

BREAST CANCER HORMONAL TREATMENT

Classification	Generic (Brand)	Dose	Common Side Effects (>10%)*
Selective Estrogen Receptor Modulators (SERMs)	Tamoxifen (Nolvadex®)	10 mg PO BID	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. <i>Less common:</i> thromboembolic events (1/100), uterine/endometrial malignancy (1.7/1000); retinitis and cataracts.
	Raloxifene (Evista®)	60 mg PO QD. Patients with hepatic dysfunction may be at greater risk for adverse events. No specific dosing adjustment recommendations at this time	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.
	Toremifene (Fareston®)	60 mg PO QD Adjustments may be required in liver disease	Similar to tamoxifen.
Estrogen Receptor Down-regulators	Fulvestrant (Faslodex®)	250 mg IM Q month	Flushing, nausea/vomiting, constipation, diarrhea, weakness, back pain, headache <i>Less common:</i> vaginal bleeding, thromboembolic events, leukopenia.
Aromatase Inhibitors (AIs) – Post menopausal only	Anastrozole (Arimidex®)	1 mg PO QD	Less risk of thromboemboli and endometrial hyperplasia/carcinoma vs. tamoxifen Increased incidence osteoporosis.
	Letrozole (Femara®)	2.5 mg PO QD	Similar to anastrozole.
	Exemestane (Aromasin®)	25 mg PO QD	Similar to anastrozole.
Progestins	Megestrol acetate (Megace®)	40 mg PO QID	Edema, breakthrough bleeding and amenorrhea, weakness, weight gain, rash <i>Less common:</i> thromboembolic events.
LHRH Analogs	Goserelin (Zoladex®)	3.6 mg SC Q 28 days	Gynecomastia, menopausal symptoms, sexual dysfunction, hot flashes; osteoporosis.
	Leuprolide acetate (Lupron®, Lupron Depot®; Eligard®) Not FDA approved Not well studied in trials	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	Depression, pain, hot flashes, weight gain, nausea/vomiting.

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

References: [Drug Information Handbook](#), 11th edition. Lexi-Comp, Inc. 2003 – 4; [Clinical Pharmacology Online](#), Gold Standard Multimedia. 2005; [Vogel VG, et al. JAMA 2006;295:23:2727 – 41](#); [ASCO Clinical Guidelines on Aromatase Inhibitors, 2004](#).

BREAST CANCER

BREAST CANCER HORMONAL THERAPY

I. ADJUVANT HORMONAL THERAPY

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

Reference: [The Arimidex, Tamoxifen Alone or in Combination Trialists' Group. *Lancet* 2002; 359:2131 – 9.](#)

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

References: [The Breast International Group \(BIG\) 1–98 Collaborative Group. *N Engl J Med* 2005; 353:2747 – 57;](#) [Coates AS, et al. *J Clin Oncol* 2007 Jan 2;\[Epub ahead of print\].](#)

Tamoxifen 20 mg PO QD x 5 years.

Reference: [Early Breast Cancer Trialists' Collaborative Group. *Lancet* 1998;351:1451– 67.](#)

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.

Reference: [Jakesz R, et al. *Lancet* 2005;366:455 – 62.](#)

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

Reference: [Goss PE, et al. *J Natl Cancer Inst* 2005; 97:1262 – 71.](#)

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.

Reference: [Coombes RC, et al. *N Engl J Med* 2004;350:1081 – 92.](#)

II. METASTATIC HORMONAL THERAPY

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

References: [Bonnetterre J, et al. *Cancer* 2001;92:2247 – 58 \(A\).](#)
[Bonnetterre J, et al. *J Clin Oncol* 2000;18:3748 – 57 \(A\).](#)
[Nabholtz JM, et al. *J Clin Oncol* 2000;18:3758 – 67 \(A\).](#)
[Mouridsen H, et al. *J Clin Oncol* 2003;21:2101 – 09 \(L\).](#)

Fulvestrant 250 mg IM QMonth (postmenopausal)

References: [Howell A, et al. *J Clin Oncol* 2004;22:1605 – 13.](#) First line.
[Osborne CK, et al. *J Clin Oncol* 2002;20:3386 – 95.](#) Second line.
[Howell A, et al. *J Clin Oncol* 2002;20:3396 – 403.](#) Second line.
[Howell A, et al. *Cancer* 2005; 104: 236 – 9.](#) Combined Second Line Update.
[Ingle JN, et al. *J Clin Oncol* 2006; 24:1052 – 6.](#) Third line.

