Bristol-Myers Squibb to Present New Data Across a Broad Range of Blood Cancers at the 59th Annual Meeting & Exposition of the American Society of Hematology

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- #ASH17
- #BMS
- #cancer
- #oncology
- #Opdivo
- #Sprycel
- #Yervoy
- $BMY
- BMS
- BMY
- Bristol-Myers
- Cancer
caregiver
- CheckMate
doctor
- Immuno-Oncology
- Immunotherapy
- ipilimumab
- nivolumab
- nurse
- Oncology
- Opdivo
- patients
- Research
- sprycel
- Squibb
treatment
- Yervoy

Dateline City:
PRINCETON, N.J.

Seven company oral presentations include first disclosure of data from CheckMate -205, evaluating Opdivo (nivolumab) as frontline therapy in newly-diagnosed, untreated patients with advanced-stage classical Hodgkin lymphoma

Phase 2 data from study CA180-372 evaluating Sprycel (dasatinib) in newly-diagnosed pediatric acute lymphoblastic leukemia among presentations

Updated safety and efficacy data for Opdivo in combination with ADCETRIS (brentuximab vedotin) in relapsed/refractory Hodgkin lymphoma to be presented

PRINCETON, N.J.--(BUSINESS WIRE)--Bristol-Myers Squibb Company (NYSE: BMY) announced today 33 presentations from Company-sponsored studies, collaborations and investigator-sponsored research evaluating Opdivo (nivolumab), Sprycel (dasatinib) and Empliciti (elotuzumab), will be featured at the 59th Annual Meeting & Exposition of the American Society of Hematology (ASH) in Atlanta, Ga. from December 9-12.

Presentations across tumor types, including Hodgkin and non-Hodgkin lymphomas, leukemia and multiple myeloma, reinforce Bristol-Myers Squibb's deep expertise in hematologic cancers and commitment to
advancing science to improve patient outcomes.

Data to be presented by Bristol-Myers Squibb include:

**Classical and Non-Hodgkin Lymphoma**

- **Results from a phase 1/2 study of brentuximab vedotin in combination with nivolumab in patients with relapsed or refractory Hodgkin lymphoma**
  
  **Author:** A. Herrera  
  **Abstract:** #649  
  **Oral Session:** 624. Hodgkin Lymphoma and T/NK Cell-Lymphoma-Clinical Studies: Hodgkin Lymphoma Immunotherapy studies; nodular lymphocyte predominant Hodgkin Lymphoma clinical studies  
  **Monday, December 11, 10:30 AM EST**, Georgia World Congress Center, Building A, Level 4, Marcus Auditorium

- **Nivolumab treatment beyond investigator-assessed progression: outcomes in patients with relapsed/refractory classical Hodgkin lymphoma from the phase 2 CheckMate -205 study**
  
  **Author:** J. Cohen  
  **Abstract:** #650  
  **Oral Session:** 624. Hodgkin Lymphoma and T/NK Cell-Lymphoma-Clinical Studies: Hodgkin Lymphoma Immunotherapy studies; nodular lymphocyte predominant Hodgkin Lymphoma clinical studies  
  **Monday, December 11, 10:45 AM EST**, Georgia World Congress Center, Building A, Level 4, Marcus Auditorium

- **Nivolumab for newly diagnosed advanced-stage classical Hodgkin lymphoma: results from the phase 2 CheckMate -205 study**
  
  **Author:** R. Ramchandren  
  **Abstract:** #651  
  **Oral Session:** 624. Hodgkin Lymphoma and T/NK Cell-Lymphoma-Clinical Studies: Hodgkin Lymphoma Immunotherapy studies; nodular lymphocyte predominant Hodgkin Lymphoma clinical studies  
  **Monday, December 11, 11 AM EST**, Georgia World Congress Center, Building A, Level 4, Marcus Auditorium

- **Safety and efficacy of the combination of ibrutinib and nivolumab in patients with relapsed non-Hodgkin lymphoma or chronic lymphocytic leukemia**
  
