Project Summary

The combination of paclitaxel and carboplatin is the standard first-line chemotherapy for ovarian, fallopian tube and primary peritoneal cancer, and is conventionally given via intravenous route every three weeks. Several trials have demonstrated a clinically significant survival advantage associated with intraperitoneal (IP) chemotherapy compared to intravenous chemotherapy and the best outcomes are consistently seen for women who have no residual disease. The Japanese Gynecologic Oncology Group (JGOG) challenged the community standard of 21-day intravenous regimen by demonstrating the superiority of dose-dense weekly paclitaxel in improving the survival of women with stage II-IV cancer.

This retrospective study aimed at comparing the clinical outcomes of women with advanced ovarian, fallopian tube or primary peritoneal cancer treated with frontline IP versus dose-dense chemotherapy, without addition of bevacizumab. It was performed at the Department of Obstetrics and Gynecology of Far Eastern Memorial Hospital from March 2006 to June 2019. The medical records of all consecutive women aged 20 and above, with advanced ovarian, fallopian tube or primary peritoneal cancer [The International Federation of Gynecology and Obstetrics (FIGO) stage II-IV] who received postoperative frontline chemotherapy or neoadjuvant chemotherapy with platinum/paclitaxel were reviewed. Women who received at least one cycle of IP chemotherapy were allocated to the IP group; otherwise, the dose-dense group.

It was anticipated that the IP group would confer a better survival benefit than the dose-dense group.

General Information

Protocol title:
Comparisons of Clinical Outcomes in Women with Advanced Ovarian Cancer Treated with Frontline Intraperitoneal versus Dose-dense Platinum/Paclitaxel Chemotherapy

Clinical Trial Registration Number and date of registration:
NCT04135521, 22/10/2019

Number of IRB and date of approval:
108137-E, 14/10/2019

Name and address of the sponsor/funder:
Far Eastern Memorial Hospital
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Name and title of the investigator:
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Study Goals and Objectives

This study aims at comparing the clinical outcomes of women with advanced ovarian, fallopian tube or primary peritoneal cancer treated with frontline IP versus dose-dense chemotherapy, without addition of bevacizumab. The secondary objective of this study is to identify the predictors of progression free survival (PFS) and overall survival (OS).

Study Design

This is a retrospective cohort study conducted between March 2006 and June 2019. No written informed consent is needed due to its retrospective nature.

Inclusion criteria:

Women aged ≧20 years old with stage II-IV ovarian, fallopian tube or primary peritoneal cancer who EITHER

1) received debulking surgery, followed by postoperative IP or dose-dense platinum/paclitaxel chemotherapy and were consecutively followed up till disease progression or death; OR

2) received neoadjuvant IP or dose-dense platinum/paclitaxel chemotherapy, followed by debulking surgery and postoperative IP or dose-dense platinum/paclitaxel chemotherapy and were consecutively followed up till disease progression or death

Exclusion criteria:

Women without a complete treatment course or discontinued treatment due to reasons other than disease progression or death

Methodology

Group allocation:

Women who received at least one cycle of IP chemotherapy were allocated to the IP group; otherwise, they were allocated to the dose-dense group.

Surgical Method

- Debulking surgery including total abdominal hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic and para-aortic lymphadenectomy, omentectomy, appendectomy (for mucinous adenocarcinoma or appendiceal involvement), excision of peritoneal implants, ascites cytology
- Optimal debulking surgery: defined as having residual tumor with a maximal diameter less than 1 cm after cytoreductive surgery

Drug Administration Schedule:

- Intraperitoneal group: 135 mg/m2 intravenous paclitaxel over a 3 or 24 hours period on day 1, followed by 75-100 mg/m2 IP cisplatin on day 2 and 60 mg/m2 IP paclitaxel on day 8
- Dose-dense group: intravenous carboplatin at AUC of 6 mg/mL per min on day 1, followed by 80 mg/m2 intravenous paclitaxel on days 1, 8, and 15

Rules for Dose Modification:

- For women with significantly impaired renal function (i.e., estimated glomerular filtration rate<50 mL/min/1.73 m2), carboplatin AUC=6 was used instead of cisplatin.
- The carboplatin or cisplatin dose was reduced when febrile neutropenia occurred, an absolute neutrophil count less than 0.5 x 10^9 cells per L persisted for 7 days or more, the platelet count was less than 10 x 10^9 per L, the platelet count was between 10 x 10^9 per L and 50 x 10^9 per L with bleeding tendencies, or the treatment was delayed for haematological toxicity for more than 1 week.
- The dose of paclitaxel was reduced in patients who had grade 2 or higher peripheral neuropathy.

Measurements:

1) Response criteria:

- Complete response → the disappearance of all evidence (including CA-125 and image) of tumor for at least 4 weeks, it could not be determined by CA-125 alone
- Partial response → a ≥50% reduction in the products of each measurable lesion or a ≥50% reduction of CA-125 for at least 4 weeks
- Progressive disease → a ≥25% increase in the size of one or more measurable lesions, the appearance of new lesions, or a ≥25% increase of CA-125
- Stable disease → any condition not meeting any of the above criteria

2) Definitions of survival and methods of measurement

- Overall survival → the time interval from the date of surgery to the date of death from any cause or the last follow-up
- Progression free survival → the time interval from the date of surgery to clinically defined recurrence, disease progression, or the last follow-up

Reasons for early cessation of trial therapy:

Disease progression, death or grade 3-4 chemotherapy related adverse events

Data Management and Statistical Analysis

All the data collected will be kept confidential and anonymous, and the results reported in the aggregate. Information on individuals is only used by the principal and co-investigators for the purpose of the study, it will not be shared with the third party, except when applicable by law. Each individual will be designated a research number as the substitute for her name.

The research results will be analyzed and published in scientific journal using Stata version 11.0 (Stata Corp, College Station, TX). Survival curves are generated using the Kaplan–Meier method, and differences in the survival curves were calculated with the log-rank test. A p-value less than 0.05 is considered statistically significant. A Cox proportional hazards model was used to identify predictors of PFS and OS.

Dissemination of Results and Publication Policy

The results of the study will be written into a manuscript and submitted for publication in English international journal by both the principal and co-investigators.

Ethics

This study has been approved by the Research Ethics Committee of Far Eastern Memorial Hospital.

Other support for the Project: Not applicable

Collaboration with other scientists or research institutions: Not applicable

Links to other projects: Not applicable

Financing and Insurance: Not applicable