CURRENT MANAGEMENT OF OVARIAN CANCER

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Disclosure

This speaker has no conflicts of interest to disclose relative to the contents of this presentation.
Objectives

At the end of this presentation, participants should be able to:

• Explain the rationale for surgical staging
• Understand the role of cytoreductive surgery
• Summarize the utilization of chemotherapy
Natural History and Management of Ovarian Cancer

Primary Staging or Cytoreduction → Interval Cytoreduction* → Second Look Surgery → Secondary Cytoreduction (Tertiary, Quarternary...) → Palliative Surgery

Dx Primary Chemotherapy ("Neoadjuvant Chemotherapy")

1st Remission

1st, 2nd, 3rd Recurrence

*Also, setting for first cytoreduction after "neoadjuvant chemotherapy"
Patterns of Spread of Epithelial Ovarian Cancer

1) Lymphatics

2) Direct extension

3) Exfoliation of clonogenic cells
FIGO Ovarian Cancer Staging
Effective Jan 1, 2014

<table>
<thead>
<tr>
<th>STAGE I: Tumor confined to ovaries</th>
<th>OLD</th>
<th>NEW</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA Tumor limited to 1 ovary, capsule intact, no tumor on surface, negative washings/ascites.</td>
<td>IA Tumor limited to 1 ovary, capsule intact, no tumor on surface, negative washings.</td>
<td>No IIC</td>
</tr>
</tbody>
</table>
**“Simplified” FIGO Staging of Ovarian Carcinoma**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Tumor confined to the ovaries</td>
</tr>
<tr>
<td>II</td>
<td>Extension to other pelvic structures</td>
</tr>
<tr>
<td>III</td>
<td>Abdominal or lymph node involvement</td>
</tr>
<tr>
<td>IV</td>
<td>Distant metastases</td>
</tr>
</tbody>
</table>
## Distribution and Five-Year Survival By FIGO Stage for Ovarian Carcinoma

*Pecorelli S et al. Int J Gyn Obstet 2003*

<table>
<thead>
<tr>
<th>Stage</th>
<th>Distribution</th>
<th>Five-Year Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>27%</td>
<td>78-90%</td>
</tr>
<tr>
<td>II</td>
<td>10%</td>
<td>68-79%</td>
</tr>
<tr>
<td>III</td>
<td>50%</td>
<td>29-49%</td>
</tr>
<tr>
<td>IV</td>
<td>13%</td>
<td>13%</td>
</tr>
</tbody>
</table>

N = 4116
## Results of Repeat Staging in Apparent Stage I and II Ovarian Cancer

<table>
<thead>
<tr>
<th>Initial Stage</th>
<th>No. Patients</th>
<th>Upstaged</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>37</td>
<td>16%</td>
</tr>
<tr>
<td>IB</td>
<td>10</td>
<td>30%</td>
</tr>
<tr>
<td>IC</td>
<td>2</td>
<td>0%</td>
</tr>
<tr>
<td>IIA</td>
<td>4</td>
<td>100%</td>
</tr>
<tr>
<td>IIB</td>
<td>38</td>
<td>39%</td>
</tr>
<tr>
<td>IIC</td>
<td>9</td>
<td>33%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>100</strong></td>
<td><strong>31%</strong></td>
</tr>
</tbody>
</table>

Young RC et al. JAMA 1983
## Results of Complete Surgical Staging in Pts Thought to Have Stage I or II Ovarian Cancer

<table>
<thead>
<tr>
<th>Site of Biopsy</th>
<th>Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Para-aortic lymph nodes</td>
<td>12%</td>
</tr>
<tr>
<td>Omentum</td>
<td>11%</td>
</tr>
<tr>
<td>Pelvic lymph nodes</td>
<td>9%</td>
</tr>
<tr>
<td>Random abdominal biopsies</td>
<td>9%</td>
</tr>
<tr>
<td>Random pelvic biopsies</td>
<td>9%</td>
</tr>
<tr>
<td>Cul-de-sac</td>
<td>6%</td>
</tr>
<tr>
<td>Diaphragm</td>
<td>3%</td>
</tr>
</tbody>
</table>

