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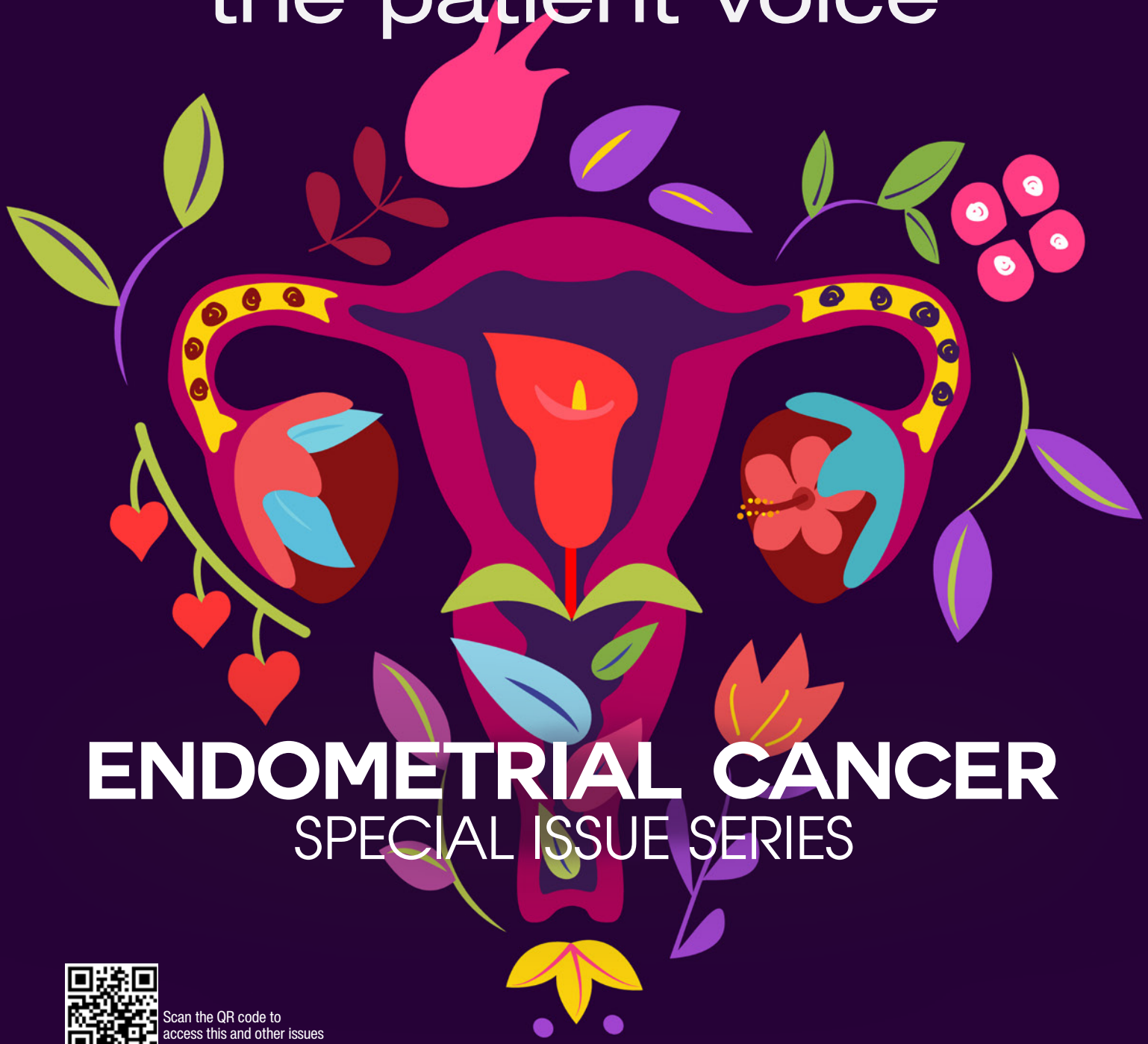

ENDOMETRIAL CANCER

SPECIAL ISSUE SERIES

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For people with certain types of advanced endometrial cancer

Living longer is possible with KEYTRUDA + LENVIMA

In a clinical study of patients with certain types of advanced endometrial cancer, **52% (181 out of 346) of patients taking KEYTRUDA + LENVIMA were alive at the time of follow-up** compared to 42% (148 out of 351) of patients receiving the chemotherapy medicines doxorubicin or paclitaxel.

KEYTRUDA and LENVIMA are prescription medicines used together to treat a kind of uterine cancer called advanced endometrial carcinoma when a laboratory test shows that your tumor is mismatch repair proficient (pMMR) or not microsatellite instability-high (MSI-H), **and** you have received anti-cancer treatment, and it is no longer working, **and** your cancer cannot be cured by surgery or radiation.

It is not known if LENVIMA is safe and effective in children.

KEYTRUDA + LENVIMA is not chemotherapy.

Important Safety Information for KEYTRUDA

KEYTRUDA is a medicine that may treat certain cancers by working with your immune system. KEYTRUDA can cause your immune system to attack normal organs and tissues in any area of your body and can affect the way they work. These problems can sometimes become severe or life-threatening and can lead to death. You can have more than one of these problems at the same time. These problems may happen any time during treatment or even after your treatment has ended.

Call or see your health care provider right away if you develop any signs or symptoms of the following problems or if they get worse. These are not all of the signs and symptoms of immune system problems that can happen with KEYTRUDA:

Lung problems: cough, shortness of breath, or chest pain.

Intestinal problems: diarrhea (loose stools) or more frequent bowel movements than usual; stools that are black, tarry, sticky, or have blood or mucus; or severe stomach-area (abdomen) pain or tenderness.

Liver problems: yellowing of your skin or the whites of your eyes; severe nausea or vomiting; pain on the right side of your stomach area (abdomen); dark urine (tea colored); or bleeding or bruising more easily than normal.

Hormone gland problems: headaches that will not go away or unusual headaches; eye sensitivity to light; eye problems; rapid heartbeat; increased sweating; extreme tiredness; weight gain or weight loss; feeling more hungry or thirsty than usual; urinating more often than usual; hair loss; feeling cold; constipation; your voice gets deeper; dizziness or fainting; changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness.

Kidney problems: decrease in the amount of your urine; blood in your urine; swelling of your ankles; loss of appetite.

Skin problems: rash; itching; skin blistering or peeling; painful sores or ulcers in your mouth or in your nose, throat, or genital area; fever or flu-like symptoms; swollen lymph nodes.

Important Safety Information for KEYTRUDA continued on the next page.

KEYTRUDA® (pembrolizumab) Injection 100 mg

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

Actor portrayal.

