



# THE INSTITUTE FOR CANCER CARE AT MERCY

PHYSICIANS ON THE LEADING EDGE OF EXCELLENCE

## Hyperthermic Intraperitoneal Chemotherapy: *An Effective Treatment for Advanced Stage Abdominal Cancers*

Armando Sardi, M.D. | Surgical Oncology

Peritoneal carcinomatosis is a condition characterized by the diffuse spread of cancer throughout the abdominal cavity. It includes extensive peritoneal involvement and may or may not involve solid organs, such as the liver, spleen, and lymph nodes.

This condition can be caused by tumors of the appendix, colon, rectum, small bowel, ovary, fallopian tube, and stomach, as well as from primary peritoneal tumors, sarcomas, and mesothelioma.

Advanced cancers with peritoneal spread typically have limited treatment options and result in high mortality rates. However, there is hope with an aggressive therapeutic surgical technique coupling cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC).

Cancers with peritoneal spread, commonly thought to be incurable tumors, have responded well to CRS and HIPEC. CRS refers to the removal of all visible tumors from the abdominal cavity, often including colectomy, splenectomy, liver resection(s), as well as peritonectomies from the pelvis to the diaphragm, depending on the extent of tumor involvement.



Armando Sardi, M.D., director of Surgical Oncology at Mercy, is widely regarded for his training and skills in utilizing Hyperthermic Intraperitoneal Chemotherapy (HIPEC) to treat advanced stages of abdominal cancer.

A complete cytoreduction is defined as <2.5 mm of residual disease (CC=0) and has been associated with longer survival. The goal of cytoreductive surgery is to remove all visible disease; however, it is likely that microscopic disease remains.

To eradicate these microscopic cells, CRS is immediately followed by hyperthermic intraperitoneal chemotherapy (HIPEC) while in the operating room. The chemotherapy agent is heated to a temperature of 42°

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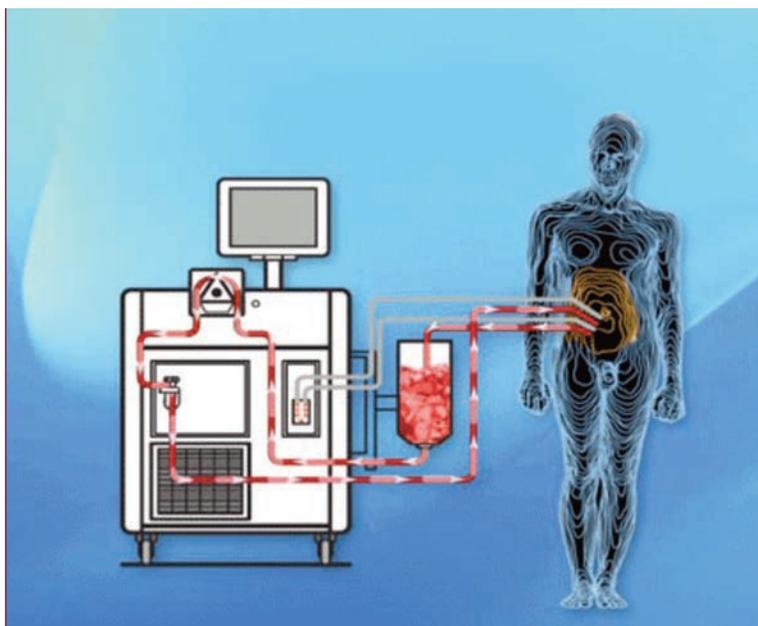
# Hyperthermic Intraperitoneal Chemotherapy *continued from page 1*

Centigrade (107.6° Fahrenheit) and perfused directly into the abdominal cavity, circulating for 90 minutes, allowing direct contact of the chemotherapy to all peritoneal surfaces. The hyperthermic temperatures kill the cancer cells and enhance the efficacy of the chemotherapy agents while the peritoneal perfusion during surgery improves the regional effect of the chemotherapy.

Peritoneal carcinomatosis is often associated with disease progression and poor prognosis, and because systemic chemotherapy has not been shown to improve survival, it has traditionally been treated with palliative intent. However, CRS/HIPEC has proven considerably more valuable than traditional surgery alone. HIPEC used in conjunction with CRS can improve survival and quality of life for patients who would otherwise have no hope in effectively treating their advanced cancer.

