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Cited rationale for variance in the use of primary intraperitoneal chemotherapy following optimal cytoreduction for stage III ovarian carcinoma at a high intraperitoneal chemotherapy utilization center

Brooke A. Schlappe, MD¹, Jennifer J. Mueller, MD¹, Oliver Zivanovic, MD^{1,2}, Ginger J. Gardner, MD^{1,2}, Kara Long Roche, MD^{1,2}, Yukio Sonoda, MD^{1,2}, Dennis S. Chi, MD^{1,2}, and Roisin E. O'Cearbhaill, MD^{3,4}

¹Gynecology Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY, USA

²Department of Obstetrics and Gynecology, Weill Cornell Medical College, New York, NY, USA

³Gynecologic Medical Oncology Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA

⁴Department of Medicine, Weill Cornell Medical College, New York, NY, USA

Abstract

Objective—Studies have demonstrated improved ovarian cancer survival with the administration of a combination of intravenous (IV) and intraperitoneal (IP) chemotherapy following optimal cytoreduction. Despite this, IV/IP chemotherapy is not uniformly used. In this retrospective cohort study, we assessed the documented reasons for giving IV-only chemotherapy.

Methods—All patients who had optimal primary cytoreductive surgery for stage III ovarian, fallopian tube, or primary peritoneal carcinoma, met eligibility criteria for GOG-172, and received primary chemotherapy at our institution between 2006 and 2013 were identified. Patients who received at least one cycle of adjuvant IV/IP therapy were included in the IP group. Patient characteristics, treatment information, and reason cited for not administering IP therapy were collected.

Results—Of the patients evaluated, 330 met inclusion criteria. The majority (n=261, 79%) received at least one IV/IP cycle (median, 6; range, 1–6), and 62% completed 6 cycles. The most common reason for giving IV-only therapy was postoperative status (i.e., delayed wound healing, performance status), accounting for 18 (26%) of the 69 IV-only patients (5% of the entire cohort).

Corresponding author: Roisin O'Cearbhaill, MD, Department of Medicine, Memorial Sloan Kettering Cancer Center, 1275 York Avenue, New York, NY 10065, Tel. 1646-888-4227, ocarbhr@mskcc.org.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts to disclose.

Other cited reasons were baseline comorbidities (15%) and IP port complications (12%). Receipt of 1 cycle of IP chemotherapy (HR 0.51; 95% CI, 0.32–0.80) and no gross residual disease (HR 0.47; 95% CI, 0.31–0.71) were associated with improved overall survival.

Conclusion—Potentially modifiable factors identified as leading to the use of IV-only chemotherapy were postoperative status and IP port complications, which if altered, could potentially lead to increased IP chemotherapy use.

Keywords

intraperitoneal chemotherapy; rationale; optimal cytoreduction; serous ovarian cancer; National Cancer Institute guideline adherence; GOG-172

INTRODUCTION

Multiple randomized trials have demonstrated a survival advantage in women with stage III ovarian cancer treated with a combination of intraperitoneal (IP) and intravenous (IV) chemotherapy following optimal cytoreduction (1–4). Gynecologic Oncology Group trial 172 (GOG-172), published in 2006, demonstrated the greatest survival advantage in this patient population (3) and led to the subsequent National Cancer Institute (NCI) recommendation that women with optimally cytoreduced stage III ovarian, fallopian tube, or primary peritoneal cancer should be informed of the advantages of combined IV/IP chemotherapy and offered this regimen (5). Despite this recommendation, IV/IP chemotherapy has not been uniformly adopted. A recent report revealed that IV/IP chemotherapy use in eligible patients ranges from 4–67% in six National Comprehensive Cancer Network (NCCN) sites, where, presumably, there should have been no logistical barriers to IP chemotherapy administration (6). Other reports confirm the poor utilization of this therapy despite the NCI recommendation (7–9). The lay media has also reported on this discrepancy, exposing an opportunity for quality improvement (10).

General impediments to IV/IP therapy and relevant patient factors have previously been reported; however, no study has evaluated cited rationale for not administering IV/IP chemotherapy in an eligible patient. Some of the general objections reported include concern for inadequate treatment of extraperitoneal disease, toxicity, cost, IP port-related impediments, complexity of the regimen, required nursing skills, and increased chemotherapy unit time (6, 11–13). Reported patient factors associated with the use of IV/IP chemotherapy include a younger age and fewer comorbidities (6).

