

National Comprehensive
Cancer Network[®]

Ovarian Cancer Guideline

Version 1.2002

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Continue

Table of Contents

[NCCN Ovarian Cancer Panel Members](#)

[Epithelial Ovarian Cancer:](#)

- [Clinical Presentation, Work-Up, Primary Treatment \(OV-1\)](#)
- [Diagnosis by Previous Surgery: Findings and Primary Treatment \(OV-2\)](#)
- [Pathologic Staging Primary Chemotherapy/Primary Adjuvant \(OV-3\)](#)
- [Secondary Adjuvant \(OV-4\)](#)
- [Monitoring/Follow-Up, Recurrent Disease \(OV-5\)](#)
- [Recurrence Therapy \(OV-6\)](#)

[Borderline Epithelial Ovarian Cancer \(Low Malignant Potential\) \(OV-7\)](#)

[Principles of Primary Surgery \(OV-A\)](#)

[Ancillary Surgical Procedures \(OV-B\)](#)

[Acceptable Recurrence Regimens \(OV-C\)](#)

[Guidelines Index](#)

[Print the Ovarian Cancer Guideline](#)

[For help using these documents, please click here](#)

[Staging](#)

[Manuscript](#)

[References](#)

Clinical Trials: The NCCN believes that the best management for any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

NCCN Categories of Consensus: All recommendations are Category 2A unless otherwise specified. See [NCCN Categories of Consensus](#)

These guidelines are a statement of consensus of the authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these guidelines is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network makes no representations or warranties of any kind, regarding their content use or application and disclaims any responsibility for their application or use in any way. These guidelines are copyrighted by National Comprehensive Cancer Network. All rights reserved. These guidelines and the illustrations herein may not be reproduced in any form without the express written permission of NCCN. ©2001.

CLINICAL
PRESENTATION

WORK-UP

PRIMARY TREATMENT ^{a,b}

Suspicious pelvic mass and/or ascites, abdominal distention, or symptoms without other obvious source of malignancy

- Barium enema/colonoscopy if clinically indicated
- Chest x-ray
- CA-125
- CBC
- Ultrasound or abdominopelvic CT if clinically indicated
- Chemistry profile
- Consider family history evaluation ([See NCCN Genetics/Cancer Screening Guidelines](#))

Laparotomy/TAH/BSO with comprehensive staging^c or USO (with comprehensive staging if patient desires fertility)

Cytoreductive surgery^c if clinical stage II, III, or IV

Consider neoadjuvant chemotherapy/interval cytoreduction for patients with bulky stage III/IV who are not surgical candidates up front (diagnosis by FNA or paracentesis)

[See Pathologic Staging \(OV-3\)](#)

Diagnosis by previous surgery

- Chest x-ray
- CA-125
- CBC
- Ultrasound or abdominopelvic CT if clinically indicated
- Chemistry profile
- Consider family history evaluation ([See NCCN Genetics/Screening Guidelines](#))

[See Findings and Primary Treatment \(OV-2\)](#)

^aStandard recommendation includes a patient evaluation by a gynecologic oncologist.

^c[See Surgical Staging \(OV-A\).](#)

^bPatients receiving primary chemotherapy will be monitored as follows:

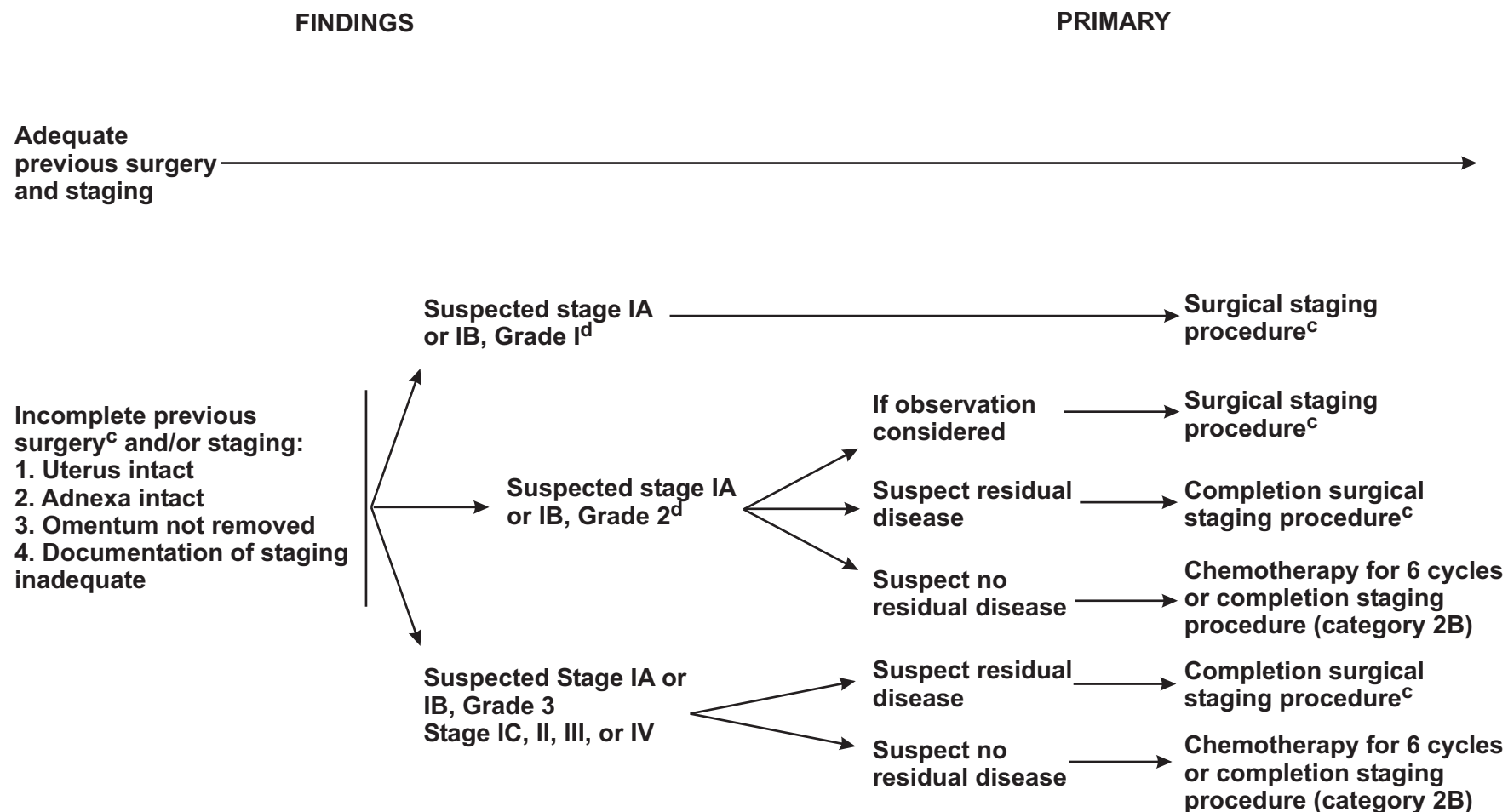
1. Pelvic exams at least every 2 cycles
2. Interim CBC with platelets as indicated
3. Chemistry profiles if indicated
4. CA-125 levels prior to each cycle of chemotherapy, if informative
5. Radiographic imaging if indicated