  **Author:** A. Younes  
  **Abstract:** #833  
  **Oral Session:** 642. CLL: Therapy, excluding Transplantation: New Agents, Infections and PET/CT  
  **Monday, December 11, 5:30 PM EST**, Georgia World Congress Center, Building B, Level 5, Murphy BR 3-4

- **Expression of major histocompatibility complex class II, but not MHC class I, predicts outcome in patients with classical Hodgkin lymphoma treated with nivolumab (programmed death-1 [PD-1] blockade)**
  
  **Author:** M. Roemer  
  **Abstract:** #1450  
  **Poster Session:** 621. Lymphoma-Genetic/Epigenetic Biology: Poster I  
  **Saturday, December 9, 5:30-7:30 PM EST**, Georgia World Congress Center, Building A, Level 1, Hall A2

- **Cost effectiveness of nivolumab for the treatment of relapsed/refractory classical Hodgkin lymphoma after failure of autologous stem cell transplantation and treatment with brentuximab vedotin treatment in Australia**
  
  **Author:** M. Tan  
  **Abstract:** #2166  
  **Poster Session:** 904. Outcomes Research-Malignant Conditions: Poster I  
  **Saturday, December 9, 5:30-7:30 PM EST**, Georgia World Congress Center, Building A, Level 1, Hall A2

- **Effect of nivolumab on patient-reported outcomes in patients with relapsed/refractory classical Hodgkin lymphoma after autologous transplantation: results from the multicohort phase 2 CheckMate -205 study**
  
  **Author:** A. Engert  
  **Abstract:** #3441  
  **Poster Session:** 904. Outcomes Research-Malignant Conditions: Poster II  
  **Sunday, December 10, 6-8 PM EST**, Georgia World Congress Center, Building A, Level 1, Hall A2

- **Economic burden in U.S. patients with relapsed or refractory classical Hodgkin lymphoma treated with brentuximab vedotin or chemotherapy after failure of autologous
hematopoietic cell transplantation
Author: C. Chen
Abstract: #4705
Poster Session: 902. Health Services Research-Malignant Conditions: Poster III
Monday, December 11, 6-8 PM EST, Georgia World Congress Center, Building A, Level 1, Hall A2

Multiple Myeloma

- Elotuzumab plus lenalidomide/dexamethasone vs Ld in patients with newly diagnosed multiple myeloma: phase 2, randomized, open-label study in Japan
  Author: N. Takezako
  Abstract: #434
  Oral Session: 653. Myeloma: Therapy, excluding Transplantation: Upfront Therapy for Multiple Myeloma: Induction and Maintenance
  Sunday, December 10, 12:15 PM EST, Georgia World Congress Center, Building C, Level 1, Hall C4

- Duration of treatment of multiple myeloma regimens in patients with relapsed or refractory multiple myeloma: findings in U.S. clinical practice settings
  Author: R. Potluri
  Abstract: #1844
  Poster Session: 653. Myeloma: Therapy, excluding Transplantation: Poster I
  Saturday, December 9, 5:30-7:30 PM EST, Georgia World Congress Center, Building A, Level 1, Hall A2

- Treatment sequencing patterns observed in patients treated initially with lenalidomide/dexamethasone combination as frontline multiple myeloma therapy
  Author: C. Chen
  Abstract: #3127
  Poster Session: 653. Myeloma: Therapy, excluding Transplantation: Poster II
  Sunday, December 10, 6-8 PM EST, Georgia World Congress Center, Building A, Level 1, Hall A2

- Treatment patterns and associated outcomes in patients with relapsed or refractory multiple myeloma in the U.S. and non-U.S. countries: findings from PREAMBLE
  Author: R. Vij
  Abstract: #3123
  Poster Session: 653. Myeloma: Therapy, excluding Transplantation: Poster II
  Sunday, December 10, 6-8 PM EST, Georgia World Congress Center, Building A, Level 1, Hall A2

- Healthcare resource utilization and costs associated with different treatment modalities of relapsed/refractory multiple myeloma patients in the U.S.: findings from PREAMBLE
  Author: D. Kuter
  Abstract: #3157
  Poster Session: 653. Myeloma: Therapy, excluding Transplantation: Poster II
  Sunday, December 10, 6-8 PM EST, Georgia World Congress Center, Building A, Level 1, Hall A2