## HIPEC at Mercy

The Surgical Oncology Department at Mercy Medical Center is proud to be an internationally recognized center in the treatment of peritoneal surface malignancies with CRS/HIPEC. Led by Armando Sardi, M.D., chief of Surgical Oncology and medical director of



Following cytoreductive surgery, the HIPEC technique is used to destroy microscopic cancer cells. The patient is connected to a series of catheters and a pumping device that bathes the entire abdominal cavity with heated chemotherapy for 90 minutes.

The Institute for Cancer Care at Mercy, a multidisciplinary team of physicians is dedicated to advancing breakthrough treatments for cancer management, while keeping hope alive through every stage of treatment, recovery, and survivorship.

The patient-centered approach is mastered through the combined knowledge and expertise of select medical and radiation oncologists, radiologists, pathologists, primary care physicians, physician assistants, specialized nurses and nurse

navigators, registered dietitians, and other cancer specialists.

Considered a leading expert in CRS/HIPEC, Dr. Armando Sardi has performed more than 550 successful procedures since 1994, with patients traveling nationally and internationally for his expertise in HIPEC treatment.

Early referral is essential when peritoneal carcinomatosis is diagnosed or suspected.

“The sooner the patient comes to us, the better the results. We will be able to protect as many organs as possible. Patients who have been told they were going to soon

die and are still alive 19 years later,” Dr. Sardi says. He reiterates that “HIPEC requires a great deal of expertise, so it is important for patients to ask their surgeon how long he/she has been doing the procedure and how many they perform annually. Poor understanding of peritoneal carcinomatosis by physicians has led to late referrals. Moreover, in women, gastrointestinal cancers are often misdiagnosed and mistreated as ovarian cancer. Patients often receive the wrong operations and traditional systemic chemotherapy, which does not work very well in peritoneal carcinomatosis cases. [As a result], many people come to us after multiple surgeries and failed chemotherapy treatments.”

## HIPEC Results

### Appendiceal Carcinomatosis

- Complete removal of tumor (complete cytoreduction) is feasible in the majority of our patients (87%) even when patients present with gross peritoneal disease or with poor histology.
- The 5- and 10-year survival of appendiceal cancers is 61% and 53%, respectively.
- When complete removal of tumor is not possible, survival decreases to 33% and 22% at 5- and 10-years, respectively.

### Survival by Completeness of Cytoreduction

	1-y	3-y	5-y	10-y	
Overall (Median: NR)	92%	72%	61%	53%	
CC-0/1 (Median: NR)	96%	76%	67%	59%	P<0.001
CC-2/3 (Median: 40 mos.)	71%	51%	33%	22%	

CC: Complete cytoreduction; CC-0: no residual disease; CC-1: <2.5 mm; CC-2: 2.5mm-2.5cm; CC-3: >2.5cm

#### Colorectal Carcinoma

- The second most common site for colorectal cancer metastases is the peritoneum and is associated with poor prognosis and treatment has palliative intent.
- The American Society of Peritoneal Surface Malignancies published guidelines on standardizing the delivery of HIPEC in colorectal cancer.
- CRS/HIPEC can be offered to select patients with a curative intent and with similar morbidity of that of other extensive surgical procedures.
- A median overall survival of 48 months with a 5-year survival of 45% has been reported.

#### Gynecologic Primary Sites

- Primary peritoneal carcinoma with HIPEC has yielded a 1-, and 3-, and 5-year disease free survival rate of 80%, 75%, and 59%, respectively.
- Our peritoneal surface malignancy center has demonstrated a 5-year survival of 65% in uterine sarcoma with peritoneal dissemination.
- A recent review of seven international HIPEC centers showed a median overall survival rate of 37 months in uterine sarcoma with a 1-, 3-, and 5-year survival of 76%, 54%, and 32%, respectively.
- Mercy is the first institution in the United States to investigate the role of CRS/HIPEC as an initial treatment option in newly diagnosed ovarian, primary

peritoneal, and fallopian tube cancers. We are currently enrolling patients in a phase II randomized clinical trial. [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov), NCT02124421. (See *Research and Collaborations for more details*)

#### Gastric Cancer

- Peritoneal spread in gastric cancer is currently regarded as systemic spread of disease. Treatments options are palliative systemic chemotherapy with limited efficacy.
- Patients who undergo CRS/HIPEC and have a complete removal of tumor have a median overall survival of 12 months.
- The role of HIPEC may help prolong survival in patients with gastric cancer.

