NCCN Guidelines® Insights

Ovarian Cancer, Version 3.2012

Featured Updates to the NCCN Guidelines

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Abstract

These NCCN Guidelines Insights focus on the major updates for the 2012 NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Ovarian Cancer by describing how and why the new recommendations were made. The 6 update topics were selected based on recent important updates in the guidelines and on debate among panel members about recent clinical trials, and include: 1) screening, 2) diagnostic tests for assessing pelvic masses, 3) primary treatment using neoadjuvant chemotherapy, 4) primary adjuvant treatment using bevacizumab in combination with chemotherapy, 5) therapy for recurrent disease, and 6) management of drug/hypersensitivity reactions. These NCCN Guidelines Insights also discuss why some recommendations were not made (eg, panel members did not feel the new data warranted changing the guideline). See "Updates" in the NCCN Guidelines for Ovarian Cancer for a complete list of all the recent revisions. *(JNCCN* 2012;10:1339–1349)

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Disclosures for the NCCN Ovarian Cancer Panel

Individual disclosures of potential conflicts of interest for the NCCN Ovarian Cancer Panel can be found online at NCCN.org.

Please Note

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) are a statement of consensus of the authors regarding their views of currently accepted approaches to treatment. **The NCCN Guidelines® Insights highlight important changes in the NCCN Guidelines® recommendations from previous versions. Colored markings in the algorithm show changes and the discussion aims to further understanding of these changes by summarizing salient portions of the Panel's discussion, including the literature reviewed.**

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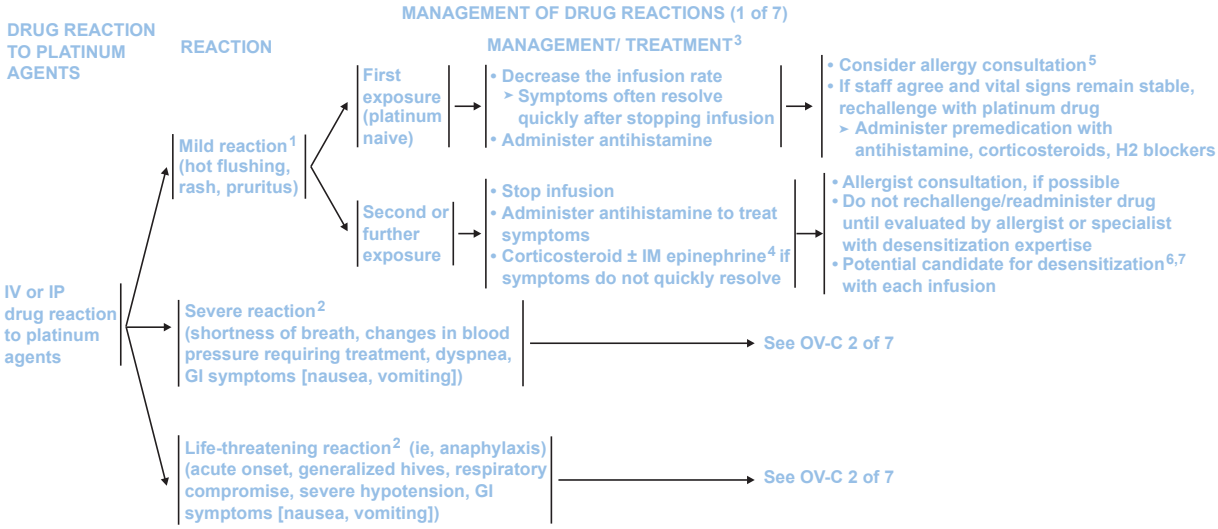
The full and most current version of these NCCN Guidelines is available at NCCN.org.



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[2]Most severe reactions are allergic reactions and more commonly are caused by platinum agents.
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[4]In the setting of acute cardiopulmonary arrest, standard resuscitation (ACLS) procedures should be followed.

See Drug Reaction to Taxane, Liposomal Doxorubicin, or Biotherapeutic Agents on OV-C 3 of 7

[5]Mild reactions can progress to severe reactions by re-exposure. An allergy consultation may provide skin testing and evaluate sensitization and the risk for further, more severe reactions
[6]Referral to academic center with expertise in desensitization is preferred.
[7]Castells MC, Tennant NM, Sloane DE, et al. Hypersensitivity reactions to chemotherapy: Outcomes and safety of rapid desensitization in 413 cases. J Allergy Clin Immunol 2008;122:574-580.