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

Reference: [Lonning PE, et al. *J Clin Oncol* 2000;18:2234 – 44.](#)

[ASCO 2004 Aromatase Inhibitor Use Guidelines](#)

BREAST CANCER CHEMOTHERAPY

NEOADJUVANT CHEMOTHERAPY TREATMENT

AC → DOCETAXEL

Doxorubicin	60 mg/m ²	IV	Day 1
Cyclophosphamide	600 mg/m ²	IV	Day 1

Repeat cycle every 21 days for 4 cycles.

THEN, following a 3 week delay

Docetaxel [‡]	100 mg/m ²	IV	Day 1
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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 $1.5 \times 10^9/L$ 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.

References: [Bear HD, et al. *J Clin Oncol* 2003;21:4165 – 74;](#) [Bear HD, et al. *J Clin Oncol* 2006;24:2019 – 27.](#)

BREAST CANCER ADJUVANT CHEMOTHERAPY TREATMENT
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AC (DOXORUBICIN – CYCLOPHOSPHAMIDE)

Doxorubicin	60 mg/m ²	IV	Day 1
Cyclophosphamide	600 mg/m ²	IV	Day 1

Repeat cycle every 21 days for 4 cycles.

References: [Fisher B, et al. / Clin Oncol 1990;8:1483 – 96](#); [Fisher B, et al. / Clin Oncol 1997;15: 1858 – 69](#).

AC → DOCETAXEL – TRASTUZUMAB (AC → TH)

Doxorubicin	60 mg/m ²	IV	Day 1
Cyclophosphamide	600 mg/m ²	IV	Day 1

Repeat cycle every 21 days for 4 cycles.

THEN, following a 3 week delay

Doxcetaxel [‡]	100 mg/m ²	IV*	Day 1
Trastuzumab	4 mg/kg load	IV**	Day 1, Week 1

Followed by

Trastuzumab	2 mg/kg	IV***	Weekly
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[‡]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
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*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.

Reference: Slamon D, et al. San Antonio Breast Cancer Conference Program and Proceedings 2005. Abstract 1. Available at <http://www.sabcs.org/>. Accessed 06/20/06.

AC → PACLITAXEL

Doxorubicin	60 mg/m ²	IV	Day 1
Cyclophosphamide	600 mg/m ²	IV	Day 1

Repeat cycle every 21 days for 4 cycles.

THEN, following a 3 week delay

Paclitaxel‡	175 ¹ –225 ² mg/m ²	IV*	Day 1
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‡Routine premedication required; *Administer over 3 hours.

Repeat cycle every 21 days for 4 cycles.

NOTE: Used for node positive patients.

References: ¹[Henderson IC, et al. / Clin Oncol 2003;21:976 – 83](#); ²[Mamounas EP, et al. / Clin Oncol 2005;23:3686 – 96](#).

AC → PACLITAXEL (DOSE DENSE)

Doxorubicin	60 mg/m ²	IV	Day 1
Cyclophosphamide	600 mg/m ²	IV	Day 1
Filgrastim	5 mcg/kg/day*	SQ	Days 3 – 10 of each cycle

Repeat cycle every 14 days for 4 cycles.

THEN, following a 2 week delay

Paclitaxel‡	175 mg/m ²	IV**	Day 1
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Repeat cycle every 14 days for 4 cycles.

‡Routine premedication required; *Dose can be rounded to nearest 300 microgram or 480 microgram vial/syringe; **Administer over 3 hours.

References: [Citron ML, et al. / Clin Oncol 2003;21:1431 – 9](#); Hudis C, et al. San Antonio Breast Cancer Conference Program and Proceedings 2005. Abstract 41. Available at <http://www.sabcs.org/>. Accessed 06/20/06.

AC → PACLITAXEL – TRASTUZUMAB

Doxorubicin	60 mg/m ²	IV	Day 1
Cyclophosphamide	600 mg/m ²	IV	Day 1

Repeat cycle every 21 days for 4 cycles.

THEN, following a 3 week delay

Paclitaxel [‡]	¹ 175 mg/m ²	IV	Day 1
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OR

Paclitaxel [‡]	² 80 mg/m ²	IV	Weekly
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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
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Followed by

Trastuzumab	2 mg/kg	IV	Weekly*, starting Day 1, Week 2
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MAINTENANCE THERAPY (STARTING THE WEEK FOLLOWING THE LAST TRASTUZUMAB DOSE):

Trastuzumab	2 mg/kg ^{1,2}	IV	Weekly
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OR

Trastuzumab	6 mg/kg ³	IV	Day 1**
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[‡]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.

