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Not intended for UK-based media

Multiple New Analyses Reinforce the Role of BAVENCIO® (avelumab) First-Line Maintenance as a Standard of Care in Patients with Locally Advanced or Metastatic Urothelial Carcinoma

- **Abstracts to be presented at the 2024 American Society of Clinical Oncology's annual Genitourinary Cancers Symposium provide insights into treatment selection and sequencing, as well as quality of life**
- **Latest real-world data show median overall survival (OS) from start of first-line chemotherapy of about 30 months for patients treated with the JAVELIN Bladder regimen without progression following chemotherapy**
- **Exploratory analyses suggest that in patients who received ADC therapy after the JAVELIN Bladder regimen, median OS from start of first-line chemotherapy reached 40 months in real-world study**

Darmstadt, Germany, January 22, 2024 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced new real-world data that continue to reinforce the JAVELIN Bladder regimen of first-line platinum-based chemotherapy followed by BAVENCIO® (avelumab) maintenance as a standard of care for eligible patients with locally advanced or metastatic urothelial carcinoma (UC) who do not progress on first-line chemotherapy. Data include real-world studies that confirm median overall survival (OS) of approximately 30 months in patients without progression after first-line chemotherapy. Additional analyses offer insights into treatment sequencing outcomes in the real world, with the first analysis of OS by next-line treatment, including in patients who received an antibody-drug

conjugate (ADC) such as enfortumab vedotin after the JAVELIN Bladder regimen. These and other analyses will be presented at the 2024 American Society of Clinical Oncology's annual Genitourinary Cancers Symposium, January 25-27, in San Francisco.

"Avelumab in the first-line maintenance setting is a standard of care for patients with locally advanced or metastatic bladder cancer, with a well-established efficacy and safety profile and supported by years of real-world experience. These new analyses add to the large body of evidence, showing avelumab maintenance treatment can help extend overall survival while potentially providing a favorable quality of life," said Philippe Barthélémy, Institut de Cancérologie Strasbourg Europe, France. "The ongoing exploratory analysis of the real-world AVENANCE study may provide new insights indicating that the initial use of the JAVELIN Bladder regimen, followed by a second-line antibody-drug conjugate treatment like enfortumab vedotin, could greatly enhance overall survival outcomes for patients. These findings underscore the importance of strategic treatment sequencing in optimizing patient outcomes."

Real-world insights into treatment sequencing following the JAVELIN Bladder regimen

Real-world data and analyses by subsequent treatment from the ongoing, real-world, ambispective (retrospective and prospective) AVENANCE study in France continue to support the use of BAVENCIO first-line maintenance while also demonstrating the impact of subsequent therapies once BAVENCIO treatment is discontinued. With a median follow-up since initiation of BAVENCIO of 26.3 months, median OS from the start of BAVENCIO maintenance was 21.3 months (n=595; 95% CI, 17.6 to 24.6) in patients who did not progress on first-line platinum-based chemotherapy and received BAVENCIO first-line maintenance. In an exploratory analysis, median OS from the start of platinum-based chemotherapy was 26.5 months (95% CI, 23.4 to 30.1). Subgroup analyses evaluated outcomes in the 330 patients who received second-line therapy, with median OS from the start of BAVENCIO maintenance of 31.3 months (95% CI, 29.1 to NE) in the 62 patients who received a second-line ADC (enfortumab vedotin: n=56; sacituzumab govitecan: n=6) and 16.7 months (95% CI, 13.6 to 22.8) in the 81 patients who received second-line platinum-based chemotherapy. Among the patients who

received a second-line ADC, median OS measured from the start of chemotherapy was 40.8 months (95% CI, 32.6 to 42.1) in the exploratory analysis.

Long-term efficacy with the JAVELIN Bladder regimen in the real world

Real-world analyses of BAVENCIO first-line maintenance show median OS from the start of chemotherapy of at least 30 months in this population of patients who do not progress on first-line platinum-based chemotherapy, consistent with previously reported results of a long-term exploratory analysis from JAVELIN Bladder 100.

