**BREAST CANCER (INVASIVE) TREATMENT REGIMENS**  
(Part 1 of 4)

**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 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 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.

### Neoadjuvant/Adjuvant Chemotherapy

**NOTE:** All recommendations are category 2A unless otherwise indicated.

#### Preferred Regimens for HER2-negative Disease

<table>
<thead>
<tr>
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| **Dose-dense AC followed by paclitaxel (Category 1)** | **Day 1:** Doxorubicin 60mg/m² IV  
**Day 1:** Cyclophosphamide 600mg/m² IV.  
Repeat cycle every 14 days for 4 cycles (all cycles are with myeloid growth factor support; refer to NCCN Guidelines for Myeloid Growth Factors), followed by:  
**Day 1:** Paclitaxel 175mg/m² via 3-hour IV infusion.  
Repeat cycle every 14 days for 4 cycles (all cycles are with myeloid growth factor support). |

| **Dose-dense AC followed by weekly paclitaxel (Category 1)** | **Day 1:** Doxorubicin 60mg/m² IV  
**Day 1:** Cyclophosphamide 600mg/m² IV.  
Repeat cycle every 14 days for 4 cycles, followed by:  
**Day 1:** Paclitaxel 80mg/m² via 1-hour IV infusion weekly for 12 weeks. |

| **TC (Category 1)** | **Day 1:** Docetaxel 75mg/m² IV  
**Day 1:** Cyclophosphamide 600mg/m² IV.  
Repeat cycle every 21 days for 4 cycles (all cycles are with myeloid growth factor support). |

#### Other Regimens for HER2-negative Disease

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| **Dose-dense AC (Category 1)** | **Day 1:** Doxorubicin 60mg/m² IV  
**Day 1:** Cyclophosphamide 600mg/m² IV.  
Repeat cycle every 14 days for 4 cycles (all cycles are with myeloid growth factor support). |

| **AC (Category 2B)** | **Day 1:** Doxorubicin 60mg/m² IV  
**Day 1:** Cyclophosphamide 600mg/m² IV.  
Repeat cycle every 21 days for 4 cycles. |

| **TAC (Category 1)** | **Day 1:** Docetaxel 75mg/m² IV  
**Day 1:** Doxorubicin 50mg/m² IV  
**Day 1:** Cyclophosphamide 500mg/m² IV.  
Repeat cycle every 21 days for 6 cycles (all cycles are with myeloid growth factor support). |

| **CMF (Category 1)** | **Days 1-14:** Cyclophosphamide 100mg/m² orally  
**Days 1 and 8:** Methotrexate 40mg/m² IV  
**Days 1 and 8:** 5-fluorouracil 600mg/m² IV.  
Repeat cycle every 28 days for 6 cycles. |

| **AC followed by docetaxel (Category 1)** | **Day 1:** Doxorubicin 60mg/m² IV  
**Day 1:** Cyclophosphamide 600mg/m² IV.  
Repeat cycle every 21 days for 4 cycles, followed by:  
**Day 1:** Docetaxel 100mg/m² IV.  
Repeat cycle every 21 days for 4 cycles. |

| **AC followed by weekly paclitaxel (Category 1)** | **Day 1:** Doxorubicin 60mg/m² IV  
**Day 1:** Cyclophosphamide 600mg/m² IV.  
Repeat cycle every 21 days for 4 cycles, followed by:  
**Day 1:** Paclitaxel 80mg/m² via 1-hour IV infusion weekly for 12 weeks. |

| **EC (Category 1)** | **Day 1:** Epirubicin 100mg/m² IV  
**Day 1:** Cyclophosphamide 830mg/m² IV.  
Repeat cycle every 21 days for 8 cycles. |
## Preferred Regimens for HER2-positive Disease

