**NON-SMALL CELL LUNG CANCER TREATMENT REGIMENS** (Part 1 of 9)

**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.

### Chemotherapy Regimens For Neoadjuvant and Adjuvant Therapy†

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

<table>
<thead>
<tr>
<th>REGIMEN</th>
<th>DOSING</th>
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<tbody>
<tr>
<td><strong>Cisplatin + vinorelbine</strong>&lt;sup&gt;3,4&lt;/sup&gt;</td>
<td>Days 1 and 8: Cisplatin 50mg/m&lt;sup&gt;2&lt;/sup&gt; IV&lt;br&gt;Days 1, 8, 15, and 22: Vinorelbine 25mg/m&lt;sup&gt;2&lt;/sup&gt; IV.&lt;br&gt;Repeat cycle every 4 weeks for 4 cycles.&lt;br&gt;<strong>OR</strong>&lt;br&gt;Day 1: Cisplatin 100mg/m&lt;sup&gt;2&lt;/sup&gt; IV&lt;br&gt;Days 1, 8, 15, and 22: Vinorelbine 30mg/m&lt;sup&gt;2&lt;/sup&gt; IV.&lt;br&gt;Repeat cycle every 4 weeks for 4 cycles.&lt;br&gt;<strong>OR</strong>&lt;br&gt;Day 1: Cisplatin 75–80mg/m&lt;sup&gt;2&lt;/sup&gt;&lt;br&gt;Days 1 and 8: Vinorelbine 25–30mg/m&lt;sup&gt;2&lt;/sup&gt;.&lt;br&gt;Repeat every 3 weeks for 4 cycles.</td>
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<tr>
<td><strong>Cisplatin + etoposide</strong>&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Day 1: Cisplatin 100mg/m&lt;sup&gt;2&lt;/sup&gt; IV&lt;br&gt;Days 1–3: Etoposide 100mg/m&lt;sup&gt;2&lt;/sup&gt; IV.&lt;br&gt;Repeat cycle every 4 weeks for 4 cycles.</td>
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<tr>
<td><strong>Cisplatin + gemcitabine</strong>&lt;sup&gt;5&lt;/sup&gt;</td>
<td>Day 1: Cisplatin 75mg/m&lt;sup&gt;2&lt;/sup&gt; IV&lt;br&gt;Days 1 and 8: Gemcitabine 1,250mg/m&lt;sup&gt;2&lt;/sup&gt; IV.&lt;br&gt;Repeat cycle every 3 weeks.</td>
</tr>
<tr>
<td><strong>Cisplatin + docetaxel</strong>&lt;sup&gt;6&lt;/sup&gt;</td>
<td>Day 1: Docetaxel 75mg/m&lt;sup&gt;2&lt;/sup&gt; IV + cisplatin 75mg/m&lt;sup&gt;2&lt;/sup&gt; IV.&lt;br&gt;Repeat every 3 weeks for 4 cycles.</td>
</tr>
<tr>
<td><strong>Cisplatin + pemetrexed</strong>&lt;sup&gt;7&lt;/sup&gt;</td>
<td>Day 1: Cisplatin 75mg/m&lt;sup&gt;2&lt;/sup&gt; IV + pemetrexed 500mg/m&lt;sup&gt;2&lt;/sup&gt; IV.&lt;br&gt;Repeat every 3 weeks for 4 cycles.</td>
</tr>
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</table>

**For patients with comorbidities or patients not able to tolerate cisplatin**<sup>1</sup>

| **Paclitaxel + carboplatin**<sup>9</sup> | Day 1: Paclitaxel 200mg/m<sup>2</sup> IV + carboplatin AUC 6mg • min/mL IV.<br>Repeat cycle every 3 weeks for 4 cycles. |

