For the treatment of patients with advanced endometrial carcinoma that is pMMR as determined by an FDA-approved test or not MSI-H, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation

KEYTRUDA + LENVIMA:

Phase 3 results from KEYNOTE-775/Study 309

The ONLY CATEGORY 1, PREFERRED second-line systemic treatment option for patients with advanced endometrial carcinoma whose tumors are non-MSI-H/non-dMMR[1]

PREFERRED

NCCN Guidelines® recommend pembrolizumab (**KEYTRUDA**) + lenvatinib (**LENVIMA**) as a **PREFERRED** second-line systemic treatment option (**CATEGORY 1**) for advanced endometrial carcinoma in patients whose tumors are non-MSI-H/non-dMMR[1,a,b]

[a]Preferred intervention = Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.
[b]Category 1 = Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
National Comprehensive Cancer Network® (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.
MSI-H = microsatellite instability-high; dMMR = mismatch repair deficient.

Indication for KEYTRUDA + LENVIMA

KEYTRUDA, in combination with LENVIMA, is indicated for the treatment of patients with advanced endometrial carcinoma that is mismatch repair proficient (pMMR) as determined by an FDA-approved test or not microsatellite instability-high (MSI-H), who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation.

Selected Safety Information for KEYTRUDA® (pembrolizumab)

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.

Selected Safety Information for LENVIMA® (lenvatinib)

Hypertension

- In differentiated thyroid cancer (DTC), hypertension occurred in 73% of patients on LENVIMA (44% grade 3-4). In advanced renal cell carcinoma (RCC), hypertension occurred in 42% of patients on LENVIMA + everolimus (13% grade 3). Systolic blood pressure ≥160 mmHg occurred in 29% of patients, and 21% had diastolic blood pressure ≥100 mmHg. In unresectable hepatocellular carcinoma (HCC), hypertension occurred in 45% of LENVIMA-treated patients (24% grade 3). Grade 4 hypertension was not reported in HCC.
- Serious complications of poorly controlled hypertension have been reported. Control blood pressure prior to initiation. Monitor blood pressure after 1 week, then every 2 weeks for the first 2 months, and then at least monthly thereafter during treatment. Withhold and resume at reduced dose when hypertension is controlled or permanently discontinue based on severity.

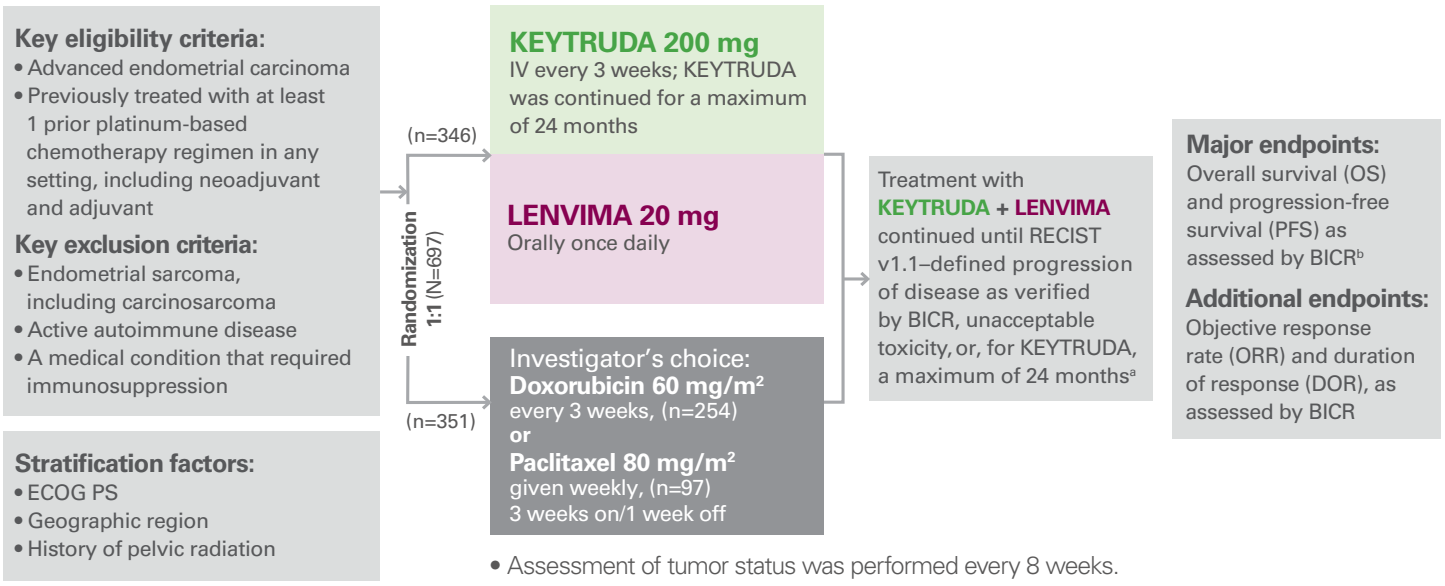
Before prescribing KEYTRUDA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information. The Medication Guide also is available. Before prescribing LENVIMA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information and Patient Information.

KEYTRUDA® (pembrolizumab) Injection 100 mg

LENVIMA® (lenvatinib) capsules | 10 mg and 4 mg

For the treatment of patients with advanced endometrial carcinoma that is pMMR as determined by an FDA-approved test or not MSI-H, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation

KEYNOTE-775/Study 309: A pivotal (N=827), multicenter, open-label, randomized, active-controlled, head-to-head phase 3 trial of **KEYTRUDA + LENVIMA** vs doxorubicin or paclitaxel in patients with advanced endometrial carcinoma. Among the 827 patients, 697 were pMMR or not MSI-H



[a]Treatment was permitted beyond RECIST v1.1–defined disease progression if the treating investigator considered the patient to be deriving clinical benefit and the treatment was tolerated.
[b]According to RECIST v1.1, modified to follow a maximum of 10 target lesions and a maximum of 5 target lesions per organ.
ECOG PS = Eastern Cooperative Oncology Group performance status; IV = intravenously; RECIST v1.1 = Response Evaluation Criteria In Solid Tumors v1.1; BICR = blinded independent central review.

Selected Safety Information for KEYTRUDA® (pembrolizumab) (*continued*)

Severe and Fatal Immune-Mediated Adverse Reactions (*continued*)

- 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.

Selected Safety Information for LENVIMA® (lenvatinib) (*continued*)

Cardiac Dysfunction

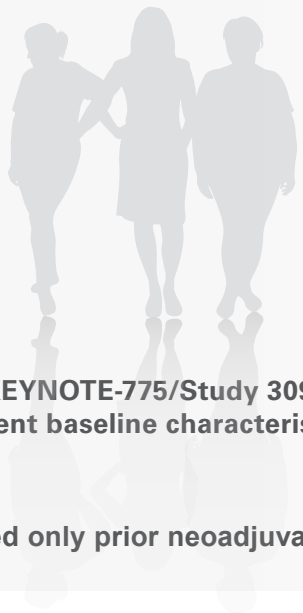
- Serious and fatal cardiac dysfunction can occur with LENVIMA. Across clinical trials in 799 patients with DTC, RCC, and HCC, grade 3 or higher cardiac dysfunction occurred in 3% of LENVIMA-treated patients. Monitor for clinical symptoms or signs of cardiac dysfunction. Withhold and resume at reduced dose upon recovery or permanently discontinue based on severity.

Before prescribing KEYTRUDA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information. The Medication Guide also is available. Before prescribing LENVIMA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information and Patient Information.

KEYTRUDA® (pembrolizumab) Injection 100 mg
LENVIMA® (lenvatinib) capsules | 10 mg and 4 mg

For the treatment of patients with advanced endometrial carcinoma that is pMMR as determined by an FDA-approved test or not MSI-H, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation

KEYNOTE-775/Study 309 enrolled patients with advanced endometrial carcinoma that was pMMR or not MSI-H across histological subtypes and treatment histories (N=697)



KEYNOTE-775/Study 309: Patient baseline characteristics

Histology

55%	Endometrioid
30%	Serous
7%	Clear cell
4%	Mixed
3%	Other

Race

62%	White
22%	Asian
3%	Black

ECOG PS

60%	0
40%	1

Prior Systemic Therapies

- **67%** had 1
- **30%** had 2
- **3%** had 3 or more

Age

- Median age of 65 years (range: 30–86)
- 52% age 65 or older

37% of patients received only prior neoadjuvant or adjuvant therapy.

