NON-SMALL CELL LUNG CANCER TREATMENT REGIMENS (Part 1 of 8)

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 health care 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 become 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 NCCN 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[1]

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

REGIMEN	DOSING
Cisplatin + vinorelbine[2-4]	**Days 1 and 8:** Cisplatin 50mg/m² IV **Days 1, 8, 15 and 22:** Vinorelbine 25mg/m² IV. Repeat cycle every 4 weeks for 4 cycles. **OR** **Day 1:** Cisplatin 100mg/m² IV **Days 1, 8, 15 and 22:** Vinorelbine 30mg/m² IV. Repeat cycle every 4 weeks for 4 cycles. **OR** **Day 1:** Cisplatin 75–80mg/m² **Days 1 and 8:** Vinorelbine 25–30mg/m². Repeat every 3 weeks for 4 cycles.
Cisplatin + etoposide[3]	**Day 1:** Cisplatin 100mg/m² IV **Days 1–3:** Etoposide 100mg/m² IV. Repeat cycle every 4 weeks for 4 cycles.
Cisplatin + gemcitabine[5]	**Day 1:** Cisplatin 75mg/m² IV **Days 1 and 8:** Gemcitabine 1,250mg/m² IV. Repeat cycle every 3 weeks.
Cisplatin + docetaxel[6]	**Day 1:** Docetaxel 75mg/m² IV + cisplatin 75mg/m² IV. Repeat every 3 weeks for 4 cycles.
Cisplatin + pemetrexed[7]	**Day 1:** Cisplatin 75mg/m² IV + pemetrexed 500mg/m² IV.* Repeat every 3 weeks for 4 cycles.
For patients with comorbidities or patients not able to tolerate cisplatin[1]	
Paclitaxel + carboplatin[8]	**Day 1:** Paclitaxel 200mg/m² IV + carboplatin AUC 6mg • min/mL IV. Repeat cycle every 3 weeks for 4 cycles.

Chemotherapy Regimens Used With Radiation Therapy (RT)[1]

Concurrent Chemotherapy/RT[1]	
Cisplatin + etoposide[9,10,a,b]	**Days 1, 8, 29 and 36:** Cisplatin 50mg/m² IV **Days 1–5 and 29–33:** Etoposide 50mg/m² IV Concurrent thoracic radiotherapy 1.8Gy/day for 5 days/week (total dose, 61Gy).
Cisplatin + vinblastine[10,a,b]	**Days 1 and 29:** Cisplatin 100mg/m² IV **Days 1, 8, 15, 22 and 29:** Vinblastine 5mg/m² IV with concurrent thoracic radiotherapy (total dose, 60Gy).
Carboplatin + pemetrexed (nonsquamous)[11,a,b]	**Day 1:** Carboplatin AUC 5mg • min/mL IV **Day 1:** Pemetrexed 500 mg/m² IV with concurrent thoracic radiotherapy. Repeat every 3 weeks for 4 cycles.
Cisplatin + pemetrexed (nonsquamous)[12,13]	**Day 1:** Cisplatin 75 mg/m² IV. **Day 1:** Pemetrexed 500 mg/m² IV with concurrent thoracic radiotherapy.[a,b] Repeat every 3 weeks for 3 cycles ± additional 4 cycles of pemetrexed 500mg/m².[b]
Paclitaxel + carboplatin[14]	Paclitaxel 45-50mg/m² IV + carboplatin AUC 2mg • min/mL IV weekly with concurrent thoracic radiotherapy (total dose, 60Gy)[a,b] given 5 days per weeks in 2Gy fractions[a,b] ± additional 2 cycles of paclitaxel 200mg/m² and carboplatin AUC 6mg • min/mL IV.[b]
Sequential Chemotherapy/RT (Adjuvant)[1]	
Cisplatin + vinblastine[10]	**Days 1 and 29:** Cisplatin 100mg/m² IV. **Days 1, 8, 15, 22 and 29:** Vinblastine 5mg/m² IV; followed by thoracic radiotherapy with 60Gy in 30 fractions beginning on Day 50.
Paclitaxel + carboplatin[15]	**Day 1:** Paclitaxel 200mg/m² IV over 3 hours + carboplatin AUC 6mg • min/mL IV over 1 hour. Repeat every 3 weeks for 2 cycles; **followed by** thoracic radiotherapy 63Gy beginning on Day 42.
Consolidation Therapy[1]	
Note: For patients with unresectable stage III NSCLC, PS 0-1, and no disease progression after 2 or more cycles of definitive chemoradiation	
Durvalumab[16]	**Day 1:** Durvalumab 10mg/kg Repeat every 2 weeks for up to 12 months.

continued

NON-SMALL CELL LUNG CANCER TREATMENT REGIMENS (Part 2 of 8)

Systemic Therapy for Advanced & Metastatic Disease[1]

Principles of Therapy[1]

- 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[1]

Principles of Therapy[1]

- 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 2 cycles, then every 2–4 cycles with CT of known sites of disease with or without contrast or when clinically indicated.

