

## News Release

Your Contact

noelle.piscitelli@emdserono.com

Phone: +1 (781) 427-4351

February 13, 2023

### **Not intended for UK-based media**

## **New Analyses Reinforce Survival Benefit of BAVENCIO First-Line Maintenance Treatment in Patients With Advanced Urothelial Carcinoma**

- **Long-term follow-up of the Phase III JAVELIN Bladder 100 study demonstrated median overall survival from start of chemotherapy of 29.7 months among patients receiving BAVENCIO, establishing a new reference point for treatment outcomes in clinical studies**
- **Similar OS benefit seen for patients who were progression-free following either carboplatin- or cisplatin-based chemotherapy**
- **Evidence from non-interventional studies in France and also Italy shows consistent benefit for the JAVELIN Bladder regimen in real-world settings**

Darmstadt, Germany, February 13, 2023 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced findings of a new analysis of long-term follow-up data from the Phase III JAVELIN Bladder 100 trial. These analyses reinforce the proven survival benefits of BAVENCIO® (avelumab) in the first-line maintenance setting for patients with locally advanced or metastatic urothelial carcinoma (UC). With median follow-up of at least 38 months from randomization, patients who were progression-free following platinum-based chemotherapy who received BAVENCIO first-line maintenance plus best supportive care (BSC) had longer median overall survival (OS) than those who received BSC alone in the maintenance setting. This benefit was seen regardless of whether their initial chemotherapy regimens included cisplatin or carboplatin. This analysis, as



## News Release

well as multiple studies of BAVENCIO in the real-world setting, are being presented at the 2023 American Society of Clinical Oncology's annual Genitourinary Cancers Symposium, February 16-18, 2023.

"Based on the significant improvement in overall survival demonstrated in the Phase III JAVELIN Bladder 100 study, platinum-based chemotherapy followed by avelumab maintenance treatment in patients without evidence of disease progression, has become a standard of care for advanced urothelial carcinoma. The findings presented today reinforce that all patients eligible for platinum-based chemotherapy, either cisplatin or carboplatin, can benefit from avelumab maintenance therapy. These findings reported here provide a reference point for outcomes of ongoing and future clinical trials in advanced bladder cancer," said Srikala Sridhar, MD, MSc, FRCPC, Princess Margaret Cancer Centre, Toronto, Ontario, Canada.

In the overall population, patients who received BAVENCIO plus BSC had a median OS of 29.7 months (95% CI, 25.2-34.0) as measured from the start of first-line chemotherapy, compared with 20.5 months (95% CI, 19.0-23.5) in patients who received BSC alone (HR, 0.77; 95% CI, 0.636-0.921). This result further supports the JAVELIN Bladder 100 regimen of BAVENCIO first-line maintenance in patients with advanced UC who are progression-free following first-line platinum-based chemotherapy as standard of care.

The analysis also confirmed that the overall survival of BAVENCIO first-line maintenance were similar regardless of whether patients received cisplatin- or carboplatin-based chemotherapy.

- In patients who received cisplatin plus gemcitabine (n=389), median OS from start of chemotherapy was 31.0 months (95% CI, 24.9-37.1) in the BAVENCIO plus BSC arm (n=183), compared with 23.0 months (95% CI, 19.2-30.9) for BSC alone (n=206) (HR, 0.79; 95% CI, 0.613-1.024).
- In patients who received carboplatin plus gemcitabine (n=269), median OS from start of chemotherapy was 25.8 months (95% CI, 22.8-33.3) for BAVENCIO plus BSC (n=147), compared with 17.6 months (95% CI, 14.8-21.3) for BSC alone (n=122) (HR, 0.69; 95% CI, 0.514-0.920).

## News Release

Long-term safety was similar in both the cisplatin plus gemcitabine and carboplatin plus gemcitabine subgroups, with no new safety concerns identified. Grade 3 or greater treatment-related adverse events were 16 percent and 23 percent for cisplatin and carboplatin cohorts, respectively.

“BAVENCIO remains the only immunotherapy to show improved overall survival in advanced UC patients in the first-line maintenance setting in a Phase III trial. The large, randomized Phase III JAVELIN Bladder 100 trial established BAVENCIO first-line maintenance treatment following platinum-based chemotherapy as a standard of care, and long-term and real-world data such as these presented at ASCO GU 2023 continue adding to the evidence supporting its benefits for patients with advanced bladder cancer,” said Tamas Sütö, MD, PhD, Senior Vice President & Head of Medical Unit Oncology, Merck KGaA, Darmstadt, Germany.

