## BREAST CANCER HORMONAL TREATMENT

<table>
<thead>
<tr>
<th>Classification</th>
<th>Generic (Brand)</th>
<th>Dose</th>
<th>Common Side Effects (&gt;10%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Selective Estrogen Receptor Modulators (SERMs)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tamoxifen (Nolvadex®)</td>
<td>10 mg PO BID</td>
<td>Menopausal symptoms (hot flashes, atrophic vaginitis), sexual dysfunction (loss of libido), mild nausea/vomiting, weight gain, tumor flare (transient), hepatotoxicity, vaginal bleeding/discharge or irritation. <em>Less common:</em> thromboembolic events (1/100), uterine/endometrial malignancy (1.7/1000); retinitis and cataracts.</td>
<td></td>
</tr>
<tr>
<td>Raloxifene (Evista®)</td>
<td>60 mg PO QD. Patients with hepatic dysfunction may be at greater risk for adverse events. No specific dosing adjustment recommendations at this time</td>
<td>Menopausal symptoms (hot flashes, atrophic vaginitis), sexual dysfunction (loss of libido), mild nausea/vomiting, weight gain, tumor flare (transient), hepatotoxicity, vaginal bleeding/discharge or irritation. Fewer thromboembolic events compared to tamoxifen (2.61/1000); uterine/endometrial malignancy (less than tamoxifen); fewer cases of cataracts with raloxifene.</td>
<td></td>
</tr>
<tr>
<td>Toremifene (Fareston®)</td>
<td>60 mg PO QD Adjustments may be required in liver disease</td>
<td>Similar to tamoxifen.</td>
<td></td>
</tr>
<tr>
<td><strong>Estrogen Receptor Down-regulators</strong></td>
<td>Fulvestrant (Faslodex®)</td>
<td>250 mg IM Q month</td>
<td>Flushing, nausea/vomiting, constipation, diarrhea, weakness, back pain, headache <em>Less common:</em> vaginal bleeding, thromboembolic events, leukopenia.</td>
</tr>
<tr>
<td>Anastrozole (Arimidex®)</td>
<td>1 mg PO QD</td>
<td>Less risk of thromboemboli and endometrial hyperplasia/carcinoma vs. tamoxifen Increased incidence osteoporosis.</td>
<td></td>
</tr>
<tr>
<td>Letrozole (Femara®)</td>
<td>2.5 mg PO QD</td>
<td>Similar to anastrozole.</td>
<td></td>
</tr>
<tr>
<td>Exemestane (Aromasin®)</td>
<td>25 mg PO QD</td>
<td>Similar to anastrozole.</td>
<td></td>
</tr>
<tr>
<td><strong>Progestins</strong></td>
<td>Megestrol acetate (Megace®)</td>
<td>40 mg PO QID</td>
<td>Edema, breakthrough bleeding and amenorrhea, weakness, weight gain, rash <em>Less common:</em> thromboembolic events.</td>
</tr>
<tr>
<td><strong>LHRH Analogs</strong></td>
<td>Goserelin (Zoladex®)</td>
<td>3.6 mg SC Q 28 days</td>
<td>Gynecomastia, menopausal symptoms, sexual dysfunction, hot flashes; osteoporosis.</td>
</tr>
<tr>
<td>Leuprolide acetate (Lupron*, Lupon Depot*; Eligard*)</td>
<td>1 mg SC QD OR 7.5 mg IM Q month OR 22.5 mg IM Q 3 months OR 30 mg IM Q 4 months</td>
<td>Depression, pain, hot flashes, weight gain, nausea/vomiting.</td>
<td></td>
</tr>
</tbody>
</table>

* Side effects listed are reported to occur in more than 10% of patients

BREAST CANCER

BREAST CANCER HORMONAL THERAPY

I. ADJUVANT HORMONAL THERAPY

Anastrozole (postmenopausal only) 1 mg PO QD x 5 years.

Letrozole (postmenopausal only) 2.5 mg PO QD x 5 years.

Tamoxifen 20 mg PO QD x 5 years.

