



NEWS RELEASE

Merck's KEYTRUDA® (pembrolizumab) Plus Pemetrexed (ALIMTA®) and Platinum Chemotherapy Reduced the Risk of Death by Half Compared with Chemotherapy Alone as First-Line Treatment for Advanced Nonsquamous NSCLC in Phase 3 KEYNOTE-189 Study

4/16/2018

KEYTRUDA Combination Improved Overall Survival in Patients Regardless of PD-L1 Expression, Including Patients Who Tested Negative for PD-L1

Results Presented Today at AACR 2018 and Published in The New England Journal of Medicine Also Show Significant Improvement in Progression-Free Survival, with Risk of Progression or Death Reduced by Nearly Half

Merck (NYSE: MRK), known as MSD outside the United States and Canada, today announced results from KEYNOTE-189, a pivotal Phase 3 trial evaluating KEYTRUDA®, Merck's anti-PD-1 therapy, in combination with pemetrexed (ALIMTA®) and cisplatin or carboplatin for the first-line treatment of metastatic nonsquamous non-small cell lung cancer (NSCLC). Findings showed that the KEYTRUDA-pemetrexed-platinum chemotherapy combination significantly improved overall survival (OS), reducing the risk of death by half compared with chemotherapy alone (HR=0.49 [95% CI, 0.38-0.64]; $p < 0.00001$). In pre-specified exploratory analyses, an OS benefit was observed regardless of PD-L1 expression in the three PD-L1 categories that were evaluated, including: patients whose tumors were negative for PD-L1 (HR=0.59 [95% CI, 0.38-0.92]); patients whose tumors had PD-L1 tumor proportion scores (TPS) of 1-49 percent (HR=0.55 [95% CI, 0.34-0.90]); and patients who had a TPS of greater than or equal to 50 percent (HR=0.42 [95% CI, 0.26-0.68]). The addition of KEYTRUDA to pemetrexed plus platinum chemotherapy also

achieved a significant improvement in progression-free survival (PFS), with a reduction in the risk of progression or death of nearly half for patients in the KEYTRUDA combination arm, compared with chemotherapy alone (HR=0.52 [95% CI, 0.43-0.64]; $p < 0.00001$). A PFS improvement in the KEYTRUDA combination group was observed in patients whose tumors were negative for PD-L1 (HR=0.75 [95% CI, 0.53-1.05]); patients with a TPS of 1-49 percent (HR=0.55 [95% CI, 0.37-0.81]); and patients with a TPS greater than or equal to 50 percent (HR=0.36 [95% CI, 0.25-0.52]). These results are being presented today in a plenary session at the American Association for Cancer Research (AACR) Annual Meeting 2018 (Abstract #CT075), with simultaneous publication in The New England Journal of Medicine.

“In this trial, KEYTRUDA in combination with pemetrexed and platinum chemotherapy, compared with chemotherapy alone, prolonged overall survival and progression-free survival in patients with advanced nonsquamous non-small cell lung cancer regardless of PD-L1 expression,” said Dr. Leena Gandhi, director of thoracic medical oncology at NYU Langone’s Perlmutter Cancer Center and lead author of The New England Journal of Medicine paper. “There is good scientific rationale for combining KEYTRUDA with pemetrexed and platinum chemotherapy, and these clinical data now suggest this combination as a new standard of care for the first-line treatment of these nonsquamous non-small cell lung cancer patients.”

“Our goal is to extend the lives of patients with lung cancer, and the unambiguous survival findings from KEYNOTE-189 showing the risk of death was reduced by half in the KEYTRUDA arm are important not only for patients but also for the medical community,” said Dr. Roger M. Perlmutter, president, Merck Research Laboratories. “The results of this trial have the potential to change the treatment paradigm for patients with nonsquamous non-small cell lung cancer in the first-line setting, including patients whose tumors are either PD-L1 negative or are untested.”

KEYTRUDA is the first immunotherapy to significantly extend survival of patients with nonsquamous NSCLC in combination with chemotherapy as a first-line treatment. KEYNOTE-189 is the confirmatory trial for KEYNOTE-021 (Cohort G), a Phase 2 study that made KEYTRUDA the only FDA-approved anti-PD-1 therapy in combination with chemotherapy (pemetrexed plus carboplatin) for the first-line treatment of patients with metastatic nonsquamous NSCLC, regardless of PD-L1 expression. Merck is working to submit data from KEYNOTE-189 to regulatory agencies in the United States and around the world.