Leukemia

- CA180-372: An international collaborative phase 2 trial of dasatinib and chemotherapy in pediatric patients with newly diagnosed Philadelphia chromosome positive acute lymphoblastic leukemia
  Author: S. Hunger
  Abstract #98
  Oral Session: 612. Acute Lymphoblastic Leukemia: Clinical Studies: Advances in the Treatment of ALL
  Saturday, December 9, 9:45 AM EST, Georgia World Congress Center, Building C, Level 2, Hall C211-C213

- Dasatinib discontinuation in patients with chronic-phase chronic myeloid leukemia and stable deep molecular response
  Author: N. Shah
  Abstract: #314
  Oral Session: 632: Chronic Myeloid Leukemia: Therapy: Treatment Discontinuation, Dose Reduction and Prognostic Indicators
  Sunday, December 10, 7:45 AM EST, Georgia World Congress Center, Building A, Level 4, Marcus Auditorium

- Impact of earlier vs. later monitoring on disease progression and economic outcomes among patients with chronic myeloid leukemia in the real-world setting
  Author: E. Jabbour
  Abstract: #2175
Cytogenetic and molecular responses by two years in SIMPLICITY, an observational study of chronic-phase chronic myeloid leukemia patients in routine clinical practice
Author: J. Cortes
Abstract: #2894
Poster Session: 632. Chronic Myeloid Leukemia: Therapy: Poster II
Sunday, December 10, 6-8 PM EST, Georgia World Congress Center, Building A, Level 1, Hall A2

Economic modeling of the potential impact of chronic myeloid leukemia monitoring on healthcare costs
Author: E. Jabbour
Abstract: #3378
Poster Session: 902. Health Services Research—Malignant Conditions: Poster II
Sunday, December 10, 6-8 PM EST, Georgia World Congress Center, Building A, Level 1, Hall A2

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 programs 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/I-O, 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’ individual 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®

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 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 adult 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

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 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. For patients without HCC, withhold OPDIVO for Grade 2 and permanently discontinue OPDIVO for Grade 3 or 4. For patients with HCC, withhold OPDIVO and administer corticosteroids if AST/ALT is within normal limits at baseline and increases to >3 and up to 5 times the upper limit of normal (ULN), if AST/ALT is >1 and up to 3 times ULN at baseline and increases to >5 and up to 10 times the ULN, and if AST/ALT is >3 and up to 5 times ULN at baseline and increases to >8 and up to 10 times the ULN. Permanently discontinue OPDIVO and administer corticosteroids if AST or ALT increases to >10 times the ULN or total bilirubin increases >3 times the ULN. 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 Checkmate 040, immune-mediated hepatitis requiring systemic corticosteroids occurred in 5% (8/154) of patients receiving OPDIVO.

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 OPDIVO 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, hypothyroidism or thyroiditis resulting in hyperthyroidism 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 lifethreatening 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 the adverse reaction, permanently discontinue or withhold OPDIVO, administer high-dose corticosteroids, and, if appropriate, initiate hormone-replacement therapy. Across clinical trials of OPDIVO monotherapy or in combination with YERVOY, the following clinically significant immune-mediated adverse reactions, some with fatal outcome, occurred in <1.0% of patients receiving OPDIVO: myocarditis, rhabdomyolysis, myositis, 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), 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 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 1.7%), 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, 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 20% of patients. The most frequent serious adverse reactions reported in ≥1% of patients were pneumonia, infusion-related reaction, pyrexia, colitis or diarrhea, pleural effusion, pneumonitis, and rash. Eleven patients died 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, diarrhea, small intestine obstruction, and general physical health deterioration. In Checkmate 040, serious adverse reactions occurred in 49% of patients (n=154). The most frequent serious adverse reactions reported in at least 2% of patients were pyrexia, ascites, back pain, general physical health deterioration, abdominal pain, and pneumonia.