### Chemotherapy Regimens Used With Radiation Therapy (RT)<sup>1,4</sup>

**Concurrent Chemotherapy/RT<sup>4,8</sup>**

| **Cisplatin + etoposide**<sup>3,10</sup> | Days 1, 8, 29 and 36: Cisplatin 50mg/m<sup>2</sup> IV<br>Days 1–5 and 29–33: Etoposide 50mg/m<sup>2</sup> IV<br>Concurrent thoracic radiotherapy 1.8Gy/day for 5 days/week (total dose, 61Gy). |
| **Cisplatin + vinblastine**<sup>11</sup> | Days 1 and 29: Cisplatin 100mg/m<sup>2</sup> IV<br>Days 1, 8, 15, 22 and 29: Vinblastine 5mg/m<sup>2</sup> IV with concurrent thoracic radiotherapy (total dose, 60Gy). |
| **Carboplatin + pemetrexed (nonsquamous)**<sup>11</sup> | Day 1: Carboplatin AUC 5mg • min/mL IV<br>Day 1: Pemetrexed 500 mg/m<sup>2</sup> IV with concurrent thoracic radiotherapy.<br>Repeat every 3 weeks for 4 cycles. |
| **Cisplatin + pemetrexed (nonsquamous)**<sup>12</sup> | Day 1: Cisplatin 75mg/m<sup>2</sup> IV.<br>Day 1: Pemetrexed 500 mg/m<sup>2</sup> IV with concurrent thoracic radiotherapy.<br>Repeat every 3 weeks for 3 cycles. |
| **Paclitaxel + carboplatin**<sup>13</sup> | Paclitaxel 45mg/m<sup>2</sup> IV + carboplatin AUC 2mg • min/mL IV weekly with concurrent thoracic radiotherapy (total dose, 60Gy) given 5 days per week in 2Gy fractions. |

**Sequential Chemotherapy/RT (Adjuvant)**<sup>13</sup>

| **Cisplatin + vinblastine**<sup>10</sup> | Days 1 and 29: Cisplatin 100mg/m<sup>2</sup> IV.<br>Days 1, 8, 15, 22 and 29: Vinblastine 5mg/m<sup>2</sup> IV; followed by thoracic radiotherapy with 60Gy in 30 fractions beginning on Day 50. |
| **Paclitaxel + carboplatin**<sup>14</sup> | Day 1: Paclitaxel 200mg/m<sup>2</sup> IV over 3 hours + carboplatin AUC 6mg • min/mL IV over 1 hour.<br>Repeat every 3 weeks for 2 cycles; followed by thoracic radiotherapy 63Gy beginning on Day 42. |

*continued*
### Concurrent Chemotherapy/RT Followed by Chemotherapy

<table>
<thead>
<tr>
<th>REGIMEN</th>
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<tr>
<td>Paclitaxel + carboplatin&lt;sup&gt;14&lt;/sup&gt;</td>
<td>Day 1 (weekly): Paclitaxel 45–50mg/m² IV and carboplatin AUC 2mg • min/mL IV. Concurrent thoracic radiotherapy; followed by 2 additional cycles of paclitaxel 200mg/m² IV and carboplatin AUC 6mg • min/mL IV.</td>
</tr>
<tr>
<td>Cisplatin + etoposide&lt;sup&gt;10&lt;/sup&gt;</td>
<td>Days 1, 8, 29, and 36: Cisplatin 50mg/m² IV. Days 1–5, 29–33: Etoposide 50mg/m² IV with concurrent thoracic radiotherapy; followed by 2 additional cycles of cisplatin 50mg/m² IV and etoposide 50mg/m² IV.</td>
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### Systemic Therapy for Advanced & Metastatic Disease<sup>1</sup>

#### Principles of Therapy<sup>1</sup>
- The drug regimen with the highest likelihood of benefit, with toxicity deemed acceptable to both the physician and the patient, should be given as initial therapy for advanced lung cancer.
- Stage, weight loss, performance status (PS), and gender predict survival.
- Platinum-based chemotherapy prolongs survival, improves symptom control, and yields superior quality of life compared to best supportive care.
- Histology of NSCLC is important in the selection of systemic therapy.
- New agent/platinum combinations have generated a plateau in overall response rate (25%–35%), time to progression (4–6 months), median survival (8–10 months), 1-year survival rate (30%–40%), and 2-year survival rate (10%–15%) in fit patients.
- Unfit patients of any age (PS 3–4) do not benefit from cytotoxic treatment, except erlotinib for those who are epidermal growth factor receptor (EGFR) mutation-positive.

