

# Occult Primary Treatment Regimens

**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 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 Therapy<sup>1</sup>

- 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.

REGIMEN	DOSING
<b>Adenocarcinoma<sup>1</sup></b>	
Paclitaxel + carboplatin <sup>2</sup>	<b>Day 1:</b> Carboplatin AUC 6mg • min/mL IV over 30 minutes + paclitaxel 200mg/m <sup>2</sup> 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 + etoposide <sup>3</sup>	<b>Day 1:</b> Paclitaxel 200mg/m <sup>2</sup> IV over 3 hours + carboplatin AUC 6mg • min/mL IV <b>Days 1–10:</b> Etoposide 50mg orally alternating with 100mg orally. Repeat cycle every 3 weeks for 4–8 cycles.
Docetaxel + carboplatin <sup>4</sup>	<b>Day 1:</b> Docetaxel 65mg/m <sup>2</sup> IV over 1 hour + carboplatin AUC 6mg • min/mL IV. Repeat cycle every 3 weeks for a max of 8 cycles.
Gemcitabine + cisplatin <sup>5</sup>	<b>Day 1:</b> Cisplatin 100mg/m <sup>2</sup> IV <b>Day 1 and 8:</b> Gemcitabine 1250mg/m <sup>2</sup> IV. Repeat cycle every 3 weeks for 4 cycles.
Gemcitabine + docetaxel <sup>6</sup>	<b>Day 1 and 8:</b> Gemcitabine 1000mg/m <sup>2</sup> IV over 30 minutes <b>Day 8:</b> Docetaxel 75mg/m <sup>2</sup> IV over 1 hour. Repeat cycle every 3 weeks for a maximum of 6 cycles.
CapeOX <sup>7</sup>	<b>Day 1:</b> Oxaliplatin 130mg/m <sup>2</sup> IV over 2 hours <b>Day 1–14:</b> Capecitabine 850–1000mg/m <sup>2</sup> orally twice daily. Repeat cycle every 3 weeks for 16 cycles.
mFOLFOX6 <sup>7,8</sup>	<b>Day 1:</b> Oxaliplatin 85mg/m <sup>2</sup> IV over 2 hours + leucovorin 400mg/m <sup>2</sup> IV over 2 hours + 5-FU 400mg/m <sup>2</sup> IV bolus <b>then</b> <b>Days 1 and 2:</b> 5-FU 1200mg/m <sup>2</sup> (total 2400mg/m <sup>2</sup> over 46–48 hours) IV continuous infusion. Repeat cycle every 2 weeks for 24 cycles.
Docetaxel + cisplatin <sup>9</sup>	<b>Day 1:</b> Docetaxel 75mg/m <sup>2</sup> IV + cisplatin 75mg/m <sup>2</sup> IV. Repeat cycle every 3 weeks for up to 6 cycles.
Irinotecan + carboplatin <sup>10</sup>	<b>Day 1:</b> Carboplatin AUC 5mg • min/mL IV <b>Days 1, 8, and 15:</b> Irinotecan 60mg/m <sup>2</sup> IV. Repeat cycle every 4 weeks for up to 6 cycles.
Irinotecan + gemcitabine <sup>11</sup>	<b>Days 1 and 8:</b> Irinotecan 100mg/m <sup>2</sup> IV + gemcitabine 1000mg/m <sup>2</sup> IV. Repeat cycle every 3 weeks for 6 cycles.

continued

# Occult Primary Treatment Regimens

## ► Systemic Therapy for Occult Primary (continued)

REGIMEN	DOSING
<b>Squamous Cell Carcinoma<sup>1</sup></b>	
Paclitaxel + carboplatin <sup>2</sup>	<b>Day 1:</b> Carboplatin AUC 6mg • min/mL IV over 30 minutes + paclitaxel 200mg/m <sup>2</sup> 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.
Cisplatin + gemcitabine <sup>5</sup>	<b>Day 1:</b> Cisplatin 100mg/m <sup>2</sup> IV <b>Day 1 and 8:</b> Gemcitabine 1250mg/m <sup>2</sup> IV. Repeat every 3 weeks for 4 cycles.
mFOLFOX6 <sup>7,8</sup>	<b>Day 1:</b> Oxaliplatin 85mg/m <sup>2</sup> IV over 2 hours + leucovorin 400mg/m <sup>2</sup> IV over 2 hours + 5-FU 400mg/m <sup>2</sup> IV bolus <b>then</b> <b>Days 1 and 2:</b> 5-FU 1200mg/m <sup>2</sup> (total 2400mg/m <sup>2</sup> over 46–48 hours) IV continuous infusion. Repeat cycle every 2 weeks for 24 cycles.
Docetaxel + cisplatin + 5-FU <sup>13</sup>	<b>Day 1:</b> Docetaxel 75mg/m <sup>2</sup> IV + cisplatin 75mg/m <sup>2</sup> IV. <b>Days 1–5:</b> 5-FU 750mg/m <sup>2</sup> /day IV via continuous infusion over 24 hours. Repeat cycle every 3 weeks for 3 cycles.
Paclitaxel + cisplatin <sup>15</sup>	<b>Day 1:</b> Paclitaxel 175mg/m <sup>2</sup> IV + cisplatin 60mg/m <sup>2</sup> IV. Repeat cycle every 3 weeks.
Docetaxel + carboplatin <sup>16</sup>	<b>Day 1:</b> Docetaxel 75mg/m <sup>2</sup> IV over 30 minutes + carboplatin AUC 5mg • min/mL IV over 30 minutes. Repeat cycle every 3 weeks for 8 cycles.
Docetaxel + cisplatin <sup>9,12</sup>	<b>Day 1:</b> Docetaxel 60mg/m <sup>2</sup> IV + cisplatin 80mg/m <sup>2</sup> IV. Repeat cycle every 3 weeks for 2 cycles and an additional 4 cycles until disease progression is demonstrated. <b>OR</b> <b>Day 1:</b> Docetaxel 75mg/m <sup>2</sup> IV + cisplatin 75mg/m <sup>2</sup> IV. Repeat cycle every 3 weeks for up to 6 cycles.
Cisplatin + fluorouracil <sup>14</sup>	<b>Days 1–5:</b> Cisplatin 20mg/m <sup>2</sup> IV <b>Days 1–5:</b> Fluorouracil 700mg/m <sup>2</sup> /day IV via continuous infusion over 24 hours. Repeat cycle every 4 weeks for 3 cycles.

### Neuroendocrine Tumors<sup>1</sup>

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

## References

1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines<sup>®</sup>) for Occult Primary (Cancer of Unknown Primary [CUP]). V1.2018. Available at: [https://www.nccn.org/professionals/physician\\_gls/pdf/occult.pdf](https://www.nccn.org/professionals/physician_gls/pdf/occult.pdf). Accessed July 12, 2018.
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