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 (n=313) 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 (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=418) were fatigue (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 (46%), musculoskeletal pain (30%), nausea (24%), rash (28%) and pruritus (24%). 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%), diarrhea (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%). In Checkmate 404, the most common adverse reactions (≥20%) reported in patients receiving OPDIVO (n=154) were fatigue (38%), musculoskeletal pain (36%), abdominal pain (34%), pruritus (27%), diarrhea (27%), rash (26%), cough (23%), 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, diarrhea, nausea, asthenia, cough, dyspnea, constipation, decreased appetite, back pain, arthralgia, upper respiratory tract infection, and 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; Checkmate 040 – hepatocellular carcinoma.

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

About Sprycel

Sprycel first received FDA approval in 2006 for the treatment of adults with Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in chronic phase (CP) who are resistant or intolerant to prior therapy including imatinib. At that time, Sprycel was also approved for adults with Ph+ acute lymphoblastic leukemia (ALL) who are resistant or intolerant to prior therapy. Sprycel is approved and marketed worldwide for these indications in more than 60 countries.

Sprycel is also an FDA-approved treatment for adults with newly diagnosed CP Ph+ CML, and in November 2017, Sprycel received FDA approval for the expanded indication for treatment in pediatric patients with CP Ph+ CML. The adult indication is approved in more than 50 countries.

U.S. FDA-APPROVED INDICATIONS FOR SPRYCEL ®

SPRYCEL® (dasatinib) is indicated for the treatment of adults with:

- Newly diagnosed adults with Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in chronic phase.
- Chronic, accelerated, or myeloid or lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy including imatinib.
- Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL) with resistance or intolerance to prior therapy.
- Pediatric patients with Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in chronic phase.

IMPORTANT SAFETY INFORMATION

Myelosuppression

Treatment with SPRYCEL is associated with severe (NCI CTCAE Grade 3/4) thrombocytopenia, neutropenia, and anemia, which occur earlier and more frequently in patients with advanced phase CML or Ph+ ALL than in patients with chronic phase CML. Myelosuppression was reported in patients with normal baseline laboratory values as well as in patients with pre-existing laboratory abnormalities.
In patients with chronic phase CML, perform complete blood counts (CBCs) every 2 weeks for 12 weeks, then every 3 months thereafter, or as clinically indicated. In patients with advanced phase CML or Ph+ ALL, perform CBCs weekly for the first 2 months and then monthly thereafter, or as clinically indicated. Myelosuppression is generally reversible and usually managed by withholding SPRYCEL temporarily and/or dose reduction. In clinical studies, myelosuppression may have also been managed by discontinuation of study therapy. Hematopoietic growth factor has been used in patients with resistant myelosuppression.

**Bleeding-Related Events**

SPRYCEL can cause serious and fatal bleeding. In all CML or Ph+ ALL clinical studies, Grade ≥3 central nervous system (CNS) hemorrhages, including fatalities, occurred in <1% of patients receiving SPRYCEL. The incidence of Grade 3/4 hemorrhage, occurred in 5.8% of adult patients and generally required treatment interruptions and transfusions. The incidence of Grade 5 hemorrhage occurred in 0.4% of adult patients. The most frequent site of hemorrhage was gastrointestinal.

- Most bleeding events in clinical studies were associated with severe thrombocytopenia
- In addition to causing thrombocytopenia in human subjects, dasatinib caused platelet dysfunction *in vitro*
- Concomitant medications that inhibit platelet function or anticoagulants may increase the risk of hemorrhage

**Fluid Retention**

SPRYCEL may cause fluid retention. After 5 years of follow-up in the adult randomized newly diagnosed chronic phase CML study (n=258), grade 3/4 fluid retention was reported in 5% of patients, including 3% of patients with grade 3/4 pleural effusion. In adult patients with newly diagnosed or imatinib resistant or intolerant chronic phase CML, grade 3/4 fluid retention occurred in 6% of patients treated with SPRYCEL at the recommended dose (n=548). In adult patients with advanced phase CML or Ph+ ALL treated with SPRYCEL at the recommended dose (n=304), grade 3/4 fluid retention was reported in 8% of patients, including grade 3/4 pleural effusion reported in 7% of patients. In pediatric patients with chronic phase CML cases of Grade 1 or 2 fluid retention were reported in 10.3% of patients.

