

Bavencio (avelumab) Approved for Merkel Cell Carcinoma in Japan

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First-ever treatment indicated for curatively unresectable Merkel cell carcinoma (MCC) and first anti-PD-L1 to be available in Japan Japanese Ministry of Health, Labour and Welfare (MHLW) decision based on Javelin Merkel 200 study, the largest registrational trial for an immunotherapy in MCC First Asian approval for BAVENCIO follows approvals in the US and Europe

Merck KGaA, Darmstadt, Germany, and Pfizer Inc. (NYSE: PFE) today announced that the Japanese Ministry of Health, Labour and Welfare (MHLW) has approved BAVENCIO® (avelumab, genetically recombinant Injection 200mg/mL for intravenous use) as the first and only treatment indicated for curatively unresectable Merkel cell carcinoma (MCC), a rare and aggressive cancer, in Japan.

"Today marks the approval of the first-ever treatment indicated for Merkel cell carcinoma in Japan, making this a significant milestone for patients living with this devastating type of skin cancer," said Luciano Rossetti, M.D., Executive Vice President, Global Head of Research & Development at the biopharma business of Merck KGaA, Darmstadt, Germany, which operates as EMD Serono in the US and Canada. "This decision by the MHLW also signifies the first approval of an anti-PD-L1 in Japan."

"This is the fifth approval for BAVENCIO in 2017 and the first in an Asian market," said Andreas Penk, M.D., Regional President Oncology International Developed Markets, Pfizer Oncology. "Today's announcement demonstrates our continued determination to provide access to our immunotherapy for people around the world living with hard-to-treat cancers such as Merkel cell carcinoma."

MCC is a designated rare disease in Japan and is estimated to affect fewer than 100 patients.[2],[3] BAVENCIO previously received Orphan Drug Designation from the MHLW in December 2016.

"Until now, there were no licensed treatments for MCC in Japan," said Dr Naoya Yamazaki, Chief of the Department of Dermatologic Oncology, National Cancer Center Hospital, Japan. "As a cancer that progresses quickly and has, for so many, a poor prognosis, today's approval is a huge step forward for people impacted by this destructive disease."

This approval is based on data from JAVELIN Merkel 200, an international, multicenter, single-arm, open-label, Phase II study in patients with metastatic MCC.[1]

The JAVELIN Merkel 200 study is the largest registrational clinical trial for an immunotherapy in metastatic MCC. The results of this study were previously presented at the June 2016 American Society of Clinical Oncology annual congress and published in the October 2016 edition of Lancet Oncology.

The MHLW's decision follows BAVENCIO's recent approval by the European Commission on September 18, 2017, as a monotherapy for the treatment of adult patients with metastatic MCC (mMCC). BAVENCIO was also granted marketing authorization by Swissmedic on September 05, 2017, for the treatment of patients with mMCC, whose disease has progressed after at least one chemotherapy treatment. Earlier this year, the US Food and Drug Administration (FDA) granted accelerated approval* for BAVENCIO for the treatment of mMCC and patients with locally advanced or metastatic urothelial carcinoma (UC) who have disease progression during or following platinum-containing chemotherapy.

The clinical development program for BAVENCIO, known as JAVELIN, involves at least 30 clinical programs and more than 6,300 patients evaluated across more than 15 different tumor types. In addition to mMCC, these cancers include breast, gastric/gastro-esophageal junction, head and neck, Hodgkin's lymphoma, melanoma, mesothelioma, non-small cell lung, ovarian, renal cell carcinoma and urothelial carcinoma.