#### First-line Systemic Therapy Options<sup>1</sup>

**Principles of Therapy**
- There is superior efficacy and reduced toxicity for cisplatin/pemetrexed in patients with nonsquamous histology compared with cisplatin/gemcitabine.
- There is superior efficacy for cisplatin/gemcitabine in patients with squamous histology, in comparison to cisplatin/pemetrexed.
- Two drug regimens are preferred; a third cytotoxic drug increases response rate but not survival.
- Single-agent therapy may be appropriate in select patients.
- Response assessment after 1–2 cycles, then every 2–4 cycles.

**Adenocarcinoma, Large Cell, NSCLC NOS (PS 0-1)**

**Bevacizumab + carboplatin + paclitaxel (Category 1)**<sup>15</sup>

| Day 1: | Paclitaxel 200mg/m² IV + carboplatin AUC 6mg • min/mL IV. Repeat cycle every 3 weeks for 6 cycles. |

| Day 1: | Bevacizumab 15mg/kg IV every 3 weeks until disease progression. |

**Bevacizumab + carboplatin + pemetrexed**<sup>16</sup>

| Day 1: | Pemetrexed 500mg/m² IV + carboplatin AUC 6mg • min/mL IV + bevacizumab 15mg/kg IV. Repeat cycle every 3 weeks for up to 4 cycles, followed by: |

| Day 1: | Pemetrexed 500mg/m² IV + bevacizumab 15mg/kg IV. Repeat cycle every 3 weeks until disease progression or unacceptable toxicity. |

**Bevacizumab + cisplatin + pemetrexed**<sup>17</sup>

| Day 1: | Bevacizumab 7.5mg/kg IV + cisplatin 75mg/m² IV + pemetrexed 500mg/m² IV. Repeat cycle every 3 weeks for 4 cycles, followed by: |

| Day 1: | Bevacizumab 7.5mg/kg IV + pemetrexed 500mg/m² IV. Repeat cycle every 3 weeks until disease progression or unacceptable toxicity. |

**Carboplatin + albumin-bound paclitaxel (Category 1)**<sup>18</sup>

| Day 1: | Carboplatin AUC 6mg • min/mL IV |

| Days 1, 8, and 15: | Nab-paclitaxel 100mg/m² IV. Repeat cycle every 3 weeks until disease progression or unacceptable toxicity. |

**Carboplatin + docetaxel (Category 1)**<sup>16</sup>

| Day 1: | Docetaxel 75mg/m² IV + carboplatin AUC 6mg • min/mL IV. Repeat cycle every 3 weeks until disease progression or unacceptable toxicity. |

**Carboplatin + etoposide (Category 1)**<sup>20,21</sup>

| Day 1: | Carboplatin 325mg/m² IV |

| Days 1, 2, and 3: | Etoposide 100mg/m³ IV. Repeat cycle every 3 to 4 weeks until disease progression or unacceptable toxicity. |

**OR**

**First Course**

| Day 1: | Carboplatin AUC 4mg • min/mL IV |

| Days 1–14: | Etoposide 50mg orally twice daily |

**Second Course**

| Day 1: | Carboplatin AUC 5mg • min/mL IV |

| Days 1–14: | Etoposide 50mg orally twice daily |

**Third Course**

| Day 1: | Carboplatin AUC 5mg • min/mL IV |

| Days 1–21: | Etoposide 50mg orally twice daily. Patients achieving a complete or partial response should receive an additional 3 courses at the same doses given in the third course. |
## Systemic Therapy for Advanced & Metastatic Disease