Merck has an extensive clinical development program in lung cancer and is advancing multiple registration-enabling studies with KEYTRUDA in combination with other treatments and as monotherapy. The program, which is comprised of nearly 9,000 patients across 15 clinical studies, is evaluating KEYTRUDA across multiple settings and stages of the disease.

“The reality is, there remains a significant need for treatment options for patients with lung cancer. At the Bonnie J. Addario Lung Cancer Foundation (ALCF), we are devoted exclusively to eradicating lung cancer through research, early detection, education and treatment. And, the survival benefit achieved by the KEYTRUDA combination in the

KEYNOTE-189 study represents a meaningful advance and may offer hope for patients newly diagnosed with one of the most common and deadly cancers,” said Bonnie J. Addario, a 14-year lung cancer survivor and ALCF founder.

Additional Data and Safety Information from KEYNOTE-189 (Abstract #CT075)

KEYNOTE-189, a randomized, double-blind, placebo-controlled, Phase 3 study, evaluated KEYTRUDA in combination with pemetrexed and cisplatin or carboplatin, compared with pemetrexed and cisplatin or carboplatin alone, in 616 untreated patients with metastatic nonsquamous NSCLC, regardless of PD-L1 expression. Patients had no sensitizing EGFR or ALK genomic tumor aberrations, and had not previously received systemic therapy for advanced disease. The dual primary endpoints were OS and PFS; secondary endpoints include overall response rate (ORR) and duration of response (DOR).

With a median follow-up of 10.5 months (range, 0.2-20.4), KEYTRUDA in combination with pemetrexed and a platinum chemotherapy demonstrated superior improvements in OS, with a 51 percent reduction in the risk of death, compared with pemetrexed plus platinum chemotherapy alone (HR=0.49 [95% CI, 0.38-0.64]; $p < 0.00001$). This finding includes the 50 percent of patients randomized to the chemotherapy alone group who discontinued all study therapy (n=170) and went on to receive subsequent anti-PD-1 or PD-L1 therapy, including 67 patients who received KEYTRUDA monotherapy as part of study crossover. Median OS was not reached in the KEYTRUDA combination group (95% CI, not estimable) and was 11.3 months in the chemotherapy alone group (95% CI, 8.7-15.1). In the study, 69.2 percent of patients were estimated to be alive at 12 months in the KEYTRUDA treatment group (95% CI, 64.1-73.8%) compared with 49.4 percent in the chemotherapy alone group (95% CI, 42.1-56.2%).

In KEYNOTE-189 there was also a significant improvement in PFS for KEYTRUDA in combination with pemetrexed and platinum chemotherapy with a 48 percent reduction in the risk of progression or death compared with pemetrexed plus platinum chemotherapy alone (HR=0.52 [95% CI, 0.43-0.64]; $p < 0.00001$). The median PFS was 8.8 months for the KEYTRUDA combination (95% CI, 7.6-9.2) compared with 4.9 months for chemotherapy alone (95% CI, 4.7-5.5). The percentage of patients who were alive with no progression of disease at 12 months was 34.1 percent in the KEYTRUDA combination group (95% CI, 28.8-39.5%), which was nearly double the percentage of the pemetrexed plus platinum chemotherapy group (17.3 percent [95% CI, 12.0-23.5%]). In addition, improvements in OS and PFS were observed in other patient subgroups evaluated, including age, sex, EGOG performance-status score, smoking status, brain metastases at baseline and type of platinum chemotherapy prescribed (carboplatin or cisplatin).

In the study, KEYTRUDA plus pemetrexed and a platinum chemotherapy also showed an ORR that was more than double the ORR of chemotherapy alone (47.6 percent [95% CI, 42.6-52.5%] compared to 18.9 percent [95% CI, 13.8-25.0%], respectively, $p < 0.00001$). Among patients in the KEYTRUDA arm, the median duration of response was 11.2 months (range, 1.1+ to 18.0+ months) compared with 7.8 months in the chemotherapy alone group (range, 2.1+ to

16.4+ months). The improvement in response rate occurred in all PD-L1 patient subgroups.

