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GOC Statement Regarding Neoadjuvant Chemotherapy versus Upfront Debulking Surgery for Treatment of Advanced Stage Cancer of the Ovaries

The standard treatment for what is commonly referred to as ovarian cancer of advanced stage (ie cancer has spread beyond the ovaries), is initial surgery with the goal of removing all visible tumor (maximal debulking) followed by chemotherapy. A woman's prognosis is improved when complete debulking of all visible tumor is achieved. However, in some advanced stage cancers (bulky stage IIIC or stage IV disease), this surgical goal may not be technically possible or may put the patient at risk for significant complications. When this is the case, chemotherapy may be given before surgery (neoadjuvant chemotherapy). The chemotherapy will usually decrease the tumor burden so that complete debulking can then be achieved. In addition, in women with poor health due to their cancer who may not tolerate an extensive initial surgery, chemotherapy first can, by shrinking the cancer, improve their health so that the needed surgery can then take place with a greater chance of success and lesser chance of resulting complications for the individual (1).

To determine which women would benefit from neoadjuvant chemotherapy, a large international clinical trial was conducted that randomly assigned patients with advanced stage ovarian cancer to either neoadjuvant chemotherapy followed by surgery and then completion of chemotherapy, or initial surgery followed by chemotherapy (2). The overall survival (ie. the number of women alive over time) in the two treatment groups was the same, maximal debulking occurred more frequently in women who received chemotherapy first. In addition, in this group, women experienced less postoperative complications such as increased blood loss, infection and blood clots. One major criticism of this study was that not all women with stage III and IV disease were included and that participation was based on individual doctor decisions. As a result, not all surgeons agree that upfront or delayed surgery are equivalent and will continue to recommend surgery first whenever possible.

Factors used by the health care team to determine the optimal mode of treatment for advanced stage ovarian cancer are individualized to the specific patient and her cancer and include the following:

- *Large metastatic tumor burden in stage IIIC or IV cancers* – Women with large tumor burdens have been shown to have equivalent outcomes when treated first with either chemotherapy or surgery. Patients who have stage IV disease with tumors more than 4.5cm

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in size do better with neoadjuvant chemotherapy. This is most often based on the inability to completely remove all the cancer. However in some settings, the surgeon can completely remove the cancer despite the large amounts of cancer.

- *General poor conditioning* – A woman's overall health, including both symptoms from the cancer and other medical conditions, help indicate whether she will be able to tolerate an extensive surgery. If the cancer treatment team feels that a woman is too sick for surgery, then neoadjuvant chemotherapy may be offered.

- *Inability to maximally debulk (eliminate) tumors* – During the assessment period, imaging such as CT scans are done to help determine the size and location of tumor. Maximal debulking is unlikely to be achieved when the disease has spread to certain organs within the abdomen or when it has spread beyond the abdomen. In these situations neoadjuvant chemotherapy may be recommended.

This statement was prepared by Dr. Marette Lee and Dr. Shannon Salvador with input from the GOC Executive.

References

1. Morrison J, Haldar K, Kehoe S, Lawrie TA. Chemotherapy versus surgery for initial treatment in advanced ovarian epithelial cancer. *Cochrane Database Syst Rev* 2012;8.
2. Vergote I, Tropé CG, Amant F, Kristensen GB, Ehlen T, Johnson N, et al. Neoadjuvant chemotherapy or primary surgery in stage IIIC or IV ovarian cancer. *N Engl J Med* 2010, Sep 2;363(10):943-53.
3. van Meurs HS, Tajik P, Hof MH, Vergote I, Kenter GG, Mol BW, et al. Which patients benefit most from primary surgery or neoadjuvant chemotherapy in stage IIIC or IV ovarian cancer? An exploratory analysis of the European organisation for research and treatment of cancer 55971 randomised trial. *Eur J Cancer* 2013, Oct;49(15):3191-201.

Our Mission

The Society of Gynecologic Oncology of Canada is a nonprofit organization consisting of physicians, nurses, scientists and other health care professionals specializing in gynecologic oncology. Its purpose is to improve the care of women with or at risk of gynecologic cancer by raising standards of practice, encouraging ongoing research, promoting innovation in prevention, care and discovery, and advancing awareness. GOC also seeks to disseminate knowledge to practitioners, patients and the general public on gynecologic cancer as well as cooperate with other organizations committed to women's health care, oncology, and related fields.