Ask your doctor today if KEYTRUDA + LENVIMA is right for you
KeytrudaLenvima.com/AdvancedEndo

Important Safety Information for LENVIMA

LENVIMA may cause serious side effects, including:

High blood pressure (hypertension): High blood pressure is a common side effect of LENVIMA and can be serious. Your blood pressure should be well controlled before you start taking LENVIMA. Your healthcare provider should check your blood pressure regularly during treatment with LENVIMA. If you develop blood pressure problems, your healthcare provider may prescribe medicine to treat your high blood pressure.

Heart problems: LENVIMA can cause serious heart problems that may lead to death. Call your healthcare provider right away if you get symptoms of heart problems, such as shortness of breath or swelling of your ankles.

Problem with blood clots in your blood vessels (arteries): Get emergency medical help right away if you get any of the following symptoms: severe chest pain or pressure; pain in your arms, back, neck, or jaw; shortness of breath; numbness or weakness on one side of your body; trouble talking; sudden severe headache; sudden vision changes.

Liver problems: LENVIMA may cause liver problems that may lead to liver failure and death. Your healthcare provider will check your liver function before and during treatment with LENVIMA. Tell your healthcare provider right away if you have any of the following symptoms: your skin or the white part of your eyes turn yellow (jaundice); dark "tea-colored" urine; light-colored bowel movements (stools); feeling drowsy, confused or loss of consciousness.

Kidney problems: Kidney failure, which can lead to death, has happened with LENVIMA treatment. Your healthcare provider should do regular blood tests to check your kidneys.

Increased protein in your urine (proteinuria): Proteinuria is a common side effect of LENVIMA and can be serious. Your healthcare provider should check your urine for protein before and during your treatment with LENVIMA.

Diarrhea: Diarrhea is a common side effect of LENVIMA and can be serious. If you get diarrhea, ask your healthcare provider about what medicines you can take to treat your diarrhea. It is important to drink more water when you get

Important Safety Information for LENVIMA continued on the next page.

Important Safety Information for KEYTRUDA *(continued)*

Problems can also happen in other organs and tissues. Signs and symptoms of these problems may include: chest pain; irregular heartbeat; shortness of breath; swelling of ankles; confusion; sleepiness; memory problems; changes in mood or behavior; stiff neck; balance problems; tingling or numbness of the arms or legs; double vision; blurry vision; sensitivity to light; eye pain; changes in eyesight; persistent or severe muscle pain or weakness; muscle cramps; low red blood cells; bruising.

Infusion reactions that can sometimes be severe or life-threatening. Signs and symptoms of infusion reactions may include chills or shaking, itching or rash, flushing, shortness of breath or wheezing, dizziness, feeling like passing out, fever, and back pain.

Rejection of a transplanted organ. Your health care provider should tell you what signs and symptoms you should report and they will monitor you, depending on the type of organ transplant that you have had.

Complications, including graft-versus-host disease (GVHD), in people who have received a bone marrow (stem cell) transplant that uses donor stem cells (allogeneic). These complications can be serious and can lead to death. These complications may happen if you underwent transplantation either before or after being treated with KEYTRUDA. Your health care provider will monitor you for these complications.

Getting medical treatment right away may help keep these problems from becoming more serious. Your health care provider will check you for these problems during treatment with KEYTRUDA. They may treat you with corticosteroid or hormone replacement medicines. They may also need to delay or completely stop treatment with KEYTRUDA if you have severe side effects.

Before you receive KEYTRUDA, tell your health care provider if you have immune system problems such as Crohn's disease, ulcerative colitis, or lupus; have had an organ transplant or have had or plan to have a bone marrow (stem cell) transplant that uses donor stem cells (allogeneic); have had radiation treatment in your chest area; have a condition that affects your nervous system, such as myasthenia gravis or Guillain-Barré syndrome.

If you are pregnant or plan to become pregnant, tell your health care provider. KEYTRUDA can harm your unborn baby. If you are able to become pregnant, you will be given a pregnancy test before you start treatment. Use effective birth control during treatment and for at least 4 months after your final dose of KEYTRUDA. Tell them right away if you think you may be pregnant or you become pregnant during treatment with KEYTRUDA.

Tell your health care provider if you are breastfeeding or plan to breastfeed. It is not known if KEYTRUDA passes into your breast milk. Do not breastfeed during treatment with KEYTRUDA and for 4 months after your final dose of KEYTRUDA.

Tell your health care provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Common side effects of KEYTRUDA when given with LENVIMA include low levels of thyroid hormone; high blood pressure; feeling tired; diarrhea; joint and muscle pain; nausea; decreased appetite; vomiting; mouth sores; weight loss; stomach-area (abdominal) pain; urinary tract infection; protein in your urine; constipation; headache; bleeding; blisters or rash on the palms of your hands and soles of your feet; hoarseness; rash; liver problems; and kidney problems.

These are not all the possible side effects of KEYTRUDA. Talk to your health care provider for medical advice about side effects.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit **www.fda.gov/medwatch** or call 1-800-FDA-1088.

Please read the adjacent Important Information about KEYTRUDA and discuss it with your doctor.

Speak with your doctor today to discuss if KEYTRUDA + LENVIMA could be right for you

KEYTRUDA® (pembrolizumab) Injection 100 mg

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

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Important Safety Information for LENVIMA *(continued)*

diarrhea. Tell your healthcare provider or go to the emergency room, if you are unable to drink enough liquids and your diarrhea is not able to be controlled.

An opening in the wall of your stomach or intestines (perforation) or an abnormal connection between two or more body parts (fistula): Get emergency medical help right away if you have severe stomach (abdomen) pain.

Changes in the electrical activity of your heart called QT prolongation: QT prolongation can cause irregular heartbeats that can be life threatening. Your healthcare provider will do blood tests before and during your treatment with LENVIMA to check the levels of potassium, magnesium, and calcium in your blood, and may check the electrical activity of your heart with an ECG.

Low levels of blood calcium (hypocalcemia): Your healthcare provider will check your blood calcium levels during treatment with LENVIMA and may tell you to take a calcium supplement if your calcium levels are low.

A condition called Reversible Posterior Leukoencephalopathy Syndrome (RPLS): Call your healthcare provider right away if you get severe headache, seizures, weakness, confusion, or blindness or change in vision.

Bleeding: LENVIMA may cause serious bleeding problems that may lead to death. Tell your healthcare provider if you have any signs or symptoms of bleeding during treatment with LENVIMA, including severe and persistent nose bleeds; vomiting blood; red or black (looks like tar) stools; blood in your urine; coughing up blood or blood clots; heavy or new onset vaginal bleeding.

Change in thyroid hormone levels: Your healthcare provider should check your thyroid hormone levels before starting and every month during treatment with LENVIMA.