*Young RC et al. JAMA 1983*
Standard Surgical Staging of Apparent Early Stage Ovarian Carcinoma

- Cytologic washings
- Intact tumor removal
- TAH/BSO (USO in selected cases)
- Infracolic omentectomy
- Random peritoneal biopsies
- Biopsy all adhesions and suspicious lesions
- Bilateral pelvic and para-aortic lymph node sampling
Can Comprehensive Staging be Performed Minimally Invasively?
Laparoscopic Removal of Right Ovarian Cancer Without Intraperitoneal Capsule Rupture
LSC Right External Iliac LND
LSC Left Obturator and Hypogastric LND
LSC Right PAN Dissection
Completed PAN Dissection
Laparoscopic Omentectomy
# Oncology

## Staging laparoscopy for the management of early-stage ovarian cancer: a metaanalysis

Hyun Jong Park, MD; Dong Wook Kim, PhD; Ga Won Yim, MD; Eun Ji Nam, MD, PhD; Sunghoon Kim, MD, PhD; Young Tae Kim, MD, PhD

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### TABLE 1

Patient characteristics and study designs in 11 enrolled observational studies

<table>
<thead>
<tr>
<th>Study (period)</th>
<th>Total patients, mean age, y (SD) [range]</th>
<th>Median follow-up, mo [range]</th>
<th>Method of data collection</th>
<th>Diagnosis of disease stage</th>
<th>Fertility-sparing surgery, n/total (%)</th>
<th>Incomplete staging at initial surgery, n/total (%)</th>
<th>Invasive epithelial carcinoma, n/total (%)</th>
<th>Conducting rate of AC, n/total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leblanc et al., 2004 (1991 through 2001)</td>
<td>n = 53, 41.3 (13.9) [18–63]</td>
<td>54 [8–116]</td>
<td>Retrospective</td>
<td>Clinical</td>
<td>9/53 (17.0)</td>
<td>53/53 (100)</td>
<td>44/53 (83.0)</td>
<td>19/53 (35.8)</td>
</tr>
<tr>
<td>Chi et al., 2005 (2000 through 2003)</td>
<td>n = 20, 47.3 (11.2)</td>
<td>Not reported</td>
<td>LSARC</td>
<td>Clinical</td>
<td>Not reported</td>
<td>13/20 (65.0)</td>
<td>17/20 (85.0)</td>
<td>Not reported</td>
</tr>
<tr>
<td>Park, 2008 (2001 through 2006)</td>
<td>n = 17, 43.2 (12.3)</td>
<td>19 [5–56]</td>
<td>LSARC</td>
<td>Clinical</td>
<td>Not reported</td>
<td>6/17 (35.3)</td>
<td>17/17 (100.0)</td>
<td>10/17 (58.8)</td>
</tr>
<tr>
<td>Park, 2008 (2004 through 2007)</td>
<td>n = 19, 43.9 (9.8)</td>
<td>17 [2–40]</td>
<td>LSARC</td>
<td>Clinical</td>
<td>3/19 (15.8)</td>
<td>7/19 (36.8)</td>
<td>19/19 (100.0)</td>
<td>15/19 (78.9)</td>
</tr>
<tr>
<td>Nezhat et al., 2009 (1995 through 2007)</td>
<td>n = 36, 47.8 [17–89]</td>
<td>55.9</td>
<td>Retrospective</td>
<td>Clinical</td>
<td>11/38 (30.6)</td>
<td>9/36 (25.0)</td>
<td>20/36 (55.6)</td>
<td>10/36 (27.8)</td>
</tr>
<tr>
<td>Lee et al., 2011 (2005 through 2010)</td>
<td>n = 26, 42.2 (10.8)</td>
<td>12 [1–42]</td>
<td>Retrospective</td>
<td>Clinical</td>
<td>Not reported</td>
<td>9/26 (34.6)</td>
<td>22/26 (84.6)</td>
<td>17/26 (65.4)</td>
</tr>
<tr>
<td>Schreuder et al., 2012 (2001 through 2009)</td>
<td>n = 25, 49.7 [18–79]</td>
<td>43 [1–116]</td>
<td>Retrospective</td>
<td>Clinical</td>
<td>Not reported</td>
<td>24/25 (96.0)</td>
<td>20/25 (80.0)</td>
<td>14/25 (56.0)</td>
</tr>
<tr>
<td>Tozzi et al., 2004 (1996 through 2003)</td>
<td>n = 24, 36.8 [19–76]</td>
<td>46.4 [2–72]</td>
<td>Prospective</td>
<td>Pathologic</td>
<td>10/24 (41.7)</td>
<td>11/24 (45.8)</td>
<td>18/24 (75.0)</td>
<td>5/24 (20.8)</td>
</tr>
<tr>
<td>Colomer et al., 2008 (2003 through 2008)</td>
<td>n = 20, 42.8 [16–67]</td>
<td>24.7 [1–61]</td>
<td>Prospective</td>
<td>Clinical</td>
<td>8/20 (40.0)</td>
<td>17/20 (85.0)</td>
<td>11/20 (55.0)</td>
<td>12/20 (60.0)</td>
</tr>
<tr>
<td>Jung et al., 2009 (2004 through 2007)</td>
<td>n = 24, 52.8 (11.3)</td>
<td>10 [2–39]</td>
<td>Prospective</td>
<td>Clinical</td>
<td>1/24 (4.2)</td>
<td>5/24 (20.8)</td>
<td>16/24 (66.7)</td>
<td>21/24 (87.5)</td>
</tr>
<tr>
<td>Ghezzi et al., 2012 (not suggested)</td>
<td>n = 82, 56 [13–80]</td>
<td>28.5 [3–86]</td>
<td>Prospective</td>
<td>Clinical</td>
<td>14/82 (17.1)</td>
<td>19/82 (23.2)</td>
<td>75/82 (91.5)</td>
<td>64/82 (78.0)</td>
</tr>
</tbody>
</table>