Additional data presented at the meeting include updates from real-world studies of patient populations in France, Italy, Germany, and the U.S. This includes the first full analysis from the AVENANCE real-world study investigating the efficacy and safety of BAVENCIO first-line maintenance therapy in advanced UC patients in France, and the READY study of real-world data from a compassionate use program in Italy, which supports the findings of JAVELIN Bladder 100 in real-world settings.

- In the ongoing (median follow-up 15.2 months) noninterventional AVENANCE study of 593 patients in France with advanced UC that had not progressed with first-line platinum-based chemotherapy who received BAVENCIO as a first-line maintenance treatment, median OS from start of BAVENCIO treatment was 20.7 months (95% CI, 17.1-not estimable) and the 12-month OS rate was 65.4% (95% CI, 61.0-69.4). Median progression-free survival (PFS) was 5.7 months (95% CI, 5.3-7.0).
- In the READY study of 464 patients in Italy who received BAVENCIO first-line maintenance treatment following platinum-based chemotherapy, median OS was not reached and the 12-month OS rate from the start of BAVENCIO treatment was 69.2% (95% CI, 64.8%-73.7%). The median PFS was 8.1 months (95% CI, 6.1-10.4) with a 12-month PFS rate of 44.3% (95% CI, 39.5-49.1).

## News Release

Data for BAVENCIO as well as real-world analyses in urothelial cancer, being presented at ASCO GU include:

Title	Lead Author, Abstract # and Session Details (all times PT)
Avelumab first-line (1L) maintenance for advanced urothelial carcinoma (UC): long-term follow-up from the JAVELIN Bladder 100 trial in subgroups defined by 1L chemotherapy regimen and analysis of overall survival (OS) from start of 1L chemotherapy	SS Sridhar  <b>Abstract #508</b> <b>Poster Session B:</b> Prostate Cancer and Urothelial Carcinoma Friday, Feb 17, 2023 12:30-2:00 PM; 5:15-6:15 PM
Full analysis from AVENANCE: A real-world study of avelumab first-line (1L) maintenance treatment in patients (pts) with advanced urothelial carcinoma (aUC)	P Barthélémy  <b>Abstract #471</b> <b>Poster Session B:</b> Prostate Cancer and Urothelial Carcinoma Friday, Feb 17, 2023 12:30-2:00 PM; 5:15-6:15 PM
Treatment patterns, indicators of receiving systemic treatment, and clinical outcomes in metastatic urothelial carcinoma: a retrospective analysis of real-world data in Germany	G Niegisch  <b>Abstract #464</b> <b>Poster Session B:</b> Prostate Cancer and Urothelial Carcinoma Friday, Feb 17, 2023 12:30-2:00 PM; 5:15-6:15 PM
Real-world treatment patterns and sequencing in patients with locally advanced or metastatic urothelial cancer (la/mUC) in the US	M Kearney  <b>Abstract #572</b> <b>Poster Session B:</b> Prostate Cancer and Urothelial Carcinoma Friday, Feb 17, 2023 12:30-2:00 PM; 5:15-6:15 PM
Baseline characteristics from a retrospective, observational, US-based, multicenter, 'real-world' (RW) study of avelumab first-line maintenance (1LM) in locally advanced/metastatic urothelial carcinoma (la/mUC) (PATRIOT-II)	P Grivas  <b>Abstract #465</b> <b>Poster Session B:</b> Prostate Cancer and Urothelial Carcinoma Friday, Feb 17, 2023 12:30-2:00 PM; 5:15-6:15 PM
READY: Real-world Data from an Italian compassionate use program of avelumab first-line maintenance (1LM) treatment for locally advanced or metastatic urothelial carcinoma (la/mUC)	L Antonuzzo  <b>Abstract #469</b> <b>Poster Session B:</b> Prostate Cancer and Urothelial Carcinoma Friday, Feb 17, 2023 12:30-2:00 PM; 5:15-6:15 PM
Assessment of treatment patterns and real-world outcomes following changes in the treatment paradigm for locally advanced/metastatic urothelial carcinoma (la/mUC) in the US	M Kirker  <b>Abstract #468</b> <b>Poster Session B:</b> Prostate Cancer and Urothelial Carcinoma Friday, Feb 17, 2023 12:30-2:00 PM; 5:15-6:15 PM
SPADE: Design of a real-world observational study of avelumab first-line (1L) maintenance in advanced	P-J Su