The safety of KEYTRUDA was consistent with what has been seen in previous trials among patients with metastatic NSCLC. Grade 3-5 adverse events from any cause occurred in 67.2 percent of patients in the KEYTRUDA plus pemetrexed and platinum chemotherapy group and 65.8 percent in the chemotherapy alone arm. Adverse events of any grade and from any cause with an incidence of 15 percent or more in the KEYTRUDA group were nausea (55.6%), anemia (46.2%), fatigue (40.7%), constipation (34.8%), diarrhea (30.9%), decreased appetite (28.1%), neutropenia (27.2%), vomiting (24.2%), cough (21.5%), dyspnea (21.2%), asthenia (20.5%), rash (20.2%), pyrexia (19.5%), edema peripheral (19.3%), thrombocytopenia (18.0%) and increased lacrimation (17.0%). The most common immune-mediated adverse events of any grade in patients receiving KEYTRUDA plus pemetrexed and platinum chemotherapy were hypothyroidism (6.7%), pneumonitis (4.4%), hyperthyroidism (4.0%), infusion reactions (2.5%), colitis (2.2%), severe skin toxicity (2.0%), nephritis (1.7%) and hepatitis (1.2%). There were three treatment-related deaths from pneumonitis in the KEYTRUDA plus pemetrexed and platinum chemotherapy group.

About KEYNOTE-189

KEYNOTE-189 (ClinicalTrials.gov, NCT02578680) enrolled 616 patients who were randomized 2:1 to one of two treatment groups, and were treated until disease progression, unacceptable toxicity, physician decision or consent withdrawal, as follows:

- KEYTRUDA (200 mg fixed dose every three weeks) plus pemetrexed (500 mg/m²) (with vitamin supplementation) plus cisplatin (75 mg/m²) or carboplatin AUC 5 mg/mL/min on day 1 every three weeks (Q3W) for four cycles, followed by KEYTRUDA 200 mg plus pemetrexed (500 mg/m²) Q3W; or
- Saline placebo plus pemetrexed (500 mg/m²) (with vitamin supplementation) plus cisplatin (75 mg/m²) or carboplatin AUC 5 mg/mL/min on day 1 every three weeks (Q3W) for four cycles, followed by placebo plus pemetrexed (500 mg/m²) Q3W.

Patients on the control arm who experienced disease progression, verified by central independent review, were permitted to undergo treatment assignment unblinding and crossover to receive open-label KEYTRUDA. The KEYNOTE-189 study was conducted in collaboration with Eli Lilly and Company, the makers of pemetrexed (ALIMTA).

About Lung Cancer

Lung cancer, which forms in the tissues of the lungs, usually within cells lining the air passages, is the leading cause of cancer death worldwide. Each year, more people die of lung cancer than die of colon, breast and prostate cancers combined. The two main types of lung cancer are non-small cell and small cell. NSCLC is the most common type of lung cancer, accounting for about 85 percent of all cases. The five-year survival rate for patients diagnosed in the United States with any stage of lung cancer is estimated to be 18 percent.

Merck Investor Webcast

Merck will hold a live investor audio webcast in conjunction with the AACR 2018 Annual Meeting on Monday, April 16 at 6:45 p.m. CDT (7:45 p.m. EDT). Those interested in participating can register and join [here](#).

About KEYTRUDA® (pembrolizumab) Injection 100mg

KEYTRUDA is an anti-PD-1 therapy that works by increasing the ability of the body's immune system to help detect and fight tumor cells. KEYTRUDA is a humanized monoclonal antibody that blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2, thereby activating T lymphocytes which may affect both tumor cells and healthy cells.

Merck has the industry's largest immuno-oncology clinical research program, which currently involves more than 700 trials studying KEYTRUDA across a wide variety of cancers and treatment settings. The KEYTRUDA clinical program seeks to understand the role of KEYTRUDA across cancers and the factors that may predict a patient's likelihood of benefitting from treatment with KEYTRUDA, including exploring several different biomarkers.

