

## **Gynaecologic Oncology Cancer Disease Site Group**

### **Policy for Intraperitoneal Chemotherapy (IP) Delivery**

*(see guideline for Ovarian, Fallopian Tube and Primary Peritoneal Cancers)*

#### Background and Rationale

The established standard of care in both adjuvant and advanced epithelial ovarian cancer (EOC) in the front-line setting, in Kingston, is carboplatin AUC5 and paclitaxel 175 mg/m<sup>2</sup> both IV every three/four weeks for six-nine cycles.

Several landmark studies that compared intraperitoneal (IP) and intravenous (IV) routes of chemotherapy administration have consistently demonstrated improved disease control and survival parameters with IP chemotherapy (1-3). As a consequence, both the National Cancer Institute in the United States (4) and the Society of Gynecologic Oncologists of Canada (GOC) (5) issued clinical announcements recommending IP chemotherapy as a new standard of care in the optimally debulked Stage III subset of ovarian cancer patients. The Gynecology Oncology Disease Site Group at CCSEO therefore decided in 2007 to adopt an IP-based chemotherapy regimen for this patient population.

Because the randomized published studies have almost exclusively been limited to IP cisplatin, the group agreed to IP cisplatin in the protocol, pending evidence confirming at least non-inferiority of IP carboplatin. The Armstrong protocol (1) is considered impractical due to a IP treatment completion rate below 50%. The utility of a day 8 paclitaxel remains unclear and the DSG have concerns about excess toxicity.

There is no consensus within Ontario or Canada on the most appropriate IP regimen. The reasons include: 1) comparison of an IP-based regimen to the current standard of IV carboplatin and paclitaxel is lacking; 2) the choice of IP drug or drugs is different across the published studies; 3) significant toxicities limit the ability to deliver full doses of IP regimens; 4) finally, technical aspects of IP chemotherapy delivery pose some logistical challenges (for instance a decision to insert port needs to be considered prior to debulking surgery, as ivr insertion requires presence of ascites).

#### CCSEO IP Regimen

The DSG consensus IP regimen is CISPPACL(IP) q21 days (paclitaxel 175 mg/m<sup>2</sup> IV over 3 hours followed by cisplatin at a dose of 100 mg/m<sup>2</sup> IP day 1), with a total planned 6 cycles. A cycle of treatment is four weeks, based on local experience and retrospective published data (6). Carboplatin AUC6 IP delivery was considered suitable if cisplatin contraindicated (7). Although the landmark studies did not include stage II disease, the local consensus was to recommend IP protocol to suitable stage II patients. Port is to be inserted intra-operatively wherever possible and with appropriate patient consent prior to surgery; chemotherapy may commence following resection when patient is fit.

Based on an increasing use of peri-operative chemotherapy with interval debulking surgery, the OV.21 Protocol (8) is a trial of IP plus IV chemotherapy versus IV carboplatin plus paclitaxel in patients with epithelial ovarian cancer optimally debulked at surgery following neoadjuvant intravenous chemotherapy. The phase III portion of the trial was activated on February 3, 2014, eliminating Arm 2 with IP cisplatin. Randomization was between the control arm (IV Paclitaxel/IV Carboplatin – Arm 1) and Arm 3 (IV Paclitaxel/IP Carboplatin + day 8 IP Paclitaxel). Accrual has now been completed. Resulting from the OV.21 experience the DSG considers IP carboplatin/IP paclitaxel as an additional standard regimen (STFM PACL CARBO IP/IV ADJ). However, clinical adoption of IP chemotherapy following interval debulking awaits trial publication.

**Inclusion criteria for IP chemotherapy:**

- Stage II and III EOC
- Primary debulking surgery completed
- Maximally debulked, thus <1 cm residual disease
- Good performance status

**Cautions/Exclusions:**

- Adhesions evident at surgery
- Bowel resection
- Interval debulked patients (pending results of OV.21)
- History of active IBD

**References:**

1. Armstrong. NEJM 354, 34-43, 2006.
2. Markman. JCO 19, 1001-7, 2001.
3. Alberts. NEJM 335, 1950-5, 1996.
4. <http://www.gog.org/IPChemoEd/clinicalann.pdf>
5. [http://g-o-c.org/en/news/positionstatements/ip\\_en.aspx](http://g-o-c.org/en/news/positionstatements/ip_en.aspx)
6. Fujiwara, Int J Gynecol Cancer 2005, 15, 426–431
7. Molckovsky, Int J Gynecol Cancer 2008, 18, 8–13  
Decreased dose density of standard chemotherapy does not compromise survival for ovarian cancer patients

8. OV.21 Protocol: A Phase II/III Trial of Intraperitoneal (IP) Plus Intravenous (IV) Chemotherapy Versus IV Carboplatin Plus Paclitaxel in Patients With Epithelial Ovarian Cancer Optimally Debulked at Surgery Following Neoadjuvant Intravenous Chemotherapy.