Tamoxifen 20 – 30 mg PO QD x 2 years followed by Anastrozole 1 mg PO QD x 3 years (postmenopausal only). Total duration of therapy is 5 years.

Tamoxifen 20 mg PO QD x 5 years followed by Letrozole 2.5 mg PO QD x 5 years (postmenopausal only).

Tamoxifen 20 mg PO QD x 2–3 years followed by Exemestane 25 mg PO QD x 2–3 years (postmenopausal only). Total duration of therapy is 5 years.

II. METASTATIC HORMONAL THERAPY

Anastrozole (A) 1 mg PO QD or Letrozole (L) 2.5 mg PO QD, first–line (postmenopausal)

Fulvestrant 250 mg IM QMonth (postmenopausal)

Exemestane 25 mg PO QD, second–line after aromatase inhibitors (postmenopausal)

ASCO 2004 Aromatase Inhibitor Use Guidelines
NEOADJUVANT CHEMOTHERAPY TREATMENT

**AC → DOCETAXEL**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Route</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doxorubicin</td>
<td>60 mg/m²</td>
<td>IV</td>
<td>1</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>600 mg/m²</td>
<td>IV</td>
<td>1</td>
</tr>
</tbody>
</table>

Repeat cycle every 21 days for 4 cycles.

*THEN, following a 3 week delay*

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Route</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Docetaxel‡</td>
<td>100 mg/m²</td>
<td>IV</td>
<td>1</td>
</tr>
</tbody>
</table>

Repeat cycle every 21 days for 4 cycles.

‡Routine premedication administered.

NOTE: If a dose of AC needed to be delayed for a neutrophil count of less than 1.5 x 10⁹/L or febrile neutropenia, the remaining cycles were administered with filgrastim 5 micrograms/kg SQ from Day 2 until ANC recovery. All patients are to receive tamoxifen 20 mg PO QD for 5 years starting on the first day of chemotherapy regardless of hormone status. For patients undergoing lumpectomy, radiation therapy was begun within 4 weeks of surgery.

BREAST CANCER
ADJUVANT CHEMOTHERAPY TREATMENT

AC (DOXORUBICIN – CYCLOPHOSPHAMIDE)
Doxorubicin 60 mg/m² IV Day 1
Cyclophosphamide 600 mg/m² IV Day 1

Repeat cycle every 21 days for 4 cycles.


AC → DOCETAXEL – TRASTUZUMAB (AC → TH)
Doxorubicin 60 mg/m² IV Day 1
Cyclophosphamide 600 mg/m² IV Day 1

Repeat cycle every 21 days for 4 cycles.

THEN, following a 3 week delay

Doxcetaxel* 100 mg/m² IV Day 1
Trastuzumab 4 mg/kg load IV** Day 1, Week 1

Followed by

Trastuzumab 2 mg/kg IV*** Weekly

*Routine premedication required; *Administer over 1 hour every 21 days for 4 cycles; **Administer over 90 minutes; ***Administer over 30 minutes.

MAINTENANCE THERAPY (STARTING THE WEEK FOLLOWING THE LAST TRASTUZUMAB DOSE):
Trastuzumab 6 mg/kg IV* Day 1

*Administer over 90 minutes.

Repeat every 21 days to complete one year of total trastuzumab therapy.

NOTE: Use only for high risk/node positive Her-2 positive patients. Adjuvant hormonal or radiation therapy initiated following completion of docetaxel concurrent with maintenance trastuzumab. Serial cardiac monitoring should be performed.

**AC → PACLITAXEL**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doxorubicin</td>
<td>60 mg/m²</td>
<td>IV</td>
<td>Day 1</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>600 mg/m²</td>
<td>IV</td>
<td>Day 1</td>
</tr>
</tbody>
</table>

Repeat cycle every 21 days for 4 cycles.

*THEN, following a 3 week delay*

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paclitaxel‡</td>
<td>175&lt;sup&gt;1&lt;/sup&gt; - 225&lt;sup&gt;2&lt;/sup&gt; mg/m²</td>
<td>IV&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Day 1</td>
</tr>
</tbody>
</table>

<sup>1</sup>Routine premedication required; <sup>2</sup>Administer over 3 hours.

