CERVICAL CANCER TREATMENT REGIMENS (Part 1 of 3)

Clinical Trials: The National Comprehensive Cancer Network 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 NCCN 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.

Advanced Cervical Cancer[1,a]

NOTE: All recommendations are category 2A unless otherwise indicated.

First-line Therapy[b]

REGIMEN	DOSING
Cisplatin[2,3]	Cisplatin 40mg/m² IV once weekly for up to 6 doses (total dose not to exceed 70mg per week).
Cisplatin + 5-FU[4,5]	**Days 1–5 of radiotherapy:** Cisplatin 75mg/m² IV over 4 hours, followed by 5-FU 4,000mg/m² IV over 96 hours (begin chemotherapy within 16 hours after radiotherapy). Repeat cycle every 3 weeks for 2 additional cycles. **OR** **Days 1 and 29:** Cisplatin 50mg/m² IV infusion (4 hours prior to external-beam radiotherapy) at 1mg/minute with standard hydration, **plus** **Days 2–5, and 30–33:** 5-FU 1,000mg/m² IV continuous infusion over 24 hours (total dose 4,000mg/m² each course).

Metastatic or Recurrent Cervical Cancer[1,c]

First-line Combination Therapy[d]

Cisplatin + paclitaxel + bevacizumab (Category 1)[6]	**Day 1:** Cisplatin 50mg/m² IV + paclitaxel 135–175mg/m² IV + bevacizumab 15mg/kg IV. Repeat cycle every 21 days until disease progression, unacceptable toxicity, or complete response.
Paclitaxel + cisplatin (Category 1)[7,8]	**Day 1:** Paclitaxel 135mg/m² IV over 24 hours **Day 2:** Cisplatin 50mg/m² IV at a rate of 1mg/minute. Repeat cycle every 3 weeks for 6 cycles.
Topotecan + paclitaxel + bevacizumab (Category 1)[6]	**Day 1:** Bevacizumuab 15mg/kg IV + Paclitaxel 175 mg/m² over 3 hours **Days 1–3:** Topotecan 0.75mg/m² IV over 30 minutes. Repeat cycle every 21 days until disease progression or unacceptable toxicity.
Paclitaxel + carboplatin (Category 1 for patients with prior cisplatin therapy)[9,10]	**Day 1:** Paclitaxel 175mg/m² IV over 3 hours, followed by 1-hour carboplatin IV at AUC 5mg•mL/min. Repeat cycle every 3 weeks for a maximum of 6 cycles or until disease progression or unacceptable toxicity.
Carboplatin + paclitaxel + bevacizumab[6,10]	**Day 1:** Paclitaxel 175mg/m² IV over 3 hours, followed by 1-hour carboplatin IV at AUC 5mg•mL/min + bevacizumab 15mg/kg IV. Repeat cycle every 3 weeks for a maximum of 6 cycles or until disease progression or unacceptable toxicity.
Cisplatin + topotecan[11]	**Days 1–3:** Topotecan 0.75mg/m² IV over 30 minutes, **followed by** **Day 1:** Cisplatin 50mg/m² IV. Repeat cycle every 3 weeks.
Topotecan + paclitaxel[6e]	**Days 1–3:** Topotecan 0.75mg/m² IV over 30 minutes, **followed by** **Day 1:** Paclitaxel 175 mg/m² IV.
Cisplatin + gemcitabine (Category 3)[12]	**Days 1 and 8:** Cisplatin 30mg/m² IV followed by gemcitabine 800mg/m² IV. Repeat cycle every 4 weeks.

Possible First-Line Single-Agent Therapy

Cisplatin (preferred as a single agent)[8]	**Day 1:** Cisplatin 50mg/m² IV. Repeat every 3 weeks for 6 cycles.
Carboplatin[13]	**Day 1:** Carboplatin 400mg/m² IV. Repeat every 4 weeks.
Paclitaxel[14]	**Day 1:** Paclitaxel 250mg/m² IV over 3 hours. Repeat every 3 weeks.

continued

CERVICAL CANCER TREATMENT REGIMENS (Part 2 of 3)

Metastatic or Recurrent Cervical Cancer[1c] (continued)

Second-Line Therapy

Note: Agents listed below are category 2B unless otherwise indicated.

REGIMEN	DOSING
Bevacizumab[15]	**Day 1:** Bevacizumab 15mg/kg IV. Repeat cycle every 3 weeks until disease progression or unacceptable toxicity.
Albumin-bound paclitaxel (nab-paclitaxel)[16]	**Days 1, 8, and 15:** Nab-paclitaxel 125mg/m^2 IV over 30 minutes. Repeat cycle every 4 weeks until disease progression or unacceptable toxicity.
Docetaxel[17]	**Day 1:** Docetaxel 100mg/m^2 IV over 1 hour. Repeat cycle every 3 weeks until disease progression or unacceptable toxicity.
5-FU[18]	**Days 1–5:** Leucovorin 200mg/m^2 IV bolus + 5-FU 370mg/m^2 IV bolus every 4 weeks for the first 2 courses with subsequent courses given every 5 weeks.
Gemcitabine[19]	**Days 1, 8, and 15:** Gemcitabine 800mg/m^2 IV over 30 minutes, with a 1-week rest until disease progression or unacceptable toxicity.
Ifosfamide[20,21]	**Days 1–5:** Ifosfamide 1.5g/m^2 IV over 30 minutes; dose reduced to 1.2g/m^2 in patients with prior radiotherapy. Repeat cycle every 3 weeks.
Irinotecan[22]	Irinotecan 125mg/m^2 IV over 90 minutes weekly for 4 weeks. Repeat cycle every 6 weeks.
Mitomycin[23]	**Day 1:** Mitomycin 6mg/m^2 IV. Repeat cycle every 4 weeks.
Pemetrexed[24]	**Day 1:** Pemetrexed 900mg/m^2 IV over 10 minutes. Repeat cycle every 21 days.
Topotecan[25,26]	**Days 1–5:** Topotecan 1.5mg/m^2 IV. Repeat cycle every 3 to 4 weeks.
Vinorelbine[27]	**Days 1 and 8:** Vinorelbine 30mg/m^2; dose omitted on day 8 for grade 3 or 4 neutropenia **OR** reduced to 20 mg/m^2 for grade 2 neutropenia. Repeat cycle every 3 weeks.

[a] Includes patients with stage 2B to 4A disease, but can be extended to include patients with 1B2 and 2A2 disease in the advanced disease category.

[b] Given concurrently with pelvic radiotherapy and brachytherapy; category 1 for patients without nodal disease or with disease limited to the pelvis as determined through surgical staging. In patients with positive para-aortic and pelvic lymph nodes on imaging studies, extraperitoneal lymph node dissection should be considered, followed by extended-field radiotherapy, concurrent cisplatin-containing chemotherapy, and brachytherapy.

[c] Cisplatin, carboplatin, docetaxel, and paclitaxel may cause drug reactions, which can be managed following recommendations in NCCN Guidelines for Ovarian Cancer—Management of Drug Reaction [OV-C].

[d] Cost and toxicity should be carefully considered when selecting an appropriate regimen for treatment.

[e] Although topotecan + paclitaxel was not shown to be superior to cisplatin + paclitaxel, it may be considered an alternative in patients who are not candidates for cisplatin.

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