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

Bevacizumab + carboplatin + paclitaxel (Category 1)[17,c,d]	**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[18,d]	**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[19,d]	**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)[20]	**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)[21,c]	**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)[22,23]	**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/mLIV Days 1–14: Etoposide 50mg orally twice daily **Third Course** Day 1: Carboplatin AUC 5mg • min/mLIV 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)[24]	**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)[25,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 (Category 1)[26]	**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)[21,c]	**Day 1:** Cisplatin 75mg/m² IV + docetaxel 75mg/m² IV. Repeat cycle every 3 weeks.

continued

Systemic Therapy for Advanced & Metastatic Disease[1] (continued)

First-line Systemic Therapy Options[1] (continued)

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

REGIMEN	DOSING
Cisplatin + etoposide (Category 1)[27]	**Day 1:** Cisplatin 100mg/m² IV **Days 1–3:** Etoposide 100mg/m² IV. Repeat cycle every 3 weeks for up to 6 cycles.
Cisplatin + gemcitabine (Category 1)[25,28]	**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.
Cisplatin + paclitaxel (Category 1)[29,c]	**Day 1:** Paclitaxel 135mg/m² IV over 24 hours **Day 2:** Cisplatin 75mg/m² IV. Repeat cycle every 3 weeks.
Cisplatin + pemetrexed (Category 1)[28]	**Day 1:** Pemetrexed 500mg/m² IV + cisplatin 75mg/m² IV. Repeat cycle every 3 weeks.
Gemcitabine + docetaxel (Category 1)[30,c]	**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 (Category 1)[31]	**Days 1 and 8:** Vinorelbine 25mg/m² IV + gemcitabine 1,000mg/m² IV. Repeat cycle every 3 weeks.
Pembrolizumab + carboplatin + pemetrexed[32,f]	**Days 1:** Pembrolizumab 200mg IV + pemetrexed 500mg/m² IV + carboplatin AUC 5mg · min/mL IV. Repeat cycle every 3 weeks for up to 4 cycles; **followed by:** **Days 1:** Pembrolizumab 200mg IV every 3 weeks for 24 months **Days 1:** Pemetrexed 500mg/m² IV every 3 weeks (optional, indefinite)
Adenocarcinoma, Large Cell, NSCLC NOS (PS 2)[1]	
Albumin-bound paclitaxel[33,c]	**Day 1:** Albumin-bound paclitaxel 260mg/m² IV. Repeat cycle every 3 weeks.
Carboplatin + albumin-bound paclitaxel[34,35]	**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[21,c]	**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[22,23]	**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[24]	**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[25,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[26]	**Day 1:** Pemetrexed 500mg/m² IV + carboplatin AUC 6mg • min/mL IV. Repeat cycle every 3 weeks for up to 6 cycles.
Docetaxel[36,37,c]	**Day 1:** Docetaxel 75mg/m² IV over 1 hour. Repeat cycle every 3 weeks.
Gemcitabine[38-40]	**Days 1 and 8:** Gemcitabine 1,250mg/m² IV. Repeat cycle every 3 weeks.
Gemcitabine + docetaxel[30,c]	**Days 1 and 8:** Gemcitabine 1,000mg/m² IV **Day 8:** Docetaxel 85mg/m² IV. Repeat cycle every 3 weeks for 8 cycles.

continued

Systemic Therapy for Advanced & Metastatic Disease[1] (continued)

First-line Systemic Therapy Options[1,c] (continued)

Adenocarcinoma, Large Cell, NSCLC NOS (PS 2)[1] (continued)

REGIMEN	DOSING
Gemcitabine + vinorelbine[31]	**Days 1 and 8:** Vinorelbine 25mg/m² IV + gemcitabine 1,000mg/m² IV. Repeat cycle every 3 weeks.
Paclitaxel[41-43,c]	**Days 1, 8, and 15:** Paclitaxel 80mg/m² IV. Repeat cycle every 4 weeks for up to 4 cycles.
Pemetrexed[44]	**Day 1:** Pemetrexed 500mg/m² IV. Repeat cycle every 3 weeks.