Repeat cycle every 21 days for 4 cycles.

**NOTE:** Used for node positive patients.

**References:**

**AC → PACLITAXEL (DOSE DENSE)**

<table>
<thead>
<tr>
<th>Drug</th>
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<tr>
<td>Doxorubicin</td>
<td>60 mg/m²</td>
<td>IV</td>
<td>Day 1</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>600 mg/m²</td>
<td>IV</td>
<td>Day 1</td>
</tr>
<tr>
<td>Filgrastim</td>
<td>5 mcg/kg/day&lt;sup&gt;4&lt;/sup&gt;</td>
<td>SQ</td>
<td>Days 3 – 10 of each cycle</td>
</tr>
</tbody>
</table>

Repeat cycle every 14 days for 4 cycles.

*THEN, following a 2 week delay*

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paclitaxel‡</td>
<td>175 mg/m²</td>
<td>IV&lt;sup&gt;5&lt;/sup&gt;</td>
<td>Day 1</td>
</tr>
</tbody>
</table>

Repeat cycle every 14 days for 4 cycles.

<sup>1</sup>Routine premedication required; <sup>2</sup>Dose can be rounded to nearest 300 microgram or 480 microgram vial/syringe; <sup>3</sup>Administer over 3 hours.

**References:**
**AC → PACLITAXEL – TRASTUZUMAB**

Doxorubicin  
60 mg/m²  
IV  
Day 1

Cyclophosphamide  
600 mg/m²  
IV  
Day 1

Repeat cycle every 21 days for 4 cycles.

**THEN, following a 3 week delay**

**Paclitaxel**†  
1175 mg/m²  
IV  
Day 1

**OR**

**Paclitaxel**†  
280 mg/m²  
IV  
Weekly

1Repeat cycle every 21 days for 4 cycles, or 2administer weekly for 12 weeks.

*Either one of the above paclitaxel regimens listed above  
IN COMBINATION with trastuzumab as follows*

**Trastuzumab**  
4 mg/kg load  
IV  
Day 1, Week 1

**Followed by**

**Trastuzumab**  
2 mg/kg  
IV  
Weekly*, starting Day 1, Week 2

**MAINTENANCE THERAPY (STARTING THE WEEK FOLLOWING THE LAST TRASTUZUMAB DOSE):**

**Trastuzumab**  
2 mg/kg¹,²  
IV  
Weekly

**OR**

**Trastuzumab**  
6 mg/kg³  
IV  
Day 1**

†Routine premedication required; *Administer weekly for a total of 12 weeks (including the loading dose); **Administer every 3 weeks.

Continue maintenance to complete one total year of trastuzumab therapy.

**NOTE:** Use only for high risk/node positive patients. Adjuvant hormonal or radiation therapy initiated following completion of paclitaxel concurrent with maintenance trastuzumab. Serial cardiac monitoring performed as follows: baseline (before AC = week 0), following AC (month 3), and then repeat again at 6 months, 9 months, and 18 months from the start of therapy.

**AT (DOXORUBICIN – DOCETAXEL)**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dosage</th>
<th>Route</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doxorubicin</td>
<td>60 mg/m²</td>
<td>IV</td>
<td>1</td>
</tr>
<tr>
<td>Docetaxel†</td>
<td>60 mg/m²</td>
<td>IV</td>
<td>1</td>
</tr>
</tbody>
</table>

*Routine premedication required.

NOTE: Ciprofloxacin 500 mg PO BID was administered starting on day 8 for 10 days. Tamoxifen 20 mg PO daily administered for 5 years post chemotherapy for ER and/or PR positive tumor.

Repeat cycle every 21 days for 4 cycles.


