

OCULT PRIMARY TUMORS 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 provided only 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.

Principles of Therapy¹

- In a majority of patients, occult primary tumors are refractory to systemic treatments and chemotherapy is only palliative and does not significantly improve long-term survival.
- Consider chemotherapy in symptomatic patients with performance status (PS) 1-2 or asymptomatic patients with aggressive cancer and PS 0.
- In certain situations, special studies can identify subsets of patients more responsive to chemotherapy based on presumed primary site. These include:
 - adenocarcinoma cervical node: head and neck cancer (HNC)
 - adenocarcinoma mediastinal metastasis:
 - men under 50 years: testicular
 - women under 50 years: ovarian
 - any patient 50 and older: non-small cell lung cancer (NSCLC)
 - adenocarcinoma axillary site: breast
 - squamous cell carcinoma in head, neck or supraclavicular area: HNC
 - squamous cell carcinoma in mediastinum: NSCLC

Systemic Therapy for Occult Primary

Note: All recommendations are Category 2A unless otherwise indicated.

Adenocarcinoma¹

REGIMEN	DOSING
Paclitaxel + carboplatin²	Day 1: Carboplatin AUC 6mg • min/mL IV over 30 minutes + paclitaxel 200mg/m ² IV over 3 hours. Repeat cycle every 3 weeks for 8 cycles in responding patients and for 6 cycles maximum in patients with stable disease.
Paclitaxel + carboplatin + etoposide³	Day 1: Paclitaxel 200mg/m ² IV over 3 hours + carboplatin AUC 6mg • min/mL IV Days 1-10: Etoposide 50mg orally alternating with 100mg orally. Repeat cycle every 3 weeks for 4-8 cycles.
Docetaxel + carboplatin⁴	Day 1: Docetaxel 65mg/m ² IV over 1 hour + carboplatin AUC 6mg • min/mL IV. Repeat cycle every 3 weeks for a max of 8 cycles.
Docetaxel + cisplatin⁵	Day 1: Docetaxel 75mg/m ² IV + cisplatin 75mg/m ² IV. Repeat cycle every 3 weeks for up to 6 cycles.
Gemcitabine + cisplatin⁶	Day 1: Cisplatin 100mg/m ² IV Day 1 and 8: Gemcitabine 1250mg/m ² IV. Repeat cycle every 3 weeks for 4 cycles.
Gemcitabine + docetaxel⁷	Day 1 and 8: Gemcitabine 1000mg/m ² IV over 30 minutes Day 8: Docetaxel 75mg/m ² IV over 1 hour. Repeat cycle every 3 weeks for a maximum of 6 cycles.
mFOLFOX6^{8,9}	Day 1: Oxaliplatin 85mg/m ² IV over 2 hours + leucovorin 400mg/m ² IV over 2 hours + 5-FU 400mg/m ² IV bolus then Days 1 and 2: 5-FU 1200mg/m ² (total 2400mg/m ² over 46-48 hours) IV continuous infusion. Repeat cycle every 2 weeks for 24 cycles.
CapeOX⁸	Day 1: Oxaliplatin 130mg/m ² IV over 2 hours Day 1-14: Capecitabine 850-1000mg/m ² orally twice daily. Repeat cycle every 3 weeks for 16 cycles.
Irinotecan + carboplatin¹⁰	Day 1: Carboplatin AUC 5mg • min/mL IV Days 1, 8, and 15: Irinotecan 60mg/m ² IV. Repeat cycle every 4 weeks for up to 6 cycles.
Irinotecan + gemcitabine¹¹	Days 1 and 8: Irinotecan 100mg/m ² IV + gemcitabine 1000mg/m ² IV. Repeat cycle every 3 weeks for 6 cycles.

Squamous Cell Carcinoma¹

Paclitaxel + carboplatin²	Day 1: Carboplatin AUC 6mg • min/mL IV over 30 minutes + paclitaxel 200mg/m ² IV over 3 hours. Repeat cycle every 3 weeks for 8 cycles in responding patients and for 6 cycles maximum in patients with stable disease.
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continued

OCCULT PRIMARY TUMORS TREATMENT REGIMENS (Part 2 of 2)

Systemic Therapy for Occult Primary (continued)

Squamous Cell Carcinoma¹ (continued)

REGIMEN	DOSING
Cisplatin + gemcitabine⁶	Day 1: Cisplatin 100mg/m ² IV Day 1 and 8: Gemcitabine 1250mg/m ² IV. Repeat every 3 weeks for 4 cycles.
mFOLFOX6^{8,9}	Day 1: Oxaliplatin 85mg/m ² IV over 2 hours + leucovorin 400mg/m ² IV over 2 hours + 5-FU 400mg/m ² IV bolus then Days 1 and 2: 5-FU 1200mg/m ² (total 2400mg/m ² over 46–48 hours) IV continuous infusion. Repeat cycle every 2 weeks for 24 cycles.
Docetaxel + cisplatin + 5-FU¹²	Day 1: Docetaxel 75mg/m ² IV + cisplatin 75mg/m ² IV. Days 1–5: 5-FU 750mg/m ² /day IV via continuous infusion over 24 hours. Repeat cycle every 3 weeks for 3 cycles.
Paclitaxel + cisplatin¹³	Day 1: Paclitaxel 175mg/m ² IV + cisplatin 60mg/m ² IV. Repeat cycle every 3 weeks.
Docetaxel + carboplatin¹⁴	Day 1: Docetaxel 75mg/m ² IV over 30 minutes + carboplatin AUC 5mg • min/mL IV over 30 minutes. Repeat cycle every 3 weeks for 8 cycles.
Docetaxel + cisplatin^{5,15}	Day 1: Docetaxel 60mg/m ² IV + cisplatin 80mg/m ² IV. Repeat cycle every 3 weeks for 2 cycles and an additional 4 cycles until disease progression is demonstrated. OR Day 1: Docetaxel 75mg/m ² IV + cisplatin 75mg/m ² IV. Repeat cycle every 3 weeks for up to 6 cycles.
Cisplatin + fluorouracil¹⁶	Days 1–5: Cisplatin 20mg/m ² IV Days 1–5: Fluorouracil 700mg/m ² /day IV via continuous infusion over 24 hours. Repeat cycle every 4 weeks for 3 cycles.