KEYTRUDA (pembrolizumab) Indications and Dosing

Melanoma

KEYTRUDA is indicated for the treatment of patients with unresectable or metastatic melanoma at a fixed dose of 200 mg every three weeks until disease progression or unacceptable toxicity.

Lung Cancer

KEYTRUDA, as a single agent, is indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have high PD-L1 expression [tumor proportion score (TPS) $\geq 50\%$] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations.

KEYTRUDA, as a single agent, is also indicated for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS $\geq 1\%$) as determined by an FDA-approved test, with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving KEYTRUDA.

KEYTRUDA, in combination with pemetrexed and carboplatin, is indicated for the first-line treatment of patients with metastatic nonsquamous NSCLC. This indication is approved under accelerated approval based on tumor response rate and progression-free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

In metastatic NSCLC, KEYTRUDA is administered at a fixed dose of 200 mg every three weeks until disease

progression, unacceptable toxicity, or up to 24 months in patients without disease progression.

When administering KEYTRUDA in combination with chemotherapy, KEYTRUDA should be administered prior to chemotherapy when given on the same day. See also the Prescribing Information for pemetrexed and carboplatin.

Head and Neck Cancer

KEYTRUDA is indicated for the treatment of patients with recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) with disease progression on or after platinum-containing chemotherapy. This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials. In HNSCC, KEYTRUDA is administered at a fixed dose of 200 mg every three weeks until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression.

Classical Hodgkin Lymphoma

KEYTRUDA is indicated for the treatment of adult and pediatric patients with refractory classical Hodgkin lymphoma (cHL), or who have relapsed after three or more prior lines of therapy. This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials. In adults with cHL, KEYTRUDA is administered at a fixed dose of 200 mg every three weeks until disease progression or unacceptable toxicity, or up to 24 months in patients without disease progression. In pediatric patients with cHL, KEYTRUDA is administered at a dose of 2 mg/kg (up to a maximum of 200 mg) every three weeks until disease progression or unacceptable toxicity, or up to 24 months in patients without disease progression.

Urothelial Carcinoma

KEYTRUDA is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-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 the confirmatory trials.

KEYTRUDA is also indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

In locally advanced or metastatic urothelial carcinoma, KEYTRUDA is administered at a fixed dose of 200 mg every three weeks until disease progression or unacceptable toxicity, or up to 24 months in patients without disease progression.

Microsatellite Instability-High (MSI-H) Cancer

KEYTRUDA is indicated for the treatment of adult and pediatric patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR)

- solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options, or
- colorectal cancer that has progressed following treatment with fluoropyrimidine, oxaliplatin, and irinotecan.

This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials. The safety and effectiveness of KEYTRUDA in pediatric patients with MSI-H central nervous system cancers have not been established.

In adult patients with MSI-H cancer, KEYTRUDA is administered at a fixed dose of 200 mg every three weeks until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression. In children with MSI-H cancer, KEYTRUDA is administered at a dose of 2 mg/kg (up to a maximum of 200 mg) every three weeks until disease progression or unacceptable toxicity, or up to 24 months in patients without disease progression.

Gastric Cancer

KEYTRUDA is indicated for the treatment of patients with recurrent locally advanced or metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma whose tumors express PD-L1 [Combined Positive Score (CPS) ≥ 1] as determined by an FDA-approved test, with disease progression on or after two or more prior lines of therapy including fluoropyrimidine- and platinum-containing chemotherapy and if appropriate, HER2/neu-targeted therapy. This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials. The recommended dose of KEYTRUDA is 200 mg every three weeks until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression.

Selected Important Safety Information for KEYTRUDA®

KEYTRUDA can cause immune-mediated pneumonitis, including fatal cases. Pneumonitis occurred in 94 (3.4%) of 2799 patients receiving KEYTRUDA, including Grade 1 (0.8%), 2 (1.3%), 3 (0.9%), 4 (0.3%), and 5 (0.1%) pneumonitis, and occurred more frequently in patients with a history of prior thoracic radiation (6.9%) compared to those without (2.9%). Monitor patients for signs and symptoms of pneumonitis. Evaluate suspected pneumonitis with radiographic imaging. Administer corticosteroids for Grade 2 or greater pneumonitis. Withhold KEYTRUDA for Grade 2; permanently discontinue KEYTRUDA for Grade 3 or 4 or recurrent Grade 2 pneumonitis.

