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Risk factors for readmission in patients with ovarian, fallopian tube, and primary peritoneal carcinoma who are receiving front-line chemotherapy on a clinical trial (GOG 218): an NRG oncology/gynecologic oncology group study (ADS-1236)*

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Abstract

Background—Readmission within 30 days is a measure of care quality. Ovarian cancer patients are at high risk for readmission, but specific risk factors are not defined. This study was designed to determine risk factors in patients with ovarian cancer receiving upfront surgery and chemotherapy.

Methods—The study population was enrolled to GOG 0218. Factors predictive of admission within 30 days of a previous admission or 40 days of cytoreductive surgery were investigated. Categorical variables were compared by Pearson chi-square test, continuous variables by

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Wilcoxon–Mann–Whitney test. A logistic regression model was used to evaluate independent prognostic factors and to estimate covariate-adjusted odds. All tests were two-tailed, $\alpha = 0.05$.

Results—Of 1873 patients, 197 (10.5%) were readmitted, with 59 experiencing >1 readmission. One-hundred-forty-four (73%) readmissions were post-operative (readmission rate 7.7%). Significant risk factors include: disease stage (stage 3 vs 4, $p = 0.008$), suboptimal cytoreduction (36% vs 64%, $p = 0.001$), ascites, ($p = 0.018$), BMI (25.4 vs 27.6, $p < 0.001$), poor PS ($p < 0.001$), and higher baseline CA 125 ($p = 0.017$). Patients readmitted within 40 days of surgery had a significantly shorter interval from surgery to chemotherapy initiation (22 versus 32 days, $p < 0.0001$). Patients treated with bevacizumab had higher readmission rates in the case of patients with >1 readmission. On multivariate analysis, the odds of re-hospitalization increased with doubling of BMI (OR = 1.81, 95% CI: 1.07–3.07) and PS of 2 (OR = 2.05, 95% CI 1.21–3.48).

Conclusion—Significant risk factors for readmission in ovarian cancer patients undergoing primary surgery and chemotherapy include stage, residual disease, ascites, high BMI and poor PS. Readmissions are most likely after the initial surgical procedure, a discrete period to target with a prospective intervention.

Keywords

Readmissions; Ovarian cancer; Chemotherapy

1. Introduction

Re-hospitalization within 30 days of prior admission has been identified by the Obama Administration as a target for reducing health care spending as well as a measure of quality of care [1]. The 2007 and 2008 Medicare Payment Advisory Commission report to Congress identified hospital readmission as a marker of poor quality and high cost [2]. The Affordable Care Act subsequently incorporated this report into Section 3025, which assesses a payment penalty on hospitals with higher than expected rates of readmission. Initially imposed with respect to three specific medical conditions (heart failure, heart attack and pneumonia), these penalties currently encompass other medical and surgical conditions.

The use of readmission rates as a measure of quality presumes that readmission is primarily due to a poor coordination of care between settings. This poor coordination is believed to occur as a result of a payment environment that rewards volume of services rather than quality of care over time. Payment penalties, therefore, are intended to incentivize medical centers to improve coordination of care and therefore decrease readmission rates. A high-profile study by Jencks et al. reported a 19.6% readmission rate within 30 days of the index hospitalization among Medicare beneficiaries; only 10% of readmissions were estimated to be planned [3]. The authors cited poor communication with patients, insufficient outpatient follow-up, and a lack of care coordination to explain this high readmission rate, and estimated the cost of unplanned re-hospitalization in 2004 alone to be \$17.4 billion [3].

Published studies regarding unplanned hospital readmission have primarily focused on Medicare patients with chronic illnesses (not including cancer) and surgical patients following specific procedures such as joint replacement or intestinal surgery. There are

limited data specific to patients with cancer. The national cost of cancer care is substantial and expected to increase because of population changes alone [4]. As the US population ages, patients with cancer will generate an increasingly higher proportion of health care costs, and addressing the cost of their care will be crucial.

