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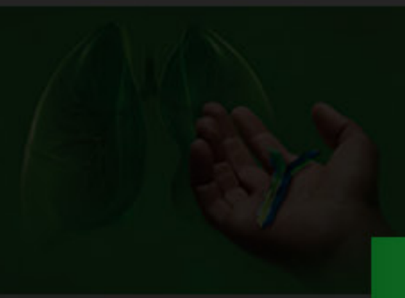

HELPING TO REDEFINE SURVIVAL EXPECTATIONS for your patients in the following indications:

I AM A HEALTH CARE PROFESSIONAL

I AM NOT A HEALTH CARE PROFESSIONAL

The information on this site is intended for health care professionals in the United States, its territories, and Puerto Rico, and is not intended for the general public.

Full Indications −

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1L Combo Therapy —Nonsquamous

FIRST-LINE COMBINATION THERAPY IN NONSQUAMOUS mNSCLC: KEYTRUDA, in combination with pemetrexed and platinum chemotherapy, is indicated for the first-line treatment of patients with metastatic nonsquamous non–small cell lung cancer (NSCLC), with no EGFR or ALK genomic tumor aberrations.

FIRST-LINE COMBINATION THERAPY IN SQUAMOUS mNSCLC: KEYTRUDA, in combination with carboplatin and either paclitaxel or paclitaxel protein-bound, is indicated for the first-line treatment of patients with metastatic squamous NSCLC.

FIRST-LINE MONOTHERAPY IN NONSQUAMOUS AND SQUAMOUS ADVANCED NSCLC: KEYTRUDA, as a single agent, is indicated for the first-line treatment of patients with NSCLC expressing PD-L1 [tum proportion score (TPS) ≥1%] as determined by an FDA-approved test, with no EGFR or ALK genomic tu aberrations, and is stage III where patients are not candidates for surgical resection or definitive chemoradiation, or metastatic.

Key Chat

SELECTED SAFETY INFORMATION

EXPAND +

Severe and Fatal Immune-Mediated Adverse Reactions

- KEYTRUDA is a monoclonal antibody that belongs to a class of drugs that bind to either the programmed death receptor-1 (PD-1) or the programmed death ligand 1 (PD-L1), blocking the PD-1/PD-L1 pathway, thereby removing inhibition of the immune response, potentially breaking peripheral tolerance and inducing immune-mediated adverse reactions. Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue, can affect more than one body system simultaneously, and can occur at any time after starting treatment or after discontinuation of treatment. Important immune-mediated adverse

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1L Combo Therapy —Squamous

1L Monotherapy

2L Monotherapy

Safety

FIRST-LINE COMBINATION THERAPY IN NONSQUAMOUS mNSCLC: KEYTRUDA, in combination with pemetrexed and platinum chemotherapy, is indicated for the first-line treatment of patients with metastatic nonsquamous non–small cell lung cancer (NSCLC), with no EGFR or ALK genomic tumor aberrations.

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SECOND-LINE OR GREATER MONOTHERAPY IN NONSQUAMOUS AND SQUAMOUS mNSCLC: KEYTRUDA, as a single agent, is indicated for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥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.

mNSCLC = metastatic NSCLC; EGFR = epidermal growth factor receptor; ALK = anaplastic lymphoma kinase; PD-L1 = programmed death ligand 1.

Key Chat

SELECTED SAFETY INFORMATION

EXPAND +

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1L Combo Therapy —Squamous

1L Monotherapy

1L

Nonsquamous mNSCLC

KEYTRUDA, in combination with pemetrexed and platinum chemotherapy, is indicated for the first-line treatment of patients with metastatic nonsquamous non–small cell lung cancer (NSCLC), with no EGFR or ALK genomic tumor aberrations.

SUPERIOR OS

with KEYTRUDA + plat/pem vs plat/pem alone (HR=0.49; 95% CI, 0.38–0.64; *P*<0.0001)[a]

DURABLE OS

with KEYTRUDA + plat/pem vs plat/pem alone at protocol-specified final analysis (HR=0.56; 95% CI, 0.46–0.69)

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SUPERIOR OS

with KEYTRUDA +
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DURABLE OS

with KEYTRUDA +
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KEYTRUDA ® (pembrolizumab) Assistant

Hi, I'm KeyChat, your virtual assistant. I'm here to help answer questions you may have about KEYTRUDA.

How can I help you today?

Please type your text here

Send

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SELECTED SAFETY INFORMATION

EXPAND +

Severe and Fatal Immune-Mediated Adverse Reactions

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1L

Nonsquamous mNSCLC
KEYTRUDA, in combination with pemetrexed and platinum chemotherapy, is indicated for the first-line treatment of patients with metastatic nonsquamous non–small cell lung cancer (NSCLC), with no EGFR or ALK genomic tumor aberrations.

SUPERIOR OS
with KEYTRUDA + plat/pem vs plat/pem alone (HR=0.49; 95% CI, 0.38–0.64; *P*<0.0001)[a]

DURABLE OS
with KEYTRUDA + plat/pem vs plat/pem alone at protocol-specified final analysis (HR=0.56; 95% CI, 0.46–0.69)

1L

Squamous mNSCLC
KEYTRUDA, in combination with carboplatin and either paclitaxel or paclitaxel protein-bound, is indicated for the first-line treatment of patients with metastatic squamous NSCLC.

SUPERIOR OS
with KEYTRUDA + carbo + paclitaxel or paclitaxel protein-bound vs carbo + paclitaxel or paclitaxel protein-bound (HR=0.64; 95% CI, 0.49–0.85; *P*=0.0017)[a]

DURABLE OS
with KEYTRUDA + carbo + paclitaxel or paclita ein-bound vs carbo + paclitaxel or paclitaxel protei at protocol-specified final analysis (HR=0.71; 95% CI, 0.58–

Key Chat

SELECTED SAFETY INFORMATION

EXPAND +

Severe and Fatal Immune-Mediated Adverse Reactions

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COLLAPSE

FIRST-LINE COMBINATION THERAPY IN NONSQUAMOUS mNSCLC: KEYTRUDA, in combination with pemetrexed and platinum chemotherapy, is indicated for the first-line treatment of patients with metastatic nonsquamous non-small cell lung cancer (NSCLC), with no EGFR or ALK genomic tumor aberrations.

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FIRST-LINE MONOTHERAPY IN NONSQUAMOUS AND SQUAMOUS ADVANCED NSCLC: KEYTRUDA, as a single agent, is indicated for the first-line treatment of patients with NSCLC expressing PD-L1 tumor proportion score (TPS) ≥1%] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and is stage III where patients are not candidates for surgical resection or definitive chemoradiation, or metastatic.

SECOND-LINE OR GREATER MONOTHERAPY IN NONSQUAMOUS AND SQUAMOUS mNSCLC: KEYTRUDA, as a single agent, is indicated for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥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.

mNSCLC = metastatic NSCLC; EGFR = epidermal growth factor receptor; ALK = anaplastic lymphoma kinase; PD-L1 = programmed death ligand 1.

SELECTED SAFETY INFORMATION

Severe and Fatal Immune-Mediated Adverse Reactions

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- Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Early identification and management are essential to ensure safe use of anti–PD-1/PD-L1 treatments. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.
- Withhold or permanently discontinue KEYTRUDA depending on severity of the immune-mediated adverse reaction. In general, if KEYTRUDA requires interruption or discontinuation, administer systemic corticosteroid therapy (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose adverse reactions are not controlled with corticosteroid therapy.

Immune-Mediated Pneumonitis

- KEYTRUDA can cause immune-mediated pneumonitis. The incidence is higher in patients who have received prior thoracic radiation. Immune-mediated pneumonitis occurred in 3.4% (94/2799) of patients receiving KEYTRUDA, including fatal (0.1%), Grade 4 (0.3%), Grade 3 (0.9%), and Grade 2 (1.3%) reactions. Systemic corticosteroids were required in 67% (63/94) of patients. Pneumonitis led to permanent discontinuation of KEYTRUDA in 1.3% (36) and withholding in 0.9% (26) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement; of these, 23% had recurrence. Pneumonitis resolved in 59% of the 94 patients.
- Pneumonitis occurred in 8% (31/389) of adult patients with cHL receiving KEYTRUDA as a single agent, including Grades 3–4 in 2.3% of patients. Patients received high-dose corticosteroids for a median duration of 10 days (range: 2 days to 53 months). Pneumonitis rates were similar in patients with and without prior thoracic radiation. Pneumonitis led to discontinuation of KEYTRUDA in 5.4% (21) of patients. Of the patients who developed pneumonitis, 42% interrupted KEYTRUDA, 68% discontinued KEYTRUDA, and 77% had resolution.

Immune-Mediated Colitis

- KEYTRUDA can cause immune-mediated colitis, which may present with diarrhea. Cytomegalovirus infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies. Immune-mediated colitis occurred in 1.7% (48/2799) of patients receiving KEYTRUDA, including Grade 4 (<0.1%), Grade 3 (1.1%), and Grade 2 (0.4%) reactions. Systemic corticosteroids were required in 69% (33/48); additional immunosuppressant therapy was required in 4.2% of patients. Colitis led to permanent discontinuation of KEYTRUDA in 0.5% (15) and withholding in 0.5% (13) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement; of these, 23% had recurrence. Colitis resolved in 85% of the 48 patients.

Hepatotoxicity and Immune-Mediated Hepatitis

KEYTRUDA as a Single Agent

- KEYTRUDA can cause immune-mediated hepatitis. Immune-mediated hepatitis occurred in 0.7% (19/2799) of patients receiving KEYTRUDA, including Grade 4 (<0.1%), Grade 3 (0.4%), and Grade 2 (0.1%) reactions. Systemic corticosteroids were required in 68% (13/19) of patients; additional immunosuppressant therapy was required in 11% of patients. Hepatitis led to permanent discontinuation of KEYTRUDA in 0.2% (6) and withholding in 0.3% (9) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement; of these, none had recurrence. Hepatitis resolved in 79% of the 19 patients.

KEYTRUDA With Axitinib

- KEYTRUDA in combination with axitinib can cause hepatic toxicity. Monitor liver enzymes before initiation of and periodically throughout treatment. Consider monitoring more frequently as compared to when the drugs are administered as single agents. For elevated liver enzymes, interrupt KEYTRUDA and axitinib, and consider administering corticosteroids as needed. With the combination of KEYTRUDA and axitinib, Grades 3 and 4 increased alanine aminotransferase (ALT) (20%) and increased aspartate aminotransferase (AST) (13%) were seen at a higher frequency compared to KEYTRUDA alone. Fifty-nine percent of the patients with increased ALT received systemic corticosteroids. In patients with ALT ≥3 times upper limit of normal (ULN) (Grades 2–4, n=116), ALT resolved to Grades 0–1 in 94%. Among the 92 patients who were rechallenged with either KEYTRUDA (n=3) or axitinib (n=34) administered as a single agent or with both (n=55), recurrence of ALT ≥3 times ULN was observed in 1 patient receiving KEYTRUDA, 16 patients receiving axitinib, and 24 patients receiving both. All patients with a recurrence of ALT ≥3 ULN subsequently recovered from the event.

Immune-Mediated Endocrinopathies

Adrenal Insufficiency

- KEYTRUDA can cause primary or secondary adrenal insufficiency. For Grade 2 or higher, initiate symptomatic treatment, including hormone replacement as clinically indicated. Withhold KEYTRUDA depending on severity. Adrenal insufficiency occurred in 0.8% (22/2799) of patients receiving KEYTRUDA, including Grade 4 (<0.1%), Grade 3 (0.3%), and Grade 2 (0.3%) reactions. Systemic corticosteroids were required in 77% (17/22) of patients; of these, the majority remained on systemic corticosteroids. Adrenal insufficiency led to permanent discontinuation of KEYTRUDA in <0.1% (1) and withholding in 0.3% (8) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement.

Hypophysitis

- KEYTRUDA can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field defects. Hypophysitis can cause hypopituitarism. Initiate hormone replacement as indicated. Withhold or permanently discontinue KEYTRUDA depending on severity. Hypophysitis occurred in 0.6% (17/2799) of patients receiving KEYTRUDA, including Grade 4 (<0.1%), Grade 3 (0.3%), and Grade 2 (0.2%) reactions. Systemic corticosteroids were required in 94% (16/17) of patients; of these, the majority remained on systemic corticosteroids. Hypophysitis led to permanent discontinuation of KEYTRUDA in 0.1% (4) and withholding in 0.3% (7) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement.

Thyroid Disorders

- KEYTRUDA can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement for hypothyroidism or institute medical management of hyperthyroidism as clinically indicated. Withhold or permanently discontinue KEYTRUDA depending on severity. Thyroiditis occurred in 0.6% (16/2799) of patients receiving KEYTRUDA, including Grade 2 (0.3%). None discontinued, but KEYTRUDA was withheld in <0.1% (1) of patients.
- Hyperthyroidism occurred in 3.4% (96/2799) of patients receiving KEYTRUDA, including Grade 3 (0.1%) and Grade 2 (0.8%). It led to permanent discontinuation of KEYTRUDA in <0.1% (2) and withholding in 0.3% (7) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement. Hypothyroidism occurred in 8% (227/2799) of patients receiving KEYTRUDA, including Grade 3 (0.1%) and Grade 2 (6.2%). It led to permanent discontinuation of KEYTRUDA in <0.1% (1) and withholding in 0.5% (14) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement. The majority of patients with hypothyroidism required long-term thyroid hormone replacement. The incidence of new or worsening hypothyroidism was higher in 1185 patients with HNSCC, occurring in 16% of patients receiving KEYTRUDA as a single agent or in combination with platinum and FU, including Grade 3 (0.3%) hypothyroidism. The incidence of new or worsening hypothyroidism was higher in 389 adult patients with cHL (17%) receiving KEYTRUDA as a single agent, including Grade 1 (6.2%) and Grade 2 (10.8%) hypothyroidism.

Type 1 Diabetes Mellitus (DM), Which Can Present With Diabetic Ketoacidosis

- Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Withhold KEYTRUDA depending on severity. Type 1 DM occurred in 0.2% (6/2799) of patients receiving KEYTRUDA. It led to permanent discontinuation in <0.1% (1) and withholding in <0.1% (1) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement.

Immune-Mediated Nephritis With Renal Dysfunction

- KEYTRUDA can cause immune-mediated nephritis. Immune-mediated nephritis occurred in 0.3% (9/2799) of patients receiving KEYTRUDA, including Grade 4 (<0.1%), Grade 3 (0.1%), and Grade 2 (0.1%) reactions. Systemic corticosteroids were required in 89% (8/9) of patients. Nephritis led to permanent discontinuation of KEYTRUDA in 0.1% (3) and withholding in 0.1% (3) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement; of these, none had recurrence. Nephritis resolved in 56% of the 9 patients.

Immune-Mediated Dermatologic Adverse Reactions

- KEYTRUDA can cause immune-mediated rash or dermatitis. Exfoliative dermatitis, including Stevens-Johnson syndrome, drug rash with eosinophilia and systemic symptoms, and toxic epidermal necrolysis, has occurred with anti–PD-1/PD-L1 treatments. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate nonexfoliative rashes. Withhold or permanently discontinue KEYTRUDA depending on severity. Immune-mediated dermatologic adverse reactions occurred in 1.4% (38/2799) of patients receiving KEYTRUDA, including Grade 3 (1%) and Grade 2 (0.1%) reactions. Systemic corticosteroids were required in 40% (15/38) of patients. These reactions led to permanent discontinuation in 0.1% (2) and withholding of KEYTRUDA in 0.6% (16) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement; of these, 6% had recurrence. The reactions resolved in 79% of the 38 patients.

Other Immune-Mediated Adverse Reactions

- The following clinically significant immune-mediated adverse reactions occurred at an incidence of <1% (unless otherwise noted) in patients who received KEYTRUDA or were reported with the use of other anti–PD-1/PD-L1 treatments. Severe or fatal cases have been reported for some of these adverse reactions. *Cardiac/Vascular:* Myocarditis, pericarditis, vasculitis. *Endocrine:* Diabetes insipidus; adrenal insufficiency. *Gastrointestinal:* Pancreatitis, enteritis, duodenitis, gastritis, duodenitis. *Musculoskeletal and Connective Tissue:* Myositis/polymyositis, rhabdomyolysis (and associated sequelae, including renal failure), arthritis (1.5%), polymyalgia rheumatica; *Endocrine:* Hypoparathyroidism; *Hematologic/Immune:* Hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenic purpura, solid organ transplant rejection.

Infusion-Related Reactions

- KEYTRUDA can cause severe or life-threatening infusion-related reactions, including hypersensitivity and anaphylaxis, which have been reported in 0.2% of 2799 patients receiving KEYTRUDA. Monitor for signs and symptoms of infusion-related reactions. Interrupt or slow the rate of infusion for Grade 1 or Grade 2 reactions. For Grade 3 or Grade 4 reactions, stop infusion and permanently discontinue KEYTRUDA.

Complications of Allogeneic Hematopoietic Stem Cell Transplantation (HSCT)

- Fatal and other serious complications can occur in patients who receive allogeneic HSCT before or after anti–PD-1/PD-L1 treatments. Transplant-related complications include hyperacute graft-versus-host-disease (GVHD), acute graft-versus-host-disease, hepatic veno-occlusive disease after reduced intensity conditioning and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between anti–PD-1/PD-L1 treatments and allogeneic HSCT. Follow patients closely for evidence of these complications and intervene promptly. Consider the benefit vs risks of using anti–PD-1/PD-L1 treatments prior to or after an allogeneic HSCT.

Increased Mortality in Patients With Multiple Myeloma

- In 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 an anti–PD-1/PD-L1 treatment in this combination is not recommended outside of controlled trials.

Embryofetal Toxicity

- Based on its mechanism of action, KEYTRUDA can cause fetal harm when administered to a pregnant woman. Advise women of this potential risk. In females of reproductive potential, verify pregnancy status prior to initiating KEYTRUDA and advise them to use effective contraception during treatment and for 4 months after the last dose.

Adverse Reactions

- In KEYNOTE-006, KEYTRUDA was discontinued due to adverse reactions in 9% of 555 patients with advanced melanoma; adverse reactions leading to permanent 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%). The most common adverse reactions (≥20%) with KEYTRUDA were fatigue (28%), diarrhea (26%), rash (24%), and nausea (21%).
- In KEYNOTE-054, KEYTRUDA was permanently discontinued due to adverse reactions in 14% of 509 patients; the most common (≥1%) were pneumonitis (1.4%), colitis (1.2%), and diarrhea (1%). Serious adverse reactions occurred in 25% of patients receiving KEYTRUDA. The most common adverse reaction (≥20%) with KEYTRUDA was diarrhea (28%).
- In KEYNOTE-189, when KEYTRUDA was administered with pemetrexed and platinum chemotherapy in metastatic nonsquamous NSCLC, KEYTRUDA was discontinued due to adverse reactions in 20% of 405 patients. The most common adverse reactions resulting in permanent discontinuation of KEYTRUDA were pneumonitis (3%) and acute kidney injury (2%). The most common adverse reactions (≥20%) with KEYTRUDA were nausea (56%), fatigue (56%), constipation (35%), diarrhea (31%), decreased appetite (28%), rash (25%), vomiting (24%), cough (21%), dyspnea (21%), and pyrexia (20%).
- In KEYNOTE-407, when KEYTRUDA was administered with carboplatin and either paclitaxel or paclitaxel protein-bound in metastatic squamous NSCLC, KEYTRUDA was discontinued due to adverse reactions in 15% of 101 patients. The most frequent serious adverse reactions reported in at least 2% of patients were febrile neutropenia, pneumonitis, and urinary tract infection. Adverse reactions observed in KEYNOTE-407 were similar to those observed in KEYNOTE-189 with the exception that increased incidences of alopecia (47% vs 36%) and peripheral neuropathy (31% vs 25%) were observed in the KEYTRUDA and chemotherapy arm compared to the placebo and chemotherapy arm in KEYNOTE-407.
- In KEYNOTE-042, KEYTRUDA was discontinued due to adverse reactions in 19% of 636 patients with advanced NSCLC; the most common were pneumonitis (3%), death due to unknown cause (1.6%), and pneumonia (1.4%). The most frequent serious adverse reactions reported in at least 2% of patients were pneumonia (7%), pneumonitis (3.9%), pulmonary embolism (2.4%), and pleural effusion (2.2%). The most common adverse reaction (≥20%) was fatigue (25%).
- In KEYNOTE-010, KEYTRUDA monotherapy was discontinued due to adverse reactions in 8% of 682 patients with metastatic NSCLC; the most common was pneumonitis (1.8%). The most common adverse reactions (≥20%) were decreased appetite (25%), fatigue (25%), dyspnea (23%), and nausea (20%).
- In KEYNOTE-048, KEYTRUDA monotherapy was discontinued due to adverse events in 12% of 300 patients with HNSCC; the most common adverse reactions leading to permanent discontinuation were sepsis (1.7%) and pneumonia (1.3%). The most common adverse reactions (≥20%) were fatigue (33%), constipation (20%), and rash (20%).
- In KEYNOTE-048, when KEYTRUDA was administered in combination with platinum (cisplatin or carboplatin) and FU chemotherapy, KEYTRUDA was discontinued due to adverse reactions in 16% of 276 patients with HNSCC. The most common adverse reactions resulting in permanent discontinuation of KEYTRUDA were pneumonia (2.5%), pneumonitis (1.8%), and septic shock (1.4%). The most common adverse reactions (≥20%) were nausea (51%), fatigue (49%), constipation (37%), vomiting (32%), mucosal inflammation (31%), diarrhea (29%), decreased appetite (29%), stomatitis (26%), and cough (22%).
- 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 (≥20%) 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 who received KEYTRUDA as a monotherapy, with the exception of increased incidences of facial edema and new or worsening hypothyroidism.
- In KEYNOTE-204, KEYTRUDA was discontinued due to adverse reactions in 14% of 148 patients with cHL. Serious adverse reactions occurred in 30% of patients receiving KEYTRUDA; those ≥1% were pneumonitis, pneumonia, pyrexia, myocarditis, acute kidney injury, febrile neutropenia, and sepsis. Three patients died from causes other than disease progression; 2 from complications after allogeneic HSCT and 1 from unknown cause. The most common adverse reactions (≥20%) were upper respiratory tract infection (41%), musculoskeletal pain (32%), diarrhea (22%), and pyrexia, fatigue, rash, and cough (20% each).
- In KEYNOTE-087, KEYTRUDA was discontinued due to adverse reactions in 5% of 210 patients with cHL. Serious adverse reactions occurred in 16% of patients; those ≥1% were pneumonia, pneumonitis, pyrexia, dyspnea, GVHD, and herpes zoster. Two patients died from causes other than disease progression: 1 from GVHD after subsequent allogeneic HSCT and 1 from septic shock. The most common adverse reactions (≥20%) were fatigue (26%), pyrexia (24%), cough (24%), musculoskeletal pain (21%), diarrhea (20%), and rash (20%).
- In KEYNOTE-170, KEYTRUDA was discontinued due to adverse reactions in 8% of 53 patients with PMBCL. Serious adverse reactions occurred in 26% of patients and included arrhythmia (4%), cardiac tamponade (2%), myocardial infarction (2%), pericardial effusion (2%), and pericarditis (2%). Six (11%) patients died within 30 days of start of treatment. The most common adverse reactions (≥20%) were musculoskeletal pain (30%), upper respiratory tract infection and pyrexia (28% each), cough (26%), fatigue (23%), and dyspnea (21%).
- In KEYNOTE-052, KEYTRUDA was discontinued due to adverse reactions in 11% of 370 patients with locally advanced or metastatic urothelial carcinoma. Serious adverse reactions occurred in 42% of patients; those ≥2% were urinary tract infection, hematuria, acute kidney injury, pneumonitis, and urosepsis. The most common adverse reactions (≥20%) were fatigue (38%), musculoskeletal pain (24%), decreased appetite (22%), constipation (21%), rash (21%), and diarrhea (20%).
- 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 was pneumonitis (1.9%). Serious adverse reactions occurred in 39% of KEYTRUDA-treated patients; those ≥2% were urinary tract infection, pneumonia, anemia, and pneumonitis. The most common adverse reactions (≥20%) in patients who received KEYTRUDA were fatigue (38%), musculoskeletal pain (32%), pruritus (23%), decreased appetite (21%), nausea (21%), and rash (20%).
- In KEYNOTE-057, KEYTRUDA was discontinued due to adverse reactions in 11% of 148 patients with high-risk NMIBC. The most common adverse reaction resulting in permanent discontinuation of KEYTRUDA was pneumonitis (1.4%). Serious adverse reactions occurred in 28% of patients; those ≥2% were pneumonia (3%), cardiac ischemia (2%), colitis (2%), pulmonary embolism (2%), sepsis (2%), and urinary tract infection (2%). The most common adverse reactions (≥20%) were fatigue (29%), diarrhea (24%), and rash (24%).
- Adverse reactions occurring in patients with MSI-H or dMMR CRC were similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy.
- Adverse reactions occurring in patients with gastric cancer were similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy.
- In KEYNOTE-590, when KEYTRUDA was administered with cisplatin and fluorouracil to patients with metastatic or locally advanced esophageal or GEJ (tumors with epicenter 1 to 5 centimeters above the GEJ) carcinoma who were not candidates for surgical resection or definitive chemoradiation, KEYTRUDA was discontinued due to adverse reactions in 15% of 370 patients. The most common adverse reactions resulting in permanent discontinuation of KEYTRUDA (≥1%) were pneumonitis (1.6%), acute kidney injury (1.1%), and pneumonia (1.1%). The most common adverse reactions (≥20%) with KEYTRUDA in combination with chemotherapy were nausea (67%), fatigue (57%), decreased appetite (44%), constipation (40%), diarrhea (36%), vomiting (34%), stomatitis (27%), and weight loss (24%).
- Adverse reactions occurring in patients with esophageal cancer who received KEYTRUDA as a monotherapy were similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy.
- In KEYNOTE-158, KEYTRUDA was discontinued due to adverse reactions in 8% of 98 patients with recurrent or metastatic cervical cancer. Serious adverse reactions occurred in 39% of patients receiving KEYTRUDA; the most frequent (≥1%) were fistulas, hemorrhage, pneumonitis, and infections [except urinary tract infections] (4.1% each). The most common adverse reactions (≥20%) were fatigue (43%), musculoskeletal pain (27%), diarrhea (23%), pain and abdominal pain (22% each), and decreased appetite (21%).
- Adverse reactions occurring in patients with hepatocellular carcinoma (HCC) were generally similar to those in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy, with the exception of increased incidences of ascites (8% Grades 3–4) and immune-mediated hepatitis (2.9%). Laboratory abnormalities (Grades 3–4) that occurred at a higher incidence were elevated AST (20%), ALT (9%), and hyperbilirubinemia (10%).
- Among the 50 patients with MCC enrolled in study KEYNOTE-017, adverse reactions occurring in patients with MCC were generally similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy. Laboratory abnormalities (Grades 3–4) that occurred at a higher incidence were elevated AST (11%) and hyperglycemia (19%).
- In KEYNOTE-426, when KEYTRUDA was administered in combination with axitinib, fatal adverse reactions occurred in 3.3% of 429 patients. Serious adverse reactions occurred in 40% of patients, the most frequent (≥1%) were hepatotoxicity (7%), dyspnea (4.2%), acute kidney injury (2.3%), dehydration (1%), and pneumonitis (1%). Permanent discontinuation due to adverse reactions occurred in 31% of patients; KEYTRUDA only (13%), axitinib only (13%), and the combination (8%); the most common were hepatotoxicity (13%), diarrhea/colitis (1.9%), acute kidney injury (1.6%), and cerebrovascular accident (1.2%). The most common adverse reactions (≥20%) were diarrhea (56%), fatigue/asthenia (52%), hypertension (48%), hepatotoxicity (39%), hypothyroidism (35%), decreased appetite (30%), palmar-plantar erythrodysesthesia (28%), nausea (28%), stomatitis/mucosal inflammation (27%), dysphonia (25%), rash (25%), cough (21%), and constipation (21%).
- Adverse reactions occurring in patients with TMB-H cancer were similar to those occurring in patients with other solid tumors who received KEYTRUDA as a single agent.
- Adverse reactions occurring in patients with cSCC were similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy.
- In KEYNOTE-355, when KEYTRUDA and chemotherapy (paclitaxel, paclitaxel protein-bound, or gemcitabine and carboplatin) were administered to patients with locally recurrent unresectable or metastatic TNBC who had not been previously treated with chemotherapy in the metastatic setting (n=596), fatal adverse reactions occurred in 2.5% of patients; cardio-respiratory arrest (0.7%) and septic shock (0.3%). Serious adverse reactions occurred in 30% of patients receiving KEYTRUDA in combination with chemotherapy; the serious reactions in ≥2% were pneumonia (2.9%), anemia (2.2%), and thrombocytopenia (2%). KEYTRUDA was discontinued in 11% of patients due to adverse reactions. The most common reactions resulting in permanent discontinuation (≥1%) were increased ALT (2.2%), increased AST (1.5%), and pneumonitis (1.2%). The most common adverse reactions (≥20%) in patients receiving KEYTRUDA in combination with chemotherapy were fatigue (48%), nausea (44%), alopecia (34%), diarrhea and constipation (28% each), vomiting and rash (26% each), cough (23%), decreased appetite (21%), and headache (20%).

Lactation

- Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment and for 4 months after the final dose.

Pediatric Use

- In KEYNOTE-051, 161 pediatric patients (62 pediatric patients aged 6 months to younger than 12 years and 99 pediatric patients aged 12 years to 17 years) were administered KEYTRUDA 2 mg/kg every 3 weeks. The median duration of exposure was 2.1 months (range: 1 day to 24 months).
- Adverse reactions that occurred at a ≥10% higher rate in pediatric patients when compared to adults were pyrexia (33%), vomiting (30%), leukopenia (30%), upper respiratory tract infection (29%), neutropenia (26%), headache (25%), and Grade 3 anemia (17%).

cHL = classical Hodgkin lymphoma; CRC = colorectal cancer; cSCC = cutaneous squamous cell carcinoma; dMMR = mismatch repair deficient; FU = fluorouracil; GEJ = gastroesophageal junction; HNSCC = head and neck squamous cell carcinoma; MCC = Merkel cell carcinoma; MSI-H = microsatellite instability-high; NMIBC = non-muscle invasive bladder cancer; NSCLC = non-small cell lung cancer; PMBCL = primary mediastinal large B-cell lymphoma; TMB-H = tumor mutational burden-high; TNBC = triple-negative breast cancer.

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information. The Medication Guide also is available.

HELPING TO REDEFINE SURVIVAL EXPECTATIONS for your patients in the following indications:

1L

Nonsquamous mNSCLC
KEYTRUDA, in combination with pemetrexed and platinum chemotherapy, is indicated for the first treatment of patients with metastatic nonsquamous non–small cell lung cancer (NSCLC), with no EGFR or ALK genomic tumor aberrations.

SUPERIOR OS
with KEYTRUDA + platinum vs platinum alone (HR=0.49; 95% CI, 0.38-0.64; *P*<0.0001)[1]

DURABLE OS
with KEYTRUDA + platinum vs platinum alone at protocol-specified final analysis (HR=0.56; 95% CI, 0.46-0.69)

Watch Video Reviewing Clinical Data

View Efficacy Data

Learn About Appropriate Patients

1L

Squamous mNSCLC
KEYTRUDA, in combination with carboplatin and either paclitaxel or paclitaxel protein-bound, is indicated for the first-line treatment of patients with metastatic squamous NSCLC.

SUPERIOR OS
with KEYTRUDA + carbo + paclitaxel or paclitaxel protein-bound vs carbo + paclitaxel or paclitaxel protein-bound at protocol-specified final analysis (HR=0.71; 95% CI, 0.58–0.88)

Watch Video Reviewing Clinical Data

View Efficacy Data

Learn About Appropriate Patients

1L

Monotherapy in nonsquamous and squamous advanced NSCLC
KEYTRUDA, as a single agent, is indicated for the first-line treatment of patients with NSCLC expressing programmed death ligand 1 (PD-L1) [tumor proportion score (TPS) ≥1%] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and is stage III where patients are not candidates for surgical resection or definitive chemoradiation, or metastatic.

SUPERIOR OS
with KEYTRUDA vs platinum-based chemotherapy in patients with PD-L1 ≥1% (HR=0.81; 95% CI, 0.71–0.93; *P*=0.0036)[2]

View Efficacy Data

Learn About Appropriate Patients

FOR A BROAD RANGE OF PATIENTS

Superior overall survival with KEYTRUDA first line in multiple phase 3 studies.[1-4]

*HR based on the stratified Cox proportional hazard model. *P* value based on stratified log-rank test.
†Compared to a *P* value boundary of 0.0291.

1L = first line; ALK = anaplastic lymphoma kinase; carbo = carboplatin; CI = confidence interval; EGFR = epidermal growth factor receptor; HR = hazard ratio; mNSCLC = metastatic NSCLC; OS = overall survival; paclitaxel = cisplatin or carboplatin and paclitaxel.

Key Clinical Trial

FIRST-LINE COMBINATION THERAPY IN NONSQUAMOUS mNSCLC: KEYTRUDA, in combination with pemetrexed and platinum chemotherapy, is indicated for the first-line treatment of patients with metastatic nonsquamous non–small cell lung cancer (NSCLC), with no EGFR or ALK genomic tumor aberrations.

FIRST-LINE COMBINATION THERAPY IN SQUAMOUS mNSCLC: KEYTRUDA, in combination with carboplatin and either paclitaxel or paclitaxel protein-bound, is indicated for the first-line treatment of patients with metastatic squamous NSCLC.

FIRST-LINE MONOTHERAPY IN NONSQUAMOUS AND SQUAMOUS ADVANCED NSCLC: KEYTRUDA, as a single agent, is indicated for the first-line treatment of patients with NSCLC expressing PD-L1 [tumor proportion score (TPS) ≥1%] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and is stage III where patients are not candidates for surgical resection or definitive chemoradiation, or metastatic.

SECOND-LINE OR GREATER MONOTHERAPY IN NONSQUAMOUS AND SQUAMOUS mNSCLC: KEYTRUDA, as a single agent, is indicated for the treatment of patients with metastatic NSCLC and whose tumors express PD-L1 (TPS ≥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.

mNSCLC = metastatic NSCLC; EGFR = epidermal growth factor receptor; ALK = anaplastic lymphoma kinase; PD-L1 = programmed death ligand 1

SELECTED SAFETY INFORMATION

Severe and Fatal Immune-Mediated Adverse Reactions

- KEYTRUDA is a monoclonal antibody that belongs to a class of drugs that bind to either the programmed death receptor-1 (PD-1) or the programmed death ligand 1 (PD-L1), blocking the PD-1/PD-L1 pathway, thereby removing inhibition of the immune response, potentially breaking peripheral tolerance and inducing immune-mediated adverse reactions. Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue, can affect more than one body system simultaneously, and can occur at any time after starting treatment or after discontinuation of treatment. Important immune-mediated adverse reactions listed here may not include all possible severe and fatal immune-mediated adverse reactions.
- Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Early identification and management are essential to ensure safe use of anti-PD-1/PD-L1 treatments. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management, including corticosteroids, promptly to begin treatment of toxicity, as appropriate.
- Withhold or permanently discontinue KEYTRUDA depending on severity of the immune-mediated adverse reaction. In general, if KEYTRUDA requires interruption or discontinuation, administer systemic corticosteroids (1 to 2 mg/kg prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose adverse reactions are not controlled with corticosteroid therapy.

Immune-Mediated Pneumonitis

- KEYTRUDA can cause immune-mediated pneumonitis. The incidence is higher in patients who have received prior thoracic radiation. Immune-mediated pneumonitis occurred in 3% (94/2799) of patients receiving KEYTRUDA, including death (0.1%), Grade 4 (0.1%), Grade 3 (0.9%), and Grade 2 (1.3%) reactions. Systemic corticosteroids were required in 67% (63/94) of patients. Pneumonitis led to permanent discontinuation of KEYTRUDA in 1.3% (36) and withholding in 0.9% (20) of patients, all patients who were withheld resinitiated KEYTRUDA after symptom improvement; of these, 23% had recurrence. Pneumonitis resolved in 59% of the 94 patients.
- Pneumonitis occurred in 8% (31/389) of adult patients with cHL receiving KEYTRUDA as a single agent, including Grades 3–4 in 2.3% of patients. Patients received high-dose corticosteroids for a median duration of 10 days (range: 2 days to 53 months). Pneumonitis rates were similar in patients with and without prior thoracic radiation. Pneumonitis led to discontinuation of KEYTRUDA in 5.4% (21) of patients. Of the patients who developed pneumonitis, 42% interrupted KEYTRUDA, 68% discontinued KEYTRUDA, and 77% had resolution.

Immune-Mediated Colitis

- KEYTRUDA can cause immune-mediated colitis, which may present with diarrhea. Cytomegalovirus infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies. Immune-mediated colitis occurred in 1.7% (48/2799) of patients receiving KEYTRUDA, including Grade 4 (<0.1%), Grade 3 (1.1%), and Grade 2 (0.4%) reactions. Systemic corticosteroids were required in 67% (63/94) of patients. Pneumonitis led to permanent discontinuation of KEYTRUDA in 1.3% (36) and withholding in 0.9% (20) of patients, all patients who were withheld resinitiated KEYTRUDA after symptom improvement; of these, 23% had recurrence. Pneumonitis resolved in 59% of the 94 patients.

