Bristol-Myers Squibb to Present Data That Advances Understanding of Effects of Immuno-Oncology Therapies on Cancer Biology and Patient Outcomes at AACR 2017

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First report of data evaluating investigational selective IDO1 inhibitor alone and in combination with Opdivo

Initial presentation of overall survival data from Phase 3 CheckMate - 067 assessing Opdivo monotherapy or in combination with Yervoy versus Yervoy alone in patients with advanced melanoma

First report of five-year survival results for Opdivo in previously treated advanced non-small cell lung cancer from CA209-003, to be presented

Ten presentations highlighting translational medicine research in multiple tumor types including lung, melanoma and head & neck

PRINCETON, N.J.--(BUSINESS WIRE)--Bristol-Myers Squibb Company (NYSE: BMY) today announced that new clinical data will be presented at the American Association for Cancer Research (AACR) Annual Meeting 2017 in Washington, D.C., from April 1-5. Research to be presented represents the company’s ongoing commitment to investigating long-term survival and safety data in advanced cancers, and to exploring the interaction between biomarkers and Immuno-Oncology (I-O) therapy across multiple tumor types. Results will be disclosed for Opdivo (nivolumab), as a single-agent and in combination with Yervoy (ipilimumab), as well as an investigational, optimized, once-daily IDO1 inhibitor alone or in combination with Opdivo. IDO is part of Bristol-Myers Squibb’s robust early clinical development pipeline and one of 21 oncology compounds in clinical study. Bristol-Myers Squibb will also share data generated as part of the International Immuno-Oncology Network (II-ON), a global peer-to-peer collaboration with academia established in 2012 and focused on advancing the science of I-O through a series of preclinical, translational and biology-focused research objectives.

“At Bristol-Myers Squibb, we are committed to translational research as we advance the development of next-generation Immuno-Oncology therapies and conduct biomarker research that will help us determine which patients are most likely to benefit from our treatments,” said Fouad Namouni, M.D., head of development, Oncology, Bristol-Myers Squibb. “In all of our research efforts, we are driven by our overarching goal of changing the way patients live with cancer.”

The full set of data to be presented by Bristol-Myers Squibb includes:

Melanoma / Skin Cancer

- Overall survival results from a phase III trial of nivolumab combined with ipilimumab in treatment-naïve patients with advanced melanoma (CheckMate -067)
  Author: James Larkin
  Abstract # CT075
  Minisymposium: Update, Novel Indication, and New Immuno-oncology Clinical Trials
  Monday, April 3, 2017, 3:35 – 3:50 p.m., Ballroom C, Level 3

- Non-comparative, open-label, multiple cohort, phase 1/2 study to evaluate nivolumab in patients with virus-associated tumors (CheckMate -358): Efficacy and safety in Merkel cell carcinoma
  Author: Suzanne Topalian
Abstract # CT074
Minisymposium: Update, Novel Indication, and New Immuno-oncology Clinical Trials
Monday, April 3, 2017, 3:05 – 3:20 p.m. Ballroom C, Level 3

- **Overall survival and safety experience from an expanded access program of nivolumab for patients with advanced melanoma who progressed after prior ipilimumab treatment (CheckMate -168)**
  Author: Milton Barros e Silva
  Abstract # LB-055
  Late-Breaking Poster Session: Clinical Research 1
  Monday, April 3, 2017, 8:00 a.m. – 12:00 p.m., Poster Section 34; Poster Board #18

**Lung**

- **Impact of tumor mutation burden on the efficacy of first-line nivolumab in stage IV or recurrent non-small cell lung cancer: an exploratory analysis of CheckMate -026**
  Author: Solange Peters
  Abstract # CT082
  Minisymposium: Update, Novel Indication, and New Immuno-oncology Clinical Trials
  Monday, April 3, 2017, 5:20 – 5:30 p.m., Ballroom C, Level 3

- **Five-year follow-up from the CA209-003 study of nivolumab in previously treated advanced non-small cell lung cancer: Clinical characteristics of long-term survivors**
  Author: Julie Renee Brahmer
  Abstract # CT077

