OVARIAN CANCER TREATMENT REGIMENS (Part 1 of 3)

Clinical Trials: The NCCN recommends cancer patient participation in clinical trials as the gold standard for treatment. Cancer therapy selection, dosing, administration, and the management of related adverse events can be a complex process that should be handled by an experienced healthcare team. Clinicians must choose and verify treatment options based on the individual patient; drug dose modifications and supportive care interventions should be administered accordingly. The cancer treatment regimens below may include both U.S. Food and Drug Administration-approved and unapproved indications/regimens. These regimens are only provided to supplement the latest treatment strategies. These Guidelines are a work in progress that may be refined as often as new significant data becomes available. The NCCN Guidelines® are a consensus statement of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN 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 warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

Primary Chemotherapy/Primary Adjuvant Therapy *,†,‡

Stage 1A or 1B (grade 2, 3, or clear cell) & Stage 1C (grade 1-3)

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<tr>
<th>REGIMEN</th>
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<tbody>
<tr>
<td>Paclitaxel + carboplatin</td>
<td>Day 1: Paclitaxel 175mg/m² IV over 3 hours; followed by carboplatin (AUC 5–7.5) IV over 1 hour. Repeat every 3 weeks for 3–6 cycles.</td>
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Stage 2-4 (IV/IP regimen) 5, 6

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<tr>
<td>Paclitaxel + cisplatin</td>
<td>Day 1: Paclitaxel 135mg/m² continuous IV infusion over 3 or 24 hours. Day 2: Cisplatin 75–100mg/m² IP; followed by Day 8: Paclitaxel 60mg/m² IP (maximum BSA 2m²). Repeat every 3 weeks for 6 cycles.</td>
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Stage 2-4 (IV regimens) *

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<td>Paclitaxel + carboplatin</td>
<td>Day 1: Paclitaxel 175mg/m² IV over 3 hours; followed by carboplatin (AUC 5–7.5) IV over 1 hour. Repeat every 3 weeks for 6–8 cycles.</td>
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Dose-dense paclitaxel + carboplatin

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<td>Day 1: Paclitaxel 80mg/m² IV over 1 hour; plus carboplatin (AUC 6) IV over 1 hour. Day 8 and 15: Paclitaxel 80mg/m² IV over 1 hour. Repeat every 3 weeks for 6 cycles.</td>
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Docetaxel + carboplatin

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<tr>
<td>Day 1: Docetaxel 60–75mg/m² IV over 1 hour; followed by carboplatin (AUC 5–6) IV over 1 hour. Repeat every 3 weeks for 6 cycles.</td>
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Stage 2-4 (bevacizumab-containing IV regimens)**

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<tr>
<td>Paclitaxel + carboplatin + bevacizumab</td>
<td>Day 1: Paclitaxel 175 mg/m² IV over 3 hours; plus carboplatin (AUC 5–6) IV over 1 hour; plus bevacizumab 7.5 mg/kg IV over 30–90 minutes. Repeat every 3 weeks for 5–6 cycles. Continue bevacizumab for up to 12 additional cycles. OR Day 1: Paclitaxel 175 mg/m² IV over 3 hours; plus carboplatin (AUC 6) IV over 1 hour. Repeat every 3 weeks × 6 cycles. Starting Day 1 of cycle 2: Bevacizumab 15 mg/kg IV over 30–90 minutes every 3 weeks for up to 22 cycles.</td>
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Principals of Chemotherapy *¹

For patients with newly diagnosed ovarian, fallopian tube, or primary peritoneal cancer

- If they are eligible for chemotherapy, patients should be informed about the different options that are available—that is, IV chemotherapy, a combination of IP and IV chemotherapy, or a clinical trial—so they can decide which is the most the appropriate option.
- Prior to the administration of the combined IP and IV regimen, patients must be apprised of the increased toxicities with the combined regimen when compared to using IV chemotherapy alone (increased myelosuppression, renal toxicities, abdominal pain, neuropathy, GI toxicities, metabolic toxicities, and hepatic toxicities).
- Patients considered for the IP cisplatin and IP/IV paclitaxel regimen should have normal renal function prior to starting, a medically appropriate performance status based on the future toxicities of the IP/IV regimen, and no prior evidence of medical problems that could significantly worsen during chemotherapy (e.g., pre-existing neuropathy).
- Prior to receiving and after receiving each cycle of IP cisplatin, adequate amounts of IV fluids need to be administered in order to prevent renal toxicity. After each cycle has been completed, patients need to be monitored carefully for myelosuppression, dehydration, electrolyte loss, end-organ toxicities (such as renal and hepatic damage), and all other toxicities. Patients often require postchemotherapy IV fluids in the out-patient setting to prevent or help treat dehydration.
- Refer to the original references in the discussion section of the guideline for full toxicity data, doses, schedule, and dose modifications.
Principals of Chemotherapy\(^*\) (continued)