Hepatotoxicity and Immune-Mediated Hepatitis

KEYTRUDA as a Single Agent

- KEYTRUDA can cause immune-mediated hepatitis. Immune-mediated hepatitis occurred in 0.7% (19/2799) of patients receiving KEYTRUDA, including Grade 4 (<0.1%), Grade 3 (0.4%), and Grade 2 (0.1%) reactions. Systemic corticosteroids were required in 68% (13/19) of patients; additional immunosuppressant therapy was required in 1% of patients. Hepatitis led to permanent discontinuation of KEYTRUDA in 0.2% (4) and withholding in 0.3% (9) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement; of these, none had recurrence. Hepatitis resolved in 79% of the 19 patients.

KEYTRUDA With Axitinib

- KEYTRUDA in combination with axitinib can cause hepatic toxicity. Monitor liver enzymes before initiation of and periodically throughout treatment. Consider monitoring more frequently as compared to when drugs are administered as single agent. In patients with cancer of the kidney, interrupt KEYTRUDA and axitinib, and consider administering corticosteroids as needed. With the combination of KEYTRUDA and axitinib, Grades 3 and 4 increased alanine aminotransferase (ALT) (20%) and increased aspartate aminotransferase (AST) (13%) were seen in a phase 3 study in treatment-naïve RCC patients. Of the 20% Grade 3 and 4 ALT events, all patients with increased ALT received systemic corticosteroids. In patients with ALT 3 times upper limit of normal (ULN) (Grades 2–4, n=116), ALT resolved to Grades 0–1 in 84%. Among the 84% patients who were rechallenged with either KEYTRUDA (n=5) or axitinib (n=21), ALT recurred as a single agent in 0% (0/5) and recurrence of ALT 3 times ULN was observed in 1 patient receiving KEYTRUDA. 16 patients receiving axitinib, and 24 patients receiving both. All patients with a recurrence of ALT ≥3 ULN subsequently recovered from the event.

Immune-Mediated Endocrinopathies

Adrenal Insufficiency

- KEYTRUDA can cause primary or secondary adrenal insufficiency. For Grade 2 or higher, initiate symptomatic treatment, including hormone replacement as clinically indicated. Withhold KEYTRUDA depending on severity. Adrenal insufficiency occurred in 0.8% (22/2799) of patients receiving KEYTRUDA, including Grade 4 (<0.1%), Grade 3 (0.3%), and Grade 2 (0.3%) reactions. Systemic corticosteroids were required in 77% (17/22) of patients; of these, the majority remained on systemic corticosteroids. Adrenal insufficiency led to permanent discontinuation of KEYTRUDA in <0.1% (1) and withholding in 0.3% (8) of patients. All patients who were withheld resinitiated KEYTRUDA after symptom improvement.

Hypophysitis

- KEYTRUDA can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, phlebitis, or visual field defects. Hypophysitis can cause hypopituitarism. Initiate hormone replacement as indicated. Withhold or permanently discontinue KEYTRUDA depending on severity. Hypophysitis occurred in 0.6% (17/2799) of patients receiving KEYTRUDA, including Grade 4 (<0.1%), Grade 3 (0.3%), and Grade 2 (0.2%) reactions. Systemic corticosteroids were required in 94% (16/17) of patients; of these, the majority remained on systemic corticosteroids. Hypophysitis led to permanent discontinuation of KEYTRUDA in 0.1% (4) and withholding in 0.3% (7) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement.

Thyroid Disorders

- KEYTRUDA can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement for hypothyroidism or institute medical management of hyperthyroidism as clinically indicated. Withhold or permanently discontinue KEYTRUDA depending on severity. Thyroiditis occurred in 0.6% (16/2799) of patients receiving KEYTRUDA, including Grade 2 (0.3%). None discontinued, but KEYTRUDA was withheld in <0.1% (1) of patients.
- Hyperthyroidism occurred in 3.4% (96/2799) of patients receiving KEYTRUDA, including Grade 3 (0.1%) and Grade 2 (0.8%). It led to permanent discontinuation of KEYTRUDA in <0.1% (2) and withholding in 0.3% (7) of patients. All patients who were withheld resinitiated KEYTRUDA after symptom improvement. Hypothyroidism occurred in 8% (237/2799) of patients receiving KEYTRUDA, including Grade 3 (0.1%) and Grade 2 (6.2%). It led to permanent discontinuation of KEYTRUDA in <0.1% (1) of patients. All patients who were withheld resinitiated KEYTRUDA after symptom improvement. The majority of patients with hypothyroidism required long-term thyroid hormone replacement. The incidence of new or worsening hypothyroidism was higher in 1185 patients with HNSCC, including 2.4% (28) who developed hypothyroidism as a single agent; or concurrent with chemotherapy and PD-L1 blockade (Study 1). In 1185 hypothyroidism. The incidence of new or worsening hypothyroidism was higher in 389 adult patients with cHL (17%) receiving KEYTRUDA as a single agent, including Grade 1 (6.2%) and Grade 2 (10.8%) hypothyroidism.

Type 1 Diabetes Mellitus (DM), Which Can Present With Diabetic Ketoacidosis

- Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Withhold KEYTRUDA depending on severity. Type 1 DM occurred in 0.2% (6/2799) of patients receiving KEYTRUDA, including Grade 3 (0.1%) and Grade 2 (0.1%). It led to permanent discontinuation of KEYTRUDA in <0.1% (1) of patients. All patients who were withheld resinitiated KEYTRUDA after symptom improvement.

Immune-Mediated Nephritis With Renal Dysfunction

- KEYTRUDA can cause immune-mediated nephritis. Immune-mediated nephritis occurred in 0.3% (9/2799) of patients receiving KEYTRUDA, including Grade 4 (<0.1%), Grade 3 (0.1%), and Grade 2 (0.1%) reactions. Systemic corticosteroids were required in 88% (8/9) of patients. Nephritis led to permanent discontinuation of KEYTRUDA in 0.1% (3) and withholding in 0.1% (3) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement; of these, none had recurrence. Nephritis resolved in 56% of the 9 patients.

Immune-Mediated Dermatologic Adverse Reactions

- KEYTRUDA can cause immune-mediated rash or dermatitis. Exfoliative dermatitis, including Stevens-Johnson syndrome, drug rash with eosinophilia and systemic symptoms, and toxic epidermal necrolysis, has occurred with anti-PD-1/PD-L1 treatment. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate cases. Withhold or permanently discontinue KEYTRUDA depending on severity. Immune-mediated dermatologic adverse reactions occurred in 1.4% (38/2799) of patients receiving KEYTRUDA, including Grade 3 (1%) and Grade 2 (0.1%) reactions. Systemic corticosteroids were required in 45% (17/38) of patients. These reactions led to permanent discontinuation of KEYTRUDA in 0.6% (16) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement; of these, 6% had recurrence. The reactions resolved in 79% of the 38 patients.

Other Immune-Mediated Adverse Reactions

- The following clinically significant immune-mediated adverse reactions occurred at an incidence of <1% (unless otherwise noted) in patients who received KEYTRUDA or were treated with the use of other anti-PD-1/PD-L1 treatments. Severe or fatal cases have been reported for some of these adverse reactions. Cardiac/Vascular: Myocarditis, pericarditis, vasculitis; Nervous System: Meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis (including exacerbation); Endocrine: Diabetic ketoacidosis; Gastrointestinal: Pancreatitis, to include fatal cases, enteritis, pancreatitis, and other rare gastrointestinal toxicities occur. Some cases can be associated with retinal detachment. Various grades of visual impairment, including blindness, can occur. If uveitis occurs in combination with other immune-mediated adverse reactions, consider a Vogt-Koyanagi-Harada-like syndrome, as this may impede treatment with systemic corticosteroids and steroid-sparing therapy (without an identified infectious cause). These complications may occur despite intervening therapy between anti-PD-1/PD-L1 treatment and ocular surgery. Musculoskeletal: Arthritis, polymyalgia rheumatica, sarcoidosis, rare cases of myositis (1.5%), polymyalgia rheumatica; *Endocrine*: Hypoparathyroidism; *Hematologic/Immune*: Hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, rare cases of graft-versus-host disease (GVHD), solid organ transplant rejection.

Infusion-Related Reactions

- KEYTRUDA can cause severe or life-threatening infusion-related reactions, including hypersensitivity and anaphylaxis, which have been reported in 0.2% of 2799 patients receiving KEYTRUDA. Monitor for signs and symptoms of infusion-related reactions. Interrupt or slow the rate of infusion for Grade 1 or Grade 2 reactions. For Grade 3 or Grade 4 reactions, stop infusion and permanently discontinue KEYTRUDA.

Complications of Allogeneic Hematopoietic Stem Cell Transplantation (HSCT)

- Fatal and other serious complications can occur in patients who receive allogeneic HSCT before or after anti-PD-1/PD-L1 treatments. Transplant-related complications include hyperacute graft-versus-host disease (GVHD), acute and chronic GVHD, hepatic veno-occlusive disease after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between anti-PD-1/PD-L1 treatment and allogeneic HSCT. Follow patients closely for evidence of these complications and intervene promptly. Consider the benefit vs risks of using anti-PD-1/PD-L1 treatments prior to or after an allogeneic HSCT.

Increased Mortality in Patients With Multiple Myeloma

- In 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 an anti-PD-1/PD-L1 treatment in this combination is not recommended outside of controlled trials.

Embryofetal Toxicity

- Based on its mechanism of action, KEYTRUDA can cause fetal harm when administered to a pregnant woman. Advise women of this potential risk. In females of reproductive potential, verify pregnancy status prior to initiating KEYTRUDA and advise them to use effective contraception during treatment and for 4 months after the last dose.

Adverse Reactions

- In NEYNOTE-006, KEYTRUDA was discontinued due to adverse reactions in 9% of 555 patients with advanced melanoma; adverse reactions leading to permanent discontinuation in more than one patient were colitis (1.4%), autoimmune hepatitis (1.2%), allergic reaction (0.4%), pulmonaritis (0.4%), and cardiac failure (0.4%). The most common adverse reactions (≥20%) with KEYTRUDA were fatigue (28%), diarrhea (26%), rash (24%), and nausea (21%).
- In KEYNOTE-024, KEYTRUDA was permanently discontinued due to adverse reactions in 14% of 508 patients; the most common (≥1%) were pneumonitis (1.4%), colitis (1.2%), and diarrhea (1%). Serious adverse reactions occurred in 25% of patients receiving KEYTRUDA. The most common adverse reaction (≥20%) with KEYTRUDA was diarrhea (22%).
- In KEYNOTE-189, when KEYTRUDA was administered with pemetrexed and platinum chemotherapy in metastatic nonsquamous NSCLC, KEYTRUDA was discontinued due to adverse reactions in 20% of 405 patients. The most common adverse reactions (≥5%) in permanent discontinuation of KEYTRUDA were pneumonitis (3%) and acute kidney injury (2%). The most common adverse reactions (≥20%) with KEYTRUDA were nausea (56%), fatigue (42%), constipation (35%), diarrhea (31%), decreased appetite (28%), rash (25%), vomiting (24%), cough (21%), dyspnea (21%), and pyrexia (20%).
- In KEYNOTE-407, when KEYTRUDA was administered with carboplatin and either paclitaxel or protein-bound in metastatic squamous NSCLC, KEYTRUDA was discontinued due to adverse reactions in 15% of 101 patients. The most frequent serious adverse reactions reported in at least 2% of patients were febrile neutropenia, anemia, and urinary tract infection. The most common adverse reactions (≥20%) in KEYTRUDA treated patients were anemia (51%), decreased appetite (37%), nausea (31%), alopecia (24%), and peripheral neuropathy (21% vs 25%) were observed in the KEYTRUDA and chemotherapy arms, respectively, in the pooled safety population in KEYNOTE-407.
- In NEYNOTE-042, KEYTRUDA was discontinued due to adverse reactions in 19% of 636 patients with advanced NSCLC; the most common were pneumonitis (3%), death due to unknown cause (2%), and acute kidney injury (2%). The most frequent serious adverse reactions reported in at least 2% of patients were pneumonitis (7%), pneumonia (3.9%), pulmonary embolism (2.4%), and pleural effusion (2.2%). The most common adverse reaction (≥20%) was fatigue (25%).
- In KEYNOTE-045, KEYTRUDA monotherapy was discontinued due to adverse reactions in 8% of 266 patients with advanced urothelial cancer; the most common were pneumonitis (1.8%). The most common adverse reactions (≥20%) were decreased appetite (25%), fatigue (25%), dyspnea (23%), and nausea (20%).
- In 945 patients in KEYNOTE-189 monotherapy was discontinued due to adverse events in 12% of 300 patients with HNSCC; the most common adverse reactions leading to permanent discontinuation were pneumonitis (2.3%), and pneumonia (1.3%). The most common adverse reactions (≥20%) were fatigue (44%), constipation (25%), and nausea (20%).
- In NEYNOTE-048, when KEYTRUDA was administered in combination with platinum (cisplatin or carboplatin) and FU chemotherapy, KEYTRUDA was discontinued due to adverse reactions in 16% of 276 patients with HNSCC. The most common adverse reactions resulting in permanent discontinuation of KEYTRUDA were pneumonia (2.5%), pneumonitis (1.8%), and septic shock (1.4%). The most common adverse reactions (≥20%) were nausea (51%), fatigue (49%), constipation (37%), vomiting (32%), mucosal inflammation (31%), diarrhea (29%), decreased appetite (29%), stomatitis (26%), and cough (22%).
- In KEYNOTE-012, KEYTRUDA was discontinued due to adverse reactions in 17% of 192 patients with hepatocellular carcinoma. 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 (≥20%) 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 who received KEYTRUDA as a monotherapy, with the exception of increased incidences of fatigue and hypothyroidism.
- In KEYNOTE-204, KEYTRUDA was discontinued due to adverse reactions in 14% of 148 patients with cHL. Serious adverse reactions occurred in 30% of patients receiving KEYTRUDA; those ≥1% were pneumonitis, pneumonia, pyrexia, hypercalcemia, acute kidney injury, febrile neutropenia, diarrhea, and sepsis. Three patients died from causes other than disease progression; 2 from complications after allogeneic HSCT and 1 from unknown cause. The most common adverse reactions (≥20%) were upper respiratory tract infection (41%), musculoskeletal pain (32%), diarrhea (23%), fatigue (22%), rash, and cough (20% each).
- In KEYNOTE-087, KEYTRUDA was discontinued due to adverse reactions in 5% of 210 patients with cHL. Serious adverse reactions occurred in 16% of patients; those ≥1% were pneumonia, pneumonitis, pyrexia, dyspnea, GVHD, and herpes zoster. Two patients died from causes other than disease progression; 1 from GVHD after subsequent allogeneic HSCT and 1 from septic shock. The most common adverse reactions (≥20%) were fatigue (26%), pyrexia (24%), cough (24%), musculoskeletal pain (21%), diarrhea (20%), and rash (20%).
- In KEYNOTE-170, KEYTRUDA was discontinued due to adverse reactions in 8% of 53 patients with PMBCL. Serious adverse reactions occurred in 26% of patients and included pyrexia (4%), cardiac tamponade (2%), myocardial infarction (2%), pericardial effusion (2%), and pericarditis (2%). Six (11%) patients died within 30 days of start of treatment. The most common adverse reactions (≥20%) were musculoskeletal pain (40%), upper respiratory tract infection and pyrexia (28% each), cough (26%), fatigue (23%), and dyspnea (21%).
- In KEYNOTE-052, KEYTRUDA was discontinued due to adverse reactions in 11% of 370 patients with locally advanced or metastatic urothelial carcinoma. Serious adverse reactions occurred in 42% of patients; those ≥2% were urinary tract infection, hematuria, acute kidney injury, pneumonia, and urosepsis. The most common adverse reactions (≥20%) were peripheral edema (34%), musculoskeletal pain (24%), decreased appetite (22%), constipation (21%), rash (20%), and diarrhea (20%).
- 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%). Serious adverse reactions occurred in 39% of KEYTRUDA-treated patients; those ≥2% were urinary tract infection, pneumonia, anemia, and pelvic pain. The most common adverse reactions (≥20%) in patients who received KEYTRUDA were fatigue (38%), musculoskeletal pain (32%), pruritus (23%), decreased appetite (21%), nausea (21%), and rash (20%).
- In KEYNOTE-427, KEYTRUDA was discontinued due to adverse reactions in 11% of 149 patients with aRCC. Serious adverse reactions occurred in 47% of patients resulting in permanent discontinuation of KEYTRUDA was pneumonitis (1.4%). Serious adverse reactions occurred in 28% of patients; those ≥2% were pneumonia (2%), cardiac failure (2%), pulmonary embolism (2%), sepsis (2%), and acute kidney injury (2%). The most common adverse reactions (≥20%) were fatigue (29%), diarrhea (24%), and rash (24%).
- Adverse reactions occurring in patients with MSI-H or dMMR CRC were similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy.
- Adverse reactions occurring in patients with gastric cancer were similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy.
- In NEYNOTE-590, when KEYTRUDA was administered with cisplatin and fluorouracil to patients with metastatic or locally advanced esophageal or GEJ (tumors with epicenter 1 to 5 centimeters above the GEJ) carcinoma who were not candidates for surgery or definitive chemoradiation, KEYTRUDA was discontinued due to adverse reactions in 15% of 370 patients. The most common adverse reactions resulting in permanent discontinuation of KEYTRUDA (≥1%) were pneumonitis (1.9%), acute kidney injury (1.1%), and pneumonia (1.1%). The most common adverse reactions (≥20%) with KEYTRUDA in combination with chemotherapy were nausea (67%), fatigue (57%), decreased appetite (44%), constipation (40%), diarrhea (36%), vomiting (34%), stomatitis (27%), and weight loss (24%).
- Adverse reactions occurring in patients with esophageal cancer who received KEYTRUDA as a monotherapy were similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy.
- In NEYNOTE-158, KEYTRUDA was discontinued due to adverse reactions in 8% of 98 patients with recurrent or metastatic cervical cancer. Serious adverse reactions occurred in 49% of patients receiving KEYTRUDA; the most frequent included anemia (7%), fistula, hemorrhage, and urinary tract infection (5% each), and pelvic inflammatory tract infections(4.1% each). The most common adverse reactions (≥20%) were fatigue (42%), musculoskeletal pain (27%), diarrhea (23%), pain and abdominal pain (22% each), and decreased appetite (21%).
- Adverse reactions occurring in patients with hepatocellular carcinoma (HCC) were generally similar to those in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy, with the exception of increased incidences of ascites (8% Grades 3–4) and immune-mediated hepatitis (2.9%). Laboratory abnormalities (Grades 3 and 4) that occurred at a higher incidence were elevated AST (2%), ALT (2%), and hyperbilirubinemia (10%).
- Among the 50 patients with MCC enrolled in study KEYNOTE-017, adverse reactions occurring in patients with MCC were generally similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy. Laboratory abnormalities (Grades 3–4) that occurred at a higher incidence were elevated AST (11%) and hyperglycemia (19%).
- In KEYNOTE-426, when KEYTRUDA was administered in combination with axitinib, fatal adverse reactions occurred in 3.3% of 429 patients. Serious adverse reactions occurred in 40% of patients, the most frequent (≥1%) were hepatotoxicity (7%), diarrhea (4.2%), acute kidney injury (2.3%), dehydration (1%), and pneumonitis (1%). Permanent discontinuation due to adverse reaction occurred in 31% of patients; adverse reactions leading to discontinuation in ≥1% were diarrhea (2%), and hepatotoxicity (1%). The most common adverse reactions (≥20%) with KEYTRUDA in combination with axitinib were diarrhea (59%), fatigue/asthenia (52%), hypertension (46%), hepatotoxicity (39%), decreased appetite (31%), vomiting (30%), stomatitis (27%), and weight loss (24%).
- Adverse reactions occurring in patients with TMB-H cancer were similar to those occurring in patients with other solid tumors who received KEYTRUDA as a single agent.
- Adverse reactions occurring in patients with cSCC were similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy.
- In KEYNOTE-355, when KEYTRUDA and chemotherapy (paclitaxel, paclitaxel protein-bound, or gemcitabine and carboplatin) were administered to patients with locally recurrent unresectable or metastatic TNBC who had not been previously treated with chemotherapy in the metastatic setting (n=596), fatal adverse reactions occurred in 2.2% of patients, including cardio-respiratory arrest (0.7%) and septic shock (0.3%). Serious adverse reactions occurred in 30% of patients receiving KEYTRUDA in combination with chemotherapy; the serious reactions in ≥2% were pneumonia (2.9%), anemia (2.2%), and thrombocytopenia (2%). KEYTRUDA was discontinued in 11% of patients due to adverse reactions. The most common adverse reactions (≥20%) in patients receiving KEYTRUDA in combination with chemotherapy were fatigue (46%), nausea (44%), alopecia (34%), diarrhea and constipation (28% each), vomiting and rash (26% each), cough (23%), decreased appetite (21%), and headache (20%).

Lactation

- Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment and for 4 months after the final dose.

Pediatric Use

- In NEYNOTE-051, 161 pediatric patients (62 pediatric patients aged 6 months to younger than 12 years and 99 pediatric patients aged 12 years to 17 years) were administered KEYTRUDA 2 mg/kg every 3 weeks. The median duration of exposure was 2.1 months (range: 1 day to 24 months).
- Adverse reactions that occurred at a ≥10% higher rate in pediatric patients when compared to adults were pyrexia (33%, vomiting (30%), leukopenia (30%), upper respiratory tract infection (29%), neutropenia (26%), headache (25%), and Grade 3 anemia (17%).

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information. The Medication Guide also is available.

References: 1. Gandhi L, Rodriguez-Abreu D, Gadgeel S, et al for the KEYNOTE-407 investigators. Pembrolizumab plus chemotherapy for squamous non-small cell lung cancer. *N Engl J Med.* 2018;379(2):2078–2092. 2. Paz-Ares L, Luft A, Vicente D, et al. for the KEYNOTE-407 investigators. Pembrolizumab plus chemotherapy for squamous non-small cell lung cancer. *N Engl J Med.* 2018;379(2):2040–2051. 3. Reck M, Rodriguez-Abreu D, Robinson AG, et al for the KEYNOTE-189 investigators. Pembrolizumab plus chemotherapy for metastatic non-squamous non-small cell lung cancer with PD-L1 tumor proportion score of 50% or greater. Co-Occur. 2019;37(537):548–554. 4. Yu HA, Kasahara K, et al. Pembrolizumab versus chemotherapy for previously untreated, PD-L1-expressing, locally advanced or metastatic non-small-cell lung cancer (KEYNOTE-042): a randomised, open-label, controlled, phase 3 trial. Lancet. 2019;393(10173):1819–1830.

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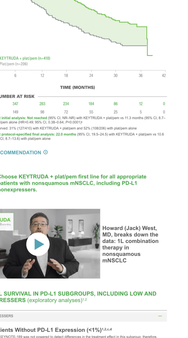
US-LAM-0095812021

DURABLE OVERALL SURVIVAL achieved first line with KEYTRUDA + platinum vs platinum alone

In nonsquamous mNSCLC with no EGFR or ALK genomic aberrations

Increased Survival with KEYTRUDA + platinum vs platinum alone

HR=0.56; 95% CI, 0.46–0.69

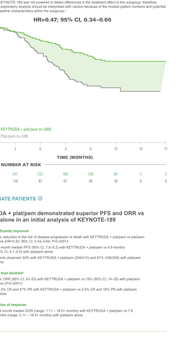


- **Median OS at initial analysis: Not reached for KEYTRUDA + platinum vs 11.3 months for platinum (n=206)**
  - Events observed: 21% (215/1018) with KEYTRUDA + platinum and 30% (151/501) with platinum alone
- **Median OS at protocol-specified final analysis: 22.0 months** (95% CI, 19.3-24.5) with KEYTRUDA + platinum vs 10.6 months (95% CI, 9.4-11.6) with platinum alone

NCCN® RECOMMENDATION ⓘ

> **Choose KEYTRUDA + platinum first line for all appropriate patients with nonsquamous mNSCLC, including PD-L1 nonexpressers.**

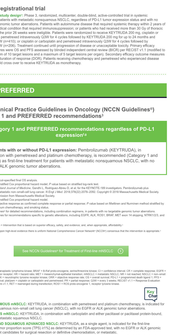
OVERALL SURVIVAL IN PD-L1 SUBGROUPS, INCLUDING LOW AND NONEXPRESSERS (exploratory analyses)[1,2]



OS in Patients With PD-L1 Expression (≤1%)[1,2,4]

LIMITATIONS: KEYNOTE-189 was not powered to detect differences in the treatment effect in this subgroup. Therefore, results from this exploratory analysis should be interpreted with caution because of the modest patient numbers and potential imbalances in baseline characteristics within the subgroup.[1]

HR=0.49; 95% CI, 0.38–0.62



OS in Patients With PD-L1 Expression (≥1%)[1,4]

LIMITATIONS: KEYNOTE-189 was not powered to detect differences in the treatment effect in this subgroup. Therefore, results from this exploratory analysis should be interpreted with caution because of the modest patient numbers and potential imbalances in baseline characteristics within the subgroup.[1]

HR=0.47; 95% CI, 0.34–0.66

Howard (Jack) West, MD, breaks down the data: 1L combination therapy in nonsquamous mNSCLC

APPROPRIATE PATIENTS ⓘ

KEYTRUDA + platinum demonstrated superior PFS and ORR vs platinum alone in an initial analysis of KEYNOTE-189

PFS — **Significantly improved**
- 24% reduction in the risk of disease progression or death with KEYTRUDA + platinum vs platinum alone (HR=0.52; 95% CI, 0.43-0.64; P<0.0001)
  - 9-month median PFS (95% CI): 8.8-12.4 with KEYTRUDA + platinum vs 4.9-6 months with platinum
  - Events observed: 35% (355/1018) with KEYTRUDA + platinum (245/510) and 61% (306/500) with platinum alone

ORR — **More than double!**
- 57.9% (95% CI, 53.45-62.34) with KEYTRUDA + platinum vs 19% (95% CI, 15-20) with platinum alone (P<0.0001)
  - 0.5% CR and 57% PR with KEYTRUDA + platinum vs 0.3% CR and 18% PR with platinum

OS — **Duration of response**
- 12.2-month median DOR (range: 1.1+ - 18.5+ months) with KEYTRUDA + platinum vs 7.8 months (range: 2.1+ - 18.4+ months) with platinum alone

Phase 3 randomized trial

KEYNOTE-189 study design: Phase 3, randomized, multicenter, double-blind, active-controlled trial in systemic chemotherapy–naïve patients with metastatic nonsquamous NSCLC with no EGFR or ALK genomic tumor aberrations. Patients with no EGFR or ALK genomic tumor aberrations. Patients with autoimmune disease that required systemic therapy within 2 years of treatment; a medical condition that required immunosuppression; or patients who had received more than 30 Gy of thoracic radiation within the prior 26 weeks were ineligible. Randomization (2:2:1) was stratified by PD-L1 TPS (≥50% vs 1-49% vs <1%), chemotherapy, and prespecified tumorigenic CDH for a total of 616 patients. KEYTRUDA 200 mg for up to 24 months or pemetrexed (500 mg/m²) + cisplatin or carboplatin and pemetrexed chemotherapy (CDH for a total of 616 patients). Pemetrexed was given in combination with cisplatin (75 mg/m²) or carboplatin (AUC=5) on day 1 of each 21-day cycle. Patients received up to 4 cycles of chemotherapy. Patients with nonprogressive disease at the end of chemotherapy could continue pemetrexed maintenance. Patients with squamous histology were ineligible for the study. Tumor assessments were performed every 6 weeks for the first 18 months and every 12 weeks thereafter. Patients were ineligible for the study if they had a history of other malignancies except for adequately treated basal cell or squamous cell skin cancer or in situ cancer of the cervix or breast. Tumor assessments were CR and duration of response (DOR). Patients receiving chemotherapy and pemetrexed who experienced disease progression could cross over to receive KEYTRUDA as monotherapy.

PREFERRED

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)
Category 1 and PREFERRED recommendations[3]

Category 1 and PREFERRED recommendations regardless of PD-L1 expression[3]

> **For patients with or without PD-L1 expression:** Pembrolizumab (KEYTRUDA), in combination with pemetrexed and platinum chemotherapy, is recommended (Category 1 and Preferred) as first-line treatment for patients with metastatic nonsquamous NSCLC, with no EGFR or ALK genomic tumor aberrations.

Based on the recommendation that PD-L1 testing is not required to select patients for treatment with KEYTRUDA, KEYTRUDA + platinum chemotherapy is preferred over the chemotherapy-only treatment regimen tested in KEYNOTE-189, last circa2 in the NCCN Guidelines. Pembrolizumab plus chemotherapy is recommended regardless of PD-L1 status (Category 1 and Preferred) in the NCCN Guidelines for Non-Small Cell Lung Cancer (NSCLC). Reprinted with permission from Massachusetts Medical Society.
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*Platinum: Best results for patients treated with platinum-based chemotherapy regimens or partial responses. ‡Value based on Medicare and Nuvinsur market shares by Medicare Part B and commercial payers.
Take NCCN Guidelines® for detailed recommendations, including contraindications, regimens, & options within the hospitals governing bodies (formulary). Visit NCCN Guidelines® for complete details, such as dosing, administration, & supportive care. ©2019 NCCN, NCCN GRAPHIC, NCCN, and NCCN Logo are trademarks of NCCN.
Preferred intervention: Intervention that is based on superior efficacy, safety, and/or convenience, and when appropriate, affordability.[3]
Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.[3]

Go to Appropriate Patients

1. Gandhi L, Rodriguez-Abreu D, Gadgeel S, et al. for the KEYNOTE-189 Investigators. Pembrolizumab plus chemotherapy in metastatic non-small cell lung cancer. N Engl J Med. 2018;378:2078-2092. doi:10.1056/NEJMoa1801005. 2. Rodriguez-Abreu D, Powell SF, Hochmair MJ, et al. for the KEYNOTE-189 Investigators. Pembrolizumab plus chemotherapy in metastatic non-small cell lung cancer: 2-year outcomes from the randomized, phase 3 KEYNOTE-189 study. Presented at: 2020 ASCO Annual Meeting; May 29-31, 2020; Virtual. 3. Ettinger DS, Wood DE, Aisner DL, et al. NCCN Guidelines® Insights: Non-Small Cell Lung Cancer, Version 2.2018. J Natl Compr Cancer Net. 2018;16(807-821). 4. Data on file. Merck & Co., Inc., Rahway, NJ, USA.

Scan to learn more about KEYTRUDA

FIRST-LINE COMBINATION THERAPY IN NONSQUAMOUS mNSCLC. KEYTRUDA, in combination with pemetrexed and platinum chemotherapy, is indicated for the first-line treatment of patients with metastatic nonsquamous non-small cell lung cancer (NSCLC), with no EGFR or ALK genomic tumor aberrations.

FIRST-LINE MONOTHERAPY IN PD-L1–HIGH NSCLC. KEYTRUDA, as a single agent, is indicated for the first-line treatment of adult patients with PD-L1–expressing metastatic NSCLC, as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and is stage III patients who are not candidates for definitive chemoradiotherapy.

FIRST LINE MONOTHERAPY IN NONSQUAMOUS AND SQUAMOUS mNSCLC. KEYTRUDA, as a single agent, is indicated for the first-line treatment of adult patients with metastatic NSCLC, with no EGFR or ALK genomic tumor aberrations, and is stage III patients who are not candidates for definitive chemoradiotherapy.

SECOND-LINE OR GREATER MONOTHERAPY IN NONSQUAMOUS AND SQUAMOUS mNSCLC. KEYTRUDA, as a single agent, is indicated for the treatment of adult patients with metastatic NSCLC, with no EGFR or ALK genomic tumor aberrations, who have disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should receive targeted therapy before KEYTRUDA.

Pembrolizumab (KEYTRUDA)

RELATED SAFETY INFORMATION

Serious and Fatal Immune-Mediated Adverse Reactions
KEYTRUDA is a monoclonal antibody that belongs to a class of drugs that bind to either the programmed death receptor-1 (PD-1) or the programmed death ligand (PD-L1) and block the PD-1/PD-L1 interaction, resulting in inhibition of the PD-1 pathway. Immune-mediated adverse reactions, which may be severe, include inflammatory adverse reactions in the skin, lung, intestine, endocrine glands, liver, and kidney. Most cases of immune-mediated adverse reactions resolve after initiation of corticosteroids or immunosuppressant therapy. Most cases of immune-mediated adverse reactions occur within 6 months of initiation of KEYTRUDA, but other immune-mediated adverse reactions have been reported as late onset. Immune-mediated adverse reactions, which may be severe, can also occur after discontinuation of KEYTRUDA. Depending on the severity of the immune-mediated adverse reaction, treatment with KEYTRUDA may need to be delayed or discontinued. Administer corticosteroids and, if clinically indicated, other immunosuppressants to patients with a severe immune-mediated adverse reaction. Early identification and management are essential to ensure safe use of KEYTRUDA. Treatments, Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. Immune-mediated adverse reactions, which may be severe, can also occur after discontinuation of KEYTRUDA. Immune-mediated adverse reactions include medical management grading (severity) and recommendations for treatment, including:
- Withhold or permanently discontinue KEYTRUDA depending on severity of the immune-mediated adverse reaction. In general, if KEYTRUDA requires interruption or discontinuation, administer systemic corticosteroids (1 to 2 mg/kg/day prednisone or equivalent) until improvement to grade 1 or less. Upon improvement to grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients in whom corticosteroids are contraindicated or patients who do not improve or worsen despite corticosteroids.

Hepatitis and Immune-Mediated Hepatitis
Immune-Mediated Pneumonitis
- KEYTRUDA can cause immune-mediated pneumonitis. The incidence higher in patients who have received prior thoracic radiation. Immune-mediated pneumonitis occurred in 3.4% (94/2705) of patients receiving KEYTRUDA, including Grad 2(1%), Grade 3 (0.8%), and Grade 5 (0.2%) reactions. Immune-mediated pneumonitis occurred in 1.2% (4/333) of patients who received prior thoracic radiation, including Grade 3 (0.6%) and Grade 4 (0.3%) reactions. Of the 94 patients with pneumonitis, 61% (57/94) resolved, 19% (18/94) improved, and 20% (19/94) had unknown resolution status. Of the 18 patients who had improvement, 2 (2% had recurrence. Pneumonitis occurred in 8% (21/260) of adult patients with cHL receiving KEYTRUDA as a single agent, including Grade 3 in 2.4% (6/250) of patients. Patients received high-dose corticosteroids for a median duration of 10 days (range: 2 to 31 days) in 19 patients. Pneumonitis resolved in 81% (17/21) of patients with cHL. Pneumonitis resolved after discontinuation of KEYTRUDA in 4.0% (2/1) of patients. Of the patients who developed pneumonitis, 42% interrupted KEYTRUDA, 19% discontinued KEYTRUDA, and 76% and 71% resolution.

Immune-Mediated Colitis
KEYTRUDA can cause immune-mediated colitis, which may present with diarrhea. Cytomegalovirus infection/reactivation has been reported in patients with immune-mediated colitis in the literature. Immune-mediated colitis occurred in 2.1% (58/2705) of patients receiving KEYTRUDA, including Grade 3 in 0.7% (19/2705) of patients. Immune-mediated colitis occurred in 1.7% (6/333) of patients who received prior thoracic radiation, including Grade 3 in 0.3% (1/333) of patients. Systemic corticosteroids were required in 89% (24/6), additional immunosuppressant therapy was required in 4.2% of patients. Colitis led to permanent discontinuation of KEYTRUDA in 0.4% (11/2705) of patients, and 0.3% (1/333) of patients who received prior thoracic radiation. Of the 58 patients with immune-mediated colitis, 71% (41/58) resolved, 14% (8/58) improved, and 14% (8/58) had unknown resolution.

Hypophysitis and Immune-Mediated Hepatitis
Immune-Mediated Nephritis
- KEYTRUDA can cause immune-mediated nephritis. Immune-mediated nephritis occurred in 0.7% (19/2705) of patients receiving KEYTRUDA, including Grade 4 (<1%), Grade 3 (0.4%), and Grade 2 (0.1%) reactions. Systemic corticosteroids were required in 58% (11/19) of patients; additional immunosuppressant therapy was required in 0.4% (1/2705) of patients. Nephritis led to permanent discontinuation of KEYTRUDA in 0.3% (7/2705) of patients, and 0.3% (1/333) of patients who received prior thoracic radiation. Of the 19 patients with immune-mediated nephritis, 37% (7/19) resolved, 26% (5/19) improved, and 37% (7/19) had unknown resolution.

Immune-Mediated Pancreatitis
- KEYTRUDA can cause immune-mediated pancreatitis. Immune-mediated pancreatitis occurred in 0.7% (19/2705) of patients receiving KEYTRUDA, including Grade 4 (<1%), Grade 3 (0.4%), and Grade 2 (0.1%) reactions. Systemic corticosteroids were required in 58% (11/19) of patients; additional immunosuppressant therapy was required in 4.2% of patients. Colitis led to permanent discontinuation of KEYTRUDA in 0.3% (7/2705) of patients, and 0.3% (1/333) of patients who received prior thoracic radiation. Of the 19 patients with immune-mediated pancreatitis, 37% (7/19) resolved, 26% (5/19) improved, and 37% (7/19) had unknown resolution.

