Focus on
OVERALL RESPONSE RATE
for your patients with advanced non-MSI-H/dMMR EC


KEYTRUDA®, in combination with LENVIMA®, is indicated for the treatment of adult patients with advanced endometrial carcinoma that is not microsatellite instability high (MSI-H) or mismatch repair deficient (dMMR), who have disease progression following prior platinum-based systemic therapy and are not candidates for curative surgery or radiation.
This indication is approved based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.[1,2]

Consider KEYTRUDA® + LENVIMA® for your appropriate patients with advanced endometrial carcinoma that is not MSI-H or dMMR, who have disease progression following prior chemotherapy in a metastatic setting and are not candidates for curative surgery or radiation.[1]

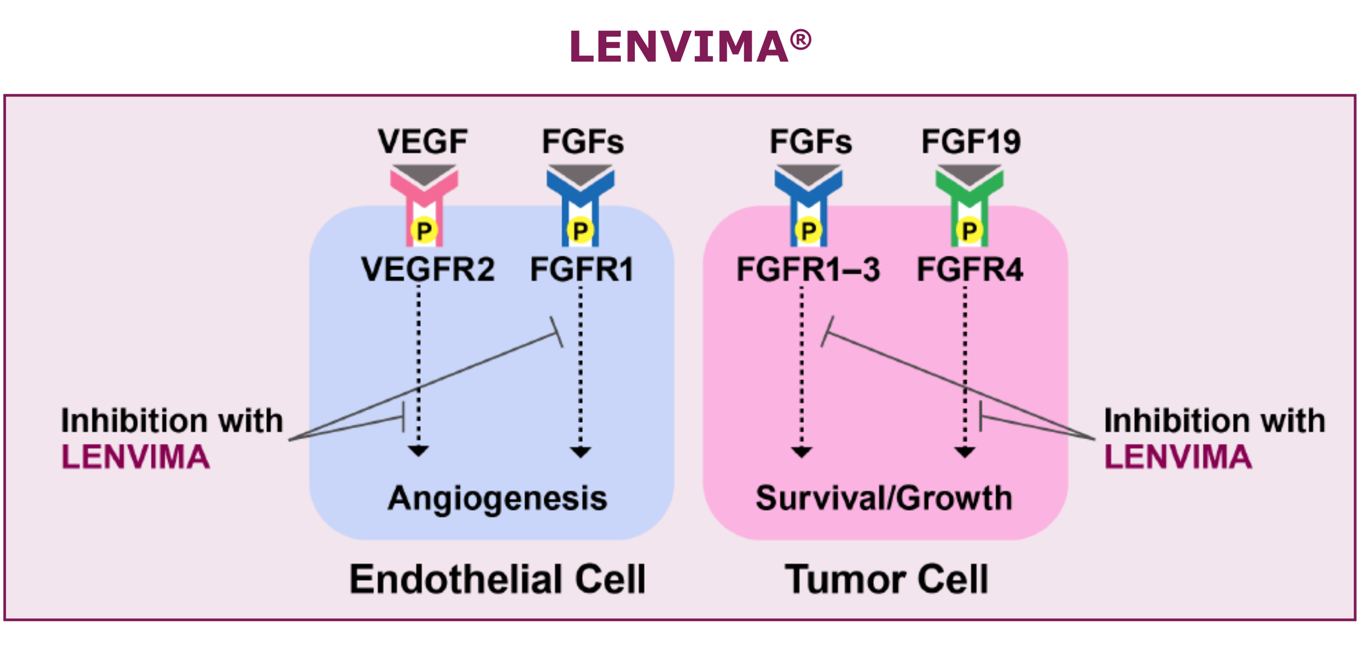
PATIENT CHARACTERISTICS recruited in KEYNOTE-146 (N=108)[3,4,a]

- 87% (n=94) of patients had tumors that were not MSI-H/dMMR Tumor MSI-H/dMMR[3,4,b]
- **Median age:** 66 years (62% aged 65 or older)
- **Prior Systemic Therapy:** 51% had 1; 38% had 2 and 11% had more than 2
- **Histological Subtypes:** Endometroid adenocarcinoma, serious adenocarcinoma, clear cell adenocarcinoma, adenocarcinoma (not otherwise specified) and other[b]