KEYTRUDA can cause immune-mediated colitis. Colitis occurred in 48 (1.7%) of 2799 patients receiving KEYTRUDA,

including Grade 2 (0.4%), 3 (1.1%), and 4 (<0.1%) colitis. Monitor patients for signs and symptoms of colitis. Administer corticosteroids for Grade 2 or greater colitis. Withhold KEYTRUDA for Grade 2 or 3; permanently discontinue KEYTRUDA for Grade 4 colitis.

KEYTRUDA can cause immune-mediated hepatitis. Hepatitis occurred in 19 (0.7%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.1%), 3 (0.4%), and 4 (<0.1%) hepatitis. Monitor patients for changes in liver function. Administer corticosteroids for Grade 2 or greater hepatitis and, based on severity of liver enzyme elevations, withhold or discontinue KEYTRUDA.

KEYTRUDA can cause hypophysitis. Hypophysitis occurred in 17 (0.6%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.2%), 3 (0.3%), and 4 (<0.1%) hypophysitis. Monitor patients for signs and symptoms of hypophysitis (including hypopituitarism and adrenal insufficiency). Administer corticosteroids and hormone replacement as clinically indicated. Withhold KEYTRUDA for Grade 2; withhold or discontinue for Grade 3 or 4 hypophysitis.

KEYTRUDA can cause thyroid disorders, including hyperthyroidism, hypothyroidism, and thyroiditis. Hyperthyroidism occurred in 96 (3.4%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.8%) and 3 (0.1%) hyperthyroidism. Hypothyroidism occurred in 237 (8.5%) of 2799 patients receiving KEYTRUDA, including Grade 2 (6.2%) and 3 (0.1%) hypothyroidism. The incidence of new or worsening hypothyroidism was higher in patients with HNSCC, occurring in 28 (15%) of 192 patients with HNSCC, including Grade 3 (0.5%) hypothyroidism. Thyroiditis occurred in 16 (0.6%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.3%) thyroiditis. Monitor patients for changes in thyroid function (at the start of treatment, periodically during treatment, and as indicated based on clinical evaluation) and for clinical signs and symptoms of thyroid disorders. Administer replacement hormones for hypothyroidism and manage hyperthyroidism with thionamides and beta-blockers as appropriate. Withhold or discontinue KEYTRUDA for Grade 3 or 4 hyperthyroidism.

KEYTRUDA can cause type 1 diabetes mellitus, including diabetic ketoacidosis, which have been reported in 6 (0.2%) of 2799 patients. Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Administer insulin for type 1 diabetes, and withhold KEYTRUDA and administer antihyperglycemics in patients with severe hyperglycemia.

KEYTRUDA can cause immune-mediated nephritis. Nephritis occurred in 9 (0.3%) of 2799 patients receiving KEYTRUDA, including Grade 2 (0.1%), 3 (0.1%), and 4 (<0.1%) nephritis. Monitor patients for changes in renal function. Administer corticosteroids for Grade 2 or greater nephritis. Withhold KEYTRUDA for Grade 2; permanently discontinue KEYTRUDA for Grade 3 or 4 nephritis.

Immune-mediated rashes, including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) (some cases

with fatal outcome), exfoliative dermatitis, and bullous pemphigoid, can occur. Monitor patients for suspected severe skin reactions and based on the severity of the adverse reaction, withhold or permanently discontinue KEYTRUDA and administer corticosteroids. For signs or symptoms of SJS or TEN, withhold KEYTRUDA and refer the patient for specialized care for assessment and treatment. If SJS or TEN is confirmed, permanently discontinue KEYTRUDA.

KEYTRUDA can cause other clinically important immune-mediated adverse reactions. These immune-mediated reactions may occur in any organ system. For suspected immune-mediated adverse reactions, ensure adequate evaluation to confirm etiology or exclude other causes. Based on the severity of the adverse reaction, withhold KEYTRUDA and administer corticosteroids. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Based on limited data from clinical studies in patients whose immune-related adverse reactions could not be controlled with corticosteroid use, administration of other systemic immunosuppressants can be considered. Resume KEYTRUDA when the adverse reaction remains at Grade 1 or less following corticosteroid taper. Permanently discontinue KEYTRUDA for any Grade 3 immune-mediated adverse reaction that recurs and for any life-threatening immune-mediated adverse reaction.