### Research and Collaborations

Dr. Sardi and his team are dedicated to raising awareness and furthering research to better understand peritoneal carcinomatosis. The Surgical Oncology Department at Mercy has cultivated a database and tumor bank of more than 700 patients that has been used to publish in peer-reviewed journals and to present at national/international conferences.

Currently, there are multiple open clinical studies for appendiceal cancer investigating the immunologic and microbiologic characteristics to better understand the etiology, disease progression, and the role of HIPEC.

(Visit <https://mdmercy.com/centers-of-excellence/cancer> Research Activities and Publications section for more details)

In addition, the Department of Surgical Oncology at Mercy has developed a unique collaboration with Dr. Teresa Diaz-Montes, the Associate Director of the Lya Segall Ovarian Cancer Institute at Mercy, and her colleagues Dr. Hyung Ryu and Dr. Jennifer Ducie. Gynecologic and surgical oncologists are working together to ensure improved outcomes in patients with advanced ovarian cancers.

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The gynecologic-surgical oncology collaborative aims to advance ovarian cancer diagnosis and treatment through cutting edge research and to provide a more comprehensive approach for better surgical outcomes and to improve long-term patient survival.

In 2014, Dr. Sardi and Dr. Diaz-Montes opened a randomized clinical trial investigating the role of CRS/HIPEC as the initial treatment for advanced ovarian cancers. Other trials have studied the role of HIPEC in recurrent disease; however, this trial is the first in the United States to explore the role of HIPEC as a first line treatment. The trial is currently enrolling patients newly diagnosed with ovarian, primary peritoneal and fallopian tube cancers without prior treatment. More information can be found on [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov), NCT02124421.

*(See article on page 6 – Why Use HIPEC to Treat Ovarian Cancer? for more details)*

## Clinical Fellowship Program

In 2008, the division of Surgical Oncology at Mercy developed a two-year peritoneal surface malignancy fellowship training program aimed to increase the number of physicians experienced in these complex procedures and cancers. Fellows are offered a balance of clinical, surgical, and

“The sooner the patient comes to us, the better the results. We will be able to protect as many organs as possible. Patients who have been told they were going to soon die, are still alive 19 years later.” *Dr. Armando Sardi*

research experience. The training program offers the opportunity and practice necessary for the multidisciplinary approach and management of peritoneal surface malignancies.

## Heat It to Beat It

A group of grateful patients organized the first “Heat It to Beat It” walk in 2010. The event raises awareness and funding for peritoneal carcinomatosis and HIPEC research and has raised more than \$870,000 to support the research led by Dr. Sardi. This patient led event is focused on generating awareness for the life-saving HIPEC treatment and celebrating patients, as they come together with family and friends and share their experiences with other survivors.

## Areas of Focus

Dr. Sardi and his colleagues, Dr. Vadim Gushchin and Dr. Kurtis Campbell, perform a vast array of complex surgical oncologic procedures for gastrointestinal, pancreatic, and soft tissue cancers, thyroid conditions and melanomas.

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# HIPEC for Peritoneal Mesothelioma

Vadim Gushchin, M.D. | Surgical Oncology

Peritoneal mesothelioma is a rare aggressive tumor of the peritoneum. It accounts for about 30 percent of all mesotheliomas. There are approximately 300 to 400 new cases each year in the United States. The typical average age of diagnosis is 65 years of age.

Peritoneal mesothelioma is difficult to diagnose. Peritoneal mesothelioma (PM) often presents with symptoms that are mistaken for other benign conditions of the abdomen which leads to delay in the diagnosis and treatment. The disease often presents with symptoms similar to irritable bowel syndrome, hernia and other abdominal cancers.

Peritoneal mesothelioma occurs in the peritoneum, a thin membrane that covers most of the abdominal organs. It can spread to tissues and over the peritoneal lining of the abdomen. It sometimes spreads to other organs such as the liver and lungs, as well as to the bones.

The patients' longevity and well-being is closely related to disease progression within the peritoneum. It can possibly lead to bowel obstruction, malnutrition, cachexia and death. Early treatments like palliative "debulking" surgery, systemic chemotherapy, and radiation therapy have not shown any drastic improvements in patient survival. However, there is hope for select patients with PM.