[Go Back To Ovarian Cancer Table of Contents](#)

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DIAGNOSIS BY PREVIOUS SURGERY



[See
Pathologic
staging
\(OV-3\)](#)

^cSee [Surgical Staging \(OV-A\)](#).

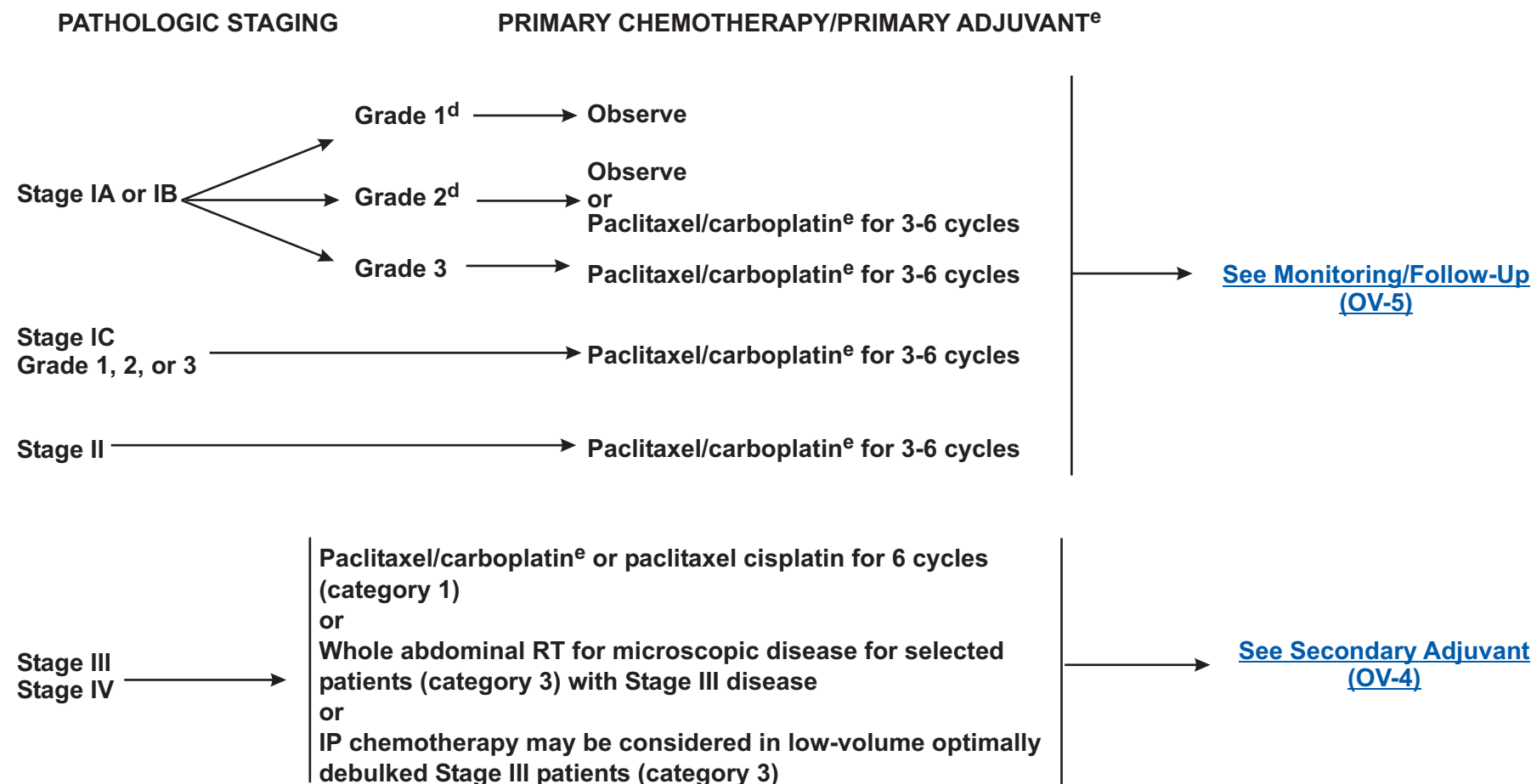
^dClear-cell pathology is grade 3.

[Go Back To Ovarian Cancer
Table of Contents](#)

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OV-2



^dClear-cell pathology is Grade 3.

^ePreferred regimen is:

1. Carboplatin, AUC 5.0-7.5, + paclitaxel, 175 mg/m², over 3h for 6 cycles for stage III or IV disease and for 3-6 cycles for lower-stage disease (preferred due to decreased toxicity)