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• EBL for LSC sig lower than for LAP
• Overall upstaging rate: 22.6%
• Overall conversion from LSC to LAP: 3.7%
• Overall rate of recurrence 9.9%
• Operative outcomes of LSC comparable to LAP
**PRINCIPLES OF SURGERY (1 of 2)**

**General considerations**
- In most instances, a vertical midline abdominal incision should be used in patients with a suspected malignant ovarian/Fallopian tube/primary peritoneal neoplasm in whom a surgical staging procedure, a primary debulking procedure, an interval debulking procedure, or secondary cytoreduction is planned.
- Intraoperative pathologic evaluation with frozen sections may assist in management.
- For select patients, a minimally invasive surgical approach may be employed by an experienced surgeon to achieve the surgical staging and debulking principles subsequently described. In addition, minimally invasive surgical approaches may be useful when evaluating whether maximum cytoreduction can be achieved in patients with newly diagnosed or recurrent ovarian cancer.
- Surgeons should quantify and document the extent of initial and residual disease in operative notes.
- It is recommended that a gynecologic oncologist perform the appropriate surgery.

The following surgical procedures should be considered for patients with newly diagnosed invasive epithelial ovarian cancer apparently confined to an ovary or to the pelvis:
- On entering the abdomen, aspiration of ascites or peritoneal lavage should be performed for peritoneal cytologic examinations.
- All peritoneal surfaces should be visualized, and any peritoneal surface or adhesion suspicious for harboring metastasis should be selectively excised or biopsied. In the absence of any suspicious areas, random peritoneal biopsies should be taken from the pelvis, paracolic gutters, and undersurfaces of the diaphragm (diaphragm scraping for Papanicolaou stain is an acceptable alternative).
- Bilateral salpingo-oophorectomy (BSO) and hysterectomy should be performed with every effort to keep an encapsulated mass intact during removal.
- For selected patients desiring to preserve fertility, unilateral salpingo-oophorectomy (USO) may be considered.
- Omentectomy should be performed.
- Para-aortic lymph node dissection should be performed by stripping the nodal tissue from the vena cava and the aorta bilaterally to at least the level of the inferior mesenteric artery and preferably to the level of the renal vessels.
- The preferred method of dissecting pelvic lymph nodes is bilateral removal of lymph nodes ecting and anterolateral to the common iliac vessels, overlying and medial to the external iliac, overlying and medial to the hypogastric vessels, and from the obturator fossa at a minimum anterior to the obturator nerve.

