Hot chemotherapy in to the abdomen is called HİPEK. This abbreviation is derived from the initials of the English term "Hyperthermic Intraperitoneal Chemotherapy" (HIPEC).

So, why administer chemotherapy into the abdomen?
Many cancer types originating from intra-abdominal organs can involve intra-abdominal membrane called "peritoneum". Peritoneum is a tissue that ensures viscosity of intra-abdominal organs and internal surface of abdominal wall by secreting a thin, low amount of fluid that covers the surface of organs. In a cancer originating from intra-abdominal organs, cancer cells can involve peritoneum by collapsing into the abdomen or adjacency. This generally shows that cancer has progressed to the terminal stage. Systemic, or intravenous, chemotherapy regimes are insufficient when dealing with cancers involving peritoneum. In these treatments, medications cannot access peritoneum. The fundamental principle in this treatment is to consider peritoneum as an organ, and resect the involved peritoneum and other organs in cancers involving peritoneum. Intra-abdominal chemotherapy is administered following this surgery, in other words removal of all tumor tissues. The goal here is to strike a hard blow to the remaining microscopic metastases.

What's the Logic behing HIPEC?
Why do we heat up the chemotherapy agent? What is the impact of heat?

Heat makes it easy for the medication to penetrate in to the tissue
Heat increases the likelihood of selected agent to kill cancer cell.
Heat itself has an antitumor effect
Intraoperative chemotherapy can be guided by hand to penetrate in to the abdomen, and heat contributes to an equal dissemination of the agent on all surfaces.
The medication's negative effects on kidney and urine outflow can be monitorized effectively during surgery (they can be followed and due precautions can be taken).
A lot of physiological parameters of a patient can be normalized during HIPEC (body heat, coagulation, haemodynamics etc.).
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Which patients and diseases can HIPEC be utilized for?
It is most frequently used for treating ovarian cancer in women. Furthermore, it could also be utilized for treating large intestines (colon-rectum), stomach, appendix cancers along with peritoneal cancers (pseudomyxoma peritonei). It has begun to be used for also treating pancreatic cancer in recent years.

There is usually an accumulation of fluid (acids) in peritoneum involvement. This fluid causes the patient's abdomen to swell, and also helps cancer cells diffuse on to diaphragm and other intra-

abdominal areas. Sometimes, the amount of fluid accumulation may not allow the patient to lie down. These fluids may be externally discharged, but that doesn't always solve the problem. The acid accumulation persists so long as the underlying cause does. Majority of these patients are told that they are at the terminal stage of the disease, and that nothing much can be done. So, they are sent home. This is where cytoreductive surgery and HIPEC comes in. They can be used for such patients.
Is HIPEC sufficient on its own?
No. HIPEC is not sufficient on its own. HIPEC is a part of treatment. This treatment has 3 pillars.

Firstly, a complete or near-complete cytoreductive surgery where peritoneum and organs involved (large intestine, ovary, gallbladder, involved portions of stomach) are resected and all tumor tissues are cleaned is required. In this surgery, the abdomen is extensively opened and all abdomen is assessed. Involved peritoneum and organs are removed. Meanwhile, removing a portion of small and/or large intestines and intestines being anastomosed to the abdominal wall (colostomy or ileostomy) might be necessary. This is mostly a temporary step and intestines are moved back in once surgery is done. Without this surgery, administering HIPEC is of no good use. Or without the HIPEC, such a procedure has no role to play. Cytoreductive surgery and HIPEC must be followed by systemic chemotherapy.

"Cytoreductive Surgery + HIPEC + Systemic Chemotherapy" trio, so to speak...
In which situations HIPEC can't be administered?
It has no role to play for involvements outside abdomen (brain, lung, bone metastases etc.). Disease must be limited to abdomen. In addition, HIPEC has no role to play in patients with several liver metastases, or liver metastasis that can no be resected. Three or fewer resectable liver metastases cause no problem for HIPEC to be administered.

