The Effect of Intraperitoneal Chemotherapy After Interval Cytoreductive Surgery on Recurrence and Survival in Patients with Advanced Stage Ovarian Carcinoma

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ABSTRACT

Objectives: To compare recurrence-free survival (RFS) and overall survival (OS) in patients with Stage III/IV ovarian cancer (OC) who received intraperitoneal (IP) chemotherapy after neoadjuvant intravenous (IV) chemotherapy and interval cytoreductive surgery.

Methods: An institutional ovarian cancer database was developed from 01/2012 to 08/2018. A sub-group of advanced stage patients who received neoadjuvant chemotherapy followed by interval cytoreductive surgery were identified. Post-operative adjuvant chemotherapy regimens were either IV or IP platinum / taxane therapies. The dataset was analyzed for patient demographics, histology, stage, initial sites of disease, CA125 levels, BRCA status, debulking status, and use of bevacizumab. Death record searches were used to confirm current survival status for all patients lost to follow-up prior to 12-months. RFS defined as diagnosis to first recurrence. OS defined as diagnosis to death or last follow-up.

Results: 143 patients with OC underwent neoadjuvant chemotherapy: 93 had IV and 50 had IP adjuvant chemotherapy. Patients receiving IV only were older than the IP group (69.8±10.7 vs. 63.2±9.9 years; p<0.001). There was no difference between groups by other demographic measures. Complete (R0) debulking was performed on 80.4% of patients, and 96.5% of patients had optimal debulking (R0+R1), with no differences between IV and IP groups. Median follow-up time was 54.4±2.6 months. Median RFS was 19.8 months and 33.7 months for IV vs. IP, respectively (p=0.04). Median OS was 43.4 months and 69.4 months for IV vs. IP, respectively (p=0.05). The 5-year Kaplan-Meier projected OS was 53% for IP arm and 35% for IV arm.

Conclusions: In this retrospective study, IP therapy was shown to be associated with improved survival compared to IV therapy for patients who received adjuvant chemotherapy following neoadjuvant chemotherapy and interval cytoreductive surgery.

BACKGROUND

- Intraperitoneal (IP) chemotherapy for advanced ovarian cancer has previously demonstrated improvement in the overall and disease-free survival in several multi-institutional randomized clinical trials[1-3].
- Catheter complications and the tolerability of IP chemotherapy used in some regimens have kept IP administration from routine clinical practice, despite the availability of level 1 evidence supporting its use.
- Results from the more recent GOG 252 trial call into question the benefit of IP chemotherapy, given the widespread use of bevacizumab in front-line therapy[4].

OBJECTIVE

- To compare recurrence-free survival (RFS) and overall survival (OS) in patients with Stage III/IV ovarian cancer (OC) who received IP chemotherapy after neoadjuvant intravenous (IV) chemotherapy and interval cytoreductive surgery.

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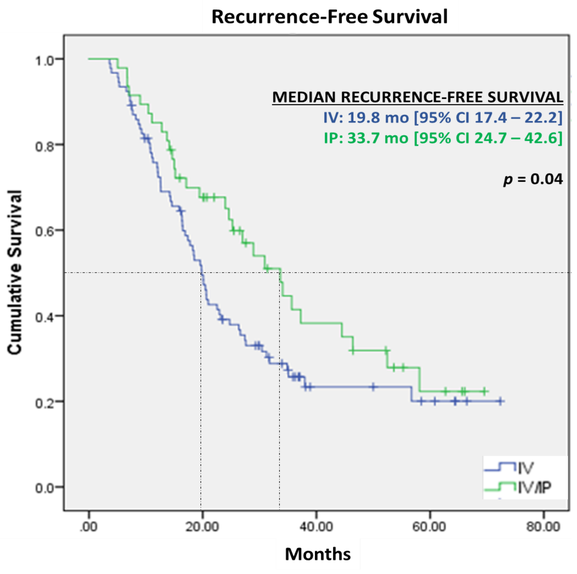
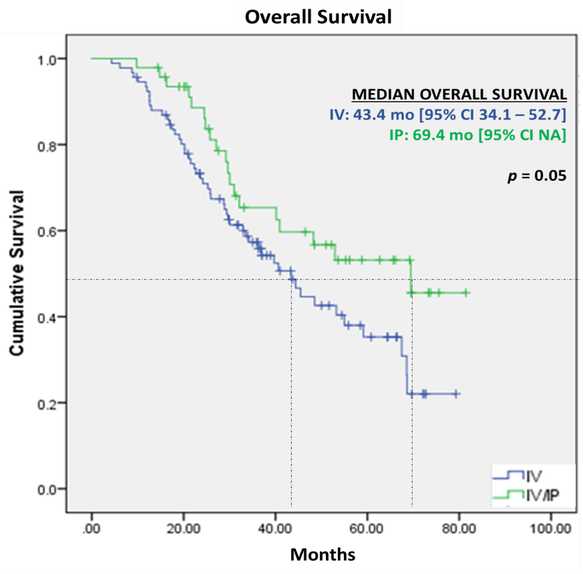
METHODS