The following clinically significant immune-mediated adverse reactions occurred in less than 1% (unless otherwise indicated) of 2799 patients: arthritis (1.5%), uveitis, myositis, Guillain-Barré syndrome, myasthenia gravis, vasculitis, pancreatitis, hemolytic anemia, and partial seizures arising in a patient with inflammatory foci in brain parenchyma. In addition, myelitis and myocarditis were reported in other clinical trials, including classical Hodgkin lymphoma, and postmarketing use.

Solid organ transplant rejection has been reported in postmarketing use of KEYTRUDA. Treatment with KEYTRUDA may increase the risk of rejection in solid organ transplant recipients. Consider the benefit of treatment with KEYTRUDA vs the risk of possible organ rejection in these patients.

KEYTRUDA can cause severe or life-threatening infusion-related reactions, including hypersensitivity and anaphylaxis, which have been reported in 6 (0.2%) of 2799 patients. Monitor patients for signs and symptoms of infusion-related reactions, including rigors, chills, wheezing, pruritus, flushing, rash, hypotension, hypoxemia, and fever. For Grade 3 or 4 reactions, stop infusion and permanently discontinue KEYTRUDA.

Immune-mediated complications, including fatal events, occurred in patients who underwent allogeneic hematopoietic stem cell transplantation (HSCT) after being treated with KEYTRUDA. Of 23 patients with cHL who proceeded to allogeneic HSCT after treatment with KEYTRUDA on any trial, 6 patients (26%) developed graft-versus-host disease (GVHD), one of which was fatal, and 2 patients (9%) developed severe hepatic veno-occlusive disease (VOD) after reduced-intensity conditioning, one of which was fatal. Cases of fatal hyperacute GVHD after allogeneic HSCT have also been reported in patients with lymphoma who received a PD-1 receptor–blocking antibody before

transplantation.

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.

In clinical trials in patients with multiple myeloma, the addition of KEYTRUDA to a thalidomide analogue plus dexamethasone resulted in increased mortality. Treatment of these patients with a PD-1 or PD-L1 blocking antibody in this combination is not recommended outside of controlled clinical trials.

Based on its mechanism of action, KEYTRUDA can cause fetal harm when administered to a pregnant woman. If used during pregnancy, or if the patient becomes pregnant during treatment, apprise the patient of the potential hazard to a fetus. Advise females of reproductive potential to use highly effective contraception during treatment and for 4 months after the last dose of KEYTRUDA.

In KEYNOTE-006, KEYTRUDA was discontinued due to adverse reactions in 9% of 555 patients with advanced melanoma; adverse reactions leading to discontinuation in more than one patient were colitis (1.4%), autoimmune hepatitis (0.7%), allergic reaction (0.4%), polyneuropathy (0.4%), and cardiac failure (0.4%). Adverse reactions leading to interruption of KEYTRUDA occurred in 21% of patients; the most common ($\geq 1\%$) was diarrhea (2.5%). The most common adverse reactions with KEYTRUDA vs ipilimumab were fatigue (28% vs 28%), diarrhea (26% with KEYTRUDA), rash (24% vs 23%), and nausea (21% with KEYTRUDA). Corresponding incidence rates are listed for ipilimumab only for those adverse reactions that occurred at the same or lower rate than with KEYTRUDA.

In KEYNOTE-010, KEYTRUDA monotherapy was discontinued due to adverse reactions in 8% of 682 patients with metastatic NSCLC. The most common adverse event resulting in permanent discontinuation of KEYTRUDA was pneumonitis (1.8%). Adverse reactions leading to interruption of KEYTRUDA occurred in 23% of patients; the most common ($\geq 1\%$) were diarrhea (1%), fatigue (1.3%), pneumonia (1%), liver enzyme elevation (1.2%), decreased appetite (1.3%), and pneumonitis (1%). The most common adverse reactions (occurring in at least 20% of patients and at a higher incidence than with docetaxel) were decreased appetite (25% vs 23%), dyspnea (23% vs 20%), and nausea (20% vs 18%).