### First-line Systemic Therapy Options (continued)

#### Adenocarcinoma, Large Cell, NSCLC NOS (PS 0-1) (continued)

<table>
<thead>
<tr>
<th>REGIMEN</th>
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</table>
| **Carboplatin + gemcitabine (Category 1)**<sup>22</sup> | Day 1: Carboplatin AUC 5mg • min/mL IV  
Days 1, 8, and 15: Gemcitabine 1,000mg/m² IV  
Repeat cycle every 4 weeks for 4 cycles. |
| **Carboplatin + paclitaxel (Category 1)**<sup>23b</sup> | Day 1: Paclitaxel 200mg/m² IV + carboplatin AUC 6mg • min/mL IV.  
Repeat every 3 weeks until disease progression or unacceptable toxicity. |
| **Carboplatin + pemetrexed (Category 1)**<sup>24</sup> | Day 1: Pemetrexed 500mg/m² IV + carboplatin AUC 6mg • min/mL IV.  
Repeat cycle every 3 weeks for up to 6 cycles. |
| **Cisplatin + docetaxel (Category 1)**<sup>19c</sup> | Day 1: Cisplatin 75mg/m² IV + docetaxel 75mg/m² IV.  
Repeat cycle every 3 weeks. |
| **Cisplatin + paclitaxel (Category 1)**<sup>25</sup> | Day 1: Paclitaxel 135mg/m² IV over 24 hours  
Day 2: Cisplatin 75mg/m² IV.  
Repeat cycle every 3 weeks. |
| **Cisplatin + etoposide (Category 1)**<sup>20,21</sup> | Day 1: Cisplatin 80mg/m² IV  
Days 1 and 8: Etoposide 100mg/m² IV.  
Repeat cycle every 3 weeks for up to 6 cycles.  
**OR**  
First Course  
Day 1: Cisplatin AUC 4mg • min/mL IV  
Days 1–14: Etoposide 50mg orally twice daily  
Second Course  
Day 1: Cisplatin AUC 5mg • min/mL IV  
Days 1–14: Etoposide 50mg orally twice daily  
Third Course  
Day 1: Cisplatin AUC 5mg • min/mL IV  
Days 1–21: Etoposide 50mg orally twice daily.  
Patients achieving a complete or partial response should receive an additional 3 courses at the same doses given in the third course. |
| **Gemcitabine + docetaxel (Category 1)**<sup>19c</sup> | Day 1: Gemcitabine 1,000mg/m² IV  
Day 8: Docetaxel 85mg/m² IV.  
Repeat cycle every 3 weeks for 8 cycles. |
| **Gemcitabine + vinorelbine (Category 1)**<sup>31</sup> | Days 1 and 8: Vinorelbine 25mg/m² IV + gemcitabine 1,000mg/m² IV.  
Repeat cycle every 3 weeks. |

#### Adenocarcinoma, Large Cell, NSCLC NOS (PS 2)

<table>
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| **Albumin-bound paclitaxel**<sup>12</sup> | Day 1: Albumin-bound paclitaxel 260mg/m² IV.  
Repeat cycle every 3 weeks. |
| **Carboplatin + albumin-bound paclitaxel**<sup>12,34</sup> | Day 1: Carboplatin AUC 6mg • min/mL IV  
Days 1, 8, and 15: Albumin-bound paclitaxel 100mg/m² IV.  
Repeat cycle every 3 weeks until disease progression or unacceptable toxicity. |
| **Carboplatin + docetaxel**<sup>19c</sup> | Day 1: Docetaxel 75mg/m² IV + carboplatin AUC 6mg • min/mL IV.  
Repeat cycle every 3 weeks until disease progression or unacceptable toxicity. |
| **Carboplatin + etoposide**<sup>20,21</sup> | Day 1: Carboplatin 325mg/m² IV  
Days 1, 2, and 3: Etoposide 100mg/m² IV.  
Repeat cycle every 3 to 4 weeks until disease progression or unacceptable toxicity.  
**OR**  
First Course  
Day 1: Carboplatin AUC 4mg • min/mL IV  
Days 1–14: Etoposide 50mg orally twice daily  
Second Course  
Day 1: Carboplatin AUC 5mg • min/mL IV  
Days 1–14: Etoposide 50mg orally twice daily  
Third Course  
Day 1: Carboplatin AUC 5mg • min/mL IV  
Days 1–21: Etoposide 50mg orally twice daily.  
Patients achieving a complete or partial response should receive an additional 3 courses at the same doses given in the third course. |
## First-line Systemic Therapy Options