- **An Open-label Phase 3b/4 Safety Trial of Flat-Dose Nivolumab in Combination With Ipilimumab in Patients With Advanced Non-Small Cell Lung Cancer**
  Author: Rathi N. Pillai
  Abstract # CT070
  Poster Session: Phase I/III Clinical Trials in Progress
  Monday, April 3, 2017, 1:00 – 5:00 p.m. ET, Halls A-C, Poster Section 33, Poster Board #20

**Head and Neck Cancer**

- **Treatment Beyond Progression With Nivolumab in Patients With Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck in the Phase 3 Checkmate -141 Study**
  Author: Robert Haddad
  Abstract # CT157
  Poster Session: Phase I/III Clinical Trials in Progress
  Monday, April 3, 2017, 1:00 – 5:00 p.m. ET, Halls A-C, Poster Section 33

**Pipeline**

- **BMS-986205, an optimized indoleamine 2,3-dioxygenase 1 (IDO1) inhibitor, is well tolerated with potent pharmacodynamic activity, alone and in combination with nivolumab in advanced cancers in a phase 1/2a trial**
  Author: Lillian L. Siu
  Abstract # CT116
  Plenary Session: Novel Immuno-oncology Agent Clinical Trials
  Tuesday, April 4, 2017, 11:13 – 11:28 a.m., Ballroom C, Level 3

- **Structure, in vitro biology and in vivo pharmacodynamic characterization of a novel clinical stage IDO1 inhibitor**
  Author: John T. Hunt
  Abstract # 4964
  Minisymposium: Novel Approaches for Experimental Therapeutics
  Tuesday, April 4, 2017, 3:20 – 3:35 p.m. ET, Room 144, Level 1

**Biomarkers and Dosing**

- **Evaluation of oral microbiome profiling as a response biomarker in squamous cell carcinoma of the head and neck: Analyses from CheckMate -141**
  Author: Robert L. Ferris
  Abstract # CT022
  Clinical Trials Plenary Session: Immuno-oncology Biomarkers in Clinical Trials
  Sunday, April 2, 2017, 4:48 – 5:03 p.m., Hall D-E, Level 2

- **Tumor-associated immune cell PD-L1 expression and peripheral immune profiling: Analyses from CheckMate -141**
  Author: Robert L. Ferris
  Abstract # CT021
  Clinical Trials Plenary Session: Immuno-oncology Biomarkers in Clinical Trials
  Sunday, April 2, 2017, 4:33 – 4:48 p.m., Hall D-E, Level 2

- **Immunogenomic analyses of tumor cells and microenvironment in patients with advanced melanoma before and after treatment with nivolumab**
  Author: Timothy A. Chan
  Abstract # 2988
• Immunomodulatory effects of nivolumab and ipilimumab in combination or nivolumab monotherapy in advanced melanoma patients: CheckMate -038
  Author: Antoni Ribas
  Abstract # CT073
  Minisymposium: Update, Novel Indication, and New Immuno-oncology Clinical Trials
  Monday, April 3, 2017, 3:20 – 3:35 p.m., Ballroom C, Level 3

• A model-based exposure-response assessment of a nivolumab 4-weekly (Q4W) dosing schedule across multiple tumor types
  Author: Xiaochen Zhao
  Abstract # 4015
  Poster Session: Phase I Clinical Trials
  Tuesday, April 4, 2017, 8:00 a.m. – 12:00 p.m. ET, Halls A-C, Poster Section 33

• A Comparative Study of PD-L1 IHC 22C3 and 28-8 FDA-Approved Diagnostic Assays in Cancer
  Author: Cory Batenchuk
  Abstract # #4015
  Poster Session: Assay Technology
  Tuesday, April 4, 2017, 1:00 – 5:00 p.m. ET, Halls A-C, Poster section 1

• Soluble HLA-G and -E (sHLA-G/E) as potential biomarkers of clinical outcomes in patients with advanced, refractory squamous (SQ) NSCLC treated with nivolumab: CheckMate -063
  Author: Vera Rebmann
  Abstract # CT126
  Poster Session: Phase I-III Clinical Trials and Pediatric Clinical Trials
  Tuesday, April 4, 2017, 1:00 – 5:00 p.m. ET, Halls A-C, Poster Section 33