Selected Safety Information for KEYTRUDA® (pembrolizumab) (*continued*)

Severe and Fatal Immune-Mediated Adverse Reactions (*continued*)

- 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.

Selected Safety Information for LENVIMA® (lenvatinib) (*continued*)

Arterial Thromboembolic Events

- Among patients receiving LENVIMA or LENVIMA + everolimus, arterial thromboembolic events of any severity occurred in 2% of patients in RCC and HCC and 5% in DTC. Grade 3-5 arterial thromboembolic events ranged from 2% to 3% across all clinical trials.
- Among patients receiving LENVIMA with KEYTRUDA, arterial thrombotic events of any severity occurred in 5% of patients in CLEAR, including myocardial infarction (3.4%) and cerebrovascular accident (2.3%).
- Permanently discontinue following an arterial thrombotic event. The safety of resuming after an arterial thromboembolic event has not been established and LENVIMA has not been studied in patients who have had an arterial thromboembolic event within the previous 6 months.

Before prescribing KEYTRUDA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information. The Medication Guide also is available. Before prescribing LENVIMA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information and Patient Information.

KEYTRUDA® (pembrolizumab) Injection 100 mg

LENVIMA® (lenvatinib) capsules | 10 mg and 4 mg

For the treatment of patients with advanced endometrial carcinoma that is pMMR as determined by an FDA-approved test or not MSI-H, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation

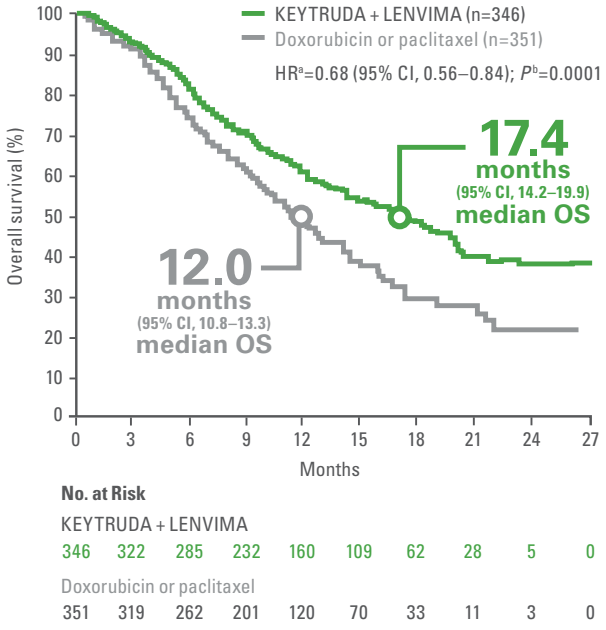
Superior OS (major endpoint): 32% reduction in the risk of death vs doxorubicin or paclitaxel alone

- **HR[a]=0.68 (95% CI, 0.56–0.84); *P*[b]=0.0001**
- Events observed: 48% (165/346) with KEYTRUDA + LENVIMA vs 58% (203/351) with doxorubicin or paclitaxel
- OS was a major endpoint with PFS in KEYNOTE-775/Study 309

Patients lived a median of **5.4 months longer** with **KEYTRUDA + LENVIMA** (n=346) vs doxorubicin or paclitaxel (n=351).

[a]Based on the stratified Cox regression model.
[b]Based on stratified log-rank test.
HR = hazard ratio; CI = confidence interval.

Kaplan-Meier estimates for OS in KEYNOTE-775/Study 309 (pMMR or not MSI-H) (N=697)



Selected Safety Information for KEYTRUDA® (pembrolizumab) (*continued*)

Severe and Fatal Immune-Mediated Adverse Reactions (*continued*)

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.

Selected Safety Information for LENVIMA® (lenvatinib) (*continued*)

Hepatotoxicity

- Across clinical studies enrolling 1,327 LENVIMA-treated patients with malignancies other than HCC, serious hepatic adverse reactions occurred in 1.4% of patients. Fatal events, including hepatic failure, acute hepatitis and hepatorenal syndrome, occurred in 0.5% of patients. In HCC, hepatic encephalopathy occurred in 8% of LENVIMA-treated patients (5% grade 3-5). Grade 3-5 hepatic failure occurred in 3% of LENVIMA-treated patients. 2% of patients discontinued LENVIMA due to hepatic encephalopathy and 1% discontinued due to hepatic failure.

Before prescribing KEYTRUDA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information. The Medication Guide also is available. Before prescribing LENVIMA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information and Patient Information.

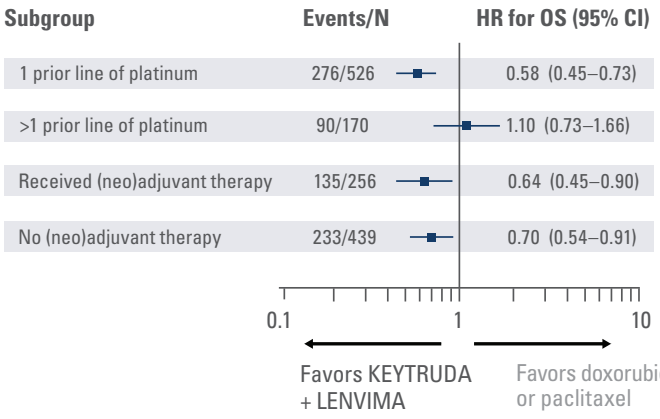
KEYTRUDA® (pembrolizumab) Injection 100 mg
LENVIMA® (lenvatinib) capsules | 10 mg and 4 mg

For the treatment of patients with advanced endometrial carcinoma that is pMMR as determined by an FDA-approved test or not MSI-H, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation

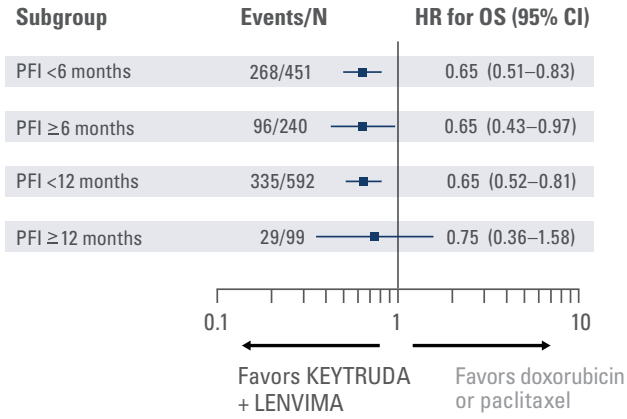
Post hoc analysis: OS[c] in patients with advanced endometrial carcinoma that was pMMR or not MSI-H[2,3]

LIMITATIONS: KEYNOTE-775/Study 309 was not powered to detect differences in the treatment effect in these subgroups and no statistical testing was planned for this exploratory analysis. No conclusions can be drawn.

OS by prior therapy



OS by PFI



[c]Randomization was stratified by MMR status. Data cutoff: October 26, 2020.
PFI = platinum-free interval from most recent platinum-containing regimen; MMR = mismatch repair.

Selected Safety Information for KEYTRUDA® (pembrolizumab) (*continued*)

Severe and Fatal Immune-Mediated Adverse Reactions (*continued*)

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.

Selected Safety Information for LENVIMA® (lenvatinib) (*continued*)

Hepatotoxicity (*continued*)

- Monitor liver function prior to initiation, then every 2 weeks for the first 2 months, and at least monthly thereafter during treatment. Monitor patients with HCC closely for signs of hepatic failure, including hepatic encephalopathy. Withhold and resume at reduced dose upon recovery or permanently discontinue based on severity.

