Bristol-Myers Squibb Data at ESMO 2017 Demonstrate Company’s Innovative Research Approach to Treating Cancer from All Angles

Release Date:
Wednesday, August 30, 2017 6:05 pm EDT

Terms:
$BMY

Dateline City:
PRINCETON, N.J.

Late-breaking data evaluating Opdivo as adjuvant therapy for resected high-risk melanoma and in combination with Yervoy in previously untreated renal cell carcinoma to be presented

New analyses of emerging biomarkers in four tumor types to help inform patient selection

Research in advanced melanoma assesses potential of Opdivo plus anti-LAG-3 antibody relatlimab in patients whose disease progressed during anti–PD-1/PD-L1 therapy

Long-term survival and safety data to be presented for Opdivo in advanced melanoma, non-small cell lung cancer and head and neck cancer

PRINCETON, N.J.--(BUSINESS WIRE)-- Bristol-Myers Squibb Company (NYSE:BMY) today announced more than 60 presentations, including seven late-breaking abstracts, from its Oncology portfolio will be featured at the European Society for Medical Oncology (ESMO) 2017 Congress in Madrid, Spain, September 8-12. Presentations of data from company-sponsored studies, clinical collaborations and investigator-sponsored research will explore the potential role of Opdivo (nivolumab) as monotherapy and in combination with Yervoy (ipilimumab); with relatlimab (formerly known as BMS-986016), a fully human monoclonal antibody that targets lymphocyte activation gene-3 (LAG-3); or with chemotherapy in 13 types of cancer and analyses that provide insights into the potential role of biomarkers to predict patients’ treatment response.

Presentations that illustrate the company’s approach include the following:

- Late-breaking research to be featured in Presidential Symposia from CheckMate -238 evaluating the safety and efficacy of adjuvant Opdivo in resected high-risk melanoma, and from CheckMate -214 on Opdivo in combination with Yervoy in previously untreated advanced renal cell carcinoma.
- Additional late-breaking presentations featuring the first disclosures of data on Opdivo in advance of surgery in squamous cell cancer of the head and neck, from CheckMate -358, and for Opdivo following induction treatment in triple-negative breast cancer.
- Late-breaking updated efficacy results from an ongoing study of relatlimab in combination with Opdivo in patients with melanoma who progressed during prior anti-PD-1/PD-L1 therapy in all-comer and biomarker-enriched populations.
- Analyses of emerging biomarkers, including tumor mutation burden, microsatellite instability, LAG-3, T cell infiltration and immune cell profiles, that may help inform more precise treatment approaches. Data on the clinical impact of a fixed duration of Opdivo in non-small cell lung cancer from CheckMate -153 will also be presented.
- Additional data evaluating Opdivo-based combinations that are rationally designed based on BMS’ deep understanding of cancer biology, including studies of Opdivo in combination with Yervoy, and the first disclosure of data from ONO-37 on the safety and clinical activity of Opdivo in combination with chemotherapy in previously untreated gastric/gastroesophageal junction cancer.

The full set of data from research investigating the company’s I-O medicines includes the following:
**Gastrointestinal Malignancies**

- **A phase 3 study of nivolumab in previously treated advanced gastric or gastroesophageal junction cancer: updated results and subset analysis by PD-L1 expression (ATTRACTION-02/ONO-4538-12)**
  
  Author: N. Boku
  
  Abstract #617O
  
  Poster Display Session: Gastrointestinal Tumors, Non-Colorectal 1
  
  Friday, September 8, 2:51–3:03 PM CEST, Barcelona Auditorium

- **Two-year survival and safety update for esophageal squamous cell carcinoma treated with nivolumab (ATTRACTION-01/ONO-4538-07)**
  
  Author: Y. Kitagawa
  
  Abstract #638P
  
  Poster Display Session
  
  Saturday, September 9, 1:15–2:15 PM CEST, Hall 8

- **Interim safety and clinical activity of nivolumab in combination with S-1/capecitabine plus oxaliplatin in patients with previously untreated unresectable advanced or recurrent gastric/gastroesophageal junction cancer: part 1 study of ATTRACTION-04/ONO-4538-37**
  
  Author: Y-K. Kang
  
  Abstract #671P
  
  Poster Display Session
  
  Saturday, September 9, 1:15–2:15 PM CEST, Hall 8

- **Nivolumab in patients with advanced chemotherapy-refractory esophagogastric cancer according to microsatellite instability status: CheckMate -032**
  
  Author: P. Ott
  
  Abstract #674P
  
  Poster Display Session
  
  Saturday, September 9, 1:15–2:15 PM CEST, Hall 8

- **ATTRACTION-04/ONO-4538-37: A randomized, multicenter, phase 2/3 study of nivolumab plus chemotherapy in patients with previously untreated advanced or recurrent gastric or gastroesophageal junction cancer**
  