References: ¹[Romond E, et al. *N Engl J Med* 2005;353:1673 – 84](#) (NASBP-B-31); ²Perez EA, et al. NCCTG-N9831 [data accessed online at www.asco.org on 05/19/05]; ³[Piccart-Gebhart MJ, et al. *N Engl J Med* 2005;353:1659 – 72](#) and [Smith I, et al. *Lancet* 2007;369:29 – 36](#). (HERA)

AT (DOXORUBICIN – DOCETAXEL)

Doxorubicin	60 mg/m ²	IV	Day 1
Docetaxel [‡]	60 mg/m ²	IV	Day 1

[‡]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.

Reference: [Goldstein L, et al. *Proc Am Soc Clin Oncol* 2005;23:7s \[Abstract 512\].](#)

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

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: 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.

References: [Tancini G, et al. *J Clin Oncol* 1983;1:2 – 10;](#) [Bonadonna G, et al. *N Engl J Med* 1995;332:901 – 6.](#)

DOCETAXEL – CYCLOPHOSPHAMIDE

Docetaxel [‡]	75 mg/m ²	IV	Day 1
Cyclophosphamide	600 mg/m ²	IV	Day 1

[‡]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.

Reference: [Jones SE, et al. *J Clin Oncol* 2006;24:5381 – 7.](#)

EPIRUBICIN → CMF

Epirubicin	100 mg/m ²	IV	Day 1
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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.

Reference: [Poole CJ, et al. *N Engl J Med* 2006;355:1851 – 62.](#)

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.

References: [Buzdar AU, et al. *Am J Clin Oncol* 1989;12:123 – 8;](#) [Hortobagyi G, et al. *Cancer* 1979;43:1225 – 33.](#) NOTE: *Cancer* reference for metastatic disease.

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.

Reference: [Levine MN, et al. *J Clin Oncol* 1998;16:2651 – 8.](#)

FE₁₀₀C

5-Fluorouracil	500 mg/m ²	IV	Day 1
Epirubicin	100 mg/m ²	IV	Day 1
Cyclophosphamide	500 mg/m ²	IV	Day 1

Repeat cycle every 21 days for 6 cycles.

Reference: [French Adjuvant Study Group. *J Clin Oncol* 2001;19:602 – 11.](#)

FE₁₀₀C → DOCETAXEL

5-Fluorouracil	500 mg/m ²	IV	Day 1
Epirubicin	100 mg/m ²	IV	Day 1
Cyclophosphamide	500 mg/m ²	IV	Day 1

Repeat cycle every 21 days for 3 cycles.

Followed by

Docetaxel [‡]	100 mg/m ²	IV	Day 1
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[‡]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.

Reference: [Roche H, et al. *J Clin Oncol* 2006;24:5664 – 71.](#)

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

5-Fluorouracil	600 mg/m ²	IV	Day 1
Epirubicin	60 mg/m ²	IV	Day 1
Cyclophosphamide	600 mg/m ²	IV	Day 1
Filgrastim	5 mcg/kg/day	SQ	Days 4 – 11

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.

Reference: [Venturini M, et al. *J Natl Cancer Inst* 2005;97:1724 – 33.](#)

TAC (DOCETAXEL – DOXORUBICIN – CYCLOPHOSPHAMIDE)

Doxorubicin	50 mg/m ²	IV*	Day 1
Cyclophosphamide	500 mg/m ²	IV**	Day 1

Followed 1 hour later by

Docetaxel [‡]	75 mg/m ²	IV***	Day 1
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[‡]Routine premedication required; *Administer over 15 minutes; **Administer over 1–5 minutes; ***Administer over 1 hour.

Repeat cycle every 21 days for 6 cycles.

Reference: [Martin M, et al. N Engl J Med 2005;352:2302 – 13.](#)

TCH (DOCETAXEL – CARBOPLATIN – TRASTUZUMAB)

Docetaxel [‡]	75 mg/m ²	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*
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Repeat cycle every 21 days for 6 cycles.

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

Trastuzumab	6 mg/kg	IV	Day 1**
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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.

Reference: Slamon D, et al. San Antonio Breast Cancer Conference Program and Proceedings 2005. [Abstract 1]. Available at <http://www.sabcs.org/>. Accessed 06/20/06.

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.

References: [Blum JL, et al. *J Clin Oncol* 1999;17:485 – 93](#); [Michaud L, et al. *Proc Am Soc Clin Oncol* 2000;19:104a \[Abstract 402\]](#).

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.

References: [Burstein HJ, et al. *J Clin Oncol* 2000;18:1212 – 9](#); [Taberero J, et al. *Ann Oncol* 2004;15:1358 – 65](#).

DOCETAXEL (EVERY 3 WEEKS)

Docetaxel[‡] 160 – 2100 mg/m² IV* Day 1

[‡]Routine premedication administered; *Administer over 1 hour.