Wound healing problems: Wound healing problems have happened in some people who take LENVIMA. Tell your healthcare provider if you plan to have any surgery before or during treatment with LENVIMA.

- You should stop taking LENVIMA at least 1 week before planned surgery.
- Your healthcare provider should tell you when you may start taking LENVIMA again after surgery.

Severe jaw bone problems (osteonecrosis). Severe jaw bone problems have happened in some people who take LENVIMA. Certain risk factors such as taking a bisphosphonate medicine or the medicine denosumab, having dental disease, or an invasive dental procedure may increase your risk of getting jaw bone problems. Your healthcare provider should examine your mouth before you start and during treatment with LENVIMA. Tell your dentist that you are taking LENVIMA. It is important for you to practice good mouth care during treatment with LENVIMA. Tell your healthcare provider right away if you have any signs or symptoms of jaw bone problems during treatment with LENVIMA, including jaw pain, toothache, or sores on your gums, and if you plan to have any dental procedures before or during treatment with LENVIMA.

- You should stop taking LENVIMA at least 1 week before planned dental surgery or invasive dental procedures.
- Your healthcare provider should tell you when you may start taking LENVIMA again after dental procedures.

The most common side effects of LENVIMA when given with KEYTRUDA include decrease in thyroid hormone levels, increased blood pressure, tiredness, diarrhea, joint and muscle pain, nausea, decreased appetite, vomiting, mouth sores, weight loss, stomach-area (abdominal) pain, urinary tract infection, protein in your urine, constipation, headache, bleeding, rash, redness, itching, or peeling of your skin on your hands and feet, hoarseness, and rash.

LENVIMA may cause fertility problems in males and females and can harm your unborn baby. Tell your healthcare provider if you are:

- pregnant or plan to become pregnant. For females who are able to become pregnant, your healthcare provider should do a pregnancy test before you start treatment with LENVIMA. Use an effective method of birth control during treatment with LENVIMA and for at least 30 days after the last dose of LENVIMA
- breastfeeding or plan to breastfeed. It is not known if LENVIMA passes into your breast milk. Do not breastfeed during treatment with LENVIMA and for at least 1 week after the last dose

Your healthcare provider may need to reduce your dose of LENVIMA, or delay or completely stop treatment if you have certain side effects.

These are not all the possible side effects of LENVIMA. Call your doctor for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088 or visit **www.fda.gov/medwatch**.

Please read the adjacent Important Information about LENVIMA and discuss it with your doctor.

Important Information About KEYTRUDA® (pembrolizumab) injection 100 mg. Please speak with your healthcare professional regarding KEYTRUDA (pronounced key-true-duh). Only your healthcare professional knows the specifics of your condition and how KEYTRUDA may work with your overall treatment plan. If you have any questions about KEYTRUDA, speak with your healthcare professional. **℞ONLY**

What is the most important information I should know about KEYTRUDA?

KEYTRUDA is a medicine that may treat certain cancers by working with your immune system. KEYTRUDA can cause your immune system to attack normal organs and tissues in any area of your body and can affect the way they work. These problems can sometimes become severe or life-threatening and can lead to death. You can have more than one of these problems at the same time. These problems may happen anytime during treatment or even after your treatment has ended.

Call or see your healthcare provider right away if you develop any new or worsening signs or symptoms, including:

Lung problems

- cough
- shortness of breath
- chest pain

Intestinal problems

- diarrhea (loose stools) or more frequent bowel movements than usual
- stools that are black, tarry, sticky, or have blood or mucus
- severe stomach-area (abdomen) pain or tenderness

Liver problems

- yellowing of your skin or the whites of your eyes
- severe nausea or vomiting
- pain on the right side of your stomach area (abdomen)
- dark urine (tea colored)
- bleeding or bruising more easily than normal

Hormone gland problems

- headaches that will not go away or unusual headaches
- eye sensitivity to light
- eye problems
- rapid heartbeat
- increased sweating
- extreme tiredness
- weight gain or weight loss
- feeling more hungry or thirsty than usual
- urinating more often than usual
- hair loss
- feeling cold
- constipation
- your voice gets deeper
- dizziness or fainting
- changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness

Kidney problems

- decrease in your amount of urine
- swelling of your ankles
- loss of appetite
- blood in your urine

Skin problems

- rash
- itching
- skin blistering or peeling
- painful sores or ulcers in your mouth or in your nose, throat, or genital area
- fever or flu-like symptoms
- swollen lymph nodes

Problems can also happen in other organs and tissues. These are not all of the signs and symptoms of immune system problems that can happen with KEYTRUDA. Call or see your healthcare provider right away for any new or worsening signs or symptoms, which may include:

- chest pain, irregular heartbeat, shortness of breath, swelling of ankles
- confusion, sleepiness, memory problems, changes in mood or behavior, stiff neck, balance problems, tingling or numbness of the arms or legs
- double vision, blurry vision, sensitivity to light, eye pain, changes in eyesight
- persistent or severe muscle pain or weakness, muscle cramps
- low red blood cells, bruising

Infusion reactions that can sometimes be severe or life-threatening. Signs and symptoms of infusion reactions may include:

- chills or shaking
- dizziness
- itching or rash
- feeling like passing out
- flushing
- fever
- shortness of breath or wheezing
- back pain

Rejection of a transplanted organ. Your healthcare provider should tell you what signs and symptoms you should report and monitor you, depending on the type of organ transplant that you have had.

Complications, including graft-versus-host-disease (GVHD), in people who have received a bone marrow (stem cell) transplant that uses donor stem cells (allogeneic). These complications can be serious and can lead to death. These complications may happen if you underwent transplantation either before or after being treated with KEYTRUDA. Your healthcare provider will monitor you for these complications.

Continued on next page.

Getting medical treatment right away may help keep these problems from becoming more serious. Your healthcare provider will check you for these problems during treatment with KEYTRUDA. Your healthcare provider may treat you with corticosteroid or hormone replacement medicines. Your healthcare provider may also need to delay or completely stop treatment with KEYTRUDA if you have severe side effects.

What is KEYTRUDA?

KEYTRUDA is a prescription medicine used to treat:

- a kind of kidney cancer called renal cell carcinoma (RCC).
  - KEYTRUDA may be used with the medicine lenvatinib as your first treatment when your kidney cancer has spread or cannot be removed by surgery (advanced RCC).
- a kind of uterine cancer called advanced endometrial carcinoma.

KEYTRUDA may be used with the medicine lenvatinib:

- when a laboratory test shows that your tumor is mismatch repair proficient (pMMR) or not microsatellite instability-high (MSI-H), **and**
- you have received anti-cancer treatment, and it is no longer working, **and**
- your cancer cannot be cured by surgery or radiation.