  Author: L-T. Chen
  
  Abstract #777TiP
  
  Poster Display Session
  
  Saturday, September 9, 1:15–2:15 PM CEST, Hall 8

- **ATTRACTION-05/ONO-4538-38/BMS CA209844: A randomized, multicenter, double-blind, placebo-controlled phase 3 study of nivolumab in combination with adjuvant chemotherapy in Stage III gastric and esophagogastric junction cancer**
  
  Author: M. Terashima
  
  Abstract #778TiP
  
  Poster Display Session
  
  Saturday, September 9, 1:15–2:15 PM CEST, Hall 8

- **Real-world productivity, healthcare resource utilization, and quality of life in patients with advanced gastric cancer in Canada and Europe**
  
  Author: G. Maglinte
  
  Abstract #1112PD
  
  Poster Discussion Session: Public Health Policy and Health Economics
• **Analysis of tumor PD-L1 expression and biomarkers in relation to clinical activity in patients with deficient DNA mismatch repair/high microsatellite instability metastatic colorectal cancer treated with nivolumab + ipilimumab: CheckMate -142**  
  Author: T. André  
  Abstract #484PD  
  Poster Discussion Session: Gastrointestinal Tumors, Colorectal  
  Sunday, September 10, 3–4 PM CEST, Sevilla Auditorium

**Genitourinary Cancer**

• **Medical costs and health care resource use in elderly U.S. patients with newly diagnosed metastatic or surgically unresectable urothelial carcinoma using Surveillance, Epidemiology, and End Results (SEER) Medicare data**  
  Author: A. Aly  
  Abstract #1131P  
  Poster Display Session  
  Sunday, September 10, 1:15–2:15 PM CEST, Hall 8

• **A phase 3, randomized, double-blind, multicenter study of adjuvant nivolumab vs placebo in patients with high-risk invasive urothelial carcinoma (CheckMate -274)**  
  Author: D. Bajorin  
  Abstract #921TiP  
  Poster Display Session  
  Sunday, September 10, 1:15–2:15 PM CEST, Hall 8

• **Impact of tumor mutation burden on nivolumab efficacy in second-line urothelial carcinoma patients: exploratory analysis of the phase 2 CheckMate -275 study**  
  Author: M. Galsky  
  Abstract #848PD  
  Poster Discussion Session: Genitourinary Tumors, Non-Prostate  
  Sunday, September 10, 2:45–4:15 PM CEST, Cordoba Auditorium

• **Epithelial-mesenchymal transition, T cell infiltration, and outcomes with nivolumab in urothelial cancer**  
  Author: M. Galsky  
  Abstract #850PD  
  Poster Discussion Session: Genitourinary Tumors, Non-Prostate  
  Sunday, September 10, 2:45–4:15 PM CEST, Cordoba Auditorium

• **CheckMate -214: Efficacy and safety of nivolumab + ipilimumab vs sunitinib for treatment-naïve advanced or metastatic renal cell carcinoma, including IMDC risk and PD-L1 expression subgroups**  
  Author: B. Escudier  
  Abstract #LBA5  
  Presidential Symposium II  
  Sunday, September 10, 4:30–6:20 PM CEST, Madrid Auditorium

**Glioblastoma**

• **Nivolumab in combination with radiotherapy ± temozolomide: updated safety results from CheckMate -143 in patients with methylated or unmethylated newly diagnosed glioblastoma**
Head and Neck Cancer

- **An open-label, multicohort, phase 1/2 study in patients with virus-associated cancers (CheckMate -358): safety and efficacy of neoadjuvant nivolumab in squamous cell carcinoma of the head and neck**
  
  Author: R. Ferris
  
  Abstract #LBA46
  
  Poster Discussion Session: Head and Neck Cancer
  
  Saturday, September 9, 2:45–4:15 PM CEST, Alicante Auditorium

- **Nivolumab vs investigator’s choice in patients with recurrent or metastatic squamous cell carcinoma of the head and neck: treatment effect on clinical outcomes by best overall response in CheckMate -141**
  
  Author: L. Licitra
  
  Abstract #1055P
  
  Poster Display Session
  
  Sunday, September 10, 1:15–2:15 PM CEST, Hall 8

- **Estimated costs of treatment-related adverse events for recurrent or metastatic squamous cell carcinoma of the head and neck in the CheckMate -141 trial**
  
  Author: M. Venkatachalam
  
  Abstract #1056P
  
  Poster Display Session
  
  Sunday, September 10, 1:15–2:15 PM CEST, Hall 8

- **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: a biomarker analysis and updated clinical outcomes**
  
