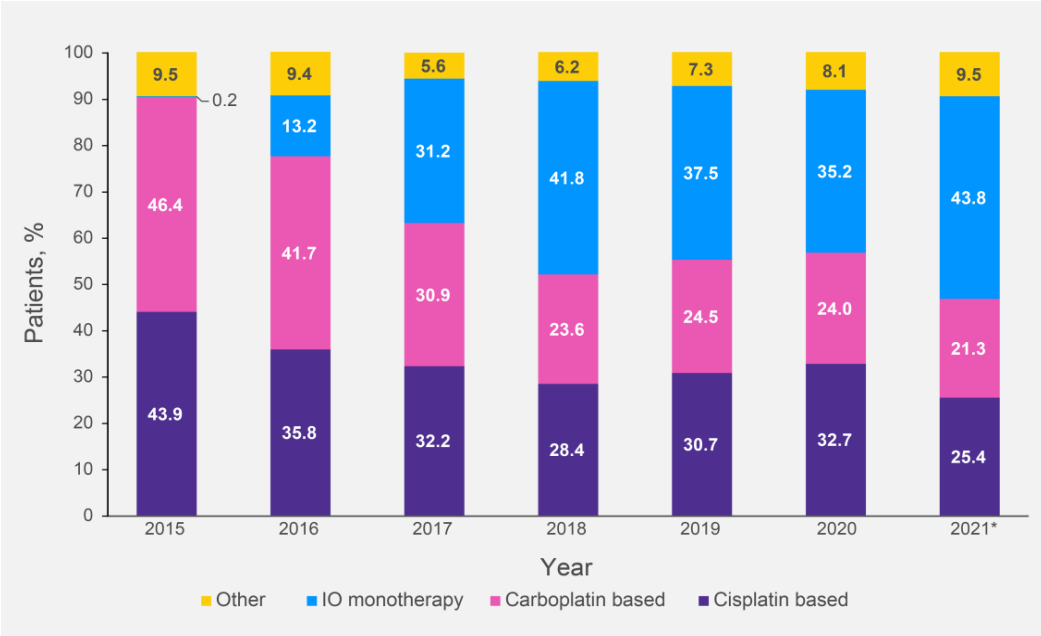
Flatiron I: Treatment Patterns by Index Year

Retrospective cohort study of patients with la/mUC using data from the Flatiron Health database (N= 4387). Study period: January 1, 2015, to July 31, 2021

4387 patients met selection criteria

- 3706 (84.5%) received systemic treatments; of these,
  - 1235 (33.3%) received cisplatin
  - 1147 (30.9%) received carboplatin
  - 1038 (28.0%) received IO monotherapy
  - 286 (7.7%) received other therapies

Due to the recent approval of IO therapies in the 1L, there was a decrease in the proportion of patients receiving 1L PBC and an increase in those receiving 1L IO from 2015 to 2021

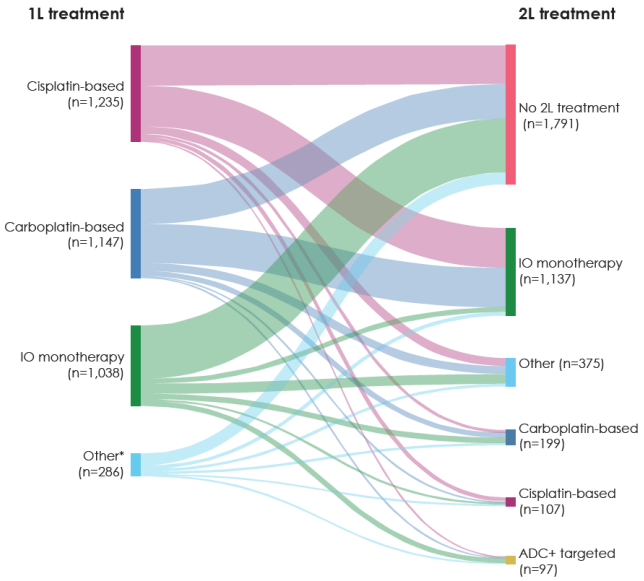


Limitations: The Flatiron Health data are not fully generalizable to the wider US population, electronic health record data are often incomplete, and data on visits to non–Flatiron Health clinics were unavailable. Only the first 6 months of 2021 were included in the study. The study period ended prior to recent changes in the FDA approvals of pembrolizumab and atezolizumab.
IO, immuno-oncology; other, other platinum-based therapies (eg, oxaliplatin) and any other treatments not falling into any previous drug class.
1 L, first line; 1 LM, first line maintenance; PBC, platinum-based chemotherapy; IO, immuno-oncology
Kirker M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Flatiron I: Treatment Patterns by Index Year

Retrospective cohort study of patients with la/mUC using data from the Flatiron Health database (N= 4387). Study period: January 1, 2015, to July 31, 2021.

Proportion of patients with treatment sequence from 1L to 2L



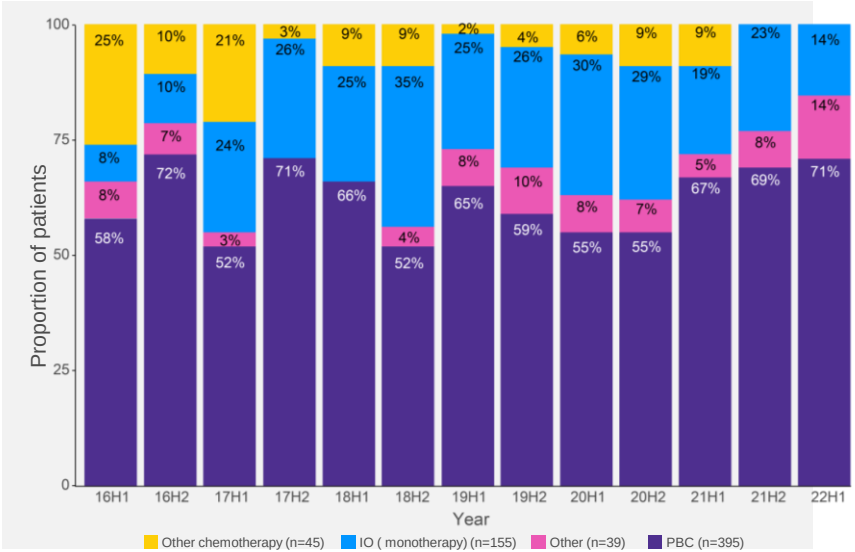
		2L treatment					
Patients, n (%) 3706 (100.0)		Cisplatin-based	Carboplatin-based	IO monotherapy	ADC + target	Other	No 2L treatment†
1L treatment	Cisplatin-based	50 (4.0)	35 (2.8)	522 (42.3)	18 (1.5)	110 (8.9)	500 (40.5)
	Carboplatin-based	17 (1.5)	66 (5.8)	508 (44.3)	10 (0.9)	103 (9.0)	443 (38.6)
	IO monotherapy	22 (2.1)	69 (6.6)	63 (6.1)	65 (6.3)	128 (12.3)	691 (66.6)
	Other*	18 (6.3)	29 (10.1)	44 (15.4)	4 (1.4)	34 (11.9)	157 (54.9)

Limitations : The Flatiron Health data are not fully generalizable to the wider US population, electronic health record data are often incomplete, and data on visits to non–Flatiron Health clinics were unavailable. Of patients treated with 1L therapy, 4.1% of those treated with cisplatin-based therapy and 3.3% of those treated with carboplatin-based therapy received avelumab 1LM treatment; 58.4% were still receiving avelumab 1LM at the end of follow-up. "Other" includes other platinum-based therapies (eg, oxaliplatin) and any other treatments not falling into any previous drug class. Treatment groups are mutually exclusive. Patients were placed into each group regardless of cross-treatment group combination with this hierarchy: IO, targeted, ADC, cisplatin, carboplatin, any other. Percentages represent row percentages.
*Inclusive of ADC+ targeted. †Inclusive of patients still receiving 1L at end of follow-up: cisplatin-based therapy (48.6%); carboplatin-based therapy (62.3%); IO monotherapy (79.9%); other (61.1%).
1L, first-line; 1LM, first-line maintenance; 2L, second-line; ADC, antibody-drug conjugates; IO, immuno-oncology.
Kirker M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Tempus I: Trends in 1L Therapy and Treatment Sequencing

Retrospective, observational study based on deidentified patient-level structured and unstructured data from the Tempus database, a US longitudinal EHR database (N= 821). Study period: January 1, 2016 to February 23, 2022.

Proportion of patients receiving 1L systemic therapy by time period (n=634)*



Treatment sequencing

	1L PBC end date pre-avelumab 1LM approval (n=243) n/N (%)
Received IO therapy as 2L or 1LM following 1L PBC	87/243 (36)
Received IO therapy as 2L	59/87 (68)
Received IO therapy as 1LM	28/87 (32)
Received 2L tx after progression on IO 1LM	9/28 (32) Enfortumab vedotin: 4/9 (44) PBC: 5/9 (56)
Did not receive IO therapy after 1L PBC but received 2L or later tx	110/243 (45)

Limitations : Data were collected primarily in the oncology clinical practice setting through routine clinical care and not for research purposes; therefore, nonrandom missingness may be present for several variables of interest, and data on healthcare received outside of the Tempus network of practices are not available. Complete medical history outside of the oncology EHR was not captured, which may lead to underreporting of treatments received . Algorithms used to identify 1LM and 2L agents may not reflect the definitions used in clinical practice. Patients who initiated 1L systemic therapy later in the study period may not have had enough follow-up time to observe 2L and subsequent treatment rates, which may have led to underestimates in these lines of treatment. Similarly, the study was limited in its ability to comprehensively understand
the use of avelumab in 1LM as it was approved by the FDA3 on June 30, 2020.

*The distribution of systemic 1L therapy initiated according to treatment class is summarized by 6-month time intervals

1L, first line; 1 LM, first line maintenance; 2L, second line; HER, electronic health record; Ia/mUC, locally advanced/metastatic urothelial carcinoma; IO, immuno-oncology; IQR, interquartile range; PBC, platinum- based chemotherapy; PD-L1, programmed death ligand; tx, treatment.

Kearney M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Post-avelumab 1LM UC

Study details

- AVENANCE
- AVENANCE Low Tumor Burden Subgroups
- READY CUP
- JAVEMACS Chart Review
- Tempus I
- Tempus II
- Flatiron II
- Flatiron III
- Flatiron III Tumor Burden
- Flatiron Safety
- PATRIOT-II
- SPEAR Bladder II
- IMPACT UC III
- Bakaloudi et al

Baseline characteristics

Treatment patterns and sequencing

Effectiveness

- OS & PFS
- OS from start of 1L chemotherapy
- ORR
- Subgroup analysis: OS

Safety

RWE studies overview

1LM, first-line maintenance, CUP, compassionate use program; OS, overall survival; PFS, progression-free survival; UC, urothelial carcinoma.

AVENANCE

Study details: ongoing, real-world, ambispective study evaluating the effectiveness and safety of avelumab 1L maintenance in patients with aUC who have not progressed with PBC in France. Data collection started on July 13, 2021, and data cutoff for this analysis was December 7, 2023

- **595 patients** received avelumab

- At data cutoff (December 7, 2023), median follow-up since avelumab initiation was 26.3 months (range: 0.6-43.7) in the full analysis set.

1L, first line; aUC, advanced urothelial carcinoma; CI, confidence interval; ddMVAC, dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin; ECOG PS, Eastern Cooperative Group performance status; PBC, platinum-based chemotherapy.

Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 561) January 25-27, 2024; San Francisco, CA

AVENANCE Low Tumor Burden Subgroups

Study details: post hoc analyses of an ongoing, real-world, ambispective study evaluating the effectiveness and safety of avelumab 1L maintenance in the low tumor burden subgroup of patients with aUC who have not progressed with PBC in France. Patients had low tumor burden at the start of 1L chemotherapy. Data collection started on July 13, 2021, and data cutoff for this analysis was December 2, 2024.

- **595 patients** received avelumab

- At data cutoff (December 2, 2024), median follow-up since avelumab initiation was 33.2 months (95% CI, range: 31.7-34.0) in the full analysis set

- **Characteristics of low tumor burden (n=186)**
  - Locally advanced disease (n=47)
  - Nonvisceral metastases* (n=79)
  - Lymph node-only disease (n=60)

*Bone metastases were considered visceral metastases

1L, first line; 1LM, first line maintenance; aUC, advanced urothelial carcinoma; CI, confidence interval; PBC, platinum-based chemotherapy.

Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 718) February 13-15, 2025; San Francisco, CA

READY CUP

Study details: prospective, noninterventional, multicentre compassionate use program (CUP) of avelumab 1LM conducted across 140 centres among 464 patients with histologically confirmed unresectable la/mUC (stage IV) in Italy

- Patients with:
  - No disease progression after 4-6 cycles of 1L PBC
  - Received their last dose of PBC 4-10 weeks prior to starting avelumab

- Study period: January 18, 2021 – March 7, 2022
- Median follow-up was 20.30 months (95% CI, 19.78-20.93)
- Median duration of avelumab treatment was 3.8 months (interquartile range, 2.0-8.3)

1L, first line; 1LM, first-line maintenance; CUP, compassionate use program; la/mUC, locally advanced or metastatic urothelial carcinoma; PBC, platinum-based chemotherapy

Antonuzzo, L., et al., ESMO Real World Data and Digital Oncology, 2024. 5: p. 100068.

JAVEMACS Chart Review

Study details: multicenter, noninterventional, retrospective study based on data from medical charts of patients with la/mUC in Japan treated at university hospitals and cancer institutes

- Patients with no disease progression following 1L PBC
- 350 patients received ≥1 dose of avelumab 1LM between February 2021 and December 2023

- 26 centers in Japan
- Data collection was retrospective

- At data cutoff (June 2024), 67 patients (19.1%) were still receiving avelumab maintenance
- At cutoff date, 200 patients (57.1%) were alive with ongoing follow-up

- Median observation period
  - 14.6 months (range, 0.16-38.5 months) from avelumab 1LM initiation
  - 20.0 months (range, 2.9-114.4 months) from PBC initiation
- Median duration of avelumab maintenance: 14.3 weeks (IQR, 7.1-30.9 weeks)

1L, first line; 1LM, first-line maintenance; IQR, interquartile range; la/mUC, locally advanced or metastatic urothelial carcinoma; PBC, platinum-based chemotherapy

Kitamura H, et al. Presented at the ASCO Genitourinary Cancers Symposium (Abstract No. 701), February 13-15, 2025; San Francisco, CA.

Tempus I

Study details: retrospective, observational study based on deidentified patient-level structured and unstructured data from the Tempus database, a US longitudinal electronic health record (EHR) database, to describe baseline demographic and clinical characteristics, real-world treatment patterns, and treatment sequencing in patients with la/mUC.

- Patients aged 18 years and older and diagnosed with la/mUC (T4b, N2/3, and/or M1 or overall cancer stage 3/4) between January 1, 2016, and February 23, 2022, were included

- Patients who completed 1L PBC and then received an IO therapy were categorized as 1LM or 2L
- 1LM was differentiated from 2L treatment based on a stated clinical intent of 1LM or initiation of IO therapy within 180 days of 1L PBC completion without disease progression

- Patients were then split into pre- and post-avelumab based on when they completed their 1L PBC treatment in relation to avelumab's 1LM US approval (June 30, 2020)

1L maintenance definition

If a patient…

- Received an IO therapy within 180 days of completing PBC

and

- Did not have a progression event in the same period, this IO therapy will be classified as 1LM
  - Permits CR, PR, and SD in period

2L therapy (subsequent)

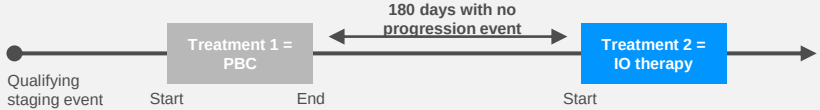
If a patient…

- Received an IO therapy >180 days after completing PBC

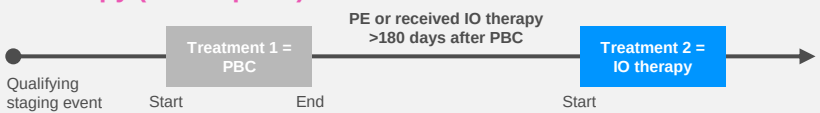
or

- Had a progression event between PBC and IO therapy

Defining 1L maintenance



2L therapy (subsequent)



1LM, first-line maintenance; 2L, second-line; CR, complete response; IO, immuno-oncology; la/mUC, locally advanced/metastatic urothelial carcinoma; PBC, platinum-based chemotherapy; PR, partial response; SD, stable disease; US, United States.

Kearney M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Tempus II

Study details: retrospective, observational study based on deidentified patient-level structured and unstructured data from the Tempus database, a US longitudinal electronic health record (EHR) database, to describe baseline demographic and clinical characteristics, real-world treatment patterns, and treatment sequencing in patients with la/mUC.

- Patients aged 18 years and older and diagnosed with la/mUC (T4b, N2/3, and/or M1 or overall cancer stage 3/4) between January 1, 2016, and March 13, 2023, were included

- Patients who completed 1L PBC and then received an IO therapy were categorized as 1LM or 2L
  - 1LM was differentiated from 2L treatment based on a stated clinical intent of 1LM or initiation of IO therapy within 180 days of 1L PBC completion without disease progression

1L maintenance definition

If a patient…

- Received an IO therapy within 180 days of completing PBC

and

- Did not have a progression event in the same period, this IO therapy will be classified as 1LM
  - Permits CR, PR, and SD in period

2L therapy (subsequent)

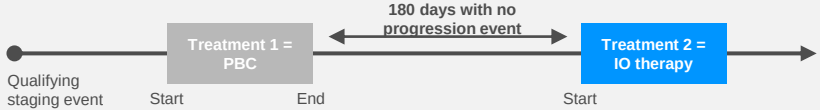
If a patient…

- Received an IO therapy >180 days after completing PBC

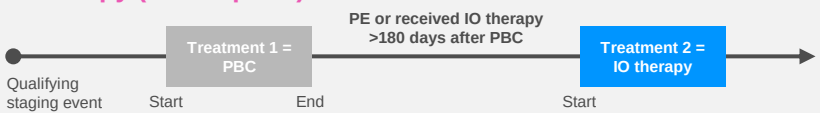
or

- Had a progression event between PBC and IO therapy

Defining 1L maintenance



2L therapy (subsequent)



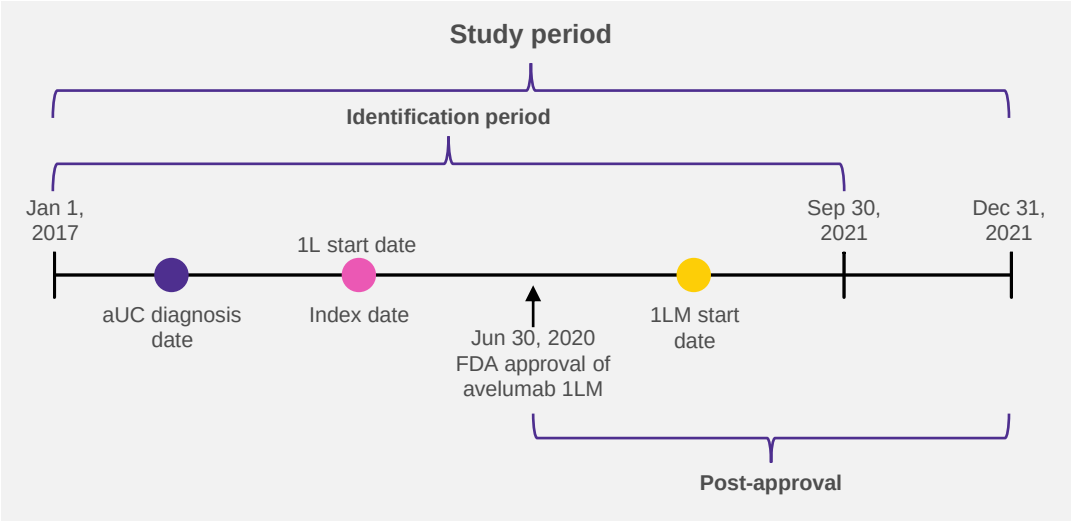
1L, first-line; 1LM, first-line maintenance; 2L, second-line; CR, complete response; IO, immuno-oncology; la/mUC, locally advanced/metastatic urothelial carcinoma; OS, overall survival; PBC, platinum-based chemotherapy; PR, partial response; SD, stable disease.

Carson K, et al. Poster presented at: ESMO Congress (Abstract 2387P); October 20-24, 2023; Madrid, Spain.

Flatiron II

Study details: noninterventional, retrospective cohort study of patients with aUC in the US aimed to assess current real-world response rates and outcomes in patients treated with 1L PBC and to understand patient eligibility for avelumab 1LM and early utilization following the FDA approval on June 30, 2020. The study used Flatiron Health's EHR database from approximately 280 cancer clinics.

- Study period: January 1, 2017, to December 31, 2021
- Identification period: January 1, 2017, to September 30, 2021, to ensure ≥3 months of follow-up unless a patient died
  - The index date was the start date for 1L treatment in the identification period
- Patients were classified as having received avelumab 1LM if they had received 1L PBC, initiated avelumab within 180 days of 1L PBC discontinuation, and had no documented progression before initiating avelumab

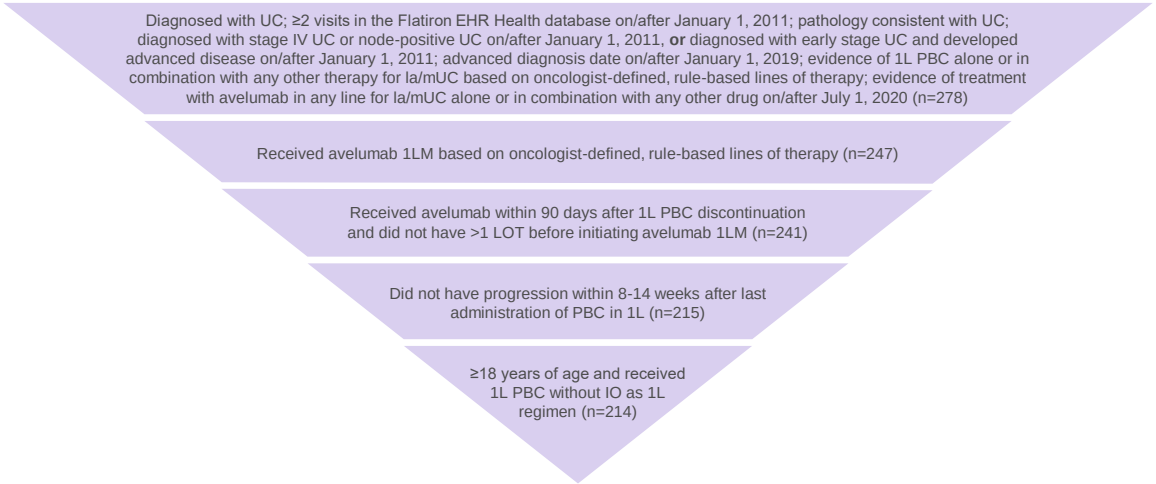


1L, first-line; 1LM, first-line maintenance; aUC, advanced urothelial carcinoma; EHR, electronic health record; FDA, Food and Drug Administration; PBC, platinum-based chemotherapy.

Moon HH, et al. Poster presented at: ASCO Annual Meeting; June 2-6, 2023; Chicago, IL.

Flatiron III

Study details: noninterventional, retrospective cohort study of patients with la/mUC in the US using the nationwide Flatiron Health electronic health record–derived database, which is comprised of deidentified patient-level structured and unstructured data, curated via technology-enabled abstraction.



During the study period (January 1, 2011-December 31, 2022), the deidentified data originated from **approximately 280 cancer clinics**

1L, first line; 1LM, first-line maintenance; EHR, electronic health record; IO, immuno-oncology; la/mUC, locally advanced/metastatic urothelial carcinoma; LOT, line of therapy; PBC, platinum-based chemotherapy; UC, urothelial carcinoma.

Moon HH, et al. Curr Oncol. 2024;31(9):5662-5676.

Flatiron III Tumor Burden

Study details: noninterventional, retrospective cohort study assessing real-world clinical outcomes based on tumor burden in patients with la/mUC with no disease progression after 1L PBC who received avelumab 1LM in the US. This study used the nationwide Flatiron Health Electronic Health Record–derived database, which is comprised of deidentified patient-level data.

- N=290
- Age ≥18 years
- Diagnosed with la/mUC between January 1, 2019, and July 31, 2023
- Avelumab 1LM initiation on or after July 1, 2020, and within 90 days after discontinuing 1L PBC
- No disease progression for 8-14 weeks after the last administration of 1L PBC

- **Subgroup analyses based on tumor burden:**
  - Nonvisceral metastases (including bone only) vs visceral metastases (including visceral sites and bone)
  - Lymph node-only metastases (including distant lymph nodes) vs distant metastases

- At data cutoff (July 31, 2023), 156 patients (53.8%) were still receiving avelumab 1LM

- Median follow-up from avelumab 1LM initiation: 8.7 months (IQR, 3.7-16.9)

1L, first line; 1LM, first line maintenance; EHR, electronic health record; IQR, interquartile range; la/mUC, locally advanced/metastatic urothelial carcinoma; PBC, platinum-based chemotherapy; US, United States.
Moon HH, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 764) February 13-15, 2025; San Francisco, CA.

Flatiron Safety

Study details: retrospective observational cohort study describing the real-world safety profiles of current 1L systemic treatments initiated by patients with la/mUC in the US from January 2016 to October 2023. This study use the nationwide, longitudinal, electronic health record-derived, deidentified Flatiron Health database, comprising patient-level data curated via technology-enabled abstraction or extraction.

- **≈280 US cancer clinics (≈800 sites of care)**
  - Patients diagnosed with la/mUC on or after January 1, 2016
  - Treatment with a 1L regimen of interest ≥6 months prior to data cutoff (April 30, 2024)

- **Regimens of interest**
  - Enfortumab vedotin + pembrolizumab
  - ICI monotherapy (pembrolizumab or atezolizumab)
  - Cisplatin-based chemotherapy followed by avelumab maintenance
  - Carboplatin-based chemotherapy followed by avelumab maintenance
  - Cisplatin-based chemotherapy without avelumab maintenance
  - Carboplatin-based chemotherapy without avelumab maintenance

- rwTEAEs assessed from the start of 1L treatment to the earliest of 90 days after last 1L treatment dose, start of subsequent treatment, or death

[a]la/mUC defined as stage IV or node-positive (stage IIIA [N1] or IIIB [N2-N3]) UC or diagnosed with early-stage UC and subsequently developed advanced disease.

1L, first line; 1LM, first line maintenance; ICI, immune checkpoint inhibitor; la/mUC, locally advanced/metastatic urothelial carcinoma; rwTEAE, real-world treatment emergent adverse event; UC, urothelial carcinoma.

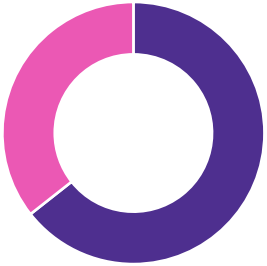
Nizam A, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 759) February 13-15, 2025; San Francisco, CA.

PATRIOT II

Study details: observational, retrospective chart review study that examined real-world outcomes, treatment patterns, and HCRU prior to and during avelumab 1LM in 160 patients with la/mUC in routine clinical practice in the United States.

Study conducted across **37 geographically dispersed sites** consisting of both community oncology practices and centers affiliated with academic institutions

60 patients (37.5%) received **1L carboplatin**



100 patients (62.5%) received **1L cisplatin**-based chemotherapy

1L, first line; 1LM, first-line maintenance; HCRU, healthcare resource utilization; la/mUC, locally advanced/metastatic urothelial carcinoma; US, United states.

Grivas P, et al. Clin Genitourin Cancer. 2024;22(6):102238.

SPEAR Bladder II

Study details: retrospective, observational study describing the real-world treatment patterns, treatment sequencing post-avelumab 1LM, and OS in 1,658 patients with la/mUC who initiated 1L treatment in the US community oncology setting

- Data was collected from the US Oncology Network iKnowMed™ EHR data system

- Adults with a diagnosis of la/mUC who initiated 1L systemic anticancer treatment between December 1, 2019, and November 30, 2023, were included and followed up till the end of the study (February 28, 2024)

Patients were categorized by 1L systemic anticancer treatment received:

- IO monotherapy
- cisplatin-based PBC only
- carboplatin-based PBC only
- cisplatin-based PBC with avelumab 1LM
- carboplatin-based PBC with avelumab 1LM
- ADCs
- other treatments

- Combination therapy: drugs administered within 28 days of the current treatment
- Next line of therapy: New treatments administered ≥28 days after the current therapy or with a gap of >90 days
- Maintenance treatment: If avelumab was administered within 90 days of completion of 1L PBC

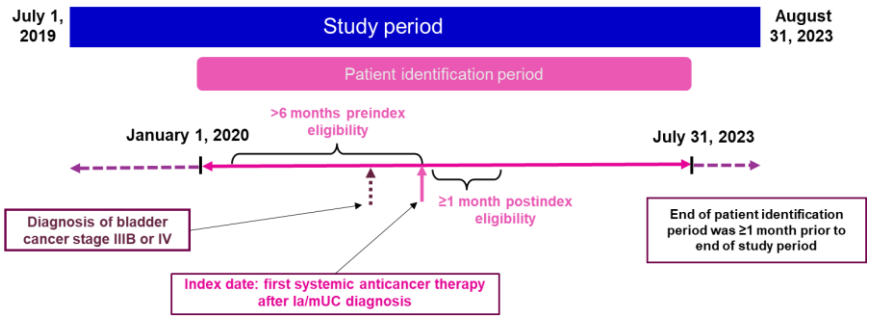
1L, first-line treatment; 1 LM, first line maintenance; ADC, antibody drug conjugate; EHR, electronic health record; la/mUC, locally advanced/metastatic urothelial carcinoma; IO, immuno-oncology; OS, overall survival; PBC, platinum-based chemotherapy

Sura S, et al. Current Oncology. 2025;32(4):187.

IMPACT UC III

Study details: noninterventional, retrospective cohort evaluating patient characteristics, treatment patterns, and clinical outcomes among 2,820 patients with la/mUC receiving 1L systemic treatment and avelumab 1LM in the United States

- Data was collected from
  - Carelon Research's Healthcare Integrated Research Database
  - Health plan's Cancer Care Quality Program (claims and clinical data)



- Adults with a diagnosis of la/mUC who initiated 1L systemic treatment (index date) from January 1, 2020-July 31, 2023, were included
- la/mUC was defined as stage IIIB or IV disease or ≥2 medical claims with metastatic disease
- Study period (July 1, 2019-August 31, 2023) allowed a ≥6-month baseline period and ≥1 month of follow-up after index date
- Avelumab 1LM use was defined as use on or after June 30, 2020, and within 90 days after completion of 1L PBC

1L, first-line treatment; 1LM, first line maintenance; la/mUC, locally advanced/metastatic urothelial carcinoma; PBC, platinum- based chemotherapy.

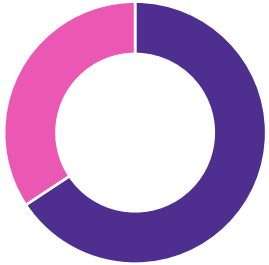
Moon H., et al. Presented at: ASCO QCS, (Poster No. 390), September 27-28, 2024; San Francisco, CA, USA.

Bakaloudi et al

Study details: multicenter retrospective cohort study of real-world patient characteristics and clinical outcomes with avelumab switch maintenance to compare with data from the JAVELIN Bladder 100 trial.

Patients from **14 academic centers** who had received 1L avelumab maintenance after no progression on PBC for aUC were included

37 (34.3%) received carboplatin



71 patients (65.7%) received cisplatin-based chemotherapy

1L, first-line treatment; 1LM, first line maintenance; aUC, advanced urothelial carcinoma; PBC, platinum-based chemotherapy.

Bakaloudi DR, et al. Clin Genitourin Cancer. 2023;S1558-7673(23)00147-7.

AVENANCE: Baseline Characteristics (1/3)

Ongoing, real-world, ambispective study in patients with aUC who have not progressed with PBC in France (N= 595).
Study period: July 13, 2021, to December 7, 2023.

	Overall effectiveness population (N=595)	2L treatment: chemotherapy (n=244)	2L treatment: ADC (n=62)	2L treatment: other (n=24)
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)

1L, first line; 1LM, first line maintenance; ADC, antibody drug conjugate; aUC, advanced urothelial carcinoma; IQR, interquartile range; PBC, platinum-based chemotherapy.
Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 561) January 25-27, 2024; San Francisco, CA.

AVENANCE: Baseline Characteristics (2/3)

Ongoing, real-world, ambispective study in patients with aUC who have not progressed with PBC in France (N= 595). Study period: July 13, 2021, to December 7, 2023.

	Overall effectiveness population (N=595)	2L treatment: chemotherapy (n=244)	2L treatment: ADC (n=62)	2L treatment: other (n=24)
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**
0	147 (31.1)	53 (28.5)	13 (26.5)	7 (35.0)
1	251 (53.1)	100 (53.8)	27 (55.1)	13 (65.0)
≥2	75 (15.9)	33 (17.7)	9 (18.4)	0

1L, first line; 1LM, first line maintenance; aUC, advanced urothelial carcinoma; ECOG PS, Eastern Cooperative Group performance status; PBC, platinum-based chemotherapy.

Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 561) January 25-27, 2024; San Francisco, CA.

AVENANCE: Baseline Characteristics (3/3)

Ongoing, real-world, ambispective study in patients with aUC who have not progressed with PBC in France (N= 595). Study period: July 13, 2021, to December 7, 2023.

	Overall effectiveness population (N=595)	2L treatment: chemotherapy (n=244)	2L treatment: ADC (n=62)	2L treatment: other (n=24)
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 + gemcitabine	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)	16 (25.8)	5 (20.8)
Partial response	332 (56.3)	140 (58.1)	32 (51.6)	12 (50.0)
Stable disease	136 (23.1)	57 (23.7)	11 (17.7)	7 (29.2)
Disease progression	4 (0.7)	1 (0.4)	3 (4.8)	0
Nonevaluable	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)

*This category includes patients who switched platinum-based regimens while receiving 1L chemotherapy.
1L, first line; 1 LM, first line maintenance; aUC, advanced urothelial carcinoma; CI, confidence interval; ddMVAC, dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin; IQR, interquartile range; PBC, platinum-based chemotherapy.
Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 561) January 25-27, 2024; San Francisco, CA.

AVENANCE Low Tumor Burden Subgroups: Baseline Characteristics (1/2)

Post hoc analysis of ongoing, real-world, ambispective study in patients with aUC who have not progressed with PBC in France and had low tumor burden at start of PBC (n=186)
Study start: July 13, 2021; Data cut-off: December 2, 2024

Characteristic	Locally advanced disease (n=47)	Nonvisceral metastases (n=79)	Lymph node-only metastases (n=60)
Age, median (IQR), years	70.7 (64.7-77.3)	72.3 (66.0-76.3)	70.7 (66.1-74.7)
Sex, n (%)			
Female	7 (14.9)	14 (17.7)	11 (18.3)
Male	40 (85.1)	65 (82.3)	49 (81.7)
ECOG PS at start of avelumab, n (%)	n=36	n=71	n=54
0	11 (30.6)	22 (31.0)	18 (33.3)
≥1	25 (69.4)	49 (69.0)	36 (66.7)
Primary tumor site, n (%)			
Lower tract	33 (70.2)	67 (84.8)	49 (81.7)
Upper tract	14 (29.8)	12 (15.2)	11 (18.3)
Prior treatment for localized invasive UC, n (%)	17 (36.2)	35 (44.3)	27 (45.0)
Received neoadjuvant chemotherapy	3 (6.4)	8 (10.1)	7 (11.7)
Received adjuvant chemotherapy	5 (10.6)	9 (11.4)	8 (13.3)

1LM, first line maintenance; ECOG PS, Eastern Cooperative Oncology Group performance status; IQR, inter-quartile range; UC, urothelial carcinoma.
Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 718) February 13-15, 2025; San Francisco, CA

AVENANCE Low Tumor Burden Subgroups: Baseline Characteristics (2/2)

Post hoc analysis of ongoing, real-world, ambispective study in patients with aUC who have not progressed with PBC in France and had low tumor burden at start of PBC (n=186)
Study start: July 13, 2021; Data cut-off: December 2, 2024

Characteristic	Locally advanced disease (n=47)	Nonvisceral metastases (n=79)	Lymph node-only metastases (n=60)
Disease stage at start of 1L chemotherapy, n (%)			
Metastatic	0	79 (100)	60 (100)
Locally advanced	47 (100)	0	0
1L chemotherapy regimen, n (%)			
Carboplatin + gemcitabine	26 (55.3)	53 (67.1)	38 (63.3)
Cisplatin + gemcitabine	14 (29.8)	19 (24.1)	16 (26.7)
Methotrexate, vinblastine, doxorubicin, and cisplatin	1 (2.1)	4 (5.1)	4 (6.7)
Other or switched*	6 (12.8)	3 (3.8)	2 (3.3)
No. of 1L chemotherapy cycles, median (range)	4 (1–10)	5 (3–10)	5 (3–10)
Response to 1L chemotherapy, n (%)	n=46		
Complete response	3 (6.5)	25 (31.6)	21 (35.0)
Partial response	30 (65.2)	35 (44.3)	28 (46.7)
Stable disease	13 (28.3)	18 (22.8)	10 (16.7)
Other	0 (0.0)	1 (1.3)	1 (1.7)

*Patients who switched platinum regimens while receiving 1L chemotherapy
1L, first line; 1LM, first line maintenance.
Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 718) February 13-15, 2025; San Francisco, CA.

READY CUP: Baseline Characteristics

Prospective, noninterventional CUP of avelumab 1LM conducted among 464 patients with la/mUC in Italy

Characteristic	Evaluable patients (n=414)
Age, median (interquartile range), years	71 (64-76)
Sex, n (%)	
Male	328 (79.2)
Female	86 (20.8)
ECOG PS, n (%)	
0	293 (70.8)
1	120 (29.0)
Not reported	1 (0.2)
Site of primary tumor, n (%)	
Upper urinary tract	123 (29.7)
Lower urinary tract	286 (69.1)
Not reported	5 (1.2)
Creatinine clearance, n (%)	
≤60 mL/min	151 (36.5)
>60 mL/min	226 (54.6)
Not reported	37 (8.9)

Characteristic	Evaluable patients (n=414)
Bellmunt prognostic risk factors, n (%)	
0 or 1	280 (67.6)
2	74 (17.9)
≥3	23 (5.6)
Not reported	37 (8.9)
1L chemotherapy regimen, n (%)	
Cisplatin + gemcitabine	184 (44.4)
Carboplatin + gemcitabine	221 (53.4)
MVAC	1 (0.2)
Other	8 (1.9)
No. of 1L chemotherapy cycles, median	5
Best response to 1L chemotherapy, n (%)	
CR	42 (10.1)
PR	235 (56.8)
SD	137 (33.1)

1L, first line; CR, complete response; CUP; compassionate use program; ECOG PS, Eastern Cooperative Oncology Group performance status; MVAC, methotrexate, vinblastine, doxorubicin, and cisplatin; PR, partial response; SD, stable disease.

Antonuzzo, L., et al., ESMO Real World Data and Digital Oncology, 2024. 5: p. 100068.

Multicenter, retrospective study based on data from medical charts of 350 patients with la/mUC in Japan
Study period: February 2021, to December 2023.

JAVEMACS Chart Review: Baseline Characteristics at Avelumab 1LM Initiation (1/2)

Characteristic	Overall population (n=350)
Age, median (interquartile) [range], years	73 (67-78) [43-93]
<65 years, n (%)	61 (17.4)
≥65 and <75 years, n (%)	145 (41.4)
≥75 and <80 years, n (%)	87 (24.9)
≥80 years, n (%)	57 (16.3)
Sex, n (%)	
Male	259 (74.0)
Female	91 (26.0)
BMI (kg/m²), n (%)	
<18.5	20 (5.7)
≥18.5 and <25	229 (65.4)
≥25	76 (21.7)
Unknown	25 (7.1)

Characteristic	Overall population (n=350)
Smoking status, n (%)	
Yes	228 (65.1)
No	110 (31.4)
Unknown	12 (3.4)
ECOG Performance Status, n (%)	
0	284 (81.1)
1	56 (16.0)
≥2	6 (1.7)
Unknown	4 (1.1)
Site of Primary Tumor, n (%)	
Ureter or renal pelvis	168 (48.0)
Bladder	177 (50.6)
Urethra	5 (1.4)

1L, first line; 1LM, first lime maintenance; BMI, body mass index; ECOG, Eastern Cooperative Oncology Group.

Kitamura H, et al. Presented at the ASCO Genitourinary Cancers Symposium (Abstract No. 701), February 13-15, 2025; San Francisco, CA.

Multicenter, retrospective study based on data from medical charts of 350 patients with la/mUC in Japan
Study period: February 2021, to December 2023.

JAVEMACS Chart Review: Baseline Characteristics at Avelumab 1LM Initiation (2/2)

Characteristic	Overall population (n=350)
Metastatic site, n (%)	
Metastases	293 (83.7%)
Regional lymph node	184 (52.6%)
Distant lymph node	105 (30.0%)
Visceral	113 (32.3%)
Lung	75 (21.4%)
Liver	24 (6.9%)
Peritoneum	14 (4.0%)
Other organs	10 (2.9%)
Bone	55 (15.7%)
Other	12 (3.4%)
Year of avelumab initiation, n (%)	
2021	115 (32.9%)
≥2022	235 (67.1%)

1L, first line; 1LM, first line maintenance.
Kitamura H, et al. Presented at the ASCO Genitourinary Cancers Symposium (Abstract No. 701), February 13-15, 2025; San Francisco, CA.

JAVEMACS Chart Review: Characteristics of 1L PBC Prior to Avelumab 1LM

Multicenter, retrospective study based on data from medical charts of 350 patients with la/mUC in Japan
Study period: February 2021, to December 2023.

Characteristic	Overall population (n=350)
1L PBC regimen, n (%)	
Cisplatin + gemcitabine	196 (56.0%)
Carboplatin + gemcitabine	116 (33.1%)
ddMVAC	32 (9.1%)
Others	6 (1.7%)
No. of cycles, n (%)	
Median (IQR)	4 (4-4)
1-3	68 (19.4%)
4	205 (58.6%)
5/6	61 (17.4%)
≥7	16 (4.6%)
Duration of 1L PBC*	
Median (IQR), weeks	19.3 (15.4-24.1)
Platinum dose reduction, n (%)	114 (32.6%)
First cycle when platinum dose reduction occurred, median (IQR)	2 (1-2)

Characteristic	Overall population (n=350)
Best Response to 1L PBC, n (%)	
CR	32 (9.1%)
PR	180 (51.4%)
SD	138 (39.4%)
Treatment-Free Interval, n (%)**	
Median (IQR), weeks	5.1 (3.6-7.1)
<4 weeks	95 (27.1%)
4-10 weeks	218 (62.3%)
>10 weeks	36 (10.3%)

*From start of 1L PBC to start of avelumab maintenance. 1 patient with unknown start and end dates of 1L PBC was excluded. **From last dose of 1L PBC to start of avelumab maintenance.
1L, first line; 1LM, first line maintenance; CR, complete response; ddMVAC, dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin; IQR, interquartile range; PBC, platinum-based chemotherapy; PR, partial response; SD, stable disease.
Kitamura H, et al. Presented at the ASCO Genitourinary Cancers Symposium (Abstract No. 701), February 13-15, 2025; San Francisco, CA.

Tempus I: Baseline Characteristics (1/2)

Retrospective, observational study based on deidentified patient-level structured and unstructured data from the Tempus database, a US longitudinal EHR database (N= 821). Study period: January 1, 2016 to February 23, 2022.

	Overall cohort, N=821
Race, n (%)	
American Indian or Alaska Native	1 (0.1)
Black or African American	53 (6.5)
Other	48 (5.8)
Unknown	200 (24)
White	519 (63)
Region, n (%)	
Midwest	214 (46)
Northeast	33 (7)
South	108 (23)
West	115 (24)
Unknown	351 (43)
Data source, n (%)	
Academic centers	221 (27)
Community centers	169 (21)
Other	426 (52)
Unknown	5 (1)

	Overall cohort, N=821
Systemic treatment, n (%)	
Treated, curated	634 (77)
Untreated	187 (23)
Follow-up from la/mUC diagnosis, median (range), months	9.20 (3.71-18.80)
Age at la/mUC diagnosis, median (IQR), years	69 (62-76)
Year of la/mUC diagnosis, n (%)	
2016	90 (11)
2017	95 (12)
2018	110 (13)
2019	182 (22)
2020	207 (25)
2021	129 (16)
2022	8 (1)
Sex, n (%)	
Male	600 (73)
Female	221 (27)

IQR, interquartile range; la/mUC, locally advanced/metastatic urothelial carcinoma; PD-L1, programmed death ligand 1.
Kearney M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Tempus I: Baseline Characteristics (2/2)

Retrospective, observational study based on deidentified patient-level structured and unstructured data from the Tempus database, a US longitudinal EHR database (N= 821). Study period: January 1, 2016 to February 23, 2022.

	Overall cohort, N=821
Smoking status, n (%)	
History of smoking	361 (63)
Never	212 (37)
Unknown	248
Histology type, n (%)	
Ambiguous carcinoma	131 (16)
Other	30 (3.7)
Squamous	2 (0.2)
Transitional	658 (80)
Histopathology grade, n (%)	
Grade 2 (moderately differentiated)	8 (1.6)
Grade 3 (poorly differentiated)	67 (14)
Grade 4 (undifferentiated)	1 (0.2)
High	416 (84)
Low	1 (0.2)
Unknown	328

	Overall cohort, N=821
Comorbidities, n (%)	
1	147 (37)
2	86 (22)
3	54 (14)
4+	106 (27)
Unknown	428
Death records, n (%)	305 (37)
PD-L1 status, n (%)	
Negative	123 (64)
Positive	70 (36)
Unknown	628

IQR, interquartile range; la/mUC, locally advanced/metastatic urothelial carcinoma; PD-L1, programmed death ligand 1.
Kearney M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Tempus II: Baseline Characteristics (1/2)

Retrospective, observational study based on deidentified patient-level structured and unstructured data from the Tempus database, a US longitudinal EHR database (N= 1939).
Study period: January 1, 2016 to March 13, 2023.

Characteristic	Overall cohort, N=1,939
Follow-up from la/mUC diagnosis, median (range), months	19 (17-22)
Age at la/mUC diagnosis, median (range), years	70 (62-76)
Year of la/mUC diagnosis, n (%)	
2016	112 (6)
2017	161 (8)
2018	219 (11)
2019	381 (20)
2020	429 (22)
2021	431 (22)
2022	199 (10)
2023	7 (<1)
Sex, n (%)	
Male	1,431 (74)
Female	508 (26)

Characteristic	Overall cohort, N=1,939
Race, n (%)	
White	1,212 (63)
Black or African American	100 (5)
Asian	39 (2)
American Indian or Alaska Native	6 (<1)
Native Hawaiian or Other Pacific Islander	2 (<1)
Other race	70 (4)
Unknown	510 (26)
Region, n (%)	
Midwest	337 (43)
South	203 (26)
West	175 (22)
Northeast	65 (8)
Unknown	1,159

la/mUC, locally advanced/metastatic urothelial carcinoma.
Carson K, et al. Poster presented at: ESMO Congress (Abstract 2387P); October 20-24, 2023; Madrid, Spain.

Tempus II: Baseline Characteristics (2/2)

Retrospective, observational study based on deidentified patient-level structured and unstructured data from the Tempus database, a US longitudinal EHR database (N= 1939).
Study period: January 1, 2016 to March 13, 2023.

Characteristic	Overall cohort, N=1,939
Data source, n (%)	
Academic centers	567 (40)
Community centers	375 (26)
Other	474 (33)
Histology type, n (%)	
Transitional	1,713 (88)
Ambiguous carcinoma	152 (8)
Other	73 (4)
Comorbidities, n (%)	
1	347 (48)
2	142 (20)
3	74 (10)
4+	154 (21)
Unknown	1,222
Deceased records, n (%)	795 (41)

la/mUC, locally advanced/metastatic urothelial carcinoma.
Carson K, et al. Poster presented at: ESMO Congress (Abstract 2387P); October 20-24, 2023; Madrid, Spain.

Flatiron II: Baseline Characteristics (1/2)

Noninterventional, retrospective cohort study of patients with aUC in the US using Flatiron Health's EHR database from approximately 280 cancer clinics (N= 998).
Study period: January 1, 2017, to December 31, 2021.

Characteristic	rwCR/rwPR	rwSD
Total, n (%)	752 (100)	246 (100)
Age at aUC diagnosis, years		
Mean (SD)	69.6 (9.0)	69.6 (10.1)
Sex, n (%)		
Female	209 (27.8)	54 (22.0)
Male	543 (72.2)	192 (78.0)
Race, n (%)		
Asian	12 (1.6)	2 (0.8)
Black or African American	40 (5.3)	11 (4.5)
Hispanic or Latino	1 (0.1)	1 (0.4)
White	493 (65.6)	169 (68.7)
Other race	127 (16.9)	41 (16.7)
Unknown	79 (10.5)	22 (8.9)

Characteristic	rwCR/rwPR	rwSD
Region of residence, n (%)		
Northeast	88 (11.7)	39 (15.9)
Midwest	107 (14.2)	30 (12.2)
South	350 (46.5)	114 (46.3)
West	115 (15.3)	33 (13.4)
Other territories	3 (0.4)	3 (1.2)
Unknown	89 (11.8)	27 (11.0)

aUC, advanced urothelial carcinoma; EHR, electronic health record, rwCR, real-world complete response; rwPR, real-world partial response; rwSD; real-world stable disease.
Moon HH, et al. Poster presented at: ASCO Annual Meeting; June 2-6, 2023; Chicago, IL.

Flatiron II: Baseline Characteristics (2/2)

Noninterventional, retrospective cohort study of patients with aUC in the US using Flatiron Health's EHR database from approximately 280 cancer clinics (N= 998).
Study period: January 1, 2017, to December 31, 2021.

Characteristic	rwCR/rwPR	rwSD
Total, n (%)	752 (100)	246 (100)
Site of disease, n (%)		
Bladder	553 (73.5)	183 (74.4)
Renal pelvis	112 (14.9)	38 (15.4)
Ureter	84 (11.2)	21 (8.5)
Urethra	3 (0.4)	4 (1.6)
Disease grade, n (%)		
High grade (G2/G3/G4)	652 (86.7)	210 (85.4)
Low grade (G1)	35 (4.7)	12 (4.9)
Unknown/ not documented	65 (8.6)	24 (9.8)
Stage at initial UC diagnosis, n (%)		
Stage 0	4 (0.5)	1 (0.4)
Stage I	17 (2.3)	4 (1.6)
Stage II	38 (5.1)	10 (4.1)
Stage III	82 (10.9)	27 (11.0)
Stage IV	340 (45.2)	94 (38.2)
Unknown/ not documented	271 (36.0)	110 (44.7)

Characteristic	rwCR/rwPR	rwSD
ECOG PS at aUC diagnosis date, n (%)		
0	264 (35.1)	82 (33.3)
1	254 (33.8)	85 (34.6)
2+	63 (8.4)	25 (10.2)
Unknown/ not documented	171 (22.7)	54 (22.0)
PD-L1 at aUC diagnosis date, n (%)		
Negative	89 (11.8)	35 (14.2)
Positive	38 (5.1)	12 (4.9)
Unknown/ not documented	625 (83.1)	199 (80.9)
GFR level at aUC diagnosis date, mL/min/1.73m^2		
Mean (SD)	67.8 (23.8)	65.5 (26.9)
Treatment group, n (%)		
Carboplatin-based	311 (41.4)	110 (44.7)
Cisplatin-based	441 (58.6)	135 (54.9)
Oxaliplatin-based	0	1 (0.4)

aUC, advanced urothelial carcinoma; ECOG PS, Eastern Cooperative Oncology Group performance status; EHR, electronic health record, G, grade; GFR, glomerular filtration rate; rwCR, real-world complete response; rwPR, real-world partial response; rwSD; real-world stable disease; UC, urothelial carcinoma.
Moon HH, et al. Poster presented at: ASCO Annual Meeting; June 2-6, 2023; Chicago, IL.

Flatiron III: Baseline Characteristics (1/3)

Noninterventional, retrospective cohort study of patients with la/mUC in the US using the nationwide Flatiron Health EHR–derived database (N= 214).
Study period: January 1, 2011 to December 21, 2022.

Characteristic	Avelumab 1LM N=214
Age at diagnosis, years	
Mean (SD)	69 (9.2)
Year of index date, n (%)	
2020	43 (20.1)
2021	75 (35.0)
2022	96 (44.9)
Sex, n (%)	
Female	50 (23.4)
Male	164 (76.6)
Race, n (%)	
White	142 (66.4)
Unknown	33 (15.4)
Other	31 (14.5)
Black or African American	6 (2.8)
Asian	2 (0.9)

Characteristic	Avelumab 1LM N=214
Region of residence, n (%)	
South	99 (46.3)
Northeast	37 (17.3)
Midwest	30 (14.0)
Unknown	24 (11.2)
West	23 (10.7)
Other	1 (0.5)
Setting, n (%)	
Community	191 (89.3)
Academic	18 (8.4)
Both	5 (2.3)
Follow-up, median (IQR), months	8.7 (4.5-15.7)

1L, first line; 1LM, first-line maintenance; EHR, electronic health record; G, grade; IQR, interquartile range; la/mUC, locally advanced or metastatic urothelial carcinoma.
Moon HH, et al. Curr Oncol. 2024;31(9):5662-5676.

Flatiron III: Baseline Characteristics (2/3)

Noninterventional, retrospective cohort study of patients with la/mUC in the US using the nationwide Flatiron Health EHR–derived database (N= 214).
Study period: January 1, 2011 to December 21, 2022.

Characteristic	Avelumab 1LM N=214
Site of disease, n (%)	
Bladder	158 (73.8)
Renal pelvis	30 (14.0)
Ureter	24 (11.2)
Urethra	2 (0.9)
Disease grade, n (%)	
High (G2/G3/G4)	174 (81.3)
Low (G1)	12 (5.6)
Unknown/not documented	28 (13.1)
Stage at initial diagnosis, n (%)	
0	2 (0.9)
I	3 (1.4)
II	9 (4.2)
III	7 (3.3)
IV	99 (46.3)
Unknown/not documented	94 (43.9)

Characteristic	Avelumab 1LM N=214
ECOG performance status at diagnosis, n (%)	
0	69 (32.2)
1	96 (44.9)
2+	21 (9.8)
Unknown/ not documented	28 (13.1)
Treatment group in 1L, n (%)	
Cisplatin based	115 (53.7)
Carboplatin based	99 (46.3)
Body mass index category, n (%)	
Underweight (<18.5 kg/m^2)	9 (4.2)
Normal (18.5-24.9 kg/m^2)	69 (32.2)
Overweight (25-29.9 kg/m^2)	59 (27.6)
Obese (≥30 kg/m^2)	60 (28.0)
Unknown	17 (7.9)

1L, first line; 1LM, first-line maintenance; EHR, electronic health record; G, grade; la/mUC, locally advanced or metastatic urothelial carcinoma.

Moon HH, et al. Curr Oncol. 2024;31(9):5662-5676.

Flatiron III: Baseline Characteristics (3/3)

Noninterventional, retrospective cohort study of patients with la/mUC in the US using the nationwide Flatiron Health EHR–derived database (N= 214).
Study period: January 1, 2011 to December 31 2022.

Characteristic	Avelumab 1LM N=214
Site of metastases, n (%)	
Distant lymph node	122 (57.0)
Bone	63 (29.4)
Lung	58 (27.1)
Liver	37 (17.3)
Soft tissue	21 (9.8)
Peritoneum	8 (3.7)
Other	6 (2.8)
Pleura	5 (2.3)
Adrenal	5 (2.3)
Brain	2 (0.9)
Skin	1 (0.5)
Kidney	1 (0.5)

1L, first line; 1LM, first-line maintenance; EHR, electronic health record; G, grade; la/mUC, locally advanced or metastatic urothelial carcinoma.

Moon HH, et al. Curr Oncol. 2024;31(9):5662-5676.

Flatiron III Tumor Burden: Baseline Characteristics (1/2)

Subgroup analyses of a multicenter, retrospective cohort study in the US conducted in 290 patients with la/mUC having low tumor burden
Data cut-off: July 2023

Characteristic	N=290
Age, years	
Median (IQR)	71.0 (64.0-76.0)
Mean (SD)	70.0 (9.0)
Age group, n (%)	
18 to <45 years	4 (1.4)
45 to <55 years	14 (4.8)
55 to <65 years	52 (17.9)
65 to <75 years	122 (42.1)
≥75 years	98 (33.8)
Sex, n (%)	
Female	70 (24.1)
Male	220 (75.9)
Ethnicity, n (%)	
Hispanic or Latino	12 (4.1)
Not Hispanic or Latino	191 (65.9)
Unknown	87 (30.0)

Characteristic	N=290
Race, n (%)	
Asian	2 (0.7)
Black or African American	8 (2.8)
White	205 (70.7)
Other	27 (9.3)
Unknown	48 (16.6)
ECOG PS, n (%)	
0	95 (32.8)
1	132 (45.5)
≥2	23 (7.9)
Missing	40 (13.8)

1LM, first-line maintenance; ECOG PS, Eastern Cooperative Group performance score; IQR, interquartile range; SD, standard deviation.
Moon HH, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 764) February 13-15, 2025; San Francisco, CA.

Flatiron III Tumor Burden: Baseline Characteristics (2/2)

Subgroup analyses of a multicenter, retrospective cohort study in the US conducted in 290 patients with la/mUC having low tumor burden
Data cut-off: July 2023

Characteristic	N=290
Sites of metastases prior to avelumab 1LM, n (%)	
Visceral	
Lung	77 (26.6)
Liver	49 (16.9)
Soft tissue	31 (10.7)
Peritoneum	8 (2.8)
Pleura	8 (2.8)
Adrenal	6 (2.1)
Brain	2 (0.7)
Kidney	1 (0.3)
Ovary	1 (0.3)
Other	8 (2.8)
Nonvisceral	
Distant lymph node	172 (59.3)
Bone	74 (25.5)
Skin	2 (0.7)
None	24 (8.3)

1LM, first-line maintenance.
Moon HH, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 764) February 13-15, 2025; San Francisco, CA.