For patients who have recurrent ovarian, fallopian tube, or primary peritoneal cancer

- Patients should be informed about the following:
  - Availability of clinical trials, including the risks and benefits of various treatments, which will depend on the number of prior lines of chemotherapy the patient has received, and
  - The patient's performance status, end-organ status, and pre-existing toxicities from prior regimens. If appropriate, palliative care should also be discussed as a possible treatment choice. (See NCCN Guidelines for Palliative Care).
- Because of prior platinum exposure, myelosuppression occurs more frequently with any myelotoxic agent given in the recurrent setting.
- With repeat use of either carboplatin and/or cisplatin, patients are at an increased risk of developing a hypersensitivity reaction (also called an allergic reaction) that could be life-threatening. Thus, patients should be counseled about the risk that a hypersensitivity reaction may occur, educated about the signs and symptoms of hypersensitivity reactions, treated by medical staff who know how to manage hypersensitivity reactions, and treated in a medical setting where appropriate medical equipment is available in case of an allergic reaction. (See NCCN Guidelines for Management of Drug Reactions [OV-C]).
- Before any chemotherapy drug is given in the recurrent setting, the clinician should be familiar with the drug's metabolism (i.e., renal and hepatic) and should make certain that the patient is an appropriate candidate for the drug (e.g., that the patient has adequate renal or hepatic function).
- Clinicians should be familiar with toxicity management and appropriate dose reduction.
- The schedule, toxicity, and potential benefits of any treatment should be thoroughly discussed with the patient and caregivers. Patient education should also include a discussion of precautions and measures to reduce the severity and duration of complications.
- Patients who progress on 2 consecutive therapy regimens without evidence of clinical benefits have diminished likelihood of benefitting from additional therapy. Decisions to offer clinical trials, supportive care only, or additional therapy should be made on a highly individual basis.

For elderly patients (>65 years) and/or those with comorbidities

- Elderly patients and those with comorbidities may be intolerant to the combination chemotherapy regimens recommended in the NCCN Guidelines. Single-agent platinum agents may be appropriate in selected patients. Algorithms have been developed for predicting chemotherapy toxicity. (See the NCCN Guidelines for Senior Adult Oncology).

NOTE: Carboplatin dosing may be revised based on changes in serum creatinine methodology. See the FDA dosing statement at: http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm228974.htm.

* Patients receiving primary chemotherapy should be monitored as follows: 1) pelvic exams at least every 2-3 cycles, 2) interim CBC with platelets as indicated, 3) chemistry profiles if indicated. 4) CA-125 levels or other tumor markers as clinically indicated prior to each cycle of chemotherapy, 5) radiographic imaging if indicated.
† All primary chemotherapy/primary adjuvant therapy regimens (including the combined IV/IP chemotherapy) may be used for epithelial ovarian, fallopian tube, and primary peritoneal cancers.
‡ Stage 1A or 1B (grade 2) can be observed or treated with chemotherapy.
§ Intraperitoneal (IP) chemotherapy in <1 cm optimally debulked stage 2 and stage 3 patients (category 1 for stage III).
¶ All women undergoing surgery for ovarian cancer should be counseled about the clinical benefit associated with combined IV and IP chemotherapy administration prior to surgery.
¶ A 3-hour infusion of paclitaxel has not been proven to be equivalent to a 24-hour infusion, although it has been reported to be more convenient, easier to tolerate, and less toxic.\(^{16}\)
# IV regimens may be considered for neoadjuvant therapy.
** Bevacizumab-containing IV regimens based on the ICON-7 and GOG-218 trials. For additional information regarding the controversy over this regimen, please see the NCCN Ovarian Cancer Guidelines for Anti-Angiogenesis Agents (v 2.2014, page 51).\(^1\)

References