Hypothyroidism
- KEYTRUDA can cause hypothyroidism. Hypothyroidism occurred in 21% (567/2705) of patients receiving KEYTRUDA, including Grade 3 (<1%) and Grade 2 (21%) reactions. Systemic corticosteroids were required in 18% (102/567) of patients; hormone replacement therapy was required in 91% (516/567) of patients. Hypothyroidism led to permanent discontinuation of KEYTRUDA in 0.1% (4) and withholding in 0.3% (7) of patients. All patients who were without immune-mediated hypothyroidism prior to KEYTRUDA treatment were ineligible for the study.

Hyperthyroidism
- KEYTRUDA can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Immune-mediated thyroid disorders occurred in 7.1% (192/2705) of patients receiving KEYTRUDA, including Grade 3 (0.3%) and Grade 2 (6.8%) reactions. Hyperthyroidism occurred in 3.8% (103/2705) of patients receiving KEYTRUDA, including Grade 3 (0.1%) and Grade 2 (3.6%) reactions. Thyroiditis occurred in 0.7% (19/2705) of patients who received prior thoracic radiation. The incidence of new or worsening hypothyroidism was 20% (522/2605) of patients with NSCLC, occurring in 16% of patients receiving KEYTRUDA as a single agent or in combination with platinum and FU, including Grade 3 (0.2%). Hyperthyroidism occurred in 3.8% (103/2705) of patients receiving KEYTRUDA, including Grade 3 (0.1%) and Grade 2 (3.6%) reactions. Thyroiditis occurred in 0.7% (19/2705) of patients who received prior thoracic radiation.

Type 1 Diabetes Mellitus (DM), Which Can Present With Diabetic Ketoacidosis
KEYTRUDA can cause type 1 diabetes mellitus, which may present with diabetic ketoacidosis. Monitor treatment with insulin as clinically indicated. Withhold KEYTRUDA depending on severity. Type 1DM occurred in 0.3% (8/2705) of patients receiving KEYTRUDA. Type 1 diabetes mellitus occurred in 0.1% (2/2705) of patients receiving KEYTRUDA, including Grade 3 (<1%) and Grade 2 (0.1%) reactions. Diabetic ketoacidosis occurred in 0.1% (2/2705) of patients receiving KEYTRUDA. All patients who were without immune-mediated hypothyroidism prior to KEYTRUDA treatment were ineligible for the study.

Immune-Mediated Adrenal Insufficiency
- KEYTRUDA can cause a secondary adrenal insufficiency. Grade 3 or higher. Initiate symptomatic treatment, including hormone replacement as clinically indicated. Withhold KEYTRUDA depending on severity. Adrenal insufficiency occurred in 0.8% (22/2705) of patients receiving KEYTRUDA, including Grade 3 (0.4%) and Grade 2 (0.4%) reactions. Adrenal insufficiency occurred in 0.3% (1/333) of patients who received prior thoracic radiation, resulting in permanent discontinuation of KEYTRUDA in 0.3% (1/333) of patients. All patients who were without pituitary disease prior to KEYTRUDA treatment were ineligible for the study.

Hypophysitis
- KEYTRUDA can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, phenylalgia, or visual field defects. Hypopituitism can cause hypothyroidism. Initiate hormone replacement as indicated. Withhold or permanently discontinue KEYTRUDA depending on severity. Hypophysitis occurred in 0.2% (6/2705) of patients receiving KEYTRUDA, including Grade 3 (0.1%) and Grade 2 (0.2%) reactions. Systemic corticosteroids were required in 67% (4/6) of patients; hormone replacement therapy was required in 67% (4/6) of patients. Hypophysitis led to permanent discontinuation of KEYTRUDA in 0.1% (4) and withholding in 0.3% (7) of patients. All patients who were without immune-mediated hypothyroidism prior to KEYTRUDA treatment were ineligible for the study.

Immune-Mediated Hypophysitis
- KEYTRUDA can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, phenylalgia, or visual field defects. Hypopituitism can cause hypothyroidism. Initiate hormone replacement as indicated. Withhold or permanently discontinue KEYTRUDA depending on severity. Hypophysitis occurred in 0.2% (6/2705) of patients receiving KEYTRUDA, including Grade 3 (0.1%) and Grade 2 (0.2%) reactions. Systemic corticosteroids were required in 67% (4/6) of patients; hormone replacement therapy was required in 67% (4/6) of patients. Hypophysitis led to permanent discontinuation of KEYTRUDA in 0.1% (4) and withholding in 0.3% (7) of patients. All patients who were without immune-mediated hypothyroidism prior to KEYTRUDA treatment were ineligible for the study.

Immune-Mediated Nephritis With Renal Dysfunction
- KEYTRUDA can cause immune-mediated nephritis. Immune-mediated nephritis occurred in 0.3% (8/2705) of patients receiving KEYTRUDA, including Grade 4 (<1%), Grade 3 (0.1%), and Grade 2 (0.1%) reactions. Systemic corticosteroids were required in 58% (11/19) of patients; additional immunosuppressant therapy was required in 0.4% (1/2705) of patients. Nephritis led to permanent discontinuation of KEYTRUDA in 0.3% (7/2705) of patients, and 0.3% (1/333) of patients who received prior thoracic radiation. Of the 19 patients with immune-mediated nephritis, 37% (7/19) resolved, 26% (5/19) improved, and 37% (7/19) had unknown resolution.

KEYTRUDA With Axitinib
- Fatal and other serious complications with axitinib can cause hepatic toxicity. Monitor liver enzyme tolerance of and permanently throughout treatment. Consider monitoring more frequently as compared to when the drug is administered alone. Withhold or permanently discontinue axitinib depending on severity. Fatal and other serious complications with axitinib can cause arterial thrombosis. Consider permanently discontinuing axitinib as needed. With the combination of KEYTRUDA and axitinib, Grades 3 and 4 increased arterial administrative (2%), hypertension (4%), and hypothyroidism (4%) occurred. Hepatotoxicity, including Grade 3 (2%) and Grade 4 (<1%) reactions, occurred in 2% (5/2) of patients with renal cell carcinoma treated with KEYTRUDA and axitinib. In patients with cHL treated with KEYTRUDA and axitinib, a fatal hepatic reaction occurred in 1 patient (<1%). Among the 92 patients who were rechallenged with either KEYTRUDA (n=0) or axitinib (n=92) administered as a single agent or with both (n=0), hepatitis recurred in 0 patients. Immune-mediated adverse reactions, including Grade 3 (<1%) pneumonitis occurring within 2 weeks of initiation of KEYTRUDA with a duration of 14.2 (1.8-24) weeks, occurred in 1 patient (<1%).

Immune-Mediated Encephalitis
- KEYTRUDA can cause immune-mediated encephalitis. Grade 2 or higher. Initiate symptomatic treatment, including hormone replacement as clinically indicated. Withhold KEYTRUDA depending on severity. Adrenal insufficiency occurred in 0.8% (22/2705) of patients receiving KEYTRUDA, including Grade 3 (0.4%) and Grade 2 (0.4%) reactions. Adrenal insufficiency occurred in 0.3% (1/333) of patients who received prior thoracic radiation, resulting in permanent discontinuation of KEYTRUDA in 0.3% (1/333) of patients. All patients who were without endocrinopathy prior to KEYTRUDA treatment were ineligible for the study.

Immune-Mediated Myocarditis
- KEYTRUDA can cause immune-mediated myocarditis. Myocarditis can present with acute symptoms associated with mass effect such as headache, phenylalgia, or visual field defects. Hypopituitism can cause hypothyroidism. Initiate hormone replacement as indicated. Withhold or permanently discontinue KEYTRUDA depending on severity. Hypophysitis occurred in 0.2% (6/2705) of patients receiving KEYTRUDA, including Grade 3 (0.1%) and Grade 2 (0.2%) reactions. Systemic corticosteroids were required in 67% (4/6) of patients; hormone replacement therapy was required in 67% (4/6) of patients. Hypophysitis led to permanent discontinuation of KEYTRUDA in 0.1% (4) and withholding in 0.3% (7) of patients. All patients who were without immune-mediated hypothyroidism prior to KEYTRUDA treatment were ineligible for the study.

Immune-Mediated Myositis/Polymyositis
- KEYTRUDA can cause immune-mediated myositis, which may present with diffuse weakness, elevated serum creatinine, and myalgia. Initiate treatment with corticosteroids as clinically indicated. Withhold KEYTRUDA depending on severity. Type 1DM occurred in 0.3% (8/2705) of patients receiving KEYTRUDA. Type 1 diabetes mellitus occurred in 0.1% (2/2705) of patients receiving KEYTRUDA, including Grade 3 (<1%) and Grade 2 (0.1%) reactions. Diabetic ketoacidosis occurred in 0.1% (2/2705) of patients receiving KEYTRUDA. All patients who were without endocrinopathy prior to KEYTRUDA treatment were ineligible for the study.

Immune-Mediated Rhabdomyolysis
- KEYTRUDA can cause immune-mediated rhabdomyolysis. Immune-mediated rhabdomyolysis occurred in 0.1% (1/2705) of patients receiving KEYTRUDA, including Grade 4 (0.1%) reactions. Immune-mediated rhabdomyolysis occurred in 0.3% (1/333) of patients who received prior thoracic radiation, resulting in permanent discontinuation of KEYTRUDA in 0.3% (1/333) of patients. All patients who were without endocrinopathy prior to KEYTRUDA treatment were ineligible for the study.

Immune-Mediated Dermatologic Adverse Reactions
- KEYTRUDA can cause immune-mediated rash or dermatitis. Exfoliative dermatitis, including Stevens-Johnson syndrome, drug rash with eosinophilia and systemic symptoms, and toxic epidermal necrosis, has occurred with anti-PD-1/PD-L1 treatments. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate rash or dermatitis. Withhold or permanently discontinue KEYTRUDA depending on severity. Immune-mediated dermatologic adverse reactions occurred in 4% (108/2705) of patients receiving KEYTRUDA, including Grade 3 (1%) and Grade 2 (3%) reactions. Exfoliative dermatitis occurred in 0.1% (2/2705) of patients who received prior thoracic radiation, resulting in permanent discontinuation in 0.3% (2) and withholding in KEYTRUDA in 0.3% (2) of patients. All patients who were without immune-mediated dermatitis prior to KEYTRUDA treatment were ineligible for the study.

Other Immune-Mediated Adverse Reactions
- The following clinically significant immune-mediated adverse reactions occurred at an incidence of <1% (unless otherwise noted) in patients who received KEYTRUDA: Immune-mediated adverse reactions involving the heart and vascular: Myocarditis, including Grade 3 (0.1%) and Grade 2 (0.1%) reactions, resulting in permanent discontinuation of KEYTRUDA in 0.1% (1/333) of patients who received prior thoracic radiation. Immune-mediated adverse reactions involving the gastrointestinal: Pancreatitis, including Grade 3 (0.1%) reactions, resulting in permanent discontinuation of KEYTRUDA in 0.1% (1/333) of patients who received prior thoracic radiation. Immune-mediated adverse reactions involving the hepatobiliary: Hepatitis, including Grade 3 (0.1%) reactions, resulting in permanent discontinuation of KEYTRUDA in 0.1% (1/333) of patients who received prior thoracic radiation. Immune-mediated adverse reactions involving the musculoskeletal and connective tissue: Myositis/polymyositis, including Grade 3 (0.1%) reactions, resulting in permanent discontinuation of KEYTRUDA in 0.1% (1/333) of patients who received prior thoracic radiation. Immune-mediated adverse reactions involving the endocrine: Hypophysitis, including Grade 3 (0.1%) reactions, resulting in permanent discontinuation of KEYTRUDA in 0.1% (1/333) of patients who received prior thoracic radiation. Immune-mediated adverse reactions involving the nervous: Encephalitis, including Grade 3 (0.1%) reactions, resulting in permanent discontinuation of KEYTRUDA in 0.1% (1/333) of patients who received prior thoracic radiation. Immune-mediated adverse reactions involving the eye: Uveitis, including Grade 3 (0.1%) reactions, resulting in permanent discontinuation of KEYTRUDA in 0.1% (1/333) of patients who received prior thoracic radiation. Immune-mediated adverse reactions involving the hematopoietic/lymphatic/immune: Hemolytic anemia/hemolysis, including Grade 3 (0.1%) reactions, resulting in permanent discontinuation of KEYTRUDA in 0.1% (1/333) of patients who received prior thoracic radiation.

Infusion-Related Reactions
- KEYTRUDA can cause severe or life-threatening infusion-related reactions, including hypersensitivity and anaphylaxis, which have been reported in 0.2% (7/38 of patients receiving KEYTRUDA. Monitor for signs and symptoms of infusion reactions. Interrupt or slow the rate of infusion for Grade 1 or Grade 2 reactions. For Grade 3 or Grade 4 reactions, stop infusion and permanently discontinue KEYTRUDA.

Complications of Allogeneic Hematopoietic Stem Cell Transplantation (HSCT)
- Fatal and other serious complications can occur in patients who receive allogeneic HSCT before or after anti-PD-1/PD-L1 treatments. Transplant-related complications include hyperacute graft-versus-host-disease (GVHD), severe acute GVHD, severe hepatic veno-occlusive disease, and severe pulmonary toxicity. Consider the risk of severe GVHD in patients with a history of allogeneic HSCT. Monitor patients for signs and symptoms of GVHD. Treatment with anti-PD-1/PD-L1 treatments and allogeneic HSCT. Follow patients closely for evidence of these complications and intervene promptly. Consider the benefit vs risk of treatment with a PD-1/PD-L1 blockade administered before or after allogeneic HSCT.

Increased Mortality in Patients With Multiple Myeloma
- In trials in patients with multiple myeloma, the addition of KEYTRUDA to a thalidomide analogue plus dexamethasone resulted in increased mortality. Treatment of patients with multiple myeloma with a PD-1 blockade in this combination is not recommended for patients in these studies.

Embryo-Fetal Toxicity
- Based on its mechanism of action, KEYTRUDA can cause fetal harm when administered to a pregnant woman. Advise women of the potential risk. In females of reproductive potential, verify pregnancy status prior to initiating KEYTRUDA and advise them to use effective contraception during treatment and for 4 months after the last dose.

Adverse Reactions
- In KEYNOTE-189, KEYTRUDA was discontinued due to adverse reactions in 9% of 555 patients with advanced melanoma; adverse reactions leading to permanent discontinuation in more than one patient were colitis (1.4%), autoimmune hepatitis (1.4%), pneumonitis (1.4%), hypophysitis (0.4%), and cardiac failure (0.4%). The most common adverse reactions (≥20%) with KEYTRUDA were fatigue (28%), diarrhea (24%), and nausea (21%).
- In KEYNOTE-045 KEYTRUDA was discontinued due to adverse reactions in 14% of 149 patients; the most common adverse reactions (≥1%) were pneumonitis (2.7%), colitis (2.7%), and diarrhea (1.3%). Serious adverse reactions occurred in 23% of patients receiving KEYTRUDA. The most common adverse reactions (≥20%) were fatigue (26%), diarrhea (21%), and nausea (20%).
- In KEYNOTE-087 and -089 KEYTRUDA was administered with pemetrexed and platinum chemotherapy. In KEYNOTE-089 KEYTRUDA was discontinued due to adverse reactions in 20% of 405 patients. The most common adverse reactions resulting in permanent discontinuation of KEYTRUDA were pneumonitis (2.5%), renal failure (2.5%), and pneumonitis (1.5%). Serious adverse reactions occurred in 42% of patients receiving KEYTRUDA. The most common adverse reactions (≥20%) were anemia (49%), diarrhea (27%), decreased appetite (21%), and rash (20%).
- In KEYNOTE-407, when KEYTRUDA was administered with carboplatin and either paclitaxel or protein-bound paclitaxel or nanoparticle albumin-bound paclitaxel, KEYTRUDA was discontinued due to adverse reactions in 19% of 559 patients with squamous NSCLC. The most common adverse reactions resulting in permanent discontinuation of KEYTRUDA were pneumonitis (2.5%), renal failure (1.4%), and pneumonitis (1.4%). Serious adverse reactions occurred in 69% of patients receiving KEYTRUDA. The most common adverse reactions (≥20%) were fatigue (37%), decreased appetite (27%), nausea (23%), diarrhea (21%), constipation (20%), and rash (20%).
- In KEYNOTE-407, when KEYTRUDA was administered with carboplatin and either paclitaxel or paclitaxel protein-bound or nanoparticle albumin-bound, KEYTRUDA was discontinued due to adverse reactions in 16% of 616 patients with nonsquamous NSCLC. The most common adverse reactions resulting in permanent discontinuation of KEYTRUDA were pneumonitis (1.3%), renal failure (1.3%), and pneumonitis (1.1%). Serious adverse reactions occurred in 65% of patients receiving KEYTRUDA. The most common adverse reactions (≥20%) were fatigue (31%), decreased appetite (26%), nausea (23%), diarrhea (21%), constipation (20%), and rash (20%).
- In KEYNOTE-042 KEYTRUDA was discontinued due to adverse reactions in 9% of 637 patients with advanced NSCLC; the most common adverse reactions resulting in permanent discontinuation of KEYTRUDA were pneumonitis (1.3%), pneumonitis (1.3%), and sepsis (0.9%). The most frequent serious adverse reactions reported in at least 2% of patients were pneumonia (3.8%), pneumonitis (2.8%), and sepsis (2.2%). The most common adverse reactions (≥20%) were fatigue (31%), decreased appetite (21%), and cough (20%).
- In KEYNOTE-189 KEYTRUDA was discontinued due to adverse reactions in 9% of 405 patients with advanced NSCLC; the most common adverse reactions resulting in permanent discontinuation of KEYTRUDA were pneumonitis (2.5%), renal failure (2.5%), and pneumonitis (1.5%). The most common adverse reactions (≥20%) were decreased appetite (33%), fatigue (31%), nausea (25%), diarrhea (23%), vomiting (21%), and rash (20%). The most frequent serious adverse reactions reported in at least 2% of patients were pneumonia (3.7%), pneumonitis (2.5%), and renal failure (2.5%).
- In KEYNOTE-021 KEYTRUDA was administered in combination with platinum (carboplatin or cisplatin) and FU chemotherapy. KEYTRUDA was discontinued due to adverse reactions in 16% of 123 patients with NSCLC. The most common adverse reactions resulting in permanent discontinuation of KEYTRUDA were pneumonitis (2.5%), pneumonitis (1.8%), and septic shock (1.8%). The most common adverse reactions (≥20%) were nausea (51%), fatigue (41%), decreased appetite (31%), vomiting (29%), constipation (27%), diarrhea (24%), and rash (21%).
- In KEYNOTE-407 KEYTRUDA was discontinued due to adverse reactions in 19% of 559 patients with squamous NSCLC; the most common adverse reactions resulting in permanent discontinuation of KEYTRUDA were pneumonitis (2.5%), renal failure (1.4%), and pneumonitis (1.4%). The most frequent serious adverse reactions reported in at least 2% of patients were pneumonia, dyspnea, confusional state, vomiting, pleural effusion, pulmonary embolism, and renal failure. The most common adverse reactions (≥20%) were fatigue (37%), decreased appetite (27%), nausea (23%), diarrhea (21%), constipation (20%), and rash (20%).
- In KEYNOTE-407 KEYTRUDA was discontinued due to adverse reactions in 16% of 616 patients with nonsquamous NSCLC; the most common adverse reactions resulting in permanent discontinuation of KEYTRUDA were pneumonitis (1.3%), renal failure (1.3%), and pneumonitis (1.1%). Serious adverse reactions occurred in 65% of patients receiving KEYTRUDA. The most common adverse reactions (≥20%) were fatigue (31%), decreased appetite (26%), nausea (23%), diarrhea (21%), constipation (20%), and rash (20%).
- In KEYNOTE-189 KEYTRUDA was discontinued due to adverse reactions in 11% of 198 patients with high-PD-L1 expression; the most common adverse reaction resulting in permanent discontinuation of KEYTRUDA was pneumonitis (2.5%). The most common adverse reactions (≥20%) were decreased appetite (31%), fatigue (31%), nausea (25%), diarrhea (23%), vomiting (21%), and rash (20%). The most frequent serious adverse reactions reported in at least 2% of patients were pneumonitis (3.5%), renal failure (2.5%), and pneumonitis (2.5%).
- In KEYNOTE-021 KEYTRUDA was discontinued due to adverse reactions in 11% of 198 patients with high-PD-L1 expression; the most common adverse reaction resulting in permanent discontinuation of KEYTRUDA was pneumonitis (2.5%). The most common adverse reactions (≥20%) were nausea (51%), fatigue (41%), decreased appetite (31%), vomiting (29%), constipation (27%), diarrhea (24%), and rash (21%).
- In KEYNOTE-407 KEYTRUDA was discontinued due to adverse reactions in 11% of 198 patients with high-PD-L1 expression; the most common adverse reaction resulting in permanent discontinuation of KEYTRUDA was pneumonitis (2.5%). The most common adverse reactions (≥20%) were fatigue (37%), decreased appetite (27%), nausea (23%), diarrhea (21%), constipation (20%), and rash (20%).
- In KEYNOTE-407 KEYTRUDA was discontinued due to adverse reactions in 11% of 198 patients with high-NSMRC; the most common adverse reaction resulting in permanent discontinuation of KEYTRUDA was pneumonitis (2.5%). The most common adverse reactions (≥20

Full Indications +

Overview

Clinical Data

1L Combo Therapy —Nonsquamous

1L Combo Therapy —Squamous

1L Monotherapy

2L Monotherapy

Safety

NCCN Guidelines®

Choose KEYTRUDA + plat/pem first line for all appropriate patients with nonsquamous mNSCLC, including PD-L1 nonexpressers.

Howard (Jack) West, MD, breaks down the data: 1L combination therapy in nonsquamous mNSCLC

OVERALL SURVIVAL IN PD-L1 SUBGROUPS, INCLUDING LOW AND NONEXPRESSERS (exploratory analyses)[1,2]

Key Chat

SELECTED SAFETY INFORMATION EXPAND +

Severe and Fatal Immune-Mediated Adverse Reactions

- KEYTRUDA is a monoclonal antibody that belongs to a class of drugs that bind to either the programmed death receptor-1 (PD-1) or the programmed death ligand 1 (PD-L1), blocking the PD-1/PD-L1 pathway, thereby removing inhibition of the immune response, potentially breaking peripheral tolerance and inducing immune-mediated adverse reactions. Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue, can affect more than one body system simultaneously, and can occur at any time after starting treatment or after discontinuation of treatment. Important immune-mediated adverse

DURABLE OVERALL SURVIVAL achieved first line with KEYTRUDA + carbo + paclitaxel or paclitaxel protein-bound vs carbo + paclitaxel or paclitaxel protein-bound[1]

In squamous mNSCLC

Durable overall survival with KEYTRUDA + carbo + paclitaxel or paclitaxel protein-bound vs carbo + paclitaxel or paclitaxel protein-bound[1]

HR=0.71; 95% CI, 0.58–0.88

- **Median OS at initial analysis (median follow-up time: 7.8 months)[1]: 15.9 months** with KEYTRUDA + carbo + paclitaxel or paclitaxel protein-bound vs **13.0 months** with carbo + paclitaxel or paclitaxel protein-bound (n=559)
  - 6-12-18-24-30-36 mo: 65%, 54%, 41%, 33%, 28%, 23%, 20%, 17%
  - Events observed: 213 (76%) patients with KEYTRUDA + carbo + paclitaxel or paclitaxel protein-bound and 235 (83%) patients with carbo + paclitaxel or paclitaxel protein-bound
- **Median OS at prespecified final analysis (median follow-up time: 12.7 months): 17.1 months** with KEYTRUDA + carbo + paclitaxel or paclitaxel protein-bound (95% CI, 14.9-19.3) vs 11.6 months (95% CI, 10.1-13.2) with carbo + paclitaxel or paclitaxel protein-bound

NCCN® RECOMMENDATION ①

Choose KEYTRUDA + carbo + paclitaxel or paclitaxel protein-bound first line for all appropriate patients with squamous mNSCLC, including PD-L1 nonexpressers.

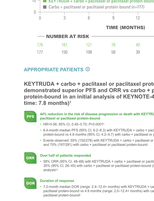
Howard (Jack) West, MD, breaks down the data: 1L combination therapy in squamous mNSCLC

OVERALL SURVIVAL IN PD-L1 SUBGROUPS (exploratory analyses)

NONEXPRESSERS

OS in Patients Without PD-L1 Expression (1%)[1,2,3,4]

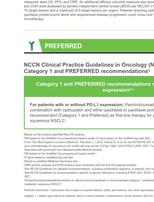
LIMITATION: KEYNOTE-407 was not powered to detect differences in OS in the treatment effect in this subgroup; therefore, results from this exploratory analysis should be interpreted with caution because of the modest patient numbers and limited statistical power to detect a treatment effect in these subgroups.



EXPRESSERS

OS in Patients With PD-L1 Expression (1%)[1,2,4]

LIMITATION: KEYNOTE-407 was not powered to detect differences in OS in the treatment effect in this subgroup; therefore, results from this exploratory analysis should be interpreted with caution because of the modest patient numbers and limited statistical power to detect a treatment effect in these subgroups.



APPROPRIATE PATIENTS ①

KEYTRUDA + carbo + paclitaxel or paclitaxel protein-bound demonstrated superior PFS and ORR vs carbo + paclitaxel or paclitaxel protein-bound in an initial analysis of KEYNOTE-407 (median follow-up time: 7.8 months)[1]

PFS	**40% relative risk reduction in the risk of disease progression or death with KEYTRUDA + carbo + paclitaxel or paclitaxel protein-bound** • HR=0.60; 95% CI, 0.49-0.73; 95% CI, 0.49-0.73 • 6-9-12-18-24 mo: 60%, 47%, 38%, 32%, 24% • Events observed: 191 (68%) patients with KEYTRUDA + carbo + paclitaxel or paclitaxel protein-bound and 264 (94%) patients with carbo + paclitaxel or paclitaxel protein-bound
ORR	**Over half of patients responded** • 58% ORR (95% CI: 46-69) with KEYTRUDA + carbo + paclitaxel or paclitaxel protein-bound vs 35% ORR (95% CI: 24-45) with carbo + paclitaxel or paclitaxel protein-bound (P=0.0081 in primary analysis)[1]
Duration of response	• 7.2 month median DOR (range: 2.4-12 m months) with KEYTRUDA + carbo + paclitaxel or paclitaxel protein-bound vs 5.5 months (range: 2.0-14.9 months) with carbo + paclitaxel or paclitaxel protein-bound[1]

Phase 3 registrational trial

KEYNOTE-407 study design: Phase 3, randomized, multicenter, double-blind, placebo-controlled trial in patients (mesp-ecoG 0-1) with previously untreated squamous NSCLC (AJCC 7th edition stage IIB-IV) tumor tissue samples were assessed for disease that expressed programmed death-ligand 1 (PD-L1) protein by a medical condition that expected immunosuppression in patients who had received more than 30 Gy of thoracic radiation within the prior 26 weeks were ineligible. Patients were randomized (1:1) to receive 4 cycles of KEYTRUDA + carbo + paclitaxel or paclitaxel protein-bound followed by KEYTRUDA monotherapy or carbo + paclitaxel or paclitaxel protein-bound chemotherapy. Tumor assessments were performed every 6 weeks for the first 18 months and every 12 weeks thereafter. Patients with progressive disease underwent CT scans every 6 weeks. Tumor assessments were evaluated per RECIST v1.1 (Response Evaluation Criteria Solid Tumors) and iRECIST v1.1 (Response Evaluation Criteria Solid Tumors for immune-based therapeutics).

Category 1 = Based upon high-level evidence, there is uniform NCCN consensus that intervention is appropriate.

PFS = Progression-free survival; ORR = Overall response rate; DOR = Duration of response; NSCLC = Non-small cell lung cancer

PREFERRED

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Category 1 and PREFERRED recommendations[5]

Category 1 and PREFERRED recommendations regardless of PD-L1 expression[5]

For patients with or without PD-L1 expression: Pembrolizumab (KEYTRUDA), in combination with platinum and pemetrexed, is a preferred first-line regimen, recommended (Category 1 and Preferred) as first-line therapy for patients with metastatic squamous NSCLC.

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SELECTED SAFETY INFORMATION

FIRST-LINE COMBINATION THERAPY IN NONSQUAMOUS mNSCLC: KEYTRUDA, in combination with pemetrexed and platinum chemotherapy, is indicated for the treatment of patients with metastatic nonsquamous NSCLC.

FIRST-LINE MONOTHERAPY IN NONSQUAMOUS AND SQUAMOUS mNSCLC: KEYTRUDA, as a single agent, is indicated for the first-line treatment of patients with metastatic NSCLC expressing PD-L1 (tumor proportion score [TPS] ≥1%) as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and is stage IV where patients are PD-L1 positive. Of the patients who received chemotherapy, 13% received prior therapy.

SECOND-LINE OR GREATER MONOTHERAPY IN NONSQUAMOUS AND SQUAMOUS mNSCLC: KEYTRUDA, as a single agent, is indicated for the treatment of patients with metastatic NSCLC expressing PD-L1 (TPS ≥1%) as determined by an FDA-approved test, with disease progression on 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.

mNSCLC = Metastatic non-small cell lung cancer; NSCLC = Non-small cell lung cancer; PD-L1 = Programmed death ligand 1

SELECTED SAFETY INFORMATION

Immune-Mediated Adverse Reactions

KEYTRUDA, a humanized monoclonal antibody that binds to PD-1, may stand to either the programmed death receptor-1 (PD-1) or the programmed death ligand-1 (PD-L1), blocking the PD-1/PD-L1 pathway, thereby removing inhibition of the immune response, potentially breaking peripheral tolerance and inducing immune-mediated adverse reactions in patients treated with KEYTRUDA. Immune-mediated adverse reactions listed here may not include all possible severe and fatal immune-mediated adverse reactions.

Immune-mediated adverse reactions listed here may not include all possible severe and fatal immune-mediated adverse reactions.

Immune-mediated adverse reactions in KEYTRUDA-treated patients were generally managed by withholding KEYTRUDA and administering immunosuppressant doses of corticosteroids, followed by prolonged taper of corticosteroids, and supportive care. Most of the immune-mediated adverse reactions were reversible with KEYTRUDA-based immunosuppressant or discontinuation, whereas systemic corticosteroids were required in 67% (336/501) of patients. Of patients who were withheld pembrolizumab because of an immune-mediated adverse reaction, 93% (46/49) resolved. Of patients who received corticosteroids for immune-mediated adverse reactions, 79% (395/501) had a median duration of 4 days (range: 1 day to 9 months). Of patients who were withheld KEYTRUDA after initiation of corticosteroids, 32% (16/50) resolved. Of patients who were withheld KEYTRUDA and received corticosteroids, 87% (43/49) had a median duration of 4 days (range: 1 day to 2 months). All patients who were withheld KEYTRUDA after initiation of corticosteroids were permanently discontinued for this adverse reaction.

Immune-Mediated Pneumonitis

Of patients who received KEYTRUDA, 3.4% (17/501) had immune-mediated pneumonitis, including 1 (0.2%) patient with Grade 5, 7 (1.4%) patients with Grade 3, and 9 (1.8%) patients with Grade 2. Pneumonitis resolved in 71% (12/17) of patients, including 2 (0.4%) patients with Grade 3 and 7 (1.4%) patients with Grade 2. Systemic corticosteroids were required in 67% (8/12) of patients. Pneumonitis led to permanent discontinuation of KEYTRUDA in 1.2% (6) and withholding in 1.2% (6) of patients. Pneumonitis led to permanent discontinuation of KEYTRUDA in 2 patients with NSCLC and 1 patient with other malignancies with other immune-mediated adverse reactions and withheld in 2 patients with NSCLC. Of the 6 patients, 5 received corticosteroids for this adverse reaction. Pneumonitis resolved in 2 patients.

Pneumonitis occurred 0.3 (21/501) of adult patients with cHL receiving KEYTRUDA as a single agent, including Grade 3 in 0.2% (1) of patients. Patients with immune-mediated pneumonitis in the KEYNOTE-087 pooled analysis (n=1,475) received KEYTRUDA as a single agent for a median duration of 4.4 months (range: 1 day to 23 months). Pneumonitis resolved in 81% (17/21) of patients, including 0.2% (3) of patients with Grade 3. Systemic corticosteroids were required in 67% (14/21) of patients. Pneumonitis led to permanent discontinuation of KEYTRUDA in 0.7% (10) and withholding in 0.2% (3) of patients. All patients who were withheld KEYTRUDA after symptom improvement, of these, 67% (2/3) resumed KEYTRUDA and 50% (1/2) of patients had no recurrence of pneumonitis.

Immune-Mediated Hepatitis

KEYTRUDA, as a single agent, administered to patients with cHL, including immune-mediated hepatitis occurred in 0.7% (7/1,059) of patients receiving KEYTRUDA, including Grade 3 in 0.4% (4) of patients. Immune-mediated hepatitis resolved in 2 patients with Grade 3. Systemic corticosteroids were required in all 7 patients. Immune-mediated hepatitis led to permanent discontinuation of KEYTRUDA in 0.2% (2) and withholding in 0.3% (3) of patients. All patients who were withheld KEYTRUDA after symptom improvement, of these, 100% (3/3) resumed KEYTRUDA and 67% (2/3) had no recurrence of hepatitis.

Immune-Mediated Colitis

KEYTRUDA in combination with ipilimumab delivered immune-mediated hepatitis occurred in 0.7% (7/1,059) of patients receiving KEYTRUDA, including Grade 3 in 0.4% (4) of patients. Immune-mediated hepatitis resolved in 2 patients with Grade 3. Systemic corticosteroids were required in all 7 patients. Immune-mediated hepatitis led to permanent discontinuation of KEYTRUDA in 0.2% (2) and withholding in 0.3% (3) of patients. All patients who were withheld KEYTRUDA after symptom improvement, of these, 100% (3/3) resumed KEYTRUDA and 67% (2/3) had no recurrence of hepatitis.

Immune-Mediated Nephritis with Renal Dysfunction

KEYTRUDA in combination with ipilimumab delivered immune-mediated nephritis occurred in 0.3% (8/2784) of patients receiving KEYTRUDA, including Grade 3 in 0.7% (2), Grade 2 in 0.7% (2), and Grade 5 in 0.1% (1) of patients. Immune-mediated nephritis resolved in 1 patient with Grade 2. Systemic corticosteroids were required in all 7 patients of KEYTRUDA in 0.1% (2) and withholding in 0.1% (3) of patients. All patients were withheld pembrolizumab KEYTRUDA after symptom improvement, of these, 100% (1/1) resumed KEYTRUDA and 50% (1/2) had no recurrence of nephritis.

Immune-Mediated Endocrine Adverse Reactions

KEYTRUDA can cause immune-mediated adrenal insufficiency, hypophysitis, diabetes, including fulminant diabetes, and thyroid disorders, beginning at any time during treatment. Most of the immune-mediated endocrine adverse reactions could result in life-threatening consequences or have permanent effects if not recognized and managed. Immune-mediated endocrine adverse reactions occurred in 1.4% (28/501) of patients receiving KEYTRUDA, including Grade 3 (1%) and Grade 2 (0.4%) reactions. Systemic corticosteroids were required in 0.8% (4/501) of patients receiving KEYTRUDA, including 0.6% (3) of patients who received greater than or equal to 40 mg prednisone or its equivalent daily for a median duration of 1 month (range: 1 day to 2 months). Of patients who were withheld KEYTRUDA because of an immune-mediated endocrine adverse reaction, 100% (2/2) resolved. Of patients who received corticosteroids for immune-mediated endocrine adverse reactions, 75% (21/28) had a median duration of 4 days (range: 1 day to 9 months). Of patients who were withheld KEYTRUDA after initiation of corticosteroids, 50% (1/2) resolved. All patients who were withheld KEYTRUDA after initiation of corticosteroids were permanently discontinued for this adverse reaction.

Immune-Mediated Adrenal Insufficiency

Immune-mediated adrenal insufficiency occurred in 0.2% (1/501) of patients receiving KEYTRUDA, including Grade 3 (0.2%) and Grade 2 (0.2%) reactions. Systemic corticosteroids were required in all patients. Immune-mediated adrenal insufficiency led to permanent discontinuation of KEYTRUDA in 0.2% (1) and withholding in 0.2% (1) of patients. All patients who were withheld KEYTRUDA after symptom improvement, of these, 100% (1/1) resumed KEYTRUDA and had no recurrence of adrenal insufficiency.

Immune-Mediated Hypophysitis

KEYTRUDA can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual defects, hypopituitarism, or hormonal deficiencies. Immune-mediated hypophysitis occurred in 0.6% (3/501) of patients receiving KEYTRUDA depending on severity. Hypophysitis occurred in 0.6% (1/159) of patients receiving KEYTRUDA, including Grade 3 (1%). Grade 3 (0.6%) and Grade 2 (0.6%) hypophysitis resolved in 2 patients. Systemic corticosteroids were required in all patients. Immune-mediated hypophysitis led to permanent discontinuation of KEYTRUDA in 0.6% (1) of patients.

Hypophysitis occurred in 0.4% (36/8706) of patients receiving KEYTRUDA, including Grade 3 (0.1%) and Grade 2 (0.4%). It led to permanent discontinuation of KEYTRUDA in 0.1% (1) and withholding in 0.3% (3) of patients. All patients were withheld KEYTRUDA after symptom improvement. The majority (97%) of patients received corticosteroids. Hypophysitis resolved in 72% (26/36) of patients, including Grade 3 in 0.1% (1) of patients. Of patients who were withheld KEYTRUDA because of hypophysitis, 92% (12/13) resolved. Of patients who received corticosteroids for hypophysitis, 72% (26/36) resolved. Of patients who received corticosteroids for hypophysitis and were withheld KEYTRUDA after initiation of corticosteroids, 92% (12/13) resolved. Of patients who were withheld KEYTRUDA for hypophysitis, 92% (12/13) were permanently discontinued for this adverse reaction.