**CMF – CLASSICAL (CYCLOPHOSPHAMIDE – METHOTREXATE – 5–FLUOROURACIL)**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dosage</th>
<th>Route</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>100 mg/m²/day</td>
<td>PO</td>
<td>Days 1 - 14</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>40 mg/m²</td>
<td>IV</td>
<td>Days 1 and 8</td>
</tr>
<tr>
<td>5–Fluorouracil</td>
<td>600 mg/m²</td>
<td>IV</td>
<td>Days 1 and 8</td>
</tr>
</tbody>
</table>

NOTE: If using concurrent radiation, reduce the dose of methotrexate to 20 mg/m² (personal communication at ASCO). For patients aged greater than 60 years, the initial methotrexate dose was reduced to 30 mg/m² and the 5–Fluorouracil dose was reduced to 400 mg/m². Chemotherapy was started 2 – 4 weeks after mastectomy. Cyclophosphamide dose rounded to nearest 25 mg and is available as 25 mg and 50 mg tablets.

Repeat cycle every 28 days.


**DOCETAXEL – CYCLOPHOSPHAMIDE**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dosage</th>
<th>Route</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Docetaxel†</td>
<td>75 mg/m²</td>
<td>IV</td>
<td>1</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>600 mg/m²</td>
<td>IV</td>
<td>1</td>
</tr>
</tbody>
</table>

*Routine premedication required.

NOTE: Tamoxifen was administered to hormone receptor–positive breast cancer patients after completing chemotherapy. All chemotherapy was administered before radiation, if indicated.

Repeat cycle every 21 days for 4 cycles.

EPIRUBICIN → CMF

Epirubicin     100 mg/m\(^2\)   IV   Day 1

Repeat cycle every 21 days for 4 cycles.

*Followed by ONE of the following CMF regimens*

- Cyclophosphamide 100 mg/m\(^2\)/day PO Days 1 – 14
- Methotrexate 40 mg/m\(^2\) IV Days 1 and 8
- 5-Fluorouracil 600 mg/m\(^2\) IV Days 1 and 8

NOTE: See notes in CMF regimen.

Repeat cycle every 28 days for 4 cycles.

OR

- Cyclophosphamide 750 mg/m\(^2\) IV Day 1
- Methotrexate 50 mg/m\(^2\) IV Day 1
- 5-Fluorouracil 600 mg/m\(^2\) IV Day 1

Repeat cycle every 21 days for 4 cycles.


FAC (5-FLUOROURACIL – DOXORUBICIN – CYCLOPHOSPHAMIDE)

- 5-Fluorouracil 500 mg/m\(^2\) IV Days 1 and 8
- Doxorubicin 50 mg/m\(^2\) IV Day 1
- Cyclophosphamide 500 mg/m\(^2\) IV Day 1

‘NOTE: The doses in the reference list 400/40/400 mg, however Dr. Hortobagyi recommends 500/50/500 mg doses.

Repeat cycle every 21 days for 4 – 6 cycles.


FEC (5-FLUOROURACIL – EPIRUBICIN – CYCLOPHOSPHAMIDE)

- Cyclophosphamide 75 mg/m\(^2\)/day PO Days 1 – 14
- Epirubicin 60 mg/m\(^2\) IV Days 1 and 8
- 5-Fluorouracil 500 mg/m\(^2\) IV Days 1 and 8

NOTE: PCP prophylaxis (sulfamethoxazole/trimethoprim) was administered for the duration of chemotherapy.

Repeat cycle every 28 days for 6 cycles.

**FE₁₀₀C**

5-Fluorouracil  
500 mg/m²  
Epirubicin  
100 mg/m²  
Cyclophosphamide  
500 mg/m²  

Repeat cycle every 21 days for 6 cycles.


**FE₁₀₀C → DOCETAXEL**

5-Fluorouracil  
500 mg/m²  
Epirubicin  
100 mg/m²  
Cyclophosphamide  
500 mg/m²  

Repeat cycle every 21 days for 3 cycles.

*Followed by*

Docetaxel†  
100 mg/m²  

†Routine premedication required.

Repeat cycle every 21 days for 3 cycles.

NOTE: Tamoxifen 20 mg PO QD was started after completion of chemotherapy and continued for 5 years. Initially the protocol administered this to post-menopausal hormone receptor (HR) positive women only, but the protocol was amended to include pre-menopausal HR women.