• Pooled analysis of PD-L1 expression across 6 tumor types in the nivolumab clinical program
  Author: Gabriel Krigsfeld
  Abstract # CT143
  Poster Session: Phase I-III Clinical Trials and Pediatric Clinical Trials
  Tuesday, April 4, 2017, 1:00 – 5:00 p.m. ET, Halls A-C, Poster Section 33

II-ON

• RNA-sequencing of tumor-educated platelets enables nivolumab immunotherapy response prediction
  Author: Mirte Muller
  Abstract # LB-248
  Poster Session: Lake-Breaking Clinical Research 2 / Endocrinology
  Tuesday, April 4, 2017, 1:00 – 5:00 p.m. ET, Poster Section 34

Bristol-Myers Squibb & Immuno-Oncology: Advancing Oncology Research
At Bristol-Myers Squibb, patients are at the center of everything we do. Our vision for the future of cancer care is focused on researching and developing transformational Immuno-Oncology (I-O) medicines that will raise survival expectations in hard-to-treat cancers and will change the way patients live with cancer.

We are leading the scientific understanding of I-O through our extensive portfolio of investigational and approved agents, including the first combination of two I-O agents in metastatic melanoma, and our differentiated clinical development program, which is studying broad patient populations across more than 35 types of cancers with 13 clinical-stage molecularly targeted agents designed to target different immune system pathways. Our deep expertise and innovative clinical trial designs uniquely position us to advance the science of combinations across multiple tumors and potentially deliver the next wave of I-O combination regimens with a sense of urgency. We also continue to pioneer research that will help facilitate a deeper understanding of the role of immune biomarkers and inform which patients will benefit most from I-O therapies.

We understand making the promise of I-O a reality for the many patients who may benefit from these therapies requires not only innovation on our part but also close collaboration with leading experts in the field. Our partnerships with academia, government, advocacy and biotech companies support our collective goal of providing new treatment options to advance the standards of clinical practice.

About Opdivo
Opdivo is a programmed death-1 (PD-1) immune checkpoint inhibitor that is designed to uniquely harness the body’s own immune system to help restore anti-tumor immune response. By harnessing the body’s own immune system to fight cancer, Opdivo has become an important treatment option across multiple cancers.

Opdivo’s leading global development program is based on Bristol-Myers Squibb’s scientific expertise in the field of Immuno-Oncology and includes a broad range of clinical trials across all phases, including Phase 3, in a variety of tumor types. To date, the Opdivo clinical development program has enrolled more than 25,000 patients. The Opdivo trials have contributed to gaining a deeper understanding of the potential role of biomarkers in patient care, particularly regarding how patients may benefit from Opdivo across the continuum of PD-L1 expression.

In July 2014, Opdivo was the first PD-1 immune checkpoint inhibitor to receive regulatory approval anywhere in the world. Opdivo is currently approved in more than 60 countries, including the United States, the European Union and Japan. In October 2015, the company’s Opdivo and Yervoy combination regimen was the first Immuno-Oncology combination to receive regulatory approval for the treatment of metastatic melanoma and is currently approved in more than 50 countries.
including the United States and the European Union.

**U.S. FDA-APPROVED INDICATIONS FOR OPDIVO®**

OPDIVO® (nivolumab) as a single agent is indicated for the treatment of patients with BRAF V600 mutation-positive unresectable or metastatic melanoma. This indication is approved under accelerated approval based on progression-free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

OPDIVO® (nivolumab) as a single agent is indicated for the treatment of patients with BRAF V600 wild-type unresectable or metastatic melanoma.

OPDIVO® (nivolumab), in combination with YERVOY® (ipilimumab), is indicated for the treatment of patients with unresectable or metastatic melanoma. This indication is approved under accelerated approval based on progression-free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

OPDIVO® (nivolumab) is indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving OPDIVO.

OPDIVO® (nivolumab) is indicated for the treatment of patients with advanced renal cell carcinoma (RCC) who have received prior anti-angiogenic therapy.

OPDIVO® (nivolumab) is indicated for the treatment of patients with classical Hodgkin lymphoma (cHL) that has relapsed or progressed after autologous hematopoietic stem cell transplantation (HSCT) and post-transplantation brentuximab vedotin. This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

OPDIVO® (nivolumab) is indicated for the treatment of patients with recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) with disease progression on or after platinum-based therapy.