Patients with ovarian cancer represent a unique group of cancer patients, because they are treated with a combination of both extensive surgery and intensive combination chemotherapy. They therefore represent an important population to study with respect to avoiding unnecessary readmission. In order to strategize how to decrease readmissions and improve patient quality of care, it is imperative to first identify predictors of readmission. To date, most studies related to unplanned readmission of patients with advanced ovarian cancer have been limited to single institution studies with retrospective capture of data. One single institution study of a gynecologic oncology inpatient service reported an overall hospital readmission rate of 13.2%; patients with ovarian cancer represented one-third of these readmissions, with the primary indication for admission non-surgical in over 90% of cases [5]. Other authors have confirmed a similar high rate of readmission in patients with ovarian cancer, also retrospectively and at the single institution level [6,7]. A prospective intervention study is crucial to determine if these readmissions are “avoidable” so we can then design methods by which they may be prevented.

The current study was designed to utilize prospectively collected data from a clinical trial managed by the Gynecologic Oncology Group (GOG) in order to retrospectively determine risk factors for rehospitalization in a nationally representative selected population of women with ovarian cancer. While patients who receive chemotherapy on clinical trial are a very special group (with likely excellent performance status, for example) this data will allow us to identify specific risk factors for re-admission in a national and therefore more generalizable population from which to design a prospective intervention. The primary objective was to determine risk factors for readmission in patients with advanced ovarian cancer after primary debulking surgery and front-line chemotherapy.

2. Materials and methods

The data set was derived from a phase III placebo-controlled, double blinded clinical trial (GOG-0218), evaluating primarily progression-free survival in women with stages III (incompletely resected) and IV epithelial ovarian, primary peritoneal, or fallopian tube cancer following primary debulking surgery [8]. The full schema for GOG-0218 is shown in Fig. 1. For the purpose of this study, the surgical hospitalization was counted as the index hospitalization.

On-study hospitalizations were captured in the case report forms (CRFs) produced by the treating institution and collected by the GOG Statistical and Data Center. All hospitalizations were recorded as adverse events according to the clinical trial protocol. Form T-PHRM for this study included the question “was the patient hospitalized as a result of reported adverse events.” This form also accounts for toxicity onset dates, allowing the determination of the interval between hospitalizations. The adverse event expedited reporting system (AdEERS) forms allowed the association of toxicity with readmission.

Data from both Form T (which includes non-severe events) and AdEERS were used. These data sets were combined, assuming that matching adverse events within 1–2 days of each other referred to the same event.

Any patient hospitalized while on the protocol within 30 days of a previous hospitalization, or within 40 days of cytoreductive surgery, was considered as readmitted. We defined any hospitalization within 40 days of surgery to be a post-surgical readmission, allowing for an up to 10 day hospital stay following date of surgical cytoreduction, recognizing that this would likely result in an over-estimation of postoperative readmissions. This decision was made because the dataset included only surgical dates and not discharge dates following surgical procedures.

Other data collected included patient demographics, medical history, clinic-pathologic information, baseline hematology and chemistry values, adverse events and toxicities and their onset dates, and any other factors related to specific hospitalization. Because exact dates of hospitalization were unavailable, they were estimated from the onset dates of adverse events recorded for each cycle of treatment. The association of readmission to potential predictors was assessed.

We examined clinicopathologic, medical, and surgical characteristics, as well as toxicities in two pairs of subgroups in GOG-0218: those patients readmitted versus not readmitted; and patients readmitted only once versus those readmitted two or more times. Categorical variables were compared between groups by the Pearson chi-square test, and continuous variables by the Wilcoxon-Mann-Whitney test [9,10]. A logistic regression model comparing the two groups of patients was used to evaluate independent prognostic factors and to estimate their covariate-adjusted odds of re-hospitalization. The nonlinearity of the effect of continuous variables was assessed using restricted cubic splines. All statistical tests were two-tailed with the significance level set at $\alpha = 0.05$, except where noted. Statistical analyses were performed using the R programming language and environment [11].

Because some patients had at least one prognostic factor missing, missing values were generated by multiple imputation while considering all the variables at once [12]. Under the assumption of data *missing at random* (MAR), we created 10 complete data sets using predictive mean matching. The previously described logistic regression model was fitted to each imputed data set and combined into a single model with averaged regression coefficients and variance and covariance estimates adjusted for imputation.