The following surgical procedures should be considered as part of the surgical management for patients with newly diagnosed invasive epithelial ovarian cancer involving the pelvis and upper abdomen:
- In general, every effort should be made to achieve maximum cytoreduction. Residual disease <1 cm defines optimal cytoreduction; however, maximal effort should be made to remove all gross disease since this offers superior survival outcomes.
- Aspiration of ascites (if present) should be performed for peritoneal cytologic examinations. All involved omentum should be removed.
- Suspicious and/or enlarged nodes should be resected, if possible.
- Those patients with tumor nodules outside the pelvis ≤2 cm (presumed stage IIB) should have bilateral pelvic and para-aortic lymph node dissection as previously described.
- Procedures that may be considered for optimal surgical cytoreduction (in all stages) include bowel resection and/or appendectomy, stripping of the diaphragm or other peritoneal surfaces, splenectomy, partial cystectomy and/or ureteroneocystotomy, partial hepatectomy, partial gastrectomy, cholecystectomy, and/or distal pancreatectomy.
- Select patients with low-volume residual disease after surgical cytoreduction for invasive epithelial ovarian or peritoneal cancer are potential candidates for IP therapy. In these patients, consideration should be given to placement of IP catheter with initial surgery.
Surgical Cytoreduction

• Also known as “tumor debulking”
• Resection of as much visible and palpable tumor as possible
• For most solid tumors, not justified
• Theoretical and clinical benefits demonstrated for ovarian carcinoma
Theoretical Benefits of Optimal Cytoreductive Surgery for Advanced Ovarian Carcinoma

- Nearly all rapid proliferation of tumor cells is in the preclinical phase
- Bulky tumors respond poorly to chemotherapy due to poor blood supply
- Removal of large bulky tumors improves the sensitivity of residual masses to postoperative chemotherapy by shifting to rapid growth phase of the cell cycle
- With less tumor volume, there is a greater likelihood of tumor eradication before chemoresistance develops
- Tumor burden of $3 \times 10^{12}$ is lethal
Clinical Benefits of Optimal Cytoreductive Surgery For Advanced Ovarian Carcinoma

- Improved pt comfort/GI function/nutrition
- Better response rate to chemotherapy
- Higher percentage of negative second-look surgeries
- Prolonged progression free interval
- Improved overall survival
Residual Disease

• The *maximum* diameter of the largest tumor mass remaining after cytoreductive surgery
• By convention, measured in cm
• Optimal versus suboptimal cytoreduction or debulking refers to the amount of residual disease in relation to a certain cutoff point (eg 1.0, 1.5, 2.0, or 3.0 cm)
• Review of 465 consecutive patients (1/89-12/03)
• No pts were stage IIIC based solely on lymph node metastasis
• 13 factors analyzed for prognostic significance
• Multivariate analysis:
  – Age
  – Ascites
  – Residual disease
What is the optimal goal of primary cytoreductive surgery for bulky stage IIIC epithelial ovarian carcinoma (EOC)?


<table>
<thead>
<tr>
<th>Residual Disease</th>
<th>Pts</th>
<th>Median OS (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Micro</td>
<td>67</td>
<td>106</td>
</tr>
<tr>
<td>&lt; 0.5 cm</td>
<td>70</td>
<td>66</td>
</tr>
<tr>
<td>0.5 – 1 cm</td>
<td>99</td>
<td>48</td>
</tr>
<tr>
<td>1 - 2 cm</td>
<td>53</td>
<td>33</td>
</tr>
<tr>
<td>&gt; 2 cm</td>
<td>176</td>
<td>34</td>
</tr>
</tbody>
</table>
What is the optimal goal of primary cytoreductive surgery for bulky stage IIIC epithelial ovarian carcinoma (EOC)?


