

CERVICAL CANCER CHEMOTHERAPY REGIMENS

The selection, dosing, and administration of anti-cancer agents and the management of associated toxicities are complex. Drug dose modifications and schedule and initiation of supportive care interventions are often necessary because of expected toxicities and because of individual patient variability, prior treatment, and comorbidities. Thus, the optimal delivery of anti-cancer agents requires a healthcare delivery team experienced in the use of such agents and the management of associated toxicities in patients with cancer. The chemotherapy regimens below may include both FDA-approved and unapproved uses/regimens and are provided as references only to the latest treatment strategies. Clinicians must choose and verify treatment options based on the individual patient.

NCCN CATEGORIES OF EVIDENCE AND CONSENSUS¹

- **Category 1:** The recommendation is based on high-level evidence (ie, high-powered randomized clinical trials or meta-analyses), and the panel has reached uniform consensus that the recommendation is indicated.
- **Category 2A:** The recommendation is based on lower level evidence, but despite the absence of higher level studies, there is uniform consensus that the recommendation is appropriate. Lower level evidence is interpreted broadly, and runs the gamut from Phase 2 to large cohort studies to case series to individual practitioner experience.
- **Category 2B:** The recommendation is based on lower level evidence, and there is non-uniform consensus that the recommendation should be made. In these instances, because the evidence is not conclusive, institutions take different approaches to the management of a particular clinical scenario.
- **Category 3:** The recommendation has engendered a major disagreement among the panel members. Several circumstances can cause major disagreements. For example, if substantial data about two interventions exist but they have never been directly compared in a randomized trial, adherents to one set of data may not accept the interpretation of the other side's results. A Category 3 designation alerts users to a major interpretation issue in the data and directs them to the manuscript for an explanation of the controversy.

REGIMEN	DOSING
---------	--------

FIRST-LINE COMBINATION THERAPY

Paclitaxel (Taxol) + cisplatin (Platinol; CDDP) (Category 2A)	Day 1: Paclitaxel 135mg/m ² IV, administered over 24 hrs plus Day 2: Cisplatin 50mg/m ² IV at a rate of 1mg/min; repeat cycle every 21 days for 6 cycles ^{2,3}
Carboplatin (Paraplatin) + paclitaxel (Category 2A)	Day 1: Carboplatin AUC= 5mg/mL/min, administered over 1 hr, followed by paclitaxel 175mg/m ² , administered over 3 hrs; repeat cycle every 21 days for 6–9 cycles or until disease progression or unacceptable toxicity ⁴
Cisplatin + topotecan (Hycamtin) (Category 2A)	Days 1–3: Topotecan 0.75mg/m ² IV, administered over 30 min plus Day 1: Cisplatin 50mg/m ² IV; repeat cycle every 21 days ⁵
Cisplatin + gemcitabine (Gemzar) (Category 2B)	Days 1 and 8: Cisplatin 30mg/m ² + gemcitabine 800mg/m ² ; repeat cycle every 28 days ⁶

FIRST-LINE MONOTHERAPY

Cisplatin (preferred as a single agent) (Category 2A)	Day 1: Cisplatin 50mg/m ² ; repeat cycle every 21 days for a total of 6 cycles ² Most patients who develop metastatic cervical cancer have received concurrent cisplatin/radiotherapy as primary treatment and may no longer be sensitive to single-agent platinum therapy ³
---	---

SECOND-LINE THERAPY

Bevacizumab (Avastin) (Category 2B)	Day 1: Bevacizumab 15mg/kg IV; repeat cycle every 21 days ⁷
Docetaxel (Taxotere) (Category 2B)	Day 1: Docetaxel 100mg/m ² IV, administered over 1 hr; repeat cycle every 21 days ⁸
Gemcitabine (Gemzar) (Category 2B)	Days 1, 8, and 15: Gemcitabine 800mg/m ² IV, administered over 30 min; repeat cycle every 28 days ⁹
Pemetrexed (Alimta) (Category 3)	Day 1: Pemetrexed 900mg/m ² IV, administered over 10 min; repeat cycle every 21 days ^{1,10}
Vinorelbine (Navelbine) (Category 3)	Days 1 and 8: Vinorelbine 30mg/m ² IV; repeat cycle every 21 days ^{1,11}

REFERENCES

<p>1. NCCN Clinical Practice Guidelines in Oncology™. Cervical Cancer. v 1.2011. Available at: http://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf. Accessed April 12, 2011.</p> <p>2. Monk BJ, Sill MW, McMeekin DS, et al. Phase III trial of four cisplatin-containing doublet combinations in stage IVB, recurrent, or persistent cervical carcinoma: a Gynecologic Oncology Group study. <i>J Clin Oncol</i>. 2009;27(28):4649–4655.</p> <p>3. Moore DH, Blessing JA, McQuellon RP, et al. Phase III study of cisplatin with or without paclitaxel in stage IVB, recurrent, or persistent squamous cell carcinoma of the cervix: a gynecologic oncology group study. <i>J Clin Oncol</i>. 2004 ;22(15):3113–3119.</p> <p>4. Pectasides D, Fountzilas G, Papaxoinis G, et al. Carboplatin and paclitaxel in metastatic or recurrent cervical cancer. <i>Int J Gynecol Cancer</i>. 2009;19:777–781.</p> <p>5. Long HJ 3rd, Bundy BN, Grendys EC Jr, et al. Gynecologic Oncology Group Study. Randomized phase III trial of cisplatin with or without topotecan in carcinoma of the uterine cervix: a Gynecologic Oncology Group Study. <i>J Clin Oncol</i>. 2005;23:4626–4633.</p> <p>6. Brewer CA, Blessing JA, Nagourney RA, McMeekin DS, Lele S, Zweigig SL. Cisplatin plus gemcitabine in previously treated squamous cell carcinoma of the cervix: a phase II study of the Gynecologic Oncology Group. <i>Gynecol Oncol</i>. 2006;100:385–388.</p>	<p>7. Monk BJ, Sill MW, Burger RA, Gray HJ, Buekers TE, Roman LD. Phase II trial of bevacizumab in the treatment of persistent or recurrent squamous cell carcinoma of the cervix: a gynecologic oncology group study. <i>J Clin Oncol</i>. 2009;27:1069–1074.</p> <p>8. Garcia AA, Blessing JA, Vaccarello L, Roman LD; Gynecologic Oncology Group Study. Phase II clinical trial of docetaxel in refractory squamous cell carcinoma of the cervix: a Gynecologic Oncology Group Study. <i>Am J Clin Oncol</i>. 2007;30:428–431.</p> <p>9. Schilder RJ, Blessing J, Cohn DE. Evaluation of gemcitabine in previously treated patients with non-squamous cell carcinoma of the cervix: a phase II study of the Gynecologic Oncology Group. <i>Gynecol Oncol</i>. 2005;96:103–107.</p> <p>10. Miller DS, Blessing JA, Bodurka DC, Bonebrake AJ, Schorge JO; Gynecologic Oncology Group. Evaluation of pemetrexed (Alimta, LY231514) as second line chemotherapy in persistent or recurrent carcinoma of the cervix: a phase II study of the Gynecologic Oncology Group. <i>Gynecol Oncol</i>. 2008;110:65–70.</p> <p>11. Muggia FM, Blessing JA, Waggoner S, Berek JS, Monk BJ, Sorosky J, Pearl ML. Evaluation of vinorelbine in persistent or recurrent nonsquamous carcinoma of the cervix: a Gynecologic Oncology Group Study. <i>Gynecol Oncol</i>. 2005;96:108–111.</p>
--	--