All patients signed an approved informed consent and authorization permitting release of personal health information prior to enrollment. All institutions required approval by their local Institutional Review Board before trial initiation.

3. Results

There were a total of 1873 patients from GOG-0218 that were enrolled in the original clinical trial; of those patients, 570 unique women (30.4%) were hospitalized while on study with 197 (10.5%) unique women readmitted by the definition above (within 30 days of a prior admission or within 40 days of surgical date). Notably, 144 of these 197 readmissions

(73%) were within 40 days of the date of surgery and so fall into the post-operative re-admission category, resulting in a total number of $144/1873 = 7.7\%$ patients readmitted after surgery. Of these 144, 10 women were re-hospitalized after surgery but before the first cycle of chemotherapy. For these 10 women, the median time for re-hospitalization before the first cycle was 3.5 days, and in this group the most common adverse event was gastrointestinal: 2 patients were readmitted with grade 3 gastrointestinal toxicity. The remaining 134 women were re-hospitalized within the 40 days from surgical date but after the first cycle of chemotherapy had been delivered. These 134 women had a median time from surgery to chemotherapy initiation of 21 days (range 15–28 days). When compared to the total group of patients on study ($N = 1676$), the 144 patients who were admitted within 40 days of surgery had a significantly shorter interval from surgery to chemotherapy initiation (22 versus 32 days, $p < 0.001$).

The characteristics of the re-hospitalized patients compared to the total population are shown in Tables 1 and 2. Patients who were re-hospitalized were evenly distributed among the 3 chemotherapy treatment arms shown in Fig. 1 (I 33.5%, II 35.5%, III 31%). The majority of patients (138 women, 70%) were re-hospitalized only once. Forty-six (23.4%) had 2 re-hospitalizations, 9 (4.6%) had 3, and 4 (2%) had 4 or more re-hospitalizations. The most common adverse event types (all defined as greater than or equal to grade 3) coded with the re-hospitalization were gastrointestinal at 63%, infection at 43%, and pain and constitutional symptoms 29% each (Table 3). With respect to specific SAEs, re-hospitalized patients were more likely to experience neutropenia, leukopenia and anemia.

Significant tumor related factors associated with re-hospitalization included: higher initial stage of disease (stage 3 vs stage 4), increased size of residual tumor after surgery (median 1.5 vs 2 cm), presence of ascites at diagnosis, and higher baseline post-operative CA 125. When considering suboptimal vs optimal cytoreduction as defined by the protocol, those women who had suboptimal cytoreduction were more likely to be readmitted (64% vs 36%, $p = 0.001$). There was no significant difference seen between tumor histology or chemotherapy treatment arm. With respect to patient factors, re-hospitalization was associated with higher BMI and poor performance status. Medical factors significantly associated with re-hospitalization included hypertension and auto-immune disease. There were no differences seen with respect to other medical co-morbidities, including diabetes. Patient age, race, and insurance payer (a surrogate for socio-economic status) were also not significantly associated with re-hospitalization. A bowel resection at the time of primary surgical cytoreduction did not significantly contribute to re-hospitalization.

Fifty-nine patients had 2 or more readmissions (Tables 4 and 5). In this group, there were differences between the treatment arms, with the 2 arms containing bevacizumab exhibiting higher re-readmission rates: Arm I (chemotherapy alone) had 12 (20.3%), arm II had 27 (45.8%) and arm 3 had 20 (33.9%) readmissions. The mean time from the first readmission to the second was 20 days (interquartile range 15–27). Patients who had multiple readmissions (rather than just one) were more likely to have had a surgery that resulted in minimal residual disease ($p = 0.03$) or requiring a bowel resection ($p = 0.039$ for small bowel and 0.036 for large bowel resection). From a medical standpoint, these women were more

likely to have autoimmune disease ($p = 0.033$). Once again race and payer were not significant.