Renal Failure or Impairment

- Serious including fatal renal failure or impairment can occur with LENVIMA. Renal impairment was reported in 14% and 7% of LENVIMA-treated patients in DTC and HCC, respectively. Grade 3-5 renal failure or impairment occurred in 3% of patients with DTC and 2% of patients with HCC, including 1 fatal event in each study. In RCC, renal impairment or renal failure was reported in 18% of LENVIMA + everolimus–treated patients (10% grade 3).

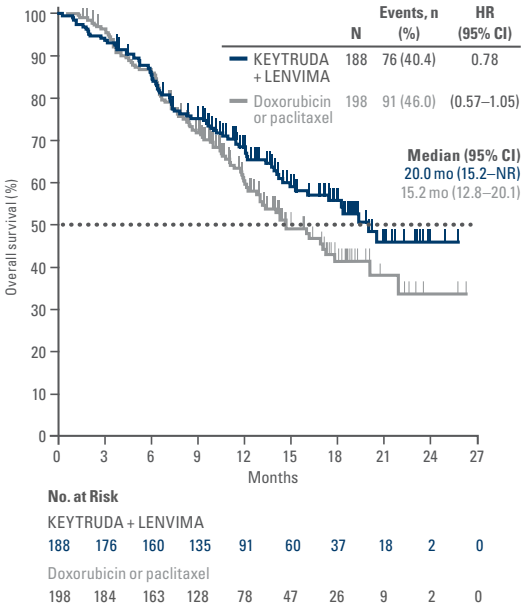
Before prescribing KEYTRUDA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information. The Medication Guide also is available. Before prescribing LENVIMA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information and Patient Information.

KEYTRUDA® (pembrolizumab) Injection 100 mg
LENVIMA® (lenvatinib) capsules | 10 mg and 4 mg

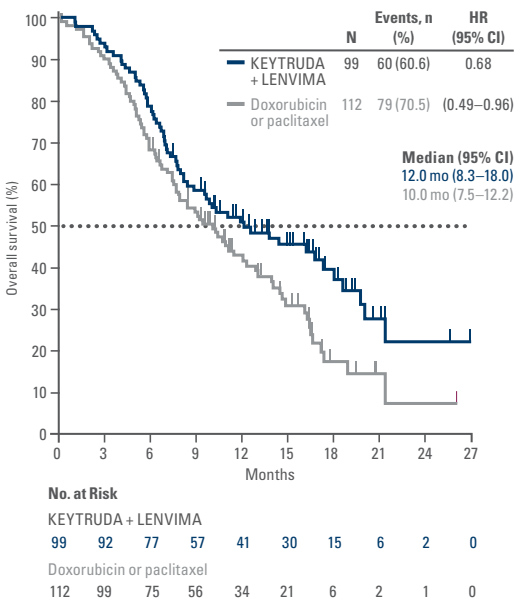
Post hoc analysis: OS[a] by histology in subgroups of patients with advanced endometrial carcinoma that was pMMR or not MSI-H[2,3]

LIMITATIONS: KEYNOTE-775/Study 309 was not powered to detect differences in the treatment effect in these subgroups and no statistical testing was planned for this exploratory analysis. No conclusions can be drawn.

Kaplan-Meier estimates for OS for endometrioid histology



Kaplan-Meier estimates for OS for serous histology



[a]Randomization was stratified by MMR status. Data cutoff: October 26, 2020.
NR = not reached.

Selected Safety Information for KEYTRUDA® (pembrolizumab) (*continued*)

Severe and Fatal Immune-Mediated Adverse Reactions (*continued*)

Hepatotoxicity and Immune-Mediated Hepatitis

- 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.

Selected Safety Information for LENVIMA® (lenvatinib) (*continued*)

Renal Failure or Impairment (*continued*)

- Initiate prompt management of diarrhea or dehydration/hypovolemia. Withhold and resume at reduced dose upon recovery or permanently discontinue for renal failure or impairment based on severity.

Proteinuria

- In DTC and HCC, proteinuria was reported in 34% and 26% of LENVIMA-treated patients, respectively. Grade 3 proteinuria occurred in 11% and 6% in DTC and HCC, respectively. In RCC, proteinuria occurred in 31% of patients receiving LENVIMA + everolimus (8% grade 3). Monitor for proteinuria prior to initiation and periodically during treatment. If urine dipstick proteinuria ≥2+ is detected, obtain a 24-hour urine protein. Withhold and resume at reduced dose upon recovery or permanently discontinue based on severity.

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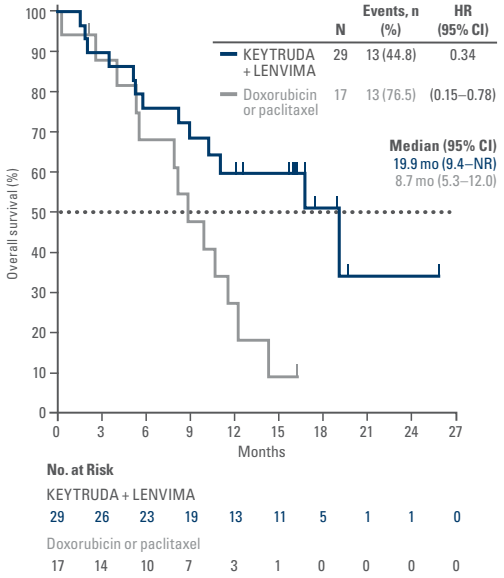
KEYTRUDA® (pembrolizumab) Injection 100 mg
LENVIMA® (lenvatinib) capsules | 10 mg and 4 mg

Post hoc analysis: OS[a] by histology in subgroups of patients with advanced endometrial carcinoma that was pMMR or not MSI-H[2,3] (cont'd)

LIMITATIONS: KEYNOTE-775/Study 309 was not powered to detect differences in the treatment effect in these subgroups and no statistical testing was planned for this exploratory analysis. No conclusions can be drawn.

Kaplan-Meier estimates for OS for clear cell histology



[a]Randomization was stratified by MMR status. Data cutoff: October 26, 2020.

Selected Safety Information for KEYTRUDA® (pembrolizumab) (*continued*)

Severe and Fatal Immune-Mediated Adverse Reactions (*continued*)

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.

Selected Safety Information for LENVIMA® (lenvatinib) (*continued*)

Diarrhea

- Of the 737 LENVIMA-treated patients in DTC and HCC, diarrhea occurred in 49% (6% grade 3). In RCC, diarrhea occurred in 81% of LENVIMA + everolimus–treated patients (19% grade 3). Diarrhea was the most frequent cause of dose interruption/reduction, and diarrhea recurred despite dose reduction. Promptly initiate management of diarrhea. Withhold and resume at reduced dose upon recovery or permanently discontinue based on severity.

Fistula Formation and Gastrointestinal Perforation

- Of the 799 patients treated with LENVIMA or LENVIMA + everolimus in DTC, RCC, and HCC, fistula or gastrointestinal perforation occurred in 2%. Permanently discontinue in patients who develop gastrointestinal perforation of any severity or grade 3-4 fistula.

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KEYTRUDA® (pembrolizumab) Injection 100 mg

LENVIMA® (lenvatinib) capsules | 10 mg and 4 mg

For the treatment of patients with advanced endometrial carcinoma that is pMMR as determined by an FDA-approved test or not MSI-H, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation

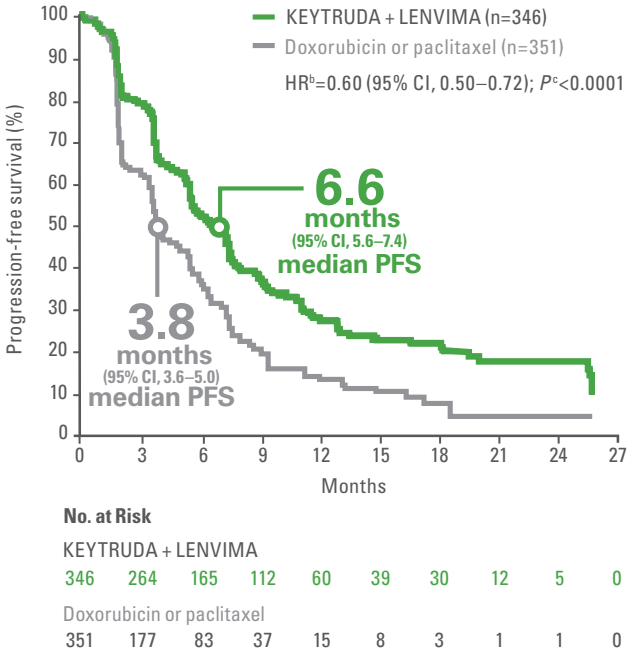
Superior PFS[a] (major endpoint): 40% reduction in the risk of disease progression or death vs doxorubicin or paclitaxel alone

- **HR[b]=0.60 (95% CI, 0.50–0.72); *P*[c]<0.0001**
- Events observed: 71% (247/346) with KEYTRUDA + LENVIMA vs 68% (238/351) with doxorubicin or paclitaxel
- PFS was a major endpoint with OS in KEYNOTE-775/Study 309

Patients lived a median of **2.8 months longer** without disease progression or death with **KEYTRUDA + LENVIMA** (n=346) vs doxorubicin or paclitaxel (n=351).