In KEYNOTE-021(G1), when KEYTRUDA was administered in combination with carboplatin and pemetrexed (carbo/pem) in advanced nonsquamous NSCLC, KEYTRUDA was discontinued in 10% of 59 patients. The most common adverse reaction resulting in discontinuation of KEYTRUDA ($\geq 2\%$) was acute kidney injury (3.4%). Adverse reactions leading to interruption of KEYTRUDA occurred in 39% of patients; the most common ($\geq 2\%$) were fatigue (8%), neutrophil count decreased (8%), anemia (5%), dyspnea (3.4%), and pneumonitis (3.4%). The most common

adverse reactions ($\geq 20\%$) with KEYTRUDA compared to carbo/pem alone were fatigue (71% vs 50%), nausea (68% vs 56%), constipation (51% vs 37%), rash (42% vs 21%), vomiting (39% vs 27%), dyspnea (39% vs 21%), diarrhea (37% vs 23%), decreased appetite (31% vs 23%), headache (31% vs 16%), cough (24% vs 18%), dizziness (24% vs 16%), insomnia (24% vs 15%), pruritus (24% vs 4.8%), peripheral edema (22% vs 18%), dysgeusia (20% vs 11%), alopecia (20% vs 3.2%), upper respiratory tract infection (20% vs 3.2%), and arthralgia (15% vs 24%). This study was not designed to demonstrate a statistically significant difference in adverse reaction rates for KEYTRUDA as compared to carbo/pem alone for any specified adverse reaction.

In KEYNOTE-012, KEYTRUDA was discontinued due to adverse reactions in 17% of 192 patients with HNSCC. Serious adverse reactions occurred in 45% of patients. The most frequent serious adverse reactions reported in at least 2% of patients were pneumonia, dyspnea, confusional state, vomiting, pleural effusion, and respiratory failure. The most common adverse reactions (reported in at least 20% of patients) were fatigue, decreased appetite, and dyspnea. Adverse reactions occurring in patients with HNSCC were generally similar to those occurring in patients with melanoma or NSCLC, with the exception of increased incidences of facial edema (10% all Grades; 2.1% Grades 3 or 4) and new or worsening hypothyroidism.

In KEYNOTE-087, KEYTRUDA was discontinued due to adverse reactions in 5% of 210 patients with cHL, and treatment was interrupted due to adverse reactions in 26% of patients. Fifteen percent (15%) of patients had an adverse reaction requiring systemic corticosteroid therapy. Serious adverse reactions occurred in 16% of patients. The most frequent serious adverse reactions ($\geq 1\%$) included pneumonia, pneumonitis, pyrexia, dyspnea, GVHD, and herpes zoster. Two patients died from causes other than disease progression; one from GVHD after subsequent allogeneic HSCT and one from septic shock. The most common adverse reactions (occurring in $\geq 20\%$ of patients) were fatigue (26%), pyrexia (24%), cough (24%), musculoskeletal pain (21%), diarrhea (20%), and rash (20%).

In KEYNOTE-052, KEYTRUDA was discontinued due to adverse reactions in 11% of 370 patients with locally advanced or metastatic urothelial carcinoma. The most common adverse reactions (in $\geq 20\%$ of patients) were fatigue (38%), musculoskeletal pain (24%), decreased appetite (22%), constipation (21%), rash (21%), and diarrhea (20%). Eighteen patients (5%) died from causes other than disease progression. Five patients (1.4%) who were treated with KEYTRUDA experienced sepsis which led to death, and 3 patients (0.8%) experienced pneumonia which led to death. Adverse reactions leading to interruption of KEYTRUDA occurred in 22% of patients; the most common ($\geq 1\%$) were liver enzyme increase, diarrhea, urinary tract infection, acute kidney injury, fatigue, joint pain, and pneumonia. Serious adverse reactions occurred in 42% of patients, the most frequent ($\geq 2\%$) of which were urinary tract infection, hematuria, acute kidney injury, pneumonia, and urosepsis.