A logistic regression analysis showed that the odds of readmission: increased 81% for a doubling of BMI (OR = 1.81, 95% CI: 1.07–3.07; $P = 0.028$); were 105% higher for patients with a performance status of 2 than for performance status 0 (OR = 2.05, 95% CI: 1.21–3.48; $P = 0.008$); decreased 25% for each unit decrease of pre-chemo hemoglobin measured (g/dL) (OR = 0.75, 95% CI: 0.66–0.86; $P < 0.001$); increased 64% for a doubling of pre-chemotherapy peripheral WBC count (mm^3) (OR = 1.64, 95% CI: 1.16–2.30; $P = 0.005$); and were 159% higher for patients with a history of autoimmune disease than for those without (OR = 2.59, 95% CI: 1.17–5.72; $P = 0.018$).

4. Discussion

Decreasing readmission rates continues to be an area of focus for the health care industry, with the ultimate goal of improving coordination of care and thus decreasing overall cost of care. Moving forward, it will be imperative that medical centers avoid costly fines imposed for the so-called “avoidable” readmissions that will not be reimbursed by Medicare and subsequently by other payers. Section 3025 of the Affordable Care Act added section 1886(q) to the Social Security Act establishing the Hospital Readmissions Reduction Program, which requires CMS to reduce payments to hospitals with excess readmissions after admissions for heart failure, acute myocardial infarction, or pneumonia (excess readmission ratio is defined as risk-adjusted predicted readmissions divided by risk-adjusted expected readmissions). Additional measures have subsequently been instituted, including penalties for those readmitted after elective knee or hip replacements, and those initially admitted for exacerbations of chronic pulmonary disease. The program, which began for discharges beginning on October 1, 2012, has increased the maximum penalty for excess admissions from 1% to 3% in 2015. In 2014, 2610 hospitals were fined a total of \$428 million [13]. While certain cancer hospitals are exempted from these readmission penalties, there remain numerous opportunities to reduce readmissions for all patients as our health care system evolves to increase financial incentives to decrease readmission rates in an effort to improve patient care.

Patients with advanced ovarian cancer are at particularly high risk for readmission because of the need for complex surgical and medical oncologic interventions as well as disease burden and age-related medical co-morbidities. This is therefore an ideal population to target with interventions aimed at decreasing this risk. Prospective clinical trials designed to institute support systems for those patients most at risk for readmission are critically needed in order to both decrease readmission rates and improve patients' overall quality of care and of life.

Retrospective studies of readmission ovarian cancer patients can be useful in identifying those women who are at highest risk, with the goal of targeting them with prospective interventions. While single institution studies are limited by a potential lack of generalizability, they may be useful in that they can quantify the scope of the problem and begin to help theorize solutions. In addition to the one retrospective single institution study

described above, two other groups have focused specifically on the population of post-operative ovarian cancer patients. Clark et al. found a readmission rate of 12% following surgical cytoreduction in their patients in Boston with stage II-IV ovarian cancer; perioperative complications placed the patient at highest risk, while age, medical comorbidities, surgical radicality did not affect the likelihood of re-admission [6]. Discharge home with ancillary services was not protective against readmission. In the same population of patients in Alabama, Fauci et al. demonstrated a re-hospitalization rate of 16%, with more than half of readmissions due to small bowel obstruction or ileus [7]. In this analysis, unlike the one in Boston, medical comorbidities were significant in both the univariate and multivariate analyses, with an increase of 1 comorbid condition associated with a 46% increase in the odds of readmission.

Most recently, Eskander et al. reported a SEER review of rehospitalizations following surgery for ovarian cancer in the United States [14]. The goal behind using SEER data is to generate more generalizable results, but specific patient and tumor related data is not available for analysis. For example, due to the nature of the SEER database, only patients older than 65 years were included in the analysis, and data regarding debulking status, histology, chemotherapy, and patient specific underlying medical problems such as obesity were not available. The authors calculated the highest rate of readmission of all the series at 19.5%, a rate not entirely surprising given the population under consideration. Risk factors for post-operative readmission in the SEER series included infection, dehydration, ileus/obstruction, metabolite/electrolyte abnormalities, and anemia. In the multivariate analysis, year of discharge was significantly associated with readmission, with the odds ratio increasing from 1.32 in the time period 1996–2000 to 1.73 in the time period 2006–2010. The authors postulate that the increase in readmission rates over time is in part due to shorter hospital stays. In addition, women readmitted within 30 days had a significantly greater 1 year mortality rate when compared with patients not readmitted. While provocative, this analysis did not allow for identification of a group of patients with specific risk factors to whom interventions might be applied.