### REGIMEN

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<tr>
<td><strong>AC followed by paclitaxel + trastuzumab</strong>&lt;sup&gt;10,j,k&lt;/sup&gt;</td>
<td><strong>Day 1:</strong> Doxorubicin 60mg/m² IV  &lt;br&gt; <strong>Day 1:</strong> Cyclophosphamide 600mg/m² IV. &lt;br&gt; Repeat cycle every 21 days for 4 cycles, <strong>followed by:</strong>  &lt;br&gt; Paclitaxel 80mg/m² via 1-hour IV infusion weekly for 12 weeks, <strong>with:</strong>  &lt;br&gt; Trastuzumab 4mg/kg IV with first dose of paclitaxel, <strong>followed by:</strong>  &lt;br&gt; Trastuzumab 2mg/kg IV weekly to complete 1 year of treatment.  &lt;br&gt; As an alternative, trastuzumab 6mg/kg IV every 21 days may be used following the completion of paclitaxel, and given to complete 1 year of trastuzumab treatment.</td>
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<td><strong>AC followed by paclitaxel + trastuzumab + pertuzumab</strong>&lt;sup&gt;10,j,k&lt;/sup&gt;</td>
<td><strong>Day 1:</strong> Doxorubicin 60mg/m² IV  &lt;br&gt; <strong>Day 1:</strong> Cyclophosphamide 600mg/m² IV.  &lt;br&gt; Repeat cycle every 21 days for 4 cycles, <strong>followed by:</strong>  &lt;br&gt; <strong>Day 1:</strong> Pertuzumab 840mg IV followed by 420mg IV  &lt;br&gt; <strong>Day 1:</strong> Trastuzumab 8mg/kg IV followed by 6mg/kg IV  &lt;br&gt; <strong>Days 1, 8, and 15:</strong> Paclitaxel 80mg/m² IV.  &lt;br&gt; Repeat cycle every 21 days for 4 cycles,  &lt;br&gt; <strong>Day 1:</strong> Trastuzumab 6mg/kg IV.  &lt;br&gt; Repeat cycle every 21 days to complete 1 year of trastuzumab therapy.</td>
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<td><strong>TCH</strong>&lt;sup&gt;12,k&lt;/sup&gt;</td>
<td><strong>Day 1:</strong> Docetaxel 75mg/m² IV  &lt;br&gt; <strong>Day 1:</strong> Carboplatin AUC 6mg • min/mL IV.  &lt;br&gt; Repeat cycle every 21 days for 6 cycles, <strong>with:</strong>  &lt;br&gt; Trastuzumab 4mg/kg IV week 1, followed by 2mg/kg IV for 17 weeks, <strong>followed by:</strong>  &lt;br&gt; Trastuzumab 6mg/kg IV every 21 days to complete 1 year of trastuzumab therapy.  &lt;br&gt; <strong>OR</strong>  &lt;br&gt; Trastuzumab 8mg/kg IV week 1, <strong>followed by:</strong>  &lt;br&gt; Trastuzumab 6mg/kg IV every 21 days to complete 1 year of trastuzumab therapy.</td>
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<td><strong>TCH chemotherapy + pertuzumab</strong>&lt;sup&gt;13,k&lt;/sup&gt;</td>
<td><strong>Day 1:</strong> Trastuzumab 8mg/kg IV followed by 6mg/kg IV  &lt;br&gt; <strong>Day 1:</strong> Pertuzumab 840mg IV followed by 420mg IV  &lt;br&gt; <strong>Day 1:</strong> Docetaxel 75mg/m² IV  &lt;br&gt; <strong>Day 1:</strong> Carboplatin AUC 6mg • min/mL IV.  &lt;br&gt; Repeat cycle every 21 days for 6 cycles, <strong>followed by:</strong>  &lt;br&gt; Trastuzumab 6mg/kg IV every 21 days to complete 1 year of trastuzumab therapy.</td>
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### Other Regimens for HER2-positive Disease<sup>5,k,g,h,i</sup>