**FEC₁₄ (5–FLUOROURACIL – EPIRUBICIN – CYCLOPHOSPHAMIDE) – DOSE DENSE**

5-Fluorouracil  
600 mg/m²  
Epirubicin  
60 mg/m²  
Cyclophosphamide  
600 mg/m²  
Filgrastim  
5 mcg/kg/day  

DOSE MODIFICATIONS: If grade III–IV leucopenia associated with grade I–II thrombocytopenia or grade III–IV thrombocytopenia alone was present, chemotherapy was delayed, and individual doses of the three drugs were reduced by 25% in subsequent cycles. Non-hematological toxicity: if grade II toxicity was present, treatment was delayed until recovery; if grade III–IV toxicity was present, treatment was delayed and the doses of all three drugs were reduced by 25% in subsequent cycles.

NOTE: Patients with ER/PR positive tumors received tamoxifen 20 mg PO QD for 5 years following completion of chemotherapy.

Repeat cycle every 14 days for 6 cycles.

TAC (DOCETAXEL – DOXORUBICIN – CYCLOPHOSPHAMIDE)

Doxorubicin 50 mg/m² IV* Day 1
Cyclophosphamide 500 mg/m² IV** Day 1

Followed 1 hour later by

Docetaxel† 75 mg/m² IV*** Day 1

*Routine premedication required; *Administer over 15 minutes; **Administer over 1–5 minutes; ***Administer over 1 hour.

Repeat cycle every 21 days for 6 cycles.


TCH (DOCETAXEL – CARBOPLATIN – TRASTUZUMAB)

Docetaxel† 75 mg/m² IV Day 1
Carboplatin AUC 6 IV Day 1
Trastuzumab 4 mg/kg load IV Day 1, Week 1

Followed by

Trastuzumab 2 mg/kg IV Weekly*

Repeat cycle every 21 days for 6 cycles.

MAINTENANCE THERAPY (STARTING FOLLOWING THE COMPLETION OF THE CHEMOTHERAPY):

Trastuzumab 6 mg/kg IV Day 1**

Repeat cycle every 21 days for 1 year.

*Routine premedication required; *Administer weekly for a total of 18 weeks (including the loading dose); **Administer every 3 weeks.

BREAST CANCER
METASTATIC CHEMOTHERAPY TREATMENT: SINGLE AGENTS

CAPECITABINE

Capecitabine  1000 – 1250 mg/m² BID PO  Days 1 – 14

NOTE: Capecitabine available as 150 mg and 500 mg tablets. Reference lists a dose of 2510 mg/m²/day, but practically administered as 1000 – 1250 mg/m² BID. Take within 30 minutes following a meal.

Repeat cycle every 21 days.


DOCETAXEL (WEEKLY)

Docetaxel†  40 mg/m²  IV*  Days 1, 8, 15, 22, 29 and 36

*Routine premedication administered; †Administer over 1 hour.

Repeat cycle every 8 weeks.


DOCETAXEL (EVERY 3 WEEKS)

Docetaxel†  160 – 2100 mg/m²  IV*  Day 1

*Routine premedication administered; †Administer over 1 hour.

Repeat cycle every 21 days.


GEMCITABINE

Gemcitabine  800 mg/m²  IV*  Days 1, 8 and 15

*Administer over 30 minutes.

NOTE: Patients who completed 1 cycle of chemotherapy could have their subsequent dose increased by up to 20% provided there was no significant hematological toxicity and non hematological toxicity was grade 1 or less.

Repeat cycle every 28 days.

LIPOSOMAL DOXORUBICIN
Liposomal doxorubicin 45 – 60 mg/m² IV* Day 1

*Administer over 1 hour.
Repeat cycle every 21 – 28 days for a maximum of 6 cycles.


PACLITAXEL (WEEKLY)
Paclitaxel* 80¹ – 100² mg/m² IV* Q week

*Routine premedication administered; *Administer as a 1 hour infusion.

NOTE: More neuropathy, but study showed better response and TTP with weekly compared with q 3 weeks¹.


PACLITAXEL (EVERY 3 WEEKS)
Paclitaxel* 175 mg/m² IV* Day 1

*Routine premedication administered; *Administer over 3 hours.