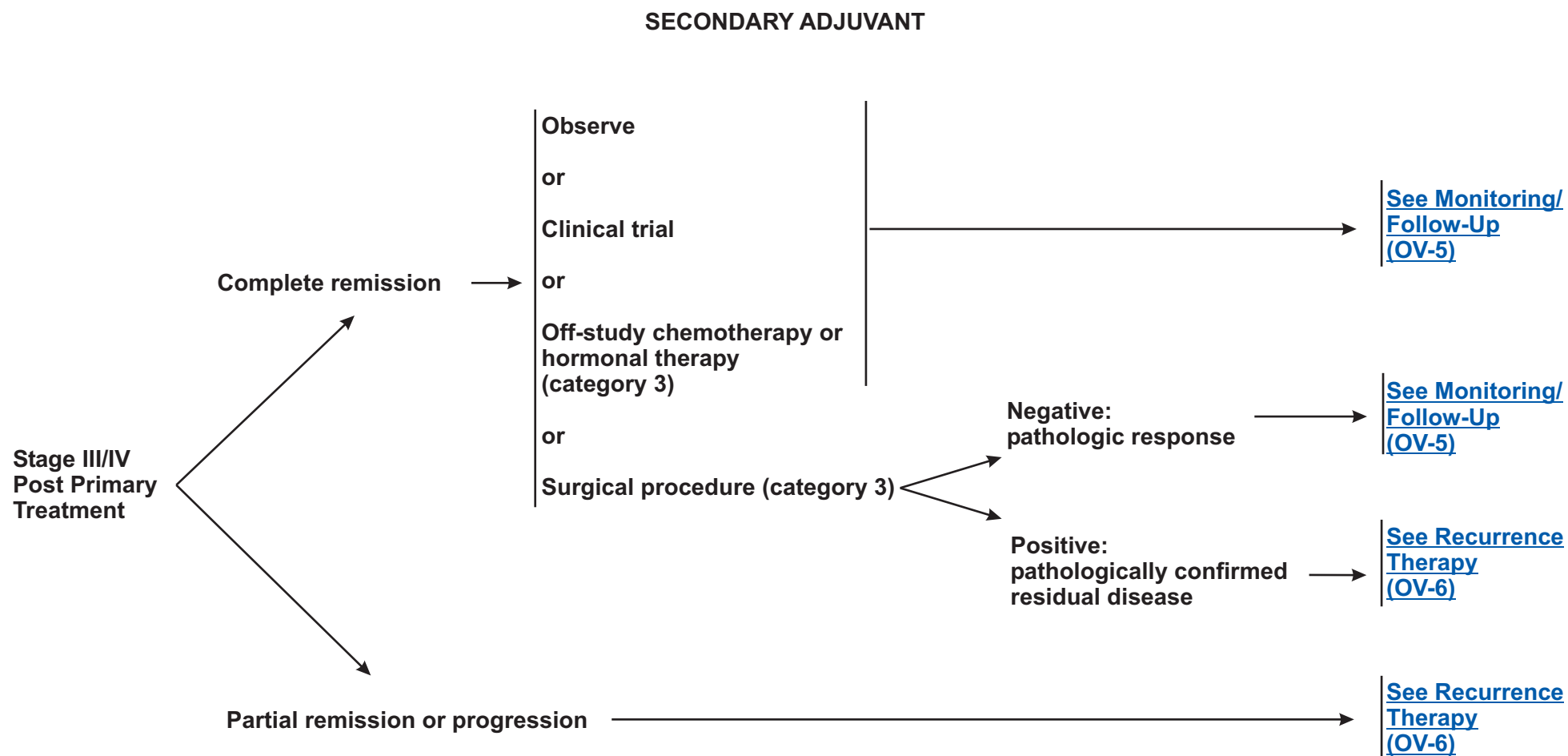
Alternative regimens include:

1. Cisplatin, 75 mg/m², + paclitaxel, 135 mg/m², over 24h
2. Whole abdominopelvic RT for microscopic disease (category 3)
3. Docetaxel/Carboplatin, AUC 5 - 6

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[Go Back To Ovarian Cancer
Table of Contents](#)



[Go Back To Ovarian Cancer
Table of Contents](#)

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OV-4

MONITORING/FOLLOW-UP

RECURRENT DISEASE

Stage I, II,
Stage III and IV
complete response

- Visits every 2-4 mo for 2 yr, then 6 mo for 3 yr
- CBC every 12 mo
- CA-125 every visit if initially elevated
- Chemistry profile as indicated
- Physical exam including pelvic exam
- Abdominopelvic CT as clinically indicated
- Chest x-ray as indicated

Rising CA-125, no previous
chemotherapy
or
Clinical relapse, no
previous chemotherapy

Laparotomy/
debulking

[See Primary
Chemotherapy/
Primary Adjuvant
\(OV-3\)](#)

Clinical relapse,
previous
chemotherapy

[See Recurrence Therapy
\(OV-6\)](#)

Rising CA-125, previous
chemotherapy

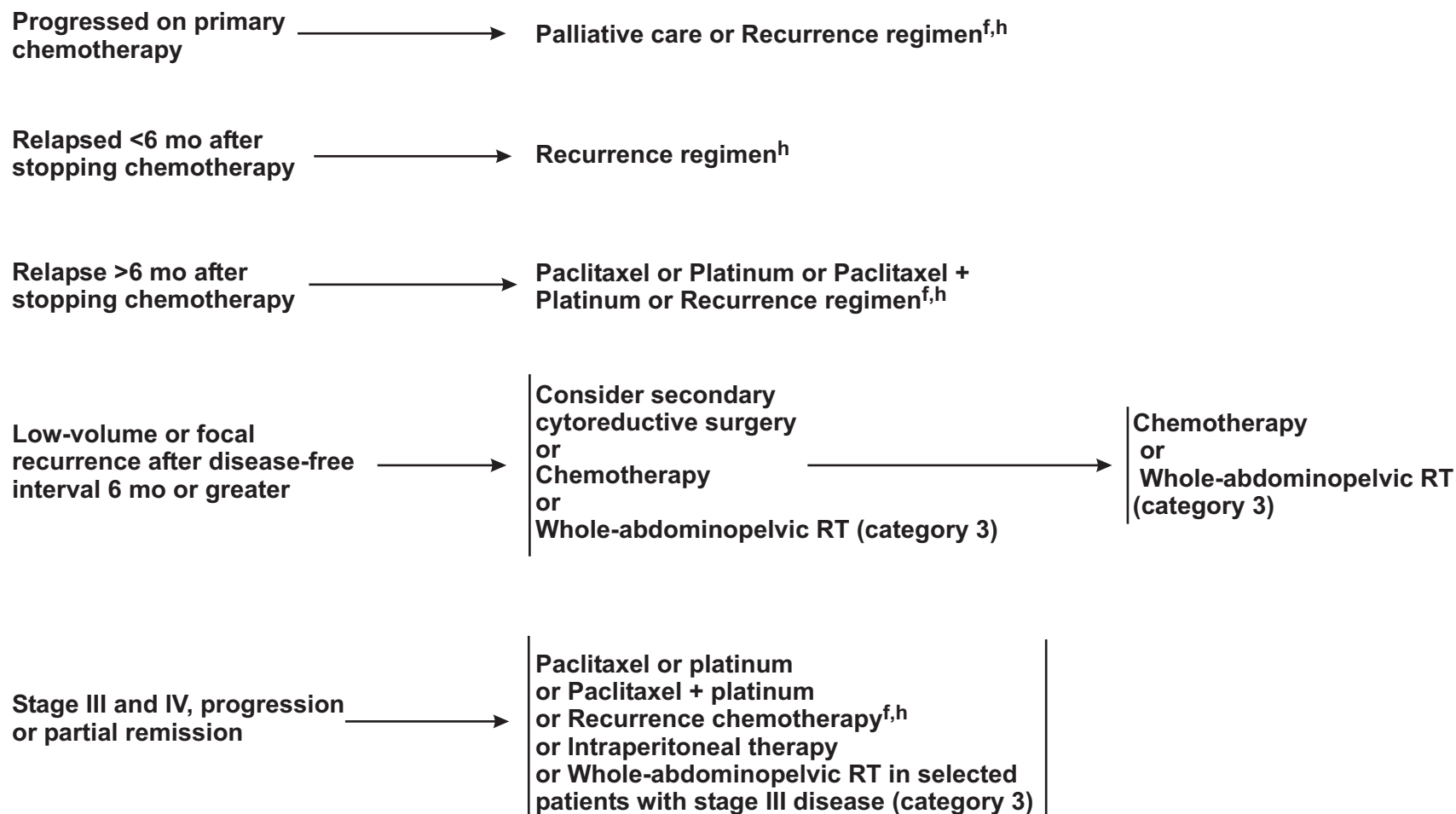
Delay until clinical relapse
(category 2B)
or
Immediate treatment for
recurrent disease: cytotoxic
chemotherapy or tamoxifen
(category 2B)