  Author: R. Haddad
  
  Abstract #1043O
  
  Proffered Paper Session: Head and Neck Cancer
  
  Monday, September 11, 3:12–3:24 PM CEST, Granada Auditorium

Melanoma

- **Characterization of complete responses in patients with advanced melanoma who received the combination of nivolumab and ipilimumab, nivolumab or IPI alone**
  
  Author: C. Robert
  
  Abstract #1213O
  
  Proffered Paper Session: Melanoma and Other Skin Tumors
  
  Saturday, September 9, 2:45–3 PM CEST, Madrid Auditorium

- **Cost-effectiveness of nivolumab + ipilimumab in first-line treatment of advanced melanoma: analysis using 28-month overall survival from CheckMate -067**
  
  Author: J. Sabater
  
  Abstract #1115P
  
  Poster Display Session
  
  Sunday, September 10, 1:15–2:15 PM CEST, Hall 8
• Late physical, psychological and social consequences of ipilimumab treatment in advanced melanoma
  Author: A. Boekhout
  Abstract #1260TIP
  Poster Display Session
  Sunday, September 10, 1:15–2:15 PM CEST, Hall 8

• Real-world use of ipilimumab and nivolumab monotherapy or in combination in patients with advanced melanoma: results from a retrospective chart review
  Author: A. Tarhini
  Abstract #1250P
  Poster Display Session
  Sunday, September 10, 1:15–2:15 PM CEST, Hall 8

• Regional differences in overall survival in patients with advanced melanoma who received nivolumab combined with ipilimumab or nivolumab alone in a phase 3 trial (CheckMate -067)
  Author: J.-J. Grob
  Abstract #1222PD
  Poster Discussion Session: Melanoma and Other Skin Tumors
  Monday, September 11, 11 AM–12:15 PM CEST, Pamplona Auditorium

• Quality-adjusted survival of combined nivolumab plus ipilimumab or NIVO alone vs IPI among treatment-naïve patients with advanced melanoma: a quality-adjusted time without symptoms or toxicity (Q-TWiST) analysis
  Author: M. Botteman
  Abstract #1223PD
  Poster Discussion Session: Melanoma and Other Skin Tumors
  Monday, September 11, 11 AM–12:15 PM CEST, Pamplona Auditorium

• Adjuvant therapy with nivolumab versus ipilimumab after complete resection of Stage III/IV melanoma: a randomized, double-blind, phase 3 trial (CheckMate -238)
  Author: J. Weber
  Abstract #LBA8
  Presidential Symposium III
  Monday, September 11, 5:15–5:30 PM CEST, Madrid Auditorium

Thoracic Malignancies

• Randomized results of fixed-duration (1-yr) vs continuous nivolumab in patients with advanced non-small cell lung cancer
  Author: D. Spigel
  Abstract #1297O
  Proffered Paper Session: NSCLC, Metastatic 1
  Friday, September 8, 4:39–4:51 PM CEST, Madrid Auditorium

• Efficiency of nivolumab in the treatment of second-line advanced non-squamous non-small cell lung cancer in Spain
  Author: P. González
  Abstract #1319P
  Poster Display Session
  Saturday, September 9, 1:15–2:15 PM CEST, Hall 8
• Three-year follow-up from CheckMate-017/057: nivolumab versus docetaxel in patients with previously treated advanced non-small cell lung cancer
  Author: E. Felip
  Abstract #1301PD
  Poster Discussion Session: NSCLC, Metastatic
  Sunday, September 10, 4:30–6 PM CEST, Barcelona Auditorium

• Nivolumab in previously treated patients with metastatic squamous NSCLC: results of a European single-arm, phase 2 trial (CheckMate-171) including patients aged ≥70 years and with poor performance status
  Author: S. Popat
  Abstract #1303PD
  Poster Discussion Session: NSCLC, Metastatic
  Sunday, September 10, 4:30–6 PM CEST, Barcelona Auditorium

**Early Assets & Cross-tumor**

• Impact of licensing and reimbursement discrepancies on patient access to cancer treatments across Europe and Canada
  Author: J. McKendrick
  Abstract #1124P
  Poster Display Session
  Sunday, September 10, 1:15–2:15 PM CEST, Hall 8

• Anti-CC-chemokine receptor 4 (CCR4) antibody mogamulizumab and nivolumab combination phase 1 study in patients with advanced or metastatic solid tumors
  Author: N. Yamamoto
  Abstract #LBA17
  Proffered Paper Session: Developmental Therapeutics
  Sunday, September 10, 4:30–4:45 PM CEST, Cordoba Auditorium

• Efficacy of BMS-986016, a monoclonal antibody that targets lymphocyte activation gene-3 (LAG-3), in combination with nivolumab in patients with melanoma who progressed during prior anti-PD-1/PD-L1 therapy in all-comer and biomarker-enriched populations
  Author: P. Ascierto
  Abstract #LBA18
  Proffered Paper Session: Developmental Therapeutics
  Sunday, September 10, 4:45–5 PM CEST, Cordoba Auditorium