Immune-Mediated Diabetes

KEYTRUDA can cause immune-mediated diabetes, including fulminant diabetes, including diseases (ketosis-prone diabetes, drug-induced diabetes with antibodies, and idiopathic diabetes). Immune-mediated diabetes occurred in 0.2% (1/501) of patients receiving KEYTRUDA. Immune-mediated diabetes resolved in 0.2% (1) of patients. Immune-mediated diabetes led to permanent discontinuation of KEYTRUDA in 0.2% (1) of patients.

Immune-mediated diabetes occurred in 0.1% (12/8706) of patients receiving KEYTRUDA, including Grade 3 (<1%) and Grade 2 (0.1%). Immune-mediated diabetes resolved in 1% (1/12) of patients receiving KEYTRUDA, including Grade 2 (<1%) and Grade 2 (0.1%). Immune-mediated diabetes led to permanent discontinuation of KEYTRUDA in 0.1% (1) of patients. All patients were withheld KEYTRUDA after symptom improvement, of these, 100% (1/1) resumed KEYTRUDA and had no recurrence of immune-mediated diabetes.

Immune-Mediated Gastrointestinal Adverse Reactions

KEYTRUDA can cause immune-mediated colitis or diarrhea. Immune-mediated colitis occurred in 0.3% (8/2784) of patients receiving KEYTRUDA, including Grade 3 (0.1%), Grade 2 (0.1%), and Grade 5 (0.1%) reactions. Immune-mediated colitis resolved in 1 patient with Grade 2. Systemic corticosteroids were required in all patients of KEYTRUDA in 0.1% (2) and withholding in 0.1% (3) of patients. All patients were withheld KEYTRUDA after symptom improvement, of these, 100% (1/1) resumed KEYTRUDA and had no recurrence of immune-mediated colitis.

Immune-Mediated Dermatologic Adverse Reactions

KEYTRUDA can cause immune-mediated rash or dermatitis. Exfoliative dermatitis, including Stevens-Johnson syndrome, drug rash with eosinophilia and systemic symptoms, and toxic epidermal necrolysis, has been reported in 0.4% of patients taking other PD-1 receptor blockade-containing products. Immune-mediated rash or dermatitis occurred in 1.4% (28/501) of patients receiving KEYTRUDA. Depending on severity, immune-mediated rash or dermatitis occurred in 1.4% (28/501) of patients receiving KEYTRUDA, including Grade 3 (1%) and Grade 2 (0.2%) reactions. Systemic corticosteroids were required in 0.6% (3/501) of patients receiving KEYTRUDA, including 0.4% (2) of patients who received greater than or equal to 40 mg prednisone or its equivalent daily for a median duration of 2 months (range: 1 day to 2 months). Immune-mediated rash or dermatitis resolved in 0.4% (1/3) of patients with Grade 3 and 0.4% (1/2) of patients with Grade 2. Of patients who received corticosteroids for immune-mediated rash or dermatitis, 75% (21/28) had a median duration of 4 days (range: 1 day to 9 months). Of patients who were withheld KEYTRUDA after initiation of corticosteroids, 50% (1/2) resolved. Of patients who received corticosteroids for immune-mediated rash or dermatitis and were withheld KEYTRUDA after initiation of corticosteroids, 50% (1/2) resolved. Of patients who were withheld KEYTRUDA for immune-mediated rash or dermatitis, 75% (3/4) were permanently discontinued for this adverse reaction.

Other Immune-Mediated Adverse Reactions

The following clinically significant immune-mediated adverse reactions occurred at an incidence of <1% (unless otherwise noted) in patients who received KEYTRUDA, or were reported with the use of other products in the class of PD-1 or PD-L1 blockers or KEYTRUDA and other PD-1 or PD-L1 blockers: myocarditis, Guillain-Barré syndrome, myasthenia gravis, polymyalgia rheumatica, vasculitis, Parkinson Syndrome, hemophagocytic lymphohistiocytosis, sarcoidosis, uveitis, and ophthalmic manifestations, hypothalamic syndrome/hypothalamitis, pancreatitis, including fulminant pancreatitis, hemolytic anemia, thrombocytopenia purpura, solid organ transplant rejection.

Immune-Mediated Myocarditis

KEYTRUDA can cause immune-mediated myocarditis. Immune-mediated myocarditis occurred in 0.4% (1/259) of patients receiving KEYTRUDA, including Grade 3 (0.4%) patients receiving KEYTRUDA. Monitor for signs and symptoms of cardiac-related toxicities. Interrupt or slow the rate of infusion for Grade 1 or Grade 2 reactions. For Grade 3 or Grade 4 reactions, permanently discontinue KEYTRUDA.

Complications of Allogeneic Hematopoietic Stem Cell Transplantation (HSCT)

Immune-mediated adverse reactions in patients who received allogeneic HSCT before or after anti-PD-1/PD-L1 treatments. Transplant-related complications included hyperacute graft-versus-host-disease (GVHD), acute and chronic GVHD, hepatic veno-occlusive disease after induced intensity conditioning regimen, and steroid-requiring febrile pneumonitis. Patients received HSCT after discontinuing KEYTRUDA. The frequency of these events in patients who underwent anti-PD-1/PD-L1 treatments and allogeneic HSCT. Follow patients closely for evidence of these complications and intervene promptly. Consider the benefit vs risks of using anti-PD-1/PD-L1 treatment prior to or after allogeneic HSCT.

Increased Mortality in Patients With Multiple Myeloma

In 2 randomized clinical trials in patients with multiple myeloma, KEYTRUDA in a thalidomide analogue plus dexamethasone resulted in increased mortality. Treatment of these patients cannot rule out this difference. Treatment of these patients with a PD-1/PD-L1 blockade in combination with these agents is not recommended.

Embryofetal Toxicity

Based on its mechanism of action, KEYTRUDA can cause fetal harm when administered to a pregnant woman. Advise women of the potential risk. In females of reproductive potential, verify their pregnancy status and advise them of the potential risk to a fetal child. Advise female patients of reproductive potential to use effective contraception for the last four months.

Adverse Reactions

In KEYNOTE-045, KEYTRUDA was discontinued due to adverse reactions in 9% of 350 patients with advanced metastatic urothelial cancer receiving KEYTRUDA. Serious adverse reactions occurred in 30% of patients receiving KEYTRUDA. The most common adverse reactions (≥20%) were fatigue (21%), and pruritus (20%). The most common adverse reactions (≥2%) were fatigue (2%), and pruritus (2%).

In KEYNOTE-052, KEYTRUDA was discontinued due to adverse reactions in 9% of 370 patients with advanced urothelial cancer. Immune-mediated adverse reactions occurred in 3.8% of patients receiving KEYTRUDA. The most common adverse reactions (≥20%) were fatigue (26%), musculoskeletal pain (22%), and pruritus (20%). The most common adverse reactions (≥2%) were fatigue (2%), and pruritus (2%).

In KEYNOTE-045, KEYTRUDA was administered with pemetrexed and platinum chemotherapy, and KEYTRUDA was discontinued due to adverse reactions in 26% of 206 patients. The most common adverse reactions (≥20%) were nausea (67%), fatigue (44%), vomiting (34%), decreased appetite (27%), diarrhea (23%), dermatitis (22%), constipation (21%), cough (21%), dyspnea (21%), and pyrexia (20%).

In KEYNOTE-407, when KEYTRUDA was administered with carboplatin and either paclitaxel or paclitaxel protein-bound in metastatic squamous NSCLC, KEYTRUDA was discontinued due to adverse reactions in 19% of 559 patients. The most common adverse reactions (≥20%) were alopecia (59%), fatigue (47%), nausea (39%), peripheral neuropathy (26%), and arthralgia (22%). The most common adverse reactions (≥2%) were fatigue (2%), and pyrexia (2%).

In KEYNOTE-189, when KEYTRUDA was administered with pemetrexed and platinum chemotherapy, and KEYTRUDA was discontinued due to adverse reactions in 14% of 405 patients. The most common adverse reactions (≥20%) were nausea (62%), fatigue (41%), vomiting (34%), diarrhea (31%), decreased appetite (28%), constipation (24%), rash (21%), and cough (20%). The most common adverse reactions (≥2%) were fatigue (2%), and pyrexia (2%).

In KEYNOTE-021, when KEYTRUDA was administered with carboplatin and pemetrexed, and KEYTRUDA was discontinued due to adverse reactions in 10% of 123 patients. The most common adverse reactions (≥20%) were fatigue (27%), nausea (26%), decreased appetite (21%), diarrhea (20%), and rash (20%). The most common adverse reactions (≥2%) were fatigue (2%), and pyrexia (2%).

In KEYNOTE-052, KEYTRUDA was administered in patients with advanced urothelial cancer (n=370) and cancer of the urinary bladder (n=18) and discontinued due to adverse reactions in 9% of 370 patients. Serious adverse reactions occurred in 30% of patients receiving KEYTRUDA. The most common adverse reactions (≥20%) were fatigue (26%), musculoskeletal pain (22%), and pruritus (20%). The most common adverse reactions (≥2%) were fatigue (2%), and pruritus (2%). Hypothyroidism occurred in 9% of patients receiving KEYTRUDA.

In KEYNOTE-045, when KEYTRUDA was administered in combination with paclitaxel, total adverse reactions occurred in 3.3% of 426 patients. Serious adverse reactions occurred in 2.1% of patients receiving KEYTRUDA. The most common adverse reactions (≥20%) were alopecia (59%), fatigue (47%), nausea (39%), peripheral neuropathy (26%), and arthralgia (22%). The most common adverse reactions (≥2%) were fatigue (2%), and pyrexia (2%).

Among the 92 patients with MCC enrolled in study KEYNOTE-017, adverse reactions occurring in patients with MCC were generally similar to those occurring in patients with other malignancies receiving KEYTRUDA. The most common adverse reactions (≥20%) were fatigue (41%), musculoskeletal pain (35%), pruritus (28%), rash (26%), diarrhea (22%), and decreased appetite (20%). The most common adverse reactions (≥2%) were fatigue (2%), and pruritus (2%).

In KEYNOTE-426, when KEYTRUDA was administered in combination with carboplatin, total adverse reactions occurred in 3.3% of 426 patients. Serious adverse reactions occurred in 39% of patients receiving KEYTRUDA. The most common adverse reactions (≥20%) were nausea (37%), fatigue (31%), vomiting (25%), diarrhea (23%), decreased appetite (21%), and rash (20%). The most common adverse reactions (≥2%) were fatigue (2%), and pyrexia (2%).

Among the 10 patients with MSI-H cancer enrolled in study KEYNOTE-016, adverse reactions occurring in patients with MSI-H cancer were generally similar to those occurring in patients with other malignancies receiving KEYTRUDA. The most common adverse reactions (≥20%) were fatigue (50%), diarrhea (40%), nausea (30%), vomiting (30%), and decreased appetite (20%). The most common adverse reactions (≥2%) were fatigue (2%), and pyrexia (2%).

In KEYNOTE-189, when KEYTRUDA was administered in combination with pemetrexed and platinum chemotherapy, and KEYTRUDA was discontinued due to adverse reactions in 14% of 405 patients. Serious adverse reactions occurred in 37% of patients receiving KEYTRUDA. The most common adverse reactions (≥20%) were nausea (62%), fatigue (41%), vomiting (34%), diarrhea (31%), decreased appetite (28%), constipation (24%), rash (21%), and cough (20%). The most common adverse reactions (≥2%) were fatigue (2%), and pyrexia (2%).

In KEYNOTE-037, KEYTRUDA was discontinued due to adverse reactions in 9% of 151 patients with RPMC. The most common adverse reaction (≥20%) was fatigue (21%). The most common adverse reactions (≥2%) were fatigue (2%), and pyrexia (2%). Hypothyroidism occurred in 7% of patients receiving KEYTRUDA.

In KEYNOTE-029, KEYTRUDA was administered in combination with chemoradiotherapy (CRT) followed by KEYTRUDA monotherapy. KEYTRUDA was discontinued due to adverse reactions in 7% of 154 patients. The most common adverse reactions (≥20%) were dermatitis (64%), pruritus (29%), and fatigue (21%). The most common adverse reactions (≥2%) were fatigue (2%), and pruritus (2%).

In KEYNOTE-053, KEYTRUDA was discontinued due to adverse reactions in 9% of 107 patients with locally advanced or metastatic urothelial carcinoma. The most common adverse reactions (≥20%) were fatigue (31%), musculoskeletal pain (25%), and diarrhea (23%). The most common adverse reactions (≥2%) were fatigue (2%), and pyrexia (2%).

In KEYNOTE-087, KEYTRUDA was discontinued due to adverse reactions in 11% of 146 patients with high-risk MMRD. The most common adverse reaction (≥20%) was fatigue (21%). The most common adverse reactions (≥2%) were fatigue (2%), and pyrexia (2%). Hypothyroidism occurred in 8% of patients receiving KEYTRUDA.

In KEYNOTE-177, KEYTRUDA was discontinued due to adverse reactions in 9% of 296 patients with locally advanced or metastatic urothelial carcinoma. The most common adverse reactions (≥20%) were pruritus (26%), rash (21%), and diarrhea (20%). The most common adverse reactions (≥2%) were pruritus (2%), and rash (2%). Hypothyroidism occurred in 8% of patients receiving KEYTRUDA.

In KEYNOTE-407, KEYTRUDA was discontinued due to adverse reactions in 11% of 198 patients with squamous NSCLC. The most common adverse reaction (≥20%) was fatigue (21%). The most common adverse reactions (≥2%) were fatigue (2%), and pyrexia (2%). Hypothyroidism occurred in 8% of patients receiving KEYTRUDA.

In KEYNOTE-042, KEYTRUDA was discontinued due to adverse reactions in 9% of 637 patients with advanced NSCLC. The most common adverse reaction (≥20%) was fatigue (21%). The most common adverse reactions (≥2%) were fatigue (2%), and pyrexia (2%). Hypothyroidism occurred in 8% of patients receiving KEYTRUDA.

In KEYNOTE-001, when KEYTRUDA was administered with cisplatin and fluorouracil to patients with metastatic or locally advanced esophageal or GEJ tumors (n=194), KEYTRUDA was discontinued due to adverse reactions in 9% of patients. Serious adverse reactions occurred in 51% of patients. KEYTRUDA was discontinued due to adverse reactions in 1% of 23 patients. The most common adverse reactions (≥20%) were diarrhea (53%), nausea (51%), decreased appetite (51%), and pyrexia (51%). The most common adverse reactions (≥2%) were diarrhea (2%), nausea (2%), and pyrexia (2%). Hypothyroidism occurred in 8% of patients receiving KEYTRUDA.

Adverse reactions occurring in patients with esophageal cancer who received KEYTRUDA as a monotherapy were similar to those occurring in patients with other malignancies receiving KEYTRUDA.

In KEYNOTE-158, KEYTRUDA was discontinued due to adverse reactions in 5% of 98 patients with cervical cancer. The most common adverse reactions (≥20%) were fatigue (31%), diarrhea (22%), and rash (20%). The most common adverse reactions (≥2%) were fatigue (2%), and pyrexia (2%).

Adverse reactions occurring in patients with gastric cancer were similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy.

In KEYNOTE-590, when KEYTRUDA was administered with cisplatin and fluorouracil to patients with metastatic or locally advanced esophageal or GEJ tumors (n=304), KEYTRUDA was discontinued due to adverse reactions in 11% of patients. Serious adverse reactions occurred in 54% of patients. KEYTRUDA was discontinued due to adverse reactions in 1% of 23 patients. The most common adverse reactions (≥20%) were diarrhea (53%), nausea (51%), decreased appetite (51%), and pyrexia (51%). The most common adverse reactions (≥2%) were diarrhea (2%), nausea (2%), and pyrexia (2%). Hypothyroidism occurred in 8% of patients receiving KEYTRUDA.

Adverse reactions occurring in patients with esophageal cancer who received KEYTRUDA as a monotherapy were similar to those occurring in patients with other malignancies receiving KEYTRUDA.

In KEYNOTE-158, KEYTRUDA was discontinued due to adverse reactions in 9% of 148 patients with advanced endometrial carcinoma. The most common adverse reactions (≥20%) were fatigue (31%), diarrhea (22%), and rash (20%). The most common adverse reactions (≥2%) were fatigue (2%), and pyrexia (2%).

Adverse reactions occurring in patients with MMR-D cancer were similar to those occurring in patients with other malignancies receiving KEYTRUDA as a monotherapy.

In KEYNOTE-158, when KEYTRUDA was administered in combination with lenvatinib, total adverse reactions occurred in 3.3% of 426 patients. Serious adverse reactions occurred in 39% of patients receiving KEYTRUDA. The most common adverse reactions (≥20%) were diarrhea (52%), fatigue (41%), musculoskeletal pain (31%), decreased appetite (31%), hypertension (31%), nausea (29%), vomiting (23%), stomatitis (22%), and rash (20%). The most common adverse reactions (≥2%) were fatigue (2%), hypertension (2%), and pyrexia (2%). Hypothyroidism occurred in 8% of patients receiving KEYTRUDA.

Adverse reactions occurring in patients with hepatocellular carcinoma (HCC) were generally similar to those in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy. In KEYNOTE-224, KEYTRUDA was discontinued due to adverse reactions in 4% of 90 patients with HCC. The most common adverse reactions (≥20%) were diarrhea (27%), and fatigue (20%). The most common adverse reactions (≥2%) were fatigue (2%), and pyrexia (2%).

In KEYNOTE-240, when KEYTRUDA was administered in combination with lenvatinib, total adverse reactions occurred in 3.3% of 426 patients. Serious adverse reactions occurred in 39% of patients receiving KEYTRUDA. The most common adverse reactions (≥20%) were diarrhea (52%), fatigue (41%), musculoskeletal pain (31%), decreased appetite (31%), hypertension (31%), nausea (29%), vomiting (23%), stomatitis (22%), and rash (20%). The most common adverse reactions (≥2%) were fatigue (2%), hypertension (2%), and pyrexia (2%). Hypothyroidism occurred in 8% of patients receiving KEYTRUDA.

Adverse reactions occurring in patients with cervical cancer were similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy.

In KEYNOTE-775, when KEYTRUDA was administered in combination with lenvatinib, total adverse reactions occurred in 3.3% of 426 patients. Serious adverse reactions occurred in 39% of patients receiving KEYTRUDA. The most common adverse reactions (≥20%) were diarrhea (52%), fatigue (41%), musculoskeletal pain (31%), decreased appetite (31%), hypertension (31%), nausea (29%), vomiting (23%), stomatitis (22%), and rash (20%). The most common adverse reactions (≥2%) were fatigue (2%), hypertension (2%), and pyrexia (2%). Hypothyroidism occurred in 8% of patients receiving KEYTRUDA.

Adverse reactions occurring in patients with endometrial carcinoma were similar to those occurring in patients with other malignancies receiving KEYTRUDA as a monotherapy.

In KEYNOTE-522, 181 patients (patients (pt) diagnosed with stage II-IIIA-IIIB-IIIC-IIIC1 disease and 18 pediatric patients (pt) 12 years to 17 years) were administered KEYTRUDA 200 mg every 3 weeks. The median duration of exposure was 11.1 months (range: 1 day to 35 months).

Adverse reactions that occurred at a ≥10% higher rate in pediatric patients when compared to adults were pyrexia (33%), vomiting (30%), leukopenia (26%), upper respiratory tract infection (22%), and abdominal pain (21%).

cHL = classical Hodgkin lymphoma; CRC = colorectal cancer; dMMR = mismatch repair deficient; EAC = esophageal adenocarcinoma; EC = endometrial carcinoma; GEJ = gastroesophageal junction; HNSCC = head and neck squamous cell carcinoma; MCC = Merkel cell carcinoma; MSI-H = microsat

DURABLE OVERALL SURVIVAL achieved first line with KEYTRUDA as monotherapy vs platinum-containing chemotherapy[1]

Durable overall survival with KEYTRUDA vs platinum-containing chemotherapy

Overall Survival (PD-L1 1%)[1,2]

At the interim analysis (median follow-up: time: 12 months)[1]:

- 40% reduction in the risk of death with KEYTRUDA vs platinum-containing chemotherapy (HR=0.60; 95% CI: 0.41-0.88; 2-sided P=0.0097)
  - Events observed in 79 patients (51.3%) with KEYTRUDA and 93% (61.6%) with platinum-containing chemotherapy

At the protocol-specified final analysis (median follow-up time: 23 months)[2]:

- **Median OS doubled: 20 months (95% CI: 15.3, 26) with KEYTRUDA vs 10 months (95% CI: 8.8-13.9) with platinum-containing chemotherapy**[2]

Durable Overall Survival in an Exploratory Updated Analysis (PD-L1 1%)[3,4]

LIMITATION: The protocol-specified analysis based on extended follow-up time of 44.4 months in KEYNOTE-024 was exploratory in nature. No formal statistical testing was planned and, therefore, no statistical conclusions can be drawn.

- **Median OS: 26.3 months (95% CI: 18.3, 40.5) vs 14.2 months in KEYNOTE-024 was exploratory in nature. No formal statistical testing was planned and, therefore, no statistical conclusions can be drawn.**
  - Events observed: 63% (97/154) with KEYTRUDA and 75% (113/151) with chemotherapy

APPROPRIATE PATIENTS ⓘ

In an interim analysis of KEYNOTE-024 (median follow-up time: 12 months)

SUPPORTIVE PFS and ORR with KEYTRUDA as monotherapy vs platinum-containing chemotherapy (PD-L1 50%)[1]

PFS ⓘ

- Patients at disease progression or death indicated by half
- HR=0.50; 95% CI, 0.37-0.68; P<0.001
- 6-month median PFS (95% CI): 5.8 months with KEYTRUDA vs 8.0 months (95% CI: 4.2-8.2) with chemotherapy
  - Events observed: 47% (73/154) with KEYTRUDA and 77% (116/151) with chemotherapy

ORR ⓘ Nearly half of patients responded

- ORR (95% CI): 27.5% (20.4-35.6) with KEYTRUDA vs 29% (20%, 31.2%) with chemotherapy
- Complete response rate: 1.9% with KEYTRUDA
  - 4% CR and 41% PR with KEYTRUDA vs 1% CR and 27% PR with chemotherapy

DOR ⓘ Duration of response

- Median DOR not reached (range: 1.9+ - 14.3+ months) with KEYTRUDA vs 8.3 months (range: 2.2+ - 22.1+ months) with chemotherapy

Phase 3 registrational trial

KEYNOTE-024 study design: Phase 3, randomized, multicenter, open-label, active-controlled trial in treatment-naive, metastatic NSCLC patients with ≥1% PD-L1 expression (n=305) and no EGFR or ALK genomic tumor aberrations. Patients received pembrolizumab (n=154) or platinum-containing chemotherapy (n=151). Patients with EGFR or ALK genomic tumor aberrations, autoimmune disease that required systemic therapy within 2 years of treatment, a medical condition that required immunosuppressive doses of corticosteroids, or active or prior CNS metastasis were ineligible. Patients received pembrolizumab 200 mg every 3 weeks or platinum-containing chemotherapy (cisplatin 75 mg/m2 or carboplatin dosed at AUC 6 mg/mL/min) plus pemetrexed 500 mg/m2 every 3 weeks. Patients with nonsquamous histology received maintenance pemetrexed, and patients with squamous histology received maintenance pemetrexed if stable or responding. Patients in chemotherapy arm received pemetrexed at progression or cisplatin-containing chemotherapy if pemetrexed was contraindicated. Tumor assessments were performed every 6 weeks. Patients in pembrolizumab arm who experienced disease progression were offered KEYTRUDA. The main efficacy outcome measure was progression-free survival (PFS). Additional efficacy outcome measures were OS and objective response rate (ORR).

PREFERRED

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)
Category 1 and PREFERRED recommendations[5]

Category 1 and PREFERRED recommendations for patients with PD-L1 ≥50%[5]

For patients with PD-L1 ≥50%: Single-agent pembrolizumab (KEYTRUDA) is recommended (Category 1 and Preferred) as first-line treatment for patients with nonsquamous or squamous (mNSCLC), and with EGFR mutations or ALK rearrangements.

See NCCN Guidelines® for Treatment of Patients with mNSCLC ⓘ

In patients with stage III NSCLC who were not candidates for surgical resection or definitive chemoradiation, and patients with mNSCLC with PD-L1 expression (≥1%) and no EGFR or ALK genomic tumor aberrations.

KEYNOTE-042

Superior overall survival first line with KEYTRUDA as monotherapy vs platinum-containing chemotherapy

Pharmacology | Dosing | Indications | Clinical Studies | Safety | Patient Information | Resources

In patients with stage III NSCLC who were not candidates for surgical resection or definitive chemoradiation, and patients with mNSCLC with PD-L1 expression (≥1%) and no EGFR or ALK genomic tumor aberrations.

KEYNOTE-042

Superior overall survival first line with KEYTRUDA as monotherapy vs platinum-containing chemotherapy

FIRST-LINE COMBINATION THERAPY IN NONSQUAMOUS mNSCLC: KEYTRUDA, in combination with pemetrexed and platinum chemotherapy, is indicated for the first line treatment of patients with metastatic nonsquamous non-small cell lung cancer, with no EGFR or ALK genomic tumor aberrations.

FIRST-LINE COMBINATION THERAPY IN SQUAMOUS mNSCLC: KEYTRUDA, in combination with carboplatin and either paclitaxel or paclitaxel protein-bound, is indicated for the first line treatment of patients with metastatic squamous non-small cell lung cancer.

FIRST-LINE MONOTHERAPY IN NONSQUAMOUS AND SQUAMOUS mNSCLC: KEYTRUDA, as a single agent, is indicated for the first line treatment of patients with NSCLC expressing PD-L1 (tumor proportion score [TPS] ≥1%) as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and is stratified for PD-L1 expression (TPS ≥50% versus TPS 1%-49%) in clinical trials.

SECOND-LINE OR ABOVE MONOTHERAPY IN NSCLC: KEYTRUDA, as a single agent, is indicated for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥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 also have disease progression on FDA-approved therapy for these aberrations.

KEYTRUDA® (PEMBROLIZUMAB) INJECTION, 100 MG | PATIENT-SPECIFIC DOSING TOOL | PATIENT-FOCUSED SUPPORT TOOLS

SELECTED SAFETY INFORMATION

Severe and Fatal Immune-Mediated Adverse Reactions

Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue, can affect more than one organ system at the same time, and can occur after discontinuation of KEYTRUDA. Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue, can affect more than one organ system at the same time, and can occur after discontinuation of KEYTRUDA. Immune-mediated adverse reactions listed here may not include all possible severe and fatal immune-mediated adverse reactions.

Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Early identification and prompt treatment of suspected immune-mediated adverse reactions may prevent severe or life-threatening sequelae. Immune-mediated pneumonitis, colitis, hepatitis, endocrinopathies, and nephritis have occurred with KEYTRUDA. Immune-mediated adverse reactions, initially manifesting after a few doses, have been observed in patients who have received KEYTRUDA. Depending on the affected organ, these may require treatment with systemic immunosuppressants or endocrine replacement therapy. Immune-mediated adverse reactions, including hypophysitis, can result in hypopituitarism, which may be exacerbated by immunosuppressant therapy. Withhold or permanently discontinue KEYTRUDA depending on severity. In addition to withholding KEYTRUDA for adverse reactions, administer corticosteroids and, if clinically appropriate, hormone replacement therapy, until improvement to ≤ Grade 1. Immune-mediated adverse reactions, including those involving endocrine and GI/liver function, may require long-term immunosuppressant therapy after initial treatment with KEYTRUDA. Consider the benefit of continuing KEYTRUDA therapy in patients with immune-mediated adverse reactions.

Immune-Mediated Pneumonitis

KEYTRUDA can cause pneumonitis, including interstitial lung disease, manifesting as dyspnea, cough, and fever. Monitor patients for signs and symptoms of pneumonitis. Evaluate suspected pneumonitis with appropriate imaging. Administer corticosteroids for ≥ Grade 2 pneumonitis. Withhold KEYTRUDA for moderate pneumonitis. Permanently discontinue KEYTRUDA for severe or life-threatening pneumonitis. In patients with lymphocytic infiltration of the lung, consider infectious etiology as part of the differential diagnosis. Infectious pneumonitis has been reported in patients who were without verified histopathologic or radiographic evidence of pneumonitis.

Immune-Mediated Colitis

KEYTRUDA can cause immune-mediated colitis, which may present with diarrhea. Cytomegalovirus infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis. In cases of corticosteroid-refractory immune-mediated colitis, consider other infectious causes. Monitor patients for signs and symptoms of colitis. Administer corticosteroids for ≥ Grade 2 colitis. Withhold KEYTRUDA for moderate colitis. Permanently discontinue KEYTRUDA for severe or life-threatening colitis.

Immune-Mediated Hepatitis and Immune-Mediated Hepatitis with Acute Liver Failure

KEYTRUDA can cause immune-mediated hepatitis. Immune-mediated hepatitis occurred in 1.5% (20/1309) patients receiving KEYTRUDA, including Grade 3 (1.4%) and Grade 4 (0.1%) hepatitis. Immune-mediated hepatitis occurred with a median time to onset of 6.9 months (range: 1 day - 22.9 months), and 9 (45%) of these patients had resolution within a median of 1.1 months (range: 1 day - 2.8+ months) after initiation of corticosteroids. Consider more frequent monitoring of liver enzymes when KEYTRUDA is administered with other anticancer drugs that are associated with liver toxicity. Withhold KEYTRUDA for ≥ Grade 3 liver enzyme elevations. Administer corticosteroids and, if clinically appropriate, hormone replacement therapy, until improvement to ≤ Grade 1. Immune-mediated adverse reactions, including those involving endocrine and GI/liver function, may require long-term immunosuppressant therapy after initial treatment with KEYTRUDA. Consider the benefit of continuing KEYTRUDA therapy in patients with immune-mediated adverse reactions.

Immune-Mediated Endocrinopathies

Adrenal Insufficiency

KEYTRUDA can cause primary or secondary adrenal insufficiency. For Grade 2 or higher, initiate symptomatic treatment, including hormone replacement as clinically indicated. Withhold KEYTRUDA depending on severity. In addition to withholding KEYTRUDA for adverse reactions, administer corticosteroids and, if clinically appropriate, hormone replacement therapy, until improvement to ≤ Grade 1. Immune-mediated adverse reactions, including those involving endocrine and GI/liver function, may require long-term immunosuppressant therapy after initial treatment with KEYTRUDA. Consider the benefit of continuing KEYTRUDA therapy in patients with immune-mediated adverse reactions.

Hypophysitis

KEYTRUDA can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual impairment, or with more subtle, nonspecific symptoms such as nausea, vomiting, and/or fatigue. Hypophysitis can result in hypopituitarism. Initiate symptomatic treatment, including hormone replacement as clinically indicated. Withhold KEYTRUDA depending on severity. In addition to withholding KEYTRUDA for adverse reactions, administer corticosteroids and, if clinically appropriate, hormone replacement therapy, until improvement to ≤ Grade 1. Immune-mediated adverse reactions, including those involving endocrine and GI/liver function, may require long-term immunosuppressant therapy after initial treatment with KEYTRUDA. Consider the benefit of continuing KEYTRUDA therapy in patients with immune-mediated adverse reactions.

Hyperthyroidism and Hypothyroidism

KEYTRUDA can cause hypothyroidism. Initiate hormone replacement therapy as clinically indicated. Withhold KEYTRUDA depending on severity. In addition to withholding KEYTRUDA for adverse reactions, administer corticosteroids until improvement to ≤ Grade 1. Hypothyroidism can result in hypopituitarism. Initiate symptomatic treatment, including hormone replacement as clinically indicated. Immune-mediated adverse reactions, including those involving endocrine and GI/liver function, may require long-term immunosuppressant therapy after initial treatment with KEYTRUDA. Consider the benefit of continuing KEYTRUDA therapy in patients with immune-mediated adverse reactions.

KEYTRUDA can cause immune-mediated hyperthyroidism. Hyperthyroidism can precipitate new onset or exacerbation of cardiac or neuromuscular disorders. Consider more frequent monitoring of thyroid function when the drugs are administered as single agents. For elevated liver enzymes, interrupt KEYTRUDA and administer corticosteroids. Upon resolution, administer KEYTRUDA at a lower dose. Withhold KEYTRUDA for ≥ Grade 3 liver enzyme elevations. In patients with renal cell carcinoma, hyperthyroidism occurred in 2.8% (4/142) patients receiving KEYTRUDA, including Grade 3 (0.7%) and Grade 2 (2.1%) events. Hyperthyroidism occurred with a median time to onset of 2.8 months (range: 0.9 - 6.4 months), and 3 (75%) of these patients had resolution within a median of 1.1 months (range: 0.9+ - 1.4+ months) after initiation of corticosteroids. In patients with NSCLC, hyperthyroidism occurred in 2.1% (31/1509) patients receiving KEYTRUDA, including Grade 3 (0.2%) and Grade 2 (1.9%) events. Hyperthyroidism occurred with a median time to onset of 2.8 months (range: 0.2 - 16.7 months), and 16 (52%) of these patients had resolution within a median of 1.1 months (range: 0.1+ - 15.2+ months) after initiation of corticosteroids. In patients with cHL, hyperthyroidism occurred in 2.7% (5/183) patients receiving KEYTRUDA, including Grade 2 (2.7%) events. Hyperthyroidism occurred with a median time to onset of 2.8 months (range: 1.4 - 5.6 months), and 3 (60%) of these patients had resolution within a median of 1.1 months (range: 1.1+ - 1.4+ months) after initiation of corticosteroids. In patients with urothelial carcinoma, hyperthyroidism occurred in 1.4% (4/281) patients receiving KEYTRUDA, including Grade 2 (1.4%) events. Hyperthyroidism occurred with a median time to onset of 2.8 months (range: 1.4 - 2.8 months), and 2 (50%) of these patients had resolution within a median of 1.1 months (range: 1.1+ - 1.1+ months) after initiation of corticosteroids. In patients with MSI-H cancer, hyperthyroidism occurred in 2.7% (3/110) patients receiving KEYTRUDA, including Grade 3 (1.8%) and Grade 2 (0.9%) events. Hyperthyroidism occurred with a median time to onset of 2.8 months (range: 2.8 - 5.6 months), and 2 (67%) of these patients had resolution within a median of 1.1 months (range: 1.1+ - 1.1+ months) after initiation of corticosteroids.

Type 1 Diabetes Mellitus (DM), Insulin-Dependent

KEYTRUDA can cause type 1 DM. Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate insulin therapy as clinically indicated. Withhold KEYTRUDA depending on severity. Type 1 DM occurred in 0.2% (3/1324) patients receiving KEYTRUDA, including Grade 3 (0.1%) and Grade 2 (0.1%) events. Type 1 DM occurred with a median time to onset of 1.4 months (range: 0.7 - 2.1 months), and 2 (67%) of these patients had resolution within a median of 1.1 months (range: 1.1+ - 1.1+ months) after initiation of KEYTRUDA withheld for adverse reaction.

Infusion-Related Reactions

KEYTRUDA can cause severe or life-threatening infusion-related reactions, including hypersensitivity and anaphylaxis, which have been reported in 0.6% (27/4839) patients receiving KEYTRUDA. Monitor for signs and symptoms of infusion-related reactions. Interrupt or slow the rate of infusion for Grade 1 or Grade 2 reactions. For Grade 3 or Grade 4 reactions, stop infusion and permanently discontinue KEYTRUDA.

Complications of Allogeneic HSCT After Indication for KEYTRUDA

Fatal and other serious complications can occur in patients who receive hematopoietic stem cell transplant (HSCT) before or after anti-PD-1/PD-L1 treatments. Transplant-related complications include hyperacute graft-versus-host-disease (GVHD), acute and chronic GVHD, hepatic veno-occlusive disease after induced intensity conditioning regimen, and steroid-requiring febrile syndrome. These complications may occur despite intervening therapies between PD-1/PD-L1 blockade and allogeneic HSCT.

Follow patients who receive KEYTRUDA prior or subsequent to allogeneic HSCT for these complications. Consider the benefit versus the risks of treatment with KEYTRUDA in patients who have undergone allogeneic HSCT.

Embryo-fetal Toxicity

Based on its mechanism of action, KEYTRUDA can cause fetal harm when administered to a pregnant woman. Advise women of the potential risk to females of reproductive potential, early pregnancy loss prior to initiating KEYTRUDA and advise them to use effective contraception during treatment and for 4 months after the last dose of KEYTRUDA.

Adverse Reactions

In NEWTON-035, KEYTRUDA was discontinued due to adverse reactions in 9% (8/92) patients with advanced melanoma; adverse reactions leading to discontinuation in ≥2% patients included pneumonitis (2%), and myocarditis (2%). The most common adverse reactions (≥20%) were fatigue (47%), pruritus (31%), and rash (25%). The most common adverse reactions (≥5%) were fatigue (5%), diarrhea (5%), and rash (5%), and pruritus (5%).

In KEYNOTE-006, KEYTRUDA was permanently discontinued due to adverse reactions in 14% of 698 patients; the most common (≥1%) were pneumonitis (1.4%), autoimmune hepatitis (1.1%), colitis (1.1%), hypophysitis (1.1%), and infusion reaction (1.1%). The most common adverse reactions (≥20%) were fatigue (29%), diarrhea (21%), and nausea (20%).