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<td><strong>AC followed by docetaxel + trastuzumab</strong>&lt;sup&gt;12,j,k&lt;/sup&gt;</td>
<td><strong>Day 1:</strong> Doxorubicin 60mg/m² IV  &lt;br&gt; <strong>Day 1:</strong> Cyclophosphamide 600mg/m² IV.  &lt;br&gt; Repeat cycle every 21 days for 4 cycles, <strong>followed by:</strong>  &lt;br&gt; <strong>Day 1:</strong> Docetaxel 100mg/m² IV.  &lt;br&gt; Repeat cycle every 21 days for 4 cycles, <strong>with:</strong>  &lt;br&gt; Trastuzumab 4mg/kg IV week 1, followed by 2mg/kg IV weekly for 11 weeks, <strong>followed by:</strong>  &lt;br&gt; Trastuzumab 6mg/kg IV every 21 days to complete 1 year of trastuzumab therapy.</td>
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<td><strong>AC followed by docetaxel + trastuzumab + pertuzumab</strong>&lt;sup&gt;13,j,k&lt;/sup&gt;</td>
<td><strong>Day 1:</strong> Doxorubicin 60mg/m² IV  &lt;br&gt; <strong>Day 1:</strong> Cyclophosphamide 600mg/m² IV.  &lt;br&gt; Repeat cycle every 21 days for 4 cycles, <strong>followed by:</strong>  &lt;br&gt; <strong>Day 1:</strong> Pertuzumab 840mg IV followed by 420mg IV  &lt;br&gt; <strong>Day 1:</strong> Trastuzumab 8mg/kg IV followed by 6mg/kg IV  &lt;br&gt; <strong>Day 1:</strong> Docetaxel 75–100mg/m² IV.  &lt;br&gt; Repeat cycle every 21 days for 4 cycles, <strong>followed by:</strong>  &lt;br&gt; Trastuzumab 6mg/kg IV every 21 days to complete 1 year of trastuzumab therapy.</td>
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| Docetaxel + cyclophosphamide + trastuzumab\textsuperscript{14,k} | Day 1: Docetaxel 75mg/m\textsuperscript{2} IV  
Day 1: Cyclophosphamide 600mg/m\textsuperscript{2} IV.  
Repeat cycle every 21 days for 4 cycles, \textit{with}: Trastuzumab 4mg/kg IV week 1, \textit{followed by}:
Trastuzumab 2mg/kg IV weekly for 11 weeks, \textit{followed by}:
Trastuzumab 6mg/kg IV every 21 days to complete 1 year of trastuzumab therapy.  
\textbf{OR}  
Trastuzumab 8mg/kg IV week 1, \textit{followed by}:
Trastuzumab 6mg/kg IV every 21 days to complete 1 year of treatment. |
| FEC followed by pertuzumab + trastuzumab + docetaxel\textsuperscript{13,l,k} | Day 1: Fluorouracil 500mg/m\textsuperscript{2} IV  
Day 1: Epirubicin 100mg/m\textsuperscript{2} IV  
Day 1: Cyclophosphamide 600mg/m\textsuperscript{2} IV.  
Repeat cycle every 21 days for 3 cycles, \textit{followed by}:
Day 1: Pertuzumab 840mg IV followed by 420mg IV  
Day 1: Trastuzumab 8mg/kg IV followed by 6mg/kg IV  
Day 1: Docetaxel 75–100mg/m\textsuperscript{2} IV.  
Repeat cycle every 21 days for 3 cycles, \textit{followed by}:
Day 1: Trastuzumab 6mg/kg IV every 21 days to complete 1 year of trastuzumab therapy. |
| FEC followed by pertuzumab + trastuzumab + paclitaxel\textsuperscript{13,l,k} | Day 1: Fluorouracil 500mg/m\textsuperscript{2} IV  
Day 1: Epirubicin 100mg/m\textsuperscript{2} IV  
Day 1: Cyclophosphamide 600mg/m\textsuperscript{2} IV.  
Repeat cycle every 21 days for 3 cycles, \textit{followed by}:
Day 1: Pertuzumab 840mg IV followed by 420mg IV  
Day 1: Trastuzumab 8mg/kg IV followed by 6mg/kg IV  
Days 1, 8, and 15: Paclitaxel 80mg/m\textsuperscript{2} IV.  
Repeat cycle every 21 days for 3 cycles, \textit{followed by}:
Day 1: Trastuzumab 6mg/kg IV every 21 days to complete 1 year of trastuzumab therapy. |
| Paclitaxel + trastuzumab\textsuperscript{15,k,l} | Day 1: Paclitaxel 80mg/m\textsuperscript{2} IV weekly for 12 weeks, \textit{with}  
Trastuzumab 4mg/kg IV with first dose of paclitaxel, \textit{followed by}:
Trastuzumab 2mg/kg IV weekly to complete 1 year of treatment.  
As an alternative, trastuzumab 6mg/kg IV every 21 days may be used following the completion of paclitaxel, and given to complete 1 year of trastuzumab therapy. |
| Pertuzumab + trastuzumab + docetaxel followed by FEC\textsuperscript{16,l,k} | Day 1: Pertuzumab 840mg IV followed by 420mg IV  
Day 1: Trastuzumab 8mg/kg IV followed by 6mg/kg IV  
Day 1: Docetaxel 75–100mg/m\textsuperscript{2} IV.  
Repeat cycle every 21 days for 4 cycles, \textit{followed by adjuvant therapy}:
Day 1: Fluorouracil 600mg/m\textsuperscript{2} IV  
Day 1: Epirubicin 90mg/m\textsuperscript{2} IV  
Day 1: Cyclophosphamide 600mg/m\textsuperscript{2} IV  
Day 1: Trastuzumab 6mg/kg IV  
Repeat cycle every 21 days for 3 cycles, \textit{followed by}:
Day 1: Trastuzumab 6mg/kg IV every 21 days to complete 1 year of trastuzumab therapy. |
| Pertuzumab + trastuzumab + paclitaxel followed by FEC\textsuperscript{16,l,k} | Day 1: Pertuzumab 840mg IV followed by 420mg IV  
Day 1: Trastuzumab 8mg/kg IV followed by 6mg/kg IV  
Days 1, 8, and 15: Paclitaxel 80mg/m\textsuperscript{2} IV.  
Repeat cycle every 21 days for 4 cycles, \textit{followed by adjuvant therapy}:
Day 1: Fluorouracil 600mg/m\textsuperscript{2} IV  
Day 1: Epirubicin 90mg/m\textsuperscript{2} IV  
Day 1: Cyclophosphamide 600mg/m\textsuperscript{2} IV  
Day 1: Trastuzumab 6mg/kg IV  
Repeat cycle every 21 days for 3 cycles, \textit{followed by}:
Day 1: Trastuzumab 6mg/kg IV every 21 days to complete 1 year of trastuzumab therapy. |
a The selection, dosing, and administration of anticancer agents and the management of associated toxicities are complex. Modifications of drug dose and schedule and initiation of supportive care interventions are often necessary because of expected toxicities and individual patient variability, prior treatment, and comorbidity. The optimal delivery of anticancer agents therefore requires a healthcare delivery team experienced in the use of anticancer agents and the management of associated toxicities in patients with cancer.