OV-C
1 of 7

NCCN Categories of Evidence and Consensus

Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

All recommendations are category 2A unless otherwise noted.

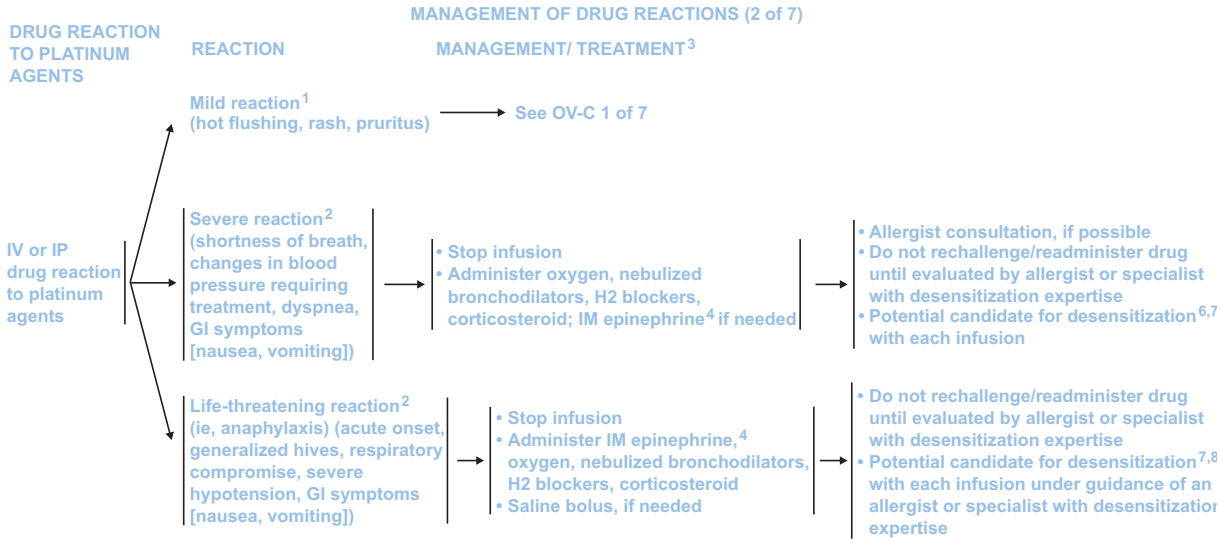
Clinical trials: NCCN believes that the best management for any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Overview

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Ovarian Cancer discuss management of epithelial ovarian cancer, which is the most common type of ovarian cancer. The guidelines also discuss borderline epithelial ovarian cancer (also known as low malignant potential), fallopian tube cancer, and primary peritoneal cancer; these neoplasms occur less frequently but are managed in a similar manner to epithelial ovarian cancer. Less common ovarian histopathologies are also described in the complete version of the NCCN Guidelines (available at NCCN.org), including malignant germ cell neoplasms, carcinosarcomas (malignant mixed Müllerian tumors of the ovary [MMMT], which are also known as poorly differentiated ovarian cancer), and sex cord-stromal tumors.

In 2012, it is estimated that 22,300 new diagnoses and 15,500 deaths from ovarian cancer will occur in the United States.[1] The complete version of the

Ovarian Cancer, Version 3.2012



NCCN Guidelines for Ovarian Cancer is available on the NCCN Web site (NCCN.org). Patient guidelines for ovarian cancer are also available (NCCN.com).