- Patients who develop symptoms of pleural effusion or other fluid retention, such as new or worsened dyspnea on exertion or at rest, pleuritic chest pain, or dry cough should be evaluated promptly with a chest x-ray or additional diagnostic imaging as appropriate
- Fluid retention events were typically managed by supportive care measures that may include diuretics or short courses of steroids
- Severe pleural effusion may require thoracentesis and oxygen therapy
- Consider dose reduction or treatment interruption

**Cardiovascular Events**

SPRYCEL can cause cardiac dysfunction. After 5 years of follow-up in the randomized newly diagnosed chronic phase CML trial in adults (n=258), the following cardiac adverse reactions occurred:

- Cardiac ischemic events (3.9% dasatinib vs 1.6% imatinib), cardiac related fluid retention (8.5% dasatinib vs 3.9% imatinib), and conduction system abnormalities, most commonly arrhythmia and palpitations (7.0% dasatinib vs 5.0% imatinib). Two cases (0.8%) of peripheral arterial occlusive disease occurred with imatinib and 2 (0.8%) transient ischemic attacks occurred with dasatinib.

Monitor patients for signs or symptoms consistent with cardiac dysfunction and treat appropriately.

**Pulmonary Arterial Hypertension (PAH)**

SPRYCEL may increase the risk of developing PAH in adult and pediatric patients, which may occur any time after initiation, including after more than 1 year of treatment. Manifestations include dyspnea, fatigue, hypoxia, and fluid retention. PAH may be reversible on discontinuation of SPRYCEL.

- Evaluate patients for signs and symptoms of underlying cardiopulmonary disease prior to initiating SPRYCEL and during treatment. If PAH is confirmed, SPRYCEL should be permanently discontinued

**QT Prolongation**

SPRYCEL may increase the risk of prolongation of QTc in patients including those with hypokalemia or hypomagnesemia, patients with congenital long QT syndrome, patients taking antiarrhythmic medicines or other medicinal products that lead to QT prolongation, and cumulative high-dose anthracycline therapy.

- Correct hypokalemia or hypomagnesemia prior to and during SPRYCEL administration
Severe Dermatologic Reactions

Cases of severe mucocutaneous dermatologic reactions, including Stevens-Johnson syndrome and erythema multiforme, have been reported in patients treated with SPRYCEL.

- Discontinue permanently in patients who experience a severe mucocutaneous reaction during treatment if no other etiology can be identified

Tumor Lysis Syndrome (TLS)

TLS has been reported in patients with resistance to prior imatinib therapy, primarily in advanced phase disease.

- Due to potential for TLS, maintain adequate hydration, correct uric acid levels prior to initiating therapy with SPRYCEL, and monitor electrolyte levels
- Patients with advanced stage disease and/or high tumor burden may be at increased risk and should be monitored more frequently

Embryo-Fetal Toxicity

Based on limited human data, SPRYCEL can cause fetal harm when administered to a pregnant woman. Hydrops fetalis, fetal leukopenia and fetal thrombocytopenia have been reported with maternal exposure to SPRYCEL. Transplacental transfer of dasatinib has been measured in fetal plasma and amniotic fluid at concentrations comparable to those in maternal plasma.

- Advise females of reproductive potential to avoid pregnancy, which may include the use of effective contraception, during treatment with SPRYCEL and for 30 days after the final dose

Effects on Growth and Development in Pediatric Patients

In pediatric trials of SPRYCEL in chronic phase CML after at least 2 years of treatment, adverse reactions associated with bone growth and development were reported in 5 (5.2%) patients, one of which was severe in intensity (Growth Retardation Grade 3). These 5 cases included cases of epiphyses delayed fusion, osteopenia, growth retardation, and gynecomastia. Of these 5 cases, 1 case of osteopenia and 1 case of gynecomastia resolved during treatment.

Lactation

No data are available regarding the presence of dasatinib in human milk, the effects of the drug on the breastfed child or the effects of the drug on milk production. However, dasatinib is present in the milk of lactating rats.

