Bristol-Myers Squibb to Present Data at 2015 American Society of Clinical Oncology (ASCO) Annual Meeting that Demonstrate the Promise of its Broad Immuno-Oncology Portfolio Across Solid Tumors and Blood Cancers Including Multiple Myeloma

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Terms:

Dateline City: PRINCETON, N.J.

- Pivotal Phase III studies (CheckMate -057 & -017) in both advanced non-squamous and squamous non-small cell lung cancer in which treatment with Opdivo demonstrated superior survival versus chemotherapy with docetaxel in previously-treated patients, to be disclosed
- First pivotal Phase III trial of investigational Opdivo+Yervoy regimen compared to Opdivo or Yervoy monotherapy in advanced melanoma, to be presented (CheckMate -067)
- First Phase III data for an investigational Immuno-Oncology agent in multiple myeloma, ELOQUENT-2 results for elotuzumab, to be presented
- Breadth and depth of Immuno-Oncology portfolio showcases Opdivo and Yervoy clinical trial results in additional tumor types, including small-cell lung cancer, renal cell carcinoma, hepatocellular carcinoma and glioblastoma

PRINCETON, N.J.--(BUSINESS WIRE)--Bristol-Myers Squibb Company (NYSE:BMY) today announced new clinical research from three of its Immuno-Oncology agents will be presented at the 51st Annual Meeting of the American Society of Clinical Oncology (ASCO) in Chicago from May 29-June 2. Building on the scientific advances the company has pioneered in Immuno-Oncology, Bristol-Myers Squibb will present data for Opdivo and Yervoy across multiple solid tumor types, as well as elotuzumab in relapsed or refractory multiple myeloma.

Data to be presented at ASCO illustrate Bristol-Myers Squibb's commitment to developing treatment options with the potential to offer patients with cancer the possibility of long-term survival through its transformative Immuno-Oncology research.

Key oral data presentations include:

- **CheckMate -057, -017**: First disclosure from Phase III trials will be presented for CheckMate -057 (Late Breaking Abstract #109) and CheckMate -017 (Abstract #8009), evaluating Opdivo in previously-treated non-squamous and squamous non-small cell lung cancer (NSCLC) against docetaxel therapy, respectively. Data from CheckMate -057 will be featured in an ASCO press conference on Friday, May 29, 1:00 - 2:00 PM CDT and presented during a Clinical Science Symposium on Saturday, May 30 from 8:51 – 9:03 AM CDT. Data from CheckMate -017 will be presented during an oral abstract session on Sunday, May 31 from 4:30 – 4:42 PM CDT.

- **CheckMate -067**: New Phase III research evaluating the Opdivo+Yervoy regimen in first-line treatment of advanced melanoma (Late Breaking Abstract #1) will be featured in an ASCO press conference on Sunday, May 31, 8:00 – 9:00 AM CDT. These data also will be presented during the plenary session on Sunday, May 31 from 1:35 – 1:50 PM CDT.

- **ELOQUENT-2**: The first presentation of a Phase III, open-label study (Abstract #8508) evaluating elotuzumab in combination with lenalidomide and dexamethasone in patients with relapsed or refractory multiple myeloma will be
featured in an ASCO presscast on Wednesday, May 13 at 12:00 PM EDT. An oral presentation of these data will take place on Tuesday, June 2 from 9:45 – 9:57 AM CDT.

- **CA209-040**: The first presentation of findings from a Phase I/II **Opdivo** trial in advanced hepatocellular carcinoma (Late Breaking Abstract #101) will be featured in an ASCO press conference on Friday, May 29, 1:00 – 2:00 PM CDT. An oral presentation of these data will take place at a Clinical Science Symposium on Saturday, May 30 from 8:27 – 8:39 AM CDT.

"At Bristol-Myers Squibb, patients are the inspiration behind our pioneering research in the field of Immuno-Oncology, which has led to the approval of novel agents for the treatment of some of the hardest to treat cancers," said Francis Cuss, MB BChir, FRCP, executive vice president and chief scientific officer, Bristol-Myers Squibb. "We are proud that our revolutionary research led to the introduction of **Yervoy** and **Opdivo**, and are excited about sharing new data at ASCO in both solid tumors and hematologic cancers."