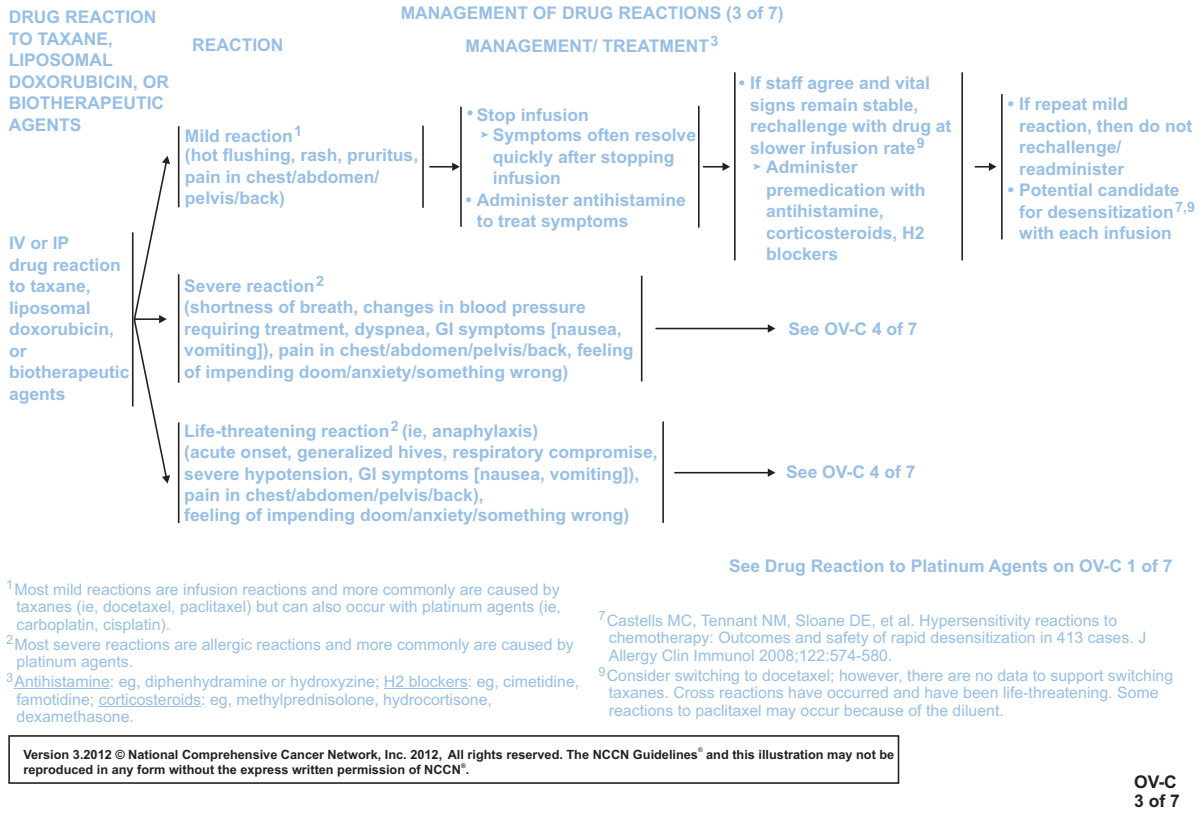
Screening Tests for Diagnosing Ovarian Cancer

Most ovarian cancer is diagnosed at an advanced stage, which accounts for the high mortality rate with this disease. More than 60% of women have advanced-stage disease (stage III–IV)[2] at diagnosis; therefore, a screening test to detect early-stage disease would be very useful. Currently, no effective and sensitive screening test for ovarian cancer is available, and none is recommended either by the NCCN Ovarian Cancer Panel or any major organization.[3–5]

Ongoing trials are assessing different approaches for ovarian cancer screening (eg, UK Collaborative Trial of Ovarian Cancer Screening [UKCTOCS]; Diagnosing Ovarian Cancer Early [DOvE]).[6,7] The Prostate, Lung, Colorectal and Ovarian [PLCO] Cancer trial is a large randomized trial involving more than 78,000 women in the United States that assessed screening with transvaginal ultrasonography and serum cancer antigen 125 (CA-125) levels. However, the PLCO trial found that this screening method did not decrease mortality from ovarian cancer.[3] In addition, false-positive results led to serious complications in some women (n=163). Although reports suggest that human epididymis protein 4 (HE4) and CA-125 may be useful in detecting ovarian cancer,[8,9] recent data show that several markers (including CA-125 and HE4) do not increase early enough to be useful in detecting early-stage ovarian cancer.[10,11]

Diagnostic Tests for Assessing Pelvic Masses

The FDA has approved the use of OVA1 as a triage diagnostic test for estimating the risk of ovarian



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[7] Castells MC, Tennant NM, Sloane DE, et al. Hypersensitivity reactions to chemotherapy: Outcomes and safety of rapid desensitization in 413 cases. J Allergy Clin Immunol 2008;122:574-580.
[9] Consider switching to docetaxel; however, there are no data to support switching taxanes. Cross reactions have occurred and have been life-threatening. Some reactions to paclitaxel may occur because of the diluent.

