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Correlation between Surgeon's assessment and radiographic evaluation of residual disease in women with advanced stage ovarian cancer reported to have undergone optimal surgical cytoreduction: An NRG Oncology/Gynecologic Oncology Group study

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Conflicts of Interest

Dr. Eskander wishes to disclose that he received personal fees from AZ Oncology, Clovis Oncology and Genentech.

Dr. Tewari reports that his institution received a research grant from Genentech and that he has participated on 2 advisory boards for Genentech.

Dr. O'Malley reports personal fees from Clovis, Astra Zeneca, Tesara, Myriad, Amgen, Novocure, Janssen Oncology, Health Analytics, outside the submitted work for advisory boards and/or consulting and that his institution receives money from multiple industrial sponsored trials that he is the local PI on.

Dr. Fujiwara reports that he has received grants from Kaken, Shionogi and Chugai, grants and personal fees from Astra Zeneca, Pfizer, Eisai, MSD, Taiho, Zeria, Ono, GSK and Lilly. Dr. Fujiwara also reports that he has received grants from Immunogen and Oncotherapy as well as personal fees from Nihon Kayaku, Novartis, Kyowahakko Kirin, Janssen, Asahikasei Medical and Daiichi Sankyo, outside of the submitted work.

Dr. Burger reports personal fees and other from Amgen, AstraZeneca, Genentech/Roche, Clovis Oncology, personal fees from Gradalis, Invitae, Janssen Research & Development, Morphotek, NuCana, Tesaro, VBL Therapeutics, outside the submitted work. All other authors have nothing to disclose.

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Abstract

Purpose: We sought to determine the level of concordance among surgeons' assessment of residual disease (RD) and pre-treatment computed tomography (CT) findings among women who underwent optimal surgical cytoreduction for advanced stage ovarian cancer.

Methods: This is a post-trial ad hoc analysis of a phase 3 randomized clinical trial evaluating the impact of bevacizumab in primary and maintenance therapy for patients with advanced stage ovarian cancer following surgical cytoreduction. All subjects underwent imaging of the chest/abdomen/pelvis to establish a post-surgical baseline prior to the initiation of chemotherapy. Information collected on trial was utilized to compare surgeon's operative assessment of RD, to pre-treatment imaging.

Results: Of 1,873 enrolled patients, surgical outcome was described as optimal (RD ≤ 1 cm) in 639 subjects. Twelve patients were excluded as they did not have a baseline, pretreatment imaging, leaving 627 participants for analysis. The average interval from surgery to baseline scan was 26 days (range: 1–109). In 251 cases (40%), the post-operative scan was discordant with surgeon assessment, demonstrating RD > 1 cm in size. RD > 1 cm was most commonly identified in the right upper quadrant (28.4%), retroperitoneal para-aortic lymph nodes (RD > 1.5 cm; 28.2%) and the left upper quadrant (10.7%). Patients with RD > 1 cm on pre-treatment CT (discordant) exhibited a significantly greater risk of disease progression (HR 1.30; 95% CI 1.08–1.56; p=0.0059).

Conclusions: Among patients reported to have undergone optimal cytoreduction, 40% were found to have lesions > 1 cm on postoperative, pretreatment imaging. Although inflammatory changes and/or rapid tumor regrowth could account for the discordance, the impact on PFS and distribution of RD may suggest underestimation by the operating surgeon.

Introduction

Epithelial ovarian cancer (EOC) remains the most lethal gynecologic malignancy. In 2017, there will be an estimated 22,440 new ovarian cancer cases in the United States with 14,080 deaths (1). Advanced stage disease is traditionally managed with surgery, followed by platinum and taxane-based combination chemotherapy (2). Several factors have been identified as prognostic for clinical outcome in patients with EOC, with extent of residual disease being investigated in numerous studies (3). The prognostic implication of optimal cytoreduction has been extensively reported in the literature, with a survival benefit described in both retrospective and non-randomized prospective studies beginning with Griffith's landmark publication in 1975 (3–6). Most recently, Landrum et al. detailed the survival outcomes of patients with no visible residual disease treated with intraperitoneal chemotherapy, reporting a median overall survival of 110 months (7). Several other authors have also validated these findings (8, 9).

Although various cutoff values have been used to define “optimal” cytoreduction, NRG Oncology currently defines optimal residual disease as 1 cm or less in largest diameter after completion of cytoreductive surgery (10). In addition to the prognostic implications discussed above, extent of residual disease may impact decisions regarding adjuvant therapy, eligibility for enrollment in clinical trials as well as the interpretation of clinical trial results (11).