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

<table>
<thead>
<tr>
<th>Title</th>
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<tr>
<td><strong>Lung Cancer</strong></td>
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<tr>
<td>Phase III, randomized trial (CheckMate -057) of nivolumab (NIVO) versus docetaxel (DOC) in advanced non-squamous cell (non-SQ) non-small cell lung cancer (NSCLC) Abstract #LBA109</td>
<td>Clinical Science Symposium Saturday, May 30th 8:51 – 9:03 AM CDT</td>
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<td>An ongoing phase III/IV safety trial of nivolumab (NIVO) in patients (pts) with advanced or metastatic non-small-cell lung cancer (NSCLC) who progressed after receiving 1 or more prior systemic regimens Abstract #3013</td>
<td>Poster Discussion Session Saturday, May 30th 3:00 – 4:15 PM CDT</td>
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<tr>
<td>Phase II study of nivolumab with or without ipilimumab for treatment of recurrent small cell lung cancer (SCLC): CA209-032 Abstract #7503</td>
<td>Oral Abstract Session Saturday, May 30th 4:00 – 4:12 PM CDT</td>
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<td>A phase III study (CheckMate -017) of nivolumab (NIVO; anti-programmed death-1 [PD-1]) vs docetaxel (DOC) in previously treated advanced or metastatic squamous (SQ) cell non-small cell lung cancer (NSCLC) Abstract #8009</td>
<td>Clinical Science Symposium Sunday, May 31st 4:30 – 4:42 PM CDT</td>
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<td>First-line monotherapy with nivolumab (NIVO; anti-programmed death-1 [PD-1]) in advanced non-small cell lung cancer (NSCLC): Safety, Efficacy and correlation of outcomes with PD-1 ligand (PD-L1) expression Abstract #8025</td>
<td>Poster Session Monday, June 1st 8:00 – 11:30 AM CDT</td>
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<td>Phase II studies of nivolumab (anti-PD-1, BMS-936558, ONO-4538) in patients with advanced squamous (sq) or nonsquamous (non-sq) non-small cell lung cancer (NSCLC) Abstract #8027</td>
<td>Poster Session Monday, June 1st 8:00 – 11:30 AM CDT</td>
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<td><strong>Melanoma</strong></td>
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<td>Clinical response, progression-free survival (PFS), and safety in patients (pts) with advanced melanoma (MEL) receiving nivolumab (NIVO) combined with ipilimumab (IPI) vs IPI monotherapy in CheckMate -069 study Abstract #9004</td>
<td>Oral Abstract Session Saturday, May 30th 2:27 – 2:39 PM CDT</td>
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<td>Efficacy and safety results from a phase III trial of nivolumab (NIVO) alone or combined with ipilimumab (IPI) versus IPI alone in treatment-naïve patients (pts) with advanced melanoma (MEL) (CheckMate -067) Abstract #LBA1</td>
<td>Plenary Session Sunday, May 31st 1:35 – 1:50 PM CDT</td>
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<td>Effect of nivolumab (NIVO) on quality of life (QoL) in patients (pts) with treatment-naïve advanced melanoma (MEL): Results of a phase III study (CheckMate -066) Abstract #9027</td>
<td>Poster Session Monday, June 1st 1:15 – 4:45 PM CDT</td>
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<td>Effect of nivolumab (NIVO) in combination with ipilimumab (IPI) versus IPI alone on quality of life (QoL) in patients (pts) with treatment-naïve advanced melanoma (MEL): Results of a phase II study (CheckMate -069) Abstract #9029</td>
<td>Poster Session Monday, June 1st 1:15 – 4:45 PM CDT</td>
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<td>A single-arm, open-label, phase II study to evaluate the safety of vemurafenib (VEM) followed by ipilimumab (IPI) in BRAF V600-mutated metastatic melanoma (MM) Abstract #9032</td>
<td>Poster Session Monday, June 1st 1:15 – 4:45 PM CDT</td>
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<td>Safety profile of nivolumab (NIVO) in patients (pts) with advanced melanoma (MEL): A pooled analysis Abstract #9018</td>
<td>Poster Discussion Session Monday, June 1st 4:45 – 6:00 PM CDT</td>
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**Hematology**
A randomized phase II study of bortezomib (Btz)/dexamethasone (dex) with or without elotuzumab (Elo) in patients with relapsed/refractory multiple myeloma (RRMM)
Abstract #8573

ELOQUENT-2: A phase III, randomized, open-label study of lenalidomide (Len)/dexamethasone (dex) with or without elotuzumab (Elo) in patients (pts) with relapsed/refractory multiple myeloma (RRMM)
Abstract #8508