### Adenocarcinoma, Large Cell, NSCLC NOS (PS 2)

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| **Carboplatin + gemcitabine**<sup>22</sup> | Day 1: Carboplatin AUC 5mg • min/mL IV  
Days 1, 8, and 15: Gemcitabine 1,000mg/m² IV  
Repeat cycle every 4 weeks for 4 cycles. |
| **Carboplatin + paclitaxel**<sup>23</sup>c | Day 1: Paclitaxel 200mg/m² IV + carboplatin AUC 6mg • min/mL IV.  
Repeat every 3 weeks until disease progression or unacceptable toxicity. |
| **Carboplatin + pemetrexed**<sup>24</sup> | Day 1: Pemetrexed 500mg/m² IV + carboplatin AUC 6mg • min/mL IV.  
Repeat cycle every 3 weeks for up to 6 cycles. |
| **Carboplatin + vinorelbine**<sup>25</sup> | Day 1: Carboplatin AUC 6mg • min/mL IV  
Days 1 and 8: Vinorelbine 30mg/m² IV  
Day 9: Pegfilgrastim 6mg SC.  
Repeat cycle every 3 weeks for 4 cycles. |

### Squamous Cell Carcinoma (PS 0-1)<sup>1</sup>

<table>
<thead>
<tr>
<th>REGIMEN</th>
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| **Carboplatin + albumin-bound paclitaxel** (Category 1)<sup>18</sup> | Day 1: Carboplatin AUC 6mg • min/mL IV  
Days 1, 8, and 15: Albumin-bound paclitaxel 100mg/m² IV.  
Repeat cycle every 3 weeks until disease progression or unacceptable toxicity. |
| **Carboplatin + docetaxel** (Category 1)<sup>19</sup> | Day 1: Docetaxel 75mg/m² IV over 1 hour.  
Repeat cycle every 3 weeks. |
| **Carboplatin + etoposide** (Category 1)<sup>20,21</sup> | Day 1: Carboplatin 325mg/m² IV  
Days 1, 2, and 3: Etoposide 100mg/m² IV.  
Repeat cycle every 3 to 4 weeks until disease progression or unacceptable toxicity.  
**OR**  
First Course  
Day 1: Carboplatin AUC 4mg • min/mL IV  
Days 1–14: Etoposide 50mg orally twice daily  
Second Course  
Day 1: Carboplatin AUC 5mg • min/mL IV  
Days 1–14: Etoposide 50mg orally twice daily  
Third Course  
Day 1: Carboplatin AUC 5mg • min/mL IV  
Days 1–21: Etoposide 50mg orally twice daily.  
Patients achieving a complete or partial response should receive an additional 3 courses at the same doses given in the third course. |
| **Carboplatin + gemcitabine** (Category 1)<sup>22</sup> | Day 1: Carboplatin AUC 5mg • min/mL IV  
Days 1, 8, and 15: Gemcitabine 1,000mg/m² IV  
Repeat cycle every 4 weeks for 4 cycles. |
| **Carboplatin + paclitaxel** (Category 1)<sup>23</sup>c | Day 1: Paclitaxel 200mg/m² IV + carboplatin AUC 6mg • min/mL IV.  
Repeat every 3 weeks until disease progression or unacceptable toxicity. |
| **Carboplatin + vinorelbine** (Category 1)<sup>25</sup> | Day 1: Carboplatin AUC 6mg • min/mL IV  
Days 1 and 8: Vinorelbine 30mg/m² IV  
Day 9: Pegfilgrastim 6mg SC.  
Repeat cycle every 3 weeks for 4 cycles. |
## Squamous Cell Carcinoma (PS 0-1)