- Because of the potential for serious adverse reactions in nursing children from SPRYCEL, breastfeeding is not recommended during treatment with SPRYCEL and for 2 weeks after the final dose

Drug Interactions

- **Strong CYP3A4 inhibitors**: The coadministration with strong CYP3A inhibitors may increase dasatinib concentrations. Increased dasatinib concentrations may increase the risk of toxicity. Avoid concomitant use of strong CYP3A4 inhibitors. If concomitant administration of a strong CYP3A4 inhibitor cannot be avoided, consider a SPRYCEL dose reduction
  - Grapefruit juice may increase plasma concentrations of SPRYCEL and should be avoided
- **Strong CYP3A4 inducers**: The coadministration of SPRYCEL with strong CYP3A inducers may decrease dasatinib concentrations. Decreased dasatinib concentrations may reduce efficacy. Consider alternative drugs with less enzyme induction potential. If concomitant administration of a strong CYP3A4 inducer cannot be avoided, consider a SPRYCEL dose increase
  - St. John's wort may decrease plasma concentrations of SPRYCEL and should be avoided
- **Gastric Acid Reducing Agents**: The coadministration of SPRYCEL with a gastric acid reducing agent may decrease the concentrations of dasatinib. Decreased dasatinib concentrations may reduce efficacy.
  - Do not administer H2 antagonists or proton pump inhibitors with SPRYCEL. Consider the use of antacids in place of H2 antagonists or proton pump inhibitors. Administer the antacid at least 2 hours prior to or 2 hours after the dose of SPRYCEL. Avoid simultaneous administration of SPRYCEL with antacids.

Adverse Reactions

The safety data reflects exposure to SPRYCEL at all doses tested in clinical studies (n=2809) including
324 adult patients with newly diagnosed chronic phase CML, 2388 adult patients with imatinib resistant or intolerant chronic or advanced phase CML or Ph+ ALL, and 97 pediatric patients with chronic phase CML.

The median duration of therapy in a total of 2712 SPRYCEL-treated adult patients was 19.2 months (range 0–93.2 months). Median duration of therapy in:

- 1618 adult patients with chronic phase CML was 29 months (range 0–92.9 months)
  - Median duration for 324 adult patients in the newly diagnosed chronic phase CML trial was approximately 60 months
  - 1094 adult patients with advanced phase CML or Ph+ ALL was 6.2 months (range 0–93.2 months)

In two non-randomized trials in 97 pediatric patients with chronic phase CML (51 patients newly diagnosed and 46 patients resistant or intolerant to previous treatment with imatinib), the median duration of therapy was 51.1 months (range 1.9 to 99.6 months).

In the newly diagnosed adult chronic phase CML trial, after a minimum of 60 months of follow-up, the cumulative discontinuation rate for 258 patients was 39%.

In the overall population of 2712 adult SPRYCEL-treated patients, 88% of patients experienced adverse reactions at some time and 19% experienced adverse reactions leading to treatment discontinuation.

Among the 1618 adult SPRYCEL-treated patients with chronic phase CML, drug-related adverse reactions leading to discontinuation were reported in 329 (20.3%) patients.

- In the adult newly diagnosed chronic phase CML trial, drug was discontinued for adverse reactions in 16% of SPRYCEL-treated patients with a minimum of 60 months of follow-up

Among the 1094 SPRYCEL-treated patients with advanced phase CML or Ph+ ALL, drug-related adverse reactions leading to discontinuation were reported in 191 (17.5%) patients. Among the 97 pediatric subjects, drug-related adverse reactions leading to discontinuation were reported in 1 patient (1%).

Patients ≥65 years are more likely to experience the commonly reported adverse reactions of fatigue, pleural effusion, diarrhea, dyspnea, cough, lower gastrointestinal hemorrhage, and appetite disturbance, and more likely to experience the less frequently reported adverse reactions of abdominal distention, dizziness, pericardial effusion, congestive heart failure, hypertension, pulmonary edema and weight decrease, and should be monitored closely.