Flatiron Safety: Baseline Characteristics (1/3)

Retrospective, observational safety study of 5,235 patients with la/mUC on 1L treatment in the US
Study period: January 2016 to October 2023

Characteristic	Overall (N=5,235)	EV + P (n=198)	ICI monotherapy (n=2,146)	Without avelumab 1LM		With avelumab 1LM	
				Cis-based CT (n=1,372)	Carbo-based CT (n=1,140)	Cis-based CT (n=197)	Carbo-based CT (n=182)
Age at index date, median (IQR), years	74 (66-80)	76 (70-82)	78 (71-83)	68 (61-74)	74 (67-79)	69 (62-74)	73 (67-78)
Age category at index date, n (%)							
18-64 years	1,051 (20)	30 (15)	240 (11)	497 (36)	188 (16)	65 (33)	31 (17)
65-74 years	1,692 (32)	52 (26)	539 (25)	541 (39)	402 (35)	88 (45)	70 (38)
75-79 years	1,070 (20)	48 (24)	432 (20)	233 (17)	287 (25)	29 (15)	41 (23)
80+ years	1,422 (27)	68 (35)	935 (43)	101 (7)	263 (23)	15 (8)	40 (22)
Race, n (%)							
Black or African American	252 (5)	16 (8)	83 (4)	77 (6)	66 (6)	8 (4)	<6
White	3,647 (70)	135 (68)	1,510 (70)	979 (71)	752 (66)	137 (70)	134 (74)
Other	671 (13)	6 (3)	285 (13)	171 (12)	174 (15)	19 (10)	16 (9)
Unknown	665 (13)	41 (21)	268 (12)	145 (11)	148 (13)	33 (17)	>26
Ethnicity, n (%)							
Hispanic or Latino	202 (4)	<8	70 (3)	59 (4)	52 (5)	9 (5)	8 (4)
Not Hispanic or Latino	3,859 (74)	>140	1,541 (72)	1,072 (78)	844 (74)	132 (67)	126 (69)
Unknown	1,174 (22)	50 (25)	535 (25)	241 (18)	244 (21)	56 (28)	48 (26)
Sex, n (%)							
Female	1,406 (27)	44 (22)	599 (28)	381 (28)	296 (26)	51 (26)	35 (19)
Male	3,828 (73)	154 (78)	1,547 (72)	990 (72)	844 (74)	146 (74)	147 (81)
Unknown	1 (<1)	0	0	1 (<1)	0	0	0

1LM, first-line maintenance; Carbo, carboplatin; Cis, cisplatin; CT, chemotherapy; EV + P, enfortumab vedotin + pembrolizumab; ICI, immune checkpoint inhibitor; IQR, interquartile range.

Nizam A, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 759) February 13-15, 2025; San Francisco, CA.

Flatiron Safety: Baseline Characteristics (2/3)

Retrospective, observational safety study of 5,235 patients with Ia/mUC on 1L treatment in the US
Study period: January 2016 to October 2023

Characteristic	Overall (N=5,235)	EV + P (n=198)	ICI monotherapy (n=2,146)	Without avelumab 1LM		With avelumab 1LM	
				Cis-based CT (n=1,372)	Carbo-based CT (n=1,140)	Cis-based CT (n=197)	Carbo-based CT (n=182)
Practice type, n (%)							
Academic	743 (14)	49 (25)	272 (13)	237 (17)	143 (13)	32 (16)	10 (5)
Community	4,112 (79)	132 (67)	1,744 (81)	1,013 (74)	914 (80)	150 (76)	159 (87)
Both	380 (7)	17 (9)	130 (6)	122 (9)	83 (7)	15 (8)	13 (7)
Primary site, n (%)							
Lower tract	4,049 (77)	165 (83)	1,666 (78)	1,120 (82)	824 (72)	137 (70)	137 (75)
Upper tract	1,179 (23)	26 (13)	480 (22)	252 (18)	316 (28)	60 (30)	45 (25)
Unknown/not documented	7 (<1)	7 (4)	0	0	0	0	0
Disease grade, n (%)							
Low (grade 1)	233 (4)	10 (5)	96 (4)	44 (3)	65 (6)	7 (4)	11 (6)
High (grade 2-4)	4,458 (85)	170 (86)	1,831 (85)	1,218 (89)	919 (81)	167 (85)	153 (84)
Unknown/not documented	544 (10)	18 (9)	219 (10)	110 (8)	156 (14)	23 (12)	18 (10)
PD-(L)1 status, n (%)							
Positive	245 (5)	15 (8)	120 (6)	38 (3)	36 (3)	12 (6)	24 (13)
Negative	446 (9)	18 (9)	198 (9)	75 (5)	114 (10)	25 (13)	16 (9)
Unknown/not tested	4,544 (87)	165 (83)	1,828 (85)	1,259 (92)	990 (87)	160 (81)	142 (78)

1LM, first-line maintenance; Carbo, carboplatin; Cis, cisplatin; CT, chemotherapy; EV + P, enfortumab vedotin + pembrolizumab; ICI, immune checkpoint inhibitor; PD-(L)1, programmed cell death 1 ligand 1

Nizam A, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 759) February 13-15, 2025; San Francisco, CA.

Flatiron Safety: Baseline Characteristics (3/3)

Retrospective, observational safety study of 5,235 patients with la/mUC on 1L treatment in the US
Study period: January 2016 to October 2023

Characteristic	Overall (N=5,235)	EV + P (n=198)	ICI monotherapy (n=2,146)	Without avelumab 1LM		With avelumab 1LM	
				Cis-based CT (n=1,372)	Carbo-based CT (n=1,140)	Cis-based CT (n=197)	Carbo-based CT (n=182)
Stage at initial diagnosis, n (%)							
I	93 (2)	2 (1)	41 (2)	24 (2)	18 (2)	1 (1)	7 (4)
II	442 (8)	23 (12)	295 (14)	62 (5)	46 (4)	6 (3)	10 (5)
III	531 (10)	17 (9)	202 (9)	216 (16)	77 (7)	8 (4)	11 (6)
IV	1,823 (35)	62 (31)	530 (25)	562 (41)	487 (43)	115 (58)	67 (37)
Unknown/Not documented	2,346 (45)	94 (47)	1078 (50)	508 (37)	512 (45)	67 (34)	87 (48)
ECOG PS at 1L, n (%)							
0	1,524 (29)	55 (28)	468 (22)	555 (40)	287 (25)	94 (48)	65 (36)
1	1,930 (37)	72 (36)	785 (37)	482 (35)	442 (39)	72 (37)	77 (42)
≥2	1,781 (34)	71 (36)	893 (42)	335 (24)	411 (36)	31 (16)	40 (22)
Unknown	0	0	0	0	0	0	0
Follow-up, median (IQR), months	9 (3-20)	7 (3-9)	5 (1-17)	11 (5-28)	8 (3-18)	17 (10-26)	14 (9-23)

1L, first line; 1LM, first-line maintenance; Carbo, carboplatin; Cis, cisplatin; CT, chemotherapy; EV + P, enfortumab vedotin + pembrolizumab; ECOG PS, Eastern Cooperative Group performance score; IQR, interquartile range; ICI, immune checkpoint inhibitor.

Nizam A, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 759) February 13-15, 2025; San Francisco, CA.

PATRIOT II: Baseline Characteristics (1/2)

Observational, retrospective chart review study patients with la/mUC in routine clinical practice in the United States (N= 160).

	All patients (N=160)
Age, median (range), years	70 (40-90)
Sex, n (%)	
Male	123 (76.9)
Female	37 (23.1)
Race, n (%)	
White	143 (89.4)
Black	5 (3.1)
Asian	4 (2.5)
American Indian/Alaskan native	1 (0.6)
Other/unknown	7 (4.4)
Ethnicity, n (%)	
Hispanic or Latino	7 (4.4)
Non-Hispanic or Latino	125 (78.1)
Unknown	28 (17.5)

	All patients (N=160)
ECOG performance status, n (%)	
0	68 (42.5)
1	53 (33.1)
≥2	12 (7.5)
Unknown	27 (16.9)
Creatinine clearance, n (%)	
≥60 mL/min	64 (40.0)
<60 mL/min	66 (41.3)
Unknown	30 (18.8)

ECOG, Eastern Cooperative Group.

Grivas P, et al. Clin Genitourin Cancer. 2024;22(6):102238.

PATRIOT II: Baseline Characteristics (2/2)

Observational, retrospective chart review study patients with la/mUC in routine clinical practice in the United States (N= 160).

	All patients (N=160)
PD-L1 status, n (%)	
Positive	44 (27.5)
Negative	33 (20.6)
Unknown	83 (51.9)
Site of metastasis at the start of 1L PBC, n (%)	
Visceral*	70 (43.8)
Nonvisceral	51 (31.9)
None	23 (14.3)
Unknown	16 (10.0)
1L PBC regimen	
Cisplatin†, n (%)	100 (62.5)
No. of cycles, median (IQR)	4 (3-6)
Carboplatin + gemcitabine, n (%)	60 (37.5)
No. of cycles, median (IQR)	5 (4-6)

	All patients (N=160)
Best response to 1L PBC, n (%)	
Complete response or partial response	130 (81.3)
Stable disease	17 (10.6)
Unknown	13 (8.1)

*Does not include bone. †Encompasses any cisplatin-based regimen.
Percentages may not add up to 100 because of rounding.
1L, first line; IQR, interquartile range; PBC, platinum-based chemotherapy.
Grivas P, et al. Clin Genitourin Cancer. 2024;22(6):102238.

SPEAR Bladder II: Baseline Characteristics

Retrospective, observational study in 1,658 patients with la/mUC using the US Oncology Network iKnowMed™ EHR

Patient characteristics	Overall study population (n=1,658)	IO monotherapy (n=683)	Cisplatin-based PBC only (n=305)	Carboplatin-based PBC only (n=233)	Cisplatin-based PBC with avelumab 1LM (n=93)	Carboplatin-based PBC with avelumab 1LM (n=93)	ADCs (n=147)	Other* (n=80)
Age at diagnosis, median (range), years	73 (31-90+)	78 (41-90+)	67 (40-87)	74 (31-90+)	67 (47-84)	74 (50-89)	73 (49-90+)	72 (40-90+)
Male, n (%)	1,238 (74.7)	497 (72.8)	246 (80.7)	173 (74.2)	67 (72.0)	75 (80.6)	112 (76.2)	54 (67.5)
Race, n (%)								
White	1,216 (73.3)	506 (74.1)	223 (73.1)	171 (73.4)	74 (79.6)	71 (76.3)	96 (65.3)	58 (72.5)
Other	192 (11.6)	71 (10.4)	37 (12.1)	28 (12.0)	11 (11.8)	8 (8.6)	18 (12.2)	15 (18.8)
Not documented	250 (15.1)	106 (15.5)	45 (14.8)	34 (14.6)	8 (8.6)	14 (15.1)	33 (22.4)	7 (8.8)
ECOG PS, n (%)								
0	213 (12.8)	81 (11.9)	56 (18.4)	27 (11.6)	19 (20.4)	7 (7.5)	14 (9.5)	8 (10.0)
1	568 (34.3)	232 (34.0)	93 (30.5)	78 (33.5)	41 (44.1)	37 (39.8)	44 (29.9)	31 (38.8)
2+	157 (9.5)	92 (13.5)	10 (3.3)	26 (11.1)	<5	<5	15 (10.2)	6 (7.5)
No information	720 (43.4)	278 (40.7)	146 (47.9)	102 (43.8)	30 (32.3)	45 (48.4)	74 (50.3)	35 (43.8)
Follow-up duration, median (range), months	9.0 (0.1-50.4)	9.4 (0.7-49.2)	9.5 (0.1-49.0)	8.2 (0.3-50.4)	12.2 (3.1-41.0)	12.7 (2.1-45.1)	5.2 (0.5-34.7)	8.2 (1.0-43.7)
Tobacco use, n (%)								
No history	279 (16.8)	115 (16.8)	58 (19.0)	34 (14.6)	15 (16.1)	20 (21.5)	19 (12.9)	13 (16.3)
Current	136 (8.2)	39 (5.7)	43 (14.1)	25 (10.7)	9 (9.7)	<5	7 (4.8)	7 (8.8)
Former	435 (26.2)	159 (23.3)	98 (32.1)	61 (26.2)	33 (35.5)	29 (31.2)	28 (19.0)	23 (28.8)
No information	808 (48.7)	370 (54.2)	106 (34.8)	113 (48.5)	36 (38.7)	42 (45.2)	93 (63.3)	37 (46.3)

1L, first line; 1LM, first-line maintenance; ADC, antibody-drug conjugate; ECOG PS, Eastern Cooperative Oncology Group performance status; EHR, electronic health record; IO, immuno-oncology; la/mUC, locally advanced or metastatic urothelial carcinoma; PBC, platinum-based chemotherapy.
*Other includes gemcitabine, erdafitinib, fluorouracil, capecitabine, and methotrexate, as monotherapy or combination

Sura S, et al. Current Oncology. 2025;32(4):187.

IMPACT UC III : Baseline Characteristics (1/2)

Retrospective cohort study in 2,820 patients with la/mUC using the Carelon Research's HIRD and health plan's Cancer Care Quality Program data in the United States

	All cohorts (n=2,820)	1L PBC (n=1,044)*	1L PBC + avelumab 1LM (n=157)†	1L IO monotherapy (n=1,099)	Other 1L therapies (n=677)
Age at index, median (IQR), years	70 (62-79)	65 (59-74)	66 (60-73)	76 (67-82)	69 (62-77)
Male sex, n (%)	1,951 (69.2)	664 (63.6)	125 (79.6)	791 (72.0)	496 (73.3)
Race and ethnicity: white (non-Hispanic or Latino), n (%)	2,058 (87.2)	767 (85.3)	123 (89.1)	783 (89.5)	508 (86.7)
Payer type, n (%)					
Commercial health plan	1,480 (52.5)	680 (65.1)	102 (65.0)	435 (39.6)	365 (53.9)
Medicare Advantage health plan	695 (24.7)	270 (25.9)	42 (26.8)	233 (21.2)	192 (28.4)
Other Medicare (supplemental) health plan	645 (22.9)	94 (9.0)	13 (8.3)	431 (39.2)	120 (17.7)

- Avelumab 1LM uptake from 2020-2023 by year was 10.8% (June-December 2020), 29.9% (2021), 34.4% (2022), and 24.8% (January-August 2023); 38.9% of patients were still receiving avelumab 1LM at the end of the study period

1L, first line; 1LM, first-line maintenance; ddMVAC, dose-dense methotrexate, vinblastine, doxorubicin, cisplatin; ECOG, Eastern Cooperative Oncology Group; HIRD; Healthcare Integrated Research Database; IO, immuno-oncology; IQR, interquartile range; PBC, platinum-based chemotherapy; SD, standard deviation.
*1L PBC cohort refers to all patients who received carboplatin, cisplatin, and ddMVAC systemic therapies. †1L PBC + avelumab 1LM is a subgroup of the 1L PBC group. ‡Diabetes with chronic complications and diabetes without chronic complications are mutually exclusive.
Moon H., et al. Presented at: ASCO QCS, (Poster No. 390), September 27-28, 2024; San Francisco, CA, USA.

IMPACT UC III : Baseline Characteristics (2/2)

Retrospective cohort study in 2,820 patients with la/mUC using the Carelon Research's HIRD and health plan's Cancer Care Quality Program data in the United States

	All cohorts (n=2,820)	1L PBC (n=1,044)*	1L PBC + avelumab 1LM (n=157)†	1L IO monotherapy (n=1,099)	Other 1L therapies (n=677)
ECOG performance score 0/1, n (%)	1,246 (91.2)	578 (93.5)	93 (94.9)	367 (86.8)	301 (92.6)
Charlson comorbidity Index, mean (SD)	1.55 (1.57)	1.37 (1.49)	1.40 (1.56)	1.75 (1.63)	1.51 (1.56)
Congestive heart failure, n (%)	348 (12.3)	103 (9.9)	13 (8.3)	170 (15.5)	75 (11.1)
Peripheral vascular disease, n (%)	644 (22.8)	207 (19.8)	29 (18.5)	295 (26.8)	142 (21.0)
Cerebrovascular disease, n (%)	321 (11.4)	80 (7.7)	11 (7.0)	165 (15.0)	76 (11.2)
Chronic pulmonary disease, n (%)	815 (28.9)	289 (27.7)	40 (25.5)	328 (29.9)	198 (29.3)
Diabetes without chronic complications, n (%)‡	715 (25.4)	255 (24.4)	28 (17.8)	288 (26.2)	172 (25.4)
Diabetes with chronic complications, n (%)‡	375 (13.3)	118 (11.3)	12 (7.6)	175 (15.9)	82 (12.1)
Renal disease, n (%)	853 (30.3)	240 (23.0)	42 (26.8)	451 (41.0)	162 (23.9)
Mild liver disease, n (%)	635 (22.5)	235 (22.5)	37 (23.6)	226 (20.6)	174 (25.7)

1L, first line; 1LM, first-line maintenance; ddMVAC, dose-dense methotrexate, vinblastine, doxorubicin, cisplatin; ECOG, Eastern Cooperative Oncology Group; HIRD; Healthcare Integrated Research Database; IO, immuno-oncology; IQR, interquartile range; PBC, platinum-based chemotherapy; SD, standard deviation.
*1L PBC cohort refers to all patients who received carboplatin, cisplatin, and ddMVAC systemic therapies. †1L PBC + avelumab 1LM is a subgroup of the 1L PBC group. ‡Diabetes with chronic complications and diabetes without chronic complications are mutually exclusive.
Moon H., et al. Presented at: ASCO QCS, (Poster No. 390), September 27-28, 2024; San Francisco, CA, USA.

Bakaloudi et al: Baseline Characteristics (1/2)

Multicenter retrospective cohort study of real-world patient characteristics and clinical outcomes with avelumab switch maintenance (N= 108).

	Overall population, N=108
Median age of cancer diagnosis (min, max)	69 (31.3, 96.2)
Sex, n (%)	
Male	87 (80.6)
Female	21 (19.4)
Race, n (%)	
White	100 (92.6)
Not white	6 (5.6)
Unknown	2 (1.9)
Smoking history, n (%)	
Yes	63 (58.3)
No	43 (39.8)
Missing	2 (1.9)
Tumor site, n (%)	
Lower urinary tract	92 (85.2)
Upper urinary tract	16 (14.8)

1L, first-line treatment; aUC, advanced urothelial carcinoma; CR, complete response; ECOG PS, Eastern Cooperative Group performance status; PBC, platinum-based chemotherapy; PR, partial response; SD, stable disease; UC, urothelial carcinoma.

Bakaloudi DR, et al. Clin Genitourin Cancer. 2023;S1558-7673(23)00147-7.

Bakaloudi et al: Baseline Characteristics (2/2)

Multicenter retrospective cohort study of real-world patient characteristics and clinical outcomes with avelumab switch maintenance (N= 108).

	Overall population, N=108
Pure UC histology, n (%)	
Yes	85 (78.7)
No	23 (21.3)
ECOG PS at PBC start, n (%)	
0	51 (47.2)
1	38 (35.2)
2	3 (2.8)
Missing	16 (14.8)
Cycles of 1L PBC, n (%)	
>4 cycles	62 (57.4)
≤4 cycles	42 (38.9)
Missing	4 (3.7)
Liver metastases, n (%)	
No	95 (88)
Yes	13 (12)

	Overall population, N=108
Weeks from last PBC to avelumab initiation, n (%)	
≤3 weeks	18 (16.7)
4-10 weeks	76 (70.3)
>10 weeks	14 (13)
Platinum agent, n (%)	
Carboplatin	37 (34.3)
Cisplatin	71 (65.7)
Best response to PBC, n (%)	
CR	18 (16.7)
PR	69 (63.9)
SD	21 (19.4)

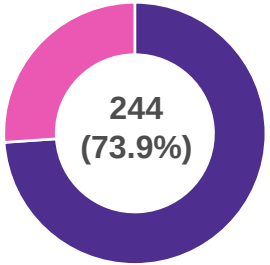
1L, first-line treatment; aUC, advanced urothelial carcinoma; CR, complete response; ECOG PS, Eastern Cooperative Group performance status; PBC, platinum-based chemotherapy; PR, partial response; SD, stable disease; UC, urothelial carcinoma.

Bakaloudi DR, et al. *Clin Genitourin Cancer*. 2023;S1558-7673(23)00147-7.

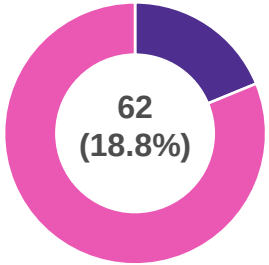
AVENANCE: Subsequent 2L Treatments

Ongoing, real-world, ambispective study in patients with aUC who have not progressed with PBC in France (N= 595).
Study period: July 13, 2021, to December 7, 2023.

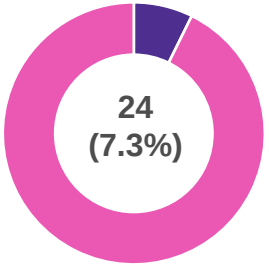
330 patients (55.5%) of the effectiveness population received 2L treatment after avelumab



244 (73.9%) received chemotherapy, including platinum-based chemotherapy (81, 24.5%) and other chemotherapy (163, 49.4%)



62 (18.8%) received an ADC, including enfortumab vedotin (56, 17.0%) and sacituzumab govitecan (6, 1.8%)



24 (7.3%) received other treatments

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in France and may not reflect US clinical practice. Exploratory analysis of mOS measured from the start of 1L platinum-based chemotherapy among those without disease progression and for patients who went on to recent 2L EV post-avelumab may be subject to immortal time bias and will need to be confirmed by additional studies.

Limitations : Conducted in France and may not reflect US clinical practice. Exploratory analysis of mOS measured from the start of 1L platinum-based chemotherapy among those without disease progression and for patients who went on to recent 2L EV post-avelumab may be subject to immortal time bias and will need to be confirmed by additional studies.
2L, second-line treatment; ADC, antibody-drug conjugate.
Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 561) January 25-27, 2024; San Francisco, CA.

AVENANCE Low Tumor Burden Subgroups: Subsequent 2L Treatments

Post hoc analysis of ongoing, real-world, ambispective study in patients with aUC who have not progressed with PBC in France and had low tumor burden at start of PBC (n=186)
Study start: July 13, 2021; Data cut-off: December 2, 2024

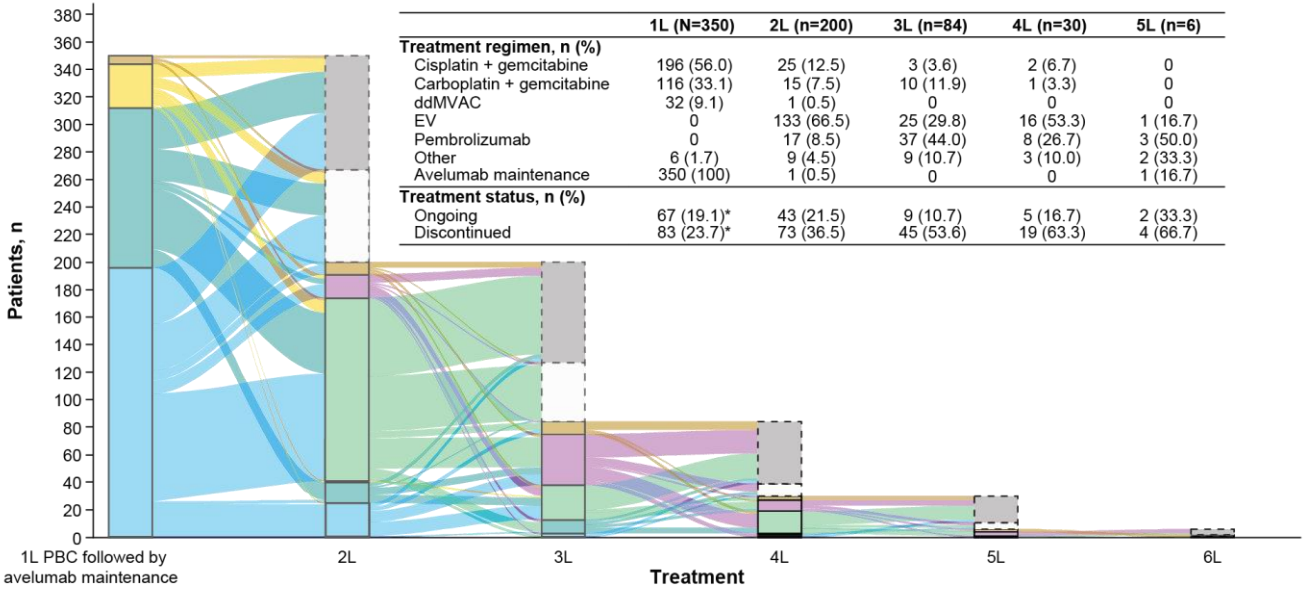
	Locally advanced disease (n=47)	Nonvisceral metastases (n=79)	Lymph node-only metastases (n=60)
Received subsequent treatment, n (%)	16 (34.0)	45 (57.0)	33 (55.0)
Chemotherapy	12 (25.5)	24 (30.4)	18 (30.0)
Enfortumab vedotin	3 (6.4)	12 (15.2)	8 (13.3)
Other ADC	0 (0.0)	1 (1.3)	1 (1.7)
Other treatment	1 (2.1)	8 (10.1)	6 (10.0)

Limitations
- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis.
- Conducted in France and may not reflect US clinical practice.

1LM, first line maintenance; 2L, second line; ADC, antibody-drug conjugate.
Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 718) February 13-15, 2025; San Francisco, CA

Multicenter, retrospective study based on data from medical charts of 350 patients with Ia/mUC in Japan
Study period: February 2021, to December 2023.

JAVEMACS Chart Review: Treatment Patterns in Patients Treated With Avelumab 1LM



	1L (N=350)	2L (n=200)	3L (n=84)	4L (n=30)	5L (n=6)
Treatment regimen, n (%)					
Cisplatin + gemcitabine	196 (56.0)	25 (12.5)	3 (3.6)	2 (6.7)	0
Carboplatin + gemcitabine	116 (33.1)	15 (7.5)	10 (11.9)	1 (3.3)	0
ddMVAC	32 (9.1)	1 (0.5)	0	0	0
EV	0	133 (66.5)	25 (29.8)	16 (53.3)	1 (16.7)
Pembrolizumab	0	17 (8.5)	37 (44.0)	8 (26.7)	3 (50.0)
Other	6 (1.7)	9 (4.5)	9 (10.7)	3 (10.0)	2 (33.3)
Avelumab maintenance	350 (100)	1 (0.5)	0	0	1 (16.7)
Treatment status, n (%)					
Ongoing	67 (19.1)*	43 (21.5)	9 (10.7)	5 (16.7)	2 (33.3)
Discontinued	83 (23.7)*	73 (36.5)	45 (53.6)	19 (63.3)	4 (66.7)

- 283 patients discontinued avelumab. Of this,
  - 200 (70.7%) received 2L treatment
  - 83 (29.3%) discontinued without 2L treatment

Limitations
- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in Japan and may not reflect US clinical practice

*Avelumab maintenance therapy.
1L, first line; 1LM, first line maintenance; 2L, second line; 3L, third line; 4L, fourth line; 5L, fifth line; 6L, sixth line; ddMVAC, dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin; EV, enfortumab vedotin.
Kitamura H, et al. Presented at the ASCO Genitourinary Cancers Symposium (Abstract No. 701), February 13-15, 2025; San Francisco, CA.

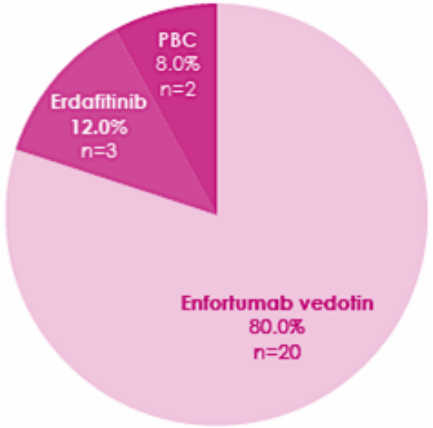
Tempus I: Treatment Patterns and Sequencing[1]

Retrospective, observational study based on deidentified patient-level structured and unstructured data from the Tempus database, a US longitudinal EHR database (N= 821). Study period: January 1, 2016 to February 23, 2022.

Treatment patterns across lines of treatment*

	All patients (N=821)	Most common tx
Untreated, n (%)	187 (22.8%)	N/A
Treated, n (%)		
1L tx	634 (77.2%)	Cisplatin + gemcitabine: 175 (27.6%) Carboplatin + gemcitabine: 124 (19.6%) Pembrolizumab: 108 (17.0%) MVAC: 45 (7.1%) Atezolizumab†: 35 (5.5%) Other: 147 (23.2%)
1LM tx	97 (24.6%) ‡	Avelumab: 63 (64.9%) Other IO therapy: 34 (35.1%)
2L tx	210 (33.1%)	Pembrolizumab: 57 (27.1%) Enfortumab vedotin: 35 (16.7%) Carboplatin + gemcitabine: 19 (9.0%) Atezolizumab†: 12 (5.7%) Avelumab: 14 (6.7%) Other: 73 (34.8%)
3L tx	65 (31.0%)	Enfortumab vedotin: 14 (21.5%) Pembrolizumab: 13 (20.0%) Avelumab: 8 (12.3%) Atezolizumab†: 7 (10.8%) Carboplatin + gemcitabine: 4 (6.2%) Other: 19 (29.2%)

2L treatments after progression on IO 1LM after avelumab approval



Limitations

- Data were collected primarily in the oncology clinical practice setting through routine clinical care and not for research purposes; therefore, nonrandom missingness may be present for several variables of interest, and data on healthcare received outside of the Tempus network of practices are not available.
- Complete medical history outside of the oncology EHR was not captured, which may lead to underreporting of treatments received. Algorithms used to identify 1LM and 2L agents may not reflect the definitions used in clinical practice.

*Data available is from both pre- and post- avelumab's 1LM US approval on June 30, 2020.[2] †Atezolizumab is no longer approved in the US to treat patients with locally advanced or metastatic urothelial carcinoma following the manufacturer's decision to withdraw its indication after consulting with the FDA. The withdrawal was made in accordance with the FDA's Accelerated Approval Program after results from the phase 3 IMvigor130 trial (NCT02807636) failed to meet the post-marketing requirement necessary to convert the accelerated approval for atezolizumab into regular approval.[3] ‡Percentage calculated from patients that received 1L platinum-based chemotherapy (n=395).

1L, first-line; 1LM, first-line maintenance; 2L, second-line; 3L, third-line; FDA, Food and Drug Administration; IO, immuno-oncology; MVAC, methotrexate, vinblastine, doxorubicin, cisplatin; tx, treatment.

1. Kearney M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA. 2. BAVENCIO® (avelumab). Prescribing information. Rockland, MA: EMD Serono, Inc. https://www.emdserono.com/us-en/pi/bavencio-pi.pdf 3. Cancer network. Atezolizumab no longer available in US for a certain type of bladder cancer. https://www.cancernetwork.com/view/atezolizumab-no-longer-available-in-us-for-a-certain-type-of-bladder-cancer. Accessed January 2024.

Tempus II: Treatment Patterns and Sequencing

Retrospective, observational study based on deidentified patient-level structured and unstructured data from the Tempus database, a US longitudinal EHR database (N= 1939). Study period: January 1, 2016 to March 13, 2023.

Treatment classes by line of therapy in patients who completed 1L treatment post avelumab approval

Treatment setting	Patients n/N (%)	Most common treatment, n (%)	
1L	974/974 (100)	• Cisplatin + gemcitabine: 297 (30) • Carboplatin + gemcitabine: 200 (21) • Pembrolizumab: 154 (16)	• MVAC: 60 (6) • Nivolumab: 36 (4) • Other: 227 (23)
1LM	219/644 (34)*	• Avelumab: 135 (62)	• Other IO therapy: 84 (38)
2L	258/974 (26)	• EV: 70 (27) • Pembrolizumab: 47 (18) • Carboplatin + gemcitabine: 34 (13) • Cisplatin + gemcitabine: 17 (7)	• Nivolumab: 17 (7) • Erdafitinib: 10 (4) • Gemcitabine: 10 (4) • Other: 53 (20)
3L	74/258 (29)	• EV: 15 (20) • Pembrolizumab: 10 (14) • Avelumab: 10 (14) • Erdafitinib: 9 (12)	• Sacituzumab govitecan: 7 (10) • Atezolizumab†: 4 (5) • Carboplatin + gemcitabine: 4 (5) • Other: 15 (20)

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Data were collected primarily in the oncology clinical practice setting through routine clinical care and not for research purposes; therefore, nonrandom missingness may be present for several variables of interest, and data on healthcare received outside of the Tempus network of practices are not available.
- Complete medical history outside of the oncology EHR was not captured, which may lead to underreporting of treatments received .
- Algorithms used to identify 1LM and 2L agents may not reflect the definitions used in clinical practice. Patients who initiated 1L systemic therapy later in the study period may not have had enough follow-up time to observe 2L and subsequent treatment rates, which may have led to underestimates in these lines of treatment.
- Similarly, the study was limited in its ability to comprehensively understand the use of avelumab in 1LM as it was approved by the FDA on June 30, 2020

*Percentage calculated from patients who received 1L platinum-based chemotherapy. †Atezolizumab is no longer approved in the US to treat patients with locally advanced or metastatic urothelial carcinoma following the manufacturer's decision to withdraw its indication after consulting with the FDA. The withdrawal was made in accordance with the FDA's Accelerated Approval Program after results from the phase 3 IMvigor130 trial (NCT02807636) failed to meet the postmarketing requirement necessary to convert the accelerated approval for atezolizumab into regular approval.
1LM, first-line maintenance; 2L, second-line; EV, enfortumab vedotin; NR, not reached; PBC, platinum-based chemotherapy; rwOS, real-world overall survival; rwPFS, real-world progression-free survival.
Carson K, et al. Poster presented at: ESMO Congress (Abstract 2387P); October 20-24, 2023; Madrid, Spain.

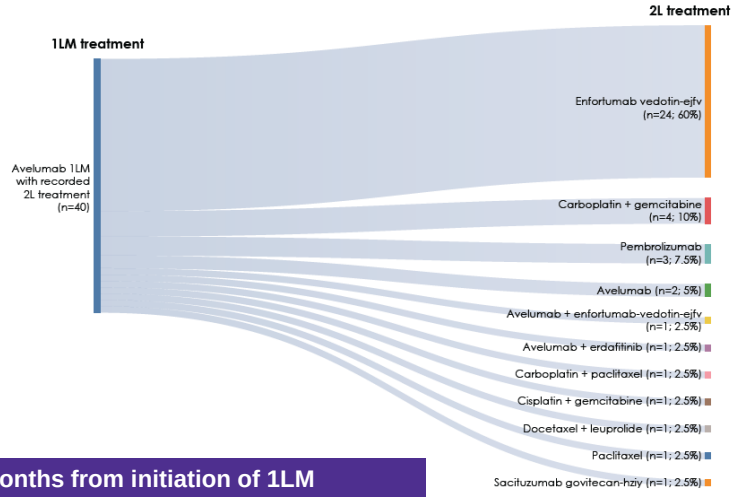
Flatiron II: Avelumab 1LM and 2L in the post–FDA Approval Period

Noninterventional, retrospective cohort study of patients with aUC in the US using Flatiron Health's EHR database from approximately 280 cancer clinics (N= 998).
Study period: January 1, 2017, to December 31, 2021.

Summary of avelumab 1LM and 2L treatment

Treatment criteria	N (% previous step)
Total study population	1245 (100)
rwCR/PR or rwSD recorded during 1L PBC	998 (80.1)
Discontinued 1L PBC after avelumab 1LM approval (June 30, 2020)	339 (34.0)
Initiated avelumab 1LM	97 (28.6)
2L treatment received after avelumab 1LM	
Received	40 (41.2)
Not received/not reported*	57 (58.8)
2L treatment not received/reported but received avelumab within 4 weeks of study period end	40 (70.2)

Treatment sequence from avelumab 1LM to 2L



The median follow-up time for patients treated with avelumab 1LM was 7.5 months from initiation of 1LM

Limitations

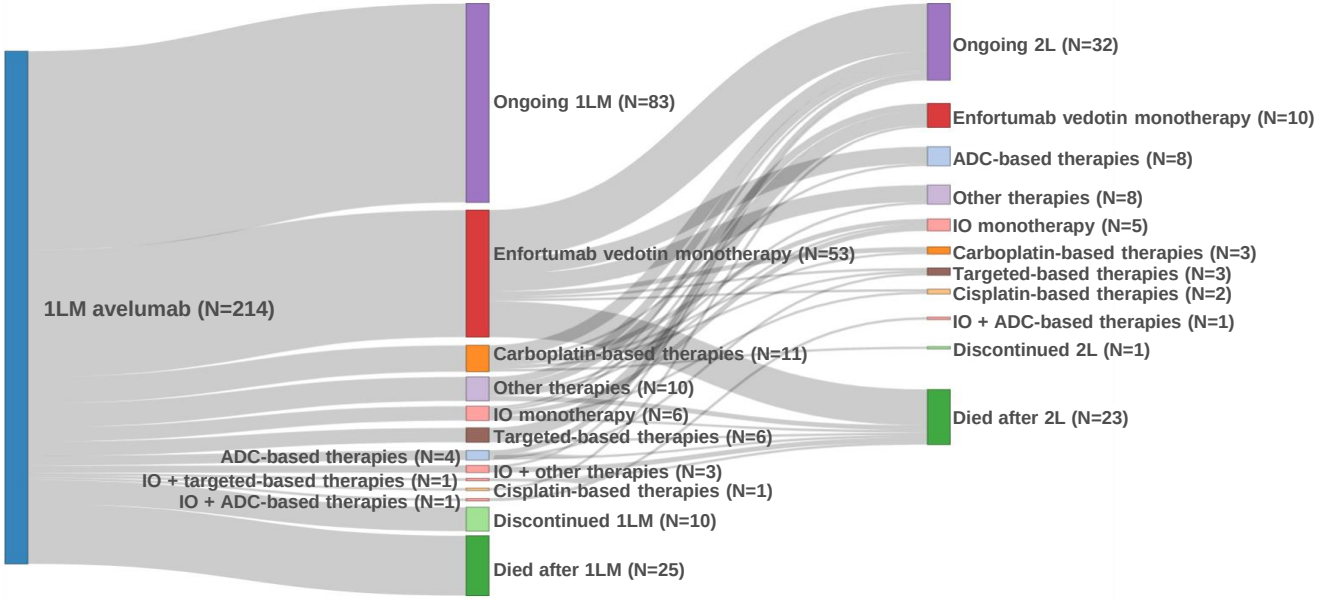
- Immortal time and selection biases since patients were required to have recorded response or SD, thus resulting in a potential overestimation of rwOS
- Retrospective study, lack of randomization, lack of granularity in specific data points (eg, site of metastasis, laboratory values), lack of central scan review, residual confounding, and short duration of study period post approval of avelumab 1LM by the FDA
- This study could not estimate true rwPFS, given that a 1L progression-free cohort was used to evaluate the avelumab 1LM-eligible population; only PFS after completion of 1L PBC was estimated

*Patients who initiated avelumab 1LM may still be receiving treatment, but data were not available.
1LM, first-line maintenance; 2L, second-line; FDA, Food and Drug Administration; rwCR, real-world complete response; rwPR, real-world partial response; rwSD; real-world stable disease; PBC, platinum-based chemotherapy.
Moon HH, et al. Poster presented at: ASCO Annual Meeting; June 2-6, 2023; Chicago, IL.

Flatiron III: Treatment Sequencing

Noninterventional, retrospective cohort study of patients with la/mUC in the US using the nationwide Flatiron Health EHR–derived database (N= 214).
Study period: January 1, 2011 to December 31 2022.

Avelumab 1LM to 2L and 3L treatment regimens during the observation period



Limitations

- Findings may not be generalizable to other populations. The lack of patient randomization and selection bias. Data maybe underreported or missing. Data elements in Flatiron Health may not be reflective of real-world practice.

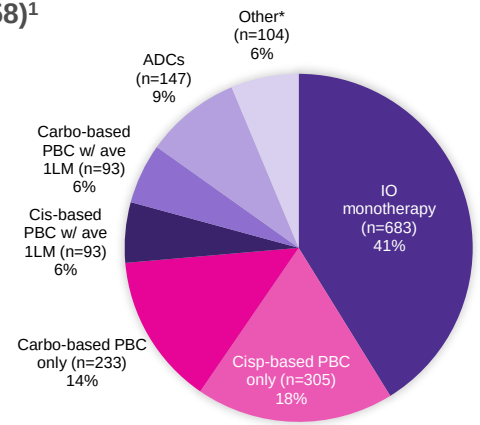
1LM, first-line maintenance; 2L, second-line; 3L, third-line; ADC, antibody-drug conjugate; IO, immuno-oncology.

Moon HH, et al. Curr Oncol. 2024;31(9):5662-5676.

SPEAR Bladder II: Treatment Sequencing

Retrospective, observational study in 1,658 patients with la/mUC using the US Oncology Network iKnowMed™ EHR

1L treatments received by patients with la/mUC (n=1,658)[1]



- Of patients in the overall study cohort who received 1L treatments (n=1,658), 598 (36.1%) and 196 (11.8%) received 2L and 3L treatments, respectively[1,2]

	2L treatments[2]	3L treatments[2]
Common treatments	• Pembrolizumab monotherapy (32.4%) • EV monotherapy (23.9%) • EV plus pembrolizumab (7.4%)	• EV monotherapy (32.1%) • Sacituzumab govitecan monotherapy (19.9%) • Pembrolizumab monotherapy (12.8%)

- Median follow-up time from index date was 9.0 months (range, 0.1-50.4)[2]
- Median follow-up from start of avelumab 1LM was 9.1 months (range, 0.5-42.2)[2]
- Rates of avelumab 1LM treatment among patients who received 1L PBC ranged from 25.0% in 2020 to 32.9% in 2023[2]
- **During the study observation period, 23.7% patients remained on avelumab 1LM** [2]
- **After discontinuation of avelumab 1LM, 43.5% patients received 2L treatment**
  - **The most common 2L treatment was EV monotherapy (59.3%)**[2]

Limitations

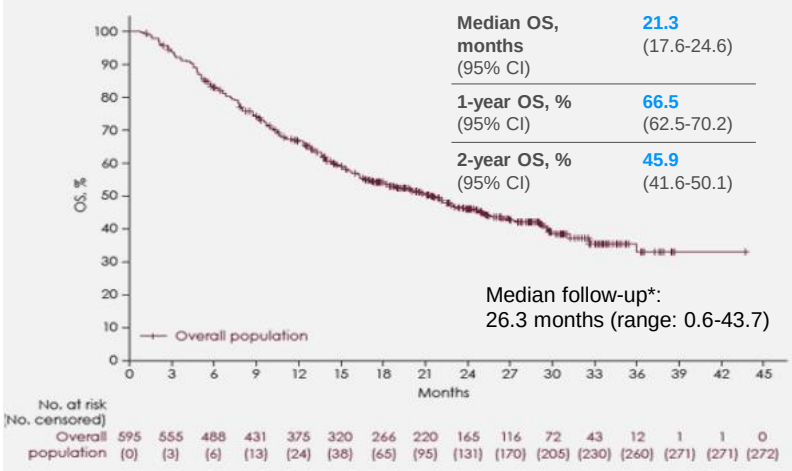
- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Data were collected primarily in the oncology clinical practice setting through routine clinical care and not for research purposes; therefore, nonrandom missingness may be present for several variables of interest, and data on healthcare received outside of the US Oncology Network iKnowMed™ EHR of practices are not available
- Complete medical history outside of the oncology EHR was not captured, which may lead to underreporting of treatments received
- Oral therapies were recorded in or prescribed through iKM, but whether those prescriptions were fulfilled was not observable
- The absence of disease progression in structured data may result in misclassification between avelumab as 1LM or 2L

1L, first line; 1LM, first-line maintenance; ADC, antibody-drug conjugate; ave, avelumab; Carbo, carboplatin; Cis, cisplatin; IO, immuno-oncology; la/mUC, locally advanced or metastatic urothelial carcinoma.
*Other includes: avelumab monotherapy (n=24), gemcitabine, erdafitinib, fluorouracil, capecitabine, and methotrexate, as monotherapy or combination (n=80)
1. Bupathi M., et al. Presented at: ASCO QCS, (Abstract No. F21), September 27-28, 2024; 2. San Francisco, CA, USA; Sura S, et al. Current Oncology. 2025;32(4):187.

AVENANCE: OS and PFS

Ongoing, real-world, ambispective study in patients with aUC who have not progressed with PBC in France (N= 595).
Study period: July 13, 2021, to December 7, 2023.

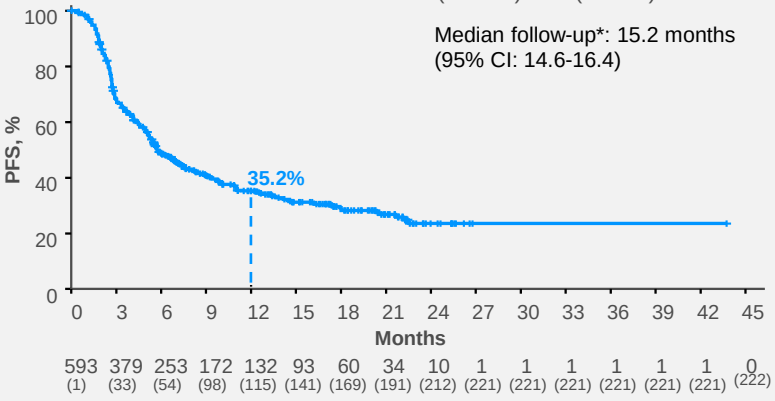
OS from start of avelumab 1L maintenance treatment[1]



Median OS, months (95% CI)	**21.3** (17.6-24.6)
1-year OS, % (95% CI)	**66.5** (62.5-70.2)
2-year OS, % (95% CI)	**45.9** (41.6-50.1)

Median follow-up*:
26.3 months (range: 0.6-43.7)

PFS from start of avelumab 1L maintenance[2]



Median PFS **5.7 months**
(95% CI) (5.3-7.0)

Median follow-up*: 15.2 months
(95% CI: 14.6-16.4)

Limitations

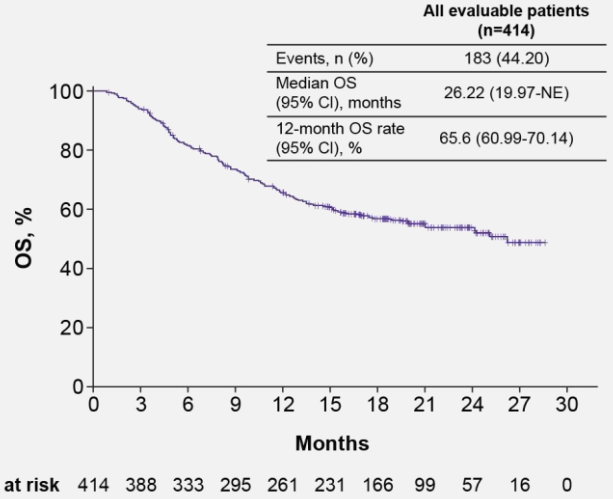
- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in France and may not reflect US clinical practice. Exploratory analysis of mOS measured from the start of 1L platinum-based chemotherapy among those without disease progression and for patients who went on to recent 2L EV post-avelumab may be subject to immortal time bias and will need to be confirmed by additional studies.

*By reverse Kaplan-Meier estimation.
1L, first-line; 1LM, first-line maintenance; aUC, advanced urothelial carcinoma; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; NE, not estimable; OS, overall survival; PBC, platinum-based chemotherapy; PFS, progression-free survival.
1. Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 561) January 25-27, 2024; San Francisco, CA. 2. Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 471.) February 16-18, 2023; San Francisco, CA.

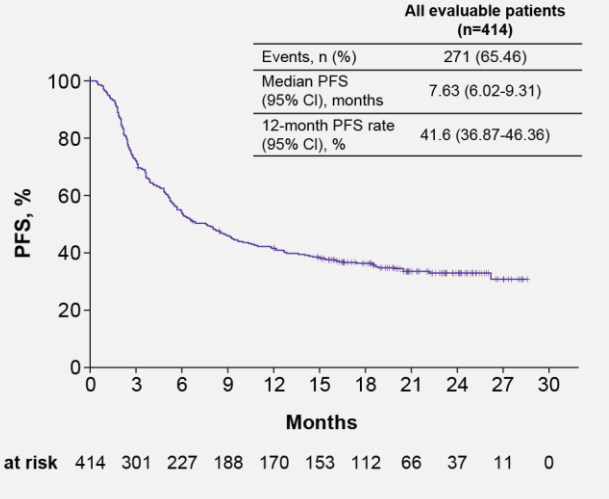
READY CUP: OS and PFS

Prospective, noninterventional CUP of avelumab 1LM conducted among 464 patients with la/mUC in Italy

OS from the start of avelumab 1L maintenance therapy in all evaluable patients



PFS from start of avelumab 1L maintenance therapy in all evaluable patients



Limitations

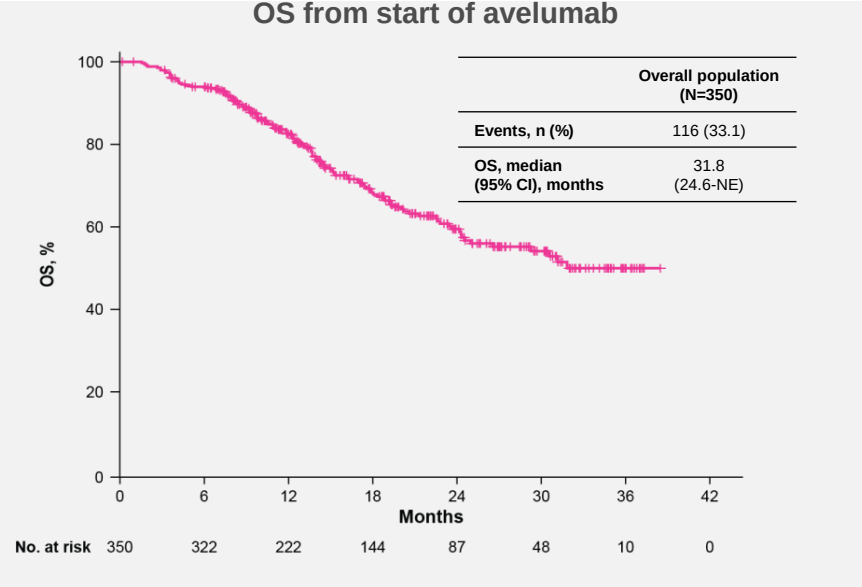
- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in Italy and may not reflect US clinical practice

1L, first line; 1LM, first line maintenance; CI, confidence interval; CUP, compassionate use program; la/mUC, locally advanced or metastatic NE, not estimable; OS, overall survival; PFS, progression-free survival; vs, versus

Antonuzzo, L., et al., ESMO Real World Data and Digital Oncology, 2024. 5: p. 100068.

JAVEMACS Chart Review: OS in the Overall Population

Multicenter, retrospective study based on data from medical charts of 350 patients with la/mUC in Japan
Study period: February 2021, to December 2023.



Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in Japan and may not reflect US clinical practice

Exploratory analyses of OS measured from the start of 1L PBC in this population of patients without disease progression after 1L PBC should be interpreted with caution.
Patients without a start date for 1L PBC were not included.
1L, first line; 1LM, first line maintenance; NE, not evaluable; OS, overall survival.
Kitamura H, et al. Presented at the ASCO Genitourinary Cancers Symposium (Abstract No. 701), February 13-15, 2025; San Francisco, CA.

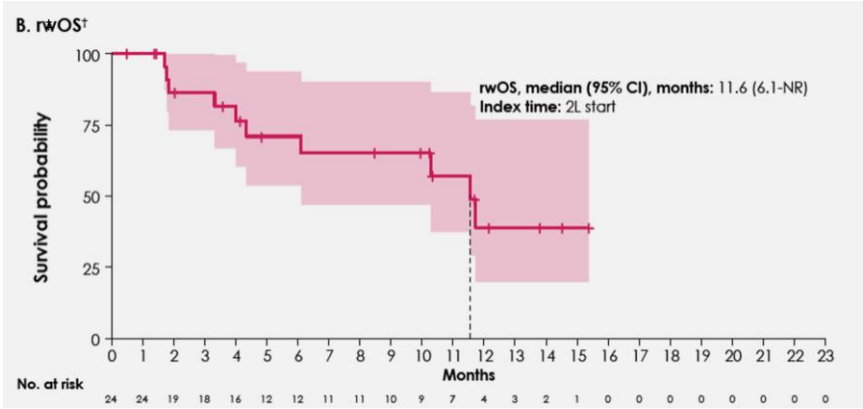
Tempus II: Overall Survival

Retrospective, observational study based on deidentified patient-level structured and unstructured data from the Tempus database, a US longitudinal EHR database (N= 1939).
Study period: January 1, 2016 to March 13, 2023.

Overall survival rates in patients: 1L PBC and avelumab 1LM

	1L PBC (n=644)*	Avelumab 1LM (n=135)†
Time on treatment, median (95% CI), months	2.73 (2.53-2.96)	3.85 (2.76-4.96)
rwOS (95% CI), %		
6-month landmark	82 (78-87)	80 (72-90)
12-month landmark	56 (50-63)	63 (52-75)
18-month landmark	42 (36-50)	43 (31-59)

OS: avelumab 1LM followed by 2L EV



Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Data were collected primarily in the oncology clinical practice setting through routine clinical care and not for research purposes; therefore, nonrandom missingness may be present for several variables of interest.
- Complete medical history outside of the Tempus database was not captured, which may lead to underreporting of treatments received.
- Algorithms used to identify 1LM and 2L agents may not reflect the definitions used in clinical practice. In addition, there was potential for misclassification based on the algorithms used.
- Patients who initiated 1L systemic therapy later in the study period may not have had enough follow-up for 2L and subsequent treatment rates to be observed

*Median follow-up from 1L PBC was 10.2 months. †Median follow-up from start of 1LM was 8.9 months. ‡This rwOS analysis included 26 of 33 patients receiving 2L EV after PBC and avelumab 1LM sequence. Not all 26 patients were at risk at time 0 due to the risk-set adjustment methodology.
1L, first-line; 1LM, first-line maintenance; 2L, second-line; HER, electronic health record; EV, enfortumab vedotin; NR, not reached; PBC, platinum-based chemotherapy; rw, real world; OS, overall survival.
Carson K, et al. Poster presented at: ESMO Congress (Abstract 2387P); October 20-24, 2023; Madrid, Spain.

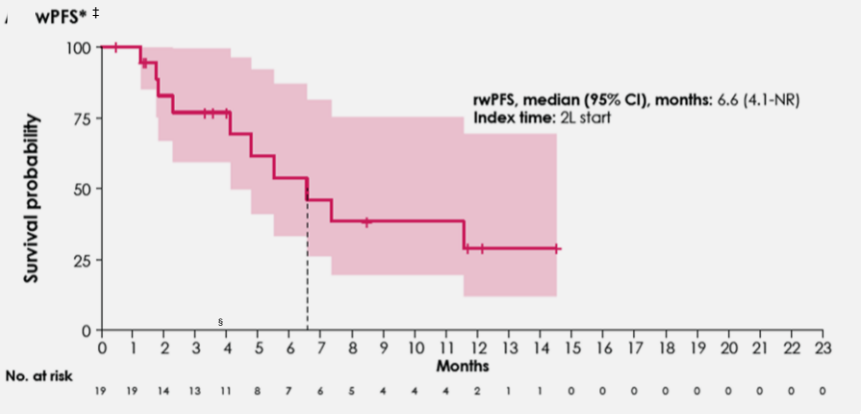
Tempus II: Progression-free Survival

Retrospective, observational study based on deidentified patient-level structured and unstructured data from the Tempus database, a US longitudinal EHR database (N= 1939).
Study period: January 1, 2016 to March 13, 2023.

Progression-free survival rates in patients: 1L PBC and avelumab 1LM

	1L PBC (n=644)*	Avelumab 1LM (n=135)†
Time on treatment, median (95% CI), months	2.73 (2.53-2.96)	3.85 (2.76-4.96)
rwPFS		
Median (95% CI), months	3.5 (3.3-4.1)	6.4 (4.6-NR)
3-month landmark (95% CI), %	65 (57-74)	73 (64-83)
6-month landmark (95% CI), %	10 (6-17)	52 (42-65)
12-month landmark (95% CI), %	2 (1-7)	40 (30-54)

PFS: avelumab 1LM followed by 2L EV



Limitations

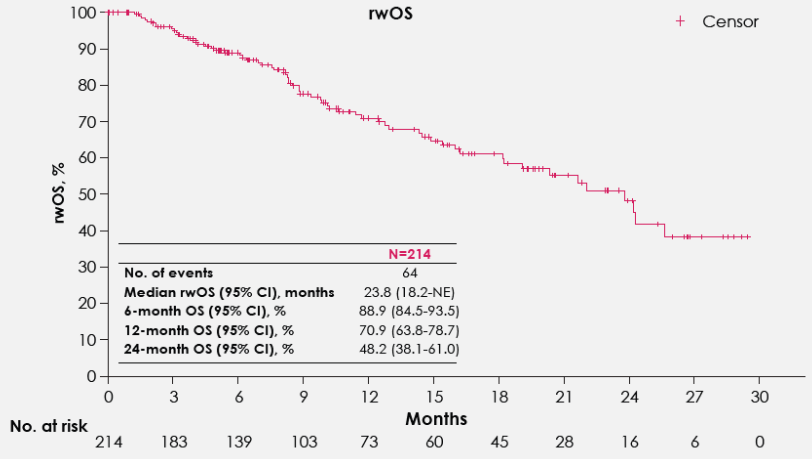
- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Data were collected primarily in the oncology clinical practice setting through routine clinical care and not for research purposes; therefore, nonrandom missingness may be present for several variables of interest.
- Complete medical history outside of the Tempus database was not captured, which may lead to underreporting of treatments received.
- Algorithms used to identify 1LM and 2L agents may not reflect the definitions used in clinical practice. In addition, there was potential for misclassification based on the algorithms used.
- Patients who initiated 1L systemic therapy later in the study period may not have had enough follow-up for 2L and subsequent treatment rates to be observed

*Median follow-up from 1L PBC was 10.2 months. †Median follow-up from start of 1LM was 8.9 months. ‡This rwPFS analysis included 20 of 33 patients receiving 2L EV after PBC and avelumab 1LM sequence. Not all 20 patients were at risk at time 0 due to the risk-set adjustment methodology.
1L, first- line; 1LM, first-line maintenance; 2L, second-line; EHR, electronic health record; EV, enfortumab vedotin; NR, not reached; PBC, platinum-based chemotherapy; rwPFS, real-world progression-free survival.
Carson K, et al. Poster presented at: ESMO Congress (Abstract 2387P); October 20-24, 2023; Madrid, Spain.

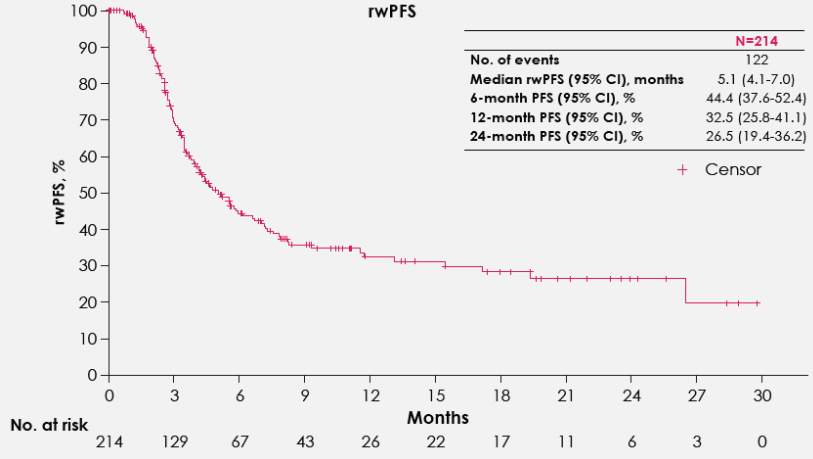
Flatiron III: OS and PFS from Avelumab 1LM Initiation

Noninterventional, retrospective cohort study of patients with la/mUC in the US using the nationwide Flatiron Health EHR–derived database (N= 214).
Study period: January 1, 2011 to December 31 2022

Real-world OS from avelumab 1LM initiation



Real-world PFS from avelumab 1LM initiation



Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Findings may not be generalizable to other populations. The lack of patient randomization and selection bias.
- Data maybe underreported or missing. Data elements in Flatiron Health may not be reflective of real-world practice.