### REGIMEN DOSING

<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>Cisplatin + docetaxel</strong> <em>(Category 1)</em></td>
<td>Day 1: Cisplatin 75mg/m² IV + docetaxel 75mg/m² IV. Repeat cycle every 3 weeks.</td>
</tr>
<tr>
<td><strong>Cisplatin + etoposide</strong> <em>(Category 1)</em></td>
<td>Day 1: Cisplatin 100mg/m² IV Days 1–3: Etoposide 100mg/m² IV. Repeat cycle every 3 weeks for up to 6 cycles.</td>
</tr>
<tr>
<td><strong>Cisplatin + gemcitabine</strong> <em>(Category 1)</em></td>
<td>Day 1: Cisplatin 80mg/m² IV Days 1 and 8: Gemcitabine 1,000mg/m² IV. Repeat cycle every 3 weeks until disease progression or unacceptable toxicity. OR Day 1: Cisplatin 75mg/m² IV Days 1 and 8: Gemcitabine 1,250mg/m² IV. Repeat cycle every 3 weeks for up to 6 cycles.</td>
</tr>
<tr>
<td><strong>Cisplatin + paclitaxel</strong> <em>(Category 1)</em></td>
<td>Day 1: Paclitaxel 135mg/m² IV over 24 hours Day 2: Cisplatin 75mg/m² IV. Repeat cycle every 3 weeks.</td>
</tr>
<tr>
<td><strong>Cisplatin + vinorelbine</strong> <em>(Category 1)</em></td>
<td>Day 1: Cisplatin 100mg/m² IV Days 1, 8, 15 and 22: Vinorelbine 25mg/m² IV over 10 minutes. Repeat cycle every 4 weeks.</td>
</tr>
<tr>
<td><strong>Cisplatin + gemcitabine + necitumumab</strong> <em>(Category 3)</em></td>
<td>Day 1: Cisplatin 75mg/m² IV over 120 minutes Days 1 and 8: Gemcitabine 1,250mg/m² IV over 30 minutes + necitumumab 800mg IV over a minimum of 50 minutes. Repeat cycle every 3 weeks for up to 6 cycles. Patients free of disease progression should continue single-agent necitumumab on the same treatment schedule until disease progression or unacceptable toxicity.</td>
</tr>
<tr>
<td><strong>Gemcitabine + docetaxel</strong> <em>(Category 1)</em></td>
<td>Days 1 and 8: Gemcitabine 1,000mg/m² IV Day 8: Docetaxel 85mg/m² IV. Repeat cycle every 3 weeks for 8 cycles.</td>
</tr>
<tr>
<td><strong>Gemcitabine + vinorelbine</strong> <em>(Category 1)</em></td>
<td>Days 1 and 8: Vinorelbine 25mg/m² IV + gemcitabine 1,000mg/m² IV. Repeat cycle every 3 weeks.</td>
</tr>
<tr>
<td><strong>Albumin-bound paclitaxel</strong></td>
<td>Day 1: Albumin-bound paclitaxel 260mg/m² IV. Repeat cycle every 3 weeks.</td>
</tr>
<tr>
<td><strong>Carboplatin + albumin-bound paclitaxel</strong></td>
<td>Day 1: Carboplatin AUC 6mg • min/mL IV Days 1, 8, and 15: Albumin-bound paclitaxel 100mg/m² IV. Repeat cycle every 3 weeks until disease progression or unacceptable toxicity.</td>
</tr>
<tr>
<td><strong>Carboplatin + docetaxel</strong></td>
<td>Day 1: Docetaxel 75mg/m² IV + carboplatin AUC 6mg • min/mL IV. Repeat cycle every 3 weeks until disease progression or unacceptable toxicity.</td>
</tr>
<tr>
<td><strong>Carboplatin + etoposide</strong></td>
<td>Day 1: Carboplatin 325mg/m² IV Days 1, 2, and 3: Etoposide 100mg/m² IV. Repeat cycle every 3 to 4 weeks until disease progression or unacceptable toxicity. OR First Course Day 1: Carboplatin AUC 4mg • min/mL IV Days 1–14: Etoposide 50mg orally twice daily Second Course Day 1: Carboplatin AUC 5mg • min/mL IV Days 1–14: Etoposide 50mg orally twice daily Third Course Day 1: Carboplatin AUC 5mg • min/mL IV Days 1–21: Etoposide 50mg orally twice daily. Patients achieving a complete or partial response should receive an additional 3 courses at the same doses given in the third course.</td>
</tr>
<tr>
<td><strong>Carboplatin + gemcitabine</strong></td>
<td>Day 1: Carboplatin AUC 5mg • min/mL IV Days 1, 8, and 15: Gemcitabine 1,000mg/m² IV. Repeat cycle every 4 weeks for 4 cycles.</td>
</tr>
<tr>
<td><strong>Carboplatin + paclitaxel</strong></td>
<td>Day 1: Paclitaxel 200mg/m² IV + carboplatin AUC 6mg • min/mL IV. Repeat every 3 weeks until disease progression or unacceptable toxicity.</td>
</tr>
<tr>
<td><strong>Carboplatin + vinorelbine</strong></td>
<td>Day 1: Carboplatin AUC 6mg • min/mL IV Days 1 and 8: Vinorelbine 30mg/m² IV Day 9: Pegfilgrastim 6mg SC. Repeat cycle every 3 weeks for 4 cycles.</td>
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Squamous Cell Carcinoma (PS 2) (continued)