We sought to evaluate adherence to the NCI recommendation at our institution and the cited rationale for administering IV chemotherapy in a prospective IV/IP patient in an attempt to identify potentially modifiable factors limiting IV/IP chemotherapy use.

METHODS

Following institutional review board approval, women with stage III ovarian, fallopian tube, or primary peritoneal carcinoma who received their primary chemotherapy at Memorial Sloan Kettering Cancer Center (MSK) following optimal surgical cytoreduction between

2006 and 2013 were identified. Patients with low-grade tumors, disease of mucinous histology or carcinosarcoma histology were excluded. Eligibility criteria for GOG-172 (3) (Table 1) were applied at the time of a patient's initial evaluation for chemotherapy as a means of excluding patients who had a medical contraindication to IV/IP chemotherapy. Only those meeting the criteria in Table 1 were included. Optimal surgical cytoreduction was defined as the presence of residual disease of ≤ 1 cm in largest diameter. Patient characteristics, including age at diagnosis, stage, body mass index (BMI, weight [kg]/height [m²]), and Karnofsky Performance Status (KPS) at initial chemotherapy evaluation, were collected. The presence of any of the following baseline comorbidities were recorded, totaled, and subsequently reported as "total comorbidities": diabetes, hypertension, pulmonary disease, coronary artery disease, renal disease, hypothyroidism, hyperthyroidism, congestive heart failure, dementia, cerebrovascular disease, hepatic disease, and peripheral vascular disease. The following treatment information was also collected: including location of primary debulking surgery, performance of a bowel resection at primary debulking surgery, presence of an ostomy, volume of residual disease, IP catheter insertion at primary debulking surgery, chemotherapy regimen administered and number of cycles, and if the patient received chemotherapy as part of a clinical trial.

In patients who received IV-only chemotherapy, the clinician's cited reason for not initiating IV/IP chemotherapy was recorded. If this reason resolved during treatment course, the reason that IV/IP chemotherapy was not administered at the time of resolution was also recorded. In those who received IV/IP chemotherapy but discontinued prior to the completion of the planned treatment, the reason for discontinuing or modifying therapy was recorded. A potentially modifiable factor was defined as any factor not present at baseline that could reasonably be prevented or altered.

Descriptive statistics were used where appropriate. Student's t-test was utilized for continuous variables, and the chi-square and Fisher exact tests (where appropriate) were used for nominal variables. Survival was analyzed using the Kaplan-Meier method and compared between chemotherapy groups using the log-rank test. Cox proportional hazards regression was used to assess the effect of variables on overall survival. Statistical significance was set at a two-sided alpha of 0.05.

RESULTS

Review of institutional databases identified 330 women who met inclusion criteria. Patient characteristics are shown in Table 2. Of these 330 women, 261 (79%) received at least one cycle of IV/IP chemotherapy. Patients who received IV/IP chemotherapy were younger ($p<0.001$), had fewer comorbidities ($p=0.02$), and higher KPS values at their initial chemotherapy evaluation ($p<0.001$). There was no difference between the two groups with regard to residual disease ($p=0.29$), BMI ($p=0.16$), histology ($p=0.28$), or stage ($p=0.41$).

The majority (175/204, 86%) of patients who received IV/IP chemotherapy outside of a clinical trial were treated with a modified GOG-172 outpatient regimen previously demonstrated by our institution to have improved tolerability and similar efficacy (14). This modified outpatient IV/IP regimen consists of a 3-h IV paclitaxel (135mg/m²)

administration, a reduced dose of IP cisplatin (75mg/m²) delivered on day 2, and IP paclitaxel (60mg/m²) on day 8. Other common modifications included the substitution of IP carboplatin for IP cisplatin (n=10, 5%), the substitution of IV paclitaxel with docetaxel combined with the elimination of the IP paclitaxel (n=5, 2.5%), and the elimination of the IP paclitaxel alone (n=9, 4%). None of the patients were treated with the exact regimen used in GOG-172 (3). Of the 57 patients in the IV/IP group who were treated on a clinical trial, 30 (53%) participated in an institutional non-randomized phase II trial (15) with the modified GOG-172 regimen previously described with the addition of bevacizumab at cycle two followed by bevacizumab maintenance.