Hepatocellular Carcinoma, Glioblastoma, and Renal Cell Carcinoma

Phase I/II safety and antitumor activity of nivolumab in patients with advanced hepatocellular carcinoma (HCC): CA209-040
Abstract #LBA101

Preclinical safety and toxicity of nivolumab and its combination with ipilimumab in recurrent glioblastoma (GBM): CheckMate -143
Abstract #3010

Immunomodulatory activity of nivolumab in metastatic renal cell carcinoma (mRCC): Association of biomarkers with clinical outcomes
Abstract #4500

Expanded cohort results from CheckMate -016: A phase I study of nivolumab in combination with ipilimumab in metastatic renal cell carcinoma (mRCC)
Abstract #4516

Analysis of real world treatment compliance in a cohort of 2,395 patients with metastatic renal cell carcinoma (mRCC)
Abstract #4546

Updated survival results from a randomized, dose-ranging phase II study of nivolumab (NIVO) in metastatic renal cell carcinoma (mRCC)
Abstract #4553

About Elotuzumab

Elotuzumab is an investigational Immuno-Oncology (more specifically defined as immuno-stimulatory) antibody targeted against Signal lymphocyte Activation Molecule (SLAMF7), a cell-surface glycoprotein that is highly and uniformly expressed on myeloma cells and Natural Killer (NK) cells but is not detected on normal solid tissues or on hematopoietic stem cells. Elotuzumab is being investigated to determine whether the compound may selectively target myeloma cells. It is believed that elotuzumab works through a dual mechanism of action: binding to SLAMF7 on NK cells, directly activating them and binding to SLAMF7 on myeloma cells, flagging them for NK cell recognition and destruction.

In May 2014, the U.S. Food and Drug Administration (FDA) granted elotuzumab Breakthrough Therapy Designation for use in combination with one of the chemotherapy treatments for multiple myeloma (lenalidomide, used in combination with dexamethasone) in patients who have received one or more prior treatments. Elotuzumab is an investigational compound and its safety and efficacy have not been evaluated by the FDA or any other health authority.

Bristol-Myers Squibb and AbbVie are co-developing elotuzumab, with Bristol-Myers Squibb leading the commercialization of the agent.

OPDIVO (nivolumab) IMPORTANT SAFETY INFORMATION

Immune-Mediated Pneumonitis

- Severe pneumonitis or interstitial lung disease, including fatal cases, occurred with OPDIVO treatment. Across the clinical trial experience in 691 patients with solid tumors, fatal immune-mediated pneumonitis occurred in 0.7% (5/691) of patients receiving OPDIVO; no cases occurred in Trial 1 or Trial 3. In Trial 1, pneumonitis, including interstitial lung disease, occurred in 3.4% (9/268) of patients receiving OPDIVO and none of the 102 patients receiving chemotherapy. Immune-mediated pneumonitis occurred in 2.2% (6/268) of patients receiving OPDIVO; one with Grade 3 and five with Grade 2. In Trial 3, immune-mediated pneumonitis occurred in 6% (7/117) of patients receiving OPDIVO, including, five Grade 3 and two Grade 2 cases. Monitor patients for signs and symptoms of pneumonitis. Administer corticosteroids for Grade 2 or greater pneumonitis. Permanently discontinue OPDIVO for Grade 3 or 4 and withhold OPDIVO until resolution for Grade 2.

Immune-Mediated Colitis

- In Trial 1, diarrhea or colitis occurred in 21% (57/268) of patients receiving OPDIVO and 18% (18/102) of patients receiving chemotherapy. Immune-mediated colitis occurred in 2.2% (6/268) of patients receiving OPDIVO; five with Grade 3 and one with Grade 2. In Trial 3, diarrhea occurred in 21% (24/117) of patients receiving OPDIVO. Grade 3 immune-mediated colitis occurred in 0.9% (1/117) of patients. Monitor patients for immune-mediated colitis. Administer corticosteroids for Grade 2 (of more than 5 days duration), 3, or 4 colitis. Withhold OPDIVO for Grade 2 or 3. Permanently discontinue OPDIVO for Grade 4 colitis or recurrent colitis upon restarting OPDIVO.