In KEYNOTE-189, when KEYTRUDA was administered with pemetrexed and platinum chemotherapy in metastatic nonsquamous NSCLC, KEYTRUDA was discontinued due to adverse reactions in 18% of patients; adverse reactions leading to discontinuation in ≥2% of patients included pneumonitis (4%), renal failure (2.1%), and pneumonia (2%). The most common adverse reactions (≥20%) were nausea (62%), fatigue (51%), constipation (37%), vomiting (29%), diarrhea (27%), decreased appetite (26%), rash (20%), cough (21%), dyspnea (21%), and pruritus (20%).

In KEYNOTE-407, when KEYTRUDA was administered in combination with carboplatin and either paclitaxel or nab-paclitaxel, KEYTRUDA was discontinued due to adverse reactions in 16% of patients; adverse reactions leading to discontinuation in ≥2% of patients included pneumonitis (2.1%), and renal failure (2.1%). The most common adverse reactions (≥20%) were fatigue (50%), nausea (41%), peripheral neuropathy (34%), alopecia (31%), constipation (27%), vomiting (26%), myalgia/arthralgia (23%), diarrhea (21%), decreased appetite (21%), rash (20%), and cough (20%). The most common adverse reactions (≥5%) were anemia (12%), neutropenia (11%), and peripheral neuropathy (5%).

In KEYNOTE-042, KEYTRUDA was discontinued due to adverse reactions in 9% of 637 patients with advanced NSCLC; the most common were pneumonitis (2%), and febrile neutropenia (2%). The most common adverse reactions (≥20%) were fatigue/asthenia (47%), nausea (29%), constipation (25%), decreased appetite (21%), pneumonia (21%), peripheral edema (20%), and dyspnea (20%). The most common adverse reactions (≥5%) were fatigue (8%).

In KEYNOTE-052, KEYTRUDA monotherapy was discontinued due to adverse reactions in 8% of 370 patients with metastatic NSCLC; the most common were hypothyroidism (1.9%), and pneumonitis (1.9%). The most common adverse reactions (≥20%) were musculoskeletal pain (31%), fatigue (28%), rash (25%), and pruritus (20%).

In KEYNOTE-045, KEYTRUDA monotherapy was discontinued due to adverse reactions in 10% of 661 patients with advanced NSCLC; the most common adverse reactions (≥1%) were renal failure (1.2%), and pneumonitis (1.2%). The most common adverse reactions (≥20%) were fatigue (30%), musculoskeletal pain (22%), nausea (21%), and rash (20%).

In KEYNOTE-024, KEYTRUDA monotherapy was discontinued due to adverse reactions in 9% of 154 patients with advanced NSCLC; the most common adverse reactions (≥1%) were pneumonitis (1.3%), hypothyroidism (1.3%), and pneumonia (1.3%). The most common adverse reactions (≥20%) were musculoskeletal pain (27%), fatigue (23%), nausea (20%), and rash (20%).

In KEYNOTE-010, KEYTRUDA monotherapy was discontinued due to adverse reactions in 9% of 1090 patients with advanced NSCLC; the most common adverse reactions (≥1%) were pneumonitis (2.1%), and fatigue (1.1%). The most common adverse reactions (≥20%) were fatigue (28%), dyspnea (26%), and cough (22%). The most common adverse reactions (≥5%) were fatigue (5%), and dyspnea (5%).

In KEYNOTE-001, advanced NSCLC patients who received KEYTRUDA as monotherapy were treated for a median duration of 12.9 months (range: 0.1+ - 52.1+ months) and 185 patients (19%) were treated for ≥24 months. Serious adverse reactions occurred in 41% of patients. The most common adverse reactions (≥20%) were dyspnea (26%), and cough (25%). The most common adverse reactions (≥5%) were dyspnea (5%), and cough (5%).

In KEYNOTE-002, KEYTRUDA monotherapy was discontinued due to adverse reactions in 16% of 628 patients with advanced melanoma (PD-1 naïve). The most common adverse reactions (≥20%) were fatigue (28%), diarrhea (21%), decreased appetite (18%), rash (20%), nausea (19%), and pruritus (18%). The most common adverse reactions (≥5%) were fatigue (5%), and diarrhea (5%).

In KEYNOTE-006, KEYTRUDA monotherapy was discontinued due to adverse reactions in 14% of 526 patients with advanced melanoma; the most common adverse reactions (≥1%) were pneumonitis (1.1%), and colitis (1.1%). The most common adverse reactions (≥20%) were fatigue (29%), diarrhea (21%), and nausea (20%). The most common adverse reactions (≥5%) were diarrhea (5%), and fatigue (5%).

In KEYNOTE-179, KEYTRUDA monotherapy was discontinued due to adverse reactions in 8% of 182 patients with relapsed or metastatic cHL; the most common adverse reactions (≥1%) were pneumonitis (1.1%), and infusion reaction (1.1%). The most common adverse reactions (≥20%) were fatigue (31%), musculoskeletal pain (27%), diarrhea (20%), and decreased appetite (20%). The most common adverse reactions (≥5%) were fatigue (5%), and diarrhea (5%).

In KEYNOTE-087, KEYTRUDA monotherapy was discontinued due to adverse reactions in 9% of 80 patients with relapsed or metastatic urothelial carcinoma. The most common adverse reactions (≥20%) were fatigue (33%), musculoskeletal pain (25%), pruritus (20%), decreased appetite (21%), nausea (21%), and rash (20%). The most common adverse reactions (≥5%) were fatigue (5%), musculoskeletal pain (5%), and decreased appetite (5%).

In KEYNOTE-052, KEYTRUDA monotherapy was discontinued due to adverse reactions in 9% of 286 patients with locally advanced or metastatic urothelial carcinoma. The most common adverse reactions (≥20%) were musculoskeletal pain (27%), fatigue (23%), and pruritus (20%). The most common adverse reactions (≥5%) were musculoskeletal pain (5%), and fatigue (5%).

In KEYNOTE-045, KEYTRUDA monotherapy was discontinued due to adverse reactions in 8% of 266 patients with locally advanced or metastatic urothelial carcinoma. The most common adverse reactions (≥20%) were fatigue (29%), nausea (21%), and pruritus (20%). The most common adverse reactions (≥5%) were fatigue (5%), and nausea (5%).

In KEYNOTE-029, KEYTRUDA monotherapy was discontinued due to adverse reactions in 9% of 148 patients with advanced GEJ adenocarcinoma; the most common adverse reactions (≥1%) were pneumonitis (2.7%), and pneumonia (2.7%). The most common adverse reactions (≥20%) were fatigue (41%), musculoskeletal pain (31%), and decreased appetite (20%). The most common adverse reactions (≥5%) were fatigue (5%), and musculoskeletal pain (5%).

In KEYNOTE-061, KEYTRUDA monotherapy was discontinued due to adverse reactions in 9% of 592 patients with locally advanced or metastatic gastric cancer; the most common adverse reactions (≥1%) were anemia (1.2%), and pneumonitis (1.2%). The most common adverse reactions (≥20%) were fatigue (28%), musculoskeletal pain (22%), and pruritus (20%). The most common adverse reactions (≥5%) were anemia (5%), and fatigue (5%).

In KEYNOTE-119, KEYTRUDA monotherapy was discontinued due to adverse reactions in 8% of 628 patients with metastatic TNBC; the most common adverse reactions (≥1%) were pneumonitis (1.1%), and renal failure (1.1%). The most common adverse reactions (≥20%) were fatigue (26%), and nausea (21%). The most common adverse reactions (≥5%) were fatigue (5%), and anemia (5%).

In KEYNOTE-158, KEYTRUDA monotherapy was discontinued due to adverse reactions in 7% of 102 patients with advanced endometrial carcinoma; the most common adverse reactions (≥1%) were pneumonitis (2.9%), and renal failure (2.9%). The most common adverse reactions (≥20%) were fatigue (31%), diarrhea (29%), decreased appetite (27%), nausea (24%), vomiting (20%), and rash (20%). The most common adverse reactions (≥5%) were fatigue (6%), diarrhea (5%), and decreased appetite (5%).

In KEYNOTE-158, KEYTRUDA monotherapy was discontinued due to adverse reactions in 9% of 90 patients with advanced cervical cancer; the most common adverse reactions (≥1%) were pneumonitis (2.2%), and renal failure (2.2%). The most common adverse reactions (≥20%) were fatigue (33%), diarrhea (27%), decreased appetite (24%), nausea (23%), and vomiting (20%). The most common adverse reactions (≥5%) were fatigue (7%), and diarrhea (5%).

In KEYNOTE-158, KEYTRUDA monotherapy was discontinued due to adverse reactions in 9% of 200 patients with locally advanced or metastatic urothelial carcinoma. The most common adverse reactions (≥20%) were musculoskeletal pain (27%), fatigue (23%), and pruritus (20%). The most common adverse reactions (≥5%) were musculoskeletal pain (5%), and fatigue (5%).

In KEYNOTE-158, KEYTRUDA monotherapy was discontinued due to adverse reactions in 7% of 763 patients with other solid tumors; the most common adverse reactions (≥1%) were pneumonitis (1.4%), and renal failure (1.4%). The most common adverse reactions (≥20%) were fatigue (29%), diarrhea (21%), decreased appetite (18%), and rash (20%). The most common adverse reactions (≥5%) were fatigue (5%), and diarrhea (5%).

In KEYNOTE-177, KEYTRUDA monotherapy was discontinued due to adverse reactions in 10% of 599 patients with advanced or metastatic colorectal cancer; the most common adverse reactions (≥1%) were pneumonitis (1.3%), and colitis (1.3%). The most common adverse reactions (≥20%) were diarrhea (25%), fatigue (23%), and rash (20%). The most common adverse reactions (≥5%) were diarrhea (5%), and fatigue (5%).

In KEYNOTE-522, KEYTRUDA was discontinued due to adverse reactions in 11% of 1000 patients with stage III TNBC; the most common adverse reactions (≥1%) were pneumonitis (1.2%), and renal failure (1.2%). The most common adverse reactions (≥20%) were fatigue (32%), nausea (29%), anemia (25%), alopecia (24%), vomiting (21%), and rash (20%). The most common adverse reactions (≥5%) were anemia (5%), and fatigue (5%).

In KEYNOTE-564, KEYTRUDA was discontinued due to adverse reactions in 9% of 821 patients with adjuvant renal cell carcinoma; the most common adverse reactions (≥1%) were pneumonitis (1.2%), and renal failure (1.2%). The most common adverse reactions (≥20%) were fatigue (26%), diarrhea (21%), and hypothyroidism (20%). The most common adverse reactions (≥5%) were fatigue (5%), and diarrhea (5%).

In KEYNOTE-671, KEYTRUDA was discontinued due to adverse reactions in 14% of 397 patients with resectable NSCLC; the most common adverse reactions (≥1%) were renal failure (2.3%), and pneumonitis (1.8%). The most common adverse reactions (≥20%) were musculoskeletal pain (27%), fatigue (23%), and nausea (21%). The most common adverse reactions (≥5%) were musculoskeletal pain (5%), and fatigue (5%).

In KEYNOTE-716, KEYTRUDA was discontinued due to adverse reactions in 8% of 296 patients with stage II to III melanoma; the most common adverse reactions (≥1%) were colitis (1.4%), and pneumonitis (1.4%). The most common adverse reactions (≥20%) were diarrhea (29%), and fatigue (21%). The most common adverse reactions (≥5%) were diarrhea (5%), and colitis (5%).

In KEYNOTE-054, KEYTRUDA was discontinued due to adverse reactions in 14% of 1360 patients with stage III melanoma; the most common adverse reactions (≥1%) were pneumonitis (1.5%), and colitis (1.1%). The most common adverse reactions (≥20%) were diarrhea (25%), and fatigue (21%). The most common adverse reactions (≥5%) were diarrhea (5%), and colitis (5%).

In KEYNOTE-630, KEYTRUDA was discontinued due to adverse reactions in 14% of 886 patients with stage III cutaneous squamous cell carcinoma; the most common adverse reactions (≥1%) were pneumonitis (1.1%), and colitis (1.1%). The most common adverse reactions (≥20%) were diarrhea (29%), and fatigue (21%). The most common adverse reactions (≥5%) were diarrhea (5%), and colitis (5%).

Adverse reactions occurring in patients with gastric cancer were similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as monotherapy.

In KEYNOTE-590, when KEYTRUDA was administered with cisplatin and fluorouracil to patients with metastatic or locally advanced esophageal or GEJ cancer with squamous (n=223) or nonsquamous (n=439) histology, serious adverse reactions occurred in 54% of patients receiving KEYTRUDA. KEYTRUDA was discontinued due to adverse reactions in 19% of 439 patients. The most common adverse reactions leading to permanent discontinuation of KEYTRUDA (≥1%) were pneumonitis (2.3%), and renal failure (1.1%). The most common adverse reactions (≥20%) were nausea (67%), fatigue (61%), vomiting (44%), decreased appetite (41%), chemotherapy toxicity (39%), fatigue (37%), decreased weight (31%), constipation (30%), diarrhea (29%), anemia (29%), abdominal pain (27%), and rash (20%). The most common adverse reactions (≥5%) were fatigue (5%), and chemotherapy toxicity (5%).

Adverse reactions occurring in patients with esophageal cancer were similar to those occurring in patients who were treated with KEYTRUDA as monotherapy were similar to those occurring in patients with melanoma or NSCLC.

In KEYNOTE-158, KEYTRUDA was discontinued due to adverse reactions in 8% of 98 patients with recurrent or metastatic cervical cancer. Serious adverse reactions occurred in 41% of patients. The most common adverse reactions (≥20%) were fatigue (33%), diarrhea (27%), decreased appetite (24%), nausea (23%), and vomiting (20%). The most common adverse reactions (≥5%) were fatigue (7%), and diarrhea (5%).

In KEYNOTE-158, KEYTRUDA was discontinued due to adverse reactions in 9% of 148 patients with recurrent or metastatic PD-L1+ squamous cell carcinoma of the anal canal. Serious adverse reactions occurred in 41% of patients. The most common adverse reactions (≥20%) were fatigue (31%), diarrhea (23%), decreased appetite (20%), rash (20%), and pruritus (20%). The most common adverse reactions (≥5%) were fatigue (5%), and diarrhea (5%).

Adverse reactions occurring in patients with MSI-H or dMMR CRC were similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as monotherapy.

In KEYNOTE-158, when KEYTRUDA was administered in combination with lenvatinib, serious adverse reactions occurred in 51% of 418 patients. Serious adverse reactions occurring in ≥2% of patients included hepatic failure (3.1%), pneumonitis (2.9%), renal failure (2.4%), and hypothyroidism (2.2%). The most common adverse reactions (≥20%) were hypertension (74%), diarrhea (67%), fatigue (61%), decreased appetite (51%), nausea (49%), decreased weight (46%), stomatitis/mucositis (41%), palmar-plantar erythrodysesthesia (29%), dysphonia (28%), stomatitis/mucositis (inflammation) (27%), dysgeusia (26%), hypothyroidism (25%), and vomiting (24%).

Adverse reactions occurring in patients with TMB-H tumors were similar to those occurring in patients with other tumors treated with KEYTRUDA.

Adverse reactions occurring in patients with cHL were similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a single agent.

In KEYNOTE-426, when KEYTRUDA was administered with carboplatin and paclitaxel or nab-paclitaxel for metastatic squamous NSCLC, KEYTRUDA was discontinued due to adverse reactions in 14% of 101 patients. Serious adverse reactions occurred in 41% of patients receiving KEYTRUDA. The most common adverse reactions (≥20%) were alopecia (57%), peripheral neuropathy (52%), fatigue (47%), nausea (44%), vomiting (32%), decreased appetite (31%), diarrhea (29%), decreased weight (29%), rash (28%), cough (27%), dyspnea (24%), and constipation (20%). The most common adverse reactions (≥5%) were fatigue (6%), and peripheral neuropathy (5%).

Adverse reactions occurring in patients with HNSCC were similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as monotherapy.

In KEYNOTE-355, when KEYTRUDA was administered in combination with carboplatin, and either paclitaxel or nab-paclitaxel, serious adverse reactions occurred in 51% of patients receiving KEYTRUDA. KEYTRUDA was discontinued for adverse reactions in 19% of patients receiving KEYTRUDA. The most common adverse reactions (≥20%) were alopecia (64%), fatigue (53%), nausea (44%), peripheral neuropathy (41%), vomiting (31%), decreased appetite (30%), diarrhea (29%), decreased weight (29%), rash (28%), cough (27%), dyspnea (24%), and constipation (20%). The most common adverse reactions (≥5%) were fatigue (6%), and peripheral neuropathy (5%).

Adverse reactions occurring in patients with cervical cancer were similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as monotherapy.

In KEYNOTE-671, when KEYTRUDA was administered in combination with cisplatin, gemcitabine, and either intravenous or subcutaneous (SC) rHuPH20, serious adverse reactions occurred in 51% of patients receiving KEYTRUDA. KEYTRUDA was discontinued for adverse reactions in 21% of patients receiving KEYTRUDA. The most common adverse reactions (≥20%) were nausea (67%), alopecia (61%), fatigue (57%), constipation (37%), vomiting (31%), rash (29%), decreased appetite (27%), diarrhea (26%), decreased weight (25%), cough (21%), dyspnea (21%), and peripheral edema (20%). The most common adverse reactions (≥5%) were fatigue (7%), nausea (6%), and anemia (5%).

Adverse reactions occurring in patients with RCC were similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a single agent.

In KEYNOTE-564, when KEYTRUDA was administered as adjuvant treatment for RCC, serious adverse reactions occurred in 37% of patients. Serious adverse reactions occurring in ≥2% of patients included pneumonitis (2.4%), renal failure (2.4%), and adrenal insufficiency (2.1%). The most common adverse reactions (≥20%) were diarrhea (41%), fatigue (37%), musculoskeletal pain (31%), hypothyroidism (29%), hepatitis (22%), decreased appetite (21%), nausea (21%), and rash (20%). The most common adverse reactions (≥5%) were diarrhea (5%), musculoskeletal pain (5%), hepat

SUPERIOR OVERALL SURVIVAL achieved second line with KEYTRUDA as monotherapy vs chemotherapy

Efficacy | Study Design

For patients with mNSCLC whose tumors express PD-L1 (TPS ≥1%) and who progressed 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.

SUPERIOR OVERALL SURVIVAL vs docetaxel in mNSCLC at all levels of PD-L1 expression (TPS ≥1%)

Efficacy Results of All Randomized Patients With TPS ≥1% in KEYNOTE-010

End point	KEYTRUDA 2 mg/kg Q3W n=124	KEYTRUDA 10 mg/kg Q3W n=123	Docetaxel 75 mg/m² Q3W n=122
OS			
Deaths (%)	172 (50%)	156 (45%)	193 (56%)
Median in months (95% CI)	10.4 (8.4–11.9)	12.7 (10.0–17.3)	8.5 (7.5–9.8)
Hazard ratio* (95% CI)	0.71 (0.58–0.88)	0.61 (0.49–0.76)	—
P value (stratified log-rank)	<0.001	<0.001	—
PFS			
Events (%)	294 (77%)	295 (74%)	257 (75%)
Median in months (95% CI)	3.9 (3.1–4.1)	4.0 (2.8–4.3)	4.0 (3.1–4.2)
Hazard ratio* (95% CI)	0.86 (0.73–1.04)	0.79 (0.66–0.94)	—
P value (stratified log-rank)	0.068	0.005	—
ORR			
ORR† (95% CI)	18% (14–23)	19% (15–25)	9% (7–13)
P value (Mettelman-Nurminen)	<0.001	<0.001	—
Median DOR in months (range)	NR (0.7+–22.1+)	NR (2.1+–17.8+)	6.2 (1.4+–8.8+)

*Based on stratified Cox proportional hazard model.
†Based on blinded independent central review using RECIST v1.1.
ALK = anaplastic lymphoma kinase; CI = confidence interval; DOR = duration of response; EGFR = epidermal growth factor receptor; mNSCLC = metastatic non-small cell lung cancer; NR = not reached; ORR = objective response rate; OS = overall survival; PD-L1 = programmed death ligand 1; PFS = progression-free survival; Q3W = every 3 weeks; RECIST v1.1 = Response Evaluation Criteria in Solid Tumors v1.1; TPS = tumor proportion score.

KEYNOTE-010 study design: An open-label, multicenter, randomized, phase 2/3 trial of single-agent KEYTRUDA vs docetaxel in 1,033 patients with squamous or nonsquamous mNSCLC. The trial included patients whose tumors were from PD-L1 positive based on a TPS ≥1%, as determined by the PD-L1 immunohistochemistry 22C3 pharmDx assay. Patients also had disease progression on platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations had to have had disease progression on FDA-approved therapy for these aberrations. Patients had an ECOG performance status of 0 or 1, modified Glasgow prognostic score of 0 or 1, and were stratified by PD-L1 expression (TPS 1%–49% vs ≥50%), prior platinum chemotherapy (1 vs ≥2 regimens), and histology (squamous vs nonsquamous), or who had received more than 30 Gy of thoracic radiation within 26 weeks were ineligible. Patients received KEYTRUDA 2 mg/kg (n=344) or 10 mg/kg (n=346) or docetaxel 75 mg/m² (n=343) Q3W until unacceptable toxicity or disease progression or for up to 24 months. Tumor status was assessed every 9 weeks. Co-primary end points were OS and PFS, as assessed by blinded independent central review using RECIST v1.1 modified to include up to 5 lesions per organ. The median follow-up was 10 target lesions and a maximum of 5 target lesions per organ. Additional efficacy outcome measures were ORR and DOR.

*Based on the 95% CI for the difference between treatments based on the stratified Cox proportional hazard model.
†Based on the 95% CI for the difference between treatments based on the stratified Miettinen and Nurminen method.

FIRST-LINE COMBINATION THERAPY IN NONSQUAMOUS mNSCLC: KEYTRUDA, in combination with pemetrexed and platinum chemotherapy, is indicated for the first-line treatment of patients with metastatic nonsquamous non-small cell lung cancer (mNSCLC), with no EGFR or ALK genomic tumor aberrations.

FIRST-LINE COMBINATION THERAPY IN SQUAMOUS mNSCLC: KEYTRUDA, in combination with carboplatin and either paclitaxel or paclitaxel protein-bound, is indicated for the first-line treatment of squamous metastatic squamous NSCLC.

FIRST-LINE MONOTHERAPY IN NONSQUAMOUS and SQUAMOUS ADVANCED NSCLC: KEYTRUDA, as a single agent, is indicated for the first-line treatment of metastatic NSCLC expressing PD-L1 (tumor proportion score [TPS] ≥1%) as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and is stage III where patients are not candidates for tumor resection or definitive chemoradiation, or metastatic.

SECOND-LINE OR GREATER MONOTHERAPY IN NONSQUAMOUS AND SQUAMOUS mNSCLC: KEYTRUDA, as a single agent, is indicated for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥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.

mNSCLC = metastatic NSCLC; EGFR = epidermal growth factor receptor; ALK = anaplastic lymphoma kinase; PD-L1 = programmed death ligand 1.

SELECTED SAFETY INFORMATION

Severe and Fatal Immune-Mediated Adverse Reactions

• KEYTRUDA is a monoclonal antibody that belongs to a class of drugs that bind to either the programmed death receptor-1 (PD-1) or the programmed death ligand 1 (PD-L1), blocking the PD-1/PD-L1 pathway, thereby removing inhibition of the immune response, potentially breaking peripheral tolerance and inducing immune mediated adverse reactions. Immune-mediated adverse reactions, which may be severe or life-threatening, can occur in any organ system or tissue. Immune-mediated adverse reactions may occur even after one or more doses of KEYTRUDA, and may be more common in patients who have had a longer duration of treatment with KEYTRUDA. Immune-mediated adverse reactions listed here may not include all possible severe and fatal immune-mediated adverse reactions.

• Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Early identification and management are essential to ensure safe use of KEYTRUDA. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude infectious causes. Based on the severity of the adverse reaction, withhold KEYTRUDA, initiate medical management promptly, including specialty consultation as appropriate.

• Without or upon recurrence of adverse reaction, depending on severity of the immune-mediated adverse reaction. In general, if KEYTRUDA requires interruption or discontinuation, administer systemic corticosteroid therapy (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose adverse reactions are not controlled with corticosteroid therapy.

Immune-Mediated Pneumonitis

• KEYTRUDA can cause immune-mediated pneumonitis. The incidence is higher in patients who have received prior thoracic radiation. Immune-mediated pneumonitis occurred in 4 (0.2%) patients receiving KEYTRUDA, including Grade 2 (n=2), Grade 3 (n=1), Grade 4 (n=1), and Grade 2 (1.5%) reactions. Systemic corticosteroids were required in 67% (8/394) of patients. Pneumonitis led to permanent discontinuation of KEYTRUDA in 1.3% (3/6) and withholding in 0.9% (2/6) of patients. Of the patients who discontinued KEYTRUDA for pneumonitis, all 3 (100%) completed follow-up. Of these, 33% had recovered. Pneumonitis resulted in 59% of the 94 patients.

• Pneumonitis occurred in 8% (31/389) of adult patients with cHL receiving KEYTRUDA as a single agent, including Grades 3-4 in 2.3% of patients. Patients received high-dose corticosteroids for a median duration of 10 days (range: 2 days to 53 months). Pneumonitis rates were similar in patients with and without prior thoracic radiation. Pneumonitis led to discontinuation of KEYTRUDA in 5.4% (21) of patients. Of the patients who developed pneumonitis, 42% interrupted KEYTRUDA, 69% discontinued KEYTRUDA, and 77% had resolution.

Immune-Mediated Colitis

• KEYTRUDA can cause immune-mediated colitis, which may present with diarrhea. Cytomegalovirus infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis. In cases of corticosteroid-refractory immune-mediated colitis, consider infectious etiology of diarrhea/colitis. Immune-mediated colitis occurred in 1.7% (462/29) of patients receiving KEYTRUDA, including Grade 4 (n=15), Grade 3 (1.1%), and Grade 2 (0.4%) reactions. Systemic corticosteroids were required in 69% (33/48) of patients with immune-mediated colitis. Immune-mediated colitis resulted in permanent discontinuation of KEYTRUDA in 0.5% (13) and withholding in 0.5% (13) of patients. All patients who were withheld resolved KEYTRUDA after symptom improvement. Of those who restarted KEYTRUDA, Colitis recurred in 85% of the 46 patients.

Hepatotoxicity and Immune-Mediated Hepatitis

• KEYTRUDA as a Single Agent

• KEYTRUDA in combination with ipilimumab can cause hepatic toxicity. Monitor liver enzymes before initiation of and periodically throughout treatment. Consider monitoring more frequently in patients who receive drugs are administered before and concomitantly with KEYTRUDA. Based on severity of liver enzyme elevations, withhold and consider administering corticosteroids as needed. With the combination of KEYTRUDA and ipilimumab, Grades 3 and 4 increased alanine aminotransferase (ALT) (3%) and increased aspartate aminotransferase (AST) (1%) occurred in patients who were administered KEYTRUDA after symptom improvement of the liver enzyme elevations in the patients with increased ALT received systemic corticosteroids. In patients with ALT ≤3 times upper limit of normal (ULN) (Grades 2-4, n=116), ALT resolved to Grades 0-1 in 94%. Among the 7 patients who were rechallenged with either KEYTRUDA (2) or ipilimumab (n=34) administered as a single agent or with both (n=55), recurrence of ALT ≥3 times ULN was observed in 1 patient receiving KEYTRUDA. The patient receiving ipilimumab, and 24 patients receiving both. All patients with a recurrence of ALT ≥3 ULN subsequently recovered from the event.

Immune-Mediated Endocrinopathies

Adrenal Insufficiency

• KEYTRUDA can cause primary or secondary adrenal insufficiency. For Grade 2 or higher, initiate symptomatic treatment, including hormone replacement as clinically indicated. Withhold KEYTRUDA depending on severity. Adrenal insufficiency occurred in 0.8% (22/29) of patients receiving KEYTRUDA, including Grade 4 (n=15), Grade 3 (0.3%), and Grade 2 (0.3%) reactions. Systemic corticosteroids were required in 77% (17/22) of patients; of these, the majority remained on systemic corticosteroids. Adrenal insufficiency led to permanent discontinuation of KEYTRUDA in <0.1% (1) and withholding in 0.3% (8) of patients. All patients who were withheld resolved KEYTRUDA after symptom improvement.

Hypophysitis

• KEYTRUDA can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual defects. Hypophysitis can cause hypopituitarism. Initiate hormone replacement as indicated. Withhold or permanently discontinue KEYTRUDA depending on severity. Hypophysitis occurred in 0.6% (12/39) of patients receiving KEYTRUDA, including Grade 4 (n0.1%), Grade 3 (0.3%), and Grade 2 (0.3%) reactions. Systemic corticosteroids were required in 83% (10/12) of patients; of these, the majority remained on systemic corticosteroids. Hypophysitis led to permanent discontinuation of KEYTRUDA in 0.1% (4) and withholding in 0.2% (2) of patients. All patients who were withheld resolved KEYTRUDA after symptom improvement.

Thyroid Disorders

• KEYTRUDA can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement for hypothyroidism or manage hypothyroidism with corticosteroids as clinically indicated. Withhold or permanently discontinue KEYTRUDA depending on severity. Thyroiditis occurred in 0.6% (16/729) of patients receiving KEYTRUDA, including Grade 2 (0.3%). None discontinued, but KEYTRUDA was withheld in 0.1% (1) of patients.

• Hyperthyroidism occurred in 3.4% (962/29) of patients receiving KEYTRUDA, including Grade 3 (0.1%) and Grade 2 (0.8%). It led to permanent discontinuation of KEYTRUDA in <0.1% (2) and withholding in 0.3% (7) of patients. All patients who were withheld resumed KEYTRUDA after symptom improvement. Hypothyroidism occurred in 8% (237/2799) of patients receiving KEYTRUDA, including Grade 3 (0.1%) and Grade 2 (6.2%). It led to permanent discontinuation of KEYTRUDA in <0.1% (2) and withholding in 0.3% (7) of patients. All patients who were withheld resumed KEYTRUDA after symptom improvement. Hypothyroidism in patients with hypothyroidism required long-term thyroid hormone replacement. The incidence of new or worsening hypothyroidism was higher in 1185 patients required in 40% (1538) of patients. These reactions led to permanent discontinuation of KEYTRUDA in 0.7% (12) and withholding in 3.1% (53) of patients. All patients who were withheld resolved KEYTRUDA after symptom improvement; of these, 6% had recurrence. The reactions resolved in 79% of the 38 patients.

Other Immune-Mediated Adverse Reactions

• The following clinically significant immune-mediated adverse reactions occurred at an incidence of <1% (unless otherwise noted) in patients who received KEYTRUDA or were reported with the use of other anti-PD-1/PD-L1 treatments: Immune-mediated adverse reactions involving the adrenal, blood, muscle, and nerve (including Guillain-Barré syndrome, myasthenia syndrome/myasthenia gravis (including exacerbation), Guillain-Barré syndrome, nerve paresis, autonomic neuropathy, neuropathy), ocular (including uveitis, iritis and other inflammatory ocular toxicities can occur. Some cases can be associated with retinal detachment. Various grades of visual impairment, including blindness, can occur. If uveitis occurs in combination with other immune-mediated adverse reactions, it may be an indicator of Vogt-Koyanagi-Harada syndrome, which has been reported in patients receiving other PD-1 and PD-L1 blockers), pancreatitis (including elevations in serum amylase and lipase), gastritis, hepatitis, sphinctero-colitis, cholecystitis, sclerosing cholangitis, Sclerosing Cholangitis of Immune Origin, hypophysitis, diabetes mellitus (and associated sequelae, including renal failure), arthritis (1.5%), polymyalgia rheumatica; dermatitis (including erythema multiforme, Stevens-Johnson syndrome, acute generalized exanthematous pustulosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenic purpura, solid organ transplant rejection.

Infusion-Related Reactions

• KEYTRUDA can cause severe or life-threatening infusion-related reactions, including hypersensitivity and anaphylaxis, which have been reported in 0.2% (7/29 patients receiving KEYTRUDA. Monitor for signs and symptoms of infusion-related reactions. Interrupt or slow the rate of infusion for Grade 1 or Grade 2 reactions. For Grade 3 or Grade 4 reactions, stop infusion and permanently discontinue KEYTRUDA.

Complications of Allogeneic HSCT after Receiving KEYTRUDA

• Fatal and other serious complications can occur in patients who receive allogeneic HSCT before or after anti-PD-1/PD-L1 treatments. Transplant-related complications include hyperacute graft-versus-host-disease (GVHD), acute graft-versus-host-disease-specified, chronic graft-versus-host-disease-specified conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between KEYTRUDA and HSCT. Monitor patients and allogeneic HSCT donors for evidence of these complications and intervene promptly. Consider the benefit vs risks of using anti-PD-1/PD-L1 treatments prior to or after an allogeneic HSCT.

Increased Mortality in Patients with Parenchymal Cancers

• In 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 anti-PD-1/PD-L1 treatment in combination with a thalidomide analogue is not recommended.

Embryofetal Toxicity

• Based on its mechanism of action, KEYTRUDA can cause fetal harm when administered to a pregnant woman. Advise women of this potential risk. In females of reproductive potential, verify pregnancy status prior to initiating KEYTRUDA and advise them to use effective contraception during treatment and for 4 months after the last dose.

Adverse Reactions

• In KEYNOTE-010, KEYTRUDA was discontinued due to adverse reactions in 9% of 555 patients with advanced pneumonitis; adverse reactions leading to permanent discontinuation in more than one patient were colitis (1.4%), autoimmune hepatitis (0.7%), allergic reaction (0.4%), polymyositis (0.4%), and cachexia (0.4%). The most common adverse reactions (≥20%) were fatigue/asthenia (39%), musculoskeletal pain (30%), rash (22%), and pruritus (20%).

• In KEYNOTE-054, KEYTRUDA was permanently discontinued due to adverse reactions in 14% of 509 patients; the most common (≥1%) were pneumonitis (1.4%), colitis (1.2%), and diarrhea (1.0%). Immune-mediated adverse reactions occurred in 25% of patients receiving KEYTRUDA. The most common adverse reactions (≥20%) were KEYTRUDA was diarrhea (28%).

• In KEYNOTE-407, when KEYTRUDA was administered with pemetrexed and platinum chemotherapy in metastatic nonsquamous NSCLC, KEYTRUDA was discontinued due to adverse reactions in 20% of 405 patients. The most common adverse reactions resulting in permanent discontinuation of KEYTRUDA were pneumonitis (3%), and acute kidney injury (2%). The most common adverse reactions (≥20%) with KEYTRUDA were nausea (56%), fatigue (38%), constipation (35%), diarrhea (31%), decreased appetite (28%), rash (25%), vomiting (24%), cough (21%), dyspnea (21%), and pyrexia (20%).

• In KEYNOTE-407, when KEYTRUDA was administered with carboplatin and paclitaxel or paclitaxel protein-bound in metastatic squamous NSCLC, KEYTRUDA was discontinued due to adverse reactions in 15% of 101 patients. The most frequent serious adverse reactions reported in at least 2% of patients were febrile neutropenia (4%), and acute kidney injury (2%). Adverse reactions occurring in at least 20% of 407 were similar to those observed in KEYNOTE-189 with the exception that increased incidences of alopecia (47% vs 36%) and peripheral neuropathy (31% vs 25%) were observed in the KEYTRUDA and chemotherapy arm compared to the placebo and chemotherapy arm, respectively.

• In KEYNOTE-042, KEYTRUDA was discontinued due to adverse reactions in 19% of 636 patients with advanced NSCLC; the most common were pneumonitis (3%), death due to unknown cause (2%), and febrile neutropenia (1.4%). The most frequent serious adverse reactions were pneumonitis (14%), febrile neutropenia, and pneumonia (7%), pneumonitis (3.9%), pulmonary embolism (2.4%), and pleural effusion (2.2%). The most common adverse reaction (≥20%) was fatigue (25%).

• In KEYNOTE-075, KEYTRUDA monotherapy was discontinued due to adverse reactions in 21% of 262 patients with advanced NSCLC; the most common was pneumonitis (1.8%). The most common adverse reactions (≥20%) were decreased appetite (25%), fatigue (25%), dyspnea (23%), and nausea (20%).

• In KEYNOTE-045, KEYTRUDA monotherapy was discontinued due to adverse reactions in 14% of 300 patients with mNSCLC; the most common adverse reactions leading to permanent discontinuation were sepsis (1.7%) and pneumonitis (1.3%). The most common adverse reactions (≥20%) were fatigue (33%), constipation (20%), and rash (20%).

• In KEYNOTE-048, when KEYTRUDA was administered in combination with platinum (cisplatin or carboplatin) and FU chemotherapy, KEYTRUDA was discontinued due to adverse reactions in 18% of 276 patients with HNSCC. The most common adverse reactions resulting in permanent discontinuation of KEYTRUDA were pneumonia (2.5%), pneumonitis (1.9%), and sepsis shock (1.4%). The most common adverse reactions (≥20%) were nausea (51%), fatigue (44%), constipation (27%), vomiting (22%), mucositis (inflammation) (21%), diarrhea (20%), decreased appetite (29%), stomatitis (28%), and cough (22%).

• 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 pneumonitis, dyspnea, confusional state, vomiting, pleural effusion, and respiratory failure. The most common adverse reactions (≥20%) were fatigue, decreased appetite, and dyspnea. Adverse reactions occurring in patients with HNSCC treated with KEYTRUDA were similar to those in patients with other cancers treated with KEYTRUDA, with the exception of a higher incidence of increased incidences of facial edema and new or worsening hypertension.