OV-C 3 of 7

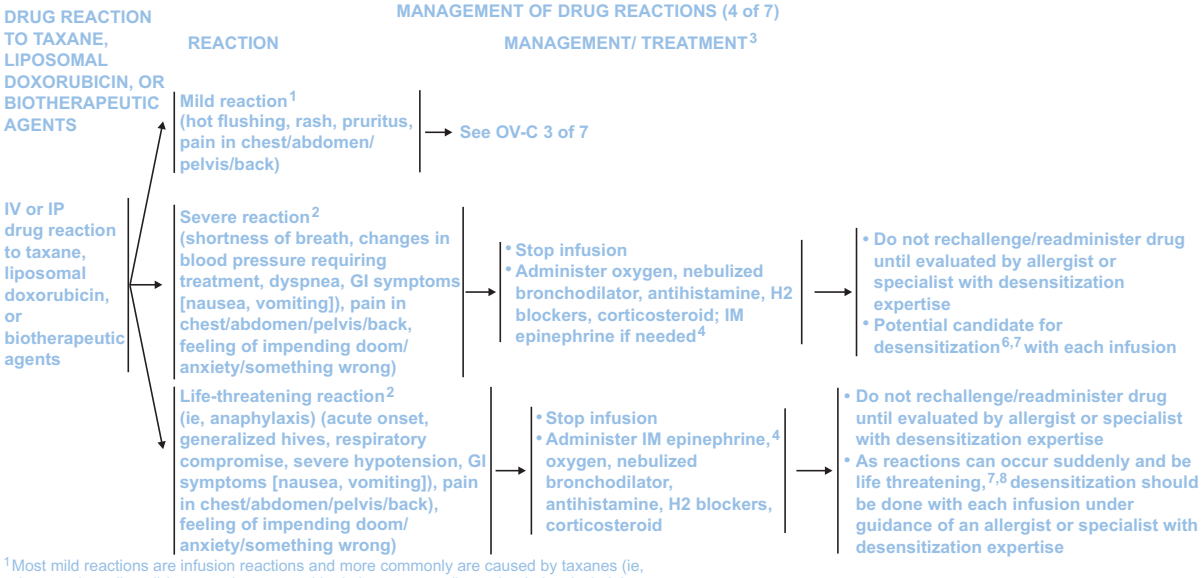
cancer in women with a pelvic mass. Note that the OVA1 test is not approved as a screening test for ovarian cancer. The OVA1 diagnostic test assesses several biomarkers (eg, CA-125), although the specific individual levels are not provided. Additional testing must be performed to obtain a CA-125 level.

Currently, the NCCN panel does not recommend the use of the OVA1 test for determining the status of an undiagnosed pelvic mass, because it increases cost without providing much benefit and because of concerns about false-positive results.[12–15] The panel recommends using the ACOG/SGO (American College of Obstetricians and Gynecologists/Society of Gynecologic Oncology) criteria to determine whether a pelvic mass is malignant (ie, suspicious) or benign, and thus whether a patient should be referred to a gynecologic oncologist.[16] The ACOG/SGO criteria recommend referral for postmenopausal women with 1) elevated CA-125, 2) nodular or fixed pelvic mass, 3) metastatic disease or ascites, or 4) family history of breast or ovarian cancer. Premenopausal women should be referred for 1) CA-125 level greater than 200 units/mL, 2) metastatic disease or ascites, or 3) strong family history of breast or ovarian cancer. However, some feel that a CA-125 level of greater than 50 units/mL (instead of a CA-125 level >200 units/mL) is a better discriminator of cancer versus benign masses for premenopausal women.[16]

Primary Treatment Using Neoadjuvant Chemotherapy

The NCCN Ovarian Cancer Panel recommends upfront primary debulking (ie, cytoreductive) surgery followed by adjuvant chemotherapy for most patients with resectable advanced ovarian cancer (including epithelial ovarian, fallopian tube, or primary perito-

Ovarian Cancer, Version 3.2012



[1] Most mild reactions are infusion reactions and more commonly are caused by taxanes (ie, docetaxel, paclitaxel) but can also occur with platinum agents (ie, carboplatin, cisplatin).
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[3] Antihistamine: eg, diphenhydramine or hydroxyzine; H2 blockers: eg, cimetidine, famotidine; corticosteroids: eg, methylprednisolone, hydrocortisone, dexamethasone.
[4] In the setting of acute cardiopulmonary arrest, standard resuscitation (ACLS) procedures should be followed.
[6] Referral to academic center with expertise in desensitization is preferred.

See Drug Reaction to Platinum Agents on OV-C 1 of 7

[7] Castells MC, Tennant NM, Sloane DE, et al. Hypersensitivity reactions to chemotherapy: Outcomes and safety of rapid desensitization in 413 cases. J Allergy Clin Immunol 2008;122:574-580.
[8] For both taxanes and platinum analogues, it is preferred that anyone with a life-threatening reaction should be evaluated and referred to an academic center if the drug is still considered first line.