## News Release

urothelial carcinoma (UC) in the Asia-Pacific (APAC) region	<p><b>Abstract #TPS577</b>  <b>Trials in Progress Poster</b>  <b>Session B: Urothelial Carcinoma</b>            Friday, Feb 17, 2023            12:30-2:00 PM; 5:15-6:15 PM</p>
C-reactive protein (CRP) as a predictive marker for outcomes with avelumab + axitinib (A + Ax) in patients with poor-risk advanced renal cell carcinoma (aRCC): exploratory analysis from JAVELIN Renal 101	<p>Y Tomita</p> <p><b>Abstract #670</b>  <b>Poster Session C: Renal Cell Cancer; Adrenal, Penile, Urethral and Testicular Cancers</b>            Saturday, Feb 18, 2023            7:00-8:00 AM; 12:30-2:00 PM</p>
A UK real-world observational study of avelumab + axitinib (A + Ax) in advanced renal cell carcinoma (aRCC): 24-month interim results	<p>P Nathan</p> <p><b>Abstract #631</b>  <b>Poster Session C: Renal Cell Cancer; Adrenal, Penile, Urethral and Testicular Cancers</b>            Saturday, Feb 18, 2023            7:00-8:00 AM; 12:30-2:00 PM</p>

### About JAVELIN Bladder 100

JAVELIN Bladder 100 (NCT02603432) is a Phase III, multicenter, multinational, randomized, open-label, parallel-arm study investigating first-line maintenance treatment with BAVENCIO plus BSC versus BSC alone in patients with locally advanced or metastatic UC. The primary endpoint was OS in the two primary populations of all patients and patients with PD-L1+ tumors defined by the Ventana SP263 assay. Secondary endpoints included progression-free survival, anti-tumor activity, safety, pharmacokinetics, immunogenicity, predictive biomarkers and patient-reported outcomes in the co-primary populations. All primary and secondary endpoints are measured from the time of randomization.

### About Urothelial Carcinoma

Bladder cancer is the tenth most common cancer worldwide.<sup>1</sup> In 2020, there were over half a million new cases of bladder cancer diagnosed, with around 200,000 deaths from the disease globally.<sup>1</sup> In the US, an estimated 83,730 cases of bladder cancer were diagnosed in 2021, with around 10,000 locally advanced or metastatic cases presented annually<sup>2</sup> UC, which accounts for about 90% of all bladder cancers,<sup>3</sup> becomes harder to treat as it advances, spreading through the layers of the bladder wall.<sup>4</sup> Only 25% to 55% of patients receive any second-line therapy after first-line chemotherapy.<sup>5</sup> In the US and EU5 markets, approximately 40% to

## News Release

50% of patients receive an immune checkpoint inhibitor in second-line therapy.<sup>2</sup> For patients with advanced UC, the five-year survival rate is 6.4%.<sup>2</sup>

### **About BAVENCIO® (avelumab)**

BAVENCIO is a human anti-programmed death ligand-1 (PD-L1) antibody. BAVENCIO has been shown in preclinical models to engage both the adaptive and innate immune functions. By blocking the interaction of PD-L1 with PD-1 receptors, BAVENCIO has been shown to release the suppression of the T cell-mediated antitumor immune response in preclinical models.<sup>6-8</sup> In November 2014, Merck KGaA, Darmstadt, Germany and Pfizer announced a strategic alliance to co-develop and co-commercialize BAVENCIO.

### **BAVENCIO Approved Indications**

BAVENCIO® (avelumab) is indicated in the US for the maintenance treatment of patients with locally advanced or metastatic urothelial carcinoma (UC) that has not progressed with first-line platinum-containing chemotherapy. BAVENCIO is also indicated for the treatment of patients with locally advanced or metastatic UC who have disease progression during or following platinum-containing chemotherapy, or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

BAVENCIO in combination with axitinib is indicated in the US for the first-line treatment of patients with advanced renal cell carcinoma (RCC).

In the US, the FDA granted accelerated approval for BAVENCIO for the treatment of adults and pediatric patients 12 years and older with metastatic Merkel cell carcinoma (MCC). This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval may be contingent upon verification and description of clinical benefit in confirmatory trials.