About Merkel Cell Carcinoma

MCC is a rare and aggressive disease in which cancer cells form in the top layer of the skin, close to nerve endings.[4],[5] MCC, which is also known as neuroendocrine carcinoma of the skin or trabecular cancer, often starts in those areas of the skin that are most often exposed to the sun, including the head and neck, and arms.[4],[6] Risk factors for MCC include sun exposure and infection with Merkel cell polyomavirus. Caucasian males older than 50 are at increased risk.[4],[6] MCC is often misdiagnosed as other skin cancers and grows at an exponential rate on chronically sun-damaged skin.[6-8] Current treatment options for MCC include surgery, radiation and chemotherapy.[5] Treatment for metastatic or Stage IV MCC is generally palliative.[5]

About JAVELIN Merkel 200

The efficacy and safety of BAVENCIO was demonstrated in the JAVELIN Merkel 200 trial, a Phase II, open-label, single-arm, multicenter study, in metastatic MCC.[1] The trial excluded patients with active or a history of central nervous system (CNS) metastasis, prior treatment with anti-PD-1, anti-PD-L1, or anti-CTLA-4 antibodies, active or a history of autoimmune disease, a history of other malignancies within the last 5 years, organ transplant, and conditions requiring therapeutic immune suppression or active infection with HIV, or hepatitis B or C. Patients received BAVENCIO 10 mg/kg as an intravenous infusion over 60 minutes every 2 weeks until disease progression or unacceptable toxicity.

The JAVELIN Merkel 200 study is the largest registrational clinical trial for an immunotherapy in metastatic MCC. The results of this study were previously presented at the June 2016 American Society of Clinical Oncology annual congress and published in the October 2016 edition of Lancet Oncology.

About BAVENCIO

BAVENCIO® (avelumab) is a human antibody specific for a protein called PD-L1, or programmed death ligand-1. BAVENCIO is designed to potentially engage both the adaptive and innate immune systems. By binding to PD-L1, BAVENCIO is thought to prevent tumor cells from using PD-L1 for protection against white blood cells, such as T cells, exposing them to anti-tumor responses. BAVENCIO has been shown to induce antibody-dependent cell-mediated cytotoxicity (ADCC) in vitro. In November 2014, Merck KGaA, Darmstadt, Germany, and Pfizer announced a strategic alliance to co-develop and co-commercialize BAVENCIO.

***Indications in the US[9]**

The US Food and Drug Administration (FDA) granted accelerated approval for BAVENCIO for the treatment of (i) mMCC in adults and pediatric patients 12 years and older and (ii) patients with locally advanced or metastatic

urothelial carcinoma (UC) who have disease progression during or following platinum-containing chemotherapy, or who have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy. These indications were approved under accelerated approval based on tumor response rate and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.

Important Safety Information from the US FDA Approved Label

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 moderate (Grade 2) and permanently discontinue for severe (Grade 3), life-threatening (Grade 4), or recurrent moderate (Grade 2) pneumonitis. Pneumonitis occurred in 1.2% (21/1738) of patients, including one (0.1%) patient with Grade 5, one (0.1%) with Grade 4, and five (0.3%) with Grade 3.

BAVENCIO can cause immune-mediated hepatitis, including fatal cases. Monitor patients for abnormal liver tests prior to and periodically during treatment. Administer corticosteroids for Grade 2 or greater hepatitis. Withhold BAVENCIO for moderate (Grade 2) immune-mediated hepatitis until resolution and permanently discontinue for severe (Grade 3) or life-threatening (Grade 4) immune-mediated hepatitis. Immune-mediated hepatitis was reported in 0.9% (16/1738) of patients, including two (0.1%) patients with Grade 5 and 11 (0.6 %) with Grade 3.

BAVENCIO can cause immune-mediated colitis. Monitor patients for signs and symptoms of colitis. Administer corticosteroids for Grade 2 or greater colitis. Withhold BAVENCIO until resolution for moderate or severe (Grade 2 or 3) colitis and permanently discontinue for life-threatening (Grade 4) or recurrent (Grade 3) colitis upon re-initiation of BAVENCIO. Immune-mediated colitis occurred in 1.5% (26/1738) of patients, including seven (0.4%) with Grade 3.

BAVENCIO can cause immune-mediated endocrinopathies, including adrenal insufficiency, thyroid disorders, and type 1 diabetes mellitus.

Monitor patients for signs and symptoms of adrenal insufficiency during and after treatment and administer corticosteroids as appropriate. Withhold BAVENCIO for severe (Grade 3) or life-threatening (Grade 4) adrenal insufficiency. Adrenal insufficiency was reported in 0.5% (8/1738) of patients, including one (0.1%) with Grade 3.