• In KEYNOTE-204, KEYTRUDA was discontinued due to adverse reactions in 14% of 148 patients with cHL. Serious adverse reactions occurred in 30% of patients. Adverse reactions occurring in at least 20% of patients, those 32% were urinary tract infection, pneumonia, pyrexia, anemia, acute kidney injury, febrile neutropenia, and urosepsis. The most common adverse reactions (≥20%) were fatigue (38%), musculoskeletal pain (24%), decreased appetite (22%), constipation (21%), rash (21%), and diarrhea (20%).

• In KEYNOTE-087, KEYTRUDA was discontinued due to adverse reactions in 9% of 216 patients with r/r cHL. Serious adverse reactions occurred in 16% of patients. Those 21% were pneumonia, pyrexia, dyspnea, GVHD, and febrile neutropenia (2%). The most common adverse reactions (≥20%) were fatigue (25%), diarrhea (22%), pain and abdominal pain (22% each), and decreased appetite (21%).

• Adverse reactions occurring in patients with hepatocellular carcinoma (HCC) were generally similar to those in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy, with the exception of increased incidences of ascites (8%, Grades 3-4) and immune-mediated hepatitis (2.9%). Laboratory abnormalities (Grades 3-4) that occurred at a higher incidence were elevated GGT (7%), ALT (5%), and AST (3%).

• Among the 50 patients with MCC enrolled in study KEYNOTE-017, adverse reactions occurring in patients with MCC were generally similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy. Laboratory abnormalities (Grades 3-4) that occurred at a higher incidence were elevated AST (11%) and hyperglycemia (19%).

• In KEYNOTE-426, KEYTRUDA when administered in combination with axitinib, fatal adverse reactions occurred in 3.3% of 429 patients. Serious adverse reactions occurred in 40% of patients, the most frequent (≥1%) were hepatotoxicity (7%), diarrhea (4.2%), acute kidney injury (2.3%), dehydration (1%), and pneumonitis (1%). Permanent discontinuation due to an adverse reaction occurred in 31% of patients. KEYTRUDA was permanently discontinued (31%) and the combination (8%); the most common were hepatotoxicity (13%), diarrhea/colitis (1.9%), acute kidney injury (1.6%), and cerebrovascular accident (1.2%). The most common adverse reactions (≥20%) were diarrhea (56%), fatigue/asthenia (53%), hypertension (48%), hepatotoxicity (43%), hypothyroidism (33%), loss of appetite (30%), palmar-plantar erythrodysesthesia (28%), nausea (28%), stomatitis/mucosal inflammation (27%), dysphonia (25%), rash (25%), cough (21%), and constipation (21%).

• Adverse reactions occurring in patients with TMB-H cancer were similar to those occurring in patients with other solid tumors who received KEYTRUDA as a single agent.

• Adverse reactions occurring in patients with cSCC were similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy.

• In KEYNOTE-355, when KEYTRUDA and chemotherapy (paclitaxel, protein-bound, or gemcitabine and carboplatin) were administered to patients with locally recurrent unresectable or metastatic TNBC who had not been previously treated with chemotherapy, the most common adverse reactions (≥20%) were nausea (41%), alopecia (37%), fatigue/asthenia (34%), peripheral neuropathy (27%), and septic shock (23%). Serious adverse reactions occurred in 30% of patients receiving KEYTRUDA. Adverse reactions resulting in permanent discontinuation of KEYTRUDA were infrequent (2%). Adverse reactions resulting in permanent discontinuation of chemotherapy were common (51% of patients due to adverse reactions. The most common reactions resulting in permanent discontinuation (≥1%) were increased ALT (2.2%), increased AST (1.5%), and pneumonitis (1.2%). The most common adverse reactions (≥20%) in patients receiving KEYTRUDA in combination with chemotherapy were fatigue (48%), nausea (44%), alopecia (34%), diarrhea and constipation (28% each), vomiting and rash (26% each), cough (23%), decreased appetite (21%), and headache (20%).

Lactation

• Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment and for 4 months after the final dose.

Pediatric Use

• In KEYNOTE-051, 161 pediatric patients (62 pediatric patients aged 6 months to younger than 12 years and 99 pediatric patients aged 12 years to 17 years) were administered KEYTRUDA 2 mg/kg every 3 weeks. The median duration of exposure was 2.1 months (range: 1 day to 24 months).

• Adverse reactions that occurred at a ≥10% higher rate in pediatric patients when compared to adults were pyrexia (33%), vomiting (30%), diarrhea (27%), abdominal pain (19%), upper respiratory tract infection (29%), neutropenia (26%), headache (22%), and Grade 3 anemia (17%).

cHL = classical Hodgkin lymphoma; CKD = chronic kidney disease; cSCC = cutaneous squamous cell carcinoma; HNSCC = recurrent/metastatic head and neck squamous cell carcinoma; MCC = Merkel cell carcinoma; MSI-H = microsatellite instability-high; MMR-D = mismatch repair deficient; PD-1 = programmed cell death protein 1; PMBCL = primary mediastinal large B-cell lymphoma; TMB-H = tumor mutational burden-high; TNBC = triple-negative breast cancer.

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information. The Medication Guide also is available.

References: 1. Herbst RS, Baas P, Kim DW, et al. Pembrolizumab versus docetaxel for previously treated, PD-L1-positive, advanced non-small cell lung cancer (KEYNOTE-010): a randomized controlled trial. *Lancet.* 2016;387(10027):1540–1550.

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US-LAM-00950 04/21

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Immune-mediated nephritis and renal dysfunction
Immune-mediated hepatitis and hepatotoxicity
Immune-mediated endocrinopathies
Immune-mediated pneumonitis
Immune-mediated colitis
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Immune-mediated hyperthyroidism
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Other immune-mediated adverse reactions
Immune-mediated adverse reactions in combination with chemotherapy for NSCLC
Immune-mediated adverse reactions in combination with chemotherapy for SCLC
Immune-mediated adverse reactions in combination with chemotherapy for TNBC
Immune-mediated adverse reactions in combination with chemotherapy for esophageal cancer
Immune-mediated adverse reactions in combination with chemotherapy for cervical cancer
Immune-mediated adverse reactions in combination with chemotherapy for HNSCC
Immune-mediated adverse reactions in combination with chemotherapy for urothelial carcinoma
Immune-mediated adverse reactions in combination with chemotherapy for MSI-H/dMMR colorectal cancer
Immune-mediated adverse reactions in combination with chemotherapy for MSI-H/dMMR gastric cancer
Immune-mediated adverse reactions in combination with chemotherapy for MSI-H/dMMR solid tumors
Immune-mediated adverse reactions in combination with chemotherapy for HCC
Immune-mediated adverse reactions in combination with chemotherapy for RCC
Immune-mediated adverse reactions in combination with chemotherapy for PMBCL
Immune-mediated adverse reactions in combination with chemotherapy for MCC
Immune-mediated adverse reactions in combination with chemotherapy for EC
Immune-mediated adverse reactions in combination with chemotherapy for GEJ adenocarcinoma
Immune-mediated adverse reactions in combination with chemotherapy for cervical adenocarcinoma
Immune-mediated adverse reactions in combination with chemotherapy for PD-L1 NSCLC
Immune-mediated adverse reactions in combination with chemotherapy for PD-L1 SCLC
Immune-mediated adverse reactions in combination with chemotherapy for PD-L1 TNBC
Immune-mediated adverse reactions in combination with chemotherapy for PD-L1 HNSCC
Immune-mediated adverse reactions in combination with chemotherapy for PD-L1 urothelial carcinoma
Immune-mediated adverse reactions in combination with chemotherapy for PD-L1 cervical cancer
Immune-mediated adverse reactions in combination with chemotherapy for PD-L1 cervical adenocarcinoma
Immune-mediated adverse reactions in combination with chemotherapy for PD-L1 HCC
Immune-mediated adverse reactions in combination with chemotherapy for PD-L1 RCC
Immune-mediated adverse reactions in combination with chemotherapy for PD-L1 PMBCL
Immune-mediated adverse reactions in combination with chemotherapy for PD-L1 MCC
Immune-mediated adverse reactions in combination with chemotherapy for PD-L1 EC
Immune-mediated adverse reactions in combination with chemotherapy for PD-L1 GEJ adenocarcinoma
Immune-mediated adverse reactions in combination with chemotherapy for PD-L1 cervical adenocarcinoma
Immune-mediated adverse reactions in combination with chemotherapy for MSI-H/dMMR colorectal cancer
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Immune-mediated adverse reactions in combination with chemotherapy for GEJ adenocarcinoma
Immune-mediated adverse reactions in combination with chemotherapy for cervical adenocarcinoma
Immune-mediated adverse reactions in combination with chemotherapy for HNSCC
Immune-mediated adverse reactions in combination with chemotherapy for urothelial car

NCCN GUIDELINES®

Full Indications
Overview
Clinical Data
1L Combo Therapy —Nonsquamous
1L Combo Therapy —Squamous
1L Monotherapy
2L Monotherapy
Safety
NCCN Guidelines®
Appropriate Patients

Pembrolizumab (**KEYTRUDA**) is a **CATEGORY 1** and **PREFERRED** 1L therapy option that is recommended for eligible patients with mNSCLC by the National Comprehensive Cancer Network® (NCCN®).[1,a-g]

1L Combination Therapy With Pembrolizumab (KEYTRUDA)[a,f]	
PD-L1 ≥50%	CATEGORY 1 & PREFERRED
PD-L1 1%–49%	CATEGORY 1 & PREFERRED
PD-L1 <1%	CATEGORY 1 & PREFERRED
1L Monotherapy With Pembrolizumab (KEYTRUDA)[c,h]	
PD-L1 ≥50%	CATEGORY 1 & PREFERRED
PD-L1 1%–49%	CATEGORY 2B & USEFUL IN CERTAIN CIRCUMSTANCES
PD-L1 <1%	NOT INDICATED & NOT RECOMMENDED

Preferred intervention = Intervention that is based on superior efficacy, safety, and evidence, and, when appropriate, affordability.
Category 1 = Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B = Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

Useful in certain circumstances = Pembrolizumab monotherapy can be considered in PD-L1 1%–49%, in patients with poor performance status or other contraindications to combination chemotherapy.

[a]See NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for detailed recommendations, including combination regimens, in patients with no targetable genomic tumor alterations.
[b]See NCCN Guidelines® for recommendations specific to genetic alterations, including EGFR, ALK, ROS1, BRAF, MET exon 14 skipping, NTRK1/2/3, and RET.
[c]Pembrolizumab/carboplatin or cisplatin/pemetrexed is recommended (category 1 and preferred) as first-line therapy for certain patients with metastatic nonsquamous NSCLC.
[d]Pembrolizumab/carboplatin/paclitaxel (paclitaxel or albumin-bound paclitaxel) is recommended (category 1 and preferred) as first-line therapy for certain patients with metastatic squamous NSCLC.

See the Broad Range of Patients for Which You Can Treat With KEYTRUDA

Key Chat

FIRST-LINE COMBINATION THERAPY IN NONSQUAMOUS mNSCLC: KEYTRUDA, in combination with pemetrexed and platinum chemotherapy, is indicated for the first-line treatment of patients with metastatic nonsquamous non–small cell lung cancer (NSCLC), with no EGFR or ALK genomic tumor aberrations.

FIRST-LINE COMBINATION THERAPY IN SQUAMOUS mNSCLC: KEYTRUDA, in combination with carboplatin and either paclitaxel or paclitaxel protein-bound, is indicated for the first-line treatment of patients with metastatic squamous NSCLC.

FIRST-LINE MONOTHERAPY IN NONSQUAMOUS AND SQUAMOUS ADVANCED NSCLC: KEYTRUDA, as a single agent, is indicated for the first-line treatment of patients with NSCLC expressing PD-L1 [tumor proportion score (TPS) ≥1%] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and is stage III where patients are not candidates for surgical resection or definitive chemoradiation, or metastatic.

SECOND-LINE OR GREATER MONOTHERAPY IN NONSQUAMOUS AND SQUAMOUS mNSCLC: KEYTRUDA, as a single agent, is indicated for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥1%) as determined by an FDA-approved test, with disease progression on 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.

mNSCLC = metastatic NSCLC; EGFR = epidermal growth factor receptor; ALK = anaplastic lymphoma kinase; PD-L1 = programmed death ligand 1.

SELECTED SAFETY INFORMATION

Severe and Fatal Immune-Mediated Adverse Reactions

- KEYTRUDA is a monoclonal antibody that belongs to a class of drugs that bind to either the programmed death receptor-1 (PD-1) or the programmed death ligand 1 (PD-L1), blocking the PD-1/PD-L1 pathway, thereby removing inhibition of the immune response, potentially breaking peripheral tolerance and inducing immune-mediated adverse reactions. Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue, can affect more than one body system simultaneously, and can occur at any time after starting treatment or after discontinuation of treatment. Important immune-mediated adverse reactions listed here may not include all possible severe and fatal immune-mediated adverse reactions.
- Immunosuppressive doses of steroids and other agents may be clinical manifestations of underlying immune-mediated adverse reactions. Early identification and management are essential to ensure safe use of anti–PD-1/PD-L1 treatments. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. For suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.
- Withhold or permanently discontinue KEYTRUDA depending on severity of the immune-mediated adverse reaction. In general, if KEYTRUDA requires interruption or discontinuation, administer systemic corticosteroid therapy (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose adverse reactions are not controlled with corticosteroid therapy.

Immune-Mediated Pneumonitis

- KEYTRUDA can cause immune-mediated pneumonitis. The incidence is higher in patients who have received prior thoracic radiation. Immune-mediated pneumonitis occurred in 3.4% (94/2799) of patients receiving KEYTRUDA, including fatal (0.1%), Grade 4 (0.3%), Grade 3 (0.9%), and Grade 2 (1.3%) reactions. Systemic corticosteroids were required in 61% (63/94) of patients. Pneumonitis led to permanent discontinuation of KEYTRUDA in 1.3% (36) and withholding in 0.9% (26) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement; of these, 23% had recurrence. Pneumonitis resolved in 59% of the 18 patients.
- Pneumonitis occurred in 8% (31/389) of adult patients with cHL receiving KEYTRUDA as a single agent, including Grades 3–4 in 2.3% of patients. Patients received high-dose corticosteroids for a median duration of 10 days (range: 2 days to 53 months). Pneumonitis rates were similar in patients with and without prior thoracic radiation. Pneumonitis led to discontinuation of KEYTRUDA in 5.4% (21) of patients. Of the patients who developed pneumonitis, 42% interrupted KEYTRUDA, 68% discontinued KEYTRUDA, and 77% had resolution.

Immune-Mediated Colitis

- KEYTRUDA can cause immune-mediated colitis, which may present with diarrhea. Cytomegalovirus infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies. Immune-mediated colitis occurred in 2.1% (59/2799) of patients receiving KEYTRUDA, including Grade 3 in 1% (1), and Grade 2 in 0.9% (25) of patients. Systemic corticosteroids were required in 69% (33/48) additional immunosuppressant therapy was required in 4.2% of patients. Colitis led to permanent discontinuation of KEYTRUDA in 0.5% (13) and withholding in 0.5% (13) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement; of these, 23% had recurrence. Colitis resolved in 85% of the 48 patients.

Hepatotoxicity and Immune-Mediated Hepatitis

KEYTRUDA as a Single Agent

- KEYTRUDA can cause immune-mediated hepatitis. Immune-mediated hepatitis occurred in 0.7% (19/2799) of patients receiving KEYTRUDA, including Grade 4 (<0.1%), Grade 3 (0.4%), and Grade 2 (0.1%) reactions. Systemic corticosteroids were required in 68% (13/19) of patients; additional immunosuppressant therapy was required in 11% of patients. Hepatitis led to permanent discontinuation of KEYTRUDA in 0.2% (6) and withholding in 0.3% (9) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement; of these, none had recurrence. Hepatitis resolved in 79% of the 19 patients.

KEYTRUDA With Axitinib

- KEYTRUDA in combination with axitinib can cause hepatic toxicity. Monitor liver enzymes before initiation of and periodically throughout treatment. Consider monitoring more frequently as compared to when the drugs are administered as single agents. For elevated liver enzymes, interrupt KEYTRUDA and axitinib, and consider administering corticosteroids. In the combination of KEYTRUDA and axitinib, Grade 3 elevated alanine aminotransferase (ALT) occurred in 4% (20/5) and increased aspartate aminotransferase (AST) (13%) were seen at a higher frequency compared to KEYTRUDA alone. Fifty-nine percent of the patients with increased ALT received corticosteroids. In patients with ALT ≤3 times upper limit of normal (ULN) at baseline, Grade 3 ALT increased in Grade 1 or 2 ALT in 9%. Among the 92 patients who were rechallenged with either KEYTRUDA (n=3) or axitinib (n=34) administered as a single agent or with both (n=55), recurrence of ALT ≥3 times ULN was observed in 1 patient receiving KEYTRUDA, 16 patients receiving axitinib, and 24 patients receiving both. All patients with a recurrence of ALT ≥3 ULN subsequently recovered from the event.

Immune-Mediated Endocrinopathies

Adrenal Insufficiency

- KEYTRUDA can cause primary or secondary adrenal insufficiency. For Grade 2 or higher, initiate symptomatic treatment, including hormone replacement as clinically indicated. Withhold KEYTRUDA depending on severity. Adrenal insufficiency occurred in 0.6% (22/2799) of patients receiving KEYTRUDA, including Grade 4 (<0.1%), Grade 3 (0.3%), and Grade 2 (0.3%) reactions. Systemic corticosteroids were required in 77% (17/22) of patients; of these, the majority remained on systemic corticosteroids. Adrenal insufficiency led to permanent discontinuation of KEYTRUDA in <0.1% (1) and withholding in 0.3% (8) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement.

Hypophysitis

- KEYTRUDA can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, phlebothrombosis, or visual field defects. Hypophysitis can cause hypopituitarism. Initiate hormone replacement as indicated. Withhold or permanently discontinue KEYTRUDA depending on severity. Hypophysitis occurred in 0.6% (16/2799) of patients receiving KEYTRUDA, including Grade 4 (<0.1%), Grade 3 (0.3%), and Grade 2 (0.2%) reactions. Systemic corticosteroids were required in 94% (16/17) of patients; of these, the majority remained on systemic corticosteroids. Hypophysitis led to permanent discontinuation of KEYTRUDA in 0.1% (4) and withholding in 0.3% (7) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement.

Thyroid Disorders

- KEYTRUDA can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement for hypothyroidism or institute medical management of hyperthyroidism as clinically indicated. Withhold or permanently discontinue KEYTRUDA depending on severity. Thyroiditis occurred in 0.6% (16/2799) of patients receiving KEYTRUDA, including Grade 3 (0.3%) and Grade 2 (0.2%) reactions. Systemic corticosteroids were required in 94% (16/17) of patients; of these, the majority remained on systemic corticosteroids. Hypothyroidism led to permanent discontinuation of KEYTRUDA in 0.1% (4) and withholding in 0.3% (7) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement.

Hypothyroidism occurred in 8% (232/2799) of patients receiving KEYTRUDA, including Grade 3 (1.1%) and Grade 2 (6.2%). It led to permanent discontinuation of KEYTRUDA in <0.1% (1) and withholding in 0.5% (14) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement. The majority of patients with hypothyroidism required long-term hormone replacement. The incidence of new or worsening hypothyroidism was higher in 1,185 patients with NSCLC, occurring in 16% of patients receiving KEYTRUDA as a single agent or in combination with platinum and FU, including Grade 3 (0.3%) hypothyroidism. The incidence of new or worsening hypothyroidism was higher in 389 adult patients with cHL (17%) receiving KEYTRUDA as a single agent, including Grade 1 (6.2%) and Grade 2 (10.8%) hypothyroidism.

Type 1 Diabetes Mellitus (DM), Which Can Present With Diabetic Ketoacidosis

- Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Withhold KEYTRUDA depending on severity. Type 1 DM occurred in 0.2% (6/2799) of patients receiving KEYTRUDA. It led to permanent discontinuation in <0.1% (1) and withholding of KEYTRUDA in <0.1% (1) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement.

Immune-Mediated Nephritis With Renal Dysfunction

- KEYTRUDA can cause immune-mediated nephritis. Immune-mediated nephritis occurred in 0.3% (9/2799) of patients receiving KEYTRUDA, including Grade 4 (<0.1%), Grade 3 (0.1%), and Grade 2 (0.1%) reactions. Systemic corticosteroids were required in 89% (8/9) of patients. Nephritis led to permanent discontinuation of KEYTRUDA in 0.1% (3) and withholding in 0.1% (3) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement; of these, none had recurrence. Nephritis resolved in 56% of the 9 patients.

Immune-Mediated Dermatologic Adverse Reactions

- KEYTRUDA can cause immune-mediated rash or dermatitis. Exfoliative dermatitis, including Stevens-Johnson syndrome, drug rash with eosinophilia and systemic symptoms, and toxic epidermal necrolysis, has occurred with anti–PD-1/PD-L1 treatments. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate nonexfoliative rashes. Withhold or permanently discontinue KEYTRUDA depending on severity. Immune-mediated dermatologic adverse reactions occurred in 14% (392/2799) of patients receiving KEYTRUDA, including Grade 3 (1%) and Grade 2 (3.1%) reactions. Systemic corticosteroids were required in 40% (157/38) of patients. These reactions led to permanent discontinuation in 0.1% (2) and withholding of KEYTRUDA in 0.6% (16) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement; of these, 6% had recurrence. The reactions resolved in 79% of the 38 patients.

Other Immune-Mediated Adverse Reactions

- The following clinically significant immune-mediated adverse reactions occurred at an incidence of <1% (unless otherwise noted) in patients who received KEYTRUDA or were reported with the use of other anti–PD-1/PD-L1 treatments. Severe or fatal cases have been reported for some of these adverse reactions. Cardiac/vascular: Myocarditis, pericarditis, vasculitis. Nervous System: Meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis (including exacerbation), Guillain-Barré syndrome, nerve paresis, autoimmune neuropathy. Ocular: Uveitis, iritis and other ocular inflammatory toxicities can occur. Some cases can be associated with retinal detachment. Various grades of visual impairment, including blindness, can occur. If uveitis occurs in combination with other immune-mediated adverse reactions, consider a Vogt-Koyanagi-Harada like syndrome, as this may require treatment with systemic steroids to reduce the risk of permanent vision loss. Gastrointestinal: Pancreatitis, to include increases in serum amylase and lipase levels, gastritis, duodenitis. Musculoskeletal and Connective Tissue: Myositis/polymyositis, rhabdomyolysis (and associated sequelae, including renal failure), arthritis (1.5%), polymyalgia rheumatica; Endocrine: Hypoparathyroidism; immune-mediated hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenic purpura, solid organ transplant rejection.

Infusion-Related Reactions

- KEYTRUDA can cause severe or life-threatening infusion-related reactions, including hypersensitivity and anaphylaxis, which have been reported in 0.2% (2799 patients receiving KEYTRUDA. Monitor for signs and symptoms of infusion-related reactions. Interrupt or slow the rate of infusion for Grade 1 or Grade 2 reactions. For Grade 3 or 4 reactions, stop infusion and permanently discontinue KEYTRUDA.

Complications of Allogeneic Hematopoietic Stem Cell Transplantation (HSCT)

- Fatal and other serious complications can occur in patients who receive allogeneic HSCT before or after anti–PD-1/PD-L1 treatments. Transplant-related complications include hyperacute graft-versus-host-disease, acute and chronic GVHD, hepatic veno-occlusive disease after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between anti–PD-1/PD-L1 treatment and allogeneic HSCT. Follow patients closely for evidence of these complications and intervene promptly. Consider the benefit vs risks of using anti–PD-1/PD-L1 treatments prior to or after an allogeneic HSCT.

Increased Mortality in Patients With Multiple Myeloma

- In 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 an anti–PD-1/PD-L1 treatment in this combination is not recommended outside of controlled trials.

Embryofetal Toxicity

- Based on its mechanism of action, KEYTRUDA can cause fetal harm when administered to a pregnant woman. Advise women of this potential risk. In females of reproductive potential, verify pregnancy status prior to initiating KEYTRUDA and advise them to use effective contraception during treatment and for 4 months after the last dose.

Adverse Reactions

- In KEYNOTE-006, KEYTRUDA was discontinued due to adverse reactions in 9% of 555 patients with advanced melanoma; adverse reactions leading to permanent discontinuation in more than one patient were colitis (1.4%), autoimmune hepatitis (0.7%), allergic reaction (0.4%), polyneuropathy (0.4%), and cardiac failure (0.2%). The most common adverse reactions (≥20%) with KEYTRUDA were fatigue (28%), diarrhea (25%), rash (24%), and nausea (21%).
- In KEYNOTE-054, KEYTRUDA was permanently discontinued due to adverse reactions in 14% of 509 patients; the most common (≥1%) were pneumonitis (1.4%), colitis (1.2%), and diarrhea (1%). Serious adverse reactions occurred in 25% of patients receiving KEYTRUDA. The most common adverse reaction (≥20%) with KEYTRUDA was diarrhea (28%).
- In KEYNOTE-189, when KEYTRUDA was administered with pemetrexed and platinum chemotherapy in metastatic nonsquamous NSCLC, KEYTRUDA was discontinued due to adverse reactions in 16% of 405 patients. The most common adverse reactions resulting in permanent discontinuation of KEYTRUDA were pneumonitis (3%) and acute kidney injury (2%). The most common adverse reactions (≥20%) with KEYTRUDA were nausea (56%), fatigue (56%), constipation (35%), diarrhea (29%), decreased appetite (26%), rash (25%), vomiting (24%), cough (21%), dyspnea (20%), and pyrexia (20%).
- In KEYNOTE-407, when KEYTRUDA was administered with carboplatin and either paclitaxel or paclitaxel protein-bound in metastatic squamous NSCLC, KEYTRUDA was discontinued due to adverse reactions in 19% of 559 patients. The most frequent adverse reactions reported in at least 20 patients in the KEYTRUDA arm of patients were febrile neutropenia, pneumonia, and urinary tract infection. Adverse reactions observed in KEYNOTE-407 were similar to those observed in KEYNOTE-189 with the exception of increased incidences of alopecia (47 vs 36%) and peripheral neuropathy (31% vs 25%) were observed in the KEYTRUDA and chemotherapy arm compared to the placebo and chemotherapy arm in KEYNOTE-407.
- In KEYNOTE-042, KEYTRUDA was discontinued due to adverse reactions in 19% of 636 patients with advanced NSCLC; the most common were pneumonitis (3%), death due to unknown cause (1.6%), and renal failure and renal impairment (1.4%). The most frequent serious adverse reactions reported in at least 2% of patients were pneumonia (7%), pneumonitis (3.9%), pulmonary embolism (2.4%), and pleural effusion (2.2%). The most common adverse reaction (≥20%) was fatigue (25%).
- In KEYNOTE-024 in 154 untreated metastatic NSCLC patients with a PD-L1 TPS ≥50%, KEYTRUDA was discontinued due to adverse reactions in 26% of patients; the most common were pneumonitis (1.8%). The most common adverse reactions (≥20%) were fatigue (33%), constipation (20%), and rash (20%).
- In KEYNOTE-048, KEYTRUDA monotherapy was discontinued due to adverse events in 12% of 300 patients with NSCLC; the most common adverse reactions leading to permanent discontinuation were pneumonitis (1.3%) and pneumonia (1.3%). The most common adverse reactions (≥20%) were fatigue (27%), constipation (20%), and rash (20%).
- In KEYNOTE-048, when KEYTRUDA was administered in combination with platinum (cisplatin or carboplatin) and FU chemotherapy, KEYTRUDA was discontinued due to adverse reactions in 16% of 276 patients with HNSCC. The most common adverse reactions resulting in permanent discontinuation of KEYTRUDA were pneumonia (2.5%), pneumonitis (1.8%), and septic shock (1.4%). The most common adverse reactions (≥20%) were nausea (51%), fatigue (49%), constipation (37%), vomiting (32%), mucosal inflammation (31%), diarrhea (29%), decreased appetite (29%), stomatitis (26%), and cough (22%).
- 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, cardiopulmonary arrest, cellulitis, and respiratory failure. The most common adverse reactions (≥20%) 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 who received KEYTRUDA as a monotherapy, with the exception of increased incidences of facial edema and new or worsening hypothyroidism.
- In KEYNOTE-204, KEYTRUDA was discontinued due to adverse reactions in 14% of 148 patients with cHL. Serious adverse reactions occurred in 30% of patients receiving KEYTRUDA; those ≥1% were pneumonitis, pneumonia, pyrexia, myocarditis, acute kidney injury, febrile neutropenia, and sepsis. Three patients died from causes other than disease progression; 2 from complications after allogeneic HSCT and 1 from unknown cause. The most common adverse reactions (≥20%) were upper respiratory tract infection (41%), musculoskeletal pain (32%), diarrhea (22%), and pyrexia, fatigue, rash, and cough (20% each).
- In KEYNOTE-087, KEYTRUDA was discontinued due to adverse reactions in 5% of 210 patients with cHL. Serious adverse reactions occurred in 16% of patients; those ≥1% were pneumonia, pneumonitis, pyrexia, dyspnea, GVHD, and herpes zoster. Two patients died from causes other than disease progression: 1 from GVHD after subsequent allogeneic HSCT and 1 from septic shock. The most common adverse reactions (≥20%) were fatigue (26%), pyrexia (24%), cough (24%), musculoskeletal pain (21%), diarrhea (20%), and rash (20%).
- In KEYNOTE-170, KEYTRUDA was discontinued due to adverse reactions in 8% of 53 patients with PMBCL. Serious adverse reactions occurred in 26% of patients and included arrhythmia (4%), cardiac tamponade (2%), myocardial infarction (2%), pericardial effusion (2%), and pericarditis (2%). Six (11%) patients died within 30 days of start of treatment. The most common adverse reactions (≥20%) were musculoskeletal pain (30%), upper respiratory tract infection and pyrexia (28% each), cough (26%), fatigue (23%), and dyspnea (21%).
- In KEYNOTE-052, KEYTRUDA was discontinued due to adverse reactions in 11% of 370 patients with locally advanced or metastatic urothelial carcinoma. Serious adverse reactions occurred in 42% of patients; those ≥2% were urinary tract infection, hematuria, acute kidney injury, pneumonia, and urosepsis. The most common adverse reactions (≥20%) were fatigue (38%), musculoskeletal pain (23%), decreased appetite (21%), rash (21%), and diarrhea (20%).
- 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%). Serious adverse reactions occurred in 39% of KEYTRUDA-treated patients; those ≥2% were urinary tract infection, pneumonia, anemia, and pneumonitis. The most common adverse reactions (≥20%) in patients who received KEYTRUDA were fatigue (38%), musculoskeletal pain (32%), pruritus (23%), decreased appetite (21%), nausea (21%), and rash (20%).
- In KEYNOTE-057, KEYTRUDA was discontinued due to adverse reactions in 11% of 148 patients with high-risk NMIBC. The most common adverse reaction resulting in permanent discontinuation of KEYTRUDA was pneumonitis (1.4%). Serious adverse reactions occurred in 28% of patients; those ≥2% were pneumonia (3%), cardiac ischemia (2%), colitis (2%), pulmonary embolism (2%), sepsis (2%), and urinary tract infection (2%). The most common adverse reactions (≥20%) were fatigue (29%), diarrhea (24%), and rash (24%).
- Adverse reactions occurring in patients with MSI-H or dMMR CRC were similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy.
- Adverse reactions occurring in patients with gastric cancer were similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy.
- In KEYNOTE-590, when KEYTRUDA was administered with cisplatin and fluorouracil to patients with metastatic or locally advanced esophageal or GEJ (tumors with epicenter 1 to 5 centimeters above the GEJ) carcinoma who were not candidates for surgical resection or definitive chemoradiation, KEYTRUDA was discontinued due to adverse reactions in 15% of 370 patients. The most common adverse reactions resulting in permanent discontinuation of KEYTRUDA (≥1%) were pneumonitis (1.6%), acute kidney injury (1.1%), and pneumonia (1.1%). The most common adverse reactions (≥20%) with KEYTRUDA in combination with chemotherapy were nausea (67%), fatigue (57%), decreased appetite (44%), constipation (40%), diarrhea (36%), vomiting (34%), stomatitis (27%), and weight loss (24%).
- Adverse reactions occurring in patients with esophageal cancer who received KEYTRUDA as a monotherapy were similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy.
- In KEYNOTE-158, KEYTRUDA was discontinued due to adverse reactions in 8% of 98 patients with recurrent or metastatic cervical cancer. Serious adverse reactions occurred in 39% of patients receiving KEYTRUDA; the most frequent included anemia (7%), fistula, hemorrhage, and infections [excepted urinary tract infections] (4.1% each). The most common adverse reactions (≥20%) were fatigue (43%), musculoskeletal pain (27%), diarrhea (23%), pain and abdominal pain (22% each), and decreased appetite (21%).
- Adverse reactions occurring in patients with hepatocellular carcinoma (HCC) were generally similar to those in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy; with the exception of increased incidences of ascites (8% Grades 3–4) and immune-mediated hepatitis (2.9%). Laboratory abnormalities (Grades 3–4) that occurred at a higher incidence were elevated AST (20%), ALT (9%), and hyperbilirubinemia (10%).
- Among the 50 patients with MCC enrolled in study KEYNOTE-017, adverse reactions occurring in patients with MCC were generally similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy. Laboratory abnormalities (Grades 3–4) that occurred at a higher incidence were elevated AST (11%) and hyperglycemia (10%).
- In KEYNOTE-426, when KEYTRUDA was administered in combination with axitinib, total adverse reactions occurred in 3.3% of 429 patients. Serious adverse reactions occurred in 40% of patients, the most frequent (≥1%) were hepatotoxicity (7%), diarrhea (4.2%), acute kidney injury (2.3%), dehydration (1%), and pneumonitis (1%). Permanent discontinuation due to an adverse reaction occurred in 31% of patients; KEYTRUDA only (13%), axitinib only (13%), and the combination (5%). The most common were hepatotoxicity (13%), diarrhea(5%), hypertension (1.9%), acute kidney injury (1.6%), and pneumonitis (1.4%). The most common adverse reactions (≥20%) were diarrhea (56%), fatigue/asthenia (52%), hypertension (48%), hepatotoxicity (39%), hypothyroidism (35%), decreased appetite (30%), palmar-plantar erythrodysesthesia (29%), nausea (28%), stomatitis/mucosal inflammation (27%), dysphonia (25%), rash (25%), cough (21%), and constipation (21%).
- Adverse reactions occurring in patients with TMB-H cancer were similar to those occurring in patients with other solid tumors who received KEYTRUDA as a single agent.
- Adverse reactions occurring in patients with urothelial carcinoma who received KEYTRUDA monotherapy or NSCLC who received KEYTRUDA as a monotherapy.
- In KEYNOTE-355, when KEYTRUDA and chemotherapy (paclitaxel, paclitaxel protein-bound, or gemcitabine and carboplatin) were administered to patients with locally recurrent unresectable or metastatic TNBC who had not been previously treated with chemotherapy in the metastatic setting (n=566), fatal adverse reactions occurred in 2.5% of patients, including cardio-respiratory arrest (0.7%) and septic shock (0.3%). Serious adverse reactions occurred in 30% of patients receiving KEYTRUDA in combination with chemotherapy; the serious reactions in ≥2% were pneumonia (2.8%), anemia (2.2%), and thromboembolic (2%). The most common adverse reactions (≥20%) were diarrhea (56%), fatigue/asthenia (52%), hypertension (48%), hepatotoxicity (39%), hypothyroidism (35%), decreased appetite (30%), palmar-plantar erythrodysesthesia (29%), nausea (28%), stomatitis/mucosal inflammation (27%), dysphonia (25%), rash (25%), cough (21%), and constipation (21%).
- Adverse reactions occurring in patients with gastric cancer who received KEYTRUDA in combination with chemotherapy were similar to those occurring in patients with other solid tumors who received KEYTRUDA as a single agent.

Lactation

- Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment and for 4 months after the final dose.

Pediatric Use

- In KEYNOTE-051, 161 pediatric patients (62 pediatric patients aged 6 months to younger than 12 years and 99 pediatric patients aged 12 years to 17 years) were administered KEYTRUDA 2 mg/kg every 3 weeks. The median duration of exposure was 2.1 months (range: 1 day to 24 months).
- Adverse reactions that occurred at a ≥10% higher rate in pediatric patients when compared to adults were pyrexia (33%), vomiting (33%), vomiting (30%), leukopenia (30%), upper respiratory tract infection (29%), neutropenia (26%), headache (25%), and Grade 3 anemia (17%).

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information. The Medication Guide also is available.

Reference: 1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer V.4.2021. © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed March 3, 2021. To view the most recent and complete version of the guidelines, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

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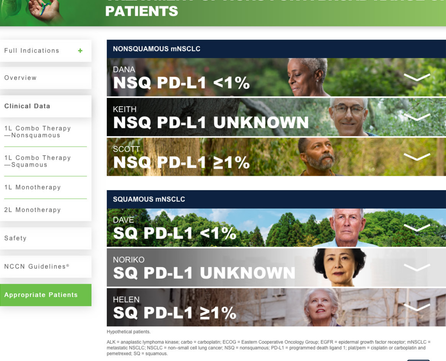
TREATMENT OPTIONS FOR A BROAD RANGE OF PATIENTS



Hypothetical patients.