BAVENCIO is currently approved for at least one indication for patients in more than 50 countries.

## News Release

### **BAVENCIO Important Safety Information from the US FDA-Approved Label**

BAVENCIO 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 BAVENCIO is recommended. For immune-mediated adverse reactions, withhold or permanently discontinue BAVENCIO depending on severity.**

In general, withhold BAVENCIO for severe (Grade 3) immune-mediated adverse reactions. Permanently discontinue BAVENCIO 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 BAVENCIO 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.

BAVENCIO can cause **immune-mediated pneumonitis**, including fatal cases. Monitor patients for signs and symptoms of pneumonitis and evaluate suspected cases with radiographic imaging. Administer corticosteroids for Grade 2 or greater

## News Release

pneumonitis. Withhold BAVENCIO for Grade 2 and permanently discontinue for Grade 3 or Grade 4 pneumonitis. Immune-mediated pneumonitis occurred in 1.2% (21/1738) 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.

BAVENCIO 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 BAVENCIO for Grade 2 or Grade 3, and permanently discontinue for Grade 4 colitis. Immune-mediated colitis occurred in 1.5% (26/1738) of patients, including Grade 3 (0.4%) and Grade 2 (0.7%) adverse reactions. Systemic corticosteroids were required in all (26/26) patients with colitis.

BAVENCIO can cause **hepatotoxicity and immune-mediated hepatitis**. Withhold or permanently discontinue BAVENCIO 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 BAVENCIO as a single agent in 0.9% (16/1738) of patients, including fatal (0.1%), Grade 3 (0.6%), and Grade 2 (0.1%) adverse reactions. Systemic corticosteroids were required in all (16/16) patients with hepatitis.

**BAVENCIO in combination with INLYTA** can cause **hepatotoxicity** with higher than expected frequencies of Grade 3 and 4 ALT and AST elevation compared to BAVENCIO alone. Consider more frequent monitoring of liver enzymes as compared to when the drugs are used as monotherapy. Withhold or permanently discontinue both BAVENCIO and INLYTA based on severity of AST, ALT, or total bilirubin elevation, and consider administering corticosteroids as needed. Consider rechallenge with BAVENCIO or INLYTA, or sequential rechallenge with both BAVENCIO and INLYTA, after recovery. In patients treated with BAVENCIO in combination with INLYTA in the advanced RCC trials, increased ALT and increased AST were reported in 9% (Grade 3) and 7% (Grade 4) of patients. Immune-mediated hepatitis was



## News Release

reported in 7% of patients including 4.9% with Grade 3 or 4 immune-mediated hepatitis. Thirty-four patients were treated with corticosteroids and one patient was treated with a non-steroidal immunosuppressant.

BAVENCIO 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 BAVENCIO for Grade 3 or Grade 4 endocrinopathies until clinically stable or permanently discontinue depending on severity. Immune-mediated adrenal insufficiency occurred in 0.5% (8/1738) of patients, including Grade 3 (0.1%) and Grade 2 (0.3%) adverse reactions. Systemic corticosteroids were required in all (8/8) patients with adrenal insufficiency.

BAVENCIO 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 BAVENCIO for Grade 3 or Grade 4 endocrinopathies until clinically stable or permanently discontinue depending on severity. Immune-mediated pituitary disorders occurred in 0.1% (1/1738) of patients, which was a Grade 2 (0.1%) adverse reaction.

BAVENCIO 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 BAVENCIO for Grade 3 or Grade 4 endocrinopathies until clinically stable or permanently discontinue depending on severity. Thyroiditis occurred in 0.2% (4/1738) of patients, including Grade 2 (0.1%) adverse reactions. Hyperthyroidism occurred in 0.4% (7/1738) of patients, including Grade 2 (0.3%) adverse reactions. Systemic corticosteroids were required in 29% (2/7) of patients with hyperthyroidism. Hypothyroidism occurred in 5% (90/1738) of patients, including Grade 3 (0.2%) and Grade 2 (3.7%) adverse reactions. Systemic corticosteroids were required in 7% (6/90) of patients with hypothyroidism.

## News Release

BAVENCIO 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 BAVENCIO for Grade 3 or Grade 4 endocrinopathies until clinically stable or permanently discontinue depending on severity. Immune-mediated type I diabetes mellitus occurred in 0.1% (2/1738) of patients, including Grade 3 (0.1%) adverse reactions.