b Retrospective evidence suggests that anthracycline-based chemotherapy regimens may be superior to nonanthracycline-based regimens in patients with HER2-positive tumors.

c Randomized clinical trials demonstrate that the addition of a taxane to anthracycline-based chemotherapy provides an improved outcome.

d CMF and radiation therapy may be given concurrently, or the CMF may be given first. All other chemotherapy regimens should be given prior to radiotherapy.

e Chemotherapy and endocrine therapy used as adjuvant therapy should be given sequentially with endocrine therapy following chemotherapy.

f Nab-paclitaxel may be substituted for paclitaxel or docetaxel due to medical necessity (ie, hypersensitivity reaction). If substituted for weekly paclitaxel or docetaxel, then the weekly dose of nab-paclitaxel should not exceed 125mg/m².

g In patients with HER2-positive and axillary node-negative breast cancer, trastuzumab should be incorporated into the adjuvant therapy (category 1). Trastuzumab should also be considered for patients with HER2-positive node-negative tumors ≥1cm (category 1).

h Trastuzumab should optimally be given concurrently with paclitaxel as part of the AC followed by paclitaxel regimen, and should be given for 1 year total duration.

i A pertuzumab-containing regimen can be administered to patients with ≥T2 or ≥N1, HER2-positive, early-stage breast cancer preoperatively. Patients who have not received a pertuzumab-containing regimen can receive adjuvant pertuzumab.

j Trastuzumab given in combination with an anthracycline is associated with significant cardiac toxicity. Concurrent use of trastuzumab and pertuzumab with an anthracycline should be avoided.

evaluate left ventricular ejection fraction (LVEF) before and during treatment. Although the optimal frequency of LVEF assessment during adjuvant trastuzumab therapy is not known, the FDA recommends LVEF measurements every 3 months during treatment.

l Paclitaxel + trastuzumab may be considered for patients with low-risk, stage I, HER2-positive disease, particularly those not eligible for other standard adjuvant regimens due to comorbidities.

References