Before receiving KEYTRUDA, tell your healthcare provider about all of your medical conditions, including if you:

- have immune system problems such as Crohn's disease, ulcerative colitis, or lupus
- have received an organ transplant
- have received or plan to receive a stem cell transplant that uses donor stem cells (allogeneic)
- have received radiation treatment to your chest area
- have a condition that affects your nervous system, such as myasthenia gravis or Guillain-Barré syndrome
- are pregnant or plan to become pregnant. KEYTRUDA can harm your unborn baby.

  Females who are able to become pregnant:
  - Your healthcare provider will give you a pregnancy test before you start treatment with KEYTRUDA.
  - You should use an effective method of birth control during and for at least 4 months after the final dose of KEYTRUDA. Talk to your healthcare provider about birth control methods that you can use during this time.
  - Tell your healthcare provider right away if you think you may be pregnant or if you become pregnant during treatment with KEYTRUDA.
- are breastfeeding or plan to breastfeed. It is not known if KEYTRUDA passes into your breast milk. Do not breastfeed during treatment with KEYTRUDA and for 4 months after your final dose of KEYTRUDA.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How will I receive KEYTRUDA?

- Your healthcare provider will give you KEYTRUDA into your vein through an intravenous (IV) line over 30 minutes.
- In adults, KEYTRUDA is usually given every 3 weeks or 6 weeks depending on the dose of KEYTRUDA that you are receiving.
- Your healthcare provider will decide how many treatments you need.
- Your healthcare provider will do blood tests to check you for side effects.
- If you miss any appointments, call your healthcare provider as soon as possible to reschedule your appointment.

What are the possible side effects of KEYTRUDA?
KEYTRUDA can cause serious side effects. See "What is the most important information I should know about KEYTRUDA?"

Common side effects of KEYTRUDA when given with lenvatinib include: low levels of thyroid hormone, high blood pressure, feeling tired, diarrhea, joint and muscle pain, nausea, decreased appetite, vomiting, mouth sores, weight loss, stomach-area (abdominal) pain, urinary tract infection, protein in your urine, constipation, headache, bleeding, blisters or rash on the palms of your hands and soles of your feet, hoarseness, rash, liver problems, and kidney problems.

These are not all the possible side effects of KEYTRUDA.

Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of KEYTRUDA

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. You can ask your pharmacist or healthcare provider for information about KEYTRUDA that is written for health professionals.

Based on Medication Guide usmg-mk3475-iv-2208r051 revised August 2022.

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PATIENT INFORMATION for LENVIMA® (lehn-veema) (lenvatinib) 10 mg and 4 mg capsules for oral use

What is LENVIMA?

LENVIMA is a prescription medicine that is used to treat people with certain kinds of cancer.

- LENVIMA is used to treat adults with a type of kidney cancer called advanced renal cell carcinoma (RCC):
  - along with the medicine pembrolizumab as your first treatment when your kidney cancer has spread or cannot be removed by surgery.
- LENVIMA is used along with another medicine called pembrolizumab to treat advanced endometrial carcinoma (EC), a type of uterine cancer:
  - when a laboratory test shows that your tumor is mismatch repair proficient (pMMR) or not microsatellite instability-high (MSI-H), **and**
  - you have received anti-cancer treatment, and it is no longer working, **and**
  - your cancer cannot be cured by surgery or radiation.

It is not known if LENVIMA is safe and effective in children.

Before you take LENVIMA, tell your healthcare provider about all of your medical conditions, including if you:

- have high blood pressure
- have heart problems
- have a history of blood clots in your arteries (type of blood vessel), including stroke, heart attack, or change in vision
- have or have had liver or kidney problems
- have a history of a tear (perforation) in your stomach or intestine, or an abnormal connection between two or more body parts (fistula)
- have headaches, seizures, or vision problems
- have any bleeding problems
- plan to have surgery, a dental procedure, or have had a recent surgery. You should stop taking LENVIMA at least 1 week before planned surgery. See **"What are the possible side effects of LENVIMA?"**
- are pregnant or plan to become pregnant. LENVIMA can harm your unborn baby.

  Females who are able to become pregnant:
  - Your healthcare provider should do a pregnancy test before you start treatment with LENVIMA.
  - You should use an effective method of birth control during treatment with LENVIMA and for at least 30 days after the last dose of LENVIMA. Talk with your healthcare provider about birth control methods you can use during this time. Tell your healthcare provider right away if you become pregnant or think you are pregnant during treatment with LENVIMA.
- are breastfeeding or plan to breastfeed. It is not known if LENVIMA passes into your breast milk. Do not breastfeed during treatment with LENVIMA and for at least 1 week after the last dose.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Especially tell your healthcare provider if you are taking, or have taken, an osteoporosis medicine.

Know the medicines you take. Keep a list of your medicines to show to your healthcare provider and pharmacist when you get a new medicine.

How should I take LENVIMA?

- Take LENVIMA exactly as your healthcare provider tells you to take it.
- Your healthcare provider will tell you how much LENVIMA to take and when to take it. Your healthcare provider may change your dose during treatment, stop treatment for some time, or completely stop treatment with LENVIMA if you have side effects.
- Take LENVIMA 1 time each day at the same time, with or without food.
- If you miss a dose of LENVIMA, take it as soon as you remember. If your next dose is due within 12 hours, skip the missed dose and take the next dose at your regular time.
- If you cannot swallow LENVIMA capsules whole:
  - Use a medicine cup to measure about one tablespoon of water or apple juice and place into a small glass.
  - Place the LENVIMA capsules into the small glass without breaking or crushing them.
  - Leave the capsules in the liquid for at least 10 minutes.
  - Stir the contents of the glass for at least 3 minutes.
  - Drink the mixture. After drinking, rinse the glass with a small amount of additional water or apple juice and swallow the liquid.
- If you take too much LENVIMA, call your healthcare provider or go to the nearest hospital emergency room right away.

What are the possible side effects of LENVIMA?

LENVIMA may cause serious side effects, including:

- **High blood pressure (hypertension).** High blood pressure is a common side effect of LENVIMA and can be serious. Your blood pressure should be well controlled before you start taking LENVIMA. Your healthcare provider should check your blood pressure regularly during treatment with LENVIMA. If you develop blood pressure problems, your healthcare provider may prescribe medicine to treat your high blood pressure.

Continued on next page.