[See
Recurrence
Therapy
\(OV-6\)](#)

[Go Back To Ovarian Cancer
Table of Contents](#)

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RECURRENCE REGIMEN^{f,g,h}

^fPatients who progress on two consecutive single-agent regimens without evidence of clinical benefits are unlikely to benefit from additional chemotherapy regimens and may be offered supportive care or a clinical trial.

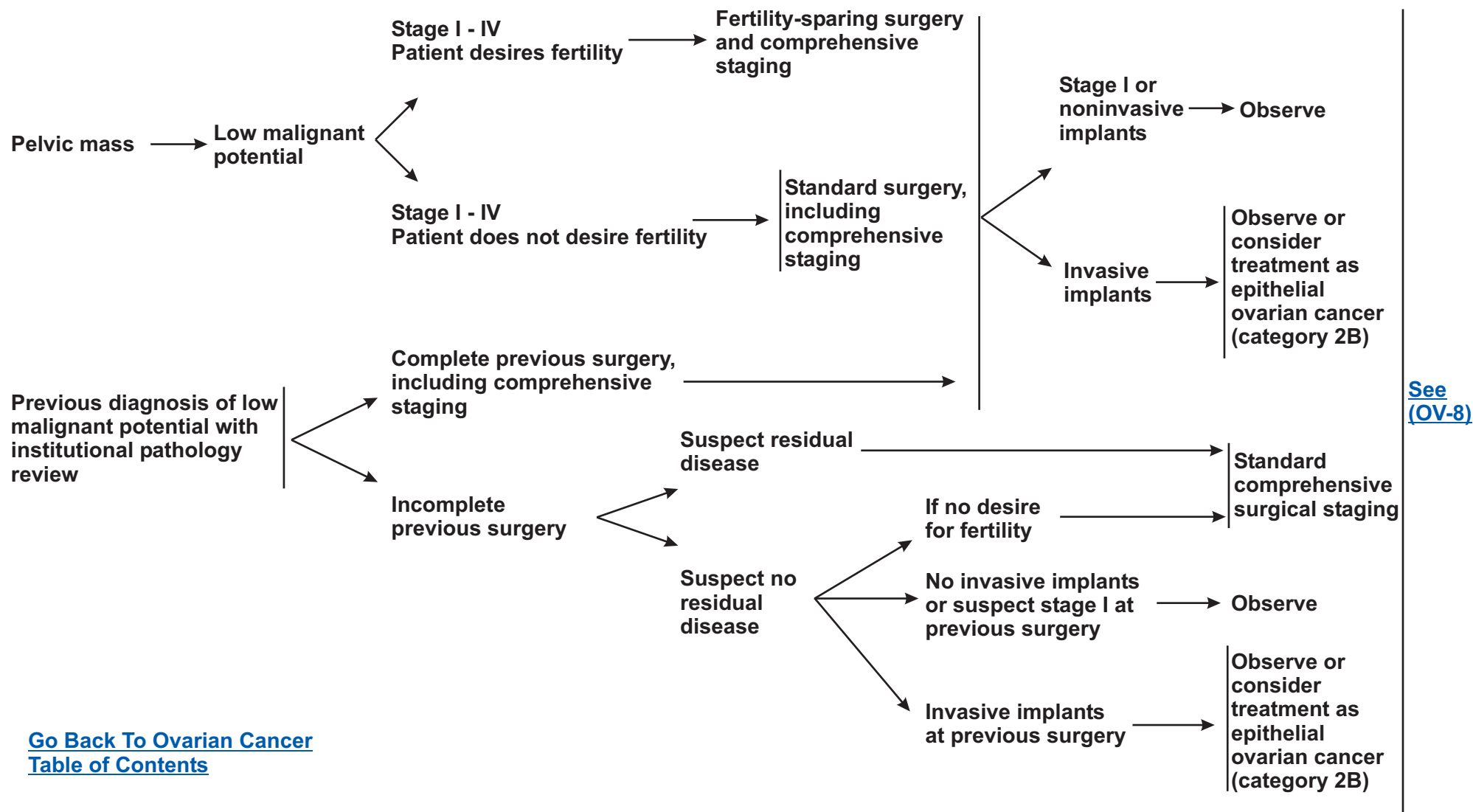
^g[For ancillary surgical procedures \(See OV-B\).](#)

^h[For acceptable recurrence regimens \(See OV-C\).](#)

[Go Back To Ovarian Cancer Table of Contents](#)