Currently, the extent of disease remaining at the completion of primary surgery is determined in a subjective manner, and not confirmed by objective means. The operating surgeon relies on visual inspection and palpation, which are limited by patient body habitus, incision size, and location of disease. Furthermore, significant interobserver variability in tumor measurements has been previously reported (12). To date, two single institution exploratory studies have been conducted examining the relationship between surgeon and imaging based assessment of residual disease. There was a consistently reported 40% discordance between surgeon assessment and baseline, pre-treatment computed tomography scan (13, 14).

Given the potential prognostic and therapeutic implications of residual disease volume, exploring the ability of the operating surgeon to accurately describe the extent of residual disease is warranted. The aim of this study was to explore the correlation between post-operative computed tomography scan and operating surgeon assessment of residual disease in patients with EOC who underwent primary surgical cytoreduction to ≤1 cm of residual disease on GOG protocol 218.

Materials and Methods

Background on GOG protocol 218.

Gynecologic Oncology Group (GOG) protocol 218, was a randomized phase 3, double blind, placebo-controlled study developed to evaluate the impact of bevacizumab in primary and maintenance therapy for patients with newly diagnosed International Federation of Gynecology and Obstetrics (FIGO) stage III and IV ovarian, fallopian tube or primary peritoneal cancer who underwent maximal effort cytoreductive surgery (15). Patients with stage III disease and residual lesions less than 1 cm in maximal diameter (as reported by operating physician) were initially excluded, but following protocol modification in July 2007, were permitted to enroll on study.

Patients were required to enroll between 1 and 12 weeks following surgery. All subjects underwent imaging (magnetic resonance imaging or computed tomography scan) of at least the abdomen and pelvis to establish a post-surgical baseline prior to the initiation of chemotherapy, and within 4 weeks of registration. Measurable lesions on radiographic imaging were defined as ≥ 10 mm in at least one dimension. CT scans were performed with contiguous cuts of 5 mm or less in slice thickness, with a contiguous reconstruction algorithm. Disease was assessed according to Response Evaluation Criteria in Solid Tumors (RECIST) (16).

Ancillary Data Statistical Analysis.

Data regarding residual disease volume (as assessed by operating surgeon), disease location, and radiographic findings on baseline pre-treatment CT scan were abstracted from the surgical reporting form (form C version 2), the surgical status form (SRGSTAT), and pre-treatment summary form (form DR version 5). Patients with FIGO stage III EOC who were reported to have undergone surgical cytoreduction to ≤ 1 cm residual disease (n = 639) subsequently underwent review of baseline, pre-treatment, radiographic scans. Patients with FIGO stage IV disease were excluded from analysis. Imaging findings, as reported on trial, were evaluated and disease location (any lesion > 1 cm in at least one dimension for soft tissue and > 1.5 cm in short axis for nodal disease) was classified as pelvis (P), right lower quadrant (RLQ), left lower quadrant (LLQ), right upper quadrant (RUQ), left upper quadrant (LUQ), para aortic lymph nodes (PA), and pelvic lymph nodes (PP). Those cases in which the surgeon reported cytoreduction to ≤ 1 cm residual disease, with baseline scan showing at least one lesion > 1 cm in largest dimension were categorized as discordant, while absence of a target lesion > 1 cm on baseline scan was considered concordant. Image analysis and interpretation were completed by radiologists at approved GOG institutions as part of the primary clinical trial.

Demographic, clinical, surgical and pathological data were collected. Descriptive statistics were used to report the frequency of discordance between operating surgeon and baseline CT scan. Categorical variables were compared between discordant and concordant subgroups using the Pearson chi-square test, and continuous variables by the Wilcoxon-Mann-Whitney test or the Kruskal-Wallis test. Logistic regression was performed to determine factors independently associated with post-operative CT scan identification of lesions more than 1 cm in dimension, including: age, stage, tumor grade, performance status, study treatment arm, body mass index, and estimated blood loss.

Survival was estimated using the Kaplan-Meier method. The proportional hazards regression model stratified by treatment, with covariates age, grade, performance status, and an indicator of lesion more than 1 cm vs. less than 1 cm was used to determine what, if any, difference in progression free and overall survival existed between concordant and discordant populations. All statistical tests were two-tailed with the significance set at α=0.05. Statistical analyses were performed using the SAS programming language and environment.

Results

Between October 2005 and June 2009, 1,873 patients were randomly assigned to one of three treatment arms. At the time of primary analysis, a significant improvement in PFS was observed for the bevacizumab-throughout arm, when compared to the control carboplatin-paclitaxel arm (HR 0.717 (95% CI, 0.625–0.824; p<0.001)) (15). No significant differences in overall survival (OS) were observed. As detailed in the primary manuscript, all treatment arms were well balanced by age, stage, grade, and performance status. Less than 50% of the enrolled subjects were optimally cytoreduced, attributed to the initial eligibility criteria.