ALK = anaplastic lymphoma kinase; carbo = carboplatin; ECOG = Eastern Cooperative Oncology Group; EGFR = epidermal growth factor receptor; mNSCLC = metastatic NSCLC; NSCLC = non-small cell lung cancer; NSQ = nonsquamous; PD-L1 = programmed death ligand 1; platinum = cisplatin or carboplatin and pemetrexed; SQ = squamous.

Key Chat

FIRST-LINE COMBINATION THERAPY IN NONSQUAMOUS mNSCLC: KEYTRUDA, in combination with pemetrexed and platinum chemotherapy, is indicated for the first-line treatment of patients with metastatic nonsquamous non-small cell lung cancer (NSCLC), with no EGFR or ALK genomic tumor aberrations.

FIRST-LINE COMBINATION THERAPY IN SQUAMOUS mNSCLC: KEYTRUDA, in combination with carboplatin and either paclitaxel or paclitaxel protein-bound, is indicated for the first-line treatment of patients with metastatic squamous NSCLC.

FIRST-LINE MONOTHERAPY IN NONSQUAMOUS AND SQUAMOUS ADVANCED NSCLC: KEYTRUDA, as a single agent, is indicated for the first-line treatment of patients with NSCLC expressing PD-L1 (tumor proportion score (TPS) ≥1%) as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and is stage III where patients are not candidates for surgical resection or definitive chemoradiation, or metastatic.

SECOND-LINE OR GREATER MONOTHERAPY IN NONSQUAMOUS AND SQUAMOUS mNSCLC: KEYTRUDA, as a single agent, is indicated for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥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.

mNSCLC = metastatic NSCLC; EGFR = epidermal growth factor receptor; ALK = anaplastic lymphoma kinase; PD-L1 = programmed death ligand 1

SELECTED SAFETY INFORMATION

Severe and Fatal Immune-Mediated Adverse Reactions

- KEYTRUDA is a monoclonal antibody that belongs to a class of drugs that bind to either the programmed death receptor-1 (PD-1) or the programmed death ligand 1 (PD-L1), blocking the PD-1/PD-L1 pathway, thereby removing immunosuppression within the immune response, potentially breaking peripheral tolerance and inducing immune-mediated adverse reactions. Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue, can affect more than one body system simultaneously, and can occur at any time after starting treatment or after discontinuation of treatment. Important immune-mediated adverse reactions listed here may not include all possible severe and fatal immune-mediated adverse reactions.
- Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Early identification and management are essential to ensure safe use of KEYTRUDA. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.
- Withhold or permanently discontinue KEYTRUDA depending on severity of the immune-mediated adverse reaction. In general, if KEYTRUDA requires interruption or discontinuation, administer systemic corticosteroid therapy (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid tapering and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose adverse reactions are not controlled with corticosteroid therapy.

Immune-Mediated Pneumonitis

- KEYTRUDA can cause immune-mediated pneumonitis. The incidence is higher in patients who have received prior thoracic radiation. Immune-mediated pneumonitis occurred in 3.4% (94/2799) of patients receiving KEYTRUDA, including fatal (0.1%), Grade 4 (0.3%), Grade 3 (0.9%), and Grade 2 (1.3%) reactions. Systemic corticosteroids were required in 1.7% (48/2799) of patients receiving KEYTRUDA, including fatal (0.1%) cases. Of these, the majority remained on systemic corticosteroids. Among the 0.9% (26) of patients who were withheld reinitiated KEYTRUDA after symptom improvement; of these, 23% had recurrence. Pneumonitis resolved in 59% of the 94 patients.
- Pneumonitis occurred in 8% (31/389) of adult patients with cHL receiving KEYTRUDA as a single agent, including Grades 3–4 in 2.3% of patients. Patients received high-dose corticosteroids for a median duration of 10 days (range: 2 days to 53 months). Pneumonitis rates were similar in patients with and without prior thoracic radiation. Pneumonitis led to discontinuation of KEYTRUDA in 5.4% (21) of patients. Of the patients who developed pneumonitis, 42% interrupted KEYTRUDA, 68% discontinued KEYTRUDA, and 77% had resolution.

Immune-Mediated Colitis

- KEYTRUDA can cause immune-mediated colitis, which may present with diarrhea. Cytomegalovirus infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies. Immune-mediated colitis occurred in 1.7% (46/2799) of patients receiving KEYTRUDA, including Grade 4 (<1%), Grade 3 (1.1%), and Grade 2 (0.4%) reactions. Systemic corticosteroids were required in 69% (33/48); additional immunosuppressant therapy was required in 42% of patients. Colitis led to permanent discontinuation of KEYTRUDA in 0.5% (15) and withholding in 0.5% (13) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement; of these, 23% had recurrence. Colitis resolved in 85% of the 48 patients.

Hepatotoxicity and Immune-Mediated Hepatitis

KEYTRUDA as a Single Agent

- KEYTRUDA can cause immune-mediated hepatitis. Immune-mediated hepatitis occurred in 0.7% (19/2799) of patients receiving KEYTRUDA, including Grade 4 (<0.1%), Grade 3 (0.4%), and Grade 2 (0.1%) reactions. Systemic corticosteroids were required in 68% (13/19) of patients; additional immunosuppressant therapy was required in 11% of patients. Hepatitis led to permanent discontinuation of KEYTRUDA in 0.2% (6) and withholding in 0.3% (9) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement; of these, none had recurrence. Hepatitis resolved in 79% of the 19 patients.

KEYTRUDA With Axitinib

- KEYTRUDA in combination with axitinib can cause hepatic toxicity. Monitor liver enzymes before initiation of and periodically throughout treatment. Consider monitoring more frequently as compared to when the drugs are administered as single agents. For elevated liver enzymes, interrupt KEYTRUDA and axitinib, and consider administering corticosteroids as needed. With the combination of KEYTRUDA and axitinib, Grades 3 and 4 increased alanine aminotransferase (ALT) (20%) and increased aspartate aminotransferase (AST) (13%) were seen at a higher frequency compared to KEYTRUDA alone. Fifty-nine percent of the patients with increased ALT received systemic corticosteroids. In patients with ALT ≥3 times upper limit of normal (ULN) (Grades 2–4, n=116), ALT resolved to Grades 0–1 in 94%. Among the 92 patients who were rechallenged with either KEYTRUDA (n=3) or axitinib (n=34) administered as a single agent or with both (n=55), recurrence of ALT ≥3 times ULN was observed in 1 patient receiving KEYTRUDA, 16 patients receiving axitinib, and 24 patients receiving both. All patients with a recurrence of ALT ≥3 ULN subsequently recovered from the event.

Immune-Mediated Endocrinopathies

Adrenal Insufficiency

- KEYTRUDA can cause primary or secondary adrenal insufficiency. For Grade 2 or higher, initiate symptomatic treatment, including hormone replacement as clinically indicated. Withhold KEYTRUDA depending on severity. Adrenal insufficiency occurred in 0.8% (22/2799) of patients receiving KEYTRUDA, including Grade 4 (<0.1%), Grade 3 (0.3%), and Grade 2 (0.5%) reactions. Systemic corticosteroids were required in 77% (17/22) of patients; in 4 of the 17 patients with adrenal insufficiency, of these, the majority remained on systemic corticosteroids. Adrenal insufficiency led to permanent discontinuation of KEYTRUDA in <0.1% (1) and withholding in 0.3% (8) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement.

Hypophysitis

- KEYTRUDA can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field defects. Hypophysitis can cause hypopituitarism. Initiate hormone replacement therapy as clinically indicated. Withhold or permanently discontinue KEYTRUDA depending on severity. Hypophysitis occurred in 0.6% (17/2799) of patients receiving KEYTRUDA, including Grade 4 (<0.1%), Grade 3 (0.3%), and Grade 2 (0.2%) reactions. Systemic corticosteroids were required in 94% (16/17) of patients. Hypophysitis led to permanent discontinuation of KEYTRUDA in 0.1% (4) and withholding in 0.3% (7) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement.

Thyroid Disorders

- KEYTRUDA can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement for hypothyroidism or manage hyperthyroidism with thionamides as medically indicated. Withhold or permanently discontinue KEYTRUDA depending on severity. Thyroiditis occurred in 0.6% (16/2799) of patients receiving KEYTRUDA, including Grade 2 (0.3%). None discontinued, but withheld in 0.3% (8) patients withheld in <0.1% (1) of patients.
- Hyperthyroidism occurred in 3.4% (96/2799) of patients receiving KEYTRUDA, including Grade 3 (0.1%) and Grade 2 (0.8%). It led to permanent discontinuation of KEYTRUDA in <0.1% (2) and withholding in 0.3% (7) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement. Hypothyroidism occurred in 8% (237/2799) of patients receiving KEYTRUDA, including Grade 4 (0.1%) and Grade 3 (0.1%) reactions. It led to permanent discontinuation of KEYTRUDA in <0.1% (1) and withholding in 0.5% (14) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement. The majority of patients with hypothyroidism required long-term hormone replacement. The incidence of new or worsening hypothyroidism was higher in 1185 patients with HNSCC, occurring in 16% of patients receiving KEYTRUDA as a single agent or in combination with platinum and FU, including Grade 3 (0.3%) hypothyroidism. The incidence of new or worsening hypothyroidism was higher in 389 adult patients with cHL (17%) receiving KEYTRUDA as a single agent, including Grade 1 (6.2%) and Grade 2 (10.8%) hypothyroidism.

Type 1 Diabetes Mellitus (DM), Which Can Present With Diabetic Ketoacidosis

- Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Withhold KEYTRUDA depending on severity. Type 1 DM occurred in 0.2% (5/2799) of patients receiving KEYTRUDA. It led to permanent discontinuation in <0.1% (1) and withholding of KEYTRUDA in <0.1% (1) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement.

Immune-Mediated Nephritis With Renal Dysfunction

- KEYTRUDA can cause immune-mediated nephritis. Immune-mediated nephritis occurred in 0.3% (9/2799) of patients receiving KEYTRUDA, including Grade 4 (<0.1%), Grade 3 (0.1%), and Grade 2 (0.1%) reactions. Systemic corticosteroids were required in 89% (8/9) of patients. Nephritis led to permanent discontinuation of KEYTRUDA in 0.1% (3) and withholding in 0.1% (3) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement; of these, none had recurrence. Nephritis resolved in 56% of the 9 patients.

Immune-Mediated Dermatologic Adverse Reactions

- KEYTRUDA can cause immune-mediated rash or dermatitis. Exfoliative dermatitis, including Stevens-Johnson syndrome, drug rash with eosinophilia and systemic symptoms, and toxic epidermal necrolysis, has occurred with anti-PD-1/PD-L1 treatments. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes. Withhold or permanently discontinue KEYTRUDA depending on severity. Immune-mediated dermatologic adverse reactions occurred in 1.4% (38/2799) of patients receiving KEYTRUDA, including Grade 3 (1%) and Grade 2 (0.1%) reactions. Systemic corticosteroids were required in 40% (15/38) of patients. These reactions led to permanent discontinuation of KEYTRUDA in 0.6% (16) of patients. All patients who were withheld reinitiated KEYTRUDA after symptom improvement; of these, 6% had recurrence. The reactions resolved in 79% of the 38 patients.

Other Immune-Mediated Adverse Reactions

- The following clinically significant immune-mediated adverse reactions occurred at an incidence of <1% (unless otherwise noted) in patients who received KEYTRUDA or were reported with the use of other anti-PD-1/PD-L1 treatments. Severe or fatal cases have been reported for some of these adverse reactions. *Cardiac/Vascular:* Myocarditis, pericarditis, vasculitis. *Nervous System:* Meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis (including exacerbation), Guillain-Barré syndrome, nerve paresis, autoimmune neuropathy; *Ocular:* Uveitis, iritis and other ocular inflammatory toxicities can occur. Some cases can be associated with retinal detachment. Various grades of visual impairment, including blindness, can occur. If uveitis occurs in combination with other immune-mediated adverse reactions, consider a Vogt-Koyanagi-Harada-like syndrome, as this may require treatment with systemic steroids to reduce the risk of permanent vision loss; *Gastrointestinal:* Pancreatitis, to include increases in serum amylase and lipase levels, gastritis, duodenitis; *Musculoskeletal and Connective Tissue:* Myositis/polymyositis, rhabdomyolysis (and associated sequelae, including renal failure), arthritis (1.5%), polymyalgia rheumatica; *Endocrine:* Hypoparathyroidism; *Hematologic/Immune:* Hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuch lymphadenitis), sarcoidosis, immune thrombocytopenic purpura, solid organ transplant rejection.

Infusion-Related Reactions

- KEYTRUDA can cause severe or life-threatening infusion-related reactions, including hypersensitivity and anaphylaxis, which have been reported in 0.2% of 2799 patients receiving KEYTRUDA. Monitor for signs and symptoms of infusion-related reactions. Interrupt or slow the rate of infusion for Grade 1 or Grade 2 reactions. For Grade 3 or Grade 4 reactions, stop infusion and permanently discontinue KEYTRUDA.

Complications of Allogeneic Hematopoietic Stem Cell Transplantation (HSCT)

- Fatal and other serious complications can occur in patients who receive allogeneic HSCT before or after anti-PD-1/PD-L1 treatments. Transplant-related complications include hyperacute graft-versus-host-disease (GVHD), acute and chronic GVHD, hepatic veno-occlusive disease after reduced intensity conditioning, and steroid-requiring febrile syndrome (without infection as a defined infectious cause). These complications may occur despite intervening therapy between anti-PD-1/PD-L1 treatments and allogeneic HSCT. Follow patients closely for evidence of these complications and intervene promptly. Consider the benefit vs risks of using anti-PD-1/PD-L1 treatments prior to or after an allogeneic HSCT.

Increased Mortality in Patients With Multiple Myeloma

- In 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 anti-PD-1/PD-L1 treatment in this combination is not recommended outside of controlled trials.

Embryofetal Toxicity

- Based on its mechanism of action, KEYTRUDA can cause fetal harm when administered to a pregnant woman. Advise women of this potential risk. In females of reproductive potential, verify pregnancy status prior to initiating KEYTRUDA and advise them to use effective contraception during treatment and for 4 months after the last dose.

Adverse Reactions

- In KEYNOTE-006, KEYTRUDA was discontinued due to adverse reactions in 9% of 555 patients with advanced melanoma; adverse reactions leading to permanent 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%). The most common adverse reactions (≥20%) with KEYTRUDA were fatigue (28%), diarrhea (26%), rash (24%), and nausea (21%).
- In KEYNOTE-054, KEYTRUDA was permanently discontinued due to adverse reactions in 14% of 509 patients; the most common (≥1%) were pneumonitis (1.4%), colitis (1.2%), and diarrhea (1%). Serious adverse reactions occurred in 25% of patients receiving KEYTRUDA. The most common adverse reaction (≥20%) with KEYTRUDA was diarrhea (26%).
- In KEYNOTE-189, when KEYTRUDA was administered with pemetrexed and platinum chemotherapy in metastatic nonsquamous NSCLC, KEYTRUDA was discontinued due to adverse reactions in 20% of 405 patients. The most common adverse reactions resulting in permanent discontinuation of KEYTRUDA were pneumonitis (3%) and acute kidney injury (2%). The most common adverse reactions (≥20%) with KEYTRUDA were nausea (56%), fatigue (56%), constipation (35%), diarrhea (31%), decreased appetite (28%), rash (25%), vomiting (24%), cough (21%), dyspnea (21%), and pyrexia (20%).
- In KEYNOTE-407, when KEYTRUDA was administered with carboplatin and either paclitaxel or nab-paclitaxel in metastatic squamous NSCLC, KEYTRUDA was discontinued due to adverse reactions in 15% of 101 patients. The most frequent serious adverse reactions reported in at least 2% of patients were pneumonia (3%) and acute kidney injury (2%). The most common adverse reactions (≥20%) with KEYTRUDA were alopecia (56%), fatigue (49%), constipation (37%), vomiting (32%), mucosal inflammation (31%), diarrhea (29%), decreased appetite (29%), stomatitis (26%), and cough (22%).
- 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 (6%), dyspnea, cellulitis, upper respiratory infection, pleural effusion, and respiratory failure. The most common adverse reactions (≥20%) 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 who received KEYTRUDA as a monotherapy, with the exception of increased incidences of facial edema and new or worsening hypothyroidism.
- In KEYNOTE-204, KEYTRUDA was discontinued due to adverse reactions in 14% of 148 patients with cHL. Serious adverse reactions occurred in 30% of patients receiving KEYTRUDA; those ≥1% were pneumonitis, pneumonia, pyrexia, myocarditis, acute kidney injury, febrile neutropenia, and sepsis. Three patients died from causes other than disease progression: 2 from complications after allogeneic HSCT and 1 from unknown cause. The most common adverse reactions (≥20%) were upper respiratory tract infection (31%), musculoskeletal pain (32%), diarrhea (22%), and pyrexia, fatigue, rash, and cough (20% each).
- In KEYNOTE-087, KEYTRUDA was discontinued due to adverse reactions in 5% of 210 patients with cHL. Serious adverse reactions occurred in 16% of patients; those ≥1% were pneumonia, pneumonitis, pyrexia, dyspnea, GVHD, and herpes zoster. Two patients died from causes other than disease progression; 1 from GVHD after subsequent allogeneic HSCT and 1 from septic shock. The most common adverse reactions (≥20%) were fatigue (26%), pyrexia (24%), cough (24%), musculoskeletal pain (21%), diarrhea (20%), and rash (20%).
- In KEYNOTE-170, KEYTRUDA was discontinued due to adverse reactions in 8% of 53 patients with PMBCL. Serious adverse reactions occurred in 26% of patients and included arrhythmia (4%), cardiac tamponade (2%), myocardial infarction (2%), pericardial effusion (2%), and pericarditis (2%). Six (11%) patients died within 30 days of start of treatment. The most common adverse reactions (≥20%) were musculoskeletal pain (30%), upper respiratory tract infection and pyrexia (28% each), cough (26%), fatigue (23%), and dyspnea (21%).
- In KEYNOTE-052, KEYTRUDA was discontinued due to adverse reactions in 11% of 370 patients with locally advanced or metastatic urothelial carcinoma. Serious adverse reactions occurred in 42% of patients; those ≥2% were urinary tract infection, hematuria, acute kidney injury, pneumonia, and urosepsis. The most common adverse reactions (≥20%) were fatigue (38%), musculoskeletal pain (24%), decreased appetite (22%), constipation (21%), rash (21%), and diarrhea (20%).
- 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%). Serious adverse reactions occurred in 39% of KEYTRUDA-treated patients; those ≥2% were urinary tract infection, pneumonia, sepsis, and pneumonitis. The most common adverse reactions (≥20%) in patients who received KEYTRUDA were fatigue (38%), musculoskeletal pain (32%), pruritus (23%), decreased appetite (21%), nausea (21%), and rash (20%).
- In KEYNOTE-057, KEYTRUDA was discontinued due to adverse reactions in 11% of 148 patients with high-risk NMIBC. The most common adverse reaction resulting in permanent discontinuation of KEYTRUDA was pneumonitis (1.4%). Serious adverse reactions occurred in 28% of patients; those ≥2% were pneumonia (3%), cardiac ischemia (2%), colitis (2%), pulmonary embolism (2%), sepsis (2%), and urinary tract infection (2%). The most common adverse reactions (≥20%) were fatigue (29%), diarrhea (24%), and rash (24%).
- Adverse reactions occurring in patients with MSI-H or dMMR CRC were similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy.
- Adverse reactions occurring in patients with gastric cancer were similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy.
- In KEYNOTE-590, when KEYTRUDA was administered with cisplatin and fluorouracil to patients with metastatic or locally advanced esophageal or GEJ tumors with esophageal 1 to 5 centimeters above the GEJ, carcinoma who were not candidates for surgical resection or definitive chemoradiation, KEYTRUDA was discontinued due to adverse reactions in 15% of 370 patients. The most common adverse reactions resulting in permanent discontinuation of KEYTRUDA (≥1%) were pneumonitis (1.6%), acute kidney injury (1.4%), and pneumonia (1.1%). The most common adverse reactions (≥20%) with KEYTRUDA in combination with chemotherapy were nausea (67%), fatigue (57%), decreased appetite (44%), constipation (40%), diarrhea (36%), vomiting (34%), stomatitis (27%), and weight loss (24%).
- Adverse reactions occurring in patients with esophageal cancer who received KEYTRUDA as a monotherapy were similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy.
- In KEYNOTE-158, KEYTRUDA was discontinued due to adverse reactions in 8% of 98 patients with recurrent or metastatic cervical cancer. Serious adverse reactions occurred in 39% of patients receiving KEYTRUDA; the most frequent included anemia (7%), fistula, hemorrhage, and infections (except urinary tract infections) (4.1% each). The most common adverse reactions (≥20%) were fatigue (43%), musculoskeletal pain (27%), diarrhea (23%), pain and abdominal pain (22% each), and decreased appetite (21%).
- Adverse reactions occurring in patients with hepatocellular carcinoma (HCC) were generally similar to those in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy, with the exception of increased incidences of ascites (8% Grades 3–4) and immune-mediated hepatitis (2.9%). Laboratory abnormalities (Grades 3–4) that occurred in higher rates included AST (20%), ALT (7%), and hyperbilirubinemia (10%).
- Among the 50 patients with MCC enrolled in study KEYNOTE-017, adverse reactions occurring in patients with MCC were generally similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy. Laboratory abnormalities (Grades 3–4) that occurred at a higher incidence were elevated AST (11%) and hyperglycemia (19%).
- In KEYNOTE-426, when KEYTRUDA was administered in combination with axitinib, fatal adverse reactions occurred in 3.3% of 429 patients. Serious adverse reactions occurred in 40% of patients; the most frequent (≥1%) were hepatotoxicity (7%), diarrhea (4.2%), acute kidney injury (2.3%), dehydration (1%), and pneumonitis (1%). Permanent discontinuation due to an adverse reaction occurred in 31% of patients; KEYTRUDA only (13%), axitinib only (13%), and the combination (8%). The most common were hepatotoxicity (13%), diarrhea/colitis (3%), acute kidney injury (1.6%), and cardiovascular accident (1.2%). The most common adverse reactions (≥20%) were diarrhea (56%), fatigue/asthenia (52%), hypertension (48%), hepatotoxicity (39%), hypothyroidism (35%), decreased appetite (30%), palmar-plantar erythrodysesthesia (28%), nausea (28%), stomatitis/mucosal inflammation (27%), dysphonia (25%), rash (25%), cough (21%), and constipation (21%).
- Adverse reactions occurring in patients with TMB-H cancer were similar to those occurring in patients with other solid tumors who received KEYTRUDA as a single agent.
- Adverse reactions occurring in patients with cSCC were similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy.
- In KEYNOTE-355, when KEYTRUDA and chemotherapy (paclitaxel, paclitaxel protein-bound, or gemcitabine and carboplatin) were administered to patients with locally recurrent unresectable or metastatic TNBC who had not been previously treated with chemotherapy in the metastatic setting (n=596), fatal adverse reactions occurred in 2.3% of patients, including cardiopulmonary arrest (0.7%) and septic shock (0.3%). Serious adverse reactions occurred in 30% of patients receiving KEYTRUDA in combination with chemotherapy; the serious reactions in ≥2% were pneumonia (2.9%), anemia (2.2%), and thrombocytopenia (2%). KEYTRUDA was discontinued in 11% of patients due to adverse reactions. The most common reactions resulting in permanent discontinuation (≥1%) were increased ALT (2.2%), increased AST (1.5%), and pneumonitis (1.2%). The most common adverse reactions (≥20%) in patients receiving KEYTRUDA in combination with chemotherapy were fatigue (48%), nausea (44%), alopecia (34%), diarrhea and constipation (28% each), vomiting and rash (26% each), cough (23%), decreased appetite (21%), and headache (20%).

Lactation

- Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment and for 4 months after the final dose.

Pediatric Use

- In KEYNOTE-051, 161 pediatric patients (62 pediatric patients aged 6 months to younger than 12 years and 99 pediatric patients aged 12 years to 17 years) were administered KEYTRUDA 2 mg/kg every 3 weeks. The median duration of exposure was 2.1 months (range: 1 day to 24 months).
- Adverse reactions that occurred at a ≥10% higher rate in pediatric patients than compared to adults were pyrexia (33%), vomiting (30%), leukopenia (30%), upper respiratory tract infection (29%), neutropenia (26%), headache (25%), and Grade 3 anemia (17%).

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information. The Medication Guide also is available.

MERCK

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US-LAM-0095812

cHL = classical Hodgkin lymphoma; CRC = colorectal cancer; cSCC = cutaneous squamous cell carcinoma; dMMR = mismatch repair deficient; FU = fluorouracil; GEJ = gastroesophageal junction; HNSCC = head and neck squamous cell carcinoma; MCC = Merkel cell carcinoma; MSI-H = microsatellite instability-high; NMIBC = non-muscle-invasive bladder cancer; NSCLC = non-small cell lung cancer; PMBCL = primary mediastinal large B-cell lymphoma; TMB-H = tumor mutational burden-high; TNBC = triple-negative breast cancer.

KEYTRUDA (pembrolizumab)

CANCER TYPE | DOSING | DETECTED ADVERSE REACTIONS | RECOGNIZING OF ACTION | PATHOLOGIST CENTER | NURSE CENTER

TREATMENT OPTIONS FOR A BROAD RANGE OF PATIENTS

Full Indications +
Overview
Clinical Data
1L Combo Therapy —Nonsquamous
1L Combo Therapy —Squamous
1L Monotherapy
2L Monotherapy
Safety
NCCN Guidelines®
Appropriate Patients

NONSQUAMOUS mNSCLC

DANIEL
NSQ PD-L1 <1%

72 YEARS OLD
NONSQUAMOUS NSCLC
A retired lawyer and avid cook, Dave has refused to be frightened of his diagnosis, nonsquamous mNSCLC.

WHAT YOU SEE
- ECOG STATUS: 1
- PD-L1 EXPRESSION: <1%
- METASTASES: Liver
- SMOKING STATUS: 30-pack-year history; quit 2 years ago
- PHYSICAL ACTIVITY LEVEL: Low

WHO I AM
- EGFR/ALK: Negative
- Married 35 years
- Two adult sons
- Mother of grown adopted children
- Volunteer librarian
- Plays piano for relax

TREATMENT OPTIONS

KEYTRUDA + PLATINUM

KEITH
NSQ PD-L1 UNKNOWN

60 YEARS OLD
NONSQUAMOUS NSCLC
A strong performer and other pickleball champion in the community garden, Keith was recently diagnosed with nonsquamous mNSCLC.

WHAT YOU SEE
- EGFR/ALK: Negative
- ECOG STATUS: 0
- PD-L1 EXPRESSION: Unknown
- METASTASES: Liver
- SMOKING STATUS: Never smoked
- PHYSICAL ACTIVITY LEVEL: High

WHO I AM
- Married 35 years
- Father of 3, one has grandfather of 2
- Retired school teacher
- Youth soccer coach
- Nature enthusiast

TREATMENT OPTIONS

KEYTRUDA + PLATINUM

KEYTRUDA MONO

DAVE
NSQ PD-L1 ≥1%

62 YEARS OLD
NONSQUAMOUS NSCLC
Scott barber or a soap box is Montreal and was subsequently diagnosed with nonsquamous mNSCLC.

WHAT YOU SEE
- EGFR/ALK: Negative
- ECOG STATUS: 1
- PD-L1 EXPRESSION: 10%
- METASTASES: Brain
- SMOKING STATUS: 20-pack-year history; quit 11 years ago
- PHYSICAL ACTIVITY LEVEL: Moderate

WHO I AM
- Father of 3 and new grandfather
- Loves tent-camping
- Award-winning architect
- Local barbecue enthusiast

TREATMENT OPTIONS

KEYTRUDA + PLATINUM

KEYTRUDA MONO

SQUAMOUS mNSCLC

CHRIS
SQ PD-L1 <1%

69 YEARS OLD
SQUAMOUS NSCLC
Diagnosed with squamous mNSCLC, Chris is determined to beat the disease.

WHAT YOU SEE
- ECOG STATUS: 1
- PD-L1 EXPRESSION: <1%
- METASTASES: Liver
- SMOKING STATUS: Current smoker
- PHYSICAL ACTIVITY LEVEL: Low

WHO I AM
- Father of 2; married 38 years
- Retired sheriff
- Former softball coach; coached the county team to state championships
- Planning a trip to Europe

TREATMENT OPTIONS

KEYTRUDA + CARBO + PACLITAXEL
OR PACLITAXEL PROTEIN-BOUND

NORIKO
SQ PD-L1 UNKNOWN

58 YEARS OLD
SQUAMOUS NSCLC
An experienced venture capitalist, Noriko just discovered she has squamous mNSCLC.

WHAT YOU SEE
- ECOG STATUS: 1
- PD-L1 EXPRESSION: Unknown
- METASTASES: Liver
- SMOKING STATUS: 10-pack-year history; quit 30 years ago
- PHYSICAL ACTIVITY LEVEL: Moderate

WHO I AM
- Married; mother of 2
- Accomplished chef; loves cooking for family and friends
- Enjoys yoga
- Wants to provide financial consultation to the disadvantaged when she retires

TREATMENT OPTIONS

KEYTRUDA + CARBO + PACLITAXEL
OR PACLITAXEL PROTEIN-BOUND

HELEN
SQ PD-L1 ≥1%

73 YEARS OLD
SQUAMOUS NSCLC
The head of the local theater, Helen was recently diagnosed with squamous mNSCLC.

WHAT YOU SEE
- ECOG STATUS: 1
- PD-L1 EXPRESSION: 20%
- METASTASES: Bone
- SMOKING STATUS: Current smoker
- PHYSICAL ACTIVITY LEVEL: Low

WHO I AM
- Father of the arts, loves all kinds of acting
- Amateur cartographer
- Likes to host events for visiting international artists
- Retired banking executive

TREATMENT OPTIONS

KEYTRUDA + CARBO + PACLITAXEL
OR PACLITAXEL PROTEIN-BOUND

KEYTRUDA MONO

Hypothetical patients.

ALK = anaplastic lymphoma kinase; carbo = carboplatin; ECOG = Eastern Cooperative Oncology Group; EGFR = epidermal growth factor receptor; mNSCLC = metastatic NSCLC; NSCLC = non-small cell lung cancer; NSQ = nonsquamous; PD-L1 = programmed death ligand 1; platinum = cisplatin or carboplatin

Fact Check

FIRST-LINE COMBINATION THERAPY IN NONSQUAMOUS mNSCLC: KEYTRUDA, in combination with pemetrexed and platinum chemotherapy, is indicated for the first-line treatment of patients with metastatic nonsquamous non-small cell lung cancer (NSCLC), with no EGFR or ALK genomic tumor aberrations.

FIRST-LINE COMBINATION THERAPY IN SQUAMOUS mNSCLC: KEYTRUDA, in combination with carboplatin and either paclitaxel or paclitaxel protein-bound chemotherapy, is indicated for the first-line treatment of patients with metastatic squamous NSCLC.

FIRST-LINE MONOTHERAPY IN NONSQUAMOUS ADVANCED NSCLC: KEYTRUDA, as a single agent, is indicated for the first-line treatment of patients with NSCLC expressing PD-L1 tumor proportion score (TPS) ≥1% as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and is stratified for PD-L1 TPS ≥50% versus 1%-49% in the overall population or in patients with non-squamous NSCLC.

SECOND-LINE OR LATER TREATMENT IN NONSQUAMOUS OR SQUAMOUS mNSCLC: KEYTRUDA, as a single agent, is indicated for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥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 also have disease progression on FDA-approved therapy for these aberrations prior to receiving KEYTRUDA.

mNSCLC = metastatic non-small cell lung cancer; NSCLC = non-small cell lung cancer; PD-L1 = programmed death ligand 1

SELECTED SAFETY INFORMATION

Severe and Fatal Immune-Mediated Adverse Reactions

- KEYTRUDA is a monoclonal antibody that belongs to a class of drugs that bind to either the programmed death receptor-1 (PD-1) or the programmed death ligand (PD-L1) proteins, blocking the PD-1/PD-L1 pathway, thereby removing immune inhibition that may result in the stimulation of an immune response to normal cells and tissues. Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue, can affect more than one body system simultaneously, and can occur at any time after starting treatment or after discontinuation of treatment. Important immune-mediated adverse reactions listed here may not include all possible severe and life-threatening adverse reactions.
- Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Early identification and management are essential to ensure safe use of KEYTRUDA. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies. Depending on severity, initiate medical management promptly, including specialty consultation as appropriate.
- Withhold or permanently discontinue KEYTRUDA depending on severity of immune-mediated adverse reaction. In general, if KEYTRUDA requires interruption or discontinuation, administer systemic corticosteroid therapy (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid tapering and continue to taper over at least 1 month. Consider administration of other immunosuppressants in patients whose adverse reaction is not controlled with corticosteroids.

Immune-Mediated Pneumonitis

- KEYTRUDA can cause immune-mediated pneumonitis. The incidence is higher in patients who have received prior thoracic radiation. Immune-mediated pneumonitis occurred in 3.4% (94/2799) of patients receiving KEYTRUDA, including fatal (0.1%), Grade 4 (0.3%), Grade 3 (1.2%) reactions. Median time to onset is 5.4 months (range: 1 day to 16.8 months), and 42% (40/94) of these events occurred after 6 months of KEYTRUDA therapy. Of the 94 patients with pneumonitis, 52% (49) of patients had resolution, 22% (21) of patients were withheld permanently from KEYTRUDA, and 77% had resolution of pneumonitis.
- Pneumonitis occurred in 8% (31/388) of adult patients with cHL receiving KEYTRUDA as a single agent, including Grades 3-4 in 2.3% of patients. Patients received high-dose corticosteroids for a median duration of 10 days (range: 2 days to 53 months). Pneumonitis rates were similar in patients with and without prior thoracic radiation. Pneumonitis resolved in 85% (22/26) of patients with cHL who withheld KEYTRUDA and 100% (5/5) of patients who discontinued KEYTRUDA. Of patients who developed pneumonitis and received corticosteroids, 88% (23/26) resolved.

Immune-Mediated Colitis

- KEYTRUDA can cause immune-mediated colitis, which may present with diarrhea. Cytomegalovirus infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies. Immune-mediated colitis occurred in 2.2% (62/2799) of patients receiving KEYTRUDA, including Grade 3 (0.7%) and Grade 2 (1.4%) reactions. Median time to onset is 6.5 months (range: 15 days to 22.9 months). Systemic corticosteroids were required in 87% (53/61) patients with immune-mediated colitis, and immunosuppressant was required in 21% (13/61) patients. Immune-mediated colitis resulted in permanent discontinuation of KEYTRUDA in 0.5% (15) and permanent withdrawal in 0.9% (13) of patients. All patients who were withheld permanently from KEYTRUDA had resolution of the adverse reaction. Adrenal insufficiency has been reported in patients who received KEYTRUDA in 10.1% (1/10) and withholding in 2.3% (8) of patients. All patients who were withheld permanently from KEYTRUDA had symptom improvement.

Hepatotoxicity and Immune-Mediated Hepatitis

- KEYTRUDA can cause hepatotoxicity.
- KEYTRUDA can cause immune-mediated hepatitis. Immune-mediated hepatitis occurred in 0.7% (19/2799) of patients receiving KEYTRUDA, including Grade 4 (10.1%), Grade 3 (0.4%), and Grade 2 (0.1%) reactions. Systemic corticosteroids were required in 68% (13/19) of patients, and immune-suppressant therapy was required in 11% of patients. Hepatitis led to permanent discontinuation of KEYTRUDA in 0.3% (8) and withholding in 0.3% (8) of patients. All patients who were withheld permanently from KEYTRUDA had symptom improvement, of these, none had recurrence. Hepatitis resolved in 79% of the 19 patients.

Immune-Mediated Nephritis

- KEYTRUDA is a potential cause of renal dysfunction. Immune-mediated nephritis with renal dysfunction occurred in 0.3% (8/2799) of patients receiving KEYTRUDA. Consider monitoring more frequently as compared to when the drugs are administered as single agents. For elevated liver enzymes, interrupt KEYTRUDA and administer corticosteroids. Immune-mediated nephritis with renal dysfunction occurred in 0.8% (3/388) of adult patients with relapsed or refractory classical Hodgkin lymphoma (cHL) treated with pembrolizumab administered at 200 mg every 3 weeks. Immune-mediated nephritis with renal dysfunction occurred in 2% (20/1025) of patients receiving KEYTRUDA, including Grade 3 (0.5%) and Grade 2 (1.2%) reactions. Median time to onset is 4.4 months (range: 1 day to 22.9 months). All patients with cHL who had immune-mediated nephritis with renal dysfunction received KEYTRUDA as a single agent and with both cytotoxic chemotherapy and brentuximab vedotin. Immune-mediated nephritis with renal dysfunction resulted in permanent discontinuation of KEYTRUDA in 0.5% (5) and permanent withdrawal in 0.9% (9) of patients. All patients who were withheld permanently from KEYTRUDA had resolution of the adverse reaction. Of patients who developed immune-mediated nephritis with renal dysfunction and received corticosteroids, 88% (23/26) resolved.