Thyroid disorders can occur at any time during treatment. Monitor patients for changes in thyroid function at the start of treatment, periodically during treatment, and as indicated based on clinical evaluation. Manage hypothyroidism with hormone replacement therapy and hyperthyroidism with medical management. Withhold BAVENCIO for severe (Grade 3) or life threatening (Grade 4) thyroid disorders. Thyroid disorders including hypothyroidism, hyperthyroidism, and thyroiditis were reported in 6% (98/1738) of patients, including three (0.2%) with Grade 3.

Type 1 diabetes mellitus, including diabetic ketoacidosis: Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Withhold BAVENCIO and administer antihyperglycemics or insulin in patients with severe or life-threatening (Grade 3 equal to or greater) hyperglycemia and resume treatment when metabolic control is achieved. Type 1 diabetes mellitus without an alternative etiology occurred in 0.1% (2/1738) of patients, including two cases of Grade 3 hyperglycemia.

BAVENCIO can cause immune-mediated nephritis and renal dysfunction. Monitor patients for elevated serum creatinine prior to and periodically during treatment. Administer corticosteroids for Grade 2 or greater nephritis. Withhold BAVENCIO for moderate (Grade 2) or severe (Grade 3) nephritis until resolution to Grade 1 or lower. Permanently discontinue BAVENCIO for life-threatening (Grade 4) nephritis. Immune-mediated nephritis occurred in 0.1% (1/1738) of patients.

BAVENCIO can result in other severe and fatal immune-mediated adverse reactions involving any organ system during treatment or after treatment discontinuation. For suspected immune-mediated adverse reactions evaluate to confirm or rule out an immune-mediated adverse reaction and to exclude other causes. Depending on the severity of the adverse reaction, withhold or permanently discontinue BAVENCIO, administer high-dose corticosteroids, and initiate hormone replacement therapy if appropriate. Resume BAVENCIO when the immune-mediated adverse reaction remains at Grade 1 or lower following a corticosteroid taper. Permanently discontinue BAVENCIO for any severe (Grade 3) immune-mediated adverse reaction that recurs and for any life-threatening (Grade 4) immune-mediated adverse reaction. The following clinically significant immune-mediated adverse reactions occurred in less than 1% of 1738 patients treated with BAVENCIO: myocarditis with fatal cases, myositis, psoriasis, arthritis, exfoliative dermatitis, erythema multiforme, pemphigoid, hypopituitarism, uveitis, Guillain-Barré syndrome, and systemic inflammatory response.

BAVENCIO can cause severe (Grade 3) or life-threatening (Grade 4) infusion-related reactions. Patients should be premedicated with an antihistamine and acetaminophen prior to the first 4 infusions and for subsequent doses 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 mild (Grade 1) or moderate (Grade 2) infusion-related reactions. Permanently discontinue BAVENCIO for severe (Grade 3) or life-threatening (Grade 4) infusion-related reactions. Infusion-related reactions occurred in 25% (439/1738) of patients, including three (0.2%) patients with Grade 4 and nine (0.5%) with Grade 3.

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 one 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 one 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, greater than or equal to 20%) in patients with metastatic Merkel cell carcinoma (MCC) were fatigue (50%), musculoskeletal pain (32%), diarrhea (23%), nausea (22%), infusion-related reactions (22%), rash (22%), decreased appetite (20%), and peripheral edema (20%).

Selected treatment-emergent laboratory abnormalities (all grades, greater than or equal to 20%) in patients with metastatic MCC were lymphopenia (49%), anemia (35%), increased aspartate aminotransferase (34%), thrombocytopenia (27%), and increased alanine aminotransferase (20%).

The most common adverse reactions (all grades greater than or equal to 20%) in patients with locally advanced or metastatic urothelial carcinoma (UC) were fatigue (41%), infusion-related reaction (30%), musculoskeletal pain (25%), nausea (24%), decreased appetite/hypophagia (21%) and urinary tract infection (21%).

