The GCS Project
2795 Estates Drive
Park City, UT 84060
www.gcsproject.org

TRANSCRIPT FOR VIDEO #7: DIAGNOSIS AND TREATMENT—WITH DR. MARCELA DEL CARMEN

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(MDC—Marcela del Carmen, MD)

Slide: **What is Carcinosarcoma?**

MDC: With regards to carcinosarcoma—that is defined as being an exceedingly rare form or cell type of cancer of the ovary or cancer of the uterus. When you look at all women that develop ovarian cancer or uterine cancer, fewer than 5% of those patients will have this particular cell type. The cell type is tricky to treat because it is pretty aggressive based on its inherent biology. These tumors are basically comprised of a combination of what we call *epithelial carcinoma*—these are your regular “garden variety” serous ovarian and endometrial ovarian cancers, for example—and then the second component of the tumor is a *sarcoma type*. So this combination of epithelial carcinoma and sarcoma is what makes it “triple MT” [MMMT] or a carcinosarcoma, and these tumors tend to be aggressive in how quickly they spread and then how refractory they can be sometimes to surgical and systemic treatment or chemotherapies.

Slide: **DIAGNOSIS:**
- **Choose GYN Pathology Specialist**
- **Ensure you have correct cell type**
- **Many are misclassified**

MDC: If you are talking about a cancer that occurs with a frequency of 5% of the time, it’s going to take an expert pair of eyes to be able to make the accurate diagnosis. So to me, the first part of it is making sure that if you have been diagnosed with a carcinosarcoma of the uterus or of the ovary, make sure that *that* diagnosis has been rendered by an expert gynecologic pathologist. And those pathologists usually live in tertiary care centers or coronary health care centers, mostly affiliated to big academic centers. So whether it is the MGH or the Brigham, Sloan-Kettering, Hopkins, the Mayo Clinic, MD Anderson, but places where all they do, day in and day out, is read gynecological cancers as opposed to what happens in a lot of other places where a general pathologist is reading prostate cancer today, they're reading colon cancer tomorrow and then the next day they are going to read ovarian cancer. So because of the rarity associated with this diagnosis, I think the first step is to make sure that you have a solid diagnosis based on expert pathology review.

Slide: **If you or someone you love is diagnosed with a GYN Carcinosarcoma (or MMMT) what do you do?**

MDC: First of all, I think the most important thing that a patient can do to advocate for her care is to really go to a place that has expertise in dealing with gynecological cancers. When you think of gynecological cancers, specifically cancer of the ovary, it is defined, irrespective of cell type, by the National Cancer Institute [NCI] as being a rare cancer. So already, you are beginning to see how you're not going to have every hospital, every physician, is going to be able to offer the appropriate expertise around care. When it comes to cancer of the ovary treatment, again, irrespective of cell type, there are data—largely out of the United States—that show that **your outcome, how long you live and how well you live during that time is really, really contingent on who takes care of you.** So finding that expert team of doctors and clinicians who are going to take the lead in helping you make decisions about your care is probably the most critical piece to your care and to the ultimate outcome of your cancer treatment.

I think after that, if it is indeed a carcinosarcoma, you really need to put together a team of experts who have a lot of experience managing these cancers. Both a gynecologic oncologist, who's going to weigh in as to whether surgery is indicated and appropriate—and if that's the case, the timing of surgery becomes really relevant—and then I think a medical oncologist is helpful in making some recommendations regarding what is the role of chemo and what kind of chemotherapy you should have. And then part of that conversation oftentimes involves around the accessibility of a clinical trial.

Clinical trials can be tricky. They're not for everyone. But for many patients they're the right choice to make. And I think that having a team of doctors and included in that may be—depending on the stage and what else is going on—radiation oncologists to see if there's any role for radiation treatment in the therapy that's going to be individualized for that patient.

Slide: **TREATMENT**
Now that I have been diagnosed, what can I expect?

MDC: But for the most part, when you're talking about early stage carcinosarcoma, you're talking about a tumor that is either confined to the uterus, if it's coming from the uterus, or confined to the ovary, if it's arising from the ovary. The information about that confinement, meaning that we know with 100% certainty that the cancer has not spread, is based on surgical findings.