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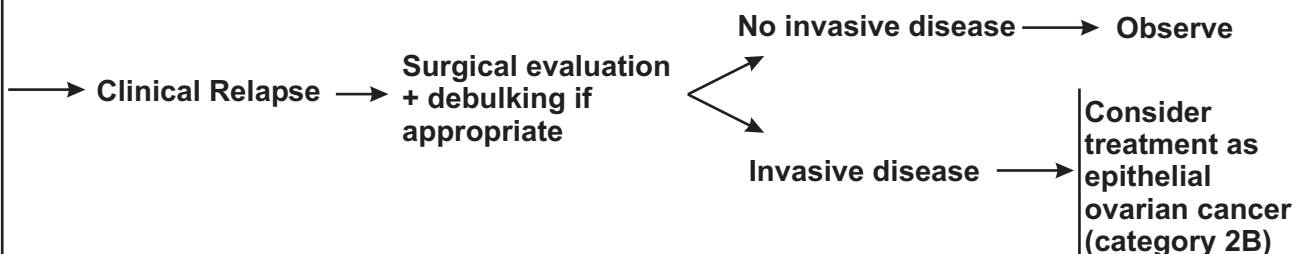
[Go Back To Ovarian Cancer Table of Contents](#)

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MONITORING/FOLLOW-UP

- After completion of childbearing in patients who underwent unilateral salpingoophorectomy, consider completion surgery (category 2B)
- Visits every 2-4 mo for 2 yr, then every 6 mo for 6 visits
- CA-125 every visit if initially elevated or Stage I or limited Stage II
- CBC every 12 mo
- Chemistry profile as indicated
- Consider family history
([See NCCN Genetics/Cancer Screening Guidelines](#))



[Go Back To Ovarian Cancer Table of Contents](#)

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OV-8

PRINCIPLES OF PRIMARY SURGERY*

A vertical incision should be used

On entering the abdomen, aspiration of ascites or peritoneal lavage should be performed for peritoneal cytologic examinations. Specimens should be taken from:

- Pelvis
- Right and left paracolic gutters
- The undersurfaces of the right and left hemidiaphragms

An encapsulated mass should be removed intact if possible

Adhesions should be noted and marked

All intestinal surfaces should be evaluated and any suspicious area should be biopsied

Omentectomy and random peritoneal biopsies should be performed

Aortic lymph node sampling should be performed by stripping the nodal tissue from the vena cava and the aorta to the level of the left renal hilus

Pelvic lymph nodes should be sampled

Total hysterectomy, salpingectomy, and oophorectomy should be performed

Surgical Cytoreduction

Every attempt should be made to achieve maximal cytoreduction in appropriate circumstances

USO for patients desiring to preserve fertility may be considered in selected patients

*All procedures may not be indicated in all patients

[Go Back To Ovarian Cancer
Table of Contents](#)

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OV-A

ANCILLARY SURGICAL PROCEDURES*

- Paracentesis
- Thoracentesis/pleurodesis
- Ureteral stents/nephrostomy
- Surgical relief of intestinal obstruction
- Enteral feeding tube
- Gastrostomy tube
- Vascular access device

* These may be appropriate in selected patients

[Go Back To Ovarian Cancer
Table of Contents](#)

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OV-B

ACCEPTABLE RECURRENCE REGIMENS

Tamoxifen

Topotecan

Gemcitabine

Oral Etoposide

Altretamine

Alkylating agent

Vinorelbine

Liposomal Doxorubicin

Radiation therapy

Taxane

Platinum compound

Patients who progress on two consecutive single-agent regimens without evidence of clinical benefit are unlikely to benefit from additional chemotherapy regimens and may be offered best supportive care or clinical trial.

[Go Back To Ovarian Cancer
Table of Contents](#)

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OV-C

Staging

Table 1		
American Joint Committee on Cancer (AJCC) TNM and FIGO Staging System for Ovarian Cancer		
Primary Tumor (T)		
TNM	FIGO	
categories	stages	
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
T1	I	Tumor limited to ovaries (one or both)
T1a	IA	Tumor limited to one ovary; capsule intact, no tumor on ovarian surface. No malignant cells in ascites or peritoneal washings*
T1b	IB	Tumor limited to both ovaries; capsules intact, no tumor on ovarian surface. No malignant cells in ascites or peritoneal washings.*
T1c	IC	Tumor limited to one or both ovaries with any of the following: capsule ruptured, tumor on ovarian surface, malignant cells in ascites, or peritoneal washings*
T2	II	Tumor involves one or both ovaries with pelvic extension*
T2a	IIA	Extension and/or implants on uterus and/or tube(s). No malignant cells in ascites or peritoneal washings.
T2b	IIB	Extension to other pelvic tissues. No malignant cells in ascites or peritoneal washings.
T2c	IIC	Pelvic extension (2a or 2b) with malignant cells in ascites or peritoneal washings
TNM	FIGO	
T3	III	Tumor involves one or both ovaries with microscopically confirmed peritoneal metastasis
and/or		outside the pelvis and/or regional lymph node metastasis
N1		
T3a	IIIA	Microscopic peritoneal metastasis beyond pelvis
T3b	IIIB	Macroscopic peritoneal metastasis beyond pelvis 2 cm or less in greatest dimension
T3c	IIIC	Peritoneal metastasis beyond pelvis more than 2 cm in greatest dimension and/or regional
and/or		lymph node metastasis
N1		
M1	IV	Distant metastasis (excludes peritoneal metastasis)

*Note: The presence of nonmalignant ascites is not classified. The presence of ascites does not affect staging unless malignant cells are present.

Note: Liver capsule metastases are T3/Stage III; liver parenchymal metastasis, M1/Stage IV. Pleural effusion must have positive cytology for M1/Stage IV.

Continued

Table 1 Continued**Regional Lymph Nodes (N)****NX** Regional lymph nodes cannot be assessed**N0** No regional lymph node metastasis**N1** Regional lymph node metastasis**Distant Metastasis (M)****MX** Distant metastasis cannot be assessed**M0** No distant metastasis**M1** Distant metastasis (excludes peritoneal metastasis)**Stage Grouping****Stage IA** T1a N0 M0**Stage IB** T1b N0 M0**Stage IC** T1c N0 M0**Stage IIA** T2a N0 M0**Stage IIB** T2b N0 M0**Stage IIC** T2c N0 M0**Stage IIIA** T3a N0 M0**Stage IIIB** T3b N0 M0**Stage IIIC** T3c N0 M0

Any T N1 M0

Stage IV Any T Any N M1

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Manuscript

NCCN Categories of Consensus

Category 1: There is uniform NCCN consensus, based on high-level evidence, that the recommendation is appropriate.