- Retrospective analysis of serial patients with stage III or IV high grade ovarian, fallopian tube, or primary peritoneal cancers (Jan 2012 to Aug 2018) treated at AHCI. Inclusion criteria:
  - Advanced stage III or IV patients
  - Histologies: HG-serous, HG-endometrioid, clear cell, carcinosarcoma
  - Received neoadjuvant chemotherapy followed by interval cytoreductive surgery
  - Post-operative adjuvant chemotherapy regimens were either IV or IP platinum / taxane therapies by attending preference
- The dataset was analyzed for patient demographics, histology, stage, initial sites of disease, presence of ascites or pleural effusions, CA-125 levels, BRCA status, debulking status, and use of bevacizumab.
- Bevacizumab was given in the neoadjuvant, adjuvant, and maintenance settings at attending discretion.
- Death record searches were used to confirm current survival status for all patients lost to follow-up prior to 12-months.
- RFS calculated from diagnosis to first recurrence. OS calculated from diagnosis to death or last follow-up.
- Follow-up time was calculated using the reverse Kaplan-Meier method.

RESULTS

N = 143	IV only (N = 93)	IV / IP (N = 50)	*p*-Value
Age, Year, mean (Std Dev)	69.8 (10.7)	63.2 (9.9)	**< 0.001**
BMI, kg/m^2, median (IQR)	25.5 (22-30)	25.3 (22-30)	0.80
Pre-op clinical stage, N (%) III IV	 52 (55.9%) 41 (44.1%)	 34 (68.0%) 16 (32.0%)	 0.21
Histology type, N (%) Serous Non-serous	 87 (93.5) 6 (6.5%)	 45 (90.0%) 5 (10.0%)	 0.52
BRCA status Negative BRCA1 positive BRCA2 positive Unknown	 62 (66.7%) 5 (5.4%) 5 (5.4%) 21 (22.6%)	 36 (72.0%) 6 (12.0%) 5 (10.0%) 3 (6.0%)	 0.22
# Neoadjuvant cycles total, median (IQR)	3 (3-4)	3 (2-3)	**< 0.001**
# Treatment cycles w/ bevacizumab, N (%)	16 (17.2)	6 (12.0)	0.41
# Maintenance cycles w/ bevacizumab, N (%)	10 (10.8)	8 (16.0)	0.37
Change in CA-125 during NAC, median (IQR) Fractional change in CA-125, median % (IQR) CA-125 less than 35 after NAC, N (%)	778 (273-3052) 95.0 (79.2-98.2) 44 (47.3)	897 (326-2406) 92.1 (75.3-97.9) 17 (34.0)	0.86 0.42 0.13
Residual disease after debulking, N (%) R0 R1 R2	 75 (80.6%) 13 (14.0%) 5 (5.4%)	 40 (80.0%) 10 (20.0%) 0 (0.0%)	 0.18
# Adjuvant chemo cycles, median (IQR)	3 (3-6)	4 (4-6)	**0.007**
Total # chemotherapy cycles given (IQR)	7 (6-9)	7 (6-9)	0.48





SUMMARY OF RESULTS

- 93 IV and 50 IP adjuvant chemotherapy patients
- Baseline characteristics were similar between arms in regard to stage, BMI, histology, debulking status, total # chemo cycles, and use of bevacizumab. IV-treated patients were older than the IP-treated arm (69.8 vs. 63.2 years; p<0.001).
- R0 debulking was achieved in 80.4% patients; optimal debulking (R0+R1) in 96.5% patients.
- Median follow-up time was 54.4 ± 2.6 months.
- Median RFS was 19.8 months and 33.7 months for IV vs. IP, respectively (p=0.04).
- Median OS was 43.4 months and 69.4 months for IV vs. IP, respectively (p=0.05).
- Estimated 5-yr OS for IP arm is 53% and for the IV arm is 35%.

CONCLUSION

- In this retrospective study, IP therapy was shown to be associated with improved survival compared to IV therapy for patients who received adjuvant chemotherapy following neoadjuvant chemotherapy and interval cytoreductive surgery.
- Patients treated with neoadjuvant chemotherapy generally have worse prognostic factors than those who undergo primary cytoreductive surgery. Our outcomes for RFS and OS are comparable to patients in other GOG trials that underwent primary surgical debulking followed by adjuvant IV therapy, including studies that incorporated bevacizumab.

REFERENCES

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