Squamous Cell Carcinoma (PS 0-1)[1]

Carboplatin + albumin-bound paclitaxel (Category 1)[20,c]	**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)[21,c]	**Day 1:** Docetaxel 75mg/m² IV + carboplatin AUC 6mg • min/mL IV. Repeat cycle every 3 weeks until disease progression or unacceptable toxicity.
Carboplatin + gemcitabine (Category 1)[24]	**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)[25,c]	**Day 1:** Paclitaxel 200mg/m² IV + carboplatin AUC 6mg • min/mL IV. Repeat every 3 weeks until disease progression or unacceptable toxicity.
Cisplatin + docetaxel (Category 1)[21,c]	**Day 1:** Cisplatin 75mg/m² IV + docetaxel 75mg/m² IV. Repeat cycle every 3 weeks.
Cisplatin + etoposide (Category 1)[27]	**Day 1:** Cisplatin 100mg/m² IV **Days 1–3:** Etoposide 100mg/m² IV. Repeat cycle every 3 weeks for up to 6 cycles.
Cisplatin + gemcitabine (Category 1)[25,28]	**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.
Cisplatin + paclitaxel (Category 1)[29,c]	**Day 1:** Paclitaxel 135mg/m² IV over 24 hours **Day 2:** Cisplatin 75mg/m² IV. Repeat cycle every 3 weeks.
Gemcitabine + docetaxel (Category 1)[30,c]	**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 (Category 1)[31]	**Days 1 and 8:** Vinorelbine 25mg/m² IV + gemcitabine 1,000mg/m² IV. Repeat cycle every 3 weeks.

Squamous Cell Carcinoma (PS 2)[1]

Albumin-bound paclitaxel[33]	**Day 1:** Albumin-bound paclitaxel 260mg/m² IV. Repeat cycle every 3 weeks.
Carboplatin + albumin-bound paclitaxel[34,35]	**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[21,c]	**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[22,23]	**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[24]	**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.

continued

Systemic Therapy for Advanced & Metastatic Disease[1] (continued)

First-line Systemic Therapy Options[1,c] (continued)

Squamous Cell Carcinoma (PS 2)[1] (continued)

REGIMEN	DOSING
Carboplatin + paclitaxel[25,c]	**Day 1:** Paclitaxel 200mg/m² IV + carboplatin AUC 6mg • min/mL IV. Repeat every 3 weeks until disease progression or unacceptable toxicity.
Docetaxel[36,37,c]	**Day 1:** Docetaxel 75mg/m² IV over 1 hour. Repeat cycle every 3 weeks.
Gemcitabine[38-40]	**Days 1 and 8:** Gemcitabine 1,250mg/m² IV. Repeat cycle every 3 weeks.
Gemcitabine + docetaxel[30,c]	**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[31]	**Days 1 and 8:** Vinorelbine 25mg/m² IV + gemcitabine 1,000mg/m² IV. Repeat cycle every 3 weeks.
Paclitaxel[41-43]	**Days 1, 8, and 15:** Paclitaxel 80mg/m² IV. Repeat cycle every 4 weeks for up to 4 cycles.

Maintenance Therapy for Advanced & Metastatic Disease[1]

Principles of Maintenance Therapy[1]

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 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 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[1]

Principles of Subsequent Therapy[1]

- In patients who have experienced disease progression either during or after first-line therapy, single-agent docetaxel, or pemetrexed 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.
- If not already given, options for patients with PS 0–2 include docetaxel, pemetrexed (nonsquamous), erlotinib, or gemcitabine (category 2B for all options).
- Response assessment with CT of known sites with or without contrast every 6–12 weeks.

REGIMEN	DOSING
Nivolumab (Category 1)[45,46]	**Day 1:** Nivolumab 240mg IV over 60 minutes every 2 weeks until disease progression or unacceptable toxicity.
Pembrolizumab (Category 1)[47,57,e,f]	**Day 1:** Pembrolizumab 2mg/kg IV. Repeat cycle every 3 weeks until disease progression or unacceptable toxicity.
Atezolizumab (Category 1)[48,65,f]	**Day 1:** Atezolizumab 1200mg IV over 1 hour. Repeat cycle every 3 weeks until disease progression or unacceptable toxicity.
Docetaxel[36,37]	**Day 1:** Docetaxel 75mg/m² IV over 1 hour. Repeat cycle every 3 weeks.
Pemetrexed[44]	**Day 1:** Pemetrexed 500mg/m² IV. Repeat cycle every 3 weeks.
Gemcitabine[38-40]	**Days 1 and 8:** Gemcitabine 1,250mg/m² IV. Repeat cycle every 3 weeks.
Ramucirumab + docetaxel[49]	**Day 1:** Ramucirumab 10mg/kg IV + docetaxel 75mg/m² IV. Repeat cycle every 3 weeks.

continued

NON-SMALL CELL LUNG CANCER TREATMENT REGIMENS (Part 6 of 8)

First-line Targeted Therapy for Advanced & Metastatic Disease[1]

Sensitizing *EGFR* Mutation Positive[1]

REGIMEN	DOSING
Erlotinib (Category 1)[58]	Erlotinib 150mg orally once daily until disease progression or unacceptable toxicity.
Afatinib (Category 1)[59]	Afatinib 40mg orally once daily until disease progression or unacceptable toxicity.
Gefitinib (Category 1)[60]	Gefitinib 250mg orally once daily until disease progression or unacceptable toxicity.

