

Ovarian Cancer Treatment Options

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Treatment Guidelines

- Surgical debulking
- Intravenous chemotherapy
- Intraperitoneal chemotherapy
- Consolidation therapy
- Second-line therapy
- Investigational therapies

Surgical Debulking

- Rationale to reduce tumor mass
 - Relieve symptoms of mass, ascites, obstruction
 - Improve chemotherapy delivery
 - Promote tumor growth phase and improve cytotoxicity

Surgical staging

- Complete hysterectomy & removal of tubes and ovaries
- Lymph node evaluation
- Omentectomy
- Intestinal resection
- Peritoneal stripping/Tumor debulking
- Conservative management for those desiring to preserve fertility with early stage disease

Primary chemotherapy

- Carboplatin plus Taxol
- Carboplatin plus Taxotere
- Cisplatin plus Taxol
- Treatment regimens of 6-8 cycles for advanced disease, 3-6 cycles for early stage disease

Current Standard Therapy

- Carboplatin/Taxol
 - 6-8 cycles intravenous
 - +/- Consolidation with one year of Taxol

Intraperitoneal Chemotherapy

- Rationale
 - Direct intra-abdominal infusion
 - High dose delivered to tumor cells
 - Longer contact time of chemotherapy with cancer cells
- Disadvantages
 - Need for peritoneal catheter
 - More difficult to administer
 - Nursing, patient discomfort,
 - Unsure of chemotherapy coverage of all tumor sites

Intraperitoneal Chemotherapy Trials

- GOG 104: IV vs. IP Cisplatin (both with IV Cytosin) Median Survival 49 vs. 41 months
- GOG 114: 2 cycles IV Carboplatin then IP Cisplatin and IV Taxol vs IV Taxol/Cisplatin: 63 vs. 52 months
- GOG 172: IV Cisplatin/Taxol vs. IV Taxol then IP Cisplatin then IP Taxol: 67 vs. 49 months

Intraperitoneal Chemotherapy

- Requirements
 - Small volume residual tumor implants
 - No extra-abdominal disease
 - Free flow in abdomen (no adhesions)
 - Peritoneal infusion catheter

Intraperitoneal chemotherapy

- Side Effects
 - Abdominal bloating and pain
 - Nausea
 - Catheter complications
 - Perforation
 - Infection
 - Enhanced chemotherapy toxicity due to longer dwell time in body

Intraperitoneal chemotherapy

- Study regimen
 - Day 1: Intravenous 24 hour infusion of Taxol
 - Day 2: Intraperitoneal Cisplatin
 - Day 8: Intraperitoneal Taxol
- Only 42% completed all 6 cycles of IP vs. 83% completed all 6 IV courses
- 32% discontinued therapy due to catheter complications

Table 2. Frequency of Grade 3 or 4 Adverse Events.

Adverse Event	Intravenous- Therapy Group (N = 210)	Intraperitoneal- Therapy Group (N = 201)*	P Value†
	no. (%)		
Leukopenia‡	134 (64)	152 (76)	<0.001
Platelet count <25,000/mm ³	8 (4)	24 (12)	0.002
Other hematologic event	190 (90)	188 (94)	0.87
Gastrointestinal event	51 (24)	92 (46)	<0.001
Renal or genitourinary event	5 (2)	14 (7)	0.03
Pulmonary event	5 (2)	7 (3)	0.50
Cardiovascular event	10 (5)	19 (9)	0.06
Neurologic event	18 (9)	39 (19)	0.001
Cutaneous change	2 (1)	2 (1)	0.96
Event involving lymphatic system	0	3 (1)	0.07
Fever	8 (4)	19 (9)	0.02
Infection	12 (6)	33 (16)	0.001
Fatigue	9 (4)	36 (18)	<0.001
Metabolic event	15 (7)	55 (27)	<0.001
Pain	3 (1)	23 (11)	<0.001
Hepatic event	1 (<1)	6 (3)	0.05
Other	1 (<1)	6 (3)	0.05

* Four patients did not receive any protocol-based therapy.

† P values were calculated by the Wilcoxon rank-sum test (grades 0, 1, and 2 vs. grades 3 and 4).

‡ A white-cell count below 1000 per cubic millimeter was considered to indicate leukopenia.

Peritoneal Portacath



Univ. Oklahoma. SGO presentation on peritoneal Portacath Insertion.

Consolidation Therapy

- GOG trial #178
 - 3 months vs. 12 months Taxol
 - Improvement in progression-free survival
 - Actual survival data unavailable since trial closed early by NCI
 - Some feel that consolidation is really 2nd line therapy started prior to recurrence and the results in survival will be equivalent

Management of Recurrence

- Rising CA-125
 - Clinical relapse usually within 2-6 months
 - Observation until symptoms then chemotherapy
 - Immediate chemotherapy
 - Hormonal therapy
 - Clinical trial

Management of Recurrence

- Failure to respond to primary therapy
 - Second line therapy
 - Alteration in schedule of Taxol (weekly)
 - Clinical trial looking for active agents
- Failure within 6 months
 - Similar to above
- Failure after 6 months
 - Combination therapy
 - Carboplatin/Taxol
 - Carboplatin/Gemcitabine
 - Single Agent therapy
 - Surgical secondary cytoreduction

Management of Recurrence

- Second line agents

Doxil	Alkeran
Gemcitabine	Cytosan
Topotecan	Tamoxifen
Taxotere	Lupron
Navelbine	Avastin (antiangiogenesis)
Oral Etoposide	
Oral Altretamine (Hexalen)	

Clinical Research Trials

- TOPA
 - Patupilone vs. Doxil for platinum resistant
 - VEGF GSK GW786034 for platinum sensitive
- UTSW
 - GOG #126-Q Alimta (ie, Pemetrexed) for platinum resistant
 - GOG #146-O Irofulven for platinum-sensitive