[a]Per independent radiology review.
[b]Based on the stratified Cox regression model.
[c]Based on stratified log-rank test.

Kaplan-Meier estimates for PFS in KEYNOTE-775/Study 309 (pMMR or not MSI-H) (N=697)



No. at Risk

KEYTRUDA + LENVIMA	346	264	165	112	60	39	30	12	5	0
Doxorubicin or paclitaxel	351	177	83	37	15	8	3	1	1	0

Selected Safety Information for KEYTRUDA® (pembrolizumab) (*continued*)

Severe and Fatal Immune-Mediated Adverse Reactions (*continued*)

Immune-Mediated Endocrinopathies (*continued*)

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.

Selected Safety Information for LENVIMA® (lenvatinib) (*continued*)

QT Interval Prolongation

- In DTC, QT/QTc interval prolongation occurred in 9% of LENVIMA-treated patients and QT interval prolongation of >500 ms occurred in 2%. In RCC, QTc interval increases of >60 ms occurred in 11% of patients receiving LENVIMA + everolimus and QTc interval >500 ms occurred in 6%. In HCC, QTc interval increases of >60 ms occurred in 8% of LENVIMA-treated patients and QTc interval >500 ms occurred in 2%.
- Monitor and correct electrolyte abnormalities at baseline and periodically during treatment. Monitor electrocardiograms in patients with congenital long QT syndrome, congestive heart failure, bradyarrhythmias, or those who are taking drugs known to prolong the QT interval, including Class Ia and III antiarrhythmics. Withhold and resume at reduced dose upon recovery based on severity.

QTc = corrected QT interval.

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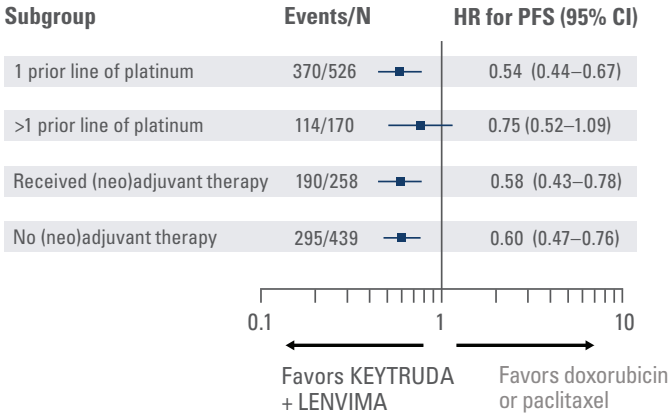
KEYTRUDA® (pembrolizumab) Injection 100 mg
LENVIMA® (lenvatinib) capsules | 10 mg and 4 mg

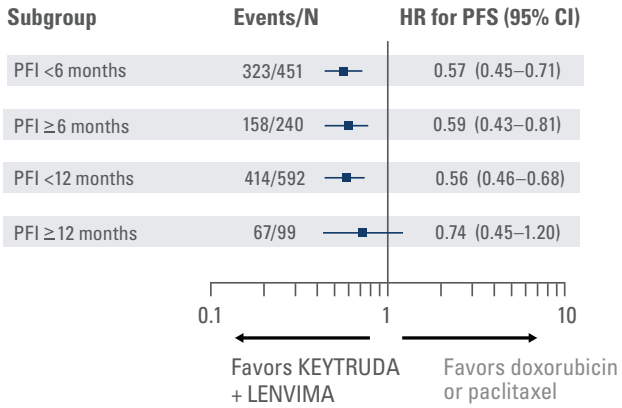
Post hoc analysis: PFS[d] in patients with advanced endometrial carcinoma that was pMMR or not MSI-H[2,3]

LIMITATIONS: KEYNOTE-775/Study 309 was not powered to detect differences in the treatment effect in these subgroups and no statistical testing was planned for this exploratory analysis. No conclusions can be drawn.

PFS by prior therapy



PFS by PFI



[d]Per RECIST v1.1 by BICR. Data cutoff: October 26, 2020.
PFI = platinum-free interval from most recent platinum-containing regimen.

Selected Safety Information for KEYTRUDA® (pembrolizumab) (*continued*)

Severe and Fatal Immune-Mediated Adverse Reactions (*continued*)

Immune-Mediated Endocrinopathies (*continued*)

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.

Selected Safety Information for LENVIMA® (lenvatinib) (*continued*)

Hypocalcemia

- In DTC, grade 3-4 hypocalcemia occurred in 9% of LENVIMA-treated patients. In 65% of cases, hypocalcemia improved or resolved following calcium supplementation with or without dose interruption or dose reduction. In RCC, grade 3-4 hypocalcemia occurred in 6% of LENVIMA + everolimus–treated patients. In HCC, grade 3 hypocalcemia occurred in 0.8% of LENVIMA-treated patients. Monitor blood calcium levels at least monthly and replace calcium as necessary during treatment. Withhold and resume at reduced dose upon recovery or permanently discontinue depending on severity.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS)

- Across clinical studies of 1,823 patients who received LENVIMA as a single agent, RPLS occurred in 0.3%. Confirm diagnosis of RPLS with MRI. Withhold and resume at reduced dose upon recovery or permanently discontinue depending on severity and persistence of neurologic symptoms.

MRI = magnetic resonance imaging.

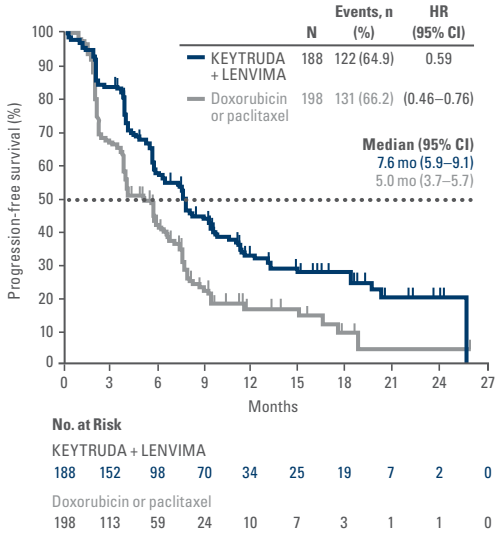
Before prescribing KEYTRUDA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information. The Medication Guide also is available. Before prescribing LENVIMA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information and Patient Information.

KEYTRUDA® (pembrolizumab) Injection 100 mg
LENVIMA® (lenvatinib) capsules | 10 mg and 4 mg

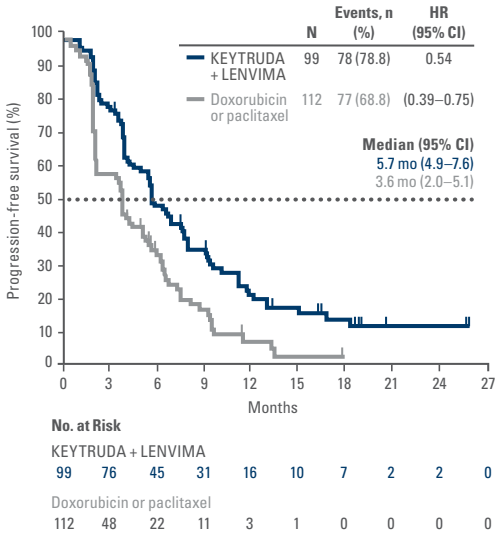
Post hoc analysis: PFS[a] by histology in subgroups of patients with advanced endometrial carcinoma that was pMMR or not MSI-H[2,3]

LIMITATIONS: KEYNOTE-775/Study 309 was not powered to detect differences in the treatment effect in these subgroups and no statistical testing was planned for this exploratory analysis. No conclusions can be drawn.