Category 2A: There is uniform NCCN consensus, based on lower-level evidence including clinical experience, that the recommendation is appropriate.

Category 2B: There is nonuniform NCCN consensus (but no major disagreement), based on lower-level evidence including clinical experience, that the recommendation is appropriate.

Category 3: There is major NCCN disagreement that the recommendation is appropriate.

All recommendations are category 2A unless otherwise noted.

Overview

Epithelial ovarian cancer is the leading cause of death from gynecologic cancer in the United States, and the country's fifth most common cause of cancer mortality in women. In the year 2001 there will be an estimated 23,400 new diagnoses and an estimated 13,900 deaths from this neoplasm (Greenlee et al, 2001). The incidence increases with age and is most prevalent in the eighth decade of life, with an incidence rate of 57/100,000 women. The median age at the time of diagnosis is 63 years, and 70% of patients present with advanced disease (Ozols et al, 1997).

Epidemiologic studies have identified risk factors as important in the etiology of ovarian cancer. A history of pregnancy with age at first

birth 25 years or younger, the use of oral contraceptives, and/or breast-feeding confers a 30% to 60% decreased risk (Ozols et al, 1997). Conversely, nulliparity or age at first birth older than 35 years confers an increased risk. Family history (primarily patients having two or more first-degree relatives with ovarian cancer), including linkage with BRCA1 and BRCA2 genotypes, has been found to be associated with early-onset disease; however, these patients account for only 5% of all women who have ovarian cancer (Ozols et al, 1997). Environmental factors have been investigated, but so far have not been conclusively associated with the development of this neoplasm.

The basic structure of the ovarian cancer guidelines has not changed since their 1997 publication. The guidelines continue to reflect the importance of stage and grade of disease. Ovarian cancer is classified primarily as stage I, II, III, or IV. In the past year, there have not been any significant changes in the TNM and FIGO (International Federation of Gynecology and Obstetrics) staging system for ovarian cancer ([Staging](#)).

Pathologic grading continues to be an important prognostic factor and is used in the selection of therapy, primarily for early-stage disease. Grading is labeled as 1, 2, or 3. Except for those with stage I, grade 1 tumors, in whom survival is greater than 95% following comprehensive laparotomy, patients in all other stages of ovarian cancer should be encouraged to enter clinical trials for both primary and recurrence therapy.

Recommended Work-up

The NCCN ovarian cancer guidelines begin with the management of an undiagnosed pelvic mass or a prior diagnosis of a malignant

epithelial ovarian tumor. Many such patients come to NCCN member institutions after having had previous surgery at other institutions.

Undiagnosed Pelvic Mass

There was general agreement on the primary work-up of a patient with an undiagnosed pelvic mass, and there have not been any significant changes made to the previous guidelines. The standard work-up for such patients should include an ultrasound or abdominopelvic computed tomography (CT) scan (if clinically indicated) after a complete physical examination and appropriate laboratory studies, including a CA 125 determination, have been completed. A consultation for a family history of ovarian and breast cancer should also be obtained (see the NCCN Genetics/Cancer Screening Guidelines).

While there continues to be no direct evidence that a chest x-ray is necessary, the panel felt that it should be part of the overall evaluation of a patient prior to surgical staging. Additional diagnostic studies, such as colonoscopy or barium studies of the gastrointestinal tract, are not routinely recommended, although they could prove useful in specific clinical situations.

Prior Diagnosis of Malignancy

Patients are often referred to NCCN institutions only after they have already been diagnosed with ovarian cancer. Many times, they have also been adequately staged (having met the standards for surgical staging of the Gynecologic Oncology Group [GOG]) and have undergone cytoreductive surgery. However, in some instances they are referred after having had “incomplete” staging (eg, uterus and/or adnexa intact, omentum not removed, or absence of documentation of surgical stage). The components of surgical staging are listed on [OV-A](#).

Primary Treatment

Primary treatment for presumed ovarian cancer consists of appropriate surgical staging and cytoreduction, followed in most (but not all) patients by systemic chemotherapy. Initial surgery should be a comprehensive staging laparotomy, including a total abdominal hysterectomy (TAH) and bilateral salpingo-oophorectomy (BSO). For a young patient who wants to maintain fertility, a unilateral salpingo-oophorectomy (USO) is adequate for stage I, grade 1 tumors. Observation alone is also recommended for these low-grade, low-stage tumors, since survival is greater than 90% for laparotomy.

For patients with clinical stage III or IV disease, the usual recommendation continues to be cytoreductive surgery. There is a recommendation that neo-adjuvant chemotherapy should also be considered for patients with bulky stage III and IV disease who are not surgical candidates. The pathologic diagnosis should be confirmed, however, by fine needle aspiration or paracentesis in this group of patients.

Incompletely Staged Patients

Recommendations regarding the treatment of incompletely staged patients continue to generate discussion. There was consensus on the following three treatment possibilities:

1. A surgical staging procedure is recommended for all patients with suspected stage Ia, grade 1 or stage Ib, grade 1 tumors, because if this stage is confirmed, no further adjuvant therapy is indicated.
2. If residual disease is suspected, a completion surgical staging procedure and debulking is recommended for all stages.

3. For stages higher than stage Ia, grade 1 or stage Ib, grade 1, if no residual disease is suspected, chemotherapy for six cycles or a completion surgical staging procedure with debulking are options (category 2B).

Patients who are stage Ia, grade 2 or stage Ib, grade 2 and have a negative restaging procedure may be followed with observation or receive adjuvant chemotherapy. All other restaged groups should routinely receive adjuvant chemotherapy.

Primary Adjuvant Chemotherapy

Most patients with epithelial ovarian cancer will receive postoperative systemic chemotherapy. Observation is recommended for stage Ia, grade 1 tumors, owing to their high cure rate (Young et al, 1990). Some disagreement continues regarding stage I, grade 2 tumors for which the panel felt that observation alone or chemotherapy would be appropriate recommendations. For patients with higher-grade and/or higher-stage tumors, systemic chemotherapy is indicated.