- Cytoreduction to > 1 cm residual has no benefit on overall survival
- There is a survival benefit associated with cytoreduction to ≤ 1 cm residual
- Within the gross residual but ≤ 1 cm category, the closer to no gross residual, the longer the median survival
Optimal Cytoreduction Rates in Advanced Ovarian Carcinoma with *Standard* Surgical Techniques

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>No. Pts</th>
<th>Optimally Cytoreduced</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smith</td>
<td>1979</td>
<td>792</td>
<td>24%</td>
</tr>
<tr>
<td>Wharton</td>
<td>1984</td>
<td>395</td>
<td>39%</td>
</tr>
<tr>
<td>Neijt</td>
<td>1993</td>
<td>265</td>
<td>46%</td>
</tr>
<tr>
<td>Makar</td>
<td>1995</td>
<td>455</td>
<td>27%</td>
</tr>
<tr>
<td>Chi</td>
<td>2001</td>
<td>282</td>
<td>25%</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>2189</td>
<td>30%</td>
</tr>
</tbody>
</table>
Primary Cytoreduction: Meta-Analysis

• Study selection
  • Medline database 1989 – 1998
  • Stage III-IV ovarian cancer: Surgery + Platinum
  • “Maximum cytoreduction” = % patients “optimal”
• 6,885 patients in 81 patient cohorts
• Mean weighted median survival - 29.0 months
• Multiple linear regression analysis
  - each 10% increase in maximum cytoreductive surgery was associated with a 5.5% increase in median survival time

Conclusions

- Percent Maximum Cytoreduction
  - Independent determinant of survival
- “Expert” vs. less-experienced centers
  - $\leq 25\%$ maximal cytoreduction:
    weighted median OS: 22.7 months
  - $> 75\%$ maximal cytoreduction:
    weighted median OS: 33.9 months
  - *increase of 50%*

**Studies with ≥ 75% Maximal Cytoreduction Rate in Bristow Meta-Analysis**

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>No. Pts</th>
<th>Cutoff Maximal Cytoreduction</th>
<th>Maximal Cytoreduction</th>
<th>Chemotherapy Study?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omura /1989</td>
<td>349</td>
<td>≤ 1 cm</td>
<td>100%</td>
<td>Yes</td>
</tr>
<tr>
<td>Piver/1991*</td>
<td>61</td>
<td>≤ 2 cm</td>
<td>79%</td>
<td>No</td>
</tr>
<tr>
<td>Gershenson/1992</td>
<td>116</td>
<td>≤ 2 cm</td>
<td>100%</td>
<td>Yes</td>
</tr>
<tr>
<td>Marchetti/1993 *</td>
<td>70</td>
<td>≤ 2 cm</td>
<td>91%</td>
<td>No</td>
</tr>
<tr>
<td>Baker/1994 **</td>
<td>136</td>
<td>≤ 2 cm</td>
<td>83%</td>
<td>No</td>
</tr>
<tr>
<td>Alberts/1996</td>
<td>546</td>
<td>≤ 2 cm</td>
<td>100%</td>
<td>Yes</td>
</tr>
<tr>
<td>Meerpohl/1997</td>
<td>158</td>
<td>≤ 2 cm</td>
<td>100%</td>
<td>Yes</td>
</tr>
<tr>
<td>Vallejos/1997</td>
<td>30</td>
<td>&lt; 1 cm</td>
<td>87%</td>
<td>Yes</td>
</tr>
<tr>
<td>Eisenkop/1998</td>
<td>163</td>
<td>≤ 1 cm</td>
<td>99%</td>
<td>No</td>
</tr>
</tbody>
</table>

*studies from SUNY Buffalo, **40% maximal cytoreduction rate for ≤ 1 cm cutoff
“Clearing the Pelvis”
Modified Posterior Exenteration (MPE, 1997-current)
The impact of bulky upper abdominal disease cephalad to the greater omentum on surgical outcome for stage IIIC epithelial ovarian, fallopian tube, and primary peritoneal cancer.