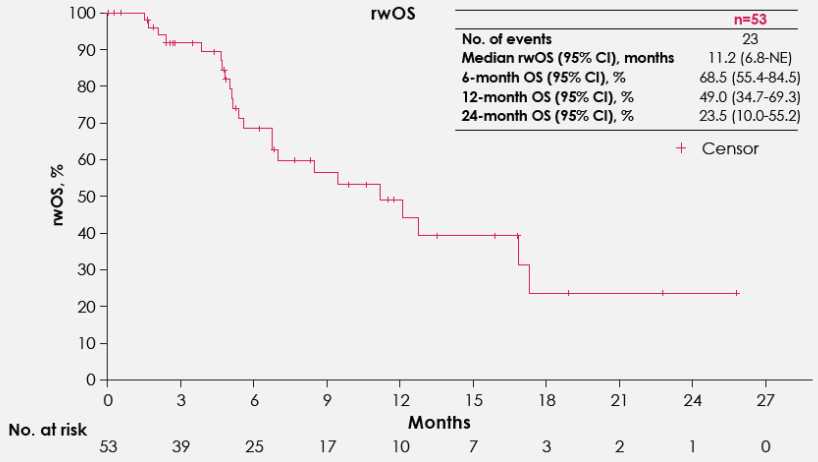
1LM, first line maintenance; EHR, electronic health record; CI, confidence interval; CUP, compassionate use program; la/mUC, locally advanced or metastatic urothelial carcinoma; NE, not estimable; OS, overall survival; PFS, progression-free survival; vs, versus

Antonuzzo, L., et al., ESMO Real World Data and Digital Oncology, 2024. 5: p. 100068.

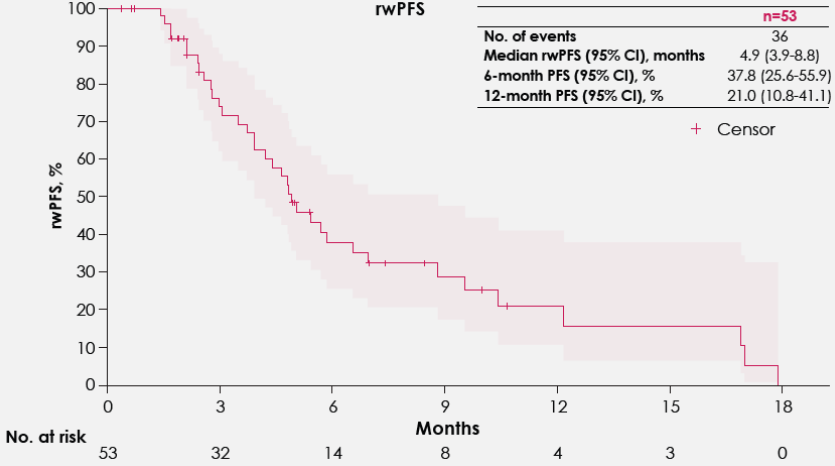
Flatiron III: OS and PFS from 2L Therapy Initiation

Noninterventional, retrospective cohort study of patients with la/mUC in the US using the nationwide Flatiron Health EHR–derived database (N= 214).
Study period: January 1, 2011 to December 31 2022.

Real-world OS from 2L EV monotherapy initiation



Real-world PFS from 2L EV monotherapy initiation



Limitations

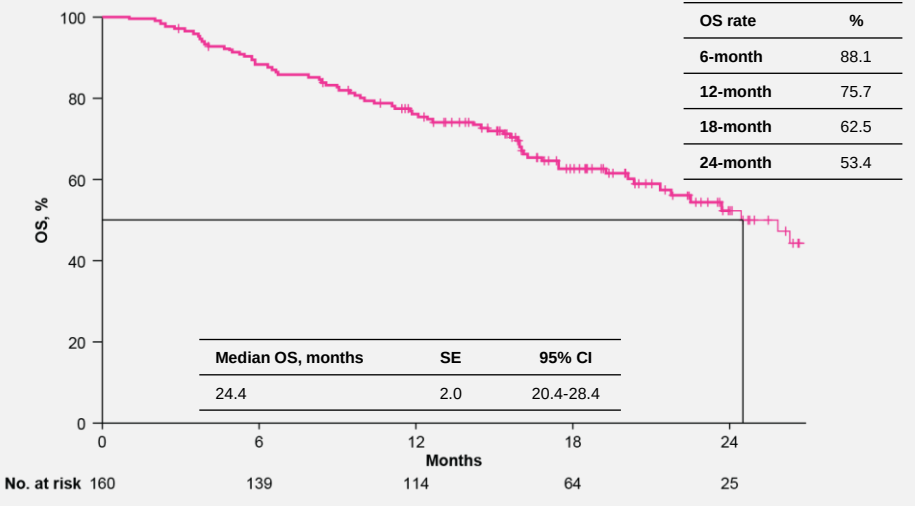
- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Findings may not be generalizable to other populations. The lack of patient randomization and selection bias. Data maybe underreported or missing.
- Data elements in Flatiron Health may not be reflective of real-world practice.

2L, second-line; CI, confidence interval; EV, enfortumab vedotin; NE, not estimable; OS, overall survival; PFS, progression-free survival; rwOS, real-world overall survival; rwPFS, real-world progression-free survival.
Moon HH, et al. Curr Oncol. 2024;31(9):5662-5676.

PATRIOT II: OS and PFS

Observational, retrospective chart review study patients with la/mUC in routine clinical practice in the United States (N= 160).

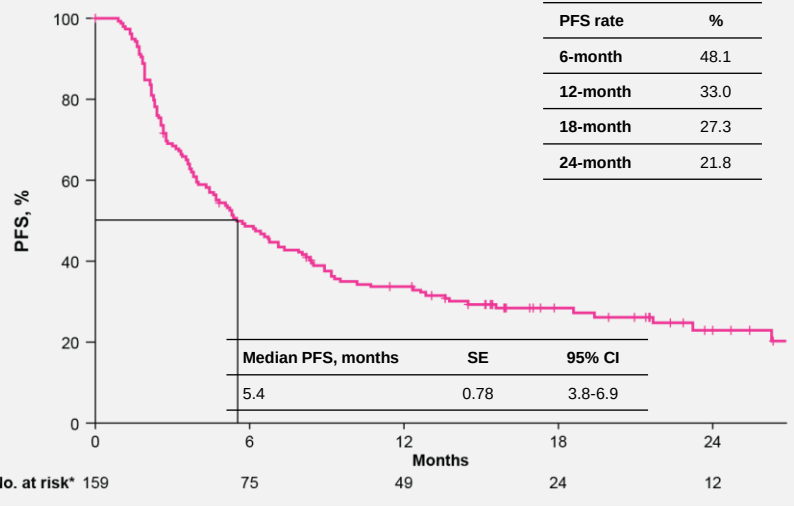
Real-world OS from the start of avelumab 1LM



OS rate	%
6-month	88.1
12-month	75.7
18-month	62.5
24-month	53.4

Median OS, months	SE	95% CI
24.4	2.0	20.4-28.4

Real-world PFS from the start of avelumab 1LM



PFS rate	%
6-month	48.1
12-month	33.0
18-month	27.3
24-month	21.8

Median PFS, months	SE	95% CI
5.4	0.78	3.8-6.9

Median follow-up was 16 months (IQR, 11-21 months)

Limitations

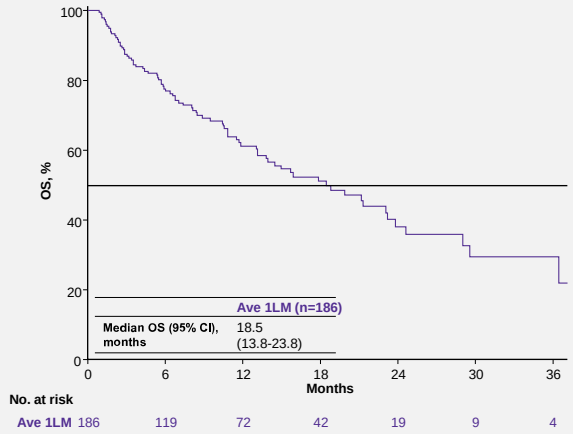
- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Studies using real-world data include lack of central imaging review, missing or unknown data, potential selection bias, and confounding factors due to the lack of randomization

1LM, first-line maintenance; IQR, interquartile range; OS, overall survival; PFS, progression-free survival.
*Date of progression was not available for 1 patient. Progression status was unknown for 3 patients; these patients were censored at the most recent follow-up date.
Grivas P, et al. Clin Genitourin Cancer. 2024;22(6):102238.

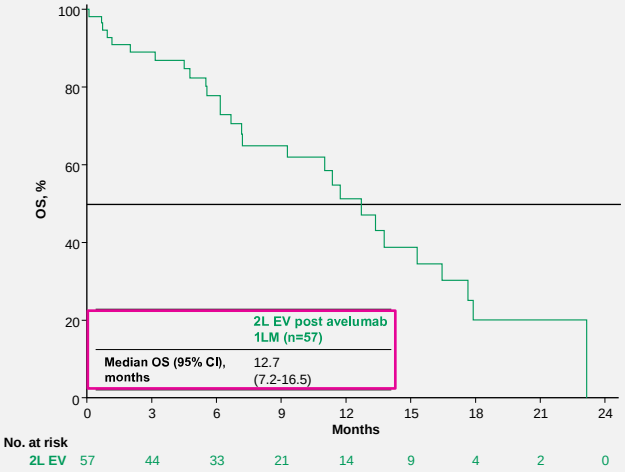
SPEAR Bladder II: Overall Survival

Retrospective, observational study in 1,658 patients with la/mUC using the US Oncology Network iKnowMed™ EHR

Median OS from the start of avelumab 1LM[1,2]



Median OS from the start of 2L EV after avelumab 1LM[1,2]



Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Data were collected primarily in the oncology clinical practice setting through routine clinical care and not for research purposes; therefore, nonrandom missingness may be present for several variables of interest, and data on healthcare received outside of the US Oncology Network iKnowMed™ EHR of practices are not available
- Complete medical history outside of the oncology EHR was not captured, which may lead to underreporting of treatments received
- Oral therapies were recorded in or prescribed through iKM, but whether those prescriptions were fulfilled was not observable
- The absence of disease progression in structured data may result in misclassification between avelumab as 1LM or 2L

1L, first line; 1LM, first-line maintenance; 2L, second line; ave, avelumab; Cis, cisplatin; Carbo, carboplatin; EHR, electronic health record; EV, enfortumab vedotin; la/mUC, locally advanced or metastatic urothelial carcinoma; OS, overall survival; PBC, platinum-based chemotherapy.

1. Sura S, et al. Current Oncology. 2025;32(4):187; 2. Sura S, et al. Current Oncology. (suppl) 2025;32(4):187.

IMPACT UC III: Overall Survival (1/2)

Retrospective cohort study in 2,820 patients with la/mUC using the Carelon Research's HIRD and health plan's Cancer Care Quality Program data in the United States

	1L PBC (n=1,044)	1L PBC + avelumab 1LM (n=157)	1L IO monotherapy (n=1,099)	Other 1L therapies (n=677)
Median follow-up (IQR), months	11.2 (5.56-20.26)	14.6 (9.23-21.32)	8.6 (4.04-17.69)	10.1 (4.63-21.45)
Median TTNT (IQR), months	4.8 (2.76-8.28)	7.6 (6.21-12.25)	5.5 (2.76-11.04)	4.1 (1.38-7.59)
OS rates (95% CI), %				
1 year	74 (71-77)	84 (78-91)	60 (57-63)	72 (68-76)
2 year	56 (52-60)	68 (58-78)	47 (43-51)	57 (52-62)
3 year	45 (40-51)	65 (55-77)	36 (32-41)	49 (44-55)
Median OS (95% CI), months	29.7 (25.1-37.2)	NE (NE-NE)*	20.0 (17.1-25.6)	34.3 (25.6-NE)

Limitations

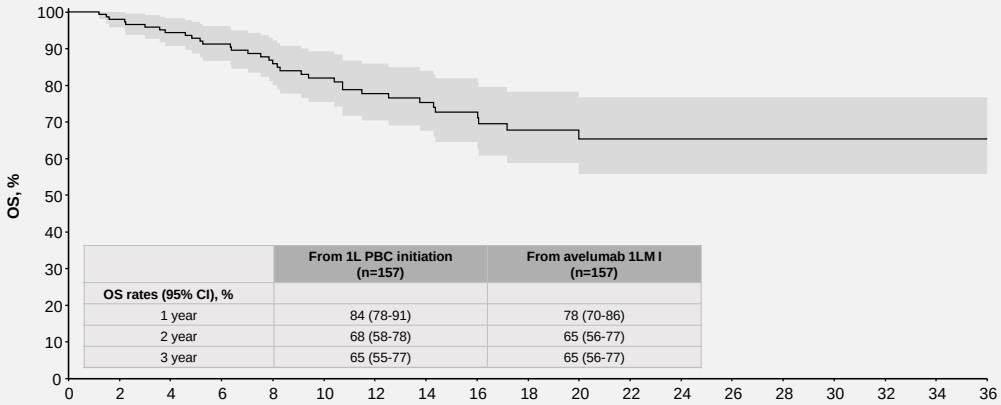
- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- The population in this analysis was queried from US commercially insured and Medicare Advantage enrollees with available clinical data from HIRD, which may limit the generalizability of these results for other population segments such as traditional fee-for-service Medicare and the uninsured
- Administrative claims data are primarily collected for billing and reimbursement purposes and are subject to potential coding biases, inconsistencies, and missing data
- Complete medical history outside of the oncology HIRD was not captured, which may lead to underreporting of treatments received
- Response data or eligibility for 1LM, and avelumab used in 2L could not be differentiated from that used in 1LM
- This was a descriptive study; thus, no comparative analyses were performed, no adjustment for baseline characteristics was made, and no logistic regression was undertaken

1L, first line; 1LM, first-line maintenance; 2L, second line; HIRD, Healthcare Integrated Research Database; IO, immuno-oncology; IQR, interquartile range; NE, not estimable; OS, overall survival; PBC, platinum-based chemotherapy; TTNT, time to next treatment.
*Median OS was not estimable because >50% of patients remained alive at the end of the study period.
Moon H., et al. Presented at: ASCO QCS, (Poster No. 390), September 27-28, 2024; San Francisco, CA, USA.

IMPACT UC III: Overall Survival (2/2)

Retrospective cohort study in 2,820 patients with la/mUC using the Carelon Research's HIRD and health plan's Cancer Care Quality Program data in the United States

Median OS for patients who received 1L PBC followed by avelumab 1LM*



	From 1L PBC initiation (n=157)	From avelumab 1LM I (n=157)
OS rates (95% CI), %		
1 year	84 (78-91)	78 (70-86)
2 year	68 (58-78)	65 (56-77)
3 year	65 (55-77)	65 (56-77)

- Median treatment-free interval from end of 1L PBC to start of avelumab 1LM was 2.7 weeks (IQR, 1.1-4.6)
- Median time on avelumab treatment was 5.0 months (IQR, 1.8-10.2)

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- The population in this analysis was queried from US commercially insured and Medicare Advantage enrollees with available clinical data from HIRD, which may limit the generalizability of these results for other population segments such as traditional fee-for-service Medicare and the uninsured
- Administrative claims data are primarily collected for billing and reimbursement purposes and are subject to potential coding biases, inconsistencies, and missing data
- Complete medical history outside of the oncology HIRD was not captured, which may lead to underreporting of treatments received
- Response data or eligibility for 1LM, and avelumab used in 2L could not be differentiated from that used in 1LM
- This was a descriptive study; thus, no comparative analyses were performed, no adjustment for baseline characteristics was made, and no logistic regression was undertaken

1L, first line; 1LM, first-line maintenance; HIRD; Healthcare Integrated Research Database; IQR, interquartile range; la/mUC, locally advanced or metastatic urothelial carcinoma; OS, overall survival; PBC, platinum-based chemotherapy.
*Median OS was not estimable because >50% of patients remained alive at the end of the study period.
Moon H., et al. Presented at: ASCO QCS, (Poster No. 390), September 27-28, 2024; San Francisco, CA, USA.

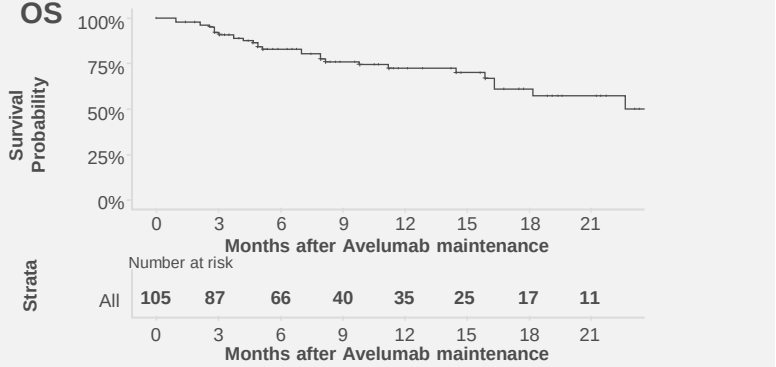
Bakaloudi et al: OS and PFS for the Entire Population

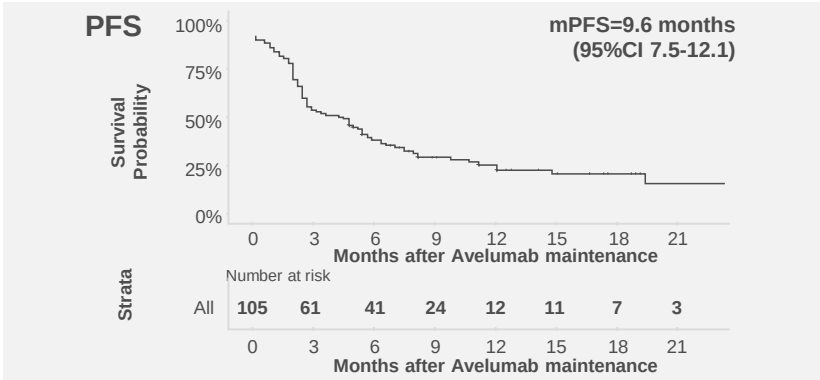
Multicenter retrospective cohort study of real-world patient characteristics and clinical outcomes with avelumab switch maintenance (N= 108).

OS and PFS at last follow-up:

- 76 (70.3%) patients were alive
- 30 (27.8%) patients had died
- 2 (1.9%) patients had unknown vital status

- Median OS: NR
  - OS rate at 1 year: 72.5% (CI: 63.2%-83.1%)
- Median PFS: 9.6 months (CI: 7.5-12.1)





Limitations

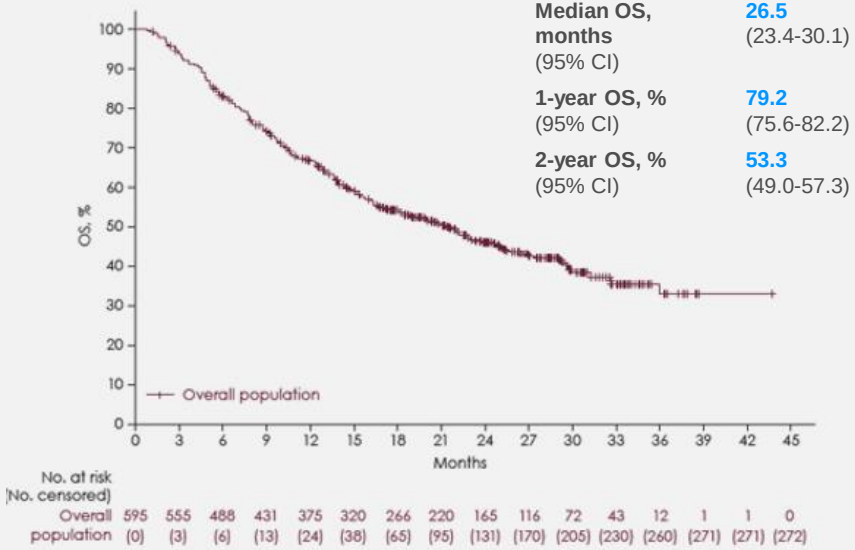
- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Moderate sample size, the relatively limited number of events and the retrospective design which is characterized by lack of randomization and of central scan review, with potential selection and confounding biases.
- The involvement of multiple institutions can lead to slightly different clinical practices (eg, imaging scheduled intervals, which can affect PFS) as well as interpretation of scan review regarding therapy response or SD versus progression.

CI, confidence interval; mPFS, median PFS; NR, not reached; OS, overall survival; PFS, progression-free survival.

Bakaloudi DR, et al. Clin Genitourin Cancer. 2023;S1558-7673(23)00147-7.

AVENANCE: OS from the Start of 1L Platinum-based Chemotherapy

Patients with aUC in the observational AVENANCE study (N=595) performed in France



Ongoing, real-world, ambispective study in patients with aUC who have not progressed with PBC in France (N= 595).
Study period: July 13, 2021, to December 7, 2023.

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in France and may not reflect US clinical practice. Exploratory analysis of mOS measured from the start of 1L platinum-based chemotherapy among those without disease progression and for patients who went on to recent 2L EV post-avelumab may be subject to immortal time bias and will need to be confirmed by additional studies.

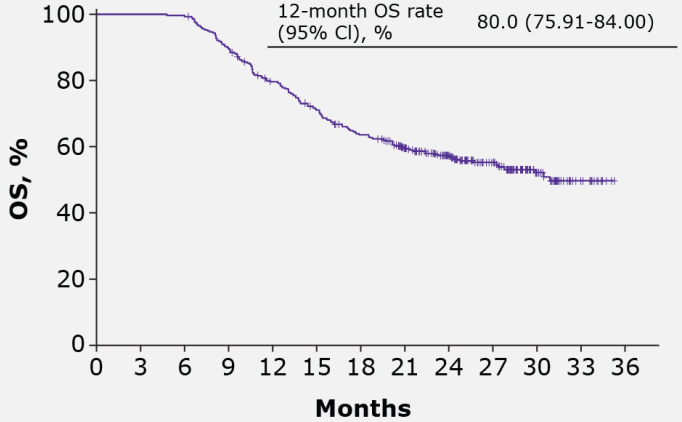
*By reverse Kaplan-Meier estimation.
1L, first-line; 1LM, first line maintenance; 2L second line treatment; aUC, advanced urothelial carcinoma; CI, confidence interval; EV, Enfortumab vedotin; m, median; OS, overall survival; PBC, platinum- based chemotherapy.
Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 561) January 25-27, 2024; San Francisco, CA.

READY CUP: OS from the Start of 1L Platinum-based Chemotherapy

Prospective, noninterventional CUP of avelumab 1LM conducted among 464 patients with la/mUC in Italy

OS from the start of 1L chemotherapy in all evaluable patients

	Evaluable patients (n=377)
Events, n (%)	166 (44.03)
Median OS (95% CI), months	30.86 (25.69-NE)
12-month OS rate (95% CI), %	80.0 (75.91-84.00)



Limitations

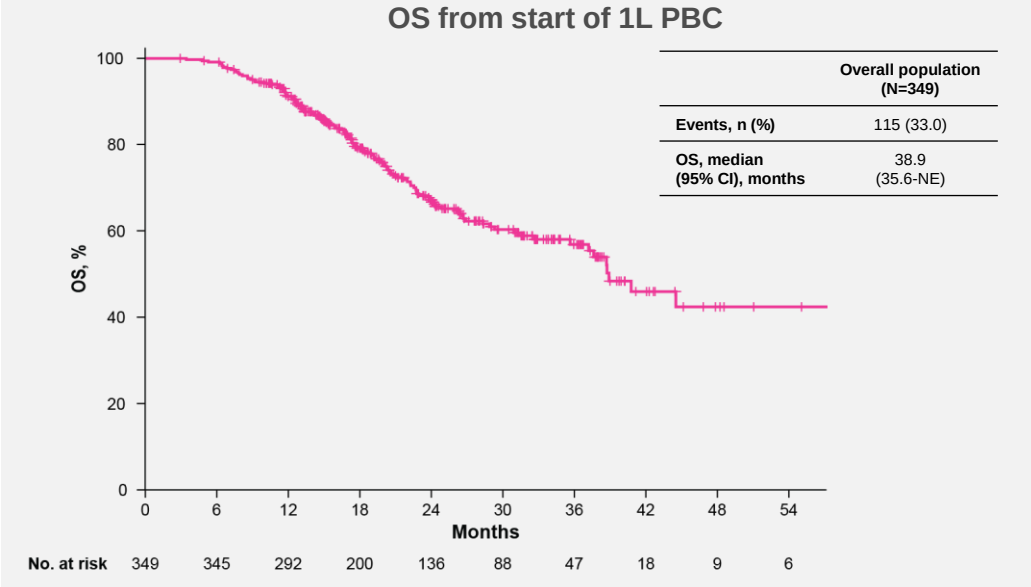
- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in Italy and may not reflect US clinical practice

1L, first line; 1LM, first line maintenance; CI, confidence interval; CUP, compassionate use program; NE, not estimable; OS, overall survival.

Antonuzzo, L., et al., ESMO Real World Data and Digital Oncology, 2024. 5: p. 100068.

Multicenter, retrospective study based on data from medical charts of 350 patients with Ia/mUC in Japan
Study period: February 2021, to December 2023.

JAVEMACS Chart Review: OS From Start of 1L PBC



Limitations

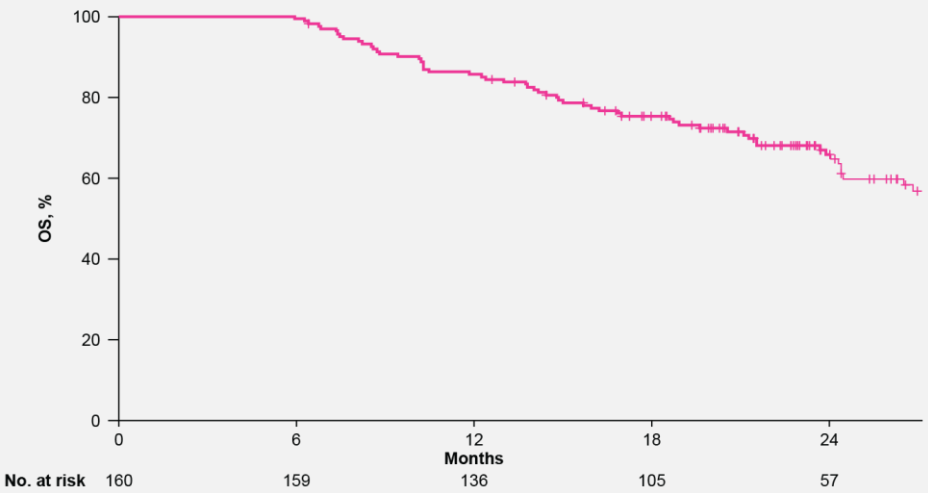
- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in Japan and may not reflect US clinical practice

Exploratory analyses of OS measured from the start of 1L PBC in this population of patients without disease progression after 1L PBC should be interpreted with caution.
Patients without a start date for 1L PBC were not included.
1L, first line; 1LM, first line maintenance; NE, not evaluable; OS, overall survival; PBC, platinum-based chemotherapy.
Kitamura H, et al. Presented at the ASCO Genitourinary Cancers Symposium (Abstract No. 701), February 13-15, 2025; San Francisco, CA.

PATRIOT II: OS From the Start of 1L PBC

Observational, retrospective chart review study of patients with la/mUC in routine clinical practice in the United States (N= 160).

Real-world OS from start of 1L PBC



OS rate	%
6-month	99.4
12-month	85.6
18-month	74.9
24-month	65.4

In this patient cohort without disease progression after 1L PBC, median real-world OS from the start of 1L PBC was 30.5 months (95% CI, 23.4-37.6 months)

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Studies using real-world data include lack of central imaging review, missing or unknown data, potential selection bias, and confounding factors due to the lack of randomization

*Date of progression was not available for 1 patient. Progression status was unknown for 3 patients; these patients were censored at the most recent follow-up date

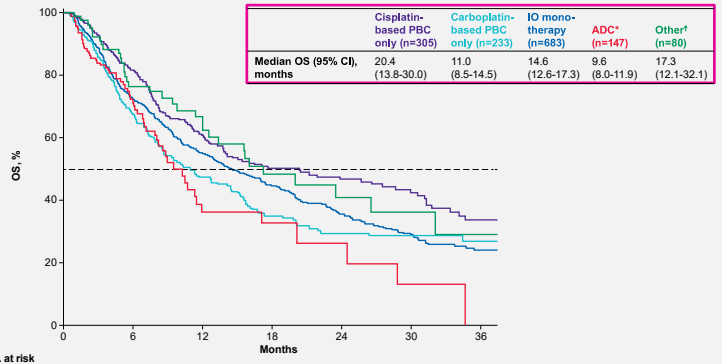
1L, first-line; 1LM, first-line maintenance; CI, confidence interval; OS, overall survival; PBC, platinum-based chemotherapy

Grivas P, et al. Clin Genitourin Cancer. 2024;22(6):102238.

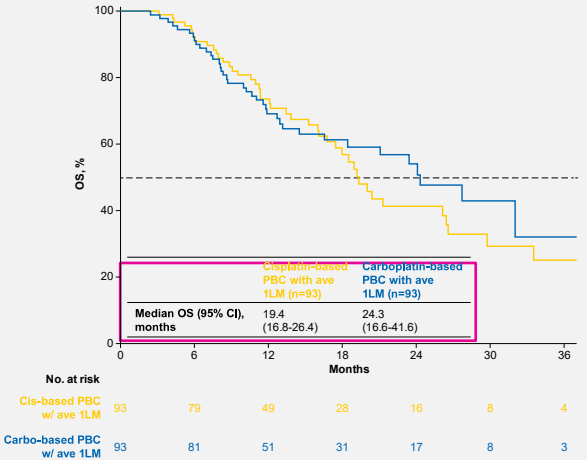
SPEAR Bladder II: OS from Start of 1L Treatment

Retrospective, observational study in 1,658 patients with la/mUC using the US Oncology Network iKnowMed™ EHR

OS from start of 1L treatment[1,2]



OS from start of 1L cisplatin- or carboplatin-based PBC[2]



Limitations

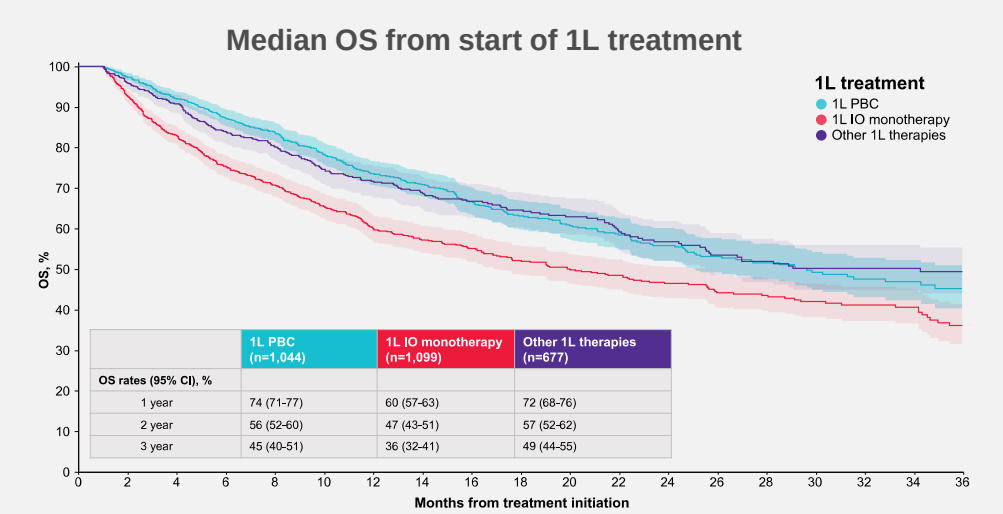
- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Data were collected primarily in the oncology clinical practice setting through routine clinical care and not for research purposes; therefore, nonrandom missingness may be present for several variables of interest, and data on healthcare received outside of the US Oncology Network iKnowMed™ EHR of practices are not available
- Complete medical history outside of the oncology EHR was not captured, which may lead to underreporting of treatments received
- Oral therapies were recorded in or prescribed through iKM, but whether those prescriptions were fulfilled was not observable
- The absence of disease progression in structured data may result in misclassification between avelumab as 1LM or 2L

1L, first line; 1LM, first-line maintenance; ADC, antibody-drug conjugate; ave, avelumab; Carbo, carboplatin; Cis, cisplatin; CI, confidence interval; HER, electronic health record; EV, enfortumab vedotin; iKM, iKnowMed IO, immuno-oncology; la/mUC, locally advanced or metastatic urothelial carcinoma; OS, overall survival; PBC, platinum-based chemotherapy.
*ADC includes EV plus pembrolizumab (59.2%) and EV monotherapy (35.4%). †Other includes gemcitabine, erdafitinib, fluorouracil, capecitabine, and methotrexate, as monotherapy or combination.

.1. Sura S, et al. Current Oncology. 2025;32(4):187; 2. Bupathi M., et al. Presented at: ASCO QCS, (Abstract No. F21), September 27-28, 2024; San Francisco, CA, USA.

IMPACT UC III: OS from the Start of 1L Treatment

Retrospective cohort study in 2,820 patients with la/mUC using the Carelon Research's HIRD and health plan's Cancer Care Quality Program data in the United States



	1L PBC (n=1,044)	1L IO monotherapy (n=1,099)	Other 1L therapies (n=677)
OS rates (95% CI), %			
1 year	74 (71-77)	60 (57-63)	72 (68-76)
2 year	56 (52-60)	47 (43-51)	57 (52-62)
3 year	45 (40-51)	36 (32-41)	49 (44-55)

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- The population in this analysis was queried from US commercially insured and Medicare Advantage enrollees with available clinical data from HIRD, which may limit the generalizability of these results for other population segments such as traditional fee-for-service Medicare and the uninsured
- Administrative claims data are primarily collected for billing and reimbursement purposes and are subject to potential coding biases, inconsistencies, and missing data
- Complete medical history outside of the oncology HIRD was not captured, which may lead to underreporting of treatments received
- Response data or eligibility for 1LM, and avelumab used in 2L could not be differentiated from that used in 1LM
- This was a descriptive study; thus, no comparative analyses were performed, no adjustment for baseline characteristics was made, and no logistic regression was undertaken

1L, first line; 1 LM, first line maintenance; 2L, second line treatment; HIRD, Healthcare Integrated Research Database IO, immuno-oncology; la/mUC, locally advanced or metastatic urothelial carcinoma; OS, overall survival; PBC, platinum-based chemotherapy.

Moon H., et al. Presented at: ASCO QCS, (Poster No. 390), September 27-28, 2024; San Francisco, CA, USA.

Bakaloudi et al: Overall Response Rate

Multicenter retrospective cohort study of real-world patient characteristics and clinical outcomes with avelumab switch maintenance (N= 108).

- Median time from avelumab maintenance initiation to last follow-up: **8.8 months** (min-max: 1-42.7)
- Median interval between last chemotherapy dose and avelumab maintenance initiation: **6 weeks** (min-max: 1-30)

	Overall population, N=108
Best response to avelumab maintenance treatment	
CR	19 (17.6)
PR	12 (11.1)
SD	32 (29.6)
PD	29 (26.9)
Unknown*	16 (14.8)
Overall response rate (ORR), %	28.7

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Moderate sample size, the relatively limited number of events and the retrospective design which is characterized by lack of randomization and of central scan review, with potential selection and confounding biases.
- The involvement of multiple institutions can lead to slightly different clinical practices (eg, imaging scheduled intervals, which can affect PFS) as well as interpretation of scan review regarding therapy response or SD versus progression.

*Most of those patients did not have response evaluation or were lost to follow-up.
1LM, first- maintenance; CR, complete response; PD, progressive disease; ORR, objective response rate; PFS, progression-free survival; PR, partial response; SD, stable disease.
Bakaloudi DR, et al. Clin Genitourin Cancer. 2023;S1558-7673(23)00147-7.

AVENANCE: Subgroup Analysis, OS from the Start of Avelumab 1L Maintenance Treatment

Ongoing, real-world, ambispective study in patients with aUC who have not progressed with PBC in France (N= 595).
Study period: July 13, 2021, to December 7, 2023.

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)
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)

Subgroup	Patients, n	mOS (95% CI), months
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)

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in France and may not reflect US clinical practice. Exploratory analysis of mOS measured from the start of 1L platinum-based chemotherapy among those without disease progression and for patients who went on to recent 2L EV post-avelumab may be subject to immortal time bias and will need to be confirmed by additional studies.

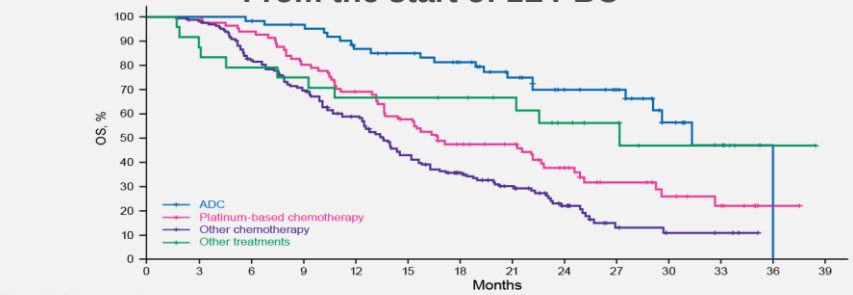
1L, first-line; 1LM, first-maintenance; 2L, second-line; ADC, antibody-drug conjugate; CI, confidence interval; ddMVAC, dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin; EVP, enfortumab vedotin; m, median; OS, overall survival; NE, not estimable; NR, not reached; UC, urothelial carcinoma.

Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 561) January 25-27, 2024; San Francisco, CA.

AVENANCE Subgroup Analysis: OS Based on 2L Treatment Subgroups

Ongoing, real-world, ambispective study in patients with aUC who have not progressed with PBC in France (N= 595).
Study period: July 13, 2021, to December 7, 2023.

From the start of 1L PBC

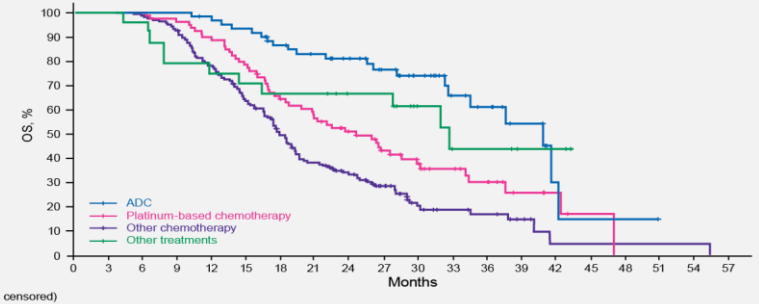


No at risk (No. censored)

ADC	62 (0)	62 (0)	61 (0)	58 (2)	51 (3)	48 (5)	42 (9)	33 (15)	25 (21)	20 (26)	9 (34)	4 (38)	0 (41)	0 (41)
Platinum-based chemotherapy	81 (0)	81 (0)	76 (0)	65 (0)	55 (1)	45 (2)	35 (4)	31 (8)	20 (13)	13 (17)	9 (19)	6 (21)	1 (26)	0 (27)
Other chemotherapy	163 (0)	159 (1)	132 (2)	112 (2)	91 (6)	65 (8)	47 (15)	35 (20)	19 (28)	7 (34)	4 (36)	3 (37)	0 (40)	0 (40)
Other treatments	24 (0)	21 (0)	19 (0)	18 (0)	16 (0)	16 (0)	15 (1)	13 (3)	9 (5)	7 (7)	4 (9)	4 (9)	1 (12)	0 (13)

	ADC (n=62)	Platinum-based chemotherapy (n=81)	Other chemotherapy (n=163)	Other treatments (n=24)
mOS (95% CI), months	31.3 (29.1-NE)	16.7 (13.6-22.8)	13.6 (12.3-15.2)	27.2 (9.3-NE)
1-year OS (95% CI), %	86.71 (75.16-93.12)	69.14 (57.84-77.97)	58.95 (50.92-66.10)	66.67 (44.28-81.73)
2-year OS (95% CI), %	70.06 (55.42-80.70)	37.88 (26.87-48.82)	22.09 (15.28-29.71)	56.41 (33.81-73.92)

From start of avelumab 1LM



No at risk (No. censored)

ADC	61 (0)	61 (0)	61 (0)	61 (0)	58 (1)	56 (1)	49 (4)	45 (6)	38 (12)	32 (16)	24 (23)	15 (30)	12 (32)	7 (36)	2 (39)	1 (39)	1 (39)	0 (40)	0 (40)	0 (40)
Platinum-based chemotherapy	79 (0)	79 (0)	79 (0)	76 (0)	70 (0)	62 (0)	49 (2)	43 (2)	34 (7)	26 (10)	19 (14)	15 (17)	11 (19)	5 (24)	3 (26)	1 (27)	0 (27)	0 (27)	0 (27)	0 (27)
Other chemotherapy	162 (0)	162 (0)	160 (0)	149 (1)	125 (2)	100 (3)	76 (6)	58 (7)	44 (14)	31 (21)	15 (30)	11 (33)	9 (34)	5 (37)	1 (39)	1 (39)	1 (39)	1 (39)	1 (39)	0 (39)
Other treatments	24 (0)	24 (0)	23 (0)	19 (0)	18 (0)	17 (0)	16 (0)	16 (0)	13 (3)	13 (3)	7 (8)	4 (9)	4 (9)	2 (11)	2 (11)	0 (13)	0 (13)	0 (13)	0 (13)	0 (13)

	ADC (n=61)	Platinum-based chemotherapy (n=79)	Other chemotherapy (n=162)	Other treatments (n=24)
mOS (95% CI), months	40.8 (32.6-42.1)	24.5 (19.8-29.8)	17.9 (16.5-19.2)	32.6 (14.3-NE)
1-year OS (95% CI), %	96.69 (87.42-99.16)	88.61 (79.25-93.90)	78.17 (70.94-83.81)	75.00 (52.62-87.91)
2-year OS (95% CI), %	81.08 (68.40-89.06)	51.03 (39.39-61.53)	33.48 (26.12-40.99)	66.67 (44.28-81.73)

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in France and may not reflect US clinical practice. Exploratory analysis of mOS measured from the start of 1L platinum-based chemotherapy among those without disease progression and for patients who went on to recent 2L EV post-avelumab may be subject to immortal time bias and will need to be confirmed by additional studies.

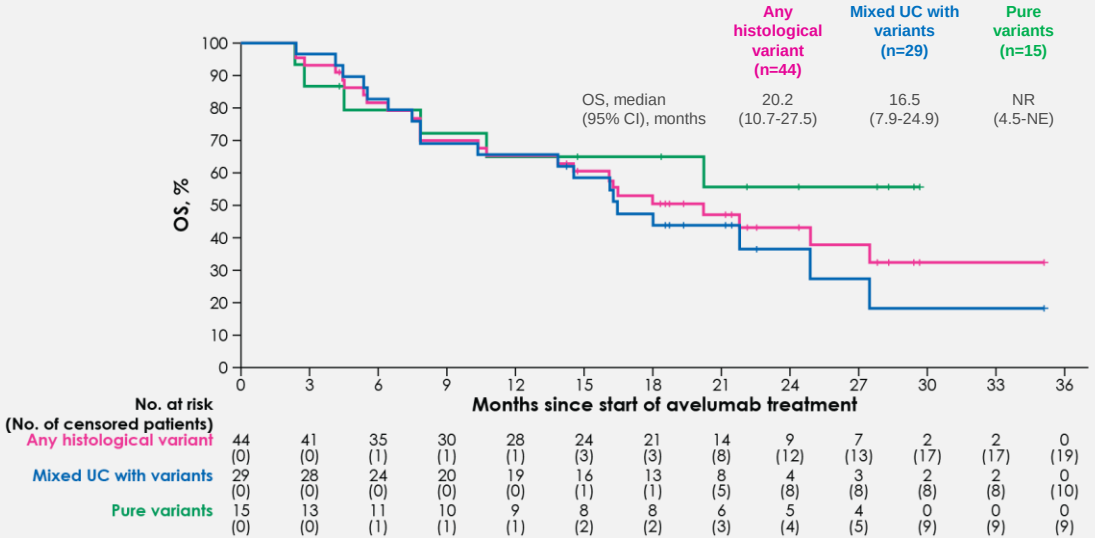
1L, first-line therapy; 1LM, first-line maintenance 2L, second-line; ADC, antibody-drug conjugate; CI, confidence interval; mOS, median overall survival; NE, not estimable; OS, overall survival; PBC: platinum based chemotheraphy.

Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 561) January 25-27, 2024; San Francisco, CA.

AVENANCE Subgroup Analysis: OS by Histologic Variants

Ongoing, real-world, ambispective study in patients with aUC who have not progressed with PBC in France (N= 595).
Study period: July 13, 2021, to December 7, 2023.

OS from the start of avelumab treatment in patients with histological variants



- As of the data cutoff (31 May 2023)
- Median follow-up from start of avelumab 1L maintenance (by reverse Kaplan-Meier estimation):
  - 22.5 months (95% CI, 19.4-28.3 months) in all patients with histological variants
  - 21.5 months (95% CI, 18.8 months-NE) in patients with UC-V
  - 24.4 months (95% CI, 14.7-29.4 months) in patients with PV

Limitations

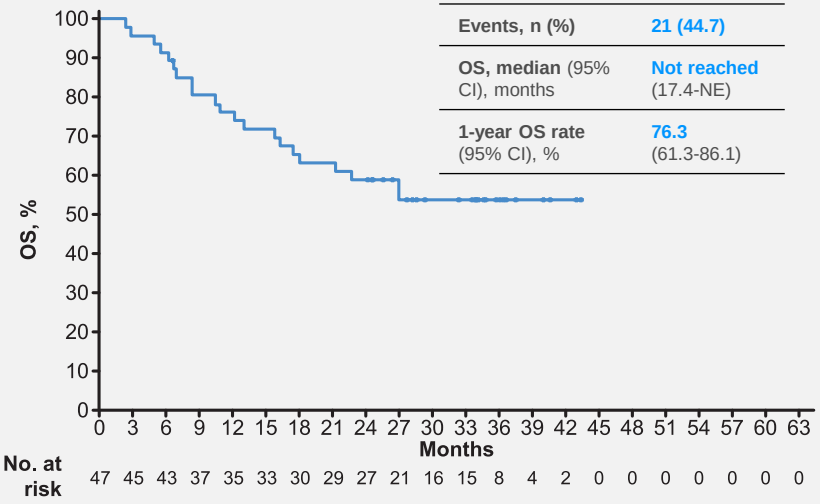
- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in France and may not reflect US clinical practice. Exploratory analysis of mOS measured from the start of 1L platinum-based chemotherapy among those without disease progression and for patients who went on to recent 2L EV post-avelumab may be subject to immortal time bias and will need to be confirmed by additional studies.

1L, first-line therapy; 1LM, first-line maintenance therapy; CI, confidence interval; mOS, median overall survival; NE, not estimable; NR, not reached; UC, urothelial carcinoma.
Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 561) January 25-27, 2024; San Francisco, CA.

AVENANCE Low Tumor Burden Subgroups: OS from Start of Avelumab 1L Maintenance Treatment

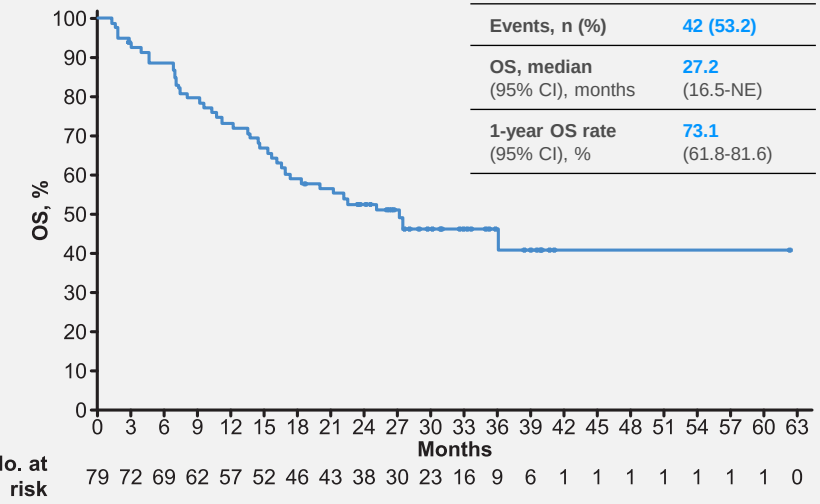
Post hoc analysis of ongoing, real-world, ambispective study in patients with aUC who have not progressed with PBC in France and had low tumor burden at start of PBC (n=186)
Study start: July 13, 2021; Data cut-off: December 2, 2024

Locally advanced disease (n=47)



Events, n (%)	21 (44.7)
OS, median (95% CI), months	Not reached (17.4-NE)
1-year OS rate (95% CI), %	76.3 (61.3-86.1)

Nonvisceral metastases (n=79)



Events, n (%)	42 (53.2)
OS, median (95% CI), months	27.2 (16.5-NE)
1-year OS rate (95% CI), %	73.1 (61.8-81.6)

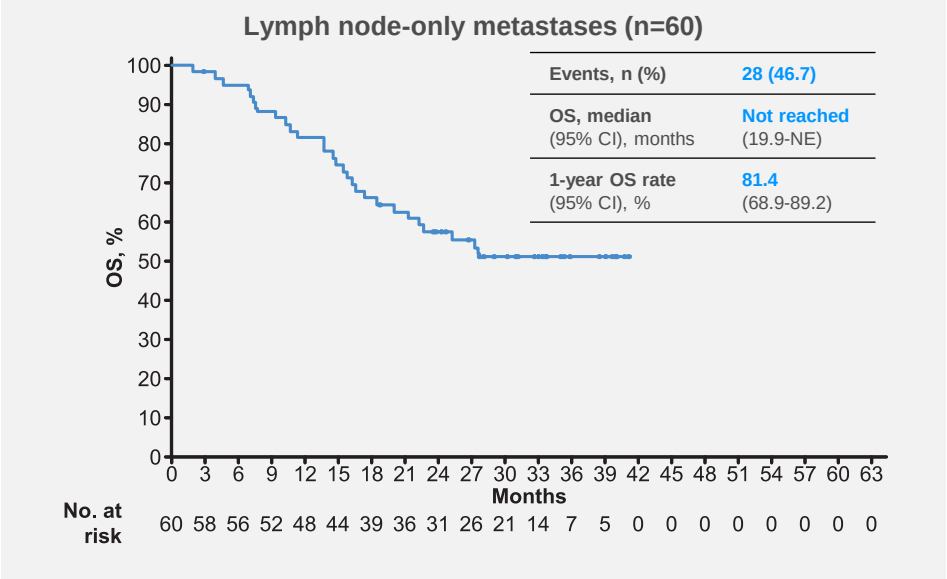
Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in France and may not reflect US clinical practice

1L, first-line; 1LM, first line maintenance; CI, confidence interval; NE, not estimable; OS, overall survival.
Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 718) February 13-15, 2025; San Francisco, CA.

AVENANCE Low Tumor Burden Subgroups: OS from Start of Avelumab 1L Maintenance Treatment

Post hoc analysis of ongoing, real-world, ambispective study in patients with aUC who have not progressed with PBC in France and had low tumor burden at start of PBC (n=186)
Study start: July 13, 2021; Data cut-off: December 2, 2024



Limitations

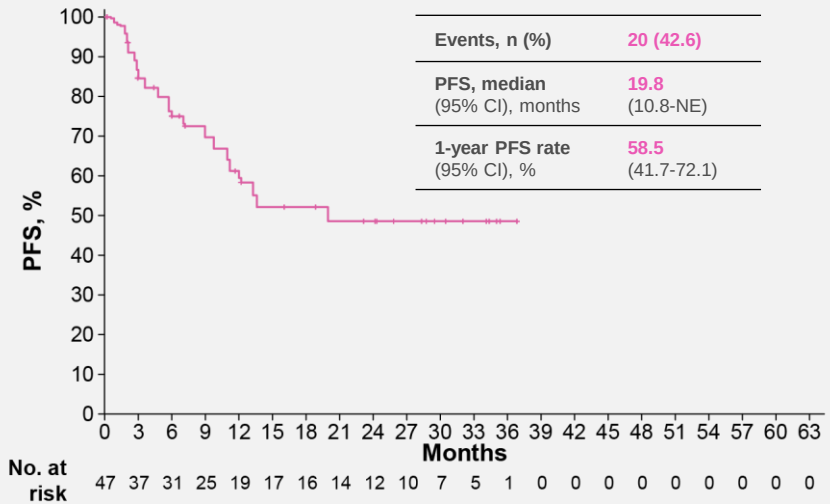
- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in France and may not reflect US clinical practice

1L, first-line; 1LM, first line maintenance; CI, confidence interval; NE, not estimable; OS, overall survival.
Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 718) February 13-15, 2025; San Francisco, CA.

AVENANCE Low Tumor Burden Subgroups: PFS from Start of Avelumab 1L Maintenance Treatment

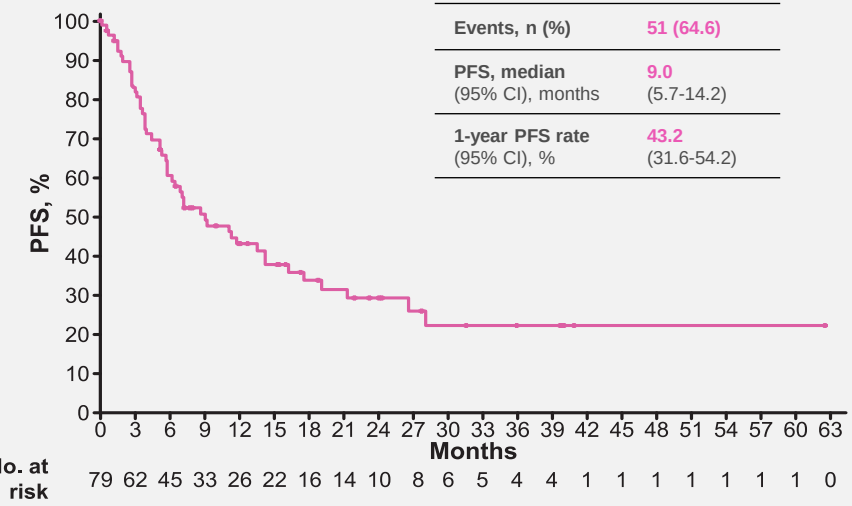
Post hoc analysis of ongoing, real-world, ambispective study in patients with aUC who have not progressed with PBC in France and had low tumor burden at start of PBC (n=186)
Study start: July 13, 2021; Data cut-off: December 2, 2024

Locally advanced disease (n=47)



Events, n (%)	20 (42.6)
PFS, median (95% CI), months	19.8 (10.8-NE)
1-year PFS rate (95% CI), %	58.5 (41.7-72.1)

Nonvisceral metastases (n=79)



Events, n (%)	51 (64.6)
PFS, median (95% CI), months	9.0 (5.7-14.2)
1-year PFS rate (95% CI), %	43.2 (31.6-54.2)

Limitations

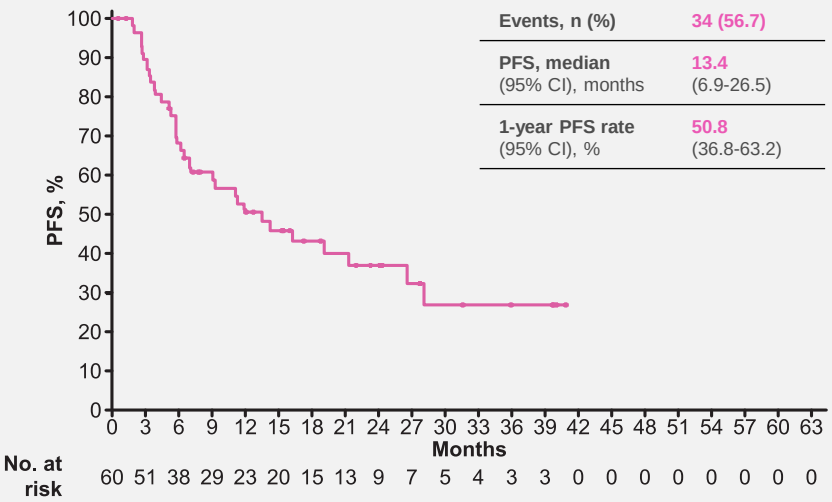
- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in France and may not reflect US clinical practice

1L, first-line; 1LM, first line maintenance; CI, confidence interval; NE, not estimable; PFS, progression-free survival.
Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 718) February 13-15, 2025; San Francisco, CA.

AVENANCE Low Tumor Burden Subgroups: PFS from Start of Avelumab 1L Maintenance Treatment

Post hoc analysis of ongoing, real-world, ambispective study in patients with aUC who have not progressed with PBC in France and had low tumor burden at start of PBC (n=186)
Study start: July 13, 2021; Data cut-off: December 2, 2024

Lymph node-only metastases (n=60)



Events, n (%)	**34 (56.7)**
PFS, median (95% CI), months	**13.4** (6.9-26.5)
1-year PFS rate (95% CI), %	**50.8** (36.8-63.2)

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in France and may not reflect US clinical practice

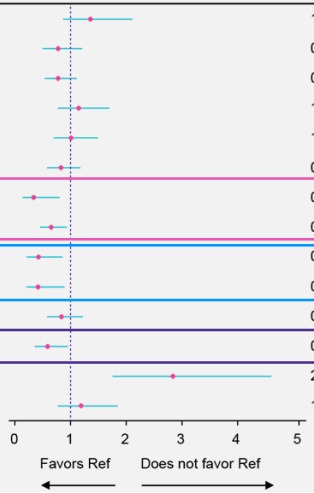
1L, first-line; 1LM, first line maintenance; CI, confidence interval; NE, not estimable; PFS, progression-free survival.
Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 718) February 13-15, 2025; San Francisco, CA.

READY CUP: Subgroup Analysis of OS (1/2)

Prospective, noninterventional CUP of avelumab 1LM conducted among 464 patients with la/mUC in Italy

Forest plot of subgroup analysis of OS from the start of avelumab 1L maintenance

Subgroup	Ref (n)		(n)	HR (95% CI)
Age	≥65 years (298)	vs	<65 years (116)	1.35 (0.87 - 2.12)
Sex	Female (86)	vs	Male (328)	0.78 (0.49 - 1.21)
Weight	≥75 kg (191)	vs	<75 kg (223)	0.78 (0.54 - 1.12)
ECOG PS	1 (120)	vs	0 (293)	1.15 (0.77 - 1.71)
1L chemotherapy regimen	Carboplatin (221)	vs	Cisplatin (184)	1.01 (0.69 - 1.48)
No. of 1L chemotherapy cycles	6 (158)	vs	4 (204)	0.83 (0.58 - 1.18)
Best response to 1L chemotherapy	CR (42)	vs	SD (137)	0.33 (0.14 - 0.81)
Best response to 1L chemotherapy	PR (235)	vs	SD (137)	0.65 (0.44 - 0.94)
Bellmunt prognostic risk factors	0 or 1 (280)	vs	≥3 (23)	0.42 (0.21 - 0.85)
Bellmunt prognostic risk factors	2 (74)	vs	≥3 (23)	0.42 (0.20 - 0.89)
Creatinine clearance	>60 mL/min (226)	vs	≤60 mL/min (151)	0.84 (0.57 - 1.23)
Lymph node only metastasis	Yes (138)	vs	No (210)	0.58 (0.36 - 0.95)
Liver metastasis	Yes (53)	vs	No (295)	2.85 (1.75 - 4.62)
Lung metastasis	Yes (83)	vs	No (265)	1.19 (0.76 - 1.86)



OS

HRs for OS were lower in patients with
- CR or PR to 1L chemotherapy vs SD
- Bellmunt score of 0-2 vs ≥3
- Lymph node–only metastasis vs no lymph node–only metastasis

Limitations
- Since AEs were reported at the treating physician's discretion in this CUP, AEs may have been underreported
- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in Italy and may not reflect US clinical practice
- There was the potential for investigator bias and some of the inclusion criteria, including ECOG PS of 0/1, number of chemotherapy cycles, and interval time between chemotherapy and maintenance, which would have excluded some patients who could receive avelumab treatment in clinical practice
- Median duration of avelumab treatment was shorter in the READY study compared with the JAVELIN Bladder 100 and AVENANCE studies

1L, first-line; 1LM, first-line maintenance; CI, confidence interval; CR, complete response; CUP, compassionate use program; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; la/mUC, locally advanced or metastatic urothelial carcinoma; OS, overall survival; PR, partial response; Ref, reference; SD, stable disease.