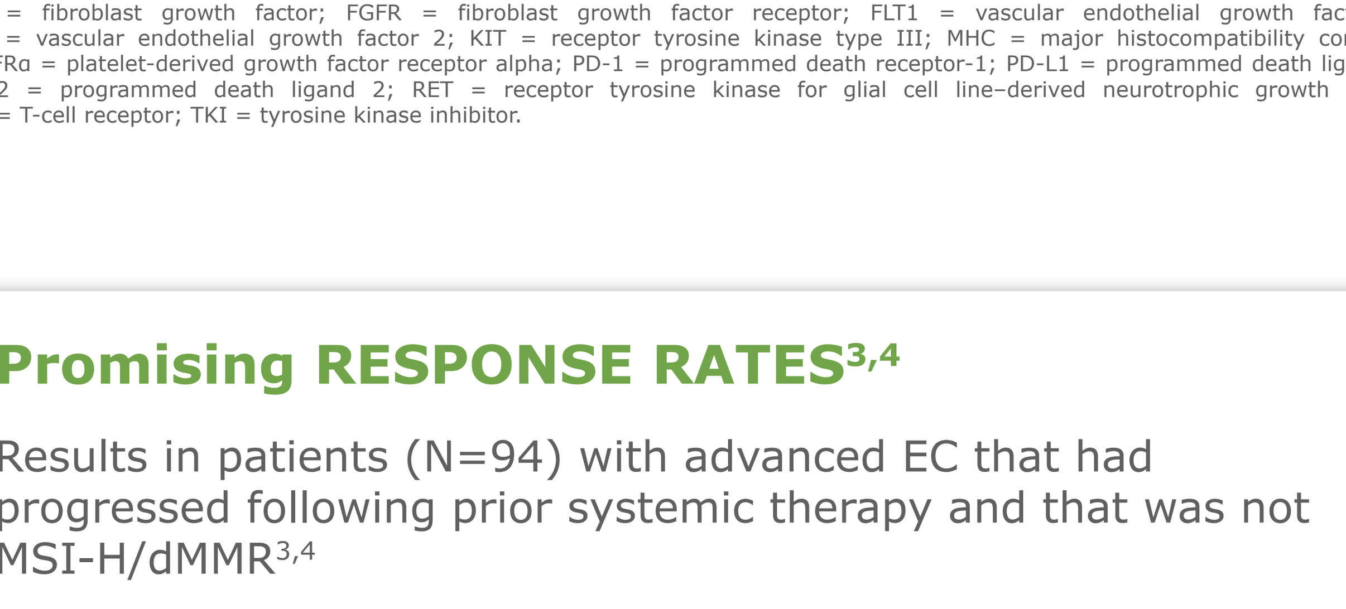
[a]Tumor MSI status was determined using a polymerase chain reaction (PCR) test and tumor MMR status was determined using an immunohistochemistry (IHC) test.
[b]Predominantly mixed histology.[3]
dMMR = mismatch repair deficient; MMR = mismatch repair; MSI-H = microsatellite instability-high.

Two mechanisms of action target advanced endometrial carcinoma[5,6]

KEYTRUDA®



LENVIMA®



FGF = fibroblast growth factor; FGFR = fibroblast growth factor receptor; FLT1 = vascular endothelial growth factor 1; KDR = vascular endothelial growth factor 2; KIT = receptor tyrosine kinase type III; MHC = major histocompatibility complex; PDGFRα = platelet-derived growth factor receptor alpha; PD-1 = programmed death receptor-1; PD-L1 = programmed death ligand 1; PD-L2 = programmed death ligand 2; RET = receptor tyrosine kinase for glial cell line–derived neurotrophic growth factor; TCR = T-cell receptor; TKI = tyrosine kinase inhibitor.

Promising RESPONSE RATES[3,4]

Results in patients (N=94) with advanced EC that had progressed following prior systemic therapy and that was not MSI-H/dMMR[3,4]

38.3% objective response rate (95% CI, 29%-49%)

10.6% complete response

27.7% partial response

40.4% stable disease

Median duration of response (DOR) had not been reached at time of analysis.[a] Among the 36 responding patients, the DOR ranged from 1.2+ to 33.1+ months.