OV-C
4 of 7

neal cancers).[17–19] Upfront cytoreductive surgery (to achieve a gross total resection) is considered the preferred treatment (ie, gold standard) in the United States.[20–22] After aggressive cytoreductive surgery, many patients with advanced ovarian cancer (even those with widespread intra-abdominal metastases, or high-grade serous carcinoma) have increased survival.[18] Thus, the management of advanced ovarian cancer differs from many other cancers in which surgery is only recommended for early-stage disease.

Neoadjuvant chemotherapy (NACT) can be considered (category 1) for patients with bulky stage III (ie, stage IIIC) or IV ovarian cancer who are not surgical candidates. The panel upgraded the option for considering NACT in this setting to a category 1 recommendation based on recent published data.[17,18,23–25] If clinically appropriate, NACT can also be considered for patients with stage II–III disease who are not surgical candidates and for select patients with MMMT (ie, poorly differentiated carcinoma) who are not surgical candidates. In select patients, NACT may be followed by interval cytoreduction (eg, NACT is given for 3 cycles followed by interval cytoreduction if possible, and then the remaining NACT regimen is given). For those having interval cytoreduction, approximately 50% of patients undergo complete resection.[23,24] NACT is defined as upfront chemotherapy given before surgery or as a stand-alone option if interval cytoreduction is not feasible.

Whether NACT followed by interval cytoreduction is appropriate as primary treatment for patients with potentially resectable disease (eg, those with stage IIIC or IV disease who are surgical candidates) is a matter of controversy.[24,26–30] A recent international trial assessed NACT with interval cytoreduction versus up-front primary cytoreduction in patients with extensive stage IIIC/IV ovar-

PRIMARY CHEMOTHERAPY/PRIMARY ADJUVANT THERAPY REGIMENS FOR STAGE II-IV[a,b]

1. **Paclitaxel 135 mg/m^2 IV continuous infusion over 24 h Day 1; cisplatin 75-100 mg/m^2 IP, Day 2 after IV paclitaxel; paclitaxel 60 mg/m^2 IP Day 8 (max BSA 2.0 m^2). Repeat every 3 weeks x 6 cycles. (category 1)**
2. **Paclitaxel 175 mg/m^2 IV over 3 hours followed by carboplatin AUC 5- 7.5 IV over 1 hour Day 1. Repeat every 3 weeks x 6 cycles. (category 1)**
3. **Docetaxel 60-75 mg/m^2 IV over 1 hour followed by carboplatin AUC 5 - 6 IV over 1 hour Day 1. Repeat every 3 weeks x 6 cycles. (category 1)**
4. **Dose-dense paclitaxel 80 mg/m^2 IV over 1 hour Days 1, 8, and 15 and carboplatin AUC 6 IV over 1 hour Day 1. Repeat every 3 weeks x 6 cycles. (category 1)**
5. **Bevacizumab-containing regimens per ICON-7 and GOG-218:**
   Paclitaxel 175 mg/m^2 IV over 3 hours, carboplatin AUC 6 IV over 1 hour, and bevacizumab 7.5 mg/kg IV over 30-90 minutes Day 1. Repeat every 3 weeks x 5-6 cycles. Continue bevacizumab for up to 12 additional cycles. (category 3)
   or
   Paclitaxel 175 mg/m^2 IV over 3 hours and carboplatin AUC 6 IV over 30 minutes Day 1. Repeat every 3 weeks x 6 cycles. Starting Day 1 of cycle 2, give bevacizumab 15 mg/kg IV over 30-90 minutes every 3 weeks for up to 22 cycles. (category 3)

See Management (OV-3)

[a] See Discussion for references (available at NCCN.org).
[b] The NCCN Ovarian Cancer panel recognizes that data for first-line and maintenance bevacizumab are becoming available and encourages participation in clinical trials.

ian, primary peritoneal, and fallopian tube carcinoma.[23] Median overall survival was equivalent in these patients (29 vs. 30 months), but patients receiving NACT with interval cytoreduction had fewer complications.[25] Based on the results of this trial, some oncologists feel that NACT is now appropriate for many patients with stage IIIC or IV ovarian cancer.[31] However, the panel only recommends NACT for select patients with stage IIIC or IV cancer who are not candidates for up-front aggressive cytoreduction (eg, those with medical comorbidities, advanced age, extra-abdominal disease, and no access to experienced gynecologic oncologist; those for whom optimal cytoreduction is not possible or for whom extensive debilitating surgery would be required to achieve up-front optimal debulking; those who refuse surgery).[17,25,32] Patients should be considered for palliative care (rather than definitive surgery and/or chemotherapy) if they have severely impaired renal function, expected survival less than 2 months, and/or performance status greater than 2.