Antonuzzo, L., et al., ESMO Real World Data and Digital Oncology, 2024. 5: p. 100068.

READY CUP: Subgroup Analysis of OS (2/2)

Prospective, noninterventional CUP of avelumab 1LM conducted among 464 patients with la/mUC in Italy

Median OS from the start of avelumab 1L maintenance in subgroups

Subgroup	n	Median OS (95% CI), months
1L CT regimen		
Cisplatin + gemcitabine	184	NR (16.05-NE)
Carboplatin + gemcitabine	221	25.10 (19.97-NE)
Best response to 1L CT		
CR	42	NR (24.21-NE)
PR	235	26.22 (21.22-NE)
SD	137	13.65 (10.56-NE)
Number of 1L CT cycles		
4 cycles	204	19.97 (13.65-NE)
6 cycles	158	NR (24.01-NE)
Age at the start of avelumab		
<65 years	116	NR (24.21-NE)
≥65 years	298	25.10 (17.43-NE)
Creatinine clearance		
≤60 mL/min	151	18.91 (13.95-NE)
>60 mL/min	226	NR (24.21-NE)

Limitations

- Since AEs were reported at the treating physician's discretion in this CUP, AEs may have been underreported
- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in Italy and may not reflect US clinical practice
- There was the potential for investigator bias and some of the inclusion criteria, including ECOG PS of 0/1, number of chemotherapy cycles, and interval time between chemotherapy and maintenance, which would have excluded some patients who could receive avelumab treatment in clinical practice
- Median duration of avelumab treatment was shorter in the READY study compared with the JAVELIN Bladder 100 and AVENANCE studies

1L, first-line; 1LM, first-line maintenance; CR, complete response; CUP, compassionate use program; CT, chemotherapy; la/mUC, locally advanced or metastatic urothelial carcinoma; NE, not estimable; NR, not reached; OS, overall survival; PR, partial response; SD, stable disease.

Antonuzzo, L., et al., ESMO Real World Data and Digital Oncology, 2024. 5: p. 100068.

JAVEMACS Chart Review: Univariate Analysis of Factors Associated With OS From Start of Avelumab 1LM Initiation (1/4)

Multicenter, retrospective study based on data from medical charts of 350 patients with la/mUC in Japan
Study period: February 2021, to December 2023.

Subgroup	Events/patients	OS, median (95% CI), months	HR (95% CI)	p value
Age				
<80 years (ref)	99/293	NR (24.6-NE)	–	0.74
≥80 years	17/57	25.0 (17.5-NE)	1.09 (0.65-1.83)	
Sex				
Male (ref)	86/259	31.8 (24.6-NE)	–	0.55
Female	30/91	NR (19.5-NE)	1.14 (0.75-1.72)	
BMI, kg/m²				
<18.5	10/20	12.2 (8.4-NE)	2.62 (1.35-5.09)	0.003
≥18.5 to <25 kg/m²	77/229	31.8 (24.3-NE)	–	
≥25	21/76	NR (29.3-NE)	0.72 (0.44-1.16)	
ECOG performance status				
0 (ref)	86/284	NR (26.5-NE)	–	<0.001
1	23/56	30.6 (16.3-NE)	1.44 (0.91-2.29)	
≥2	4/6	7.7 (1.5-NE)	7.40 (2.66-20.60)	

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in Japan and may not reflect US clinical practice

1L, first line; 1LM, first line maintenance; BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; NE, not evaluable; NR, not reached; OS, overall survival; ref, reference.
Kitamura H, et al. Presented at the ASCO Genitourinary Cancers Symposium (Abstract No. 701), February 13-15, 2025; San Francisco, CA.

JAVEMACS Chart Review: Univariate Analysis of Factors Associated With OS From Start of Avelumab 1LM Initiation (2/4)

Multicenter, retrospective study based on data from medical charts of 350 patients with la/mUC in Japan
Study period: February 2021, to December 2023.

Subgroup	Events/patients	OS, median (95% CI), months	HR (95% CI)	p value
Primary tumor location				
Bladder (ref)	57/177	NR (23.6-NE)	–	0.78
Renal pelvis/ureter	58/168	31.2 (24.2-NE)	1.11 (0.77-1.60)	
Urethra	1/5	NR (20.6-NE)	0.68 (0.09-4.92)	
Variant histology				
Pure UC (ref)	93/277	31.8 (24.6-NE)	–	0.60
UC with variant or pure non-UC	16/50	NR (20.6-NE)	0.87 (0.51-1.48)	
Visceral metastases				
No (ref)	69/236	NR (30.6-NE)	–	0.004
Yes	47/113	22.6 (17.1-NE)	1.73 (1.19-2.50)	
Eligibility				
Cis eligible (ref)	35/100	31.2 (20.0-NE)	–	0.98
Cis ineligible/pt eligible	64/185	31.8 (22.6-NE)	1.02 (0.68-1.54)	
Pt ineligible	9/30	30.6 (19.5-NE)	0.96 (0.46-2.00)	

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in Japan and may not reflect US clinical practice

1L, first line; 1LM, first line maintenance; carbo, carboplatin; cis, cisplatin; ddMVAC, dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin; HR, hazard ratio; NE, not evaluable; NR, not reached; OS, overall survival; pt, platinum; ref, reference; UC, urothelial carcinoma.

Kitamura H, et al. Presented at the ASCO Genitourinary Cancers Symposium (Abstract No. 701), February 13-15, 2025; San Francisco, CA.

JAVEMACS Chart Review: Univariate Analysis of Factors Associated With OS From Start of Avelumab 1LM Initiation (3/4)

Multicenter, retrospective study based on data from medical charts of 350 patients with la/mUC in Japan
Study period: February 2021, to December 2023.

Subgroup	Events/patients	OS, median (95% CI), months	HR (95% CI)	p value
1L PBC regimen				
Cis + gem (ref)	61/196	NR (31.2-NE)	–	0.08
Carbo + gem	47/116	24.3 (19.5-30.6)	1.53 (1.04-2.24)	
ddMVAC	7/32	NR (20.0-NE)	0.77 (0.35-1.69)	
Others	1/6	NR (10.9-NE)	0.54 (0.08-3.92)	
No. of 1L PBC cycles				
1-3	26/68	25.0 (15.2-NE)	1.39 (0.88-2.20)	0.54
4 (ref)	61/205	NR (29.3-NE)	–	
5/6	21/61	31.2 (18.0-NE)	1.12 (0.68-1.84)	
≥7	8/16	23.6 (19.3-NE)	1.29 (0.62-2.70)	
Best response to 1L PBC				
CR	5/32	NR (30.6-NE)	0.32 (0.13-0.81)	0.03
PR (ref)	61/180	31.2 (22.6-NE)	–	
SD	50/138	26.5 (20.2-NE)	1.12 (0.77-1.62)	

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in Japan and may not reflect US clinical practice

1L, first line; 1LM, first line maintenance; carbo, carboplatin; cis, cisplatin; CR, complete response; ddMVAC, dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin; HR, hazard ratio; NE, not evaluable; NR, not reached; OS, overall survival; PBC, platinum-based chemotherapy; PR, partial response; ref, reference; SD, stable disease.

Kitamura H, et al. Presented at the ASCO Genitourinary Cancers Symposium (Abstract No. 701), February 13-15, 2025; San Francisco, CA.

JAVEMACS Chart Review: Univariate Analysis of Factors Associated With OS From Start of Avelumab 1LM Initiation (4/4)

Multicenter, retrospective study based on data from medical charts of 350 patients with la/mUC in Japan
Study period: February 2021, to December 2023.

Subgroup	Events/patients	OS, median (95% CI), months	HR (95% CI)	p value
Treatment-free interval				
<4 weeks	35/95	29.3 (19.5-NE)	1.07 (0.71-1.61)	0.33
≥4 to ≤10 weeks (ref)	70/218	NR (24.2-NE)	–	
>10 weeks	10/36	NR (20.6-NE)	0.63 (0.33-1.22)	

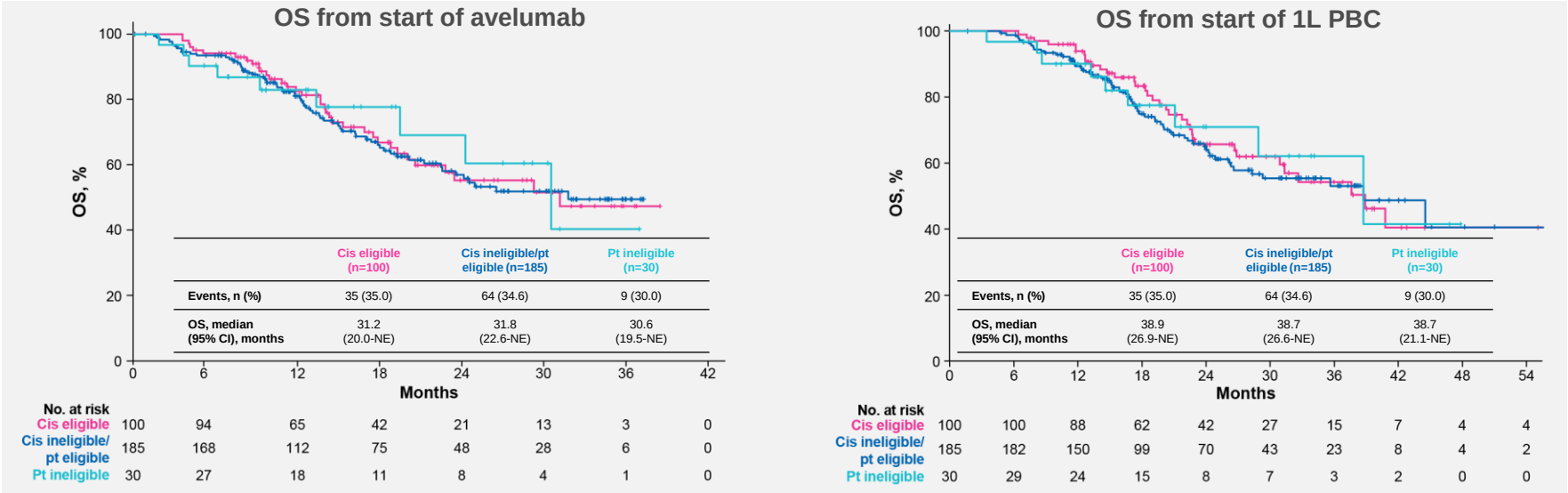
Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in Japan and may not reflect US clinical practice

1L, first line; 1LM, first line maintenance; CI, confidence interval; NE, not evaluable; OS, overall survival; ref, reference.
Kitamura H, et al. Presented at the ASCO Genitourinary Cancers Symposium (Abstract No. 701), February 13-15, 2025; San Francisco, CA.

JAVEMACS Chart Review: OS in Subgroups Defined by Cisplatin and Platinum Eligibility

Multicenter, retrospective study based on data from medical charts of 350 patients with la/mUC in Japan
Study period: February 2021, to December 2023.



Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in Japan and may not reflect US clinical practice

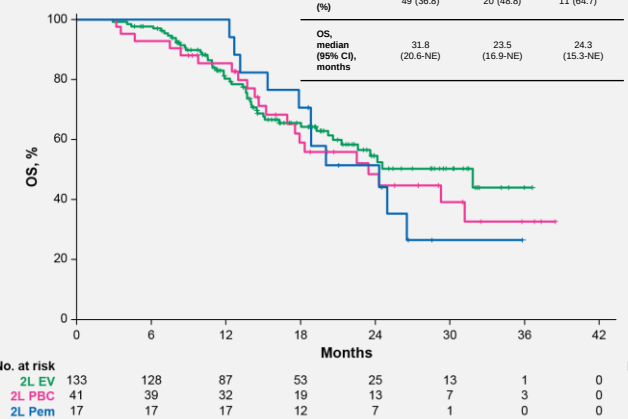
Exploratory analyses of OS measured from the start of 1L PBC in this population of patients without disease progression after 1L PBC should be interpreted with caution.
Patients without a start date for 1L PBC were not included.
1L, first line; 1LM, first line maintenance; carbo, carboplatin; cis, cisplatin; ddMVAC, dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin; NE, not evaluable; OS, overall survival; PBC, platinum-based chemotherapy; pt, platinum.
Kitamura H, et al. Presented at the ASCO Genitourinary Cancers Symposium (Abstract No. 701), February 13-15, 2025; San Francisco, CA.

JAVEMACS Chart Review: OS in Patients Receiving 2L Treatment

Multicenter, retrospective study based on data from medical charts of 350 patients with la/mUC in Japan
Study period: February 2021, to December 2023.

OS from start of avelumab

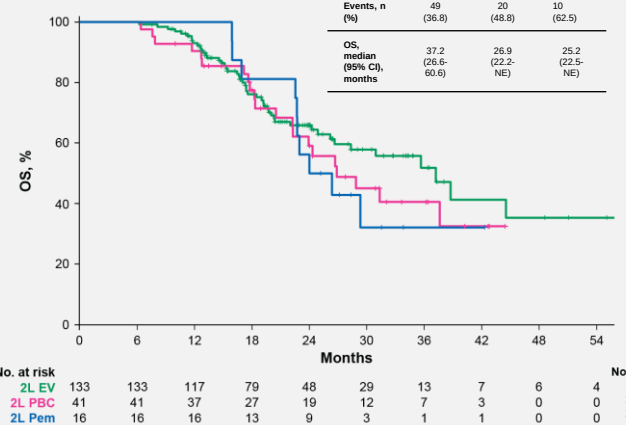
	2L EV (n=133)	2L PBC (n=41)	2L Pem (n=17)
Events, n (%)	49 (36.8)	20 (48.8)	11 (64.7)
OS, median (95% CI), months	31.8 (20.6-NE)	23.5 (16.9-NE)	24.3 (15.3-NE)



No. at risk								
2L EV	133	128	87	53	25	13	1	0
2L PBC	41	39	32	19	13	7	3	0
2L Pem	17	17	17	12	7	1	0	0

OS from start of 1L PBC

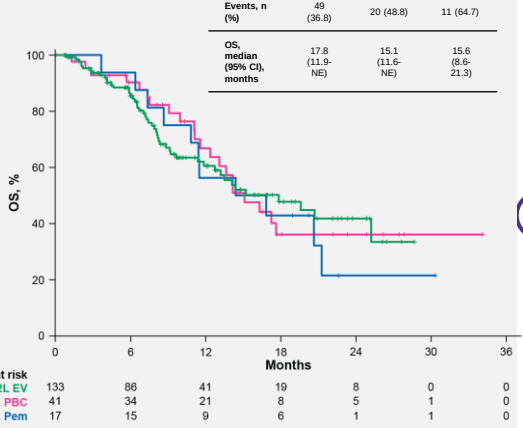
	2L EV (n=133)	2L PBC (n=41)	2L Pem (n=16)
Events, n (%)	49 (36.8)	20 (48.8)	10 (62.5)
OS, median (95% CI), months	37.2 (26.6-60.6)	26.9 (22.2-NE)	25.2 (22.5-NE)



No. at risk										
2L EV	133	133	117	79	48	29	13	7	6	4
2L PBC	41	41	37	27	19	12	7	3	0	0
2L Pem	16	16	16	13	9	3	1	1	0	0

OS from start of 2L treatment

	2L EV (n=133)	2L PBC (n=41)	2L Pem (n=17)
Events, n (%)	49 (36.8)	20 (48.8)	11 (64.7)
OS, median (95% CI), months	17.8 (11.9-NE)	15.1 (11.6-NE)	15.6 (8.6-21.3)



No. at risk							
2L EV	133	86	41	19	8	0	0
2L PBC	41	34	21	8	5	1	0
2L Pem	17	15	9	6	1	1	0

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in Japan and may not reflect US clinical practice

Exploratory analyses of OS measured from the start of 1L PBC in this population of patients without disease progression after 1L PBC should be interpreted with caution.
Patients without a start date for 1L PBC were not included.
1L, first line; 1LM, first line maintenance; 2L, second line; EV, enfortumab vedotin; NE, not evaluable; OS, overall survival; PBC, platinum-based chemotherapy; Pem, pembrolizumab.
Kitamura H, et al. Presented at the ASCO Genitourinary Cancers Symposium (Abstract No. 701), February 13-15, 2025; San Francisco, CA.

Flatiron III Tumor Burden: Clinical Outcomes by Disease Burden in Patients with Metastases at Avelumab 1LM Initiation

Subgroup analyses of a multicenter, retrospective cohort study in the US conducted in 290 patients with la/mUC having low tumor burden
Data cut-off: July 2023

Outcomes in the overall population

- Median rwOS from avelumab 1LM initiation: 22.0 months (95% CI, 18.2-24.8)
- Median rwPFS from avelumab 1LM initiation: 5.0 months (95% CI, 3.9-5.8)
- rwORR in patients who had a tumor assessment during avelumab 1LM (n=236): 34.7%

Outcomes by disease burden in patients with metastases at avelumab 1LM initiation

Outcome from avelumab 1LM initiation, median (95% CI), months	Patients with Metastases (n=266)	
	Nonvisceral (n=124)	Visceral (n=142)
rwOS	23.8 (15.4–NE)	19.1 (12.5–23.8)
rwPFS	5.6 (4.1–7.8)	3.6 (3.1–5.0)
TTNT	6.6 (6.6–9.8)	6.0 (4.3–7.4)
TTD	5.3 (4.2–10.1)	4.4 (3.5–5.7)
	Lymph node only (n=83)	Distant (n=183)
rwOS	24.3 (20.7–NE)	16.5 (12.5–22.6)
rwPFS	8.7 (5.0–NE)	3.6 (3.1-4.6)
TTNT	8.1 (6.2–23.8)	5.2 (4.3–6.7)
TTD	10.1 (4.9–NE)	4.2 (3.3–5.5)

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- The noninterventional, retrospective nature of this study limited control over data collection and introduced potential biases, including selection and information biases
- Reliance on the nationwide Flatiron Health EHR-derived deidentified database may have resulted in incomplete or inconsistent data, particularly for tumor assessments and treatment patterns
- Real-world treatment practices and follow-up schedules may vary, impacting the comparability and generalizability of results
- Factors such as comorbidities, genomic data, and detailed measures of tumor biology were not captured and may have influenced outcomes, but were not accounted for in the analysis

1LM, first-line maintenance; EHR, electronic health record; CI, confidence interval; rwOS, real-world overall survival; rwORR, real-world objective response rate; rwPFS, real-world progression-free survival; TTD, time to treatment discontinuation; TTNT, time to next treatment.

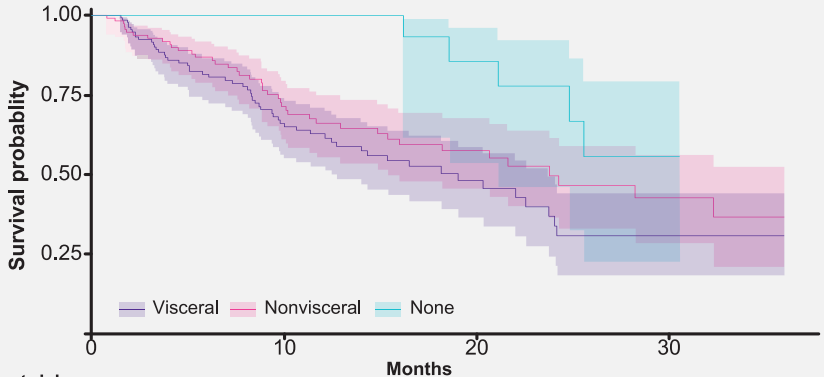
Moon HH, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 764) February 13-15, 2025; San Francisco, CA.

Flatiron III Tumor Burden: rwOS by Metastatic Site

Subgroup analyses of a multicenter, retrospective cohort study in the US conducted in 290 patients with la/mUC having low tumor burden
Data cut-off: July 2023

rwOS for visceral vs nonvisceral metastases

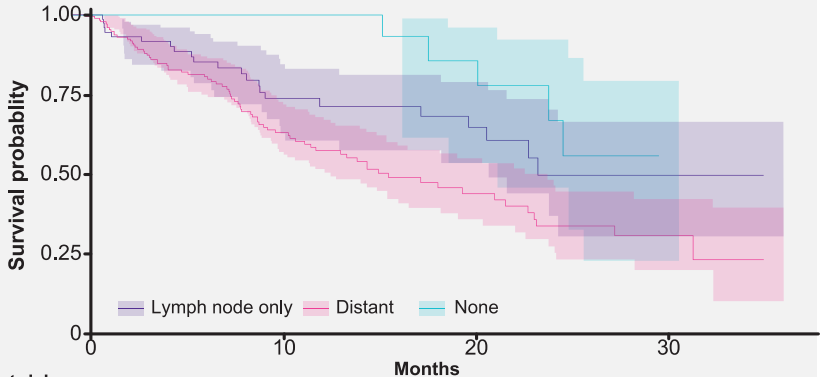
Median rwOS: 19.1 (12.5-23.8) vs 23.8 (15.4-NE)



No. at risk				
Visceral	142	62	19	5
Nonvisceral	124	57	25	9
None	24	17	11	2

rwOS for lymph node–only vs distant metastases

Median rwOS: 24.3 (20.7-NE) vs 16.5 (12.5-22.6)



No. at risk				
Lymph node only	83	39	19	6
Distant	183	79	25	8
None	24	17	11	2

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- The noninterventional, retrospective nature of this study limited control over data collection and introduced potential biases, including selection and information biases
- Reliance on the nationwide Flatiron Health EHR-derived deidentified database may have resulted in incomplete or inconsistent data, particularly for tumor assessments and treatment patterns
- Real-world treatment practices and follow-up schedules may vary, impacting the comparability and generalizability of results
- Factors such as comorbidities, genomic data, and detailed measures of tumor biology were not captured and may have influenced outcomes, but were not accounted for in the analysis

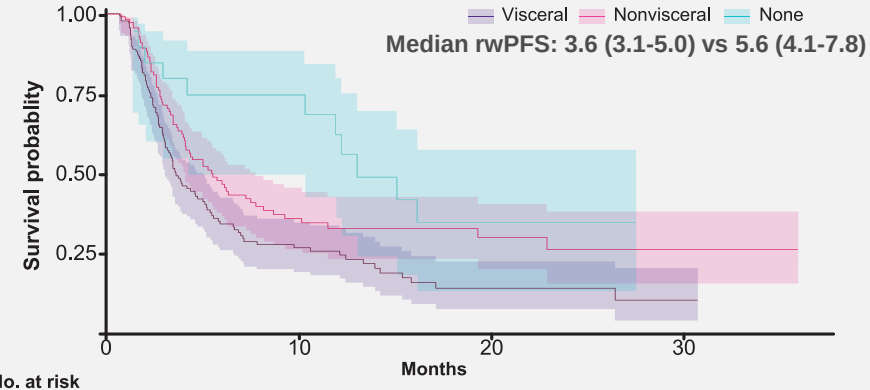
1LM, first-line maintenance; EHR, electronic health record; NE, not estimable; rwOS, real-world overall survival.

Moon HH, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 764) February 13-15, 2025; San Francisco, CA.

Flatiron III Tumor Burden: rwPFS by Metastatic Site

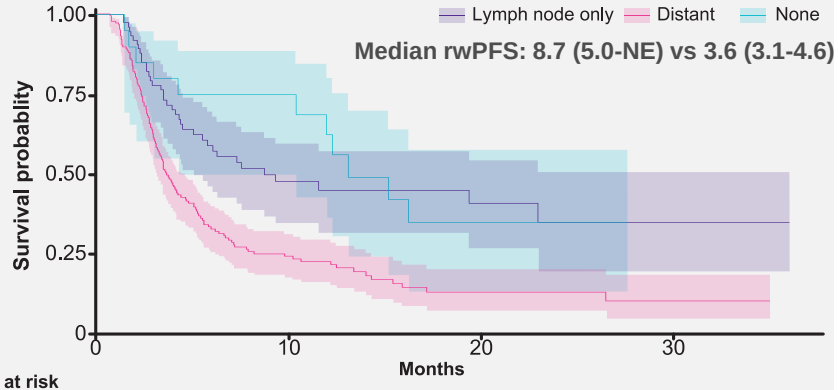
Subgroup analyses of a multicenter, retrospective cohort study in the US conducted in 290 patients with la/mUC having low tumor burden
Data cut-off: July 2023

rwPFS for visceral vs nonvisceral metastases



No. at risk				
Visceral	142	26	8	2
Nonvisceral	124	27	10	4
None	24	12	5	0

rwPFS for lymph node–only vs distant metastases



No. at risk				
Lymph node only	83	39	9	3
Distant	183	30	9	3
None	24	12	5	0

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- The noninterventional, retrospective nature of this study limited control over data collection and introduced potential biases, including selection and information biases
- Reliance on the nationwide Flatiron Health EHR-derived deidentified database may have resulted in incomplete or inconsistent data, particularly for tumor assessments and treatment patterns
- Real-world treatment practices and follow-up schedules may vary, impacting the comparability and generalizability of results
- Factors such as comorbidities, genomic data, and detailed measures of tumor biology were not captured and may have influenced outcomes, but were not accounted for in the analysis

1LM, first-line maintenance; ; EHR, electronic health record; NE, not estimable; rwPFS, real-world progression-free survival.
Moon HH, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 764) February 13-15, 2025; San Francisco, CA.

Bakaloudi et al: Subgroup analysis, OS and PFS

Multicenter retrospective cohort study of real-world patient characteristics and clinical outcomes with avelumab switch maintenance (N= 108).

OS	HR	95% CI
Sex (Female vs. Male)	1.76	0.68-4.50
Smoking History (No vs. Yes)	0.70	0.27-1.78
Upper vs. lower tract	1.19	0.33-4.29
Histology (pure vs. mixed UC)	1.09	0.37-3.21
PBC Regimen (Cis vs. Carbo)	2.25	0.88-5.77
Cycles of PBC (≤4 vs. >4)	0.80	0.30-2.15
Liver mets at start of PBC (Yes vs. No)*	1.06	0.35-3.18
ECOG PS (0 vs. ≥1) at start of PBC*	**0.15**	**0.05-0.47**
Best response to PBC (CR/PR vs. SD)*	**0.33**	**0.13-0.87**
Weeks from PBC end to avelumab initiation (≤3 vs. 4-10)	1.46	0.48-4.41
Weeks from PBC end to avelumab initiation (>10 vs. 4-10)	0.59	0.13-2.75

PFS	HR	95% CI
Sex (Female vs. Male)	1.29	0.70-2.36
Smoking History (No vs. Yes)	0.94	0.57-1.55
Upper vs. Lower tract	1.32	0.64-2.74
Histology (pure vs. mixed UC)	0.91	0.52-1.57
PBC Regimen (Cis vs. Carbo)	1.58	0.90-2.76
Cycles of PBC (≤ 4 vs. >4)	1.13	0.67-1.91
Liver mets at start of PBC (Yes vs. No)[a]	**2.32**	**1.17-4.59**
ECOG PS (0vs. ≥1) at start of PBC[a]	0.64	0.38-1.06
Best response to PBC (CR/PR vs. SD)[a]	0.61	0.34-1.08
Weeks from PBC end to avelumab initiation (≤3 vs. 4-10)	1.59	0.84-3.00
Weeks from PBC end to avelumab initiation (>10 vs. 4-10)	0.44	0.19-1.05

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Moderate sample size, the relatively limited number of events and the retrospective design which is characterized by lack of randomization and of central scan review, with potential selection and confounding biases.
- The involvement of multiple institutions can lead to slightly different clinical practices (eg, imaging scheduled intervals, which can affect PFS) as well as interpretation of scan review regarding therapy response or SD versus progression.

*Significant variables (a = 0.05)

1LM, first-line maintenance; Carbo, carboplatin; Cis, cisplatin; CI, confidence interval; CR, complete response; ECOG PS, Eastern Cooperative Group performance status; HR, hazard ratio; OS, overall survival; PBC, platinum-based chemotherapy; PFS, progression-free survival; PR, partial response; SD, stable disease; UC, urothelial carcinoma.

Bakaloudi DR, et al. Clin Genitourin Cancer. 2023;S1558-7673(23)00147-7.

AVENANCE: Safety

Safety of avelumab and most common TEAEs of any grade

Ongoing, real-world, ambispective study in patients with aUC who have not progressed with PBC in France (N= 593).
Study period: July 13, 2021, to December 1, 2022.

Adverse events, n (%)	Overall safety population (N=593)
TEAE*	428 (72.2)
Serious TEAE	200 (33.7)
TEAE leading to temporary/permanent discontinuation	171 (28.8)
TEAE leading to death	99 (16.7)
TRAE	254 (42.8)
Serious TRAE	31 (5.2)
TRAE leading to temporary/permanent discontinuation	78 (13.2)
TRAE leading to death	5 (0.8)

Events, n (%)	Overall safety population (N=593)
Asthenia	115 (19.4)
Pruritus	59 (9.9)
General physical health deterioration	44 (7.4)
Neoplasm progression	44 (7.4)
Intentional product misuse	43 (7.3)
Diarrhea	36 (6.1)
Nausea	34 (5.7)

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in France and may not reflect US clinical practice. Exploratory analysis of mOS measured from the start of 1L platinum-based chemotherapy among those without disease progression and for patients who went on to recent 2L EV post-avelumab may be subject to immortal time bias and will need to be confirmed by additional studies.

*Adverse events were considered treatment emergent if their start date was on or after avelumab initiation.
1L, first-line; 1LM, first-line maintenance;2L, second- line; aUC, advanced urothelial carcinoma; EVP, enfortumab vedotin; mOS, median overall survival; PBC, platinum-based chemotherapy; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.
Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 471) February 16-18, 2023; San Francisco, CA.

AVENANCE Low Tumor Burden Subgroups: Safety

Post hoc analysis of ongoing, real-world, ambispective study in patients with aUC who have not progressed with PBC in France and had low tumor burden at start of PBC (n=186)
Study start: July 13, 2021; Data cut-off: December 2, 2024

	Locally advanced disease (n=48)	Nonvisceral metastases (n=79)	Lymph node–only metastases (n=60)
TEAE, n (%)	40 (83.3)	60 (75.9)	48 (80.0)
Serious TEAE	20 (41.7)	13 (16.5)	10 (16.7)
TEAE leading to temporary/permanent discontinuation	31 (64.6)	42 (53.2)	36 (60.0)
TEAE leading to death	2 (4.2)	3 (3.8)	1 (1.7)
TRAE, n (%)	32 (66.7)	45 (57.0)	37 (61.7)
Serious TRAE	6 (12.5)	5 (6.3)	5 (8.3)
TRAE leading to temporary/permanent discontinuation	19 (39.6)	33 (41.8)	29 (48.3)
TRAE leading to death	0	0	0

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in France and may not reflect US clinical practice

Reported AEs occurred during the on-treatment period (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)..
1LM, first line maintenance; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.
Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 718) February 13-15, 2025; San Francisco, CA.

READY CUP: Safety

Prospective, noninterventional CUP of avelumab 1LM conducted among 464 patients with la/mUC in Italy

Patients, n (%)	All evaluable patients (n=414)
Any AE	175 (42.3)
Serious AEs	24 (5.8)
AEs leading to permanent discontinuation of avelumab	24 (5.8)
Any TRAE	112 (27.1)
Most common TRAEs*	
Pruritus	15 (3.6)
Asthenia	13 (3.1)
Fatigue	11 (2.7)
Arthralgia	10 (2.4)
Hypothyroidism	10 (2.4)
Pyrexia	10 (2.4)
Hyperthyroidism	9 (2.2)
Infusion-related reaction	7 (1.7)
Rash	6 (1.5)
Immune-related AEs	76 (18.4)

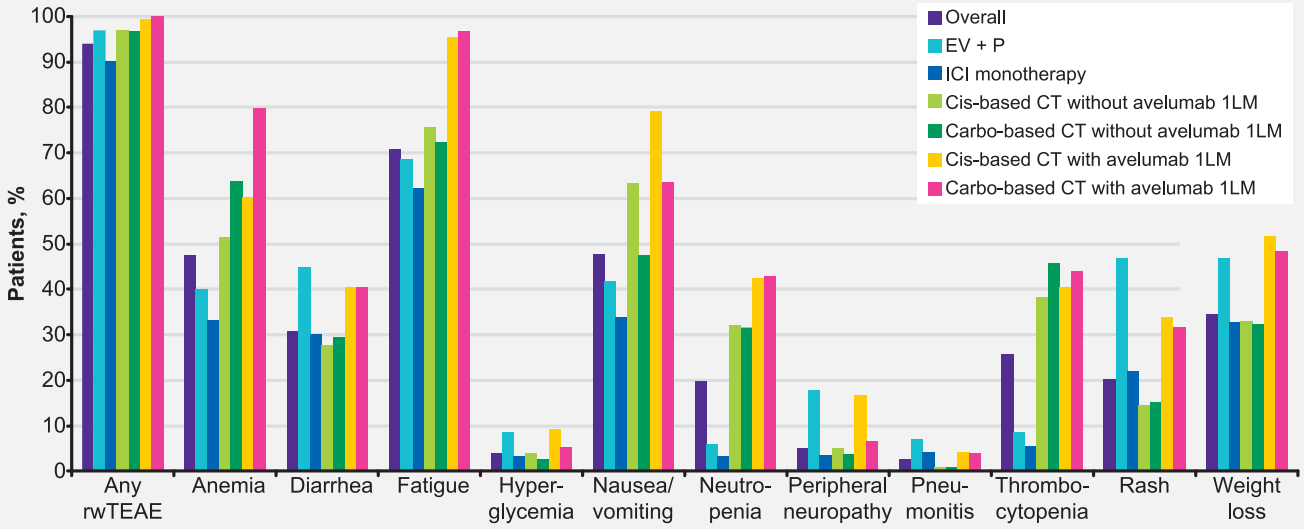
Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in Italy and may not reflect US clinical practice

*AEs/TRAEs occurring in ≥1.5% of evaluable patients are listed.
1LM, first line maintenance; AE, adverse event; CUP, compassionate use program; TRAE, treatment-related adverse event.
Antonuzzo, L., et al., ESMO Real World Data and Digital Oncology, 2024. 5: p. 100068.

Flatiron Safety: Incidence of Select rwTEAEs by 1L Regimen

Retrospective, observational safety study of 5,235 patients with Ia/mUC in the US
Study period: January 2016 to October 2023



- **296 patients** (6% of the overall population) did not have documented evidence of any rwTEAEs of interest
- Most common rwTEAEs overall:
  - fatigue (71%)
  - anemia (48%)
  - nausea (48%)

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Evaluation of rwTEAEs was limited to those occurring during 1L treatment; however, the occurrence of AEs after discontinuation was expected to be relatively low
- Line of treatment was determined using oncologist-defined, rules-based algorithms, which may have resulted in misclassification of 1L regimens
- Information on the severity/grade of rwTEAEs was not available, and the management and associated outcomes of rwTEAEs were not reported
- The study focused on descriptive analyses across the six 1L regimens without adjustment for heterogeneity in baseline patient characteristics, and statistical comparisons were not conducted; thus, caution should be exercised when attempting to compare safety data between cohorts
- The study only captured the incidence of a prespecified list of 30 AEs, and other clinically relevant AEs may have occurred that were not captured; furthermore, AEs may have been underreported, including low-grade events that are challenging to detect and measure, such as peripheral sensory neuropathy

1L, first line; 1LM, first-line maintenance; AE, adverse event Carbo, carboplatin; Cis, cisplatin; CT, chemotherapy; EV + P, enfortumab vedotin + pembrolizumab; ICI, immune checkpoint inhibitor; rwAEs, real-world adverse events; rwTEAE, real-world treatment-emergent adverse event.

Nizam A, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 759) February 13-15, 2025; San Francisco, CA.

Flatiron Safety: Incidence and Treatment-adjusted Rates of Select rwTEAEs by 1L Regimen (1/3)

Retrospective, observational safety study of 5,235 patients with Ia/mUC in the US
Study period: January 2016 to October 2023

Incidence of rwTEAEs, % (treatment-adjusted incidence rate per 1,000 patient-months on treatment)	Overall (N=5,235)	EV + P (n=198)	ICI monotherapy (n=2,146)	Without avelumab 1LM		With avelumab 1LM	
				Cis-based CT (n=1,372)	Carbo-based CT (n=1,140)	Cis-based CT (n=197)	Carbo-based CT (n=182)
Any rwTEAE	94.3 (1130.7)	97 (1491.2)	90.3 (757.9)	96.9 (1614.3)	96.7 (1755.4)	99.5 (1723.7)	100.0 (1542.2)
Anemia	47.6 (108.5)	40.0 (83.6)	33.2 (56.3)	51.5 (159.1)	63.8 (267.7)	60.4 (49.9)	79.7 (108.4)
Constipation	41.4 (89.1)	48.0 (109.7)	33.2 (55.1)	45.9 (143.3)	42.5 (125.6)	70.6 (80.9)	58.2 (51.3)
Diarrhea	30.7 (58.2)	45.0 (98.4)	30.2 (49.5)	27.8 (66.9)	29.5 (74.9)	40.6 (24.9)	40.7 (29.1)
Fatigue	70.7 (266.6)	68.7 (234.3)	62.2 (172)	75.7 (406.9)	72.5 (380.4)	95.4 (371.3)	96.7 (375.5)
Hyperglycemia	3.9 (5.6)	8.6 (12.7)	3.4 (4.1)	3.9 (7.9)	2.7 (5.4)	9.1 (4.0)	5.5 (2.6)

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Evaluation of rwTEAEs was limited to those occurring during 1L treatment; however, the occurrence of AEs after discontinuation was expected to be relatively low
- Line of treatment was determined using oncologist-defined, rules-based algorithms, which may have resulted in misclassification of 1L regimens
- Information on the severity/grade of rwTEAEs was not available, and the management and associated outcomes of rwTEAEs were not reported
- The study focused on descriptive analyses across the six 1L regimens without adjustment for heterogeneity in baseline patient characteristics, and statistical comparisons were not conducted; thus, caution should be exercised when attempting to compare safety data between cohorts
- The study only captured the incidence of a prespecified list of 30 AEs, and other clinically relevant AEs may have occurred that were not captured; furthermore, AEs may have been underreported, including low-grade events that are challenging to detect and measure, such as peripheral sensory neuropathy

1L, first line; 1LM, first-line maintenance; Carbo, carboplatin; Cis, cisplatin; CT, chemotherapy; EV + P, enfortumab vedotin + pembrolizumab; ICI, immune checkpoint inhibitor; rwTEAE, real-world treatment-emergent adverse event.

Nizam A, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 759) February 13-15, 2025; San Francisco, CA.

Flatiron Safety: Incidence and Treatment-adjusted Rates of Select rwTEAEs by 1L Regimen (2/3)

Retrospective, observational safety study of 5,235 patients with la/mUC in the US
Study period: January 2016 to October 2023

Incidence of rwTEAEs, % (treatment-adjusted incidence rate per 1,000 patient-months on treatment)	Overall (N=5,235)	EV + P (n=198)	ICI monotherapy (n=2,146)	Without avelumab 1LM		With avelumab 1LM	
				Cis-based CT (n=1,372)	Carbo-based CT (n=1,140)	Cis-based CT (n=197)	Carbo-based CT (n=182)
Hypothyroidism	1.3 (8.9)	9.1 (13.9)	9.0 (12.0)	2.5 (4.9)	2.2 (4.3)	11.7 (5.2)	8.8 (4.3)
Musculoskeletal pain	41.2 (88.1)	31.3 (57.6)	41.1 (75.4)	38.5 (105.3)	38.6 (105.5)	65.0 (66.0)	65.4 (63.0)
Nausea/vomiting	47.6 (108.4)	41.9 (85.6)	33.9 (55.0)	63.4 (258.1)	47.5 (152.7)	79.2 (115.8)	63.7 (65.9)
Neutropenia	20.0 (33.4)	6.1 (8.8)	3.3 (4.0)	32.2 (86.8)	31.5 (86.2)	42.6 (28.0)	42.9 (28.7)
Peripheral neuropathy	5.2 (7.6)	17.7 (29.0)	3.6 (4.4)	5.3 (10.9)	3.8 (7.6)	16.8 (8.4)	6.6 (2.8)
Pneumonitis	2.7 (3.9)	7.1 (10.2)	4.2 (5.2)	0.8 (1.6)	1.0 (1.9)	4.1 (1.8)	3.9 (2.0)

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Evaluation of rwTEAEs was limited to those occurring during 1L treatment; however, the occurrence of AEs after discontinuation was expected to be relatively low
- Line of treatment was determined using oncologist-defined, rules-based algorithms, which may have resulted in misclassification of 1L regimens
- Information on the severity/grade of rwTEAEs was not available, and the management and associated outcomes of rwTEAEs were not reported
- The study focused on descriptive analyses across the six 1L regimens without adjustment for heterogeneity in baseline patient characteristics, and statistical comparisons were not conducted; thus, caution should be exercised when attempting to compare safety data between cohorts
- The study only captured the incidence of a prespecified list of 30 AEs, and other clinically relevant AEs may have occurred that were not captured; furthermore, AEs may have been underreported, including low-grade events that are challenging to detect and measure, such as peripheral sensory neuropathy

1L, first line; 1LM, first-line maintenance; AE, adverse event; Carbo, carboplatin; Cis, cisplatin; CT, chemotherapy; EV + P, enfortumab vedotin + pembrolizumab; ICI, immune checkpoint inhibitor; rwTEAE, real-world treatment-emergent adverse event.

Nizam A, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 759) February 13-15, 2025; San Francisco, CA.

Flatiron Safety: Incidence and Treatment-adjusted Rates of Select rwTEAEs by 1L Regimen (3/3)

Retrospective, observational safety study of 5,235 patients with la/mUC in the US
Study period: January 2016 to October 2023

Incidence of rwTEAEs, % (treatment-adjusted incidence rate per 1,000 patient-months on treatment)	Overall N=5,235	EV + P n=198	ICI monotherapy n=2,146	Without avelumab 1LM		With avelumab 1LM	
				Cis-based CT n=1,372	Carbo-based CT n=1,140	Cis-based CT n=197	Carbo-based CT n=182
Pruritus	14.5 (24.3)	36.9 (72.5)	19.9 (30.7)	6.1 (12.4)	7.8 (16.4)	23.4 (13.0)	21.4 (13.4)
Thrombocytopenia	25.7 (44.7)	8.6 (12.7)	5.6 (6.9)	38.4 (108)	45.8 (147.1)	40.6 (26.1)	44.0 (30.2)
Rash	20.3 (35.6)	47.0 (108.7)	21.9 (33.5)	14.7 (32.5)	15.3 (34.4)	34.0 (20.1)	31.9 (20.8)
Weight loss	34.6 (66.6)	47.0 (102.2)	32.9 (53.2)	33.0 (84.1)	32.5 (84.9)	51.8 (35.1)	48.4 (34.6)

Limitations

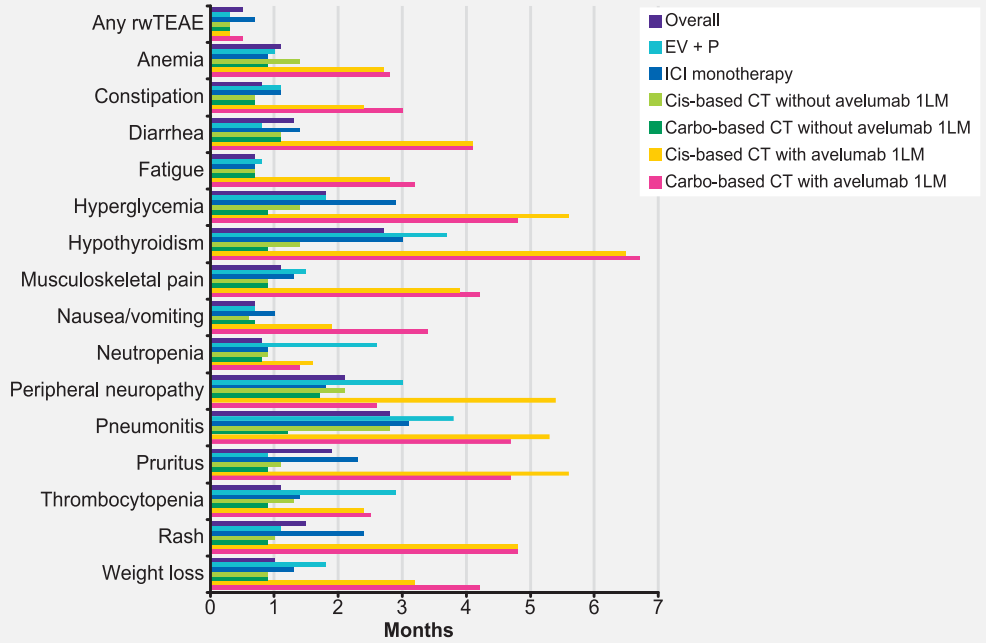
- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Evaluation of rwTEAEs was limited to those occurring during 1L treatment; however, the occurrence of AEs after discontinuation was expected to be relatively low
- Line of treatment was determined using oncologist-defined, rules-based algorithms, which may have resulted in misclassification of 1L regimens
- Information on the severity/grade of rwTEAEs was not available, and the management and associated outcomes of rwTEAEs were not reported
- The study focused on descriptive analyses across the six 1L regimens without adjustment for heterogeneity in baseline patient characteristics, and statistical comparisons were not conducted; thus, caution should be exercised when attempting to compare safety data between cohorts
- The study only captured the incidence of a prespecified list of 30 AEs, and other clinically relevant AEs may have occurred that were not captured; furthermore, AEs may have been underreported, including low-grade events that are challenging to detect and measure, such as peripheral sensory neuropathy

1L, first line; 1LM, first-line maintenance; Carbo, carboplatin; Cis, cisplatin; CT, chemotherapy; EV + P, enfortumab vedotin + pembrolizumab; ICI, immune checkpoint inhibitor; rwTEAE, real-world treatment-emergent adverse event.

Nizam A, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 759) February 13-15, 2025; San Francisco, CA.

Flatiron Safety: Median Time to Onset of Select rwTEAEs by 1L Regimen

Retrospective, observational safety study of 5,235 patients with la/mUC in the US
Study period: January 2016 to October 2023



- In patients who had any rwTEAE, median time to onset of the first rwTEAE after 1L initiation was 0.5 months (IQR, 0.2-0.7)
- 4 rwTEAEs had a median time to onset of <1 month after 1L initiation:
  - fatigue (0.7 months [IQR, 0.3-1.4])
  - nausea/vomiting (0.7 months [IQR, 0.3-1.6])
  - constipation (0.8 months [IQR, 0.3-2.0])
  - neutropenia (0.8 months [IQR, 0.5-1.8])
- rwTEAEs with the longest median time to onset after 1L initiation in the overall population:
  - pneumonitis (2.8 months [IQR, 1.1-7.3])
  - hypothyroidism (2.7 months [IQR, 0.8-5.5])

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Evaluation of rwTEAEs was limited to those occurring during 1L treatment; however, the occurrence of AEs after discontinuation was expected to be relatively low
- Line of treatment was determined using oncologist-defined, rules-based algorithms, which may have resulted in misclassification of 1L regimens
- Information on the severity/grade of rwTEAEs was not available, and the management and associated outcomes of rwTEAEs were not reported
- The study focused on descriptive analyses across the six 1L regimens without adjustment for heterogeneity in baseline patient characteristics, and statistical comparisons were not conducted; thus, caution should be exercised when attempting to compare safety data between cohorts
- The study only captured the incidence of a prespecified list of 30 AEs, and other clinically relevant AEs may have occurred that were not captured; furthermore, AEs may have been underreported, including low-grade events that are challenging to detect and measure, such as peripheral sensory neuropathy

1L, first line; 1LM, first-line maintenance; Carbo, carboplatin; Cis, cisplatin; CT, chemotherapy; EV + P, enfortumab vedotin + pembrolizumab; ICI, immune checkpoint inhibitor; IQR, interquartile range; rwTEAE, real-world treatment-emergent adverse event.

Nizam A, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 759) February 13-15, 2025; San Francisco, CA.

PATRIOT II: Safety

Observational, retrospective chart review study patients with la/mUC in routine clinical practice in the United States (N= 160).

TRAEs:

- TRAEs occurred in **62 patients (38.8%)**

- **The most common TEAEs were:**
  - fatigue (n=7 [4.4%])
  - hypothyroidism (n=7 [4.4%])
  - anemia (n=6 [3.8%])
  - infusion-related reaction (n=6 [3.8%])
  - nausea (n=6 [3.8%])
  - elevated creatinine (n=5 [3.1%])
  - diarrhea (n=4 [2.5%])
  - rash (n=4 [2.5%])

Summary of long-term safety for avelumab 1LM

	All patients (N=160)
Any TRAE, n (%)	62 (38.8)
Time to onset from avelumab initiation, mean (SD), days	95 (127)
Median (range)	56 (0-793)
Any immune-related AE, n (%)	35 (21.9)
Time to onset from avelumab initiation, mean (SD), days	146 (173)
Median (range)	91 (0-793)
Therapy stopped due to any TRAE, n (%)	16 (10.0)
Received steroid (including topical due to any TRAE, n(%)	36 (32.1)
Received high-dose systemic steroid due to TRAE, n(%)	23 (14.3)

	All patients (N=160)
TRAE(s) outcome, n (%)	**N=165***
Resolved	105 (63.6)
Unresolved	32 (19.4)
Resolved with sequelae	2 (1.2)
Unknown	26 (15.8)
Duration of TRAE(s), days†	**N=165***
Mean (SD)	97 (151)
Median (range)	31 (0-657)
Hospitalized due to TRAE, n (%)	
Yes	13 (8.1)
No	147 (91.9)

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Studies using real-world data include lack of central imaging review, missing or unknown data, potential selection bias, and confounding factors due to the lack of randomization
- This analysis of OS measured from the start of 1L PBC in this selected population without progression on 1L PBC should be interpreted with caution

*N represents number of AEs; duplicated in data file. †Most recent follow-up date used if unresolved.
1L, first-line; 1LM, first-line maintenance; AE, adverse event; la/mUC, locally advanced or metastatic urothelial carcinoma; PBC, platinum-based chemotherapy; OS, overall survival; SD, standard deviation; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

Grivas P, et al. Clin Genitourin Cancer. 2024;22(6):102238.

Bakaloudi et al: Safety

Multicenter retrospective cohort study of real-world patient characteristics and clinical outcomes with avelumab switch maintenance (N= 108).

At the time of the analysis, **48 patients (44.4%)** were still receiving avelumab maintenance

60 (55.6%) had discontinued avelumab

	Overall population, N=108
Reason for avelumab discontinuation	
Clinical progression	12 (11.1)
Radiographic progression	34 (31.5)
Toxicity	6 (5.6)
Other	8 (7.4)
Patient still on treatment	48 (44.4)

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Moderate sample size, the relatively limited number of events and the retrospective design which is characterized by lack of randomization and of central scan review, with potential selection and confounding biases.
- The involvement of multiple institutions can lead to slightly different clinical practices (eg, imaging scheduled intervals, which can affect PFS) as well as interpretation of scan review regarding therapy response or SD versus progression.

Bakaloudi DR, et al. *Clin Genitourin Cancer*. 2023;S1558-7673(23)00147-7.

RW Studies Have Generated Data from Heterogenous Populations for Avelumab Maintenance (1/2)

US					
Bakaloudi et al[1]	Tempus II[2]	Flatiron III[3]	Flatiron III Tumor Burden[4]	PATRIOT II[5]	SPEAR BLADDER II[6]
N=108	N=135*	N=214	N=266	N=160	N=1,658
mOS†: NR 12-month OS: 72.5%	**mOS†: NE** 12-month OS: 63%	**mOS†: 23.8 months** 12-month OS: 70.9%	**rwOS‡: 23.8, 19.1, 24.3, 16.5 months**	**mOS†: 24.4 months** 12-month OS: 75.7%	**mOS†: 18.5 months**
mPFS†: 9.6 months	**mPFS†: 6.4 months**	**mPFS†: 5.1 months** 12-month PFS: 32.5%	**mPFS‡: 5.6, 3.6, 8.7, 3.7 months**	**mPFS†: 5.4 months** 12-month PFS: 33%	-
TRAEs: 10%	N/A	N/A	N/A	TRAEs: 38.8%	-
Objective response rate Subgroup analysis	Sequencing	Sequencing	Subgroup analysis		Sequencing

*Number of patients in the study that completed first-line treatment post avelumab 1LM approval and received avelumab as 1LM. † Index date is start of 1LM. ‡ Presented in the metastases subgroup order of nonvisceral, visceral, lymph node only and distant.

1LM, first-line maintenance; (m)OS, (median) overall survival; (m)PFS, (median) progression-free survival; NE, not evaluated; NR, not reached; RW, real world; TRAE, treatment-related adverse event.

1. Bakaloudi D, et al. Clin Genitourin Cancer 2023;21:584-593. 2. Carson K, et al. Poster presented at: ESMO Congress (Abstract 2387P); October 20-24, 2023; Madrid, Spain; 3. Moon HH, et al. Curr Oncol. 2024;31(9):5662-5676. 4. Moon HH, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 764) February 15-18, 2023; San Francisco, CA. 5. Grass J, et al. Clin Genitourin Cancer. 2024;22(6):102238. 6. Sura S, et al. Current Oncology. 2025;32(4):187.

RW Studies Have Generated Data from Heterogenous Populations for Avelumab Maintenance (2/2)

FRANCE		ITALY	JAPAN
AVENANCE[1]	AVENANCE Low Tumor Burden[2]	READY CUP[3]	JAVEMACS Chart Review[4]
N=595	**N=186**	**N=464**	**N=350**
mOS†: 21.3 months 12-month OS: 66.5%	**mOS‡: NR, 27.2 months, NR**	**mOS†: NR** 12-month OS: 69.2%	**mOS: 31.8 months**
mPFS†: 5.7 months 12-month PFS: 35.2%	**mPFS‡: 19.8, 9.0, 13.4 months**	**mPFS†: 8.1 months** 12-month PFS: 44.3%	-
TRAEs: 59.1%	TRAEs‡: 66.7%; 57.0%; 61.7%	Grade 3/4 AEs: 7.1%	-
Subgroup analysis Histologic variants Sequencing	Subgroup analysis	-	Sequencing Subgroup analysis

*Number of patients in the study that completed first-line treatment post avelumab 1LM approval and received avelumab as 1LM. † Index date is start of 1LM. ‡ Presented in the subgroup order of locally advanced disease, nonvisceral metastases, and lymph node-only disease.

1LM, first-line maintenance; AE, adverse events; CUP, compassionate use program; (m)OS, (median) overall survival; (m)PFS, (median) progression-free survival; NE, not evaluated; NR, not reached; RW, real world; TRAE, treatment-related adverse event.

1. Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 561) January 25-27, 2024; San Francisco, CA.; 2. Barthelemy P, et al. Presented at the ASCO Genitourinary Cancers

Studies

Pre-avelumab 1LM

US-based, retrospective studies

Flatiron I

Tempus I

Post-avelumab 1LM

French-based, ambispective study
- AVENANCE
- AVENANCE Low Tumor Burden Subgroups

Italy-based, prospective study
- READY CUP

Japan-based, restrospective study
- JAVEMACS Chart Review

US-based, retrospective studies
- Tempus I
- Tempus II
- Flatiron II
- Flatiron III
- Flatiron III Tumor Burden
- Flatiron Safety
- PATRIOT-II
- SPEAR Bladder II
- IMPACT UC III

Multicenter, retrospective study based on data from Europe and the US
- Bakaloudi et al

1L, first line; 1LM, first-line maintenance; CUP, compassionate use program; UC, urothelial carcinoma.

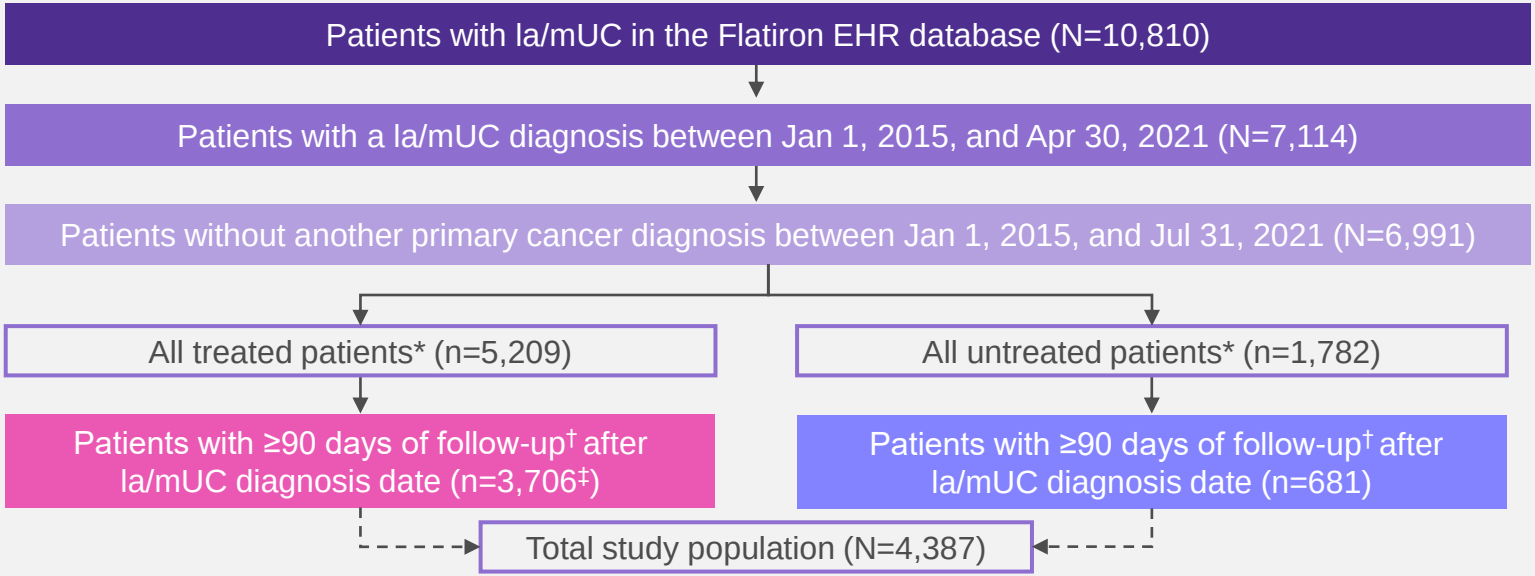
Pre-avelumab 1LM

US-based, retrospective studies

- Flatiron I
- Tempus I

Flatiron I

Study details: retrospective cohort study of patients with la/mUC using data from the Flatiron Health database from January 1, 2015, to July 31, 2021, to understand treatment patterns and real-world outcomes in patients with la/mUC in the US, including the early implementation of avelumab 1LM since its US FDA approval in June 2020.