Kaplan-Meier estimates for PFS for endometrioid histology



Kaplan-Meier estimates for PFS for serous histology



[a]Per RECIST v1.1 by BICR. Randomization was stratified by MMR status. Data cutoff: October 26, 2020.

Selected Safety Information for KEYTRUDA® (pembrolizumab) (*continued*)

Severe and Fatal Immune-Mediated Adverse Reactions (*continued*)

Immune-Mediated Endocrinopathies (*continued*)

Thyroid Disorders (*continued*)

- 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 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.

Selected Safety Information for LENVIMA® (lenvatinib) (*continued*)

Hemorrhagic Events

- Serious including fatal hemorrhagic events can occur with LENVIMA. In DTC, RCC, and HCC clinical trials, hemorrhagic events, of any grade, occurred in 29% of the 799 patients treated with LENVIMA as a single agent or in combination with everolimus. The most frequently reported hemorrhagic events (all grades and occurring in at least 5% of patients) were epistaxis and hematuria. In DTC, grade 3-5 hemorrhage occurred in 2% of LENVIMA-treated patients, including 1 fatal intracranial hemorrhage among 16 patients who received LENVIMA and had CNS metastases at baseline. In RCC, grade 3-5 hemorrhage occurred in 8% of LENVIMA + everolimus–treated patients, including 1 fatal cerebral hemorrhage. In HCC, grade 3-5 hemorrhage occurred in 5% of LENVIMA-treated patients, including 7 fatal hemorrhagic events.

CNS = central nervous system.

Before prescribing KEYTRUDA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information. The Medication Guide also is available. Before prescribing LENVIMA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information and Patient Information.

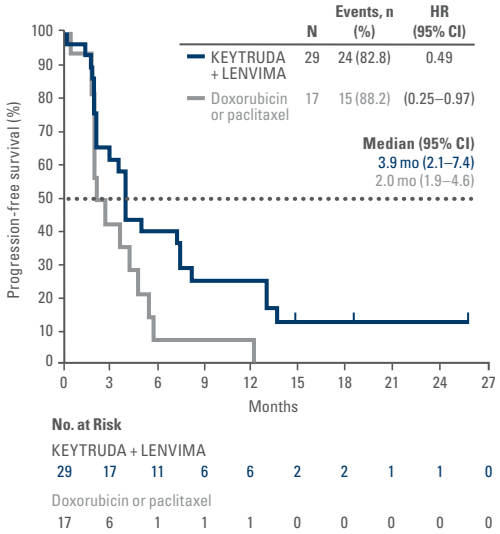
KEYTRUDA® (pembrolizumab) Injection 100 mg

LENVIMA® (lenvatinib) capsules | 10 mg and 4 mg

Post hoc analysis: PFS[a] by histology in subgroups of patients with advanced endometrial carcinoma that was pMMR or not MSI-H[2,3] (cont'd)

LIMITATIONS: KEYNOTE-775/Study 309 was not powered to detect differences in the treatment effect in these subgroups and no statistical testing was planned for this exploratory analysis. No conclusions can be drawn.

Kaplan-Meier estimates for PFS for clear cell histology



[a]Per RECIST v1.1 by BICR. Randomization was stratified by MMR status. Data cutoff: October 26, 2020.

Selected Safety Information for KEYTRUDA® (pembrolizumab) (*continued*)

Severe and Fatal Immune-Mediated Adverse Reactions (*continued*)

Immune-Mediated Endocrinopathies (*continued*)

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.

Selected Safety Information for LENVIMA® (lenvatinib) (*continued*)

Hemorrhagic Events (*continued*)

Serious tumor-related bleeds, including fatal hemorrhagic events, occurred in LENVIMA-treated patients in clinical trials and in the postmarketing setting. In postmarketing surveillance, serious and fatal carotid artery hemorrhages were seen more frequently in patients with anaplastic thyroid carcinoma (ATC) than other tumors. Safety and effectiveness of LENVIMA in patients with ATC have not been demonstrated in clinical trials.

- Consider the risk of severe or fatal hemorrhage associated with tumor invasion or infiltration of major blood vessels (eg, carotid artery). Withhold and resume at reduced dose upon recovery or permanently discontinue based on severity.

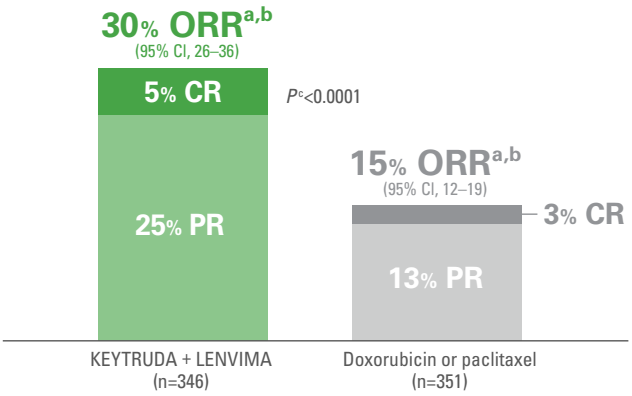
Before prescribing KEYTRUDA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information. The Medication Guide also is available. Before prescribing LENVIMA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information and Patient Information.

KEYTRUDA® (pembrolizumab) Injection 100 mg

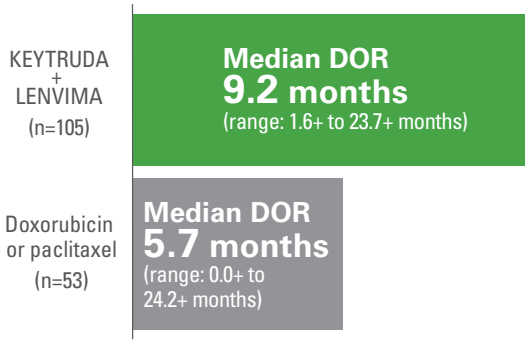
LENVIMA® (lenvatinib) capsules | 10 mg and 4 mg

Additional endpoints: Objective response rate and duration of response

Superior ORR, 2x that of doxorubicin or paclitaxel



Longer median DOR vs doxorubicin or paclitaxel



[a]Response: Best objective response as confirmed by CR or PR.
[b]Per independent radiology review.
[c]Based on Miettinen and Nurminen method stratified by ECOG PS, geographic region, and history of pelvic radiation.
ORR = objective response rate; CR = complete response; PR = partial response; DOR = duration of response.

Selected Safety Information for KEYTRUDA® (pembrolizumab) (*continued*)

Severe and Fatal Immune-Mediated Adverse Reactions (*continued*)

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.

Selected Safety Information for LENVIMA® (lenvatinib) (*continued*)

Impairment of Thyroid Stimulating Hormone Suppression/Thyroid Dysfunction

- LENVIMA impairs exogenous thyroid suppression. In DTC, 88% of patients had baseline thyroid stimulating hormone (TSH) level ≤0.5 mU/L. In patients with normal TSH at baseline, elevation of TSH level >0.5 mU/L was observed post baseline in 57% of LENVIMA-treated patients. In RCC and HCC, grade 1 or 2 hypothyroidism occurred in 24% of LENVIMA + everolimus–treated patients and 21% of LENVIMA-treated patients, respectively. In patients with normal or low TSH at baseline, elevation of TSH was observed post baseline in 70% of LENVIMA-treated patients in HCC and 60% of LENVIMA + everolimus–treated patients in RCC.
- Monitor thyroid function prior to initiation and at least monthly during treatment. Treat hypothyroidism according to standard medical practice.

Before prescribing KEYTRUDA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information. The Medication Guide also is available. Before prescribing LENVIMA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information and Patient Information.