Neuroendocrine Tumors¹

- For poorly differentiated (high-grade or anaplastic) or small cell subtype, refer to the NCCN Small Cell Lung Cancer guidelines.
- For moderate and well-differentiated neuroendocrine tumors, refer to the NCCN Neuroendocrine Tumors guidelines (Carcinoid tumors).

References

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| <ol style="list-style-type: none"> 1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Occult Primary (Cancer of Unknown Primary [CUP]). V2.2016. Available at: http://www.nccn.org. Accessed September 16, 2016. 2. Briasoulis E, Kalofonos H, Bafaloukos D, et al. Carboplatin plus paclitaxel in unknown primary carcinoma: A phase II Hellenic Cooperative Oncology Group Study. <i>J Clin Oncol</i>. 2000;18:3101–3107. 3. Greco F, Burris, H, Erland J, et al. Carcinoma of unknown primary site: Long term follow-up after treatment with paclitaxel, carboplatin, and etoposide. <i>Cancer</i>. 2000;89:2655–2660. 4. Greco F, Erland J, Morrissey H, et al. Carcinoma of unknown primary site: Phase II trials with docetaxel plus cisplatin or carboplatin. <i>Ann Oncol</i>. 2000;11:211–215. 5. Demirci U, Coskun U, Karaca H, et al. Docetaxel and cisplatin in first line treatment of patients with unknown primary cancer: a multicenter study of the anatolian society of medical oncology. <i>Asian Pac J Cancer Prev</i>. 2014;15(4):1581–1584. 6. Gross-Goupil M, Fourcade A, Blot E, et al. Cisplatin alone or combined with gemcitabine in carcinomas of unknown primary: Results of the randomised GEFCAPI 02 trial. <i>Eur J Cancer</i>. 2012;48:721–727. 7. Pouessel D, Culine S, Becht C, et al. Gemcitabine and docetaxel as front-line chemotherapy in patients with carcinoma of an unknown primary site. <i>Cancer</i>. 2004;100:1257–1261. 8. Cassidy J, Clarke S, Diaz Rubio E, et al. Randomized phase III study of capecitabine plus oxaliplatin compared with fluorouracil/folinic acid plus oxaliplatin as first-line therapy for metastatic colorectal cancer. <i>J Clin Oncol</i>. 2008;26:2006–2012. | <ol style="list-style-type: none"> 9. Cheeseman SL, Joel SP, Chester JD, et al. A "modified de Gramont" regimen of fluorouracil, alone and with oxaliplatin, for advanced colorectal cancer. <i>Br J Cancer</i>. 2002;87:393–399. 10. Yonemori K, Ando M, Yunokawa M, et al. Irinotecan plus carboplatin for patients with carcinoma of unknown primary site. <i>Br J Cancer</i>. 2009;100(1):50–55. 11. Hainsworth JD, Spigel DR, Clark BL, et al. Paclitaxel/ carboplatin/etoposide versus gemcitabine/irinotecan in the first-line treatment of patients with carcinoma of unknown primary site: a randomized, phase III Sarah Cannon Oncology Research Consortium Trial. <i>Cancer J</i>. 2010;16(1):70–75. 12. Pointreau Y, Garaud P, Chapet S, et al. Randomized trial of induction chemotherapy with cisplatin and 5-fluorouracil with or without docetaxel for larynx preservation. <i>J Natl Cancer Inst</i>. 2009;101:498–506. 13. Park YH, Ryoo BY, Choi SJ, et al. A phase II study of paclitaxel plus cisplatin chemotherapy in an unfavourable group of patients with cancer of unknown primary site. <i>Jpn J Clin Oncol</i>. 2004;34:681–685. 14. Pantheroudakis G, Briasoulis E, Kalofonos HP, et al. Docetaxel and carboplatin combination chemotherapy as outpatient palliative therapy in carcinoma of unknown primary: a multicenter Hellenic Cooperative Oncology Group phase II study. <i>Acta Oncol</i>. 2008;47:1148–1155. 15. Mukai H, Katsumata N, Ando M, et al. Safety and efficacy of a combination of docetaxel and cisplatin in patients with unknown primary cancer. <i>Am J Clin Oncol</i>. 2010;33:32–35. 16. Kusaba H, Shibata Y, Arita S, et al. Infusional 5-fluorouracil and cisplatin as first-line chemotherapy in patients with carcinoma of unknown primary site. <i>Med Oncol</i>. 2007;24:259–264. |
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