ALK Positive[1]

Crizotinib (Category 1)[56,61]	Crizotinib 250mg orally twice daily until disease progression or unacceptable toxicity.
Alectinib (Category 1) Preferred[52,53,64]	**Day 1:** Alectinib 600mg orally twice daily. Repeat until disease progression or unacceptable toxicity.
Ceritinib (Category 1)[54,55,63]	**Day 1:** Ceritinib 750mg orally once daily. Repeat until disease progression or unacceptable toxicity.

ROS1 Rearrangement Positive[1]

Crizotinib[56,61]	**Day 1:** Crizotinib 250mg orally twice daily. Repeat until disease progression or unacceptable toxicity.

BRAF V600E Mutation Positive[1]

Dabrafenib + trametinib[50,68,69,g]	**Day 1:** Dabrafenib 150mg orally twice daily **Day 1:** Trametinib 2mg orally once daily Repeat until disease progression or unacceptable toxicity.

See First-line therapy options for adenocarcinoma/squamous cell carcinoma.

PD-L1 Expression Positive[1]

Pembrolizumab (Category 1)[51,e]	**Day 1:** Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks until disease progression or unacceptable toxicity

Subsequent Targeted Therapy for Advanced & Metastatic Disease[1]

Sensitizing *EGFR* Mutation Positive[1,h]

Osimertinib (Category 1)[62,i]	Osimertinib 80mg orally once daily until disease progression or unacceptable toxicity.
Erlotinib[58]	Erlotinib 150mg orally once daily until disease progression or unacceptable toxicity.
Afatinib[59]	Afatinib 40mg orally once daily until disease progression or unacceptable toxicity.
Gefitinib[60]	Gefitinib 250mg orally once daily until disease progression or unacceptable toxicity.

ALK Positive[1]

Crizotinib[56,61]	Crizotinib 250mg orally twice daily until disease progression or unacceptable toxicity.
Ceritinib[54,55,63]	Ceritinib 750mg orally once daily until disease progression or unacceptable toxicity.
Alectinib[52,53,64]	Alectinib 600mg orally twice daily until disease progression or unacceptable toxicity.
Brigatinib[67]	**Days 1-7:** Brigatinib 90mg orally once daily **followed by**: **Day 1:** Brigatinib 180mg orally once daily Repeat until disease progression or unacceptable toxicity. Refer to guidelines.

ROS1 Rearrangement Positive[1]

See first-line therapy options for adenocarcinoma, squamous cell carcinoma, or PD-L1 expression positive (>50%)

BRAF V600E Mutation Positive[1]

If progression occurs after dabrafenib + trametinib, recommendation is first-line therapy options for adenocarcinoma/squamous cell carcinoma.
If progression occurs after first-line therapy options for adenocarcinoma/squamous cell carcinoma, recommendation is dabrafenib + trametinib.

PD-L1 Expression Positive[1]

See first-line therapy options for adenocarcinoma or squamous cell carcinoma

[a] Regimens can be used as neoadjuvant/preoperative/induction chemoradiotherapy.
[b] Regimens can be used as adjuvant or definitive concurrent chemotherapy/RT.
[c] Albumin-bound paclitaxel may be substituted for either paclitaxel or docetaxel in patients who have experienced hypersensitivity reactions after receiving paclitaxel or docetaxel despite premedication, or for patients where the standard premedications (ie. Dexamethasone, H2 blockers, H1 blockers) are contraindicated.
[d] Bevacizumab should be given until progression.
[e] Pembrolizumab is approved for patients with NSCLC with PD-L1 expression levels >1%, as determined by an FDA-approved test.
[f] If pembrolizumab not previously given.
[g] Single-agent vemurafenib or dabrafenib are treatment options if the combination of dabrafenib + trametinib is not tolerated.
[h] T790M testing should be performed upon progression.
[i] Osimertinib if T790M(+) disease, if T790M(-) refer to first line therapy options for adenocarcinoma, squamous cell carcinoma, or PD-L1 expression positive (>50%). Refer to Treatment Guidelines.

continued

References

1. Referenced with permission from NCCN Clinical Practice Guidelines in Oncology™ Non-Small Cell Lung Cancer. v 9.2017. Available at: http://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed October 3, 2017.
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