So, let me kind of walk you through a sort of generic patient experience in early stage tumors. These patients come in either with a biopsy of the lining of the uterus or the endometrium that shows that they have a carcinosarcoma that began in the endometrium, and then they usually get imaging before they go to the operating room, and we do usually a PET CT to look for cancer outside of the [uterine] lining.

If the PET CT does not show any evidence if there's any metastases, then those patients are triaged to surgery. And they will have a full hysterectomy [removal of the uterus], they will have removal of their ovaries and fallopian tubes, and they will have a comprehensive lymph node dissection, where they have lymph nodes in the pelvic area and along the aorta removed. All that tissue gets sent to pathology, it gets looked at under the microscope and based on what is shown under the microscope with regards to any microscopic metastases, we assign that person's cancer a stage.

If the cancer is confined, let's say in the example of uterine primary—if it's confined to the uterus, even it's really, really early, ***because these tumors have a very aggressive biology, almost all patients will get recommendations for chemotherapy, because we have one shot of curing it, and we want to be as aggressive as we can.*** If the cancer comes back, it's a lot harder to treat it. And generally, it's not curable if it recurs. So, most patients, even if they have an early stage cancer, they will go through surgery. ***The surgery is part of the treatment, but it's also the staging portion of the management.*** And then even in early stage disease, these patients usually end up getting six cycles of chemotherapy, primarily Taxol [paclitaxel] and carboplatinum [Carboplatin]. There are emerging data that that doublet [Taxol-Carboplatin] is as good as the other chemotherapies that we had before with less toxicity. And then depending on the finer details around the pathology report, they may end up needing a little bit of radiation therapy, something called brachytherapy to the top of the vagina.

If the cancer has spread microscopically to the lymph nodes, then that already manifests; it changes the staging to a more advanced stage, meaning Stage 3. However, the likely outcome is probably better than if you present with big, bulky metastatic disease up front. So, I would say largely, patients that appear to have disease confined to the uterus will go through surgery for treatment. The surgery is also part of the staging. Most of these patients will have 6 rounds of chemotherapy and maybe some radiation to the top of the vagina.

For women that have metastatic disease up front—meaning that there is already a recognition by the clinician that the cancer has left its site of origin, and it has spread at other places—the presentation of the patient can be different. They can present with something else and then as part of that something else, they have a workup [testing] that includes a CT scan of the abdomen and pelvis and then that shows that they have implants that look like cancer implants.

We first need to figure out where the cancer is coming from. So, many of these patients will have a radiology-guided biopsy. So they have tissue that is procured by a radiologist either through an ultrasound guidance or CT-guided procedure, and then that tissue gets looked at under the microscope, and we confirm a diagnosis. If that is the case, then the next question that we have to ask—we already know it is cancer, we already know that it has spread—then the next question is, **"What is the role of surgery?"** *Can surgery be done and remove all cancer so that at the end of the surgical procedure there is no cancer left to the eyes of the surgeon? If that is the case, then surgery is the first line of treatment, followed by the same chemotherapy that you would get if you had early stage disease.*

If the operation would not lead to a complete resection, then surgery has no role, because it doesn't add any value. It just delays the institution of systemic treatment (chemotherapy). So, if the surgeon looks at the scans and says there's tumor in areas that are not resectable because of the anatomy or the location, then we give chemotherapy. And again, the general standard is Taxol-carboplatinum [paclitaxel-carboplatin], usually 6 cycles, and then we start to think about—is the chemotherapy working to shrink everything and then surgery may be an option? Now, that paradigm, where you would give chemo and then do surgery after the chemo, is completely "outside of the box." We don't have any data from any randomized trials that that is an effective way to treat these cancers. But sometimes we have to think creatively, and we think outside of the box not infrequently in medicine because not every patient is going to have a tumor that has read the textbook. So, I think that’s why, getting back full circle to the initial part of our conversation, that it is so critical that you have a multidisciplinary group of doctors who are experts in the management of gynecological cancers looking in as to what is the best treatment strategy individualized to your cancer, both to the stage of your cancer, your age, your medical co-morbidities, what else you bring to the table that should factor into how best to treat your cancer.