- In adult newly diagnosed chronic phase CML patients:
  - Drug-related serious adverse reactions (SARs) were reported for 16.7% of patients. Serious adverse reactions reported in ≥5% of patients included pleural effusion (5%)
  - Grade 3/4 laboratory abnormalities included neutropenia (29%), thrombocytopenia (22%), anemia (13%), hypophosphatemia (7%), hypocalcemia (4%), elevated bilirubin (1%), and elevated creatinine (1%)

- In adult patients resistant or intolerant to prior imatinib therapy:
  - Drug-related SARs were reported for 26.1% of SPRYCEL-treated patients treated at the recommended dose of 100 mg once daily in the randomized dose-optimization trial of patients with chronic phase CML resistant or intolerant to prior imatinib therapy. Serious adverse reactions reported in ≥5% of patients included pleural effusion (10%)
  - Grade 3/4 hematologic laboratory abnormalities in chronic phase CML patients resistant or intolerant to prior imatinib therapy who received SPRYCEL 100 mg once daily with a minimum follow up of 60 months included neutropenia (36%), thrombocytopenia (24%), and anemia (13%). Other grade 3/4 laboratory abnormalities included: hypophosphatemia (10%), and hypokalemia (2%)
  - Among chronic phase CML patients with resistance or intolerance to prior imatinib therapy, cumulative grade 3/4 cytopenias were similar at 2 and 5 years including: neutropenia (36% vs 36%), thrombocytopenia (23% vs 24%), and anemia (13% vs 13%)
  - Grade 3/4 elevations of transaminases or bilirubin and Grade 3/4 hypocalcemia, hypokalemia, and hypophosphatemia were reported in patients with all phases of CML
  - Elevations in transaminases or bilirubin were usually managed with dose reduction or interruption
  - Patients developing Grade 3/4 hypocalcemia during the course of SPRYCEL therapy often had recovery with oral calcium supplementation

- In pediatric subjects with Ph+ CML in chronic phase
  - Drug-related SARs were reported for 14.4% of pediatric patients
  - In the pediatric studies, the rates of laboratory abnormalities were consistent with the known profile for laboratory parameters in adults

Most common adverse reactions (≥15%) in patients included myelosuppression, fluid retention
events, diarrhea, headache, skin rash, hemorrhage, dyspnea, fatigue, nausea, and musculoskeletal pain

Please see the US full Prescribing Information here.

About Empliciti

Empliciti is an immunostimulatory antibody that specifically targets Signaling Lymphocyte Activation Molecule Family member 7 (SLAMF7), a cell-surface glycoprotein. SLAMF7 is expressed on myeloma cells independent of cytogenetic abnormalities. SLAMF7 is also expressed on Natural Killer cells, plasma cells and at lower levels on specific immune cell subsets of differentiated cells within the hematopoietic lineage.

Empliciti has a dual mechanism-of-action. It directly activates the immune system through Natural Killer cells via the SLAMF7 pathway. Empliciti also targets SLAMF7 on myeloma cells, tagging these malignant cells for Natural Killer cell-mediated destruction via antibody-dependent cellular toxicity.

Bristol-Myers Squibb and AbbVie are co-developing Empliciti, with Bristol-Myers Squibb solely responsible for commercial activities.

U.S. FDA-APPROVED INDICATION FOR EMPLICITI ¶

EMPLICITI™ (elotuzumab) is indicated in combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received one to three prior therapies.

IMPORTANT SAFETY INFORMATION

Infusion Reactions

EMPLICITI can cause infusion reactions. Common symptoms include fever, chills, and hypertension. Bradycardia and hypotension also developed during infusions. In the trial, 5% of patients required interruption of the administration of EMPLICITI for a median of 25 minutes due to infusion reactions, and 1% of patients discontinued due to infusion reactions. Of the patients who experienced an infusion reaction, 70% (23/33) had them during the first dose. If a Grade 2 or higher infusion reaction occurs, interrupt the EMPLICITI infusion and institute appropriate medical and supportive measures. If the infusion reaction recurs, stop the EMPLICITI infusion and do not restart it on that day. Severe infusion reactions may require permanent discontinuation of EMPLICITI therapy and emergency treatment.

Premedicate with dexamethasone, H1 Blocker, H2 Blocker, and acetaminophen prior to infusing with EMPLICITI.