A total of 639 patients with FIGO stage III EOC were reported to have undergone surgical cytoreduction to ≤ 1 cm residual disease. Among those, 12 did not have a baseline imaging study, leaving 627 subjects eligible for inclusion and data analysis. Table 1 summarizes the patient and tumor characteristics for the cohort of 627 subjects. The majority of the cohort was white, with performance status of 0–1, and had high-grade epithelial ovarian cancer. The interval from surgery to baseline scan is shown in Figure 1. The mean number of days from surgery to scan was 26, with a range of 1 to 109. The majority of eligible patients had baseline scan completed within 4 weeks of surgery (N= 468, 75%), with only 8 subjects (1%) receiving baseline scans 8 weeks or more after primary cytoreduction.

In 251 cases (40%), the postoperative computed tomography scan findings reported a lesion > 1 cm in at least one dimension (> 1.5 cm in short axis for nodal disease), and were discordant from the operating surgeon's report of residual disease volume at completion of surgical resection (Table 2). In the 251 discordant cases, as many as 9 target lesions measuring larger than 1 cm in size were reported on baseline, pre-treatment scan, with 109 subjects (43.4%) having at least 3 separate identifiable masses (Table 3). Residual masses > 1 cm in size were most frequently reported in the following locations: 28.2% in the para-aortic lymph nodes (> 1.5 cm in short axis), 28.4% in the right upper quadrant (including liver and diaphragm), and 10.7% in the left upper quadrant (including spleen and diaphragm) (Figure 2).

Logistic regression analysis was completed on the cohort of 627 subjects to determine if specific variables were associated with CT evidence of residual disease > 1 cm on baseline scan. Importantly, body mass index (BMI) (dichotomized as BMI < 30 and ≥ 30), and estimated blood loss were not significantly associated with residual disease. To evaluate the impact of interval from surgery to baseline scan, and the possibility of tumor regrowth, time from surgery to scan was examined as both a continuous and dichotomous variable (mean number of days to scan) in both the concordant and discordant cohorts, and once again no significant association was identified (p = 0.37).

Additionally, the impact of discordance on oncologic outcomes was examined in the cohort of patients who were reported to have undergone cytoreduction to ≤ 1 cm residual disease, and by study treatment arm. The presence of a discordant lesion on baseline imaging was associated with a significant increase in the risk of disease progression (HR 1.3; 95% CI 1.077–1.558; p = 0.0059). The median progression-free survival (PFS) in the non-discordant population was 18.3 months vs. 12.8 months in the discordant cohort (Figure 3; p = 0.0059). Conversely, no significant difference in overall survival was identified (HR 0.99; 95% CI 0.802–1.232). Lastly, the rate of discordance was not significantly different across treatment arms on trial.

Discussion

The goal of surgical cytoreduction in patients with advanced stage ovarian, fallopian tube and primary peritoneal cancer has evolved, and the contemporary surgical objective is resection of all visible disease (no gross residual, NGR). Prior investigators have detailed the survival advantage associated with aggressive surgical efforts, and the use of more extensive

procedures to achieve NGR has been adopted by many centers (17–22). Despite the accepted prognostic relevance of residual disease volume, the measure is subjective, and reported by the surgeon at completion of surgery. This is in contrast to patient age, FIGO stage, grade, performance status, and BRCA mutation status, which are objective and prognostic.

Furthermore, residual disease volume may impact patient counseling and clinical trial eligibility and end-points. Within the ovarian cancer clinical trial arena, pathologic complete response at the time of interval cytoreduction following neoadjuvant chemotherapy is emerging as a potentially clinically meaningful end-point (23). The identified rate of discordance between surgeon assessment of residual disease and radiographic imaging may fundamentally impact our ability to define pathologic complete response in ovarian cancer. If the para aortic lymph nodes and upper abdomen are not surgically explored, and harbor unidentified, measurable disease, patients may be incorrectly defined as having a pathologic complete response.

Historically, physicians have been shown to preferentially underestimate, rather than overestimate the volume of residual disease, with significant inter-observer variability in surgical models (12). Despite the above, limited data exists evaluating operating surgeons' ability to accurately assess residual disease after primary surgical cytoreduction in patients with advanced stage ovarian cancer (13, 14, 24). Chi et al. compared post-operative CT findings and primary surgeon evaluation in 78 eligible patients with EOC who underwent cytoreduction to ≤ 1 cm. Within this cohort, there was a 52% correlation between surgeon assessment and postoperative computed tomography scan evaluation of residual disease (13). Follow up studies failed to show an independent association between discordant findings and oncologic outcome (24). Given the small sample size, this study may have lacked power to show a difference in outcome. In an alternate study, Sala et al. analogously examined the correlation between postoperative computed tomography (CT) findings, and surgeon reported residual disease in a small cohort of 51 subjects (14). There was a 59% correlation between the surgical assessment and postoperative CT findings of residual disease in patients reported to have undergone optimal resection. Most recently, prognostic clinical models incorporating postoperative baseline computed tomography scans showed that CT evidence of residual disease > 1 cm in optimally cytoreduced patients was associated with an increased risk of disease progression and death (25).