Sixty-nine patients (21% of all patients included in the study) received IV-only chemotherapy. The most common standard chemotherapy regimen given was carboplatin and paclitaxel administered every 21 days (28/61, 46%). Fourteen patients (23%) received at least one cycle of carboplatin and weekly paclitaxel outside of a clinical trial. In the 8 patients (12%) who participated in a clinical trial, the most common regimen was carboplatin, weekly paclitaxel and bevacizumab with bevacizumab maintenance on GOG-252 (6/8, 75%) (16).

A postoperative issue was the most common reason cited for not initiating IV/IP chemotherapy, noted in 18 (26%) of the 69 patients who received IV chemotherapy and comprising 5.4% of the entire cohort (Table 3). The most common postoperative issue cited was delayed wound healing, documented in 10 patients, comprising 15% of the IV-only cohort and 3% of the entire cohort. The second most common reason cited for avoiding IV/IP chemotherapy was baseline comorbidities (10, 15%) including hearing impairment in 4 (40%), advanced age in 2 (20%), peripheral neuropathy in 1 (10%), cardiac disease in 1 (10%), and a combination of these comorbidities in 2 (20%) patients. In those who had a postoperative issue that prevented the initial administration of IV/IP chemotherapy, the issue resolved in 11 (61%) of 18 patients. The most common issue to resolve was delayed wound healing (6/11, 55%) followed by poor postoperative performance status (3/11, 27%). The reasons cited for not initiating IV/IP chemotherapy after resolution of the initial issue included the presence of a new issue precluding IP chemotherapy administration in 2 patients (18%), an IP port complication in 2 patients (18%), late resolution of the original reason (between cycles 5 and 6) in 2 patients (18%), and 1 patient declined IP chemotherapy (9%). The reason for not initiating at a later time was not stated in 4 patients (36%).

In patients who received at least one cycle of IV/IP chemotherapy, the median number of completed IV/IP cycles was 6 (range, 1–6), with 162 patients (62%) receiving 6 cycles and 216 patients (83%) receiving 4 or more cycles. Forty of the 261 patients in the IV/IP group (15%) started with IV-only chemotherapy (Table 4). Among these 40 patients, the most common reason cited for starting with IV chemotherapy was delayed wound healing (n=12). Other commonly cited reasons were infection (n=8), poor performance status (n=6), and desire to avoid delay in chemotherapy administration for IP port placement (n=5).

Of patients who received IV/IP chemotherapy, 63 (24%) transitioned to an IV-only regimen and 3 (1%) discontinued therapy altogether prior to the completion of 6 cycles. Among these 66 patients, toxicity was the most commonly cited reason for treatment modification or

discontinuation (44/66, 67%), which included fatigue in 8, abdominal pain in 5, nephrotoxicity in 5, nausea in 4, bowel obstruction in 4, neuropathy in 3, and a combination of these toxicities in 11 patients. No patients receiving bevacizumab discontinued IV/IP therapy due to hypertension. In patients receiving bevacizumab, there was no difference in dose delays due to hypertension between patients receiving IV/IP chemotherapy and IV-only chemotherapy ($p=0.57$) or in patients receiving regimens containing IP cisplatin ($p=0.22$). Four patients had IV/IP chemotherapy discontinued at their request and transitioned to IV-only chemotherapy. In the entire cohort of 330 patients, neuropathy was identified as one of the reasons for treatment modification in 11 patients (4%) who received IV/IP chemotherapy and 2 patients (3%) who received IV chemotherapy ($p=1.00$).

Median follow-up time for the entire cohort was 51.7 months (range, 12.9–122.8 months). Median progression-free survival (PFS) in the IV/IP chemotherapy group was 27 months vs 20 months in the IV-only group, although this did not reach statistical significance ($p=0.07$). Five-year overall survival (OS) was significantly longer in patients who received IV/IP chemotherapy (69% vs 51%, $p<0.001$). When PFS was evaluated by residual disease, patients who had no gross residual disease and received IV/IP chemotherapy had a PFS of 36.9 months compared with 21.3 months in those with optimal but gross residual disease receiving IV/IP chemotherapy ($P<0.001$). For those patients who had no gross residual disease and received IV-only chemotherapy, PFS was 21 months compared with 17.6 months for those with optimal but residual disease receiving IV-only chemotherapy ($P=0.52$). Receipt of at least 1 cycle of IV/IP chemotherapy (HR 0.51; 95% CI, 0.32–0.80) and no gross residual disease at the time of primary debulking surgery (HR 0.47; 95% CI, 0.31–0.71) were associated with improved OS. Age (HR 0.99; 95% CI, 0.97–1.01), stage (stage IIIC referent, stage IIIA HR 1.10, 95% CI, 0.47–2.6; stage IIIB HR 0.50, 95% CI, 0.18–1.37), and baseline comorbidities (HR 1.06; 95% CI, 0.84–1.34) did not affect overall survival.

