CERVICAL CANCER TREATMENT REGIMENS (Part 1 of 2)

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.

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NOTE: All recommen	idations are category	24 unless	otherwise indicated.

First-line	Therapy with	th Radiotherap	y
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REGIMEN	DUSING	
Cisplatin ^{2,3}	40mg/m² IV once weekly for up to 6 doses (total dose not to exceed 70mg per week).	
Cisplatin + 5-FU ⁴	Days 1 and 29: Cisplatin 50mg/m² IV infusion (4 hours prior to external-beam radiotherapy) at 1mg/minute with standard hydration, <u>plus</u> Days 2-5, and 30-33: 5-FU 1,000mg/m² IV continuous infusion over 24 hours (total dose 4,000mg/m² each course).	

Cisplatin + 5-FU ⁵	Days 1-5 of radiotherapy: Cisplatin 75mg/m ² 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.

Cisplatin + 5-FU + hydroxyurea ³	Days 1 and 29: Cisplatin 50mg/m ² IV, followed by 4,000mg/m ² 5-FU over
	96 hours, plus
	Hydroxyurea 2,000mg PO twice weekly for 6 weeks.

Cisplatin + gemcitabine + radiotherapy + brachytherapy⁶

Induction therapy

·Cisplatin 40mg/m² IV over 1 hour, followed by gemcitabine 125mg/m² IV over 30-60 minutes.

Repeat cycle every week for 6 weeks (both drugs to be given 1-2 hours before external-beam radiotherapy 50.4Gy in 28 fractions).

• The above completed chemotherapy schedule should be **immediately followed by** brachytherapy 30-35Gy in 96 hours.

Adjuvant therapy (following a 2-week rest)

• Day 1: Cisplatin 50mg/m², plus

• Davs 1 and 8: Gemcitabine 1.000mg/m².

Repeat every 3 weeks for 2 cycles.

Metastatic or Recurrent Cervical Cancer¹

First-line Therapy with Radiotherapy

Paclitaxel + cisplatin ^{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.
Carboplatin + paclitaxel ^{9*}	Day 1: Paclitaxel 175mg/m² IV over 3 hours, followed by carboplatin (AUC=5) in 500mL 5% dextrose/water over 1 hour. Repeat cycle every 3 weeks for 6-9 cycles or until disease progression or unacceptable toxicity.
Cisplatin + topotecan ¹⁰	Days 1-3: Topotecan 0.75mg/m² IV over 30 minute, <u>followed by</u> Day 1: Cisplatin 50mg/m² IV. Repeat cycle every 3 weeks.
Cisplatin + gemcitabine ¹¹	Days 1 and 8: Cisplatin 30mg/m² <u>followed by</u> gemcitabine 800mg/m². Repeat cycle every 4 weeks.

First-line Monotherapy

Cisplatin (preferred as a single	Day 1: Cisplatin 50mg/m2 at a rate of 1mg/minute.
agent) ^{7,8†}	Repeat cycle every 3 weeks for a total of 6 cycles.

continued

CERVICAL CANCER TREATMENT REGIMENS (Part 2 of 2)

Metastatic or Recurrent Cervical Cancer¹ (continued)

Second-line Therapy		
REGIMEN	DOSING	
Bevacizumab ¹²	Day 1: Bevacizumab 15mg/kg IV. Repeat cycle every 3 weeks.	
Docetaxel ¹³	Day 1: Docetaxel 100mg/m² IV over 1 hour. Repeat cycle every 3 weeks.	
Gemcitabine ¹⁴	Days 1, 8 and 15: Gemcitabine 800mg/m² IV over 30 minutes, with a 1-week rest until progression or adverse events prohibit further therapy.	

- * For patients receiving paclitaxel, consider pretreating with dexamethasone, diphenhydramine, and an H2 receptor antagonist (e.g., cimetidine or ranitidine).
- † 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.

References

- NCCN Clinical Practice Guidelines in Oncology™. Cervical Cancer. v 1.2012. Available at: http://www.nccn.org/professionals/ physician_gls/pdf/cervical.pdf. Accessed March 4. 2014.
- Keys HM, Bundy BN, Stehman FB, et al. Cisplatin, radiation, and adjuvant hysterectomy compared with radiation and adjuvant hysterectomy for bulky stage IB cervical carcinoma. N Engl J Med. 1999;340:1154-1161.
- Rose PG, Bundy BN, Watkins EB, et al. Concurrent cisplatinbased radiotherapy and chemotherapy for locally advanced cervical cancer. N Engl J Med. 1999;340:1144-1153.
- 4. Whitney CW, Sause W, Bundy BN, et al. Randomized comparison of fluorouracil plus cisplatin versus hydroxyurea as an adjunct to radiotherapy in stage IIB-IVA carcinoma of the cervix with negative para-aortic lymph nodes: A Gynecologic Oncology Group and Southwest Oncology Group study. J Clin Oncol. 1999;17:1339–1348.
- Morris M, Eifel PF, Lu J, et al. Pelvic radiation with concurrent chemotherapy compared with pelvic and para-aortic radiation for high-risk cervical cancer. N Engl J Med. 1999;340(15):1137–1143.
- Dueñas-González A, Zarbá JJ, et al. Phase III, open-label, randomized study comparing concurrent gemcitabine plus cisplatin and radiation followed by adjuvant gemcitabine and cisplatin versus concurrent cisplatin and radiation in patients with stage IIB to IVA carcinoma of the cervix. J Clin Oncol. 2011:29(13):1678-1685.
- 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. J Clin Oncol. 2009;27(28):4649-4655.

- 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. J Clin Oncol. 2004;22(15): 3113-3119.
- Pectasides D, Fountzilas G, Papaxoinis G, et al. Carboplatin and paclitaxel in metastatic or recurrent cervical cancer. Int J Gynecol Cancer. 2009;19:777–781.
- 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. J Clin Oncol. 2005; 23:4626–4633.
- 11. Brewer CA, Blessing JA, Nagourney RA, et al. Cisplatin plus gemcitabine in previously treated squamous cell carcinoma of the cervix: a phase II study of the Gynecologic Oncology Group. Gynecol Oncol. 2006;100:385–388.
- Monk BJ, Sill MW, Burger RA, et al. Phase II trial of bevacizumab in the treatment of persistent or recurrent squamous cell carcinoma of the cervix: a gynecologic oncology group study. J Clin Oncol. 2009;27:1069–1074.
- Garcia AA, Blessing JA, Vaccarello L, et al. Phase II clinical trial of docetaxel in refractory squamous cell carcinoma of the cervix: a Gynecologic Oncology Group Study. Am J Clin Oncol. 2007;30:428-431.
- 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. Gynecol Oncol. 2005;96:103–107.

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