KEYTRUDA® (pembrolizumab) Injection 100 mg
LENVIMA® (lenvatinib) capsules | 10 mg and 4 mg

For the treatment of patients with advanced endometrial carcinoma that is pMMR as determined by an FDA-approved test or not MSI-H, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation

The safety of KEYTRUDA in combination with LENVIMA was investigated in KEYNOTE-775/Study 309, a multicenter, open-label, randomized (1:1) active-controlled trial of patients with advanced endometrial carcinoma that was pMMR or not MSI-H, who were previously treated with at least 1 prior platinum-based chemotherapy regimen in any setting. The adverse reactions listed reflect the adverse reaction profile of this population treated with KEYTRUDA in combination with LENVIMA (n=342) in the study.

Adverse reactions in KEYNOTE-775/Study 309

Fatal adverse reactions occurred in 4.7% of patients treated with KEYTRUDA + LENVIMA, including 2 cases of pneumonia, and 1 case of the following:

- Acute kidney injury
- Acute myocardial infarction
- Colitis
- Decreased appetite
- Intestinal perforation
- Lower gastrointestinal hemorrhage
- Malignant gastrointestinal obstruction
- Multiple organ dysfunction syndrome
- Myelodysplastic syndrome
- Pulmonary embolism
- Right ventricular dysfunction

Serious adverse reactions occurred in 50% of patients receiving KEYTRUDA + LENVIMA. Serious adverse reactions (≥3%) were:

- Hypertension (4.4%)
- Urinary tract infection (3.2%)

Selected Safety Information for KEYTRUDA® (pembrolizumab) (*continued*)

Severe and Fatal Immune-Mediated Adverse Reactions (*continued*)

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.

Selected Safety Information for LENVIMA® (lenvatinib) (*continued*)

Impaired Wound Healing

- Impaired wound healing has been reported in patients who received LENVIMA. Withhold LENVIMA for at least 1 week prior to elective surgery. Do not administer for at least 2 weeks following major surgery and until adequate wound healing. The safety of resumption of LENVIMA after resolution of wound healing complications has not been established.

Before prescribing KEYTRUDA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information. The Medication Guide also is available. Before prescribing LENVIMA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information and Patient Information.

KEYTRUDA® (pembrolizumab) Injection 100 mg

LENVIMA® (lenvatinib) capsules | 10 mg and 4 mg

For the treatment of patients with advanced endometrial carcinoma that is pMMR as determined by an FDA-approved test or not MSI-H, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation

Discontinuation and interruption rates for **KEYTRUDA** and **LENVIMA** and **dose reduction** rates for **LENVIMA** in KEYNOTE-775/Study 309 due to adverse reactions

	KEYTRUDA	LENVIMA
Median duration of exposure (months)	6.8 (range: 1 day–25.8 months)	6.7 (range: 1 day–26.8 months)

	KEYTRUDA	LENVIMA
Discontinuation	15%	26%
Dose reduction	N/A[a]	67%
Dose interruption	48%	58%

[a]No dose reductions are recommended for KEYTRUDA.

Median duration of study treatment: **7.2** months (range: 1 day–26.8 months).

Selected Safety Information for KEYTRUDA® (pembrolizumab) (*continued*)

Severe and Fatal Immune-Mediated Adverse Reactions (*continued*)

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;

Selected Safety Information for LENVIMA® (lenvatinib) (*continued*)

Osteonecrosis of the Jaw (ONJ)

- ONJ has been reported in patients receiving LENVIMA. Concomitant exposure to other risk factors, such as bisphosphonates, denosumab, dental disease or invasive dental procedures, may increase the risk of ONJ.

  Perform an oral examination prior to treatment with LENVIMA and periodically during LENVIMA treatment. Advise patients regarding good oral hygiene practices and to consider having preventive dentistry performed prior to treatment with LENVIMA and throughout treatment with LENVIMA.

  Avoid invasive dental procedures, if possible, while on LENVIMA treatment, particularly in patients at higher risk. Withhold LENVIMA for at least 1 week prior to scheduled dental surgery or invasive dental procedures, if possible. For patients requiring invasive dental procedures, discontinuation of bisphosphonate treatment may reduce the risk of ONJ.

  Withhold LENVIMA if ONJ develops and restart based on clinical judgement of adequate resolution.

Before prescribing KEYTRUDA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information. The Medication Guide also is available. Before prescribing LENVIMA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information and Patient Information.

KEYTRUDA® (pembrolizumab) Injection 100 mg

LENVIMA® (lenvatinib) capsules | 10 mg and 4 mg

Adverse reactions that led to **discontinuation** in KEYNOTE-775/Study 309

Discontinuation of KEYTRUDA due to an adverse reaction occurred in 15% of patients.
Discontinuation of LENVIMA due to an adverse reaction occurred in 26% of patients.

The most common adverse reaction (≥1%) leading to discontinuation of KEYTRUDA was:

Increased alanine aminotransferase (1.2%).

The most common adverse reactions (≥1%) leading to discontinuation of LENVIMA were:

Hypertension (2%)	Diarrhea (1.2%)	Proteinuria (1.2%)
Asthenia (1.8%)	Decreased appetite (1.2%)	Vomiting (1.2%)

Selected Safety Information for KEYTRUDA® (pembrolizumab) (*continued*)

Severe and Fatal Immune-Mediated Adverse Reactions (*continued*)

Other Immune-Mediated Adverse Reactions (*continued*)

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.

Selected Safety Information for LENVIMA® (lenvatinib) (*continued*)

Embryo-Fetal Toxicity

- Based on its mechanism of action and data from animal reproduction studies, LENVIMA can cause fetal harm when administered to pregnant women. In animal reproduction studies, oral administration of LENVIMA during organogenesis at doses below the recommended clinical doses resulted in embryotoxicity, fetotoxicity, and teratogenicity in rats and rabbits. Advise pregnant women of the potential risk to a fetus; and advise females of reproductive potential to use effective contraception during treatment with LENVIMA and for 30 days after the last dose.

Before prescribing KEYTRUDA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information. The Medication Guide also is available. Before prescribing LENVIMA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information and Patient Information.

KEYTRUDA® (pembrolizumab) Injection 100 mg
LENVIMA® (lenvatinib) capsules | 10 mg and 4 mg

For the treatment of patients with advanced endometrial carcinoma that is pMMR as determined by an FDA-approved test or not MSI-H, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation

Most **common adverse reactions** that led to **dose interruption** in KEYNOTE-775/Study 309

Dose interruption of KEYTRUDA due to an adverse reaction occurred in 48% of patients.
Dose interruption of LENVIMA due to an adverse reaction occurred in 58% of patients.

The most common adverse reactions (≥3%) leading to interruption of KEYTRUDA were:

Diarrhea (8%)	Increased aspartate aminotransferase (3.8%)
Increased alanine aminotransferase (4.4%)	Hypertension (3.5%)

The most common adverse reactions (≥2%) leading to interruption of LENVIMA were:

Hypertension (11%)	Nausea (3.5%)
Diarrhea (11%)	Abdominal pain (2.9%)
Proteinuria (6%)	Weight decreased (2.6%)
Decreased appetite (5%)	Urinary tract infection (2.6%)
Vomiting (5%)	Increased aspartate aminotransferase (2.3%)
Increased alanine aminotransferase (3.5%)	Asthenia (2.3%)
Fatigue (3.5%)	Palmar-plantar erythrodysesthesia (2%)

Selected Safety Information for KEYTRUDA® (pembrolizumab) (*continued*)

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 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.

Selected Safety Information for LENVIMA® (lenvatinib) (*continued*)

Adverse Reactions

- In endometrial carcinoma, the most common adverse reactions (≥20%) observed in LENVIMA + KEYTRUDA-treated patients were hypothyroidism (67%), hypertension (67%), fatigue (58%), diarrhea (55%), musculoskeletal disorders (53%), nausea (49%), decreased appetite (44%), vomiting (37%), stomatitis (35%), decreased weight (34%), abdominal pain (34%), urinary tract infection (31%), proteinuria (29%), constipation (27%), headache (26%), hemorrhagic events (25%), palmar-plantar erythrodysesthesia (23%), dysphonia (22%), and rash (20%).