**REGIMEN**

Cisplatin + gemcitabine + necitumumab (Category 3)

**DOISING**

Day 1: Cisplatin 75mg/m² IV over 120 minutes
Days 1 and 8: Gemcitabine 1,250mg/m² IV over 30 minutes + necitumumab 800mg IV over a minimum of 50 minutes.
Repeat cycle every 3 weeks for up to 6 cycles. Patients free of disease progression should continue single-agent necitumumab on the same treatment schedule until disease progression or unacceptable toxicity.

Docetaxel

Day 1: Docetaxel 75mg/m² IV over 1 hour.
Repeat cycle every 3 weeks.

Etoposide

Days 1–21: Etoposide 50mg/m² orally daily.
Repeat cycle every 4 to 5 weeks.

Gemcitabine

Days 1 and 8: Gemcitabine 1,250mg/m² IV.
Repeat cycle every 3 weeks.

Gemcitabine + docetaxel

Days 1 and 8: Gemcitabine 1,000mg/m² IV.
Day 8: Docetaxel 85mg/m² IV.
Repeat cycle every 3 weeks for 8 cycles.

Gemcitabine + vinorelbine

Days 1 and 8: Vinorelbine 25mg/m² IV + gemcitabine 1,000mg/m² IV.
Repeat cycle every 3 weeks.

Irinotecan

Day 1: Irinotecan 300mg/m² IV.
Repeat cycle every 3 weeks.

Paclitaxel

Days 1, 8, and 15: Paclitaxel 80mg/m² IV.
Repeat cycle every 4 weeks for up to 4 cycles.

Vinorelbine

Days 1, 8, and 15: Vinorelbine 30mg/m² IV.
Repeat cycle every 3 weeks.

**Principles of Maintenance Therapy**

Continuation maintenance refers to the use of at least one of the agents given in first line, beyond 4 to 6 cycles, in the absence of disease progression. Switch maintenance refers to the initiation of a different agent, not included as part of the first-line regimen, in the absence of disease progression, after 4 to 6 cycles of initial therapy.

- **Continuation Maintenance:** Bevacizumab and cetuximab given in combination with chemotherapy should be continued until evidence of disease progression or unacceptable toxicity, as per the design of the clinical trials supporting their use.
  - Continuation of bevacizumab after 4–6 cycles of platinum-doublet chemotherapy and bevacizumab (category 1).
  - Continuation of cetuximab after 4–6 cycles of cisplatin, vinorelbine, and cetuximab (category 1).
  - Continuation of pemetrexed after 4–6 cycles of cisplatin and pemetrexed chemotherapy, for patients with histologies other than squamous cell carcinoma (category 1).
  - Continuation of bevacizumab + pemetrexed after 4–6 cycles of bevacizumab, pemetrexed, cisplatin/carboplatin, for patients with histologies other than squamous cell carcinoma.
  - Continuation of gemcitabine after 4–6 cycles of platinum-doublet chemotherapy (category 2B).

- **Switch Maintenance:** Two studies have shown a benefit in progression-free and overall survival with the initiation of pemetrexed or erlotinib after first-line chemotherapy, in patients without disease progression after 4–6 cycles of therapy.
  - Initiation of pemetrexed after 4–6 cycles of first-line platinum-doublet chemotherapy for patients with histologies other than squamous cell carcinoma (category 2B).
  - Initiation of erlotinib after 4–6 cycles of first-line platinum-doublet chemotherapy (category 2B).
  - Initiation of docetaxel after 4–6 cycles of first-line platinum-doublet chemotherapy in patients with squamous cell carcinoma (category 2B).