Selected laboratory abnormalities (grades 3-4, greater than or equal to 3%) in patients with locally advanced or metastatic UC were hyponatremia (16%), increased gamma-glutamyltransferase (12%), lymphopenia (11%), hyperglycemia (9%), increased alkaline phosphatase (7%), anemia (6%), increased lipase (6%), hyperkalemia (3%), and increased aspartate aminotransferase (3%).

Please see full US Prescribing Information and Medication Guide available at www.BAVENCIO.com.

Alliance between Merck KGaA, Darmstadt, Germany, and Pfizer Inc., New York, US

Immuno-oncology is a top priority for Merck KGaA, Darmstadt, Germany, and Pfizer Inc. The global strategic alliance between Merck KGaA, Darmstadt, Germany, and Pfizer Inc., New York, US, enables the companies to benefit from each other's strengths and capabilities and further explore the therapeutic potential of avelumab, an anti-PD-L1 antibody initially discovered and developed by Merck KGaA, Darmstadt, Germany. The immuno-oncology alliance will jointly develop and commercialize avelumab and advance Pfizer's PD-1 antibody. The alliance is focused on developing high-priority international clinical programs to investigate avelumab as a monotherapy, as well as in combination regimens, and is striving to find new ways to treat cancer.

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About Merck KGaA, Darmstadt, Germany

Merck KGaA, Darmstadt, Germany, is a leading science and technology company in healthcare, life science and performance materials. Around 50,000 employees work to further develop technologies that improve and enhance life - from biopharmaceutical therapies to treat cancer or multiple sclerosis, cutting-edge systems for scientific research and production, to liquid crystals for smartphones and LCD televisions. In 2016, Merck KGaA, Darmstadt, Germany, generated sales of €15.0 billion in 66 countries.

Founded in 1668, Merck KGaA, Darmstadt, Germany, is the world's oldest pharmaceutical and chemical company. The founding family remains the majority owner of the publicly listed corporate group. Merck KGaA, Darmstadt, Germany, operates as EMD Serono, MilliporeSigma and EMD Performance Materials in the United States and Canada.

Pfizer Inc.: Working together for a healthier world®

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of healthcare products. Our global portfolio includes medicines and vaccines, as well as many of the world's best-known consumer healthcare products. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with healthcare providers, governments and local communities to support and expand access to reliable, affordable healthcare around the world. For more than 150 years, Pfizer has worked to make a difference for all who rely on us. To learn more, please visit us at www.pfizer.com. In addition, to learn more, follow us on Twitter at @Pfizer and @Pfizer_News, LinkedIn and like us on Facebook at [Facebook.com/Pfizer](https://www.facebook.com/Pfizer).

Pfizer Disclosure Notice

The information contained in this release is as of September 27, 2017. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about BAVENCIO (avelumab), including a new indication in Japan for the treatment of curatively unresectable Merkel cell carcinoma, the Merck KGaA, Darmstadt, Germany-Pfizer Alliance involving anti-PD-L1 and anti-PD-1 therapies, and clinical development plans, including their potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, uncertainties regarding the commercial success of BAVENCIO; the uncertainties inherent in research and development, including the ability to meet anticipated clinical study commencement and completion dates and regulatory submission dates, as well as the possibility of unfavorable study results, including unfavorable new clinical data and additional analyses of existing clinical data; risks associated with interim data; the risk that clinical trial data are subject to differing interpretations, and, even when we view data as sufficient to support the safety and/or effectiveness of a product candidate, regulatory authorities may not share our views and may require additional data or may deny approval altogether; whether and when any other drug applications may be filed in any jurisdictions for potential indications for BAVENCIO, combination therapies or other product candidates; whether and when regulatory authorities in any other jurisdictions where applications are pending or may be submitted for BAVENCIO, combination therapies or other product candidates may approve any such applications, which will depend on the assessment by such regulatory authorities of the benefit-risk profile suggested by the totality of the efficacy and safety information submitted; decisions by regulatory authorities regarding labeling and other matters that could affect the availability or commercial potential of BAVENCIO, combination therapies or other product candidates; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2016, and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

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