Infections

In a clinical trial of patients with multiple myeloma (N=635), infections were reported in 81.4% of patients in the EMPLICITI with lenalidomide/dexamethasone arm (ERd) and 74.4% in the lenalidomide/dexamethasone arm (Rd). Grade 3-4 infections were 28% (ERd) and 24.3% (Rd). Opportunistic infections were reported in 22% (ERd) and 12.9% (Rd). Fungal infections were 9.7% (ERd) and 5.4% (Rd). Herpes zoster was 13.5% (ERd) and 6.9% (Rd). Discontinuations due to infections were 3.5% (ERd) and 4.1% (Rd). Fatal infections were 2.5% (ERd) and 2.2% (Rd). Monitor patients for development of infections and treat promptly.

Second Primary Malignancies

In a clinical trial of patients with multiple myeloma (N=635), invasive second primary malignancies (SPM) were 9.1% (ERd) and 5.7% (Rd). The rate of hematologic malignancies were the same between ERd and Rd treatment arms (1.6%). Solid tumors were reported in 3.5% (ERd) and 2.2% (Rd). Skin cancer was reported in 4.4% (ERd) and 2.8% (Rd). Monitor patients for the development of SPMs.

Hepatotoxicity

Elevations in liver enzymes (AST/ALT greater than 3 times the upper limit, total bilirubin greater than 2 times the upper limit, and alkaline phosphatase less than 2 times the upper limit) consistent with hepatotoxicity were 2.5% (ERd) and 0.6% (Rd). Two patients experiencing hepatotoxicity discontinued treatment; however, 6 out of 8 patients had resolution and continued treatment. Monitor liver enzymes periodically. Stop EMPLICITI upon Grade 3 or higher elevation of liver enzymes. After return to baseline values, continuation of treatment may be considered.

Interference with Determination of Complete Response

EMPLICITI is a humanized IgG kappa monoclonal antibody that can be detected on both the serum protein electrophoresis and immunofixation assays used for the clinical monitoring of endogenous M-protein. This interference can impact the determination of complete response and possibly relapse from complete
This interference can impact the determination of complete response and possibly relapse from complete response in patients with IgG kappa myeloma protein.

**Pregnancy/Females and Males of Reproductive Potential**

There are no studies with EMPLICITI with pregnant women to inform any drug associated risks. There is a risk of fetal harm, including severe life-threatening human birth defects associated with lenalidomide and it is contraindicated for use in pregnancy. Refer to the lenalidomide full prescribing information for requirements regarding contraception and the prohibitions against blood and/or sperm donation due to presence and transmission in blood and/or semen and for additional information.

**Adverse Reactions**

Infusion reactions were reported in approximately 10% of patients treated with EMPLICITI with lenalidomide and dexamethasone. All reports of infusion reaction were Grade 3 or lower. Grade 3 infusion reactions occurred in 1% of patients.

Serious adverse reactions were 65.4% (ERd) and 56.5% (Rd). The most frequent serious adverse reactions in the ERd arm compared to the Rd arm were: pneumonia (15.4%, 11%), pyrexia (6.9%, 4.7%), respiratory tract infection (3.1%, 1.3%), anemia (2.8%, 1.9%), pulmonary embolism (3.1%, 2.5%), and acute renal failure (2.5%, 1.9%).

The most common adverse reactions in ERd and Rd, respectively (>20%) were fatigue (61.6%, 51.7%), diarrhea (46.9%, 36.0%), pyrexia (37.4%, 24.6%), constipation (35.5%, 27.1%), cough (34.3%, 18.9%), peripheral neuropathy (26.7%, 20.8%), nasopharyngitis (24.5%, 19.2%), upper respiratory tract infection (22.6%, 17.4%), decreased appetite (20.8%, 12.6%), and pneumonia (20.1%, 14.2%).

Please see the full Prescribing Information for EMPLICITI.

**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, Sprycel, Empliciti or any of the compounds mentioned above will receive regulatory approval in the US 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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#MEDIA: $BMY announces new blood cancer data to be presented at #ASH17