Most patients in the United States undergoing primary cytoreduction followed by postoperative intravenous chemotherapy for advanced ovarian cancer have better progression-free and overall survivals (overall survival averages 50 months in US trials) than those reported in the international trial.[17,33] The median overall survival in the international trial is 20 months lower than that reported in US trials using accepted therapeutic interventions (ie, up-front primary cytoreduction followed by chemotherapy). However, this difference may have occurred because the international trial did not include patients with stage IIIB or earlier-stage cancer. In addition, primary or interval cytoreduction in the international trial may not have been optimal (ie, patients may

Ovarian Cancer, Version 3.2012

ACCEPTABLE RECURRENCE THERAPIES (1 of 2)†

Agents	Cytotoxic Therapy	Hormonal Therapy	Targeted Therapy	Radiation Therapy
Preferred Agents	**Combination if platinum sensitive‡ ¶** Carboplatin/paclitaxel (category 1)[1] Carboplatin/weekly paclitaxel[2] Carboplatin/docetaxel[3,4] Carboplatin/gemcitabine[5] Carboplatin/liposomal doxorubicin[6] Cisplatin/gemcitabine[7] **Single-agent if platinum sensitive** Carboplatin[5] Cisplatin[5] **Single-agent non-platinum based if platinum resistant** Docetaxel[8] Etoposide, oral[9] Gemcitabine[10,11] Liposomal doxorubicin[10,11] Paclitaxel, weekly[12] Topotecan[13,14]		Bevacizumab	
Other Potentially Active Agents	**Single Agents**[15] Altretamine Capecitabine Cyclophosphamide Ifosfamide Irinotecan Melphalan Oxaliplatin Paclitaxel Paclitaxel, albumin bound (nab-paclitaxel) Pemetrexed Vinorelbine	Anastrozole Letrozole Leuprolide acetate Megestrol acetate Tamoxifen		Palliative localized radiation therapy

†Patients who progress on two consecutive therapy regimens without evidence of clinical benefits have diminished likelihood of benefitting from additional therapy. (Griffiths RW, et al. Outcomes after multiple lines of chemotherapy for platinum-resistant epithelial cancers of the ovary, peritoneum, and fallopian tube. Int J Gyn Ca 2011;21:58-65.) Decisions to offer clinical trials, supportive care, or additional therapy should be made on a highly individual basis.

‡In general, the panel would recommend combination regimens based on randomized trial data especially in first relapses.

¶Platinum-based combination therapy should be considered for platinum-sensitive recurrences.

See References (OV-E 2 of 2)

OV-E 1 of 2

have had >1 cm of residual disease) or equivalent between the 2 arms.[17,26] The NCCN Guidelines recommend optimal cytoreduction (ie, to yield a gross total resection) for patients with ovarian cancer.[20–22]

The panel believes that more data are necessary before NACT can be recommended in patients with potentially resectable ovarian cancer.[20] Thus, up-front cytoreductive surgery remains the preferred treatment in the United States for most patients with resectable advanced ovarian cancer (including epithelial, fallopian tube, or primary peritoneal cancer). Note that the authors of the international trial believe that up-front primary cytoreduction should remain the standard of care for patients with stage IIIB or earlier-stage cancer, but that NACT with interval cytoreduction is an option for those with extensive stage IIIC or stage IV disease.[23]

Primary Adjuvant Treatment Using Bevacizumab in Combination With Chemotherapy

The panel members had a major disagreement about recommending the addition of bevacizumab to up-front therapy with carboplatin/paclitaxel or using bevacizumab as maintenance therapy; this disagreement is reflected as a category 3 recommendation. Most panel members believe that bevacizumab should not be added to up-front chemotherapy in patients with ovarian cancer, because recent data from 2 phase III randomized trials (ie, GOG-0218 and ICON7) have not shown a statistically significant increase in overall survival and/or improved quality of life.[34,35] The magnitude of the clinical benefit versus the potential for serious side effects (eg, <3% of patients had gastrointestinal perforation or fistula) and cost were also discussed by the panel, with varying opinions.[36,37]

The panel recommends (category 3) that if bevacizumab is used with up-front chemotherapy followed by maintenance therapy, then either the GOG-0218 or ICON7 regimen should be used (see OV-D, page 1344).[34,35] The only GOG-0218 regimen that is recommended (category 3) is bevacizumab up-front with carboplatin/paclitaxel followed by maintenance bevacizumab. Note that a category 3 recommendation indicates that more than 25% of the panel members believe that the intervention is not appropriate.