Other groups have considered readmission rates for surgical patients undergoing colorectal surgery, a population with surgical risk factors in common with ovarian cancer patients [15–20]. In these series, most of which focus on patients with colorectal cancer, the most common risk factors for readmission include: the occurrence of post-operative complications, older age, medical comorbidities, and lower socioeconomic status [15–20]. When considering the oncology patient population, most of whom are admitted to medical oncology inpatient units, the most common risk factors for readmission include: gastrointestinal cancer, nausea within 24 h of discharge, financial and insurance concerns, or caregiver difficulty [21]. Finally, measures of pre-operative risk other than performance status (PS) are available in the population of women with gynecologic malignancy that may assist in identifying those women at increased risk, including frailty and poor pre-operative quality of life [22,23].

Potentially impacting the rate of readmission, there has also been an effort to reduce length of stay (LOS) as a means of reducing cost of care over the past few decades. Eskander's SEER study is notable for the increase in re-hospitalization rates over time, associated with a

corresponding decrease in length of stay (LOS) over time [14]. Another study in the gynecology oncology population of patients suggested that LOS could be safely decreased with an overall 5% readmission rate [24]. However, 44 patients in their series were readmitted, and 52% of them had a cancer diagnosis. Importantly, only a diagnosis of ovarian cancer was significantly related to readmission. Similar data is available in the colorectal cancer population: readmission rates after colectomy for colon cancer have increased over the past 2 decades while mean LOS has decreased [19]. The overall rate of readmission in the colorectal cancer population in this study was 11.2%. Obviously a careful balance needs to be maintained between optimal LOS following cancer surgery and rates of readmission.

The current study has identified several important risk factors for readmission that can subsequently be targeted in prospective intervention trials. First, the majority of the readmissions identified in this study (73%) occurred within 40 days of the index surgery but after the first cycle of chemotherapy was delivered. This finding suggests that targeting this unique vulnerable time period would be valuable in decreasing risk. A longer delay from surgery to chemotherapy initiation may have decreased the readmission rate in this group of patients. Second, the majority of patients (70%) were readmitted only once, lending credence to the theory that targeting this time period of surgical recovery and initiation of chemotherapy would be valuable. Third, those patients at risk for multiple readmissions are the patients who had a surgery that either required a bowel resection or left them with the smallest volume of residual disease. Since these surgical factors can be identified at the time of first hospital discharge, this particular population can be targeted for increased intervention moving forward. Finally, increased BMI and poor performance status are significant risk factors in the multivariate model for readmission. Those patients who are obese and have a poor performance status at the time of initial diagnosis could therefore be considered either for other treatment strategies (such as neoadjuvant chemotherapy) or alternatively for increased support following primary treatment aimed at decreasing readmission risk.

What interventions might be appropriate for the advanced ovarian cancer population, either post-operatively or during their chemotherapy course? Telephone intervention has been shown in some reports to decrease readmission rates, but none of these studies have focused only on the cancer patient population. In one study, completion of telephone follow-up was a significant predictor of lower 30 day readmissions [25]. A Cochrane review of 33 studies (total of 5110 patients) concluded that most studies had low methodological quality [26]. While some reports found the intervention was favorable, overall the research did not show an advantage to telephone follow-up. However, limited prospective data is available. The data from Clark et al. suggest that the addition of ancillary home services following discharge does not impact the re-hospitalization rates; however, these data were obtained from a metropolitan area tertiary care institution and therefore may not be generalizable [6].