*All patients were aged ≥18 years; †Unless in the case of death; ‡To reach this patient number, additional eligibility criteria were met: (1) no systemic treatment for la/mUC in the baseline period (n=5118); (2) <180 days between la/mUC diagnosis date and administration of 1L treatment (n=4634); (3) no clinical study drug during the study period (n=4532).
1L, first-line; 1LM, first-line maintenance; EHR, electronic health record; FDA, Food and Drug Administration; la/mUC, locally advanced/metastatic urothelial carcinoma; US, United States.
Kirker M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Flatiron: Limitations

The Flatiron Health data are not fully generalizable to the wider US population, electronic health record data are often incomplete, and data on visits to non–Flatiron Health clinics were unavailable

Kirker M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Flatiron I: Baseline Characteristics (1/4)

	All treated, n (%)	Cisplatin-based, n (%)	Carboplatin-based, n (%)	IO monotherapy, n (%)	Other, n (%)	Avelumab 1LM, n (%)
	3706 (100.0)	1235 (33.3)	1147 (30.9)	1038 (28.0)	286 (7.7)	89 (2.4)
Age at la/mUC diagnosis, mean (SD), years	71.0 (9.0)	67.0 (8.9)	72.1 (8.0)	74.6 (8.2)	71.6 (8.9)	69.2 (10.1)
Sex						
Female	984 (26.6)	335 (27.1)	284 (24.8)	290 (27.9)	75 (26.2)	20 (22.5)
Male	2721 (73.4)	899 (72.8)	863 (75.2)	748 (72.1)	211 (73.8)	69 (77.5)
Unknown	1 (<0.1)	1 (0.1)	0	0	0	0
Race						
White	2585 (69.8)	867 (70.2)	796 (69.4)	716 (69.0)	206 (72.0)	54 (60.7)
Black	168 (4.5)	57 (4.6)	53 (4.6)	39 (3.8)	19 (6.6)	2 (2.3)
Hispanic or Latino	5 (0.1)	1 (0.1)	4 (0.3)	0	0	0
Asian	48 (1.3)	22 (1.8)	13 (1.1)	11 (1.1)	2 (0.7)	0
Other	596 (16.1)	192 (15.5)	183 (16.0)	185 (17.8)	36 (12.6)	23 (25.8)
Unknown	304 (8.2)	96 (7.8)	98 (8.5)	87 (8.4)	23 (8.0)	10 (11.2)

1LM, first-line maintenance; IO, immuno-oncology; la/mUC, locally advanced/metastatic urothelial carcinoma; SD, standard deviation.

Kirker M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Flatiron I: Baseline Characteristics (2/4)

	All treated, n (%)	Cisplatin-based, n (%)	Carboplatin-based, n (%)	IO monotherapy, n (%)	Other, n (%)	Avelumab 1LM n (%)
Region of residence						
Northeast	492 (13.3)	172 (13.9)	136 (11.9)	144 (13.9)	40 (14.0)	14 (15.7)
Midwest	464 (12.5)	157 (12.7)	147 (12.8)	123 (11.8)	37 (12.9)	14 (15.7)
South	1723 (46.5)	552 (44.7)	554 (48.3)	489 (47.1)	128 (44.8)	41 (46.1)
West	511 (13.8)	174 (14.1)	164 (14.3)	144 (13.9)	29 (10.1)	13 (14.6)
Other territories	41 (1.1)	10 (0.8)	13 (1.1)	14 (1.3)	4 (1.4)	0
Unknown	475 (12.8)	170 (13.8)	133 (11.6)	124 (11.9)	48 (16.8)	7 (7.9)

Of 4,387 patients included in the study, 3,706 (84.5%) received systemic anticancer treatments

1LM, first-line maintenance; IO, immuno-oncology.

Kirker M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Flatiron I: Baseline Characteristics (3/4)

	All treated, n (%)	Cisplatin-based, n (%)	Carboplatin-based, n (%)	IO monotherapy, n (%)	Other, n (%)	Avelumab 1LM n (%)
	3706 (100.0)	1235 (33.3)	1147 (30.9)	1038 (28.0)	286 (7.7)	89 (2.4)
Site of disease						
Bladder	2825 (76.2)	990 (80.2)	832 (72.5)	794 (76.5)	209 (73.1)	73 (82.0)
Renal pelvis	485 (13.1)	141 (11.4)	175 (15.3)	127 (12.2)	42 (14.7)	9 (10.1)
Ureter	366 (9.9)	91 (7.4)	128 (11.2)	116 (11.2)	31 (10.8)	7 (7.9)
Urethra	30 (0.8)	13 (1.1)	12 (1.0)	1 (0.1)	4 (1.4)	0
Disease grade						
High grade (grades 2-4)	3185 (85.9)	1093 (88.5)	951 (82.9)	890 (85.7)	251 (87.8)	70 (78.7)
Low grade (grade 1)	174 (4.7)	50 (4.0)	58 (5.1)	52 (5.0)	14 (4.9)	4 (4.5)
Unknown/not documented	347 (9.4)	92 (7.4)	138 (12.0)	96 (9.2)	21 (7.3)	15 (16.9)
Smoking status						
History of smoking	2717 (73.3)	908 (73.5)	850 (74.1)	747 (72.0)	212 (74.1)	59 (66.3)
No history of smoking	975 (26.3)	322 (26.1)	292 (25.5)	287 (27.6)	74 (25.9)	29 (32.6)
Unknown/not documented	14 (0.4)	5 (0.4)	5 (0.4)	4 (0.4)	0	1 (1.1)
Stage at initial diagnosis						
0	13 (0.4)	5 (0.4)	4 (0.3)	4 (0.4)	0	1 (1.1)

1LM, first-line maintenance; IO, immuno-oncology.

Kirker M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Flatiron I: Baseline Characteristics (4/4)

	All treated, n (%)	Cisplatin-based, n (%)	Carboplatin-based, n (%)	IO monotherapy, n (%)	Other, n (%)	Avelumab 1LM n (%)
Stage at initial diagnosis						
I	66 (1.8)	20 (1.6)	22 (1.9)	20 (1.9)	4 (1.4)	3 (3.4)
II	286 (7.7)	52 (4.2)	54 (4.7)	149 (14.4)	31 (10.8)	6 (6.7)
III	335 (9.0)	139 (11.3)	68 (5.9)	103 (9.9)	25 (8.7)	3 (3.4)
IV	1415 (38.2)	593 (48.0)	480 (41.8)	246 (23.7)	96 (33.6)	40 (44.9)
Unknown/not documented	1591 (42.9)	426 (34.5)	519 (45.2)	516 (49.7)	130 (45.5)	36 (40.5)
PD-L1 testing status						
Yes						
Negative	342 (9.2)	107 (8.7)	115 (10.0)	94 (9.1)	26 (9.1)	15 (16.9)
Positive	393 (10.6)	117 (9.5)	107 (9.3)	144 (13.9)	25 (8.7)	20 (22.5)
Unknown	365 (9.8)	106 (8.6)	97 (8.5)	127 (12.2)	35 (12.2)	15 (16.9)
No	2606 (70.3)	905 (73.3)	828 (72.2)	673 (64.8)	200 (69.9)	39 (43.8)
GFR (mL/min/1.73m^2) at la/mUC diagnosis date (±30 days)						
30-60	128 (3.5)	6 (0.5)	53 (4.6)	57 (5.5)	12 (4.2)	20 (22.5)
<30	845 (22.8)	171 (13.8)	319 (27.8)	279 (26.9)	76 (26.6)	0
>60	800 (21.6)	363 (29.4)	221 (19.3)	163 (15.7)	53 (18.5)	30 (33.7)
Unknown	1933 (52.2)	695 (56.3)	554 (48.3)	539 (51.9)	145 (50.7)	39 (43.8)

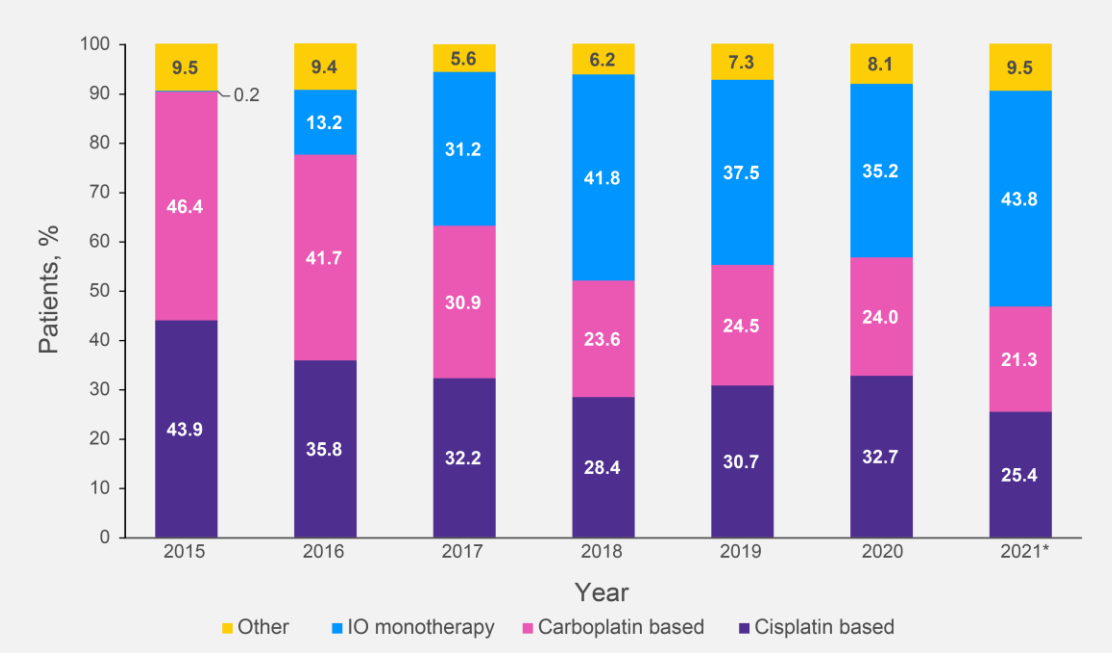
1LM, first-line maintenance; GFR, glomerular filtration rate; IO, immuno-oncology; PD-L1, programmed cell death protein ligand 1.
Kirker M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Flatiron I: Treatment Patterns by Index Year

4387 patients met selection criteria

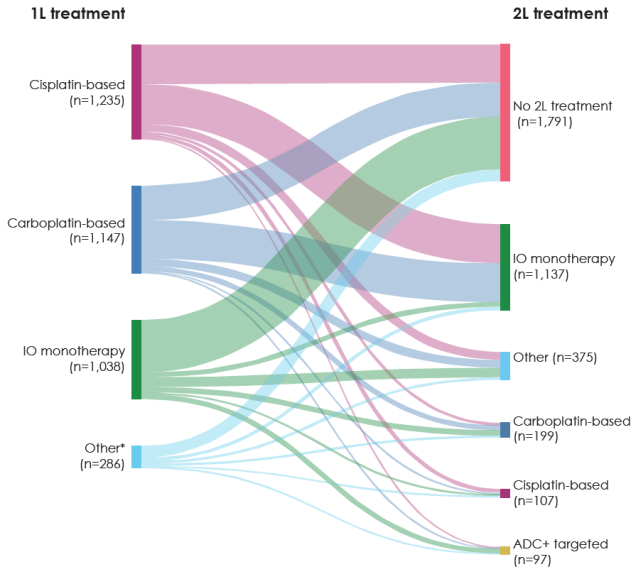
- 3706 (84.5%) received systemic treatments; of these,
  - 1235 (33.3%) received cisplatin
  - 1147 (30.9%) received carboplatin
  - 1038 (28.0%) received IO monotherapy
  - 286 (7.7%) received other therapies

Due to the recent approval of IO therapies in the 1L, there was a decrease in the proportion of patients receiving 1L PBC and an increase in those receiving 1L IO from 2015 to 2021



Limitations: The Flatiron Health data are not fully generalizable to the wider US population, electronic health record data are often incomplete, and data on visits to non–Flatiron Health clinics were unavailable.
*Only the first 6 months of 2021 were included in the study. The study period ended prior to recent changes in the FDA approvals of pembrolizumab and atezolizumab.
IO, immuno-oncology; other, other platinum-based therapies (eg, oxaliplatin) and any other treatments not falling into any previous drug class.
Kirker M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Flatiron I: Treatment Patterns



Proportion of patients with treatment sequence from 1L to 2L

		2L treatment					
Patients, n (%) 3706 (100.0)		Cisplatin-based	Carboplatin-based	IO monotherapy	ADC + target	Other	No 2L treatment†
1L treatment	Cisplatin-based	50 (4.0)	35 (2.8)	522 (42.3)	18 (1.5)	110 (8.9)	500 (40.5)
	Carboplatin-based	17 (1.5)	66 (5.8)	508 (44.3)	10 (0.9)	103 (9.0)	443 (38.6)
	IO monotherapy	22 (2.1)	69 (6.6)	63 (6.1)	65 (6.3)	128 (12.3)	691 (66.6)
	Other*	18 (6.3)	29 (10.1)	44 (15.4)	4 (1.4)	34 (11.9)	157 (54.9)

Limitations: The Flatiron Health data are not fully generalizable to the wider US population, electronic health record data are often incomplete, and data on visits to non–Flatiron Health clinics were unavailable. Of patients treated with 1L therapy, 4.1% of those treated with cisplatin-based therapy and 3.3% of those treated with carboplatin-based therapy received avelumab 1LM treatment; 58.4% were still receiving avelumab 1LM at the end of follow-up. "Other" includes other platinum-based therapies (eg, oxaliplatin) and any other treatments not falling into any previous drug class. Treatment groups are mutually exclusive. Patients were placed into each group regardless of cross-treatment group combination with this hierarchy: IO, targeted, ADC, cisplatin, carboplatin, any other. Percentages represent row percentages.
*Inclusive of ADC+ targeted. †Inclusive of patients still receiving 1L at end of follow-up: cisplatin-based therapy (48.6%); carboplatin-based therapy (62.3%); IO monotherapy (79.9%); other (61.1%).
1L, first-line; 1LM, first-line maintenance; 2L, second-line; ADC, antibody-drug conjugates; IO, immuno-oncology.

Tempus I

Study details: retrospective, observational study based on deidentified patient-level structured and unstructured data from the Tempus database, a US longitudinal electronic health record (EHR) database, to describe baseline demographic and clinical characteristics, real-world treatment patterns, and treatment sequencing in patients with la/mUC.

- Patients aged 18 years and older and diagnosed with la/mUC (T4b, N2/3, and/or M1 or overall cancer stage 3/4) between January 1, 2016, and February 23, 2022, were included

- Patients who completed 1L PBC and then received an IO therapy were categorized as 1LM or 2L
- 1LM was differentiated from 2L treatment based on a stated clinical intent of 1LM or initiation of IO therapy within 180 days of 1L PBC completion without disease progression

- Patients were then split into pre- and post-avelumab based on when they completed their 1L PBC treatment in relation to avelumab's 1LM US approval (June 30, 2020)

1L maintenance definition

If a patient…

- Received an IO therapy within 180 days of completing PBC

and

- Did not have a progression event in the same period, this IO therapy will be classified as 1LM
  - Permits CR, PR, and SD in period

2L therapy (subsequent)

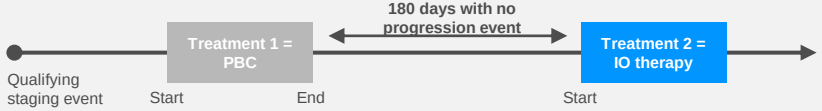
If a patient…

- Received an IO therapy >180 days after completing PBC

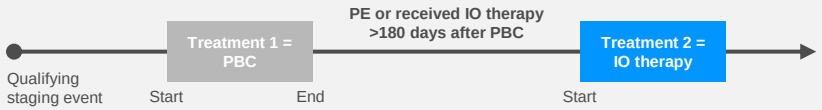
or

- Had a progression event between PBC and IO therapy

Defining 1L maintenance



2L therapy (subsequent)



1LM, first-line maintenance; 2L, second-line; CR, complete response; IO, immuno-oncology; la/mUC, locally advanced/metastatic urothelial carcinoma; PBC, platinum-based chemotherapy; PE, progression event; PR, partial response; SD, stable disease; US, United States.

Kearney M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Tempus I: Limitations

- Data were collected primarily in the oncology clinical practice setting through routine clinical care and not for research purposes; therefore, nonrandom missingness may be present for several variables of interest, and data on healthcare received outside of the Tempus network of practices are not available
- Complete medical history outside of the oncology EHR was not captured, which may lead to underreporting of treatments received
- Algorithms used to identify 1LM and 2L agents may not reflect the definitions used in clinical practice
- Patients who initiated 1L systemic therapy later in the study period may not have had enough follow-up time to observe 2L and subsequent treatment rates, which may have led to underestimates in these lines of treatment
- Similarly, the study was limited in its ability to comprehensively understand the use of avelumab in 1LM as it was approved by the FDA on June 30, 2020

1L, first-line; 1LM, first-line maintenance; 2L, second-line; EHR, electronic health record

Kearney M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Tempus I: Baseline Characteristics (1/2)

	Overall cohort, N=821
Race, n (%)	
American Indian or Alaska Native	1 (0.1)
Black or African American	53 (6.5)
Other	48 (5.8)
Unknown	200 (24)
White	519 (63)
Region, n (%)	
Midwest	214 (46)
Northeast	33 (7)
South	108 (23)
West	115 (24)
Unknown	351
Data source, n (%)	
Academic centers	221 (27)
Community centers	169 (21)
Other	426 (52)
Unknown	5

	Overall cohort, N=821
Systemic treatment, n (%)	
Treated, curated	634 (77)
Untreated	187 (23)
Follow-up from la/mUC diagnosis, median (range), months	9.20 (3.71-18.80)
Age at la/mUC diagnosis, median (IQR), years	69 (62-76)
Year of la/mUC diagnosis, n (%)	
2016	90 (11)
2017	95 (12)
2018	110 (13)
2019	182 (22)
2020	207 (25)
2021	129 (16)
2022	8 (1)
Sex, n (%)	
Male	600 (73)
Female	221 (27)

IQR, interquartile range; la/mUC, locally advanced/metastatic urothelial carcinoma; PD-L1, programmed death ligand 1.
Kearney M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Tempus I: Baseline Characteristics (2/2)

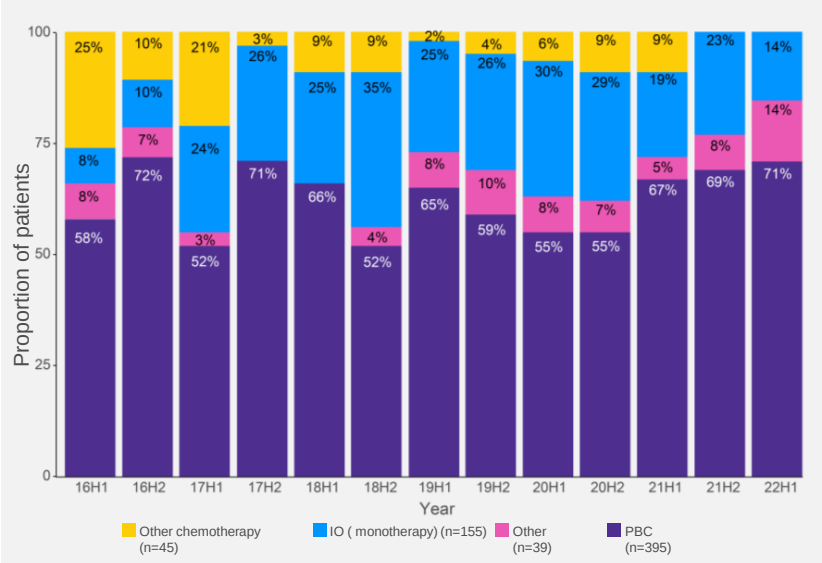
	Overall cohort, N=821
Smoking status, n (%)	
History of smoking	361 (63)
Never	212 (37)
Unknown	248
Histology type, n (%)	
Ambiguous carcinoma	131 (16)
Other	30 (3.7)
Squamous	2 (0.2)
Transitional	658 (80)
Histopathology grade, n (%)	
Grade 2 (moderately differentiated)	8 (1.6)
Grade 3 (poorly differentiated)	67 (14)
Grade 4 (undifferentiated)	1 (0.2)
High	416 (84)
Low	1 (0.2)
Unknown	328

	Overall cohort, N=821
Comorbidities, n (%)	
1	147 (37)
2	86 (22)
3	54 (14)
4+	106 (27)
Unknown	428
Death records, n (%)	305 (37)
PD-L1 status, n (%)	
Negative	123 (64)
Positive	70 (36)
Unknown	628

IQR, interquartile range; la/mUC, locally advanced/metastatic urothelial carcinoma; PD-L1, programmed death ligand 1.
Kearney M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Tempus I: Trends in 1L Therapy and Treatment Sequencing

Proportion of patients receiving 1L systemic therapy by time period (n=643)*



Treatment sequencing

	1L PBC end date pre-avelumab 1LM approval (n=243) n/N (%)
Received IO therapy as 2L or 1LM following 1L PBC	87/243 (36)
Received IO therapy as 2L	59/87 (68)
Received IO therapy as 1LM	28/87 (32)
Received 2L tx after progression on IO 1LM	9/28 (32) Enfortumab vedotin: 4/9 (44) PBC: 5/9 (56)
Did not receive IO therapy after 1L PBC but received 2L or later tx	110/243 (45)

Limitations: Data were collected primarily in the oncology clinical practice setting through routine clinical care and not for research purposes; therefore, nonrandom missingness may be present for several variables of interest, and data on healthcare received outside of the Tempus network of practices are not available. Complete medical history outside of the oncology EHR was not captured, which may lead to underreporting of treatments received . Algorithms used to identify 1LM and 2L agents may not reflect the definitions used in clinical practice. Patients who initiated 1L systemic therapy later in the study period may not have had enough follow-up time to observe 2L and subsequent treatment rates, which may have led to underestimates in these lines of treatment. Similarly, the study was limited in its ability to comprehensively understand the use of avelumab in 1LM as it was approved by the FDA3 on June 30, 2020.

*The distribution of systemic 1L therapy initiated according to treatment class is summarized by 6-month time intervals

IQR, interquartile range; la/mUC, locally advanced/metastatic urothelial carcinoma; PD-L1, programmed death ligand

1. Kearney M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Post-avelumab 1LM

French-based, ambispective study
- AVENANCE
- AVENANCE Low Tumor Burden Subgroups

Italy-based, prospective study
- READY CUP

Japan-based, retrospective study
- JAVEMACS Chart Review

US-based, retrospective studies
- Tempus I
- Tempus II
- Flatiron II
- Flatiron III
- Flatiron III Tumor Burden
- Flatiron Safety
- PATRIOT-II
- SPEAR Bladder II
- IMPACT UC III

Multicenter, retrospective study based on data from Europe and the US
- Bakaloudi et al

1LM, first-line maintenance; CUP, compassionate use program; UC, urothelial carcinoma.

AVENANCE

Study details: ongoing, real-world, ambispective study evaluating the effectiveness and safety of avelumab 1L maintenance in patients with aUC who have not progressed with PBC in France. Data collection started on July 13, 2021, and data cutoff for this analysis was December 7, 2023.

- **595 patients** received avelumab

- At data cutoff (December 7, 2023), median follow-up since avelumab initiation was 26.3 months (range: 0.6-43.7) in the full analysis set.

1L, first line; aUC, advanced urothelial carcinoma; CI, confidence interval; ddMVAC, dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin; ECOG PS, Eastern Cooperative Group performance status; PBC, platinum-based chemotherapy.

Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 561) January 25-27, 2024; San Francisco, CA

AVENANCE: Limitations

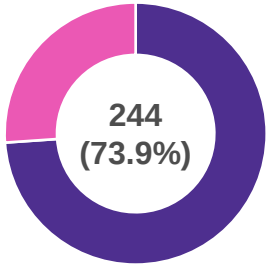
- Conducted in France and may not reflect US clinical practice.
- Exploratory analysis of mOS measured from the start of 1L platinum-based chemotherapy among those without disease progression and for patients who went on to recent 2L EV post-avelumab may be subject to immortal time bias and will need to be confirmed by additional studies.

1L, first line; aUC, advanced urothelial carcinoma; CI, confidence interval; ddMVAC, dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin; ECOG PS, Eastern Cooperative Group performance status; PBC, platinum-based chemotherapy.

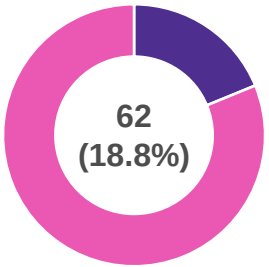
Barthélémy P, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

AVENANCE: Subsequent 2L Treatments

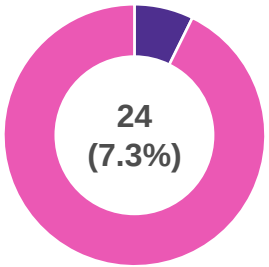
330 patients (55.5%) of the effectiveness population received 2L treatment after avelumab



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

ADC, antibody-drug conjugate.

Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 561) January 25-27, 2024; San Francisco, CA.

AVENANCE: Baseline Characteristics (1/3)

	Overall effectiveness population (N=595)	2L treatment: chemotherapy (n=244)	2L treatment: ADC (n=62)	2L treatment: other (n=24)
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 (12.0)	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)

1L, first line; 2l, second line; ADC, antibody-drug conjugate; IQR, inter-quartile range

Barthélémy P, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

AVENANCE: Baseline Characteristics (2/3)

	Overall effectiveness population (N=595)	2L treatment: chemotherapy (n=244)	2L treatment: ADC (n=62)	2L treatment: other (n=24)
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**
0	147 (31.1)	53 (28.5)	13 (26.5)	7 (35.0)
1	251 (53.1)	100 (53.8)	27 (55.1)	13 (65.0)
≥2	75 (15.9)	33 (17.7)	9 (18.4)	0

1L, first line; 2L, second line; ADC, antibody-drug conjugate; ECOG, eastern cooperative Group.

Barthélémy P, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

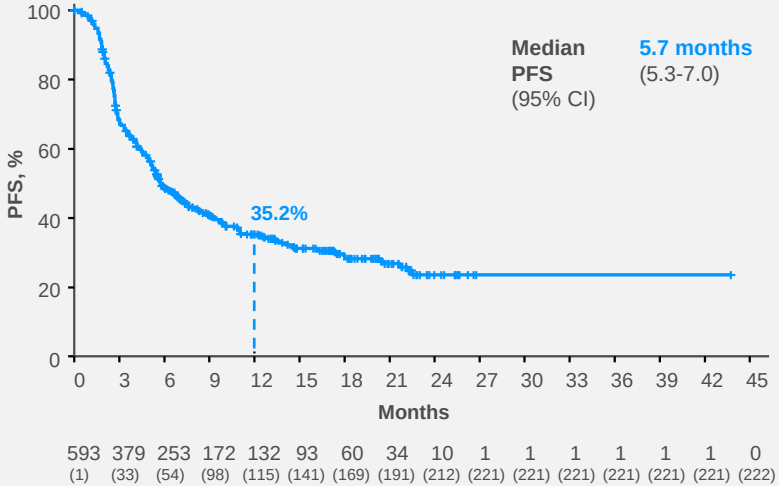
AVENANCE: Baseline Characteristics (3/3)

	Overall effectiveness population (N=595)	2L treatment: chemotherapy (n=244)	2L treatment: ADC (n=62)	2L treatment: other (n=24)
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 + gemcitabine	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)	16 (25.8)	5 (20.8)
Partial response	332 (56.3)	140 (58.1)	32 (51.6)	12 (50.0)
Stable disease	136 (23.1)	57 (23.7)	11 (17.7)	7 (29.2)
Disease progression	4 (0.7)	1 (0.4)	3 (4.8)	0
Nonevaluable	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)

*This category includes patients who switched platinum-based regimens while receiving 1L chemotherapy.
1L, first line; 2l, second line; ADC, antibody-drug conjugate; IQR, inter quartile range; ddMVAC, dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin;
Barthélémy P, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

AVENANCE: Progression-free Survival

PFS from start of avelumab 1L maintenance treatment in patients with aUC in the observational AVENANCE study (N=593) performed in France



Median follow-up*: 15.2 months
(95% CI: 14.6-16.4)

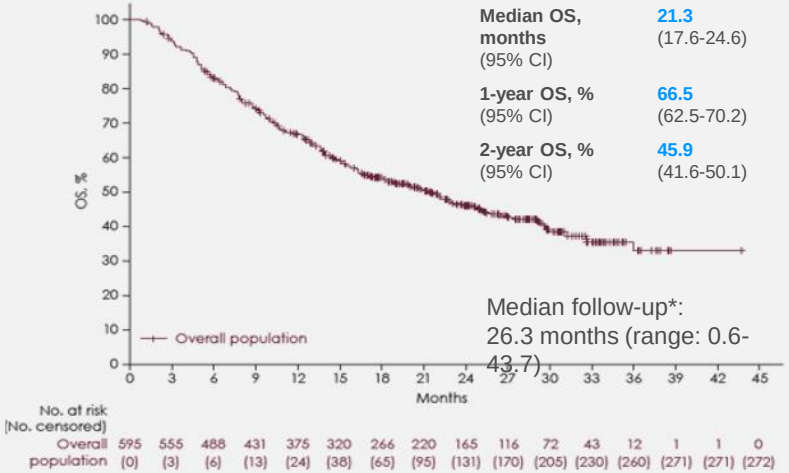
Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in France and may not reflect US clinical practice. Exploratory analysis of mOS measured from the start of 1L platinum-based chemotherapy among those without disease progression and for patients who went on to recent 2L EV post-avelumab may be subject to immortal time bias and will need to be confirmed by additional studies.

*By reverse Kaplan-Meier estimation.
1L, first-line; aUC, advanced urothelial carcinoma; CI, confidence interval; PFS, progression-free survival.
Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 471.) February 16-18, 2023; San Francisco, CA.

AVENANCE: Overall Survival

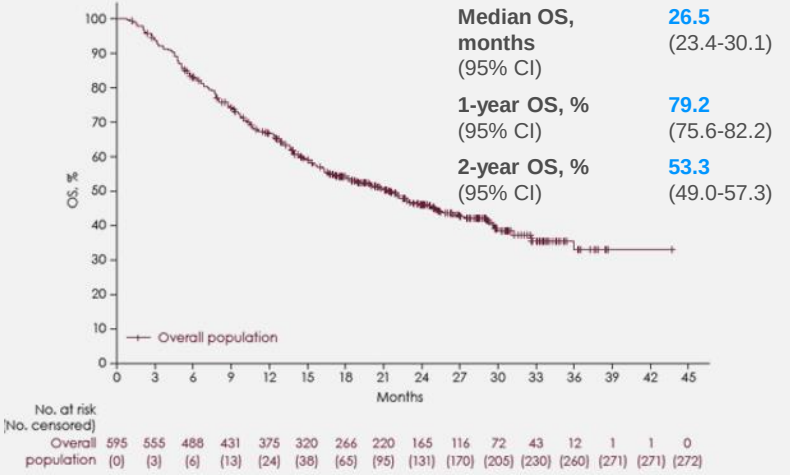
OS from start of avelumab 1L maintenance treatment (N=595)



Median OS, months (95% CI)	**21.3** (17.6-24.6)
1-year OS, % (95% CI)	**66.5** (62.5-70.2)
2-year OS, % (95% CI)	**45.9** (41.6-50.1)

Median follow-up*: 26.3 months (range: 0.6-43.7)

OS from the start of 1L platinum-based chemotherapy (N=595)



Median OS, months (95% CI)	**26.5** (23.4-30.1)
1-year OS, % (95% CI)	**79.2** (75.6-82.2)
2-year OS, % (95% CI)	**53.3** (49.0-57.3)

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in France and may not reflect US clinical practice. Exploratory analysis of mOS measured from the start of 1L platinum-based chemotherapy among those without disease progression and for patients who went on to recent 2L EV post-avelumab may be subject to immortal time bias and will need to be confirmed by additional studies.

*By reverse Kaplan-Meier estimation.
1L, first-line; aUC, advanced urothelial carcinoma; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; NE, not estimable; OS, overall survival; PFS, progression-free survival.
Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 561) January 25-27, 2024; San Francisco, CA.

AVENANCE Subgroup Analysis: OS from the Start of Avelumab 1L Maintenance Treatment

Subgroup	Patient, 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)
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)

Subgroup	Patient, n	mOS (95% CI), months
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)

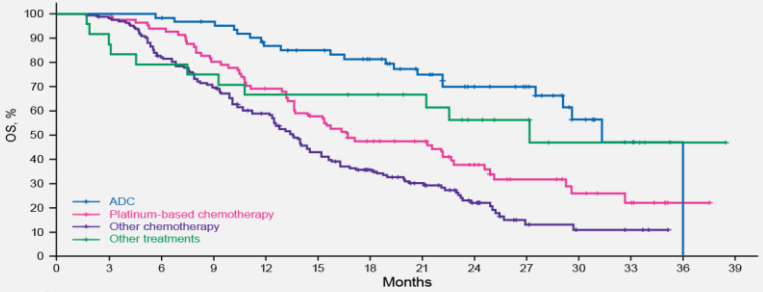
Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in France and may not reflect US clinical practice. Exploratory analysis of mOS measured from the start of 1L platinum-based chemotherapy among those without disease progression and for patients who went on to recent 2L EV post-avelumab may be subject to immortal time bias and will need to be confirmed by additional studies.

Subgroups with <20 patients are not shown.
1L, first-line therapy; CI, confidence interval; ddMVAC, dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin; NE, not estimable; NR, not reached; OS, overall survival.
Barthélémy P, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; January 25-27, 2024; San Francisco, CA.

AVENANCE Subgroup Analysis: OS Based on 2L Treatment Subgroups

From the start of 1L PBC

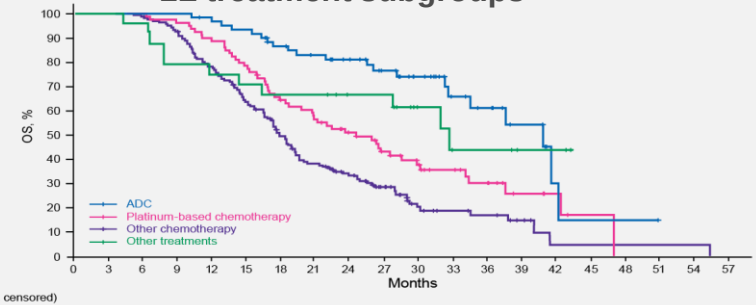


No at risk (No. censored)

ADC	62	62 (0)	61 (0)	58 (2)	51 (3)	48 (5)	42 (9)	33 (15)	25 (21)	20 (26)	9 (34)	4 (38)	0 (41)	0 (41)
Platinum-based chemotherapy	81	81 (0)	76 (0)	65 (0)	55 (1)	45 (2)	35 (4)	31 (8)	20 (13)	13 (17)	9 (19)	6 (21)	1 (26)	0 (27)
Other chemotherapy	163	159 (1)	132 (2)	112 (2)	91 (6)	65 (8)	47 (15)	35 (20)	19 (28)	7 (34)	4 (36)	3 (37)	0 (40)	0 (40)
Other treatments	24	21 (0)	19 (0)	18 (0)	16 (0)	16 (0)	15 (1)	13 (3)	9 (5)	7 (7)	4 (9)	4 (9)	1 (12)	0 (13)

	ADC (n=62)	Platinum-based chemotherapy (n=81)	Other chemotherapy (n=163)	Other treatments (n=24)
mOS (95% CI), months	31.3 (29.1-NE)	16.7 (13.6-22.8)	13.6 (12.3-15.2)	27.2 (9.3-NE)
1-year OS (95% CI), %	86.71 (75.16-93.12)	69.14 (57.84-77.97)	58.95 (50.92-66.10)	66.67 (44.28-81.73)
2-year OS (95% CI), %	70.06 (55.42-80.70)	37.88 (26.87-48.82)	22.09 (15.28-29.71)	56.41 (33.81-73.92)

2L treatment subgroups



No at risk (No. censored)

ADC	61	61 (0)	61 (0)	61 (0)	58 (1)	56 (1)	49 (4)	45 (6)	38 (12)	32 (16)	24 (23)	15 (30)	12 (32)	7 (36)	2 (39)	1 (39)	1 (39)	0 (40)	0 (40)	0 (40)
Platinum-based chemotherapy	79	79 (0)	79 (0)	76 (0)	70 (0)	62 (0)	49 (2)	43 (2)	34 (7)	26 (10)	19 (14)	15 (17)	11 (19)	5 (24)	3 (26)	1 (27)	0 (27)	0 (27)	0 (27)	0 (27)
Other chemotherapy	162	162 (0)	160 (0)	149 (1)	125 (2)	100 (3)	76 (6)	58 (7)	44 (14)	31 (21)	15 (30)	11 (33)	9 (34)	5 (37)	1 (39)	1 (39)	1 (39)	1 (39)	1 (39)	0 (39)
Other treatments	24	24 (0)	23 (0)	19 (0)	18 (0)	17 (0)	16 (0)	16 (0)	13 (3)	13 (3)	7 (8)	4 (9)	4 (9)	2 (11)	2 (11)	0 (13)	0 (13)	0 (13)	0 (13)	0 (13)

	ADC (n=61)	Platinum-based chemotherapy (n=79)	Other chemotherapy (n=162)	Other treatments (n=24)
mOS (95% CI), months	40.8 (32.6-42.1)	24.5 (19.8-29.8)	17.9 (16.5-19.2)	32.6 (14.3-NE)
1-year OS (95% CI), %	96.89 (87.42-99.16)	88.61 (79.25-93.90)	78.17 (70.94-83.81)	75.00 (52.62-87.91)
2-year OS (95% CI), %	81.08 (68.40-89.06)	51.03 (39.39-61.53)	33.48 (26.12-40.99)	66.67 (44.28-81.73)

Limitations

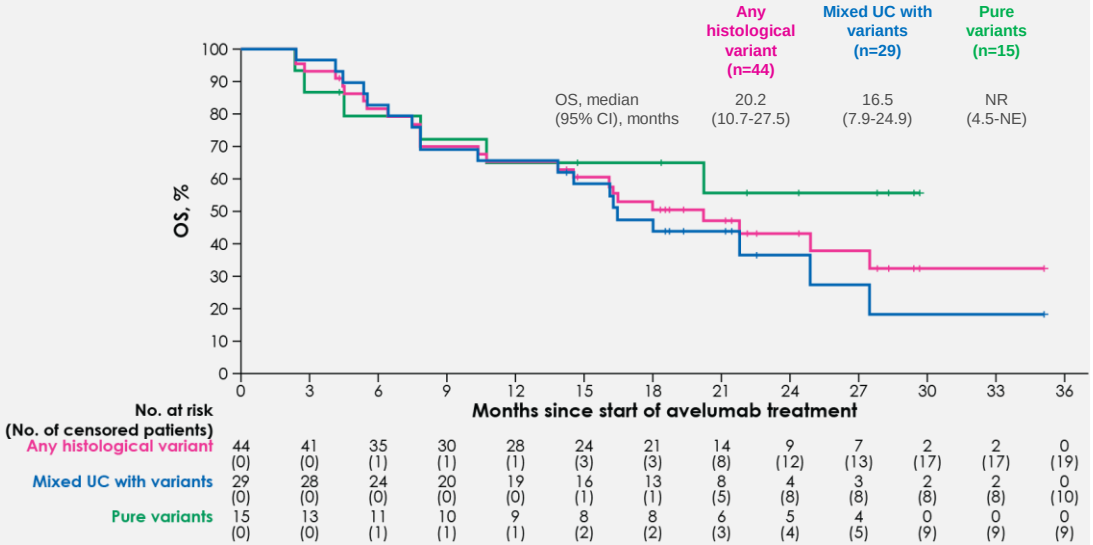
- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in France and may not reflect US clinical practice. Exploratory analysis of mOS measured from the start of 1L platinum-based chemotherapy among those without disease progression and for patients who went on to recent 2L EV post-avelumab may be subject to immortal time bias and will need to be confirmed by additional studies.

1L, first-line therapy; 1LM, first-line maintenance 2L, second-line; ADC, antibody-drug conjugate; CI, confidence interval; mOS, median overall survival; NE, not estimable; OS, overall survival; PBC: platinum based chemotheraphy.

Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 561) January 25-27, 2024; San Francisco, CA.

AVENANCE Subgroup Analysis: OS by Histologic Variants

OS from the start of avelumab treatment in patients with histological variants



- As of the data cutoff (31 May 2023)
- Median follow-up from start of avelumab 1L maintenance (by reverse Kaplan-Meier estimation):
  - 22.5 months (95% CI, 19.4-28.3 months) in all patients with histological variants
  - 21.5 months (95% CI, 18.8 months-NE) in patients with UC-V
  - 24.4 months (95% CI, 14.7-29.4 months) in patients with PV

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in France and may not reflect US clinical practice. Exploratory analysis of mOS measured from the start of 1L platinum-based chemotherapy among those without disease progression and for patients who went on to recent 2L EV post-avelumab may be subject to immortal time bias and will need to be confirmed by additional studies.

1L, first-line therapy; 1LM, first-line maintenance therapy; CI, confidence interval; mOS, median overall survival; NE, not estimable; NR, not reached; UC, urothelial carcinoma.

Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 561) January 25-27, 2024; San Francisco, CA.

AVENANCE: Safety

Adverse events, n (%)	Overall safety population (N=593)
TEAE*	428 (72.2)
Serious TEAE	200 (33.7)
TEAE leading to temporary/permanent discontinuation	171 (28.8)
TEAE leading to death	99 (16.7)
TRAE	254 (42.8)
Serious TRAE	31 (5.2)
TRAE leading to temporary/permanent discontinuation	78 (13.2)
TRAE leading to death	5 (0.8)

Events, n (%)	Overall safety population (N=593)
Asthenia	115 (19.4)
Pruritus	59 (9.9)
General physical health deterioration	44 (7.4)
Neoplasm progression	44 (7.4)
Intentional product misuse	43 (7.3)
Diarrhea	36 (6.1)
Nausea	34 (5.7)

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in France and may not reflect US clinical practice. Exploratory analysis of mOS measured from the start of 1L platinum-based chemotherapy among those without disease progression and for patients who went on to recent 2L EV post-avelumab may be subject to immortal time bias and will need to be confirmed by additional studies.

Adverse events were considered treatment emergent if their start date was on or after avelumab initiation.
TEAE, treatment-emergent adverse event; TRAE, treatment-related and -emergent adverse event.
Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 471) February 16-18, 2023; San Francisco, CA.

AVENANCE Low Tumor Burden Subgroups

Study details: post hoc analyses of an ongoing, real-world, ambispective study evaluating the effectiveness and safety of avelumab 1L maintenance in the low tumor burden subgroup of patients with aUC who have not progressed with PBC in France. Patients had low tumor burden at the start of 1L chemotherapy. Data collection started on July 13, 2021, and data cutoff for this analysis was December 2, 2024.

- **595 patients** received avelumab

- At data cutoff (December 2, 2024), median follow-up since avelumab initiation was 33.2 months (95% CI, range: 31.7-34.0) in the full analysis set

- **Characteristics of low tumor burden (n=186)**
  - Locally advanced disease (n=47)
  - Nonvisceral metastases* (n=79)
  - Lymph node-only disease (n=60)

*Bone metastases were considered visceral metastases

1L, first line; 1LM, first line maintenance; aUC, advanced urothelial carcinoma; CI, confidence interval; PBC, platinum-based chemotherapy.

Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 718) February 13-15, 2025; San Francisco, CA

AVENANCE Low Tumor Burden Subgroups

No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis

Conducted in France and may not reflect US clinical practice

1LM, first line maintenance.

Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 718) February 13-15, 2025; San Francisco, CA

AVENANCE Low Tumor Burden Subgroups: Baseline Characteristics (1/2)

Characteristic	Locally advanced disease (n=47)	Nonvisceral metastases (n=79)	Lymph node-only metastases (n=60)
Age, median (IQR), years	70.7 (64.7-77.3)	72.3 (66.0-76.3)	70.7 (66.1-74.7)
Sex, n (%)			
Female	7 (14.9)	14 (17.7)	11 (18.3)
Male	40 (85.1)	65 (82.3)	49 (81.7)
ECOG PS at start of avelumab, n (%)	n=36	n=71	n=54
0	11 (30.6)	22 (31.0)	18 (33.3)
≥1	25 (69.4)	49 (69.0)	36 (66.7)
Primary tumor site, n (%)			
Lower tract	33 (70.2)	67 (84.8)	49 (81.7)
Upper tract	14 (29.8)	12 (15.2)	11 (18.3)
Prior treatment for localized invasive UC, n (%)	17 (36.2)	35 (44.3)	27 (45.0)
Received neoadjuvant chemotherapy	3 (6.4)	8 (10.1)	7 (11.7)
Received adjuvant chemotherapy	5 (10.6)	9 (11.4)	8 (13.3)

1LM, first line maintenance; ECOG PS, Eastern Cooperative Oncology Group performance status; IQR, inter-quartile range; UC, urothelial carcinoma.

Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 718) February 13-15, 2025; San Francisco, CA

AVENANCE Low Tumor Burden Subgroups: Baseline Characteristics (2/2)

Characteristic	Locally advanced disease (n=47)	Nonvisceral metastases (n=79)	Lymph node-only metastases (n=60)
Disease stage at start of 1L chemotherapy, n (%)			
Metastatic	0	79 (100)	60 (100)
Locally advanced	47 (100)	0	0
1L chemotherapy regimen, n (%)			
Carboplatin + gemcitabine	26 (55.3)	53 (67.1)	38 (63.3)
Cisplatin + gemcitabine	14 (29.8)	19 (24.1)	16 (26.7)
Methotrexate, vinblastine, doxorubicin, and cisplatin	1 (2.1)	4 (5.1)	4 (6.7)
Other or switched*	6 (12.8)	3 (3.8)	2 (3.3)
No. of 1L chemotherapy cycles, median (range)	4 (1–10)	5 (3–10)	5 (3–10)
Response to 1L chemotherapy, n (%)	n=46		
Complete response	3 (6.5)	25 (31.6)	21 (35.0)
Partial response	30 (65.2)	35 (44.3)	28 (46.7)
Stable disease	13 (28.3)	18 (22.8)	10 (16.7)
Other	0 (0.0)	1 (1.3)	1 (1.7)

*Patients who switched platinum regimens while receiving 1L chemotherapy
1L, first line; 1LM, first line maintenance.
Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 718) February 13-15, 2025; San Francisco, CA.

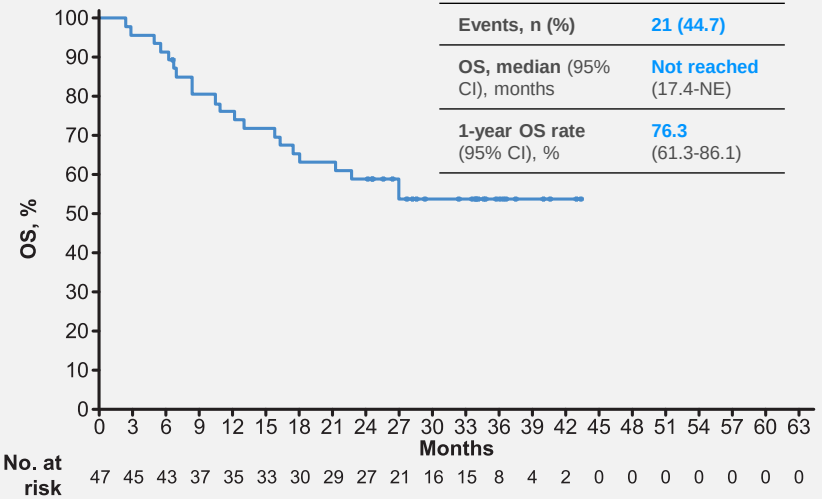
AVENANCE Low Tumor Burden Subgroups: Subsequent 2L Treatments

	Locally advanced disease (n=47)	Nonvisceral metastases (n=79)	Lymph node-only metastases (n=60)
Received subsequent treatment, n (%)	16 (34.0)	45 (57.0)	33 (55.0)
Chemotherapy	12 (25.5)	24 (30.4)	18 (30.0)
Enfortumab vedotin	3 (6.4)	12 (15.2)	8 (13.3)
Other ADC	0 (0.0)	1 (1.3)	1 (1.7)
Other treatment	1 (2.1)	8 (10.1)	6 (10.0)

1LM, first line maintenance; 2L, second line; ADC, antibody-drug conjugate.
Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 718) February 13-15, 2025; San Francisco, CA

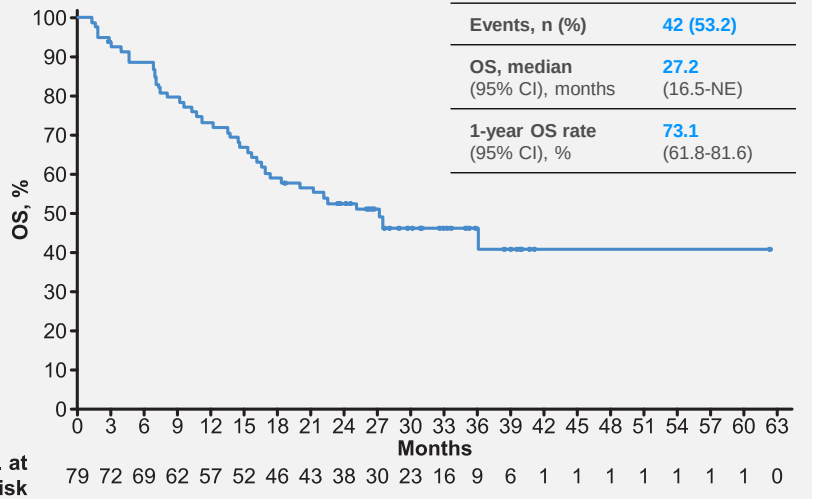
AVENANCE Low Tumor Burden Subgroups: OS from Start of Avelumab 1L Maintenance Treatment

Locally advanced disease (n=47)



Events, n (%)	21 (44.7)
OS, median (95% CI), months	Not reached (17.4-NE)
1-year OS rate (95% CI), %	76.3 (61.3-86.1)

Nonvisceral metastases (n=79)



Events, n (%)	42 (53.2)
OS, median (95% CI), months	27.2 (16.5-NE)
1-year OS rate (95% CI), %	73.1 (61.8-81.6)

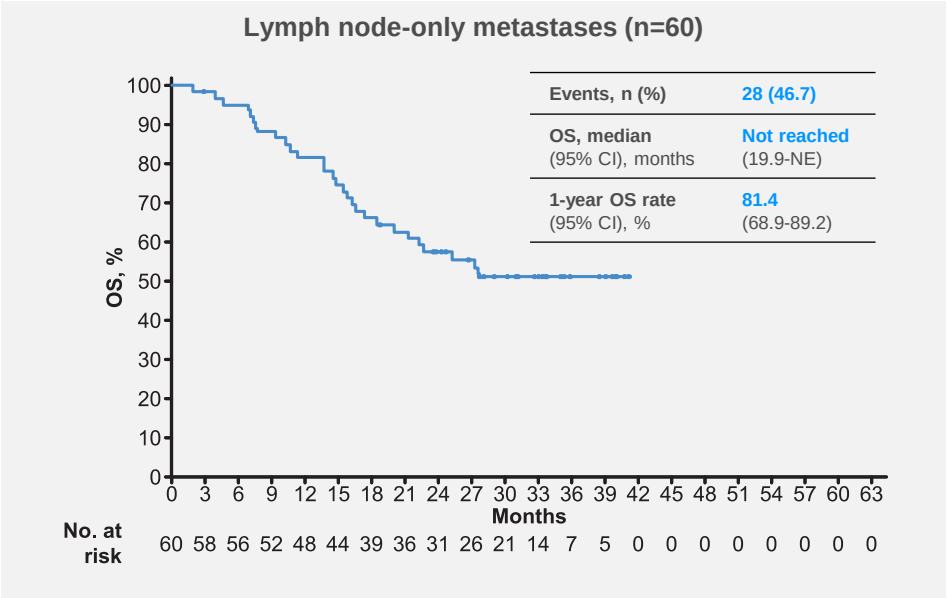
Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis.
- Conducted in France and may not reflect US clinical practice.

1L, first-line; 1LM, first line maintenance; CI, confidence interval; NE, not estimable; OS, overall survival.

Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 718) February 13-15, 2025; San Francisco, CA.

AVENANCE Low Tumor Burden Subgroups: OS from Start of Avelumab 1L Maintenance Treatment



Limitations

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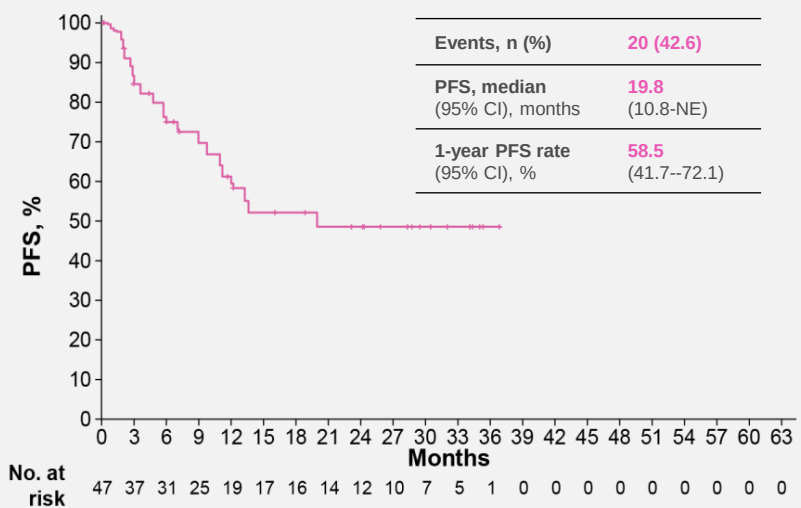
- Conducted in France and may not reflect US clinical practice.

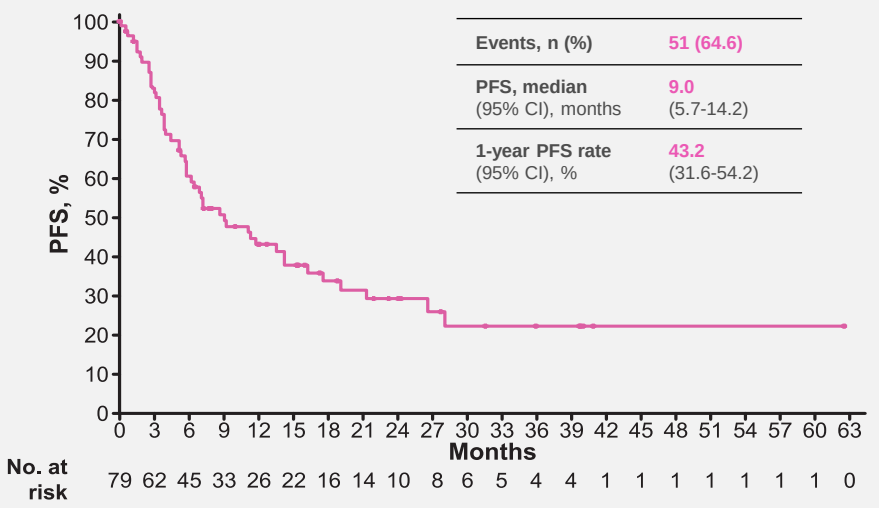
1LM, first line maintenance; CI, confidence interval; NE, not estimable; OS, overall survival.
Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 718) February 13-15, 2025; San Francisco, CA.

AVENANCE Low Tumor Burden Subgroups: PFS from Start of Avelumab 1L Maintenance Treatment

Locally advanced disease (n=47)



Nonvisceral metastases (n=79)



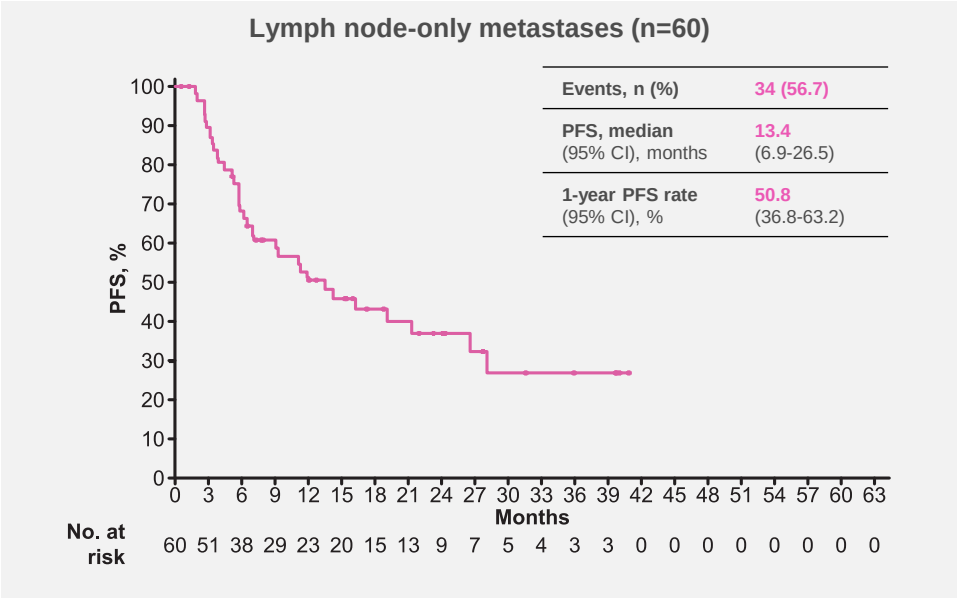
Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in France and may not reflect US clinical practice

1L, first-line; 1LM, first line maintenance; CI, confidence interval; NE, not estimable; PFS, progression-free survival.

Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 718) February 13-15, 2025; San Francisco, CA.

AVENANCE Low Tumor Burden Subgroups: PFS from Start of Avelumab 1L Maintenance Treatment



Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis.
- Conducted in France and may not reflect US clinical practice.

LM, first line maintenance; CI, confidence interval; NE, not estimable; PFS, progression-free survival.
Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 718) February 13-15, 2025; San Francisco, CA.

AVENANCE Low Tumor Burden Subgroups: Safety

	Locally advanced disease (n=48)	Nonvisceral metastases (n=79)	Lymph node–only metastases (n=60)
TEAE, n (%)	40 (83.3)	60 (75.9)	48 (80.0)
Serious TEAE	20 (41.7)	13 (16.5)	10 (16.7)
TEAE leading to temporary/permanent discontinuation	31 (64.6)	42 (53.2)	36 (60.0)
TEAE leading to death	2 (4.2)	3 (3.8)	1 (1.7)
TRAE, n (%)	32 (66.7)	45 (57.0)	37 (61.7)
Serious TRAE	6 (12.5)	5 (6.3)	5 (8.3)
TRAE leading to temporary/permanent discontinuation	19 (39.6)	33 (41.8)	29 (48.3)
TRAE leading to death	0	0	0

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis.
- Conducted in France and may not reflect US clinical practice.

Reported AEs occurred during the on-treatment period (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)..
1LM, first line maintenance; TEAE, treatment-emergent adverse event; TRAE, treatment-related and -emergent adverse event.
Barthélémy P, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 718) February 13-15, 2025; San Francisco, CA.

READY CUP

Study details: prospective, noninterventional, multicentre compassionate use program (CUP) of avelumab 1LM conducted across 140 centres among 464 patients with histologically confirmed unresectable la/mUC (stage IV) in Italy

- Patients with:
  - No disease progression after 4-6 cycles of 1L PBC
  - Received their last dose of PBC 4-10 weeks prior to starting avelumab

- Study period: January 18 2021 – March 7 2022
- Median follow-up was 20.30 months (95% CI, 19.78-20.93).
- Median duration of avelumab treatment was 3.8 months (interquartile range, 2.0-8.3).

1L, first line; 1LM, first-line maintenance; CUP, compassionate use program; la/mUC, locally advanced or metastatic urothelial carcinoma; PBC, platinum-based chemotherapy

Antonuzzo, L., et al., ESMO Real World Data and Digital Oncology, 2024. 5: p. 100068.