- **PATRIOT-II U.S. Real-World Study:** The observational, retrospective PATRIOT-II study analyzed medical records from 160 U.S. patients, with median follow-up from the start of BAVENCIO maintenance of 16 months (range, 11-21 months). Patients who received BAVENCIO first-line maintenance treatment following chemotherapy achieved a median OS of 30.5 months measured from the start of first-line chemotherapy (95% CI, 23.4 to 37.6). Median OS was 24.4 months measured from the start of maintenance treatment (95% CI, 20.4 to 28.4).
- **READY CUP Italy Real-World Study:** The prospective, noninterventional compassionate use program (CUP) provided Italian patients with locally advanced or metastatic UC early access to BAVENCIO first-line maintenance before reimbursement. With median follow-up of 20.3 months (95% CI, 19.8 to 20.9), median OS measured from start of first-line chemotherapy was 30.9 months (95% CI, 25.7 to NE) in this population without progression after chemotherapy. Median OS from the start of maintenance treatment was 26.2 months (95% CI, 20.0 to NE).

Analyses of quality of life and efficacy in JAVELIN Bladder 100

- **Patient-Reported Outcomes from JAVELIN Bladder 100:** This post-hoc analysis assessed long-term patient-reported outcomes (PRO) data using the National Comprehensive Cancer Network/Functional Assessment of Cancer Therapy Bladder Symptom Index-18 (FBlSI-18) and EuroQoL 5 Dimensions 5 Levels (EQ-5D-5L).An analysis of scores over all cycles prior to end of BAVENCIO treatment PRO patient-reported outcomes scores were BAVENCIO treatment:, with a -2.15 mean change from baseline of -2.15 (95% CI, -3.25 to -1.04) in the FBISI-18 score and -.07 (95% CI, -.09 to -.05) in the EQ-5D-5L index score. In patients with 12 months or more of BAVENCIO treatment, there was a 1.28 mean change from baseline (95% CI, .08 to 2.49) in the FBISI-18 score and a -

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.02 mean change in the EQ-5D-5L index score further supporting the use of the JAVELIN Bladder regimen in eligible patients with advanced UC until progression or unacceptable toxicity.

- **High BMI Subgroup Analysis from JAVELIN Bladder 100:** This exploratory subgroup analysis (n=122) showed the efficacy and safety of BAVENCIO maintenance treatment in patients with a high body mass index (BMI; ≥30 kg/m^2)—a key patient population given that high BMI is a risk factor for bladder cancer, and 25% of the world's population is anticipated to have a high BMI by 2035. In patients with high BMI at baseline, median OS for patients receiving BAVENCIO maintenance therapy plus BSC was 20.8 months from the start of maintenance treatment (95% CI, 16.9 to 34.4), compared with 12.7 months (95% CI, 8.1 to 26.6 months) for BSC alone (HR: 0.77; 95% CI, 0.49 to 1.21). Long-term safety for patients with high BMI was consistent with results from the overall population.

"The JAVELIN Bladder 100 study helped transform the standard of care for patients with advanced bladder cancer, at a time when there had been few advancements in decades. By continuing to share new research on BAVENCIO, including data on health-related quality of life, key patient populations, and treatment sequencing, we can further support clinicians in making informed treatment decisions for each individual patient," said Tamas Sütö, MD, PhD, Senior Vice President & Head of Medical Unit Oncology, Merck KGaA, Darmstadt, Germany.

All company presentations in urothelial cancer at ASCO GU 2024 are listed below.

Title	**Lead Author, Abstract # and Session Details (all times PT)**
Real-world treatment patterns (tx) and clinical outcomes in patients (pts) with locally advanced or metastatic urothelial carcinoma (la/mUC) in Germany: Results of a retrospective observational study (CONVINCE)	S. Machtens **Abstract #551** **Poster Session B:** Urothelial Carcinoma Friday, Jan 26, 2024 11:30-13:00, 17:45-18:45
Avelumab first-line maintenance (1LM) in patients (pts) with locally advanced or metastatic urothelial carcinoma (la/mUC) in the Czech Republic: Interim real-world results from a national reimbursement registry	A Zemankova **Abstract #557** **Poster Session B:** Urothelial Carcinoma Friday, Jan 26, 2024 11:30-13:00, 17:45-18:45