It is notable that patients who underwent more than one readmission were a unique population: specifically they were more likely to have minimal residual disease after surgery and more likely to have a bowel resection performed. This finding would suggest an association between maximal surgical effort and hospital readmission, though a more

definitive statement regarding risk of readmission after aggressive surgical effort cannot be made because data specific to surgical effort were not collected in this study. Clearly the initial surgery is a very important factor in readmission risk in the ovarian cancer population and these patients require additional attention in the post-discharge period in order to avoid readmission. Future studies addressing risk factors for readmission specific to chemotherapy administration in this disease must consider other modalities of ovarian cancer primary treatment including intraperitoneal chemotherapy delivery and neoadjuvant chemotherapy with interval cytoreduction. Analysis of upfront chemotherapy trials that include intraperitoneal and dose dense delivery systems (such as GOG 252 (NCT00951496) and 262 (NCT01167712)) will be very useful.

The current study has several important strengths. First, we considered a large population of women with newly diagnosed ovarian cancer representing ovarian cancer patients from across the nation. Second, due to the nature of reporting in clinical trials, we had access to abundant data with respect to important patient dependent and tumor dependent factors that contribute to readmission risk. We also had extensive data regarding toxicities related to admission and were able to make conclusions regarding the additional risk of readmission incurred by the addition of bevacizumab to the treatment regimen. Finally, unlike the SEER database studies, we were able to include patients of all ages in our analysis.

The study also has some limitations. Only patients medically fit enough to be registered on GOG-0218 were included; thus we included only those patients with a GOG Performance Status of 0–2. By virtue of the inclusion and exclusion criteria for this study, patients who are treated with neoadjuvant chemotherapy for whatever reason (tumor distribution, medical illness, bowel obstruction) were not included in this analysis. The neoadjuvant chemotherapy group adds a significant degree of complexity: while they are often more medically ill with poor performance status and thus at higher risk for readmission, they are also likely to require a less complex surgical procedure, perhaps thus decreasing risk. Because we did not have access to surgical discharge dates, a post-operative length of stay was estimated, likely leading to over-estimation of the number of readmissions. We were not able to assess risk associated with intraperitoneal chemotherapy as this treatment modality was not included in the treatment regimens of GOG-0218.

In summary, this study has identified several important risk factors for readmission in the population of women undergoing primary cytoreduction and upfront chemotherapy in a clinical trial setting for the diagnosis of stages III-IV primary peritoneal, fallopian tube, and ovarian carcinoma. The majority of readmissions were related to the primary surgery and delivery of the first cycle of chemotherapy. Those patients who were readmitted within 40 days of surgery were more likely to have a significantly shorter interval from primary surgery to chemotherapy initiation, suggesting a delay of an additional 2 weeks in these patients may have decreased the readmission rate. Those patients who were optimally cytoreduced or underwent bowel resection as part of their primary surgery were also the patients who were at most risk for multiple re-admissions. Greater BMI and worse performance status are both significant predictors for rehospitalization in this population. Since both of these patient characteristics are identifiable pre-operatively, these patients may be “flagged” in the pre-operative period as high risk for re-hospitalization and targeted for

interventions aimed at decreasing this risk. It may even be appropriate to triage those patients at particularly high risk for neoadjuvant chemotherapy as primary therapy. The addition of bevacizumab to the treatment regimen increased the rate of readmission only in that group of patients who had multiple readmissions (a minority).

In conclusion, this study has identified an overall readmission rate of 10.5% in women with primary peritoneal, fallopian tube and ovarian cancer who undergo primary attempt at surgical cytoreduction followed by combination chemotherapy in a front-line clinical trial setting. Important risk factors for readmission include increased BMI and poor PS (PS = 2) suggesting that patients who have one or both of these risk factors identified pre-operatively may benefit from an alternative approach to therapy and/or increased preventative interventions post-discharge. Further study including future analysis of GOG studies 252 and 262 as well as design of prospective intervention studies will be required to decrease overall readmission rates in women with newly diagnosed advanced ovarian cancer.

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Conflicts of interest

All the co-authors have grants/grants pending for various clinical trials. Dr. Robert Burger also serves as a consultant for Genentech.

