

SWOG S0221: Phase III Trial of Continuous Schedule AC + G Q 2 Week Schedule AC, Followed by Paclitaxel Given Either Every 2 Weeks or Weekly for 12 Weeks as Post-Operative Adjuvant Therapy in Node-Positive or High-Risk Node-Negative Breast Cancer

FAST FACTS

ELIGIBILITY CRITERIA

1. Patients must be women or men with a histologically confirmed diagnosis of operable Stage I, II or III invasive breast carcinoma with known estrogen or progesterone receptor status (see Section 7.6B and c). Patients with T4 Tumors are not eligible.
2. Patients with bilateral synchronous breast cancer diagnosed within 1 month of each other are eligible if the higher TNM stage primary tumor meets the eligibility for this trial.
3. Patients must be high risk by meeting at least one of the following criteria:

- Tumor ≥ 2 cm in greatest diameter. Size must be determined from the pathology specimen. Size is equal to the maximum diameter of an entire lesion, including both invasive and intraductal components. In the case of multi-focal tumors, the largest lesion with an invasive component must be used to determine size. If the tumor is resected in pieces, the pathologist must re-orient the tumor fragments to determine maximum size.

Patients whose nodal status is “N01+” (no cluster of tumor sells in any node greater than 0.2 mm) will be considered to be node-negative, and must have primary tumors ≥ 2 cm in size or have tumors ≥ 1 cm with high risk features below. Patients registered to NCI-funded national sentinel node studies [i.e., ACOSOG Z0010, Z0011, and NSABP B-32] are eligible. **Patients who are node negative on the basis of a sentinel node procedure may be entered even if fewer than 6 axillary nodes were removed; otherwise, at least 6 axillary or intramammary nodes must be negative for a patient to be considered node negative.**

- Tumor > 1 cm in diameter and either: 1) ER-negative and PgR-negative, or 2) ER-positive or PgR-positive with a Genomic Health Recurrence Score of > 26 .
 - One or more axillary or intramammary nodes are involved by metastatic breast cancer. If one or more nodes are involved, a minimum of 6 axillary or intramammary nodes must have been examined histologically. Patients with N0 (i+) disease will be considered to be node negative.
4. Patients with HER-2 positive tumors (3+ by immunohistochemical staining or amplified by fluorescence in-situ hybridization) are eligible. Such patients must be treated in compliance with Section 7.7. The use of Trastuzumab should be documented in the treatment forms.
 5. Patients must have had either a modified radical mastectomy or local excision of all tumors plus an axillary lymph node dissection or sentinel node resection prior to registration. Final resection margins for the primary tumor must be histologically negative for invasive cancer and ductal carcinoma in-situ. Patients with resection margins positive for lobular carcinoma in-situ will be eligible. Patients must have at least 6 axillary or intramammary lymph nodes sampled, with the exception of patients who have a sentinel node procedure with all sampled nodes being uninvolved by malignancy.
 6. Patients must be registered within 84 days from the final surgical procedure required to adequately treat the primary tumor and/or axilla.
 7. Patients must NOT have received prior cytotoxic chemotherapy for this breast cancer. Patients must NOT have had prior chemotherapy with an anthracycline, anthracenedione, or a taxane for any condition.
 8. Patients must NOT have received prior radiation therapy for the current malignancy, except for partial breast irradiation (PBI) following lumpectomy. PBI must have been completed at least 2 weeks prior to registration. Patients who have received prior radiation therapy for ductal carcinoma in-situ are eligible provided that radiation therapy was completed at least 2 weeks prior to registration.
 9. Patients who have had segmental mastectomy or other breast sparing procedure will be treated with radiotherapy according to standard procedure after completion of all chemotherapy, unless treated with PBI. Participation in B-39 is allowed. Patients who have had a modified radical mastectomy may also

TREATMENT PLAN [continued]

ARMS 2 and 4: WEEKLY DOXORUBICIN WITH DAILY ORAL CYCLOPHOSPHAMIDE AND FILGRASTIM (AC + G)

AGENT	DOSE	ROUTE	DAYS	INTERVAL
Doxorubicin	24mg/m ²	IV, bolus	1	Weekly x 15 weeks
Cyclophosphamide*	60mg/m ²	PO	Daily	Continuously for 15 weeks
Filgrastim**	5mcg/kg	Sub Q	2-7	Weekly x 15 weeks
Prophylactic Trimethoprim Sulfa***	1 double-strength tablet BID	PO	4 and 5	Weekly x 15 weeks
Paclitaxel	See Section 7.4 or 7.5	See Section 7.4 or 7.5	-----	To begin 14 days following the last dose of cyclophosphamide

- * Rounded to nearly 25 mg dose. All patients should be instructed on the importance of vigorous hydration [drinking 8-10 glasses of water daily] during cyclophosphamide therapy.
- ** Begin 24 hours after the administration of doxorubicin. Rounded to the nearer of 300 or 480 µg. NOTE: In the event of a WBC > 50,000/µl or significant bone pain with a WBC > 20,000/µl, the dose of Filgrastim will be reduced by 50%. Because a rapid onset of neutropenia is observed when Filgrastim is held in this circumstance, Filgrastim should be dose-reduced rather than held.
- *** For patients who are allergic to trimethoprim sulfa, oral trimethoprim/sulfamethoxazole desensitization, pentamidine, or no prophylaxis may be administered at the discretion of the treating physician [see Appendix 19.3].
- **** Ideally, therapy will be administered at the beginning of Weeks 1,2,3,4,5,6,7,8,9,10,11,12,13,14, and 15, with the final dose of oral cyclophosphamide being administered on Day 7 of Week 15.

FOR TOXICITIES AND DOSAGE MODIFICATIONS, SEE SECTION 8.0