



# Uterine clear cell carcinoma

## WHAT SHOULD I KNOW?



### DESCRIPTION OF THE TUMOR/CANCER TYPE

Uterine or endometrial clear cell carcinoma is a rare tumor subtype, accounting for less than 5% of all endometrial cancers. Patients with clear cell carcinoma of the uterus tend to be older and have a later stage at time of presentation. The genes most commonly mutated in uterine clear cell carcinoma include *ARID1A*, *ZFHX*, *PIK3CA*, *TSPYL2*, *SPOP*, and *FBXW7*. *TP53* mutations are also found in this tumor subtype. Clear cell carcinoma of the uterus is more prevalent among East Asian patients, and the tumor has a very distinctive appearance under the microscope compared to other uterine cancers.

### SIGNS & SYMPTOMS

Patients with uterine clear cell carcinoma have symptoms similar to women with other subtypes of endometrial cancer. These symptoms include abnormal uterine bleeding which can be bleeding between periods, irregular vaginal bleeding, bleeding after sex, or bleeding after menopause. A pap smear may show abnormal findings including atypical glandular cells or endometrial cells in a postmenopausal patient. Other symptoms include abnormal vaginal discharge, pelvic pain, urinary or stool changes, blood in the urine or stool, unexplained weight loss, decreased appetite, abdominal bloating/pain, or pain with sexual activity.

### SCREENING

There is no effective screening for this cancer. If a patient develops abnormal uterine bleeding or has other concerning symptoms, an endometrial biopsy in the office or dilation and curettage in the operating room are needed to make the diagnosis.

### TREATMENT & FOLLOW-UP

*This section is intended to clarify basics and showcase how treatment and follow-up may be different for these rare types of cancer.*

#### Role of Surgery

Similar to other types of endometrial cancer, surgical removal of the uterus, cervix, tubes, and ovaries is usually the first step in treatment. The surgery may be done through small incisions (laparoscopically or robotically) or with a larger abdominal incision. Lymph node assessment (sampling or sentinel lymph node biopsy) is

an important component of surgical evaluation to assign a stage to the cancer. Abdominal washings and sampling of the omentum at the time of surgery are often done to assist with treatment recommendations.

#### Role of Chemotherapy and Radiation

The surgical stage is important in determining additional treatment recommendations. Depending on whether the tumor was invading the muscle of the uterus or has spread beyond the uterus to the lymph nodes or other parts of the body, additional treatment may include chemotherapy, radiation, or both. The two most common chemotherapy drugs used are carboplatin and paclitaxel. In early-stage disease (stage I or II), chemotherapy is often recommended with vaginal brachytherapy (radiation localized to the top of the vagina). In certain settings, a high dose of radiation to the pelvis called external beam radiation (EBRT) may be recommended with or without chemotherapy. For advanced stage disease (stage III or IV), chemotherapy is the mainstay of treatment after surgery with the possible addition of radiation (vaginal brachytherapy, EBRT, or both).

#### Targeted Therapy Options

For patients with advanced stage or recurrent disease, testing the DNA of the tumor for different molecular markers with next-generation sequencing may open the possibility for treatment with targeted therapies outside of standard chemotherapy.

#### Immunotherapy Options

If the tumor has spread beyond the uterus or has recurred, the addition of immunotherapy to standard chemotherapy may help treat the cancer more effectively. Patients with advanced stage disease or recurrent uterine clear cell carcinoma may be candidates for the use of immunotherapy. Immunotherapies target checkpoints in the immune system including PD-L1, PD-1, and CTLA-4. By blocking these checkpoints, the immune system can more effectively attack cancer cells. Examples of these drugs include pembrolizumab, dostarlimab, atezolizumab, and ipilimumab. Additionally, combining immunotherapy with another drug called lenvatinib may help treat this cancer in the recurrent setting. Lenvatinib is a multi-tyrosine kinase inhibitor which blocks new blood vessels growth in tumors and decreases signals which cause cancer cells to grow.



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### QUESTIONS YOU SHOULD ASK YOUR CARE TEAM ABOUT YOUR TREATMENT PLAN & FOLLOW-UP CARE

**If you are not already being treated by a gynecologic oncologist, consider seeking a second opinion.**

Has my pathology been reviewed at a comprehensive cancer center?

Should I have a CA-125 blood test prior to surgery?

What imaging has been ordered to assess if the cancer has spread in my body?

Has my case been presented at a multidisciplinary tumor board?

Are there clinical trials that I am a candidate for?

Has my tumor been sent for next-generation sequencing?

What is the goal of my treatment?

What side effects should I prepare for?

What are the chances my cancer will come back?

How will this affect my sex life?

When should I call and what symptoms should I be worried by?

How will we know if the treatment is working?