At Mercy, surgical oncologists Drs. Armando Sardi and Vadim Gushchin offer patients cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) as an alternative treatment option. CRS/HIPEC has become a valuable treatment option for



Vadim Gushchin, M.D., director of Gastrointestinal Oncology, discusses recently published case series on analyzed treatment results for peritoneal mesothelioma patients treated with cytoreductive surgery and HIPEC.

selected patients with PM. CRS/HIPEC involves extensive cytoreductive of tumor on visceral and peritoneal surfaces with resection of involved visceral organs followed by HIPEC.

In recently published case series, Drs. Sardi and Gushchin analyzed treatment results for patients with peritoneal mesothelioma. In spite of treating patients with advanced disease in 70% of all patients' complete removal of the tumor (complete cytoreduction) was performed in 65% of patients. The 5-year overall survival of 60% was reached, which is a remarkable result.

The Surgical Oncology team at Mercy continues research in the field of mesothelioma collaborating with other institutions for advanced molecular analysis of the removed tumors. This approach may help with new treatment strategies for this difficult to treat disease in the near future.

To learn more about the study and CRS/HIPEC treatment for peritoneal mesothelioma, please call Drs. Sardi and/or Gushchin at 410.332.9294.

# Why Use HIPEC to Treat Ovarian Cancer?

Teresa Diaz-Montes, M.D. | The Lya Segall Ovarian Cancer Institute

One of the most feared forms of gynecologic cancer, ovarian cancer is the second most common form of gynecologic cancer and the most deadly.

An estimated

**22,000**

women will be diagnosed this year,

and approximately

**14,000**

women will die of it.



## Initial Treatment for Ovarian Cancer

The initial management of ovarian cancer consists of cytoreductive surgery followed by chemotherapy. Chemotherapy can be administered as an intravenous (IV) or intraperitoneal (IP) infusion. Clinical trials have shown an advantage of IP chemotherapy versus IV chemotherapy; however, only a minority of patients are able to complete the IP treatment as established.

## Why Use HIPEC?

Why is HIPEC (hyperthermic intraperitoneal chemotherapy) being considered for management of ovarian cancer? The propensity of peritoneal spread of ovarian cancer is similar to other peritoneal surface malignancies such as colon and appendiceal cancers. HIPEC has been

explored in the management of those malignancies with success.

The advantages of this regional therapy is the administration of chemotherapy at the time of the surgery when the bulk removal of the disease in the absence of adhesions, allowing for a better distribution of the chemotherapy. Additionally, hyperthermia has been shown to increase tumor penetration of anticancer agents and synergistically enhance the cytotoxicity of platinum agents.

Mercy Medical Center has excellent results with cytoreductive surgery (CRS) and HIPEC in select patients with primary peritoneal cancer with an overall survival of 55% at 5-years. These statistics led to the development of the first clinical trial in the United States evaluating the use of HIPEC for

the initial management of ovarian, fallopian tube, and primary peritoneal cancer.

## About the Study

In April 2014, Mercy began enrolling patients in the randomized phase II clinical trial entitled, “Outcomes after cytoreduction surgery with or without carboplatin hyperthermic intraperitoneal chemotherapy followed by adjuvant chemotherapy as initial treatment of advanced state (III/IV) ovarian, fallopian tube, and primary peritoneal cancer”. The study intervention arm receives CRS with HIPEC followed by adjuvant IV / IP chemotherapy. Both gynecologic and surgical oncologists operate together, regardless of the randomization assignment.

# Mercy Welcomes New Physicians

## Preliminary Outcomes

To date, 46 patients have been evaluated with 15 patients meeting the study inclusion criteria. We have achieved complete cytoreduction in 93% of patients. The median length of stay for HIPEC arm is 13 days versus 11 days for the control arm. The median ICU stay is two days for the HIPEC versus one day for the control arm. Complications have been limited in each group with resolution of all complications.

All study participants have received adjuvant chemotherapy with completion of six cycles. Women who have received HIPEC are reporting a return to quality of life faster when compared to the control arm. However, with such small numbers, we have not seen major differences between study arms in regards to hospital stay, complications, or toxicity.

It appears that cytoreductive surgery with HIPEC may be a safe procedure for the initial treatment of advanced stage ovarian, fallopian tube and primary peritoneal cancer. Patient recruitment is ongoing.

Additionally, we have a cohort of women treated with neo-adjuvant chemotherapy who then undergo HIPEC as the interval cytoreduction. Thus far, we have approximately 14 patients enrolled in that cohort with similar findings. Due to the small numbers and recent enrollment, no conclusions about progression free survival or overall survival can be estimated.



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Women's Imaging

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