Of the 627 eligible subjects included in this analysis, 251 were found to have at least one lesion > 1 cm in dimension on baseline scan, with 43.4% of those having 3 or more separate identifiable masses. The quantification of residual disease following surgery is subjective and may be influenced by several factors including patient body habitus, operative exposure/incision size, as well as surgeon and family expectations (13). In an effort to control for potential confounders, we evaluated the impact of age, FIGO stage, tumor grade, and interval from surgery to baseline scan, none of which were significantly associated with identifiable disease on post-surgical baseline scan.

Although not seen in prior studies, the identification of lesions > 1 cm on baseline scan (discordant cohort) was associated with a significantly increased risk of disease progression (HR 1.3; 95% CI 1.077–1.558; p = 0.0059). Patients without identifiable lesions on scan had

a nearly 6-month improvement in PFS. This impact on progression-free survival argues against artifact, such as postoperative tissue inflammation, blood or tissue debris, as well as hemostatic agents being misinterpreted as residual disease, as these findings should not impact disease recurrence.

In conjunction with the discordance rate reported and the impact on PFS, another compelling finding is the distribution of residual disease identified on scan. As outlined above, the most common locations of disease on baseline imaging were the retroperitoneal para-aortic lymph nodes, right upper quadrant and left upper quadrant. Consistent with prior publications, this may represent an omission by operating surgeons to completely explore the retroperitoneum and upper abdomen, including liver mobilization and diaphragm visualization (13, 26, 27). The difference in progression-free survival may be due to underestimation of residual disease in these anatomic locations, incorrectly labeling these patients as “optimal.”

These results, while continuing to call into question the clinical validity of surgeon assessed residual disease in patients with advanced stage ovarian cancer, do not provide specific evidence that post-operative computed tomography is a definitive answer. None of the evaluated patients underwent biopsy to confirm the presence of malignancy at the identified sites on scan, and pre-surgical scans were not available for comparison. Subjecting patients to repeat procedures was not feasible within the context of this ad-hoc analysis, and may not be warranted on future studies. Furthermore, prior studies in patients with colorectal and appendiceal cancer have shown poor detection of peritoneal implants, and inter-observer differences on preoperative computed tomography scans (28, 29). In addition, interval tumor regrowth cannot be excluded in the context of the current study, as the precise size of residual disease at completion of surgery was not available.

The strengths of this study include the standardization of the surgical approach, meticulous and reliable treatment records, and mandate for pretreatment imaging of at least the abdomen and pelvis prior to protocol-directed therapy. Importantly, an independent radiologic review of over 97% of patients enrolled on GOG 218 was conducted, showing a high rate of concordance among independent reviewers and investigators (30). The collection of accurate oncologic follow up data further allowed for the evaluation of the clinical significance of discordance on cancer outcome.

In summary, in a large cohort of patients with advanced stage EOC enrolled on a prospective clinical trial, we identified a 40% discordance rate between surgeon and baseline scan with respect to residual disease. This discordance was associated with a significant reduction in progression free survival. Moving forward, in parallel with advancements in novel therapeutics, evaluation of methods facilitating the objective quantification of residual disease in this patient population is warranted. This is of particular importance if residual disease is used as an eligibility criteria and/or outcome measure on clinical trials, and in cases where residual disease directly impact therapeutic options. Prospective validation of the results from this analysis of GOG 218 are warranted in future clinical trials, and may be done in combination with the exploration of objective measures of residual disease volume.

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REFERENCES

1. Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2017. CA Cancer J Clin. 2017;67(1):7–30. [PubMed: 28055103]
2. Bookman M Trials with impact on clinical management: first line. International journal of gynecological cancer : official journal of the International Gynecological Cancer Society. 2009;19 Suppl 2:S55–62. [PubMed: 19955916]
3. Winter WE 3rd, Maxwell GL, Tian C, Carlson JW, Ozols RF, Rose PG, et al. Prognostic factors for stage III epithelial ovarian cancer: a Gynecologic Oncology Group Study. J Clin Oncol. 2007;25(24):3621–7. Epub 2007/08/21. [PubMed: 17704411]
4. Griffiths CT. Surgical resection of tumor bulk in the primary treatment of ovarian carcinoma. Natl Cancer Inst Monogr. 1975;42:101–4. [PubMed: 1234624]
5. Chang SJ, Bristow RE, Ryu HS. Impact of complete cytoreduction leaving no gross residual disease associated with radical cytoreductive surgical procedures on survival in advanced ovarian cancer. Ann Surg Oncol. 2012;19(13):4059–67. [PubMed: 22766983]