Immune-Mediated Hepatitis
Immune-Mediated Nephritis and Renal Dysfunction

- In Trial 1, there was an increased incidence of elevated creatinine in the OPDIVO-treated group as compared to the chemotherapy-treated group (13% vs 9%). Grade 2 or 3 immune-mediated nephritis or renal dysfunction occurred in 0.7% (2/268) of patients. In Trial 3, the incidence of elevated creatinine was 22%. Immune-mediated renal dysfunction (Grade 2) occurred in 0.9% (1/117) of patients. Monitor patients for elevated serum creatinine prior to and periodically during treatment. For Grade 2 or 3 serum creatinine elevation, withhold OPDIVO and administer corticosteroids; if worsening or no improvement occurs, permanently discontinue OPDIVO. Administer corticosteroids for Grade 4 serum creatinine elevation and permanently discontinue OPDIVO.

Immune-Mediated Hypothyroidism and Hyperthyroidism

- In Trial 1, Grade 1 or 2 hypothyroidism occurred in 8% (21/268) of patients receiving OPDIVO and none of the 102 patients receiving chemotherapy. Grade 1 or 2 hyperthyroidism occurred in 3% (8/268) of patients receiving OPDIVO and 1% (1/102) of patients receiving chemotherapy. In Trial 3, hypothyroidism occurred in 4.3% (5/117) of patients receiving OPDIVO. Hyperthyroidism occurred in 1.7% (2/117) of patients, including one Grade 2 case. Monitor thyroid function prior to and periodically during treatment. Administer hormone replacement therapy for hypothyroidism. Initiate medical management for control of hyperthyroidism.

Other Immune-Mediated Adverse Reactions

- In Trial 1 and 3 (n=385), the following clinically significant immune-mediated adverse reactions occurred in <2% of OPDIVO-treated patients: adrenal insufficiency, uveitis, pancreatitis, facial and abducens nerve paresis, demyelination, autoimmune neuropathy, motor dysfunction, and vasculitis. Across clinical trials of OPDIVO administered at doses 3 mg/kg and 10 mg/kg, additional clinically significant, immune-mediated adverse reactions were identified: hypophysitis, diabetic ketoacidosis, hypopituitarism, Guillain-Barré syndrome, and myasthenic syndrome. Based on the severity of adverse reaction, withhold OPDIVO, administer high-dose corticosteroids, and, if appropriate, initiate hormone-replacement therapy.

Embryofetal Toxicity

- Based on its mechanism of action, OPDIVO 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 OPDIVO and for at least 5 months after the last dose of OPDIVO.

Lactation

- It is not known whether OPDIVO 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 OPDIVO, advise women to discontinue breastfeeding during treatment.

Serious Adverse Reactions

- In Trial 1, serious adverse reactions occurred in 41% of patients receiving OPDIVO. 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 transaminase, and increased lipase.

- In Trial 3, serious adverse reactions occurred in 59% of patients receiving OPDIVO. The most frequent serious adverse drug reactions reported in ≥2% of patients were dyspnea, pneumonia, chronic obstructive pulmonary disease exacerbation, pneumonitis, hypercalcemia, pleural effusion, hemoptysis, and pain.

Common Adverse Reactions

- The most common adverse reactions (≥20%) reported with OPDIVO in Trial 1 were rash (21%) and in Trial 3 were fatigue (50%), dyspnea (38%), musculoskeletal pain (36%), decreased appetite (35%), cough (32%), nausea (29%), and constipation (24%).

Please see US Full Prescribing Information for OPDIVO.

YERVOY® (ipilimumab) INDICATION & IMPORTANT SAFETY INFORMATION

YERVOY (ipilimumab) is indicated for the treatment of unresectable or metastatic melanoma.

Important Safety Information

WARNING: IMMUNE-MEDIATED ADVERSE REACTIONS

YERVOY can result in severe and fatal immune-mediated adverse reactions due to T-cell activation and proliferation. 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) and thyroid function tests at baseline and before each dose.

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

Recommended Dose Modifications

Withhold dose for any moderate immune-mediated adverse reactions or for symptomatic endocrinopathy until return to baseline, improvement to mild severity, or complete resolution, and patient is receiving <7.5 mg prednisone or equivalent per day.