- **Heart problems.** LENVIMA can cause serious heart problems that may lead to death. Call your healthcare provider right away if you get symptoms of heart problems, such as shortness of breath or swelling of your ankles.
- **Problem with blood clots in your blood vessels (arteries).** Get emergency medical help right away if you get any of the following symptoms:
  - severe chest pain or pressure
  - pain in your arms, back, neck or jaw
  - shortness of breath
  - numbness or weakness on one side of your body
  - trouble talking
  - sudden severe headache
  - sudden vision changes
- **Liver problems.** LENVIMA may cause liver problems that may lead to liver failure and death. Your healthcare provider will check your liver function before and during treatment with LENVIMA. Tell your healthcare provider right away if you have any of the following symptoms:
  - your skin or the white part of your eyes turns yellow (jaundice)
  - dark "tea colored" urine
  - light-colored bowel movements (stools)
  - feeling drowsy, confused or loss of consciousness
- **Kidney problems.** Kidney failure, which can lead to death, has happened with LENVIMA treatment. Your healthcare provider should do regular blood tests to check your kidneys.
- **Increased protein in your urine (proteinuria).** Proteinuria is a common side effect of LENVIMA and can be serious. Your healthcare provider should check your urine for protein before and during your treatment with LENVIMA.
- **Diarrhea.** Diarrhea is a common side effect of LENVIMA and can be serious. If you get diarrhea, ask your healthcare provider about what medicines you can take to treat your diarrhea. It is important to drink more water when you get diarrhea. Tell your healthcare provider or go to the emergency room if you are unable to drink enough liquids and your diarrhea is not able to be controlled.
- **An opening in the wall of your stomach or intestines (perforation) or an abnormal connection between two or more body parts (fistula).** Get emergency medical help right away if you have severe stomach (abdomen) pain.
- **Changes in the electrical activity of your heart called QT prolongation.** QT prolongation can cause irregular heartbeats that can be life threatening. Your healthcare provider will do blood tests before and during your treatment with LENVIMA to check the levels of potassium, magnesium, and calcium in your blood, and may check the electrical activity of your heart with an ECG.
- **Low levels of blood calcium (hypocalcemia).** Your healthcare provider will check your blood calcium levels during treatment with LENVIMA and may tell you to take a calcium supplement if your calcium levels are low.
- **A condition called Reversible Posterior Leukoencephalopathy Syndrome (RPLS).** Call your healthcare provider right away if you get severe headache, seizures, weakness, confusion, or blindness or change in vision.
- **Bleeding.** LENVIMA may cause serious bleeding problems that may lead to death. Tell your healthcare provider if you have any signs or symptoms of bleeding during treatment with LENVIMA, including:
  - severe and persistent nose bleeds
  - vomiting blood
  - red or black (looks like tar) stools
  - blood in your urine
  - coughing up blood or blood clots
  - heavy or new onset vaginal bleeding
- **Change in thyroid hormone levels.** Your healthcare provider should check your thyroid hormone levels before starting and every month during treatment with LENVIMA.
- **Wound healing problems.** Wound healing problems have happened in some people who take LENVIMA. Tell your healthcare provider if you plan to have any surgery before or during treatment with LENVIMA.
  - You should stop taking LENVIMA at least 1 week before planned surgery.
  - Your healthcare provider should tell you when you may start taking LENVIMA again after surgery.
- **Severe jaw bone problems (osteonecrosis).** Severe jaw bone problems have happened in some people who take LENVIMA. Certain risk factors such as taking a bisphosphonate medicine or the medicine denosumab, having dental disease, or an invasive dental procedure may increase your risk of getting jaw bone problems. Your healthcare provider should examine your mouth before you start and during treatment with LENVIMA. Tell your dentist that you are taking LENVIMA. It is important for you to practice good mouth care during treatment with LENVIMA. Tell your healthcare provider right away if you get signs or symptoms of jaw bone problems during treatment with LENVIMA, including jaw pain, toothache, or sores on your gums. Tell your healthcare provider if you plan to have any dental procedures before or during treatment with LENVIMA. You should avoid having invasive dental procedures if possible, during treatment with LENVIMA. Stopping your bisphosphonate medicine before an invasive dental procedure may help decrease your risk of getting these jaw problems.
  - You should stop taking LENVIMA at least 1 week before planned dental surgery or invasive dental procedures.
  - Your healthcare provider should tell you when you may start taking LENVIMA again after dental procedures.

Continued on next page.

The most common side effects of LENVIMA when given with pembrolizumab include:

- decrease in thyroid hormone levels
- increased blood pressure
- tiredness
- diarrhea
- joint and muscle pain
- nausea
- decreased appetite
- vomiting
- mouth sores
- weight loss
- stomach-area (abdomen) pain
- urinary tract infection
- protein in your urine
- constipation
- headache
- bleeding
- rash, redness, itching, or peeling of your skin on your hands and feet
- hoarseness
- rash

LENVIMA may cause fertility problems in males and females. Talk to your healthcare provider if this is a concern for you.

Your healthcare provider may need to reduce your dose of LENVIMA, or delay or completely stop treatment, if you have certain side effects.

These are not all the possible side effects of LENVIMA.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store LENVIMA?

- Store LENVIMA at room temperature, between 68°F to 77°F (20°C to 25°C).

Keep LENVIMA and all medicines out of the reach of children.

General information about the safe and effective use of LENVIMA.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use LENVIMA for a condition for which it was not prescribed. Do not give LENVIMA to other people, even if they have the same symptoms you have. It may harm them. You can ask your healthcare provider or pharmacist for information about LENVIMA that is written for health professionals.

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table of contents

FOREWORD

By LILLIE D. SHOCKNEY, RN, BS, MAS, HON-ONN-CG

On behalf of the contributors to this issue of *CONQUER: the patient voice*, it is my pleasure to welcome you to this resource. You can also access these articles and past issues of *CONQUER* at www.conquer-magazine.com. I truly hope that you find the inspiration, hope, and education you need to best navigate your cancer journey in these pages.

With the ongoing COVID-19 pandemic, we would like to remind breast cancer survivors to work closely with their healthcare team to determine appropriate safety measures when receiving care.

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ECANA: Endometrial Cancer Action Network for African-Americans

An interview with Jacqueline Mbayo, Adrienne Moore, and Margie Wilson about the work of the ECANA community

By **KRISTIN SIYAHIAN**

The Endometrial Cancer Action Network for African-Americans, or ECANA, is an organization of women who come together to create support, community, and empowerment for any African-American woman affected by endometrial cancer. Many patient advocacy groups are founded by patients, but ECANA was founded by Kemi Doll, MD, of the University of Washington. Dr. Doll's vision was to bring together patients, doctors, survivors, community advocates, and professional leaders who share a common goal—improving the lives of Black women with this disease.

For newly diagnosed Black women, the ECANA website (ecanawomen.org) is a place to find educational resources about this disease, as well as a community of women who understand what they are going through. Women who are ready to give back can join ECANA in their national efforts to set a new standard of research.