In KEYNOTE-045, KEYTRUDA was discontinued due to adverse reactions in 8% of 266 patients with locally advanced or metastatic urothelial carcinoma. The most common adverse reaction resulting in permanent discontinuation of

KEYTRUDA was pneumonitis (1.9%). Adverse reactions leading to interruption of KEYTRUDA occurred in 20% of patients; the most common ($\geq 1\%$) were urinary tract infection (1.5%), diarrhea (1.5%), and colitis (1.1%). The most common adverse reactions ($\geq 20\%$) in patients who received KEYTRUDA vs those who received chemotherapy were fatigue (38% vs 56%), musculoskeletal pain (32% vs 27%), pruritus (23% vs 6%), decreased appetite (21% vs 21%), nausea (21% vs 29%), and rash (20% vs 13%). Serious adverse reactions occurred in 39% of KEYTRUDA-treated patients, the most frequent ($\geq 2\%$) of which were urinary tract infection, pneumonia, anemia, and pneumonitis.

It is not known whether KEYTRUDA is excreted in human milk. Because many drugs are excreted in human milk, instruct women to discontinue nursing during treatment with KEYTRUDA and for 4 months after the final dose.

There is limited experience in pediatric patients. In a study, 40 pediatric patients (16 children aged 2 years to younger than 12 years and 24 adolescents aged 12 years to 18 years) with advanced melanoma, lymphoma, or PD-L1-positive advanced, relapsed, or refractory solid tumors were administered KEYTRUDA 2 mg/kg every 3 weeks. Patients received KEYTRUDA for a median of 3 doses (range 1–17 doses), with 34 patients (85%) receiving KEYTRUDA for 2 doses or more. The safety profile in these pediatric patients was similar to that seen in adults treated with KEYTRUDA. Toxicities that occurred at a higher rate ($\geq 15\%$ difference) in these patients when compared to adults under 65 years of age were fatigue (45%), vomiting (38%), abdominal pain (28%), hypertransaminasemia (28%), and hyponatremia (18%).

Merck's Focus on Cancer

Our goal is to translate breakthrough science into innovative oncology medicines to help people with cancer worldwide. At Merck, helping people fight cancer is our passion and supporting accessibility to our cancer medicines is our commitment. Our focus is on pursuing research in immuno-oncology and we are accelerating every step in the journey – from lab to clinic – to potentially bring new hope to people with cancer.

As part of our focus on cancer, Merck is committed to exploring the potential of immuno-oncology with one of the fastest-growing development programs in the industry. We are currently executing an expansive research program evaluating our anti-PD-1 therapy across more than 30 tumor types. We also continue to strengthen our immuno-oncology portfolio through strategic acquisitions and are prioritizing the development of several promising immunotherapeutic candidates with the potential to improve the treatment of advanced cancers.

For more information about our oncology clinical trials, visit www.merck.com/clinicaltrials.

About Merck

For more than a century, Merck, a leading global biopharmaceutical company known as MSD outside of the United States and Canada, has been inventing for life, bringing forward medicines and vaccines for many of the world's most challenging diseases. Through our prescription medicines, vaccines, biologic therapies and animal health

products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to health care through far-reaching policies, programs and partnerships. Today, Merck continues to be at the forefront of research to advance the prevention and treatment of diseases that threaten people and communities around the world - including cancer, cardio-metabolic diseases, emerging animal diseases, Alzheimer's disease and infectious diseases including HIV and Ebola. For more information, visit www.merck.com and connect with us on [Twitter](#), [Facebook](#), [Instagram](#), [YouTube](#) and [LinkedIn](#).

Forward-Looking Statement of Merck & Co., Inc., Kenilworth, N.J., USA

This news release of Merck & Co., Inc., Kenilworth, N.J., USA (the "company") includes "forward-looking statements" within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company's management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline products that the products will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company's ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company's 2017 Annual Report on Form 10-K and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site (www.sec.gov).

Please see Prescribing Information for KEYTRUDA at https://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_pi.pdf and Patient Information/Medication Guide for KEYTRUDA at https://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_mg.pdf.

ALIMTA® is a registered trademark of Eli Lilly and Company.

Merck

Media:

Pamela Eisele, 267-305-3558

or

Kristen Drake, 908-334-4688

or

Investors:

Teri Loxam, 908-740-1986

or

Michael DeCarbo, 908-740-1807