READY CUP: Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Since AEs were reported at the treating physician's discretion in this CUP, AEs may have been underreported
- Median duration of avelumab treatment was shorter in the READY study compared with the JAVELIN Bladder 100 and AVENANCE studies
- Conducted in Italy and may not reflect US clinical practice
- There was the potential for investigator bias and some of the inclusion criteria, including ECOG PS of 0/1, number of chemotherapy cycles, and interval time between chemotherapy and maintenance, which would have excluded some patients who could receive avelumab treatment in clinical practice

1L, first line; 1LM, first-line maintenance; CUP, compassionate use program.
Antonuzzo, L., et al., ESMO Real World Data and Digital Oncology, 2024. 5: p. 100068.

READY CUP: Baseline Characteristics

Characteristic	Evaluable patients (n=414)
Age, median (interquartile range), years	71 (64-76)
Sex, n (%)	
Male	328 (79.2)
Female	86 (20.8)
ECOG PS, n (%)	
0	293 (70.8)
1	120 (29.0)
Not reported	1 (0.2)
Site of primary tumor, n (%)	
Upper urinary tract	123 (29.7)
Lower urinary tract	286 (69.1)
Not reported	5 (1.2)
Creatinine clearance, n (%)	
≤60 mL/min	151 (36.5)
>60 mL/min	226 (54.6)
Not reported	37 (8.9)

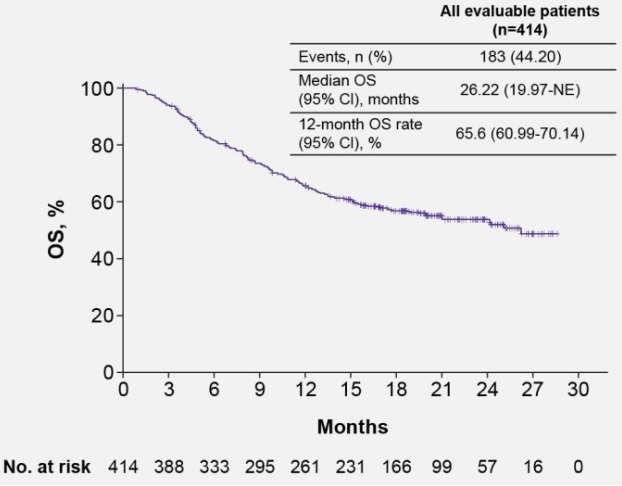
Characteristic	Evaluable patients (n=414)
Bellmunt prognostic risk factors, n (%)	
0 or 1	280 (67.6)
2	74 (17.9)
≥3	23 (5.6)
Not reported	37 (8.9)
1L chemotherapy regimen, n (%)	
Cisplatin + gemcitabine	184 (44.4)
Carboplatin + gemcitabine	221 (53.4)
MVAC	1 (0.2)
Other	8 (1.9)
No. of 1L chemotherapy cycles, median	5
Best response to 1L chemotherapy, n (%)	
CR	42 (10.1)
PR	235 (56.8)
SD	137 (33.1)

1L, first line; CR, complete response; CUP, compassionate use program; ECOG PS, Eastern Cooperative Oncology Group performance status; MVAC, methotrexate, vinblastine, doxorubicin, and cisplatin; PR, partial response; SD, stable disease.

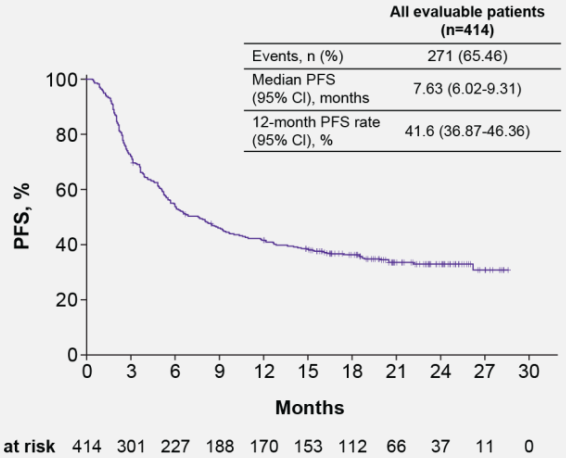
Antonuzzo, L., et al., ESMO Real World Data and Digital Oncology, 2024. 5: p. 100068.

READY CUP: OS and PFS

OS from the start of avelumab 1L maintenance therapy in all evaluable patients



PFS from start of avelumab 1L maintenance therapy in all evaluable patients



Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in Italy and may not reflect US clinical practice
- Since AEs were reported at the treating physician's discretion in this CUP, AEs may have been underreported
- There was the potential for investigator bias and some of the inclusion criteria, including ECOG PS of 0/1, number of chemotherapy cycles, and interval time between chemotherapy and maintenance, which would have excluded some patients who could receive avelumab treatment in clinical practice
- Median duration of avelumab treatment was shorter in the READY study compared with the JAVELIN Bladder 100 and AVENANCE studies

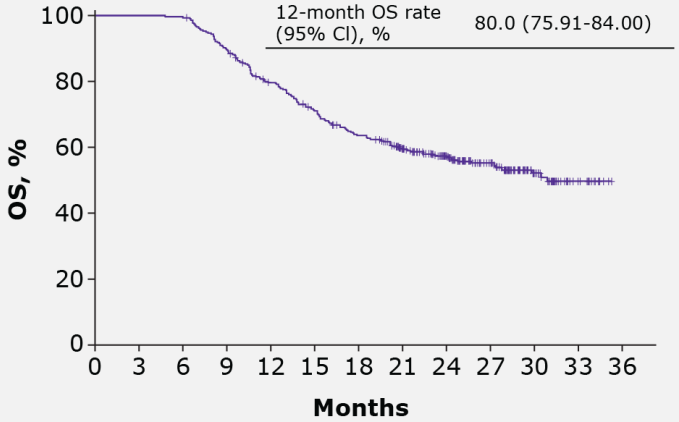
1L, first line; CI, confidence interval; CUP, compassionate use program; NE, not estimable; OS, overall survival; PFS, progression-free survival; vs, versus

Antonuzzo, L., et al., ESMO Real World Data and Digital Oncology, 2024. 5: p. 100068.

READY CUP: OS from the Start of 1L Platinum-based Chemotherapy

OS from the start of 1L chemotherapy in all evaluable patients

	Evaluable patients (n=377)
Events, n (%)	166 (44.03)
Median OS (95% CI), months	30.86 (25.69-NE)
12-month OS rate (95% CI), %	80.0 (75.91-84.00)



Limitations

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- Conducted in Italy and may not reflect US clinical practice
- Since AEs were reported at the treating physician's discretion in this CUP, AEs may have been underreported
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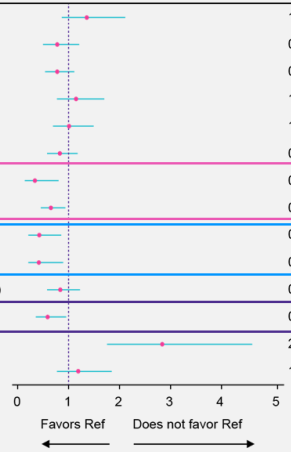
- Median duration of avelumab treatment was shorter in the READY study compared with the JAVELIN Bladder 100 and AVENANCE studies

. 1L, first line; CI, confidence interval; CUP, compassionate use program; NE, not estimable; OS, overall survival.
Antonuzzo, L., et al., ESMO Real World Data and Digital Oncology, 2024. 5: p. 100068.

READY CUP: Subgroup Analysis of OS (1/2)

Forest plot of subgroup analysis of OS from the start of avelumab 1L maintenance

Subgroup	Ref (n)		(n)	HR (95% CI)
Age	≥65 years (298)	vs	<65 years (116)	1.35 (0.87 - 2.12)
Sex	Female (86)	vs	Male (328)	0.78 (0.49 - 1.21)
Weight	≥75 kg (191)	vs	<75 kg (223)	0.78 (0.54 - 1.12)
ECOG PS	1 (120)	vs	0 (293)	1.15 (0.77 - 1.71)
1L chemotherapy regimen	Carboplatin (221)	vs	Cisplatin (184)	1.01 (0.69 - 1.48)
No. of 1L chemotherapy cycles	6 (158)	vs	4 (204)	0.83 (0.58 - 1.18)
Best response to 1L chemotherapy	CR (42)	vs	SD (137)	0.33 (0.14 - 0.81)
Best response to 1L chemotherapy	PR (235)	vs	SD (137)	0.65 (0.44 - 0.94)
Bellmunt prognostic risk factors	0 or 1 (280)	vs	≥3 (23)	0.42 (0.21 - 0.85)
Bellmunt prognostic risk factors	2 (74)	vs	≥3 (23)	0.42 (0.20 - 0.89)
Creatinine clearance	>60 mL/min (226)	vs	≤60 mL/min (151)	0.84 (0.57 - 1.23)
Lymph node only metastasis	Yes (138)	vs	No (210)	0.58 (0.36 - 0.95)
Liver metastasis	Yes (53)	vs	No (295)	2.85 (1.75 - 4.62)
Lung metastasis	Yes (83)	vs	No (265)	1.19 (0.76 - 1.86)



OS

HRs for OS were lower in patients with

- CR or PR to 1L chemotherapy vs SD
- Bellmunt score of 0-2 vs ≥3
- Lymph node–only metastasis vs no lymph node–only metastasis

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in Italy and may not reflect US clinical practice
- There was the potential for investigator bias and some of the inclusion criteria, including ECOG PS of 0/1, number of chemotherapy cycles, and interval time between chemotherapy and maintenance, which would have excluded some patients who could receive avelumab treatment in clinical practice
- Median duration of avelumab treatment was shorter in the READY study compared with the JAVELIN Bladder 100 and AVENANCE studies

1L, first line; CI, confidence interval; CR, complete response; CUP, compassionate use program; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; OS, overall survival; PR, partial response; Ref, reference; SD, stable disease.

Antonuzzo, L., et al., ESMO Real World Data and Digital Oncology, 2024. 5: p. 100068.

READY CUP: Subgroup Analysis of OS (2/2)

Median OS from the start of avelumab 1L maintenance in subgroups

Subgroup	n	Median OS (95% CI), months
1L CT regimen		
Cisplatin + gemcitabine	184	NR (16.05-NE)
Carboplatin + gemcitabine	221	25.10 (19.97-NE)
Best response to 1L CT		
CR	42	NR (24.21-NE)
PR	235	26.22 (21.22-NE)
SD	137	13.65 (10.56-NE)
Number of 1L CT cycles		
4 cycles	204	19.97 (13.65-NE)
6 cycles	158	NR (24.01-NE)
Age at the start of avelumab	116	NR (24.21-NE)
<65 years	298	25.10 (17.43-NE)
≥65 years		
Creatinine clearance		
≤60 mL/min	151	18.91 (13.95-NE)
>60 mL/min	226	NR (24.21-NE)

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in Italy and may not reflect US clinical practice
- Since AEs were reported at the treating physician's discretion in this CUP, AEs may have been underreported
- There was the potential for investigator bias and some of the inclusion criteria, including ECOG PS of 0/1, number of chemotherapy cycles, and interval time between chemotherapy and maintenance, which would have excluded some patients who could receive avelumab treatment in clinical practice
- Median duration of avelumab treatment was shorter in the READY study compared with the JAVELIN Bladder 100 and AVENANCE studies

1L, first-line; OS, overall survival; CR, complete response; CT, chemotherapy; CUP, compassionate use program; NE, not estimable; NR, not reached; PR, partial response; SD, stable disease

Antonuzzo, L., et al., ESMO Real World Data and Digital Oncology, 2024. 5: p. 100068.

READY CUP: Safety

Patients, n (%)	All evaluable patients (n=414)
Any AE	175 (42.3)
Serious AEs	24 (5.8)
AEs leading to permanent discontinuation of avelumab	24 (5.8)
Any TRAE	112 (27.1)
Most common TRAEs*	
Pruritus	15 (3.6)
Asthenia	13 (3.1)
Fatigue	11 (2.7)
Arthralgia	10 (2.4)
Hypothyroidism	10 (2.4)
Pyrexia	10 (2.4)
Hyperthyroidism	9 (2.2)
Infusion-related reaction	7 (1.7)
Rash	6 (1.5)
Immune-related AEs	76 (18.4)

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in Italy and may not reflect US clinical practice
- Since AEs were reported at the treating physician's discretion in this CUP, AEs may have been underreported
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- Median duration of avelumab treatment was shorter in the READY study compared with the JAVELIN Bladder 100 and AVENANCE studies

*AEs/TRAEs occurring in ≥1.5% of evaluable patients are listed.
AE, adverse event; CUP, compassionate use program; TRAE, treatment-related adverse event.
Antonuzzo, L., et al., ESMO Real World Data and Digital Oncology, 2024. 5: p. 100068.

JAVEMACS Chart Review

Study details: multicenter, noninterventional, retrospective study based on data from medical charts of patients with la/mUC in Japan treated at university hospitals and cancer institutes

- Patients with no disease progression following 1L PBC
- 350 patients received ≥1 dose of avelumab 1LM between February 2021 and December 2023

- 26 centers in Japan
- Data collection was retrospective

- At data cutoff (June 2024), 67 patients (19.1%) were still receiving avelumab maintenance
- At cutoff date, 200 patients (57.1%) were alive with ongoing follow-up

- Median observation period
  - 14.6 months (range, 0.16-38.5 months) from avelumab 1LM initiation
  - 20.0 months (range, 2.9-114.4 months) from PBC initiation
- Median duration of avelumab maintenance: 14.3 weeks (IQR, 7.1-30.9 weeks)

1L, first line; 1LM, first-line maintenance; la/mUC, locally advanced or metastatic urothelial carcinoma; PBC, platinum-based chemotherapy

Kitamura H, et al. Presented at the ASCO Genitourinary Cancers Symposium (Abstract No. 701), February 13-15, 2025; San Francisco, CA.

JAVEMACS Chart Review: Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in Japan and may not reflect US clinical practice

1L, first line; 1LM, first-line maintenance.
Kitamura H, et al. Presented at the ASCO Genitourinary Cancers Symposium (Abstract No. 701), February 13-15, 2025; San Francisco, CA.

JAVEMACS Chart Review: Baseline Characteristics at Avelumab 1LM Initiation (1/2)

Characteristic	Overall population (n=350)
Age, median (interquartile) [range], years	73 (67-78) [43-93]
<65 years, n (%)	61 (17.4)
≥65 and <75 years, n (%)	145 (41.4)
≥75 and <80 years, n (%)	87 (24.9)
≥80 years, n (%)	57 (16.3)
Sex, n (%)	
Male	259 (74.0)
Female	91 (26.0)
BMI (kg/m^2), n (%)	
<18.5	20 (5.7)
≥18.5 and <25	229 (65.4)
≥25	76 (21.7)
Unknown	25 (7.1)

Characteristic	Overall population (n=350)
Smoking status, n (%)	
Yes	228 (65.1)
No	110 (31.4)
Unknown	12 (3.4)
ECOG Performance Status, n (%)	
0	284 (81.1)
1	56 (16.0)
≥2	6 (1.7)
Unknown	4 (1.1)
Site of Primary Tumor, n (%)	
Ureter or renal pelvis	168 (48.0)
Bladder	177 (50.6)
Urethra	5 (1.4)

1L, first line; 1LM, first lime maintenance; BMI, body mass index; ECOG, Eastern Cooperative Oncology Group.

Kitamura H, et al. Presented at the ASCO Genitourinary Cancers Symposium (Abstract No. 701), February 13-15, 2025; San Francisco, CA.

JAVEMACS Chart Review : Baseline Characteristics at Avelumab 1LM Initiation (2/2)

Characteristic	Overall population (n=350)
Metastatic site, n (%)	
Metastases	293 (83.7%)
Regional lymph node	184 (52.6%)
Distant lymph node	105 (30.0%)
Visceral	113 (32.3%)
Lung	75 (21.4%)
Liver	24 (6.9%)
Peritoneum	14 (4.0%)
Other organs	10 (2.9%)
Bone	55 (15.7%)
Other	12 (3.4%)
Year of avelumab initiation, n (%)	
2021	115 (32.9%)
≥2022	235 (67.1%)

1L, first line; 1LM, first line maintenance.
Kitamura H, et al. Presented at the ASCO Genitourinary Cancers Symposium (Abstract No. 701), February 13-15, 2025; San Francisco, CA.

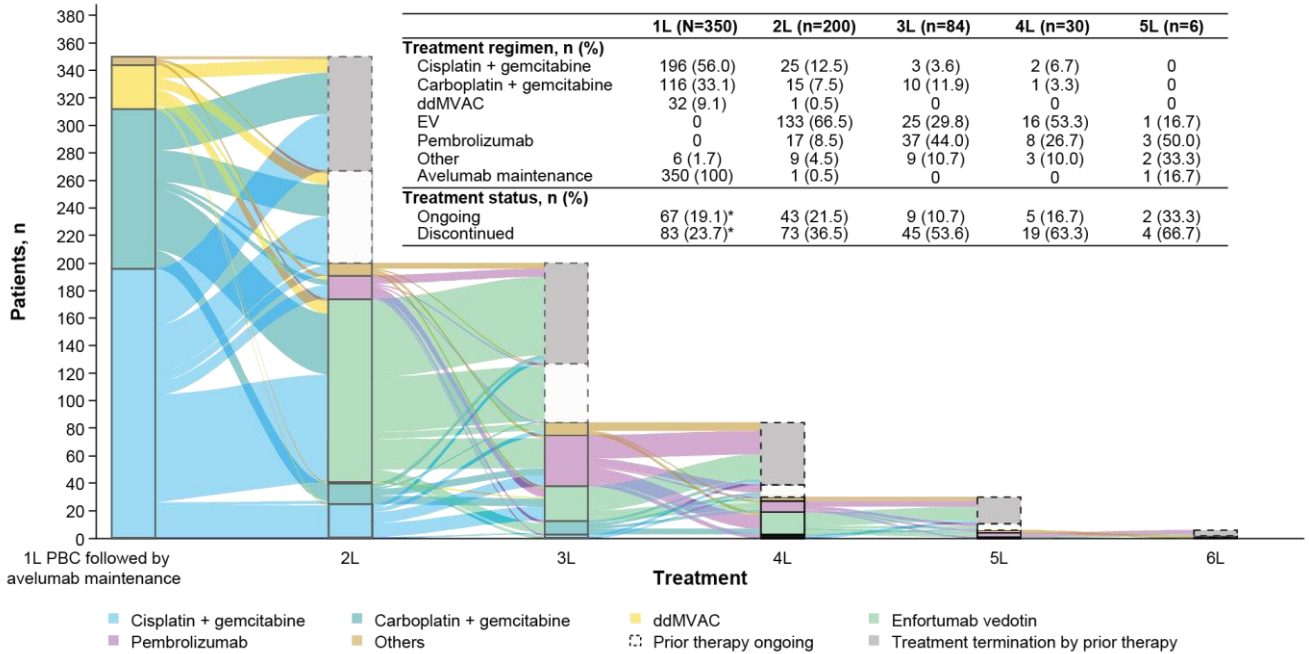
JAVEMACS Chart Review: Characteristics of 1L PBC Prior to Avelumab 1LM

Characteristic	Overall population (n=350)
1L PBC regimen, n (%)	
Cisplatin + gemcitabine	196 (56.0%)
Carboplatin + gemcitabine	116 (33.1%)
ddMVAC	32 (9.1%)
Others	6 (1.7%)
No. of cycles, n (%)	
Median (IQR)	4 (4-4)
1-3	68 (19.4%)
4	205 (58.6%)
5/6	61 (17.4%)
≥7	16 (4.6%)
Duration of 1L PBC*	
Median (IQR), weeks	19.3 (15.4-24.1)
Platinum dose reduction, n (%)	114 (32.6%)
First cycle when platinum dose reduction occurred, median (IQR)	2 (1-2)

Characteristic	Overall population (n=350)
Best Response to 1L PBC, n (%)	
CR	32 (9.1%)
PR	180 (51.4%)
SD	138 (39.4%)
Treatment-Free Interval, n (%)**	
Median (IQR), weeks	5.1 (3.6-7.1)
<4 weeks	95 (27.1%)
4-10 weeks	218 (62.3%)
>10 weeks	36 (10.3%)

*From start of 1L PBC to start of avelumab maintenance. 1 patient with unknown start and end dates of 1L PBC was excluded. **From last dose of 1L PBC to start of avelumab maintenance.
1L, first line; 1LM, first line maintenance; CR, complete response; ddMVAC, dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin; IQR, interquartile range; PBC, platinum-based chemotherapy; PR, partial response; SD, stable disease.
Kitamura H, et al. Presented at the ASCO Genitourinary Cancers Symposium (Abstract No. 701), February 13-15, 2025; San Francisco, CA.

JAVEMACS Chart Review: Treatment Patterns in Patients Treated With Avelumab 1LM



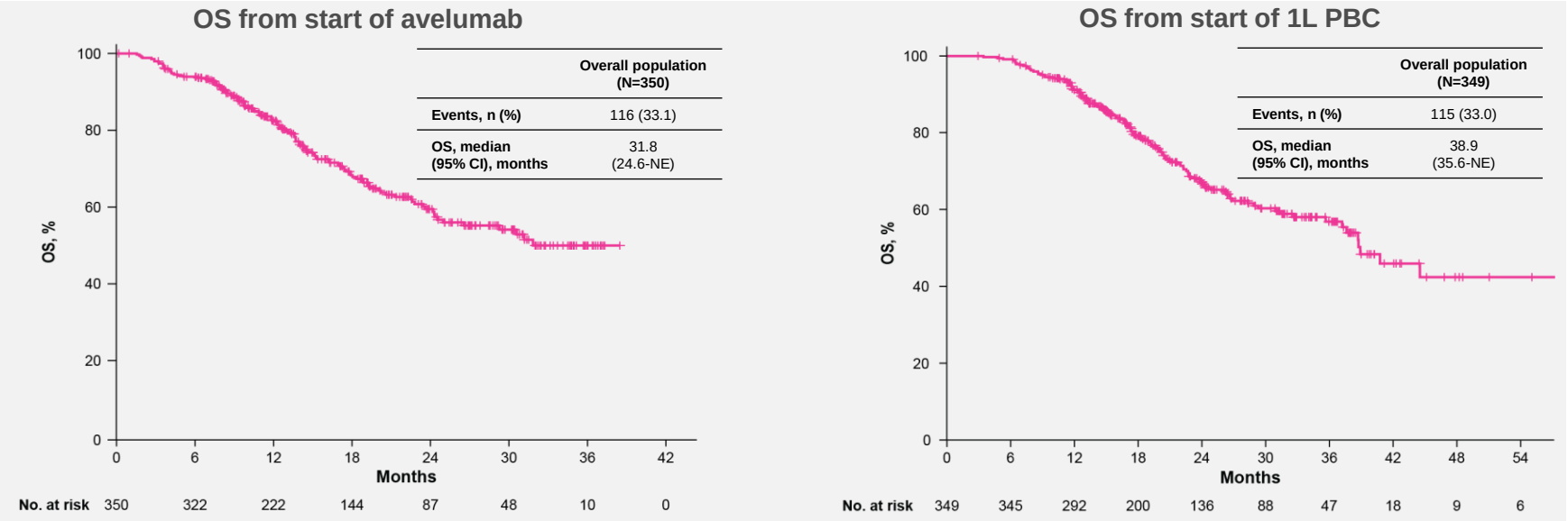
	1L (N=350)	2L (n=200)	3L (n=84)	4L (n=30)	5L (n=6)
Treatment regimen, n (%)					
Cisplatin + gemcitabine	196 (56.0)	25 (12.5)	3 (3.6)	2 (6.7)	0
Carboplatin + gemcitabine	116 (33.1)	15 (7.5)	10 (11.9)	1 (3.3)	0
ddMVAC	32 (9.1)	1 (0.5)	0	0	0
EV	0	133 (66.5)	25 (29.8)	16 (53.3)	1 (16.7)
Pembrolizumab	0	17 (8.5)	37 (44.0)	8 (26.7)	3 (50.0)
Other	6 (1.7)	9 (4.5)	9 (10.7)	3 (10.0)	2 (33.3)
Avelumab maintenance	350 (100)	1 (0.5)	0	0	1 (16.7)
Treatment status, n (%)					
Ongoing	67 (19.1)*	43 (21.5)	9 (10.7)	5 (16.7)	2 (33.3)
Discontinued	83 (23.7)*	73 (36.5)	45 (53.6)	19 (63.3)	4 (66.7)

- 283 patients discontinued avelumab. Of this,
  - 200 (70.7%) received 2L treatment
  - 83 (29.3%) discontinued without 2L treatment

Limitations
- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in Japan and may not reflect US clinical practice

*Avelumab maintenance therapy.
1L, first line; 1LM, first line maintenance; 2L, second line; 3L, third line; 4L, fourth line; 5L, fifth line; 6L, sixth line; ddMVAC, dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin; EV, enfortumab vedotin.
Kitamura H, et al. Presented at the ASCO Genitourinary Cancers Symposium (Abstract No. 701), February 13-15, 2025; San Francisco, CA.

JAVEMACS Chart Review: OS in the Overall Population



Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in Japan and may not reflect US clinical practice

Exploratory analyses of OS measured from the start of 1L PBC in this population of patients without disease progression after 1L PBC should be interpreted with caution.
Patients without a start date for 1L PBC were not included.
1L, first line; 1LM, first line maintenance; NE, not evaluable; OS, overall survival; PBC, platinum-based chemotherapy.
Kitamura H, et al. Presented at the ASCO Genitourinary Cancers Symposium (Abstract No. 701), February 13-15, 2025; San Francisco, CA.

JAVEMACS Chart Review: Univariate Analysis of Factors Associated With OS From Start of Avelumab 1LM Initiation (1/4)

Subgroup	Events/patients	OS, median (95% CI), months	HR (95% CI)	p value
Age				
<80 years (ref)	99/293	NR (24.6-NE)	–	0.74
≥80 years	17/57	25.0 (17.5-NE)	1.09 (0.65-1.83)	
Sex				
Male (ref)	86/259	31.8 (24.6-NE)	–	0.55
Female	30/91	NR (19.5-NE)	1.14 (0.75-1.72)	
BMI, kg/m²				
<18.5	10/20	12.2 (8.4-NE)	2.62 (1.35-5.09)	0.003
≥18.5 to <25 kg/m²	77/229	31.8 (24.3-NE)	–	
≥25	21/76	NR (29.3-NE)	0.72 (0.44-1.16)	
ECOG performance status				
0 (ref)	86/284	NR (26.5-NE)	–	<0.001
1	23/56	30.6 (16.3-NE)	1.44 (0.91-2.29)	
≥2	4/6	7.7 (1.5-NE)	7.40 (2.66-20.60)	

Limitations

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- Conducted in Japan and may not reflect US clinical practice

1L, first line; 1LM, first line maintenance; BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; NE, not evaluable; NR, not reached; OS, overall survival; ref, reference.

Kitamura H, et al. Presented at the ASCO Genitourinary Cancers Symposium (Abstract No. 701), February 13-15, 2025; San Francisco, CA.

JAVEMACS Chart Review: Univariate Analysis of Factors Associated With OS From Start of Avelumab 1LM Initiation (2/4)

Subgroup	Events/patients	OS, median (95% CI), months	HR (95% CI)	p value
Primary tumor location				
Bladder (ref)	57/177	NR (23.6-NE)	–	0.78
Renal pelvis/ureter	58/168	31.2 (24.2-NE)	1.11 (0.77-1.60)	
Urethra	1/5	NR (20.6-NE)	0.68 (0.09-4.92)	
Variant histology				
Pure UC (ref)	93/277	31.8 (24.6-NE)	–	0.60
UC with variant or pure non-UC	16/50	NR (20.6-NE)	0.87 (0.51-1.48)	
Visceral metastases				
No (ref)	69/236	NR (30.6-NE)	–	0.004
Yes	47/113	22.6 (17.1-NE)	1.73 (1.19-2.50)	
Eligibility				
Cis eligible (ref)	35/100	31.2 (20.0-NE)	–	0.98
Cis ineligible/pt eligible	64/185	31.8 (22.6-NE)	1.02 (0.68-1.54)	
Pt ineligible	9/30	30.6 (19.5-NE)	0.96 (0.46-2.00)	

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in Japan and may not reflect US clinical practice

1L, first line; 1LM, first line maintenance; carbo, carboplatin; cis, cisplatin; ddMVAC, dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin; HR, hazard ratio; NE, not evaluable; NR, not reached; OS, overall survival; pt, platinum; ref, reference; UC, urothelial carcinoma.

Kitamura H, et al. Presented at the ASCO Genitourinary Cancers Symposium (Abstract No. 701), February 13-15, 2025; San Francisco, CA.

JAVEMACS Chart Review: Univariate Analysis of Factors Associated With OS From Start of Avelumab 1LM Initiation (3/4)

Subgroup	Events/patients	OS, median (95% CI), months	HR (95% CI)	p value
1L PBC regimen				
Cis + gem (ref)	61/196	NR (31.2-NE)	–	0.08
Carbo + gem	47/116	24.3 (19.5-30.6)	1.53 (1.04-2.24)	
ddMVAC	7/32	NR (20.0-NE)	0.77 (0.35-1.69)	
Others	1/6	NR (10.9-NE)	0.54 (0.08-3.92)	
No. of 1L PBC cycles				
1-3	26/68	25.0 (15.2-NE)	1.39 (0.88-2.20)	0.54
4 (ref)	61/205	NR (29.3-NE)	–	
5/6	21/61	31.2 (18.0-NE)	1.12 (0.68-1.84)	
≥7	8/16	23.6 (19.3-NE)	1.29 (0.62-2.70)	
Best response to 1L PBC				
CR	5/32	NR (30.6-NE)	0.32 (0.13-0.81)	0.03
PR (ref)	61/180	31.2 (22.6-NE)	–	
SD	50/138	26.5 (20.2-NE)	1.12 (0.77-1.62)	

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in Japan and may not reflect US clinical practice

1L, first line; 1LM, first line maintenance; carbo, carboplatin; cis, cisplatin; CR, complete response; ddMVAC, dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin; HR, hazard ratio; NE, not evaluable; NR, not reached; OS, overall survival; PBC, platinum-based chemotherapy; PR, partial response; ref, reference; SD, stable disease.

Kitamura H, et al. Presented at the ASCO Genitourinary Cancers Symposium (Abstract No. 701), February 13-15, 2025; San Francisco, CA.

JAVEMACS Chart Review: Univariate Analysis of Factors Associated With OS From Start of Avelumab 1LM Initiation (4/4)

Subgroup	Events/patients	OS, median (95% CI), months	HR (95% CI)	p value
Treatment-free interval				
<4 weeks	35/95	29.3 (19.5-NE)	1.07 (0.71-1.61)	0.33
≥4 to ≤10 weeks (ref)	70/218	NR (24.2-NE)	–	
>10 weeks	10/36	NR (20.6-NE)	0.63 (0.33-1.22)	

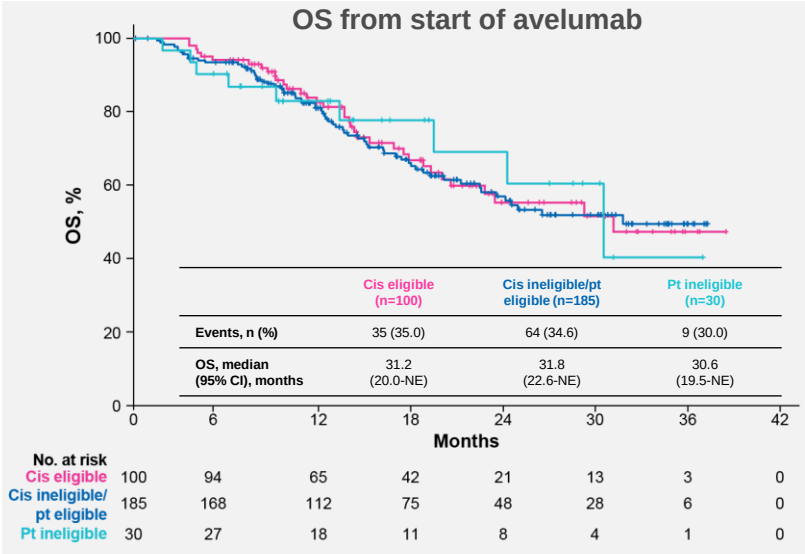
Limitations

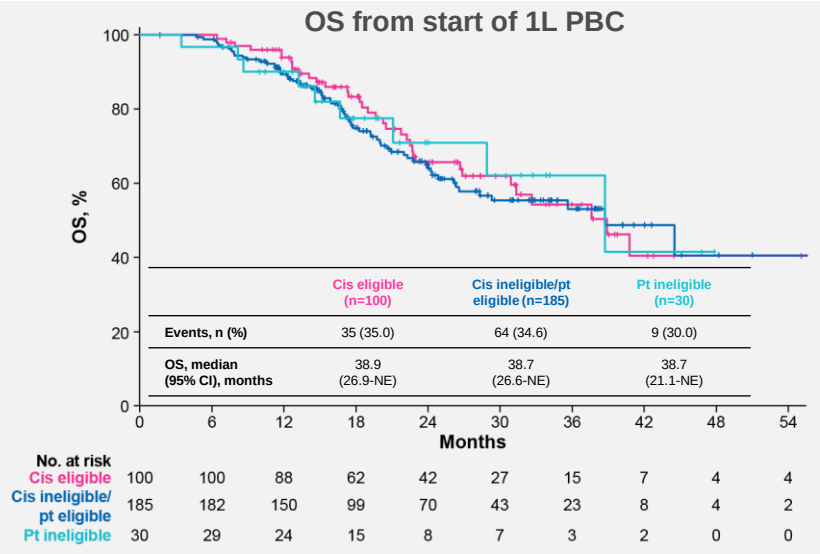
- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in Japan and may not reflect US clinical practice

1L, first line; 1LM, first line maintenance; CI, confidence interval; NE, not evaluable; OS, overall survival; ref, reference.

Kitamura H, et al. Presented at the ASCO Genitourinary Cancers Symposium (Abstract No. 701), February 13-15, 2025; San Francisco, CA.

JAVEMACS Chart Review: OS in Subgroups Defined by Cisplatin and Platinum Eligibility





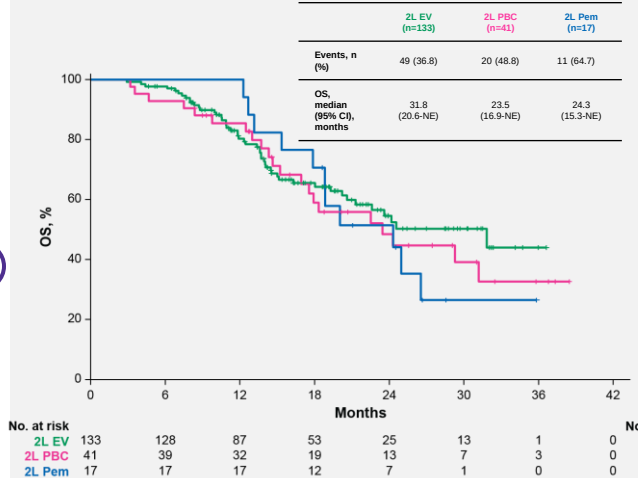
Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in Japan and may not reflect US clinical practice

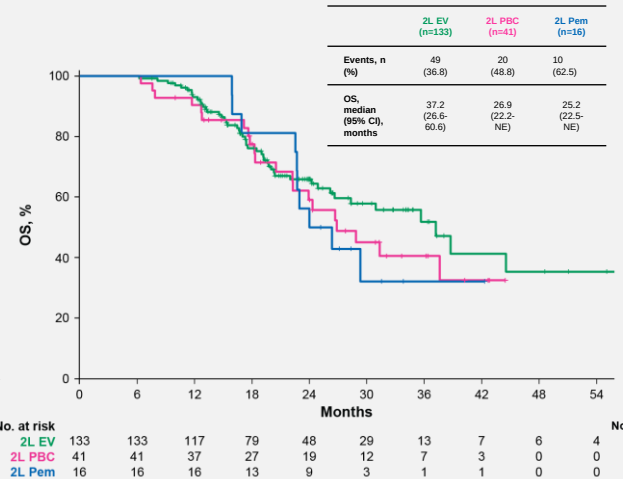
Exploratory analyses of OS measured from the start of 1L PBC in this population of patients without disease progression after 1L PBC should be interpreted with caution.
Patients without a start date for 1L PBC were not included.
1L, first line; 1LM, first line maintenance; carbo, carboplatin; cis, cisplatin; ddMVAC, dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin; NE, not evaluable; OS, overall survival; PBC, platinum-based chemotherapy; pt, platinum.
Kitamura H, et al. Presented at the ASCO Genitourinary Cancers Symposium (Abstract No. 701), February 13-15, 2025; San Francisco, CA.

JAVEMACS Chart Review: OS in Patients Receiving 2L Treatment

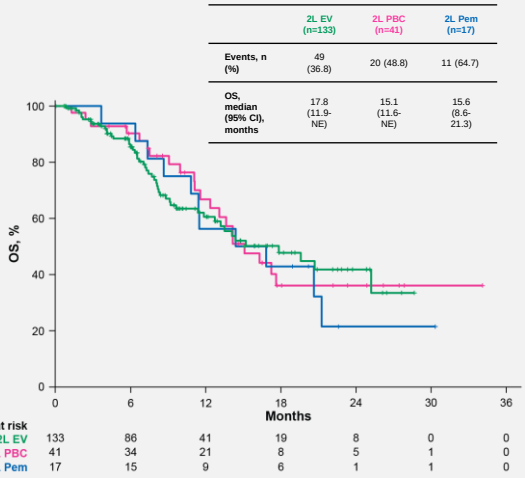
OS from start of avelumab



OS from start of 1L PBC



OS from start of 2L treatment



Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Conducted in Japan and may not reflect US clinical practice

Exploratory analyses of OS measured from the start of 1L PBC in this population of patients without disease progression after 1L PBC should be interpreted with caution.
Patients without a start date for 1L PBC were not included.
1L, first line; 1LM, first line maintenance; 2L, second line; EV, enfortumab vedotin; NE, not evaluable; OS, overall survival; PBC, platinum-based chemotherapy; Pem, pembrolizumab.
Kitamura H, et al. Presented at the ASCO Genitourinary Cancers Symposium (Abstract No. 701), February 13-15, 2025; San Francisco, CA.

Tempus I

Study details: retrospective, observational study based on deidentified patient-level structured and unstructured data from the Tempus database, a US longitudinal electronic health record (EHR) database, to describe baseline demographic and clinical characteristics, real-world treatment patterns, and treatment sequencing in patients with la/mUC.

- Patients aged 18 years and older and diagnosed with la/mUC (T4b, N2/3, and/or M1 or overall cancer stage 3/4) between January 1, 2016, and February 23, 2022, were included

- Patients who completed 1L PBC and then received an IO therapy were categorized as 1LM or 2L
- 1LM was differentiated from 2L treatment based on a stated clinical intent of 1LM or initiation of IO therapy within 180 days of 1L PBC completion without disease progression

- Patients were then split into pre- and post-avelumab based on when they completed their 1L PBC treatment in relation to avelumab's 1LM US approval (June 30, 2020)

1L maintenance definition

If a patient…

- Received an IO therapy within 180 days of completing PBC

and

- Did not have a progression event in the same period, this IO therapy will be classified as 1LM
  - Permits CR, PR, and SD in period

2L therapy (subsequent)

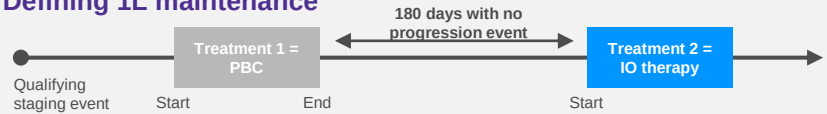
If a patient…

- Received an IO therapy >180 days after completing PBC

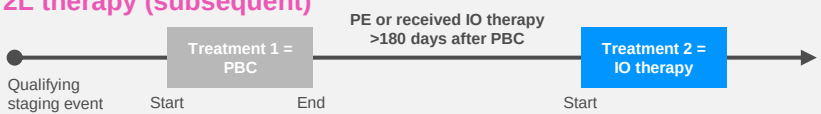
or

- Had a progression event between PBC and IO therapy

Defining 1L maintenance



2L therapy (subsequent)



1LM, first-line maintenance; 2L, second-line; CR, complete response; IO, immuno-oncology; la/mUC, locally advanced/metastatic urothelial carcinoma; PBC, platinum-based chemotherapy; PE, progression event; PR, partial response; SD, stable disease; US, United States.

Kearney M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Tempus I: Limitations

- Data were collected primarily in the oncology clinical practice setting through routine clinical care and not for research purposes; therefore, nonrandom missingness may be present for several variables of interest, and data on healthcare received outside of the Tempus network of practices are not available
- Complete medical history outside of the oncology EHR was not captured, which may lead to underreporting of treatments received
- Algorithms used to identify 1LM and 2L agents may not reflect the definitions used in clinical practice
- Patients who initiated 1L systemic therapy later in the study period may not have had enough follow-up time to observe 2L and subsequent treatment rates, which may have led to underestimates in these lines of treatment
- Similarly, the study was limited in its ability to comprehensively understand
the use of avelumab in 1LM as it was approved by the FDA on June 30, 2020

Kearney M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Tempus I: Baseline Characteristics (1/2)

	Overall cohort, N=821
Race, n (%)	
American Indian or Alaska Native	1 (0.1)
Black or African American	53 (6.5)
Other	48 (5.8)
Unknown	200 (24)
White	519 (63)
Region, n (%)	
Midwest	214 (46)
Northeast	33 (7)
South	108 (23)
West	115 (24)
Unknown	351 (43)
Data source, n (%)	
Academic centers	221 (27)
Community centers	169 (21)
Other	426 (52)
Unknown	5 (1)

	Overall cohort, N=821
Systemic treatment, n (%)	
Treated, curated	634 (77)
Untreated	187 (23)
Follow-up from la/mUC diagnosis, median (range), months	9.20 (3.71-18.80)
Age at la/mUC diagnosis, median (IQR), years	69 (62-76)
Year of la/mUC diagnosis, n (%)	
2016	90 (11)
2017	95 (12)
2018	110 (13)
2019	182 (22)
2020	207 (25)
2021	129 (16)
2022	8 (1)
Sex, n (%)	
Male	600 (73)
Female	221 (27)

IQR, interquartile range; la/mUC, locally advanced/metastatic urothelial carcinoma; PD-L1, programmed death ligand 1.
Kearney M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Tempus I: Baseline Characteristics (2/2)

	Overall cohort, N=821
Smoking status, n (%)	
History of smoking	361 (63)
Never	212 (37)
Unknown	248
Histology type, n (%)	
Ambiguous carcinoma	131 (16)
Other	30 (3.7)
Squamous	2 (0.2)
Transitional	658 (80)
Histopathology grade, n (%)	
Grade 2 (moderately differentiated)	8 (1.6)
Grade 3 (poorly differentiated)	67 (14)
Grade 4 (undifferentiated)	1 (0.2)
High	416 (84)
Low	1 (0.2)
Unknown	328

	Overall cohort, N=821
Comorbidities, n (%)	
1	147 (37)
2	86 (22)
3	54 (14)
4+	106 (27)
Unknown	428
Death records, n (%)	305 (37)
PD-L1 status, n (%)	
Negative	123 (64)
Positive	70 (36)
Unknown	628

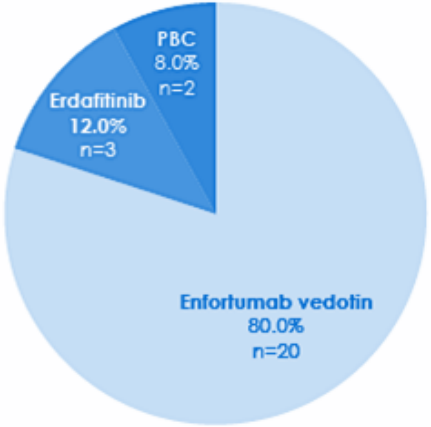
IQR, interquartile range; la/mUC, locally advanced/metastatic urothelial carcinoma; PD-L1, programmed death ligand 1.
Kearney M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA.

Tempus I: Treatment Patterns and Sequencing[1]

Treatment patterns across lines of treatment*

	All patients (N=821)	Most common tx
Untreated, n (%)	187 (22.8%)	N/A
Treated, n (%)		
1L tx	634 (77.2%)	Cisplatin + gemcitabine: 175 (27.6%) Carboplatin + gemcitabine: 124 (19.6%) Pembrolizumab: 108 (17.0%) MVAC: 45 (7.1%) Atezolizumab†: 35 (5.5%) Other: 147 (23.2%)
1LM tx	97 (24.6%)‡	Avelumab: 63 (64.9%) Other IO therapy: 34 (35.1%)
2L tx	210 (33.1%)	Pembrolizumab: 57 (27.1%) Enfortumab vedotin: 35 (16.7%) Carboplatin + gemcitabine: 19 (9.0%) Atezolizumab†: 12 (5.7%) Avelumab: 14 (6.7%) Other: 73 (34.8%)
3L tx	65 (31.0%)	Enfortumab vedotin: 14 (21.5%) Pembrolizumab: 13 (20.0%) Avelumab: 8 (12.3%) Atezolizumab†: 7 (10.8%) Carboplatin + gemcitabine: 4 (6.2%) Other: 19 (29.2%)

2L treatments after progression on IO 1LM after avelumab approval



Limitations

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- Complete medical history outside of the oncology EHR was not captured, which may lead to underreporting of treatments received. Algorithms used to identify 1LM and 2L agents may not reflect the definitions used in clinical practice.

*Data available is from both pre- and post- avelumab's 1LM US approval on June 30, 2020.[2] †Atezolizumab is no longer approved in the US to treat patients with locally advanced or metastatic urothelial carcinoma following the manufacturer's decision to withdraw its indication after consulting with the FDA. The withdrawal was made in accordance with the FDA's Accelerated Approval Program after results from the phase 3 IMvigor130 trial (NCT02807636) failed to meet the post-marketing requirement necessary to convert the accelerated approval for atezolizumab into regular approval.[3] ‡Percentage calculated from patients that received 1L platinum-based chemotherapy (n=395).
1L, first-line; 1LM, first-line maintenance; 2L, second-line; 3L, third-line; FDA, Food and Drug Administration; IO, immuno-oncology; MVAC, methotrexate, vinblastine, doxorubicin, cisplatin; tx, treatment.
1. Kearney M, et al. Poster presented at: ASCO Genitourinary Cancers Symposium; February 16-18, 2023; San Francisco, CA. 2. BAVENCIO® (avelumab). Prescribing information. Rockland, MA: EMD Serono, Inc. https://www.emdserono.com/us-en/pi/bavencio-pi.pdf 3. Cancer network. Atezolizumab no longer available in US for a certain type of bladder cancer. https://www.cancernetwork.com/view/atezolizumab-no-longer-available-in-us-for-a-certain-type-of-bladder-cancer. Accessed January 2024.

Tempus II

Study details: retrospective, observational study based on deidentified patient-level structured and unstructured data from the Tempus database, a US longitudinal electronic health record (EHR) database, to describe baseline demographic and clinical characteristics, real-world treatment patterns, and treatment sequencing in patients with la/mUC.

- Patients aged 18 years and older and diagnosed with la/mUC (T4b, N2/3, and/or M1 or overall cancer stage 3/4) between January 1, 2016, and March 13, 2023, were included

- Patients who completed 1L PBC and then received an IO therapy were categorized as 1LM or 2L
  - 1LM was differentiated from 2L treatment based on a stated clinical intent of 1LM or initiation of IO therapy within 180 days of 1L PBC completion without disease progression

1L maintenance definition

If a patient…

- Received an IO therapy within 180 days of completing PBC

and

- Did not have a progression event in the same period, this OS therapy will be classified as 1LM
  - Permits CR, PR, and SD in period

2L therapy (subsequent)

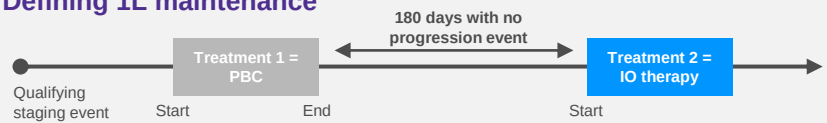
If a patient…

- Received an IO therapy >180 days after completing PBC

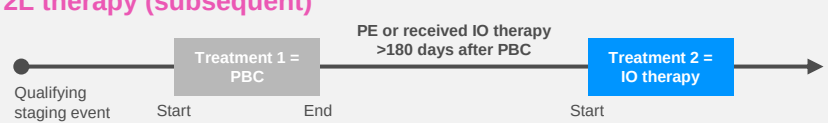
or

- Had a progression event between PBC and IO therapy

Defining 1L maintenance



2L therapy (subsequent)



1LM, first-line maintenance; 2L, second-line; IO, immuno-oncology; la/mUC, locally advanced/metastatic urothelial carcinoma; PBC, platinum-based chemotherapy; PE, progression event; PR, partial response; SD, stable disease;

Carson K, et al. Poster presented at: Presented at the ESMO Congress 2023, 20-24 October 2023; Madrid, Spain.

Tempus II: Limitations

- Data were collected primarily in the oncology clinical practice setting through routine clinical care; therefore, nonrandom missingness may be present for several variables of interest
- Algorithms used to identify 1LM and 2L agents may not reflect the definitions used in clinical practice. In addition, there was potential for misclassification based on the algorithms used
- Complete medical history outside of the Tempus database was not captured, which may lead to underreporting of treatments received
- Patients who initiated 1L systemic therapy later in the study period may not have had enough follow-up for 2L and subsequent treatment rates to be observed

1L, first-line; 1LM, first-line maintenance; 2L, second-line

Carson K, et al. Poster presented at: Presented at the ESMO Congress 2023, 20-24 October 2023; Madrid, Spain

Tempus II: Baseline Characteristics (1/2)

Characteristic	Overall cohort, N=1,939
Follow-up from la/mUC diagnosis, median (range), months	19 (17-22)
Age at la/mUC diagnosis, median (range), years	70 (62-76)
Year of la/mUC diagnosis, n (%)	
2016	112 (6)
2017	161 (8)
2018	219 (11)
2019	381 (20)
2020	429 (22)
2021	431 (22)
2022	199 (10)
2023	7 (<1)
Sex, n (%)	
Male	1,431 (74)
Female	508 (26)

Characteristic	Overall cohort, N=1,939
Race, n (%)	
White	1,212 (63)
Black or African American	100 (5)
Asian	39 (2)
American Indian or Alaska Native	6 (<1)
Native Hawaiian or Other Pacific Islander	2 (<1)
Other race	70 (4)
Unknown	510 (26)
Region, n (%)	
Midwest	337 (43)
South	203 (26)
West	175 (22)
Northeast	65 (8)
Unknown	1,159

la/mUC, locally advanced/metastatic urothelial carcinoma

Carson K, et al. Poster presented at: Presented at the ESMO Congress 2023, 20-24 October 2023; Madrid, Spain.

Tempus II: Baseline Characteristics (2/2)

Characteristic	Overall cohort, N=1,939
Data source, n (%)	
Academic centers	567 (40)
Community centers	375 (26)
Other	474 (33)
Histology type, n (%)	
Transitional	1,713 (88)
Ambiguous carcinoma	152 (8)
Other	73 (4)
Comorbidities, n (%)	
1	347 (48)
2	142 (20)
3	74 (10)
4+	154 (21)
Unknown	1,222
Deceased records, n (%)	795 (41)

la/mUC, locally advanced/metastatic urothelial carcinoma

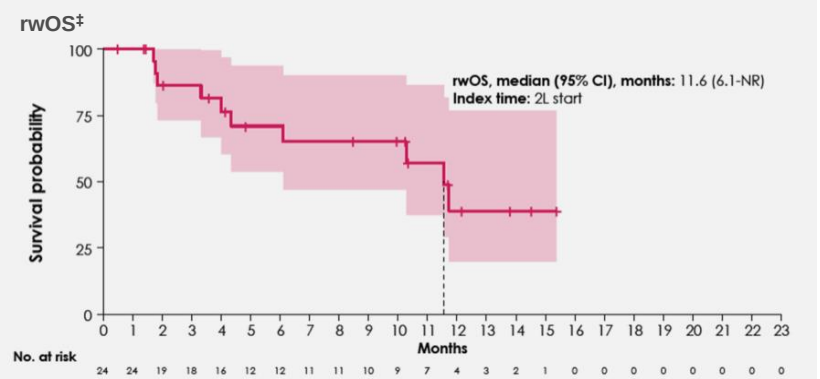
Carson K, et al. Poster presented at: Presented at the ESMO Congress 2023, 20-24 October 2023; Madrid, Spain.

Tempus II: Overall Survival

Overall survival rates in patients: 1L PBC and avelumab 1LM

	1L PBC (n=644)*	Avelumab 1LM (n=135)†
Time on treatment, median (95% CI), months	2.73 (2.53-2.96)	3.85 (2.76-4.96)
rwOS (95% CI), %		
6-month landmark	82 (78-87)	80 (72-90)
12-month landmark	56 (50-63)	63 (52-75)
18-month landmark	42 (36-50)	43 (31-59)

OS: avelumab 1LM followed by 2L EV



Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Data were collected primarily in the oncology clinical practice setting through routine clinical care and not for research purposes; therefore, nonrandom missingness may be present for several variables of interest, and data on healthcare received outside of the Tempus network of practices are not available.
- Complete medical history outside of the oncology EHR was not captured, which may lead to underreporting of treatments received .
- Algorithms used to identify 1LM and 2L agents may not reflect the definitions used in clinical practice. Patients who initiated 1L systemic therapy later in the study period may not have had enough follow-up time to observe 2L and subsequent treatment rates, which may have led to underestimates in these lines of treatment.
- Similarly, the study was limited in its ability to comprehensively understand the use of avelumab in 1LM as it was approved by the FDA on June 30, 2020

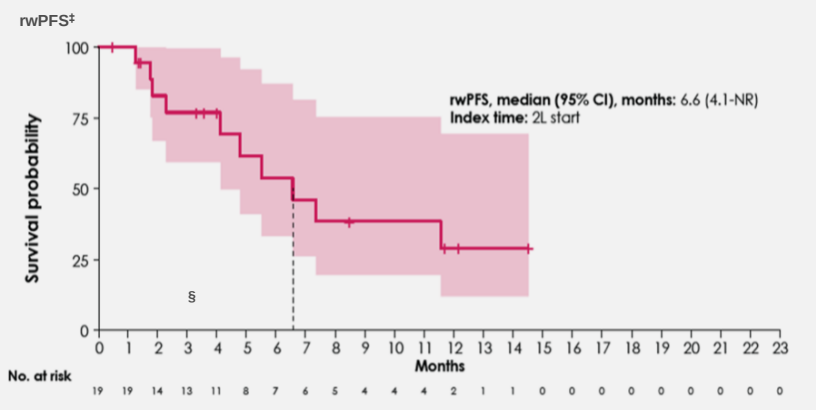
* Median follow-up from 1L PBC was 10.2 months. †Median follow-up from start of 1LM was 8.9 months. ‡This rwOS analysis included 26 of 33 patients receiving 2L EV after PBC and avelumab 1LM sequence. Not all 26 patients were at risk at time 0 due to the risk-set adjustment methodology.
1LM, first-line maintenance; 2L, second-line; EV, enfortumab vedotin; NR, not reached; PBC, platinum-based chemotherapy; rwOS, real-world overall survival; rwPFS, real-world progression-free survival.
Carson K, et al. Poster presented at: Presented at the ESMO Congress 2023, 20-24 October 2023; Madrid, Spain.

Tempus II: Progression-free Survival

Progression-free survival rates in patients: 1L PBC and avelumab 1LM

	1L PBC (n=644)*	Avelumab 1LM (n=135)†
Time on treatment, median (95% CI), months	2.73 (2.53-2.96)	3.85 (2.76-4.96)
rwPFS		
Median (95% CI), months	3.5 (3.3-4.1)	6.4 (4.6-NR)
3-month landmark (95% CI), %	65 (57-74)	73 (64-83)
6-month landmark (95% CI), %	10 (6-17)	52 (42-65)
12-month landmark (95% CI), %	2 (1-7)	40 (30-54)

PFS: avelumab 1LM followed by 2L EV



Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Data were collected primarily in the oncology clinical practice setting through routine clinical care and not for research purposes; therefore, nonrandom missingness may be present for several variables of interest, and data on healthcare received outside of the Tempus network of practices are not available.
- Complete medical history outside of the oncology EHR was not captured, which may lead to underreporting of treatments received .
- Algorithms used to identify 1LM and 2L agents may not reflect the definitions used in clinical practice. Patients who initiated 1L systemic therapy later in the study period may not have had enough follow-up time to observe 2L and subsequent treatment rates, which may have led to underestimates in these lines of treatment.
- Similarly, the study was limited in its ability to comprehensively understand the use of avelumab in 1LM as it was approved by the FDA on June 30, 2020

* Median follow-up from 1L PBC was 10.2 months. †Median follow-up from start of 1LM was 8.9 months. ‡This rwPFS analysis included 20 of 33 patients receiving 2L EV after PBC and avelumab 1LM sequence. Not all 20 patients were at risk at time 0 due to the risk-set adjustment methodology

1LM, first-line maintenance; 2L, second-line; EV, enfortumab vedotin; NR, not reached; PBC, platinum-based chemotherapy; rwOS, real-world overall survival; rwPFS, real-world progression-free survival.

Carson K, et al. Poster presented at: Presented at the ESMO Congress 2023, 20-24 October 2023; Madrid, Spain.