• Initial results of BMS-986012, a first-in-class fucosyl-GM1 mAb, in combination with nivolumab, in patients with relapsed/refractory small-cell lung cancer
  Author: Q. Chu
  Abstract #1528PD
  Poster Discussion Session: Non-metastatic NSCLC and Other Thoracic Malignancies
  Monday, September 11, 2:45–4:15 PM CEST, Pamplona Auditorium

**Clinical Collaborations**

• A phase 1/2 study on safety of rovalpituzumab tesirine in combination with nivolumab or nivolumab + ipilimumab in small cell lung cancer
  Author: C. Scripture
  Abstract #1538TP
PIVOT-02: A phase 1/2, open-label, multicenter, dose escalation and dose expansion study of NKTR-214 and nivolumab in patients with select, locally advanced or metastatic solid tumor malignancies

Author: A. Diab
Abstract #1212TIP
Poster Display Session
Sunday, September 10, 1:15–2:15 PM CEST, Hall 8

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 for hard-to-treat cancers that could potentially improve outcomes for these patients.

We are leading the scientific understanding of I-O through our extensive portfolio of investigational compounds and approved agents. Our differentiated clinical development program is studying broad patient populations across more than 50 types of cancers with 14 clinical-stage molecules designed to target different immune system pathways. Our deep expertise and innovative clinical trial designs position us to advance I-O/chemotherapy, I-O/targeted therapies and I-O/radiation therapies across multiple tumors and potentially deliver the next wave of therapies 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 how patients’ tumor biology can be used as a guide for treatment decisions throughout their journey.

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®

OPDVO® (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.

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

OPDVO® (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.

OPDVO® (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.

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

OPDVO® (nivolumab) is indicated for the treatment of adult patients with classical Hodgkin lymphoma (cHL) that has
relapsed or progressed after autologous hematopoietic stem cell transplantation (HSCT) and brentuximab vedotin or after 3 or more lines of systemic therapy that includes autologous HSCT. 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 tumor response rate and duration of response. 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 adults and pediatric (12 years and older) patients with microsatellite instability high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer (CRC) that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan. 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**

OPDIVO 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 6.0% (16/266) of patients receiving OPDIVO. Immune-mediated pneumonitis occurred in 4.9% (13/266) of patients receiving OPDIVO: Grade 3 (n=1) and Grade 2 (n=12).

**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 or 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 hospitalized 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, hyperthyroidism or thyroiditis occurring in or after thyroiditis 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 nephritis. Monitor patients for elevated serum creatinine prior to and periodically during treatment. Administer corticosteroids for Grades 2-4 increased serum creatinine. 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), some cases with fatal outcome. Administer corticosteroids for Grade 3 or 4 rash. Withhold for Grade 3 and permanently discontinue for Grade 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 other etiologies are ruled out, 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, gastitis, 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 myeloablative 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 diaphram (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 diaphram (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, diaphram, and hypercalcermia. In Checkmate 205 and 039, adverse reactions leading to discontinuation occurred in 7% and dose delays due to adverse reactions occurred in 34% of patients (n=266). Serious adverse reactions occurred in 26% of patients. The most frequent serious adverse reactions reported in ≥1% of patients were pneumonia, infusion-related reaction, pyrexia, colitis or diaphram, pleural effusion, pneumonitis, and rash. Eleven patients died from causes other than disease progression: 3 from adverse reactions within 30 days of the last OPDIVO dose, 2 from infection 8 to 9 months after completing OPDIVO, and 6 from complications of allogeneic HSCT. 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 infection, 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, diaphram, 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%), diaphram (52%), nausea (40%), pyrexia (37%), vomiting (28%), and dyspnea (20%). The most common (≥20%) adverse reactions in the OPDIVO (n=313) arm were fatigue (53%), rash (40%), diaphram (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%), diaphram (25% vs 32%), constipation (23% vs 18%), decreased appetite (23% vs 30%), back pain (21% vs 16%), and arthralgia (20% vs 14%). In Checkmate 205 and 039, the most common adverse reactions (≥20%) reported in patients receiving OPDIVO (n=266) were upper respiratory tract infection (44%), fatigue (39%), cough (36%), diaphram (33%), pyrexia (29%), musculoskeletal pain (26%), rash (24%), nausea (20%) and pruritus (20%). 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%). The most common adverse reactions (≥20%) in patients who received OPDIVO as a single agent were fatigue, rash, musculoskeletal pain, pruritus, diaphram, nausea, asthenia, cough, dyspnea, constipation, decreased appetite, back pain,
arthralgia, upper respiratory tract infection, pyrexia.

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 any of the oncology 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.