OPDIVO® (nivolumab) is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma 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. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

**IMPORTANT SAFETY INFORMATION**

**WARNING: IMMUNE-MEDIATED ADVERSE REACTIONS**

YERVOY can result in severe and fatal immune-mediated adverse reactions. These immune-mediated reactions may involve any organ system; however, the most common severe immune-mediated adverse reactions are enterocolitis, hepatitis, dermatitis (including toxic epidermal necrolysis), neuropathy, and endocrinopathy. The majority of these immune-mediated reactions initially manifested during treatment; however, a minority occurred weeks to months after discontinuation of YERVOY.

Assess patients for signs and symptoms of enterocolitis, dermatitis, neuropathy, and endocrinopathy and evaluate clinical chemistries including liver function tests (LFTs), adrenocorticotropic hormone (ACTH) level, and thyroid function tests at baseline and before each dose.

Permanently discontinue YERVOY and initiate systemic high-dose corticosteroid therapy for severe immune-mediated reactions.

**Immune-Mediated Pneumonitis**

OPDIVO can cause immune-mediated pneumonitis. Fatal cases have been reported. Monitor patients for signs with radiographic imaging and for symptoms of pneumonitis. Administer corticosteroids for Grade 2 or more severe pneumonitis. Permanently discontinue for Grade 3 or 4 and withhold until resolution for Grade 2. In patients receiving OPDIVO monotherapy, fatal cases of immune-mediated pneumonitis have occurred. Immune-mediated pneumonitis occurred in 3.1% (61/1994) of patients. In patients receiving OPDIVO with YERVOY, immune-mediated pneumonitis occurred in 6% (25/407) of patients.

In Checkmate 205 and 039, pneumonitis, including interstitial lung disease, occurred in 4.9% (13/263) of patients receiving OPDIVO. Immune-mediated pneumonitis occurred in 3.4% (9/263) of patients receiving OPDIVO: Grade 3 (n=1) and Grade 2 (n=8).

**Immune-Mediated Colitis**

OPDIVO can cause immune-mediated colitis. Monitor patients for signs and symptoms of colitis. Administer corticosteroids for Grade 2 (of more than 5 days duration), 3, or 4 colitis. Withhold OPDIVO monotherapy for Grade 2 or 3 and permanently discontinue for Grade 4 or recurrent colitis upon re-initiation of OPDIVO. When administered with YERVOY, withhold OPDIVO and YERVOY for Grade 2 and permanently discontinue for Grade 3 or 4 recurrent colitis. In patients receiving OPDIVO monotherapy, immune-mediated colitis occurred in 2.9% (58/1994) of patients. In patients receiving OPDIVO with YERVOY, immune-mediated colitis occurred in 26% (107/407) of patients including three fatal cases.

In a separate Phase 3 study of YERVOY 3 mg/kg, severe, life-threatening, or fatal (diarrhea of ≥7 stools above baseline, fever, ileus, peritoneal signs; Grade 3-5) immune-mediated enterocolitis occurred in 34 (7%) patients. Across all YERVOY-
treated patients in that study (n=511), 5 (1%) developed intestinal perforation, 4 (0.8%) died as a result of complications, and 26 (5%) were hospitalised for severe enterocolitis.

**Immune-Mediated Hepatitis**

**OPDIVO can cause immune-mediated hepatitis.** Monitor patients for abnormal liver tests prior to and periodically during treatment. Administer corticosteroids for Grade 2 or greater transaminase elevations. Withhold for Grade 2 and permanently discontinue for Grade 3 or 4 immune-mediated hepatitis. In patients receiving OPDIVO monotherapy, immune-mediated hepatitis occurred in 1.8% (35/1994) of patients. In patients receiving OPDIVO with YERVOY, immune-mediated hepatitis occurred in 13% (51/407) of patients.

In a separate Phase 3 study of YERVOY 3 mg/kg, severe, life-threatening, or fatal hepatotoxicity (AST or ALT elevations >5x the ULN or total bilirubin elevations >3x the ULN; Grade 3-5) occurred in 8 (2%) patients, with fatal hepatic failure in 0.2% and hospitalization in 0.4%.