Tempus II: Treatment Patterns and Sequencing

Treatment setting	Patients n/N (%)	Most common treatment, n (%)	
1L	974/974 (100)	• Cisplatin + gemcitabine: 297 (30) • Carboplatin + gemcitabine: 200 (21) • Pembrolizumab: 154 (16)	• MVAC: 60 (6) • Nivolumab: 36 (4) • Other: 227 (23)
1LM	219/644 (34)*	• Avelumab: 135 (62)	• Other IO therapy: 84 (38)
2L	258/974 (26)	• EV: 70 (27) • Pembrolizumab: 47 (18) • Carboplatin + gemcitabine: 34 (13) • Cisplatin + gemcitabine: 17 (7)	• Nivolumab: 17 (7) • Erdafitinib: 10 (4) • Gemcitabine: 10 (4) • Other: 53 (20)
3L	74/258 (29)	• EV: 15 (20) • Pembrolizumab: 10 (14) • Avelumab: 10 (14) • Erdafitinib: 9 (12)	• Sacituzumab govitecan: 7 (10) • Atezolizumab: 4 (5) • Carboplatin + gemcitabine: 4 (5) • Other: 15 (20)

Limitations

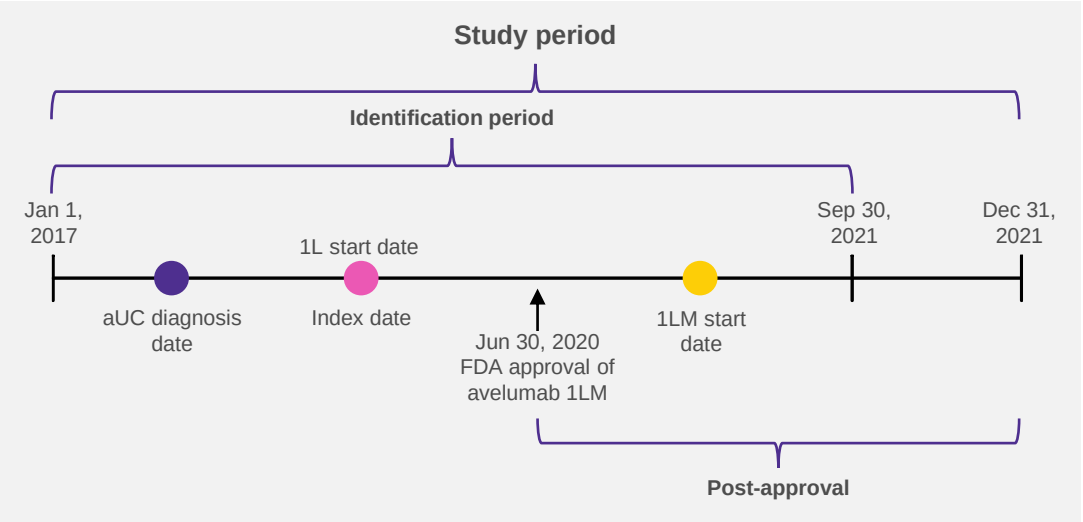
- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Data were collected primarily in the oncology clinical practice setting through routine clinical care and not for research purposes; therefore, nonrandom missingness may be present for several variables of interest, and data on healthcare received outside of the Tempus network of practices are not available.
- Complete medical history outside of the oncology EHR was not captured, which may lead to underreporting of treatments received .
- Algorithms used to identify 1LM and 2L agents may not reflect the definitions used in clinical practice. Patients who initiated 1L systemic therapy later in the study period may not have had enough follow-up time to observe 2L and subsequent treatment rates, which may have led to underestimates in these lines of treatment.
- Similarly, the study was limited in its ability to comprehensively understand the use of avelumab in 1LM as it was approved by the FDA on June 30, 2020

*Percentage calculated from patients who received 1L platinum-based chemotherapy. † Atezolizumab is no longer approved in the US to treat patients with locally advanced or metastatic urothelial carcinoma following the manufacturer's decision to withdraw its indication after consulting with the FDA. The withdrawal was made in accordance with the FDA's Accelerated Approval Program after results from the phase 3 IMvigor130 trial (NCT02807636) failed to meet the postmarketing requirement necessary to convert the accelerated approval for atezolizumab into regular approval.
1LM, first-line maintenance; 2L, second-line; EV, enfortumab vedotin; NR, not reached; PBC, platinum-based chemotherapy; rwOS, real-world overall survival; rwPFS, real-world progression-free survival.
Carson K, et al. Poster presented at: Presented at the ESMO Congress 2023, 20-24 October 2023; Madrid, Spain.

Flatiron II

Study details: noninterventional, retrospective cohort study of patients with aUC in the US aimed to assess current real-world response rates and outcomes in patients treated with 1L PBC and to understand patient eligibility for avelumab 1LM and early utilization following the FDA approval on June 30, 2020. The study used Flatiron Health's EHR database from approximately 280 cancer clinics.

- Study period: January 1, 2017, to December 31, 2021
- Identification period: January 1, 2017, to September 30, 2021, to ensure ≥3 months of follow-up unless a patient died
  - The index date was the start date for 1L treatment in the identification period
- Patients were classified as having received avelumab 1LM if they had received 1L PBC, initiated avelumab within 180 days of 1L PBC discontinuation, and had no documented progression before initiating avelumab



1L, first-line; 1LM, first-line maintenance; aUC, advanced urothelial carcinoma; EHR, electronic health record; FDA, Food and Drug Administration; PBC, platinum-based chemotherapy.

Moon HH, et al. Poster presented at: ASCO Annual Meeting; June 2-6, 2023; Chicago, IL.

Flatiron II: Limitations

- Immortal time and selection biases since patients were required to have recorded response or SD, thus resulting in a potential overestimation of rwOS
- This study could not estimate true rwPFS, given that a 1L progression-free cohort was used to evaluate the avelumab 1LM-eligible population; only PFS after completion of 1L PBC was estimated
- Retrospective study, lack of randomization, lack of granularity in specific data points (eg, site of metastasis, laboratory values), lack of central scan review, residual confounding, and short duration of study period post approval of avelumab 1LM by the FDA

Moon HH, et al. Poster presented at: ASCO Annual Meeting; June 2-6, 2023; Chicago, IL.

Flatiron II: Baseline Characteristics (1/2)

Characteristic	rwCR/rwPR	rwSD
Total, n (%)	752 (100)	246 (100)
Age at aUC diagnosis, years		
Mean (SD)	69.6 (9.0)	69.6 (10.1)
Sex, n (%)		
Female	209 (27.8)	54 (22.0)
Male	543 (72.2)	192 (78.0)
Race, n (%)		
Asian	12 (1.6)	2 (0.8)
Black or African American	40 (5.3)	11 (4.5)
Hispanic or Latino	1 (0.1)	1 (0.4)
White	493 (65.6)	169 (68.7)
Other race	127 (16.9)	41 (16.7)
Unknown	79 (10.5)	22 (8.9)

Characteristic	rwCR/rwPR	rwSD
Region of residence, n (%)		
Northeast	88 (11.7)	39 (15.9)
Midwest	107 (14.2)	30 (12.2)
South	350 (46.5)	114 (46.3)
West	115 (15.3)	33 (13.4)
Other territories	3 (0.4)	3 (1.2)
Unknown	89 (11.8)	27 (11.0)

aUC, advanced urothelial carcinoma; rwCR, real-world complete response; rwPR, real-world partial response; rwSD; real-world stable disease.
Moon HH, et al. Poster presented at: ASCO Annual Meeting; June 2-6, 2023; Chicago, IL

Flatiron II: Baseline Characteristics (2/2)

Characteristic	rwCR/rwPR	rwSD
Total, n (%)	752 (100)	246 (100)
Site of disease, n (%)		
Bladder	553 (73.5)	183 (74.4)
Renal pelvis	112 (14.9)	38 (15.4)
Ureter	84 (11.2)	21 (8.5)
Urethra	3 (0.4)	4 (1.6)
Disease grade, n (%)		
High grade (G2/G3/G4)	652 (86.7)	210 (85.4)
Low grade (G1)	35 (4.7)	12 (4.9)
Unknown/ not documented	65 (8.6)	24 (9.8)
Stage at initial UC diagnosis, n (%)		
Stage 0	4 (0.5)	1 (0.4)
Stage I	17 (2.3)	4 (1.6)
Stage II	38 (5.1)	10 (4.1)
Stage III	82 (10.9)	27 (11.0)
Stage IV	340 (45.2)	94 (38.2)
Unknown/ not documented	271 (36.0)	110 (44.7)

Characteristic	rwCR/rwPR	rwSD
ECOG PS at aUC diagnosis date, n (%)		
0	264 (35.1)	82 (33.3)
1	254 (33.8)	85 (34.6)
2+	63 (8.4)	25 (10.2)
Unknown/ not documented	171 (22.7)	54 (22.0)
PD-L1 at aUC diagnosis date, n (%)		
Negative	89 (11.8)	35 (14.2)
Positive	38 (5.1)	12 (4.9)
Unknown/ not documented	625 (83.1)	199 (80.9)
GFR level at aUC diagnosis date, mL/min/1.73m^2		
Mean (SD)	67.8 (23.8)	65.5 (26.9)
Treatment group, n (%)		
Carboplatin-based	311 (41.4)	110 (44.7)
Cisplatin-based	441 (58.6)	135 (54.9)
Oxaliplatin-based	0	1 (0.4)

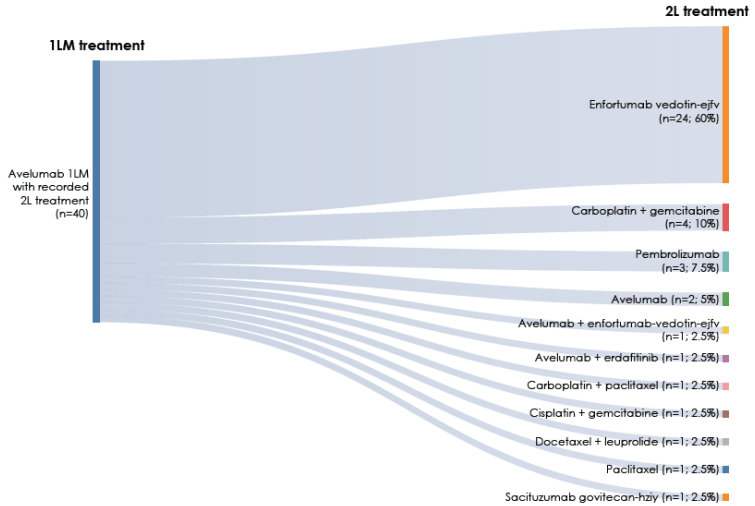
aUC, advanced urothelial carcinoma; ECOG PS, Eastern Cooperative Oncology Group performance status; G, grade; GFR, glomerular filtration rate; rwCR, real-world complete response; rwPR, real-world partial response; rwSD; real-world stable disease; UC, urothelial carcinoma.
Moon HH, et al. Poster presented at: ASCO Annual Meeting; June 2-6, 2023; Chicago, IL

Flatiron II: Avelumab 1LM and 2L in the post–FDA Approval Period

Summary of avelumab 1LM and 2L treatment

Treatment criteria	N (% previous step)
Total study population	1245 (100)
rwCR/PR or rwSD recorded during 1L PBC	998 (80.1)
Discontinued 1L PBC after avelumab 1LM approval (June 30, 2020)	339 (34.0)
Initiated avelumab 1LM	97 (28.6)
2L treatment received after avelumab 1LM	
Received	40 (41.2)
Not received/not reported*	57 (58.8)
2L treatment not received/reported but received avelumab within 4 weeks of study period end	40 (70.2)

Treatment sequence from avelumab 1LM to 2L



The median follow-up time for patients treated with avelumab 1LM was 7.5 months from initiation of 1LM

Limitations: Immortal time and selection biases since patients were required to have recorded response or SD, thus resulting in a potential overestimation of rwOS. Retrospective study, lack of randomization, lack of granularity in specific data points (eg, site of metastasis, laboratory values), lack of central scan review, residual confounding, and short duration of study period post approval of avelumab 1LM by the FDA. This study could not estimate true rwPFS, given that a 1L progression-free cohort was used to evaluate the avelumab 1LM-eligible population; only PFS after completion of 1L PBC was estimated

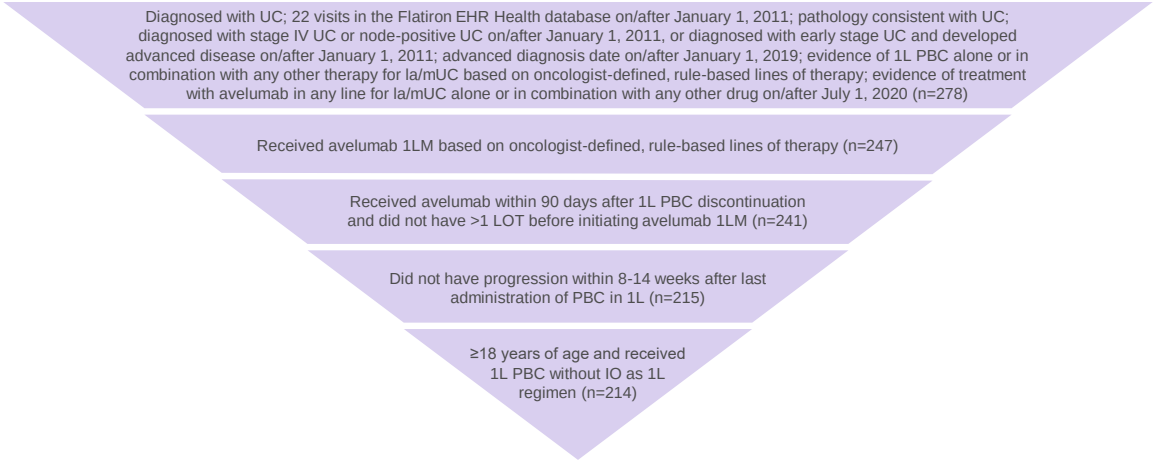
*Patients who initiated avelumab 1LM may still be receiving treatment, but data were not available.

1LM, first-line maintenance; 2L, second-line; FDA, Food and Drug Administration; rwCR, real-world complete response; rwPR, real-world partial response; rwSD; real-world stable disease; PBC, platinum-based chemotherapy.

Moon HH, et al. Poster presented at: ASCO Annual Meeting; June 2-6, 2023; Chicago, IL.

Flatiron III

Study details: noninterventional, retrospective cohort study of patients with la/mUC in the US using the nationwide Flatiron Health electronic health record–derived database, which is comprised of deidentified patient-level structured and unstructured data, curated via technology-enabled abstraction



During the study period (January 1, 2011-December 31, 2022), the deidentified data originated from **approximately 280 cancer clinics**

Moon HH, et al. Curr Oncol. 2024;31(9):5662-5676.

Flatiron III: Limitations

- Findings may not be generalizable to other populations
- The lack of patient randomization and selection bias
- Data maybe underreported or missing
- Data elements in Flatiron Health may not be reflective of real-world practice

Moon HH, et al. Curr Oncol. 2024;31(9):5662-5676.

Flatiron III: Baseline Characteristics (1/3)

Characteristic	Avelumab 1LM N=214
Age at diagnosis, years	
Mean (SD)	69 (9.2)
Year of index date, n (%)	
2020	43 (20.1)
2021	75 (35.0)
2022	96 (44.9)
Sex, n (%)	
Female	50 (23.4)
Male	164 (76.6)
Race, n (%)	
White	142 (66.4)
Unknown	33 (15.4)
Other	31 (14.5)
Black or African American	6 (2.8)
Asian	2 (0.9)

Characteristic	Avelumab 1LM N=214
Region of residence, n (%)	
South	99 (46.3)
Northeast	37 (17.3)
Midwest	30 (14.0)
Unknown	24 (11.2)
West	23 (10.7)
Other	1 (0.5)
Setting, n (%)	
Community	191 (89.3)
Academic	18 (8.4)
Both	5 (2.3)
Follow-up, median (IQR), months	8.7 (4.5-15.7)

1L, first line; 1LM, first-line maintenance; EHR, electronic health record; G, grade; IQR, interquartile range; la/mUC, locally advanced or metastatic urothelial carcinoma.

Moon HH, et al. Curr Oncol. 2024;31(9):5662-5676.

Flatiron III: Baseline Characteristics (2/3)

Characteristic	Avelumab 1LM N=214
Site of disease, n (%)	
Bladder	158 (73.8)
Renal pelvis	30 (14.0)
Ureter	24 (11.2)
Urethra	2 (0.9)
Disease grade, n (%)	
High (G2/G3/G4)	174 (81.3)
Low (G1)	12 (5.6)
Unknown/not documented	28 (13.1)
Stage at initial diagnosis, n (%)	
0	2 (0.9)
I	3 (1.4)
II	9 (4.2)
III	7 (3.3)
IV	99 (46.3)

Characteristic	Avelumab 1LM N=214
ECOG performance status at diagnosis, n (%)	
0	69 (32.2)
1	96 (44.9)
2+	21 (9.8)
Unknown/ not documented	28 (13.1)
Treatment group in 1L, n (%)	
Cisplatin based	115 (53.7)
Carboplatin based	99 (46.3)
Body mass index category, n (%)	
Underweight (<18.5 kg/m^2)	9 (4.2)
Normal (18.5-24.9 kg/m^2)	69 (32.2)
Overweight (25-29.9 kg/m^2)	59 (27.6)

1L, first line; 1LM, first-line maintenance; EHR, electronic health record; G, grade; la/mUC, locally advanced or metastatic urothelial carcinoma.

Moon HH, et al. Curr Oncol. 2024;31(9):5662-5676.

Flatiron III: Baseline Characteristics (3/3)

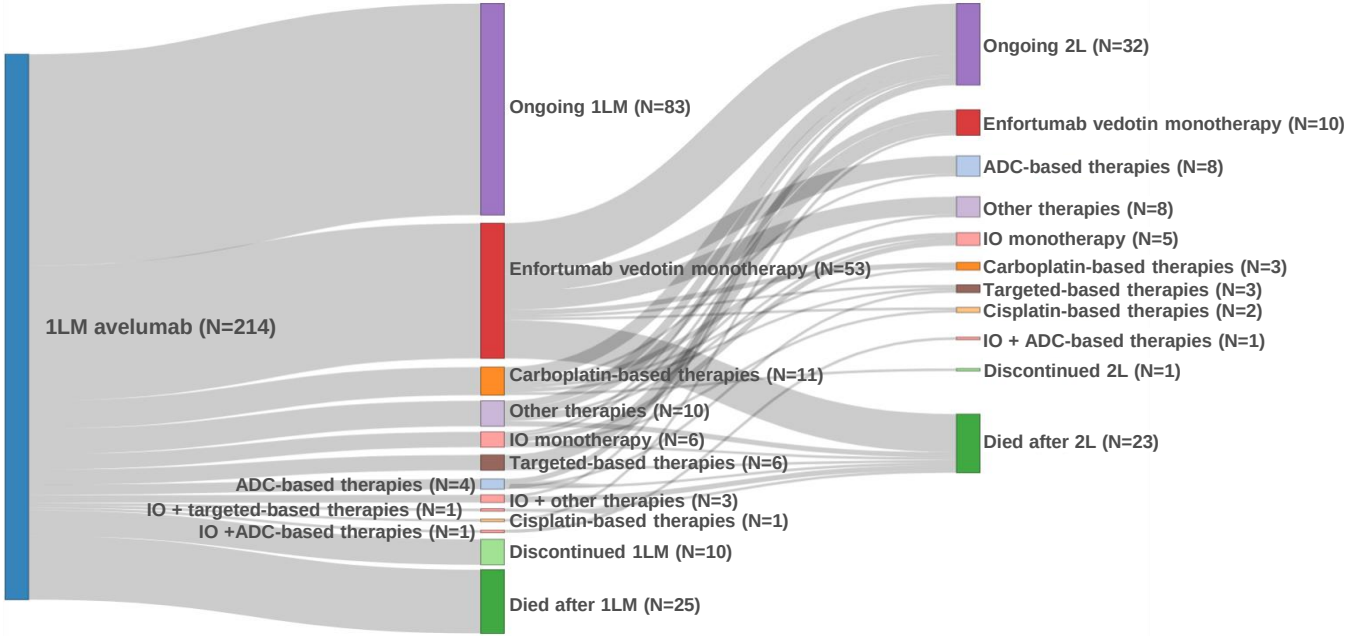
Characteristic	Avelumab 1LM N=214
Site of metastases, n (%)	
Distant lymph node	122 (57.0)
Bone	63 (29.4)
Lung	58 (27.1)
Liver	37 (17.3)
Soft tissue	21 (9.8)
Peritoneum	8 (3.7)
Other	6 (2.8)
Pleura	5 (2.3)
Adrenal	5 (2.3)
Brain	2 (0.9)
Skin	1 (0.5)
Kidney	1 (0.5)

1L, first line; 1LM, first-line maintenance; EHR, electronic health record; G, grade; la/mUC, locally advanced or metastatic urothelial carcinoma.

Moon HH, et al. Curr Oncol. 2024;31(9):5662-5676.

Flatiron III: Treatment Sequencing

Avelumab 1LM to 2L and 3L treatment regimens during the observation period



Limitations

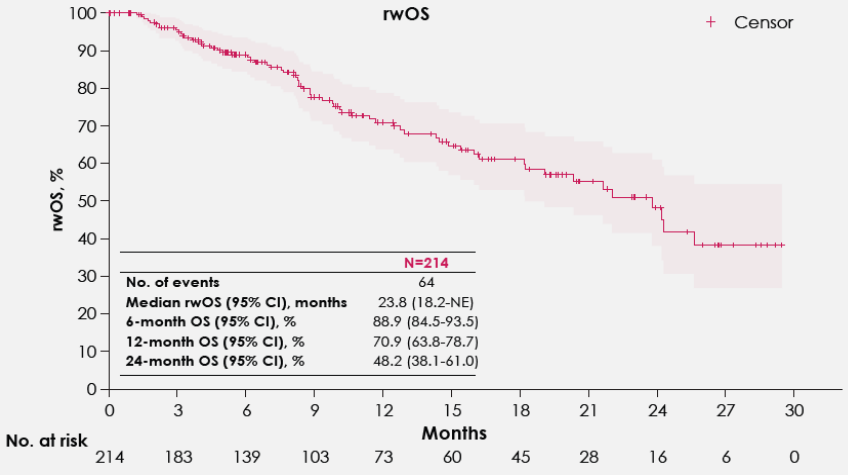
- Findings may not be generalizable to other populations
- The lack of patient randomization and selection bias
- Data maybe underreported or missing. Data elements in Flatiron Health may not be reflective of real-world practice

1L, first line; 1LM, first-line maintenance; 2L, second line; 3L, third line; ADC, antibody-drug conjugate; EV, enfortumab vedotin; IO, immuno-oncology.

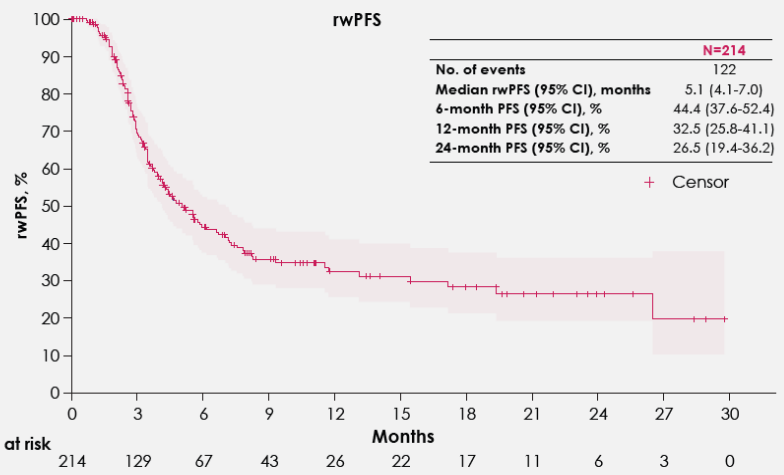
Moon HH, et al. Curr Oncol. 2024;31(9):5662-5676.

Flatiron III: OS and PFS from Avelumab 1LM Initiation

Real-world OS from avelumab 1LM initiation



Real-world PFS from avelumab 1LM initiation



Limitations

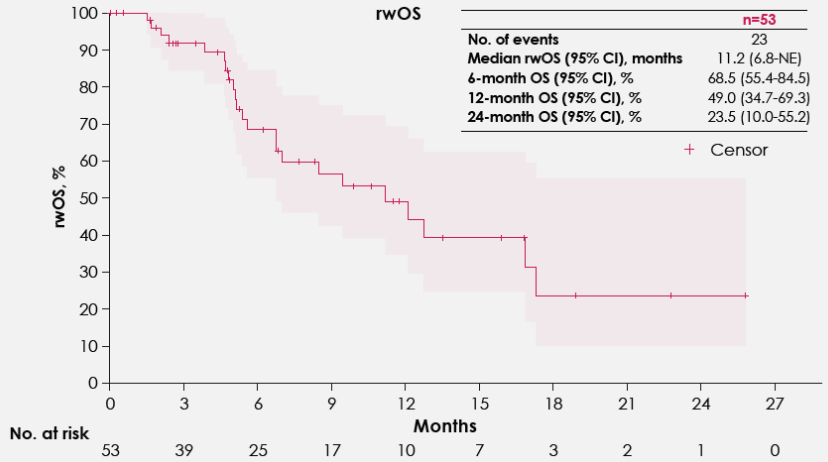
- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Findings may not be generalizable to other populations. The lack of patient randomization and selection bias.
- Data maybe underreported or missing. Data elements in Flatiron Health may not be reflective of real-world practice.

1LM, first-line maintenance; CI, confidence interval; NE, not estimable; OS, overall survival; PFS, progression-free survival; rwOS, real-world overall survival; rwPFS, real-world progression-free survival.

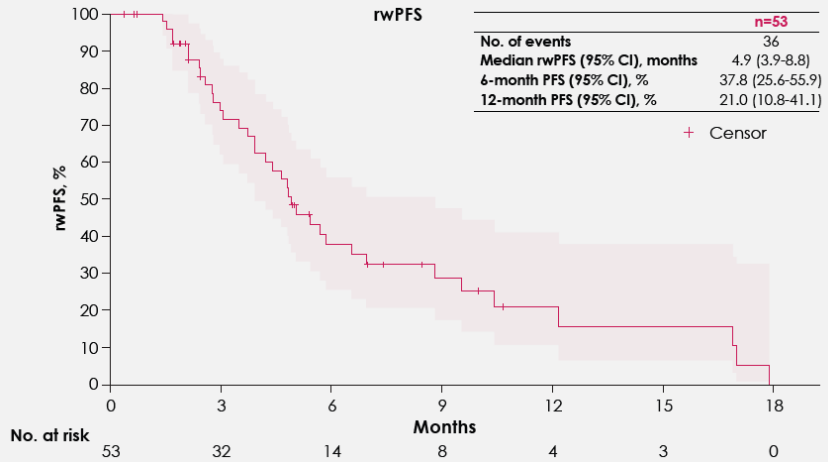
Moon HH, et al. Curr Oncol. 2024;31(9):5662-5676.

Flatiron III: OS and PFS from 2L Therapy Initiation

Real-world OS from 2L EV monotherapy initiation



Real-world PFS from 2L EV monotherapy initiation



Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Findings may not be generalizable to other populations. The lack of patient randomization and selection bias.
- Data maybe underreported or missing. Data elements in Flatiron Health may not be reflective of real-world practice.

2L, second-line; CI, confidence interval; EV, enfortumab vedotin; NE, not estimable; OS, overall survival; PFS, progression-free survival; rwOS, real-world overall survival; rwPFS, real-world progression-free survival.

Moon HH, et al. Curr Oncol. 2024;31(9):5662-5676.

Flatiron III Tumor Burden

Study details: noninterventional, retrospective cohort study assessing real-world clinical outcomes based on tumor burden in patients with la/mUC with no disease progression after 1L PBC who received avelumab 1LM in the US. This study used the nationwide Flatiron Health Electronic Health Record–derived database, which is comprised of deidentified patient-level data.

- N=290
- Age ≥18 years
- Diagnosed with la/mUC between January 1, 2019, and July 31, 2023
- Avelumab 1LM initiation on or after July 1, 2020, and within 90 days after discontinuing 1L PBC
- No disease progression for 8-14 weeks after the last administration of 1L PBC

- At data cutoff (July 31, 2023), 156 patients (53.8%) were still receiving avelumab 1LM

- **Subgroup analyses based on tumor burden:**
  - Nonvisceral metastases (including bone only) vs visceral metastases (including visceral sites and bone)
  - Lymph node-only metastases (including distant lymph nodes) vs distant metastases

- Median follow-up from avelumab 1LM initiation: 8.7 months (IQR, 3.7-16.9)

1L, first line; 1LM, first line maintenance; IQR, interquartile range; la/mUC, locally advanced/metastatic urothelial carcinoma; PBC, platinum-based chemotherapy.

Moon HH, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 764) February 13-15, 2025; San Francisco, CA.

Flatiron III Tumor Burden: Limitations

- The noninterventional, retrospective nature of this study limited control over data collection and introduced potential biases, including selection and information biases
- Reliance on the nationwide Flatiron Health EHR-derived deidentified database may have resulted in incomplete or inconsistent data, particularly for tumor assessments and treatment patterns
- Real-world treatment practices and follow-up schedules may vary, impacting the comparability and generalizability of results
- Factors such as comorbidities, genomic data, and detailed measures of tumor biology were not captured and may have influenced outcomes, but were not accounted for in the analysis

1LM, first line maintenance; EHR, electronic health record.

Moon HH, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 764) February 13-15, 2025; San Francisco, CA.

Flatiron III Tumor Burden: Baseline Characteristics (1/2)

Characteristic	N=290
Age, years	
Median (IQR)	71.0 (64.0-76.0)
Mean (SD)	70.0 (9.0)
Age group, n (%)	
18 to <45 years	4 (1.4)
45 to <55 years	14 (4.8)
55 to <65 years	52 (17.9)
65 to <75 years	122 (42.1)
≥75 years	98 (33.8)
Sex, n (%)	
Female	70 (24.1)
Male	220 (75.9)
Ethnicity, n (%)	
Hispanic or Latino	12 (4.1)
Not Hispanic or Latino	191 (65.9)
Unknown	87 (30.0)

Characteristic	N=290
Race, n (%)	
Asian	2 (0.7)
Black or African American	8 (2.8)
White	205 (70.7)
Other	27 (9.3)
Unknown	48 (16.6)
ECOG PS, n (%)	
0	95 (32.8)
1	132 (45.5)
≥2	23 (7.9)
Missing	40 (13.8)

1LM, first-line maintenance; ECOG PS, Eastern Cooperative Group performance score; IQR, interquartile range; SD, standard deviation.
Moon HH, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 764) February 13-15, 2025; San Francisco, CA.

Flatiron III Tumor Burden: Baseline Characteristics (2/2)

Characteristic	N=290
Sites of metastases prior to avelumab 1LM, n (%)	
Visceral	
Lung	77 (26.6)
Liver	49 (16.9)
Soft tissue	31 (10.7)
Peritoneum	8 (2.8)
Pleura	8 (2.8)
Adrenal	6 (2.1)
Brain	2 (0.7)
Kidney	1 (0.3)
Ovary	1 (0.3)
Other	8 (2.8)
Nonvisceral	
Distant lymph node	172 (59.3)
Bone	74 (25.5)
Skin	2 (0.7)
None	24 (8.3)

1LM, first-line maintenance.

Moon HH, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 764) February 13-15, 2025; San Francisco, CA.

Flatiron III Tumor Burden: Clinical Outcomes by Disease Burden in Patients with Metastases at Avelumab 1LM Initiation

Outcomes in the overall population

- Median rwOS from avelumab 1LM initiation: 22.0 months (95% CI, 18.2-24.8)
- Median rwPFS from avelumab 1LM initiation: 5.0 months (95% CI, 3.9-5.8)
- rwORR in patients who had a tumor assessment during avelumab 1LM (n=236): 34.7%

Outcomes by disease burden in patients with metastases at avelumab 1LM initiation

Outcome from avelumab 1LM initiation, median (95% CI), months	Patients with Metastases (n=266)	
	Nonvisceral (n=124)	Visceral (n=142)
rwOS	23.8 (15.4–NE)	19.1 (12.5–23.8)
rwPFS	5.6 (4.1–7.8)	3.6 (3.1–5.0)
TTNT	6.6 (6.6–9.8)	6.0 (4.3–7.4)
TTD	5.3 (4.2–10.1)	4.4 (3.5–5.7)
	Lymph node only (n=83)	Distant (n=183)
rwOS	24.3 (20.7–NE)	16.5 (12.5–22.6)
rwPFS	8.7 (5.0–NE)	3.6 (3.1-4.6)
TTNT	8.1 (6.2–23.8)	5.2 (4.3–6.7)
TTD	10.1 (4.9–NE)	4.2 (3.3–5.5)

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- The noninterventional, retrospective nature of this study limited control over data collection and introduced potential biases, including selection and information biases
- Reliance on the nationwide Flatiron Health EHR-derived deidentified database may have resulted in incomplete or inconsistent data, particularly for tumor assessments and treatment patterns
- Real-world treatment practices and follow-up schedules may vary, impacting the comparability and generalizability of results
- Factors such as comorbidities, genomic data, and detailed measures of tumor biology were not captured and may have influenced outcomes, but were not accounted for in the analysis

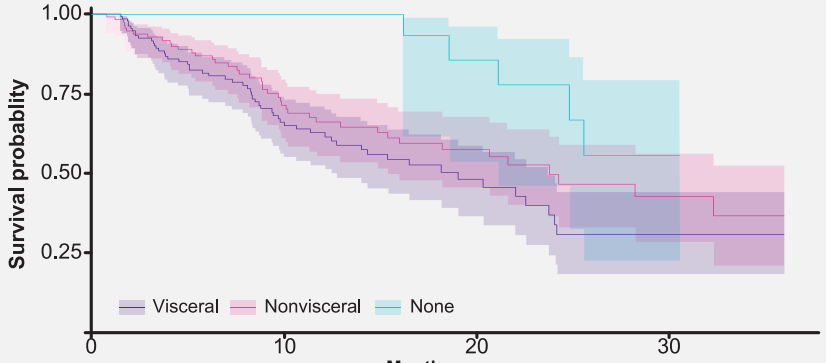
1LM, first-line maintenance; CI, confidence interval; rwOS, real-world overall survival; rwORR, real-world objective response rate; rwPFS, real-world progression-free survival; TTD, time to treatment discontinuation; TTNT, time to next treatment.

Moon HH, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 764) February 13-15, 2025; San Francisco, CA.

Flatiron III Tumor Burden: rwOS by Metastatic Site

rwOS for visceral vs nonvisceral metastases

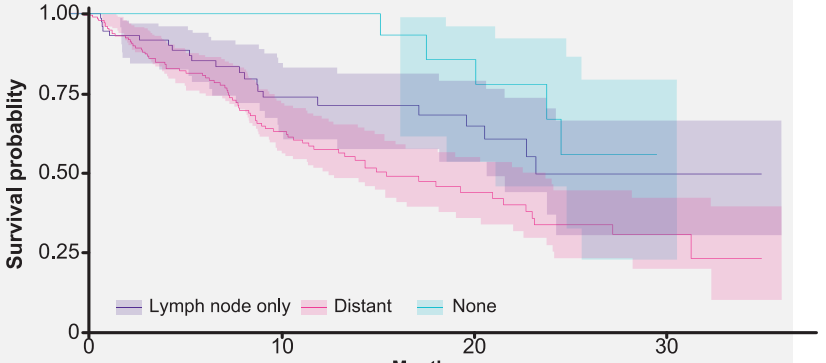
Median rwOS: 19.1 (12.5-23.8) vs 23.8 (15.4-NE)



No. at risk				
Visceral	142	62	19	5
Nonvisceral	124	57	25	9
None	24	17	11	2

rwOS for lymph node–only vs distant metastases

Median rwOS: 24.3 (20.7-NE) vs 16.5 (12.5-22.6)



No. at risk				
Lymph node only	83	39	19	6
Distant	183	79	25	8
None	24	17	11	2

Limitations

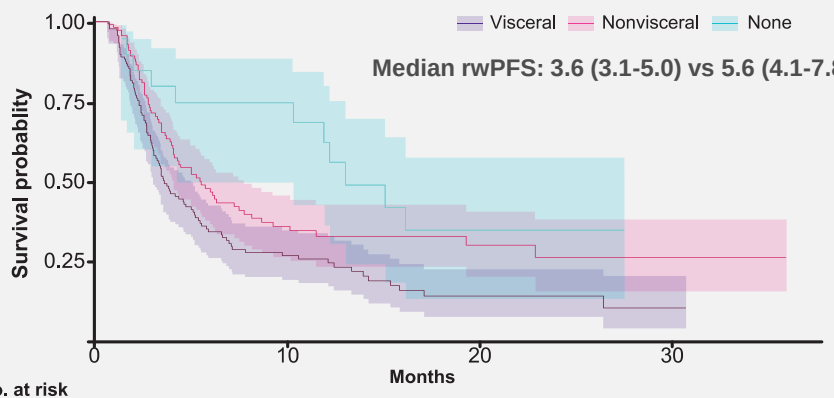
- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- The noninterventional, retrospective nature of this study limited control over data collection and introduced potential biases, including selection and information biases
- Reliance on the nationwide Flatiron Health EHR-derived deidentified database may have resulted in incomplete or inconsistent data, particularly for tumor assessments and treatment patterns
- Real-world treatment practices and follow-up schedules may vary, impacting the comparability and generalizability of results
- Factors such as comorbidities, genomic data, and detailed measures of tumor biology were not captured and may have influenced outcomes, but were not accounted for in the analysis

1LM, first-line maintenance; EHR, electronic health record; NE, not estimable; rwOS, real-world overall survival.

Moon HH, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 764) February 13-15, 2025; San Francisco, CA.

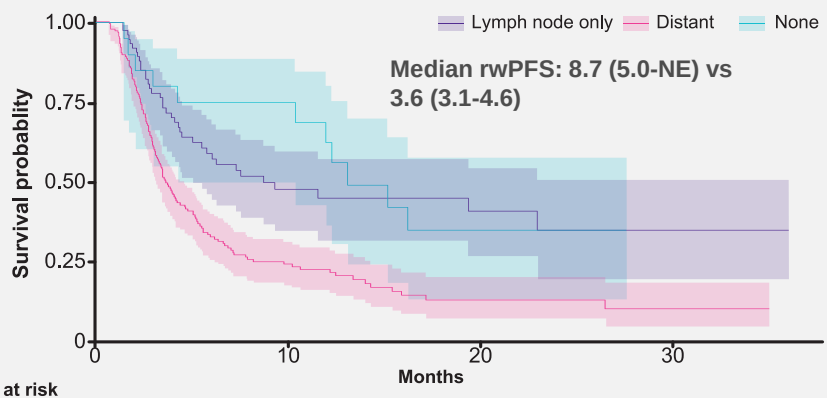
Flatiron III Tumor Burden: rwPFS by Metastatic Site

rwPFS for visceral vs nonvisceral metastases



No. at risk				
Visceral	142	26	8	2
Nonvisceral	124	27	10	4
None	24	12	5	0

rwPFS for lymph node–only vs distant metastases



No. at risk				
Lymph node only	83	39	9	3
Distant	183	30	9	3
None	24	12	5	0

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- The noninterventional, retrospective nature of this study limited control over data collection and introduced potential biases, including selection and information biases
- Reliance on the nationwide Flatiron Health EHR-derived deidentified database may have resulted in incomplete or inconsistent data, particularly for tumor assessments and treatment patterns
- Real-world treatment practices and follow-up schedules may vary, impacting the comparability and generalizability of results
- Factors such as comorbidities, genomic data, and detailed measures of tumor biology were not captured and may have influenced outcomes, but were not accounted for in the analysis

1LM, first-line maintenance; ; EHR, electronic health record; NE, not estimable; rwPFS, real-world progression-free survival.

Moon HH, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 764) February 13-15, 2025; San Francisco, CA.

Flatiron Safety

Study details: retrospective observational cohort study describing the real-world safety profiles of current 1L systemic treatments initiated by patients with la/mUC in the US from January 2016 to October 2023. This study use the nationwide, longitudinal, electronic health record-derived, deidentified Flatiron Health database, comprising patient-level data curated via technology-enabled abstraction or extraction.

- **≈280 US cancer clinics (≈800 sites of care)**
  - Patients diagnosed with la/mUC on or after January 1, 2016
  - Treatment with a 1L regimen of interest ≥6 months prior to data cutoff (April 30, 2024)

- rwTEAEs assessed from the start of 1L treatment to the earliest of 90 days after last 1L treatment dose, start of subsequent treatment, or death

- **Regimens of interest**
  - Enfortumab vedotin + pembrolizumab
  - ICI monotherapy (pembrolizumab or atezolizumab)
  - Cisplatin-based chemotherapy followed by avelumab maintenance
  - Carboplatin-based chemotherapy followed by avelumab maintenance
  - Cisplatin-based chemotherapy without avelumab maintenance
  - Carboplatin-based chemotherapy without avelumab maintenance

[a]la/mUC defined as stage IV or node-positive (stage IIIA [N1] or IIIB [N2-N3]) UC, or diagnosed with early-stage UC and subsequently developed advanced disease.
1L, first line; 1LM, first line maintenance; ICI, immune checkpoint inhibitor; la/mUC, locally advanced/metastatic urothelial carcinoma; rwTEAE, real-world treatment emergent adverse event; UC, urothelial carcinoma.
Nizam A, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 759) February 13-15, 2025; San Francisco, CA.

Flatiron Safety: Limitations

Evaluation of rwTEAEs was limited to those occurring during 1L treatment; however, the occurrence of AEs after discontinuation was expected to be relatively low

Line of treatment was determined using oncologist-defined, rules-based algorithms, which may have resulted in misclassification of 1L regimens

Information on the severity/grade of rwTEAEs was not available, and the management and associated outcomes of rwTEAEs were not reported

The study focused on descriptive analyses across the six 1L regimens without adjustment for heterogeneity in baseline patient characteristics, and statistical comparisons were not conducted; thus, caution should be exercised when attempting to compare safety data between cohorts

The study only captured the incidence of a prespecified list of 30 AEs, and other clinically relevant AEs may have occurred that were not captured; furthermore, AEs may have been underreported, including low-grade events that are challenging to detect and measure, such as peripheral sensory neuropathy

1L, first line; 1LM, first line maintenance AE, adverse event; rwTEAE, real-world treatment emergent adverse event.

Nizam A, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 759) February 13-15, 2025; San Francisco, CA.

Flatiron Safety: Baseline Characteristics (1/3)

Characteristic	Overall (N=5,235)	EV + P (n=198)	ICI monotherapy (n=2,146)	Without avelumab 1LM		With avelumab 1LM	
				Cis-based CT (n=1,372)	Carbo-based CT (n=1,140)	Cis-based CT (n=197)	Carbo-based CT (n=182)
Age at index date, median (IQR), years	74 (66-80)	76 (70-82)	78 (71-83)	68 (61-74)	74 (67-79)	69 (62-74)	73 (67-78)
Age category at index date, n (%)							
18-64 years	1,051 (20)	30 (15)	240 (11)	497 (36)	188 (16)	65 (33)	31 (17)
65-74 years	1,692 (32)	52 (26)	539 (25)	541 (39)	402 (35)	88 (45)	70 (38)
75-79 years	1,070 (20)	48 (24)	432 (20)	233 (17)	287 (25)	29 (15)	41 (23)
80+ years	1,422 (27)	68 (35)	935 (43)	101 (7)	263 (23)	15 (8)	40 (22)
Race, n (%)							
Black or African American	252 (5)	16 (8)	83 (4)	77 (6)	66 (6)	8 (4)	<6
White	3,647 (70)	135 (68)	1,510 (70)	979 (71)	752 (66)	137 (70)	134 (74)
Other	671 (13)	6 (3)	285 (13)	171 (12)	174 (15)	19 (10)	16 (9)
Unknown	665 (13)	41 (21)	268 (12)	145 (11)	148 (13)	33 (17)	>26
Ethnicity, n (%)							
Hispanic or Latino	202 (4)	<8	70 (3)	59 (4)	52 (5)	9 (5)	8 (4)
Not Hispanic or Latino	3,859 (74)	>140	1,541 (72)	1,072 (78)	844 (74)	132 (67)	126 (69)
Unknown	1,174 (22)	50 (25)	535 (25)	241 (18)	244 (21)	56 (28)	48 (26)
Sex, n (%)							
Female	1,406 (27)	44 (22)	599 (28)	381 (28)	296 (26)	51 (26)	35 (19)
Male	3,828 (73)	154 (78)	1,547 (72)	990 (72)	844 (74)	146 (74)	147 (81)
Unknown	1 (<1)	0	0	1 (<1)	0	0	0

1LM, first-line maintenance; Carbo, carboplatin; Cis, cisplatin; CT, chemotherapy; EV + P, enfortumab vedotin + pembrolizumab; ICI, immune checkpoint inhibitor; IQR, interquartile range.

Nizam A, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 759) February 13-15, 2025; San Francisco, CA.

Flatiron Safety: Baseline Characteristics (2/3)

Characteristic	Overall (N=5,235)	EV + P (n=198)	ICI monotherapy (n=2,146)	Without avelumab 1LM		With avelumab 1LM	
				Cis-based CT (n=1,372)	Carbo-based CT (n=1,140)	Cis-based CT (n=197)	Carbo-based CT (n=182)
Practice type, n (%)							
Academic	743 (14)	49 (25)	272 (13)	237 (17)	143 (13)	32 (16)	10 (5)
Community	4,112 (79)	132 (67)	1,744 (81)	1,013 (74)	914 (80)	150 (76)	159 (87)
Both	380 (7)	17 (9)	130 (6)	122 (9)	83 (7)	15 (8)	13 (7)
Primary site, n (%)							
Lower tract	4,049 (77)	165 (83)	1,666 (78)	1,120 (82)	824 (72)	137 (70)	137 (75)
Upper tract	1,179 (23)	26 (13)	480 (22)	252 (18)	316 (28)	60 (30)	45 (25)
Unknown/not documented	7 (<1)	7 (4)	0	0	0	0	0
Disease grade, n (%)							
Low (grade 1)	233 (4)	10 (5)	96 (4)	44 (3)	65 (6)	7 (4)	11 (6)
High (grade 2-4)	4,458 (85)	170 (86)	1,831 (85)	1,218 (89)	919 (81)	167 (85)	153 (84)
Unknown/not documented	544 (10)	18 (9)	219 (10)	110 (8)	156 (14)	23 (12)	18 (10)
PD-(L)1 status, n (%)							
Positive	245 (5)	15 (8)	120 (6)	38 (3)	36 (3)	12 (6)	24 (13)
Negative	446 (9)	18 (9)	198 (9)	75 (5)	114 (10)	25 (13)	16 (9)
Unknown/not tested	4,544 (87)	165 (83)	1,828 (85)	1,259 (92)	990 (87)	160 (81)	142 (78)

1LM, first-line maintenance; Carbo, carboplatin; Cis, cisplatin; CT, chemotherapy; EV + P, enfortumab vedotin + pembrolizumab; ICI, immune checkpoint inhibitor; PD-(L)1, programmed cell death 1 ligand 1

Nizam A, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 759) February 13-15, 2025; San Francisco, CA.

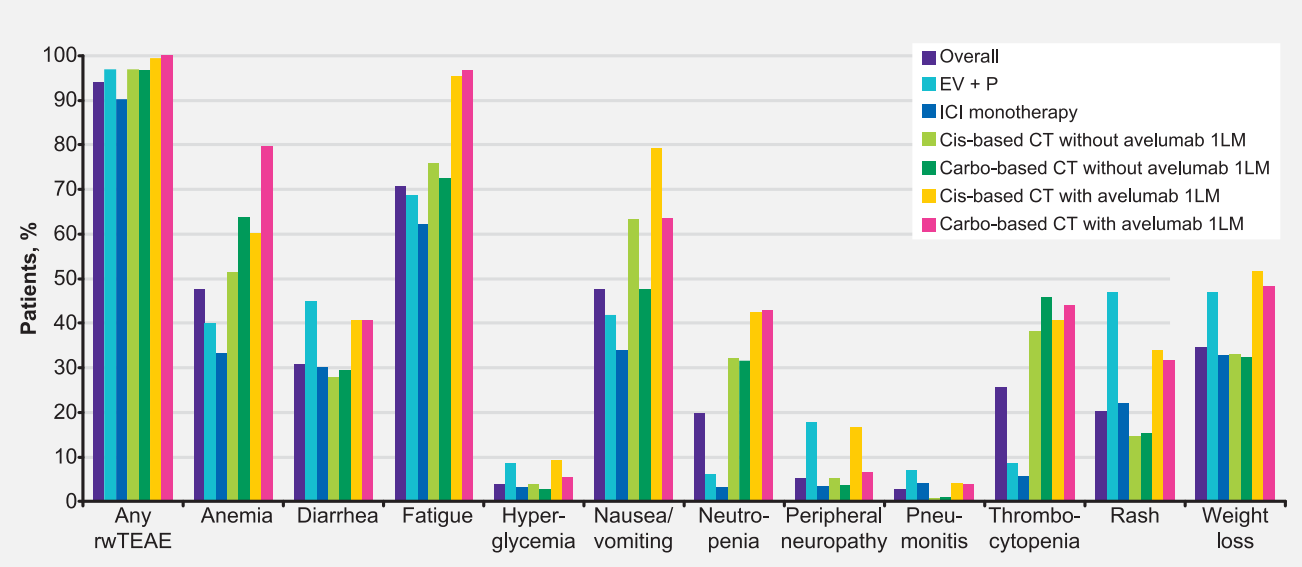
Flatiron Safety: Baseline Characteristics (3/3)

Characteristic	Overall (N=5,235)	EV + P (n=198)	ICI monotherapy (n=2,146)	Without avelumab 1LM		With avelumab 1LM	
				Cis-based CT (n=1,372)	Carbo-based CT (n=1,140)	Cis-based CT (n=197)	Carbo-based CT (n=182)
Stage at initial diagnosis, n (%)							
I	93 (2)	2 (1)	41 (2)	24 (2)	18 (2)	1 (1)	7 (4)
II	442 (8)	23 (12)	295 (14)	62 (5)	46 (4)	6 (3)	10 (5)
III	531 (10)	17 (9)	202 (9)	216 (16)	77 (7)	8 (4)	11 (6)
IV	1,823 (35)	62 (31)	530 (25)	562 (41)	487 (43)	115 (58)	67 (37)
Unknown/Not documented	2,346 (45)	94 (47)	1078 (50)	508 (37)	512 (45)	67 (34)	87 (48)
ECOG PS at 1L, n (%)							
0	1,524 (29)	55 (28)	468 (22)	555 (40)	287 (25)	94 (48)	65 (36)
1	1,930 (37)	72 (36)	785 (37)	482 (35)	375 (33)	72 (37)	77 (42)
≥2	1,724 (33)	71 (36)	893 (42)	335 (24)	63 (6)	31 (16)	40 (22)
Unknown	0	0	0	0	0	0	0
Follow-up, median (IQR), months	9 (3-20)	7 (3-9)	5 (1-17)	11 (5-28)	8 (3-18)	17 (10-26)	14 (9-23)

1L, first line; 1LM, first-line maintenance; Carbo, carboplatin; Cis, cisplatin; CT, chemotherapy; EV + P, enfortumab vedotin + pembrolizumab; ECOG PS, Eastern Cooperative Group performance score; IQR, interquartile range; ICI, immune checkpoint inhibitor.

Nizam A, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 759) February 13-15, 2025; San Francisco, CA.

Flatiron Safety: Incidence of Select rwTEAEs by 1L Regimen



- **296 patients** (6% of the overall population) did not have documented evidence of any rwTEAEs of interest
- Most common rwTEAEs overall:
  - **fatigue (71%)**
  - **anemia (48%)**
  - **nausea (48%)**

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Evaluation of rwTEAEs was limited to those occurring during 1L treatment; however, the occurrence of AEs after discontinuation was expected to be relatively low
- Line of treatment was determined using oncologist-defined, rules-based algorithms, which may have resulted in misclassification of 1L regimens
- Information on the severity/grade of rwTEAEs was not available, and the management and associated outcomes of rwTEAEs were not reported
- The study focused on descriptive analyses across the six 1L regimens without adjustment for heterogeneity in baseline patient characteristics, and statistical comparisons were not conducted; thus, caution should be exercised when attempting to compare safety data between cohorts
- The study only captured the incidence of a prespecified list of 30 AEs, and other clinically relevant AEs may have occurred that were not captured; furthermore, AEs may have been underreported, including low-grade events that are challenging to detect and measure, such as peripheral sensory neuropathy

1L, first line; 1LM, first-line maintenance; AE, adverse event Carbo, carboplatin; Cis, cisplatin; CT, chemotherapy; EV + P, enfortumab vedotin + pembrolizumab; ICI, immune checkpoint inhibitor; rwAEs, real-world adverse events; rwTEAE, real-world treatment-emergent adverse event.

Nizam A, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 759) February 13-15, 2025; San Francisco, CA.

Flatiron Safety: Incidence and Treatment-adjusted Rates of Select rwTEAEs by 1L Regimen (1/3)

Incidence of rwTEAEs, % (treatment-adjusted incidence rate per 1,000 patient-months on treatment)	Overall (N=5,235)	EV + P (n=198)	ICI monotherapy (n=2,146)	Without avelumab 1LM		With avelumab 1LM	
				Cis-based CT (n=1,372)	Carbo-based CT (n=1,140)	Cis-based CT (n=197)	Carbo-based CT (n=182)
Any rwTEAE	94.3 (1130.7)	97 (1491.2)	90.3 (757.9)	96.9 (1614.3)	96.7 (1755.4)	99.5 (1723.7)	100.0 (1542.2)
Anemia	47.6 (108.5)	40.0 (83.6)	33.2 (56.3)	51.5 (159.1)	63.8 (267.7)	60.4 (49.9)	79.7 (108.4)
Constipation	41.4 (89.1)	48.0 (109.7)	33.2 (55.1)	45.9 (143.3)	42.5 (125.6)	70.6 (80.9)	58.2 (51.3)
Diarrhea	30.7 (58.2)	45.0 (98.4)	30.2 (49.5)	27.8 (66.9)	29.5 (74.9)	40.6 (24.9)	40.7 (29.1)
Fatigue	70.7 (266.6)	68.7 (234.3)	62.2 (172)	75.7 (406.9)	72.5 (380.4)	95.4 (371.3)	96.7 (375.5)
Hyperglycemia	3.9 (5.6)	8.6 (12.7)	3.4 (4.1)	3.9 (7.9)	2.7 (5.4)	9.1 (4.0)	5.5 (2.6)

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Evaluation of rwTEAEs was limited to those occurring during 1L treatment; however, the occurrence of AEs after discontinuation was expected to be relatively low
- Line of treatment was determined using oncologist-defined, rules-based algorithms, which may have resulted in misclassification of 1L regimens
- Information on the severity/grade of rwTEAEs was not available, and the management and associated outcomes of rwTEAEs were not reported
- The study focused on descriptive analyses across the six 1L regimens without adjustment for heterogeneity in baseline patient characteristics, and statistical comparisons were not conducted; thus, caution should be exercised when attempting to compare safety data between cohorts
- The study only captured the incidence of a prespecified list of 30 AEs, and other clinically relevant AEs may have occurred that were not captured; furthermore, AEs may have been underreported, including low-grade events that are challenging to detect and measure, such as peripheral sensory neuropathy

1L, first line; 1LM, first-line maintenance; Carbo, carboplatin; Cis, cisplatin; CT, chemotherapy; EV + P, enfortumab vedotin + pembrolizumab; ICI, immune checkpoint inhibitor; rwTEAE, real-world treatment-emergent adverse event.

Nizam A, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 759) February 13-15, 2025; San Francisco, CA.

Flatiron Safety: Incidence and Treatment-adjusted Rates of Select rwTEAEs by 1L Regimen (2/3)

Incidence of rwTEAEs, % (treatment-adjusted incidence rate per 1,000 patient-months on treatment)	Overall (N=5,235)	EV + P (n=198)	ICI monotherapy (n=2,146)	Without avelumab 1LM		With avelumab 1LM	
				Cis-based CT (n=1,372)	Carbo-based CT (n=1,140)	Cis-based CT (n=197)	Carbo-based CT (n=182)
Hypothyroidism	1.3 (8.9)	9.1 (13.9)	9.0 (12.0)	2.5 (4.9)	2.2 (4.3)	11.7 (5.2)	8.8 (4.3)
Musculoskeletal pain	41.2 (88.1)	31.3 (57.6)	41.1 (75.4)	38.5 (105.3)	38.6 (105.5)	65.0 (66.0)	65.4 (63.0)
Nausea/vomiting	47.6 (108.4)	41.9 (85.6)	33.9 (55.0)	63.4 (258.1)	47.5 (152.7)	79.2 (115.8)	63.7 (65.9)
Neutropenia	20.0 (33.4)	6.1 (8.8)	3.3 (4.0)	32.2 (86.8)	31.5 (86.2)	42.6 (28.0)	42.9 (28.7)
Peripheral neuropathy	5.2 (7.6)	17.7 (29.0)	3.6 (4.4)	5.3 (10.9)	3.8 (7.6)	16.8 (8.4)	6.6 (2.8)
Pneumonitis	2.7 (3.9)	7.1 (10.2)	4.2 (5.2)	0.8 (1.6)	1.0 (1.9)	4.1 (1.8)	3.9 (2.0)

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Evaluation of rwTEAEs was limited to those occurring during 1L treatment; however, the occurrence of AEs after discontinuation was expected to be relatively low
- Line of treatment was determined using oncologist-defined, rules-based algorithms, which may have resulted in misclassification of 1L regimens
- Information on the severity/grade of rwTEAEs was not available, and the management and associated outcomes of rwTEAEs were not reported
- The study focused on descriptive analyses across the six 1L regimens without adjustment for heterogeneity in baseline patient characteristics, and statistical comparisons were not conducted; thus, caution should be exercised when attempting to compare safety data between cohorts
- The study only captured the incidence of a prespecified list of 30 AEs, and other clinically relevant AEs may have occurred that were not captured; furthermore, AEs may have been underreported, including low-grade events that are challenging to detect and measure, such as peripheral sensory neuropathy

1L, first line; 1LM, first-line maintenance; AE, adverse event; Carbo, carboplatin; Cis, cisplatin; CT, chemotherapy; EV + P, enfortumab vedotin + pembrolizumab; ICI, immune checkpoint inhibitor; rwTEAE, real-world treatment-emergent adverse event.

Nizam A, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 759) February 13-15, 2025; San Francisco, CA.

Flatiron Safety: Incidence and Treatment-adjusted Rates of Select rwTEAEs by 1L Regimen (3/3)

Incidence of rwTEAEs, % (treatment-adjusted incidence rate per 1,000 patient-months on treatment)	Overall N=5,235	EV + P n=198	ICI monotherapy n=2,146	Without avelumab 1LM		With avelumab 1LM	
				Cis-based CT n=1,372	Carbo-based CT n=1,140	Cis-based CT n=197	Carbo-based CT n=182
Pruritus	14.5 (24.3)	36.9 (72.5)	19.9 (30.7)	6.1 (12.4)	7.8 (16.4)	23.4 (13.0)	21.4 (13.4)
Thrombocytopenia	25.7 (44.7)	8.6 (12.7)	5.6 (6.9)	38.4 (108)	45.8 (147.1)	40.6 (26.1)	44.0 (30.2)
Rash	20.3 (35.6)	47.0 (108.7)	21.9 (33.5)	14.7 (32.5)	15.3 (34.4)	34.0 (20.1)	31.9 (20.8)
Weight loss	34.6 (66.6)	47.0 (102.2)	32.9 (53.2)	33.0 (84.1)	32.5 (84.9)	51.8 (35.1)	48.4 (34.6)

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Evaluation of rwTEAEs was limited to those occurring during 1L treatment; however, the occurrence of AEs after discontinuation was expected to be relatively low
- Line of treatment was determined using oncologist-defined, rules-based algorithms, which may have resulted in misclassification of 1L regimens
- Information on the severity/grade of rwTEAEs was not available, and the management and associated outcomes of rwTEAEs were not reported
- The study focused on descriptive analyses across the six 1L regimens without adjustment for heterogeneity in baseline patient characteristics, and statistical comparisons were not conducted; thus, caution should be exercised when attempting to compare safety data between cohorts
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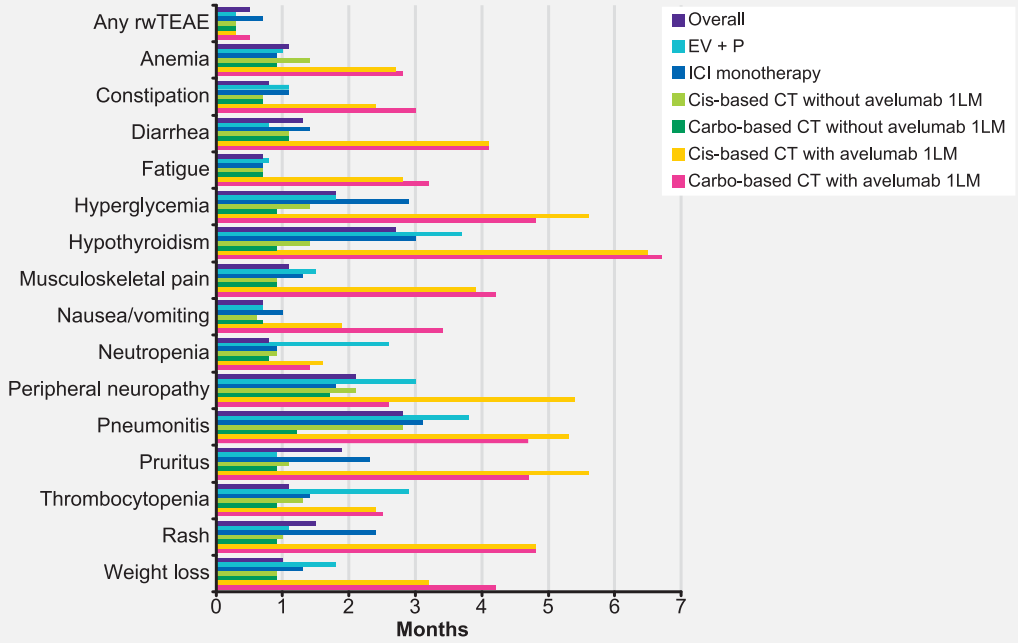
1L, first line; 1LM, first-line maintenance; Carbo, carboplatin; Cis, cisplatin; CT, chemotherapy; EV + P, enfortumab vedotin + pembrolizumab; ICI, immune checkpoint inhibitor; rwTEAE, real-world treatment-emergent adverse event.

