I was just diagnosed with Clear Cell Sarcoma. What do I do now?

With a diagnosis of Clear Cell Sarcoma (CCS), it is very important to be seen by a doctor at a large cancer center. Sarcomas are rare and CCS is a rare sarcoma making it an ultra-rare cancer. Doctors outside of large cancer centers are not likely to have previously seen a patient with CCS, which will impact their ability to treat someone with this diagnosis. Since CCS is so rare, doctors have not developed a standard of care protocol to treat it. Doctors that are not familiar with CCS may suggest treatments used for other sarcomas which at best may not be effective for CCS and at worst can be detrimental.

Why is it so important to be seen by a sarcoma specialist upon being diagnosed with Clear Cell Sarcoma?

Finding a sarcoma specialist gives the patient the best chance to be treated by a physician familiar with CCS. A doctor not familiar with CCS may have the best intentions but in reality, will not have the time necessary to research CCS thoroughly and discover impactful information, such as which therapies have proven ineffective. Sarcoma specialists may have experience with treating CCS or at least the ability to network and discuss treatment options with other sarcoma specialists that have such experience.

What is the standard of treatment for CCS tumors?

The best chance for a good outcome with soft tissue sarcoma is to remove it surgically with clear margins, therefore surgery is part of the treatment for CCS whenever possible. It's important that your surgeon and your other doctors are experienced in the treatment of sarcomas. Studies have shown that patients with sarcomas have better outcomes when they are treated at large cancer centers where specialized oncologists have more experience with the disease. Following surgery there is no standard therapy for CCS. It is important to work closely with your oncologist to determine a path forward after surgery. Options include radiation therapy, immunotherapy, chemotherapy, targeted therapy, and ablation therapy. Each of these therapies have benefits and drawbacks that need to be carefully considered. However, it should be noted that there has been no benefit shown for adjuvant chemotherapy in treating CCS.

What is the modality of choice for imaging CCS tumors?

The location and type of tumor will determine which imaging test(s) may be used. A doctor may order more than one type of imaging for a patient. MRI and CT are both commonly used to image tumors in bones, joints, and soft tissues. A CT scan is generally good for larger areas, while an MRI scan produces a better overall image of the tissue under examination. Both have risks but are relatively safe procedures. Other imaging tests that may be used are PET scans, X-rays ultrasound, and bone scans.

What is a Clear Cell Sarcoma tumor? Is it cancer? Is it sarcoma?

A tumor identified as clear cell sarcoma is malignant, meaning that it is cancer and has the ability to grow back after removal and to spread to other areas of the body (metastasize). The best outcomes are seen in individuals that have CCS tumors removed with clear margins before they are 5 cm in diameter and before it has been detected in lymph nodes or other areas of the body. Clear cell sarcoma (CCS) of the soft tissue is different than clear cell sarcoma of the kidney or clear cell carcinoma. CCS is primarily found in adolescents and young adults and arises in connective tissues such as tendons - especially in limbs, feet and hands. There is also a form of CCS that occurs in the gastrointestinal tract (GI version). CCS is a translocation-associated sarcoma, which means that pieces of two chromosomes are swapped causing an abnormal fusion of genes. The most common fusion genes seen in CCS are EWSR1-ATF1 or EWSR1-CREB1.

Can my CCS tumor be passed down to my children?

CCS occurs after a mutation takes place in an individual and a tumor grows. This mutation is somatic and is not present in germ cells (eggs or sperm) therefore the mutation will not be handed down to children. There are certain conditions that may be inherited or passed down that make an individual more likely to develop sarcoma, such as hereditary retinoblastoma, Li-Fraumeni syndrome, neurofibromatosis type I, familial adenomatous polyposis (FAP), tuberous sclerosis, Familial GIST, Gorlin syndrome, or Werners syndrome. It is more common for sarcoma to be caused sporadically than for it to be caused by a syndrome such as those mentioned above.

How do I know if my CCS is going to be cured?

The best outcomes for CCS patients occur when tumors are discovered before they have grown larger than 5 cm or have spread to other areas of the body. After surgical removal of CCS, the best course of action is to monitor for recurrence of CCS by scans. CCS may recur within a short time or it may be many years before a recurrence. CCS most commonly recurs near the original tumor but it may come back at a distant location such as lung or spine. This knowledge should be taken into consideration in determining type and location of scans. Early detection is key to survival of CCS, stay vigilant.

I have a CCS tumor. Can I get pregnant?

This is something that should be thoughtfully discussed with your doctor.

What do I need to know about clinical trials?

Clinical trials are developed to determine if a treatment is helpful for a specific disease. There are currently no treatments proven effective for CCS. However, there are treatments that have been hypothesized to be helpful. These treatments may have been

shown to be effective for other sarcomas or shown to be effective in the lab. The only way to show effectiveness of new therapies in patients is to examine the benefit through clinical trials. Clinical trials can be found at https://clinicaltrials.gov. There have been three clinical trials for CCS launched in 2020. It is important to note the phase of the clinical trial, as each phase is meant to determine something different.

Phase 1 – generally conducted on a small number of people to determine safety of the treatment.

Phase 2 - After a treatment is considered to be relatively safe, it is evaluated in a phase 2 trial to determine effectiveness for a specific cancer or disease.

Phase 3 – after a treatment is determined to be relatively safe and effective, it is then evaluated in phase 3 trial to see if it is more effective or has less side effects than the standard treatment. Remember there is currently no standard treatment for CCS.

Can CCS tumor recurrence be predicted?

It is not possible at this time to predict CCS recurrence. However, recurrence is common and the best practice is to act as if a recurrence is expected and vigilantly monitor for CCS by scans and general body awareness.

What is the significance of EWSR1-ATF1 and EWSR1-CREB1 mutations in CCS tumors?

EWSR1-ATF1 or EWSR1-CREB1 fusion genes are thought to be the main drivers for CCS tumors. This means that the presence of either of these fusion genes is enough to cause a CCS tumor to grow. There may be other mutations that develop over time to allow for faster growth or metastasis of the cancer. These fusion genes are a target for future therapeutic interventions such as CRISPR to edit out the mutated gene.

How is CCS diagnosed?

To definitively diagnose CCS, FISH testing, RT-PCR or sequencing is required to identify the presence of the fusion gene EWSR1-ATF1 (or less commonly EWSR1-CREB1). CCS is named for the presence of pale-staining or clear cells that grow in a nested growth pattern in the tumor. The more common variant (non-GI version) has features similar to malignant melanoma (expression of Melan-A, MITF, HMB-45), which can complicate diagnosis if EWSR1-ATF1, -CREB1 presence is not yet known.

What roadblocks might I encounter as a patient?

The correct diagnosis often takes two or more months, during which time doctors may be eager to start treatment. However, without an accurate diagnosis, mistakes may be made in choosing a treatment path. Currently there is no standard of care protocol for CCS and no way to track the disease (no ICD-10 code which insurance companies

use for categorizing diseases and treatment options). In addition to that, patients are often not involved in choosing treatment options with their oncologist, and not given details why one treatment is chosen over another. Considering the rarity of CCS, patients and their caregivers have to be their own advocates, educating themselves about current knowledge of CCS and treatments options.