76% duration of response ≥6 months[b]

51% duration of response ≥12 months[c]

Median follow-up time of 18.7 months

[a]DOR was assessed by BICR using RECIST 1.1.
[b]Based on KaplanMeier estimates: includes 25 patients with responses of 6 months or longer.
[c]Based on KaplanMeier estimates: includes 8 patients with responses of 12 months or longer.
MSI-H = microsatellite instability-high; dMMR = mismatch repair deficient; CI = confidence interval; BICR = blinded independent central review; RECIST 1.1 = Response Evaluation Criteria In Solid Tumors v1.1.

Promising OVERALL SURVIVAL and PROGRESSION FREE SURVIVAL[3,4,a]

Patients (N=94) with advanced EC that had progressed following prior systemic therapy and that was not MSI-H/dMMR[3,4,a]

OS rate at 12 months (n=94)
70%

PFS rate at 6 & 12 months (n=94)
49% | 33%

Median OS (95% CI, 13.5 - 25.9 months)
16.4 months

Median PFS (95% CI, 4.4 – 7.6 months)
5.4 months

- Median follow up time was 18.7 months.
- At 12 months, 70% of patients who received KEYTRUDA® + LENVIMA® for advanced endometrial carcinoma that was not MSI-H/dMMR were still alive.
- It was estimated that nearly half of patients with advanced endometrial carcinoma that was not MSI-H/dMMR had PFS at 6 months.

[a]PFS was assessed by BICR using RECIST 1.1
BICR = blinded independent central review; CI = confidence interval; dMMR = mismatch repair deficient; MSI-H = microsatellite instability high; PFS = progression-free survival; OS = overall survival

KEYNOTE-146 is a single-arm, multicenter, open-label, multicohort trial of lenvatinib plus pembrolizumab in patients with metastatic endometrial carcinoma that had progressed following at least one prior systemic therapy in any setting. Patients with active autoimmune disease or a medical condition that required immunosuppression were ineligible. 108 patients were enrolled, with a median follow-up of 18.7 months. Patients took pembrolizumab plus lenvatinib. Pembrolizumab 200 mg was given intravenously every 3 weeks until unacceptable toxicity or disease progression, as determined by the investigator plus pembrolizumab dosing was continued for a maximum of 24 months. Lenvatinib 20 mg was given orally once daily until unacceptable toxicity or disease progression, as determined by the investigator. Lenvatinib treatment could be continued beyond 24 months. Assessment of tumor status was performed at baseline and then every 6 weeks until week 24, followed by every 9 weeks thereafter. The primary end point was objective response rate (ORR) at 24 weeks (ORRWk24); secondary efficacy end points included duration of response (DOR), progression-free survival (PFS), and overall survival (OS). Tumor assessments were evaluated by investigators per immune-related RECIST.[3,4]

KEYTRUDA® SELECTED SAFETY INFORMATION

Indications

Melanoma
KEYTRUDA (pembrolizumab) is indicated for the treatment of patients with unresectable or metastatic melanoma.
KEYTRUDA is indicated for the adjuvant treatment of patients with melanoma with lymph node involvement who have undergone complete resection.

Non-Small Cell Lung Carcinoma
KEYTRUDA, in combination with pemetrexed and platinum chemotherapy, is indicated for the first-line treatment of patients with metastatic non-squamous non-small cell lung carcinoma (NSCLC), with no EGFR or ALK genomic tumor aberrations.
KEYTRUDA, in combination with carboplatin and either paclitaxel or nab-paclitaxel, is indicated for the first-line treatment of patients with metastatic squamous NSCLC.
KEYTRUDA as monotherapy is indicated for the first-line treatment of patients with metastatic NSCLC whose tumors express PD-L1 with a ≥50% tumor proportion score (TPS) as determined by a validated test, with no EGFR or ALK genomic tumor aberrations.
KEYTRUDA as monotherapy is indicated for the treatment of patients with locally advanced or metastatic NSCLC whose tumors express PD-L1 with a ≥1% TPS as determined by a validated test and who have received platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have received prior therapy for these aberrations prior to receiving KEYTRUDA.