DISCUSSION

Combination IV/IP chemotherapy following optimal cytoreduction in patients with stage III ovarian, fallopian tube, or primary peritoneal carcinoma leads to a PFS and OS advantage in large, randomized trials (3, 4). The NCI currently recommends strongly considering IV/IP chemotherapy in optimally cytoreduced stage III ovarian, fallopian tube, and primary peritoneal cancer (5). Despite these recommendations, this regimen is not widely used (6–9). A recent report showed that the overall rate of IV/IP chemotherapy use at six NCCN cancer centers after the NCI's recommendation was released in 2006 was only 47%. The authors concluded that increasing the use of IV/IP chemotherapy may improve ovarian cancer outcomes in these institutions; however, they did not identify the rationale for giving IV-only chemotherapy at these institutions (6). It is important to identify barriers to the use of IV/IP chemotherapy in order to ultimately affect a change in the rate of administration. Editorials, reviews, and surveys of Society of Gynecologic Oncology (SGO) and American Society of Clinical Oncology (ASCO) members have presented general objections providers have to IV/IP chemotherapy (11, 13, 17, 18), but this is the first study evaluating cited reasons in a cohort of patients eligible for IV/IP chemotherapy.

The main reasons cited for patients not receiving IP therapy were postoperative issues, comorbidities, IP port-related issues, presence of an ileostomy, patient preference, and clinical trial participation. We determined that some of these reasons were potentially modifiable and postulate that a concerted effort to prevent such modifiable factors could increase adherence to the NCI's recommendations. Postoperative issues, particularly delayed wound healing, was documented most commonly as the reason for selecting an IV-only regimen, although the overall rate in our cohort was low at 5%. While ovarian cancer patients are not classically obese, 15% of our cohort had a BMI ≥ 30 and 40% had a BMI ≥ 25 . With an increase in adiposity and its attendant comorbidities, delayed wound healing and surgical site infection are problems encountered across surgical specialties (19). Several modified wound closure techniques and modifications in postoperative management have been evaluated and shown to decrease complication rates (20–23). Negative pressure wound therapy has been shown to have promising results in the surgical oncology population, but with mixed results overall. Blackham et al (24) demonstrated decreased surgical site infections but no decrease in spontaneous superficial dehiscence with negative pressure wound therapy in a retrospective analysis of a surgical oncology population. Masden et al (25) performed a randomized controlled trial of negative pressure wound therapy versus standard dressings in a high-risk population and demonstrated no difference in surgical site infections or dehiscence; however, the majority of these patients (91%) underwent lower extremity wound closure, and the applicability to our population is questionable. Improved wound healing with the prophylactic use of negative pressure therapy is currently being investigated in gynecologic oncology patients in a prospective randomized fashion at our institution. New medical and surgical techniques to improve wound healing are needed to improve care in gynecologic oncology patients.

IP port complications and lack of an IP port at the initial chemotherapy visit are also potentially modifiable factors identified in our cohort. In GOG-172, 119 (58%) of those randomized to the IV/IP chemotherapy arm did not complete 6 cycles of IV/IP chemotherapy, 34% due primarily to IP port complications, most commonly infection (26). The rate of IP port complications in our cohort was 8 % (24/301). The most common complication in our cohort was port malfunction (11/24, 46%). One patient was assigned to the IV chemotherapy group as she did not have an IP port. Five patients in the IV/IP chemotherapy group who subsequently had an IP port inserted started with IV chemotherapy due to the provider not wanting to delay treatment for IP port placement. In the GOG-172 cohort, there was no difference in completion of 6 cycles of IV/IP chemotherapy when the IP port was inserted at the time of primary cytoreductive surgery versus as a separate subsequent procedure (26). An IP port should not be placed in a grossly contaminated field, but the initial concern over placing an IP port at the time of any bowel resection has subsided, as the rates of IP port infections do not appear to significantly differ when placed at a primary cytoreductive surgery in which an uncomplicated bowel resection is performed (27). The IP port infection rate in our cohort was 2%. Notably, 41% of the IP ports placed in our cohort were inserted during the primary debulking surgery in which an uncomplicated bowel resection was performed. This further supports that IP port insertion at the time of uncomplicated bowel resection is not contraindicated. Based on our data, it appears that IP port placement at the time of primary cytoreductive surgery is safe, makes a second