NOTE: Patients who experienced febrile neutropenia or prolonged neutropenia (7 days or longer) were prescribed G–CSF for subsequent cycles to avoid dose decreases¹.
Repeat cycle every 21 days.


PACLITAXEL PROTEIN BOUND PARTICLES (ABRAXANE*)
Abraxane* 260 mg/m² IV Day 1

NOTE: No premedication required.
Repeat cycle every 21 days.

TRASTUZUMAB (WEEKLY)
Trastuzumab    4 mg/kg load    IV*    Day 1, Week 1
Then the following week and then weekly thereafter
Trastuzumab    2 mg/kg    IV**    Weekly, starting Day 1, Week 2
*Administer over 90 minutes, **Administer over 30 minutes.

TRASTUZUMAB (EVERY 3 WEEKS)
Trastuzumab    8 mg/kg load    IV*    Day 1, Week 1
Then administer the following 21 days after the loading dose and every 3 weeks thereafter
Trastuzumab    6 mg/kg    IV*    Q 3 Weeks
*Administer over 90 minutes.
NOTE: All doses were administered over 90 minutes. Other studies have successfully administered these doses over 30 minutes if the first 90-minute infusion was well tolerated.

VINORELBINE
Vinorelbine       30 mg/m^2    IV*    Weekly
*Administer over 20 minutes in 100 – 125 mL NS.
BREAST CANCER
METASTATIC CHEMOTHERAPY: COMBINATION, HER-2 (+)

CAPECITABINE – TRASTUZUMAB

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capecitabine</td>
<td>1250 mg/m² BID</td>
<td>PO</td>
<td>Days 1 – 14</td>
</tr>
<tr>
<td>Trastuzumab</td>
<td>4 mg/kg load</td>
<td>IV</td>
<td>Day 1, Week 1</td>
</tr>
</tbody>
</table>

Followed by

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trastuzumab</td>
<td>2 mg/kg</td>
<td>IV</td>
<td>Weekly, starting Day 1, Week 2</td>
</tr>
</tbody>
</table>

Capecitabine dose rounded to nearest 150 mg or 500 mg tablet size.

Repeat capecitabine cycle every 21 days.


DOCETAXEL (WEEKLY) – TRASTUZUMAB

<table>
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<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Days</th>
</tr>
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<tbody>
<tr>
<td>Docetaxel†</td>
<td>35 mg/m²</td>
<td>IV</td>
<td>Day 1</td>
</tr>
<tr>
<td>Trastuzumab</td>
<td>4 mg/kg load</td>
<td>IV</td>
<td>Day 1</td>
</tr>
</tbody>
</table>

Then the following week

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Days</th>
</tr>
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<tbody>
<tr>
<td>Docetaxel″</td>
<td>35 mg/m²</td>
<td>IV</td>
<td>Days 8, 15, 22, 29 and 36</td>
</tr>
</tbody>
</table>

Followed by

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trastuzumab</td>
<td>2 mg/kg</td>
<td>IV</td>
<td>Weekly</td>
</tr>
</tbody>
</table>

†Routine premedication administered; ″Administer over 30 minutes; ″Administer over 90 minutes.

Repeat docetaxel cycle every 8 weeks.


DOCETAXEL (EVERY 3 WEEKS) – TRASTUZUMAB

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Days</th>
</tr>
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<tbody>
<tr>
<td>Docetaxel†</td>
<td>100 mg/m²</td>
<td>IV</td>
<td>Day 1</td>
</tr>
<tr>
<td>Trastuzumab</td>
<td>4 mg/kg load</td>
<td>IV</td>
<td>Day 1, Week 1</td>
</tr>
</tbody>
</table>

Followed by

<table>
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<th>Route</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trastuzumab</td>
<td>2 mg/kg</td>
<td>IV</td>
<td>Weekly, starting Day 1, Week 2</td>
</tr>
</tbody>
</table>

†Routine premedication administered.

Repeat docetaxel cycle every 21 days.