Primary Chemotherapy

The recommendations for specific primary chemotherapy/primary adjuvant therapy remain unchanged from previous guidelines. Paclitaxel plus carboplatin is recommended as the preferred regimen due to decreased toxicity. Paclitaxel plus cisplatin or carboplatin plus docetaxel are alternative regimens. (Cisplatin or carboplatin are again suggested as the primary chemotherapeutic regimens) (Bookman et al, 1996; McGuire et al, 1996; Vasey et al, 2001)). The extent of treatment varies with stage of disease. For patients with advanced-stage disease, six cycles of chemotherapy are recommended (category 1), whereas for earlier-stage disease,

three to six cycles are recommended, pending the results of an ongoing GOG study in this group of patients.

The recommended regimen of chemotherapy accepted by a consensus of the panel consists of carboplatin, dosed at an area under the curve (AUC) of 5 to 7.5, plus paclitaxel, 175 mg/m² given over 3 hours. Alternative regimens included cisplatin, 75 mg/m² plus paclitaxel, 135 mg/m² given over 24 hours, or carboplatin, dosed at an area under the curve (AUC) of 5 to 6 plus docetaxel, 75 mg/m².

Radiation Therapy

There was a major debate among the panel members regarding the role of whole abdominal radiation therapy in patients with low-bulk stage III or IV disease. Based primarily on historical data (Thomas, 1994), whole-abdominopelvic radiotherapy was listed as a primary chemotherapy/primary adjuvant therapy option for patients with low-bulk disease (category 3).

Other Areas of Controversy

Intraperitoneal (IP) Cisplatin: The panel also considered the role of IP cisplatin, as opposed to intravenous (IV) cisplatin, based upon the results of a recent SWOG/GOG clinical trial of IP cisplatin plus IV cyclophosphamide versus IV cisplatin plus IV cyclophosphamide in patients with stage III ovarian cancer (Alberts et al, 1996). This study demonstrated the decreased toxicity and increased efficacy of IP cisplatin. However, because of questions about the appropriateness of the control arm and the role of IP platinum in the presence of IV paclitaxel, panel members felt that the role of IP therapy is not clear. Some panelists felt that IP therapy could be considered in low-volume, optimally debulked, stage III patients (category 2B).

Dose Intensity: Panel members discussed the issue of dose intensity as well. Clinical trials have begun recently of high-dose chemotherapy, which requires peripheral stem cell transplantation in selected patients with previously untreated ovarian cancer, or as a consolidation strategy following induction therapy with standard drug doses. Panel members recommended that patients participate in these trials, but uniformly felt that high-dose chemotherapy that requires stem cell support be considered investigational, and not part of the current practice guidelines.

Number of Chemotherapy Cycles: There also was considerable discussion regarding the number of cycles of paclitaxel plus cisplatin or carboplatin that should be recommended for patients with advanced-stage disease. There is no existing evidence confirming that more than six cycles of combination chemotherapy are needed as part of induction chemotherapy. However, clinical trials are now evaluating the role of maintenance therapy in patients who achieve a complete remission after six cycles of chemotherapy.

Follow-up Recommendations

Stage I and Stage II Disease

After the completion of primary surgery and chemotherapy in those with lower-stage disease and poor prognostic features, the standard recommendation would be observation with follow-up. No role has been established for routine abdominopelvic CT scans in this group of patients, but these may be ordered if clinically necessary. Measurement of CA 125 levels, if initially elevated, is advocated. A consultation for a family history evaluation should also be considered if a family history suggests a genetic syndrome, as recommended in the NCCN Genetics/Cancer Screening Guidelines.

Stage III and Stage IV Disease

Patients with advanced-stage disease who have no evidence of progression while receiving treatment should undergo a clinical reevaluation after six cycles of paclitaxel plus a platinum compound. Patients who progress during initial therapy should be treated with second-line approaches (“recurrence therapy”).

There was substantial disagreement among panel members regarding the management of advanced-stage patients who are in complete remission. Options range from observation alone to additional chemotherapy or hormonal therapy, preferably in a controlled clinical trial. As previously noted, there is no evidence to support the use of additional cycles of chemotherapy as being superior to observation alone in this group of patients. In addition, the roles of second-look laparotomy or laparoscopy and debulking after primary chemotherapy remain controversial in this group of patients (category 3).

If a second-look laparotomy or laparoscopy is performed, the findings should dictate further treatment. If the findings are negative, the patient should be monitored as described previously. If the second-look findings are positive and the patient is thought to have been responding to initial chemotherapy, then the same chemotherapy regimen may be continued. In some patients, however, the second-look surgical procedure will demonstrate that they have not responded to initial chemotherapy, and these patients should be treated in a recurrence setting.

Management of a Rising CA125 Level

There was considerable discussion regarding the management of patients in clinical complete remission who, during routine monitoring and follow-up, are found to have a rising CA 125 level but

no symptoms of recurrent disease, a negative pelvic examination, and a negative abdominopelvic CT scan. Patients who have never received chemotherapy should be managed as newly diagnosed patients, undergo staging laparotomy and debulking, and be treated as described under the primary chemotherapy/primary adjuvant chemotherapy guidelines.

The median time for a clinical relapse following a rising CA 125 is 2 to 6 months. In patients who have had previous chemotherapy, there was a lack of consensus regarding the timing of recurrence therapy. Since tamoxifen has a defined response rate in recurrent disease following progression on cisplatin-based chemotherapy (Hatch et al, 1991), it is frequently administered to patients who have only a rising CA 125 level (van der Velden et al, 1995). Consequently, the panel included tamoxifen as an acceptable recommendation for this clinical situation (category 2B). Other alternatives include observation until clinical symptoms arise (category 2B) and the immediate institution of cytotoxic chemotherapy (category 2B).

Recurrent Disease

The prognosis for those who progress on primary chemotherapy is extremely poor. In light of this fact, panel members recommended several ancillary surgical and supportive care procedures for selected patients ([OV-B](#)). The importance of clinical trials to identify agents active in this group was also emphasized. Since these patients are resistant primarily to their induction regimen, retreatment with a platinum compound or paclitaxel is not recommended, although recent clinical trials suggest that altering the schedule of paclitaxel may produce secondary responses (Fennelly et al, 1997).

Patients whose disease relapses less than 6 months after chemotherapy ends are deemed platinum-resistant, and treatment with an acceptable second-line agent is recommended (Markman et al, 1991). These patients, like those who progress on primary chemotherapy, should not be treated routinely with a platinum compound or paclitaxel, given the low likelihood of a response.