474 stage IIIC patients between 1989-2005 stratified by UAD

Zivanovic O et al. Gynecol Oncol 2007

Fig. 1. Abdominopelvic regions. (A) Upper abdomen cephalad to the greater omentum. (B) Mid-abdomen. (C) Pelvis.
Role of Extensive Cytoreductive Procedures

What Are the Current Surgical Objectives, Strategies, and Technical Capabilities of Gynecologic Oncologists Treating Advanced Epithelial Ovarian Cancer?

Scott M. Eisenkop, M.D.,* and Nick M. Spirtos, M.D.†

*Womens’ Cancer Center, Encino–Tarzana, 5525 Etiwanda Avenue, Suite 311, Tarzana, California 91356; and
†Womens’ Cancer Center, Palo Alto, 900 Welch Road, Suite 300, Palo Alto, California 94304-1800

Received December 7, 2000; published online August 1, 2001

• Survey mailed to SGO membership with 61% response
• Reasons for suboptimal cytoreduction:
  • Unresectable upper abd metastases 85%
• Disease sites precluding optimal cytoreduction:
  • Disease involving base of mesentery 83%
  • Portal triad disease 77%
  • Bulky diaphragmatic metastases 76%

Eisenkop SM. Gynecol Oncol 2001
Dissection of Tumor and Peritoneum off Right Hepatic Vein
Continuation of Dissection Laterally
Right Diaphragm Peritoneectomy
Medial Mobilization of Liver with Identification of Right Kidney, Adrenal Gland and Retro-Hepatic IVC
Right Diaphragm Peritoneectomy
En bloc Omentectomy & Splenectomy
Splenectomy & Distal Pancreatectomy
Resection of Portion of Left Diaphragm with Pericardium
Liver and Diaphragm Resection

Cut edge of liver

Pleural Space
Cholecystectomy and Porta Hepatis Dissection

- Bile duct
- Hepatic artery
- Portal vein
Chi DS et al. Gynecol Oncol 2009

Survival
Adv Ovary Cancer
MSKCC 1987-2004

Weighted Median Survival (months)

Percent Maximum Cytoreductive Surgery

“increased LARs” * (1987-1994)


* (2001-2004)
Complete Gross Resection Rates at MSKCC 2001-2013
Upper Abdominal Surgery at Primary Debulking for Advanced Ovarian Cancer

Publications by Year and Country

Australia, 2
Belgium
Canada
China
France
Germany
Greece
Italy
Japan
Korea, 1
Lebanon
Portugal
Turkey
USA, 2
USA, 6
USA, 3
USA, 11
USA, 7

Dinkenspiel H et al. SGO 2012
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- In most instances, a vertical midline abdominal incision should be used in patients with a suspected malignant ovarian/Fallopian tube/primary peritoneal neoplasm in whom a surgical staging procedure, a primary debulking procedure, an interval debulking procedure, or secondary cytoreduction is planned.
- Intraoperative pathologic evaluation with frozen sections may assist in management.
- For select patients, a minimally invasive surgical approach may be employed by an experienced surgeon to achieve the surgical staging and debulking principles subsequently described. In addition, minimally invasive surgical approaches may be useful when evaluating whether maximum cytoreduction can be achieved in patients with newly diagnosed or recurrent ovarian cancer.
- Surgeons should quantify and document the extent of initial and residual disease in operative notes.
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The following surgical procedures should be considered for patients with newly diagnosed invasive epithelial ovarian cancer apparently confined to an ovary or to the pelvis:
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- The preferred method of dissecting pelvic lymph nodes is bilateral removal of lymph nodes overlying and anterolateral to the common iliac vessel, overlying and medial to the external iliac, overlying and medial to the hypogastric vessels, and from the obturator fossa at a minimum anterior to the obturator nerve.