In patients with diffuse and dense small intestinal involvements, resecting a major portion of intestines is not considered pro-life, therefore these patients are not suitable for HIPEC treatment. It's not possible to identify most of those patients before the surgery. So, these indications are observed once the patient is opened.
Are there instances where HIPEC is used on its own?
In some patients, HIPEC might be administered with a catheter laparoscopically placed in the abdomen during surgery in order to treat the acid and provide patient some comfort. However, it is generally a palliative therapy. It doesn't really contribute to the survival duration of the patient.
How is HIPEC administered?
HIPEC administration is a part of the surgical procedure. It is administered at the end of a long and arduous surgery, after the intra-abdominal tumor cleaning, and when the patient is still under anesthesia. Two drains are placed to the upper and lower quadrants of abdomen before closure of abdomen. Thruogh these drains, connection with the special device that heats up chemotherapeutic fluid is established and 2 heat probes are placed to the upper and lower sides of abdomen to track heat levels. These probes ensure that the heat is stable at the desired level during the course of chemotherapy. The temperature must be between 41 and 43 degrees. Chemotherapy lasts for 60 minutes. 3.5 liters of chemotherapeutic fluid is infused in to the abdomen. Meanwhile, for the chemotherapy to access everywhere in the abdomen, it is guided by hand, and rinsed. The fluid in abdomen is flushed and procedure is completed.

Who should the team undertaking cytoreductive surgery and HIPEK be consist of?
Operation takes about six to ten hours. It requires pelvic and hepatobiliary surgical experience. For that reason, general surgeons, a gynaecologist and and oncologist are needed. Moreover; experienced radiologists for screening the patient pre-op, medical oncologists for regulating chemotherapy regimes and treatments of patients, experienced pathologists for validating accuracy of diagnoses, nuclear medicine experts for assessing PET and other tomography results, experienced dieticians for setting and regulating patients' diets, experienced anesthesiologists for following up

patients, experienced and talented ICU personnel and nurses are indispensible parts of this team. This is a multidisciplinary treatment.

What is HIPEC's effect on survival length?
Majority of patients who are candidates for such treatment are at an advanced stage in their disease and have survival expectations limited to months. Thus, this significant details must not be forgotten when survival length is being mentioned.

HIPEC administration has differing long-term outcomes in different cancer types. Ovarian cancer is the one that most benefits from treatment, and 5 year-survival expectation is around 50 %. In large intestinal cancers, that rate is around 30 %. In stomach cancers, 1 year-survival rate is reported to be 43%, while it is 11% in 5 years. Considering life expectancy in advanced stage stomach cancers with peritoneal metastasis is less than 6 months, the given data points to significant success.

Following HIPEC, the 5 year-survival rates for pseudomyxoma peritonei and peritoneal mesothelioma vary between 66 and 97 %.

What are the risks for HIPEC therapy?
This is a complex therapy. Hence, having a higher risk rate than standard surgery. Results in patients well-prepared before, well-observed and managed during surgery are good despite the complexity of the procedure. Intestinal system shutdown for a period of time (loss of function) is observed most frequently. Complications such as bleeding, renal failure due to therapy, pulmonary or brain embolism, bone marrow failure due to chemotherapy, surgical site (scar) infections, separation of wounds, anastomosis leakeage during surgery can be observed. However; precautions taken in experienced centers and good patient management can overcome most of these issues. Even though various trials declare differing results, the risk of losing a patient following this procedure is between 0 and 7 %. Considering the stage and severity of the disease, the complication and mortality risk in a risk-benefit assessment is at an acceptable level.

RESULTS
To sum up, cytoreductive surgery and HIPEC administration take long, lots of effort, attention and care and require the presence of experienced surgeons and teams. But it is a treatment method that is hopeful, promising and contemporary. Patient and patient family's motivation of treatment and harmony with the medical team is a significant detail in improving the success of treatment.

"Cytoreductive Surgery + HIPEC + Systemic Chemotherapy" trio is the one and only treatment option for patients with peritoneal metastasis giving them long-term survival hope (20 - 50 %).