Permanently discontinue YERVOY for any of the following:

- Persistent moderate adverse reactions or inability to reduce corticosteroid dose to 7.5 mg prednisone or equivalent per day
- Failure to complete full treatment course within 16 weeks from administration of first dose
- Severe or life-threatening adverse reactions, including any of the following:
  - Colitis with abdominal pain, fever, ileus, or peritoneal signs; increase in stool frequency (≥7 over baseline), stool incontinence, need for intravenous hydration for >24 hours, gastrointestinal hemorrhage, and gastrointestinal perforation
  - AST or ALT >5 × the upper limit of normal (ULN) or total bilirubin >3 × the ULN
  - Stevens-Johnson syndrome, toxic epidermal necrolysis, or rash complicated by full-thickness dermal ulceration or necrotic, bullous, or hemorrhagic manifestations
  - Severe motor or sensory neuropathy, Guillain-Barré syndrome, or myasthenia gravis
  - Severe immune-mediated reactions involving any organ system
  - Immune-mediated ocular disease which is unresponsive to topical immunosuppressive therapy

Immune-mediated Enterocolitis:

- In the pivotal Phase 3 study in YERVOY-treated patients, 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%) and moderate (diarrhea with up to 6 stools above baseline, abdominal pain, mucus or blood in stool; Grade 2) enterocolitis occurred in 28 (5%) patients
- Across all YERVOY-treated patients (n=511), 5 (1%) developed intestinal perforation, 4 (0.8%) died as a result of complications, and 26 (5%) were hospitalized for severe enterocolitis
- Infliximab was administered to 5 of 62 (8%) patients with moderate, severe, or life-threatening immune-mediated enterocolitis following inadequate response to corticosteroids
- Monitor patients for signs and symptoms of enterocolitis (such as diarrhea, abdominal pain, mucus or blood in stool, with or without fever) and of bowel perforation (such as peritoneal signs and ileus). In symptomatic patients, rule out infectious etiologies and consider endoscopic evaluation for persistent or severe symptoms
- Permanently discontinue YERVOY in patients with severe enterocolitis and initiate systemic corticosteroids (1-2 mg/kg/day of prednisone or equivalent). Upon improvement to ≤Grade 1, initiate corticosteroid taper and continue over at least 1 month. In clinical trials, rapid corticosteroid tapering resulted in recurrence or worsening symptoms of enterocolitis in some patients
- Withhold YERVOY for moderate enterocolitis; administer anti-diarrheal treatment and, if persistent for >1 week, initiate systemic corticosteroids (0.5 mg/kg/day prednisone or equivalent)

Immune-mediated Hepatitis:

- In the pivotal Phase 3 study in YERVOY-treated patients, 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%
- 13 (2.5%) additional YERVOY-treated patients experienced moderate hepatotoxicity manifested by LFT abnormalities (AST or ALT elevations >2.5x but ≤5x the ULN or total bilirubin elevation >1.5x but ≤3x the ULN; Grade 2)
- Monitor LFTs (hepatic transaminase and bilirubin levels) and assess patients for signs and symptoms of hepatotoxicity before each dose of YERVOY. In patients with hepatotoxicity, rule out infectious or malignant causes and increase frequency of LFT monitoring until resolution
- Permanently discontinue YERVOY in patients with Grade 3-5 hepatotoxicity and administer systemic corticosteroids (1-2 mg/kg/day of prednisone or equivalent). When LFTs show sustained improvement or return to baseline, initiate corticosteroid tapering and continue over 1 month. Across the clinical development program for YERVOY, mycophenolate treatment has been administered in patients with persistent severe hepatitis despite high-dose corticosteroids
- Withhold YERVOY in patients with Grade 2 hepatotoxicity
• In a dose-finding trial, Grade 3 increases in transaminases with or without concomitant increases in total bilirubin occurred in 6 of 10 patients who received concurrent YERVOY (3 mg/kg) and vemurafenib (960 mg BID or 720 mg BID)

Immune-mediated Dermatitis:
• In the pivotal Phase 3 study in YERVOY-treated patients, severe, life-threatening, or fatal immune-mediated dermatitis (e.g., 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
• There were 63 (12%) YERVOY-treated patients with moderate (Grade 2) dermatitis
• Monitor patients for signs and symptoms of dermatitis such as rash and pruritus. Unless an alternate etiology has been identified, signs or symptoms of dermatitis should be considered immune-mediated
• Permanently discontinue YERVOY in patients with severe, life-threatening, or fatal immune-mediated dermatitis (Grade 3–5). Administer systemic corticosteroids (1-2 mg/kg/day of prednisone or equivalent). When dermatitis is controlled, corticosteroid tapering should occur over a period of at least 1 month. Withhold YERVOY in patients with severe signs and symptoms
• Treat mild to moderate dermatitis (e.g., localized rash and pruritus) symptomatically. Administer topical or systemic corticosteroids if there is no improvement within 1 week