- Close surveillance of patients without therapy is a reasonable alternative to maintenance.

**Subsequent Therapy for Advanced & Metastatic Disease**

- In patients who have experienced disease progression either during or after first-line therapy, single-agent docetaxel, pemetrexed, or erlotinib are established second-line agents.
  - Nivolumab improves survival when compared with docetaxel.
  - Pembrolizumab improves overall survival in PD-L1 positive tumors when compared with docetaxel.
  - Docetaxel is superior to vinorelbine or ifosfamide.
  - Pemetrexed is considered equivalent to docetaxel with less toxicity in patients with adenocarcinoma and large cell carcinoma.
  - Ramucirumab + docetaxel improves survival when compared to docetaxel alone.
  - Erlotinib is superior to best supportive care.

- If not already given, options for patients with PS 0–2 include docetaxel, pemetrexed (nonsquamous), erlotinib, or gemcitabine (category 2B for all options).

**continued**
### Systemic Therapy for Advanced & Metastatic Disease4 (continued)

#### Subsequent Therapy for Advanced & Metastatic Disease4 (continued)

<table>
<thead>
<tr>
<th>REGIMEN</th>
<th>DOISING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nivolumab (Category 1)51,49</td>
<td>Day 1: Nivolumab 240mg IV over 60 minutes every 2 weeks until disease progression or unacceptable toxicity.</td>
</tr>
<tr>
<td>Pembrolizumab (Category 1)50,51</td>
<td>Day 1: Pembrolizumab 2mg/kg IV. Repeat cycle every 3 weeks until disease progression or unacceptable toxicity.</td>
</tr>
<tr>
<td>Docetaxel55,36</td>
<td>Day 1: Docetaxel 75mg/m² IV over 1 hour. Repeat cycle every 3 weeks.</td>
</tr>
<tr>
<td>Pemetrexed46</td>
<td>Day 1: Pemetrexed 500mg/m² IV. Repeat cycle every 3 weeks.</td>
</tr>
<tr>
<td>Gemcitabine38-40</td>
<td>Days 1 and 8: Gemcitabine 1,250mg/m² IV. Repeat cycle every 3 weeks.</td>
</tr>
<tr>
<td>Ramucirumab + docetaxel41</td>
<td>Day 1: Ramucirumab 10mg/kg IV + docetaxel 75mg/m² IV. Repeat cycle every 3 weeks.</td>
</tr>
</tbody>
</table>

#### First-line Targeted Therapy for Advanced & Metastatic Disease4

**Sensitizing EGFR Mutation Positive1**

- **Erlotinib (Category 1)52**: Erlotinib 150mg orally once daily until disease progression or unacceptable toxicity.
- **Afatinib (Category 1)53**: Afatinib 40mg orally once daily until disease progression or unacceptable toxicity.
- **Gefitinib (Category 1)54**: Gefitinib 250mg orally once daily until disease progression or unacceptable toxicity.

**ALK Positive4**

- **Crizotinib (Category 1)55**: Crizotinib 250mg orally twice daily until disease progression or unacceptable toxicity.

**Subsequent Targeted Therapy for Advanced & Metastatic Disease4**

**Sensitizing EGFR Mutation Positive1**

- **Osimertinib56**: Osimertinib 80mg orally once daily until disease progression or unacceptable toxicity.
- **Erlotinib52**: Erlotinib 150mg orally once daily until disease progression or unacceptable toxicity.
- **Afatinib53**: Afatinib 40mg orally once daily until disease progression or unacceptable toxicity.
- **Gefitinib54**: Gefitinib 250mg orally once daily until disease progression or unacceptable toxicity.

**ALK Positive4**

- **Crizotinib55**: Crizotinib 250mg orally twice daily until disease progression or unacceptable toxicity.
- **Ceritinib57**: Ceritinib 750mg orally once daily until disease progression or unacceptable toxicity.
- **Alectinib58**: Alectinib 600mg orally twice daily until disease progression or unacceptable toxicity.

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### References

References