BAVENCIO can cause **immune-mediated nephritis with renal dysfunction**. Withhold BAVENCIO 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% (1/1738) of patients, which was a Grade 2 (0.1%) adverse reaction. Systemic corticosteroids were required in this patient.

BAVENCIO 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 BAVENCIO for suspected and permanently discontinue for confirmed SJS, TEN, or DRESS. Immune-mediated dermatologic adverse reactions occurred in 5% (90/1738) of patients, including Grade 3 (0.1%) and Grade 2 (2.0%) adverse reactions. Systemic corticosteroids were required in 29% (26/90) of patients with dermatologic adverse reactions.

BAVENCIO 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 BAVENCIO or were reported with the use of other PD-1/PD-L1 blocking antibodies. For myocarditis, permanently discontinue BAVENCIO for Grade 2, Grade 3, or Grade 4. For neurological toxicities, withhold BAVENCIO for Grade 2 and permanently discontinue for Grade 3 or Grade 4.

BAVENCIO 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

## News Release

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 BAVENCIO for Grade 3 or Grade 4 infusion-related reactions. Infusion-related reactions occurred in 25% of patients, including three (0.2%) Grade 4 and nine (0.5%) Grade 3 infusion-related reactions. Eleven (92%) of the 12 patients with Grade  $\geq 3$  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.

BAVENCIO **in combination with INLYTA** can cause **major adverse cardiovascular events (MACE)** including severe and fatal events. Consider baseline and periodic evaluations of left ventricular ejection fraction. Monitor for signs and symptoms of cardiovascular events. Optimize management of cardiovascular risk factors, such as hypertension, diabetes, or dyslipidemia. Permanently discontinue BAVENCIO and INLYTA for Grade 3-4 cardiovascular events. MACE occurred in 7% of patients with advanced RCC treated with BAVENCIO in combination with INLYTA compared to 3.4% treated with sunitinib in a randomized trial. These events included death due to cardiac events (1.4%), Grade 3-4 myocardial infarction (2.8%), and Grade 3-4 congestive heart failure (1.8%).

BAVENCIO 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 BAVENCIO and for at least 1 month after the last dose of BAVENCIO. It is not known whether BAVENCIO 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 BAVENCIO due to the potential for serious adverse reactions in breastfed infants.

## News Release

**The most common adverse reactions** (all grades,  $\geq 20\%$ ) in patients with **metastatic Merkel cell carcinoma (MCC)** were fatigue (50%), musculoskeletal pain (32%), diarrhea (23%), nausea (22%), infusion-related reaction (22%), rash (22%), decreased appetite (20%), and peripheral edema (20%).

**Selected treatment-emergent laboratory abnormalities** (all grades,  $\geq 20\%$ ) in patients with **metastatic MCC** were lymphopenia (49%), anemia (35%), increased aspartate aminotransferase (34%), thrombocytopenia (27%), and increased alanine aminotransferase (20%).

A **fatal adverse reaction** (sepsis) occurred in one (0.3%) patient with **locally advanced or metastatic urothelial carcinoma (UC)** receiving BAVENCIO + 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 BAVENCIO experienced either pneumonitis, respiratory failure, sepsis/urosepsis, cerebrovascular accident, or gastrointestinal adverse events, which led to death.

**The most common adverse reactions** (all grades,  $\geq 20\%$ ) in patients with **locally advanced or metastatic UC** receiving BAVENCIO + 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 BAVENCIO, the most common adverse reactions (all grades,  $\geq 20\%$ ) were fatigue, infusion-related reaction, musculoskeletal pain, nausea, decreased appetite, and urinary tract infection.

**Selected laboratory abnormalities** (all grades,  $\geq 20\%$ ) in patients with **locally advanced or metastatic UC** receiving BAVENCIO + 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

## News Release

amylase increased (21% vs 12%), hemoglobin decreased (28% vs 18%), and white blood cell decreased (20% vs 10%).

**Fatal adverse reactions** occurred in 1.8% of patients with **advanced renal cell carcinoma (RCC)** receiving BAVENCIO in combination with INLYTA. These included sudden cardiac death (1.2%), stroke (0.2%), myocarditis (0.2%), and necrotizing pancreatitis (0.2%).