6. Hoskins WJ, McGuire WP, Brady MF, Homesley HD, Creasman WT, Berman M, et al. The effect of diameter of largest residual disease on survival after primary cytoreductive surgery in patients with suboptimal residual epithelial ovarian carcinoma. Am J Obstet Gynecol. 1994;170(4):974–9; discussion 9–80. [PubMed: 8166218]
7. Landrum LM, Java J, Mathews CA, Lanneau GS Jr., Copeland LJ, Armstrong DK, et al. Prognostic factors for stage III epithelial ovarian cancer treated with intraperitoneal chemotherapy: a Gynecologic Oncology Group study. Gynecol Oncol. 2013;130(1):12–8. [PubMed: 23578540]
8. Bristow RE, Tomacruz RS, Armstrong DK, Trimble EL, Montz FJ. Survival effect of maximal cytoreductive surgery for advanced ovarian carcinoma during the platinum era: a meta-analysis. J Clin Oncol. 2002;20(5):1248–59. Epub 2002/03/01. [PubMed: 11870167]
9. Chi DS, Eisenhauer EL, Lang J, Huh J, Haddad L, Abu-Rustum NR, et al. What is the optimal goal of primary cytoreductive surgery for bulky stage IIIC epithelial ovarian carcinoma (EOC)? Gynecol Oncol. 2006;103(2):559–64. Epub 2006/05/23. [PubMed: 16714056]
10. Ozols R, Bundy B, Greer B, Fowler J, Clarke-Pearson D, Burger R, et al. Phase III trial of carboplatin and paclitaxel compared with cisplatin and paclitaxel in patients with optimally resected stage III ovarian cancer: a Gynecologic Oncology Group study. J Clin Oncol. 2003;21(17):3194–200. [PubMed: 12860964]
11. Armstrong DK, Bundy B, Wenzel L, Huang HQ, Baergen R, Lele S, et al. Intraperitoneal cisplatin and paclitaxel in ovarian cancer. N Engl J Med. 2006;354(1):34–43. Epub 2006/01/06. [PubMed: 16394300]
12. Prefontaine M, Gelfand AT, Donovan JT, Powell JL. Reproducibility of tumor measurements in ovarian cancer: a study of interobserver variability. Gynecol Oncol. 1994;55(1):87–90. Epub 1994/10/01. [PubMed: 7959274]
13. Chi DS, Ramirez PT, Teitcher JB, Mironov S, Sarasohn DM, Iyer RB, et al. Prospective study of the correlation between postoperative computed tomography scan and primary surgeon assessment in patients with advanced ovarian, tubal, and peritoneal carcinoma reported to have undergone primary surgical cytoreduction to residual disease 1 cm or less. J Clin Oncol. 2007;25(31):4946–51. Epub 2007/11/01. [PubMed: 17971592]
14. Sala E, Mannelli L, Yamamoto K, Griffin M, Griffin N, Grant L, et al. The value of postoperative/preadjuvant chemotherapy computed tomography in the management of patients with ovarian cancer. International journal of gynecological cancer : official journal of the International Gynecological Cancer Society. 2011;21(2):296–301. [PubMed: 21721161]
15. Burger RA, Brady MF, Bookman MA, Fleming GF, Monk BJ, Huang H, et al. Incorporation of bevacizumab in the primary treatment of ovarian cancer. N Engl J Med. 2011;365(26):2473–83. Epub 2011/12/30. [PubMed: 22204724]
16. Therasse P, Arbuck SG, Eisenhauer EA, Wanders J, Kaplan RS, Rubinstein L, et al. New guidelines to evaluate the response to treatment in solid tumors. European Organization for Research and Treatment of Cancer, National Cancer Institute of the United States, National Cancer Institute of Canada. J Natl Cancer Inst. 2000;92(3):205–16. [PubMed: 10655437]
17. Aletti GD, Dowdy SC, Gostout BS, Jones MB, Stanhope CR, Wilson TO, et al. Aggressive surgical effort and improved survival in advanced-stage ovarian cancer. Obstet Gynecol. 2006;107(1):77–85. [PubMed: 16394043]
18. Bristow RE, Montz FJ, Lagasse LD, Leuchter RS, Karlan BY. Survival impact of surgical cytoreduction in stage IV epithelial ovarian cancer. Gynecol Oncol. 1999;72(3):278–87. [PubMed: 10053096]
19. Chang SJ, Bristow RE, Chi DS, Cliby WA. Role of aggressive surgical cytoreduction in advanced ovarian cancer. Journal of gynecologic oncology. 2015;26(4):336–42. [PubMed: 26197773]
20. Colombo PE, Mourregot A, Fabbro M, Gutowski M, Saint-Aubert B, Quenet F, et al. Aggressive surgical strategies in advanced ovarian cancer: a monocentric study of 203 stage IIIC and IV patients. Eur J Surg Oncol. 2009;35(2):135–43. [PubMed: 18289825]
21. Eisenhauer EL, Abu-Rustum NR, Sonoda Y, Levine DA, Poynor EA, Aghajanian C, et al. The addition of extensive upper abdominal surgery to achieve optimal cytoreduction improves survival in patients with stages IIIC-IV epithelial ovarian cancer. Gynecol Oncol. 2006;103(3):1083–90. [PubMed: 16890277]