I had the opportunity to speak with 3 women from ECANA—Jacqueline Mbayo, Adrienne Moore, and Margie Wilson—about the mission of ECANA, the popular Survivors' Sanctuary program, and the important work of connecting survivors and researchers. What follows is our thoughtful exchange.

Jacqueline Mbayo is the director of research partnerships at ECANA. After her diagnosis in 2017, Jacqueline has devoted her life to educating, empowering, and building community with Black women diagnosed with endometrial cancer.

Adrienne Moore serves as the director of peer support for the SISTER Study at the University of Washington as well as the director of programs for ECANA. She learned about ECANA after doing research about endometrial cancer in Black women after her diagnosis of endometrial cancer in 2016.

Margie Wilson is a 5-year endometrial cancer survivor and a patient partner, advocate, advisor, and director of fundraising for ECANA. Margie has 5 grandchildren who are the joy of her life!

Can you please tell us how and why ECANA was founded?

Margie: Yes, my pleasure. ECANA was founded by Dr. Kemi Doll, a gynecologic oncologist and researcher at the University of Washington. During her studies, Dr. Doll became aware of the huge gap in survival rates of Black women who were diagnosed with endometrial cancer. In fact, Black women were dying at higher rates than any other ethnic group. Dr. Doll decided to build a community of Black endometrial cancer survivors that would also include healthcare providers and advocates who would support, encourage, and be a resource for Black women dealing with endometrial cancer. In doing so, Dr. Doll hopes to improve the survival rates of Black women.

Can you tell us about the mission and goals of ECANA?

Adrienne: I'd be happy to. We are a group of women who have come together to create support, community, and empowerment for any African American affected by endometrial cancer.

We are doctors, patients, survivors, community advocates, and professional leaders all committed to 1 purpose—improving the lives of Black people affected by this disease. We know that healthcare for Black people is not as it should be, and we are here to bridge the gap. We are realistic and optimistic. We are here to motivate survivors and listen to survivors. On the ECANA site, we hope Black women with endometrial cancer find the community and knowledge they are looking for. And when that woman is ready to give back, we hope she will join us in our national efforts to set a new standard of research on this condition. Research that respects us, that is focused on what matters to us, and that is designed to improve our health and well-being.

Our mission is built on bridging the gaps among community, education, and research for Black endometrial cancer survivors.

The ECANA website provides survivors with several educational resources. Can you describe the practical tools a survivor will find on the site and how this information can empower her?

Adrienne: Education is a primary focus within our ECANA community. We want to equip Black endometrial cancer survivors with the tools and terms grounded in a conversational approach to the science of this disease. We don't want people to shy away from learning about this cancer because they feel intimidated by it. Instead, we want them to lean in, gain a sense of familiarity, and feel empowered by their new knowledge.

For example, our Learn the Lingo tile board is a relatable and interactive resource for our community. This is a practical tool women can use to learn many of the new terms they will need to know—whether it's about anatomy, procedures, or treatments.

ECANA has created a unique community where African American survivors can connect and share their stories. Can you speak about the importance of joining a community of survivors?

Adrienne: For many of the survivors in our community, the first time they heard about endometrial cancer was the day they were diagnosed. That speaks volumes not only about the need for more awareness programs in African American communities, but also about the need to connect with other Black women as part of their support network once they are diagnosed. What we have all learned as survivors is that when we are able to see ourselves and our journeys reflected in others, it helps our community thrive and brings hope to us all. Being cancer survivors comes with the innate ability to encourage and enlighten one another through our own survivorship stories, and that is part of what makes us unique.

ECANA recently celebrated the 2-year anniversary of its Survivors' Sanctuary. We'd love to learn more about this program and its impact on survivors.

Margie: Survivors' Sanctuary meets every other Friday via Zoom. Each meeting features chair yoga and conversation. Basically, we enjoy about 30 minutes of gentle, guided movement followed by conversation and connection.

Our gentle chair yoga has proved to help many of our women get moving again and to help them realize that they are able to engage in physical activity again.

After yoga, we talk. We give participants the opportunity to share anything related to their life or their cancer journey. The women learn from each other as they share stories and their personal experiences. We encourage connection, conversation, and relatability. I can tell you, one phrase that is repeated often in the Survivors' Sanctuary is "me too!" Those words can be very reassuring to hear.

Through movement, conversation, and relatability, the Survivors' Sanctuary is a place where Black women can come and connect with other endometrial cancer survivors who share their experiences.

ECANA promotes partnerships between academic researchers and Black women who have had endometrial cancer. We'd love to hear more about these partnerships and how they are advancing care.

Jacqueline: Yes, ECANA promotes partnerships between Black survivors and academic researchers to ensure that the issues that are important to survivors are heard and understood by researchers. This program gives Black endometrial cancer survivors the opportunity to share their perspectives and care experiences to inform the planning and implementation of academic research. This is especially important because Black women with endometrial cancer are underrepresented in academic research. These partnerships are advancing care because Black women with endometrial cancer are able to address aspects of the research in a way that researchers may not have considered, and it provides researchers with new insights to view problems.

The research collaboration helps to ensure that the research outcomes are focused on the things that patients value, such as quality of life and improving treatment options, because survival is not the only desired outcome. Black endometrial cancer survivors are viewed as equal stakeholders in the research partnership, and their contributions are greatly valued by academic researchers.

What advice would you give to a woman who is newly diagnosed with endometrial cancer?

Jacqueline: I've got this one.

1. Breathe.
2. Focus on getting well, and not on the cancer diagnosis.
3. Don't be hard on yourself.
4. Do everything you can to get educated about your endometrial cancer diagnosis and treatment, and do your best to complete your treatment.
5. Ask for help.
6. Celebrate every single win, like taking a walk, or making a meal for yourself.
7. Know that you can have a great life after an endometrial cancer diagnosis.

Can you share an ECANA success story?

Adrienne: One of ECANA's earliest success stories is the incredible opportunity we were given in 2019 to bring 12 Black endometrial cancer survivors together in Hawaii for the Society of Gynecologic Oncology annual meeting. We recognize this event as the first meeting of our community-building initiative of empowering women to go out in their communities to talk about endometrial cancer. The program is an evidence-based peer education program that aims to increase knowledge about endometrial cancer to empower and improve health outcomes for Black women with this disease.

These 12 women were from all over the country and knew very little about us and even less than that about each other. Despite that, they were all willing to take a chance on us and believed that we could do more to affect Black endometrial cancer survival together than we could alone.

After that meeting, each of these women went home to their communities with training, a knowledge base, communication tools, and a survivorship plan that included a commitment to endometrial cancer advocacy.