Repeat cycle every 21 days.

References: ¹[Harvey V, et al. *J Clin Oncol* 2006;24:4963 – 70](#); ²[Jones SE, et al. *J Clin Oncol* 2005;23:5542 – 51](#).

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.

Reference: [Carmichael J, et al. *J Clin Oncol* 1995;13:2731 – 6](#).

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.

Reference: [Ranson MR, et al. *J Clin Oncol* 1997;15:3185 – 91.](#)

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.

References: ¹[Seidman AD, et al. *Proc Am Soc Clin Oncol* 2004;22\(14S\):6s \[Abstract 512\]](#); ²[Seidman AD, et al. *J Clin Oncol* 1998;16:3353 – 61](#); ²[Seidman AD, et al. *Semin Oncol* 1997;24\(Suppl 17\):S17-72 – S17-76.](#)

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.

References: [Nabholtz JM, et al. *J Clin Oncol* 1996;14:1858 – 67](#); ¹[Winer EP, et al. *J Clin Oncol* 2004;22:2061 – 8](#); [Jones SE, et al. *J Clin Oncol* 2005;23:5542 – 51.](#)

PACLITAXEL PROTEIN BOUND PARTICLES (ABRAXANE®)

Abraxane[®] 260 mg/m² IV Day 1

NOTE: No premedication required.

Repeat cycle every 21 days.

Reference: [Gradishar WJ, et al. *J Clin Oncol* 2005;23:7794 – 803.](#)

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.

Reference: [Cobleigh MA, et al. J Clin Oncol 1999;17:2639 – 48.](#)

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.

Reference: [Baselga J, et al. J Clin Oncol 2005;23:2162 – 71.](#)

VINORELBINE

Vinorelbine 30 mg/m² IV* Weekly

*Administer over 20 minutes in 100 – 125 mL NS.

References: [Garcia-Conde J, et al. Ann Oncol 1994;5:854 – 7;](#) [Degardin M, et al. Ann Oncol 1994;5:423 – 6.](#)

BREAST CANCER METASTATIC CHEMOTHERAPY: COMBINATION, HER-2 (+)
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CAPECITABINE – TRASTUZUMAB

Capecitabine	1250 mg/m ² BID	PO	Days 1 – 14
Trastuzumab	4 mg/kg load	IV	Day 1, Week 1

Followed by

Trastuzumab	2 mg/kg	IV	Weekly, starting Day 1, Week 2
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Capecitabine dose rounded to nearest 150 mg or 500 mg tablet size.

Repeat capecitabine cycle every 21 days.

Reference: Schaller G, et al. San Antonio Breast Cancer Conference Program and Proceedings 2005. Abstract 2033. Available at <http://www.sabcs.org/>. Accessed 06/20/06.

DOCETAXEL (WEEKLY) – TRASTUZUMAB

Docetaxel [‡]	35 mg/m ²	IV*	Day 1
Trastuzumab	4 mg/kg load	IV**	Day 1

Then the following week

Docetaxel [‡]	35 mg/m ²	IV*	Days 8, 15, 22, 29 and 36
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Followed by

Trastuzumab	2 mg/kg	IV*	Weekly
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[‡]Routine premedication administered; *Administer over 30 minutes; **Administer over 90 minutes.

Repeat docetaxel cycle every 8 weeks.

Reference: [Tedesco KL, et al. J Clin Oncol 2004;22:1071 – 7.](#)

DOCETAXEL (EVERY 3 WEEKS) – TRASTUZUMAB

Docetaxel [‡]	100 mg/m ²	IV	Day 1
Trastuzumab	4 mg/kg load	IV	Day 1, Week 1

Followed by

Trastuzumab	2 mg/kg	IV	Weekly, starting Day 1, Week 2
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[‡]Routine premedication administered.

Repeat docetaxel cycle every 21 days.

Reference: [Marty M, et al. J Clin Oncol 2005;23:4265 – 74.](#)

PACLITAXEL (WEEKLY) – TRASTUZUMAB

Trastuzumab	4 mg/kg load	IV*	Day 0, Week 1, <i>followed by</i>
Paclitaxel [‡]	90 mg/m ²	IV**	Day 1, Week 1

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

Paclitaxel [‡]	90 mg/m ²	IV**	Day 1, Week 2
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Followed immediately by

Trastuzumab	2 mg/kg	IV***	Day 1, Week 2
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Repeat second week paclitaxel/trastuzumab cycle every 7 days.