operation unnecessary, and may increase the rate of IV/IP chemotherapy administration by avoiding any delays for IP port insertion.

Other potentially modifiable factors can center on provider education. Data could not be found demonstrating that patients with “localized” disease or those with para-aortic lymph node involvement representing the only extrapelvic disease would not benefit from IV/IP chemotherapy. Providers should consider this modality in these situations. Resolution of all modifiable factors would increase the rate of IV/IP chemotherapy administration in this cohort from 79% to 88%.

Advanced age was cited as the only reason for administering IV-only chemotherapy in 2 patients and as a contributing reason in 2 additional patients. The age range for these 4 patients was 76 to 83 years. Notably, while the group that received IV/IP chemotherapy was statistically younger, 22 patients (8%) who received IV/IP chemotherapy were 70 years of age at diagnosis. In this small subset of patients, the median number of IV/IP cycles received was 6 (range, 1–6), with 50% (11/22) receiving 6 cycles and 91% (20/22) receiving 4 or more cycles of IV/IP chemotherapy. While age was not considered a “modifiable factor” in this study, it should be noted that data have previously shown that IV/IP chemotherapy may be safely administered in the elderly ovarian cancer population (28). Consideration for IV/IP chemotherapy should be based on functional status and not age alone.

In our cohort, 11 patients who were initially started on IV chemotherapy had resolution of the reason IV/IP chemotherapy was avoided, which most commonly was delayed wound healing. A reason for not initiating IV/IP chemotherapy at that time was given in 7 patients, leaving 4 in whom a reason for continuing IV-only chemotherapy could not be identified. A survival advantage was seen in GOG-172 despite only 42% of the IV/IP chemotherapy group receiving all 6 cycles (3). Long-term survival analyses of GOG-114 and GOG-172 demonstrated that patients who received all 6 cycles had improved survival compared with those who received 3 cycles IV/IP followed by 3 cycles IV chemotherapy; however, these results may be subject to bias, as healthier patients are more likely to receive all 6 cycles (4, 29). Others have demonstrated no difference in survival based upon the number of IV/IP chemotherapy cycles received, with patients who started with IV chemotherapy and subsequently transitioned to IV/IP chemotherapy having similar PFS and OS to those receiving all 6 adjuvant cycles as IV/IP (30). The goal should be to administer at least 1 cycle of IV/IP chemotherapy, and providers should continually reassess patients unable to start with IV/IP chemotherapy for possible transition from IV-only chemotherapy.

Recent PFS data for trial GOG-252 were presented at the 2016 annual SGO meeting. GOG-252 is a multicenter randomized phase III trial comparing IV carboplatin with IV weekly paclitaxel, IV weekly paclitaxel with IP carboplatin, and IV/IP paclitaxel with IP cisplatin. Bevacizumab was added concurrently and as maintenance in all arms. There was no difference in PFS between the three groups. It was noted, however, that the PFS in the patients with no gross residual disease treated with IV/IP paclitaxel and IP cisplatin (33.8 months) did not approach the PFS seen in this group in trial GOG-172 (60.4 months). Interestingly, the median PFS for patients in our cohort who had no gross residual disease and received IP chemotherapy was 36.9 months, similar to that of GOG-252 and shorter than