What's in the future for ECANA?

Margie: ECANA's future is bright! We are working toward developing biyearly conferences and nationwide fundraisers to promote awareness and visibility for Black women who are journeying through endometrial cancer.

Our goal is to be nationally known as the organization to come to for support and connection for Black women who are diagnosed with endometrial cancer. ♦

Beyond Chemotherapy: Immunotherapy Offers a New Treatment Option for Women with Endometrial Cancer

By **PRATIBHA S. BINDER, MD**
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Did you know that your own immune system has the ability to fight against cancer cells? Scientists have been studying the role of the immune system in recognizing and fighting cancer cells for over a century, but it has been only in the past few decades that multiple drugs that activate or turn on and regulate the immune system have been approved for the treatment of some cancers. Some of these immune activators and regulators, what is collectively called "immunotherapy," have recently been approved for the treatment of endometrial cancer, a cancer arising in the inside lining of the uterus.

The First Immunotherapy

The first immunotherapy drug tested in endometrial cancer clinical trials actually was approved very rapidly because it proved its benefit to cancer patients who had endometrial cancers with a certain immune environment, or "signature." This is known as an accelerated approval, and the drug was pembrolizumab, which is currently used for the treatment of solid organ cancers that have spread elsewhere in the body, including endometrial cancer, that expresses a specific type of immune signature. After this accelerated approval in May 2017, pembrolizumab received full approval for endometrial cancers with that same immune signature in March 2022. You may be asking "What is this pembrolizumab, how does it work, and what do you mean by immune signature?" Please allow me to explain.

How Does the Immune System Fight Cancer?

The immune system works by identifying foreign or "non-self" cells and then secreting chemicals that activate other parts of the immune system to fight against the foreign cells. This is how our body recognizes infections and then fights off bacteria and viruses that do not belong. Similarly, cancer cells are foreign because they have mutated enough to start looking different from our normal cells. However, our immune system does not fight cancer the same way it fights infections. This is because cancer cells have learned how to evade our immune system by either hiding from it or by putting on the brakes to deactivate or turn off the immune system. This is where pembrolizumab comes in. Pembrolizumab takes these brakes off and allows the immune system to recognize cancer cells as foreign again and also

OTHER IMMUNOTHERAPY MEDICATIONS THAT WORK SIMILARLY TO PEMBROLIZUMAB HAVE ALSO BEEN APPROVED IN THE TREATMENT OF ENDOMETRIAL CANCER.

allows activation of our "killer immune system" that then does the job of killing cancer cells.

What Is an Immune Signature?

Pembrolizumab itself works quite well in cancer cells that have a lot of mutations and have a lot of unrepaired DNA damage because those cancer cells look more foreign. That is the immune signature I mentioned above. Scientifically speaking, pembrolizumab is usually effective in cancers with a mismatch repair-deficient, microsatellite instability-high, or tumor mutational burden-high status. Special pathology tests are done to determine if the cancer cells display these features. Pembrolizumab was approved for the treatment of recurrent endometrial cancers with these immune signatures that cannot be cured with alternative anticancer treatment options, such as surgery, radiation, or chemotherapy.

While pembrolizumab led to a response in 46% of cancers with the above immune signature, it did not work so well in the patients with mismatch repair-*proficient*, microsatellite instability-*low*, and tumor mutational burden-*low* endometrial cancer status.[1] For these patients, another clinical trial was performed combining pembrolizumab with lenvatinib (a targeted treatment that inhibits cellular pathways and growth), and one study showed a response rate of 40% with this combination.[2] Another confirmatory study was done to show that patients receiving pembrolizumab with lenvatinib survived without their cancer progressing for almost twice as long as patients receiving chemotherapy (6.6 months vs 3.8 months).[3] The combination of pembrolizumab and lenvatinib was granted accelerated FDA approval in September 2019 and received full approval in July 2021.

Side Effects

The most common side effects of pembrolizumab can include fatigue, rash, musculoskeletal pain, diarrhea, fevers, cough, decreased appetite, itching, shortness of breath, constipation, pain, abdominal pain, and nausea. In some cases, pembrolizumab can overactivate the immune system to a point where it can affect normal glands and normal human organs, including the thyroid gland, pancreas, adrenal glands, lungs, colon, and others. Physicians using pembrolizumab are very well versed in the adverse effects and are constantly evaluating patients for early signs of any side effect. When pembrolizumab starts affecting normal organs, it is usually treated with corticosteroids, which suppresses the immune system temporarily.

The Future of Immunotherapy

Other immunotherapy medications, including dostarlimab, that work similarly to pembrolizumab have also been approved in the treatment of endometrial cancer. Immunotherapy is now also being studied in first-line treatment of endometrial cancer to see if incorporating these medications earlier can lead to higher cure rates in both early- and advanced-stage patients.

Conclusion

If you are dealing with a recurrence of your endometrial cancer and have not yet heard about immunotherapy, ask your treating oncologist if you might be a candidate now or in the near future. Some women get second opinions at large academic cancer centers so that doctors who specialize only in the treatment of endometrial cancer can weigh in on what your options may be now or later. Immunotherapy is now also being studied in endometrial cancer clinical trials at initial detection and diagnosis if the risk of recurrence is high enough to warrant anticancer therapy. Ask your treating oncologist if you are a candidate for a clinical trial near you. ♦

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Fertility After a Cancer Diagnosis

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You just received a cancer diagnosis. Panic ensues, as does a whirlwind of tests, processes, procedures, and an onslaught of questions, uncertainty, and emotions. Most patients enter fight or flight mode and focus on survival when they are told they have cancer. Focusing on what we know, what is to come, and how it impacts our life in the near and distant future is normal. However, there is a lot to consider that does not meet the eye and is not common knowledge, and that is where education and experts can help guide you.

So often, when an adolescent or young adult (AYA), defined as aged 15 to 39 years, is diagnosed with cancer, it comes as a complete surprise, *and* when presented with the possibility that fertility preservation should be considered because there is some likelihood of infertility, it is complete and utter shock. Fertility preservation becomes yet another thing to consider in the mounting list of to-dos, and unfortunately, it comes with an urgent timeline.