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

Reference: [Seidman AD, et al. *J Clin Oncol* 2001;19:2587 – 95.](#)

PACLITAXEL (EVERY 3 WEEKS) – TRASTUZUMAB (WEEKLY)

Paclitaxel [‡]	175 mg/m ²	IV	Day 1
Trastuzumab	4 mg/kg load	IV	Day 1, Week 1

Followed by

Trastuzumab	2 mg/kg	IV	Weekly, starting Day 1, Week 2
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Repeat paclitaxel cycle every 21 days for 6 cycles or beyond at physician's discretion. Continue trastuzumab treatment until disease progression.

[‡]Routine premedication administered.

Reference: [Slamon DJ, et al. *N Engl J Med* 2001;344:783 – 92.](#)

PACLITAXEL – TRASTUZUMAB (BOTH EVERY 3 WEEKS)

FIRST CYCLE

Paclitaxel [‡]	175 mg/m ²	IV*	Day 0
Trastuzumab	8 mg/kg load	IV**	Day 1

Then every 21 days thereafter

SUBSEQUENT CYCLES

Trastuzumab	6 mg/kg	IV**	Day 1
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Followed 30 minutes later by

Paclitaxel [‡]	175 mg/m ²	IV*	Day 1
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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.

Reference: [Leyland-Jones B, et al. *J Clin Oncol* 2003;21:3965 – 71.](#)

TCH (DOCETAXEL – CARBOPLATIN – TRASTUZUMAB)

Docetaxel [‡]	75 mg/m ²	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
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Repeat cycle every 21 days for 6 cycles.

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

Trastuzumab	6 mg/kg	IV*	Day 1
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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.

Reference: Slamon D, et al. San Antonio Breast Cancer Conference Program and Proceedings 2005. Abstract 1. Available at <http://www.sabcs.org/>. Accessed 10/10/06.

TCH (PACLITAXEL – CARBOPLATIN – TRASTUZUMAB)

Paclitaxel [‡]	80 mg/m ²	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
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[‡]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).

Reference: [Perez EA, et al. Clin Breast Cancer 2005;6:425 – 32.](#)

VINOURELBINE – TRASTUZUMAB

Trastuzumab	4 mg/kg load	IV*	Day 1, Week1
Vinorelbine	¹ 25 – ² 30 mg/m ²	IV***	Day 1, Week1

Then the following week and then weekly thereafter

Trastuzumab	2 mg/kg	IV**	Q week
Vinorelbine	¹ 25 – ² 30 mg/m ²	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.

References: ¹[Burstein HJ, et al. / Clin Onco/2001;19:2722 – 30](#); ²[Chan A, et al. Br J Cancer 2006;95:788 – 93](#).

BREAST CANCER METASTATIC CHEMOTHERAPY: COMBINATION, HER-2 (-)
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AT (DOXORUBICIN – DOCETAXEL)

Doxorubicin	50 mg/m ²	IV*	Day 1
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Followed 1 hour later by

Docetaxel [‡]	75 mg/m ²	IV**	Day 1
Filgrastim	5 mcg/kg/day ²	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.

References: [Nabholtz JM, et al. J Clin Oncol 2003;21:968 – 75](#); [Erratum in J Clin Oncol 2003;21:2048](#); [Bontenbal M, et al. J Clin Oncol 2005;23:7081 – 8](#).

DOCETAXEL–CAPECITABINE

Docetaxel [‡]	75 mg/m ²	IV*	Day 1
Capecitabine	1250 mg/m ² 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.

Reference: [O'Shaughnessy J, et al. J Clin Oncol 2002;20:2812 – 23](#).

EPIRUBICIN – PACLITAXEL

Epirubicin	75 mg/m ²	IV*	Day 1
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Followed immediately by

Paclitaxel [‡]	175 mg/m ²	IV**	Day 1
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‡Routine premedication administered; *Administer over 15 – 20 minutes; **Administer over 3 hours.

Repeat cycle every 21 days.

Reference: [Rischin D, et al. Br J Cancer 2000;83:438 – 42](#).

GEMCITABINE – PACLITAXEL

Gemcitabine	1250 mg/m ²	IV	Days 1 and 8
Paclitaxel [‡]	175 mg/m ²	IV	Day 1

[‡]Routine premedication administered.

Repeat cycle every 21 days.

Reference: [Moinpour C, et al. Proc Am Soc Clin Oncol 2004;22\(14S\):32s \[Abstract 621\]](#).

PACLITAXEL – BEVACIZUMAB

Paclitaxel [‡]	90 mg/m ²	IV*	Days 1, 8 and 15
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Followed on Day 1 and 15 by

Bevacizumab [#]	10 mg/kg	IV**	Days 1 and 15
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[‡]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; Accessed 6/20/06.