The following surgical procedures should be considered as part of the surgical management for patients with newly diagnosed invasive epithelial ovarian cancer involving the pelvis and upper abdomen:
- In general, every effort should be made to achieve maximum cytoreduction. Residual disease <1 cm defines optimal cytoreduction; however, maximal effort should be made to remove all gross disease since this offers superior survival outcomes.
- If present, all involved omentum should be removed.
- Suspicious and/or enlarged nodes should be resected, if possible.
- Those patients with tumor nodules outside the pelvis ≤2 cm (presumed stage IIIb) should have bilateral pelvic and para-aortic lymph node dissection as previously described.
- Procedures that may be considered for optimal surgical cytoreduction (in all stages) include bowel resection and/or appendectomy, stripping of the diaphragm or other peritoneal surfaces, splenectomy, partial cystectomy and/or ureteroneocystotomy, partial hepatectomy, partial gastrectomy, cholecystectomy, and/or distal pancreatectomy.
- Select patients with low-volume residual disease after surgical cytoreduction for invasive epithelial ovarian or peritoneal cancer are potential candidates for IP therapy. In these patients, consideration should be given to placement of IP catheter with initial surgery.
Postoperative Chemotherapy

Early Stage

Randomized phase III trial of three versus six cycles of adjuvant carboplatin and paclitaxel in early stage epithelial ovarian carcinoma: A Gynecologic Oncology Group study

Jeffrey Bell a, b, Mark F. Brady b, Robert C. Young e, Janice Lage d, Joan L. Walker c, Katherine Y. Look f, G. Scott Rose g, Nick M. Spiro t h

Survival after recurrence in early-stage high-risk epithelial ovarian cancer: A Gynecologic Oncology Group study

John K. Chan a, b, Chunqiiao Tian b, Deanna Teoh e, Bradley J. Monk f, Thomas Herzog d, Daniel S. Kapp g, Jeffrey Bell h

Cumulative Incidence of Recurrence
By Randomized Treatment including Surgical Exclusions

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Control Failed</th>
<th>Death</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin × 3</td>
<td>149</td>
<td>58</td>
<td>213</td>
</tr>
<tr>
<td>Carboplatin × 6</td>
<td>102</td>
<td>43</td>
<td>214</td>
</tr>
</tbody>
</table>

*Deaths prior to disease recurrence

Recurrence-free survival

Fig. 1. Cumulative incidence of recurrence by randomized treatment.

Fig. 2. Recurrence-free survival of serous and non-serous ovarian cancer patients treated with six versus three cycles of chemotherapy (n = 427).
Postoperative Chemotherapy
Advanced Stage

Intraperitoneal Cisplatin and Paclitaxel in Ovarian Cancer

Deborah K. Armstrong, M.D., Brian Bundy, Ph.D., Lari Wenzel, Ph.D., Helen Q. Huang, M.S., Rebecca Baergen, M.D., Shashikant Lele, M.D., Larry J. Copeland, M.D., Joan L. Walker, M.D., and Robert A. Burger, M.D., for the Gynecologic Oncology Group

Median OS (months):
- IP Regimen: 65.6
- IV Regimen: 49.7

Long-term results of dose-dense paclitaxel and carboplatin versus conventional paclitaxel and carboplatin for treatment of advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer (JGOG 3016): a randomised, controlled, open-label trial

Nanako Katsumata, Makoto Yatsuda, Seiji Itohachi, Fumitsuki Takahashi, Hirofumi Mishima, Eizo Kimura, Daisuke Aoki, Toshiko Ijobo, Unji Kodama, Fumio Kato, Yasushi Tono, Shokokusei, Kazumasa Ochiai, for the Japanese Gynecologic Oncology Group

Median OS (months):
- Conventional Regimen: 62.2
- Dose Dense Regimen: 100.5
Postoperative Chemotherapy
Advanced Stage