Every patient's cancer experience is unique. We all have our own life circumstances, different things we value and that motivate us. When considering our treatment options, the oncologist is the expert on the treatment plan, but as the patient, you are ultimately in the driver's seat. You get to decide, regardless of your reasoning, what you want to pursue or not pursue. Along with your treatment plan, fertility preservation should be one of those considerations that you get the final say in. It is worth asking your medical team about fertility-sparing treatment options whether or not you pursue fertility preservation at the time of diagnosis. It should be noted that fertility-sparing treatment for endometrial cancer is not the standard of care.[1]

Most patients do not come into a cancer diagnosis knowing that the cancer and different treatment options may cause infertility. Surgery, medications, chemotherapy, and radiation can all individually and in combination affect your future childbearing ability. The goal of fertility preservation is to preserve your ability to become pregnant. Eggs or embryos (eggs that have been fertilized by male sperm) may be preserved for future use in the event that treatment impacts your fertility. Ideally,

> MOST PATIENTS ENTER FIGHT OR FLIGHT MODE AND FOCUS ON SURVIVAL WHEN THEY ARE TOLD THEY HAVE CANCER.

fertility preservation discussions and the actual process of preserving is completed before any treatment commences.

Endometrial cancer (uterine cancer) is the most common gynecological cancer in women.[2] Depending on the staging, the grade of the cancer gives you and your medical team some indication of the impact on your future fertility. Low-grade endometrial cancer often has a bit less of a risk than high-grade. However, having a cancer in a reproductive organ should trigger a serious consideration of fertility preservation, as the chances of adverse effects to your fertility are greater than with other types of cancers.

As science and technology evolve, so do the long-term survival rates and the options for treatment, fertility preservation, and childbearing. Women with endometrial cancer have an 80% 5-year survival rate.[2] The possibility of a long and productive life is now seen more commonly, and thus the ability to build a family is something to take into consideration. Whether or not fertility preservation is pursued at the time of diagnosis and before treatment, there are options to build families, perhaps just not the way initially envisioned.

Things to Consider

Not literally, but figuratively, your voice should be the loudest in the room. You should feel empowered to voice your concerns, opinions, and desires and have them taken into consideration before a treatment plan is agreed upon. Having a mutual understanding will significantly help with compliance, satisfaction, and quality of life and hopefully lead to the health outcomes and family planning desired.

This is your health and life; you should feel comfortable with your treatment plan and medical team. You are always encouraged to seek second and third opinions.

Having the fertility preservation conversation multiple times is normal and should be encouraged. While it is most important to have this conversation before treatment, your desires and circumstances may change and influence future plans. Having posttreatment fertility assessments can help determine what your options are and the need for any interventions.

Just having the conversation about fertility preservation may provide hope. It's an ethical obligation of the medical team, and it can help manage expectations from the start.

Fertility Preservation Options

Fertility preservation is an option only for those who have reached puberty. For patients who are prepubescent, all fertility preservation options are experimental, meaning they are not the standard of care. For women, the standards of care are egg and embryo cryopreservation (a fancy way to say "freezing") or ovarian tissue cryopreservation. The latter is a process where a sample of your ovary is removed and stored. Women have 2 ovaries, 1 on either side of the uterus, and this is where your lifetime supply of immature eggs is stored. By storing this tissue, those eggs are also preserved. The other options that may be presented at this time are all experimental, but there may be some benefit to pursing them *if* standard options are not possible or available. Experimental options include ovarian suppression with a monthly injection, like Lupron, to put your ovaries into a medically induced hibernation to potentially preserve the eggs stored in them and protect them from the harmful effects of treatment.

The process of fertility preservation takes coordination. Either the educated patient brings up the topic with the medical team *or* the medical team brings it up with the patient at the time of diagnosis to allow for maximum time to pursue options and figure out logistics prior to beginning cancer treatment. The process of egg retrieval and storing eggs or embryos is similar to doing in vitro fertilization. It takes 2 to 4 weeks and requires many visits to a fertility clinic and reproductive endocrinologist and infertility (REI) specialist. It also requires daily injections to stimulate your ovaries to mature your egg follicles and subsequent blood tests to monitor the maturation of the eggs to indicate the best time for egg retrieval. Retrieving eggs is an outpatient procedure performed with anesthesia in the clinic, where many mature eggs are removed, analyzed, tested, and then frozen. Due to advances in medicine, the timing of doing fertility preservation does not have to coincide with your menstrual cycle. The

injections stimulate your hormones, and thus ovaries and eggs, to expedite the process.

If egg retrieval is initiated, it takes coordination between the REI specialist and the medical oncologist to ensure that a delay in starting treatment is not going to cause more harm than good. It also requires the REI specialist to do a thorough exam and consult, assess your health, weight, and medications to determine if this process is safe to consider. Often REI specialists will not do in-clinic fertility preservation and egg retrieval on patients with a body mass index over 45.

As a former AYA patient navigator, it was my job to inform my patients about fertility preservation and educate them on its importance and what the process would entail. In almost every instance where fertility preservation was pursued, the patient was able to do only 1 round of egg retrieval. To most patients, that is all that time and/or finances would allow. To most, it was something, and better than not pursuing it at all! I did have 1 patient with endometrial cancer do 2 rounds of egg retrieval prior to treatment to maximize her future chances of a biological child. Fortunately for her, this process was covered by her insurance due to a state mandate.

Check with your insurance to see if any part of the fertility process is covered. Even partial coverage is better than nothing at all. To find out if your state has a fertility preservation mandate, check the Alliance for Fertility Preservation website at www.allianceforfertilitypreservation.org.

Treatment Considerations for Endometrial Cancer

One of the more common, conservative, and noninvasive treatment options for low-grade, early-stage endometrial cancer is progestin hormone therapy. However, over time, the side effects of this treatment make compliance less likely.

Levonorgestrel-releasing intrauterine devices (IUDs) and gonadotropin-releasing hormones are other more conservative treatment options that can be used individually or in combination.

Adding in progesterone in combination with an IUD has been shown to lead to better outcomes and more successful pregnancies after treatment and remission.[2] However, each treatment option has risks and benefits that need to be considered.

Women who are on more conservative treatment regimens for early-stage endometrial cancer and do not achieve remission or who have disease progression may need to consider a total hysterectomy and/or removal of both ovaries, which unfortunately would cause permanent infertility and the inability to carry a child. A total hysterectomy and bilateral ovary removal are often considered when childbearing is complete to prevent future recurrence.

Another option for treatment, if indicated, is removal of the diseased endometrial tissue and implantation of an IUD. This is a possible fertility-sparing option to be discussed with your medical team.

When possible, women with endometrial cancer should be evaluated for conservative treatment options that would be fertility sparing. This requires serious and candid discussions with your medical team so that your family planning desires are considered and your health restored. ♦

A Checklist of Things to Consider

- What is your goal regarding family planning and child bearing?
- Have you talked with your medical team and/or reproductive endocrinologist and infertility specialist about fertility preservation?
- How will your treatments impact your future fertility?
  - If you want to pursue fertility preservation, can you delay the start of treatment? If so, by how much time?
- Does your insurance cover fertility preservation? Does your state have a fertility preservation mandate? Do you qualify for coverage?

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