**Immune-Mediated Neuropathies**

In a separate Phase 3 study of YERVOY 3 mg/kg, 1 case of fatal Guillain-Barré syndrome and 1 case of severe (Grade 3) peripheral motor neuropathy were reported.

**Immune-Mediated Endocrinopathies**

**OPDIVO can cause immune-mediated hypophysitis, immune-mediated adrenal insufficiency, autoimmune thyroid disorders, and Type 1 diabetes mellitus.** Monitor patients for signs and symptoms of hypophysitis, signs and symptoms of adrenal insufficiency, thyroid function prior to and periodically during treatment, and hyperglycemia. Administer hormone replacement as clinically indicated and corticosteroids for Grade 2 or greater hypophysitis. Withhold for Grade 2 or 3 and permanently discontinue for Grade 4 hypophysitis. Administer corticosteroids for Grade 3 or 4 adrenal insufficiency. Withhold for Grade 2 and permanently discontinue for Grade 3 or 4 adrenal insufficiency. Administer hormone-replacement therapy for hypothyroidism. Initiate medical management for control of hyperthyroidism. Withhold OPDIVO for Grade 3 and permanently discontinue for Grade 4 hyperglycemia.

In patients receiving OPDIVO monotherapy, hypophysitis occurred in 0.6% (12/1994) of patients. In patients receiving OPDIVO with YERVOY, hypophysitis occurred in 9% (36/407) of patients. In patients receiving OPDIVO monotherapy, adrenal insufficiency occurred in 1% (20/1994) of patients. In patients receiving OPDIVO with YERVOY, adrenal insufficiency occurred in 5% (21/407) of patients. In patients receiving OPDIVO monotherapy, hypothyroidism or thyroiditis resulting in hypothyroidism occurred in 9% (171/1994) of patients. Hyperthyroidism occurred in 2.7% (54/1994) of patients receiving OPDIVO monotherapy. In patients receiving OPDIVO with YERVOY, immune-mediated hypophysitis occurred in 22% (89/407) of patients. Hyperthyroidism occurred in 8% (34/407) of patients receiving OPDIVO with YERVOY. In patients receiving OPDIVO monotherapy, diabetes occurred in 0.9% (17/1994) of patients. In patients receiving OPDIVO with YERVOY, diabetes occurred in 1.5% (6/407) of patients.

In a separate Phase 3 study of YERVOY 3 mg/kg, severe to life-threatening immune-mediated endocrinopathies (requiring hospitalization, urgent medical intervention, or interfering with activities of daily living; Grade 3-4) occurred in 9 (1.8%) patients. All 9 patients had hypopituitarism, and some had additional concomitant endocrinopathies such as adrenal insufficiency, hypogonadism, and hypothyroidism. 6 of the 9 patients were hospitalized for severe endocrinopathies.

**Immune-Mediated Nephritis and Renal Dysfunction**

**OPDIVO can cause immune-mediated rash, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), some cases with fatal outcome.** Administer corticosteroids for Grade 3 or 4 rash. Withhold OPDIVO for Grade 2 or 3 and permanently discontinue for Grade 4 increased serum creatinine. In patients receiving OPDIVO monotherapy, immune-mediated nephritis and renal dysfunction occurred in 1.2% (23/1994) of patients. In patients receiving OPDIVO with YERVOY, immune-mediated nephritis and renal dysfunction occurred in 2.2% (9/407) of patients.

**Immune-Mediated Skin Adverse Reactions and Dermatitis**

**OPDIVO can cause immune-mediated rash, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), severe cases with fatal outcome.** Administer corticosteroids for Grade 3 or 4 rash. Withhold OPDIVO for Grade 3 and 4 rash. For symptoms or signs of SJS or TEN, withhold OPDIVO and refer the patient for specialized care for assessment and treatment; if confirmed, permanently discontinue. In patients receiving OPDIVO monotherapy, immune-mediated rash occurred in 9% (171/1994) of patients. In patients receiving OPDIVO with YERVOY, immune-mediated rash occurred in 22.6% (92/407) of patients.

In a separate Phase 3 study of YERVOY 3 mg/kg, severe, life-threatening, or fatal immune-mediated dermatitis (eg, Stevens-Johnson syndrome, toxic epidermal necrolysis, or rash complicated by full thickness dermal ulceration, or necrotic, bullous, or hemorrhagic manifestations; Grade 3-5) occurred in 13 (2.5%) patients. 1 (0.2%) patient died as a result of toxic epidermal necrolysis. 1 additional patient required hospitalization for severe dermatitis.