Incorporation of Bevacizumab in the Primary Treatment of Ovarian Cancer

Robert A. Burger, M.D., Mark F. Brady, Ph.D., Michael A. Bookman, M.D., Gini F. Fleming, M.D., Bradley J. Monk, M.D., Helen Huang, M.S., Robert S. Mannel, M.D., Howard D. Humesley, M.D., Jeffrey Fowler, M.D., Benjamin E. Greer, M.D., Matthew Boente, M.D., Michael J. Birrer, M.D., Ph.D., and Sharon X. Liang, M.D., for the Gynecologic Oncology Group

1873 Patients were enrolled and underwent randomization

625 Were assigned to control therapy:
Cycles 1–6: Carboplatin, AUC 6 Paclitaxel, 175 mg/m² Placebo (starting in cycle 2) every 3 wk Cycles 7–22: Placebo every 3 wk

625 Were assigned to bevacizumab-initiation therapy:
Cycles 1–6: Carboplatin, AUC 6 Paclitaxel, 175 mg/m² Bevacizumab, 15 mg/kg (starting in cycle 2) every 3 wk Cycles 7–22: Placebo every 3 wk

623 Were assigned to bevacizumab-throughout therapy:
Cycles 1–6: Carboplatin, AUC 6 Paclitaxel, 175 mg/m² Bevacizumab, 15 mg/kg (starting in cycle 2) every 3 wk Cycles 7–22: Bevacizumab, 15 mg/kg every 3 wk
NCCN Guidelines for Postoperative Chemotherapy

Epithelial Ovarian Cancer/ Fallopian Tube Cancer/ Primary Peritoneal Cancer

**PATHOLOGIC STAGING**

- **Stage IA or IB**
  - Grade 1 → Observe
  - Grade 2 → Observe or Intravenous (IV) taxane/carboplatin\(^k\) for 3-6 cycles
  - Grade 3 or clear cell → IV taxane/carboplatin\(^k\) for 3-6 cycles

- **Stage IC**
  - Grade 1, 2, or 3 → IV taxane/carboplatin\(^k\) for 3-6 cycles

- **Stage II**
- **Stage III**
- **Stage IV**

**PRIMARY CHEMOTHERAPY/PRIMARY ADJUVANT THERAPY**

- • Chemotherapy\(^n\)
  - \(i, k\) in <1 cm optimally debulked stage II and stage III patients (category 1 for stage III) or
  - Intravenous taxane/carboplatin\(^k\) for a total of 6-8 cycles (category 1)
  - Completion surgery as indicated by tumor response and potential resectability in selected patients\(^j\)

See Monitoring/Follow-Up (OV-5)
See Secondary Adjuvant Therapy (OV-4)
# Current Management of Ovarian Cancer

## Summary

<table>
<thead>
<tr>
<th>Stage</th>
<th>Surgery</th>
<th>Chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA, IB (grade 1, 2)</td>
<td>TAH/BSO (USO for &lt; 40 yo), staging procedure</td>
<td>None</td>
</tr>
<tr>
<td>IA, IB (grade 3), IC</td>
<td>TAH/BSO (USO for &lt; 40 yo), staging procedure</td>
<td>IV Taxol/Carbo x 3-6</td>
</tr>
<tr>
<td>II-IIIC, IV (intraperitoneal)</td>
<td>PDS including TAH/BSO or NACT with IDS</td>
<td>IV/IP Taxol, IP Cisplatin x 6 or IV Taxol/Carbo x 6</td>
</tr>
<tr>
<td>IV (extraperitoneal)</td>
<td>PDS including TAH/BSO or NACT with IDS</td>
<td>IV Taxol/Carbo X 6</td>
</tr>
<tr>
<td>Platinum Sensitive Recurrence</td>
<td>Consider repeat debulking</td>
<td>IV platinum-based doublet</td>
</tr>
<tr>
<td>Platinum-Resistant Recurrence</td>
<td>Only for palliation (eg bowel obstruction)</td>
<td>IV or oral single agent therapy based on toxicity</td>
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