The ICON7 and GOG-0218 (phase III, randomized) trials assessed bevacizumab in combination with intravenous carboplatin/paclitaxel as up-front adjuvant therapy (after up-front cytoreductive surgery) compared with carboplatin/paclitaxel alone in patients with stage III–IV ovarian cancer.[34,35] In GOG-0218, the median progression-free survival was slightly increased (3.8 months) in patients receiving bevacizumab up-front and as maintenance therapy compared with chemotherapy alone.[34] Whether use of maintenance bevacizumab therapy alone in GOG-0218 would have yielded the same progression-free survival results is unclear. Although the progression-free survival data from ICON7 confirm the findings of GOG-0218, the benefits were also modest (1.7 month increase in progression-free survival). Quality of life was similar between the arms in both trials. Overall survival was also similar between the arms in GOG-0218. Mature data regarding overall survival have not been reported yet for ICON7.

ICON7 had some important differences compared with GOG-0218 (eg, the dose of bevacizumab in ICON7 was decreased by 50% to 7.5 mg/kg).[35] After an unplanned post hoc subset analysis in ICON7, an apparent overall survival advantage was reported in patients with stage III suboptimal and stage IV disease (30% of participants). However, this overall survival advantage was not seen in GOG-0218, in which 65% to 70% of patients had similar high-risk features; any potential benefit may have been obscured by the availability of bevacizumab after progression of disease in the United States. This topic is discussed in greater detail in the NCCN Guidelines (available at NCCN.org).

Therapy for Recurrent Disease

Chemotherapy

Most patients (≈75%) respond to initial treatment for ovarian cancer, although they often experience recurrence. Many patients have platinum-sensitive disease. For patients with platinum-sensitive disease, platinum-based combination regimens should be considered for recurrent disease.[38] Combination regimens are recommended based on randomized trial data, especially for first relapses (see OV-E, page 1345). *Platinum-sensitive* refers to disease that recurs more than 6 months after primary treatment, whereas *platinum-resistant* refers to disease that recurs after less than 6 months (or remains stable). *Refractory* usually refers to disease that has progressed while on platinum-based chemotherapy or does not respond to treatment. *Persistent* refers to disease that remains after initial chemotherapy treatment, which can be stable or smaller. *Stable* indicates that the tumor nodules have not grown or shrunk.

Platinum-resistant epithelial ovarian, fallopian tube, and primary peritoneal cancers are difficult to treat; prognosis is poor because most patients do not respond well to therapy.[39,40] The NCCN Guidelines recommend single agents for platinum-resistant disease; the preferred agents are docetaxel, oral etoposide, gemcitabine, liposomal doxorubicin, weekly paclitaxel, or topotecan (see OV-E, page 1345).[40] These preferred agents can also be used for persistent and refractory disease.[40] The choice of agent for recurrent or persistent platinum-resistant disease is often based on expert opinion (eg, decreased toxicity and/or marginally increased effectiveness).[39] Although liposomal doxorubicin is widely used, other agents may also be used.[39,41–44] Data are lacking to define the appropriate sequence of agents in this setting. All therapy in this setting is highly individualized and often based on the practice patterns of the physician and preferences of the patient.

Targeted Therapy

Currently, single-agent bevacizumab is recommended in the NCCN Guidelines as a preferred recurrence therapy for patients with epithelial ovarian, fallopian tube cancer, or primary peritoneal cancer.[45,46] For example, bevacizumab is a reasonable option for patients with recurrent disease that is platinum-resistant.[47] Bevacizumab is active (21%) in both platinum-sensitive and -resistant patients.[45] Several trials are assessing combination therapy with bevacizumab for recurrent ovarian cancer (ie, OCEANS, AURELIA).[48,49] Other therapies are in clinical trials.[46,50,51]