that of GOG-172 (31-32). It has been postulated that the decreased dose of IP cisplatin may contribute to this discrepancy. The dose of IP cisplatin given to the majority of patients in our cohort was the same as in the IV/IP paclitaxel and IP cisplatin arm of GOG-252 and decreased from the GOG-172 regimen. The addition of bevacizumab to all arms in GOG-252 also makes these results challenging to interpret, as bevacizumab may negate the benefits of weekly paclitaxel as was seen in the subset analysis of GOG-262 (33). Given the current available data, bevacizumab does not improve overall survival in the primary adjuvant setting in patients with minimal residual disease and should not be used in this setting outside of a clinical trial (34). Finally, data from several IP trials demonstrated improved survival with an IP regimen, while only one trial demonstrated improved survival with a weekly paclitaxel regimen (1-4, 35). Several ongoing clinical trials may provide more information, but given these current data, the NCI is unlikely to change their recommendation for strong consideration of IV/IP chemotherapy in those that are eligible. At our institution, IV/IP chemotherapy remains our standard, off-protocol, primary chemotherapy regimen for patients with advanced ovarian carcinoma who have undergone optimal primary debulking surgery.

Our adherence to the NCI recommendation is higher than that recently reported at six NCCN institutions, despite similar patient characteristics and likely similar logistical considerations (6). While current data would suggest that this increased administration of IV/IP chemotherapy is beneficial for our patients, the high percentage of patients receiving at least 1 cycle of IV/IP chemotherapy is a limitation in this current study evaluating the rationale for not administering IV/IP chemotherapy. In our large academic center, IV/IP chemotherapy has been broadly used since prior to the NCI recommendation. This may make our results less generalizable. The reasons cited for not administering IV/IP chemotherapy may be very different in other institutions where the modality is not used as commonly or there are logistical barriers to administering IP chemotherapy.

Our study is a retrospective cohort study and has all the limitations associated with retrospective studies. Given that IV/IP chemotherapy is standard at our institution, providers generally provided a clear reason for not administering IV/IP chemotherapy in an eligible patient, but there were some cases in which this information was not available. Documentation of the specific eligibility criteria for GOG-172 in patients not being assessed for eligibility at the time of their visit could also potentially bias our study, as some patients who were eligible may have been nonetheless excluded.

CONCLUSIONS

The NCI currently recommends strong consideration for IV/IP chemotherapy in patients with optimally cytoreduced stage III ovarian, fallopian tube, and primary peritoneal cancer (5). There are potentially modifiable factors preventing the adherence to these guidelines, which if modified, can lead to the increased use of this regimen. Providers should also be aware that the benefit of IV/IP chemotherapy is potentially achievable regardless of the total number of cycles delivered. Given this, initiating an IV-only regimen should not preclude transition to an IV/IP regimen when possible.

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Research Highlights

1. IP chemotherapy was given to 79% of eligible patients in our cohort
2. Potentially modifiable factors were identified as prohibiting IP chemotherapy use
3. Postoperative status is the most cited reason for giving IV-only chemotherapy

Table 1

GOG-172 inclusion and exclusion criteria utilized (3).

Inclusion Criteria:

- Adequate bone marrow, renal, and hepatic function as defined by WBC ≥ 3000 cells/mcl, platelets ≥ 100,000/mcl, serum creatinine ≤ 2 mg/dcl, bilirubin ≤ 1.5 times normal, alkaline phosphatase and SGOT ≤ 3 times normal.
- Patients with a GOG performance status of 0, 1, or 2.
- Patients must be entered no more than six weeks postoperatively.

Exclusion Criteria:

- Patients with epithelial ovarian carcinoma of low malignant potential (borderline carcinomas).
- Patients with suboptimal (>1cm) residual disease.
- Patients who have received radiotherapy or chemotherapy.
- Patients with septicemia, severe infection, or acute hepatitis.
- Patients with severe gastrointestinal bleeding.
- Patients whose circumstances do not permit completion of study or required follow-up.
- Patients with a GOG performance status of 3 or 4.
- Patients with other invasive malignancies, with the exception of non-melanoma skin cancer, who had (or have) any evidence of the other cancer present within the last 5 years or whose previous cancer treatment contraindicates this protocol therapy.
- Patients with unstable angina or those who have had a myocardial infarction within the past six months. Patients with evidence of abnormal cardiac conduction (e.g. bundle branch block, heart block) are eligible if their disease has been stable for the past six months.

Table 2

Patient characteristics.