**Immune-Mediated Encephalitis**

**OPDIVO can cause immune-mediated encephalitis.** Evaluation of patients with neurologic symptoms may include, but not be limited to, consultation with a neurologist, brain MRI, and lumbar puncture. Withhold OPDIVO in patients with new-onset moderate to severe neurologic signs or symptoms and evaluate to rule out other causes. If this ruleout is not completed, administer corticosteroids and permanently discontinue OPDIVO for immune-mediated encephalitis. In patients receiving OPDIVO monotherapy, encephalitis occurred in 0.2% (3/1994) of patients. Fatal limbic encephalitis occurred in one patient after 7.2 months of exposure despite discontinuation of OPDIVO and administration of corticosteroids. Encephalitis occurred in one patient receiving OPDIVO with YERVOY (0.2%) after 1.7 months of exposure.

**Other Immune-Mediated Adverse Reactions**
Based on the severity of adverse reaction, permanently discontinue or withhold treatment, administer high-dose corticosteroids, and, if appropriate, initiate hormone-replacement therapy. Across clinical trials of OPDIVO the following clinically significant immune-mediated adverse reactions occurred in <1.0% of patients receiving OPDIVO: uveitis, iritis, pancreatitis, facial and abducens nerve paresis, demyelination, polymyalgia rheumatica, autoimmune neuropathy, Guillain-Barré syndrome, hypopituitarism, systemic inflammatory response syndrome, gastritis, duodenitis, sarcoidosis, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), myositis, myocarditis, rhabdomyolysis, motor dysfunction, vasculitis, and myasthenic syndrome.

**Infusion Reactions**

OPDIVO can cause severe infusion reactions, which have been reported in <1.0% of patients in clinical trials. Discontinue OPDIVO in patients with Grade 3 or 4 infusion reactions. Interrupt or slow the rate of infusion in patients with Grade 1 or 2. In patients receiving OPDIVO monotherapy, infusion-related reactions occurred in 6.4% (127/1994) of patients. In patients receiving OPDIVO with YERVOY, infusion-related reactions occurred in 2.5% (10/407) of patients.

**Complications of Allogeneic HSCT after OPDIVO**

Complications, including fatal events, occurred in patients who received allogeneic HSCT after OPDIVO. Outcomes were evaluated in 17 patients from Checkmate 205 and 039, who underwent allogeneic HSCT after discontinuing OPDIVO (15 with reduced-intensity conditioning, 2 with myeloblastic conditioning). Thirty-five percent (6/17) of patients died from complications of allogeneic HSCT after OPDIVO. Five deaths occurred in the setting of severe or refractory GVHD. Grade 3 or higher acute GVHD was reported in 29% (5/17) of patients. Hyperacute GVHD was reported in 20% (n=2) of patients. A steroid-requiring febrile syndrome, without an identified infectious cause, was reported in 35% (n=6) of patients. Two cases of encephalitis were reported: Grade 3 (n=1) lymphocytic encephalitis without an identified infectious cause, and Grade 3 (n=1) suspected viral encephalitis. Hepatic veno-occlusive disease (VOD) occurred in one patient, who received reduced-intensity conditioned allogeneic HSCT and died of GVHD and multi-organ failure. Other cases of hepatic VOD after reduced-intensity conditioned allogeneic HSCT have also been reported in patients with lymphoma who received a PD-1 receptor blocking antibody before transplantation. Cases of fatal hyperacute GVHD have also been reported. These complications may occur despite intervening therapy between PD-1 blockade and allogeneic HSCT.

Follow patients closely for early evidence of transplant-related complications such as hyperacute GVHD, severe (Grade 3 to 4) acute GVHD, steroid-requiring febrile syndrome, hepatic VOD, and other immune-mediated adverse reactions, and intervene promptly.

**Embryo-Fetal Toxicity**

Based on their mechanisms of action, OPDIVO and YERVOY can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with an OPDIVO- or YERVOY- containing regimen and for at least 5 months after the last dose of OPDIVO.