Immune-mediated Neuropathies:
• In the pivotal Phase 3 study in YERVOY-treated patients, 1 case of severe Guillain-Barré syndrome and 1 case of severe (Grade 3) peripheral motor neuropathy were reported
• Across the clinical development program of YERVOY, myasthenia gravis and additional cases of Guillain-Barré syndrome have been reported
• Monitor for symptoms of motor or sensory neuropathy such as unilateral or bilateral weakness, sensory alterations, or paresthesia. Permanently discontinue YERVOY in patients with severe neuropathy (interfering with daily activities) such as Guillain-Barré-like syndromes
• Institute medical intervention as appropriate for management of severe neuropathy. Consider initiation of systemic corticosteroids (1-2 mg/kg/day of prednisone or equivalent) for severe neuropathies. Withhold YERVOY in patients with moderate neuropathy (not interfering with daily activities)

Immune-mediated Endocrinopathies:
• In the pivotal Phase 3 study in YERVOY-treated patients, 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
• Moderate endocrinopathy (requiring hormone replacement or medical intervention; Grade 2) occurred in 12 (2.3%) YERVOY-treated patients and consisted of hypothyroidism, adrenal insufficiency, hypopituitarism, and 1 case each of hyperthyroidism and Cushing’s syndrome
• Median time to onset of moderate to severe immune-mediated endocrinopathy was 11 weeks and ranged up to 19.3 weeks after the initiation of YERVOY
• Monitor patients for clinical signs and symptoms of hypophysitis, adrenal insufficiency (including adrenal crisis), and hyper- or hypothyroidism
  • Patients may present with fatigue, headache, mental status changes, abdominal pain, unusual bowel habits, and hypotension, or nonspecific symptoms which may resemble other causes such as brain metastasis or underlying disease. Unless an alternate etiology has been identified, signs or symptoms should be considered immune-mediated
  • Monitor thyroid function tests and clinical chemistries at the start of treatment, before each dose, and as clinically indicated based on symptoms. In a limited number of patients, hypophysitis was diagnosed by imaging studies through enlargement of the pituitary gland
• Withhold YERVOY in symptomatic patients. Initiate systemic corticosteroids (1-2 mg/kg/day of prednisone or equivalent) and initiate appropriate hormone replacement therapy. Long-term hormone replacement therapy may be necessary

Other Immune-mediated Adverse Reactions, Including Ocular Manifestations:
• In the pivotal Phase 3 study in YERVOY-treated patients, clinically significant immune-mediated adverse reactions seen in <1% were: nephritis, pneumonitis, meningitis, pericarditis, uveitis, iritis, and hemolytic anemia
• Across the clinical development program for YERVOY, likely immune-mediated adverse reactions also reported with <1% incidence were: myocarditis, angiopathy, temporal arteritis, vasculitis, polymyalgia rheumatica, conjunctivitis, biephalitis, episcleritis, scleritis, leukocyctoclastic vasculitis, erythema multiforme, scle, psoriasis, pancreatitits, arthritis, autoimmune thyroiditis, sarcoidosis, neurosensory hypoacusis, autoimmune central neuropathy (encephalitis), myositis, polymyositis, and ocular myositis
Permanently discontinue YERVOY for clinically significant or severe immune-mediated adverse reactions. Initiate systemic corticosteroids (1-2 mg/kg/day of prednisone or equivalent) for severe immune-mediated adverse reactions. Administer corticosteroid eye drops for uveitis, iritis, or episcleritis. Permanently discontinue YERVOY for immune-mediated ocular disease unresponsive to local immunosuppressive therapy.

**Pregnancy & Nursing:**
- YERVOY is classified as pregnancy category C. There are no adequate and well-controlled studies of YERVOY in pregnant women. Use YERVOY during pregnancy only if the potential benefit justifies the potential risk to the fetus.
- Human IgG1 is known to cross the placental barrier and YERVOY is an IgG1; therefore, YERVOY has the potential to be transmitted from the mother to the developing fetus.
- It is not known whether YERVOY is secreted in human milk. Because many drugs are secreted in human milk and because of the potential for serious adverse reactions in nursing infants from YERVOY, a decision should be made whether to discontinue nursing or to discontinue YERVOY.

**Common Adverse Reactions:**
- 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%).

**Language:**
English

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