The **most common adverse reactions** (all grades,  $\geq 20\%$ ) in patients with **advanced RCC** receiving BAVENCIO in combination with INLYTA (vs sunitinib) were diarrhea (62% vs 48%), fatigue (53% vs 54%), hypertension (50% vs 36%), musculoskeletal pain (40% vs 33%), nausea (34% vs 39%), mucositis (34% vs 35%), palmar-plantar erythrodysesthesia (33% vs 34%), dysphonia (31% vs 3.2%), decreased appetite (26% vs 29%), hypothyroidism (25% vs 14%), rash (25% vs 16%), hepatotoxicity (24% vs 18%), cough (23% vs 19%), dyspnea (23% vs 16%), abdominal pain (22% vs 19%), and headache (21% vs 16%).

**Selected laboratory abnormalities** (all grades,  $\geq 20\%$ ) worsening from baseline in patients with **advanced RCC** receiving BAVENCIO in combination with INLYTA (vs sunitinib) were blood triglycerides increased (71% vs 48%), blood creatinine increased (62% vs 68%), blood cholesterol increased (57% vs 22%), alanine aminotransferase increased (ALT) (50% vs 46%), aspartate aminotransferase increased (AST) (47% vs 57%), blood sodium decreased (38% vs 37%), lipase increased (37% vs 25%), blood potassium increased (35% vs 28%), platelet count decreased (27% vs 80%), blood bilirubin increased (21% vs 23%), and hemoglobin decreased (21% vs 65%).

Please see full [US Prescribing Information](#) and [Medication Guide](#) available at <http://www.BAVENCIO.com>.

All Merck KGaA, Darmstadt, Germany, press releases are distributed by e-mail at the same time they become available on the EMD Group website. In case you are a resident of the USA or Canada, please go to [www.emdgroup.com/subscribe](http://www.emdgroup.com/subscribe) to register online, change your selection or discontinue this service.

### **About Merck KGaA, Darmstadt, Germany**

Merck KGaA, Darmstadt, Germany, a leading science and technology company, operates across life science, healthcare and electronics. More than 60,000 employees work to make a positive difference to millions of people's lives every day by creating more joyful and sustainable ways to live. From providing

## News Release

products and services that accelerate drug development and manufacturing as well as discovering unique ways to treat the most challenging diseases to enabling the intelligence of devices – the company is everywhere. In 2021, Merck KGaA, Darmstadt, Germany, generated sales of € 19.7 billion in 66 countries.

The company holds the global rights to the name and trademark “Merck” internationally. The only exceptions are the United States and Canada, where the business sectors of Merck KGaA, Darmstadt, Germany, operate as MilliporeSigma in life science, EMD Serono in healthcare and EMD Electronics in electronics. Since its founding in 1668, scientific exploration and responsible entrepreneurship have been key to the company’s technological and scientific advances. To this day, the founding family remains the majority owner of the publicly listed company.

### References

1. Sung H, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: A Cancer Journal for Clinicians*. 2021;0:1–41.
2. SEER. Cancer stat facts: bladder cancer. <https://seer.cancer.gov/statfacts/html/urinb.html>. Accessed February 2022.
3. Cancer.net. Bladder cancer: introduction. <https://www.cancer.net/cancer-types/bladder-cancer/introduction>. Accessed February 2022.
4. American Cancer Society. What is bladder cancer? <https://www.cancer.org/cancer/bladder-cancer/about/what-is-bladder-cancer.html>. Accessed February 2022.
5. Cheeseman S, et al. Current treatment and outcomes benchmark for locally advanced or metastatic urothelial cancer from a large UK-based single centre. *Front Oncol*. 2020;10:167.
6. Boyerinas B, Jochems C, Fantini M, et al. Antibody-dependent cellular cytotoxicity activity of a novel anti-PD-L1 antibody avelumab (MSB0010718C) on human tumor cells. *Cancer Immunol Res*. 2015;3(10):1148-1157.
7. Dolan DE, Gupta S. PD-1 pathway inhibitors: changing the landscape of cancer immunotherapy. *Cancer Control*. 2014;21(3):231-237.
8. Dahan R, Sega E, Engelhardt J, et al. FcγRs modulate the anti-tumor activity of antibodies targeting the PD-1/PD-L1 axis. *Cancer Cell*. 2015;28(3):285-295.