Nizam A, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 759) February 13-15, 2025; San Francisco, CA.

Flatiron Safety: Median Time to Onset of Select rwTEAEs by 1L Regimen



- In patients who had any rwTEAE, median time to onset of the first rwTEAE after 1L initiation was 0.5 months (IQR, 0.2-0.7)
- 4rwTEAEs had a median time to onset of <1 month after 1L initiation:
  - fatigue (0.7 months [IQR, 0.3-1.4])
  - nausea/vomiting (0.7 months [IQR, 0.3-1.6])
  - constipation (0.8 months [IQR, 0.3-2.0])
  - neutropenia (0.8 months [IQR, 0.5-1.8])
- rwTEAEs with the longest median time to onset after 1L initiation in the overall population:
  - pneumonitis (2.8 months [IQR, 1.1-7.3])
  - hypothyroidism (2.7 months [IQR, 0.8-5.5])

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Evaluation of rwTEAEs was limited to those occurring during 1L treatment; however, the occurrence of AEs after discontinuation was expected to be relatively low
- Line of treatment was determined using oncologist-defined, rules-based algorithms, which may have resulted in misclassification of 1L regimens
- Information on the severity/grade of rwTEAEs was not available, and the management and associated outcomes of rwTEAEs were not reported
- The study focused on descriptive analyses across the six 1L regimens without adjustment for heterogeneity in baseline patient characteristics, and statistical comparisons were not conducted; thus, caution should be exercised when attempting to compare safety data between cohorts
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1L, first line; 1LM, first-line maintenance; Carbo, carboplatin; Cis, cisplatin; CT, chemotherapy; EV + P, enfortumab vedotin + pembrolizumab; ICI, immune checkpoint inhibitor; IQR, interquartile range; rwTEAE, real-world treatment-emergent adverse event.

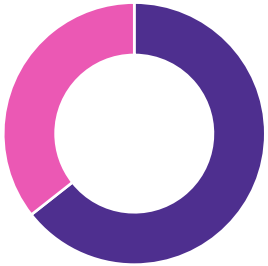
Nizam A, et al. Presented at the ASCO Genitourinary Cancers Symposium, (Abstract No. 759) February 13-15, 2025; San Francisco, CA.

PATRIOT II

Study details: observational, retrospective chart review study, which examined real-world outcomes, treatment patterns, and HCRU prior to and during avelumab 1LM in 160 patients with la/mUC in routine clinical practice in the United States.

Study conducted across **37 geographically dispersed sites** consisting of both community oncology practices and centers affiliated with academic institutions

60 patients (37.5%) received **1L carboplatin**



100 patients (62.5%) received **1L cisplatin**-based chemotherapy

Grivas P, et al. Clin Genitourin Cancer. 2024;22(6):102238.

PATRIOT II: Limitations

Limitations of studies using real-world data include lack of central imaging review, missing or unknown data, potential selection bias, and confounding factors due to the lack of randomization

Grivas P, et al. Clin Genitourin Cancer. 2024;22(6):102238.

PATRIOT II: Baseline Characteristics (1/2)

	All patients (N=160)
Age, median (range), years	70 (40-90)
Sex, n (%)	
Male	123 (76.9)
Female	37 (23.1)
Race, n (%)	
White	143 (89.4)
Black	5 (3.1)
Asian	4 (2.5)
American Indian/ Alaskan native	1 (0.6)
Other/Unknown	7 (4.4)
Ethnicity, n (%)	
Hispanic or Latino	7 (4.4)
Non-Hispanic or Latino	125 (78.1)
Unknown	28 (17.5)

	All patients (N=160)
ECOG performance status, n (%)	
0	68 (42.5)
1	53 (33.1)
≥2	12 (7.5)
Unknown	27 (16.9)
Creatinine clearance, n (%)	
≥60 mL/min	64 (40.0)
<60 mL/min	66 (41.3)
Unknown	30 (18.8)

Grivas P, et al. Clin Genitourin Cancer. 2024;22(6):102238.

PATRIOT II: Baseline Characteristics (2/2)

	All patients (N=160)
PD-L1 status, n (%)	
Positive	44 (27.5)
Negative	33 (20.6)
Unknown	83 (51.9)
Site of metastatic at the start of 1L PBC, n (%)	
Visceral*	70 (43.8)
Nonvisceral	51 (31.9)
None	23 (14.3)
Unknown	16 (10.0)
1L PBC regimen	
Cisplatin, n (%)	100 (62.5)
No. of cycles, median (IQR)	4 (3-6)
Carboplatin + gemcitabine, n (%)	60 (37.5)
No. of cycles, median (IQR)	5 (4-6)

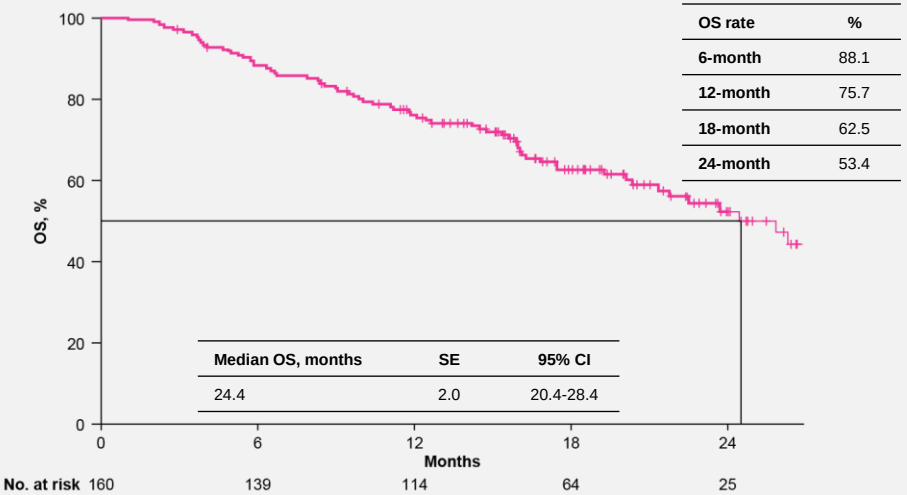
	All patients (N=160)
Best response to 1L PBC, n (%)	
Complete response or partial response	130 (81.3)
Stable disease	17 (10.6)
Unknown	13 (8.1)

*Does not include bone. †Encompasses any cisplatin-based regimen.
IQR, interquartile range;
Grivas P, et al. Clin Genitourin Cancer. 2024;22(6):102238.

PATRIOT II: OS and PFS

Observational, retrospective chart review study patients with la/mUC in routine clinical practice in the United States (N= 160).

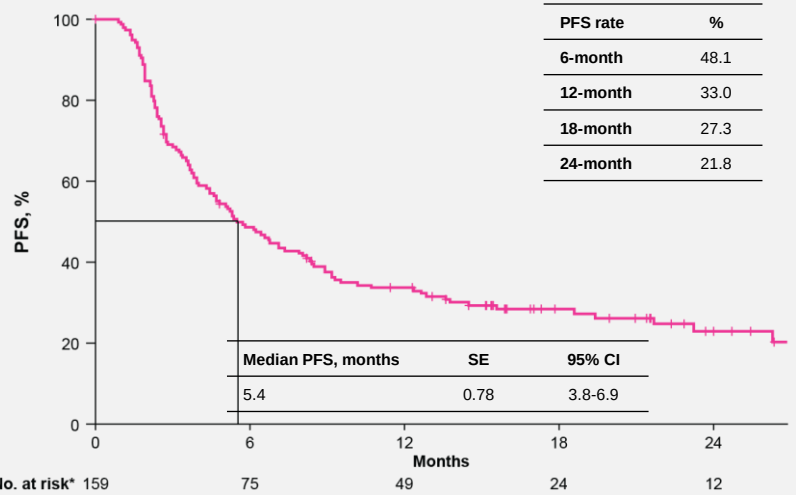
Real-world OS from the start of avelumab 1LM



OS rate	%
6-month	88.1
12-month	75.7
18-month	62.5
24-month	53.4

Median OS, months	SE	95% CI
24.4	2.0	20.4-28.4

Real-world PFS from the start of avelumab 1LM



PFS rate	%
6-month	48.1
12-month	33.0
18-month	27.3
24-month	21.8

Median PFS, months	SE	95% CI
5.4	0.78	3.8-6.9

Median follow-up was 16 months (IQR, 11-21 months)

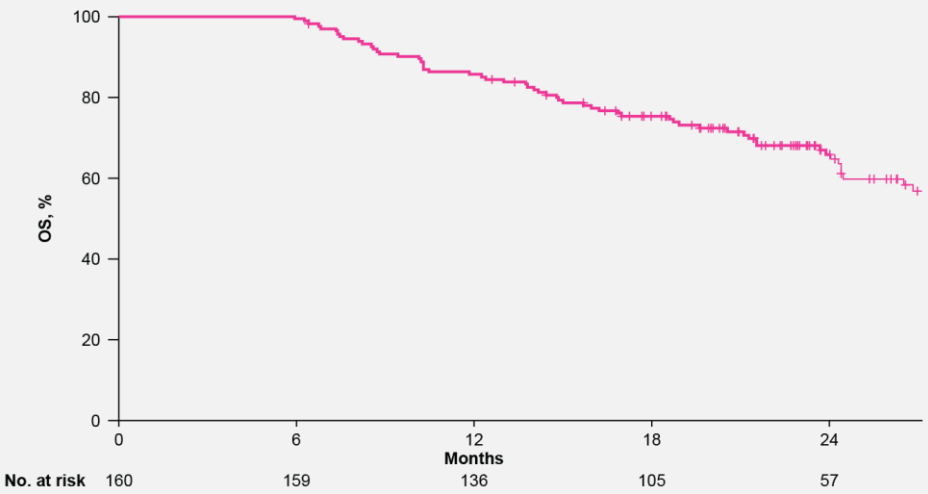
Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Studies using real-world data include lack of central imaging review, missing or unknown data, potential selection bias, and confounding factors due to the lack of randomization

1LM, first-line maintenance; IQR, interquartile range; OS, overall survival; PFS, progression-free survival.
*Date of progression was not available for 1 patient. Progression status was unknown for 3 patients; these patients were censored at the most recent follow-up date.
Grivas P, et al. Clin Genitourin Cancer. 2024;22(6):102238.

PATRIOT II: OS From the Start of 1L PBC

Real-world OS from start of 1L PBC



OS rate	%
6-month	99.4
12-month	85.6
18-month	74.9
24-month	65.4

In this patient cohort without disease progression after 1L PBC, median real-world OS from the start of 1L PBC was 30.5 months (95% CI, 23.4-37.6 months)

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Studies using real-world data include lack of central imaging review, missing or unknown data, potential selection bias, and confounding factors due to the lack of randomization

*Date of progression was not available for 1 patient. Progression status was unknown for 3 patients; these patients were censored at the most recent follow-up date

1L, first-line; 1LM, first-line maintenance; CI, confidence interval; OS, overall survival; PBC, platinum-based chemotherapy

Grivas P, et al. Clin Genitourin Cancer. 2024;22(6):102238.

PATRIOT II: Safety

TEAEs:

- Any TRAEs occurred in **62 patients (38.8%)**

- **The most common TEAE were:**
  - fatigue (n=7 [4%]),
  - hypothyroidism (n=7 [4%]),
  - anemia (n=6 [4%]),
  - infusion-related reaction (n=6 [4%]),
  - nausea (n=6 [4%]),
  - elevated creatinine (n=5 [3%]),
  - diarrhea (n=4 [3%]), and rash (n=4 [3%])

Summary of long-term safety for avelumab 1LM

	All patients (N=160)
Any TRAE, n (%)	62 (38.8)
Time to onset from avelumab initiation, mean (SD), days	95 (127)
Median (range)	56 (0-793)
Any immune-related AE, n (%)	35 (21.9)
Time to onset from avelumab initiation, mean (SD), days	146 (173)
Median (range)	91 (0-793)
Therapy stopped due to any TRAE, n (%)	16 (10.0)
Received steroid (including topical due to any TRAE, n(%)	36 (32.1)
Received high-dose systemic steroid due to TRAE, n(%)	23 (14.3)

	All patients (N=160)
TRAE(s) outcome, n (%)	**N=165***
Resolved	105 (63.6)
Unresolved	32 (19.4)
Resolved with sequelae	2 (1.2)
Unknown	26 (15.8)
Duration of TRAE(s), days†	**N=165***
Mean (SD)	97 (151)
Median (range)	31 (0-657)
Hospitalized due to TRAE, n (%)	
Yes	13 (8.1)
No	147 (91.9)

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Studies using real-world data include lack of central imaging review, missing or unknown data, potential selection bias, and confounding factors due to the lack of randomization

1LM, first-line maintenance; AE, adverse event; TRAE, treatment-related adverse event.
*N represents number of AEs, duplicated in data file. †Most recent follow-up date used if unresolved.
Grivas P, et al. Clin Genitourin Cancer. 2024;22(6):102238.

SPEAR Bladder II

Study details: retrospective, observational study describing the real-world treatment patterns, treatment sequencing post-avelumab 1LM, and OS in 1,658 patients with la/mUC who initiated 1L treatment in the US community oncology setting

- Data was collected from the US Oncology Network iKnowMed™ EHR data system

- Adults with a diagnosis of la/mUC who initiated 1L systemic anticancer treatment between
- December 1, 2019, and November 30, 2023, were included and followed up till the end of the study (February 28, 2024)

Patients were further categorized by 1L systemic anticancer treatment received:

- IO monotherapy
- cisplatin-based PBC only
- carboplatin-based PBC only
- cisplatin-based PBC with avelumab 1LM
- carboplatin-based PBC with avelumab 1LM
- ADCs
- other treatments

- Combination therapy: drugs administered within 28 days of the current treatment
- New treatments administered ≥28 days after the current therapy or with a gap of >90 days were considered the next line of therapy
- If avelumab was administered within 90 days of completion of 1L PBC, the avelumab regimen was considered maintenance treatment

1L, first-line treatment; EHR, electronic health record; la/mUC, locally advanced/metastatic urothelial carcinoma; OS, overall survival; PBC, platinum-based chemotherapy

Sura S, et al. Current Oncology. 2025;32(4):187.

SPEAR Bladder II: Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Oral therapies were recorded in or prescribed through iKM, but whether those prescriptions were fulfilled was not observable
- Data were collected primarily in the oncology clinical practice setting through routine clinical care and not for research purposes; therefore, nonrandom missingness may be present for several variables of interest, and data on healthcare received outside of the US Oncology Network iKnowMed™ EHR of practices are not available
- The absence of disease progression in structured data may result in misclassification between avelumab as 1LM or 2L
- Complete medical history outside of the oncology EHR was not captured, which may lead to underreporting of treatments received

1L, first-line treatment; EHR, electronic health record; la/mUC, locally advanced/metastatic urothelial carcinoma; OS, overall survival; PBC, platinum-based chemotherapy

Sura S, et al. Current Oncology. 2025;32(4):187.

SPEAR Bladder II: Baseline Characteristics

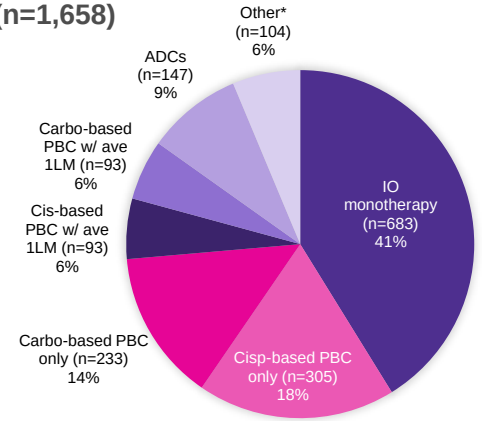
Patient characteristics	Overall study population (n=1,658)	IO monotherapy (n=683)	Cisplatin-based PBC only (n=305)	Carboplatin-based PBC only (n=233)	Cisplatin-based PBC with avelumab 1LM (n=93)	Carboplatin-based PBC with avelumab 1LM (n=93)	ADCs (n=147)	Other* (n=80)
Age at diagnosis, median (range), years	73 (31-90+)	78 (41-90+)	67 (40-87)	74 (31-90+)	67 (47-84)	74 (50-89)	73 (49-90+)	72 (40-90+)
Male, n (%)	1,238 (74.7)	497 (72.8)	246 (80.7)	173 (74.2)	67 (72.0)	75 (80.6)	112 (76.2)	54 (67.5)
Race, n (%)								
White	1,216 (73.3)	506 (74.1)	223 (73.1)	171 (73.4)	74 (79.6)	71 (76.3)	96 (65.3)	58 (72.5)
Other	192 (11.6)	71 (10.4)	37 (12.1)	28 (12.0)	11 (11.8)	8 (8.6)	18 (12.2)	15 (18.8)
Not documented	250 (15.1)	106 (15.5)	45 (14.8)	34 (14.6)	8 (8.6)	14 (15.1)	33 (22.4)	7 (8.8)
ECOG PS, n (%)								
0	213 (12.8)	81 (11.9)	56 (18.4)	27 (11.6)	19 (20.4)	7 (7.5)	14 (9.5)	8 (10.0)
1	568 (34.3)	232 (34.0)	93 (30.5)	78 (33.5)	41 (44.1)	37 (39.8)	44 (29.9)	31 (38.8)
2+	157 (9.5)	92 (13.5)	10 (3.3)	26 (11.1)	<5	<5	15 (10.2)	6 (7.5)
No information	720 (43.4)	278 (40.7)	146 (47.9)	102 (43.8)	30 (32.3)	45 (48.4)	74 (50.3)	35 (43.8)
Follow-up duration, median (range), months	9.0 (0.1-50.4)	9.4 (0.7-49.2)	9.5 (0.1-49.0)	8.2 (0.3-50.4)	12.2 (3.1-41.0)	12.7 (2.1-45.1)	5.2 (0.5-34.7)	8.2 (1.0-43.7)
Tobacco use, n (%)								
No history	279 (16.8)	115 (16.8)	58 (19.0)	34 (14.6)	15 (16.1)	20 (21.5)	19 (12.9)	13 (16.3)
Current	136 (8.2)	39 (5.7)	43 (14.1)	25 (10.7)	9 (9.7)	<5	7 (4.8)	7 (8.8)
Former	435 (26.2)	159 (23.3)	98 (32.1)	61 (26.2)	33 (35.5)	29 (31.2)	28 (19.0)	23 (28.8)
No information	808 (48.7)	370 (54.2)	106 (34.8)	113 (48.5)	36 (38.7)	42 (45.2)	93 (63.3)	37 (46.3)

1L, first line; 1LM, first-line maintenance; ADC, antibody-drug conjugate; ECOG PS, Eastern Cooperative Oncology Group performance status; EHR, electronic health record; IO, immuno-oncology; la/mUC, locally advanced or metastatic urothelial carcinoma; PBC, platinum-based chemotherapy.
*Other includes gemcitabine, erdafitinib, fluorouracil, capecitabine, and methotrexate, as monotherapy or combination

Sura S, et al. Current Oncology. 2025;32(4):187.

SPEAR Bladder II: Treatment Sequencing

1L treatments received by patients with la/mUC (n=1,658)



- Of patients in the overall study cohort who received 1L treatments (n=1,658), 598 (36.1%) and 196 (11.8%) received 2L and 3L treatments, respectively

	2L treatments[2]	3L treatments[2]
Common treatments	• Pembrolizumab monotherapy (32.4%) • EV monotherapy (23.9%) • EV plus pembrolizumab (7.4%)	• EV monotherapy (32.1%) • Sacituzumab govitecan monotherapy (19.9%) • Pembrolizumab monotherapy (12.8%)

- Median follow-up time from index date was 9.0 months (range, 0.1-50.4)
- Median follow-up from start of avelumab 1LM was 9.1 months (range, 0.5-42.2)
- Rates of avelumab 1LM treatment among patients who received 1L PBC ranged from 25.0% in 2020 to 32.9% in 2023
- **During the study observation period, 23.7% patients remained on avelumab 1LM**
- **After discontinuation of avelumab 1LM, 43.5% patients received 2L treatment**
  - **The most common 2L treatment was EV monotherapy (59.3%)**

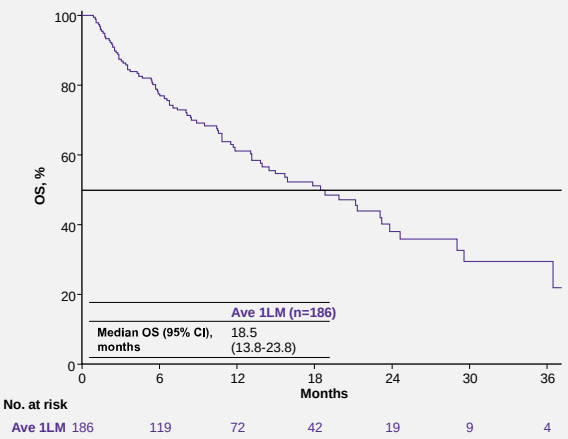
Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Data were collected primarily in the oncology clinical practice setting through routine clinical care and not for research purposes; therefore, nonrandom missingness may be present for several variables of interest, and data on healthcare received outside of the US Oncology Network iKnowMed™ EHR of practices are not available
- Complete medical history outside of the oncology EHR was not captured, which may lead to underreporting of treatments received
- Oral therapies were recorded in or prescribed through iKM, but whether those prescriptions were fulfilled was not observable
- The absence of disease progression in structured data may result in misclassification between avelumab as 1LM or 2L

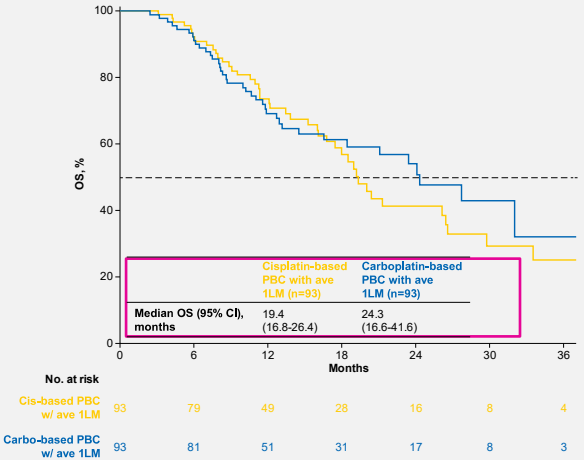
1L, first line; 1LM, first-line maintenance; ADC, antibody-drug conjugate; ave, avelumab; Carbo, carboplatin; Cis, cisplatin; IO, immuno-oncology; la/mUC, locally advanced or metastatic urothelial carcinoma.
*Other includes: avelumab monotherapy (n=24), gemcitabine, erdafitinib, fluorouracil, capecitabine, and methotrexate, as monotherapy or combination (n=80)
Sura S, et al. Current Oncology. 2025;32(4):187.

SPEAR Bladder II: OS (1/2)

Median OS from the start of avelumab 1LM[1,2]



OS from start of 1L cisplatin- or carboplatin-based PBC[3]



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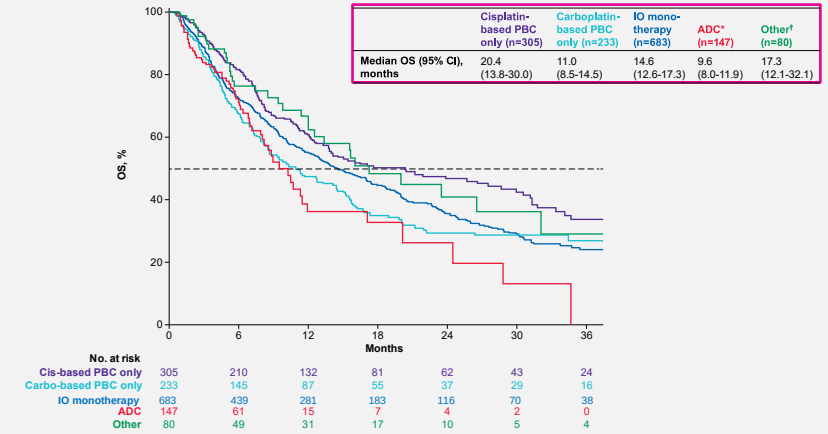
- Complete medical history outside of the oncology EHR was not captured, which may lead to underreporting of treatments received
- Oral therapies were recorded in or prescribed through iKM, but whether those prescriptions were fulfilled was not observable
- The absence of disease progression in structured data may result in misclassification between avelumab as 1LM or 2L

1L, first line; 1LM, first-line maintenance; ave, avelumab; Cis, cisplatin; Carbo, carboplatin; la/mUC, locally advanced or metastatic urothelial carcinoma; OS, overall survival; PBC, platinum-based chemotherapy

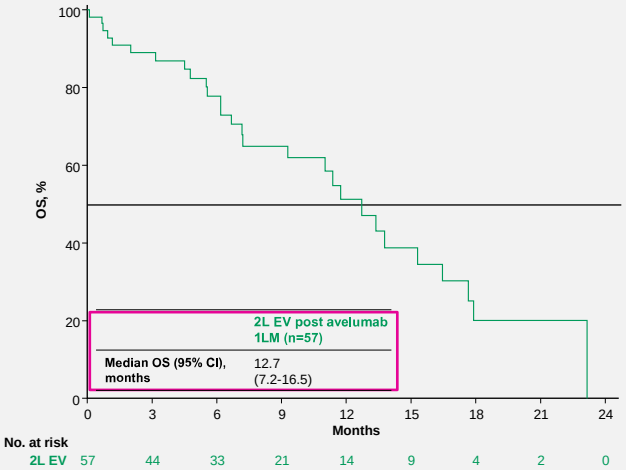
1. Sura S, et al. Current Oncology. 2025;32(4):187; 2. Sura S, et al. Current Oncology. (suppl) 2025;32(4):187; 3. Bupathi M., et al. Presented at: ASCO QCS, (Abstract No. F21), September 27-28, 2024; San Francisco, CA, USA;

SPEAR Bladder II: OS (2/2)

OS from start of 1L treatment[1]



Median OS from the start of 2L EV after avelumab 1LM[2,3]



Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Data were collected primarily in the oncology clinical practice setting through routine clinical care and not for research purposes; therefore, nonrandom missingness may be present for several variables of interest, and data on healthcare received outside of the US Oncology Network iKnowMed™ EHR of practices are not available
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- Oral therapies were recorded in or prescribed through iKM, but whether those prescriptions were fulfilled was not observable
- The absence of disease progression in structured data may result in misclassification between avelumab as 1LM or 2L

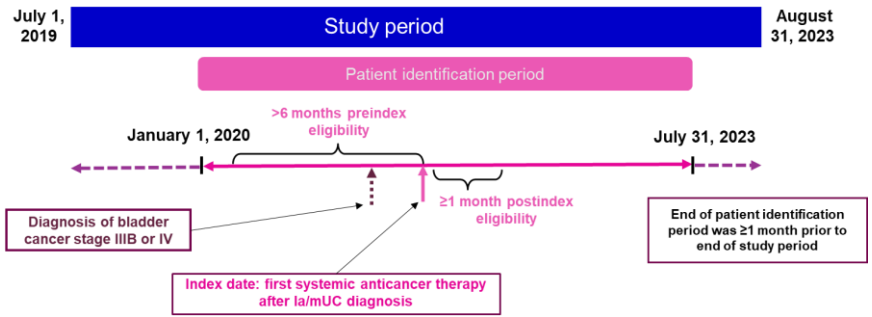
1L, first line; ADC, antibody-drug conjugate; Carbo, carboplatin; Cis, cisplatin; EV, enfortumab vedotin; IO, immuno-oncology; la/mUC, locally advanced or metastatic urothelial carcinoma; OS, overall survival; PBC, platinum-based chemotherapy.*ADC includes EV plus pembrolizumab (59.2%) and EV monotherapy (35.4%). †Other includes gemcitabine, erdafitinib, fluorouracil, capecitabine, and methotrexate, as monotherapy or combination.

1. Bupathi M., et al. Presented at: ASCO QCS, (Abstract No. F21), September 27-28, 2024; San Francisco, CA, USA; 2. Sura S, et al. Current Oncology. 2025;32(4):187; 3. Sura S, et al. Current Oncology. (suppl) 2025;32(4):187.

IMPACT UC III

Study details: noninterventional, retrospective cohort study evaluated healthcare resource utilization and direct medical costs in 2,820 patients with la/mUC receiving 1L systemic treatment with or without avelumab 1LM in the United States[1,2]

- Data was collected from[1,2]
  - Carelon Research's Healthcare Integrated Research Database
  - Health plan's Cancer Care Quality Program (claims and clinical data)



- Adults with a diagnosis of la/mUC who initiated 1L systemic treatment (index date) from January 1, 2020-July 31, 2023, were included[1,2]
- Study period (July 1, 2019-August 31, 2023) allowed a ≥6-month baseline period and ≥1 month of follow-up after index date[1,2]
- Avelumab 1LM use was defined as use on or after June 30, 2020, and within 90 days after completion of 1L PBC [,2]

[a]la/mUC was defined as stage IIIB or IV disease or ≥2 medical claims with metastatic disease.

1L, first-line treatment; 2L, second- line treatment; HCEI, healthcare economic information; la/mUC, locally advanced/metastatic urothelial carcinoma; PBC, platinum-based chemotherapy; UC, urothelial carcinoma.

1. Ike C., et al. Presented at: AMCP Nexus , (Poster No. N6), October 14-17, 2024; Las Vegas, NV, USA; 2. Moon H., et al. Presented at: ASCO QCS, (Poster No. 390), September 27-28, 2024; San Francisco, CA, USA.

IMPACT UC III: Limitations

The population in this analysis was queried from US commercially insured and Medicare Advantage enrollees with available clinical data from HIRD, which may limit the generalizability of these results for other population segments such as traditional fee-for-service Medicare and the uninsured

Administrative claims data are primarily collected for billing and reimbursement purposes and are subject to potential coding biases, inconsistencies, and missing data

Complete medical history outside of the oncology HIRD was not captured, which may lead to underreporting of treatments received

Response data or eligibility for 1LM, and avelumab used in 2L could not be differentiated from that used in 1LM

This was a descriptive study; thus, no comparative analyses were performed, no adjustment for baseline characteristics was made, and no logistic regression was undertaken

1L, first-line treatment; 1LM, first-line maintenance; 2L, second-line treatment; HIRD; Healthcare Integrated Research Database; Ia/mUC, locally advanced/metastatic urothelial carcinoma;
Moon H., et al. Presented at: ASCO QCS, (Poster No. 390), September 27-28, 2024; San Francisco, CA, USA.

IMPACT UC III: Baseline Characteristics (1/2)

	All cohorts (n=2,820)	1L PBC (n=1,044)*	1L PBC + avelumab 1LM (n=157)†	1L IO monotherapy (n=1,099)	Other 1L therapies (n=677)
Age at index, median (IQR), years	70 (62-79)	65 (59-74)	66 (60-73)	76 (67-82)	69 (62-77)
Male sex, n (%)	1,951 (69.2)	664 (63.6)	125 (79.6)	791 (72.0)	496 (73.3)
Race and ethnicity: white (non-Hispanic or Latino), n (%)	2,058 (87.2)	767 (85.3)	123 (89.1)	783 (89.5)	508 (86.7)
Payer type, n (%)					
Commercial health plan	1,480 (52.5)	680 (65.1)	102 (65.0)	435 (39.6)	365 (53.9)
Medicare Advantage health plan	695 (24.7)	270 (25.9)	42 (26.8)	233 (21.2)	192 (28.4)
Other Medicare (supplemental) health plan	645 (22.9)	94 (9.0)	13 (8.3)	431 (39.2)	120 (17.7)

- Avelumab 1LM uptake from 2020-2023 by year was 10.8% (June-December 2020), 29.9% (2021), 34.4% (2022), and 24.8% (January-August 2023); 38.9% of patients were still receiving avelumab 1LM at the end of the study period

1L, first line; 1LM, first-line maintenance; ddMVAC, dose-dense methotrexate, vinblastine, doxorubicin, cisplatin; ECOG, Eastern Cooperative Oncology Group; HIRD; Healthcare Integrated Research Database; IO, immuno-oncology; IQR, interquartile range; PBC, platinum-based chemotherapy; SD, standard deviation.
*1L PBC cohort refers to all patients who received carboplatin, cisplatin, and ddMVAC systemic therapies. †1L PBC + avelumab 1LM is a subgroup of the 1L PBC group. ‡Diabetes with chronic complications and diabetes without chronic complications are mutually exclusive.
Moon H., et al. Presented at: ASCO QCS, (Poster No. 390), September 27-28, 2024; San Francisco, CA, USA.

IMPACT UC III: Baseline Characteristics (2/2)

	All cohorts (n=2,820)	1L PBC (n=1,044)*	1L PBC + avelumab 1LM (n=157)†	1L IO monotherapy (n=1,099)	Other 1L therapies (n=677)
ECOG performance score 0/1, n (%)	1,246 (91.2)	578 (93.5)	93 (94.9)	367 (86.8)	301 (92.6)
Charlson comorbidity Index, mean (SD)	1.55 (1.57)	1.37 (1.49)	1.40 (1.56)	1.75 (1.63)	1.51 (1.56)
Congestive heart failure, n (%)	348 (12.3)	103 (9.9)	13 (8.3)	170 (15.5)	75 (11.1)
Peripheral vascular disease, n (%)	644 (22.8)	207 (19.8)	29 (18.5)	295 (26.8)	142 (21.0)
Cerebrovascular disease, n (%)	321 (11.4)	80 (7.7)	11 (7.0)	165 (15.0)	76 (11.2)
Chronic pulmonary disease, n (%)	815 (28.9)	289 (27.7)	40 (25.5)	328 (29.9)	198 (29.3)
Diabetes without chronic complications, n (%)‡	715 (25.4)	255 (24.4)	28 (17.8)	288 (26.2)	172 (25.4)
Diabetes with chronic complications, n (%)‡	375 (13.3)	118 (11.3)	12 (7.6)	175 (15.9)	82 (12.1)
Renal disease, n (%)	853 (30.3)	240 (23.0)	42 (26.8)	451 (41.0)	162 (23.9)
Mild liver disease, n (%)	635 (22.5)	235 (22.5)	37 (23.6)	226 (20.6)	174 (25.7)

1L, first line; 1LM, first-line maintenance; ddMVAC, dose-dense methotrexate, vinblastine, doxorubicin, cisplatin; ECOG, Eastern Cooperative Oncology Group; HIRD; Healthcare Integrated Research Database; IO, immuno-oncology; IQR, interquartile range; PBC, platinum-based chemotherapy; SD, standard deviation.
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Moon H., et al. Presented at: ASCO QCS, (Poster No. 390), September 27-28, 2024; San Francisco, CA, USA.

IMPACT UC III: Overall Survival (1/2)

	1L PBC (n=1,044)	1L PBC + avelumab 1LM (n=157)	1L IO monotherapy (n=1,099)	Other 1L therapies (n=677)
Median follow-up (IQR), months	11.2 (5.56-20.26)	14.6 (9.23-21.32)	8.6 (4.04-17.69)	10.1 (4.63-21.45)
Median TTNT (IQR), months	4.8 (2.76-8.28)	7.6 (6.21-12.25)	5.5 (2.76-11.04)	4.1 (1.38-7.59)
OS rates (95% CI), %				
1 year	74 (71-77)	84 (78-91)	60 (57-63)	72 (68-76)
2 year	56 (52-60)	68 (58-78)	47 (43-51)	57 (52-62)
3 year	45 (40-51)	65 (55-77)	36 (32-41)	49 (44-55)
Median OS (95% CI), months	29.7 (25.1-37.2)	NE (NE-NE)*	20.0 (17.1-25.6)	34.3 (25.6-NE)

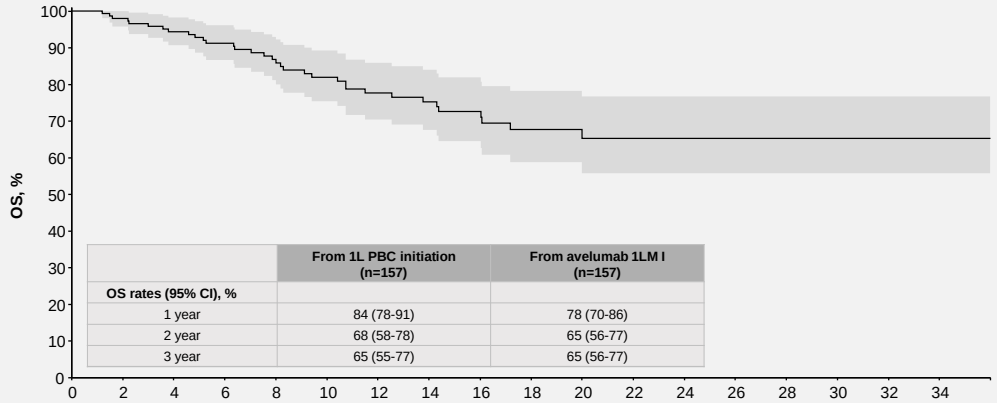
Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- The population in this analysis was queried from US commercially insured and Medicare Advantage enrollees with available clinical data from HIRD, which may limit the generalizability of these results for other population segments such as traditional fee-for-service Medicare and the uninsured
- Administrative claims data are primarily collected for billing and reimbursement purposes and are subject to potential coding biases, inconsistencies, and missing data
- Complete medical history outside of the oncology HIRD was not captured, which may lead to underreporting of treatments received
- Response data or eligibility for 1LM, and avelumab used in 2L could not be differentiated from that used in 1LM
- This was a descriptive study; thus, no comparative analyses were performed, no adjustment for baseline characteristics was made, and no logistic regression was undertaken

1L, first line; 1LM, first-line maintenance; IO, immuno-oncology; IQR, interquartile range; NE, not estimable; OS, overall survival; PBC, platinum-based chemotherapy; TTNT, time to next treatment.
*Median OS was not estimable because >50% of patients remained alive at the end of the study period.
Moon H., et al. Presented at: ASCO QCS, (Poster No. 390), September 27-28, 2024; San Francisco, CA, USA.

IMPACT UC III: Overall Survival (2/2)

Median OS for patients who received 1L PBC followed by avelumab 1LM*



	From 1L PBC initiation (n=157)	From avelumab 1LM I (n=157)
OS rates (95% CI), %		
1 year	84 (78-91)	78 (70-86)
2 year	68 (58-78)	65 (56-77)
3 year	65 (55-77)	65 (56-77)

- Median treatment-free interval from end of 1L PBC to start of avelumab 1LM was 2.7 weeks (IQR, 1.1-4.6)
- Median time on avelumab treatment was 5.0 months (IQR, 1.8-10.2)

Limitations

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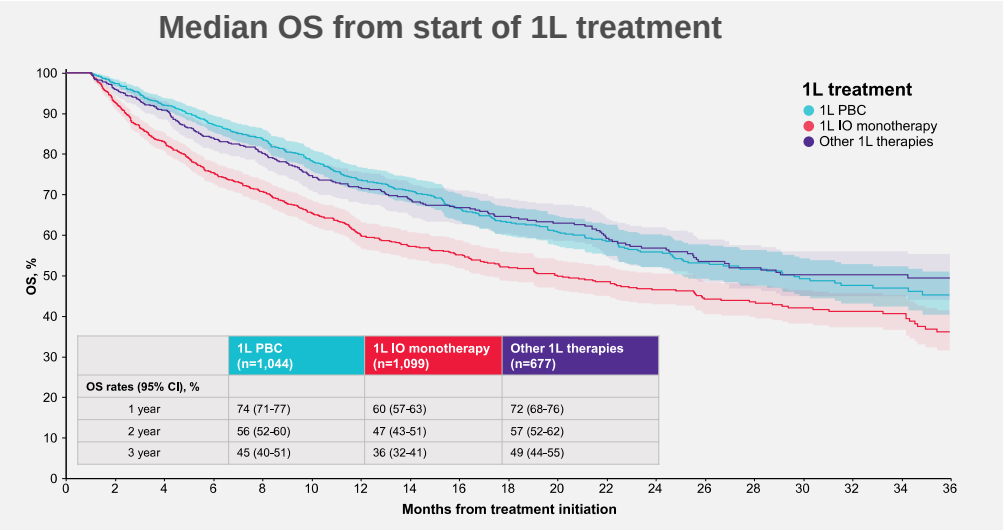
1L, first line; 1LM, first-line maintenance; HIRD; Healthcare Integrated Research Database; la/mUC, locally advanced or metastatic urothelial carcinoma; OS, overall survival; PBC, platinum-based chemotherapy.
*Median OS was not estimable because >50% of patients remained alive at the end of the study period.
Moon H., et al. Presented at: ASCO QCS, (Poster No. 390), September 27-28, 2024; San Francisco, CA, USA.

IMPACT UC III: Overall Survival



	1L PBC (n=1,044)	1L IO monotherapy (n=1,099)	Other 1L therapies (n=677)
OS rates (95% CI), %			
1 year	74 (71-77)	60 (57-63)	72 (68-76)
2 year	56 (52-60)	47 (43-51)	57 (52-62)
3 year	45 (40-51)	36 (32-41)	49 (44-55)

Limitations

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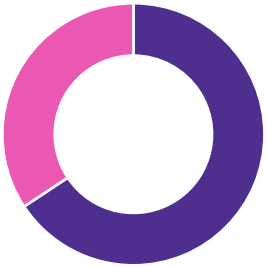
Moon H., et al. Presented at: ASCO QCS, (Poster No. 390), September 27-28, 2024; San Francisco, CA, USA.

Bakaloudi et al

Study details: multicenter retrospective cohort study of real-world patient characteristics and clinical outcomes with avelumab switch maintenance to compare with data from the JAVELIN Bladder 100 trial.

Patients from **14 academic centers** who had received 1L avelumab maintenance after no progression on PBC for aUC were included

37 (34.3%) received carboplatin



71 patients (65.7%) received cisplatin-based chemotherapy

1L, first-line treatment; aUC, advanced urothelial carcinoma; CR, complete response; ECOG PS, Eastern Cooperative Group performance status; PBC, platinum-based chemotherapy; PR, partial response; SD, stable disease; UC, urothelial carcinoma.

Bakaloudi DR, et al. *Clin Genitourin Cancer*. 2023;S1558-7673(23)00147-7.

Bakaloudi et al: Limitations

- Limitations of our study include the moderate sample size, the relatively limited number of events and the retrospective design which is characterized by lack of randomization and of central scan review, with potential selection and confounding biases.
- The involvement of multiple institutions can lead to slightly different clinical practices (eg, imaging scheduled intervals, which can affect PFS) as well as interpretation of scan review regarding therapy response or SD versus progression.

PFS: progression free survival; SD, stable disease.

Bakaloudi et al DR, et al. *Clin Genitourin Cancer*. 2023;S1558-7673(23)00147-7

Bakaloudi et al: Baseline Characteristics (1/2)

	Overall population, N=108
Median age of cancer diagnosis (min, max)	69 (31.3, 96.2)
Sex, n (%)	
Male	87 (80.6)
Female	21 (19.4)
Race, n (%)	
White	100 (92.6)
Not white	6 (5.6)
Unknown	2 (1.9)
Smoking history, n (%)	
Yes	63 (58.3)
No	43 (39.8)
Missing	2 (1.9)
Tumor site, n (%)	
Lower urinary tract	92 (85.2)
Upper urinary tract	16 (14.8)

1L, first-line treatment; aUC, advanced urothelial carcinoma; CR, complete response; ECOG PS, Eastern Cooperative Group performance status; PBC, platinum-based chemotherapy; PR, partial response; SD, stable disease; UC, urothelial carcinoma.

Bakaloudi et al DR, et al. *Clin Genitourin Cancer*. 2023;S1558-7673(23)00147-7.

Bakaloudi et al: Baseline Characteristics (2/2)

	Overall population, N=108
Tumor site, n (%)	
Lower urinary tract	92 (85.2)
Upper urinary tract	16 (14.8)
Pure UC histology, n (%)	
Yes	85 (78.7)
No	23 (21.3)
ECOG PS at PBC start, n (%)	
0	51 (47.2)
1	38 (35.2)
2	3 (2.8)
Missing	16 (14.8)
Cycles of 1L PBC, n (%)	
> 4 cycles	62 (57.4)
≤ 4 cycles	42 (38.9)
Missing	4 (3.7)

	Overall population, N=108
Liver metastases, n (%)	
No	95 (88)
Yes	13 (12)
Weeks from last PBC to avelumab initiation, n (%)	
≤ 3 weeks	18 (16.7)
4-10 weeks	76 (70.3)
> 10 weeks	14 (13)
Platinum agent, n (%)	
Carboplatin	37 (34.3)
Cisplatin	71 (65.7)
Best response to PBC, n (%)	
CR	18 (16.7)
PR	69 (63.9)
SD	21 (19.4)

1L, first-line treatment; aUC, advanced urothelial carcinoma; CR, complete response; ECOG PS, Eastern Cooperative Group performance status; PBC, platinum-based chemotherapy; PR, partial response; SD, stable disease; UC, urothelial carcinoma.

Bakaloudi et al DR, et al. *Clin Genitourin Cancer*. 2023;S1558-7673(23)00147-7.

Bakaloudi et al et al: Overall Response Rate

- Median time from avelumab maintenance initiation to last follow-up: **8.8 months** (min-max: 1-42.7)
- Median interval between last chemotherapy dose and avelumab maintenance initiation: **6 weeks** (min-max: 1-30)

	Overall population, N=108
Best response to avelumab maintenance treatment	
CR	19 (17.6)
PR	12 (11.1)
SD	32 (29.6)
PD	29 (26.9)
Unknown*	16 (14.8)
Overall response rate (ORR), %	28.7

Limitations

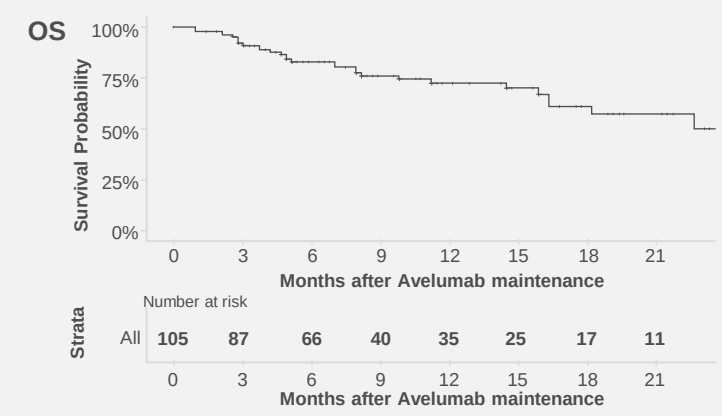
- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Moderate sample size, the relatively limited number of events and the retrospective design which is characterized by lack of randomization and of central scan review, with potential selection and confounding biases.
- The involvement of multiple institutions can lead to slightly different clinical practices (eg, imaging scheduled intervals, which can affect PFS) as well as interpretation of scan review regarding therapy response or SD versus progression.

*Most of those patients did not have response evaluation or were lost to follow-up.
CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease.
Bakaloudi et al DR, et al. *Clin Genitourin Cancer*. 2023;S1558-7673(23)00147-7.

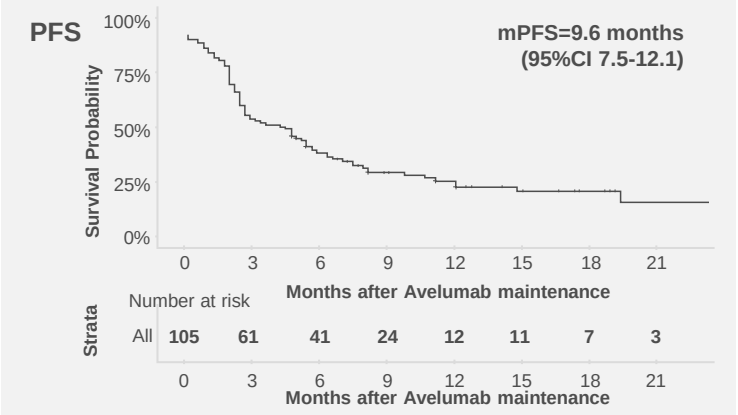
Bakaloudi et al: OS and PFS for the Entire Population

OS and PFS at last follow-up:

- 76 (70.3%) patients were alive
- 30 (27.8%) patients had died
- 2 (1.9%) patients had unknown vital status



- Median OS: NR
  - OS rate at 1 year: 72.5% (CI: 63.2%-83.1%)
- Median PFS: 9.6 months (CI: 7.5-12.1)



Limitations

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- The involvement of multiple institutions can lead to slightly different clinical practices (eg, imaging scheduled intervals, which can affect PFS) as well as interpretation of scan review regarding therapy response or SD versus progression.

CI, confidence interval; mPFS, median PFS; NR, not reached; OS, overall survival; PFS, progression-free survival.

Bakaloudi DR, et al. *Clin Genitourin Cancer*. 2023;S1558-7673(23)00147-7.

Bakaloudi et al, Subgroup Analysis: OS and PFS

OS	HR	95% CI
Sex (Female vs. Male)	1.76	0.68-4.50
Smoking History (No vs. Yes)	0.70	0.27-1.78
Upper vs. lower tract	1.19	0.33-4.29
Histology (pure vs. mixed UC)	1.09	0.37-3.21
PBC Regimen (Cis vs. Carbo)	2.25	0.88-5.77
Cycles of PBC (≤4 vs. >4)	0.80	0.30-2.15
Liver mets at start of PBC (Yes vs. No)*	1.06	0.35-3.18
ECOG PS (0 vs. ≥1) at start of PBC*	**0.15**	**0.05-0.47**
Best response to PBC (CR/PR vs. SD)*	**0.33**	**0.13-0.87**
Weeks from PBC end to avelumab initiation (≤3 vs. 4-10)	1.46	0.48-4.41
Weeks from PBC end to avelumab initiation (>10 vs. 4-10)	0.59	0.13-2.75

PFS	HR	95% CI
Sex (Female vs. Male)	1.29	0.70-2.36
Smoking History (No vs. Yes)	0.94	0.57-1.55
Upper vs. Lower tract	1.32	0.64-2.74
Histology (pure vs. mixed UC)	0.91	0.52-1.57
PBC Regimen (Cis vs. Carbo)	1.58	0.90-2.76
Cycles of PBC (≤ 4 vs. >4)	1.13	0.67-1.91
Liver mets at start of PBC (Yes vs. No)[a]	**2.32**	**1.17-4.59**
ECOG PS (0vs. ≥1) at start of PBC[a]	0.64	0.38-1.06
Best response to PBC (CR/PR vs. SD)[a]	0.61	0.34-1.08
Weeks from PBC end to avelumab initiation (≤3 vs. 4-10)	1.59	0.84-3.00
Weeks from PBC end to avelumab initiation (>10 vs. 4-10)	0.44	0.19-1.05

Limitations

- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Moderate sample size, the relatively limited number of events and the retrospective design which is characterized by lack of randomization and of central scan review, with potential selection and confounding biases.
- The involvement of multiple institutions can lead to slightly different clinical practices (eg, imaging scheduled intervals, which can affect PFS) as well as interpretation of scan review regarding therapy response or SD versus progression.

.*Significant variables (a = 0.05)
CI, confidence interval; CR, complete response; ECOG PS, Eastern Cooperative Group performance status; HR, hazard ratio; OS, overall survival; PBC, platinum-based chemotherapy; PFS, progression-free survival; PR, partial response; SD, stable disease.
Bakaloudi DR, et al. *Clin Genitourin Cancer*. 2023;S1558-7673(23)00147-7.

Bakaloudi et al: Safety

At the time of the analysis, **48 patients (44.4%)** were still receiving avelumab maintenance

60 (55.6%) had discontinued avelumab

	Overall population, N=108
Reason for avelumab discontinuation	
Clinical progression	12 (11.1)
Radiographic progression	34 (31.5)
Toxicity	6 (5.6)
Other	8 (7.4)
Patient still on treatment	48 (44.4)

Limitations

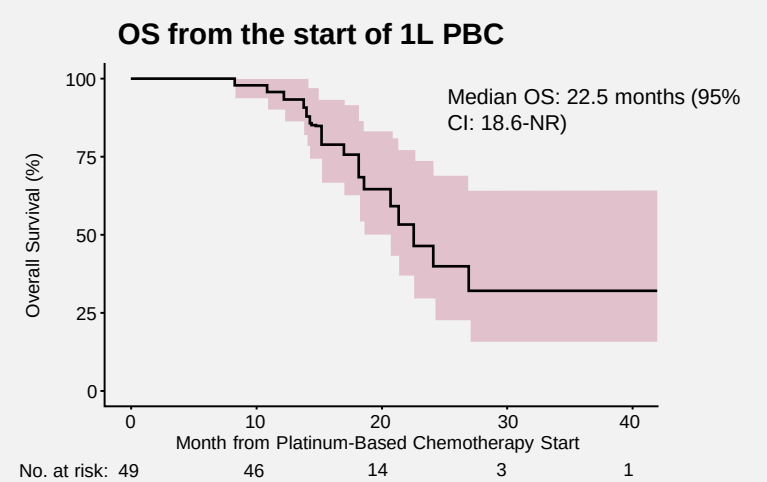
- No conclusions should be drawn, and no treatment decisions should be made based on this real-world analysis
- Moderate sample size, the relatively limited number of events and the retrospective design which is characterized by lack of randomization and of central scan review, with potential selection and confounding biases.
- The involvement of multiple institutions can lead to slightly different clinical practices (eg, imaging scheduled intervals, which can affect PFS) as well as interpretation of scan review regarding therapy response or SD versus progression.

.Bakaloudi et al DR, et al. *Clin Genitourin Cancer*. 2023;S1558-7673(23)00147-7.

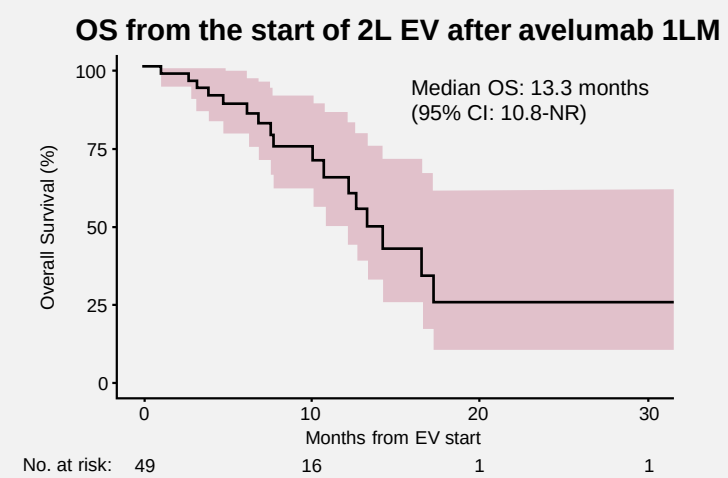
Reactive Appendix

UNITE study: Overview

Study details: Multicentre, retrospective cohort study of patients with aUC treated with EV after PBC and AVE 1LM in the US (N=49)



Median follow-up from PBC start: 19.4 months (95% CI: 16.6-24.6)



Median follow-up from EV start: 8.5 months (95% CI: 6.7-15.0)

Limitations

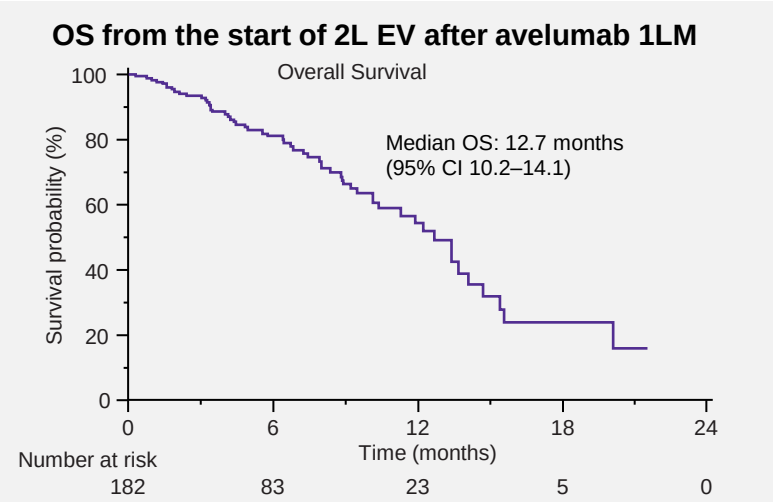
- This study had a retrospective design with limited sample size
- There were chances of selection and confounding bias
- There was a lack of central review of imaging

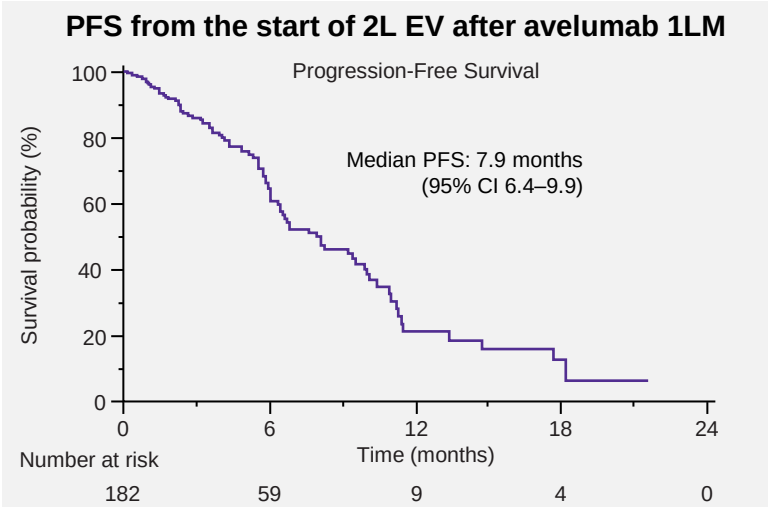
1L, first-line; 2L, second-line; 1LM, first-line maintenance; aUC, advanced urothelial carcinoma; EV, enfortumab vedotin; PBC, platinum-based chemotherapy; rwOS, real-world overall survival.

1. Nizam A, et al. Poster presented at: ASCO Genitourinary Cancers Symposium, (Abstract No. 537); January 25-27, 2024; San Francisco, CA

ARON-2^{EV} study: Overview

Study details: Multicentre, observational study of patients with mUC treated with EV after PBC and AVE 1LM from 15 countries (N=182); median follow-up: 12.0 months (95% CI 5.9–21.6)





Limitations

- This study had a retrospective design with limited sample size
- There were chances of selection and confounding bias
- There was a lack of central review of imaging

.1LM, first-line maintenance; 2L, second-line; EV, enfortumab vedotin; mUC, metastatic urothelial carcinoma; OS, overall survival; PBC, platinum-based chemotherapy; PFS, progression free survival.

Fiala O, et al. Targ Oncol. 2024;19:905–915.