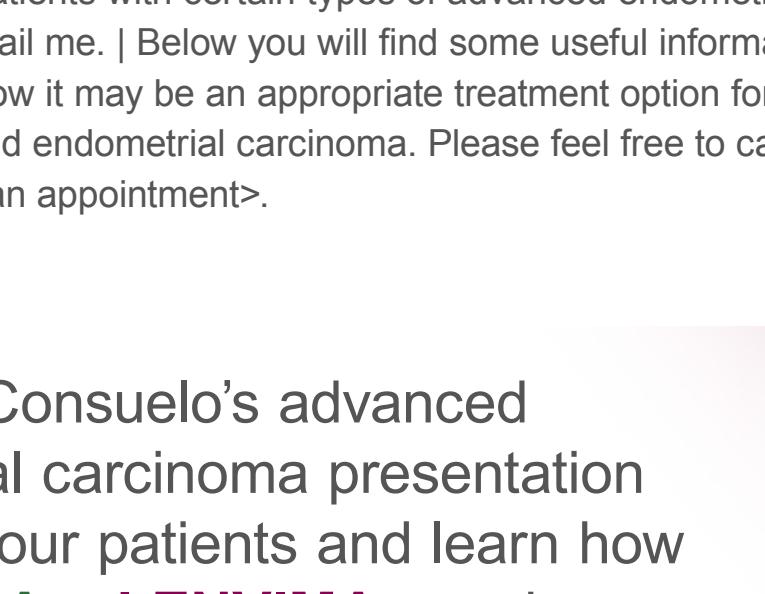


From: {{customText##accLname####accFname####accFname## ##accLname##}},

Subject: How would you treat a patient with Consuelo's characteristics?

Review the following profile and consider how you would treat similarly eligible patients.



HTML alt text:
KEYTRUDA® (pembrolizumab)
Injection 100 mg; LENVIMA®
(lenvatinib) capsules 10mg and
4 mg

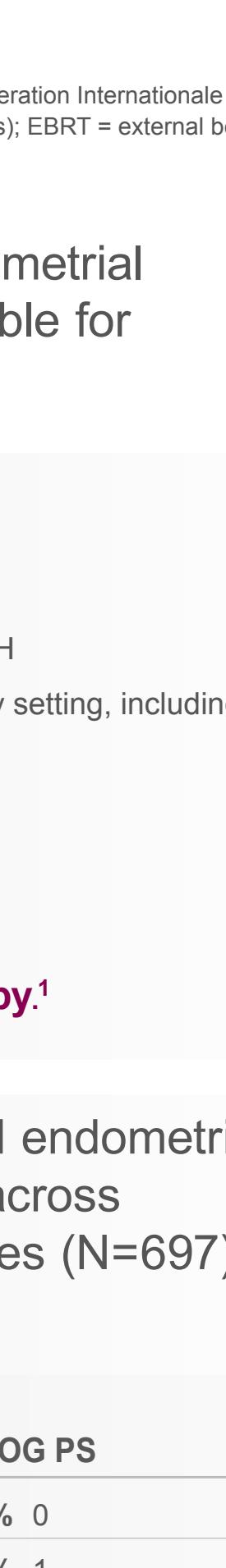
{}{{customText##Dear##Hello##Hi##Good morning##Good afternoon##Good evening##}};

{}{{customText##Dr##Mr##Ms##Miss##Prof##}};

{}{{customText###accLname####accFname####accFname## ##accLname##}};

<I'm sorry to have missed you during my recent visit. Below is some useful information about KEYTRUDA + LENVIMA and how it may be an appropriate treatment option for your patients with certain types of advanced endometrial carcinoma. Please feel free to call or email me if you have questions or would like to schedule an appointment. I was great meeting you during my last visit to your office. As discussed, below is some useful information about KEYTRUDA + LENVIMA and how it may be an appropriate treatment option for your patients with certain types of advanced endometrial carcinoma. Please feel free to call or email me. I below will find some useful information about KEYTRUDA + LENVIMA and how it may be an appropriate treatment option for your patients with certain types of advanced endometrial carcinoma. Please feel free to call or email me if you would like to schedule an appointment>

Compare Consuelo's advanced endometrial carcinoma presentation to that of your patients and learn how **KEYTRUDA + LENVIMA** may be an appropriate treatment option



Hypothetical patient.

Indication for KEYTRUDA + LENVIMA

LENVIMA, in combination with KEYTRUDA, 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.

Summary of Warnings and Precautions for LENVIMA

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.

See below for additional Selected Safety Information for LENVIMA.

Consuelo:

• 69-year-old woman

Initial Presentation:

- Diagnosis: Grade 3 endometrial carcinoma
- Endometrial biopsy grade: Grade 3 endometrial carcinoma
- Comorbidities: Type 2 diabetes
- Biomarker status: pMMR or not MSI-H
- ECOG PS: 1

Initial Treatment:

- Surgery: Total abdominal hysterectomy with bilateral salpingo-oophorectomy
- Surgical staging: FIGO stage III
- Adjuvant treatment: Carboplatin/paclitaxel/EBRT
- Treatment response: Recurrence at 2-month follow-up (lung metastases)

Consuelo may be an appropriate patient for KEYTRUDA + LENVIMA.

ECOG PS = Eastern Cooperative Oncology Group performance status; FIGO = Federation Internationale de Gynecologie et d'Obstetrique (International Federation of Gynecology and Obstetrics); EBRT = external beam radiation therapy.