Patient Characteristic	IV Chemotherapy (n=69)	IV/IP Chemotherapy (n=261)	p value
Median Age, years (range)	63 (40 – 83)	59 (30 – 79)	<0.001 ^a
Median BMI, kg/m ² (range)	24 (16 – 43)	24 (17 – 46)	0.16 ^a
Total comorbidities: median (range)	1 (0 – 3)	0 (0 – 3)	0.02 ^a
Stage: n (%)			0.41 ^b
IIIA	2 (3%)	19 (7%)	
IIIB	4 (6%)	16 (6%)	
IIIC	63 (91%)	226 (87%)	
Histology: n (%)			
Serous adenocarcinoma	65 (94%)	242 (93%)	
Endometrioid adenocarcinoma	1 (1.5%)	1 (0.4%)	
Clear cell carcinoma	3 (4%)	6 (2%)	
Undifferentiated carcinoma	0 (0%)	4 (1.5%)	
Mixed carcinoma	0 (0%)	8 (3%)	
Residual Disease: n (%)			0.29 ^b
No gross residual	31 (45%)	136 (52%)	
1 cm	38 (55%)	125 (48%)	
PDS Location: n (%)			
MSKCC	53 (77%)	201 (77%)	
Outside institution	16 (23%)	60 (23%)	
Bowel resection at PDS: n (%)	36 (52%)	105 (40%)	0.07 ^b
Ostomy at PDS: n (%)	9 (13%)	3 (1%)	<0.001 ^b
IP port placed at PDS: n (%)	37 (54%)	215 (82%)	<0.001 ^b
KPS at initial chemotherapy evaluation: median (range)	80 (50 – 100)	90 (60 – 100)	<0.001 ^a
Participated in a clinical trial: n (%)	8 (12%)	57 (22%)	0.06 ^b
Total adjuvant chemotherapy cycles: median (range)	6 (2 – 8)	6 (3 – 9)	0.75 ^a

IV = intravenous, IP = intraperitoneal, BMI = body mass index (weight [kg]/height [m²]), MSKCC = Memorial Sloan Kettering Cancer Center, PDS = primary debulking surgery, KPS = Karnofsky Performance Status.

^aTwo-sided t-test.

^bChi-square.

Table 3

Reasons cited for not giving IV/IP chemotherapy in patients who received IV chemotherapy (N=69).

Primary Reason Cited for Not Giving IV/IP Chemotherapy	n (%)
Postoperative issue	18 (26%)
Wound infection	2 (3%)
Delayed wound healing	10 (15%)
Performance status	6 (9%)
Baseline comorbidities	10 (15%)
IP port complication	8 (12%)
Clinical trial	6 (9%)
Patient choice	6 (9%)
Ileostomy present	5 (7%)
Intra-abdominal adhesions	3 (4%)
Other	9 (13%)
Disease thought to be localized	1 (1.4%)
Stage III by PALN involvement	1 (1.4%)
Avoid delay for IP port placement	1 (1.4%)
Severe taxane allergy with first infusion	2 (3%)
Recent cerebrovascular accident	1 (1.4%)
Tenckhoff catheter in place	1 (1.4%)
Extensive nature of PDS	1 (1.4%)
Recent LBO requiring stent	1 (1.4%)
Not stated	4 (6%)

IP = intraperitoneal, PALN = para-aortic lymph node, PDS = primary debulking surgery, LBO = large bowel obstruction.

Table 4

In patients who received at least one cycle of IV/IP chemotherapy (N=261), cited rationale for starting with IV-only chemotherapy or discontinuing IV/IP chemotherapy early

Cited Rationale	n (%)
IV-only chemotherapy started initially	40 (15%)
Delayed wound healing	12 (5%)
Infection	8 (3%)
Low KPS	6 (2%)
Avoid delay for IP port placement	5 (2%)
IP port malfunction	3 (1%)
Ileostomy	2 (1%)
Other	4 (1.5%)
IV/IP chemotherapy discontinued early	66 (25%)
Toxicity	44 (17%)
Fatigue	8 (3%)
Abdominal pain	5 (2%)
Nephrotoxicity	5 (2%)
Nausea	4 (1.5%)
Bowel obstruction	4 (1.5%)
Neuropathy	3 (1%)
Multiple	11 (4%)
Other	4 (1.5%)
IP port malfunction	6 (2%)
Patient request	4 (1.5%)
Not stated	3 (1%)
Progression of disease	2 (1%)
Other	7 (3%)