22. Eisenkop SM, Spirtos NM, Friedman RL, Lin WC, Pisani AL, Perticucci S. Relative influences of tumor volume before surgery and the cytoreductive outcome on survival for patients with advanced ovarian cancer: a prospective study. Gynecol Oncol. 2003;90(2):390–6. [PubMed: 12893206]

23. Petrillo M, Zannoni GF, Tortorella L, Pedone Anchora L, Salutari V, Ercoli A, et al. Prognostic role and predictors of complete pathologic response to neoadjuvant chemotherapy in primary unresectable ovarian cancer. Am J Obstet Gynecol. 2014;211(6):632 e1–8. [PubMed: 24954656]

24. Chi DS, Barlin JN, Ramirez PT, Levenback CF, Mironov S, Sarasohn DM, et al. Follow-up study of the correlation between postoperative computed tomographic scan and primary surgeon assessment in patients with advanced ovarian, tubal, or peritoneal carcinoma reported to have undergone primary surgical cytoreduction to residual disease of 1 cm or smaller. International journal of gynecological cancer : official journal of the International Gynecological Cancer Society. 2010;20(3):353–7. Epub 2010/04/09. [PubMed: 20375796]

25. Burger IA, Goldman DA, Vargas HA, Kattan MW, Yu C, Kou L, et al. Incorporation of postoperative CT data into clinical models to predict 5-year overall and recurrence free survival after primary cytoreductive surgery for advanced ovarian cancer. Gynecol Oncol. 2015;138(3):554–9. [PubMed: 26093061]

26. Aletti GD, Dowdy SC, Podratz KC, Cliby WA. Surgical treatment of diaphragm disease correlates with improved survival in optimally debulked advanced stage ovarian cancer. Gynecol Oncol. 2006;100(2):283–7. [PubMed: 16182350]

27. Schwartz L, Schrot-Sanyan S, Brigand C, Baldauf JJ, Wattiez A, Akladios C. Impact of Pelvic and Para-aortic Lymphadenectomy in Advanced Ovarian Cancer After Neoadjuvant Chemotherapy. Anticancer Res. 2015;35(10):5503–9. [PubMed: 26408716]

28. Coakley FV, Choi PH, Gougoutas CA, Pothuri B, Venkatraman E, Chi D, et al. Peritoneal metastases: detection with spiral CT in patients with ovarian cancer. Radiology. 2002;223(2):495–9. [PubMed: 11997559]

29. de Bree E, Koops W, Kroger R, van Ruth S, Witkamp AJ, Zoetmulder FA. Peritoneal carcinomatosis from colorectal or appendiceal origin: correlation of preoperative CT with intraoperative findings and evaluation of interobserver agreement. J Surg Oncol. 2004;86(2):64–73. [PubMed: 15112247]

30. Burger RA, Brady MF, Rhee J, Sovak MA, Kong G, Nguyen HP, et al. Independent radiologic review of the Gynecologic Oncology Group Study 0218, a phase III trial of bevacizumab in the primary treatment of advanced epithelial ovarian, primary peritoneal, or fallopian tube cancer. Gynecol Oncol. 2013;131(1):21–6. [PubMed: 23906656]

Research Highlights

- A 40% discordance was identified between surgeon and CT imaging with respect to residual disease
- The most frequently identified areas of discordance include the retroperitoneum and upper abdomen
- Objective measures of residual disease volume should be explored