**Lactation**

It is not known whether OPDIVO or YERVOY is present in human milk. Because many drugs, including antibodies, are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from an OPDIVO-containing regimen, advise women to discontinue breastfeeding during treatment. Advise women to discontinue nursing during treatment with YERVOY and for 3 months following the final dose.

**Serious Adverse Reactions**

In Checkmate 037, serious adverse reactions occurred in 41% of patients receiving OPDIVO (n=268). Grade 3 and 4 adverse reactions occurred in 42% of patients receiving OPDIVO. The most frequent Grade 3 and 4 adverse drug reactions reported in 2% to <5% of patients receiving OPDIVO were abdominal pain, hyponatremia, increased aspartate aminotransferase, and increased lipase. In Checkmate 066, serious adverse reactions occurred in 36% of patients receiving OPDIVO (n=206). Grade 3 and 4 adverse reactions occurred in 41% of patients receiving OPDIVO. The most frequent Grade 3 and 4 adverse reactions reported in ≥2% of patients receiving OPDIVO were gamma-glutamyltransferase increase (3.9%) and diarrhea (3.4%). In Checkmate 067, serious adverse reactions (73% and 37%), adverse reactions leading to permanent discontinuation (43% and 14%) or to dosing delays (55% and 28%), and Grade 3 or 4 adverse reactions (72% and 44%) all occurred more frequently in the OPDIVO plus YERVOY arm (n=313) relative to the OPDIVO arm (n=313). The most frequent (≥10%) serious adverse reactions in the OPDIVO plus YERVOY arm and the OPDIVO arm, respectively, were diarrhea (13% and 2.6%), colitis (10% and 1.6%), and pyrexia (10% and 0.6%). In Checkmate 017 and 057, serious adverse reactions occurred in 46% of patients receiving OPDIVO (n=418). The most frequent serious adverse reactions reported in at least 2% of patients receiving OPDIVO were pneumonia, pulmonary embolism, dyspnea, pyrexia, pleural effusion, pneumonitis, and respiratory failure. In Checkmate 025, serious adverse reactions occurred in 47% of patients receiving OPDIVO (n=406). The most frequent serious adverse reactions reported in ≥2% of patients were acute kidney injury, pleural effusion, pneumonia, diarrhea, and hypercalcemia. In Checkmate 025 and 039, among all patients (safety population n=263), adverse reactions leading to discontinuation (4.2%) or to dosing delays (23%) occurred. The most frequent serious adverse reactions reported in ≥1% of patients were infusion-related reaction, pneumonia, pleural effusion, pyrexia, rash and pneumonitis. Ten patients died from causes other than disease progression, including 6 who died from complications of allogeneic HSCT. Serious adverse reactions occurred in 21% of patients in the safety population (n=263) and 27% of patients in the subset of patients evaluated for efficacy (efficacy population n=95). In Checkmate 141, serious adverse reactions occurred in 49% of patients receiving OPDIVO. The most frequent serious adverse reactions reported in at least 2% of patients receiving OPDIVO were pneumonia, dyspnea, respiratory failure, respiratory tract infections, and sepsis. In Checkmate 275, serious adverse reactions occurred in 54% of patients receiving OPDIVO (n=270). The most frequent serious adverse reactions reported in at least 2% of patients receiving OPDIVO were urinary tract infection, sepsis, diarrhea, small intestine obstruction, and general physical health deterioration.