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HIGHLIGHTS

- Ovarian cancer patients undergoing primary treatment are at high risk for readmission.
- Risk factors for readmission include higher BMI and poor performance status.
- Interventions to decrease readmissions should be designed to improve care quality.

Arm I Standard chemotherapy	Carboplatin	every 21 days for 6 cycles
	Paclitaxel	every 21 days for 6 cycles
	Placebo	day 1 every 21 days beginning with cycle 2 x 5 cycles
	Placebo	day 1 every 21 days cycles 7 through 22
Arm II Concurrent bevacizumab	Carboplatin	every 21 days for 6 cycles
	Paclitaxel	every 21 days for 6 cycles
	Bevacizumab	day 1 every 21 days beginning with cycle 2 x 5 cycles
	Placebo	day 1 every 21 days cycles 7 through 22
Arm III Extended bevacizumab	Carboplatin	every 21 days for 6 cycles
	Paclitaxel	every 21 days for 6 cycles
	Bevacizumab	day 1 every 21 days beginning with cycle 2 x 5 cycles
	Bevacizumab	day 1 every 21 days cycles 7 through 22

Fig. 1.
Schema for GOG 0218.

Table 1

Characteristics of re-hospitalized patients.

	<u>Not rehospitalized</u>	<u>Rehospitalized</u>	
	N = 1676	N = 197	p
Age (years)	59.8	62	0.063
Race/ethnicity			
White	83.3%	86.3%	0.096
Asian	6.6%	3.0%	
Black	4.0%	6.6%	
Hispanic	4.1%	2.5%	
Other	2.0%	1.5%	
Payer			
Private	60.8%	57.9%	0.146
Medicare	10.5%	9.6%	
Medicare + private	12.3%	19.8%	
Medicaid	2.6%	3.0%	
Medicaid + Medicare	1.0%	1.0%	
Military	0.5%	0.5%	
Self/uninsured	5.5%	4.1%	
Unknown	6.6%	4.1%	
BMI kg/m2	25.4	27.6	<0.001
Performance status			
0	51.3%	35.5%	<0.001
1	42.5%	49.2%	
2	6.2%	15.2%	
Histology			
Serous	84.2%	88.3%	0.552
Mixed epithelial	4.8%	2.5%	
Endometrioid	3.2%	2.5%	
Clear cell/mucinous	4.1%	3.0%	
Other	3.8%	3.6%	
Surgical stage			
III	75.2%	66.5%	0.008
IV	24.8%	33.5%	
Tumor grade			
1	4.4%	5.1%	0.586
2	15.5%	18.3%	
3	71.3%	70.6%	
Excluded	4.7%	3.6%	
Not graded	4.2%	2.5%	
Residual tumor, cm	1.5	2.0	0.029
Ascites			

	<u>Not rehospitalized</u>	<u>Rehospitalized</u>	
	N = 1676	N = 197	<i>p</i>
No	22.0%	14.7%	0.018
Yes	78.0%	85.2%	
Baseline CA 125, IU/ml	304	405	0.017
Treatment arm			
I	33.4%	33.5%	0.719
II	33.1%	35.5%	
III	33.5%	31.0%	

BMI = body mass index.

Table 2

Hospitalized patients: medical history and surgical details.

	<u>Not rehospitalized</u>	<u>Rehospitalized</u>	<i>p</i>
	N = 1676	N = 197	
Hypertension			<0.001
No	63.5%	47.8%	
Yes	36.5%	52.2%	
Peripheral vascular disease			0.307
No	99.5%	98.9%	
Yes	0.5%	1.1%	
MI or CVA			0.38
No	97.7%	96.7%	
Yes	2.3%	3.3%	
Smoker			0.617
No	87.0%	88.3%	
Yes	13.0%	11.7%	
Diabetes			0.77
No	91.8%	90.6%	
Yes	8.2%	9.5%	
Autoimmune disease			0.009
No	97.7%	94.4%	
Yes	2.3%	5.6%	
Intestinal obstruction			0.753
No	97.1%	96.7%	
Yes	2.9%	3.3%	
Small bowel resection			0.748
No	90.9%	91.7%	
Yes	9.1%	3.3%	
Large bowel resection			0.227
No	82.0%	78.3%	
Yes	18.0%	21.7%	

Table 3

Rehospitalization toxicities.