Patients whose disease relapses more than 6 months after initial chemotherapy are considered drug-sensitive and have the greatest number of potential options for second-line therapy ([OV-C](#)). There is no evidence that combination chemotherapy is superior to single-agent therapy in this situation, although many of these patients are treated with the same combination that produced their initial remission. Alternatively, patients can be treated with single-agent paclitaxel or platinum and then crossed over to the other drug as necessary. In addition, there is no evidence that retreatment with paclitaxel or a platinum compound in patients with drug-sensitive recurrent ovarian cancer that recurs is superior to using newer agents as the first chemotherapy option for recurrent disease.

For patients with small-volume residual disease or recurrent disease, the recommendation for whole abdominal radiotherapy (category 3) instead of chemotherapy remained controversial among panel members (Schray et al, 1988).

Secondary cytoreductive surgery was endorsed for patients who have a low-grade or focal recurrence after a long disease-free interval (Hoskins et al, 1989). The exact length of the disease-free interval has not been established, although there was a consensus among panel members that it should be 6 months or greater for the surgery to be beneficial.

Acceptable Recurrence Regimens

In the last 8 years, the efficacy of several new agents in ovarian cancer has been described. The activity of the following agents appears to be similar: topotecan, 20% (ten Bokkel Huinink et al, 1997); gemcitabine, 19% (Lund et al, 1994); vinorelbine, 20% (Bajetta et al, 1996); liposomal doxorubicin, 26% (Muggia et al, 1997); and oral etoposide, 27% in platinum-resistant patients and 35% in platinum-sensitive patients (Rose et al, 1992). Altretamine, with a 14% response rate (Vergote et al, 1992), and ifosfamide, with a 12% response rate (Markman et al, 1992), have also been proven to be active in recurrent ovarian cancer, although less information regarding their use in paclitaxel-refractory patients is available. In addition, radiation therapy can provide an effective palliation when radiation ports are tailored to specific symptomatic disease sites (Corn et al, 1994).

Most patients in the GOG group trial of etoposide (Rose et al, 1992) had prior therapy with paclitaxel, making these results particularly relevant to the management of those whose initial therapy consisted of paclitaxel plus a platinum compound. Gemcitabine has been shown to be synergistic with platinum in ovarian cancer cell lines; at this point, however, there is no evidence that combination chemotherapy with gemcitabine and cisplatin is superior to gemcitabine alone for recurrent ovarian cancers. Liposomal doxorubicin is associated with a relatively prolonged survival (progression-free survival, 5.7 months; and median survival, 11 months) in heavily treated patients.

The panel felt that no single chemotherapeutic agent should be considered the treatment of choice for recurrent ovarian carcinoma. They also felt that in vitro chemosensitivity testing to choose a chemotherapy regimen for recurrent disease situations could not be

recommended, owing to the lack of demonstrable efficacy for such an approach. However, regardless of which regimen is selected initially, reevaluation should follow after two cycles of chemotherapy to determine whether there is any clinical benefit. If there are two successive therapeutic failures, then supportive care should be offered.

Borderline Epithelial Ovarian Cancer

Diagnosis

Borderline epithelial ovarian cancer--epithelial ovarian cancer of low malignant potential--identifies a tumor whose histological characteristics suggest malignancy but whose clinical behavior reflects an excellent prognosis (Fort et al, 1989), with a 5-year survival exceeding 80% (Barakat et al, 1995) despite a morphological appearance consistent with epithelial ovarian cancer. While the diagnostic pathologic characteristic of typical epithelial ovarian cancer consists of peritoneal implants microscopically and/or macroscopically invading the peritoneum, borderline epithelial ovarian cancer is manifested by the gross appearance of peritoneal carcinomatosis and a microscopic appearance that characteristically fails to reveal evidence of frank invasion by the tumor nodules.

The appearance of invasive implants portends a less favorable prognosis and postoperative chemotherapy can be considered for these patients if there is microscopic demonstration of invasive implants on the peritoneal surfaces (Gershenson and Silva, 1990). In contrast to patients with frankly invasive ovarian carcinoma, women with borderline disease tend to be younger and are often diagnosed with stage I disease (Leake et al, 1992; Barnhill et al, 1995). The benefit of postoperative chemotherapy has not been

demonstrated for patients who have no microscopically demonstrable invasive implants (Sutton et al, 1991; Trope et al, 1993).

Treatment

Treatment guidelines for this tumor depend on the histological and clinical characteristics, the age of the patient (Barnhill et al, 1995), and the stage of the disease at the time of diagnosis. At NCCN institutions, patients may be initially evaluated with an undiagnosed pelvic mass or with an established diagnosis of ovarian cancer of low malignant potential lesion following a laparotomy. If the patient desires to maintain her fertility, a unilateral oophorectomy may be performed at the time of comprehensive staging. If the patient does not desire fertility-sparing surgery, standard ovarian cancer debulking surgery is recommended, accompanied by comprehensive staging ([OV-A](#)).

Patients previously diagnosed with a low malignant potential lesion but who were incompletely staged, are suspected of having residual disease, or have no desire to maintain fertility should undergo a completion comprehensive staging. Conversely, patients who are suspected of having no residual disease (suspected stage I) or who desire to maintain fertility should be observed.

Follow-up

Treatment recommendations following comprehensive staging depend on the presence or absence of invasive implants. There was nonuniform consensus among the panel regarding the initial therapeutic approach. Patients having invasive implants may be observed or consideration can be given to treating patients according to the guidelines for epithelial ovarian cancer (category 2B). Patients with noninvasive implants should be observed and monitored (Leake et al, 1992; Kennedy and Hail, 1996) by a physician every 2 to 4 months for 2 years and every 6 months for 3 years. If the CA 125 level is initially elevated, it should be monitored at each visit; in addition, a complete blood count should be obtained once a year, and chemistry profiles should be monitored as clinically indicated.

Patients who had chosen fertility-sparing surgery should be considered for exploratory surgery and standard debulking following the completion of childbearing. All patients should be considered for a family history evaluation according to the NCCN Genetics/Cancer Screening Guidelines.

At the time of clinical relapse, a surgical evaluation and debulking should be considered. Patients who have invasive implants at this time may be considered for treatment according to the guidelines as recommended for epithelial ovarian cancer; those without invasive implants should be observed or enrolled in a clinical trial.

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& References marked with this symbol provided the basis for the algorithms.