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Updated subgroup analyses from READY: REAl-world Data from an Italian compassionate use program (CUP) of avelumab first-line maintenance (1LM) treatment for locallY advanced or metastatic urothelial carcinoma (la/mUC)	S Bracarda **Abstract #558** **Poster Session B:** Urothelial Carcinoma Friday, Jan 26, 2024 11:30-13:00, 17:45-18:45
Updated results from AVENANCE: Real-world effectiveness of avelumab first-line maintenance (1LM) in patients (pts) with advanced urothelial carcinoma (aUC) and analysis of subsequent treatment	P Barthélémy **Abstract #561** **Poster Session B:** Urothelial Carcinoma Friday, Jan 26, 2024 11:30-13:00, 17:45-18:45
Avelumab first-line maintenance (1LM) for advanced urothelial carcinoma (aUC): Long-term patient-reported outcomes (PROs) in the phase 3 JAVELIN Bladder 100 trial	P Grivas **Abstract #581** **Poster Session B:** Urothelial Carcinoma Friday, Jan 26, 2024 11:30-13:00, 17:45-18:45
Clinical outcomes with split-dose cisplatin-based regimens in patients (pts) with locally advanced or metastatic urothelial carcinoma (la/mUC): results of a systematic literature review (SLR) and network meta-analysis (NMA)	R O'Dwyer **Abstract #589** **Poster Session B:** Urothelial Carcinoma Friday, Jan 26, 2024 11:30-13:00, 17:45-18:45
Avelumab first-line (1L) maintenance for advanced urothelial carcinoma (aUC): long-term outcomes from the JAVELIN Bladder 100 trial in patients (pts) with high body mass index (BMI)	J Aragon-Ching **Abstract #600** **Poster Session B:** Urothelial Carcinoma Friday, Jan 26, 2024 11:30-13:00, 17:45-18:45
Real-world (rw) treatment patterns, sequencing, and outcomes in patients (pts) with locally advanced or metastatic urothelial carcinoma (la/mUC) receiving avelumab first-line maintenance (1LM) in the US	HH Moon **Abstract #605** **Poster Session B:** Urothelial Carcinoma Friday, Jan 26, 2024 11:30-13:00, 17:45-18:45
Platinum eligibility (PE) criteria for patients with metastatic urothelial carcinoma (mUC): results of a physician survey in 5 European countries	S Gupta **Abstract #696** **Poster Session B:** Urothelial Carcinoma Friday, Jan 26, 2024 11:30-13:00, 17:45-18:45
Avelumab first-line maintenance therapy for locally advanced/metastatic urothelial carcinoma: results from the real-world PATRIOT-II study	P Grivas **Abstract #697** **Poster Session B:** Urothelial Carcinoma Friday, Jan 26, 2024 11:30-13:00, 17:45-18:45

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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.[1] In 2020, there were over half a million new cases of bladder cancer diagnosed, with around 200,000 deaths from the disease globally.[1] 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.[2] UC, which accounts for about 90% of all bladder cancers,[3] becomes harder to treat as it advances, spreading through the layers of the bladder wall.[4] Only 25% to 55% of patients receive any second-line therapy after first-line chemotherapy.[5] In the US and EU5 markets, approximately 40% to 50% of patients receive an immune checkpoint inhibitor in second-line therapy.[2] For patients with advanced UC, the five-year survival rate is 6.4%.[2]

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.[6-8]

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, BAVENCIO is indicated for the treatment of adults and pediatric patients 12 years and older with metastatic Merkel cell carcinoma (MCC).

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

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 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 axitinib*** 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 axitinib based on severity of AST, ALT, or total bilirubin elevation, and consider administering corticosteroids as needed. Consider rechallenge with BAVENCIO or axitinib, or sequential rechallenge with both BAVENCIO and axitinib, after recovery. In patients treated with BAVENCIO in combination with axitinib 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 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.

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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.

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 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 ≥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 axitinib** 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.

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Permanently discontinue BAVENCIO and axitinib for Grade 3-4 cardiovascular events. MACE occurred in 7% of patients with advanced RCC treated with BAVENCIO in combination with axitinib 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.

The most common adverse reactions (all grades, ≥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, ≥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, ≥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, ≥20%) were fatigue, infusion-related reaction, musculoskeletal pain, nausea, decreased appetite, and urinary tract infection.

Selected laboratory abnormalities (all grades, ≥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 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 axitinib. 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, ≥20%) in patients with **advanced RCC** receiving BAVENCIO in combination with axitinib (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, ≥20%) worsening from baseline in patients with **advanced RCC** receiving BAVENCIO in combination with axitinib (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

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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.

About Merck KGaA, Darmstadt, Germany
Merck KGaA, Darmstadt, Germany, a leading science and technology company, operates across life science, healthcare and electronics. More than 64,000 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 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 2022, Merck KGaA, Darmstadt, Germany, generated sales of € 22.2 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.

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