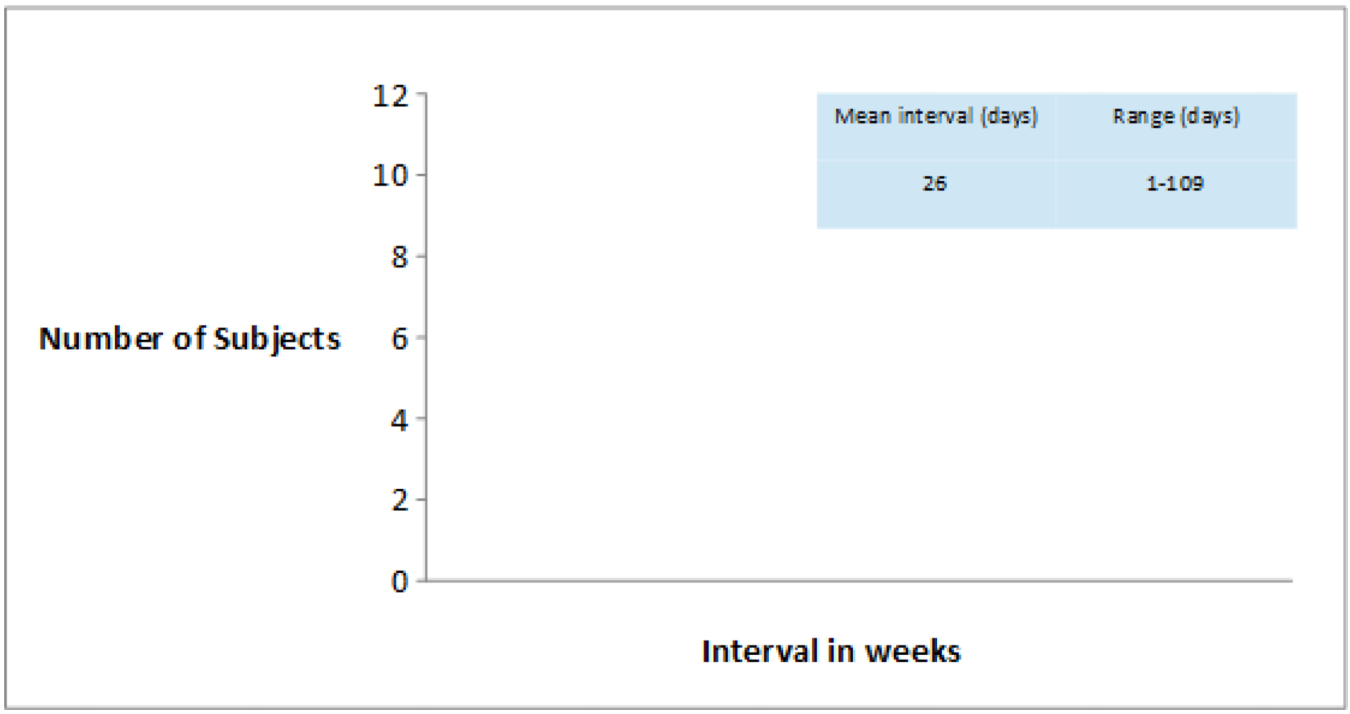

Figure 1:
Time interval from surgery to baseline computed tomography scan

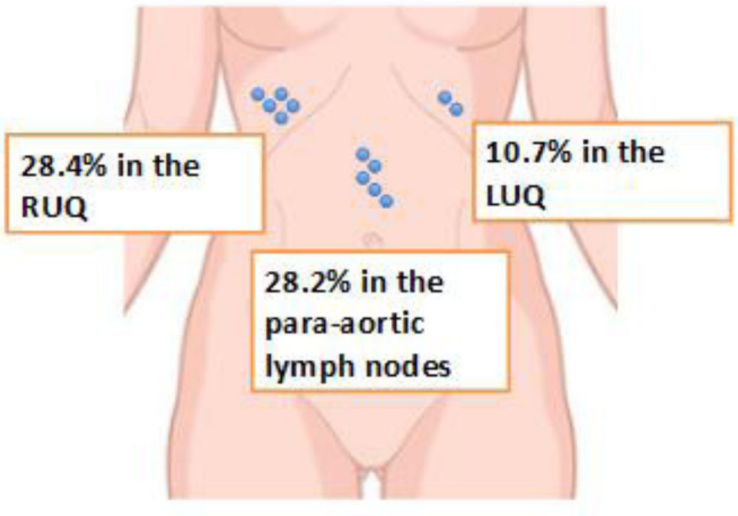

Figure 2:
Location of residual disease identified on baseline scan

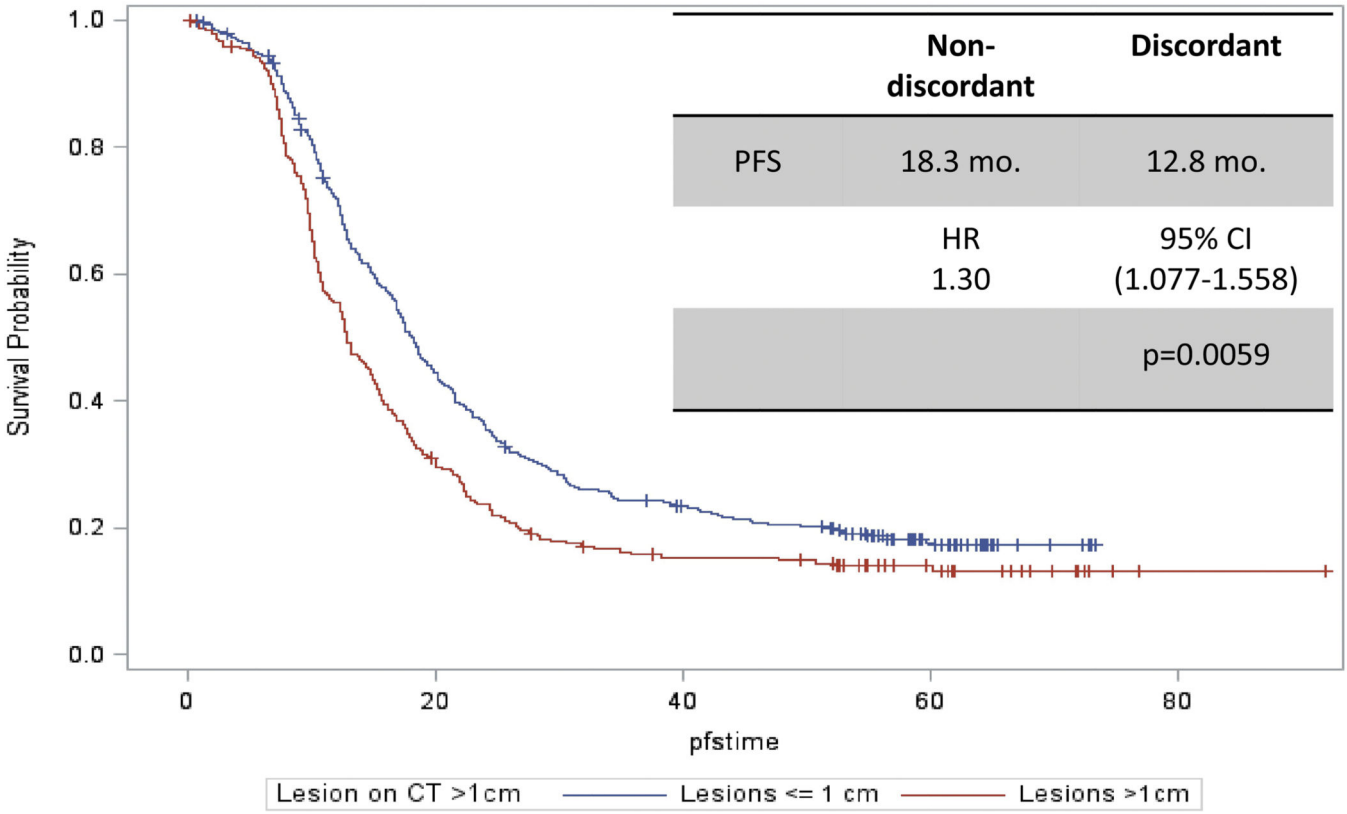

Figure 3:
Progression free survival in the discordant and concordant cohorts

Table 1:

Patient and tumor characteristics

Patient and Tumor Characteristic	Patients (N = 627*)	
	No	%
Age		
20–29	5	1
30–39	20	3
40–49	98	16
50–59	194	31
60–69	197	31
70–79	103	16
80–89	10	2
Race		
Unknown	12	2
Asian	41	7
Black/African American	22	3
American Indian/Alaskan Native	2	0
Native Hawaiian/Pacific Islander	1	0
White	549	88
Performance Status		
0	354	56
1	248	40
2	25	4
BMI		
< 30	469	75
> 30	158	25
FIGO Stage		
3A	15	2
3B	45	7
3C	557	89
3N	10	2
Grade		
1	31	5
2	90	15
3	448	71
Not reported	58	9

*=number of subjects enrolled on GOG 218 with FIGO stage III EOC who underwent optimal surgical cytoreduction and had a baseline CT scan

3N = stage 3 not otherwise specified on the clinical trial protocol form

Table 2:

Residual lesion status by baseline computed tomography scan in patients reported to have undergone optimal surgical cytoreduction

Radiographic reported outcome	Patients (N = 627)	
	No.	%
Masses ≤ 1 cm	376	60
Masses > 1 cm	251	40

Table 3:

Frequency of target lesions identified on baseline computed tomography scanin the discordant population

Number of target lesions	Patients (N = 251)	
	No.	%
1	73	29.0
2	69	27.5
3	43	17.1
4	21	8.4
5	14	5.6
6	15	6.0
7	8	3.2
8	2	0.8
9	6	2.4