Ovarian Cancer, Version 3.2012

Management of Drug/ Hypersensitivity Reactions

Virtually all drugs have the potential to cause drug/hypersensitivity reactions, either during or after the infusion.[52–54] Drugs used in gynecologic oncology treatment that more commonly cause adverse reactions include carboplatin, cisplatin, docetaxel, liposomal doxorubicin, oxaliplatin, and paclitaxel. Drug reactions can occur with either intravenous or intraperitoneal administration of these drugs.[55] Most of these drug reactions are mild infusion reactions (ie, skin reactions, cardiovascular reactions, respiratory or throat tightness), but more severe allergic reactions (ie, life-threatening anaphylaxis) can sometimes occur.[56,57] Infusion reactions are more common with paclitaxel,[58] but mild reactions can also occur with liposomal doxorubicin.[59] Allergic/hypersensitivity reactions (ie, true drug allergies) are more common with platinum agents (ie, carboplatin, cisplatin, oxaliplatin).[58,60] Although severe reactions to biotherapeutic agents (eg, bevacizumab) are rare, they can also occur.[58]

Management of drug reactions is discussed in the NCCN Guidelines. New algorithms are now provided for management of mild, severe, and life-threatening reactions after intravenous or intraperitoneal infusion (see OV-C, pages 1340–1343).[61] Previously, only an appendix (but no algorithm) appeared for this topic. Typically, the infusion should be stopped in patients experiencing a drug reaction; further management is provided in the new algorithms. In many patients who have experienced drug reactions, desensitization may be used to enable further use of chemotherapy. These drug reaction algorithms are also useful for patients with other cancers (eg, cervical and uterine cancers).

Summary of the Major Updates

Six update topics are discussed in these NCCN Guidelines Insights: 1) screening, 2) diagnostic tests for assessing pelvic masses, 3) primary treatment using NACT, 4) primary adjuvant treatment using bevacizumab in combination with chemotherapy, 5) therapy for recurrent disease, and 6) management of drug/hypersensitivity reactions.

Screening for ovarian cancer is not recommended either by the NCCN Ovarian Cancer Panel or by any major organization.[3–5]

The panel does not recommend use of the OVA1 test for determining the status of an undiagnosed pelvic mass.[12–15] The panel feels that guidelines from ACOG/SGO should be used to assess whether a pelvic mass is malignant or benign, and thus whether a patient should be referred to a gynecologic oncologist.

NACT can be considered (category 1) for patients with bulky stage III (ie, stage IIIC) or IV ovarian cancer who are not surgical candidates. The panel upgraded the option for considering NACT in this setting to a category 1 recommendation.[17,18,23–25,62] Previously, NACT was a category 2A recommendation in the guidelines. However, the panel recommends up-front primary debulking (ie, cytoreductive) surgery followed by adjuvant chemotherapy for most patients with resectable advanced ovarian cancer (including epithelial ovarian, fallopian tube, or primary peritoneal cancers).[17–19]

The panel had a major disagreement about recommending the addition of bevacizumab to up-front therapy with carboplatin/paclitaxel or using bevacizumab as maintenance therapy; this disagreement is reflected as a category 3 recommendation. Most panel members believe that bevacizumab should not be added to up-front chemotherapy in patients with ovarian cancer, because data from GOG-0218 and ICON7 have not shown an increase in overall survival and/or improved quality of life.[34,35] However, the panel recommends (category 3) that if bevacizumab is used with up-front chemotherapy, then either the GOG-0218 or ICON7 regimens should be used (see OV-D, page 1344).[34,35]

Most patients (≈75%) respond to initial treatment for ovarian cancer, although they often experience a recurrence. For patients with platinum-sensitive disease, platinum-based combination regimens are preferred for persistent, recurrent, or refractory disease.[38] The NCCN Guidelines recommend single agents for platinum-resistant disease; the preferred chemotherapeutic agents are docetaxel, oral etoposide, gemcitabine, liposomal doxorubicin, weekly paclitaxel, or topotecan.[40] These preferred agents can also be used for persistent and refractory disease.[40] Currently, bevacizumab is recommended in the NCCN Guidelines as a preferred single-agent targeted therapy for patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancers.[45,46] For example, bevacizumab is a reasonable

option as second- or third-line therapy in patients with persistent or recurrent disease that is platinum-resistant.[47]

Management of drug reactions is discussed in the NCCN Guidelines. New algorithms are now provided for management of mild, severe, or life-threatening drug reactions after intravenous or intraperitoneal infusion (see OV-C, pages 1340–1343).[61] Drugs used in gynecologic oncology treatment that more commonly cause adverse reactions include carboplatin, cisplatin, docetaxel, liposomal doxorubicin, oxaliplatin, and paclitaxel. In many patients who have had drug reactions, desensitization may be used to enable further use of chemotherapy. These drug reaction guidelines are also useful for patients with other cancers (eg, cervical and uterine cancers).

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