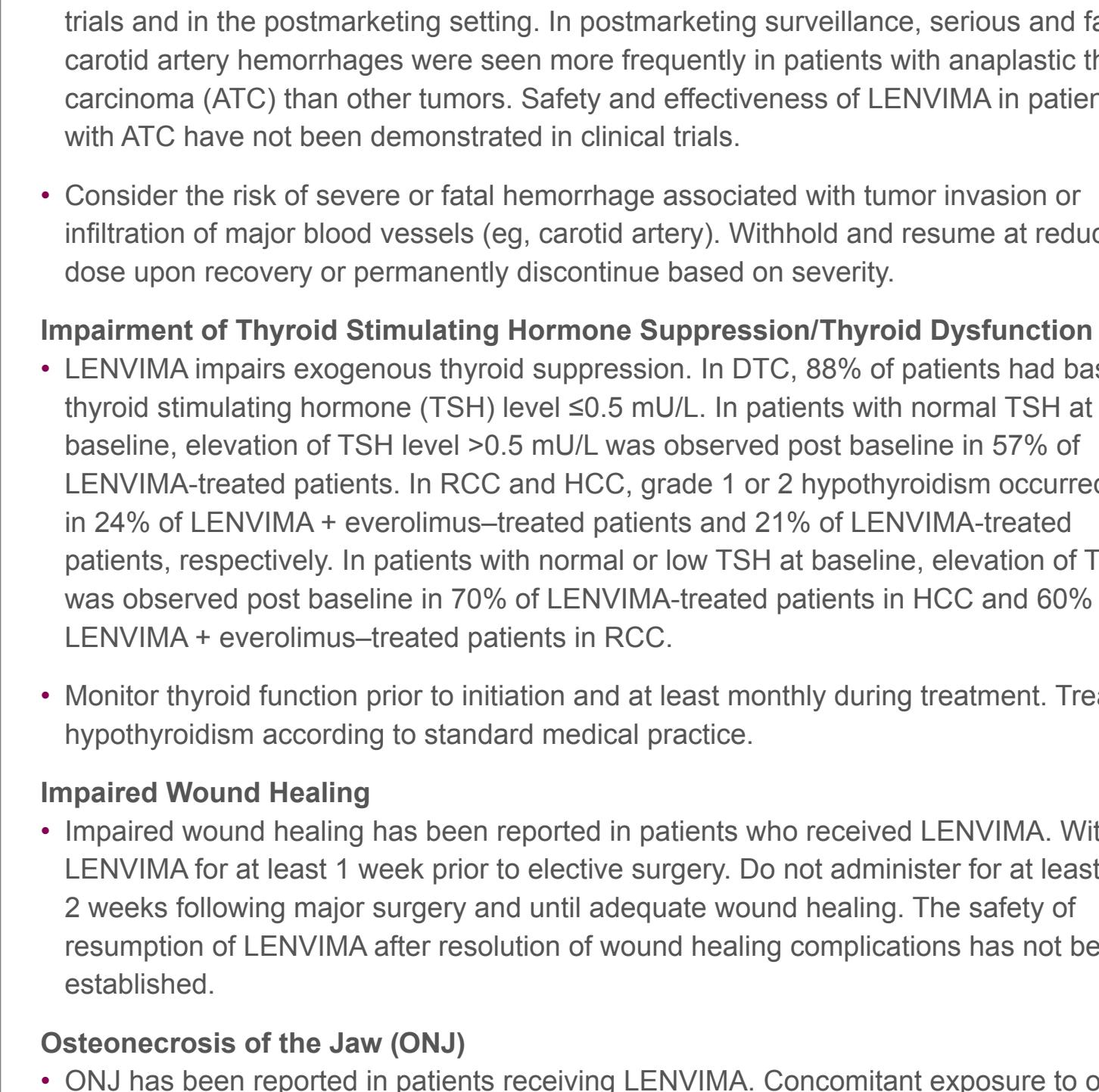
Identify other patients with advanced endometrial carcinoma like Consuelo who may be eligible for treatment with **KEYTRUDA + LENVIMA**.

Eligibility Criteria (all criteria must be met):

- ✓ Advanced endometrial carcinoma
- ✓ pMMR, as determined by an FDA-approved test, or not MSI-H
- ✓ Disease progression following a prior systemic therapy in any setting, including in the neoadjuvant and adjuvant settings
- ✓ Not a candidate for curative surgery or radiation

Earliest eligibility for KEYTRUDA + LENVIMA: Following prior systemic therapy.¹

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



Selected Safety Information for LENVIMA

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. Withdraw and resume at reduced dose when hypertension is controlled or permanently discontinue based on severity.

See below for additional Selected Safety Information for LENVIMA.

Choose KEYTRUDA + LENVIMA for your appropriate patients with advanced endometrial carcinoma.

See Efficacy and Safety Information >

Links to the Endo page of the KEYTRUDA + LENVIMA HCP Landing Page.

Selected Safety Information for LENVIMA (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. Withdraw and resume at reduced dose upon recovery or permanently discontinue based on severity.

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.

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.

• 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. Withdraw and resume at reduced dose upon recovery or permanently discontinue based on severity.

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. Withdraw 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.

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, bradycardia, tachycardia, or those who are taking drugs known to prolong the QTc interval, including class Ia and III antiarrhythmics. Withdraw and resume at reduced dose upon recovery based on severity.

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. Withdraw 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. Withdraw and resume at reduced dose upon recovery or permanently discontinue depending on severity and persistence of neurologic symptoms.

Hemorrhagic Events

- Serious including fatal hemorrhagic events can occur with LENVIMA. In DTC, RCC, and HCC clinical trials, hemorrageic 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 6% of LENVIMA + everolimus-treated patients, and 1 fatal cerebral hemorrhage in 1%. In HCC, grade 3-5 hemorrhage occurred in 5% of LENVIMA-treated patients, including 7 fatal hemorrhagic events. 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). Withdraw and resume at reduced dose upon recovery or permanently discontinue 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. 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).

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

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