Immune-Mediated Dermatitis

- KEYTRUDA can cause immune-mediated rash or dermatitis. Exfoliative dermatitis, including Stevens-Johnson syndrome, drug rash with eosinophilia and systemic symptoms, and toxic epidermal necrosis, has occurred with anti-PD-1/PD-L1 treatments. Topical emollients and/or topical corticosteroids may be adequate to resolve mild to moderate rash in patients treated with KEYTRUDA. Immune-mediated rash or dermatitis occurred in 1.8% (52/2799) of patients receiving KEYTRUDA, including Grade 3 (0.7%) and Grade 2 (1.1%) reactions. Median time to onset is 2.1 months (range: 1 day to 22.9 months). Corticosteroids were required in 40% (19/38) of patients. These reactions led to permanent discontinuation in 0.1% (2) and withholding of KEYTRUDA in 0.4% (16) of patients. All patients who were withheld permanently from KEYTRUDA after adverse reaction resolved. The reactions resolved in 79% (27) of the patients.

Other Immune-Mediated Adverse Reactions

- The immune-mediated adverse reactions listed below have been identified as immune-mediated adverse reactions in patients who received KEYTRUDA or were reported with the use of other anti-PD-1/PD-L1 antibodies. Severe or fatal cases have been reported for some of these adverse reactions. Cardiac/Vascular: Myocarditis, pericarditis, vasculitis. Nervous System: Meningitis, encephalitis, myositis and demyelination; myasthenic syndrome/myasthenia gravis (including exacerbation); demyelinating polyradiculoneuropathy; and Guillain-Barré syndrome. Endocrine: Hypophysitis including cases resulting in pituitary gland insufficiency; pituitary gland inflammation; and pituitary hemorrhage which in some cases resulted in adrenal insufficiency; diabetes mellitus, including cases in patients who developed diabetic ketoacidosis; diabetic ketoacidosis; adrenal insufficiency; and acute kidney injury (AKI). The most common adverse reactions (≥20%) were rash (24%), fatigue (21%), pruritus (21%), and pyrexia (20%), and pyrexia (20%), and pyrexia (20%).
- Immune-mediated adverse reactions, which may be severe or life-threatening, have occurred in patients who received KEYTRUDA in combination with other immune-mediated adverse reactions, consider a high-dose corticosteroid, and if clinically indicated, initiate immunosuppressant therapy. Immune-mediated adverse reactions, which may be severe or life-threatening, have occurred in patients who received KEYTRUDA in combination with chemotherapy. Consider the appropriate medical therapy for these adverse reactions, as clinically indicated.

Infusion-Related Reactions

- KEYTRUDA can cause severe or life-threatening infusion-related reactions, including hypersensitivity and anaphylaxis, which have been reported in 0.2% (2/799) patients receiving KEYTRUDA. Monitor for signs and symptoms of infusion-related reactions. Interrupt or slow the rate of infusion for Grade 1 or Grade 2 reactions. For severe or life-threatening infusion-related reactions, stop KEYTRUDA infusion permanently.

Complications of Allogeneic Hematopoietic Stem Cell Transplantation (HSCT)

- Fatal and other serious complications can occur in patients who receive allogeneic HSCT before and after anti-PD-1/PD-L1 treatments. Transplant-related complications include hyperacute graft-versus-host-disease (GVHD), acute GVHD, chronic GVHD, hepatic veno-occlusive disease after myeloablative conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between KEYTRUDA and HSCT. Follow patients who receive KEYTRUDA before or after allogeneic HSCT for these complications. Consider the benefit vs. risks of using anti-PD-1/PD-L1 treatments prior to or after an allogeneic HSCT.

Increased Mortality in Patients With Multiple Myeloma

- In 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 an anti-PD-1/PD-L1 treatment in this combination is not recommended outside of controlled trials.

Embryofetal Toxicity

- Based on its mechanism of action, KEYTRUDA can cause fetal harm when administered to a pregnant woman. Advise women of this potential risk. In females of reproductive potential, verify pregnancy status prior to initiating KEYTRUDA and for 4 months after the last dose to ensure effective contraception during treatment and for 4 months after the last dose.

Adverse Reactions

- In KEYNOTE-006, KEYTRUDA was discontinued due to adverse reactions in 9% of 555 patients with advanced melanoma; adverse reactions leading to permanent discontinuation in more than one patient were colitis (1.4%), autoimmune hepatitis (0.7%), allergic reaction (0.4%), polymyositis (0.4%), and cardiac arrest (0.2%). The most common adverse reactions (≥20%) were fatigue (37%), diarrhea (28%), rash (25%), and nausea (21%).
- In KEYNOTE-054, KEYTRUDA was permanently discontinued due to adverse reactions in 14% of 509 patients; the most common (≥1%) were pneumonitis (1.4%), colitis (1.4%), and diarrhea (1%). The most common adverse reactions were diarrhea (38%), rash (29%), and pruritus (19%), and the most common adverse reactions (≥2%) in KEYTRUDA were diarrhea (28%).
- In KEYNOTE-189, when KEYTRUDA was administered with pemetrexed and platinum chemotherapy in metastatic nonsquamous NSCLC, KEYTRUDA was discontinued due to adverse reactions in 16% of 405 patients. The most frequent adverse reactions leading to permanent discontinuation of KEYTRUDA were pneumonitis (2.5%) and acute kidney injury (2%). The most common adverse reactions (≥20%) were nausea (62%), fatigue (56%), constipation (34%), diarrhea (31%), decreased appetite (28%), rash (25%), vomiting (24%), cough (21%), dyspnea (21%), and pyrexia (20%).
- In KEYNOTE-407, when KEYTRUDA was administered with carboplatin and either paclitaxel or paclitaxel protein-bound chemotherapy in metastatic squamous NSCLC, KEYTRUDA was discontinued due to adverse reactions in 10% of 101 patients. The most frequent serious adverse reactions reported in at least 2% of patients were febrile neutropenia (3%) and pneumonitis (2%). The most common adverse reactions (≥20%) were alopecia (54%), fatigue (51%), nausea (47%), rash (26%), and diarrhea (21%). With the exception that increased incidence of alopecia (47% vs 37%) and peripheral neuropathy (17% vs 13%) were observed in the KEYTRUDA arm, the adverse reactions in chemotherapy arm compared to the placebo and chemotherapy arm in KEYNOTE-407.
- In KEYNOTE-042, KEYTRUDA was discontinued due to adverse reactions in 18% of 1034 patients with advanced NSCLC; the most common were pneumonitis (2%), death due to unknown cause (1.6%), and pneumonitis (1.4%). The most frequent serious adverse reactions reported in at least 2% of patients were pneumonitis (4.8%), pneumonia (2.9%), pleural effusion (2.4%), and pleural effusion (2.2%). The most common adverse reactions (≥20%) were fatigue (28%), cough (25%), musculoskeletal pain (25%), dyspnea (22%), and rash (20%).
- In KEYNOTE-119, KEYTRUDA monotherapy was discontinued due to adverse reactions in 8% of 1682 patients with metastatic NSCLC; the most common was pneumonitis (1.2%) and pneumonia (1.1%). The most frequent adverse reactions reported in at least 2% of patients were pneumonia (5.8%) and pneumonitis (2.8%).
- In KEYNOTE-177, KEYTRUDA monotherapy was discontinued due to adverse events in 17% of 299 patients with mMSI-H cancer. Serious adverse events occurred in 57% of patients and included pyrexia (4%), cardiac failure (2%), myocardial infarction (2%), pancreatitis (2%), pneumonitis (2%), and pneumonia (2%). The most common adverse events (≥20%) were fatigue (32%), musculoskeletal pain (26%), diarrhea (25%), and rash (20%).
- In KEYNOTE-045, KEYTRUDA was discontinued due to adverse events in 15% of 270 patients with locally advanced or metastatic urothelial carcinoma. Serious adverse events occurred in 49% of patients. The most common adverse events (≥20%) were fatigue (36%), musculoskeletal pain (26%), decreased appetite (22%), constipation (21%), rash (21%), and diarrhea (20%).
- In KEYNOTE-048, KEYTRUDA was discontinued due to adverse events in 8% of 298 patients with locally advanced or metastatic urothelial carcinoma. The most common adverse events (≥20%) were fatigue (28%), musculoskeletal pain (26%), decreased appetite (22%), constipation (21%), rash (21%), and diarrhea (20%).
- In KEYNOTE-087, KEYTRUDA was discontinued due to adverse events in 13% of 370 patients with relapsed or refractory cHL. Serious adverse events occurred in 30% of patients. The most common adverse events (≥20%) were upper respiratory tract infection (25%), musculoskeletal pain (25%), diarrhea (24%), fever (22%), fatigue, rash, and cough (20% each).
- In KEYNOTE-087, KEYTRUDA was discontinued due to adverse events in 5% of 210 patients with cHL. Serious adverse events occurred in 16% of patients. The most common adverse events (≥20%) were upper respiratory tract infection (29%), musculoskeletal pain (25%), diarrhea (23%), fever (22%), fatigue (21%), and cough (20%).
- In KEYNOTE-170, KEYTRUDA monotherapy was discontinued due to adverse events in 17% of 300 patients with PMBCL. Serious adverse events occurred in 27% of patients and included pyrexhia (4%), cardiac tamponade (2%), myocardial infarction (2%), pericardial effusion (2%), and pericarditis (2%). The 10 patients (3%) who had a fatal adverse event included 2 patients with cardiac failure, 2 with cardiac tamponade, 2 with cardiac arrest, 1 with myocarditis, and 1 with pyrexia (28% each), cough (26%), fatigue (25%), and dyspnea (20%).
- In KEYNOTE-002, KEYTRUDA was discontinued due to adverse reactions in 11% of 320 patients with locally advanced or metastatic unresectable melanoma. Serious adverse reactions occurred in 41% of patients. Those 22% were serious renal events, acute kidney injury, renal failure, and renal impairment. The most common adverse reactions (≥20%) were fatigue (38%), musculoskeletal pain (26%), decreased appetite (22%), constipation (21%), rash (21%), and diarrhea (20%).
- 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 reactions (≥20%) were fatigue (36%), musculoskeletal pain (26%), decreased appetite (22%), constipation (21%), rash (21%), and diarrhea (20%).
- In KEYNOTE-087, KEYTRUDA was discontinued due to adverse events in 12% of 183 patients with relapsed or refractory cHL. Serious adverse events occurred in 30% of patients. The most common adverse events (≥20%) were upper respiratory tract infection (29%), musculoskeletal pain (25%), diarrhea (23%), fever (22%), fatigue (21%), and cough (20%).
- In KEYNOTE-170, KEYTRUDA monotherapy was discontinued due to adverse events in 17% of 200 patients with PMBCL. Serious adverse events occurred in 27% of patients and included pyrexhia (4%), cardiac tamponade (2%), myocardial infarction (2%), pericardial effusion (2%), and pericarditis (2%). The 10 patients (3%) who had a fatal adverse event included 2 patients with cardiac failure, 2 with cardiac tamponade, 2 with cardiac arrest, 1 with myocarditis, and 1 with pyrexia (28% each), cough (26%), fatigue (25%), and dyspnea (20%).
- In KEYNOTE-002, KEYTRUDA was discontinued due to adverse reactions in 11% of 320 patients with locally advanced or metastatic unresectable melanoma. Serious adverse reactions occurred in 41% of patients. Those 22% were serious renal events, acute kidney injury, renal failure, and renal impairment. The most common adverse reactions (≥20%) in patients who received KEYTRUDA were fatigue (38%), musculoskeletal pain (26%), decreased appetite (22%), constipation (21%), rash (21%), and diarrhea (20%).
- 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 reactions (≥20%) in patients who received KEYTRUDA were fatigue (36%), musculoskeletal pain (26%), decreased appetite (22%), constipation (21%), rash (21%), and diarrhea (20%).
- In KEYNOTE-087, KEYTRUDA was discontinued due to adverse events in 12% of 183 patients with relapsed or refractory cHL. Serious adverse events occurred in 30% of patients. The most common adverse events (≥20%) were upper respiratory tract infection (29%), musculoskeletal pain (25%), diarrhea (23%), fever (22%), fatigue (21%), and cough (20%).
- In KEYNOTE-170, KEYTRUDA monotherapy was discontinued due to adverse events in 17% of 200 patients with PMBCL. Serious adverse events occurred in 27% of patients and included pyrexhia (4%), cardiac tamponade (2%), myocardial infarction (2%), pericardial effusion (2%), and pericarditis (2%). The 10 patients (3%) who had a fatal adverse event included 2 patients with cardiac failure, 2 with cardiac tamponade, 2 with cardiac arrest, 1 with myocarditis, and 1 with pyrexia (28% each), cough (26%), fatigue (25%), and dyspnea (20%).
- In KEYNOTE-002, KEYTRUDA was discontinued due to adverse events in 17% of 320 patients with locally advanced or metastatic unresectable melanoma. Serious adverse events occurred in 49% of patients. The most common adverse events (≥20%) were fatigue (36%), musculoskeletal pain (26%), decreased appetite (22%), constipation (21%), rash (21%), and diarrhea (20%).
- In KEYNOTE-045, KEYTRUDA was discontinued due to adverse events in 15% of 266 patients with locally advanced or metastatic urothelial carcinoma. Serious adverse events occurred in 49% of patients. The most common adverse events (≥20%) were fatigue (36%), musculoskeletal pain (26%), decreased appetite (22%), constipation (21%), rash (21%), and diarrhea (20%).
- In KEYNOTE-087, KEYTRUDA was discontinued due to adverse events in 12% of 183 patients with relapsed or refractory cHL. Serious adverse events occurred in 30% of patients. The most common adverse events (≥20%) were upper respiratory tract infection (29%), musculoskeletal pain (25%), diarrhea (23%), fever (22%), fatigue (21%), and cough (20%).
- In KEYNOTE-170, KEYTRUDA monotherapy was discontinued due to adverse events in 17% of 200 patients with PMBCL. Serious adverse events occurred in 27% of patients and included pyrexhia (4%), cardiac tamponade (2%), myocardial infarction (2%), pericardial effusion (2%), and pericarditis (2%). The 10 patients (3%) who had a fatal adverse event included 2 patients with cardiac failure, 2 with cardiac tamponade, 2 with cardiac arrest, 1 with myocarditis, and 1 with pyrexia (28% each), cough (26%), fatigue (25%), and dyspnea (20%).
- Adverse reactions occurring in patients with MSI-H or dMMR CRC were similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy.
- Adverse reactions occurring in patients with gastric cancer were similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy.
- In KEYNOTE-590, when KEYTRUDA was administered with cisplatin and fluorouracil to patients with metastatic or locally advanced esophageal or GEJ carcinoma with squamous 1 to 5 centimeters above the GEJ carcinoma who were not candidates for surgical resection or definitive chemoradiotherapy, KEYTRUDA was discontinued due to adverse reactions in 16% of 370 patients. The most common adverse reactions resulting in permanent discontinuation of KEYTRUDA were pneumonitis (1.6%), acute kidney injury (1.1%), and pneumonia (1.1%). The most common adverse reactions (≥20%) with KEYTRUDA in combination with chemotherapy were nausea (67%), fatigue (62%), decreased appetite (44%), vomiting (41%), diarrhea (38%), vomiting (34%), stomatitis (27%), and pyrexia (24%).
- Adverse reactions occurring in patients with esophageal cancer who received KEYTRUDA as a monotherapy were similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy.
- In KEYNOTE-158, KEYTRUDA was discontinued due to adverse reactions in 9% of 98 patients with recurrent or metastatic cervical cancer. Serious adverse events occurred in 53% of patients. The most common adverse events (≥20%) were fatigue (31%), diarrhea (29%), nausea (26%), musculoskeletal pain (25%), and pneumonitis (1%). Pancreatitis due to an adverse reaction occurred in 2 patients (2%) receiving KEYTRUDA monotherapy, with fever (1%), and the combination (8%), the most common were hepatotoxicity (13%), diarrhea/colitis (13%), acute kidney injury (11 8%), and cerebrovascular accident (2 2%). The most common adverse reactions (≥20%) were fatigue (47%), musculoskeletal pain (37%), diarrhea (32%), nausea (29%), decreased appetite (28%), pulmonary embolism (20%), pain (20%), cough (21%), and dyspnea (20%).
- Adverse reactions occurring in patients with TMB-H cancer were similar to those occurring in patients with other solid tumors who received KEYTRUDA as a single agent.
- Adverse reactions occurring in patients with dMCC were similar to those occurring in patients with melanoma or NSCLC who received KEYTRUDA as a monotherapy.
- In KEYNOTE-355, when KEYTRUDA and chemotherapy (paclitaxel, protein-bound paclitaxel, or gemcitabine and carboplatin) were administered to patients with locally recurrent unresectable or metastatic TNBC,who had not received prior chemotherapy in the metastatic setting (n=595), Most adverse reactions occurred in 37% of patients. Including cardio-respiratory arrest (0.7%) and sepsis (focus 2.5%). Serious adverse reactions occurred in 30% of patients receiving KEYTRUDA in combination with chemotherapy. the serious reactions occurred in 22% were pneumonia, febrile neutropenia, and pyrexia. The most common adverse reactions (≥20%) in patients who received KEYTRUDA were fatigue (51%), nausea (47%), alopecia (54%), diarrhea and constipation (28% each), vomiting and rash (26% each), cough (21%), decreased appetite (21%), and headache (20%).

Caution

- Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment and for 4 months after the final dose.

Pediatric Use

- In KEYNOTE-051, 161 pediatric patients (62 pediatric patients aged 6 months to younger than 12 years and 99 pediatric patients aged 12 years to 17 years) were administered KEYTRUDA at 2 mg/kg every 3 weeks or 200 mg every 3 weeks. The safety profile in these patients was similar to that in adults.
- Adverse reactions that occurred at a ≥10% higher rate in pediatric patients when compared to adults were pyrexia (25%), vomiting (20%), hedonema (20%), upper respiratory tract infection (20%), headache (20%), and Grade 3 anemia (11%).

cHL = classical Hodgkin lymphoma; CRC = colorectal cancer; dMMR = mismatch repair deficient; dMCC = Merkel cell carcinoma; EGFR = epidermal growth factor receptor; mNSCLC = metastatic NSCLC; mMSI-H = metastatic high microsatellite instability; NSCLC = non-small cell lung cancer; PMBCL = primary mediastinal large B-cell lymphoma; TMB-H = high tumor mutational burden; TNBC = triple-negative breast cancer

Before prescribing KEYTRUDA, please read the accompanying Prescribing Information. The Medication Guide also is available.

US-NON-5899-0421

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Overview

HELPING TO REDEFIN SURVIVAL EXPECTAT for your patients in the following indications:

Key Chat

SELECTED SAFETY INFORMATION for KEYTRUDA® (pembrolizumab) +

Severe and Fatal Immune-Mediated Adverse Reactions

- KEYTRUDA is a monoclonal antibody that

Advanced NSCLC

KEYTRUDA, in combination with pemetrexed and platinum chemotherapy, is indicated for the first-line treatment of patients with metastatic nonsquamous non–small cell lung cancer (NSCLC), with no EGFR or ALK genomic tumor aberrations.

KEYTRUDA, in combination with carboplatin and either paclitaxel or paclitaxel protein-bound, is indicated for the first-line treatment of patients with metastatic squamous NSCLC.

KEYTRUDA, as a single agent, is indicated for the first-line treatment of patients with NSCLC expressing PD-L1 [tumor proportion score (TPS) ≥1%] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and is stage III where patients are not candidates for surgical resection or definitive chemoradiation, or metastatic.

KEYTRUDA, as a single agent, is indicated for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥1%) as determined by an FDA-approved test, with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic

CLOSE ✕

SELECTED SAFETY INFORMATION for KEYTRUDA® (pembrolizumab)

+

Severe and Fatal Immune-Mediated Adverse Reactions

- KEYTRUDA is a monoclonal antibody that

ALK genomic tumor aberrations.

KEYTRUDA, in combination with carboplatin and either paclitaxel or paclitaxel protein-bound, is indicated for the first-line treatment of patients with metastatic squamous NSCLC.

KEYTRUDA, as a single agent, is indicated for the first-line treatment of patients with NSCLC expressing PD-L1 [tumor proportion score (TPS) ≥1%] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and is stage III where patients are not candidates for surgical resection or definitive chemoradiation, or metastatic.

KEYTRUDA, as a single agent, is indicated for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥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.

EGFR = epidermal growth factor receptor;

ALK = anaplastic lymphoma kinase;

PD-L1 = programmed death ligand 1.

CLOSE ✕

SELECTED SAFETY INFORMATION for KEYTRUDA® (pembrolizumab)

+

Severe and Fatal Immune-Mediated Adverse Reactions

- KEYTRUDA is a monoclonal antibody that

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Overview

HELPING TO REDEFIN SURVIVAL EXPECTAT

Key Chat for your patients in the following indications:

SELECTED SAFETY INFORMATION for KEYTRUDA® (pembrolizumab)

Severe and Fatal Immune-Mediated Adverse Reactions

- KEYTRUDA is a monoclonal antibody that

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KEYTRUDA® (pembrolizumab) Injection 100mg

MENU

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KEYTRUDA ® (pembrolizumab) Assistant

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How can I help you today?

Please type your text here

Send

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SELECTED SAFETY INFORMATION for KEYTRUDA® (pembrolizumab)

Severe and Fatal Immune-Mediated Adverse Reactions

- KEYTRUDA is a monoclonal antibody that

RECENT SAFETY INFORMATION

Deaths due to adverse reactions (5.1)

Severe and Life-threatening Hemorrhagic Events including Serious Gastrointestinal Bleeding (5.2)

Severe hypertension (5.3)

Hepatotoxicity (5.4)

Hypertension, Renal Adverse Events, and Electrolyte Abnormalities in Patients with Renal Impairment (5.5)

Hypertension in Patients with Hepatic Impairment (5.6)

Hypertension in Patients Taking Concomitant Medications that Increase Blood Pressure (5.7)

Adverse reactions (6.1)

Hypersensitivity (6.2)

Drug interactions (7.1)

Lactation (8.2)

Effects on fertility (8.3)

INDICATIONS AND USAGE

RETEVMO is a kinase inhibitor indicated for the treatment of adult patients with:

- RET fusion-positive non-small cell lung cancer (NSCLC) as detected by a test cleared or approved by the FDA (5.1), (12.1), (14.1)
- RET fusion-positive thyroid cancer (TC) as detected by a test cleared or approved by the FDA (5.1), (12.1), (14.1)
- RET mutation-positive medullary thyroid cancer (MTC) as detected by a test cleared or approved by the FDA (5.1), (12.1), (14.1)
- RET mutation-positive medullary thyroid cancer (MTC) as detected by a test cleared or approved by the FDA, and who require systemic therapy (5.1), (12.1), (14.1)

DOSAGE AND ADMINISTRATION

- Recommended dose is 160 mg orally twice daily (2.1)
- Patients with RET fusion-positive NSCLC or RET fusion-positive TC who require a dose reduction due to adverse reactions, the recommended dose is 120 mg orally twice daily (2.2)
- Patients with RET mutation-positive MTC who require a dose reduction due to adverse reactions, the recommended dose is 80 mg orally twice daily (2.2)
- Patients unable to tolerate a further dose of 80 mg orally twice daily due to adverse reactions, discontinue RETEVMO (2.2)
- Patients with moderate hepatic impairment, the recommended dose is 40 mg orally twice daily (2.3)
- Patients with moderate renal impairment, the recommended dose is 80 mg orally twice daily (2.3)
- Patients with moderate hepatic impairment and moderate renal impairment, the recommended dose is 40 mg orally twice daily (2.3)
- Patients with severe renal impairment or end stage renal disease (ESRD), the recommended dose is 40 mg orally twice daily (2.3)
- Patients taking strong CYP3A inhibitors, the recommended dose is 40 mg orally twice daily (2.4)
- Patients taking strong CYP3A inducers, the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking proton pump inhibitors (PPI), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking short-acting antacids or histamine-2 receptor antagonists (H2RA), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that increase blood pressure, the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that increase QT interval, the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of P-glycoprotein (P-gp), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of breast cancer resistance protein (BCRP), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of multidrug and toxin extrusion protein 1 (MATE1), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of organic cation transporter 2 (OCT2), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of multidrug and toxin extrusion protein 2-K (MATE2-K), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of organic anion transporting polypeptide 1B1 (OATP1B1), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of organic anion transporting polypeptide 1B3 (OATP1B3), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of organic anion transporter 3 (OAT3), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of organic anion transporter 1 (OAT1), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of organic anion transporter 2 (OAT2), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of multidrug resistance protein 1 (MRP1), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of multidrug resistance protein 4 (MRP4), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium/hydrogen exchanger isoform 1 (NHE1), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium/hydrogen exchanger isoform 2 (NHE2), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium/hydrogen exchanger isoform 3 (NHE3), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium/hydrogen exchanger isoform 5 (NHE5), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium/hydrogen exchanger isoform 6 (NHE6), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium/hydrogen exchanger isoform 7 (NHE7), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium/hydrogen exchanger isoform 8 (NHE8), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium/hydrogen exchanger isoform 9 (NHE9), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium/hydrogen exchanger isoform 1 regulatory factor (NHE1RF), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium/hydrogen exchanger isoform 8 regulatory factor (NHE8RF), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium/hydrogen exchanger isoform 9 regulatory factor (NHE9RF), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium/hydrogen exchanger isoform 10 (NHE10), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium/hydrogen exchanger isoform 11 (NHE11), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium/hydrogen exchanger isoform 12 (NHE12), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium-dependent phosphate transporter 1 (NPT1), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium-dependent phosphate transporter 4 (NPT4), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium-dependent phosphate transporter 5 (NPT5), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium-dependent phosphate transporter 1 regulatory factor (NPT1RF), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium-dependent phosphate transporter 4 regulatory factor (NPT4RF), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium-dependent phosphate transporter 5 regulatory factor (NPT5RF), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium-dependent vitamin C transporter 1 (SVCT1), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium-dependent vitamin C transporter 2 (SVCT2), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium-dependent vitamin C transporter 1 regulatory factor (SVCT1RF), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium-dependent vitamin C transporter 2 regulatory factor (SVCT2RF), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium-dependent glucose transporter 1 (SGLT1), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium-dependent glucose transporter 2 (SGLT2), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium-dependent glucose transporter 1 regulatory factor (SGLT1RF), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium-dependent glucose transporter 2 regulatory factor (SGLT2RF), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium-dependent multivitamin transporter (SMVT), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium-dependent multivitamin transporter regulatory factor (SMVTRF), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium-dependent lysophosphatidylcholine transporter 1 (NLPCT1), the recommended dose is 160 mg orally twice daily (2.4)
- Patients taking oral medications that are substrates of sodium-dependent lysophosphatidylcholine transporter 1 regulatory factor (NLPCT1RF), the recommended dose is 160 mg orally twice daily (2.4)
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- Patients taking oral medications that are substrates of sodium-dependent lysophosphat

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KEYTRUDA® (pembrolizumab) Injection 100 mg

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HELPING TO REDEFINE SURVIVAL EXPECTATIONS for your patients in the following indications:

Nonsquamous mNSCLC

KEYTRUDA, in combination with pemetrexed and platinum chemotherapy, is indicated for the first-line treatment of patients with metastatic nons[illegible]us non–small cell lung cancer ([illegible]), with no EGFR or ALK genom[illegible]r aberrations.

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+

Severe and Fatal Immune-Mediated Adverse Reactions

- KEYTRUDA is a monoclonal antibody that

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1L Monotherapy

2L Monotherapy

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Yoga is a practice of self-discovery and self-mastery.

Yoga is a practice of self-discovery and self-mastery.

YOGA LIFE COMMUNITY TEMPLE IN MALAYSIA Yoga Life Community Temple in Malaysia is a place where people can come together to practice yoga, meditation, and other spiritual practices. The temple is a place of peace and tranquility, and it is a place where people can feel at home and connect with their spirituality.

Prostate Cancer, Version 1.2026 — February 12, 2026

Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

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ALL OF 1A COMMENTARY

APPROPRIATE PATIENTS ☑

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Howard (Jack) West, MD, breaks down the data: 1L combination therapy in nonsquamous mNSCLC

OVERALL SURVIVAL IN PD-L1 SUBGROUPS, INCLUDING LOW AND NONEXPRESSERS (exploratory analyses)[1,2]

NONEXPRESSERS

OS in Patients Without PD-L1 Expression (<1%)[1,2,c,d]

LIMITATIONS: KEYNOTE-189 wa[illegible]owered to detect differences in the treatme[illegible]t in this subgroup; therefore, results from this exploratory analysis should be interpreted with

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SELECTED SAFETY INFORMATION for KEYTRUDA® (pembrolizumab)

Severe and Fatal Immune-Mediated Adverse Reactions

- KEYTRUDA is a monoclonal antibody that

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Evaluation of a web portal with computer tailored content for adolescents living with a chronic illness: a randomized controlled trial

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Ultrafast and ultrasensitive ferroelectric transistors and switches for visual perception and human-machine interaction

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Abstract

Ultrafast and ultrasensitive electronic devices are critical for advanced visual perception and human-machine interaction. Ferroelectric transistors (FETs) and switches (FSWs) have emerged as promising candidates due to their rapid polarization switching and high sensitivity. However, challenges remain in achieving ultrafast operation, ultrasensitive detection, and multifunctional integration. This review systematically examines the fundamental mechanisms, device architectures, and performance metrics of FETs and FSWs, with a focus on their ultrafast response, ultrasensitive detection, and multifunctional integration for visual perception and human-machine interaction. Key advancements in ultrafast FETs and FSWs, including optimized ferroelectric materials, high-mobility channels, and low-capacitance interfaces, are discussed, alongside ultrasensitive detection strategies leveraging ferroelectric polarization modulation and interface engineering. Multifunctional integration, including ferroelectric memory, neuromorphic computing, and sensor fusion, is also explored, highlighting its potential for enhancing visual perception and human-machine interaction. This review concludes with a discussion of current challenges and future prospects, including material optimization, scalable manufacturing, and system-level integration, to guide the development of next-generation ultrafast and ultrasensitive ferroelectric transistors and switches for advanced visual perception and human-machine interaction.

Keywords: ferroelectric transistors, ferroelectric switches, ultrafast response, ultrasensitive detection, visual perception, human-machine interaction

Introduction

Ultrafast and ultrasensitive electronic devices are critical for advanced visual perception and human-machine interaction, enabling rapid data processing and high-precision detection in applications such as autonomous vehicles, medical imaging, and smart interfaces. Ferroelectric transistors (FETs) and switches (FSWs) have emerged as promising candidates due to their rapid polarization switching and high sensitivity. However, challenges remain in achieving ultrafast operation, ultrasensitive detection, and multifunctional integration. This review systematically examines the fundamental mechanisms, device architectures, and performance metrics of FETs and FSWs, with a focus on their ultrafast response, ultrasensitive detection, and multifunctional integration for visual perception and human-machine interaction. Key advancements in ultrafast FETs and FSWs, including optimized ferroelectric materials, high-mobility channels, and low-capacitance interfaces, are discussed, alongside ultrasensitive detection strategies leveraging ferroelectric polarization modulation and interface engineering. Multifunctional integration, including ferroelectric memory, neuromorphic computing, and sensor fusion, is also explored, highlighting its potential for enhancing visual perception and human-machine interaction. This review concludes with a discussion of current challenges and future prospects, including material optimization, scalable manufacturing, and system-level integration, to guide the development of next-generation ultrafast and ultrasensitive ferroelectric transistors and switches for advanced visual perception and human-machine interaction.

Ultrafast FETs and FSWs

Ultrafast FETs

Ultrafast FETs are critical for high-speed data processing and real-time visual perception, leveraging ferroelectric polarization switching to achieve rapid response times. Key advancements include optimized ferroelectric materials, high-mobility channels, and low-capacitance interfaces, which collectively enhance the performance of these devices. For instance, ferroelectric materials with low coercive fields and high polarization switching speeds are used to achieve sub-microsecond response times, while high-mobility channels such as graphene and transition metal dichalcogenides (TMDs) further boost the overall speed and efficiency. Low-capacitance interfaces minimize parasitic capacitance, ensuring minimal signal delay and maximum bandwidth. These advancements are pivotal for applications in autonomous vehicles, medical imaging, and smart interfaces, where rapid data processing and high-precision detection are essential.

Ultrafast FSWs

Ultrafast FSWs are critical for high-speed data processing and real-time visual perception, leveraging ferroelectric polarization switching to achieve rapid response times. Key advancements include optimized ferroelectric materials, high-mobility channels, and low-capacitance interfaces, which collectively enhance the performance of these devices. For instance, ferroelectric materials with low coercive fields and high polarization switching speeds are used to achieve sub-microsecond response times, while high-mobility channels such as graphene and transition metal dichalcogenides (TMDs) further boost the overall speed and efficiency. Low-capacitance interfaces minimize parasitic capacitance, ensuring minimal signal delay and maximum bandwidth. These advancements are pivotal for applications in autonomous vehicles, medical imaging, and smart interfaces, where rapid data processing and high-precision detection are essential.

Ultrasensitive FETs and FSWs

Ultrasensitive FETs

Ultrasensitive FETs are critical for high-precision detection and low-power applications, leveraging ferroelectric polarization modulation and interface engineering to achieve high sensitivity. Key advancements include optimized ferroelectric materials, high-mobility channels, and low-capacitance interfaces, which collectively enhance the performance of these devices. For instance, ferroelectric materials with low coercive fields and high polarization switching speeds are used to achieve sub-microsecond response times, while high-mobility channels such as graphene and transition metal dichalcogenides (TMDs) further boost the overall speed and efficiency. Low-capacitance interfaces minimize parasitic capacitance, ensuring minimal signal delay and maximum bandwidth. These advancements are pivotal for applications in autonomous vehicles, medical imaging, and smart interfaces, where rapid data processing and high-precision detection are essential.

Ultrasensitive FSWs

Ultrasensitive FSWs are critical for high-precision detection and low-power applications, leveraging ferroelectric polarization modulation and interface engineering to achieve high sensitivity. Key advancements include optimized ferroelectric materials, high-mobility channels, and low-capacitance interfaces, which collectively enhance the performance of these devices. For instance, ferroelectric materials with low coercive fields and high polarization switching speeds are used to achieve sub-microsecond response times, while high-mobility channels such as graphene and transition metal dichalcogenides (TMDs) further boost the overall speed and efficiency. Low-capacitance interfaces minimize parasitic capacitance, ensuring minimal signal delay and maximum bandwidth. These advancements are pivotal for applications in autonomous vehicles, medical imaging, and smart interfaces, where rapid data processing and high-precision detection are essential.

Multifunctional integration

Multifunctional integration, including ferroelectric memory, neuromorphic computing, and sensor fusion, is also explored, highlighting its potential for enhancing visual perception and human-machine interaction. This review concludes with a discussion of current challenges and future prospects, including material optimization, scalable manufacturing, and system-level integration, to guide the development of next-generation ultrafast and ultrasensitive ferroelectric transistors and switches for advanced visual perception and human-machine interaction.

Conclusion

Ultrafast and ultrasensitive electronic devices are critical for advanced visual perception and human-machine interaction, enabling rapid data processing and high-precision detection in applications such as autonomous vehicles, medical imaging, and smart interfaces. Ferroelectric transistors (FETs) and switches (FSWs) have emerged as promising candidates due to their rapid polarization switching and high sensitivity. However, challenges remain in achieving ultrafast operation, ultrasensitive detection, and multifunctional integration. This review systematically examines the fundamental mechanisms, device architectures, and performance metrics of FETs and FSWs, with a focus on their ultrafast response, ultrasensitive detection, and multifunctional integration for visual perception and human-machine interaction. Key advancements in ultrafast FETs and FSWs, including optimized ferroelectric materials, high-mobility channels, and low-capacitance interfaces, are discussed, alongside ultrasensitive detection strategies leveraging ferroelectric polarization modulation and interface engineering. Multifunctional integration, including ferroelectric memory, neuromorphic computing, and sensor fusion, is also explored, highlighting its potential for enhancing visual perception and human-machine interaction. This review concludes with a discussion of current challenges and future prospects, including material optimization, scalable manufacturing, and system-level integration, to guide the development of next-generation ultrafast and ultrasensitive ferroelectric transistors and switches for advanced visual perception and human-machine interaction.

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SELECTIVE SOODING PRICE TIMES

Selective sooding is a method of pricing in which the price of a product is determined by the number of units sold. The more units sold, the higher the price. This method is used by companies that want to maintain a high level of quality and exclusivity, as it allows them to control the supply of their product and ensure that it remains in high demand.

The selective sooding price times method is a variation of selective sooding that takes into account the time of day when the product is sold. The price is set at a higher level during peak hours, when the demand is high, and at a lower level during off-peak hours, when the demand is low. This method is used by companies that want to maximize their profits by taking advantage of the fluctuations in demand.

The selective sooding price times method is a complex pricing strategy that requires a deep understanding of the market and the customer. The company must be able to predict the demand for its product at different times of the day and set the price accordingly. The company must also be able to monitor the market and adjust the price in real-time to ensure that it remains competitive.

The selective sooding price times method is a powerful pricing strategy that can be used to maximize profits and maintain a high level of quality and exclusivity. The company must be able to predict the demand for its product at different times of the day and set the price accordingly. The company must also be able to monitor the market and adjust the price in real-time to ensure that it remains competitive.

SELECTIVE SOODING PRICE TIMES FOR THE YEAR 2023

Month	Price	Units Sold	Revenue
January	$10	100	$1,000
February	$10	100	$1,000
March	$10	100	$1,000
April	$10	100	$1,000
May	$10	100	$1,000
June	$10	100	$1,000
July	$10	100	$1,000
August	$10	100	$1,000
September	$10	100	$1,000
October	$10	100	$1,000
November	$10	100	$1,000
December	$10	100	$1,000
Total		1,200	$12,000

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