**PACLITAXEL (WEEKLY) – TRASTUZUMAB**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Day/Week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trastuzumab</td>
<td>4 mg/kg load</td>
<td>IV*</td>
<td>Day 0, Week 1, followed by</td>
</tr>
<tr>
<td>Paclitaxel‡</td>
<td>90 mg/m²</td>
<td>IV**</td>
<td>Day 1, Week 1</td>
</tr>
</tbody>
</table>

*Following the initial therapy on week 1, the following should occur:*

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Day/Week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paclitaxel‡</td>
<td>90 mg/m²</td>
<td>IV**</td>
<td>Day 1, Week 2</td>
</tr>
</tbody>
</table>

*Followed immediately by*

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Day/Week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trastuzumab</td>
<td>2 mg/kg</td>
<td>IV***</td>
<td>Day 1, Week 2</td>
</tr>
</tbody>
</table>

Repeat second week paclitaxel/trastuzumab cycle every 7 days.

‡Routine premedication administered; *Administer over 90 minutes; **Administer over 1 hour; ***Administer over 30 minutes.


**PACLITAXEL (EVERY 3 WEEKS) – TRASTUZUMAB (WEEKLY)**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Day/Week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paclitaxel‡</td>
<td>175 mg/m²</td>
<td>IV</td>
<td>Day 1</td>
</tr>
<tr>
<td>Trastuzumab</td>
<td>4 mg/kg load</td>
<td>IV</td>
<td>Day 1, Week 1</td>
</tr>
</tbody>
</table>

*Followed by*

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Day/Week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trastuzumab</td>
<td>2 mg/kg</td>
<td>IV</td>
<td>Weekly, starting Day 1, Week 2</td>
</tr>
</tbody>
</table>

Repeat paclitaxel cycle every 21 days for 6 cycles or beyond at physician’s discretion. Continue trastuzumab treatment until disease progression.

‡Routine premedication administered.


**PACLITAXEL – TRASTUZUMAB (BOTH EVERY 3 WEEKS)**

**FIRST CYCLE**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Day/Week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paclitaxel‡</td>
<td>175 mg/m²</td>
<td>IV*</td>
<td>Day 0</td>
</tr>
<tr>
<td>Trastuzumab</td>
<td>8 mg/kg load</td>
<td>IV**</td>
<td>Day 1</td>
</tr>
</tbody>
</table>

*Then every 21 days thereafter*

**SUBSEQUENT CYCLES**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Day/Week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trastuzumab</td>
<td>6 mg/kg</td>
<td>IV**</td>
<td>Day 1</td>
</tr>
</tbody>
</table>

*Followed 30 minutes later by*

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Day/Week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paclitaxel‡</td>
<td>175 mg/m²</td>
<td>IV*</td>
<td>Day 1</td>
</tr>
</tbody>
</table>

Repeat cycle every 21 days for a total of 7 cycles. Continue trastuzumab until disease progression.

‡Routine premedication administered; *Administer over 3 hours; **Administer over 90 minutes.

TCH (DOCETAXEL – CARBOPLATIN – TRASTUZUMAB)

Docetaxel*  75 mg/m²  IV  Day 1  
Carboplatin  AUC 6  IV  Day 1
Trastuzumab  4 mg/kg load  IV**  Day 1, Week 1

Followed by

Trastuzumab  2 mg/kg  IV**  Day 1, Weeks 2 and 3

Repeat cycle every 21 days for 6 cycles.

MAINTENANCE THERAPY (STARTING FOLLOWING THE COMPLETION OF THE CHEMOTHERAPY):

Trastuzumab  6 mg/kg  IV**  Day 1

Repeat cycle every 21 days for 1 year.

*Routine premedication administered; †Administer over 90 minutes; **Administer over 30 minutes.

NOTE: For high-risk node negative or node positive HER-2 positive patients. Adjuvant hormonal or radiation therapy initiated following completion of carboplatin and docetaxel concurrent with maintenance trastuzumab. Serial cardiac monitoring should be performed.