Head and Neck Cancer
KEYTRUDA, as monotherapy or in combination with platinum and 5-fluorouracil (5-FU) chemotherapy, is indicated for the first line treatment of patients with metastatic or unresectable recurrent head and neck squamous cell carcinoma (HNSCC) whose tumours express PD-L1 with a CPS ≥ 1.

Classical Hodgkin Lymphoma
KEYTRUDA is indicated for the treatment of adult and pediatric patients aged 3 years and above, with relapsed or refractory classical Hodgkin lymphoma (cHL), who have failed autologous stem cell transplant (ASCT) or following at least two prior therapies when ASCT is not a treatment option.

Urothelial Carcinoma
KEYTRUDA is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma whose tumours express PD-L1 with a combined positive score (CPS) ≥10 as determined by a validated test, and who are not eligible for cisplatin-containing chemotherapy.
KEYTRUDA is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who have received prior platinum-containing chemotherapy.

Esophageal Cancer
KEYTRUDA, in combination with platinum and fluoropyrimidine based chemotherapy, is indicated for the first-line treatment of patients with locally advanced or metastatic carcinoma of the esophagus or HER2 negative gastroesophageal junction (GEJ) adenocarcinoma (tumors with epicenter 1 to 5 centimeters above the GEJ) that is not amenable to surgical resection or definitive chemoradiation.

Colorectal Cancer
KEYTRUDA is indicated for the first-line treatment of patients with metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer (CRC).

Renal Cell Carcinoma
KEYTRUDA, in combination with axitinib, is indicated for the first-line treatment of patients with advanced renal cell carcinoma (RCC).

Endometrial Carcinoma
KEYTRUDA, in combination with lenvatinib, is indicated for the treatment of patients with advanced endometrial carcinoma that is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR), who have disease progression following prior chemotherapy in the metastatic setting and are not candidates for curative surgery or radiation.

Triple Negative Breast Cancer
KEYTRUDA, in combination with chemotherapy, is indicated for the treatment of patients with locally recurrent unresectable or metastatic triple negative breast cancer (TNBC) whose tumors express PD L1 (CPS ≥10) as determined by a validated test and who have not received prior chemotherapy for metastatic disease.

Dosing
KEYTRUDA is administered as an intravenous infusion over 30 minutes.
The recommended dose of KEYTRUDA in adults with HNSCC, cHL, urothelial carcinoma, CRC, RCC, endometrial carcinoma, TNBC, previously untreated NSCLC, or for the adjuvant treatment of melanoma is either:
- 200 mg every 3 weeks or
- 400 mg every 6 weeks.

The recommended dose of KEYTRUDA in adults with previously treated NSCLC or for unresectable or metastatic melanoma is 2 mg/kg every 3 weeks. Patients should be treated with KEYTRUDA until disease progression or unacceptable toxicity.
For the adjuvant treatment of melanoma, KEYTRUDA should be administered for up to one year or until disease recurrence or unacceptable toxicity.

Contraindications
KEYTRUDA is contraindicated in patients with hypersensitivity to pembrolizumab or any of the inactive ingredients.

Precautions/Warnings
Immune-mediated adverse reactions, including severe and fatal cases, have occurred in patients receiving KEYTRUDA. List of immune-mediated adverse reactions include but are not limited to: pneumonitis; colitis; hepatitis; nephritis; endocrinopathies; severe skin reactions. Transplant-related adverse reaction such as risk of rejection in solid organ transplant recipients; complications of allogeneic HSCT after treatment with KEYTRUDA; graft-versus-host disease (GVHD) and hepatic veno-occlusive disease (VOD) have been observed. Elevated liver enzymes when KEYTRUDA is given in combination with axitinib for RCC. Increased mortality in patients with multiple myeloma when KEYTRUDA is added to a thalidomide analogue and dexamethasone. Infusion-related reactions including hypersensitivity and anaphylaxis.