Broad category hospitalization adverse events	N (197) **
Death	1.00%
Hemorrhage/bleeding	7.10%
Peripheral neuropathy	7.10%
Neurology	13.20%
Pulmonary/upper respiratory	14.70%
Vascular	15.70%
Cardiac	17.30%
Dermatology/skin	20.30%
Metabolic/laboratory	26.40%
Constitutional symptoms	29.90%
Pain	29.90%
Infection	43.10%
Gastrointestinal	63.50%

** The totals exceed 100% since patients could be classified as having more than one broad category of adverse event during a rehospitalization.

Table 4

Patients with 2 or more Rehospitalizations.

	<u>Rehospitalized × 1</u>	<u>Rehospitalized × 2+</u>	
	N = 138	N = 59	p
Age (years)	62	61.3	0.864
Race/ethnicity			
White	86.2%	86.4%	0.439
Asian	2.9%	3.4%	
Black	7.2%	5.1%	
Hispanic	1.4%	5.1%	
Other	2.2%	0.0%	
Payer			
Private	58.7%	55.9%	0.607
Medicare	10.1%	8.5%	
Medicare + private	18.1%	23.7%	
Medicaid	2.9%	3.4%	
Medicaid + Medicare	1.4%	0.0%	
Military	0.0%	1.7%	
Self/uninsured	5.1%	1.7%	
Unknown	3.6%	5.1%	
BMI kg/m2	27.6	27.4	0.842
Performance status			
0	37.0%	32.2%	0.237
1	45.7%	57.6%	
2	17.4%	10.2%	
Histology			0.561
Serous	87.7%	89.8%	
Mixed epithelial	2.9%	1.7%	
Endometrioid	3.6%	0.0%	
Clear cell/mucinous	2.9%	3.4%	
Other	2.9%	5.1%	
Surgical stage			0.684
III	67.4%	64.4%	
IV	32.6%	35.6%	
Tumor grade			0.576
1	6.5%	1.7%	
2	17.4%	20.3%	
3	70.3%	71.2%	
Excluded	2.9%	5.1%	
Not graded	2.9%	1.7%	
Residual tumor cm	2.0	1.5	0.03
Ascites			

	<u>Rehospitalized × 1</u>	<u>Rehospitalized × 2+</u>	
	N = 138	N = 59	<i>p</i>
No	15.9%	11.9%	0.459
Yes	84.1%	88.1%	
Baseline CA 125 iU/ml	380	430	0.913
Treatment arm			
I	39.1%	20.3%	0.029
II	31.2%	45.8%	
III	29.7%	33.9%	

Table 5

Patients with 2 or more Re-hospitalizations: medical and surgical characteristics.

	<u>Rehospitalized × 1</u>	<u>Rehospitalized × 2+</u>	<i>p</i>
	N = 138	N = 59	
Hypertension			0.297
No	45.2%	53.7%	
Yes	54.8%	46.3%	
Peripheral vascular disease			0.535
No	99.2%	98.1%	
Yes	0.8%	1.9%	
MI or CVA			0.856
No	96.8%	96.3%	
Yes	3.2%	3.7%	
Smoker			0.51
No	87.3%	90.7%	
Yes	12.7%	9.3%	
Diabetes			0.513
No	89.7%	92.6%	
Yes	10.1%	7.4%	
Autoimmune disease			0.033
No	96.8%	88.9%	
Yes	3.2%	11.1%	
Intestinal obstruction			0.856
No	96.8%	96.3%	
Yes	3.2%	3.7%	
Small bowel resection			0.039
No	94.4%	85.2%	
Yes	5.6%	14.8%	
Large bowel resection			0.036
No	82.5%	68.5%	
Yes	17.5%	31.5%	

MI = myocardial infarction.

CVA = cerebral vascular accident.