Before prescribing KEYTRUDA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information. The Medication Guide also is available. Before prescribing LENVIMA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information and Patient Information.

KEYTRUDA® (pembrolizumab) Injection 100 mg
LENVIMA® (lenvatinib) capsules | 10 mg and 4 mg

For the treatment of patients with advanced endometrial carcinoma that is pMMR as determined by an FDA-approved test or not MSI-H, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation

Most **common adverse reactions** that led to **dose reduction** in KEYNOTE-775/Study 309

Dose reduction of LENVIMA due to an adverse reaction occurred in 67% of patients.

The most common adverse reactions (≥5%) resulting in dose reduction of LENVIMA were:

Hypertension (18%)	Fatigue (7%)
Diarrhea (11%)	Decreased appetite (6%)
Palmar-plantar erythrodysesthesia syndrome (9%)	Asthenia (5%)
Proteinuria (7%)	Weight decreased (5%)

- No dose reduction for KEYTRUDA is recommended.

Selected Safety Information for KEYTRUDA® (pembrolizumab) (*continued*)

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.

Selected Safety Information for LENVIMA® (lenvatinib) (*continued*)

Adverse Reactions (*continued*)

Fatal adverse reactions among these patients occurred in 4.7% of those treated with LENVIMA and KEYTRUDA, including 2 cases of pneumonia, and 1 case of the following: acute kidney injury, acute myocardial infarction, colitis, decreased appetite, intestinal perforation, lower gastrointestinal hemorrhage, malignant gastrointestinal obstruction, multiple organ dysfunction syndrome, myelodysplastic syndrome, pulmonary embolism, and right ventricular dysfunction.

Serious adverse reactions occurred in 50% of these patients receiving LENVIMA and KEYTRUDA. Serious adverse reactions with frequency ≥3% were hypertension (4.4%), and urinary tract infection (3.2%).

Discontinuation of LENVIMA due to an adverse reaction occurred in 26% of these patients. The most common (≥1%) adverse reactions leading to discontinuation of LENVIMA were hypertension (2%), asthenia (1.8%), diarrhea (1.2%), decreased appetite (1.2%), proteinuria (1.2%), and vomiting (1.2%).

Dose reductions of LENVIMA due to adverse reactions occurred in 67% of patients. The most common (≥5%) adverse reactions resulting in dose reduction of LENVIMA were hypertension (18%), diarrhea (11%), palmar-plantar erythrodysesthesia syndrome (9%), proteinuria (7%), fatigue (7%), decreased appetite (6%), asthenia (5%), and weight decreased (5%).

Before prescribing KEYTRUDA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information. The Medication Guide also is available. Before prescribing LENVIMA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information and Patient Information.

KEYTRUDA® (pembrolizumab) Injection 100 mg

LENVIMA® (lenvatinib) capsules | 10 mg and 4 mg

For the treatment of patients with advanced endometrial carcinoma that is pMMR as determined by an FDA-approved test or not MSI-H, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation

Adverse reactions occurring in ≥20% of patients receiving **KEYTRUDA + LENVIMA** in KEYNOTE-775/Study 309

Adverse Reaction	KEYTRUDA + LENVIMA (n=342)		Doxorubicin or Paclitaxel (n=325)	
	All Grades[a] (%)	Grades 3–4 (%)	All Grades[a] (%)	Grades 3–4 (%)
Hypothyroidism[b]	67	0.9	0.9	0
Hypertension[c]	67	39	6	2.5
Fatigue[d]	58	11	54	6
Diarrhea[e]	55	8	20	2.8
Musculoskeletal disorders[f]	53	5	27	0.6
Nausea	49	2.9	47	1.5
Decreased appetite[g]	44	7	21	0
Vomiting	37	2.3	21	2.2
Stomatitis[h]	35	2.6	26	1.2
Abdominal pain[i]	34	2.6	21	1.2
Weight loss	34	10	6	0.3
Urinary tract infection[j]	31	5	13	1.2
Proteinuria[k]	29	6	3.4	0.3
Constipation	27	0	25	0.6
Headache	26	0.6	9	0.3
Hemorrhagic events[l]	25	2.6	15	0.9
Palmar-plantar erythrodysesthesia[m]	23	2.9	0.9	0
Dysphonia	22	0	0.6	0
Rash[n]	20	2.3	4.9	0

[a]Graded per NCI-CTCAE v4.03.
[b]Includes hypothyroidism, blood thyroid stimulating hormone increased, thyroiditis, primary hypothyroidism, secondary hypothyroidism.
[c]Includes hypertension, blood pressure increased, hypertensive crisis, secondary hypertension, blood pressure abnormal, hypertensive encephalopathy, blood pressure fluctuation.
[d]Includes fatigue, asthenia, malaise, lethargy.
[e]Includes diarrhea, gastroenteritis.
[f]Includes arthralgia, myalgia, back pain, pain in extremity, bone pain, neck pain, musculoskeletal pain, arthritis, musculoskeletal chest pain, musculoskeletal stiffness, non-cardiac chest pain, pain in jaw.
[g]Includes decreased appetite, early satiety.
[h]Includes stomatitis, mucosal inflammation, oropharyngeal pain, aphthous ulcer, mouth ulceration, cheilitis, oral mucosal erythema, tongue ulceration.
[i] Includes abdominal pain, abdominal pain upper, abdominal pain lower, abdominal discomfort, gastrointestinal pain, abdominal tenderness, epigastric discomfort.
[j] Includes urinary tract infection, cystitis, pyelonephritis.
[k]Includes proteinuria, protein urine present, hemoglobinuria.
[l] Includes epistaxis, vaginal hemorrhage, hematuria, gingival bleeding, metrorrhagia, rectal hemorrhage, contusion, hematochezia, cerebral hemorrhage, conjunctival hemorrhage, gastrointestinal hemorrhage, hemoptysis, hemorrhage urinary tract, lower gastrointestinal hemorrhage, mouth hemorrhage, petechiae, uterine hemorrhage, anal hemorrhage, blood blister, eye hemorrhage, hematoma, hemorrhage intracranial, hemorrhagic stroke, injection site hemorrhage, melena, purpura, stoma site hemorrhage, upper gastrointestinal hemorrhage, wound hemorrhage, blood urine present, coital bleeding, ecchymosis, hematemesis, hemorrhage subcutaneous, hepatic hematoma, injection site bruising, intestinal hemorrhage, laryngeal hemorrhage, pulmonary hemorrhage, subdural hematoma, umbilical hemorrhage, vessel puncture site bruise.
[m]Includes palmar-plantar erythrodysesthesia syndrome, palmar erythema, plantar erythema, skin reaction.
[n]Includes rash, rash maculo-papular, rash pruritic, rash erythematous, rash macular, rash pustular, rash papular, rash vesicular, application site rash.
NCI-CTCAE = National Cancer Institute-Common Terminology Criteria for Adverse Events.

Before prescribing KEYTRUDA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information. The Medication Guide also is available. Before prescribing LENVIMA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information and Patient Information.

KEYTRUDA® (pembrolizumab) Injection 100 mg
LENVIMA® (lenvatinib) capsules | 10 mg and 4 mg

Selected Safety Information (*continued*)

Selected Safety Information for KEYTRUDA® (pembrolizumab) (*continued*)

Adverse Reactions

- In KEYNOTE-775, when KEYTRUDA was administered in combination with LENVIMA to patients with advanced endometrial carcinoma that was pMMR or not MSI-H (n=342), fatal adverse reactions occurred in 4.7% of patients. Serious adverse reactions occurred in 50% of these patients; the most common (≥3%) were hypertension (4.4%) and urinary tract infections (3.2%).
- Discontinuation of KEYTRUDA due to an adverse reaction occurred in 15% of these patients. The most common adverse reaction leading to discontinuation of KEYTRUDA (≥1%) was increased ALT (1.2%).
- The most common adverse reactions for KEYTRUDA in combination with LENVIMA (reported in ≥20% patients) were hypothyroidism and hypertension (67% each), fatigue (58%), diarrhea (55%), musculoskeletal disorders (53%), nausea (49%), decreased appetite (44%), vomiting (37%), stomatitis (35%), abdominal pain and weight loss (34% each), urinary tract infections (31%), proteinuria (29%), constipation (27%), headache (26%), hemorrhagic events (25%), palmar-plantar erythrodysesthesia (23%), dysphonia (22%), and rash (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.