Adverse Reactions
Most frequent adverse reactions (reported ≥ 20% patients) were: KEYTRUDA as monotherapy: fatigue, nausea, and diarrhoea. KEYTRUDA in combination with chemotherapy: nausea, anaemia, fatigue, constipation, decreased appetite, diarrhoea, neutropenia and vomiting. KEYTRUDA in combination with axitinib: diarrhoea, hypertension, fatigue, hypothyroidism, decreased appetite, palmar-plantar erythrodysaesthesia syndrome, nausea, ALT increased, AST increased,dysphonia, cough, and constipation. KEYTRUDA in combination with lenvatinib: hypertension, diarrhea, fatigue, decreased appetite, hypothyroidism, nausea, vomiting, stomatitis, decreased weight, arthralgia, headache, constipation, dysphonia, urinary tract infection, abdominal pain, hypomagnesemia, palmar-plantar erythrodysesthesia, dyspnea, cough, myalgia, and back pain

Before prescribing Keytruda, please consult full prescribing information. Full prescribing information is available upon request.

LENVIMA® Abbreviated Prescribing Information

Indications:
LENVIMA® is indicated for the treatment of patients with locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer (DTC).
LENVIMA® is indicated in combination with everolimus for the treatment of patients with advanced renal cell carcinoma (RCC) following one prior vascular endothelial growth factor (VEGF)-targeted therapy.
LENVIMA® is indicated for the first-line treatment of patients with unresectable hepatocellular carcinoma (HCC).
LENVIMA®, in combination with pembrolizumab, is indicated for the treatment of patients with advanced endometrial carcinoma that is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR), who have disease progression following prior chemotherapy in the metastatic setting and are not candidates for curative surgery or radiation.

Contraindications:
Hypersensitivity to the active substance or to any of the excipients.

Adverse Reactions (all grades):
Differentiated Thyroid Cancer
The most frequently reported adverse reactions in (occurring in ≥30% of patients) are hypertension, fatigue, diarrhea, arthralgia/myalgia, decreased appetite, weight decreased, nausea, stomatitis, headache, vomiting, proteinuria, and palmar-plantar erythrodysaesthesia syndrome (PPE), abdominal pain, and dysphonia.

Renal Cell Carcinoma
The most frequently reported adverse reactions in the LENVIMA plus everolimus-treated group (occurring in ≥30% of patients) are diarrhea, fatigue, arthralgia/myalgia, decreased appetite, vomiting, nausea, stomatitis/oral inflammation, hypertension, peripheral edema, cough, abdominal pain, dyspnea, rash, weight decreased, hemorrhagic events, and proteinuria.

Hepatocellular Carcinoma
The most common adverse reactions observed in the LENVIMA-treated patients (≥20%) were, in order of decreasing frequency, hypertension, fatigue, diarrhea, decreased appetite, arthralgia/myalgia, decreased weight, abdominal pain, palmar-plantar erythrodysesthesia syndrome, proteinuria, dysphonia, hemorrhagic events, hypothyroidism, and nausea.

Endometrial Carcinoma
The most commonly reported adverse reactions (≥40% of subjects) were hypertension, diarrhea, fatigue, decreased appetite, hypothyroidism and nausea.
For further information, refer to the product package insert.

References:
1. KEYTRUDA® Local Product Circular Feb 2022.
2. LENVIMA® Prescribing Information Nov 2020.
3. Makker V, Taylor M, Aghajanian C, et al. Lenvatinib plus pembrolizumab in patients with advanced endometrial cancer. *J Clin Oncol*. 2020;38:1–13. doi:10.1200/JCO.19.02627. Online ahead of print. Accessed May 22, 2020
4. Makker V, Taylor M, Aghajanian C, et al. Supplementary appendix to: Lenvatinib plus pembrolizumab in patients with advanced endometrial cancer. (https://ascopubs.org/doi/suppl/10.1200/JCO.19.02627. Online ahead of print.) Accessed March 17, 2020.
5. Pardoll DM. The blockade of immune checkpoints in cancer immunotherapy. *Nat Rev Cancer*. 2012;12(4):252–264.
6. Kudo M. Lenvatinib may drastically change the treatment landscape of hepatocellular carcinoma. *Liver Cancer*. 2018;7(1):1–19.

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