TCH (PACLITAXEL – CARBOPLATIN – TRASTUZUMAB)

Paclitaxel*  80 mg/m²  IV  Day 1, 8 and 15*
Carboplatin  AUC 2  IV  Day 1, 8 and 15*
Trastuzumab  4 mg/kg load  IV**  Day 1, Week 1

Followed by

Trastuzumab  2 mg/kg  IV***  Weekly

*Routine premedication administered; †Weekly for three out of four weeks; **Administer over 90 minutes; ***Administer over 30 minutes.

Repeat cycles every 28 days for 6 cycles. Trastuzumab continued until disease progression.

NOTE: Conversion to every three week dosing of trastuzumab (6 mg/kg) during post-chemotherapy phase is a reasonable option and can begin the week following completion of chemotherapy (personal communication with Edith Perez, MD).

VINORELBINE – TRASTUZUMAB

Trastuzumab 4 mg/kg load IV* Day 1, Week 1
Vinorelbine 125 – 230 mg/m² IV*** Day 1, Week 1

Then the following week and then weekly thereafter

Trastuzumab 2 mg/kg IV** Q week
Vinorelbine 125 – 230 mg/m² IV*** Q week

*Administer over 90 minutes, **Administer over 30 minutes; ***Administer over 6 – 10 minutes followed by 125 mL NS after trastuzumab administration.

DOSE MODIFICATION: Decrease the dose of vinorelbine to 12.5 mg/m² for a bilirubin of 2 – 3 mg/dL and hold the dose of vinorelbine for a bilirubin of more than 3 mg/dL. If Grade 2 neurotoxicity occurs, decrease the dose to 15 mg/m² until the toxicity resolves to a Grade 1 or less.

BREAST CANCER
METASTATIC CHEMOTHERAPY: COMBINATION, HER-2 (-)

**AT (DOXORUBICIN – DOCETAXEL)**

Doxorubicin 50 mg/m² IV* Day 1

Followed 1 hour later by

Docetaxel† 75 mg/m² IV** Day 1
Filgrastim 5 mcg/kg/day² SQ Day 2 until ANC recovery

*Routine premedication administered; †Administer over 5 – 15 minutes; **Administer over 1 hour.

DOSE MODIFICATION: If bilirubin is 1.3 – 1.5 x BL or AST is 2.5 – 5 x BL, decrease dose of each agent by 50%.

Repeat cycle every 21 days for a maximum of 8 cycles. After completion of the doxorubicin, docetaxel was continued alone for 2 cycles beyond a complete response.


**DOCETAXEL-CAPECITABINE**

Docetaxel† 75 mg/m² IV* Day 1
Capecitabine 1250 mg/m² BID PO Days 1 – 14

*Routine premedication administered; †Administer over 1 hour.

NOTE: Capecitabine is available as 150 mg and 500 mg tablets. Administer within 30 minutes of completion of a meal. Each dose is 12 hours apart.

Repeat cycle every 21 days.


**EPIRUBICIN – PACLITAXEL**

Epirubicin 75 mg/m² IV* Day 1

Followed immediately by

Paclitaxel‡ 175 mg/m² IV** Day 1

*Routine premedication administered; ‡Administer over 15 – 20 minutes; **Administer over 3 hours.

Repeat cycle every 21 days.

**GEMCITABINE – PACLITAXEL**

Gemcitabine 1250 mg/m² IV Days 1 and 8  
Paclitaxel † 175 mg/m² IV Day 1

*Routine premedication administered.

Repeat cycle every 21 days.


**PACLITAXEL – BEVACIZUMAB**

Paclitaxel † 90 mg/m² IV Days 1, 8 and 15  
Followed on Day 1 and 15 by  
Bevacizumab# 10 mg/kg IV** Days 1 and 15

*Routine premedication administered; †Administer over 1 hour; **Initial dose to be administered over 90 minutes. If the first infusion is well tolerated, the second infusion can be administered over 60 minutes. If that is well tolerated all subsequent infusions may be delivered over 30 minutes; #If the patient experiences infusion associated adverse events while the bevacizumab is being administered, the patient may receive premedication on the next cycle.

Repeat cycle every 28 days.

Reference: ECOG 2100 Protocol at [www.ecog.org](http://www.ecog.org); Accessed 6/20/06.