ALT = alanine aminotransferase.

Selected Safety Information for LENVIMA® (lenvatinib) (*continued*)

Adverse Reactions (*continued*)

Dose interruptions of LENVIMA due to an adverse reaction occurred in 58% of these patients. The most common (≥2%) adverse reactions leading to interruption of LENVIMA were hypertension (11%), diarrhea (11%), proteinuria (6%), decreased appetite (5%), vomiting (5%), increased alanine aminotransferase (3.5%), fatigue (3.5%), nausea (3.5%), abdominal pain (2.9%), weight decreased (2.6%), urinary tract infection (2.6%), increased aspartate aminotransferase (2.3%), asthenia (2.3%), and palmar-plantar erythrodysesthesia (2%).

Use in Specific Populations

- Because of the potential for serious adverse reactions in breastfed children, advise women to discontinue breastfeeding during treatment and for 1 week after last dose. LENVIMA may impair fertility in males and females of reproductive potential.
- No dose adjustment is recommended for patients with mild (creatinine clearance [CLcr] 60-89 mL/min) or moderate (CLcr 30-59 mL/min) renal impairment. LENVIMA concentrations may increase in patients with DTC, RCC, or endometrial carcinoma and severe (CLcr 15-29 mL/min) renal impairment. Reduce the dose for patients with DTC, RCC, or endometrial carcinoma and severe renal impairment. There is no recommended dose for patients with HCC and severe renal impairment. LENVIMA has not been studied in patients with end stage renal disease.
- No dose adjustment is recommended for patients with HCC and mild hepatic impairment (Child-Pugh A). There is no recommended dose for patients with HCC with moderate (Child-Pugh B) or severe (Child-Pugh C) hepatic impairment. No dose adjustment is recommended for patients with DTC, RCC, or endometrial carcinoma and mild or moderate hepatic impairment. LENVIMA concentrations may increase in patients with DTC, RCC, or endometrial carcinoma and severe hepatic impairment. Reduce the dose for patients with DTC, RCC, or endometrial carcinoma and severe hepatic impairment.

Before prescribing KEYTRUDA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information. The Medication Guide also is available. Before prescribing LENVIMA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information and Patient Information.

KEYTRUDA® (pembrolizumab) Injection 100 mg

LENVIMA® (lenvatinib) capsules | 10 mg and 4 mg

For the treatment of patients with advanced endometrial carcinoma that is pMMR as determined by an FDA-approved test or not MSI-H, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation

In KEYNOTE-775/Study 309: KEYTRUDA + LENVIMA demonstrated superiority in OS, PFS, and ORR vs doxorubicin or paclitaxel alone

Major endpoint: Superior overall survival (OS) vs doxorubicin or paclitaxel:

- **HR[a]=0.68; 95% CI, 0.56–0.84; *P*[b]=0.0001**
- Events observed: 48% (165/346) with KEYTRUDA + LENVIMA vs 58% (203/351) with doxorubicin or paclitaxel
- Median OS: 17.4 months (95% CI, 14.2–19.9) with KEYTRUDA + LENVIMA vs 12.0 months (95% CI, 10.8–13.3) with doxorubicin or paclitaxel

32% reduced risk of death with KEYTRUDA + LENVIMA

Major endpoint: Superior progression-free survival (PFS)[c] vs doxorubicin or paclitaxel:

- **HR[a]=0.60; 95% CI, 0.50–0.72; *P*[b]<0.0001**
- Events observed: 71% (247/346) with KEYTRUDA + LENVIMA vs 68% (238/351) with doxorubicin or paclitaxel
- Median PFS: 6.6 months (95% CI, 5.6–7.4) with KEYTRUDA + LENVIMA vs 3.8 months (95% CI, 3.6–5.0) with doxorubicin or paclitaxel

40% reduction in the risk of disease progression or death with KEYTRUDA + LENVIMA

Additional endpoint: Superior objective response rate (ORR)[c,d] vs doxorubicin or paclitaxel:

- ORR: 30% (95% CI, 26–36) with KEYTRUDA + LENVIMA (n=346) vs 15% (95% CI,12–19) with doxorubicin or paclitaxel (n=351); *P*[e]<0.0001
  - Complete response (CR): 5% with KEYTRUDA + LENVIMA vs 3% with doxorubicin or paclitaxel
  - Partial response (PR): 25% with KEYTRUDA + LENVIMA vs 13% with doxorubicin or paclitaxel

2x the ORR (30%) with KEYTRUDA + LENVIMA vs doxorubicin or paclitaxel alone (15%)

[a]Based on the stratified Cox regression model.
[b]Based on stratified log-rank test.
[c]Per independent radiology review.
[d]Response: Best objective response as confirmed by CR or PR.
[e]Based on Miettinen and Nurminen method stratified by ECOG PS, geographic region, and history of pelvic radiation.

Summary of Warnings and Precautions for KEYTRUDA® (pembrolizumab)

Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue and can affect more than one body system simultaneously. Immune-mediated adverse reactions can occur at any time during or after treatment with KEYTRUDA, including pneumonitis, colitis, hepatitis, endocrinopathies, nephritis, dermatologic reactions, solid organ transplant rejection, and complications of allogeneic hematopoietic stem cell transplantation. Important immune-mediated adverse reactions listed here may not include all possible severe and fatal immune-mediated adverse reactions. Early identification and management of immune-mediated adverse reactions are essential to ensure safe use of KEYTRUDA. Based on the severity of the adverse reaction, KEYTRUDA should be withheld or permanently discontinued and corticosteroids administered if appropriate. KEYTRUDA can also cause severe or life-threatening infusion-related reactions. Based on its mechanism of action, KEYTRUDA can cause fetal harm when administered to a pregnant woman.

Summary of Warnings and Precautions for LENVIMA® (lenvatinib)

Adverse reactions, some of which can be serious or fatal, may occur with LENVIMA, including hypertension, cardiac dysfunction, arterial thromboembolic events, hepatotoxicity, renal failure or impairment, proteinuria, diarrhea, fistula formation and gastrointestinal perforation, QT interval prolongation, hypocalcemia, reversible posterior leukoencephalopathy syndrome, hemorrhagic events, impairment of thyroid stimulating hormone suppression/thyroid dysfunction, impaired wound healing, osteonecrosis of the jaw, and embryo-fetal toxicity. Based on its mechanism of action and data from animal reproduction studies, LENVIMA can cause fetal harm when administered to a pregnant woman. Females of reproductive potential should be advised to use effective contraception. Based on the severity of the adverse reaction, LENVIMA should be interrupted, reduced, and/or discontinued.

Before prescribing KEYTRUDA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information. The Medication Guide also is available. Before prescribing LENVIMA, please read the additional Selected Safety Information included throughout this document, and the accompanying Prescribing Information and Patient Information.

References: 1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Uterine Neoplasms V.1.2022. © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed August 30, 2022. To view the most recent and complete version of the guidelines, go online to NCCN.org. **2.** Data available on request from Merck, Professional Services-DAP, WP1-27, PO Box 4, West Point, PA 19486-0004. Please specify information package US-KLE-00796. **3.** Colombo N, Lorusso D, Casado Herráez A, et al. Outcomes by histology and prior therapy with lenvatinib plus pembrolizumab vs treatment of physician's choice in patients with advanced endometrial cancer (Study 309/KEYNOTE-775). Mini oral session presented at: European Society for Medical Oncology (ESMO) Virtual Congress; September 16–21, 2021. **4.** Makker V, Colombo N, Casado Herráez A, et al. Lenvatinib plus pembrolizumab for advanced endometrial cancer. *N Engl J Med.* 2022;386(5):437–448. doi:10.1056/NEJMoa2108330

For more information visit KeytrudaLenvimaHCP.com.

MERCK Eisai

KEYTRUDA® (pembrolizumab) Injection 100 mg
LENVIMA® (lenvatinib) capsules | 10 mg and 4 mg