**Common Adverse Reactions**
In Checkmate 037, the most common adverse reaction (≥20%) reported with OPDIVO (n=268) was rash (21%). In Checkmate 066, the most common adverse reactions (≥20%) reported with OPDIVO (n=206) vs dacarbazine (n=205) were fatigue (49% vs 39%), musculoskeletal pain (32% vs 25%), rash (28% vs 12%), and pruritus (23% vs 12%). In Checkmate 067, the most common (≥20%) adverse reactions in the OPDIVO plus YERVOY arm (n=313) were fatigue (59%), rash (53%), diarrhea (52%), nausea (40%), pyrexia (37%), vomiting (28%), and dyspnea (20%). The most common (≥20%) adverse reactions in the OPDIVO arm were fatigue (53%), rash (40%), diarrhea (31%), and nausea (28%). In Checkmate 017 and 057, the most common adverse reactions (≥20%) in patients receiving OPDIVO (n=418) were fatigue, musculoskeletal pain, cough, dyspnea, and decreased appetite. In Checkmate 025, the most common adverse reactions (≥20%) reported in patients receiving OPDIVO (n=406) vs everolimus (n=397) were asthenic conditions (56% vs 57%), cough (34% vs 38%), nausea (28% vs 29%), rash (28% vs 36%), dyspnea (27% vs 31%), diarrhea (25% vs 32%), constipation (23% vs 18%), decreased appetite (25% vs 30%), back pain (21% vs 16%), and arthralgia (20% vs 14%). In Checkmate 205 and 039, among all patients (safety population n=263) and the subset of patients in the efficacy population (n=95), respectively, the most common adverse reactions (≥20%) were fatigue (32% and 43%), upper respiratory tract infection (28% and 48%), pyrexia (24% and 35%), diarrhea (23% and 30%), and cough (22% and 35%). In the subset of patients in the efficacy population (n=95), the most common adverse reactions also included rash (31%), musculoskeletal pain (27%), pruritus (25%), nausea (23%), arthralgia (21%), and peripheral neuropathy (21%). In Checkmate 141, the most common adverse reactions (≥10%) in patients receiving OPDIVO were cough and dyspnea at a higher incidence than investigator's choice. In Checkmate 275, the most common adverse reactions (≥20%) reported in patients receiving OPDIVO (n=270) were fatigue (46%), musculoskeletal pain (30%), nausea (22%), and decreased appetite (22%).

In a separate Phase 3 study of YERVOY 3 mg/kg, the most common adverse reactions (≥5%) in patients who received YERVOY at 3 mg/kg were fatigue (41%), diarrhea (32%), pruritus (31%), rash (29%), and colitis (8%).

Checkmate Trials and Patient Populations

Checkmate 067 - advanced melanoma alone or in combination with YERVOY; Checkmate 037 and 066 - advanced melanoma; Checkmate 017 - squamous non-small cell lung cancer (NSCLC); Checkmate 057 - non-squamous NSCLC; Checkmate 025 - renal cell carcinoma; Checkmate 205/039 - classical Hodgkin lymphoma; Checkmate 141 - squamous cell carcinoma of the head and neck; Checkmate 275 - urothelial carcinoma.

Please see U.S. Full Prescribing Information for OPDIVO and YERVOY, including Boxed WARNING regarding immune-mediated adverse reactions for YERVOY.

About the Bristol-Myers Squibb and Ono Pharmaceutical Co., Ltd. Collaboration

In 2011, through a collaboration agreement with Ono Pharmaceutical Co., Ltd (Ono), Bristol-Myers Squibb expanded its territorial rights to develop and commercialize Opdivo globally except in Japan, South Korea and Taiwan, where Ono had retained all rights to the compound at the time. On July 23, 2014, Bristol-Myers Squibb and Ono further expanded the companies’ strategic collaboration agreement to jointly develop and commercialize multiple immunotherapies – as single agents and combination regimens – for patients with cancer in Japan, South Korea and Taiwan.

About Bristol-Myers Squibb

Bristol-Myers Squibb is a global biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. For more information about Bristol-Myers Squibb, visit us at BMS.com or follow us on LinkedIn, Twitter, YouTube and Facebook.

Bristol-Myers Squibb Forward-Looking Statement

This press release contains "forward-looking statements" as that term is defined in the Private Securities Litigation Reform Act of 1995 regarding the research, development and commercialization of pharmaceutical products. Such forward-looking statements are based on current expectations and involve inherent risks and uncertainties, including factors that could delay, divert or change any of them, and could cause actual outcomes and results to differ materially from current expectations. No forward-looking statement can be guaranteed. Among other risks, there can be no guarantee that Opdivo, Yervoy or any of the compounds mentioned in this release will receive regulatory approval for an additional indication. Forward-looking statements in this press release should be evaluated together with the many uncertainties that affect Bristol-Myers Squibb's business, particularly those identified in the cautionary factors discussion in Bristol-Myers Squibb's Annual Report on Form 10-K for the year ended December 31, 2016 in our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K. Bristol-Myers Squibb undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.

Language:

English

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